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Formation of [gamma]-lactams and lactones by radical cyclizations, homolytic aromatic alkylations, and preparation of levoglucosenone and its chiral derivatives

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Formation of γ–lactams and lactones by radical cyclizations, homolytic aromatic alkylations, and preparation of levoglucosenone and its chiral derivatives

by

Chen Wang

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ABSTRACT

Radical cyclization methodology has been explored for the formation of functionalized γ-lactams and γ-lactones in the addition of $PhSO_2Br$, under photolysis, to diene amides, or diene and enyne esters, respectively.

With *N*-allyl acrylamides $CH_2=CH_2C(O)NRCH_2CH=CH_2$, only $C_\alpha \rightarrow C_\beta$ cyclization is observed where $PhSO_2\bullet$ adds only to the acrylic C=C bond and then the adduct radical intramolecularly cyclizes by adding into the allyl C=C bond by a 5-exo mode. This cyclization shows trans selectivity and its chemoselectivity is confirmed by competition experiments: the acrylic C=C bond is about 10 times as reactive as the allyl C=C bond towards the sulfonyl radical. The $C_\beta \rightarrow C_\alpha$ cyclization is observed with *N*-allyl 3,3-dimethylacrylamides $Me_2C=CHC(O)NRCH_2CH=CH_2$ which show no cis/trans selectivity. The R groups in both types of amides influence the conformation population of the amides which affects the yields of lactams. Usually, the yield of a lactam is excellent or good when R is an allyl, *tert*-butyl, benzyl, or methyl group, but low or zero when R is a phenyl group or hydrogen atom.

The formation of γ-lactones in the addition of $PhSO_2Br$ to allyl acrylates $CH_2=CHC(O)OCR^1R^2CH=CH_2$ can be observed with trans selectivity when R^1 and R^2 are alkyl groups. The introduction of trace amounts of pyridine into the reactions can inhibit the acid-catalyzed hydrolysis and dehydration of the corresponding esters and therefore increase the yields of lactones. The gem-dialkyl effect has also been explored for the formation of lactones from propargyl acrylates and allyl propiolates. Reactions of β-substituted acrylates and propiolates yield lactones with different functionality.

Homolytic base-promoted aromatic alkylations can be observed with alkyl halides, $(Bu_3Sn)_2$, and DABCO in C_6H_6 at 60 °C. These results suggest that base-promoted homolytic aromatic substitutions may be a rather general process for aromatic compounds with electron-withdrawing substituents. Alkylations by alkyl halides have a much shorter kinetic chain

length than those involving alkylmercury halides and usually need a longer reaction time. Yields vary from low to high depending on the substrates and are much higher if recovered starting benzene derivatives are taken into account. Usually the reactivity and initial kinetic chain length decrease from 1,2- to 1,3- to 1,4- disubstituted benzenes.

A convenient procedure for the preparation of levoglucosenone from cellulose has been investigated. Cellulose and H_3PO_4 are added to a vegetable oil, such as soybean oil, and the mixture is heated to 270-310 °C under reduced pressure (20-30 mm Hg); within seconds levoglucosenone, water, and charcoal begin to form, and the water and the levoglucosenone are distilled from the mixture and condensed. Changes in the kind of vegetable oil and other aspects of the procedure have been explored. The yield of levoglucosenone is in the range of 5-10 wt % depending on the vegetable oil and heating rate, and its purity was *ca* 70 wt % . Preparation of several chiral derivatives of levoglucosenone have been investigated.

LIST OF ABBREVIATIONS

AIBN	2,2'-azobisisobutyronitrile
Bn	benzyl
BPO	benzoyl peroxide
Bu	butyl
calcd	calculated
CIMS	chemical ionization mass spectrum
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-diazabicyyclo[5.4.0]undec-7-ene
DEAD	diethyl azodicarboxylate
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
DTBN	di-tert-butyl nitroxide
EIMS	electron ionization mass spectrum
Et	ethyl
GC	gas chromatography
HMBC	heteroatom muitiple bond correlation
HREIMS	high resolution EIMS
i	*iso*
IR	infra-red
KCL	kinetic chain length
mCPBA	3-chloroperoxybenzoic acid
Me	methyl
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance

NOE	nuclear Overhauser effect
NOESY	NOE correlation spectroscopy
Ph	phenyl
Pr	propyl
r.t.	room temperature
t	*tertiary*
THF	tetrahydrofurane
TLC	thin-layer chromatography
Tol	ortho-methylphenyl
wt	weight

GENERAL INTRODUCTION

Radical cyclization methodology has proved to be a powerful tool for the synthesis of cyclic compounds. Radical cyclization involving molecular chains containing heteroatoms can produce lactams, lactones, or other heterocyclic compounds which are very useful both in organic synthesis and medical applications. However, a heteroatom and/or carbonyl group substituted linkage is not as flexible as an all-carbon chain linkage, and the corresponding molecule usually populates a conformation which disfavors a cyclization process, and therefore yields of heterocyclic compounds are often low. The reactions need to be conducted in very low concentration or high temperatures, and the functional groups which can facilitate further structural modification are often lost.

The use of diene or enyne amides or esters as precursors to functionalized lactams and lactones respectively is a promising route. We investigated the reaction of $PhSO_2Br$ and *N*-allyl acrylamides, allyl acrylates, and other dienes and enynes. The conformational control is achieved by the third substituted group on the amide N atom for amides, or gem-dialkyl groups for esters, so that the molecules populate a conformer which favors cyclization and thus higher yields of heterocyclic compounds can be obtained.

The alkylation of aromatic compounds by the Friedel-Crafts reaction is well known. Usually, this methodology works readily for electron-rich aromatic compounds, not electron-poor ones. Homolytic alkylations of aromatic compounds were only thought of as being of theoretical interest because of the low yields of products. However, by simply introducing a base to convert the adduct radical to a radical anion, homolytic alkylations give much higher yields of alkylated aromatic compounds, specifically for electron-poor aromatic compounds.

Levoglucosenone is a very versatile chiral chemical in organic synthesis. A very economical way to prepare this compound is the vacuum pyrolysis of preacidified cellulose powder. Due to the unavoidable heat and mass transfer problems, the yield of

levoglucosenone obtained by this method is in the range of 2-5%, and even lower when the reaction is scaled up to hundreds of grams. The use of a vegetable oil in the pyrolysis of cellulose is a creative idea because the vegetable oil can serve as a medium facilitating heat and mass transfer. This new procedure gives a higher yield of levoglucosenone (5-10%) in good purity (70 wt %). Optimization of this new procedure and preparation of potentially valuable chiral derivatives of levoglucosenone have been investigated.

Dissertation Organization

This thesis has four chapters. Chapters I and II focus on the formation by radical cyclizations of functionalized lactams and lactones, respectively. Chapter III discusses the homolytic alkylation of aromatic compounds by alkyl halides. Chapter IV describes the preparation of levoglucosenone and its chiral derivatives. All chapters are written in the style of the Journal of Organic Chemistry, which includes introduction, results and discussion, conclusions, experimental section, references, and an appendix. The first three chapters contain published and unpublished material. The unpublished studies are the addition of $BrCH(CN)_2$ to amides (Chapter 1), radical cyclizations initiated by $CH_3C(O)SH$, $BrCH(CN)_2$, and *t*-BuHgCl (Chapter II), and the reactions of diacetylbenzenes (Chapter III). This unpublished material is insufficient to be written as a separate chapter, and the significance of each component can be well understood within the context of the chapter it is put in. Compared to the corresponding published papers, each of these three chapters has an extended introduction. General conclusions of the four chapters are also provided.

CHAPTER I. CHEMOSELECTIVE LACTAM FORMATION IN THE ADDITION OF BENZENESULFONYL BROMIDE TO *N*-ALLYL ACRYLAMIDES AND *N*-ALLYL 3,3-DIMETHYLACRYLAMIDES

A paper, portions of which were published on the Journal of Organic Chemistry*

Chen Wang and Glen A. Russell

Introduction

The γ-lactam skeleton is present in a wide variety of molecules of importance in medicine and agriculture.[1] Also, functionalized lactams are versatile intermediates in the synthesis of pyrrolidines,[2] γ-amino acids,[3] and other bioactive natural products.[4] Synthesis of functionalized lactams has been reported over a long period of time. Although the γ-lactam skeleton can be constructed through formation of an acyl-*N* bond,[5] this methodology seems to be of less interest because it does not introduce new functional groups into the final lactams and its stereoselectivity is usually poor. In recent years, cyclizations involving formation of the C_α-C_β bond have received attention. Pd-catalysed cyclization[6] and radical cyclization[7] are good methods for construction of the γ-lactam skeleton through the formation of the C_α-C_β bond, and examples of these are shown in Scheme 1.

Among the radical cyclization examples, the α-carbamoyl radical, generated from the corresponding halide[7a,b], mercury halide[7c], or other precursor under thermolysis, photolysis, or mediation of Cu^{+1}, Ni^0, Fe^0, Mn^{3+}, et al., intramolecularly adds to another C=C bond in a 5-exo or 5-endo mode.[7d-g] This kind of cyclization is defined as $C_\alpha \rightarrow C_\beta$ radical cyclization in this paper (Scheme 2, for simplicity only exo-cyclization is depicted). Even the Pd-catalyzed cyclization proceeds from C_α to C_β. Surprisingly, we have not found any report of $C_\beta \rightarrow C_\alpha$

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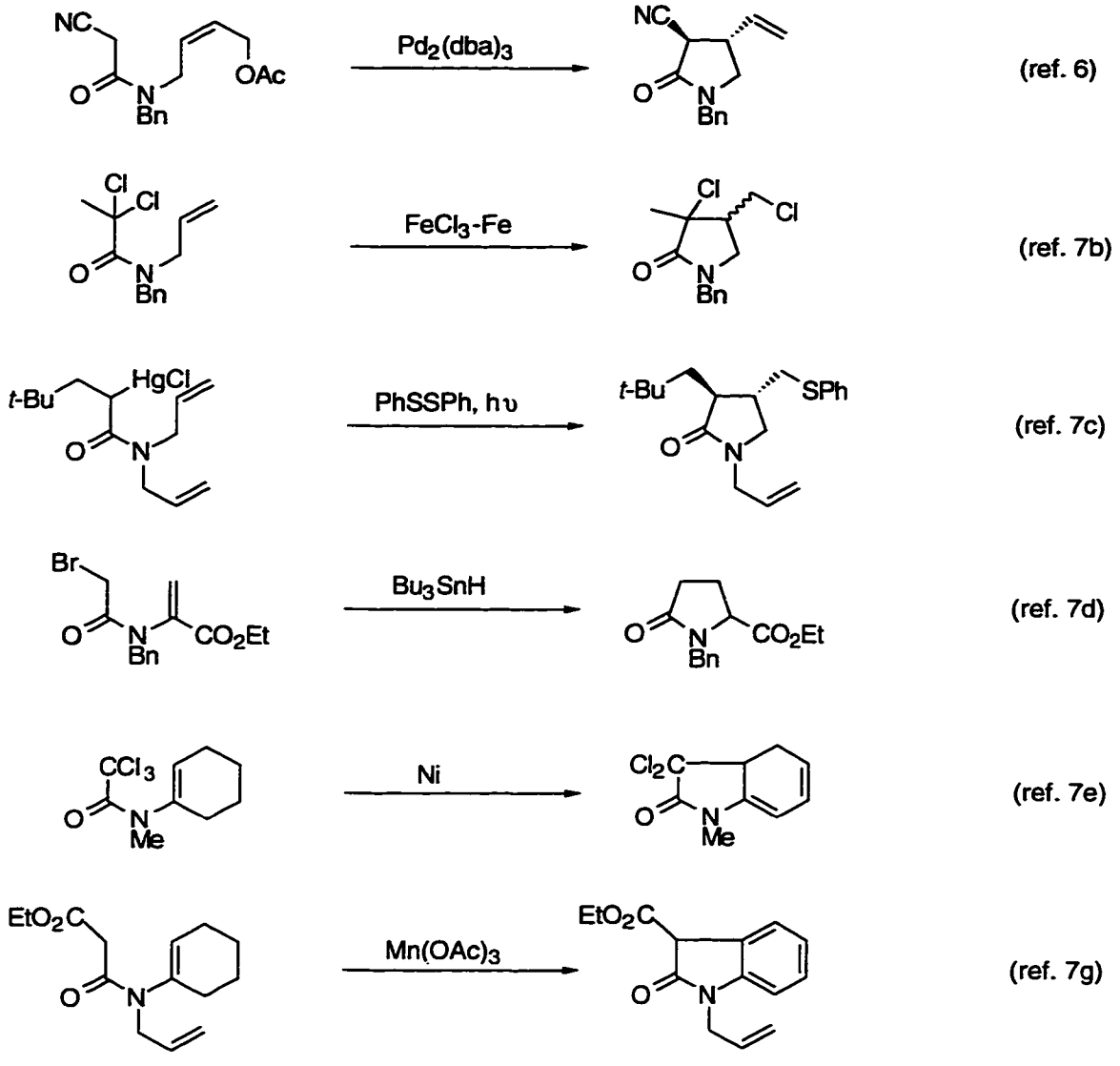
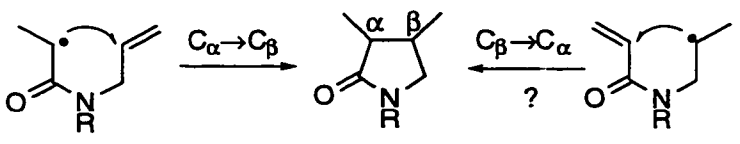
cyclization, which, if possible, would provide a new approach to the γ-lactam skeleton with different functionality.

