1-1-2002

Synthesis of benzo[b]thiophenes and indoles via palladium-catalyzed coupling and electrophilic cyclization of terminal acetylenes

Dawei Yue
Iowa State University

Recommended Citation

Yue, Dawei, "Synthesis of benzo[b]thiophenes and indoles via palladium-catalyzed coupling and electrophilic cyclization of terminal acetylenes" (2002). *Retrospective Theses and Dissertations*. 21368.
https://lib.dr.iastate.edu/rtd/21368

Synthesis of benzo[*b*]thiophenes and indoles via palladium-catalyzed coupling and electrophilic cyclization of terminal acetylenes

by

Dawei Yue

A thesis submitted to the graduate faculty
in partial fulfillment of the requirements for the degree of
MASTER OF SCIENCE

Major: Organic Chemistry
Program of Study Committee:
Richard C. Larock (Major Professor)
Dennis C. Johnson
William S. Jenks

Iowa State University
Ames, Iowa
2002

Graduate College

Iowa State University

This is to certify that the master's thesis of

Dawei Yue

has met the thesis requirements of Iowa State University

To my parents and my wife,

for their love, patience, support and encouragement.

LIST OF ABBREVIATIONS

aq	aqueous
Bu	butyl
t-Bu	*tert*-butyl
cat.	catalytic
d	doublet
dd	doublet of doublet
eq	equation
equiv	equivalent
Et	ethyl
h	hour(s)
HRMS	high resolution mass spectroscopy
Hz	Hertz
IR	infrared
m	multiplet
Me	methyl
ml	milliliter(s)
mol	mole(s)
mp	melting point
MS	mass spectrometry
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance
o	ortho

o-tol	*o*-tolyl
Ph	phenyl
q	quartet
s	singlet
satd	saturate
t	triplet
tert	tertiary
TLC	thin layer chromatography
TMS	trimethylsilyl

GENERAL INTRODUCTION

Benzo[*b*]thiophenes and indoles are important heterocyclic ring system in organic chemistry, because of their occurrence in natural products and their wide range of biological and physiological effects.[1] Research directed towards concise, new syntheses of 2,3-disubstituted benzo[*b*]thiophenes and indoles are highly desirable.

Electrophilic cyclization[2] has been widely used in organic synthesis. However, this type of cyclization is generally limited to the cyclization of carbon-carbon double bonds. The cyclization of compounds with carbon-carbon triple bonds is relatively unexplored. Previous work by Cacchi[3], Flynn[4] and Larock[5] shows that iodine and other electrophiles can be used for the synthesis of benzo[*b*]furans, benzo[*b*]thiophenes and isoquinolines. This type of cyclization is generally viewed as proceeding through an intramolecular, stepwise electrophilic addition and dealkylation mechanism involving a cationic intermediate. The mild reaction conditions and high efficiency encouraged us to further explore the generality of this approach for benzo[*b*]thiophenes and indoles utilizing various electrophiles.

Thesis Organization

This thesis is composed of two chapters. The chapters presented herein are written following the guidelines for a full paper in the *Journal of Organic Chemistry* and are composed of an abstract, introduction, results and discussion, conclusion, experimental, acknowledgement, and references.

Chapter 1 is a publication that describes the synthesis of 2,3-disubstituted benzo[*b*]thiophenes by the palladium-catalyzed coupling and electrophilic cyclization of terminal alkynes. This process has proven to be highly efficient. Various electrophiles undergo this process and give high yields of the desired cyclization products.

Chapter 2 presents the synthesis of indoles by electrophilic cyclization. The overall synthetic process involves the coupling of a terminal acetylene with an *N,N*-dialkyl-*o*-iodoaniline by a palladium-catalyzed coupling reaction, followed by electrophilic cyclization. Iodine is the most effective electrophile for this process. It gives high yields of 3-iodoindoles, which can be further functionalized by utilizing palladium-catalyzed couplings.

Finally, all of the ^{1}H and ^{13}C NMR spectra for the thioanisole and aniline starting materials and the electrophilic cyclization products have been compiled in appendices A and B following the general conclusions for this thesis.

References

1. (a) Pinny, K. G.; Bounds, A. D.; Dubgenab, K. M.; Mocharla, V. P.; Pettit, G. R.; Hamel, E. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1081. (b) Pinny, K. G.; Pettit, G. R.; Mocharla, V. P.; Del, P. M.; Shirali, A. *PCT Int. Appl. WO 98 39 323 (Chem. Abs.,* **1998**, *129, 245037c*). (c) Sundberg, R. *J. Prog. Heterocyclic Chem.* **1989**, *1*, 111. (d) Saxon, J. E. *Nat. Prod. Rep.* **1986**, *3*, 357; **1987**, *4*, 591; **1989**, *6*, 1.
2. Ren. X-F.; Turos, E. *Tetrahedron Lett.* **1993**, *34*, 1575.
3. Arcadi, A.; Cacchi, S.; Giancarlo, F.; Marinelli, F.; Moro, L. *Synlett.* **1999**, 1432.
4. Flynn, B. L; Verdier-Pinard, P.; Hamel, E. *Org. Lett.* **2001**, *5*, 651.
5. Yue, D.; Larock, R. C.; *J. Org. Chem.*, **2002**, *67*, 1905.

CHAPTER 1. SYNTHESIS OF 2,3-DISUBSTITUTED BENZO[*b*]THIOPHENES VIA PALLADIUM-CATALYZED COUPLING AND ELECTROPHILIC CYCLIZATION OF TERMINAL ACETYLENES

A paper submitted to the *Journal of Organic Chemistry*

Dawei Yue and Richard C. Larock*

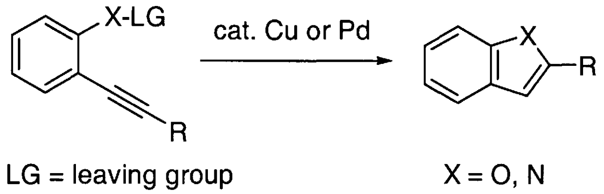
Department of Chemistry, Iowa State University, Ames, IA 50011

Abstract

2,3-Disubstituted benzo[*b*]thiophenes have been prepared in excellent yields via coupling of terminal acetylenes with commercially available *o*-iodothioanisole in the presence of a palladium catalyst and subsequent electrophilic cyclization of the resulting *o*-(1-alkynyl)thioanisole derivatives. I_2, Br_2, NBS, *p*-$O_2NC_6H_4SCl$ and PhSeCl have been utilized as electrophiles. Aryl-, vinylic-, and alkyl-substituted terminal acetylenes undergo this coupling and cyclization to produce excellent yields of benzo[*b*]thiophenes. Trimethylsilyl acetylene also undergoes this coupling/cyclization process with I_2, NBS, and the sulfur and selenium electrophiles to afford the corresponding 2-(trimethylsilyl)benzo[*b*]-thiophenes.

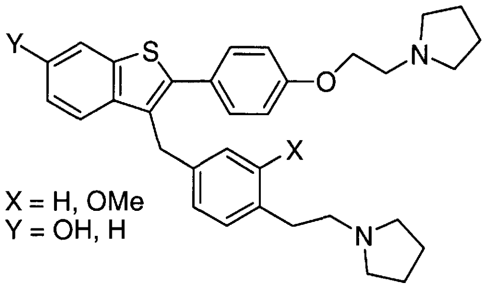
Introduction

The transition metal-catalyzed cyclization of disubstituted alkynes possessing a nucleophile in proximity to the triple bond by either copper or palladium reagents has been shown to be extremely effective for the synthesis of a wide variety of carbo- and heterocycles (eq 1).[1] Generally, this methodology requires a good leaving group on the nucleophile. However,due to sulfur's affinity for transition metals, sulfur-containing heterocycles, like benzo[*b*]thiophenes, have never been synthesized using this strategy.



(1)

Benzo[*b*]thiophenes are of interest, because of their frequent occurrence in nature and their wide range of biological and physiological effects.[2] Benzo[*b*]thiophene derivatives, which are antimitotic agents,[3] estrogen receptor antagonists, and antitumor, anti-inflammation and anti-fungal agents[4] are currently in pharmaceutical use or development. Diaminobenzothiophene derivatives like **1** have been identified as active site directed thrombin inhibitors.[5] Thus, research directed towards concise, new syntheses of 2,3-disubstituted benzo[*b*]thiophenes has been actively pursued in recent years.[1,6]



1

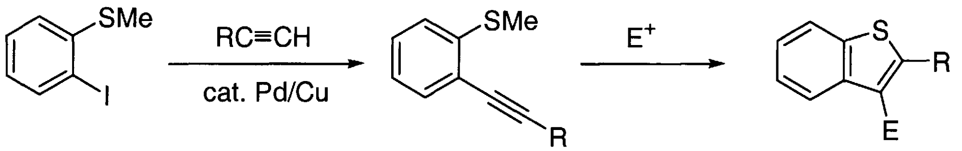
The electrophilic cyclization of unsaturated compounds has proven to be an efficient method for constructing heterocycles.[7] These reactions are generally viewed as proceeding through an intramolecular, stepwise electrophilic addition and dealkylation mechanism involving a cationic intermediate. Taniguchi and co-workers have explored the cyclization of vinylic cations as a route to heterocycles, but found significant limitations in generating the vinylic cations.[8] Although mechanistic and synthetic work on the preparation of benzofuran and indole derivatives have been carried out by Cacchi and co-workers[9] and ourselves,[10] the synthesis of benzo[*b*]thiophenes by this approach remains relatively unexplored.

Recently, Flynn and co-workers treated *o*-(1-alkynyl)phenyl benzyl sulfides with iodine to obtain 3-iodobenzo[*b*]thiophene derivatives through a 5-endo-dig iodocyclization.[4c] The limited availability of the requisite starting sulfides, the low yields obtained in their preparation, the incompatibility of functional groups with this methodology and the failure to demonstrate the scope of this methodology have encouraged us to report our related studies.[11] Herein, we report the successful application of this electrophilic cyclization strategy as a convenient and general synthetic methodology for the synthesis of 2,3-disubstituted benzo[*b*]thiophenes.

Results and Discussion

A two step approach to benzo[*b*]thiophenes has been examined involving (i) the Sonagashira coupling of commercially available *o*-iodothioanisole with terminal alkynes, and (ii) electrophilic cyclization (Scheme 1).

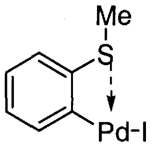
Scheme 1



$E^+ = I_2, Br_2$, NBS, p-$O_2NC_6H_4SCl$, PhSeCl

To assess the generality of this approach, the scope of the Sonogashira coupling of *o*-iodothioanisole has been studied. Treatment of *o*-iodothioanisole with a variety of terminal alkynes under standard Sonogashira coupling conditions (5 mmol of *o*-iodothioanisole, 1.2 equivs of terminal alkyne, 2 mol % of $PdCl_2(PPh_3)_2$, 1 mol % CuI, 12.5 ml of Et_3N at room temperature for 3-5 h) affords almost quantitative yields of the coupling products (Table 1).

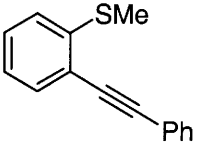
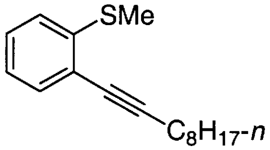
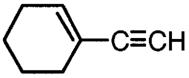
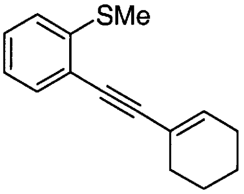
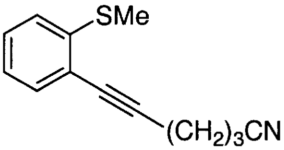
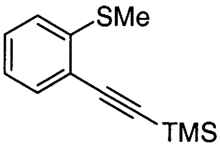
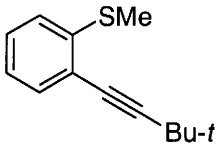
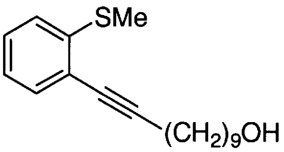
o-Iodothioanisole shows high reactivity towards the Sonogashira coupling and this allows the preparation of a wide variety of functionally substituted *o*-(1-alkynyl)thioanisoles. This high reactivity may be attributed to the coordination of sulfur to palladium in the presumed intermediate (**2**), which stabilizes the arylpalladium



2

intermediate and reduces its tendency to undergo homo-coupling. Alkynes with all sorts of substituents, including phenyl, trimethylsilyl, vinylic, bulky alkyl, and alkyl groups bearing functional groups, such as hydroxy and cyano groups, have been successfully employed in the Sonagashira coupling of *o*-iodothioanisole. Almost quantitative yields were obtained in all cases (Table 1).

Table 1. Sonogashira Coupling of *o*-Iodothioanisole and Terminal Acetylenes (Scheme 1).[a]

entry	terminal acetylene	arylalkyne	reaction time (h)	% isolated yield
1	$PhC\equiv CH$	 (**3**)	3	100
2	n-$C_8H_{17}C\equiv CH$	 (**4**)	3	93
3		 (**5**)	3	100
4	$NC(CH_2)_3C\equiv CH$	 (**6**)	5	99
5	$Me_3SiC\equiv CH$	 (**7**)	3	97
6	t-$BuC\equiv CH$	 (**8**)	3	99
7	$HO(CH_2)_9C\equiv CH$	 (**9**)	5	99

[a] All reactions were run with 5 mmol of *o*-iodothioanisole, 1.2 equivs of the terminal acetylene, 2 mol % of $PdCl_2(PPh_3)_2$, 1 mol % of CuI, and 12.5 mL of Et_3N at reaction temperature.

We have found that *o*-(phenylethynyl)thioanisole (**3**), when treated with I_2 in CH_2Cl_2, undergoes smooth iodocyclization at room temperature and affords a nearly quantitative yield of the corresponding2,3-disubstituted benzo[*b*]thiophene (**10**) (Scheme 1; Table 2, entry 1). The mild reaction conditions, as well as the high yield of this reaction, encouraged us to extend this methodology to a range of *o*-(1-alkynyl)thioanisoles (Table 2; entries 5, 9, 14, 18, 23 and 28). The yieldsin all cases are essentially quantitative. It makes little difference if the substituent on the other end of the alkyne is aryl, vinylic, alkyl, functionally-substituted or silyl. Even hindered trimethylsilyl- (**7**) or *tert*-butyl- (**8**) substituted alkynes react rapidly and quantitatively.

The sulfur moiety in this approach to benzo[*b*]thiophenes comes from commercially available *o*-iodothioanisole. The approach used by Flynn and co-workers[4c] introduces the sulfur through a series of steps starting with 2-iodoaniline or 2-bromo-1-iodobenzene and is thus less practical. We were pleased to find that the methyl group on the sulfur is easily removed during the cyclization step, which makes introduction of the benzylsulfide group of Flynn and co-workers unnecessary.[4c] This represents the first general route to 2,3-disubstituted benzo[*b*]thiophenes by an electrophilic cyclization strategy.

In order to explore the scope of this electrophilic cyclization strategy, four other electrophiles, Br_2, NBS, *p*-$O_2NC_6H_4SCl$ and PhSeCl have been employed. The reactions have all been monitored by thin layer chromatography and most of the reactions were complete within half an hour. In virtually all cases examined, excellent yields of benzo[*b*]thiophene of around 90% have been obtained. The results are summarized in Table 2.

Table 2. Electrophilic Cyclization of *o*-(1-Alkynyl)thioanisoles to 2,3-Disubstituted Benzo[*b*]thiophenes (Scheme 1).[a]

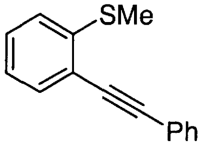
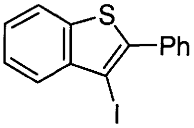
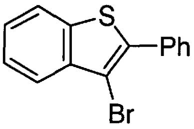
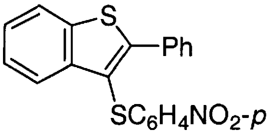
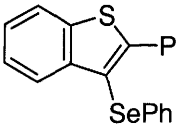
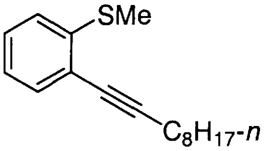
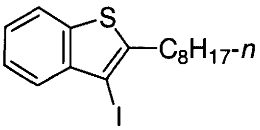
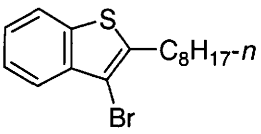
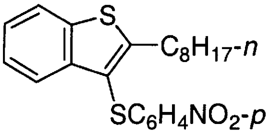
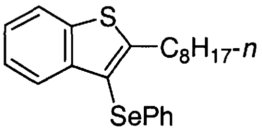
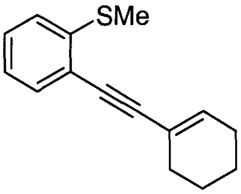
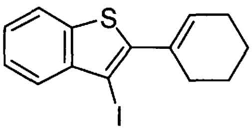
entry	*o*-(1-alkynyl)thioanisole	electrophile	time (min)	product	yield (%)
1		I_2	10	 **(10)**	100
2		Br_2	10	 **(11)**	92
3		p-$O_2NC_6H_4SCl$	10	 **(12)**	97
4		PhSeCl	10	 **(13)**	100
5		I_2	10	 **(14)**	100
6		Br_2	10	 **(15)**	91
7		p-$O_2NC_6H_4SCl$	10	 **(16)**	70
8		PhSeCl	10	 **(17)**	91
9		I_2	10	 **(18)**	97

Table 2. (Continued)

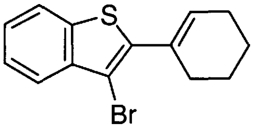
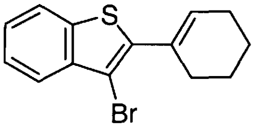
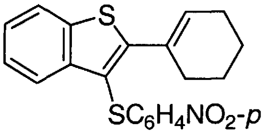
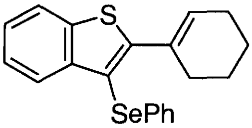
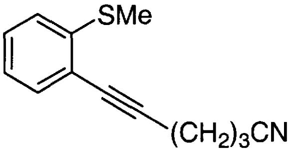
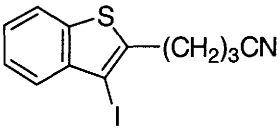
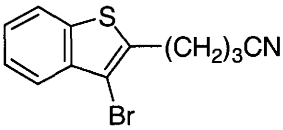
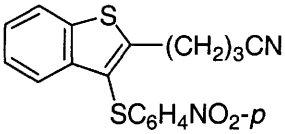
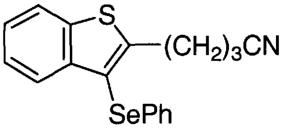
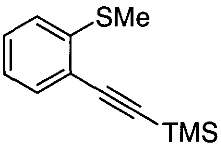
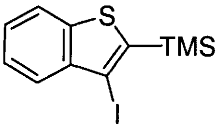
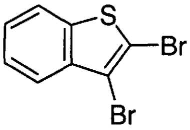
10		Br_2	10	 **(19)**	–
11		NBS	2 d	 **(19)**	74^b
12		p-$O_2NC_6H_4SCl$	10	 **(20)**	95
13		PhSeCl	10	 **(21)**	97
14		I_2	10	 **(22)**	98
15		Br_2	10	 **(23)**	79
16		p-$O_2NC_6H_4SCl$	10	 **(24)**	25^c
17		PhSeCl	10	 **(25)**	78
18		I_2	10	 **(26)**	100
19		Br_2	60	 **(27)**	95^d

Table 2. (Continued)

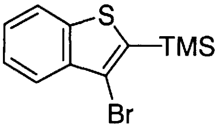
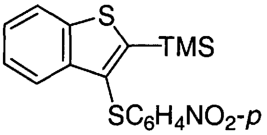
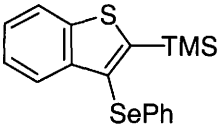
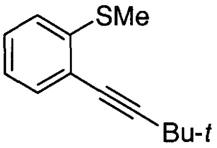
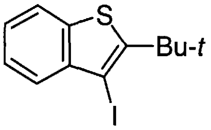
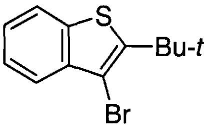
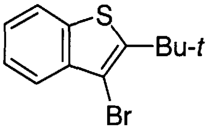
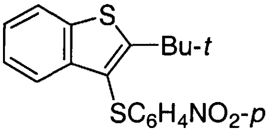
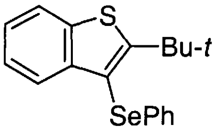
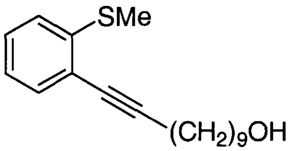
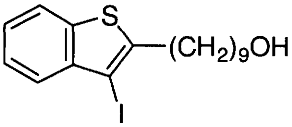
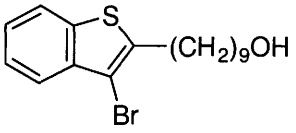
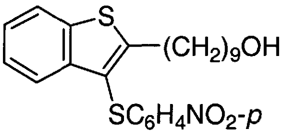
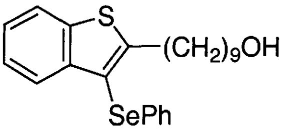
20		NBS	2 d	 **(28)**	65
21		*p*-$O_2NC_6H_4SCl$	10	 **(29)**	100
22		PhSeCl	10	 **(30)**	100
23		I_2	20	 **(31)**	98
24		Br_2	30	 **(32)**	67
25		NBS	6 h	 **(32)**	52
26		*p*-$O_2NC_6H_4SCl$	20	 **(33)**	80
27		PhSeCl	20	 **(34)**	82
28		I_2	30	 **(35)**	98

Table 2. (Continued)

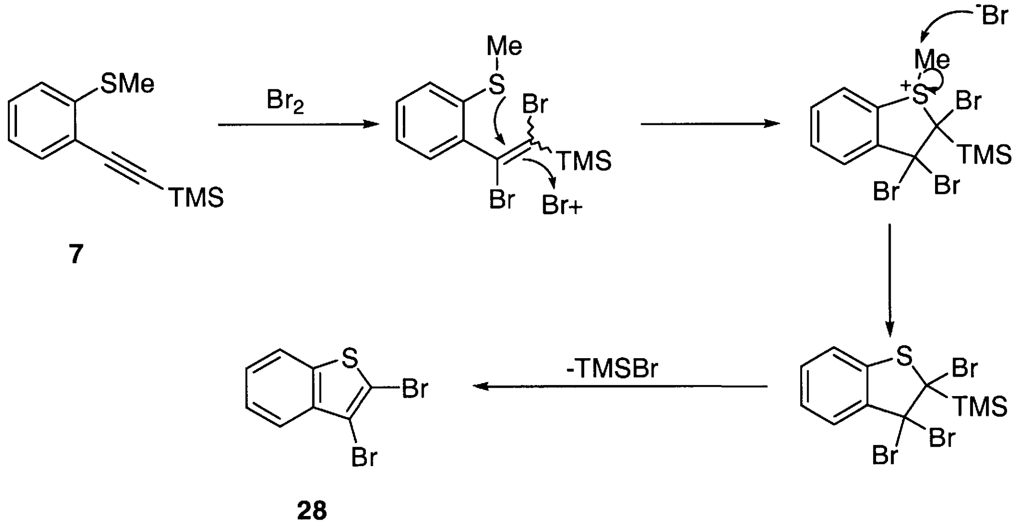
29	Br_2	30	 **(36)**	70
30	p-$O_2NC_6H_4SCl$	30	 **(37)**	60
31	PhSeCl	30	 **(38)**	95

[a]All reactions were run with 0.25 mmol of the *o*-(1-alkynyl)thioanisole, 1.5 equivs of electrophile in 5 mL of CH_2Cl_2 at 25 °C unless otherwise indicated. All NBS reactions were run using 1.2 equivs of NBS in 10 mL of CH_2Cl_2. [b]1.2 Equivs of NBS at 25 °C for 2 d. [c]The desired benzo[*b*]thiophene **24** was obtained as an inseparable 1:3 mixture of **24** and the product of addition of the *p*-nitrophenylsulfenyl chloride to the alkyne triple bond. The yield was determined by ^1H NMR spectroscopy. [d]1 Equiv of Br_2 gave the product of bromine addition to the triple bond; 1.5 equivs of NBS gave a mixture of the simple alkyne addition product and 2,3-dibromobenzo[*b*]thiophene, and 2 equiv of Br_2 gave 2,3-dibromobenzo[*b*]thiophene. The yield here is of 2,3-dibromobenzo[*b*]thiophene.

The nature of the electrophile plays an important role in these cyclization reactions. The iodocyclization reactions are most efficient and general. All functional groups that we have studied tolerate the reaction conditions and yields above 97% were obtained in all cases (Table 2, entries 1, 5, 9, 14, 18, 23 and 28). Aryl- (entry 1) and long chain alkyl- (entry 5) substituted alkynes are readily accommodated and the presence of an olefin (entry 9), a nitrile (entry 14) or an alcohol (entry 28) group presents no difficulties. *o*-(Trimethylsilylethynyl)thioanisole (entry 18) undergoes iodocyclization smoothly without desilylation, which provides an efficient method for the preparation of 3- iodo-2-silylbenzo[*b*]thiophenes. Even an alkyne with a bulky *tert*-butyl group (entry 23) gave almost a quantitative isolated yield (98%) of the cyclization product in only 10 min reaction time. The success of this reaction is presumably due to the highly nucleophilic nature of the iodide ion formed after the cyclization, which facilitates methyl group removal from the sulfonium intermediate presumably generated upon cyclization.

The reactions with Br_2 gave somewhat different results than those of I_2. While most alkynes reacted fairly cleanly with Br_2 to afford good to excellent yields of 3-bromobenzo[*b*]thiophenes (entries 2, 6, 15, 24 and 29), there were also complications not encountered previously using I_2. The carbon-carbon double bond present in alkyne **5** was found to be more reactive towards Br_2 than the triple bond and only a trace of the desired bromobenzo[*b*]thiophene product was detected (entry 10). However, by changing the electrophile from Br_2 to NBS, the desired cyclization product **19** was obtained in 74% yield (entry 11). The reaction of silyl alkyne **7** with Br_2 led to a mixture of 2,3-dibromobenzo[*b*]thiophene (**27**) and products of simple addition of the Br_2 to the carbon-carbon triple bond. The formation of **27** can be explained by either bromocyclization in the desired manner, followed by more rapid bromodesilylation, or by the mechanism described in Scheme 2, where the bromine first adds to the triple bond to form the simple addition product. Attack of another equivalent of Br_2 on the simple addition product might then lead to cyclization and formation of a 2,3-dihydrobenzo[*b*]thiophene bearing 3 bromine atoms and a silyl group. Elimination of trimethylsilyl bromide would afford **27**. By changing the electrophile from Br_2 to NBS, the desired cyclization product 3-bromo-2-silylbenzo[*b*]thiophene **28** was obtained in 65% yield. The bromocyclization reaction times of NBS and *o*-(1-alkynyl)thioanisoles (entries 11, 20 and 25) are generally longer than the bromocyclization reaction times employing Br_2 and the yields are generally lower.

Scheme 2



The commercially available reagents p-$O_2NC_6H_4SCl$ and PhSeCl are generally good electrophiles in this cyclization reaction, when there is no nucleophilic functionality present in the *o*-(1-alkynyl)thioanisoles. *o*-(1-Alkynyl)thioanisoles **3**, **4**, **5**, **7** and **8** all give decent yields of the desired disubstituted benzo[*b*]thiophene products. However, the yields from p-$O_2NC_6H_4SCl$ cyclizations are generally lower than those of the PhSeCl cyclizations, which are in turn lower than those of the iodocyclization reactions. The reason for this is not clear at this time, but factors to be considered include the electrophilicity and hardness of the electrophiles.

Substituents on the triple bond of the *o*-(1-alkynyl)thioanisoles also affect the yields of the cyclization reactions. Substrates with substituents, which are in conjugation with the triple bond, such as the phenyl group in alkyne **3** and the vinylic group in alkyne **5**, appear to cyclize more rapidly and generally produce higher yields of products. Bulky substrates, like the *tert*-butyl group in alkyne **6** tend to hinder cyclization. Longer reaction times are often needed and lower yields often result. However, no products involving simple addition of the electrophile to the alkyne triple bond are observed with this alkyne.

Long alkyl chains also play a role in the cyclization. The presence of an *n*-octyl group on the triple bond, as in alkyne **2**, lowered the yields of the *p*-nitrophenylsulfenyl and phenylselenyl cyclization reactions (entries 7 and 8), relative to the halocyclization processes (entries 5 and 6). Some product of the simple addition of *p*-$O_2NC_6H_4SCl$ to the carbon-carbon triple bond of the *o*-(1-alkynyl)thioanisole **2** was observed (entry 7).

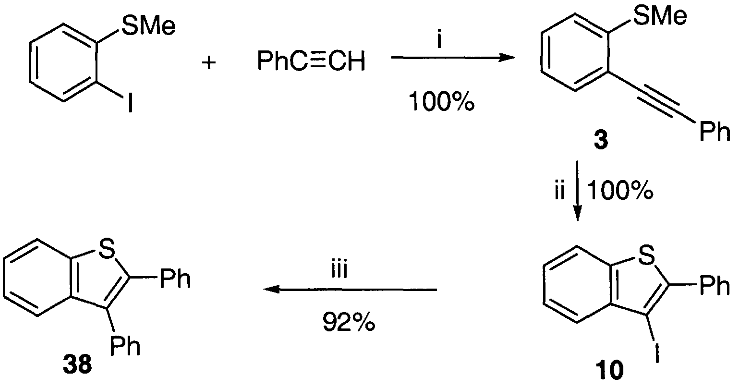
Due apparently to the electron-withdrawing effect of the cyano group on the alkyl chain, the reactions of 5-(2-methylmercaptophenyl)-5-hexynenitrile (**6**) with the sulfur and selenium electrophiles (entries 16 and 17) gave lower yields than the simple alkyl-substituted alkyne **2**. In fact, *p*-$O_2NC_6H_4SCl$ gave mainly the product of simple addition of the electrophile to the carbon-carbon triple bond and only a 25% yield of the desired product was obtained (entry 16). The cyano group here could serve as a nucleophile, which possibly interacts with the sulfur and selenium electrophiles and lowers the yields of the cyclization reactions.

An alcohol group can also interfere in the cyclization process. While the yield for the iodocyclization of the *o*-(1-alkynyl)thioanisole **9** with an hydroxyl group on the end of the long alkyl chain of the alkyne is still high, the Br_2 and *p*-$O_2NC_6H_4SCl$ cyclizations give much lower yields (entries 29 and 30). The hydroxyl group of alkyne **7** may be reacting directly with the *p*-$O_2NC_6H_4SCl$ generating HCl and a *p*-nitrophenylsulfenyloxy group on the end of the alkyl chain.

The 3-substituted benzo[*b*]thiophenes produced by this new chemistry should be very useful for the synthesis of additional benzo[*b*]thiophenes. For example, the 3-

iodobenzo[*b*]thiophenes produced by this strategy can be further functionalized by applying palladium-mediated coupling techniques(Scheme 3). This methodology has been successfully employed by Flynn and co-workers in the synthesis of tubulin binding agents.[4c] We have found that 2,3-diphenylbenzo[*b*]thiophene can be obtained in a 92% overall yield from *o*-iodothioanisole and phenyl acetylene by our two step coupling/cyclization process, followed by Suzuki cross-coupling of the intermediate 3-iodo-2-phenylbenzo[*b*]thiophene with $NaBPh_4$. One should be able to prepare many other 2,3-disubstituted benzo[*b*]thiophenes using these iodo substrates and known palladium methodology.

Scheme 3



Reagents and reaction conditions: i. 2 mol % $PdCl_2(Ph_3)_2$, 1 mol % CuI, Et_3N, 25 °C for 6 h; ii. I_2, CH_2Cl_2, 25 °C for 10 min; iii. 5 mol % $Pd(OAc)_2$, $NaBPh_4$, 1:1 DMF/H_2O, 1 equiv of Na_2CO_3, 100 °C for 12 h.

Conclusions

A very efficient synthesis of 2,3-disubstituted benzo[*b*]thiophenes has been developed by a two step approach involving the Sonagashira cross-coupling of terminal alkynes and commercially available *o*-iodothioanisole, followed by electrophilic cyclization using I_2, Br_2, NBS, and sulfur and selenium electrophiles. All electrophiles give benzo[*b*]thiophenes in good to excellent yields. A wide variety of thioanisole-containing acetylenes with various functional groups undergo this overall process in good to excellent yields. The steric and electronic effects of the substituents on the carbon-carbon triple bond of the alkynylthioanisole intermediates have been studied.

Experimental Section

General. All ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz. 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). All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at a voltage of 70 eV. All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of ethyl ether, hexanes, ethyl acetate, methylene chloride and DMF were purchased from Fisher Scientific Co. 2-Iodothioanisole, phenylacetylene, 1-decyne, 1-cyclohexenyl acetylene, 11-undecyn-1-ol, *tert*-butyl acetylene, trimethylsilyl acetylene, 5-hexynenitrile and Et_3N were purchased from Aldrich Chemical Co., Inc. The palladium salts were donated by Johnson Matthey Inc. and Kawaken Fine Chemicals Co. Ltd.

General Procedure for the Palladium-Catalyzed Formation of *o*-(1-Alkynyl)thioanisoles. To a solution of Et_3N (12.5 mL), $PdCl_2(PPh_3)_2$ (0.070 g, 2 mol %), 5 mmol of *o*-iodothioanisole and 6 mmol of terminal acetylene (stirring for 5 min beforehand), CuI (0.010 g, 1 mol %) was added and stirring was continued for another 2 min before flushing with Ar and the flask was then sealed. The mixture was allowed to stir at room temperature for 3-6 h and the resulting solution was filtered and washed with a satd aq NaCl solution and extracted with diethyl ether (2 x 10 mL). The combined ether fractions were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by flash chromatography on silica gel using ethyl acetate/hexane as the eluent.

o-(1-Alkynyl)thioanisoles Prepared

***o*-(Phenylethynyl)thioanisole (3).** The product was obtained as a yellow oil. The ^1H and ^{13}C NMR spectral data were in good agreement with the literature data.[12] Characterization of all other *o*-(1-alkynyl)thioanisoles prepared in this study can be found in the supporting information.

***o*-(1-Decynyl)thioanisole (4).** The product was obtained as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 0.8 Hz, 3H), 1.29-1.31 (m, 8 H), 1.50 (q, J = 7.6 Hz, 2H), 1.65 (q, J = 7.2 Hz, 2H), 2.47 (s, 3H), 2.48 (t, J = 6.8 Hz, 2H), 7.05 (t, J = 7.6 Hz, 1H), 7.11 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 15.2, 19.9, 22.9, 29.0, 29.1, 29.4, 29.4, 32.1, 78.3, 97.7, 122.3, 123.9, 124.3, 128.2, 132.4, 141.3; IR (neat, cm^{-1}) 3058, 2926, 2855, 2227, 1464, 1435, 749; HRMS cald for $C_{17}H_{24}S$ 260.15987. Found 260.16021.

***o*-(Cyclohex-1-enylethynyl)thioanisole (5).** The product was obtained as a yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 1.54-1.62 (m, 4H), 2.07-2.09 (m, 2H), 2.12-2.20 (m, 2H), 2.40 (s, 3H), 6.19 (m, 1H), 6.96 (d, J = 1.2 Hz, 1H), 7.03 (t, J = 4.2 Hz, 1H), 7.16 (t, J =

3.9 Hz, 1H) 7.25 (d, $J = 1.5$ Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 15.2, 21.7, 22.5, 26.0, 29.3, 84.4, 98.1, 120.9, 121.9, 124.0, 124.3, 128.4, 132.1, 135.7, 141.4; IR (neat, cm^{-1}) 2925, 2857, 1461, 1434, 749; HRMS calcd for $C_{15}H_{16}S$ 228.09727. Found 228.09766.

5-(2-Methylmercaptophenyl)-5-hexynenitrile (6). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (t, $J = 6.8$ Hz, 2H), 2.40 (s, 3H), 2.58 (m, 4H), 6.99 (t, $J = 7.6$ Hz, 1H), 7.05 (d, $J = 8.0$ Hz, 1H), 7.20 (td, $J = 15.6$, 1.2 Hz, 1H), 7.28 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0, 16.1, 16.3, 17.6, 18.9, 24.4, 24.8, 70.5, 80.1, 93.9, 119.5, 121.2, 123.9, 124.3, 128.7, 132.3, 141.5; IR (neat, cm^{-1}) 3058, 2922, 2247, 1464, 1432, 735; HRMS calcd for $C_{13}H_{13}NS$ 215.07687. Found 215.07723.

***o*-(Trimethylsilylethynyl)thioanisole (7).** The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.29 (s, 9H), 2.49 (s, 3H), 7.07 (td, $J = 7.6$, 1.0 Hz, 1H), 7.14 (d, $J = 8.0$ Hz, 1H), 7.29 (td, $J = 8.0$, 1.4 Hz, 1H), 7.43 (dd, $J = 8.0$, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.2, 15.2, 101.6, 102.3, 121.3, 124.1, 124.5, 129.1, 132.8, 142.2; IR (neat, cm^{-1}) 3059, 2959, 2920, 2155, 1461, 1434, 1249, 843; HRMS calcd for $C_{12}H_{16}SSi$ 220.07420. Found 220.07455.

***o*-(3,3-Dimethyl-1-butynyl)thioanisole (8).** The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 9H), 2.46 (s, 3H), 7.04 (t, $J = 7.8$ Hz, 1H), 7.10 (d, $J = 7.6$ Hz, 1H), 7.23 (t, $J = 8.4$ Hz, 1H), 7.33 (d, $J = 7.2$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 28.5, 30.8, 31.2, 76.8, 105.7, 122.0, 123.8, 124.2, 128.2, 132.2, 141.5; IR (neat, cm^{-1}) 2968, 2922, 2234; HRMS calcd for $C_{13}H_{16}S$ 204.09727. Found 204.09765.

o-(9-Hydroxy-1-undecynyl)thioanisole (9). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.33 (m, 9H), 1.48-1.52 (m, 2H), 1.54-1.58 (m, 2H), 1.60-1.66 (m, 2H), 1.47 (s, 3H), 1.49 (t, J = 6.8 Hz, 2H), 3.63 (t, J = 6.8 Hz, 2H), 7.05 (t, J = 7.6 Hz, 1H), 7.11 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 7.6 Hz, 1H); ^{13}C NMR (400 MHz, CDCl$_3$) δ 15.2, 19.8, 25.9, 28.9, 29.0, 29.3, 29.6, 29.7, 33.0, 63.2, 78.3, 97.6, 122.2, 123.9, 124.3, 128.2, 132.4, 141.3; IR (neat, cm^{-1}) 3312, 3057, 2927, 2854, 2226, 1464, 1435, 750; HRMS calcd for $C_{18}H_{26}OS$ 290.17044. Found 290.17097.

General Procedure for the Iodo- and Bromocyclizations. To a solution of 0.25 mmol of the o-(1-alkynyl)thioanisole and 3 mL of CH_2Cl_2, 2 equivs of I_2 or Br_2 dissolved in 2 mL of CH_2Cl_2 was added gradually. The reaction mixture was flushed with Ar and allowed to stir at room temperature for 30 min. The excess I_2 or Br_2 was removed by washing with a satd aq soln of $Na_2S_2O_3$. The aqueous solution was then extracted by diethyl ether (2 x 10 mL). The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under a vacuum to yield the crude product, which was purified by flash chromatography on silica gel using ethyl acetate/hexanes as the eluent.

3-Halobenzo[*b*]thiophenes Prepared

3-Iodo-2-phenylbenzo[*b*]thiophene (10). The product was obtained as a yellow oil. The ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature data.[12] Characterization of all other 3-halobenzo[*b*]thiophenes prepared in this study can be found in the supporting information.

3-Bromo-2-phenylbenzo[*b*]thiophene (11). The product was obtained as pale yellow crystals: lit[13] mp 63-64 °C, found 63-64 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 5H), 7.75 (dd, $J = 9.0$, 1.5 Hz, 2H), 7.79 (d, $J = 6.0$ Hz, 1H), 7.87 (d, $J = 9.0$ Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 105.2, 122.4, 123.9, 125.5, 125.7, 128.8, 129.0, 129.9, 133.3, 137.9, 138.4, 139.4; IR (neat, cm^{-1}) 3060, 2925, 2853; HRMS calcd for $C_{14}H_9BrS$ 287.96083. Found 287.96116.

3-Iodo-2-*n*-octylbenzo[*b*]thiophene (14). The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91-0.96 (t, $J = 9.2$ Hz, 3H), 1.33-1.41 (m, 10H), 1.78 (m, 2 H), 2.98 (t, $J = 7.8$ Hz, 2H), 7.36 (d, $J = 8.4$ Hz, 1H), 7.43 (t, $J = 0.6$ Hz, 1H), 7.72 (t, $J = 0.6$ Hz, 1H), 7.73 (d, $J = 1.2$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 22.9, 29.3, 29.4, 29.6, 30.8, 32.1, 33.2, 80.3, 122.4, 124.9, 125.2, 125.2, 138.2, 141.3, 145.0; IR (neat, cm^{-1}) 2924, 2853, 2354, 1454, 1432, 749; HRMS calcd for $C_{16}H_{21}IS$ 372.04087. Found 372.04128.

3-Bromo-2-*n*-octylbenzo[*b*]thiophene (15). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, $J = 9$ Hz, 3H), 1.30-1.45 (m, 10H), 1.70-1.77 (m, 2H), 2.95 (t, $J = 10.2$ Hz, 2H), 7.33 (td, J = 12.0, 1.6 Hz, 1H), 7.43 (td, $J = 12.0$, 2.0 Hz, 1H), 7.76 (dd, $J = 12.0$, 1.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 22.9, 29.3, 29.4, 29.5, 30.1, 30.6, 32.1, 105.9, 122.5, 122.8, 124.9, 125.0, 137.3, 138.6, 141.2; IR (neat, cm^{-1}) 2953, 2925, 2854; HRMS calcd for $C_{16}H_{21}BrS$ 324.05473. Found 324.05523.

2-(Cyclohex-1-enyl)-3-iodobenzo[*b*]thiophene (18). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.69-1.71 (m, 2H), 1.79-1.80 (m, 2H), 2.23-

2.25 (m, 2H), 2.44-2.45 (m, 2H), 6.17-6.19 (m, 1H), 7.31 (td, *J* = 7.4, 0.8 Hz, 1H), 7.40 (td, *J* = 8.0, 1.2 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 23.0, 25.8, 30.1, 77.6, 122.3, 125.2, 125.3, 125.9, 132.4, 132.7, 138.1, 141.7, 145.3; IR (neat, cm^{-1}) 2925, 2855, 1432, 749; HRMS calcd for $C_{14}H_{13}IS$ 339.97827. Found 339.97881.

3-Bromo-2-(cyclohex-1-enyl)benzo[*b*]thiophene (19).[14] The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.67-1.72 (m, 2H), 1.76-1.82 (m, 2H), 2.24-2.25 (m, 2H), 2.51 (m, 2H), 6.31 (s, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.78 (d, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 23.0, 26.0, 29.6, 103.3, 122.2, 123.3, 125.1, 125.1, 130.9, 132.3, 136.9, 139.2, 141.3; IR (neat, cm^{-1}) 2934, 2860; HRMS calcd for $C_{14}H_{13}BrS$ 291.99213. Found 291.99258.

4-(3-Iodobenzo[*b*]thiophen-2-yl)butanenitrile (22). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09-2.21 (m, 2H), 2.44 (t, *J* = 7.2 Hz, 2H), 3.12 (t, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.6, 26.4, 31.7, 81.8, 119.3, 122.5, 125.5, 125.6, 125.6, 138.2, 141.2, 141.2; IR (neat, cm^{-1}) 3056, 2923, 2850, 2247, 1453, 1433, 1265, 753; HRMS calcd for $C_{12}H_{10}INS$ 326.95787. Found 326.95832.

4-(3-Bromobenzo[*b*]thiophen-2-yl)butanenitrile (23). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (q, *J* = 3.2 Hz, 2H), 2.42 (t, *J* = 2.8 Hz, 2H), 3.10 (t, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.6, 26.2, 28.8, 107.4, 119.3, 122.6, 123.1, 125.4, 125.5, 137.3, 137.4, 138.4; IR (neat, cm^{-1}) 3062, 2921, 2850, 2250, cm^{-1}; HRMS calcd for $C_{12}H_{10}BrNS$ 278.97173. Found 278.97219.

3-Iodo-2-(trimethylsilyl)benzo[*b*]thiophene (26). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.51 (s, 9H), 7.37 (td, *J* = 8.0, 1.2 Hz, 1H), 7.43 (td, *J* = 7.2, 1.2 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.4, 87.3, 122.1, 125.2, 125.4, 125.5, 140.9, 141.4, 143.1; IR (neat, cm^{-1}) 2954, 2923, 1470, 839, 750; HRMS calcd for $C_{11}H_{13}ISSi$ 331.95520. Found 331.95571.

2,3-Dibromobenzo[*b*]thiophene (27). The product was obtained as pale yellow crystals: lit[15] mp 58-59 °C, found 58-59 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.41 (m, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 111.9, 114.4, 122.1, 123.5, 125.7, 125.9, 137.7, 139.1; IR (neat, cm^{-1}) 3072, 2963; HRMS calcd for $C_8H_4Br_2S$ 291.83800. Found 291.83852.

3-Bromo-2-(trimethylsilyl)benzo[*b*]thiophene (28). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.47 (s, 9H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.6, 114.9, 122.4, 123.1, 125.0, 125.3, 136.2, 140.0, 141.6; IR (neat, cm^{-1}) 3072, 2956, 2924; HRMS calcd for $C_{11}H_{13}BrSSi$ 283.96906. Found 283.96949.

2-*t*-Butyl-3-iodobenzo[*b*]thiophene (31). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (s, 9H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5, 36.0, 75.0, 121.9, 125.0, 125.2, 125.4, 136.3, 143.1, 151.6; IR (neat, cm^{-1}) 3056, 2961, 2925, 1429, 750; HRMS calcd for $C_{12}H_{13}IS$ 315.97827. Found 315.97879.

3-Bromo-2-*t*-butylbenzo[*b*]thiophene (32). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.59 (s, 9H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 30.2, 35.7, 102.9, 122.1, 122.8, 124.9, 125.0, 135.7, 140.2, 149.0; IR (neat, cm^{-1}) 3071, 2963, 2866; HRMS calcd for $C_{12}H_{13}BrS$ 267.99213. Found 267.99254.

2-(9-Hydroxynonyl)-3-iodobenzo[*b*]thiophene (35). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.32-1.42 (m, 11H), 1.54-1.57 (m, 2H), 1.74 (q, *J* = 7.6 Hz, 2H), 2.95 (t, *J* = 7.6 Hz, 2H), 3.63 (t, *J* = 6.0 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), ^{13}C NMR (100 MHz, CDCl$_3$) δ 25.9, 29.2, 29.5, 29.6, 29.6, 30.7, 33.0, 33.1, 63.3, 80.3, 122.4, 125.0, 125.2, 125.2, 138.2, 141.3, 145.0; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{17}H_{23}IOS$ 402.05144. Found 402.05195.

3-Bromo-2-(9-hydroxynonyl)benzo[*b*]thiophene (36). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.31-1.40 (m, 11H), 1.55 (t, *J* = 10.0 Hz, 2H), 1.73 (m, 2H), 2.93 (t, *J* = 8.0 Hz, 2H), 3.62 (t, *J* = 6.4 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 25.9, 29.2, 29.4, 29.6, 29.6, 30.1, 30.5, 33.0, 63.2, 105.9, 122.4, 122.8, 124.9, 125.0, 137.3, 138.6, 141.1; IR (neat, cm^{-1}) 3386, 3050, 2926, 2853; HRMS calcd for $C_{17}H_{23}BrOS$ 354.06530. Found 354.06573.

General Procedure for the *p*-$O_2NC_6H_4SCl$ and PhSeCl cyclizations. To a solution of 0.25 mmol of the *o*-(1-alkynyl)thioanisole and CH_2Cl_2 (3 mL), a solution of 0.375 mmol of *p*-$O_2NC_6H_4SCl$ and PhSeCl and CH_2Cl_2 (2 mL) was added. The mixture was stirred for 2 min and the flask was flushed with Ar and allowed to stir at the designated temperature for 30 min. The reaction mixture was washed with 20 mL of water and extracted with diethyl ether. The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product, which was further purified by flash chromatography on silica gel using ethyl acetate/hexanes as the eluent.

3-Thio- and 3-Selenobenzo[*b*]thiophenes Prepared

3-(*p*-Nitrophenylsulfenyl)-2-phenylbenzo[*b*]thiophene (12). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.8 Hz, 2H), 7.42-7.46 (m, 5H), 7.65-7.67 (m, 2H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.8, 122.6, 123.4, 124.1, 124.2, 125.6, 125.8, 128.8, 129.5, 129.7, 132.9, 138.6, 140.3, 145.3, 147.8, 151.3; IR (neat, cm^{-1}) 3061, 2918, 2849, 1577, 1512, 1337, 753; HRMS calcd for $C_{20}H_{13}NO_2S_2$ 363.03877. Found 363.03943. Characterization of all other 3-thio and 3-seleno benzo[*b*]thiophenes prepared in this study can be found in the supporting information.

2-Phenyl-3-(phenylselenyl)benzo[*b*]thiophene (13). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16-7.22 (m, 5H), 7.41-7.47 (m, 5H), 7.70 (dd, *J* = 1.6, 2.4 Hz, 2H), 7.90-7.93 (m, 1H), 7.94-7.97 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 115.7, 122.3, 125.3, 126.1, 127.9, 128.5, 129.1, 129.4, 129.4, 130.3, 131.7, 133.0, 134.3, 139.3, 142.2; IR (neat, cm^{-1}) 3055, 2919, 2849, 1576, 1475; HRMS calcd for $C_{20}H_{14}SSe$ 367.99833. Found 367.99903.

3-(*p*-Nitrophenylsulfenyl)-2-*n*-octylbenzo[*b*]thiophene (16). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.85 (t, *J* = 6.8 Hz, 3H), 1.21-1.36 (m, 10H), 1.67-1.72 (m, 2H), 3.07 (t, *J* = 7.6 Hz, 2H), 7.04 (dd, *J* = 8.8, 2.4 Hz, 2H), 7.33-7.36 (m, 2H), 7.62-7.64 (m, 1H), 8.01 (dd, *J* = 8.8, 2.4 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.3, 22.8, 29.3 (2C), 29.4, 29.8, 31.5, 32.0, 116.2, 122.6, 122.8, 124.2, 125.1, 125.3, 125.6, 138.2, 139.8, 145.4, 147.9, 155.3; IR (neat, cm^{-1}) 2925, 2853, 1578, 1515, 1337; HRMS calcd for $C_{22}H_{15}S_2NO_2$ 399.13267. Found 399.13346.

2-*n*-Octyl-3-(phenylselenyl)benzo[*b*]thiophene (17). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.86 (t, *J* = 6.8 Hz, 3H), 1.22-1.33 (m, 10H), 1.67-1.70 (m, 2H), 3.13 (t, *J* = 8.0 Hz, 2H), 7.08-7.14 (m, 5H), 7.28-7.31 (m, 2H), 7.77-7.80 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.3, 22.9, 29.4, 29.5, 31.2, 31.8, 32.0, 116.1, 122.3, 124.3, 124.6, 125.0, 126.1, 129.1, 129.3, 132.9, 138.6, 141.8, 152.8; IR (neat, cm^{-1}) 3057, 2924, 2853, 1577, 1476, 1434; HRMS cald for $C_{22}H_{26}SSe$ 402.09204. Found 402.09268.

2-(Cyclohex-1-enyl)-3-(*p*-nitrophenylsulfenyl)benzo[*b*]thiophene (20). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.56-1.57 (m, 2H), 1.63-1.65 (m, 2H), 2.10-2.12 (m, 2H), 2.41-2.41 (m, 2H), 6.11 (m, 1H), 6.98 (d, *J* = 9.2 Hz, 2H), 7.25 (m, 2H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 21.7, 22.9, 26.0, 30.0, 114.1, 122.6, 122.9, 124.3, 125.3, 125.4, 125.6, 131.1, 133.0, 137.8, 140.4, 145.3, 148.4, 154.6; IR (neat, cm^{-1}) 3055, 2930, 2857, 1577, 1475, 1434, 754, 731; HRMS calcd for $C_{20}H_{17}NO_2S_2$ 367.07007. Found 367.07053.

2-(Cyclohex-1-enyl)-3-(phenylselenyl)benzo[*b*]thiophene (21). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.64-1.66 (m, 2H), 1.73-1.74 (m, 2H), 2.19-2.21 (m, 2H), 2.50-2.51 (m, 2H), 6.10 (m, 1H), 7.10-7.15 (m, 5H), 7.28-7.31 (m, 2H), 7.76-7.79 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 21.9, 23.0, 25.9, 30.4, 114.0, 122.2, 124.7, 124.8, 125.0, 126.0, 129.3, 131.7, 132.0, 132.4, 133.3, 138.4, 142.0, 152.1; IR (neat, cm^{-1}) 3055, 2929, 1577, 1475, 1433, 754, 731; HRMS calcd for $C_{20}H_{18}SeS$ 370.02944. Found 370.02987.

4-(3-(*p*-Nitrophenylsulfenyl)benzo[*b*]thiophen-2-yl)butanenitrile (24). The compound was obtained as an inseparable 1:3 mixture of benzo[*b*]thiophene **24** and the product of addition of the *p*-$O_2NC_6H_4SCl$ to the alkyne triple bond. Compound **24**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.37-2.44 (m, 2H), 2.93 (t, J = 7.0 Hz, 2H), 3.26 (t, J = 7.6 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 7.35-7.41 (m, 2H), 7.66 (d, J = 7.6 Hz, 1H), 7.87 (d, J = 7.2 Hz, 1H), 8.02 (d, J = 8.8 Hz, 2H); IR (neat, cm^{-1}) 3095, 2920, 2849, 2249, 1735, 1577, 1513, 1338; HRMS calcd for $C_{20}H_{14}N_2O_2S_2$ 354.04967. Found 354.05038.

4-(3-(Phenylselenyl)benzo[*b*]thiophen-2-yl)butanenitrile (25). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.00-2.04 (m, 2H), 2.32 (t, J = 7.2 Hz, 2H), 3.27 (t, J = 7.6 Hz, 2H), 7.13 (m, 5H), 7.33-7.36 (m, 2H), 7.80-7.85 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 16.7, 27.2, 29.9, 119.2, 122.4, 124.5, 125.2, 125.3, 126.4, 129.2, 129.5, 132.3, 134.2, 138.5, 141.6, 148.7; IR (neat, cm^{-1}) 3055, 2934, 2246, 1576, 1475, 1434, 757, 734; HRMS calcd for $C_{18}H_{15}NSSe$ 357.00904. Found 357.00971.

3-(*p*-Nitrophenylsulfenyl)-2-(trimethylsilyl)benzo[*b*]thiophene (29). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.40 (s, 9H), 7.01 (d, J = 8.8 Hz, 1H), 7.35 (t, J = 7.8 Hz, 1H), 7.40 (t, J = 7.2 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.3, 122.5, 124.1, 125.2, 125.3, 125.4, 126.3, 141.1, 142.9, 145.2, 148.1, 151.5; IR (neat, cm^{-1}) 3064, 2956, 2898, 1578, 1514, 1337; HRMS calcd for $C_{17}H_{17}NO_2S_2Si$ 359.04700. Found 359.04769.

3-Phenylselenyl-2-(trimethylsilyl)benzo[*b*]thiophene (30). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.43 (s, 9H), 7.06-7.10 (m, 5H), 7.29-7.36 (m, 2H), 7.81 (d, J = 7.4 Hz, 1H), 7.88 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.2, 122.3, 124.3, 124.9, 125.0, 125.4, 125.9, 128.7, 129.3, 133.6, 142.8, 143.2, 149.3; IR (neat, cm^{-1}) 3057, 2954, 1577, 1476, 1247; HRMS calcd for $C_{17}H_{18}SSeSi$ 362.00637. Found 362.00687.

2-*t*-Butyl-3-(*p*-nitrophenylsulfenyl)benzo[*b*]thiophene (33). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58 (s, 9H), 7.01 (d, J = 8.6 Hz, 2H), 7.27-7.36 (m, 2H), 7.57 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 36.5, 114.1, 122.2, 122.4, 124.2, 125.0, 125.3, 125.4, 136.6, 141.2, 145.2, 148.3, 164.1; IR (neat, cm^{-1}) 3062, 2963, 1578, 1513, 1337; HRMS calcd for $C_{18}H_{17}NO_2S_2$ 343.07007. Found 343.07076.

2-*t*-Butyl-3-(phenylselenyl)benzo[*b*]thiophene (34). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (s, 9H), 7.04-7.12 (m, 5H), 7.25-7.30 (m, 2H), 7.74 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.5, 36.7, 121.9, 124.1, 124.5, 124.9, 125.7, 127.9, 128.3, 129.3, 129.4, 131.7, 133.8, 143.2; IR (neat, cm^{-1}) 3055, 2960, 2920, 1577, 1475; HRMS calcd for $C_{18}H_{18}SSe$ 346.02944. Found 346.02983.

2-(9-Hydroxynonyl)-3-(*p*-nitrophenylsulfenyl)benzo[*b*]thiophene (37). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.24-1.32 (m, 11H), 1.51-1.55 (m, 2H), 1.65-1.72 (m, 2H), 3.08 (t, *J* = 8.0 Hz, 2H), 3.62 (t, *J* = 6.4 Hz, 2H), 7.05 (d, *J* = 9.2 Hz, 2H), 7.34-7.37 (m, 2H), 7.63 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.85 (dd, *J* = 8.0, 2.0 Hz, 1H), 8.02 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 25.9, 29.3, 29.3, 29.5, 29.6, 29.8, 31.5, 33.0, 63.2, 116.3, 122.6, 122.8, 124.3, 125.2, 125.4, 125.6, 138.2, 139.8, 145.4, 147.9, 155.3; IR (neat, cm^{-1}) 3347, 2926, 2853, 1578, 1513, 1337; HRMS calcd for $C_{23}H_{27}NO_3S_2$ 429.14324. Found 429.14398.

2-(9-Hydroxynonyl)-3-(phenylselenyl)benzo[*b*]thiophene (38). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.25-1.32 (m, 11H), 1.54 (q, *J* = 7.6 Hz, 2H), 1.69 (q, *J* = 7.2 Hz, 2H), 3.14 (t, *J* = 7.6 Hz, 2H), 3.62 (t, *J* = 6.8 Hz, 2H), 7.10-7.13 (m, 5H), 7.30-7.32 (m, 2H), 7.78-7.81 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 25.9, 29.3, 29.4, 29.5, 29.6, 31.2, 31.7, 33.0, 63.2, 116.1, 122.3, 124.2, 124.6, 125.0, 126.1, 129.1, 129.3, 132.8, 138.6, 141.8, 152.7; IR (neat, cm^{-1}) 3341, 3056, 2925, 2854, 1577, 1475; HRMS calcd for $C_{23}H_{28}OSSe$ 432.10261. Found 432.10322.

2,3-Diphenylbenzo[*b*]thiophene (39). This benzo[*b*]thiophene was prepared by the following procedure. Into 10 mL of a 2:1 DMF/H_2O solution containing 5 mmol of 3-iodo-2-phenylbenzo[*b*]thiophene, 5 mmol of Na_2CO_3 and 1.25 mmol of $NaBPh_4$ were added and the reaction mixture was stirred for 2 min. $Pd(OAc)_2$ (5 mol %) was then added and the flask was flushed with Ar, sealed and allowed to stir at 100 °C for 12 h. The resulting reaction mixture was extracted with ethyl ether (2 x 10 mL). The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to afford a white solid product. Crystallization afforded a 92 % yield of a crystalline solid. The product was obtained as white needles: lit[16] mp 113-114 °C, found 114-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12-7.14 (m, 3H), 7.20-7.29 (m, 9H), 7.50 (d, J = 7.6 Hz, 1H), 7.75-7.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 122.3, 123.6, 124.7, 124.8, 127.6, 127.9, 128.6, 128.9, 129.9, 130.7, 133.5, 134.5, 135.7, 139.1, 141.1; IR (neat, cm^{-1}) 3057, 3024, 1599; HRMS calcd for $C_{20}H_{14}S$ 286.08162. Found 286.08219.

Acknowledgements. We gratefully acknowledge partial financial support from the Petroleum Research Fund administered by the American Chemical Society, and we thank Johnson Matthey, Inc., and Kawaken Fine Chemicals Co., Ltd. for providing the palladium salts.

References

1. (a) Roesch, K. R.; Larock, R. C. *Org. Lett.* **1999**, *4*, 553. (b) Nan, Y.; Miao, H.; Yang, Z. *Org. Lett.* **2000**, *2*, 297. (c) Larock, R. C.; Yum, E. K. *J. Am. Chem. Soc.* **1991**, *113*, 6689. (d) Larock, R. C.; Yum, E. K.; Refvik, M. D. *J. Org. Chem.* **1998**, *63*, 7652. (e) Roesch, K. R.; Larock, R. C. *J. Org. Chem.* **1998**, *63*, 5306. (f) Cacchi, S.; Fabrizi, G.; Moro, L. *Tetrahedron Lett.* **1998**, *39*, 5101. (g) Cacchi, S.; Fabrizi, G.; Moro, L. *Synlett* **1998**, 741. (h) Arcadi, A.; Cacchi, S.; Rosario, M. D.; Fabrizi, G.; Marinelli, F. *J. Org. Chem.* **1996**, *61*, 9280. (i) Cacchi, S.; Carnicelli, V.; Marinelli, F. *J. Organomet. Chem.* **1994**, *475*, 289. (j) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1992**, *33*, 3915. (k) Cacchi, S. *J. Organomet. Chem.* **1999**, *576*, 42.

2. Bradley, D. A.; Godfrey, A. G.; Schmid, C. R. *Tetrahedron Lett.* **1999**, *40*, 5155.
3. (a) Pinny, K. G.; Bounds, A. D.; Dubgenab, K. M.; Mocharla, V. P.; Pettit, G. R.; Bai, R.; Hamel, E. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1081. (b) Pinny, K. G.; Pettit, G. R.; Mocharla, V. P.; Del, P. M.; Shirali, A. *PCT Int. Appl. WO* 98 39 323 (*Chem. Abs.*, **1998**, *129*, 245037c).
4. (a) Magarian, R. A.; Overacre, L. B.; Singh, S.; Meyer, K. L. *Curr. Med. Chem.* **1994**, *1*, 61. (b) Bryant, H. U.; Dere, W. H. *Proc. Soc. Exp. Biol. Med.* **1998**, *217*, 45. (c) Flynn, B. L; Verdier-Pinard, P.; Hamel, E. *Org. Lett.* **2001**, *5*, 651.
5. (a) Su, T.; Naughton, M. A. H.; Smyth, M. S.; Rose, J. W.; Arfsten, A. E.; McCowan, J. R.; Jakubowski, J. A.; Wyss, V. L.; Ruterbories, K. J.; Sall, D. J; Scarborough, R. M. *J. Med. Chem.* **1997**, *40*, 4308. (b) Takeuchi, K.; Kohn, T. J.; Bastian, J. A.; Chirgadze, N. Y.; Denney, M. L.; Harper, R. W.; Lin, H.; Mccowan, J. R.; Gifford-Moore, D. S.; Richett, M. E.; Sall, D. J.; Smith, G. F.; Zhang, M. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 759. (c) Sall, D. J.; Bastian, J. A.; Briggs, S. L.; Buben, J. A.; Chirgadze, N. Y.; Clawson, D. K.; Denney, M. L.; Giera, D. D.; Gifford-Moore, D. S.; Harper, R. W.; Hauser, K. L.; Klimkowski, V. J.; Kohn, T. J.; Lin, H.; McCowan, J. R.; Palkowitz, A. D.; Smith, G. F.; Takeuchi, K.; Thrasher, K. J.; Tinsley, J. M.; Utterback, B. G.; Yan, S. B.; Zhang, M. *J. Med. Chem.* **1997**, *40*, 3489.
6. (a) Tony, Y. Z.; O'Toole, J.; Proctor, C. S. *Sulfur Reports* **1999**, *22*, 1. (b) Pelkey, E. T. *Prog. Heterocycl. Chem.* **1999**, *11,* 102. (c) Bianchini, C.; Meli, A. *Synlett* **1997**, 643. (d) Russell, R. K.; Press, J. B. *Compr. Heterocycl. Chem. II* **1996**, *2*, 679. (e) Irie, M.; Uchida, K. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 985. (f) Gallagher, T.; Pardoe, D. A.; Porter, R. A. *Tetrahedron Lett.* **2000**, *41*, 5415. (g) Arnau, N.; Moreno-Manas,

M.; Pleixats, R. *Tetrahedron* **1993**, *49*, 11019. (h) McDonald, F. E.; Burova, S. A.; Huffman, L. G. Jr. *Synthesis* **2000**, 970.

7. Ren, X-F.; Turos, E. *Tetrahedron Lett.* **1993**, *34*, 1575.
8. (a) Sonada, T.; Kawakami, M.; Ikeda, T.; Kobayashi, S.; Taniguchi, H. *J. Chem. Soc., Chem. Commun.* **1976**, 612. (b) Kitamura, T.; Kobayashi, S.; Taniguchi, H.; Hori, K. *J. Am. Chem. Soc.* **1991**, *113*, 6240. (c) Kitamura, T.; Takachi, T.; Kawasato, H.; Taniguchi, H.; *J. Chem. Soc., Perkin Trans. 1* **1992**, 1969.
9. Arcadi, A.; Cacchi, S.; Giancarlo, F.; Marinelli, F.; Moro, L. *Synlett* **1999**, 1432.
10. Larock, R. C.; Harrison L. W. *J. Am. Chem. Soc.* **1984**, *106*, 4218.
11. For a previous communication, see: Larock, R. C.; Yue, D. *Tetrahedron Lett.,* **2001**, *42,* 6011-6013.
12. Campo, M. A.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3675.
13. (a) Pinto, D. J. P.; Copeland, R. A.; Covington, M. B.; Pitts, W. J.; Batt, D. G.; Orwat, M. J.; Lam, G. N.; Joshi, A.; Chan, Y.; Wang, S.; Trzaskos, J. M.; Magolda, R. L.; Kornhauser, D. M. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2907. (b) Buquet, A; Couture, A.; Lablache-Lombier, A. *Tetrahedron*, **1981**, *37*, 75.
14. Iddon, B.; Dickinson, R. P. *J. Chem. Soc. C* **1970**, *18*, 2592.
15. (a) Sura, T. P.; MacDowell, D. W. H. *J. Org. Chem.* **1993**, *58* 4360. (b) Ried, W.; Bender, H. *Chem. Ber.* **1955**, *34*, 88.
16. (a) Benati, L.; Montevecchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1992**, *13*, 1659. (b) Albertazzi, A.; Leardini, R.; Pedulli, G. F.; Tundo, A.; Zanrdi, G. *J. Org. Chem.* **1984**, *49*, 4482.

CHAPTER 2. SYNTHESIS OF 3-IODOINDOLES VIA PALLADIUM-CATALYZED COUPLING AND ELECTROPHILIC CYCLIZATION OF TERMINAL ACETYLENES

A paper to be submitted to the *Journal of Organic Chemistry*

Dawei Yue and Richard C. Larock*

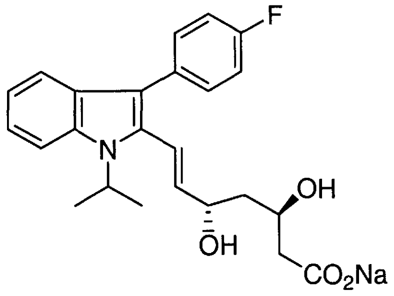
Department of Chemistry, Iowa State University, Ames, IA 50011

Abstract

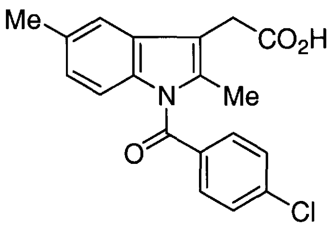
3-Iodoindoles have been prepared in excellent yields via coupling of terminal acetylenes with *N,N*-dialkyl-*o*-iodoanilines in the presence of a palladium catalyst and subsequent electrophilic iodocyclization of the resulting *N,N*-dialkyl-*o*-(1-alkynyl)aniline derivatives. Aryl-, vinylic-, alkyl- and silyl-substituted terminal acetylenes undergo this process to produce excellent yields of 3-iodoindoles.

Introduction

The indole nucleus is prevalent in natural products and important in medicinal chemistry.[1] 2,3-Disubstituted indoles, like lescol 1, which has been identified as an HMG-CoA reductase inhibitor,[1c] and indomethacin, which is an anti-tumor agent for endometrial cancers, are good examples.[1d] Thus, research directed towards concise and novel syntheses of substituted indoles is highly desirable.



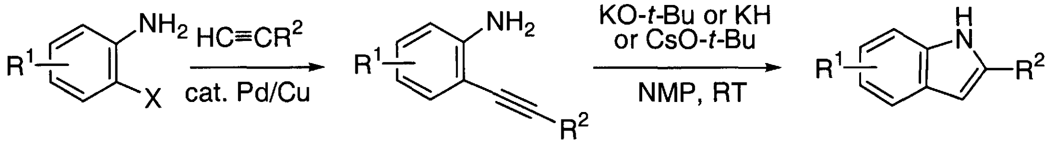
Lescol 1



Indomethacin

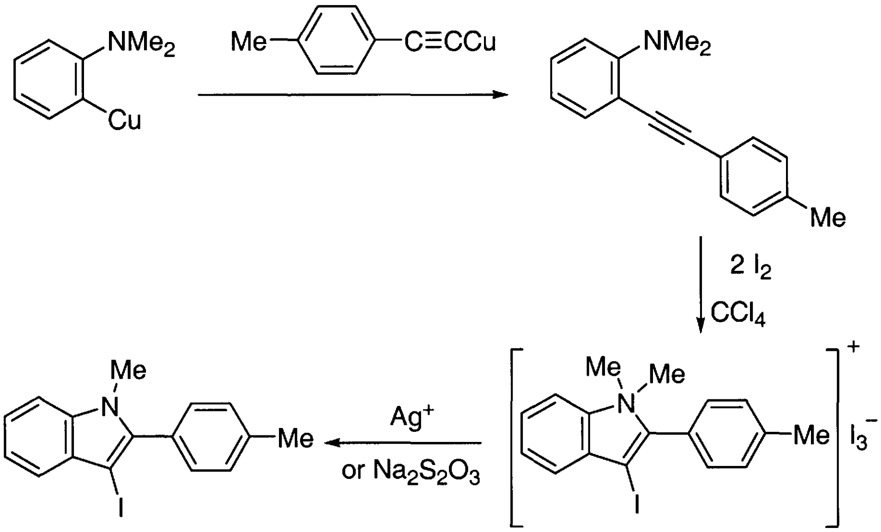
Many useful syntheses of indoles have recently been reported.[2] Knochel has reported a versatile indole synthesis by the *5-endo-dig* cyclization of *o*-alkynylanilines mediated by potassium or cesium bases.[2c] This highly efficient ring closure process requires an excess of a strong base and sometimes a high temperature (Scheme 1). On the other hand, the electrophilic cyclization of unsaturated compounds has proven to be an efficient method for constructing heterocycles.[3] This process is generally viewed as proceeding through an intramolecular, stepwise electrophilic addition and dealkylation mechanism involving a cationic intermediate. Taniguchi has explored the cyclization of vinylic cations as a route to heterocycles, but found significant limitations in generating the vinylic cations.[4] Although mechanistic and synthetic work on the preparation of benzo[*b*]furan,[3a] benzo[*b*]thiophene,[3b,c] isoquinoline,[3d] and furopyridine[3e] derivatives by electrophilic cyclization[5] of the corresponding functionally-substituted arylalkynes have been carried out, the synthesis of indole derivatives by this novel method remains relatively unknown.

Scheme 1



Hoedt has reported an approach to the synthesis of 1-methyl-2-*p*-tolylindole and the corresponding 3-iodo- derivative by related processes involving electrophilic cyclization (Scheme 2).[6] Unfortunately, the separation of the triiodide salt and the stepwise addition of an expensive silver reagent or $Na_2S_2O_3$ are not particularly attractive synthetically. Furthermore, the yield of the above process was only 66% or less and the scope of the cyclization step has not been examined. Herein, we report the successful application of this electrophilic cyclization strategy as a convenient and general synthetic methodology for the synthesis of a wide variety of 3-iodoindoles.

Scheme 2

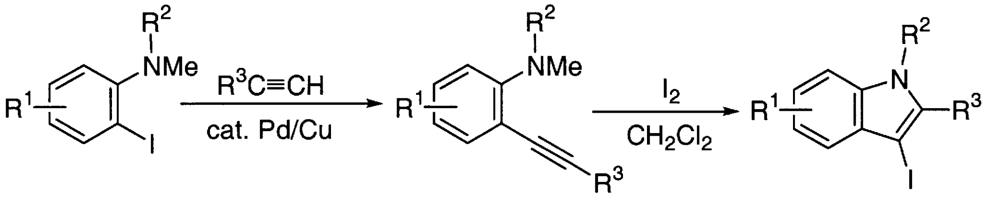


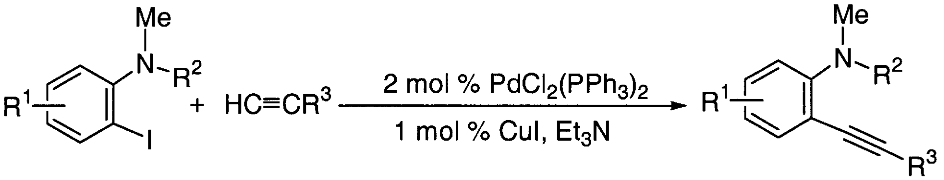
Results and Discussion

A two step approach to 3-iodoindoles has been examined involving (i) the Sonogashira coupling[7] of *N*,*N*-dialkyl-*o*-iodoanilines with terminal alkynes, and (ii) electrophilic cyclization (Scheme 3).

To assess the generality of this approach, the scope of the Sonogashira coupling of various *N,N*-dialkyl-*o*-iodoaniline derivatives and terminal alkynes has been studied. Treatment of *N,N*-dialkyl-*o*-iodoanilines bearing different functionality with a variety of terminal alkynes under standard Sonogashira coupling conditions[9] (5 mmol of *N,N*-dialkyl-*o*-iodoaniline, 1.2 equivs of terminal alkyne, 2 mol % of $PdCl_2(PPh_3)_2$, 1 mol % of CuI, 12.5 ml of Et_3N at room temperature for 5-24 h) affords high yields of the coupling products (eq 1, Table 1).

Scheme 3





(1)

N,N-Dialkyl-*o*-iodoanilines exhibit high reactivity towards Sonogashira coupling, allowing the preparation of a wide variety of functionally-substituted *N,N*-dialkyl-*o*-(1-alkynyl)anilines. *N,N*-Dialkyl-*o*-iodoanilines bearing nitro, ester, methyl and methoxy groups undergo smooth Sonogashira coupling with terminal alkynes bearing various substituents, including aryl, vinylic, alkyl and silyl groups. High yields have been obtained in almost all cases (Table 1). However, because it is extremely active towards homocoupling, 5-hexynenitrile affords only a relatively low yield and a large amount of the homocoupled diyne product of 5-hexynenitrile is formed (entry 6). 1-Octyne has also given a low yield on occasion (entries 12 and 18) for reasons that are not obvious.

Table 1. Sonogashira Coupling of *N*,*N*-Dialkyl-2-iodoanilines and Terminal Acetylenes (eq 1).[a]

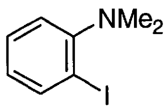
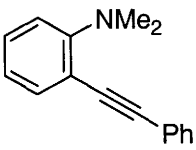
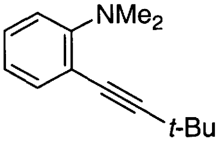
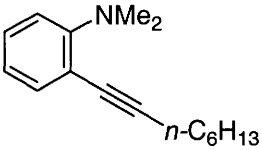
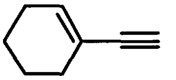
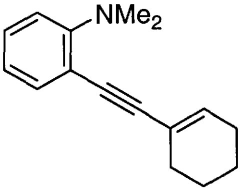
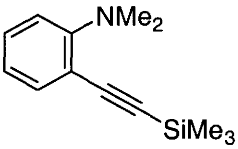
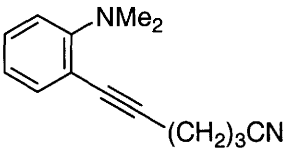
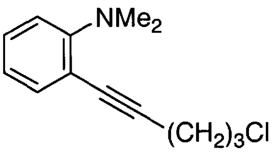
entry	*N*,*N*-dialkyl-2-iodoaniline	terminal acetylene	arylalkyne	time (h)	yield (%)
1	 **1**	$PhC\equiv CH$	 **2**	7	84
2		t-$BuC\equiv CH$	 **3**	7	85
3		n-$C_6H_{13}C\equiv CH$	 **4**	7	94
4			 **5**	5	84
5		Me_3Si—≡	 **6**	7	70
6		$HC\equiv C(CH_2)_3CN$	 **7**	7	40
7		$HC\equiv C(CH_2)_3Cl$	 **8**	7	87

Table 1. (Continued)

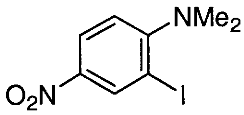
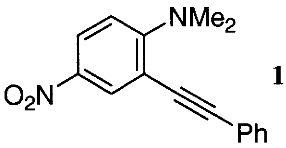
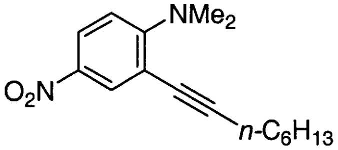
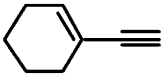
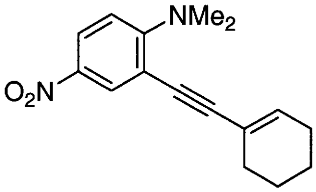
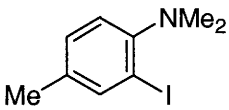
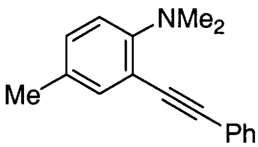
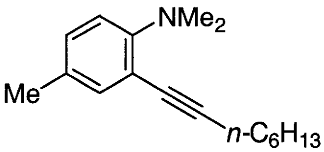
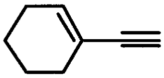
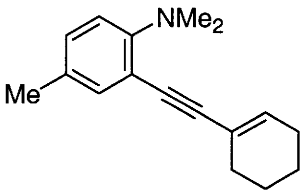
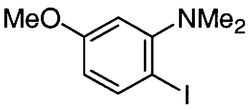
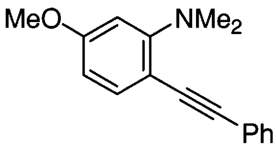
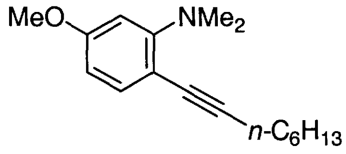
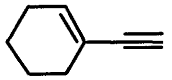
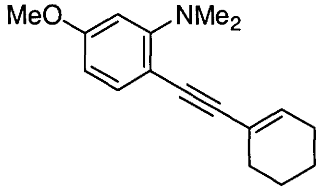
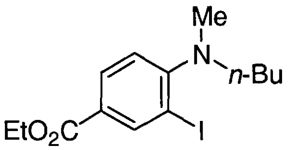
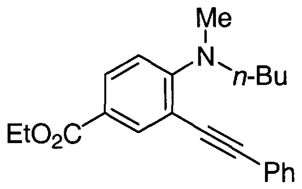
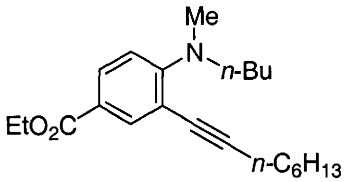
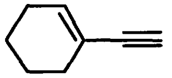
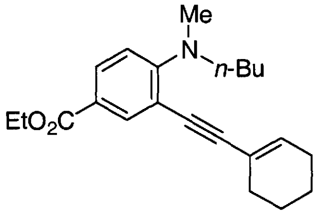
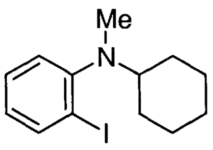
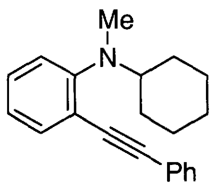
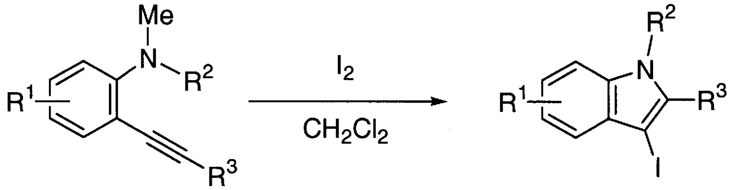
8	 **9**	$PhC\equiv CH$	 **10**	5	89
9		$n\text{-}C_6H_{13}C\equiv CH$	 **11**	5	83
10			 **12**	5	100
11	 **13**	$PhC\equiv CH$	 **14**	5	98
12		$n\text{-}C_6H_{13}C\equiv CH$	 **15**	5	67
13			 **16**	5	83
14	 **17**	$PhC\equiv CH$	 **18**	24	98

Table 1. (Continued)

15		n-$C_6H_{13}C{\equiv}CH$		**19**	24	93
16				**20**	24	100
17	 **21**	PhC≡CH		**22**	5	100
18		n-$C_6H_{13}C{\equiv}CH$		**23**	5	54
19				**24**	5	95
20	 **25**	PhC≡CH		**26**	24	80

[a] All reactions were run with 5 mmol of the *N*,*N*-dialkyl-2-iodoaniline, 1.2 equiv of the terminal acetylene, 2 mol % of $PdCl_2(PPh_3)_2$, 1 mol % of CuI, and 12.5 mL of Et_3N at 50 °C.

We have found that *N*,*N*-dimethyl-*o*-(phenylethynyl)aniline (**2**), when treated with 2 equiv of I_2 in CH_2Cl_2, undergoes smooth iodocyclization at room temperature and affords a nearly quantitative yield of the corresponding 3-iodo-2-phenylindole (**33**) (Table 2, entry 1). Only a trace of the triiodide salt was observed upon TLC analysis. However, under Hoedt's reaction conditions, using CCl_4 as the solvent, the triiodide salt is the major product. The mild reaction conditions, as well as the high yield of this reaction, encouraged us to extend this methodology to a range of *N,N*-dimethyl-*o*-(1-alkynyl)-anilines (eq 2; Table 2, entries 1-7). It makes little difference if the substituent on the other end of the alkyne is aryl, vinylic, alkyl, functionally-substituted alkyl or silyl. Even hindered *tert*-butyl- (**3**) (entry 2) or trimethylsilyl- (**6**) (entry 5) substituted alkynes react rapidly in high yields.



(2)

Substituents on the remote end of the triple bond of the *N,N*-dimethyl-*o*-(1-alkynyl)anilines also affect the yields of the cyclization reactions. The reactions of 6-(2-*N,N*-dimethylaminophenyl)-5-hexynenitrile (**7**) and *N,N*-dimethyl-2-(5-chloro-1-pentynyl)aniline (**8**) with iodine (entries 6 and 7) afford slightly lower yields than the simple alkyl-substituted alkyne **4** (entry 3). This may be because the electron-withdrawing cyano and chloro groups on the alkyl chain make the vinylic cation intermediates less stable or it may be the result of some side reaction of which we are unaware at this time. No products involving simple addition of the electrophile I_2 to the alkyne triple bond are observed with any of these alkynes. The 3-iodo-1-methyl-2-(trimethylsilyl)indole (**31**) obtained by iodocyclization of the silylalkyne **6** is extremely

Table 2. Synthesis of 3-Iodoindoles (eq 2).[a]

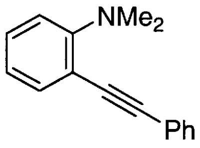
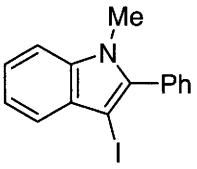
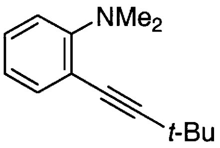
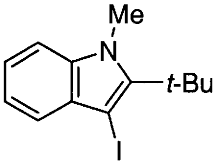
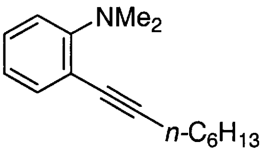
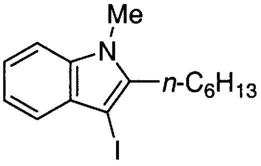
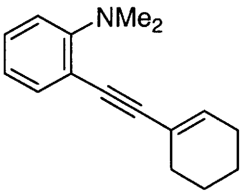
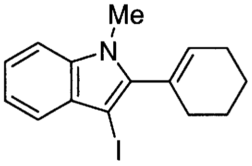
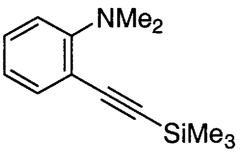
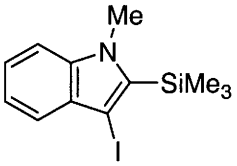
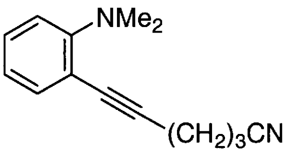
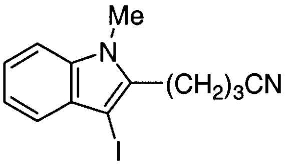
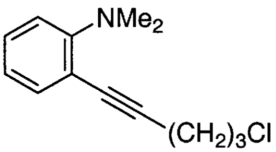
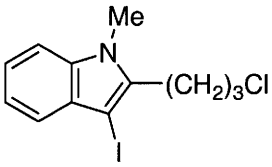
entry	alkyne	time (h)	product	Yield (%)
1	 **2**	2	 **27**	100
2	 **3**	2	 **28**	96
3	 **4**	2	 **29**	94
4	 **5**	2	 **30**	85
5	 **6**	4	 **31**	80
6	 **7**	4	 **32**	86
7	 **8**	4	 **33**	73

Table 2. (Continued)

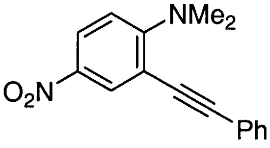
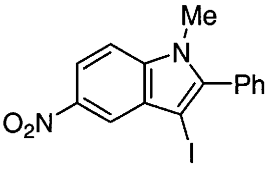
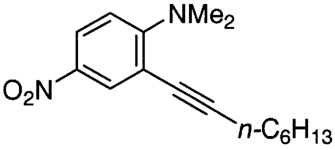
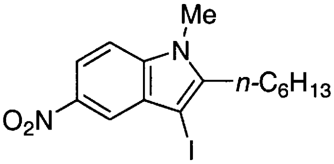
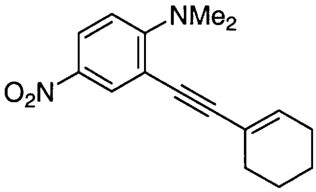
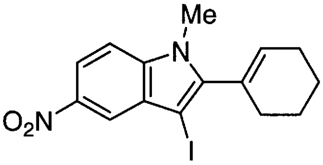
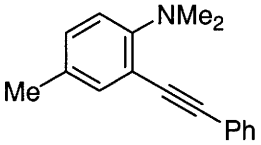
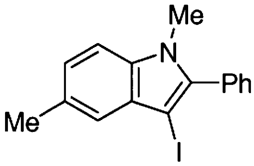
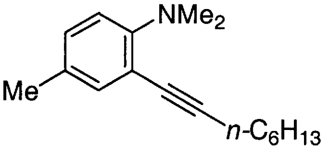
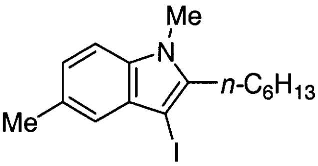
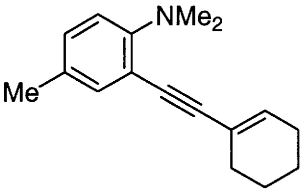
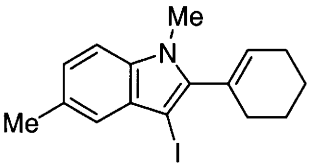
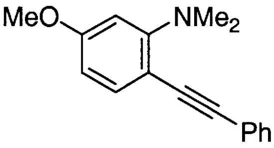
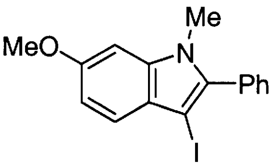
8	 **10**	0.5	 **34**	100
9	 **11**	0.5	 **35**	95
10	 **12**	0.5	 **36**	100
11	 **14**	0.5	 **37**	100
12	 **15**	0.5	 **38**	100
13	 **16**	0.5	 **39**	98
14	 **18**	2	 **40**	84

Table 2. (Continued)

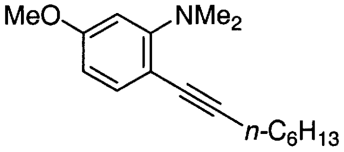
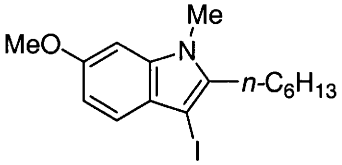
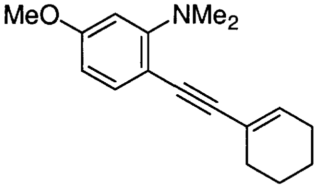
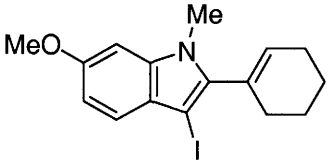
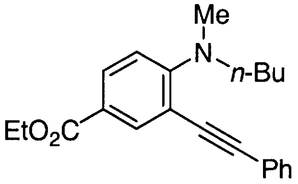
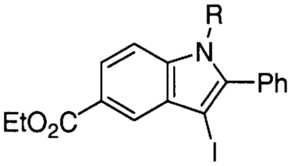
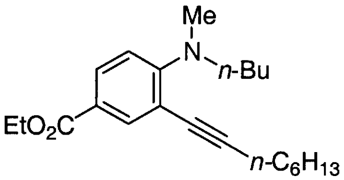
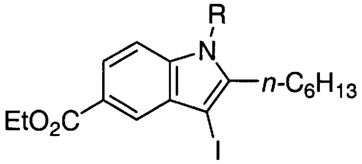
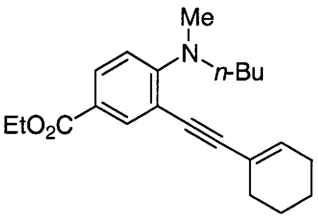
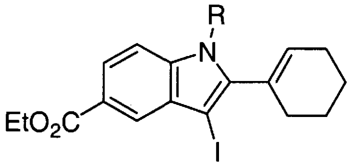
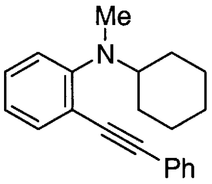
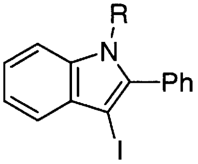
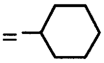
15	 **19**	2	 **41**	84
16	 **20**	2	 **42**	100
17	 **22**	0.5	 R = *n*-Bu R = Me **43** **44**	98 (72:28)
18	 **23**	0.5	 R = *n*-Bu R = Me **45** **46**	84 (62:38)
19	 **24**	0.5	 R = *n*-Bu R = Me **47** **48**	92 (66:34)

Table 2. (Continued)

20	 **26**	2	 R = Me **27** R =  **49**	50 (90:10)

^{a}All reactions were run with 0.25 mmol of the alkyne and 2 equiv of I_2 in 5 mL of CH_2Cl_2 at 25 °C, followed by the addition of 5 mL of satd aq $Na_2S_2O_3$ to remove the excess I_2.

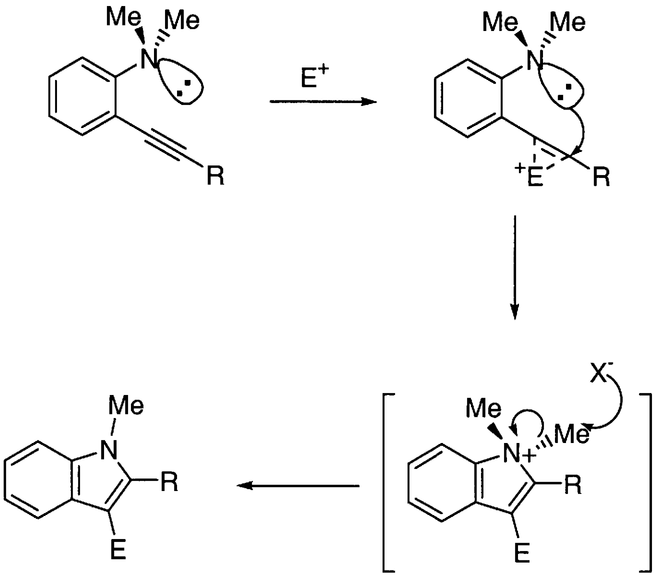
unstable. Although the cyclization product was detected by TLC analysis, we were unable to cleanly separate and characterize the corresponding 3-iodoindole. Substituents on the aniline ring play a role in the cyclization. Electron-withdrawing groups, such as a nitro or an ester group, enhance the electrophilic cyclization. The reaction times are shorter and higher yields are obtained (entries 8-10 and 17-19). Electron-donating groups, such as a methoxy group, make the triple bonds more electron rich and, therefore, make the cationic intermediate less reactive towards attack by the nitrogen. Longer reaction times are therefore needed and lower yields of the desired cyclization products are obtained (entries 14 and 15). Anilines with a less electron-donating group, such as a methyl group, undergo rapid iodocyclization and give high yields of the desired cyclization products (entries 11-13).

We were pleased to find that the methyl group on the nitrogen is easily removed during the cyclization step. This represents the first general route to 3-iodoindoles by an electrophilic cyclization strategy. The use of two different alkyl groups on the nitrogen of the aniline raises interesting selectivity questions. Compounds **22-24** with a methyl and an *n*-butyl group on the nitrogen undergo electrophilic cyclization smoothly and the total conversions are almost quantitative (entries 17-19). The less hindered methyl is more easily removed than is the *n*-butyl group. Thus, cleavage in this case appears to involve S_N2 displacement of the less hindered alkyl group. The corresponding 1-*n*-butyl-3-iodoindoles and 3-iodo-1-methylindoles were generally obtained in approximately a 2 to 1 ratio. The chemistry of compound **26** bearing a methyl and a cyclohexyl group on the nitrogen of the aniline was also of interest (entry 20). We expected to obtain mainly the *N*-cyclohexylindole if loss of the alkyl group proceeds by an S_N2 mechanism. If loss of the alkyl group proceeds by an S_N1 process, we would expect to obtain the *N*-methylindole. In fact, we isolated 45% of the *N*-methylindole and about 5% of the *N*-cyclohexylindole was formed. This suggests that loss of the alkyl group can occur by either an S_N1 or an S_N2 mechanism depending upon what groups are attached to the nitrogen of the aniline.

We believe that these cyclizations proceed by anti attack of the electrophile and the nitrogen of the *N,N*-dialkylamino group of the alkyne to produce an indolium salt, which loses an alkyl group via either S_N1 or S_N2 substitution by the iodide nucleophile present in the reaction mixture after cyclization (Scheme 4). The success of this reaction is presumably due to several factors. First, the two alkyl groups on the nitrogen make the nitrogen highly nucleophilic. Second, the interaction between the two alkyl groups and the internal triple bond favors an orientation of the nitrogen with its lone pair of electrons pointing towards the triple bond. Third, the highly nucleophilic iodide ion formed after the cyclization facilitates removal of the methyl or other alkyl group.

In order to explore the scope of this electrophilic cyclization strategy, four other electrophiles, Br_2, NBS, *p*-$O_2NC_6H_4SCl$ and PhSeCl have been employed in the reaction

Scheme 4

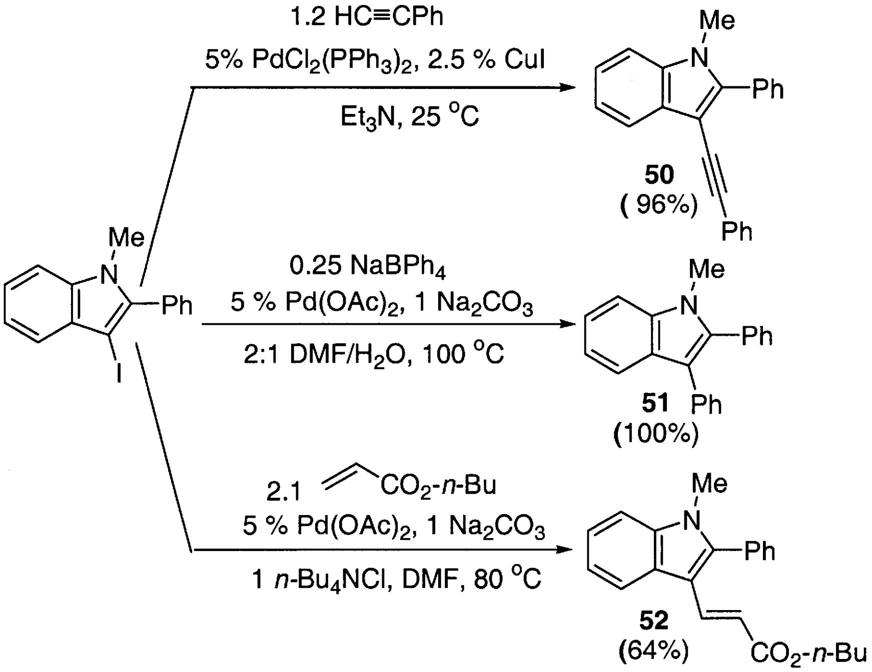


of alkyne **2**. Only iodine exhibits high reactivity towards electrophilic cyclization. These electrophiles do not provide good yields of cyclization products.

The 3-iodoindoles produced by this chemistry should be very useful for the synthesis of additional indoles. For example, the 3-iodo-2-phenylindole produced by this strategy can be further functionalized by applying palladium-catalyzed coupling reactions. We have found that 1-methyl-2-phenyl-3-(phenylethynyl)indole (**50**), 1-methyl-2,3-diphenylindole (**51**) and *n*-butyl (*E*)-3-[1-methyl-2-phenylindol-3-yl]propenoate (**52**) can be obtained in 92%, 90% and 64% overall yields respectively from *N,N*-dimethyl-*o*-iodoaniline and phenyl acetylene by our two step coupling/cyclization process, followed by palladium-catalyzed cross-coupling processes involving the Sonogashira,[7] Suzuki,[8] and Heck[9] reactions (Scheme 5). One should be able to prepare many other 2,3-

disubstituted indoles using these iodoindole substrates and other known palladium methodology.[10]

Scheme 5



Conclusions

A very efficient synthesis of 2,3-disubstituted indoles has been developed by a two step approach involving the Sonogashira cross-coupling of terminal alkynes and *N,N*-dialkyl-*o*-iodoanilines, followed by electrophilic cyclization using I_2 in CH_2Cl_2. While I_2 gives 3-iodoindoles in excellent yields, Br_2, NBS, *p*-$O_2NC_6H_4SCl$ and PhSeCl give mixtures of both cyclization products and products of simple addition to the triple bond with the latter predominating. A wide variety of aniline-containing acetylenes with various functional groups on the arene moiety undergo this overall process in good to excellent yields. The steric and electronic effects of the substituents on the carbon-

carbon triple bond of the *N,N*-dialkyl-2-(1-alkynyl)aniline intermediates have been studied. A study of the N-alkyl bond cleavage of the dialkylamino group reveals that this chemistry can undergo either S_N1 or S_N2 displacement.

Experimental Section

General. All ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz. 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). All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at a voltage of 70 eV. All reagents were used directly as obtained commercially unless otherwise noted. Anhydrous forms of ethyl ether, hexanes, ethyl acetate, methylene chloride and DMF were purchased from Fisher Scientific Co. 2-Iodoaniline, phenylacetylene, 1-octyne, 1-cyclohexenyl acetylene, *tert*-butyl acetylene, trimethylsilyl acetylene, 5-hexynenitrile and Et_3N were purchased from Aldrich Chemical Co., Inc. The palladium salts were donated by Johnson Matthey Inc. and Kawaken Fine Chemicals Co. Ltd.

Preparation of 2-Iodoanilines. 2-Iodo-4-nitroaniline,[11] 2-iodo-4-methylaniline,[11] 2-iodo-5-methoxyaniline[11] and ethyl 3-iodo-4-(*n*-butylamino)benzoate[12] were prepared according to literature procedures. The ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature data.[11,12]

Ethyl 4-(*n*-butylamino)-3-iodobenzoate. The compound was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, J = 7.2 Hz, 3H), 1.36 (t, J = 6.9 Hz, 3H), 1.40-

1.52 (m, 2H), 1.63-1.72 (m, 2H), 3.18-3.22 (m, 2H), 4.31 (q, J = 7.2 Hz, 2H), 4.61 (s, 1H), 6.49 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 8.33 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 14.6, 20.4, 31.2, 43.8, 60.7, 83.8, 108.9, 120.0, 131.7, 140.8, 150.7, 165.7; IR (neat, cm^{-1}) 3394, 2959, 2930, 2871, 1711. The product was used for the next step without further characterization.

General Procedure for the Preparation of *N,N*-Dialkyl-*o*-iodoanilines. These compounds were prepared by a procedure reported by Cadogan.[13] A solution of the corresponding aniline (2.0 mmol) and iodomethane (0.85 g, 6.0 mmol) in DMF (10 ml) containing K_2CO_3 (0.55 g, 4.0 mmol) was stirred for 48 h at room temperature. Water (10 ml) was then added, and the solution was extracted with ethyl ether (3 x 10 ml). The organic extracts were washed with water (4 x 20 ml) to remove any remaining DMF, and then dried (Na_2SO_4) and the solvent was removed under reduced pressure to yield the crude product, which was further purified by flash chromatography on silica gel using ethyl acetate/hexane as the eluent.

N,N-Dialkyl-2-iodoanilines Prepared

***N,N*-Dimethyl-2-iodoaniline (1)**. The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.76 (s, 6H), 6.76 (t, J= 8.2 Hz, 1H), 7.08 (d, J = 9.3 Hz, 1H), 7.30 (t, J= 7.7 Hz, 1H), 7.83 (d, J= 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.2, 97.3, 120.6, 125.2, 129.2, 140.4, 155.1; IR (neat, cm^{-1}) 3002, 1944, 2830, 2783; HRMS calcd for $C_8H_{10}IN$ 246.98580. Found 246.98605.

