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Advances in C-H activation by palladium: migration and cyclocarbonylation

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Advances in C-H activation by palladium: migration and cyclocarbonylation

by

Marino Andres Campo Molina

A dissertation submitted to the graduate faculty

in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

Major: Organic Chemistry

Program of Study Committee:

Richard C. Larock, Major Professor

Valerie Sheares Ashby

Keith Woo

Walter S. Trahanovsky

David Hoffman

Iowa State University

Ames, Iowa

2003

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Graduate College

Iowa State University

This is to certify that the doctoral dissertation of

Marino Andres Campo Molina

has met the dissertation requirements of Iowa State University

Signature was redacted for privacy.

Major Professor

Signature was redacted for privacy.

For the Major Program

To all of those who believed in me.

Thank you, I could not have done it alone.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

Ac	acetyl
aq	aqueous
Ar	argon
br	broad
br s	broad singlet
n-Bu	butyl
cat.	catalytic
concd	concentrated
d	doublet
dba	dibenzylideneacetone
dd	doublet of doublets
DDQ	2,3-dichloro-5,6-dicyanoquinone
DEAD	Diethyl azodicarboxylate
DMA	*N,N*-dimethylacetamide
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
dt	doublet of triplets
eq	equation
equiv	equivalent
Et	ethyl
h	hour
HRMS	high resolution mass spectroscopy

Hz	Hertz
IR	infrared
m	multiplet
Me	methyl
mL	milliliters
mol	mole(s)
mp	melting point
Ms	methanesulfonyl
MS	mass spectrometry
n	normal
NMP	*N*-methylpyrrolidone
NMR	nuclear magnetic resonance
o	ortho
p	para
Ph	phenyl
q	quartet
s	singlet
t	triplet
TBAC	tetra-*n*-butylammonium chloride
td	triplet of doublets
Ts	*p*-toluenesulfonyl
tt	triplet of triplets

ABSTRACT

Palladium-catalyzed intramolecular C-H activation of *o*-halobiaryls has been used to carry out important chemical transformations. For instance, in the presence of catalytic amounts of Pd(0), *o*-halobiaryls are readily cyclocarbonylated under an atmosphere of CO to produce fluorenones in high yields with good regioselectivity. This methodology has been successfully applied to the preparation of polycyclic fluorenones and fluorenones containing fused isoquinoline, indole, pyrrole, thiophene, benzothiophene, and benzofuran rings.

A novel 1,4-Pd migration between the *o*- and *o*'-positions of biaryls has been observed in organopalladium intermediates derived from *o*-halobiaryls. The organopalladium intermediates generated by this unique C-H activation-migration process have been trapped by way of a Heck reaction and Suzuki-Miyaura cross-coupling with arylboronic acids. Similarly, organopalladium intermediates generated by 1,4-Pd migration have been trapped by intramolecular arylation to produce fused polycycles. This unique migration-arylation methodology have been used to prepare complex polycyclic compounds containing fused benzofuran, quinoline, oxepine, indole, phenanthrene, and naphthalene rings.

GENERAL INTRODUCTION

Palladium methodology is a powerful tool in organic synthesis due to the ability of this metal to catalyze a wide range of reactions. Most commonly, organopalladium intermediates are prepared in situ from the oxidative addition of organic halides or triflates to Pd(0). A more attractive approach to organopalladium intermediates involves C-H activation, which offers a more direct route to such intermediates as well as better atom economy.

Our own interest in Pd-catalyzed methodology involving C-H activation led us to examine intramolecular versions of this process in *o*-halobiaryls. First of all, we cyclocarbonylated *o*-halobiaryls to fluorenones using carbon monoxide. We have also discovered that palladium is able to migrate between the *o*- and *o*'-positions of these biaryls through a five-membered palladacycle intermediate. We have been able to show that such palladium migration is compatible with other Pd-catalyzed reactions, such as Heck, Suzuki, and alkyne annulation. Furthermore, we have developed a two step C-H activation process to tranform *o*-halobiaryls into complex fused polycycles.

Dissertation Organization

This dissertation is divided into three chapters. Each of these chapters is written by the following guidelines for a full paper in the *Journal of Organic Chemistry.*

Chapter 1 describes the synthesis of fluoren-9-ones and other cyclic ketones by the palladium catalyzed cyclocarbonylation of *o*-halobiaryls. The regioselectivity and general scope of this methodology for preparing carbocyclic and heterocyclic ketones is examined in detailed in terms of electronic and steric effects.

Chapter 2 describes experimental results aimed to establish a 1,4-palladium migration in organopalladium intermediates derived from *o*-halobiaryls. In order to accomplish this goal, the key arylpalladium intermediates generated by 1,4-palladium migration were trapped by Heck, Suzuki and alkyne annulation reactions. Our experimental results point to the intermediacy of an electrophilic palladium species, which prefers to reside in the more electron-rich position of the biaryl.

Chapter 3 describes the synthetic aspect of this 1,4-palladium migration. This methodology makes use of a palladium migration to generate key organopalladium intermediates, which undergo intramolecular arylation producing polycycles containing fused benzofuran, quinoline, oxepine, indole, phenanthrene, and naphthalene rings.

Finally, all the ^{1}H and ^{13}C NMR spectra for the starting materials and the palladium-catalyzed reaction products have been compiled in appendices A-C.

CHAPTER 1. SYNTHESIS OF FLUOREN-9-ONES BY THE PALLADIUM-CATALYZED CYCLOCARBONYLATION OF *o*-HALOBIARYLS

Based on a paper published in the *Journal of Organic Chemistry*

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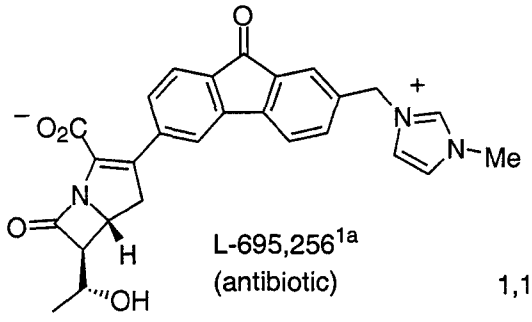
Abstract

The synthesis of various substituted fluoren-9-ones has been accomplished by the palladium-catalyzed cyclocarbonylation of *o*-halobiaryls. The cyclocarbonylation of 4'-substituted 2-iodobiphenyls produces very high yields of 2-substituted fluoren-9-ones bearing either electron-donating or electron-withdrawing substituents. 3'-Substituted 2-iodobiphenyls afford 3-substituted fluoren-9-ones in excellent yields with good regioselectivity. This chemistry has been successfully extended to polycyclic fluorenones and fluorenones containing fused isoquinoline, indole, pyrrole, thiophene, benzothiophene, and benzofuran rings.

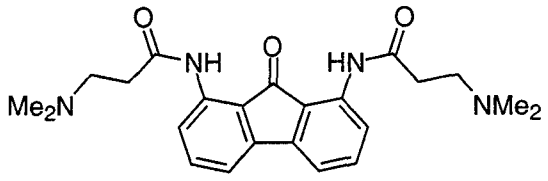
Introduction

Fluoren-9-ones are a family of natural products displaying a wide range of biological activity,[1] such as antibiotic[1a] and inhibitory activity for human telomerase[1b] and protein kinase-C[1c] (Figure 1). In recent years, fluorenones have attracted much interest because of

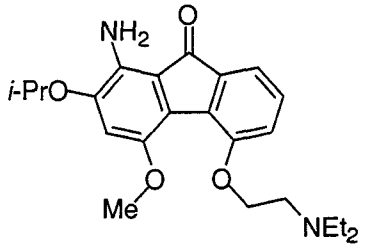
groundbreaking discoveries in the biomedical field,[1] which include their use as probes for DNA redox chemistry.[1d] Furthermore, fluorenones have been prepared as key synthetic intermediates for the total synthesis of natural products, such as stealthin and prekinamycin.[2]



L-695,256[1a]
(antibiotic)



1,1-bis(*N,N*-dimethylaminopropionamido)fluoren-9-one[1b]
(human telomerase inhibitor)



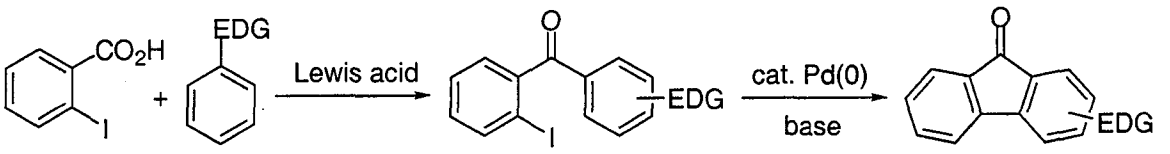
1-amino-2-isopropoxy-4-methoxy-5-[2-(*N,N*-diethylamino)ethoxy]fluoren-9-one[1c]
(protein kinase-C inhibitor)

Figure 1. Biologically active fluoren-9-ones.

The most useful syntheses of fluorenones include Friedel-Crafts ring closures of biarylcarboxylic acids and derivatives,[3] intramolecular [4 + 2] cycloaddition reactions of conjugated enynes,[4] oxidation of fluorenes,[5] and remote metalation of 2-biphenylcarboxamides or 2-biphenyloxazolines.[6] Unfortunately, these methods suffer some drawbacks, mainly because they employ harsh reaction conditions, such as a strong Lewis acid,[3] heat,[3,4] or a nucleophilic base,[6] which do not tolerate many organic functional groups. Alternatively, fluorenones have been synthesized by the palladium-catalyzed cyclization of *o*-iodobenzophenones [7] (Scheme 1). Although, this reported methodology employs relatively

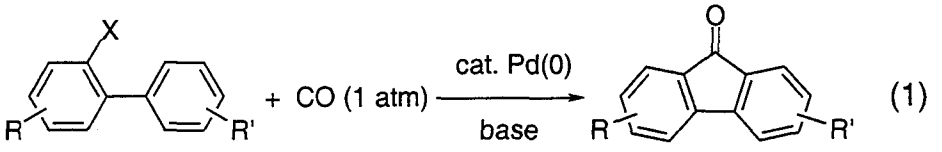
mild reaction conditions, the *o*-iodobenzophenones used as starting materials are difficult to prepare and require the use of a synthetically limited Friedel-Crafts type reaction.

Scheme 1



EDG: electron-donating group (OMe, OH)

Our interest in fluorenones has led to the development of a novel palladium-catalyzed cyclocarbonylation of readily available *o*-halobiaryls, which provides a highly efficient and direct route to the fluoren-9-one skeleton, as well as other related cyclic aromatic ketones (eq 1).[8] Herein, we report the full details of this new fluorenone synthesis.



(1)

Results and Discussion

In order to develop an optimum set of reaction conditions, we first studied the palladium-catalyzed cyclocarbonylation of commercially available 2-iodobiphenyl (**1**) to fluoren-9-one (**2**) as our model system. All of the optimization reactions have been carried out using 0.25 mmol of 2-iodobiphenyl (**1**) in DMF (6 mL) at 110 °C for 7 h under one atm of carbon monoxide. It is evident from the results listed in Table 1, that the base added, as well as the ligand present on palladium, are critical elements in this reaction. For instance, the use of chelating ligands, such as 1,2-bis(diphenylphosphino)ethane (dppe), 1,1'-

bis(diphenylphosphino)ferrocene (dppf), and 1,10-phenanthroline gave poor yields of the desired fluoren-9-one (**2**) (entries 1-3). Monodentate phosphine ligands have a major effect on the yield of the cyclocarbonylation reaction. Use of the electron-deficient ligands tri(*p*-fluorophenyl)phosphine and tri(*p*-chlorophenyl)phosphine gave low yields of fluoren-9-one (33 % and 37 % respectively), while the more electron-rich triphenylphosphine produced a 58 % yield (entries 4-6). Following this electronic trend, we have observed that the bulky, electron-rich ligand tricyclohexylphosphine was by far the most effective ligand, producing a quantitative yield of the desired compound **2** (entry 7). Finally, we explored the effect of different bases on the yield of fluoren-9-one and found that replacing the unusual cesium pivalate (CsPiv) base with NaOAc or Cs_2CO_3 was detrimental to the reaction (entries 8 and 9), the yield dropping from 100% to 92% and 82% respectively. The use of organic bases, such as pyridine and diisopropylethylamine, gave negligible yields of fluoren-9-one (entries 10 and 11).

The results of this optimization study have led to the development of a standard set of reaction conditions employing one atm of carbon monoxide, one equiv of the aryl halide (0.25 mmol), 5 mol % of commercially available $Pd(PCy_3)_2$, and 2 equiv of anhydrous cesium pivalate in DMF (6 ml) at 110 ^{0}C for 7 h. This procedure has been applied to a wide range of aryl halides (Table 2). 2-Iodobiphenyl produces fluoren-9-one (**2**) in a quantitative yield (entry 2). Under our reaction conditions, 2-bromobiphenyl is also converted to fluoren-9-one (**2**) in a quantitative yield (entry 1). However, biphenyl-2-yl trifluoromethanesulfonate fails to afford the desired product.

Table 1. Palladium-catalyzed cyclocarbonylation of 2-iodobiphenyl (**1**) to fluoren-9-one (**2**).[a]

entry	base	Pd catalyst	ligand (mol %)	time (h)	% isolated yield of **2**
1	CsPiv[b]	$Pd(OAc)_2$	dppe (5)	7	46
2	CsPiv	$Pd(OAc)_2$	dppf (5)	7	25
3	CsPiv	$Pd(OAc)_2$	1,10-phenanthroline (5)	7	< 5
4	CsPiv	$Pd(OAc)_2$	$(p\text{-}FC_6H_5)_3P$ (10)	7	33
5	CsPiv	$Pd(OAc)_2$	$(p\text{-}ClC_6H_5)_3P$ (10)	7	37
6	CsPiv	$Pd(OAc)_2$	Ph_3P (10)	7	58 (38[c])
7	CsPiv	$Pd(PCy_3)_2$	-[d]	7	100
8	NaOAc	$Pd(PCy_3)_2$	-[d]	7	92
9	Cs_2CO_3	$Pd(PCy_3)_2$	-[d]	7	84
10	pyridine	$Pd(PCy_3)_2$	-[d]	24	< 5
11	$(i\text{-}Pr)_2NEt$	$Pd(PCy_3)_2$	-[d]	24	< 5

[a]All reactions were run with 0.25 mmol of 2-iodobiphenyl (**1**), 2 equiv of base, 5 mol % of Pd catalyst, and 5 or 10 mol % of an appropriate ligand in 6 mL of DMF at 110 ^{0}C for 7 h under one atm of CO. [b]CsPiv = cesium pivalate. [c]The amount of DMF solvent was reduced from 6 ml to 1 ml. [d]The palladium catalyst contains 10 mol % of tricyclohexylphosphine, so no further ligand was added to the reaction mixture.

The utility of this reaction for the synthesis of 2-substituted fluoren-9-ones has been assessed by studying the cyclocarbonylation of readily prepared[9] 4'-substituted 2-iodobiphenyls (entries 2-6). As indicated, the reaction works well, tolerating both electron-donating, as well as electron-withdrawing substituents.

We have also addressed the question of regiochemistry in the cyclocarbonylation of 3'-substituted 2-iodobiphenyls[9] (entries 7 and 8). Cyclocarbonylation of the electron-rich 2-iodo-3'-methylbiphenyl (**12**) and the electron-poor 3-(2-iodophenyl)benzaldehyde (**15**)

Table 2. Synthesis of fluoren-9-ones by the Pd-catalyzed cyclocarbonylation of *o*-halobiaryls.[a]

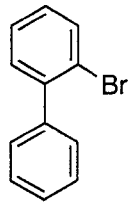
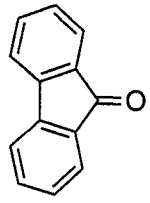
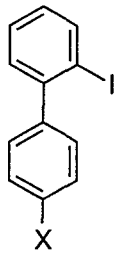
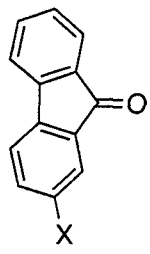
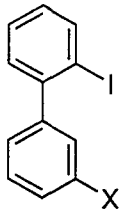
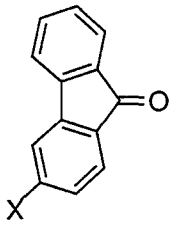
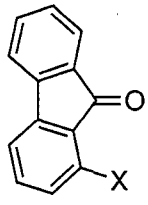
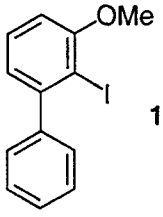
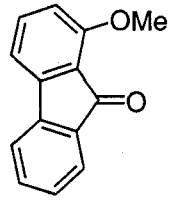
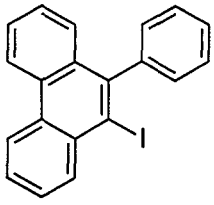
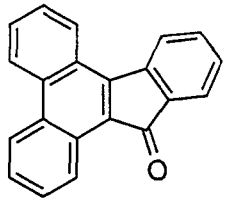
entry	substrate	product(s)	% yield
1	 **3**	 **2**	100
2	 X = H (**1**)	 **2**	100
3	X = Me (**4**)	**5**	97
4	X = OMe (**6**)	**7**	100
5	X = CH_2OMe (**8**)	**9**	100
6	X = CHO (**10**)	**11**	100
7	 X = Me (**12**)	 **13** +  **14**	90 + 10
8	X = CHO (**15**)	**16** **17**	94 (9:1)[b]
9	 **18**	 **19**	99
10	 **20**	 **21**	98

Table 2. (Continued)

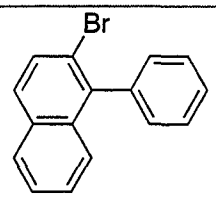
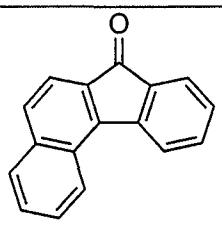
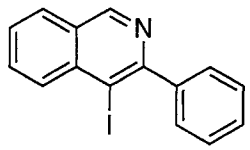
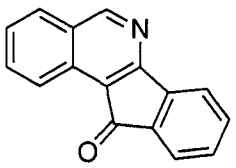
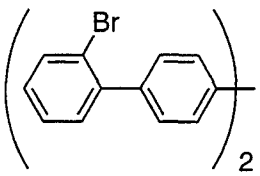
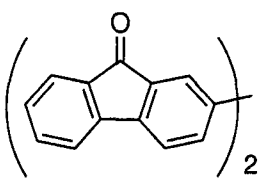
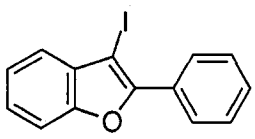
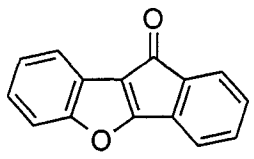
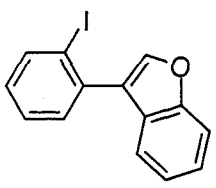
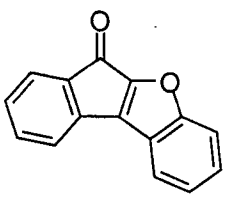
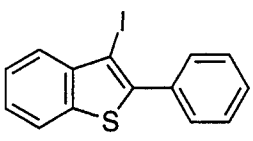
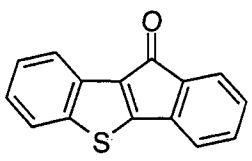
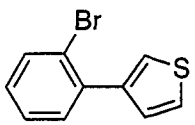
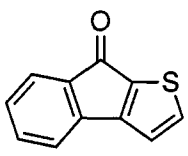
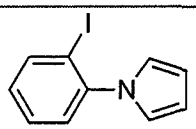
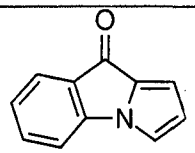
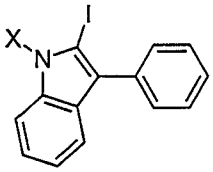
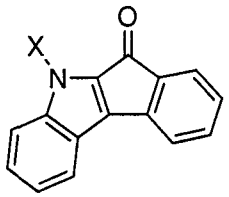
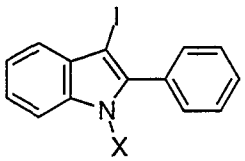
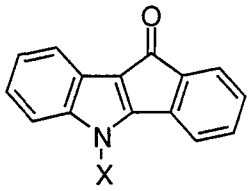
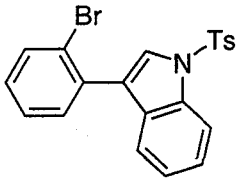
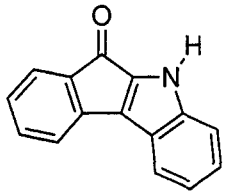
entry	substrate		product(s)		% yield
11		**22**		**23**	96
12		**24**		**25**	95
13		**26**		**27**	87[c,d]
14		**28**		**29**	0
15		**30**		**31**	81
16		**32**		**33**	67
17		**34**		**35**	86[d]

Table 2. (Continued)

entry	substrate	product(s)	% yield
18	 **36**	 **37**	96
19	 X = H (**38**)	 X = H (**39**)	0
20	X = Me (**40**)	X = Me (**41**)	49
21	 X = H (**42**)	 X = H (**43**)	0
22	X = Me (**44**)	X = Me (**45**)	21
23	X = Ts (**46**)	X = H (**43**)	45
24	 **47**	 **39**	55[e]

[a]All reactions were carried out under the optimal conditions described in the text. [b]The product ratio was determined by ^{1}H NMR spectroscopic analysis. [c]In order to keep the equivalents of aryl halide consistent, we employed 0.125 mmol of aryl dibromide **26**. [d]The reaction period was extended to 14 h. [e]A 42 % yield of compound **47** was recovered at the end of the reaction.

affords similar 9:1 regiochemical mixtures in excellent yields. In both cases, the predominant isomer arises from ring closure distal to the substituent. These experimental results seem to indicate that there is only a weak electronic effect during the cyclization process, and that a more important steric effect favors the less hindered isomers **13** and **16**.

This cyclocarbonylation does not appear to be significantly affected by the presence of substituents *ortho* to the halo group. For example, the palladium-catalyzed reaction of 2-iodo-3-methoxybiphenyl[10] (**18**) produces 1-methoxyfluoren-9-one (**19**) in 99 % yield (entry 9).

Interestingly, this palladium-catalyzed transformation can be readily employed on biaryl systems containing either polycyclic or heterocyclic rings. Thus, treatment of 9-iodo-10-phenylphenanthrene (**20**) with carbon monoxide under our standard reaction conditions produces indene[1,2-*l*]phenanthren-13-one[11] (**21**) in a 98% yield (entry 10). Similarly, 2-bromo-1-phenylnaphthalene[12] (**22**) produces a 96% yield of benzo[*c*]flouren-7-one[13] (**23**) (entry 11). Furthermore, cyclocarbonylation of the nitrogen-containing heterocycle 4-iodo-3-phenylisoquinoline[14] (**24**) produces 11-oxoindeno[1,2-*c*]isoquinoline[15] (**25**) in a 95% yield (entry 12).

This palladium reaction is also effective for the double cyclocarbonylation of 2,2'''-dibromo-*p*-quaterphenyl[16] (**26**) (entry 13). Under our standard reaction conditions, but 14 h reaction time, substrate **26** produces the desired [2,2']bifluorenyl-9,9'-dione[17] (**27**) in 87 % yield.

So far, we have demonstrated the utility of this chemistry by preparing a variety of fluorenones in high yields with good regioselectivity from *o*-halobiaryls containing six-membered ring aromatics, such as benzene, naphthalene, phenanthrene, etc. (Table 2, entries 1-13). We next turned our attention to applying this palladium methodology to *o*-halobiaryls in which one of the aromatic rings is a five-membered ring heterocycle, such as a benzofuran, a benzothiophene, a thiophene, a pyrrole or an indole (entries 14-24). We began

by studying the electronic effects of the cyclocarbonylation of *o*-iodobiaryls containing a benzofuran. When 3-iodo-2-phenylbenzofuran[18] (**28**) was subjected to the standard reaction conditions, it failed to give any of the desired benz[*b*]indeno[2,1-*d*]furan-10-one (**29**) (entry 14). On the other hand, the cyclocarbonylation of 3-(2-iodophenyl)benzofuran (**30**), in which ring closure takes place onto the electron-rich benzofuran ring, produced the desired benz[*b*]indeno[1,2-*d*]furan-6-one (**31**) in 81% yield (entry 15). In these benzofuran-containing systems, cyclocarbonylation occurred onto the more reactive benzofuran moiety of the biaryl (entry 15), but failed to do so onto the less electron-rich phenyl ring of the biaryl (entry 14). Similar electronic effects have also been observed with *o*-halobiaryls containing either benzothiophene or thiophene rings. For instance, 3-iodo-2-phenylbenzothiophene[19] (**32**) produced a 67 % yield of 10-oxo-10*H*-benz[*b*]indeno[1,2-*d*]thiophene[20] (**33**) (entry 16), while 3-(2-bromophenyl)thiophene[21] (**34**) produced an 86 % yield of indeno[2,1-*d*]thiophen-8-one[22] (**35**) with excellent C-2 regioselectivity (entry 17). It is noteworthy that switching from the oxygen heterocycle of entry 14 to the sulfur analogue of entry 16 resulted in a substantial increase in yield. In like manner, the pyrrole derivative 1-(2-iodophenyl)pyrrole (**36**) gave a 96 % yield of pyrrolo[1,2-*a*]indol-9-one[23] (**37**) (entry 18).

The yield of the palladium-catalyzed cyclocarbonylation of *o*-halobiaryls containing an indole was not only dependent on electronic effects, but also on the nature of the protecting group on the indole nitrogen. To illustrate, 2-iodo-3-phenyl-1*H*-indole (**38**) and 3-iodo-2-phenyl-1*H*-indole[24] (**42**), both of which have unprotected nitrogens, failed to give the desired indenoindolones under the standard reaction conditions (entries 19 and 21). However, the *N*-methyl substituted indole analogues 2-iodo-1-methyl-3-phenylindole (**40**)

and 3-iodo-1-methyl-2-phenylindole (**44**) produced the desired 5-methyl-5*H*-indeno[2,1-*b*]indol-6-one[7d, 25] (**41**) and 5-methyl-5*H*-indeno[1,2-*b*]indol-10-one[26] (**45**) in 49% and 21% yields respectively (entries 20 and 22). In an attempt to increase the yield of indeno[1,2-*b*]indol-10-one, 3-iodo-2-phenyl-1-(4-toluenesulfonyl)indole (**46**) was prepared and subsequently cyclocarbonylated under our standard reaction conditions to produce 5*H*-indeno[1,2-*b*]indol-10-one[27] (**43**) in a 45% yield (entry 23). It is worth emphasizing that compound **46** led to the cyclocarbonylated product **43** in which the sulfonamide functionality had been removed under the relatively mild reaction conditions employed. This unusual deprotection was also observed in the cyclocarbonylation of 3-(2-bromophenyl)-1-(4-toluenesulfonyl)indole (**47**), which led to 5*H*-indeno[2,1-*b*]indol-6-one (**39**) in 55 % yield (entry 24). Furthermore, 42 % of the 3-(2-bromophenyl)-1-(4-toluenesulfonyl)indole (**47**) was recovered at the end of the reaction, which seems to indicate that removal of the sulfonamide functionality occurs during or after the cyclocarbonylation reaction, not before.

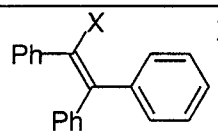
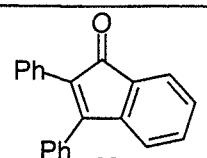
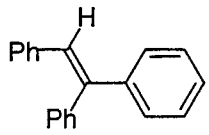
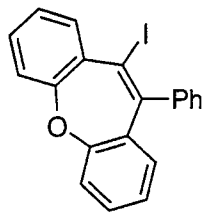
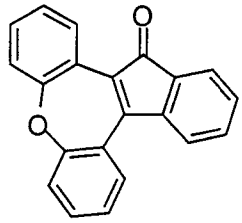
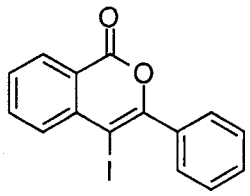
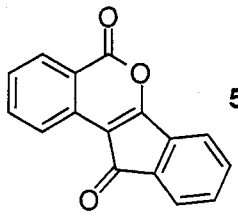
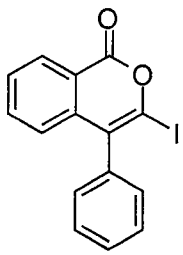
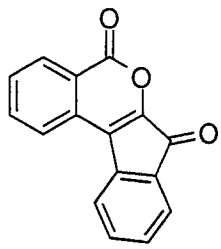
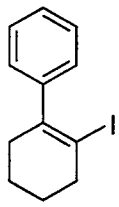
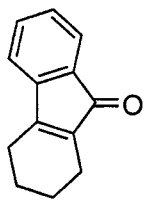
In summary, the synthesis of fluorenones have been accomplished in excellent yields with good regioselectivity by the cyclocarbonylation of *o*-halobiaryls containing six-membered ring aromatics (Table 2, entries 1-13). Similarly, this palladium-catalyzed reaction can also be used to prepare more strained fluorenones containing two fused five-membered rings (Table 2, entries 14-24). In the latter reactions, the yield of fluorenone is strongly dependent on electronic effects. This fact can be rationalized in terms of the ring strain of the palladium intermediates (see the latter mechanistic discussion and Scheme 2) leading to such fluorenones. The transformation is more favorable if cyclization occurs onto an electron-rich system, such as a benzofuran [81 % yield (entry 15)], a thiophene [86% yield

(entry 17)], a pyrrole [96 % yield (entry 18)] or an indole [97 % yield based on percent conversion (entry 24)] versus cyclization onto a relatively unreactive phenyl group [0-67 % yields (entries 14, 16 and 19-23)].

Finally, this chemistry can also be applied to vinylic halides for the preparation of indenones. For instance, the cyclocarbonylation of commercially available 1-bromo-1,2,2-triphenylethene (**48**) led to 2,3-diphenyl-1-indenone (**49**) in 81 % yield (Table 3, entry 1); however, 1-iodo-1,2,2-triphenylethene[28] (**51**) led to the desired product **49** in only a 61 % yield along with 24 % of triphenylethene (**50**) (entry 2). Furthermore, 5-iodo-6-phenyldibenz[*b*,*f*]oxepine[29] (**52**) produced indeno[5,6]dibenz-[*b*,*f*]oxepin-14-one (**53**) in 80 % yield (entry 3). Similar attempts to cyclocarbonylate 3-iodo-4-phenylisocoumarin (**54**) or 4-iodo-3-phenylisocoumarin (**56**) under our standard reaction conditions resulted in failure (entries 4 and 5). It is unclear why substrates **54** and **56** failed to successfully undergo the cyclocarbonylation reaction, but it is possibly due to unfavorable electronic effects during the cyclization process. Finally, the cyclocarbonylation of 1-iodo-2-phenylcyclohexene[30] (**58**) produced 1,2,3,4-tetrahydrofluoren-9-one[31] (**59**) in 34 % yield. This indicates that the palladium-catalyzed cyclocarbonylation of vinylic halides to indenones does not appear to be as general as the cyclocarbonylation of *o*-halobiaryls to fluorenones. This observation can be rationalized in terms of unfavorable electronic effects during the cyclocarbonylation of vinylic halides or possibly the instability of the desired indenone products.

We propose a possible reaction mechanism for this palladium-catalyzed synthesis of fluorenones involving (1) oxidative addition of the aryl halide to Pd(0), (2) CO insertion to

Table 3. Palladium-catalyzed cyclocarbonylation of vinylic halides to indenones.[a]

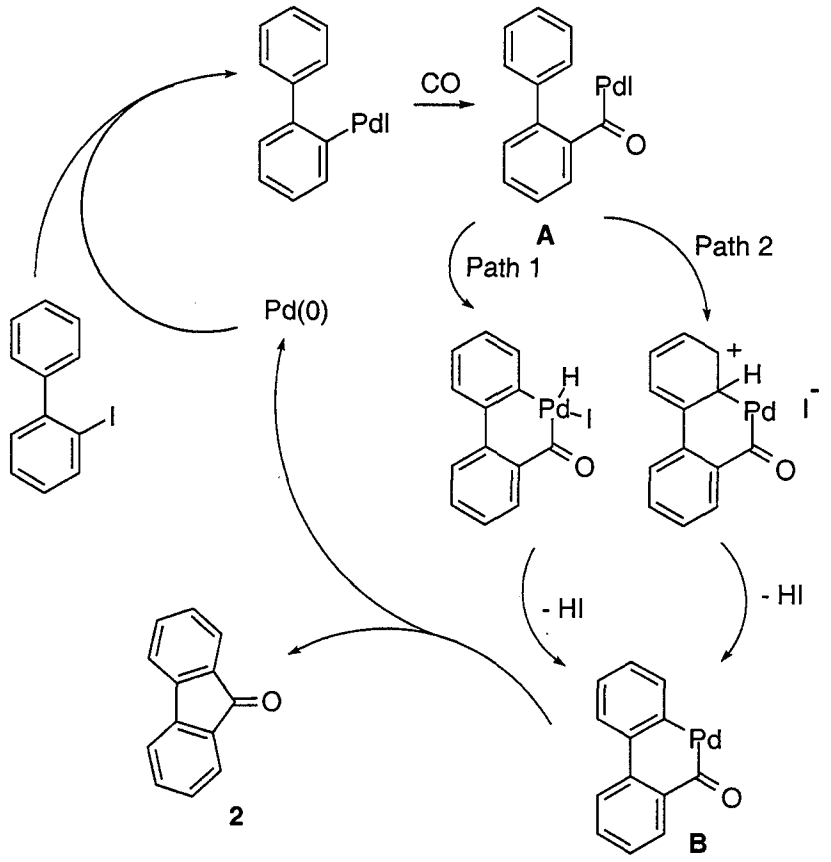
entry	substrate	product(s)	% yield
1	 X = Br (**48**)	 **49** +  **50**	81[b] + 0
2	X = I (**51**)		61 + 24
3	 **52**	 **53**	80
4	 **54**	 **55**	0
5	 **56**	 **57**	0
6	 **58**	 **59**	34

[a]All reactions were carried out under the optimal conditions described in the text. [b]The reaction time was extended to 24 h.

generate the acylpalladium intermediate **A**, (3) either oxidative addition of the neighboring aryl C-H to the acylpalladium to generate a Pd(IV) intermediate (path 1)[32] or electrophilic

palladation (path 2)[33] and subsequent elimination of HI to generate the neighboring aryl C-H to the acylpalladium to generate a Pd(IV) intermediate (path 1)[32] or electrophilic palladation (path 2)[33] and subsequent elimination of HI to generate intermediate **B**, and (4) reductive elimination of the ketone with simultaneous regeneration of the Pd(0) catalyst (Scheme 2).

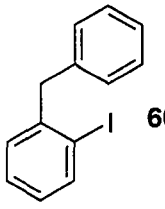
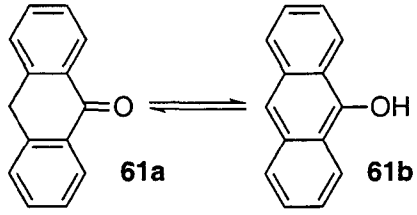
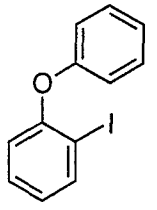
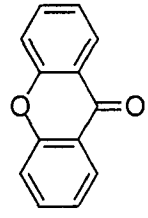
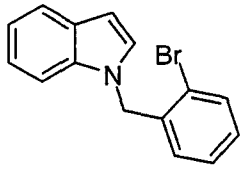
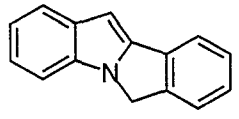
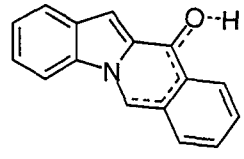
Scheme 2



Finally, we have explored the use of our cyclocarbonylation methodology to prepare six-membered ring ketones. Unfortunately, treating 1-benzyl-2-iodobenzene[34] (**60**) with CO under our standard reaction conditions failed to give the desired product **61a** or tautomer **61b** (Table 4, entry 1). Similarly, the more electron-rich (2-iodophenyl)phenyl ether[29] (**62**) failed

to produce the desired xanthen-9-one (**63**) under our standard reaction conditions (entry 2). A similar attempt to cyclocarbonylate 1-(2-bromobenzyl)indole[35] (**64**) led exclusively to

Table 4. Palladium-catalyzed cyclocarbonylation of aryl halides to six-membered ring ketones.[a]

entry	substrate	product(s)	% yield
1	 **60**	 **61a** **61b**	0
2	 **62**	 **63**	0
3	 **64**	 **65** +  **66a, 66b**	70 + 0

[a]All reactions were carried out under the optimal conditions described in the text.

direct cyclization, without CO insertion, producing 6-*H*-isoindolo[2,1-*a*]indole[36] (**65**) in 70 % yield and none of the desired cyclic ketone product **66a** or tautomer **66b** (entry 3). We speculate that the cyclocarbonylation of aryl halides to six-membered ring ketones is unfavorable due to the difficulty in forming a seven-membered ring organopalladium intermediate analogous to **B**, which would be required prior to cyclization (Scheme 2).

Therefore, we conclude that the preparation of six-membered ring ketones by this methodology is probably not feasible, at least under our present reaction conditions.

Conclusion

The palladium-catalyzed cyclocarbonylation of *o*-halobiaryls provides a short, straightforward route to a variety of substituted fluoren-9-ones under mild reaction conditions and short reaction times. Our success in extending this reaction to other biaryl systems, as well as some vinylic halides, indicates its potential for the synthesis of a wide variety of five-membered carbocyclic and heterocyclic aromatic ketones. We were unable to extend this chemistry to the preparation of six-membered cyclic ketones.

Experimental Section

General procedures. All ^{1}H and ^{13}C spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5 %) + 300 mL of H_2O]. All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV.

Reagents. All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of DME, THF, DMF, diethyl ether, ethyl acetate and hexanes were purchased from Fisher Scientific Co. 2-Iodobiphenyl (**1**), 2-iodothioanisole and thiophene-3-

boronic acid were obtained from Lancaster Synthesis Ltd. 2-Iodoaniline, triphenylethene (**50**), 1,2,2-triphenyl-1-bromoethene (**48**), 2-bromobiphenyl (**3**), 1-bromo-2-iodobenzene, 4-bromotoluene, 3-bromotoluene, 2-fluoroanisole, 4-bromoanisole, 2,5-dihydro-2,5-dimethoxyfuran, 2-bromophenylboronic acid, 4,4'-diiodobiphenyl, phenyllithium, phenylacetylene, cesium carbonate, cesium fluoride, pivalic acid and triethylamine were obtained from Aldrich Chemical Co., Inc. Bis(tricyclohexylphosphine)palladium(0) was purchased from Strem Chemicals, Inc.

Synthesis of the *o*-Halobiaryls

2-Iodo-4'-methylbiphenyl (4). 2-Iodo-4'-methylbiphenyl (**4**) was prepared by a procedure reported by Hart.[9] A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 4-methylphenylmagnesium bromide [prepared from 4-bromotoluene (1.71 g, 10.0 mmol) and Mg (0.246 g, 10.0 mmol) in THF (30 mL)], and the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I_2 (3.8 g, 15.0 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I_2 was destroyed by adding 10% aq $NaHSO_3$ (35 mL); the organic layer was separated and rewashed with brine (20 mL). Finally, the organic layer was dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The residue was chromatographed using 20:1 hexanes/ethyl acetate to afford 0.88 g (60 %) of the desired compound **3** as a colorless liquid with spectral properties identical to those previously reported.[37]

2-Iodo-4'-methoxybiphenyl (6). This biphenyl was prepared by the same method used to prepare **4**, but 4-bromoanisole (1.71 g, 10.0 mmol) was employed. The residue was

chromatographed using 20:1 hexanes/ethyl acetate to afford 0.610 g (39 %) of the desired compound **6** as a yellow solid. This compound was further purified by recrystallization from hexanes to yield a white solid: mp 58-60 ^{0}C; ^{1}H NMR ($CDCl_3$) δ 3.86 (s, 3H), 6.94-7.02 (m, 3H), 7.26-7.30 (m, 3H), 7.36 (td, J = 7.2, 0.9 Hz, 1H), 7.93 (dd, J = 8.0, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.5, 99.4, 113.5, 128.4, 128.8, 130.4, 130.7, 137.0, 139.7, 146.5, 159.3; HRMS *m/z* 309.98594 (calcd for $C_{13}H_{11}IO$, 309.98547).

2-Iodo-4'-methoxymethylbiphenyl (8). This iodobiphenyl was prepared in two steps from 2-iodo-4'-methylbiphenyl (**4**). Compound **4** was brominated by the procedure of Ponchant[37] to afford 4'-bromomethyl-2-iodobiphenyl (**67**): ^{1}H NMR ($CDCl_3$) δ 4.54 (s, 2H), 7.01-7.07 (m, 1H), 7.26-7.41 (m, 6H), 7.94-7.97 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 33.4, 98.2, 128.2, 128.3, 129.1, 129.4, 130.1, 130.2, 130.4, 137.5, 139.6, 144.6, 145.8 . A solution of 4'-bromomethyl-2-iodobiphenyl (**67**) (0.228 g, 0.611 mmol) and NaOMe (0.162 g, 3.0 mmol) in 10 mL of anhydrous methanol was stirred for 16 h at room temperature. The mixture was diluted with diethyl ether (50 mL) and washed with brine (25 ml). The organic layer was dried ($MgSO_4$), filtered, and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 7:1 hexanes/ethyl acetate to afford 0.172 g (87 %) of the desired compound **8** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 3.44 (s, 3H), 4.51 (s, 2H), 6.99-7.04 (m, 1H), 7.26-7.41 (m, 6H), 7.94 (dd, J = 8.1, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 58.6, 74.8, 98.8, 127.6, 128.4, 129.0, 129.6, 130.4, 137.9, 139.7, 143.8, 146.6; IR (CH_2Cl_2) 3049, 2985, 1463 cm^{-1}; HRMS *m/z* 324.0016 (calcd for $C_{14}H_{13}IO$, 324.0011).

4-(2-Iodophenyl)benzaldehyde (10). Compound **67** was oxidized to aldehyde **10** using the following procedure: a solution of $AgClO_4$ (0.29 g, 1.4 mmol) in DMSO (5 mL)

was added quickly with stirring to 4'-bromomethyl-2-iodobiphenyl (0.50 g, 1.3 mmol) in DMSO (2 mL). The resulting mixture was allowed to stand for 30 min at room temperature in the dark. At this point, triethylamine (0.81 g, 8.0 mmol) was added and the mixture stirred for an additional 20 min. The reaction mixture was quenched with brine (25 mL) and extracted with diethyl ether (60 mL). The aqueous layer was reextracted with diethyl ether (20 mL), and the organic layers were combined, dried ($MgSO_4$) and filtered. The solvent was removed under reduced pressure, and the resulting yellow oil was purified by column chromatography using 5:1 hexanes/ethyl acetate to afford 0.308 g (77 %) of 4-(2-iodophenyl)benzaldehyde (**10**) as a white solid: mp 79-80 °C (lit.[38] mp 80-81 °C). The spectral properties were identical to those previously reported.[38]

2-Iodo-3'-methylbiphenyl (12). This biphenyl was prepared by the same method used to prepare **4**, but 3-bromotoluene (1.71 g, 10.0 mmol) was employed. It was obtained as a colorless liquid (0.84 g, 57 %): ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 7.04 (td, J = 7.6, 2.0 Hz, 1H), 7.16-7.18 (m, 2H), 7.22-7.24 (m, 1H), 7.31-7.41 (m, 3H), 7.97 (dd, J = 8.0, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.6, 98.8, 126.5, 127.9, 128.1, 128.4, 128.8, 130.1, 130.2, 137.6, 139.5, 144.2, 146.8; HRMS *m/z* 293.99093 (calcd for $C_{13}H_{11}I$, 293.99055).

3-(2-Iodophenyl)benzaldehyde (15). This aldehyde was prepared in two steps from 2-iodo-3'-methylbiphenyl (**12**) by the same method used to prepare 4-(2-iodophenyl)benzaldehyde (**10**). Bromination[37] of **12** produced 3'-bromomethyl-2-iodo-biphenyl (**68**) in 70 % yield: ^{1}H NMR ($CDCl_3$) δ 4.54 (s, 2H), 7.04 (td, J = 8.55, 1.8 Hz, 1H), 7.26-7.42 (m, 6H), 7.95 (dd, J = 7.8, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 33.4, 98.6, 128.3, 128.4, 128.5, 129.1, 129.5, 130.1, 130.2, 137.5, 139.7, 144.7, 146.0. Oxidation of **68** (0.485 g, 1.3

mmol) using DMSO (7 mL) and $AgClO_4$ (0.29 g, 1.4 mmol) gave 0.300 g (75 %) of the desired product **15** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 7.06 (td, J = 7.8, 1.8 Hz, 1H), 7.30 (dd, J = 7.8, 1.8 Hz, 1H), 7.41 (td, J = 7.4, 1.2 Hz, 1H), 7.56-7.64 (m, 2H), 7.85-7.86 (m, 1H), 7.91 (dt, J = 6.9, 1.8 Hz, 1H), 7.96 (dd, J = 7.8, 1.2 Hz, 1H), 10.06 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 98.3, 128.5, 128.8, 128.9, 129.5, 130.1, 130.8, 135.5, 136.3, 139.8, 145.0, 145.2, 192.1; IR ($CHCl_3$) 1698 cm^{-1}; HRMS *m/z* 307.97049 (calcd for $C_{13}H_9IO$, 307.96982).

2-Iodo-3-methoxybiphenyl (18). 1-Lithio-2-methoxybiphenyl was prepared *in situ* from 2-fluoroanisole (1.134 g, 9.0 mmol) and phenyllithium (10 mL of 1.8 M solution in hexanes) in diethyl ether (20 ml) by the procedure of Huisgen.[10] The reaction mixture was cooled to 0 °C using an ice bath and I_2 (3.5 g, 13.8 mmol) was added slowly with constant stirring. The mixture was stirred for an additional 30 min, then the excess I_2 was destroyed by adding 10% aq $NaHSO_3$ (35 mL). The organic layer was rewashed with brine (20 mL), dried ($MgSO_4$) and filtered. Removal of solvent under reduced pressure gave a yellow oil that was purified by chromatography using 20:1 hexanes/ethyl acetate to afford 1.02 g (36 %) of the desired compound **18** as a yellow solid. Recrystallization from hexanes/ethyl acetate gave the desired product as a white solid: mp 83-84 °C; ^{1}H NMR ($CDCl_3$) δ 3.94 (s, 3H), 6.82 (dd, J = 8.2, 1.2 Hz, 1H), 6.92 (dd, J = 7.5, 1.2 Hz, 1H), 7.30-7.43 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 56.7, 91.4, 109.5, 122.8, 127.6, 127.9, 129.0, 129.4, 144.6, 148.9, 158.4; HRMS *m/z* 309.98594 (calcd for $C_{13}H_{11}IO$, 309.98547).

9-Iodo-10-phenylphenanthrene (20). This iodobiaryl was prepared from 9-phenyl-10-(trimethylsilyl)phenanthrene[39] using an iodination procedure from the literature.[40] To a solution of 9-phenyl-10-(trimethylsilyl)phenanthrene (0.133 g, 0.4 mmol) in CH_2Cl_2 (2 mL)

was added ICl (0.078 g, 0.48 mmol) in CH_2Cl_2 (2 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 1 h, then the excess ICl was destroyed by adding 10% aq $Na_2S_2O_3$ (10 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The remaining solid was recrystallized from methanol/CH_2Cl_2 to afford 0.13 g (85 %) of the desired compound **20** as a white solid: mp 118-120 °C; ^{1}H NMR ($CDCl_3$) δ 7.28 (dd, J = 6.0, 1.8 Hz, 2H), 7.38 (d, J = 3.9 Hz, 2H), 7.50-7.56 (m, 3H), 7.60-7.70 (m, 3H), 8.44-8.47 (m, 1H), 8.63-8.70 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 106.6, 122.6, 122.7, 127.0, 127.1, 127.5, 127.8, 128.1, 128.5, 128.7, 130.0, 130.3, 130.6, 132.3, 132.4, 134.7, 145.3, 145.4; IR ($CDCl_3$) 3064, 3025, 1481 cm^{-1}; HRMS *m/z* 380.0062 (calcd for $C_{20}H_{13}I$, 380.0062).

2-Bromo-1-phenylnaphthalene (22). This starting material was prepared by the procedure of Wittig[12]: ^{1}H NMR ($CDCl_3$) δ 7.27-7.31 (m, 2H), 7.32-7.36 (m, 1H), 7.41-7.52 (m, 5H), 7.65-7.72 (m, 2H), 7.79-7.82 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 121.8, 126.3, 127.0, 127.1, 128.1, 128.2, 128.6, 129.2, 130.2, 130.4, 132.6, 134.2, 139.9, 140.1.

4-Iodo-3-phenylisoquinoline (24). This aryl iodide was prepared by the procedure of Larock *et al*[14]: ^{1}H NMR ($CDCl_3$) δ 7.45-7.53 (m, 3H), 7.61-7.71 (m, 3H), 7.83 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 9.17 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 98.2, 128.0, 128.1, 128.1, 128.4, 129.9, 132.4, 132.5, 138.7, 143.7, 152.1, 157.1 (one sp^2 carbon missing due to overlap); IR (neat) 3055, 1630, 1549 cm^{-1}; HRMS *m/z* 330.9852 (calcd for $C_{15}H_{10}IN$, 330.9858).

2,2'''-Dibromo-*p*-quaterphenyl (26). This aryl dibromide was prepared by a selective Suzuki-Miyaura cross-coupling reaction as follows. 4,4'-Diiodobiphenyl (0.406 g, 1.0 mmol), 2-bromophenylboronic acid (0.44 g, 2.2 mmol), CsF (0.608 g, 4.0 mmol),

$Pd(dba)_2$ (0.0576 g, 0.10 mmol), and PPh_3 (0.052 g, 0.2 mmol) in 1,2-dimethoxyethane (DME) (5 mL) were stirred under Ar at 90 ^{0}C for 6 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The residue was purified by crystallization from ethanol/acetone to afford 0.318 g (68 % yield) of the desired compound **26** as a yellow solid: mp 170-171 ^{0}C (lit[16] mp 174.8 ^{0}C); ^{1}H NMR ($CDCl_3$) δ 7.21-7.26 (m, 1H), 7.39-7.41 (m, 2H), 7.51-7.55 (m, 2H), 7.70-7.76 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 122.9, 126.9, 127.7, 129.0, 130.1, 131.6, 133.5, 140.1, 140.4, 142.4; IR (CH_2Cl_2) 3054, 1466 cm^{-1}; HRMS *m/z* 463.9607 (calcd for $C_{24}H_{16}Br_2$, 463.9598).

3-Iodo-2-phenylbenzofuran (28). This compound was prepared by the procedure of Cacchi *et al.*[18] The spectral properties were identical to those previously reported.[18]

3-(2-Iodophenyl)benzofuran (30). This starting material was prepared by the procedure of Jørgensen *et al*[41] from 1-(2-iodophenyl)-2-phenoxyethanone[42] (**69**) [^{1}H NMR ($CDCl_3$) δ 5.10 (s, 1H), δ 6.91 (dd, *J* = 7.5, 1.2 Hz, 2H), 6.98 (tt, *J* = 7.4, 1.0 Hz, 1H) 7.14-7.18 (m, 1H), 7.25-7.30 (m, 2H), 7.40-7.44 (m, 2H), 7.92 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 71.6, 91.7, 114.9, 121.9, 128.1, 128.7, 129.7, 132.4, 140.8, 141.5, 157.7, 199.9]. To a solution of **69** (0.2 g, 0.59 mmol) in CH_2Cl_2 (8 mL) was added methanesulfonic acid (0.39 mL, ~ 6 mmol). The resulting solution was stirred at 55 ^{0}C for 40 h. The reaction mixture was diluted with diethyl ether (30 mL) and washed with brine (30 mL). The organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 18:1 hexanes/ethyl acetate to afford 0.122 g (64 %) of the desired compound **30** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 7.05-7.09 (m,

1H), 7.25 (td, J = 7.4, 1.2 Hz, 1H), 7.33 (td, J = 7.6, 1.2 Hz, 1H), 7.39-7.41 (m, 2H), 7.46 (d, J = 7.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.76 (s, 1H), 8.00 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 99.8, 111.8, 121.0, 122.9, 124.2, 124.7, 127.1, 128.3, 129.5, 131.2, 136.8, 140.0, 143.0, 155.0; IR (CH_2Cl_2) 3049, 3068 cm^{-1}; HRMS *m/z* 319.9702 (calcd for $C_{14}H_9IO$, 319.9698).

3-Iodo-2-phenylbenzothiophene (32). This starting material was prepared in two steps from commercially available 2-iodothioanisole. To a solution of 2-iodo-thioanisole (1.53 g, 6.1 mmol) and phenylacetylene (0.75 g, 7.3 mmol) in Et_3N (25 mL) was added $PdCl_2(PPh_3)_2$ (86 mg, 2.0 mol %). The mixture was stirred for 5 min under Ar and CuI (11 mg, 1.0 mol %) was added. The resulting mixture was then heated under an Ar atmosphere at 60 °C for 2 h. The reaction mixture was allowed to cool to room temperature, and the ammonium iodide salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography using 20:1 hexanes/ethyl acetate to afford 1.26 g (92 %) of 2-(2-phenylethynyl)thioanisole (**70**) as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 2.51 (s, 3H), 7.10 (td, J = 7.5, 1.2 Hz, 1H), 7.17 (dd, J = 7.8, 0.9 Hz, 1H), 7.27-7.37 (m, 4H), 7.48 (ddd, J = 7.5, 1.2, 0.6 Hz, 1H), 7.56-7.60 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 15.3, 87.1, 96.1, 123.4, 124.4, 124.4, 124.5, 128.6, 128.6, 129.0, 131.8, 132.5, 141.9; IR (CH_2Cl_2) 1599, 1491 cm^{-1}; HRMS *m/z* 224.06627 (calcd for $C_{15}H_{12}S$, 224.06597). 3-Chloromercurio-2-phenylbenzothiophene was prepared *in situ* from **70** by the procedure of Larock *et al.*[19] To a suspension of $Hg(OAc)_2$ (0.318 g, 1.0 mmol) in glacial HOAc (3 mL) at room temperature was added 2-(2-phenylethynyl)thioanisole (0.224 g, 1.0 mol), and the resulting solution was stirred at room temperature for 30 min. The reaction mixture was

quenched by adding I_2 (0.38 g, 1.5 mmol), and the mixture was stirred vigorously for an additional 30 min. Excess I_2 was destroyed by adding 10% aq $Na_2S_2O_3$ (30 mL), and the aqueous layer was extracted with diethyl ether (50 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The residue was purified by column chromatography using 30:1 hexanes/ethyl acetate to afford 0.304 g (90 %) of 3-iodo-2-phenylbenzothiophene as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.34-7.40 (td, J = 7.5, 1.5 Hz, 1H), 7.42-7.50 (m, 4H), 7.66-7.69 (m, 2H), 7.75-7.78 (m, 1H), 7.81-7.84 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 79.7, 122.4, 125.7, 125.8, 126.6, 128.8, 129.2, 130.3, 134.9, 139.2, 142.2, 142.4; IR (CH_2Cl_2) 3065, 1601, 1477, 1433 cm^{-1}; HRMS *m/z* 335.94745 (calcd for $C_{14}H_9IS$, 335.94697).

3-(2-Bromophenyl)thiophene (34). This aryl bromide was prepared by a selective Suzuki-Miyaura cross-coupling reaction as follows. 1-Bromo-2-iodobenzene (0.2829 g, 1.0 mmol), thiophene-3-boronic acid (0.140 g, 1.1 mmol), cesium fluoride (0.304 g, 2.0 mmol), $Pd(dba)_2$ (0.0288 g, 0.05 mmol), and PPh_3 (0.026 g, 0.1 mmol) in DME (5 mL) were stirred under Ar at 90 ^{0}C for 6 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (30 mL). The organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using hexanes to afford 0.210 g (88 %) of the desired compound **34** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 7.17 (td, J = 7.6, 0.4 Hz, 1H), 7.28-7.40 (m, 5H), 7.65 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 122.6, 124.0, 124.8, 127.4, 128.7, 129.0, 131.3, 133.4, 137.6, 141.1; IR (CH_2Cl_2) 3112, 3048, 1468 cm^{-1}; HRMS *m/z* 237.9455 (calcd for $C_{10}H_7BrS$, 237.9452).

1-(2-Iodophenyl)pyrrole (36). This aryl iodide was prepared by the condensation of 2-iodoaniline with 2,5-dihydro-2,5-dimethoxyfuran. To a solution of citric acid monohydrate (4.2 g, 20 mmol) in water (20 ml) was added 2,5-dihydro-2,5-dimethoxyfuran (1.716 g, 13 mmol) and the mixture was stirred vigorously for approximately 8 min at room temperature. At this point a homogeneous solution was obtained, and the mixture was diluted with methanol (10 mL), followed by addition of 2-iodoaniline (2.19 g, 10 mmol) in methanol (20 mL). The mixture was stirred at room temperature for 14 h, then diluted with diethyl ether (75 ml) and washed with brine (75 mL). The aqueous layer was reextracted with diethyl ether (25 mL) and the organic layers were combined, dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 20:1 hexanes/ethyl acetate to afford 2.28 g (85 %) of the desired compound **36** as a clear oil: ^{1}H NMR ($CDCl_3$), δ 6.34 (t, J = 2.0 Hz, 2H), 6.81 (t, J = 2.0 Hz, 2H), 7.09 (td, J = 7.6, 1.6 Hz, 1H), 7.30 (dd, J = 7.6, 1.6 Hz, 1H), 7.40 (td, J = 7.6, 1.2 Hz, 1H), 7.94 (dd, J = 7.6, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 96.1, 109.4, 122.4, 128.3, 129.2, 129.6, 140.2, 144.2; IR (CH_2Cl_2) 3049, 1496 cm^{-1}; HRMS *m/z* 268.9705 (calcd for $C_{10}H_8IN$, 268.9702).

2-Iodo-3-phenyl-1*H*-indole (38). This indole derivative was prepared from 2-trimethylsilyl-3-phenyl-1*H*-indole[43] using an iodination procedure from the literature.[40] To a solution of 2-trimethylsilyl-3-phenyl-1*H*-indole (0.265 g, 1.0 mmol) in CH_2Cl_2 (2 mL) was added ICl (0.1785 g, 1.1 mmol) in CH_2Cl_2 (3 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 1 h. Then the excess ICl was destroyed by adding 10% aq $Na_2S_2O_3$ (15 mL). The organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 7:1 hexanes/ethyl

acetate to afford 0.249 g (78 %) of the desired compound **38** as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.06-7.18 (m, 2H), 7.25-7.28 (m, 1H), 7.32-7.38 (m, 1H), 7.44-7.50 (m, 2H), 7.56-7.63 (m, 3H), 8.02 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 77.3, 110.5, 119.0, 120.6, 122.9, 123.8, 127.1, 127.3, 128.7, 129.9, 134.6, 139.8; IR (CH_2Cl_2) 3446, 3053, 1404 cm^{-1}; HRMS *m/z* 318.9862 (calcd for $C_{14}H_{10}IN$, 318.9858).

2-Iodo-1-methyl-3-phenylindole (40). This indole derivative was prepared in two steps from 3-phenyl-1*H*-indole. To a suspension of NaH (0.0528 g, 2.2 mmol) in DMF (4 mL) at 0 °C was added 3-phenyl-1*H*-indole (0.338 g, 1.7 mmol) in DMF (4 mL) and the mixture was stirred at room temperature for 30 min. At this point MeI (2.414 g, 17.0 mmol) in DMF (4 mL) was added and the reaction mixture stirred at room temperature for 14 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent removed under reduced pressure. The residue was purified by column chromatography using 9:1 hexanes/ethyl acetate to afford 0.350 g (78 %) of the desired 1-methyl-3-phenyllindole (**71**) as a yellow oil with spectral properties identical to those previously reported.[44] To a solution of **71** (0.343 g, 1.61 mmol) in THF (10 mL) at 0 °C was added *n*-butyllithium (0.76 mL of 2.5 M in hexanes, 1.9 mmol) and the reaction mixture was stirred at 0 °C for 4 h and then for 40 min at room temperature. The reaction mixture was cooled again to 0 °C and I_2 (0.762 g, 3.0 mmol) was added slowly over a 5 min period and the stirring was continued for an additional 10 min. At this point, the reaction mixture was diluted with diethyl ether (35 mL) and excess I_2 was destroyed by adding 10 % aq $Na_2S_2O_3$ (40 mL). The organic layer was dried ($MgSO_4$), filtered, and the solvent

removed under reduced pressure. The residue was purified by column chromatography using 18:1 hexanes/ethyl acetate to afford 0.383 g (70 %) of the desired compound **40** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3H), 7.06-7.11 (m, 1H), 7.18-7.23 (m, 1H), 7.33-7.39 (m, 2H), 7.45-7.50 (m, 2H), 7.56-7.61 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 34.8, 87.0, 110.0, 119.2, 120.2, 122.5, 123.2, 127.1, 127.8, 128.6, 130.2, 135.4, 138.8; IR (CH_2Cl_2) 3048, 2941, 1460, 1323 cm^{-1}; HRMS *m/z* 333.0019 (calcd for $C_{15}H_{12}IN$, 333.0015).

3-Iodo-2-phenyl-1*H*-indole (42). This indole derivative was prepared by the procedure of Bocci and Palla.[24] The spectral properties were identical to those previously reported.[24]

3-Iodo-1-methyl-2-phenylindole (44). This indole derivative was prepared from **42.** To a suspension of NaH (0.031 g, 1.3 mmol) in DMF (2 mL) at 0 ^{0}C was added **42** (0.320 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point, MeI (1.42 g, 10.0 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 14 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent removed under reduced pressure. The residue was purified by column chromatography using 9:1 hexanes/ethyl acetate to afford 0.310 g (93 %) of the desired 3-iodo-1-methyl-2-phenylindole (**44**) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.65 (s, 1H), 7.21-7.25 (m, 1H), 7.29-7.30 (m, 2H), 7.44-7.51 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 32.1, 59.0, 109.9, 120.8, 121.5, 123.0, 128.5, 128.9, 130.5, 131.0, 131.7, 137.8, 141.8; IR (CH_2Cl_2) 3047, 2944, 1463 cm^{-1}; HRMS *m/z* 333.0019 (calcd for $C_{15}H_{12}IN$, 333.0015).

3-Iodo-2-phenyl-1-(4-toluenesulfonyl)indole (46). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added 3-iodo-2-phenyl-1*H*-indole (0.320 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point *p*-toluenesulfonyl chloride (0.305 g, 1.6 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 14 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent removed under reduced pressure. The residue was purified by column chromatography using 5:1 hexanes/ethyl acetate to afford 0.30 g (68 %) of the desired compound **46** as a white solid: mp 118-120 °C; ^{1}H NMR ($CDCl_3$) δ 2.32 (s, 3H), 7.07-7.10 (m, 2H), 7.30-7.50 (m, 10H), 8.30 (dt, J = 8.1, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.8, 76.0, 116.2, 122.4, 124.9, 126.3, 127.1, 127.7, 129.5, 129.7, 131.8, 132.0, 132.5, 135.3, 137.2, 141.3, 145.2; IR (CH_2Cl_2) 3065, 2982, 1377, 1260, 1178 cm^{-1}; HRMS *m/z* 472.9955 (calcd for $C_{15}H_{12}O_2$, 472.9946).

3-(2-Bromophenyl)-1-(4-toluenesulfonyl)indole (47). This indole derivative was prepared by a selective Suzuki-Miyaura cross-coupling reaction as follows. 2-Bromophenylboronic acid (0.221 g, 1.1 mmol), 3-iodo-1-(4-toluenesulfonyl)indole[45] (0.3974 g, 1.0 mmol) [mp 130-131 °C; ^{1}H NMR ($CDCl_3$) δ 2.31 (s, 3H), 7.20 (d, J = 8.0 Hz, 2H), 7.28-7.36 (m, 3H), 7.68 (s, 1H), δ 7.75-7.77 (m, 2H), 7.93-7.96 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 21.7, 66.9, 113.4, 122.0, 124.0, 125.7, 127.0, 129.8, 130.1, 132.5, 134.4, 134.9, 145.4], CsF (0.304 g, 2.0 mmol), $Pd(dba)_2$ (0.0288 g, 0.05 mmol), and PPh_3 (0.026 g, 0.1 mmol) in DME (5 mL) were stirred under Ar at 90 °C for 5 h. The reaction mixture was diluted with diethyl

ether (50 mL) and washed with brine (30 mL). The organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 5:1 hexanes/ethyl acetate to afford 0.349 g (82 %) of the desired compound **47** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 2.32 (s, 3H), 7.20-7.25 (m, 4H), 7.34-7.42 (m, 4H), 7.71 (dd, J = 8.0, 1.2 Hz, 1H), 7.75 (s, 1H), 7.80-7.83 (m, 2H), 8.04 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.6, 113.8, 120.8, 122.6, 123.5, 123.9, 124.9, 125.4, 127.0, 127.5, 129.4, 130.0, 130.1, 132.0, 133.5, 133.6, 134.8, 135.2, 145.1; IR (CH_2Cl_2) 3066, 2981, 1373, 1177 cm^{-1}; HRMS *m/z* 425.0091 (calcd for $C_{15}H_{12}O_2$, 425.0085).

2-Iodo-1,2,2-triphenylethene (51). This vinylic iodide was prepared by the procedure of Miller et al.[28]

5-Iodo-6-phenyldibenz[*b,f*]oxepine (52). This vinylic iodide was prepared by the procedure of Kitamura *et al.*[29] The spectral properties were identical to those previously reported.[29]

4-Iodo-3-phenylisocoumarin (54). To a solution of methyl 2-(phenylethylnyl)benzoate[46] (0.0708 g, 0.3 mmol) in CH_2Cl_2 (3 mL) under Ar was added ICl (0.0584 g, 0.36 mmol) in CH_2Cl_2 (0.5 mL) dropwise via syringe. The reaction was stirred for 30 min at room temperature then diluted with diethyl ether (50 mL), washed with 10 % aq $Na_2S_2O_3$ (25 mL), dried ($MgSO_4$), and filtered. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography using 10:1 hexanes/ethyl acetate to afford 94.6 mg (90 %) of the indicated compound **54** as a white solid: mp 169-170 °C; ^{1}H NMR ($CDCl_3$) δ 7.47-7.49 (m, 3H), 7.59 (t, J = 7.8 Hz, 1H), 7.68-7.71 (m, 2H), 7.83-7.92 (m, 2H), 8.31 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 76.7, 120.5, 128.3, 129.5, 129.9,

130.2, 130.4, 131.7, 135.4, 135.9, 138.4, 155.0, 161.7; IR (CH_2Cl_2) 1736 cm^{-1}; HRMS *m/z* 347.9652 (calcd for $C_{15}H_9IO_2$, 347.9647).

3-Iodo-4-phenylisocoumarin (56). To a solution of 4-phenyl-3-(trimethylsilyl)isocoumarin[47] (0.441g, 1.5 mL) and I_2 (1.14 g, 4.5 mmol) in CH_3CN (15 mL) under Ar was added AgOTf (0.78 g, 3.0 mmol) in CH_3CN (5 mL) at room temperature. The reaction mixtute was stirred at 55 °C for 5 d. The mixture was allowed to cool to room temperature, diluted with diethyl ether (100 mL), and filtered. The filtrate was washed with 10 % aq $Na_2S_2O_3$ (25 mL) and the organic layer dried ($MgSO_4$), and filtered. The solvent was evaporated under reduced pressure and the residue purified by column chromatography using 9:1 hexanes/ethyl acetate to afford 501 mg (96 %) of the indicated compound **56** as a white solid: mp 170-171 °C; ^1H NMR ($CDCl_3$) δ 6.98 (d, *J* = 12.0 Hz, 1H), 7.27 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.50-7.63 (m, 5H), 8.31 (dd, *J* = 8.0, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 107.9, 119.6, 125.6, 127.4, 128.7, 128.9, 129.1, 129.9, 130.5, 135.2, 137.0, 137.3, 161.2.

1-Iodo-2-phenylcyclohexene (58). This vinylic iodide was prepared by the procedure of Larock *et al.*[30]

1-Benzyl-2-iodobenzene (60). To a solution of 2-iodobenzyl bromide (1.485 g, 5.0 mmol) in benzene (25 mL) was added $AgClO_4$ (2.07 g, 10 mmol) at room temperature and stirred for 7 h. The resulting mixture was filtered and diluted with Et_2O (30 mL). The organic layer was washed twice with H_2O (30 mL), dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 50:1 hexanes/ethyl acetate to obtain 1.529 g (86 %) of the desired product **60** as a clear oil with spectral properties identical to those previously reported.[34]

(2-Iodophenyl)phenyl ether (62). Compound **62** was prepared by the procedure of Kitamura *et al.*[29]

1-(2-Bromobenzyl)indole (64). Compound **64** was prepared by the procedure of Kozikowski *et al.*[35]

General Procedure for the Pd-Catalyzed Cyclocarbonylation of *o*-Halobiaryls. DMF (6 mL), $Pd(PCy_3)_2$ (8.4 mg, 0.0125 mmol), anhydrous cesium pivalate (0.117 g, 0.5 mmol), and the *o*-halobiaryl (0.25 mmol) were stirred under an Ar atmosphere at room temperature for 5 min. The mixture was flushed with CO and fitted with a CO filled balloon. The reaction mixture was heated to 110 °C with vigorous stirring for 7 h. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

Fluoren-9-one (2). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 45.1 mg (100 %) of the indicated compound as a yellow solid: mp 82-83 °C. This compound was identified by comparing the ^{1}H NMR and ^{13}C NMR spectra and melting point with an authentic sample obtained from Aldrich Chemical Co., Inc.

2-Methylfluoren-9-one (5). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 47.1 mg (97 %) of the indicated compound as a yellow solid: mp 90-91 °C (lit.[48] mp 92 °C); ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3H), 7.19-7.24 (m, 2H), 7.33 (d, J = 7.6 Hz, 1H), 7.04- 7.41 (m, 3H), 7.58 (d, J = 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.4, 120.0,

120.2, 124.2, 125.0, 128.6, 134.3, 134.4, 134.7, 135.1, 139.3, 141.8, 144.7, 194.2. The spectral properties were identical to those previously reported.[48]

2-Methoxyfluoren-9-one (7). The reaction mixture was chromatographed using 6:1 hexanes/ethyl acetate to afford 52.6 mg (100 %) of the indicated compound as a yellow solid: mp 78-79 °C (lit.[48] mp 78 °C); ^{1}H NMR ($CDCl_3$) δ 3.82 (s, 3H), 6.94 (dd, J = 8.4, 2.8 Hz, 1H), 7.14-7.18 (m, 2H), 7.34-7.41 (m, 3H), 7.56 (d, J = 7.6 Hz, 1H); IR (CH_2Cl_2) 1717 cm^{-1}. The spectral properties were identical to those previously reported.[49]

2-Methoxymethylfluoren-9-one (9). The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 56.0 mg (100 %) of the indicated compound as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 3.41 (s, 3H), 4.46 (s, 2H), 7.26-7.30 (m, 1H), 7.45-7.50 (m, 4H), 7.62-7.65 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 58.3, 74.1, 120.3, 123.6, 124.4, 129.1, 133.9, 134.4, 134.4, 134.8, 139.8, 143.9, 144.3, 193.8 (missing one sp^2 carbon due to overlap); IR (CH_2Cl_2) 3054, 2930, 1718 cm^{-1}; HRMS *m/z* 224.0840 (calcd for $C_{15}H_{12}O_2$, 224.0837).

9-Oxofluorene-2-carbaldehyde (11). The reaction mixture was chromatographed using 2:1 hexanes/ethyl acetate to afford 52.0 mg (100 %) of the indicated compound as a yellow solid: mp 204-205 °C (lit.[49] mp 203-204 °C); ^{13}C NMR ($CDCl_3$) δ 121.0, 121.7, 125.0, 130.8, 135.0, 135.1, 135.4, 136.4, 137.5, 143.3, 149.9, 190.8, 192.4. The spectral properties were identical to those previously reported.[50]

3-Methylfluoren-9-one (13). The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 43.7 mg (90 %) of the indicated compound as a yellow solid: mp 66-67 °C (lit.[51] mp 65 °C); ^{13}C NMR ($CDCl_3$) δ 22.2, 120.1, 121.3, 124.2, 124.3, 129.0,

129.6, 131.9, 134.5, 134.7, 144.3, 144.8, 145.9, 193.3. The other spectral properties were identical to those previously reported.[52]

1-Methylfluoren-9-one (14). The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 4.9 mg (10 %) of the indicated compound as a yellow solid: mp 98-99 °C (lit.[53] mp 98-99 °C). The spectral properties were identical to those previously reported.[53]

9-Oxofluorene-3-carbaldehyde (16) and 9-oxofluorene-1-carbaldehyde (17). The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 48.9 mg (94 %) of the indicated compounds as a 9:1 inseparable mixture of isomers (the ratio was determined by ^{1}H NMR spectroscopic analysis). **9-Oxofluorene-1-carbaldehyde** (minor isomer): ^{1}H NMR ($CDCl_3$) δ 11.06 (s, 1H) (as a characteristic peak); ^{13}C NMR ($CDCl_3$) δ 120.7, 124.9, 125.2, 126.3, 130.0, 133.6, 134.0, 134.7, 135.6, 143.8, 144.5, 145.0, 190.5, 194.4; IR (CH_2Cl_2) 1695, 1711 cm^{-1}; HRMS *m/z* 208.05281 (calcd for $C_{14}H_8O_2$, 208.05243). **9-Oxofluorene-3-carbaldehyde** (major isomer). This isomer was purified by recrystallization from hexanes/ethyl acetate to afford 29.2 mg (56 %) of the desired compound as a yellow solid: mp 148-149 °C (lit.[54] mp 149-150 °C); ^{1}H NMR ($CDCl_3$) δ 7.37 (td, J = 7.5, 1.2 Hz, 1H), 7.57 (td, J = 7.5, 1.2 Hz, 1H), 7.62-7.64 (m, 1H), 7.71 (d, J = 7.5 Hz, 1H), 7.82-7.82 (m, 2H), 8.03 (t, J = 0.9, 1H), 10.10 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 119.7, 121.2, 124.8, 125.0, 130.1, 132.7, 134.4, 135.7, 138.8, 141.2, 143.6, 145.2, 191.7, 193.0; IR ($CHCl_3$) 1719, 1701 cm^{-1}; HRMS *m/z* 208.05281 (calcd for $C_{14}H_8O_2$, 208.05243).

1-Methoxyfluoren-9-one (19). The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 52.0 mg (99 %) of the indicated compound as a yellow solid:

mp 142-143 °C (lit.[55] mp 141-142 °C); ^{1}H NMR ($CDCl_3$) δ 3.97 (s, 3H), 6.81 (d, J = 8.1 Hz, 1H), 7.11 (dd, J = 7.2, 0.6 Hz, 1H), 7.27 (td, J = 6.9, 1.2 Hz, 1H), 7.40-7.49 (m, 3H), 7.63 (dt, J = 7.2, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 56.2, 113.1, 113.3, 120.3, 120.4, 124.1, 129.4, 134.1, 134.7, 137.0, 143.4, 146.7, 158.6, 187.5. The spectral properties were identical to those previously reported.[55]

Indene[1,2-*l*]phenanthrene-13-one (21). The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 68.7 mg (98 %) of the indicated compound as an orange solid: mp 183-184 °C (ethanol/acetone) (lit.[11] mp 185-187 °C); ^{1}H NMR ($CDCl_3$) δ 7.25-7.34 (m, 1H), 7.48 (td, J = 8.2, 1.2 Hz, 1H), 7.62-7.79 (m, 5H), 8.02 (d, J = 7.5 Hz, 1H), 8.57-8.63 (m, 2H), 8.70 (d, J = 8.1 Hz, 1H), 9.21-9.24 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 122.8, 123.5, 123.7, 124.0, 125.5, 125.9, 126.2, 127.4, 127.5, 127.7, 127.8, 128.6, 129.0, 129.4, 131.2, 134.1, 134.5, 134.8, 144.0, 144.8, 196.0. The spectral properties were identical to those previously reported.[11]

Benzo[*c*]fluoren-7-one (23). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 55.3 mg (96 %) of the indicated compound as an orange solid: mp 160-161 °C (lit.[13] mp 161-162 °C). The spectral properties were identical to those previously reported.[13]

11-Oxoindeno[1,2-*c*]isoquinoline (25). The reaction mixture was chromatographed using 1:1 hexanes/ethyl acetate to afford 54.9 mg (95 %) of the indicated compound as a yellow solid: mp 198-200 °C (lit.[14] mp 199-200 °C); ^{13}C NMR ($CDCl_3$) δ 119.8, 120.7, 123.6, 123.9, 127.7, 128.8, 129.3, 130.6, 132.6, 133.6, 134.7, 135.0, 143.9, 158.4, 162.5, 194.2. The spectral properties were identical to those previously reported.[14]

[2,2']Bifluorenyl-9,9'-dione (27). In order to keep the equiv of aryl halide consistent, we employed 0.125 mmol of aryl dibromide **26** and the reaction period was extended to 14 h. The reaction mixture was diluted with water (20 mL) and a yellow solid crystallized from the reaction mixture. The solid was filtered and washed with water (10 mL) and then ethanol (5 mL) to yield 0.039 g (87 %) of the desired compound **27**. The indicated compound was further purified by crystallization from $CHCl_3$/toluene to afford a green-yellow solid: mp 295-296 °C (lit.[16] mp 295-297 °C); ^{1}H NMR ($CDCl_3$) δ 7.33 (t, J = 7.2 Hz, 1H), 7.55-7.63 (m, 3H), 7.70 (d, J = 6.8 Hz, 1H), 7.77 (d, J = 7.2 Hz, 1H), 7.93 (s, 1H); ^{13}C NMR and IR were not obtained for this compound due to its poor solubility in common organic solvents; HRMS *m/z* 358.1001 (calcd for $C_{26}H_{14}O_2$, 358.0994).

Benz[*b*]indeno[1,2-*d*]furan-6-one (31). The reaction mixture was chromatographed using 7:1 hexanes:ethyl acetate to afford 44.6 mg (81 %) of the indicated compound as an orange solid: mp 109-110 °C; ^{1}H NMR ($CDCl_3$) δ 7.12-7.18 (m, 2H), 7.29-7.38 (m, 3H), 7.44 (td, J = 7.8, 1.2 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.71 (dd, J = 8.0, 0.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 113.8, 120.3, 122.0, 124.1, 124.8, 128.6, 128.7, 133.9, 134.9, 136.0, 141.4, 154.6, 161.6, 180.7; IR (CH_2Cl_2) 3025, 1714 cm^{-1}; HRMS *m/z* 220.0526 (calcd for $C_{15}H_8O_2$, 220.0524).

10-Oxo-10-*H*-benz[*b*]indeno[1,2-*d*]thiophene (33). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 39.6 mg (67 %) of the indicated compound as an orange solid: mp 203-204 °C (lit.[20] mp 205-206 °C); ^{1}H NMR ($CDCl_3$) δ 7.17-7.49 (m, 6H), 7.76-7.80 (m, 1H), 8.10-8.14 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 120.4, 123.1,

123.3, 123.7, 125.5, 126.8, 129.7, 132.6, 133.8, 135.0, 137.1, 138.8, 144.2, 162.4, 187.4; IR (CH_2Cl_2) 1718, 1697, 1608 cm^{-1}; HRMS *m/z* 236.03008 (calcd for $C_{15}H_8OS$, 236.02959).

Indeno[2,1-*d*]thiophen-8-one (35). The reaction period was extended to 14 h. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 40.1 mg (86 %) of the indicated compound as a yellow solid: mp 109-110 °C (lit.[22] mp 107-110 °C); ^{13}C NMR ($CDCl_3$) δ 119.7, 120.3, 124.1, 128.2, 133.8, 137.1, 138.0, 139.3, 139.8, 158.8, 185.7. The other spectral properties were identical to those previously reported.[22]

Pyrrolo[1,2-*a*]indol-9-one (37). The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 40.5 mg (96 %) of the indicated compound as a yellow solid: mp 121-122 °C (lit.[23] mp 119.5-121.5 °C); ^{13}C NMR ($CDCl_3$) δ 110.5, 114.2, 116.2, 119.7, 124.7, 125.7, 130.5, 132.2, 134.4, 144.0, 179.9. The other spectral properties were identical to those previously reported.[23]

5*H*-Indeno[2,1-*b*]indol-6-one (39). This compound was prepared from compound **47**. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 30.6 mg (55 %) of the indicated compound as a purple solid: mp 259-260 °C; ^1H NMR ($CDCl_3$) δ 7.02 (t, *J* = 7.4 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 6.8 Hz, 1H), 7.25-7.38 (m, 4H), 7.83 (d, *J* = 8.0 Hz, 1H) (missing one proton due to exchange); ^{13}C NMR ($CDCl_3$) δ 114.8, 119.9, 121.1, 121.9, 122.4, 123.6, 126.7, 127.2, 134.4, 134.8, 136.9, 140.6, 143.4, 184.1 (missing one sp^2 carbon due to overlap); IR (CH_2Cl_2) 3444, 3055, 1705 cm^{-1}; HRMS *m/z* 219.0686 (calcd for $C_{15}H_9NO$, 219.0684).

5-Methyl-5*H*-indeno[2,1-*b*]indol-6-one (41). The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 28.5 mg (49 %) of the indicated

compound as a dark red solid: mp 145-146 °C (lit.[7b,25] mp 147-148 °C); ^{1}H NMR ($CDCl_3$) δ 3.87 (s, 3H), 6.94-6.99 (m, 1H), 7.08-7.10 (m, 1H), 7.14-7.20 (m, 1H), 7.22-7.30 (m, 4H), 7.65 (dt, J = 8.1, 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 30.8, 111.7, 119.2, 121.4, 121.9, 122.1, 123.7, 126.2, 126.6, 133.7, 134.1, 137.4, 140.6, 144.1, 147.2, 185.0; IR (CH_2Cl_2) 3054, 1704 cm^{-1}; HRMS *m/z* 233.0843 (calcd for $C_{16}H_{11}NO$, 233.0841).

5*H*-Indeno[1,2-*b*]indol-10-one (43). This compound was prepared from compound **46**. The reaction mixture was chromatographed using 2:1 hexanes/ethyl acetate to afford 24.9 mg (45 %) of the indicated compound as a red solid: mp 334-336 °C (sublimes) (lit.[27] mp 333-336 °C); ^{13}C NMR (DMSO-d_6) δ 114.4, 114.8, 119.8, 120.0, 123.1, 123.2, 123.6, 123.8, 130.5, 133.3, 135.3, 141.1, 142.5, 159.3, 185.2. The other spectral properties were identical to those previously reported.[27]

5-Methyl-5*H*-indeno[1,2-*b*]indol-10-one (45). The reaction mixture was chromatographed using 2:1 hexanes/ethyl acetate to afford 12.2 mg (21 %) of the indicated compound as a red solid: mp 217-218 °C (lit.[26] mp 216-218 °C). The spectral properties were identical to those previously reported.[26]

2,3-Diphenyl-1-indenone (49). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 57.2 mg (81 %) of the indicated compound as a red solid: mp 152-153 °C. This compound was identified by comparing the ^{1}H NMR and ^{13}C NMR spectra and melting point with an authentic sample obtained from Aldrich Chemical Co., Inc.

2,3-Diphenyl-1-indenone (49) and triphenylethene (50). These two compounds were obtained from the cyclocarbonylation of compound **51**. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 43.0 mg (61 %) of the indenone

49 as a red solid, mp 152-153 °C; in addition, 15.4 mg (24 %) of compound **50** were isolated from the reaction mixture as a white solid, mp 68-69 °C. Compound **50** was identified by comparing the ^{1}H NMR and ^{13}C NMR spectra and melting point with an authentic sample obtained from Aldrich Chemical Co., Inc.

Indeno[5,6]dibenz[*b,f*]oxepin-14-one (53). The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 58.9 mg (80 %) of the indicated compound as a red solid: mp 162-164 °C; ^{1}H NMR ($CDCl_3$) δ 7.22-7.47 (m, 8H), 7.49-7.55 (m, 1H), 7.60-7.63 (m, 1H), 7.75 (dd, J = 7.8, 1.5 Hz, 1H), 7.90-7.93 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 121.3, 121.9, 122.7, 123.7, 125.4, 125.4, 125.6, 126.8, 127.7, 129.5, 129.7, 130.0, 130.7, 131.9, 133.1, 133.7, 143.4, 153.2, 157.9, 158.8, 195.3; IR (CH_2Cl_2) 3076, 1707 cm^{-1}; HRMS *m/z* 296.0842 (calcd for $C_{21}H_{12}O_2$, 296.0837).

1,2,3,4-Tetrahydrofluoren-9-one (59). The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 15.7 mg (34 %) of the indicated compound **59** as a yellow oil with spectral properties identical to those previously reported.[31]

6-*H*-Isoindolo[2,1a]indole (65). The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 58.9 mg (70 %) of the indicated compound as a white solid: mp 226-228 °C (lit.[37] mp 209-211 °C) with spectral properties identical to those previously reported.[37]

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References

(1) (a) Greenlee, M. L.; Laub, J. B.; Rouen, G. P.; DiNinno, F.; Hammond, M. L; Huber, J. L.; Sundelof, J. G.; Hammond, G. G. *Biorg. Med. Chem. Lett.* **1999**, *9*, 3225. (b) Perry, P. J.; Read, M. A.; Davies, R. T.; Gowan, S. M.; Reszka, A. P.; Wood, A. A.; Kelland, L. R.; Neidle, S. *J. Med. Chem.* **1999**, *42*, 2679. (c) Jones, W. D.; Ciske, F. L.; Dinerstein, R. J.; Diekema, K, A. U.S. Patent No. 6,004,959, **1999**. (d) Tierney, M. T.; Grinstaff, M. W. *J. Org. Chem.* **2000**, *65*, 5355. (e) Han, Y.; Bisello, A.; Nakamoto, C.; Rosenblatt, M; Chorev, M. *J. Pept. Res.* **2000**, *55*, 230.

(2) (a) Koyama, H.; Kamikawa, T. *Tetrahedron Lett.* **1997**, *38*, 3973. (b) Carney, J. R. *J. Org. Chem.* **1997**, *62*, 320.

(3) (a) Olah, G. A.; Mathew, T.; Farnia, M.; Prakash, S. *Synlett* **1999**, 1067. (b) Yu, Z.; Velasco, D. *Tetrahedron Lett.* **1999**, *40*, 3229.

(4) (a) Danheiser, R. L.; Gould, A. E.; Pradilla, R. F.; Helgason, A. L. *J. Org. Chem.* **1994**, *59*, 5514.

(5) (a) Hashemi, M.; Beni, Y. *J. Chem. Res. (S),* **1999**, 434. (b) Nikalje, M.; Sudalai, A. *Tetrahedron* **1999**, *55*, 5903.

(6) (a) Ciske, F.; Jones, W. D., Jr. *Synthesis* **1998**, 1195. (b) Wang, W.; Snieckus, V. *J. Org. Chem.* **1992**, *57*, 424.

(7) (a) Qabaja, G.; Jones, G. B. *Tetrahedron Lett.* **2000**, *41*, 5317. (b) Kozikowski, A. P.; Ma, D. *Tetrahedron Lett.* **1991**, *32*, 3317.

(8) For a preliminary communication and full paper, see: (a) Campo, M. A.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3675. (b) Campo, M. A.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 5616.

(9) These starting materials were prepared using the procedure of Hart, H.; Harada, K.; Du, C. *J. Org. Chem.* **1985**, *50*, 3104.

(10) This starting material was prepared using the procedure of Huisgen, R.; Rist, H. *Liebigs Ann. Chem.* **1955**, *594*, 137.

(11) (a) Sprinzak, Y. *J. Am. Chem. Soc.* **1958**, *80*, 5449. (b) Horspool, W. M. *J. Chem. Soc. C* **1971**, 400. (c) Pandey, B.; Mahajan, M. P.; Tikare, R. K.; Muneer, M.; Rath, N. P.; Kamat, P. V.; George, M. V. *Res. Chem. Intermed.* **1991**, *15*, 271.

(12) Wittig, G.; Hellwinkel, D. *Chem. Ber.* **1964**, *97*, 769.

(13) (a) Fu, J.; Zhao, B.; Sharp, M. J.; Snieckus, V. *J. Org. Chem.* **1991**, *56*, 1683. (b) Harvey, R. G.; Abu-shqara, E.; Yang, C. *J. Org. Chem.* **1992**, *57*, 6313.

(14) This aryl iodide was prepared by the procedure of Huang, Q.; Hunter, J. A.; Larock, R. C. *Org. Lett.* **2001**, *3*, 2973.

(15) (a) Wawzonec, S.; Stowell, J. K.; Karll, R. E. *J. Org. Chem.* **1966**, *31*, 1004. (b) Dusemund, J.; Kroeger, E. *Arch. Pharm.* **1987**, *320*, 617.

(16) Fujioka, Y. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 3494.

(17) Barnett, M. D.; Daub, G. H.; Hayes, N.; Ott, D. G. *J. Am. Chem. Soc.* **1959**, *81*, 4583.

(18) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Moro, L. *Synlett* **1999**, 1432.

(19) This starting material was prepared using the procedure of Larock, R. C.; Harrison, L. W. *J. Am. Chem. Soc.* **1984**, *106*, 4218.

(20) Sauter, F.; Dzerovicz, A. *Monatsh. Chem.* **1969**, *100*, 913.

(21) Martelli, G.; Spagnolo, P.; Tiecco, M. *J. Chem. Soc. B* **1968**, 901.

(22) MacDowell, D. W. H.; Patrick, T. B. *J. Org. Chem.* **1967**, *32*, 2441.

(23) (a) Mazzola, V. J.; Bernady, K. F.; Franck, R. W. *J. Org. Chem.* **1967**, *32*, 486. (b) Flitsch, W.; Kappenberg, F.; Schmitt, H. *Chem. Ber.* **1978**, 111, 2407.

(24) This substrate was prepared by the procedure of Bocchi, V.; Palla, G. *Synthesis* **1982**, 1096.

(25) Borsche, W.; Klein, A. *Liebigs Ann. Chem.* **1941**, *548*, 64.

(26) Itahara, T.; Sakakibara, T. *Synthesis* **1978**, 607.

(27) Eisch, J. J.; Abraham, T. *Tetrahedron Lett.* **1976**, 1647.

(28) Miller, L. L.; Kaufman, D. A. *J. Am. Chem. Soc.* **1968**, *90*, 7282.

(29) Kitamura, T.; Takachi, H.; Taniguchi, K.; Taniguchi, H. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1969.

(30) Larock, R. C.; Tian, Q. *J. Org. Chem.* **1998**, *63*, 2002.

(31) Parham, W. E.; Czuba, L. J. *J. Org. Chem.* **1969**, *34*, 1899.

(32) Gretz, E.; Oliver, T. F.; Sen, A. *J. Am. Chem. Soc.* **1987**, *109*, 8109.

(33) (a) Catellani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1992**, *425*, 151. (b) Stock, L. M.; Tse, Kwok-tuen; Vorvick, L. J.; Walstrum, S. A. *J. Org. Chem.* **1981**, *46*, 1757.

(34) Geahigan, K. B.; Taintor, R. J.; George, B. M.; Meagher, D. A.; Nalli, T. W. *J. Org. Chem.* **1998**, *63*, 6141.

(35) Kozikowski, A. P.; Ma, D. *Tetrahedron Lett.* **1991**, *32*, 3317.

(36) Caddick, S.; Aboutayab, K.; Jenkins, K.; Robert, I. *J. Chem. Soc., Perkin Trans. 1* **1996**, 675.

(37) Ponchant, M.; Demphel, S.; Hinnen, F.; Crouzel, C. *Eur. J. Med. Chem. Chim. Ther.* **1997**, *32*, 747.

(38) Brown. J. W.; Butcher, J. L.; Byron, D. J.; Gunn, E. S.; Rees, M.; Wilson, R. C. *Mol. Cryst. Liq. Cryst.* **1988**, 255.

(39) Larock, R. C.; Doty, M. J.; Tian, Q.; Zenner, J. M. *J. Org. Chem.* **1997**, *62*, 7536.

(40) Miller, R. B.; McGarvey, G. *Synth. Commun.* **1978**, *8*, 291.

(41) Jørgensen, M.; Krebs, F. C.; Bechgaard, K. *J. Org. Chem.* **2000**, *65*, 8783.

(42) Barton, J. W.; Rogers, A. M.; Barney, M. E. *J. Chem. Soc.* **1965**, 5537.

(43) Larock, R. C.; Yum, E. K.; Refvik, M. D. *J. Org. Chem.* **1998**, *63*, 7652.

(44) Nishio, T. *J. Org. Chem.* **1988**, *53*, 1323.

(45) This indole derivative was prepared by the procedure of Ciattini, P. G.; Morera, E.; Orta, G. *Synth. Commun.* **1995**, *25*, 2883.

(46) Yao, T.; Larock, R. C. *Tetrahedron Lett.*, (in press).

(47) Larock, R. C.; Doty, M. J.; Han, X. *J. Org. Chem.* **1999**, *64*, 8870.

(48) Lansbury, P. T.; Spitz, R. P.; *J. Org. Chem.* **1967**, *32*, 2623.

(49) Hauser, A.; Thurner, J.; Hinzman, B. *J. Prakt. Chem.* **1988**, *330*, 367.

(50) Bullock, P. J.; Byron, D. J.; Harwood, D. J.; Wilson, R. C.; Woodward, A. M. *J. Chem. Soc., Perkin Trans.* 2 **1984**, 2121.

(51) Colonge, J.; Daunis, H. *Bull. Soc. Chim. Fr.* **1961**, 2238.

(52) (a) Collins, M. J.; Gready, J. E.; Sternhell, S.; Charles, W. *Aust. J. Chem.* **1990**, *43*, 1547. (b) Bell, J. H.; Ireland, S.; Spears, A. W. *Anal. Chem.* **1969**, *41*, 310.

(53) (a) Tomioka, H.; Kawasaki, H.; Kobayashi, N.; Hirai, K. *J. Am. Chem. Soc.* **1995**, *117*, 4483. (b) Ford, W. T.; Thompson, T. B.; Snoble, A. J.; Timko, J. M. *J. Am. Chem. Soc.* **1975**, *97*, 95.

(54) Urezkaja G.; Kraft M. Y. *J. Gen. Chem. USSR* (English Transl.) **1963**, *33*, 2978.

(55) Russell, J.; Thomson, R. H. *J. Chem. Soc.* **1962**, 3379.

CHAPTER 2. NOVEL 1,4-PALLADIUM MIGRATION IN ORGANOPALLADIUM INTERMEDIATES DERIVED FROM *o*-HALOBIARYLS

Based on a communication published in the *Journal of the American Chemical Society* and a paper to be published in the *Journal of the American Chemical Society*

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Abstract

A novel 1,4-palladium migration between the *o*- and *o*'-positions of biaryls has been observed in organopalladium intermediates derived from *o*-halobiaryls. The organopalladium intermediates generated by this palladium migration have been trapped by way of a Heck reaction with ethyl acrylate and a Suzuki cross-coupling with arylboronic acids. The ratios of Heck and Suzuki products indicate that palladium has a tendency to migrate from a more electron-poor to a more electron-rich position in the biaryl.

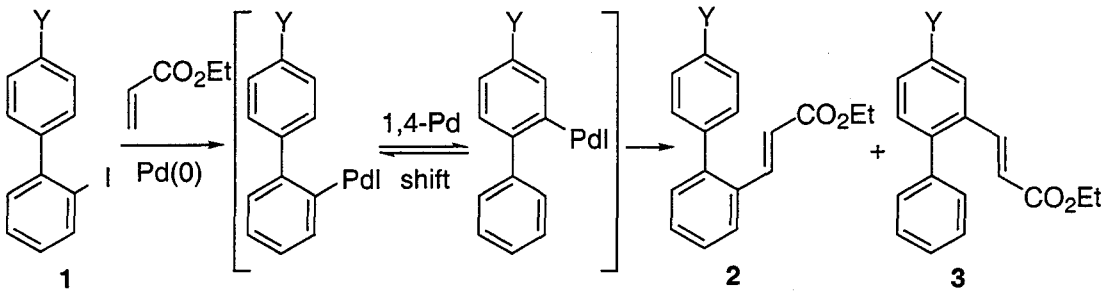
Introduction

The extraordinary C-C bond forming ability of palladium places it among the most versatile and useful metals in organic synthesis. Organopalladium intermediates are often prepared by oxidative addition of an organic halide or triflate to Pd(0) and subsequent C-C bond formation normally occurs at the position originally occupied by the halogen or triflate.

Among the most important Pd-catalyzed C-C bond forming reactions is the Heck reaction for which there are numerous applications in the literature,[1] including a few employing *o*-bromobiaryls.[2]

To our surprise, upon studying the palladium-catalyzed olefination of unsymmetrical *o*-halobiphenyls with ethyl acrylate, we obtained, under certain modified reaction conditions, the expected *o*-olefinated biphenyl (**2**) along with the *o*'-olefinated biphenyl (**3**) (Scheme 1).[3]

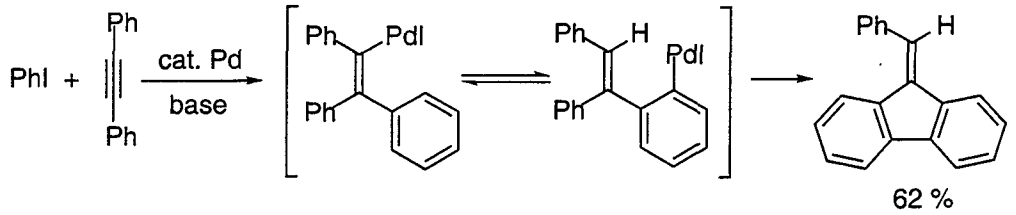
Scheme 1



The observed mixture of Heck products points to the existence of arylpalladium intermediates in which the metal moiety is located in each of the two different ortho positions of the unsymmetrical biphenyl. This through-space relocation of the metal moiety between the ortho positions of biaryls amounts to an overall 1,4-palladium shift. The novel palladium migration observed in our *o*-halobiaryl systems has also been simultaneously reported by Gallagher, et al., who studied the Heck reaction of pyridine-containing biaryls.[4] However, the results reported by Gallagher suggested that palladium migration occurred only in minor amounts in such biaryls, and that electron-withdrawing nitro groups were critical to migration. Furthermore, Larock, et al. have previously proposed a vinylic to aryl palladium migration to account for the formation of 9-benzylidene-9*H*-fluorene from diphenylacetylene

and iodobenzene (Scheme 2).[5] We now wish to report the full details of this novel palladium aryl to aryl migration chemistry.

Scheme 2

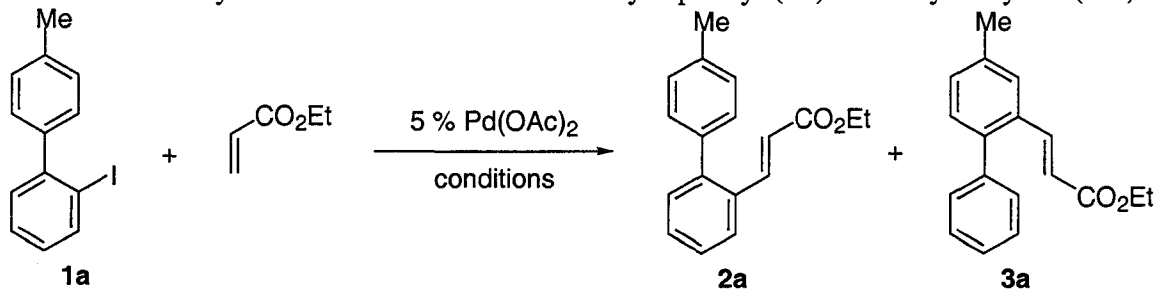


Results and Discussion

In order to obtain a clear picture of how various reaction variables effect the palladium biaryl migration, we have studied the behavior of 2-iodo-4'-methylbiphenyl (**1a**) and ethyl acrylate under various reaction conditions (Table 1). We have found that under the classical reaction conditions described by Jeffrey,[6] the expected ethyl *E*-3-(4'-methylbiphen-2-yl)acrylate (**2a**) was obtained exclusively in a quantitative yield (Table 1, entry 1). By simply diluting the reaction mixture 4-fold, we began to observe small amounts of the migration product ethyl *E*-3-(4-methylbiphen-2-yl)acrylate (**3a**) (entry 2), and 23 % of **3a** was obtained under the more dilute conditions obtained by reducing the number of equivalents of ethyl acrylate from 4 to 1 (entry 3). We have obtained almost equal amounts of the direct olefination product **2a** and the rearranged product **3a** when using CsO_2CCMe_3 (CsPiv) as the base (entry 4). Furthermore, under these conditions, the *n*-Bu_4NCl (TBAC) additive was unnecessary to achieve virtually the same results (entry 5). The use of phosphine ligands, such as 1,1-bis(diphenylphosphino)methane (dppm) and PPh_3, in the reaction further changed the isomer distribution to 50:50 (entries 6 and 7). The solubility of

the base in the reaction mixture seems to play a critical role in determining the isomer distribution. Thus, under identical conditions CsPiv, CsOAc, and NaOAc, which are listed in decreasing order of apparent solubility in DMF, gave decreasing amounts of isomer **3a** (entries 6, 8 and 9). To further illustrate this phenomenon, we have run the reaction under our standard migration

Table 1. Pd-Catalyzed reaction of 2-iodo-4'-methylbiphenyl (**1a**) and ethyl acrylate (EA).[a]



1a **2a** **3a**

entry	equiv EA	conditions	time (d)	mol ratio **2a**:**3a**[b]	% yield
1	4	TBAC, $NaHCO_3$[c]	1.0	100:0	100
2	4	TBAC, $NaHCO_3$	1.0	95:5	100
3	1	TBAC, $NaHCO_3$	1.0	77:23	92
4	1	TBAC, CsPiv	1.5	55:45	89
5	1	CsPiv	1.5	54:46	93
6	1	5 % dppm, CsPiv	1.5	50:50	88
7	1	10 % PPh_3, CsPiv	1.5	50:50	87
8	1	5 % dppm, CsOAc	1.5	55:45	90
9	1	5 % dppm, NaOAc	1.0	69:31	75
10	1	5 % dppm, CsPiv[d]	1.0	75:25	94
11	1	5 % dppm, Et_3N	1.0	100:0	90

[a]The reaction was run using 0.25 mmol of the iodobiaryl, ethyl acrylate (EA), 2 equiv of an appropriate base, and 1 equiv of *n*-Bu_4NCl (TBAC) where indicated in 4 ml of DMF at 100 °C unless otherwise indicated. [b]The mole ratio was determined by ^1H NMR spectroscopic analysis. [c]One mL of DMF as solvent. [d]Four mL of toluene as solvent.

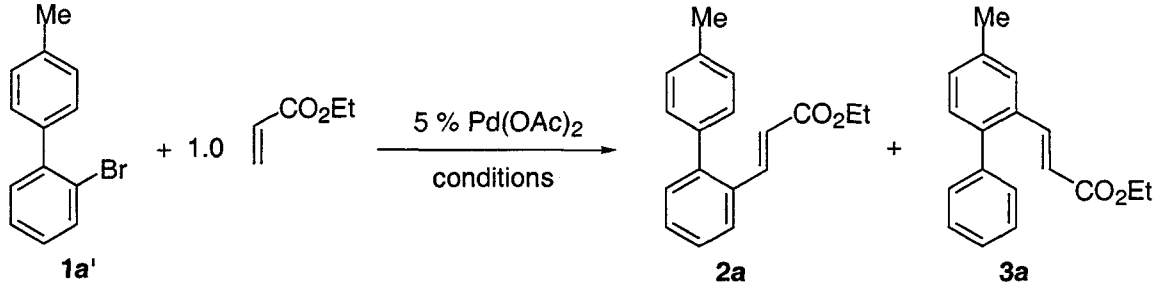
conditions, but used a less polar solvent toluene in which the CsPiv base has a much lower solubility than in DMF, and we obtained only 25 % of **3a** (entry 10 versus entry 6). The use of Et_3N as a base completely inhibited the migration process. Using Et_3N instead of CsPiv

and conditions identical to those of entry 6, we obtained isomer **2a** exclusively in a 90 % yield (entry 11). It is important to note at this point that by manipulating the reaction conditions, we can switch the palladium migration "on" or "off" in this biphenyl system. Thus, our optimal migration conditions for activating palladium migration are those described in entry 6 of Table 1 (conditions A), and the conditions to prevent this process are those described in entry 1. Furthermore, it turned out that ethyl acrylate was superior to other olefins as a Heck trap. For instance, the reaction of **1a** with either methyl vinyl ketone or styrene under conditions A favoring migration gave complex mixtures and no desired Heck products were isolated.

To investigate whether palladium migration will also occur with less reactive *o*-bromobiphenyls, we examined the Heck reaction of 2-bromo-4'-methylbiphenyl (**1a'**) and ethyl acrylate under various reaction conditions (Table 2). We first carried out the reaction of **1a'** under migration conditions A, but failed to observe any significant amount of Heck products after 3 days (entry 1, Table 2). In attempting to promote the reaction, we increased the temperature from 100 °C to 110 °C, but TLC analysis of the reaction mixture indicated that **1a'** had failed to react (entry 2). We then resorted to the use of highly active palladium catalyst systems employing a combination of 5 mol % $Pd(OAc)_2$ and 10 mol % of a hindered, electron-rich phosphine ligand, such as 2-(di-*t*-butylphosphino)biphenyl or 2-(dicyclohexylphosphino)biphenyl.[7] Unfortunately, the results were unfruitful (entries 3 and 4). Similarly, the use of air-stable and highly active Pd(di-*t*-butylphosphinous acid)$_2$Cl$_2$ as catalyst[8] failed to promote the Heck reaction of **1a'** (entry 5). It is somewhat surprising that the palladium catalysts described in entries 3-5 failed to promote the Heck reaction of 2-

bromo-4'-methylbiphenyl with ethyl acrylate, especially since these catalysts have been reported to activate aryl bromides, as well as aryl chlorides, towards Negishi, Suzuki, and amination reactions.[7,8] Fortunately, we were able to circumvent the poor reactivity of 2-bromo-4'-methylbiphenyl by simply carrying the reaction out under conditions A, but we replaced the DMF solvent with wet DMF (5 % H_2O by volume) as the reaction solvent. Thus, compound **1a'** produced a 50:50 mixture of **2a** and **3a** in a 49 % yield along with 45 %

Table 2. Pd-Catalyzed reaction of 2-bromo-4'-methylbiphenyl (**1a'**) and ethyl acrylate.[a]



1a' 2a 3a

entry	conditions	mol ratio **2a**:**3a**[b]	% yield
1	5 % dppm, 2.0 CsPiv, DMF (4 mL), 100 °C, 3 d	-	trace
2	5 % dppm, 2.0 CsPiv, DMF (4 mL), 110 °C, 2 d	-	trace
3	10 % 2-(di-*t*-butylphosphino)biphenyl, 2.0 CsPiv, DMF (4 mL), 100 °C, 2 d	-	trace
4	10 % 2-(dicyclohexylphosphino)biphenyl, 2.0 CsPiv, DMF (4 mL), 100 °C, 2 d	-	trace
5	5 % Pd(di-*t*-butylphosphinous acid)$_2$Cl$_2$[c], 2.0 CsPiv, DMF (4 mL), 100 °C, 2 d	-	trace
6	5 % dppm, 2.0 CsPiv, DMF (3.8 mL), H_2O (0.2 mL) 100 °C, 1 d	49 (45)[d]	50:50
7[e]	5 % dppm, 2.0 CsPiv, DMF (3.8 mL), H_2O (0.2 mL), 100 °C, 1 d	85	50:50

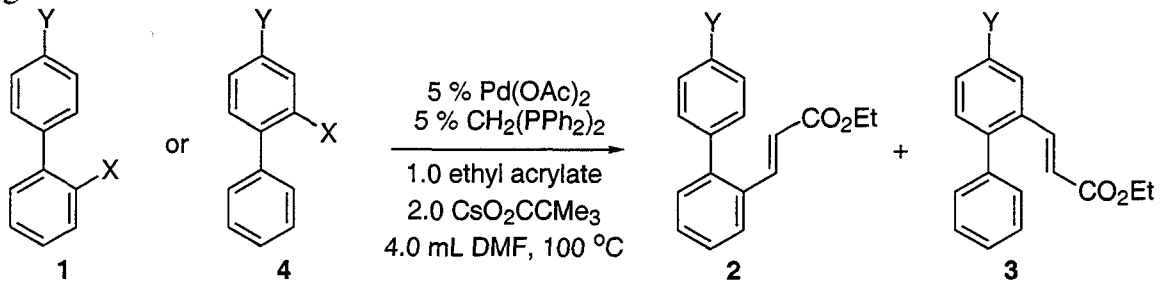
[a]The reaction was run using 0.25 mmol of the bromobiphenyl. [b]The mole ratio was determined by ^{1}H NMR spectroscopic analysis. [c]The $Pd(OAc)_2$ catalyst was omitted. [d]The yield in parentheses corresponds to the amount of isolated 4-methylbiphenyl. [e]Compound **1a** was used in place of **1a'**.

of 4-methylbiphenyl[9], which corresponds to the product arising from C-Br reduction to a C-H bond (entry 6). We were also pleased to find that 2-iodo-4'-methylbiphenyl and ethyl acrylate reacted under the reaction conditions described in entry 6 of Table 2 to produce a 50:50 mixture of **2a** and **3a** in an 85 % yield (entry 7), verifying that **1a** and **1a'** generate identical mixtures of **2a** and **3a**. Thus far, two sets of migration reaction conditions have been developed, namely conditions A, which are described in entry 6 of Table 1, and conditions B, which are described in entry 6 of Table 2.

An obvious question to answer is whether under our standard reaction conditions 2-iodo-4-methylbiphenyl (**4a**) and ethyl acrylate would generate the same distribution of isomers **2a** and **3a** as previously obtained from **1a** and ethyl acrylate. Indeed, substrate **4a** generated a 49:51 mixture of isomers **2a** and **3a** in an 86 % yield under our optimized migration conditions A (entry 6, Table 3). This interesting result seems to indicate that under our reaction conditions, the arylpalladium intermediates generated from either **1a** or **4a** undergo apparent equilibration prior to olefin-trapping to generate essentially identical mixtures of **2a** and **3a** (compare entries 5 and 6 of Table 3). Once again, we can suppress the Pd migration by carrying the reaction out under the conditions described by Jeffrey (Table 4). Thus, 2-iodo-4-methylbiphenyl (**4a**) produced **3a** exclusively in a 93 % yield under the Jeffrey conditions (entry 6, Table 4).

In order to examine a possible correlation between electronic effects in the *o*-halobiphenyls and the ratio of Heck products they produce, we studied the reaction of various *p*-substituted *o*-halobiphenyls with ethyl acrylate under our standard migration conditions

Table 3. Heck reaction of *p*-substituted *o*-halobiphenyls with ethyl acrylate under Pd-migration conditions.[a]



1 4 2 3

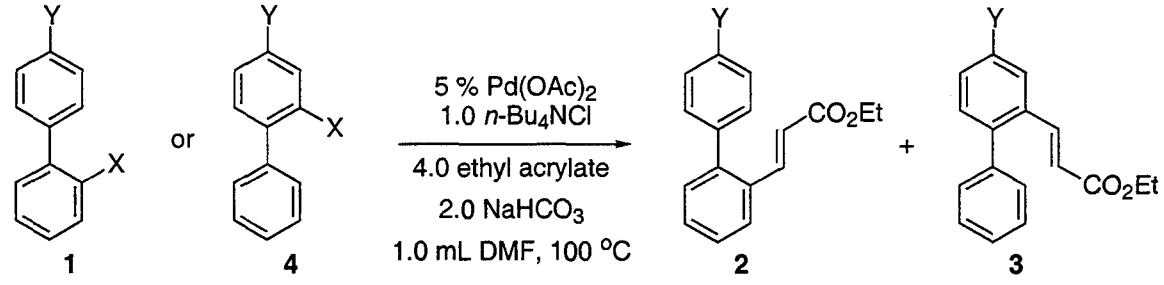
entry	substrate	Y	X	time (d)	% yield	mol ratio **2**:**3**[b]
1	**1a**	Me	I	1.5	88	50:50
2	**4a**	Me	I	1.5	86	49:51
3	**1b**	NMe_2	I	1	90	55:45
4	**4b**	NMe_2	I	1.5	93	49:51
5	**1c**	OMe	I	2	93	52:48
6	**4c**	OMe	I	2	92	48:52
7	**1d**	CO_2Et	Br	1[c]	45 (45)[d]	47:53
8	**4d**	CO_2Et	I	1[c]	83	42:58
9	**1e**	NO_2	I	2.5[c]	46 (40)[d]	39:61
10	**4e**	NO_2	I	2.5[c]	37 (50)[d]	33:67

[a]The reaction was run using 0.25 mmol of the halobiphenyl. [b]The mole ratio was determined by ^1H NMR spectroscopic analysis. [c]Wet DMF was used as the reaction solvent: 3.8 mL of DMF plus 0.2 mL of H_2O (conditions B). [d]The yield in parentheses indicates the amount of isolated product in which C-X was reduced to C-H.

(Table 3). First of all, we used strong electron-donating dimethylamino-substituted biphenyls. For instance, the reaction of 4'-dimethylamino-2-iodobiphenyl (**1b**) with ethyl acrylate under migration conditions A produced a 55:45 mixture of isomers **2b** and **3b** respectively in a 90 % yield (entry 3, Table 3). Similarly, the reaction of 4-dimethylamino-2-iodobiphenyl (**4b**) and ethyl acrylate produced a 49:51 mixture of **2b** and **3b** respectively in a 93 % yield (entry 4). Notice that the Heck product ratios obtained from **1b** and **4b** differ by approximately 6 mol %, indicating that the migration kinetics for the arylpalladium intermediates derived from these dimethylamino-substituted biphenyls is apparently somewhat slower than the kinetics of their

methyl-substituted counterparts. Nevertheless, for practical purposes we can assume that the arylpalladium intermediates generated from **1b** and **4b** pretty much equilibrate prior to olefin-trapping by ethyl acrylate. Furthermore, we calculated the average ratio of **2b** and **3b** to be 52:48, indicating only a very slight preference for the formation of isomer **2b**. In addition, we suppressed the palladium migration by carrying out the reaction of **1b** and **4b** under Jeffrey's reaction conditions (Table 4). Thus, **1b** produced **2b** exclusively in an 80 % yield, while **4b** produced **3b** exclusively in a 100 % yield (entries 3 and 4 of Table 4).

Table 4. Heck reaction of *p*-substituted *o*-halobiphenyls with ethyl acrylate under Jeffrey's conditions.[a]



1 4 2 3

entry	substrate	Y	X	time (d)	% yield	mol ratio **2**:**3**[b]
1	**1a**	Me	I	1.0	100	100:0
2	**4a**	Me	I	1.0	93	0:100
3	**1b**	NMe_2	I	1.0	80	100:0
4	**4b**	NMe_2	I	1.0	100	0:100
5	**1c**	OMe	I	2.0	100	100:0
6	**4c**	OMe	I	2.0	99	0:100
7	**1d**	CO_2Et	Br	2.0[c]	77 + 11	-
8	**4d**	CO_2Et	I	1.0	99	0:100
9	**1e**	NO_2	I	1.0[d]	85	100:0
10	**4e**	NO_2	I	1.0[d]	89	0:100

[a]The reaction was run using 0.25 mmol of the halobiphenyl. [b]The mole ratio was determined by ^1H NMR spectroscopic analysis. [c]Ten mol % of 2-(di-*t*-butylphosphino)biphenyl was used as the ligand. [d]2.0 Equiv of Et_3N were used as the base.

We continued our investigation by examining the reaction of methoxy-substituted biphenyls **1c** and **4c** under our standard palladium migration conditions A. Thus, compound **1c** produced a 52:48 mixture of isomers **2c** and **3c** respectively in a 93 % yield (entry 5, Table 3), while compound **4c** produced a 48:52 mixture of **2c** and **3c** respectively in a 92 % yield (entry 6, Table 3). These results validate the idea that our migration reaction conditions promote the near equilibration of arylpalladium intermediates derived from methoxy-substituted biphenyls **1b** and **4b**, and in this case the ratio of Heck products differs by only approximately 4 mol %. Similar to our results with other biphenyls bearing electron-donating substituents, the 50:50 average ratio of Heck products **2c** and **3c** indicates no preference for the formation of either one of these two isomers. At this point, we conclude that *p*-substituted biphenyls bearing electron-donating groups, such as Me, MeO, and Me_2N, produce nearly 50:50 mixtures of Heck products. To finalize our examination of the methoxy-substituted biphenyls **1c** and **4c,** we carried out the Heck reaction under Jeffrey's conditions (Table 4). Thus, **1b** produced **2b** in a quantitative yield (entry 5), while **4a** gave **3b** exclusively in a 99% yield (entry 6).

Next, we switched our attention to the Heck reactions of biphenyls bearing electron-withdrawing substituents. To begin with, we considered the Heck reaction of biphenyls **1d** and **4d** bearing a CO_2Et group. Although the Pd-catalyzed reactions of **1d** and **4d** with ethyl acrylate were unsuccessful under migration conditions A, the reaction proceeded smoothly under conditions B. Thus, **1d** produced a 47:53 mixture of **2d** and **3d** in a 45 % yield, along with ethyl 4-phenylbenzoate[10] in 45 % yield, while **4d** produced a 42:58 mixture of **2d** and **3d** in an 83 % yield. Again, we found that the Heck product ratios produced by **1d** and **4d**

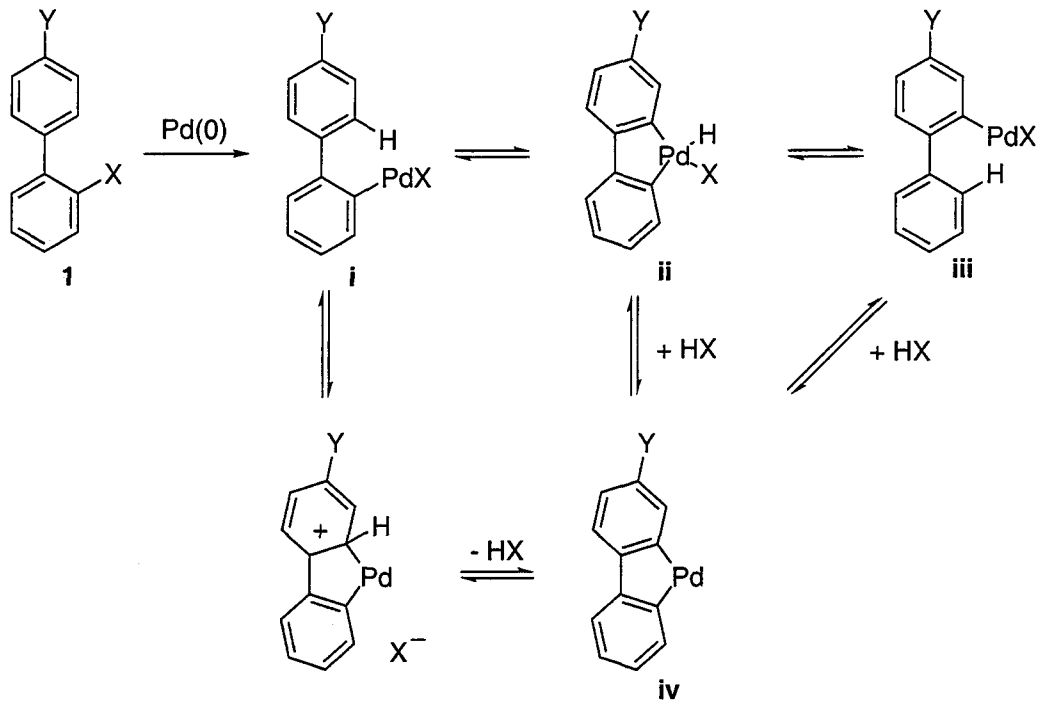
differed by approximately 5 mol %, indicating near equilibration of the corresponding arylpalladium intermediates. Furthermore, the average ratio of **2d** and **3d** turned out to be 44:56, which indicates that there is a slight tendency for these halobiphenyls to form isomer **3d**. Furthermore, the reaction of **1d** with ethyl acrylate under Jeffrey's conditions was unsuccessful, but the addition of 2-(dicyclohexylphosphino)biphenyl[7] as a ligand produced **2d** in a 77 % yield along with an 11 % yield of isomer **3d** (entry 7, Table 4). Thus, under these conditions, some migration appears to be taking place. Similarly, under Jeffrey's reaction conditions, compound **4d** produced the expected isomer **3d** exclusively in a 99 % yield (entry 8, Table 4).

Finally, the Heck reactions of strong electron-withdrawing nitro-substituted biphenyls **1e** and **4e** have displayed a trend similar to that observed previously with the ester-substituted biphenyls. For instance, using aqueous DMF (conditions B), **1e** generated a 39:61 mixture of **2e** and **3e** respectively in a 46 % yield, plus a 40 % yield of reduction product (entry 9, Table 3). Under the same conditions, aryl iodide **4e** produced a 33:67 mixture of **2e** and **3e** respectively in a 37 % yield, plus a 50 % yield of the reduction product (entry 11). The average ratio of **2e** and **3e** is 36:64, which clearly indicates a preference for the formation of isomer **3e** arising from the arylpalladium intermediate having the metal moiety located on the nitro-substituted phenyl ring of the biphenyl. It is worth mentioning that under the migration conditions B the Heck reaction of biphenyls **1e** and **4e** was sluggish. Thus, after the prolonged heating required to complete these reactions, we isolated considerable amounts of 4-nitrobiphenyl[11] (40 % and 50 % yields respectively from **1e** and **4e**) as a side product arising from reduction of the C-I bond to a C-H bond. On the other hand, aryl iodides **1e** and **4e**

smoothly underwent the Heck reaction under Jeffrey's conditions using Et_3N as the base to produce **2e** in an 85 % yield and **3e** in an 89 % yield respectively (entries 9 and 10, Table 4). It is worth noting that the use of Et_3N as a base for the Heck reaction of **1e** and **4e** was necessary to eliminate small amounts of migration products.

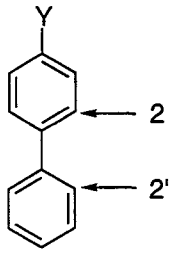
We propose a possible mechanism (Scheme 3) for the palladium migration in organopalladium intermediates derived from *o*-halobiaryls which involves oxidative addition of the aryl halide to Pd(0) to generate intermediate **i**, which can either (a) undergo oxidative addition of a neighboring C-H bond to produce a hydridopallada(IV)cycle (**ii**), followed by reductive elimination of CH to generate **iii** or **i**, or (b) electrophilic palladation to generate intermediate **iv**, followed by either protonolysis of a C-Pd bond to generate **iii** or **i** or oxidative addition to HX to generate **ii**. In regard to the mechanism, we would like to point out that not all ligands on palladium are shown for simplicity. We believe that the intermediacy of **iv** is highly unlikely for two main reasons. First of all, it is improbable that intermediate **iv** could react with HX under the basic reaction conditions we employed. Second of all, Catellani and Chiusoli have demonstrated that pallada(II)cycles, analogous to intermediate **iv**, easily undergo oxidative addition to aryl and alkyl halides to generate palladium(IV) intermediates, which after a series of rearrangements lead to unique polycyclic compounds.[12] Thus, the presence of intermediate **iv** in our reaction would lead to the formation of signature compounds, which we were unable to observe under our reaction conditions. As a result, we favor the reversible interconversion between **i** and **iii** via hydridopallada(IV)cycle **ii**. It is also important to realize that palladium migration involves intramolecular C-H activation.

Scheme 3



In order to rationalize the Heck product distributions in terms of electronic effects, we must consider the possible factors influencing these ratios. To begin with, we must consider the reactivity of the corresponding arylpalladium intermediates towards the olefin trap. To illustrate, the more reactive intermediate should be trapped faster by the olefin, giving rise to mixtures enriched with that isomer. However, since we were not able to find any such reactivity data in the literature, we have no way of predicting how electronic effects might influence the reactivities of such arylpalladium intermediates. Thus, for the time being, we can simplify our discussion by assuming that the reactivities of arylpalladium intermediates generated by palladium migration are fairly similar, and that the ratio of Heck products will not be significantly affected by such reactivities. With this argument in mind, the critical factor determining the ratio of Heck products is the actual distribution of the arylpalladium intermediates generated by palladium migration. Thus, this distribution must be determined

by the electronic preference of the palladium within the biphenyl. Since the palladium species involved in the intramolecular C-H activation required for palladium migration is most likely electrophilic in nature,[13] we speculate that palladium, as any other electrophile, will prefer the more electron-rich position of the biphenyl. HF/6-31G(d) calculations using the GAMESS suite of programs[14] show that biphenyls with electron-donating substituents, such as Me and OMe, have relatively similar Mulliken electron densities between the 2 and 2' positions (see Figure 1). These calculations are consistent with the near 50:50 mol ratio of Heck products **2a** and **2c** to **3a** and **3c** obtained with iodobiphenyls substituted with Me and



Y	2	2'	$\lvert\Delta\rvert$
NMe_2	-0.1973	-0.2200	0.0227
OMe	- 0.2102	- 0.2171	0.0069
Me	- 0.2090	- 0.2169	0.0079
CO_2Et	- 0.2299	- 0.2126	0.0173
NO_2	- 0.2306	- 0.2119	0.0187

Figure 1. Mulliken Electron Charges Calculated by HF/6-31G(d).

OMe groups under our palladium migration conditions (entries 1, 2, 5 and 6; Table 3). On the other hand, the Me_2N- substituted biphenyl has a relatively larger concentration of charge on the 2' position. Thus, this biphenyl should favor palladium migration to the more electron-rich 2 position. Indeed, we obtained Heck products slightly enriched with isomer **2b** (entries 3 and 4). In contrast, substituted biphenyls bearing electron-withdrawing groups, such as CO_2Et

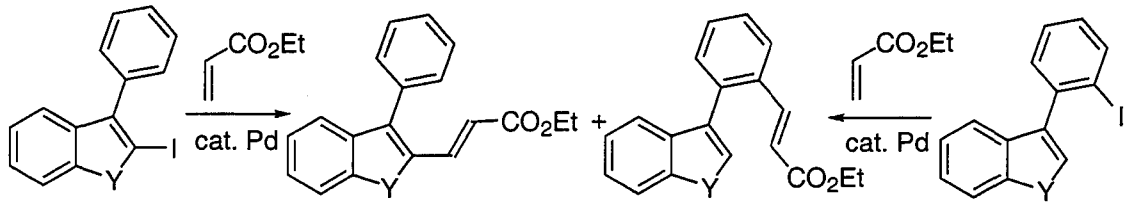
and NO_2, have greater electron density in the 2 position of the substituted phenyl moiety of the biphenyl. Thus, it is not surprising that we have obtained Heck reaction mixtures enriched with isomers **3d** and **3e** (entries 7-10, Table 3), which indicates a tendency for palladium to migrate to the more electron-rich position of these biphenyls. As a result, we conclude that electron density calculations can be used in a qualitative fashion to predict the preference of palladium within these biphenyls. Furthermore, these results are consistent with the intermediacy of an electrophilic palladium species.

At this time, we are unable to find any obvious correlation between our results and those reported by Gallagher.[4] Gallagher has observed that electron-withdrawing nitro groups are critical to migration in his systems. However, it is impossible to compare his experimental data with ours, since equilibration of the corresponding palladium intermediates was apparently never established in his reactions. Therefore, in his system we cannot deduce whether the nitro group is promoting migration directly or indirectly by simply retarding the Heck reaction and allowing enough time for the palladium migration to take place.

We have continued to investigate the electronic effects of other unsymmetrical *o*-halobiaryls and found a more marked effect on the Heck product distribution in the reaction of 2-iodo-3-phenylbenzofuran (**5a**) and ethyl acrylate, which under our standard migration conditions A gives exclusively ethyl *E*-3-(3-phenylbenzofuran-2-yl)acrylate (**6a**) in an 85 % yield (entry 1, Table 5). This unexpected result showing no apparent 1,4-Pd shift suggested that palladium has a strong preference for the 2-position of the benzofuran moiety. To test this hypothesis 3-(2-iodophenyl)benzofuran (**8a**) was allowed to react with ethyl acrylate under our standard migration conditions A. Acrylate **6a** was produced in a 78 % yield,

alongside only ~5 % of isomer **7a** (entry 2), indicating a strong preference for palladium to migrate from the phenyl to the benzofuran ring. These results are consistent with the idea of an electrophilic palladium preferring the more reactive 2-position of the benzofuran moiety.[15] However, keep in mind that very different reactivities of the two arylpalladium intermediates could be favoring the formation of **6a**. Once again, compound **7a** was prepared in a 75 % yield from **8a** by carrying out the Heck reaction with ethyl acrylate under Jeffrey's reaction conditions (entry 3, Table 5).

Table 5. Heck reaction of *o*-halobiaryls with ethyl acrylate.



5 **6** **7** **8**

entry	substrate	Y	conditions	% yield	mol ratio **6**:**7**[a]
1	**5a**	O	A, 1.0 d	85	100:0
2	**8a**	O	A, 1.0 d	83	94:6
3	**8a**	O	5 % $Pd(OAc)_2$, 4.0 ethyl acrylate, 1.0 *n*-Bu_4NCl, 2.0 $NaHCO_3$, DMF (1.0 mL), 80 °C, 1.0 d	75	0:100
4	**5b**	NMe	A, 1.0 d	94	100:0
5	**8b**	NMe	A, 1.0 d	90	85:15
6	**8b**	NMe	5 % $Pd(OAc)_2$, 4.0 ethyl acrylate, 1.0 *n*-Bu_4NCl, 2.0 $NaHCO_3$, DMF (1.0 mL), 80 °C, 1.0 d	85	100:0

[a]The product ratio was determined by ^1H NMR spectroscopic analysis.

Similarly, we have studied the Heck reaction of indole-containing biaryls (Table 5). As expected, the Pd-catalyzed reaction of 2-iodo-1-methyl-3-phenylindole (**5b**) and ethyl

acrylate under migration conditions A, produced ethyl *E*-3-(1-methyl-3-phenylindol-2-yl)acrylate (**6b**) exclusively in a 94 % yield (entry 4). Clearly this result supports the idea that palladium prefers to reside on the 2 position of the indole, rather than the phenyl moiety of the biaryl. On the other hand, the Heck reaction of 3-(2-iodophenyl)-1-methylindole (**8b**), under migration conditions A, produced an 85:15 mixture of **6b** and **7b** in a 90 % yield (entry 5). Although this latter result indicates a tendency for palladium to migrate to the indole ring, the arylpalladium intermediates formed were far from having reached equilibrium. We believe that the 15 mol % of retained product is a result of slow palladium migration kinetics, which might be due to unfavorable steric interactions imposed on the palladium when migrating to the relatively hindered 2 position of the 1-methylindole (Figure 2). Therefore, we postulate that steric hindrance might be a significant factor in this palladium migration chemistry disfavoring sterically congested arylpalladium intermediates.

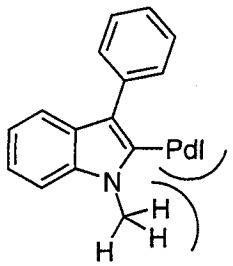
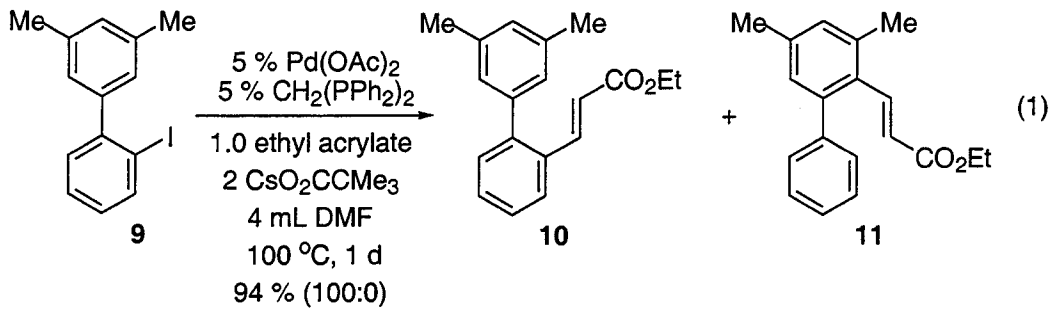


Figure 2. Unfavorable steric interactions in 1-methyl-3-phenylindol-2-ylpalladium iodide.

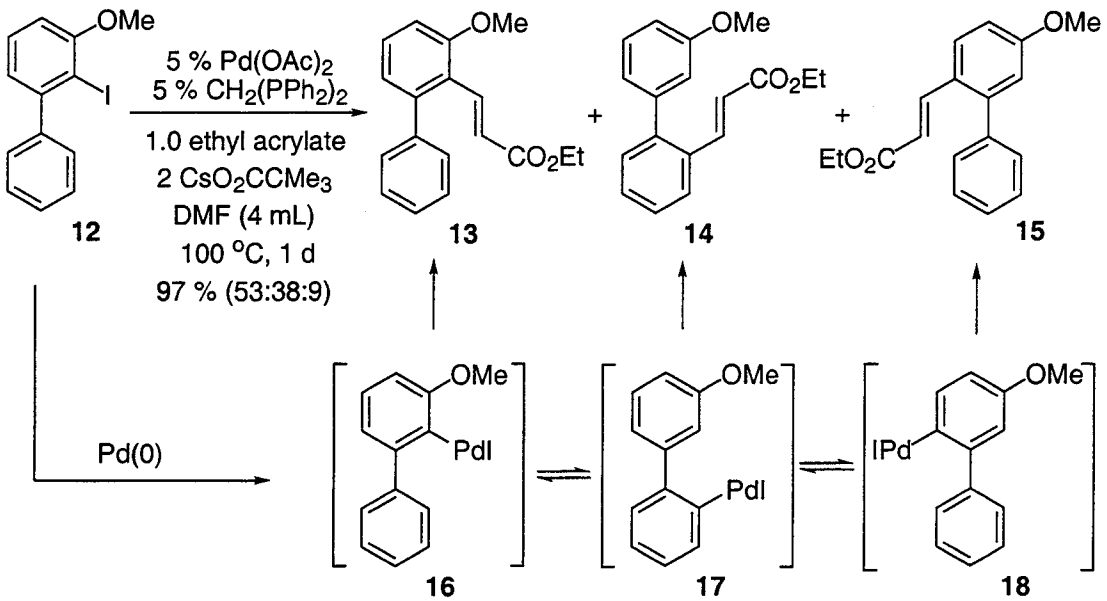
In order to study the effect of steric hindrance on the palladium migration, we have prepared 2-iodo-3',5'-dimethylbiphenyl (**9**). We chose this dimethyl-substituted biphenyl for two main reasons. First of all, methyl substituents are not likely to chelate palladium. Second of all, based on previous observations with biphenyls **1a** and **4a**, methyl groups

should be essentially electronically neutral in the palladium migration. We began by carrying out the reaction of **9** under Jeffrey's conditions to obtain the expected compound **10** exclusively in a 97 % yield (eq 1). Similarly, compound **9** also reacted with ethyl acrylate under our standard migration conditions A to generate compound **10** exclusively in a 94 % yield (eq 1). This result clearly indicates that the steric effect of the methyl substituents completely inhibited palladium migration to the dimethyl-substituted phenyl ring of the biphenyl.

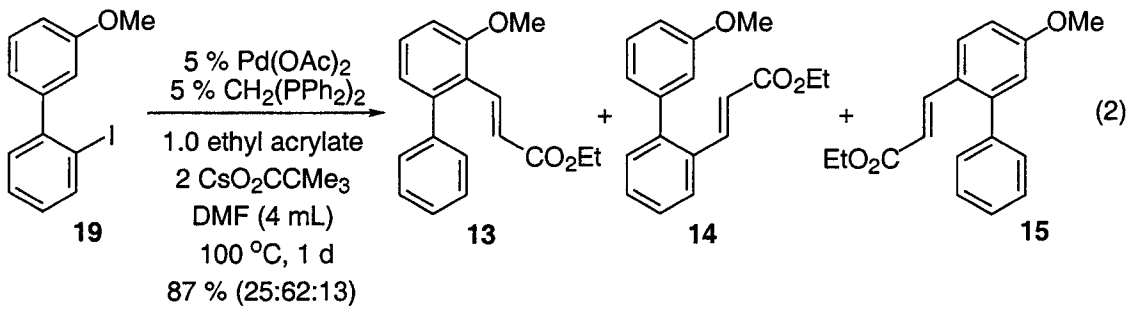


There is no reason to believe that these migrations should be restricted to a single 1,4-Pd shift. In fact, we have established a double 1,4-Pd shift in organopalladium intermediates generated from 2-iodo-3-methoxybiphenyl (**12**) (Scheme 4). Hypothetically, the palladium-catalyzed reaction involving compound **12** should give rise to three different arylpalladium intermediates **16-18** after a series of 1,4-Pd shifts, which should produce three different Heck products **13-15**. Indeed, the reaction of **12** with ethyl acrylate under our standard migration conditions A produced a mixture of compounds **13**, **14** and **15** (53:38:9 respectively) in an overall 97 % yield (Scheme 4). The presence of the key intermediate **18**, generated after a minimum of two 1,4-Pd shifts between the 2-, 2'-, and 6-positions of the biphenyl, explains the formation of isomer **15**. Interestingly, the reaction of 2-iodo-3'-methoxybiphenyl (**19**)

Scheme 4

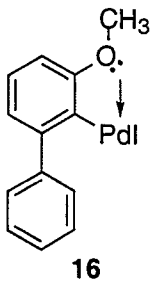


and ethyl acrylate under our standard migration conditions A, produced a mixture of compounds **13**, **14** and **15** (25:62:13 respectively) in an 87 % overall yield (eq 2). The wide discrepancy in the Heck product distribution obtained from the reaction of **12** versus **19**,



indicates that palladium is unable to achieve equilibrium between the three different positions of the biphenyl prior to olefin trapping. This is not an unexpected result, since equilibration of the palladium moiety in this biphenyl requires a more kinetically demanding double 1,4-Pd shift between the three distinct positions of the biphenyl prior to ethyl acrylate trapping. Finally, another factor adding to the complexity of this biphenyl system involves the

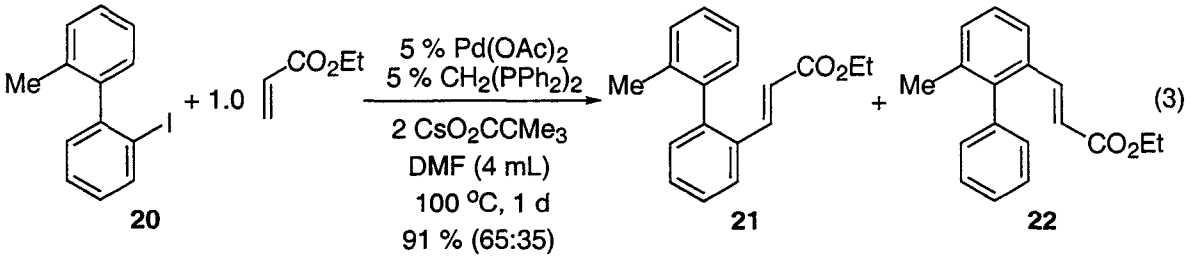
possibility of intramolecular oxygen chelation in the arylpalladium intermediate **16** (Figure 3).