Scheme 1

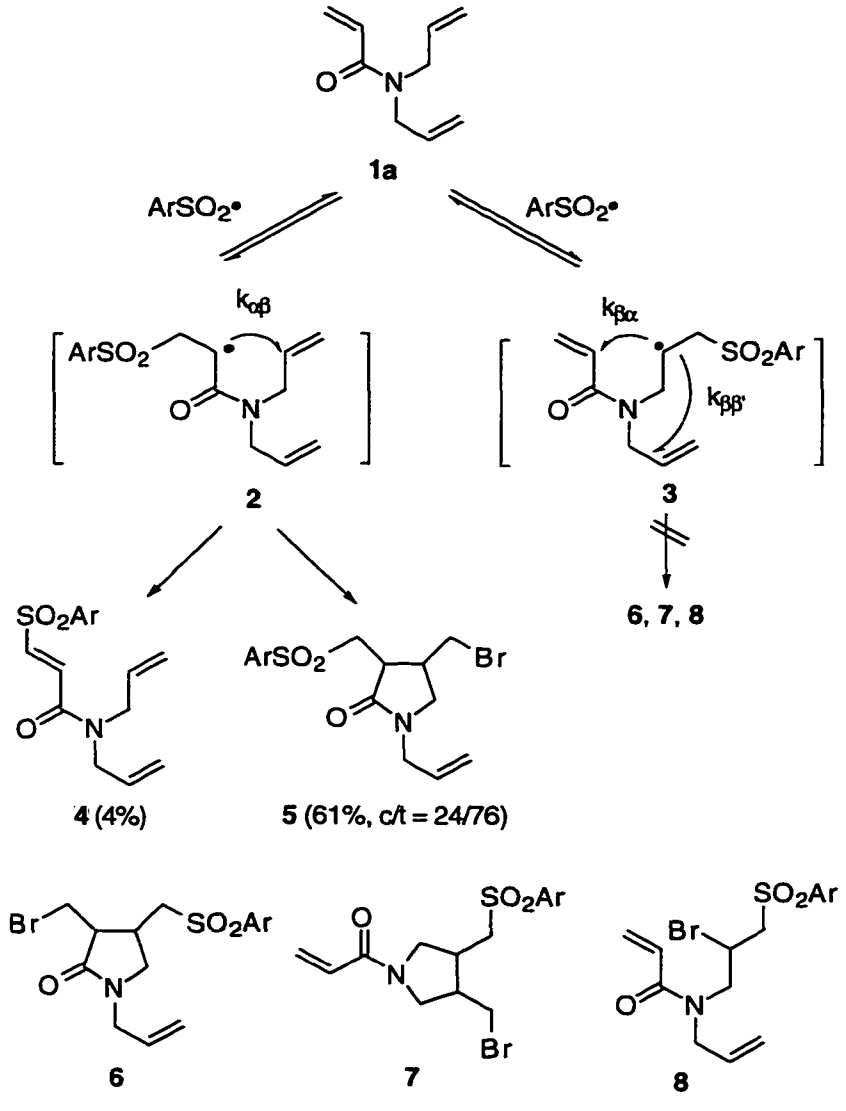


Scheme 2



In fact, $C_\beta \rightarrow C_\alpha$ radical cyclization has been attempted by M. P. Bertrand and his colleagues (Scheme 3).[8] They reported that the reaction of toluenesulfonyl bromide ($TolSO_2Br$) with amide **1a** yielded only sulfones **4** and **5**, which originate from radical adduct **2**. Compounds **6**, **7**, and **8**, originating from intermediate **3**, were not found. The absence of products **6**, **7**, and **8** contrasts with what is predicted based on polar effects, because the electrophilic radical $TolSO_2^\bullet$, generated by photolysis of $TolSO_2Br$, would be expected to add preferentially to the nucleophilic allyl C=C bond, rather than the electrophilic acrylic C=C bond of **1a**. Bertrand explained this observation by postulating that the initial additions of $TolSO_2^\bullet$

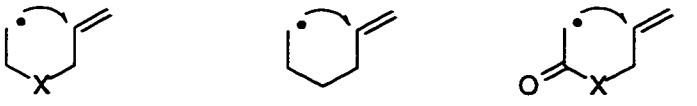
Scheme 3



to the acrylic and allyl C=C bonds are reversible, and the cyclization rate constant $k_{\alpha\beta}$ is significantly greater than $k_{\beta\alpha}$ and $k_{\beta\beta\cdot}$ (Scheme 3). Since **3** only undergoes slow cyclization processes ($k_{\beta\alpha}$ and $k_{\beta\beta\cdot}$), it can regenerate **1a**, which in turn produces intermediate **2** which yields product **5** due to the rapid $k_{\alpha\beta}$ cyclization process, and a small amount of uncyclized product **4**.[8a]

Though plausible, Bertrand's explanation has yet to be confirmed. While reversible addition of the sulfonyl radical to C=C bonds has been observed in many cases,[9] there is no report confirming Bertrand's postulate as to the relative rates of $k_{\alpha\beta}$ and $k_{\beta\alpha}$. On the other hand, based on the heteroatom (N atom)-accelerating and carbonyl group-decelerating effects on the rate of radical 5-exo cyclizations,[10] we know the following sequence of rates of radical cyclizations which spreads over a range of 100 (Scheme 4), and believe that at least $k_{\alpha\beta}$ is unlikely to be greater than $k_{\beta\beta\cdot}$. Also, Bertrand's explanation could not account for the fact that acrylic C=C bond mono adduct **4** was the only uncyclized product,[8a] and allyl C=C bond mono adduct **8** was not observed. As we see, even if **3** fails to cyclize ($k_{\beta\alpha}$ and $k_{\beta\beta\cdot}$) to yield **6** and/or **7**, it still can be intercepted by the bromine transfer step from $TolSO_2Br$ to yield **8**.

Scheme 4



fast
X = O, NSO_2Ar

intermediate

slow
X = O, NR

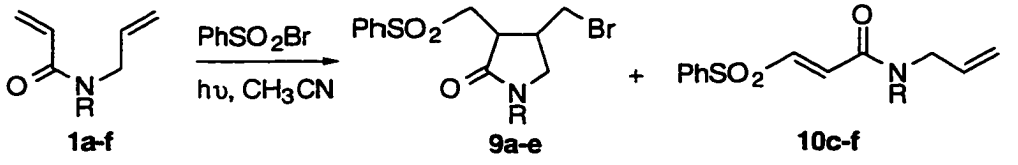
Bertrand's reaction successfully incorporates sulfonyl and halide groups into diene amides to form lactams chemoselectively in one step. This is different from those reports shown in Scheme 1 where the transferred functional groups, such as halides, sulfides, must be first incorporated into the substrates.

Thus we set out to try to understand the chemoselectivity observed in Scheme 3 and to try to realize $C_\beta \rightarrow C_\alpha$ radical cyclizations. Since the sulfonyl group is a very versatile functional group in organic synthesis[11] and $PhSO_2\bullet$ is a stronger electrophilic radical than $TolSO_2\bullet$, we decided to use $PhSO_2Br$ to investigate the addition and cyclization reactions with *N*-allylacrylamides, and *N*-allyl-3,3-dimethylacrylamides where the $C_\beta \rightarrow C_\alpha$ cyclizations can be forced by steric effects.

Results and Discussion

1. Addition of $PhSO_2Br$ to *N*-Allyl Acrylamides

Table 1 summarizes the reactions of $PhSO_2Br$ and *N*-allylacrylamides (eq 1) under sunlamp irradiation in acetonitrile. Typically, 0.20 M of an amide along with 1.1 equiv of $PhSO_2Br$ in acetonitrile was irritiated at room temperature. The uncyclized acryl C=C bond adducts could not be isolated in a pure form due to their partial dehydrobromination on TLC plate, so they were treated with 2 equiv of triethylamine at room temperature for about 30 min, and then the dehydrobrominated products **10c-f** were isolated by another TLC separation.



1a-f **9a-e** **10c-f** (1)

The *cis*/*trans* configurations of the products **9a-e** were determined by 2D NOE; there is NOE coupling between $PhSO_2CH_2$ and $BrCH_2$ for the *cis* products but no NOE coupling between them for the *trans* products. This method of assigning the stereochemistry of the products gives the same results as Bertrand's method, where the ^{13}C NMR chemical shift of the *cis* $PhSO_2CH_2$ is about 63 ppm, while that of the *trans* isomer is about 57 ppm. NOE coupling between the two methine H's can be observed in both *cis* and *trans* products, and therefore can not be used as a criterion for the stereo configuration assignment. Another possible structure with the groups

$PhSO_2$ and Br reversed in **9** is excluded by H-H COSY, H-C COSY, and HMBC (Heteroatom Multiple Bonds Correlation) 2D spectroscopy. In the HMBC spectrum (Figure 1), one methine H correlates to C=O (δ ~ 171 ppm) and $PhSO_2CH_2$ (δ ~ 63 or 57 ppm), while the other methine H correlates to CH_2NR (δ ~ 50 ppm) and $BrCH_2$ (δ ~ 35 ppm). Overall, $C_\alpha \rightarrow C_\beta$ cyclization shows trans selectivity.

The results presented in Table 1 are consistent with Bertrand's report: only $C_\alpha \rightarrow C_\beta$ cyclized products could be observed. The electrophilicity of the sulfonyl radicals does not promote $C_\beta \rightarrow C_\alpha$ cyclizations (Scheme 2). Also the trend in yields of products **9** is consistent

Table 1. Reactions of $PhSO_2Br$ and *N*-Allyl Acrylamides under Sunlamp Irradiation in Acetonitrile

amide, R =	products (yield % [a])	
1a, $CH_2CH=CH_2$	**9a** (83, c/t=1/6.1)	
1b, CMe_3	**9b** (93, c/t=1/5.0)	
1c, CH_2Ph	**9c** (46, c/t=1/4.6)	**10c** (15)
1d, Me	**9d** (50, c/t=1/2.5)	**10d** (41)
1e, Ph	**9e** (25, trans only)	**10e** (20)
1f, H		**10f** (46)

[a] Isolated yields based on the starting amides.

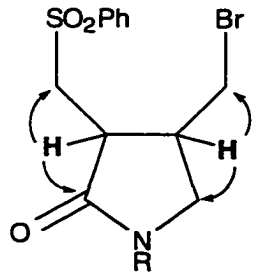


Figure 1. HMBC of compound **9**.

with the report that the *cis-trans* rotamer population of amide **1** is controlled by its second substituent R (Scheme 5 and Table 2). [8a, 12] Amide **1** is about 100% *cis*-populated when R is *tert*-Bu, and 100% *trans*-populated when R is Ph or H. While the cis rotamer favors the cyclization, the *trans* rotamer disfavors this process. The rotation barrier of C(O)-N bond is about 16-22 kcal/mol,[8a] but it may be lower in the adduct radicals.

Scheme 5

Table 2. Conformational Population of Amides 1a-f in $CHCl_3$ at r.t.

amide, R =	*cis* (%)	*trans* (%)
1a, $-CH_2CH=CH_2$	50	50
1b, -*t*-Bu	100	0
1c, $-CH_2Ph$	60	40
1d, $-CH_3$	40	60
1e, -Ph	0	100
1f, -H	0	100

It is interesting to find that while the uncyclized products **10c-f** are commonly presented in Table 1, no allyl C=C bond adduct (like **8** shown in Scheme 2) is observed. The result from **1f** is especially striking: uncyclized product **10f** is the only product isolated. This observation shows that the chemoselectivity here is not related to any cyclization process and attack on the acrylic C=C bond is strongly preferred to attack on the allyl C=C bond.