***N,N*-Dimethyl-2-iodo-4-nitroaniline (9)**. The compound was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.94 (s, 6H), 6.98 (d, *J* = 9.0 Hz, 1H), 8.16 (d, *J* = 9.0 Hz, 1H), 8.69 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.4, 90.6, 118.6, 124.8, 136.8, 160.7; IR (neat, cm^{-1}) 2947, 2871, 2843, 2794; HRMS calcd for $C_8H_9IN_2O_2$ 291.97088. Found 291.97104.

***N,N*-Dimethyl-2-iodo-4-methylaniline (13).** The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.26 (s, 3H), 2.72 (s, 6H), 6.99 (d, *J* = 9.0 Hz, 1H), 7.11 (d, *J* = 9.0 Hz, 1H), 7.68 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 45.4, 97.6, 120.3, 130.0, 135.1, 140.7, 152.7; IR (neat, cm^{-1}) 3058, 2926, 2855, 2227, 1464, 1435, 749; HRMS calcd for $C_9H_{12}IN$ 261.00165. Found 261.00198.

***N,N*-Dimethyl-2-iodo-5-methoxyaniline (17).** The compound was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75 (s, 6H), 3.78 (s, 3H), 6.38 (d, *J* = 10.4 Hz, 1H), 6.66 (s, 1H), 7.68 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.0, 55.5, 85.4, 107.8, 110.0, 140.3, 156.1, 160.9; IR (neat, cm^{-1}) 2293, 2829, 2780; HRMS calcd for $C_9H_{12}INO$ 276.99637. Found 276.99697.

Ethyl 4-(*N*-*n*-butyl-*N*-methylamino)-3-iodobenzoate (21). The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.5 Hz, 3H), 1.30-1.40 (m, 5H), 2.78 (s, 3H), 3.03 (t, *J* = 9.0 Hz, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 1H), 7.96 (dd, *J* = 8.4, 2.1 Hz, 1H), 8.49 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 14.6, 20.4, 29.7, 41.9, 56.1, 61.2, 95.7, 120.7, 126.2, 130.5, 142.0, 158.9, 165.4; IR (neat, cm^{-1}) 3004, 2922, 1713; HRMS calcd for $C_{14}H_{20}INO_2$ 361.05388. Found 361.05433.

N-Cyclohexyl-N-methyl-2-iodoaniline (25). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08-1.13 (m, 4H), 1.32 (q, J = 12.0 Hz, 2H), 1.74-1.84 (m, 4H), 2.62 (s, 3H), 2.97-3.03 (m, 1H), 6.75 (t, J = 7.2 Hz, 1H), 7.07 (d, J = 7.2 Hz, 1H), 7.27 (t, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.8, 26.3, 29.3, 35.6, 62.2, 100.2, 123.8, 125.1, 128.6, 140.2, 154.3; HRMS calcd for $C_{13}H_{18}IN$ 315.00637. Found 315.00684.

General Procedure for the Palladium/Copper-Catalyzed Formation of N,N-Dialkyl-2-(1-alkynyl)anilines. To a solution of Et_3N (12.5 ml), $PdCl_2(PPh_3)_2$ (0.070 g, 2 mol %), 5 mmol of N,N-dialkyl-o-iodoaniline and 6.0 mmol of terminal acetylene (stirring for 5 min beforehand), CuI (0.010 g, 1 mol %) was added and stirring was continued for another 2 min before flushing with Ar. The flask was then sealed. The mixture was allowed to stir at room temperature for the desired time and the resulting solution was filtered, washed with a satd aq NaCl solution and extracted with diethyl ether (2 x 10 ml). The combined ether fractions were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by flash chromatography on silica gel using ethyl acetate/hexane as the eluent.

N,N-Dialkyl-2-(1-alkynyl)anilines Prepared

N,N-Dimethyl-2-(phenylethynyl)aniline (2). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.01 (s, 6H), 6.88-6.94 (m, 2H), 7.25 (t, J = 6.3 Hz, 1H), 7.31-7.37 (m, 3H), 7.49 (d, J = 5.7 Hz, 1H), 7.54 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.8, 89.1, 95.0, 115.3, 117.2, 120.7, 124.1, 128.2, 128.5, 129.5, 131.5, 134.6, 155.0; IR (neat, cm^{-1}) 3059, 2943, 2833, 2785, 2209; HRMS calcd for $C_{16}H_{15}N$ 221.12045. Found 221.12076.

***N,N*-Dimethyl-2-(3,3-dimethyl-1-butynyl)aniline (3).** The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 9H), 2.92 (s, 6H), 6.80-6.86 (m, 2H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.5, 31.2, 43.6, 78.5, 104.0, 116.2, 116.9, 120.5, 128.5, 134.5, 154.6; IR (neat, cm^{-1}) 3004, 2923, 2147; HRMS calcd for $C_{14}H_{18}N$ 200.14392. Found 200.14417.

***N,N*-Dimethyl-2-(1-octynyl)aniline (4).** The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, *J* = 6.9 Hz, 3H), 1.29-1.34 (m, 4 H), 1.46-1.49 (m, 2H), 1.62 (q, *J* = 3.8 Hz, 2H), 2.47 (t, *J* = 7.2 Hz, 2H), 2.91 (s, 3H), 6.83-6.90 (m, 2H), 7.18 (t, *J* = 5.0 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 20.1, 22.8, 28.9, 29.0, 31.6, 43.8, 79.7, 96.1, 116.8, 117.1, 120.9, 128.5, 134.5, 154.8; IR (neat, cm^{-1}) 2930, 2858, 2782, 2242; HRMS calcd for $C_{16}H_{23}N$ 229.18305. Found 229.18336.

***N,N*-Dimethyl-2-(cyclohex-1-enylethynyl)aniline (5).** The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62-1.68 (m, 4H), 2.13-2.15 (m, 2H), 2.25-2.27 (m, 2H), 2.93 (s, 6H), 6.18-6.19 (m, 1H), 6.84-6.89 (m, 2H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 22.5, 25.9, 29.3, 43.6, 86.3, 96.8, 115.9, 117.0, 120.6, 121.3, 128.8, 134.2, 134.4, 154.6; IR (neat, cm^{-1}) 2932, 2859, 2832, 2196; HRMS calcd for $C_{16}H_{19}N$ 225.15175. Found 225.15209.

***N,N*-Dimethyl-2-(trimethylsilylethynyl)aniline (6).** The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 9H), 2.98 (s, 3H), 6.83 (dd, *J* = 9.0, 6.0 Hz, 2H), 7.21 (t, *J* = 9.0 Hz, 1H), 7.41 (d, *J* = 9.0, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.2, 43.5, 99.7, 104.9, 114.9, 116.9, 120.3, 129.6, 135.1, 155.3; IR (neat, cm^{-1}) 3059, 2959, 2920, 2155, 1461, 1434, 1249, 843; HRMS calcd for $C_{13}H_{18}NSi$ 216.12085. Found 216.12100.

6-(2-*N,N*-Dimethylaminophenyl)-5-hexynenitrile (7). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.97 (t, *J* = 7.2 Hz, 2H), 2.57 (t, *J* = 7.2 Hz, 2H), 2.67 (t, *J* = 6.8 Hz, 2H), 2.90 (s, 6H), 6.87 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 19.1, 24.9, 43.8, 81.6, 92.3, 115.9, 117.3, 119.4, 121.0, 129.1, 134.4, 155.0; IR (neat, cm^{-1}) 3061, 2942, 2834, 2785, 2247; HRMS calcd for $C_{14}H_{16}N_2$ 212.13135. Found 212.13172.

***N,N*-Dimethyl-2-(5-chloro-1-pentynyl)aniline (8).** The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.04-2.11 (m, 2H), 2.68 (t, *J* = 6.8 Hz, 2H), 2.91 (s, 6H), 3.74 (t, *J* = 6.3 Hz, 2H), 6.84-6.92 (m, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.6, 31.7, 43.8, 44.0, 80.8, 93.6, 116.3, 117.3, 121.0, 128.9, 134.5, 154.9; IR (neat, cm^{-1}) 2943, 2832, 2784, 2259; HRMS calcd for $C_{13}H_{16}ClN$ 221.69713. Found 221.69754.

***N,N*-Dimethyl-4-nitro-2-(phenylethynyl)aniline (10).** The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.26 (s, 6H), 6.78 (d, *J* = 9.2 Hz, 1H), 7.36-7.38 (m, 3H), 7.50-7.52 (m, 2H), 8.06 (dd, *J* = 9.2, 2.4 Hz, 1H), 8.35 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.7, 87.7, 95.3, 110.4, 114.7, 123.0, 125.1, 128.6, 128.7, 131.1, 131.4, 138.5, 157.5; IR (neat, cm^{-1}) 2954, 2917, 2849, 2133; HRMS calcd for $C_{16}H_{14}N_2O_2$ 266.10553. Found 266.10592.

***N,N*-Dimethyl-4-nitro-2-(1-octynyl)aniline (11).** The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, *J* = 6.8 Hz, 3H), 1.30-1.34 (m, 4H), 1.43-1.48 (m, 2H), 1.62 (q, *J* = 7.2 Hz, 2H), 2.45 (t, *J* = 7.1 Hz, 2H), 3.15 (s, 6H), 6.73 (d, *J* = 9.3 Hz, 1H), 7.99 (dd, *J* = 9.3, 2.7 Hz, 1H), 8.20 (d, *J* = 2.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 19.9, 22.7, 28.7, 28.9, 31.5, 42.8, 78.7, 97.3, 112.4, 114.9, 124.5, 131.4, 138.9, 158.0; IR (neat, cm^{-1}) 2930, 2857, 2806, 2224; HRMS calcd for $C_{16}H_{22}N_2O_2$ 274.16813. Found 274.16830.

***N,N*-Dimethyl-2-(cyclohex-1-enylethynyl)-4-nitroaniline (12).** The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61-1.71 (m, 4H), 2.15-2.20 (m, 2H), 2.20-2.22 (m, 2H), 3.18 (s, 6H), 6.20-6.21 (m, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 12.0 Hz, 1H), 8.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 22.3, 25.8, 28.8, 42.7, 85.0, 97.5, 111.5, 114.6, 120.7, 124.6, 131.0, 135.4, 138.7, 157.5; IR (neat, cm^{-1}) 2924, 2853, 2354, 1454, 1432, 749; HRMS calcd for $C_{16}H_{18}N_2O_2$ 270.13683. Found 270.13735.

***N,N*-Dimethyl-4-methyl-2-(phenylethynyl)aniline (14)**. The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.26 (s, 3H), 2.95 (s, 6H), 6.83 (d, *J* = 8.1 Hz, 1H), 7.04 (d, *J* = 9.0 Hz, 1H), 7.22-7.33 (m, 4H), 7.52-7.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 44.0, 89.1, 94.7, 115.6, 117.3, 124.2, 128.2, 128.5, 130.3, 130.3, 131.6, 134.8, 152.8; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{17}H_{17}N$ 235.13610. Found 235.13582.

***N,N*-Dimethyl-4-methyl-2-(1-octynyl)aniline (15).** The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.83 (t, *J* = 6.0 Hz, 3H), 1.24-1.26 (m, 4H), 1.37-1.41 (m, 2H), 1.55 (q, *J* = 8.0 Hz, 2H), 2.16 (s, 3H), 2.40 (t, *J* = 8.0 Hz, 2H), 2.79 (s, 6H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 7.12 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.3, 20.1, 20.4, 22.8, 28.9, 29.0, 31.6, 44.0, 79.6, 95.7, 116.9, 117.2, 129.2, 130.4, 134.9, 152.5; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{17}H_{25}N$ 243.19870. Found 243.19908.

***N,N*-Dimethyl-2-(cyclohex-1-enylethynyl)-4-methylaniline (16).** The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.52-1.63 (m, 4H), 2.05-2.06 (m, 2H), 2.15-2.17 (m, 5H), 2.81 (s, 3H), 6.09-6.11 (m, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 7.12 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.4, 21.8, 22.6, 25.9, 29.3, 43.8, 86.2, 96.6, 116.1, 117.0, 121.3, 129.5, 130.1, 134.4, 134.5, 152.5; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{17}H_{21}N$ 239.16740. Found 239.16779.

***N,N*-Dimethyl-5-methoxy-2-(phenylethynyl)aniline (18).** The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.99 (s, 6H), 3.79 (s, 3H), 6.44 (d, *J* = 8.0 Hz, 2H), 7.23-7.34 (m, 3H), 7.41 (d, *J* = 8.8 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 43.5, 55.4, 89.2, 93.5, 103.8, 105.3, 107.6, 124.4, 127.8, 131.2, 135.6, 156.3, 160.8; IR (neat, cm^{-1}) 2924, 2853, 2354, 1454, 1432, 749; HRMS calcd for $C_{17}H_{17}NO$ 251.13101. Found 251.13132.

***N,N*-Dimethyl-5-methoxy-2-(1-octynyl)aniline (19).** The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, CDCl$_3$) δ 0.90 (t, *J* = 6.8 Hz, 3H), 1.30-1.33 (m, 4H), 1.42-1.49 (m, 2H), 1.62 (q, J = 7.6 Hz, 2H), 2.45 (t, J = 6.8 Hz, 2H), 2.90 (s, 6H), 3.77 (s, 3H), 6.36-6.42 (m, 2H), 7.29 (d, J = 8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 20.0, 22.8, 28.9, 29.1, 31.6, 43.6, 55.3, 79.5, 94.2, 104.1, 105.3, 109.2, 135.4, 156.1, 160.0; IR (neat, cm^{-1}) 2924, 2853, 2354, 1454, 1432, 749; HRMS calcd for $C_{17}H_{25}NO$ 259.19361. Found 259.19389.

***N,N*-Dimethyl-2-(cyclohex-1-enylethynyl)-5-methoxyaniline (20).** The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59-1.68 (m, 4H), 2.12-2.14 (m, 2H), 2.22-2.24 (m, 2H), 2.92 (s, 6H), 3.78 (s, 3H), 6.13-6.15 (m, 1H), 6.38-6.41 (m, 2H), 7.29 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 22.6, 25.9, 29.4, 43.4, 55.3, 86.2, 95.3, 103.8, 105.2, 108.3, 121.4, 133.6, 135.3, 156.0, 160.3; IR (neat, cm^{-1}) 2932, 2834, 2786, 2194; HRMS calcd for $C_{17}H_{21}NO$ 255.16231. Found 255.16270.

Ethyl 4-(*N*-*n*-butyl-*N*-methylamino)-3-(phenylethynyl)benzoate (22). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, J = 7.4 Hz, 3H), 1.25-1.31 (m, 2H), 1.37 (t, J = 7.0 Hz, 3H), 1.63-1.69 (m, 2H), 3.02 (s, 3H), 3.54 (t, J = 7.8 Hz, 2H), 4.34 (q, J = 7.2 Hz, 2H), 6.81 (d, J = 8.8 Hz, 1H), 7.31-7.35 (m, 3H), 7.49-7.51 (m, 2H), 7.86 (d, J = 8.8 Hz, 1H), 8.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.6, 20.4, 30.1, 39.8, 54.9, 60.7, 89.0, 94.2, 111.7, 115.8, 120.5, 123.8, 128.2, 128.5, 130.8, 131.3, 137.1, 156.6, 166.2; IR (neat, cm^{-1}) 2957, 2929, 2870, 2203; HRMS calcd for $C_{22}H_{25}NO_2$ 335.18853. Found 335.18887.

Ethyl 4-(*N*-*n*-butyl-*N*-methylamino)-3-(1-octynyl)benzoate (23). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81-0.87 (m, 6H), 1.19-1.40 (m, 11H), 1.50-1.58 (m, 4H), 2.87 (s, 3H), 3.39 (q, J = 8.0 Hz, 2H) , 4.25 (q, J = 8.0 Hz, 2H), 6.71 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.94 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.3, 14.6, 20.1, 20.4, 22.8, 28.9, 28.9, 30.0, 31.6, 39.7, 54.9, 60.6, 79.6, 95.7, 113.4, 116.0, 120.8, 130.1, 137.0, 156.9, 166.4; IR (neat, cm^{-1}) 2924, 2853, 2354, 1454, 1432, 749; HRMS calcd for $C_{22}H_{33}NO_2$ 343.25113. Found 343.25150.

Ethyl 4-(*N*-*n*-butyl-*N*-methylamino)-3-(cyclohex-1-enylethynyl)benzoate (24). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, J = 8.0 Hz, 3H), 1.20-1.28 (m, 5H), 1.54-1.59 (m, 6H), 2.06-2.15 (m, 4H), 2.89 (s, 3H), 3.39 (q, J = 8.0 Hz, 2H), 4.24 (t, J = 8.0 Hz, 2H), 6.09 (m, 1H), 6.69 (d, J = 8.0 Hz, 1 H), 7.73 (d, J = 8.0 Hz, 1H), 7.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 14.6, 20.4, 21.7, 22.5, 25.9, 29.2, 30.0, 39.7, 54.8, 60.6, 86.1, 96.3, 112.6, 115.8, 120.5, 121.2, 130.3, 134.5, 136.8, 156.5, 166.3; IR (neat, cm^{-1}) 2924, 2853, 2354, 1454, 1432, 749; HRMS calcd for $C_{22}H_{29}NO_2$ 339.21983. Found 339.22025.

***N*-Cyclohexyl-*N*-methyl-2-(phenylethynyl)aniline (26).** The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07-1.28 (m, 4H), 1.51-1.62 (m, 2H), 1.78 (d, J = 13.2 Hz, 2H), 1.88 (d, J = 12.0 Hz, 2H), 2.77 (s, 3H), 3.80-3.85 (m, 1H), 6.87 (t, J = 7.2 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 7.23 (d, J = 7.2 Hz, 1H), 7.30-7.33 (m, 3H), 7.50 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.3, 26.4, 29.9, 32.8, 62.6, 89.2, 94.3, 116.0, 119.0, 120.3, 124.2, 128.0, 128.5, 129.1, 131.5, 134.7, 154.8; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{21}H_{23}N$ 289.0144. Found 289.0251.

General Procedure for Iodocyclization. To a solution of 0.25 mmol of the *N,N*-dialkyl-2-(1-alkynyl)aniline and 3 ml of CH_2Cl_2, 2 equivs of I_2 dissolved in 2 ml of CH_2Cl_2 was added gradually. The reaction mixture was flushed with Ar and allowed to stir at room temperature for the desired time. The excess I_2 was removed by washing with a satd aq soln of $Na_2S_2O_3$. The aqueous solution was then extracted by diethyl ether (2 x 10 ml). The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under a vacuum to yield the crude product, which was purified by flash chromatography on silica gel using ethyl acetate/hexanes as the eluent.

3-Iodoindoles Prepared

3-Iodo-1-methyl-2-phenylindole (27). The product was obtained as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 3.63 (s, 3H), 7.21-7.28 (m, 3H), 7.43-7.51 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.2, 59.0, 110.0, 120.9, 121.6, 123.1, 128.6, 129.0, 130.5, 131.1, 131.8, 137.9, 141.9; IR (neat, cm^{-1}) 3054, 2937; HRMS calcd for $C_{15}H_{12}IN$ 333.00145. Found 333.00194.

2-*t*-Butyl-3-iodo-1-methylindole (28). The product was obtained as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 1.67 (s, 9H), 3.92 (s, 3H), 7.16-7.25 (m, 3H), 7.52 (t, J = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.4, 32.4, 34.7, 54.5, 109.0, 120.5, 122.4, 122.8, 131.6, 138.6, 144.4; IR (neat, cm^{-1}) 3004, 2966, 2922; HRMS calcd for $C_{13}H_{16}IN$ 312.02492. Found 312.02515.

2-*n*-Hexyl-3-iodo-1-methylindole (29). The product was obtained as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 7.0 Hz, 3H), 1.30-1.43 (m, 6H), 1.56-1.59 (m, 2H), 2.82 (t, *J* = 8.0 Hz, 2H), 3.70 (s, 3H), 7.12-7.20 (m, 3H), 7.37 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.3, 22.8, 27.3, 29.2, 29.5, 30.8, 31.8, 57.9, 109.4, 120.4, 120.7, 122.1, 130.2, 137.6, 142.0; IR (neat, cm^{-1}) 3053, 2926, 2855; HRMS calcd for $C_{15}H_{20}IN$ 341.06405. Found 341.06452.

2-(Cyclohex-1-enyl)-3-iodo-1-methylindole (30). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.73-1.76 (m, 2H), 1.81-1.84 (m, 2H), 2.22-2.30 (m, 4H), 3.68 (s, 3H), 5.88-5.90 (m, 1H), 7.17-7.19 (m, 1H), 7.22-7.24 (m, 2H), 7.41 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 22.1, 22.9, 25.7, 29.4, 31.5, 57.0, 109.7, 120.5, 121.2, 122.4, 130.0, 130.3, 133.8, 137.3, 144.4; IR (neat, cm^{-1}) 2921, 2850; HRMS calcd for $C_{15}H_{16}IN$ 337.03275. Found 337.03300.

3-Iodo-1-methyl-2-(trimethylsilyl)indole (31). The product was obtained as an inseparable mixture of the desired product and decomposed product.

4-(3-Iodo-1-methylindol-2-yl)butanenitrile (32). The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.99 (q, *J* = 7.4 Hz, 2H), 2.42 (t, *J* = 7.1 Hz, 2H), 3.02 (t, *J* = 7.5 Hz, 2H), 3.77 (s, 3H), 7.17-7.21 (m, 1H), 7.24-7.26 (m, 2H), 7.38 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 16.8, 25.4, 26.0, 30.9, 59.3, 109.6, 119.5, 120.8, 121.0, 122.8, 130.0, 137.8, 138.8; IR (neat, cm^{-1}) 2935, 2869, 2246; HRMS calcd for $C_{13}H_{13}IN_2$ 324.01235. Found 324.01269.

2-(3-Chloropropyl)-3-iodo-1-methylindole (33). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.04-2.11 (m, 2H), 3.02 (t, *J* = 7.6 Hz, 2H), 3.60 (t, *J* = 7.8 Hz, 2H), 3.76 (s, 3H), 7.14-7.18 (m, 1H), 7.22-7.23 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 24.6, 30.9, 32.3, 44.4, 58.6, 109.6, 120.6, 120.8, 122.5, 130.1, 137.7, 140.0; IR (neat, cm^{-1}) 2956, 2928, 2869; HRMS calcd for $C_{12}H_{13}ClIN$ 333.57813. Found 333.57851.

3-Iodo-1-methyl-5-nitro-2-phenylindole (34). The compound was obtained as pale yellow crystals: the compound decomposes at 125 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (s, 3H), 7.36 (d, *J* = 9.0 Hz, 1H), 7.46-7.59 (m, 2H), 7.53-7.57 (m, 3H), 8.19 (dd, *J* = 9.0, 2.4 Hz, 1H), 8.45 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.6, 32.7, 61.3, 110.2, 118.6, 119.0, 128.9, 129.8, 130.2, 130.7, 130.9, 140.9, 142.7, 145.4; IR (neat, cm^{-1}) 2924, 2852; HRMS calcd for $C_{15}H_{11}IN_2O_2$ 378.01168. Found 378.01242.

2-*n*-Hexyl-3-iodo-1-methyl-5-nitroindole (35). The product was obtained as pale yellow crystals: the compound decomposes at 118 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, *J* = 7.1 Hz, 3H), 1.31-1.37 (m, 4H), 1.39-1.46 (m, 2H), 1.57-1.64 (m, 2H), 2.87 (t, *J* = 7.5 Hz, 2H), 3.81 (s, 3H), 7.25 (d, *J* = 8.4 Hz, 1H), 8.09 (dd, *J* = 9.0, 2.4 Hz, 1H), 8.32 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 16.6, 22.8, 27.6, 29.3, 31.4, 31.7, 60.3, 109.5, 117.8, 118.0, 130.0, 140.8, 142.4, 145.9; IR (neat, cm^{-1}) 3004, 2964, 2923; HRMS calcd for $C_{15}H_{19}IN_2O_2$ 386.04913. Found 386.04988.

2-(Cyclohex-1-enyl)-3-iodo-1-methyl-5-nitroindole (36). The compound was obtained as pale yellow crystals: mp 112 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (s, 3H), 7.36 (d, *J* = 9.0 Hz, 1H), 7.46-7.57 (m, 5H), 8.19 (d, *J* = 12.0 Hz, 1H), 8.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.6, 32.7, 61.3, 110.2, 118.6, 119.0, 128.9, 129.8, 130.2, 130.7, 130.9, 140.9, 142.7, 145.4; IR (neat, cm^{-1}) 3095, 2920, 2849, 2249, 1735, 1577, 1513, 1338; HRMS calcd for $C_{15}H_{15}IN_2O_2$ 382.01783. Found 382.01837.

3-Iodo-1,5-dimethyl-2-phenylindole (37). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.54 (s, 3H), 7.03 (d, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.20 (s, 1H), 7.37-7.41 (m, 5H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.6, 32.2, 58.4, 109.8, 121.2, 124.7, 128.6, 128.9, 130.4, 130.7, 131.1, 131.9, 136.4, 141.8; IR (neat, cm^{-1}) 3055, 2919, 2849, 1576, 1475; HRMS calcd for $C_{16}H_{14}IN$ 347.01710. Found 347.01747.

2-*n*-Hexyl-3-iodo-1,5-dimethylindole (38). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, *J* = 6.8 Hz, 3H), 1.24-1.34 (m, 6H), 1.49 (q, *J* = 7.6 Hz, 2H), 2.39 (s, 3H), 2.73 (t, *J* = 8.0 Hz, 2H), 3.61 (s, 3H), 6.94 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 7.08 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 14.3, 21.6, 22.8, 27.3, 29.2, 29.5, 30.8, 31.8, 57.3, 109.1, 120.4, 123.6, 129.8, 130.3, 136.0, 141.9; IR (neat, cm^{-1}) 3055, 2919, 2849, 1576, 1475; HRMS calcd for $C_{16}H_{22}IN$ 355.07970. Found 355.08037.

2-(Cyclohex-1-enyl)-3-iodo-1,5-dimethylindole (39). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64-1.74 (m, 4H), 2.15-2.19 (m, 4H), 2.39 (s, 3H), 3.56 (s, 3H), 5.79 (m, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 7.11 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 21.6, 22.1, 22.9, 25.7, 29.4, 31.5, 56.4, 109.5, 120.8, 124.0, 129.9, 130.0, 130.4, 133.6, 135.7, 144.4; IR (neat, cm^{-1}) 3055, 2919, 2849, 1576, 1475; HRMS calcd for $C_{16}H_{18}IN$ 351.04840. Found 351.04879.

3-Iodo-6-methoxy-1-methyl-2-phenylindole (40). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 3H), 3.89 (s, 3H), 6.77 (s, 1H), 6.89 (d, *J* = 12.0 Hz, 1H), 7.37 (d, *J* = 12.0 Hz, 1H), 7.40-7.51 (m, 5H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 32.2, 56.0, 58.7, 93.5, 110.7, 122.3, 125.0, 128.6, 128.8, 131.1, 131.9, 138.5, 140.9, 157.4; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{16}H_{14}INO$ 363.01202. Found 363.01270.

2-*n*-Hexyl-3-iodo-6-methoxy-1-methylindole (41). The product was obtained as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, *J* = 6.8 Hz, 3H), 1.31-1.33 (m, 4H), 1.40-1.42 (m, 2H), 1.56 (q, *J* = 7.6 Hz, 2H), 2.79 (t, *J* = 8.0 Hz, 2H), 3.66 (s, 3H), 3.86 (s, 3H), 6.70 (s, 1H), 6.81 (d, *J* = 8.8 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 22.8, 27.3, 29.2, 29.6, 30.8, 31.8, 56.1, 57.4, 93.4, 109.8, 121.3, 124.5, 138.1, 140.9, 156.8; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{16}H_{22}INO$ 371.07462. Found 371.07537.

2-(1-Cyclohexenyl)-3-iodo-6-methoxy-1-methylindole (42). The product was obtained as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) δ 1.72-1.75 (m, 2H), 1.79-1.82 (m, 2H), 2.22-2.26 (m, 4H), 3.61 (s, 3H), 3.86 (s, 3H), 5.87 (s, 1H), 6.70 (d, *J* = 2.0 Hz, 1H), 6.82 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 22.9, 25.7, 29.5, 31.5, 56.0, 56.5, 93.4, 110.1, 121.8, 124.6, 130.0, 133.7, 137.8, 143.5, 157.0; IR (neat, cm^{-1}) 2925, 2855; HRMS calcd for $C_{16}H_{18}INO$ 367.06332. Found 367.06396.

Ethyl 1-*n*-butyl-3-iodo-2-phenylindole-5-carboxylate (43). The product was obtained as a pale yellow solid: mp. 103-105 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (t, *J* = 7.2 Hz, 3H), 3.62 (s, 3H), 4.36 (q, *J* = 7.2 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.38-7.48 (m, 5H), 7.94 (d, *J* = 8.8 Hz, 1H), 8.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 32.4, 60.6, 61.0, 109.8, 123.3, 124.4, 124.5, 128.7, 129.3, 130.2, 131.0, 131.3, 140.5, 143.4, 167.6; IR (neat, cm^{-1}) 2978, 2933, 1705; HRMS calcd for $C_{18}H_{16}INO_2$ 405.02258. Found 405.02306.

Ethyl 3-iodo-1-methyl-2-phenylindole-5-carboxylate (44). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.67 (t, *J* = 7.2 Hz, 3H), 1.02-1.07 (m, 2H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.47-1.51 (m, 2H), 4.00 (t, *J* = 7.2 Hz, 2H), 4.34 (t, *J* = 7.0 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 1H), 7.34-7.43 (m, 5H), 7.91 (d, *J* = 8.4 Hz, 1H), 8.17 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 13.7, 14.7, 20.0, 32.2, 45.2, 60.9, 61.2, 110.1, 123.2, 124.2, 124.5, 128.7, 129.3, 130.3, 130.9, 131.7, 139.6, 143.3, 167.6; IR (neat, cm^{-1}) 3058, 2959, 2932, 2872, 1709; HRMS calcd for $C_{21}H_{22}INO_2$ 447.06953. Found 447.07000.

Ethyl 1-*n*-butyl-2-*n*-hexyl-3-iodoindole-5-carboxylate (45). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.83 (t, *J* = 6.0 Hz, 3H), 1.25-1.26 (m, 4H), 1.34-1.38 (m, 5H), 1.53 (q, *J* = 8.0 Hz, 2H), 2.78 (t, *J* = 8.0 Hz, 2H), 3.70 (s, 3H), 4.34 (q, *J* = 8.0 Hz, 2H), 7.17 (t, *J* = 8.8 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 8.05 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.3, 14.7, 22.8, 27.4, 29.2, 29.4, 31.1, 31.8, 59.5, 60.9, 109.1, 122.8, 123.5, 123.6, 129.9, 140.3, 143.7, 167.7; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{18}H_{24}INO_2$ 413.08518. Found 413.08573.

Ethyl 2-*n*-hexyl-3-iodo-1-methylindole-5-carboxylate (46). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.83-0.90 (m, 6H), 1.26-1.37 (m, 11H), 1.52-1.55 (m, 2H), 1.64-1.67 (m, 2H), 2.76 (t, *J* = 8.0 Hz, 2H), 4.06 (t, *J* = 8.0 Hz, 2H), 4.34 (q, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 12.0 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 1H), 8.05 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.0, 14.3, 14.7, 20.5, 22.8, 27.4, 29.4, 29.6, 31.7, 32.7, 44.7, 59.8, 60.8, 109.4, 122.7, 123.4, 123.5, 130.0, 139.5, 143.2, 167.7; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{21}H_{30}INO_2$ 455.13213. Found 455.13262.

Ethyl 1-*n*-butyl-2-(cyclohex-1-enyl)-3-iodoindole-5-carboxylate (47). The product was obtained as a pale yellow solid: mp. 121-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, *J* = 8.0 Hz, 3H), 1.68-1.77 (m, 4H), 2.17-2.22 (m, 4H), 3.64 (s, 3H), 4.34 (q, *J* = 8.0 Hz, 2H), 5.85 (m, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 8.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 14.7, 20.0, 32.2, 45.2, 60.9, 61.2, 110.1, 123.2, 124.2, 124.5, 128.7, 129.3, 130.3, 130.9, 131.7, 139.6, 143.3, 167.6; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{18}H_{20}INO_2$ 409.05388. Found 409.05434.

Ethyl 2-(cyclohex-1-enyl)-3-iodo-1-methylindole-5-carboxylate (48). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 8.0 Hz, 3H), 1.21-1.27 (m, 2H), 1.35 (t, *J* = 8.0 Hz, 3H), 1.58-1.75 (m, 6H), 2.18-2.19 (m, 4H), 4.00 (q, *J* = 8.0 Hz, 2H), 4.33 (q, *J* = 8.0 Hz, 2H), 5.83 (m, 1H), 7.18 (d, *J* = 12.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 8.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.7, 20.3, 22.0, 22.9, 25.7, 29.6, 32.6, 45.1, 59.0, 60.8, 109.8, 122.7, 123.7, 124.0, 129.8, 130.1, 134.2, 139.2, 145.6, 167.7; IR (neat, cm^{-1}) 3378, 3057, 2925, 2853, 1453, 1433, 750; HRMS calcd for $C_{21}H_{26}INO_2$ 451.10083. Found 451.10169.

1-Methyl-2-phenyl-3-(phenylethynyl)indole (50). This indole was prepared by the following procedure. Into a well mixed Et_3N solution (5 ml) containing 5.0 mmol of 3-iodo-2-phenylindole, 6.0 mmol of phenylacetylene and $PdCl_2(PPh_3)_2$ (5 mol %), CuI (2.5 mol %) was added and the flask was flushed with Ar, sealed and allowed to stir at room temperature for 2 h. The resulting precipitate was filtered off and washed with ethyl ether (10 ml). The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to afford a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.69 (s, 3H), 7.21-7.32 (m, 6H), 7.41-7.44 (m, 3H), 7.49 (t, J = 7.2 Hz, 2H), 7.65 (dd, J = 10.8, 2.0 Hz, 2H), 7.85 (dd, J = 10.4, 2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.8, 84.5, 91.9, 110.0, 120.2, 121.0, 123.1, 124.7, 127.4, 128.1, 128.4, 128.5, 128.7, 129.0, 130.4, 131.0, 131.3, 137.4, 144.0; IR (neat, cm^{-1}) 3004, 2962, 2923, 2204; HRMS calcd for $C_{23}H_{17}N$ 307.13610. Found 307.13698.

1-Methyl-2,3-diphenylindole (51). This indole was prepared according to a literature procedure.[14] Into 10 ml of a 2:1 DMF/H_2O solution containing 5.0 mmol of 3-iodo-2-phenylindole, 5.0 mmol of Na_2CO_3 and 1.25 mmol of $NaBPh_4$ were added and the reaction mixture was stirred for 2 min. $Pd(OAc)_2$ (5 mol %) was then added and the flask was flushed with Ar, sealed and allowed to stir at 100 °C for 2 h. The resulting reaction mixture was extracted with ethyl ether (2 x 10 ml). The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to afford a white solid. Recrystallization afforded a 92 % yield of a crystalline solid. The product was obtained as white needles: mp 136-137 °C, lit[15] mp 137-138 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.67 (s, 3H), 7.16-7.39 (m, 13H), 7.80 (d, J = 10.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.1, 109.8, 115.3, 119.8, 120.4, 122.4, 125.7, 127.2, 128.2, 128.4, 128.6, 130.1, 131.4, 132.1, 135.4, 137.5, 137.9; IR (neat, cm^{-1}) 3058, 2923, 2849; HRMS calcd for $C_{21}H_{17}N$ 283.13610. Found 283.13690.

***n*-Butyl 2(*E*)-3-[1-methyl-2-phenylindol-3-yl]propenoate (52).** This indole was prepared by the following procedure. Into 1 ml of DMF containing 0.25 mmol of 3-iodo-

2-phenylindole, 0.25 mmol of Na_2CO_3 and 0.25 mmol of *n*-Bu_4NCl, 0.525 mmol of *n*-butyl acrylate were added and the reaction mixture was stirred for 2 min. $Pd(OAc)_2$ (5 mol %) was then added and the flask was flushed with Ar, sealed and allowed to stir at 80 °C for 24 h.[16] The resulting reaction mixture was extracted with ethyl ether (2 x 10 ml). The combined ether layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to afford a pale yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, *J* = 7.5 Hz, 3H), 1.37-1.44 (m, 2H), 1.62-1.67 (m, 2H), 3.61 (s, 3H), 4.15 (t, *J* = 6.6 Hz, 2H), 6.48 (d, *J* = 15.9 Hz, 1H), 7.32-7.40 (m, 5H), 7.50-7.53 (m, 3H), 7.72 (d, *J* = 16.2 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 19.4, 31.1, 31.3, 64.0, 110.2, 110.6, 113.1, 120.9, 121.9, 123.2, 125.8, 128.8, 129.4, 130.2, 131.1, 138.1, 139.0, 145.6, 168.8; IR (neat, cm^{-1}) 3004, 2963, 2925, 1711; HRMS calcd for $C_{22}H_{23}NO_2$ 333.17288. Found 333.17370.

Acknowledgements. We gratefully acknowledge partial financial support from the Petroleum Research Fund administered by the American Chemical Society, and thank Johnson Matthey, Inc., and Kawaken Fine Chemicals Co., Ltd. for providing the palladium salts.

References

1. For reviews see: (a) Sundberg, R. *J. Prog. Heterocyclic Chem.* **1989**, *1*, 111. (b) Saxon, J. E. *Nat. Prod. Rep.* **1986**, *3*, 357; **1987**, *4*, 591; **1989**, *6*, 1. (c) Sundberg, R. J. "*Indoles*," Academic Press: New York, **1996**. (d) Mori, H.; Yoshimi, N. *Mutation Research* **2001**, *480*, 201. (e) Gribble, G. W.; *J. Chem. Soc., Perkin Trans 1* **2000**, *7*, 1045. (f) Toyota, M.; Ihara, M.; *Nat. Prod. Rep.* **1998**, *15*, 327.

(g) Lobo, A. M.; Prabhakar, S.; *J. Heterocyclic Chem.* **2002**, *39*, 429. (h) Tokuyama, H.; Fukuyama, T. *Kagaku Kogyo* **2001**, *52*, 416. (i) Xiong, W. N.; Yang, C. G.; Jiang, B. *Bioorg. Med. Chem.* **2001**, *9*, 1773. (j) Ezquerra, J.; Pedregal, C.; Lamas, C. *J. Org. Chem.* **1996**, *61*, 5804.

2. (a) Pete, B.; Toke, L. *Tetrahedron Lett.* **2001**, *42*, 3373. (b) Kuroda, T. F. **2001**, *37*, 67. (c) Rodriguez, A. L.; Koradin, C.; Dohle, W.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 2488. (d) Takeda, A.; Kamijo, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 5662. (e) Roesch, K. R.; Larock, R. C. *Org. Lett.* **1999**, *4*, 553. (f) Roesch, K. R.; Larock, R. C. *J. Org. Chem.* **1998**, *63*, 5306. (e) Larock, R. C.; Yum, E. K.; Refvik, M. D. *J. Org. Chem.* **1998**, *63*, 7652. (g) Larock, R. C.; Yum, E. K. *J. Am. Chem. Soc.* **1991**, *113*, 6689. (h) Cacchi, S. *J. Organomet. Chem.* **1999**, *576*, 42. (i) Cacchi, S.; Fabrizi, G.; Moro, L. *Tetrahedron Lett.* **1998**, *39*, 5101. (j) Cacchi, S.; Fabrizi, G.; Moro, L. *Synlett* **1998**, 741. (k) Arcadi, A.; Cacchi, S.; Rosario, M. D.; Fabrizi, G.; Marinelli, F. *J. Org. Chem.* **1996**, *61*, 9280.
3. (a) Arcadi, A.; Cacchi, S.; Giancarlo, F.; Marinelli, F.; Moro, L. *Synlett* **1999**, 1432. (b) Yue, D.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 1905. (c) Flynn, B. L; Verdier-Pinard, P.; Hamel, E. *Org. Lett.* **2001**, *5*, 651. (d) Huang, Q.; Hunter, J. A.; Larock, R. C. *J. Org. Chem.* **2002,** *67,* 3437. (e) Arcadi, A.; Cacchi, S.; Di Giuseppe, S.; Fabrizi., G.; Marinelli, F. *Org. Lett.* **2002**, *4*, 2409.
4. (a) Sonada, T.; Kawakami, M.; Ikeda, T.; Kobayashi, S.; Taniguchi, H. *J. Chem. Soc., Chem. Commun.* **1976**, 612. (b) Kitamura, T.; Kobayashi, S.; Taniguchi, H.; Hori, K. *J. Am. Chem. Soc.* **1991**, *113*, 6240.

5. For other examples of iodine-promoted cyclization of alkynes to give heterocycles, see: (a) Knight, D. W.; Redfern, A. L.; Gilmore, J. *J. Chem. Soc., Perkin Trans. 1* **2002**, 622. (b) Bellina, F.; Biagetti, M.; Carpita, A.; Rossi, R. *Tetrahedron Lett.* **2001**, *42*, 2859. (c) Bellina, F.; Biagetti, M.; Carpita, A.; Rossi, R. *Tetrahedron* **2001**, *57*, 2857. (d) Djuardi, E.; McNelis, E. *Tetrahedron Lett.* **1999**, *40*, 7193. (e) Marshall, J. A.; Yanik, M. M. *J. Org. Chem.* **1999**, *64*, 3798. (f) Knight, D. W.; Redfern, A. L.; Gilmore, J. *J. Chem. Soc., Chem. Commun.* **1998**, 2207. (g) Redfern, A. L.; Gilmore, J. *Synlett* **1998**, 731. (h) Ren, X.-F., Konaklieva, M. I.; Shi, H.; Dicy, H.; Lim, D. V.; Gonzales, J.; Turos, E. *J. Org. Chem.* **1998**, *63*, 8898. (k) Bew, S. P.; Knight, D. W. *J. Chem. Soc., Chem. Commun.* **1996**, 1007.
6. Hoedt, W. M. R.; Van Koten, G.; Noltes, J. G. *Synth. Commun.* **1977**, *7*, 61.
7. Sonogashira, K. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F.; Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; Chap. 5, pp 203-229.
8. Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147.
9. Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.
10. Li, J.; Gribble, G. W. *App. Organomet. Chem.* **2002**, *16*, 616.
11. Ma, C.; Liu, X.; Li, X.; Flippen-Anderson, J.; Yu, S.; Cook, J. M. *J. Org. Chem.* **2001**, *66*, 4525.
12. Hill, M. L.; Raphael, R. A. *Tetrahedron* **1990**, *46*, 4587.
13. Cadogan, J. T. G.; Hickson, C. L.; Husband, J. B.; McNab, H. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1891.
14. Bumagin, N.; Bykov, V. V. *Tetrahedron* **1997**, *53*, 14437.

15. Fuerstner, A.; Hupperts, A.; Ptock, A.; Janssen, E. *J. Org. Chem.* **1994**, *59*, 5215.

16. Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, *19*, 1287.

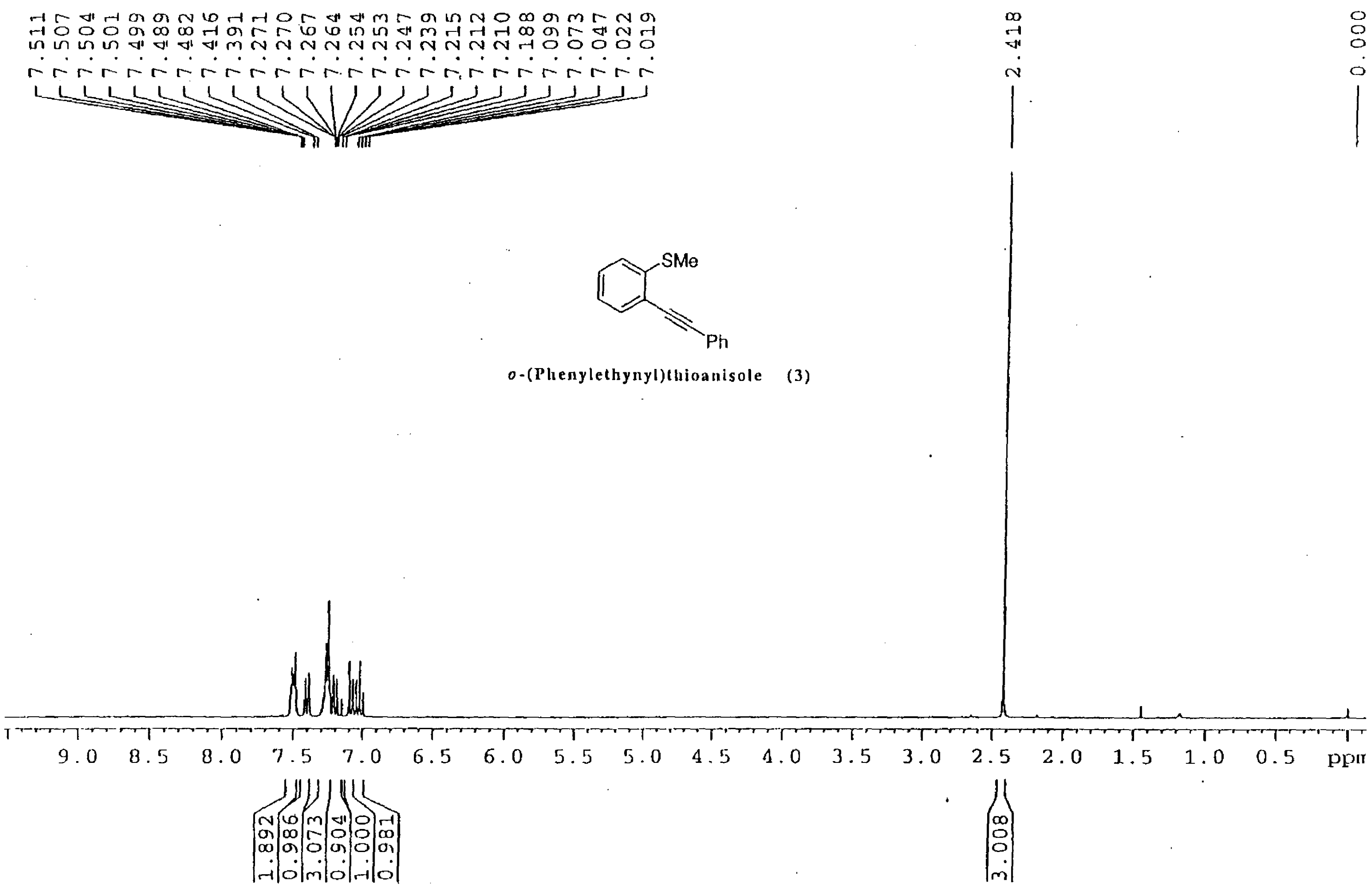
GENERAL CONCLUSIONS

In this thesis, the scope and limitations of syntheses of substituted benzo[*b*]thiophenes and indoles by electrophilic cyclization reactions have been presented. Various electrophiles have been employed in this study and highly efficient synthetic methodologies have been developed.

Chapter 1 describes the synthesis of 2,3-disubstituted benzo[*b*]thiophenes by the palladium-catalyzed coupling and electrophilic cyclization of terminal acetylenes. Various benzo[*b*]thiophenes have been synthesized by this approach in high yields. I_2, Br_2, NBS, *p*-$O_2NC_6H_4SCl$ and PhSeCl have been utilized as electrophiles. Aryl-, vinylic-, and alkyl-substituted terminal acetylenes undergo this coupling and cyclization to produce excellent yields of benzo[*b*]thiophenes. Trimethylsilyl acetylene also undergoes this coupling/cyclization process with I_2, NBS, and the sulfur and selenium electrophiles to afford the corresponding 2-(trimethylsilyl)benzo[*b*]thiophenes.

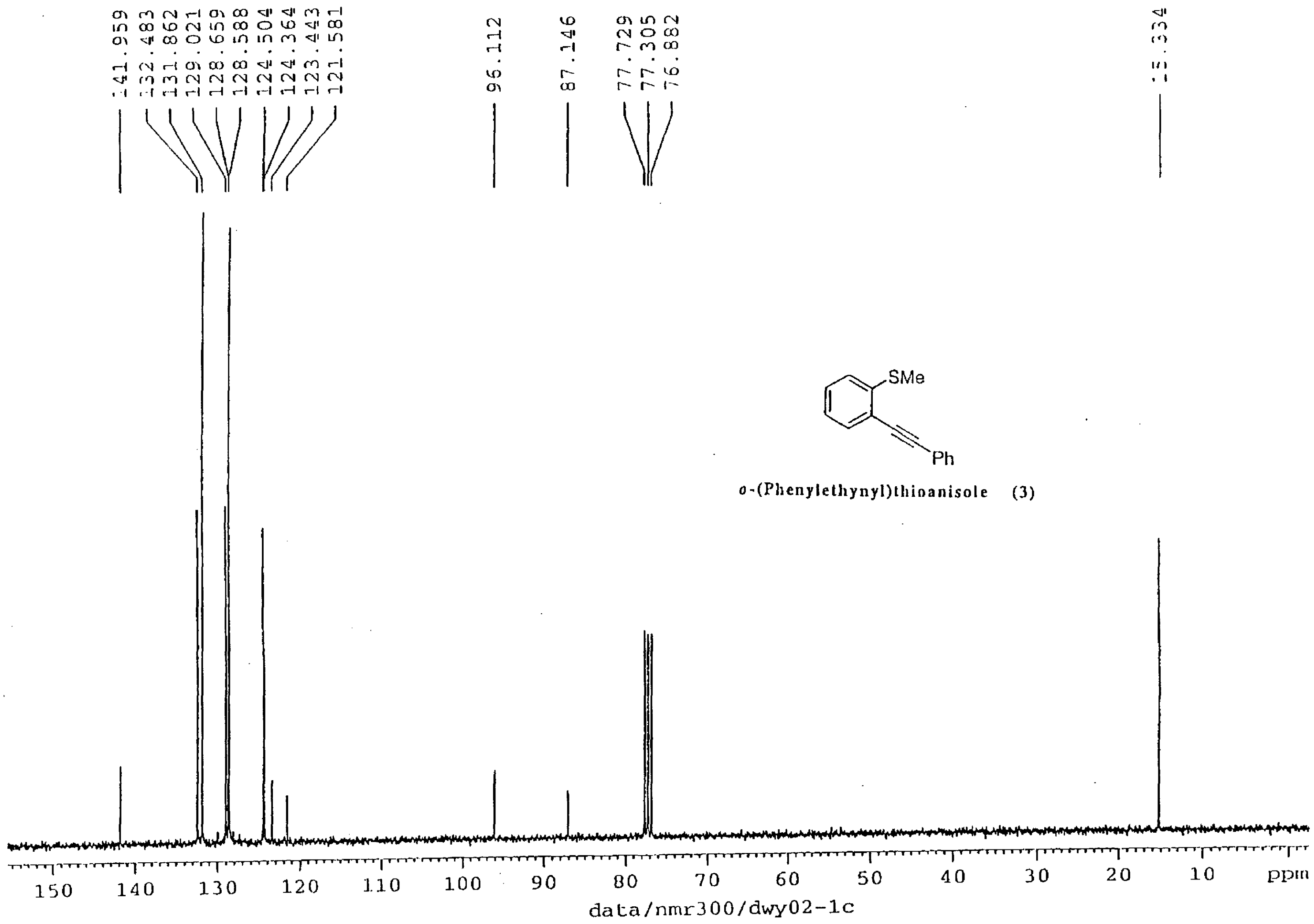
Chapter 2 presents a synthesis of 3-iodoindoles via coupling of terminal acetylenes with *N,N*-dialkyl-*o*-iodoanilines in the presence of a palladium catalyst and subsequent electrophilic iodocyclization of the resulting *N,N*-dialkyl-*o*-(1-alkynyl)aniline derivatives. Aryl-, vinylic-, alkyl- and silyl-substituted terminal acetylenes undergo this process to produce excellent yields of 3-iodoindoles.

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

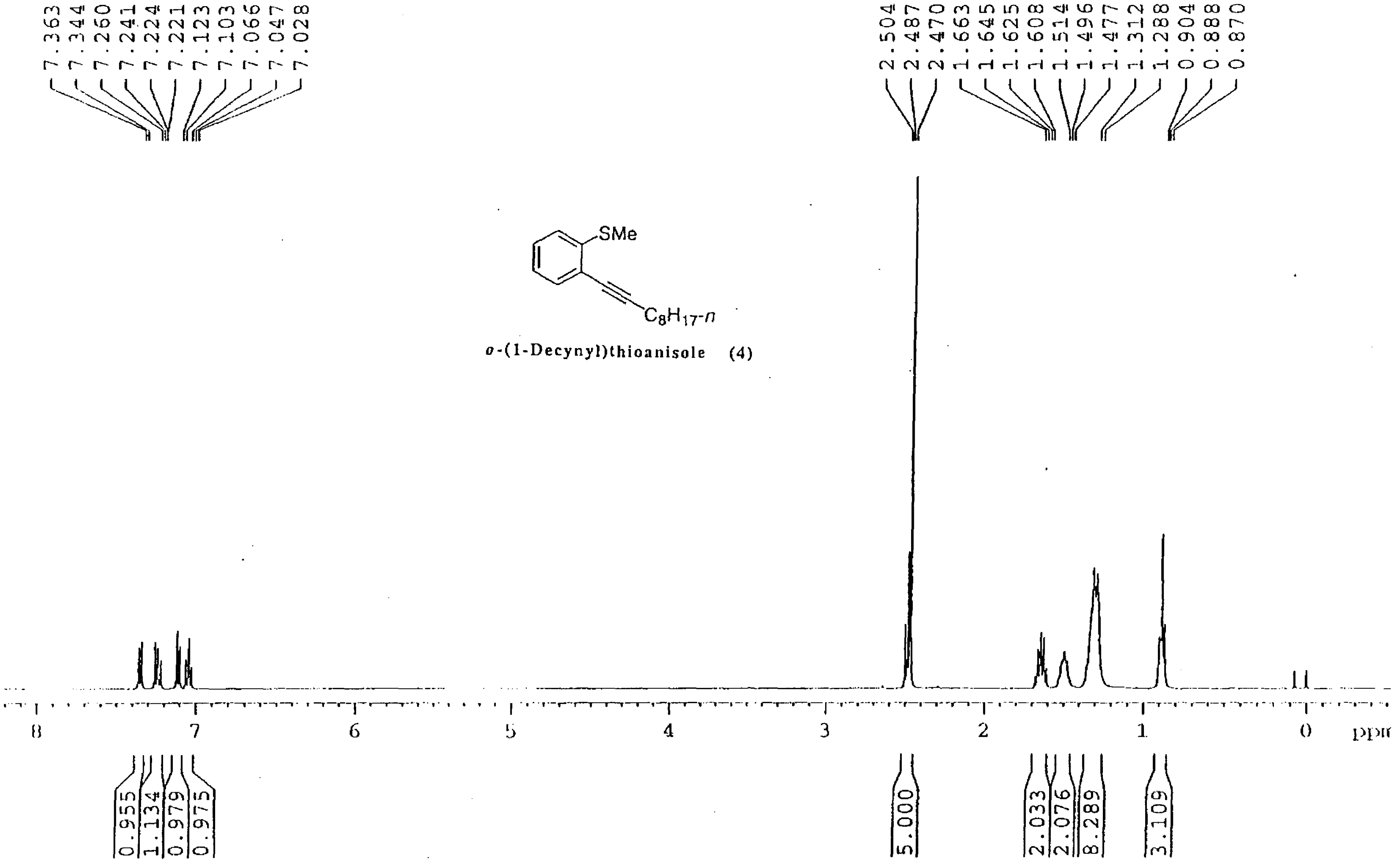


o-(Phenylethynyl)thioanisole (3)

data/nmr300/dwy02-1

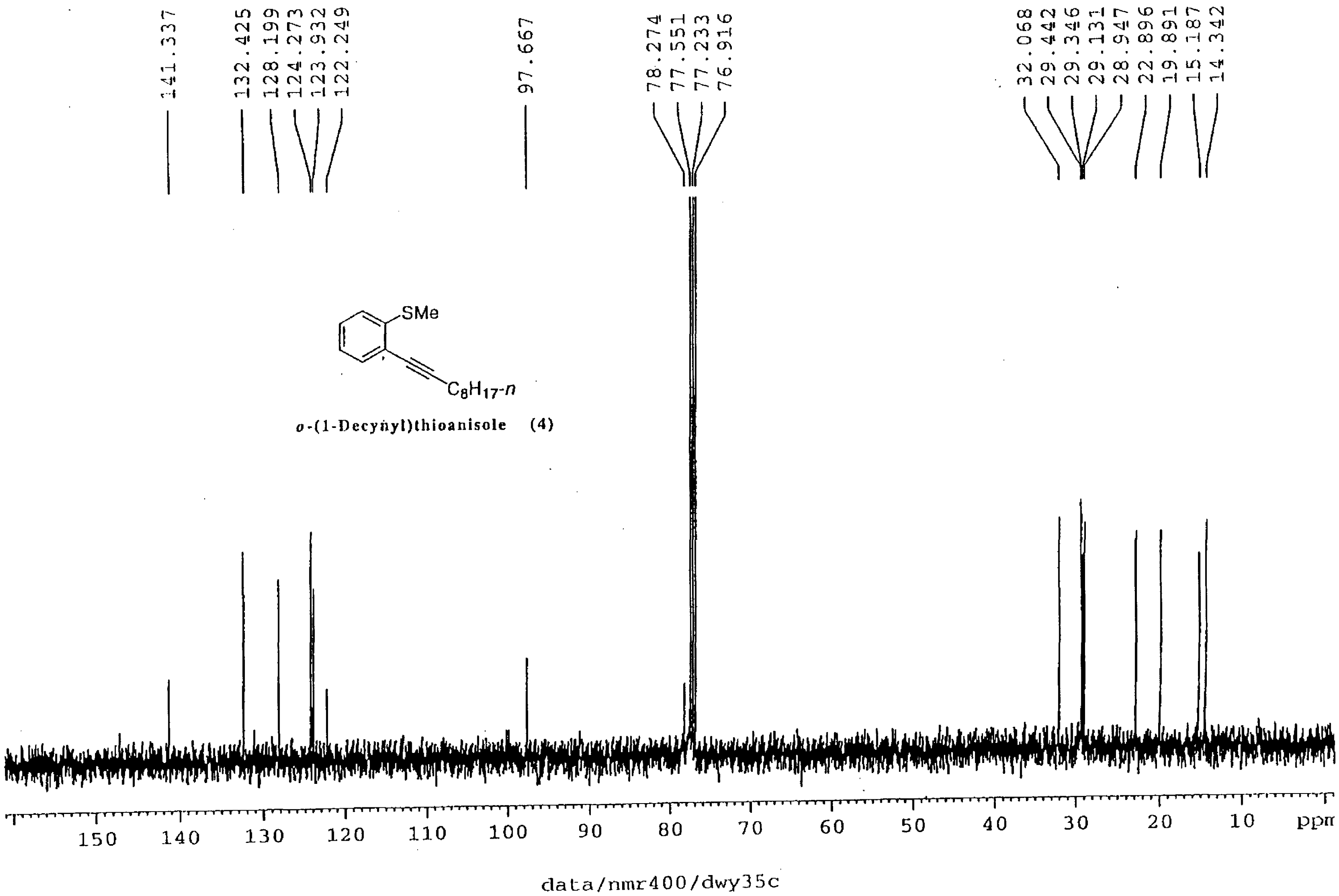


o-(Phenylethynyl)thioanisole (3)

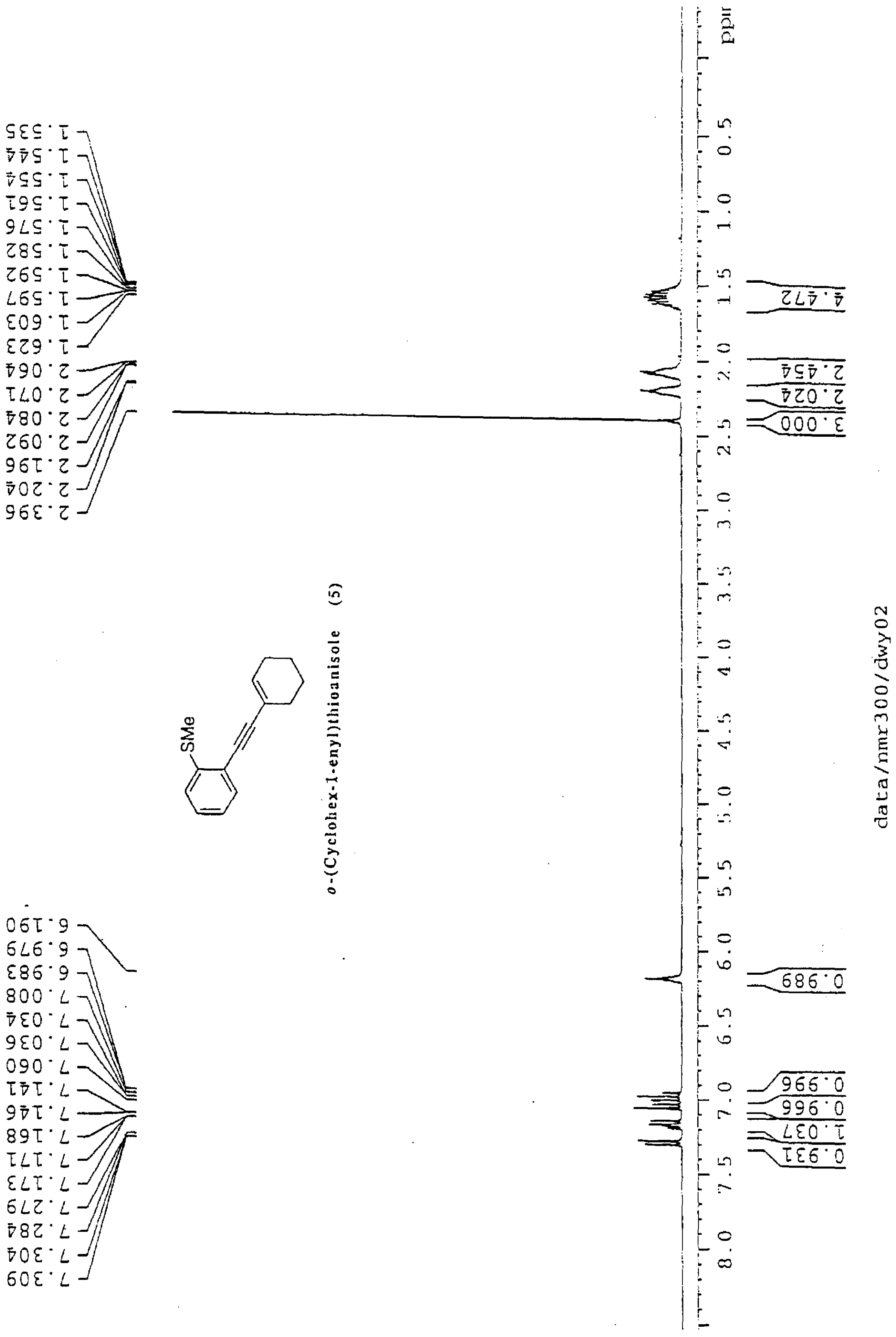


o-(1-Decynyl)thioanisole (4)

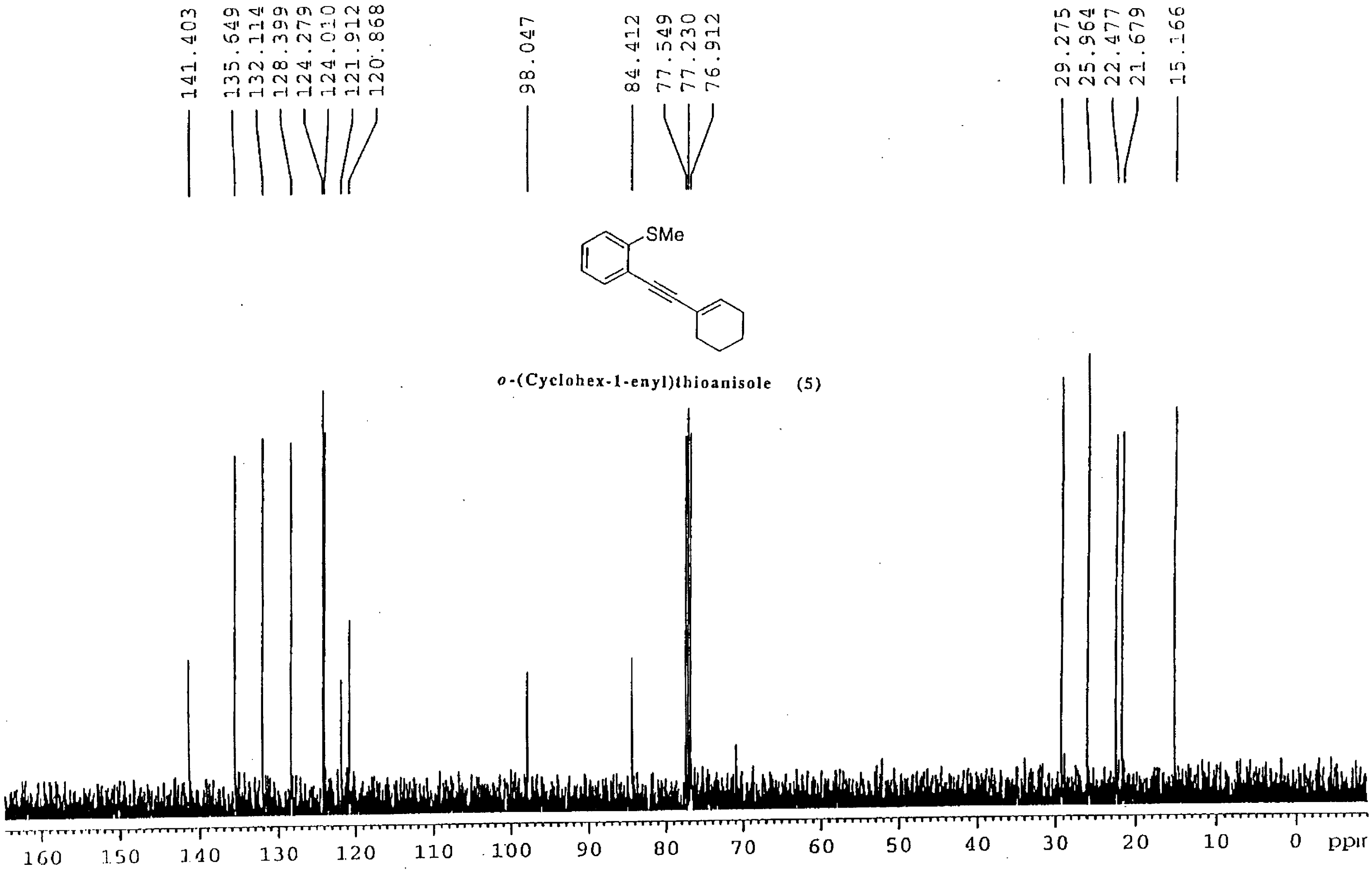
data/nmr400/dwy35



o-(1-Decynyl)thioanisole (4)

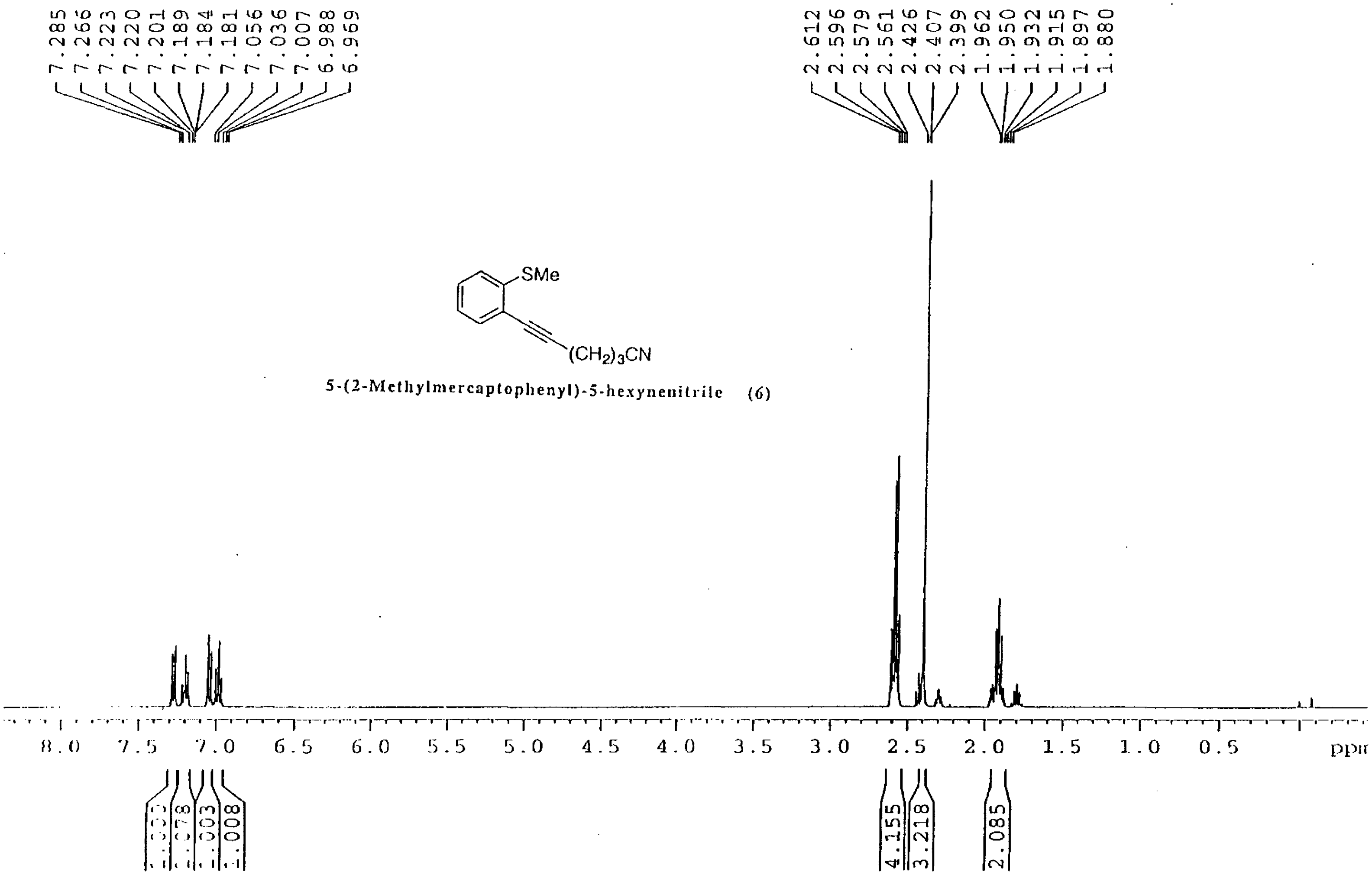


***o*-(Cyclohex-1-enyl)thioanisole (5)**



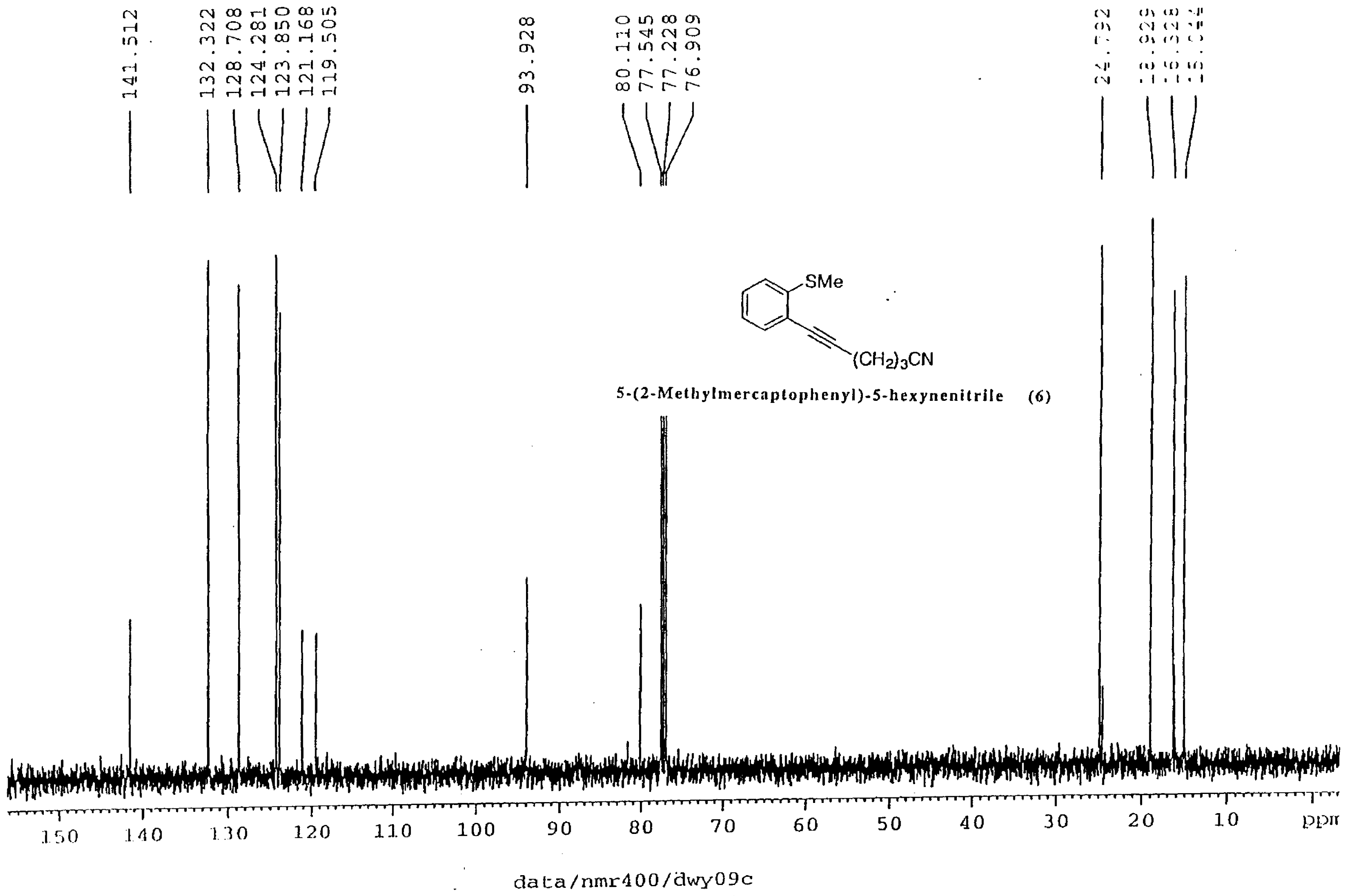
o-(Cyclohex-1-enyl)thioanisole (5)

data/nmr400/dwy02c

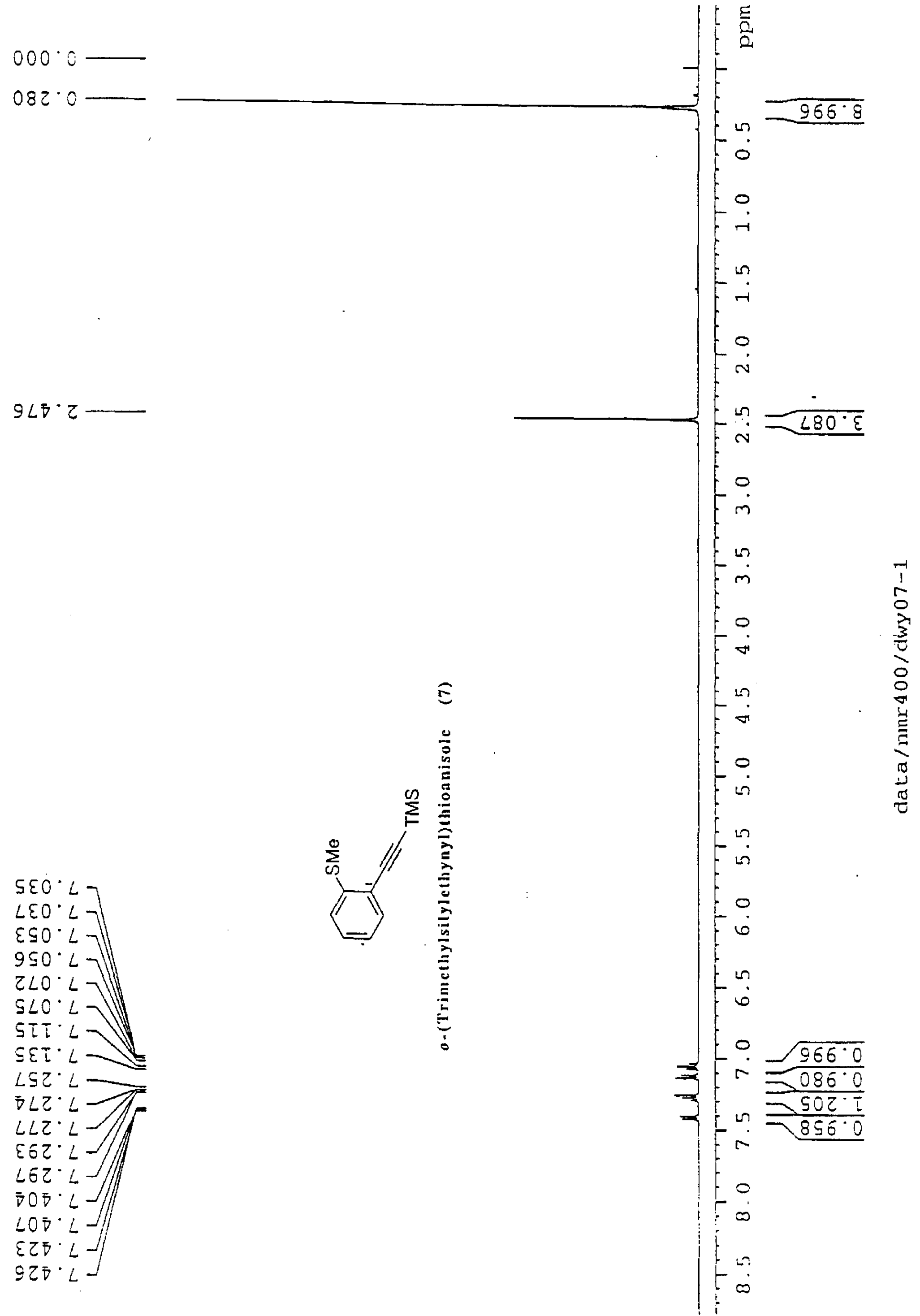


5-(2-Methylmercaptophenyl)-5-hexynenitrile (6)

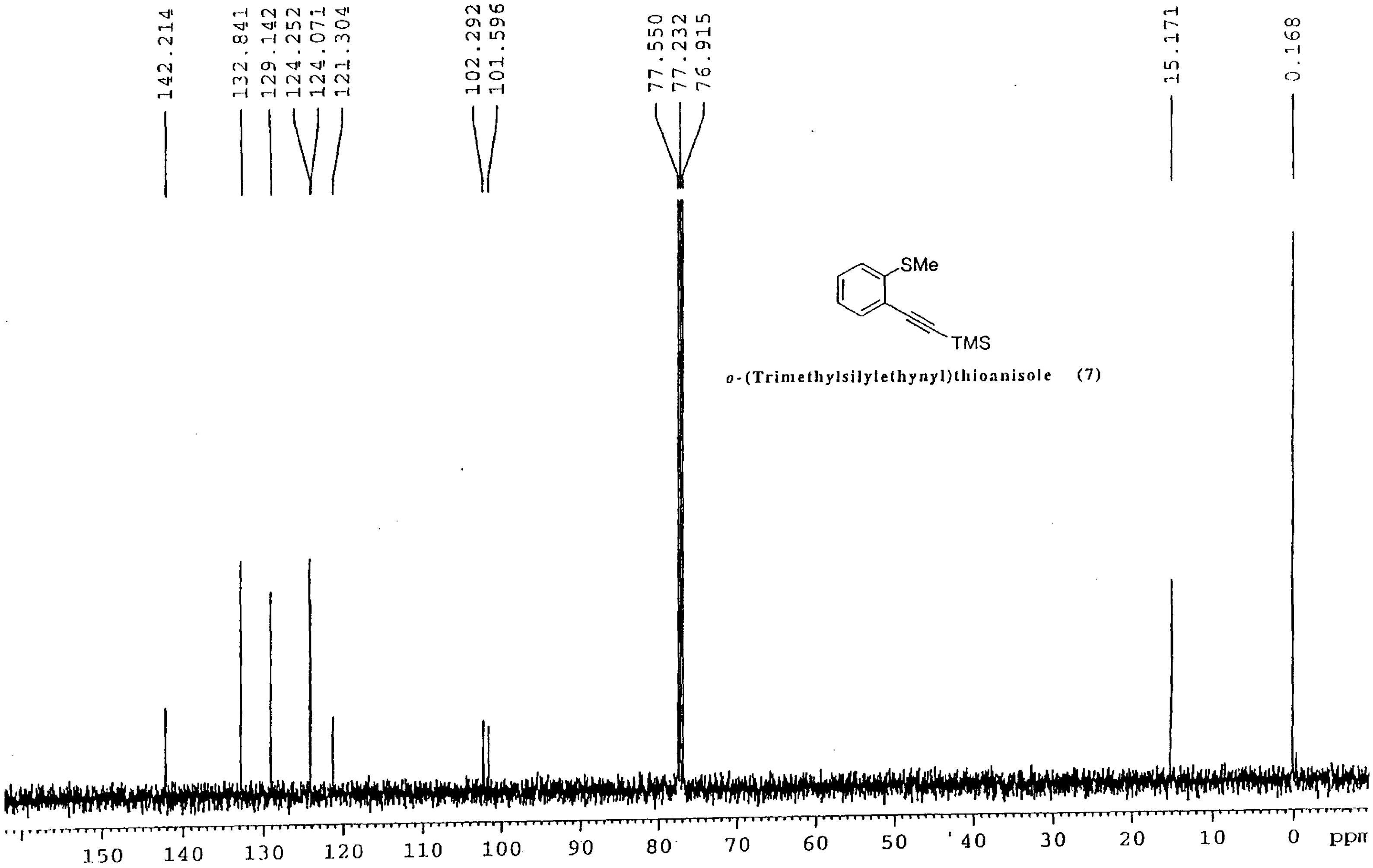
data/nmr400/dwy09



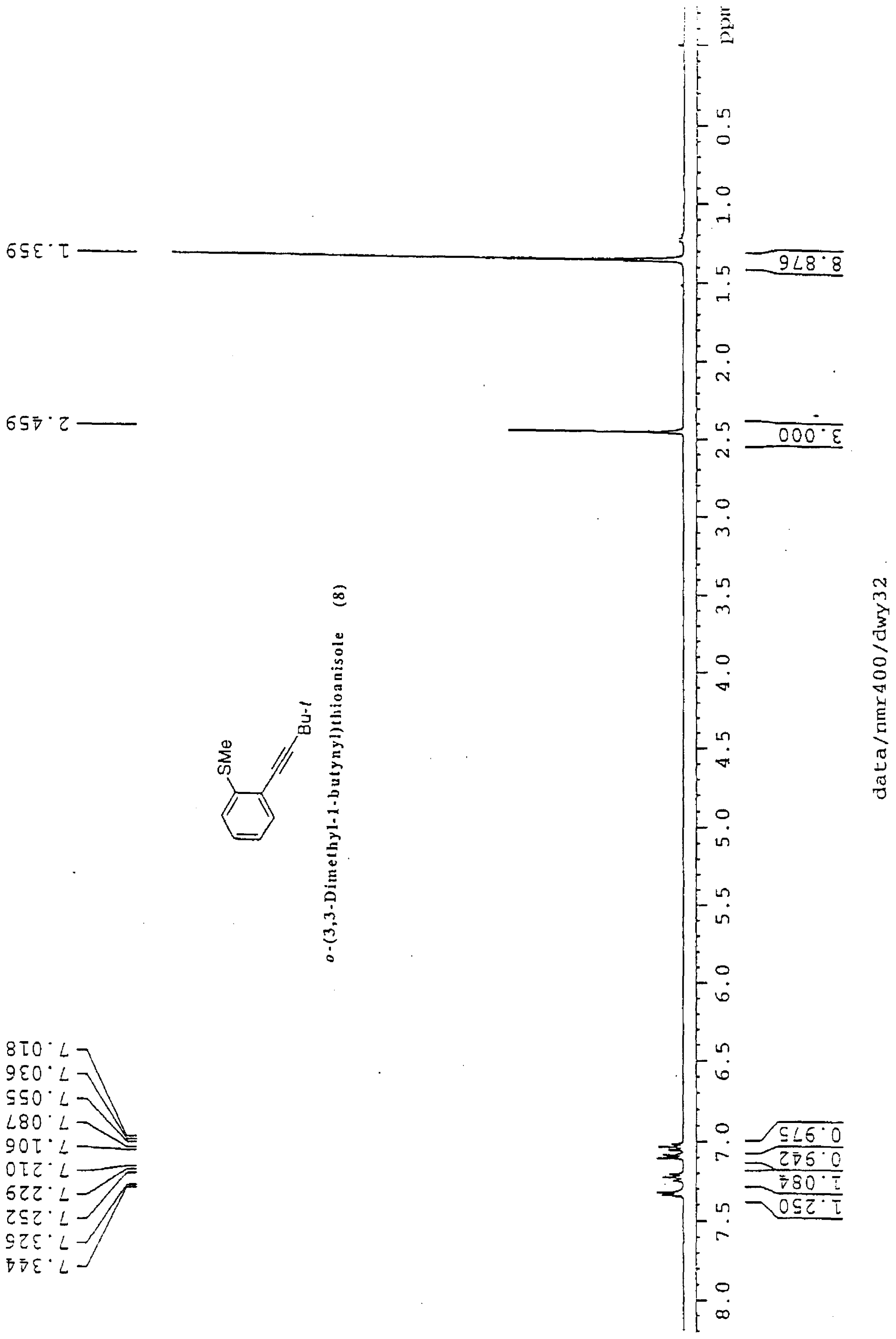
5-(2-Methylmercaptophenyl)-5-hexynenitrile (6)



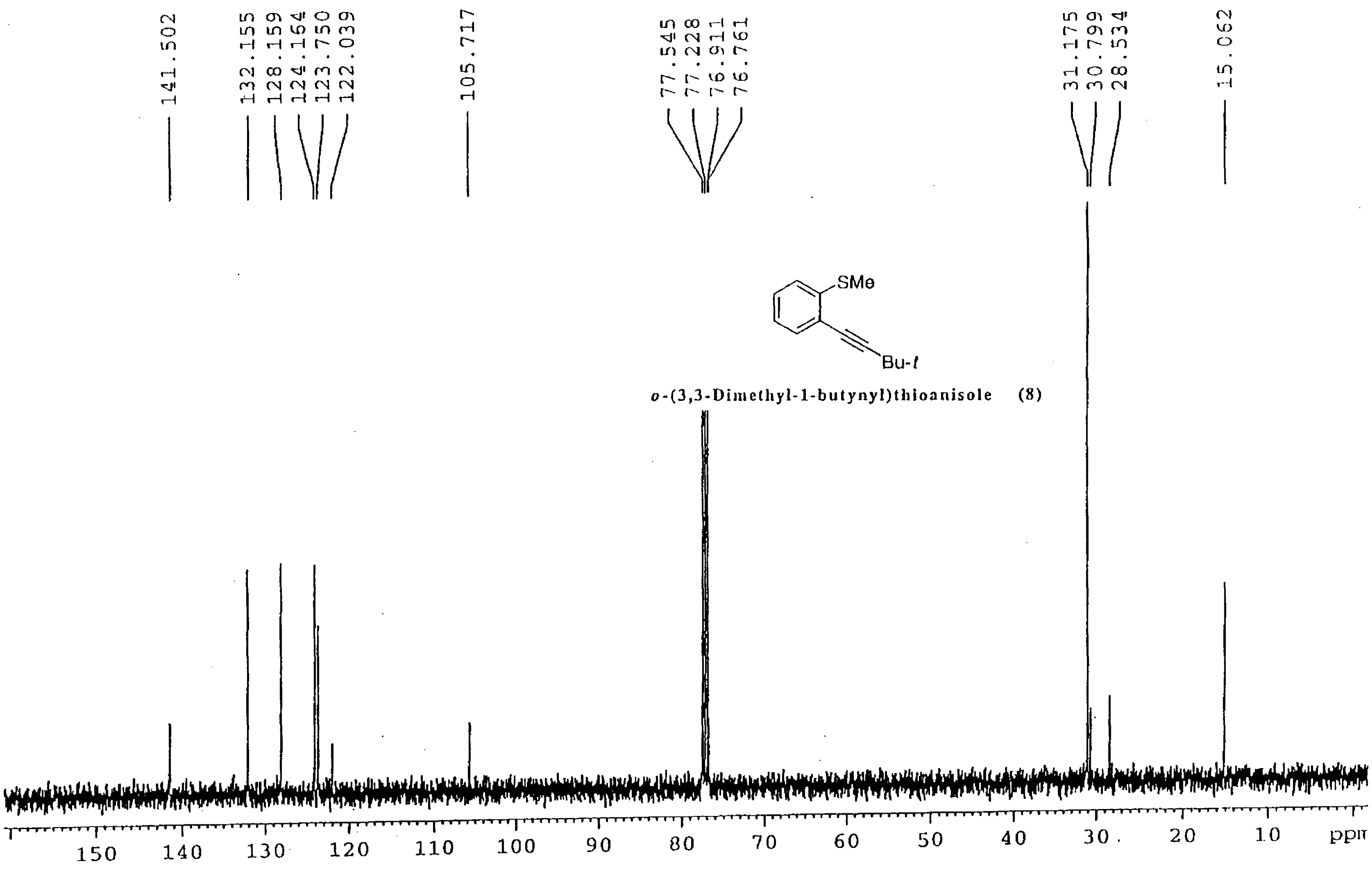
o-(Trimethylsilylethynyl)thioanisole (7)



o-(Trimethylsilylethynyl)thioanisole (7)

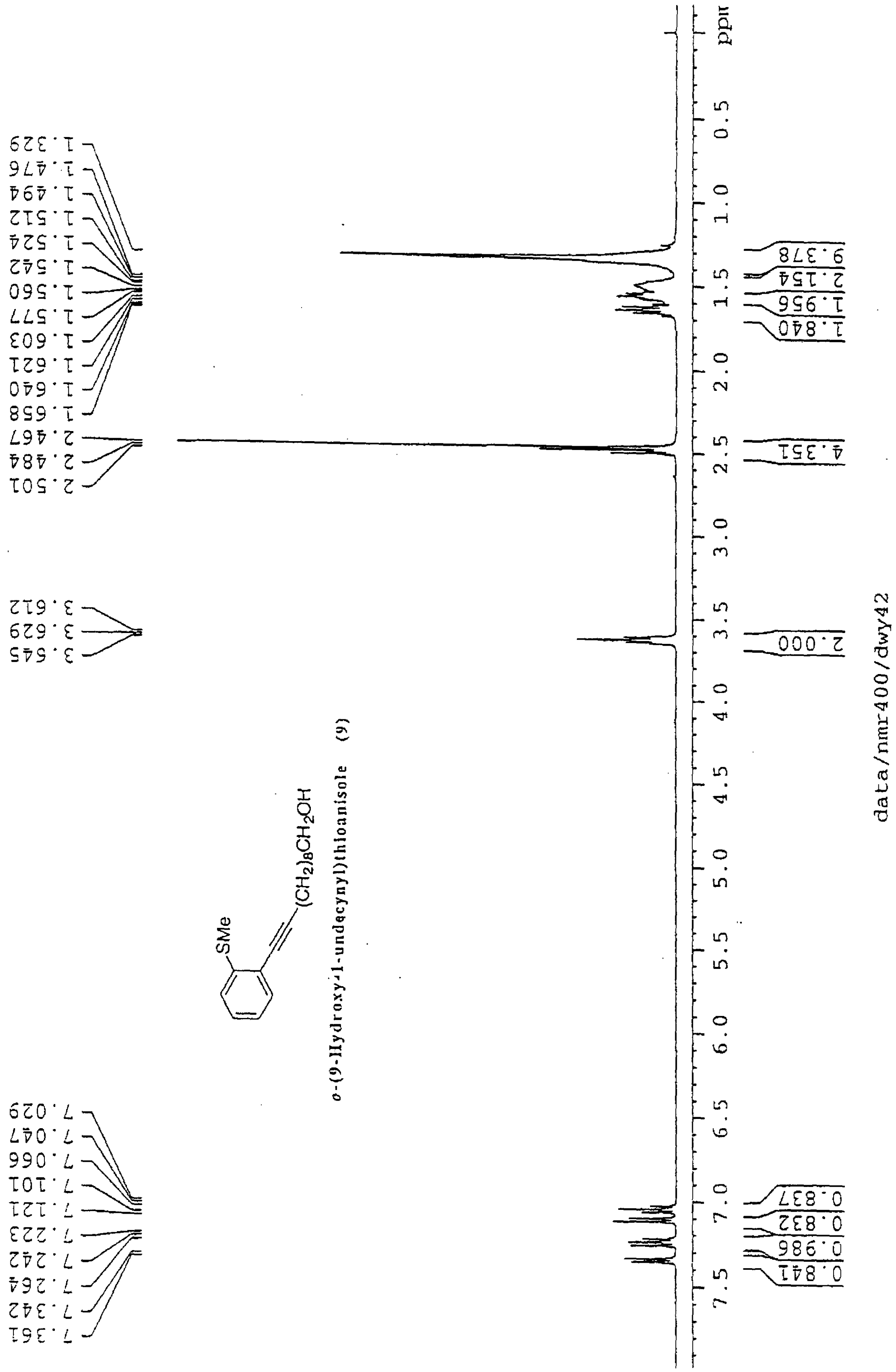


o-(3,3-Dimethyl-1-butynyl)thioanisole (8)

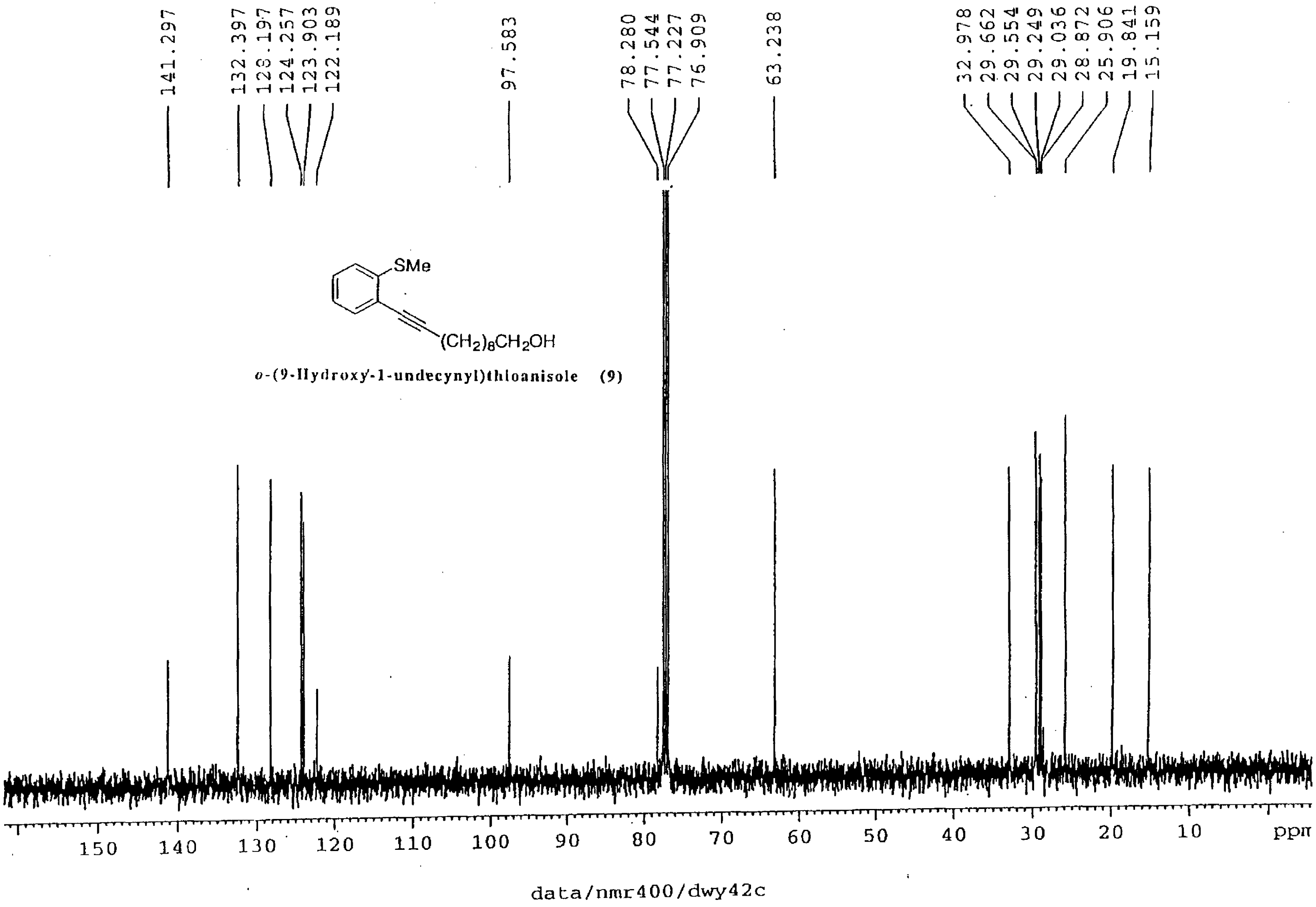


o-(3,3-Dimethyl-1-butynyl)thioanisole (8)

data/nmr400/dwy32c

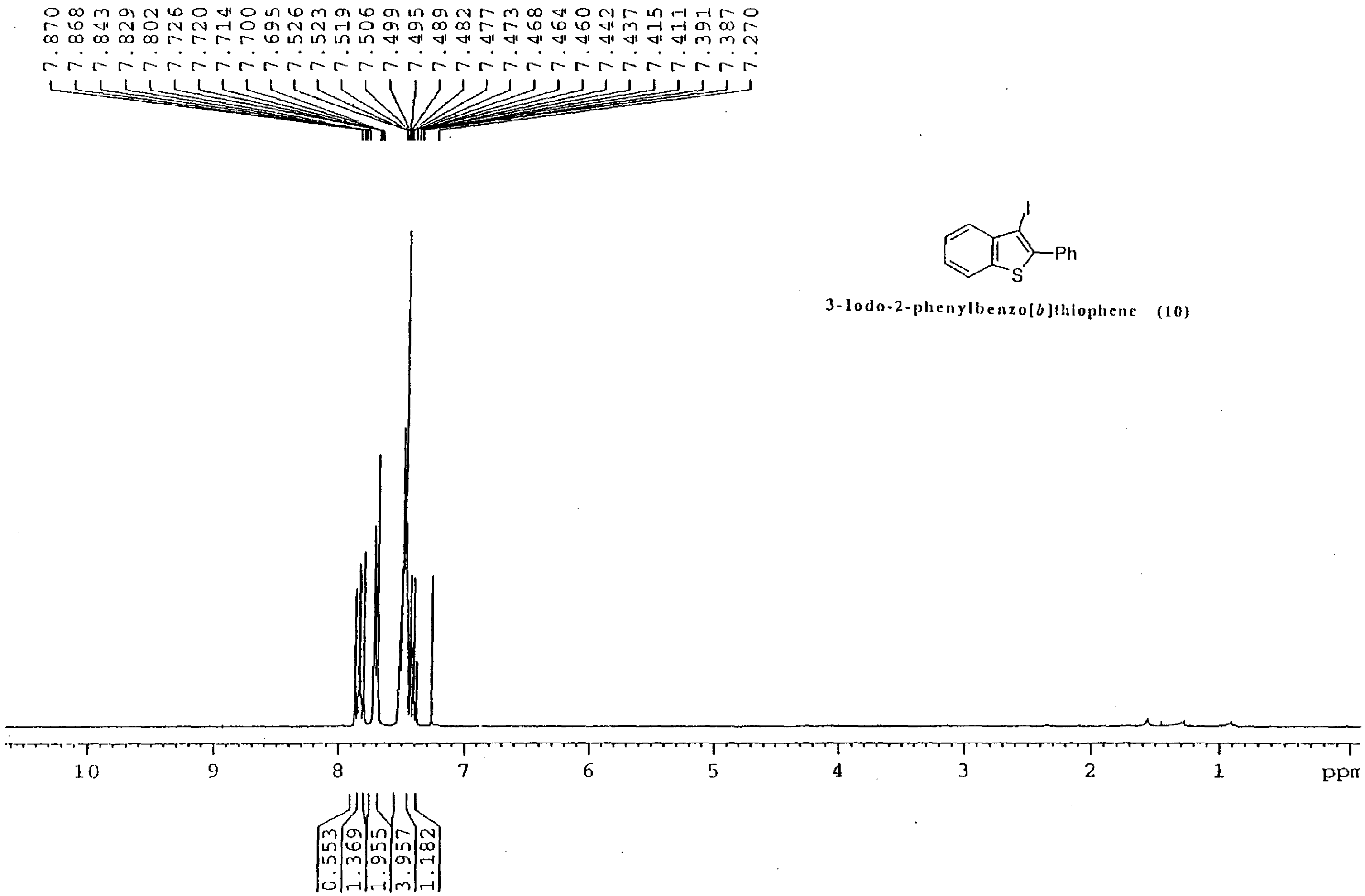


o-(9-Hydroxy-1-undecynyl)thioanisole (9)