16

Figure 3. Intramolecular chelation by oxygen.

Another interesting example of palladium migration involves the use of 2-iodo-2'-methylbiphenyl (**20**) in the Heck reaction (eq 3). Notice that in this biphenyl, there is only one vacant position for palladium migration on the methyl-substituted phenyl ring versus two vacant positions on the other ring. Therefore, statistically speaking, we expect to obtain a 2:1 (67:33) mixture of isomers **21** and **22**. To our satisfaction, the reaction of compound **20** with ethyl acrylate under migration conditions A produced a nearly theoretical 65:35 mixture of **21** and **22** in a 91 % yield. Furthermore, the reaction of compound **20** with ethyl acrylate under Jeffrey's conditions produced **21** exclusively in a 92 % yield.

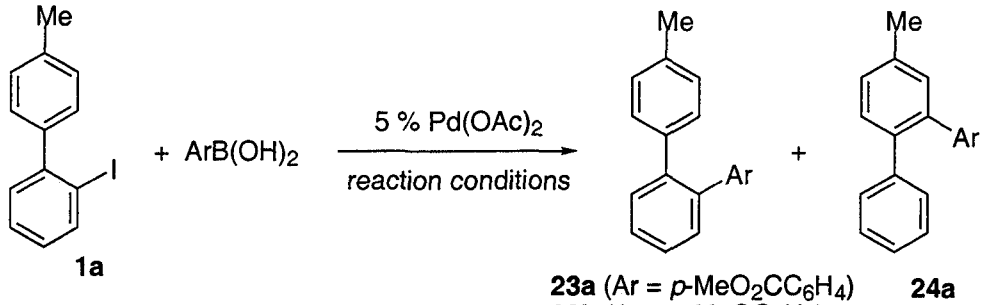


20 **21** **22** (3)

After exploring the Heck reaction, we proceeded to examine the Suzuki-Miyaura cross-coupling[16] of the same *o*-halobiaryls with arylboronic acids. First of all, we studied the coupling of 2-iodo-4'-methylbiphenyl (**1a**) with arylboronic acids under a variety of reaction

conditions (Table 6). For instance, the palladium-catalyzed coupling of **1a** with 4-(methoxycarbonyl)phenylboronic acid under conditions described by Wright, et al.[16c] produced methyl 4-(4'-methylbiphen-2-yl)benzoate (**23a**) exclusively in a 62 % yield (entry 1). Clearly under these conditions, the coupling reaction proceeds without any palladium migration. We then carried out the coupling reaction of **1a** with 4-(methoxycarbonyl)-phenylboronic acid under our standard migration conditions A, but after 3 d only trace amounts of the Suzuki-Miyaura product **23a** could be identified by TLC analysis of the reaction mixture (entry 2). In order to improve the yield, we carried out this reaction with the more electron-rich 4-methoxyphenylboronic acid and obtained a 57:43 mixture of 2-(4-methoxyphenyl)-4'-methylbiphenyl (**23b**) and 2-(4-methoxyphenyl)-4-methylbiphenyl (**24b**) in a 33 % yield, indicating that palladium migration had indeed occurred under these conditions. Even though we had obtained a low yield of Suzuki-Miyaura products under migration conditions A, we were encouraged by this positive result. We also suspected that the yield of this reaction could be improved by using water as an additive.[17] Therefore, we proceeded to carry out the coupling reaction of **1a** with 4-methoxyphenylboronic acid under migration conditions B, which employ 5% H_2O by volume in DMF as the reaction solvent and we obtained a 66:34 mixture of isomers **23b** and **24b** in a substantially higher 77 % overall yield. It should be pointed out that the addition of water to the reaction mixture improved the overall yield of the Suzuki reaction, but it lowered the amount of migration product **24b** (compared entries 3 and 4). Furthermore, the Suzuki coupling of **1a** with the electron-deficient 4-(methoxycarbonylphenyl)boronic acid under migration conditions B,

Table 6. Suzuki-Miyaura cross-coupling of 2-iodo-4'-methylbiphenyl (**1a**) with arylboronic acids.[a]



1a

23a (Ar = *p*-$MeO_2CC_6H_4$) **24a**
23b (Ar = *p*-$MeOC_6H_4$) **24b**

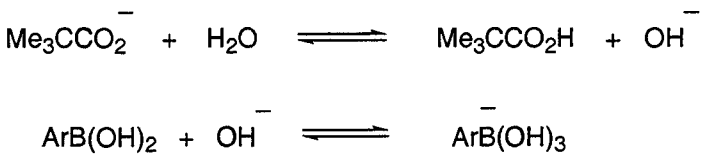
entry	reaction conditions	Ar/equiv	% yield	ratio (**23**:**24**)[b]
1	10 % PPh_3, 2.2 CsF, DME (1.0 mL), 90 °C, 8 h	*p*-$MeO_2CC_6H_4$/1.2	62	100:0
2	5 % dppm, 2 CsPiv, DMF (4.0 mL), 100 °C, 72 h	*p*-$MeO_2CC_6H_4$/1.0	trace	-
3	5 % dppm, 2 CsPiv, DMF (4.0 mL), 100 °C, 72 h	*p*-$MeOC_6H_4$/1.0	33	57:43
4	5 % dppm, 2 CsPiv, DMF (3.8 mL), 44 H_2O (0.2 mL) 100 °C, 8 h	*p*-$MeOC_6H_4$/1.0	77	66:34
5	5 % dppm, 2 CsPiv, DMF (3.8 mL), 44 H_2O (0.2 mL) 100 °C, 8 h	C_6H_5/1.0	complex mixture	-
6	5 % dppm, 2 CsPiv, DMF (3.8 mL), 44 H_2O (0.2 mL) 100 °C, 8 h	$C_6H_5BF_3K$/1.0	complex mixture	-
7	5 % dppm, 2 CsPiv, DMF (3.8 mL), 44 H_2O (0.2 mL) 100 °C, 8 h	*p*-$MeO_2CC_6H_4$/ 1.0	61	60:40
8	5 % dppm, 2 CsPiv, DMF (4.0 mL), 20 H_2O, 100 °C, 8 h	*p*-$MeO_2CC_6H_4$/ 1.0	55	57:43
9	5 % dppm, 2 CsPiv, 2 Me_3CCO_2H, DMF (4.0 mL), 20 H_2O, 100 °C, 24 h (buffered)	*p*-$MeO_2CC_6H_4$/ 1.0	57	50:50
10	5 % dppm, 2 CsPiv, 2 Me_3CCO_2H, DMF (4.0 mL), 100 °C, 24 h (buffered)	*p*-$MeO_2CC_6H_4$/ 1.0	trace	-
11	5 % dppm, 2 CsPiv, 2 Me_3CCO_2H, DMF (4.0 mL), 20 H_2O, 100 °C, 24 h (buffered)	*p*-$MeOC_6H_4$/1.0	38	52:48
12	5 % dppm, 2 CsPiv, 2 Me_3CCO_2H, DMF (4.0 mL), 20 H_2O, 100 °C, 24 h (buffered)	*p*-$MeO_2CC_6H_4$/ 1.4	71	51:49

[a]The reaction was run using 0.25 mmol of the aryl iodide. [b]The mole ratio was determined by ^1H NMR spectroscopic analysis.

produced a 60:40 mixture of **23a** and **24a** in a 61 % yield (entry 7). Obviously, the use of 4-(methoxycarbonylphenyl)boronic acid in place of 4-methoxyphenylboronic acid improved the amount of migration product, presumably due to the lower reactivity of the electron-deficient arylboronic acid.

At this stage, we looked more closely at the possible role of water in the Suzuki-Miyaura coupling reaction and realized that, in the presence of base, water may serve as a source of hydroxide ions. In turn, hydroxide ions probably activate the arylboronic acid by generating a more reactive arylboronate species (Scheme 5). So our new strategy aimed to control the relatively fast arylpalladium trapping kinetics by arylboronic acids by controlling

Scheme 5



the concentration of hydroxide ions in the reaction mixture and thus reducing the concentration of the more reactive boronate anion. The first step was to carry out the coupling of **1a** with 4-(methoxycarbonyl)phenylboronic acid under conditions B, but we also reduced the amount of water from 44 equiv (corresponding to conditions B) to 20 equiv. Under these conditions, the coupling reaction produced a 57:43 mixture of **23a** and **24a** in a 55 % overall yield (entry 8), indicating only a slight improvement in the isomer ratio (compare this with a 60:40 ratio previously obtained using conditions B). At this point, we decided to buffer the reaction mixture by using a combination of 2 equiv of CsPiv plus 2 equiv of pivalic acid. To our satisfaction, the coupling of **1a** and 4-(methoxycarbonyl)phenylboronic acid under these buffered conditions produced a 50:50

mixture of **23a** and **24a** in a 57 % overall yield (entry 9). Naturally, we carried out the same reaction in the absence of water and observed only trace amounts of Suzuki-Miyaura products after 1 d of reaction (entry 10).

Now that we had apparently developed a set of optimal migration conditions for the Suzuki-Miyaura reaction, we proceeded to examine the use of the more electron-rich 4-methoxyphenylboronic acid as the coupling agent. As expected, the Suzuki-Miyaura coupling of **1a** with this arylboronic acid produced a 52:48 mixture of isomers **23b** and **24b** in a disappointingly low 38 % overall yield. This experiment confirmed the idea that the more electron-rich 4-methoxyphenylboronic acid trapped the arylpalladium intermediates somewhat faster than the electron-poor 4-(methoxycarbonyl)phenylboronic acid, thus producing the observed ratio of isomers, which is slightly enriched with the direct coupling product **23b**. On the other hand, the overall low yields obtained in the Suzuki-Miyaura reaction under our buffered conditions (entries 9 and 11) might be due to a side reaction involving protonation of the corresponding arylboronic acids by pivalic acid (eq 4). Thus, in

$$Me_3CCO_2H + ArB(OH)_2 \longrightarrow Me_3CCO_2B(OH)_2 + Ar\text{-}H \quad (4)$$

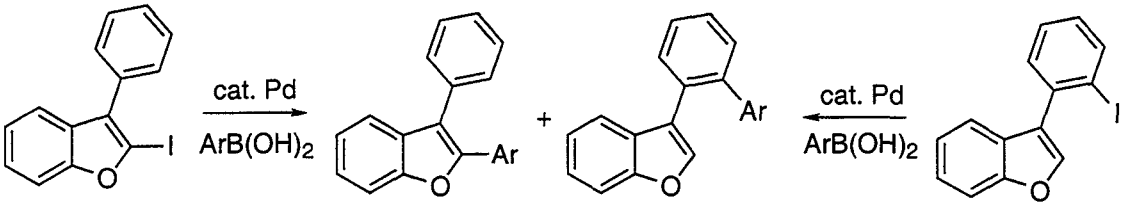
an attempt to improve the reaction yield, we carried out the Suzuki cross-coupling of **1a** with 1.4 equiv of 4-(methoxycarbonyl)phenylboronic acid as opposed to the usual 1.0 equiv (entry 12). Using this protocol, we obtained a 51:49 mixture of **23a** and **24a** in a 71 % overall yield. As a result, we chose this latter set of reaction conditions, described in entry 12 of Table 6, as our standard migration conditions (conditions C) for the Suzuki-Miyaura cross-coupling of *o*-halobiaryls with arylboronic acids. Equally significant is the fact that we can

suppress the palladium migration in the Suzuki-Miyaura reaction by simply employing the conditions described in entry 1 of Table 6.

As discussed previously, there are two possible factors determining the ratio of Heck products from the corresponding *o*-halobiaryls, namely the distribution of arylpalladium intermediates and/or their relative reactivities towards ethyl acrylate. Naturally, the same argument applies to the Suzuki-Miyaura reaction. Recall that we have previously assumed that the reactivities of the arylpalladium intermediates generated via palladium migration are similar, and differing reactivities does not significantly affect the ratio of Heck products. If such an assumption were true, there should be very little difference between the ratios of Heck versus Suzuki-Miyaura products, since the determining factor for such product ratios is a pre-established distribution of the arylpalladium intermediates independent of their reactivities. On the other hand, if the reactivity of the arylpalladium intermediates is playing a significant role in determining the ratio of the reaction products, we should expect a significant difference between the ratios of Heck and Suzuki-Miyaura products. With this argument in mind, it is important to point out that under our migration conditions, aryl iodide **1a** produced nearly identical mixtures of Heck and Suzuki-Miyaura products. This is a very significant finding since this similarity supports our hypothesis that a pre-established distribution of arylpalladium intermediates determines these ratios. In order to further test this hypothesis, we have carried out the Suzuki-Miyaura cross-coupling of 2-iodo-3-phenylbenzofuran (**5a**) with 4-(methoxycarbonyl)-phenylboronic acid under our standard migration conditions C and obtained 2-(4-methoxycarbonylphenyl)-3-phenylbenzofuran (**25**) exclusively in a 79 % yield (entry 1, Table 7). Similarly, the reaction of 3-(2-iodophenyl)-

benzofuran (**8a**) with 4-(methoxycarbonyl)phenylboronic acid under our standard migration conditions C produced compound **25** in a 78 % overall yield, along with only a small amount (< 5 %) of the direct coupling product **26** (entry 2). In addition, the Suzuki-Miyaura reaction of **8a** under Wright's conditions produced the expected compound **26** in a 78 % yield, along with compound **25** in a 7 % yield. Clearly, both the Heck and Suzuki-Miyaura experiments with the benzofuran-containing biaryls **5a** and **8a** give very similar results indicating a tendency for palladium to migrate from the phenyl to the benzofuran moiety of the biaryl (see Tables 5 and 7). Furthermore, the similarities in Heck and Suzuki-Miyaura product ratios obtained under our migration conditions support the hypothesis that a pre-established distribution of arylpalladium intermediates rather than their relative reactivities determines such product ratios.

Table 7. Suzuki-Miyaura cross-coupling of benzofuran-containing biaryls.[a]



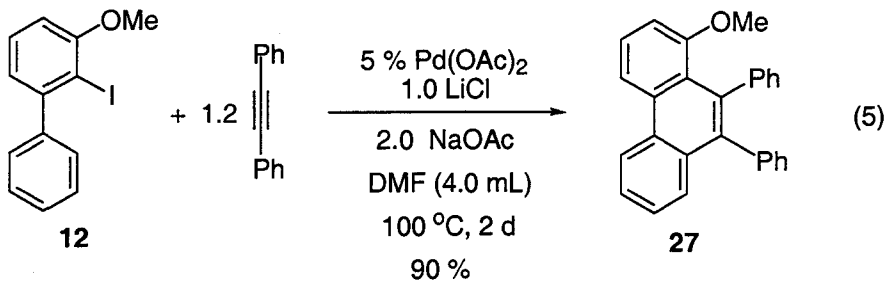
5a **25** **26** **8a**

Ar = *p*-$MeO_2CC_6H_4$

entry	substrate	reaction conditions	% yield **25** + **26**
1	**5a**	C, 1.0 d	79 + 0
2	**8a**	C, 1.0 d	78 + < 5
3	**8a**	5 % $Pd(OAc)_2$, 10 % PPh_3, 2.2 CsF, 1.2 *p*-$MeO_2CC_6H_4B(OH)_2$, DME (1.0 mL), 90 °C, 6 h	7 + 75

[a]The reaction was run using 0.25 mmol of the corresponding aryl iodide.

To further explore the scope of this Pd migration process, we have carried out the palladium-catalyzed reaction of diphenylacetylene and aryl iodide **12** in the hope that the arylpalladium intermediates generated by a 1,4-Pd shift could be trapped by way of alkyne insertion-annulation chemistry described earlier by Larock et al.[18] First, the reaction was carried out under the previously described annulation conditions employing 1.2 equiv of the acetylene, 5 mol % $Pd(OAc)_2$, 1 equiv of LiCl and 2 equiv of NaOAc in DMF at 100 °C for 2 d. As expected, we obtained 1-methoxy-9,10-diphenylphenanthrene (**27**) in a 90 % yield (eq 5). We then switched "on" the palladium migration by allowing **12** to react with 1.2 equiv of

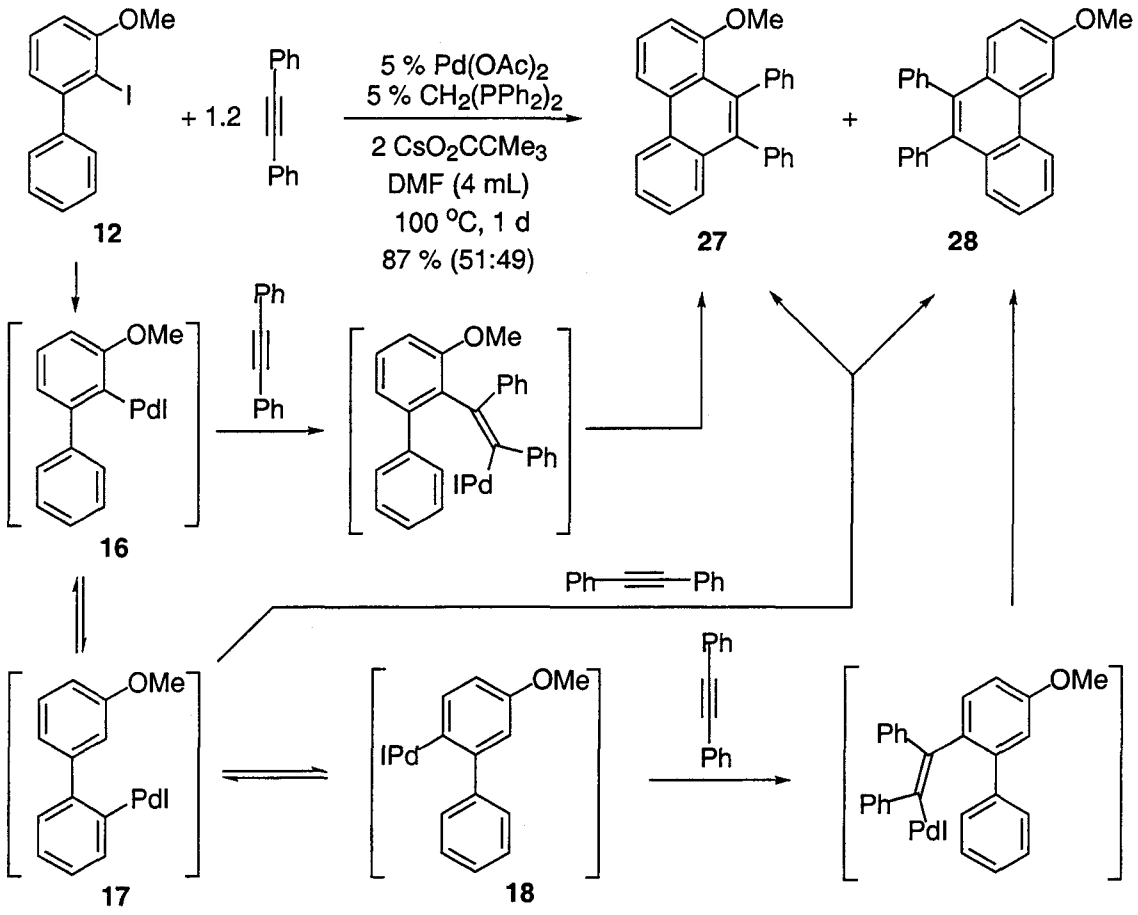


(5)

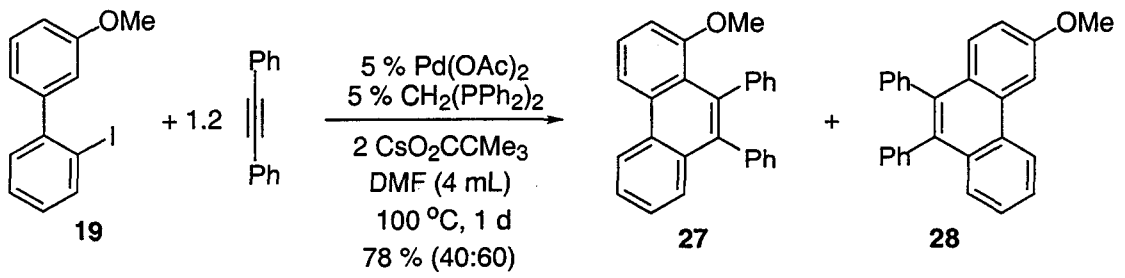
diphenylacetylene under our standard Pd migration conditions A to obtain a 51:49 mixture of phenanthrenes **27** and **28** respectively in an 87 % overall yield (Scheme 6). The mechanism for the formation of phenanthrenes **27** and **28** is described in Scheme 6. Notice that there are multiple paths for the formation of isomer **28** (as well as **27**). It is important to note that in these alkyne reactions the formation of product **28** cannot arise directly from the intermediacy of a simple bridged pallada(II)cycle,[19] but instead its formation requires complete migration of the palladium moiety from the methoxy-bearing ring to the other aromatic ring. Similarly, aryl iodide **19** reacted with diphenylacetylene under our standard migration conditions A to generate a 40:60 mixture of phenanthrenes **27** and **28** respectively

in a 78 % overall yield (Scheme 7), indicating that the arylpalladium intermediates derived from **12** and **19** have not reached equilibrium under these conditions. These interesting

Scheme 6



Scheme 7



migration results suggest that there is the exciting possibility of trapping arylpalladium intermediates generated by 1,4-Pd shifts by many other synthetically useful palladium methodologies.

Conclusion

In conclusion, we have been able to establish a 1,4-palladium migration in organopalladium intermediates derived from *o*-halobiaryls. These arylpalladium intermediates have been generated under relatively mild reaction conditions compatible with the Heck, Suzuki and alkyne annulation reactions. We have developed standard migration conditions, which allow arylpalladium intermediates to approach equilibrium prior to the trapping step. The palladium migration can be activated or suppressed at will by simple manipulation of the reaction conditions. The nearly identical ratio of isomers obtained from the Heck and Suzuki reactions seem to indicate that there is a direct correlation between these ratios and the distribution of arylpalladium intermediates generated by palladium migration.

Experimental

General procedures. All ^{1}H and ^{13}C spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5 %) + 300 mL of H_2O]. All melting points are

uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV.

Reagents. All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of THF, DME, DMF, diethyl ether, ethyl acetate and hexanes were purchased from Fisher Scientific Co. Tetra-*n*-butylammonium chloride (TBAC) was purchased from Lancaster Synthesis, Inc. 3-Bromoanisole, 1-bromo-2-iodobenzene, diphenylacetylene and ethyl acrylate were purchased from Aldrich Chemical Co., Inc. Cesium pivalate was prepared according to the procedure of Larock and Campo.[20] Compounds **1a, 1b, 5b, 8a, 13** and **10** have been previously reported[20] (see chapter 1 of this thesis).

Synthesis of the *o*-halobiaryls

2-Bromo-4'-methylbiphenyl (1a'). A mixture of 2-iodo-4'-methylbiphenyl (**1a**) (0.147 g, 0.5 mmol), CuBr (1.435 g, 5.0 mmol), and KBr (0.595 g, 5.0 mmol) in DMF (12 mL) was stirred at 145 °C under Ar for 1 d. The reaction mixture was diluted with diethyl ether (80 mL) and filtered. The filtrate was washed with brine (50 mL), and the organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using hexanes to obtain 0.105 g (85 %) of the indicated compound as a clear oil: ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 3H), 7.16-7.20 (m, 1H), 7.23-7.25 (m, 2H), 7.30-7.34 (m, 4H), 7.64-7.66 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 21.3, 122.8, 127.4, 128.6, 128.8, 129.3, 131.4, 133.1, 137.4, 138.3, 142.6. The other spectral properties were identical to those previously reported.[21]

2-Iodo-4-methylbiphenyl (4a). This compound was prepared by the procedure of Hellwinkel:[22] ^{1}H NMR ($CDCl_3$) δ 2.35 (s, 3H), 7.18-7.19 (m, 2H), 7.30-7.41 (m, 5H), 7.79-7.80 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 20.7, 98.7, 127.7, 128.1, 129.2, 129.6, 129.9, 139.1, 140.2, 144.0, 144.3; IR (CH_2Cl_2) 3024, 2920, 1603, 1473 cm^{-1}; HRMS *m/z* 293.9910 (calcd for $C_{13}H_{11}I$, 293.9906).

***N,N*-Dimethyl-4-(2-iodophenyl)aniline (1b).** Compound **1b** was prepared in two steps from compound **1e**. To a solution of **1e** (0.389 g, 1.19 mmol), $FeCl_3$•$6H_2O$ (5.0 mg, 0.018 mmol), and activated charcoal (2.4 mg) in methanol (10 mL) under reflux was added N_2H_4•$1H_2O$ (0.115 g, 3.03 mmol) dropwise over 10 min. The mixture was refluxed for an additional 14 h and then allowed to cool to room temperature. The reaction mixture was diluted with diethyl ether (50 mL) and the organic layer was washed with water (50 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent evaporated under reduced pressure to obtain a yellow oil [presumed to be 4-(2-iodophenyl)aniline], which without further purification or characterization was dissolved in acetonitrile (8 mL). To this acetonitrile solution was added 37 % aq formaldehyde (0.96 mL) and $NaBH_3CN$ (0.230 g, 3.66 mmol). The resulting reaction mixture was stirred at room temperature while glacial acetic acid (0.12 mL) was added dropwise over 10 min. After the addition, the reaction mixture was stirred for 40 min, then another portion of glacial acetic acid (0.12 mL) was added at once and stirring continued for an additional 30 min. The reaction mixture was diluted with diethyl ether (50 mL) and washed with 5 % aq NaOH. The organic layer was dried (Na_2SO_4), filtered, and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 9:1 hexanes/ethyl acetate to afford

36.9 mg (96 %) of the indicated compound **1b** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 3.00 (s, 6H), 6.75-6.77 (m, 2H), 6.94-6.98 (m, 1H), 7.23-7.26 (m, 2H), 7.29-7.36 (m, 2H), 7.93 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 40.5, 99.6, 111.5, 128.1, 128.2, 130.1, 130.3, 132.4, 139.5, 146.8, 149.9; IR (CH_2Cl_2) 2917, 2849, 1612, 1525, 1461, 1351 cm^{-1}; HRMS *m/z* 323.0176 (calcd for $C_{14}H_{14}IN$, 323.0171).

***N,N*-Dimethyl-3-iodo-4-phenylaniline (4b).** Compound **4b** was prepared in two steps from 2-iodo-4-nitrobiphenyl (**4e**) by a procedure similar to that used for **1d**. The reaction mixture was purified by chromatography on a silica gel column using 9:1 hexanes/ethyl acetate to afford 38.1 mg (98 %) of the indicated compound (**4b**) as a yellow solid: mp 76-77 °C; ^{1}H NMR ($CDCl_3$) δ 2.96 (s, 6H), 6.75 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 2.8 Hz, 1H), 7.33-7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 40.5, 99.5, 112.3, 122.9, 127.0, 127.8, 129.8, 130.1, 134.4, 144.3, 150.4; IR (CH_2Cl_2) 2917, 2849, 1598, 1486, 1511, 1442 cm^{-1}; HRMS *m/z* 323.0176 (calcd for $C_{14}H_{14}IN$, 323.0171).

2-Iodo-4-methoxybiphenyl (4c). This compound was prepared by the Sandmeyer reaction of diazotized 5-methoxy-2-phenylaniline:[23] ^{1}H NMR ($CDCl_3$) δ 3.60-3.79 (br s, 2H), 3.79 (s, 3H), 6.32 (d, *J* = 2.4 Hz, 1H), 6.41 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 7.29-7.33 (m, 1H), 7.39-7.42 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 55.3, 101.2, 104.4, 120.9, 126.9, 128.8, 129.3, 131.4, 139.4, 144.6, 160.1. To a solution of 5-methoxy-2-phenylaniline (0.66 g, 3.3 mmol) in a mixture of H_2O (9 ml), H_2SO_4 (0.8 ml), and DME (20 ml) at 0 °C was added slowly with stirring $NaNO_2$ (0.33 g, 4.8 mmol) and the resulting solution stirred for an additional 30 min at 0 °C. The resulting mixture was added slowly to a solution of NaI (3 g, 20 mmol) in H_2O (7 ml) and the mixture was stirred vigorously for an additional 15 min.

The I_2 present was destroyed by adding 10% aq $Na_2S_2O_3$ (20 mL) and the reaction mixture was subsequently extracted with diethyl ether (100 ml). The organic layer was dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 20:1 hexanes/ethyl acetate to afford 0.635 g (62 %) of the desired compound **4c** as a yellow solid, which was recrystallized from methanol: mp 83-84 °C; ^{1}H NMR ($CDCl_3$) δ 3.83 (s, 3 H), 6.94 (dd, J = 8.4, 2.4 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 7.31-7.33 (m, 2H), 7.36-7.41 (m, 3 H), 7.48 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.6, 98.5, 114.3, 124.5, 127.4, 127.9, 129.6, 130.3, 139.2, 143.9, 158.9; IR (CH_2Cl_2) 3051, 2966, 1554, 1592, 1475 cm^{-1}; HRMS *m/z* 309.9859 (calcd for $C_{13}H_{11}IO$, 309.9855).

Ethyl 4-(2-bromophenyl)benzoate (1d). Compound **1d** was prepared by a selective Suzuki-Miyaura cross-coupling reaction as follows. 2-Bromophenylboronic acid (0.462 g, 2.3 mmol), ethyl 4-iodobenzoate (0.552 g, 2.0 mmol), CsF (0.668 g, 4.4 mmol), $Pd(OAc)_2$ (0.022 g, 5 mol %), and PPh_3 (0.052 g, 10 mol %) in DME (10 mL) were stirred under Ar at 90 °C for 7 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (30 mL). The organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography using 9:1 hexanes/ethyl acetate to afford 0.493 g (81 %) of the desired compound **1d** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.42 (t, J = 7.2 Hz, 3H), 4.41 (q, J = 7.2 Hz, 2H), 7.21-7.26 (m, 1H), 7.31-7.33 (m, 1H), 7.36-7.40 (m, 1H), 7.48-7.50 (m, 2H), 7.68 (dd, J = 8.0, 1.2 Hz, 1H), 8.10-8.12 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.4, 61.1, 122.3, 127.5, 129.3, 129.5, 129.7, 131.1, 133.3, 141.7, 145.5, 166.5 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 2980, 1715, 1611, 1466, 1275 cm^{-1}; HRMS *m/z* 304.0104 (calcd for $C_{15}H_{13}BrO_2$, 304.0099).

Ethyl 3-iodo-4-phenylbenzoate (4d). Compound **4d** was prepared from ethyl 4-iodo-3-nitrobenzoate.[24] First, we carried out a Suzuki-Miyaura cross-coupling of ethyl 2-iodo-3-nitrobenzoate and $NaBPh_4$ as follows. $NaBPh_4$ (1.69 g, 4.94 mmol), ethyl 4-iodo-3-nitrobenzoate (1.38 g, 4.3 mmol), LiCl (0.182 g, 4.3 mmol), $Pd(OAc)_2$ (48.0 mg, 5 mol %), and PPh_3 (0.113 g, 10 mol %) in DMF (10 mL) were stirred under Ar at 70 °C for 2 d. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (50 mL). The organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure to obtain a yellow oil (presumed to be ethyl 3-nitro-4-phenylbenzoate), which without further purification was dissolved in 50 mL of a mixture of DME/EtOH/AcOH (50:40:10 % by volume respectively). To this solution was added $SnCl_2$ (5.71 g, 30.1 mmol) and the resulting mixture was stirred at 60 °C under Ar for 16 h. The reaction mixture was diluted with diethyl ether (100 mL) and washed with 10 % aq Na_2CO_3 (100 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column using 3:1 hexanes/ethyl acetate to obtain ~0.93 g (90 %) of ethyl 3-amino-4-phenylbenzoate as a yellow oil, which quickly decomposed as a neat liquid (no spectral data was obtained for this compound due to its instability). Ethyl 3-amino-4-phenylbenzoate was diazotized and iodinated by the following procedure. To a solution of ethyl 3-amino-4-phenylbenzoate (~0.93 g, 3.86 mmol) in DME (10 mL) was added water (8 mL) containing H_2SO_4 (0.7 mL). This reaction mixture was stirred at 0 °C while $NaNO_2$ (0.386 g, 5.60 mmol) in H_2O (2 mL) was added dropwise over 30 min. After the addition, the mixture was stirred for an additional 20 min at 0 °C, then this mixture was added to NaI (3.0 g, 20.0 mmol) in H_2O (7 mL). Any I_2 formed was

destroyed by adding 10% aq $Na_2S_2O_3$ (10 mL) and the mixture was extracted twice with diethyl ether (50 mL x 2). The organic layers were combined, dried (Na_2SO_4), filtered, and the solvent evaporated under reduced pressure. The residue was purified by column chromatography on a silica gel column using 7:1 hexanes/ethyl acetate to obtain 1.06 g (78 %) of the title compound **4d** as a white solid: mp 76-77 °C; ^{1}H NMR ($CDCl_3$) δ 1.41 (t, J = 7.2 Hz, 3H), 4.40 (q, J = 7.2 Hz, 2H), 7.33-7.37 (m, 3H), 7.41-7.45 (m, 3H), 8.04 (dd, J = 8.0, 1.6 Hz, 1H), 8.61 (d, J = 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.4, 61.4, 98.1, 128.2, 128.2, 129.0, 129.2, 129.9, 130.8, 140.6, 143.4, 150.9, 165.0; IR (CH_2Cl_2) 2973, 2818, 1722, 1276, 1378 cm^{-1}; HRMS *m/z* 351.9966 (calcd for $C_{15}H_{13}IO_2$, 351.9960); Anal. C, 51.14, H, 3.34 (calcd for $C_{15}H_{13}IO_2$: C, 51.16; H, 3.72)

2-Iodo-4'-nitrobiphenyl (1e). Compound **1e** was prepared by the procedure of Ozasa et al.[25]

2-Iodo-4-nitrobiphenyl (4e). Compound **4e** was prepared in two steps from 2-iodo-4-nitroaniline.[26] First of all, 2-iodo-4-nitroaniline was diazotized by the following procedure. To a solution of 2-iodo-4-nitroaniline (1.09 g, 4.13 mmol), and 48-50 % aq HBF_4 (3.0 g) in methanol (20 mL) was added $NaNO_2$ (0.342 g, 4.96 mmol) in H_2O (0.5 mL) at room temperature. The reaction mixture was stirred for 30 min, and then the reaction mixture was concentrated to 10 mL by passing a stream of Ar over it. At this point, a yellow solid had precipitated out of solution, and further crystallization was induced by cooling the mixture to -20 °C. The solid was filtered and washed repeatedly with diethyl ether. Recrystallization from methanol/diethyl ether afforded 0.673 g (49 %) of 4-nitro-2-iodophenyldiazonium tetrafluoroborate as a yellow solid. 4-Nitro-2-iodophenyldiazonium tetrafluoroborate (82.7

mg, 0.25 mmol) was dissolved in dry DMSO (2.0 mL), then diluted with dry benzene (8.0 mL). The reaction mixture was stirred at 80 °C for 2 h under Ar. The reaction mixture was diluted with diethyl ether (20 mL) and washed with brine (30 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 12:1 hexanes/ethyl acetate to obtain 35.8 mg (44 %) of the indicated compound **4e** as a yellow solid: mp 91-92 °C; ^{1}H NMR ($CDCl_3$) δ 7.33-7.35 (m, 2H), 7.45-7.48 (m, 4H), 8.25 (dd, J = 8.4, 2.4 Hz, 1H), 8.80 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 97.9, 123.1, 128.4, 128.8, 130.2, 134.5, 142.3, 147.0, 153.1 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 2918, 2850, 1523, 1349 cm^{-1}; HRMS *m/z* 324.9606 (calcd for $C_{12}H_8INO_2$, 324.9600); Anal. C, 44.29, H, 2.29; N, 4.11 (calcd for $C_{12}H_8INO_2$: C, 44.33; H, 2.48; N, 4.34).

2-Iodo-3-phenylbenzofuran (5a). This iodobiaryl was prepared from 3-phenyl-2-(triisopropylsilyl)benzofuran (**29**)[27] using an iodination procedure from the literature.[28] To a solution of **29** (0.329 g, 0.938 mmol) in CH_2Cl_2 (2 mL) was added ICl (0.162 g, 1.0 mmol) in CH_2Cl_2 (3 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min, then the excess ICl was destroyed by adding 10 % aq $Na_2S_2O_3$ (10 mL) and diluted with 50 ml of Et_2O. The organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The remaining oil was purified by column chromatography using 30:1 hexanes/ethyl acetate to afford 0.267 g (89 %) of the desired compound **5a** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.19-7.28 (m, 2H), 7.38-7.43 (m, 1 H), 7.46-7.61 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 97.2, 111.2, 119.4, 123.4, 124.7, 128.0, 128.1, 128.9, 128.9, 129.2, 131.7, 158.4;

IR (CH_2Cl_2) 3062, 3030, 1444, 1335, 1090 cm^{-1}; HRMS *m/z* 319.9702 (calcd for $C_{14}H_9IO$, 319.9698).

3-(2-Iodophenyl)-1-methylindole (8b). Compound **8b** was prepared in two steps from 2-(2-iodophenyl)acetaldehyde.[29] A solution of 2-(2-iodophenyl)acetaldehyde (0.216 g, 0.88 mmol), phenylhydrazine (0.105 g, 0.97 mmol), and methanesulfonic acid (17 mg, 0.18 mmol) in absolute ethanol (5.0 mL) was stirred at room temperature for 40 min under Ar. Then methanesulfonic acid (0.152 g, 1.58 mmol) was added and the mixture was stirred at 85 °C for 1.5 d under Ar. The reaction mixture was diluted with diethyl ether (50 mL) and washed with satd aq NH_4Cl (30 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using hexanes/ethyl acetate 3:1 to afford 11.5 mg (41 %) of 3-(2-iodophenyl)indole as a brown oil: ^1H NMR ($CDCl_3$) δ 6.99 (m, 1H), 7.13-7.17 (m, 1H), 7.21-7.25 (m, 1H), 7.32-7.47 (m, 4H), 7.53 (d, *J* = 8.0 Hz, 1H), 8.00 (dd, *J* = 8.0, 0.8 Hz, 1H), 8.18 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 100.9, 111.4, 120.2, 122.5, 123.7, 126.6, 128.1, 128.4, 131.5, 135.7, 139.9, 140.0 (two sp^2 carbons missing due to overlap). To a suspension of NaH (0.031 g, 1.3 mmol) in DMF (2.0 mL) at 0 °C was added 3-(2-iodophenyl)indole (0.319 g, 1.0 mmol) in DMF (3.0 mL) and the mixture was stirred at room temperature for 30 min. At this point, MeI (1.42 g, 10.0 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 14 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent removed under reduced pressure. The residue was purified by column

chromatography using 5:1 hexanes/ethyl acetate to afford 0.320 g (96 %) of the desired 3-(2-iodophenyl)-1-methylindole (**8b**) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.84 (s, 3H), 6.97-7.01 (m, 1H), 7.12-7.16 (m, 1H), 7.22-7.28 (m, 2H), 7.35-7.40 (m, 2H), 7.45 (dd, J = 7.6, 1.6 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.99 (dd, J = 7.6, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 33.1, 100.8, 109.5, 118.5, 119.7, 120.3, 122.0, 127.0, 128.1, 128.2, 128.4, 131.5, 136.6, 139.9, 140.1; IR (CH_2Cl_2) 3050, 2922, 1547, 1478, 1459, 1376 cm^{-1}; HRMS *m/z* 333.0024 (calcd for $C_{15}H_{12}IN$, 333.0014).

2-Iodo-3',5'-dimethybiphenyl (9). 2-Iodo-3',5'-dimethylbiphenyl (**9**) was prepared by a procedure reported by Hart.[30] A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 3,5-dimethylphenylmagnesium bromide [prepared from 1-bromo-3,5-dimethylbenzene (1.85 g, 10 mmol) and Mg (0.246 g, 10 mmol) in THF (30 mL)], and the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I_2 (3.8 g, 15 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I_2 was destroyed by adding 10% aq $NaHSO_3$ (35 mL) and the organic layer was separated and rewashed with brine (20 mL). Finally, the organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using hexanes to afford 0.836 g (54 %) of the desired compound **9** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 6H), 6.95-7.02 (m, 4H), 7.33-7.82 (m, 1H), 7.92-7.94 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 21.6, 98.9, 127.3, 128.3, 128.8, 129.4, 130.3, 137.6, 139.6, 144.3, 147.1; IR (CH_2Cl_2) 2917, 2849, 1602, 1461, 1015 cm^{-1}; HRMS *m/z* 308.0070 (calcd for $C_{14}H_{13}I$, 308.0062).

2-Iodo-3'-methoxybiphenyl (19). Compound **19** was prepared by a procedure reported by Hart.[30] A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 3-methoxyphenylmagnesium bromide [prepared from 3-bromoanisole (1.87 g, 10 mmol) and Mg (0.246 g, 10 mmol) in THF (30 mL)], and the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I_2 (3.8 g, 15 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I_2 was destroyed by adding 10% aq $NaHSO_3$ (35 mL) and the organic layer was separated and rewashed with brine (20 mL). Finally, the organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using 30:1 hexanes/ethyl acetate to afford 0.620 g (40 %) of the desired compound **19** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.84 (s, 3H), 6.88-6.95 (m, 3H), 7.01-7.05 (m, 1H), 7.29-7.38 (m, 3H), 7.95 (dd, J = 8.0, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.4, 98.5, 113.4, 115.0, 121.8, 128.1, 128.9, 129.1, 130.1, 139.6, 145.5, 146.5, 159.1; HRMS *m/z* 309.9859 (calcd for $C_{13}H_{11}IO$, 309.9855).

2-Iodo-2'-methylbiphenyl (20). Compound **20** was prepared by a procedure reported by Hart.[30] A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 2-methylphenylmagnesium bromide [prepared from 2-bromotoluene (1.71 g, 10 mmol) and Mg (0.246 g, 10 mmol) in THF (30 mL)], and the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I_2 (3.8 g, 15 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I_2 was destroyed by adding 10% aq $NaHSO_3$ (35 mL) and the organic layer was separated and rewashed with brine (20 mL). Finally, the organic

layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using hexanes to afford 0.97 g (66 %) of the desired compound **20** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 2.07 (s, 3H), 7.01-7.07 (m, 2H), 7.20-7.31 (m, 4H), 7.36-7.40 (m, 1H), 7.92-7.94 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 20.1, 100.1, 125.6, 128.0, 128.1, 128.7, 129.2, 129.7, 129.9, 135.7, 138.9, 144.4, 146.8; IR (CH_2Cl_2) 3056, 3018, 2921, 1461, 1428 cm^{-1}; HRMS *m/z* 293.9910 (calcd for $C_{14}H_{13}I$, 293.9906).

Heck reactions

The following procedures are representative of the palladium-catalyzed Heck reactions with ethyl acrylate.

Migration reaction conditions A: The appropriate aryl halide (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol), CsO_2CCMe_3 (CsPiv) (0.117 g, 0.5 mmol) and ethyl acrylate (0.025 g, 0.25 mmol) in DMF (4.0 ml) under Ar at 100 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

Migration reaction conditions B: The appropriate aryl halide (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol), CsO_2CCMe_3 (CsPiv) (0.117 g, 0.5 mmol) and ethyl acrylate (0.025 g, 0.25 mmol) in wet DMF (5 % H_2O by volume) (4.0 mL) under Ar at 100 °C were stirred for the specified length

of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

Jeffrey's reaction conditions:[6] The appropriate aryl iodide (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), *n*-Bu_4NCl (0.0694 g, 0.25 mmol), $NaHCO_3$ (0.042 g, 0.5 mmol) and ethyl acrylate (0.10 g, 1.0 mmol) in DMF (1 ml) under Ar at 100 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

Ethyl *E*-3-(4'-methylbiphen-2-yl)acrylate (2a). 2-Iodo-4'-methylbiphenyl (**1a**) (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 day. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 66.6 mg (100 %) of the indicated compound as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.2 Hz, 3H), 2.41 (s, 3H), 4.21 (q, J = 7.2 Hz, 2H), 6.39 (d, J = 16.0 Hz, 1H), 7.18-7.26 (m, 4H), 7.34-7.42 (m, 3H), 7.67-7.70 (m, 1H), 7.75 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.4, 21.2, 60.4, 119.0, 126.8, 127.5, 129.1, 129.8, 129.9, 130.6, 132.7, 137.0, 137.4, 143.0, 144.0, 167.0; IR (CH_2Cl_2) 3024, 2977, 1712, 1631 cm^{-1}; HRMS *m/z* 266.1312 (calcd for $C_{18}H_{18}O_2$, 266.1307).

Ethyl *E*-3-(4-methylbiphen-2-yl)acrylate (3a). Compound **4a** (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 61.9 mg (93 %) of the indicated compound as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.2 Hz, 3H), 2.42 (s, 3H), 4.20 (q, J = 7.2 Hz, 2H), 6.39 (d, J = 16.0 Hz, 1H), 7.25-7.31 (m, 4H), 7.36-7.44 (m, 3H), 7.51-7.51 (m, 1H), 7.72 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.3, 21.2, 60.4, 119.0, 127.3, 127.4, 128.3, 130.0, 130.5, 130.8, 132.5, 137.4, 139.9, 140.3, 143.9, 167.0; IR (CH_2Cl_2) 3026, 2980, 1633, 1711 cm^{-1}; HRMS *m/z* 266.1312 (calcd for $C_{18}H_{18}O_2$, 266.1307).

Ethyl *E*-3-(4'-methylbiphen-2-yl)acrylate (2a) and ethyl *E*-3-(4-methylbiphen-2-yl)acrylate (3a). Compound **1a** (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1.5 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 58.6 mg (88 %) of the indicated compounds as a clear oil in a 50:50 ratio. Similarly, compound **4a** (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1.5 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 57.3 mg (86 %) of the indicated compounds as a clear oil in a 49:51 ratio.

Ethyl *E*-3-(4'-dimethylaminobiphen-2-yl)acrylate (2b). *N,N*-Dimethyl-4-(2-iodophenyl)aniline (**1b**) (80.8 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 day. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 59.0 mg (80 %) of the indicated compound as a yellow solid: mp 117-118 °C; ^{1}H NMR ($CDCl_3$) δ 1.30 (t, J = 7.0 Hz, 3H), 3.01 (s, 6H), 4.22 (q, J = 7.2 Hz, 2H), 6.39 (d, J = 15.6 Hz, 1H), 6.78-6.80 (m, 2H), 7.20-7.22 (m, 2H), 7.31-7.40 (m, 3H),

7.66 (d, J = 7.2 Hz, 1H), 7.84 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.4, 40.6, 60.3, 112.2, 118.5, 126.7, 126.9, 127.7, 129.8, 130.4, 130.7, 132.6, 143.2, 144.7, 150.0, 167.2; IR (CH_2Cl_2) 2975, 2926, 2857, 1715, 1612, 1631, 1526 cm^{-1}; HRMS *m/z* 295.1580 (calcd for $C_{19}H_{21}NO_2$, 295.1572); Anal. C, 77.05, H, 7.29; N, 4.57 (calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.77).

Ethyl *E*-3-(4-dimethylaminobiphen-2-yl)acrylate (3b). *N,N*-Dimethyl-3-iodo-4-phenylaniline (**4b**) (80.8 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 73.8 mg (100 %) of the indicated compound as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.2 Hz, 3H), 3.01 (s, 6H), 4.21 (q, J = 7.2 Hz, 2H), 6.39 (d, J = 15.6 Hz, 1H), 6.85 (dd, J = 8.8, 2.8 Hz, 1H), 6.97 (d, J = 2.8 Hz, 1H), 7.24-7.34 (m, 4H), 7.38-7.42 (m, 2H), 7.77 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.4, 40.6, 60.4, 109.8, 114.7, 118.7, 126.8, 128.2, 130.0, 131.3, 131.6, 133.1, 140.2, 145.1, 149.8, 167.1; IR (CH_2Cl_2) 2975, 2920, 1711, 1632, 1605, 1174 cm^{-1}; HRMS *m/z* 295.1577 (calcd for $C_{19}H_{21}NO_2$, 295.1572).

Ethyl *E*-3-(4'-dimethylaminobiphen-2-yl)acrylate (2b) and ethyl *E*-3-(4-dimethylaminobiphen-2-yl)acrylate (3b). Compound **1b** (80.8 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 66.4 mg (90 %) of the indicated compounds as a clear oil in a 55:45 ratio. Similarly, compound **4b** (80.8 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using

5:1 hexanes/ethyl acetate to afford 68.6 mg (93 %) of the indicated compounds as a clear oil in a 49:51 ratio.

Ethyl *E*-3-(4'-methoxybiphen-2-yl)acrylate (2c). 2-Iodo-4'-methoxybiphenyl (**1c**) (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 70.6 mg (100 %) of the indicated compound as a white solid: mp 67-68 °C; ^{1}H NMR ($CDCl_3$) δ 1.29 (t, J = 7.2 Hz, 3H), 3.86 (s, 3H), 4.21 (q, J = 7.2 Hz, 2H), 6.40 (d, J = 16.0 Hz, 1H), 6.96-6.98 (m, 2H), 7.23-7.25 (m, 2H), 7.34-7.36 (m, 2H), 7.34-7.41 (m, 1H), 7.67-7.69 (m, 1H), 7.75 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.4, 55.4, 60.4, 113.8, 119.0, 126.9, 127.3, 129.9, 130.6, 131.0, 132.3, 132.7, 142.6, 144.1, 159.2, 167.0; IR (CH_2Cl_2) 3060, 2979, 1710, 1631, 1516 cm^{-1}; HRMS *m/z* 282.1259 (calcd for $C_{18}H_{18}O_3$, 282.1256).

Ethyl *E*-3-(4-methoxybiphen-2-yl)acrylate (3c). Compound **4c** (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 69.9 mg (99 %) of the indicated compound as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.2 Hz, 3H), 3.87 (s, 3H), 4.20 (q, J = 7.2 Hz, 2H), 6.38 (d, J = 15.6 Hz, 1H), 7.00 (dd, J = 5.6, 2.8 Hz, 1H), 7.19 (d, J = 2.8 Hz, 1H), 7.27-7.31 (m, 3H), 7.35-7.42 (m, 3H), 7.71 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.5, 55.7, 60.6, 111.4, 116.4, 119.6, 127.4, 128.5, 130.1, 131.9, 133.8, 136.1, 139.9, 144.0, 159.2, 167.0; IR (CH_2Cl_2) 2980, 2935, 1711, 1633, 1481 cm^{-1}; HRMS *m/z* 282.1259 (calcd for $C_{18}H_{18}O_3$, 282.1256).

Ethyl *E*-3-(4'-methoxybiphen-2-yl)acrylate (2c) and ethyl *E*-3-(4-methoxybiphen-2-yl)acrylate (3c). Compound **1c** (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 65.6 mg (93 %) of the indicated compounds as a clear oil in a 52:48 ratio. Similarly, compound **4c** (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 64.9 mg (92 %) of the indicated compounds as a clear oil in a 48:52 ratio.

Ethyl *E*-3-(4'-ethoxycarbonylbiphen-2-yl)acrylate (2d). Ethyl 4-(2-bromophenyl)benzoate (**1d**) (76.2 mg, 0.25 mmol) was allowed to react for 2 d under Jeffrey's reaction conditions with ethyl acrylate plus added 2-(di-*t*-butylphosphino)biphenyl (7.46 mg, 10 mol %). The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 62.4 mg (77 %) of the indicated compound (**2d**) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.0 Hz, 3H), 1.42 (t, J = 7.2 Hz, 3H), 4.21 (q, J = 7.2 Hz, 2H), 4.42 (q, J = 7.2 Hz, 2H), 6.41 (d, J = 15.6 Hz, 1H), 7.36-7.46 (m, 5H), 7.66 (d, J = 16.0 Hz, 1H), 7.70-7.72 (m, 1H), 8.11-8.13 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.3, 14.4, 60.5, 61.1, 119.8, 127.0, 128.3, 129.6, 129.7, 129.9, 130.0, 130.4, 132.7, 141.8, 143.2, 144.5, 166.4, 166.7; IR (CH_2Cl_2) 2880, 2933, 1713, 1633 cm^{-1}; HRMS *m/z* 324.1368 (calcd for $C_{20}H_{20}O_4$, 324.1362). In addition, we also obtained 8.9 mg (11 %) of compound **3d** as a clear oil.

Ethyl *E*-3-(4-ethoxycarbonylbiphen-2-yl)acrylate (3d). Ethyl 3-iodo-4-phenylbenzoate (**4d**) (76.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1

hexanes/ethyl acetate to afford 80.2 mg (99 %) of the indicated compound (**3d**) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.30 (t, J = 7.2 Hz, 3H), 1.43 (t, J = 7.0 Hz, 3H), 4.22 (q, J = 7.2 Hz, 2H), 4.42 (q, J = 7.2 Hz, 2H), 6.52 (d, J = 16.0 Hz, 1H), 7.32-7.33 (m, 2H), 7.42-7.48 (m, 4H), 7.72 (d, J = 16.0 Hz, 1H), 8.08-8.10 (m, 1H), 8.38 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.3, 14.4, 60.6, 61.3, 120.4, 128.2, 128.5, 129.7, 129.9, 130.5, 130.7, 132.9, 139.0, 142.8, 146.9, 166.0, 166.7 (one sp^2 carbon missing due to overlap) ; IR (CH_2Cl_2) 2980, 1717, 1636, 1285, 1245 cm^{-1}; HRMS *m/z* 324.1368 (calcd for $C_{20}H_{20}O_4$, 324.1362).

Ethyl *E*-3-(4'-ethoxycarbonylbiphen-2-yl)acrylate (2d) and ethyl *E*-3-(4-ethoxycarbonylbiphen-2-yl)acrylate (3d). Compound **1d** (76.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions B for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 36.4 mg (45 %) of the indicated compounds as a clear oil in a 47:53 ratio. In addition, we obtained 26.0 mg (46 %) of ethyl 4-phenylbenzoate as a white solid with spectral properties identical to those previously described in the literature.[10] Similarly, compound **4d** (76.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions B for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 67.2 mg (83 %) of the indicated compounds as a clear oil in a 42:58 ratio.

Ethyl *E*-3-(4'-nitrobiphen-2-yl)acrylate (2e). Compound **1e** (81.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions, but Et_3N (50.5 mg, 0.5 mmol) was used in place of $NaHCO_3$ as the base. After 1 d, the reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 63.1 mg (85 %) of the indicated compound **3e** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.29 (t, J = 7.0 Hz, 3H), 4.22 (q, J = 7.2

Hz, 2H), 6.43 (d, J = 16.0 Hz, 1H), 7.36-7.38 (m, 1H), 7.46-7.51 (m, 4H), 7.60 (d, J = 15.6 Hz, 1H), 7.72-7.74 (m, 1H), 8.29-8.32 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.3, 60.7, 120.5, 123.6, 127.3, 129.0, 130.1, 130.3, 130.7, 132.7, 140.3, 142.4, 146.7, 147.3, 166.6; IR (CH_2Cl_2) 2917, 1710, 1517, 1348, 1314, 1179 cm^{-1}; HRMS *m/z* 297.1010 (calcd for $C_{17}H_{15}NO_4$, 297.1001).

Ethyl *E*-3-(4-nitrobiphen-2-yl)acrylate (3e). Compound **4e** (81.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions, but Et_3N (50.5 mg, 0.5 mmol) was used in place of $NaHCO_3$ as the base. After 1 d, the reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 66.1 mg (89 %) of the indicated compound **3e** as a yellow solid: mp = 118-119 °C, ^{1}H NMR ($CDCl_3$) δ 1.31 (t, J = 7.2 Hz, 3H), 4.24 (q, J = 7.2 Hz, 2H), 6.55 (d, J = 15.9 Hz, 1H), 7.31-7.34 (m, 2H), 7.46-7.56 (m, 4H), 7.69 (d, J = 15.9 Hz, 1H), 8.26 (dd, J = 8.4, 2.4 Hz, 1H), 8.55 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.5, 61.0, 122.2, 122.2, 124.2, 128.9, 129.1, 129.7, 131.8, 134.4, 138.1, 141.6, 147.5, 148.8, 166.3; IR (CH_2Cl_2) 2974, 2917, 2849, 1719, 1523, 1347, 1179, 1118 cm^{-1}; HRMS *m/z* 297.1010 (calcd for $C_{17}H_{15}NO_4$, 297.1001); Anal. C, 68.41; H, 4.84; N, 4.51 (calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71).

Ethyl *E*-3-(4'-nitrobiphen-2-yl)acrylate (2e) and ethyl *E*-3-(4-nitrobiphen-2-yl)acrylate (3e). Compound **1e** (81.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions B for 2.5 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 34.2 mg (46 %) of the indicated compounds as a yellow oil in a 39:61 ratio. In addition, we obtained 19.9 mg (40 %) of 4-nitrobiphenyl as a yellow solid with spectral properties identical to those previously

reported.[11] Similarly, compound **4e** (81.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions B for 2.5 d. The reaction mixture was chromatographed using 5:1 hexanes/ethyl acetate to afford 27.5 mg (37 %) of the indicated compounds as a yellow oil in a 33:67 ratio. In addition, we obtained 24.9 mg (50 %) of 4-nitrobiphenyl as a yellow solid with spectral properties identical to those previously reported.[11]

Ethyl *E*-3-(3-phenylbenzofuran-2-yl)acrylate (6a). Compound **5a** (80.0 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 62.1 mg (85 %) of the indicated compound as a white solid: mp 84-85 °C, ^{1}H NMR ($CDCl_3$) δ 1.32 (t, J = 7.2 Hz, 3H), 4.25 (q, J = 7.2 Hz, 2H), 6.68 (d, J = 15.6 Hz, 1H), 7.25-7.29 (m, 1H), 7.40-7.54 (m, 7H), 7.63-7.68 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.4, 60.7, 111.6, 119.4, 121.0, 123.5, 125.7, 127.0, 128.4, 128.4, 129.2, 129.6, 130.3, 131.2, 148.3, 155.0, 167.0; IR (CH_2Cl_2) 3062, 2979, 1709, 1628, 1450 cm^{-1}; HRMS *m/z* 292.1104 (calcd for $C_{19}H_{16}O_3$, 292.1099). Similarly, compound **8a** (80.0 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 57.0 mg (78 %) of the indicated compound as a yellow solid: mp 82-84 °C.

Ethyl *E*-3-[2-(benzofuran-3-yl)phenyl]acrylate (7a). Compound **8a** (80.0 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions at 80 °C for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 54.8 mg (75 %) of the indicated compound as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.24 (t, J = 7.0

Hz, 3H), 4.18 (q, J = 7.2 Hz, 2H), 6.44 (d, J = 16.0 Hz, 1H), 7.24-7.28 (m, 1H), 7.33-7.58 (m, 6H), 7.60 (s, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.86 (d, J = 15.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.3, 60.5, 111.8, 119.8, 119.8, 120.5, 123.2, 124.9, 127.1, 127.6, 128.2, 130.1, 130.7, 132.2, 133.7, 143.1, 143.5, 155.3, 166.8; IR (CH_2Cl_2) 3060, 2979, 1711, 1633, 1452 cm^{-1}; HRMS *m/z* 292.1104 (calcd for $C_{19}H_{16}O_3$, 292.1099).

Ethyl *E*-3-(1-methyl-3-phenylindol-2-yl)acrylate (6b). Compound **5b** (83.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 71.2 mg (94 %) of the indicated compound **6b** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.29 (t, J = 7.2 Hz, 3H), 3.90 (s, 3H), 4.22 (q, J = 7.2 Hz, 2H), 6.23 (d, J = 16.4 Hz, 1H), 7.12-7.14 (m, 1H), 7.33-7.39 (m, 3H), 7.45-7.48 (m, 4H), 7.62 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 16.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.4, 31.7, 60.6, 109.7, 118.7, 120.6, 120.6, 122.7, 124.6, 127.0, 127.2, 128.8, 130.4, 131.1, 133.3, 134.2, 139.1, 167.2; IR (CH_2Cl_2) 3057, 2975, 2927, 1708, 1625, 1369, 1289, 1180 cm^{-1}; HRMS *m/z* 305.1420 (calcd for $C_{20}H_{19}NO_2$, 305.1416).

Ethyl *E*-3-(2-(1-methylindol-3-yl)phenyl)acrylate (7b). Compound **8b** (83.2 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions at 75 °C for 2 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 64.4 mg (85 %) of the indicated compound as a white solid: mp 130-131 °C; ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 3H), 3.85 (s, 3H), 4.19 (q, J = 7.2 Hz, 2H), 6.43 (d, J = 16.0 Hz, 1H), 7.01 (s, 1H), 7.14-7.18 (m, 1H), 7.27-7.39 (m, 3H), 7.42-7.46 (m, 1H), 7.60-7.64 (m, 2H), 7.73 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.4, 33.0,

60.3, 109.5, 113.9, 118.5, 120.0, 120.1, 122.2, 126.6, 127.0, 127.4, 129.4, 129.9, 131.0, 133.2, 136.0, 137.0, 144.6, 167.2; IR (CH_2Cl_2) 2918, 2848, 1712, 1631, 1314 cm^{-1}; HRMS *m/z* 305.1420 (calcd for $C_{20}H_{19}NO_2$, 305.1416); Anal. C, 78.36; H, 6.28; N, 4.45 (calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59).

Ethyl *E*-3-(3',5'-dimethylbiphen-2-yl)acrylate (10). Compound **9** (77.0 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 69.0 mg (97 %) of the indicated compound **10** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, *J* = 7.2 Hz, 3H), 2.36 (s, 6H), 4.20 (q, *J* = 7.2 Hz, 2H), 6.38 (d, *J* = 16.0 Hz, 1H), 6.92 (s, 2H), 7.02 (s, 1H), 7.33-7.41 (m, 3H), 7.67-7.69 (m, 1H), 7.75 (d, *J* = 15.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.4, 21.4, 60.3, 118.9, 126.6, 127.5, 127.8, 129.2, 129.8, 130.5, 132.6, 137.8, 139.9, 143.3, 143.9, 167.0; IR (CH_2Cl_2) 2918, 2976, 1712, 1632, 1313 cm^{-1}; HRMS *m/z* 280.1468 (calcd for $C_{19}H_{20}O_2$, 280.1463).

Ethyl *E*-3-(3-methoxybiphen-2-yl)acrylate (13). Compound **12** (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 55.1 mg (78 %) of the indicated compound **13** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.25 (t, *J* = 7.2 Hz, 3H), 3.94 (s, 3H), 4.16 (q, *J* = 7.2 Hz, 2H), 6.61 (d, *J* = 16.4 Hz, 1H), 6.94-6.96 (m, 2H), 7.28-7.41 (m, 6H), 7.63 (d, *J* = 16.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.3, 55.7, 60.2, 110.0, 121.5, 122.4, 123.0, 127.5, 128.2, 129.9, 130.0, 139.8, 140.6, 145.5, 159.3, 168.0; IR (CH_2Cl_2) 3054, 2985, 2926, 1705, 1265, cm^{-1}; HRMS 282.1256*m/z* (calcd for $C_{18}H_{18}O_3$, 282.1256).

Ethyl *E*-3-(3'-methoxybiphen-2-yl)acrylate (14). Compound **19** (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 60.0 mg (85 %) of the indicated compound as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.2 Hz, 3H), 3.83 (s, 3H), 4.21 (q, J = 7.2 Hz, 2H), 6.39 (d, J = 16.0 Hz, 1H), 6.85-6.95 (m, 3H), 7.32-7.43 (m, 4H), 7.68-7.70 (m, 1H), 7.75 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.3, 55.4, 60.4, 113.4, 115.4, 119.2, 122.4, 126.8, 127.8, 129.3, 129.8, 130.4, 132.7, 141.3, 142.8, 143.8, 159.4, 166.9; IR (CH_2Cl_2) 3061, 2980, 1711, 1632, 1314, 1177, cm^{-1}; HRMS *m/z* (calcd for $C_{18}H_{18}O_3$, 282.1256).

Ethyl *E*-3-(5-methoxybiphen-2-yl)acrylate (15). An authentic sample of compound **15** was prepared in two steps from 2-iodo-4-methoxybenzaldehyde[31] [mp 113-114 °C; ^{1}H NMR ($CDCl_3$) δ 3.88 (s, 3H), 6.99 (dd, J = 8.8, 2.4 Hz, 1H), 7.44 (d, J = 2.0 Hz, 1H), 7.85 (d, J = 8.8 Hz, 1H), 9.93 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 102.4, 114.9, 125.4, 128.6, 131.6, 164.4, 194.5] in the following matter. 2-Iodo-4-methoxybenzaldehyde (0.262 g, 1.0 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PPh_3 (26.2 mg, 0.1 mmol), CsF (0.334 g, 2.2 mmol) and phenylboronic acid (0.146 g, 1.2 mmol) in DME (5 ml) under Ar at 90 °C were stirred for 3 h. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column using 7:1 hexanes/ethyl acetate to afford 21.0 mg (99 %) of 2-phenyl-4-methoxybenzaldehyde as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.91 (s, 3H), 6.88 (d, J = 2.4 Hz,

1H), 6.99-7.02 (m, 1H), 7.38-7.47 (m, 5H), 8.03 (d, J = 8.8 Hz, 1H), 9.84 (d, J = 0.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.7, 114.0, 115.2, 127.4, 128.3, 128.4, 129.9, 130.0, 137.9, 148.6, 163.6, 191.1. 2-Phenyl-4-methoxybenzaldehyde (53.0 mg, 0.25 mmol) and (carboethoxymethylene)triphenylphosphorane (0.1305 g, 0.375 mmol) in CH_2Cl_2 (5 ml) were stirred at 60 °C under argon for 15 h. The reaction mixture was allowed to cool to room temperature and the solvent evaporated under reduced pressure. The resulting yellow oil was purified by column chromatography on a silica gel column using 1:9 ethyl acetate/hexanes to afford 43.7 mg (62 %) of the desired compound **15** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.2 Hz, 3H), 3.85 (s, 3H), 4.18 (q, J = 7.2 Hz, 2H), 6.29 (d, J = 15.9 Hz, 1H), 6.87 (d, J = 2.7 Hz, 1H), 6.92-6.95 (m, 1H), 7.29-7.33 (m, 2H), 7.39-7.44 (m, 3H), 7.64-7.69 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.5, 55.7, 60.4, 114.2, 115.4, 117.0, 125.6, 127.9, 128.5, 128.5, 129.9, 140.1, 143.4, 145.1, 160.9, 167.4; IR (CH_2Cl_2) 3056, 2978, 2937, 1709, 1630. 1600, 1484 cm^{-1}; HRMS *m/z* (calcd for $C_{18}H_{18}O_3$, 282.1256).

Ethyl *E*-3-(3-methoxybiphen-2-yl)acrylate (13), ethyl *E*-3-(3'-methoxybiphen-2-yl)acrylate (14), and ethyl *E*-3-(5-methoxybiphen-2-yl)acrylate (15). Compound **12** (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 2 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 68.5 mg (97 %) of the indicated compounds as a clear oil in a 53:38:9 ratio. Similarly, compound **19** (77.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 61.3 mg (87 %) of the indicated compounds as a clear oil in a 25:62:13 ratio.

Ethyl *E*-3-(2'-methylbiphen-2-yl)acrylate (21). Compound **21** (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under Jeffrey's reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 61.2 mg (92 %) of the indicated compound **21** as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.24 (t, J = 7.2 Hz, 3H), 2.03 (s, 3H), 4.16 (q, J = 7.2 Hz, 2H), 6.33 (d, J = 16.0 Hz, 1H), 7.10 (d, J = 7.2 Hz, 1H), 7.20-7.29 (m, 4H), 7.37-7.44 (m, 3H), 7.70-7.72 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.3, 20.1, 60.4, 119.0, 125.7, 126.2, 127.7, 128.0, 129.8, 129.9, 130.1, 130.5, 133.0, 136.1, 139.6, 142.9, 143.0, 166.9; IR (CH_2Cl_2) 3061, 2978, 2920, 1713, 1633, 1177 cm^{-1}; HRMS *m/z* 266.1312 (calcd for $C_{18}H_{18}O_2$, 266.1307).

Ethyl *E*-3-(2'-methylbiphen-2-yl)acrylate (21) and ethyl *E*-3-(6-methylbiphen-2-yl)acrylate (22). Compound **20** (73.5 mg, 0.25 mmol) was allowed to react with ethyl acrylate under our standard migration reaction conditions A for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 60.5 mg (91 %) of the indicated compounds as a yellow oil in a 65:35 ratio. Minor isomer **22**: ^{1}H NMR ($CDCl_3$) δ 2.08 (s, 3H), 6.27 (d, J = 16.0 Hz, 1H), 7.54-7.56 (m, 1H) as characteristic peaks; ^{13}C NMR ($CDCl_3$) δ 20.9, 60.3, 118.8, 123.8, 127.4, 127.5, 128.5, 129.7, 131.5, 133.4, 137.0, 138.9, 142.8, 143.9, 143.9 as characteristic peaks; HRMS *m/z* 266.1312 (calcd for $C_{18}H_{18}O_2$, 266.1307).

1-Methoxy-9,10-diphenylphenanthrene (27). 2-Iodo-3-methoxybiphenyl (**12**) (77.5 mg, 0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), LiCl (0.0105 g, 0.25 mmol), NaOAc (0.0175 g, 0.5 mmol) and diphenylacetylene (0.0534 g, 0.30 mmol) in DMF (4 ml) under Ar at 100 °C were stirred for 2 d. The reaction mixture was then cooled to room temperature,

diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using 25:1 hexanes/ethyl acetate to afford 81.1 mg (90 %) of the indicated compound **27** as a white solid: mp 188-189 °C; ^{1}H NMR ($CDCl_3$) δ 3.34 (s, 3H), 6.96-7.20 (m, 11H), 7.43-7.45 (m, 2H), 7.58-7.63 (m, 2H), 8.46 (d, J = 8.1 Hz, 1H), 8.77 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 109.3, 115.5, 122.6, 123.1, 124.8, 126.2, 126.2, 126.4, 126.8, 126.9, 127.4, 127.8, 129.5, 129.7, 131.3, 132.1, 132.2, 135.1, 138.2, 139.8, 144.1, 157.9; IR (CH_2Cl_2) 3026, 1576, 1462 cm^{-1}; HRMS *m/z* 360.1521 (calcd for $C_{27}H_{20}O$, 360.1514).

3-Methoxy-9,10-diphenylphenanthrene (28). Compound **12** (77.5 mg, 0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol), CsPiv (0.117 g, 0.5 mmol) and diphenylacetylene (0.0534 g, 0.30 mmol) in DMF (4 ml) under Ar at 100 °C were stirred for 2 d. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using 25:1 hexanes/ethyl acetate to afford 40.0 mg (44 %) of compound **27**, alongside 38.4 mg (43 %) of compound **28** as a white solid: mp 184-186 °C; ^{1}H NMR ($CDCl_3$) δ 4.03 (s, 3H), 7.11-7.25 (m, 11H), 7.47-7.49 (m, 2H), 7.54-7.56 (m, 1H), 7.61-7.65 (m, 1H), 8.17 (d, J = 2.4 Hz, 1H), 8.72 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.6, 104.0, 116.5, 122.6, 126.0, 126.4, 126.5, 126.6, 126.8, 127.6, 127.9, 129.4, 129.5, 131.1, 131.3, 131.5, 132.4, 135.0, 137.1, 139.7, 139.8, 158.3 (missing one sp^2 carbon due to

overlap); IR (CH_2Cl_2) 3056, 3022, 1576, 1460 cm^{-1}; HRMS *m/z* 360.1521 (calcd for $C_{27}H_{20}O$, 360.1514).

Suzuki-Miyaura reactions

The following procedures are representative of the Suzuki-Miyaura cross-coupling reactions of *o*-iodobiaryls with arylboronic acids.

Migration reaction conditions C: The appropriate aryl iodide (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol), CsO_2CCMe_3 (CsPiv) (0.117 g, 0.5 mmol), Me_3CCO_2H (0.051 g, 0.5 mmol), H_2O (0.09 g, 5.0 mmol) and the corresponding arylboronic acid (0.35 mmol) in DMF (4.0 ml) under Ar at 100 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

Wright's reaction conditions:[16c] The appropriate aryl iodide (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 5 mol %), PPh_3 (6.56 mg, 10 mol %), CsF (0.084 g, 0.55 mmol), and the corresponding arylboronic acid (0.30 mmol) in DME (1.0 ml) under Ar at 90 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

Methyl 4-(4'-methylbiphen-2-yl)benzoate (23a). Compound **1a** and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under Wright's conditions for 8 h. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 46.6 mg (62 %) of the indicated compound **23a** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 2.3 (s, 3H), 3.89 (s, 3H), 6.97-7.04 (m, 4H), 7.20-7.23 (m, 2H), 7.40-7.44 (m, 4H), 7.87-7.90 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.3, 52.3, 127.6, 128.3, 128.3, 129.0, 129.4, 129.9, 130.1, 130.6, 131.0, 136.6, 138.3, 139.7, 140.9, 146.9, 167.4; IR (CH_2Cl_2) 2918, 3023, 1724, 1277 cm^{-1}; HRMS *m/z* 302.1313 (calcd for $C_{21}H_{18}O_2$, 302.1307).

Methyl 4-(4'-methylbiphen-2-yl)benzoate (23a) and methyl 4-(4-methylbiphen-2-yl)benzoate (24a). Compound **1a** and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under our standard migration conditions C for 1 d. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 59.7 mg (71 % corrected yield) of the indicated compounds as a clear oil in a 51:49 ratio. Minor isomer **24a**: ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 3.88 (s, 3H) as characteristic peaks; HRMS *m/z* 302.1313 (calcd for $C_{21}H_{18}O_2$, 302.1307). In addition, this sample was contaminated with what is presumed to be 4,4'-bis(dimethoxycarbonyl)biphenyl (21 mol %): ^{1}H NMR ($CDCl_3$) δ 3.92 (s, 3H), as a characteristic peak.

4-(4'-Methylbiphen-2-yl)anisole (23b) and 4-(4-methylbiphen-2-yl)anisole (24b). Compound **1a** and 4-methoxyphenylboronic acid (38.0 mg, 0.25 mmol) were allowed to react under our standard migration conditions C for 1 d. The reaction mixture was chromatographed using 30:1 hexanes/ethyl acetate to afford 26.2 mg (38 %) of the indicated compounds as a clear oil in 52:48 ratio. Major isomer **23b**: ^{1}H NMR ($CDCl_3$) δ 2.31 (s, 3H),

3.77 (s, 3H) as characteristic peaks; HRMS *m/z* 274.1353 (calcd for $C_{20}H_{18}O$, 274.1358). Minor isomer **24b**: ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 3H), 3.76 (s, 3H) as characteristic peaks; HRMS *m/z* 274.1353 (calcd for $C_{20}H_{18}O$, 274.1358).

Methyl 4-(3-phenylbenzofuran-2-yl)benzoate (25). Compound **5a** and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under our standard migration conditions for 1 d. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 64.9 mg (79 %) of the indicated **25** compound as a white solid: mp 122-123 °C; ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 3H), 7.23-7.27 (m, 1H), 7.34-7.38 (m, 1H), 7.43-7.51 (m, 6H), 7.56-7.58 (m, 1H), 7.71-7.73 (m, 2H), 7.96-7.98 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 52.2, 111.3, 119.6, 120.4, 123.2, 125.5, 126.6, 128.1, 129.2, 129.4, 129.7, 130.1, 132.4, 134.9, 149.3, 154.2, 166.7 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 2917, 2849, 1727, 1609, 1453, 1278, 1118 cm^{-1}; HRMS *m/z* 328.1104 (calcd for $C_{22}H_{16}O_3$, 328.1099); Anal. C, 80.12; H, 4.81; N (calcd for $C_{22}H_{16}O_3$: C, 80.47; H, 4.91). In addition, compound **8a** and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under our standard migration conditions C for 1 d. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 63.9 mg (78 %) of the indicated compound as a white solid.

Methyl 4-[2-(benzofuran-3-yl)phenyl]benzoate (26). Compound **8a** and 4-(methoxycarbonyl)phenylboronic acid were allowed to react under Wright's conditions for 6 h. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 61.5 mg (75 %) of the indicated compound **26** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.87 (s, 3H), 7.11-7.14 (m, 1H), 7.21-7.27 (m, 2H), 7.30-7.34 (m, 3H), 7.42-7.49 (m, 4H), 7.58-7.60 (m, 1H), 7.87-7.89 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 52.3, 111.7, 120.6, 121.2, 123.0, 124.6, 127.4,

128.3, 128.4, 128.8, 129.5, 129.6, 130.1, 130.8, 131.1, 140.7, 143.1, 146.4, 155.3, 167.2; IR (CH_2Cl_2) 2850, 2973, 1723, 1609, 1452, 1279 cm^{-1}; HRMS *m/z* 328.1104 (calcd for $C_{22}H_{16}O_3$, 328.1099). In addition, we isolated 6.0 mg (7 %) of compound **25** from this reaction mixture.

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References

(1) (a) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379. (b) Gibson, S. E.; Middleton, R. J. *Contemp. Org. Synth.* **1996**, *3*, 447. (c) Overman, L. E. *Pure Appl. Chem.* **1994**, *66*, 1423. (d) Shibasaki, M.; Boden, C. D. J.; Kojima, A. *Tetrahedron* **1997**, *22*, 7371. (e) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2.

(2) (a) Diaz-Ortiz, A.; Prieto, P.; Vazquez, E. *Synlett* **1997**, 269. (b) Heck, R. F. *Org. React.* **1982**, *27*, 345.

(3) Campo, M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2002**, *124*, 14326.

(4) Karig, G.; Moon, M.-T.; Thasana, N.; Gallagher, T. *Org. Lett.* **2002**, *4*, 3115.

(5) Larock, R. C.; Tian, Q. *J. Org. Chem.* **2001**, *66*, 7372.

(6) Jeffrey, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287.

(7) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550.

(8) Li, G. Y.; Zheng, G.; Noonan, A. F. *J. Org. Chem.* **2001**, *66*, 8677.

(9) The spectral properties of this compound were identical to those previously reported, see: Bregbreiter, D. E.; Osburn, P. L.; Wilson, A.; Sink, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 9058.

(10) The spectral properties of this compound were identical to those previously reported, see: Rottlaender, M.; Knochel, P.; *J. Org. Chem.* **1998**, *63*, 203.

(11) The spectral properties of this compound were identical to those previously reported, see: Wallow, T. I.; Novak, B. M. *J. Org. Chem.* **1994**, *59*, 5034.

(12) (a) Catellani, M.; Motti, E; Minari, M. *Chem. Comm.* **2000**, 157. (b) Catellani, M.; Motti, E.; Paterlini, L. *J. Organomet. Chem.* **2000**, *593*, 240. (c) Catellani, M.; Cugini, F. *Tetrahedron* **1999**, *55*, 6595. (d) Catellani, M.; Frignani, F; Rangoni, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 119. (e) Catellani, M.; Fagnola, M. C. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2421. (f) Canty, A. J. *Acc. Chem. Res.* **1992**, *25*, 83. (g) Catellani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1985**, *286*, C13.

(13) For mechanistic studies suggesting electrophilic species in intramolecular C-H activation by palladium, see: (a) Martin-Matute, B.; Mateo, C.; Cardenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2001**, *7*, 2341. (b) Catellani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1992**, *425*, 151.

(14) Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. H.; Koseki, S.; Matsunaga, N.; Nguyen, N.; Su, S. J.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comput. Chem.* **1993**, *14*, 1347.

(15) For examples of electrophilic aromatic substitutions involving 3-phenylbenzofuran, see: (a) Callens, R. E. A.; Duquet, D.; Borremans, F. A. M.; Anteunis, M. J. O. *Bull Soc. Chim. Belg.* **1985**, *94*, 39. (b) Chatterjea, J. N.; Singh, K. R. R. P. *Indian J. Chem., Sect. B* **1981**, *20B*, 1053.

(16) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147. (c) Wright, S. W.; Hageman, D. L.; McClure, L. D. *J. Org. Chem.* **1994**, *59*, 6095.

(17) Netherton, M. R.; Dai, C.; Neushutz, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 10099.

(18) Larock, R. C.; Doty, M. J; Tian, Q.; Zenner, J. M. *J. Org. Chem.* **1997**, *62*, 7536.

(19) For similar pallada(II)cycle reactions with alkynes, see: Portscheller, J. L.; Malinakova, H. C. *Org. Lett.* **2002**, *4*, 3679 and references therein.

(20) (a) Campo, M. A.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3675. (b) Campo, M. A.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 5616.

(21) Ueyama, N.; Yanagisawa, T.; Tomiyama, T. *J. Labelled Comp. Radiopharm.* **1995**, *10*, 915.

(22) Hellwinkel, D. *Chem. Ber.* **1966**, *99*, 3642.

(23) Brandsher, C. K.; Brown, F. C.; Leake, P. H. *J. Org. Chem.* **1957**, *22*, 500.

(24) Murray, M. M.; Kaszynski, P.; Kaisaki, D. A.; Dougherty, D. A. *J. Am. Chem. Soc.* **1994**, *116*, 8152.

(25) Ozasa, S.; Fujoka, Y.; Tsukada, M.; Ibuki, E. *Chem. Pharm. Bull.* **1981**, *29*, 344.

(26) Ma, C.; Liu, X.; Li, X.; Flippen-Anderson, J.; Yu, S.; Cook, J. M. *J. Org. Chem.* **2001**, *66*, 4525.

(27) Larock, R. C.; Yum, E. K.; Doty, M. J.; Sham, K. K. C. *J. Org. Chem* **1995**, *60*, 3270.

(28) Miller, R. B.; McGarvey, G. *Synth. Commun.* **1978**, *8*, 291.

(29) Gibson, S. E.; Guillo, N.; Middleton, R. J.; Thuilliez, A.; Tozer, M. J. *J. Chem Soc. Perkin Trans. 1* **1997**, 447.

(30) Hart, H.; Harada, K.; Du, C. *J. Org. Chem.* **1985**, *50*, 3104.

(31) Karl, J.; Gust, R.; Spruss, T.; Schneider, M. R.; Schoenenberger, H.; Engel, J.; Wrobel, K. H.; Lux, F.; Haeberlin, S. T. *J. Med. Chem.* **1988**, *31*, 72.

CHAPTER 3. SEQUENTIAL 1,4-PALLADIUM MIGRATION FOLLOWED BY INTRAMOLECULAR ARYLATION: SYNTHESIS OF FUSED POLYCYCLES

Based on a communication to be submitted to the *Journal of the American Chemical Society* and a paper to be submitted to the *Journal of the American Chemical Society*

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Abstract

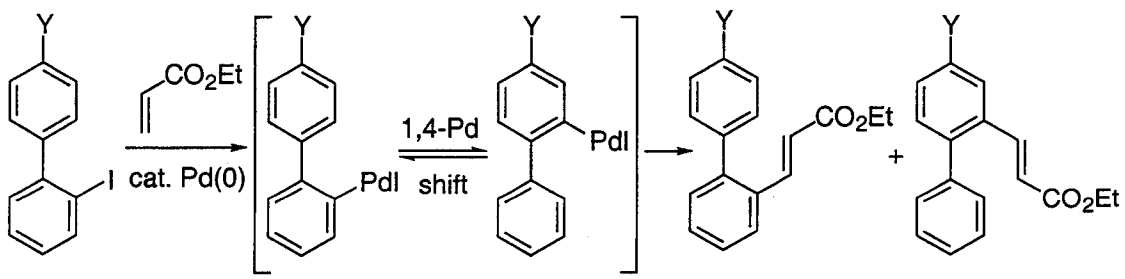
The synthesis of various fused carbocycles and heterocycles has been accomplished by the Pd-catalyzed intramolecular C-H activation of *o*-halobiaryls. This methodology makes use of a 1,4-palladium migration to generate key organopalladium intermediates, which undergo intramolecular arylation producing complex polycyclic compounds containing fused benzofuran, quinoline, oxepine, indole, phenanthrene, and naphthalene rings. This methodology offers a unique approach to the preparation of complex systems, which would be difficult to access by other known methodologies.

Introduction

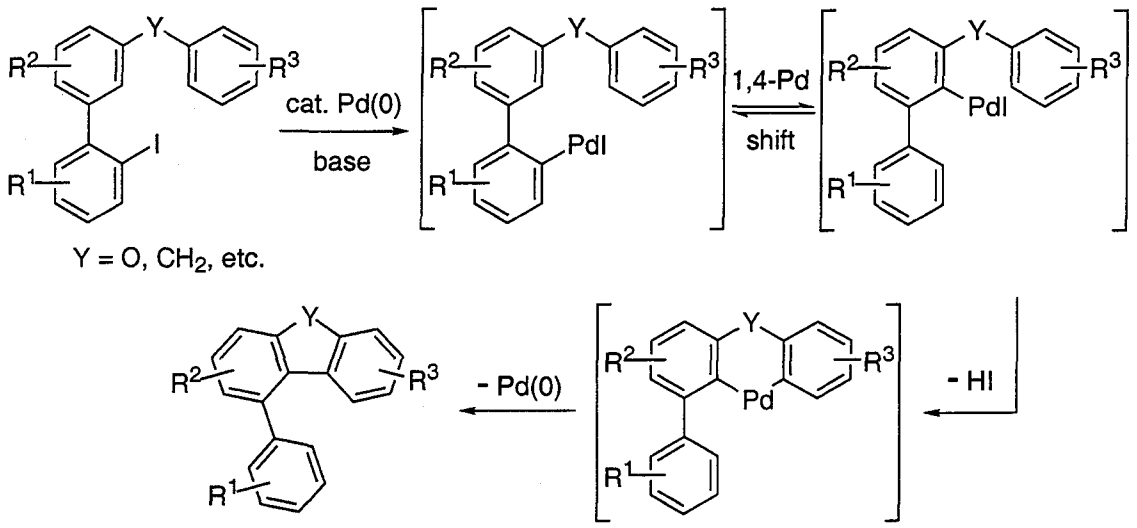
The ability of palladium to activate C-H bonds has been used extensively in organic synthesis.[1] In recent years, palladium-catalyzed C-H activation has received considerable attention due to the wide variety of reactions this metal will catalyze. For instance, catalytic amounts of Pd salts have been used to activate the addition of C-H bonds of electron-rich

arenes to alkenes and alkynes, as well as to undergo other transformations, such as carbonylation.[2] We have previously reported the synthesis of 9-benzylidene-9*H*-fluorenes by Pd-catalyzed intramolecular C-H activation involving the rearrangement of organopalladium intermediates derived from aryl halides and internal alkynes.[3] Similarly, intramolecular C-H activation in organopalladium intermediates derived from *o*-halobiaryls leads to a 1,4-palladium migration (Scheme 1).[4] We have already shown that such intermediates can be trapped by Heck, Suzuki and alkyne annulation reactions. We have recently explored the synthetic potential of this aryl-aryl migration process, and now wish to report a novel synthesis of fused polycycles using this novel rearrangement. Our strategy involves the use of palladium C-H activation to catalyze a 1,4-palladium migration within biaryls generating key arylpalladium intermediates, which subsequently undergo C-C bond formation by intramolecular arylation producing fused polycycles (Scheme 2). This process represents a very powerful new tool for the preparation of complex molecules, which might be difficult to prepare by any other present methodology.

Scheme 1



Scheme 2

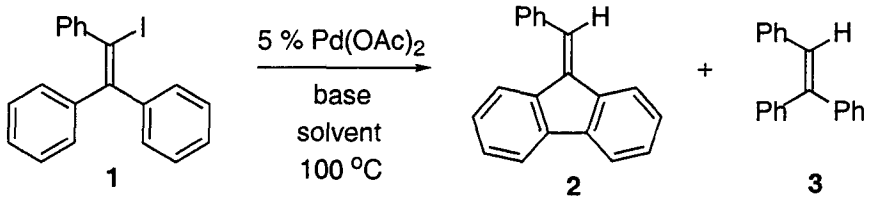


Results and Discussion

In order to obtain an optimum set of reaction conditions for migration, we have reinvestigated the palladium-catalyzed transformation of 1-iodo-1,2,2-triphenylethene (**1**) to 9-benzylidene-9*H*-fluorene (**2**) as our model system[3] (Table 1). While this system may not be the most obvious for a study of aryl to aryl Pd migrations, we had previously accumulated substantial data on this system. To begin with, we carried out this reaction using our previously reported conditions[3] and obtained a 73 % yield of the desired compound **2**, along with a 15 % yield of triphenylethene (**3**) (entry 1). The first variable to be examined was the ligand on palladium. We examined phosphines other that PPh_3. Entries 2 and 3 indicate that P(*o*-tolyl)$_3$ and $CH_2(PPh_2)_2$ (dppm) are superior to PPh_3 in affording higher yields of the fluorene **2**. However, the reactions with all of these phosphine ligands required 3 d to reach completion. In order to shorten this relatively lengthy reaction time, we eliminated *n*-Bu_4NCl (TBAC) and found that the reaction was complete after only 1 d (entry 4). Unfortunately,

this led to a much lower yield of the desired compound **2** (47 %), and the yield of reduced product **3** increased to 47 %. In order to investigate whether DMF was the hydride source for the reduction of **1** to **3**, we carried out this reaction using other solvents,

Table 1. Palladium-catalyzed transformation of 1-iodo-1,2,2-triphenylethene (**1**) to 9-benzylidenefluorene (**2**).[a]



1 2 3

entry	ligand (mol %)	base	chloride source	solvent	time (d)	% yield **1**	% yield **2**
1	PPh_3 (10)	NaOAc	TBAC[b]	DMF	3	73	15
2	P(*o*-tolyl)$_3$ (10)	NaOAc	TBAC	DMF	3	75	20
3	dppm[c] (5)	NaOAc	TBAC	DMF	3	79	15
4	dppm (5)	NaOAc	-	DMF	1	47	47
5	dppm (5)	NaOAc	-	DMA	1.5	52	48
6	dppm (5)	NaOAc	-	NMP	1	46	46
7	dppm (5)	NaOAc	-	DMSO	1	-	-
8	dppm (5)	pyridine	-	DMF	1	-	-
9	dppm (5)	*i*-Pr_2NEt	-	DMF	1	-	-
10	dppm (5)	Na_2CO_3	-	DMF	1	70	26
11	dppm (5)	$NaHCO_3$	-	DMF	1	65	23
12	dppm (5)	Na_2CO_3[d]	-	DMF	1	-	47
13	dppm (5)	Cs_2CO_3	-	DMF	1	74	22
14	dppm (5)	CsOAc	-	DMF	2	90	4
15	dppm (5)	CsO_2CCMe_3	-	DMF	1	96	4
16	dppm (5)	CsO_2CCMe_3	-	DMA	1	59	17[e]
17	dppe[f] (5)	CsO_2CCMe_3	-	DMF	1	90	10
18	dppm (5)	*n*-Bu_4NOAc	-	DMF	1	<10	-

[a]The reaction was run using 0.25 mmol of 1-iodo-1,2,2-triphenylethene (**1**), 5 mol % of $Pd(OAc)_2$ and 4 mL of solvent at 100 °C. [b]TBAC = *n*-Bu_4NCl. [c]Dppm = 1,1-bis(diphenylphosphino)methane. [d]One equiv of NaI was added. [e]Twenty four percent of **1** was recovered. [f]Dppe = 1,2-bis(diphenylphosphino)ethane.

such as DMA, NMP, and DMSO (entries 5-7). DMSO gave none of the desired fluorene **2** or any reduction product **3**. The amount of reduction was more or less the same in the other solvents. Thus, we continued our investigation using DMF as the reaction solvent.

We also examined the effect of various bases on the yield of **3**, including organic bases, such as pyridine and diisopropylethylamine (entries 8 and 9). These bases were ineffective in promoting the reaction and TLC analysis of the reaction mixtures indicated only the presence of starting vinylic halide **1**. The use of Na_2CO_3 as the base provided **2** in a 70 % yield, but we also obtained a 26 % yield of reduced product **3**. The base $NaHCO_3$ provided a 65 % yield of **2** and a 23 % yield of **3**. We believe that the solubility of these bases in the reaction mixture may be playing a critical role in determining the outcome. Thus, once again we used Na_2CO_3 as the base, but this time we added 1 equiv of NaI, which is completely soluble in DMF, as an additive to promote a sodium common ion effect intended to make Na_2CO_3 less soluble in the reaction mixture. Indeed, this experiment revealed that under such reaction conditions only reduced product **3** was produced in a 47 % yield. None of the desired product **2** was observed (compare entries 10 and 12). Although there may be a number of other effects going on under these reaction conditions, it seemed logical to assume that the yield of the reaction would improve by using more soluble inorganic bases. Thus, the use of Cs_2CO_3, which presumably has better solubility than other alkali carbonates in DMF,[5] provided a slightly higher 74 % yield of compound **2**, along with a 22 % yield of reduced product **3**. Similarly, the use of very soluble CsOAc as base provided a 90 % yield of the desired product **2**, along with 4 % of the reduced product **3** after 2 d (entry 14). We subsequently found that cesium pivalate (CsO_2CCMe_3), unlike any other

previously studied base, was completely soluble in DMF at 100 °C. In this case, we obtained an impressive 96 % yield of the desired compound **2**, along with only a small amount of the reduced product **3** (4 %) after only 1 d (entry 15). Clearly, cesium pivalate is far superior as a base in this reaction, and its high solubility in DMF seems to explain this phenomena. To illustrate, we carried out the reaction of **1** under conditions identical to those described in entry 15, but we used DMA instead of DMF as the solvent, in which cesium pivalate is not completely soluble. Under these conditions, we obtained a relatively low 59 % yield of the desired compound **2**, along with a 17 % yield of reduced product **3** (entry 16). Twenty four percent of the starting vinylic iodide **1** was also obtained. Finally, to test whether dppm was indeed critical to this reaction, we carried out the transformation using another chelating phosphine ligand, namely 1,2-bis(diphenylphosphino)ethane (dppe), and we obtained a 90 % yield of **2**, along with a 10 % yield of the reduced product **3** (entry 17). As a result, our optimal set of reaction conditions for this transformation are those listed in entry 15 of Table 1. Notice that the newly developed conditions catalyze the transformation of **1** to **2** in high yield and much shorter reaction time than our earlier reported procedure.[3] The most critical element to achieve these positive results was the use of the highly soluble cesium pivalate base. Surprisingly, the use of *n*-Bu_4NOAc as the base, which is also completely soluble in DMF under reaction conditions identical to those described in entry 15, failed to promote this reaction, affording only trace amounts of the desired product **2** after 1 d. As a result, not only the solubility, but also the exact nature of the base, appears critical in determining the reaction yield. It is interesting to note that the work of Buchwald, Hartwig and Fu has demonstrated that steric congestion imposed on palladium by bulky, electron-rich ligands

facilitate both the oxidative addition and reductive elimination steps involving palladium, and give rise to more effective catalyst systems.[6] However, nothing is apparently known about the effects of using a sterically hindered base, such as pivalate, in palladium chemistry, and whether or not it may give similar results to those obtained using bulky ligands.

With an apparently "optimal" set of reaction conditions at our disposal, we proceeded to study the sequential Pd-catalyzed migration/arylation of various 3'-substituted 2-iodobiphenyls (Table 2). We began by allowing 3'-benzyl-2-iodobiphenyl (**4**) to react under our standard reaction conditions at 100 °C, but after 2 d this substrate failed to react. However, by simply increasing the reaction temperature to 110 °C, we were able to obtain the desired compound **5** in a 40 % yield (entry 1). The disappointingly low yield obtained with this substrate might be explained by the poor reactivity of the benzyl moiety as an intramolecular trap. To test this idea, we carried out the reaction with the more electron-rich 2-iodo-3'-phenoxybiphenyl (**6**) and obtained the desired 4-phenyldibenzofuran (**7**) in an impressive 89 % yield (entry 2). Clearly, these results indicate that the electron-rich oxygen-substituted phenyl ring was superior as an arylating agent. Our finding that electron-rich arenes are superior to electron-neutral arene traps is consistent with literature reports indicating that the ease of C-H activation by palladium parallels electrophilic aromatic substitution.[7] Similarly, we were able to selectively obtain 3-chloro-5-phenyldibenzofuran (**9**) in an 82 % yield from 3-(*p*-chlorophenoxy)-2-iodobiphenyl (**8**) under our standard conditions while leaving the chloro functionality intact (entry 3).

Motivated by the ease of preparation of the following starting materials and by the knowledge that electron-rich arenes are apparently superior as intramolecular traps for our

Table 2. Palladium-catalyzed transformation of *o*-halobiaryls.[a]

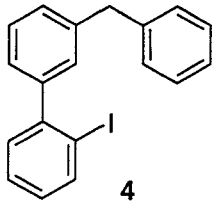
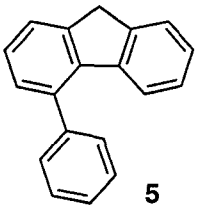
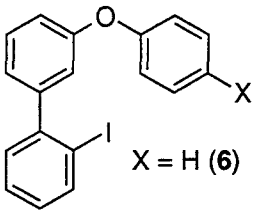
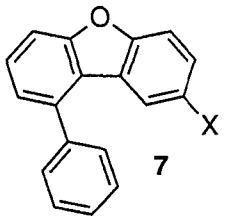
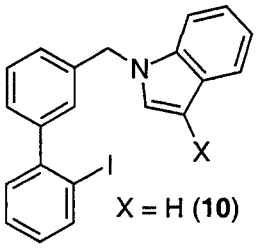
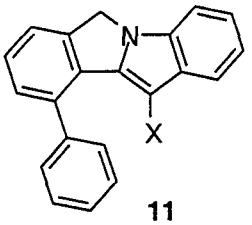
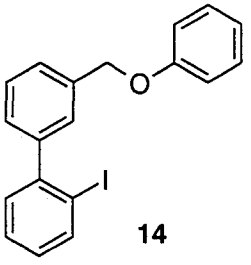
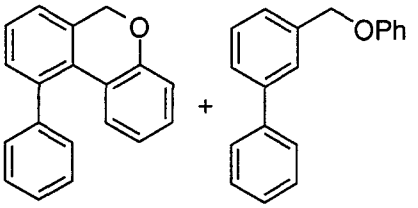
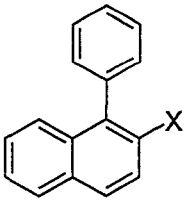
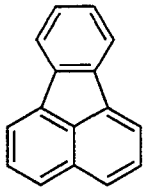
entry	substrate	product(s)	time (d)	% yield[b]
1	 **4**	 **5**	3[c]	40
2	 X = H (**6**)	 **7**	1[c]	89
3	X = Cl (**8**)	**9**	1[c]	82
4	 X = H (**10**)	 **11**	1	70
5	X = Me (**12**)	**13**	1	71
6	 **14**	 **15** **16**	2[d]	75 (60 : 40)
7	 X = I (**17**)	 **18**	1[c]	81
8	X = Br (**19**)		3[c]	70

Table 2. (continued)

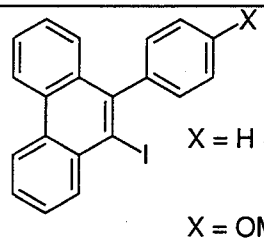
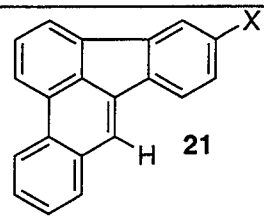
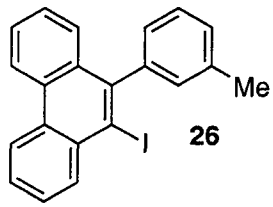
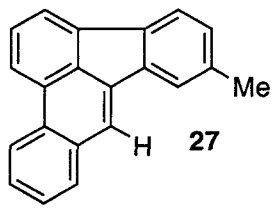
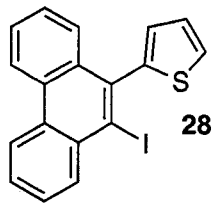
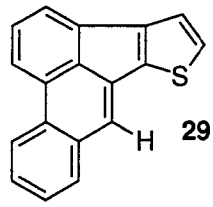
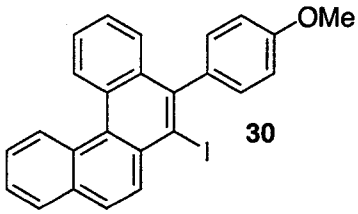
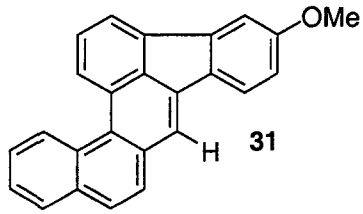
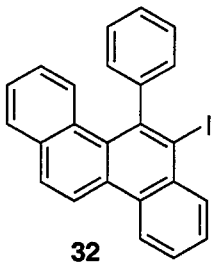
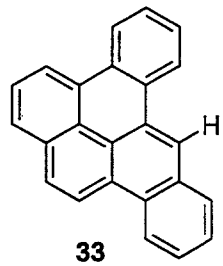
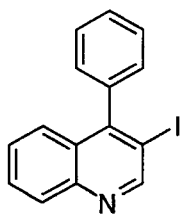
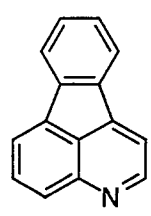
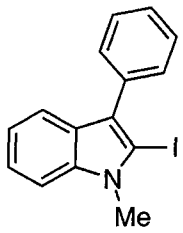
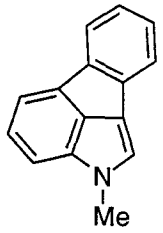
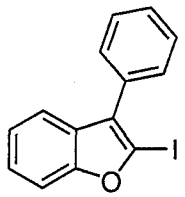
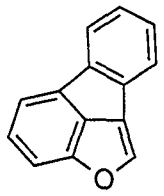
entry	substrate	product(s)	time (d)	% yield[b]
9	 X = H (**20**)	 **21**	2[c]	78 (18)
10	X = OMe (**22**)	**23**	2[c]	71 (22)
11	X = CO_2Et (**24**)	**25**	2[c]	50 (20)
12	 **26**	 **27**	2[c]	56 (37)
13	 **28**	 **29**	2[c]	0
14	 **30**	 **31**	2[c]	65
15	 **32**	 **33**	2[c]	0 (80)
16	 **34**	 **35**	2.5[c]	54

Table 2. (continued)

entry	substrate	product(s)	time (d)	% yield[b]
17	 **36**	 **37**	2[c]	0
18	 **38**	 **39**	2[c]	0

[a]The reaction was carried under the previously described standard conditions employing 0.25 mmol of the *o*-halobiaryl, 5 mol % $Pd(OAc)_2$, 5 mol % dppm, and 2 equivs of CsO_2CCMe_3 in DMF (4 mL) at 100 °C unless otherwise noted. [b]The yield in parentheses corresponds to GC yield of product in which the C-I bond has been reduced to a C-H. [c]The reaction temperature was increased to 110 °C. [d]The reaction temperature was increased to 120 °C.

arylpalladium intermediates, we synthesized the indole derivatives **10** and **12**. To our great satisfaction, compound **10** smoothly underwent the desired reaction producing the relatively strained isoindoloindole **11** in a 70 % yield (entry 4). Surprisingly, compound **12** produced the strained and sterically congested 2-methyl isoindoloindole **13** in a 71 % yield. We next examined the possibility of using an intramolecular arylation to form six-membered rings. Unfortunately, 3-(2-iodophenyl)benzyl phenyl ether (**14**) failed to react under our standard reaction conditions. Even at 110 °C, the reaction was sluggish, so the temperature was increased to 120 °C, in which case the reaction was complete after 2 d. Unfortunately, a 60:40 inseparable mixture of the desired compound **15** and reduced product **16** was obtained in a 75 % overall yield. Clearly, the formation of a six-membered ring is not as favorable as

five-membered ring formation (compare entries 2 and 6). This might be due to the intermediacy of an unfavorable seven-membered ring palladacycle (Figure 1).

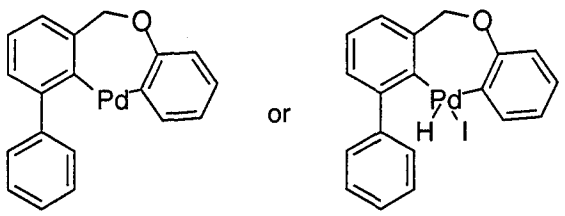
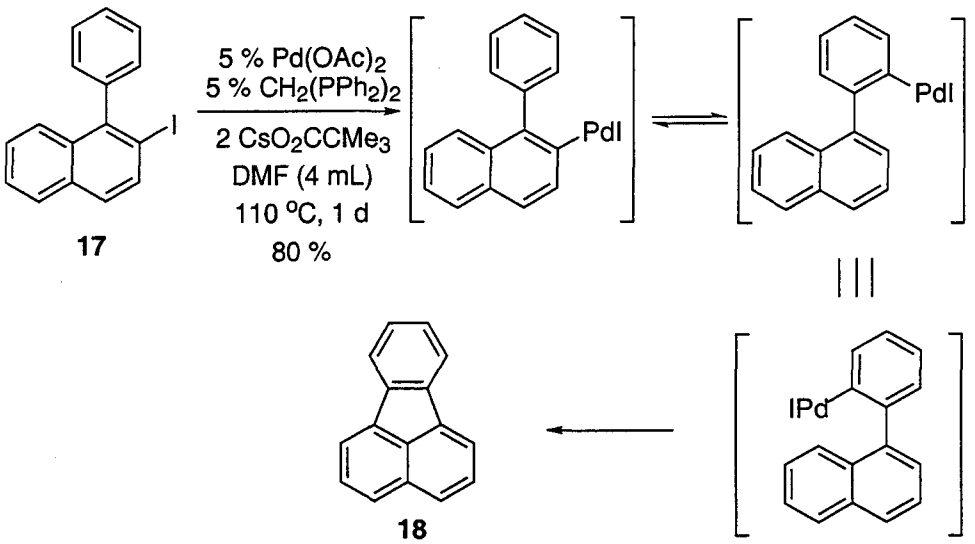


Figure 1. Unfavorable seven-membered ring palladacycle intermediates.

We proceeded to investigate the sequential migration/arylation reaction of more complex polyaromatic compounds. In theory, 2-iodo-1-phenylnaphthalene (**17**) should afford fluoranthene (**18**) using our methodology. Mechanistically, the palladium must first undergo a 1,4-palladium migration from the 2-position of the naphthalene to the *o*-position of the phenyl substituent, followed by arylation at the 8-position of the naphthalene (Scheme 3). Although the reaction did not proceed at 100 °C, at 110 °C, compound **17** produced the

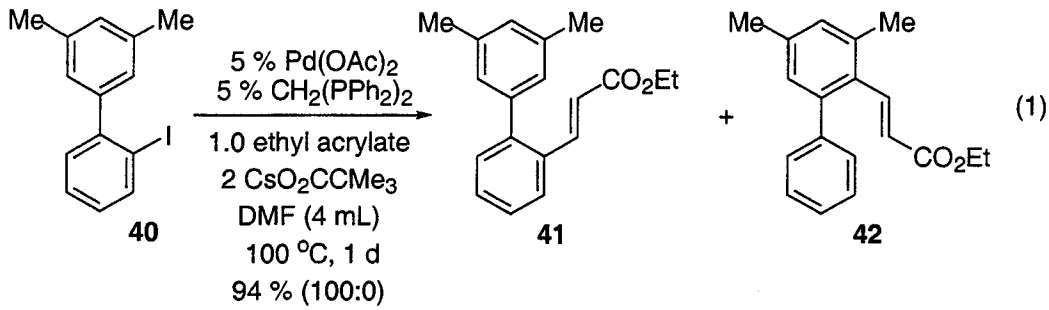
Scheme 3



desired compound **18** in an 81 % yield. Similarly, 2-bromo-1-phenylnaphthalene (**19**) produced the desired fluoranthene (**18**) in a 70 % yield, indicating that this aryl bromide also undergoes the desired transformation, but in a somewhat lower yield and a longer reaction time.

Another interesting example of this migration involves the rearrangement of easily prepared 9-iodo-10-phenylphenanthrenes[8] to benz[*e*]acephenanthrylene. In this case, the palladium migrates from the 9 position of the phenanthrene to the *ortho* position of the phenyl substituent, followed by cyclization onto the 8 position of the phenanthrene. Indeed, the reaction of 9-iodo-10-phenylphenanthrene (**20**) under our standard reaction conditions at 110 °C produced the desired benz[*e*]acephenanthrylene (**21**) in a 78 % yield (entry 9). We proceeded to investigate electronic effects in this phenanthrene reaction by looking at different substituents on the phenyl moiety. As expected, the use of an electron-donating methoxy group in compound **22** gave a good yield (71 %) of the corresponding benz[*e*]acephenanthrylene **23** (entry 10). However, the introduction of an electron-withdrawing CO_2Et group in the *para* position of the phenyl substituent was detrimental to the reaction, producing compound **25** in only a 50 % yield. We have also studied the regioselectivity of the migration by using a 3-methyl-substituted phenyl moiety in the 10-position of the 9-iodophenanthrene (entry 12). Compound **26** has two available positions for palladium migration, the more sterically-congested neighboring 2 position or the remote 6 position of the phenyl ring. The palladium-catalyzed cyclization of compound **26** generated compound **27** exclusively in a 56 % yield. This result indicates that palladium migration occurs exclusively onto the less sterically-congested 6 position of the phenyl moiety and that

the presence of a methyl group apparently completely inhibited migration to the more hindered 2 position. This result is in complete agreement with our previous observation that the Heck reaction of 2-iodo-3',5'-dimethylbiphenyl (**40**) with ethyl acrylate under our standard migration conditions afforded exclusively ester **41** and failed to produce any of the migration product **42** (eq 1).[9] Furthermore, the less statistically favorable palladium migration to only the distal 6 position of the phenyl moiety might help explain the relatively low yield obtained for this transformation.



We next tried to prepare the more strained fused thiophene **29** from phenanthrene **28**. Unfortunately, this reaction led to a very complex mixture, which produced none of the desired compound **29**. Besides the unfavorable ring strain associated with the final product **29**, intramolecular sulfur chelation of the intermediate 10-thiophen-1-ylphenanthren-9-ylpalladium iodide might be inhibiting the palladium migration step (Figure 2).

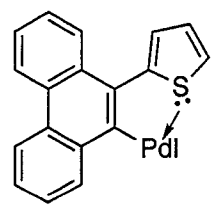


Figure 2. Intramolecular palladium chelation by sulfur.

In addition, the relatively electron-rich benzo[*e*]phenanthrene **30** also underwent the migration/arylation reaction, producing the highly conjugated hexacyclic compound **31** in a

65 % yield (entry 14). Unfortunately, compound **32** failed to generate the desired hexacycle **33** under our reaction conditions at 110 °C (entry 15). Only reduction product was isolated in 80 % yield. This example once again indicates that intramolecular annulation to form a six membered ring is rather unfavorable.

Having studied the palladium-catalyzed transformation of a variety of polycyclic aromatic halides, we switched our attention to heterocyclic aromatic compounds. To begin with, we carried out the reaction of 3-iodo-4-phenylquinoline (**34**) under our standard reaction conditions at 100 °C, but after 2 d this substrate failed to react. Fortunately, by simply increasing the reaction temperature to 110 °C, we obtained the desired indeno[1,2,3-*de*]quinoline (**35**) in a 54 % yield. Again the modest yield obtained with this electron-deficient substrate is consistent with our previous observations that electron-deficient substrates do not perform as well as more electron-rich substrates (compare entries 7 and 16). We also allowed 2-iodo-1-methyl-3-phenylindole (**36**) to react under our standard reaction conditions at 110 °C, but failed to obtain the desired tricyclic compound **37** (entry 17). A similar negative result was obtained with 2-iodo-3-phenylbenzofuran (**38**) (entry 18). The poor results obtained with substrates **36** and **38** can be explained in terms of the unfavorable ring strain of the corresponding products **37** and **39**. In addition, we have previously established, using Heck trapping experiments, that palladium prefers to reside on the benzofuran and indole moieties in these substrates (Scheme 4).[4,9]

Scheme 4

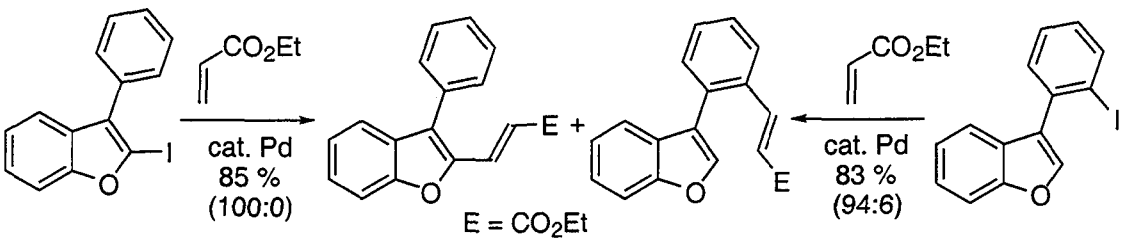
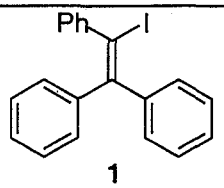
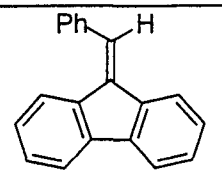
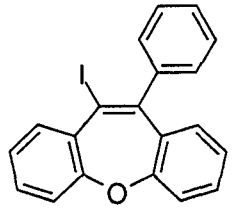
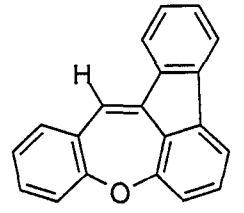
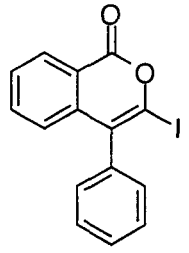
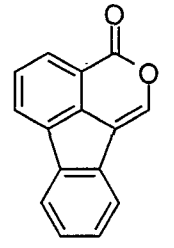
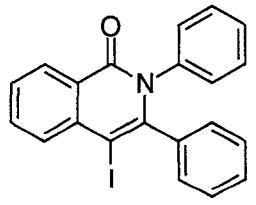
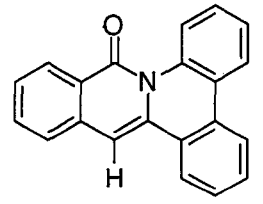


Table 3. Palladium-catalyzed migration and annulation of vinylic iodides.[a]

entry	substrate	product	time (d)	% yield[b]
1	 **1**	 **2**	1	96 (4)
2	 **43**	 **44**	2[c]	80
3	 **45**	 **46**	2	0
4	 **47**	 **48**	5[c]	0 (12)

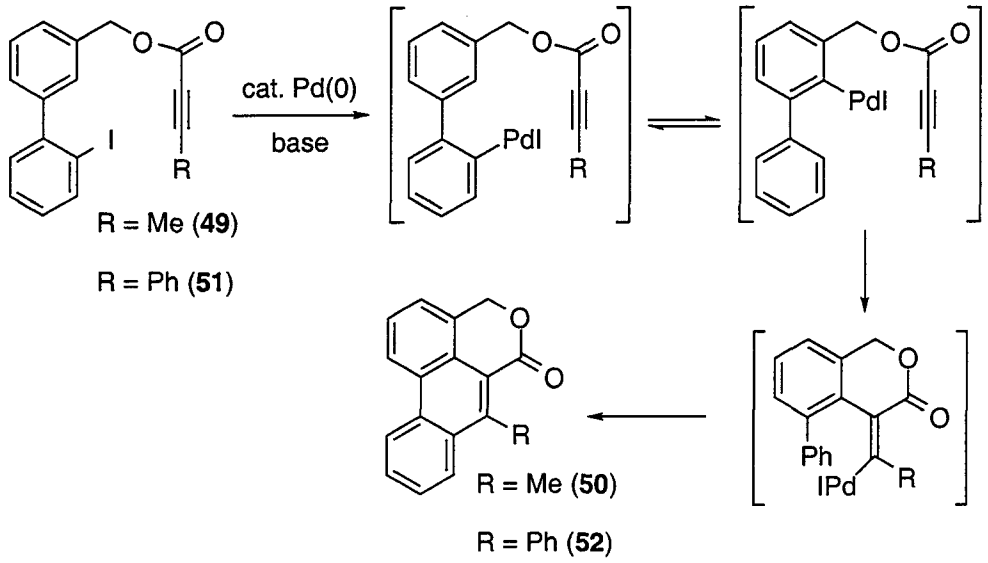
[a]The reaction was carried under the previously described standard Pd migration conditions employing 0.25 mmol of the vinylic iodide, 5 mol % of $Pd(OAc)_2$, 5 mol % of dppm, 2 equiv of CsO_2CCMe_3 in DMF (4 mL) at 100 °C, unless otherwise noted. [b]The yield in parentheses corresponds to the product in which the C-I has been reduced to a C-H bond. [c]The reaction temperature was increased to 110 °C.

While our efforts had been focused on synthesizing polycyclic compounds in which the key 1,4-palladium shift occurs from an aryl to another aryl position, we wanted to establish that our methodology could also make use of a vinylic to aryl palladium migration to generate the key intermediate for the intramolecular arylation step. We have already shown one example of such a transformation in converting compound **1** to **2** (entry 1, Table 3). Another illustration of this process involves the use of 9-iodo-10-phenyldibenz[*b,f*]oxepine (**43**). The reaction of this relatively electron-rich substrate produced the desired pentacyclic compound **44** in an 80 % yield (entry 2). On the other hand, treating the electron-deficient 3-iodo-4-phenylisocoumarin (**45**) under our standard reaction conditions gave a complex mixture, and we failed to isolate any of the desired compound **46** (entry 3). This disappointing result was not unexpected, since our experience with compound **45** has indicated that palladium easily catalyzes its decomposition. Our last attempt to generate polycycles from vinylic iodides involved the use of isoquinolone **47**. This substrate suffers the disadvantage that the intramolecular arylation step requires the formation of a six-membered ring. As expected, the reaction of substrate **47** under our standard reaction conditions at 110 °C failed to produce the desired pentacyclic product **48** and after 5 d of reaction time, we were only able to isolate the reduction product *N*-phenyl-3-phenylisoquinolone[10] in a 12 % yield as a side product (entry 4).

We have also examined the possibility of preparing polycycles using annulation reactions other than the usual intramolecular arylation. The first set of experiments involved the use of intramolecular alkyne annulation reactions (entries 1 and 2, Table 4; Scheme 5). We have previously established that the corresponding intermolecular version of this alkyne

annulation methodology works well under our migration conditions.[4] Therefore, it was surprising to find that the reaction of either compound **49** or **51** gave complex reaction mixtures and that none of the desired tetracyclic compounds **50** or **52** could be isolated. It is conceivable that intermolecular side reactions might be giving rise to dimers, trimers and other oligomers, which would account for the complexity of these reaction mixtures.

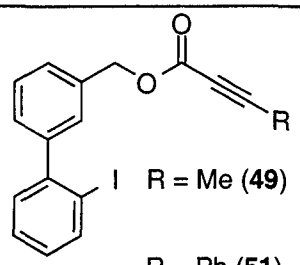
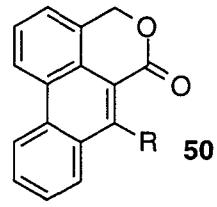
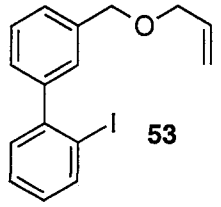
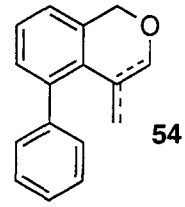
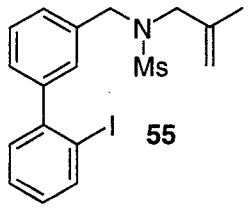
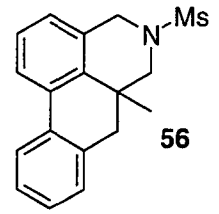
Scheme 5



We also tested whether an intramolecular version of the Heck reaction could be used to trap key arylpalladium intermediates generated via palladium migration. Therefore, we prepared two biphenyl derivatives having a strategically positioned C-C double bond. Biphenyl **53** was designed to produce the cyclic compound **54** by intramolecular Heck reaction with the allyl ether moiety (entry 3). Unfortunately, the reaction of compound **53** produced a very complex reaction mixture, and we failed to isolate the desired compound **54**. Biphenyl **55** was designed to trap the corresponding palladium intermediate by

intramolecular annulation onto the methallyl amine moiety generating a stable alkylpalladium intermediate lacking β-hydrogens. In turn, this alkylpalladium intermediate

Table 4. Attempted palladium-catalyzed intramolecular alkyne and alkene annulations of 3'-substituted 2-iodobiphenyls.[a]

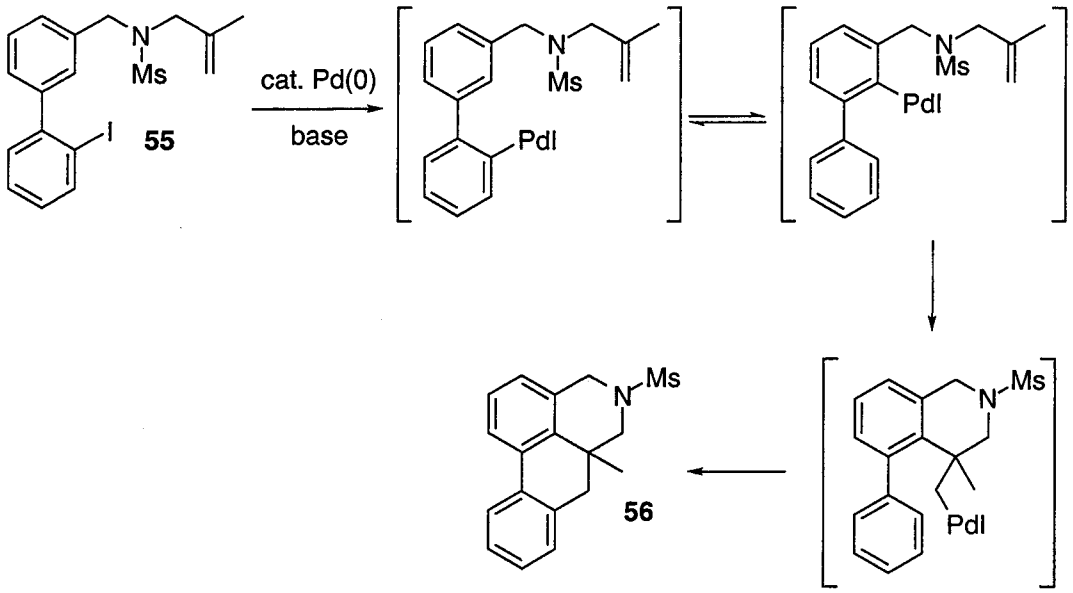
entry	substrate	anticipated product	time (d)	% yield
1	 R = Me (**49**)	 **50**	1	0
2	R = Ph (**51**)	**52**	1	0
3	 **53**	 **54**	1	0
4	 **55**	 **56**	1	0

[a]The reaction was carried out under the previously described standard reaction conditions employing 0.25 mmol of the aryl iodide, 5 mol % of $Pd(OAc)_2$, 5 mol % of dppm, 2 equiv of CsO_2CCMe_3 in DMF (4 mL) at 100 °C.

might be expected to undergo a second cyclization onto the neighboring phenyl ring via C-H activation to render the tetracyclic compound **56** (entry 4, Table 4; Scheme 6). Unfortunately, as previously observed with other substrates, compound **55** produced a very complex reaction mixture, and we failed to isolate the desired tetracycle **56**. At this point, we conclude that intramolecular Heck and alkyne annulation reactions are ineffective for the

synthesis of complex polycycles using our present methodology. These negative results can most likely be attributed to unwanted intermolecular side reactions.

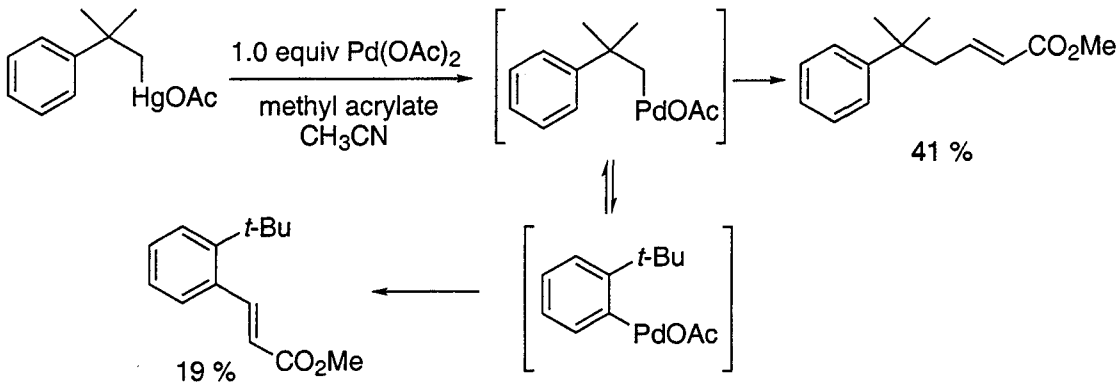
Scheme 6



We have continued to investigate the generality of our methodology for the synthesis of polycycles. Particularly, we were interested in exploiting other types of palladium migration. To elaborate, we have previously studied systems in which a 1,4-palladium shift between aryl and aryl positions or vinylic and aryl positions has been used to generated key palladium intermediates, which in turn undergo subsequent cyclization rendering the desired polycycles. We now report catalytic alkyl to aryl 1,4-palladium migration to prepare polycycles. This type of migration has been previously observed as a side reaction using stoichiometric amounts of palladium acetate and neophylmercuric acetate (Scheme 7).[11]

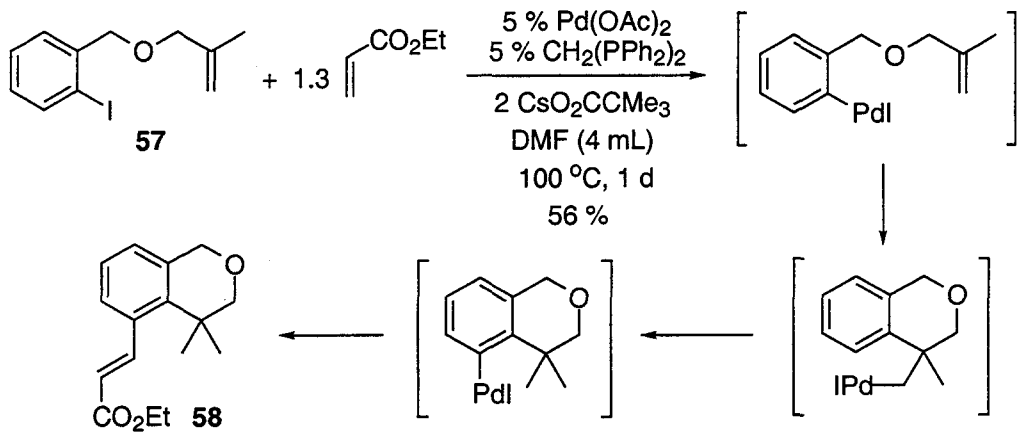
In order to accomplish this goal, we have used 2-iodobenzyl methallyl ether (**57**) as a precursor to generate a stable alkylpalladium intermediate. A stepwise examination of our experimental design reveals that the Pd-catalyzed annulation of 2-iodobenzyl methallyl ether

Scheme 7



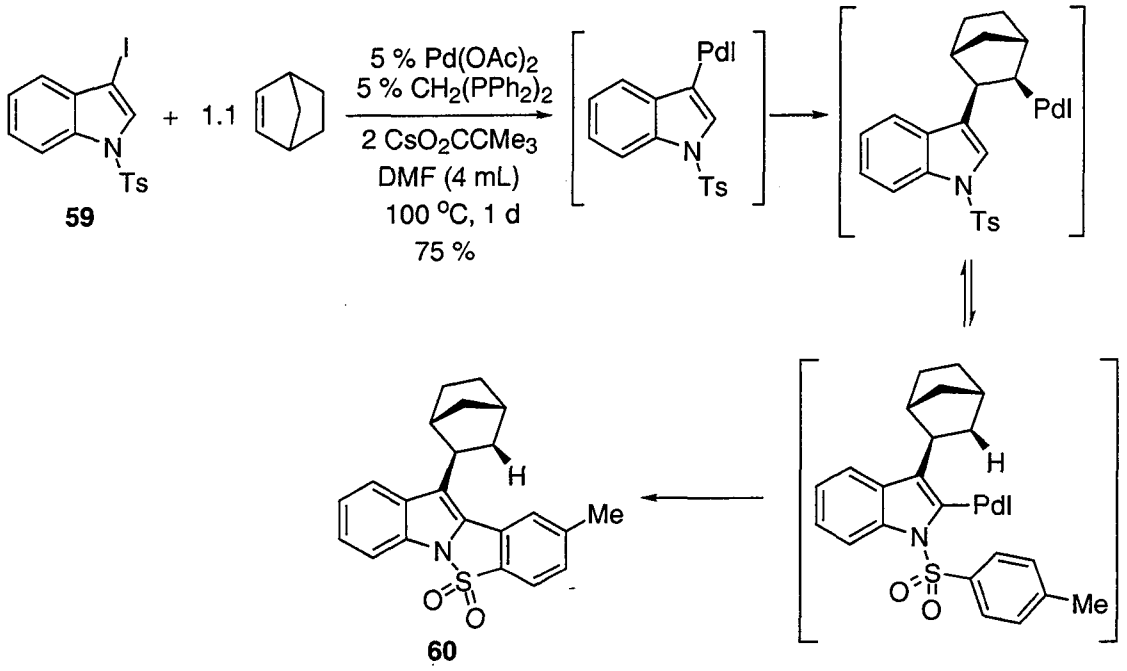
should generate a stable alkylpalladium intermediate lacking β-hydrogens (Scheme 8). In turn, this intermediate might undergo the key alkyl to aryl palladium migration generating an arylpalladium, which is subsequently trapped by way of an intramolecular Heck reaction with ethyl acrylate. Thus, the reaction of compound **57** with ethyl acrylate under our standard conditions led to the formation of polycyclic compound **58** in a 56 % yield (Scheme 8). Clearly, under our palladium-catalyzed reaction conditions the desired alkyl to aryl migration had occurred, indicating the potential of our methodology for generating polyfunctional cyclic compounds from relatively simple starting materials.

Scheme 8



A second example of a reaction involving an alkyl to aryl palladium migration to generate a functionalized polycycle was obtained during the reaction of 3-iodo-1-*p*-tosylindole (**59**) with norbornene under our standard Pd migration reaction conditions (Scheme 9). The first step of this reaction involves the cis addition of an indol-3-ylpalladium iodide to norbornene, generating a stable alkylpalladium intermediate lacking cis β-hydrogens properly aligned for β-hydride elimination. This intermediate in turn undergoes a 1,4-alkyl to aryl palladium shift to the 2-position of the indole, followed by intramolecular annulation onto the *p*-toluenesulfonyl moiety.[12] The overall transformation produced a 75 % yield of the desired polycycle **60**. The possibility of using this process to prepare other carbocycles and heterocycles is currently being investigated in our research group.

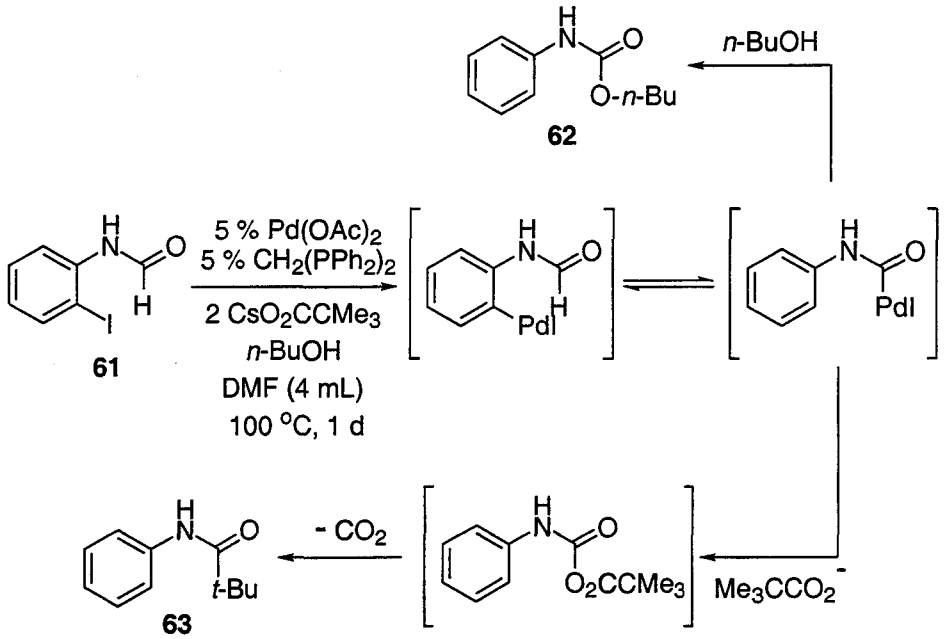
Scheme 9



To further extend the scope of our methodology, we have explored other possible palladium migrations. Next, we describe experiments aimed towards establishing an aryl to

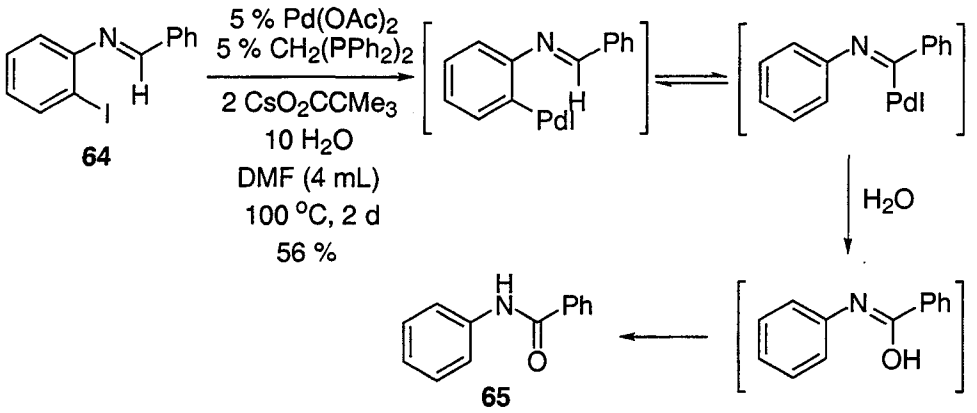
carbonyl palladium migration. First of all, we looked at an aryl to acyl palladium migration using *N*-(2-iodophenyl)formamide (**61**). Thus, the reaction of **61** under our standard migration reaction conditions in the presence of 10 equiv of *n*-butanol as a trapping agent for the anticipated acylpalladium intermediate produced the desired carbamate **62** in a 15 % yield along with the surprising pivalanilide (**63**) product in a 15 % yield. Scheme 9 shows a possible mechanism for the formation of these compounds from the key acylpalladium intermediate generated after the desired palladium migration. It is worth noting that by carrying out this reaction in the presence of 50 equiv of *n*-BuOH, we obtained the desired carbamate **62** exclusively in a 27 % yield, thus inhibiting the formation of pivalanilide (**63**). Similarly, if this reaction is carried out in the absence of *n*-BuOH, we obtained pivalanilide (**63**) exclusively in a 26 % yield.[13]

Scheme 9



Similarly, the reaction of benzylidene(2-iodophenyl)amine (**64**) under our migration conditions in the presence of 10 equiv of water produced the desired benzanilide (**65**) in a 56 % yield (Scheme 11). The formation of benzanilide suggests that a palladium migration from an aryl to an imidoyl position has taken place, generating a Pd species which upon hydrolysis and subsequent tautomerization leads to the benzanilide product.[14]

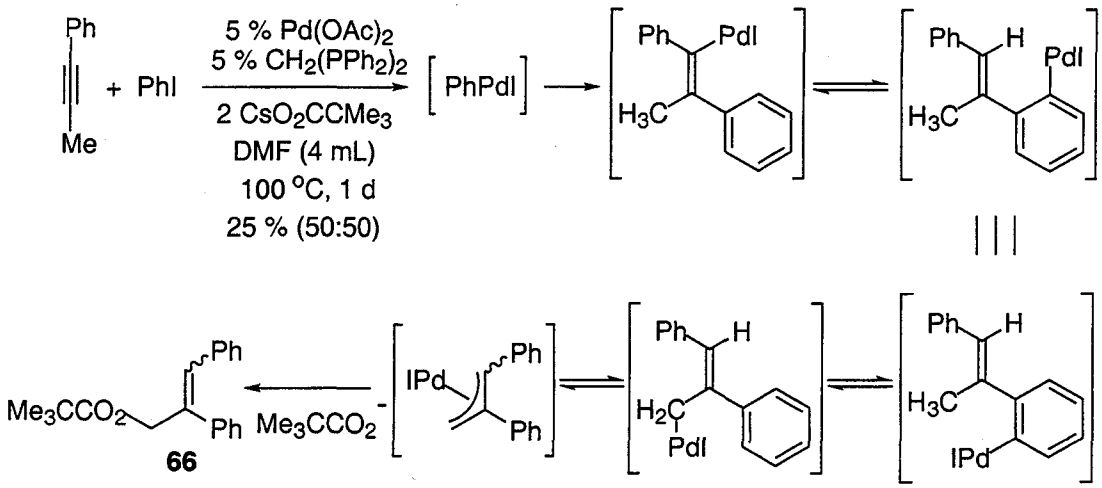
Scheme 11



Finally, we have explored the possibility of using an aryl to allyl palladium migration to prepare functionalized alkenes, as well as heterocycles. Scheme 12 illustrates a possible mechanism for the reaction of iodobenzene with 1-phenyl-1-propyne under our standard reaction conditions. Notice that the sterically-controlled, regioselective addition of phenylpalladium iodide to 1-phenyl-1-propyne should generate a vinylic palladium intermediate, which might undergo the expected 1,4-vinylic to aryl palladium migration to produce an arylpalladium intermediate. We anticipated that this arylpalladium intermediate might undergo a second migration to the methyl position, producing a π-allylpalladium species, which should react with the nucleophilic pivalate base, generating the desired

pivalate ester **66**. Indeed, this reaction produced the indicated pivalate ester **66** in a 25 % yield as a 50:50 mixture of

Scheme 12

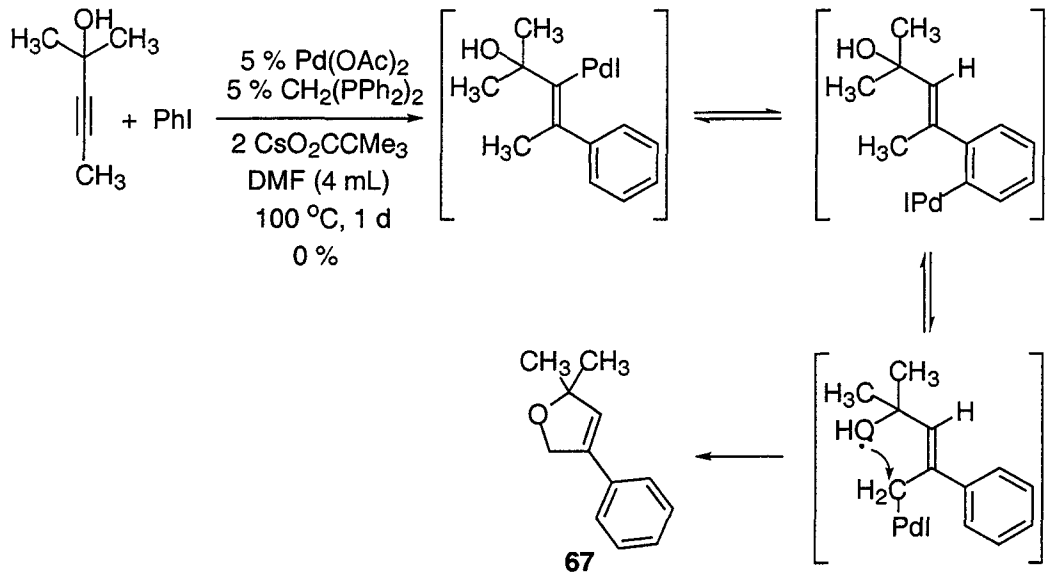


E and *Z* isomers. Having established the possibility of generating allylpalladium intermediates from aryl iodides and alkynes, we thought it should be feasible to trap such intermediates in an intramolecular fashion to generate heterocycles. Unfortunately, the reaction of iodobenzene with 2-methylpent-3-yn-2-ol failed to produce the desired cyclic ether **67** (Scheme 13). The potential of this type of annulation is currently being investigated in our research group.