2. Addition of $PhSO_2Br$ to *N*-Allyl 3,3-Dimethylacrylamides

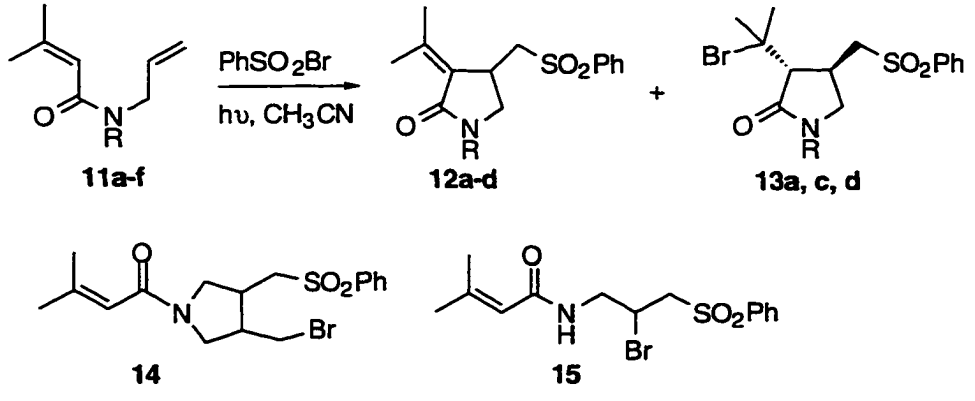
We have found that $C_\beta \rightarrow C_\alpha$ cyclizations can be observed in the reactions of $PhSO_2Br$ and *N*-allyl-3,3-dimethylacrylamides where the chemoselectivity is forced by steric effects (Table 3 and eq 2).

For the complete reactions of **11c** and **11d**, addition of 20 mol % $Bu_3SnSnBu_3$ was necessary. $C_\beta \rightarrow C_{\beta'}$ cyclized product **14** was observed from **11a**. Also, the allyl C=C bond

Table 3. Reactions of $PhSO_2Br$ and *N*-Allyl 3,3-Dimethylacrylamides under Sunlamp Irradiation in Acetonitrile

Amide, R =	Products (yield %[a])		
11a, $CH_2CH{=}CH_2$	**12a** (34)[b]	**13a** (13)[b]	**14** (37, c/t = 2 or 0.5)[c]
11b, CMe_3	**12b** (50)	**11f** (21)	
11c, CH_2Ph	**12c** (62)	**13c** (37)	
11d, Me	**12d** (37)	**13d** (15)	
11e, Ph	no reaction		
11f, H			**15** (72)

[a] Isolated yields based on the starting amides. [b] Lactams **12a** and **13a**, **12d** and **13d** are inseparable by TLC; their yields were calculated from the ^1H NMR ratio of the mixtures. [c] The isomer ratio of **14** was determined by GC-MS without assignment.



(2)

adduct **15** was also observed from **11f** and **11f** is an unexpected product in the reaction of amide **11b**. Under the same conditions, **11e** does not react with $PhSO_2Br$. The trans configuration of lactam **13** was determined by the observed NOE coupling between $PhSO_2CH_2CH$ and $BrC(CH_3)_2$, and between $CHCBrMe_2$ and $PhSO_2CH_2$. The stereoselectivity of the $C_\beta \rightarrow C_\alpha$ cyclizations cannot be measured, because the *cis* products and maybe some *trans* products, dehydrobrominated readily to yield **12** during TLC separation.

3. Competition Experiments

Since absolute rate constants for the addition of a sulfonyl radical to C=C bonds are not available from the literature, the relative reactivity of the acryl C=C bond vs. the allyl C=C bond towards PhSO2• was quantified by competition experiments using eqs 3 - 5.[13]

Eq 5 holds true only if the radical addition step is the rate-determing step and the only step involving M_1 and M_2. Though reversibility of the radical addition step may complicate the relative reactivity measurement, eq 5 has been shown to be reliable for the addition of TolSO2I to C=C bonds because of the fast iodine transfer step following the addition step.[13a] It was estimated that the bromine transfer rate from $PhSO_2Br$ is about one-third of the iodine transfer rate from $PhSO_2I$.[14]

$$PhSO_2^{\bullet} + \begin{cases} M_1 \xrightarrow{k_1} \text{Radical adduct 1} \\ M_2 \xrightarrow{k_2} \text{Radical adduct 2} \end{cases} \quad (3)$$

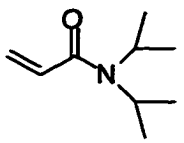
$$\alpha\,(M_1/M_2) = \{\log[M_1]_0 - \log[M_1]_t\} / \{\log[M_2]_0 - \log[M_2]_t\} \quad (4)$$

$$k_1/k_2 = \alpha\,(M_1/M_2) \quad (5)$$

$[M_1]_0$, $[M_2]_0$ are the initial concentration of olefins M_1, M_2.

$[M_1]_t$, $[M_2]_t$ are the concentration of olefins M_1, M_2 at time t.

Several reactions were set up in NMR tubes with CD_3CN as the solvent and $(Me_3Si)_2O$ as the internal standard, *N,N*-diisopropylacrylamide (**16**), *N*-allyl-*N*-benzyl acetamide (**17**), and *N,N*-diallylacetamide (**18**) were chosen as the substrates for the measurement of α (**16/17**) and α (**16/18**) (Table 4 and Figure 2).



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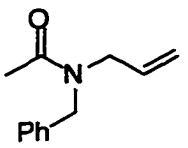

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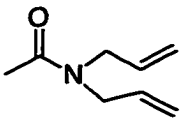

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Table 4. Measurement of α (16/17) and α (16/18)

		reaction time (min)			
entry[a]	α (M_1/M_2)	15	30	45	60
1	α (**16/17**)	9.5	10.0	8.3	6.8
2	α (**16/17**)	10.6	11.0	11.3	8.3
3	α (**16/18**)	2.3	2.2	2.0	1.7

[a] One run for each entry. Initial molar ratio for entries (by ^{1}H NMR): (1) **16** : **17** : $PhSO_2Br$ = 1.00 : 1.12 : 0.90. (2) **16** : **17** : $PhSO_2Br$ = 1.00 : 1.21 : 1.27. (3) **16** : **18** : $PhSO_2Br$ = 1.00 : 1.16 : 1.70. The concentration of amide **16** was 0.20 M initially for all runs.

From the data in Table 3 and Figure 2, we find that α (**16/17**) is about 10, significantly larger than expected. On the other hand, α (**16/18**) is only about 2.3. Since there are two allyl C=C bonds in **18**, the acrylic C=C bond of **16** is about 4.6 times as reactive as the each allyl C=C bond of **18** towards the sulfonyl radical. The allyl C=C bond of **18** is more reactive than that of **17** may be because the structures of these two amides are different, and the reversibility of the addition of the sulfonyl radical to the allyl C=C bond of **18** is inhibited by the $C_\beta \rightarrow C_\beta$· cyclization process. The reaction of **18** gives $C_\beta \rightarrow C_\beta$· cyclized product **19** (Scheme 6). Our experiments also showed that α was nearly constant within short reaction times, and not affected by either the ratios of the components, or the conversion of the reaction, showing the validity of the relative reactivity measurements. So, we believe that in amide **1** the acrylic C=C bond is more reactive than the allyl C=C bond towards $PhSO_2$•.

The higher reactivity of the acrylic C=C bond over the allyl C=C bond may be explained by stabilization effects due to delocalization of the α-carbamoyl radical over the carbonyl group. However, it is not clear why the stabilization effects overwhelm the polar effects. While the relative reactivity of olefins of a homologous series towards sulfonyl radical is predictable,[13] no general statement could be found to predict the relative reactivity of different olefins like acrylic and allyl C=C bonds.

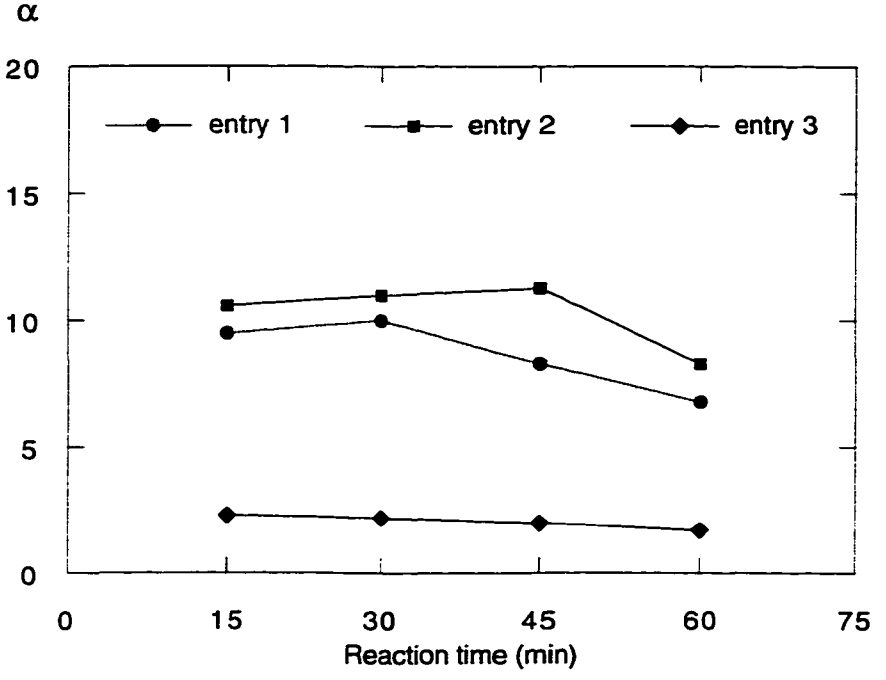
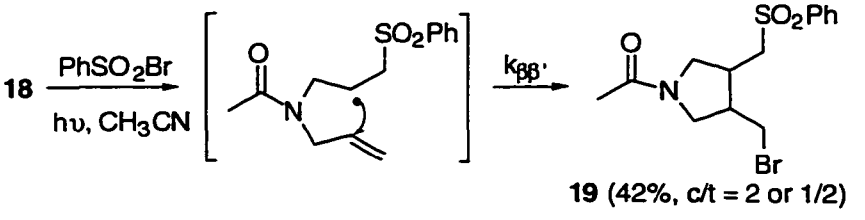


Figure 2. Relative reactivities of **16/17** and **16/18**.

Scheme 6

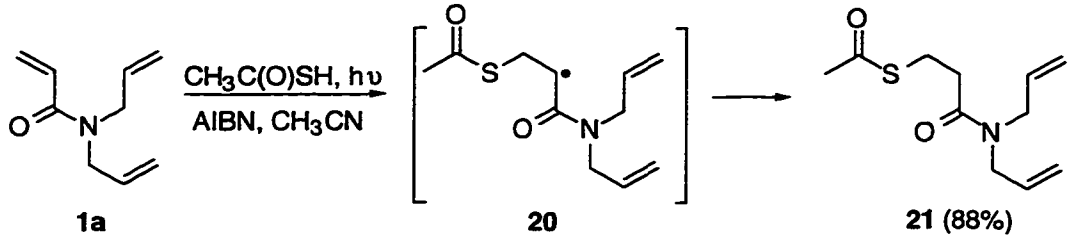


As a comparison, an acrylic C=C bond of alkyl acrylates was reported as reactive as an allyl C=C bond of alkyl allyl ethers towards a sulfonyl radical.[13c] We used similar competition experiments to find out that the acrylic C=C bond of **16** is 3 times as reactive as that of ethyl acrylate which is only 1.6 times as reactive as the allyl C=C bond of allyl acetate. The reason for the reactivity difference between acrylamides and acrylates is not clear, and may be partially explained by the N atom of acrylamides being less electronegative than the O atom of acrylates.

4. Additions and Cyclizations Initiated by Other Electrophilic Radicals

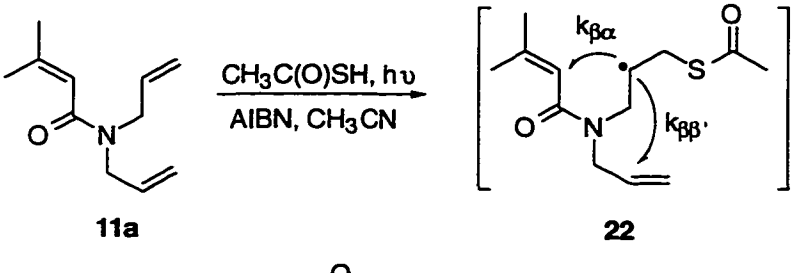
Some other electrophilic radicals, such as $CH_3C(O)S\bullet$, $Cl_3C\bullet$ and $(NC)_2CH\bullet$ were also tested in our work. The reactions which involve the addition of $CH_3C(O)SH$ to amides **1a** and **11a** are very informative (Schemes 7 and 8).