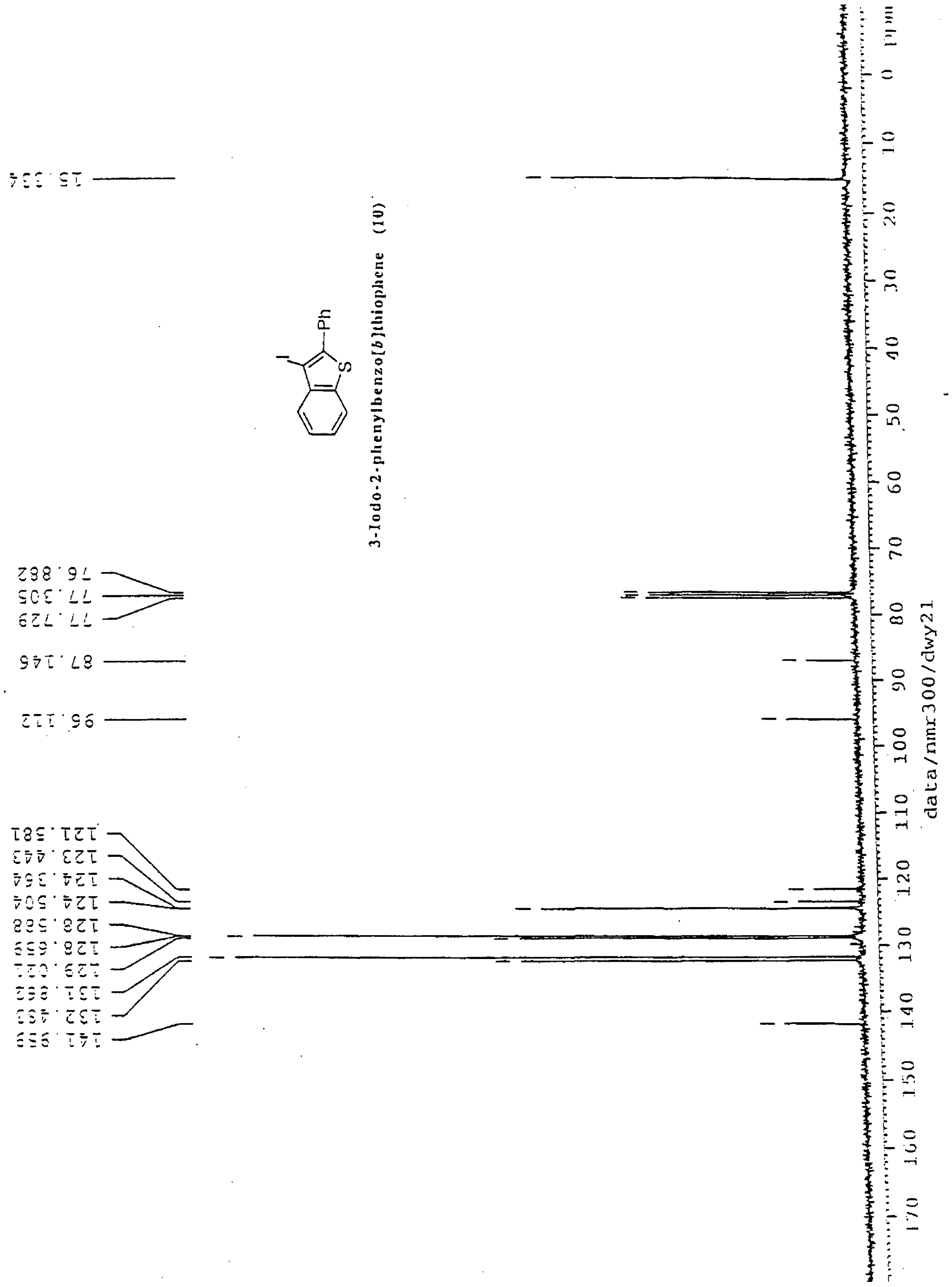


o-(9-Hydroxy-1-undecynyl)thioanisole (9)

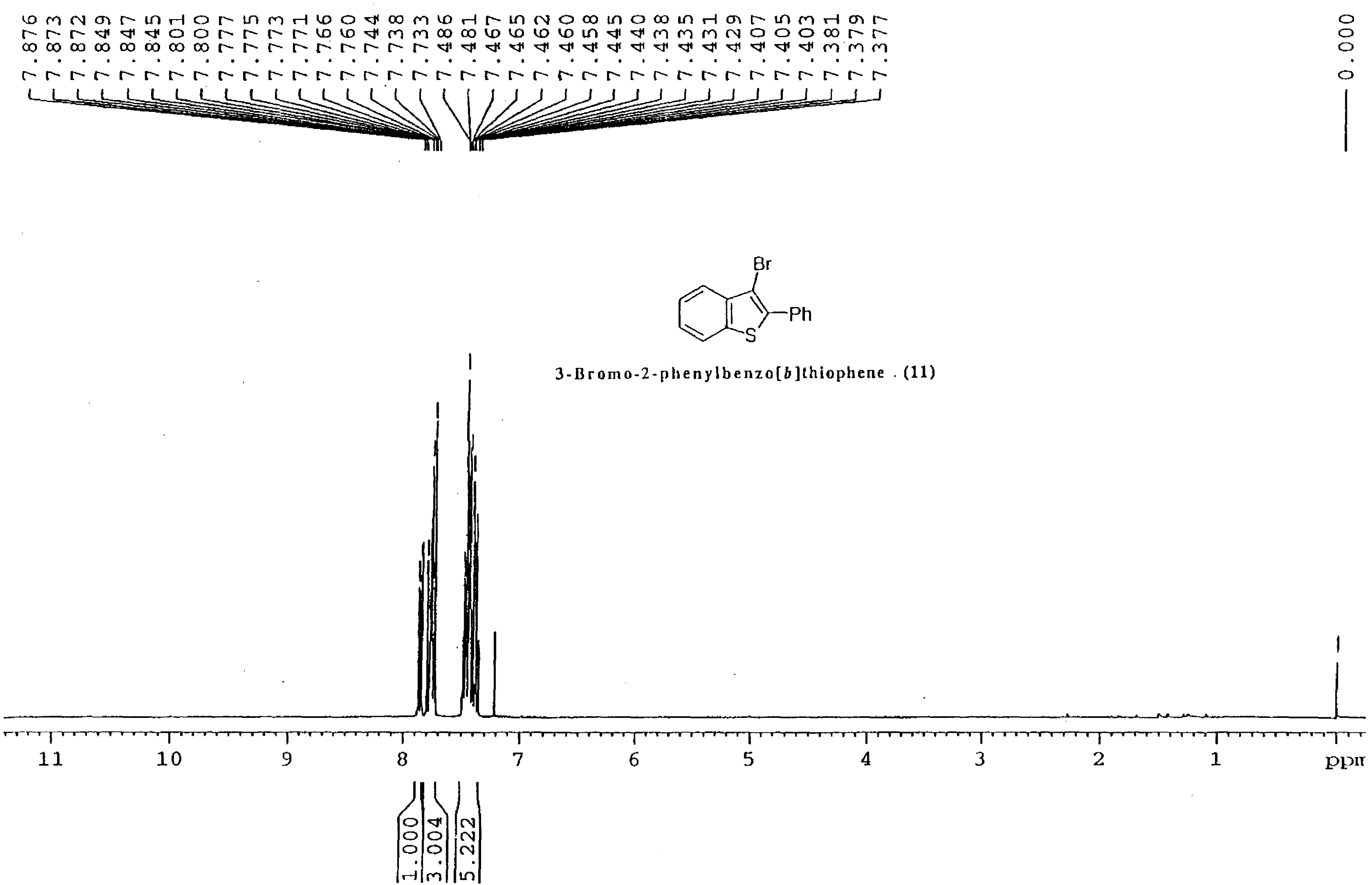
3-Iodo-2-phenylbenzo[*b*]thiophene (10)



data/nmr300/dwy21

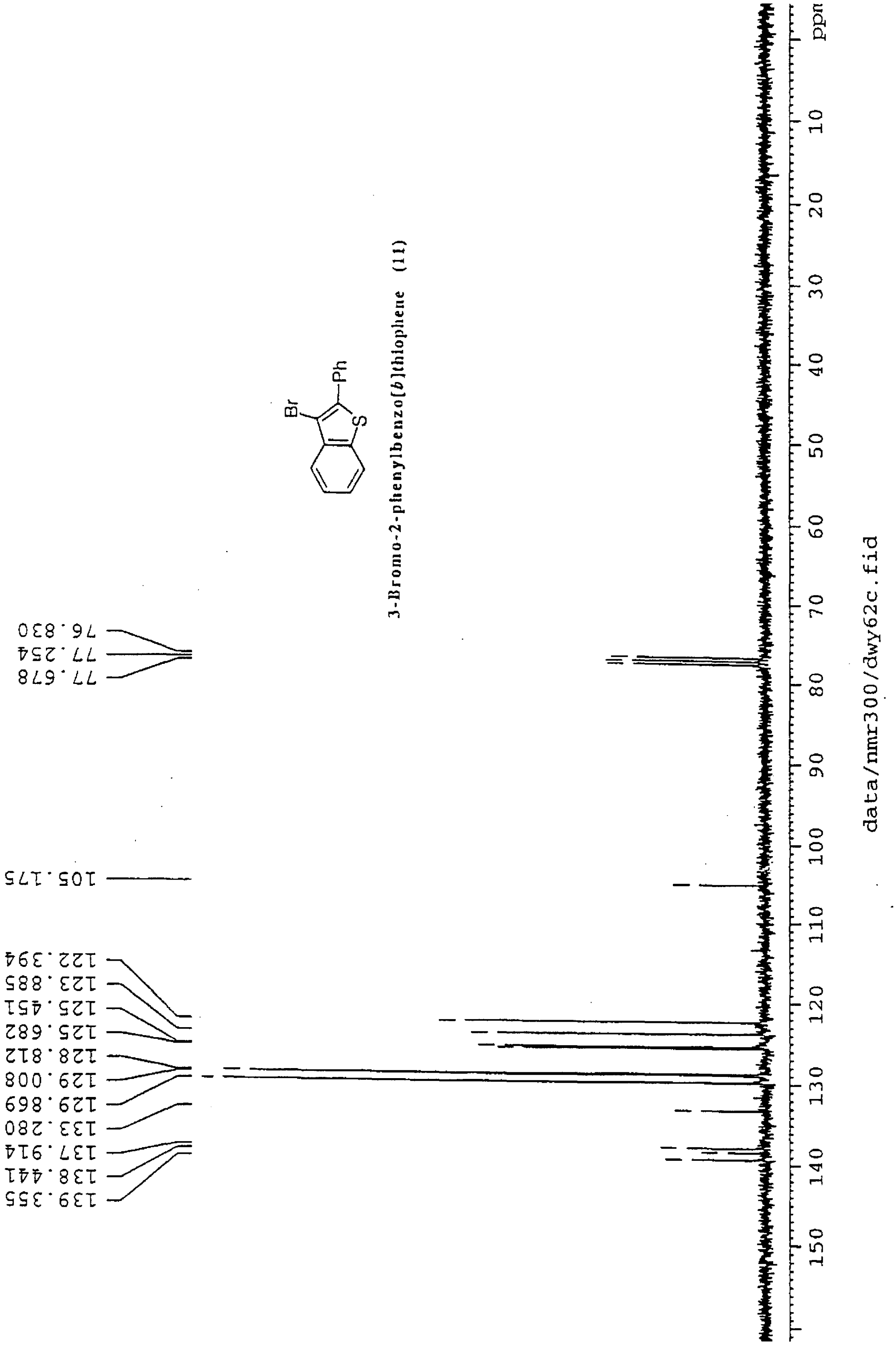


3-Iodo-2-phenylbenzo[*b*]thiophene (10)

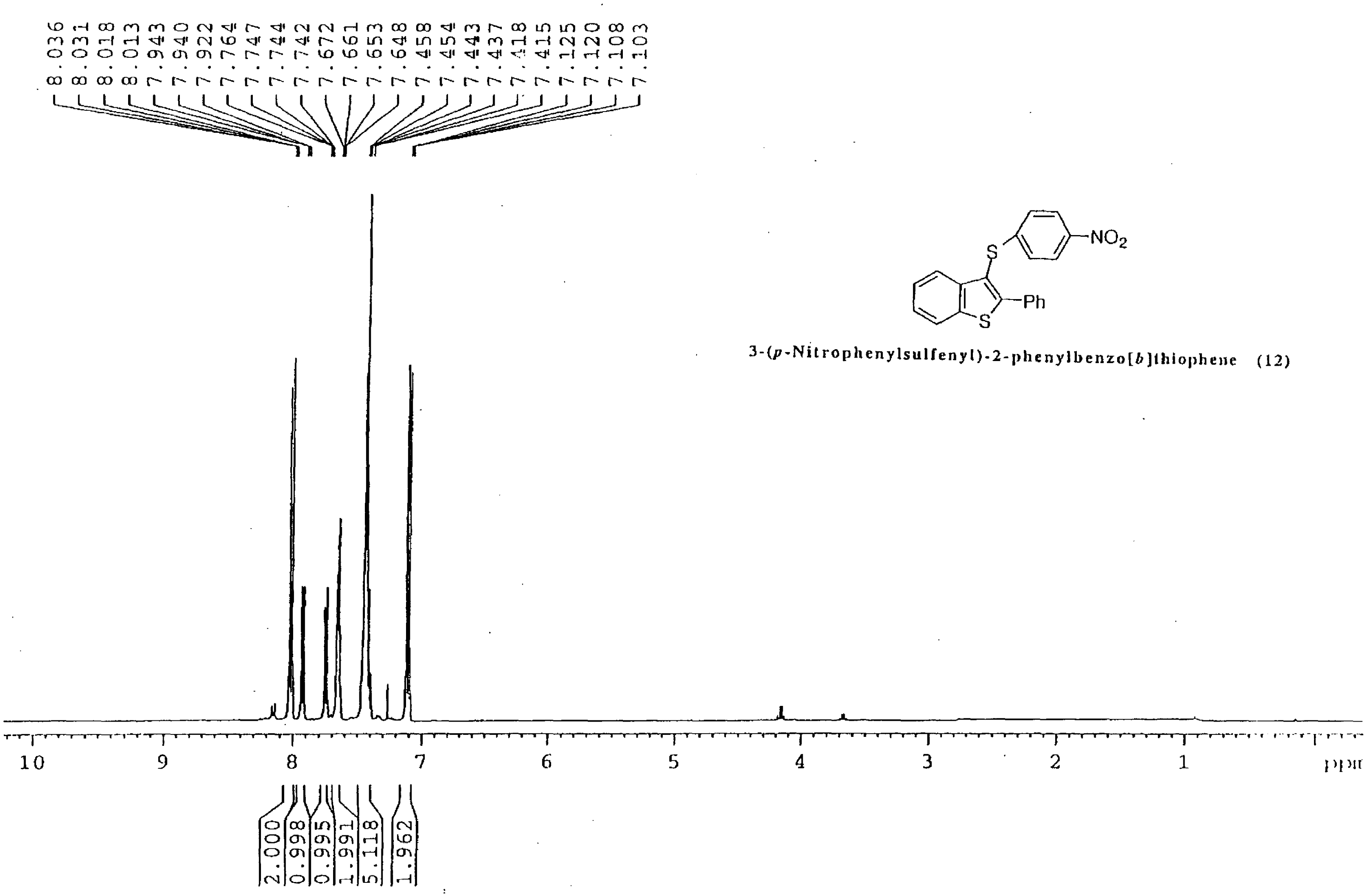


3-Bromo-2-phenylbenzo[*b*]thiophene . (11)

data/nmr300/dwy62.fid

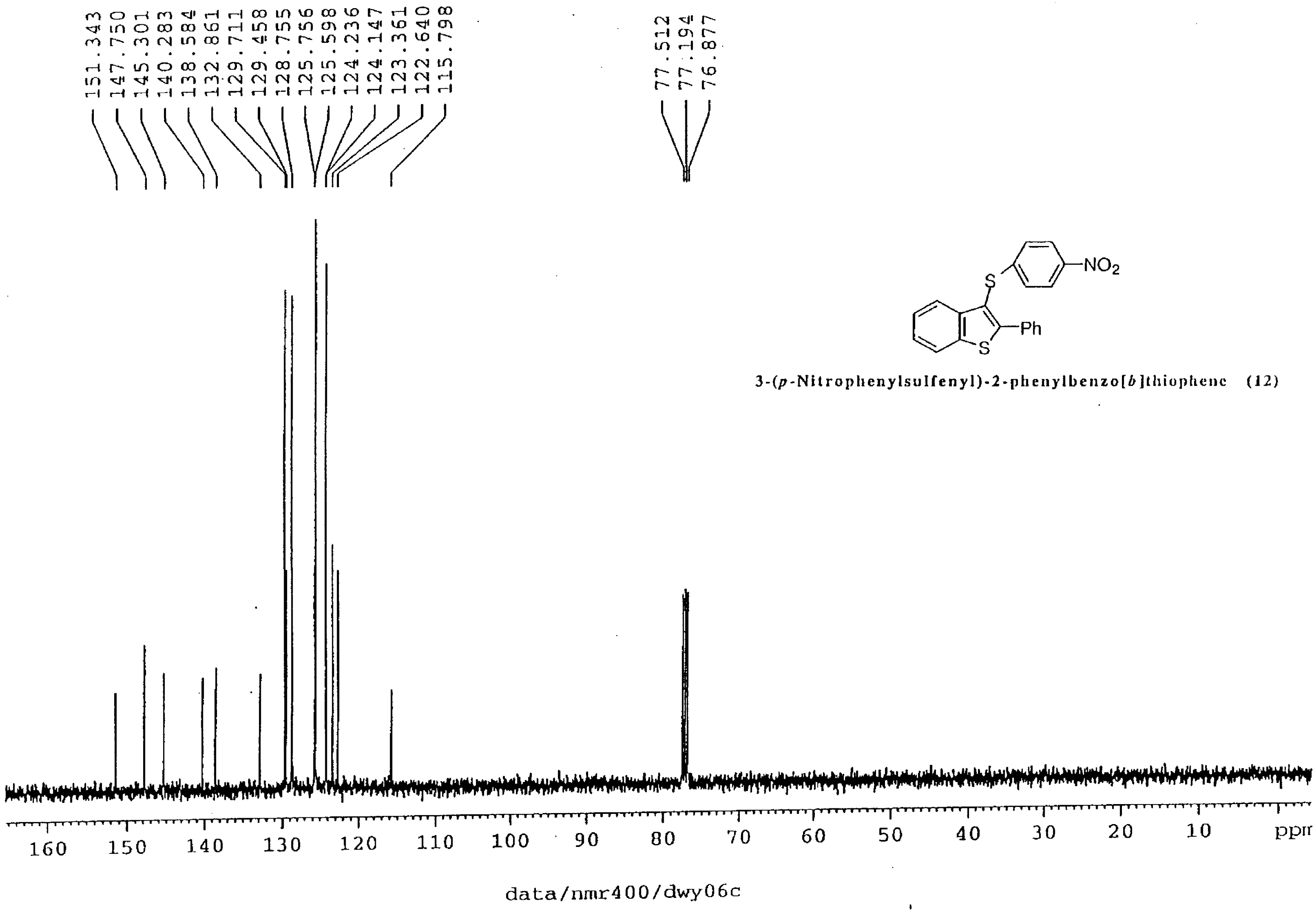


3-Bromo-2-phenylbenzo[*b*]thiophene (11)

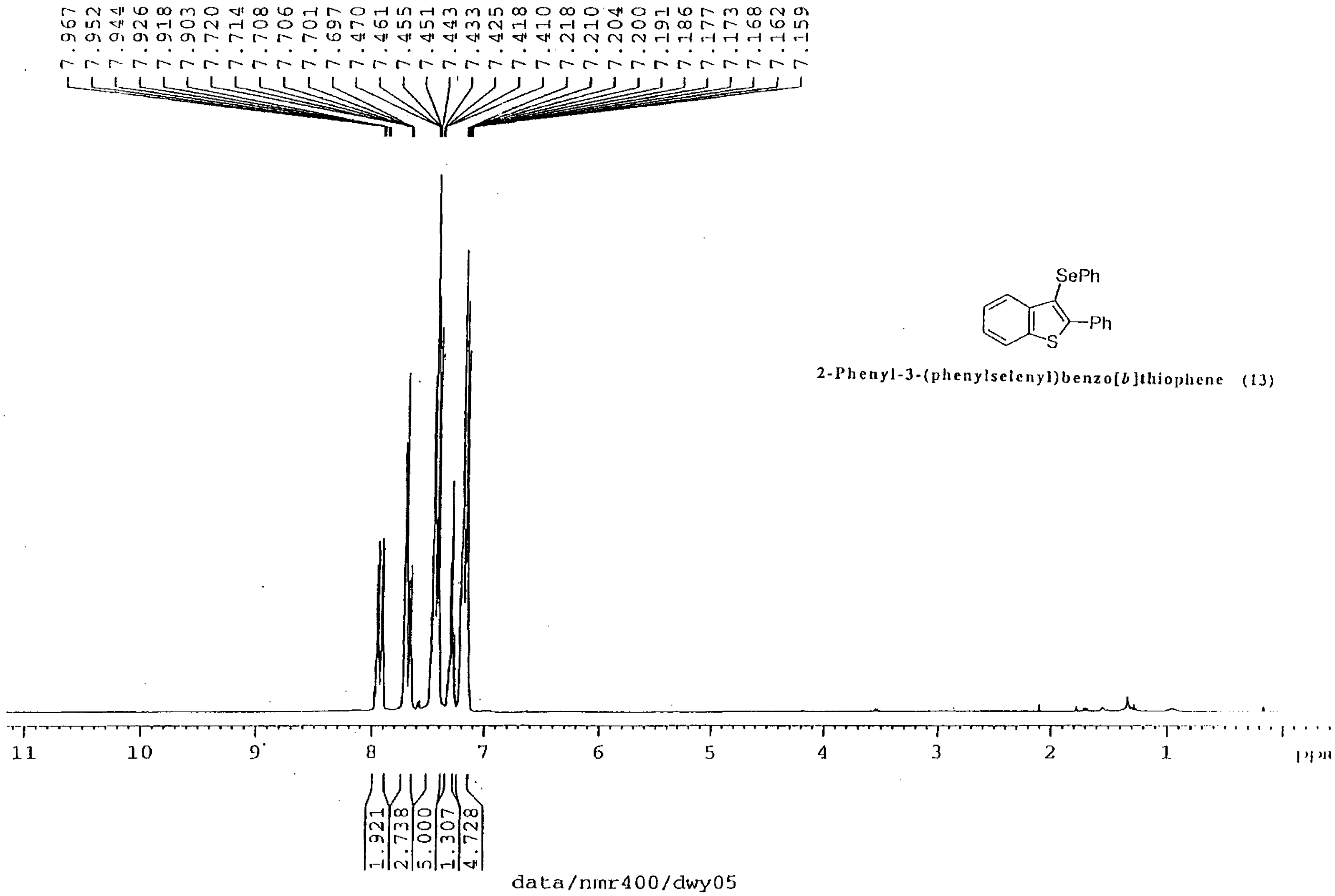


3-(*p*-Nitrophenylsulfenyl)-2-phenylbenzo[*b*]thiophene (12)

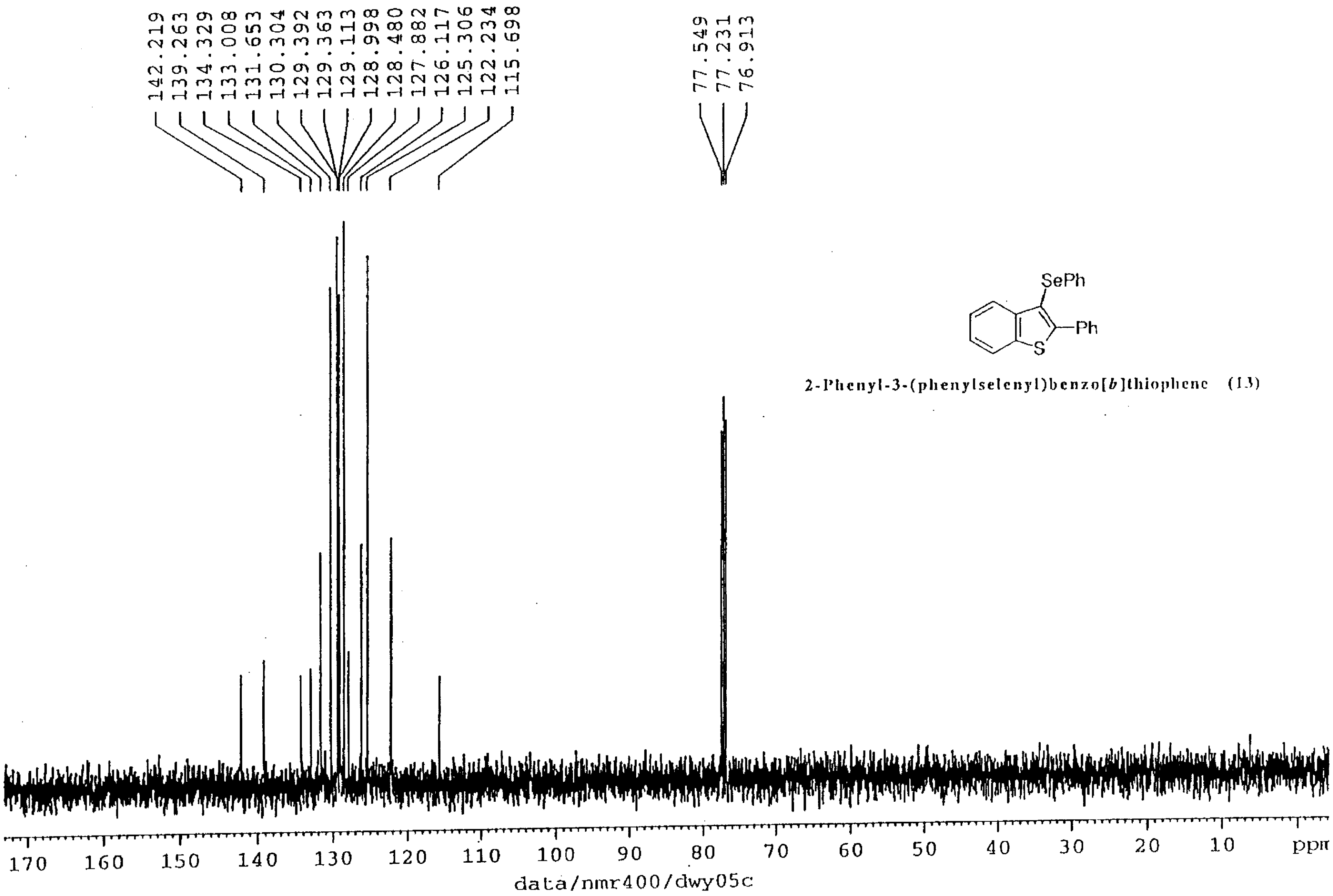
data/nmr400/dwy06



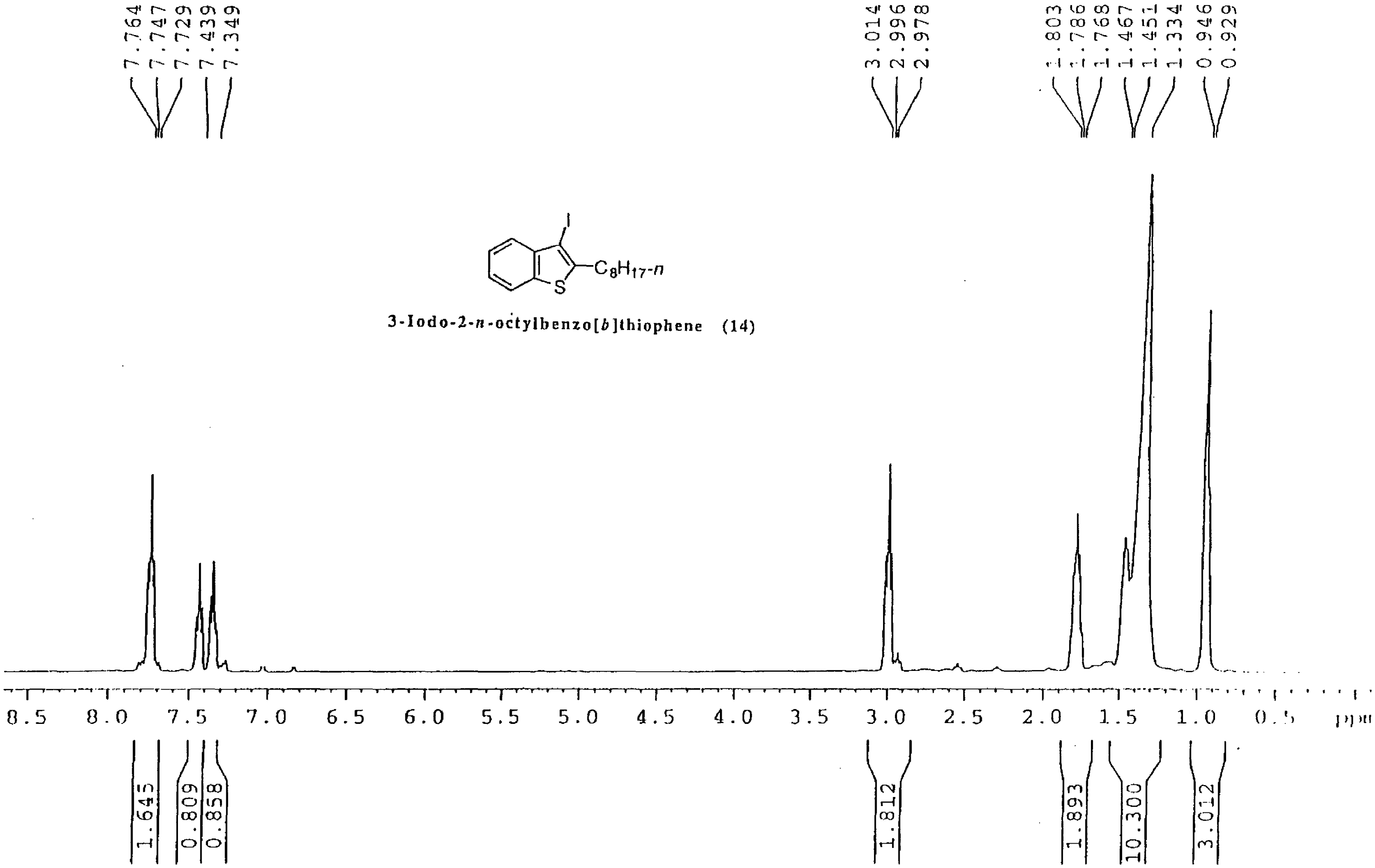
3-(*p*-Nitrophenylsulfenyl)-2-phenylbenzo[*b*]thiophene (12)



2-Phenyl-3-(phenylselenyl)benzo[*b*]thiophene (13)

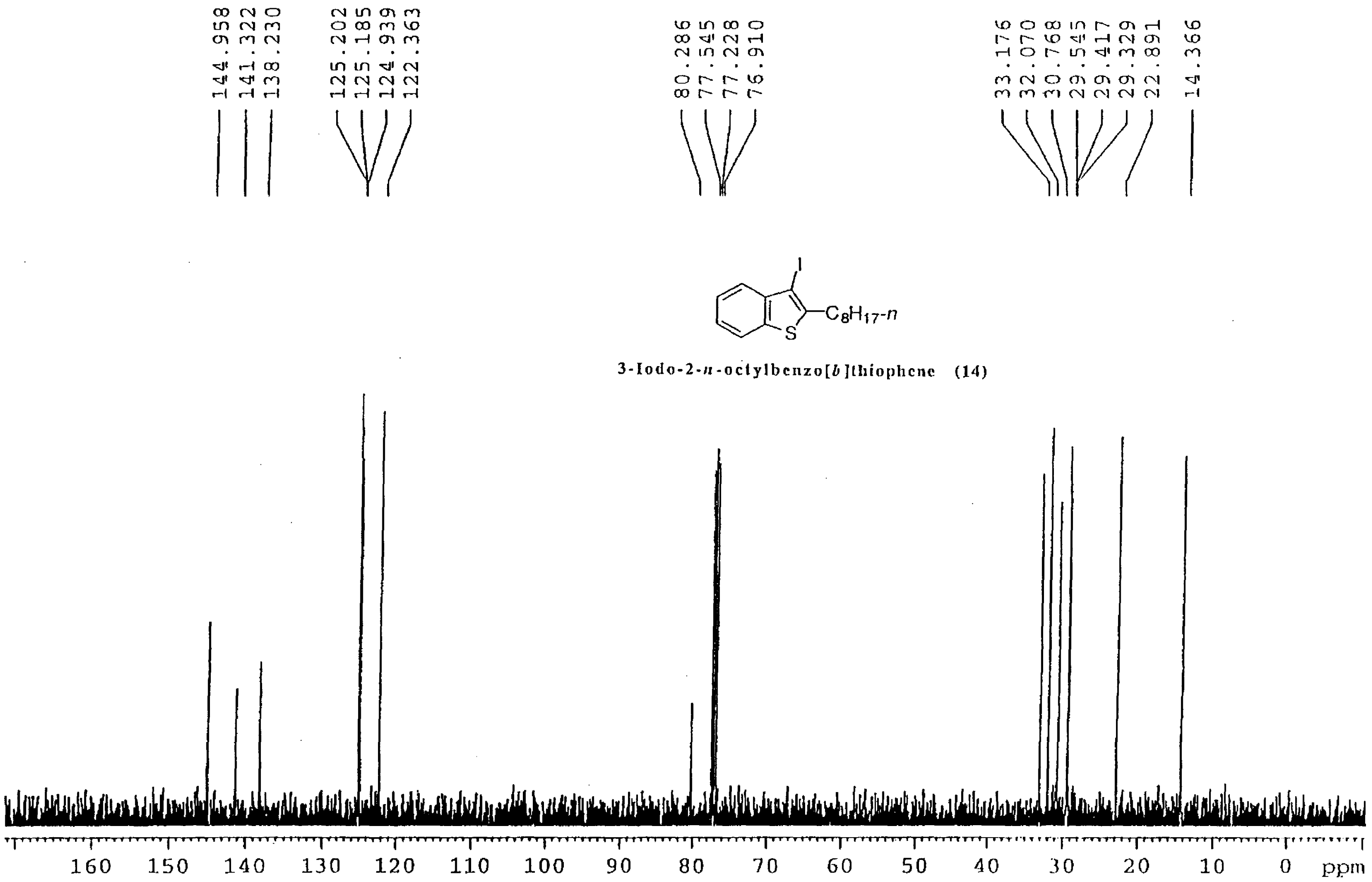


2-Phenyl-3-(phenylselenyl)benzo[*b*]thiophene (13)



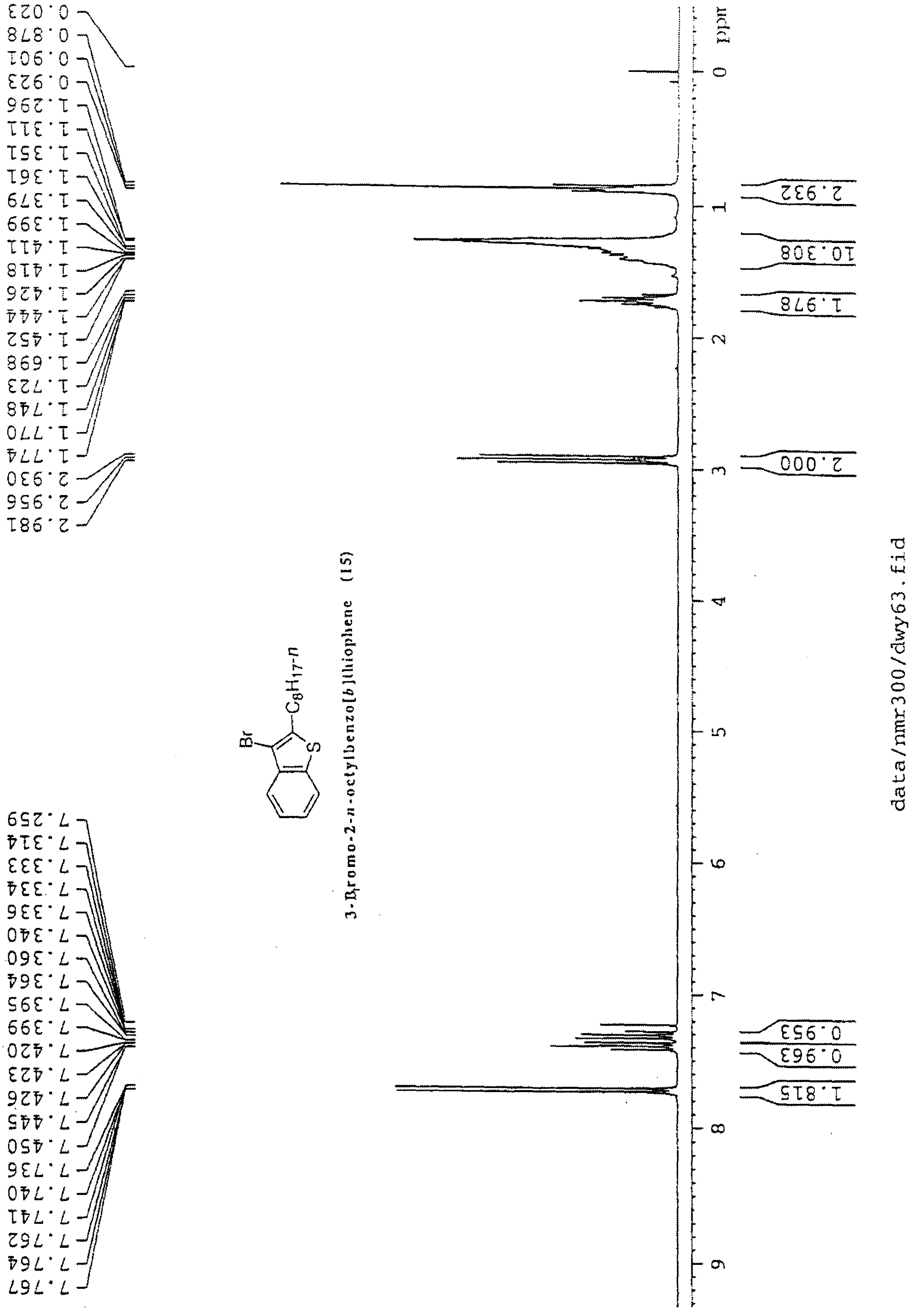
3-Iodo-2-*n*-octylbenzo[*b*]thiophene (14)

data/nmr400/dwy01

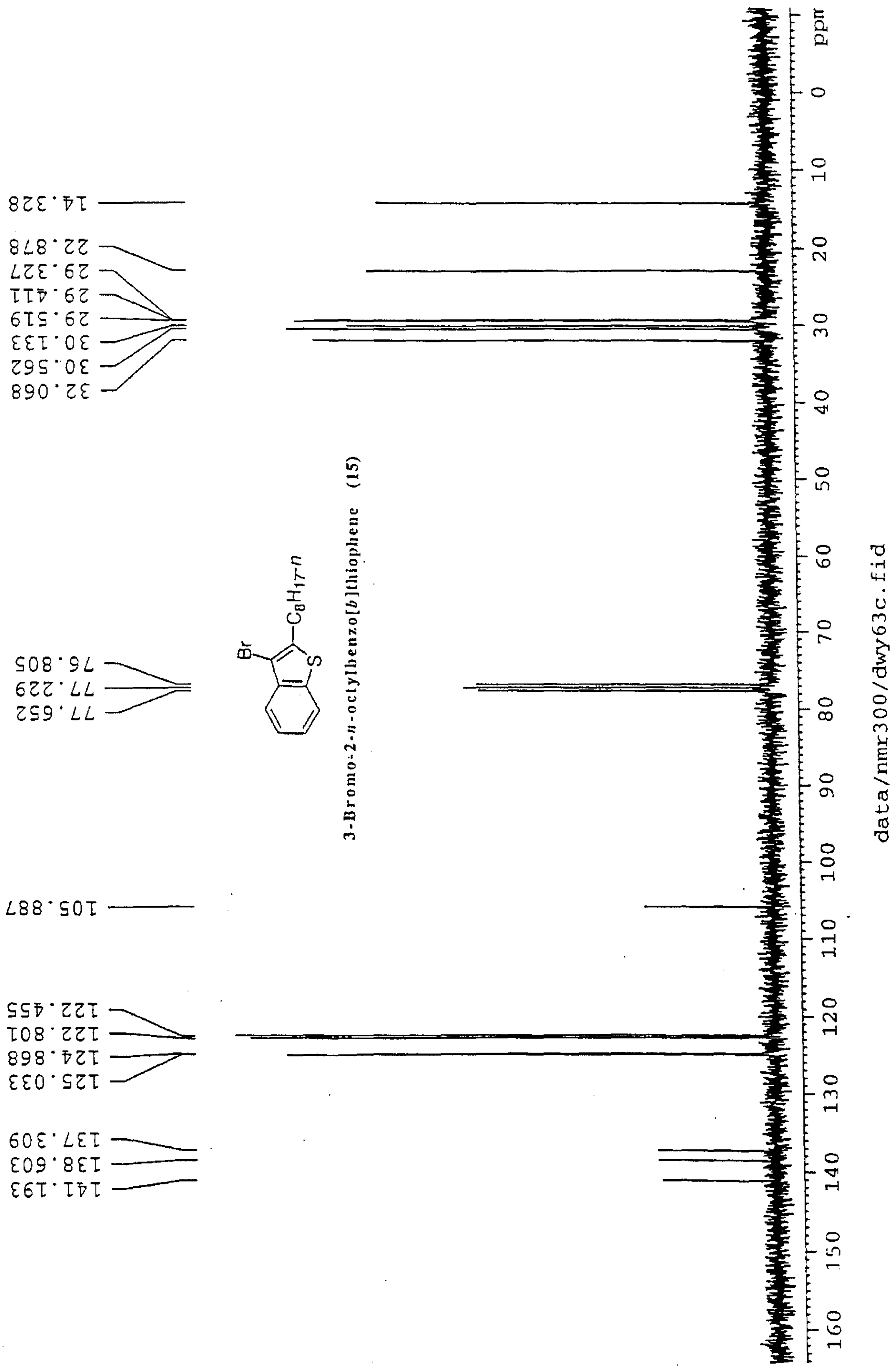


3-Iodo-2-*n*-octylbenzo[*b*]thiophene (14)

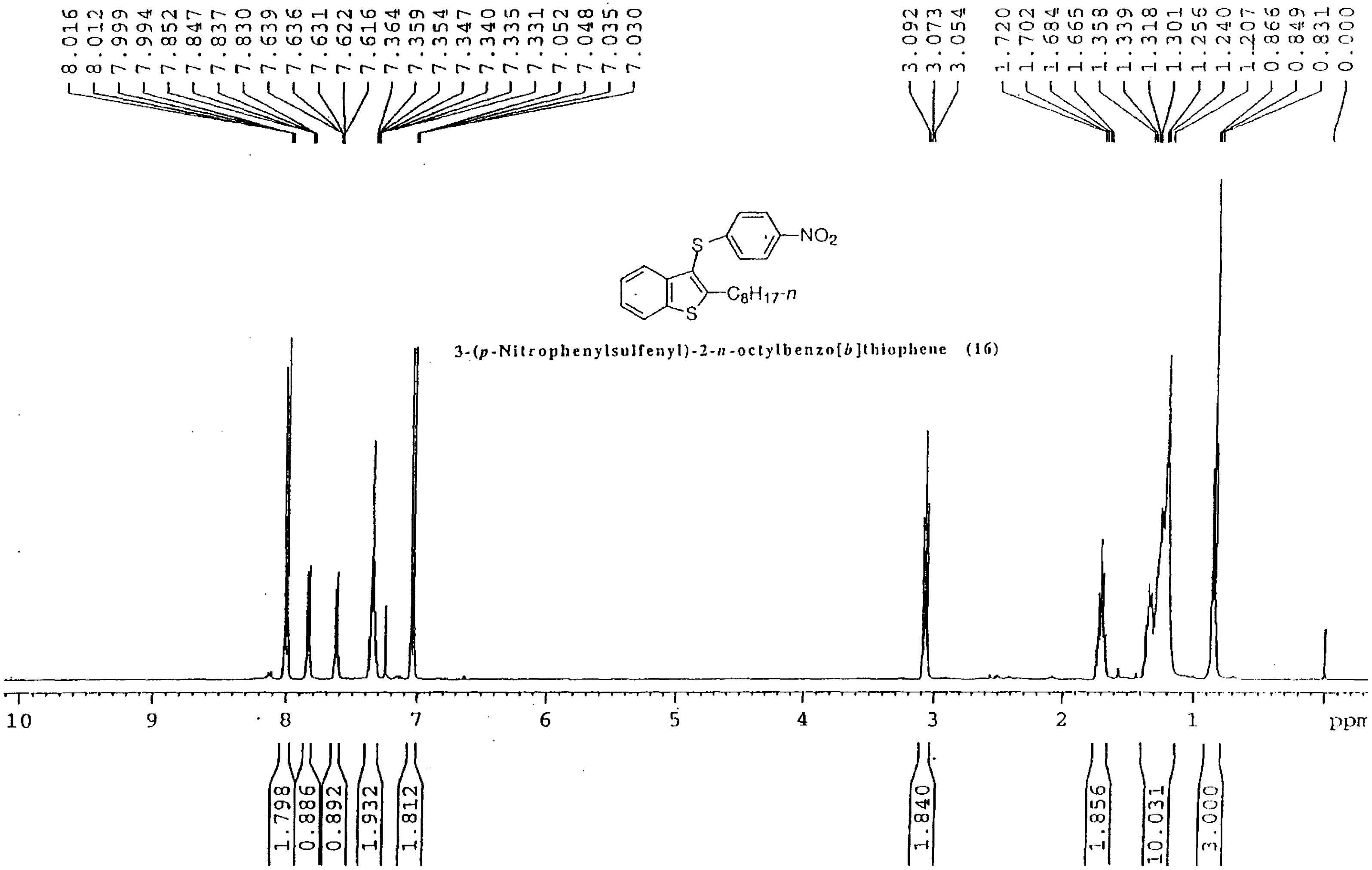
data/nmr400/dwy01c



3-Bromo-2-*n*-octylbenzo[*b*]thiophene (15)

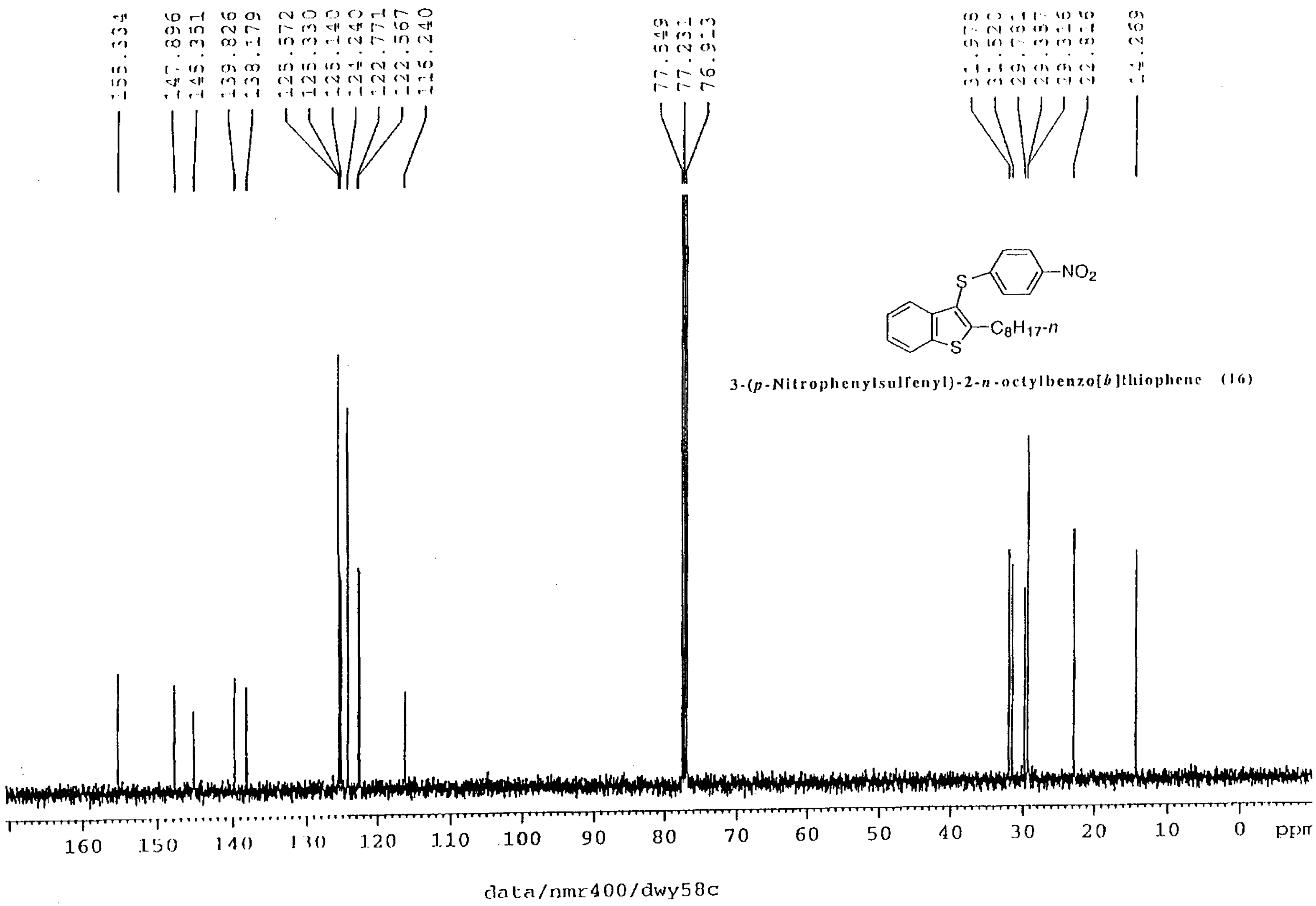


3-Bromo-2-*n*-octylbenzo[*b*]thiophene (15)

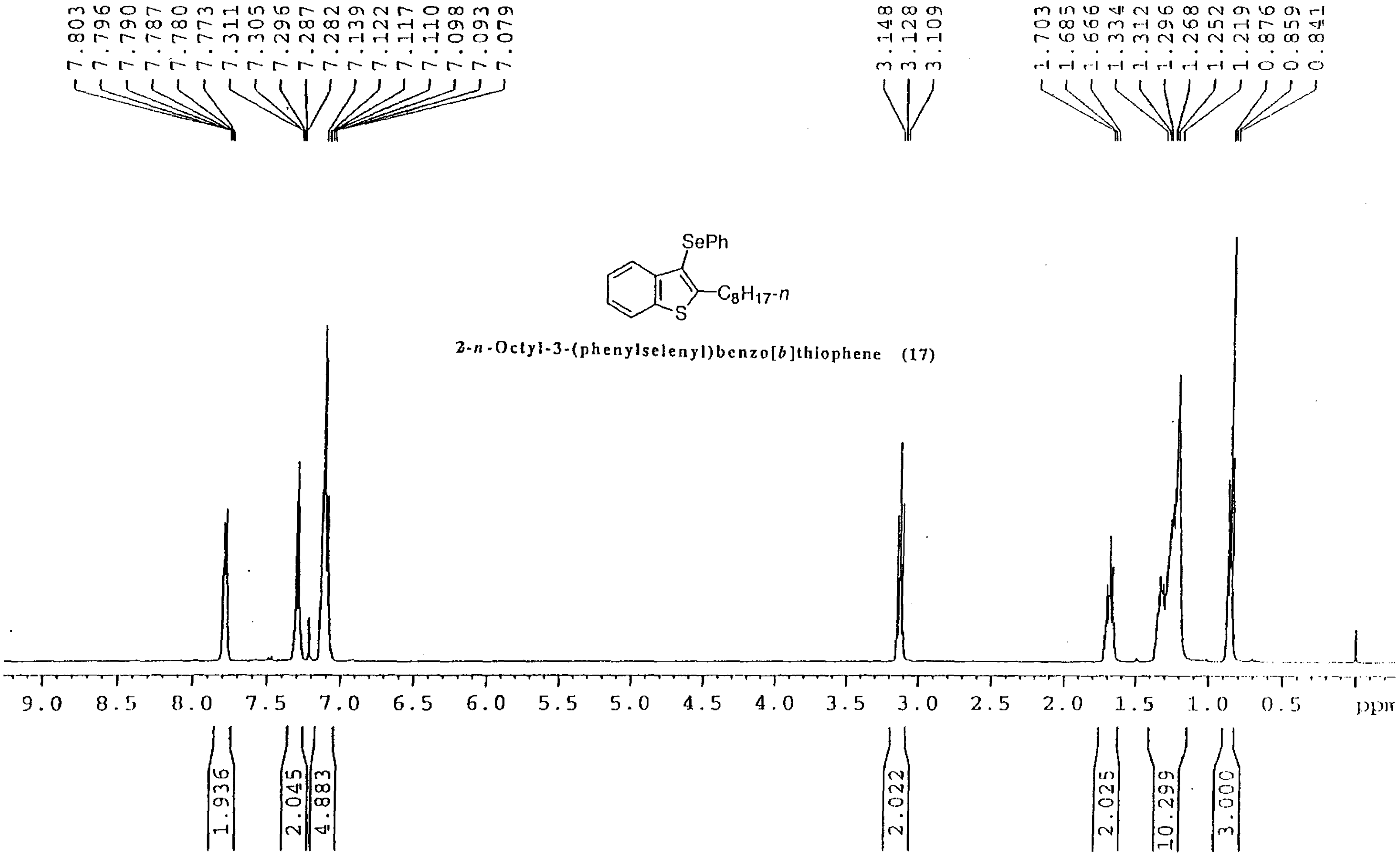


3-(*p*-Nitrophenylsulfenyl)-2-*n*-octylbenzo[*b*]thiophene (16)

data/nmr400/dwy58

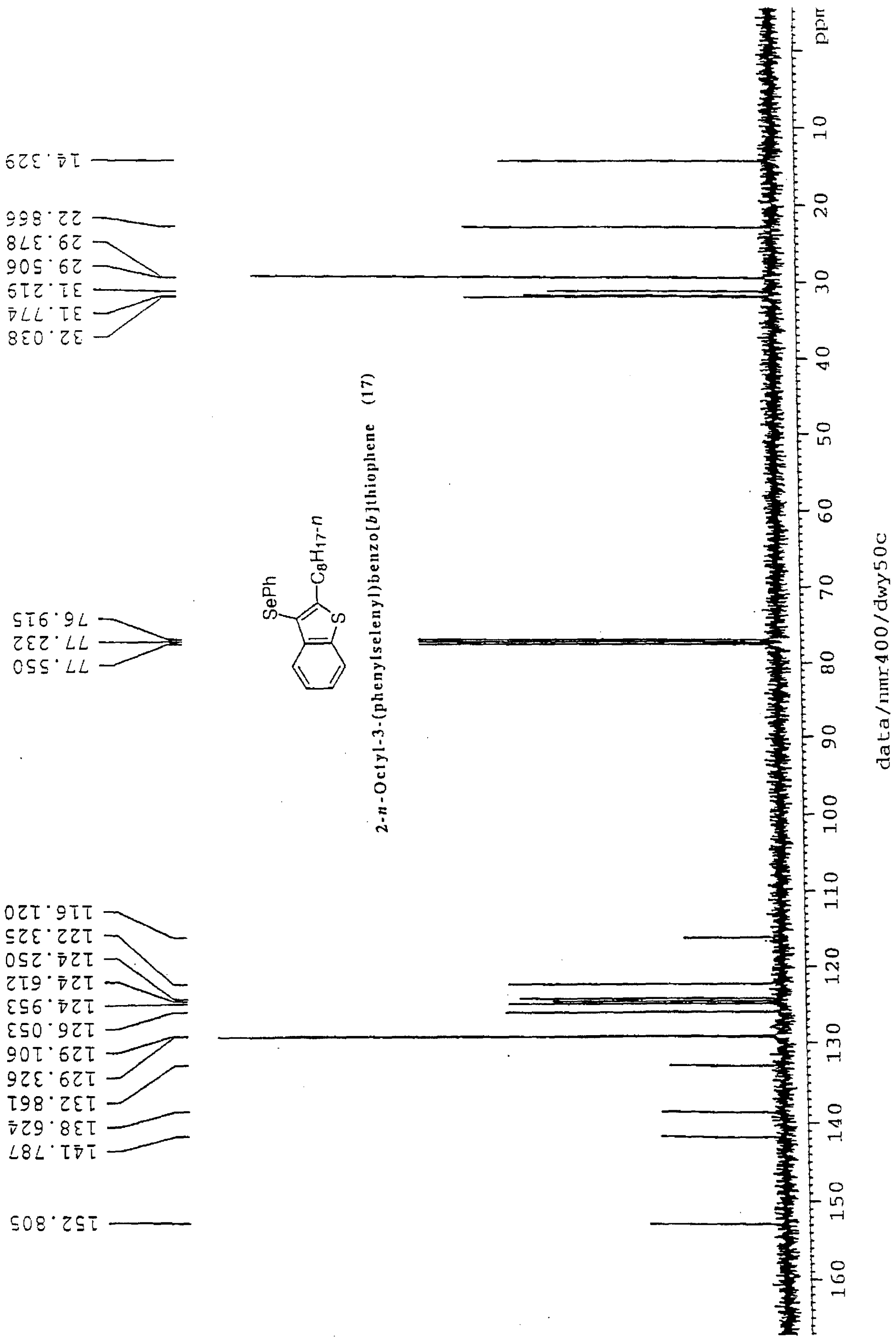


3-(*p*-Nitrophenylsulfenyl)-2-*n*-octylbenzo[*b*]thiophene (16)

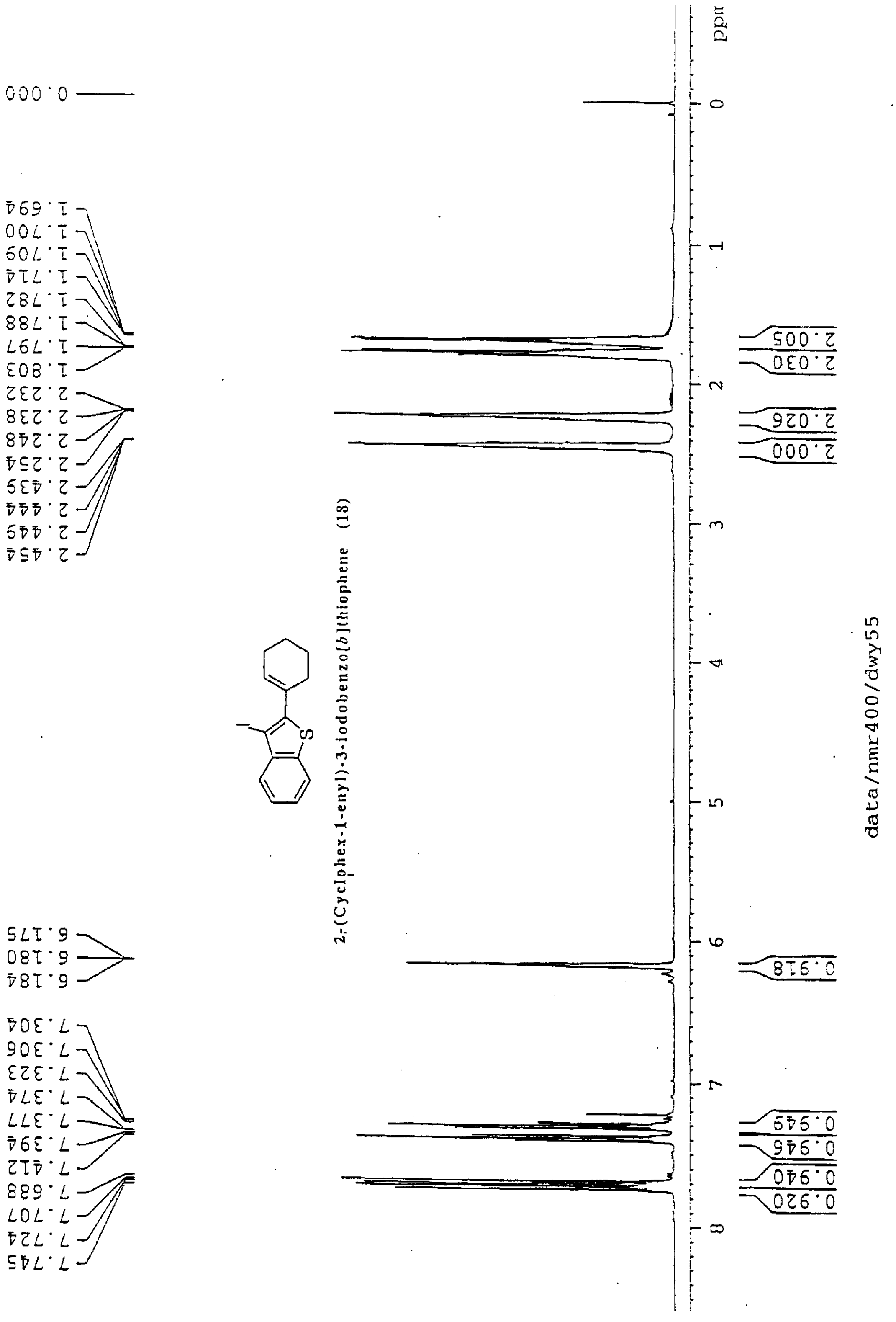


2-*n*-Octyl-3-(phenylselenyl)benzo[*b*]thiophene (17)

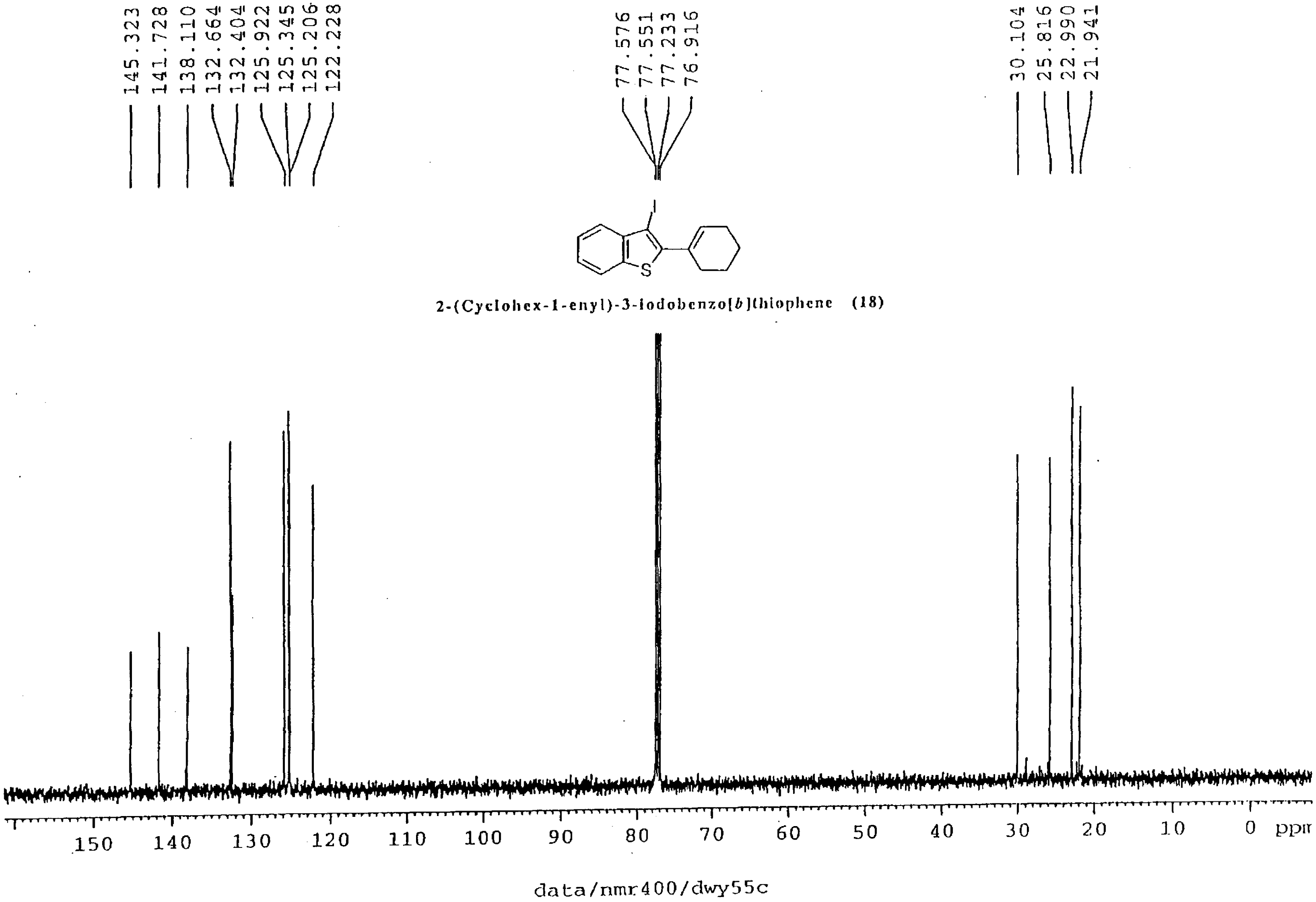
data/nmr400/dwy50



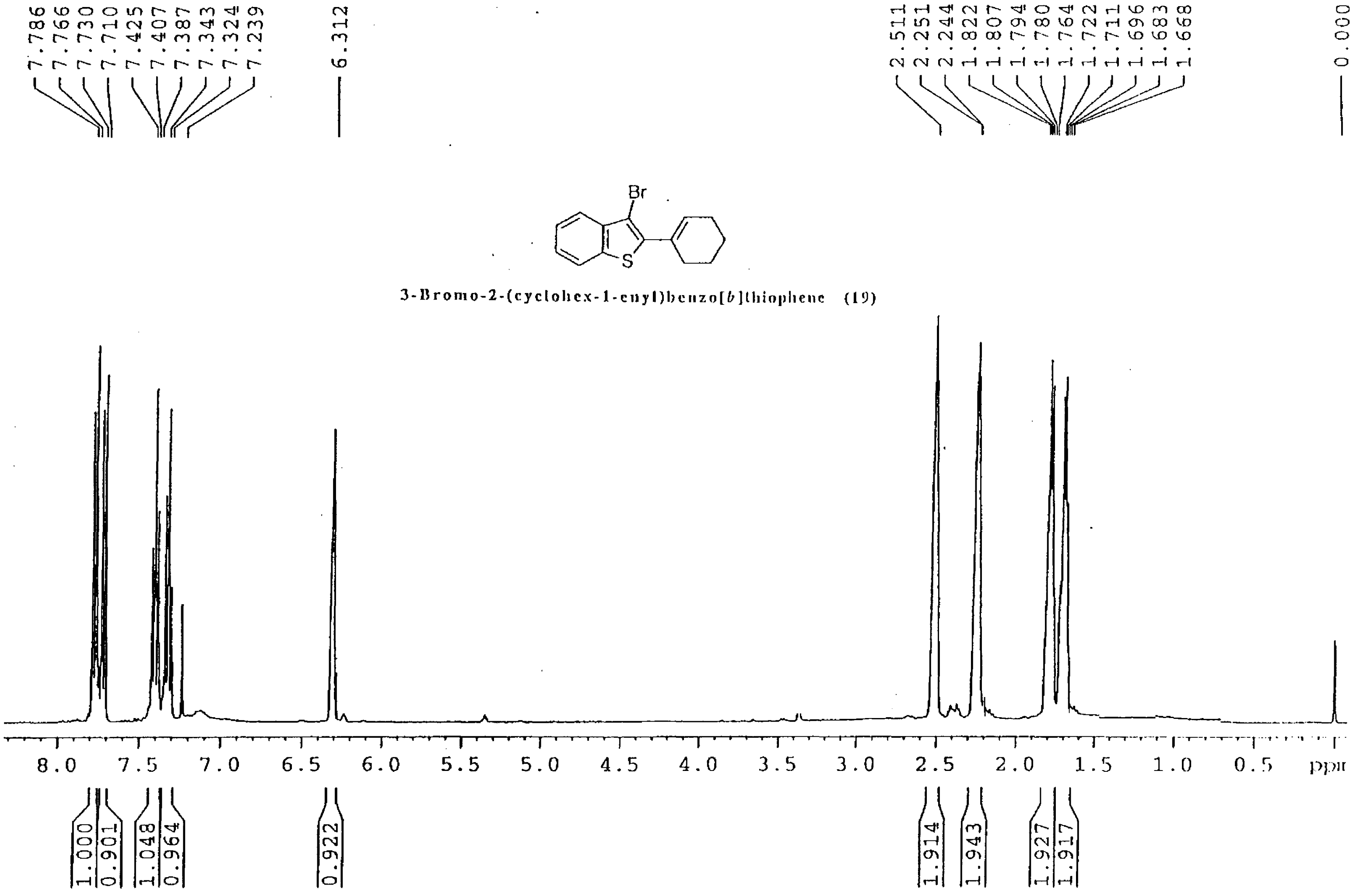
2-*n*-Octyl-3-(phenylselenyl)benzo[*b*]thiophene (17)



2-(Cyclohex-1-enyl)-3-iodobenzo[*b*]thiophene (18)

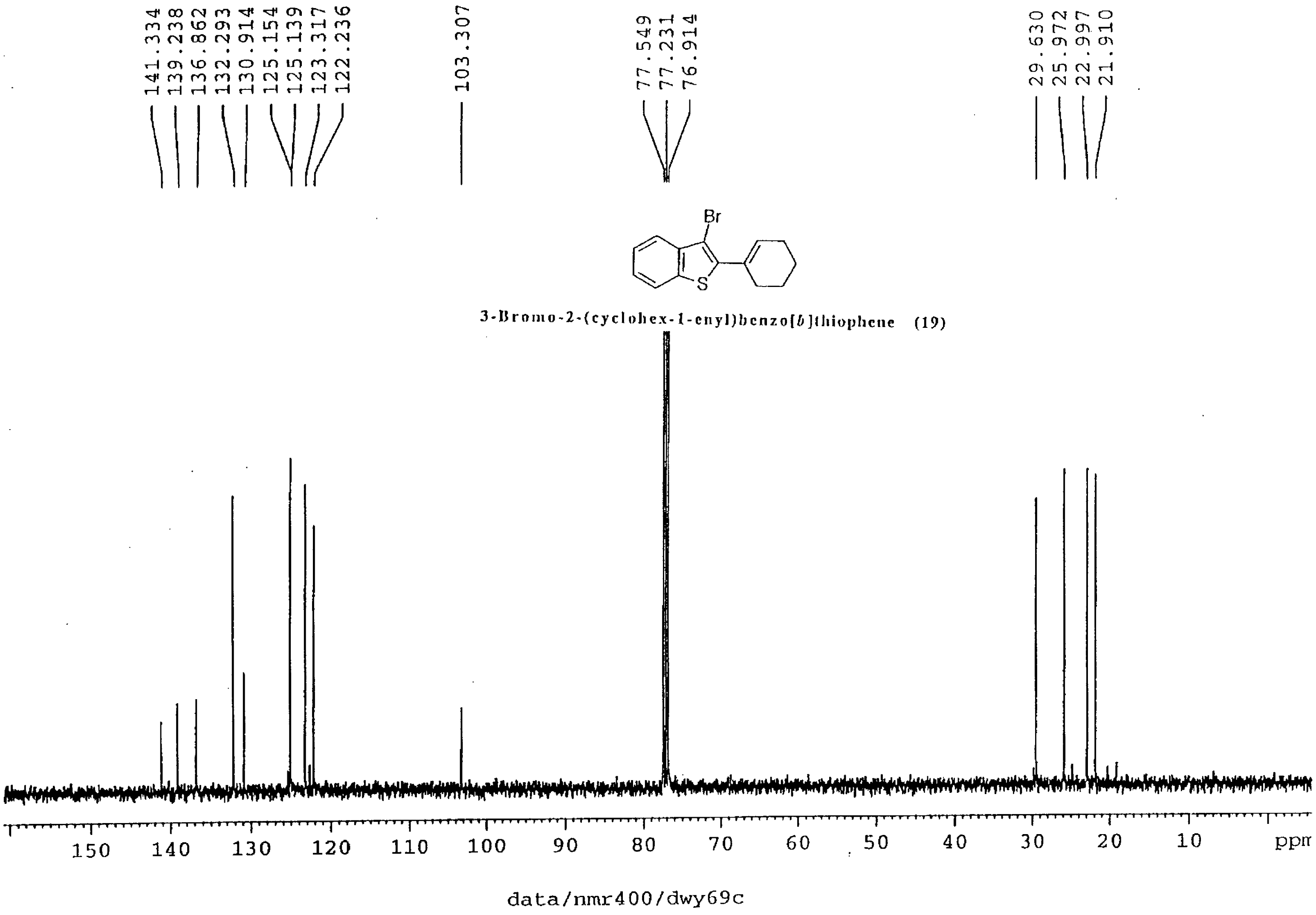


2-(Cyclohex-1-enyl)-3-iodobenzo[*b*]thiophene (18)

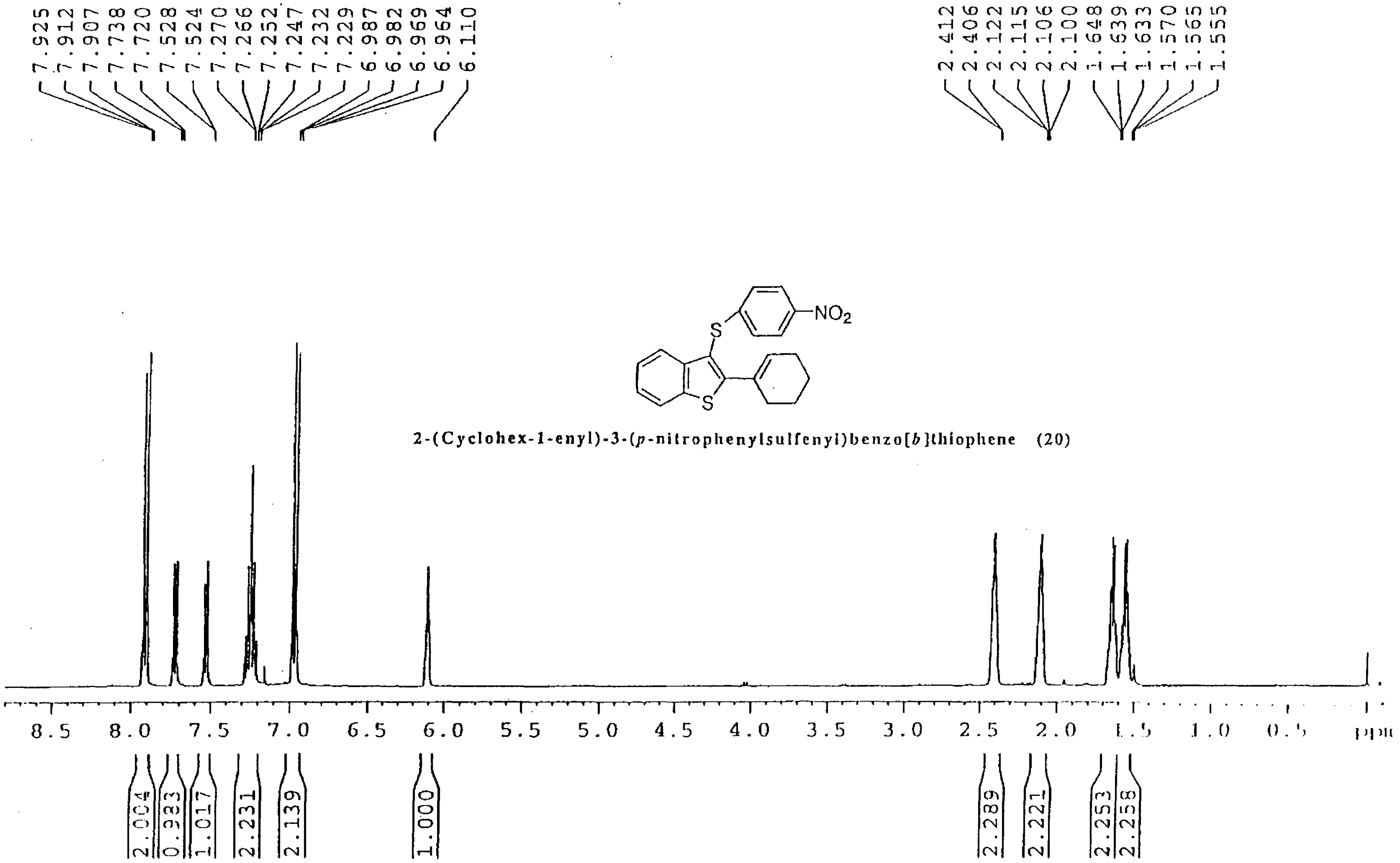


3-Bromo-2-(cyclohex-1-enyl)benzo[*b*]thiophene (19)

data/nmr400/dwy69

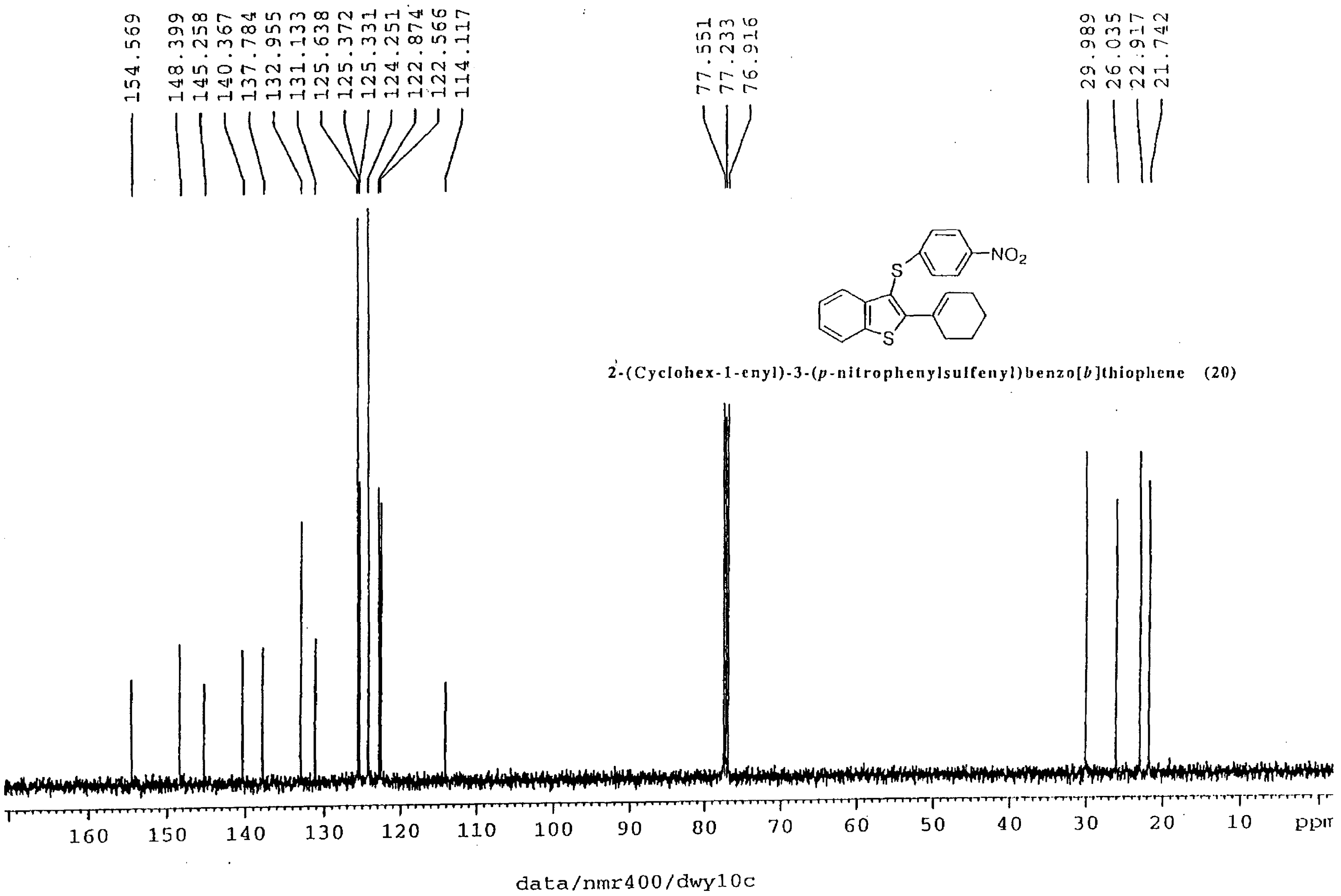


3-Bromo-2-(cyclohex-1-enyl)benzo[*b*]thiophene (19)

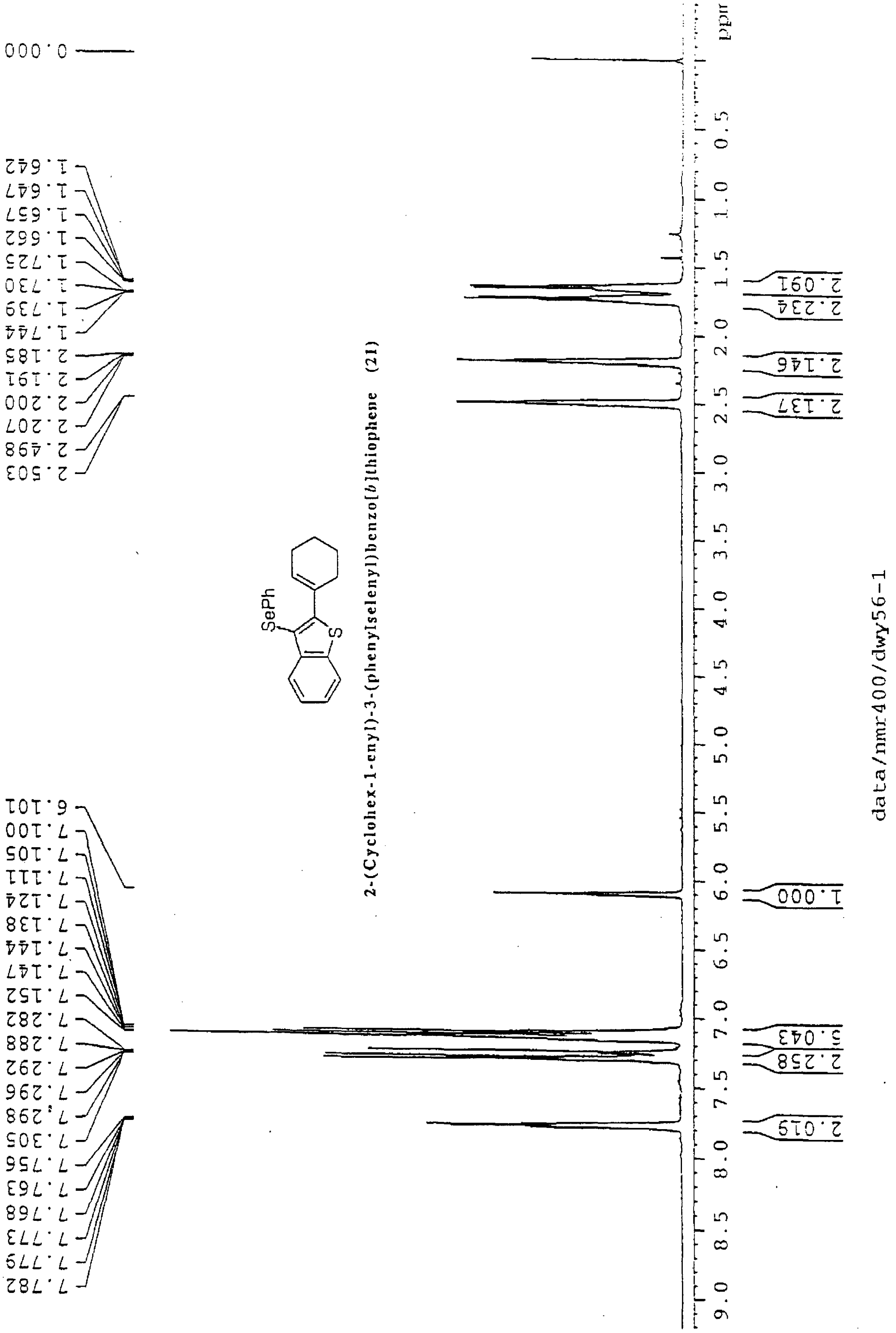


2-(Cyclohex-1-enyl)-3-(*p*-nitrophenylsulfenyl)benzo[*b*]thiophene (20)

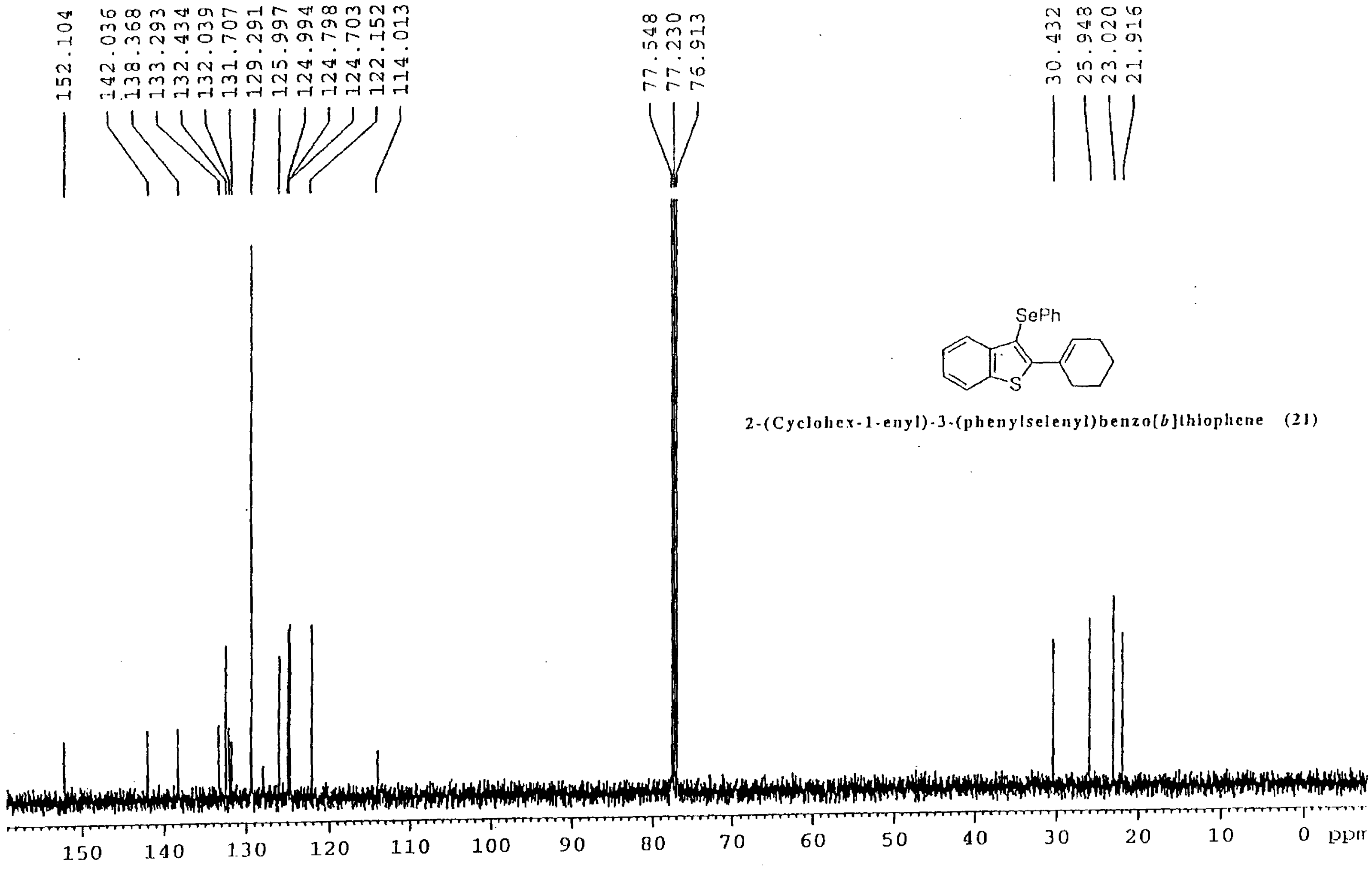
data/nmr400/dwy10



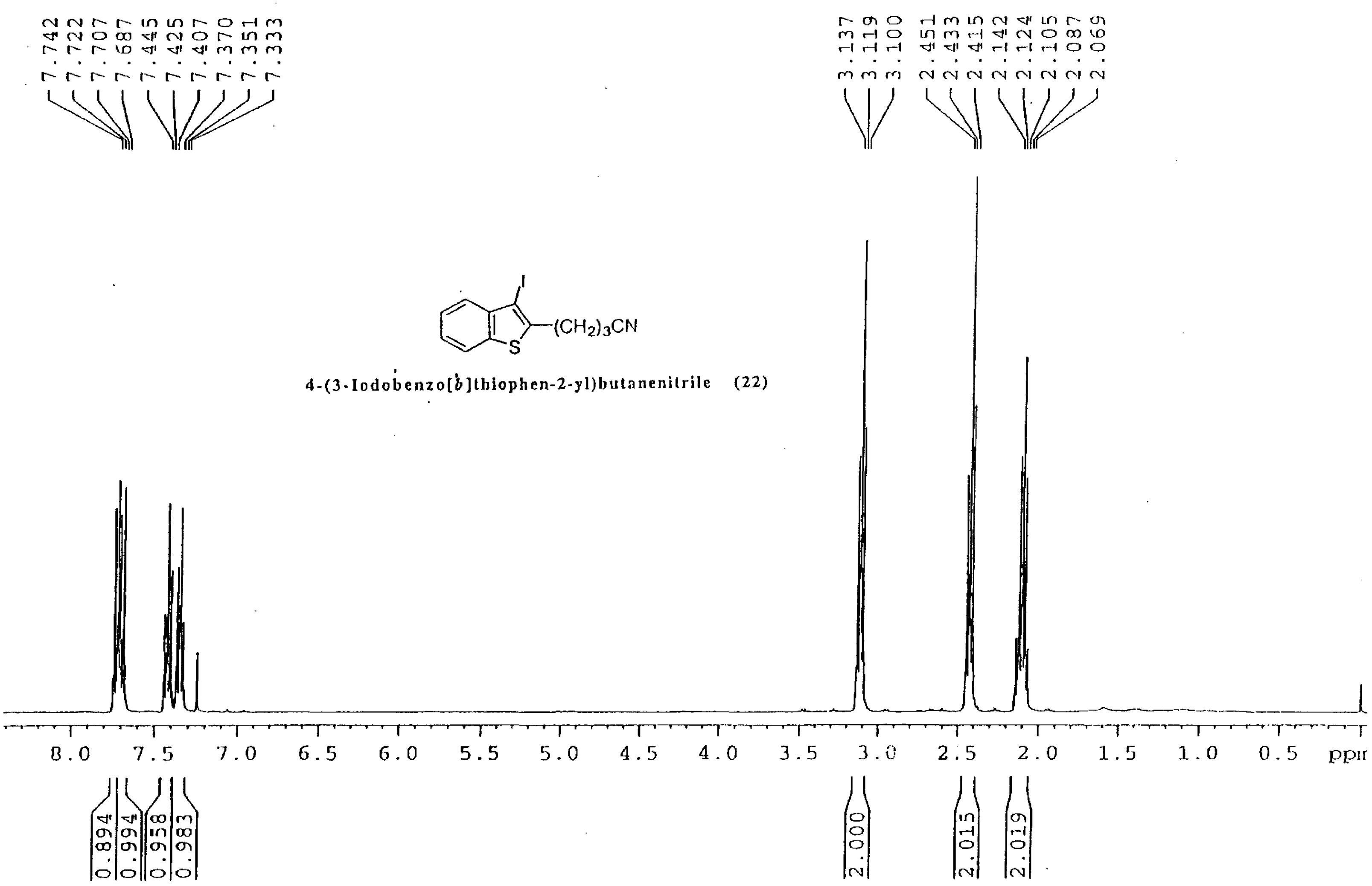
2-(Cyclohex-1-enyl)-3-(*p*-nitrophenylsulfenyl)benzo[*b*]thiophene (20)



2-(Cyclohex-1-enyl)-3-(phenylselenyl)benzo[*b*]thiophene (21)

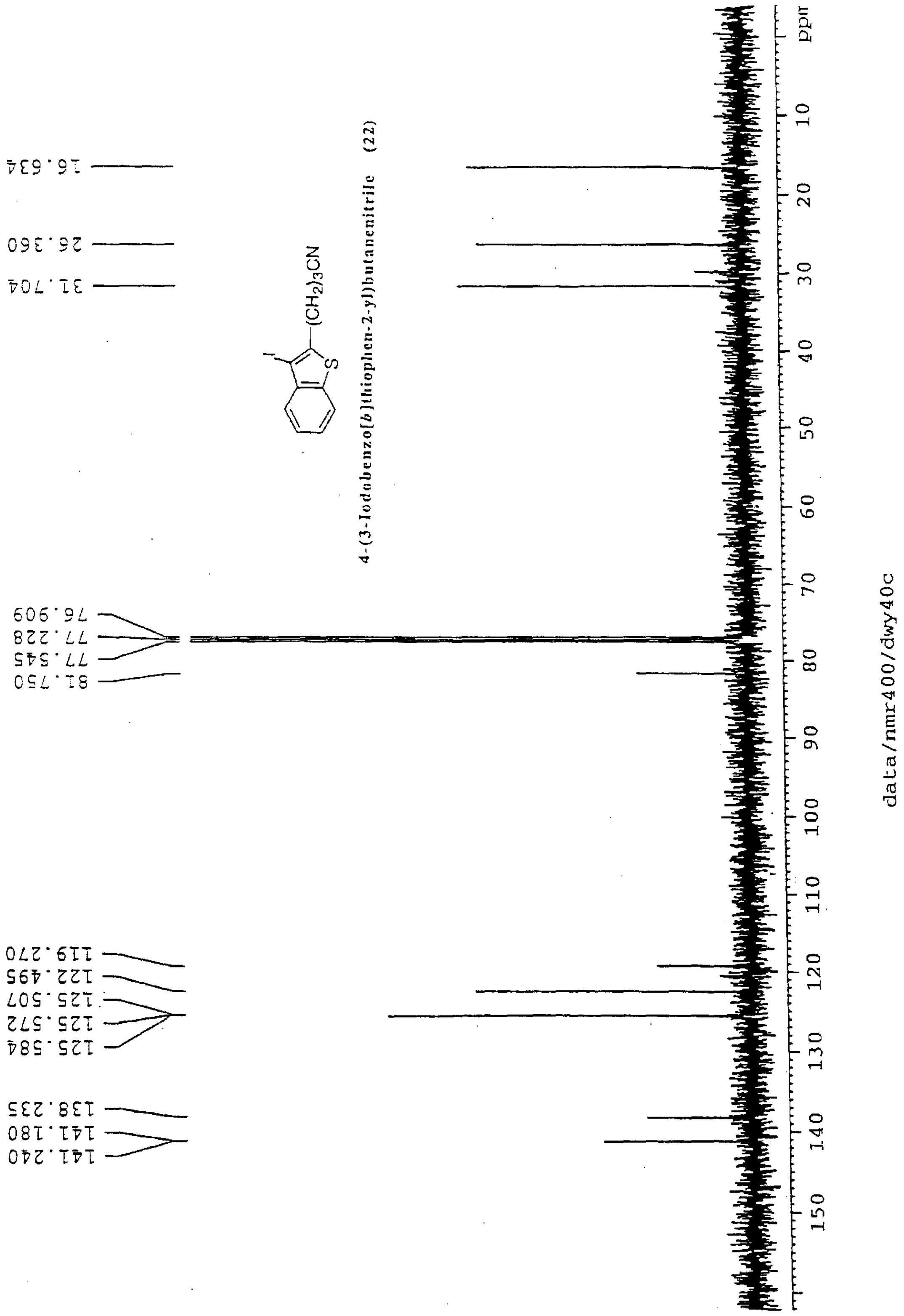


2-(Cyclohex-1-enyl)-3-(phenylselenyl)benzo[*b*]thiophene (21)

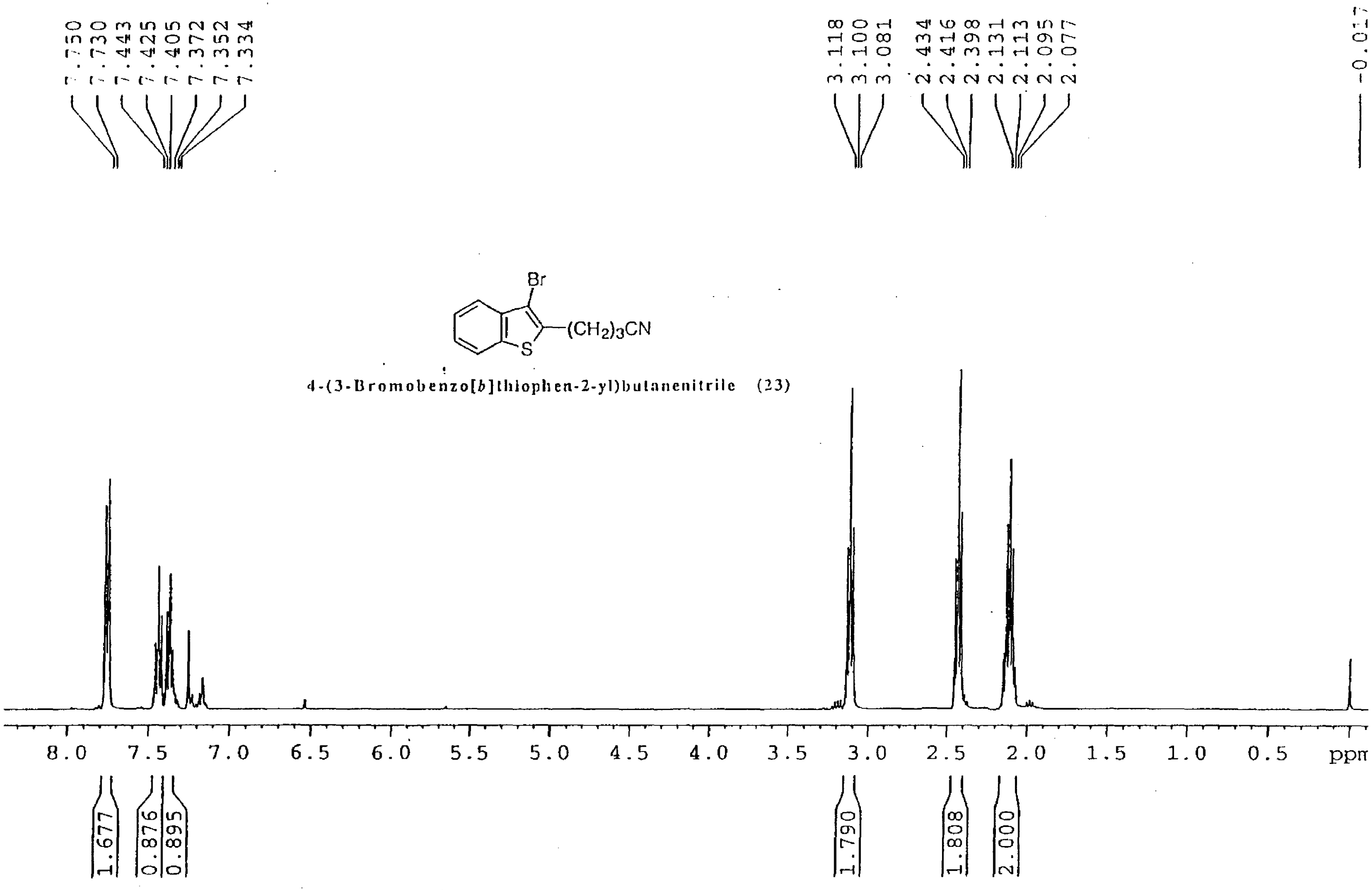


4-(3-Iodobenzo[*b*]thiophen-2-yl)butanenitrile (22)

data/nmr400/dwy40

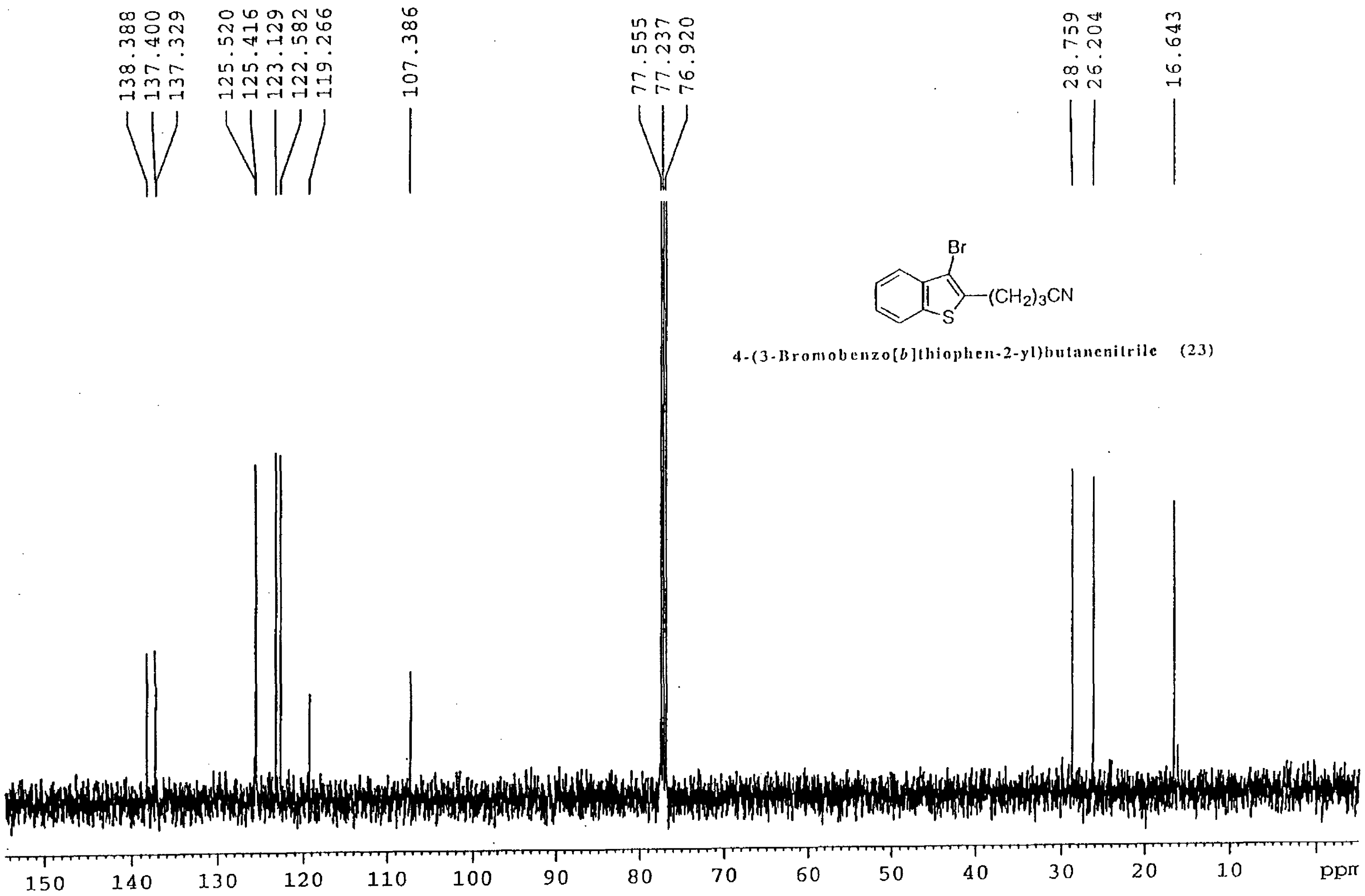


4-(3-Iodobenzo[*b*]thiophen-2-yl)butanenitrile (22)