Conclusions

In conclusion, we have developed novel methodology for the synthesis of complex fused polycycles employing two sequential Pd-catalyzed intramolecular processes involving C-H activation. This methodology exploits relatively general aryl to aryl, vinylic to aryl, and alkyl to aryl 1,4-palladium migrations combined with intramolecular arylation to prepare a wide variety of carbocycles and heterocycles. The chemistry developed here works best with

Scheme 13



67

electron-rich aromatics, which is in agreement with the idea that these palladium-catalyzed C-H activation reactions parallel electrophilic aromatic substitution.

Experimental

General procedures. All ^{1}H and ^{13}C spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5 %) + 300 mL of H_2O]. All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV.

Reagents. All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of THF, DME, DMF, benzene, diethyl ether, ethyl acetate and

hexanes were purchased from Fisher Scientific Co. *n*-Bu_4NCl (TBAC) was purchased from Lancaster Synthesis, Inc. $AgClO_4$, $Cu(OAc)_2$, 3,4-dihydro-1-phenylnaphthalene and Et_3N were purchased from Aldrich Chemical Co., Inc. Cesium pivalate was prepared according to the procedure of Larock and Campo.[15] Compounds **1**, **2**, **19**, **20**, **36**, **38**, **40**, **41**, **43**, and **59** have been previously reported[15] (see Chapter 1 of this thesis).

Synthesis of the organic halides

3'-Benzyl-2-iodobiphenyl (4). This biphenyl was prepared from 3'-bromomethyl-2-iodobiphenyl (**68**)[15] by following a procedure from the literature.[16] To a suspension of $AgClO_4$ (0.28 g, 1.4 mmol) in benzene (4.0 mL) was added **68** (0.261 g, 0.7 mmol) in benzene (4.0 mL) and the resulting mixture stirred overnight at room temperature in the dark. The reaction mixture was diluted with diethyl ether (50 mL), filtered and washed with brine (25 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 50:1 hexanes/ethyl acetate to afford 0.187 g (72 %) of the indicated compound **4** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 4.03 (s, 3H), 6.97-7.01 (m, 1H), 7.15-7.34 (m, 11H), 7.92 (dd, J = 8.0, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 42.0, 98.8, 126.2, 127.1, 128.2, 128.2, 128.3, 128.6, 128.8, 129.1, 130.1, 130.2, 139.6, 140.8, 141.0, 144.3, 146.6; IR (CH_2Cl_2) 3056, 3025, 2917, 1601, 1583, 1494, 1461 cm^{-1}; HRMS *m/z* 370.0224 (calcd for $C_{19}H_{15}I$, 370.0218).

2-Iodo-3'-methoxybiphenyl (69). Compound **69** was prepared by a procedure reported by Hart.[17] A solution of 2-bromoiodobenzene (1.415 g, 5.0 mmol) in THF (10 mL) was added slowly (90 min) to a solution of 3-methoxyphenylmagnesium bromide [prepared from 3-bromoanisole (1.87 g, 10 mmol) and Mg (0.246 g, 10 mmol) in THF (30 mL)], and

the mixture was stirred under Ar for an additional 14 h at room temperature. The reaction was quenched by adding I_2 (3.8 g, 15 mmol), and the mixture was stirred for an additional 30 min at room temperature. The excess I_2 was destroyed by adding 10% aq $NaHSO_3$ (35 mL) and the organic layer was separated and rewashed with brine (20 mL). Finally, the organic layer was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was chromatographed using 30:1 hexanes/ethyl acetate to afford 0.620 g (40 %) of the desired compound **69** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.84 (s, 3H), 6.88-6.95 (m, 3H), 7.01-7.05 (m, 1H), 7.29-7.38 (m, 3H), 7.95 (dd, J = 8.0, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.4, 98.5, 113.4, 115.0, 121.8, 128.1, 128.9, 129.1, 130.1, 139.6, 145.5, 146.5, 159.1; HRMS *m/z* 309.9859 (calcd for $C_{13}H_{11}IO$, 309.9855).

2-Iodo-3'-phenoxybiphenyl (6). This biphenyl was prepared in two steps from 2-iodo-3-methoxybiphenyl (**69**). To a solution of **69** (0.97 g, 3.14 mmol) in CH_2Cl_2 (20 mL) at -78 °C was added 1.0 M BBr_3 in CH_2Cl_2 (4.1 mL, 4.1 mmol). The resulting solution was allowed to warm to room temperature and stirred for 2 h. The mixture was worked up with ice (15 g) and extracted with diethyl ether (75 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 3:1 hexanes/ethyl acetate to afford 0.91 g (98 %) of 3-(2-iodophenyl)phenol (**70**) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 5.04 (br s, 1H), 6.80-6.81 (m, 1H), 6.85-6.90 (m, 2H), 7.00-7.05 (m, 1H), 7.25-7.31 (m, 2H), 7.37 (td, J = 7.6, 0.8 Hz, 1H), 7.94 (dd, J = 8.0, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 98.4, 114.7, 116.4, 122.0, 128.1, 128.9, 129.3, 130.0, 139.5, 145.8, 146.2, 155.0. Compound **70** was phenylated by a procedure found in the literature.[18] A suspension of **70** (0.222 g, 0.75 mmol), phenylboronic

acid (0.183 g, 1.5 mmol), $Cu(OAc)_2$ (0.163 g, 0.90 mmol), Et_3N (0.38 g, 3.75 mmol), 5 Angstrom molecular sieves (0.2 g) in CH_2Cl_2 (6.0 mL) was stirred under O_2 (1 atm) for 2 d at room temperature. The reaction mixture was diluted with diethyl ether (50 mL), filtered, and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 15:1 hexanes/ethyl acetate to afford 0.129 g (46 %) of the indicated compound **6** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 7.00-7.12 (m, 7H), 7.25-7.40 (m, 5H), 7.92 (dd, J = 8.0, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 98.4, 118.2, 119.1, 119.8, 123.4, 124.2, 128.2, 129.0, 129.4, 129.8, 130.0, 139.6, 145.9, 146.0, 156.8, 157.1; IR (CH_2Cl_2) 3058, 1578, 1488, 1460, 1222, cm^{-1}; HRMS *m/z* 372.0020 (calcd for $C_{18}H_{13}IO$, 372.0011).

2-Iodo-3'-(*p*-chlorophenoxy)biphenyl (8). This biphenyl was prepared by a procedure similar to that used for compound **6**. A suspension of **70** (0.222 g, 0.75 mmol), *p*-chlorophenylboronic acid (0.235 g, 1.5 mmol), $Cu(OAc)_2$ (0.163 g, 0.90 mmol), Et_3N (0.38 g, 3.75 mmol), 5 Angstrom molecular sieves (0.2 g) in CH_2Cl_2 (6.0 mL) was stirred under O_2 (1 atm) for 2 d at room temperature. The reaction mixture was diluted with diethyl ether (50 mL), filtered, and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 30:1 hexanes/ethyl acetate to afford 79.5 mg (26 %) of the indicated compound **6** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 6.96-7.09 (m, 6H), 7.27-7.41 (m, 5H), 7.93 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 98.4, 118.2, 119.9, 120.3, 124.6, 128.2, 128.4, 129.1, 129.6, 129.8, 130.0, 139.6, 145.8, 146.0, 155.8, 156.4; IR (CH_2Cl_2) 3057, 1576, 1484, 1460, 1228 cm^{-1}; HRMS *m/z* 405.9632 (calcd for $C_{18}H_{12}ICIO$, 405.9621).

1-[3-(2-Iodophenyl)benzyl]indole (10). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added 1*H*-indole (0.117 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point 3'-bromomethyl-2-iodobiphenyl (**68**)[15] (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at 50 °C for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 12:1 hexanes/ethyl acetate to afford 0.335 g (88 %) of the desired compound **10** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 5.34 (s, 2H), 6.54 (d, J = 2.8 Hz, 1H), 6.98 (td, J = 7.6, 1.6 Hz, 1H), 7.09-7.23 (m, 7H), 7.30-7.34 (m, 3H), 7.64 (d, J = 7.6 Hz, 1H), 7.90 (dd, J = 8.0, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 50.1, 98.6, 101.9, 109.9, 119.6, 121.1, 121.8, 126.2, 128.0, 128.2, 128.4, 128.6, 128.6, 128.9, 129.0, 130.1, 136.4, 137.4, 139.6, 144.6, 146.1; IR (CH_2Cl_2) 3052, 2972, 2922, 2863, 1462, 1437, 1316 cm^{-1}; HRMS *m/z* 409.0334 (calcd for $C_{21}H_{16}IN$, 409.0328).

1-[3-(2-Iodophenyl)benzyl]-3-methylindole (12). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added 3-methyl-1*H*-indole (0.131 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point 3'-bromomethyl-2-iodobiphenyl (**68**)[15] (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at 50 °C for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography

using 12:1 hexanes/ethyl acetate to afford 0.362 g (92 %) of the desired compound **12** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 2.33 (d, J = 0.8 Hz, 3H), 5.29 (s, 2H), 6.92-6.92 (m, 1H), 6.97-6.99 (m, 1H), 7.10-7.24 (m, 6H), 7.27-7.34 (m, 3H), 7.56-7.58 (m, 1H), 7.90-7.92 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 10.1, 50.1, 98.8, 109.9, 111.2, 119.1, 119.3, 121.9, 126.2, 126.4, 128.2, 128.4, 128.7, 128.7, 129.2, 129.3, 130.3, 136.9, 137.9, 139.8, 144.7, 146.4; IR (CH_2Cl_2) 3052,2914, 1611, 1465, 1330, 1012 cm^{-1}; HRMS *m/z* 423.0491 (calcd for $C_{22}H_{18}IN$, 423.0484).

3-(2-Iodophenyl)benzyl phenyl ether (14). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 ^{0}C was added phenol (0.094 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point, 3'-bromomethyl-2-iodobiphenyl (**68**)[15] (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 12:1 hexanes/ethyl acetate to afford 0.359 g (100 %) of the desired compound **14** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 5.13 (s, 2H), 6.96-7.04 (m, 4H), 7.26-7.33 (m, 4H), 7.39-7.46 (m, 4H), 7.94-7.96 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 69.9, 98.6, 115.0, 121.1, 126.8, 128.3, 128.4, 128.5, 129.0, 129.0, 129.6, 130.2, 137.0, 139.6, 144.5, 146.4, 158.8; IR (CH_2Cl_2) 3056, 2919, 1598, 1494, 1238 cm^{-1}; HRMS *m/z* 386.0172 (calcd for $C_{19}H_{15}IO$, 386.0168).

2-Iodo-1-phenylnaphthalene (17). To a solution of 3,4-dihydro-1-phenylnaphthalene (1.30 g, 6.3 mmol) and I_2 (2.24 g, mmol) in anhydrous CH_3CN (15 mL)

was added dropwise AgOTf (1.75 g, 6.8 mmol) in anhydrous CH_3CN (20 mL). The resulting mixture was stirred at room temperature in the dark for 1 h. The reaction was diluted with diethyl ether (70 mL) and washed with satd aq $Na_2S_2O_3$ (25 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was dissolved in benzene (25 mL). To this solution was added DDQ (2.86 g, 12.6 mmol) and the reaction heated at 65 °C for 2 d. The resulting mixture is filtered and washed with 10 % aq Na_2CO_3 (25 mL). The organic layer was filtered, dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was purified using chromatography on a silica gel column using 50:1 hexanes/ethyl acetate to afford 1.47 g (70 %) of the indicated compound **17** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 7.22-7.26 (m, 2H), 7.32-7.34 (m, 1H), 7.38-7.56 (m, 6H), 7.80-7.83 (m, 1H), 7.95 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 98.7, 126.5, 127.0, 127.4, 128.1, 128.1, 128.7, 129.3, 130.2, 133.1, 133.6, 135.8, 143.5, 144.7; IR (CH_2Cl_2) 3053, 1577, 1502, 1442, 1382, 1306 cm^{-1}; HRMS *m/z* 329.9910 (calcd for $C_{16}H_{11}I$, 329.9906).

General procedure for synthesis of the phenanthrenes[8]

The following procedure was used to prepare phenanthrenes **22**, **24**, **26**, **28**, **30** and chrysene **32**. To a solution of 2-(arylethynyl)biphenyl (0.30 mmol) in CH_2Cl_2 (3 mL) under N_2 was added ICl (1.2 equiv) in CH_2Cl_2 (0.5 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 1 h unless otherwise indicated. The reaction mixture was then diluted with diethyl ether (50 mL), washed with 25 mL of satd aq $Na_2S_2O_3$, dried ($MgSO_4$), and filtered. The solvent was evaporated under reduced pressure and the product was purified by chromatography on a silica gel column.

General procedure for preparation of the 2-(arylethynyl)biphenyls. To a solution of the corresponding aryl iodide (1.0 mmol) and the terminal alkyne (1.2 mmol, 1.2 equiv) in Et_3N (4.0 mL) were added $PdCl_2(PPh_3)_2$ (1.4 mg, 2 mol %) and CuI (2.0 mg, 1 mol %). The resulting mixture was then heated under an N_2 atmosphere at 55 °C for 3 h. The mixture was allowed to cool to room temperature, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the corresponding product.

2-[(4-Methoxyphenyl)ethynyl]biphenyl (71). 2-Ethynylbiphenyl[19] and 4-iodoanisole were employed. Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.21 g (74 %) of the product as a clear liquid: ^{1}H NMR ($CDCl_3$) δ 3.80 (s, 3H), 6.84 (dd, J = 2.4, 6.9 Hz, 2H), 7.30 (dd, J = 2.1, 6.9 Hz, 2H), 7.34-7.50 (m, 6H), 7.64-7.73 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 55.5, 88.4, 92.5, 114.2, 115.9, 122.2, 127.3, 127.6, 128.1, 128.4, 129.6, 129.7, 132.9, 133.1, 140.9, 143.9, 159.8.

2-[(3-Methylphenyl)ethynyl]biphenyl (72). 2-Ethynylbiphenyl[19] and 3-iodotoluene were employed. Purification by flash chromatography (40:1 hexane/EtOAc) afforded 0.26 g (95 %) of the product as a clear liquid: ^{1}H NMR ($CDCl_3$) δ 2.34 (s, 3H), 7.12-7.22 (m, 4H), 7.33-7.53 (m, 6H), 7.67-7.74 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 21.5, 89.3, 92.7, 122.0, 123.5, 127.3, 127.7, 128.2, 128.4, 128.7, 128.7, 129.3, 129.7, 129.7, 132.2, 133.1, 138.2, 140.9, 144.1.

Ethyl 4-(biphen-2-ylethynyl)benzoate (73). 2-Ethynylbiphenyl[19] and ethyl 4-iodobenzoate were employed. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 0.27 g (84 %) of the product as a white solid: mp 58-60 °C; ^{1}H NMR ($CDCl_3$) δ

1.38 (t, J = 6.9 Hz, 3H), 4.36 (q, J = 7.2 Hz, 2H), 7.32-7.48 (m, 8H), 7.64-7.66 (m, 3H), 7.96 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.6, 61.3, 91.7, 92.6, 121.3, 127.4, 127.9, 128.2, 128.3, 129.3, 129.63, 129.64, 129.8, 129.9, 131.4, 133.2, 140.6, 144.5, 166.3.

2-(Biphen-2-ylethynyl)thiophene (74). 2-Ethynylbiphenyl[19] and 2-iodothiophene were employed. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 0.22 g (85 %) of the product as a light yellow liquid: ^{1}H NMR ($CDCl_3$) δ 6.98-7.00 (m, 1H), 7.15-7.17 (m, 1H), 7.25-7.27 (m, 1H), 7.37-7.55 (m, 6H), 7.66-7.75 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 85.9, 93.5, 121.6, 123.8, 127.3, 127.4, 127.5, 127.8, 128.3, 129.0, 129.6, 129.8, 131.8, 132.8, 140.7, 144.0.

2-[2-(Phenylethynyl)phenyl]naphthalene (75). 2-(2-Iodophenyl)naphthalene[17] and phenylacetylene were employed. Purification by flash chromatography (40:1 hexane/EtOAc) afforded 0.29 g (96 %) of the product as a light yellow liquid: ^{1}H NMR ($CDCl_3$) δ 7.24-7.58 (m, 10H), 7.70-7.72 (m, 1H), 7.86-7.97 (m, 4H), 8.17 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 89.7, 92.7, 122.0, 123.6, 126.2, 126.3, 127.4, 127.5, 127.9, 128.0, 128.3, 128.4, 128.5, 128.9, 130.0, 131.6, 132.9, 133.3, 133.5, 138.3, 144.0 (one sp^2 carbon missing due to overlap).

2-[(4-Methoxyphenyl)ethynyl]-1-phenylnaphthalene (76). 2-Iodo-1-phenylnaphthalene and 4-ethynylanisole[20] were employed. Purification by flash chromatography (20:1 hexane/EtOAc) afforded 0.27 g (82 %) of the product as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.81 (s, 3H), 6.82 (dd, J = 6.9, 2.1 Hz, 2H), 7.17 (d, J = 6.9, 2.1 Hz, 2H), 7.43-7.60 (m, 7H), 7.68-7.72 (m, 2H), 7.83-7.94 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 55.4, 88.9, 93.5, 114, 115.7, 120.7, 126.4, 126.6, 126.8, 127.6, 127.6, 128.1, 128.2, 128.4, 130.9, 132.4, 133.0, 133.1, 139.3, 142.8, 159.7.

9-Iodo-10-(4-methoxyphenyl)phenanthrene (22). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.122 g (99 %) of the product as a white solid: mp 170-171 °C; ^{1}H NMR ($CDCl_3$) δ 3.94 (s, 3H), 7.09 (dd, J = 2.1, 6.6 Hz, 2H), 7.21 (dd, J = 2.1, 6.6 Hz, 2H), 7.40-7.49 (m, 2H), 7.64-7.72 (m, 3H), 8.45-8.49 (m, 1H), 8.67-8.78 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 55.6, 107.7, 114.0, 122.8, 122.9, 127.2, 127.3, 127.7, 128.3, 129.0, 130.5, 130.8, 131.3, 132.7, 132.9, 135.0, 138.2, 145.3, 159.4; IR (neat) 3066, 3024, 2834, 1610 cm^{-1}; HRMS *m/z* 410.0172 (calcd for $C_{21}H_{15}IO$, 410.0168).

Ethyl 4-(10-iodophenanthren-9-yl)benzoate (24). The reaction mixture was stirred at room temperature for 1 h. Purification by flash chromatography (15:1 hexane/EtOAc) afforded 0.136 g (100 %) of the product as a white solid: mp 152-153 °C; ^{1}H NMR ($CDCl_3$) δ 1.46 (t, J = 7.2 Hz, 3H), 4.47 (q, J = 7.2 Hz, 2H), 7.30-7.45 (m, 4H), 7.66-7.75 (m, 3H), 8.26 (dd, J = 1.8, 6.6 Hz, 2H), 8.45-8.49 (m, 1H), 8.68-8.78 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.6, 61.4, 106.0, 122.9, 123.0, 127.4, 127.5, 128.0, 128.4, 128.5, 130.1, 130.3, 130.4, 130.5, 130.8, 132.1, 132.5, 134.9, 144.6, 150.0, 166.7; IR (CH_2Cl_2) 3069, 2979, 1714 cm^{-1}; HRMS *m/z* 452.0278 (calcd for $C_{23}H_{17}IO_2$, 452.0273).

9-Iodo-10-(3-methylphenyl)phenanthrene (26). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.117 g (99 %) of the product as a white solid: mp 134-135 °C; ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 7.07-7.09 (m, 2H), 7.30-7.32 (m, 1H), 7.41-7.45 (m, 3H), 7.63-7.70 (m, 3H), 8.45-8.48 (m, 1H), 8.67-8.73 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.7, 106.5, 122.6, 122.7, 127.1, 127.1, 127.5, 128.1, 128.4, 128.5, 128.8, 130.3, 130.6, 130.6, 132.5, 132.5, 134.7, 138.1, 145.4, 145.5 (one sp^2 carbon missing due to

overlap); IR (CH_2Cl_2) 3067, 2971, 2921, 1602, 1563 cm^{-1}; HRMS *m/z* 394.0226 (calcd for $C_{21}H_{15}I$, 394.0219).

9-Iodo-10-(thiophen-2-yl)phenanthrene (28). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.111 g (96 %) of the product as a white solid: mp 140-142 °C; ^1H NMR ($CDCl_3$) δ 7.06-7.08 (m, 1H), 7.23-7.26 (m, 1H), 7.45-7.76 (m, 6H), 8.44-8.49 (m, 1H), 8.66-8.75 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 110.5, 122.7, 122.9, 126.5, 127.2, 127.5, 128.2, 128.4, 128.7, 128.8, 130.3, 131.1, 132.6, 133.2, 135.3, 138.4, 146.5; IR (neat) 2925, 1464, 1216 cm^{-1}; HRMS *m/z* 385.9631 (calcd for $C_{18}H_{11}IS$, 385.9626).

6-Iodo-5-(4-methoxyphenyl)benzo[*c*]phenanthrene (30). Purification by flash chromatography (30:1 hexane/EtOAc) afforded 0.138 g (97 %) of the product as a white solid: mp 186-187 °C; ^1H NMR ($CDCl_3$) δ 3.94 (s, 3H), 7.08-7.12 (m, 2H), 7.23-7.26 (m, 2H), 7.42-7.47 (m, 1H), 7.57-7.69 (m, 4H), 7.94 (d, J = 9.0 Hz, 1H), 8.04-8.06 (m, 1H), 8.42 (d, J = 9.0 Hz, 1H), 9.01-9.04 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 55.6, 107.3, 114.1, 126.4, 126.6, 126.7, 126.8, 128.4, 128.4, 128.6, 128.6, 128.8, 129.0, 129.7, 130.2, 131.3, 131.5, 132.4, 133.8, 133.8, 138.0, 145.0, 159.4; IR (neat) 2950, 1606, 1506 cm^{-1}; HRMS *m/z* 460.0330 (calcd for $C_{25}H_{17}IO$, 460.0324).

6-Iodo-5-phenylchrysene (32). Purification by flash chromatography (40:1 hexane/EtOAc) afforded 98 mg (76%) of the product as a yellow solid: mp 168-169 °C; ^1H NMR ($CDCl_3$) δ 7.07 (t, J = 6.9 Hz, 1H), 7.33-7.57 (m, 7H), 7.71-7.76 (m, 2H), 8.89 (d, J = 6.5 Hz, 1H), 8.04 (d, J = 7.6 Hz, 1H), 8.56-8.60 (m, 1H), 8.78 (d, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 111.5, 121.3, 123.7, 125.4, 126.1, 127.7, 128.2, 128.4, 128.6, 128.9, 129.0, 129.2,

129.3, 130.4, 130.7, 130.8, 131.1, 133.5, 133.8, 135.3, 144.3, 150.0; IR (neat) 2922 cm^{-1}; HRMS *m/z* 430.0025 (calcd for $C_{24}H_{15}I$, 430.0219).

3-Iodo-4-phenylquinoline (34). To a solution of *N*-phenylmethanesulfonamide[21] (0.513 g, 3.0 mmol), PPh_3 (1.18 g, 4.5 mmol) and 3-phenylpropargyl alcohol (0.594 g, 4.5 mmol) in anhydrous THF (30 mL) at 0 °C was added DEAD (0.784 g, 4.5 mmol). The resulting solution was stirred at 0 °C for 1 h and an additional 3 h at room temperature. The mixture was washed with brine (30 mL) and the organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 3:1 hexanes/ethyl acetate to obtain 0.534 g (63 %) of *N*-methanesulfonyl-*N*-(3-phenyl-2-propyn-1-yl)aniline as a white solid: mp 76-77 °C; ^{1}H NMR ($CDCl_3$) δ 3.08 (s, 3H), 4.67 (s, 2H), 7.34-7.46 (m, 8H), 7.62-7.66 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 39.2, 42.3, 84.4, 86.3, 122.3, 127.7, 128.4, 128.7, 129.1, 129.7, 131.9, 140.5. To a solution of *N*-methanesulfonyl-*N*-(3-phenyl-2-propyn-1-yl)aniline (71.2 mg, 0.25 mmol) in CH_2Cl_2 (3.0 mL) at -78 °C was added ICl (48.7 mg, 0.3 mmol) in CH_2Cl_2 (0.5 mL) and the resulting solution stirred at this temperature for 1 h. The reaction mixture was washed with satd aq $Na_2S_2O_3$ (20 mL) and the organic layer dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 5:1 hexanes/ethyl acetate to obtain 82.2 mg (80 %) of 3-iodo-1-methanesulfonyl-4-phenyl-1,2-dihydroquinoline as a white solid: mp 173-175 °C; ^{1}H NMR ($CDCl_3$) δ 2.89 (s, 3H), 4.82 (s, 2H), 6.80 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.11-7.16 (m, 3H), 7.30-7.33 (m, 1H), 7.44-7.48 (m, 3H), 7.62 (dd, *J* = 8.1, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 38.6, 56.7, 92.0, 126.9, 127.2, 127.2, 128.6, 128.8, 129.0, 129.2, 130.7, 134.5, 140.3, 143.9. A

solution of 3-iodo-1-methanesulfonyl-4-phenyl-1,2-dihydroquinoline (0.103 g, 0.25 mmol) and NaOH (0.10 g, 2.5 mmol) in EtOH (10 mL) was stirred at 50 °C under O_2 (1 atm) for 12 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column using 5:1 hexanes/ethyl acetate to afford 76.1 mg (92 %) of the desired compound **34** as a white solid: mp 131-132 °C; ^{1}H NMR ($CDCl_3$) δ 7.25-7.28 (m, 2H), 7.42-7.48 (m, 2H), 7.52-7.55 (m, 3H), 7.69-7.74 (m, 1H), 8.12 (d, J = 8.8 Hz, 1H), 9.24 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 96.4, 126.8, 127.4, 128.7, 129.0, 129.1, 129.5, 129.8, 140.4, 147.2, 152.4, 156.6 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3061, 2918, 1566, 1501, 1485 cm^{-1}; HRMS *m/z* 330.9864 (calcd for $C_{15}H_{10}IN$, 330.9858).

3-Iodo-4-phenylisocoumarin (45). A solution of 4-phenyl-3-(trimethylsilyl)isocoumarin[22] (0.435 g, 1.48 mmol), I_2 (1.13 g, 4.45 mmol), and AgOTf (0.76 g, 2.96 mmol) in CH_3CN (20 mL) was heated at 55 °C for 5 d. The reaction mixture was diluted with diethyl ether (100 mL), and washed with satd aq $Na_2S_2O_3$ (30 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure to obtain 0.498 g (97 %) of the indicated compound **45** as a yellow solid. Recrystallization from hexanes/ethyl acetate afforded the indicated compound **45** as a yellow solid: mp 170-171 °C, ^{1}H NMR ($CDCl_3$) δ 6.97 (d, J = 8.0 Hz, 1H), 7.26-7.28 (m, 2H), 7.50-7.56 (m, 4H), 7.59-7.63 (m, 1H), 8.31 (dd, J = 8.0, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 107.9, 119.6, 125.6, 127.4, 128.7, 128.9, 129.1, 129.9, 130.5, 135.2, 137.0, 137.3, 161.2; IR (CH_2Cl_2) 1736.0 cm^{-1}; HRMS *m/z* 347.9652 (calcd for $C_{15}H_9IO_2$, 347.9647).

4-Iodo-2,3-diphenyl-2*H*-isoquinolin-1-one (47). To a solution of *N*-phenyl-2-(phenylethynyl)benzamide[23] (74.2 mg, 0.25 mmol) in CH_2Cl_2 (3.0 mL) at room temperature was added ICl (48.7 mg, 0.3 mmol) in CH_2Cl_2 (0.5 mL) and the resulting solution stirred at this temperature for 1 h. The reaction mixture was washed with satd aq $Na_2S_2O_3$ (20 mL) and the organic layer dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on a silica gel column using 5:1 hexanes/ethyl acetate to obtain 42.3 mg (40 %) of the indicated compound **47** as a yellow solid: mp 129-130 °C; ^{1}H NMR ($CDCl_3$) δ 7.08-7.11 (m, 1H), 7.20-7.30 (m, 3H), 7.33-7.38 (m, 4H), 7.57-7.64 (m, 3H), 7.67-7.72 (m, 1H), 8.03-8.06 (m, 1H), 8.84-8.87 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 75.2, 124.1, 125.1, 125.1, 125.4, 128.1, 128.7, 128.7, 130.5, 130.9, 132.0, 132.7, 135.7, 140.6, 145.0, 147.8, 152.1; IR (CH_2Cl_2) 2916, 2849, 1642, 1586, 1488, 1445 cm^{-1}; HRMS *m/z* 423.0131 (calcd for $C_{15}H_9IO_2$, 423.0120).

3-(2-Iodophenyl)benzyl but-2-ynoate (49). To a solution of 3'-bromomethyl-2-iodobiphenyl (**68**)[15] (0.186 g, 0.5 mmol) and 2-butynoic acid (58.8 mg, 0.7 mmol) in DMF (2.5 mL) was added diisopropylethylamine (84.0 mg, 0.65 mmol) and the resulting solution was stirred at 50 °C for 1 d. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 7:1 hexanes/ethyl acetate to afford 0.153 g (82 %) of the indicated compound **49** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.99 (s, 3H), 5.24 (s, 2H), 7.01-7.07 (m, 1H), 7.28-7.44 (m, 6H), 7.95 (dd, J = 8.1, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 3.9, 67.3, 72.4, 86.3, 98.5, 127.7, 128.3, 128.4, 129.0, 129.4, 129.6, 130.2, 134.8, 139.6, 144.5, 146.1, 153.6;

IR (neat) 3054, 2957, 2241, 1709, 1254 cm^{-1}; HRMS *m/z* 375.9967 (calcd for $C_{17}H_{13}IO_2$, 375.9960).

3-(2-Iodophenyl)benzyl 3-phenylprop-2-ynoate (51). To a solution of 3'-bromomethyl-2-iodobiphenyl (**68**)[15] (0.186 g, 0.5 mmol), 3-phenylpropynoic acid (0.102 g, 0.7 mmol) in DMF (2.5 mL) was added diisopropylethylamine (84.0 mg, 0.65 mmol) and the resulting solution stirred at 50 °C for 1 d. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 7:1 hexanes/ethyl acetate to afford 0.197 g (90 %) of the indicated compound **51** as a colorless oil: ^1H NMR ($CDCl_3$) δ 5.32 (s, 2H), 7.04 (td, *J* = 7.8, 1.6 Hz, 1H), 7.30-7.46 (m, 9H), 7.57-7.59 (m, 2H), 7.96 (dd, *J* = 8.0, 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 67.6, 80.6, 87.0, 98.6, 119.6, 127.9, 128.3, 128.4, 128.7, 129.1, 129.5, 129.7, 130.2, 130.8, 133.1, 134.8, 139.7, 144.5, 146.0, 154.0; IR (neat) 3056, 2220, 1709, 1489 cm^{-1}; HRMS *m/z* 438.0122 (calcd for $C_{22}H_{15}IO_2$, 438.0117).

3-(2-Iodophenyl)benzyl allyl ether (53). To a solution of sodium allyl alkoxide [prepared by dissolving metallic Na (0.10 g, 4.35 mmol) in allyl alcohol (5 mL)] in allyl alcohol was added 3'-bromomethyl-2-iodobiphenyl (**68**)[15] (0.347 g, 0.93 mmol) and the resulting solution was stirred at 55 °C for 5 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent evaporated under reduced pressure. The residue was purified by chromatography on a silica gel column using 20:1 hexanes/ethyl acetate to afford 0.293 g (90 %) of the indicated compound **5** as a colorless oil: ^1H NMR ($CDCl_3$) δ 4.07 (dt, *J* = 5.7, 1.5

Hz, 1H), 4.58 (s, 2H), 5.19-5.23 (m, 1H), 5.29-5.36 (m, 1H), 5.92-5.98 (m, 1H), 6.99-7.05 (m, 1H), 7.25-7.41 (m, 6H), 7.93-7.96 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 71.3, 72.0, 98.6, 117.3, 127.0, 128.1, 128.2, 128.6, 128.7, 128.9, 130.1, 134.8, 138.1, 139.5, 144.3, 146.5; IR (neat) 3058, 2850, 1461, 1418, 1012 cm^{-1}; HRMS *m/z* 350.0171 (calcd for $C_{16}H_{15}IO$, 350.0168).

***N*-[3-(2-Iodophenyl)benzyl]-*N*-methallylmethanesulfonamide (55).** To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 °C was added *N*-methallylmethanesulfonamide [prepared from methallylamine and methanesulfonyl chloride: ^{1}H NMR ($CDCl_3$) δ 1.79 (d, *J* = 0.3 Hz, 3H), 2.97, (s, 3H), 3.69 (m, 2H), 4.64 (br s, 1H), 4.93-4.95 (m, 1H), 4.99-5.00 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 20.2, 41.1, 49.1, 113.0, 141.1] (0.149 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point 3'-bromomethyl-2-iodobiphenyl (**68**)[15] (0.347 g, 0.93 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 2:1 hexanes/ethyl acetate to afford 0.353 g (86 %) of the desired compound **55** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.75 (s, 3H), 2.82 (t, *J* = 3.4 Hz, 3H), 3.82 (s, 2H), 4.44 (s, 2H), 4.98-5.00 (m, 2H), 7.03 (t, *J* = 4.0 Hz, 1H), 7.26-7.28 (m, 3H), 7.38-7.42 (m, 3H), 7.95 (dd, *J* = 8.0, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.1, 40.3, 49.9, 52.6, 98.6, 115.0, 128.3, 128.3, 128.5, 129.0, 129.1, 129.7, 130.0, 135.5, 139.5, 139.9, 144.7, 146.2; IR (CH_2Cl_2) 3051, 2919, 1329, 1148, 1012 cm^{-1}; HRMS *m/z* 441.0267 (calcd for $C_{18}H_{20}INO_2S$, 441.0260).

2-Iodobenzyl methallyl ether (57). To a suspension of NaH (0.031 g, 1.30 mmol) in DMF (2 mL) at 0 ^{0}C was added 2-iodobenzyl alcohol (0.234 g, 1.0 mmol) in DMF (3 mL) and the mixture was stirred at room temperature for 30 min. At this point, methallyl chloride (0.122 g, 1.35 mmol) in DMF (3 mL) was added and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (60 mL). The aqueous layer was reextracted with diethyl ether (15 mL) and the organic layers were combined, dried ($MgSO_4$), and the solvent evaporated under reduced pressure. The residue was purified by column chromatography using 20:1 hexanes/ethyl acetate to afford 0.27 g (94 %) of the desired compound **57** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.80 (s, 3H), 4.02 (s, 2H), 4.47 (s, 2H), 4.95 (s, 1H), 5.05 (s, 1H), 6.96-7.00 (m, 1H), 7.33-7.37 (m, 1H), 7.46-7.48 (m, 1H), 7.81-7.83 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 19.8, 74.9, 75.9, 97.8, 112.7, 128.4, 128.9, 129.3, 139.3, 140.9, 142.2; HRMS *m/z* 288.0018 (calcd for $C_{11}H_{13}IO$, 288.0011).

***N*-(2-Iodophenyl)formamide (61).** Compound **61** was prepared according to the procedure of Fukuyama et al.[24]

Benzylidene(2-iodophenyl)amine (64). Compound **64** was prepared according to the procedure of Larock et al.[25]

Representative procedure for the palladium-catalyzed migration reactions. The appropriate aryl iodide (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol) and CsO_2CCMe_3 (CsPiv) (0.117 g, 0.5 mmol) in DMF (4 ml) under Ar at 100 °C were stirred for the specified length of time. The reaction mixture was then cooled to room temperature, diluted with diethyl

ether (35 mL) and washed with brine (30 mL). The aqueous layer was reextracted with diethyl ether (15 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on a silica gel column.

9-Benzylidenefluorene (2). Compound **1** (95.6 mg, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 61.0 mg (96 %) of the indicated compound **2** as a yellow solid with melting point and spectral properties identical to those previously reported.[3]

1,1,2-Triphenylethene (3). Compound **3** was obtained as a side product from compound **1**. This compound was characterized by comparing the melting point and ^1H and ^{13}C NMR spectra with an authentic sample obtained from Aldrich Chemical Co., Inc.

1-Phenyl-9*H*-fluorene (5). Compound **4** (92.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 3 d. The reaction mixture was chromatographed using 30:1 hexanes/ethyl acetate to afford 24.2 mg (40 %) of the indicated compound **5** as a colorless oil: ^1H NMR ($CDCl_3$) δ 3.95 (s, 2H), 6.94 (d, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 7.19-7.22 (m, 2H), 7.33 (t, J = 7.6 Hz, 1H), 7.45-7.55 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 37.0, 122.9, 124.0, 124.8, 126.3, 126.4, 127.5, 128.5, 128.8, 129.2, 137.9, 138.7, 141.3, 141.6, 143.7, 143.9 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3056, 3025, 1454, 1417, 1478 cm^{-1}; HRMS *m/z* 242.1101 (calcd for $C_{19}H_{14}$, 242.1096).

1-Phenyldibenzofuran (7). Compound **6** (93.0 mg, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed

using 30:1 hexanes/ethyl acetate to afford 54.4 mg (89 %) of the indicated compound **7** as a white solid: mp 62-63 °C (lit[26] mp 63-64 °C); ^{1}H NMR ($CDCl_3$) δ 7.10-7.14 (m, 1H), 7.24-7.26 (m, 1H), 7.37-7.42 (m, 1H), 7.46-7.64 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 110.5, 111.6, 121.8, 122.3, 122.5, 123.9, 124.0, 127.1, 127.1, 127.9, 128.6, 129.0, 138.0, 140.0, 156.4, 156.5. The other spectral properties were identical to those previously reported.[26]

7-Chloro-1-phenyldibenzofuran (9). Compound **8** (0.101 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 57.1 mg (82 %) of the indicated compound **9** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.25 (dd, J = 6.8, 1.2 Hz, 1H), 7.34 (dd, J = 8.4, 2.4 Hz, 1H), 7.45-7.60 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 110.7, 112.5, 121.0, 122.1, 124.3, 125.3, 127.1, 127.7, 127.8, 128.3, 128.8, 128.9, 138.2, 139.4, 154.7, 157.1; IR (CH_2Cl_2) 3061, 3032, 1444, 1400, 1199, 1243 cm^{-1}; HRMS *m/z* 278.0501 (calcd for $C_{18}H_{11}ClO$, 278.0498).

10-Phenyl-6*H*-isoindolo[2,1-*a*]indole (11). Compound **10** (0.102 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 49.2 mg (70 %) of the indicated compound **11** as a white solid: mp 139-140 °C; ^{1}H NMR ($CDCl_3$) δ 5.08 (s, 2H), 6.16 (s, 1H), 7.03-7.07 (m, 1H), 7.14-7.18 (m, 1H), 7.32-7.54 (m, 8H), 7.64-7.66 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 48.2, 94.3, 109.1, 119.7, 121.7, 122.4, 127.3, 128.0, 128.5, 128.8, 129.3, 131.0, 132.4, 133.7, 137.0, 139.9, 142.5, 143.2 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3053, 2916, 2850, 1471, 1551, 1446 cm^{-1}; HRMS *m/z* 281.1210 (calcd for $C_{21}H_{15}N$, 281.1204).

2-Methyl-10-phenyl-6*H*-isoindolo[2,1-*a*]indole (13). Compound **12** (0.106 g, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 12:1 hexanes/ethyl acetate to afford 52.4 mg (71 %) of the indicated compound **13** as a white solid: mp 143-145 °C (decomposes); ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 3H), 5.06 (s, 2H), 7.03-7.07 (m, 1H), 7.16-7.20 (m, 1H), 7.23-7.31 (m, 3H), 7.40-7.50 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 9.5, 48.1, 104.2, 109.0, 119.1, 120.0, 122.0, 122.4, 126.5, 127.9, 128.7, 129.9, 130.2, 132.6, 133.8, 134.0, 137.0, 140.0, 142.6, 142.8; IR (CH_2Cl_2) 3048, 2976, 2853, 1469, 2976, 2853, 1469, 1411 cm^{-1}; HRMS *m/z* 295.1369 (calcd for $C_{22}H_{17}N$, 295.1361).

10-Phenyl-6*H*-benzo[*c*]chromene (15) and phenyl 3-phenylbenzyl ether (16). Compound **14** (96.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 120 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 47.8 mg (75 %) of a 60:40 inseparable mixture of compounds **15** and **16** respectively. Major isomer **15**: ^{1}H NMR ($CDCl_3$) δ 5.02 (s, 2H) as a characteristic peak; HRMS *m/z* 258.1050 (calcd for $C_{19}H_{14}O$, 258.1045). Minor isomer **16**: ^{1}H NMR ($CDCl_3$) δ 5.11 (s, 2H) as a characteristic peak; HRMS *m/z* 260.1206 (calcd for $C_{19}H_{16}O$, 260.1201). Mixture: ^{13}C NMR ($CDCl_3$) δ 69.9, 70.2, 115.1, 117.6, 121.3, 121.3, 123.6, 124.1, 126.6, 126.7, 127.1, 127.4, 127.4, 127.5, 127.5, 127.7, 128.4, 128.9, 128.9, 128.9, 129.1, 129.1, 129.3, 129.4, 129.4, 129.8, 132.0, 135.5, 137.8, 139.3, 141.2, 141.9, 142.5, 156.6, 159.0; IR (neat) 3058, 3029, 1599, 1495, 1453, 1243 cm^{-1}.

Fluoranthene (18). Compound **17** (82.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 1 d. The reaction mixture was

chromatographed using 50:1 hexanes/ethyl acetate to afford 41.0 mg (81 %) of the indicated compound **13** as a white solid: mp 107-108 °C (lit[27] mp 106-108 °C). The other spectral properties were identical to those previously reported.[28]

Benzo[*e*]acephenanthrylene (21). Compound **20**[15] (95.0 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 49.2 mg (78 %) of the indicated compound **21** as a white solid: mp 166-167 °C (lit[29] mp 165-166 °C). The other spectral properties were identical to those previously reported.[30]

5-Methoxybenzo[*e*]acephenanthrylene (23). Compound **22** (0.103 g, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 30:1 hexanes/ethyl acetate to afford 50.1 mg (71 %) of the indicated compound **23** as a white solid: mp 188-189 °C (lit[30] mp 189-190 °C). The other spectral properties were identical to those previously reported.[30]

Ethyl benzo[*e*]acephenanthrylene-5-carboxylate (25). Compound **24** (0.113 g, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 9:1 hexanes/ethyl acetate to afford 40.5 mg (50 %) of the indicated compound **25** as a white solid: mp 153-154 °C; ^{1}H NMR ($CDCl_3$) δ 1.46 (t, J = 7.2 Hz, 3H), 4.45 (q, J = 7.2 Hz, 2H), 7.63-7.65 (m, 1H), 7.68-7.70 (m, 1H), 7.74-7.78 (m, 1H), 7.98-8.04 (m, 3H), 8.09 (dd, J = 7.6, 1.6 Hz, 1H), 8.24 (s, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.54 (d, J = 0.8 Hz, 1H), 8.64 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.5, 61.2, 120.1, 121.5, 122.1, 122.5, 123.2, 123.3, 127.0, 127.6, 127.7, 128.5, 129.0, 129.9, 130.6,

131.1, 132.4, 133.8, 134.0, 136.2, 140.7, 142.6, 166.9; IR (CH_2Cl_2) 2979, 1710, 1240, 1290 cm^{-1}; HRMS *m/z* 324.1157 (calcd for $C_{23}H_{16}O_2$, 324.1150).

6-Methylbenzo[*e*]acephenanthrylene (27). Compound **26** (98.5 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 37.2 mg (56 %) of the indicated compound **27** as a white solid: mp 149-151 °C; ^1H NMR ($CDCl_3$) δ 2.50 (s, 3H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.59-7.80 (m, 5H), 7.91 (d, *J* = 7.2 Hz, 1H), 8.01-8.02 (m, 1H), 8.17 (s, 1H), 8.40 (d, *J* = 8.0 Hz, 1H), 8.63 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.9, 119.2, 121.2, 121.3, 121.3, 122.8, 123.2, 126.8, 127.0, 127.6, 128.3, 129.0, 130.2, 130.8, 132.4, 134.1, 135.3, 137.2, 137.5, 138.2, 138.9; IR (CH_2Cl_2) 2921, 2852, 1460, 1600, 1374 cm^{-1}; HRMS *m/z* 266.1099 (calcd for $C_{21}H_{14}$, 266.1096).

10-Methoxydibenz[*e,l*]acephenanthrylene (31). Compound **30** (0.115 g, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 50:1 hexanes/ethyl acetate to afford 54.0 mg (65 %) of the indicated compound **31** as a white solid: mp 178-179 °C; ^1H NMR ($CDCl_3$) δ 3.95 (s, 3H), 6.93 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.46 (d, *J* = 2.1 Hz, 1H), 7.60-7.66 (m, 1H), 7.70-8.03 (m, 7H), 8.11 (s, 1H), 8.98 (d, *J* = 8.4 Hz, 1H), 9.19 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 107.4, 113.4, 119.6, 121.0, 122.8, 122.8, 126.0, 126.8, 127.3, 127.5, 127.8, 128.3, 128.4, 128.6, 128.7, 129.0, 131.5, 131.5, 133.8, 133.8, 136.1, 137.4, 142.6, 160.6; IR (CH_2Cl_2) 2921, 2849, 1608, 1461, 1285, 1213 cm^{-1}; HRMS *m/z* 332.1209 (calcd for $C_{25}H_{16}O$, 332.1201).

Indeno[1,2,3-*de*]quinoline (35). Compound **34** (82.8 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2.5 d. The reaction mixture was chromatographed using 3:2 hexanes/ethyl acetate to afford 27.4 mg (54 %) of the indicated compound **35** as a white solid: mp 100-101 °C (lit[31] mp 102-103 °C); ^{1}H NMR ($CDCl_3$) δ 7.35-7.51 (m, 2H), 7.72-7.77 (m, 2H), 7.84-7.91 (m, 3H), 7.99 (d, *J* = 8.4 Hz, 1H), 9.07 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 114.4, 121.0, 122.2, 123.7, 128.2, 128.4, 130.4, 131.7, 135.4, 138.2, 138.2, 140.5, 145.1, 145.7, 152.9. The other spectral properties were identical to those previously reported.[32]

Benzo[*f*]fluoreno[1,9-*b*,*c*]oxepine (44). Compound **43** (99.1 mg, 0.25 mmol) was allowed to react under our standard reaction conditions at 110 °C for 2 d. The reaction mixture was chromatographed using 18:1 hexanes/ethyl acetate to afford 53.6 mg (80 %) of the indicated compound **44** as a white solid: mp 106-107 °C; ^{1}H NMR ($CDCl_3$) δ 6.69 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.83 (s, 1H), 6.93-6.95 (m, 1H), 6.97-6.99 (m, 1H), 7.05-7.07 (m, 1H), 7.16-7.30 (m, 5H), 7.58-7.59 (m, 1H), 7.62-7.64 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 115.4, 117.2, 120.4, 120.6, 122.3, 124.8, 126.0, 127.2, 128.3, 128.7, 129.1, 131.3, 131.4, 132.4, 137.1, 137.6, 139.9, 141.0, 154.8, 155.6; IR (CH_2Cl_2) 3050, 1580, 1238, 1450, 1426 cm^{-1}; HRMS *m/z* 268.0892 (calcd for $C_{20}H_{12}O$, 268.0888).

Ethyl *E*-3-(4,4-dimethylisochroman-5-yl)acrylate (58). Compound **57** (72.0 mg, 0.25 mmol) and ethyl acrylate (32.5 mg, 0.325 mmol) were allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 7:1 hexanes/ethyl acetate to afford 36.4 mg (56 %) of the indicated compound **58** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.35 (t, *J* = 7.2 Hz, 3H), 1.38 (s, 6H), 3.54 (s, 2H), 4.28 (q, *J* = 7.2 Hz,

2H), 4.80 (s, 2H), 6.19 (d, J = 15.6 Hz, 1H), 6.98 (d, J = 7.2 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 8.30 (d, J = 15.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.5, 26.5, 34.0, 60.7, 69.6, 78.9, 119.8, 126.1, 126.3, 127.5, 134.9, 135.0, 141.5, 145.7, 167.0; IR (CH_2Cl_2) 3056.1, 2962.9, 2844.3, 1711.3, 1632.3, 1446.0 cm^{-1}; HRMS *m/z* 260.1416 (calcd for $C_{16}H_{20}O_3$, 260.1412).

8-Methyl-1*H*-indole[1,2-*b*]benzo[*d*]isothiazole-10-(*endo*-norbornan-2-yl)-5,5-dioxide (60). Compound **59**[15] (99.3 mg, 0.25 mmol) and norbornene (25.9 mg, 0.275 mmol) were allowed to react under our standard reaction conditions for 1 d. The reaction mixture was diluted with diethyl ether (50 mL) and washed with brine (25 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed under reduced pressure to afford 68.0 mg (75 %) of the indicated compound **60** as a yellow solid, which is easily recrystallized from $CHCl_3$/hexanes: mp 255-256 °C; ^{1}H NMR ($CDCl_3$) δ 1.42-1.49 (m, 3H), 1.71-1.75 (m, 2H), 1.89-1.94 (m, 2H), 2.07-2.08 (m, 1H), 2.51 (br s, 4H), 2.65 (br s, 1H), 3.28-3.31 (m, 1H), 7.18-7.23 (m, 1H), 7.26-7.28 (m, 1H), 7.31-7.36 (m, 1H), 7.60 (s, 1H), 7.68-7.72 (m, 2H), 7.83 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 22.3, 29.4, 30.7, 36.5, 37.8, 37.9, 41.1, 42.7, 112.0, 122.6, 122.8, 123.0, 123.2, 123.5, 125.5, 128.7, 129.2, 132.2, 133.0, 135.5, 145.0 (one sp2 carbon missing due to overlap); IR (neat) 2952, 2866, 1597, 1326, 1179 cm^{-1}; HRMS *m/z* 363.1300 (calcd for $C_{22}H_{21}NO_2S$, 363.1293).

***N*-Phenylcarbamic acid butyl ester (62).** Compound **61** (61.8 mg, 0.25 mmol) and *n*-BuOH (0.925 g, 12.5 mmol) were allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford

13.0 mg (27 %) of the indicated compound **62** as a yellow oil with spectral properties identical to those previously reported.[33]

Pivalanilide (63). Compound **61** (61.8 mg, 0.25 mmol) was allowed to react under our standard reaction conditions for 1 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 11.4 mg (26 %) of the indicated compound **63** as a white solid: mp 130-132 °C (lit[34] mp 133-134 °C). All the spectral properties were identical to those previously reported.[35]

Benzanilide (65). Compound **64**[25] (76.8 mg, 0.25 mmol) and H_2O (45.0 mg, 2.5 mmol) were allowed to react under our standard reaction conditions for 2 d. The reaction mixture was chromatographed using 3:1 hexanes/ethyl acetate to afford 27.6 mg (56 %) of the indicated compound **65** as a white solid: mp 163-164 °C. This compound was characterized by comparing the melting point and ^1H and ^{13}C NMR spectra with an authentic sample obtained from Aldrich Chemical Co., Inc.

***E*-2,3-Diphenylprop-2-en-1-yl pivalate (66a) and *Z*-2,3-diphenylprop-2-en-1-yl pivalate (66b).** Iodobenzene (51.0 mg, 0.25 mmol) and 1-phenyl-1-propyne (34.8 mg, 0.30 mmol) were allowed to react under our standard reaction conditions at 100 °C for 21 h. The reaction mixture was chromatographed using 30:1 hexanes/ethyl acetate to afford 18.7 mg (25 %) of the indicated compounds **66a** and **66b** as an inseparable 50:50 mixture: ^1H NMR ($CDCl_3$) δ 1.11 (s, 9H), 1.13 (s, 9H), 4.91 (br s, 2H), 5.12 (br s, 2H), 6.67 (s, 1H), 6.98-7.47 (m, 20H); ^{13}C NMR ($CDCl_3$) δ 27.2, 27.3, 62.2, 69.2, 126.7, 127.3, 127.7, 127.8, 127.8, 128.2, 128.6, 128.7, 128.8, 129.0, 129.1, 129.1, 129.5, 133.0; IR (CH_2Cl_2) 3058, 2971, 2926, 2869, 1729, 1479, 1446 cm^{-1}; HRMS *m/z* 294.1623 (calcd for $C_{20}H_{22}O_2$, 294.1620).

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References

(1) (a) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. (b) Li, Chao-Jun *Acc. Chem. Res.* **2002**, *35*, 533. (c) Catellani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1983**, *250*, 509. (d) Oyamada, J.; Jia, C.; Fujiwara, Y. *Chem. Lett.* **2002**, 2. (e) Oyamada, J.; Jia, C.; Fujiwara, Y. *Chem. Lett.* **2002**, 380. (f) Jia, C.; Piao, D.; Kitamura, T.; Fujiwara, Y. *J. Org. Chem.* **2000**, *65*, 7516.

(2) (a) Fujiwara, Y.; Jia, C. *Handbook of Organopalladium Chemistry for Organic Synthesis* **2002**, *2*, 2859. (b) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633.

(3) Larock, R. C.; Tian, Q. *J. Org. Chem.* **2001**, *66*, 7372.

(4) Campo, M. A.; Larock, R. C. *J. Am. Chem. Soc.* **2002**, *124*, 14326.

(5) Satoh, T.; Inoch, J.; Kawamura, Y.; Kawamura, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2239.

(6) (a) Old, D. W.; Harris, M. C.; Buchwald, S. L. *Org. Lett.* **2000**, *2*, 1403. (b) Mann, G.; Incarvito, C.; Rheingold, A. L.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 3224. (c) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989.

(7) For mechanistic studies suggesting electrophilic species in intramolecular C-H activation by palladium, see: (a) Martin-Matute, B.; Mateo, C.; Cardenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2001**, *7*, 2341 and references therein. (b) Catellani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1992**, *425*, 151 and references therein.

(8) Tuanli Yao, Marino A. Campo and Richard C. Larock, work in progress.

(9) For full details, see Chapter 2 of this dissertation.

(10) The spectral properties of this compound were identical to those previously reported, see: Hellwinkel, D.; Goeke, K. *Synthesis*, **1995**, 1135.

(11) Heck, R. F. *J. Organomet. Chem.* **1972**, *37*, 389. For a similar alkyl to aryl palladium migration, see: Catellani, M.; Cugini, F.; Bocelli, G. *J. Organomet. Chem.* **1999**, *584*, 63.

(12) For a similar Rh-catalyzed norbornyl to aryl type migration using arylboronic acid precursors, see: Oguma, K.; Miura, M.; Satoh, T.; Nomura, M. *J. Am. Chem. Soc.* **2000**, *122*, 10464.

(13) For an analogous rearrangement of carbamic anhydride intermediates, see: Newman, M. S.; Lee, S. H.; Garrett, A. B. *J. Am. Chem. Soc.* **1947**, *69*, 113.

(14) For nucleophilic reactions on palladium imidate intermediates, see: Saluste, C. G.; Whitby, R. J.; Furber, M. *Tetrahedron Lett.* **2001**, *42*, 6191.

(15) (a) Campo, M. A.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3675. (b) Campo, M. A.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 5616.

(16) Burton, H; Praill, P. F. G. *J. Chem. Soc.* **1953**, 827.

(17) Hart, H.; Harada, K.; Du, C. *J. Org. Chem.* **1985**, *50*, 3104.

(18) Evans, A. E.; Katz, J. L.; West, T. R. *Tetrahedron Lett.* **1998**, *39*, 2937.

(19) John, J. A.; Tour, J. M. *Tetrahedron* **1997**, *53*, 15515.

(20) Appelberg, U.; Mohell, N.; Hacksell, U. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 415.

(21) Inoue, J.; Cui, Y.-S.; Sakai, O.; Nakamura, Y.; Kogiso, H.; Kador, P. F. *Bioorg. Chem.* **2000**, *8*, 2167.

(22) Larock, R. C.; Yum, E. K.; Doty, M. J.; Sham, K. C. *J. Org. Chem.* **1995**, *60*, 3270.

(23) Kundu, N. G.; Khan, M. W. *Tetrahedron* **2000**, *56*, 4777.

(24) Fukujama, T.; Chen, X.; Peng, G. *J. Am. Chem. Soc.* **1994**, *116*, 3127.

(25) Roesch, K. R.; Larock, R. C. *J. Org. Chem.* **2001**, *66*, 412.

(26) McCall, E. B.; Neale, A. J.; Rawlings, T. J. *J. Chem Soc.* **1962**, 4900.

(27) Badger, G. M.; Donnelly, J. K.; Spotswood, T. M. *Aust. J. Chem.* **1964**, *17*, 1147.

(28) Yu, C.; Levy, G. C. *J. Am. Chem. Soc.* **1984**, *106*, 6533.

(29) Badger, G. M.; Novotny, J. *Aust. J. Chem.* **1963**, *16*, 623.

(30) Rice, J. E.; Cai, Zhen-Wei *J. Org. Chem.* **1993**, *58*, 1415.

(31) Koelsch, S. *J. Org. Chem.* **1953**, *18*, 1516.

(32) Dalgaard, M. *J. Am. Chem. Soc.* **1978**, *100*, 6887.

(33) McGhee, W.; Riley, D.; Christ, K.; Pan, Y.; Parnas, B. *J. Org. Chem.* **1995**, *60*, 2820.

(34) Suzuki, H.; Tsuji, J.; Sato, N.; Osuka, A. *Chem. Lett.* **1983**, 449.

(35) Bezombes, J. P.; Hitchcock, P. B.; Lappert, M. F.; Merle, P. G. *J. Chem. Soc. Dalton Trans.* **2001**, *6*, 816.

GENERAL CONCLUSIONS

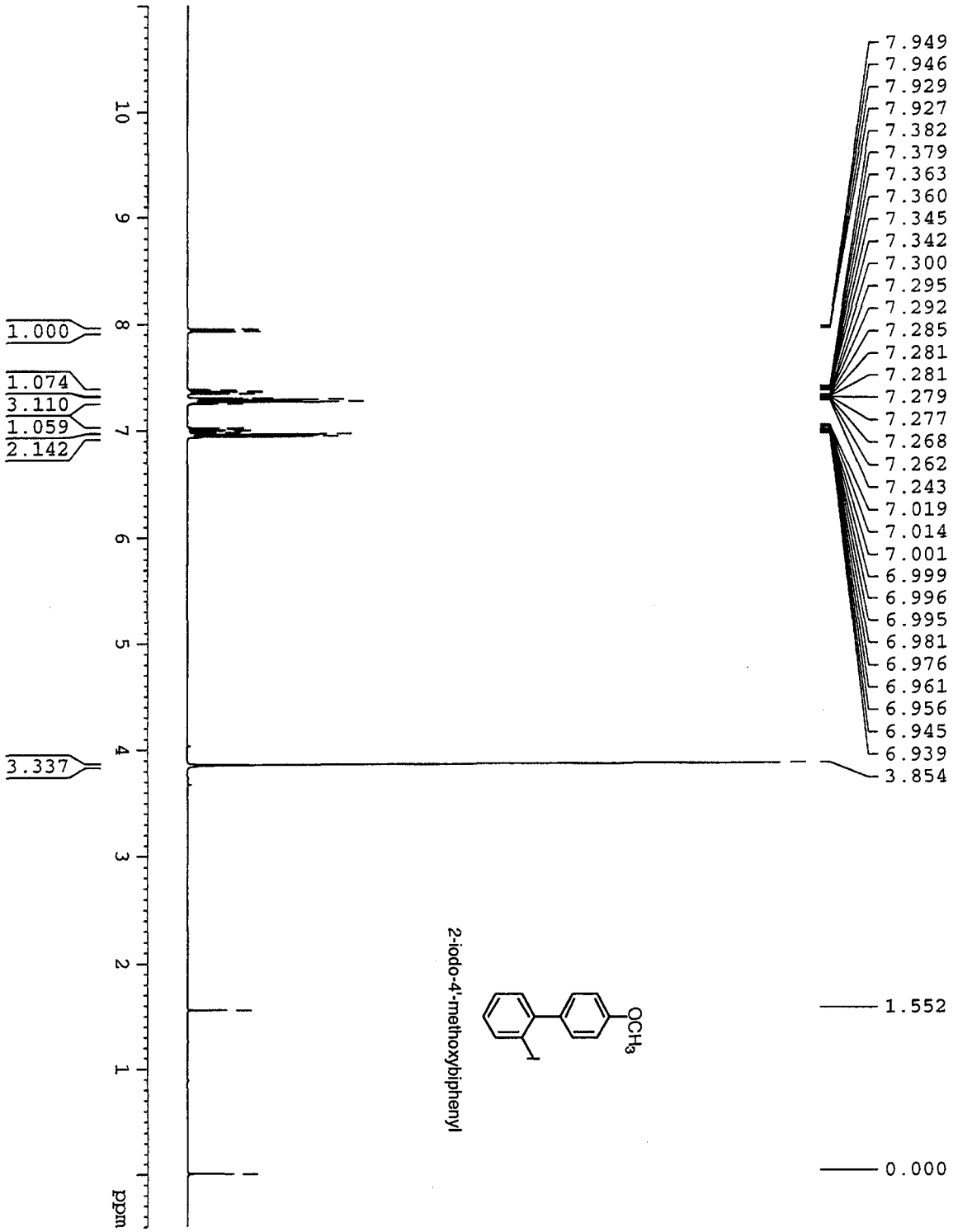
In this dissertation, the scope and limitations of several palladium-catalyzed processes have been presented. In particular, the palladium-catalyzed intramolecular C-H activation of *o*-halobiaryls has been exploited for the synthesis of a wide variety of polycycles and heterocycles.

Chapter 1 describes the synthesis of various carbocyclic and heterocyclic ketones by the palladium-catalyzed cyclocarbonylation of *o*-halobiaryls. This methodology works well for electron-rich, as well as electron-poor, *o*-halobiaryls. This reaction proceeds with good regioselectivity favoring the less sterically-congested isomer.

Chapter 2 describes Heck, Suzuki and alkyne annulation reactions with *o*-halobiaryls. These reactions have revealed that arylpalladium intermediates undergo a facile 1,4-palladium shift. After studying various reaction variables, we have learned that this palladium migration can be activated or suppressed at will by simply choosing the appropriate set of reaction conditions. These experiments consistently point to the intermediacy of an electrophilic palladium species.

Chapter 3 describes novel methodology involving the sequential transformation of *o*-halobiaryls to fused polycycles. This methodology works best for electron-rich arenes, which is in agreement with the idea that C-H activation by palladium parallels electrophilic aromatic substitution. We have been able to exploit a wide range of palladium migrations to generate the key organopalladium intermediates required for these cyclizations.

APPENDIX A. CHAPTER 1 ^{1}H AND ^{13}C NMR SPECTRA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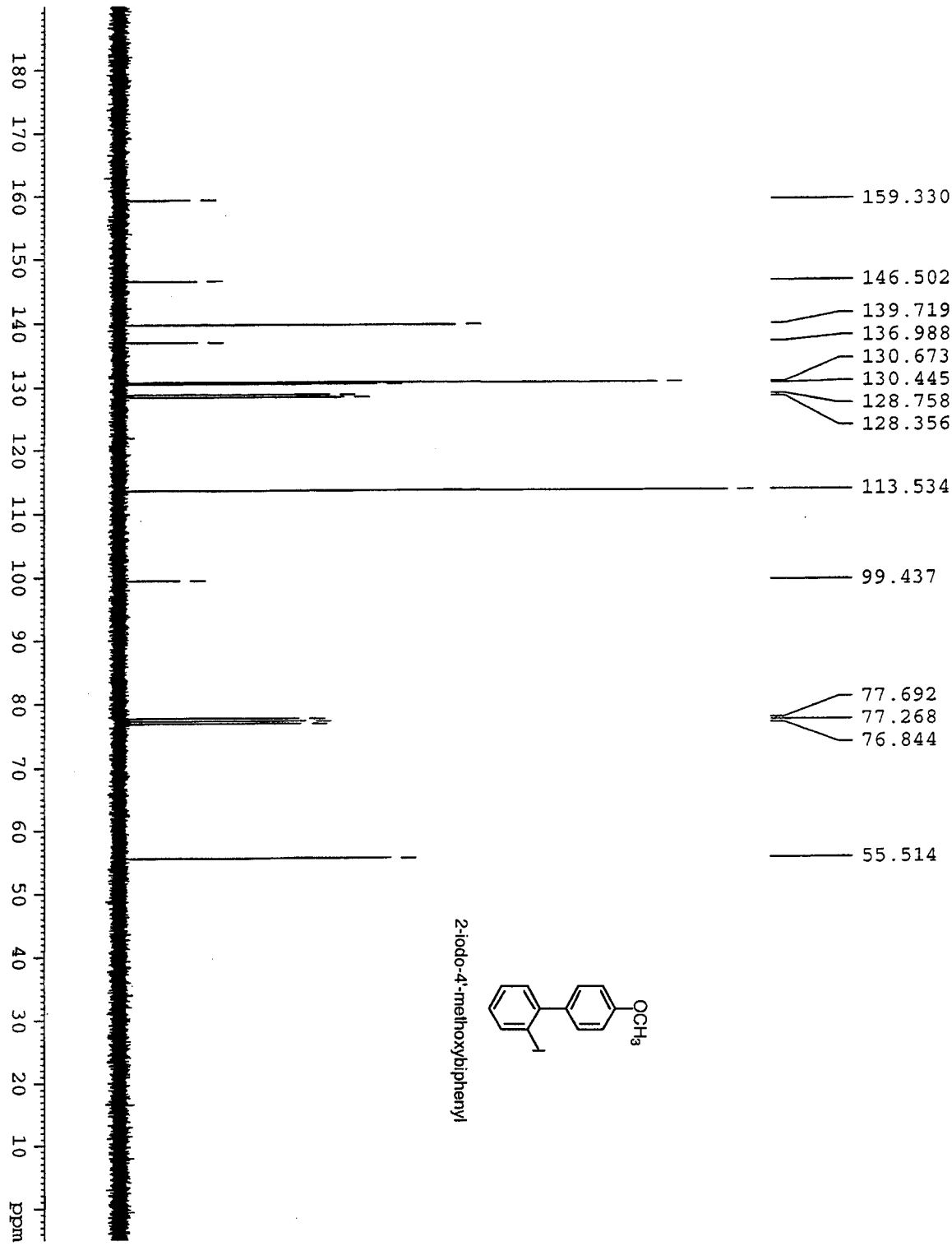
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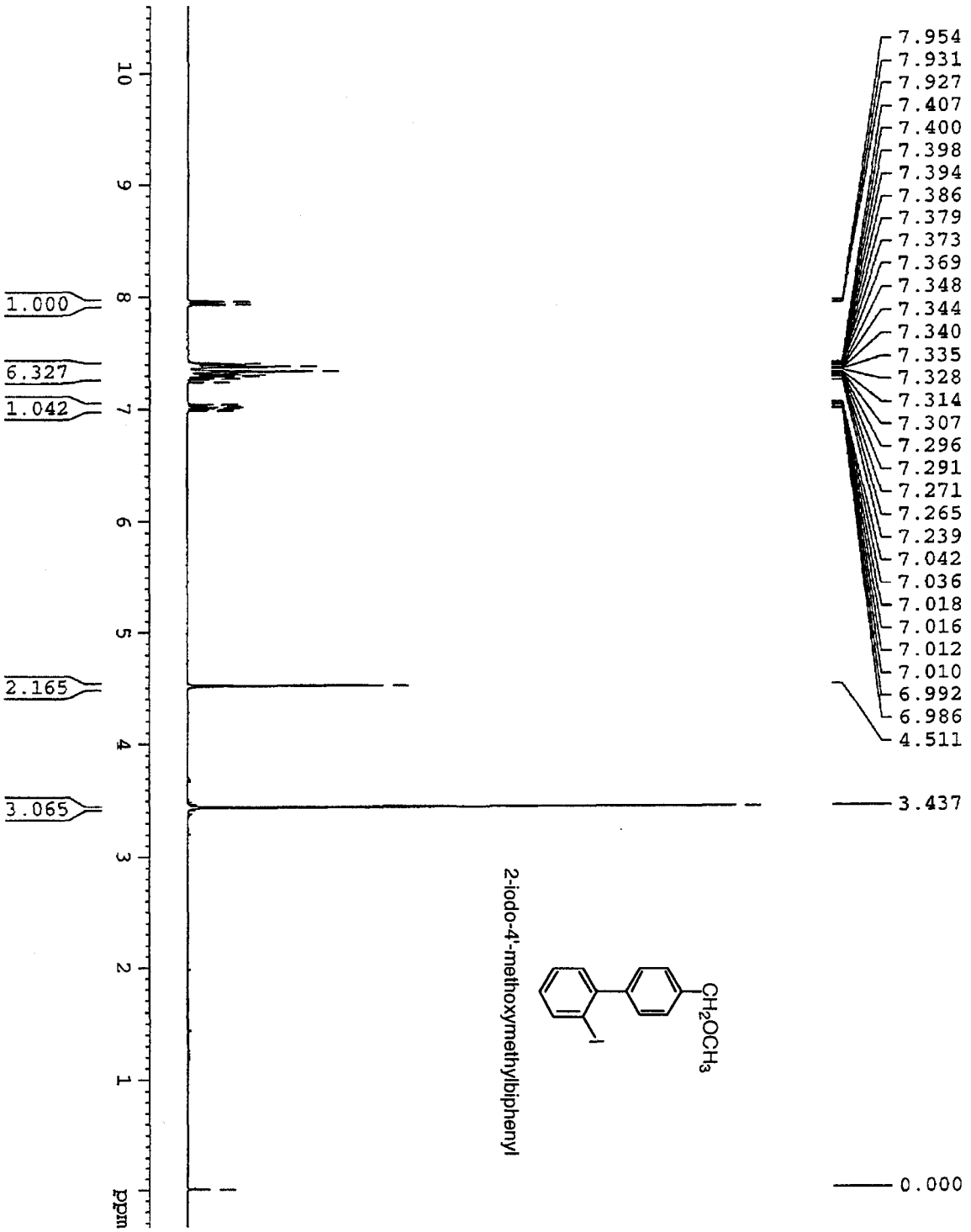
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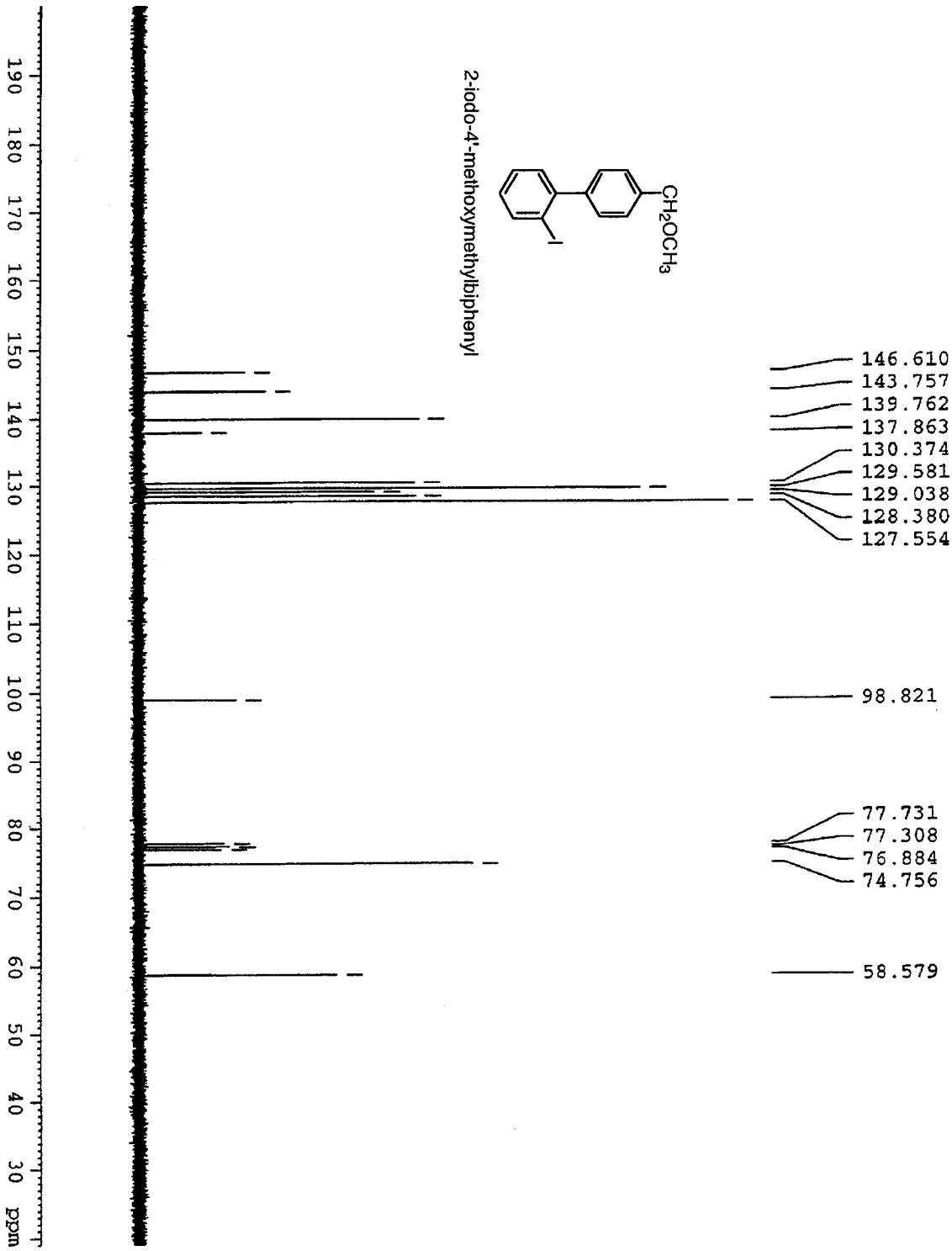
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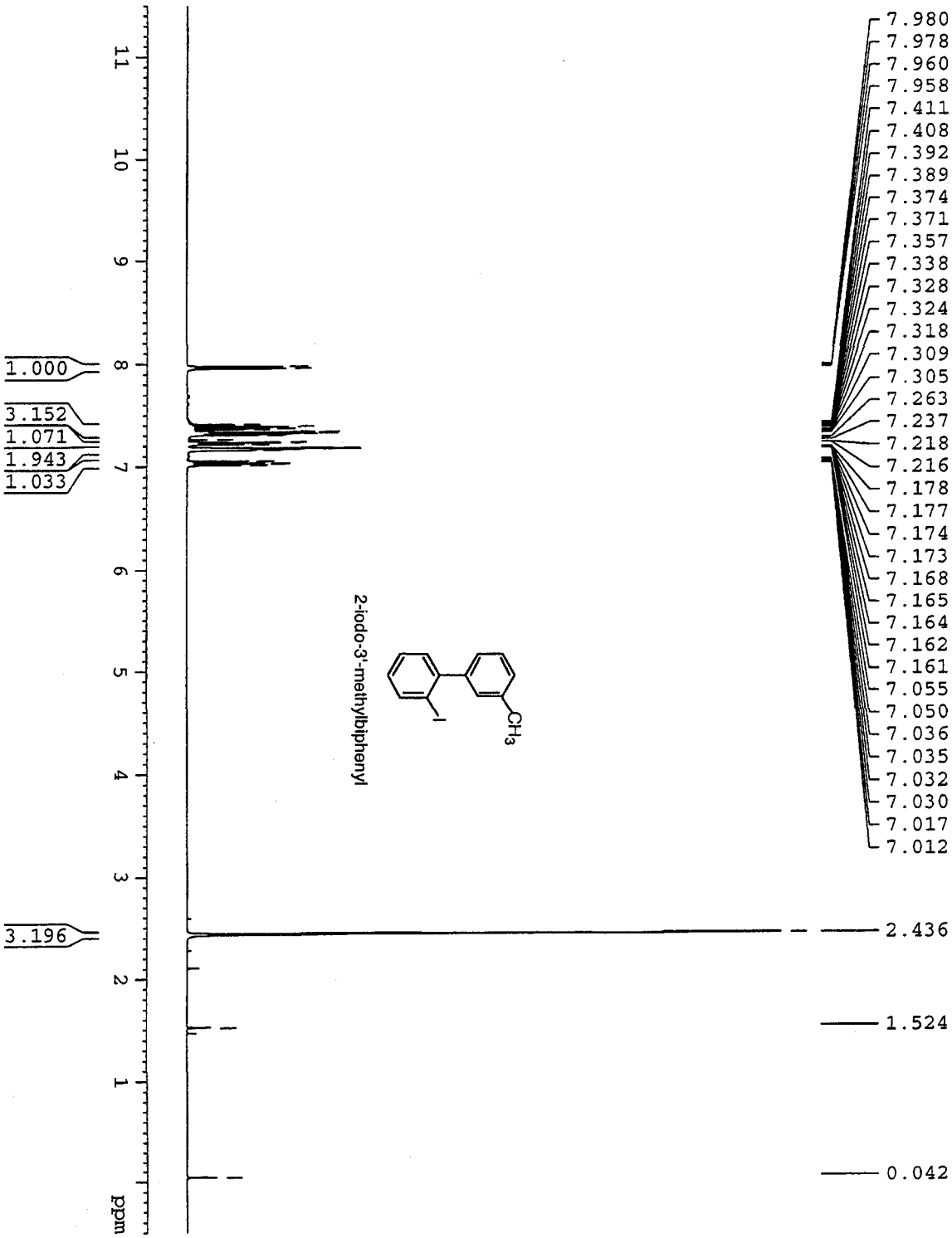
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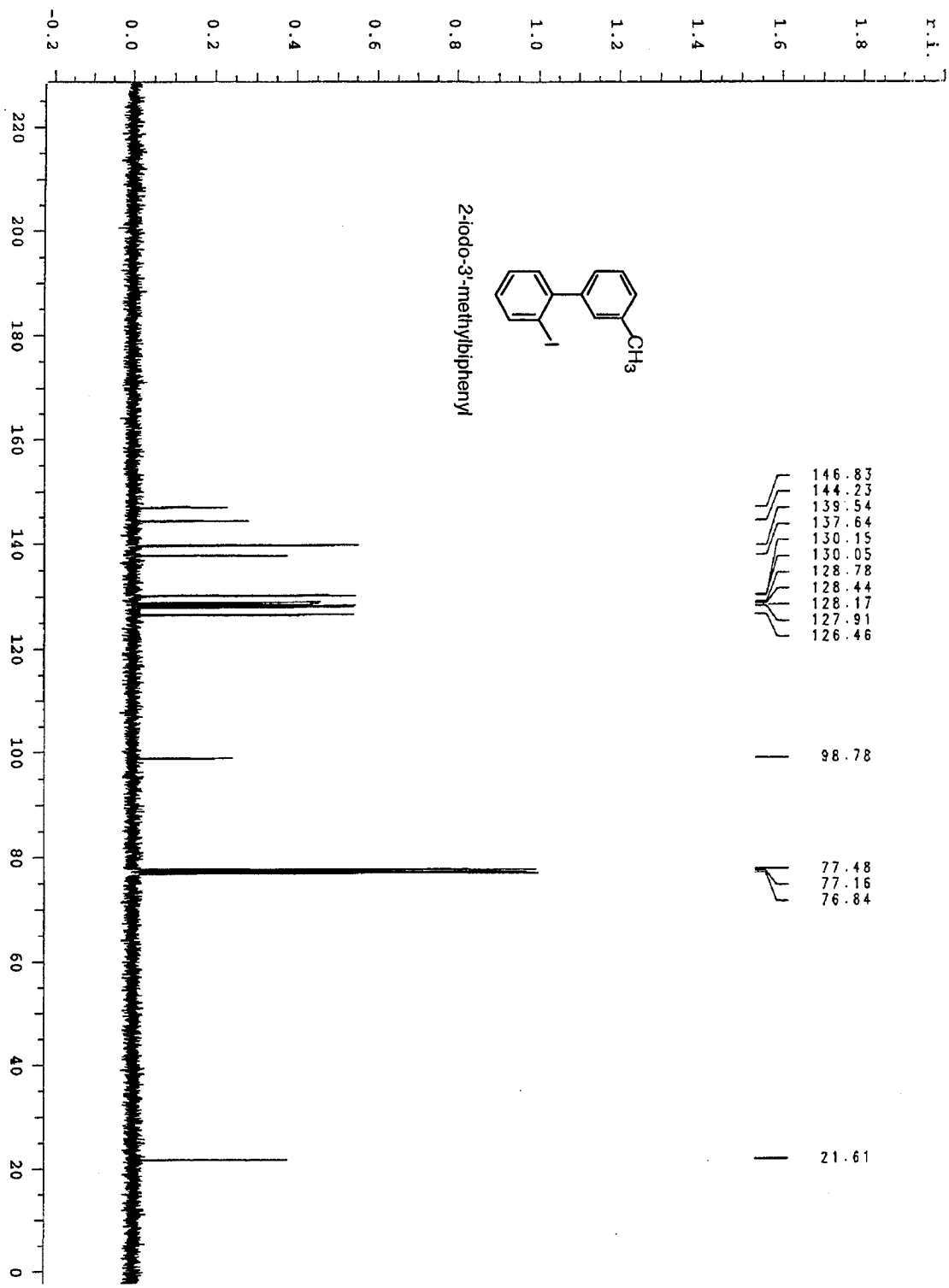
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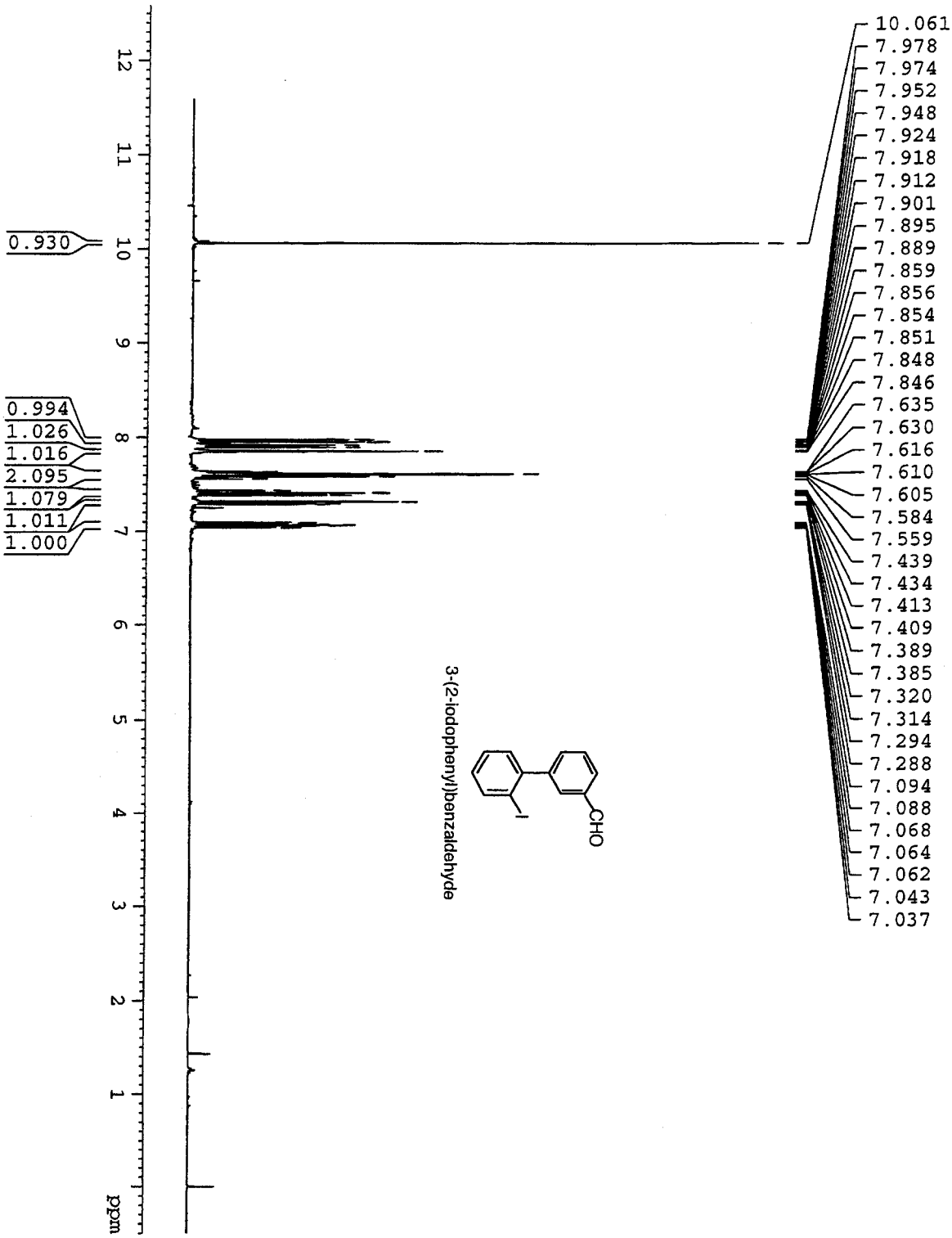
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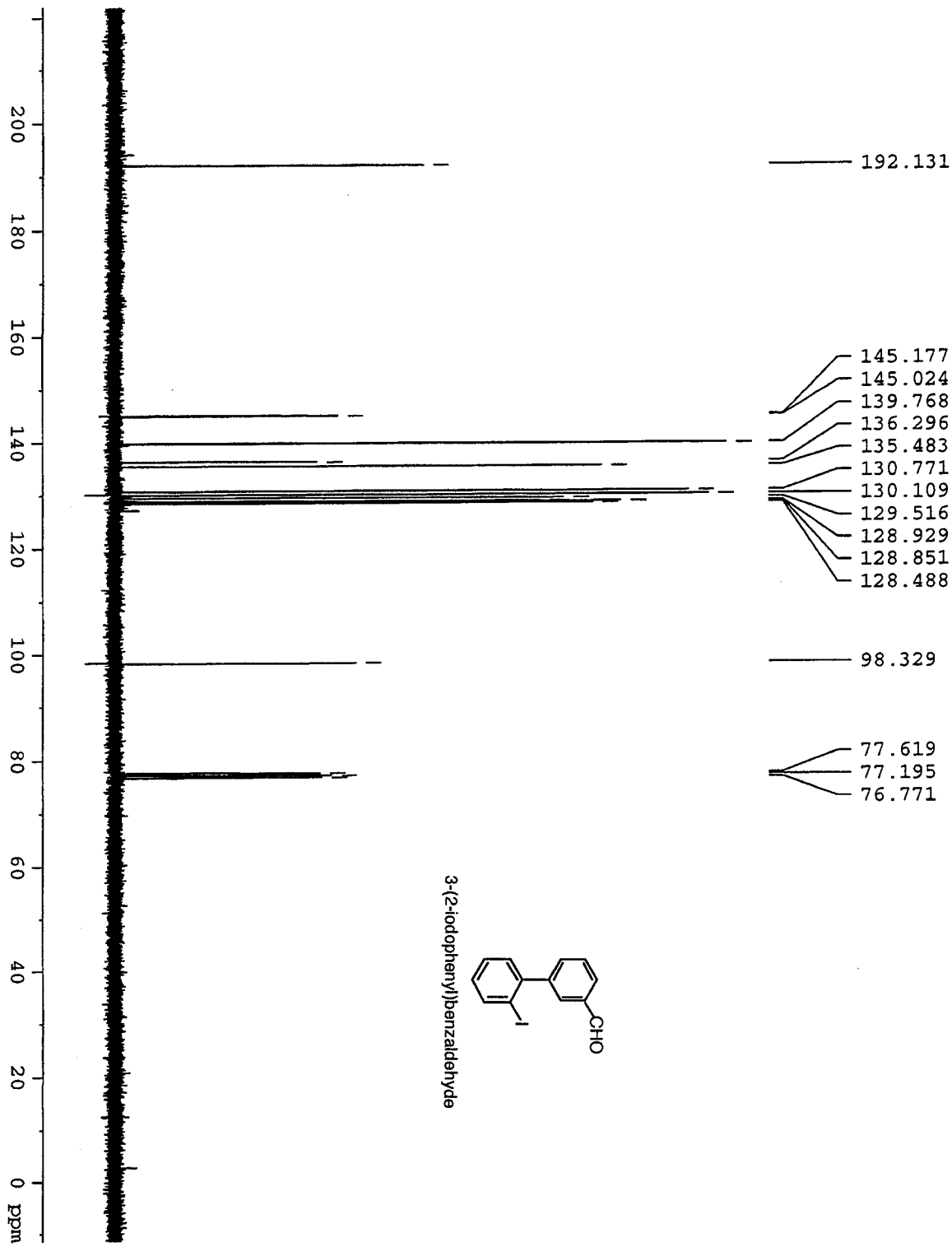
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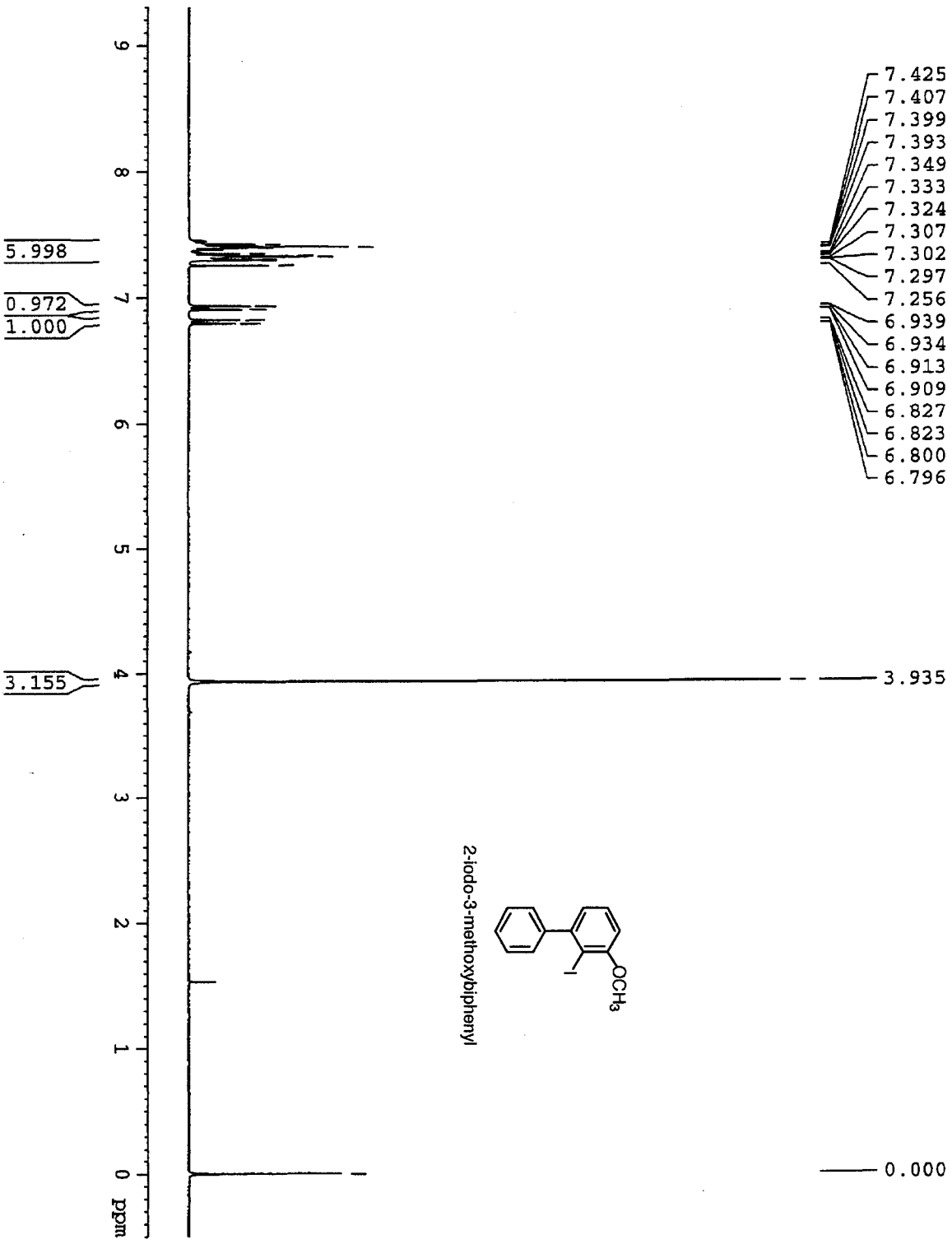
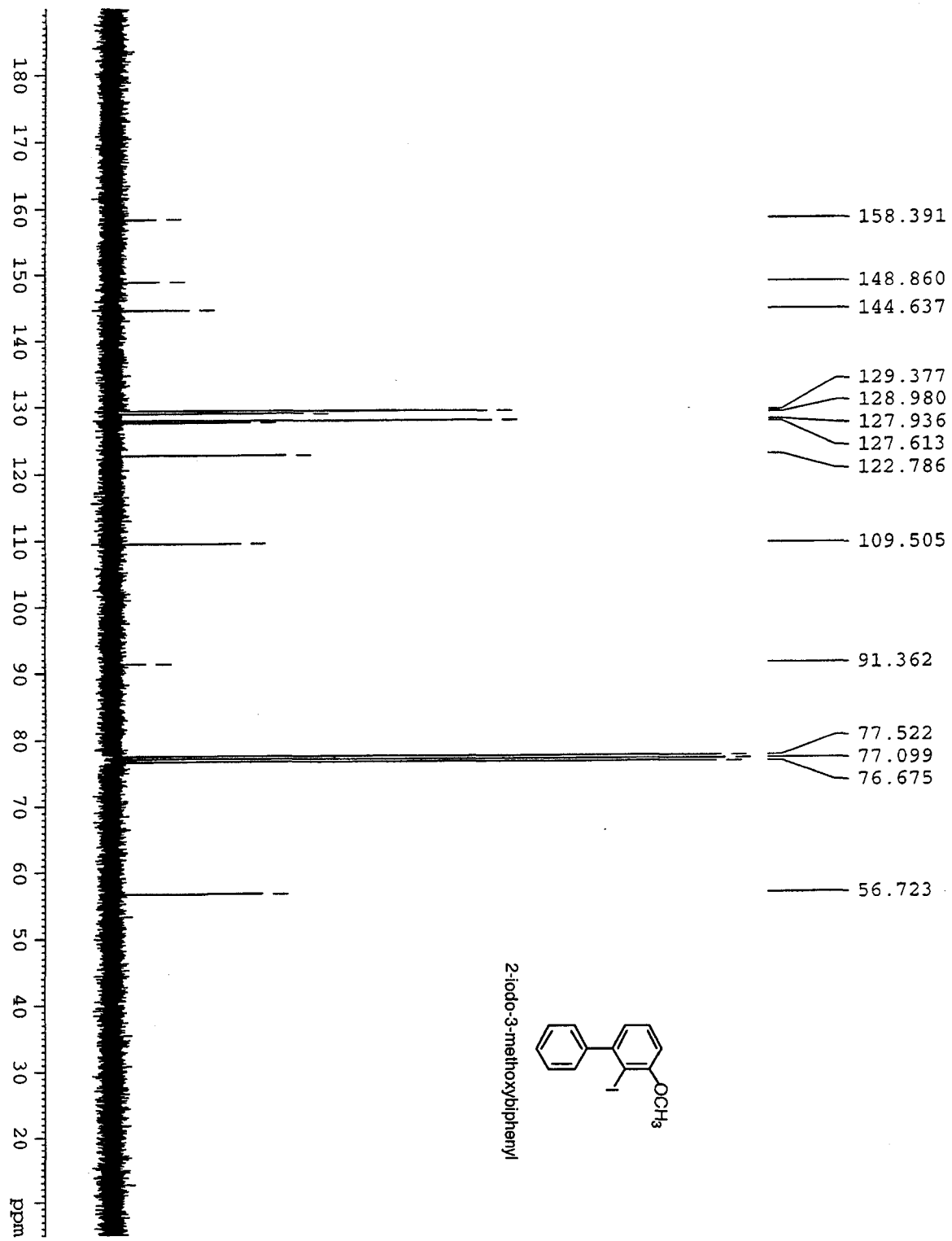
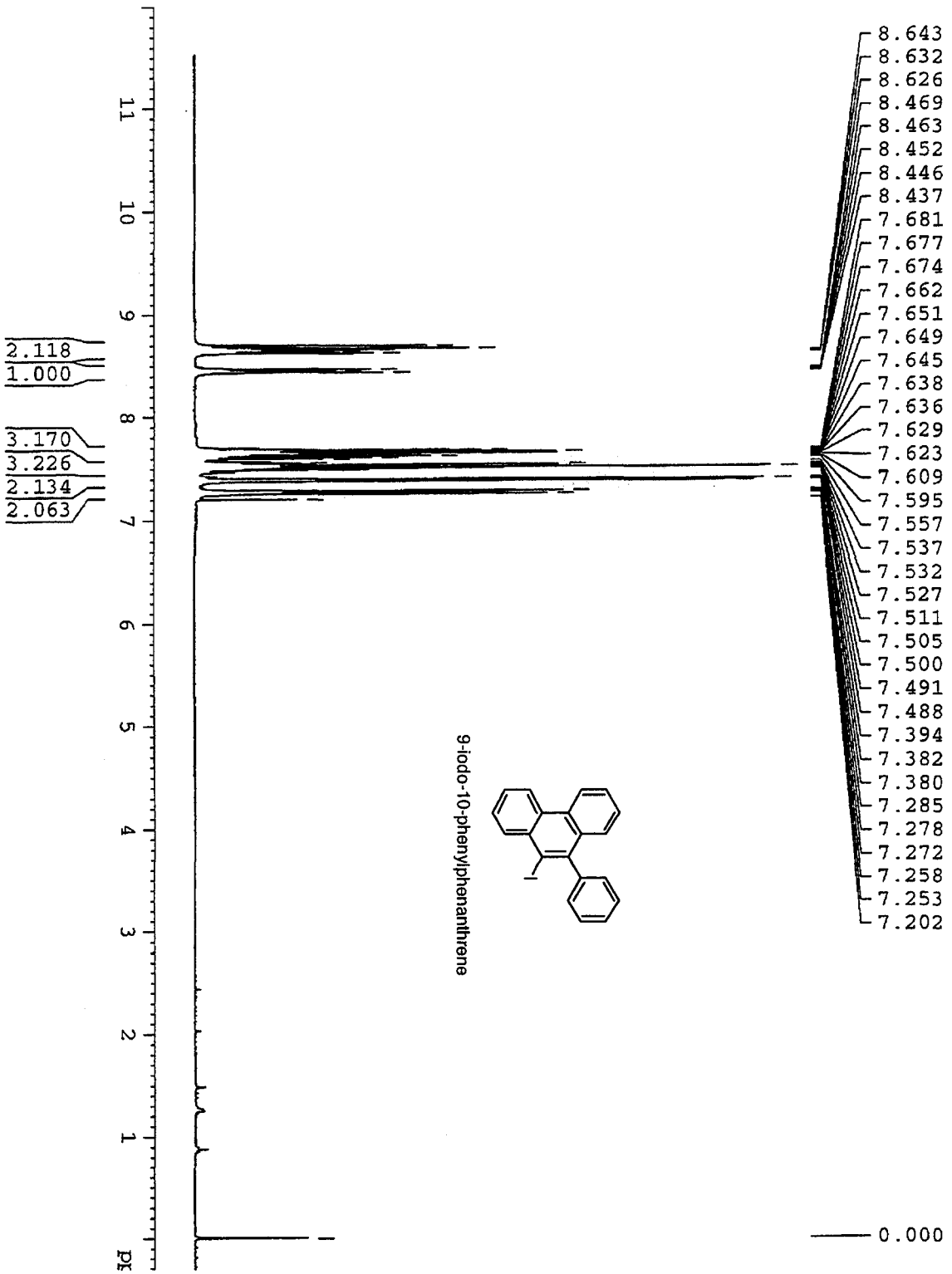
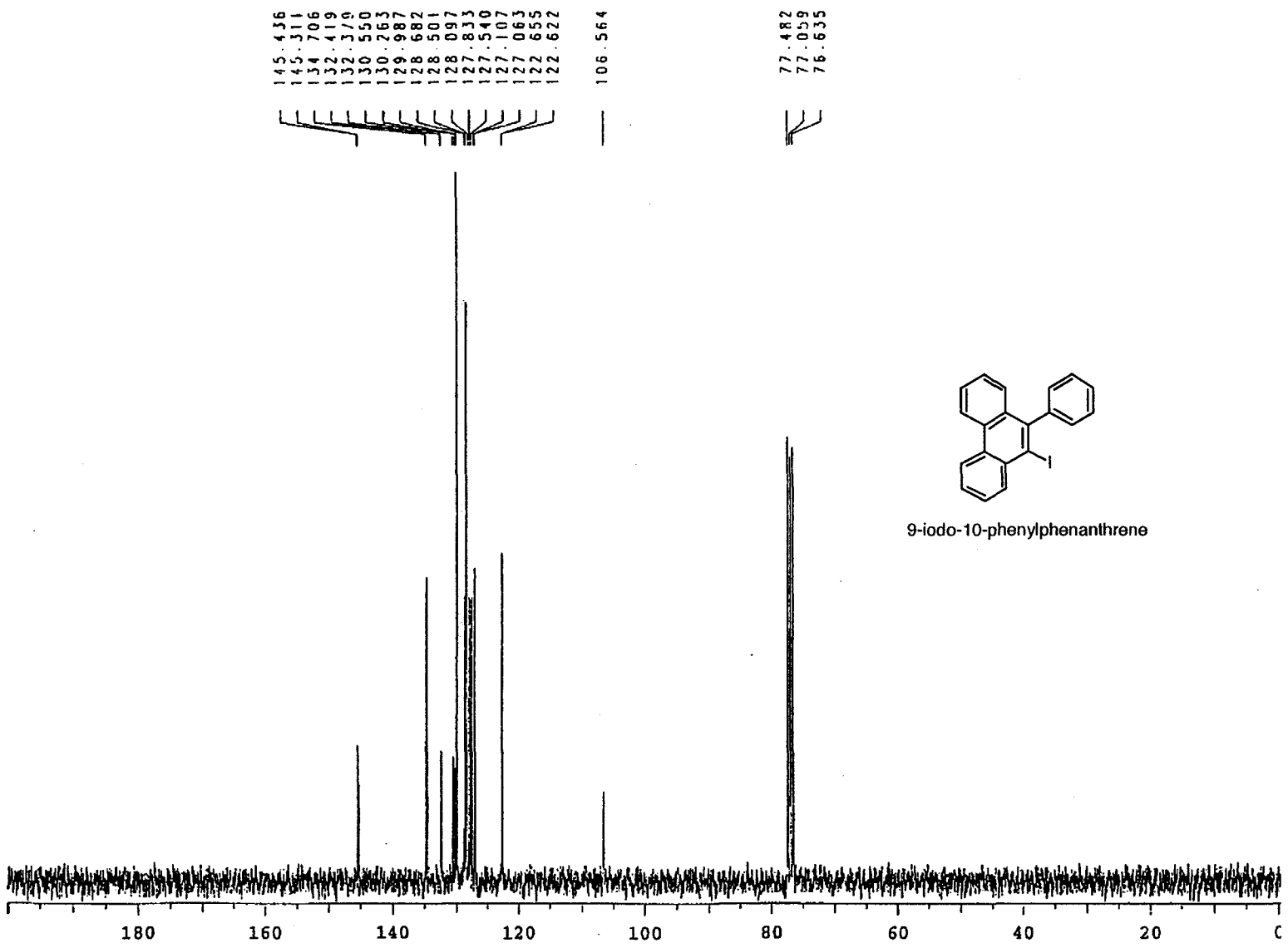
20
0 ppm
3-(2-iodophenyl)benzaldehyde
I
CHO

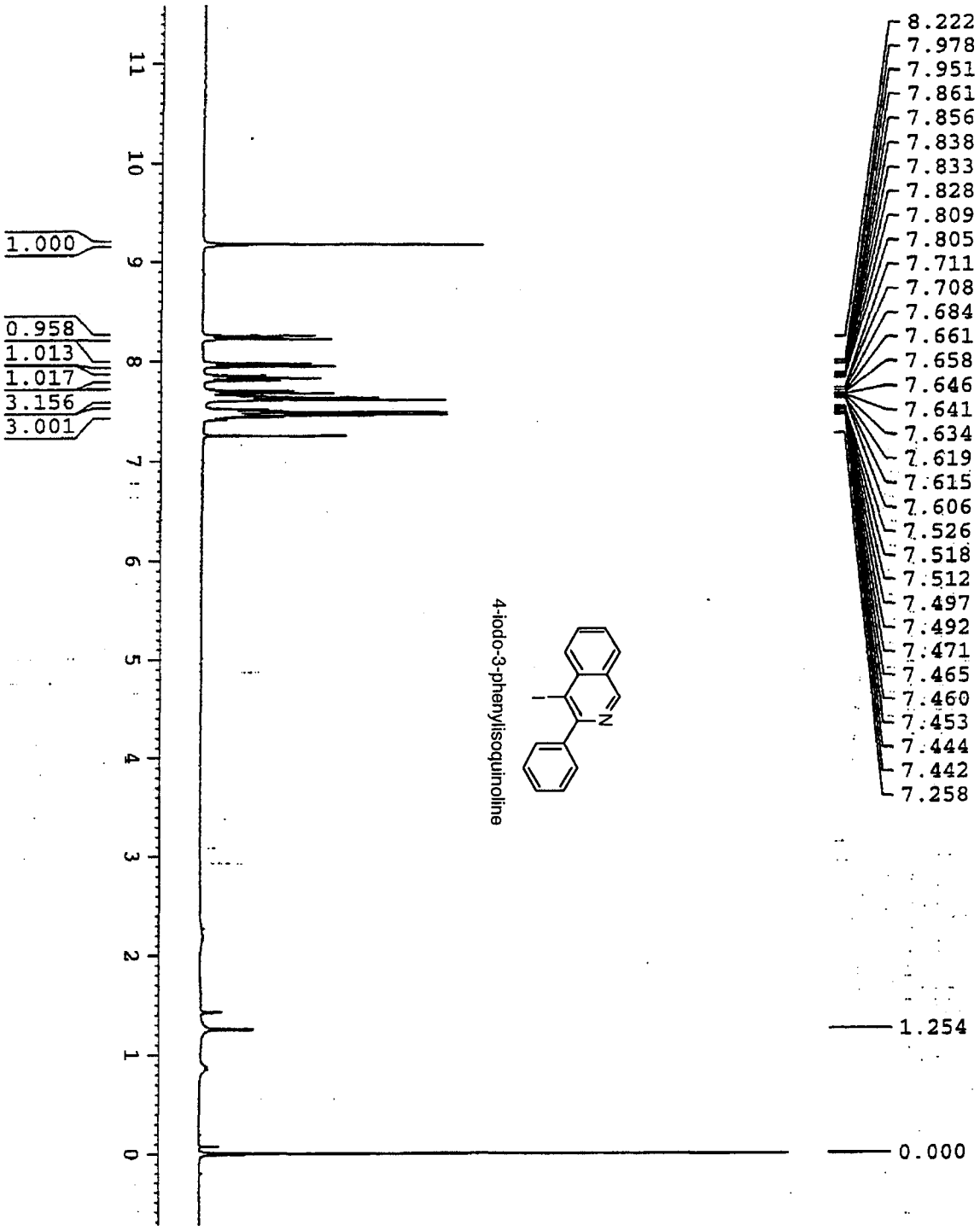

7.425
7.407
7.399
7.393
7.349
7.333
7.324
7.307
7.302
7.297
7.256
6.939
6.934
6.913
6.909
6.827
6.823
6.800
6.796
5.998
0.972
1.000
3.155
3.935
0.000
ppm
2-iodo-3-methoxybiphenyl
I
OCH3

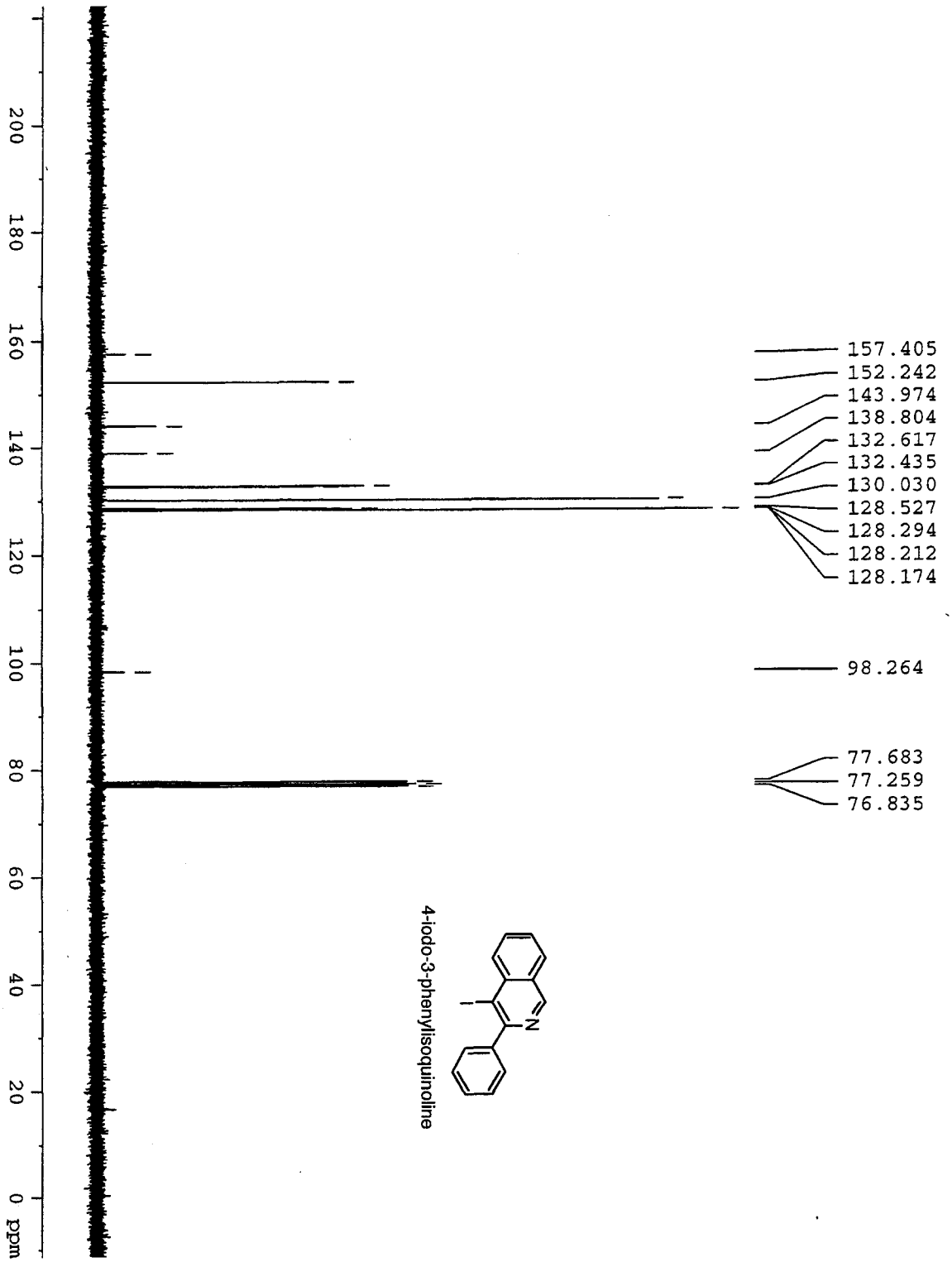

158.391
148.860
144.637
129.377
128.980
127.936
127.613
122.786
109.505
91.362
77.522
77.099
76.675
56.723
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm
2-iodo-3-methoxybiphenyl
I
OCH3

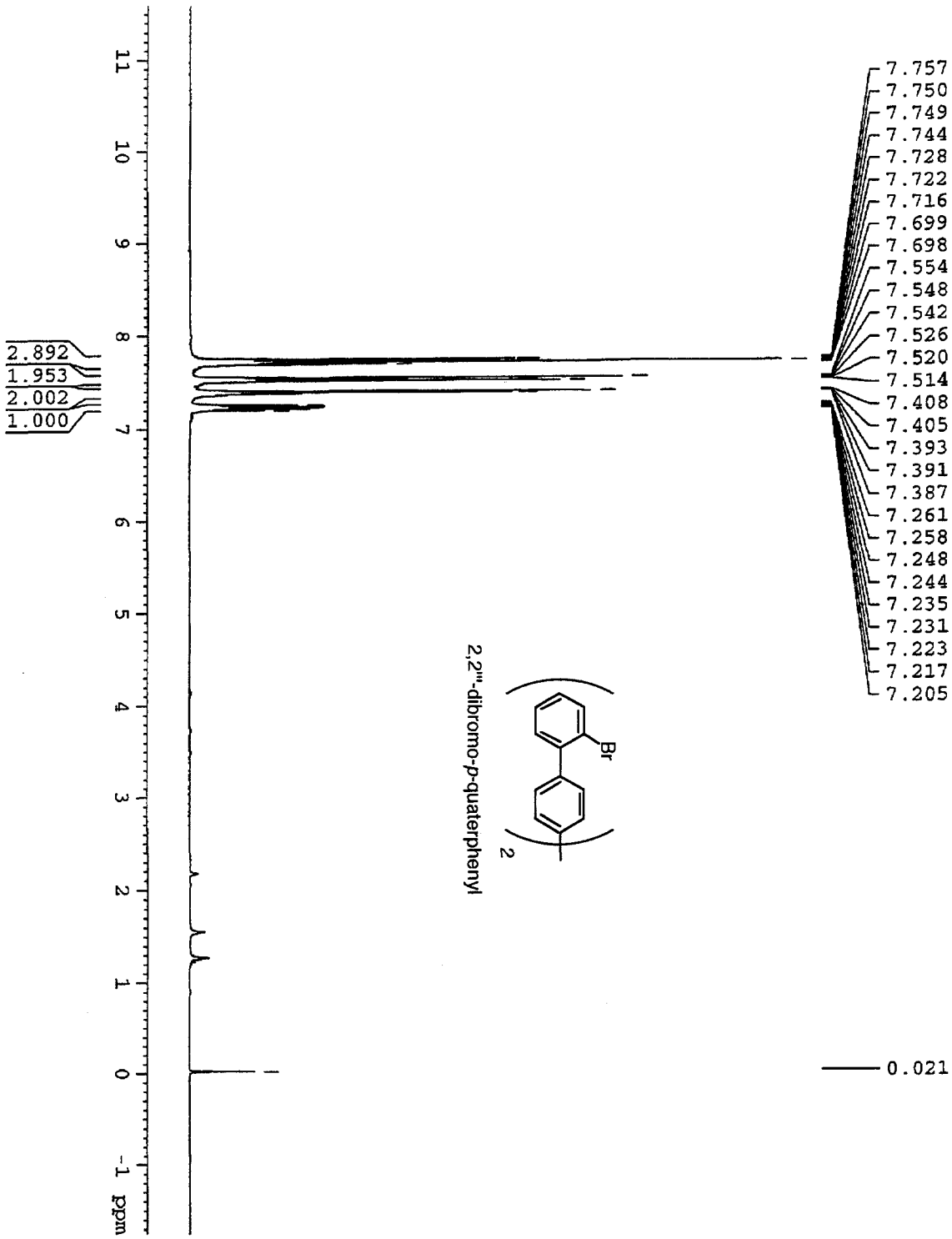

8.643
8.632
8.626
8.469
8.463
8.452
8.446
8.437
7.681
7.677
7.674
7.662
7.651
7.649
7.645
7.638
7.636
7.629
7.623
7.609
7.595
7.557
7.537
7.532
7.527
7.511
7.505
7.500
7.491
7.488
7.394
7.382
7.380
7.285
7.278
7.272
7.258
7.253
7.202
0.000
2.118
1.000
3.170
3.226
2.134
2.063
9-iodo-10-phenylphenanthrene
11
10
9
8
7
6
5
4
3
2
1
ppm

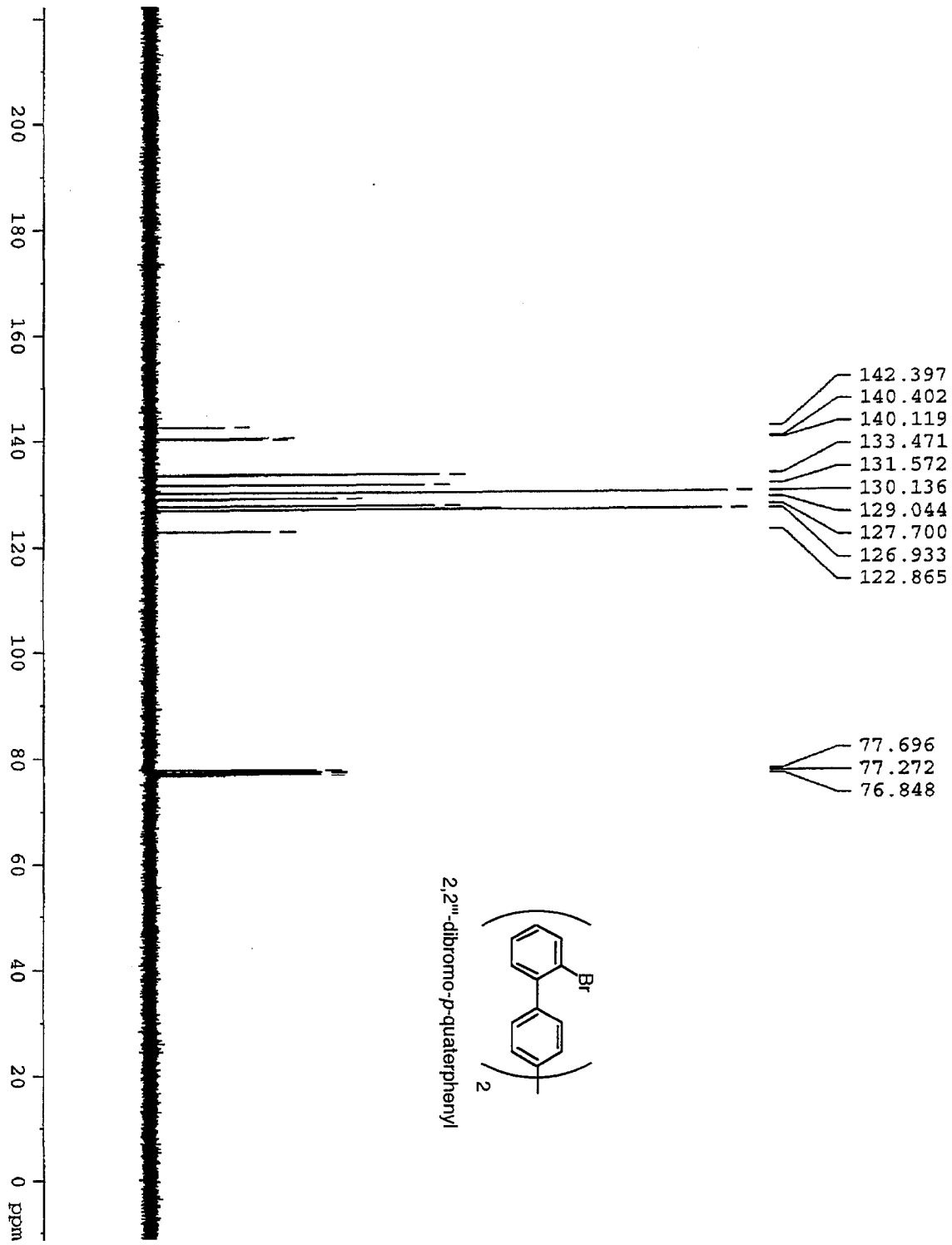


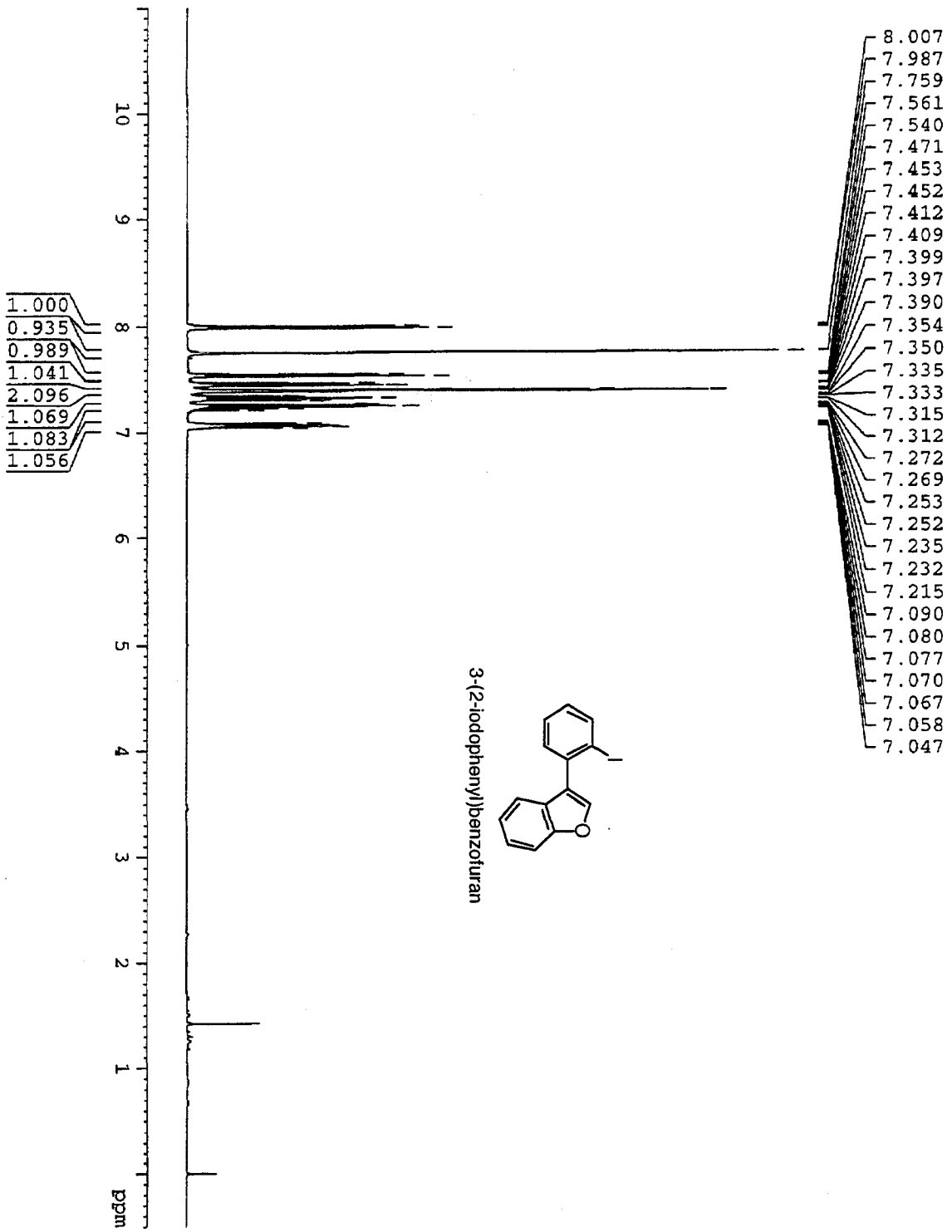
9-iodo-10-phenylphenanthrene

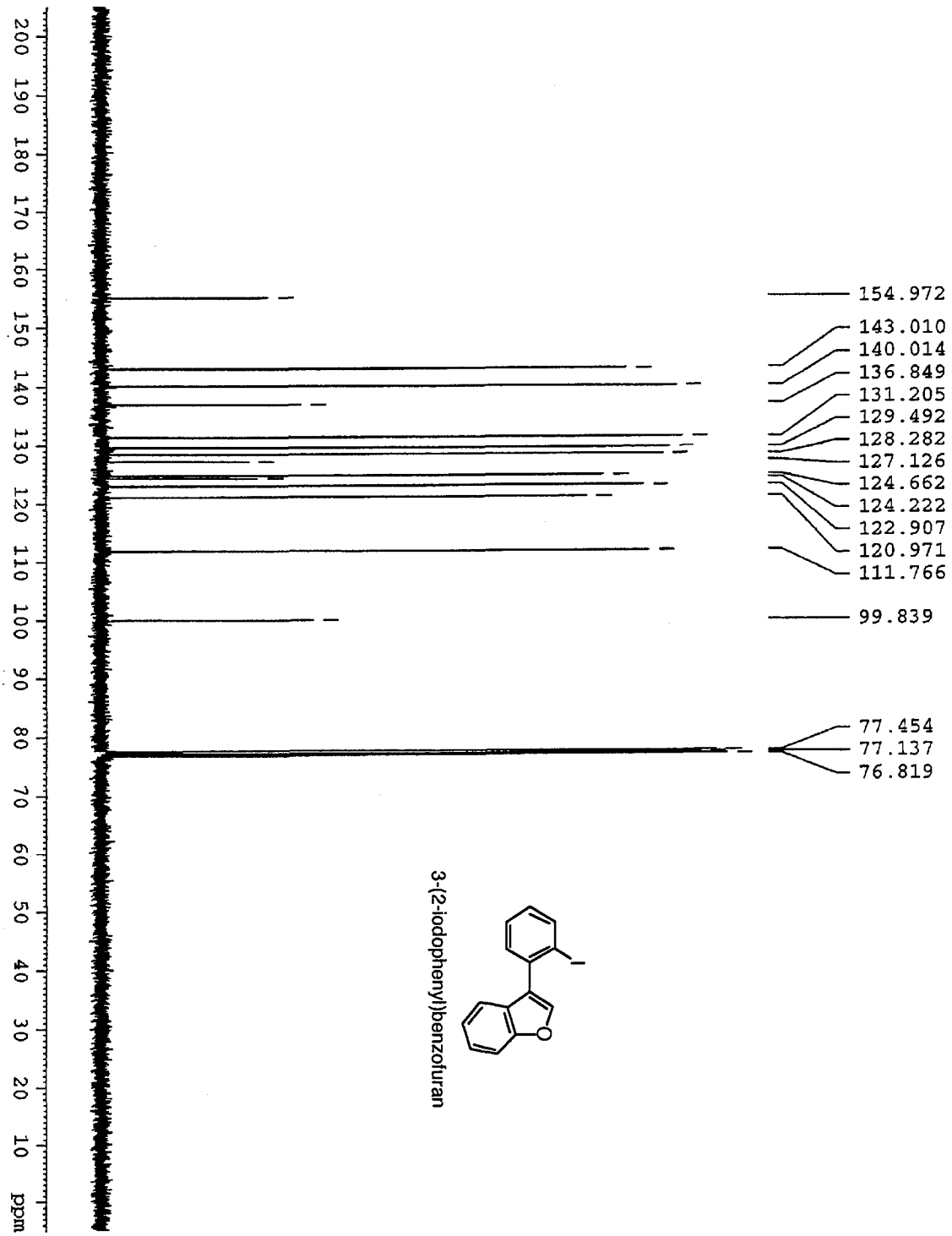

8.222
7.978
7.951
7.861
7.856
7.838
7.833
7.828
7.809
7.805
7.711
7.708
7.684
7.661
7.658
7.646
7.641
7.634
7.619
7.615
7.606
7.526
7.518
7.512
7.497
7.492
7.471
7.465
7.460
7.453
7.444
7.442
7.258
1.254
0.000
1.000
0.958
1.013
1.017
3.156
3.001
4-iodo-3-phenylisoquinoline
I
N

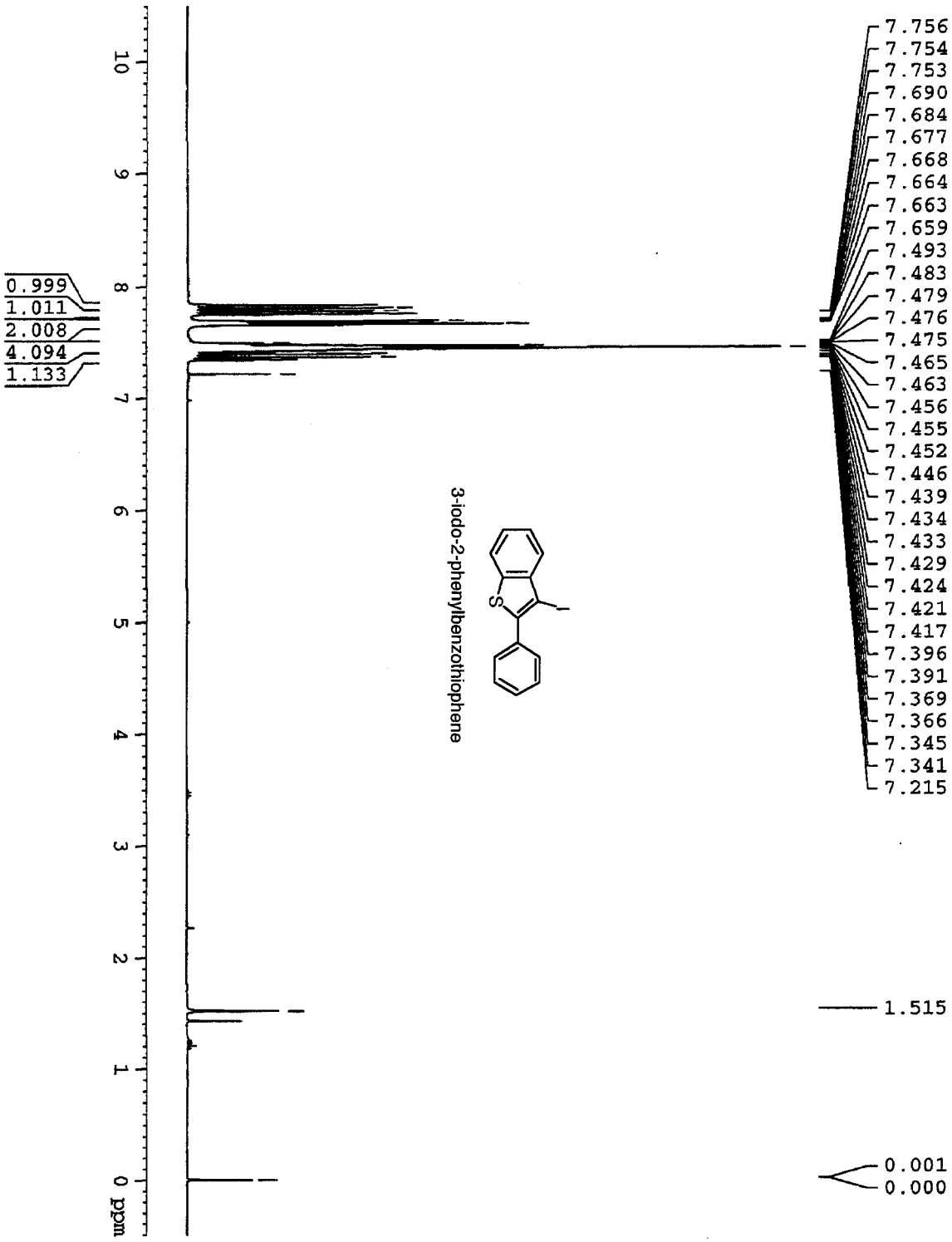

157.405
152.242
143.974
138.804
132.617
132.435
130.030
128.527
128.294
128.212
128.174
98.264
77.683
77.259
76.835
200
180
160
140
120
100
80
60
40
20
0 ppm
4-iodo-3-phenylisoquinoline
N

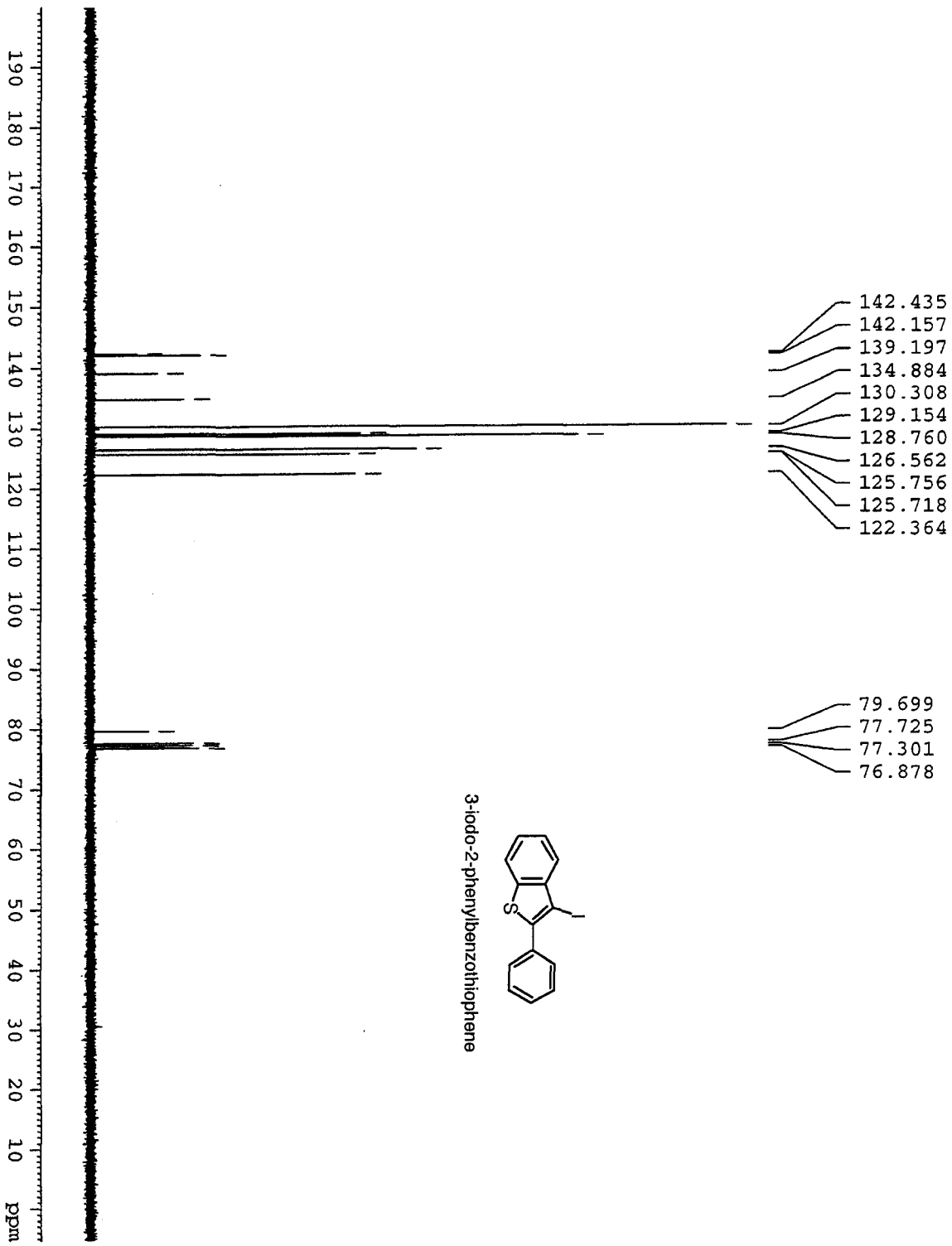

7.757
7.750
7.749
7.744
7.728
7.722
7.716
7.699
7.698
7.554
7.548
7.542
7.526
7.520
7.514
7.408
7.405
7.393
7.391
7.387
7.261
7.258
7.248
7.244
7.235
7.231
7.223
7.217
7.205
2.892
1.953
2.002
1.000
0.021
Br
2
2,2'''-dibromo-p-quaterphenyl
11
10
9
8
7
6
5
4
3
2
1
0
-1
ppm