Scheme 7

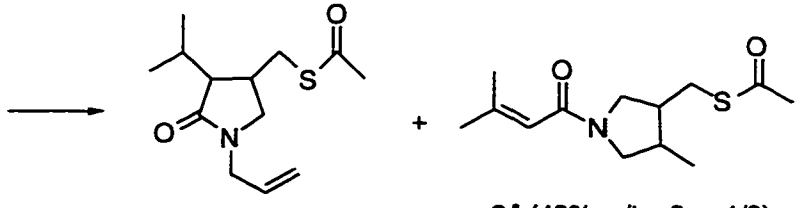


1a **20** **21** (88%)

Scheme 8



11a **22**



23 (41%, c/t = 1.5) **24** (43%, c/t = 2 or 1/2)

No cyclized product was observed for amide **1a** in Scheme 7, which means the rate of $C_\beta \rightarrow C_\alpha$ cyclization of **1a** (or adduct radical **20**), is slower (about one order of magnitude) than that of the H-transfer from $CH_3C(O)SH$ to **20**. On the other hand, the high yield of cyclized products observed for **11a** in Scheme 7 suggests that the rates of $C_\beta \rightarrow C_\alpha$ and $C_\beta \rightarrow C_{\beta'}$ cyclizations of **11a** (or adduct radical **22**) are faster (about one order of magnitude) than that of the H-transfer from $CH_3C(O)SH$ to intermediate **22**. An analogous observation that the rate of $C_\beta \rightarrow C_{\beta'}$ cyclization is faster than that of H-transfer from $CH_3C(O)SH$ was also found in Padwa's report (eq 6).[15]

(6)

The rate of the H-transfer from $CH_3C(O)SH$ to **22** should be about same as that to **20**, or the former one might be slightly faster because intermediate **20** is more stable than intermediate **22**. From the data in Table 3, the ratio of yields of $k_{\beta\alpha}$ cyclized products (**12a** and **13a**) to $k_{\beta\beta'}$ cyclized produts (**14**) is about 1.27. From the data in Scheme 8, this ratio is about 0.95. This shows that $k_{\beta\beta'}$ of **11a**, or more accurately the $k_{\beta\beta'}$ of the allyl C=C adduct radical of **11a**, is about same as that of $k_{\beta\alpha}$. It is reasonable to suppose $k_{\beta\beta'}$ (**11a**) would be about same as $k_{\beta\beta'}$ (**1a**). So, we can have the following rate sequence (Scheme 9):

Scheme 9

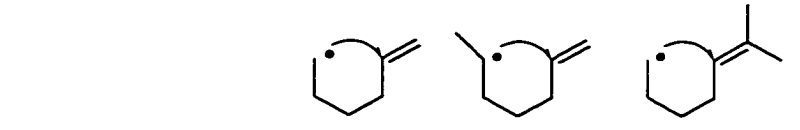
$k_{\beta\alpha}$ (**11a**) ~ $k_{\beta\beta'}$ (**11a**) ~ $k_{\beta\beta'}$ (**1a**) >> H-transfer to **22** ~ H-transfer to **20** >> $k_{\alpha\beta}$ (**1a**)

It is very conservative to say $k_{\beta\beta'}$ (**1a**) is about 100 times greater than $k_{\alpha\beta}$ (**1a**), because the radical cyclization rate has been confirmed to be accelerated by heteroatom (N atom) substitution and decelerated by the presence of a carbonyl group (Scheme 4).[10c,d] Also, the

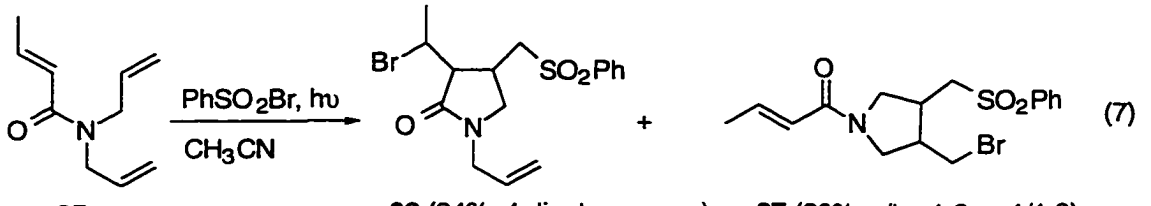
fact that uncyclized acrylic C=C mono adducts (**11**) were observed (Table 1), but no uncyclized allyl C=C mono adduct has been seen (Table 3) except for amide **15**, suggests that the $C_\beta \rightarrow C_\alpha$ and $C_\beta \rightarrow C_{\beta'}$ cyclization rates of amide **11a** are faster than the $C_\alpha \rightarrow C_\beta$ cyclization rates of amide **1a**. No $C_\beta \rightarrow C_{\beta'}$ cyclized product was observed from the reaction of amide **1a** in eq 1 even though $k_{\beta\beta'}$ (**1a**) is greater than $k_{\alpha\beta}$ (**1a**) strongly suggests that Bertrand's assumption is not correct.

Rate constants $k_{\beta\alpha}$ (**1a**) and $k_{\alpha\beta}$ (**1a**) can not be compared directly because no product from the former cyclization process is observed, $k_{\beta\alpha}$ (**1a**) may be different from $k_{\beta\alpha}$ (**11a**). Beckwith reported that the dimethyl groups at the new radical center show little effect on the cyclization rate of 5-hexenyl radicals (Scheme 10).[10d] We tentatively use the reaction of *N,N*-diallylcrotonylamide (**25**) to estimate the effect of one methyl group on the rate of $C_\beta \rightarrow C_\alpha$ cyclization (eq 7), and find that the ratio of yields of products **26/27** is 1.16, not very different from the ratio of yields of (**12a+13a**)/**14** which is 1.27 (Table 3).

Scheme 10



relative cyclization rates 1 1.4 2.4



25 **26** (34%, 4 diastereomers) **27** (30%, c/t = 1.6 or 1/1.6) (7)

However, the estimation from eq 7 does not take into account the effect of the conformational difference between amides **1a** and **11a** on rate of cyclizations. In amide **1a**, the acrylic C=C bond and the C=O bond are conjugated in a planar conformation, while in

11a, they form a dihedral angle of 60° which facilitates radical cyclizations.[16] This effect is difficult to estimate quantitatively. By guess, we postulate that the difference between $k_{\beta\alpha}$ (**1a**) and $k_{\beta\alpha}$ (**11a**) may be within one order of magnitude. As pointed out before, $k_{\beta\alpha}$ (**11a**) is about 2 orders of magnitude greater than $k_{\alpha\beta}$ (**1a**). Therefore we think $k_{\beta\alpha}$ (**1a**) may be greater than, or at least comparable to $k_{\alpha\beta}$ (**1a**).

A significant yield of the *cis* $C_\beta \rightarrow C_\alpha$ cyclized product was obtained from the reaction of amide **11a** (Scheme 8). However, the $C_\alpha \rightarrow C_\beta$ cyclization gave mainly the *trans* product (eq 1). This observation is also consistent with the general assumption that a fast cyclization process has an early transition state which gives *cis*-predominant product, while a slow cyclization process has a late transition state which gives more *trans* product.

One reason favoring Bertrand's comparison of $k_{\alpha\beta}$ (**1a**) and $k_{\beta\alpha}$ (**1a**) may come from the polarized coefficients of LUMO orbitals on C_α and C_β carbons of the acrylic C=C bond. In the LUMO orbital, the coefficient of the C_α of the acrylic C=C bond is much smaller than that of C-2 of the allyl C=C bond.[17] This difference makes the $C_\beta \rightarrow C_\alpha$ exo cyclization more difficult compared to the $C_\alpha \rightarrow C_\beta$ exo cyclization (Figure 3).

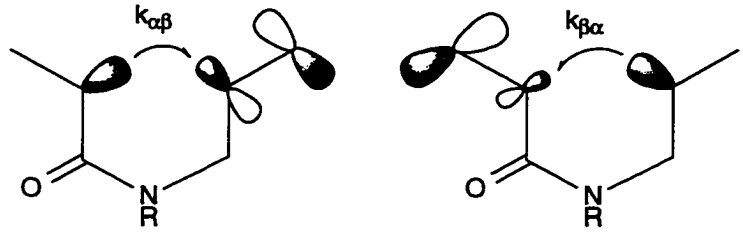


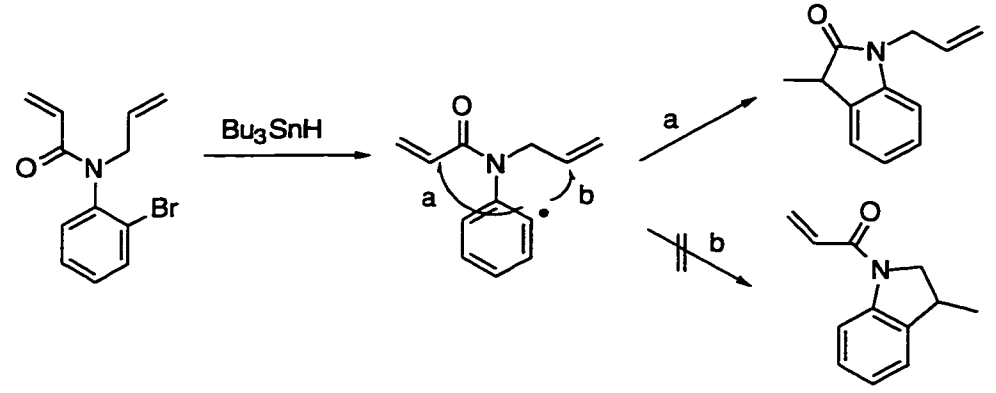
Figure 3. Comparison of LUMO orbitals of acrylic C=C bond and allyl C=C bond.

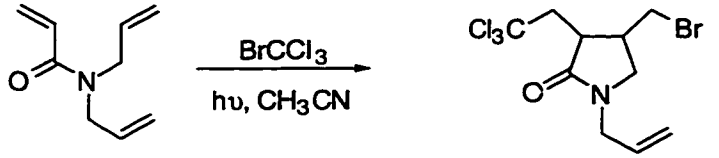
This reminded us of another long-discussed chemoselectivity shown in Scheme 11.[18] Although it is a different radical cyclization, the chemoselectivity here suggests that the coefficients of the LUMO orbitals may not always be a predominant factor. We would still like to know whether the chemoselectivity shown in eq 1 can be reversed by polar effects using

other stronger electrophilic radicals. Eq 8 shows that the strong electrophilic radical $Cl_3C^{\bullet}$ still gives only $C_\alpha \rightarrow C_\beta$ cyclized products with amide **1a**.

Some interesting results came from the $(NC)_2CH^{\bullet}$ radical generated from $BrCH(CN)_2$. As known, $BrCH(CN)_2$ can add to alkenes in a fast exothermic chain process (Scheme 12).[19]

Scheme 11



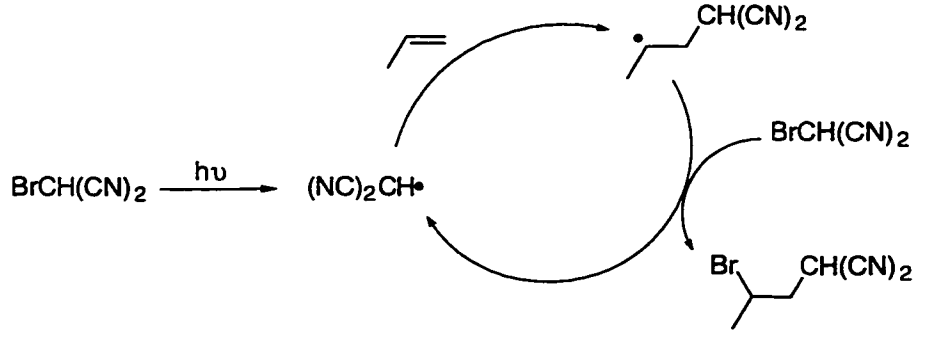


(8)

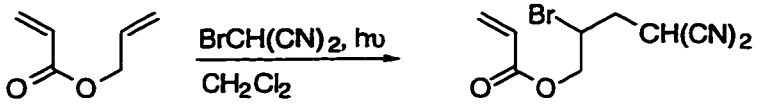
1a

28 (70%, c/t = 1/4)

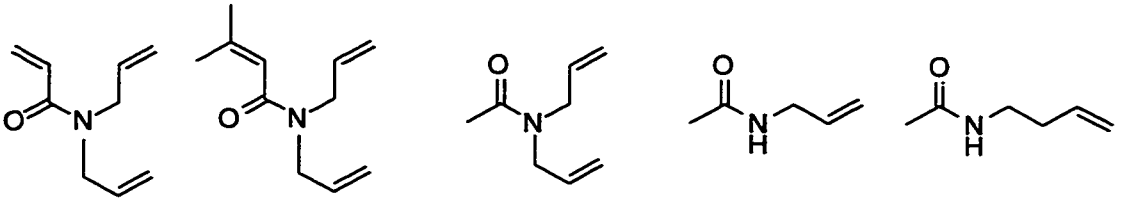
Scheme 12



We have found that $BrCH(CN)_2$ adds to the allyl C=C bond of allyl acrylate with the expected chemoselectivity based on its electrophilicity (eq 9) even though no cyclization was observed. Surprisingly, there is no reaction between $BrCH(CN)_2$ and the following unsaturated amides.