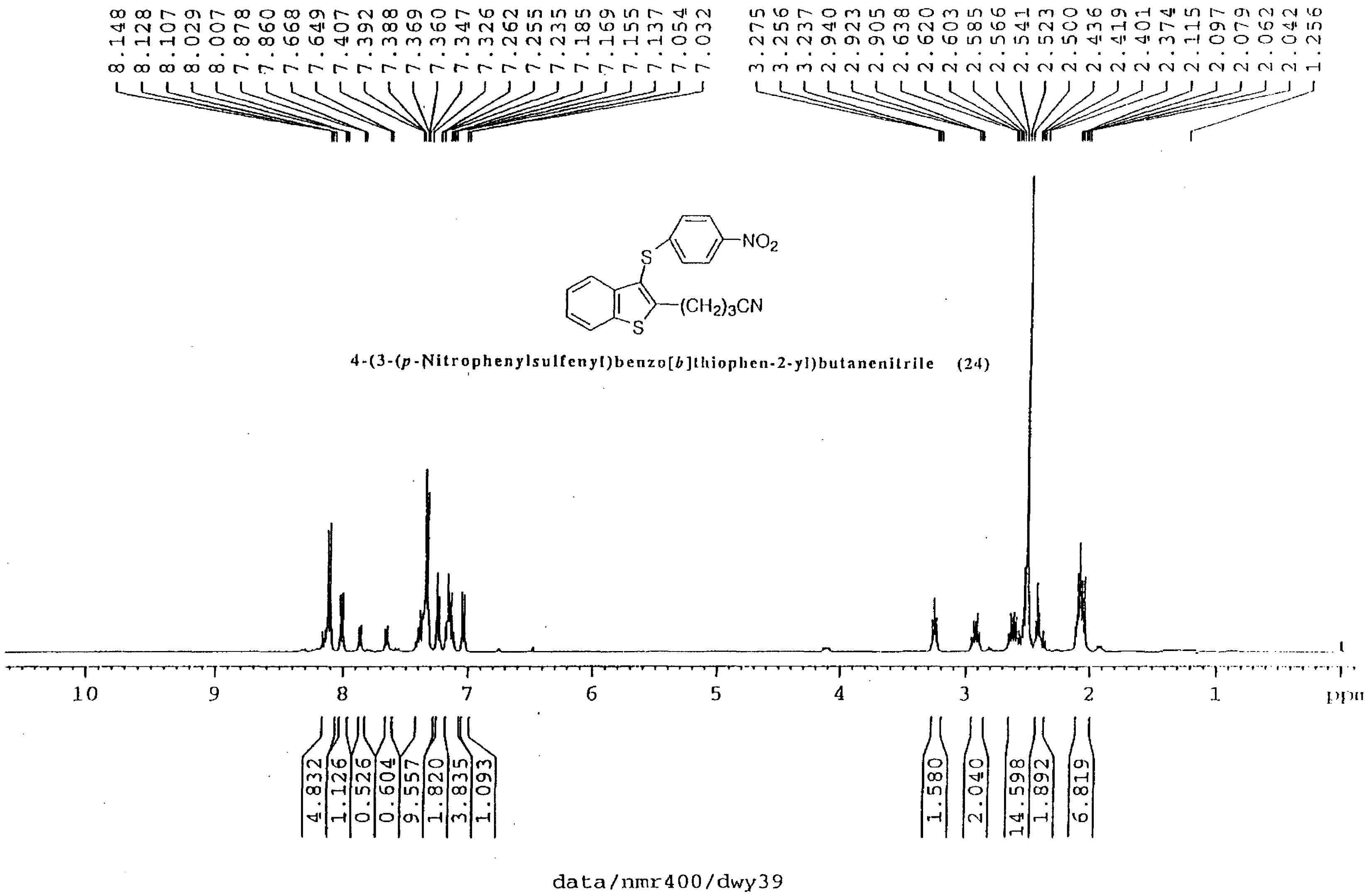


4-(3-Bromobenzo[*b*]thiophen-2-yl)butanenitrile (23)

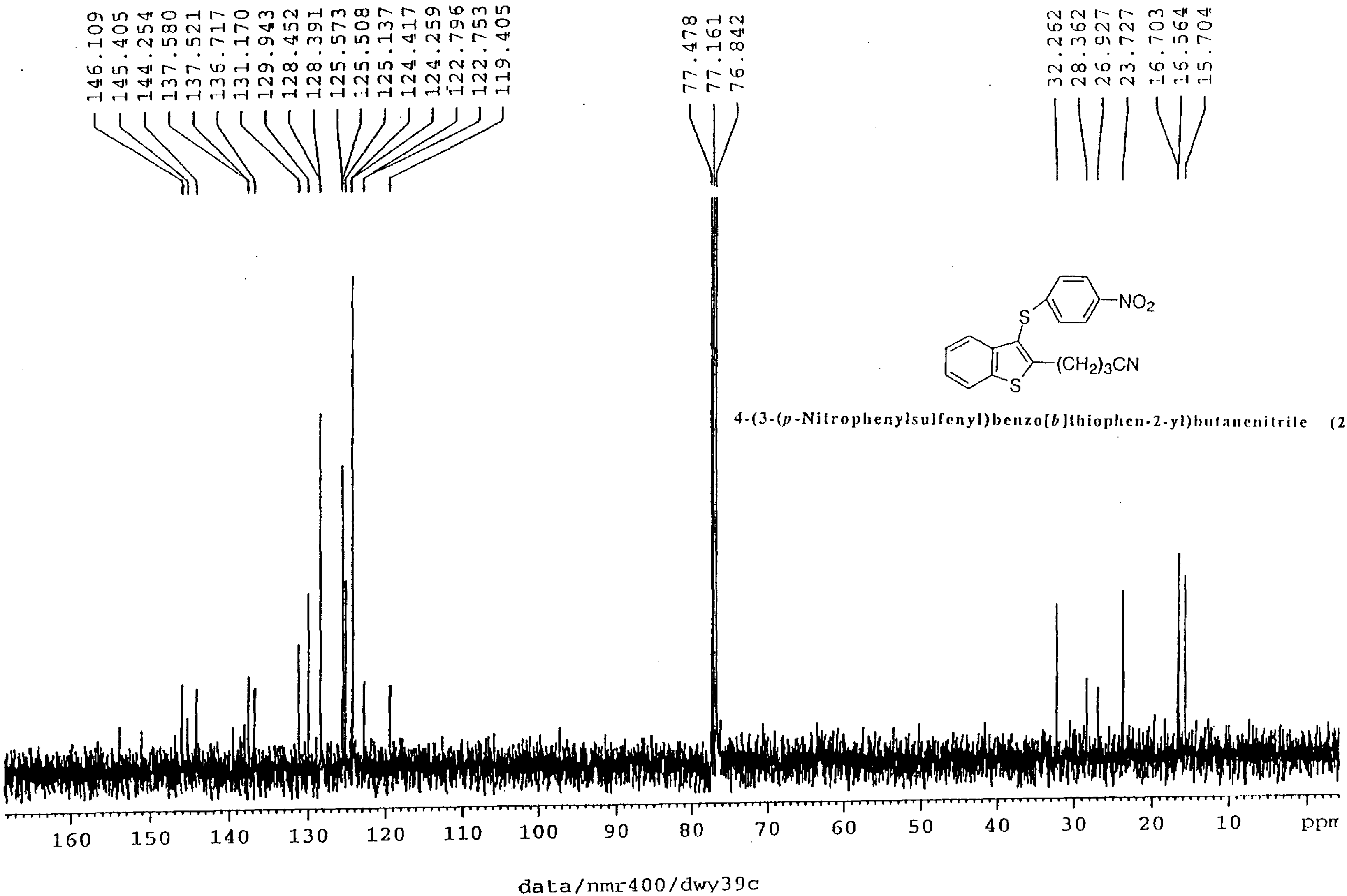
data/nmr400/dwy67



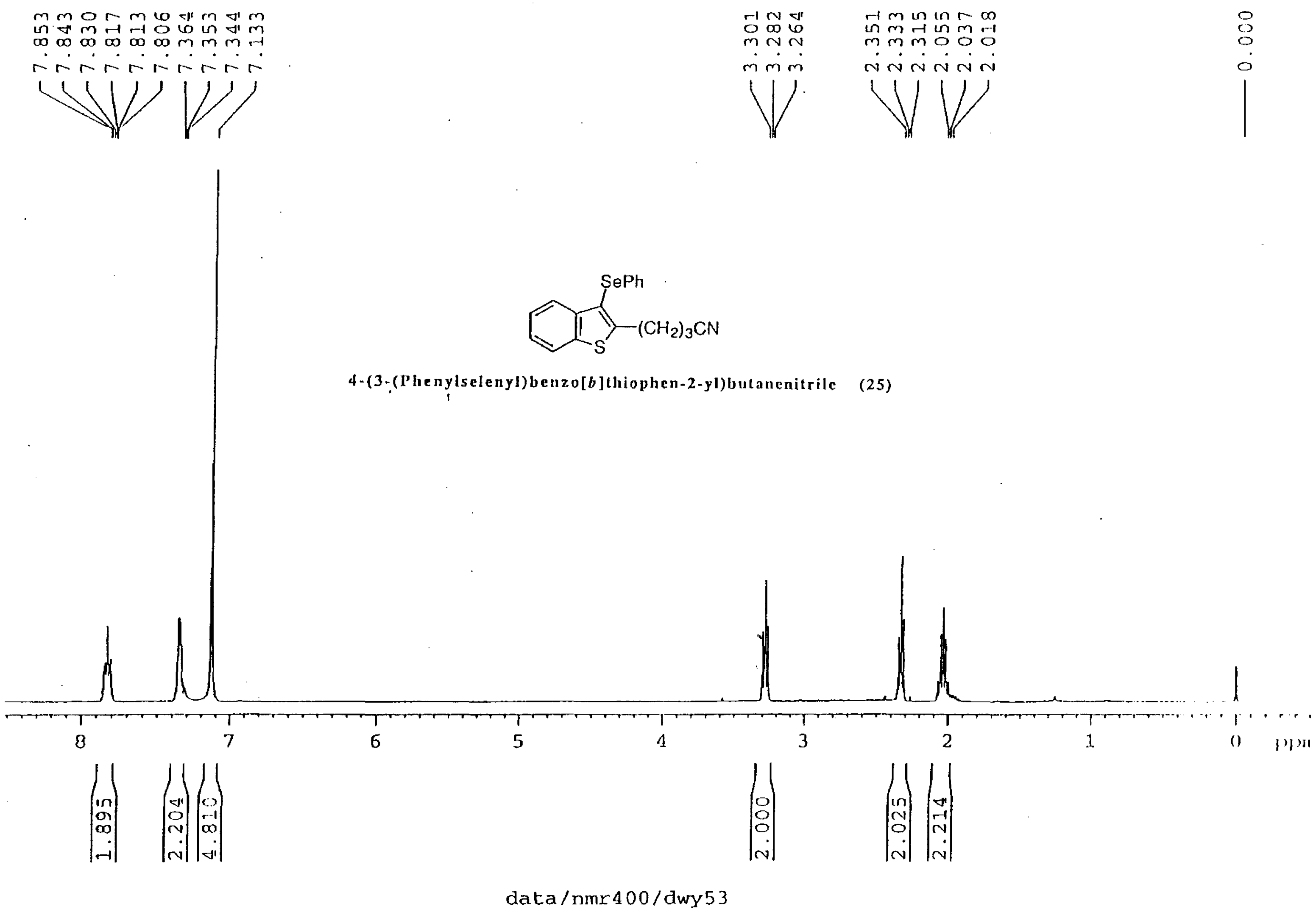
4-(3-Bromobenzo[*b*]thiophen-2-yl)butanenitrile (23)



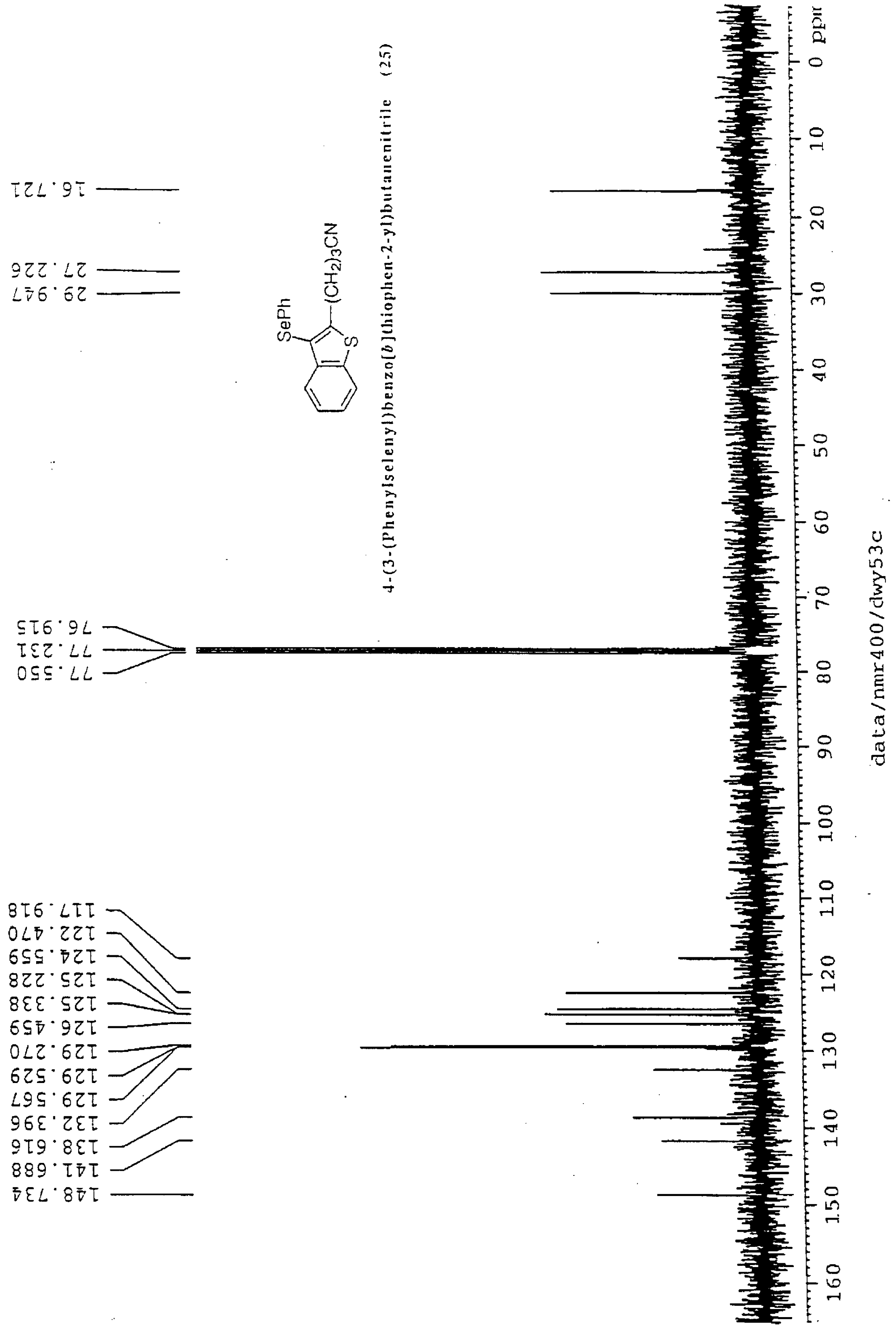
4-(3-(*p*-Nitrophenylsulfenyl)benzo[*b*]thiophen-2-yl)butanenitrile (24)



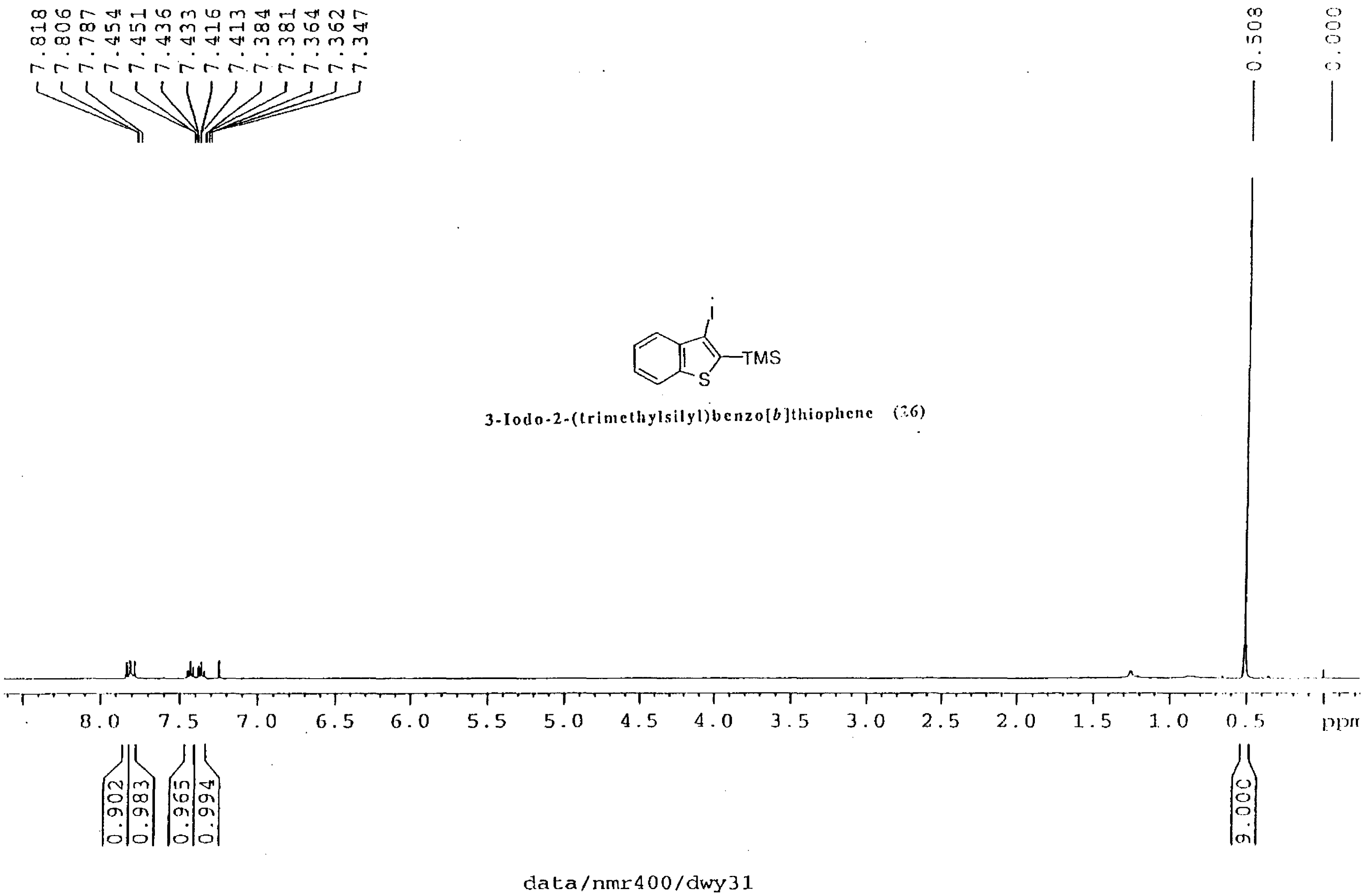
4-(3-(*p*-Nitrophenylsulfenyl)benzo[*b*]thiophen-2-yl)butanenitrile (24)



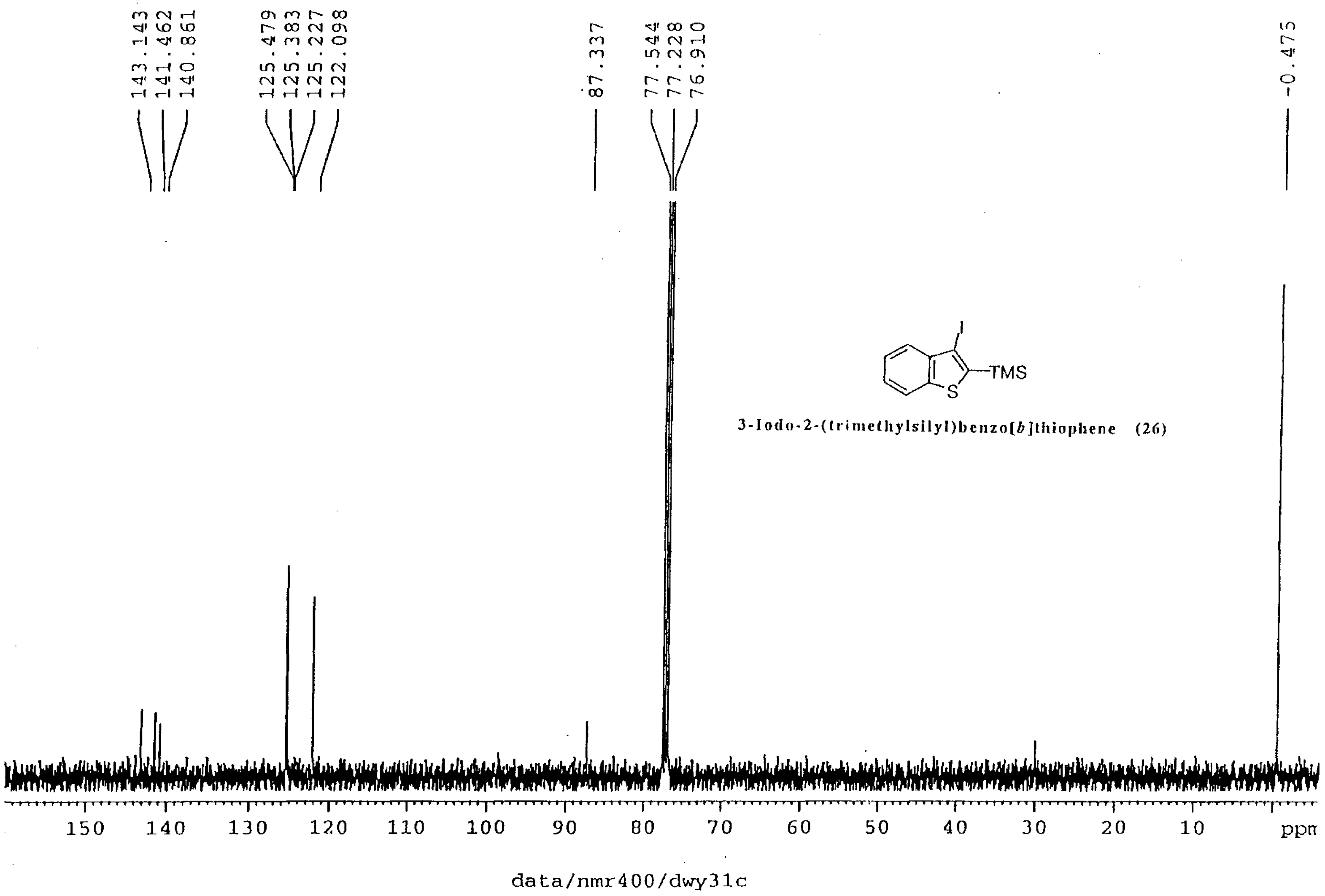
4-(3-(Phenylselenyl)benzo[*b*]thiophen-2-yl)butanenitrile (25)



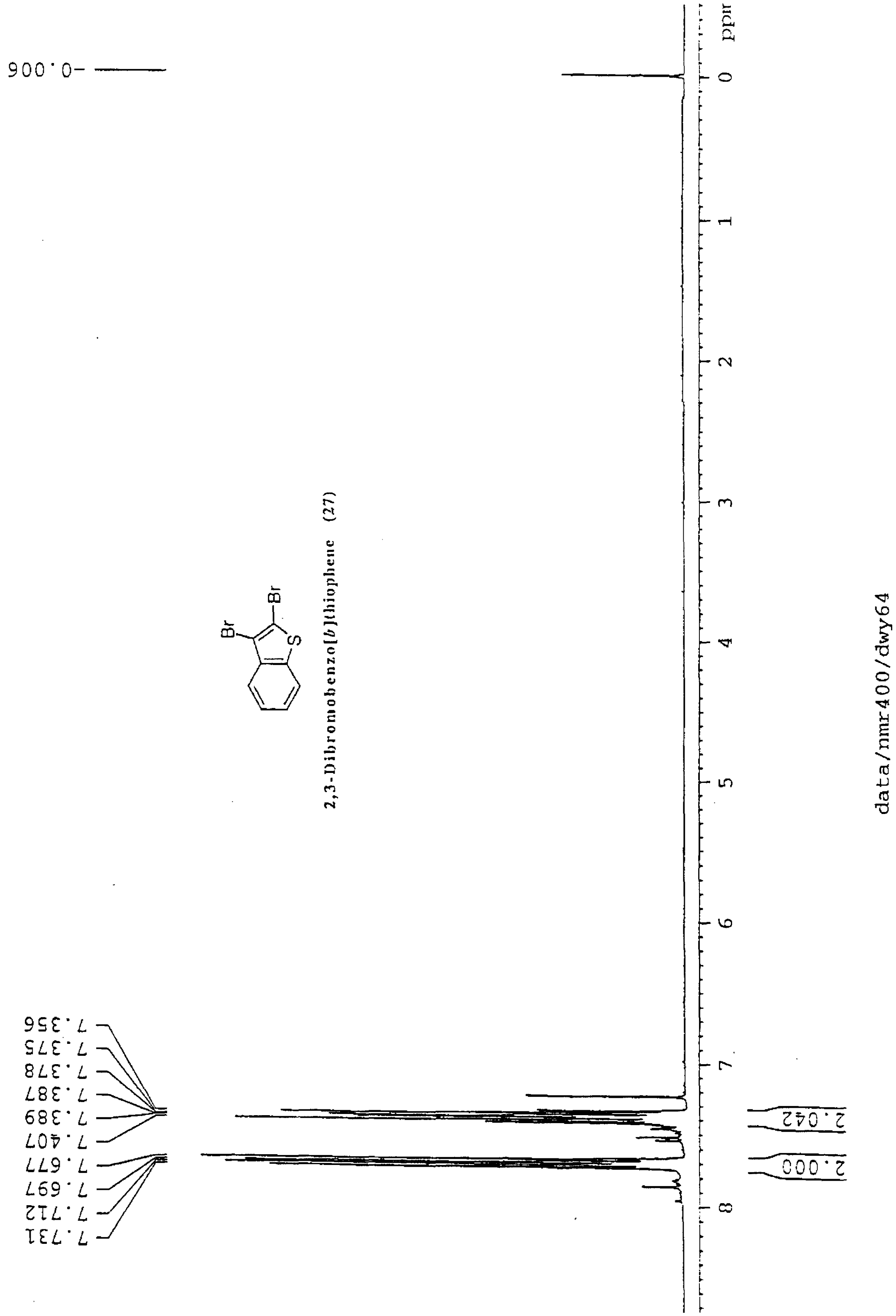
4-(3-(Phenylselenyl)benzo[*b*]thiophen-2-yl)butanenitrile (25)



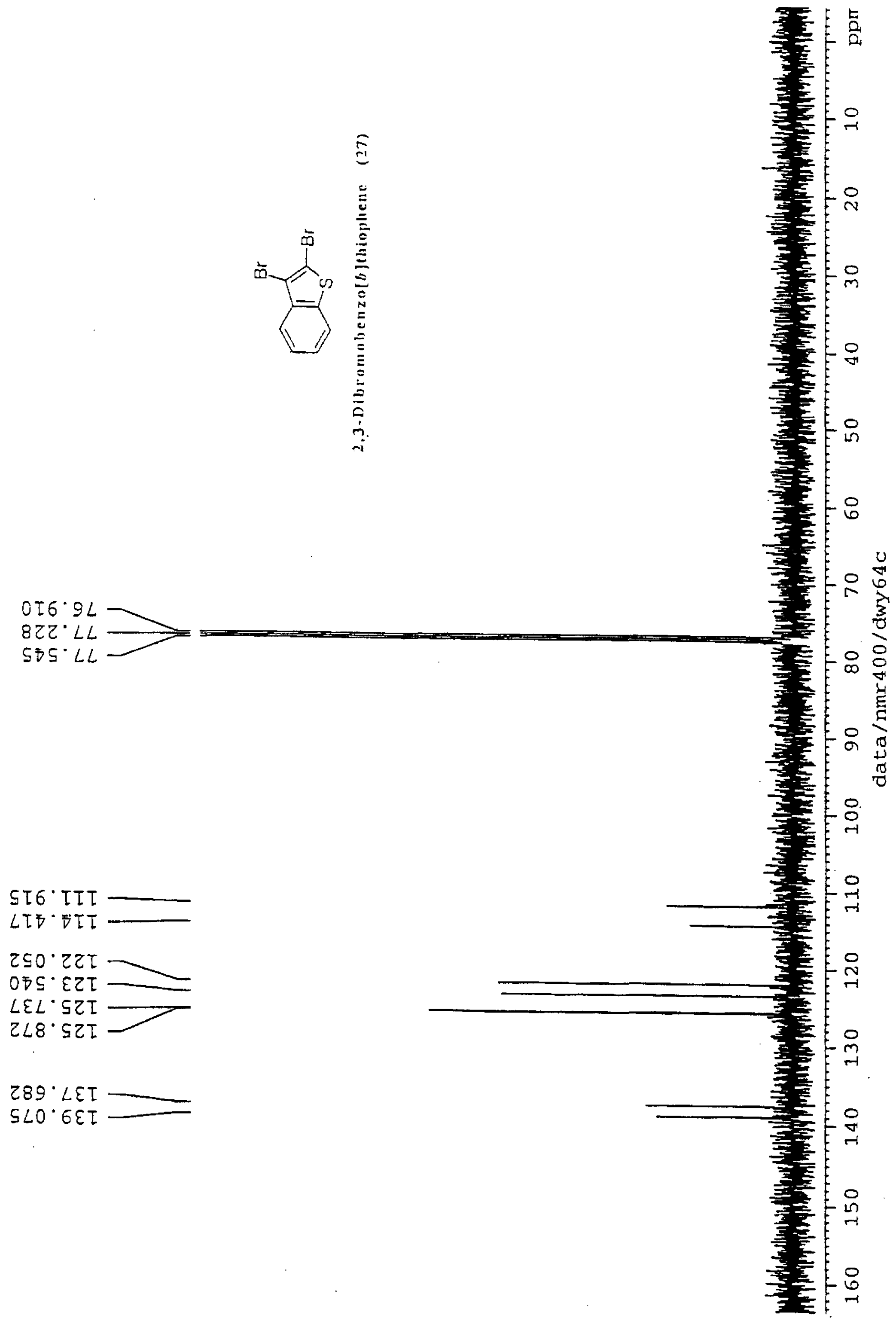
3-Iodo-2-(trimethylsilyl)benzo[*b*]thiophene (36)



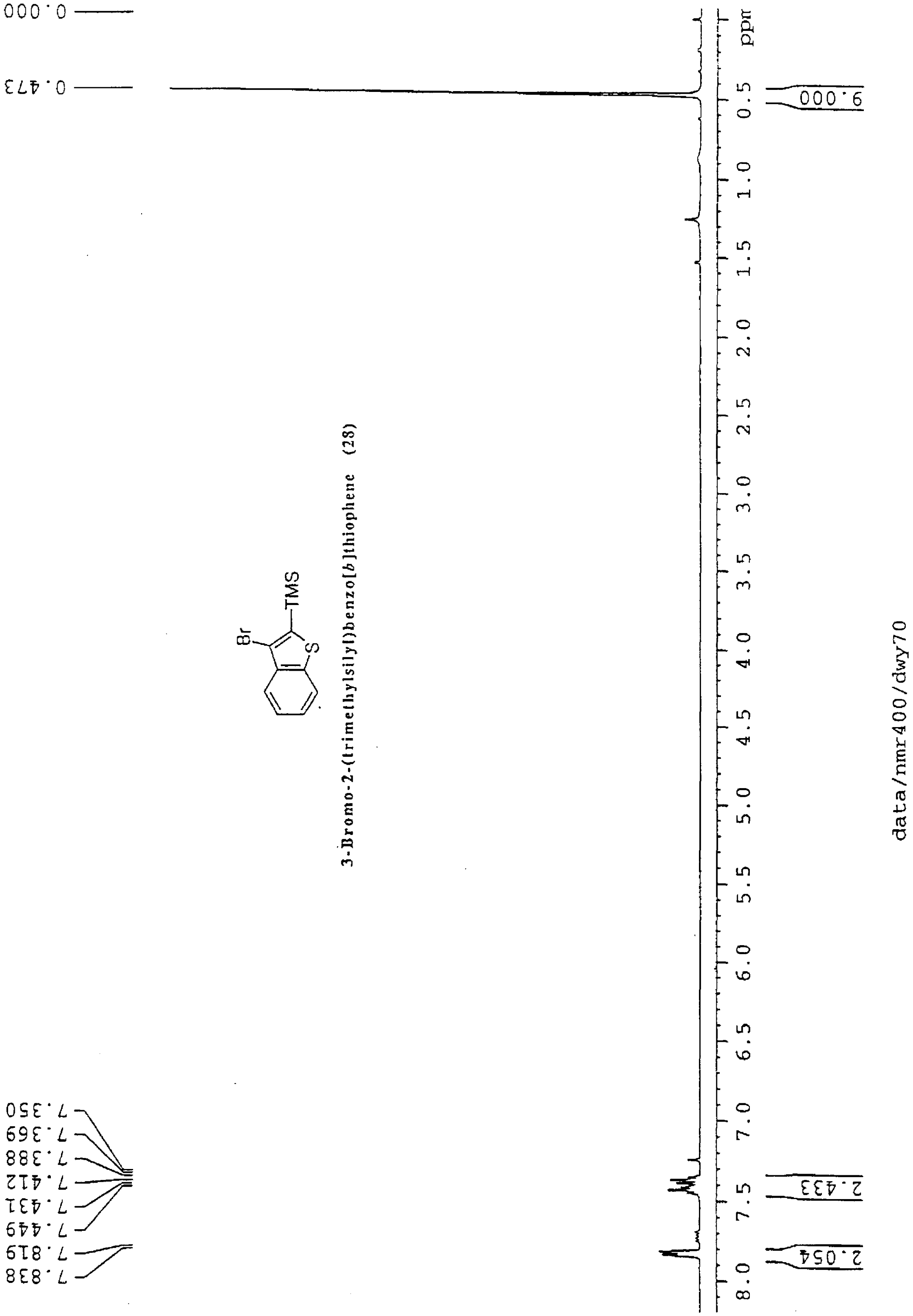
3-Iodo-2-(trimethylsilyl)benzo[*b*]thiophene (26)



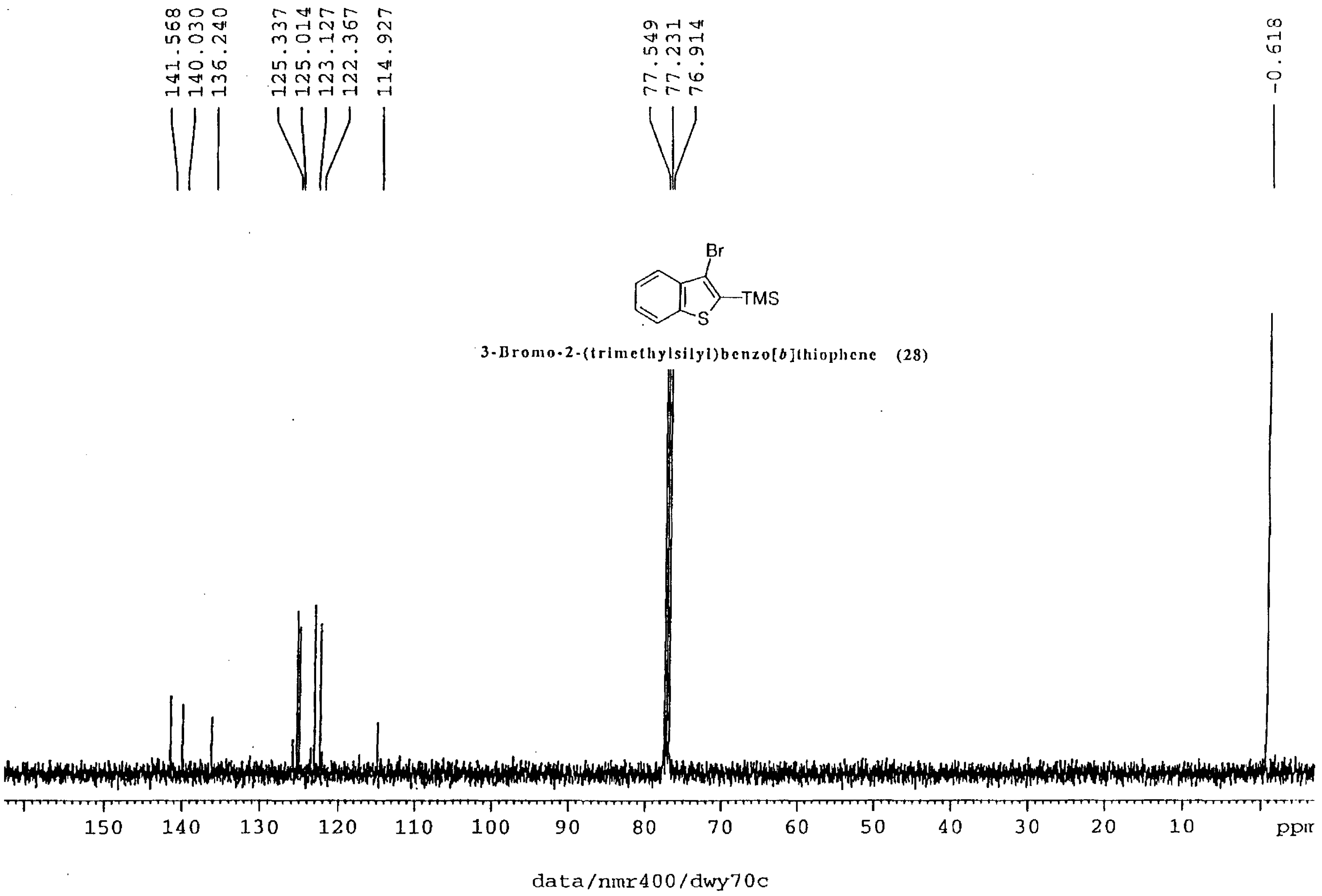
2,3-Dibromobenzo[*b*]thiophene (27)



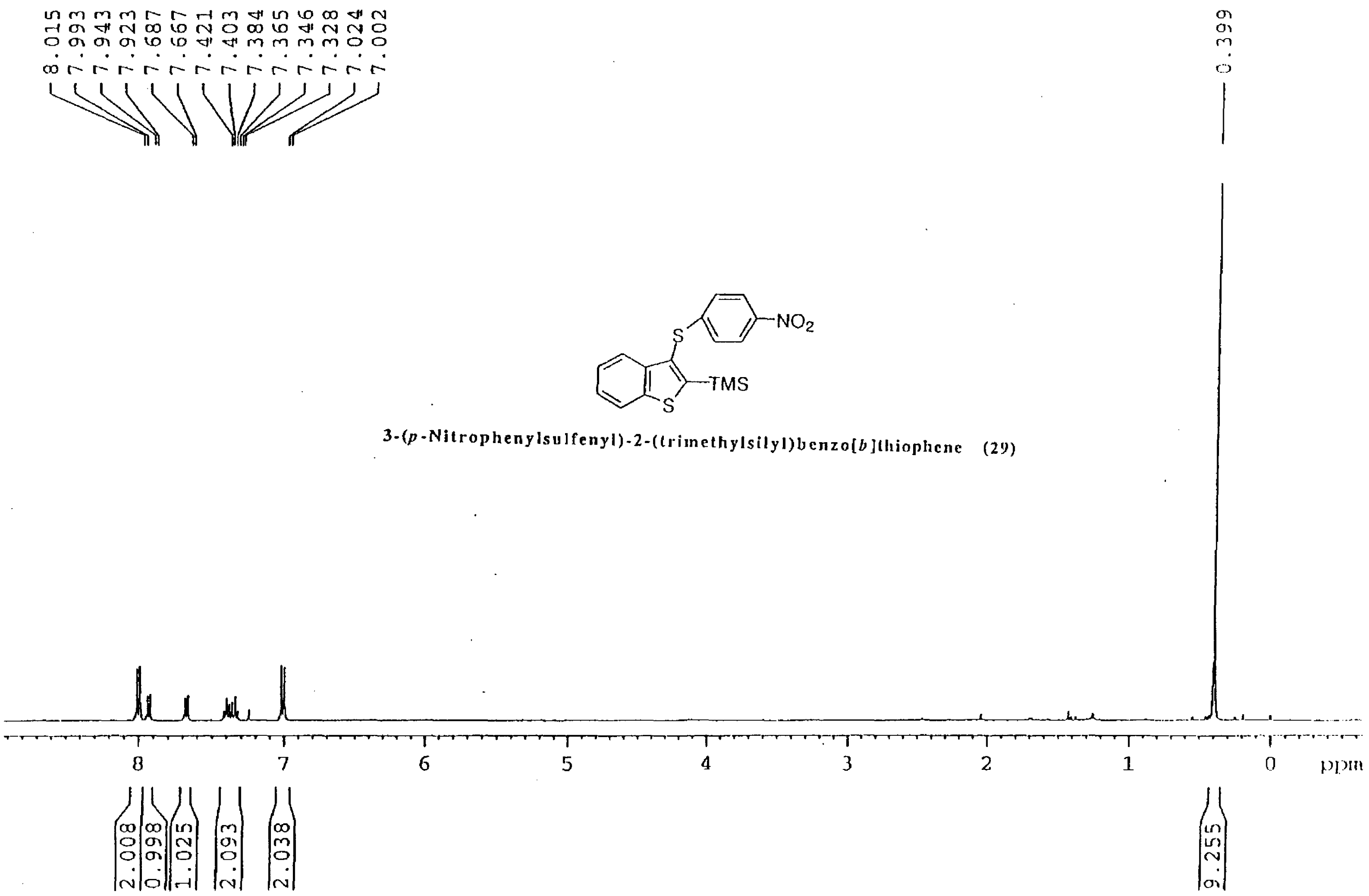
2,3-Dibromobenzo[b]thiophene (27)



3-Bromo-2-(trimethylsilyl)benzo[*b*]thiophene (28)

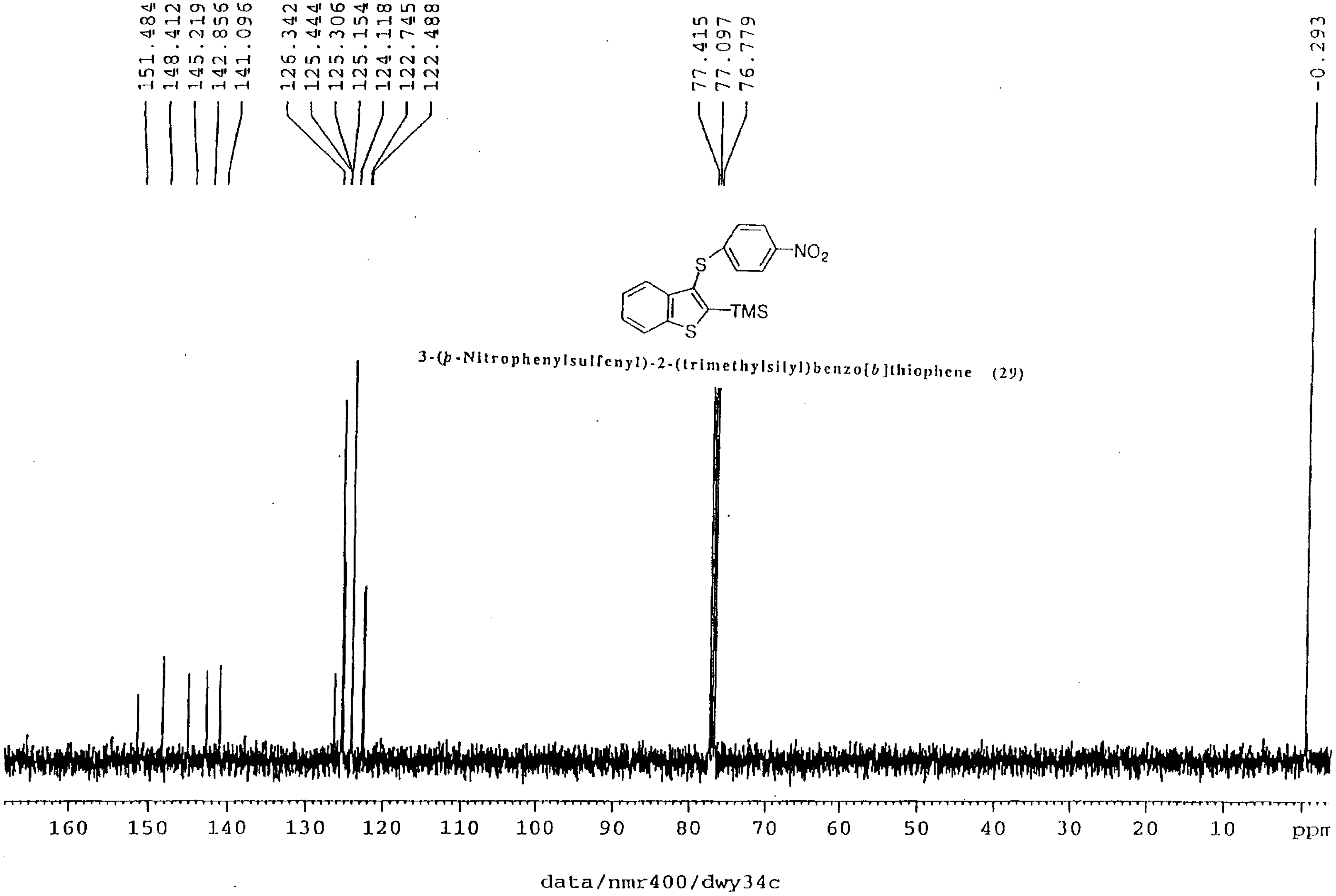


3-Bromo-2-(trimethylsilyl)benzo[*b*]thiophene (28)

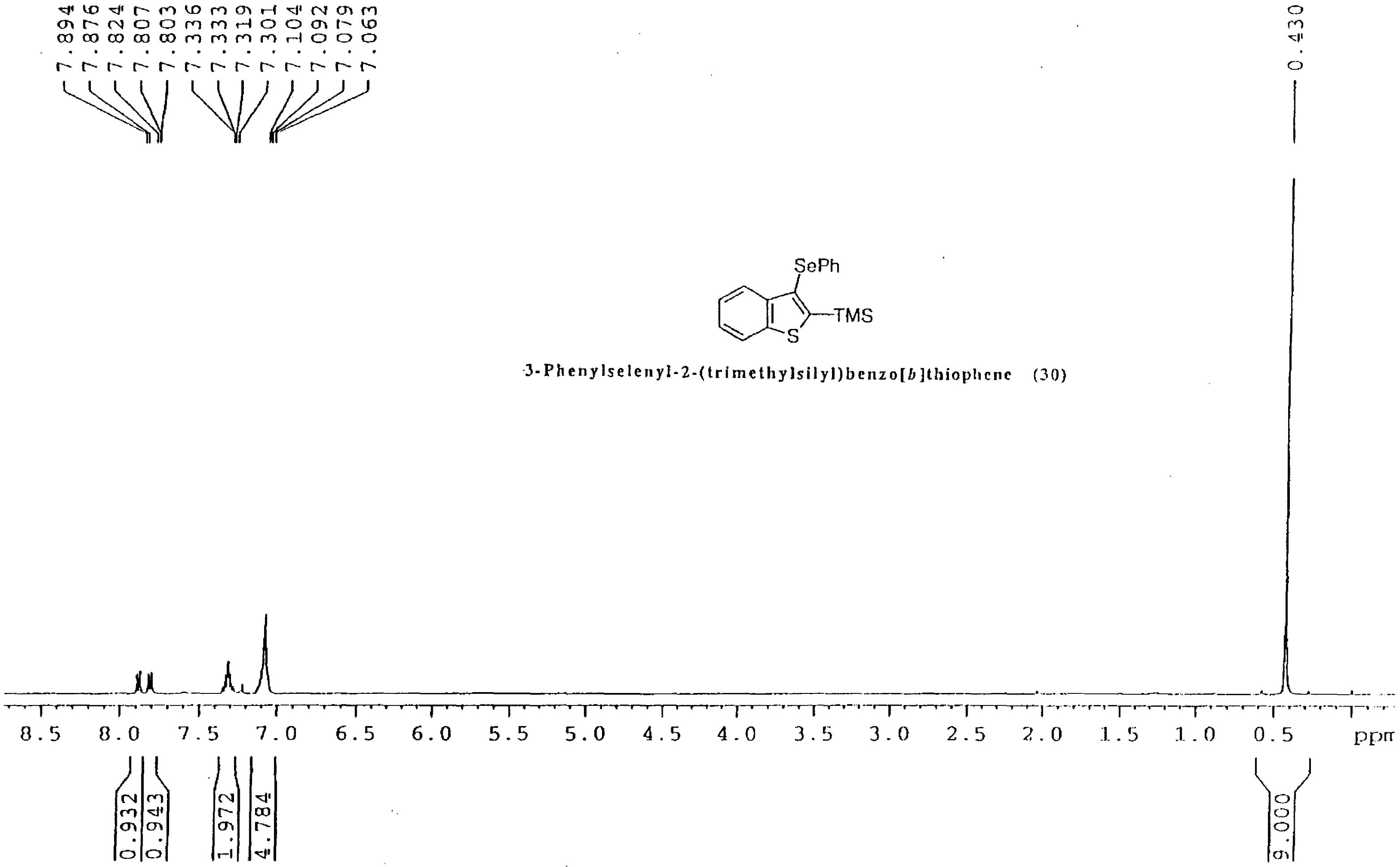


3-(*p*-Nitrophenylsulfenyl)-2-(trimethylsilyl)benzo[*b*]thiophene (29)

data/nmr400/dwy34

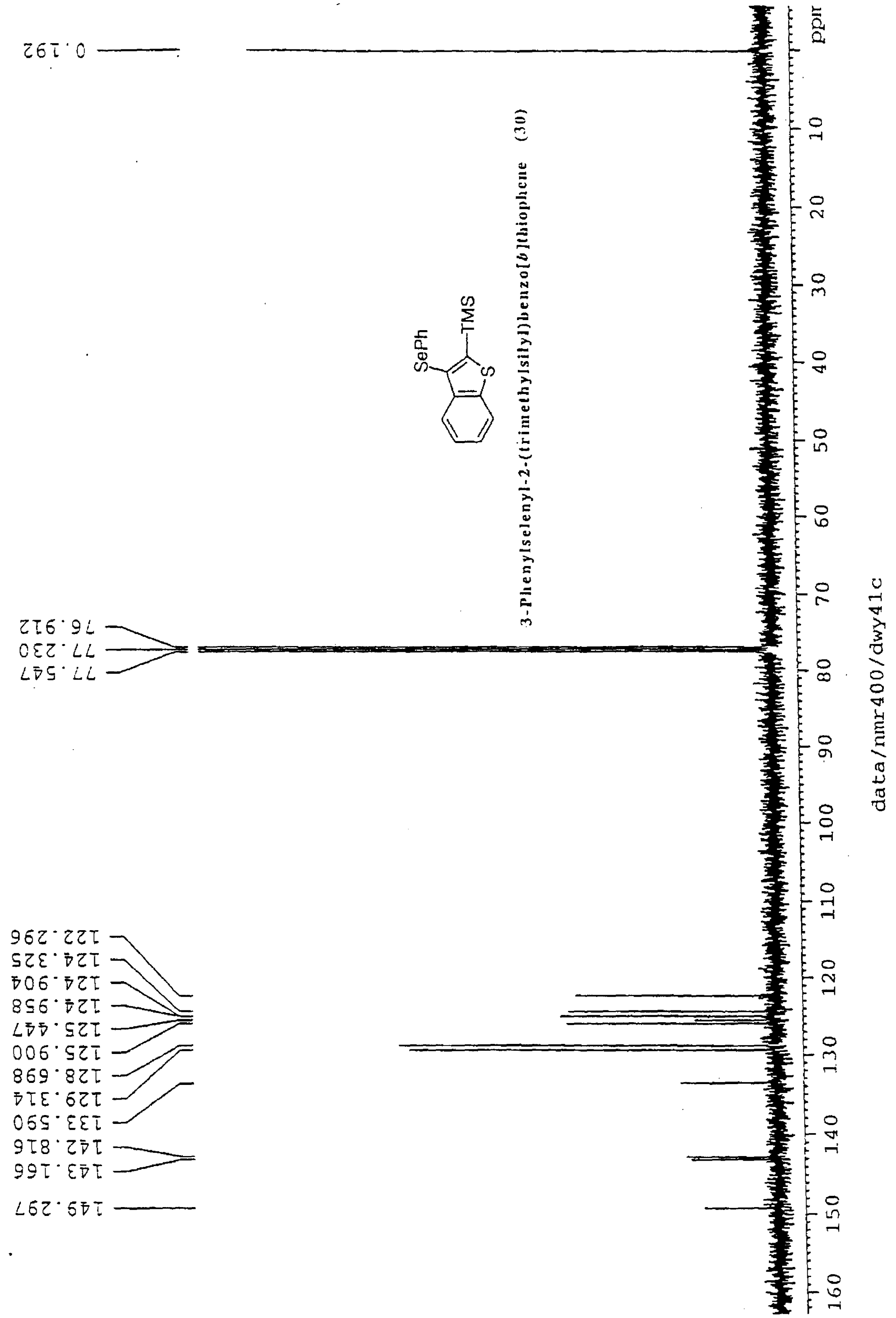


3-(*p*-Nitrophenylsulfenyl)-2-(trimethylsilyl)benzo[*b*]thiophene (29)

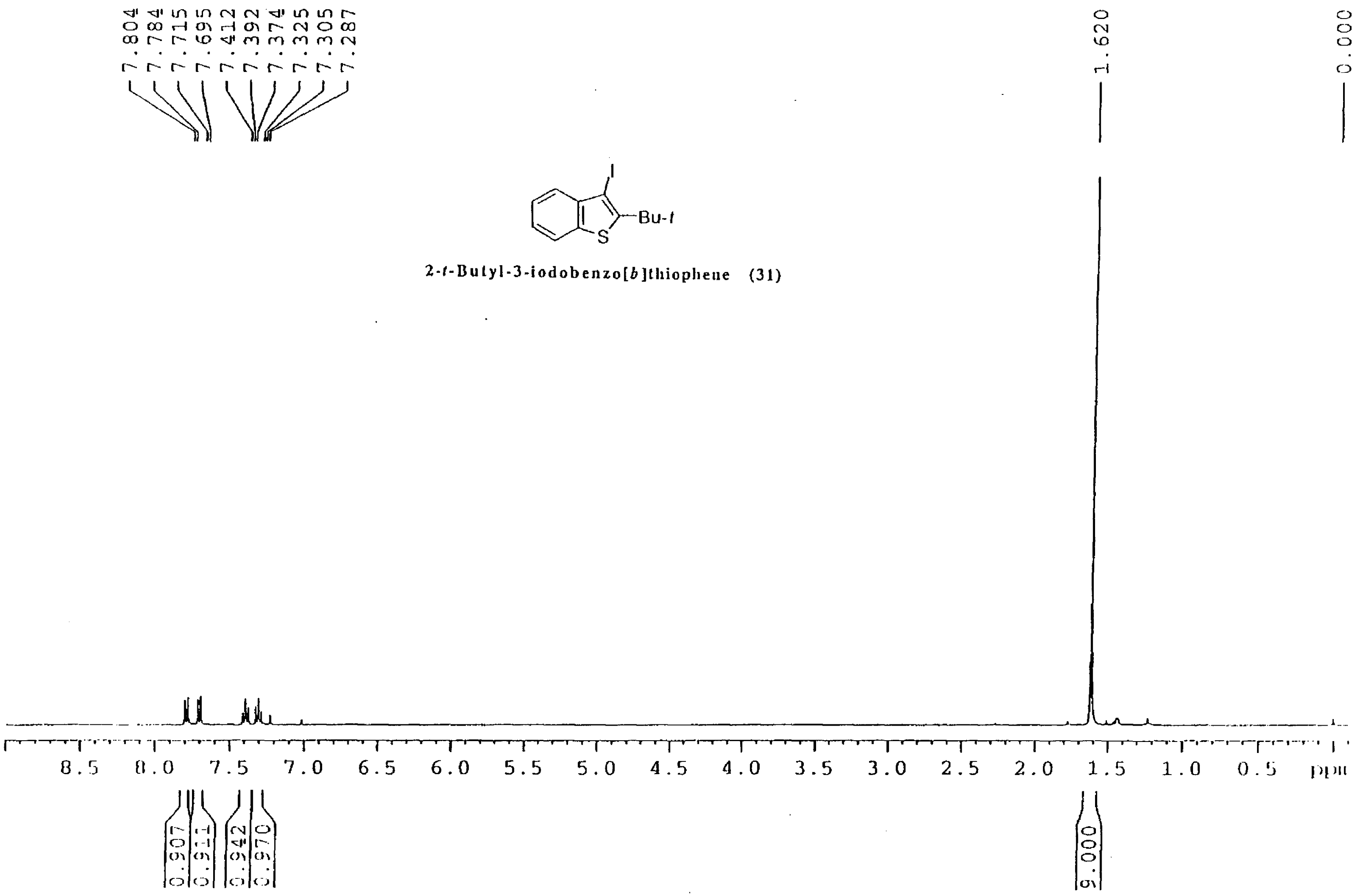


3-Phenylselenyl-2-(trimethylsilyl)benzo[*b*]thiophene (30)

data/nmr400/dwy41

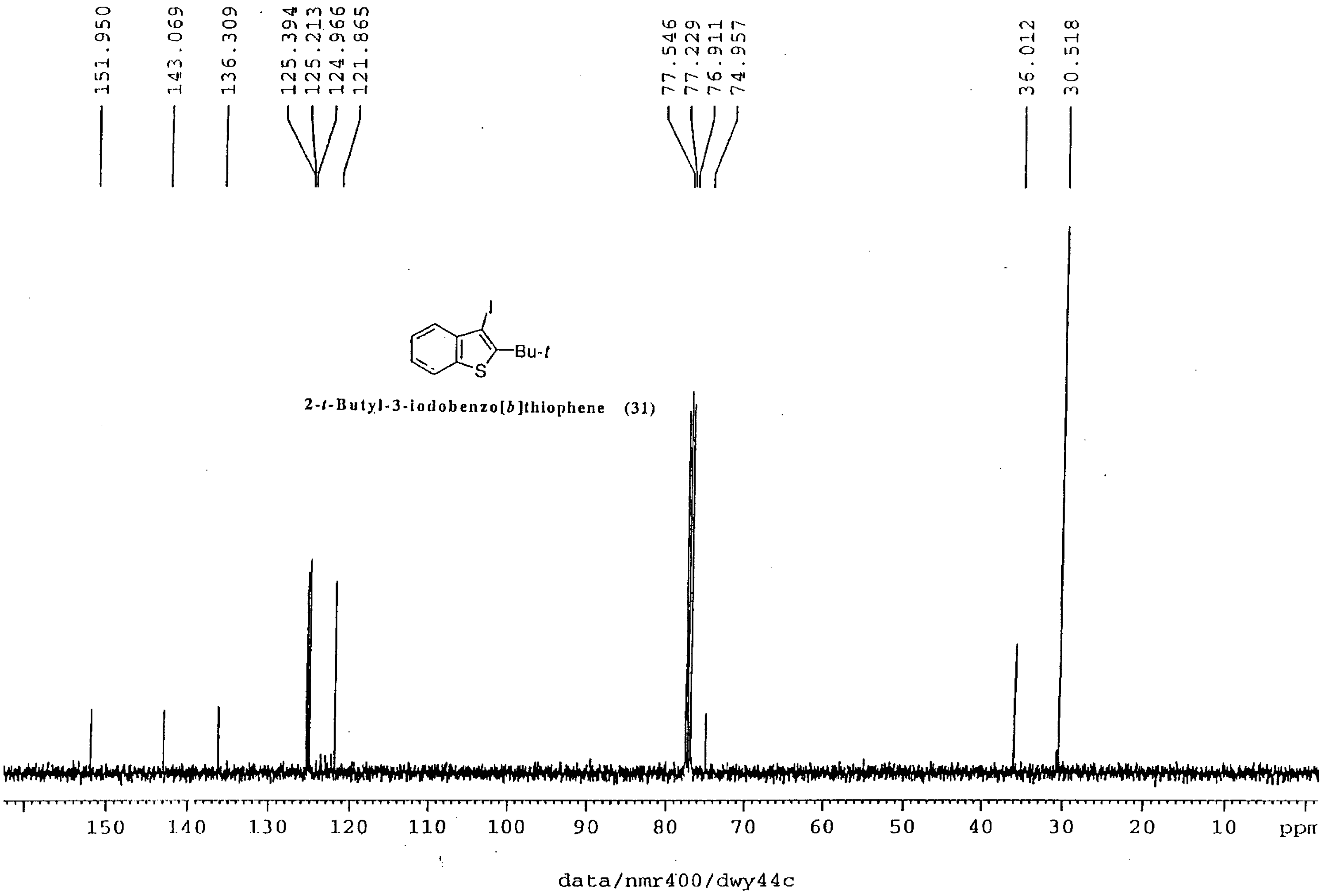


3-Phenylselenyl-2-(trimethylsilyl)benzo[*b*]thiophene (30)

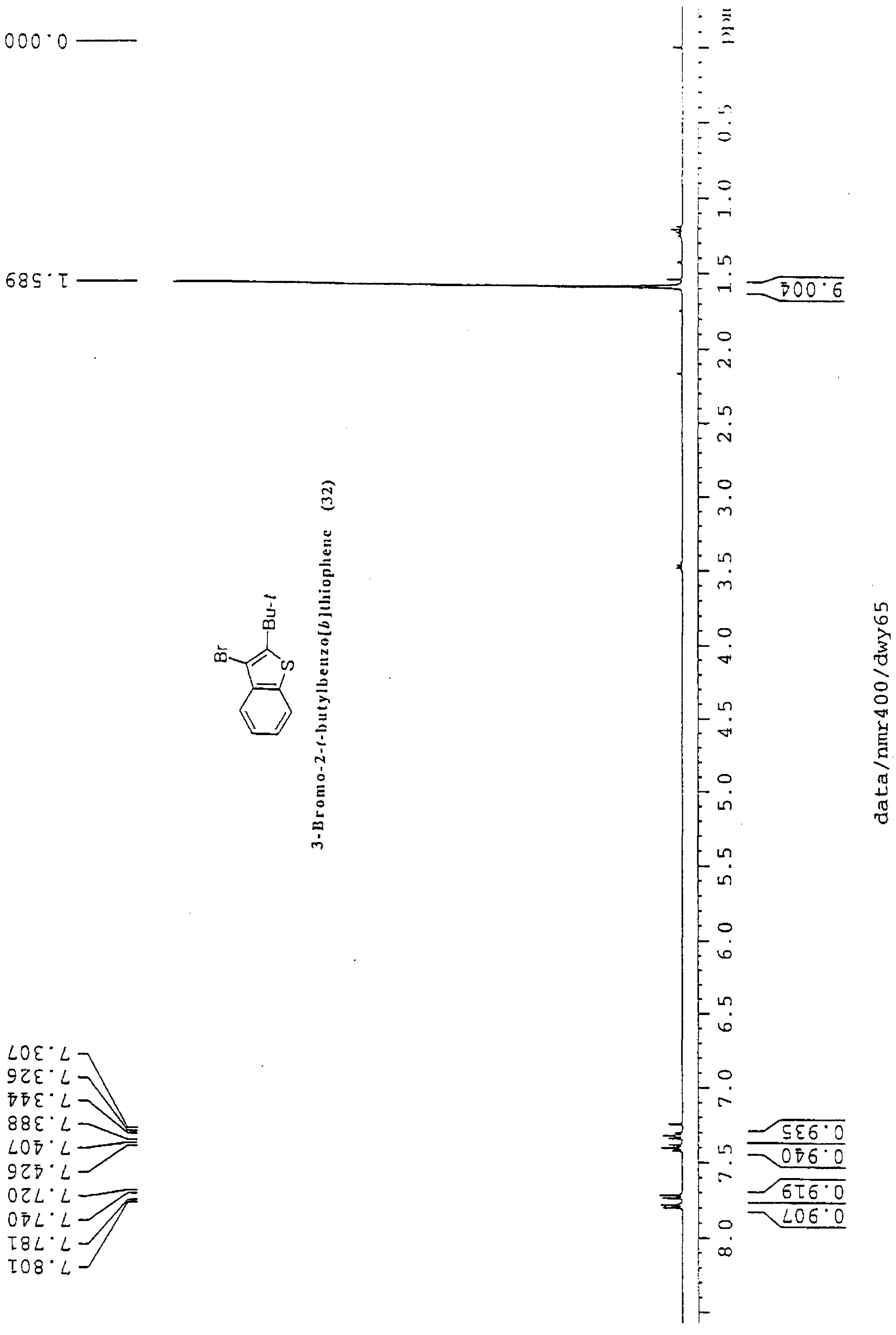


2-*t*-Butyl-3-iodobenzo[*b*]thiophene (31)

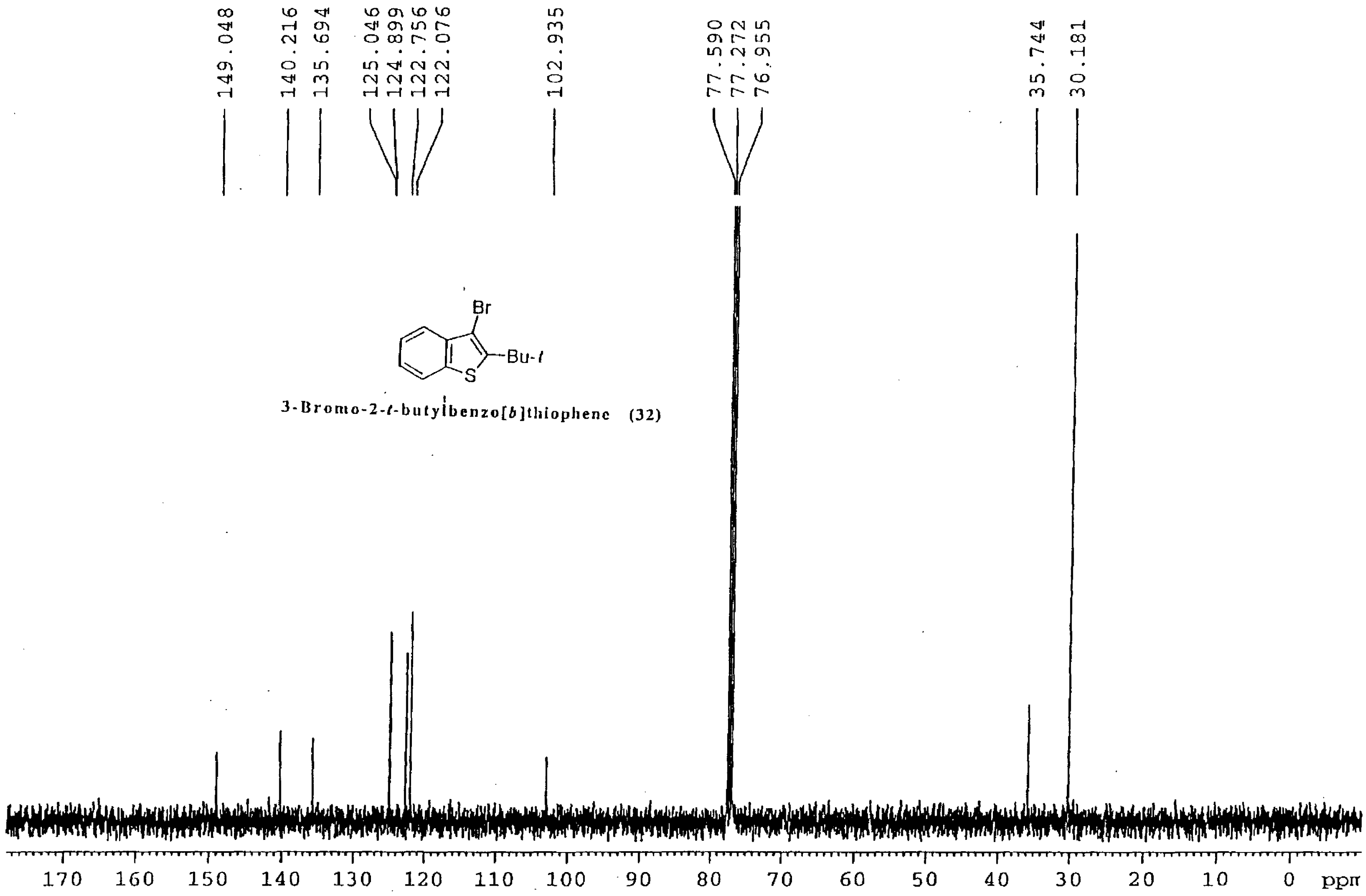
data/nmr400/dwy44



2-*t*-Butyl-3-iodobenzo[*b*]thiophene (31)

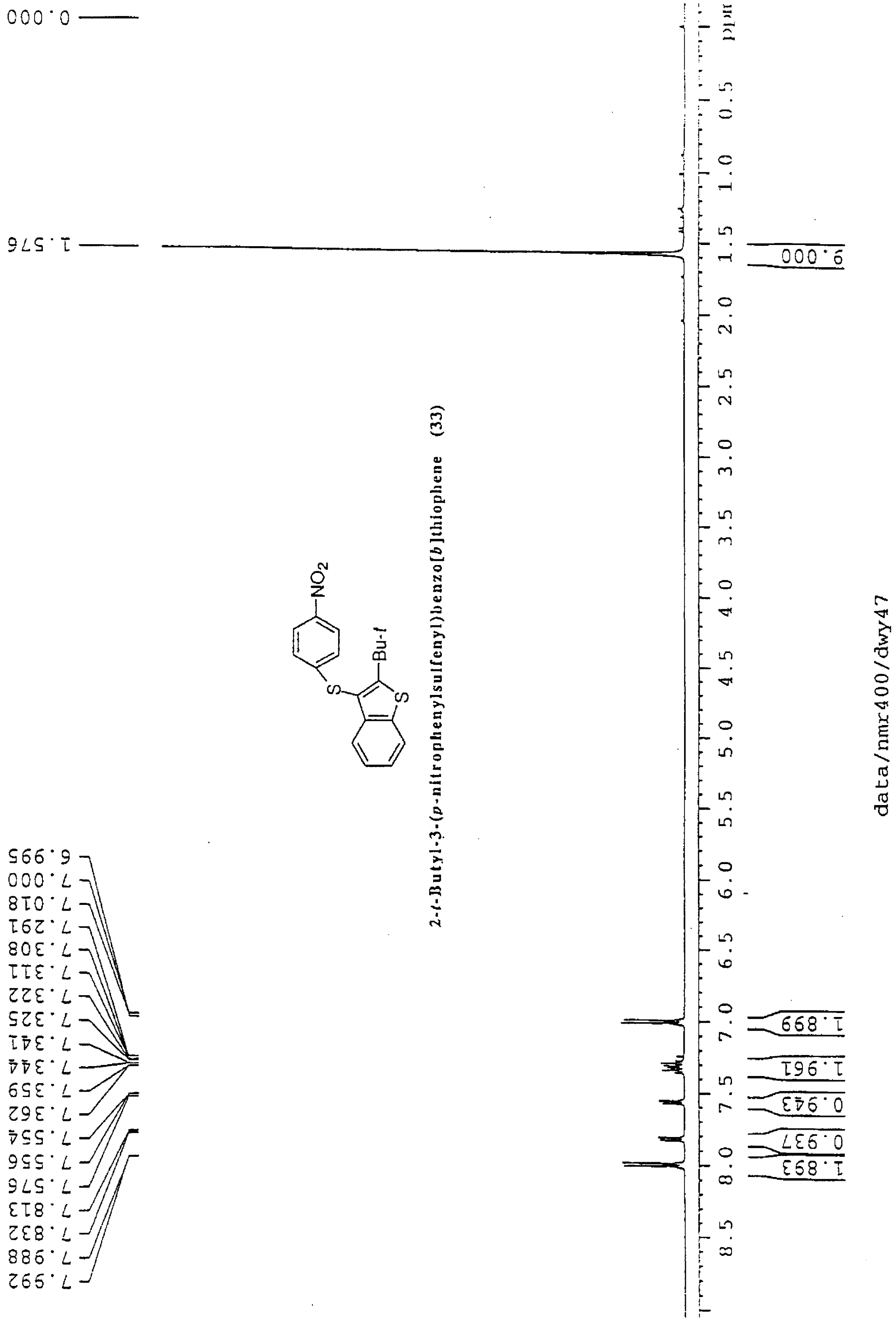


3-Bromo-2-*t*-butylbenzo[*b*]thiophene (32)

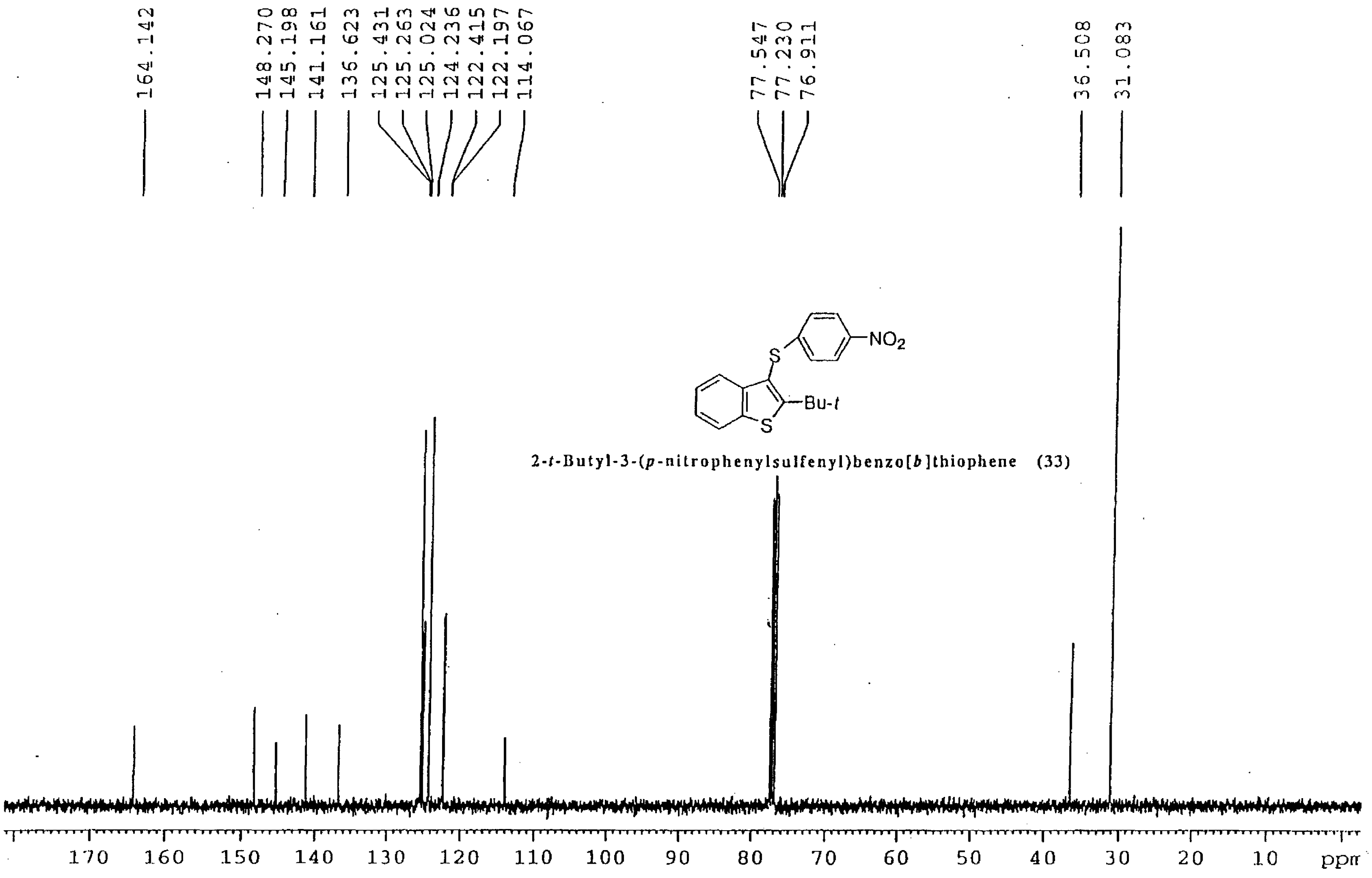


3-Bromo-2-*t*-butylbenzo[*b*]thiophene (32)

data/nmr400/dwy65c

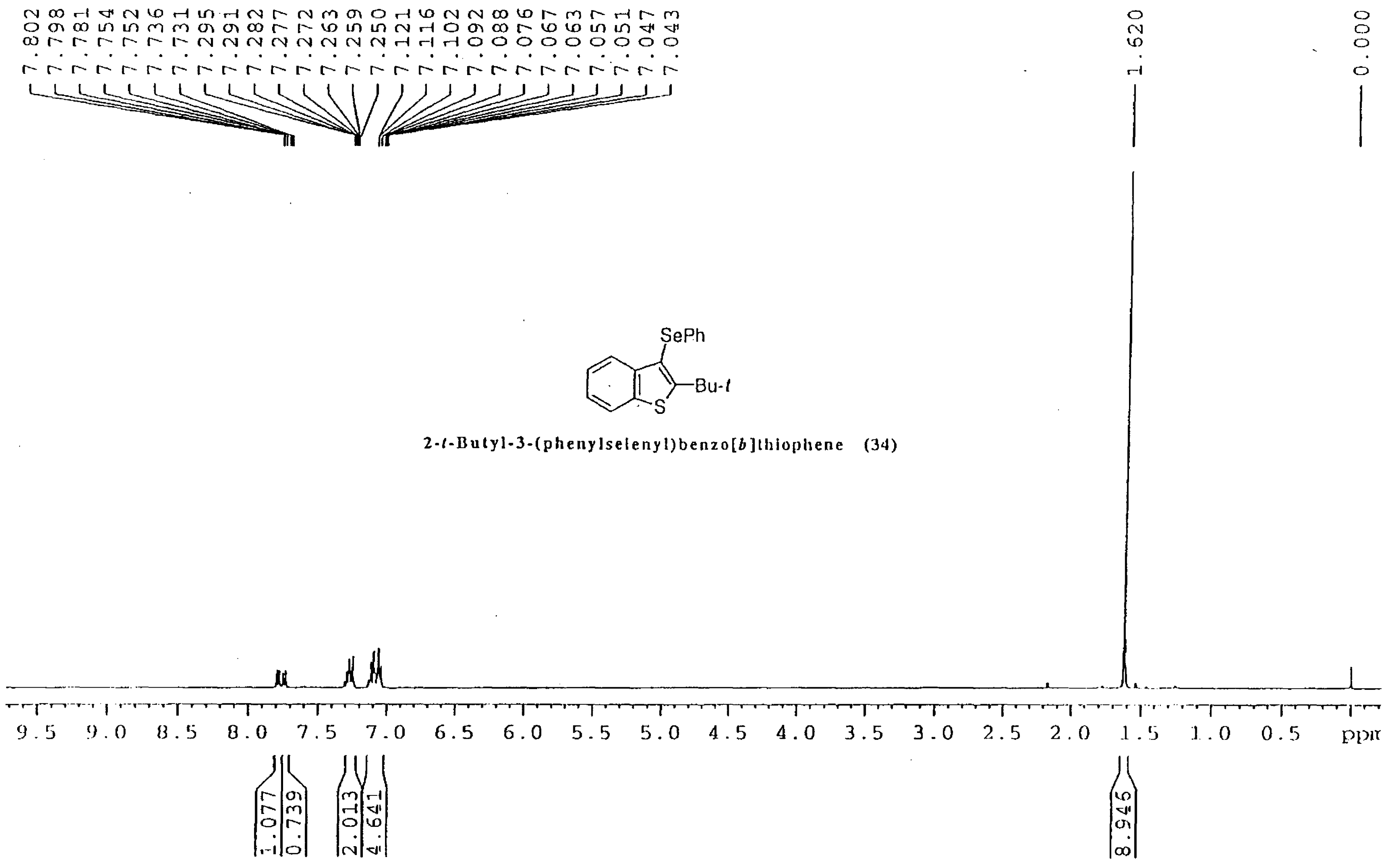


2-*t*-Butyl-3-(*p*-nitrophenylsulfenyl)benzo[*b*]thiophene (33)



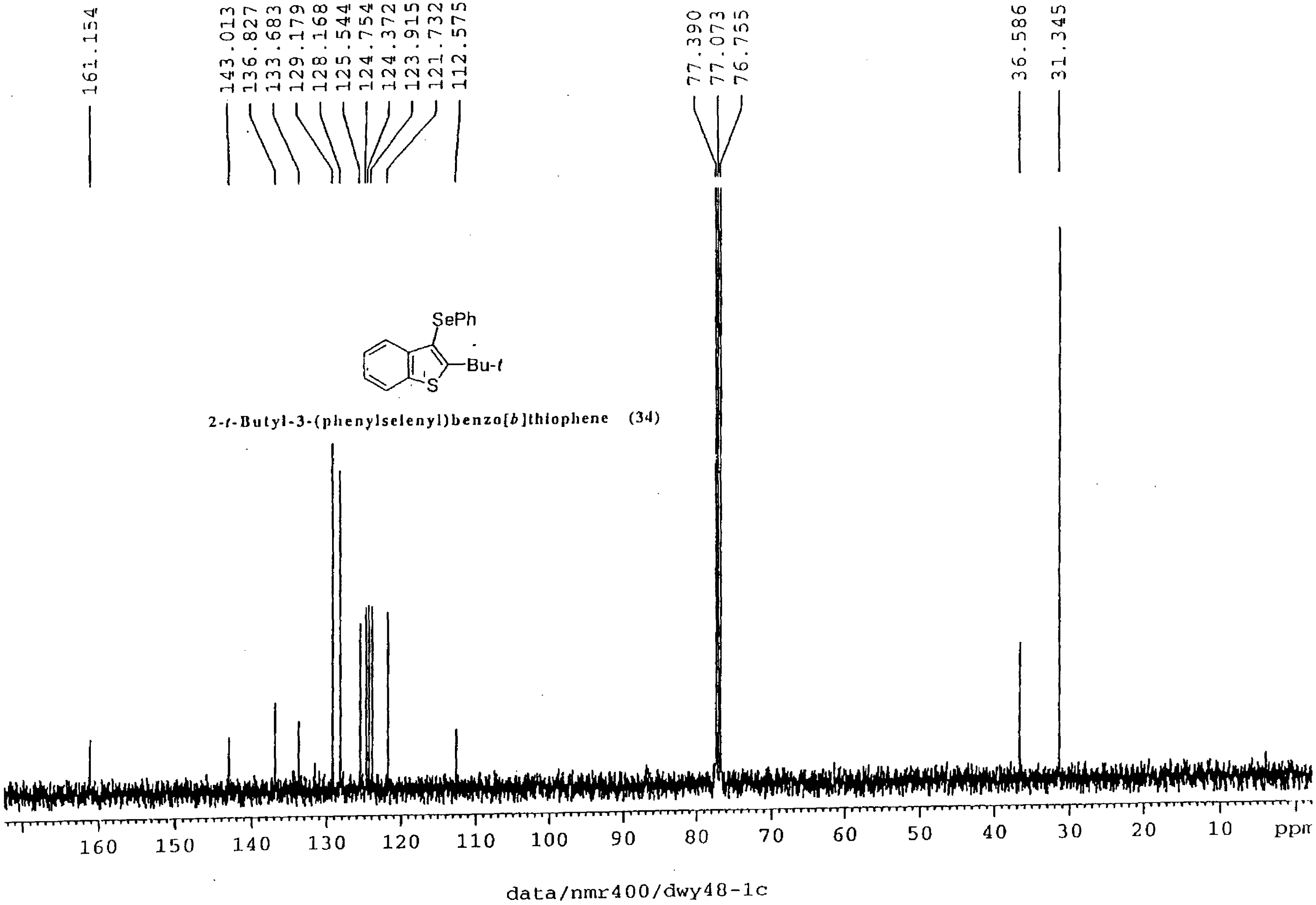
2-*t*-Butyl-3-(*p*-nitrophenylsulfenyl)benzo[*b*]thiophene (33)

data/nmr400/dwy47c

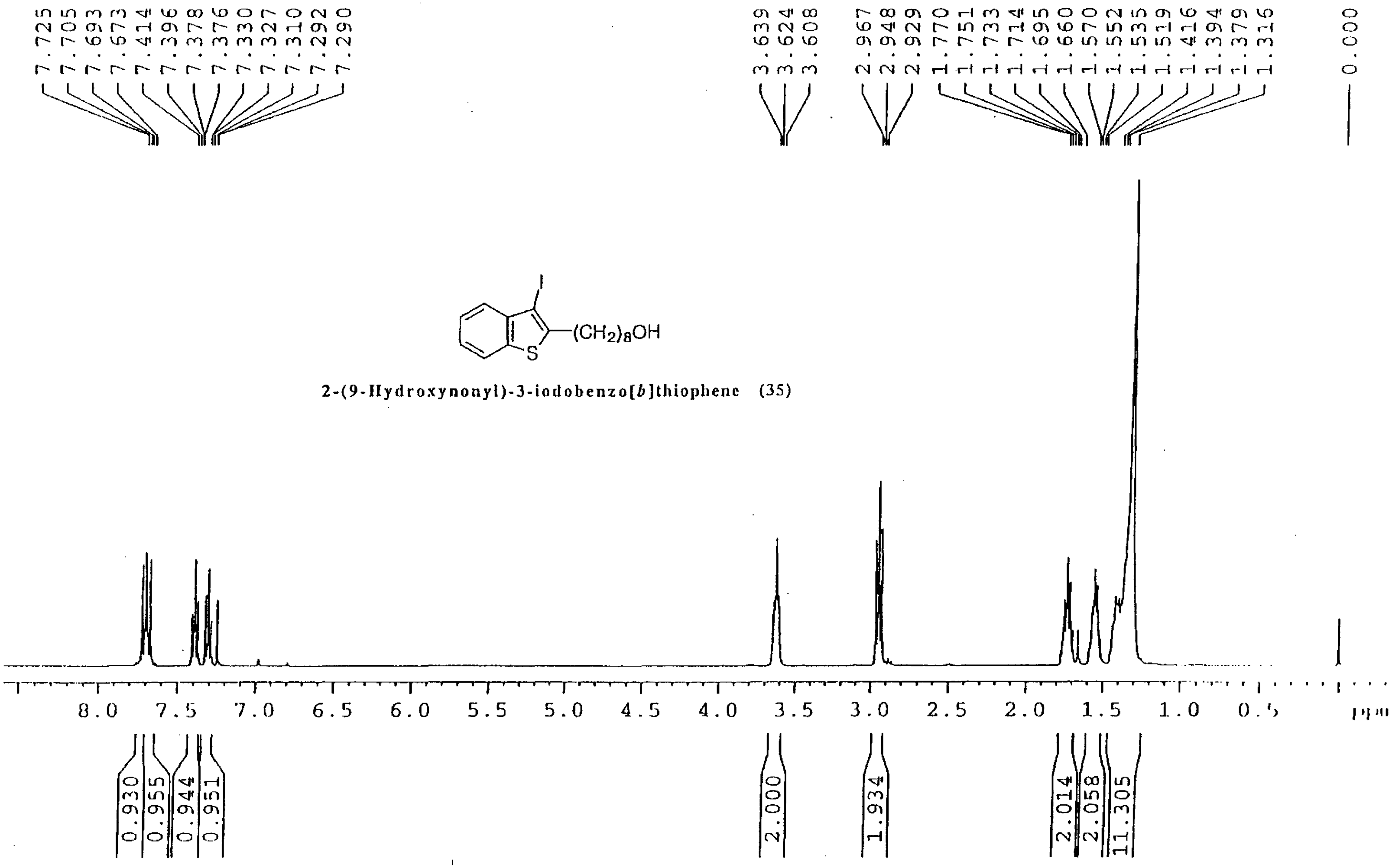


2-*t*-Butyl-3-(phenylselenyl)benzo[*b*]thiophene (34)

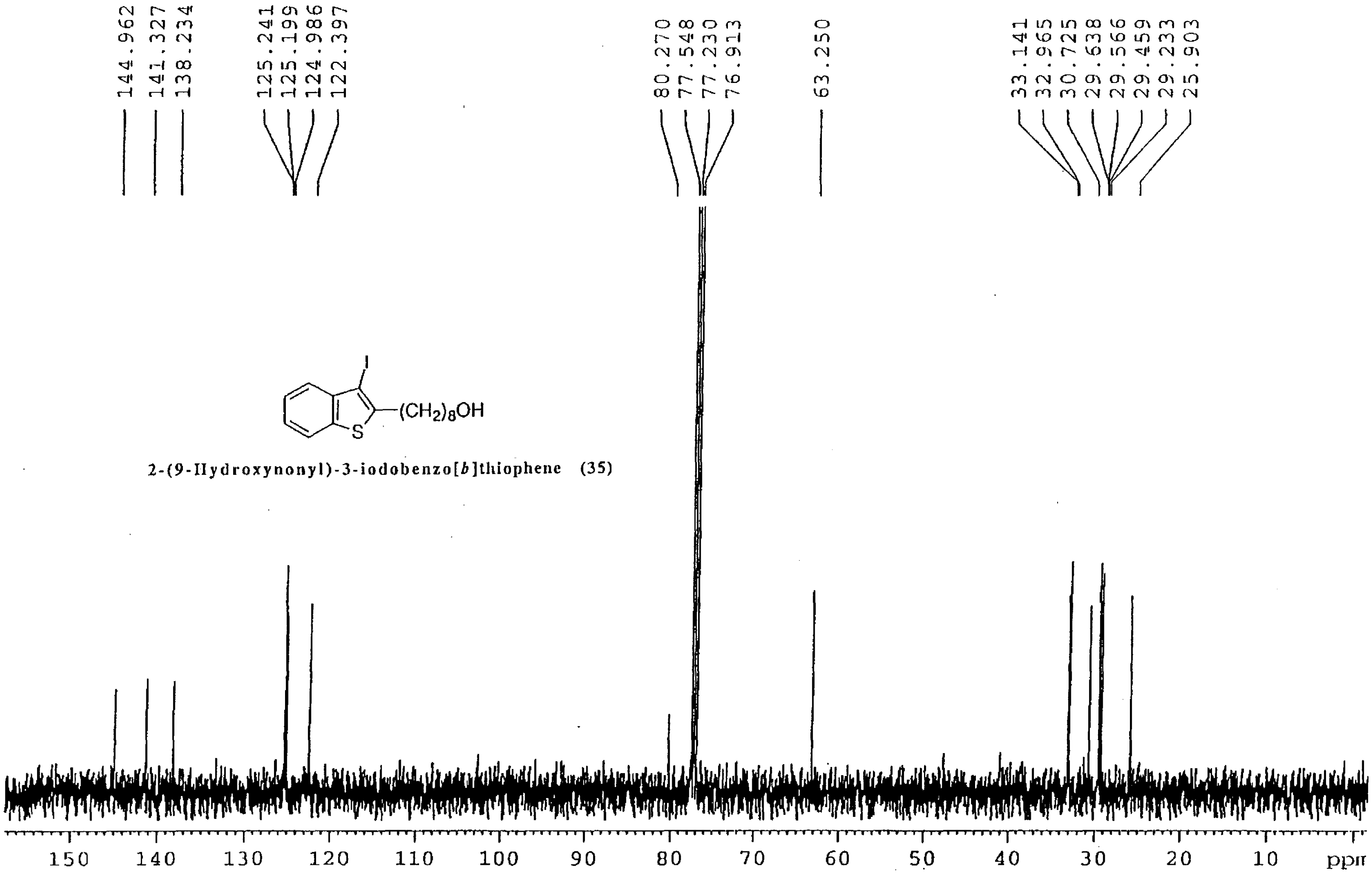
data/nmr400/dwy48-1



2-*t*-Butyl-3-(phenylselenyl)benzo[*b*]thiophene (34)

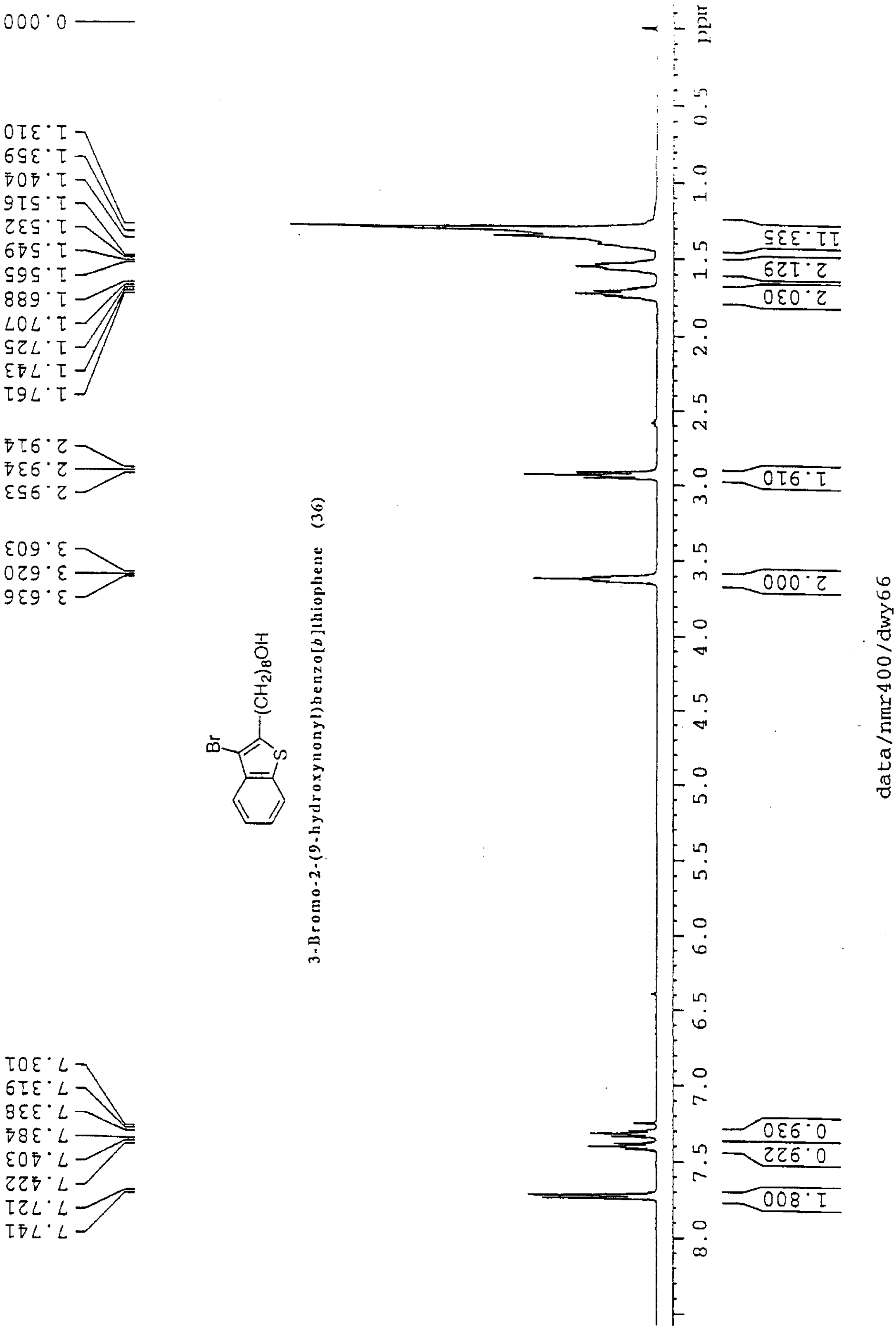


2-(9-Hydroxynonyl)-3-iodobenzo[*b*]thiophene (35)

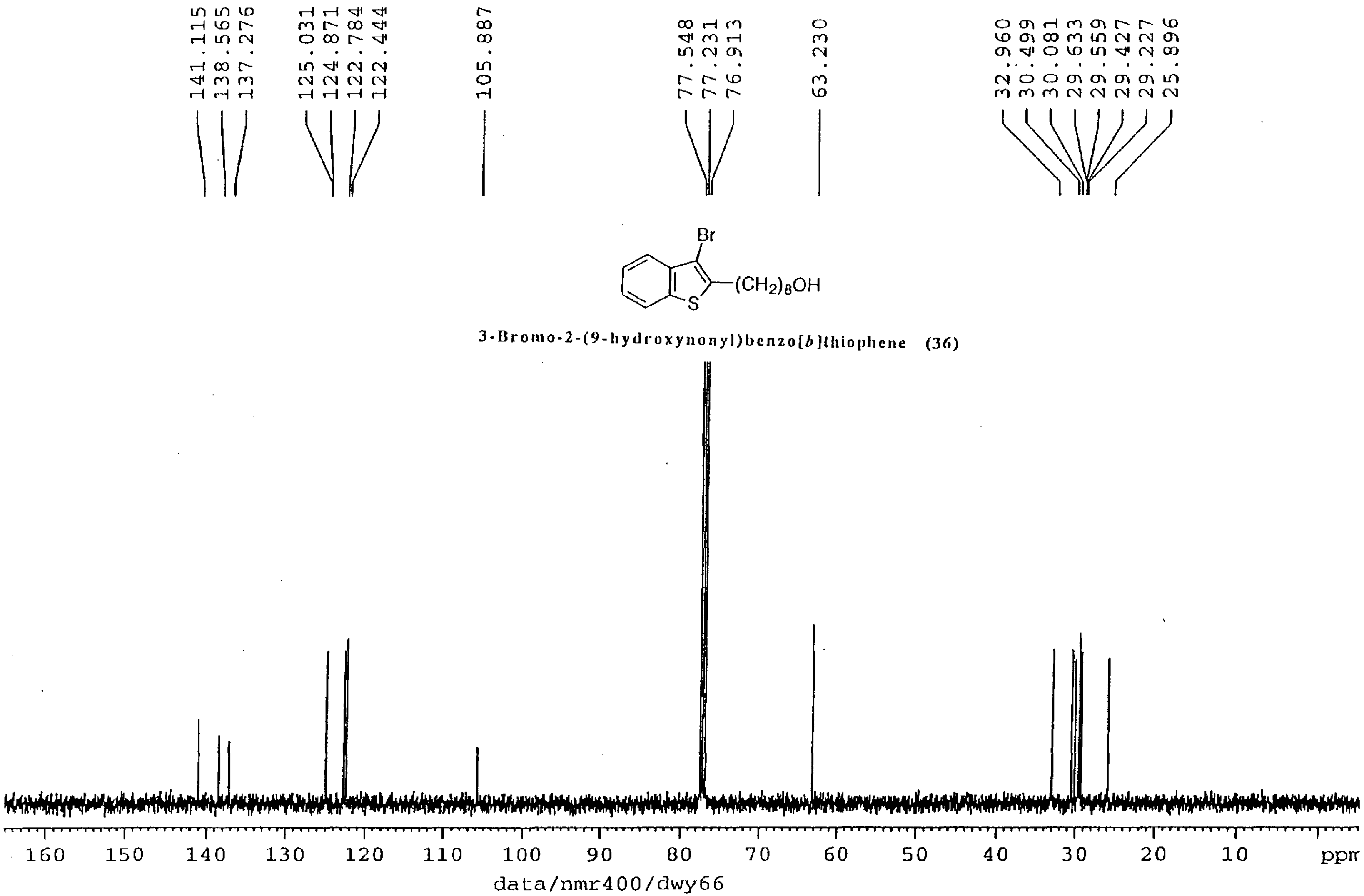


2-(9-Hydroxynonyl)-3-iodobenzo[*b*]thiophene (35)

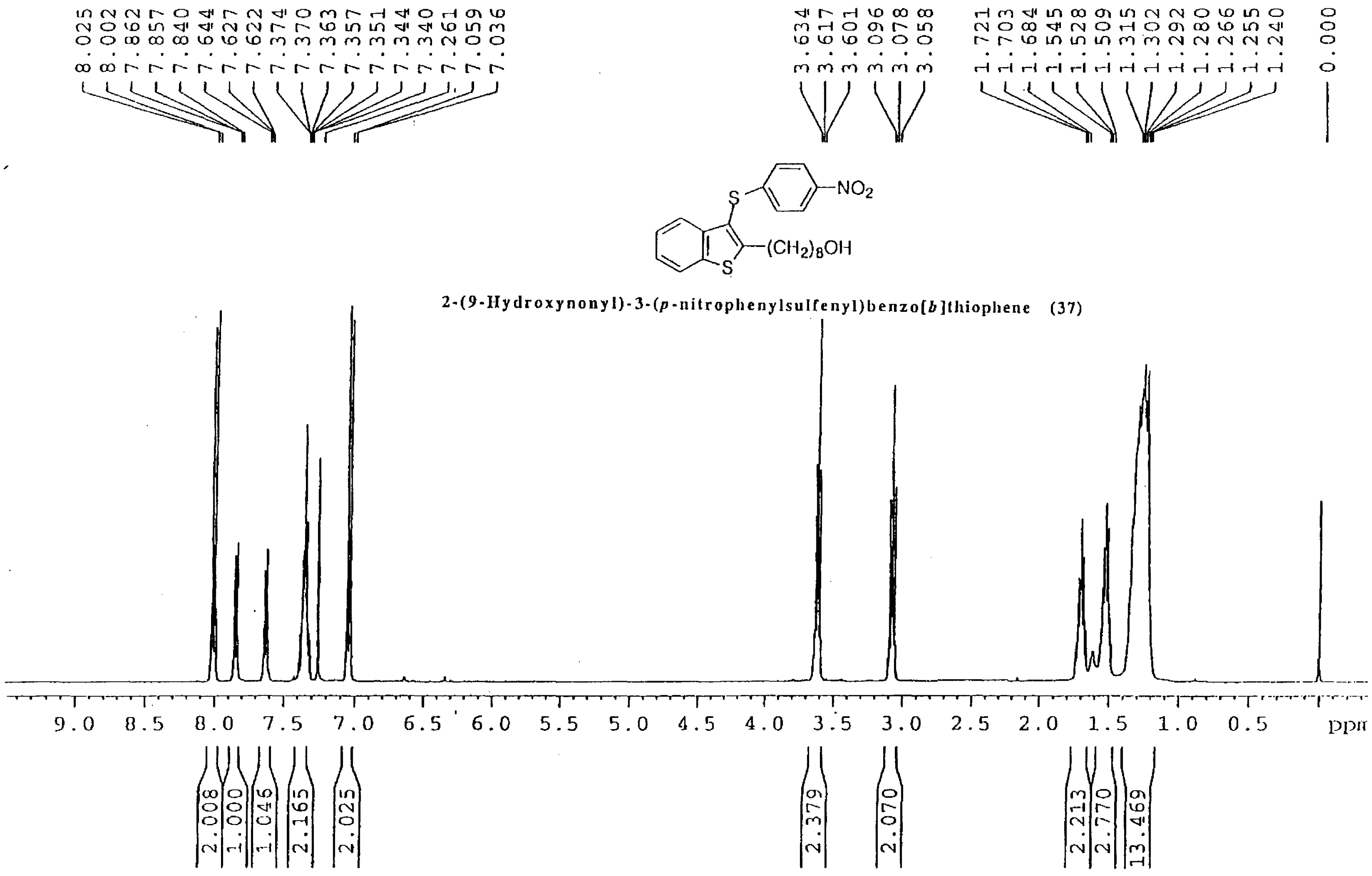
data/nmr400/dwy51c



3-Bromo-2-(9-hydroxynonyl)benzo[*b*]thiophene (36)