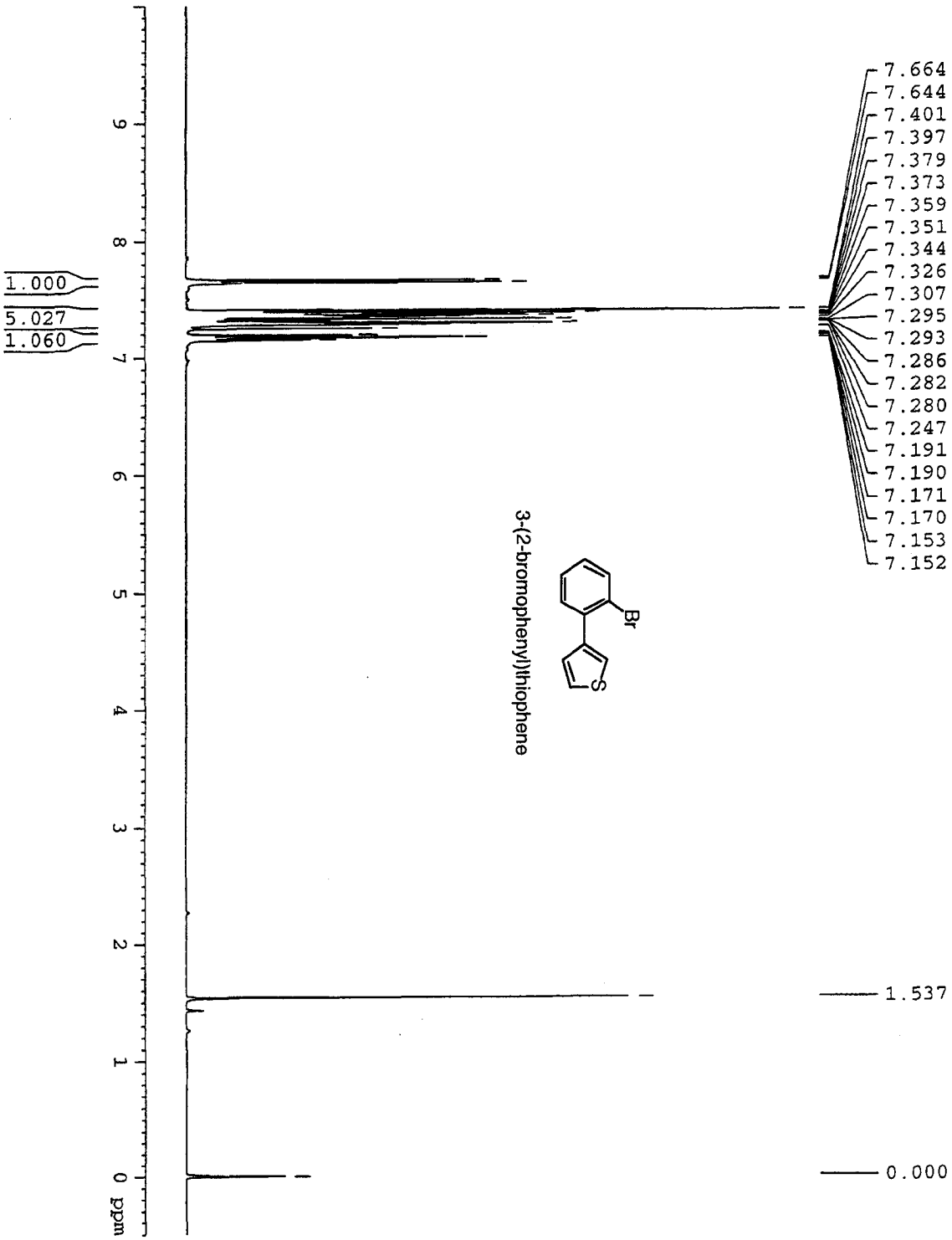

142.397
140.402
140.119
133.471
131.572
130.136
129.044
127.700
126.933
122.865
77.696
77.272
76.848
200
180
160
140
120
100
80
60
40
20
0 ppm
Br
2
2,2'''-dibromo-p-quaterphenyl

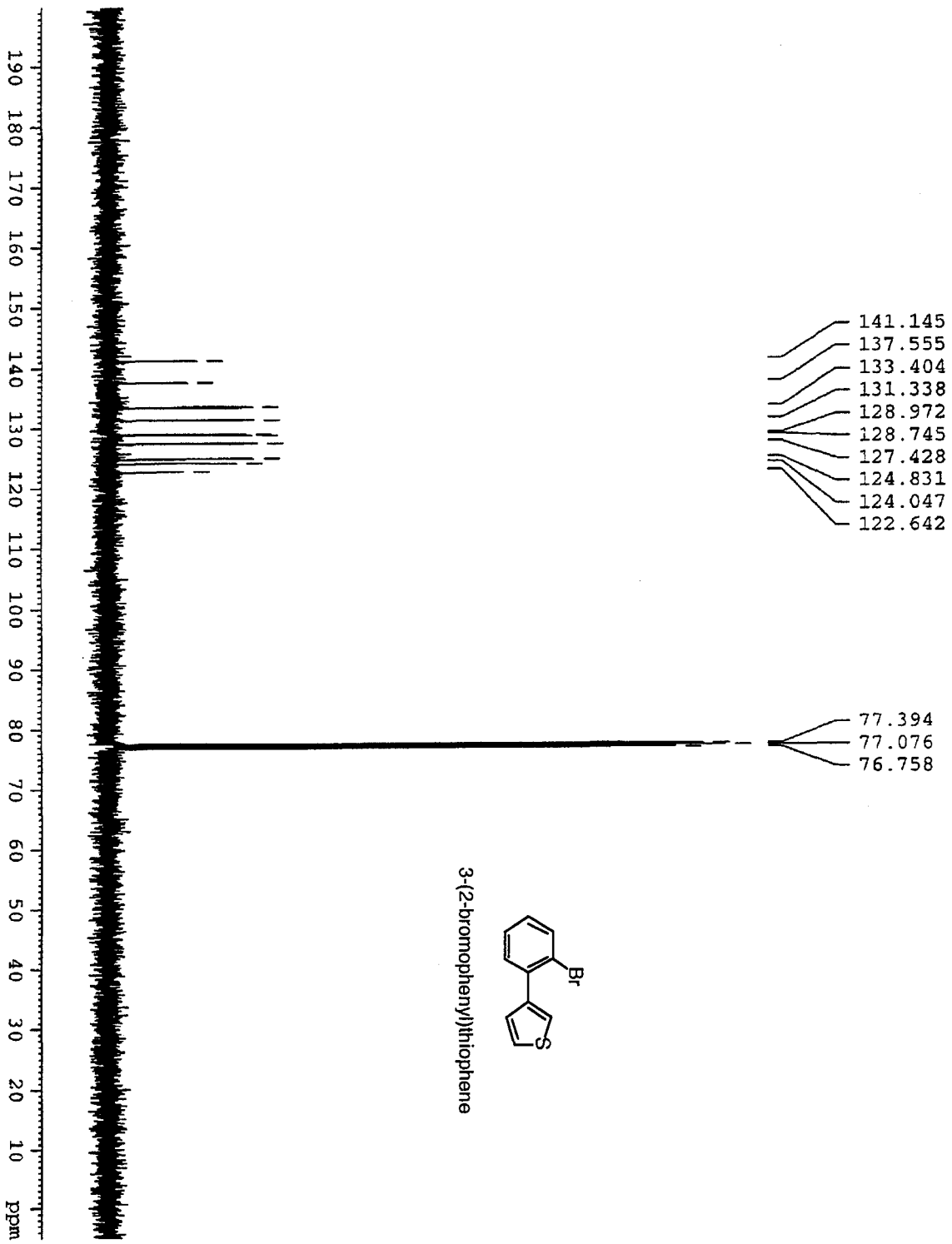

8.007
7.987
7.759
7.561
7.540
7.471
7.453
7.452
7.412
7.409
7.399
7.397
7.390
7.354
7.350
7.335
7.333
7.315
7.312
7.272
7.269
7.253
7.252
7.235
7.232
7.215
7.090
7.080
7.077
7.070
7.067
7.058
7.047
1.000
0.935
0.989
1.041
2.096
1.069
1.083
1.056
3-(2-iodophenyl)benzofuran
ppm

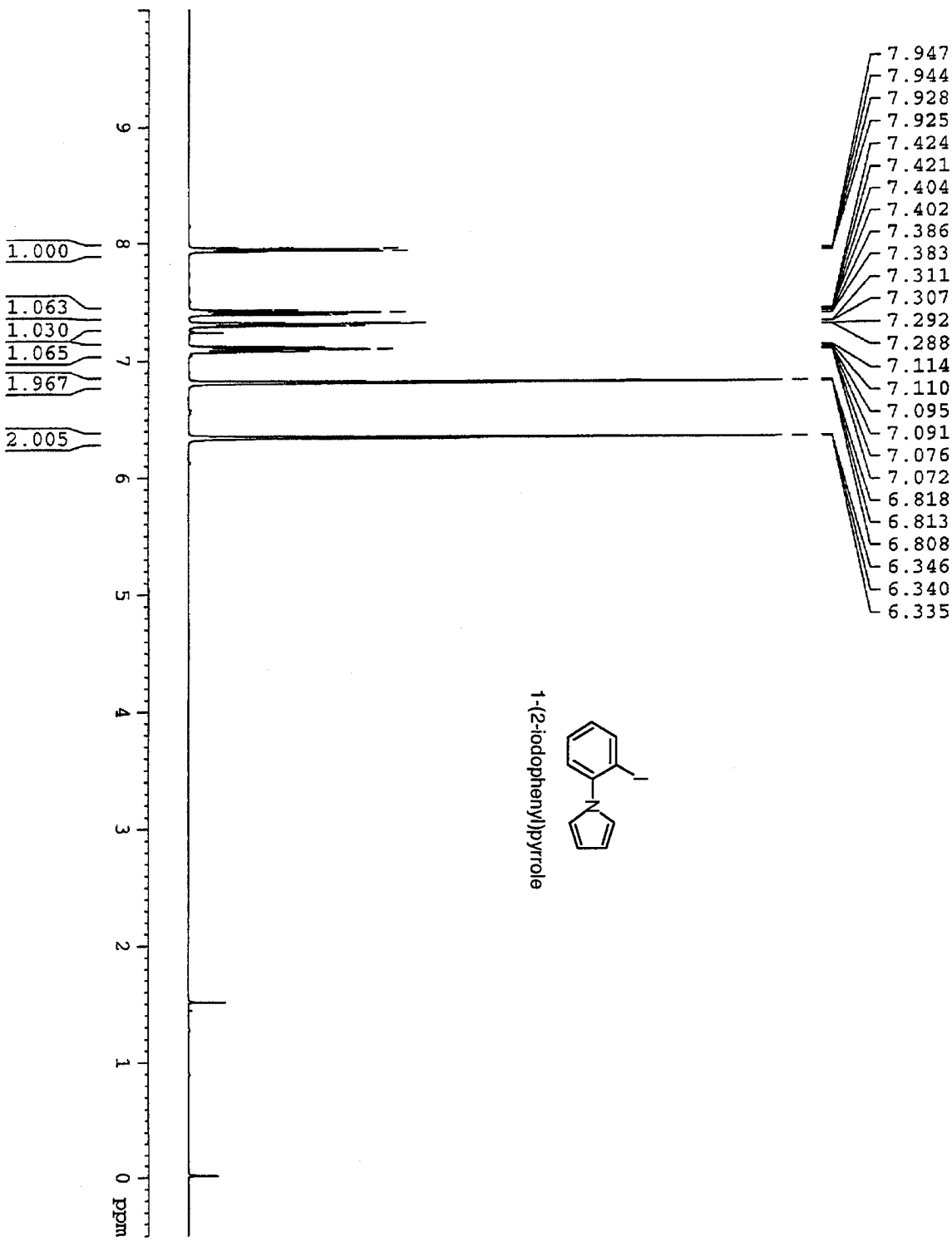

154.972
143.010
140.014
136.849
131.205
129.492
128.282
127.126
124.662
124.222
122.907
120.971
111.766
99.839
77.454
77.137
76.819
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
3-(2-iodophenyl)benzofuran

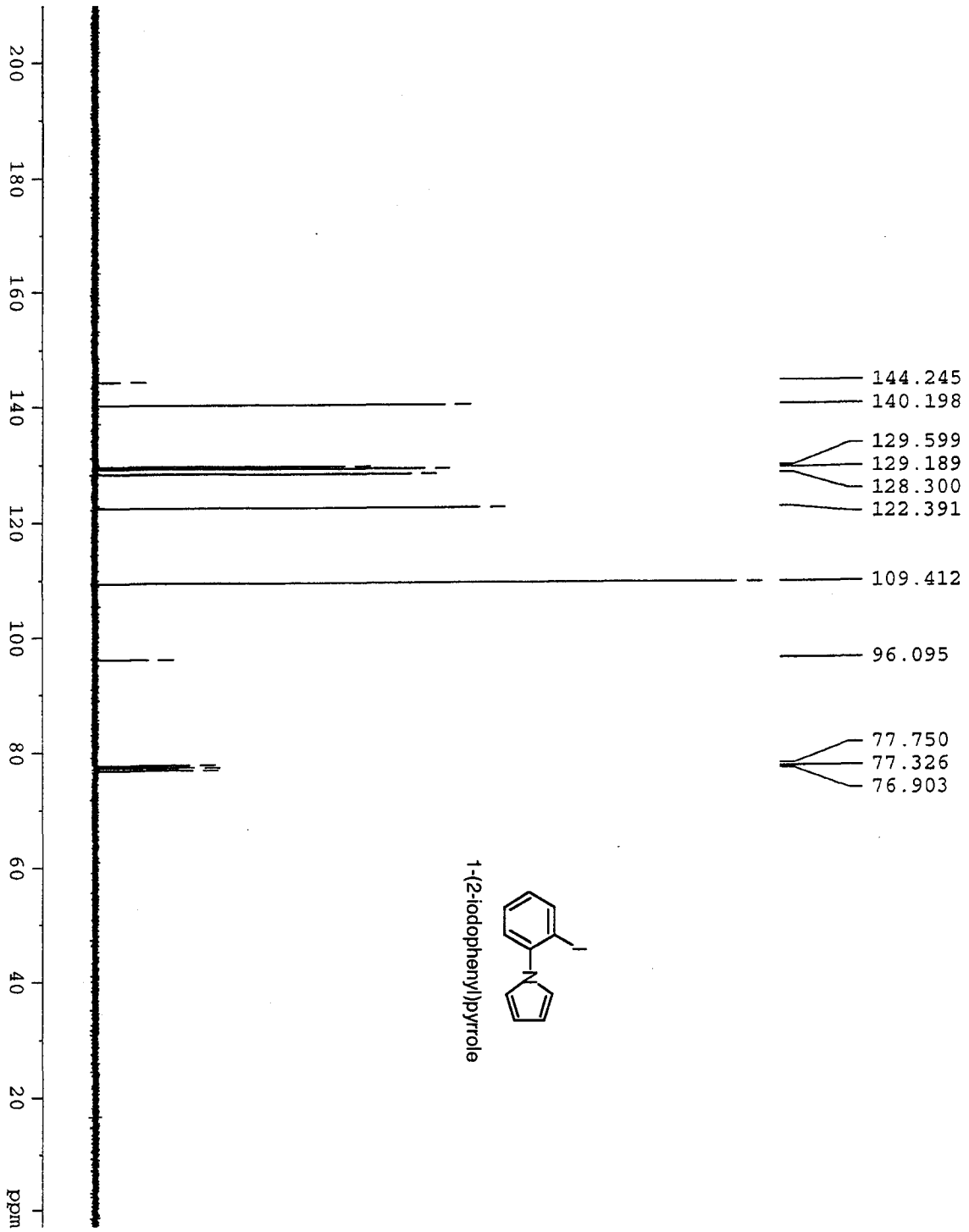

7.756
7.754
7.753
7.690
7.684
7.677
7.668
7.664
7.663
7.659
7.493
7.483
7.479
7.476
7.475
7.465
7.463
7.456
7.455
7.452
7.446
7.439
7.434
7.433
7.429
7.424
7.421
7.417
7.396
7.391
7.369
7.366
7.345
7.341
7.215
1.515
0.001
0.000
0.999
1.011
2.008
4.094
1.133
3-iodo-2-phenylbenzothiophene
S
10
9
8
7
6
5
4
3
2
1
0 ppm

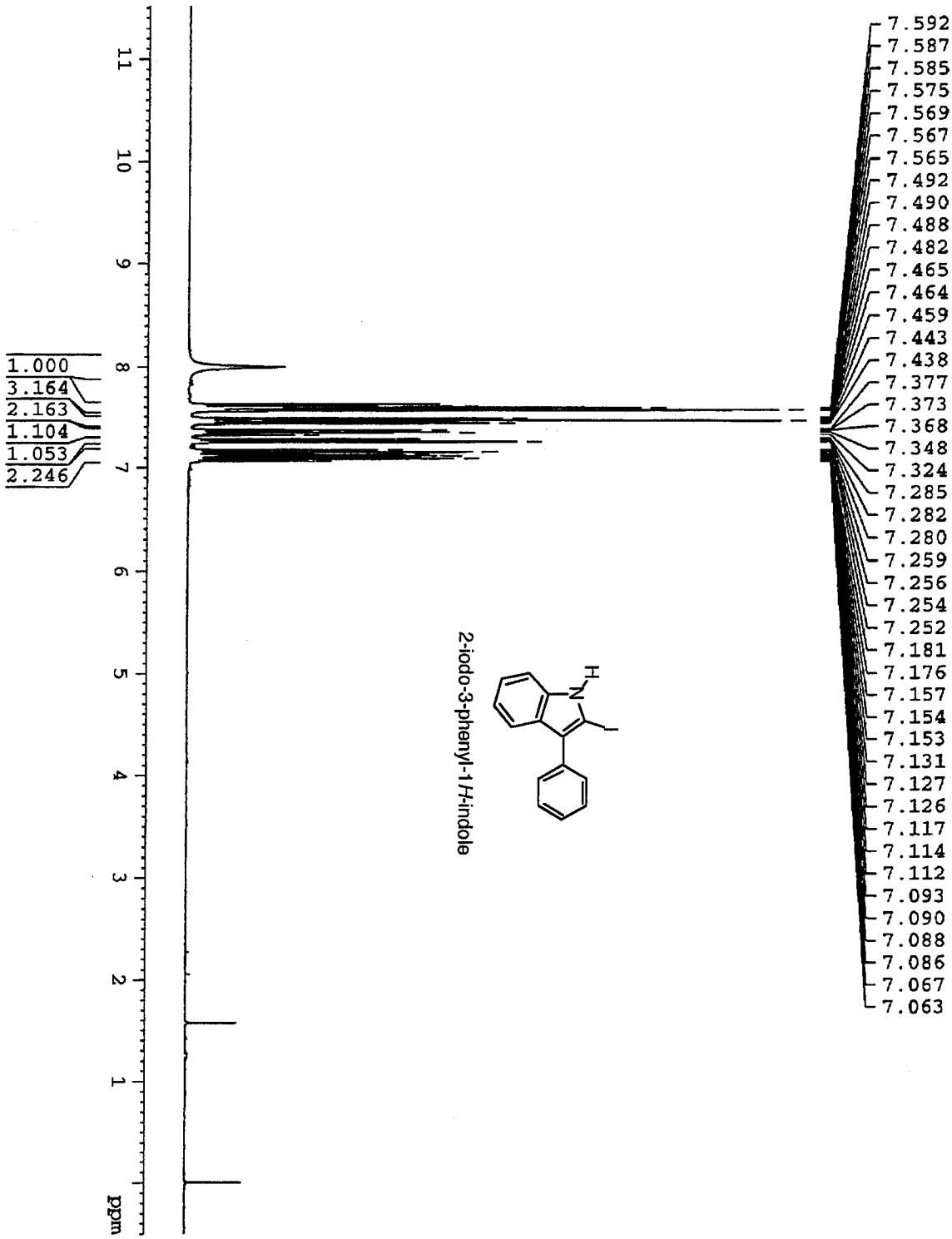

142.435
142.157
139.197
134.884
130.308
129.154
128.760
126.562
125.756
125.718
122.364
79.699
77.725
77.301
76.878
3-iodo-2-phenylbenzothiophene
S
I
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

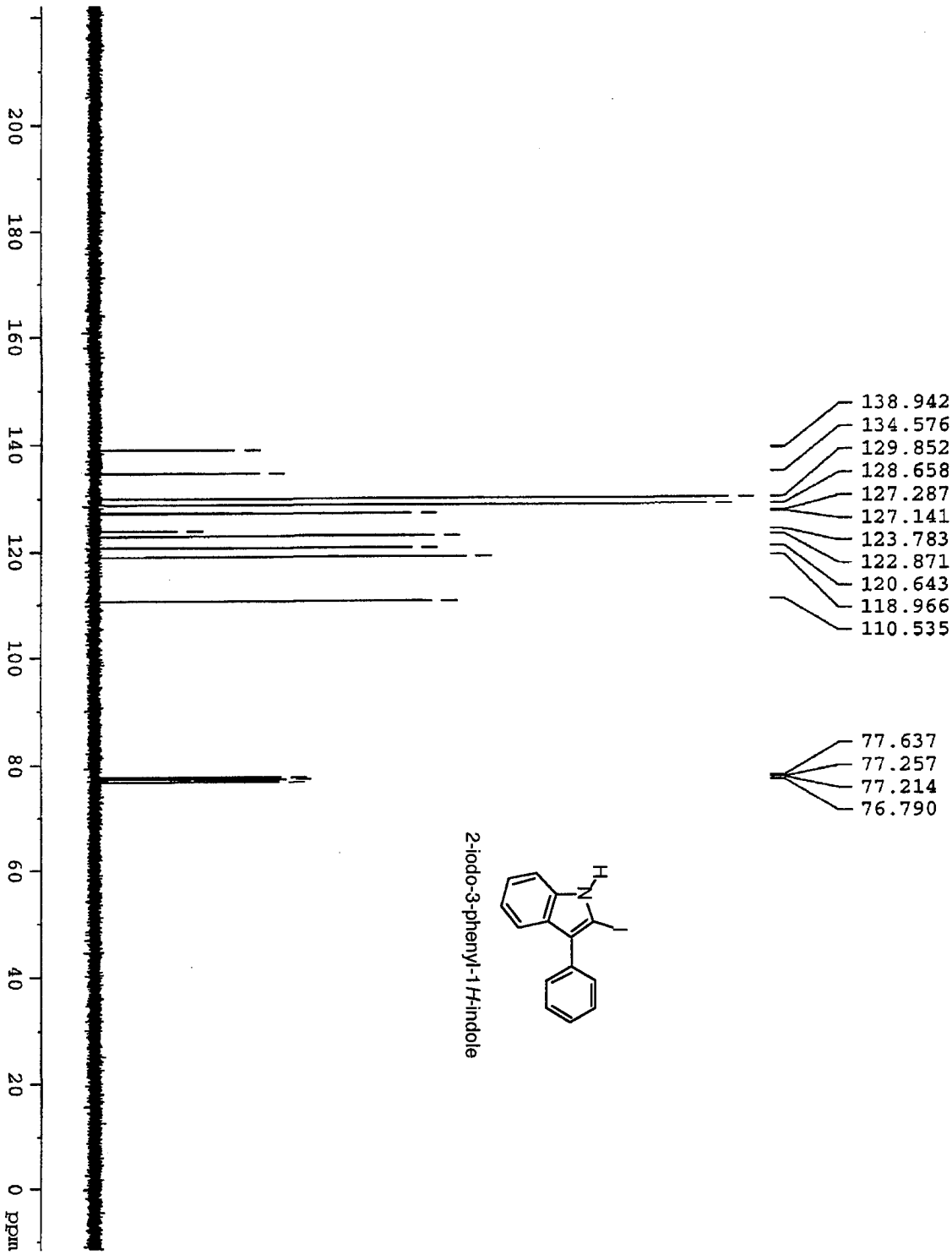

7.664
7.644
7.401
7.397
7.379
7.373
7.359
7.351
7.344
7.326
7.307
7.295
7.293
7.286
7.282
7.280
7.247
7.191
7.190
7.171
7.170
7.153
7.152
1.000
5.027
1.060
1.537
0.000
ppm
3-(2-bromophenyl)thiophene
Br
S

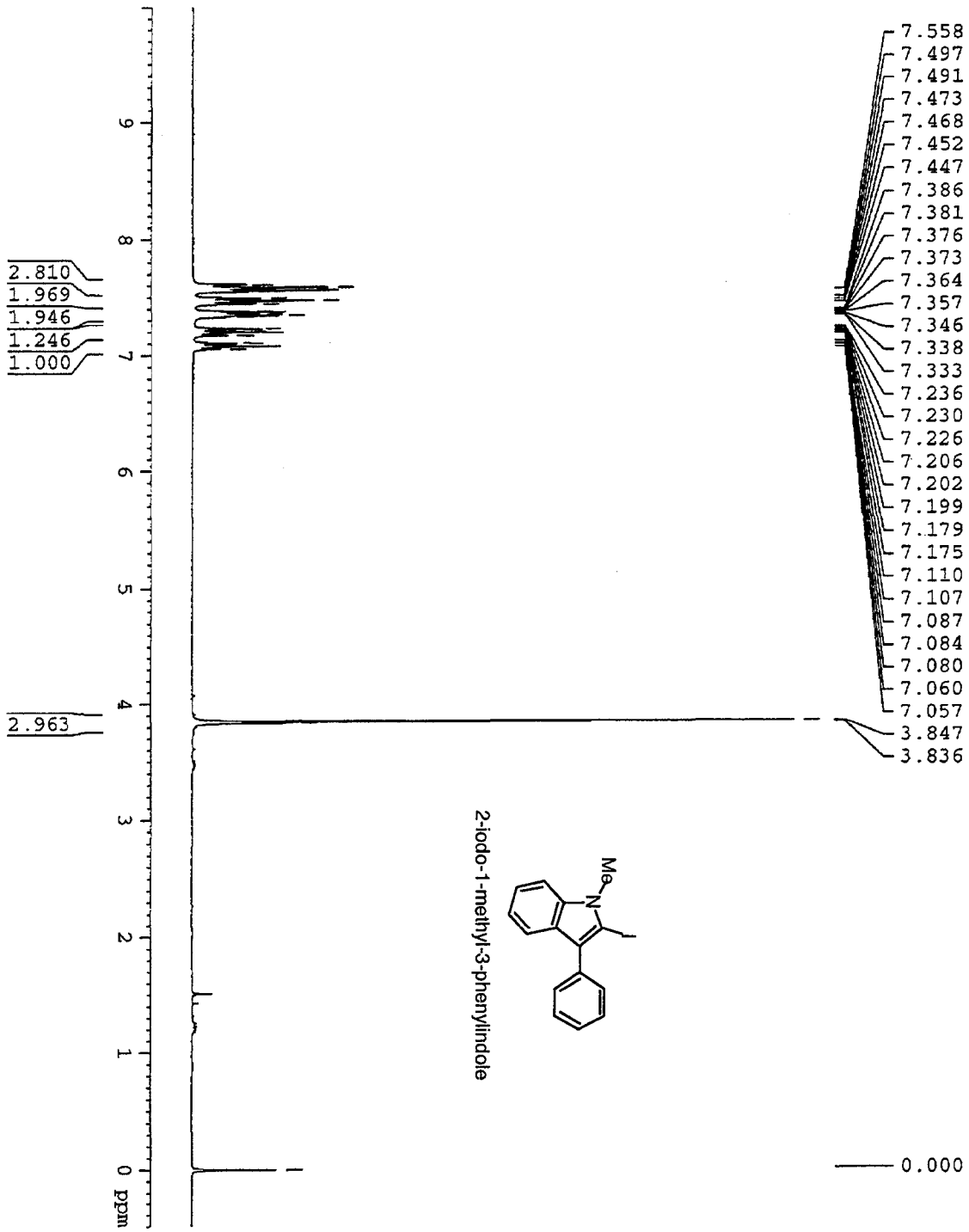

141.145
137.555
133.404
131.338
128.972
128.745
127.428
124.831
124.047
122.642
77.394
77.076
76.758
Br
S
3-(2-bromophenyl)thiophene
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

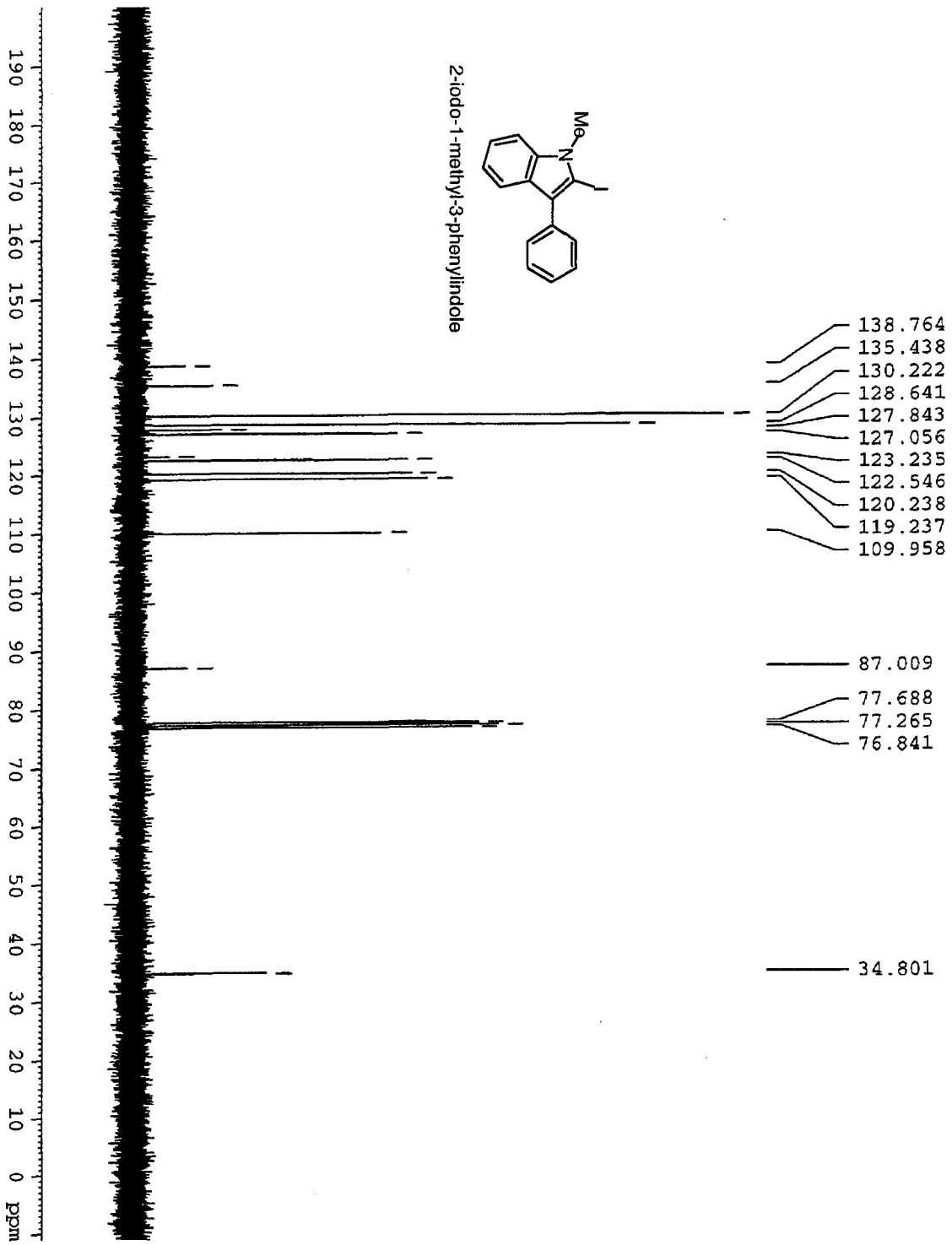

7.947
7.944
7.928
7.925
7.424
7.421
7.404
7.402
7.386
7.383
7.311
7.307
7.292
7.288
7.114
7.110
7.095
7.091
7.076
7.072
6.818
6.813
6.808
6.346
6.340
6.335
1.000
1.063
1.030
1.065
1.967
2.005
1-(2-iodophenyl)pyrrole
9
8
7
6
5
4
3
2
1
0 ppm

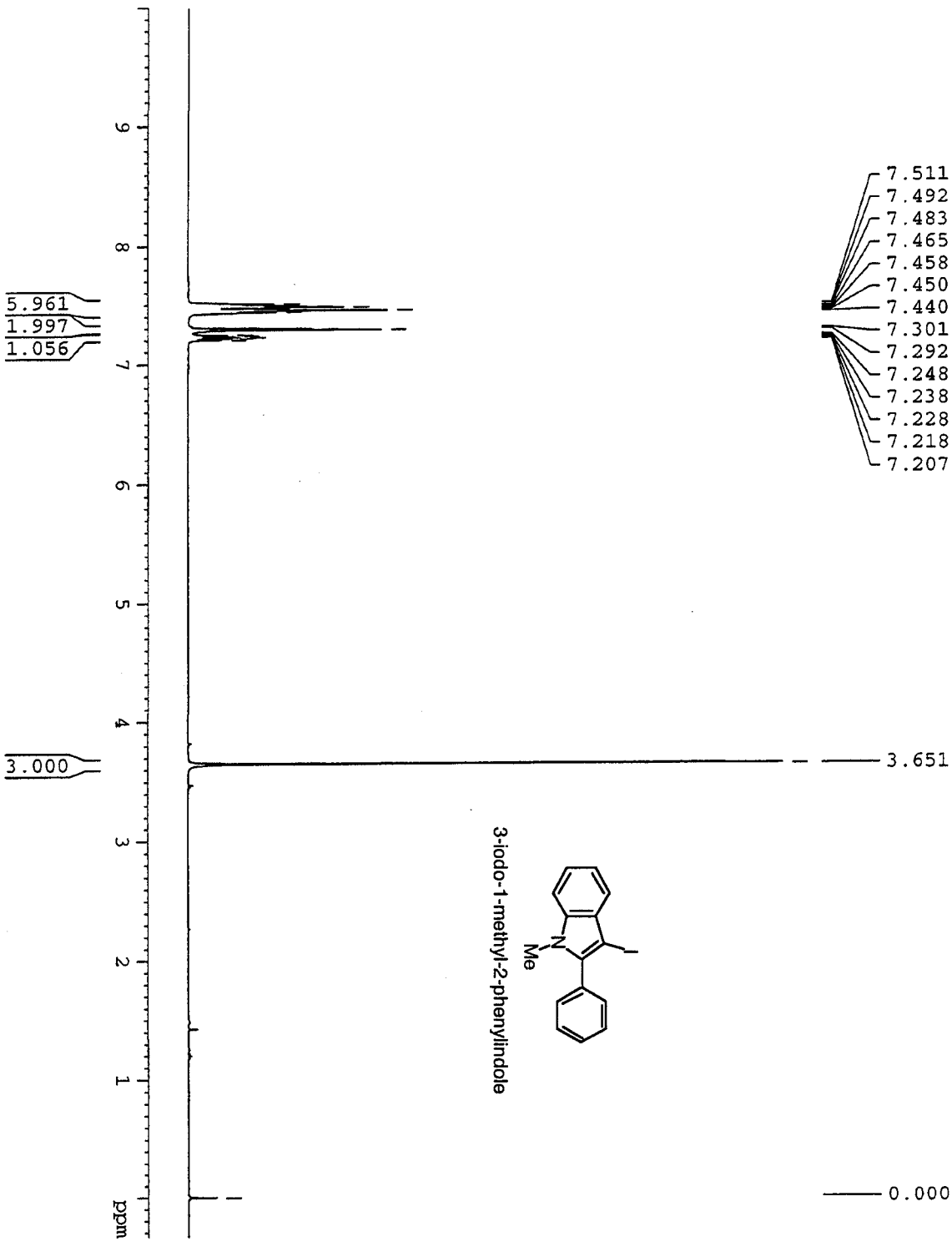

200
180
160
140
120
100
80
60
40
20
ppm
144.245
140.198
129.599
129.189
128.300
122.391
109.412
96.095
77.750
77.326
76.903
1-(2-iodophenyl)pyrrole

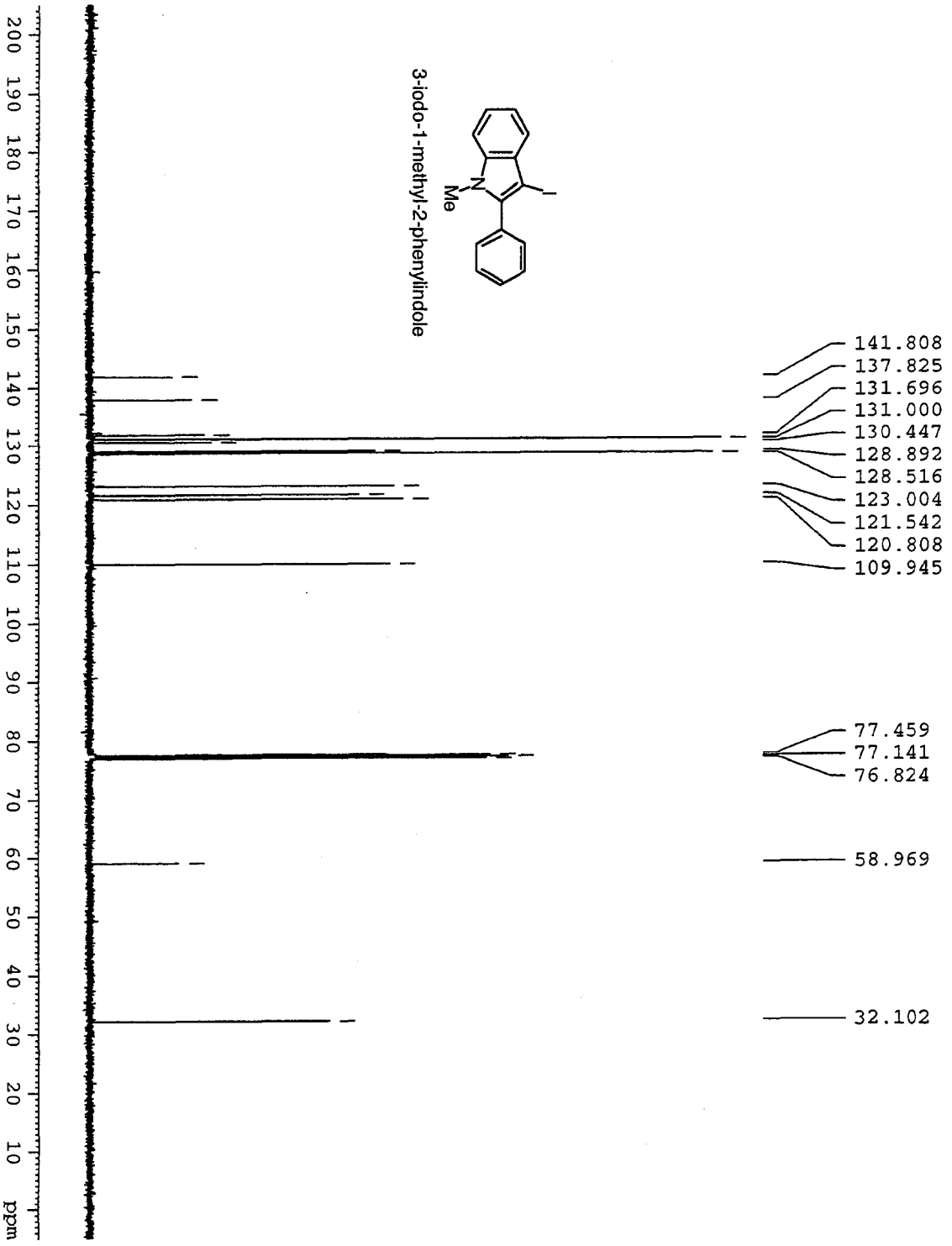

7.592
7.587
7.585
7.575
7.569
7.567
7.565
7.492
7.490
7.488
7.482
7.465
7.464
7.459
7.443
7.438
7.377
7.373
7.368
7.348
7.324
7.285
7.282
7.280
7.259
7.256
7.254
7.252
7.181
7.176
7.157
7.154
7.153
7.131
7.127
7.126
7.117
7.114
7.112
7.093
7.090
7.088
7.086
7.067
7.063
1.000
3.164
2.163
1.104
1.053
2.246
2-iodo-3-phenyl-1H-indole
ppm

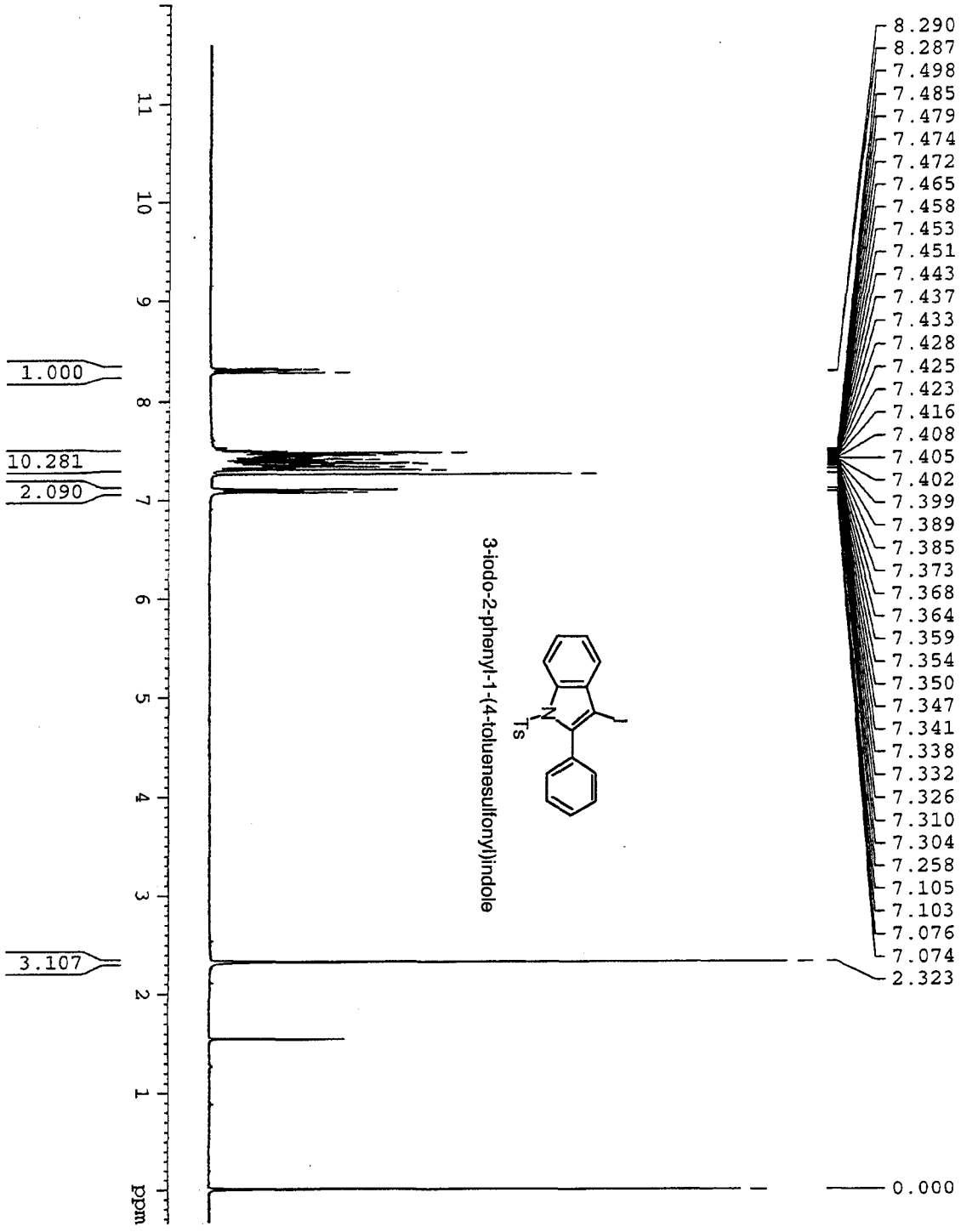

138.942
134.576
129.852
128.658
127.287
127.141
123.783
122.871
120.643
118.966
110.535
77.637
77.257
77.214
76.790
200
180
160
140
120
100
80
60
40
20
0 ppm
2-iodo-3-phenyl-1H-indole
H
N

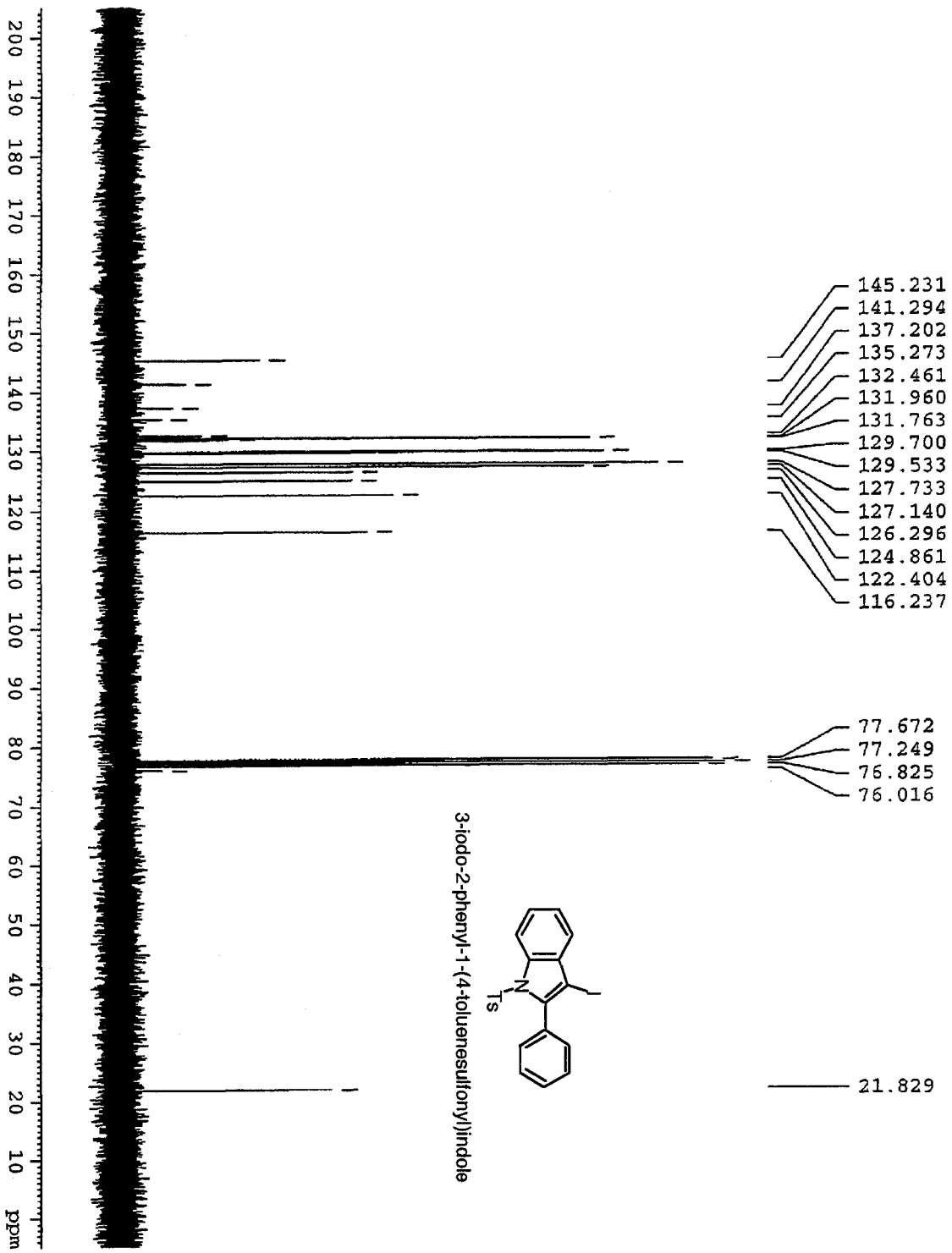

7.558
7.497
7.491
7.473
7.468
7.452
7.447
7.386
7.381
7.376
7.373
7.364
7.357
7.346
7.338
7.333
7.236
7.230
7.226
7.206
7.202
7.199
7.179
7.175
7.110
7.107
7.087
7.084
7.080
7.060
7.057
3.847
3.836
2.810
1.969
1.946
1.246
1.000
2.963
0.000
0 ppm
Me
N
2-iodo-1-methyl-3-phenylindole

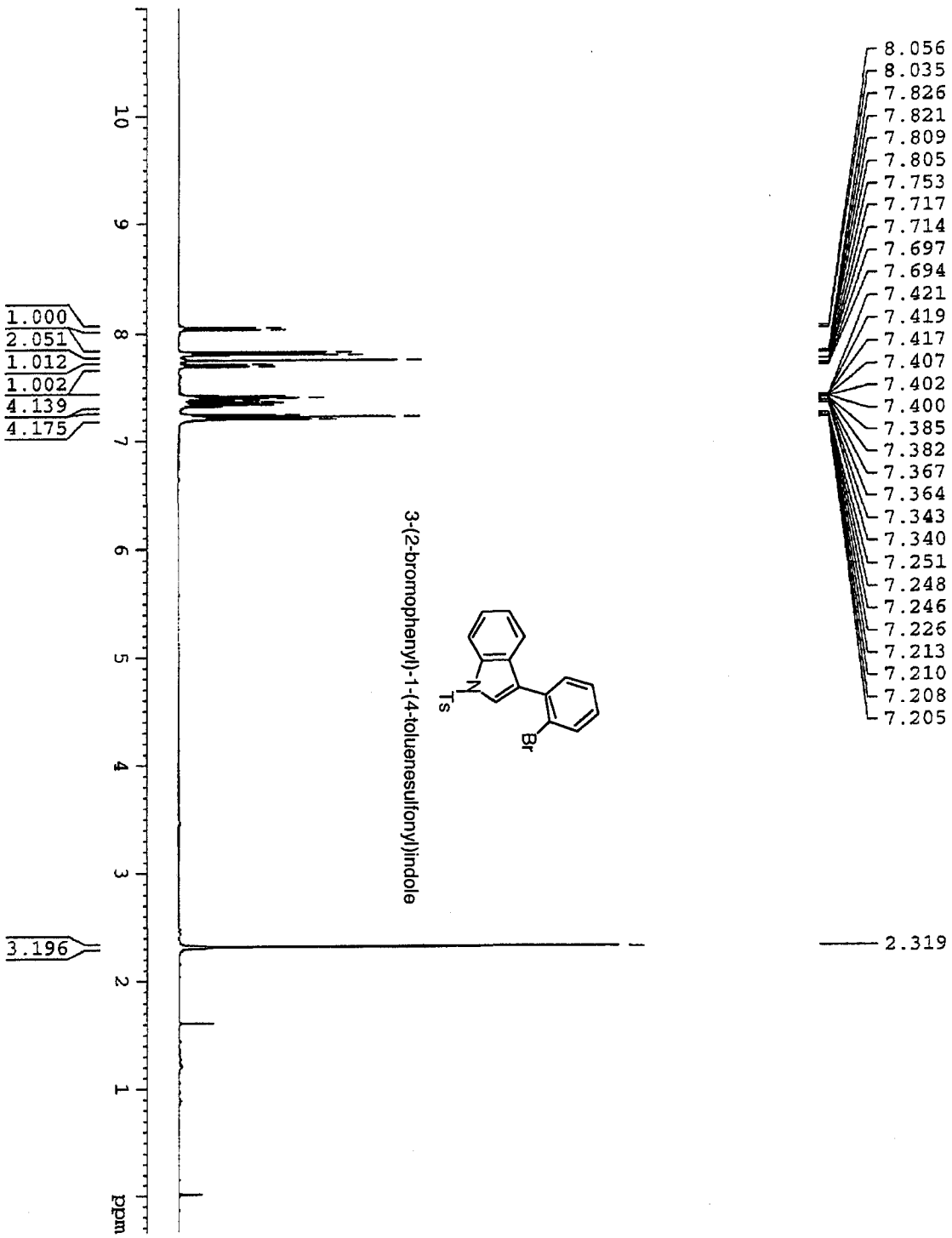

2-iodo-1-methyl-3-phenylindole
Me
138.764
135.438
130.222
128.641
127.843
127.056
123.235
122.546
120.238
119.237
109.958
87.009
77.688
77.265
76.841
34.801
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

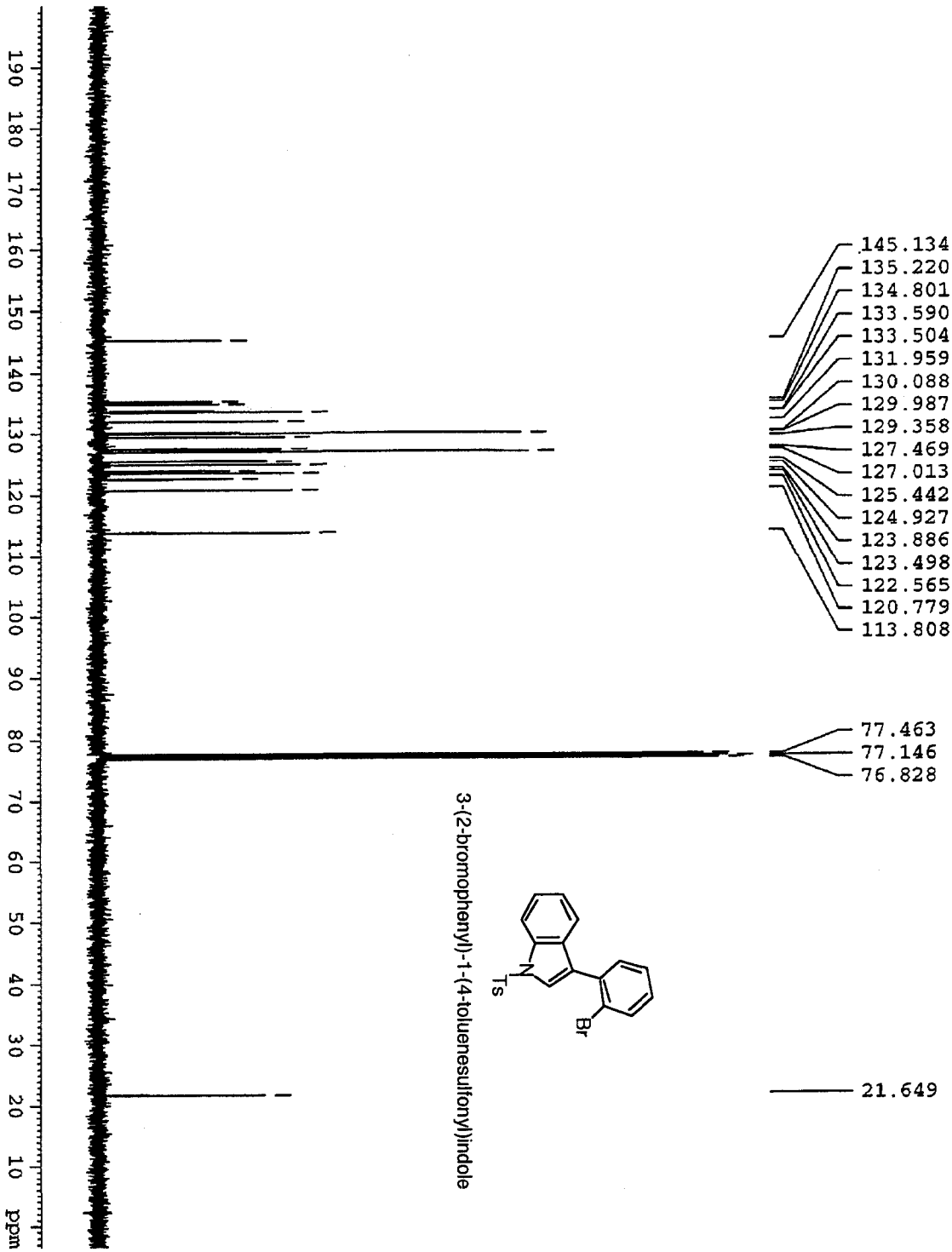

7.511
7.492
7.483
7.465
7.458
7.450
7.440
7.301
7.292
7.248
7.238
7.228
7.218
7.207
5.961
1.997
1.056
3.000
3.651
0.000
ppm
3-iodo-1-methyl-2-phenylindole
N
Me
I

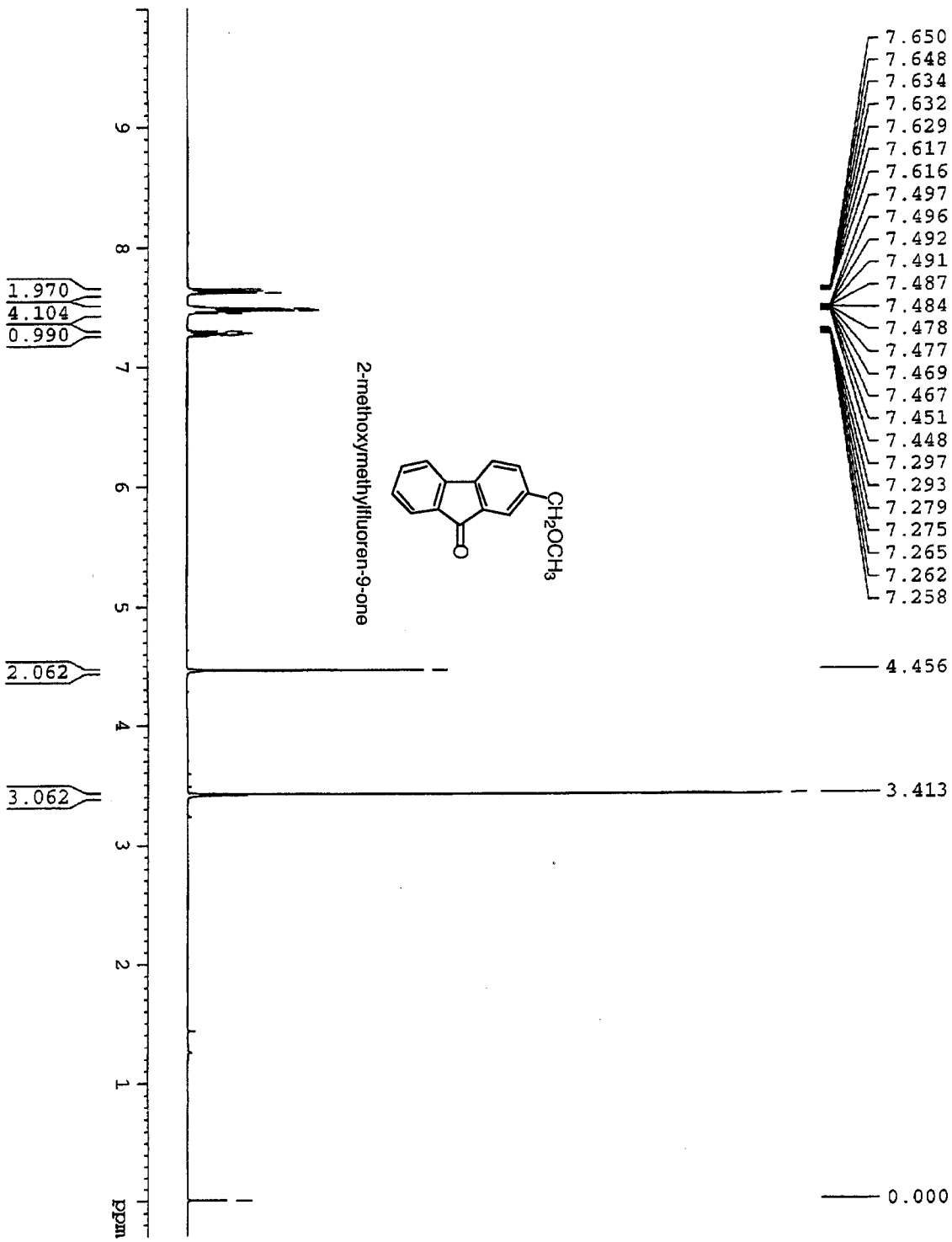

3-iodo-1-methyl-2-phenylindole
Me
I
141.808
137.825
131.696
131.000
130.447
128.892
128.516
123.004
121.542
120.808
109.945
77.459
77.141
76.824
58.969
32.102
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

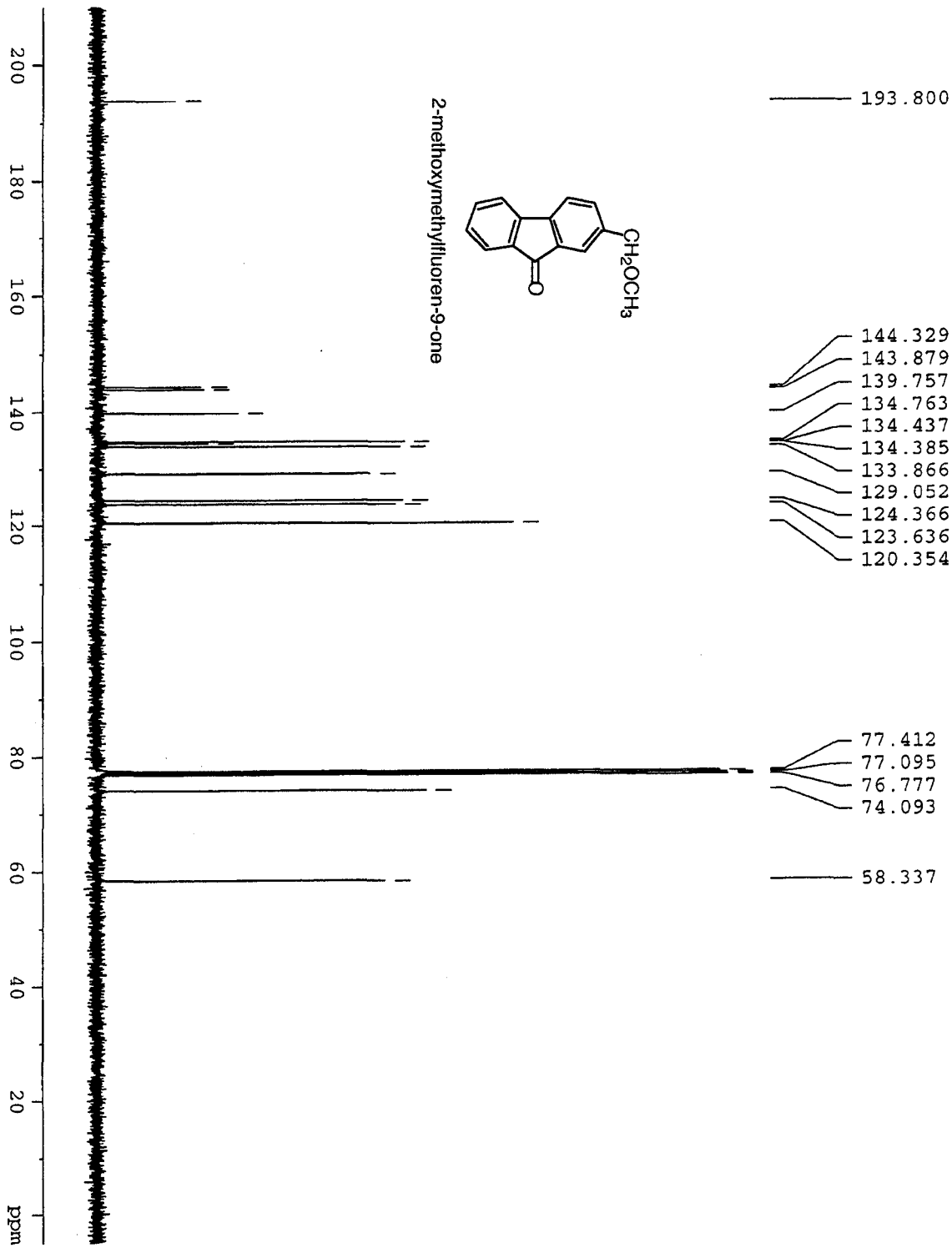

8.290
8.287
7.498
7.485
7.479
7.474
7.472
7.465
7.458
7.453
7.451
7.443
7.437
7.433
7.428
7.425
7.423
7.416
7.408
7.405
7.402
7.399
7.389
7.385
7.373
7.368
7.364
7.359
7.354
7.350
7.347
7.341
7.338
7.332
7.326
7.310
7.304
7.258
7.105
7.103
7.076
7.074
2.323
0.000
1.000
10.281
2.090
3.107
3-iodo-2-phenyl-1-(4-toluenesulfonyl)indole
Ts
ppm

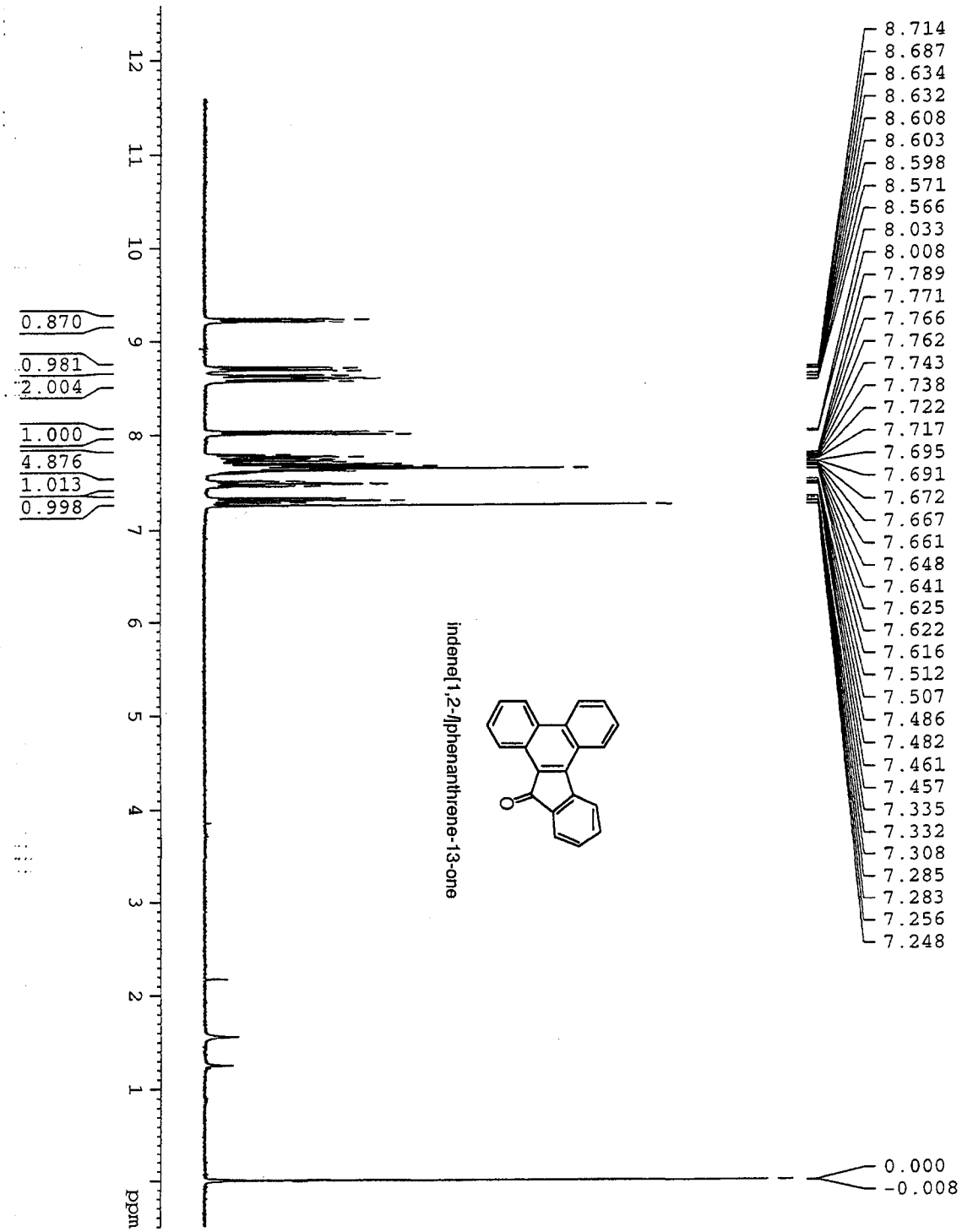

145.231
141.294
137.202
135.273
132.461
131.960
131.763
129.700
129.533
127.733
127.140
126.296
124.861
122.404
116.237
77.672
77.249
76.825
76.016
21.829
3-iodo-2-phenyl-1-(4-toluenesulfonyl)indole
Ts
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

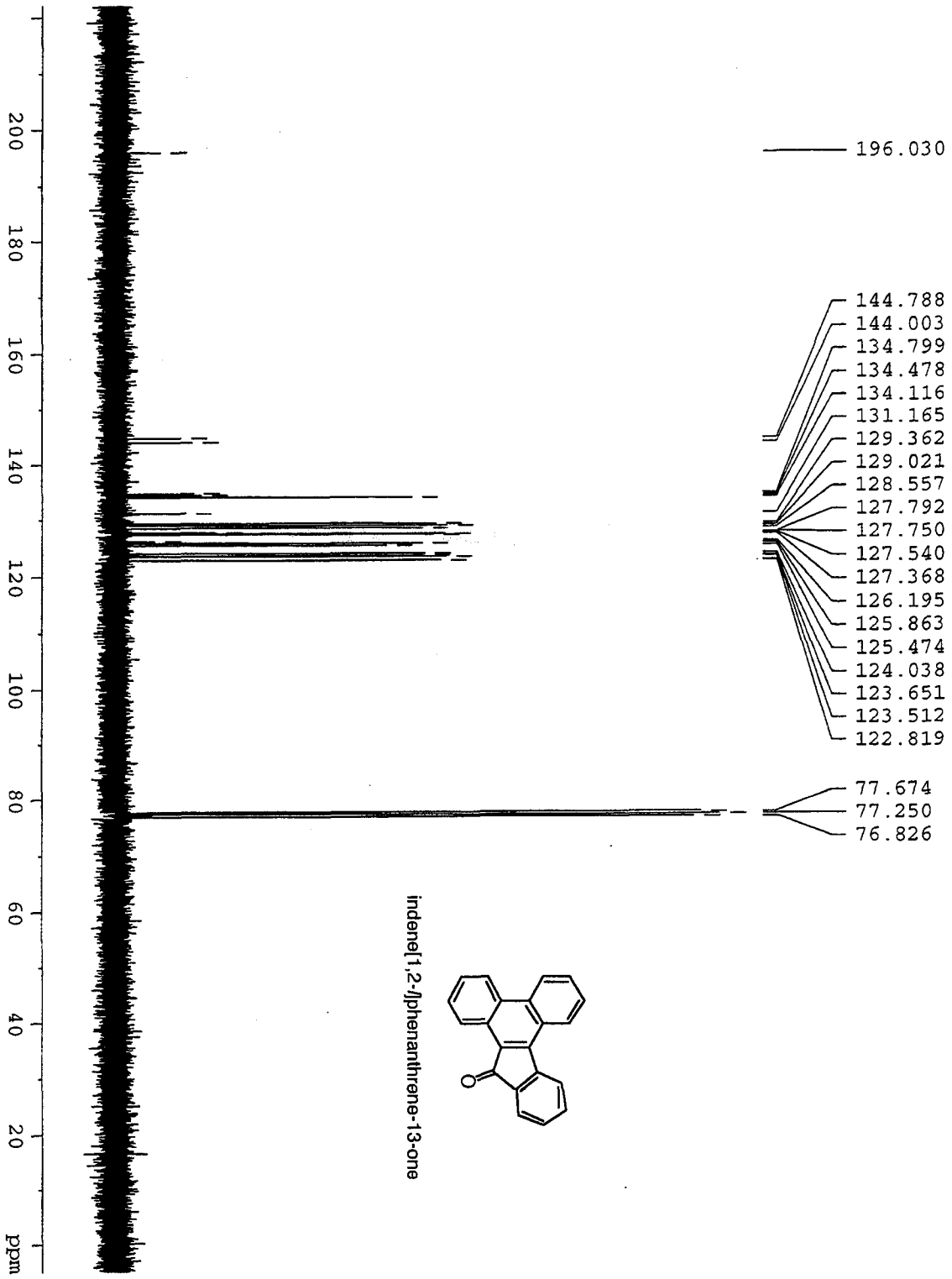

8.056
8.035
7.826
7.821
7.809
7.805
7.753
7.717
7.714
7.697
7.694
7.421
7.419
7.417
7.407
7.402
7.400
7.385
7.382
7.367
7.364
7.343
7.340
7.251
7.248
7.246
7.226
7.213
7.210
7.208
7.205
2.319
1.000
2.051
1.012
1.002
4.139
4.175
3.196
3-(2-bromophenyl)-1-(4-toluenesulfonyl)indole
Ts
Br
ppm

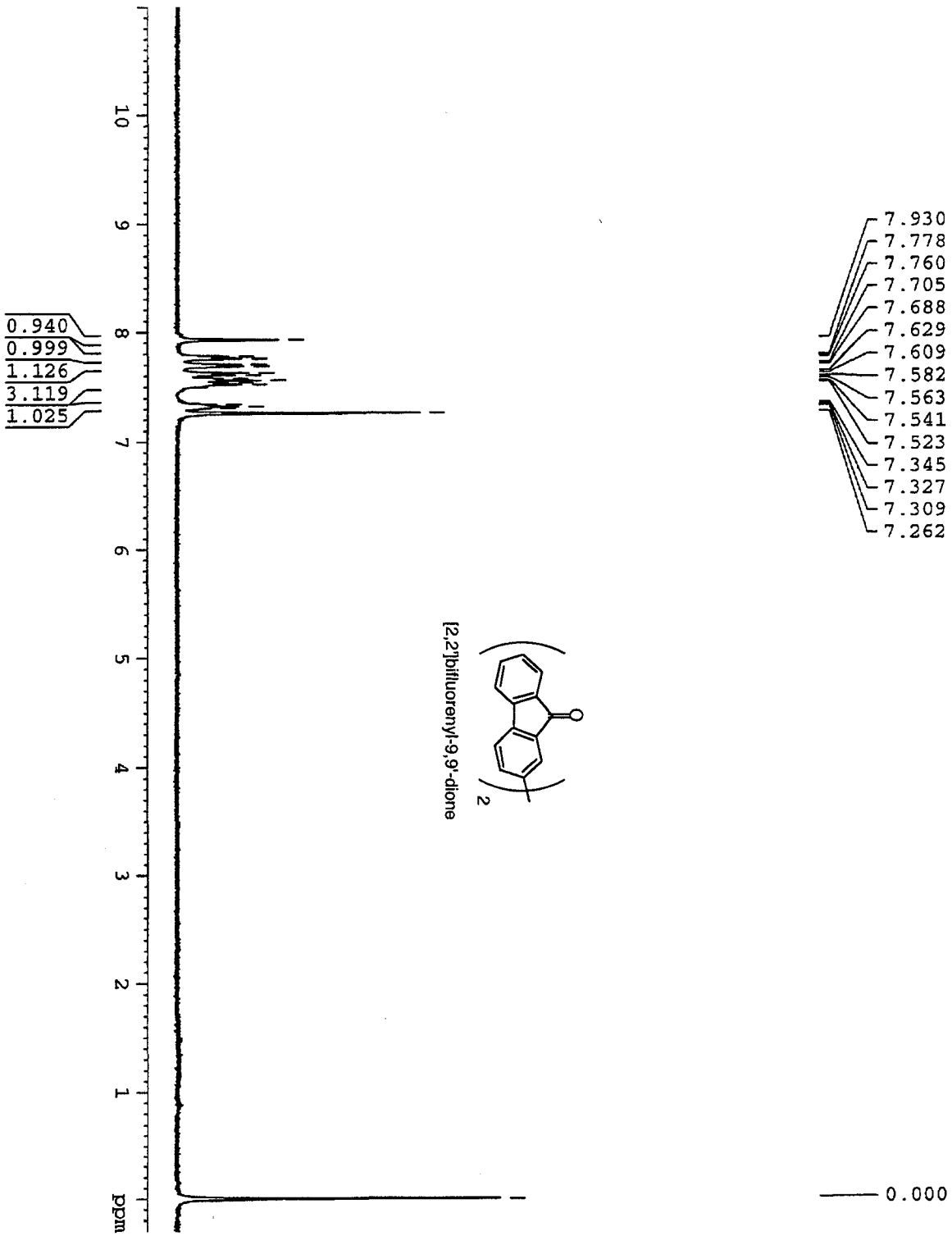

145.134
135.220
134.801
133.590
133.504
131.959
130.088
129.987
129.358
127.469
127.013
125.442
124.927
123.886
123.498
122.565
120.779
113.808
77.463
77.146
76.828
21.649
3-(2-bromophenyl)-1-(4-toluenesulfonyl)indole
Ts
Br
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

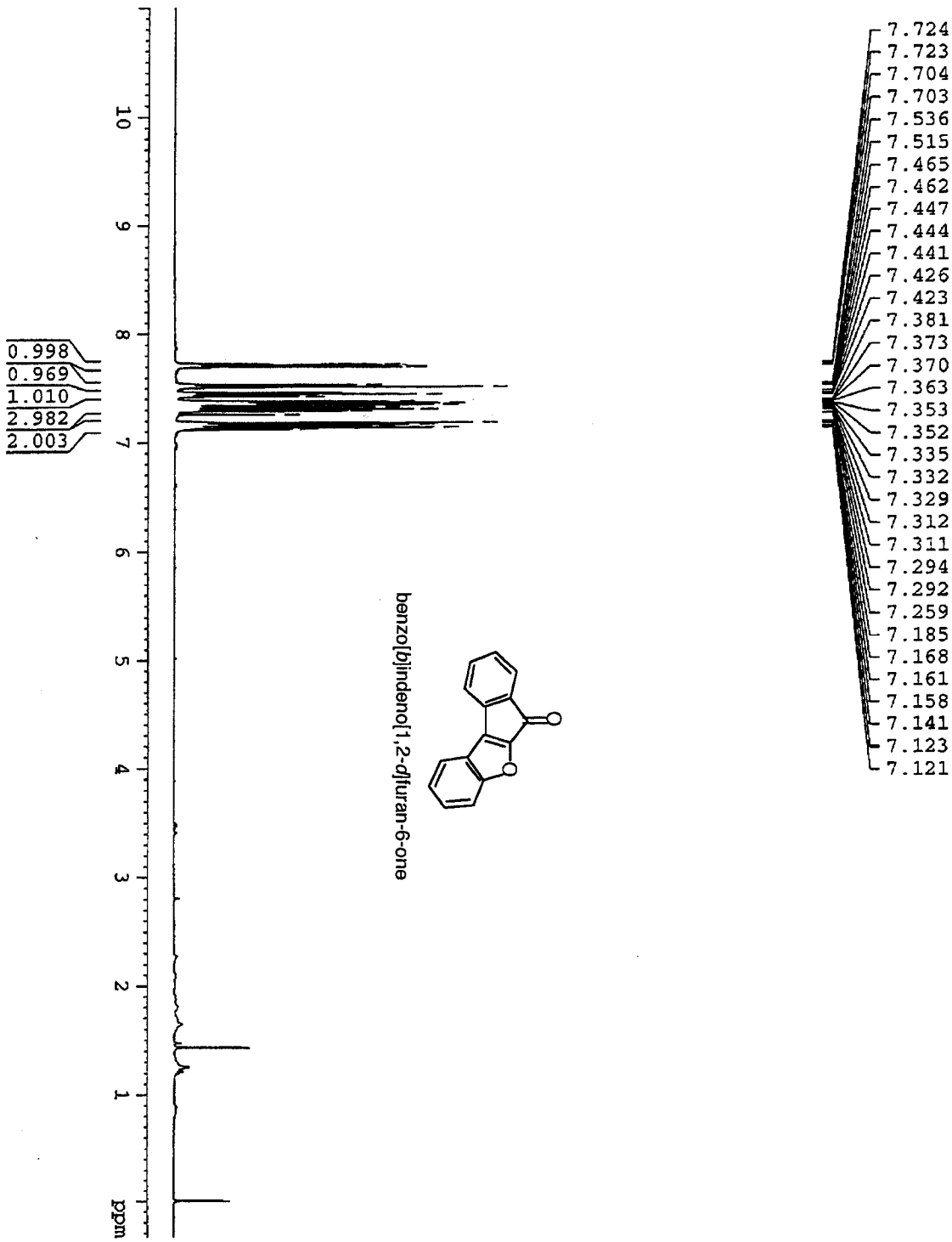

7.650
7.648
7.634
7.632
7.629
7.617
7.616
7.497
7.496
7.492
7.491
7.487
7.484
7.478
7.477
7.469
7.467
7.451
7.448
7.297
7.293
7.279
7.275
7.265
7.262
7.258
4.456
3.413
0.000
1.970
4.104
0.990
2.062
3.062
2-methoxymethylfluoren-9-one
CH2OCH3
O
ppm

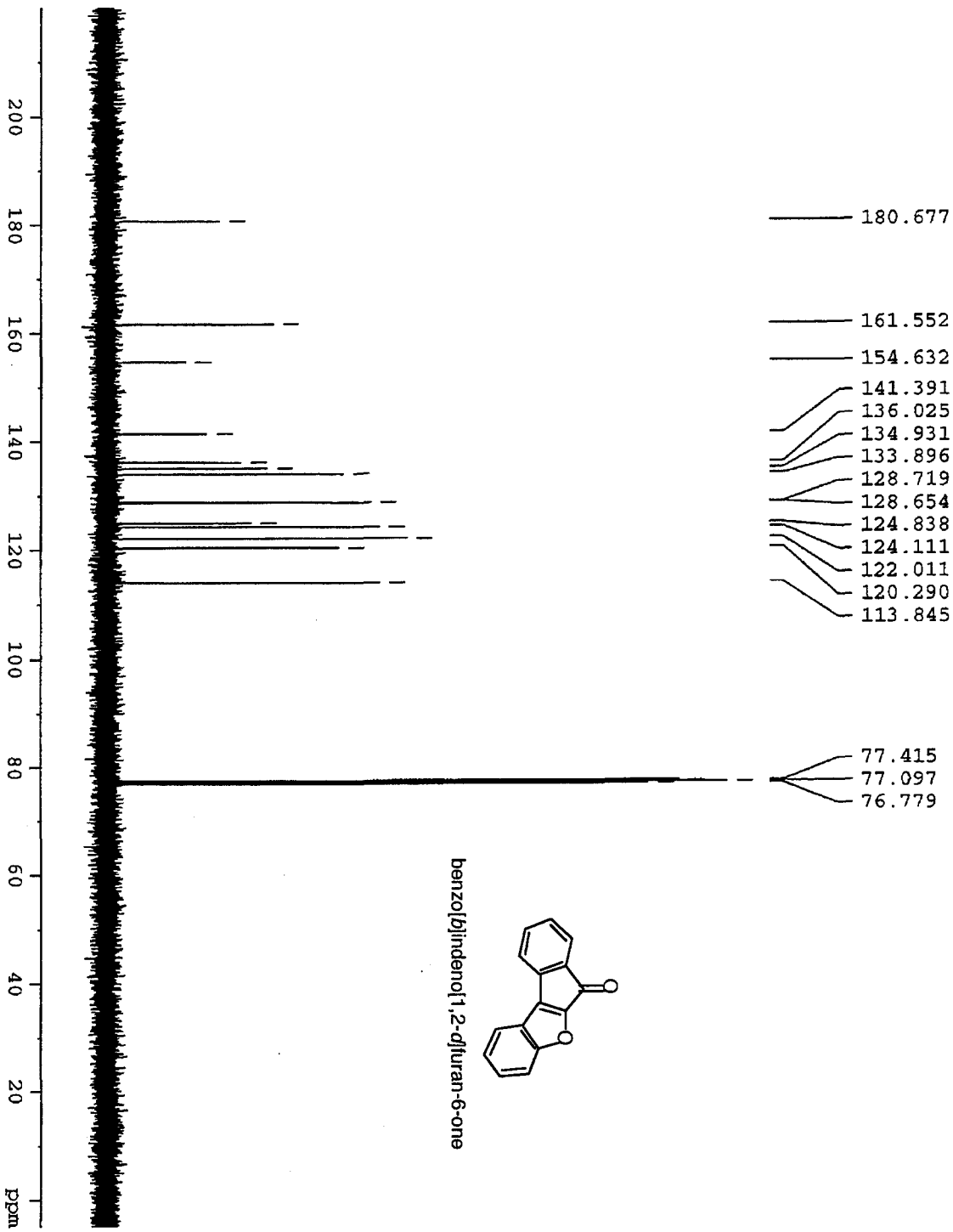

2-methoxymethylfluoren-9-one
CH2OCH3
193.800
144.329
143.879
139.757
134.763
134.437
134.385
133.866
129.052
124.366
123.636
120.354
77.412
77.095
76.777
74.093
58.337
200
180
160
140
120
100
80
60
40
20
ppm

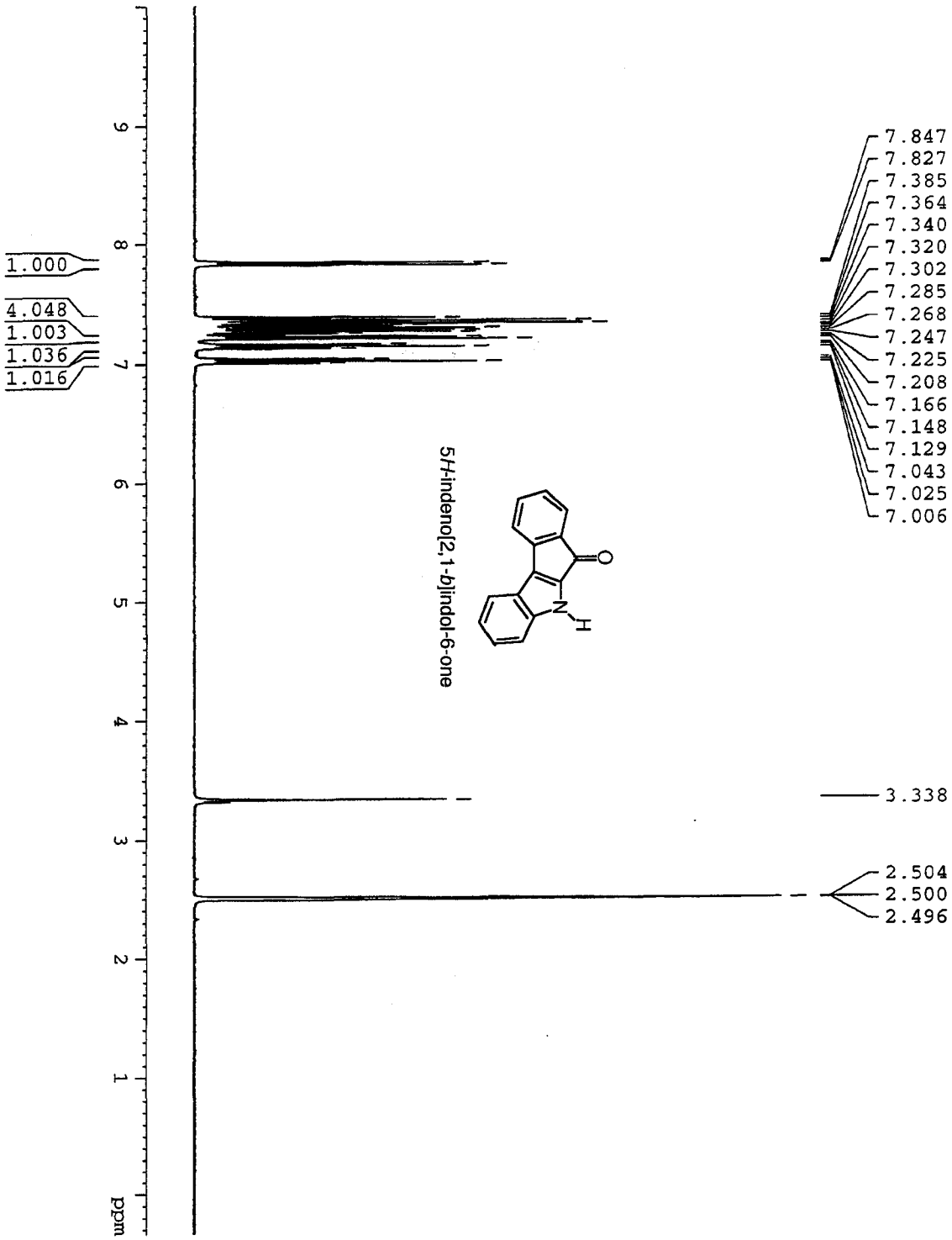

8.714
8.687
8.634
8.632
8.608
8.603
8.598
8.571
8.566
8.033
8.008
7.789
7.771
7.766
7.762
7.743
7.738
7.722
7.717
7.695
7.691
7.672
7.667
7.661
7.648
7.641
7.625
7.622
7.616
7.512
7.507
7.486
7.482
7.461
7.457
7.335
7.332
7.308
7.285
7.283
7.256
7.248
0.870
0.981
2.004
1.000
4.876
1.013
0.998
0.000
-0.008
indene[1,2-f]phenanthrene-13-one
ppm

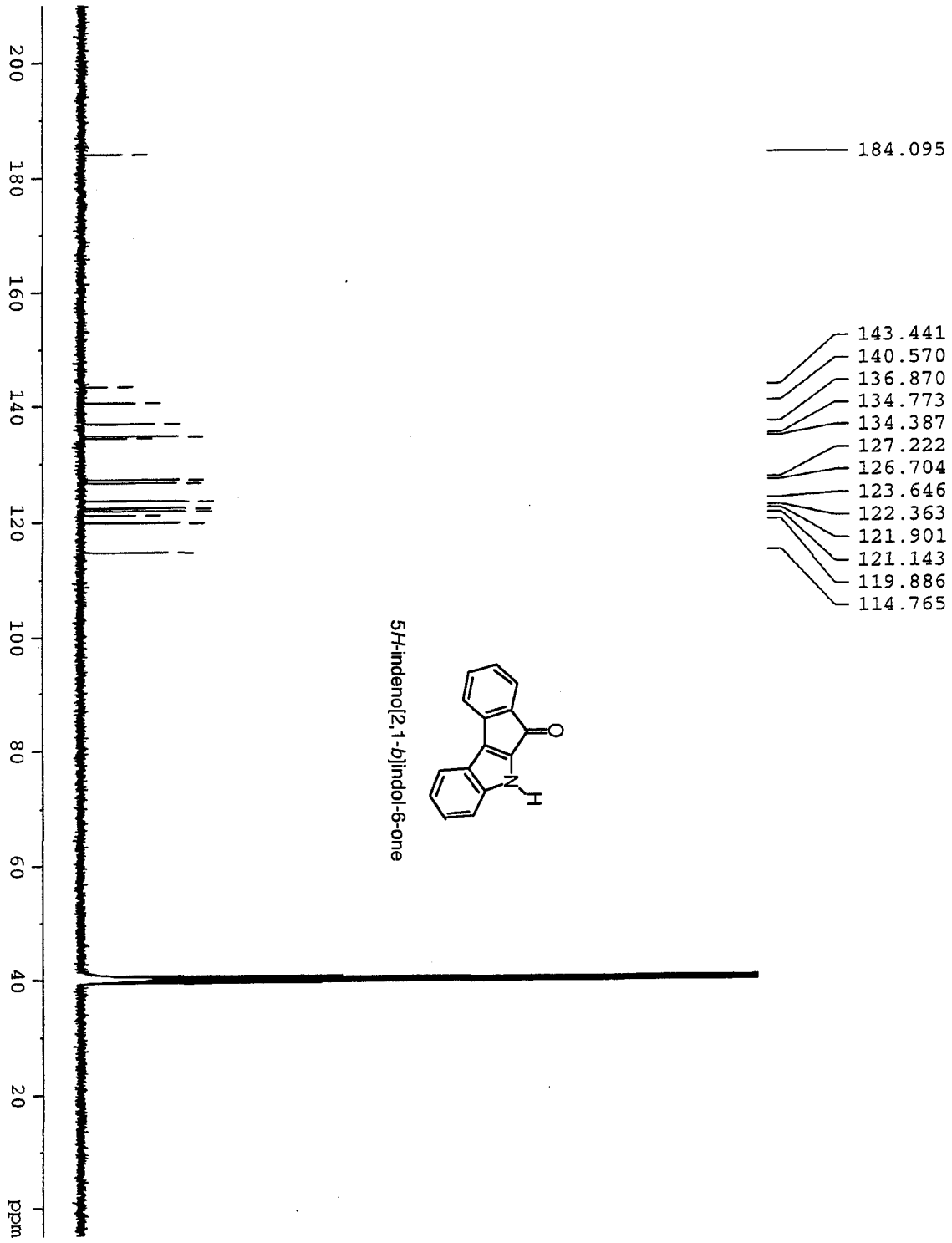

196.030
144.788
144.003
134.799
134.478
134.116
131.165
129.362
129.021
128.557
127.792
127.750
127.540
127.368
126.195
125.863
125.474
124.038
123.651
123.512
122.819
77.674
77.250
76.826
200
180
160
140
120
100
80
60
40
20
ppm
indeno[1,2-l]phenanthrene-13-one

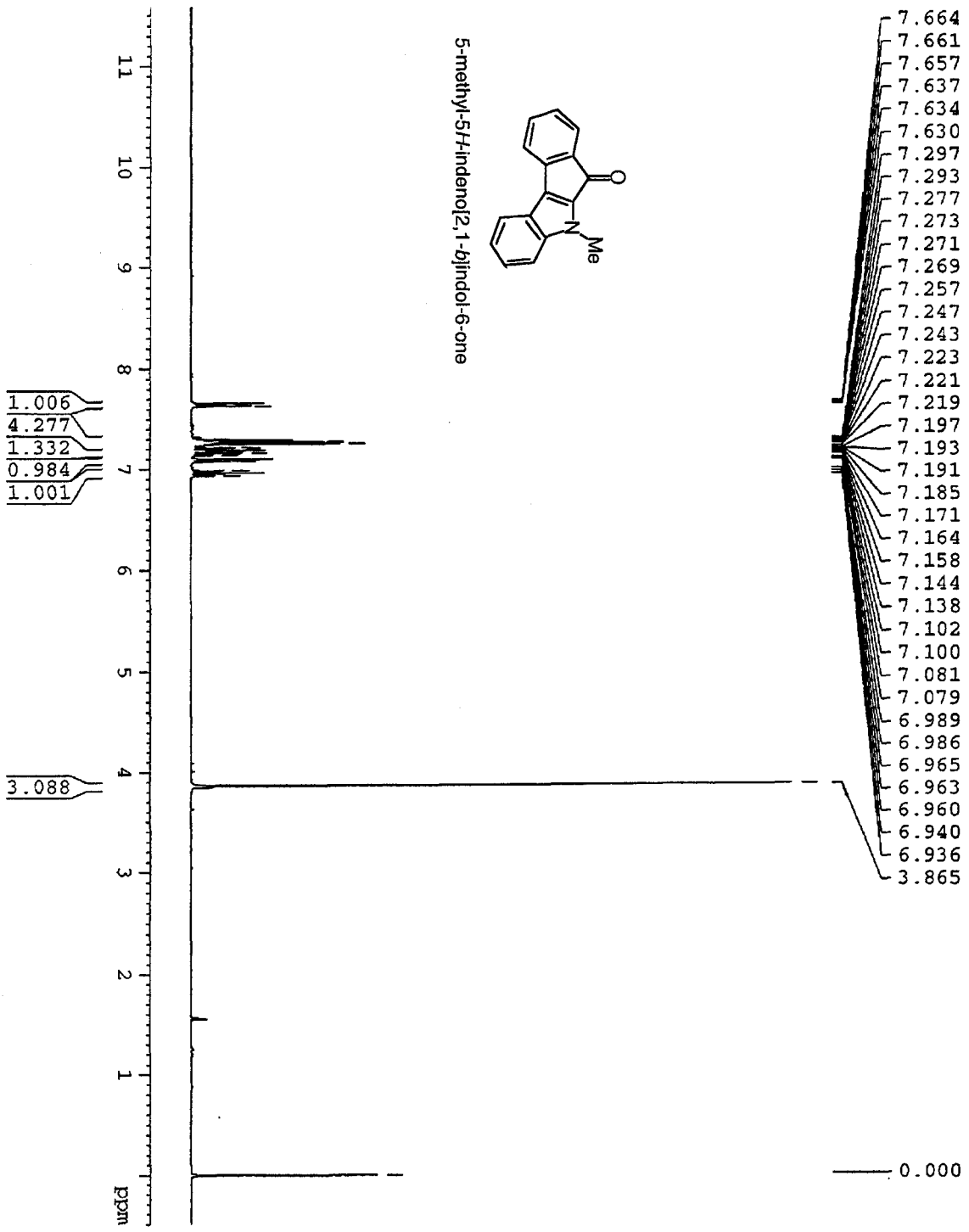

0.940
0.999
1.126
3.119
1.025
7.930
7.778
7.760
7.705
7.688
7.629
7.609
7.582
7.563
7.541
7.523
7.345
7.327
7.309
7.262
0.000
ppm
[2,2']bifluorenyl-9,9'-dione
2

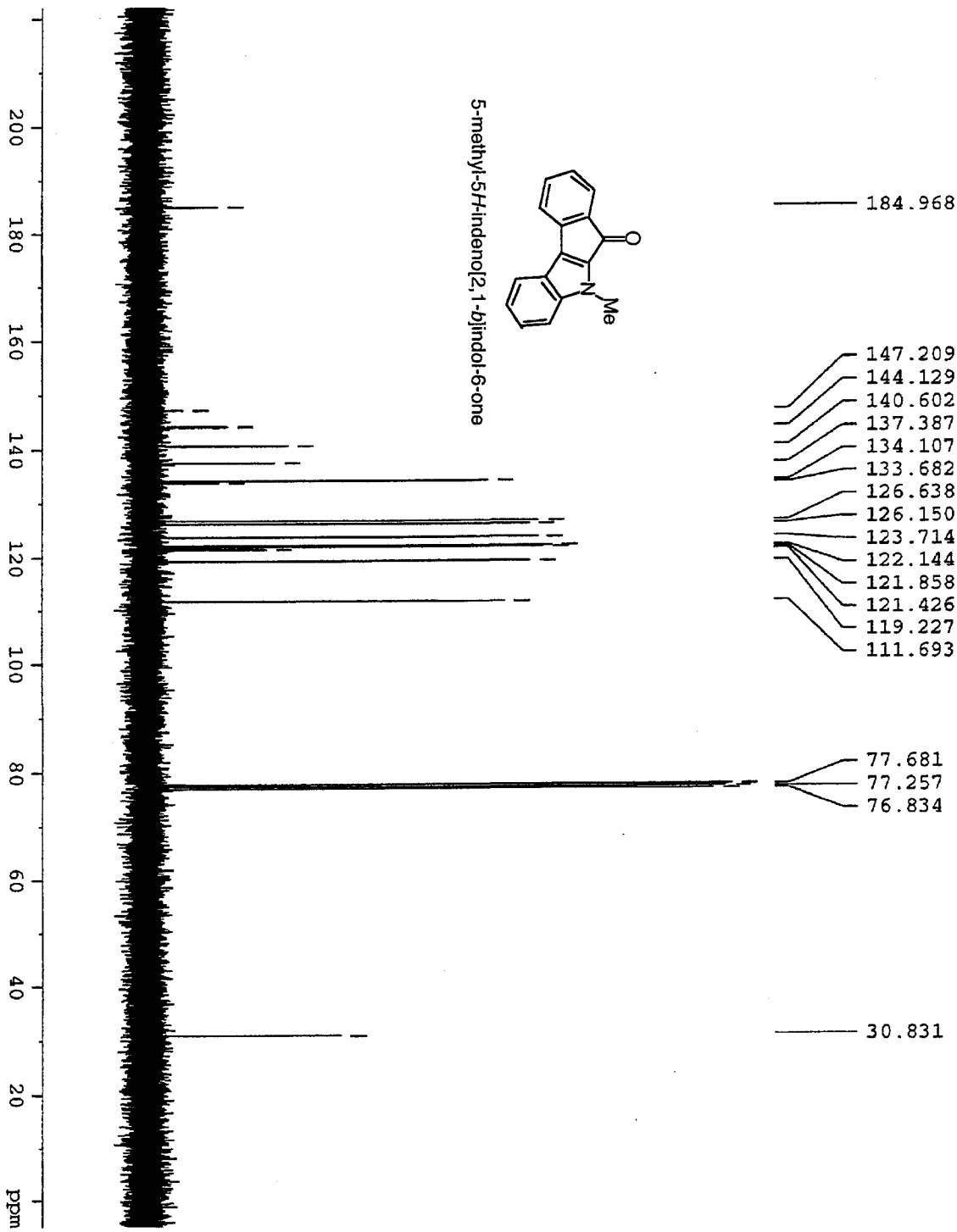

0.998
0.969
1.010
2.982
2.003
10
9
8
7
6
5
4
3
2
1
ppm
benzo[b]indeno[1,2-d]furan-6-one
7.724
7.723
7.704
7.703
7.536
7.515
7.465
7.462
7.447
7.444
7.441
7.426
7.423
7.381
7.373
7.370
7.363
7.353
7.352
7.335
7.332
7.329
7.312
7.311
7.294
7.292
7.259
7.185
7.168
7.161
7.158
7.141
7.123
7.121

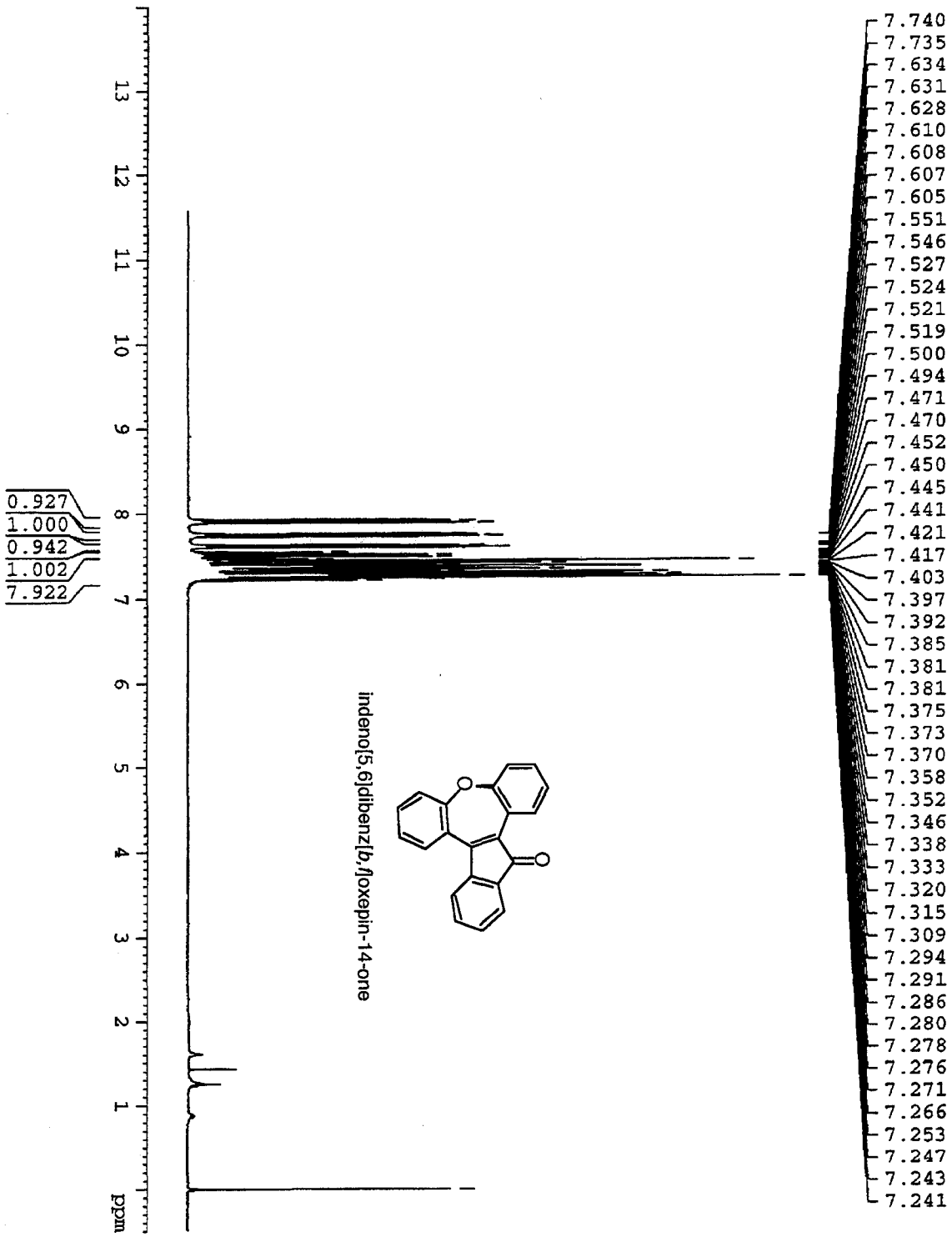

180.677
161.552
154.632
141.391
136.025
134.931
133.896
128.719
128.654
124.838
124.111
122.011
120.290
113.845
77.415
77.097
76.779
200
180
160
140
120
100
80
60
40
20
ppm
benzo[b]indeno[1,2-d]furan-6-one

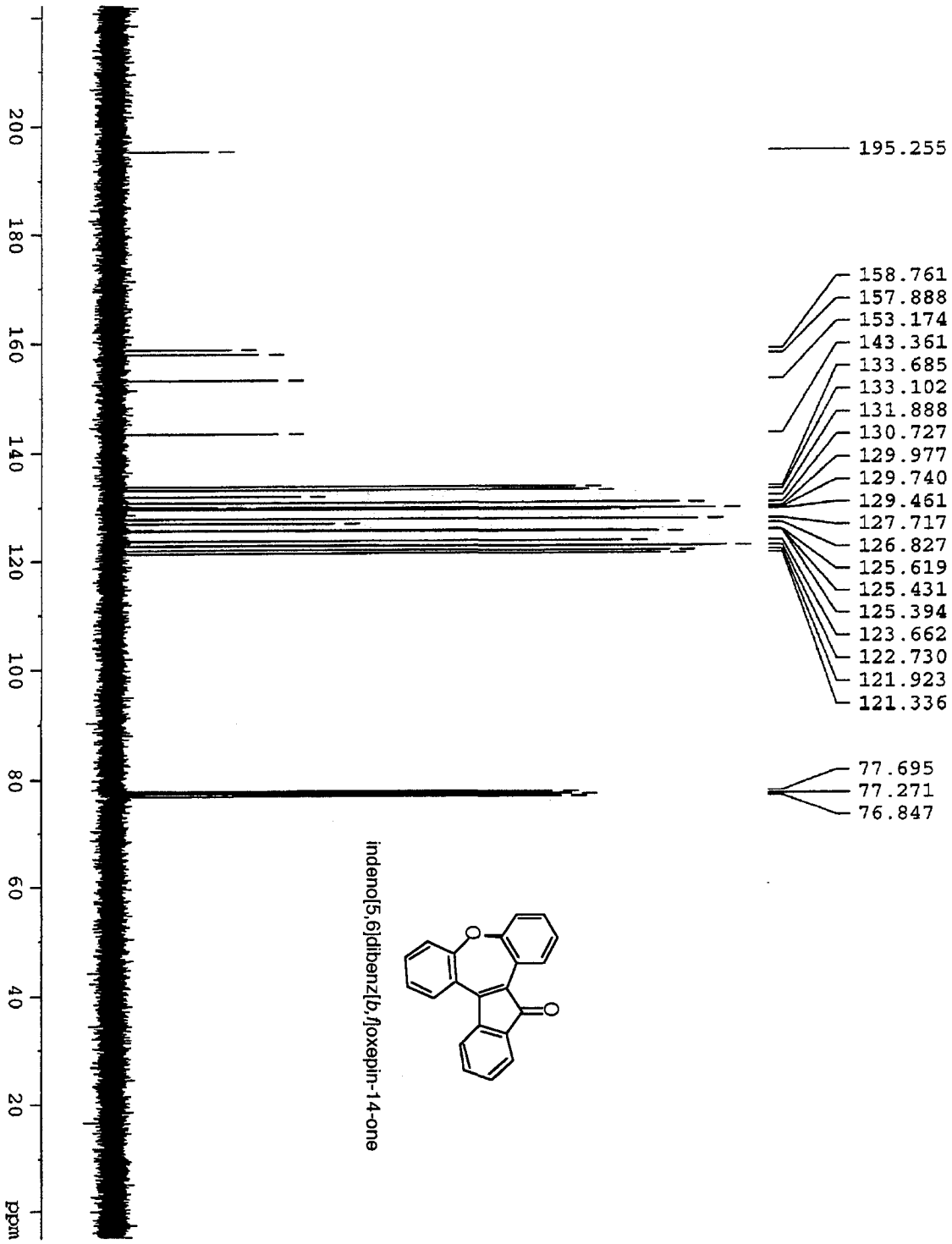

7.847
7.827
7.385
7.364
7.340
7.320
7.302
7.285
7.268
7.247
7.225
7.208
7.166
7.148
7.129
7.043
7.025
7.006
3.338
2.504
2.500
2.496
1.000
4.048
1.003
1.036
1.016
5H-indeno[2,1-b]indol-6-one
O
N
H
ppm


184.095
143.441
140.570
136.870
134.773
134.387
127.222
126.704
123.646
122.363
121.901
121.143
119.886
114.765
5H-indeno[2,1-b]indol-6-one
O
N
H
200
180
160
140
120
100
80
60
40
20
ppm

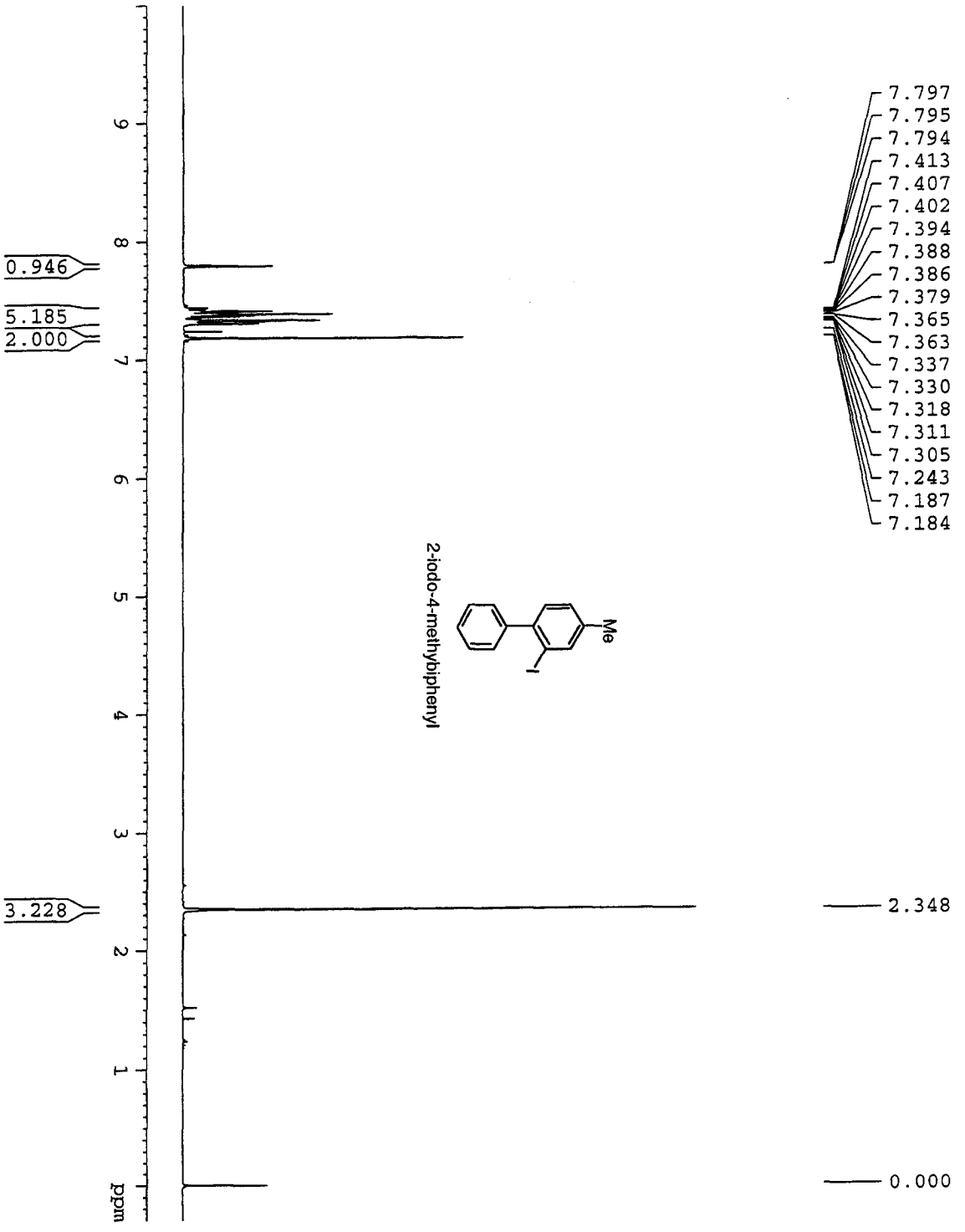

5-methyl-5H-indeno[2,1-b]indol-6-one
Me
7.664
7.661
7.657
7.637
7.634
7.630
7.297
7.293
7.277
7.273
7.271
7.269
7.257
7.247
7.243
7.223
7.221
7.219
7.197
7.193
7.191
7.185
7.171
7.164
7.158
7.144
7.138
7.102
7.100
7.081
7.079
6.989
6.986
6.965
6.963
6.960
6.940
6.936
3.865
0.000
1.006
4.277
1.332
0.984
1.001
3.088
ppm

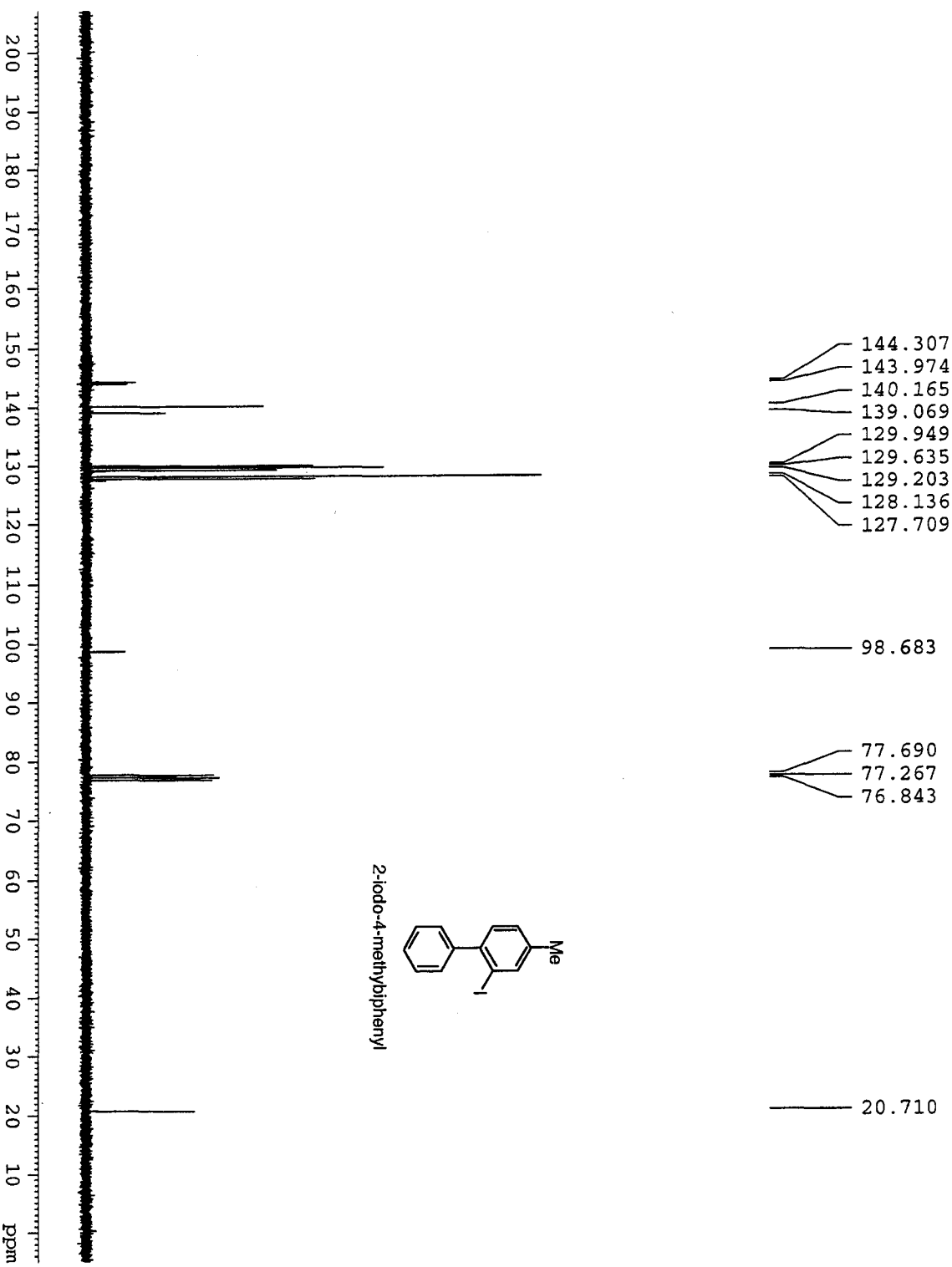

5-methyl-5H-indeno[2,1-b]indol-6-one
Me
184.968
147.209
144.129
140.602
137.387
134.107
133.682
126.638
126.150
123.714
122.144
121.858
121.426
119.227
111.693
77.681
77.257
76.834
30.831
200
180
160
140
120
100
80
60
40
20
ppm

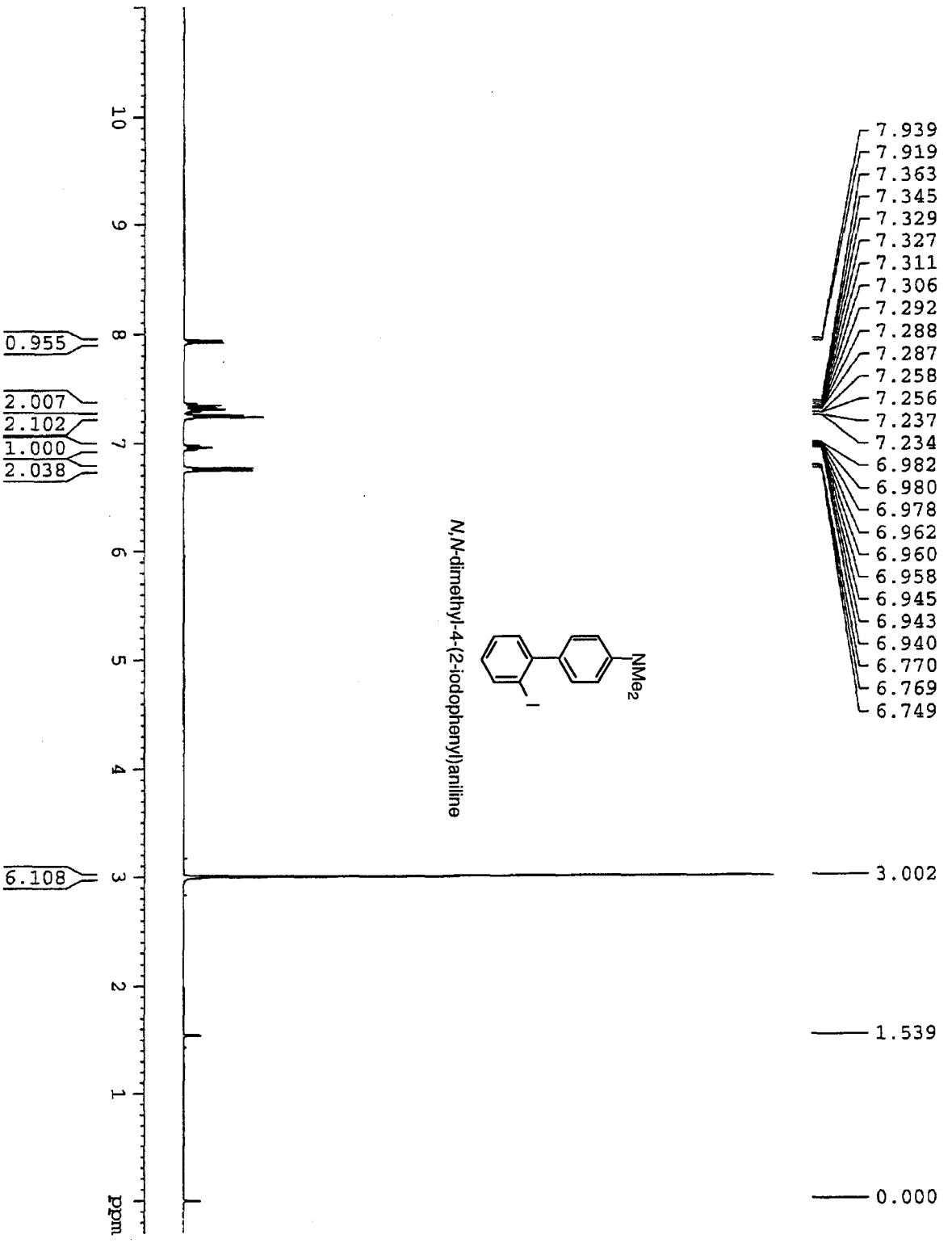

7.740
7.735
7.634
7.631
7.628
7.610
7.608
7.607
7.605
7.551
7.546
7.527
7.524
7.521
7.519
7.500
7.494
7.471
7.470
7.452
7.450
7.445
7.441
7.421
7.417
7.403
7.397
7.392
7.385
7.381
7.381
7.375
7.373
7.370
7.358
7.352
7.346
7.338
7.333
7.320
7.315
7.309
7.294
7.291
7.286
7.280
7.278
7.276
7.271
7.266
7.253
7.247
7.243
7.241
0.927
1.000
0.942
1.002
7.922
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
indeno[5,6]dibenz[b,f]oxepin-14-one

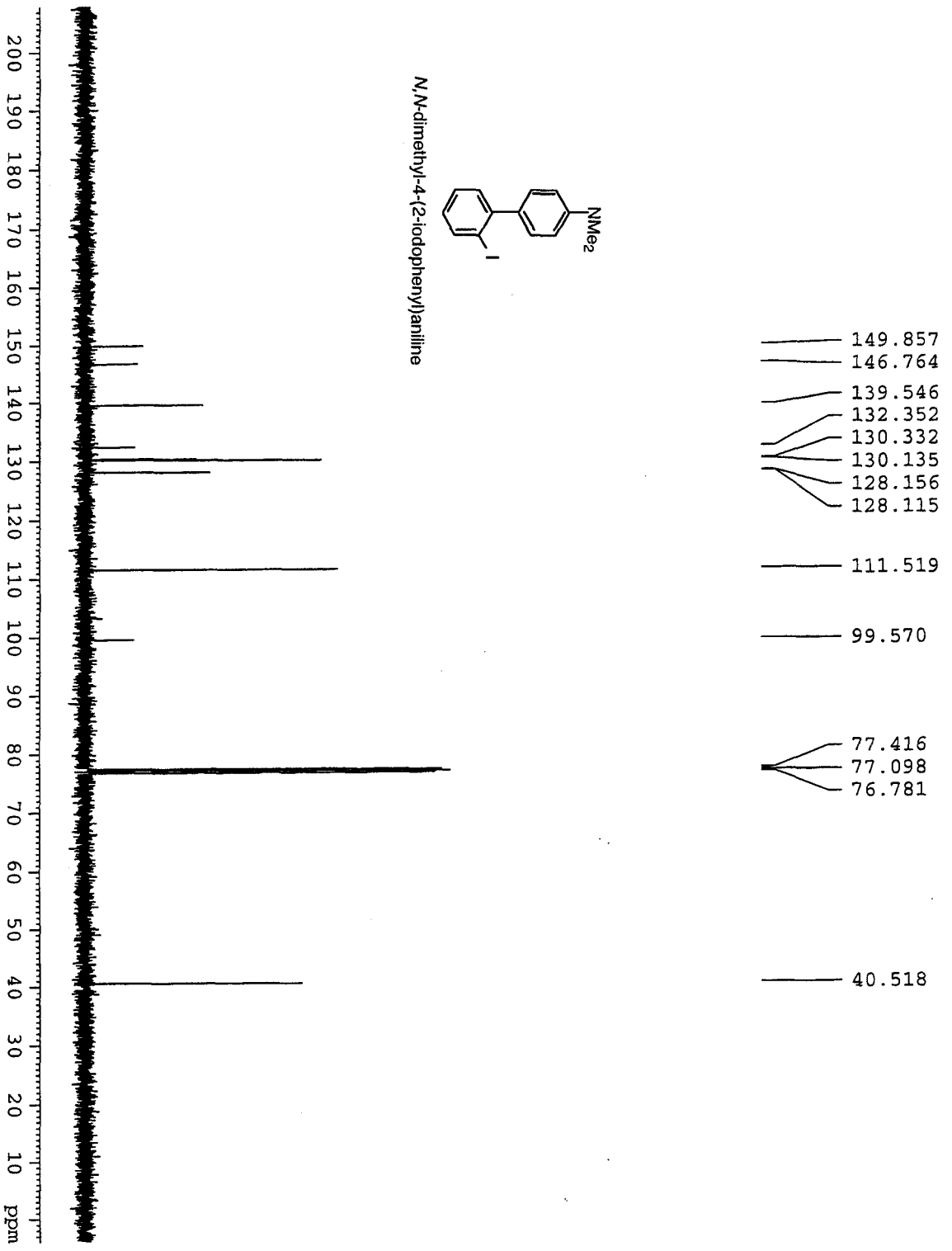

195.255
158.761
157.888
153.174
143.361
133.685
133.102
131.888
130.727
129.977
129.740
129.461
127.717
126.827
125.619
125.431
125.394
123.662
122.730
121.923
121.336
77.695
77.271
76.847
200
180
160
140
120
100
80
60
40
20
ppm
indeno[5,6]dibenz[b,f]oxepin-14-one

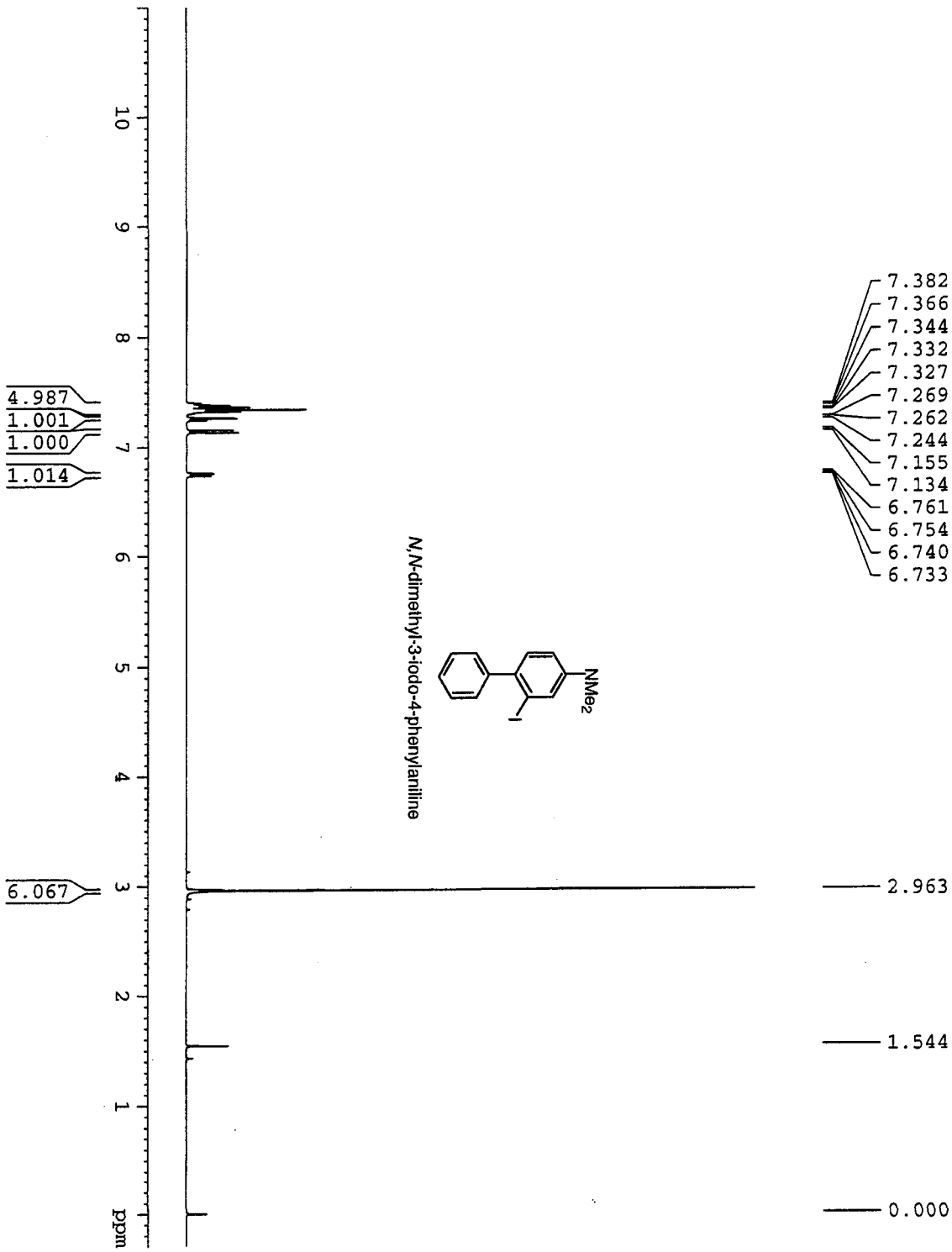
APPENDIX B. CHAPTER 2 ^{1}H AND ^{13}C NMR SPECTRA

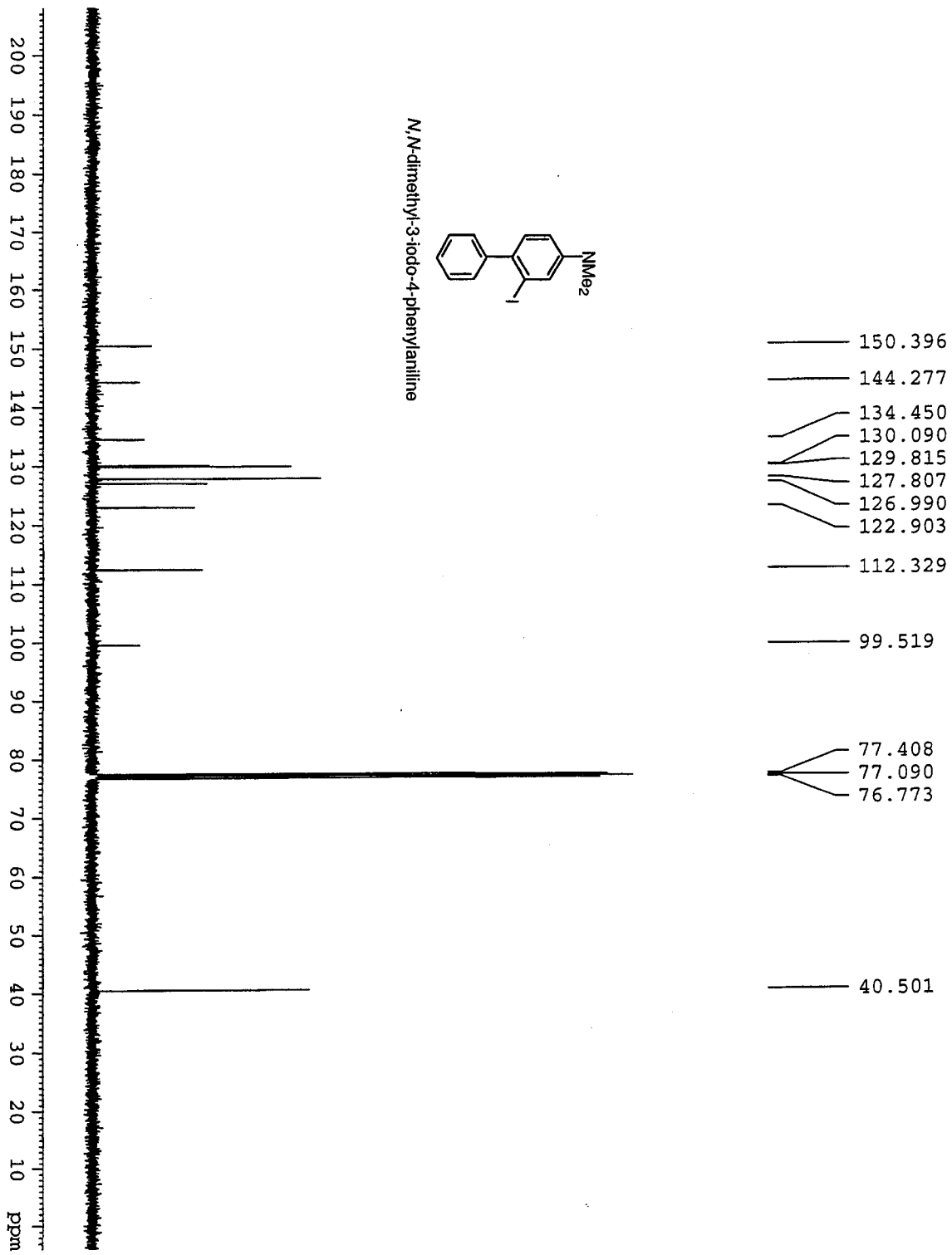

7.797
7.795
7.794
7.413
7.407
7.402
7.394
7.388
7.386
7.379
7.365
7.363
7.337
7.330
7.318
7.311
7.305
7.243
7.187
7.184
0.946
5.185
2.000
3.228
2.348
0.000
2-iodo-4-methybiphenyl
Me
I
ppm

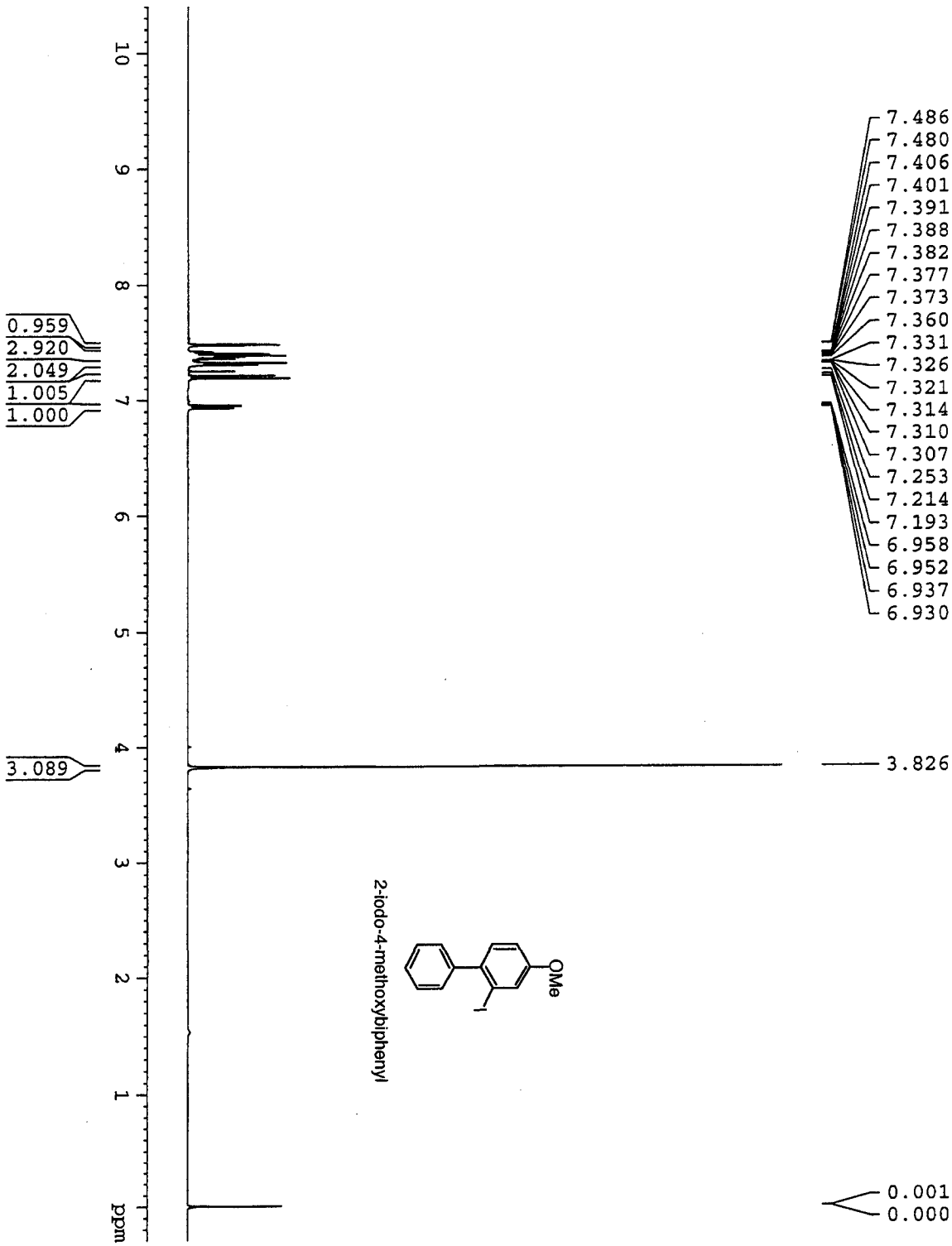

144.307
143.974
140.165
139.069
129.949
129.635
129.203
128.136
127.709
98.683
77.690
77.267
76.843
20.710
2-iodo-4-methylbiphenyl
Me
I
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