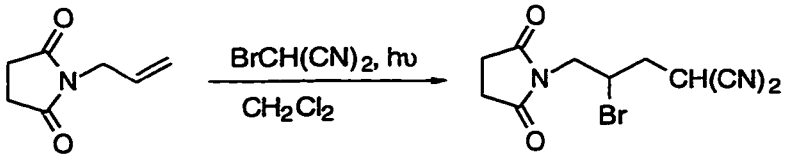


29 (58%) (9)

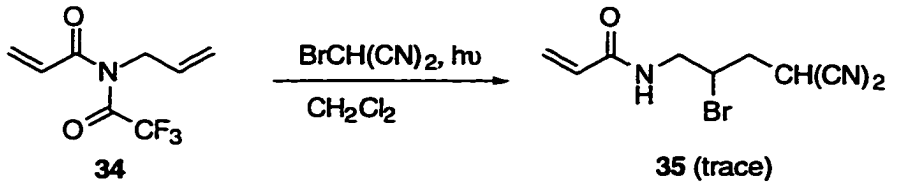


1a **11a** **18** **30** **31**

However, $BrCH(CN)_2$ adds to *N*-allylsuccinimide **32** to yield **33** (eq 10). This result suggests that two electron-withdrawing groups on the amide N may promote the addition of CH(CN)• radical to the allyl C=C bond of *N*-allyl amides. The reason for the lack of reaction with the above amides is probably related to an interaction between the basic amide and the acidic $BrCH(CN)_2$. To confirm our postulation, we studied the reactions of $BrCH(CN)_2$ with amides with two electron-withdrawing groups. The reaction of $BrCH(CN)_2$ with **34** yielded a trace of the expected allyl adduct **35** along with amide **1f** (eq 11). The trifluoroacetyl group of **34** is very labile, and **34** is converted easily to **1f** under the photolysis. The corresponding adduct product also lost trifluoroacetyl group during the TLC separation to yield **35**.

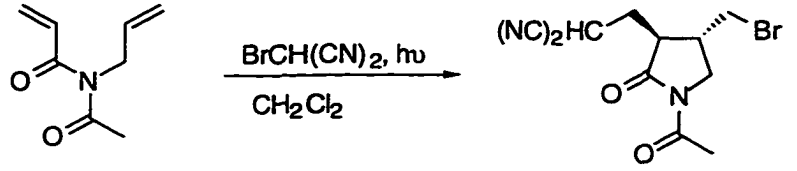


32 **33** (40%) (10)

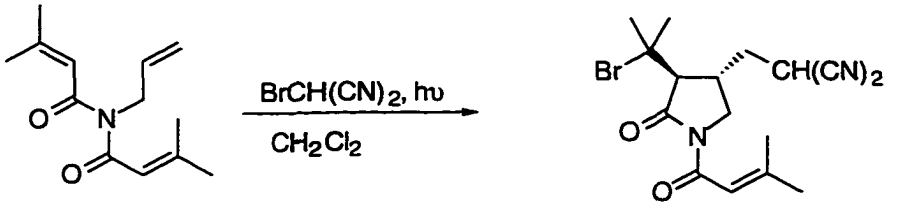


34 **35 (trace)** (11)

From the above results, we expected that the $C_\beta \rightarrow C_\alpha$ cyclization might be observed in the reaction of amide **36**. However, only trans $C_\alpha \rightarrow C_\beta$ cyclized product **37** was isolated (eq 12). The electrophilic dicyanomethane radical still attacks the acrylic C=C bond instead of the allyl C=C bond. Also, the reaction of amide **38** gives the $C_\beta \rightarrow C_\alpha$ cyclized product **39** (eq 13). Overall, it is unlikely that the electrophilicity of the attacking radical itself can shift the chemoselectivity of the addition from an acrylic C=C bond to an allyl C=C bond.



36 **37 (43%)** (12)



38 **39 (30%)** (13)

Conclusions

Chemoselectivity in the radical addition reactions of $PhSO_2Br$ to *N*-allyl acrylamides is due to the higher reactivity of the acrylic C=C bond towards the sulfonyl radical than that of the allyl C=C bond. While the $C_\beta \rightarrow C_\alpha$ cyclization process gives mainly trans product, the $C_\beta \rightarrow C_\alpha$ cyclization which can be observed in the reactions of *N*-allyl 3,3-dimethylacrylamides shows low stereoselectivity.

Experimental Section

General Considerations

NMR spectra were recorded in $CDCl_3$ or as stated otherwise (^1H at 300 or 400 MHz and ^{13}C at 75 or 100 MHz). 2D NMR spectra were obtained with a Bruker DRX400 spectrometer. CI, EIMS (70ev) were obtained with Finnigan 4000 (GC mode) and Kratos MS-50 spectrometers. All mp's were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Most products were isolated by TLC on silica gel with hexanes-ethyl acetate as the eluent. Photostimulated reactions utilized a Sylvania 275 W fluorescent sunlamp and 5-mm NMR tubes or Pyrex reaction vessels at room temperature. Yields were based on the starting acrylamides. $PhSO_2Br$ was prepared according to the literature procedure.[19] Amides **1a-f, 11a-f, 28** were prepared from acid chlorides and corresponding amines according to the literature procedure.[8a]

General Preparative Procedures and Compound Characterization

Benzenesulfonyl Bromide ($PhSO_2Br$) was prepared in two steps from $PhSO_2Cl$ according to the literature procedure.[20]

To the stirred ice-cooled solution of anhydrous hydrazine (6.4 g, 0.2 mol) and ethyl ether (30 mL) was added dropwise ethyl ether solution (10 mL) containing $PhSO_2Cl$ (17.7 g, 0.1 mol) over 40 min. The reaction stood at r.t. for another 20 min. Then the white precipitate was filtered, washed with cold water, and recrystallized from ethanol (40 mL). Finally, the white solid $PhSO_2NHNH_2$ (11.2 g, 65%) was obtained, mp 100-103 °C (lit.[20] 101-103 °C).

To the stirred ice-cooled solution of $PhSO_2NHNH_2$ (5.2 g, 0.03 mol) and 20% HCl 50 mL) was added slowly the aqueous solution (10 mL) of KBr (1.19 g, 0.01 mol) and $KBrO_3$ (3.34 g, 0.02 mol) over 30 min. The reaction solution was extracted with methylene chloride. The extract was washed with aqueous $NaHCO_3$ (5%) and NaCl solutions in sequence, and then dried over $MgSO_4$. After evaporation of the solvent under vacuum, a colorless $PhSO_2Br$ liquid (5.5 g, 83%) was obtained and was used without further purification.

Bromodicyanomethane [$BrCH(CN)_2$] was prepared according to the literature procedure.[21]

To a stirred ice-cooled 50 mL of water was added $CH_2(CN)_2$ (3.3 g, 50 mmol), and then Br_2 (8 g, 50 mmol) was added slowly to the $BrCH(CN)_2$ solution over 30 min. After the addition, the brown reaction solution turned colorless in minutes and was stirred at r.t. for 1 h. Then the reaction solution was extracted with ethyl ether. The ethereal extract was washed with saturated NaCl aqueous solution and dried over $MgSO_4$. After the evaporation of the ethyl ether, a colorless crystalline solid $BrCH(CN)_2$ (4.3 g, 60%) was obtained and was used without further purification, mp 62-64 °C (lit. [21] 63-64 °C).

General Procedure for Preparation of Amides 1, 11, 16-18, and **25**. To 10 mL of anhydrous ethyl ether containing an appropriate amine (0.02 mol) cooled to 0 °C was added the corresponding acyl chloride (0.01 mol). After the addition of the acyl chloride, the reaction stood at r.t. for about 30 min. A usual workup and purification by column chromatography gave the amide in 70-100 % yield.

General Procedure for the Addition of $PhSO_2Br$ to Amides. A mixture of an amide (0.20 mmol) and PhSO2Br (0.22 mmol) in CH_3CN (1.0 mL) was irradiated at r.t. until the starting amide disappeared as checked by TLC. Products were obtained by TLC separation on 20 x 10 cm silica gel plates with hexanes-ethyl acetate as the eluent. Yields were calculated based on the amount of amides used.

General Procedure for Competition Experiments. A mixture of two amides (about 0.20 mmol each), $PhSO_2Br$ (about 0.25 mmol) and $Me_3SiOSiMe_3$ (0.2 μL) in CD_3CN (1.0 mL) in a 5-mm NMR tube was recorded by 400 MHz ^1H NMR before irradiation. The integral areas of selected H peaks from each amide were measured relative to the internal standard $Me_3SiOSiMe_3$. The mixture was then recorded by NMR after irradiated at r.t. for every 15 min up to a total of 1 h. The relative reactivity was calculated based on the integral areas of the selected H peaks using eq 5.

***N*-Allyl-4-bromomethyl-3-(phenylsulfonyl)methyl-2-pyrrolidone (9a).** The trans isomer was isolated as a yellow oil. IR (cm^{-1}) 1689, 1307, 1151; ^1H NMR δ (C_6D_6) 2.24-2.34 (m, 1H), 2.62 (t, *J* = 9.6 Hz, 1H), 2.65 (dd, *J* = 3.0, 9.6 Hz, 1H), 2.69 (ddd, *J* = 2.0, 9.2, 9.6 Hz, 1H), 2.89 (dd, *J* = 8.8, 9.6 Hz, 1H), 3.25 (dd, *J* = 8.4, 10.0 Hz, 1H), 3.48 (dd, *J* = 6.0, 15.2 Hz, 1H), 3.66 (dd, *J* = 6.0, 15.2 Hz, 1H), 3.73 (dd, *J* = 2.0, 9.6 Hz, 1H), 3.81 (dd, *J* = 3.6, 10.0 Hz, 1H), 4.88 (dd, *J* = 1.0, 16.8 Hz, 1H), 4.92 (dd, *J* = 1.0, 10.0 Hz, 1H), 5.42 (ddt, *J* = 10.0, 16.8, 6.0 Hz, 1H), 6.80-7.70 (m, 5H); ^{13}C NMR δ 35.81, 39.67, 41.66, 45.89, 50.13, 57.72, 119.03, 128.18, 129.70, 131.65, 134.33, 139.23, 171.52; HREIMS m/z (relative intensity) 371.0179 (62, calcd for $C_{15}H_{18}{}^{79}BrNO_3S$ 371.0191), 292 (12), 230 (36), 150 (35), 136 (74), 77 (68), 40 (100). The cis isomer was isolated as a yellow solid, mp 135-137 °C. IR (cm^{-1}) 1693, 1305, 1146; ^1H NMR (C_6D_6) δ 2.56 (dd, *J* = 6.8, 10.0 Hz, 1H), 2.64 (m, 1H), 2.79 (dd, *J* = 0.8, 10.0 Hz, 1H), 2.99 (dd, *J* = 12.4, 14.0 Hz, 1H), 3.08 (ddd, *J* = 1.6, 7.2, 12.4 Hz, 1H), 3.12 (dd, *J* = 8.0, 10.4 Hz, 1H), 3.38 (dd, *J* = 3.6, 10.4 Hz, 1H), 3.53 (dd, *J* = 6.4, 15.2 Hz, 1H), 3.63 (dd, *J* = 6.4, 15.2 Hz, 1H), 3.80 (dd, *J* = 1.6, 14.0 Hz, 1H), 4.87 (dd, *J* = 1.2, 17.6 Hz, 1H), 4.90 (dd, *J* = 1.2, 10.4 Hz, 1H), 5.44 (ddt, *J* = 10.4, 17.6, 6.4 Hz, 1H), 6.82-7.67 (m, 5H); ^{13}C NMR δ 33.48, 35.54, 40.41, 45.95, 49.63, 52.68, 119.27, 128.15, 129.78, 131.92, 134.40, 139.07, 170.70; HREIMS m/z (relative intensity) 371.0184 (53, calcd for $C_{15}H_{18}{}^{79}BrNO_3S$ 371.0191), 292 (24), 230 (59), 150 (34), 136 (76), 77 (58), 40 (100).

***N-tert*-Butyl-4-bromomethyl-3-(phenylsulfonyl)methyl-2-pyrrolidone (9b)** was isolated as a 1:5 mixture of cis and trans isomers (from ^1H NMR). Only the major isomer (assigned as trans by NOESY spectrum) can be assigned from the ^1H NMR spectrum of the mixture. ^1H NMR (C_6D_6) δ 1.18 (s, 9H), 2.18-2.28 (m, 1H), 2.58 (dd, *J* = 10.0, 14.0 Hz, 1H), 2.66 (ddd, *J* = 2.0, 10.0, 14.0 Hz, 1H), 2.72 (dd, *J* = 5.6, 10.0 Hz, 1H), 3.12 (dd, *J* = 6.0, 10.0 Hz, 1H), 3.26 (dd, *J* = 8.4, 10.0 Hz, 1H), 3.75 (dd, *J* = 2.0, 14.0 Hz, 1H), 3.89 (dd, *J* = 3.6, 10.0 Hz, 1H), 6.85-7.75 (m, 5H); ^{13}C NMR δ the trans isomer 27.74,

35.76, 39.46, 42.88, 49.12, 54.98, 57.89, 128.09, 129.62, 134.20, 139.36, 171.61; the cis isomer 27.79, 33.34, 35.05, 41.69, 48.35, 52.77, 54.90, 128.03, 129.71, 134.28, 139.16, 170.60; HREIMS m/z (relative intensity) 387.0502 (42, calcd for $C_{16}H_{22}{}^{79}BrNO_3S$ 387.0504), 332 (29), 230 (100), 192 (33), 190 (34), 77 (10), 57 (27).