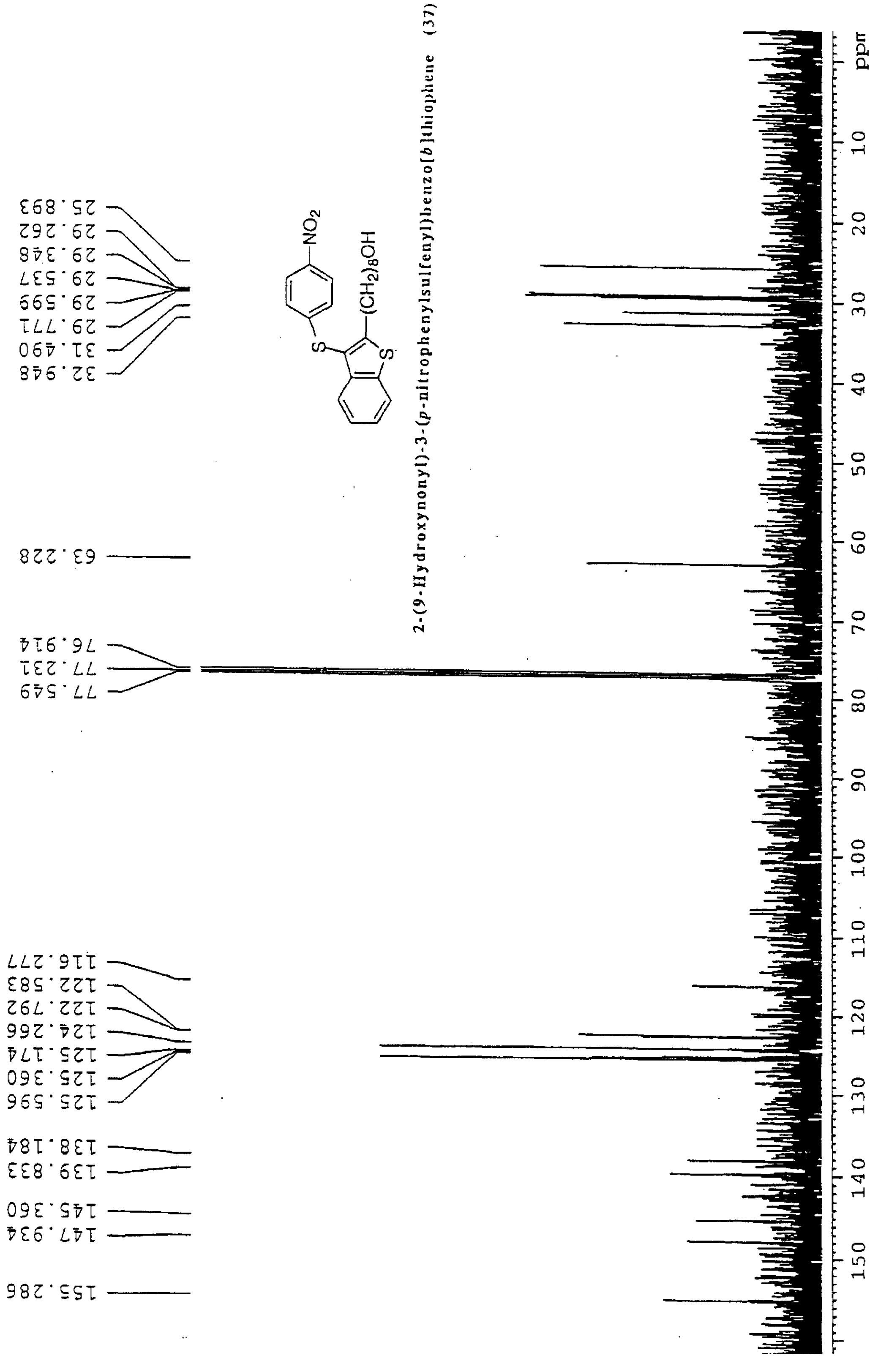


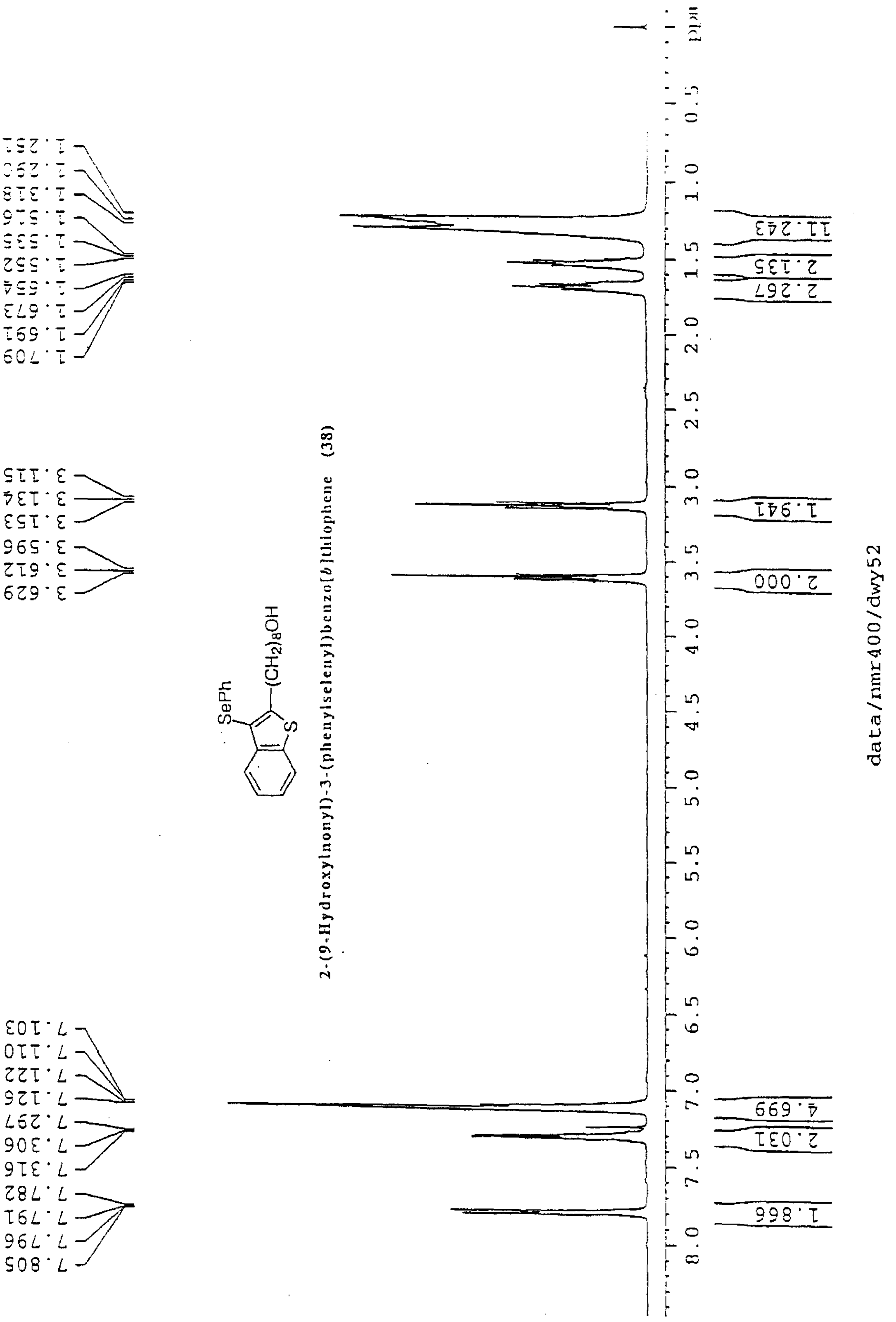
3-Bromo-2-(9-hydroxynonyl)benzo[*b*]thiophene (36)



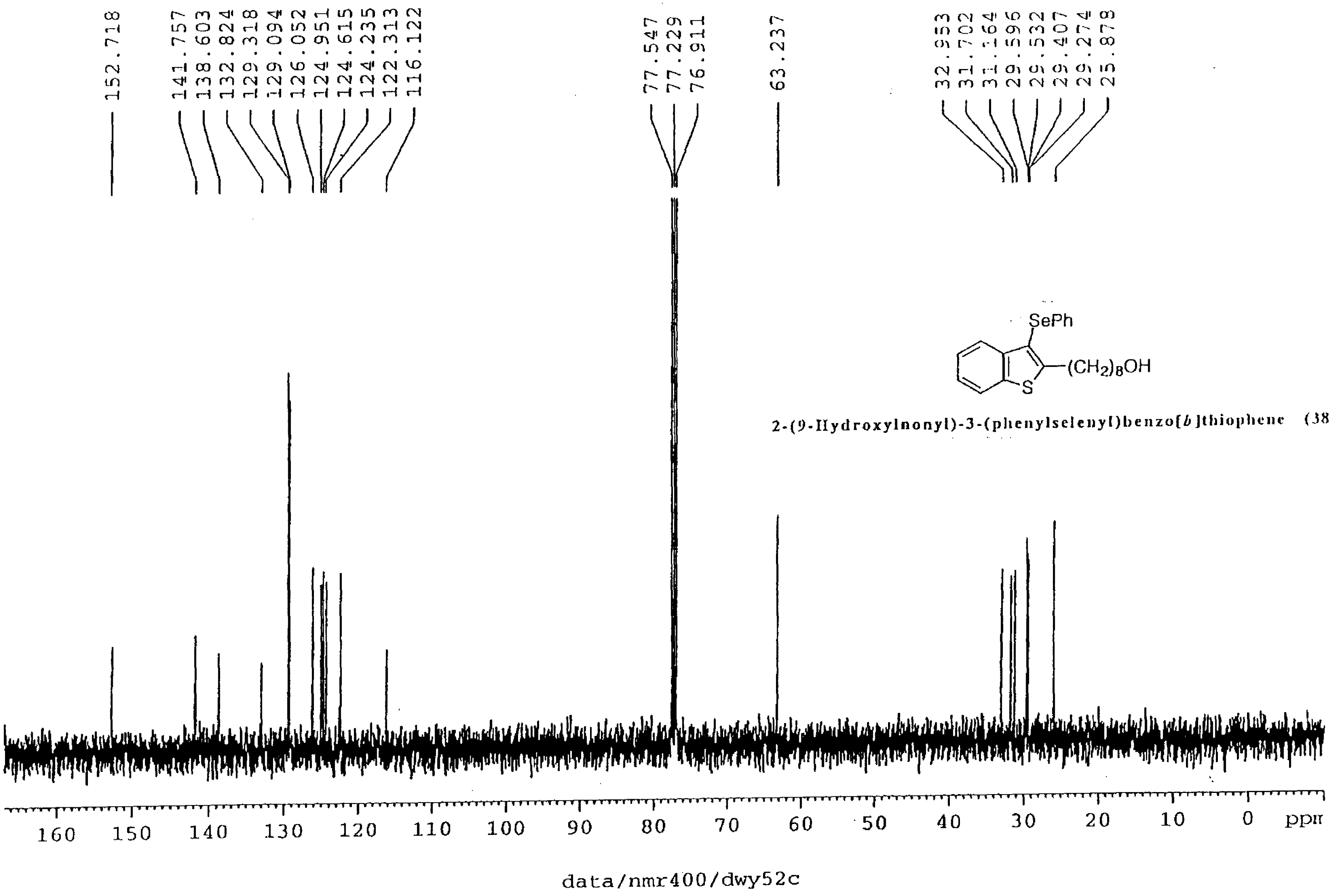
2-(9-Hydroxynonyl)-3-(*p*-nitrophenylsulfenyl)benzo[*b*]thiophene (37)

data/nmr400/dwy54

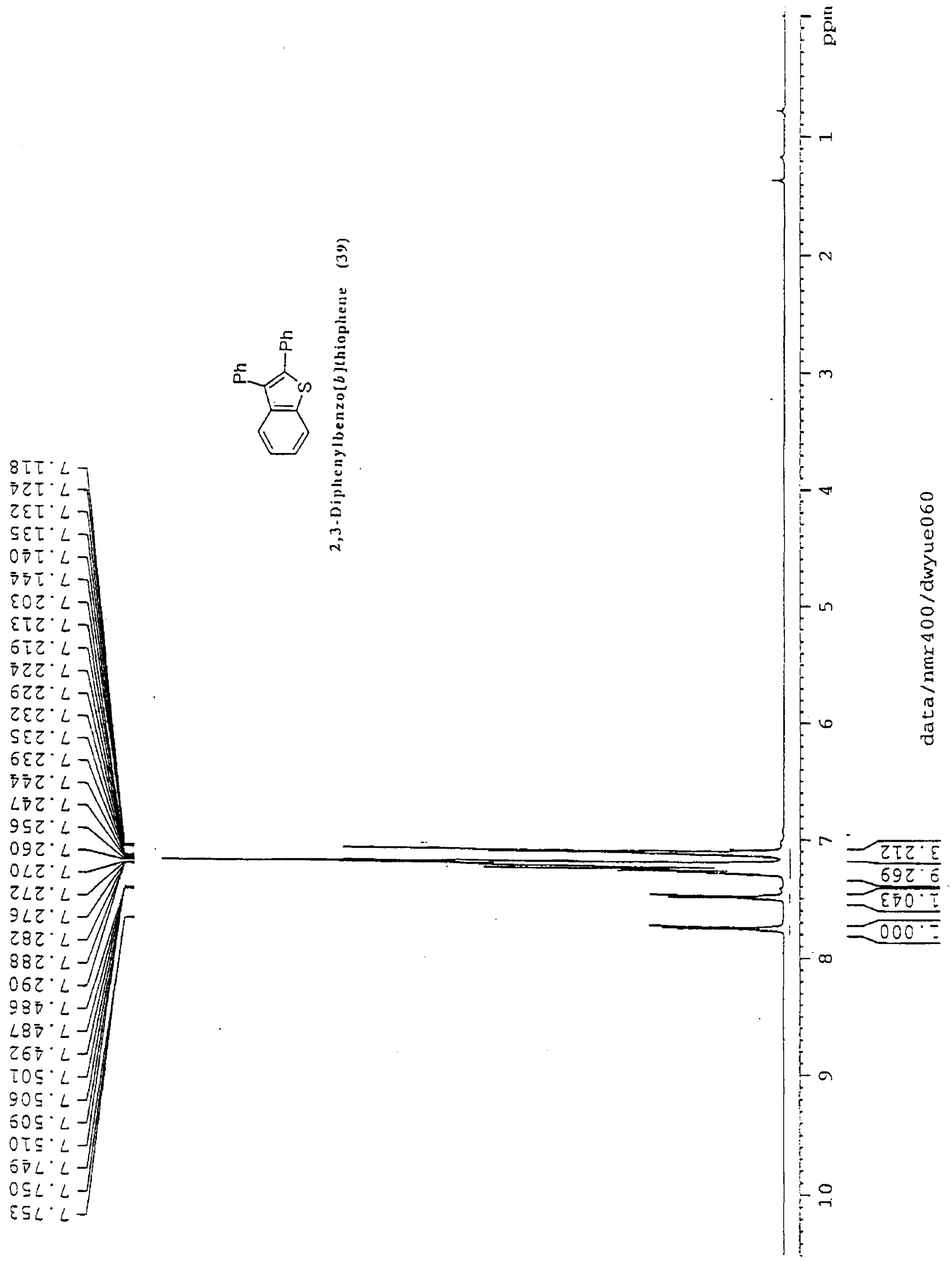

2-(9-Hydroxynonyl)-3-(*p*-nitrophenylsulfenyl)benzo[*b*]thiophene (37)



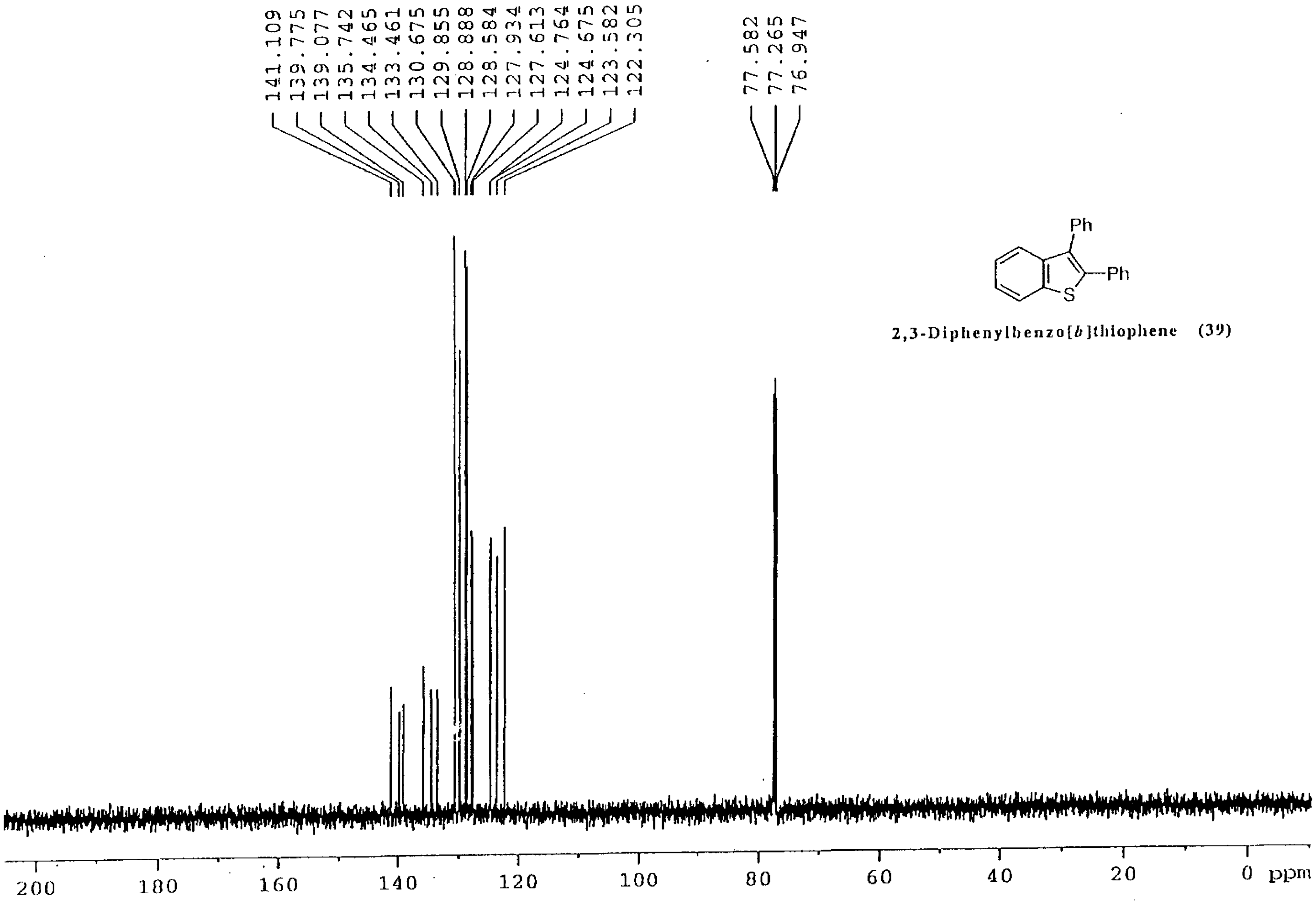
2-(9-Hydroxylnonyl)-3-(phenylselenyl)benzo[*b*]thiophene (38)



2-(9-Hydroxylnonyl)-3-(phenylselenyl)benzo[*b*]thiophene (38)



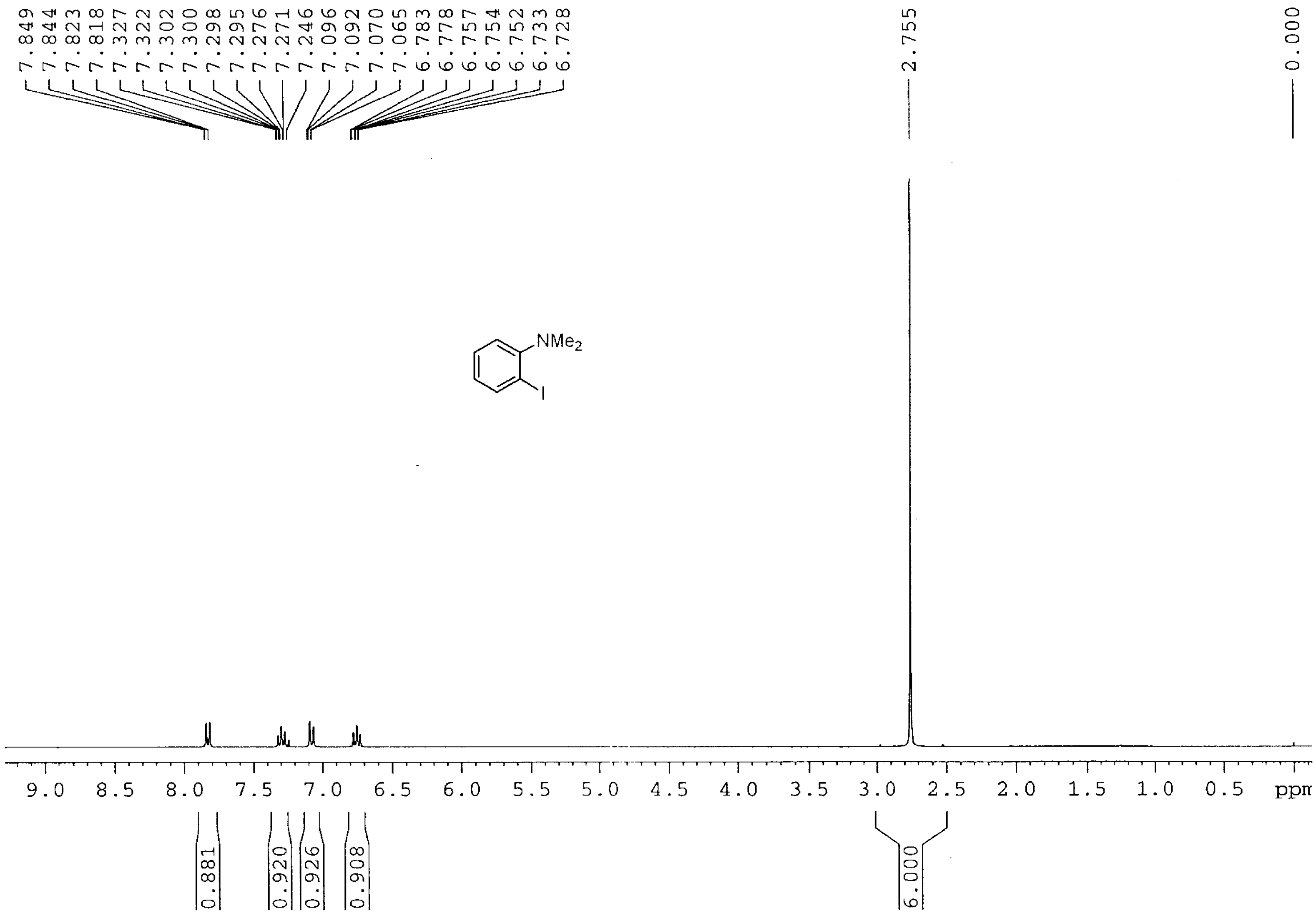
2,3-Diphenylbenzo[*b*]thiophene (39)

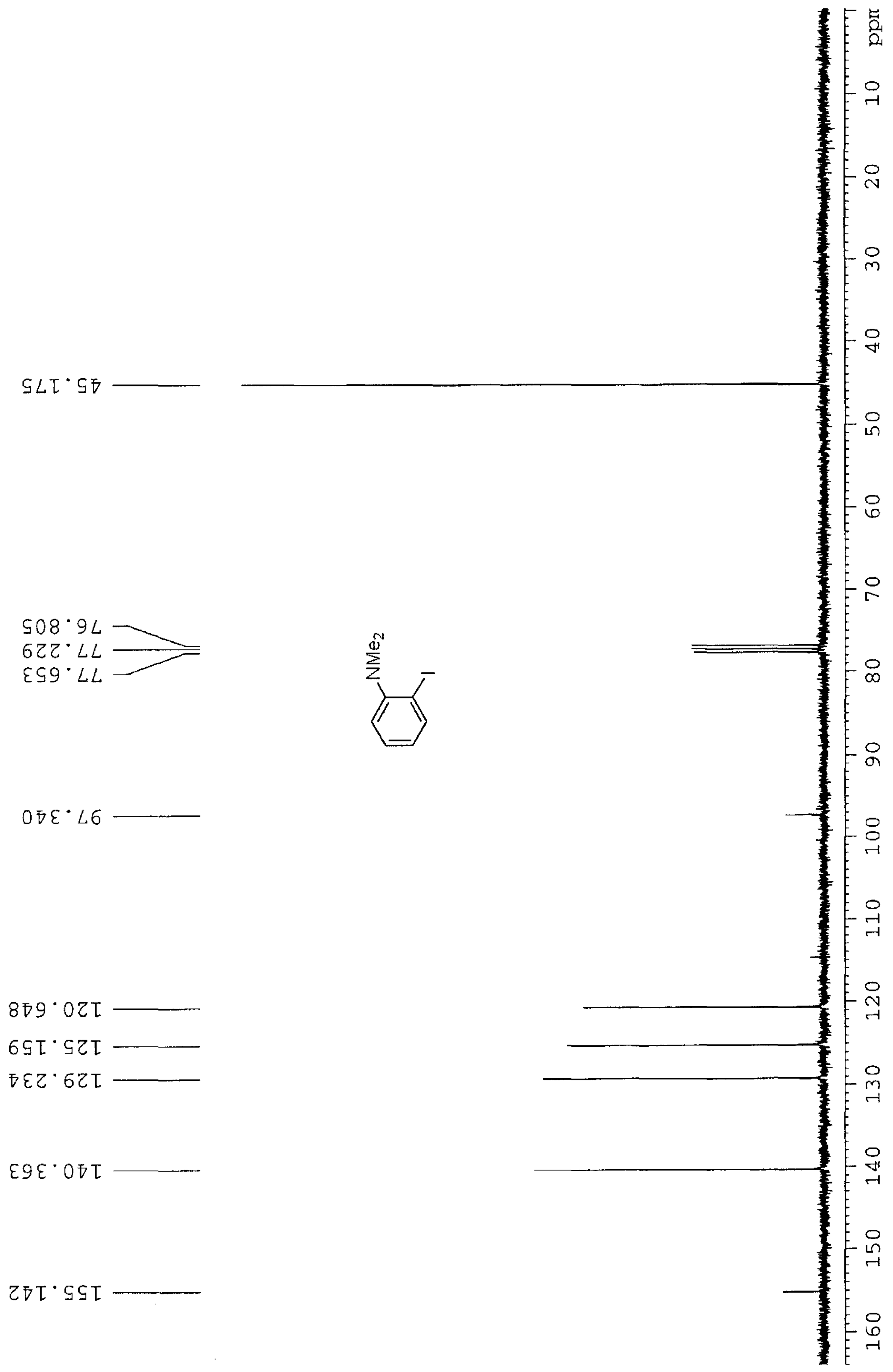


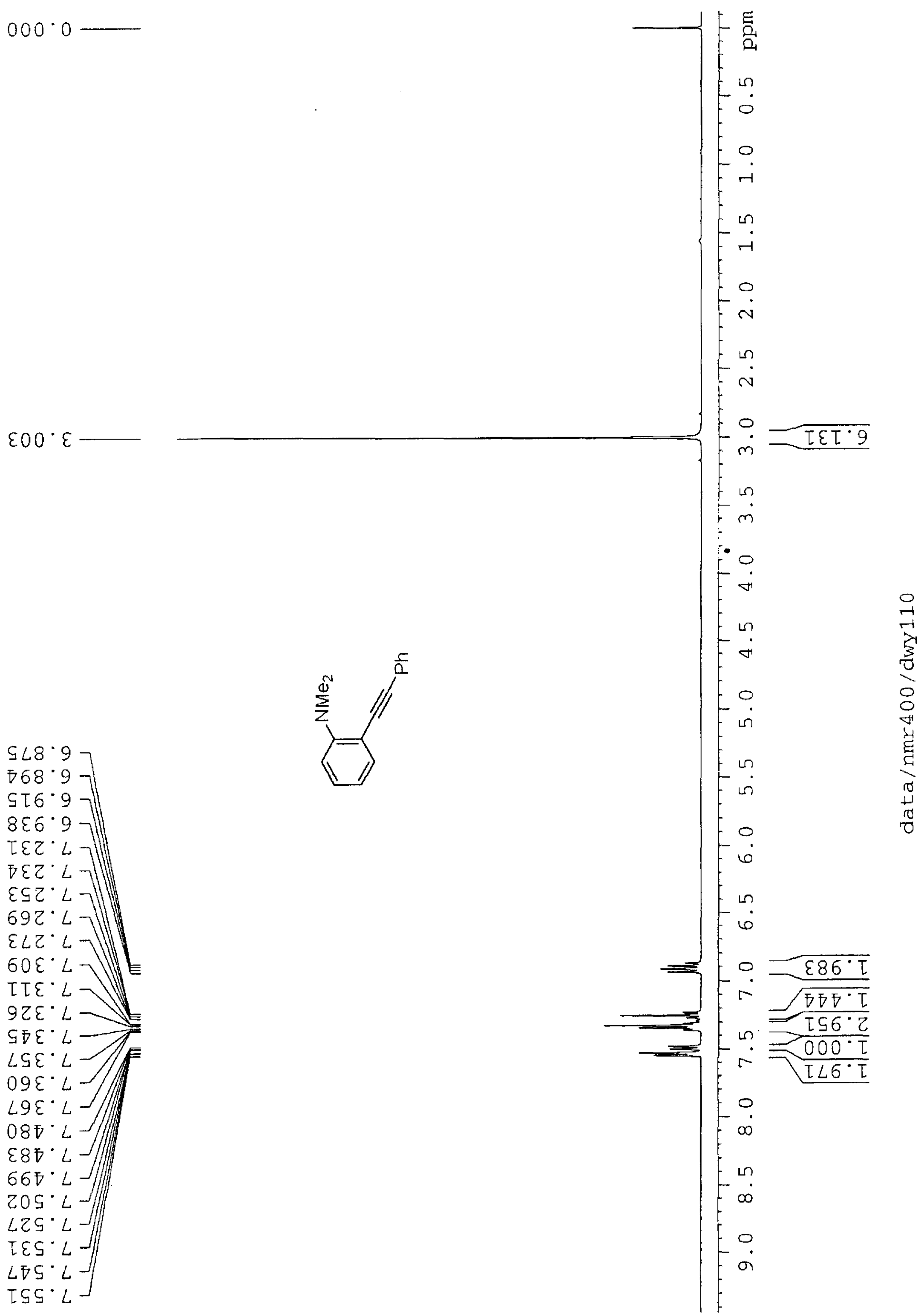
2,3-Diphenylbenzo[*b*]thiophene (39)

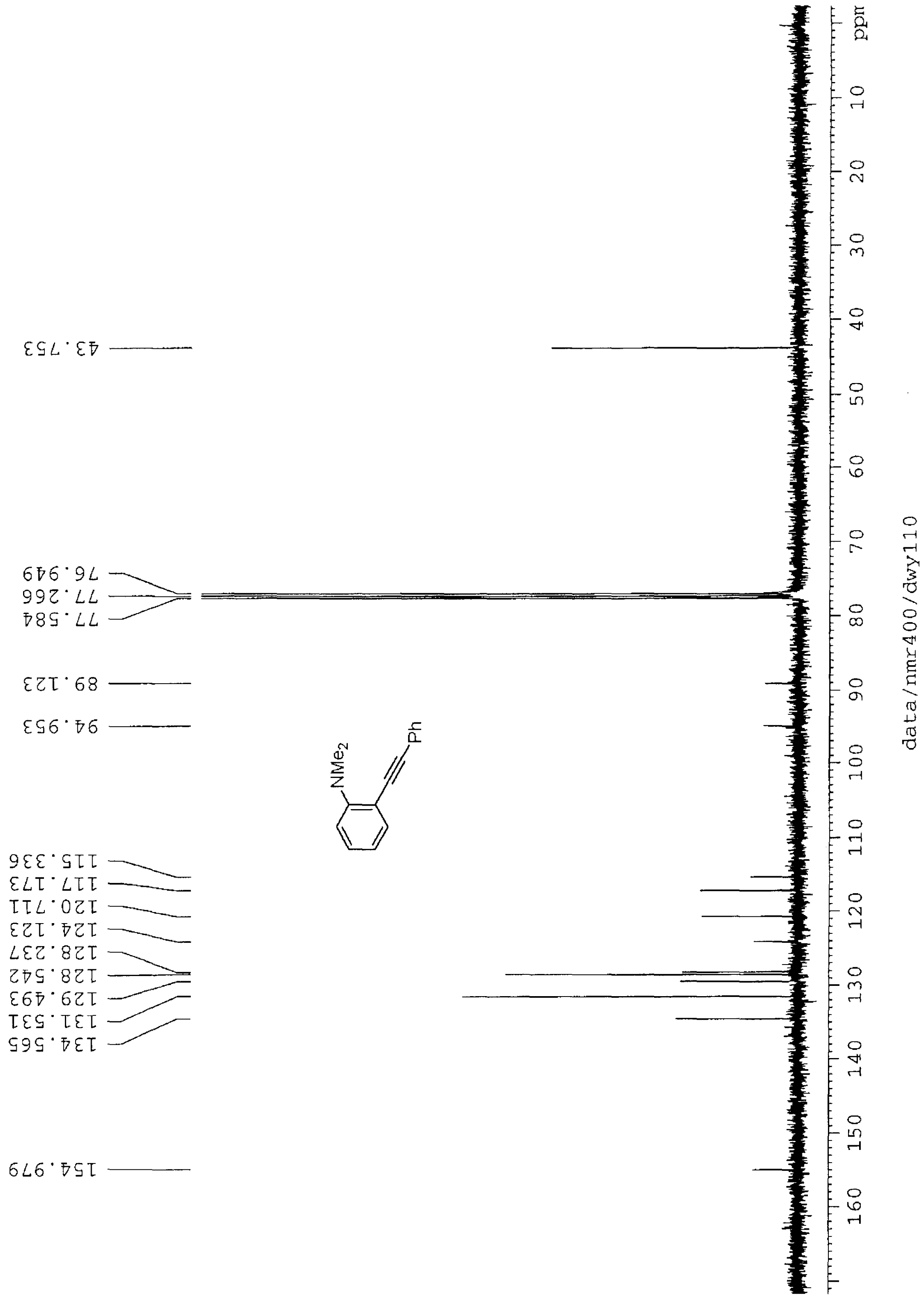
data/nmr400/dwyue060c.fid

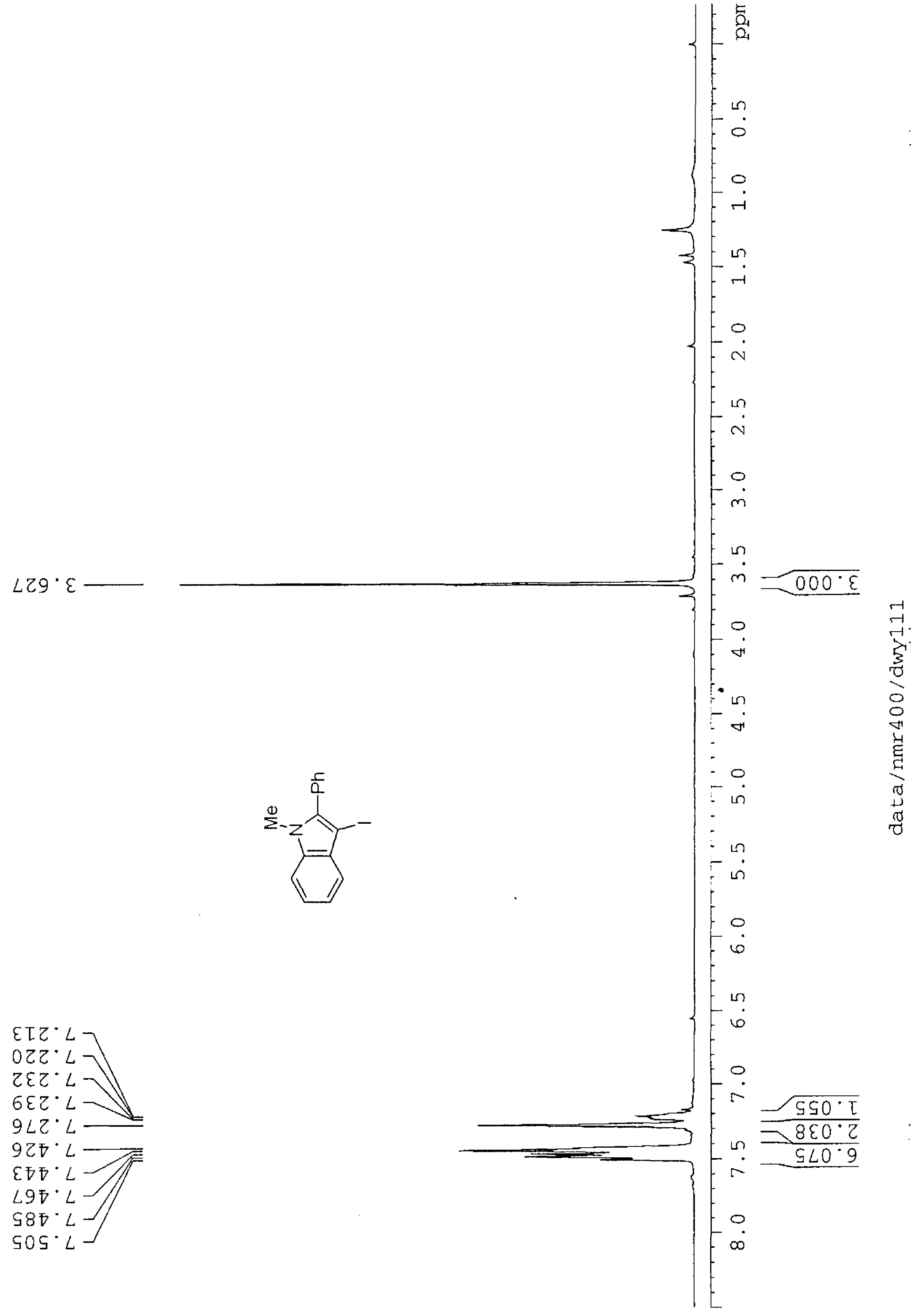
APPENDIX B. CHAPTER 2 ^{1}H AND ^{13}C NMR SPECTRA

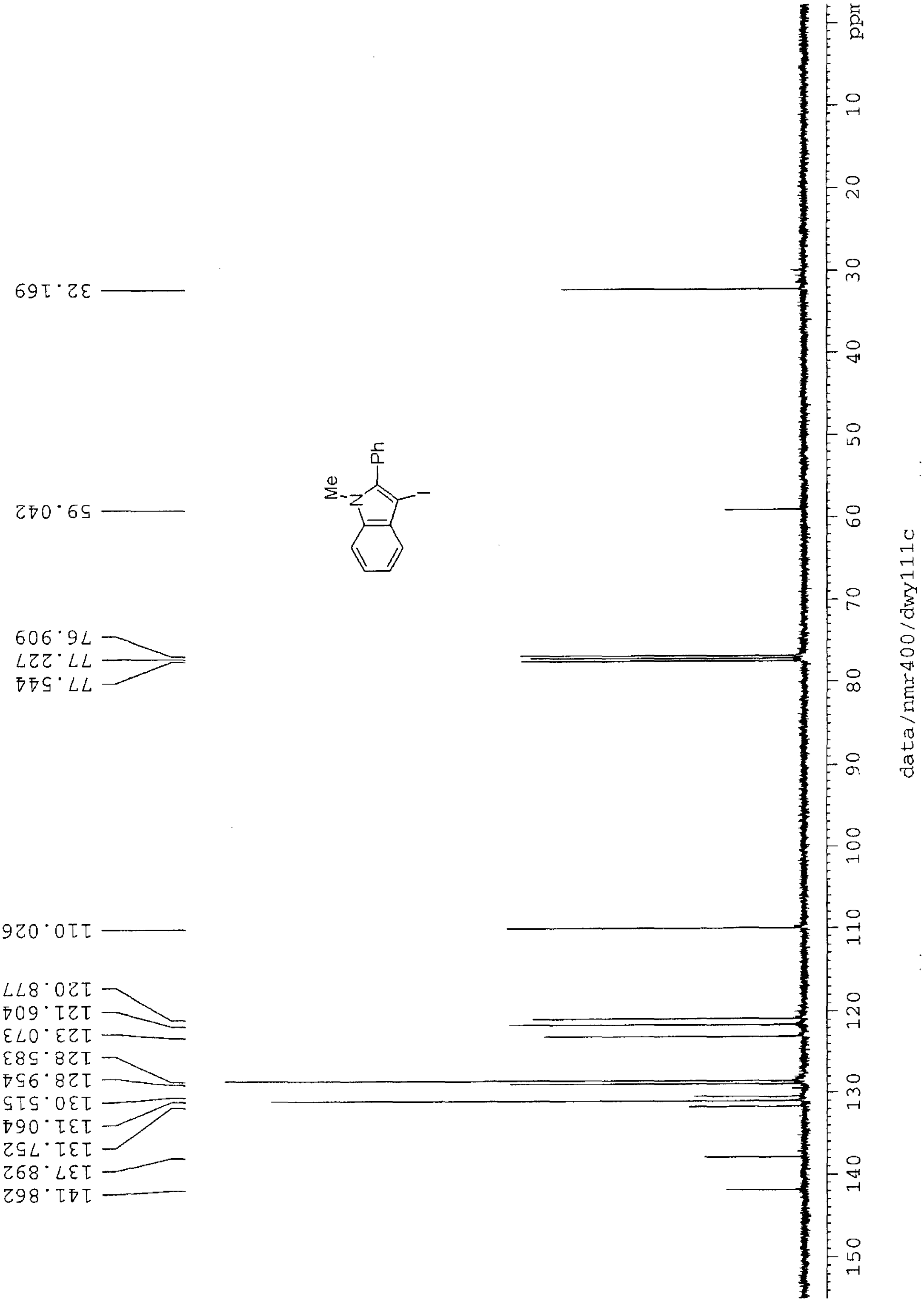

7.849
7.844
7.823
7.818
7.327
7.322
7.302
7.300
7.298
7.295
7.276
7.271
7.246
7.096
7.092
7.070
7.065
6.783
6.778
6.757
6.754
6.752
6.733
6.728
2.755
0.000
NMe2
I
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.881
0.920
0.926
0.908
6.000

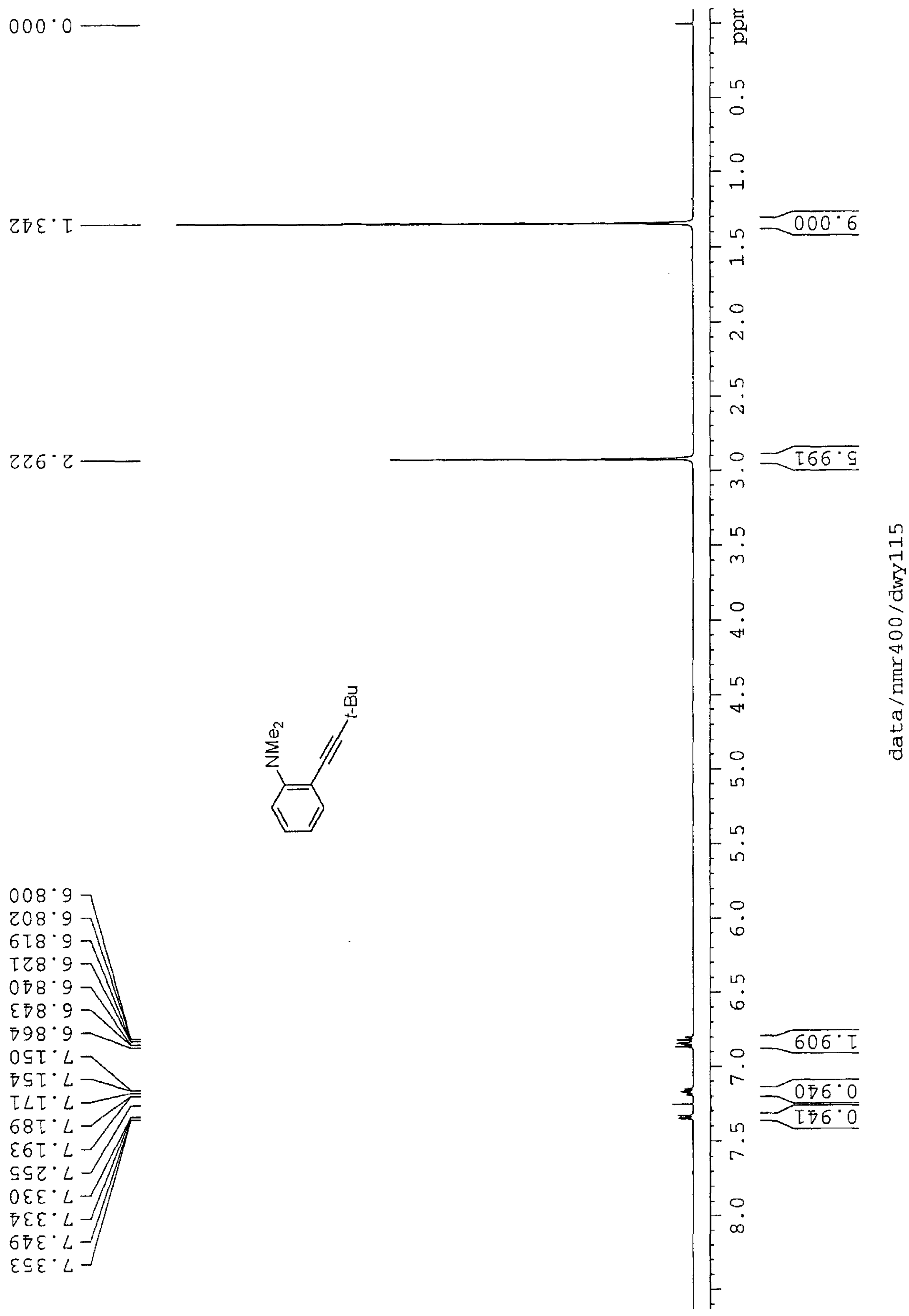

45.175
76.805
77.229
77.653
97.340
120.648
125.159
129.234
140.363
155.142
NMe2
I
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160

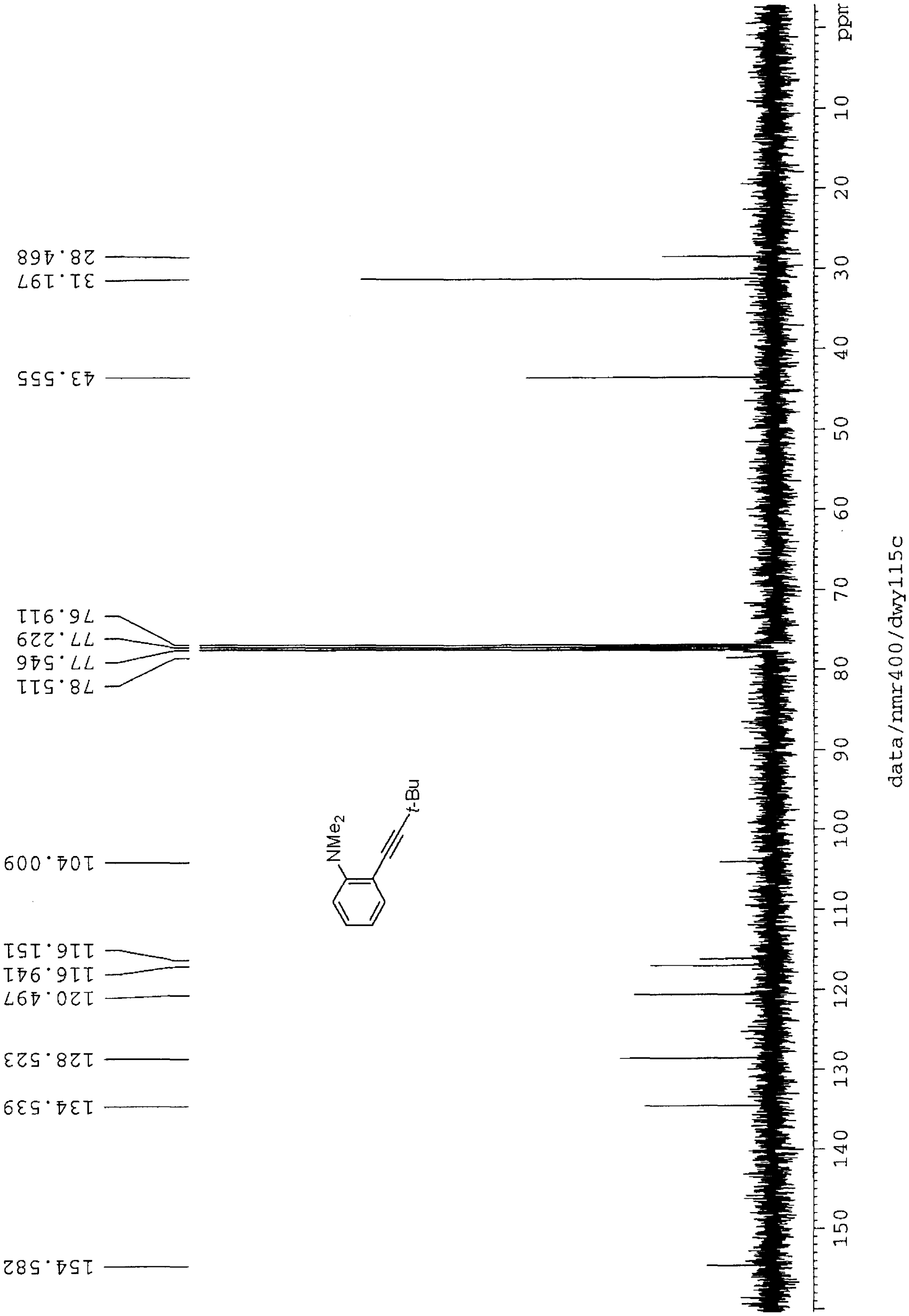

0.000
3.003
6.875
6.894
6.915
6.938
7.231
7.234
7.253
7.269
7.273
7.309
7.311
7.326
7.345
7.357
7.360
7.367
7.480
7.483
7.499
7.502
7.527
7.531
7.547
7.551
NMe2
Ph
6.131
1.983
1.444
2.951
1.000
1.971
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
data/nmr400/dwy110

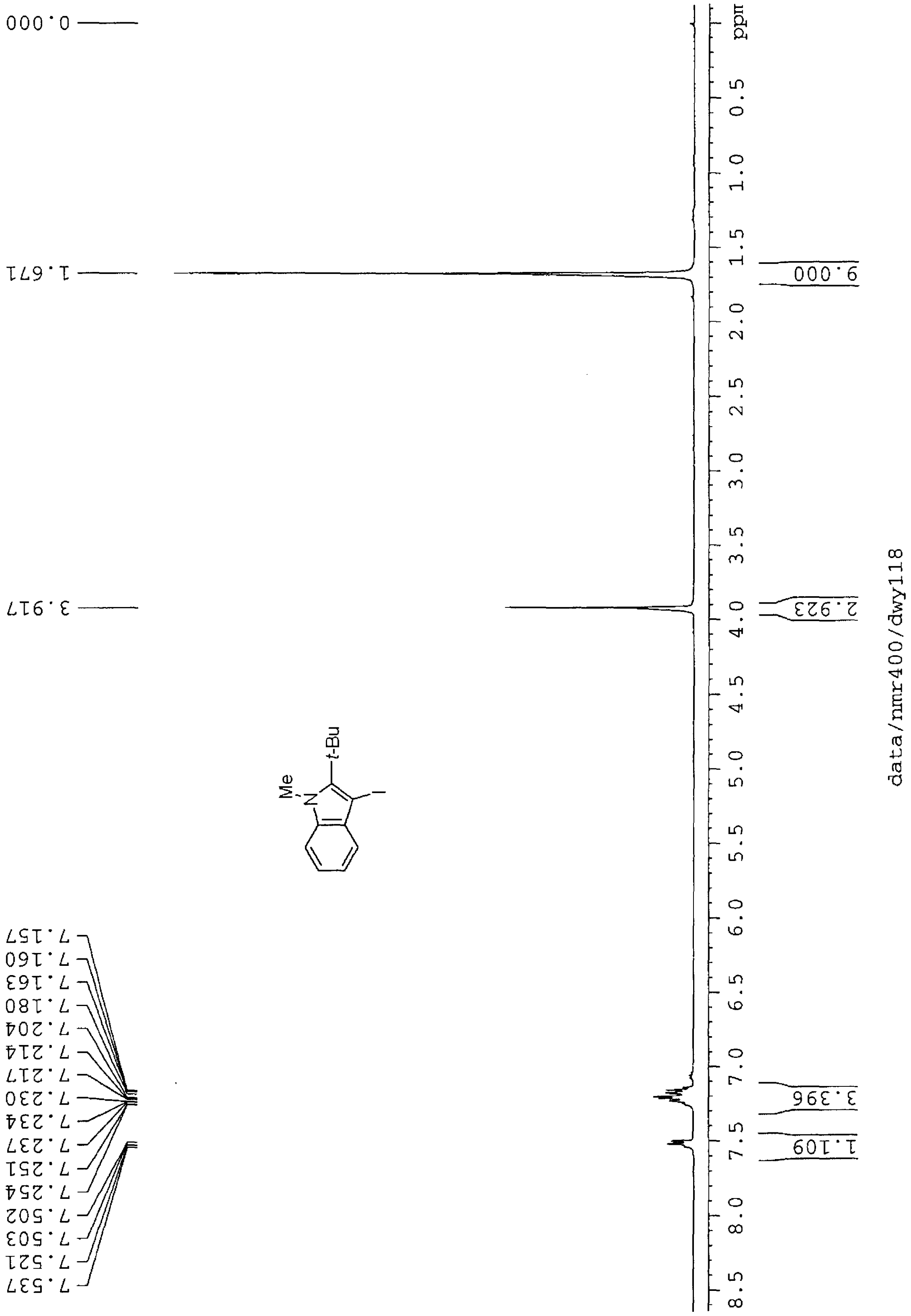

43.753
76.949
77.266
77.584
89.123
94.953
115.336
117.173
120.711
124.123
128.237
128.542
129.493
131.531
134.565
154.979
NMe2
Ph
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr400/dwy110

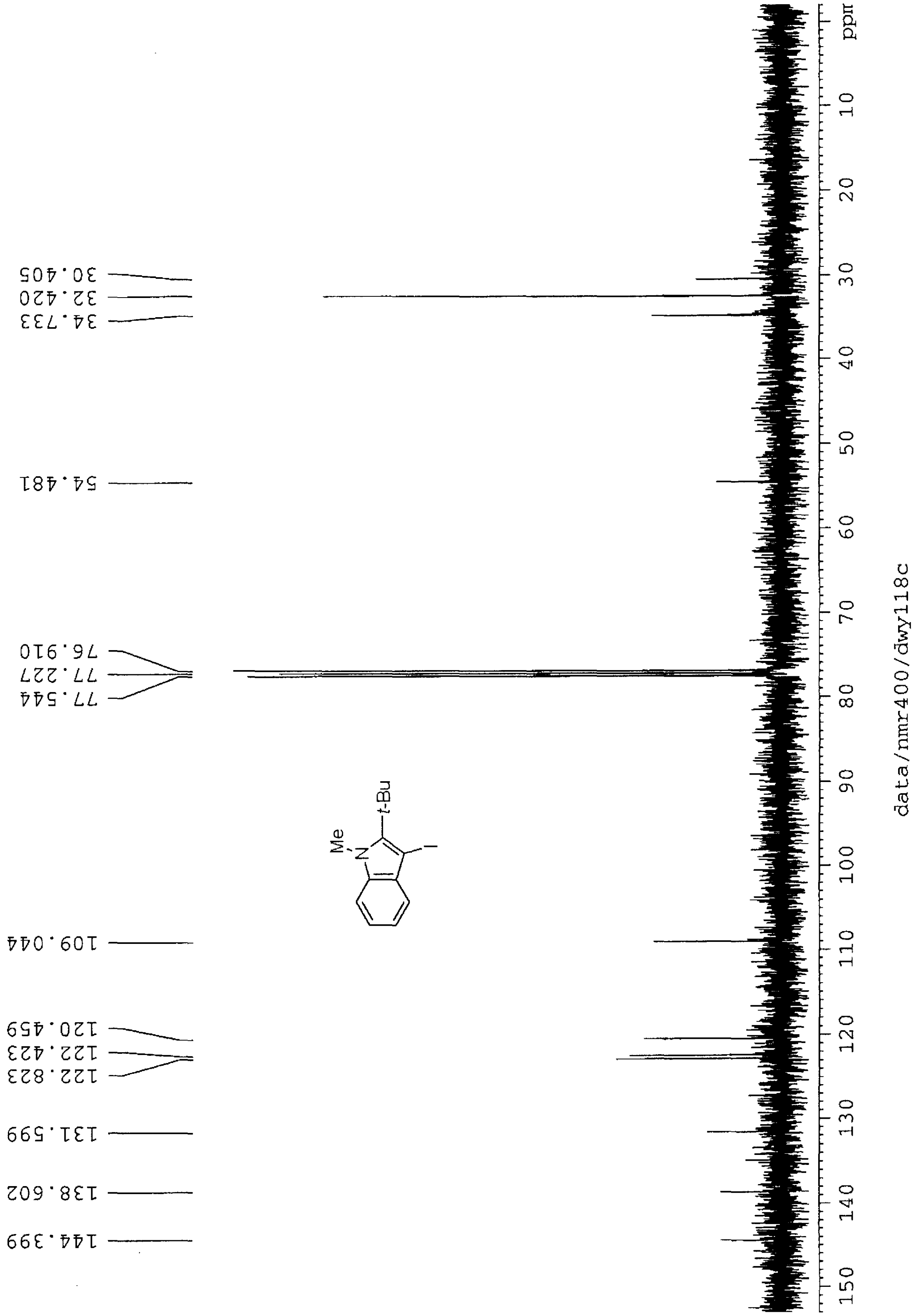

3.627
7.213
7.220
7.232
7.239
7.276
7.426
7.443
7.467
7.485
7.505
Me
N
Ph
I
3.000
1.055
2.038
6.075
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
data/nmr400/dwy111

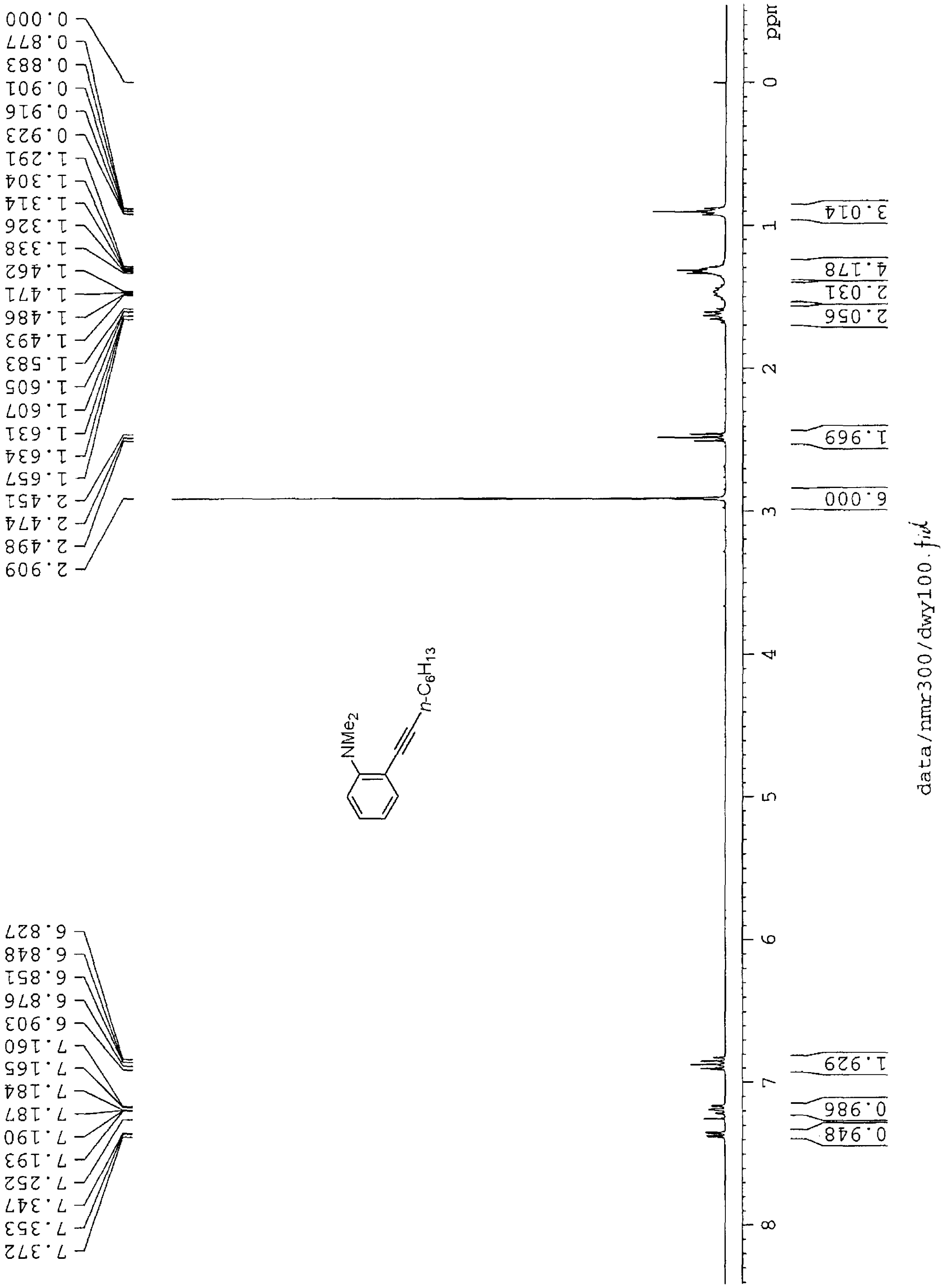

32.169
59.042
76.909
77.227
77.544
110.026
120.877
121.604
123.073
128.583
128.954
130.515
131.064
131.752
137.892
141.862
Me
N
Ph
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr400/dwy111c

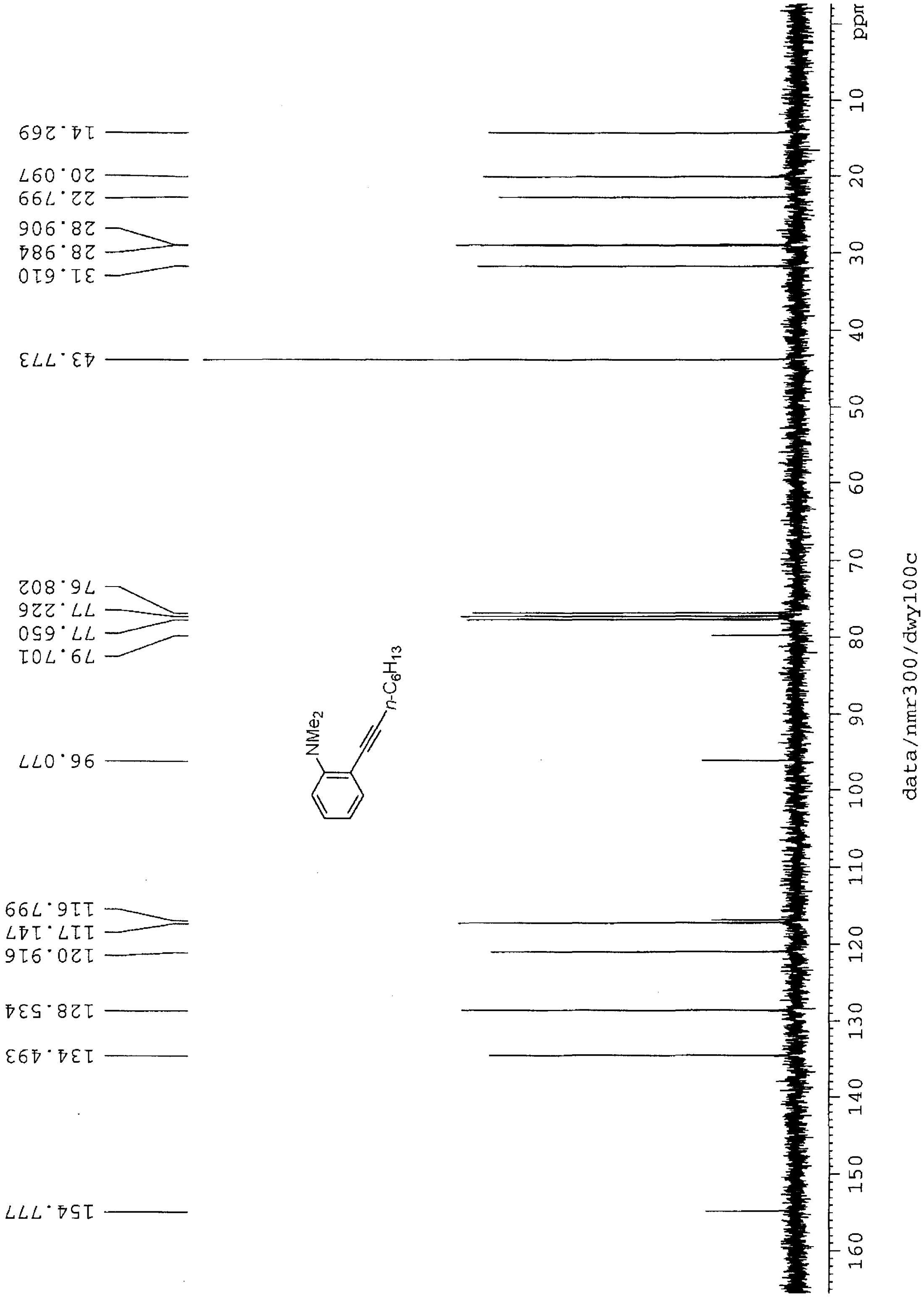

0.000
1.342
2.922
6.800
6.802
6.819
6.821
6.840
6.843
6.864
7.150
7.154
7.171
7.189
7.193
7.255
7.330
7.334
7.349
7.353
NMe2
t-Bu
9.000
5.991
1.909
0.940
0.941
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
data/nmr400/dwy115

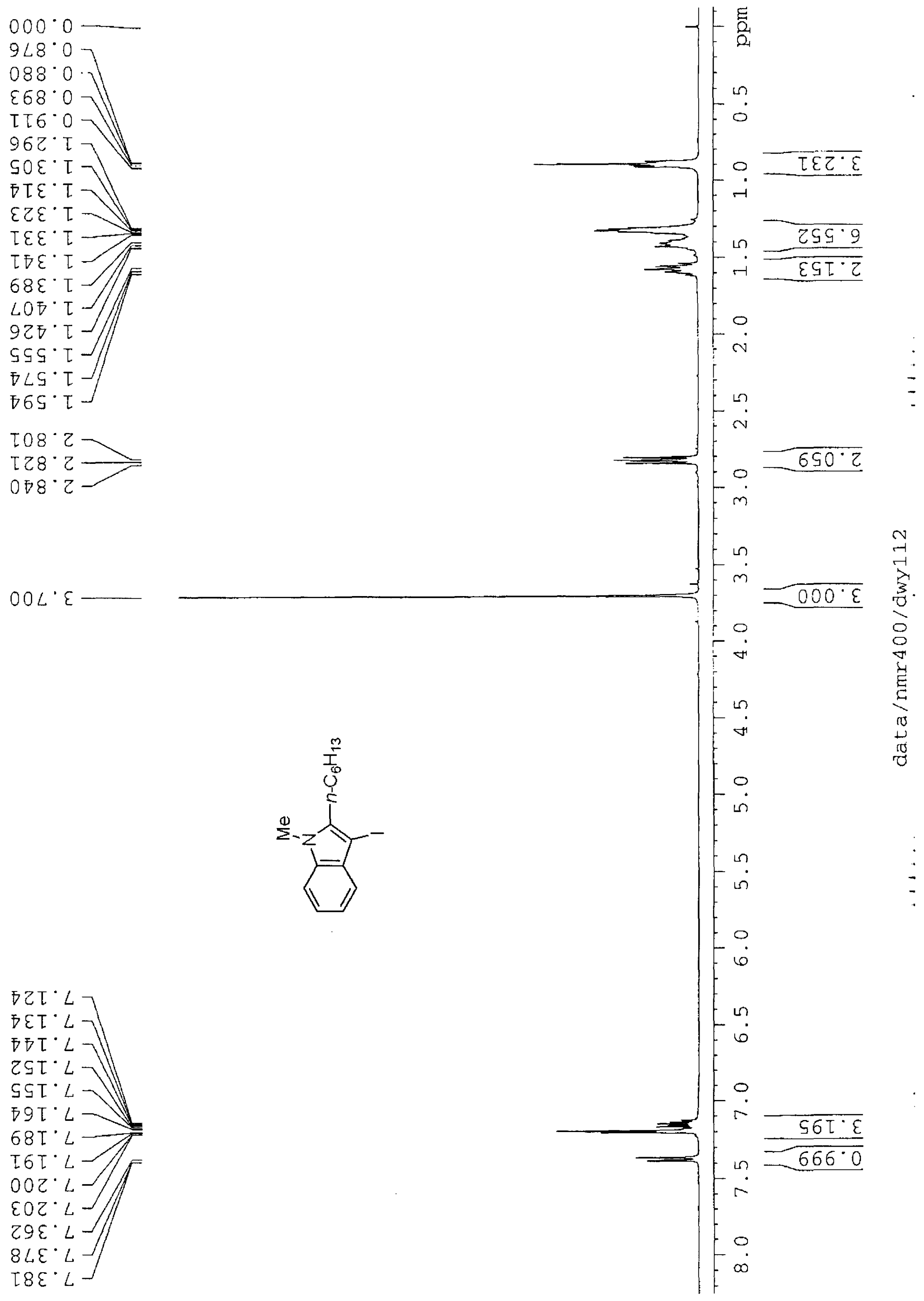

28.468
31.197
43.555
76.911
77.229
77.546
78.511
104.009
116.151
116.941
120.497
128.523
134.539
154.582
NMe$_2$
t-Bu
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr400/dwy115c

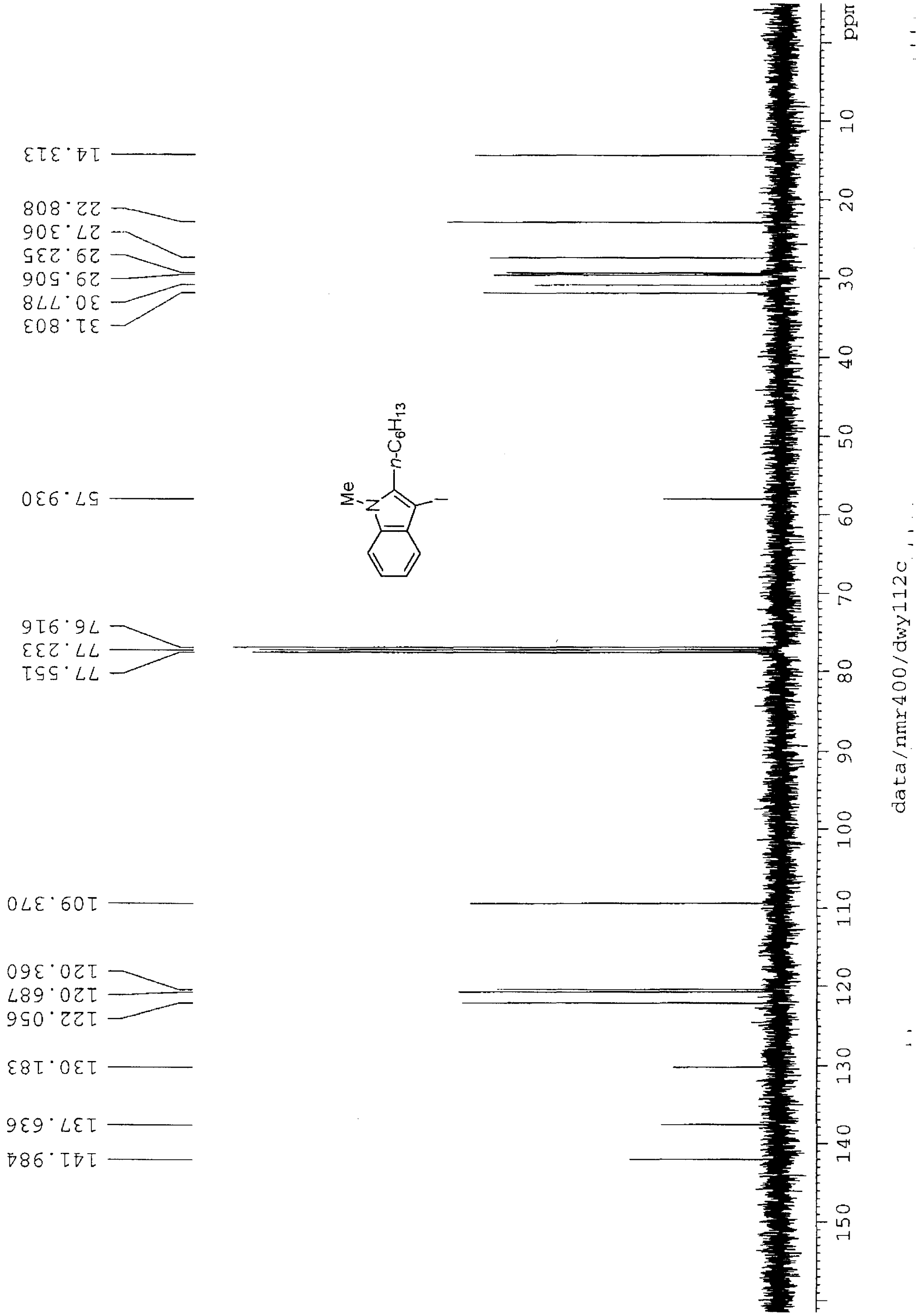

0.000
1.671
3.917
7.157
7.160
7.163
7.180
7.204
7.214
7.217
7.230
7.234
7.237
7.251
7.254
7.502
7.503
7.521
7.537
Me
N
t-Bu
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.000
2.923
3.396
1.109
data/nmr400/dwy118

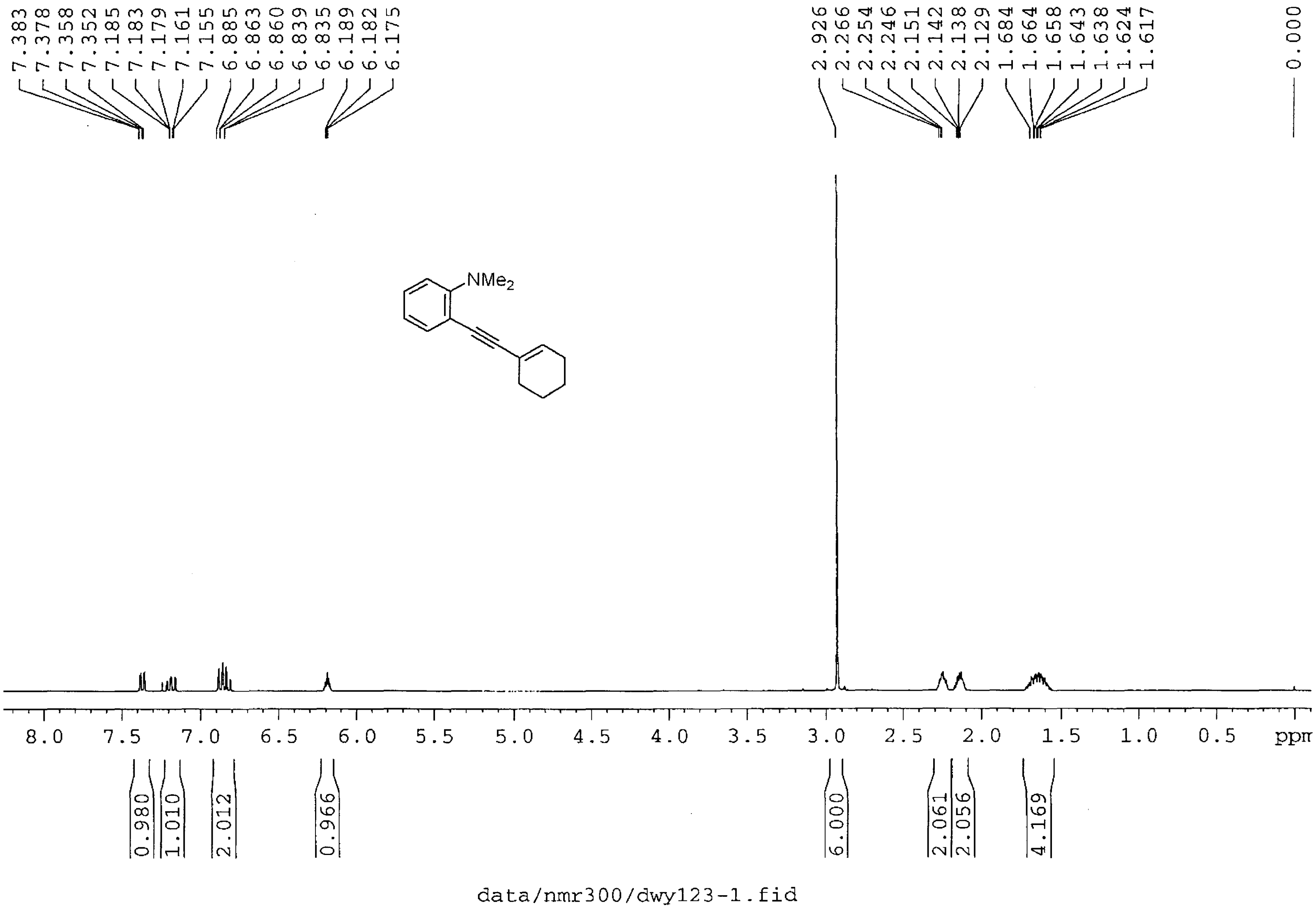

30.405
32.420
34.733
54.481
76.910
77.227
77.544
109.044
120.459
122.423
122.823
131.599
138.602
144.399
Me
N
t-Bu
I
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr400/dwy118c

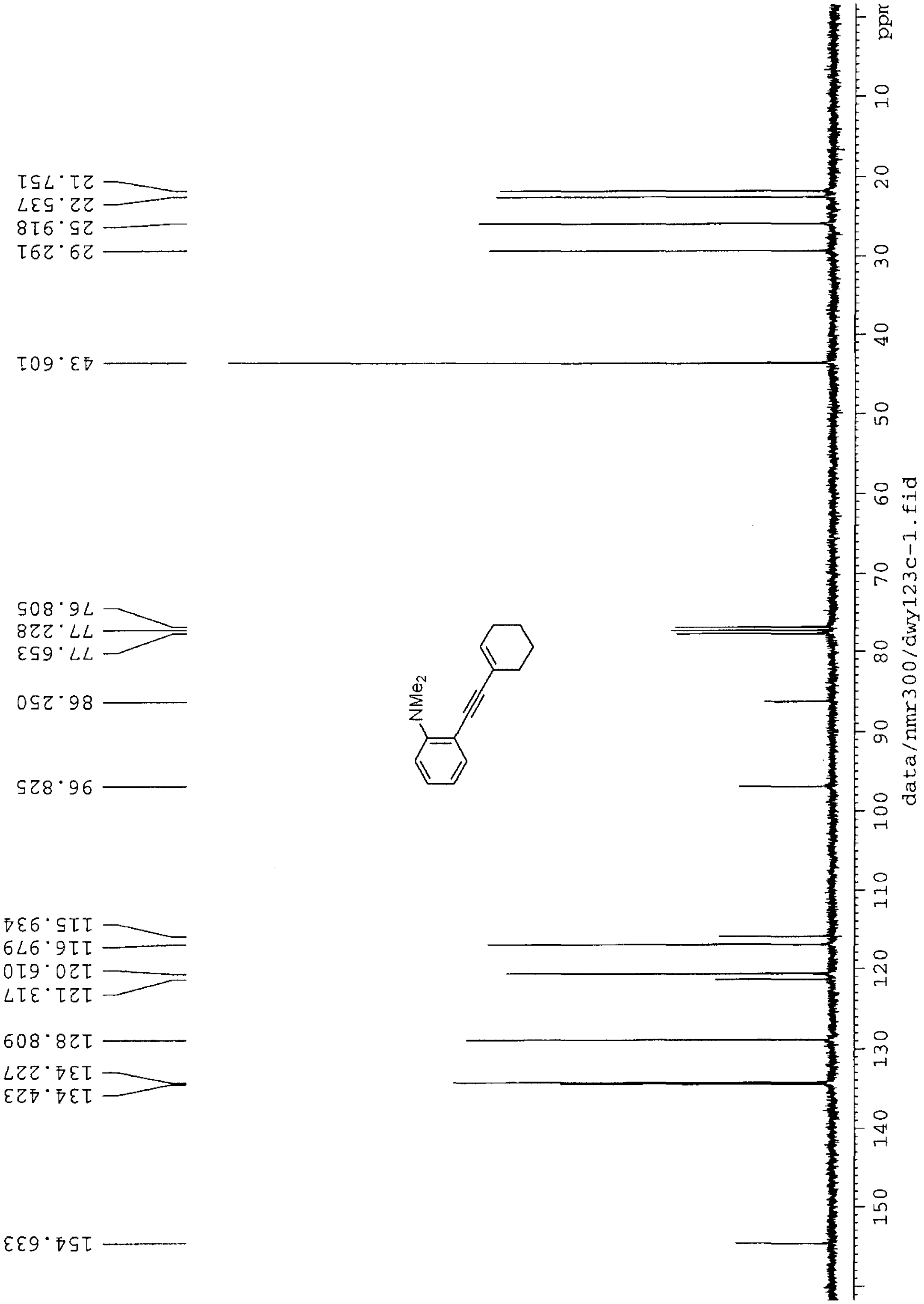

0.000
0.877
0.883
0.901
0.916
0.923
1.291
1.304
1.314
1.326
1.338
1.462
1.471
1.486
1.493
1.583
1.605
1.607
1.631
1.634
1.657
2.451
2.474
2.498
2.909
6.827
6.848
6.851
6.876
6.903
7.160
7.165
7.184
7.187
7.190
7.193
7.252
7.347
7.353
7.372
NMe2
n-C6H13
3.014
4.178
2.031
2.056
1.969
6.000
1.929
0.986
0.948
ppm
0
1
2
3
4
5
6
7
8
data/nmr300/dwy100.fid

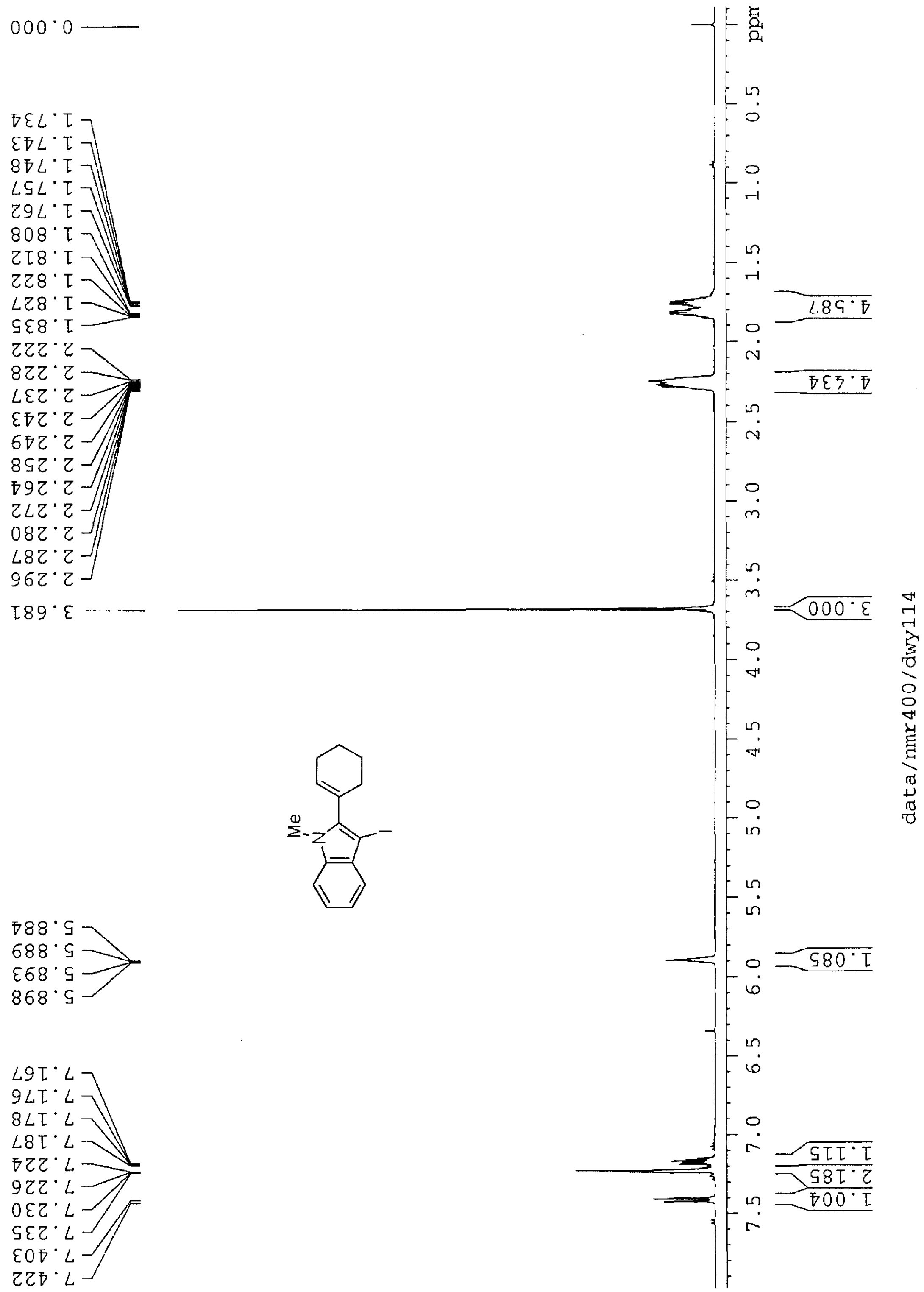

14.269
20.097
22.799
28.906
28.984
31.610
43.773
76.802
77.226
77.650
79.701
96.077
116.799
117.147
120.916
128.534
134.493
154.777
NMe2
n-C6H13
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr300/dwy100c

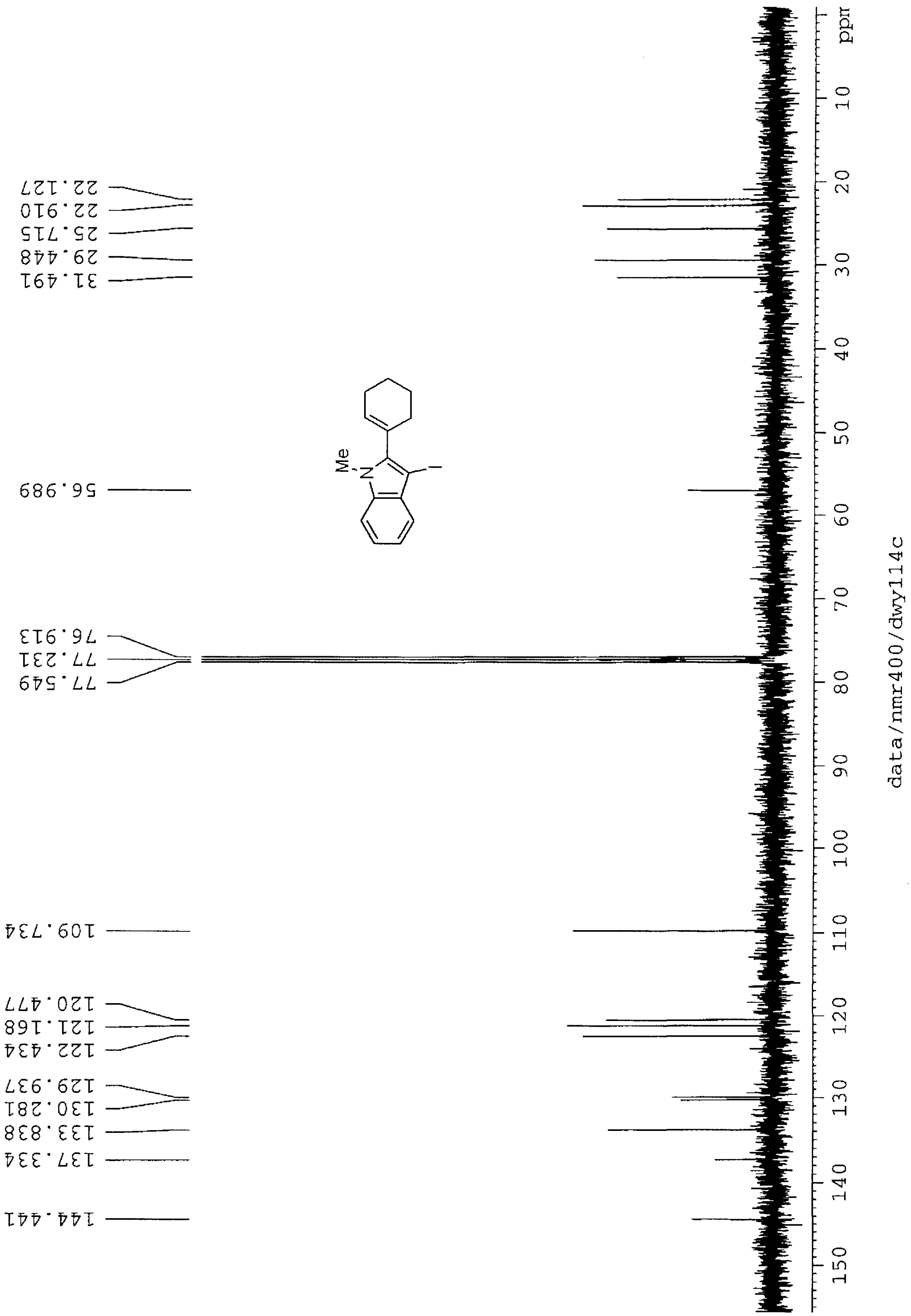

0.000
0.876
0.880
0.893
0.911
1.296
1.305
1.314
1.323
1.331
1.341
1.389
1.407
1.426
1.555
1.574
1.594
2.801
2.821
2.840
3.700
7.124
7.134
7.144
7.152
7.155
7.164
7.189
7.191
7.200
7.203
7.362
7.378
7.381
3.231
6.552
2.153
2.059
3.000
3.195
0.999
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
data/nmr400/dwy112
Me
N
n-C6H13
I

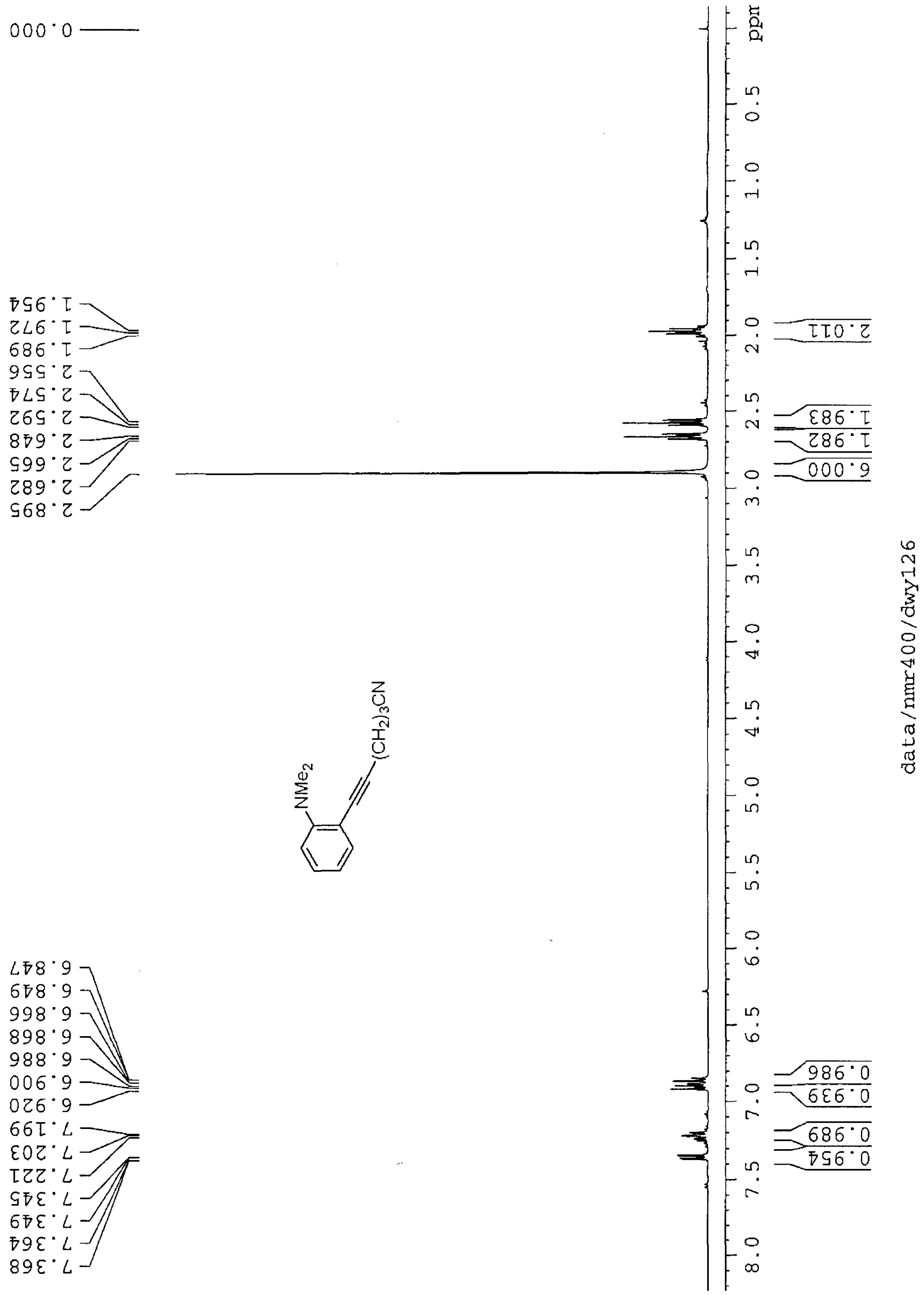

14.313
22.808
27.306
29.235
29.506
30.778
31.803
57.930
76.916
77.233
77.551
109.370
120.360
120.687
122.056
130.183
137.636
141.984
Me
N
n-C6H13
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr400/dwy112c

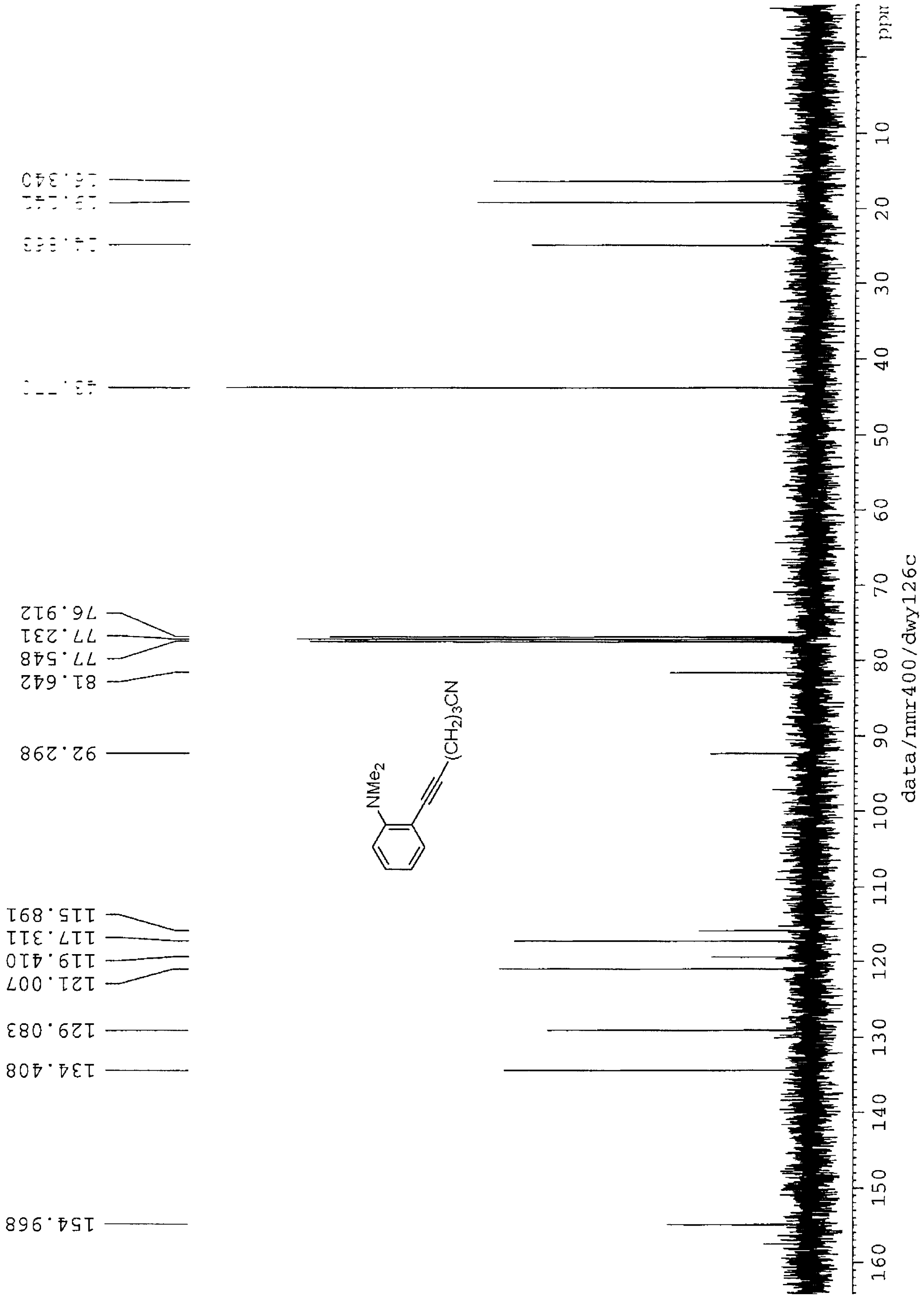

7.383
7.378
7.358
7.352
7.185
7.183
7.179
7.161
7.155
6.885
6.863
6.860
6.839
6.835
6.189
6.182
6.175
2.926
2.266
2.254
2.246
2.151
2.142
2.138
2.129
1.684
1.664
1.658
1.643
1.638
1.624
1.617
0.000
NMe2
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.980
1.010
2.012
0.966
6.000
2.061
2.056
4.169
data/nmr300/dwy123-1.fid

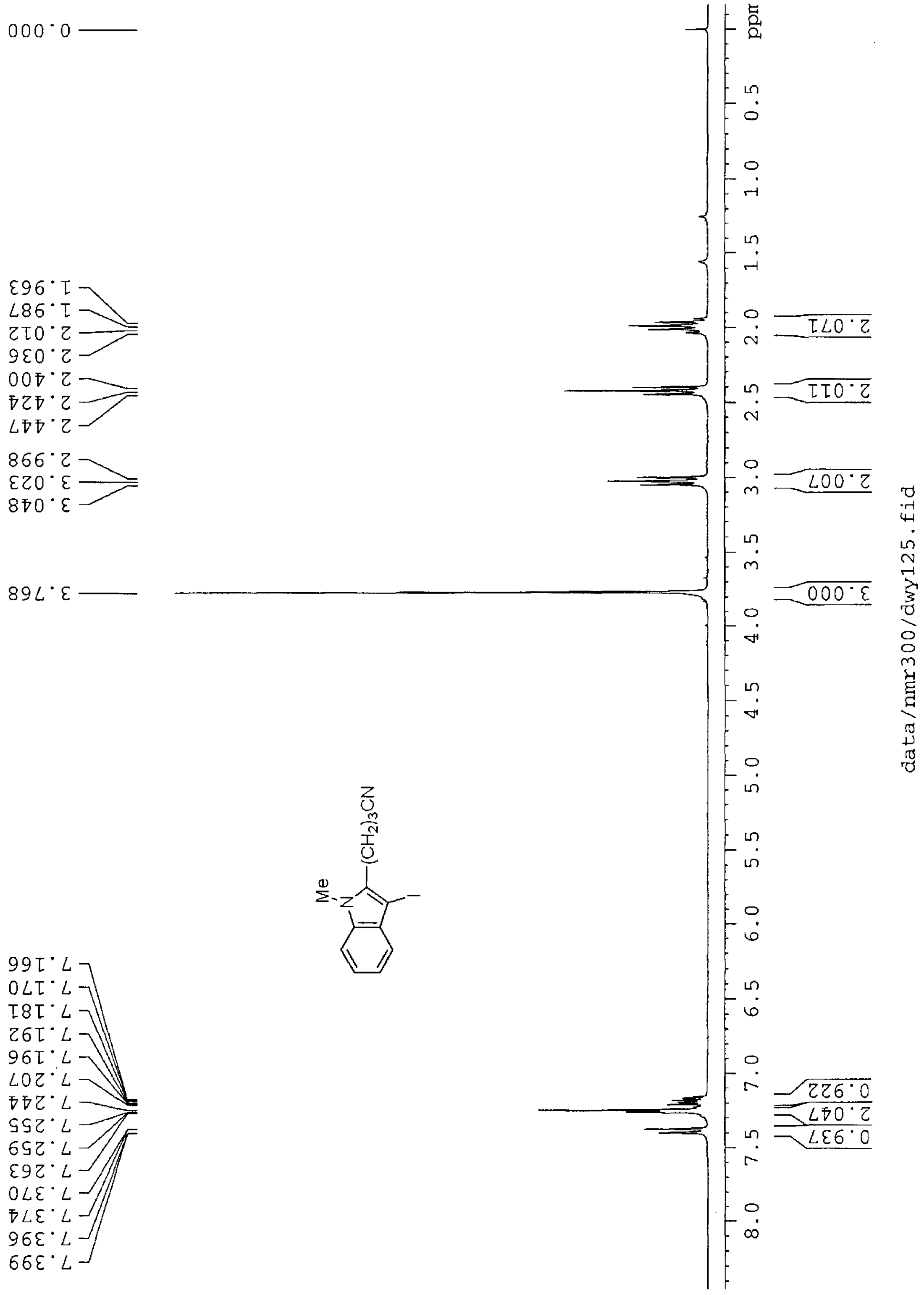

21.751
22.537
25.918
29.291
43.601
76.805
77.228
77.653
86.250
96.825
115.934
116.979
120.610
121.317
128.809
134.227
134.423
154.633
NMe$_2$
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr300/dwy123c-1.fid