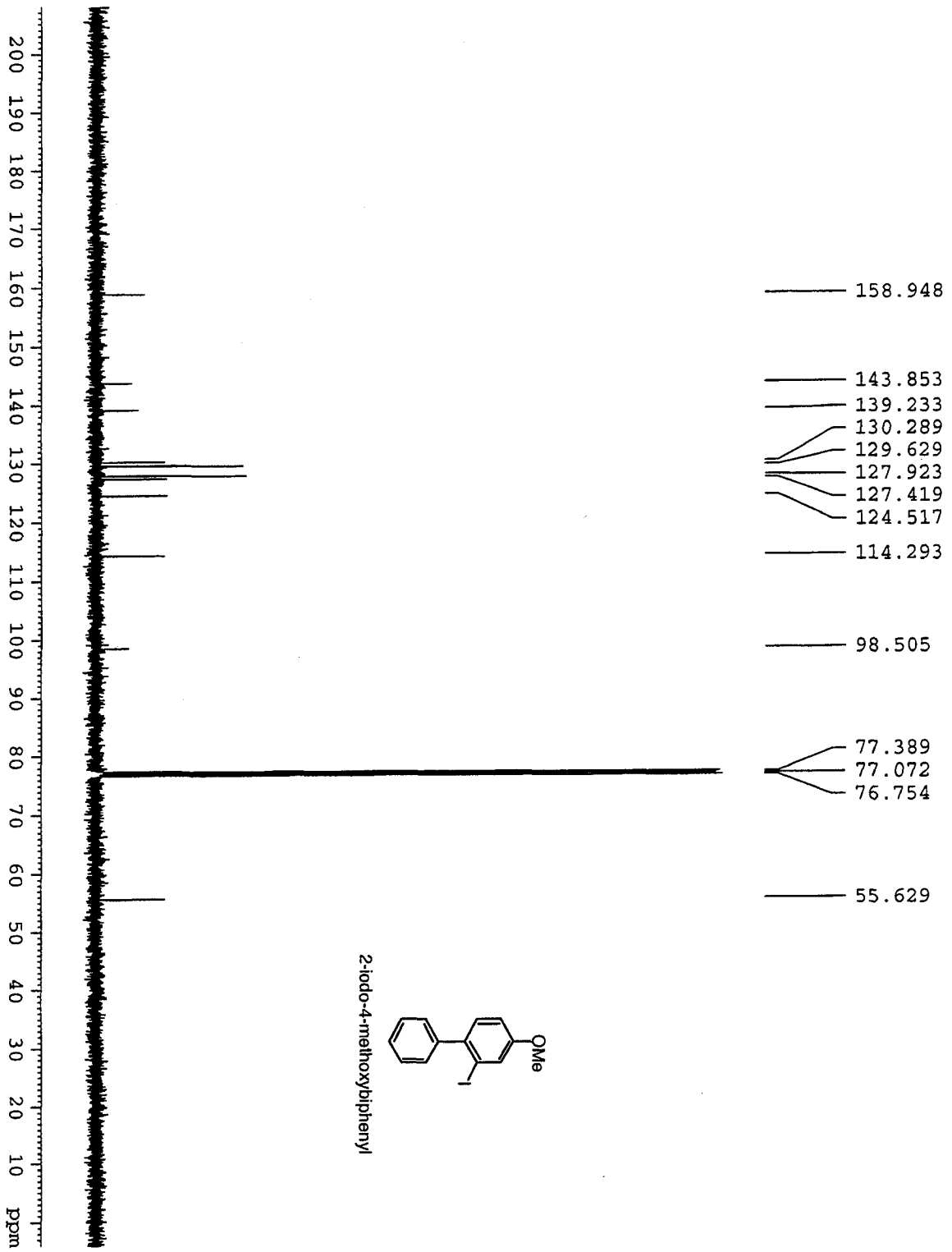

7.939
7.919
7.363
7.345
7.329
7.327
7.311
7.306
7.292
7.288
7.287
7.258
7.256
7.237
7.234
6.982
6.980
6.978
6.962
6.960
6.958
6.945
6.943
6.940
6.770
6.769
6.749
0.955
2.007
2.102
1.000
2.038
6.108
3.002
1.539
0.000
ppm
N,N-dimethyl-4-(2-iodophenyl)aniline
NMe2
I

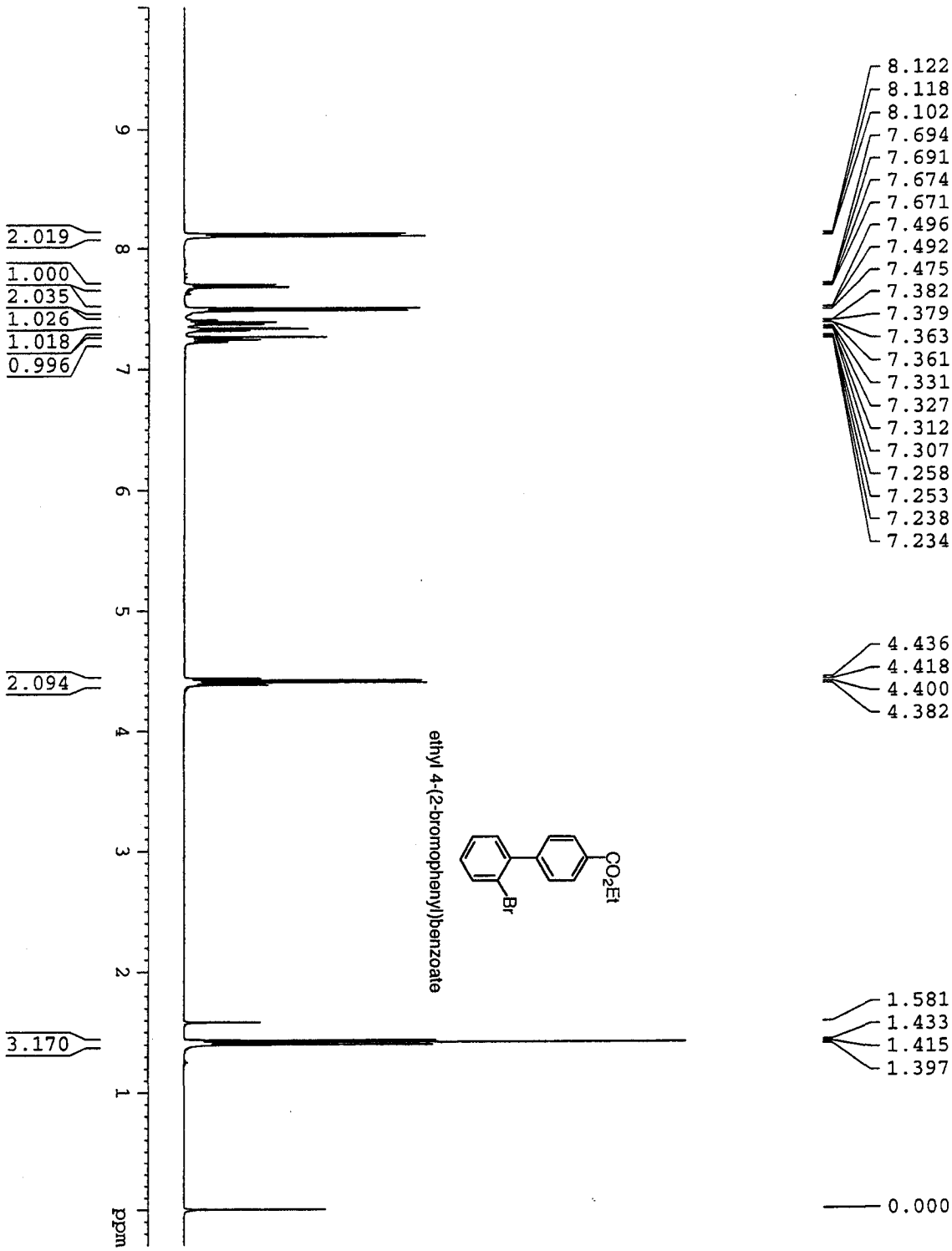

N,N-dimethyl-4-(2-iodophenyl)aniline
NMe2
I
149.857
146.764
139.546
132.352
130.332
130.135
128.156
128.115
111.519
99.570
77.416
77.098
76.781
40.518
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

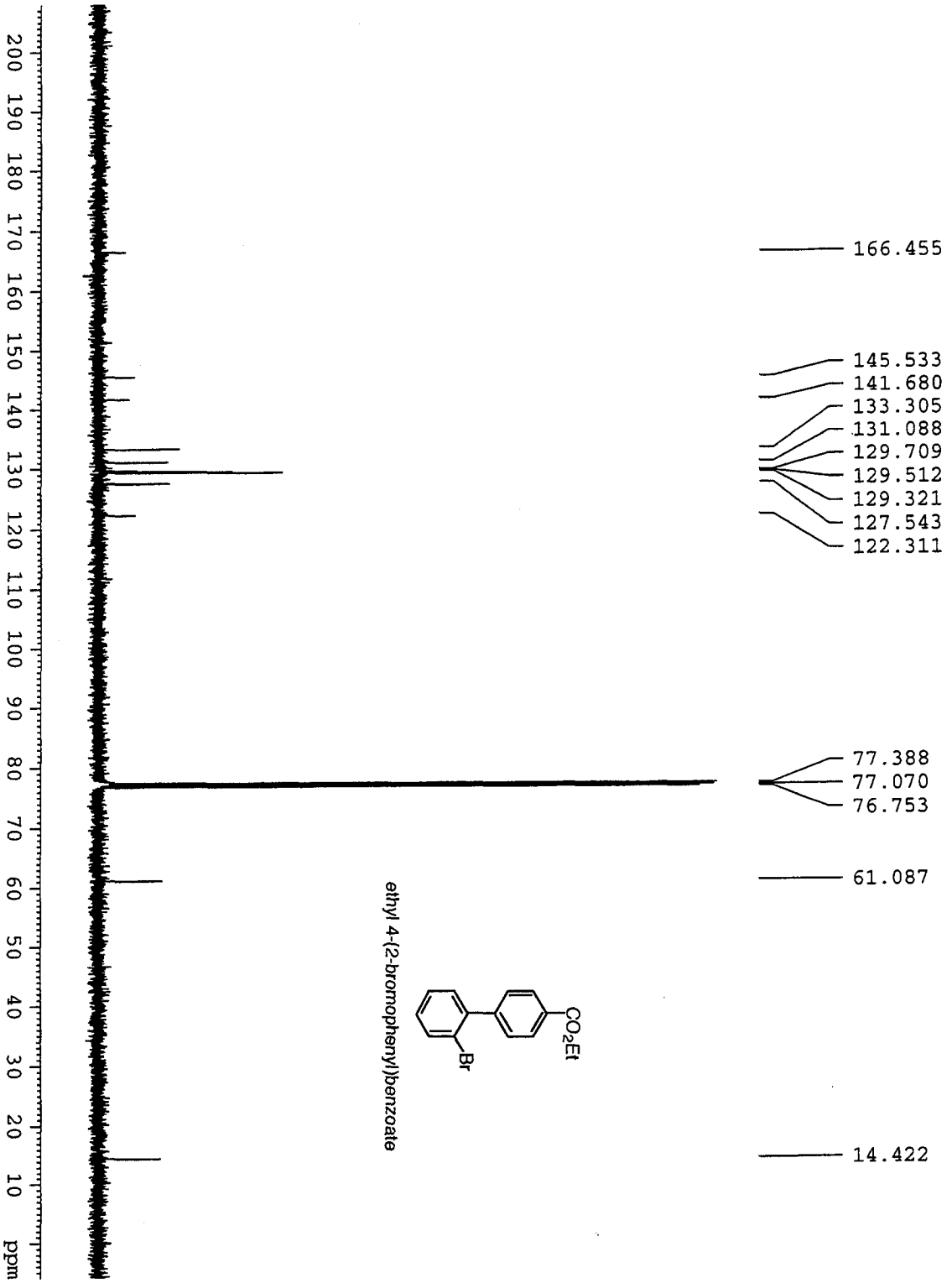

7.382
7.366
7.344
7.332
7.327
7.269
7.262
7.244
7.155
7.134
6.761
6.754
6.740
6.733
4.987
1.001
1.000
1.014
6.067
2.963
1.544
0.000
N,N-dimethyl-3-iodo-4-phenylaniline
NMe2
I
10
9
8
7
6
5
4
3
2
1
ppm

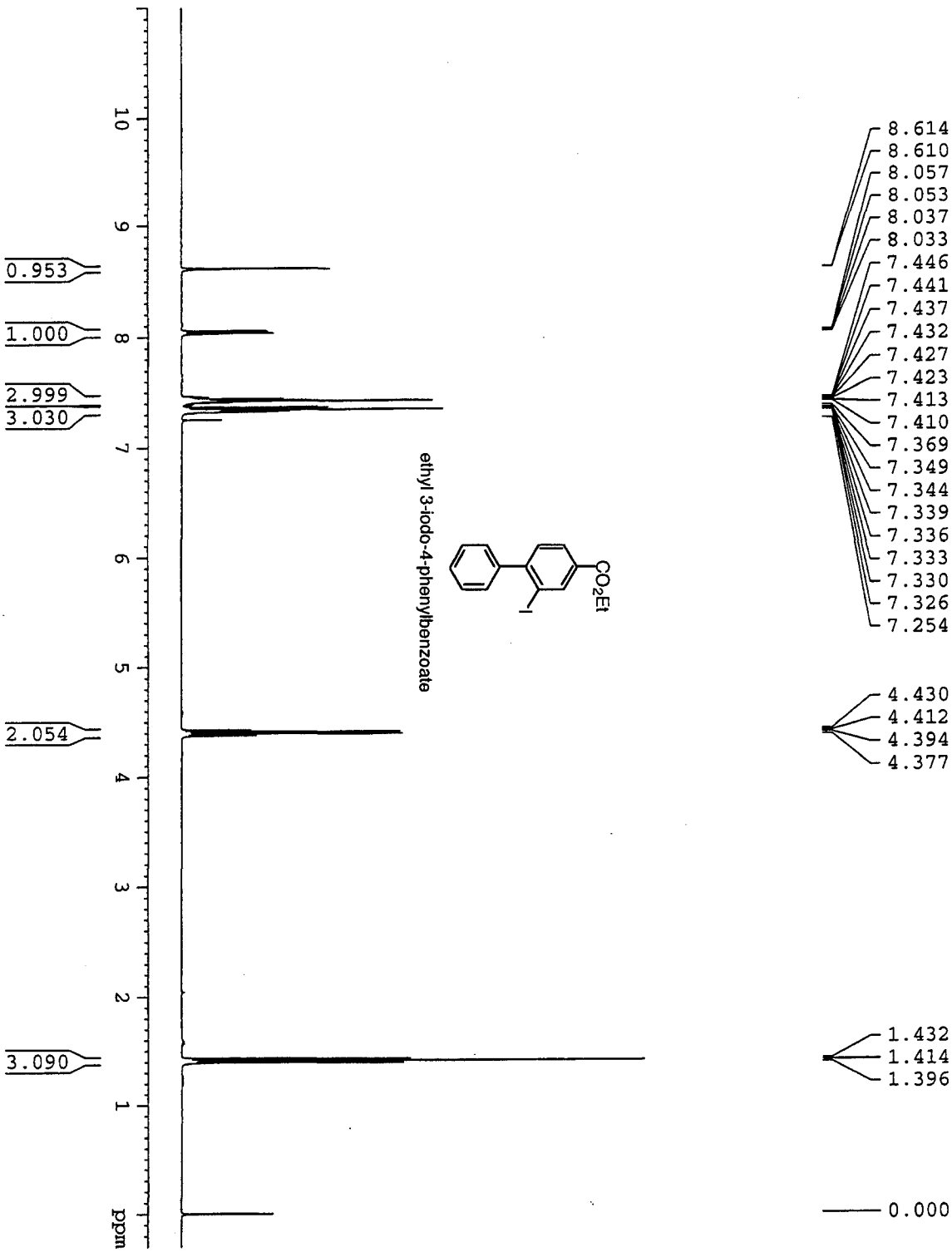

N,N-dimethyl-3-iodo-4-phenylaniline
NMe2
I
150.396
144.277
134.450
130.090
129.815
127.807
126.990
122.903
112.329
99.519
77.408
77.090
76.773
40.501
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

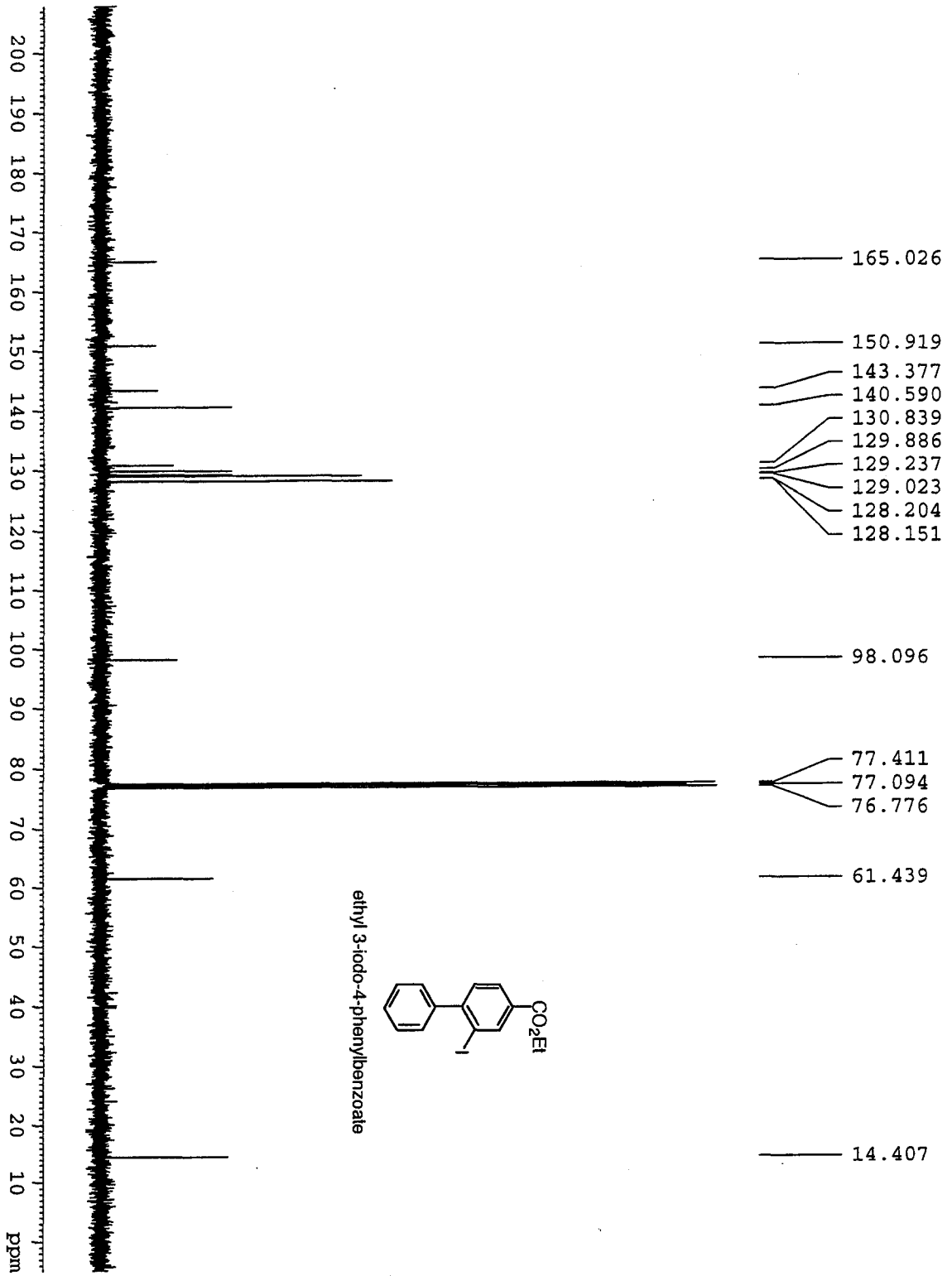

7.486
7.480
7.406
7.401
7.391
7.388
7.382
7.377
7.373
7.360
7.331
7.326
7.321
7.314
7.310
7.307
7.253
7.214
7.193
6.958
6.952
6.937
6.930
3.826
0.001
0.000
0.959
2.920
2.049
1.005
1.000
3.089
10
9
8
7
6
5
4
3
2
1
ppm
2-iodo-4-methoxybiphenyl
OMe
I

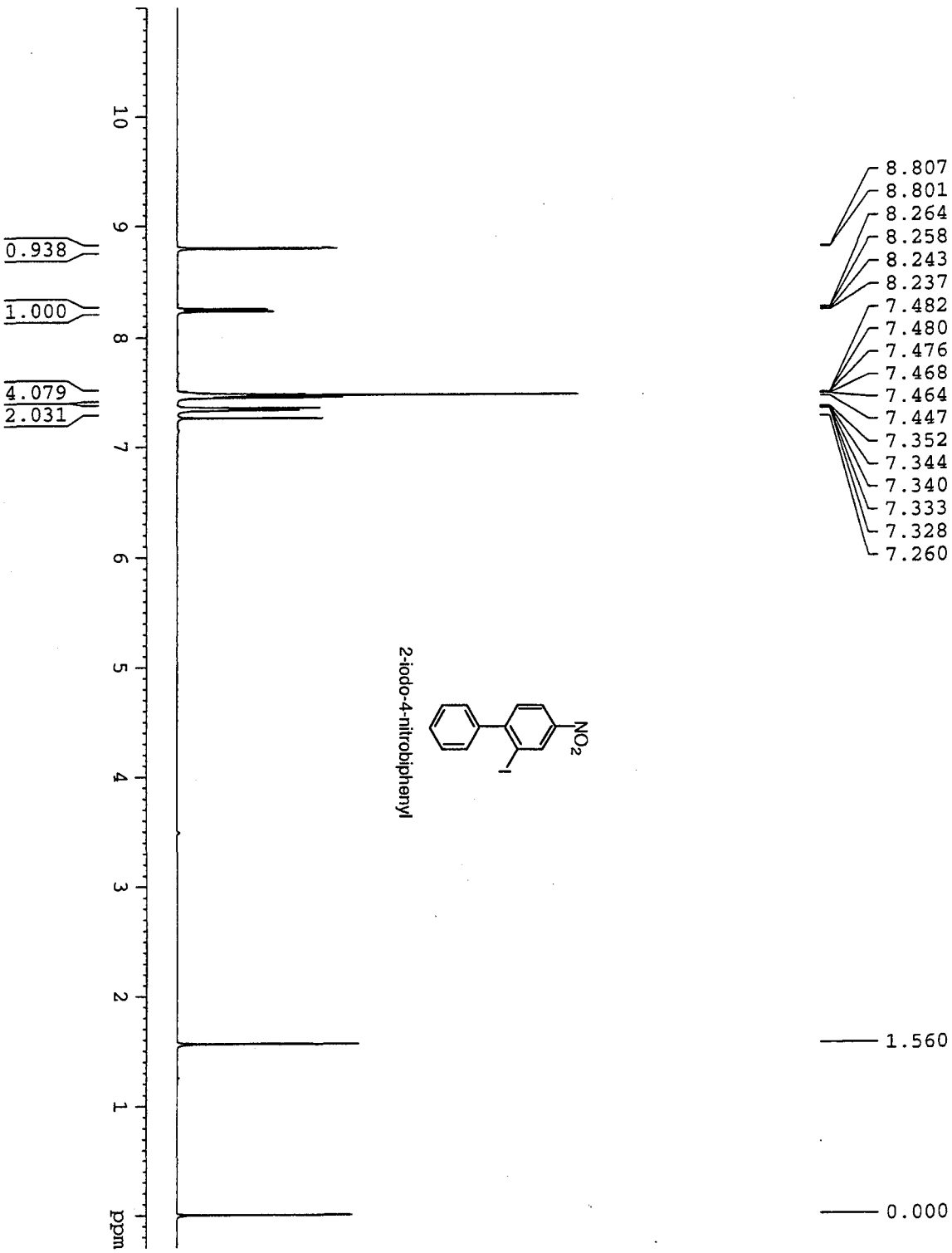

158.948
143.853
139.233
130.289
129.629
127.923
127.419
124.517
114.293
98.505
77.389
77.072
76.754
55.629
2-iodo-4-methoxybiphenyl
OMe
I
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

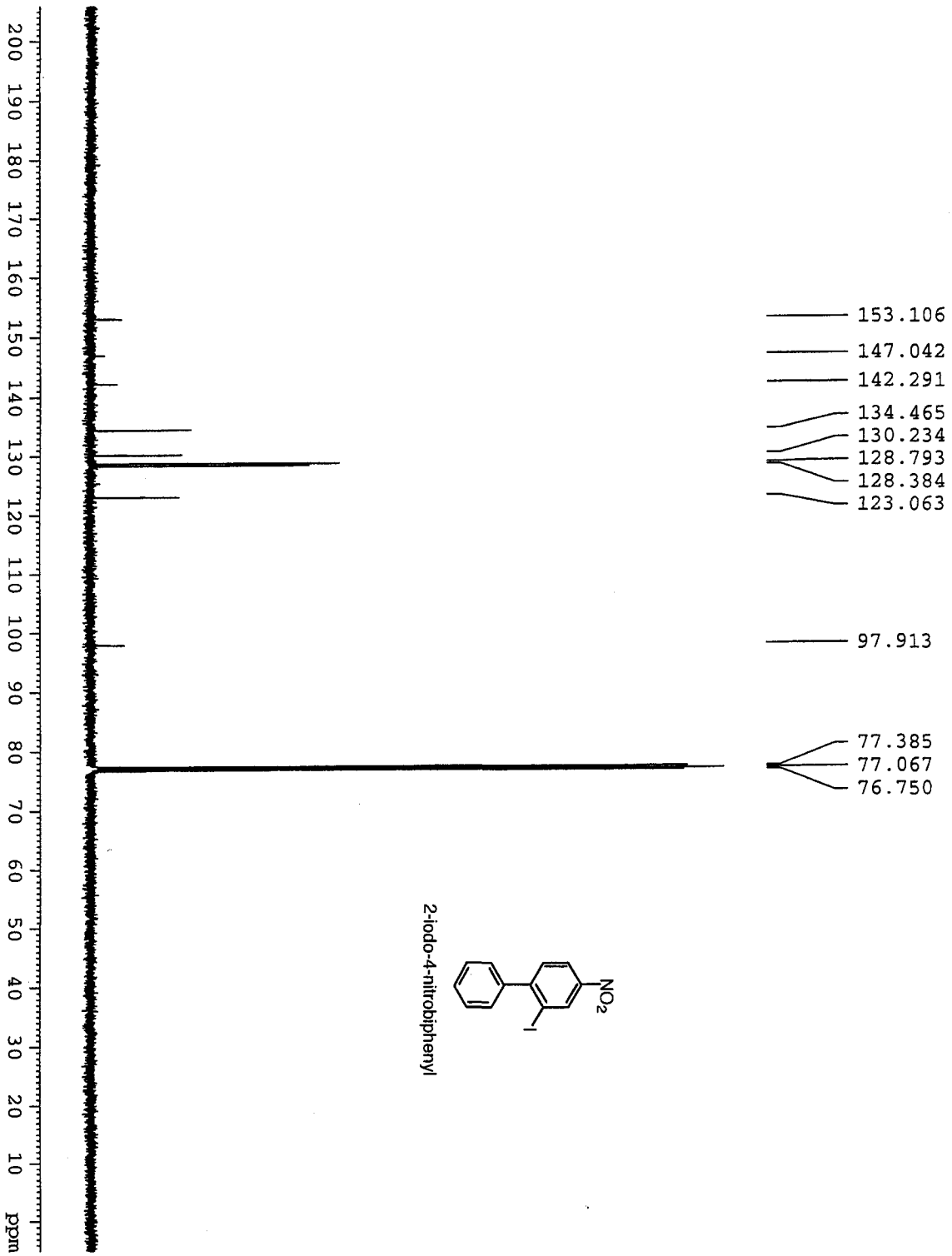

8.122
8.118
8.102
7.694
7.691
7.674
7.671
7.496
7.492
7.475
7.382
7.379
7.363
7.361
7.331
7.327
7.312
7.307
7.258
7.253
7.238
7.234
4.436
4.418
4.400
4.382
1.581
1.433
1.415
1.397
0.000
2.019
1.000
2.035
1.026
1.018
0.996
2.094
3.170
ppm
ethyl 4-(2-bromophenyl)benzoate
Br
CO2Et

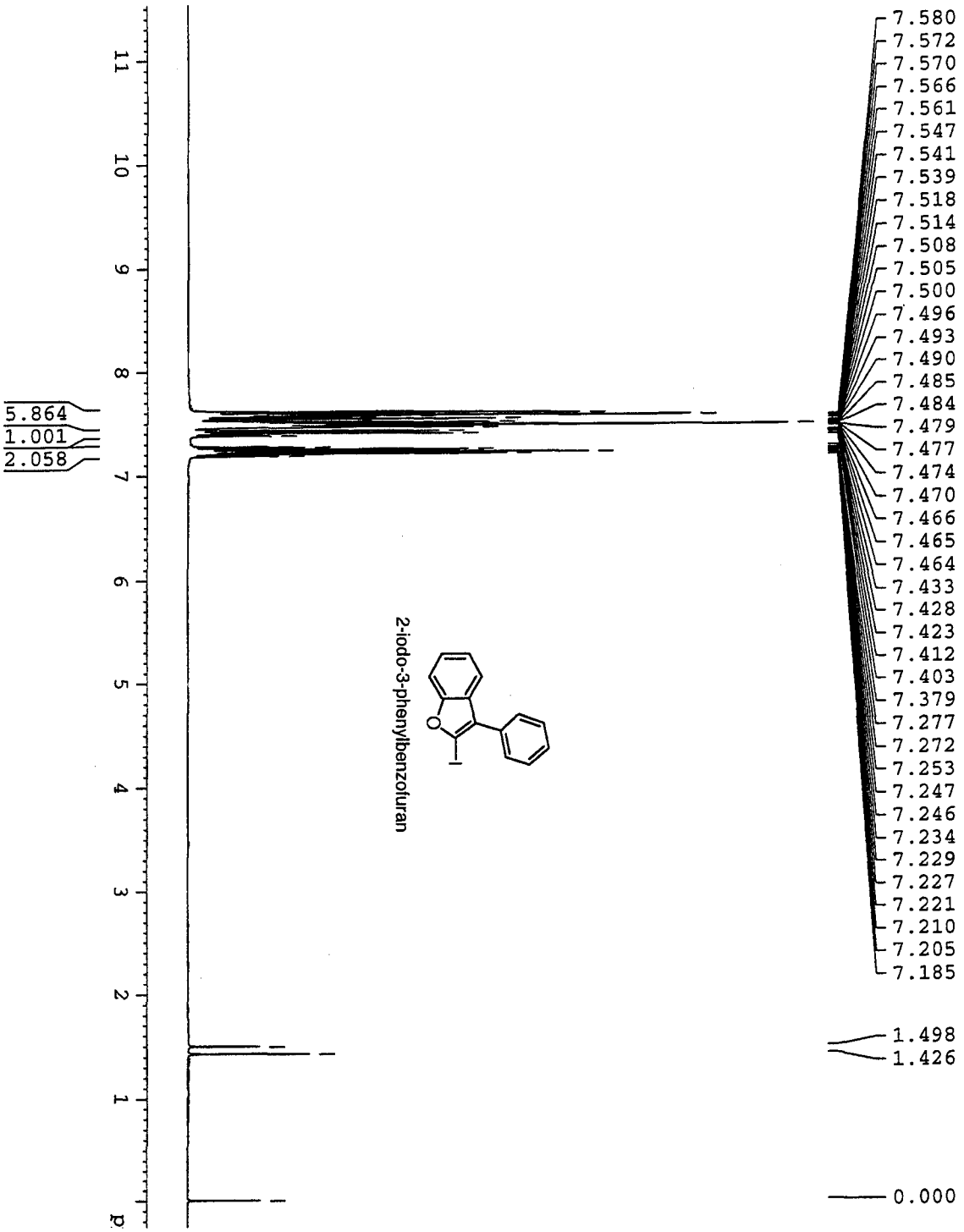

166.455
145.533
141.680
133.305
131.088
129.709
129.512
129.321
127.543
122.311
77.388
77.070
76.753
61.087
14.422
ethyl 4-(2-bromophenyl)benzoate
Br
CO2Et
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

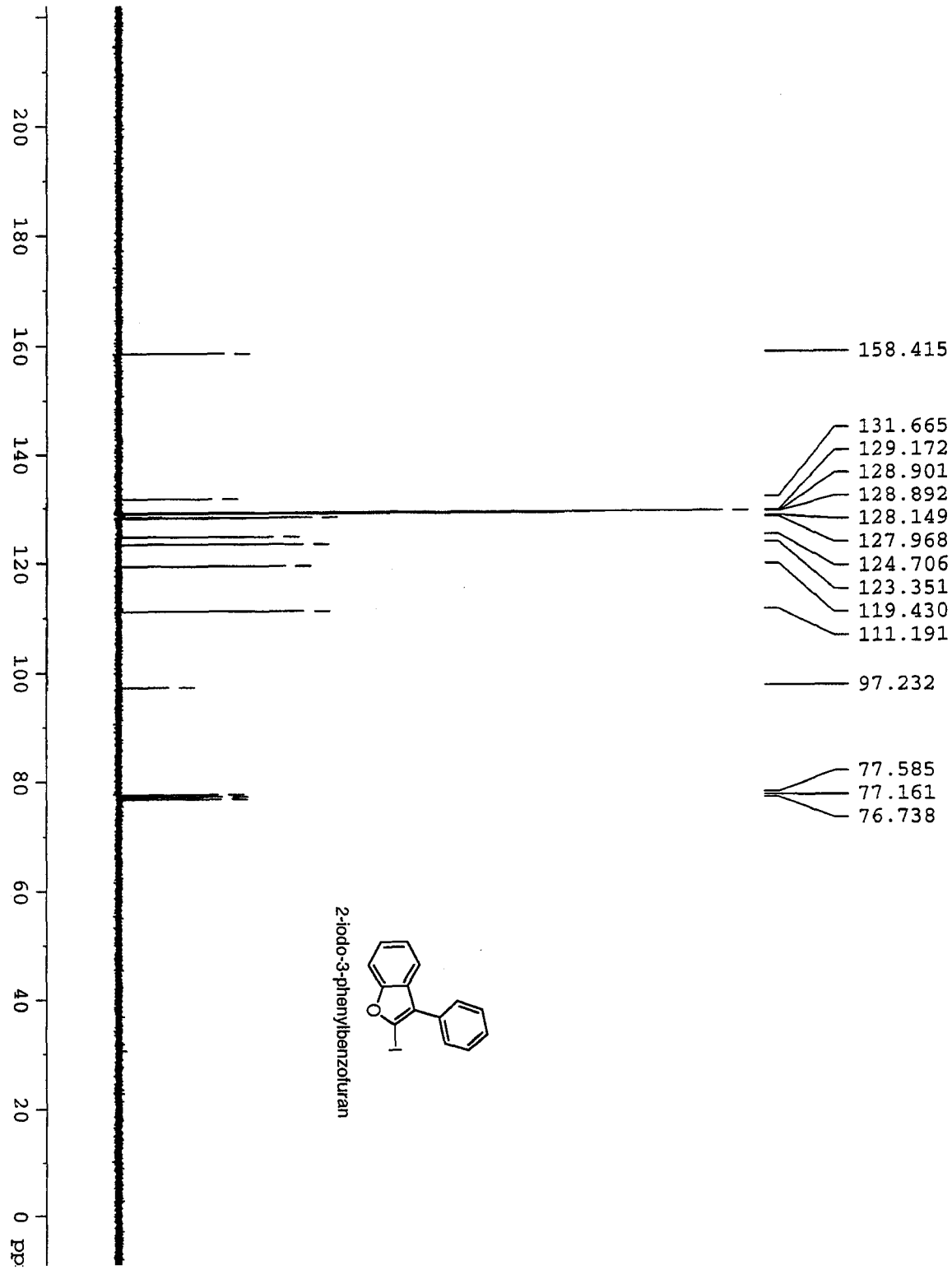

ethyl 3-iodo-4-phenylbenzoate
CO2Et
I
0.953
1.000
2.999
3.030
2.054
3.090
8.614
8.610
8.057
8.053
8.037
8.033
7.446
7.441
7.437
7.432
7.427
7.423
7.413
7.410
7.369
7.349
7.344
7.339
7.336
7.333
7.330
7.326
7.254
4.430
4.412
4.394
4.377
1.432
1.414
1.396
0.000
ppm

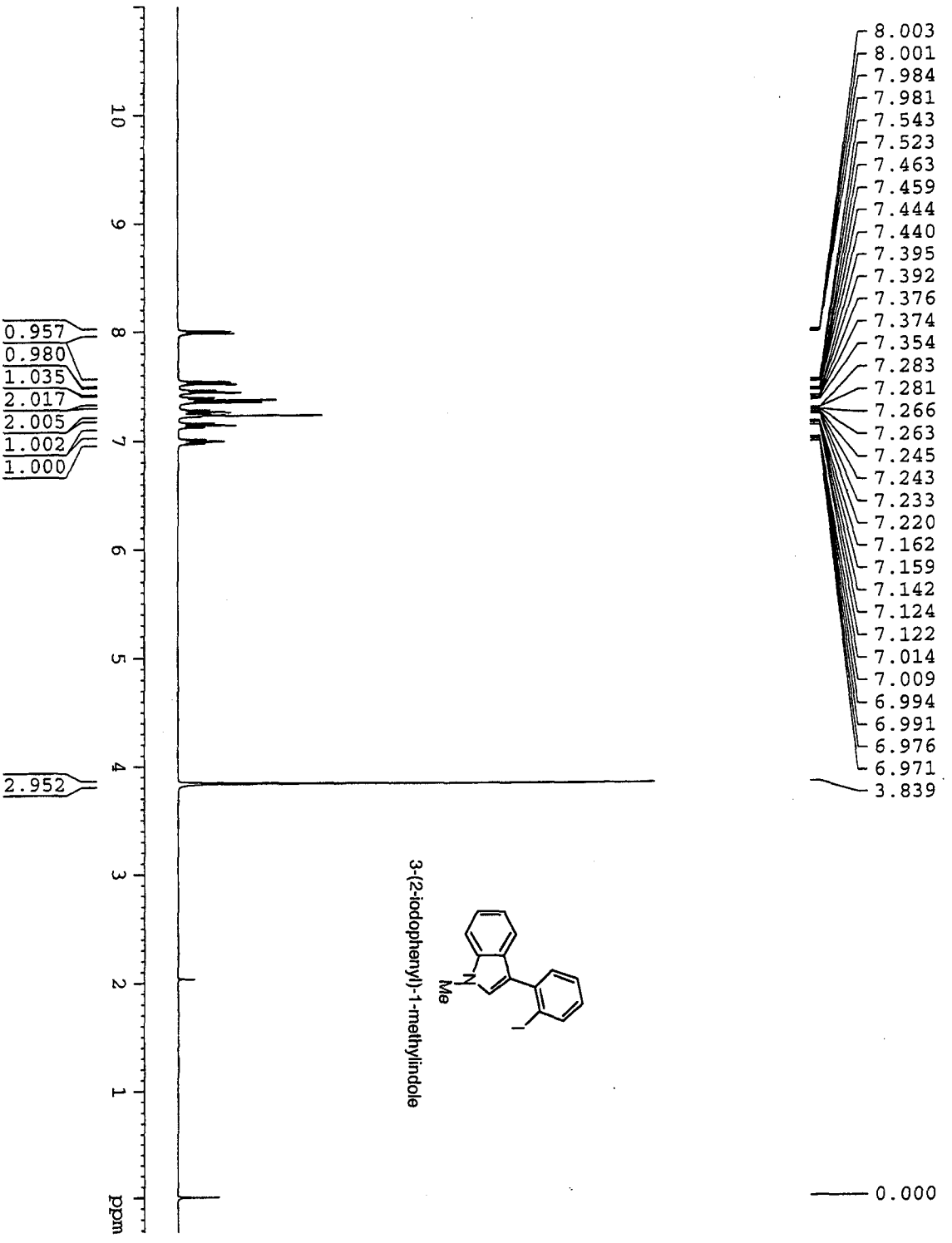

165.026
150.919
143.377
140.590
130.839
129.886
129.237
129.023
128.204
128.151
98.096
77.411
77.094
76.776
61.439
14.407
ethyl 3-iodo-4-phenylbenzoate
CO2Et
I
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

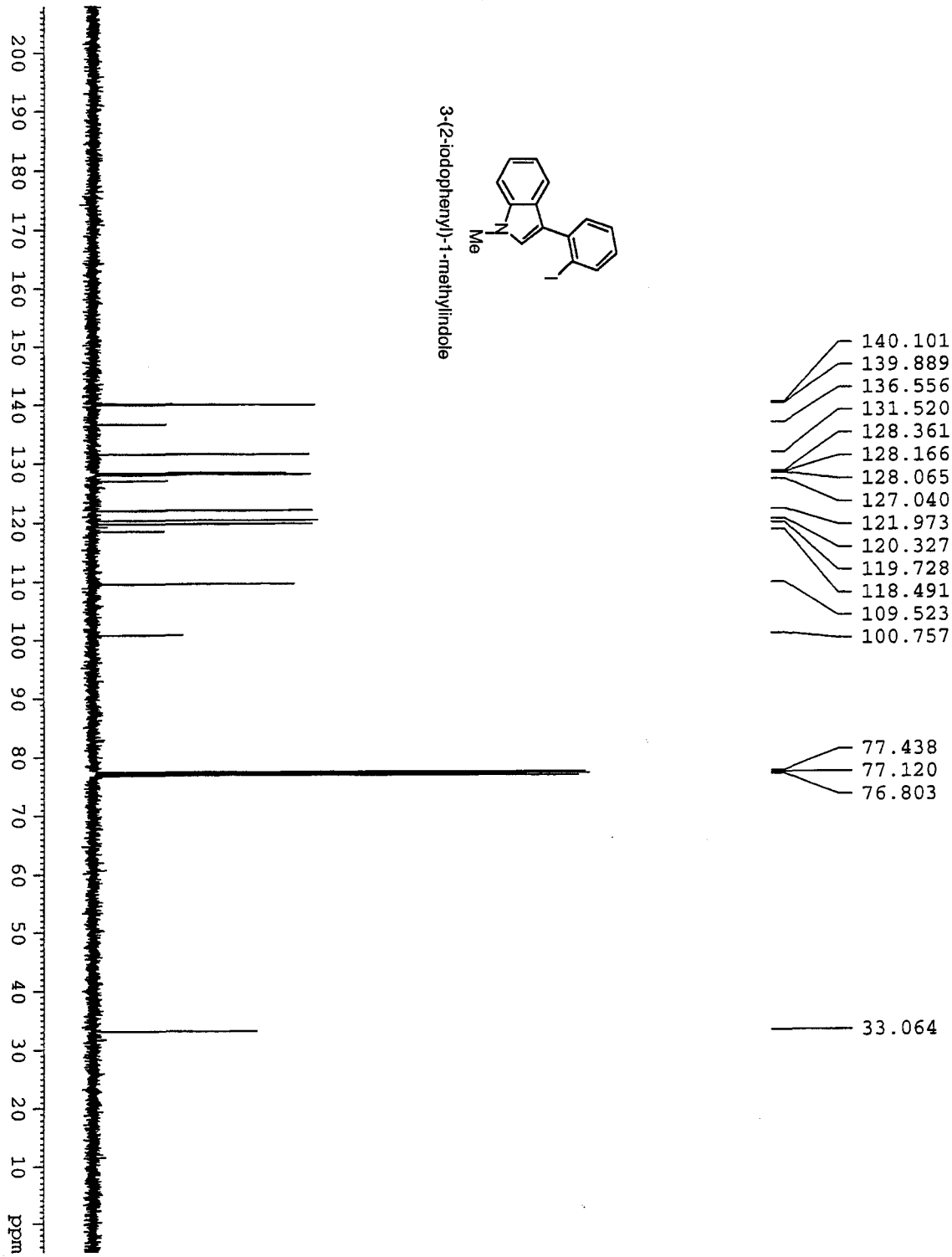

8.807
8.801
8.264
8.258
8.243
8.237
7.482
7.480
7.476
7.468
7.464
7.447
7.352
7.344
7.340
7.333
7.328
7.260
1.560
0.000
0.938
1.000
4.079
2.031
2-iodo-4-nitrobiphenyl
NO2
I
ppm

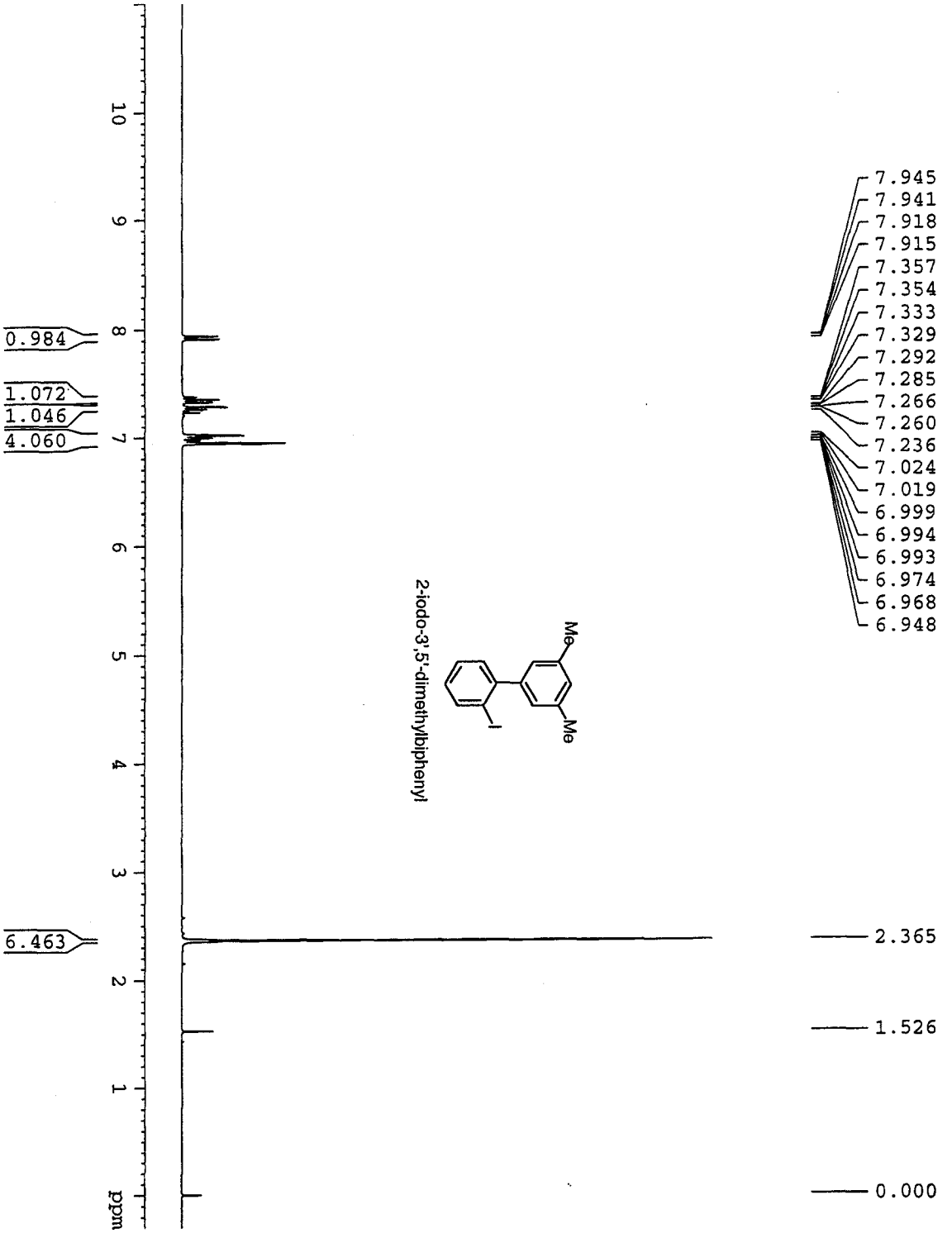

153.106
147.042
142.291
134.465
130.234
128.793
128.384
123.063
97.913
77.385
77.067
76.750
2-iodo-4-nitrobiphenyl
NO2
I
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

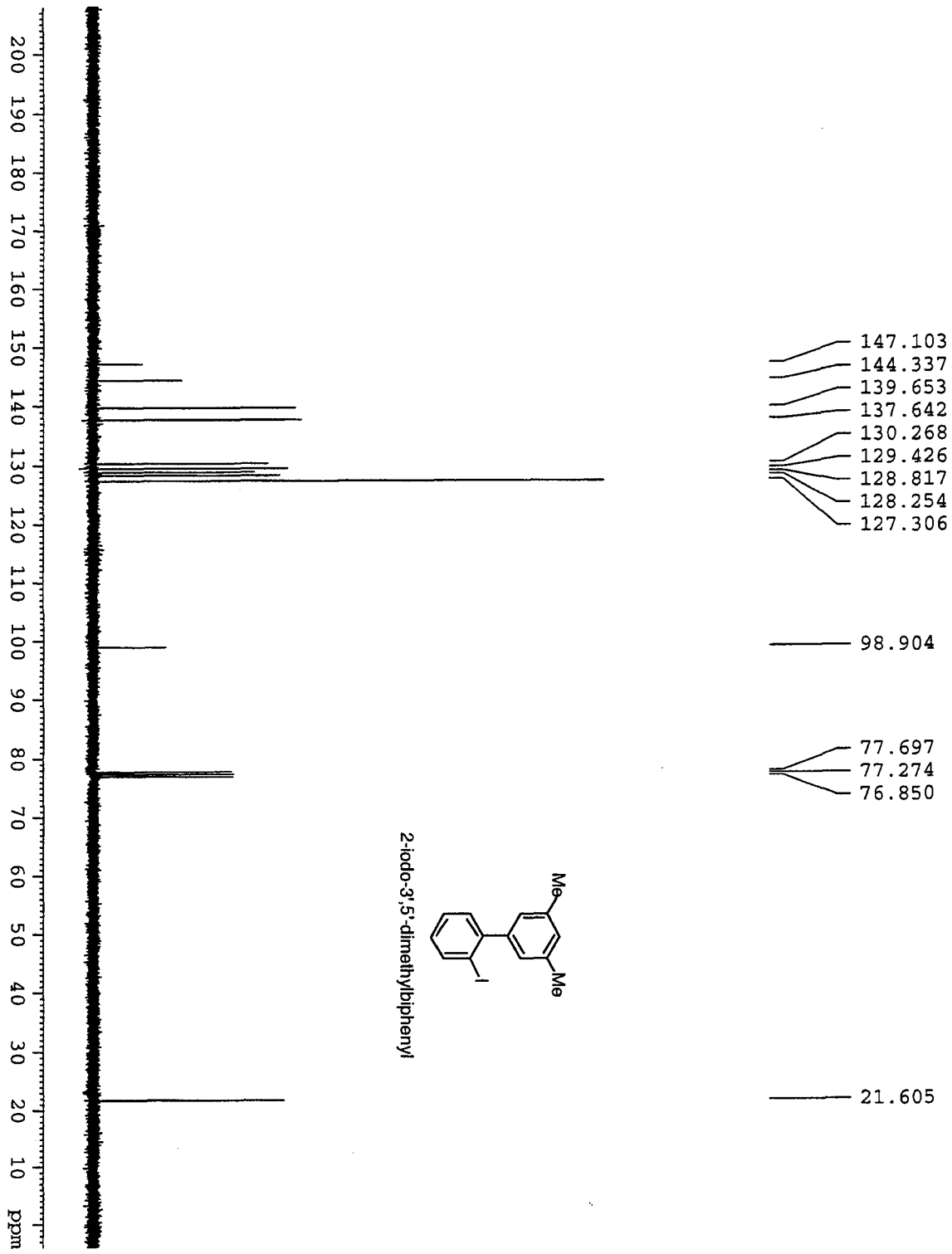

7.580
7.572
7.570
7.566
7.561
7.547
7.541
7.539
7.518
7.514
7.508
7.505
7.500
7.496
7.493
7.490
7.485
7.484
7.479
7.477
7.474
7.470
7.466
7.465
7.464
7.433
7.428
7.423
7.412
7.403
7.379
7.277
7.272
7.253
7.247
7.246
7.234
7.229
7.227
7.221
7.210
7.205
7.185
1.498
1.426
0.000
5.864
1.001
2.058
2-iodo-3-phenylbenzofuran
O
I

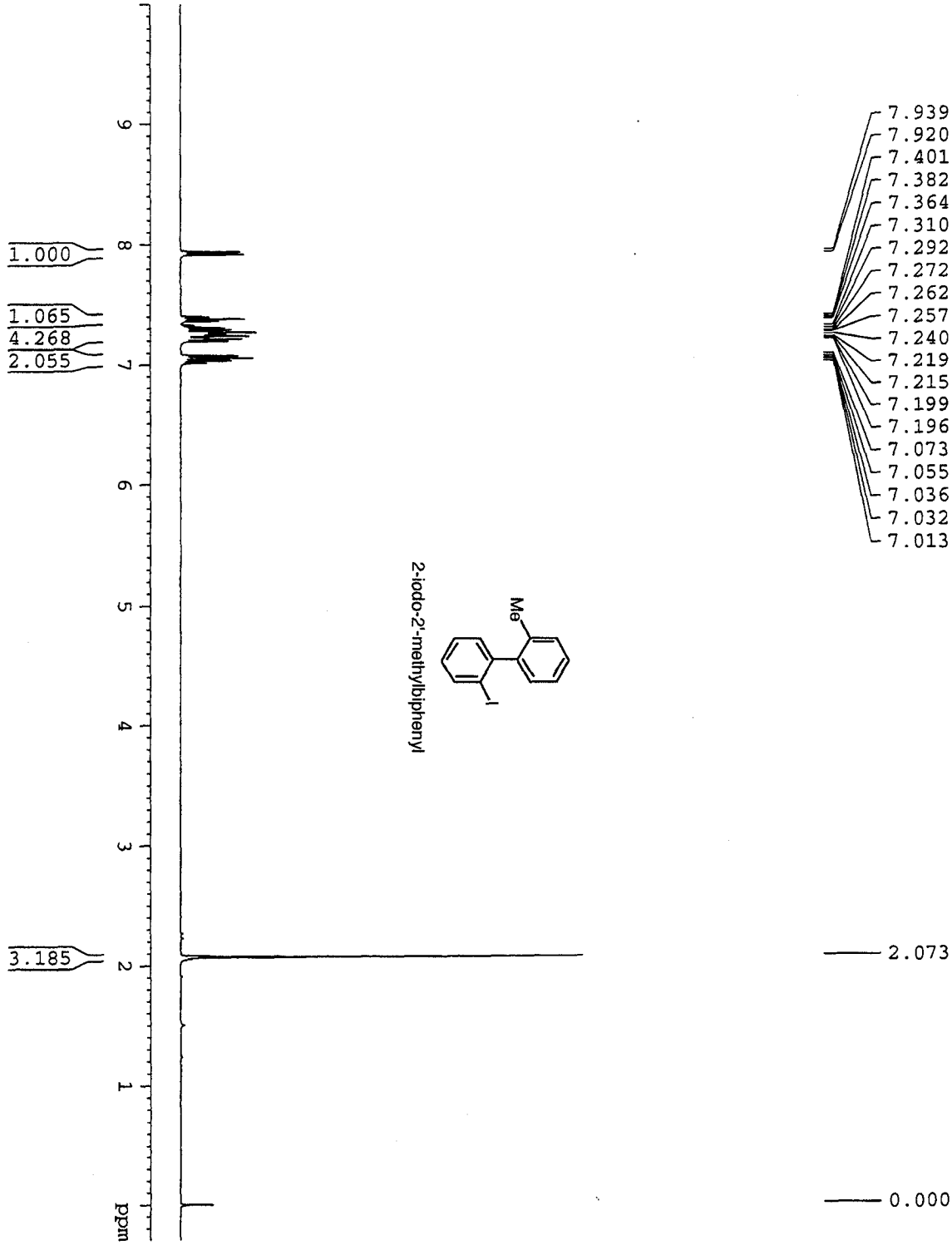

158.415
131.665
129.172
128.901
128.892
128.149
127.968
124.706
123.351
119.430
111.191
97.232
77.585
77.161
76.738
200
180
160
140
120
100
80
60
40
20
0 pp
2-iodo-3-phenylbenzofuran

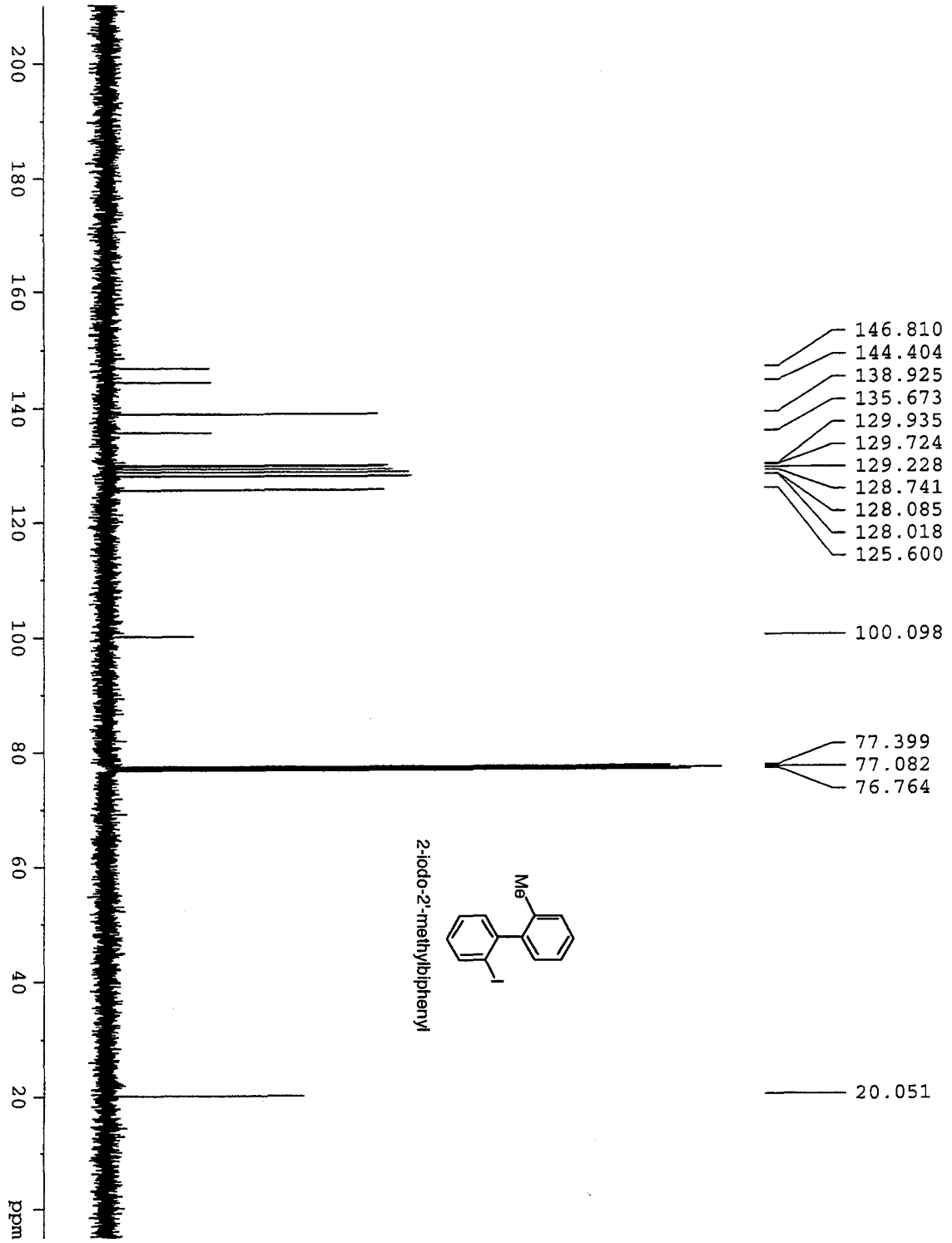

8.003
8.001
7.984
7.981
7.543
7.523
7.463
7.459
7.444
7.440
7.395
7.392
7.376
7.374
7.354
7.283
7.281
7.266
7.263
7.245
7.243
7.233
7.220
7.162
7.159
7.142
7.124
7.122
7.014
7.009
6.994
6.991
6.976
6.971
3.839
0.957
0.980
1.035
2.017
2.005
1.002
1.000
2.952
0.000
ppm
3-(2-iodophenyl)-1-methylindole
Me
I

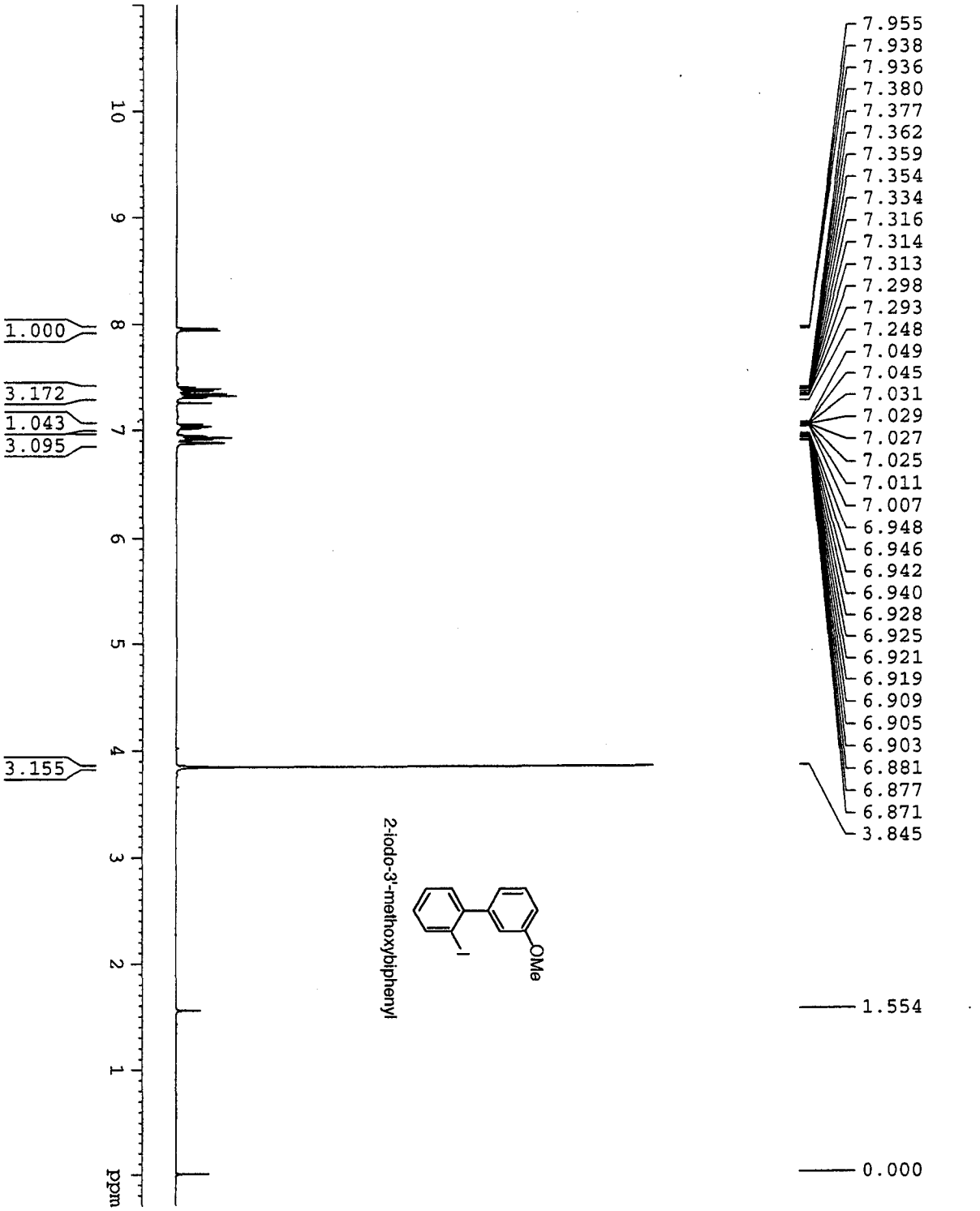

3-(2-iodophenyl)-1-methylindole
Me
I
140.101
139.889
136.556
131.520
128.361
128.166
128.065
127.040
121.973
120.327
119.728
118.491
109.523
100.757
77.438
77.120
76.803
33.064
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

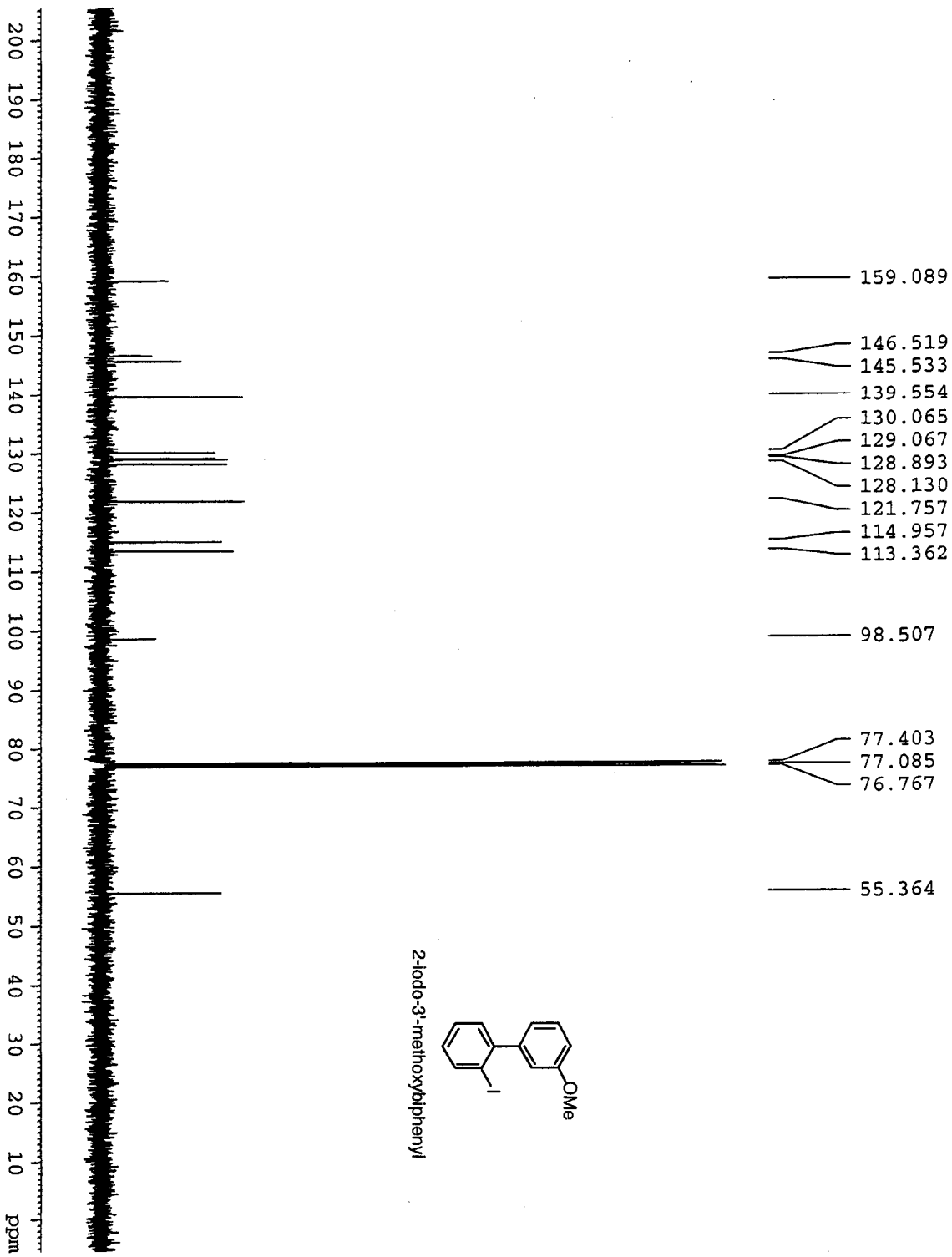

7.945
7.941
7.918
7.915
7.357
7.354
7.333
7.329
7.292
7.285
7.266
7.260
7.236
7.024
7.019
6.999
6.994
6.993
6.974
6.968
6.948
0.984
1.072
1.046
4.060
6.463
2.365
1.526
0.000
2-iodo-3',5'-dimethylbiphenyl
Me
Me
I
ppm

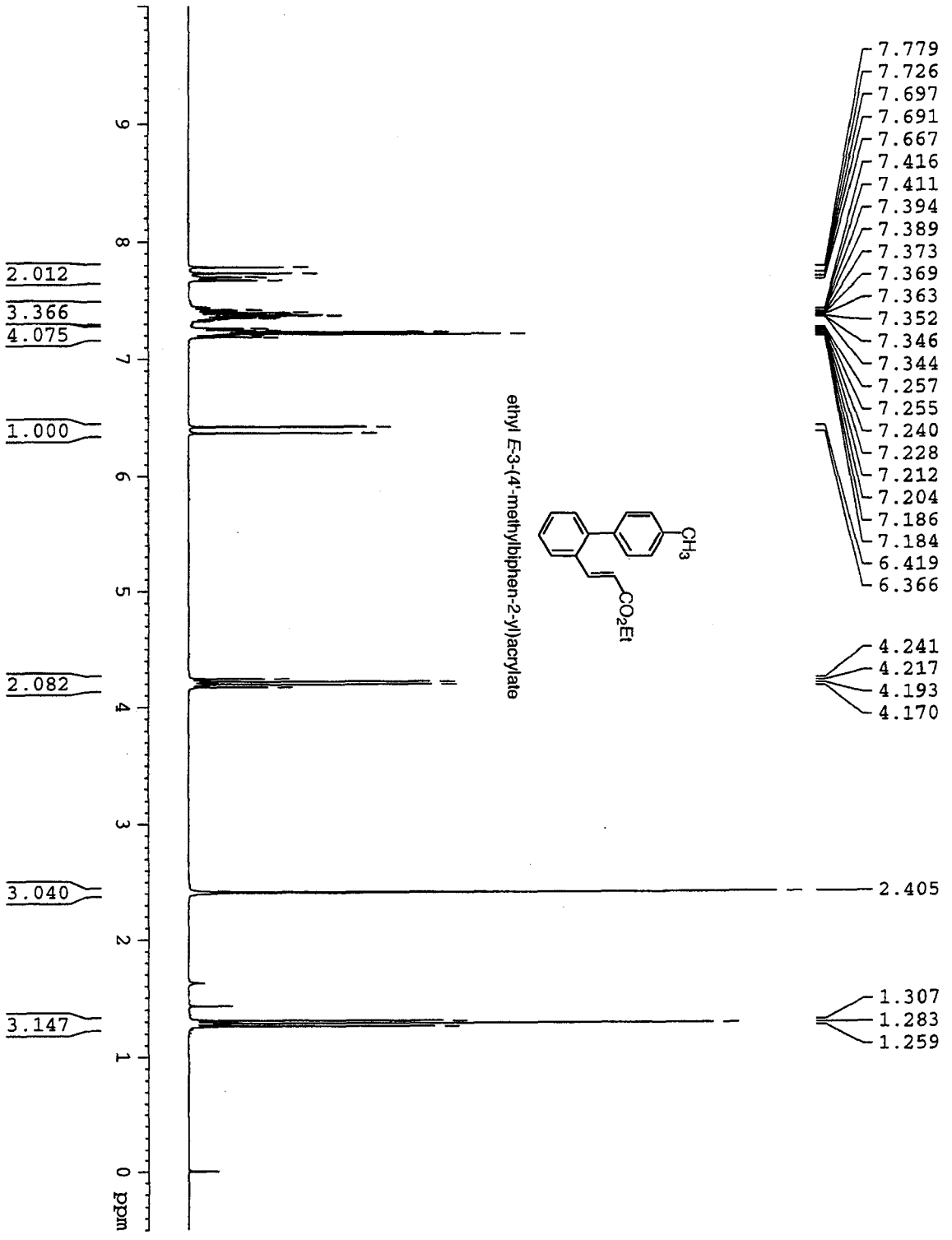

147.103
144.337
139.653
137.642
130.268
129.426
128.817
128.254
127.306
98.904
77.697
77.274
76.850
21.605
2-iodo-3',5'-dimethylbiphenyl
Me
Me
I
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

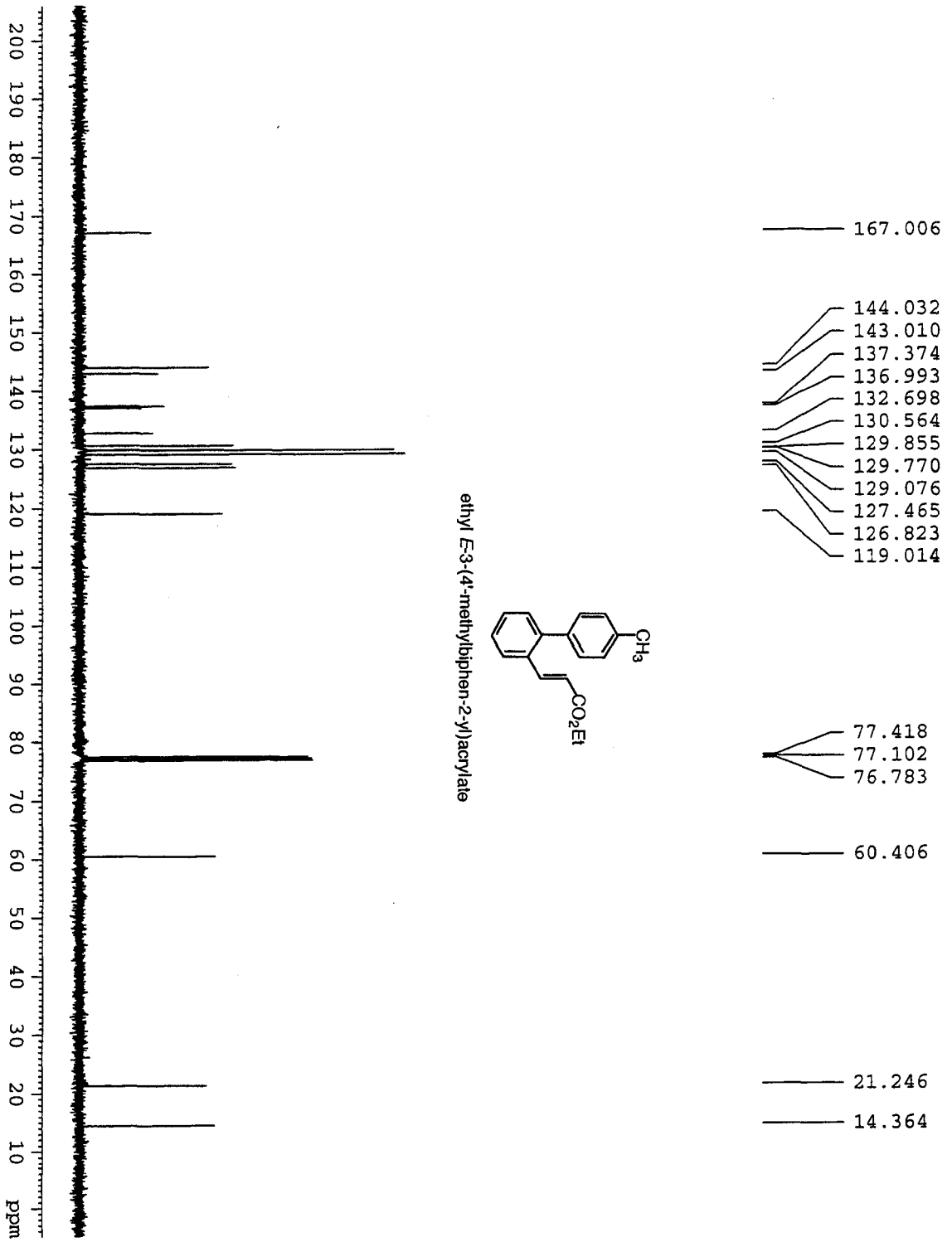

7.939
7.920
7.401
7.382
7.364
7.310
7.292
7.272
7.262
7.257
7.240
7.219
7.215
7.199
7.196
7.073
7.055
7.036
7.032
7.013
1.000
1.065
4.268
2.055
3.185
2.073
0.000
2-iodo-2'-methylbiphenyl
Me
I
ppm

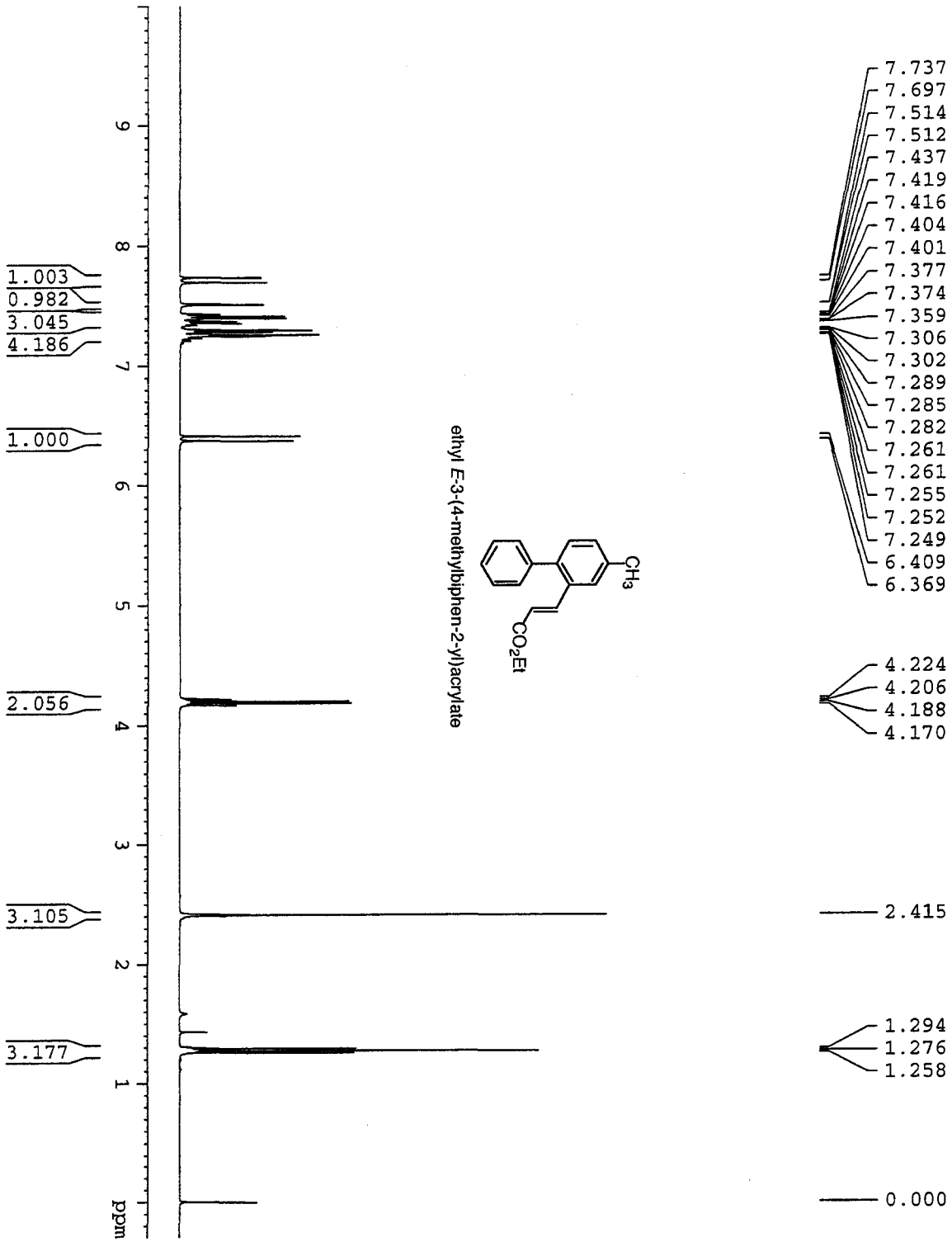

200
180
160
140
120
100
80
60
40
20
ppm
146.810
144.404
138.925
135.673
129.935
129.724
129.228
128.741
128.085
128.018
125.600
100.098
77.399
77.082
76.764
20.051
2-iodo-2'-methylbiphenyl
Me
I

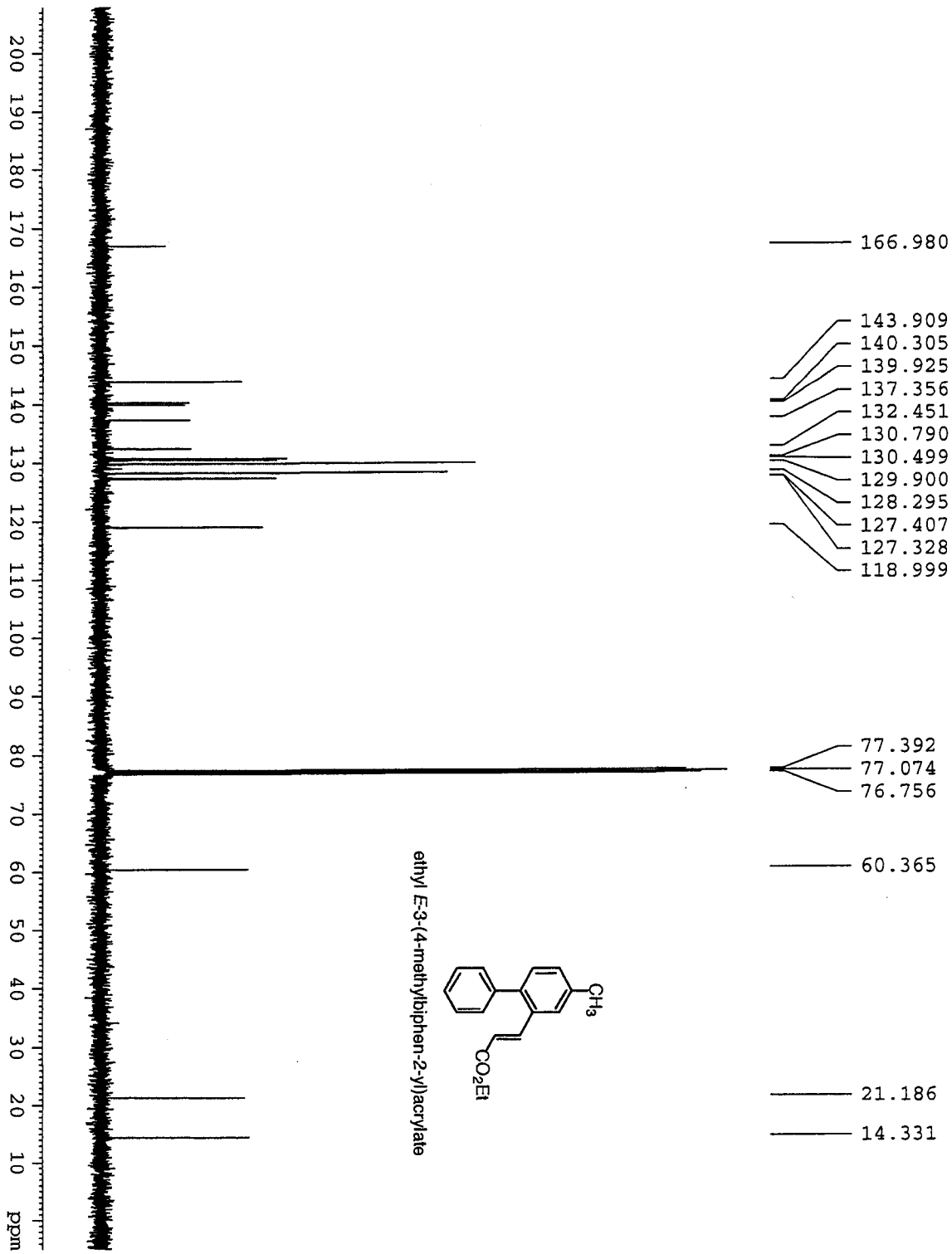

7.955
7.938
7.936
7.380
7.377
7.362
7.359
7.354
7.334
7.316
7.314
7.313
7.298
7.293
7.248
7.049
7.045
7.031
7.029
7.027
7.025
7.011
7.007
6.948
6.946
6.942
6.940
6.928
6.925
6.921
6.919
6.909
6.905
6.903
6.881
6.877
6.871
3.845
1.554
0.000
1.000
3.172
1.043
3.095
3.155
2-iodo-3'-methoxybiphenyl
I
OMe
ppm

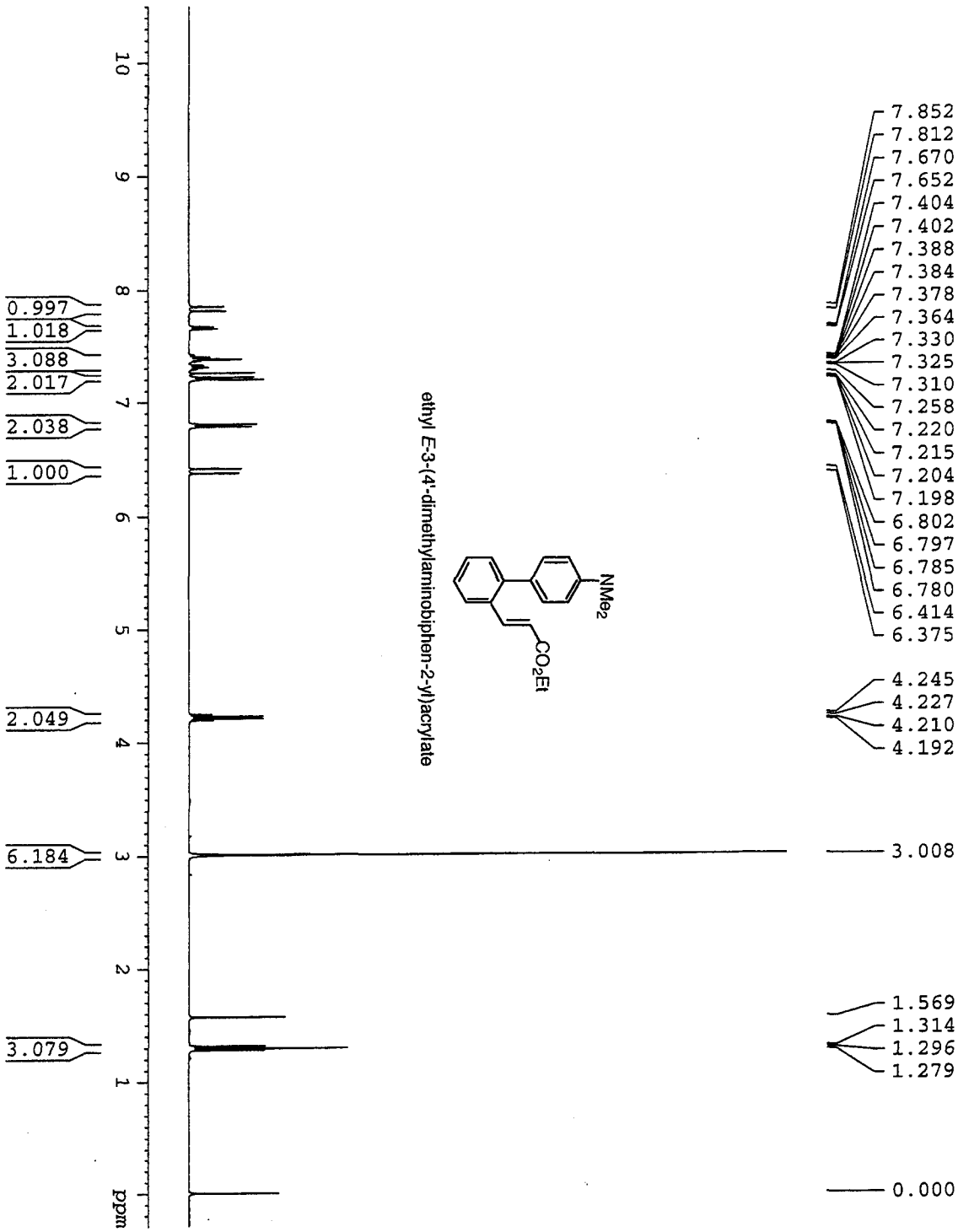

159.089
146.519
145.533
139.554
130.065
129.067
128.893
128.130
121.757
114.957
113.362
98.507
77.403
77.085
76.767
55.364
2-iodo-3'-methoxybiphenyl
I
OMe
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

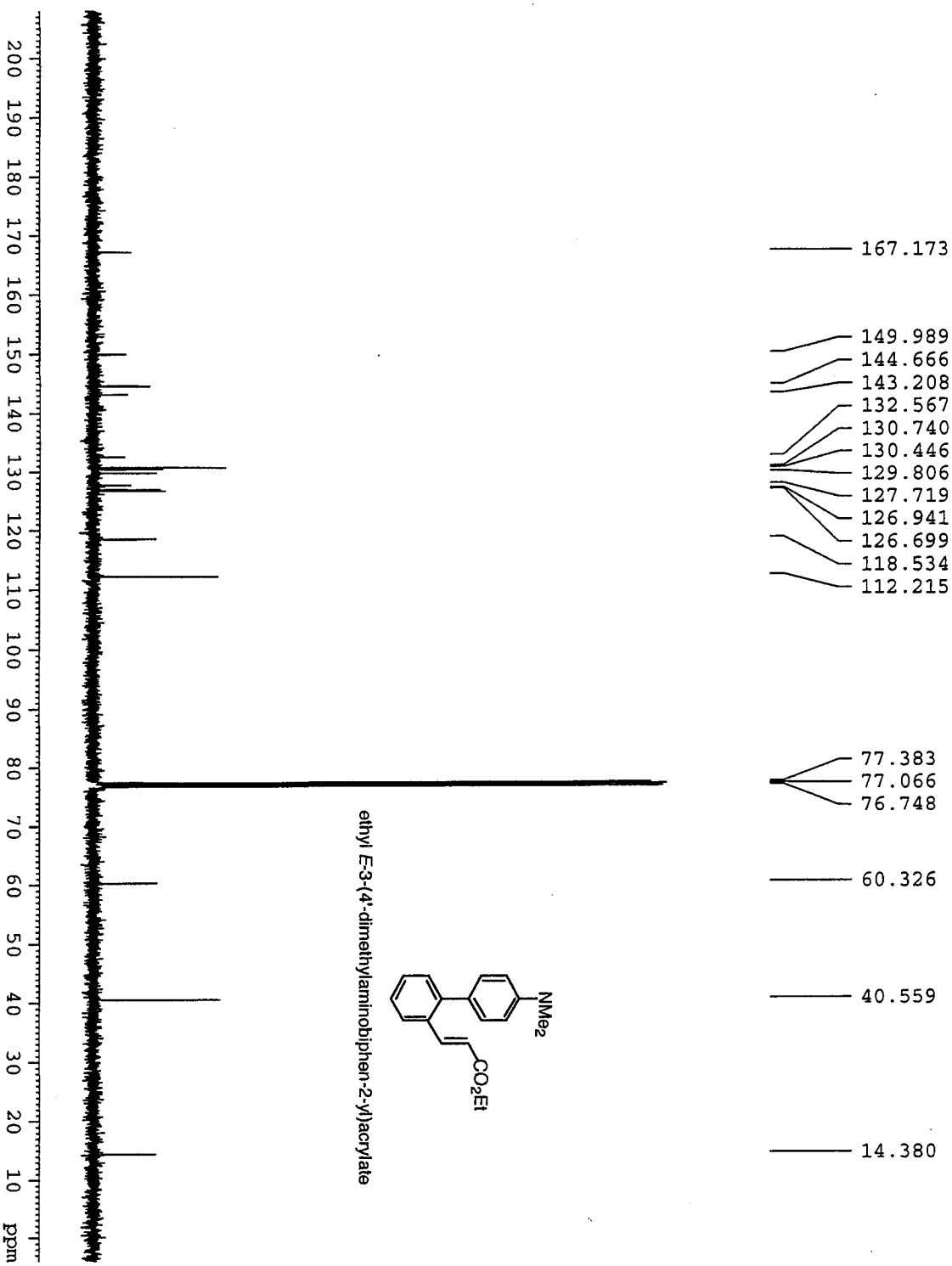

ethyl E-3-(4'-methylbiphen-2-yl)acrylate
CH3
CO2Et
7.779
7.726
7.697
7.691
7.667
7.416
7.411
7.394
7.389
7.373
7.369
7.363
7.352
7.346
7.344
7.257
7.255
7.240
7.228
7.212
7.204
7.186
7.184
6.419
6.366
4.241
4.217
4.193
4.170
2.405
1.307
1.283
1.259
2.012
3.366
4.075
1.000
2.082
3.040
3.147
ppm

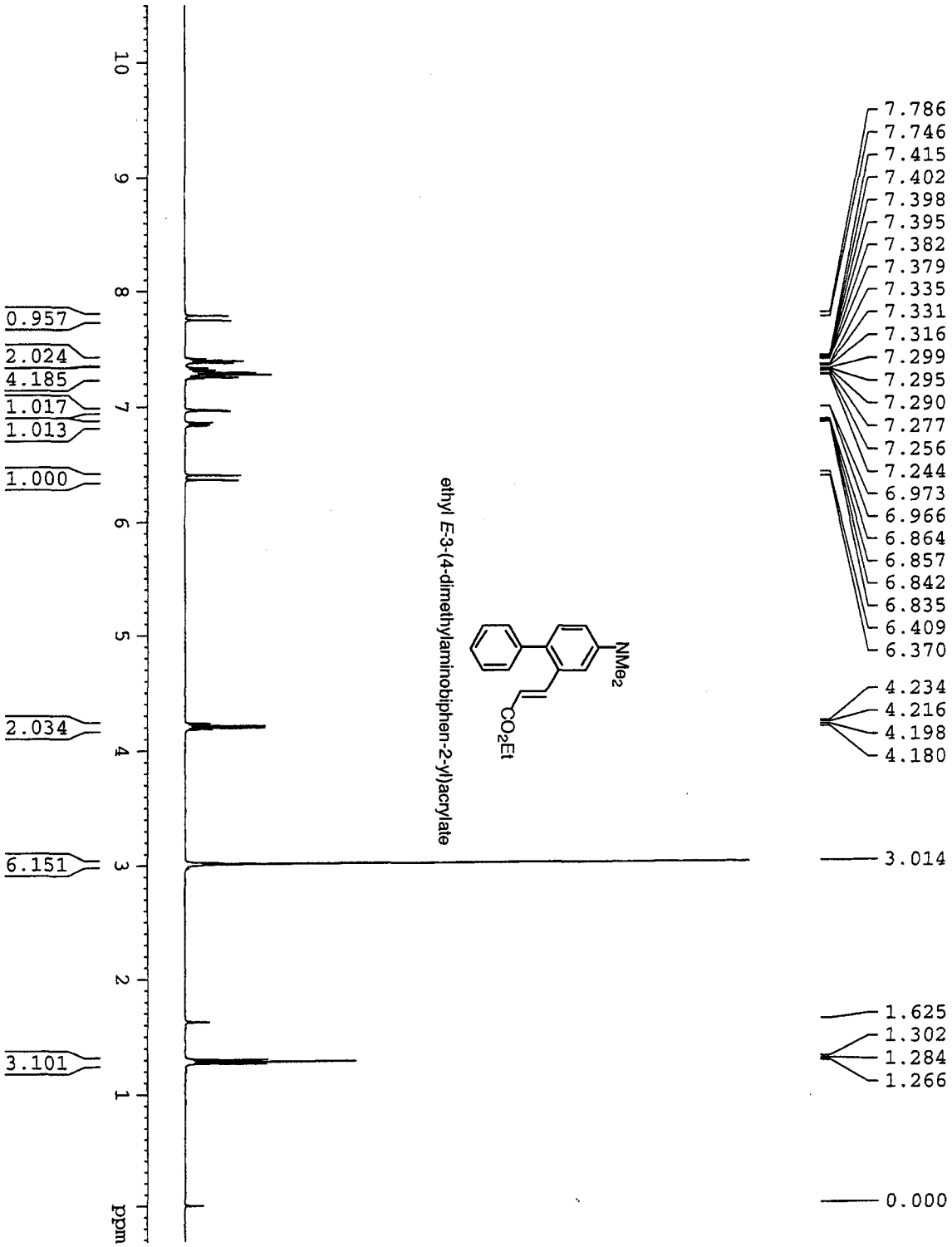

167.006
144.032
143.010
137.374
136.993
132.698
130.564
129.855
129.770
129.076
127.465
126.823
119.014
77.418
77.102
76.783
60.406
21.246
14.364
ethyl E-3-(4'-methylbiphen-2-yl)acrylate
CH3
CO2Et
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

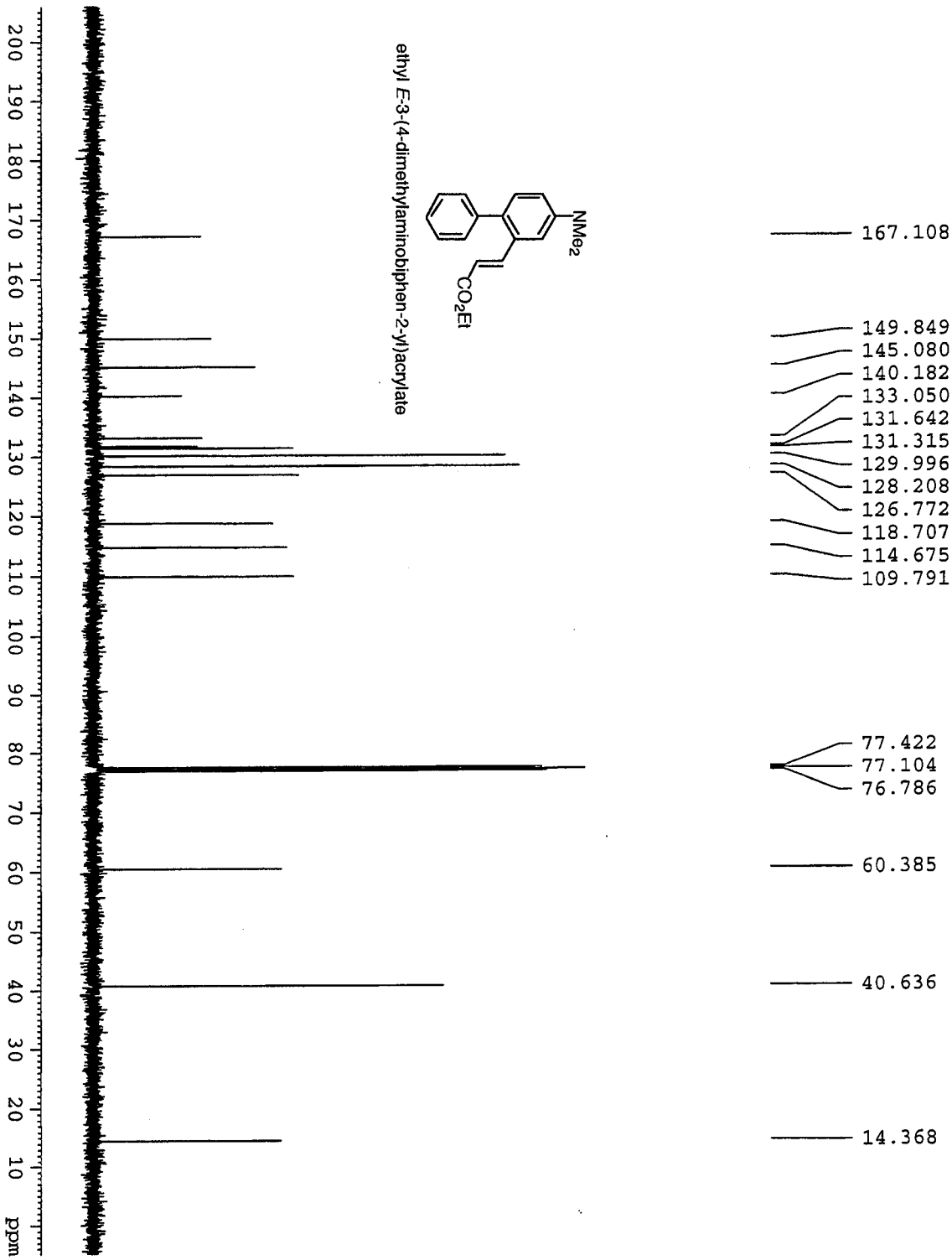

7.737
7.697
7.514
7.512
7.437
7.419
7.416
7.404
7.401
7.377
7.374
7.359
7.306
7.302
7.289
7.285
7.282
7.261
7.261
7.255
7.252
7.249
6.409
6.369
4.224
4.206
4.188
4.170
2.415
1.294
1.276
1.258
0.000
1.003
0.982
3.045
4.186
1.000
2.056
3.105
3.177
ppm
ethyl E-3-(4-methylbiphen-2-yl)acrylate
CH3
CO2Et

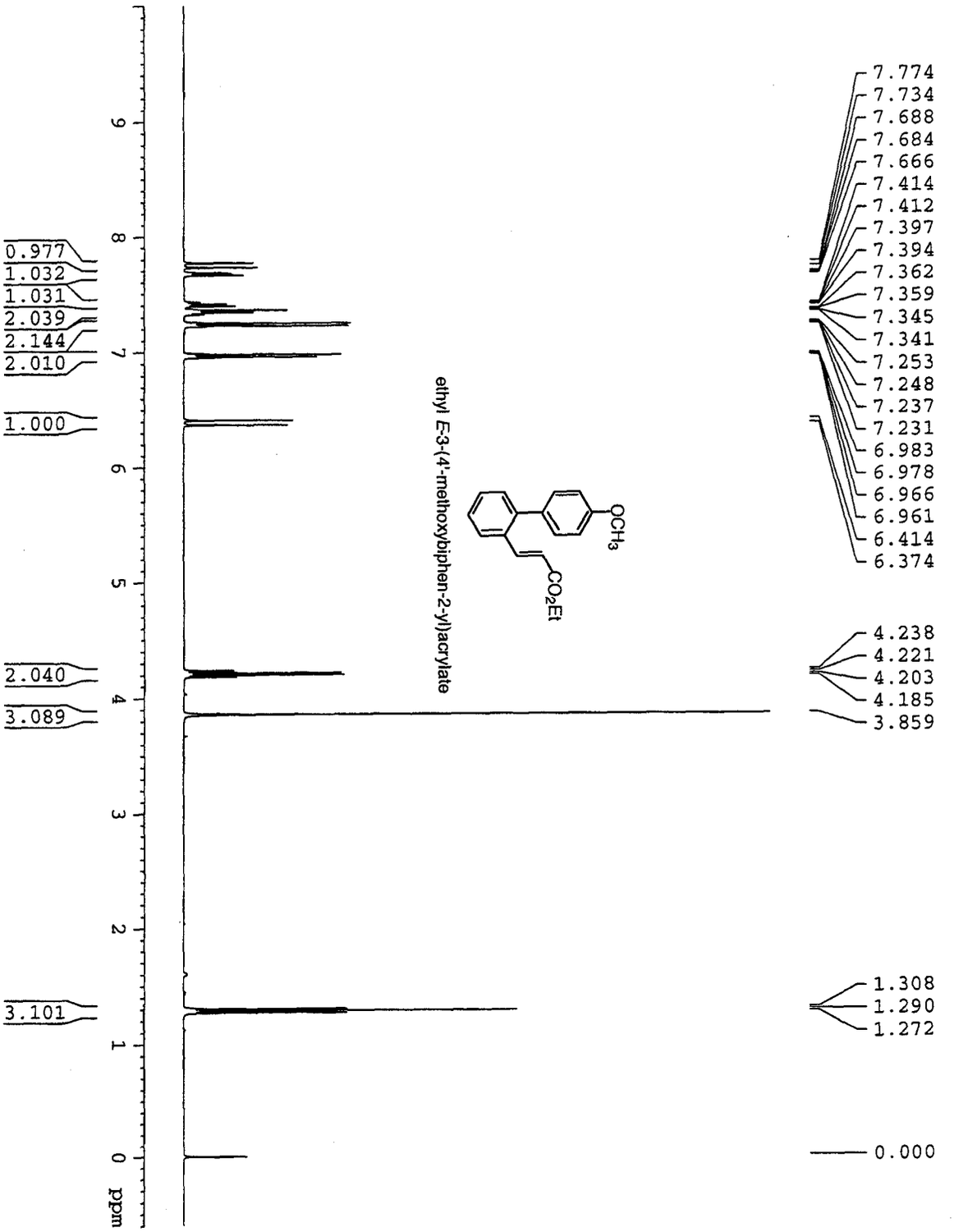

166.980
143.909
140.305
139.925
137.356
132.451
130.790
130.499
129.900
128.295
127.407
127.328
118.999
77.392
77.074
76.756
60.365
21.186
14.331
ethyl E-3-(4-methylbiphen-2-yl)acrylate
CH3
CO2Et
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

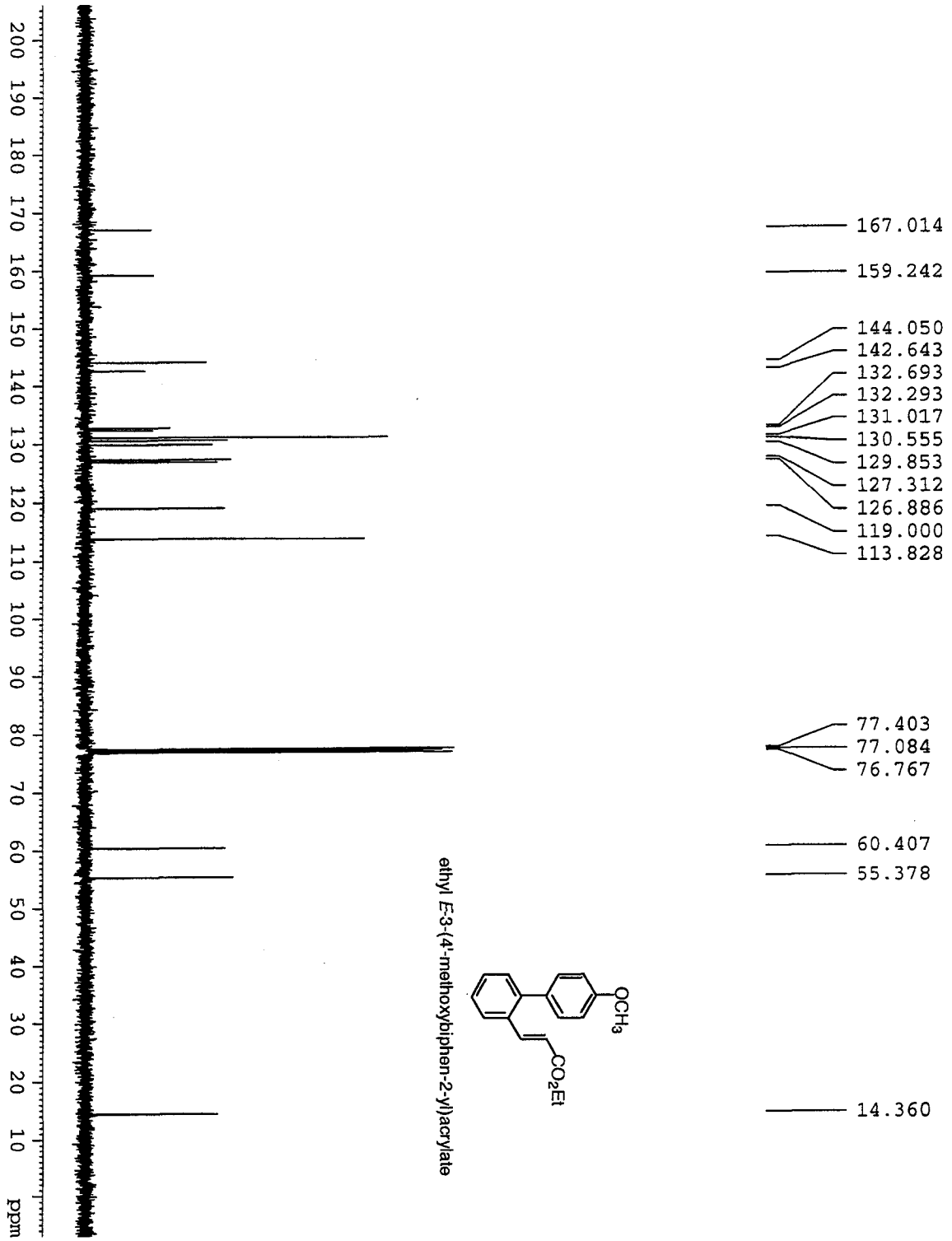

ethyl E-3-(4'-dimethylaminobiphen-2-yl)acrylate
NMe2
CO2Et
7.852
7.812
7.670
7.652
7.404
7.402
7.388
7.384
7.378
7.364
7.330
7.325
7.310
7.258
7.220
7.215
7.204
7.198
6.802
6.797
6.785
6.780
6.414
6.375
4.245
4.227
4.210
4.192
3.008
1.569
1.314
1.296
1.279
0.000
0.997
1.018
3.088
2.017
2.038
1.000
2.049
6.184
3.079
ppm

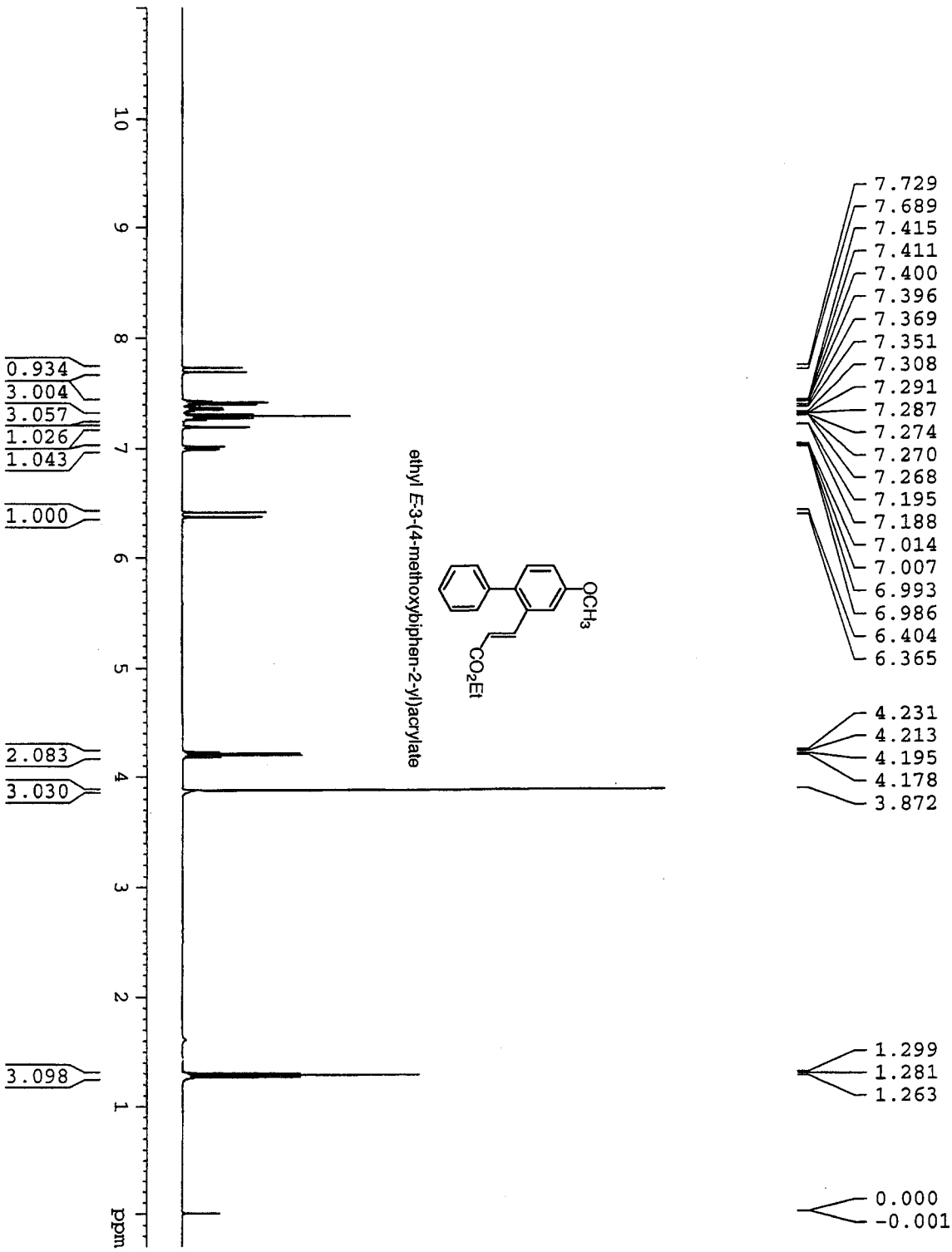

167.173
149.989
144.666
143.208
132.567
130.740
130.446
129.806
127.719
126.941
126.699
118.534
112.215
77.383
77.066
76.748
60.326
40.559
14.380
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
ethyl E-3-(4'-dimethylaminobiphen-2-yl)acrylate
NMe2
CO2Et

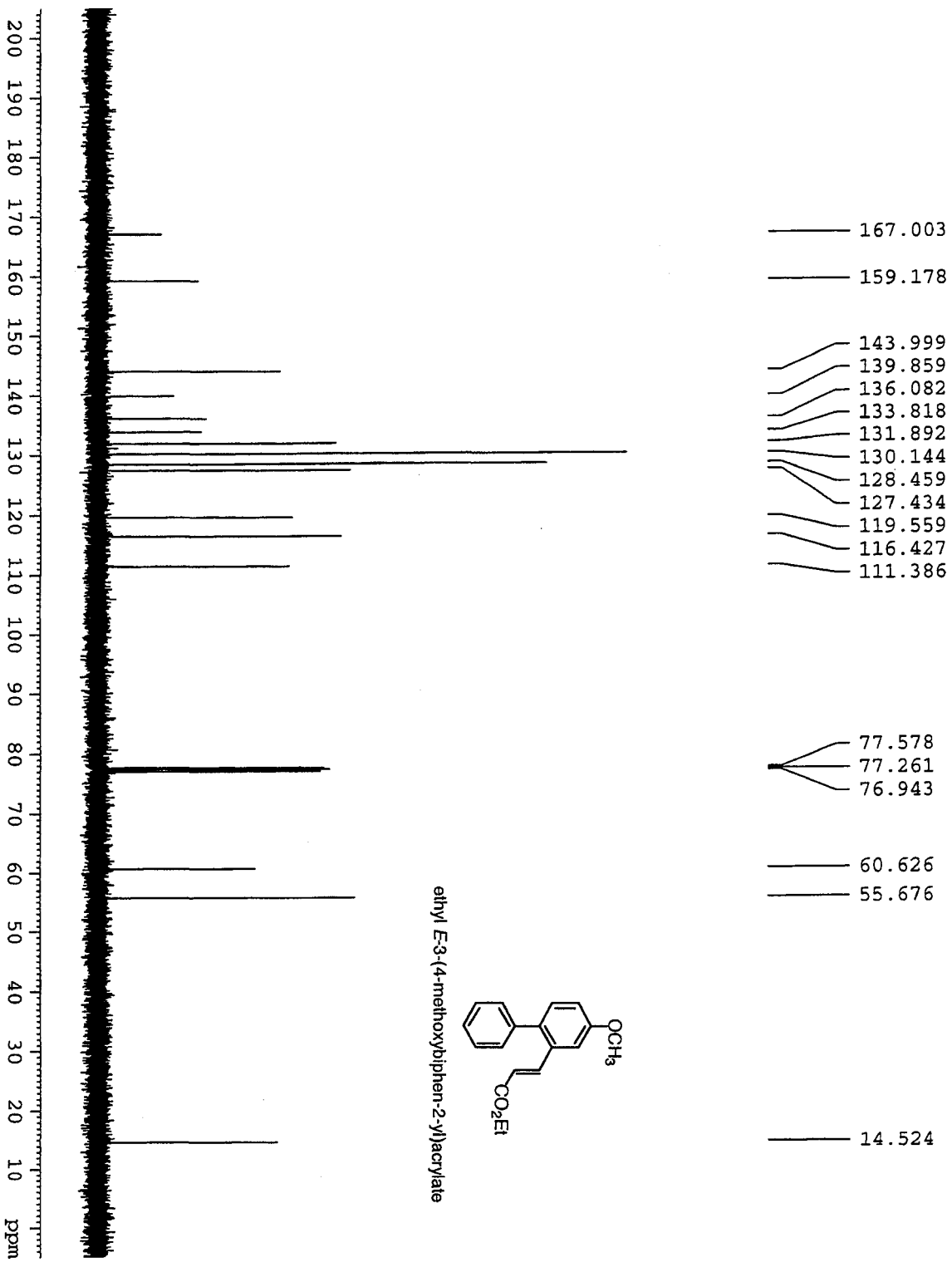

ethyl E-3-(4-dimethylaminobiphen-2-yl)acrylate
NMe2
CO2Et
0.957
2.024
4.185
1.017
1.013
1.000
2.034
6.151
3.101
7.786
7.746
7.415
7.402
7.398
7.395
7.382
7.379
7.335
7.331
7.316
7.299
7.295
7.290
7.277
7.256
7.244
6.973
6.966
6.864
6.857
6.842
6.835
6.409
6.370
4.234
4.216
4.198
4.180
3.014
1.625
1.302
1.284
1.266
0.000
ppm

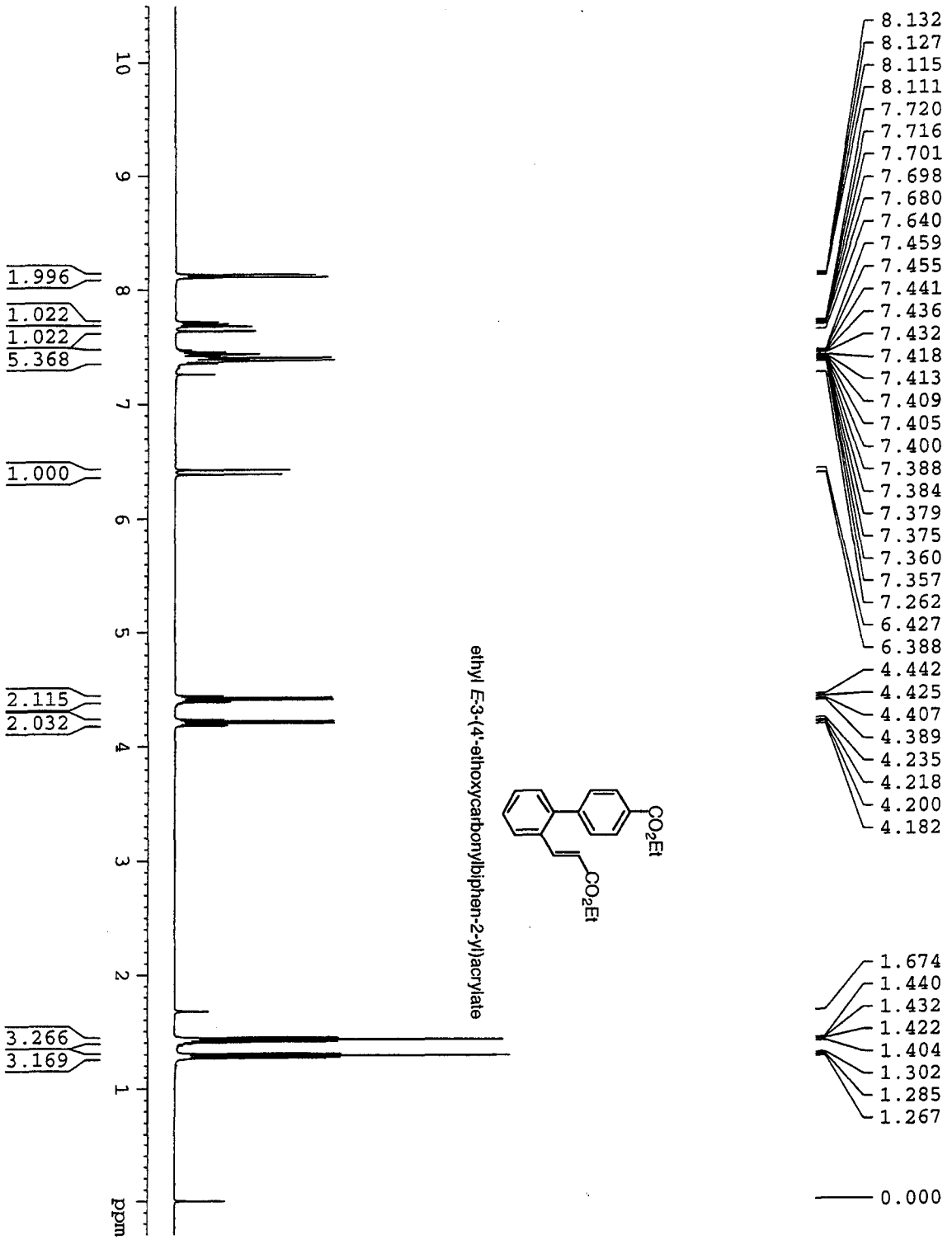

ethyl E-3-(4-dimethylaminobiphen-2-yl)acrylate
NMe2
CO2Et
167.108
149.849
145.080
140.182
133.050
131.642
131.315
129.996
128.208
126.772
118.707
114.675
109.791
77.422
77.104
76.786
60.385
40.636
14.368
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

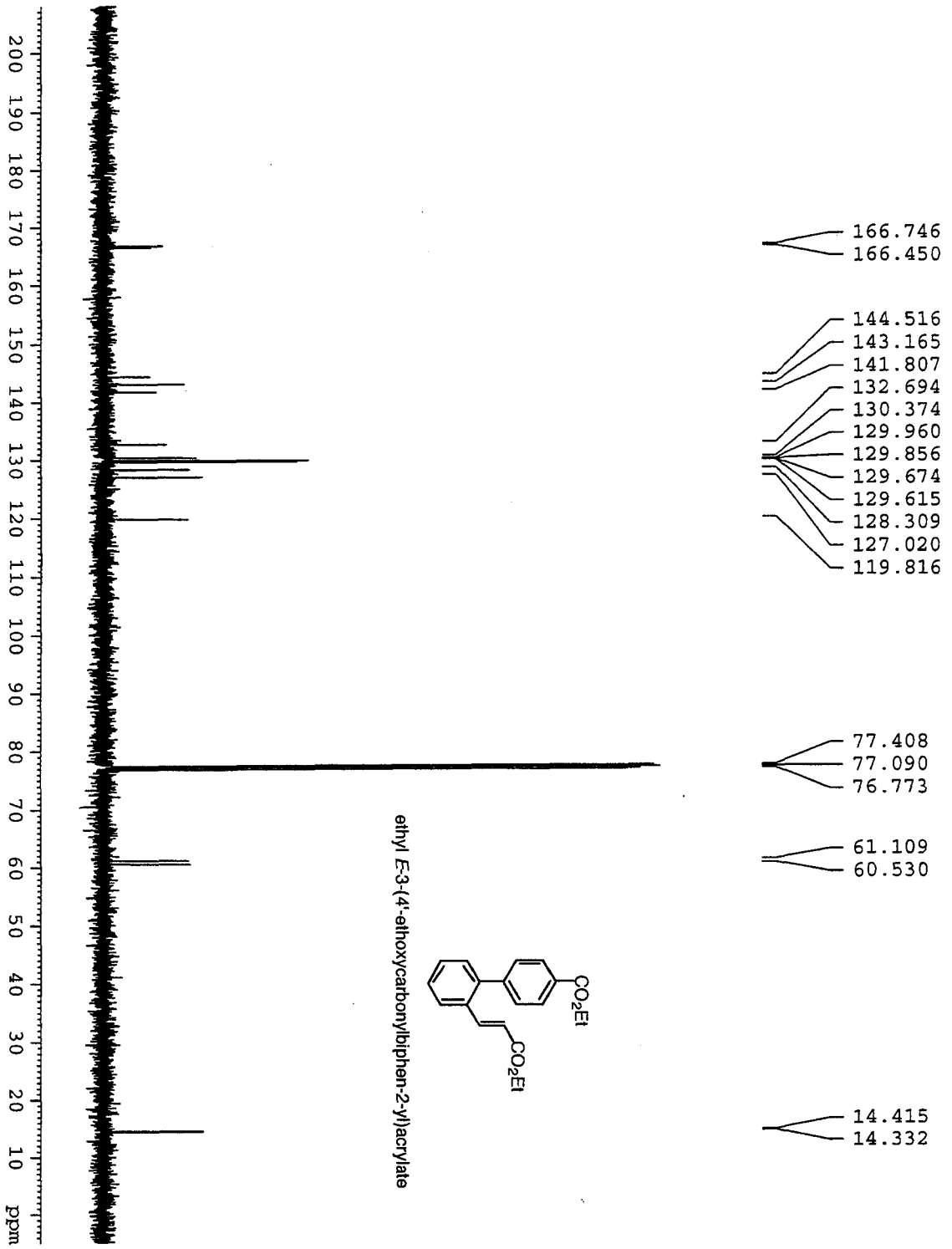

ethyl E-3-(4'-methoxybiphen-2-yl)acrylate
OCH3
CO2Et
0.977
1.032
1.031
2.039
2.144
2.010
1.000
2.040
3.089
3.101
7.774
7.734
7.688
7.684
7.666
7.414
7.412
7.397
7.394
7.362
7.359
7.345
7.341
7.253
7.248
7.237
7.231
6.983
6.978
6.966
6.961
6.414
6.374
4.238
4.221
4.203
4.185
3.859
1.308
1.290
1.272
0.000
ppm

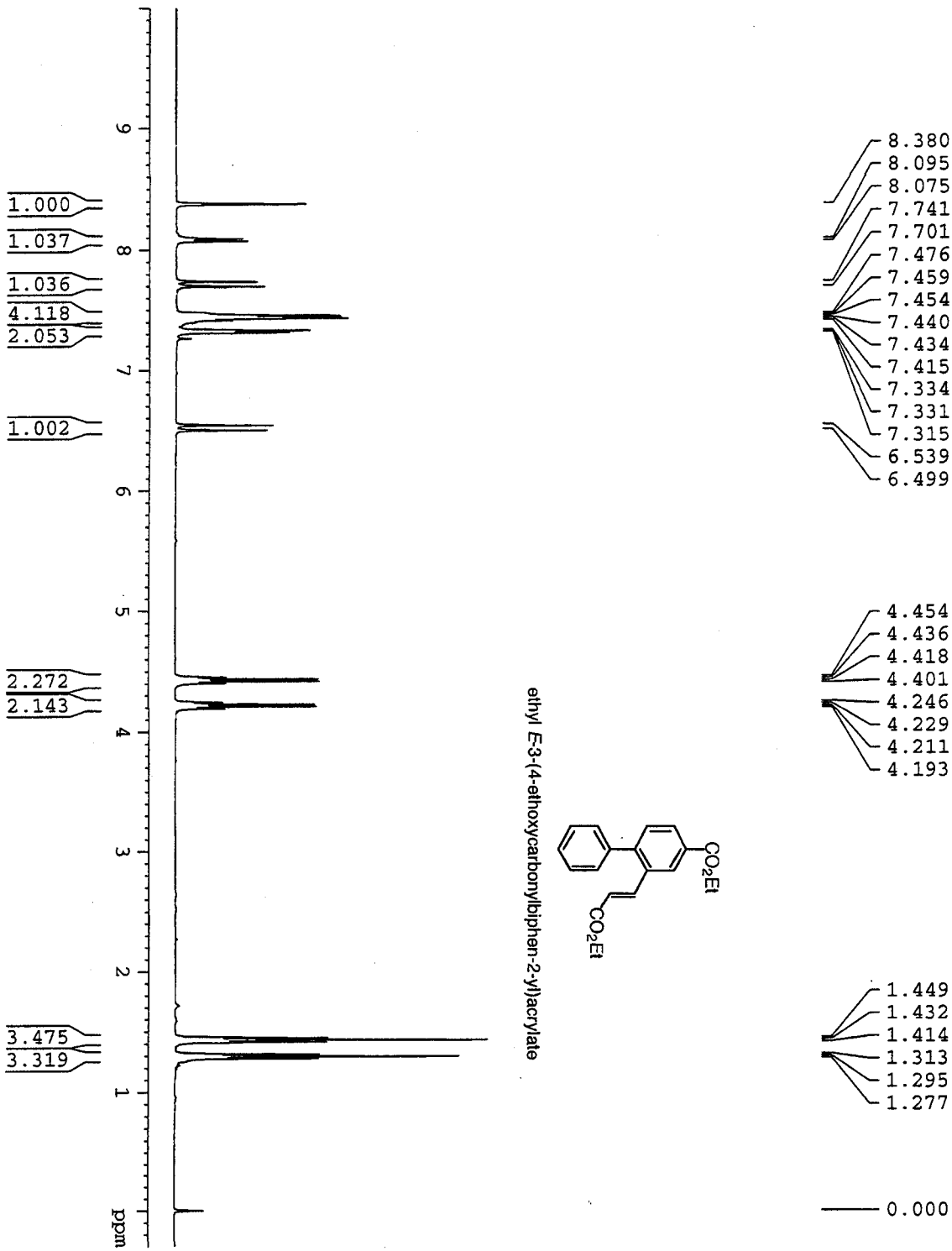

167.014
159.242
144.050
142.643
132.693
132.293
131.017
130.555
129.853
127.312
126.886
119.000
113.828
77.403
77.084
76.767
60.407
55.378
14.360
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
ethyl E-3-(4'-methoxybiphen-2-yl)acrylate
OCH3
CO2Et

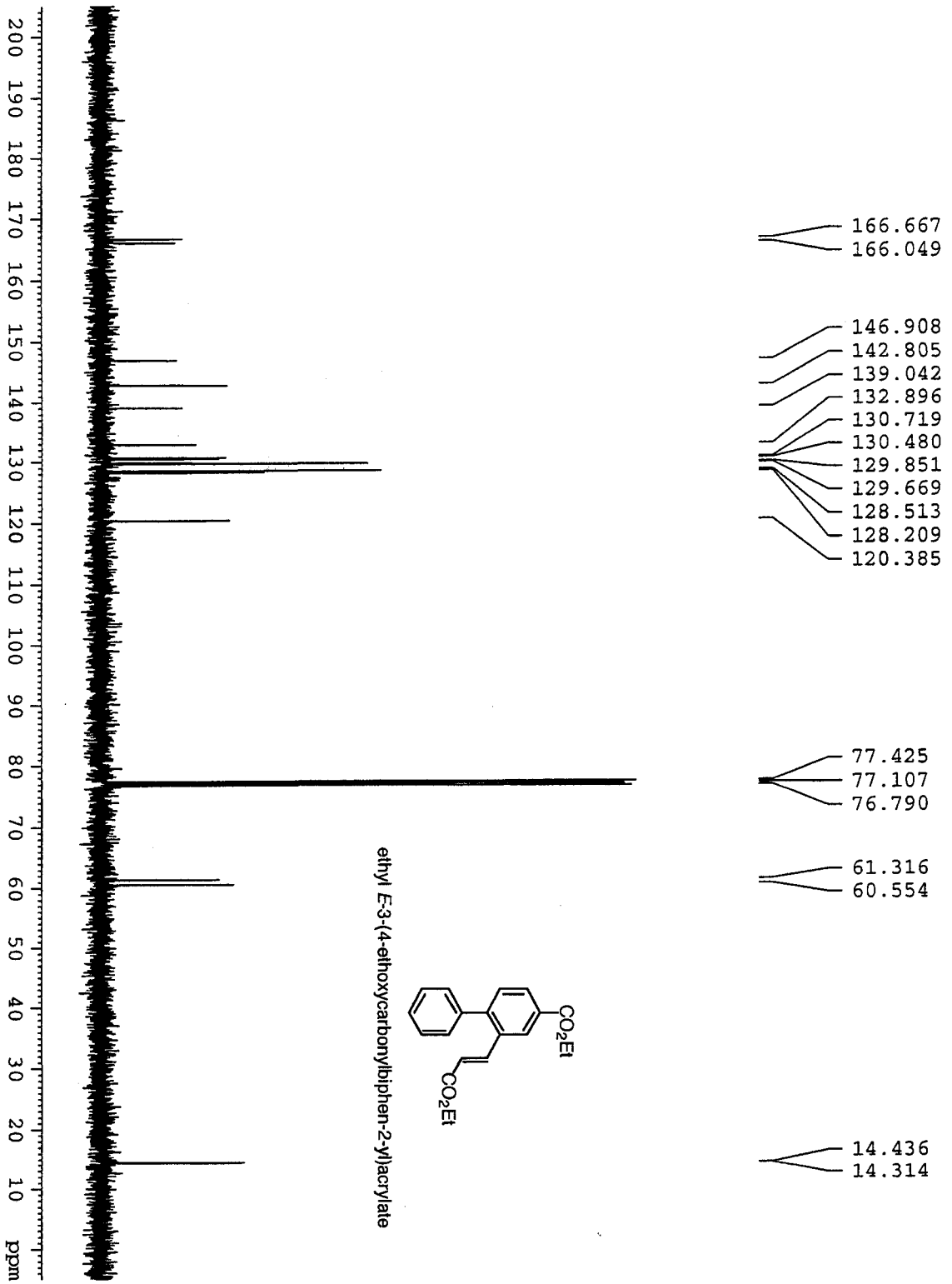

ethyl E-3-(4-methoxybiphen-2-yl)acrylate
OCH3
CO2Et
0.934
3.004
3.057
1.026
1.043
1.000
2.083
3.030
3.098
7.729
7.689
7.415
7.411
7.400
7.396
7.369
7.351
7.308
7.291
7.287
7.274
7.270
7.268
7.195
7.188
7.014
7.007
6.993
6.986
6.404
6.365
4.231
4.213
4.195
4.178
3.872
1.299
1.281
1.263
0.000
-0.001
ppm

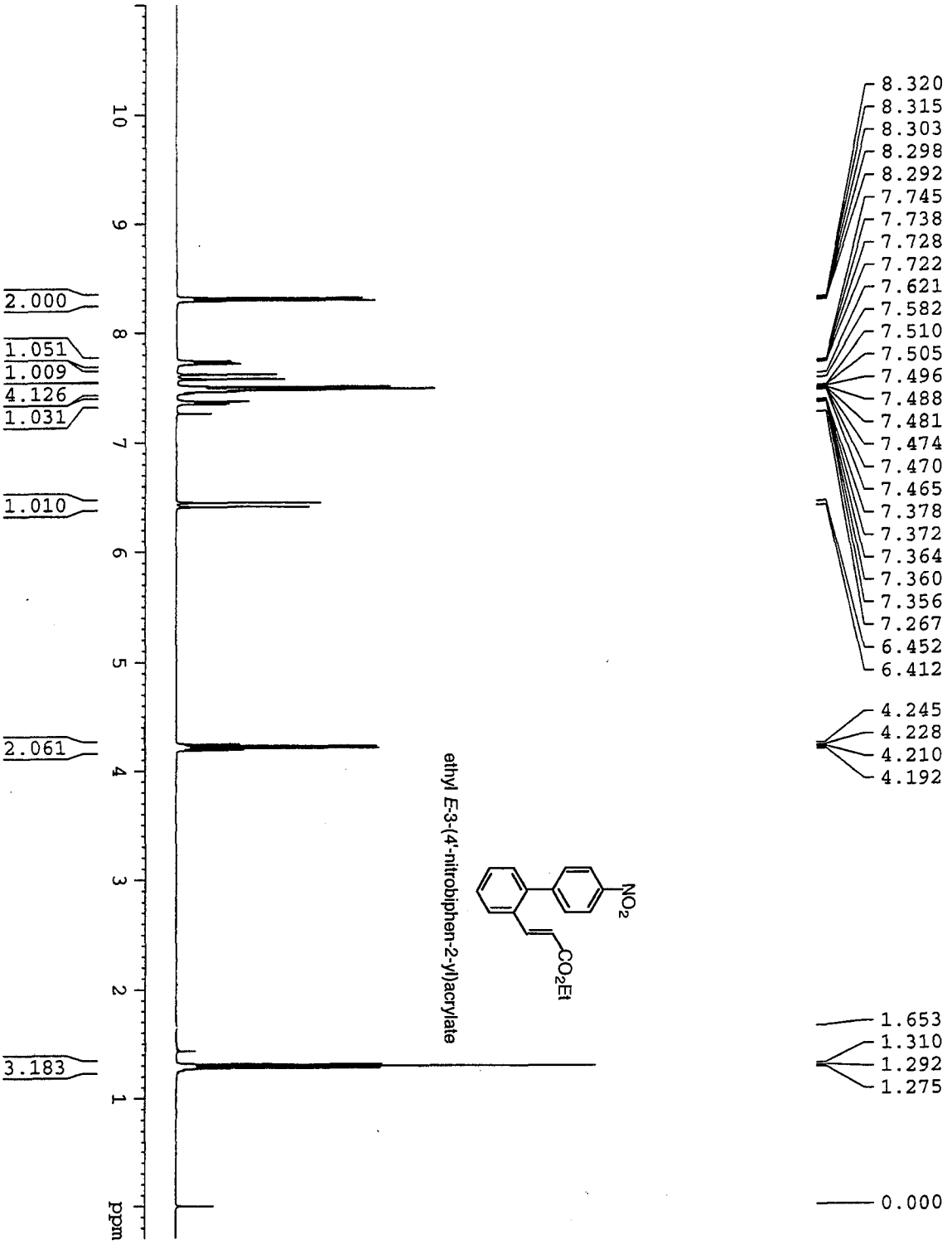

167.003
159.178
143.999
139.859
136.082
133.818
131.892
130.144
128.459
127.434
119.559
116.427
111.386
77.578
77.261
76.943
60.626
55.676
14.524
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
ethyl E-3-(4-methoxybiphen-2-yl)acrylate
OCH3
CO2Et