***N*-Benzyl-4-bromomethyl-3-(phenylsulfonyl)methyl-2-pyrrolidone (9c).** The trans isomer was isolated as a light yellow oil. IR (cm^{-1}) 1691, 1307, 1151; ^1H NMR δ 2.80-2.90 (m, 1H), 2.98 (ddd, *J* = 2.8, 9.6, 10.0 Hz, 1H), 3.17 (dd, *J* = 7.6, 10.0 Hz, 1H), 3.18 (dd, *J* = 10.0, 14.4 Hz, 1H), 3.44 (dd, *J* = 8.4, 10.0 Hz, 1H), 3.70 (dd, *J* = 7.2, 10.4 Hz, 1H), 3.85 (dd, *J* = 2.8, 14.4 Hz, 1H), 3.90 (dd, *J* = 3.2, 10.4 Hz, 1H), 4.40 (d, *J* = 14.8 Hz, 1H), 4.48 (d, *J* = 14.8 Hz, 1H), 7.20-8.10 (m, 10H); ^{13}C NMR δ 35.70, 39.62, 41.64, 47.30, 50.00, 57.68, 128.12, 128.16, 128.33, 129.05, 129.70, 134.33, 135.63, 139.25, 171.79; HREIMS m/z (relative intensity) 421.0345 (43, calcd for $C_{19}H_{20}{}^{79}BrNO_3S$ 421.0347), 252 (66), 250 (64), 186 (26), 91 (100). The cis isomer was isolated as a white solid, mp 118-120 °C. IR (cm^{-1}) 1692, 1305, 1150; ^1H NMR (C_6D_6) δ 2.52 (dd, *J* = 6.4, 10.0 Hz, 1H), 2.57 (m, 1H), 2.73 (dd, *J* = 0.4, 10.0 Hz, 1H), 3.00 (dd, *J* = 12.4, 14.4 Hz, 1H), 3.07 (dd, *J* = 8.0, 10.4 Hz, 1H), 3.15 (ddd, *J* = 2.0, 7.6, 12.4 Hz, 1H), 3.32 (dd, *J* = 3.2, 10.4 Hz, 1H), 3.85 (dd, *J* = 2.0, 14.4 Hz, 1H), 4.00 (d, *J* = 14.4 Hz, 1H), 4.30 (d, *J* = 14.4 Hz, 1H), 7.25-8.10 (m, 10H); ^{13}C NMR δ 33.33, 35.57, 40.42, 47.41, 49.65, 52.71, 128.15, 128.16, 128.63, 129.03, 129.80, 134.42, 135.71, 139.09, 170.95; HREIMS m/z (relative intensity) 421.0347 (17, calcd for $C_{19}H_{20}{}^{79}BrNO_3S$ 421.0347), 361 (15), 359 (13), 252 (8), 186 (7), 104 (8), 91 (100).

***N*-Methyl-4-bromomethyl-3-(phenylsulfonyl)methyl-2-pyrrolidone (9d).** The trans isomer was isolated as a colorless oil. IR (cm^{-1}) 1695, 1306, 1151; ^1H NMR (C_6D_6) δ 2.18-2.28 (m, 1H), 2.32 (s, 3H), 2.40 (dd, *J* = 7.6, 9.6 Hz, 1H), 2.55 (dd, *J* = 10.0, 12.0 Hz, 1H), 2.57 (ddd, *J* = 0.4, 8.0, 10.0 Hz, 1H), 2.69 (dd, *J* = 8.4, 9.6 Hz, 1H), 3.17 (dd, *J* = 8.8, 10.0 Hz, 1H), 3.74 (dd, *J* = 0.4, 12.0 Hz, 1H), 3.86 (dd, *J* = 4.0, 10.0

Hz, 1H), 6.82-7.75 (m, 5H); ^{13}C NMR δ 30.18, 35.79, 39.63, 41.39, 52.67, 57.74, 128.15, 129.67, 134.31, 139.16, 171.72; HREIMS m/z (relative intensity) 345.0035(36, calcd.for $C_{13}H_{16}{}^{79}BrNO_3S$ 345.0034), 266 (11), 252 (14), 204 (23), 202 (51), 124 (34), 110 (100). The cis isomer was isolated as a white solid, mp 95-97 °C. IR (cm^{-1}) 1690, 1304, 1149; ^1H NMR (C_6D_6) δ 2.33 (s, 3H), 2.44 (dd, *J* = 6.4, 10.0 Hz, 1H), 2.53-2.60 (m, 1H), 2.59 (dd, *J* = 0.8, 10.0 Hz, 1H), 2.98 (ddd, *J* = 1.2, 6.8, 13.2 Hz, 1H), 3.02 (dd, *J* = 1.2, 10.4 Hz, 1H), 3.09 (dd, *J* = 8.0, 10.4 Hz, 1H), 3.35 (dd, *J* = 3.6, 10.4 Hz, 1H), 3.80 (dd, *J* = 9.6, 10.4 Hz, 1H), 6.82-7.75 (m, 5H); ^{13}C NMR δ 30.05, 33.68, 35.48, 40.05, 52.22, 52.75, 128.12, 129.77, 134.39, 139.06, 170.98; HREIMS m/z (relative intensity) 345.0034 (15, calcd for $C_{13}H_{16}{}^{79}BrNO_3S$ 345.0034), 266 (18), 252 (14), 204 (31), 202 (51), 124 (30), 110 (82), 77 (45), 69 (100).

***trans*-*N*-Phenyl-4-bromomethyl-3-(phenylsulfonyl)methyl-2-pyrrolidone (9e)** was isolated as a yellow solid, mp 105-107 °C. IR (cm^{-1}) 1700, 1307, 1151; ^1H NMR δ 2.90-3.10 (m, 1H), 3.12 (ddd, *J* = 2.4, 9.0, 9.6 Hz, 1H), 3.28 (dd, *J* = 9.6, 14.1 Hz, 1H), 3.78 (dd, *J* = 7.8, 8.4 Hz, 1H), 3.81 (dd, *J* = 7.5, 10.5 Hz, 1H), 3.90 (dd, *J* = 2.4, 14.1 Hz, 1H), 4.01 (dd, *J* = 8.4, 10.0 Hz, 1H), 4.06 (dd, J = 3.6, 10.5 Hz, 1H), 7.10-8.00 (m, 10H); ^{13}C NMR δ 35.16, 39.43, 42.87, 51.84, 57.56, 120.31, 125.58, 128.23, 129.24, 129.75, 134.41, 138.68, 139.21, 170.96; HREIMS m/z (relative intensity) 407.0187 (51, calcd for $C_{18}H_{18}{}^{79}BrNO_3S$ 407.0191), 268 (98), 266 (100), 186 (37), 172 (56), 104 (26), 77 (64).

***N*-Benzyl-*N*-(2-propenyl)-3-(phenylsulfonyl)acrylamide (10c)** was isolated as a colorless oil. IR (cm^{-1}) 1653, 1320, 1148; ^1H NMR (2 rotamers) δ 3.95 (d, *J* =4.8, 1.2H), 4.06 (d, *J* = 6.0 Hz, 0.8H), 4.62 (s, 0.8H), 4.65 (s, 1.2H), 5.15-5.35 (m, 2H), 5.7-5.9 (m, 2H), 7.15-7.95 (m, 10H); ^{13}C NMR δ (2 rotamers, * for overlapping peaks) 48.97, 49.49, 49.64, 50.73, 118.12, 118.93, 126.75*, 128.06, 128.31, 128.36, 128.41, 128.57, 128.99, 129.37, 129.72, 129.76, 131.29, 132.01, 132.26, 134.32, 134.37, 135.98, 136.55, 138.99, 139.06, 141.86, 141.68, 163.31, 163.56; HREIMS m/z (relative intensity)

341.1081 (25, calcd for $C_{19}H_{19}NO_3S$ 341.1086), 300 (41), 200 (72), 146 (43), 125 (58), 106 (69), 91 (100), 77 (29).

***N*-Methyl-*N*-(2-propenyl)-3-(phenylsulfonyl)acrylamide (10d)** was isolated as a yellow oil. IR (cm^{-1}) 1651, 1321, 1151; ^1H NMR (2 rotamers) δ 3.01 (s, 1.7H), 3.09 (s, 1.3H), 4.00-4.10 (m, 2H), 5.13-5.30 (m, 2H), 5.65-5.88 (m, 1H), 7.28 (d, J = 14.7 Hz, 1H), 7.43 (d, J = 14.7 Hz, 1H), 7.55-7.95 (m, 5H); ^{13}C NMR (2 rotamers) δ 34.56, 35.27, 50.80, 52.68, 117.88, 118.61, 128.35, 128.37, 129.74, 129.76, 131.13, 131.24, 131.89, 132.08, 134.33, 134.37, 139.05, 139.10, 141.11, 141.37, 162.72, 163.38; HREIMS m/z (relative intensity) 265.0769 (36, calcd for $C_{13}H_{15}NO_3S$ 265.0773), 142 (13), 124 (79), 77 (24), 70 (100).

***N*-Phenyl-*N*-(2-propenyl)-3-(phenylsulfonyl)acrylamide (10e)** was isolated as a colorless oil. IR (cm^{-1}) 1653, 1320, 1149; ^1H NMR δ 4.36 (d, J = 6.2 Hz, 1H), 5.08-5.17 (m, 2H), 5.85 (ddt, J = 1.2, 10.2, 16.8 Hz, 1H), 6.78 (d, J = 14.7 Hz, 1H), 7.30 (d, J = 14.7 Hz, 1H), 7.13 (m, 2H), 7.40-7.80 (m, 8H); ^{13}C NMR δ 53.06, 119.00, 127.96, 128.31, 128.97, 129.66, 130.19, 132.03, 132.08, 134.24, 139.14, 140.80, 140.95, 162.18; HREIMS m/z (relative intensity) 327.0926 (4, calcd for $C_{18}H_{17}NO_3S$ 327.0929), 186 (100), 132 (30), 125 (25), 77 (34).

***N*-(2-Propenyl)-3-(phenylsulfonyl)acrylamide (10f)** was isolated as a white solid, mp 119-121 °C. IR (cm^{-1}) 1653, 1308, 1148; ^1H NMR δ 3.96 (m, 2H), 5.17-5.25 (m, 2H), 5.78-5.60 (m, 1H), 5.95-6.05 (br, 1H), 6.94 (d, J = 14.7 Hz, 1H), 7.33 (d, J = 14.7 Hz, 1H), 7.55-7.92 (m, 5H); ^{13}C NMR δ 42.71, 117.82, 128.38, 128.37, 129.80, 133.43, 134.47, 138.97, 140.77, 161.82. HREIMS m/z (relative intensity) 251.0619 (35, calcd for $C_{12}H_{13}NO_3S$ 251.0616), 142 (22), 125 (73), 110 (65), 77 (41), 56 (100), 41 (38).

***N*-Allyl-4-(phenylsulfonyl)methyl-3-isopropylidene-2-pyrrolidone (12a)** was isolated as a 2.3:1 mixture with **13a** (from ^1H NMR). ^1H NMR δ (* for overlapping peaks with **13a**) 1.63 (s, 3H), 2.21 (s, 3H), 3.0-4.2* (m, 7H), 5.21-5.30* (m, 2H), 5.68-

5.73* (m, 1H), 7.61-7.95* (m, 5H); ^{13}C NMR δ 19.39, 22.86, 31.17, 45.63, 48.45, 59.95, 118.69, 126.19, 128.19, 129.76*, 132.32, 134.31, 139.37, 144.91, 167.59; HREIMS m/z (relative intensity) 319.1242 (57, calcd for $C_{17}H_{21}NO_3S$ 319.1242), 178 (17), 164 (100), 82 (25).

***N*-*tert*-Butyl-4-(phenylsulfonyl)methyl-3-isopropylidene-2-pyrrolidone (12b)** was isolated as a white solid, mp 118-120 °C. IR (cm^{-1}) 1681, 1306, 1153; ^1H NMR δ 1.39 (s, 9H), 1.58 (s, 3H), 2.17 (s, 3H), 3.00 (dd, J = 1.2, 14.0 Hz, 1H), 3.17 (dd, J = 7.2, 14.0 Hz, 1H), 3.25-3.35 (m, 1H), 3.45 (dd, J = 6.8, 10.8 Hz, 1H), 3.59 (dd, J = 0.8, 10.8 Hz, 1H), 7.61-7.95 (m, 5H); ^{13}C NMR δ 19.22, 22.86, 27.80, 31.05, 46.79, 54.38, 59.63, 127.84, 128.18, 129.75, 134.29, 139.49, 143.39, 168.60; HREIMS m/z (relative intensity) 335.1554 (57, calcd for $C_{18}H_{25}NO_3S$ 335.1555), 320 (100), 180 (20), 124 (37).