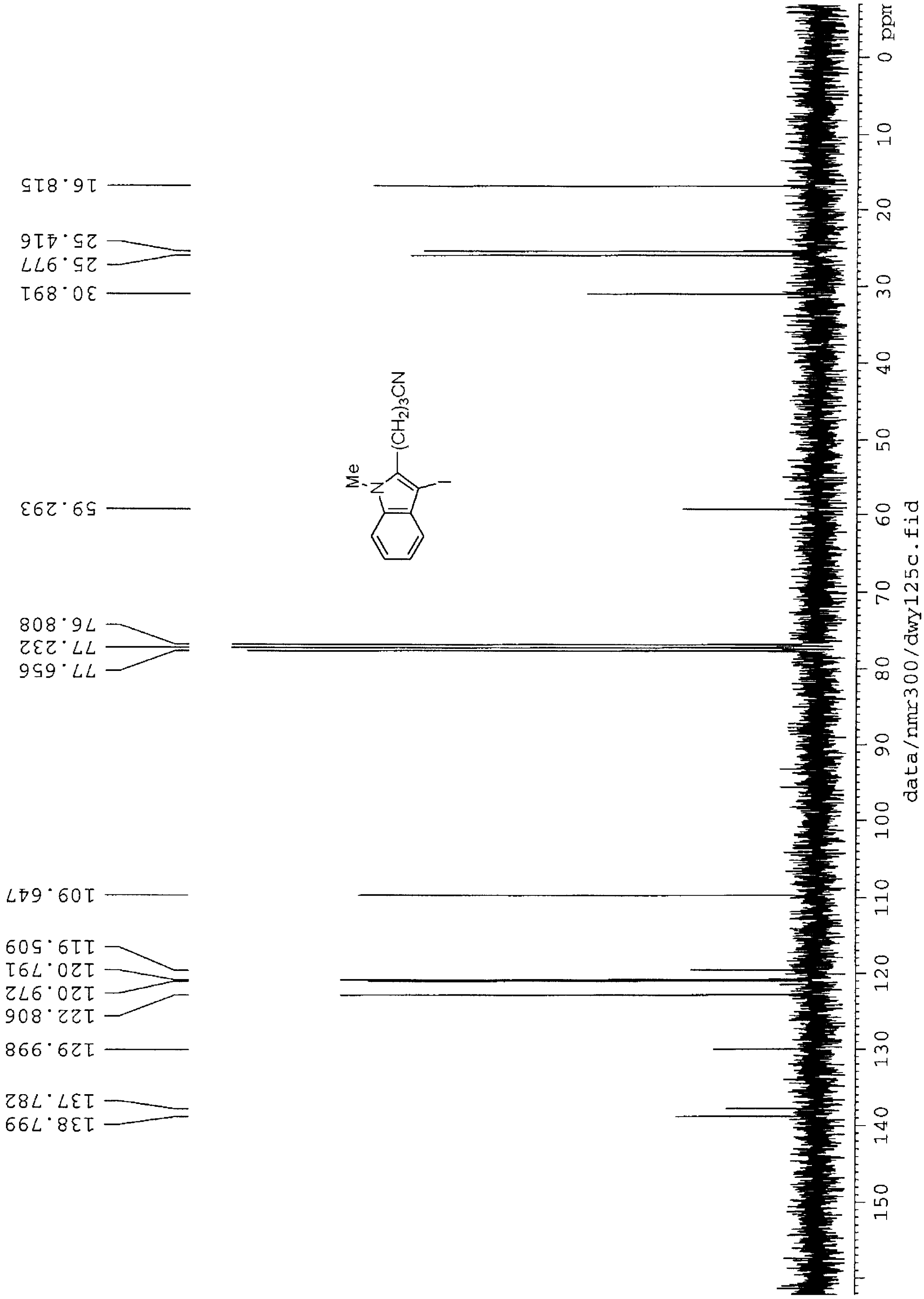

0.000
1.734
1.743
1.748
1.757
1.762
1.808
1.812
1.822
1.827
1.835
2.222
2.228
2.237
2.243
2.249
2.258
2.264
2.272
2.280
2.287
2.296
3.681
5.884
5.889
5.893
5.898
7.167
7.176
7.178
7.187
7.224
7.226
7.230
7.235
7.403
7.422
Me
N
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
4.587
4.434
3.000
1.085
1.115
2.185
1.004
data/nmr400/dwy114

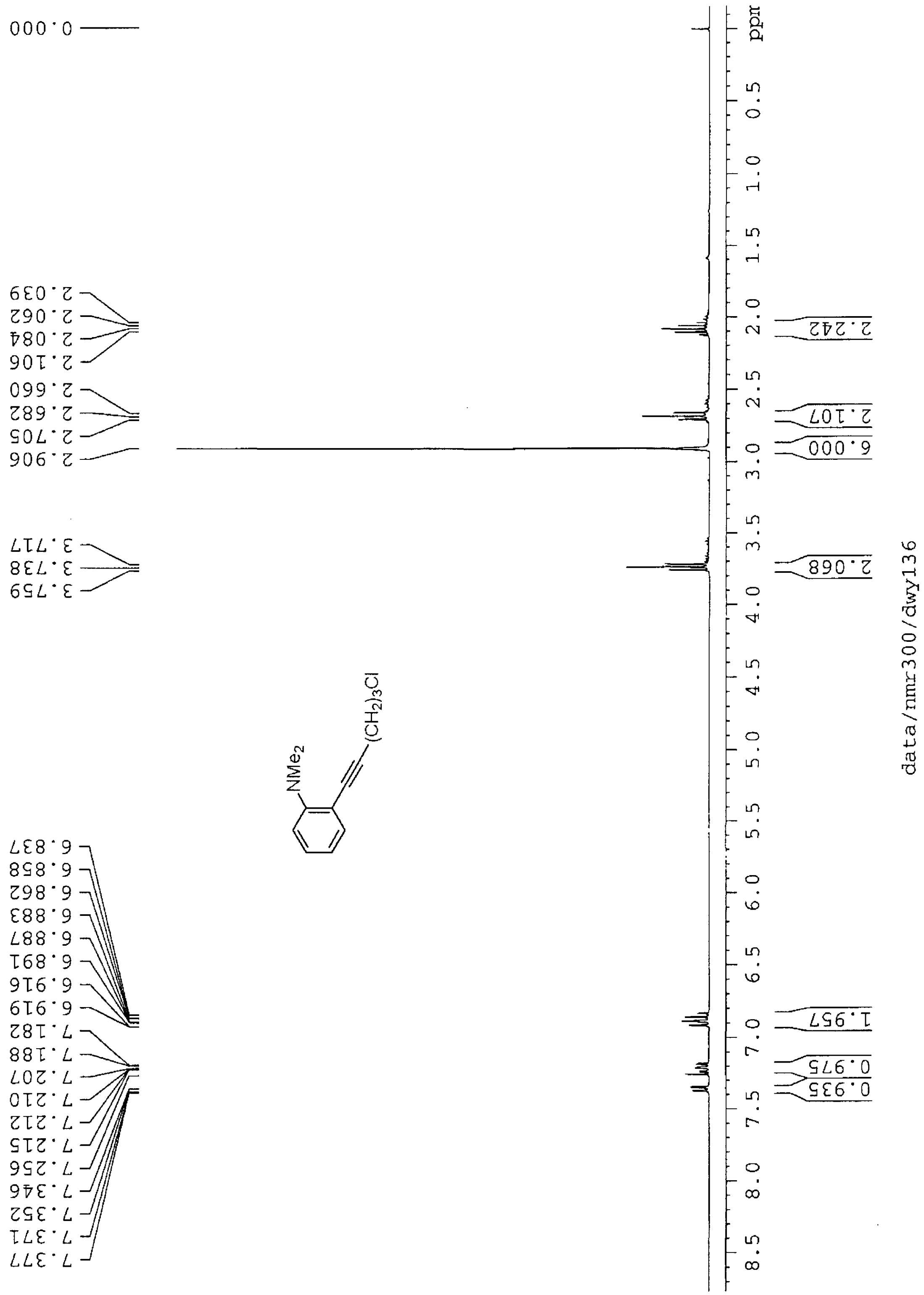

22.127
22.910
25.715
29.448
31.491
56.989
76.913
77.231
77.549
109.734
120.477
121.168
122.434
129.937
130.281
133.838
137.334
144.441
Me
N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr400/dwy114c

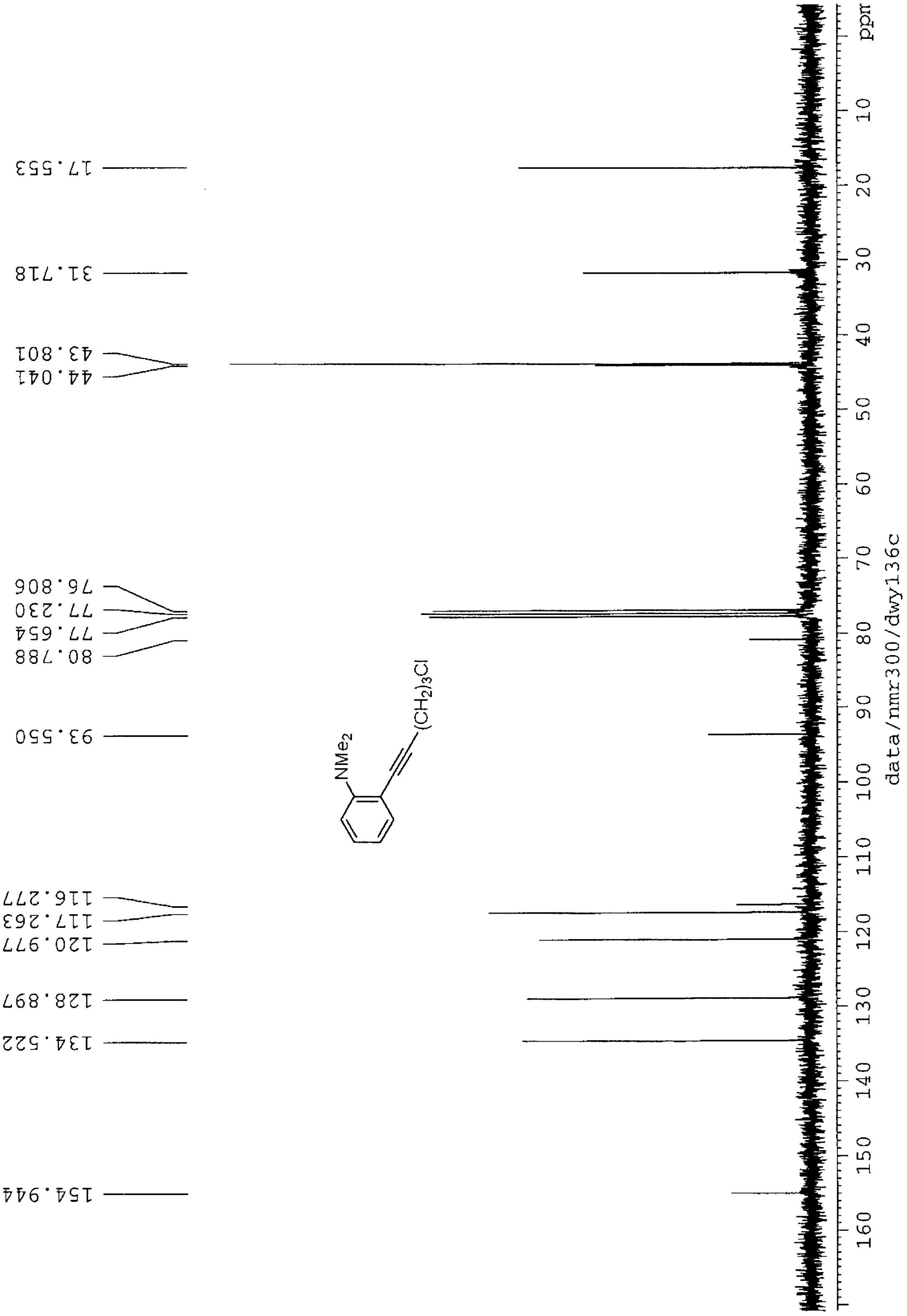

0.000
1.954
1.972
1.989
2.556
2.574
2.592
2.648
2.665
2.682
2.895
6.847
6.849
6.866
6.868
6.886
6.900
6.920
7.199
7.203
7.221
7.345
7.349
7.364
7.368
NMe$_2$
(CH$_2$)$_3$CN
2.011
1.983
1.982
6.000
0.986
0.939
0.989
0.954
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
data/nmr400/dwy126

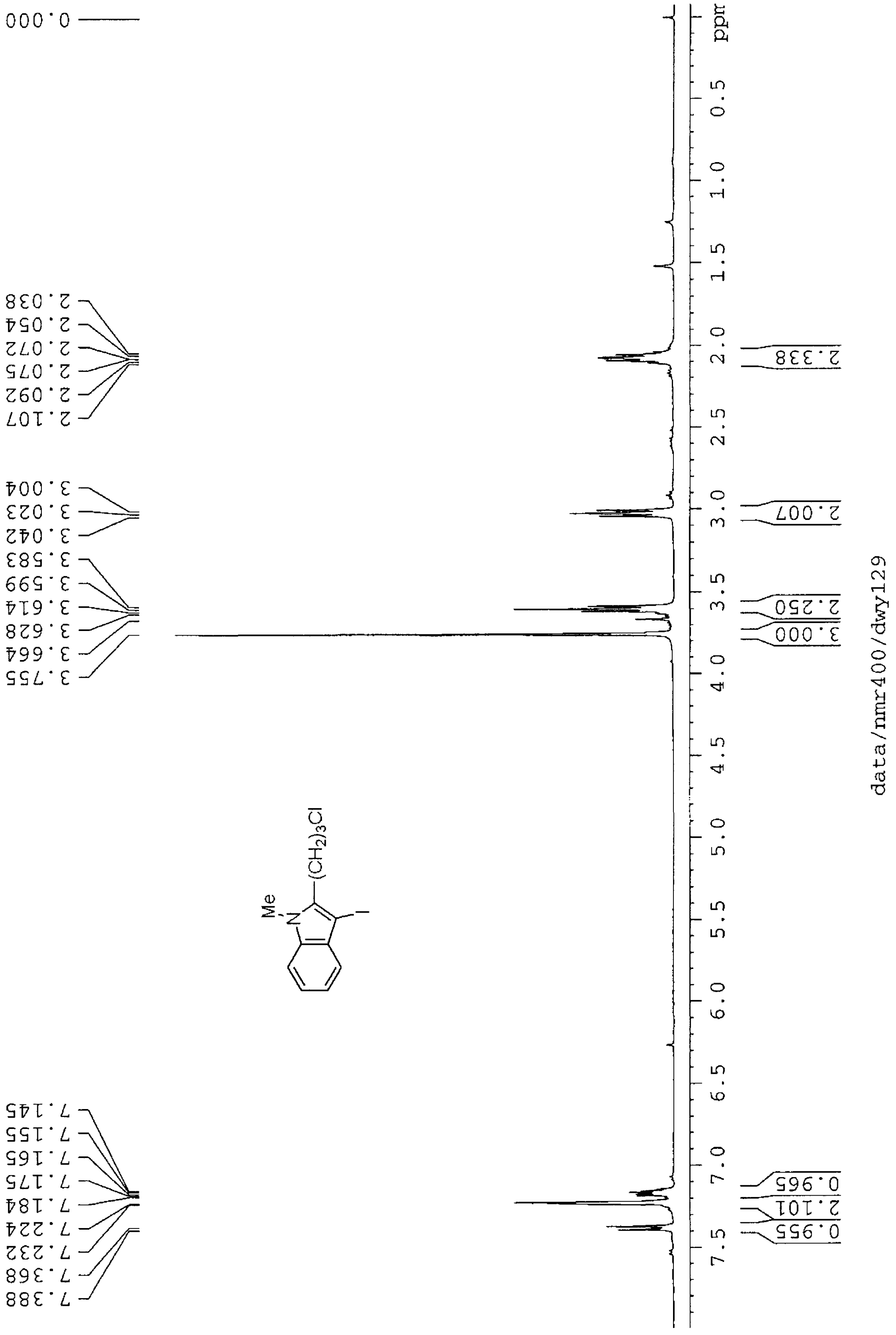

16.340
76.912
77.231
77.548
81.642
92.298
115.891
117.311
119.410
121.007
129.083
134.408
154.968
NMe2
(CH2)3CN
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr400/dwy126c

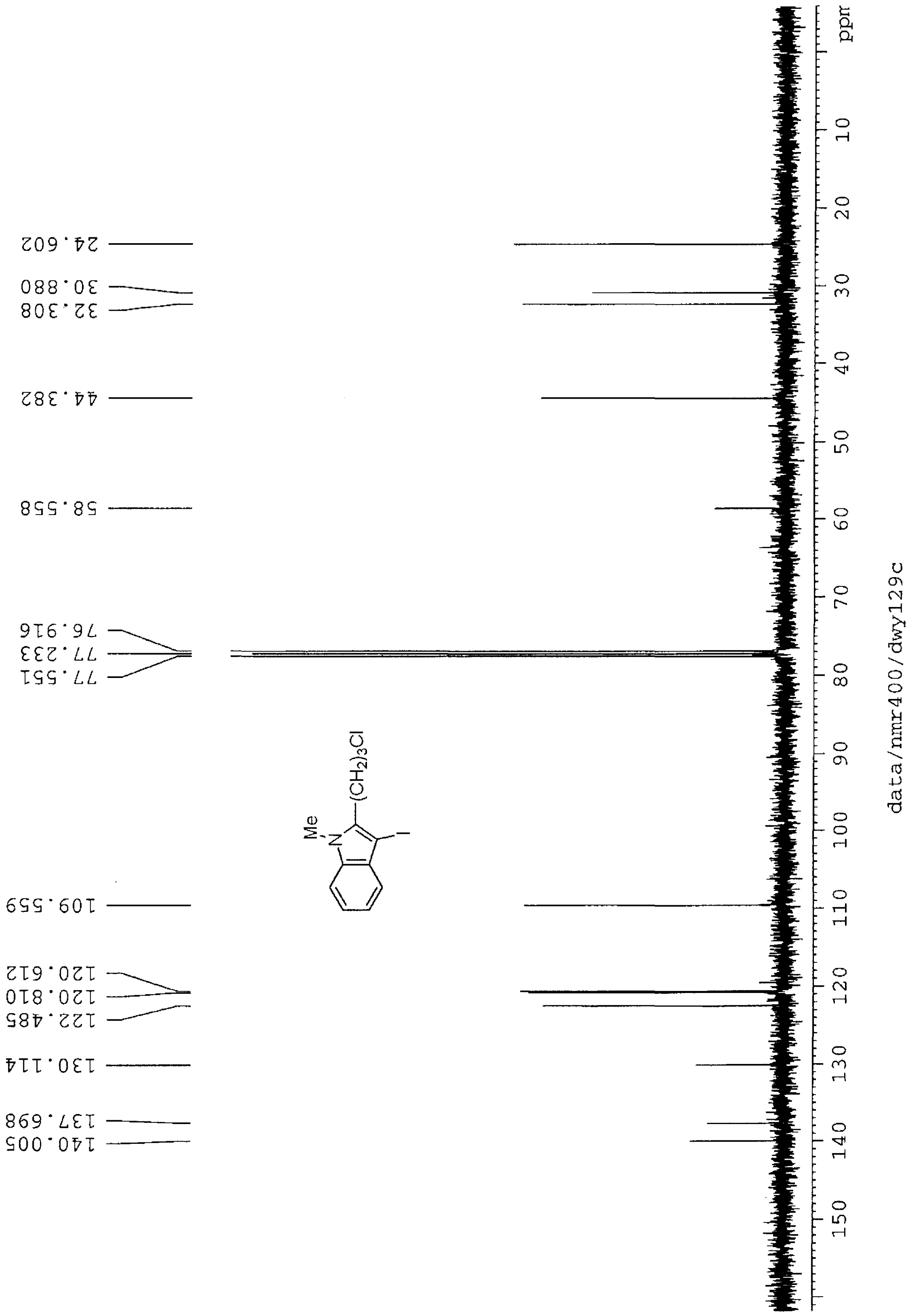

0.000
1.963
1.987
2.012
2.036
2.400
2.424
2.447
2.998
3.023
3.048
3.768
7.166
7.170
7.181
7.192
7.196
7.207
7.244
7.255
7.259
7.263
7.370
7.374
7.396
7.399
Me
N
(CH$_2$)$_3$CN
2.071
2.011
2.007
3.000
0.922
2.047
0.937
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
data/nmr300/dwy125.fid

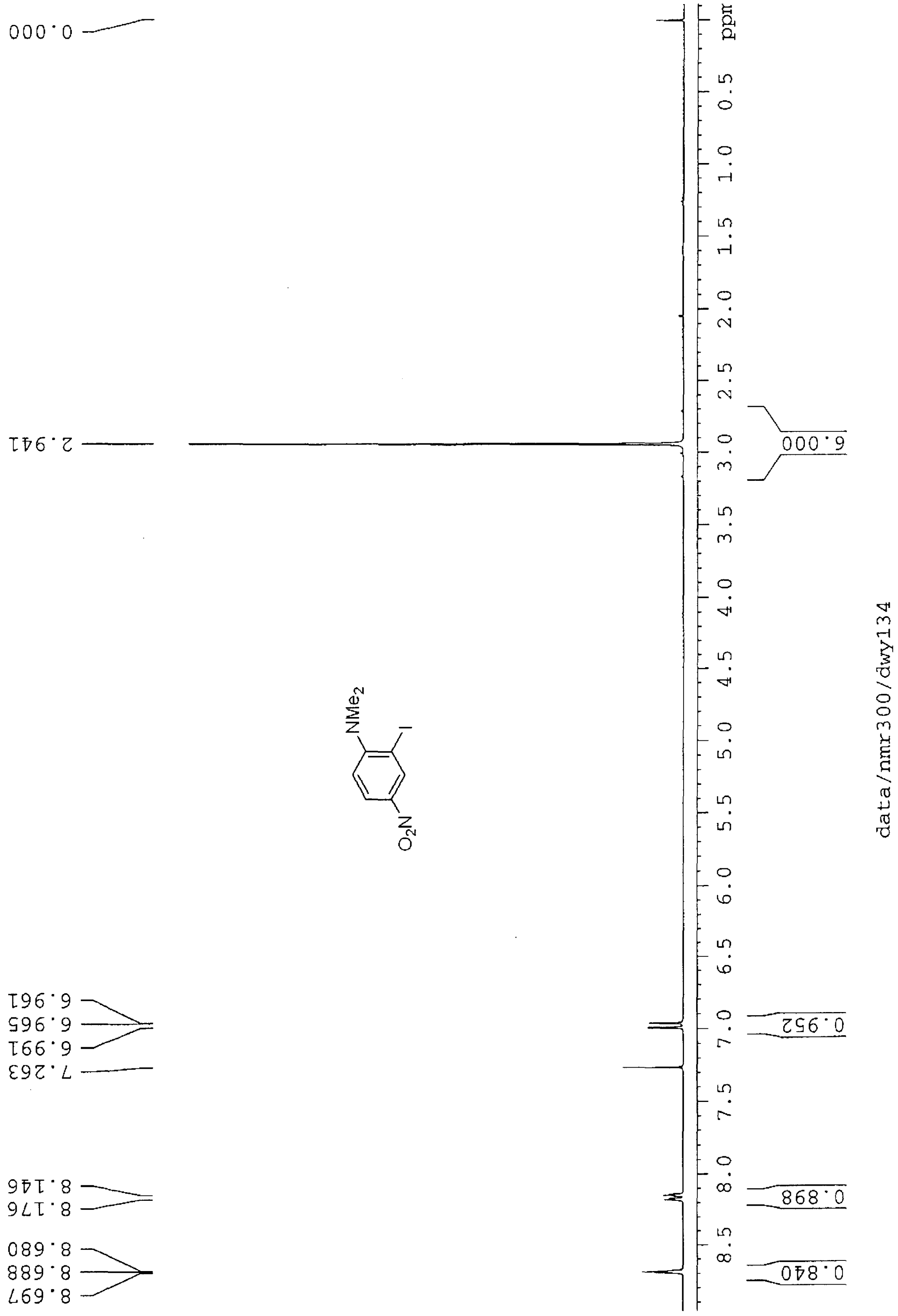

16.815
25.416
25.977
30.891
59.293
76.808
77.232
77.656
109.647
119.509
120.791
120.972
122.806
129.998
137.782
138.799
Me
N
(CH2)3CN
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
ppm
data/nmr300/dwy125c.fid

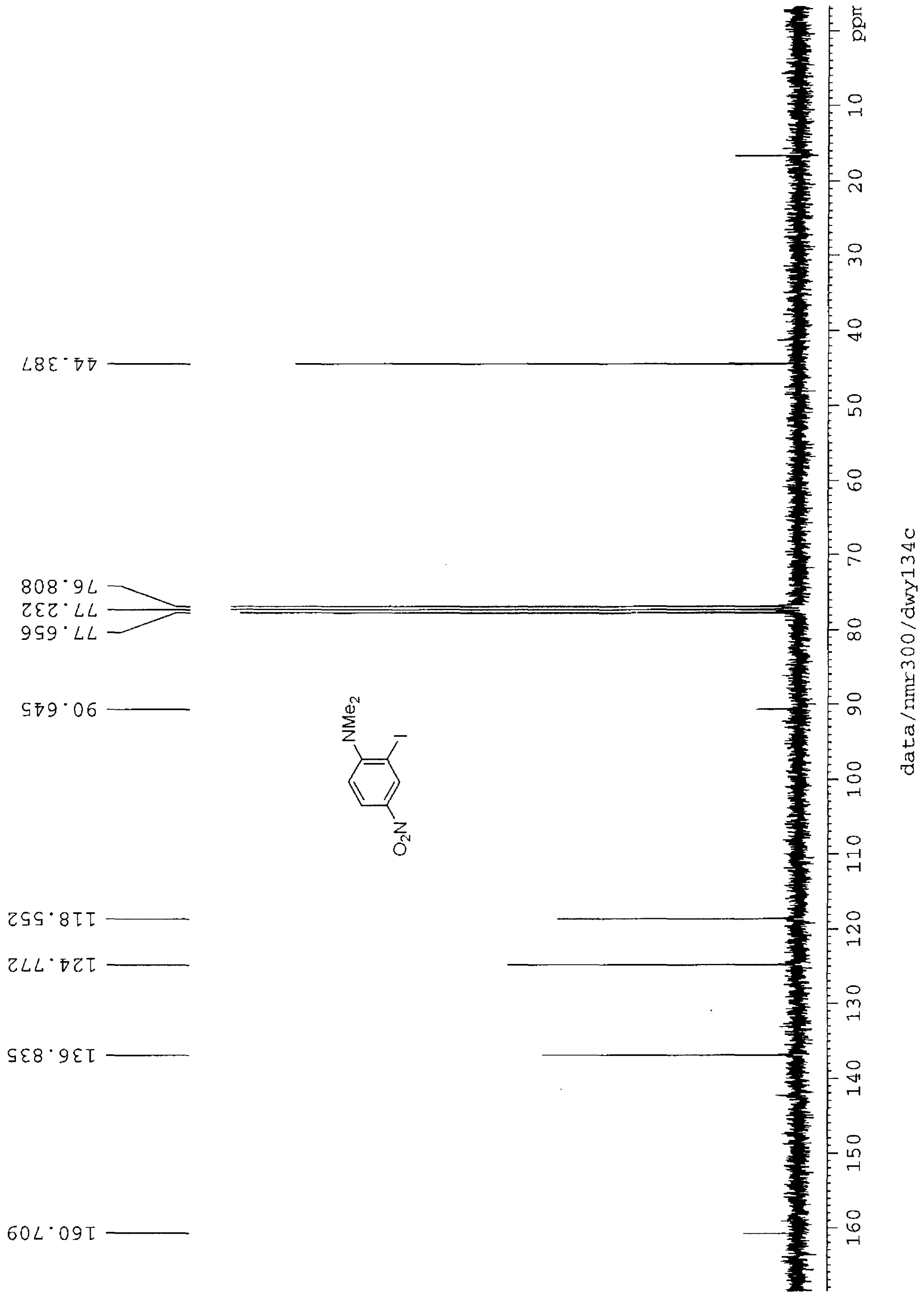

0.000
2.039
2.062
2.084
2.106
2.660
2.682
2.705
2.906
3.717
3.738
3.759
6.837
6.858
6.862
6.883
6.887
6.891
6.916
6.919
7.182
7.188
7.207
7.210
7.212
7.215
7.256
7.346
7.352
7.371
7.377
NMe2
(CH2)3Cl
2.242
2.107
6.000
2.068
1.957
0.975
0.935
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
data/nmr300/dwy136

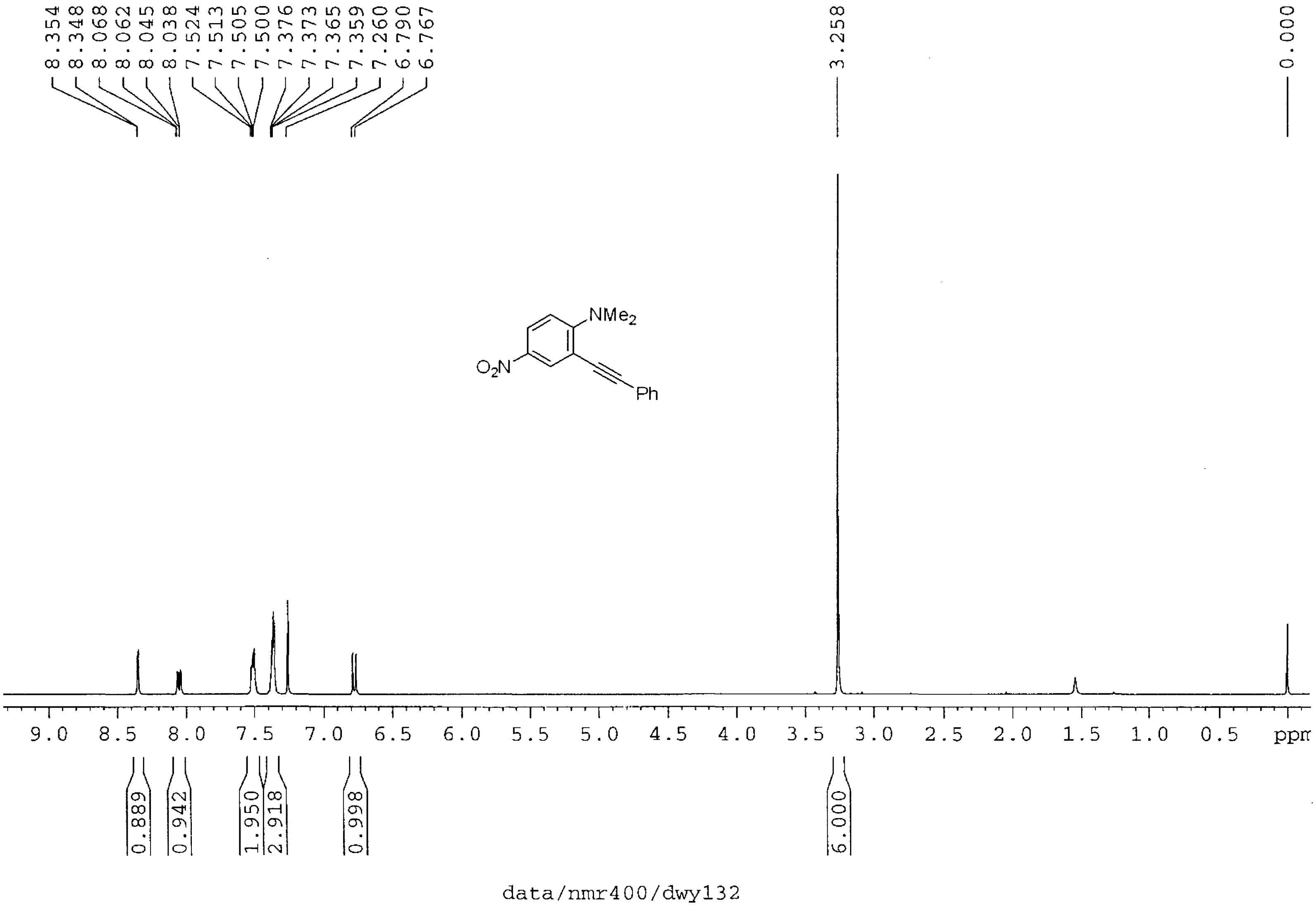

17.553
31.718
43.801
44.041
76.806
77.230
77.654
80.788
93.550
116.277
117.263
120.977
128.897
134.522
154.944
NMe$_2$
(CH$_2$)$_3$Cl
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr300/dwy136c

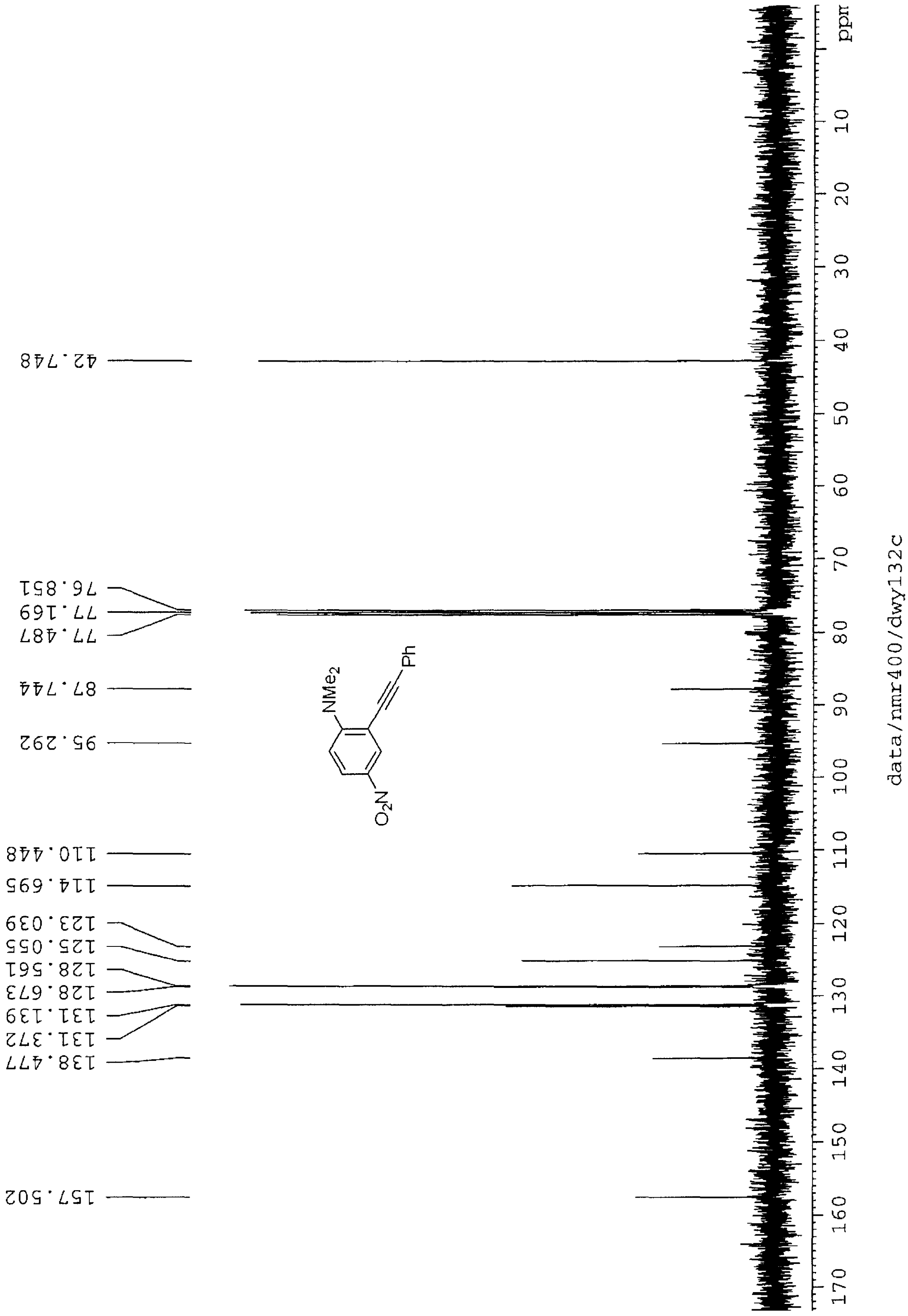

0.000
2.038
2.054
2.072
2.075
2.092
2.107
3.004
3.023
3.042
3.583
3.599
3.614
3.628
3.664
3.755
7.145
7.155
7.165
7.175
7.184
7.224
7.232
7.368
7.388
Me
N
(CH$_2$)$_3$Cl
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
2.338
2.007
2.250
3.000
0.965
2.101
0.955
data/nmr400/dwy129

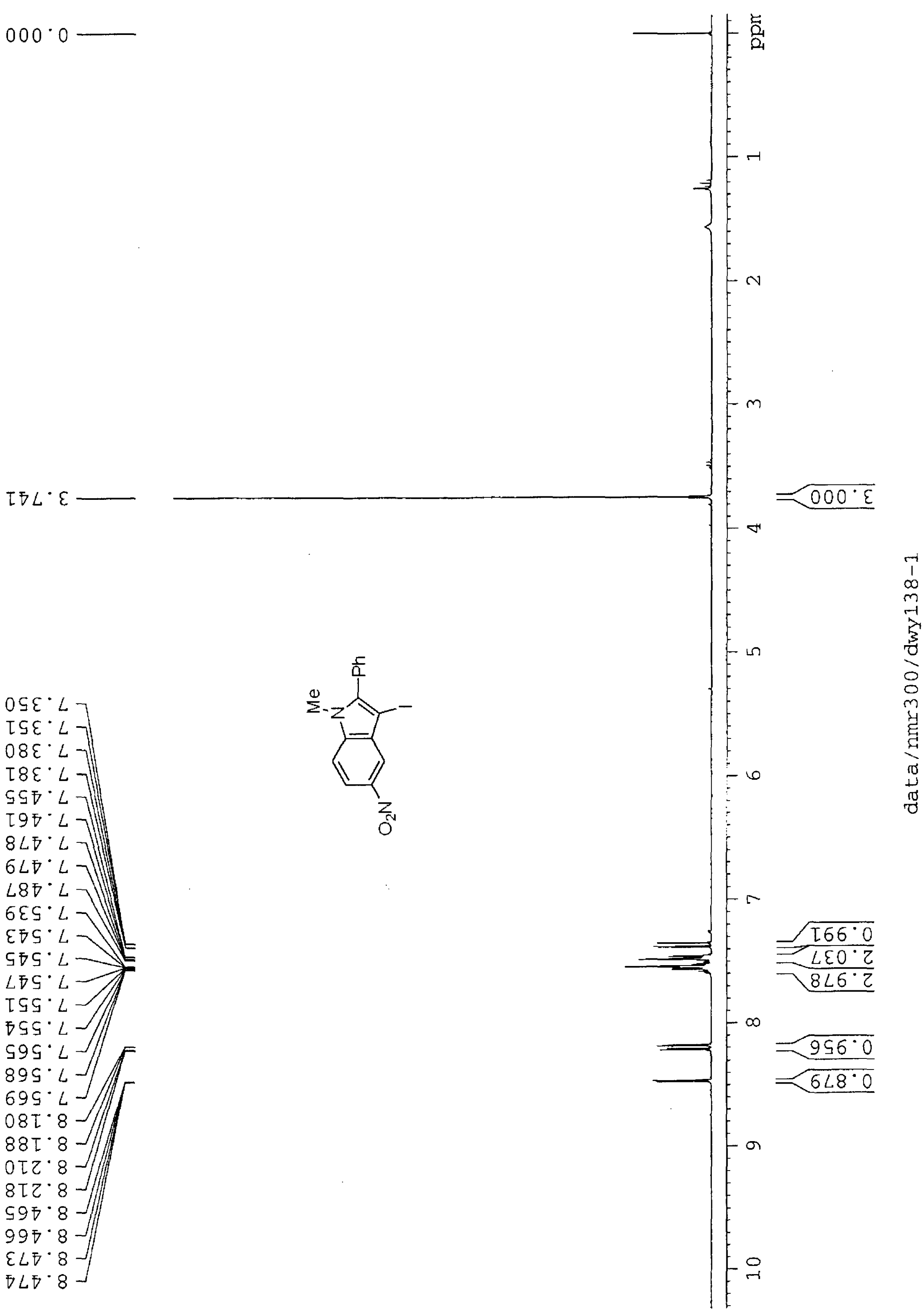

24.602
30.880
32.308
44.382
58.558
76.916
77.233
77.551
109.559
120.612
120.810
122.485
130.114
137.698
140.005
Me
N
(CH2)3Cl
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr400/dwy129c

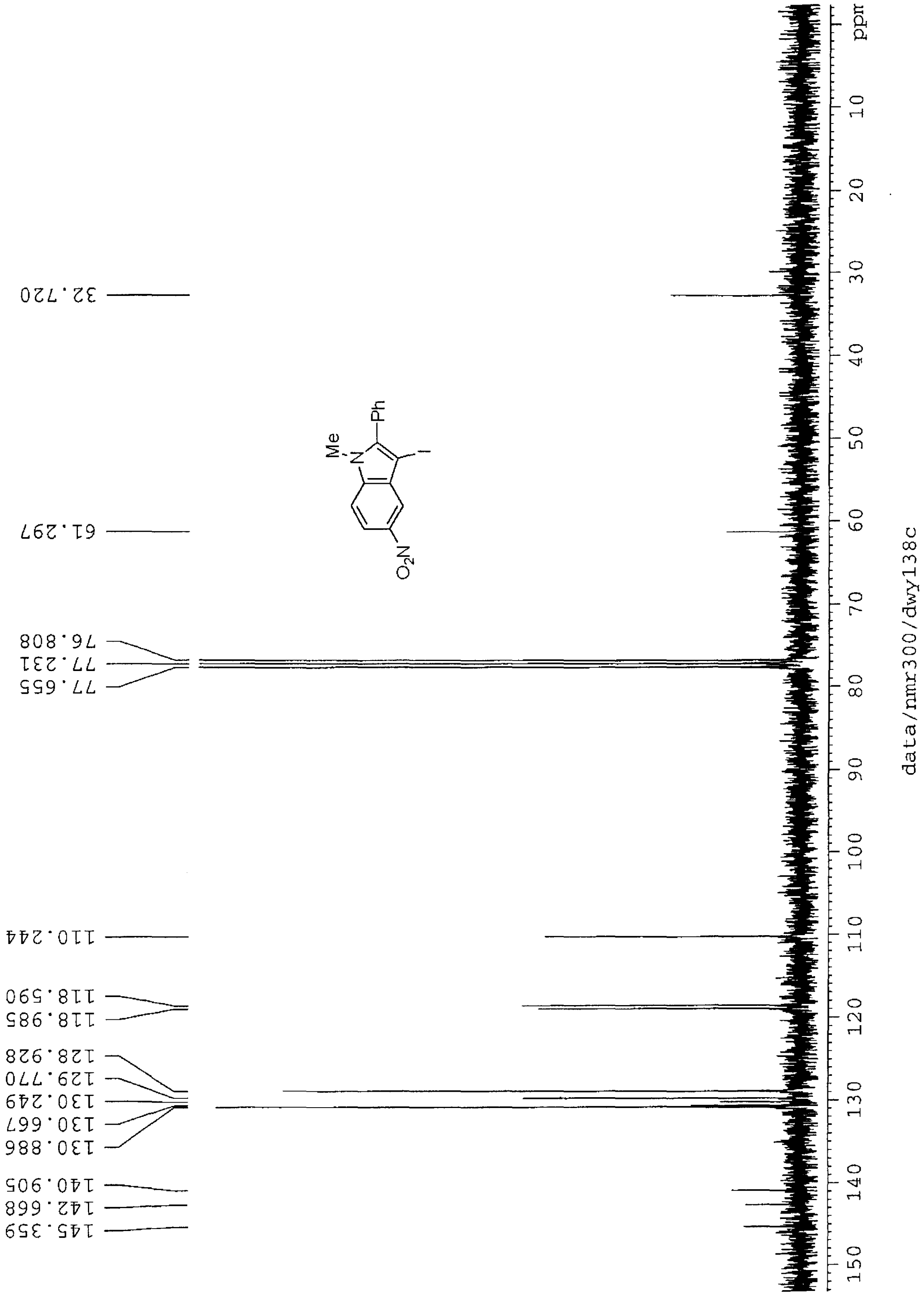

0.000
2.941
6.961
6.965
6.991
7.263
8.146
8.176
8.680
8.688
8.697
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
6.000
0.952
0.898
0.840
NMe2
I
O2N
data/nmr300/dwy134

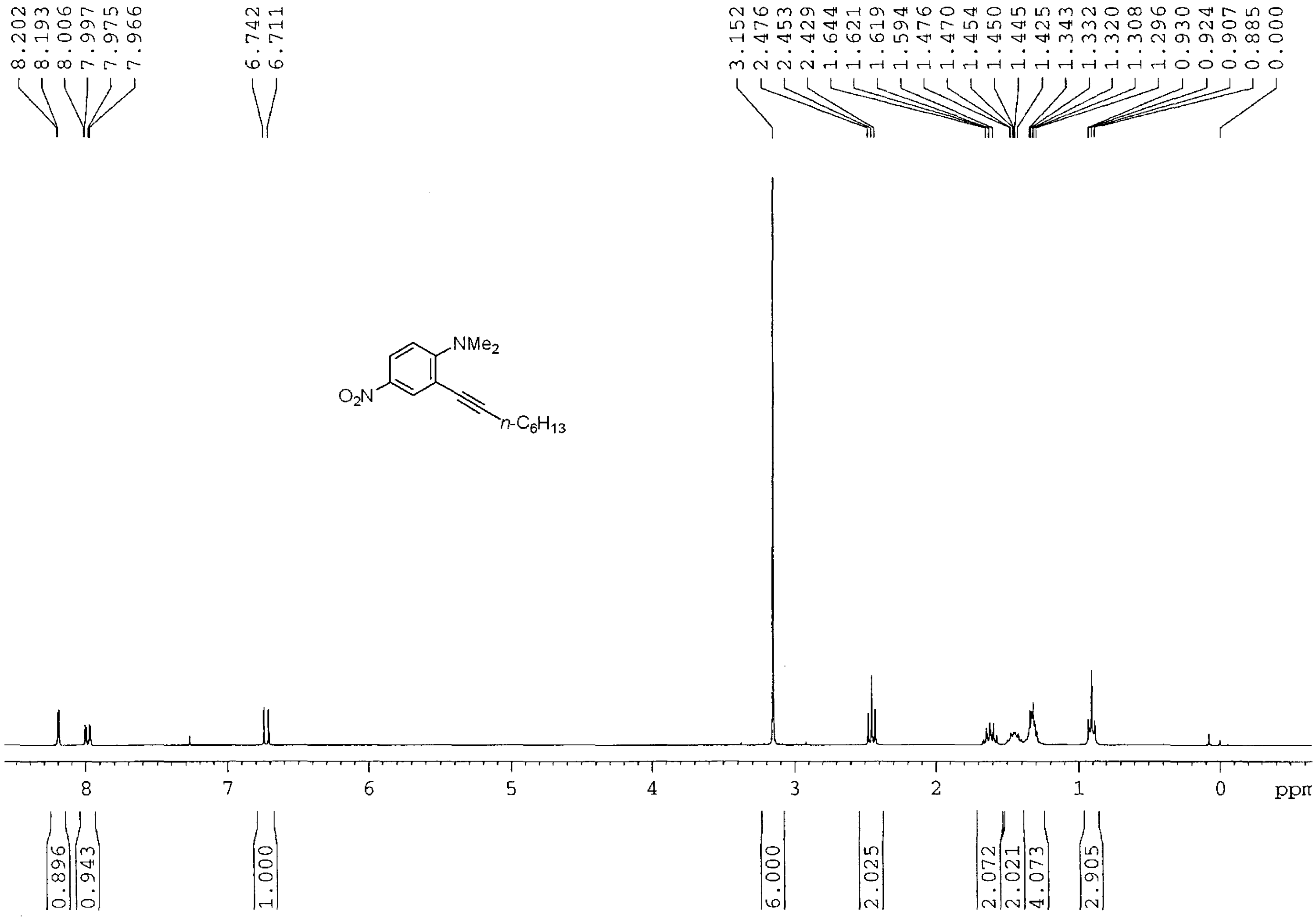

44.387
76.808
77.232
77.656
90.645
118.552
124.772
136.835
160.709
NMe$_2$
I
O$_2$N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr300/dwy134c


8.354
8.348
8.068
8.062
8.045
8.038
7.524
7.513
7.505
7.500
7.376
7.373
7.365
7.359
7.260
6.790
6.767
3.258
0.000
NMe2
O2N
Ph
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.889
0.942
1.950
2.918
0.998
6.000
data/nmr400/dwy132

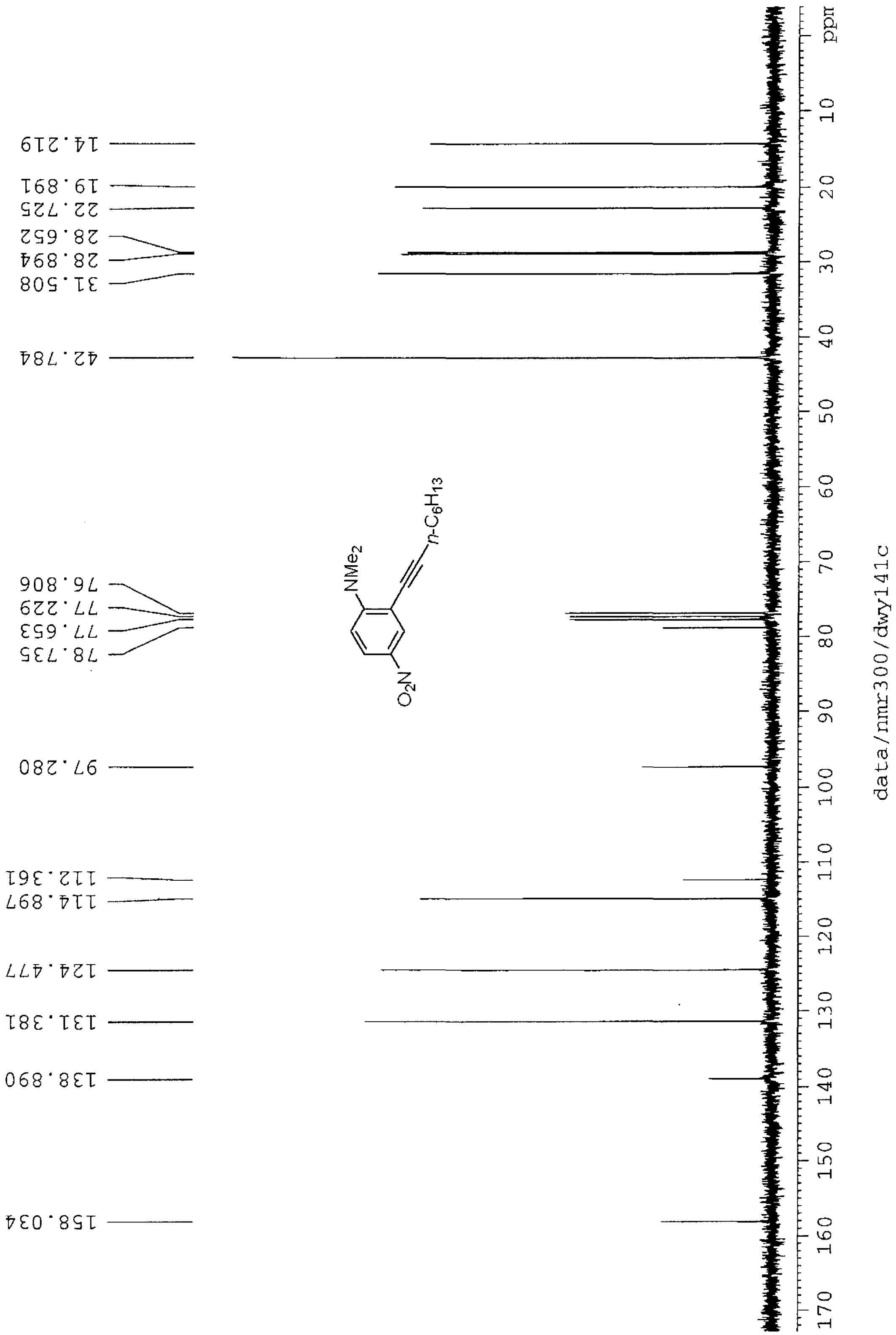

42.748
76.851
77.169
77.487
87.744
95.292
110.448
114.695
123.039
125.055
128.561
128.673
131.139
131.372
138.477
157.502
NMe$_2$
Ph
O$_2$N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy132c

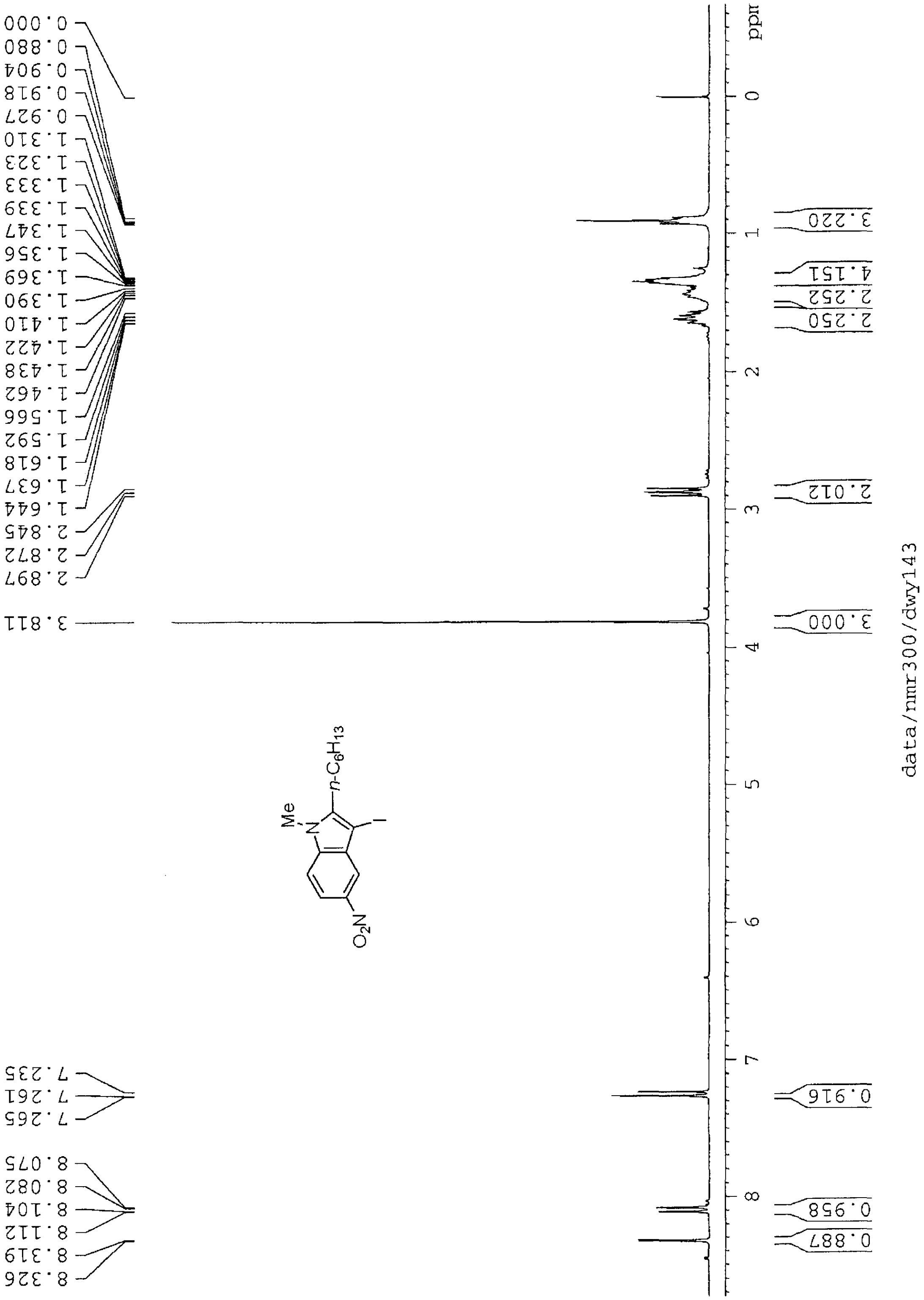

0.000
3.741
7.350
7.351
7.380
7.381
7.455
7.461
7.478
7.479
7.487
7.539
7.543
7.545
7.547
7.551
7.554
7.565
7.568
7.569
8.180
8.188
8.210
8.218
8.465
8.466
8.473
8.474
Me
N
Ph
I
O2N
3.000
0.991
2.037
2.978
0.956
0.879
ppm
1
2
3
4
5
6
7
8
9
10
data/nmr300/dwy138-1

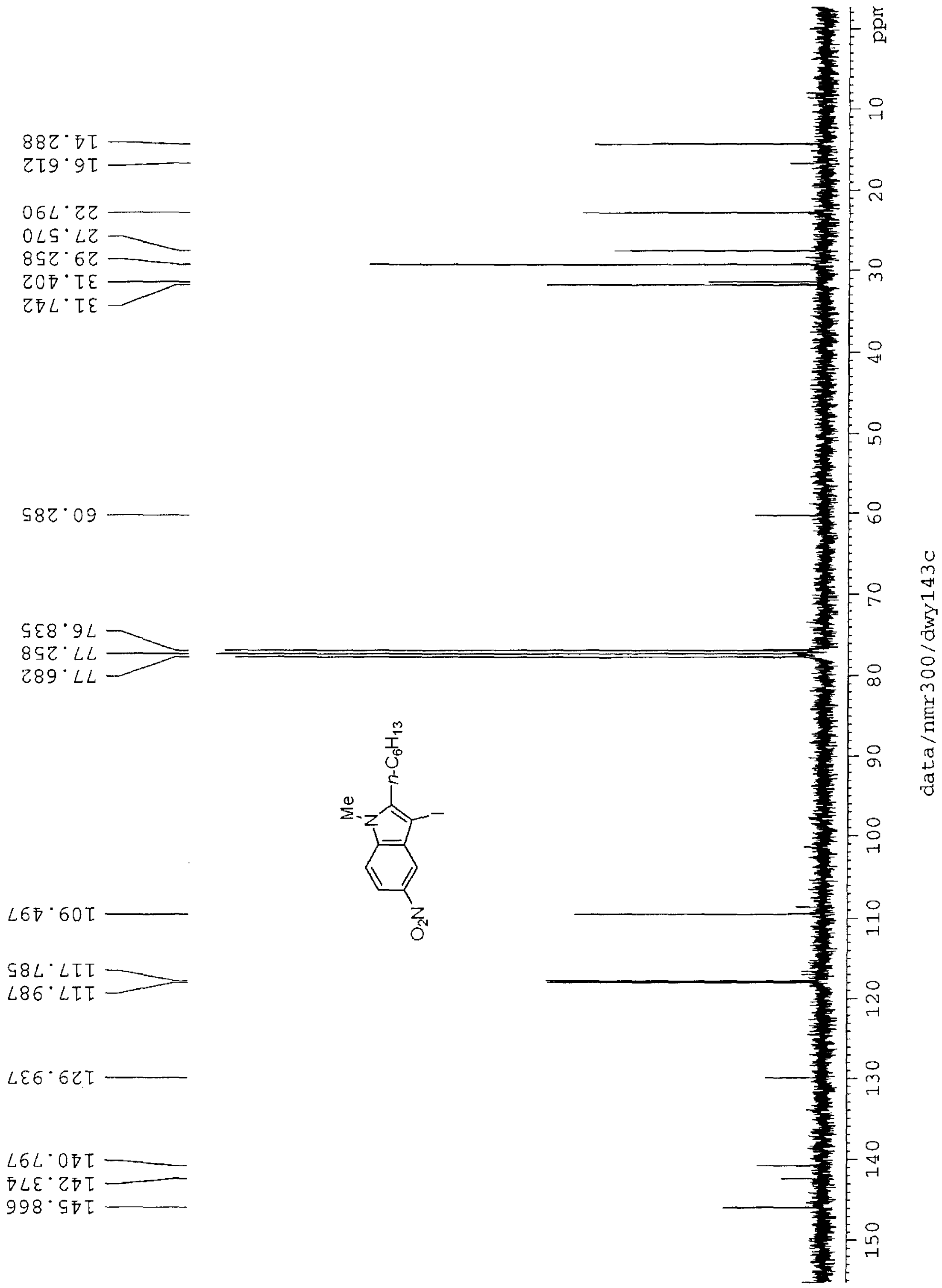

32.720
61.297
76.808
77.231
77.655
110.244
118.590
118.985
128.928
129.770
130.249
130.667
130.886
140.905
142.668
145.359
Me
N
Ph
I
O_2N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr300/dwy138c

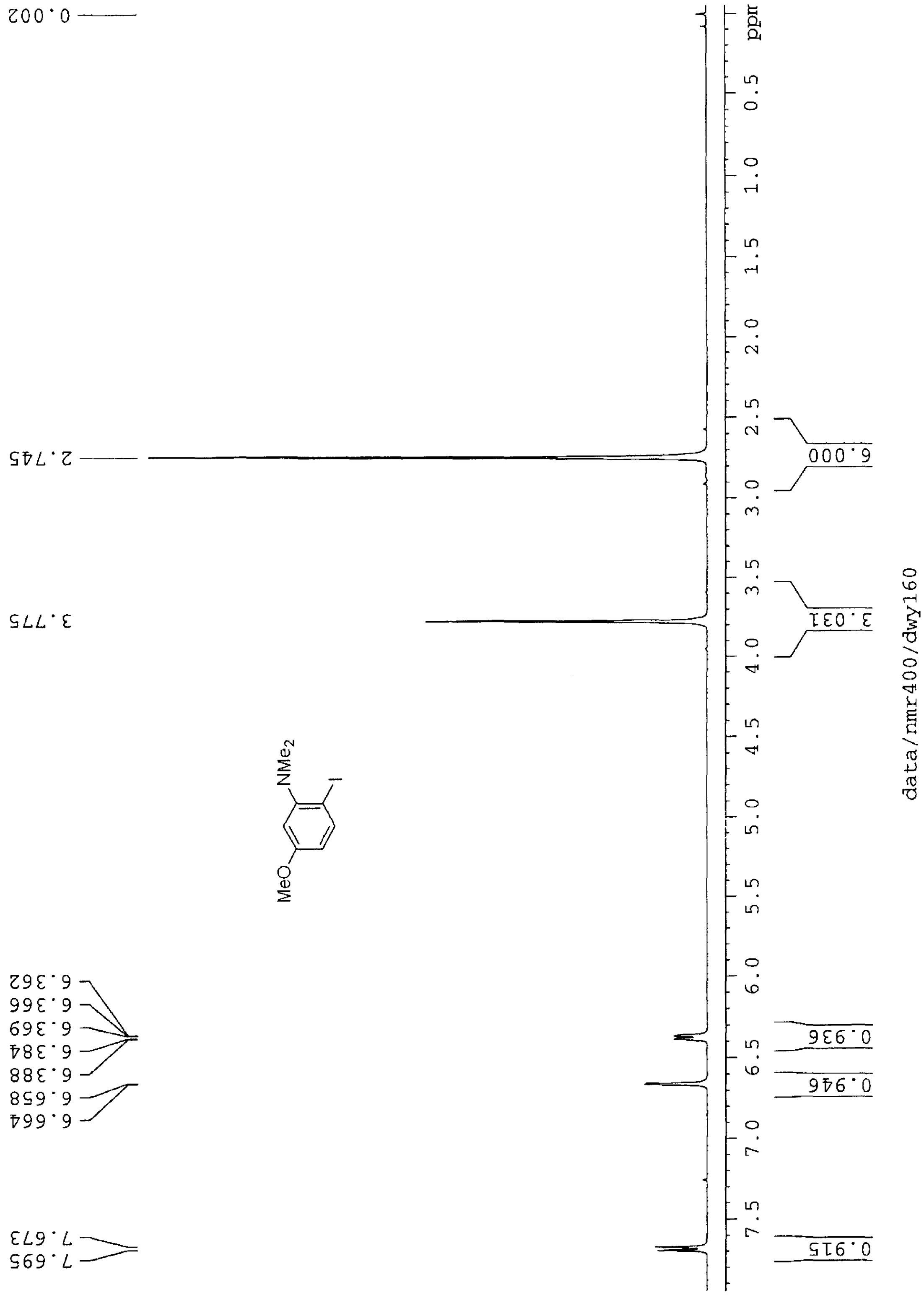


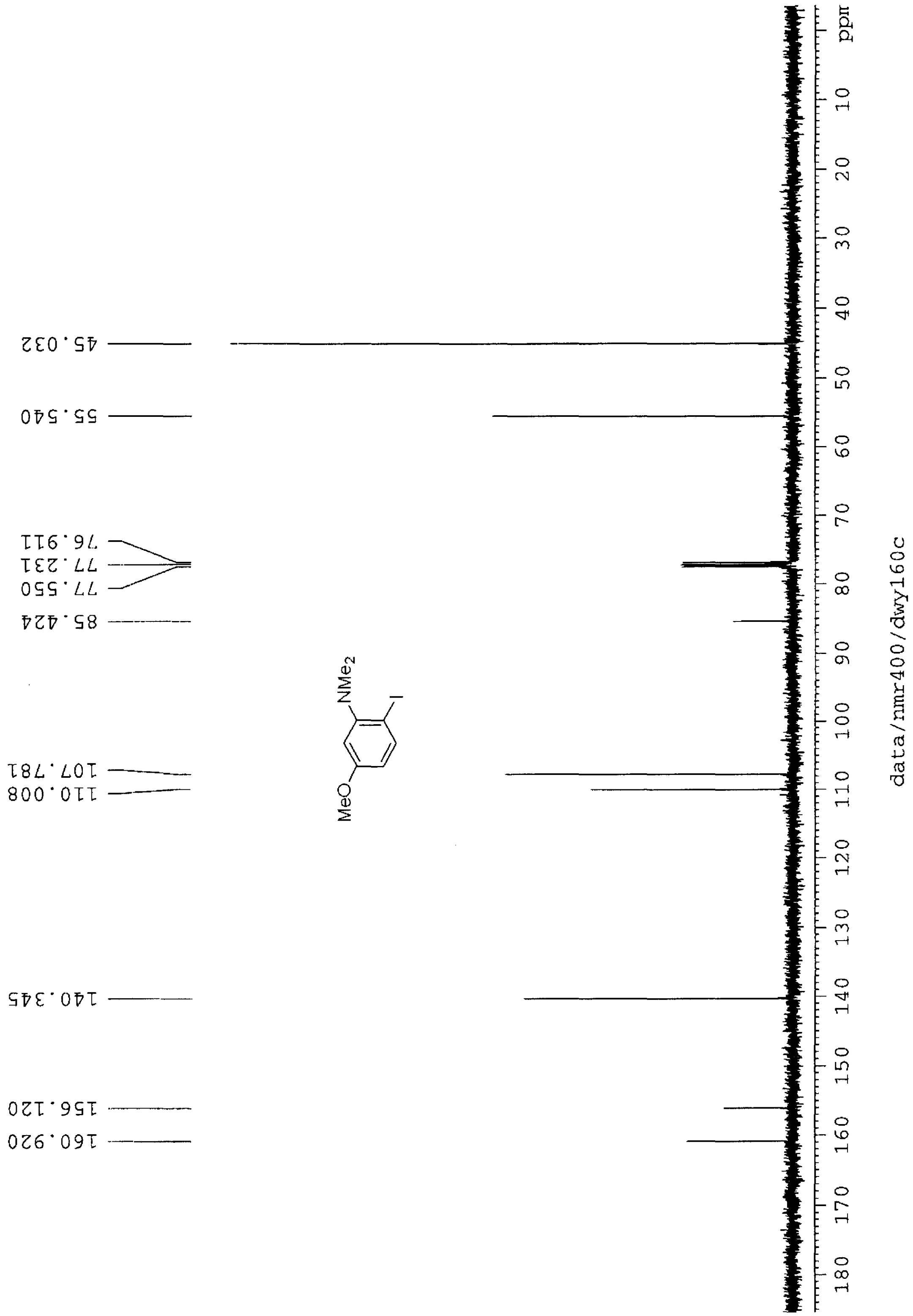
data/nmr300/dwy141

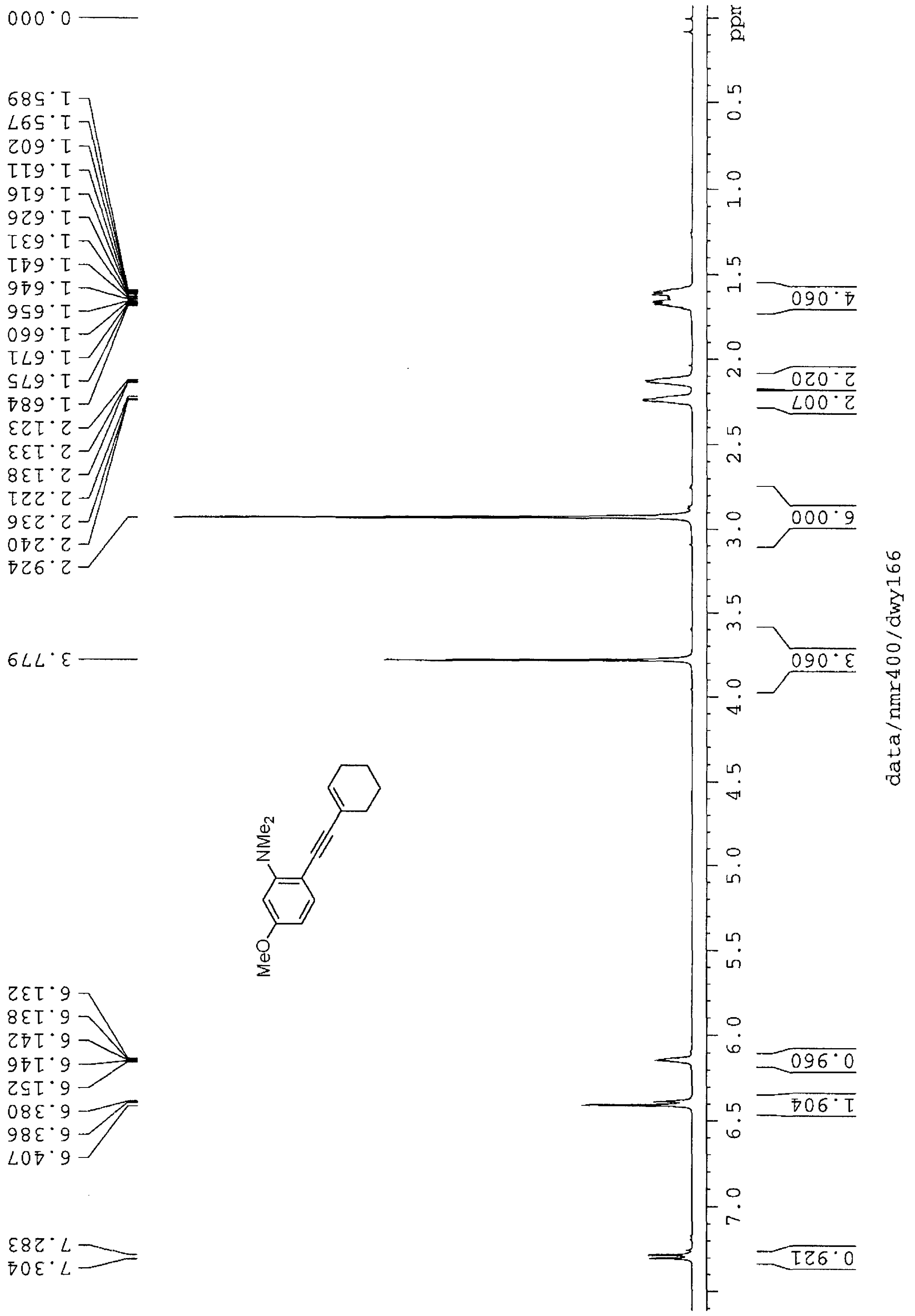

14.219
19.891
22.725
28.652
28.894
31.508
42.784
76.806
77.229
77.653
78.735
97.280
112.361
114.897
124.477
131.381
138.890
158.034
NMe2
O2N
n-C6H13
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr300/dwy141c

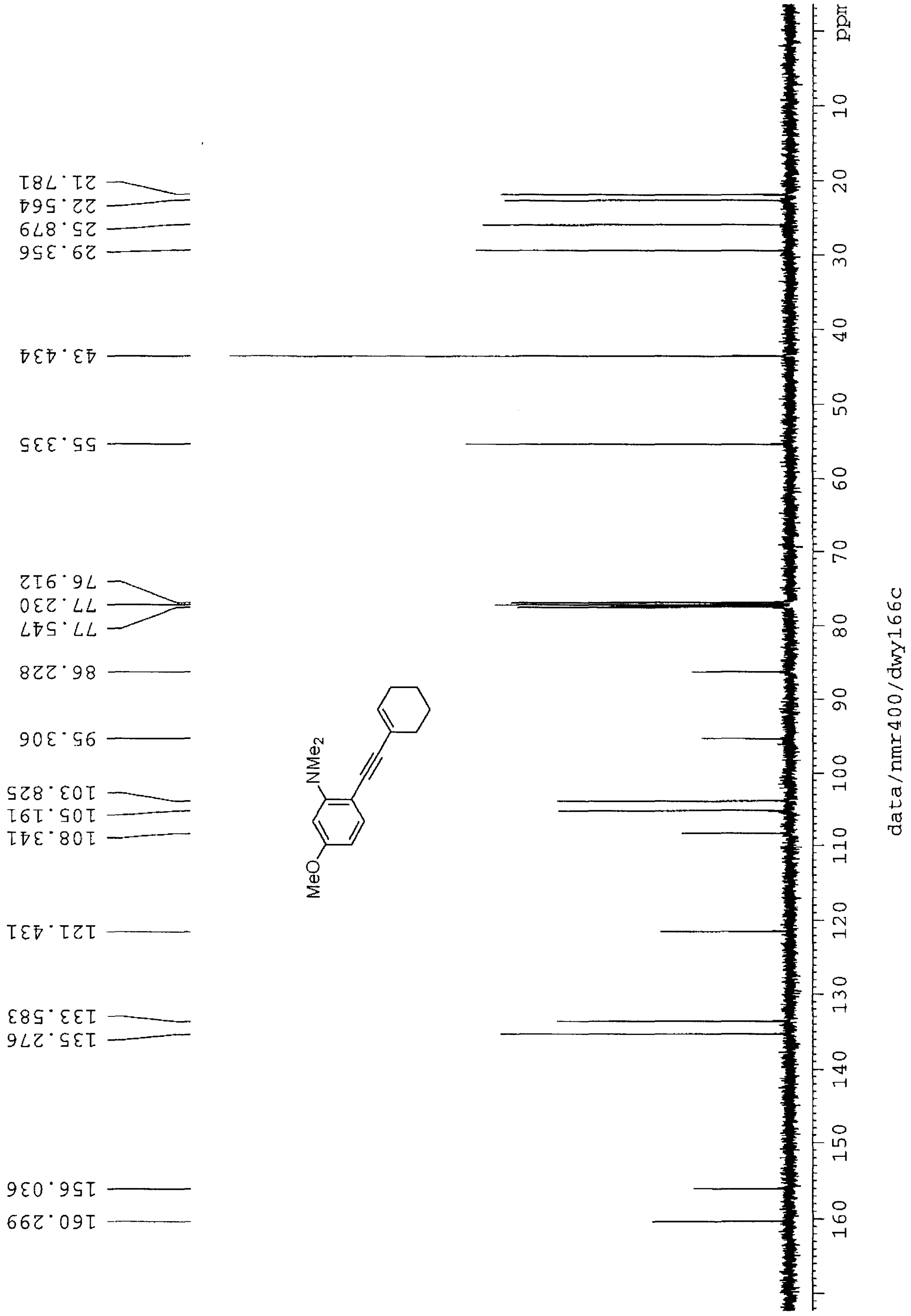

0.000
0.880
0.904
0.918
0.927
1.310
1.323
1.333
1.339
1.347
1.356
1.369
1.390
1.410
1.422
1.438
1.462
1.566
1.592
1.618
1.637
1.644
2.845
2.872
2.897
3.811
7.235
7.261
7.265
8.075
8.082
8.104
8.112
8.319
8.326
Me
N
n-C6H13
I
O2N
3.220
4.151
2.252
2.250
2.012
3.000
0.916
0.958
0.887
ppm
0
1
2
3
4
5
6
7
8
data/nmr300/dwy143

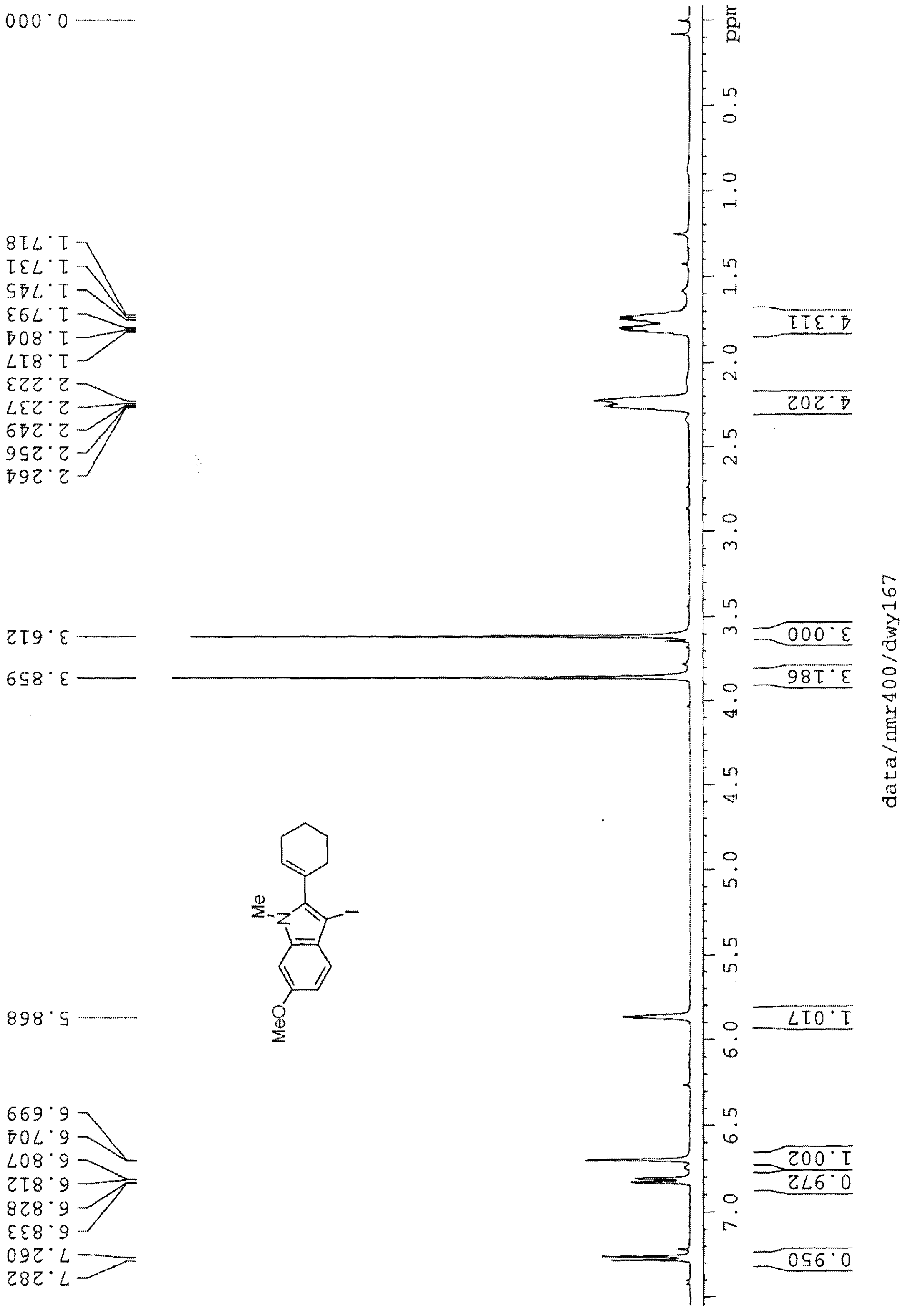

14.288
16.612
22.790
27.570
29.258
31.402
31.742
60.285
76.835
77.258
77.682
109.497
117.785
117.987
129.937
140.797
142.374
145.866
Me
N
n-C$_6$H$_{13}$
I
O$_2$N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr300/dwy143c

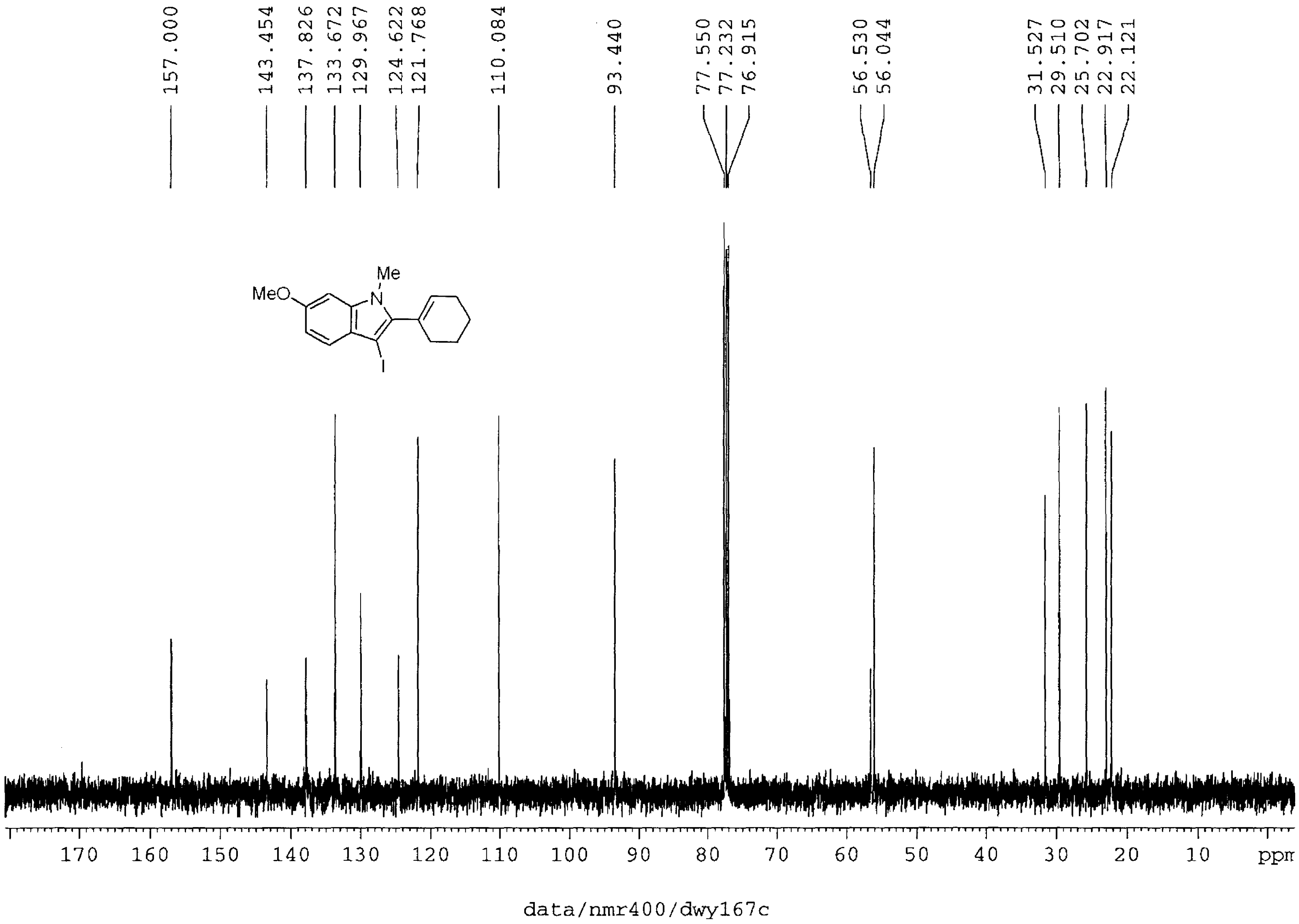

0.002
2.745
3.775
6.362
6.366
6.369
6.384
6.388
6.658
6.664
7.673
7.695
NMe2
I
MeO
6.000
3.031
0.936
0.946
0.915
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
data/nmr400/dwy160

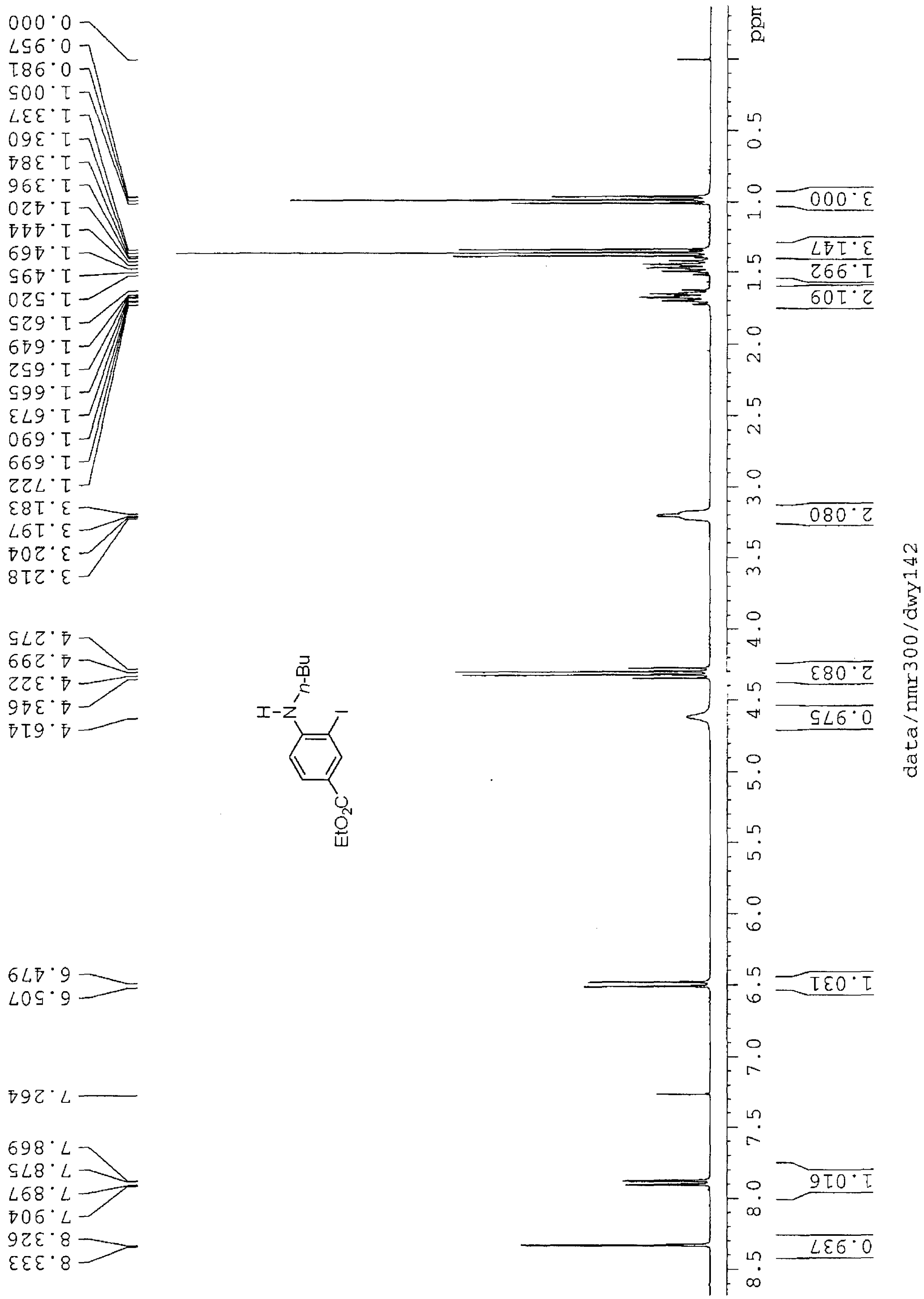

45.032
55.540
76.911
77.231
77.550
85.424
107.781
110.008
140.345
156.120
160.920
NMe2
I
MeO
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
data/nmr400/dwy160c

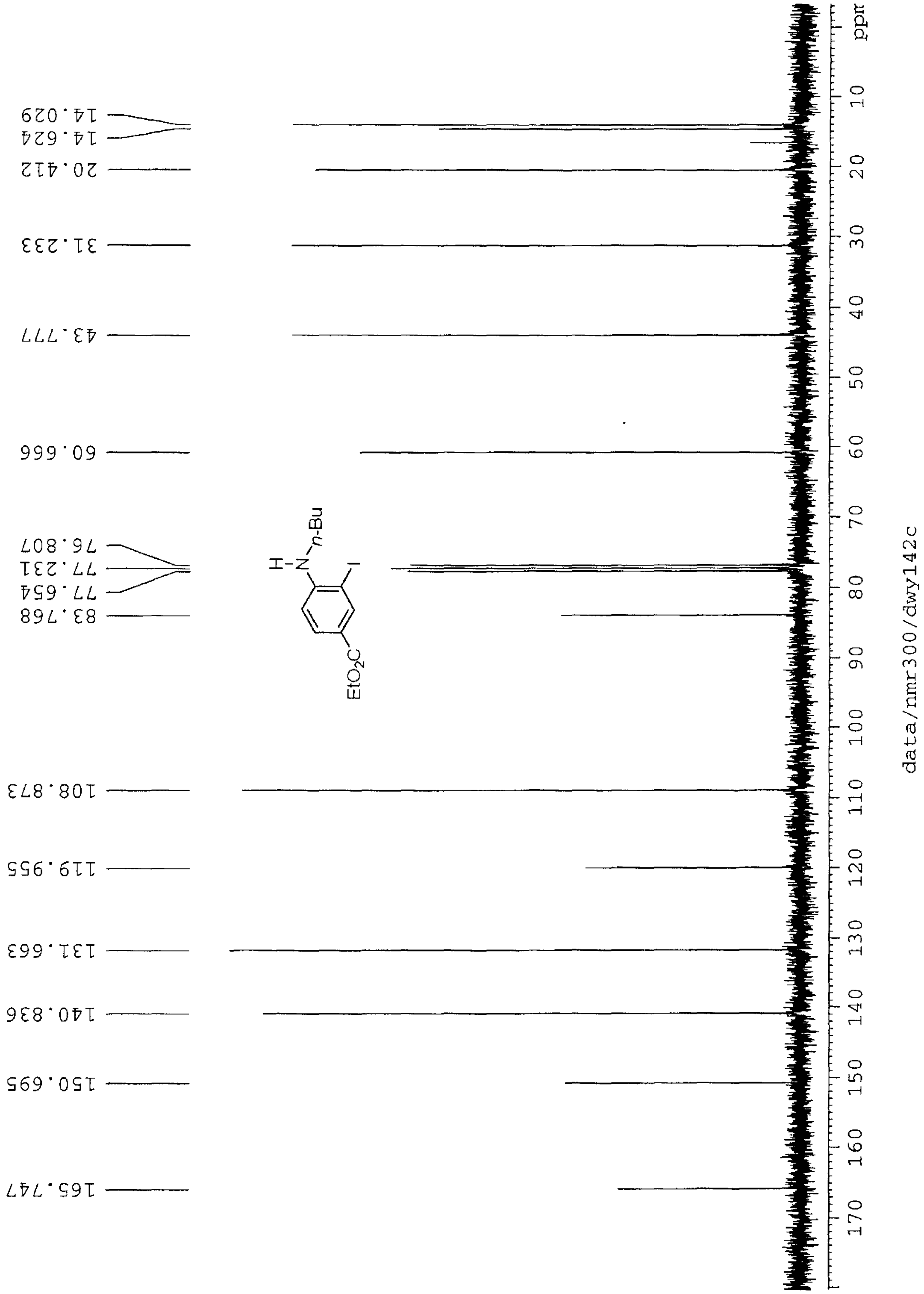

0.000
1.589
1.597
1.602
1.611
1.616
1.626
1.631
1.641
1.646
1.656
1.660
1.671
1.675
1.684
2.123
2.133
2.138
2.221
2.236
2.240
2.924
3.779
6.132
6.138
6.142
6.146
6.152
6.380
6.386
6.407
7.283
7.304
NMe2
MeO
4.060
2.020
2.007
6.000
3.060
0.960
1.904
0.921
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
data/nmr400/dwy166

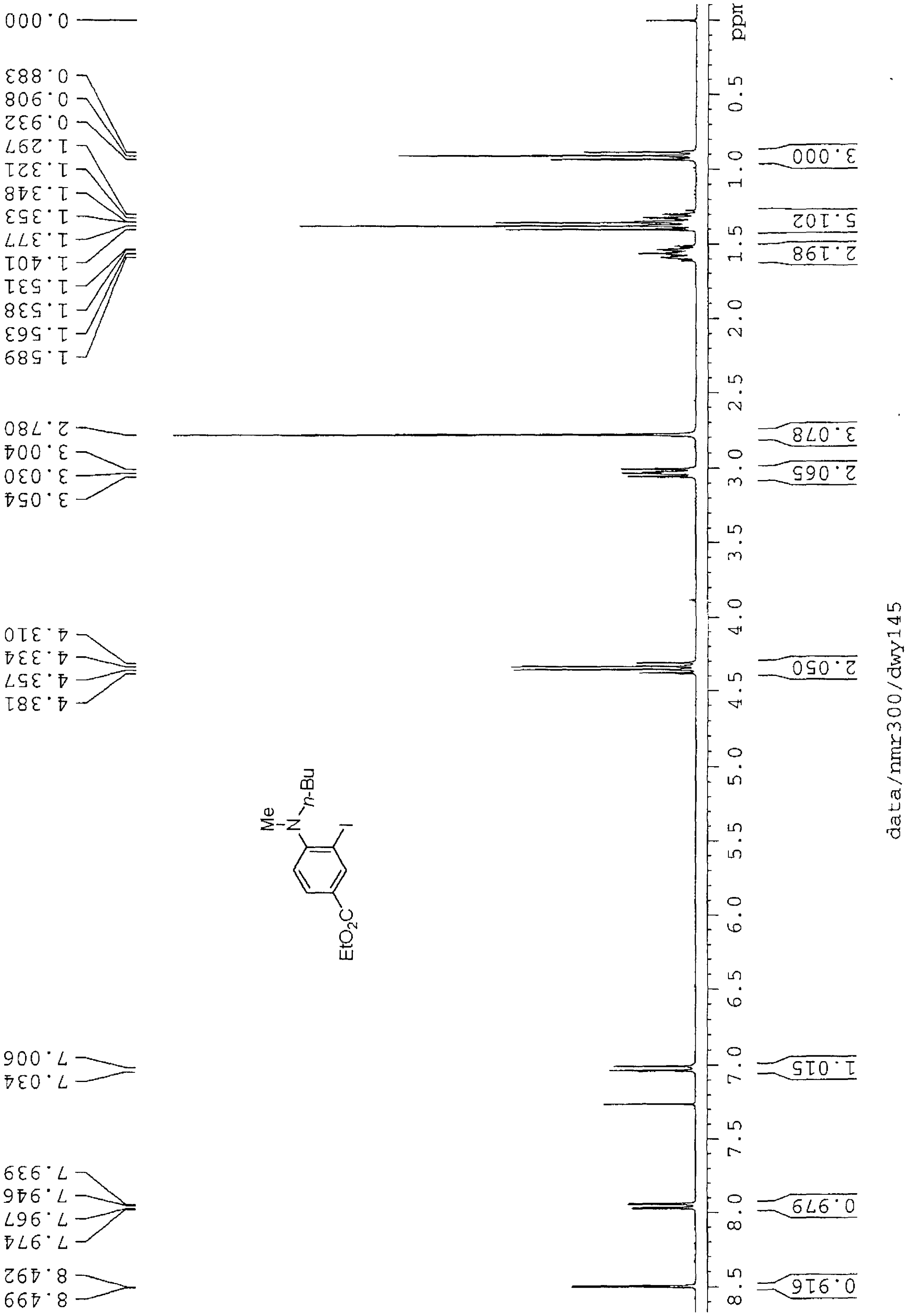

21.781
22.564
25.879
29.356
43.434
55.335
76.912
77.230
77.547
86.228
95.306
103.825
105.191
108.341
121.431
133.583
135.276
156.036
160.299
MeO
NMe$_2$
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr400/dwy166c

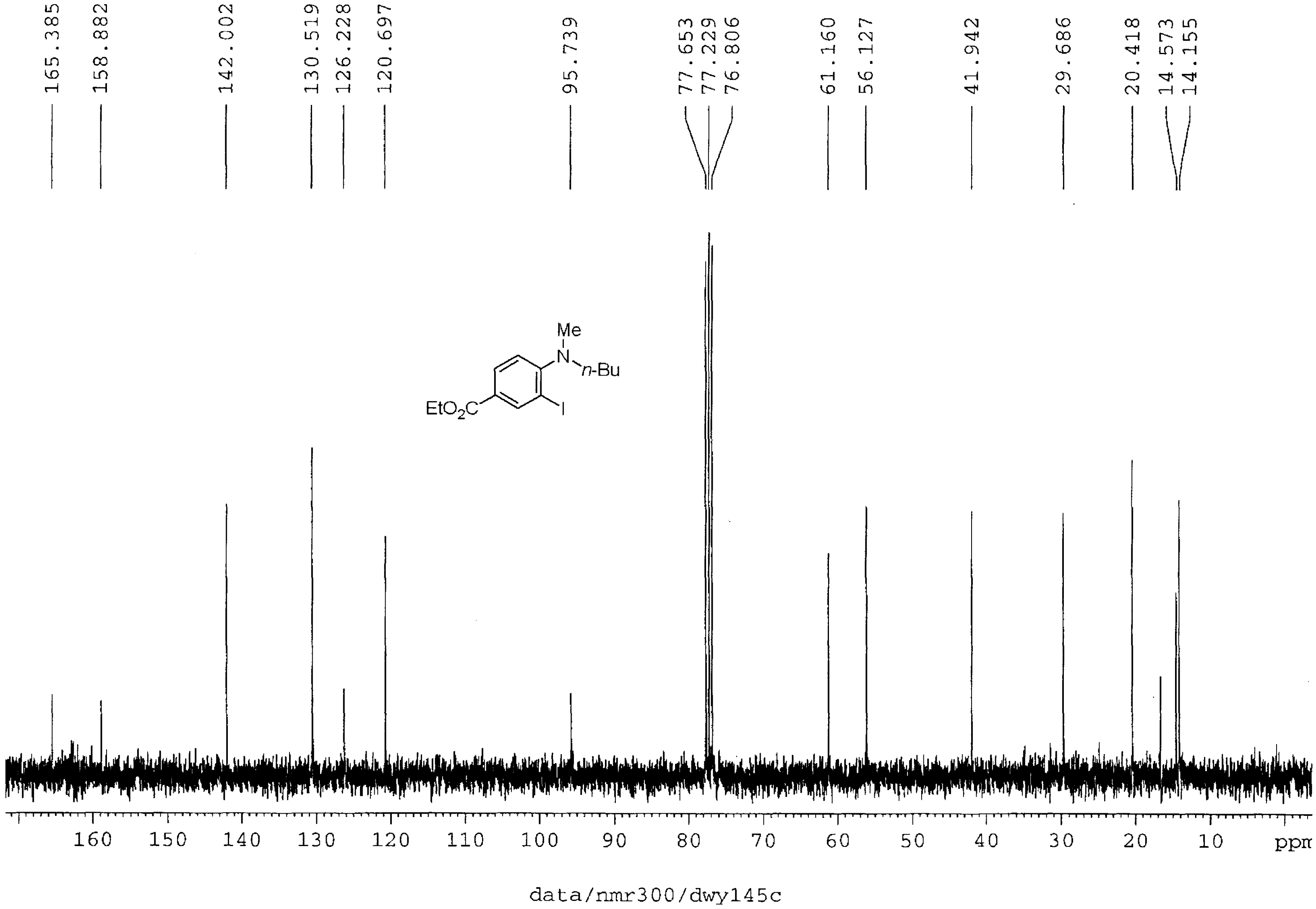

0.000
1.718
1.731
1.745
1.793
1.804
1.817
2.223
2.237
2.249
2.256
2.264
3.612
3.859
5.868
6.699
6.704
6.807
6.812
6.828
6.833
7.260
7.282
Me
N
MeO
4.311
4.202
3.000
3.186
1.017
1.002
0.972
0.950
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
data/nmr400/dwy167