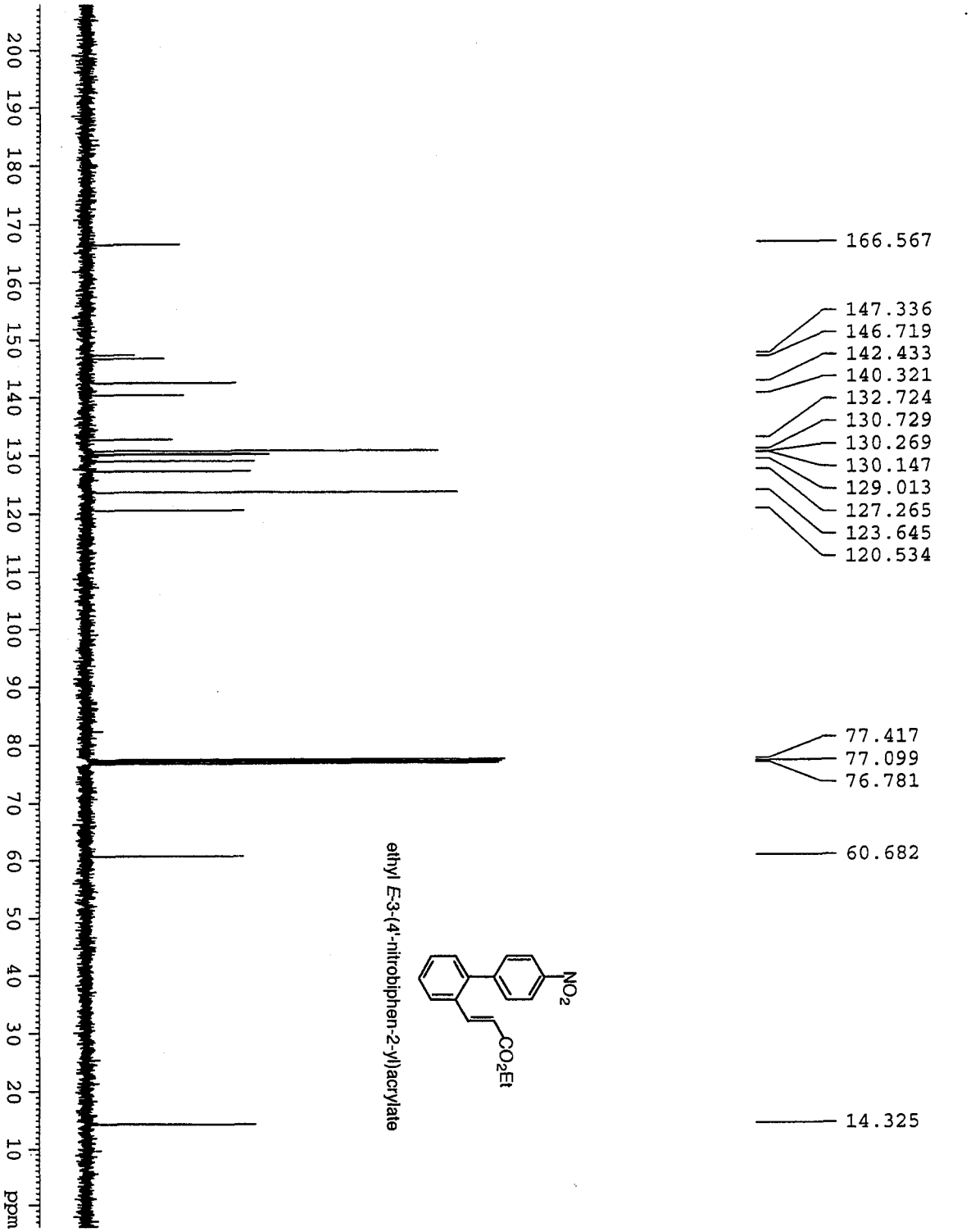

8.132
8.127
8.115
8.111
7.720
7.716
7.701
7.698
7.680
7.640
7.459
7.455
7.441
7.436
7.432
7.418
7.413
7.409
7.405
7.400
7.388
7.384
7.379
7.375
7.360
7.357
7.262
6.427
6.388
4.442
4.425
4.407
4.389
4.235
4.218
4.200
4.182
1.674
1.440
1.432
1.422
1.404
1.302
1.285
1.267
0.000
1.996
1.022
1.022
5.368
1.000
2.115
2.032
3.266
3.169
ppm
ethyl E-3-(4'-ethoxycarbonylbiphen-2-yl)acrylate
CO2Et
CO2Et

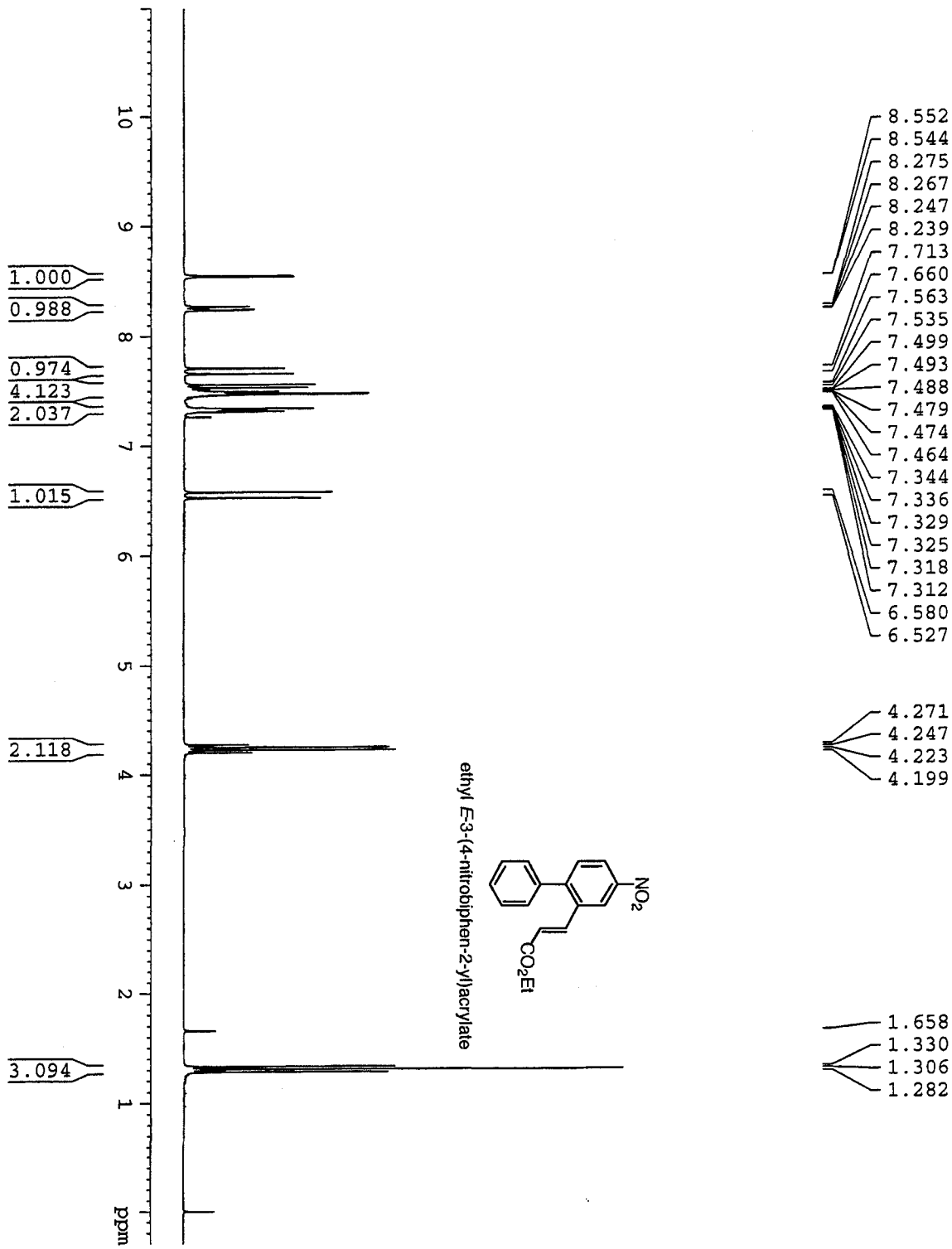

166.746
166.450
144.516
143.165
141.807
132.694
130.374
129.960
129.856
129.674
129.615
128.309
127.020
119.816
77.408
77.090
76.773
61.109
60.530
14.415
14.332
ethyl E-3-(4'-ethoxycarbonylbiphen-2-yl)acrylate
CO2Et
CO2Et
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

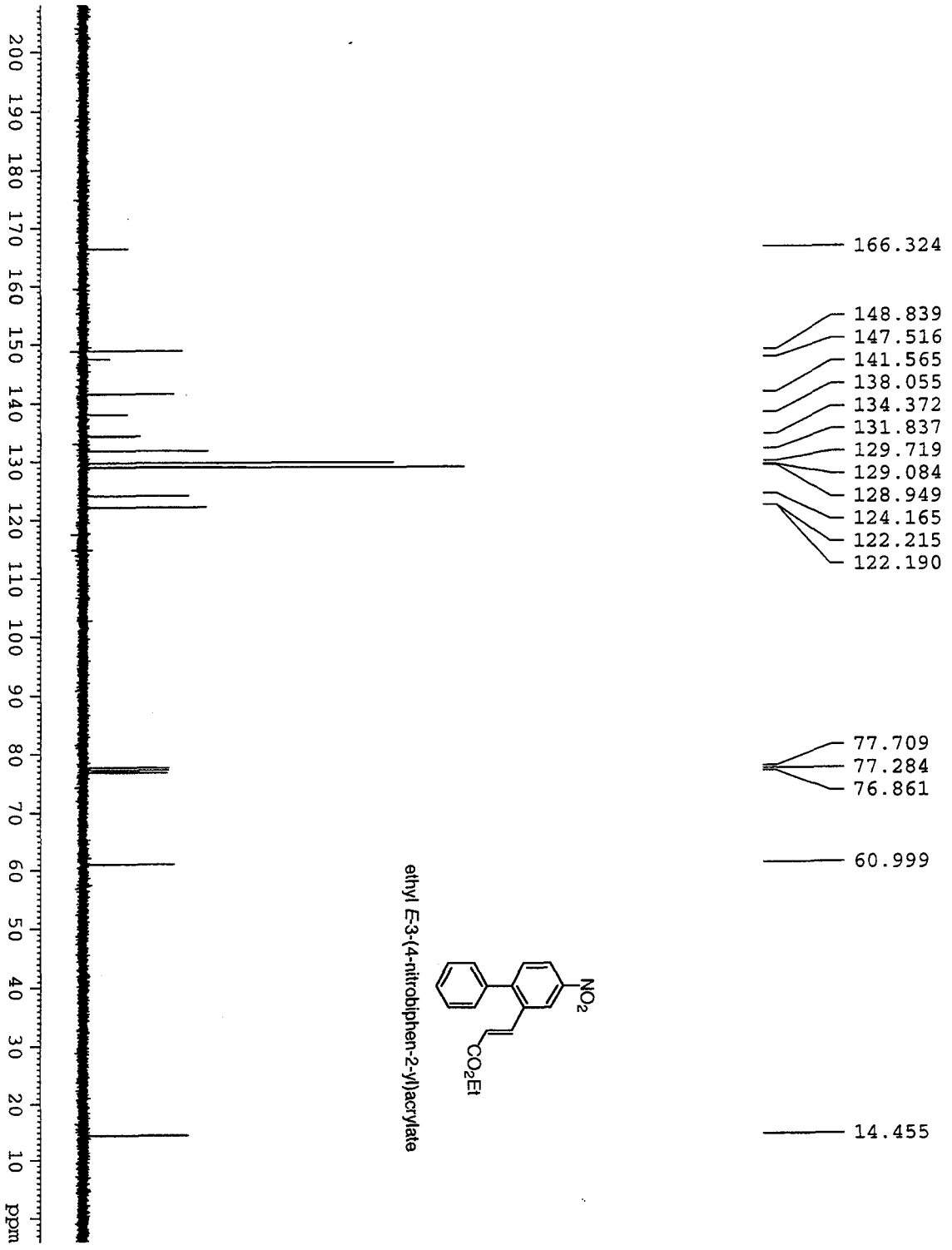

8.380
8.095
8.075
7.741
7.701
7.476
7.459
7.454
7.440
7.434
7.415
7.334
7.331
7.315
6.539
6.499
4.454
4.436
4.418
4.401
4.246
4.229
4.211
4.193
1.449
1.432
1.414
1.313
1.295
1.277
0.000
1.000
1.037
1.036
4.118
2.053
1.002
2.272
2.143
3.475
3.319
ppm
ethyl E-3-(4-ethoxycarbonylbiphen-2-yl)acrylate
CO2Et
CO2Et

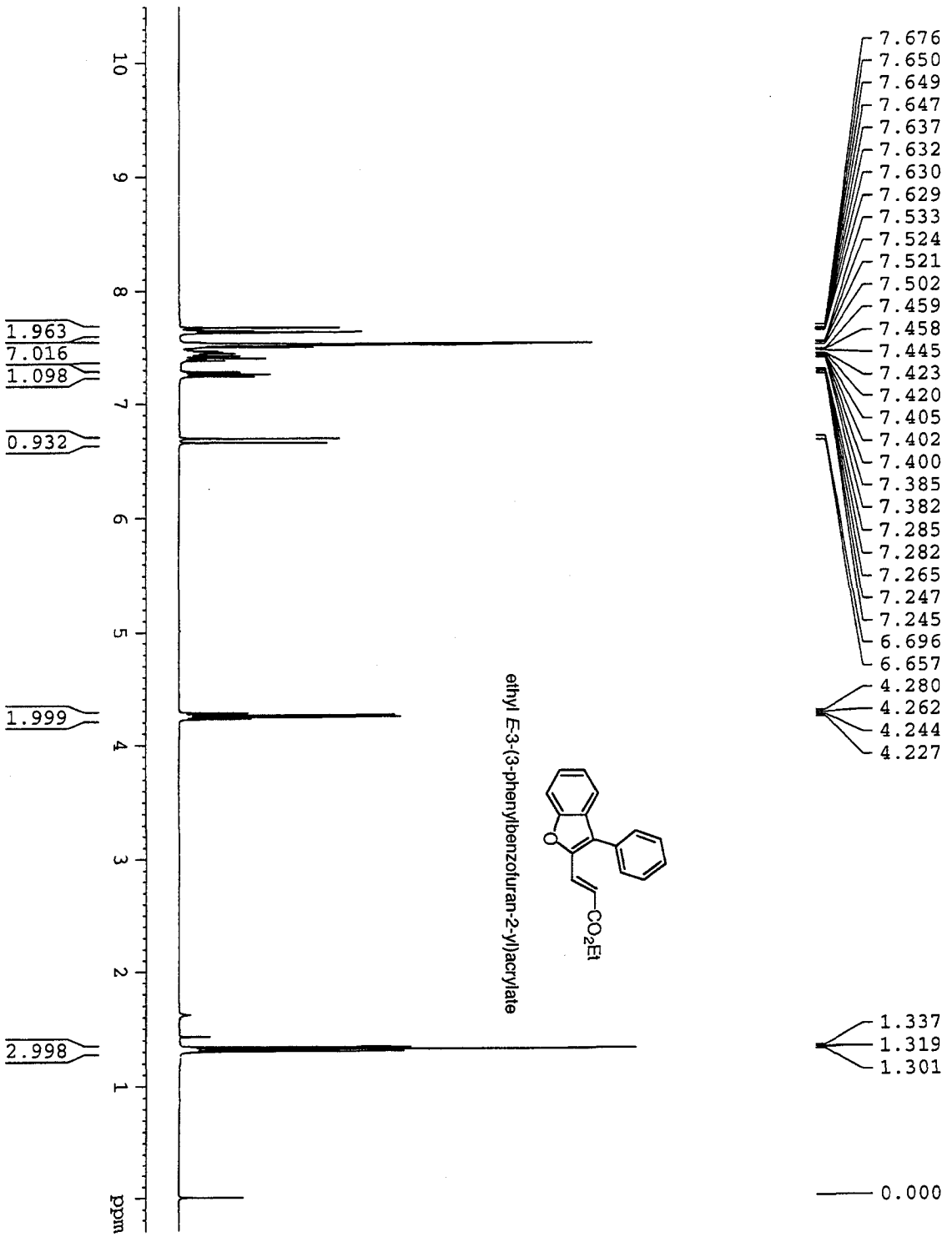

166.667
166.049
146.908
142.805
139.042
132.896
130.719
130.480
129.851
129.669
128.513
128.209
120.385
77.425
77.107
76.790
61.316
60.554
14.436
14.314
CO2Et
CO2Et
ethyl E-3-(4-ethoxycarbonylbiphen-2-yl)acrylate
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

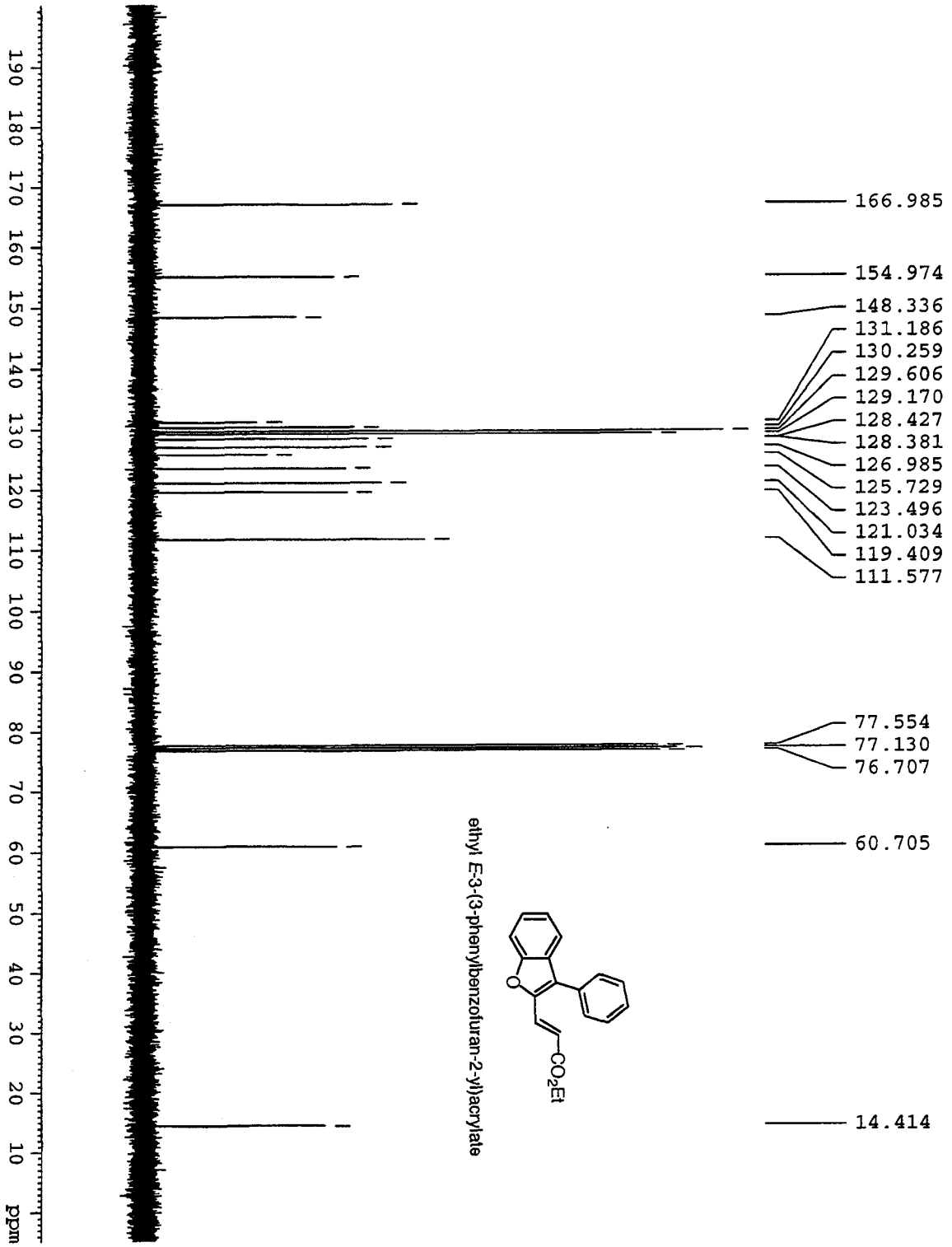

8.320
8.315
8.303
8.298
8.292
7.745
7.738
7.728
7.722
7.621
7.582
7.510
7.505
7.496
7.488
7.481
7.474
7.470
7.465
7.378
7.372
7.364
7.360
7.356
7.267
6.452
6.412
4.245
4.228
4.210
4.192
1.653
1.310
1.292
1.275
0.000
2.000
1.051
1.009
4.126
1.031
1.010
2.061
3.183
ppm
ethyl E-3-(4'-nitrobiphen-2-yl)acrylate
NO2
CO2Et

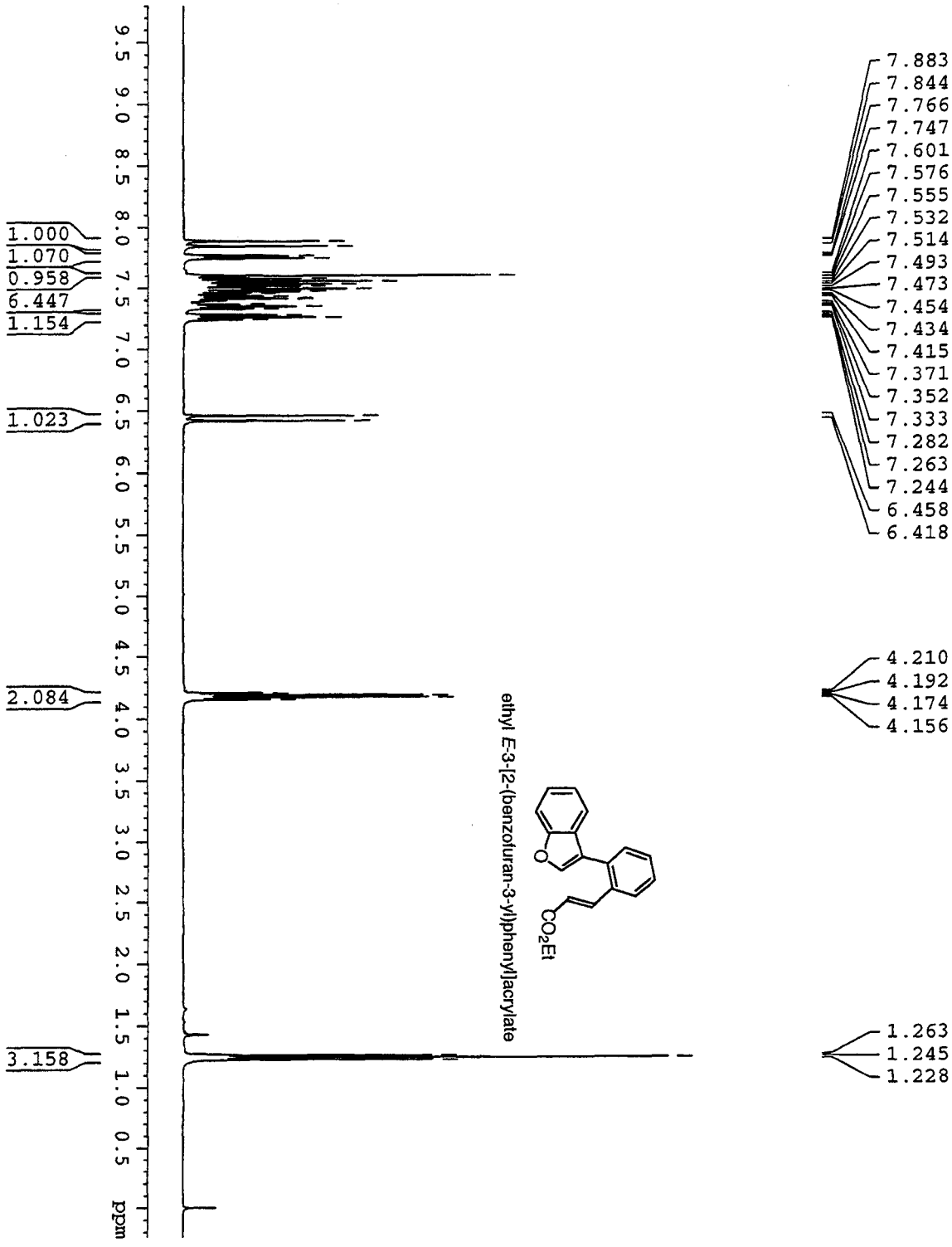

166.567
147.336
146.719
142.433
140.321
132.724
130.729
130.269
130.147
129.013
127.265
123.645
120.534
77.417
77.099
76.781
60.682
14.325
ethyl E-3-(4'-nitrobiphen-2-yl)acrylate
NO2
CO2Et
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

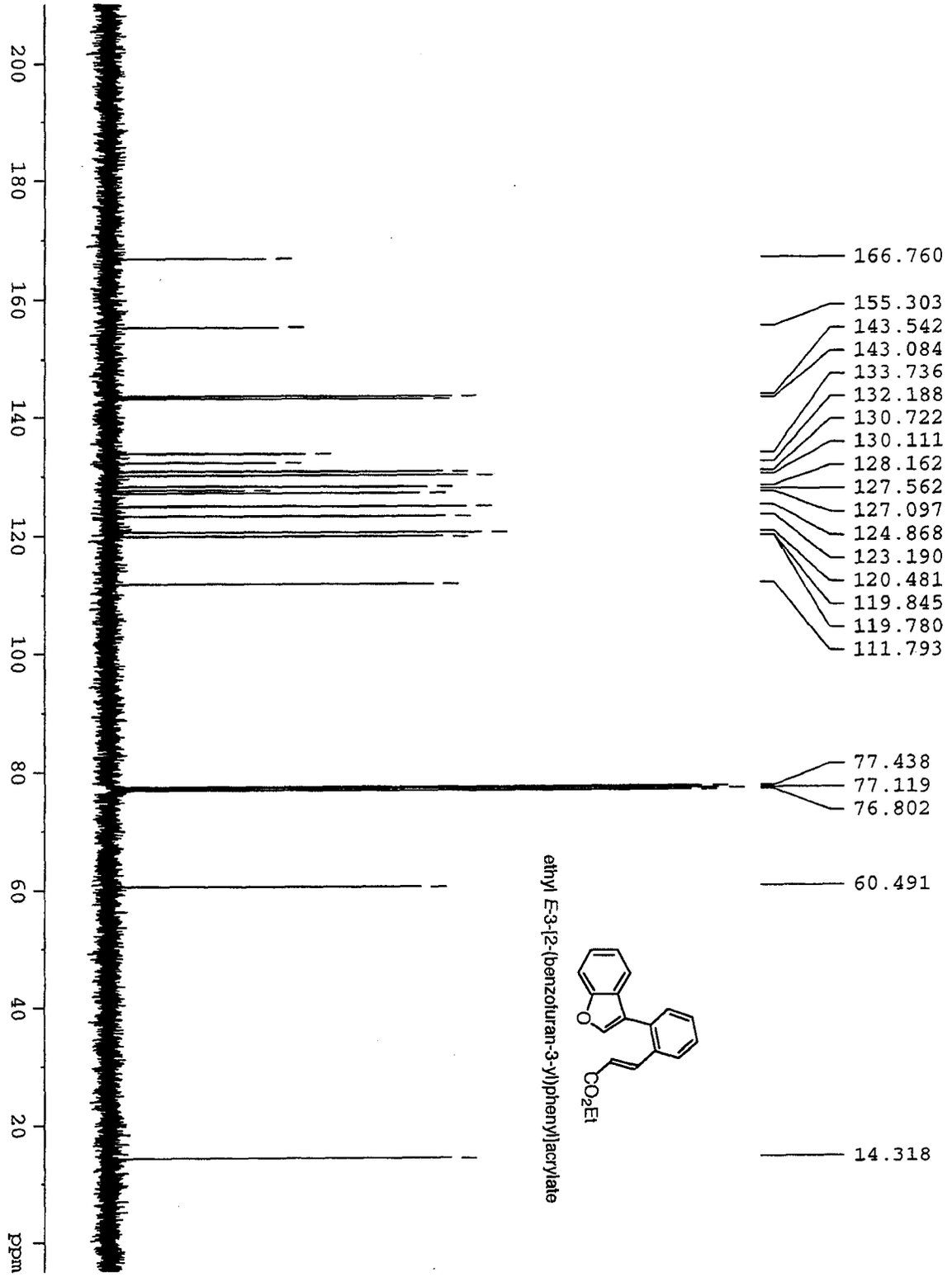

8.552
8.544
8.275
8.267
8.247
8.239
7.713
7.660
7.563
7.535
7.499
7.493
7.488
7.479
7.474
7.464
7.344
7.336
7.329
7.325
7.318
7.312
6.580
6.527
4.271
4.247
4.223
4.199
1.658
1.330
1.306
1.282
1.000
0.988
0.974
4.123
2.037
1.015
2.118
3.094
ppm
ethyl E-3-(4-nitrobiphen-2-yl)acrylate
NO2
CO2Et

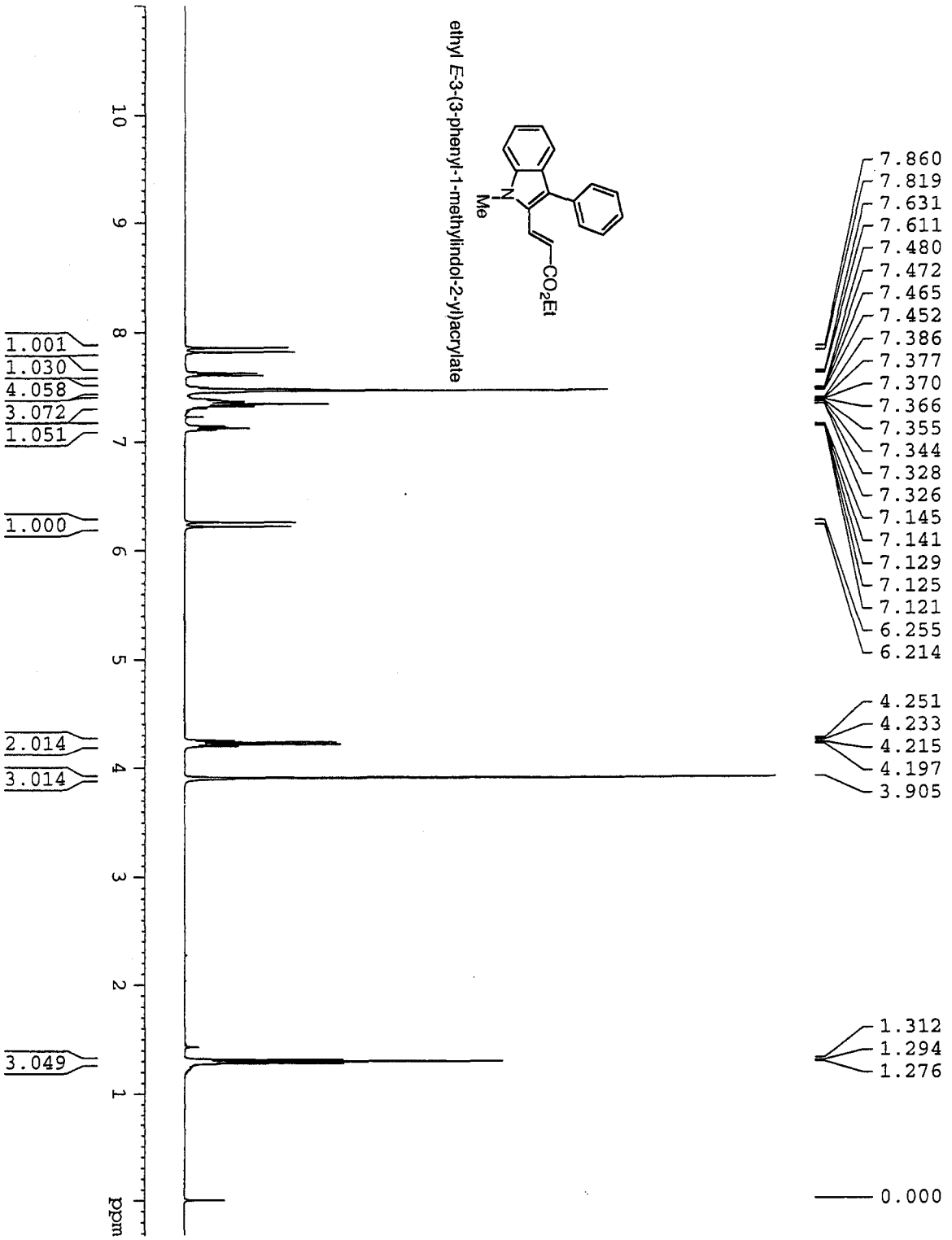

166.324
148.839
147.516
141.565
138.055
134.372
131.837
129.719
129.084
128.949
124.165
122.215
122.190
77.709
77.284
76.861
60.999
14.455
ethyl E-3-(4-nitrobiphen-2-yl)acrylate
NO2
CO2Et
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

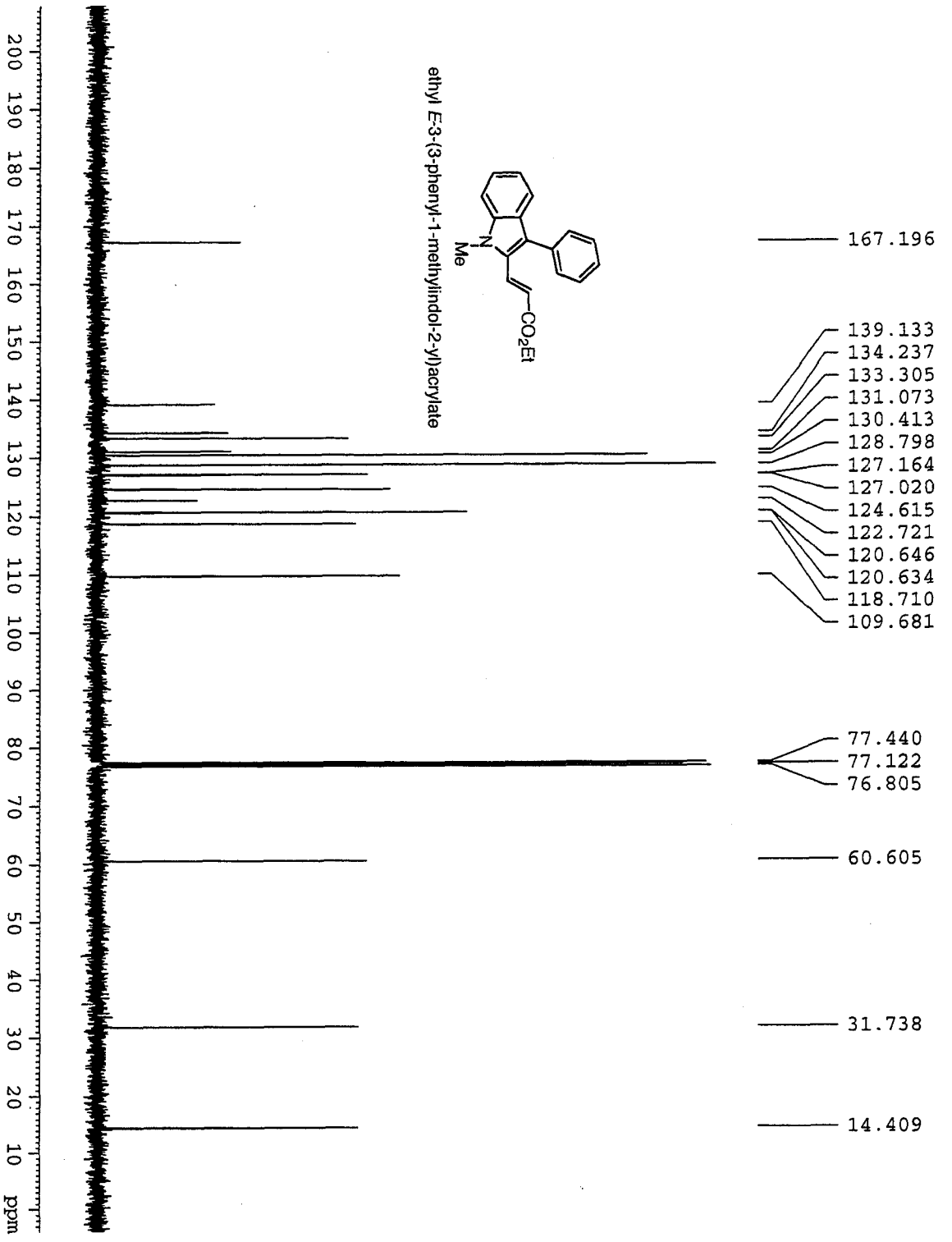

7.676
7.650
7.649
7.647
7.637
7.632
7.630
7.629
7.533
7.524
7.521
7.502
7.459
7.458
7.445
7.423
7.420
7.405
7.402
7.400
7.385
7.382
7.285
7.282
7.265
7.247
7.245
6.696
6.657
4.280
4.262
4.244
4.227
1.337
1.319
1.301
0.000
1.963
7.016
1.098
0.932
1.999
2.998
ppm
ethyl E-3-(3-phenylbenzofuran-2-yl)acrylate
CO2Et

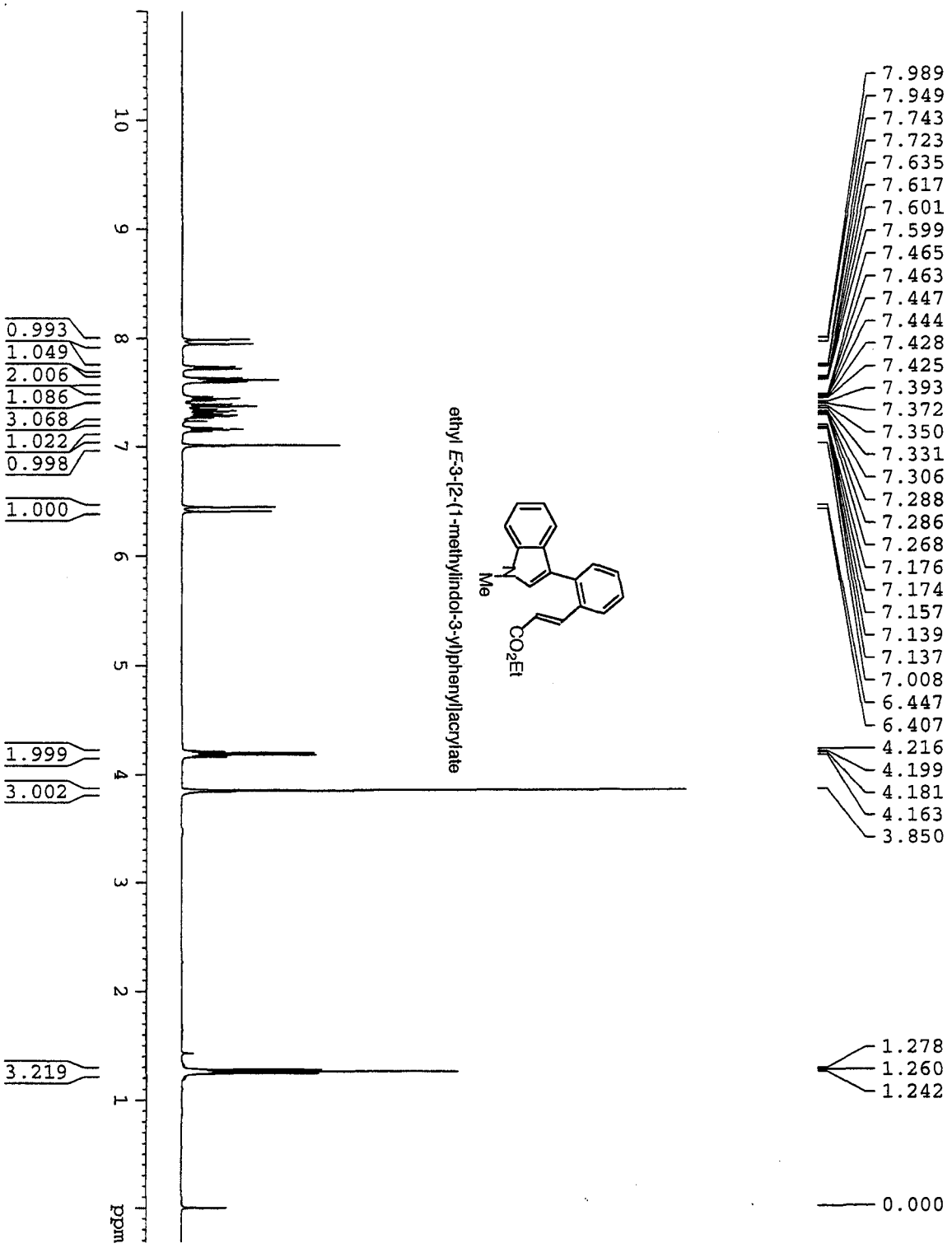

166.985
154.974
148.336
131.186
130.259
129.606
129.170
128.427
128.381
126.985
125.729
123.496
121.034
119.409
111.577
77.554
77.130
76.707
60.705
14.414
ethyl E-3-(3-phenylbenzofuran-2-yl)acrylate
CO2Et
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

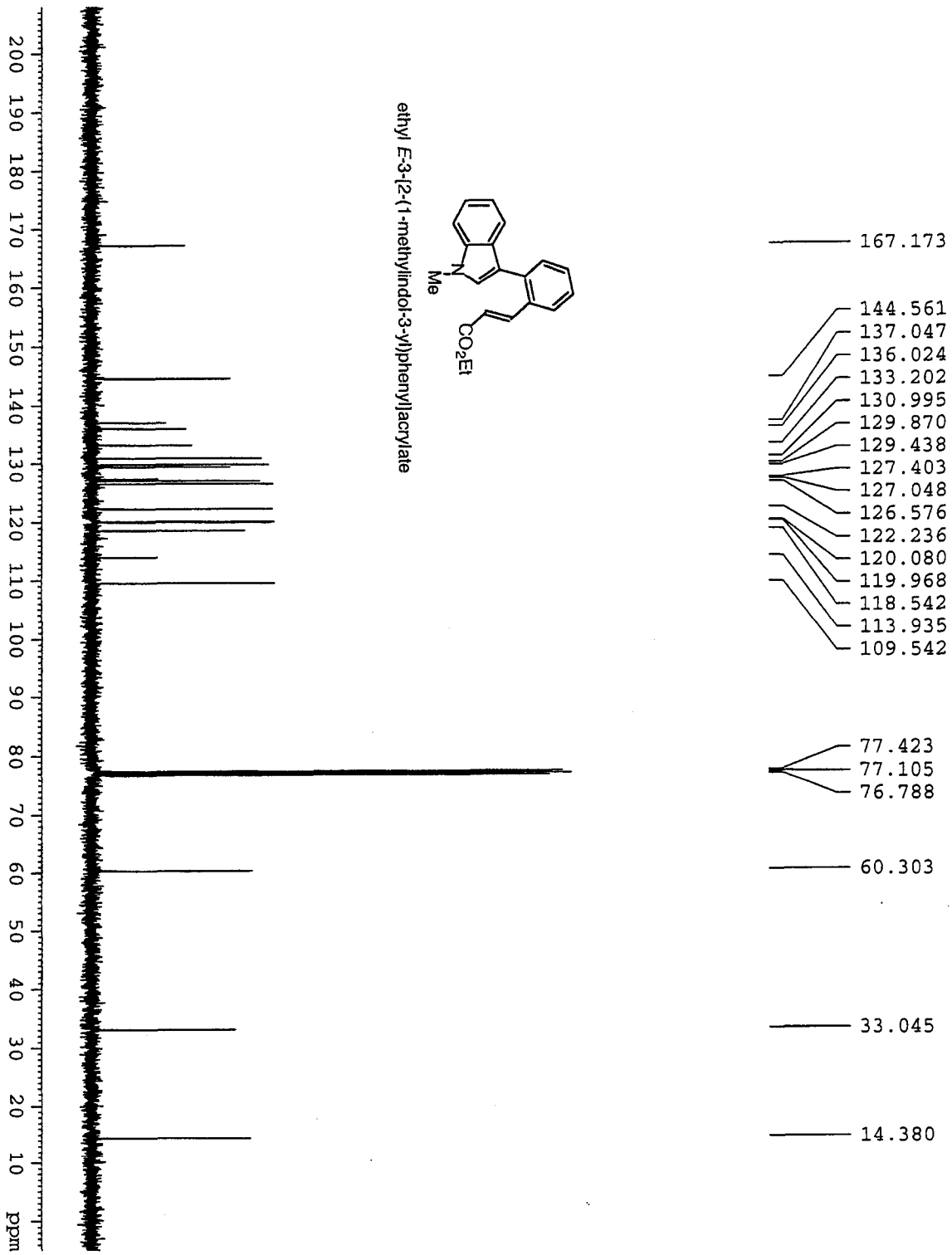

7.883
7.844
7.766
7.747
7.601
7.576
7.555
7.532
7.514
7.493
7.473
7.454
7.434
7.415
7.371
7.352
7.333
7.282
7.263
7.244
6.458
6.418
4.210
4.192
4.174
4.156
1.263
1.245
1.228
1.000
1.070
0.958
6.447
1.154
1.023
2.084
3.158
ppm
ethyl E-3-[2-(benzofuran-3-yl)phenyl]acrylate
CO2Et

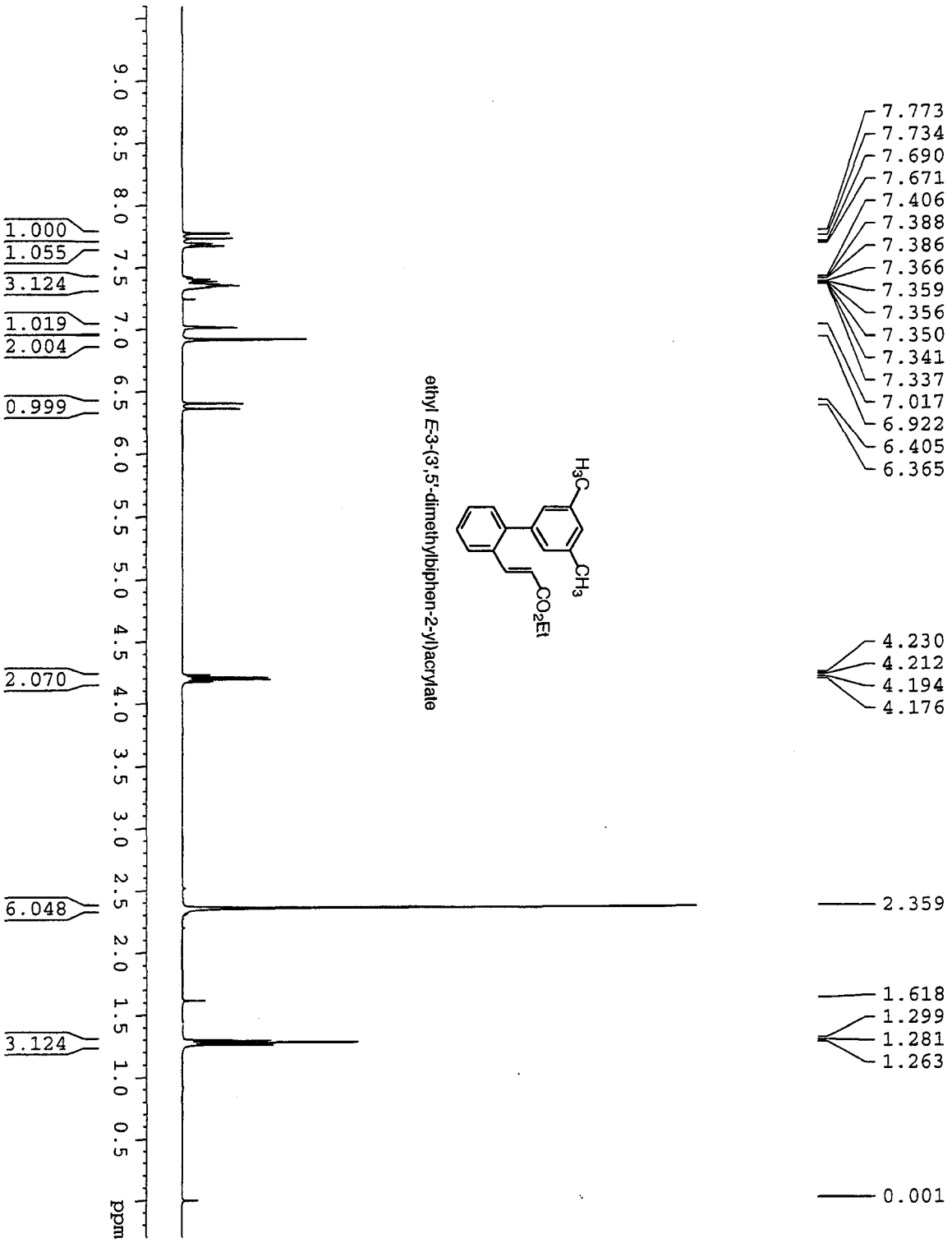

166.760
155.303
143.542
143.084
133.736
132.188
130.722
130.111
128.162
127.562
127.097
124.868
123.190
120.481
119.845
119.780
111.793
77.438
77.119
76.802
60.491
14.318
200
180
160
140
120
100
80
60
40
20
ppm
ethyl E-3-[2-(benzofuran-3-yl)phenyl]acrylate
O
CO2Et

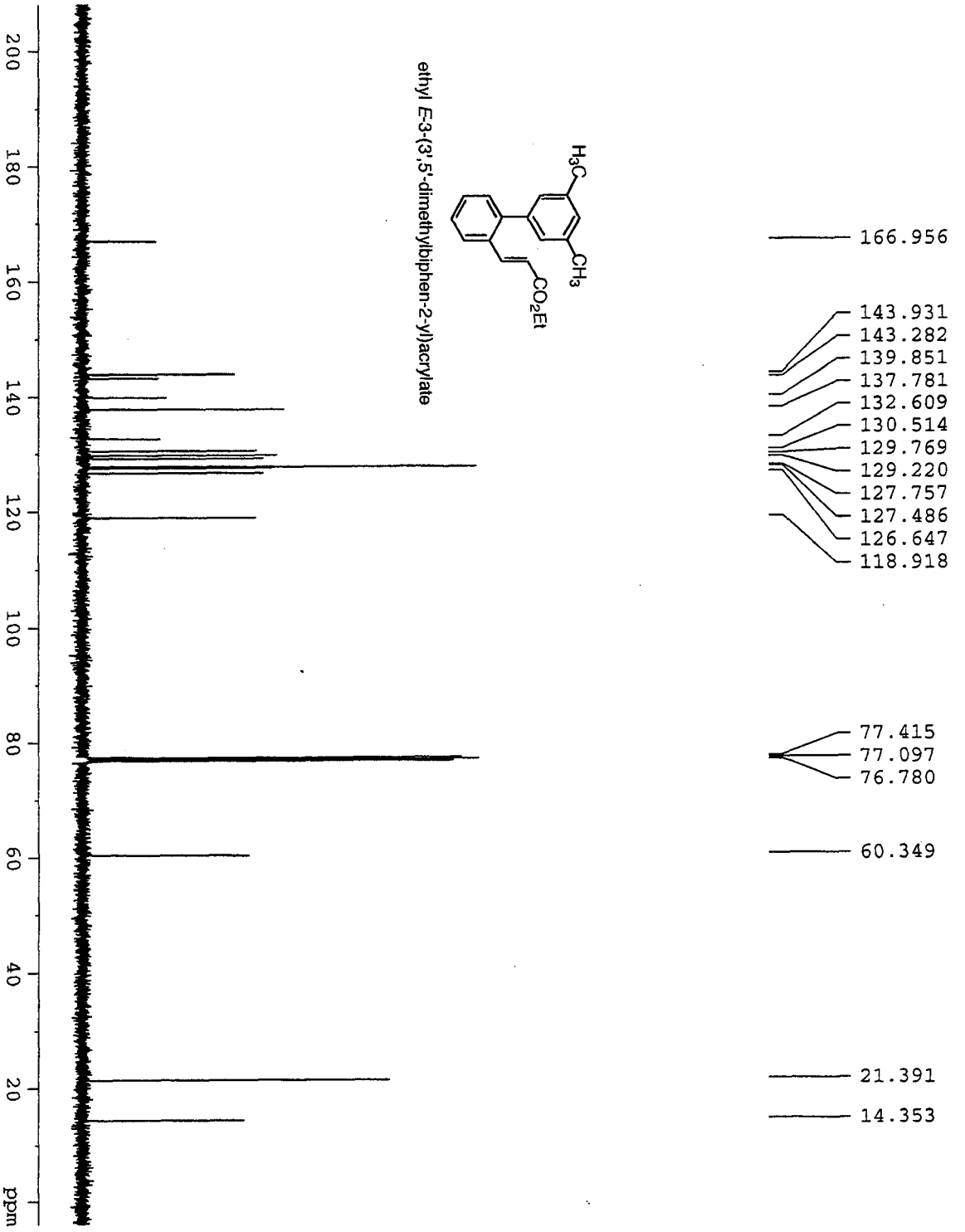

ethyl E-3-(3-phenyl-1-methylindol-2-yl)acrylate
Me
N
CO2Et
7.860
7.819
7.631
7.611
7.480
7.472
7.465
7.452
7.386
7.377
7.370
7.366
7.355
7.344
7.328
7.326
7.145
7.141
7.129
7.125
7.121
6.255
6.214
4.251
4.233
4.215
4.197
3.905
1.312
1.294
1.276
0.000
1.001
1.030
4.058
3.072
1.051
1.000
2.014
3.014
3.049
ppm

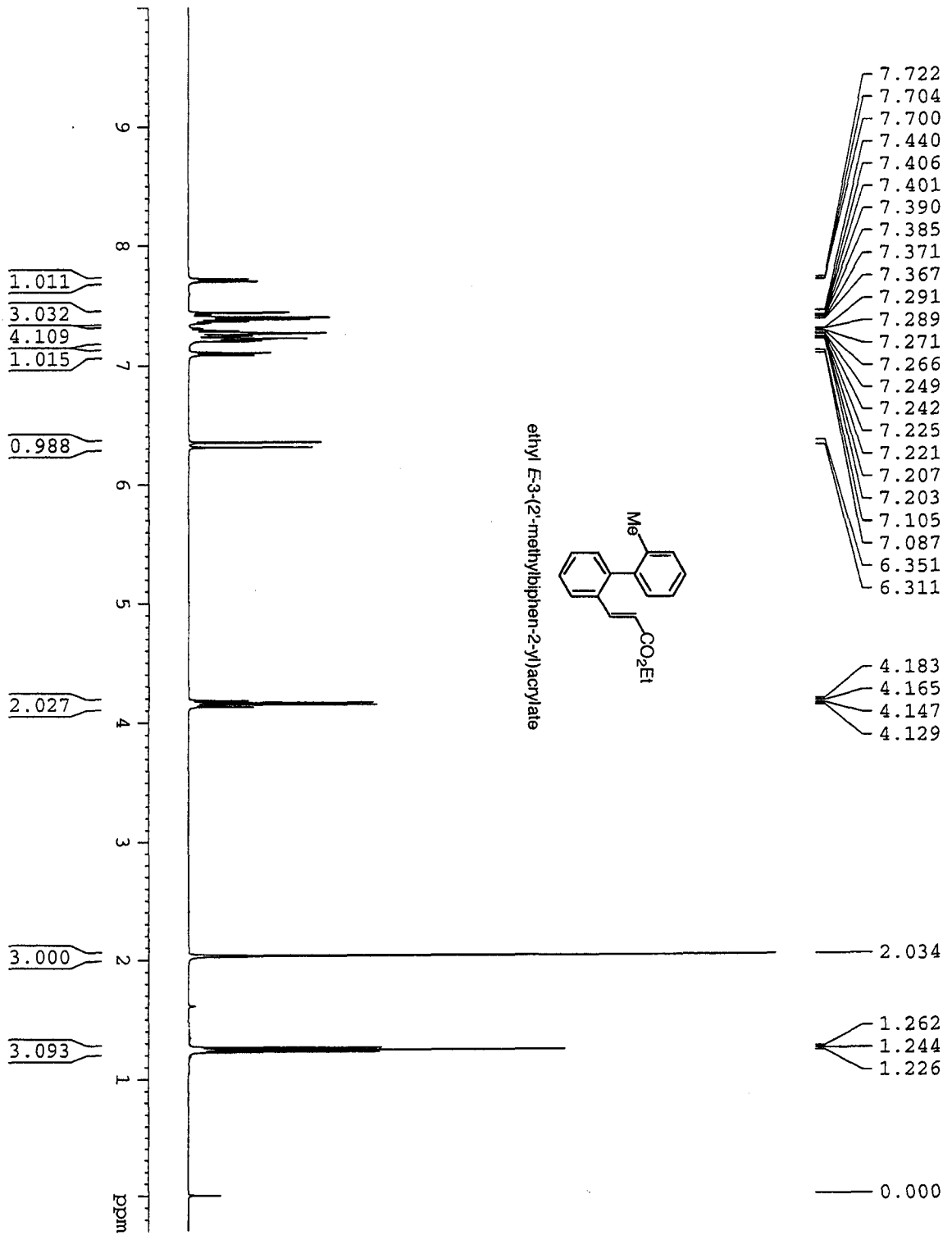

ethyl E-3-(3-phenyl-1-methylindol-2-yl)acrylate
Me
N
CO2Et
167.196
139.133
134.237
133.305
131.073
130.413
128.798
127.164
127.020
124.615
122.721
120.646
120.634
118.710
109.681
77.440
77.122
76.805
60.605
31.738
14.409
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

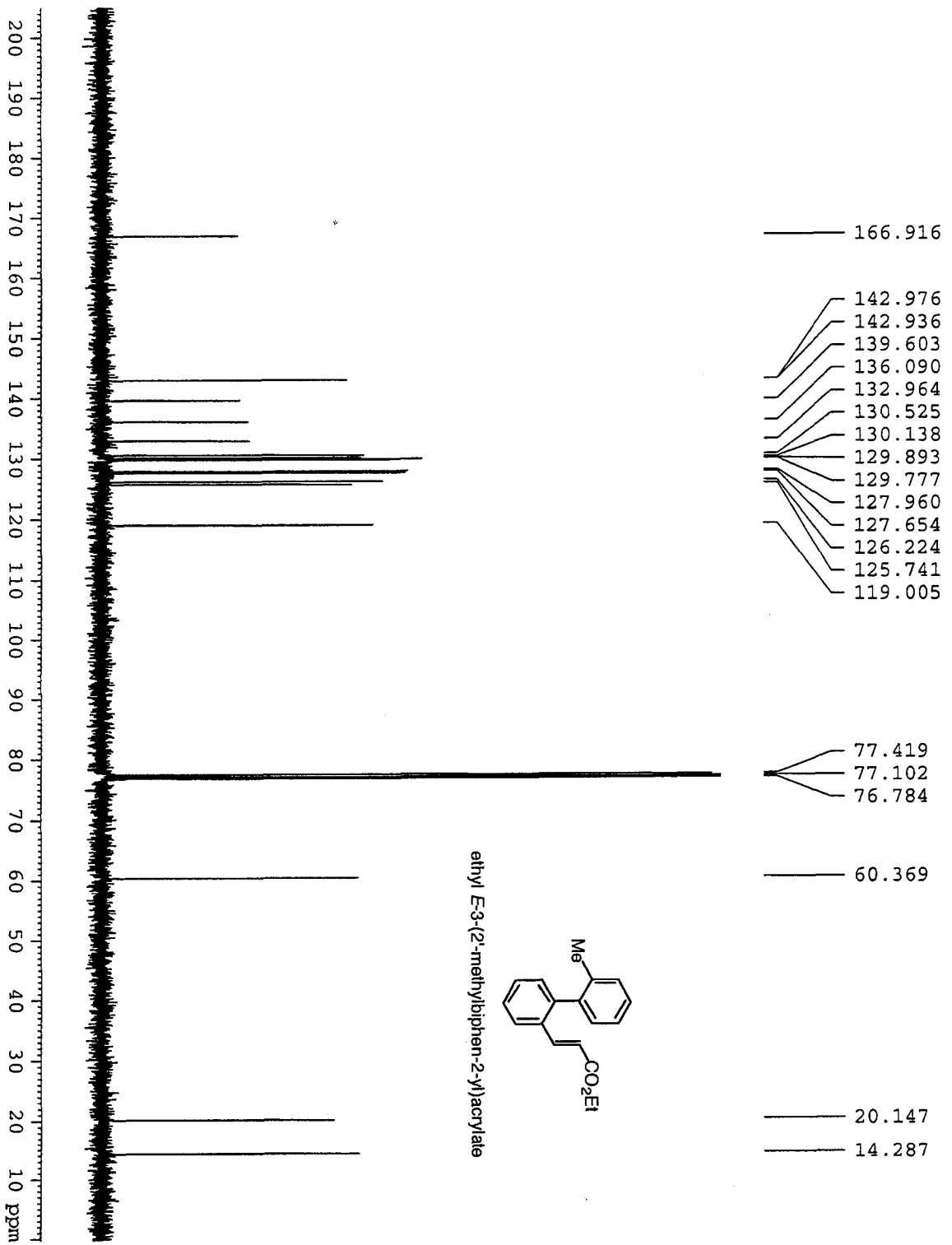

ethyl E-3-[2-(1-methylindol-3-yl)phenyl]acrylate
Me
CO2Et
7.989
7.949
7.743
7.723
7.635
7.617
7.601
7.599
7.465
7.463
7.447
7.444
7.428
7.425
7.393
7.372
7.350
7.331
7.306
7.288
7.286
7.268
7.176
7.174
7.157
7.139
7.137
7.008
6.447
6.407
4.216
4.199
4.181
4.163
3.850
1.278
1.260
1.242
0.000
0.993
1.049
2.006
1.086
3.068
1.022
0.998
1.000
1.999
3.002
3.219
ppm

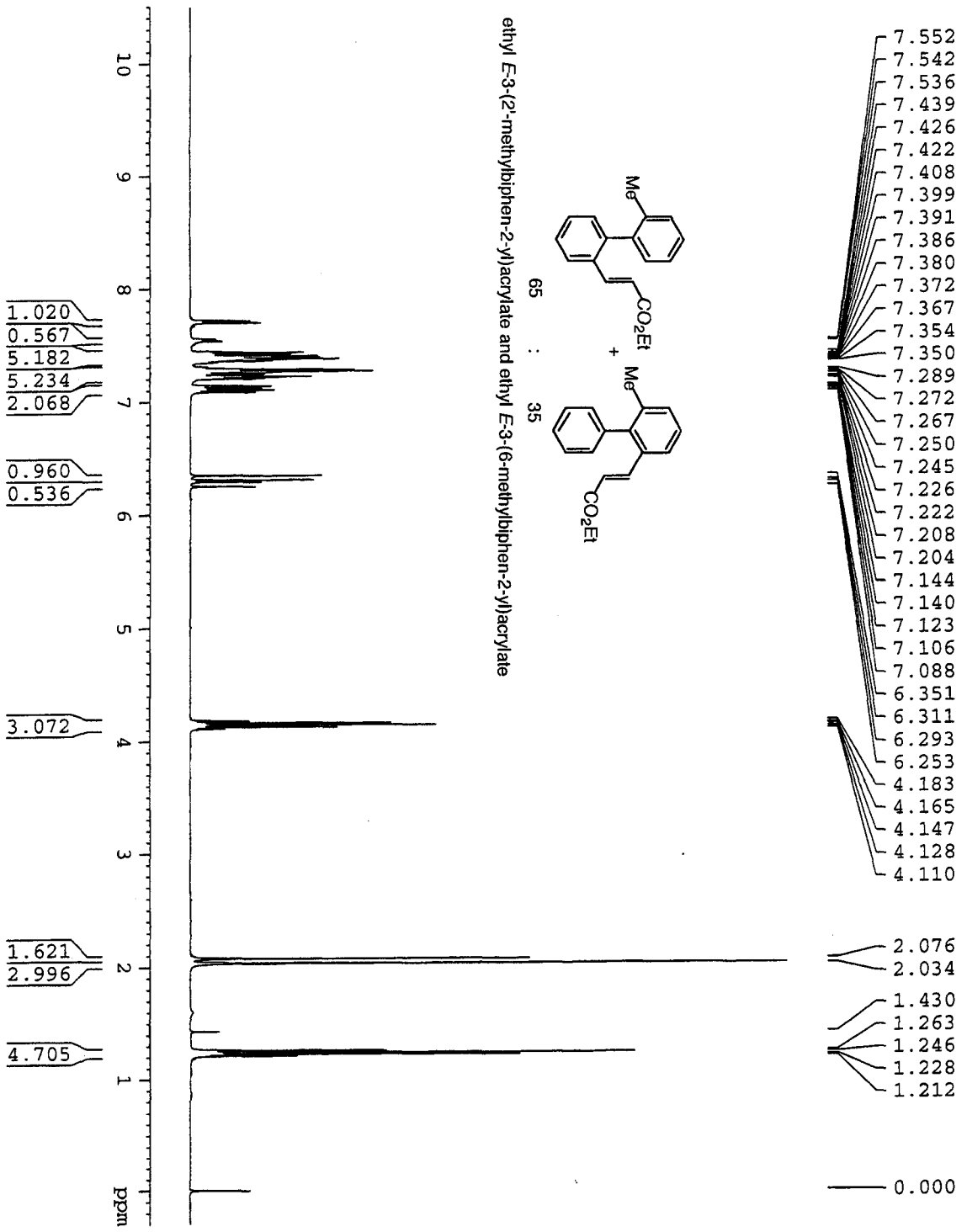

ethyl E-3-[2-(1-methylindol-3-yl)phenyl]acrylate
Me
CO2Et
167.173
144.561
137.047
136.024
133.202
130.995
129.870
129.438
127.403
127.048
126.576
122.236
120.080
119.968
118.542
113.935
109.542
77.423
77.105
76.788
60.303
33.045
14.380
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

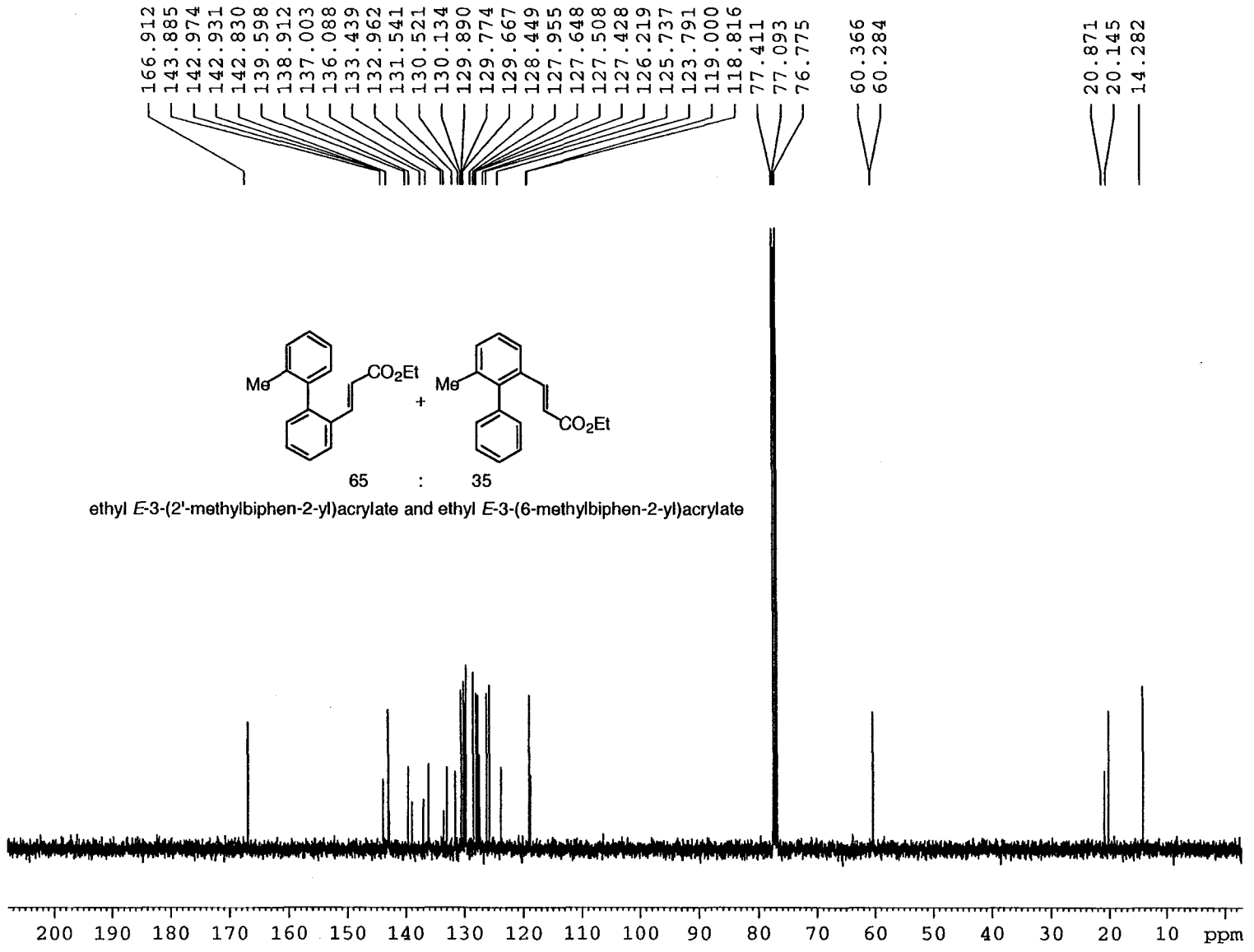

7.773
7.734
7.690
7.671
7.406
7.388
7.386
7.366
7.359
7.356
7.350
7.341
7.337
7.017
6.922
6.405
6.365
4.230
4.212
4.194
4.176
2.359
1.618
1.299
1.281
1.263
0.001
1.000
1.055
3.124
1.019
2.004
0.999
2.070
6.048
3.124
ppm
ethyl E-3-(3',5'-dimethylbiphen-2-yl)acrylate
H3C
CH3
CO2Et


ethyl E-3-(3',5'-dimethylbiphen-2-yl)acrylate
H3C
CH3
CO2Et
166.956
143.931
143.282
139.851
137.781
132.609
130.514
129.769
129.220
127.757
127.486
126.647
118.918
77.415
77.097
76.780
60.349
21.391
14.353
200
180
160
140
120
100
80
60
40
20
ppm

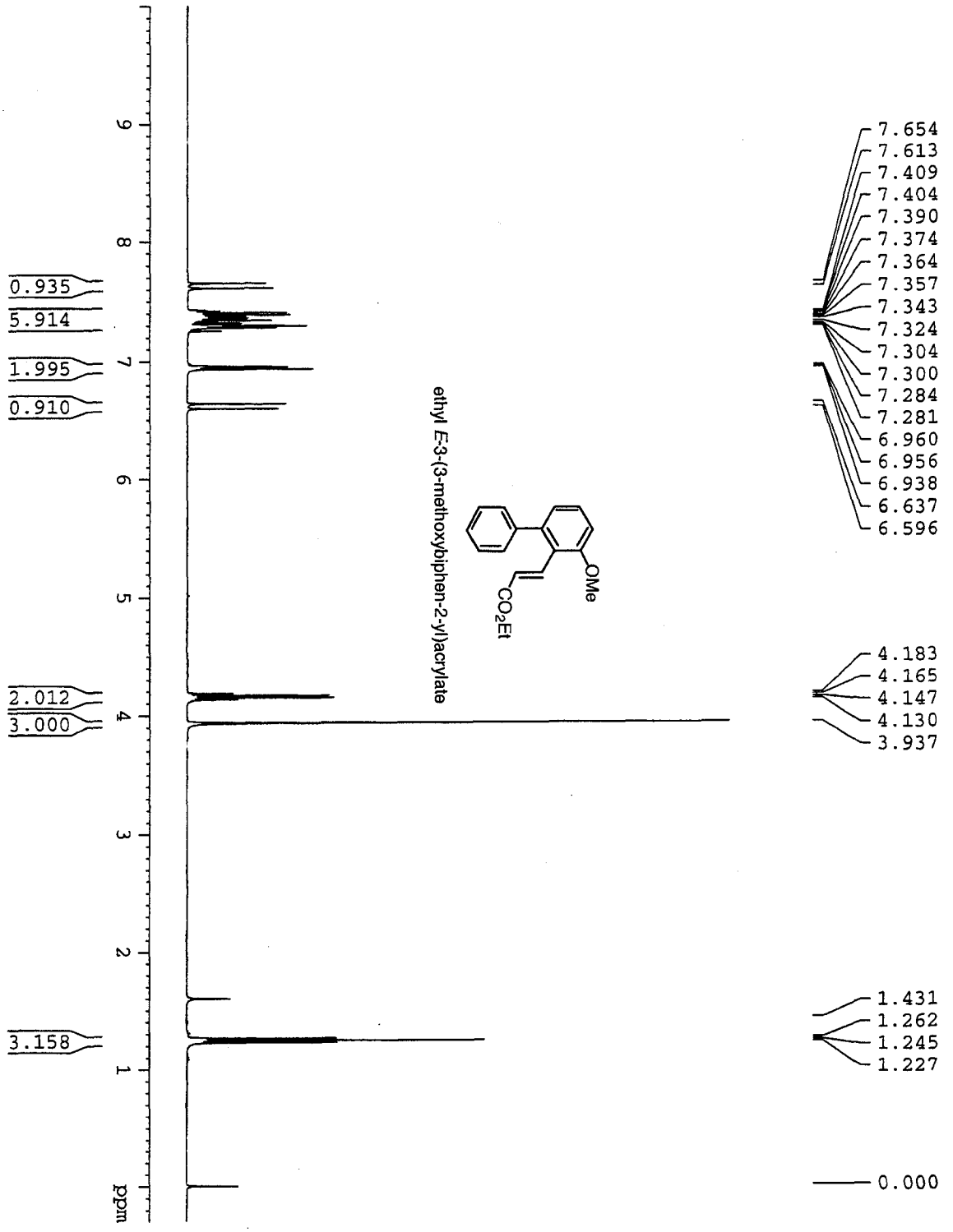

ethyl E-3-(2'-methylbiphen-2-yl)acrylate
Me
CO2Et
7.722
7.704
7.700
7.440
7.406
7.401
7.390
7.385
7.371
7.367
7.291
7.289
7.271
7.266
7.249
7.242
7.225
7.221
7.207
7.203
7.105
7.087
6.351
6.311
4.183
4.165
4.147
4.129
2.034
1.262
1.244
1.226
0.000
1.011
3.032
4.109
1.015
0.988
2.027
3.000
3.093
ppm

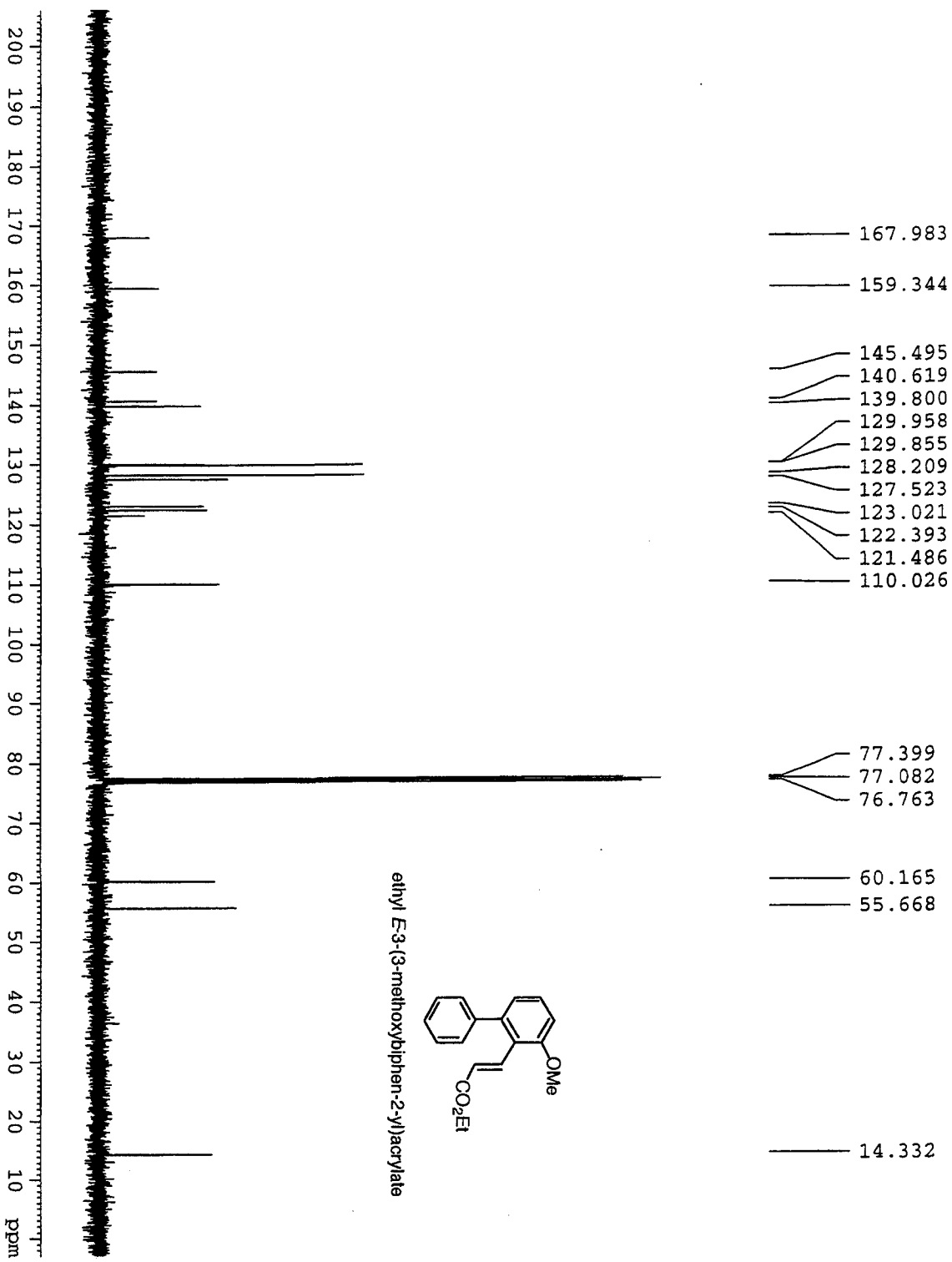

166.916
142.976
142.936
139.603
136.090
132.964
130.525
130.138
129.893
129.777
127.960
127.654
126.224
125.741
119.005
77.419
77.102
76.784
60.369
20.147
14.287
ethyl E-3-(2'-methylbiphen-2-yl)acrylate
Me
CO2Et
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

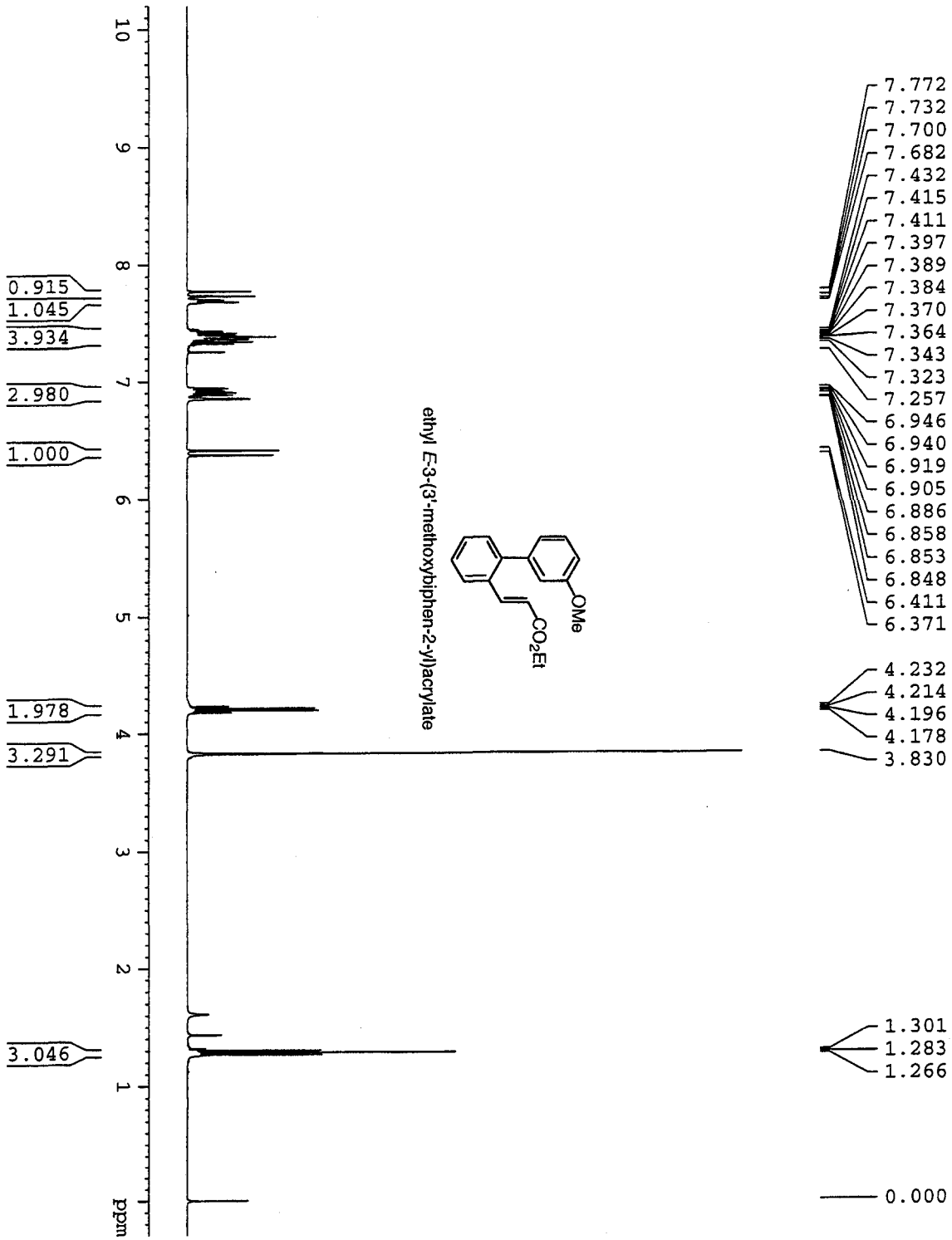

ethyl E-3-(2'-methylbiphen-2-yl)acrylate and ethyl E-3-(6-methylbiphen-2-yl)acrylate
65 : 35
Me
CO2Et
+
Me
CO2Et
7.552
7.542
7.536
7.439
7.426
7.422
7.408
7.399
7.391
7.386
7.380
7.372
7.367
7.354
7.350
7.289
7.272
7.267
7.250
7.245
7.226
7.222
7.208
7.204
7.144
7.140
7.123
7.106
7.088
6.351
6.311
6.293
6.253
4.183
4.165
4.147
4.128
4.110
2.076
2.034
1.430
1.263
1.246
1.228
1.212
0.000
1.020
0.567
5.182
5.234
2.068
0.960
0.536
3.072
1.621
2.996
4.705
10
9
8
7
6
5
4
3
2
1
ppm

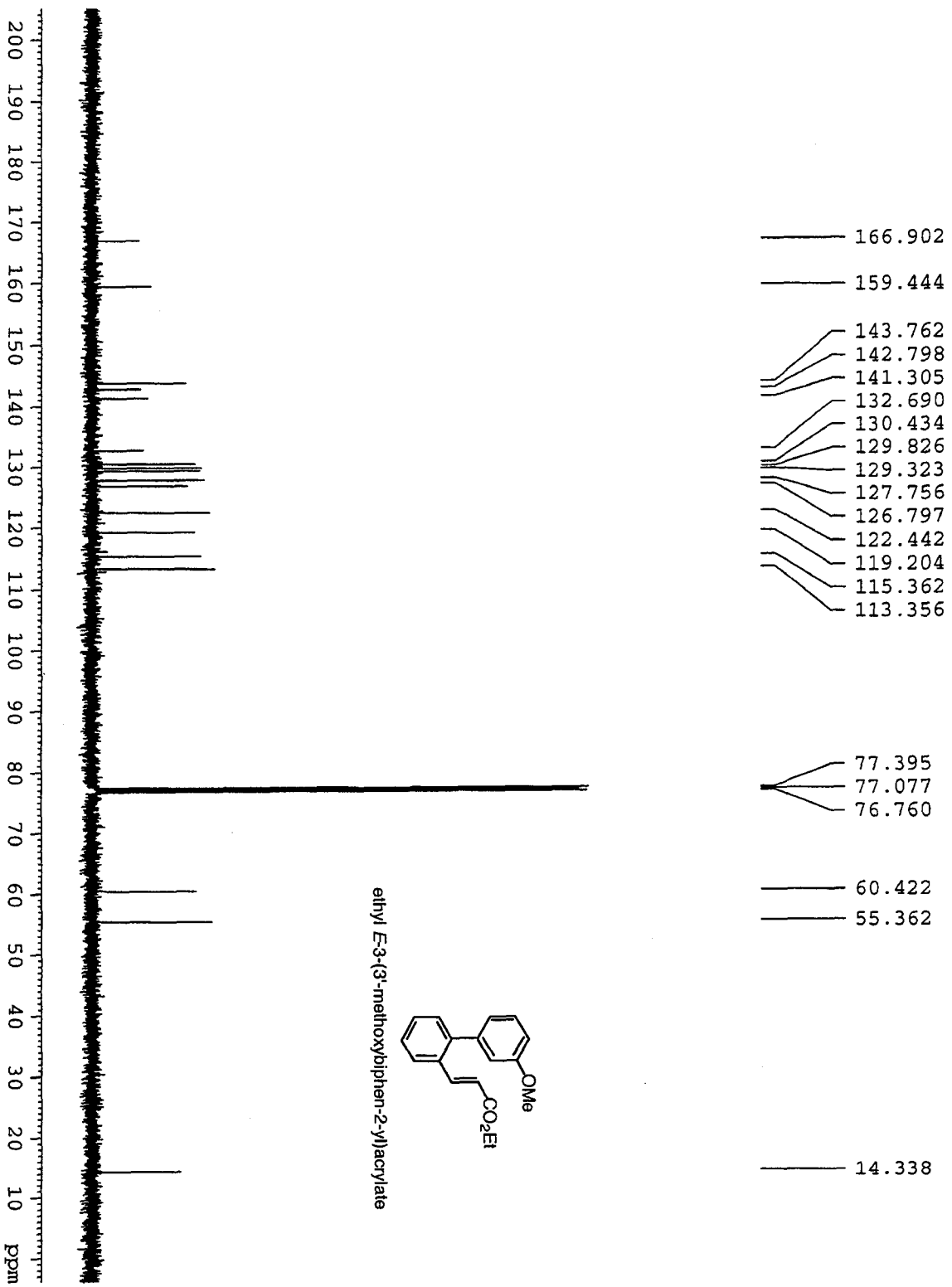


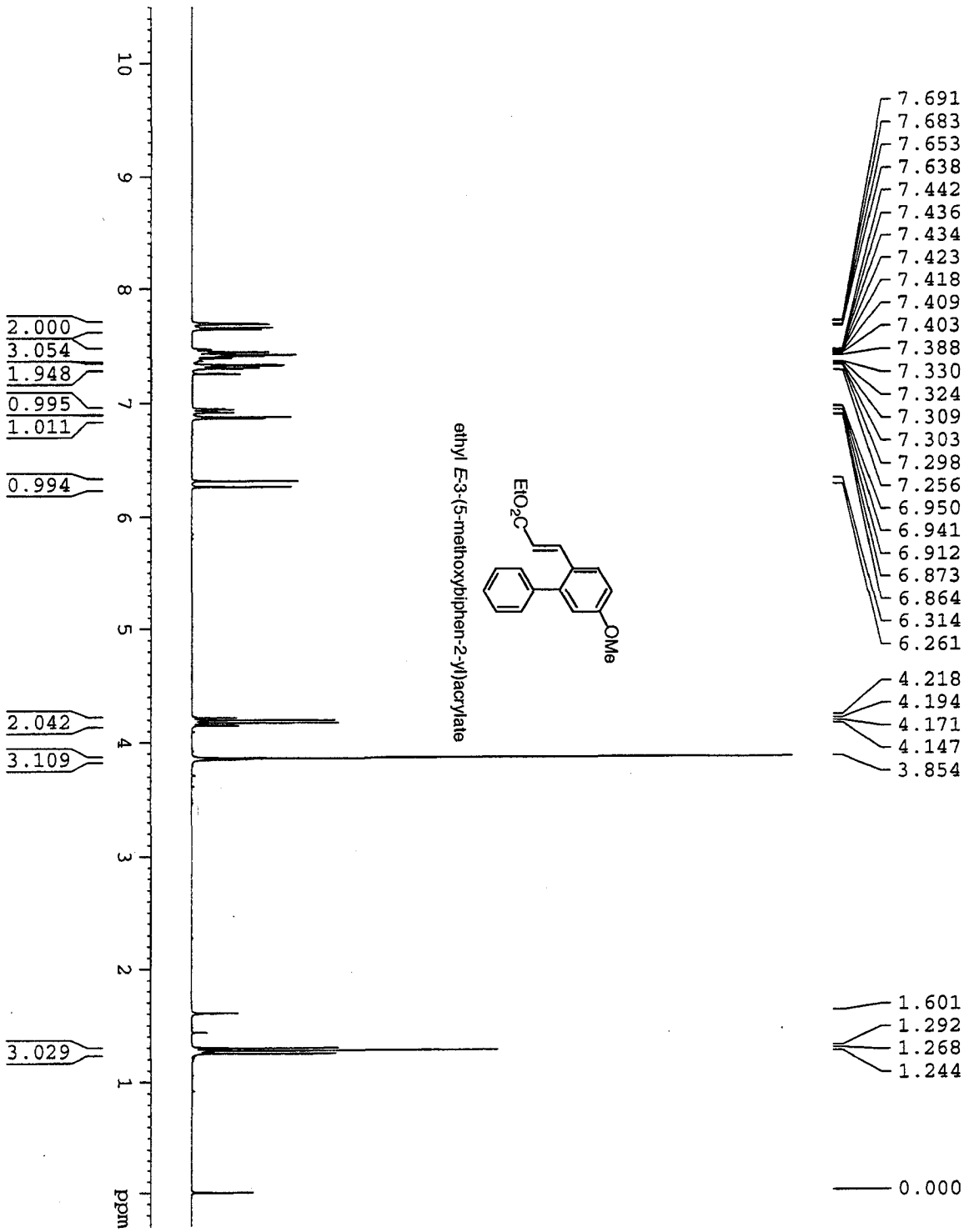
ethyl *E*-3-(2'-methylbiphen-2-yl)acrylate and ethyl *E*-3-(6-methylbiphen-2-yl)acrylate

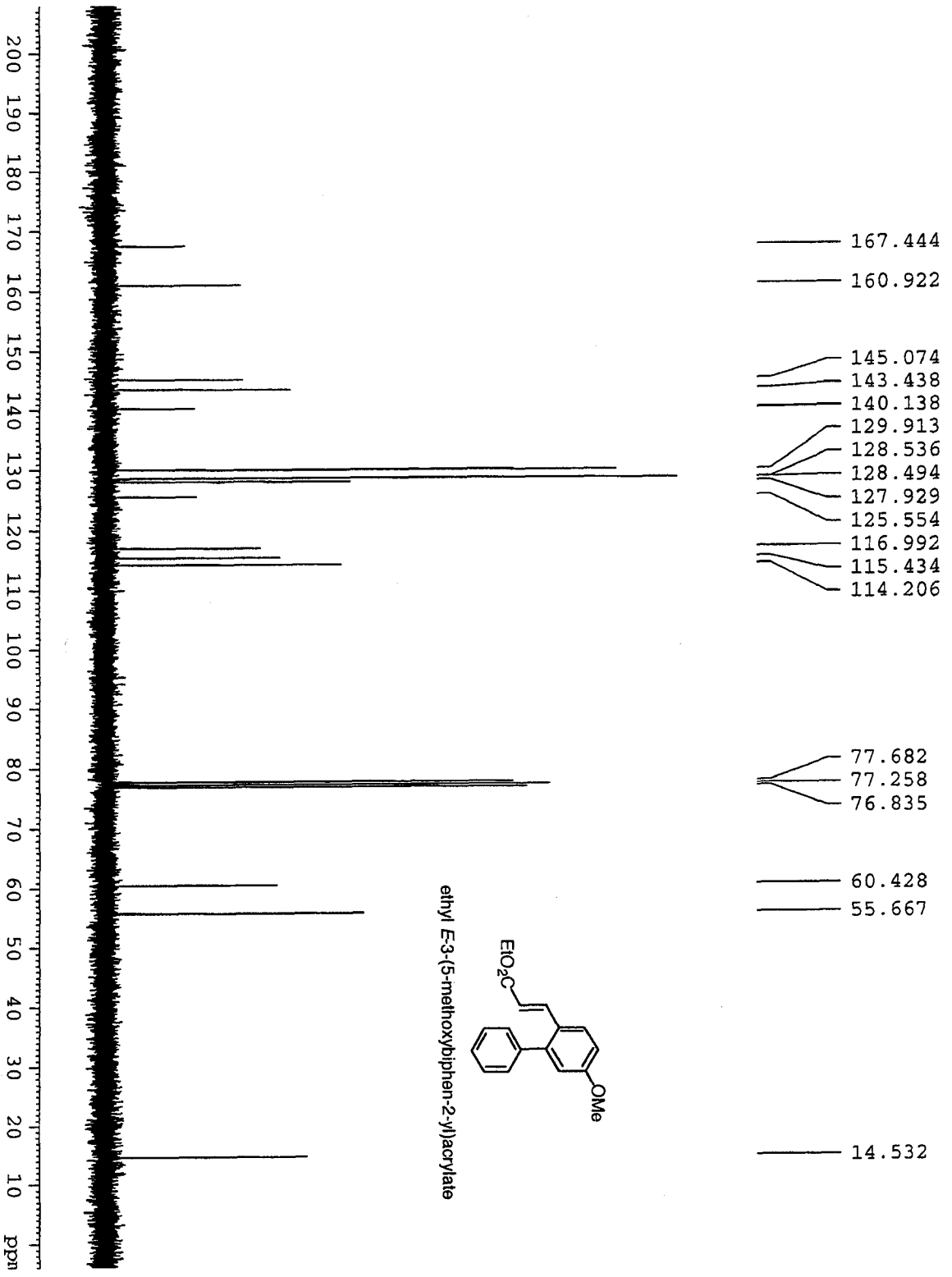

ethyl E-3-(3-methoxybiphen-2-yl)acrylate
OMe
CO2Et
0.935
5.914
1.995
0.910
2.012
3.000
3.158
7.654
7.613
7.409
7.404
7.390
7.374
7.364
7.357
7.343
7.324
7.304
7.300
7.284
7.281
6.960
6.956
6.938
6.637
6.596
4.183
4.165
4.147
4.130
3.937
1.431
1.262
1.245
1.227
0.000
ppm

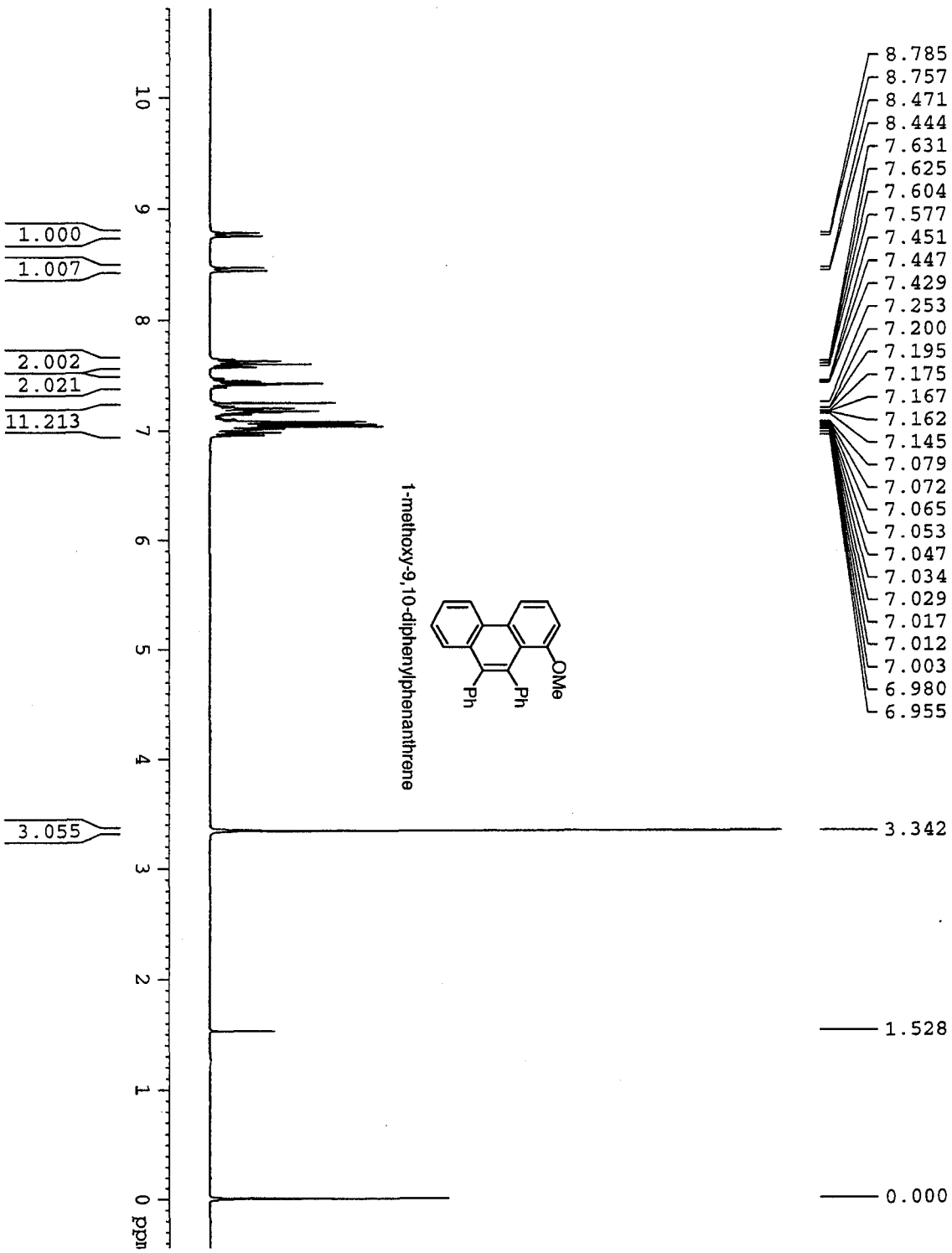

167.983
159.344
145.495
140.619
139.800
129.958
129.855
128.209
127.523
123.021
122.393
121.486
110.026
77.399
77.082
76.763
60.165
55.668
14.332
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
ethyl E-3-(3-methoxybiphen-2-yl)acrylate
OMe
CO2Et

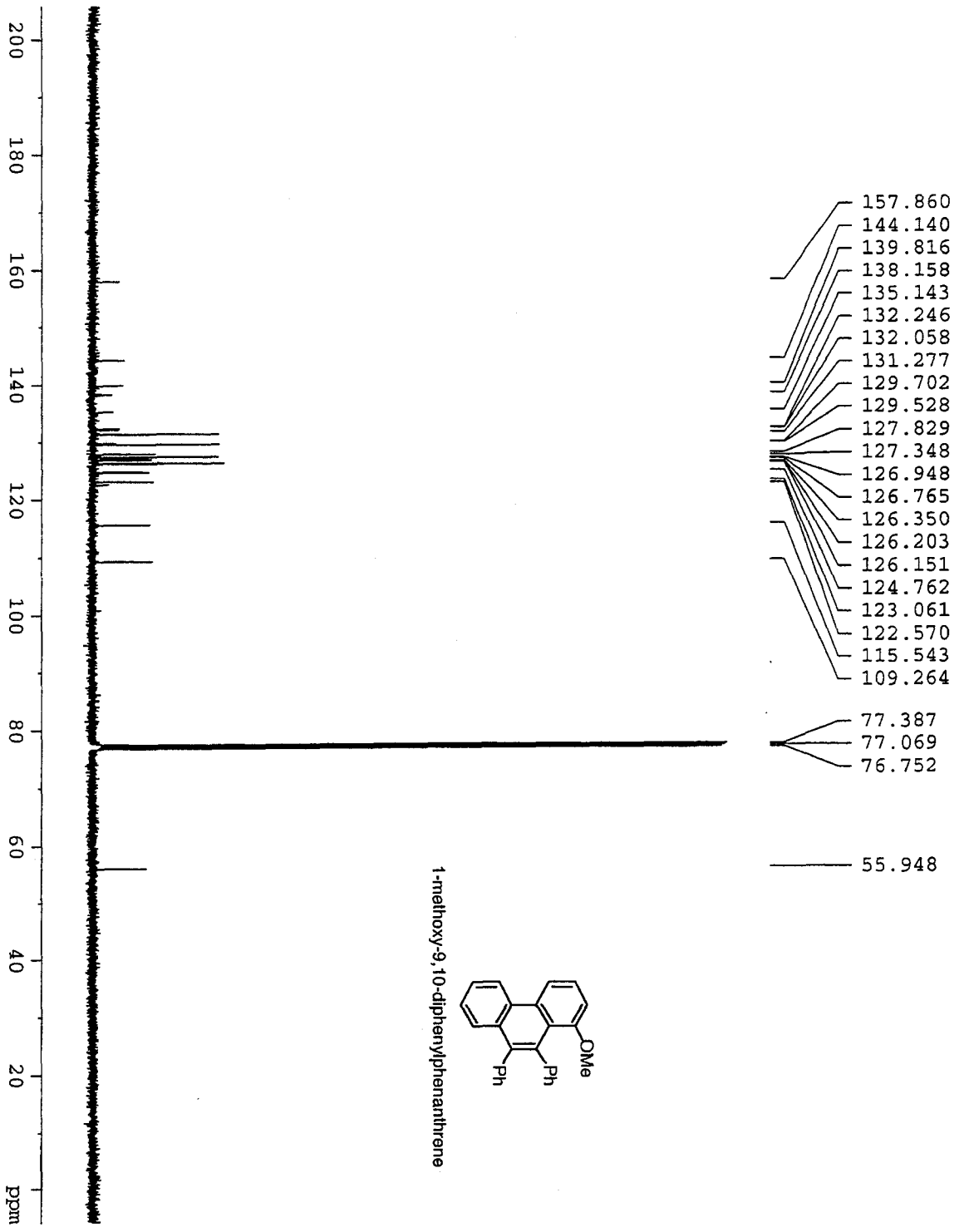

ethyl E-3-(3'-methoxybiphen-2-yl)acrylate
OMe
CO2Et
7.772
7.732
7.700
7.682
7.432
7.415
7.411
7.397
7.389
7.384
7.370
7.364
7.343
7.323
7.257
6.946
6.940
6.919
6.905
6.886
6.858
6.853
6.848
6.411
6.371
4.232
4.214
4.196
4.178
3.830
1.301
1.283
1.266
0.000
0.915
1.045
3.934
2.980
1.000
1.978
3.291
3.046
ppm

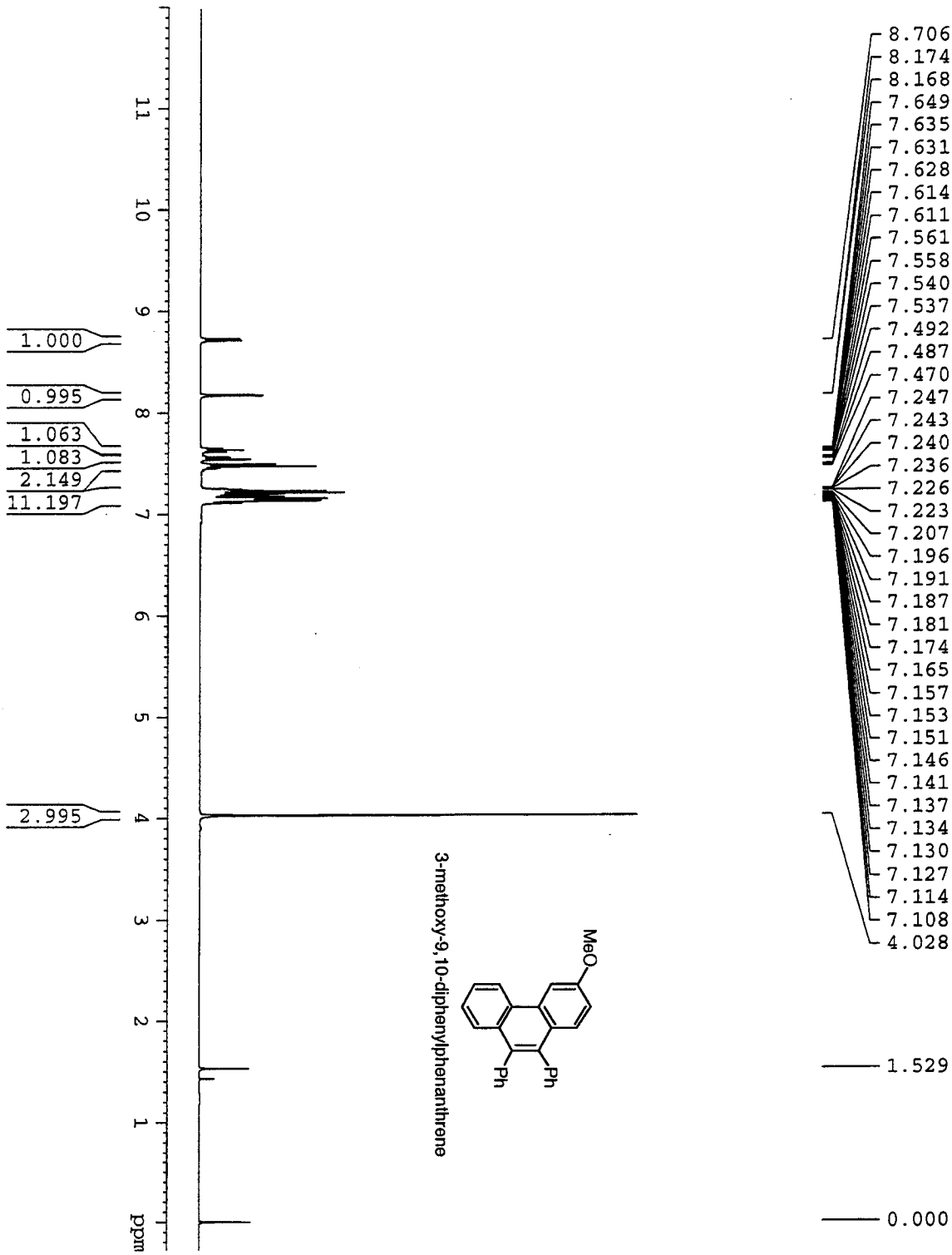

166.902
159.444
143.762
142.798
141.305
132.690
130.434
129.826
129.323
127.756
126.797
122.442
119.204
115.362
113.356
77.395
77.077
76.760
60.422
55.362
14.338
ethyl E-3-(3'-methoxybiphen-2-yl)acrylate
OMe
CO2Et
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

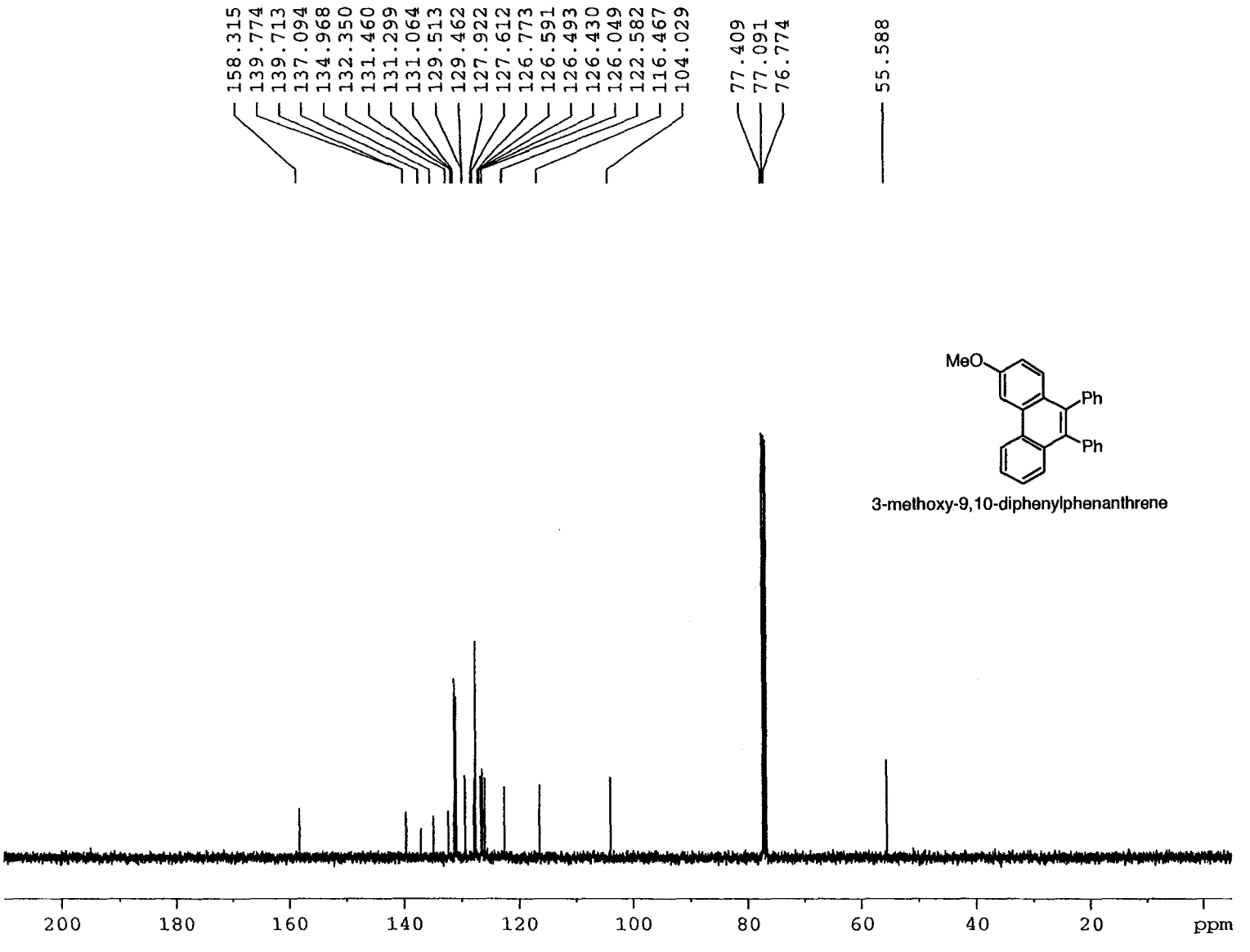

ethyl E-3-(5-methoxybiphen-2-yl)acrylate
EtO2C
OMe
7.691
7.683
7.653
7.638
7.442
7.436
7.434
7.423
7.418
7.409
7.403
7.388
7.330
7.324
7.309
7.303
7.298
7.256
6.950
6.941
6.912
6.873
6.864
6.314
6.261
4.218
4.194
4.171
4.147
3.854
1.601
1.292
1.268
1.244
0.000
2.000
3.054
1.948
0.995
1.011
0.994
2.042
3.109
3.029
ppm

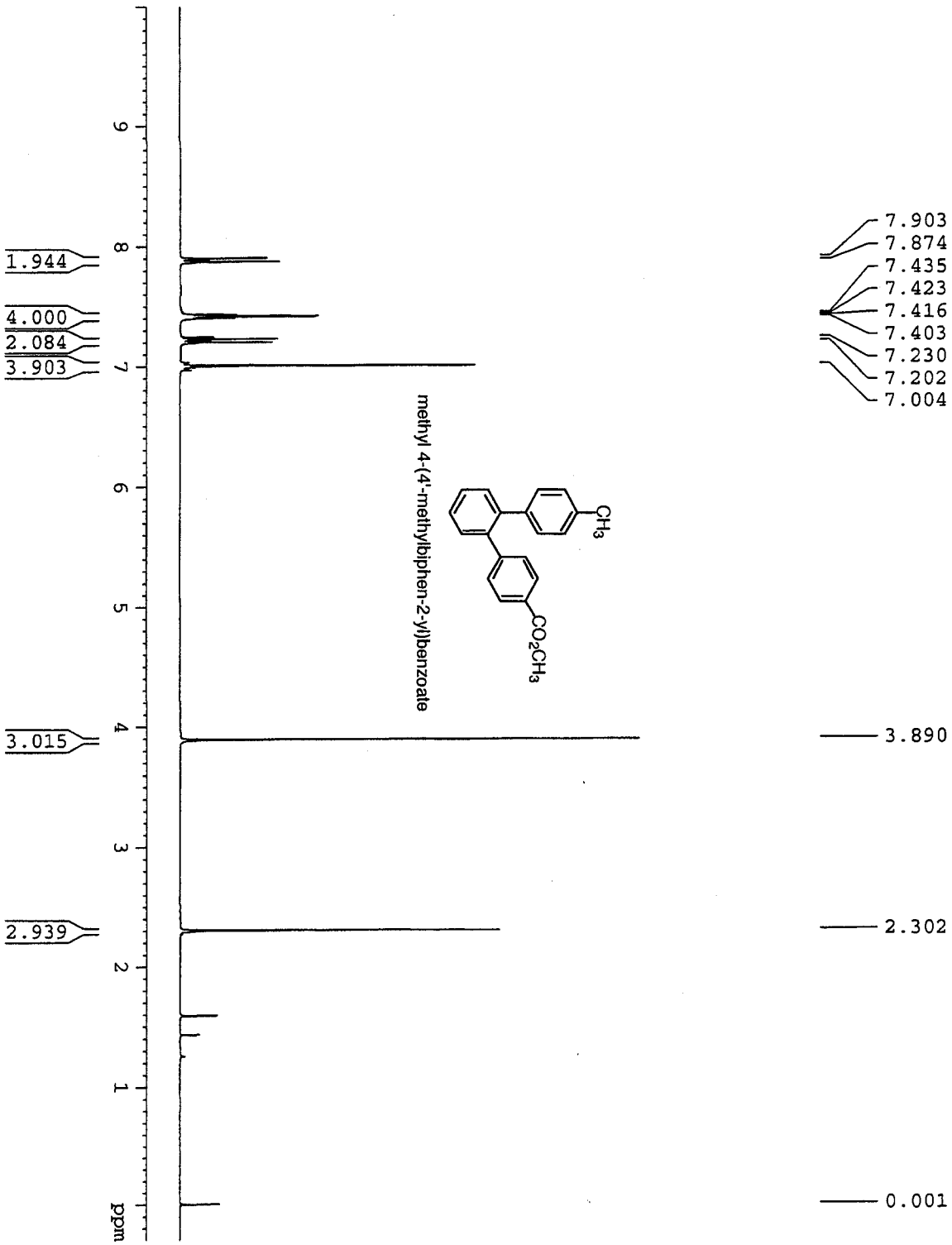

167.444
160.922
145.074
143.438
140.138
129.913
128.536
128.494
127.929
125.554
116.992
115.434
114.206
77.682
77.258
76.835
60.428
55.667
14.532
ethyl E-3-(5-methoxybiphen-2-yl)acrylate
EtO2C
OMe
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

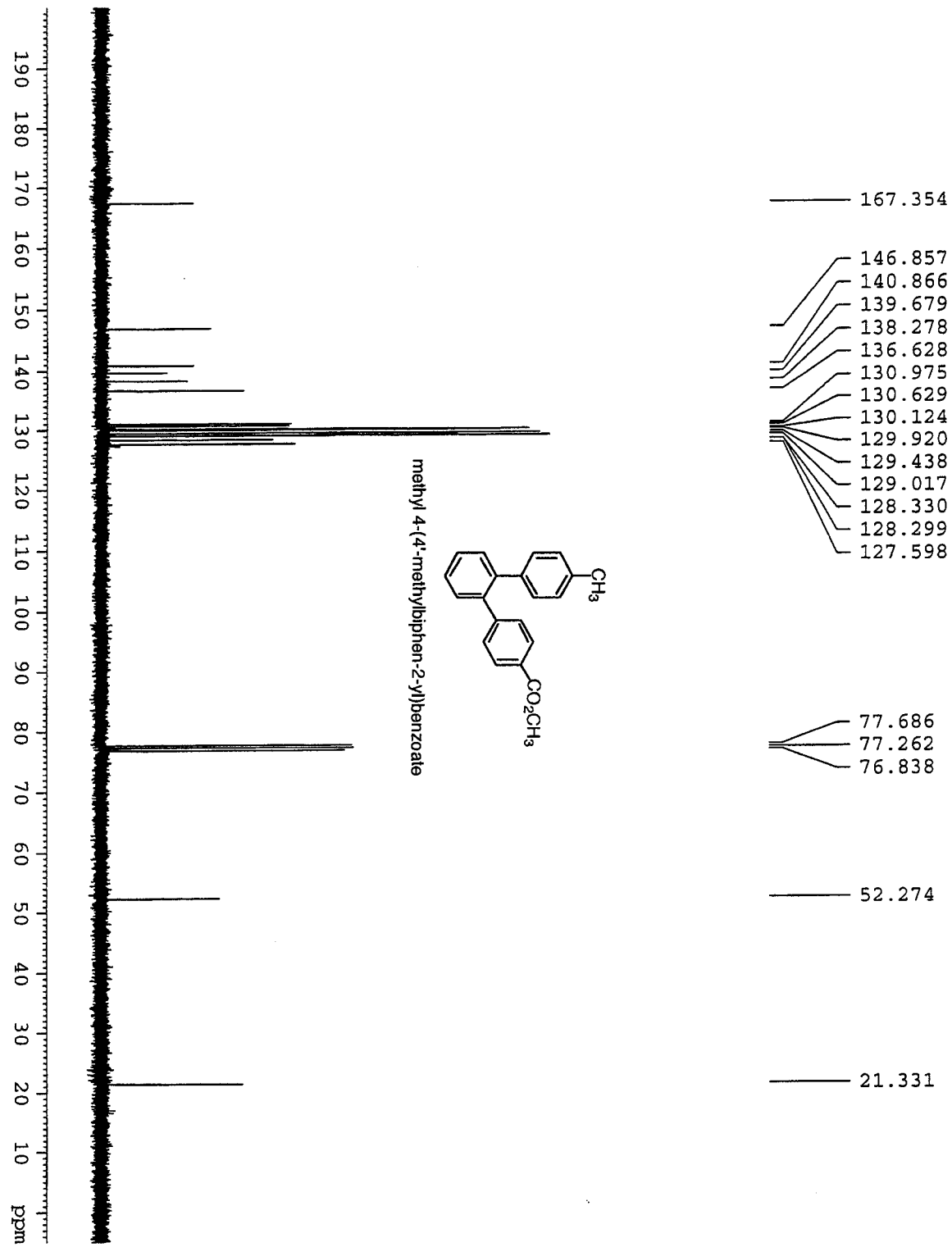

8.785
8.757
8.471
8.444
7.631
7.625
7.604
7.577
7.451
7.447
7.429
7.253
7.200
7.195
7.175
7.167
7.162
7.145
7.079
7.072
7.065
7.053
7.047
7.034
7.029
7.017
7.012
7.003
6.980
6.955
1.000
1.007
2.002
2.021
11.213
3.055
3.342
1.528
0.000
1-methoxy-9,10-diphenylphenanthrene
OMe
Ph
Ph
10
9
8
7
6
5
4
3
2
1
0 ppm

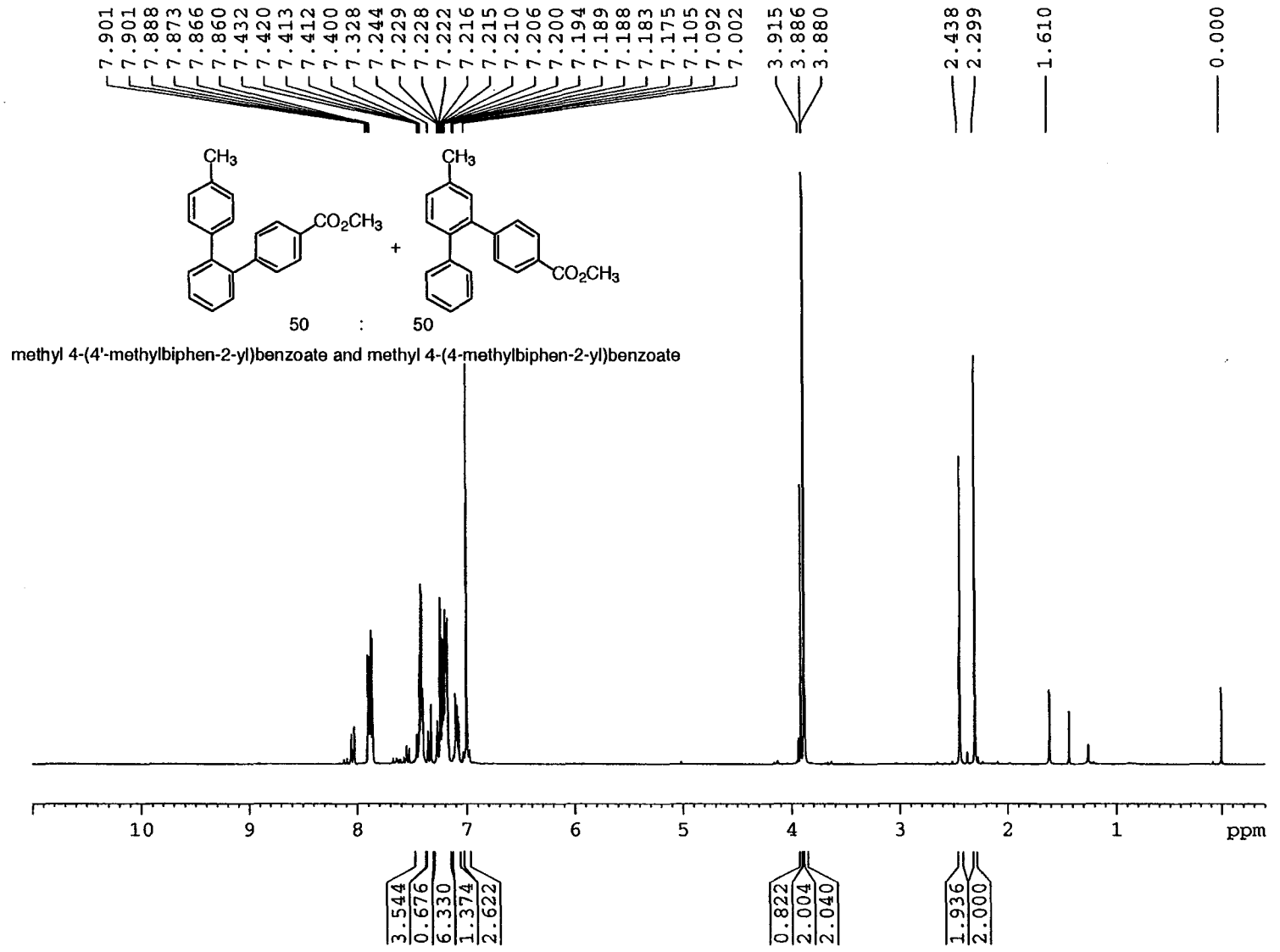

157.860
144.140
139.816
138.158
135.143
132.246
132.058
131.277
129.702
129.528
127.829
127.348
126.948
126.765
126.350
126.203
126.151
124.762
123.061
122.570
115.543
109.264
77.387
77.069
76.752
55.948
200
180
160
140
120
100
80
60
40
20
ppm
1-methoxy-9,10-diphenylphenanthrene
OMe
Ph
Ph

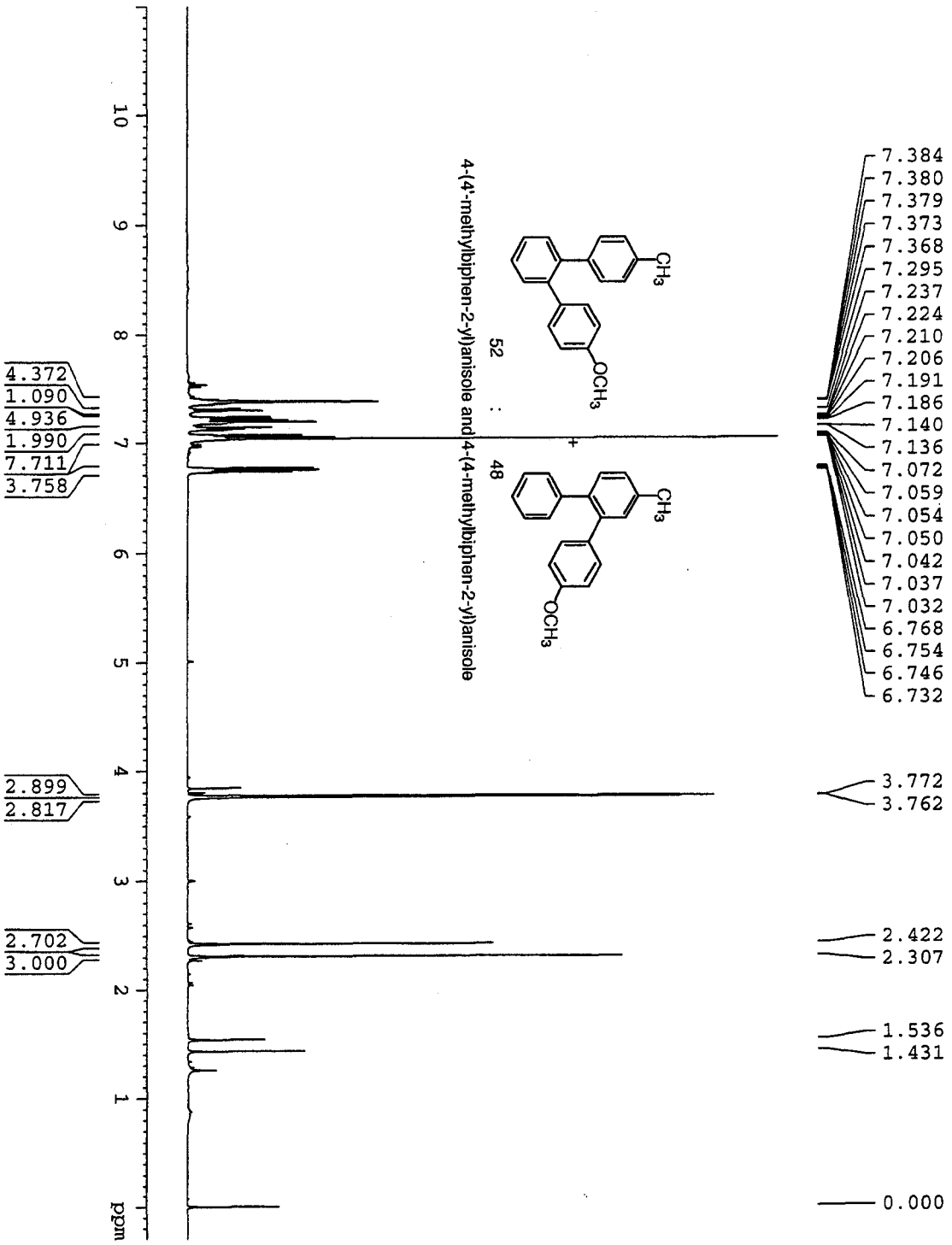

8.706
8.174
8.168
7.649
7.635
7.631
7.628
7.614
7.611
7.561
7.558
7.540
7.537
7.492
7.487
7.470
7.247
7.243
7.240
7.236
7.226
7.223
7.207
7.196
7.191
7.187
7.181
7.174
7.165
7.157
7.153
7.151
7.146
7.141
7.137
7.134
7.130
7.127
7.114
7.108
4.028
1.529
0.000
1.000
0.995
1.063
1.083
2.149
11.197
2.995
11
10
9
8
7
6
5
4
3
2
1
ppm
3-methoxy-9,10-diphenylphenanthrene
MeO
Ph
Ph

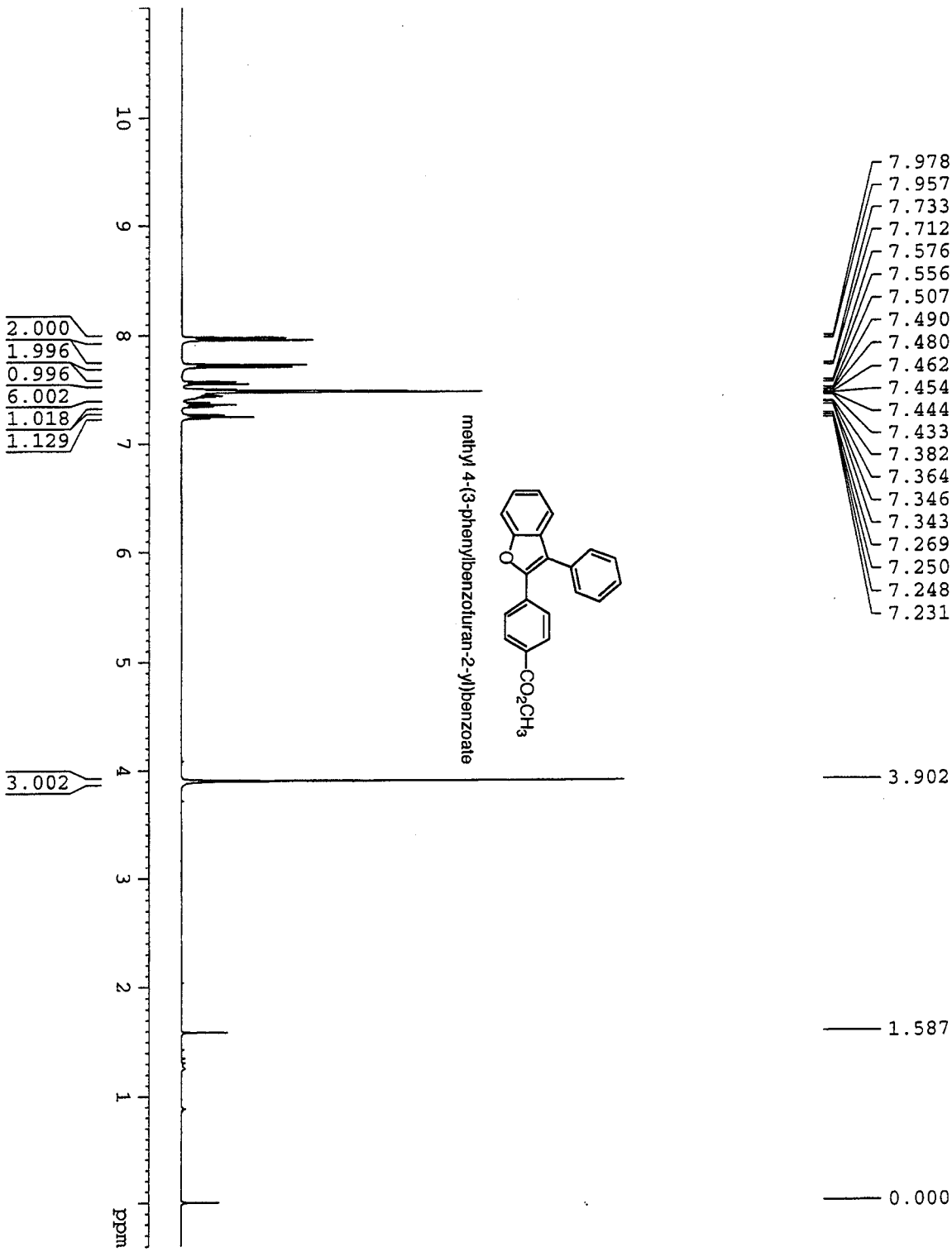

158.315
139.774
139.713
137.094
134.968
132.350
131.460
131.299
131.064
129.513
129.462
127.922
127.612
126.773
126.591
126.493
126.430
126.049
122.582
116.467
104.029
77.409
77.091
76.774
55.588
MeO
Ph
Ph
3-methoxy-9,10-diphenylphenanthrene
200
180
160
140
120
100
80
60
40
20
ppm

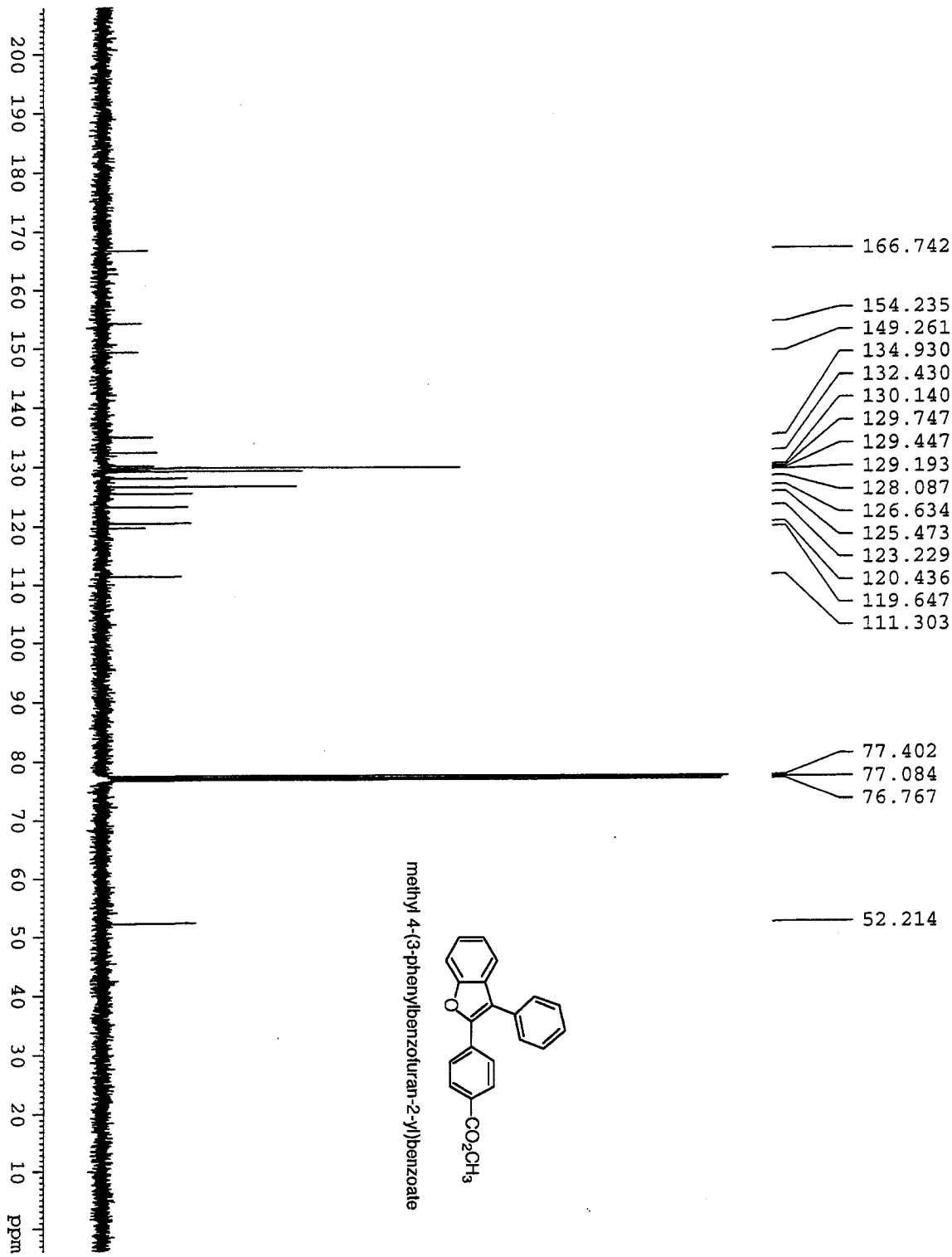

7.903
7.874
7.435
7.423
7.416
7.403
7.230
7.202
7.004
3.890
2.302
0.001
1.944
4.000
2.084
3.903
3.015
2.939
ppm
methyl 4-(4'-methylbiphen-2-yl)benzoate
CH3
CO2CH3

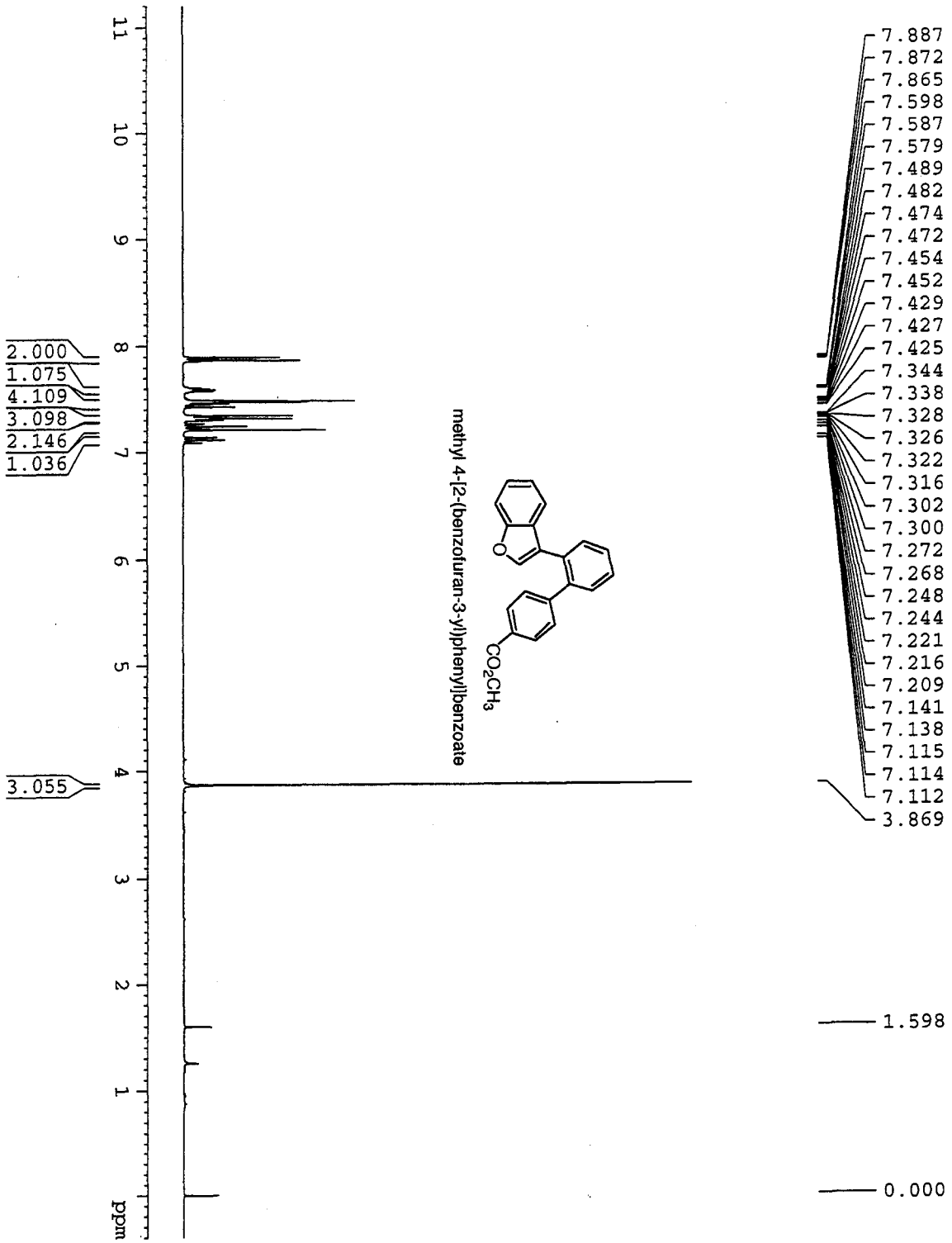

167.354
146.857
140.866
139.679
138.278
136.628
130.975
130.629
130.124
129.920
129.438
129.017
128.330
128.299
127.598
77.686
77.262
76.838
52.274
21.331
methyl 4-(4'-methylbiphen-2-yl)benzoate
CH3
CO2CH3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