***N*-Benzyl-4-(phenylsulfonyl)methyl-3-isopropylidene-2-pyrrolidone (12c)** was isolated as a yellow oil. IR (cm^{-1}) 1688, 1307, 1147; ^1H NMR (C_6D_6) δ 1.24 (s, 3H), 2.33 (s, 3H), 2.50-2.60 (m, 2H), 2.98 (dd, J = 6.8, 10.4 Hz, 1H), 3.10-3.20 (m, 1H), 3.26 (dd, J = 0.8, 10.4 Hz, 1H), 4.14 (d, J = 14.4 Hz, 1H), 4.46 (d, J = 14.4 Hz, 1H), 7.50-7.85 (m, 5H); ^{13}C NMR δ 19.87, 23.12, 31.32, 47.70, 48.88, 59.72, 125.80, 128.08, 128.12, 128.62, 129.05, 129.73, 134.30, 136.00, 139.18, 146.80, 167.96; HREIMS m/z (relative intensity) 369.1407 (74, calcd for $C_{21}H_{23}NO_3S$ 369.1399), 228 (19), 214 (72), 91 (100), 83 (30).

***N*-Methyl-4-[(phenylsulfonyl)methyl]-3-isopropylidene-2-pyrrolidone (12d)** was isolated as a 2.5:1 mixture with **13d**. ^1H NMR (C_6D_6) δ 1.25 (s, 3H), 2.31 (s, 3H), 2.52 (s, 3H), 2.52-2.60 (m, 2H), 2.87 (dd, J = 6.8, 10.4 Hz, 1H), 3.15-3.22 (m, 1H), 3.27 (dd, J = 0.8, 10.8 Hz, 1H), 6.88-6.95 (m, 3H), 7.60-7.70 (m, 2H); ^{13}C NMR δ 19.24, 22.81, 30.13, 31.06, 50.99, 59.86, 125.99, 128.14, 129.74, 134.30, 139.35, 144.27, 168.08; HREIMS m/z (relative intensity) 293.1085 (49, calcd for $C_{15}H_{19}NO_3S$ 293.1086), 138 (100), 84 (58).

***N*-Allyl-3-(1-bromo-1-methyl)ethyl-4-(phenylsulfonyl)methyl-2-pyrrolidone (13a)** was isolated as a 1:2.3 mixture with **12a** (from ^{1}H NMR). ^{1}H NMR δ (* for overlapping peaks with **12a**) 1.79 (s, 3H), 1.94 (s, 3H), 2.47 (d, *J* = 3.6 Hz, 1H), 3.0-4.2* (m, 7H), 5.21-5.30* (m, 2H), 5.68-5.73* (m, 1H), 7.61-7.95* (m, 5H); ^{13}C NMR δ 30.42, 31.32, 34.62, 45.77, 50.27, 60.04, 61.74, 67.77, 119.10, 128.26, 129.76*, 131.65, 134.40, 139.23, 169.75; HREIMS m/z (relative intensity) 399.0498 (1, calcd for $C_{17}H_{22}{}^{79}BrNO_3S$ 399.0502), 319 (60), 178 (18), 164 (100), 77 (16).

***trans*-*N*-Benzyl-3-(1-bromo-1-methyl)ethyl-4-(phenylsulfonyl) methyl-2-pyrrolidone (13c)** was isolated as a yellow oil. IR (cm^{-1}) 1682, 1292, 1146; ^{1}H NMR (C_6D_6) δ 1.65 (s, 3H), 1.85 (s, 3H), 2.05 (d, *J* = 5.2 Hz, 1H), 2.48 (dd, *J* = 11.2, 14.0 Hz, 1H), 2.80-2.90 (m, 1H), 2.99 (dd, *J* = 2.4, 14.0 Hz, 1H), 3.12 (dd, *J* = 4.0, 10.4 Hz, 1H), 3.44 (dd, *J* = 8.8, 10.4 Hz, 1H), 3.98 (d, *J* = 14.4 Hz, 1H), 4.44 (d, *J* = 14.4 Hz, 1H), 6.80-7.85 (m, 10H); ^{13}C NMR δ 30.47, 31.31, 34.66, 47.23, 50.15, 59.98, 61.72, 67.78, 128.11, 128.24, 128.57, 129.03, 129.72, 134.37, 135.86, 139.10, 169.97; HREIMS m/z (relative intensity) 369.1408 [59, calcd for $C_{21}H_{23}NO_3S$ (M - HBr) 369.1399], 228 (19), 214 (69), 91 (100); CIMS m/z 469/467 ($M + NH_4^+$).

***trans*-*N*-Methyl-3-(1-bromo-1-methyl)ethyl-4-(phenylsulfonyl)methyl-2-pyrrolidone (13d)** was isolated as a 1:2.5 mixture with **12d**. ^{1}H NMR (C_6D_6) δ 1.62 (s, 3H), 1.86 (s, 3H), 2.40 (s, 3H), 1.98 (d, *J* = 5.6 Hz, 1H), 2.52 (dd, *J* = 12.0, 14.0 Hz, 1H), 2.78-2.85 (m, 1H), 2.98 (dd, *J* = 4.4, 10.4 Hz, 1H), 3.05 (dd, *J* = 2.8, 14.0 Hz, 1H), 3.33 (dd, *J* = 8.8, 10.4 Hz, 1H), 6.88-6.95 (m, 3H), 7.60-7.70 (m, 2H); ^{13}C NMR δ 30.05, 31.31, 31.34, 34.89, 52.69, 59.80, 61.66, 67.89, 128.22, 129.74, 134.38, 139.12, 170.04; HREIMS m/z (relative intensity) 293.1085 [49, calcd for $C_{15}H_{19}NO_3S$ (M - HBr) 293.1086], 138 (100), 84 (58); CIMS m/z 376/374 ($M + H^+$).

***N*-(3,3-Dimethylacryloyl)-3-bromomethyl-2-(phenylsulfonyl)methyl pyrrolidine (14)** was isolated as a 1:2 or 2:1 (from GC-MS) mixture of cis and trans

isomers without assignment. ^{1}H NMR δ 1.88 (s, 3H), 2.10 (s, 3H), 2.5-4.0 (m, 10H), 5.76 (s, 1H), 7.61-7.95 (m, 5H); ^{13}C NMR δ major isomer 20.41, 27.36, 30.36, 36.33, 42.39, 48.80, 50.25, 54.14, 116.94, 128.18, 129.82, 134.43, 139.20, 151.45, 166.75; minor isomer 20.43, 27.38, 30.36, 35.06, 43.58, 48.80, 50.82, 54.67, 116.91, 128.18, 129.82, 134.43. 139.14, 151.31, 166.70; HREIMS m/z (relative intensity) 399.0502 (40, calcd for $C_{17}H_{22}{}^{79}BrNO_3S$ 399.0504), 320 (19), 318 (37), 246 (57), 176 (28), 83 (100), 55 (16).

***N*-(2-Bromo-3-phenylsulfonyl)propyl-3,3-dimethylacrylamide (15)** was isolated as a light yellow solid, mp 130-132 °C. IR (cm^{-1}) 1650, 1308, 1146; ^{1}H NMR δ 1.86 (s, 3H), 2.16 (s, 3H), 3.60-3.80 (m, 4H), 4.43 (pentet, J = 6.0 Hz, 1H), 5.59 (s, 1H), 5.88-5.93 (b, 1H), 7.50-8.10 (m, 5H); ^{13}C NMR δ 20.18, 27.47, 43.48, 45.27, 61.78, 117.88, 128.52, 129.70, 134.48, 139.18, 152.21, 167.08; HREIMS m/z (relative intensity) 279.0924 [22, calcd for $C_{14}H_{17}NO_3S$ (M - HBr) 279.0929], 138 (97), 83 (100), 55 (20); CIMS m/z 379/377 (M + NH_4^+).

***N*-Acetyl-3-bromomethyl-2-[(phenylsulfonyl)methyl]pyrrolidine (19)** was isolated as a 1:2 or 2:1 (from GC-MS) mixture of cis and trans isomers without assignment. ^{1}H NMR δ 2.07 (s, 3H), 2.50-4.00 (m, 10H), 7.50-8.10 (m, 5H); ^{13}C NMR δ major isomer 22.47, 29.91, 36.27, 42.62, 49.05, 50.71, 53.92, 128.17, 129.86, 134.50, 139.22, 169.87; HREIMS m/z (relative intensity) 359.0188 (16, calcd for $C_{14}H_{18}{}^{79}BrNO_3$ 359.0191), 318 (19), 316 (17), 224 (19), 204 (100), 176 (48), 137 (18), 96 (58), 77 (47), 43 (99).

***N,N*-Diallyl-3-(acetylthio)propionamide (21)** was isolated as a colorless oil. IR (cm^{-1}) 1694, 1651; ^{1}H NMR δ 2.30 (s, 3H), 2.62 (t, J = 6.6 Hz, 2H), 3.15 (t, J = 6.6 Hz, 2H), 3.83 (d, J = 4.8 Hz, 2H), 3.97 (d, J = 6.0 Hz, 2H), 5.10-5.20 (m, 4H), 5.75-5.85 (m, 2H); ^{13}C NMR δ 24.99, 30.68, 33.31, 48.23, 49.09, 116.87, 117.65, 132.66, 133.26, 171.00, 196.54; HREIMS m/z (relative intensity) 227.0984 (16, calcd for $C_{11}H_{17}BNO_2S$ 227.0980), 184 (47), 152 (49), 124 (45), 96 (25), 70 (21), 56 (87), 43 (99), 41 (100).

***N*-Allyl-3-(1-methyl)ethyl-4-(acetylthio)methyl-2-pyrrolidone (23).** The trans isomer was isolated as a colorless oil. IR (cm^{-1}) 1694; ^1H NMR δ 0.90 (d, J = 6.8 Hz, 3H), 1.03 (d, J = 6.8 Hz, 3H), 2.18 (dd, J = 4.4, 4.8 Hz, 1H), 2.22-2.27 (m, 1H), 2.30-2.40 (m, 1H), 2.35 (s, 3H), 2.91 (t, J = 13.2 Hz, 1H), 2.93 (dd, J = 4.8, 10.4 Hz, 1H), 3.06 (dd, J = 5.6, 13.2 Hz, 1H), 3.44 (dd, J = 8.4, 10.4 Hz, 1H), 3.79 (dd, J = 6.0, 15.2 Hz, 1H), 3.95 (dd, J = 6.0, 15.2 Hz, 1H), 5.10-5.20 (m, 2H), 5.69 (ddt, J = 9.6, 17.6, 6.0 Hz, 1H); ^{13}C NMR δ 18.46, 20.27, 29.23, 30.87, 32.97, 34.66, 45.36, 50.87, 54.05, 118.31, 132.53, 174.87, 195.46; HREIMS m/z (relative intensity) 255.1294 (27, calcd for $C_{13}H_{21}NO_2S$ 255.1293), 212 (37), 180 (16), 166 (7), 136 (12), 124 (100), 83 (28), 55 (10), 43 (32). The cis isomer was isolated as a colorless oil. IR (cm^{-1}) 1699; ^1H NMR δ 1.11 (d, J = 6.8 Hz, 3H), 1.15 (d, J = 6.8 Hz, 3H), 2.00 (octet, J = 6.8 Hz, 1H), 2.31 (dd, J = 6.8, 8 Hz, 1H), 2.35 (s, 3H), 2.50-2.60 (m, 1H), 2.82 (dd, J = 13.6 Hz, 14.0, 1H), 3.02 (dd, J = 5.6, 10.0 Hz, 1H), 3.13 (dd, J = 4.8, 13.6 Hz, 1H), 3.30 (dd, J = 7.2, 10.0 Hz, 1H), 3.83 (dd, J = 6.4, 15.2 Hz, 1H), 3.92 (dd, J = 6.4, 15.2 Hz, 1H), 5.15-5.25 (m, 2H), 5.70 (ddt, J = 10.0, 17.2, 6.4 Hz, 1H); ^{13}C NMR δ 20.01, 22.46, 26.78, 28.40, 30.83, 36.75, 45.40, 50.13, 51.27, 118.47, 132.76, 174.51, 195.48; HREIMS m/z (relative intensity) 255.1296 (26, calcd for $C_{13}H_{21}NO_2S$ 255.1293), 213 (28), 180 (8), 166 (26), 136 (15), 124 (100), 83 (14), 43 (32).