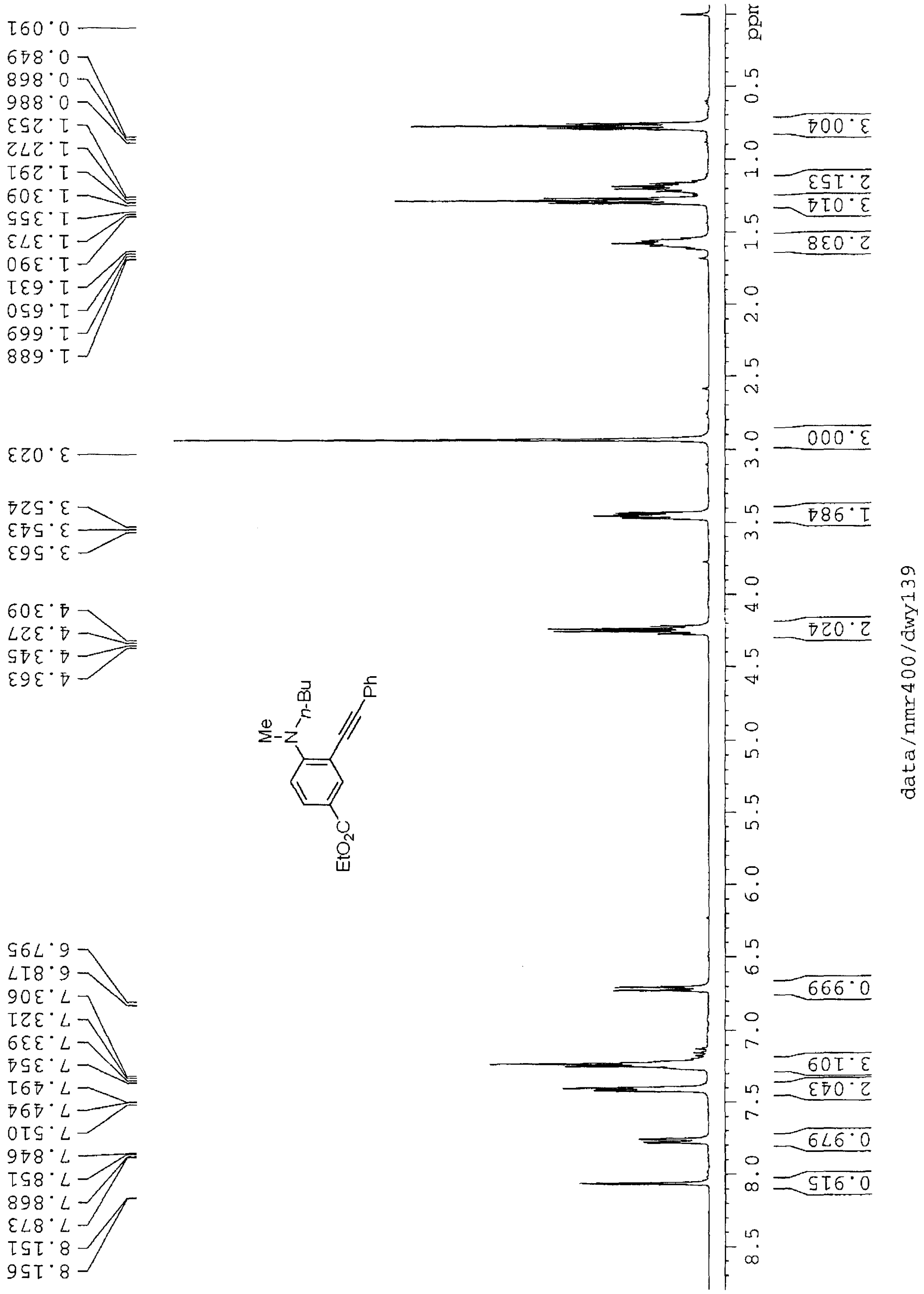

157.000
143.454
137.826
133.672
129.967
124.622
121.768
110.084
93.440
77.550
77.232
76.915
56.530
56.044
31.527
29.510
25.702
22.917
22.121
MeO
Me
N
I
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
data/nmr400/dwy167c

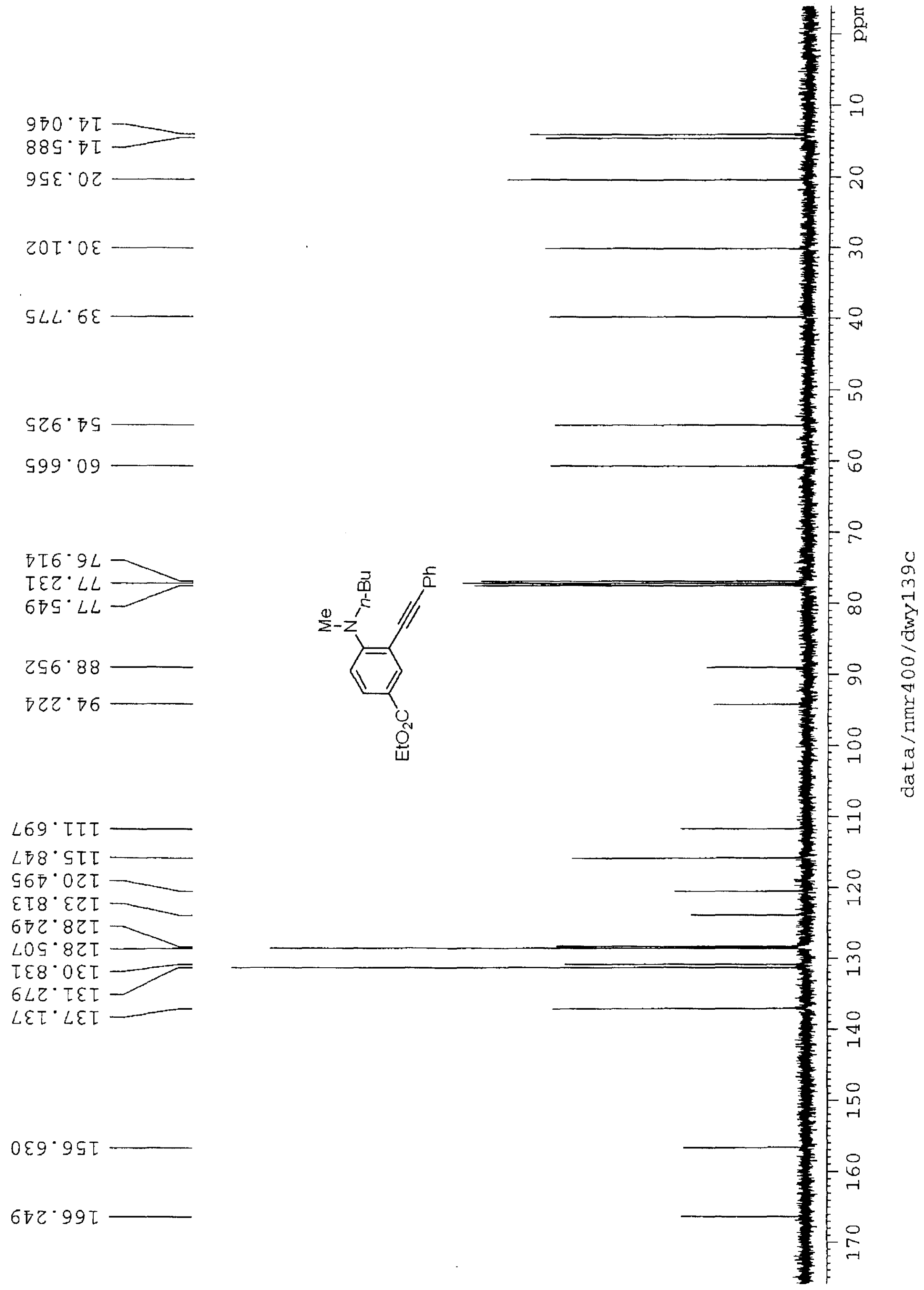

0.000
0.957
0.981
1.005
1.337
1.360
1.384
1.396
1.420
1.444
1.469
1.495
1.520
1.625
1.649
1.652
1.665
1.673
1.690
1.699
1.722
3.183
3.197
3.204
3.218
4.275
4.299
4.322
4.346
4.614
6.479
6.507
7.264
7.869
7.875
7.897
7.904
8.326
8.333
H
N
n-Bu
I
EtO2C
3.000
3.147
1.992
2.109
2.080
2.083
0.975
1.031
1.016
0.937
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
data/nmr300/dwy142

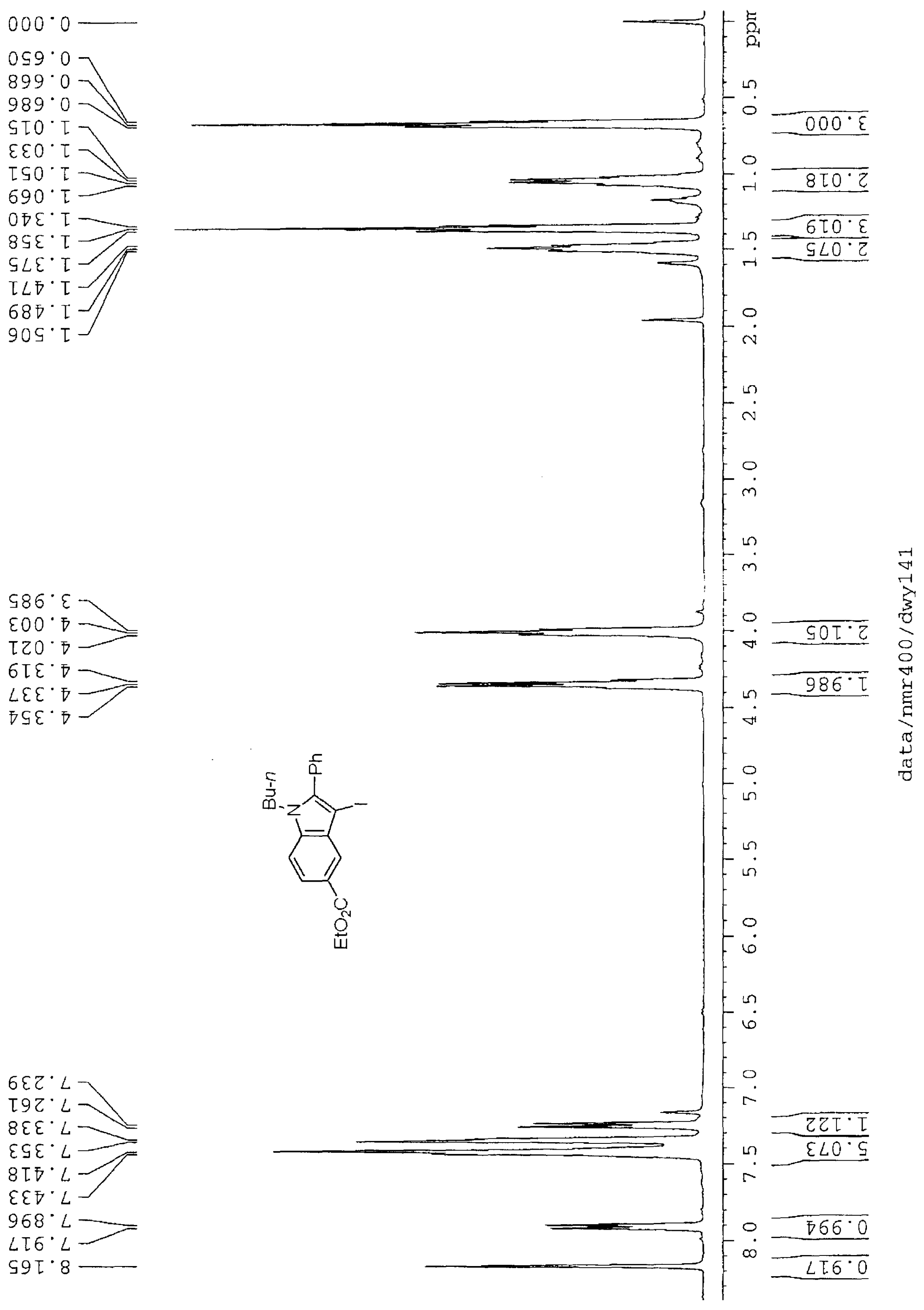

14.029
14.624
20.412
31.233
43.777
60.666
76.807
77.231
77.654
83.768
108.873
119.955
131.663
140.836
150.695
165.747
H
N
n-Bu
I
EtO2C
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr300/dwy142c

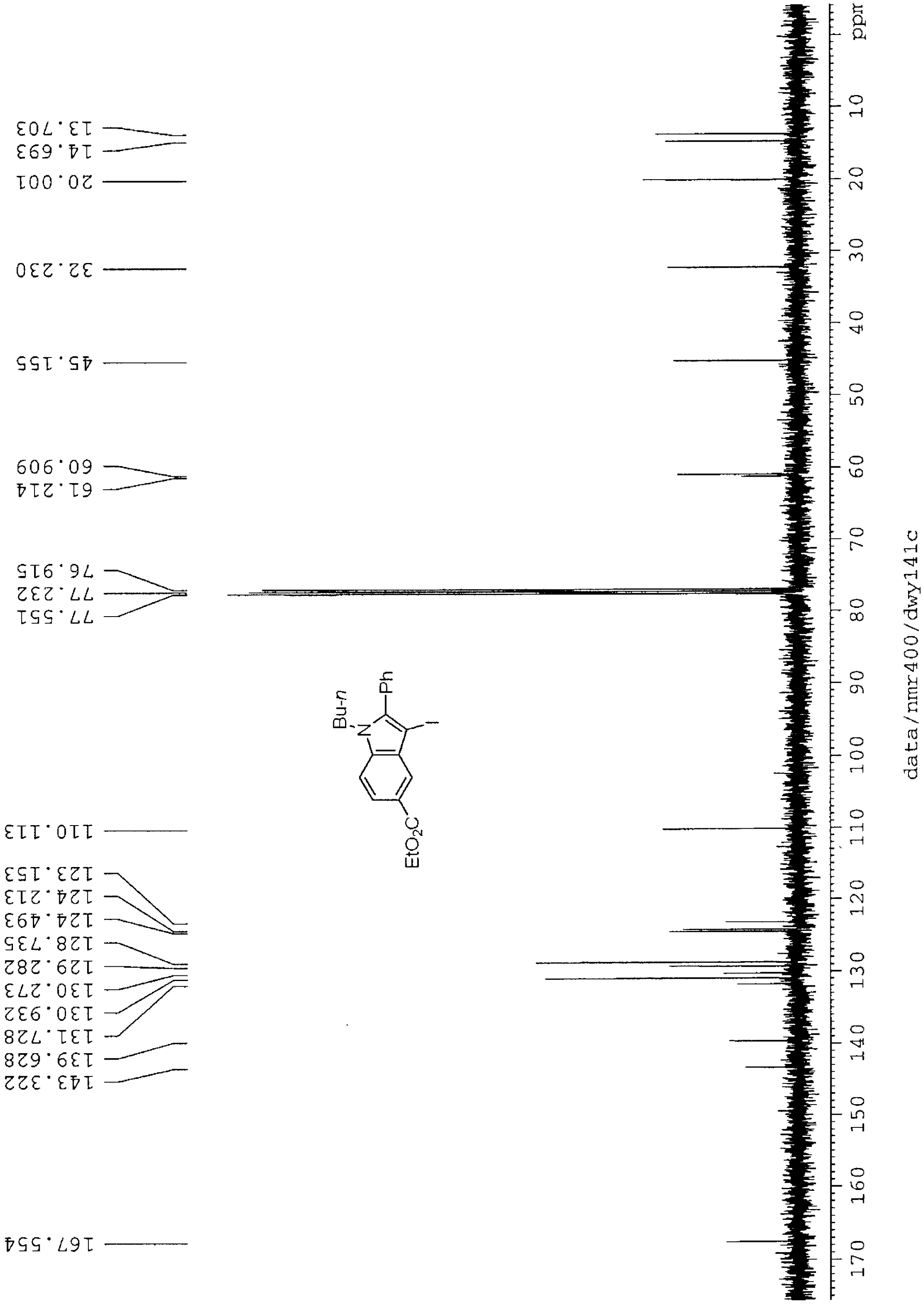

0.000
0.883
0.908
0.932
1.297
1.321
1.348
1.353
1.377
1.401
1.531
1.538
1.563
1.589
2.780
3.004
3.030
3.054
4.310
4.334
4.357
4.381
7.006
7.034
7.939
7.946
7.967
7.974
8.492
8.499
Me
N
n-Bu
I
EtO_2C
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
3.000
5.102
2.198
3.078
2.065
2.050
1.015
0.979
0.916
data/nmr300/dwy145

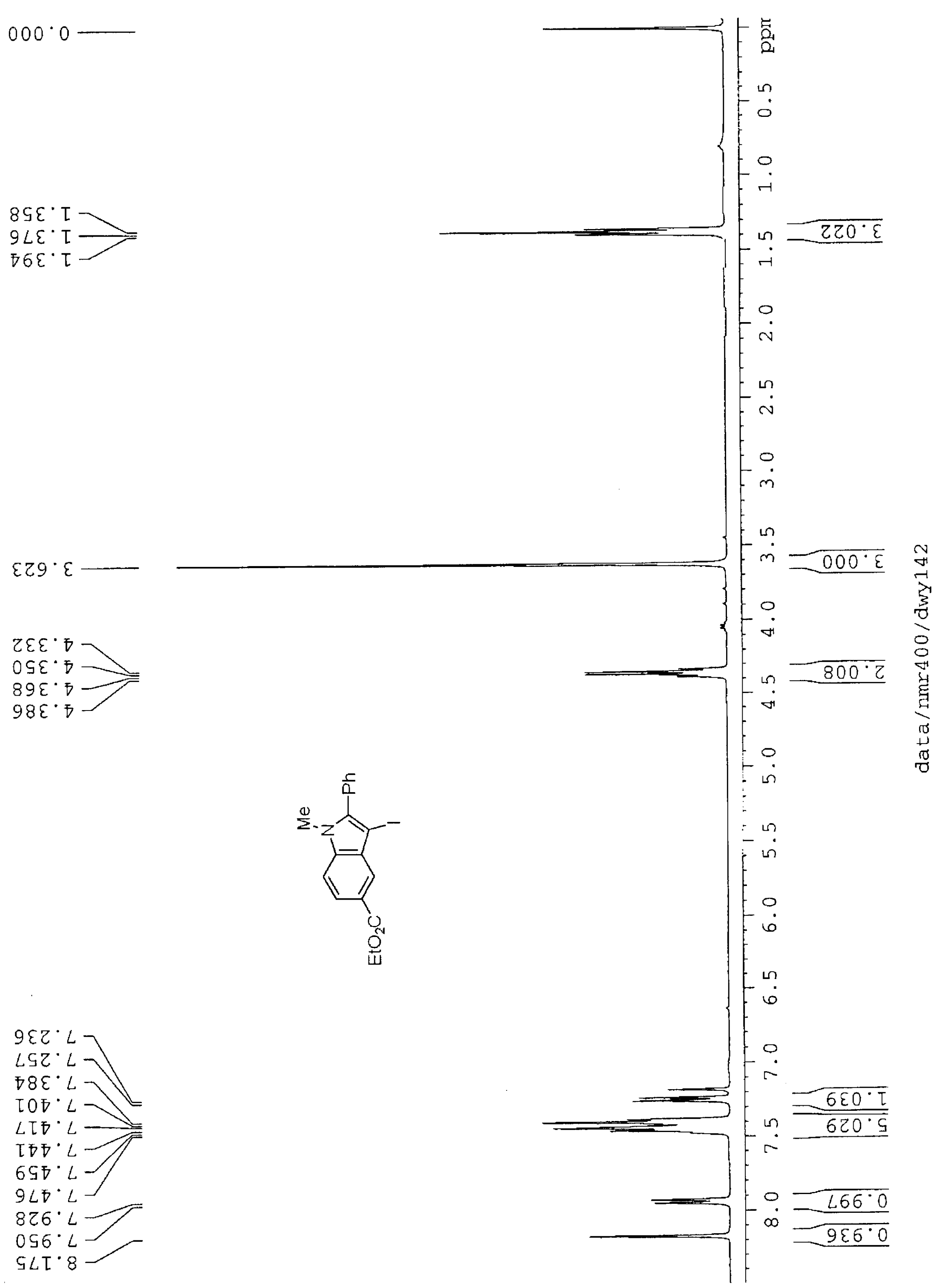

165.385
158.882
142.002
130.519
126.228
120.697
95.739
77.653
77.229
76.806
61.160
56.127
41.942
29.686
20.418
14.573
14.155
Me
N
n-Bu
EtO2C
I
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
data/nmr300/dwy145c

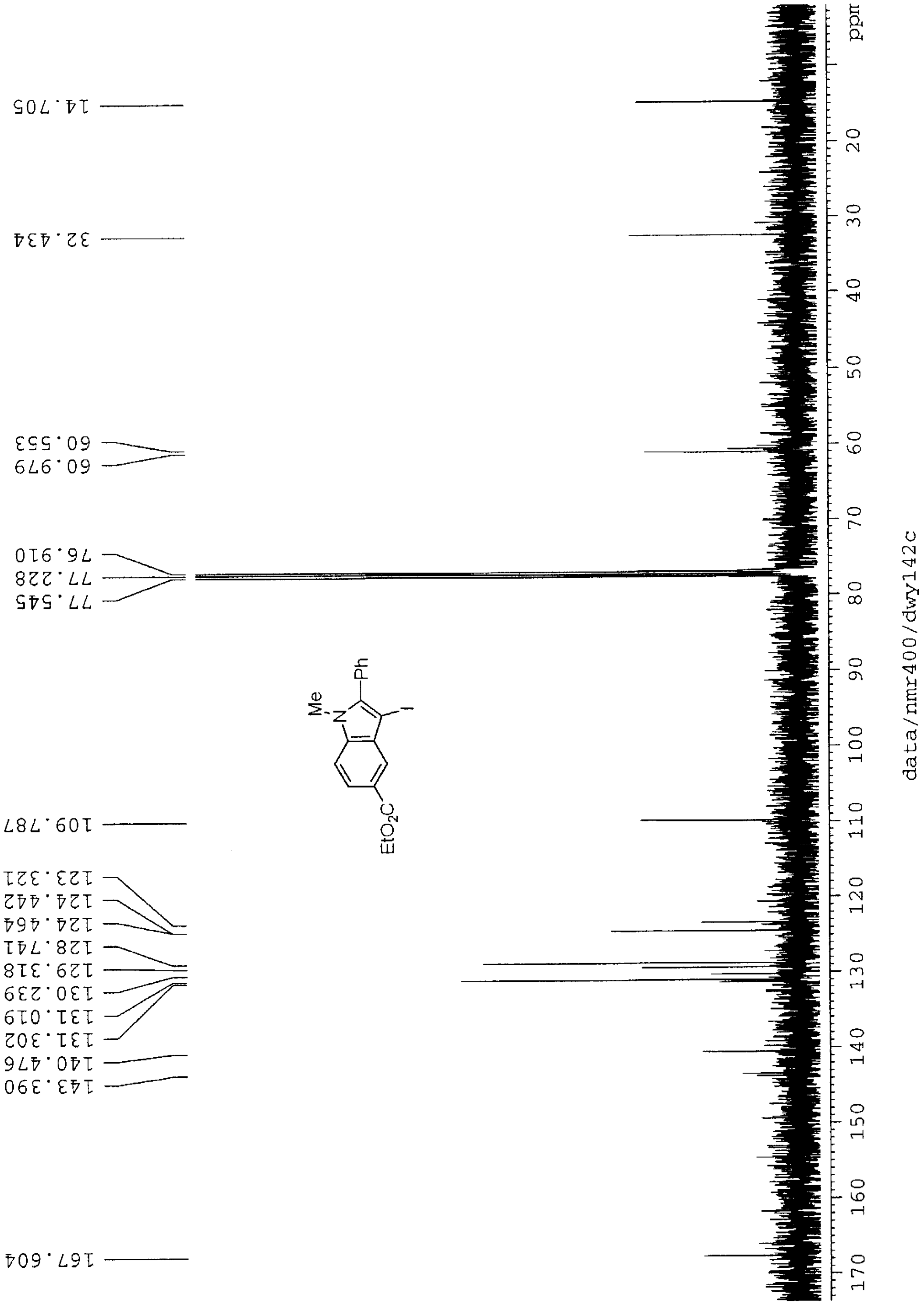

0.091
0.849
0.868
0.886
1.253
1.272
1.291
1.309
1.355
1.373
1.390
1.631
1.650
1.669
1.688
3.023
3.524
3.543
3.563
4.309
4.327
4.345
4.363
6.795
6.817
7.306
7.321
7.339
7.354
7.491
7.494
7.510
7.846
7.851
7.868
7.873
8.151
8.156
Me
N
n-Bu
Ph
EtO2C
3.004
2.153
3.014
2.038
3.000
1.984
2.024
0.999
3.109
2.043
0.979
0.915
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
data/nmr400/dwy139

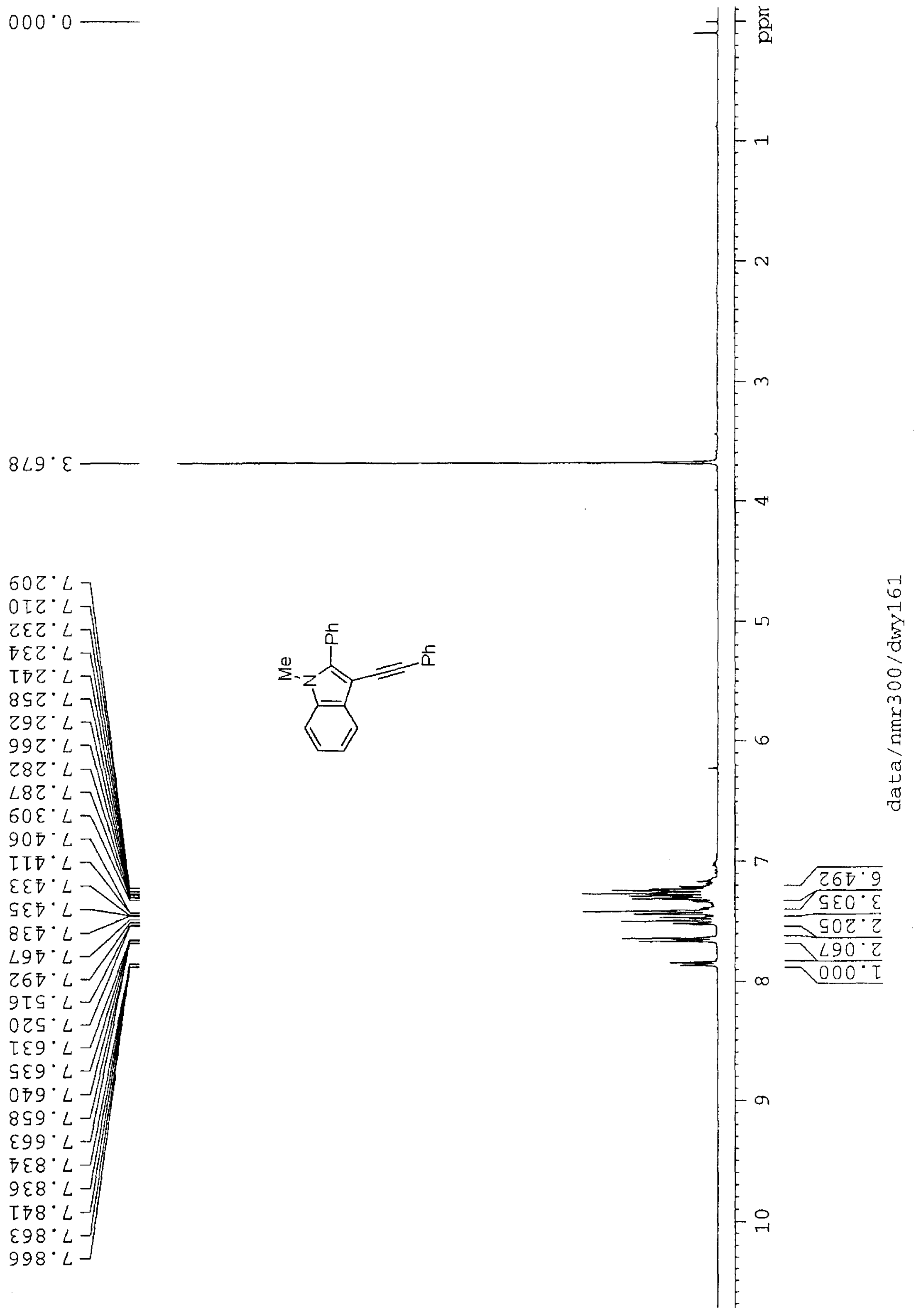

14.046
14.588
20.356
30.102
39.775
54.925
60.665
76.914
77.231
77.549
88.952
94.224
111.697
115.847
120.495
123.813
128.249
128.507
130.831
131.279
137.137
156.630
166.249
Me
N
n-Bu
Ph
EtO2C
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy139c

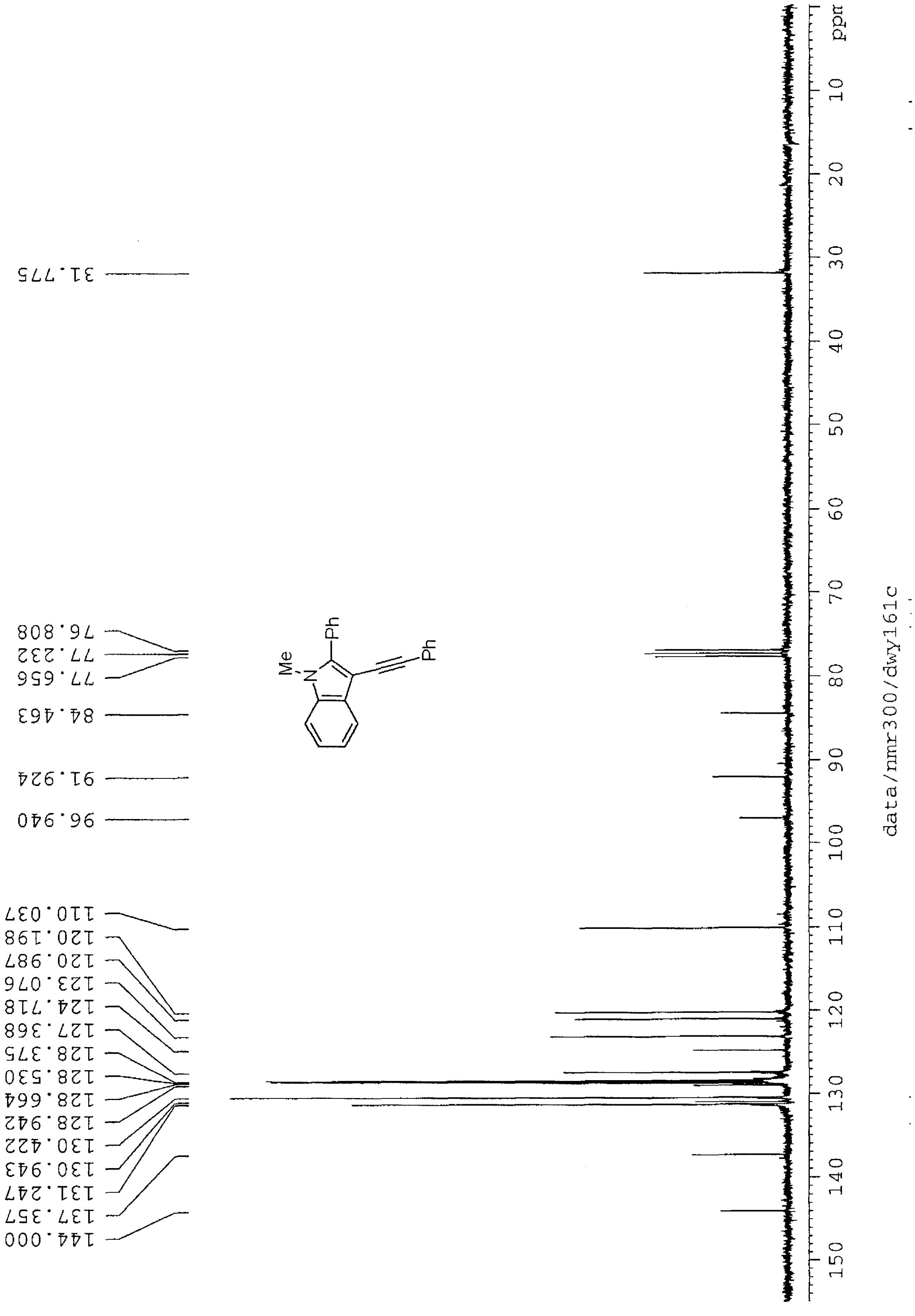

0.000
0.650
0.668
0.686
1.015
1.033
1.051
1.069
1.340
1.358
1.375
1.471
1.489
1.506
3.985
4.003
4.021
4.319
4.337
4.354
7.239
7.261
7.338
7.353
7.418
7.433
7.896
7.917
8.165
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
3.000
2.018
3.019
2.075
2.105
1.986
1.122
5.073
0.994
0.917
data/nmr400/dwy141
Bu-n
N
Ph
EtO2C

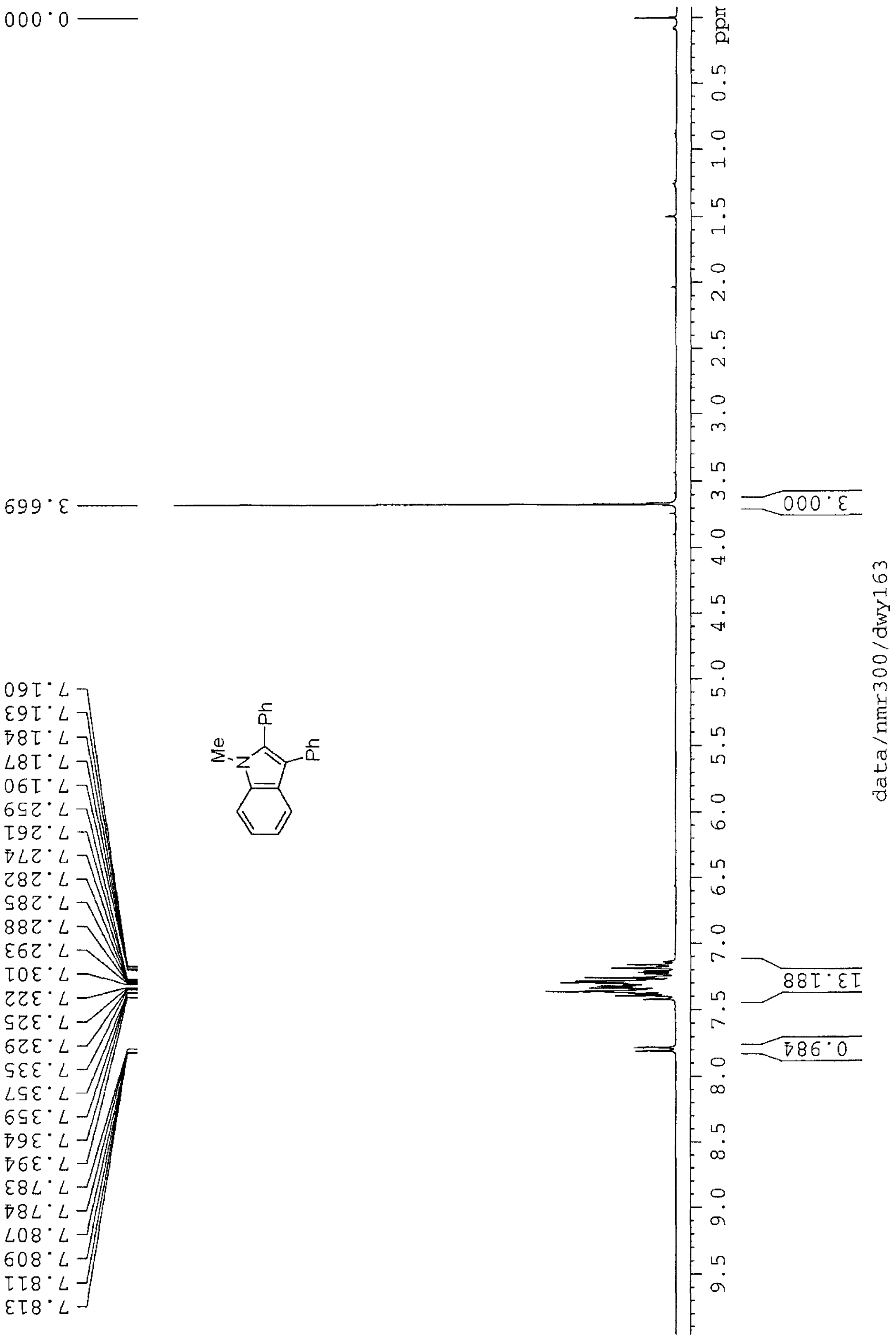

13.703
14.693
20.001
32.230
45.155
60.909
61.214
76.915
77.232
77.551
110.113
123.153
124.213
124.493
128.735
129.282
130.273
130.932
131.728
139.628
143.322
167.554
Bu-n
N
Ph
EtO2C
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy141c

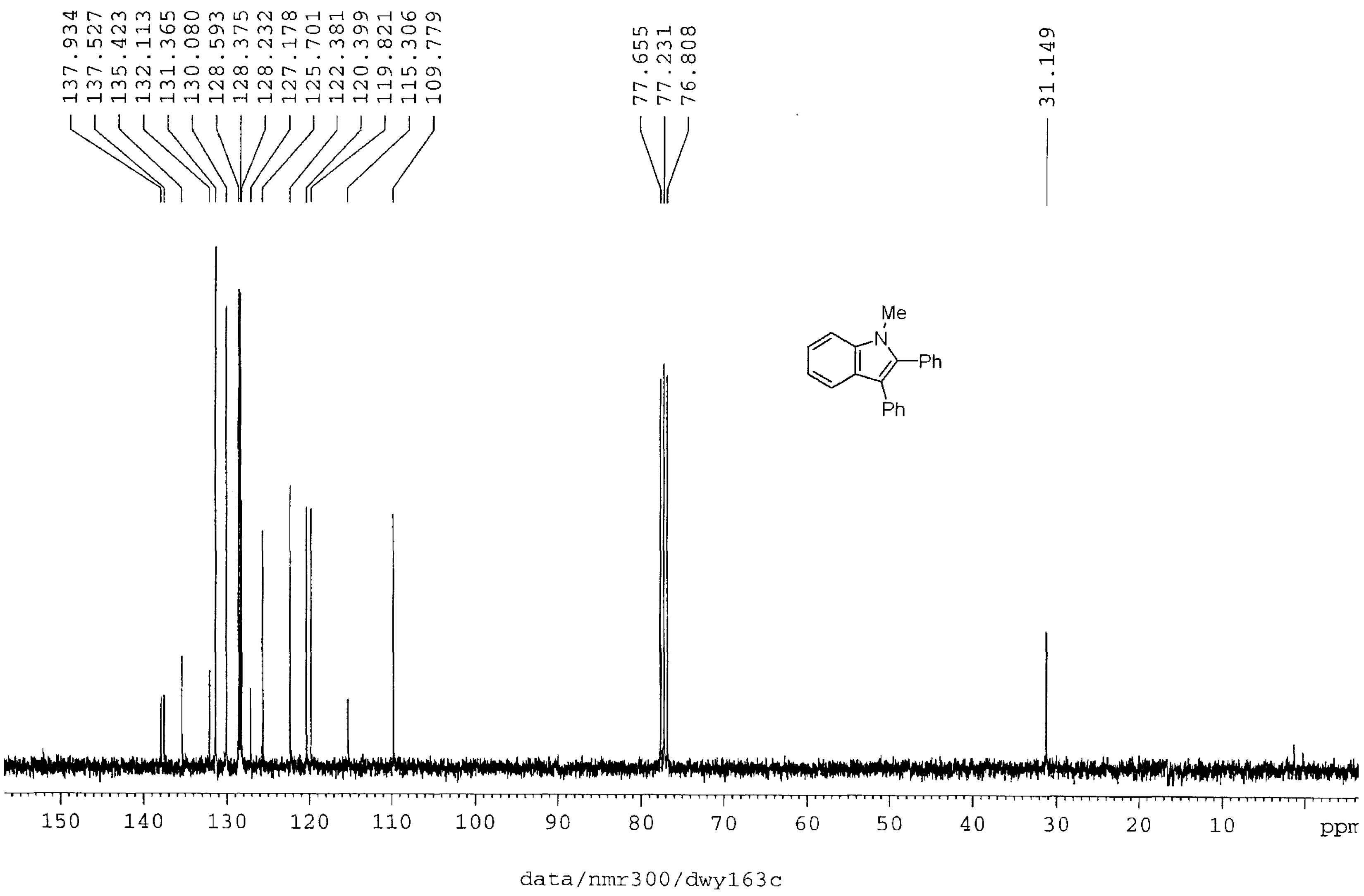

0.000
1.358
1.376
1.394
3.623
4.332
4.350
4.368
4.386
7.236
7.257
7.384
7.401
7.417
7.441
7.459
7.476
7.928
7.950
8.175
Me
N
Ph
I
EtO2C
3.022
3.000
2.008
1.039
5.029
0.997
0.936
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
data/nmr400/dwy142

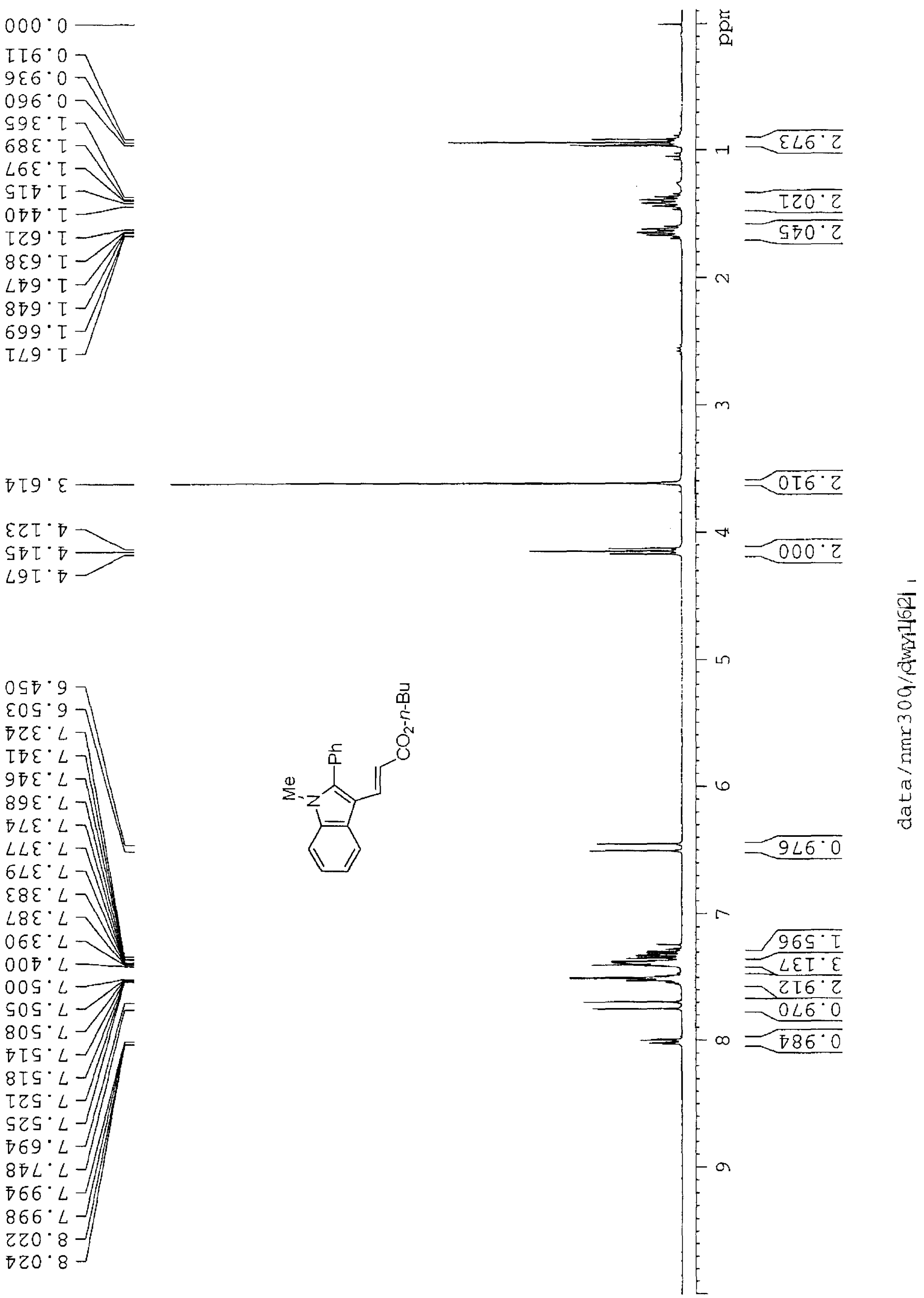

14.705
32.434
60.553
60.979
76.910
77.228
77.545
109.787
123.321
124.442
124.464
128.741
129.318
130.239
131.019
131.302
140.476
143.390
167.604
Me
N
Ph
I
EtO2C
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy142c

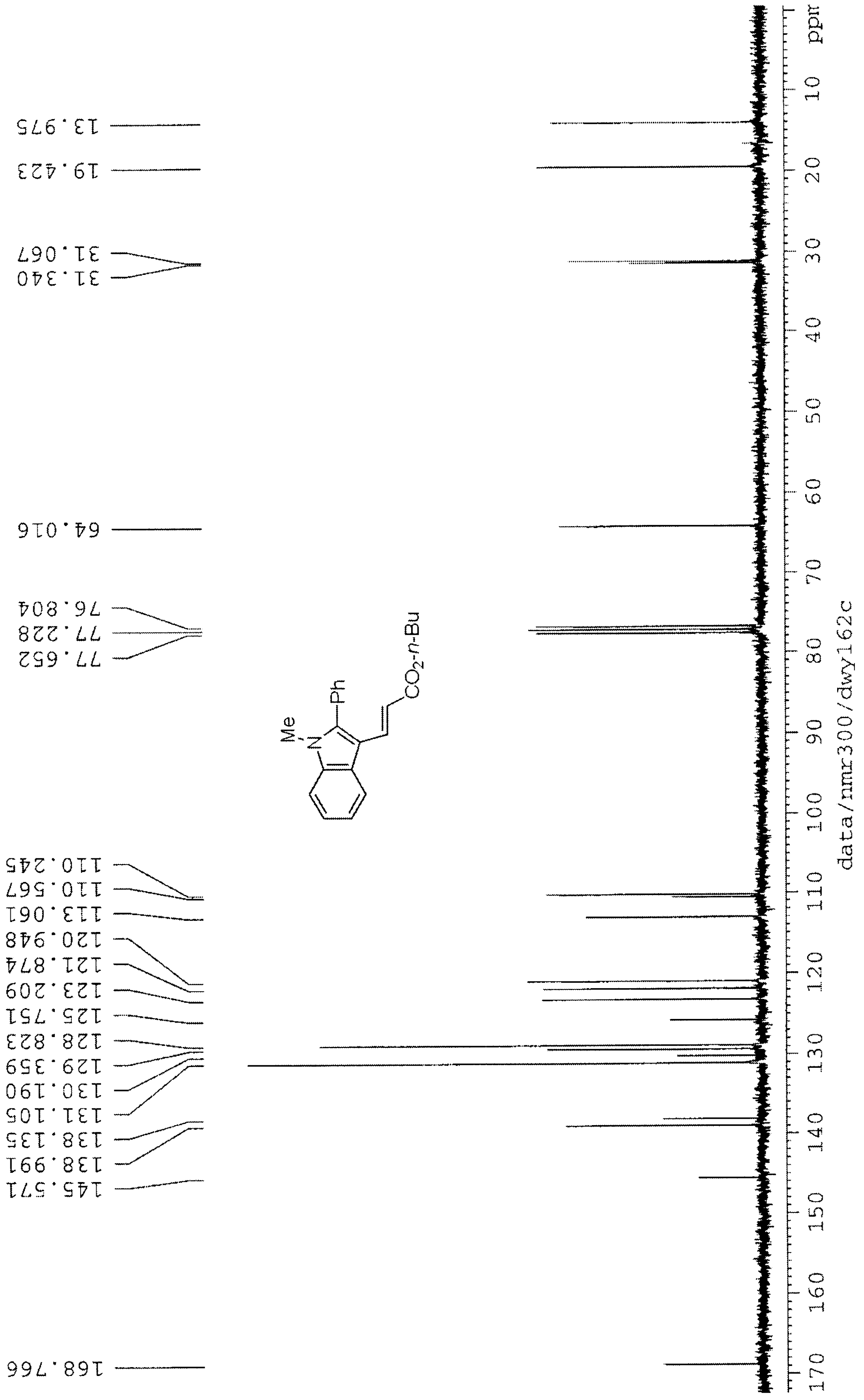

0.000
3.678
7.209
7.210
7.232
7.234
7.241
7.258
7.262
7.266
7.282
7.287
7.309
7.406
7.411
7.433
7.435
7.438
7.467
7.492
7.516
7.520
7.631
7.635
7.640
7.658
7.663
7.834
7.836
7.841
7.863
7.866
Me
N
Ph
Ph
6.492
3.035
2.205
2.067
1.000
data/nmr300/dwy161
ppm
1
2
3
4
5
6
7
8
9
10

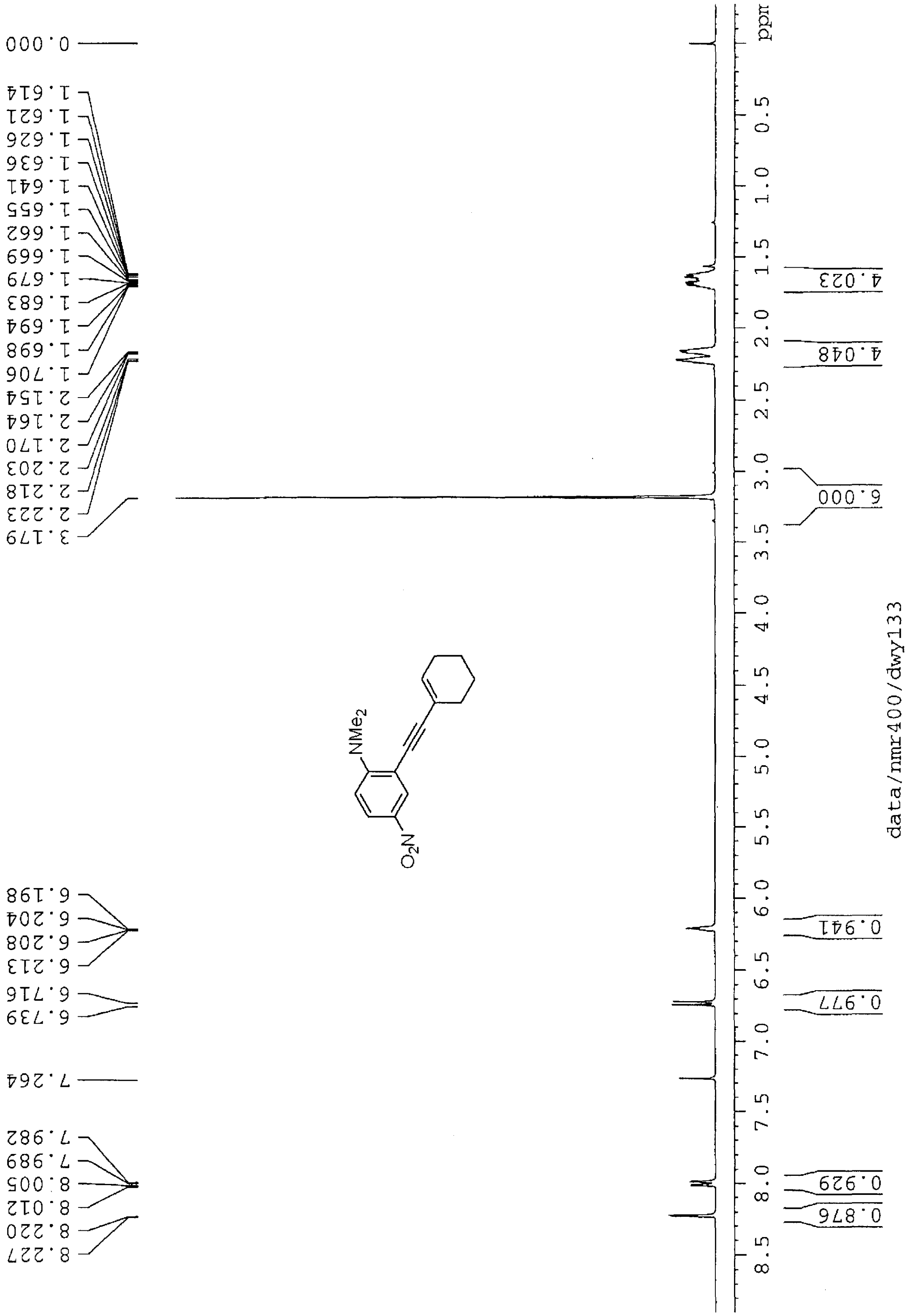

31.775
76.808
77.232
77.656
84.463
91.924
96.940
110.037
120.198
120.987
123.076
124.718
127.368
128.375
128.530
128.664
128.942
130.422
130.943
131.247
137.357
144.000
Me
N
Ph
Ph
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr300/dwy161c

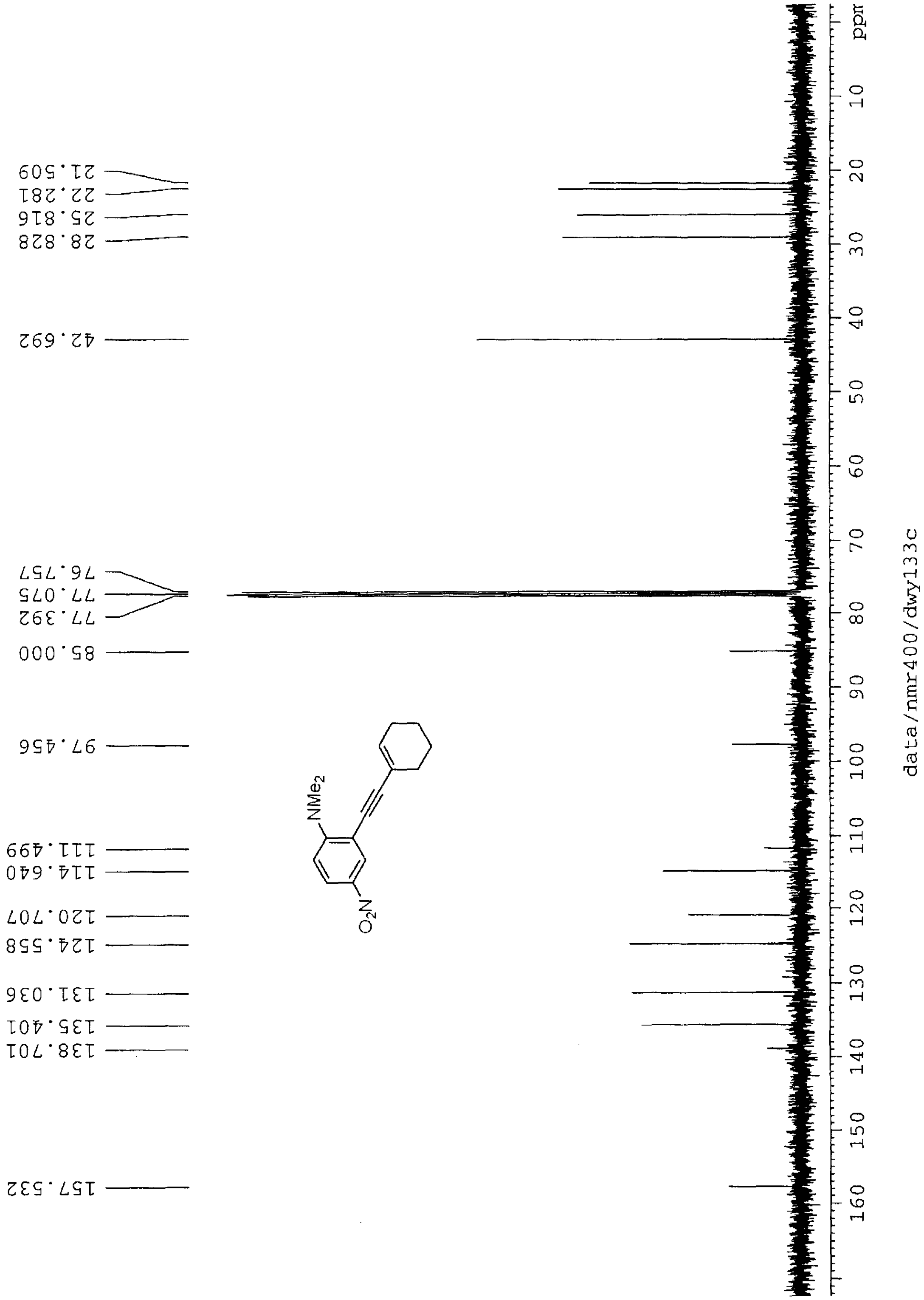

0.000
3.669
7.160
7.163
7.184
7.187
7.190
7.259
7.261
7.274
7.282
7.285
7.288
7.293
7.301
7.322
7.325
7.329
7.335
7.357
7.359
7.364
7.394
7.783
7.784
7.807
7.809
7.811
7.813
Me
N
Ph
Ph
3.000
13.188
0.984
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
data/nmr300/dwy163

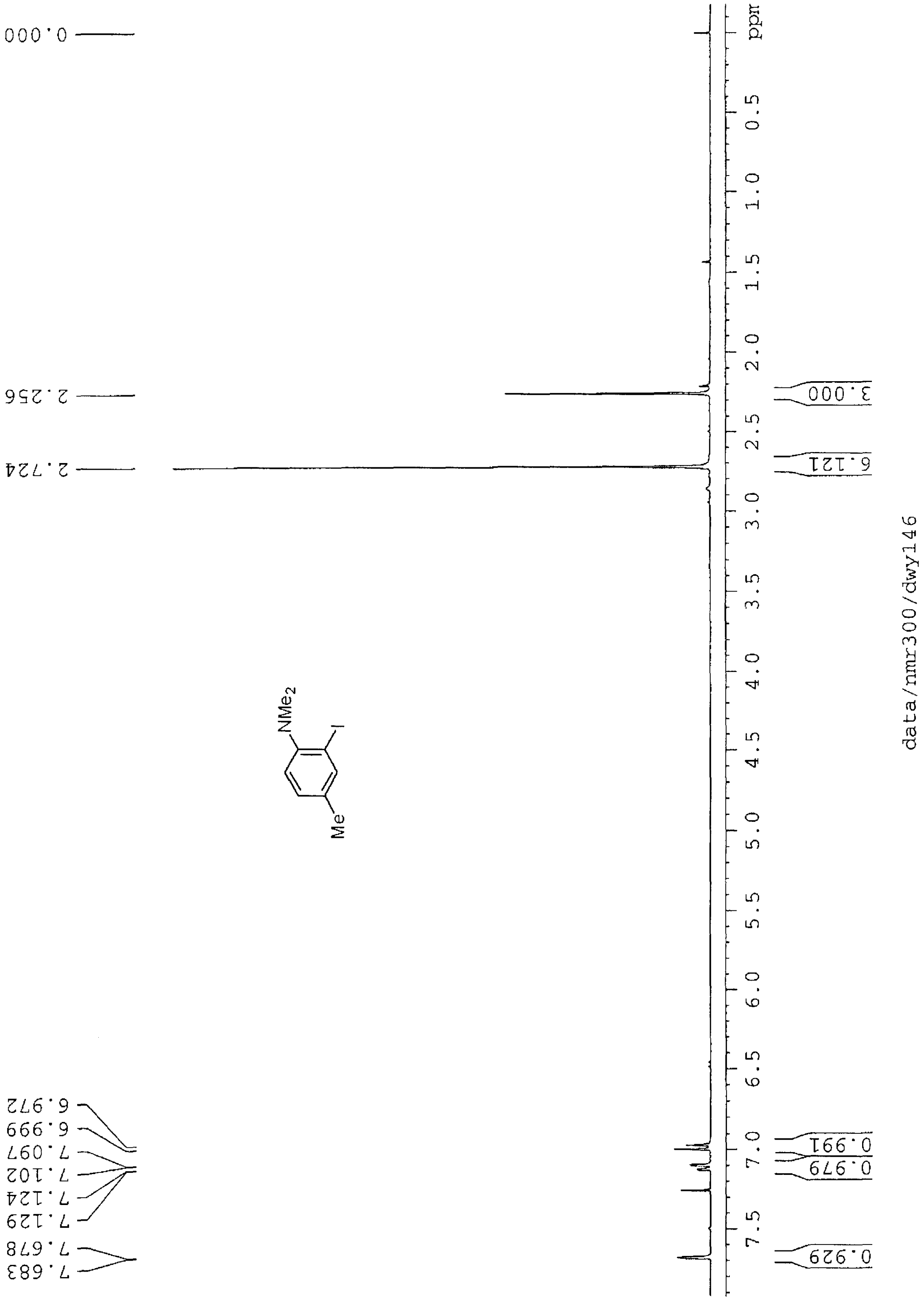

137.934
137.527
135.423
132.113
131.365
130.080
128.593
128.375
128.232
127.178
125.701
122.381
120.399
119.821
115.306
109.779
77.655
77.231
76.808
31.149
Me
N
Ph
Ph
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
data/nmr300/dwy163c

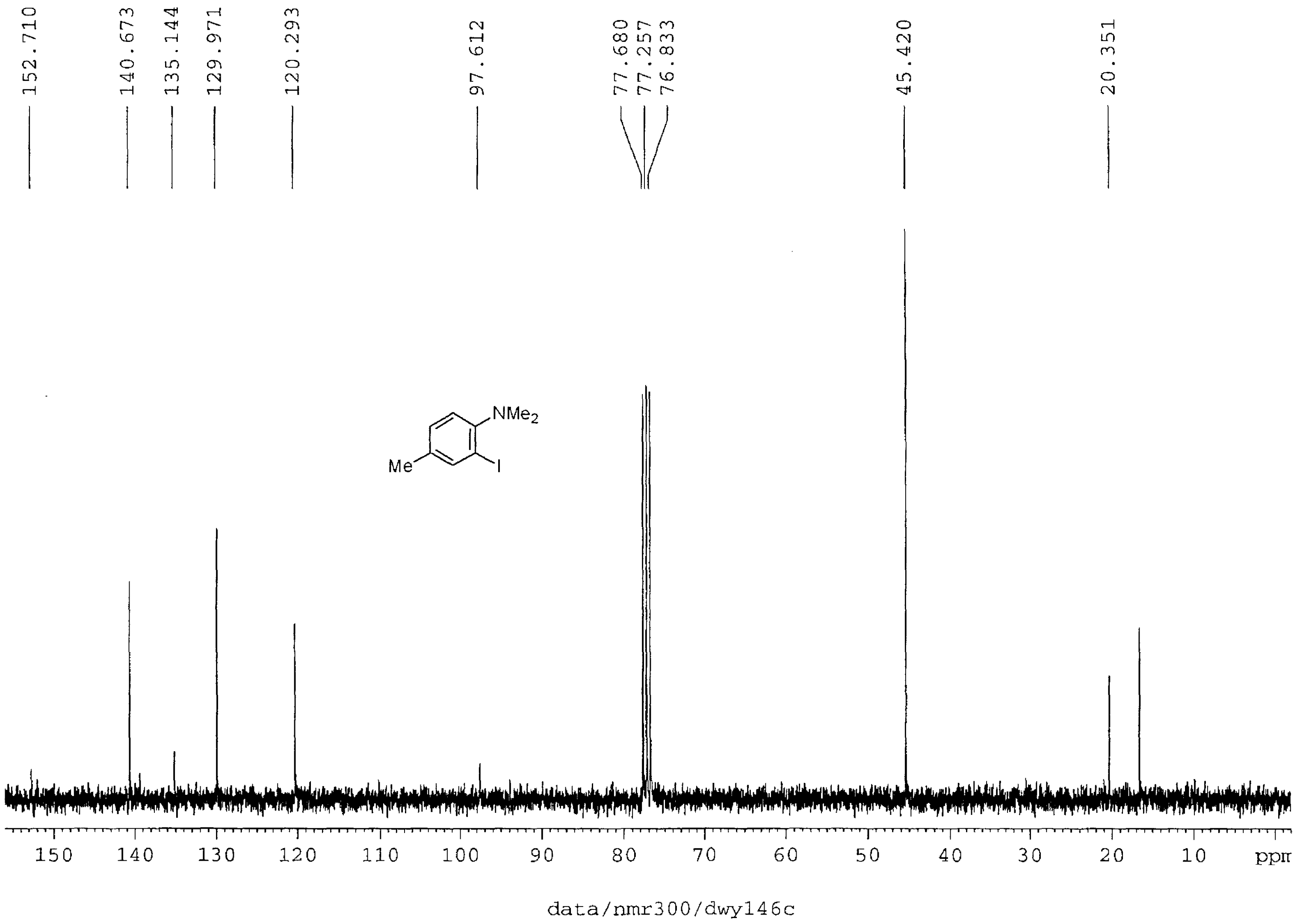

0.000
0.911
0.936
0.960
1.365
1.389
1.397
1.415
1.440
1.621
1.638
1.647
1.648
1.669
1.671
3.614
4.123
4.145
4.167
6.450
6.503
7.324
7.341
7.346
7.368
7.374
7.377
7.379
7.383
7.387
7.390
7.400
7.500
7.505
7.508
7.514
7.518
7.521
7.525
7.694
7.748
7.994
7.998
8.022
8.024
Me
N
Ph
CO2-n-Bu
2.973
2.021
2.045
2.910
2.000
0.976
1.596
3.137
2.912
0.970
0.984
ppm
1
2
3
4
5
6
7
8
9
data/nmr300/dwy1621

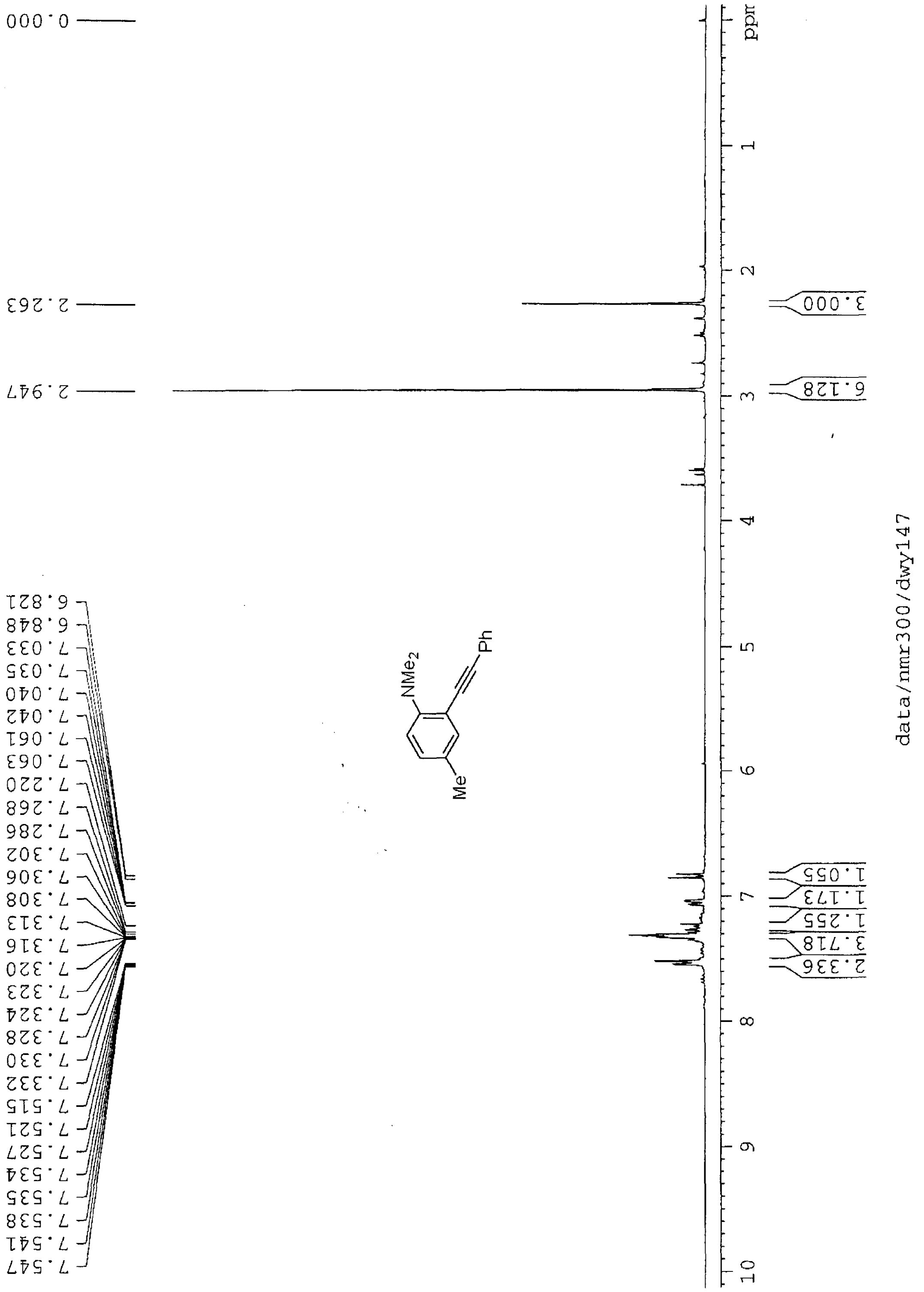

13.975
19.423
31.067
31.340
64.016
76.804
77.228
77.652
110.245
110.567
113.061
120.948
121.874
123.209
125.751
128.823
129.359
130.190
131.105
138.135
138.991
145.571
168.766
Me
N
Ph
CO2-n-Bu
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr300/dwy162c

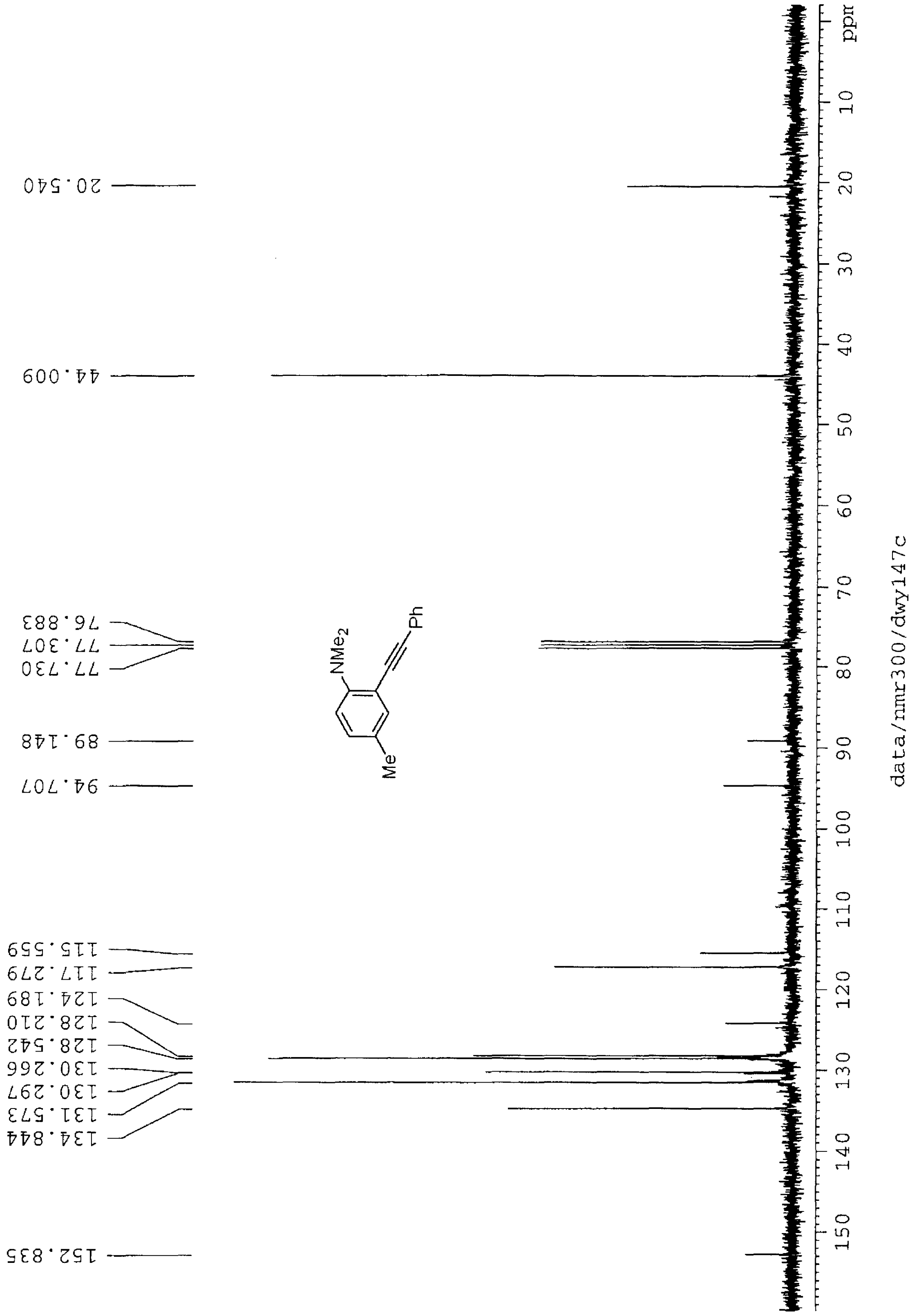

0.000
1.614
1.621
1.626
1.636
1.641
1.655
1.662
1.669
1.679
1.683
1.694
1.698
1.706
2.154
2.164
2.170
2.203
2.218
2.223
3.179
6.198
6.204
6.208
6.213
6.716
6.739
7.264
7.982
7.989
8.005
8.012
8.220
8.227
NMe2
O2N
4.023
4.048
6.000
0.941
0.977
0.929
0.876
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
data/nmr400/dwy133

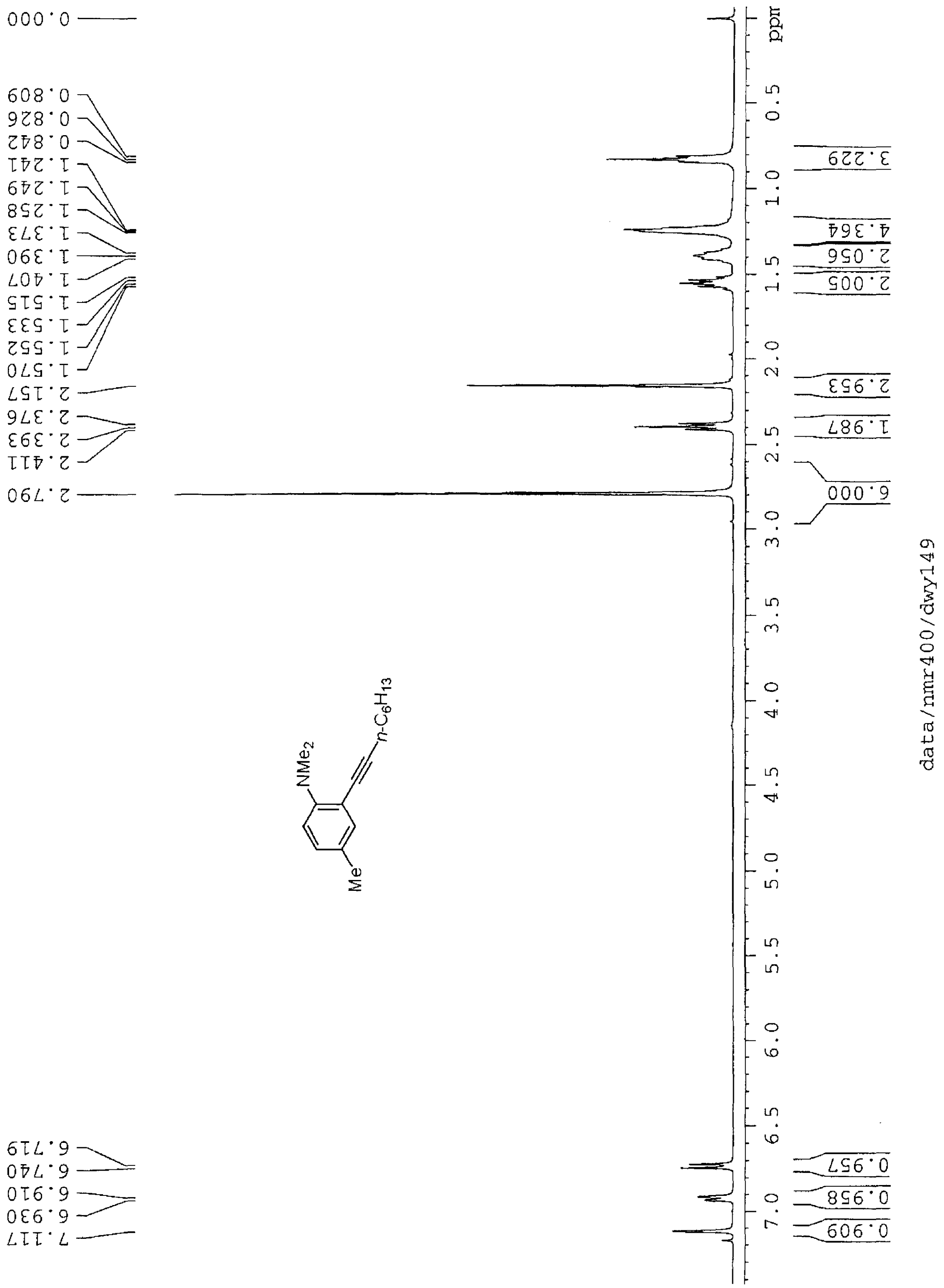

21.509
22.281
25.816
28.828
42.692
76.757
77.075
77.392
85.000
97.456
111.499
114.640
120.707
124.558
131.036
135.401
138.701
157.532
NMe$_2$
O$_2$N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr400/dwy133c

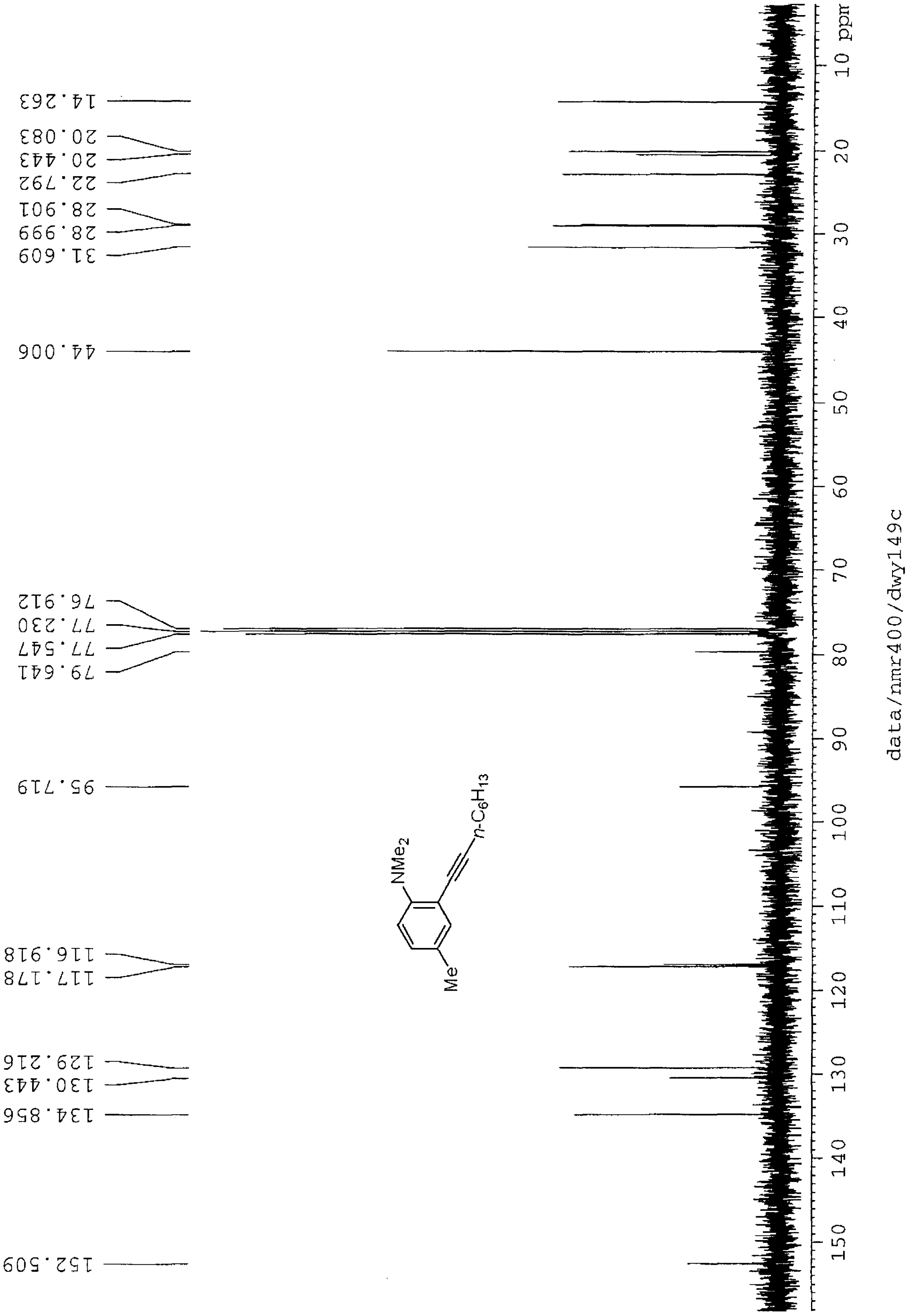

0.000
2.256
2.724
6.972
6.999
7.097
7.102
7.124
7.129
7.678
7.683
NMe$_2$
I
Me
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
3.000
6.121
0.991
0.979
0.929
data/nmr300/dwy146

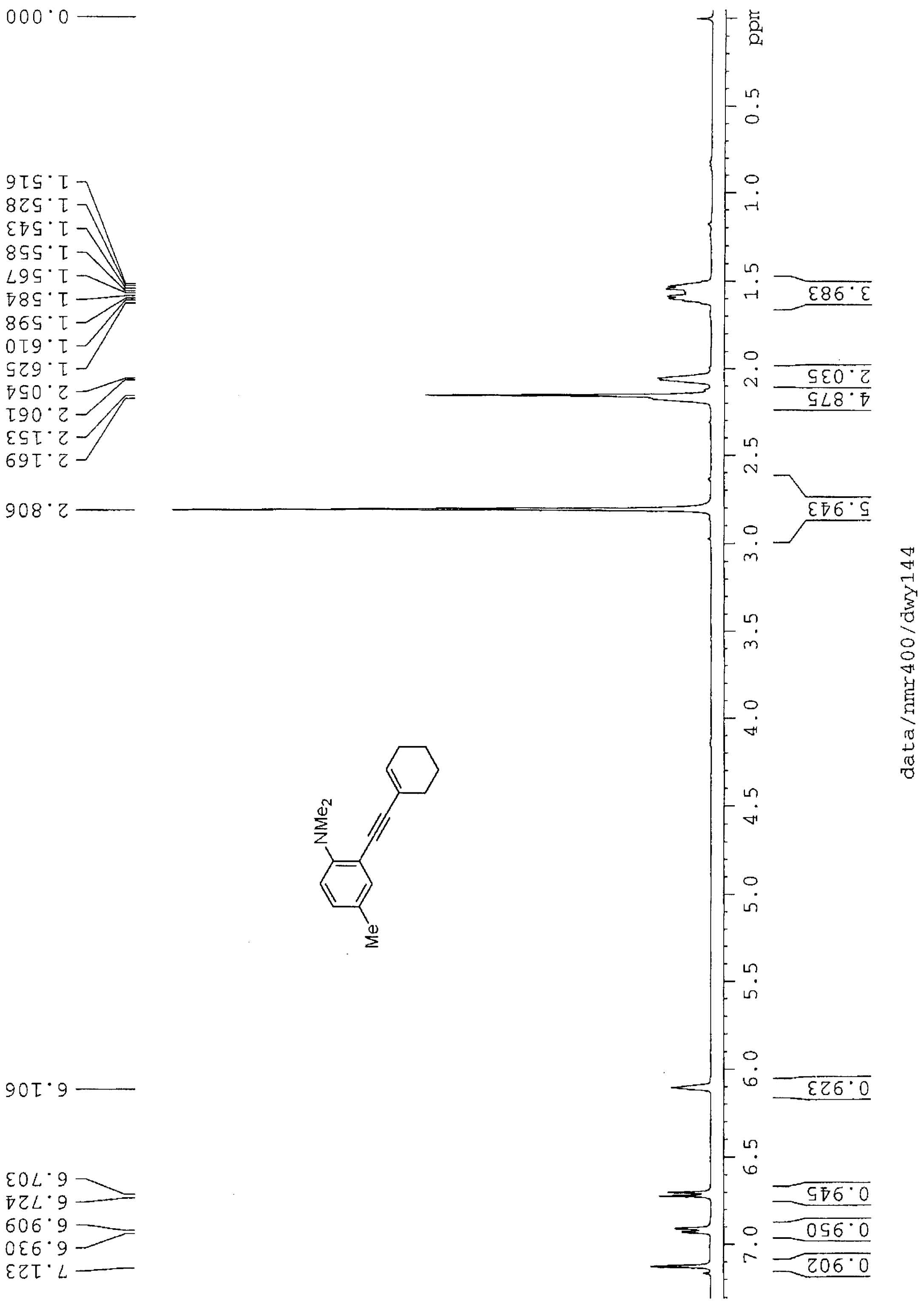

152.710
140.673
135.144
129.971
120.293
97.612
77.680
77.257
76.833
45.420
20.351
NMe$_2$
Me
I
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
data/nmr300/dwy146c

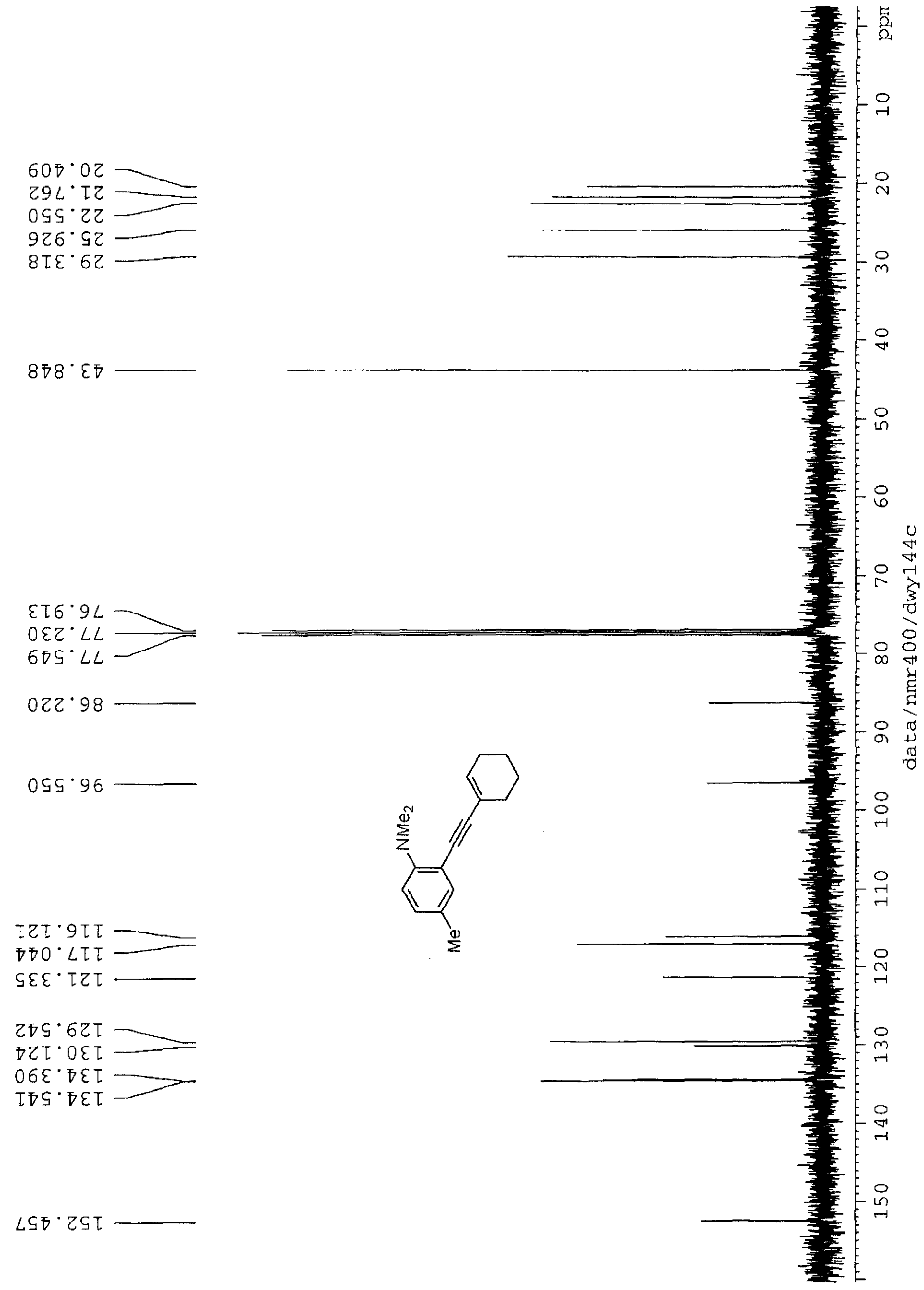

0.000
2.263
2.947
6.821
6.848
7.033
7.035
7.040
7.042
7.061
7.063
7.220
7.268
7.286
7.302
7.306
7.308
7.313
7.316
7.320
7.323
7.324
7.328
7.330
7.332
7.515
7.521
7.527
7.534
7.535
7.538
7.541
7.547
NMe2
Ph
Me
3.000
6.128
1.055
1.173
1.255
3.718
2.336
ppm
1
2
3
4
5
6
7
8
9
10
data/nmr300/dwy147

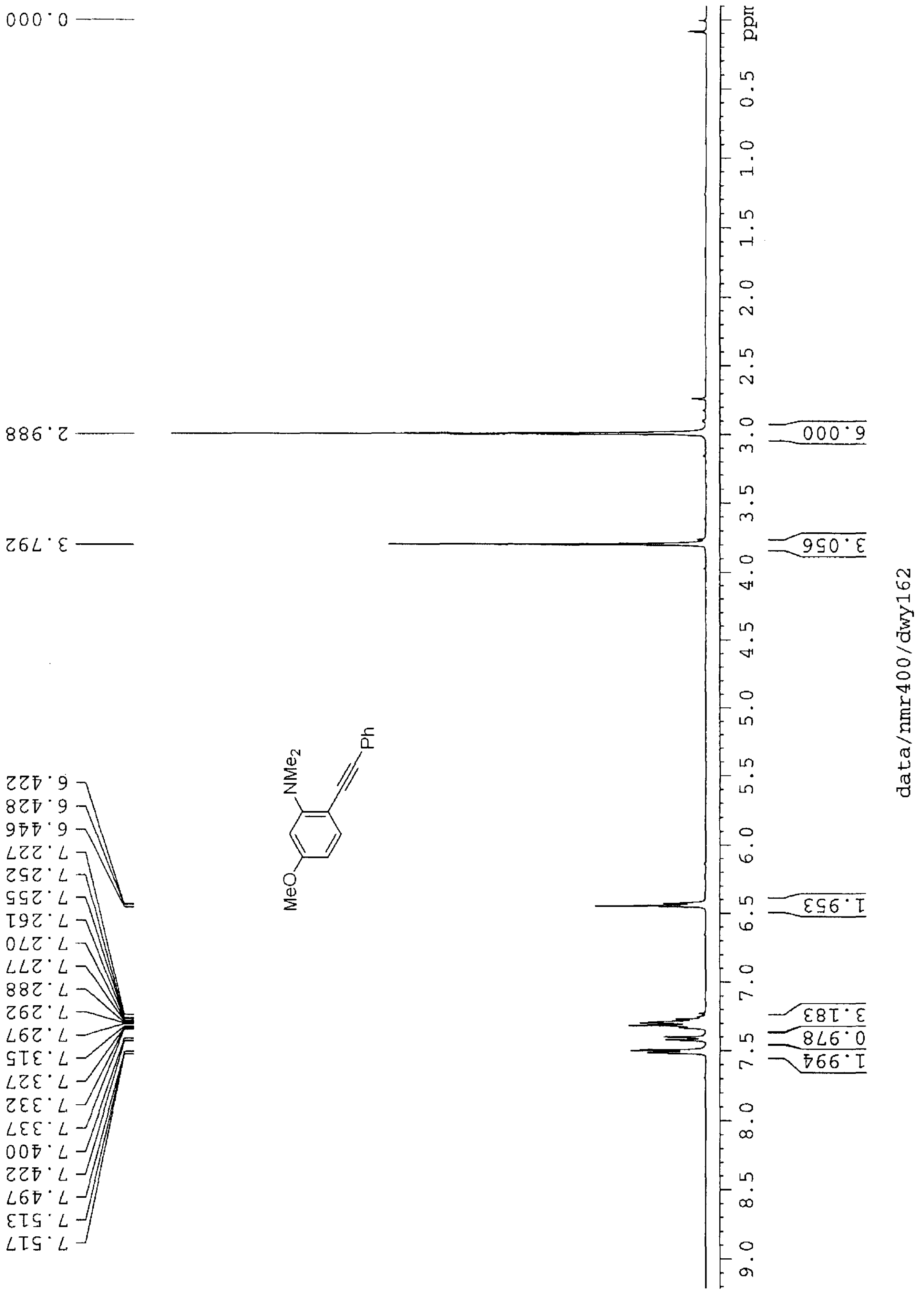

20.540
44.009
76.883
77.307
77.730
89.148
94.707
115.559
117.279
124.189
128.210
128.542
130.266
130.297
131.573
134.844
152.835
NMe$_2$
Ph
Me
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr300/dwy147c

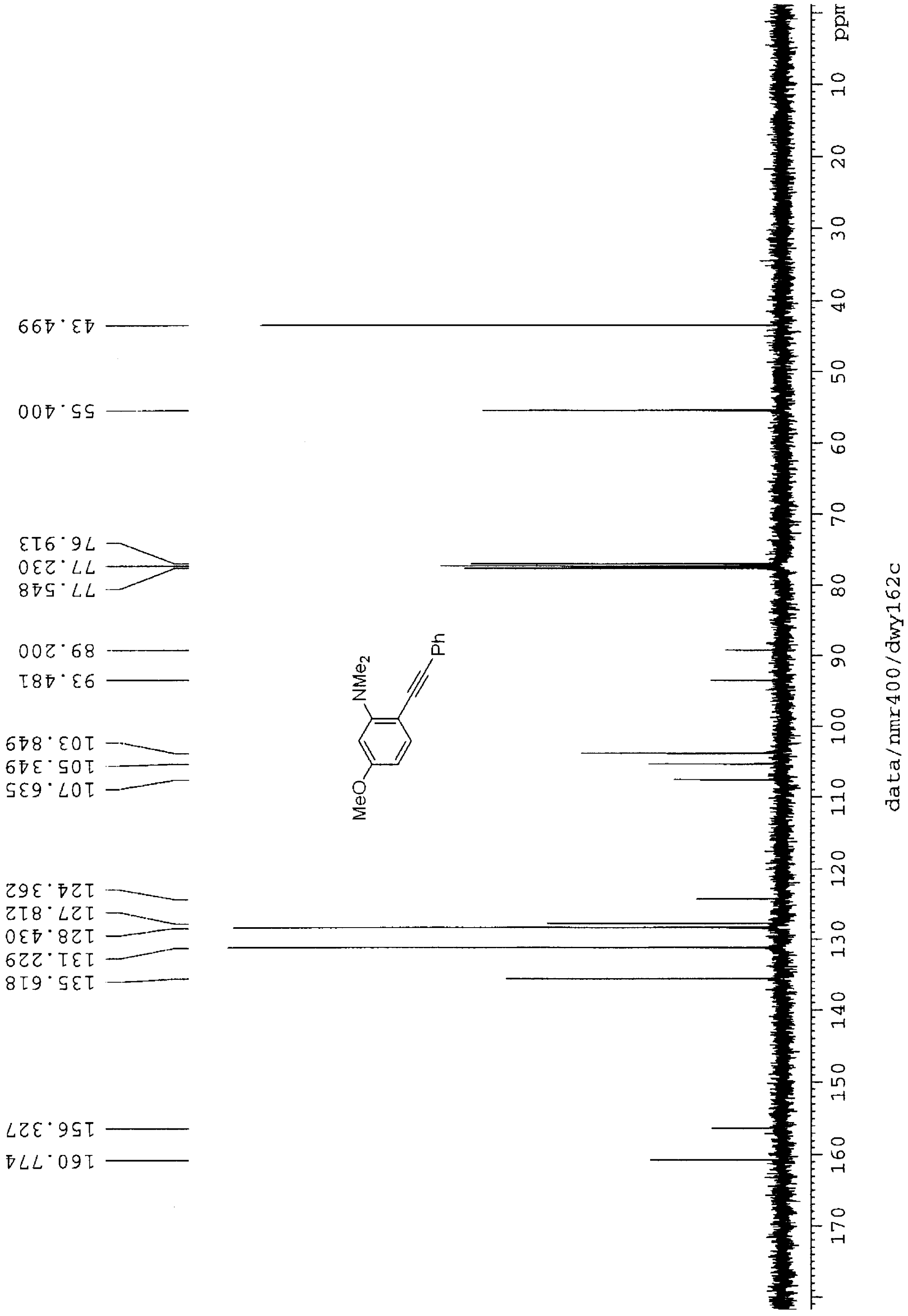

0.000
0.809
0.826
0.842
1.241
1.249
1.258
1.373
1.390
1.407
1.515
1.533
1.552
1.570
2.157
2.376
2.393
2.411
2.790
6.719
6.740
6.910
6.930
7.117
3.229
4.364
2.056
2.005
2.953
1.987
6.000
0.957
0.958
0.909
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
data/nmr400/dwy149
NMe2
n-C6H13
Me

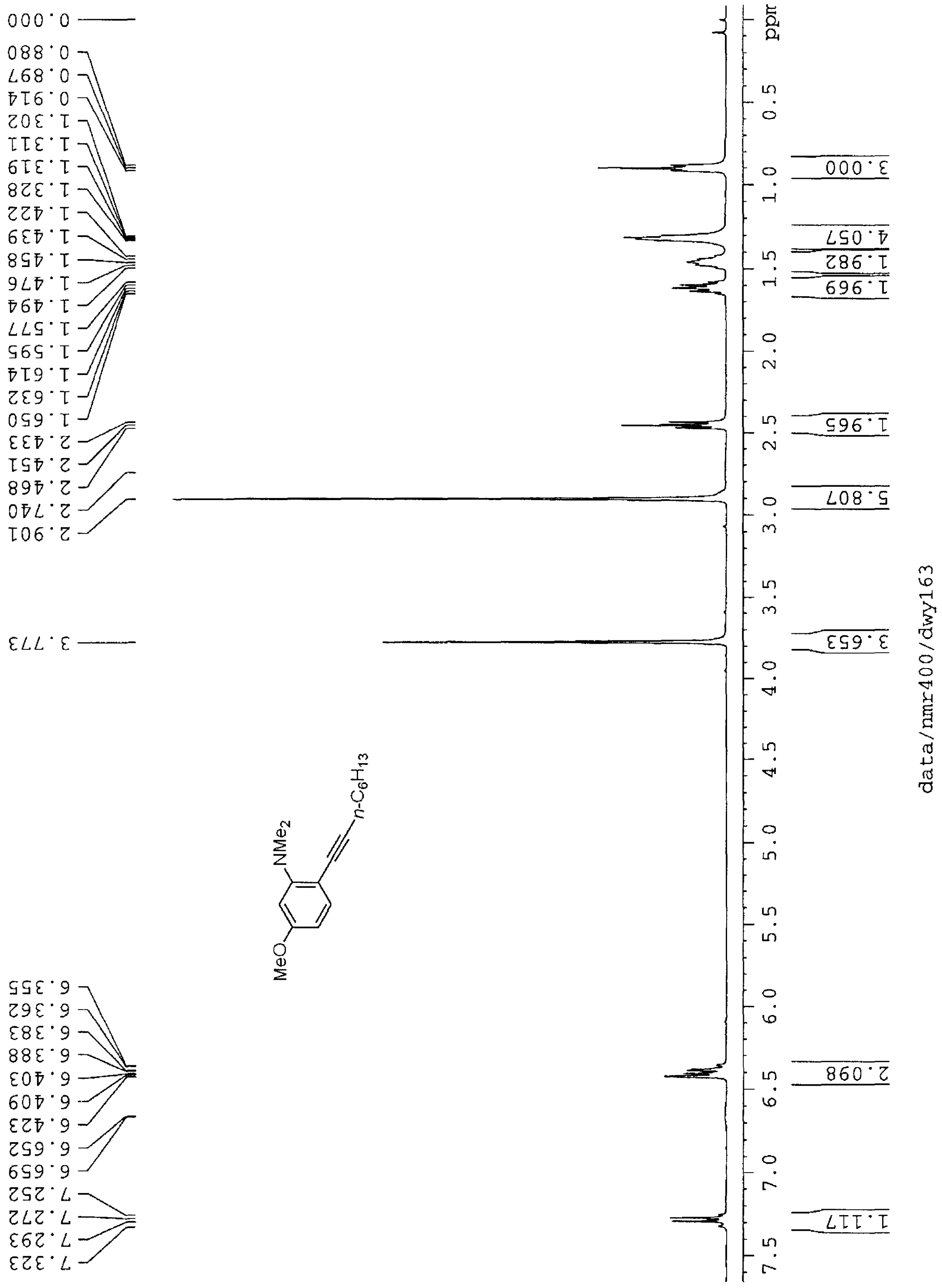

14.263
20.083
20.443
22.792
28.901
28.999
31.609
44.006
76.912
77.230
77.547
79.641
95.719
116.918
117.178
129.216
130.443
134.856
152.509
NMe$_2$
n-C$_6$H$_{13}$
Me
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
ppm
data/nmr400/dwy149c