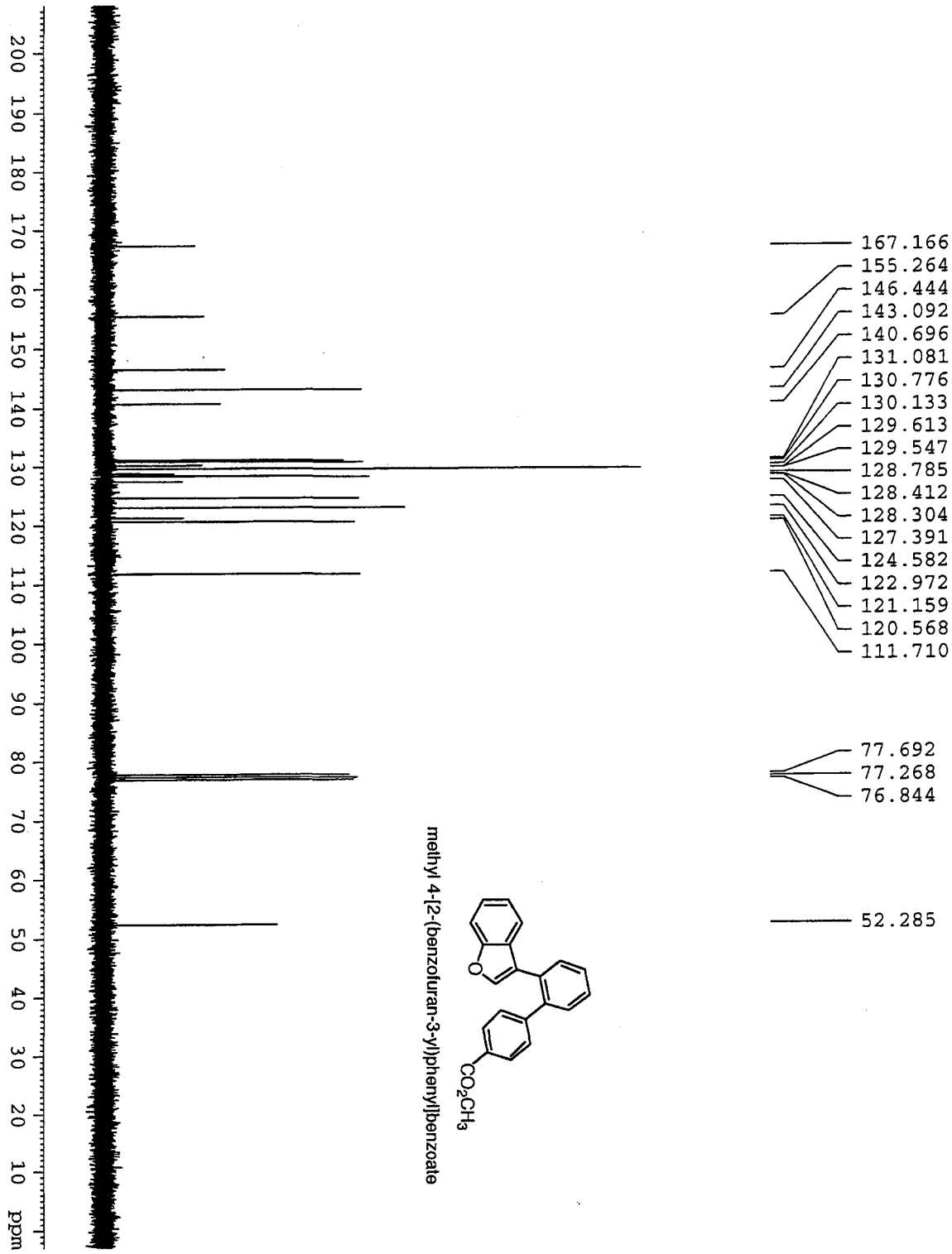

7.901
7.901
7.888
7.873
7.866
7.860
7.432
7.420
7.413
7.412
7.400
7.328
7.244
7.229
7.228
7.222
7.216
7.215
7.210
7.206
7.200
7.194
7.189
7.188
7.183
7.175
7.105
7.092
7.002
3.915
3.886
3.880
2.438
2.299
1.610
0.000
CH3
CO2CH3
+
CH3
CO2CH3
50 : 50
methyl 4-(4'-methylbiphen-2-yl)benzoate and methyl 4-(4-methylbiphen-2-yl)benzoate
10
9
8
7
6
5
4
3
2
1
ppm
3.544
0.676
6.330
1.374
2.622
0.822
2.004
2.040
1.936
2.000


4-(4'-methylbiphen-2-yl)anisole and 4-(4-methylbiphen-2-yl)anisole
52 : 48
CH3
OCH3
7.384
7.380
7.379
7.373
7.368
7.295
7.237
7.224
7.210
7.206
7.191
7.186
7.140
7.136
7.072
7.059
7.054
7.050
7.042
7.037
7.032
6.768
6.754
6.746
6.732
3.772
3.762
2.422
2.307
1.536
1.431
0.000
4.372
1.090
4.936
1.990
7.711
3.758
2.899
2.817
2.702
3.000
10
9
8
7
6
5
4
3
2
1
ppm

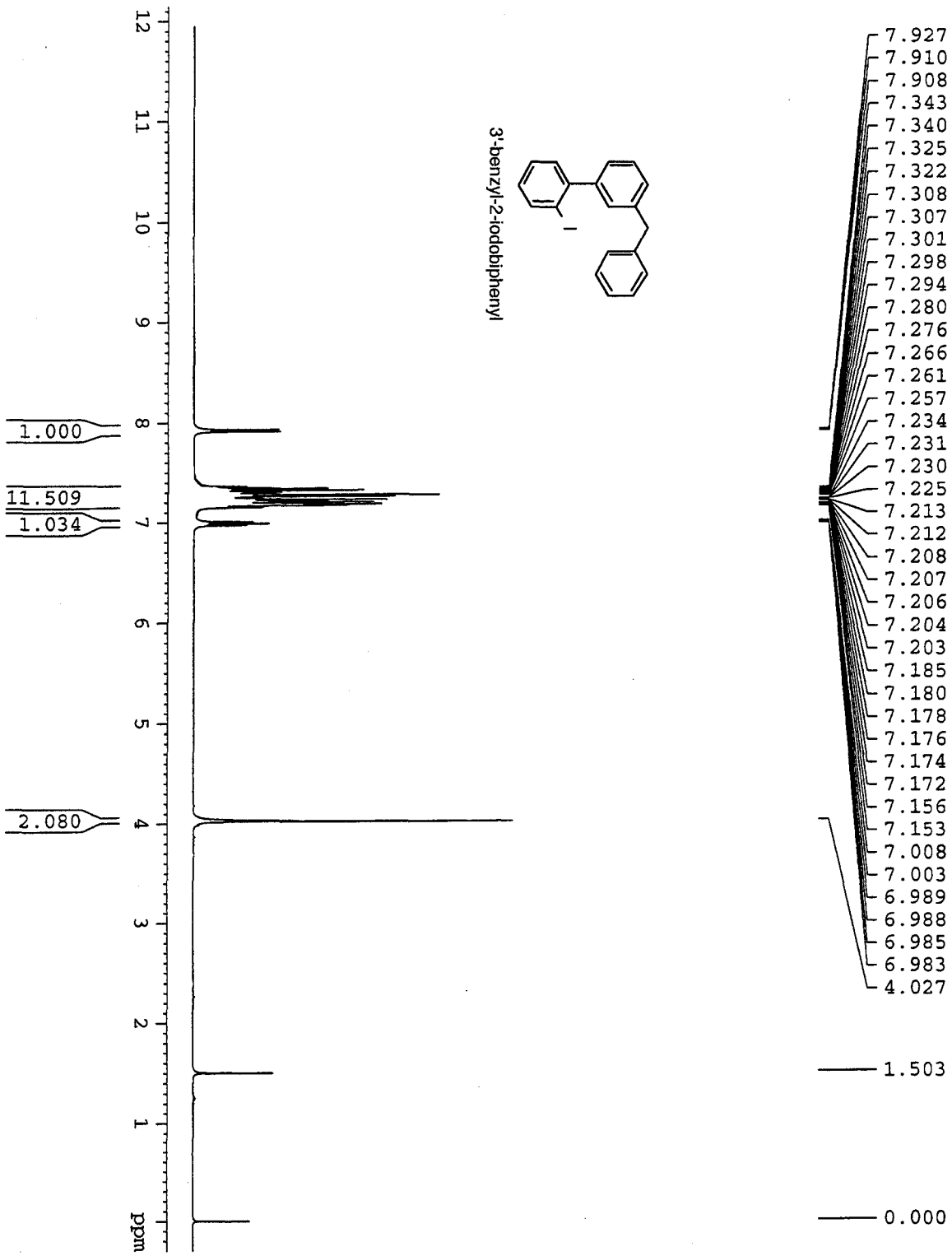

methyl 4-(3-phenylbenzofuran-2-yl)benzoate
CO_2CH_3
2.000
1.996
0.996
6.002
1.018
1.129
3.002
7.978
7.957
7.733
7.712
7.576
7.556
7.507
7.490
7.480
7.462
7.454
7.444
7.433
7.382
7.364
7.346
7.343
7.269
7.250
7.248
7.231
3.902
1.587
0.000
ppm

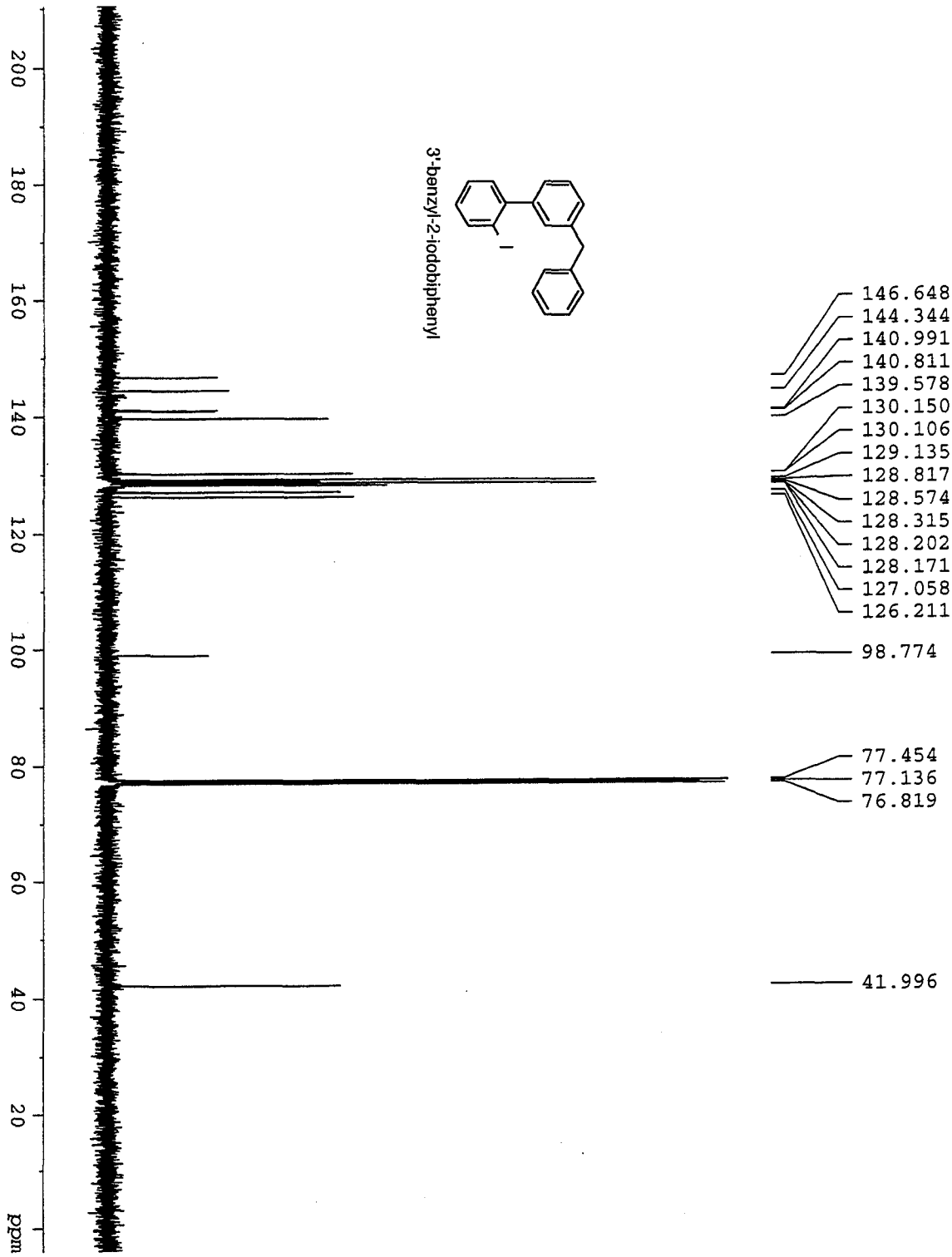

166.742
154.235
149.261
134.930
132.430
130.140
129.747
129.447
129.193
128.087
126.634
125.473
123.229
120.436
119.647
111.303
77.402
77.084
76.767
52.214
methyl 4-(3-phenylbenzofuran-2-yl)benzoate
CO2CH3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

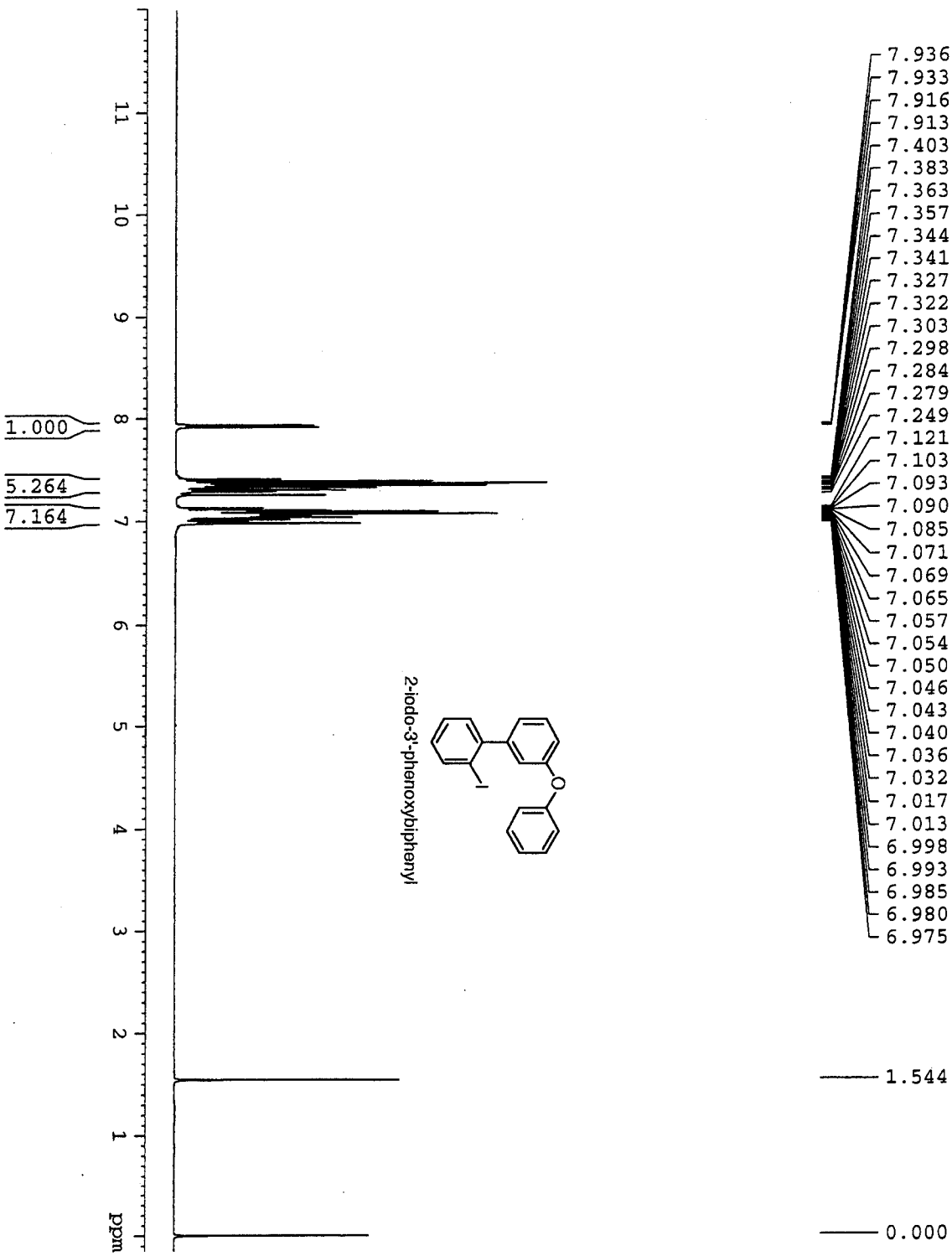

methyl 4-[2-(benzofuran-3-yl)phenyl]benzoate
CO2CH3
O
2.000
1.075
4.109
3.098
2.146
1.036
3.055
7.887
7.872
7.865
7.598
7.587
7.579
7.489
7.482
7.474
7.472
7.454
7.452
7.429
7.427
7.425
7.344
7.338
7.328
7.326
7.322
7.316
7.302
7.300
7.272
7.268
7.248
7.244
7.221
7.216
7.209
7.141
7.138
7.115
7.114
7.112
3.869
1.598
0.000
11
10
9
8
7
6
5
4
3
2
1
ppm

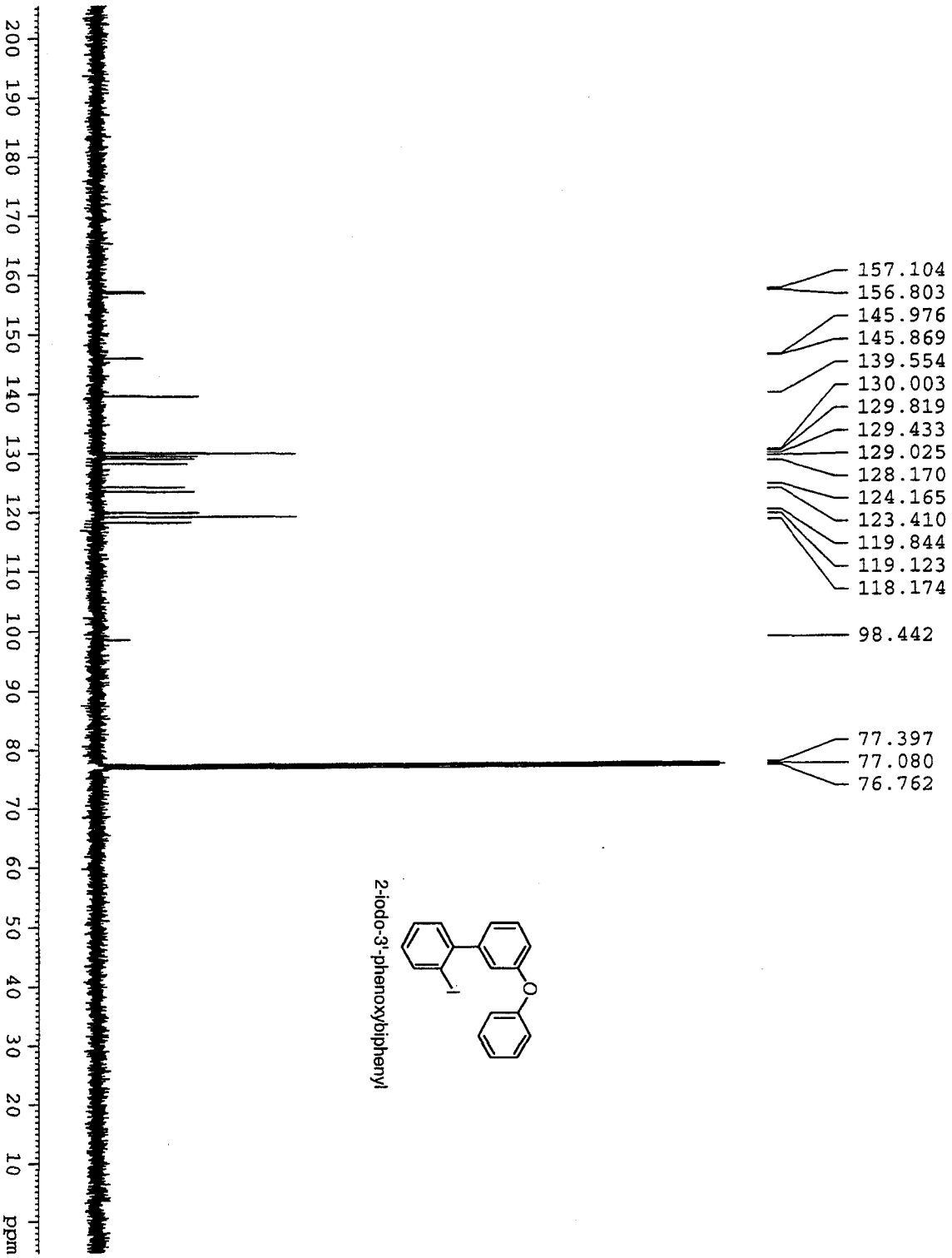

167.166
155.264
146.444
143.092
140.696
131.081
130.776
130.133
129.613
129.547
128.785
128.412
128.304
127.391
124.582
122.972
121.159
120.568
111.710
77.692
77.268
76.844
52.285
methyl 4-[2-(benzofuran-3-yl)phenyl]benzoate
CO2CH3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

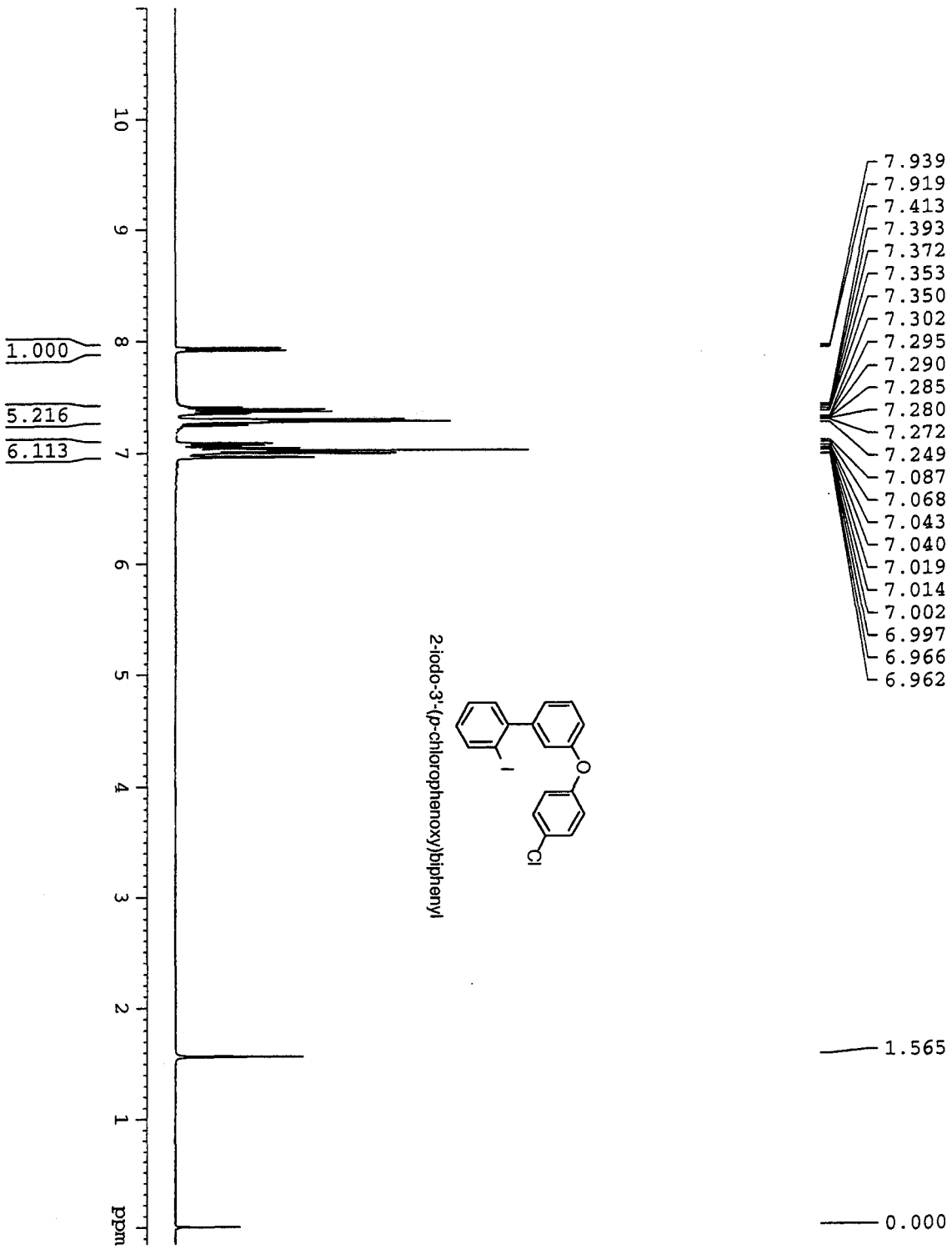
APPENDIX C. CHAPTER 3 ^{1}H AND ^{13}C NMR SPECTRA

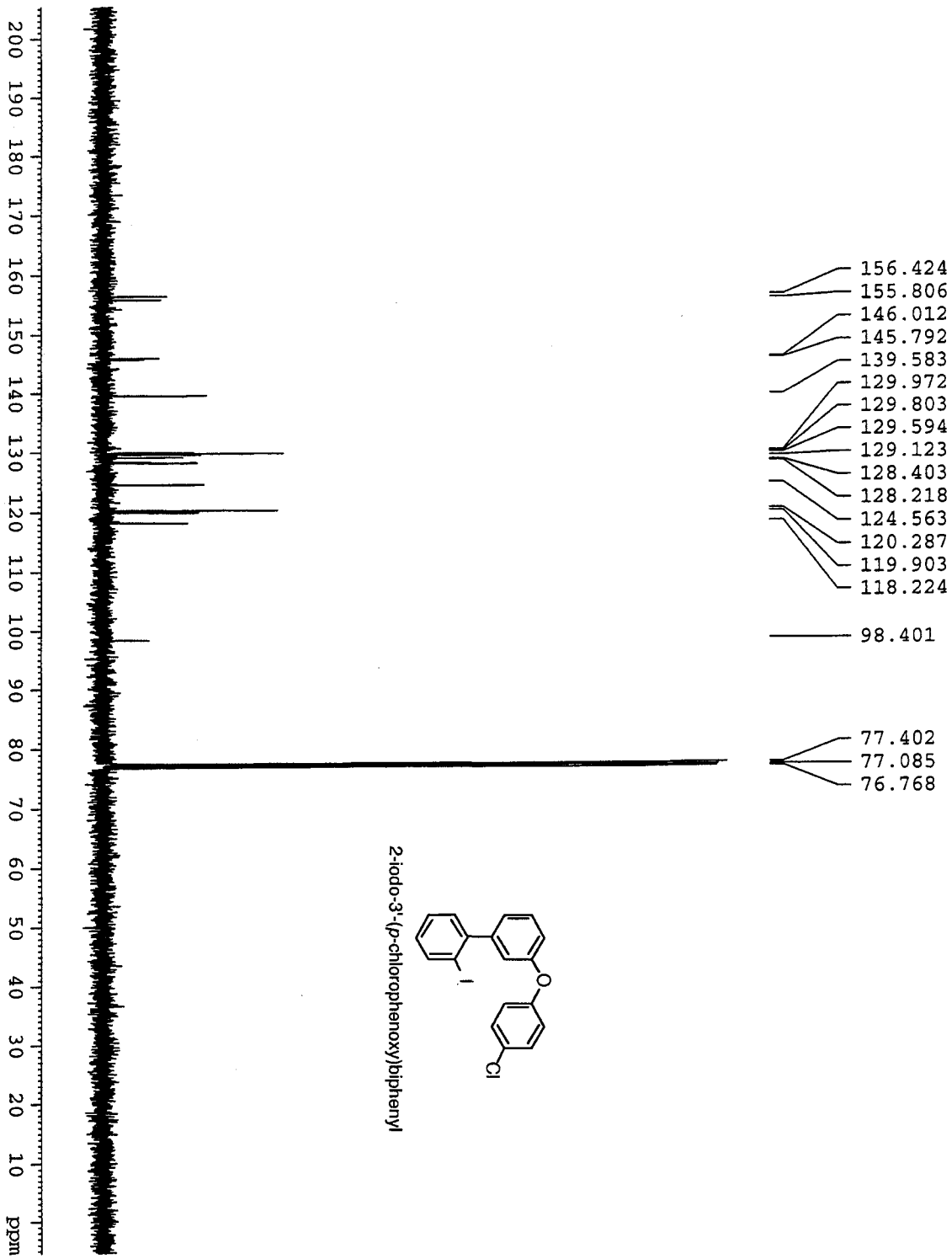

3'-benzyl-2-iodobiphenyl
I
1.000
11.509
1.034
2.080
12
11
10
9
8
7
6
5
4
3
2
1
ppm
7.927
7.910
7.908
7.343
7.340
7.325
7.322
7.308
7.307
7.301
7.298
7.294
7.280
7.276
7.266
7.261
7.257
7.234
7.231
7.230
7.225
7.213
7.212
7.208
7.207
7.206
7.204
7.203
7.185
7.180
7.178
7.176
7.174
7.172
7.156
7.153
7.008
7.003
6.989
6.988
6.985
6.983
4.027
1.503
0.000

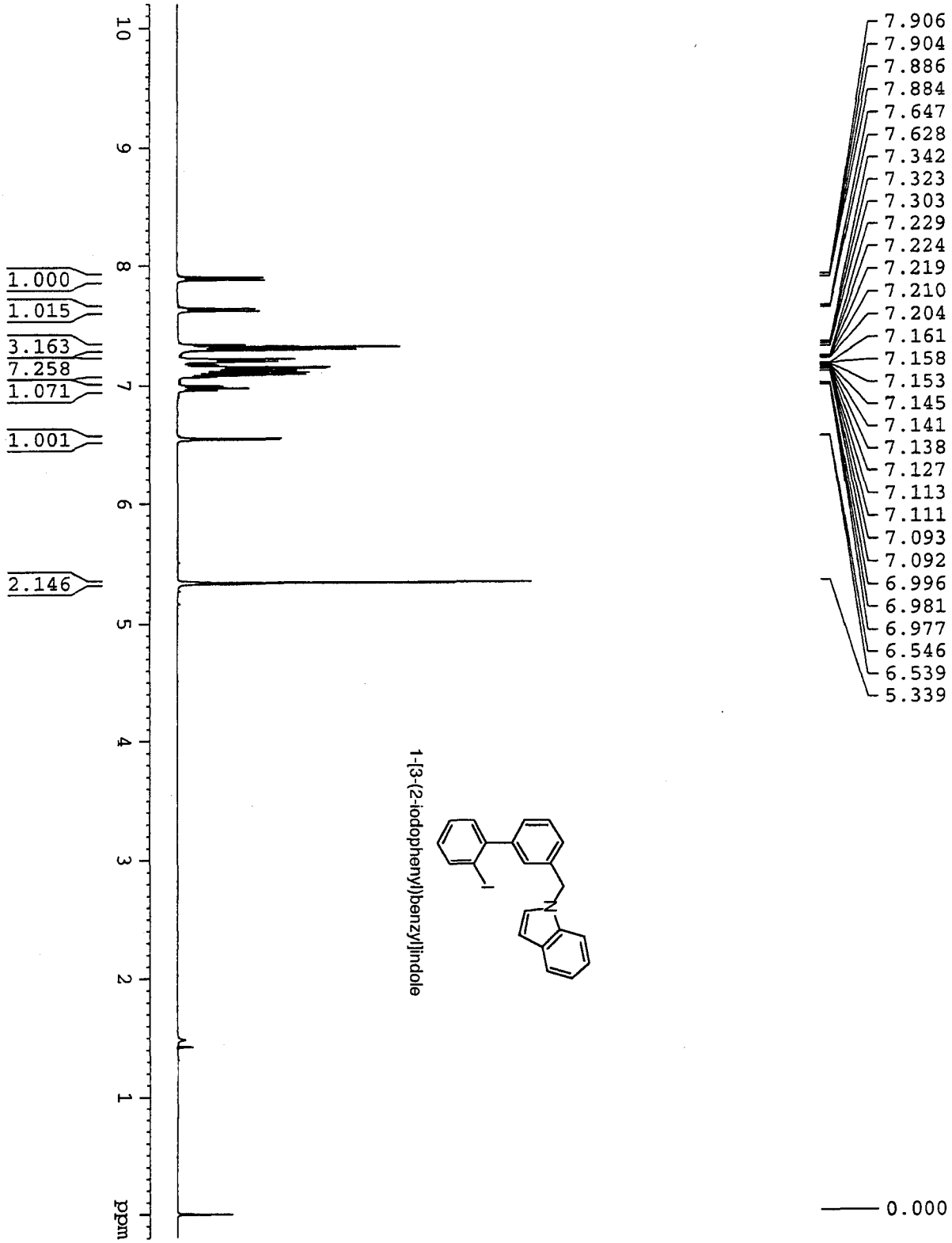

3'-benzyl-2-iodobiphenyl
I
146.648
144.344
140.991
140.811
139.578
130.150
130.106
129.135
128.817
128.574
128.315
128.202
128.171
127.058
126.211
98.774
77.454
77.136
76.819
41.996
200
180
160
140
120
100
80
60
40
20
ppm

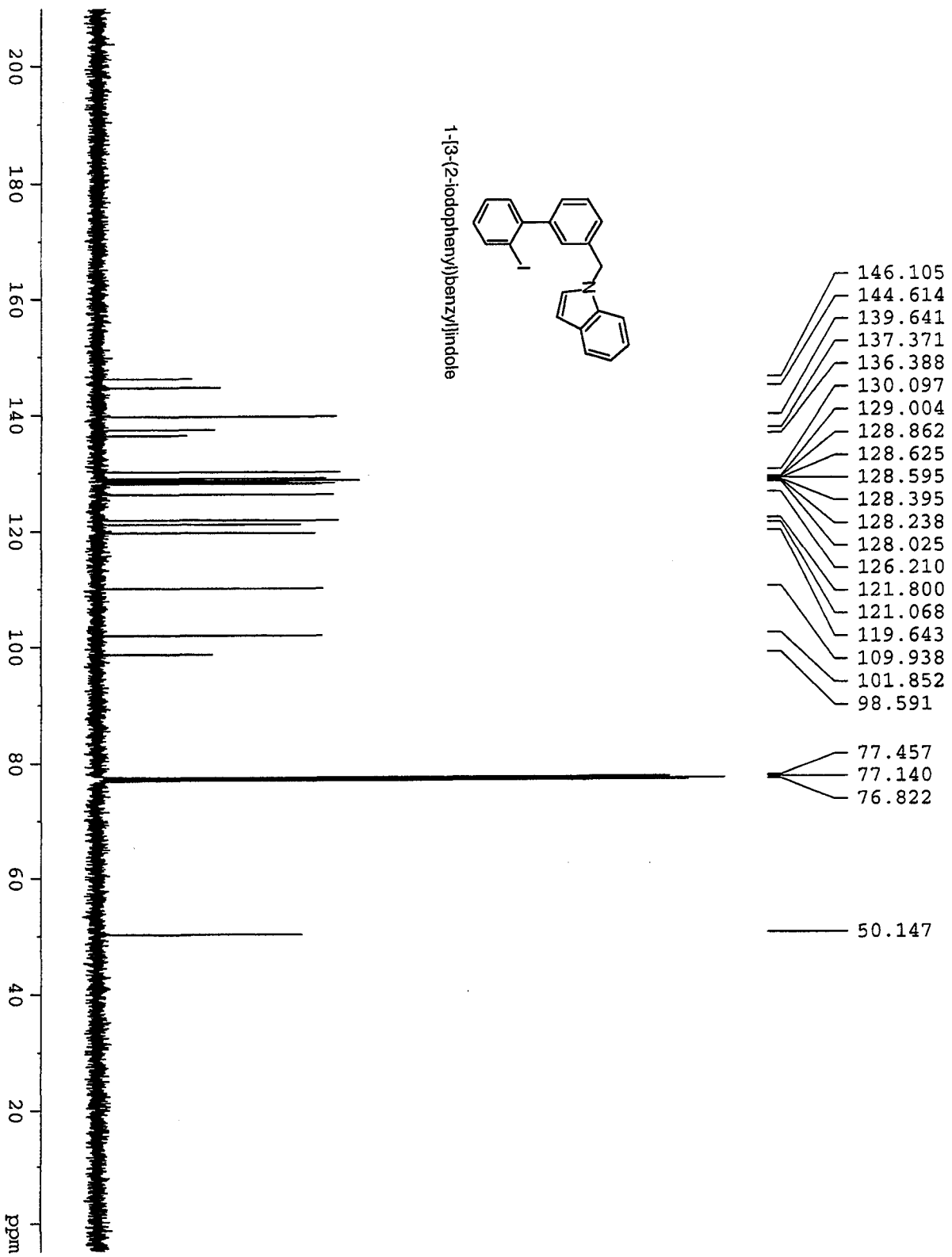

7.936
7.933
7.916
7.913
7.403
7.383
7.363
7.357
7.344
7.341
7.327
7.322
7.303
7.298
7.284
7.279
7.249
7.121
7.103
7.093
7.090
7.085
7.071
7.069
7.065
7.057
7.054
7.050
7.046
7.043
7.040
7.036
7.032
7.017
7.013
6.998
6.993
6.985
6.980
6.975
1.544
0.000
1.000
5.264
7.164
2-iodo-3'-phenoxybiphenyl
I
O
ppm

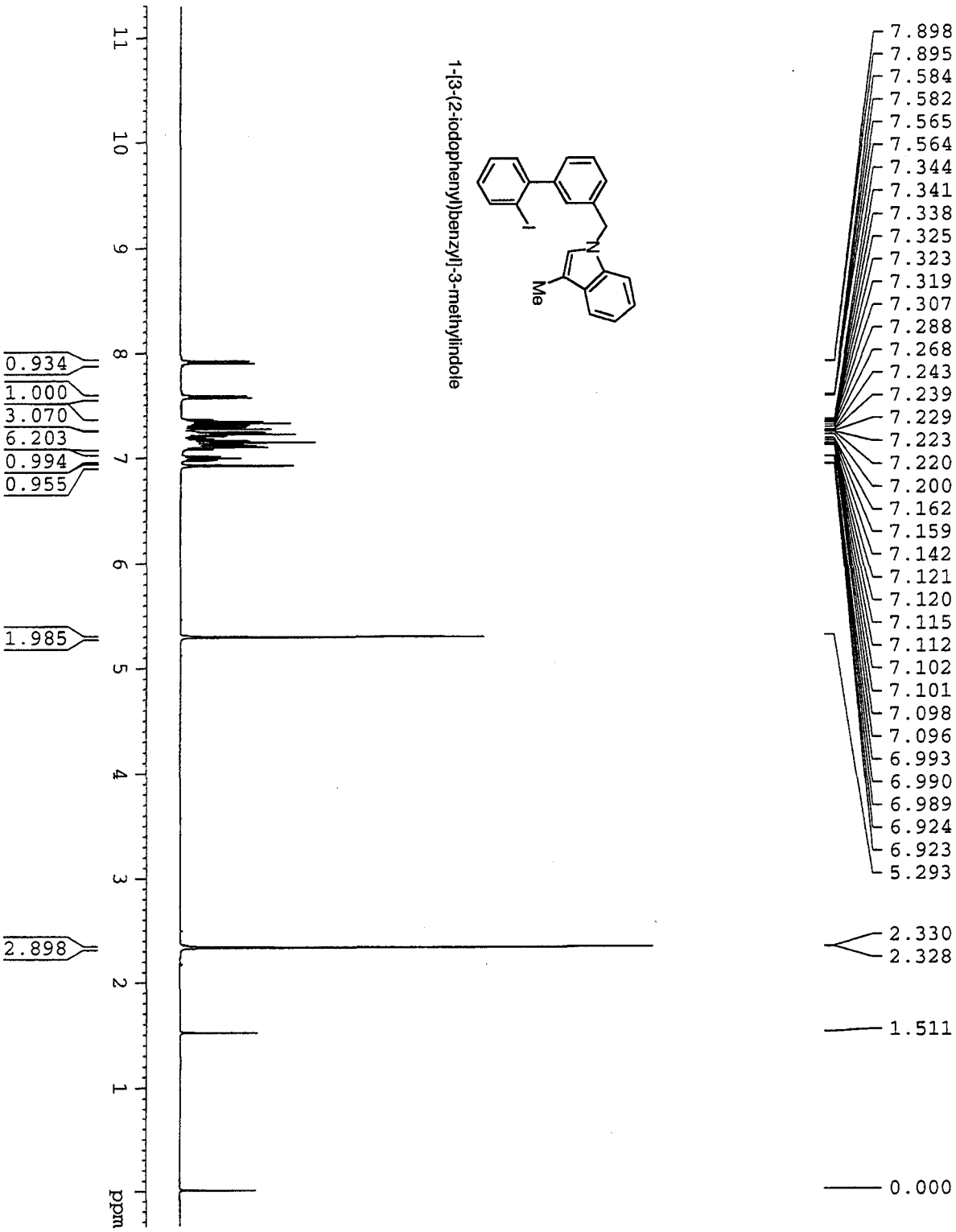

157.104
156.803
145.976
145.869
139.554
130.003
129.819
129.433
129.025
128.170
124.165
123.410
119.844
119.123
118.174
98.442
77.397
77.080
76.762
2-iodo-3'-phenoxybiphenyl
I
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

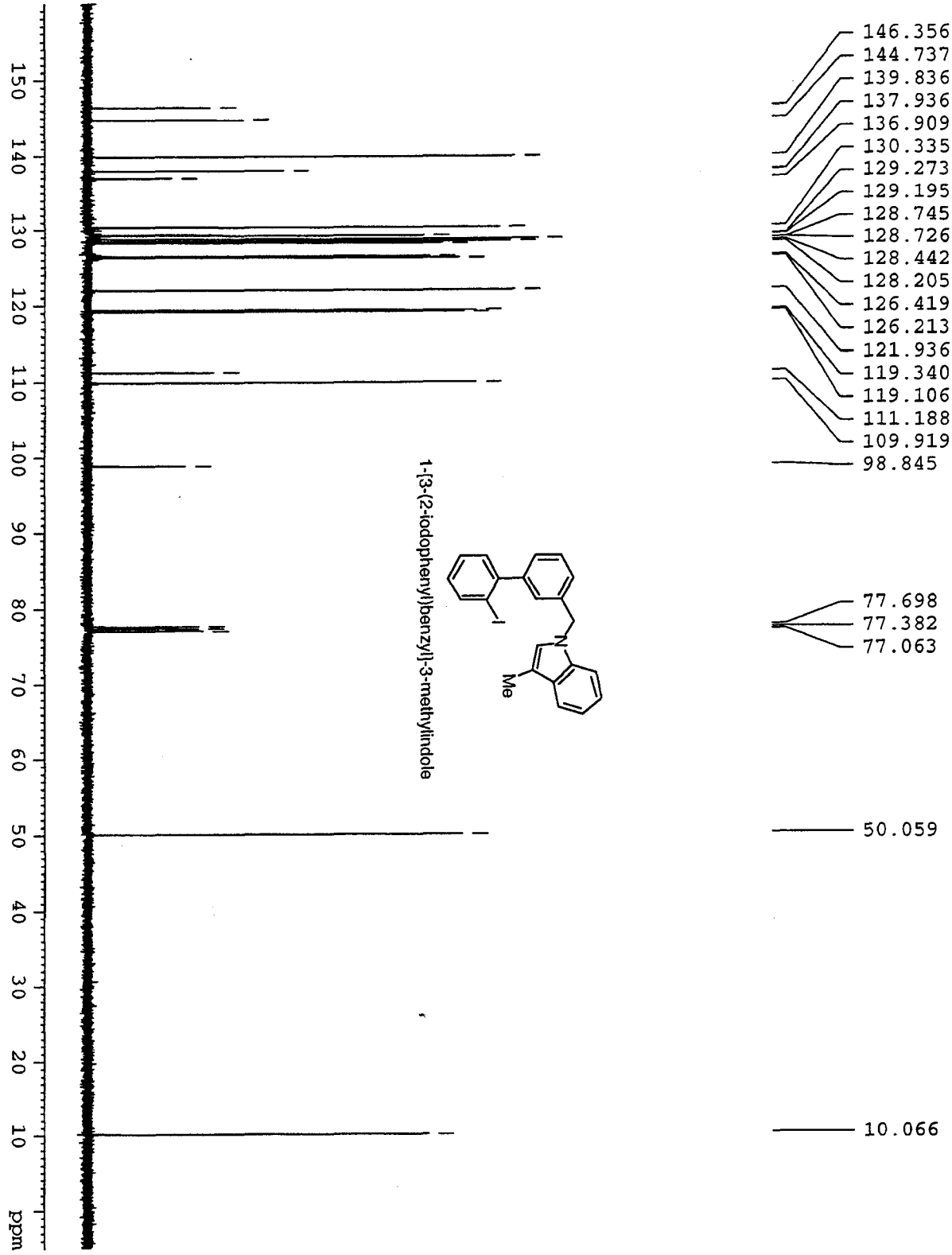

7.939
7.919
7.413
7.393
7.372
7.353
7.350
7.302
7.295
7.290
7.285
7.280
7.272
7.249
7.087
7.068
7.043
7.040
7.019
7.014
7.002
6.997
6.966
6.962
1.565
0.000
1.000
5.216
6.113
10
9
8
7
6
5
4
3
2
1
ppm
2-iodo-3'-(p-chlorophenoxy)biphenyl
O
I
Cl

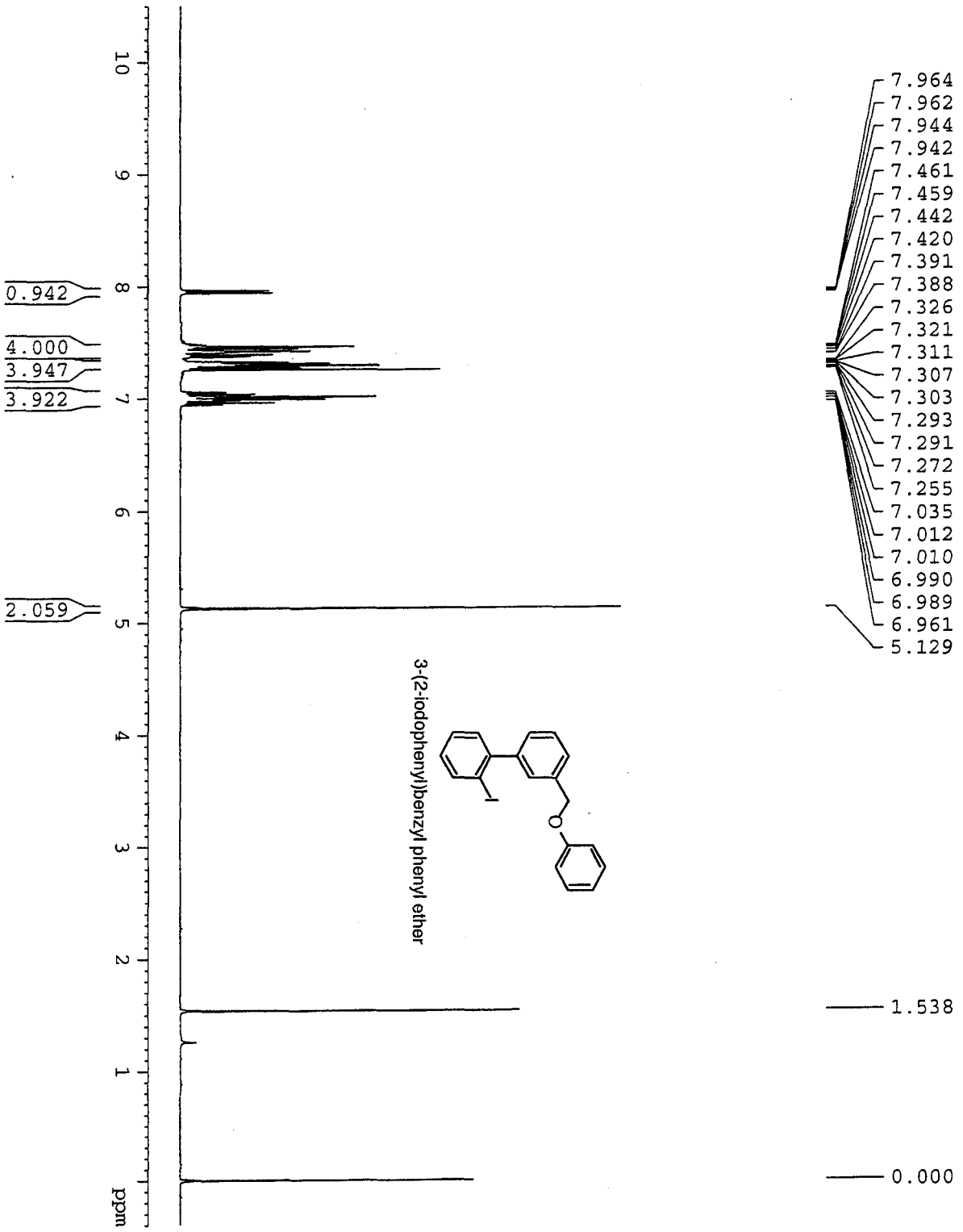

156.424
155.806
146.012
145.792
139.583
129.972
129.803
129.594
129.123
128.403
128.218
124.563
120.287
119.903
118.224
98.401
77.402
77.085
76.768
2-iodo-3'-(p-chlorophenoxy)biphenyl
I
O
Cl
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

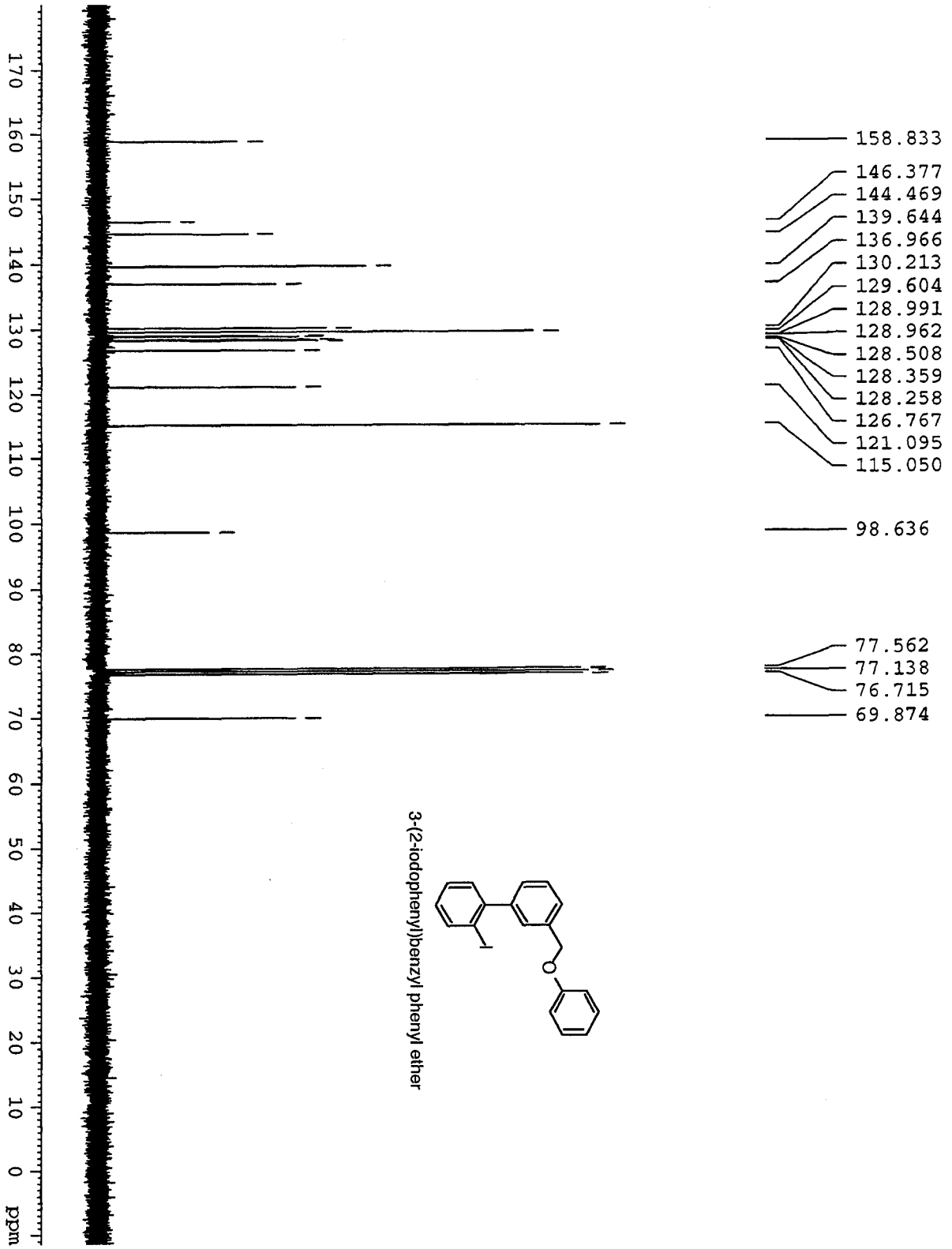

1.000
1.015
3.163
7.258
1.071
1.001
2.146
10
9
8
7
6
5
4
3
2
1
ppm
7.906
7.904
7.886
7.884
7.647
7.628
7.342
7.323
7.303
7.229
7.224
7.219
7.210
7.204
7.161
7.158
7.153
7.145
7.141
7.138
7.127
7.113
7.111
7.093
7.092
6.996
6.981
6.977
6.546
6.539
5.339
0.000
1-[3-(2-iodophenyl)benzyl]indole

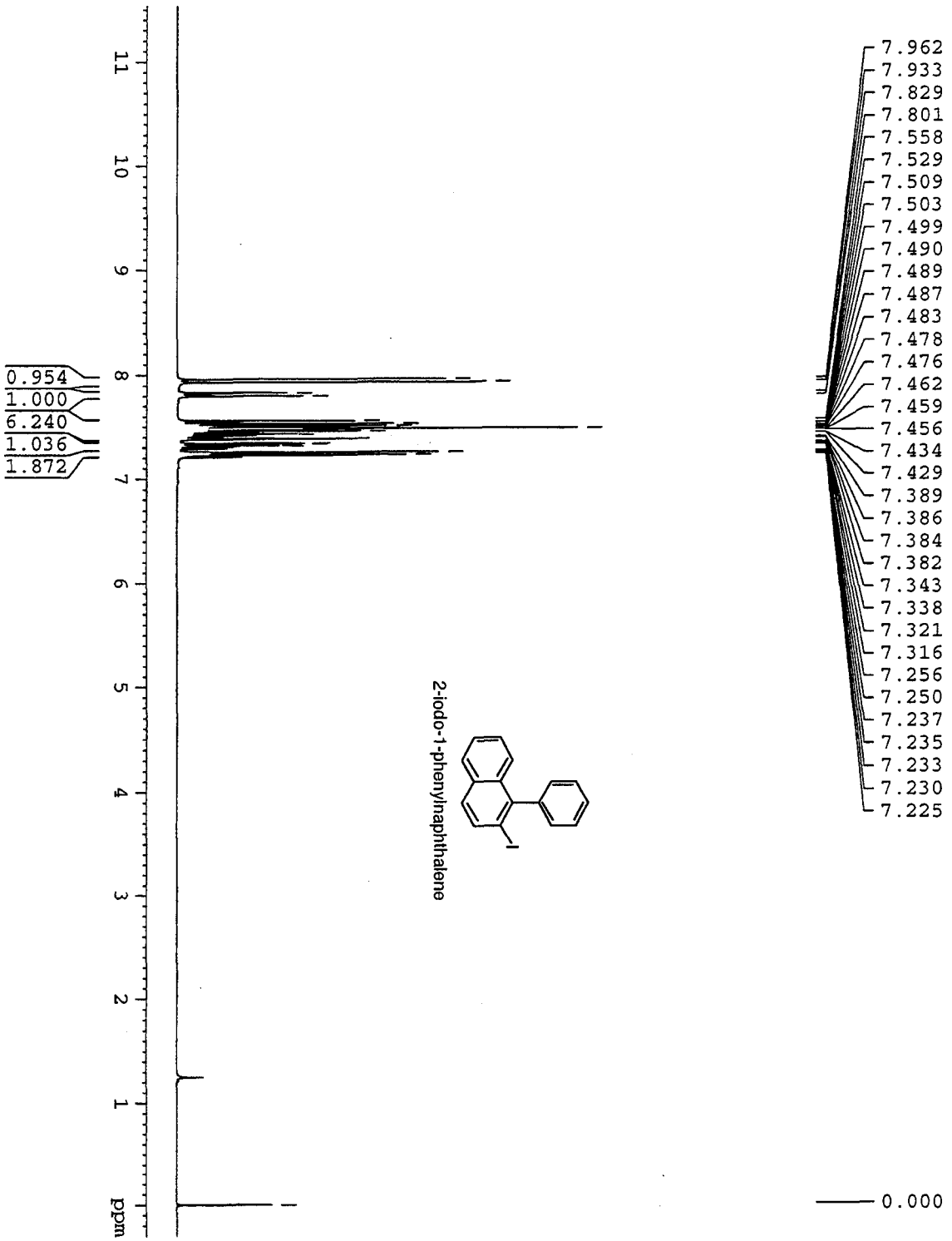

1-[3-(2-iodophenyl)benzyl]indole
146.105
144.614
139.641
137.371
136.388
130.097
129.004
128.862
128.625
128.595
128.395
128.238
128.025
126.210
121.800
121.068
119.643
109.938
101.852
98.591
77.457
77.140
76.822
50.147
200
180
160
140
120
100
80
60
40
20
ppm

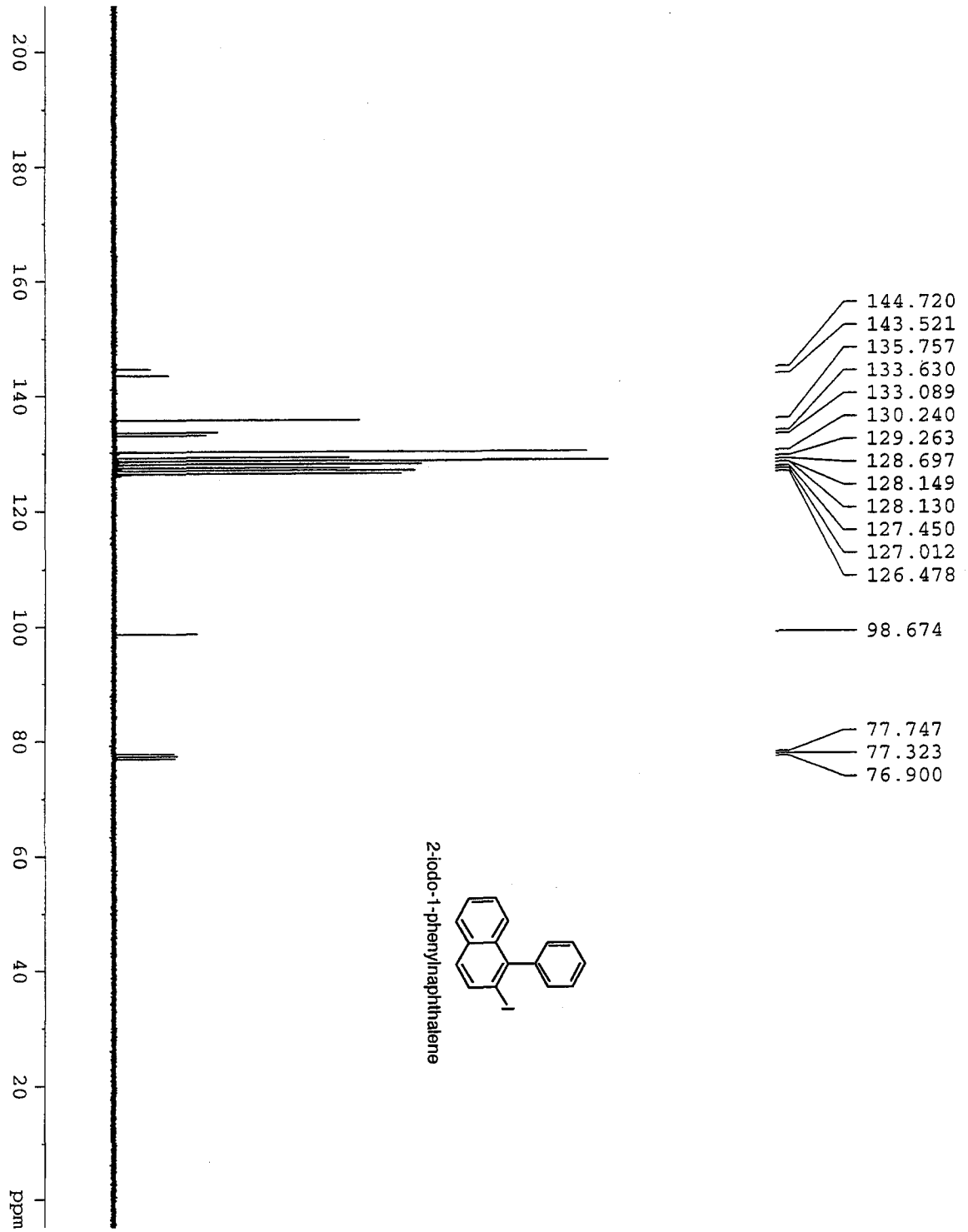

1-[3-(2-iodophenyl)benzyl]-3-methylindole
I
N
Me
0.934
1.000
3.070
6.203
0.994
0.955
1.985
2.898
11
10
9
8
7
6
5
4
3
2
1
ppm
7.898
7.895
7.584
7.582
7.565
7.564
7.344
7.341
7.338
7.325
7.323
7.319
7.307
7.288
7.268
7.243
7.239
7.229
7.223
7.220
7.200
7.162
7.159
7.142
7.121
7.120
7.115
7.112
7.102
7.101
7.098
7.096
6.993
6.990
6.989
6.924
6.923
5.293
2.330
2.328
1.511
0.000

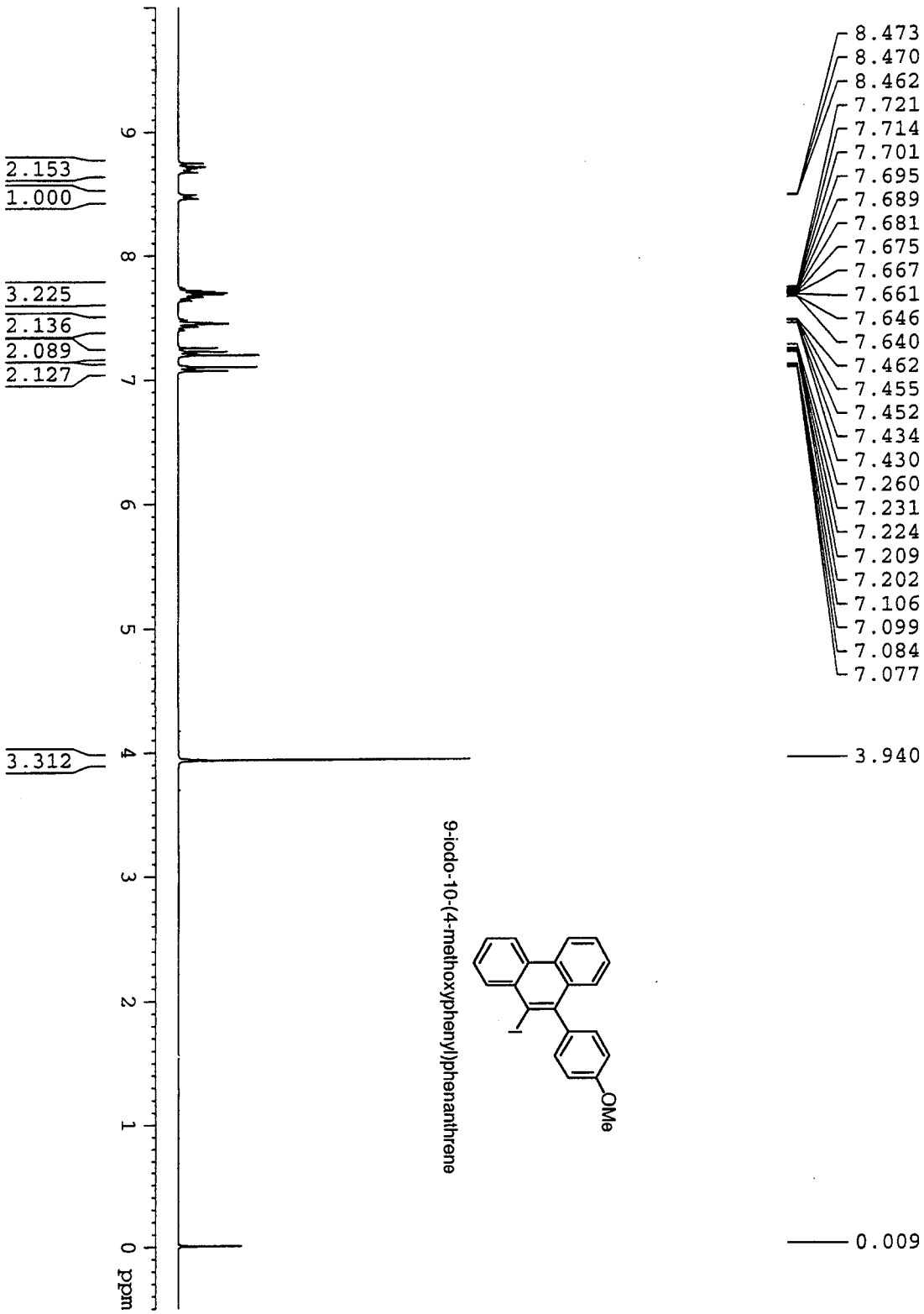

146.356
144.737
139.836
137.936
136.909
130.335
129.273
129.195
128.745
128.726
128.442
128.205
126.419
126.213
121.936
119.340
119.106
111.188
109.919
98.845
77.698
77.382
77.063
50.059
10.066
1-[3-(2-iodophenyl)benzyl]-3-methylindole
Me
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

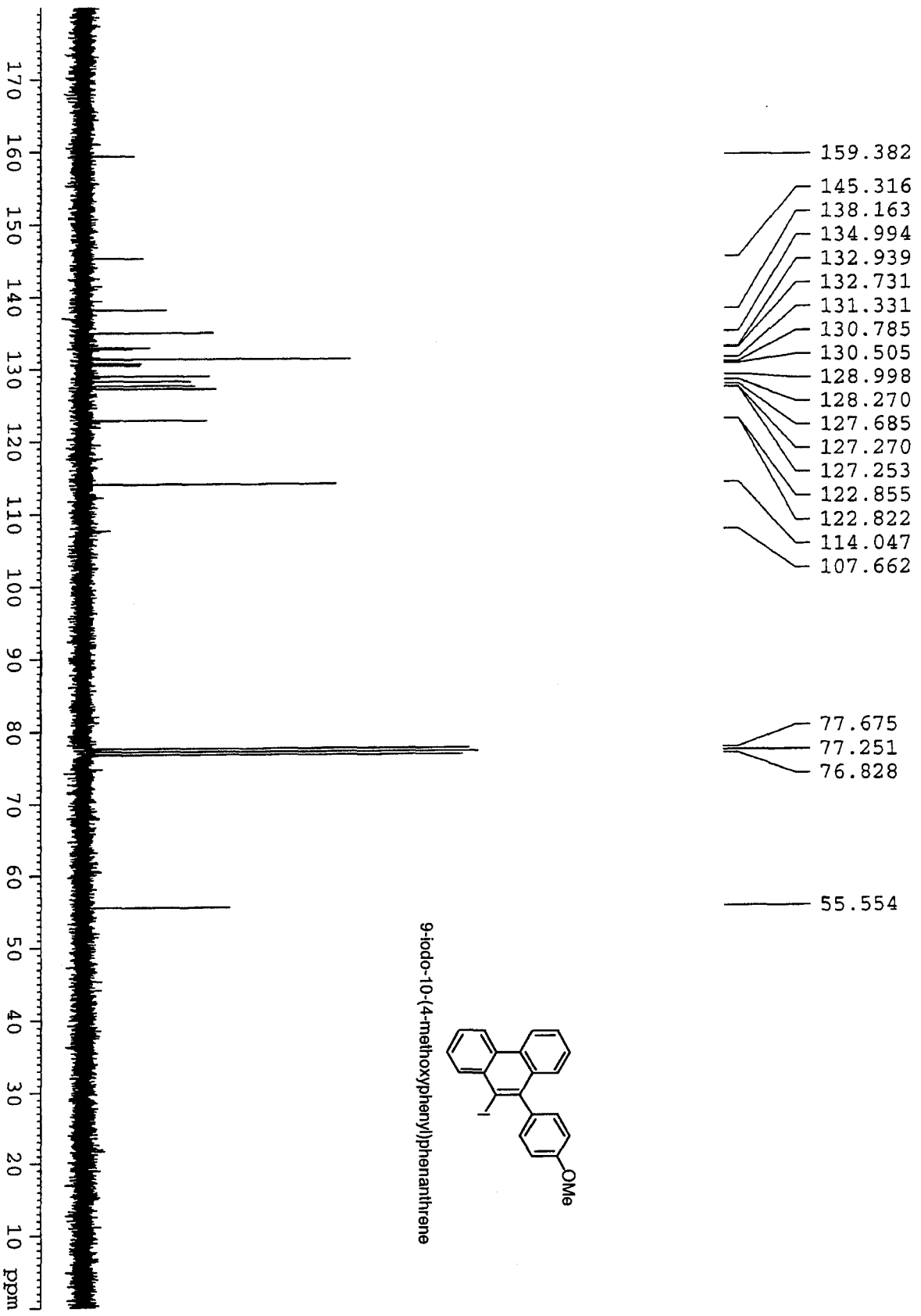

7.964
7.962
7.944
7.942
7.461
7.459
7.442
7.420
7.391
7.388
7.326
7.321
7.311
7.307
7.303
7.293
7.291
7.272
7.255
7.035
7.012
7.010
6.990
6.989
6.961
5.129
0.942
4.000
3.947
3.922
2.059
1.538
0.000
3-(2-iodophenyl)benzyl phenyl ether
ppm

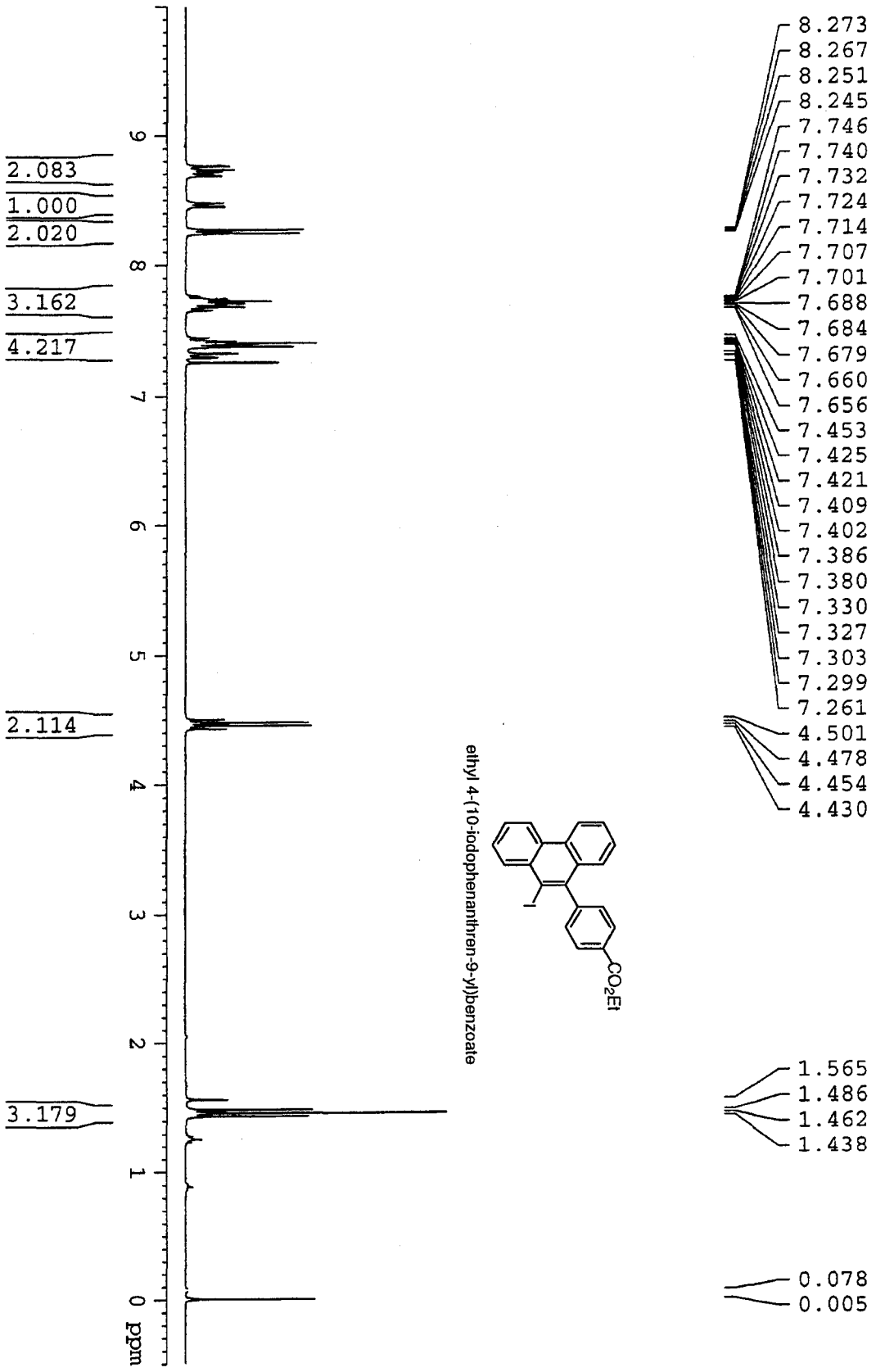

158.833
146.377
144.469
139.644
136.966
130.213
129.604
128.991
128.962
128.508
128.359
128.258
126.767
121.095
115.050
98.636
77.562
77.138
76.715
69.874
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
3-(2-iodophenyl)benzyl phenyl ether

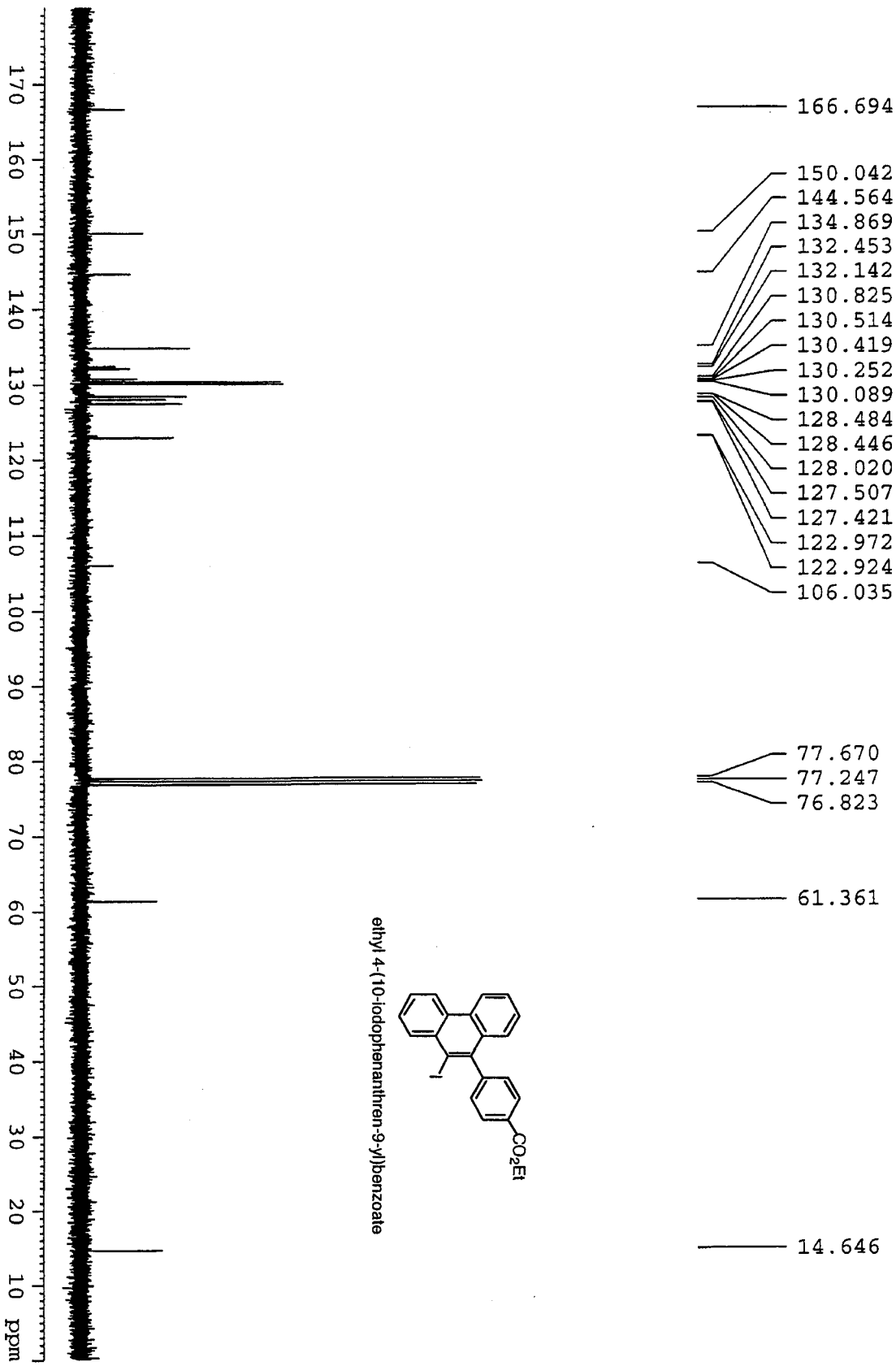

0.954
1.000
6.240
1.036
1.872
11
10
9
8
7
6
5
4
3
2
1
ppm
2-iodo-1-phenylnaphthalene
7.962
7.933
7.829
7.801
7.558
7.529
7.509
7.503
7.499
7.490
7.489
7.487
7.483
7.478
7.476
7.462
7.459
7.456
7.434
7.429
7.389
7.386
7.384
7.382
7.343
7.338
7.321
7.316
7.256
7.250
7.237
7.235
7.233
7.230
7.225
0.000

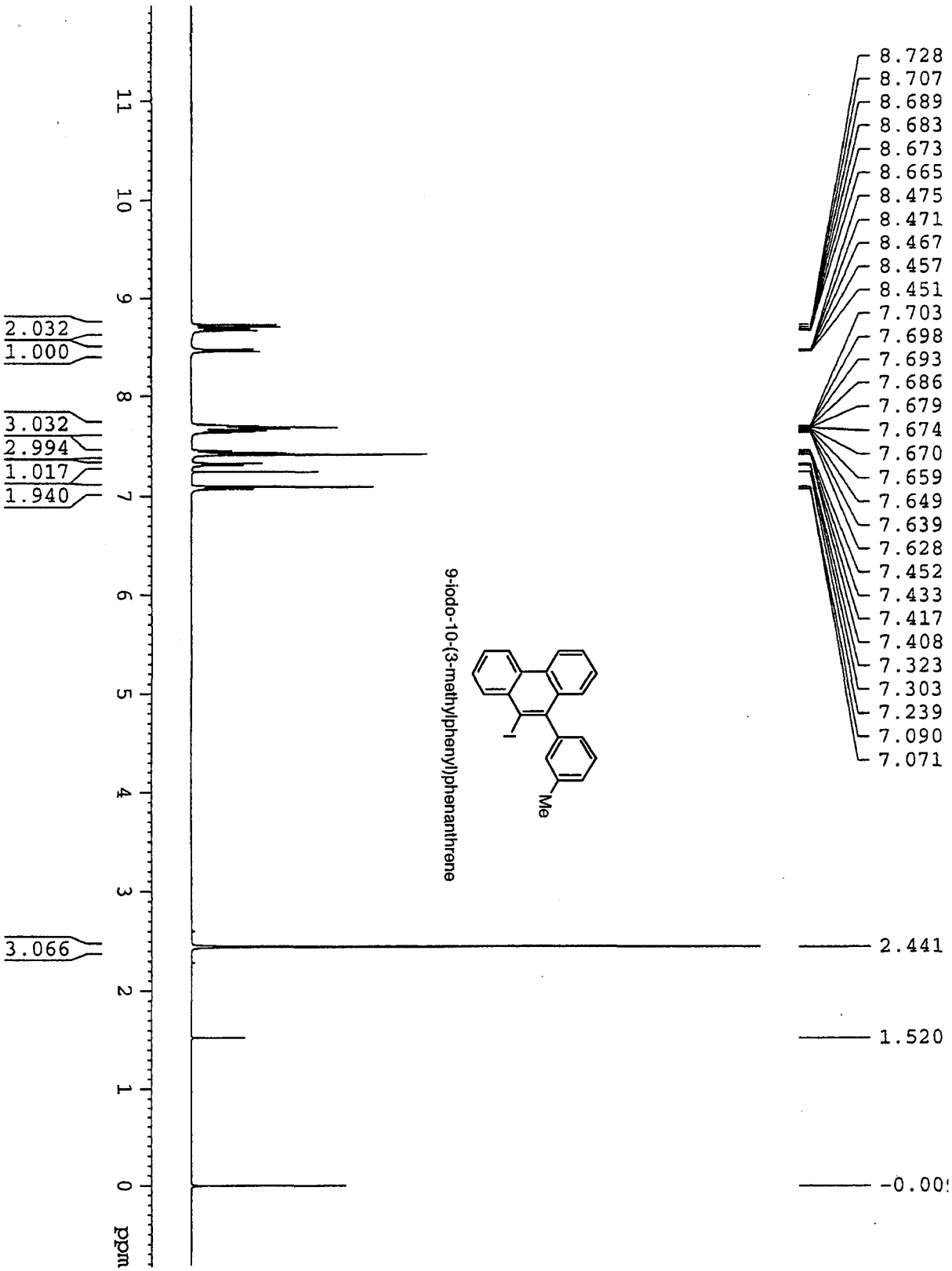

200
180
160
140
120
100
80
60
40
20
ppm
144.720
143.521
135.757
133.630
133.089
130.240
129.263
128.697
128.149
128.130
127.450
127.012
126.478
98.674
77.747
77.323
76.900
2-iodo-1-phenylnaphthalene
I

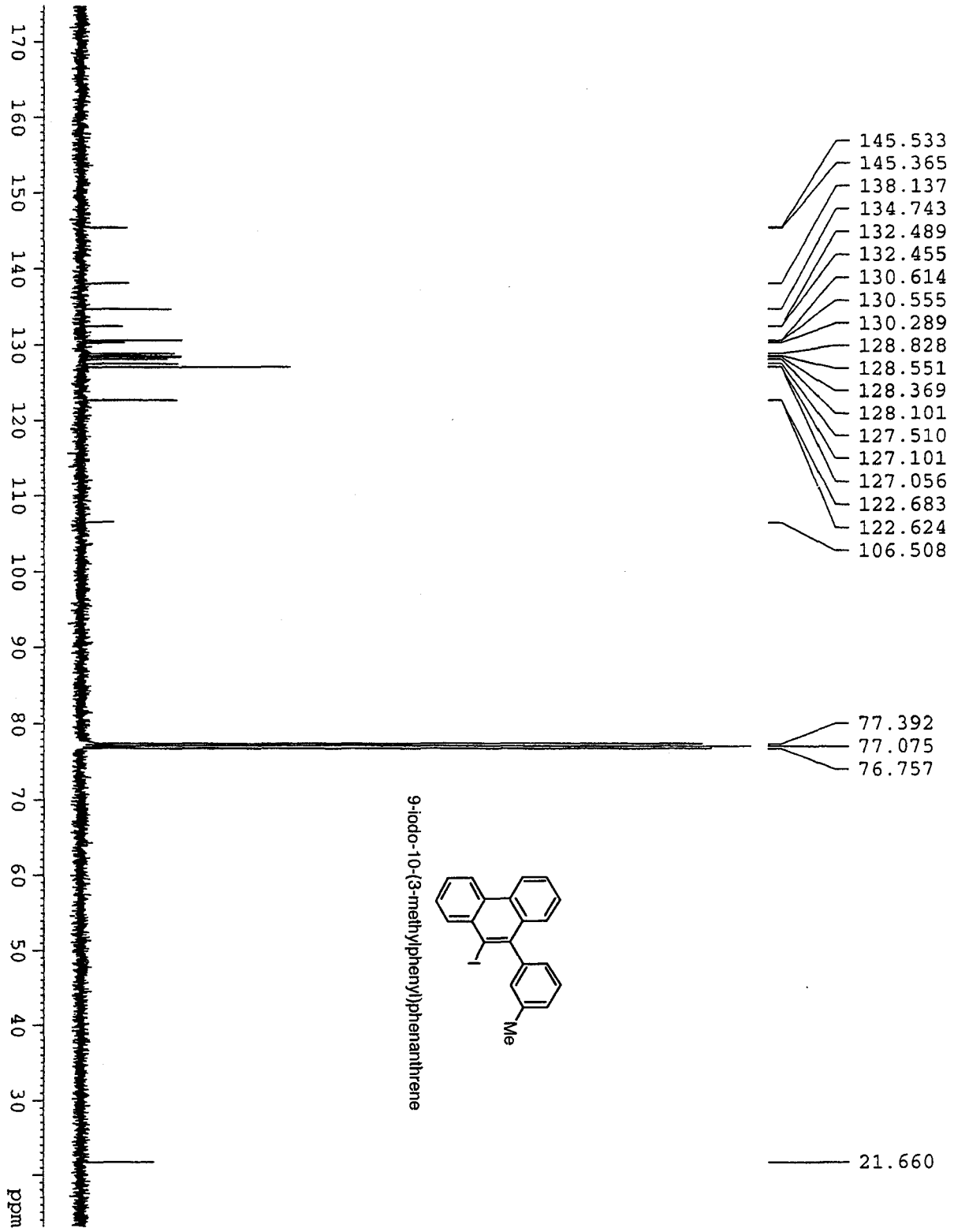

8.473
8.470
8.462
7.721
7.714
7.701
7.695
7.689
7.681
7.675
7.667
7.661
7.646
7.640
7.462
7.455
7.452
7.434
7.430
7.260
7.231
7.224
7.209
7.202
7.106
7.099
7.084
7.077
3.940
0.009
2.153
1.000
3.225
2.136
2.089
2.127
3.312
9-iodo-10-(4-methoxyphenyl)phenanthrene
OMe
I
ppm

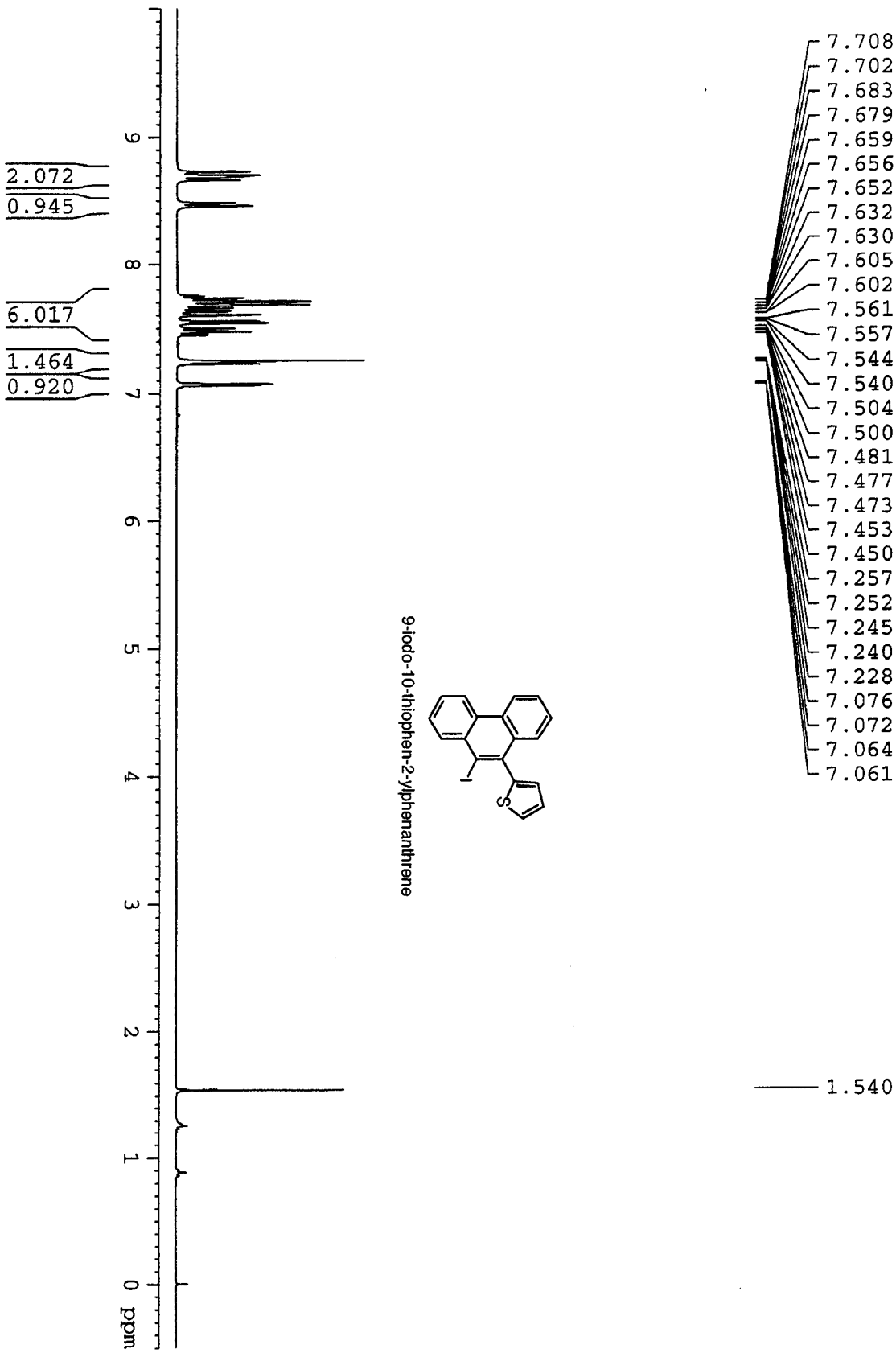

159.382
145.316
138.163
134.994
132.939
132.731
131.331
130.785
130.505
128.998
128.270
127.685
127.270
127.253
122.855
122.822
114.047
107.662
77.675
77.251
76.828
55.554
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
9-iodo-10-(4-methoxyphenyl)phenanthrene
I
OMe

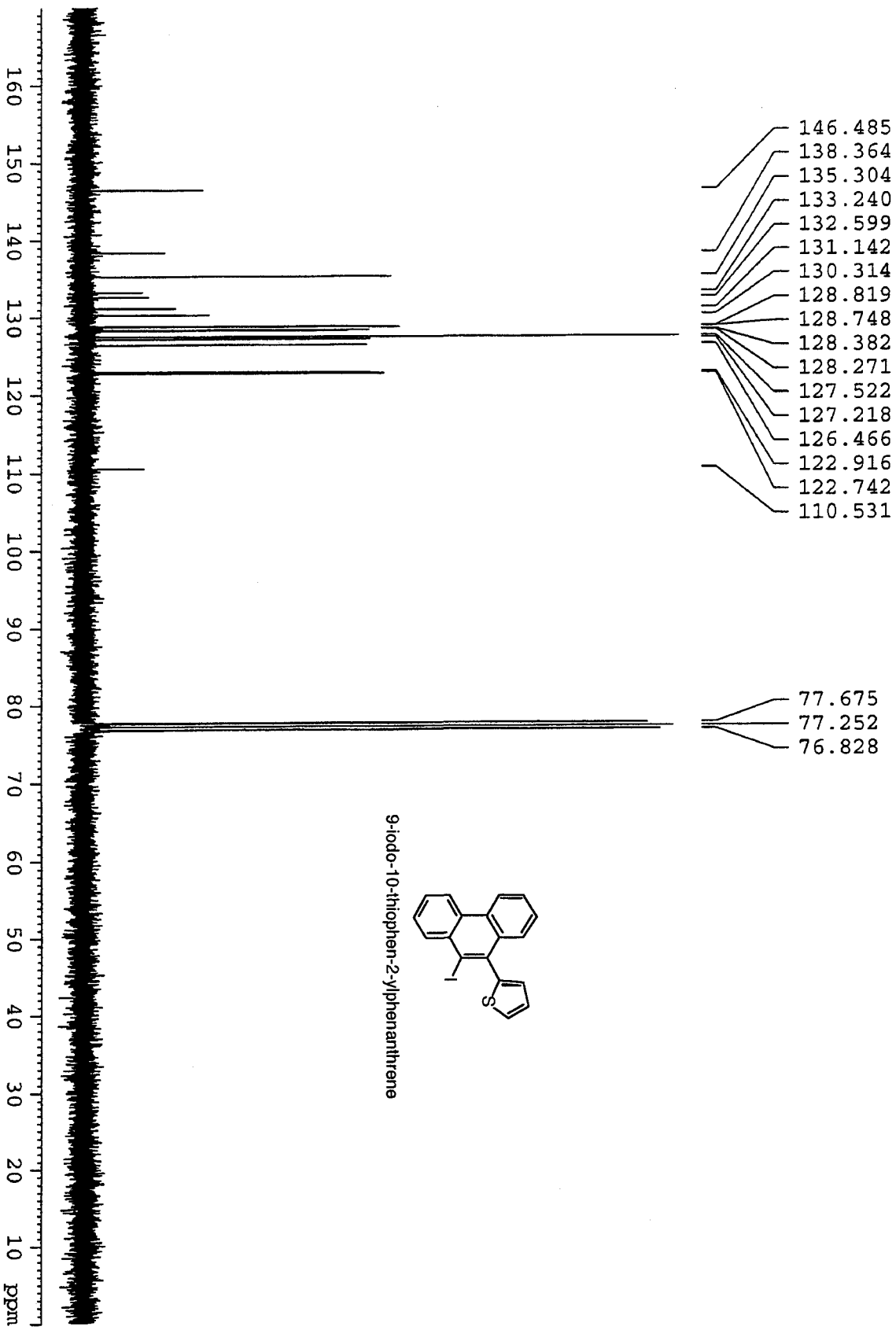

8.273
8.267
8.251
8.245
7.746
7.740
7.732
7.724
7.714
7.707
7.701
7.688
7.684
7.679
7.660
7.656
7.453
7.425
7.421
7.409
7.402
7.386
7.380
7.330
7.327
7.303
7.299
7.261
4.501
4.478
4.454
4.430
1.565
1.486
1.462
1.438
0.078
0.005
2.083
1.000
2.020
3.162
4.217
2.114
3.179
9
8
7
6
5
4
3
2
1
0 ppm
ethyl 4-(10-iodophenanthren-9-yl)benzoate
I
CO2Et

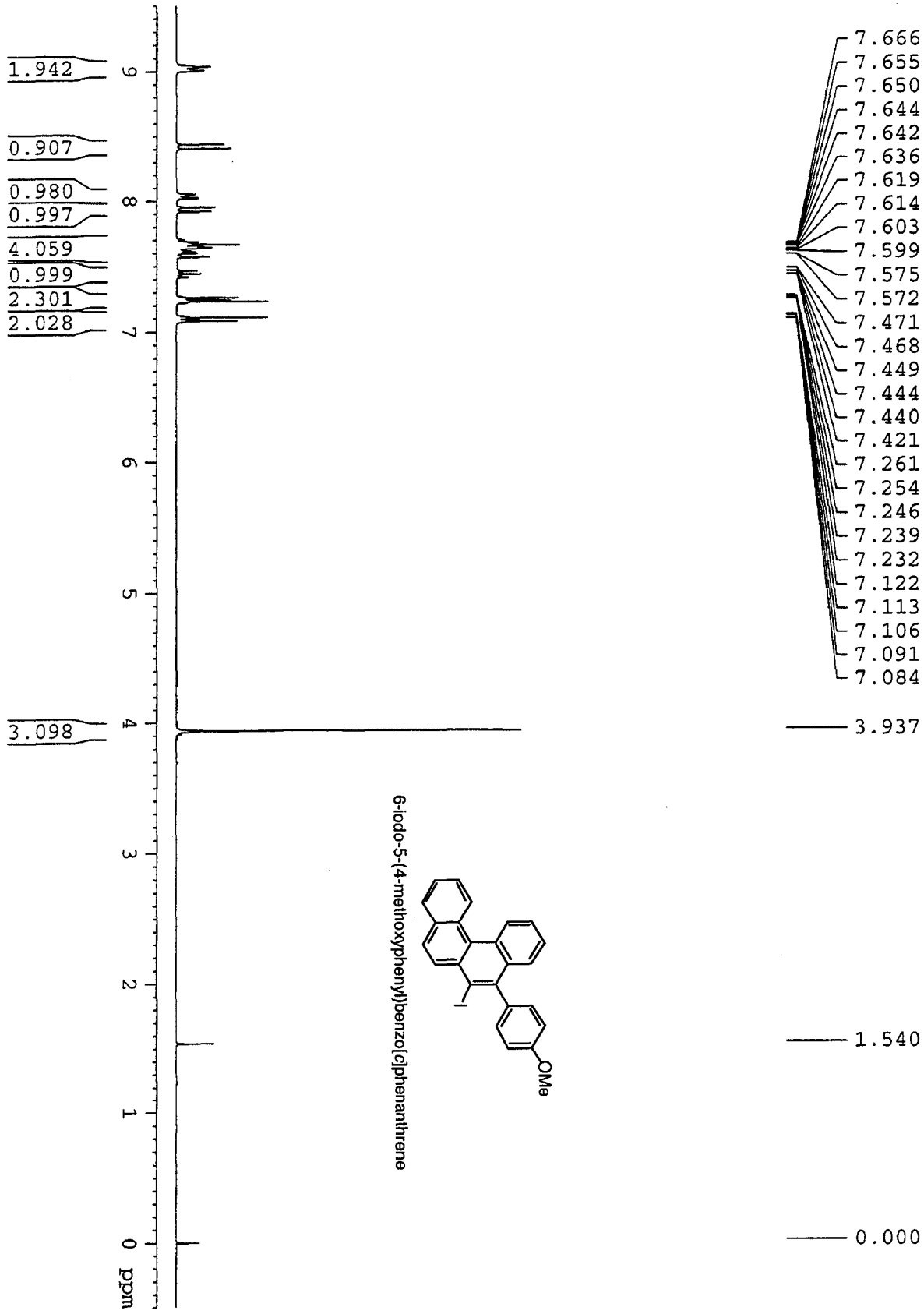

166.694
150.042
144.564
134.869
132.453
132.142
130.825
130.514
130.419
130.252
130.089
128.484
128.446
128.020
127.507
127.421
122.972
122.924
106.035
77.670
77.247
76.823
61.361
14.646
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
ethyl 4-(10-iodophenanthren-9-yl)benzoate
I
CO2Et

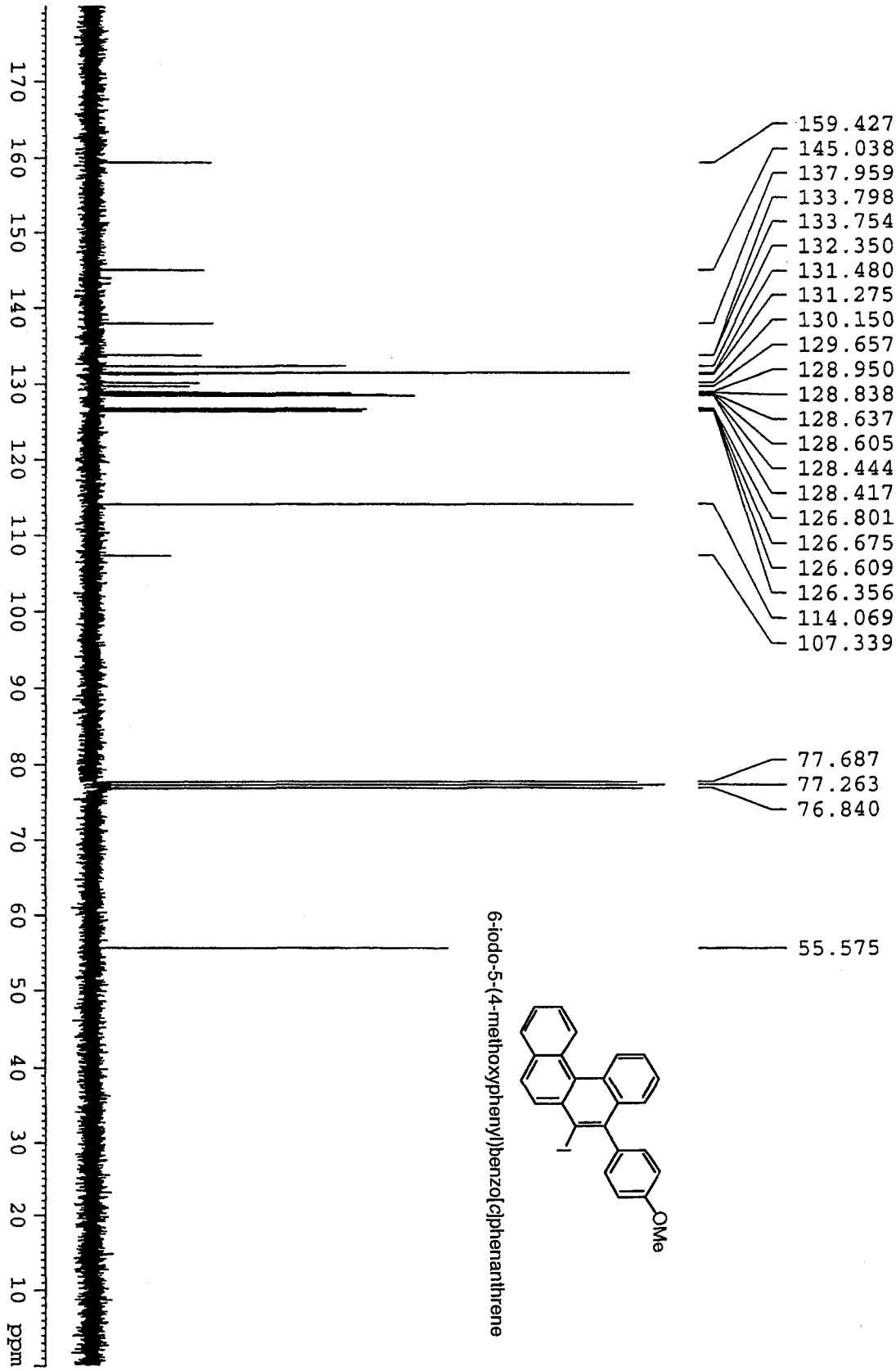

8.728
8.707
8.689
8.683
8.673
8.665
8.475
8.471
8.467
8.457
8.451
7.703
7.698
7.693
7.686
7.679
7.674
7.670
7.659
7.649
7.639
7.628
7.452
7.433
7.417
7.408
7.323
7.303
7.239
7.090
7.071
2.032
1.000
3.032
2.994
1.017
1.940
3.066
2.441
1.520
-0.00
9-iodo-10-(3-methylphenyl)phenanthrene
Me
ppm

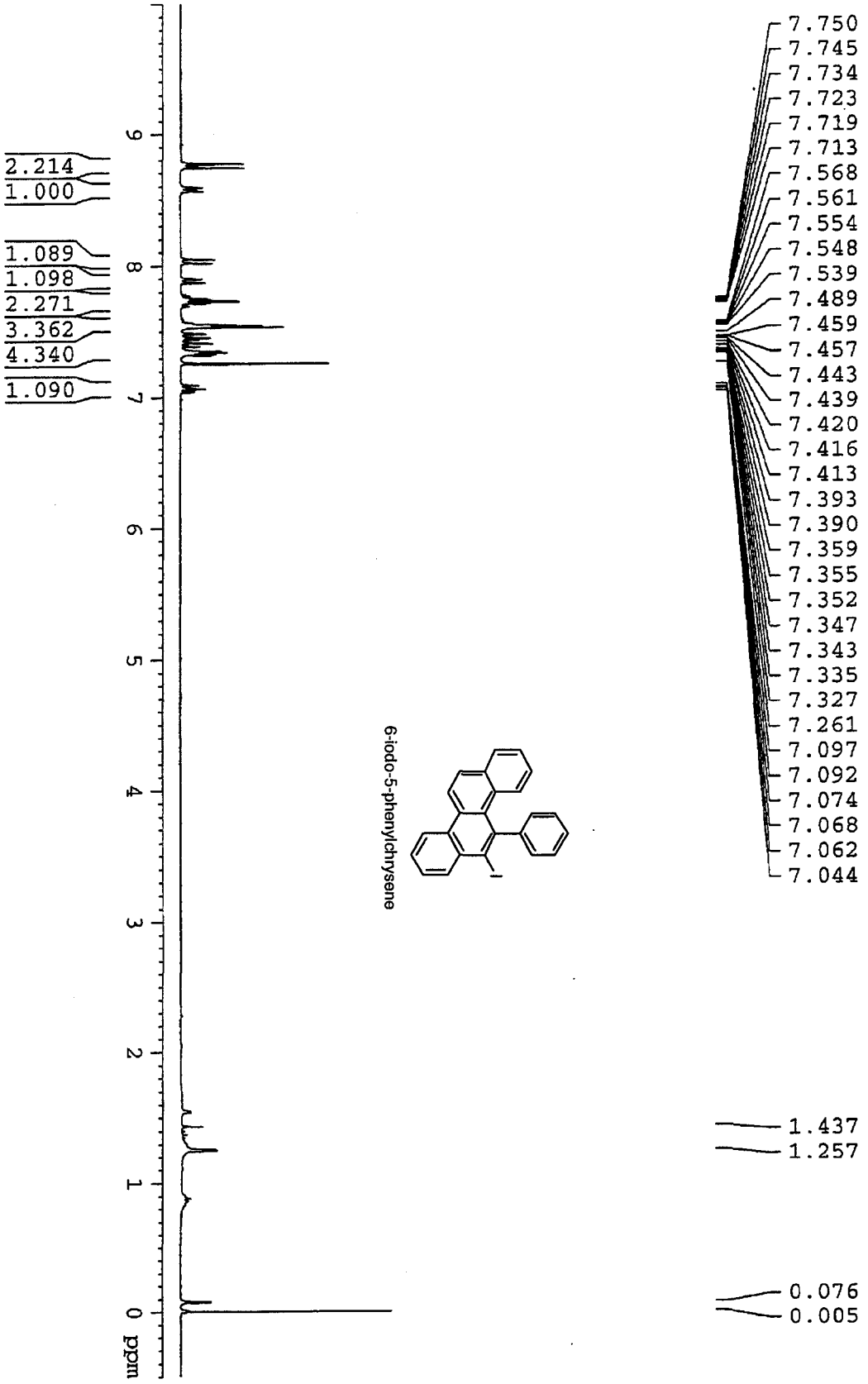

145.533
145.365
138.137
134.743
132.489
132.455
130.614
130.555
130.289
128.828
128.551
128.369
128.101
127.510
127.101
127.056
122.683
122.624
106.508
77.392
77.075
76.757
21.660
9-iodo-10-(3-methylphenyl)phenanthrene
I
Me
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

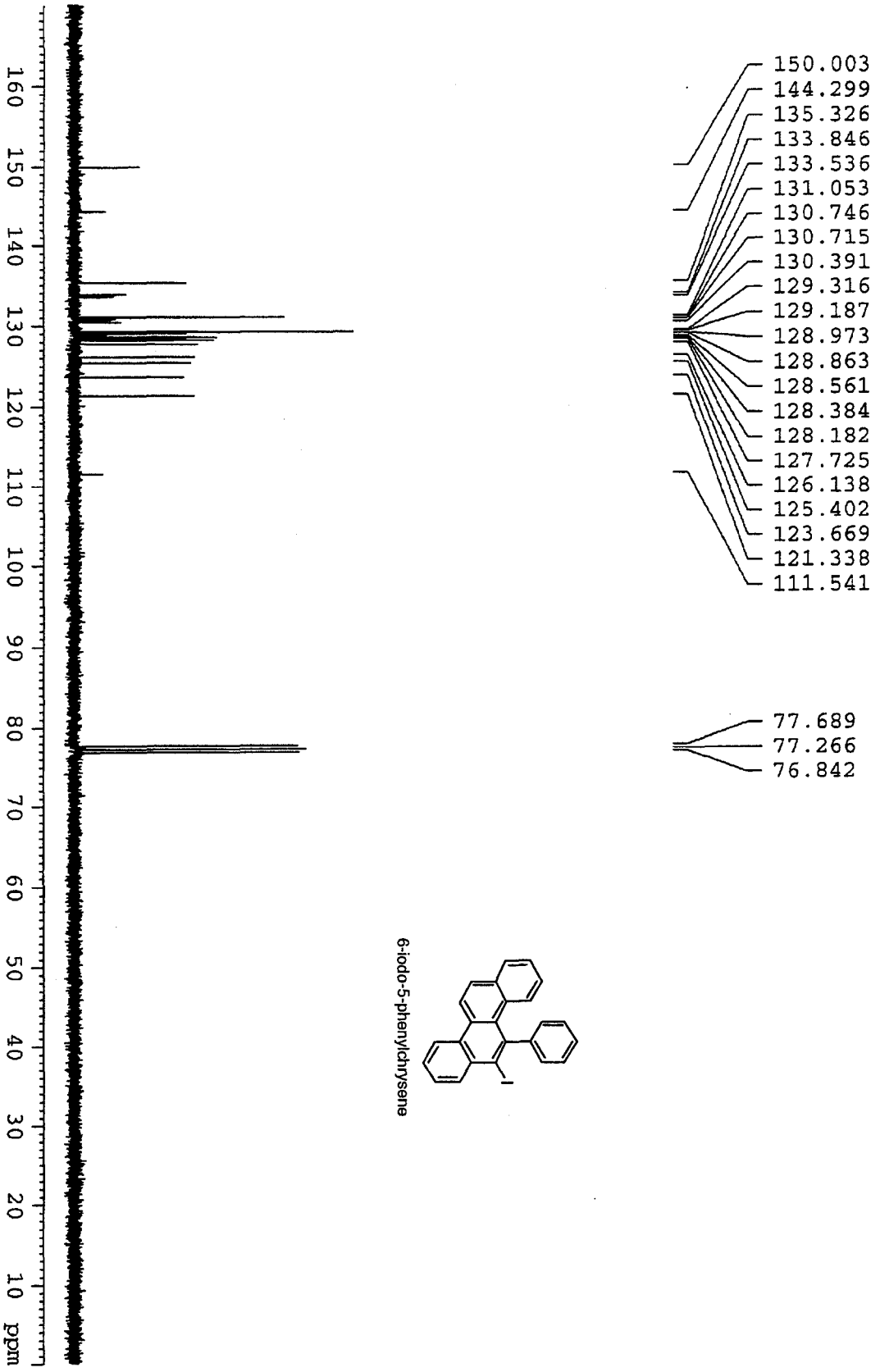

2.072
0.945
6.017
1.464
0.920
9
8
7
6
5
4
3
2
1
0
ppm
9-iodo-10-thiophen-2-ylphenanthrene
I
S
7.708
7.702
7.683
7.679
7.659
7.656
7.652
7.632
7.630
7.605
7.602
7.561
7.557
7.544
7.540
7.504
7.500
7.481
7.477
7.473
7.453
7.450
7.257
7.252
7.245
7.240
7.228
7.076
7.072
7.064
7.061
1.540

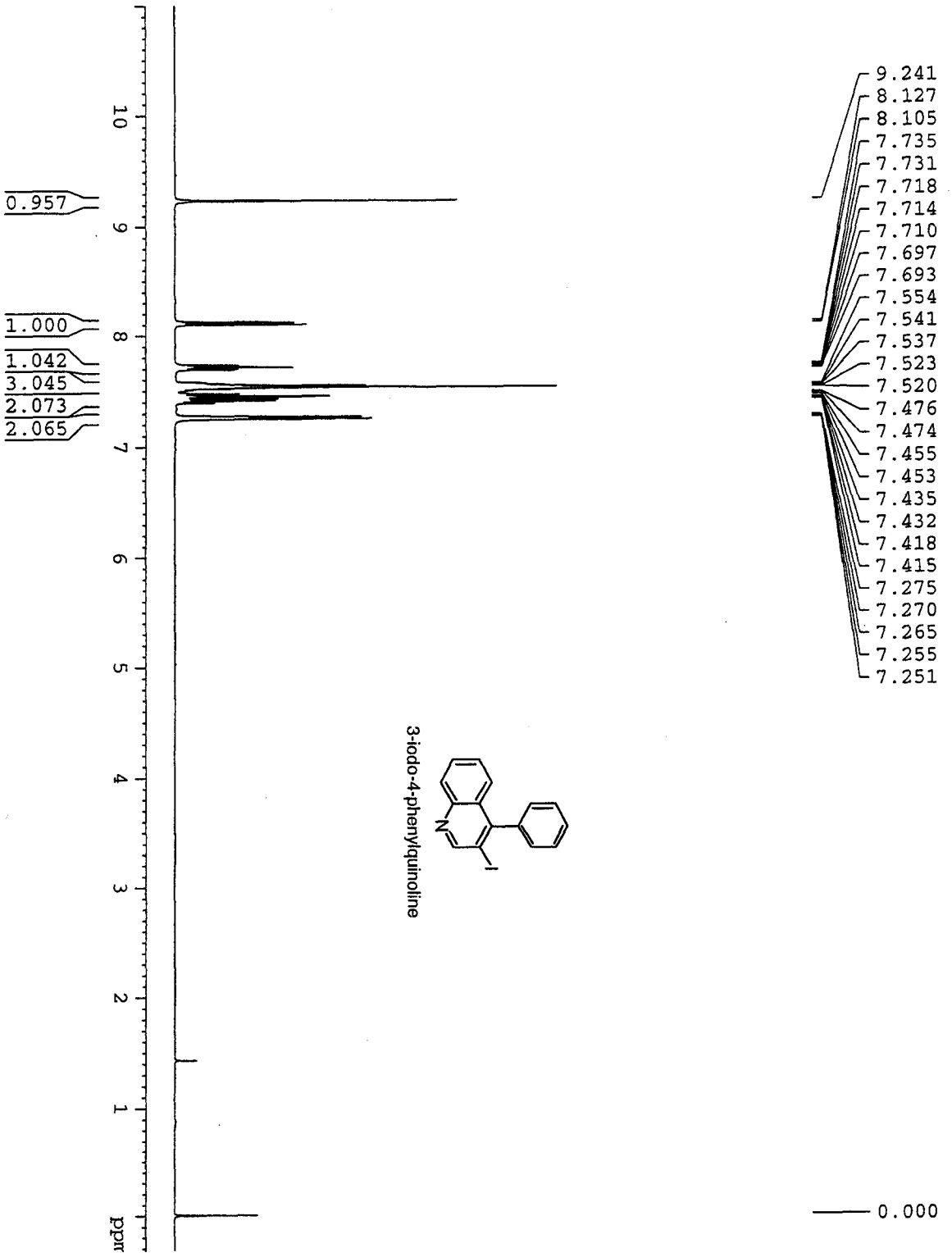

146.485
138.364
135.304
133.240
132.599
131.142
130.314
128.819
128.748
128.382
128.271
127.522
127.218
126.466
122.916
122.742
110.531
77.675
77.252
76.828
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
9-iodo-10-thiophen-2-ylphenanthrene
I
S

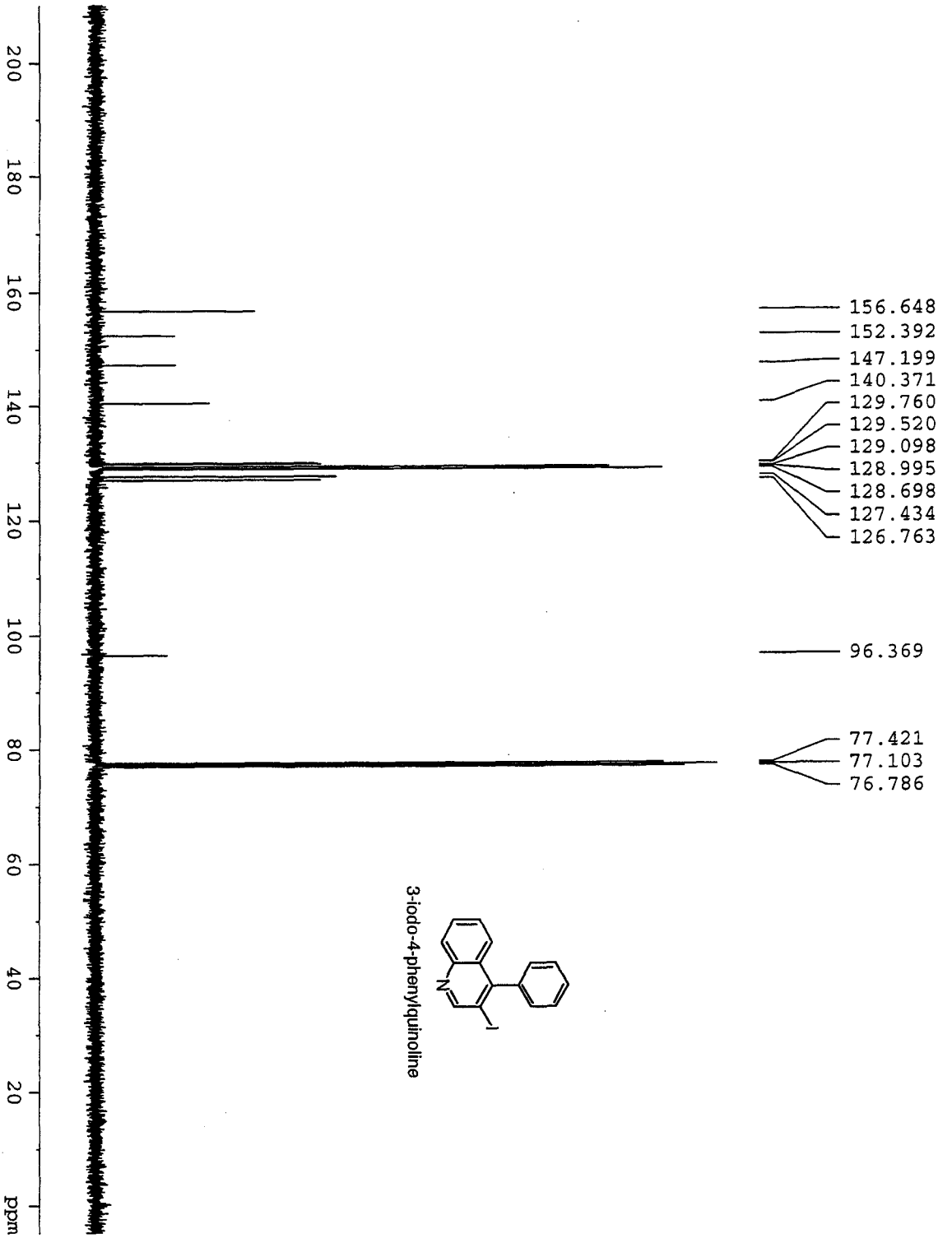

1.942
0.907
0.980
0.997
4.059
0.999
2.301
2.028
3.098
9
8
7
6
5
4
3
2
1
0
ppm
7.666
7.655
7.650
7.644
7.642
7.636
7.619
7.614
7.603
7.599
7.575
7.572
7.471
7.468
7.449
7.444
7.440
7.421
7.261
7.254
7.246
7.239
7.232
7.122
7.113
7.106
7.091
7.084
3.937
1.540
0.000
6-iodo-5-(4-methoxyphenyl)benzo[c]phenanthrene
I
OMe

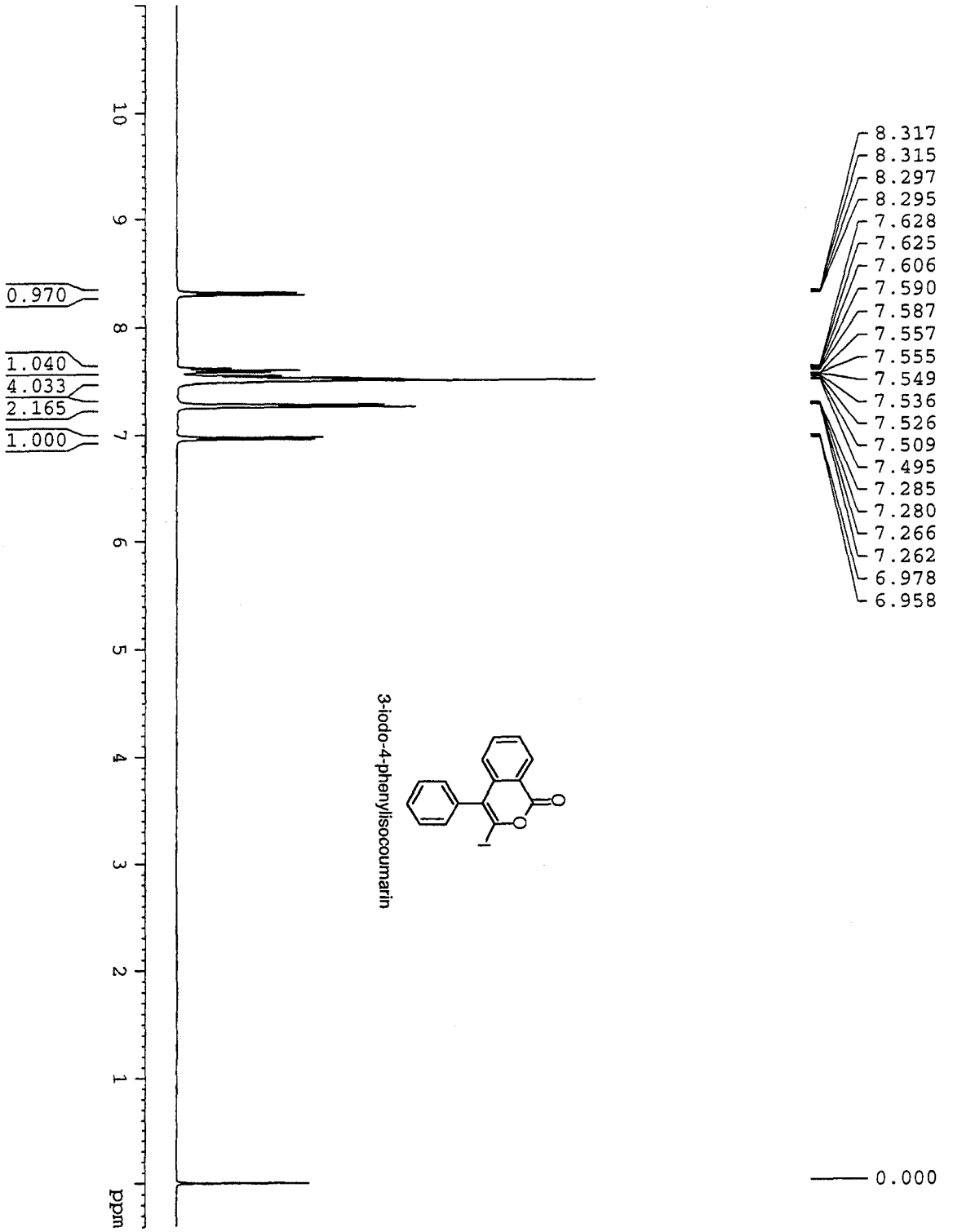

159.427
145.038
137.959
133.798
133.754
132.350
131.480
131.275
130.150
129.657
128.950
128.838
128.637
128.605
128.444
128.417
126.801
126.675
126.609
126.356
114.069
107.339
77.687
77.263
76.840
55.575
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
6-iodo-5-(4-methoxyphenyl)benzo[c]phenanthrene
I
OMe

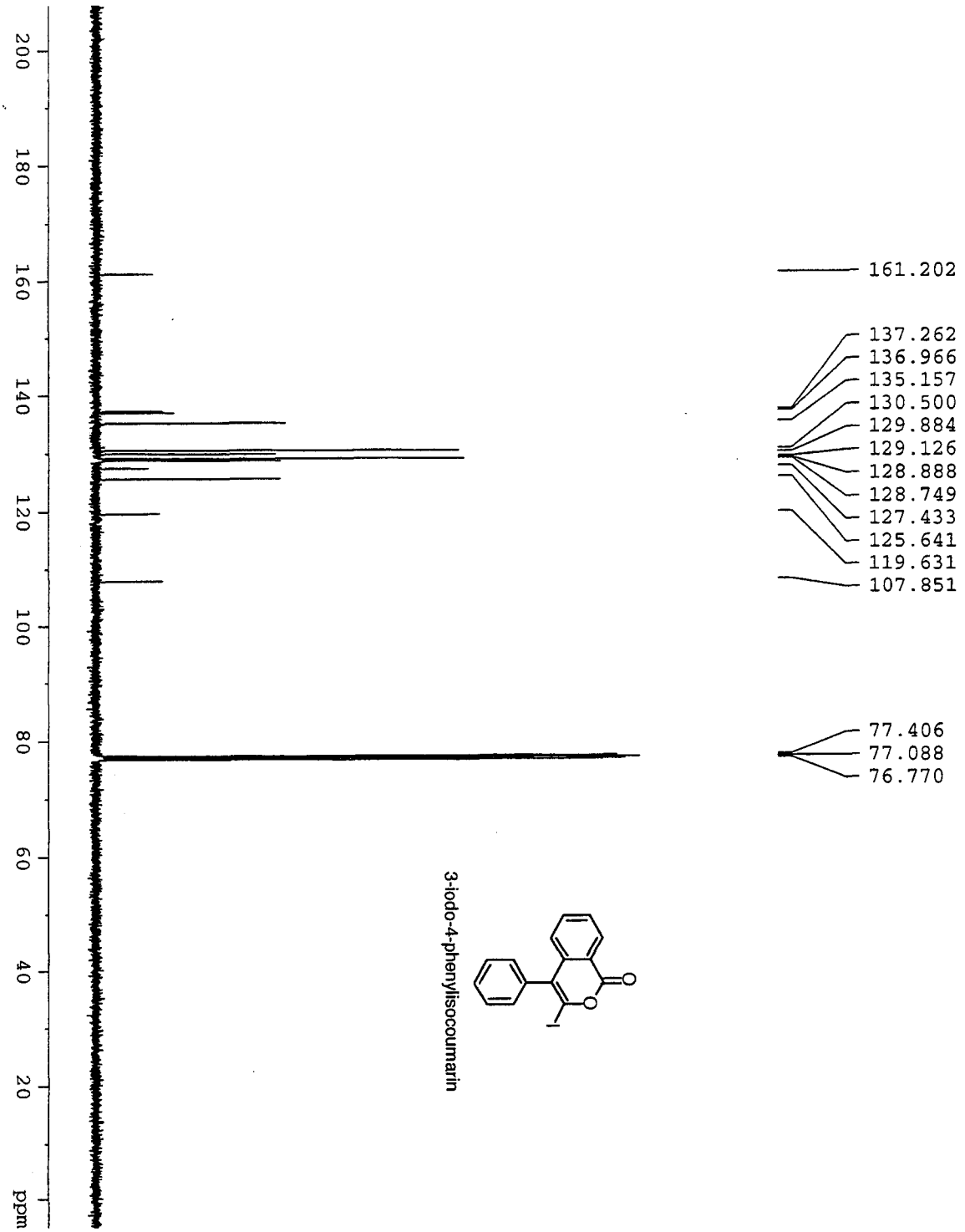

7.750
7.745
7.734
7.723
7.719
7.713
7.568
7.561
7.554
7.548
7.539
7.489
7.459
7.457
7.443
7.439
7.420
7.416
7.413
7.393
7.390
7.359
7.355
7.352
7.347
7.343
7.335
7.327
7.261
7.097
7.092
7.074
7.068
7.062
7.044
1.437
1.257
0.076
0.005
2.214
1.000
1.089
1.098
2.271
3.362
4.340
1.090
6-iodo-5-phenylchrysene
I
9
8
7
6
5
4
3
2
1
0
ppm

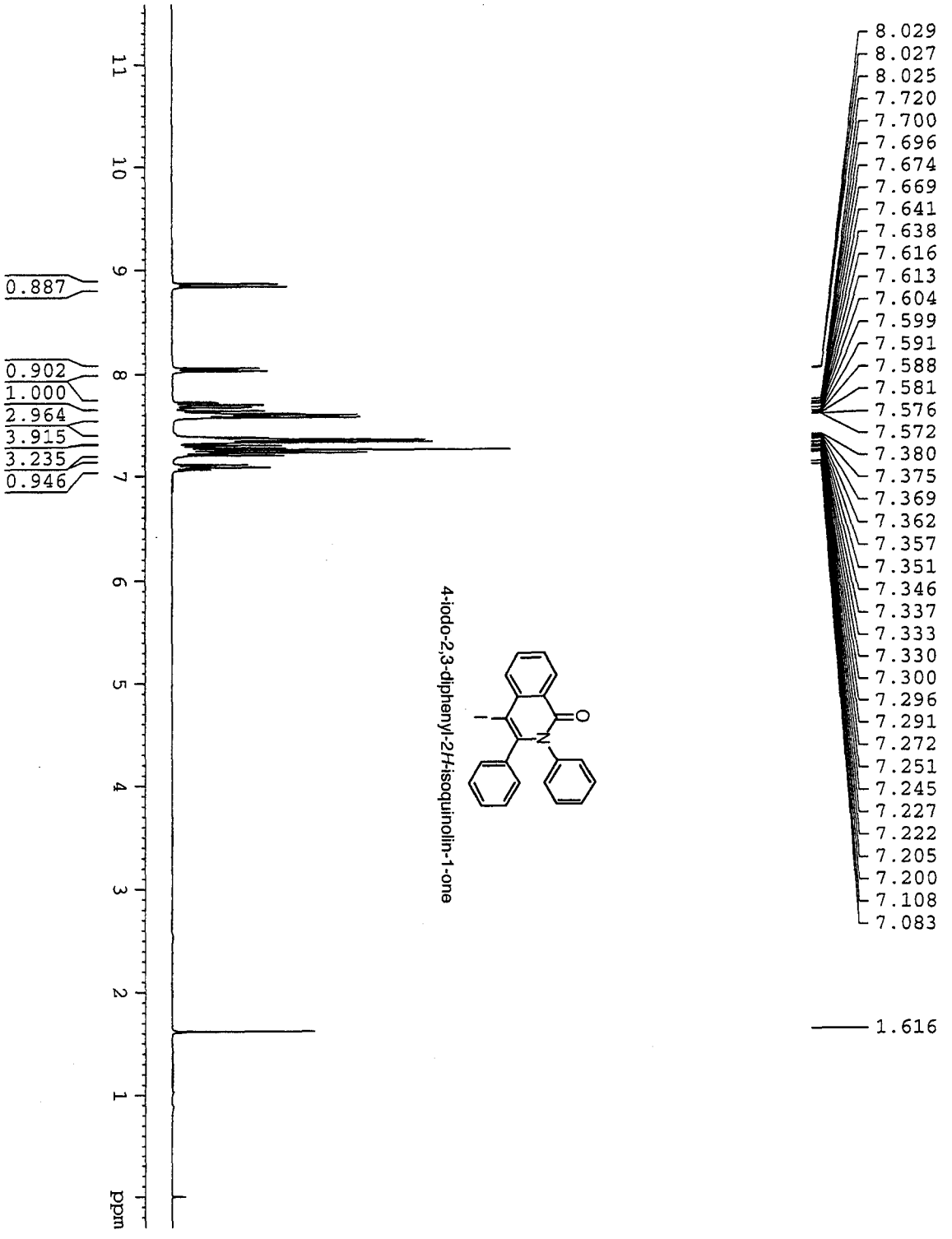

150.003
144.299
135.326
133.846
133.536
131.053
130.746
130.715
130.391
129.316
129.187
128.973
128.863
128.561
128.384
128.182
127.725
126.138
125.402
123.669
121.338
111.541
77.689
77.266
76.842
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
6-iodo-5-phenylchrysene

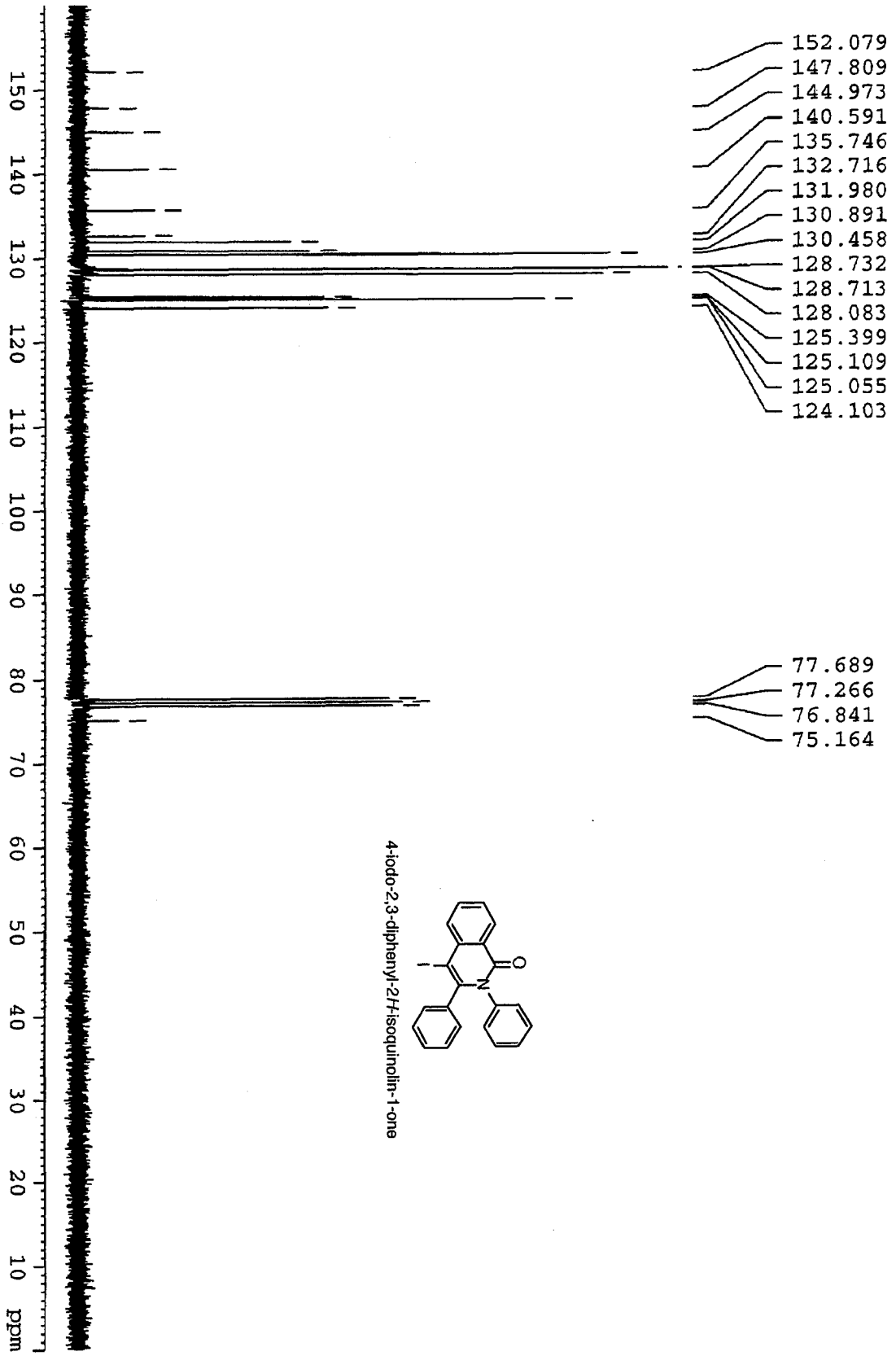

9.241
8.127
8.105
7.735
7.731
7.718
7.714
7.710
7.697
7.693
7.554
7.541
7.537
7.523
7.520
7.476
7.474
7.455
7.453
7.435
7.432
7.418
7.415
7.275
7.270
7.265
7.255
7.251
0.957
1.000
1.042
3.045
2.073
2.065
10
9
8
7
6
5
4
3
2
1
ppm
0.000
3-iodo-4-phenylquinoline
N
I