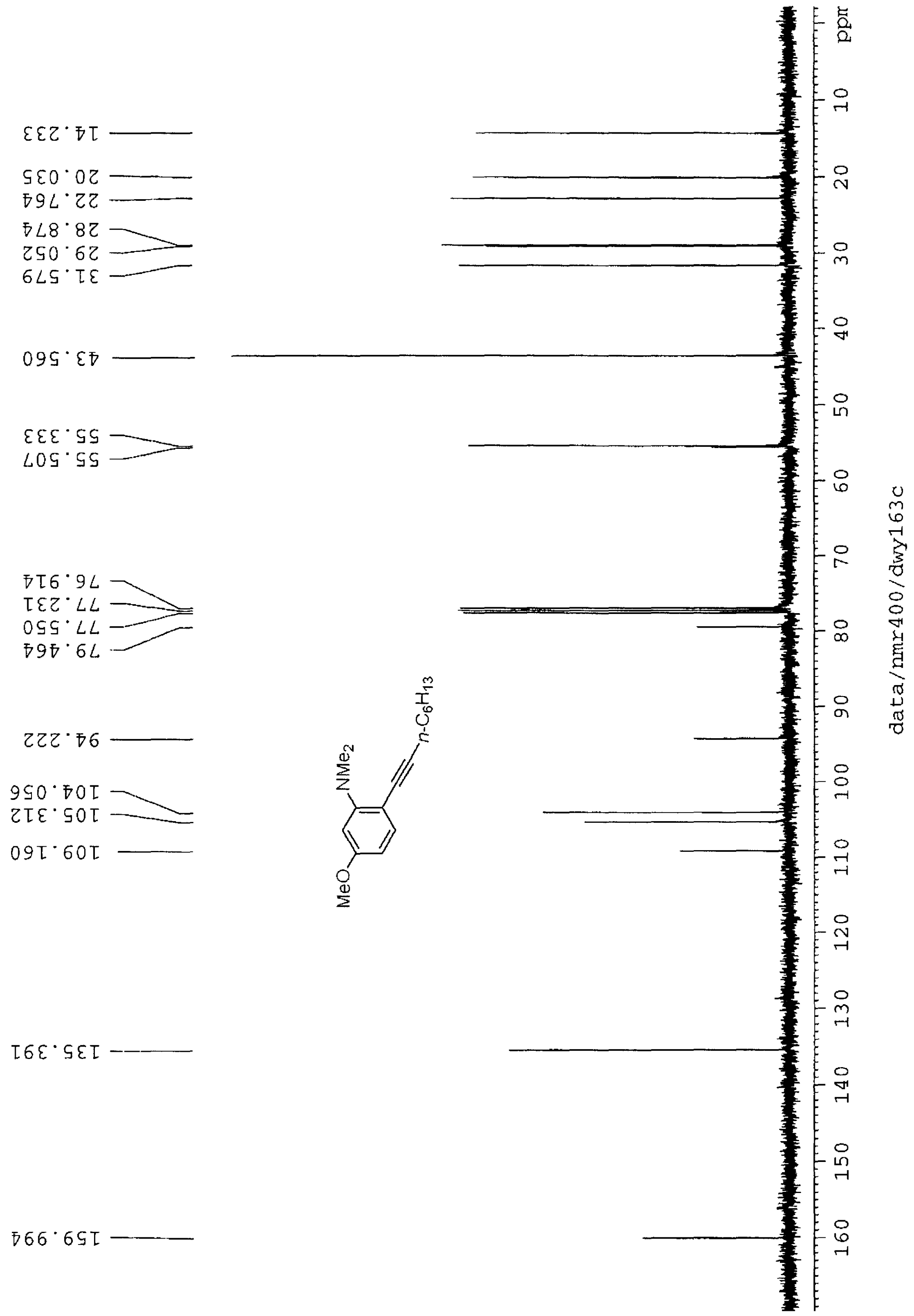

0.000
1.516
1.528
1.543
1.558
1.567
1.584
1.598
1.610
1.625
2.054
2.061
2.153
2.169
2.806
6.106
6.703
6.724
6.909
6.930
7.123
NMe$_2$
Me
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
3.983
2.035
4.875
5.943
0.923
0.945
0.950
0.902
data/nmr400/dwy144

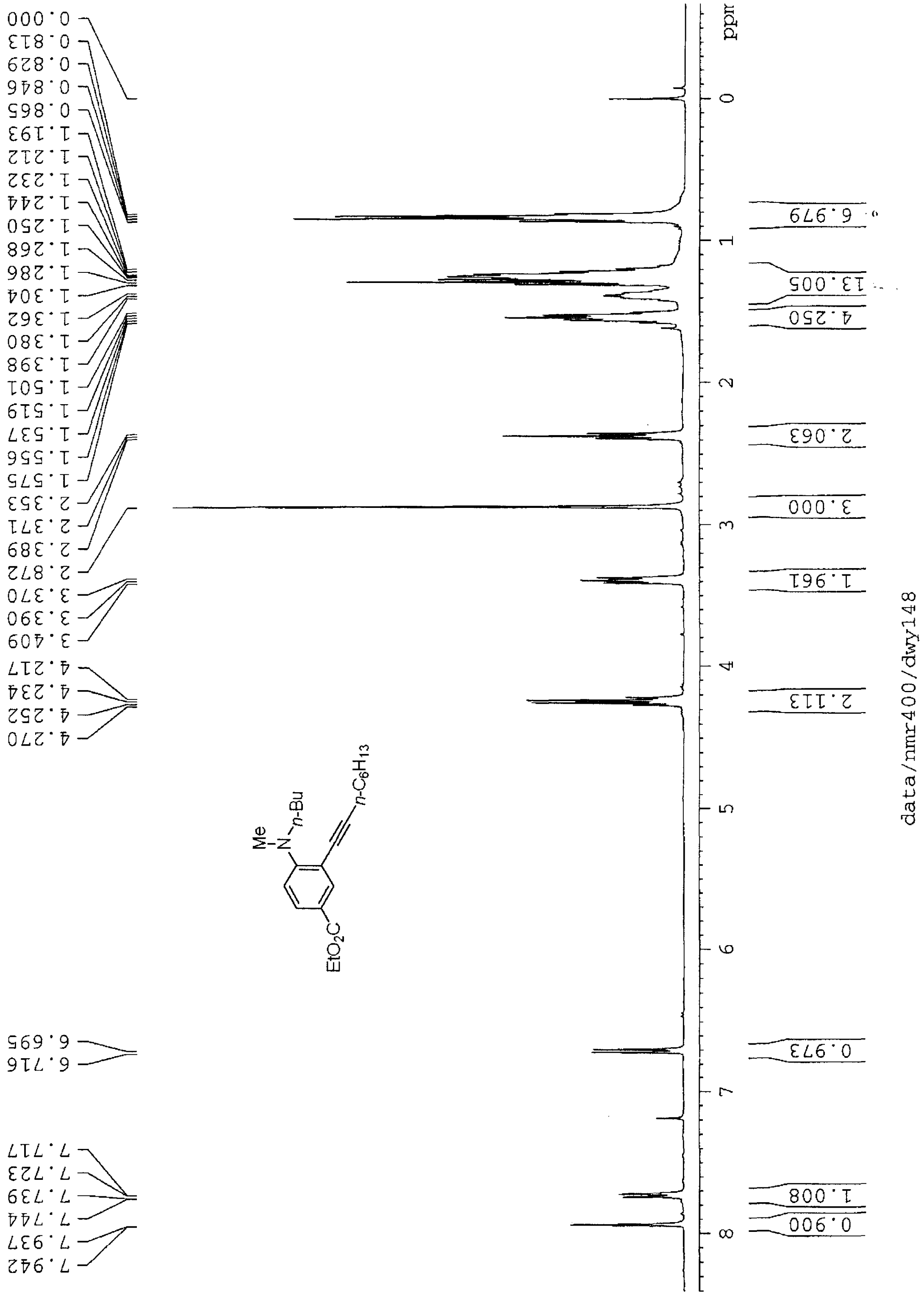

20.409
21.762
22.550
25.926
29.318
43.848
76.913
77.230
77.549
86.220
96.550
116.121
117.044
121.335
129.542
130.124
134.390
134.541
152.457
NMe2
Me
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr400/dwy144c

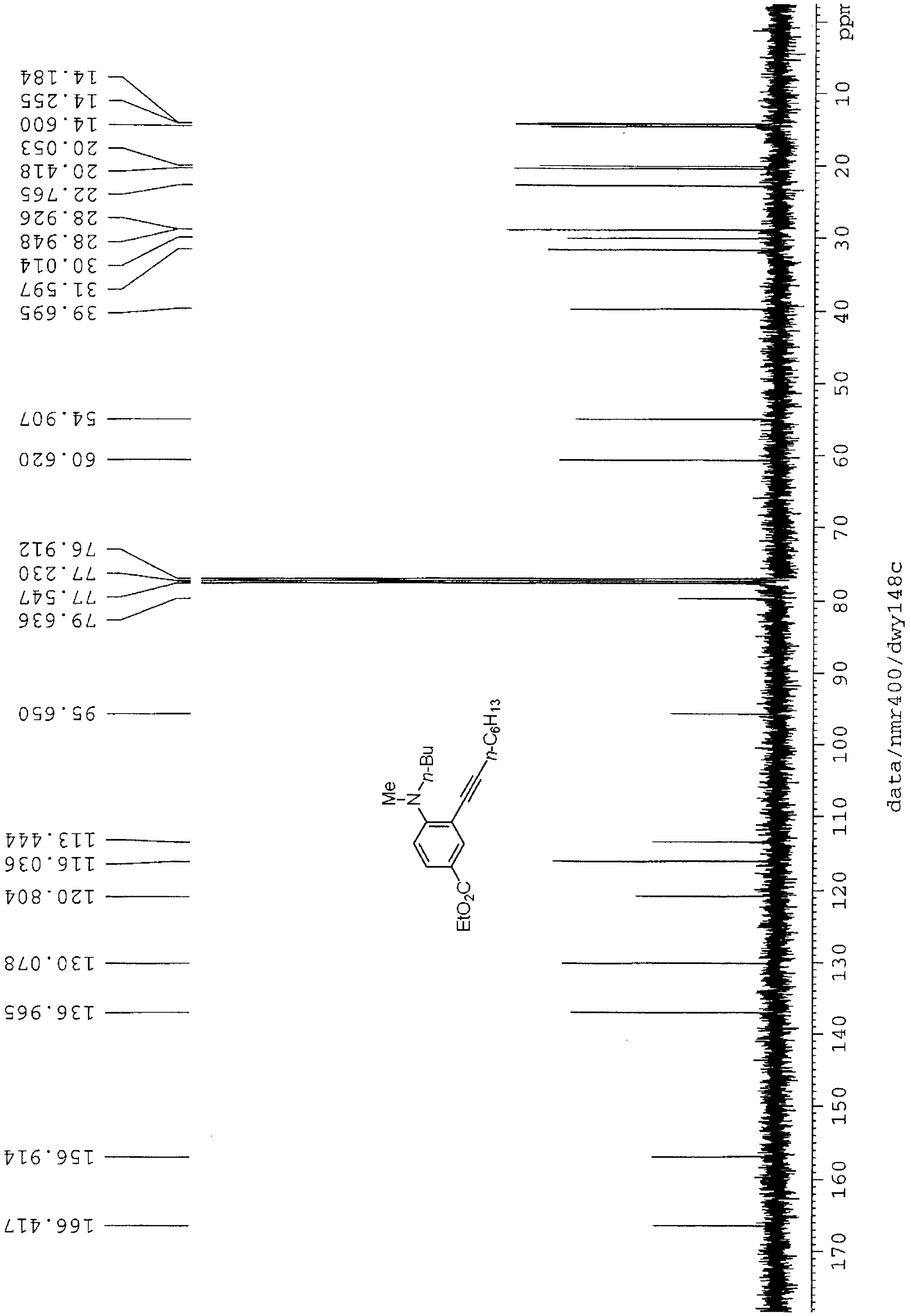

0.000
2.988
3.792
6.422
6.428
6.446
7.227
7.252
7.255
7.261
7.270
7.277
7.288
7.292
7.297
7.315
7.327
7.332
7.337
7.400
7.422
7.497
7.513
7.517
MeO
NMe2
Ph
6.000
3.056
1.953
3.183
0.978
1.994
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
data/nmr400/dwy162

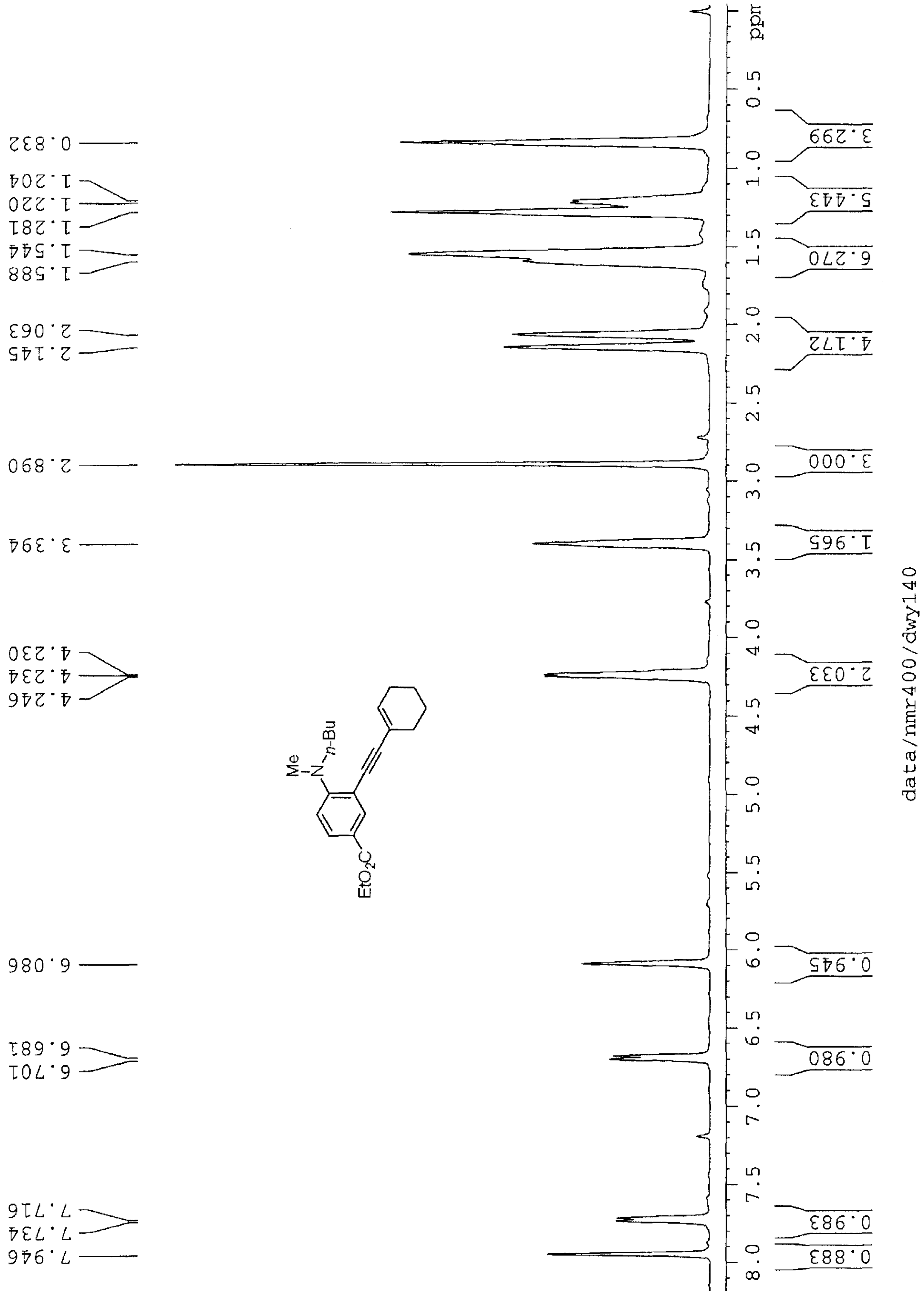

43.499
55.400
76.913
77.230
77.548
89.200
93.481
103.849
105.349
107.635
124.362
127.812
128.430
131.229
135.618
156.327
160.774
MeO
NMe2
Ph
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy162c

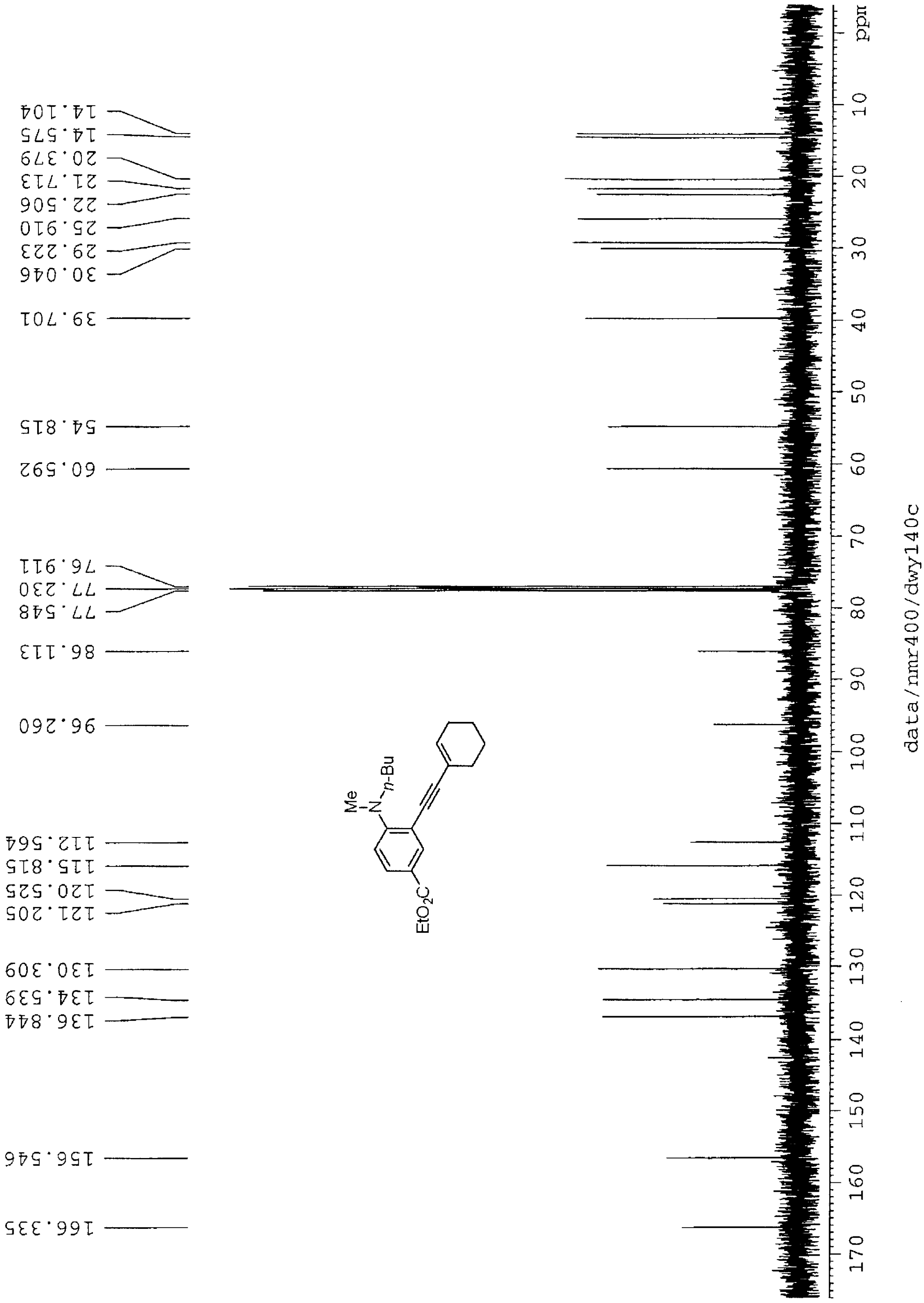

0.000
0.880
0.897
0.914
1.302
1.311
1.319
1.328
1.422
1.439
1.458
1.476
1.494
1.577
1.595
1.614
1.632
1.650
2.433
2.451
2.468
2.740
2.901
3.773
6.355
6.362
6.383
6.388
6.403
6.409
6.423
6.652
6.659
7.252
7.272
7.293
7.323
MeO
NMe2
n-C6H13
3.000
4.057
1.982
1.969
1.965
5.807
3.653
2.098
1.117
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
data/nmr400/dwy163

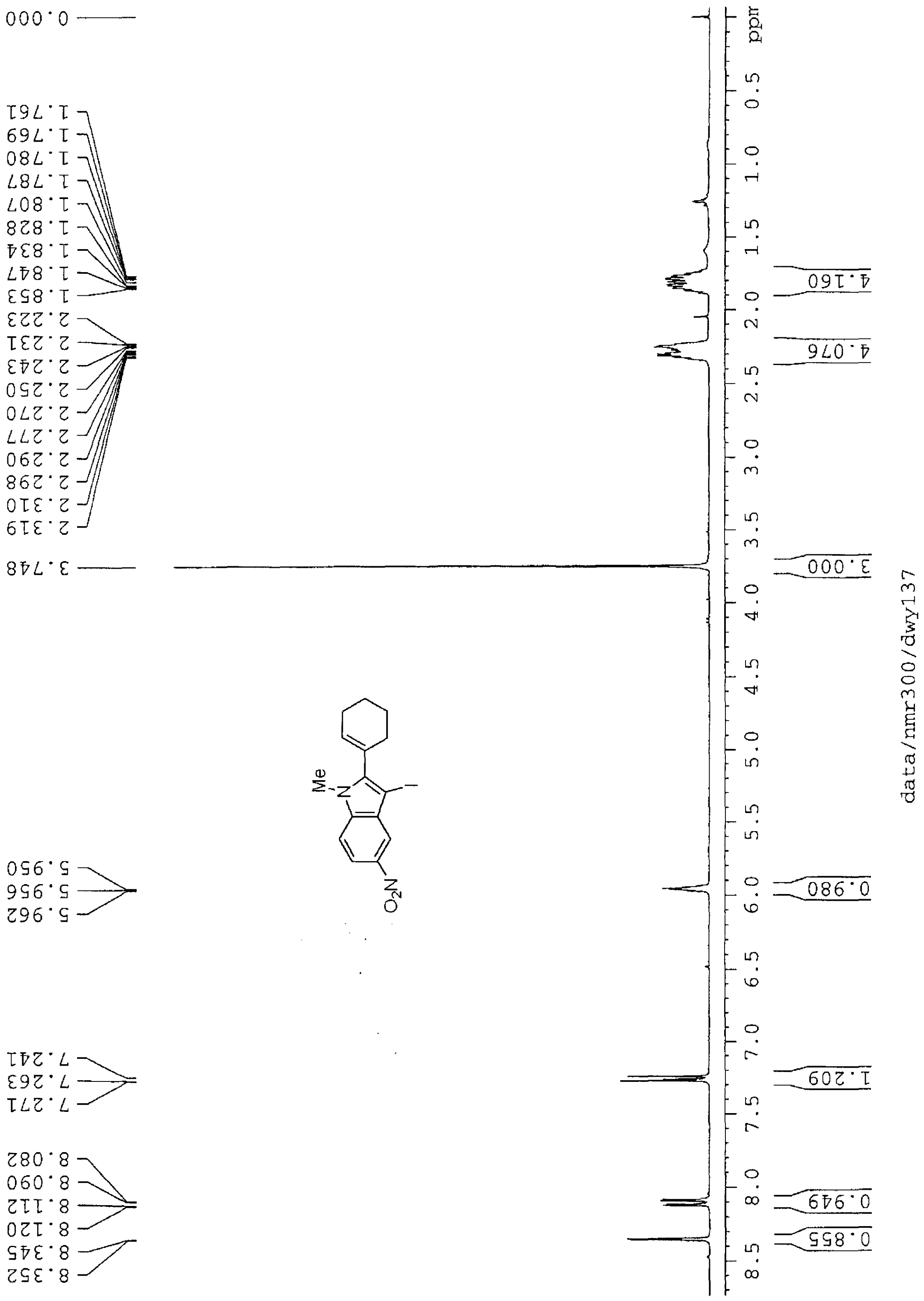

14.233
20.035
22.764
28.874
29.052
31.579
43.560
55.333
55.507
76.914
77.231
77.550
79.464
94.222
104.056
105.312
109.160
135.391
159.994
NMe2
MeO
n-C6H13
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr400/dwy163c

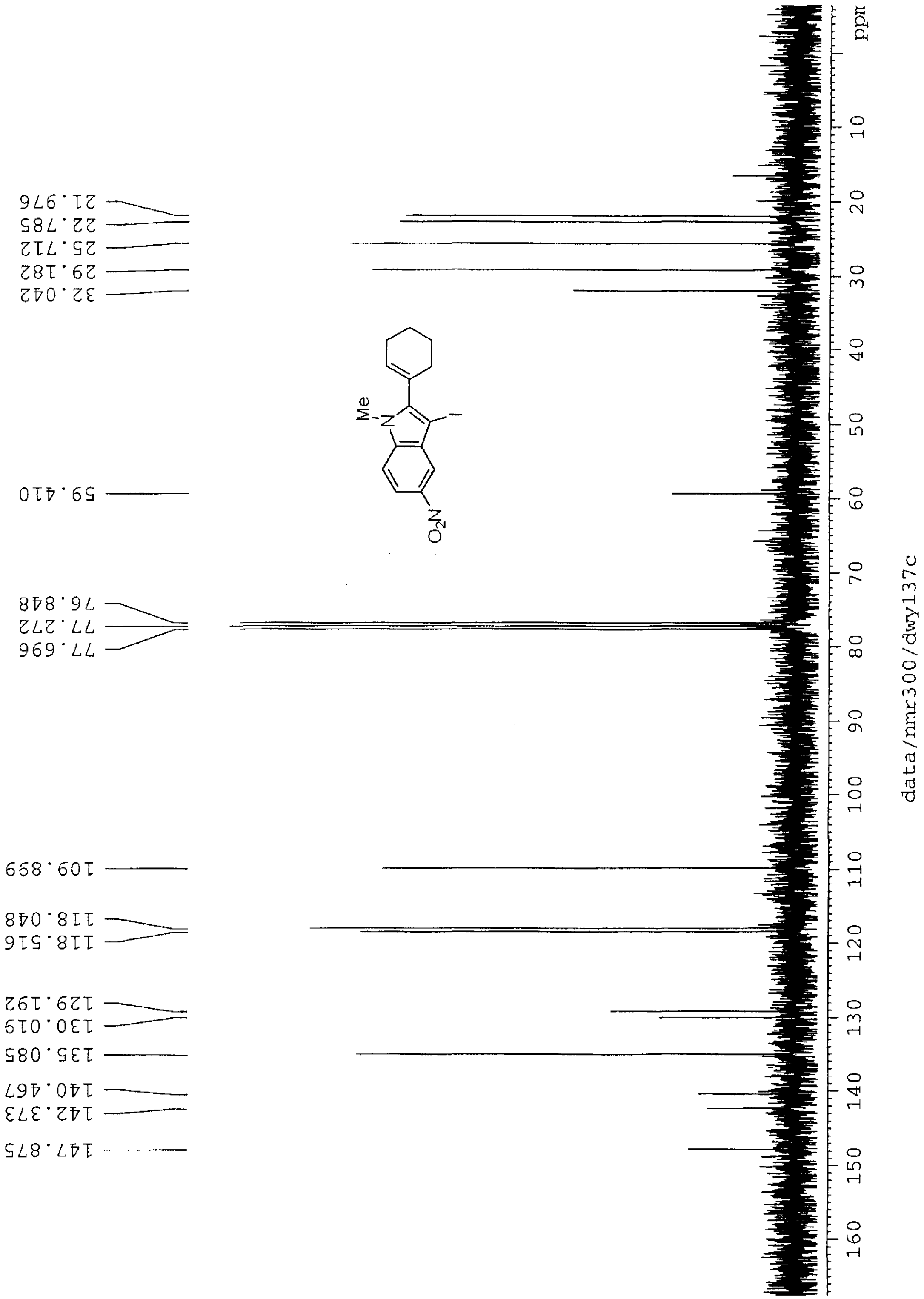

0.000
0.813
0.829
0.846
0.865
1.193
1.212
1.232
1.244
1.250
1.268
1.286
1.304
1.362
1.380
1.398
1.501
1.519
1.537
1.556
1.575
2.353
2.371
2.389
2.872
3.370
3.390
3.409
4.217
4.234
4.252
4.270
6.695
6.716
7.717
7.723
7.739
7.744
7.937
7.942
6.979
13.005
4.250
2.063
3.000
1.961
2.113
0.973
1.008
0.900
ppm
0
1
2
3
4
5
6
7
8
data/nmr400/dwy148
Me
N
n-Bu
n-C6H13
EtO2C

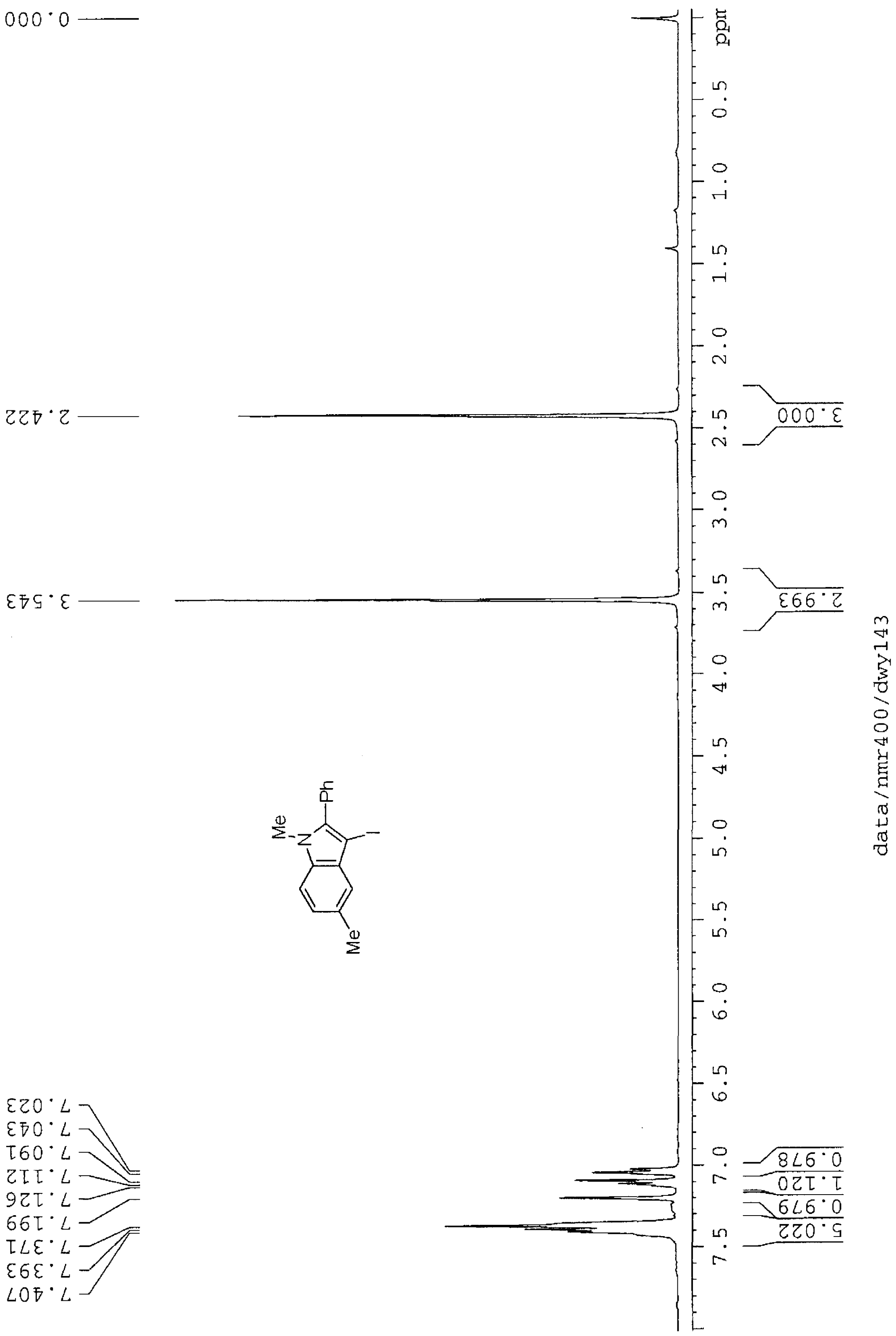

14.184
14.255
14.600
20.053
20.418
22.765
28.926
28.948
30.014
31.597
39.695
54.907
60.620
76.912
77.230
77.547
79.636
95.650
113.444
116.036
120.804
130.078
136.965
156.914
166.417
Me
N
n-Bu
n-C6H13
EtO2C
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy148c

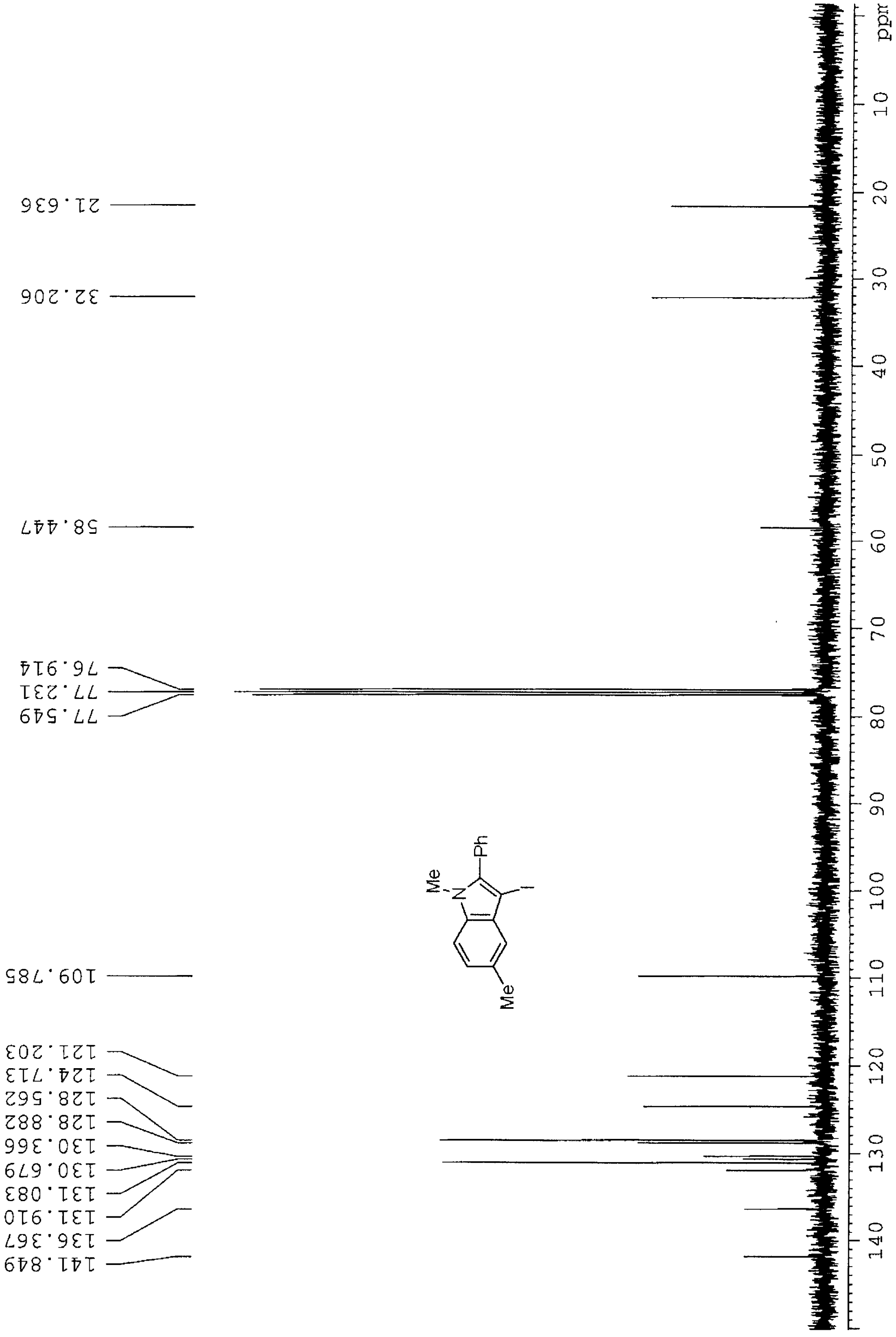

0.832
1.204
1.220
1.281
1.544
1.588
2.063
2.145
2.890
3.394
4.230
4.234
4.246
6.086
6.681
6.701
7.716
7.734
7.946
3.299
5.443
6.270
4.172
3.000
1.965
2.033
0.945
0.980
0.983
0.883
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
data/nmr400/dwy140
Me
N
n-Bu
EtO2C

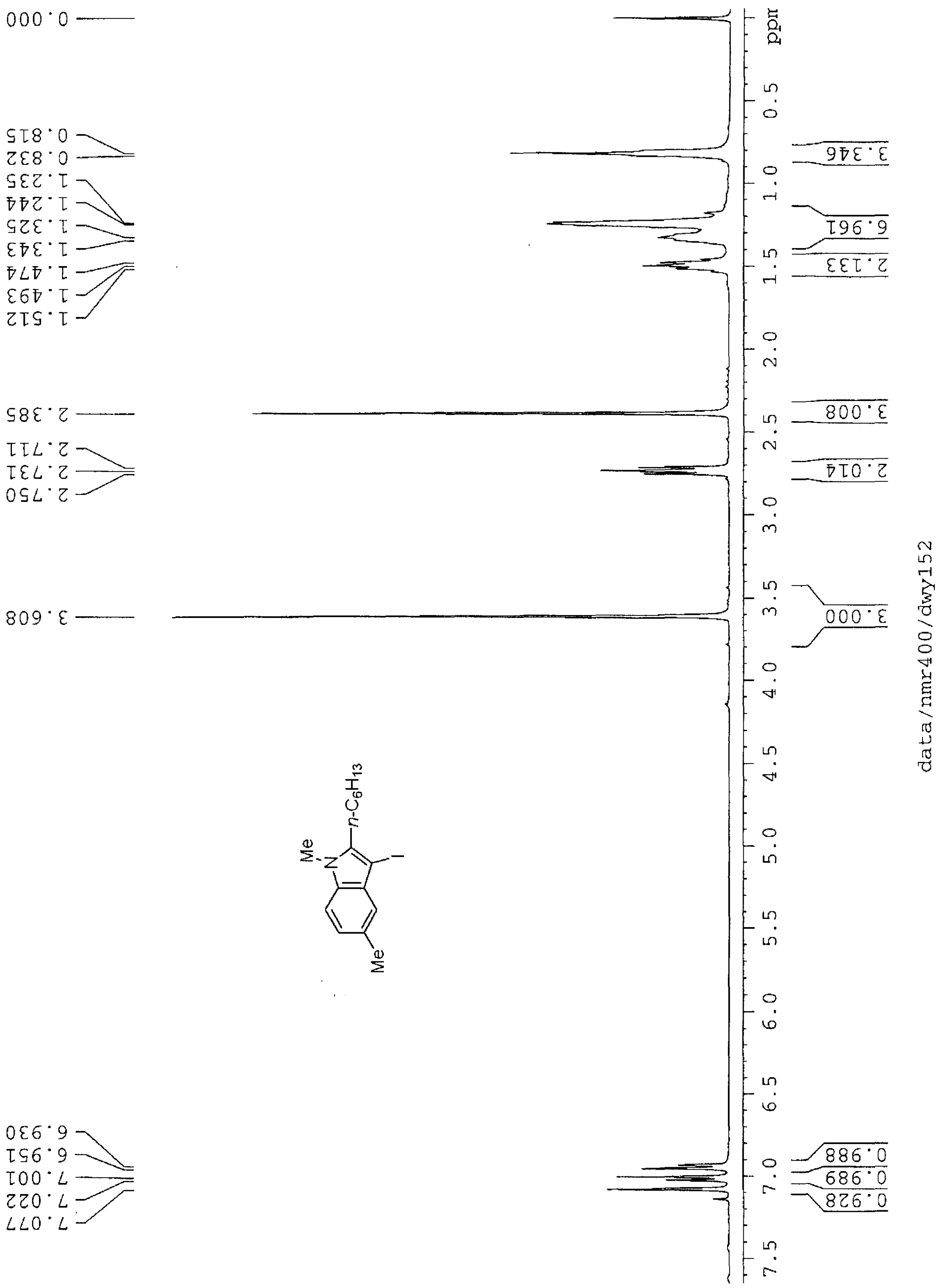

14.104
14.575
20.379
21.713
22.506
25.910
29.223
30.046
39.701
54.815
60.592
76.911
77.230
77.548
86.113
96.260
112.564
115.815
120.525
121.205
130.309
134.539
136.844
156.546
166.335
Me
N
n-Bu
EtO2C
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy140c

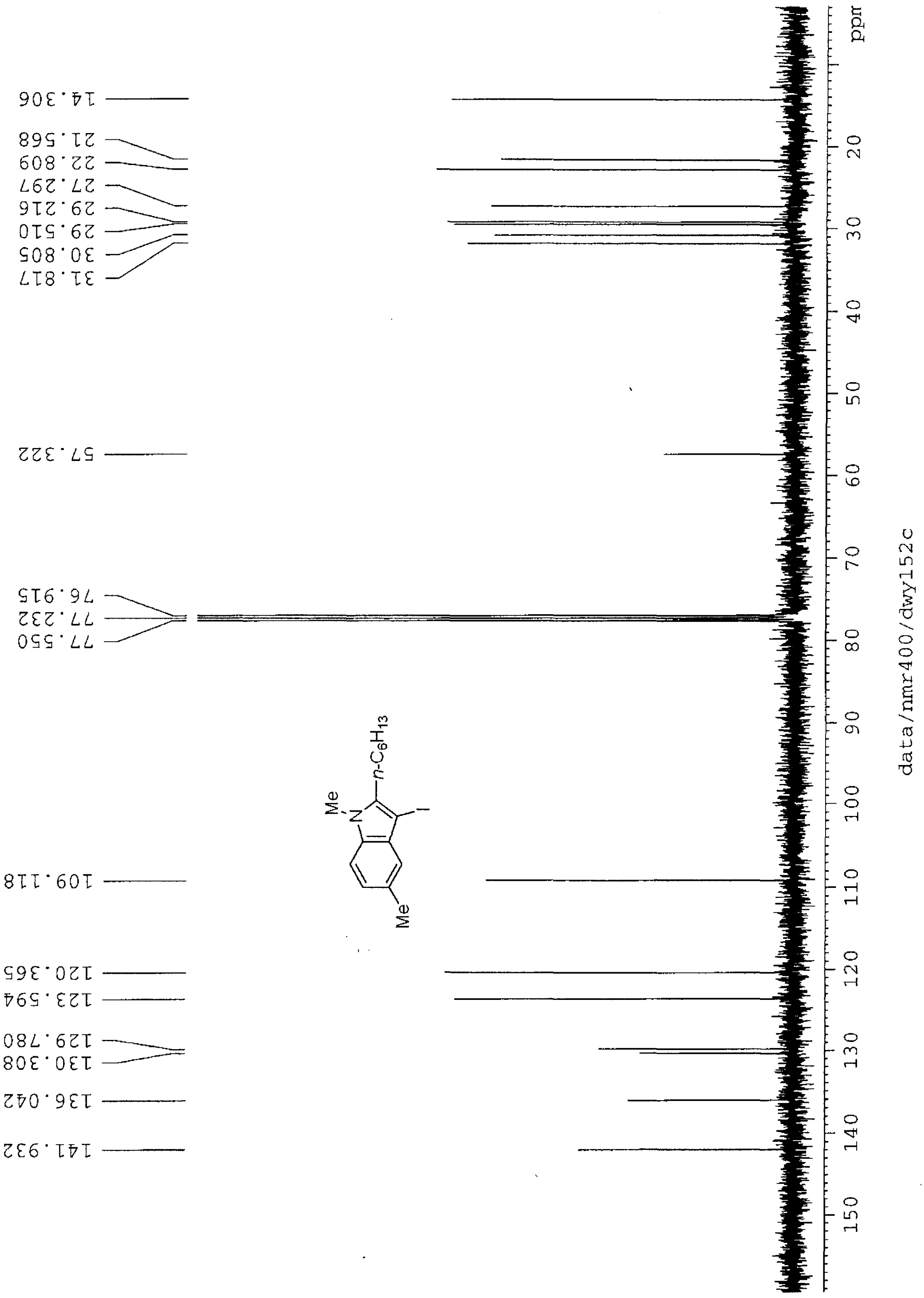

0.000
1.761
1.769
1.780
1.787
1.807
1.828
1.834
1.847
1.853
2.223
2.231
2.243
2.250
2.270
2.277
2.290
2.298
2.310
2.319
3.748
5.950
5.956
5.962
7.241
7.263
7.271
8.082
8.090
8.112
8.120
8.345
8.352
Me
N
O_2N
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
4.160
4.076
3.000
0.980
1.209
0.949
0.855
data/nmr300/dwy137

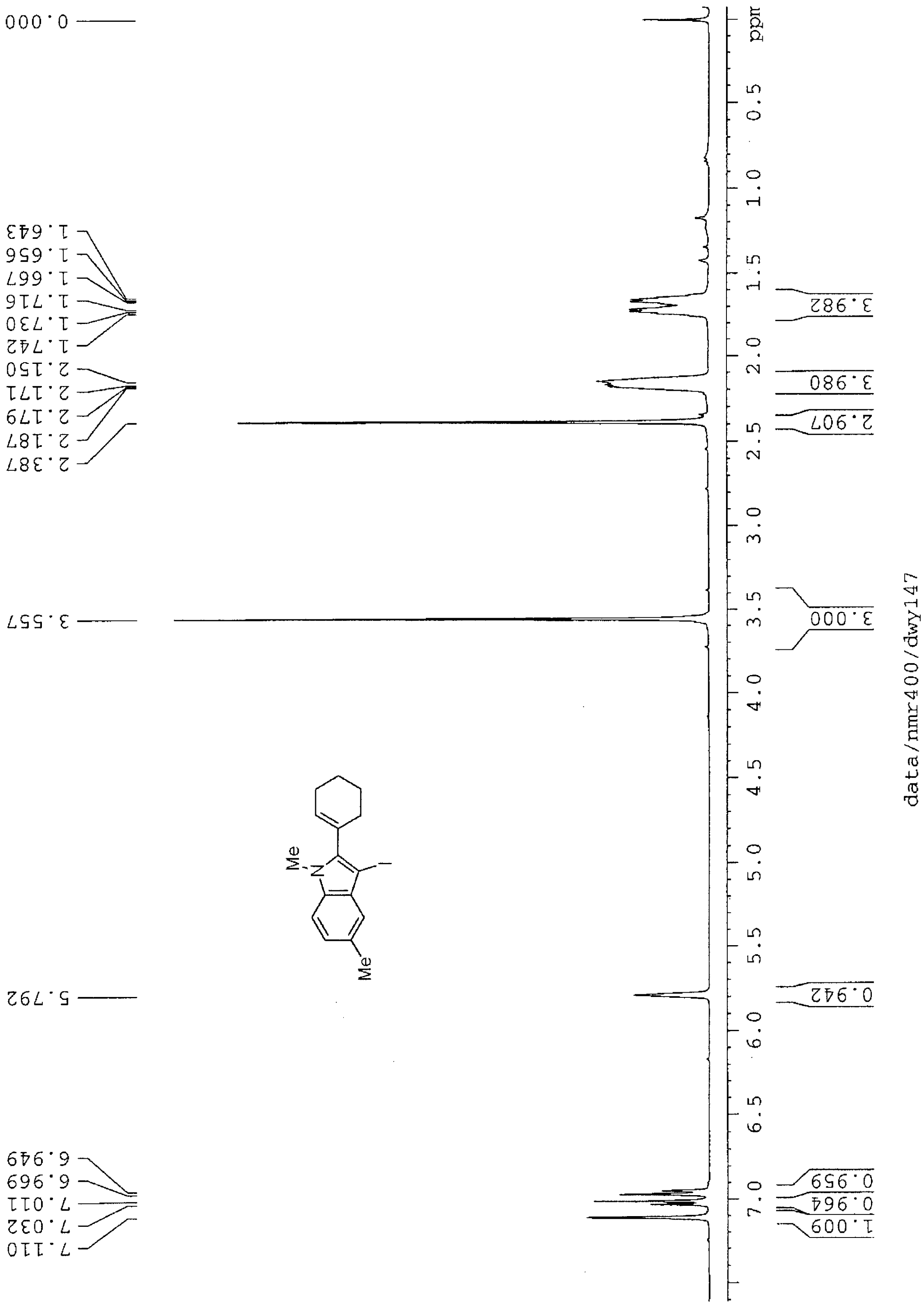

21.976
22.785
25.712
29.182
32.042
59.410
76.848
77.272
77.696
109.899
118.048
118.516
129.192
130.019
135.085
140.467
142.373
147.875
Me
N
O2N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr300/dwy137c

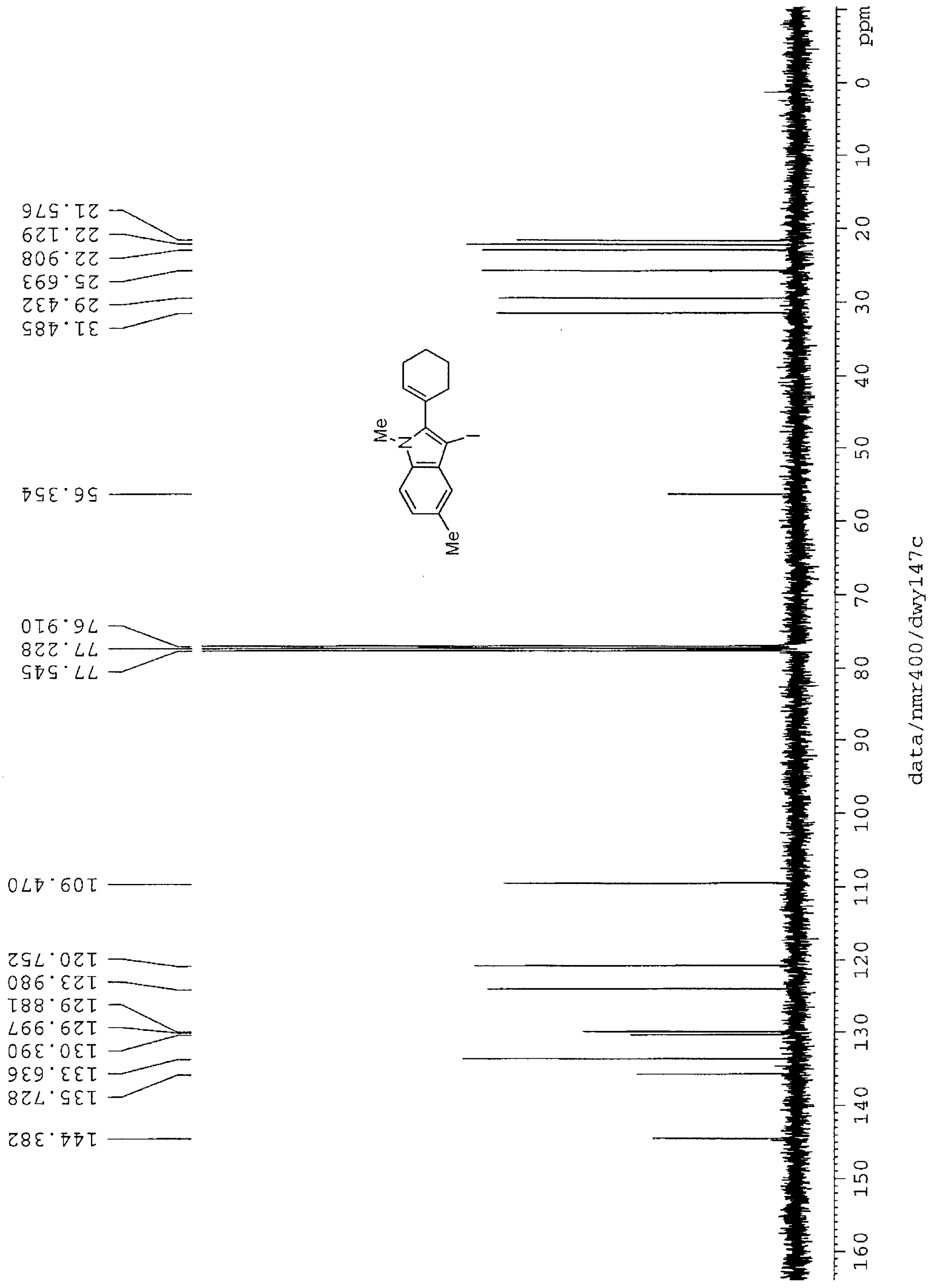

0.000
2.422
3.543
7.023
7.043
7.091
7.112
7.126
7.199
7.371
7.393
7.407
Me
N
Ph
Me
3.000
2.993
0.978
1.120
0.979
5.022
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
data/nmr400/dwy143

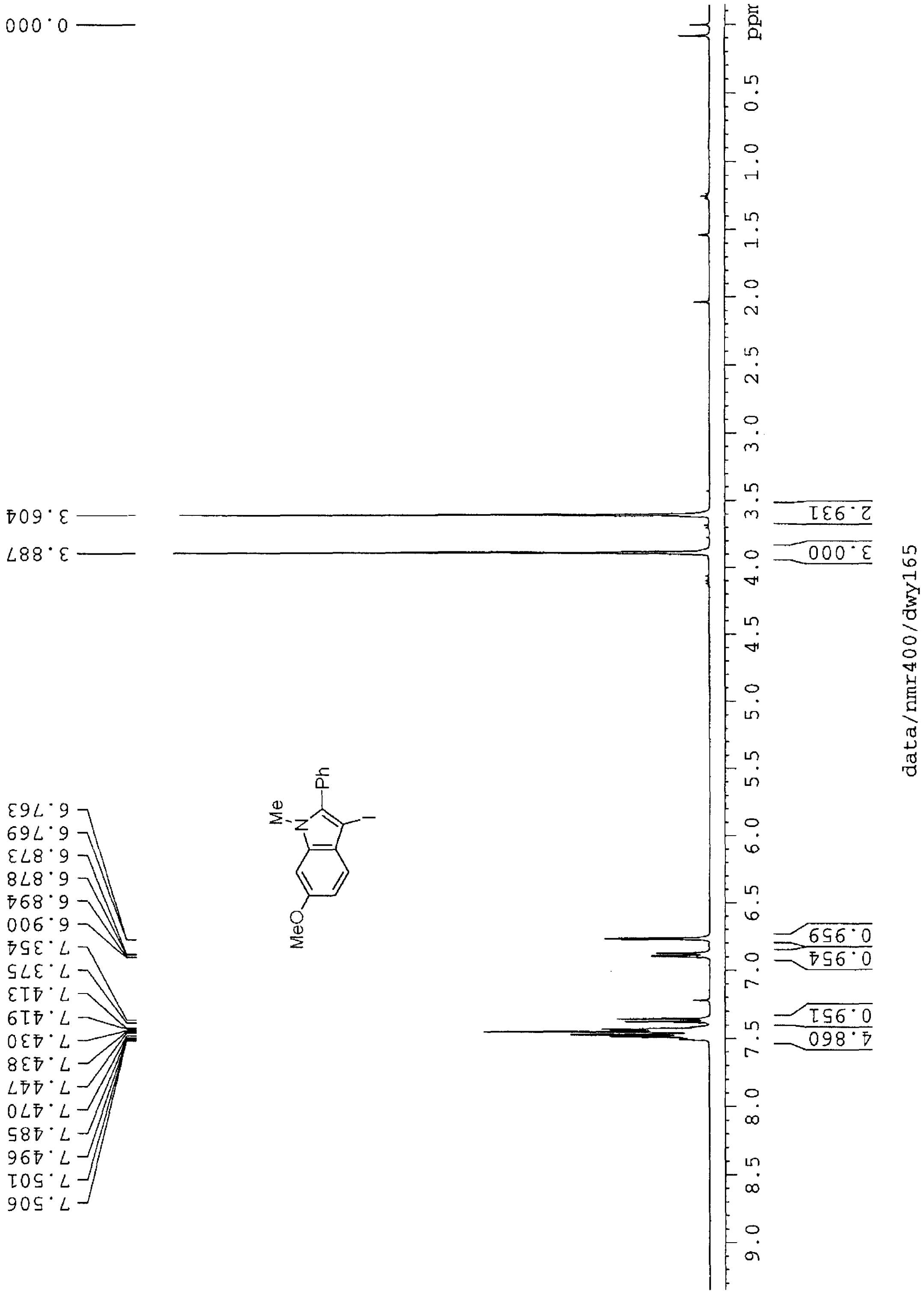

21.636
32.206
58.447
76.914
77.231
77.549
109.785
121.203
124.713
128.562
128.882
130.366
130.679
131.083
131.910
136.367
141.849
Me
N
Ph
Me
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140

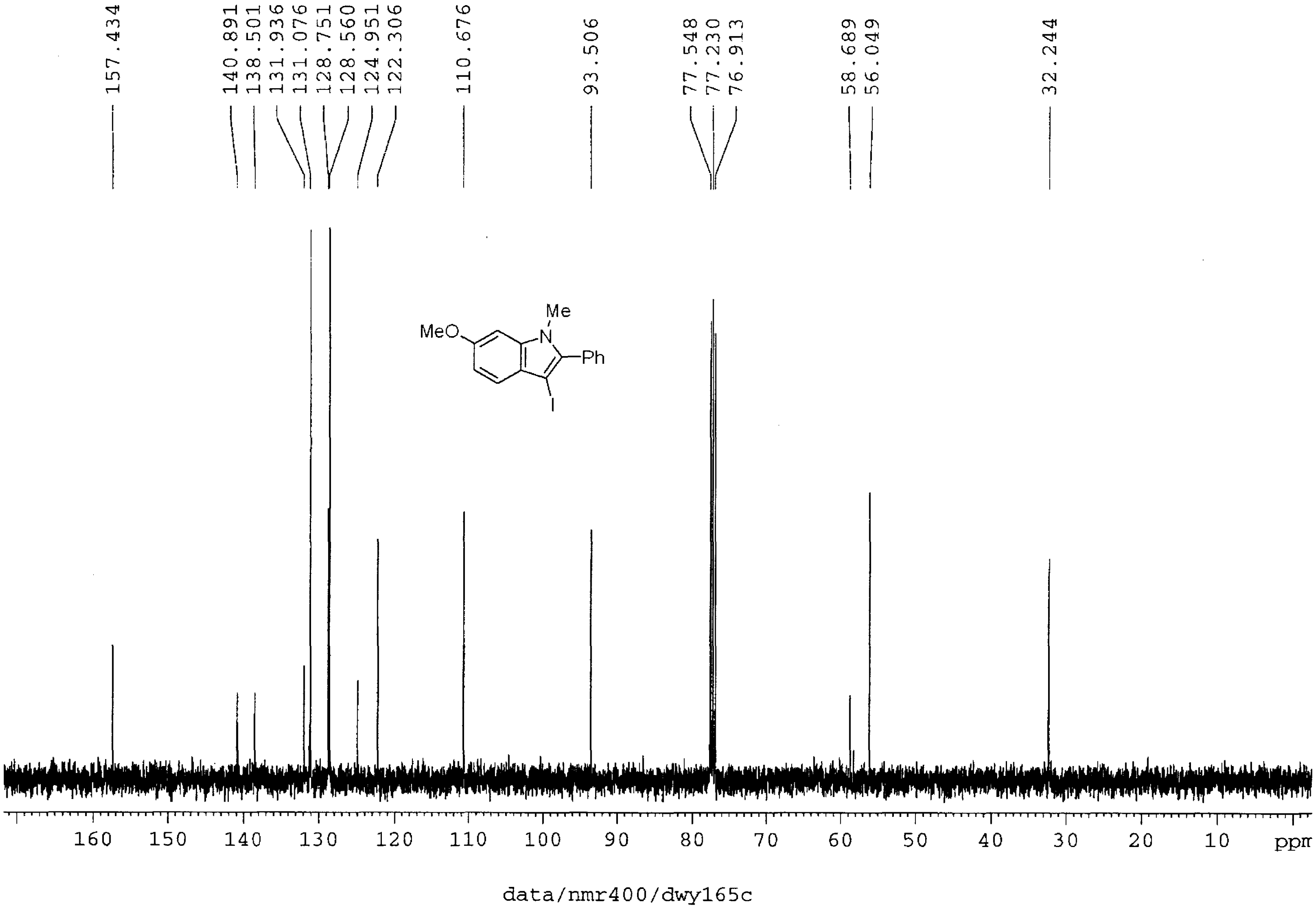

0.000
0.815
0.832
1.235
1.244
1.325
1.343
1.474
1.493
1.512
2.385
2.711
2.731
2.750
3.608
6.930
6.951
7.001
7.022
7.077
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
3.346
6.961
2.133
3.008
2.014
3.000
0.988
0.989
0.928
data/nmr400/dwy152
Me
N
n-C6H13
I
Me

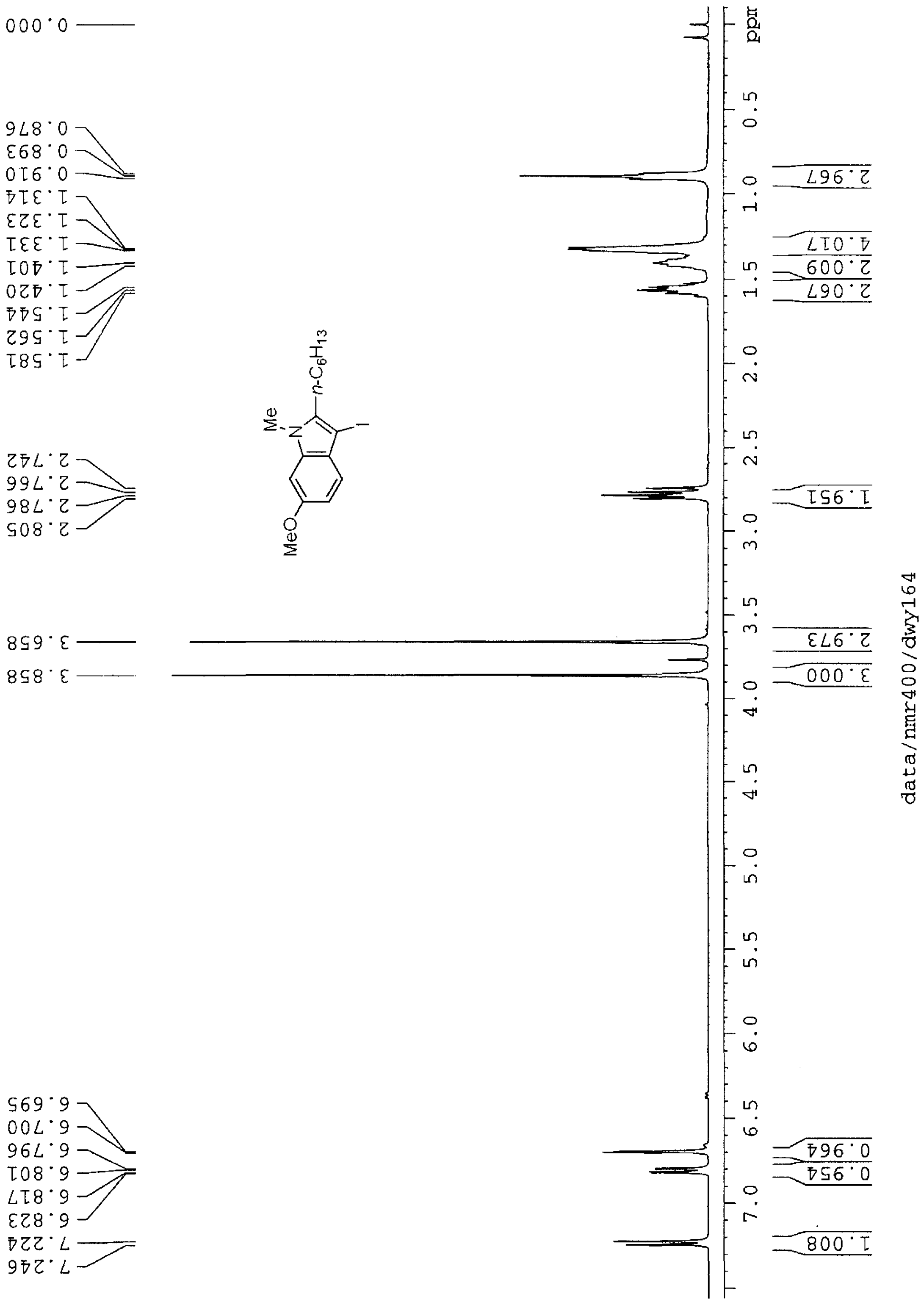

14.306
21.568
22.809
27.297
29.216
29.510
30.805
31.817
57.322
76.915
77.232
77.550
109.118
120.365
123.594
129.780
130.308
136.042
141.932
Me
N
n-C6H13
I
Me
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
data/nmr400/dwy152c

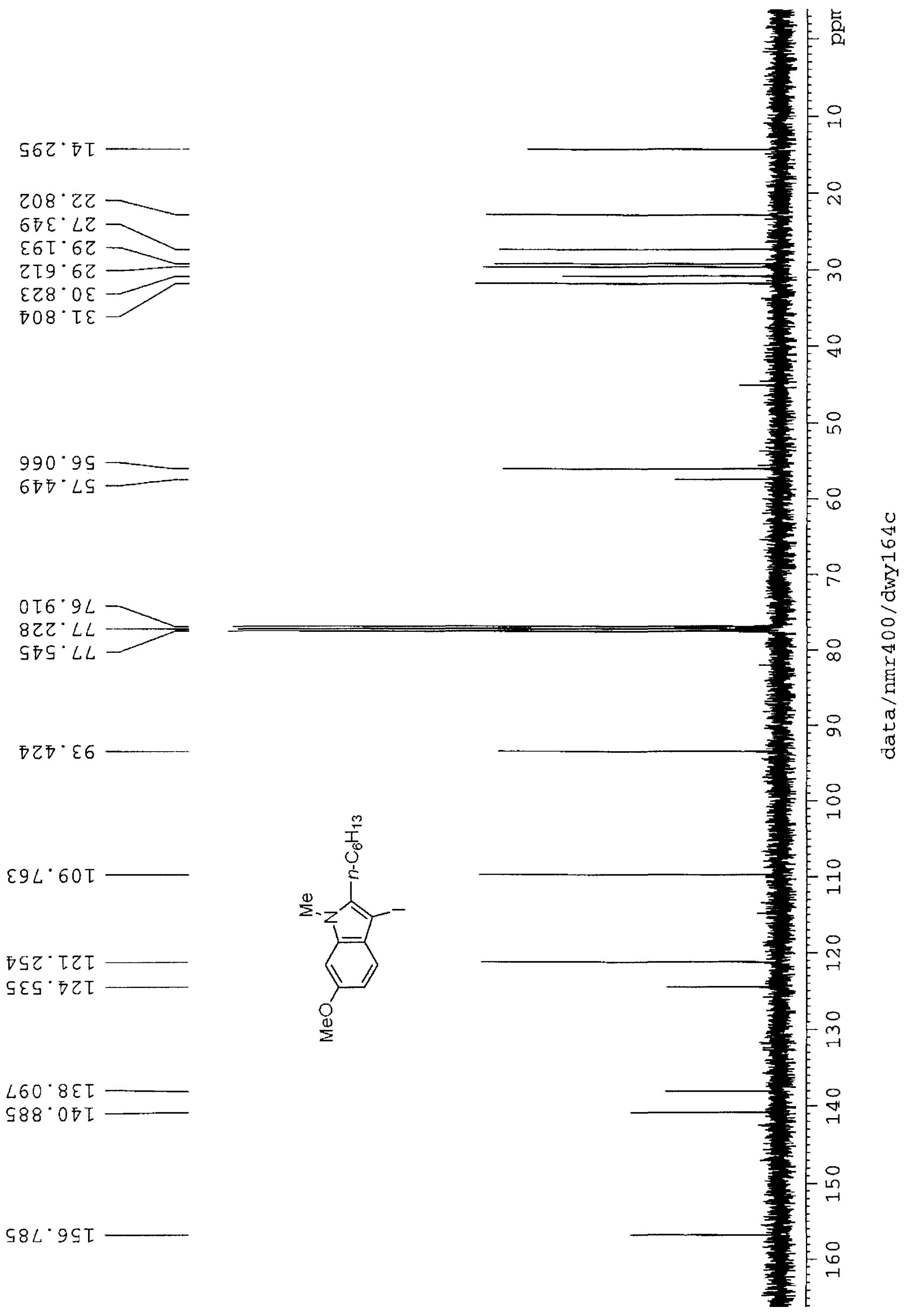

0.000
1.643
1.656
1.667
1.716
1.730
1.742
2.150
2.171
2.179
2.187
2.387
3.557
5.792
6.949
6.969
7.011
7.032
7.110
3.982
3.980
2.907
3.000
0.942
0.959
0.964
1.009
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
data/nmr400/dwy147
Me
N
Me

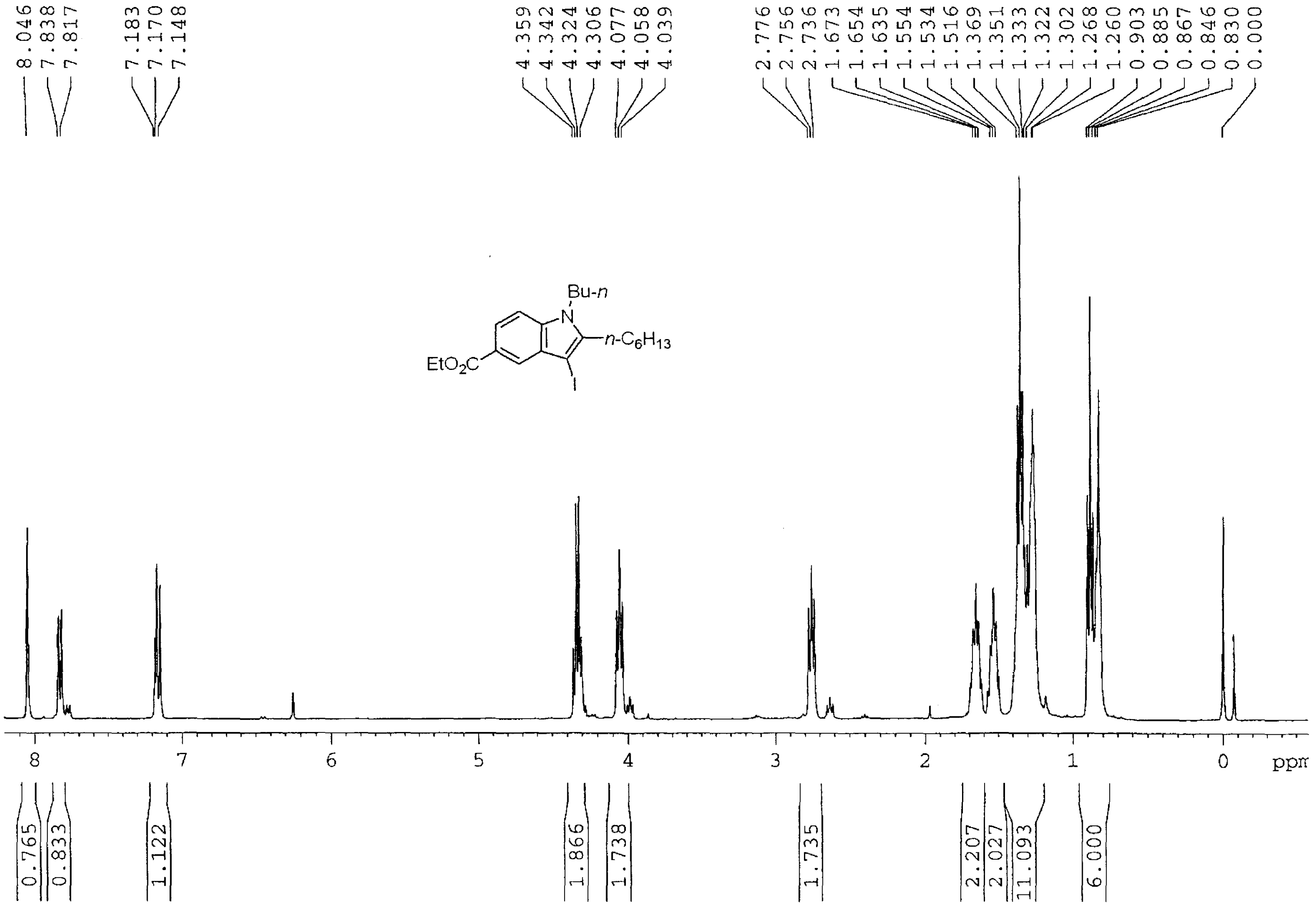

21.576
22.129
22.908
25.693
29.432
31.485
56.354
76.910
77.228
77.545
109.470
120.752
123.980
129.881
129.997
130.390
133.636
135.728
144.382
Me
N
I
Me
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr400/dwy147c


0.000
3.604
3.887
6.763
6.769
6.873
6.878
6.894
6.900
7.354
7.375
7.413
7.419
7.430
7.438
7.447
7.470
7.485
7.496
7.501
7.506
Me
N
Ph
I
MeO
2.931
3.000
0.959
0.954
0.951
4.860
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
data/nmr400/dwy165

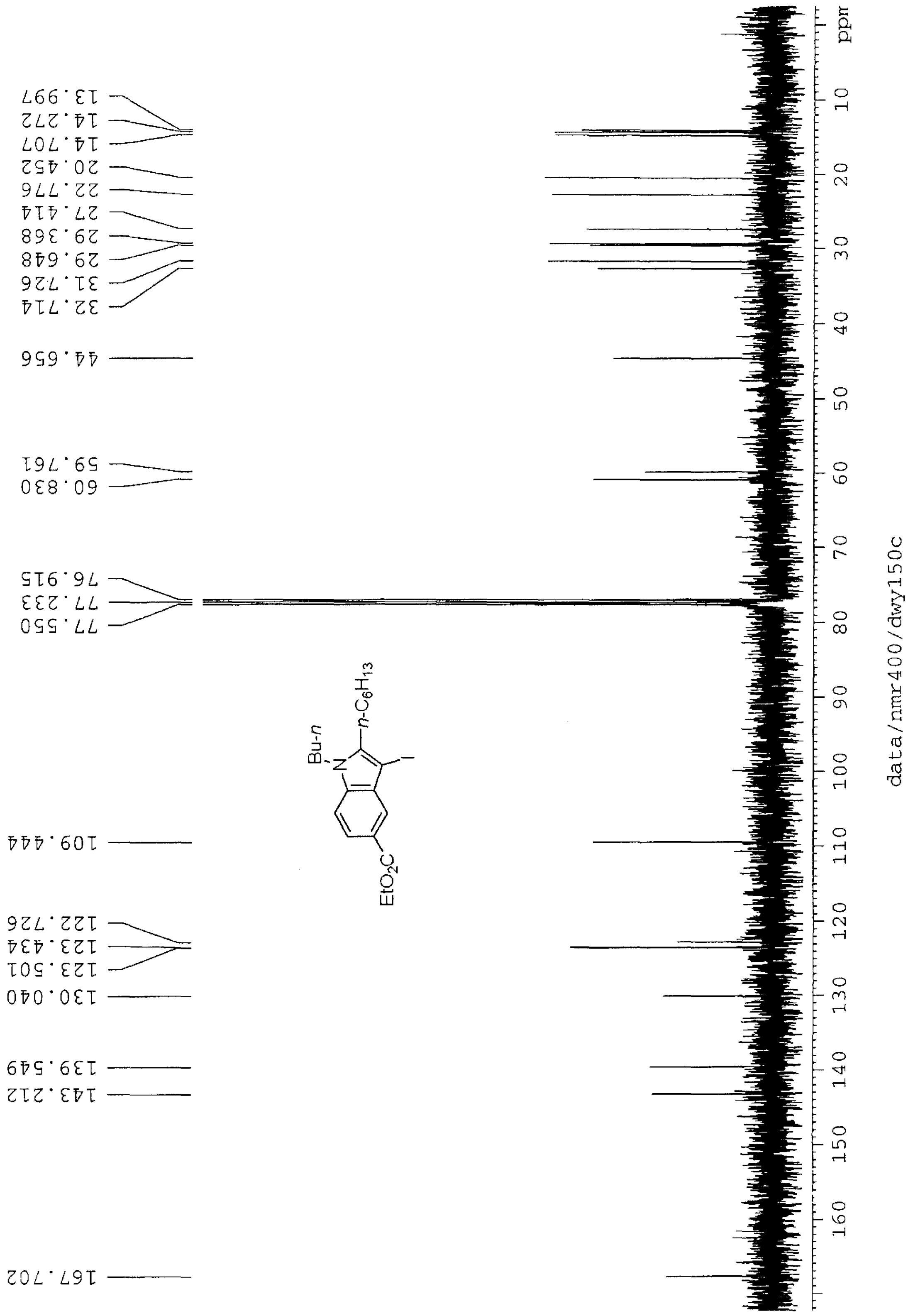

157.434
140.891
138.501
131.936
131.076
128.751
128.560
124.951
122.306
110.676
93.506
77.548
77.230
76.913
58.689
56.049
32.244
Me
MeO
N
Ph
I
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
data/nmr400/dwy165c

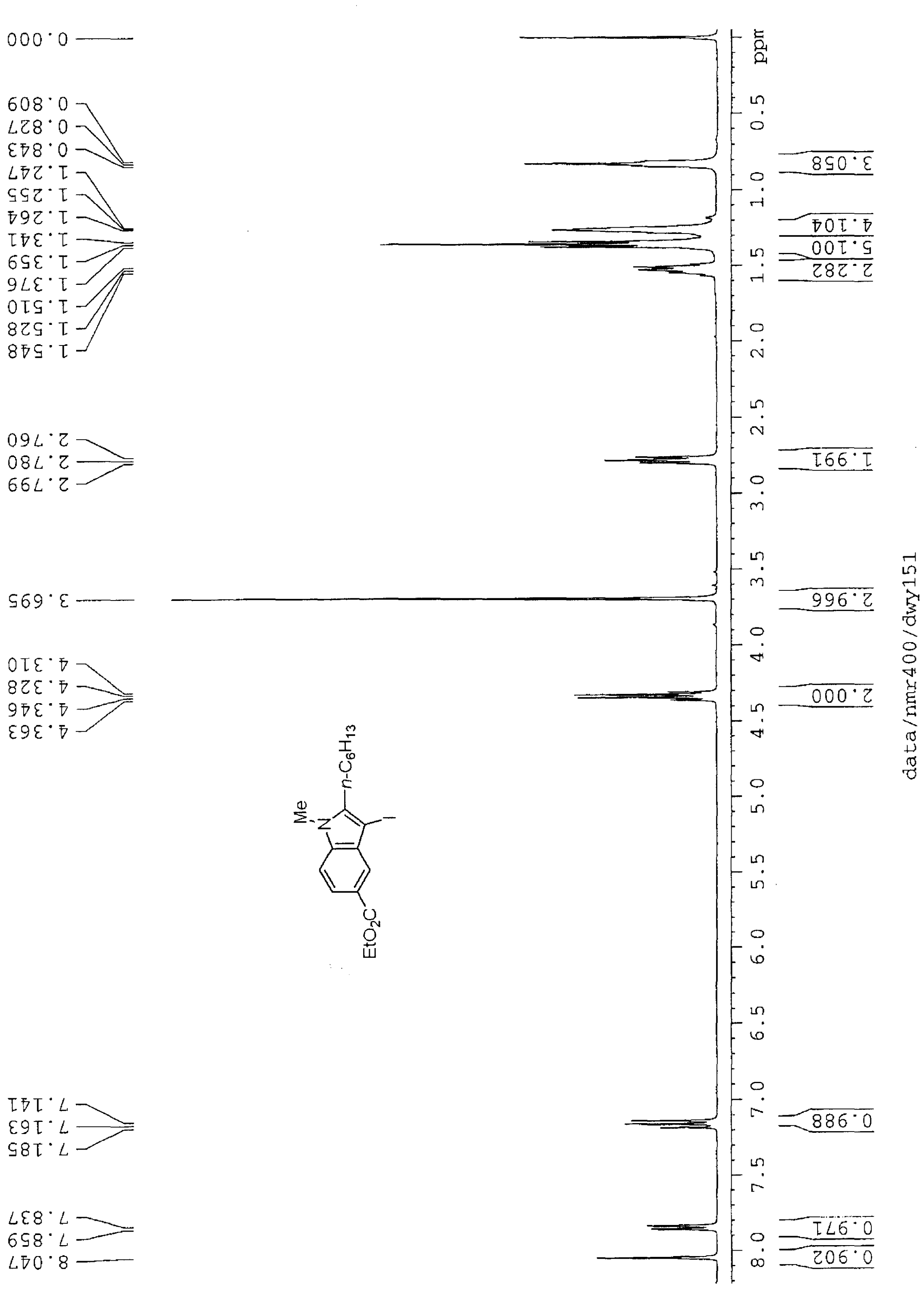

0.000
0.876
0.893
0.910
1.314
1.323
1.331
1.401
1.420
1.544
1.562
1.581
2.742
2.766
2.786
2.805
3.658
3.858
6.695
6.700
6.796
6.801
6.817
6.823
7.224
7.246
2.967
4.017
2.009
2.067
1.951
2.973
3.000
0.964
0.954
1.008
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
data/nmr400/dwy164
Me
N
n-C6H13
I
MeO

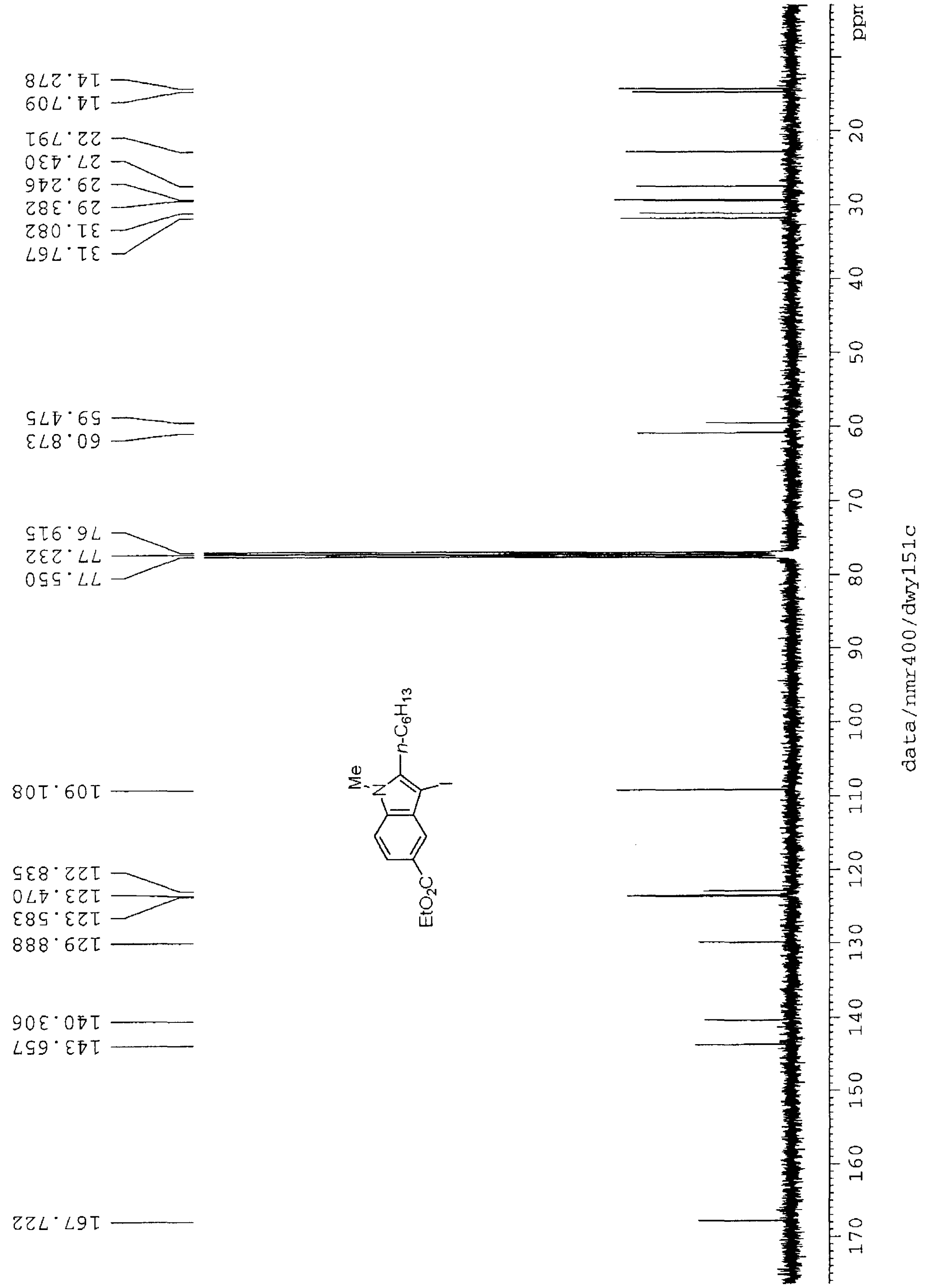

14.295
22.802
27.349
29.193
29.612
30.823
31.804
56.066
57.449
76.910
77.228
77.545
93.424
109.763
121.254
124.535
138.097
140.885
156.785
MeO
N
Me
n-C_6H_{13}
I
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr400/dwy164c

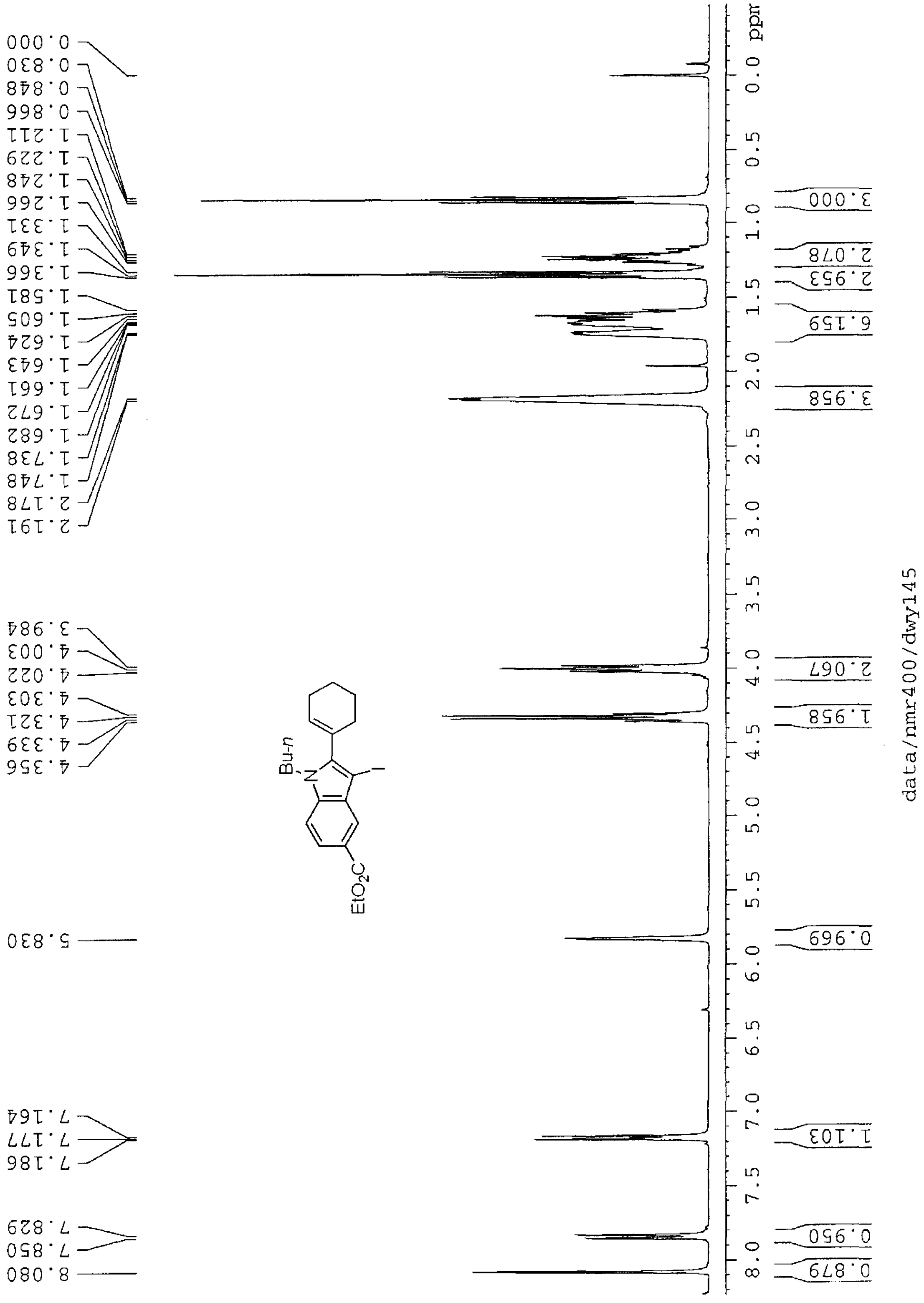


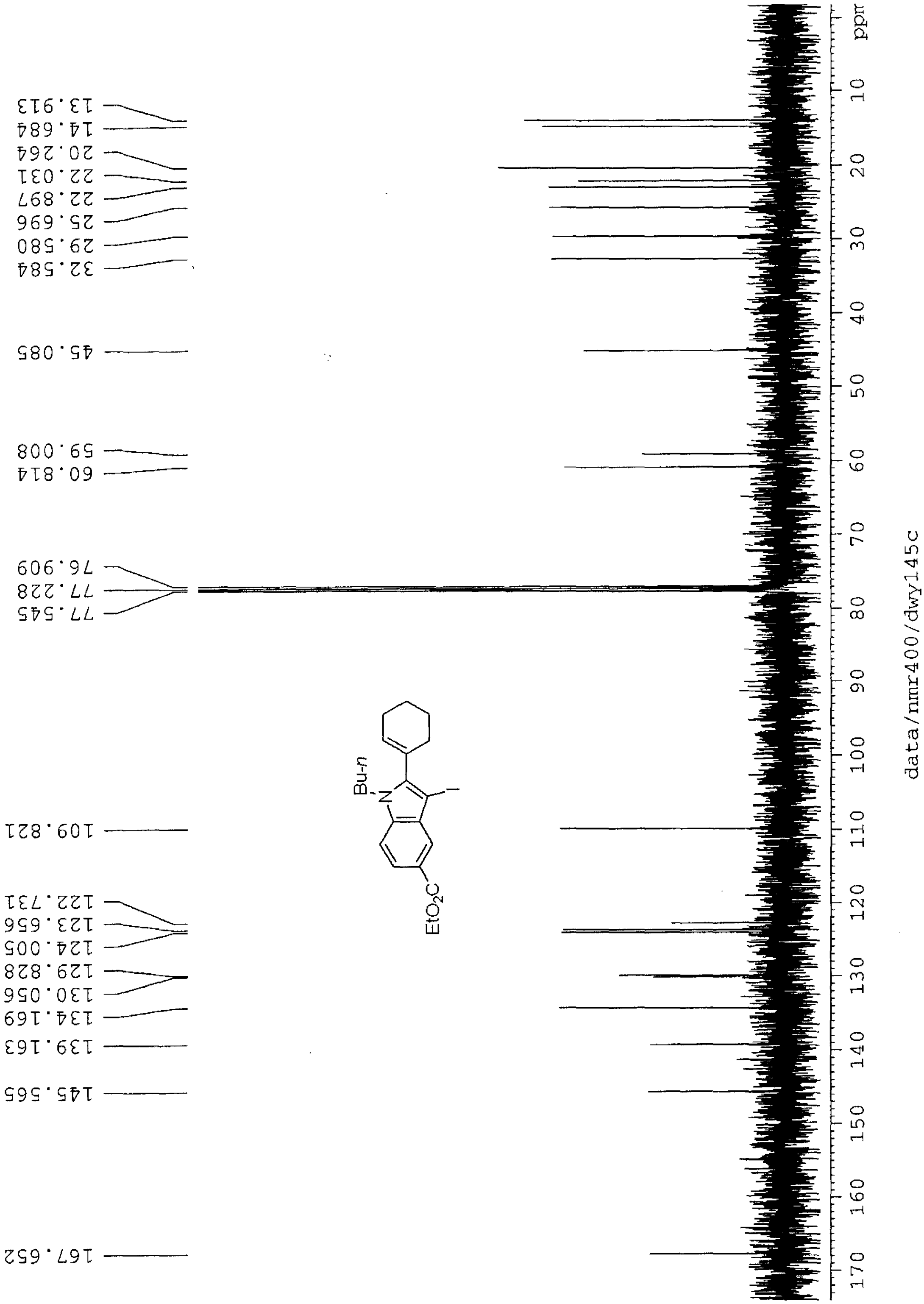
data/nmr400/dwy150

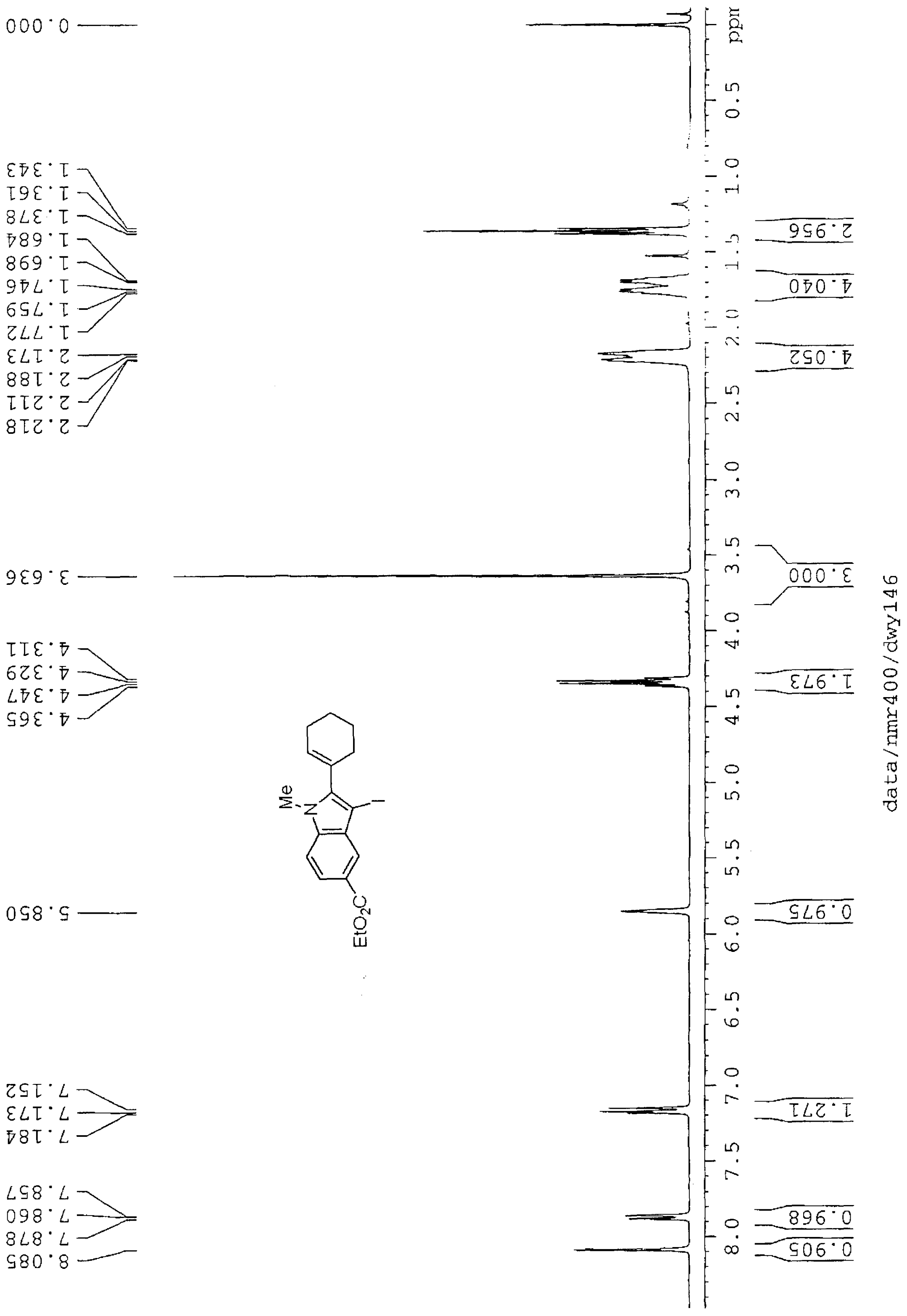

13.997
14.272
14.707
20.452
22.776
27.414
29.368
29.648
31.726
32.714
44.656
59.761
60.830
76.915
77.233
77.550
109.444
122.726
123.434
123.501
130.040
139.549
143.212
167.702
Bu-n
N
n-C6H13
EtO2C
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
data/nmr400/dwy150c

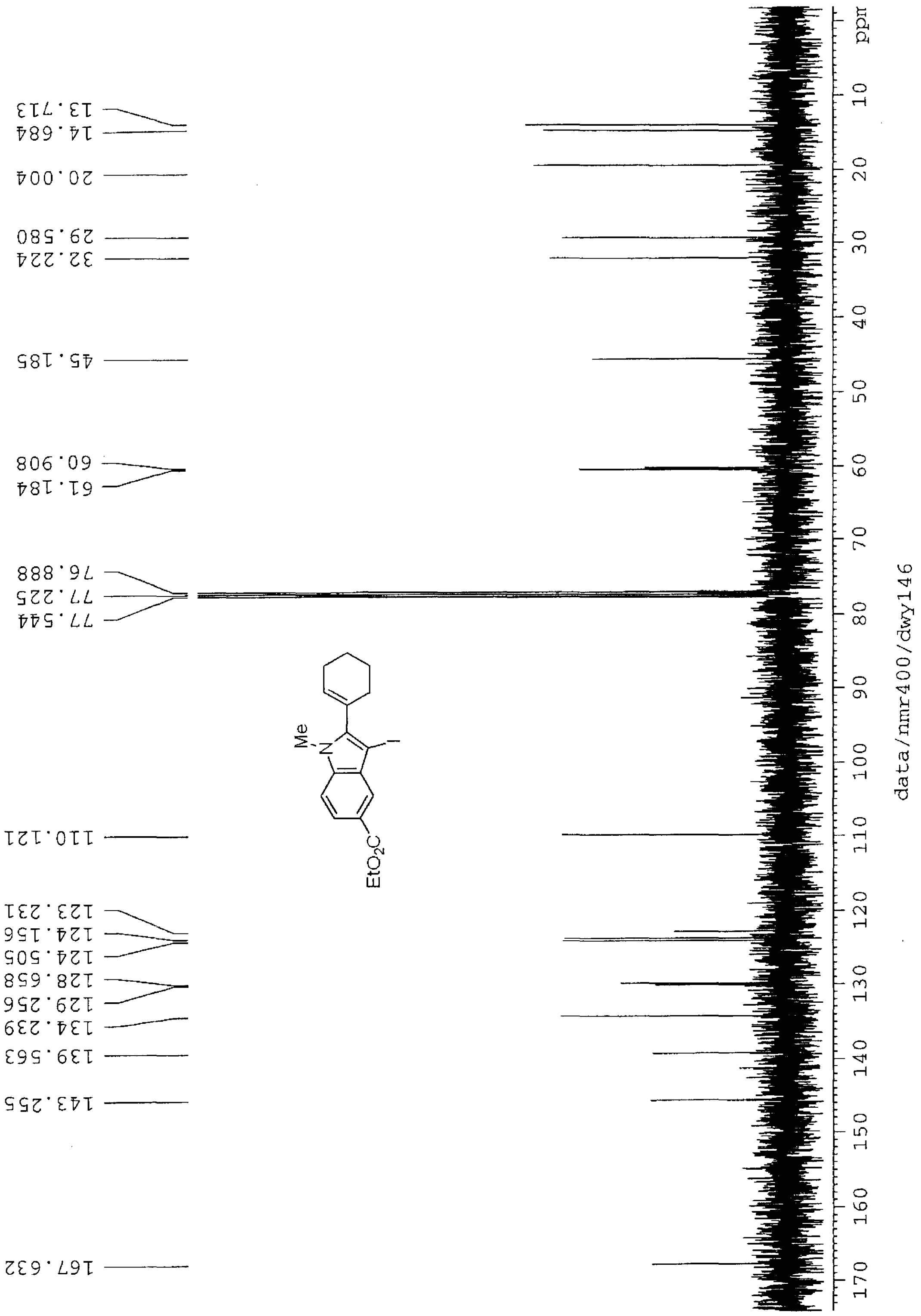

0.000
0.809
0.827
0.843
1.247
1.255
1.264
1.341
1.359
1.376
1.510
1.528
1.548
2.760
2.780
2.799
3.695
4.310
4.328
4.346
4.363
7.141
7.163
7.185
7.837
7.859
8.047
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
3.058
4.104
5.100
2.282
1.991
2.966
2.000
0.988
0.971
0.902
data/nmr400/dwy151
Me
N
n-C6H13
EtO2C


14.278
14.709
22.791
27.430
29.246
29.382
31.082
31.767
59.475
60.873
76.915
77.232
77.550
109.108
122.835
123.470
123.583
129.888
140.306
143.657
167.722
Me
N
n-C6H13
EtO2C
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy151c


0.000
0.830
0.848
0.866
1.211
1.229
1.248
1.266
1.331
1.349
1.366
1.581
1.605
1.624
1.643
1.661
1.672
1.682
1.738
1.748
2.178
2.191
3.984
4.003
4.022
4.303
4.321
4.339
4.356
5.830
7.164
7.177
7.186
7.829
7.850
8.080
3.000
2.078
2.953
6.159
3.958
2.067
1.958
0.969
1.103
0.950
0.879
ppm
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
data/nmr400/dwy145
Bu-n
N
EtO2C


13.913
14.684
20.264
22.031
22.897
25.696
29.580
32.584
45.085
59.008
60.814
76.909
77.228
77.545
109.821
122.731
123.656
124.005
129.828
130.056
134.169
139.163
145.565
167.652
Bu-n
N
I
EtO2C
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy145c


0.000
1.343
1.361
1.378
1.684
1.698
1.746
1.759
1.772
2.173
2.188
2.211
2.218
3.636
4.311
4.329
4.347
4.365
5.850
7.152
7.173
7.184
7.857
7.860
7.878
8.085
Me
N
EtO2C
2.956
4.040
4.052
3.000
1.973
0.975
1.271
0.968
0.905
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
data/nmr400/dwy146


13.713
14.684
20.004
29.580
32.224
45.185
60.908
61.184
76.888
77.225
77.544
110.121
123.231
124.156
124.505
128.658
129.256
134.239
139.563
143.255
167.632
Me
N
EtO$_2$C
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
data/nmr400/dwy146

ACKNOWLEDGMENTS

I would like to express my sincere gratitude and appreciation to Professor Richard C. Larock. I am indebted to him for his patience, understanding, and financial support.

I would like to thank the past and present member of the Larock group that I have worked with.

I would like to thank my parents and brothers for their encouragements.

I would like to thank my wife Pangao Liao, whose loving support and incredible sacrifices made all this possible.