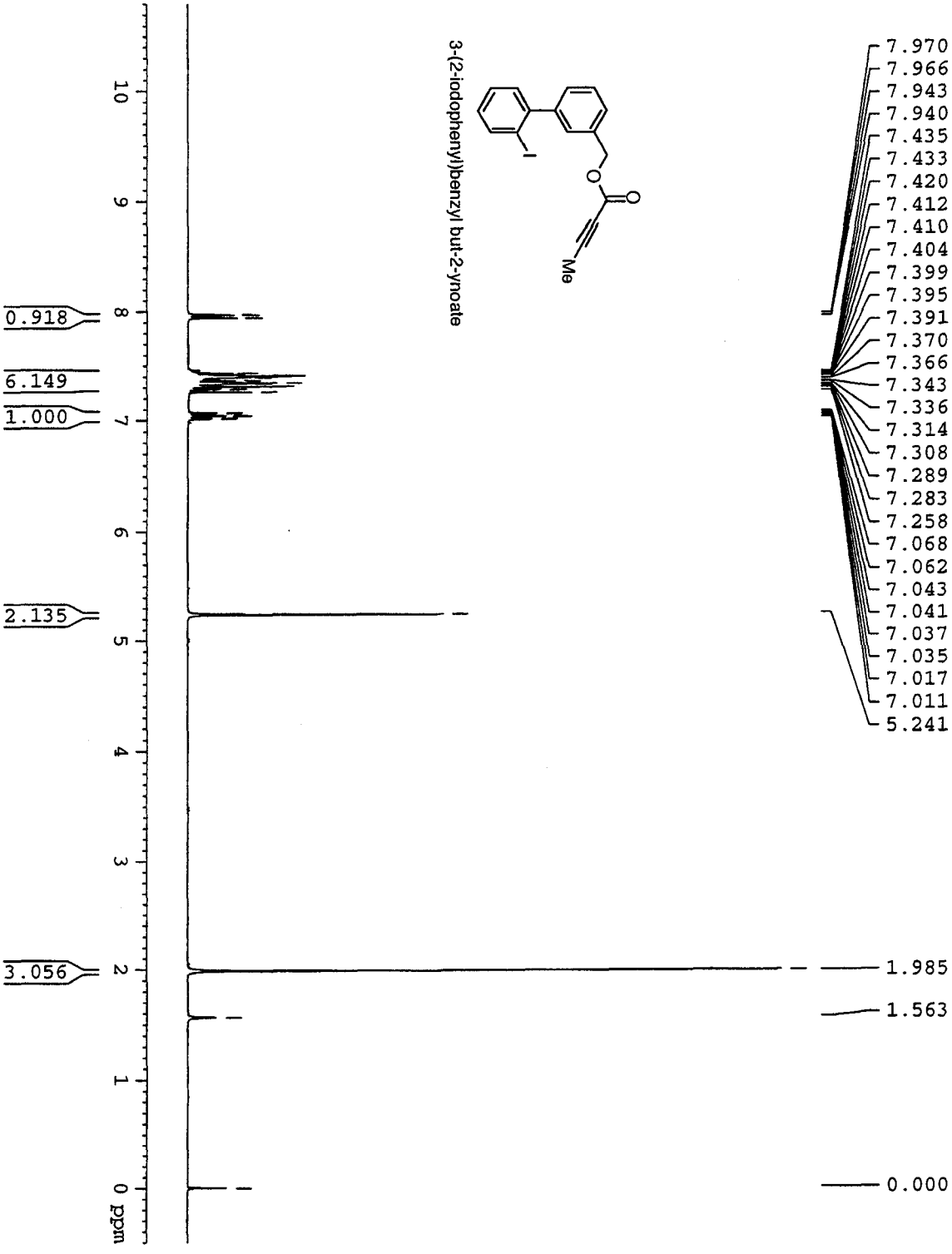

156.648
152.392
147.199
140.371
129.760
129.520
129.098
128.995
128.698
127.434
126.763
96.369
77.421
77.103
76.786
3-iodo-4-phenylquinoline
N
I
200
180
160
140
120
100
80
60
40
20
ppm

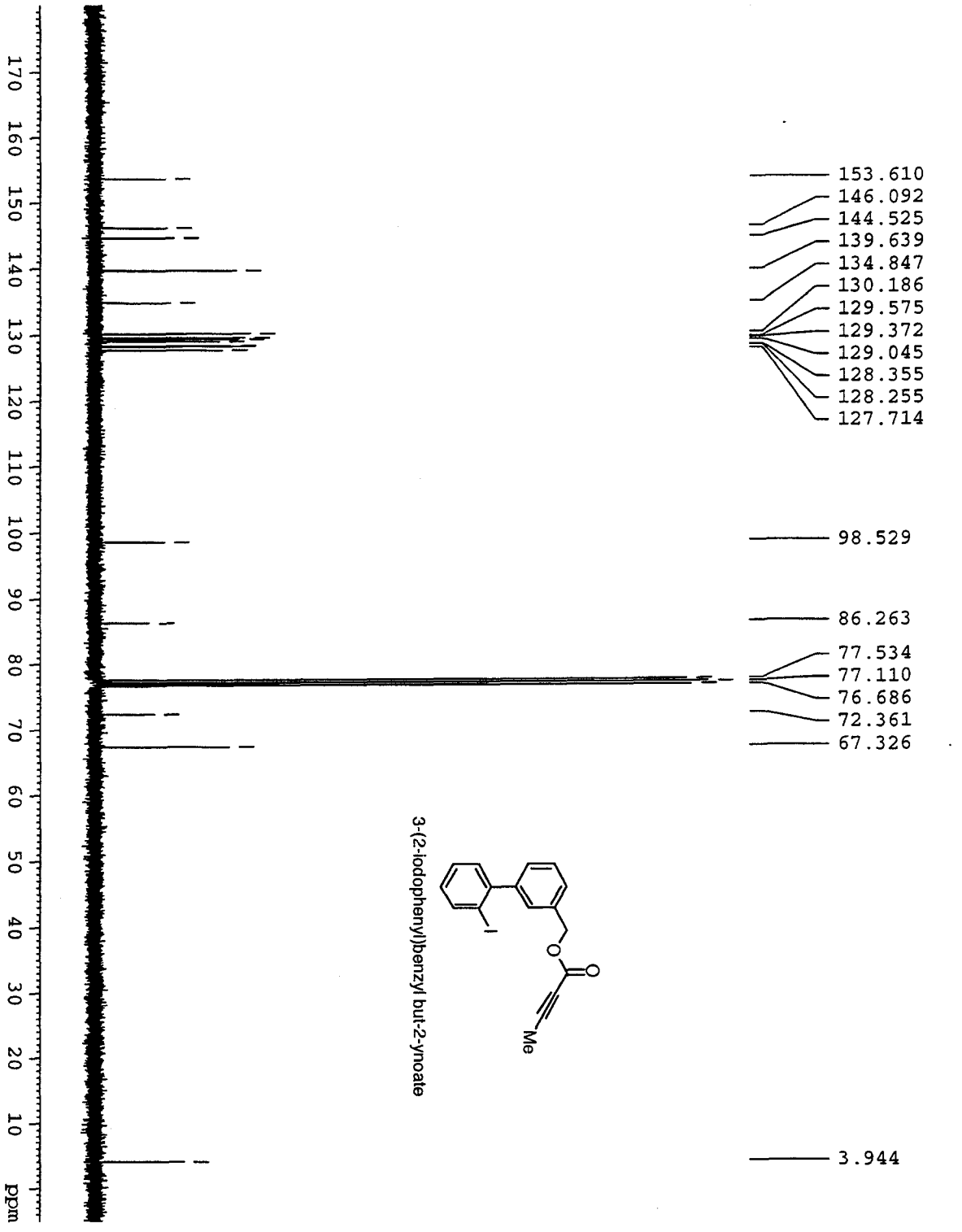

8.317
8.315
8.297
8.295
7.628
7.625
7.606
7.590
7.587
7.557
7.555
7.549
7.536
7.526
7.509
7.495
7.285
7.280
7.266
7.262
6.978
6.958
0.970
1.040
4.033
2.165
1.000
0.000
ppm
3-iodo-4-phenylisocoumarin

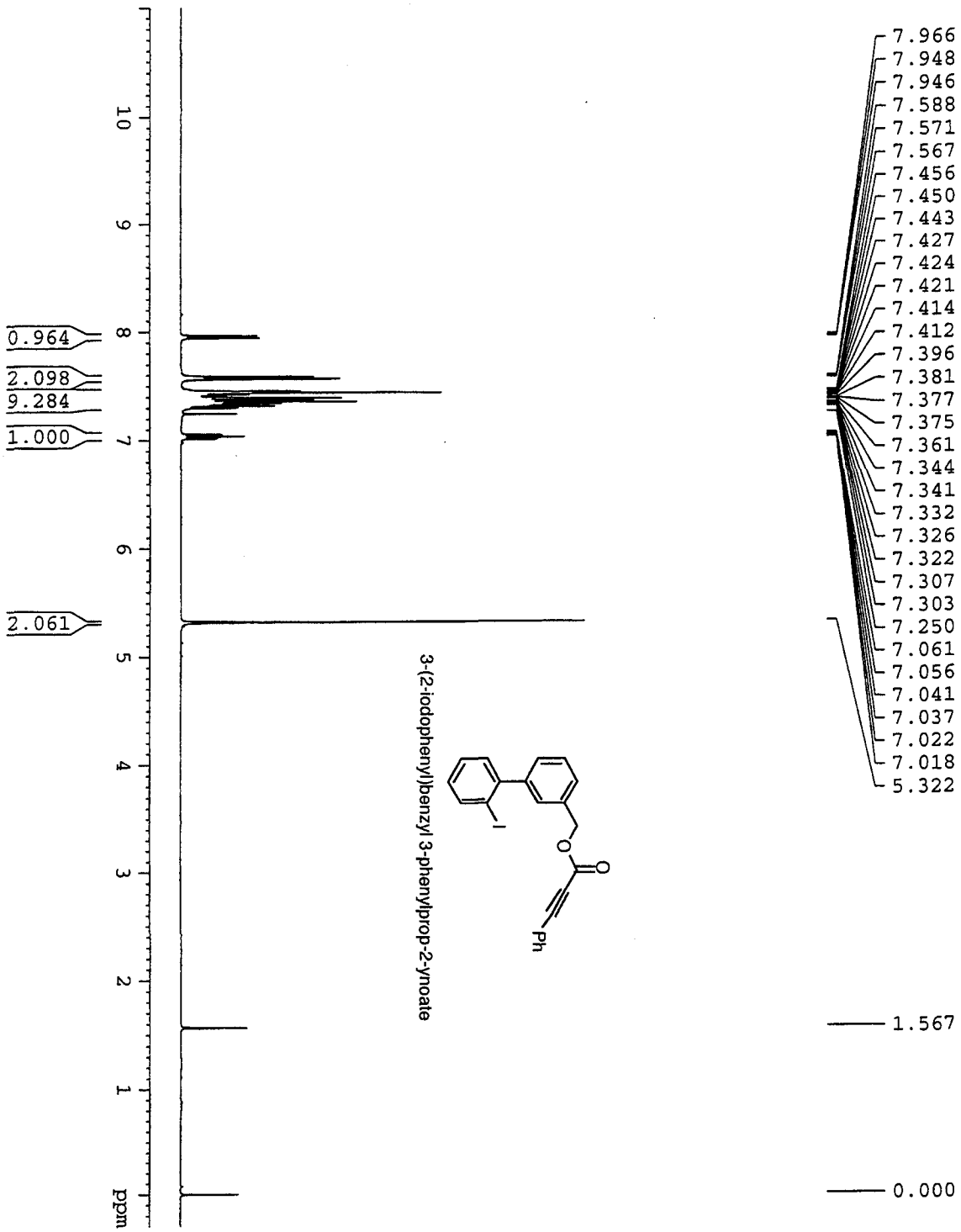

161.202
137.262
136.966
135.157
130.500
129.884
129.126
128.888
128.749
127.433
125.641
119.631
107.851
77.406
77.088
76.770
200
180
160
140
120
100
80
60
40
20
ppm
3-iodo-4-phenylisocoumarin
O
O
I

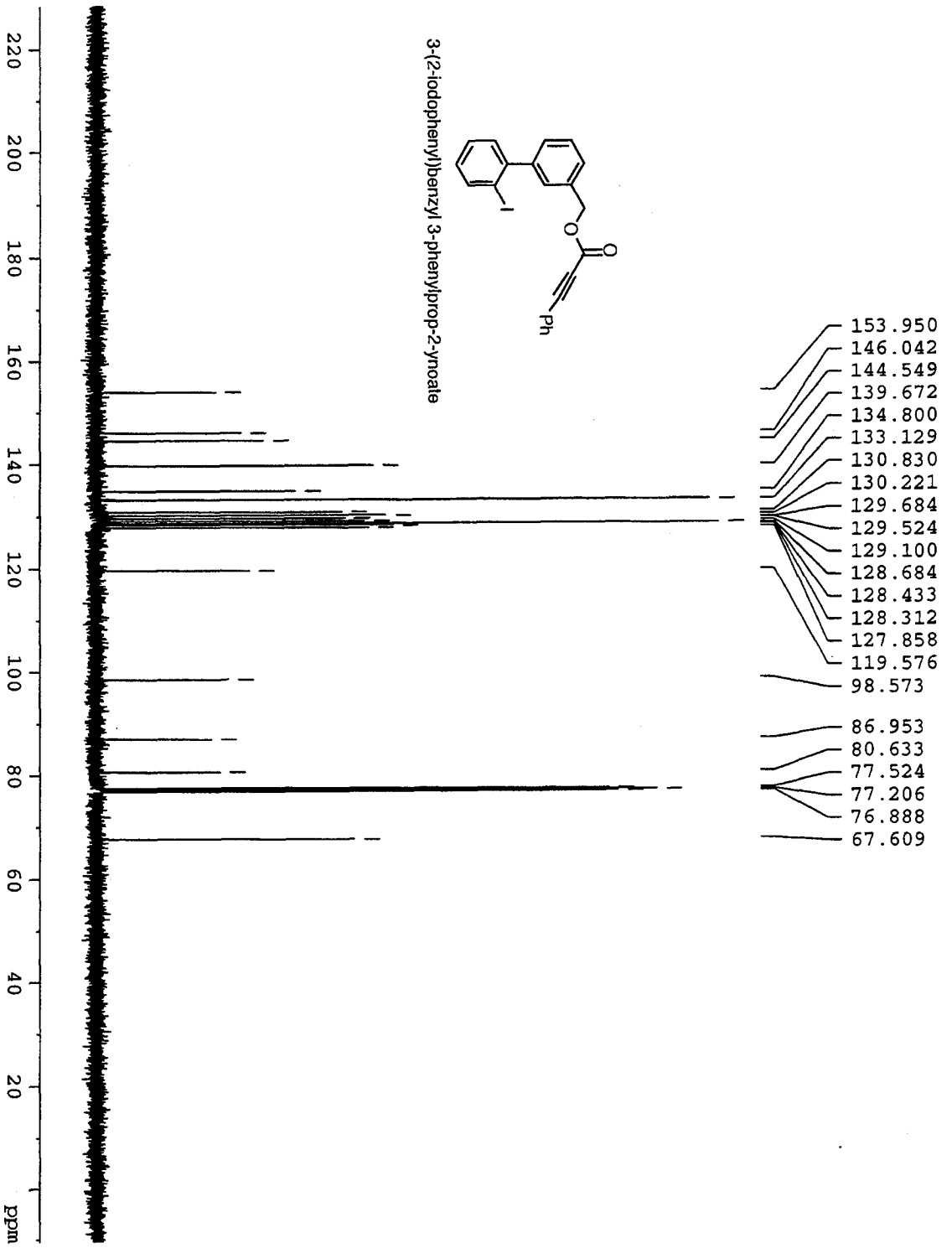

8.029
8.027
8.025
7.720
7.700
7.696
7.674
7.669
7.641
7.638
7.616
7.613
7.604
7.599
7.591
7.588
7.581
7.576
7.572
7.380
7.375
7.369
7.362
7.357
7.351
7.346
7.337
7.333
7.330
7.300
7.296
7.291
7.272
7.251
7.245
7.227
7.222
7.205
7.200
7.108
7.083
1.616
0.887
0.902
1.000
2.964
3.915
3.235
0.946
4-iodo-2,3-diphenyl-2H-isoquinolin-1-one
I
O
N
11
10
9
8
7
6
5
4
3
2
1
ppm

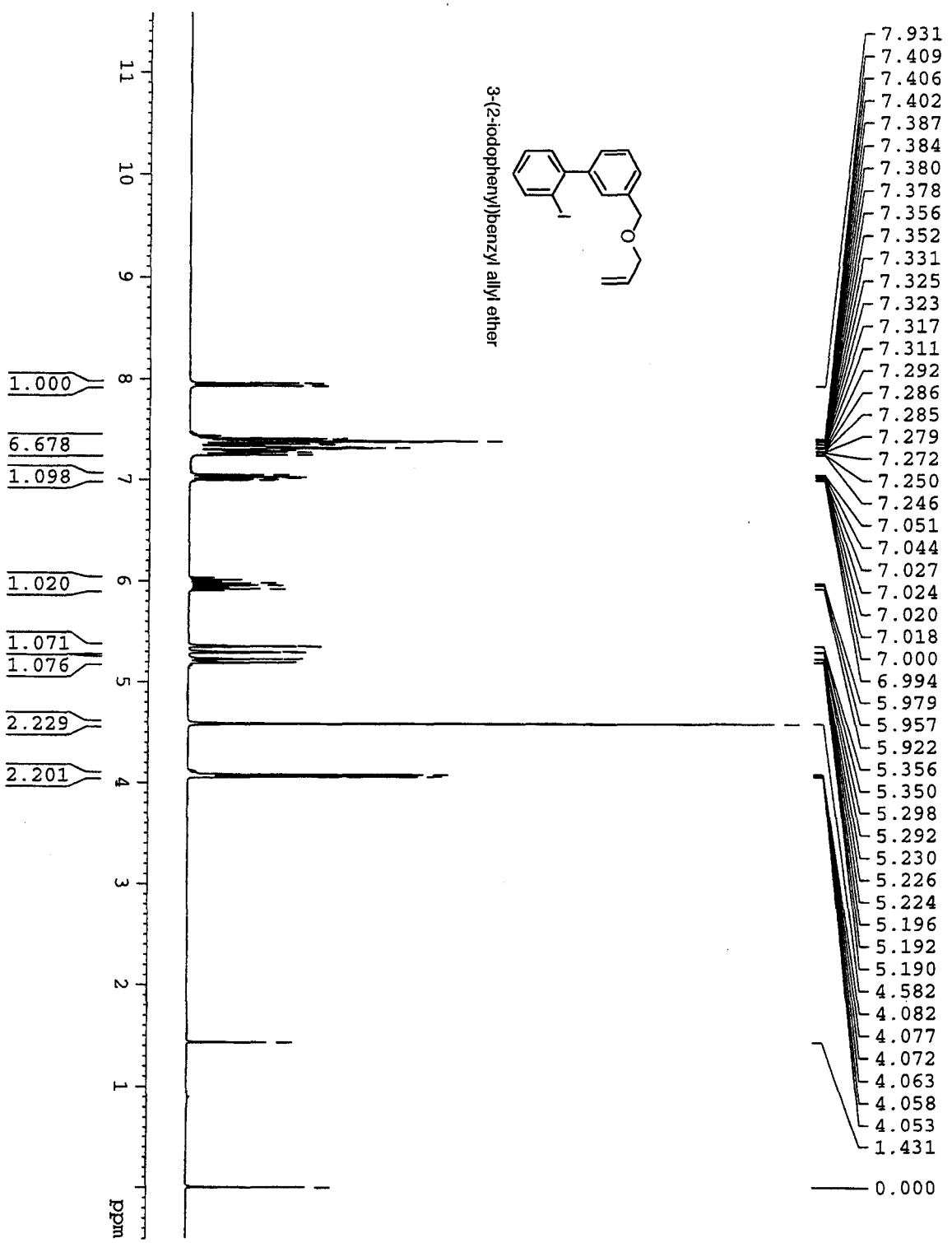

152.079
147.809
144.973
140.591
135.746
132.716
131.980
130.891
130.458
128.732
128.713
128.083
125.399
125.109
125.055
124.103
77.689
77.266
76.841
75.164
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
4-iodo-2,3-diphenyl-2H-isoquinolin-1-one
O
N

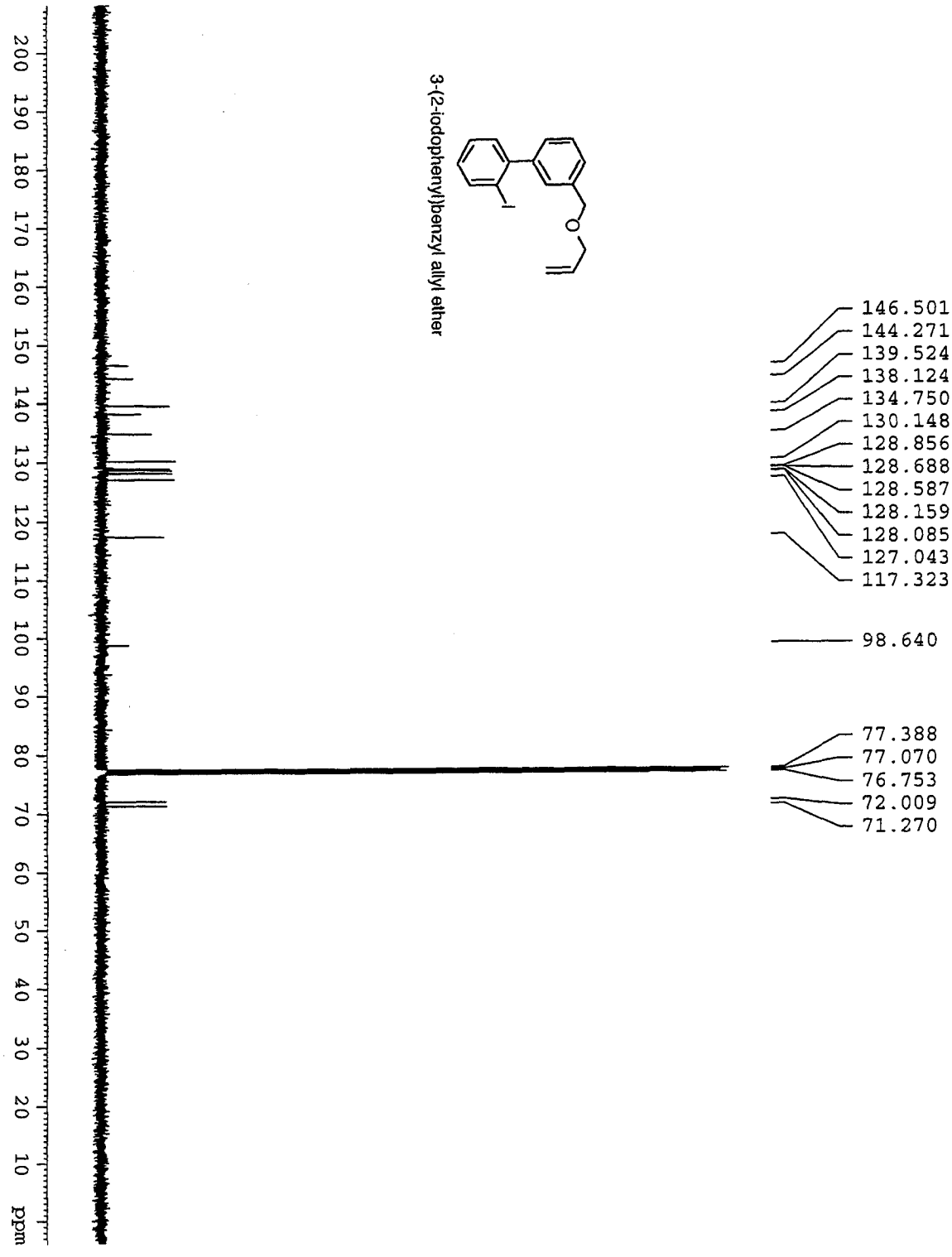

3-(2-iodophenyl)benzyl but-2-ynoate
I
O
O
Me
7.970
7.966
7.943
7.940
7.435
7.433
7.420
7.412
7.410
7.404
7.399
7.395
7.391
7.370
7.366
7.343
7.336
7.314
7.308
7.289
7.283
7.258
7.068
7.062
7.043
7.041
7.037
7.035
7.017
7.011
5.241
1.985
1.563
0.000
0.918
6.149
1.000
2.135
3.056
10
9
8
7
6
5
4
3
2
1
0
ppm

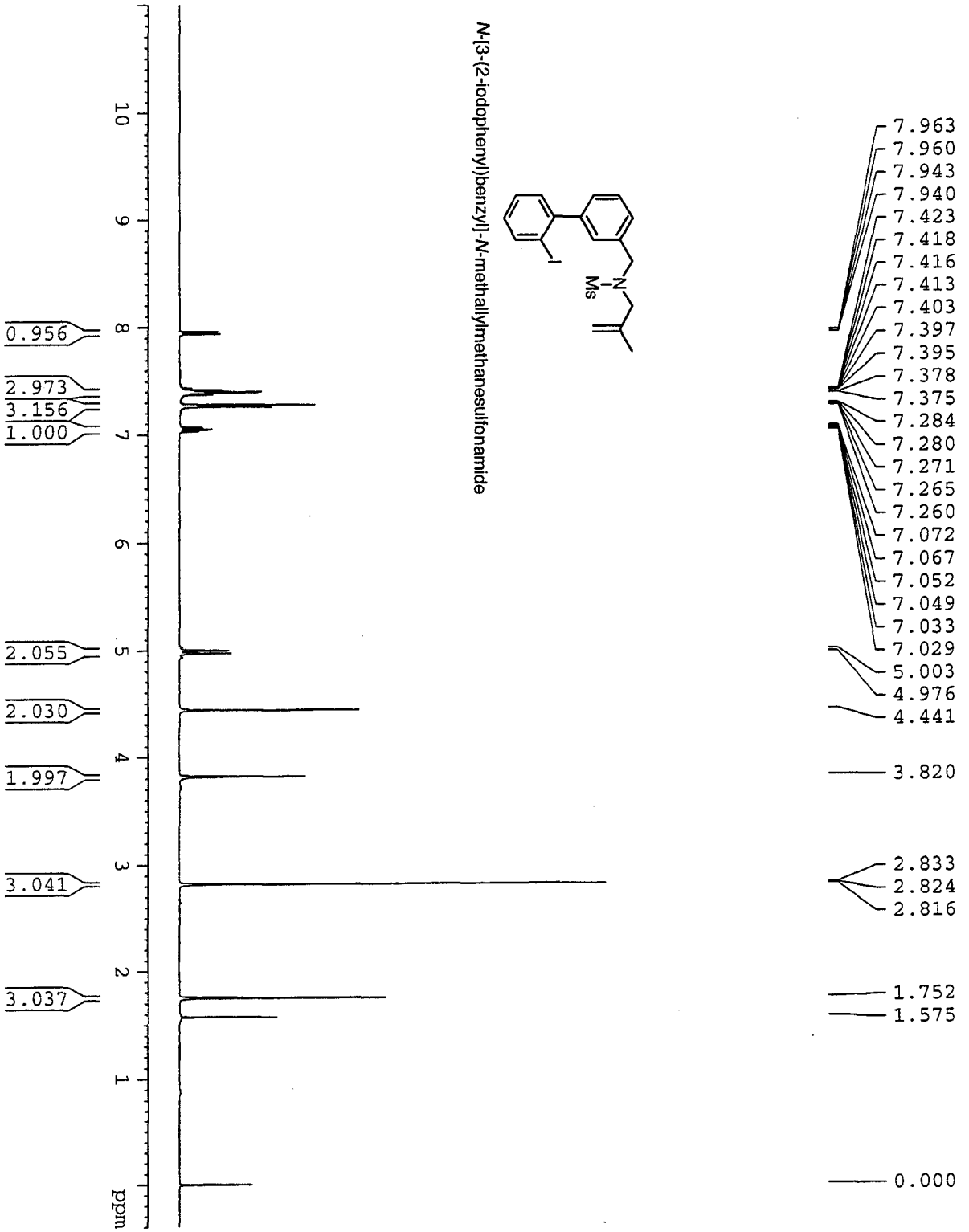

153.610
146.092
144.525
139.639
134.847
130.186
129.575
129.372
129.045
128.355
128.255
127.714
98.529
86.263
77.534
77.110
76.686
72.361
67.326
3.944
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
3-(2-Iodophenyl)benzyl but-2-ynoate
I
O
O
Me

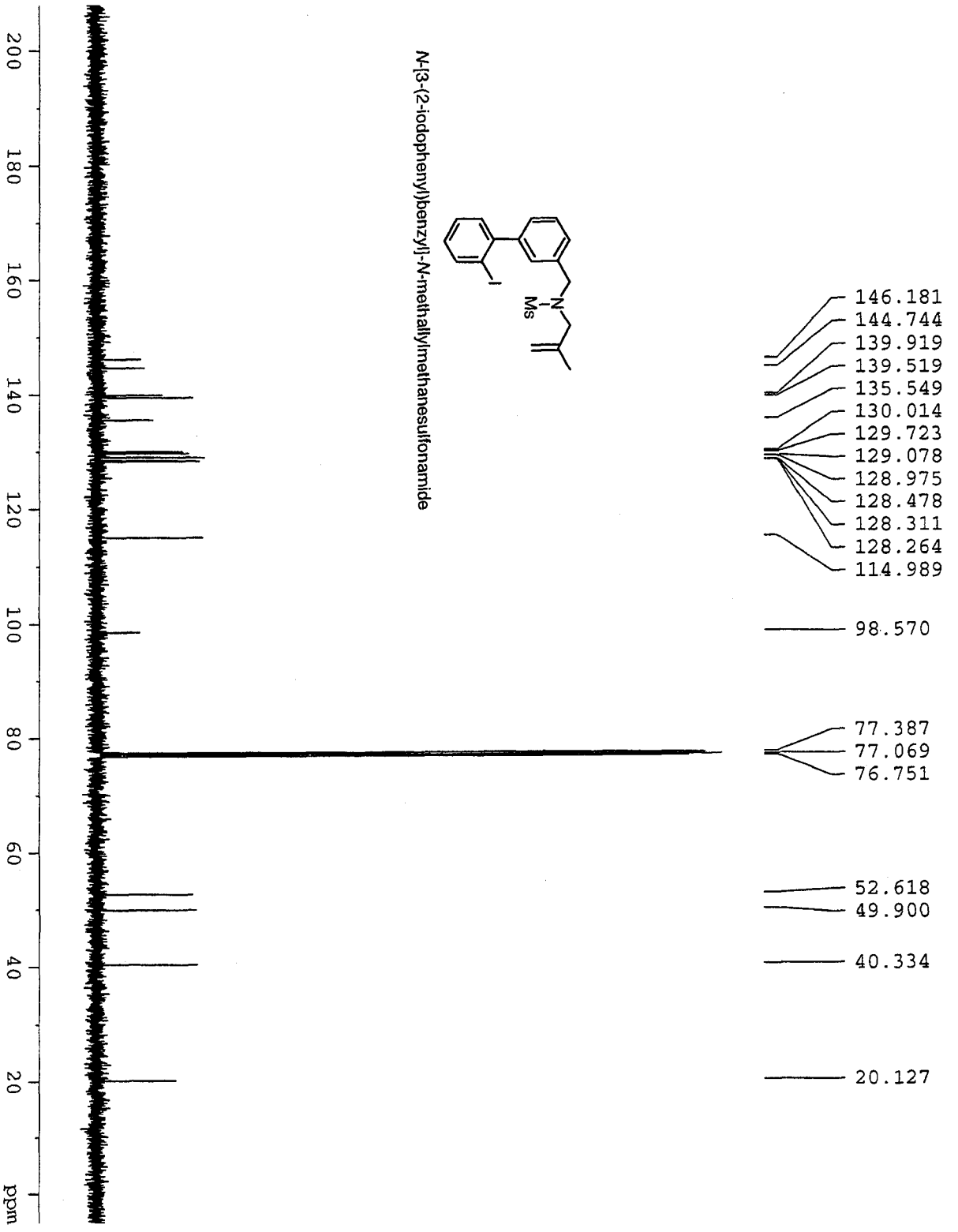

7.966
7.948
7.946
7.588
7.571
7.567
7.456
7.450
7.443
7.427
7.424
7.421
7.414
7.412
7.396
7.381
7.377
7.375
7.361
7.344
7.341
7.332
7.326
7.322
7.307
7.303
7.250
7.061
7.056
7.041
7.037
7.022
7.018
5.322
1.567
0.000
0.964
2.098
9.284
1.000
2.061
ppm
3-(2-iodophenyl)benzyl 3-phenylprop-2-ynoate
I
O
O
Ph

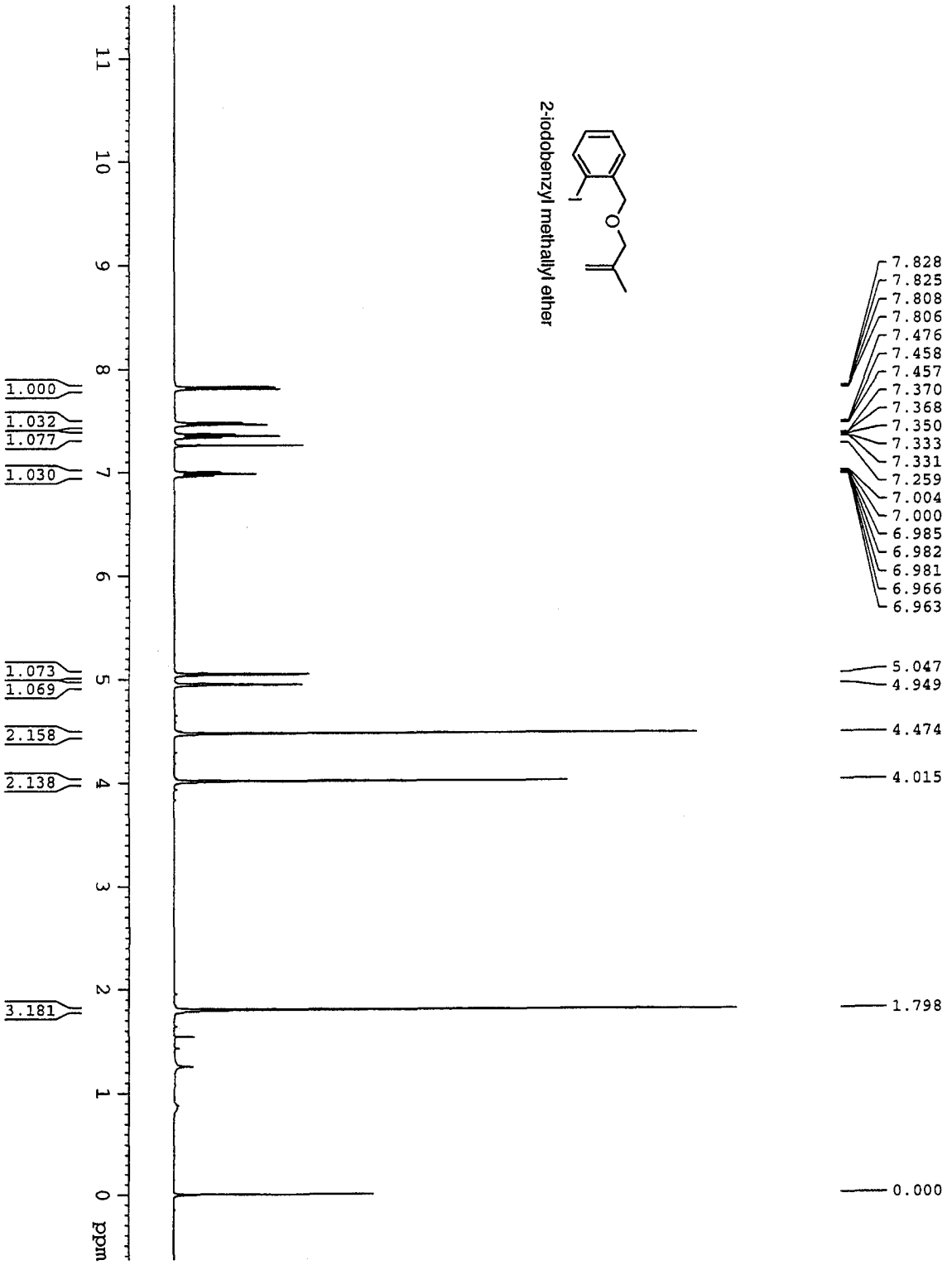

3-(2-iodophenyl)benzyl 3-phenylprop-2-ynoate
I
O
O
Ph
153.950
146.042
144.549
139.672
134.800
133.129
130.830
130.221
129.684
129.524
129.100
128.684
128.433
128.312
127.858
119.576
98.573
86.953
80.633
77.524
77.206
76.888
67.609
220
200
180
160
140
120
100
80
60
40
20
ppm

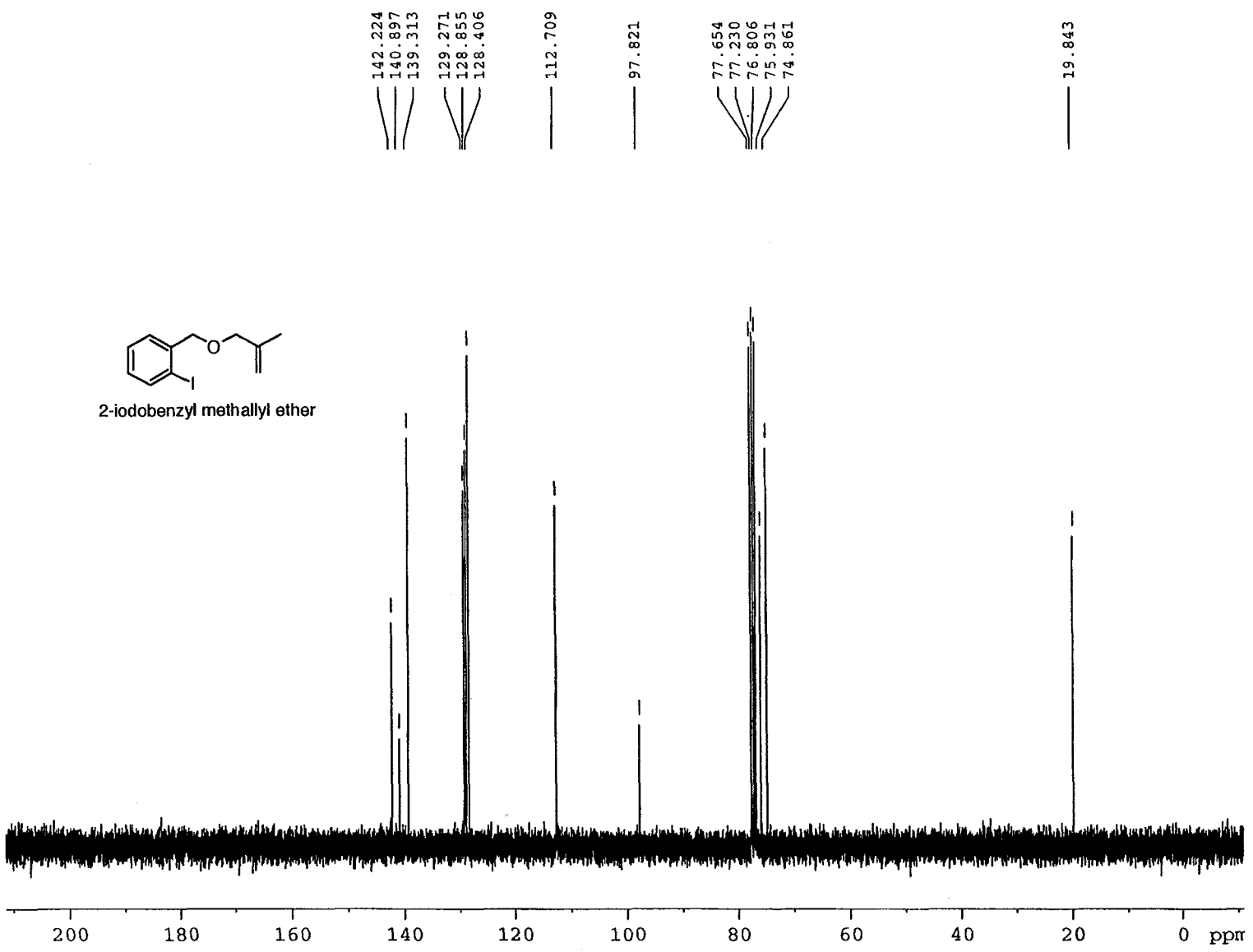

3-(2-iodophenyl)benzyl allyl ether
7.931
7.409
7.406
7.402
7.387
7.384
7.380
7.378
7.356
7.352
7.331
7.325
7.323
7.317
7.311
7.292
7.286
7.285
7.279
7.272
7.250
7.246
7.051
7.044
7.027
7.024
7.020
7.018
7.000
6.994
5.979
5.957
5.922
5.356
5.350
5.298
5.292
5.230
5.226
5.224
5.196
5.192
5.190
4.582
4.082
4.077
4.072
4.063
4.058
4.053
1.431
0.000
1.000
6.678
1.098
1.020
1.071
1.076
2.229
2.201
ppm

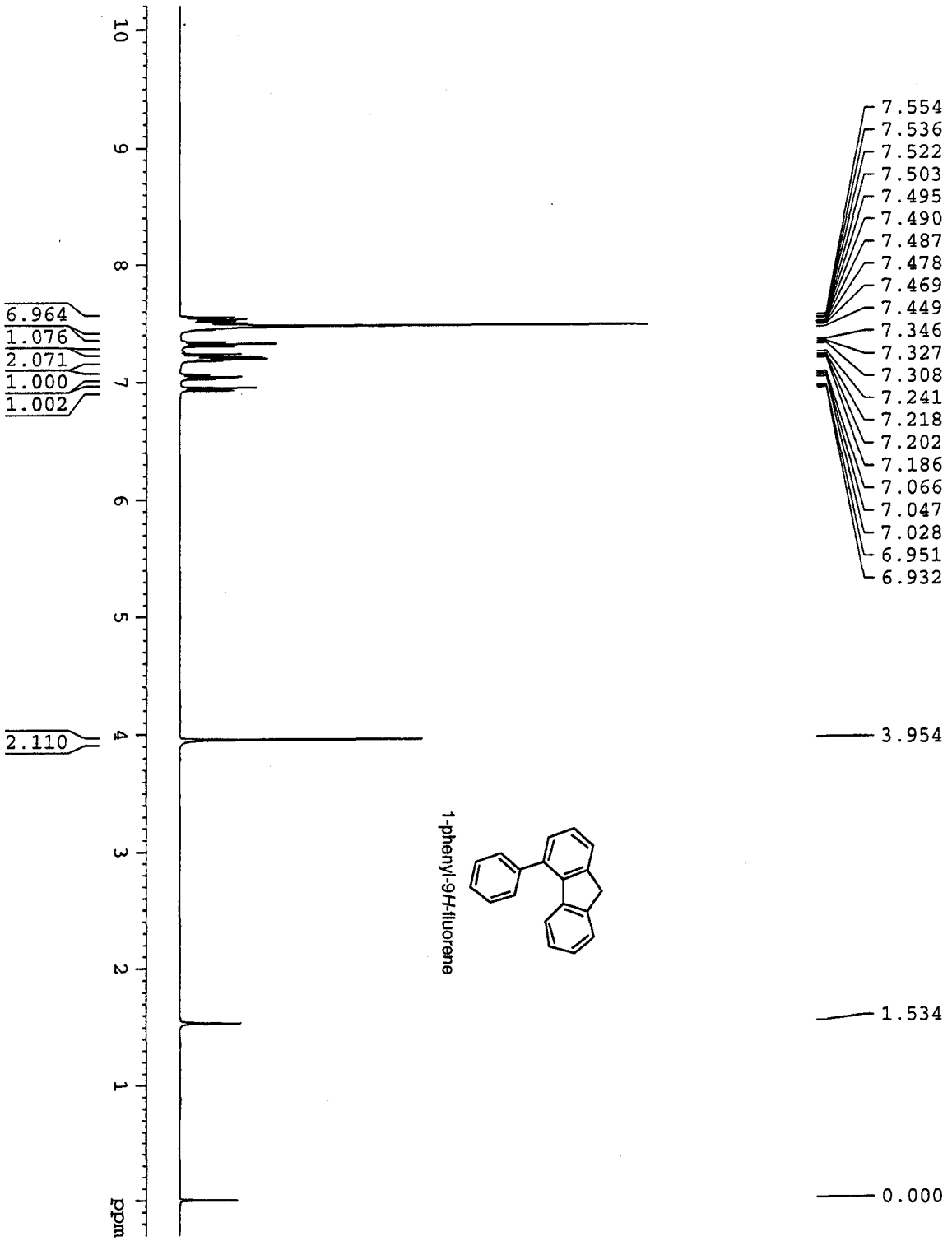

3-(2-iodophenyl)benzyl allyl ether
I
O
146.501
144.271
139.524
138.124
134.750
130.148
128.856
128.688
128.587
128.159
128.085
127.043
117.323
98.640
77.388
77.070
76.753
72.009
71.270
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

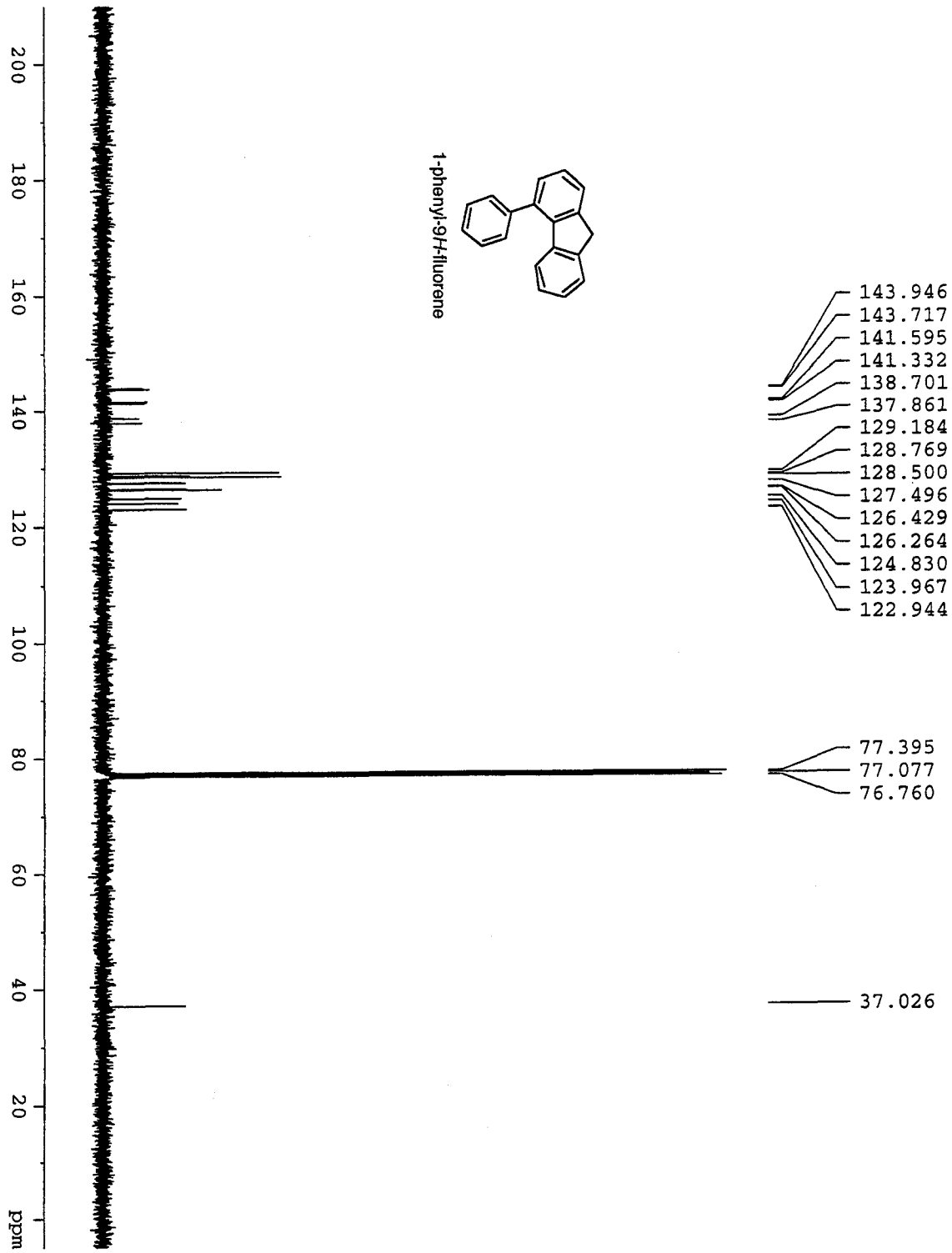

N-[3-(2-iodophenyl)benzyl]-N-methallylmethanesulfonamide
Ms
0.956
2.973
3.156
1.000
2.055
2.030
1.997
3.041
3.037
ppm
7.963
7.960
7.943
7.940
7.423
7.418
7.416
7.413
7.403
7.397
7.395
7.378
7.375
7.284
7.280
7.271
7.265
7.260
7.072
7.067
7.052
7.049
7.033
7.029
5.003
4.976
4.441
3.820
2.833
2.824
2.816
1.752
1.575
0.000

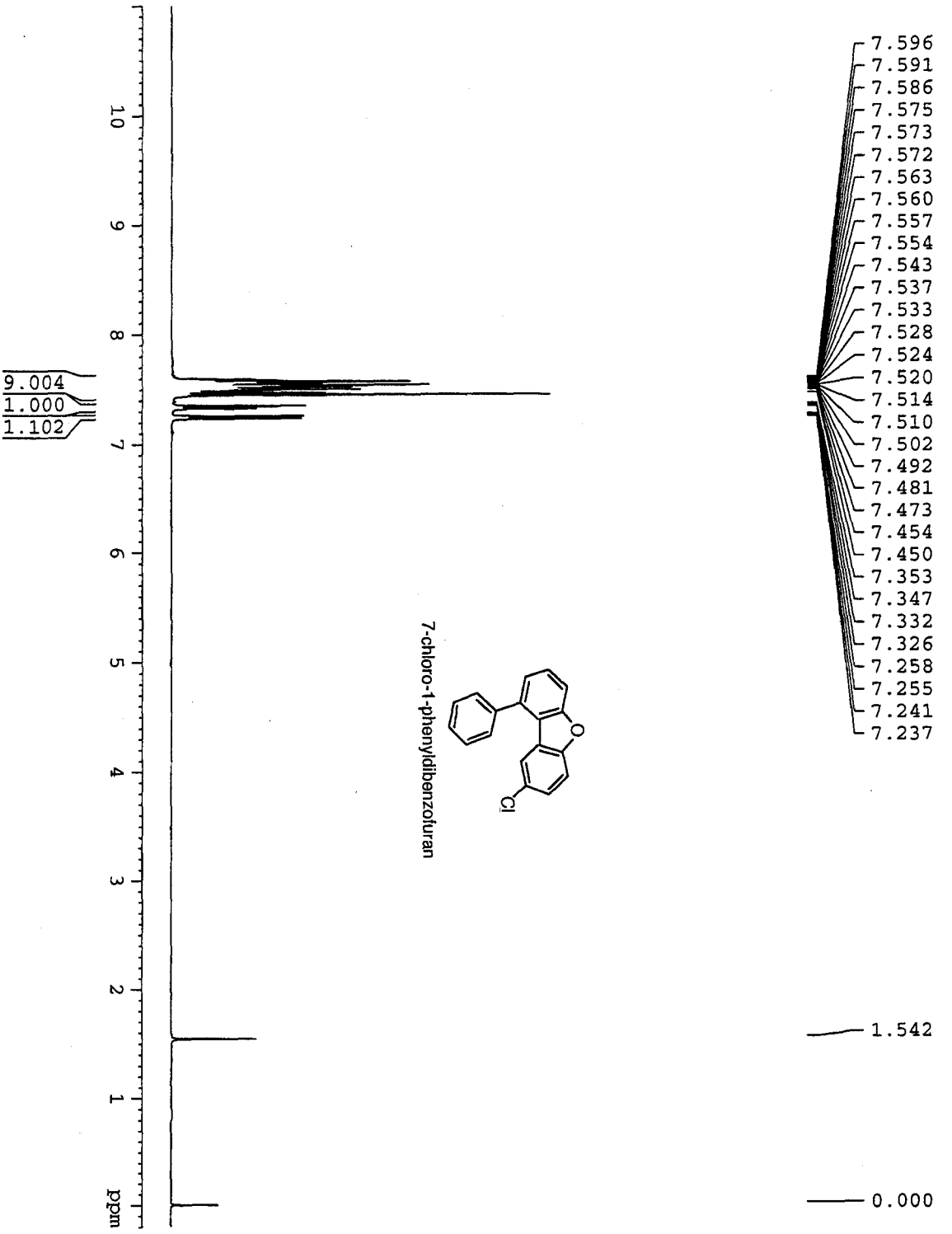

N-[3-(2-iodophenyl)benzyl]-N-methallylmethanesulfonamide
I
N
Ms
146.181
144.744
139.919
139.519
135.549
130.014
129.723
129.078
128.975
128.478
128.311
128.264
114.989
98.570
77.387
77.069
76.751
52.618
49.900
40.334
20.127
200
180
160
140
120
100
80
60
40
20
ppm

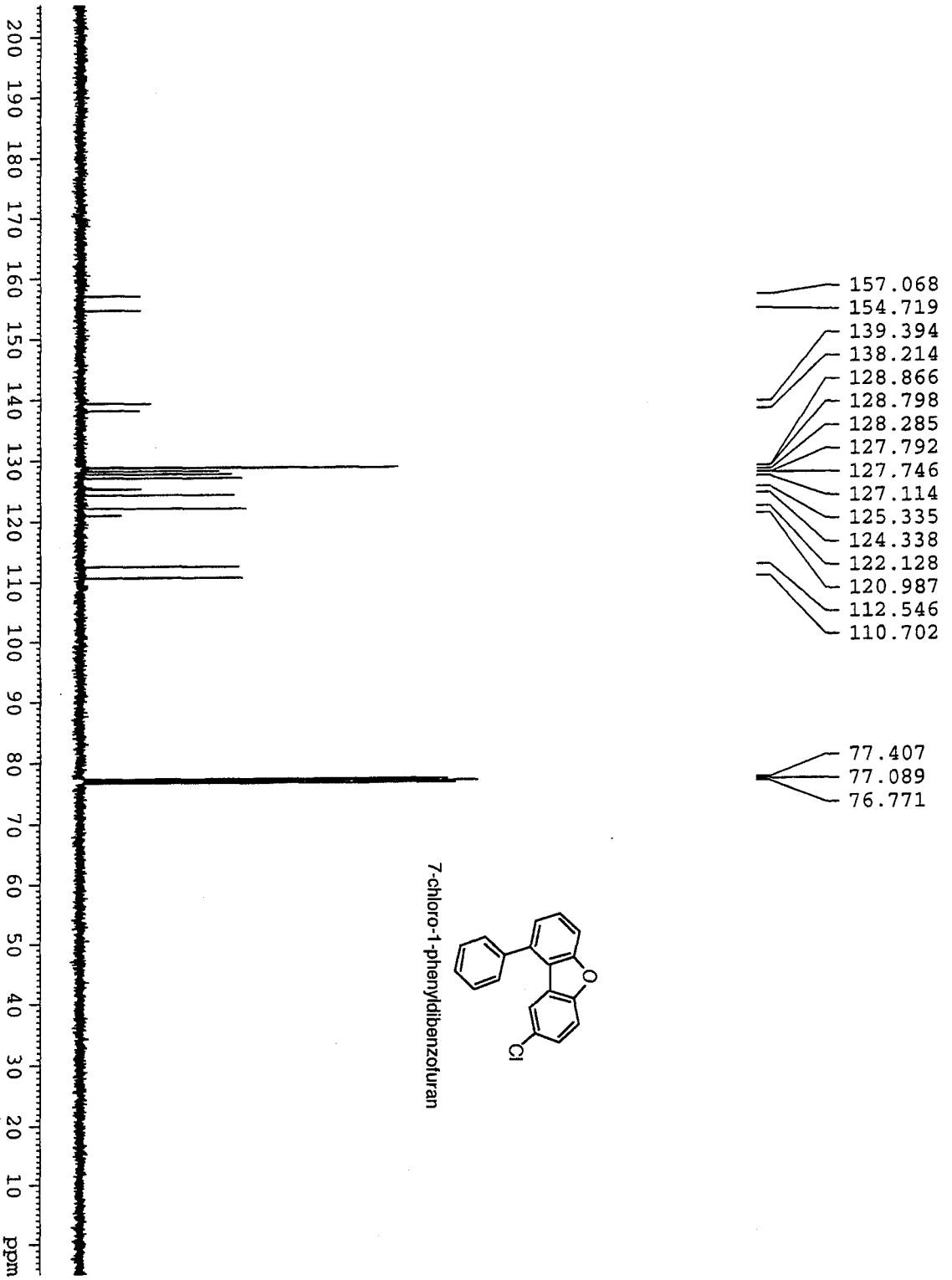

2-iodobenzyl methallyl ether
7.828
7.825
7.808
7.806
7.476
7.458
7.457
7.370
7.368
7.350
7.333
7.331
7.259
7.004
7.000
6.985
6.982
6.981
6.966
6.963
5.047
4.949
4.474
4.015
1.798
0.000
1.000
1.032
1.077
1.030
1.073
1.069
2.158
2.138
3.181
ppm

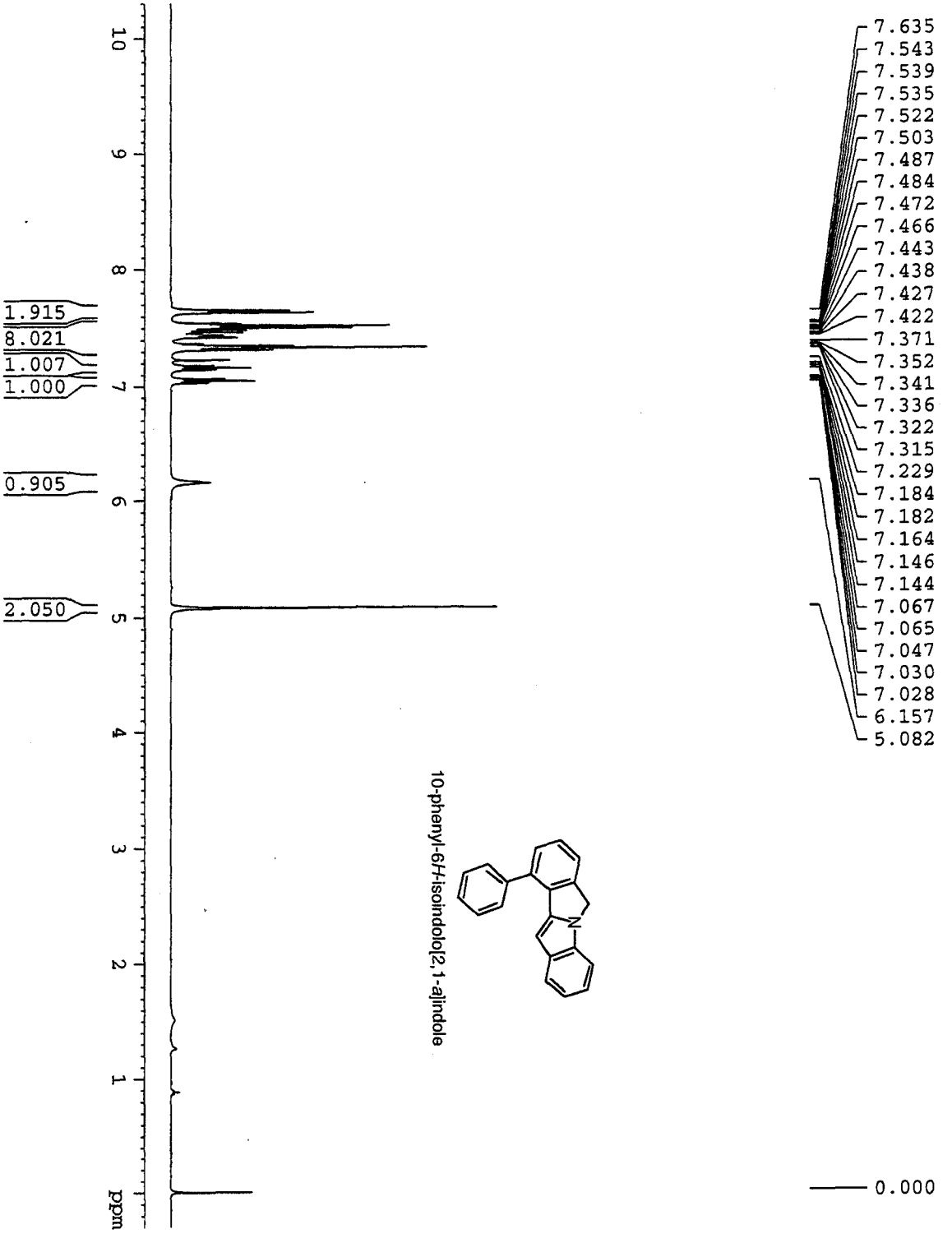

142.224
140.897
139.313
129.271
128.855
128.406
112.709
97.821
77.654
77.230
76.806
75.931
74.861
19.843
O
I
2-iodobenzyl methallyl ether
200
180
160
140
120
100
80
60
40
20
0
ppm

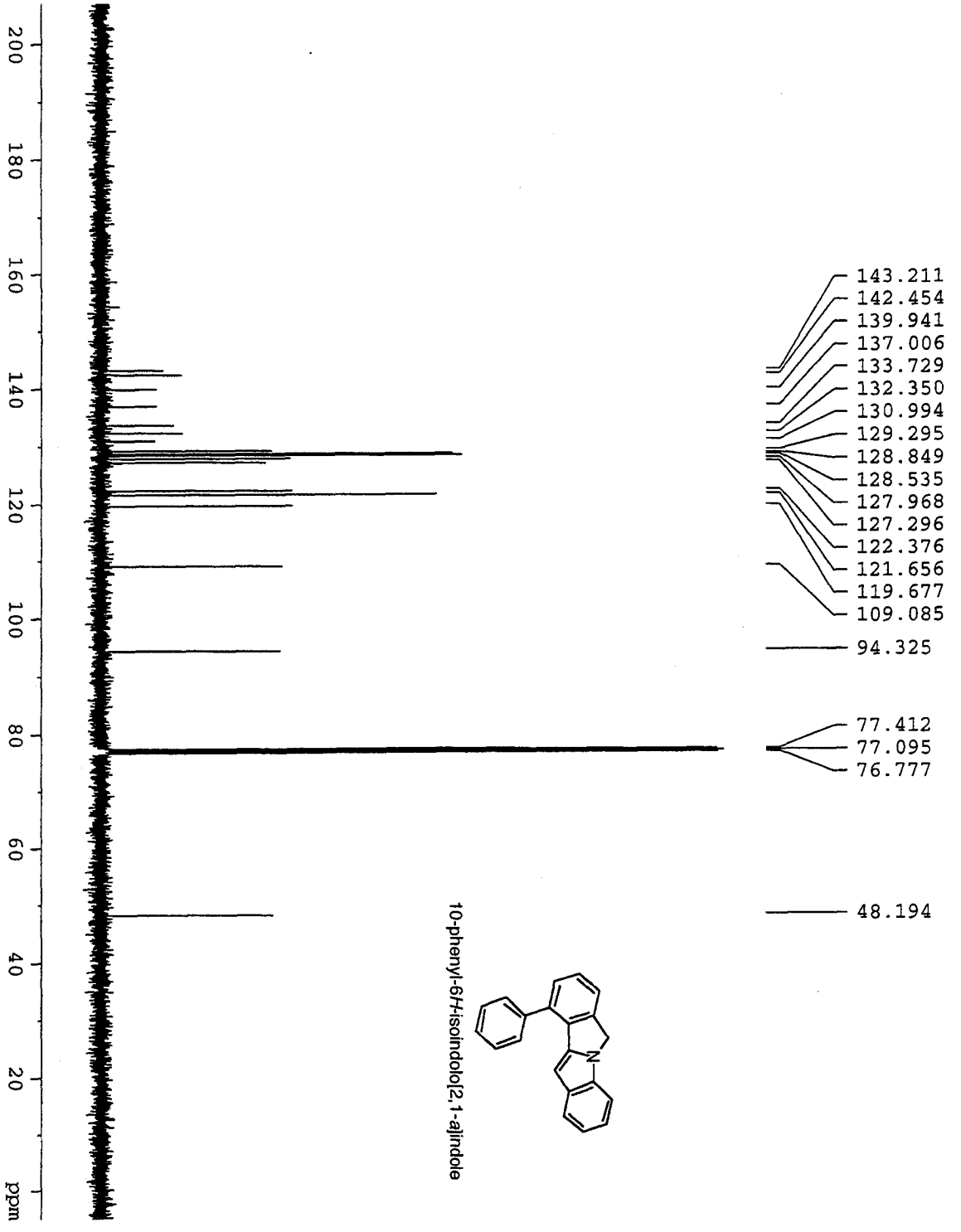

6.964
1.076
2.071
1.000
1.002
2.110
7.554
7.536
7.522
7.503
7.495
7.490
7.487
7.478
7.469
7.449
7.346
7.327
7.308
7.241
7.218
7.202
7.186
7.066
7.047
7.028
6.951
6.932
3.954
1.534
0.000
1-phenyl-9H-fluorene
ppm

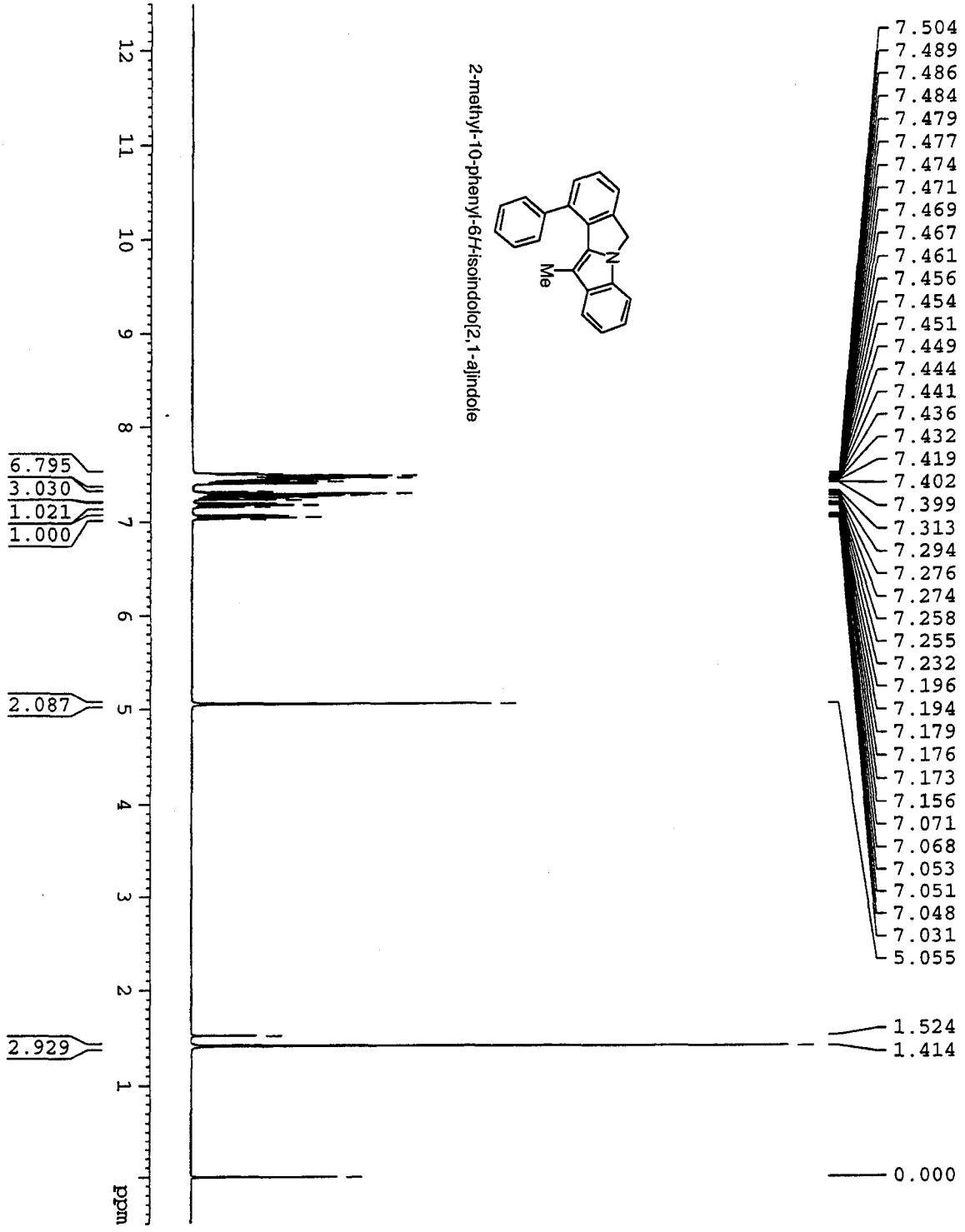

1-phenyl-9H-fluorene
143.946
143.717
141.595
141.332
138.701
137.861
129.184
128.769
128.500
127.496
126.429
126.264
124.830
123.967
122.944
77.395
77.077
76.760
37.026
200
180
160
140
120
100
80
60
40
20
ppm

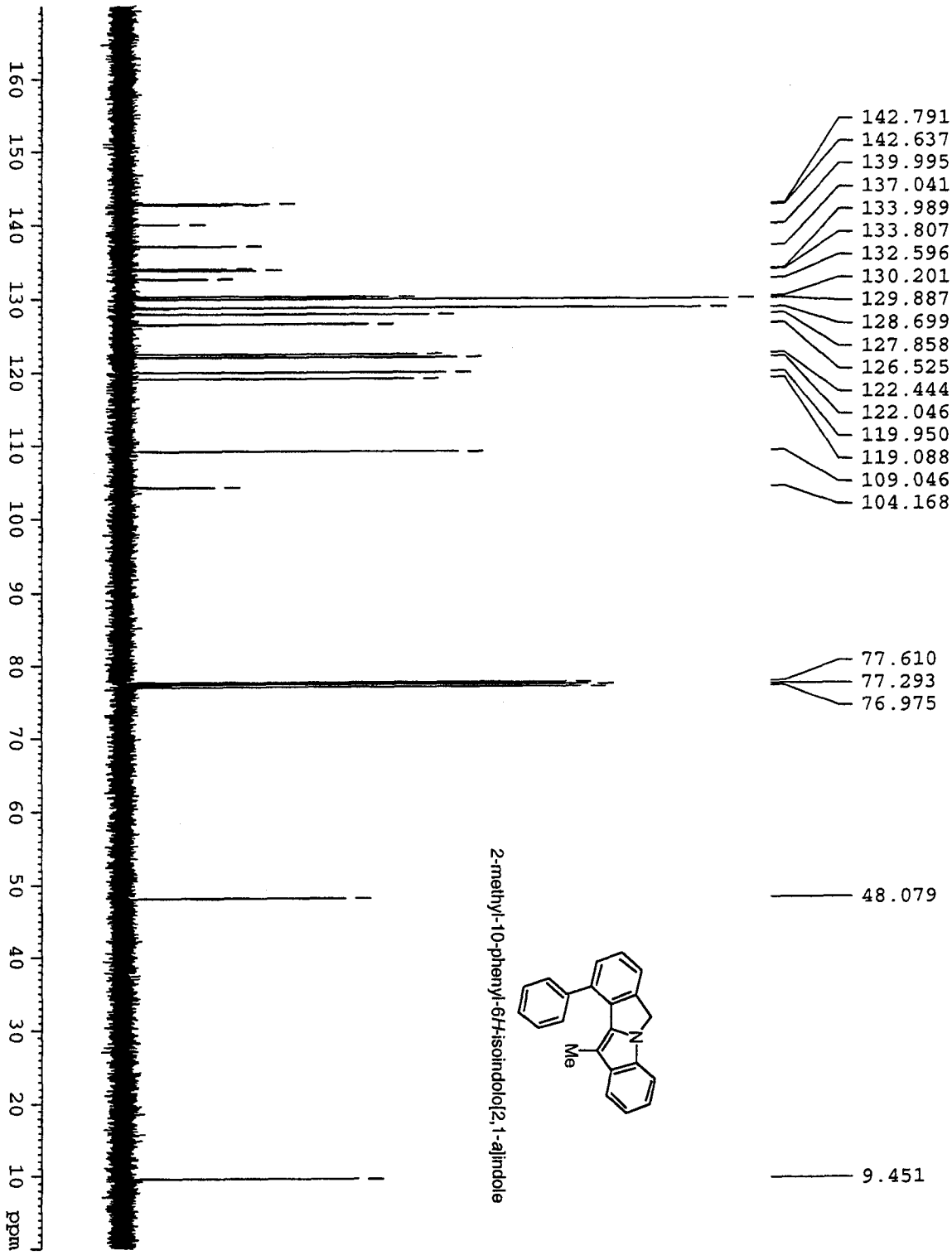

9.004
1.000
1.102
10
9
8
7
6
5
4
3
2
1
ppm
7-chloro-1-phenyldibenzofuran
O
Cl
7.596
7.591
7.586
7.575
7.573
7.572
7.563
7.560
7.557
7.554
7.543
7.537
7.533
7.528
7.524
7.520
7.514
7.510
7.502
7.492
7.481
7.473
7.454
7.450
7.353
7.347
7.332
7.326
7.258
7.255
7.241
7.237
1.542
0.000

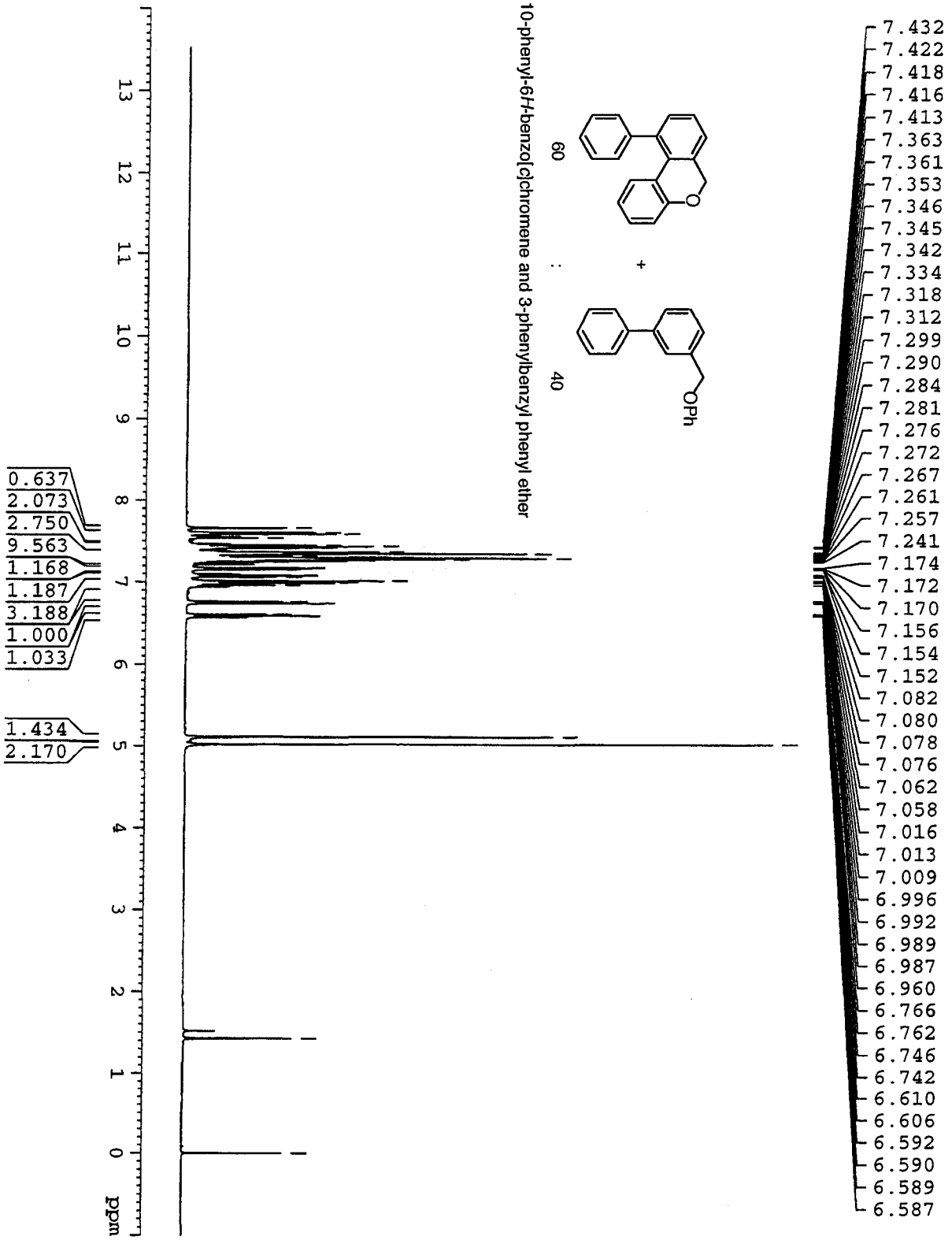

157.068
154.719
139.394
138.214
128.866
128.798
128.285
127.792
127.746
127.114
125.335
124.338
122.128
120.987
112.546
110.702
77.407
77.089
76.771
7-chloro-1-phenyldibenzofuran
O
Cl
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

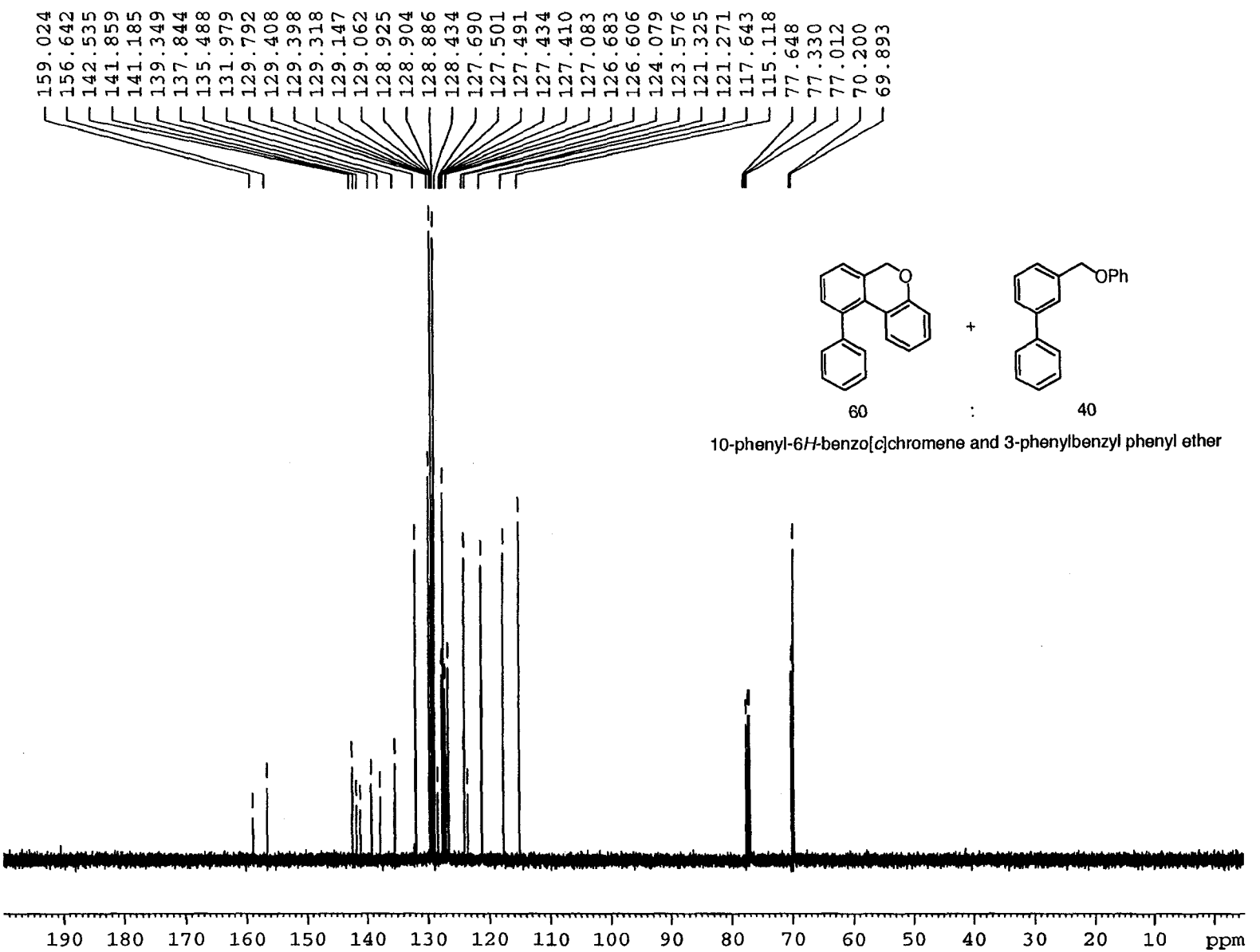

7.635
7.543
7.539
7.535
7.522
7.503
7.487
7.484
7.472
7.466
7.443
7.438
7.427
7.422
7.371
7.352
7.341
7.336
7.322
7.315
7.229
7.184
7.182
7.164
7.146
7.144
7.067
7.065
7.047
7.030
7.028
6.157
5.082
1.915
8.021
1.007
1.000
0.905
2.050
10-phenyl-6H-isoindolo[2,1-a]indole
0.000
ppm


143.211
142.454
139.941
137.006
133.729
132.350
130.994
129.295
128.849
128.535
127.968
127.296
122.376
121.656
119.677
109.085
94.325
77.412
77.095
76.777
48.194
10-phenyl-6H-isoindolo[2,1-a]indole
N
200
180
160
140
120
100
80
60
40
20
ppm

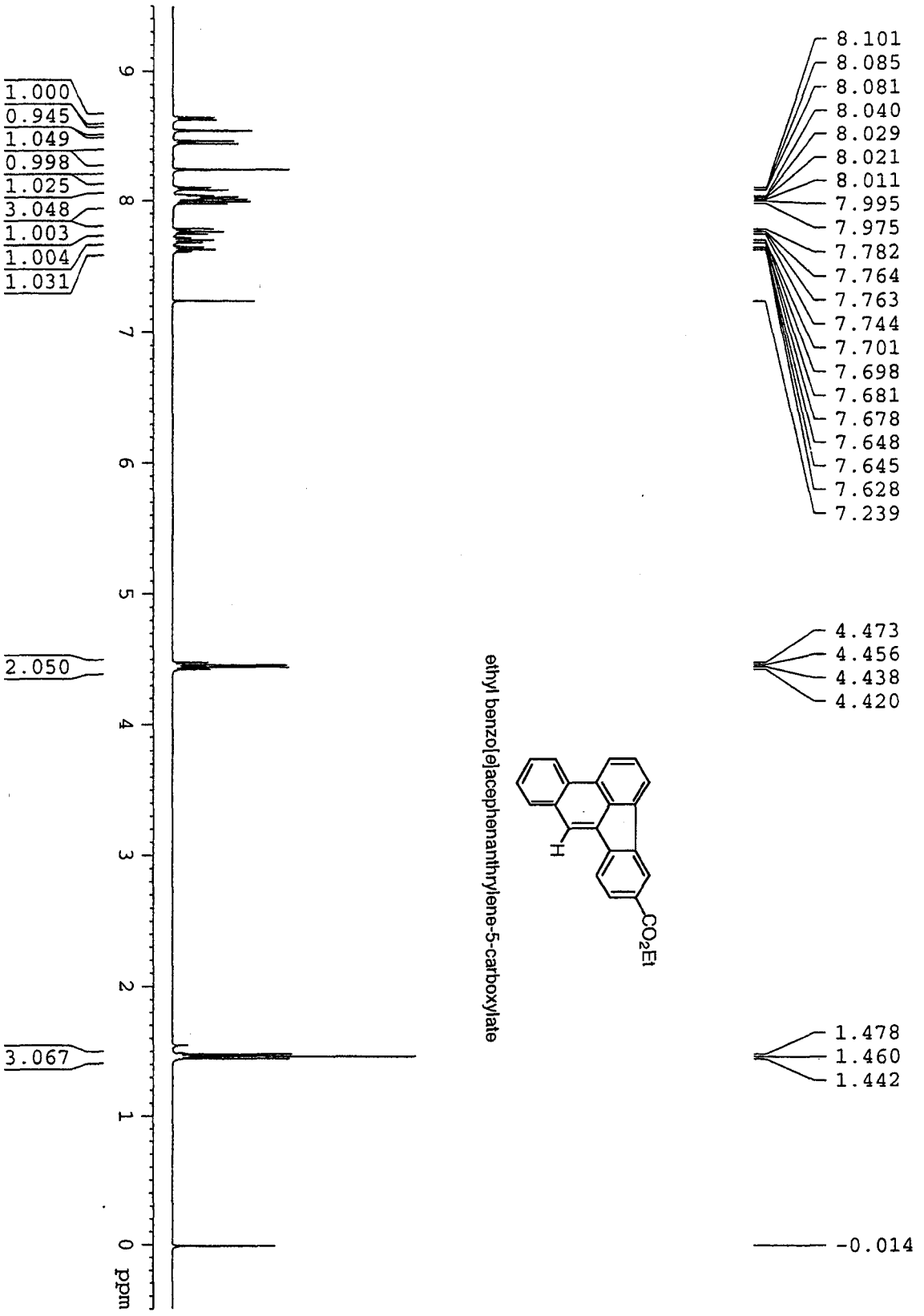

2-methyl-10-phenyl-6*H*-isoindolo[2,1-a]indole
Me
N
7.504
7.489
7.486
7.484
7.479
7.477
7.474
7.471
7.469
7.467
7.461
7.456
7.454
7.451
7.449
7.444
7.441
7.436
7.432
7.419
7.402
7.399
7.313
7.294
7.276
7.274
7.258
7.255
7.232
7.196
7.194
7.179
7.176
7.173
7.156
7.071
7.068
7.053
7.051
7.048
7.031
5.055
1.524
1.414
0.000
6.795
3.030
1.021
1.000
2.087
2.929
ppm

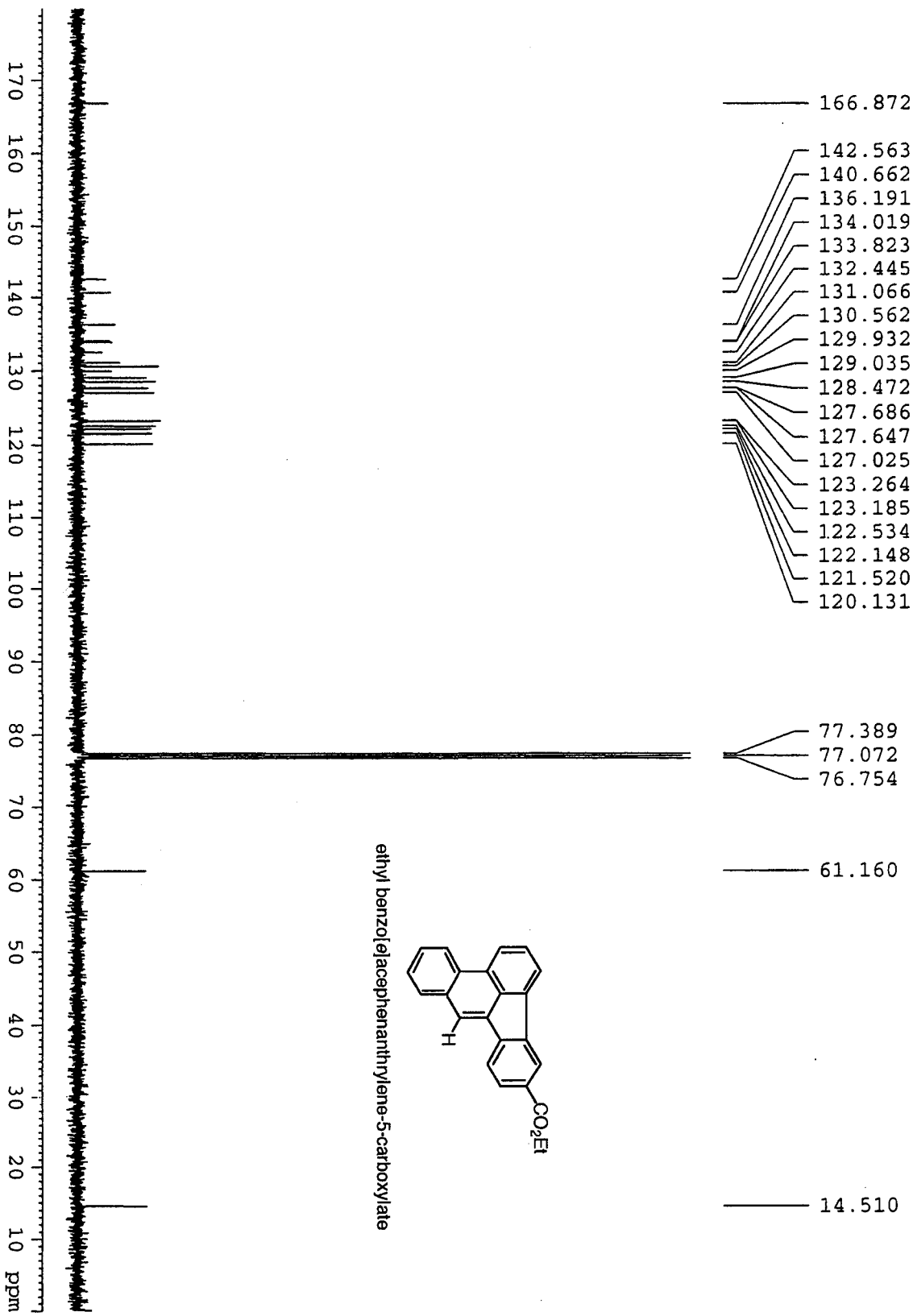

142.791
142.637
139.995
137.041
133.989
133.807
132.596
130.201
129.887
128.699
127.858
126.525
122.444
122.046
119.950
119.088
109.046
104.168
77.610
77.293
76.975
48.079
9.451
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
2-methyl-10-phenyl-6H-isoindolo[2,1-a]indole
Me
N

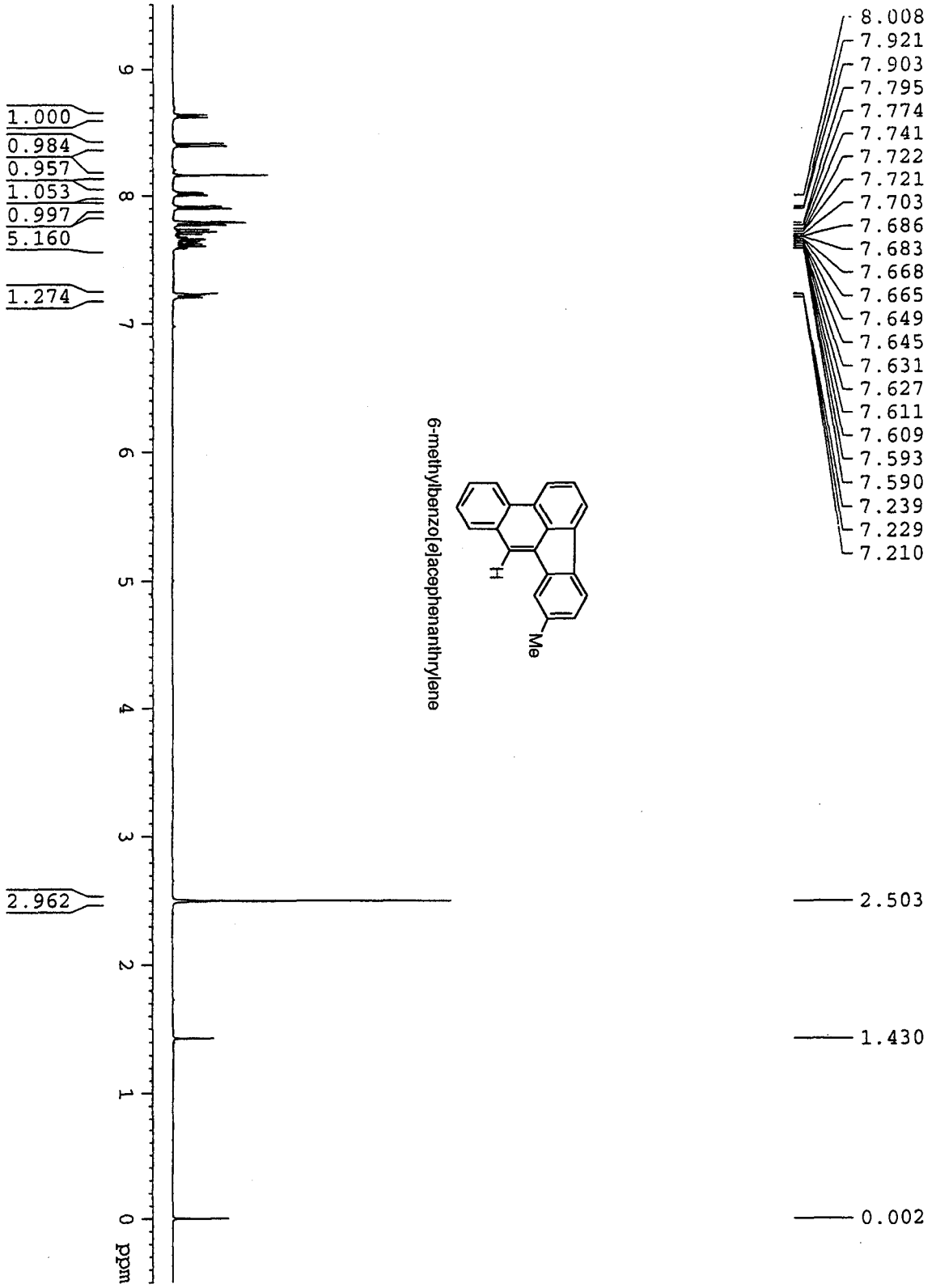

10-phenyl-6H-benzo[c]chromene and 3-phenylbenzyl phenyl ether
OPh
7.432
7.422
7.418
7.416
7.413
7.363
7.361
7.353
7.346
7.345
7.342
7.334
7.318
7.312
7.299
7.290
7.284
7.281
7.276
7.272
7.267
7.261
7.257
7.241
7.174
7.172
7.170
7.156
7.154
7.152
7.082
7.080
7.078
7.076
7.062
7.058
7.016
7.013
7.009
6.996
6.992
6.989
6.987
6.960
6.766
6.762
6.746
6.742
6.610
6.606
6.592
6.590
6.589
6.587
0.637
2.073
2.750
9.563
1.168
1.187
3.188
1.000
1.033
1.434
2.170
ppm

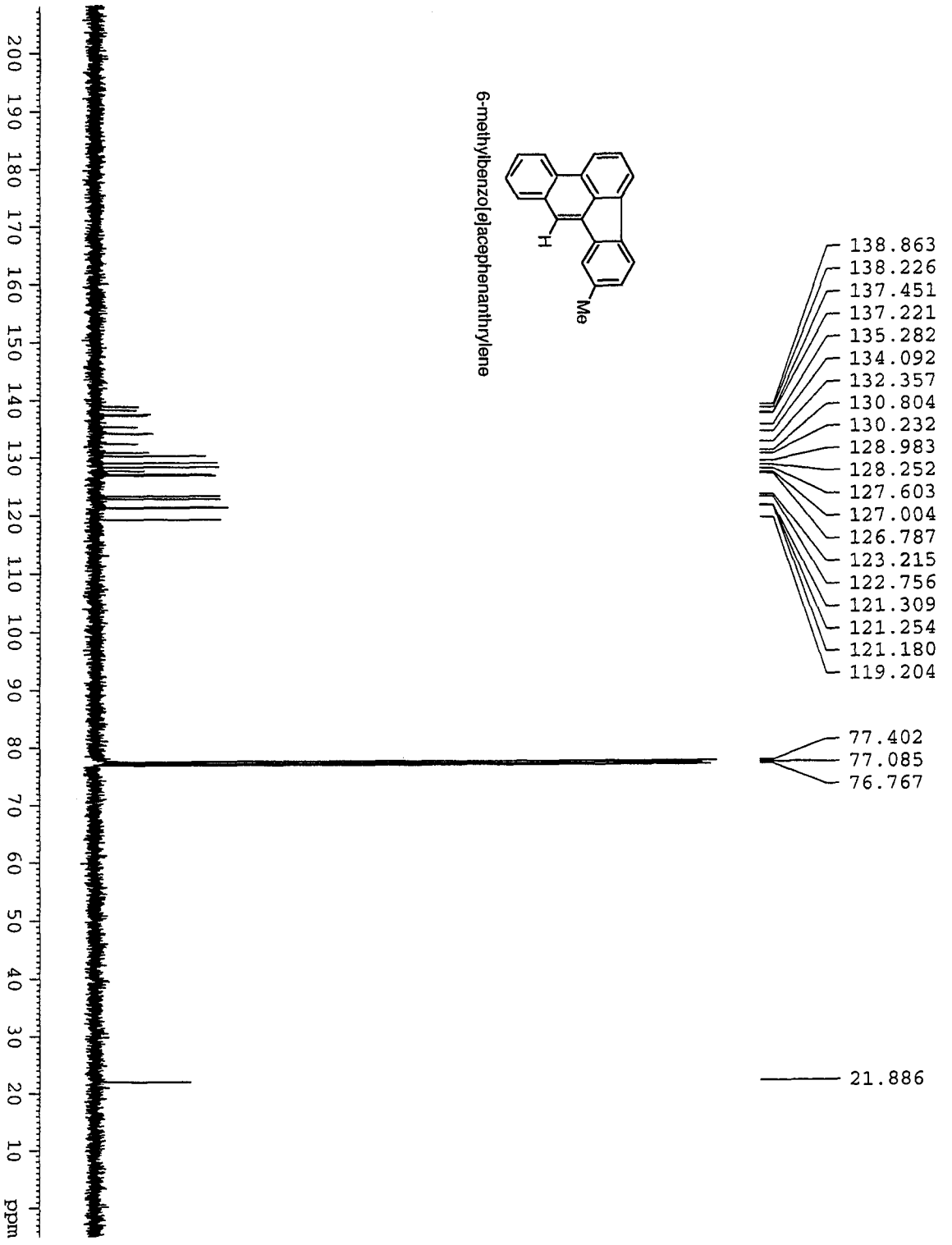


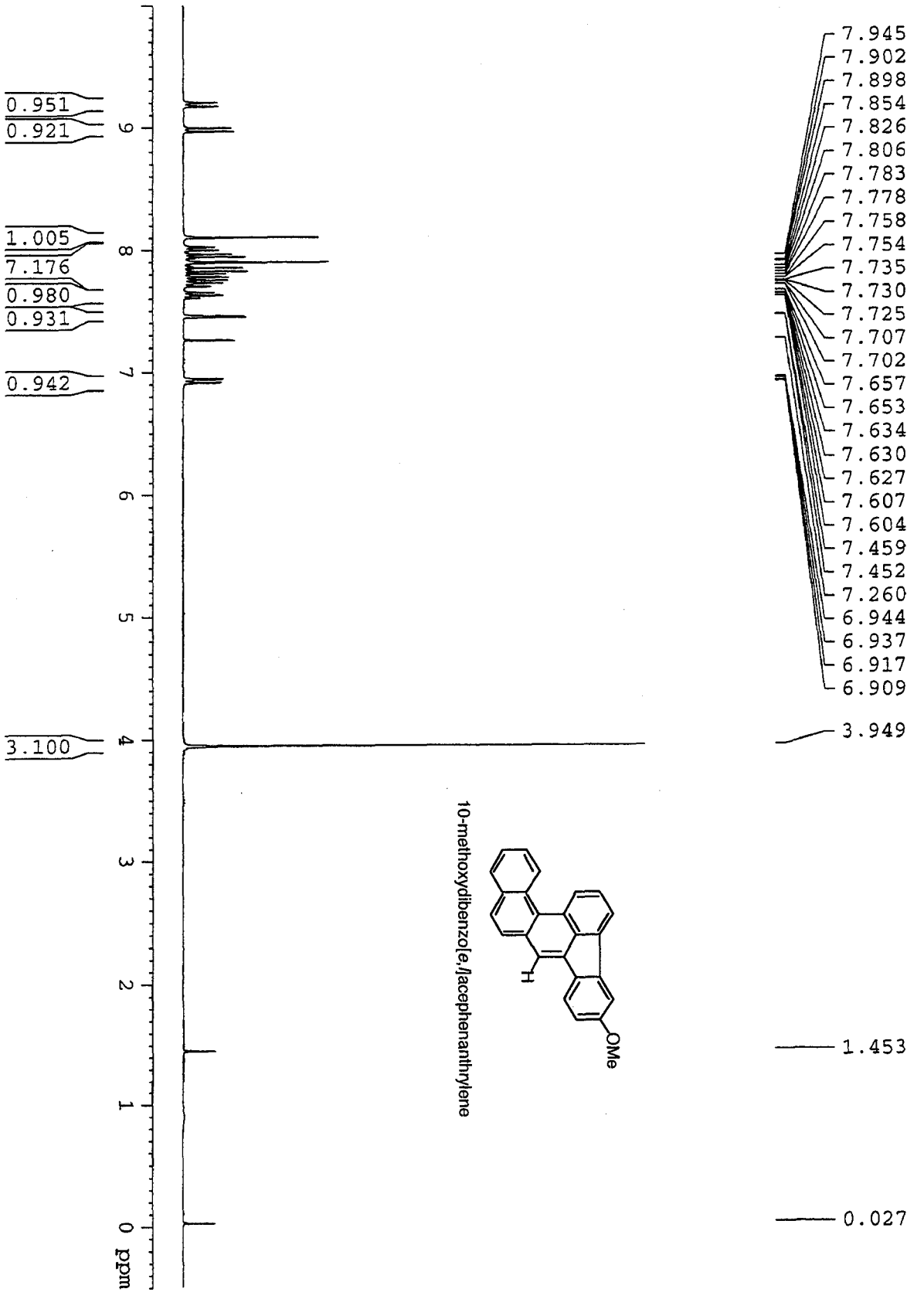
10-phenyl-6*H*-benzo[*c*]chromene and 3-phenylbenzyl phenyl ether

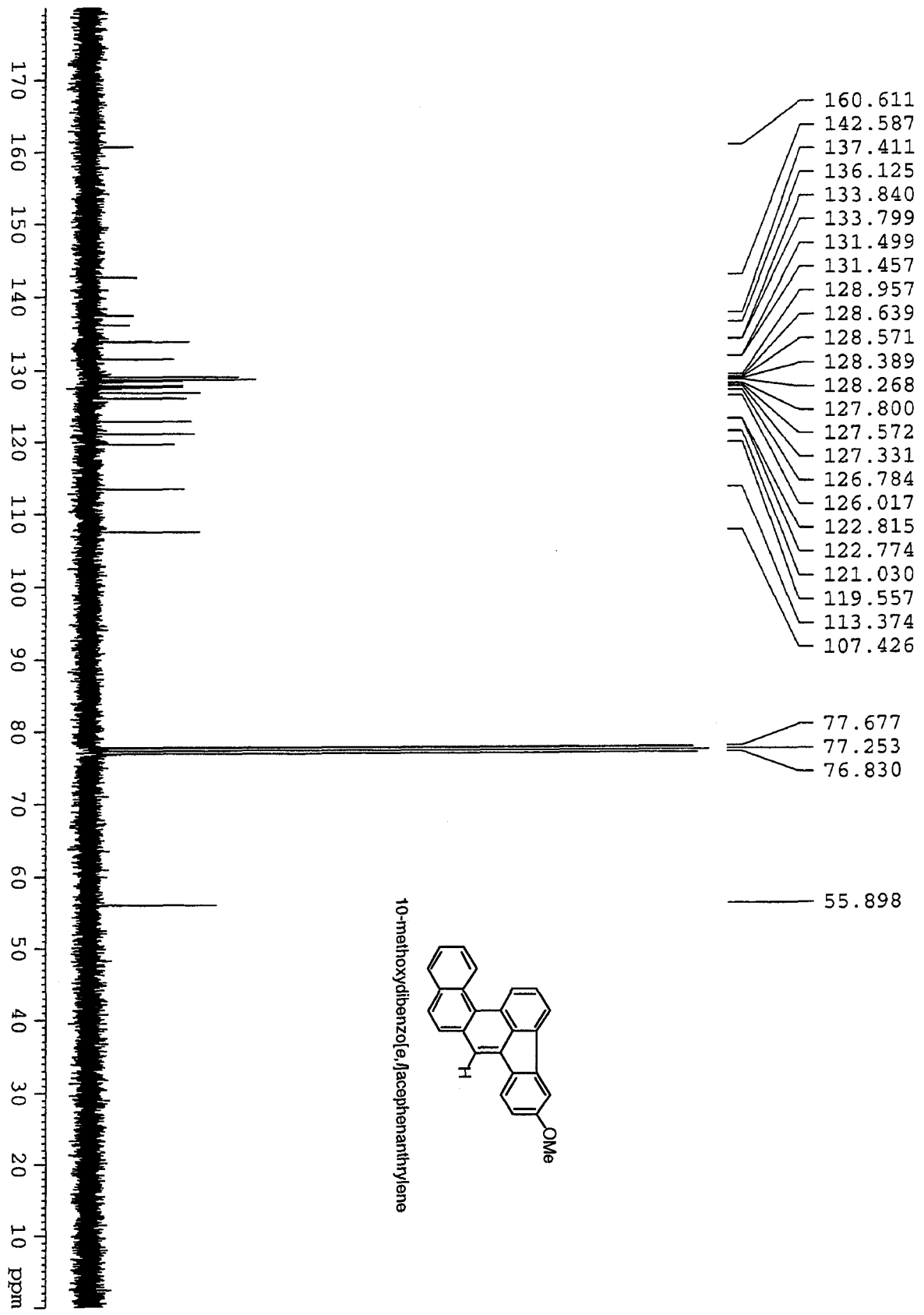

8.101
8.085
8.081
8.040
8.029
8.021
8.011
7.995
7.975
7.782
7.764
7.763
7.744
7.701
7.698
7.681
7.678
7.648
7.645
7.628
7.239
4.473
4.456
4.438
4.420
1.478
1.460
1.442
-0.014
1.000
0.945
1.049
0.998
1.025
3.048
1.003
1.004
1.031
2.050
3.067
ppm
ethyl benzo[e]acephenanthrylene-5-carboxylate
H
CO2Et

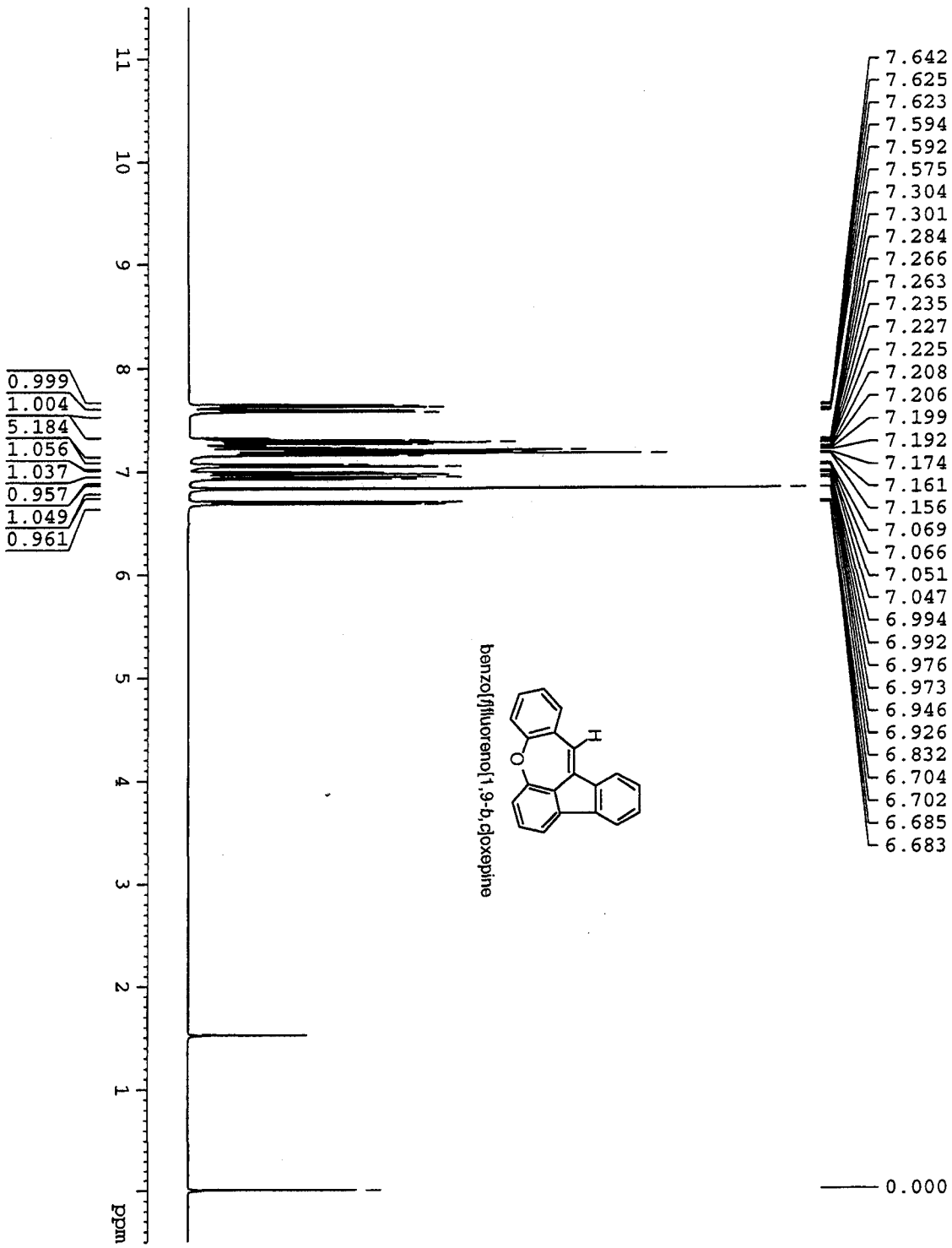

166.872
142.563
140.662
136.191
134.019
133.823
132.445
131.066
130.562
129.932
129.035
128.472
127.686
127.647
127.025
123.264
123.185
122.534
122.148
121.520
120.131
77.389
77.072
76.754
61.160
14.510
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
ethyl benzo[e]acephenanthrylene-5-carboxylate
H
CO2Et

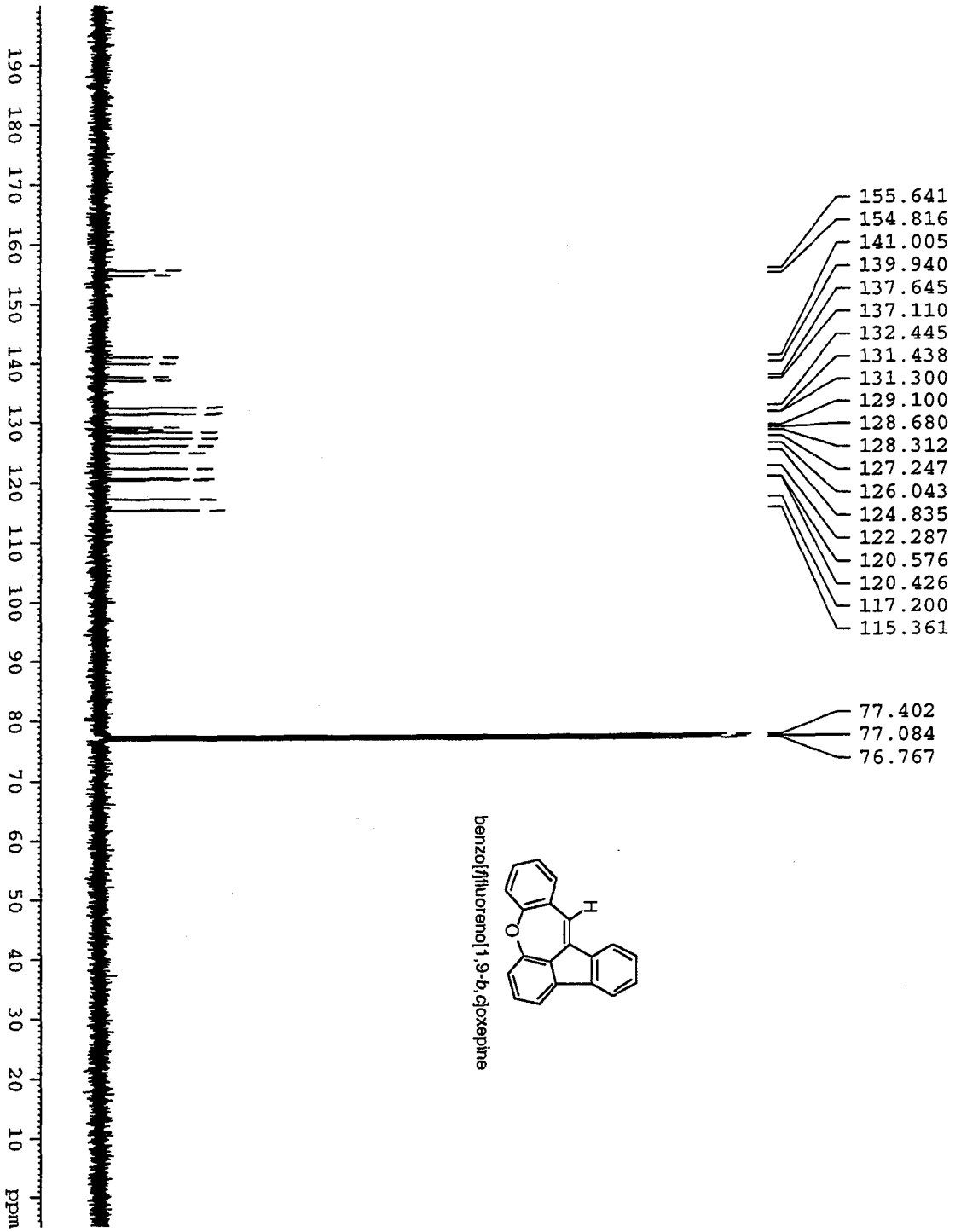

8.008
7.921
7.903
7.795
7.774
7.741
7.722
7.721
7.703
7.686
7.683
7.668
7.665
7.649
7.645
7.631
7.627
7.611
7.609
7.593
7.590
7.239
7.229
7.210
1.000
0.984
0.957
1.053
0.997
5.160
1.274
2.962
2.503
1.430
0.002
6-methylbenzo[e]acephenanthrylene
H
Me
ppm

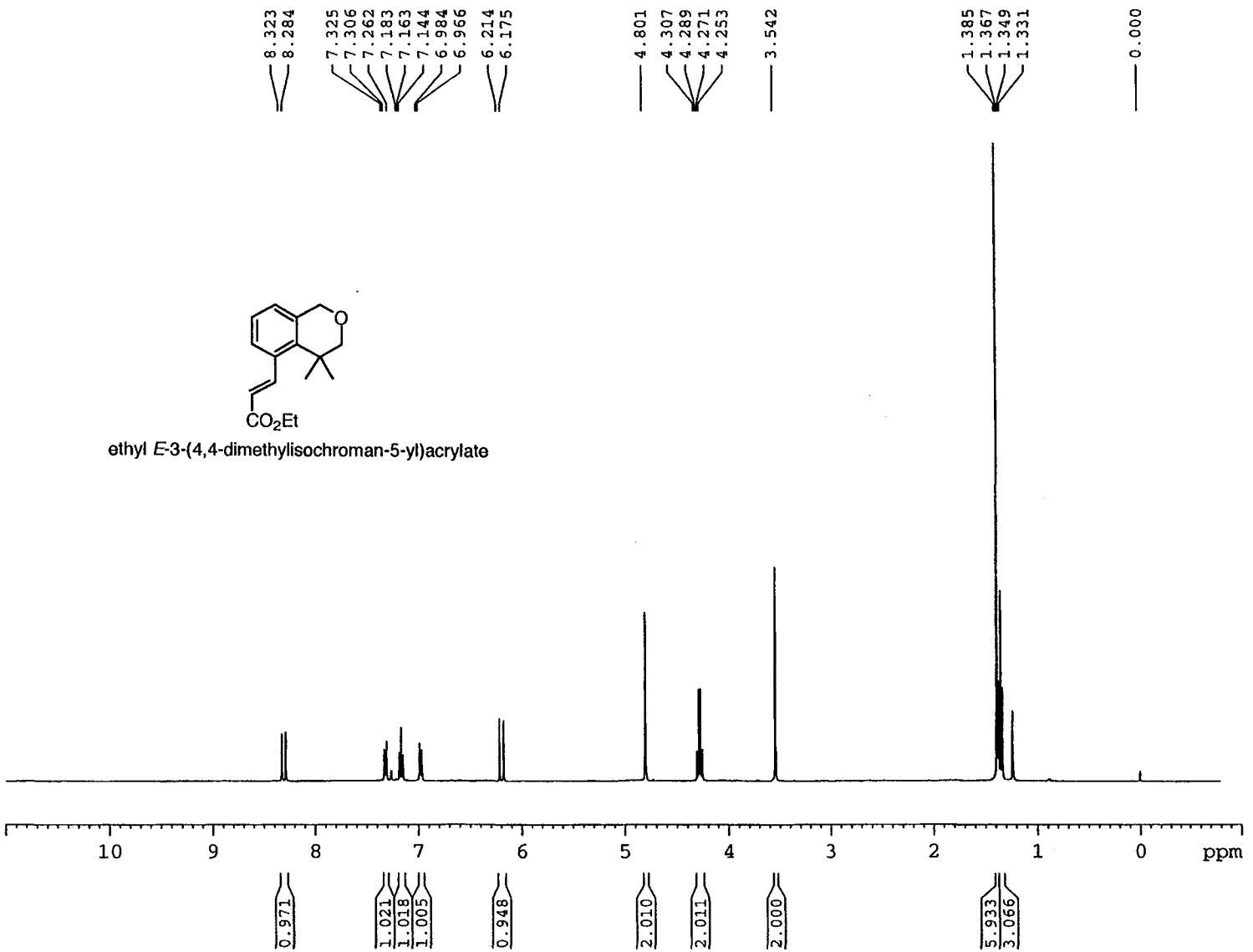

6-methylbenzo[e]acephenanthrylene
H
Me
138.863
138.226
137.451
137.221
135.282
134.092
132.357
130.804
130.232
128.983
128.252
127.603
127.004
126.787
123.215
122.756
121.309
121.254
121.180
119.204
77.402
77.085
76.767
21.886
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


0.951
0.921
1.005
7.176
0.980
0.931
0.942
3.100
9
8
7
6
5
4
3
2
1
0
ppm
7.945
7.902
7.898
7.854
7.826
7.806
7.783
7.778
7.758
7.754
7.735
7.730
7.725
7.707
7.702
7.657
7.653
7.634
7.630
7.627
7.607
7.604
7.459
7.452
7.260
6.944
6.937
6.917
6.909
3.949
1.453
0.027
10-methoxydibenzo[e,fjacephenanthrylene
H
OMe

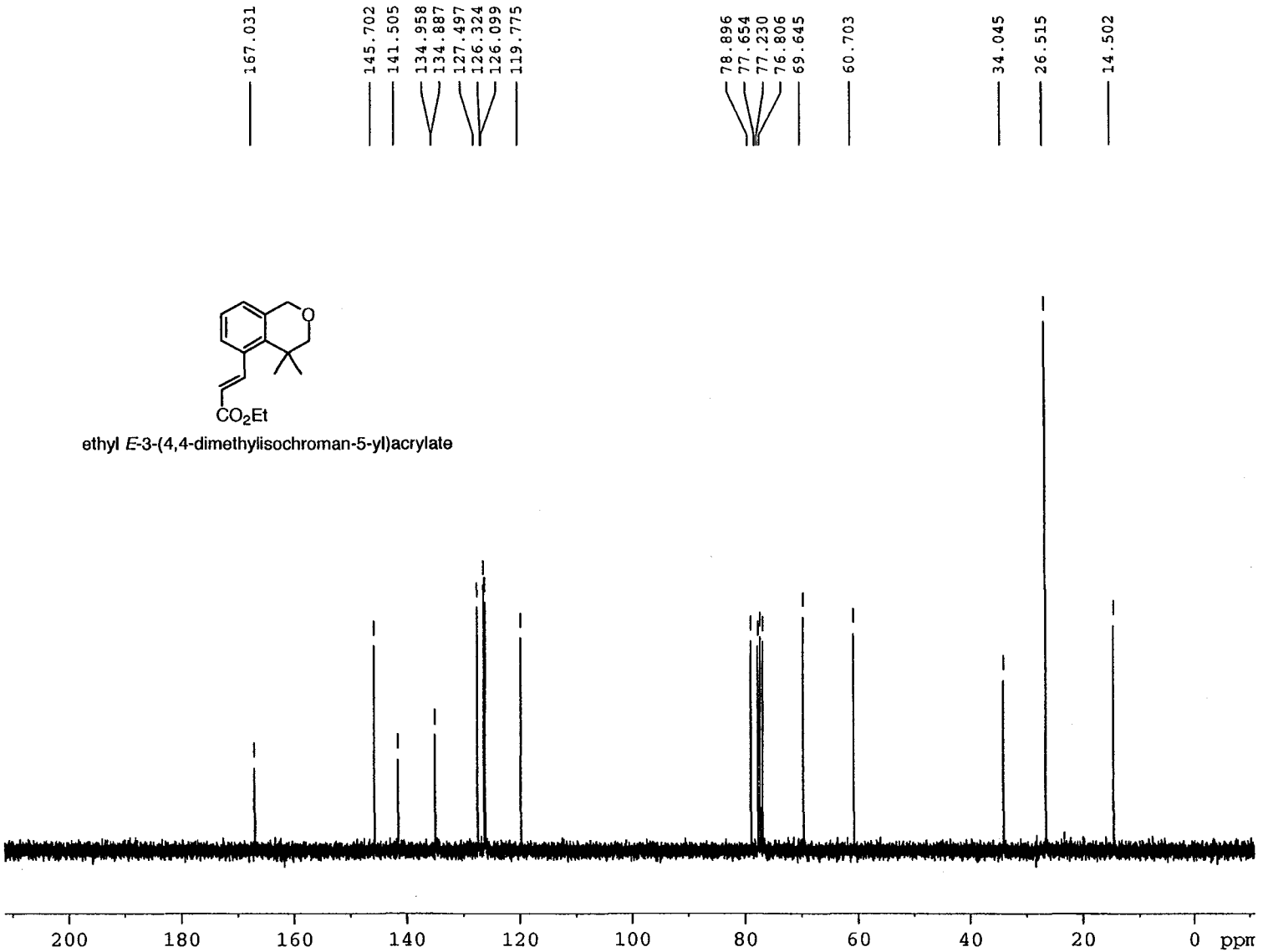

160.611
142.587
137.411
136.125
133.840
133.799
131.499
131.457
128.957
128.639
128.571
128.389
128.268
127.800
127.572
127.331
126.784
126.017
122.815
122.774
121.030
119.557
113.374
107.426
77.677
77.253
76.830
55.898
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
10-methoxydibenzo[e,l]acephenanthrylene
H
OMe


7.642
7.625
7.623
7.594
7.592
7.575
7.304
7.301
7.284
7.266
7.263
7.235
7.227
7.225
7.208
7.206
7.199
7.192
7.174
7.161
7.156
7.069
7.066
7.051
7.047
6.994
6.992
6.976
6.973
6.946
6.926
6.832
6.704
6.702
6.685
6.683
0.000
0.999
1.004
5.184
1.056
1.037
0.957
1.049
0.961
benzo[f]fluoreno[1,9-b,c]oxepine
H
O
11
10
9
8
7
6
5
4
3
2
1
ppm

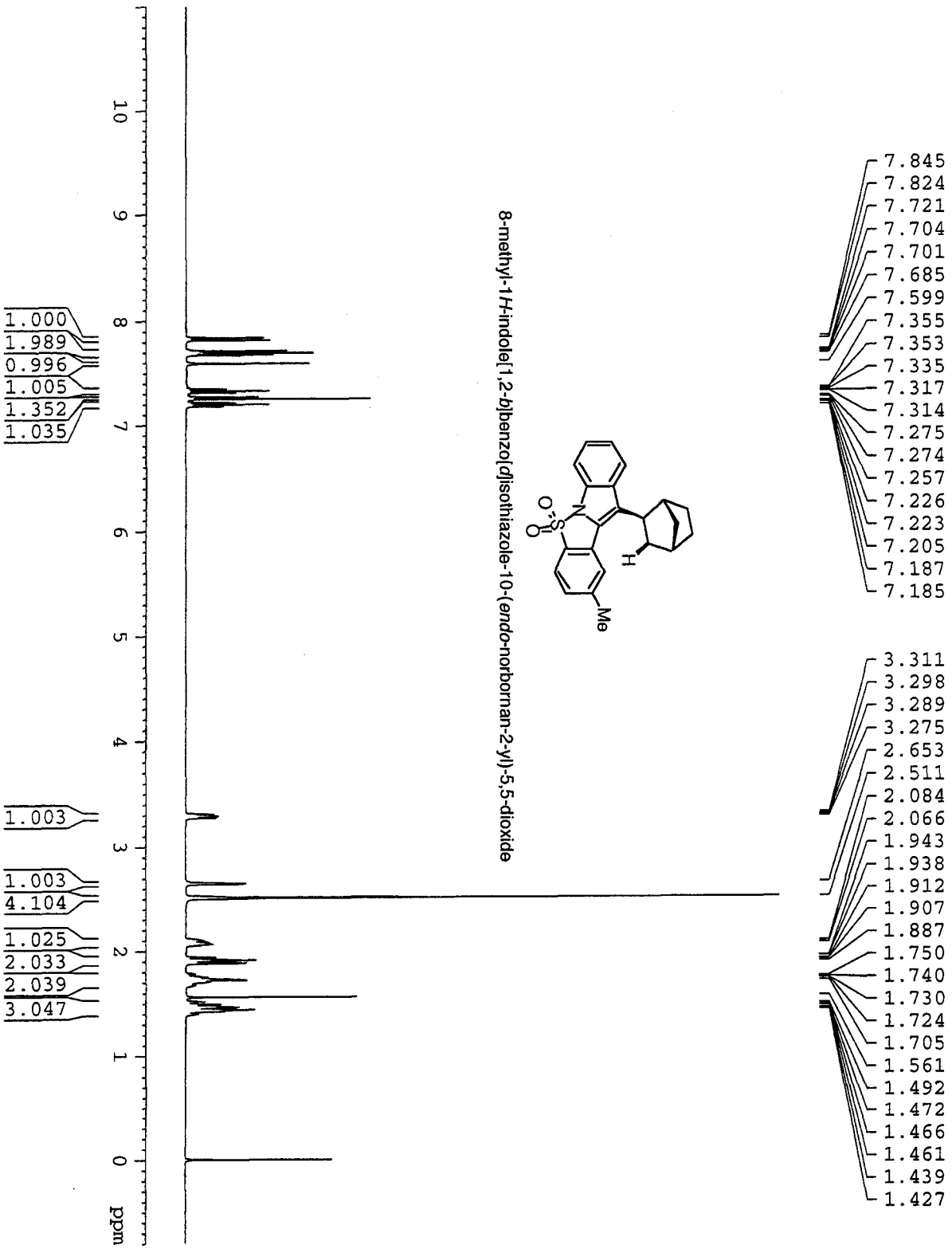

155.641
154.816
141.005
139.940
137.645
137.110
132.445
131.438
131.300
129.100
128.680
128.312
127.247
126.043
124.835
122.287
120.576
120.426
117.200
115.361
77.402
77.084
76.767
benzo[f]fluoreno[1,9-b,c]oxepine
H
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

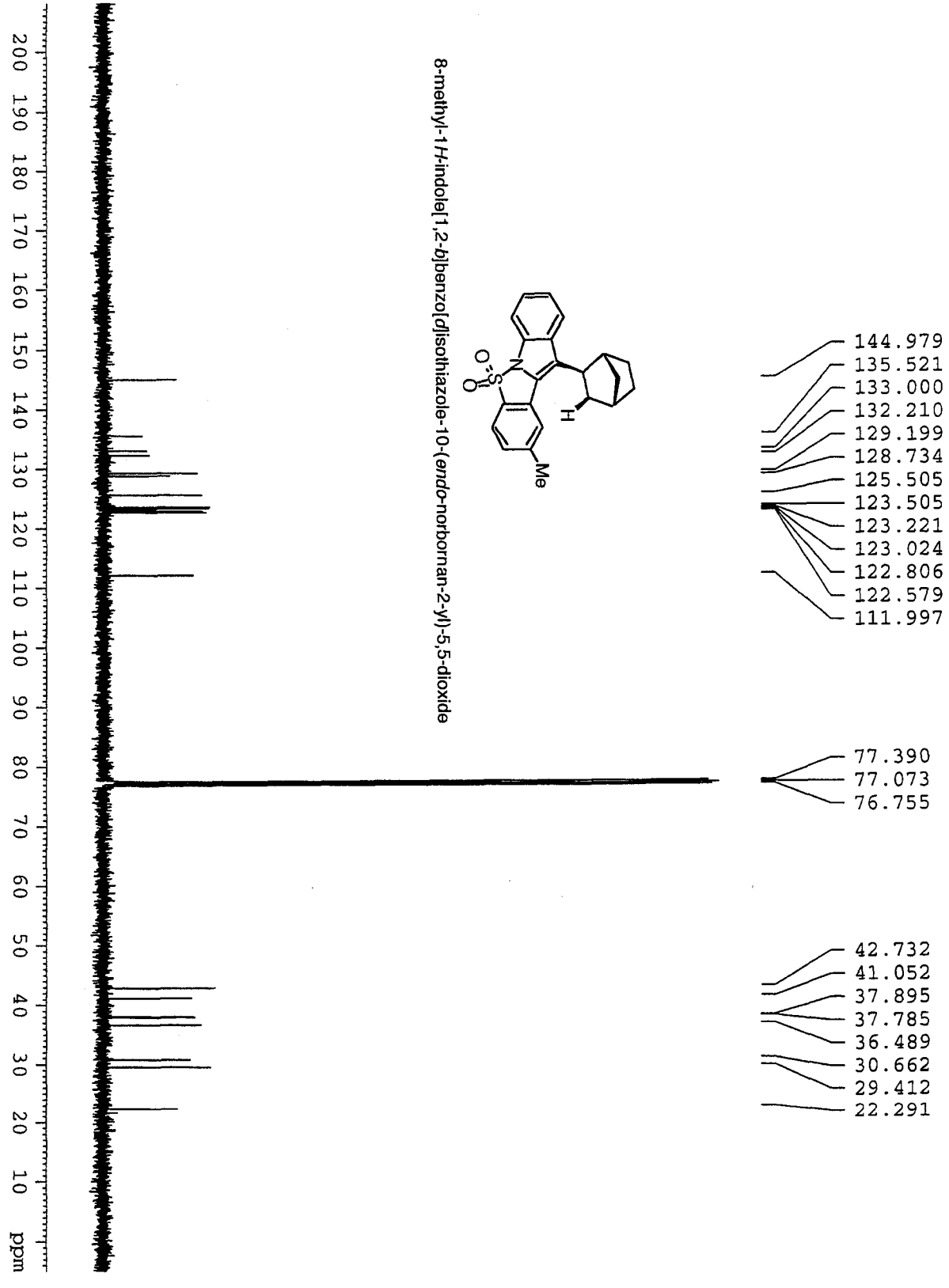


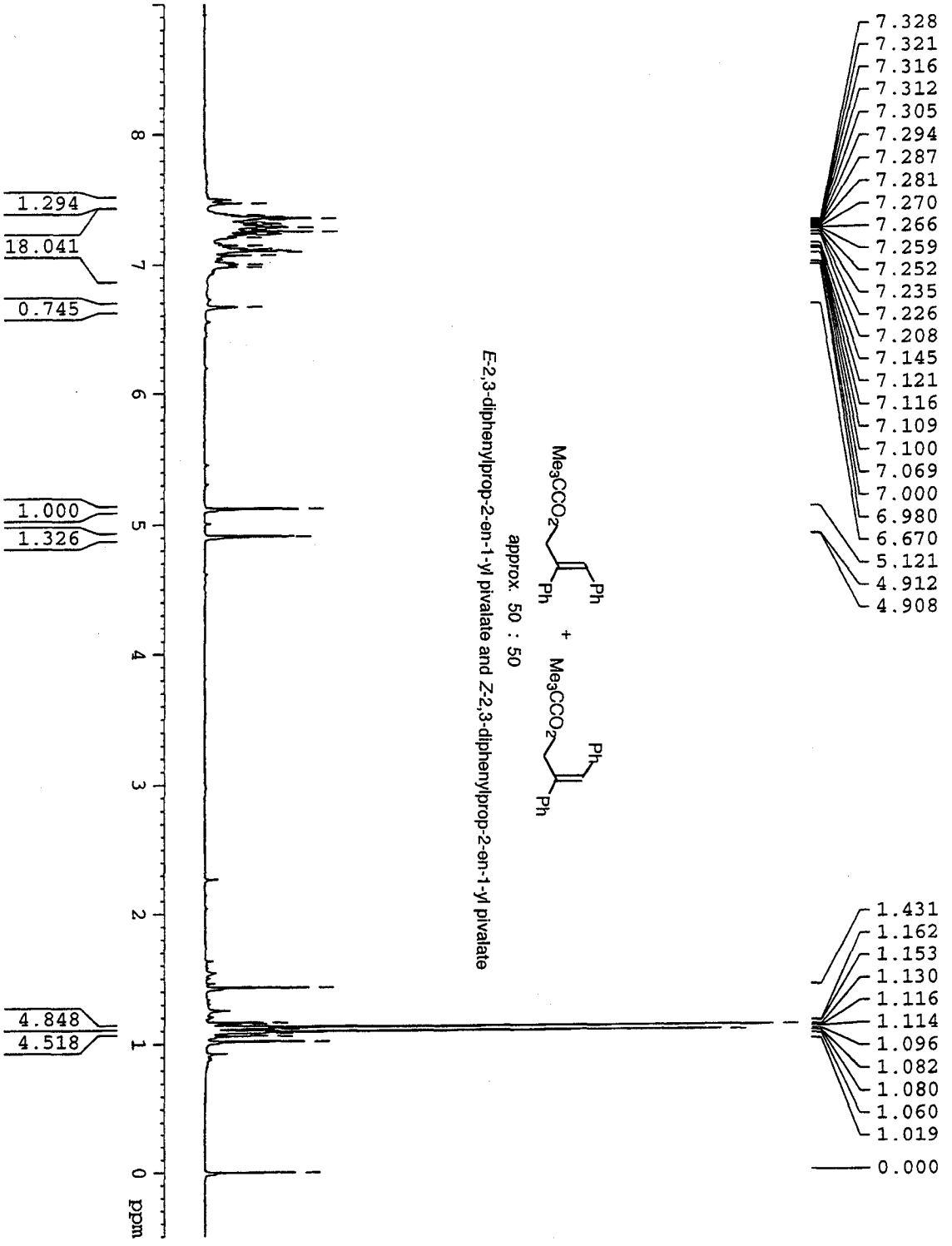
ethyl *E*-3-(4,4-dimethylisochroman-5-yl)acrylate



ethyl *E*-3-(4,4-dimethylisochroman-5-yl)acrylate


8-methyl-1H-indolo[1,2-b]benzo[d]isothiazole-10-(endo-norborman-2-yl)-5,5-dioxide
Me
H
7.845
7.824
7.721
7.704
7.701
7.685
7.599
7.355
7.353
7.335
7.317
7.314
7.275
7.274
7.257
7.226
7.223
7.205
7.187
7.185
3.311
3.298
3.289
3.275
2.653
2.511
2.084
2.066
1.943
1.938
1.912
1.907
1.887
1.750
1.740
1.730
1.724
1.705
1.561
1.492
1.472
1.466
1.461
1.439
1.427
1.000
1.989
0.996
1.005
1.352
1.035
1.003
1.003
4.104
1.025
2.033
2.039
3.047
ppm


8-methyl-1*H*-indole[1,2-*b*]benzo[*d*]isothiazole-10-(*endo*-norbornan-2-yl)-5,5-dioxide
144.979
135.521
133.000
132.210
129.199
128.734
125.505
123.505
123.221
123.024
122.806
122.579
111.997
77.390
77.073
76.755
42.732
41.052
37.895
37.785
36.489
30.662
29.412
22.291
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.328
7.321
7.316
7.312
7.305
7.294
7.287
7.281
7.270
7.266
7.259
7.252
7.235
7.226
7.208
7.145
7.121
7.116
7.109
7.100
7.069
7.000
6.980
6.670
5.121
4.912
4.908
1.431
1.162
1.153
1.130
1.116
1.114
1.096
1.082
1.080
1.060
1.019
0.000
1.294
18.041
0.745
1.000
1.326
4.848
4.518
8
7
6
5
4
3
2
1
0
ppm
Me3CCO2
Ph
Ph
+
Me3CCO2
Ph
Ph
approx. 50 : 50
E-2,3-diphenylprop-2-en-1-yl pivalate and Z-2,3-diphenylprop-2-en-1-yl pivalate

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I would also like to thank my very dear friends Kathy and David Larson for being so special and warm. Thank you for making me feel right at home.

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Unfortunately there is not enough space here to acknowledge all my aunts and uncles (Molina and Campo). Nevertheless, I would like to give special thanks to my parents Marino Campo and Margarita Molina, my brothers Mauricio Campo and Jose Luis Campo, my grandmother Stella Aristizabal, my great aunt Nubia Aristizabal, my aunts Miriam Campo and Sonia Molina, my very loving uncle Eduardo Campo, my grandfather Efren Molina, and my beloved wife Isabelle Schluep Campo for their love, encouragement and their endless support. Thank you so much for everything.