***N*-(3,3-Dimethylacryloyl)-4-methyl-3-(acetylthio)methylpyrrolidine (24)** was isolated as a 2:1 or 1:2 (from GC-MS) mixture of cis and trans isomers without assignment. ^1H NMR δ 0.96 (d, J = 6.8 Hz, 3H, minor isomer), 1.06 (d, J = 6.4 Hz, 3H, major isomer), 1.82 (s, 3H), 2.03 (s, 3H) , 2.31 (s, 3H), 2.70-4.00 (m, 8H), 5.71 (s, J =10.0 Hz, 1H); HREIMS m/z (relative intensity) 255.1296 (27, calcd for $C_{13}H_{21}NO_2S$ 255.1293), 212 (5), 166 (33), 130 (10), 83 (100), 55 (18), 43 (10).

***N*-Allyl-3-(1-bromo)ethyl-4-(phenylsulfonyl)methyl-2-pyrrolidone (26)** was isolated as an inseparable mixture of 4 diastereomers. ^1H NMR δ 1.18-1.66 (m, 3H),

2.70-4.00 (m, 9H), 5.15-5.30 (m, 2H), 5.68-5.85 (m, 1H), 7.50-8.10 (m, 5H); HREIMS m/z (relative intensity) 385.0348 (28, calcd for $C_{16}H_{20}{}^{79}BrNSO_3$ 385.0347), 305 (52), 278 (33), 246 (29), 218 (15), 164 (52), 150 (100), 136 (17), 122 (15), 77 (49).

***N*-Crotonyl-3-bromomethyl-4-[(phenylsulfonyl)methyl]pyrrolidine (27)** was isolated as an 1:1.6 or 1.6:1 mixture of cis and trans isomers (from GC-MS). ^{1}H NMR δ 1.89 (d, J = 7.2 Hz, 3H), 2.20-3.90 (m, 10H), 6.10 (d, J = 15.2 Hz, 1H), 6.95 (m, 1H), 7.50-7.95 (m, 5H); ^{13}C NMR δ major isomer 18.34, 30.24, 36.27, 42.36, 49.23, 49.87, 54.09, 122.26, 128.17, 129.83, 134.46, 139.15, 142.53, 165.36; minor isomer 18.34, 32.13, 34.96, 43.55, 49.11, 50.42, 54.56, 122.26, 128.14, 129.83, 134.46, 139.07, 142.53, 165.03; HREIMS m/z (relative intensity) 385.0348 (10, calcd for $C_{16}H_{20}{}^{79}BrNSO_3$ 385.0347), 306 (6), 278 (2), 230 (21), 176 (15), 164 (8), 150 (5), 96 (15), 77 (12), 69 (100).

***N*-Allyl-4-bromomethyl-3-(2,2,2-trichloro)ethyl-2-pyrrolidone (28)**. A mixture of cis and trans isomers was found by GC-MS (cis/trans = 1/4). Only the trans isomer was isolated pure as a yellow oil. IR (cm^{-1}) 1695; ^{1}H NMR (C_6D_6) δ 1.90-1.99 (m, 1H), 2.17 (dd, J = 7.6, 11.2 Hz, 1H), 2.31 (dt, J = 3.2, 7.6 Hz, 1H), 2.57 (dd, J = 7.2, 9.6 Hz, 1H), 2.73 (t, J = 10 Hz, 1H), 2.86 (dd, J = 8, 9.6 Hz, 1H), 3.24 (dd, J = 3.6, 10 Hz, 1H), 3.42 (dd, J = 3.2, 11.2 Hz, 1H), 3.55-3.67 (m, 2H), 4.88-4.95 (m, 2H), 5.47 (ddt, J = 10.8, 16.8, 6 Hz, 1H); ^{13}C δ NMR 35.79, 40.03, 45.68, 45.89, 50.19, 56.08, 98.70, 119.02, 131.86, 172.70; HREIMS m/z (relative intensity) 346.9243 (12, calcd for $C_{10}H_{13}{}^{79}Br^{35}Cl_3NO$ 346.9246), 314 (8), 217 (16), 122 (80), 68 (100).

2-Bromo-4,4-dicyanobutyl Acrylate (29) was isolated as a colorless oil. ^{1}H NMR δ 2.45 (ddd, J = 4.8, 11.4, 14.4 Hz, 1H), 2.70 (ddd, J = 3.3, 11.1, 14.4 Hz, 1H), 4.20 (dd, J = 4.8, 11.1 Hz, 1H), 4.30 (m, 1H), 4.42 (dd, J = 6.6, 12 Hz, 1H), 4.57 (dd, J = 5.1, 12 Hz, 1H), 5.95 (dd, J = 1.5, 10.5 Hz, 1H), 6.15 (dd, J = 10.5, 17.1 Hz, 1H), 6.50 (dd, J = 1.5, 17.1 Hz, 1H); ^{13}C NMR δ 21.86, 36.48, 44.88, 66.22, 111.24, 111.72, 127.16, 132.88, 165.10; EIMS m/z (relative intensity) 229 (4), 186 (5), 121 (11), 85 (8), 73

(17), 55 (100); CIMS m/z 276/274 ($M + NH_4^+$)

***N*-Allylsuccinimide (32)** was prepared according to the literature procedure.[22]

To a solution of succinimide (1.0 g, 10 mmol), allyl alcohol (0.9 mL, 12 mmol) and Ph_3P (3.44 g, 13 mmol) in 40 mL of anhydrous THF at 0 °C was added DEAD (2.3 g, 13 mmol). The mixture was stirred overnight. After the usual workup and purification by column chromatograph with petroleum ether-ethyl acetate as the eluent, a white solid **32** (500 mg, 36%) was obtained, mp 105-107 °C. ^1H NMR δ 2.73 (s, 4H), 4.10 (m, 2H), 5.19 (m, 2H), 5.79 (m, 1H); ^{13}C NMR δ 28.37, 41.10, 118.59, 130.86, 176.99; HREIMS m/z (relative intensity) 139.0631 (100, calcd for $C_7H_9NO_2$ 139.0633), 110 (18), 96 (7), 84 (10), 56 (57).

***N*-(2-Bromo-4,4-dicyanobutyl)succinimide (33)** was isolated as a colorless oil. ^1H NMR δ 2.39 (ddd, J = 4.5, 11.4, 14.4 Hz, 1H), 2.59 (ddd, J = 3, 11.1, 14.4 Hz, 1H), 2.82 (s, 4H), 3.88 (dd, J = 6.6, 14.1 Hz, 1H), 4.05 (dd, J = 7.2, 14.1 Hz, 1H), 4.22 (dd, J = 4.5, 11.1 Hz, 1H), 4.36 (m, 1H); ^{13}C NMR δ 22.13, 28.30, 37.28, 44.20, 45.09, 111.85, 111.28, 176.74; HREIMS m/z (relative intensity) 217.9821 [4, calcd for $C_7H_9NO_2{}^{79}Br$ (M - $CH(CN)_2$) 217.9817], 204 (10), 176 (8), 138 (28), 125 (12), 112 (80), 84 (63), 55 (100); CIMS m/z 303/301 ($M + NH_4^+$)

Preparation of *N*-Trifluoroacyl-*N*-allylacrylamide (34). To the slurry of NaH (240 mg, 10 mmol) in anhydrous ethyl ether (10 mL) cooled to 0 °C was added dropwise *N*-allylacrylamide (220 mg, 2 mmol). After the gaseous bubbling subsided, the solution was stirred for another 10 min, and then trifloroacetic anhydride (0.50 mL, 4 mmol) was added to the reaction solution. After 30 min, anhydrous ethyl ether (10 mL) was added to the reaction solution, and the top clear ethereal solution was transfer to another dry round-bottom flask and concentrated. Finally, a crude light yellow liquid **34** (400 mg, 98%) was obtained and used without further purification: ^1H NMR δ 4.39 (d, J = 5.2 Hz, 2H), 5.24 (m, 2H), 5.83 (m, 1H), 5.93 (dd, J = 1.6, 10 Hz, 1H), 6.54 (dd, J = 1.6, 17.2 Hz, 1H), 6.67 (dd, J = 10, 17.2 Hz, 1H); ^{13}C NMR δ 46.97, 115.82 (q, J = 1145 Hz), 118.57, 129.15, 131.35, 132.88,

160.01 (q, J = 156.9 Hz), 168.07; HREIMS m/z (relative intensity) 207.0510 (4, calcd for $C_8H_8NO_2F_3$ 207.0507), 179 (5), 152 (7), 84 (18), 55 (100).

***N*-(2-Bromo-4,4-dicyanobutyl)acrylamide (35)** was isolated as a light yellow oil. ^{1}H NMR δ 2.43 (ddd, J = 4.8, 6.4, 14.4 Hz, 1H), 2.60 (ddd, J = 4.8, 6.4, 14.4 Hz, 1H), 3.75 (dd, J = 4.8, 6.8 Hz, 1H), 3.91 (dd, J = 4.8, 6.8 Hz, 1H), 4.30 (pentet, J = 4.8 Hz, 1H), 4.38 (dd, J = 6.4, 9.6 Hz, 1H), 5.65 (br, 1H), 5.78 (dd, J = 1.2, 10.6 Hz, 1H), 6.16 (dd, J = 10.4, 17.2 Hz, 1H), 6.38 (dd, J = 1.2, 17.2 Hz, 1H); ^{13}C NMR δ 21.81, 36.59, 44.71, 49.51, 111.63, 111.96, 128.75, 129.78, 166.31; HREIMS m/z (relative intensity) 189.9869 [15, calcd for $C_6H_9NO^{79}Br$ (M - $CH(CN)_2$) 189.9868], 110 (11), 96 (13), 80 (20), 55 (56), 43 (100); CIMS m/z 275/274 (M + NH_4^+)

Preparation of *N*-Acetyl,*N*-allylacrylamide (36). To the slurry of NaH (240 mg, 10 mmol) in anhydrous ethyl ether (10 mL) cooled to 0 °C was added dropwise *N*-allylacryamide (220 mg, 2 mmol). After gaseous bubbling subsided, the solution was stirred for another 10 min. Then acryloyl chloride (0.32 mL, 4 mmol) was added to the reaction solution slowly. After the reaction solution was stirred for another 30 min, water was added to the reaction solution cautiously. The reaction misture was extracted with ether, and dried over $MgSO_4$. Purification by column chromatography on silica gel gave a light yellow liquid **26** (200 mg, 65%). IR (cm^{-1}) 1703, 1694; ^{1}H NMR δ 2.46 (s, 3H), 4.36 (d, J = 4.8 Hz, 2H), 5.14 (dd, J = 0.8, 16.4 Hz, 1H), 5.21 (dd, J = 0.8, 10.4 Hz, 1H), 5.80 (dd, J = 1.6, 10.4 Hz, 1H), 5.88 (ddt, J = 10.4, 16.4, 4.8 Hz, 1H), 6.43 (dd, J = 1.6, 16.8 Hz, 1H), 6.73 (dd, J = 10.4, 16.8 Hz, 1H); ^{13}C NMR δ 26.30, 46.70, 116.72, 130.53, 130.57, 133.00, 168.94, 173.39; HREIMS m/z (relative intensity) 153.0790 (11, calcd for $C_8H_{11}NO$ 153.0790), 111 (32), 98 (28), 55 (100), 43 (61).

***N*-Acetyl-4-bromomethyl-3-(2,2-dicyano)ethyl-2-pyrrolidone (37)** was isolated as a light yellow oil. IR (cm^{-1}) 2260, 1729, 1704; ^{1}H NMR δ 2.31 (ddd, J = 4.8, 10.8, 14 Hz, 1H), 2.40-2.46 (m, 1H), 2.47 (ddd, J = 10.8, 11.2, 14 Hz, 1H), 2.50 (s, 3H),

2.87 (dt, J = 3.6, 10.8 Hz, 1H), 3.47 (dd, J = 9.2, 12 Hz, 1H), 3.52 (dd, J = 6, 10.8 Hz, 1H), 3.61 (dd, J = 4.4, 10.8 Hz, 1H), 4.12 (dd, J = 8.4, 12 Hz, 1H), 4.86 (dd, J = 4.8, 11.2 Hz, 1H); ^{13}C NMR δ 20.27, 25.27, 31.11, 32.11, 38.26, 44.34, 47.69, 112.18, 112.50, 170.50, 174.39; HREIMS m/z (relative intensity) 297.0113 (5, calcd for $C_{11}H_{12}{}^{79}BrN_3O_2$ 297.0113), 271 (2), 258 (2), 221 (2), 175 (2), 139 (2), 126 (3), 84 (2), 42 (100).

***N*-Allyl-bis(3,3-dimethylacryloyl)amide (38)** was prepared similarly to amide **36** using *N*-allyl-3,3-dimethylacrylamide and 3,3-dimethylacryloyl chloride, and isolated as a colorless oil in a yield of 41%. ^{1}H NMR δ 1.91 (d, J = 1.0 Hz, 6H), 2.10 (d, J = 1.0 Hz, 6H), 4.33 (d, J = 6.8 Hz, 1H), 5.16 (m, 2H), 5.85 (m, 1H), 6.07 (m, 2H); ^{13}C NMR δ 21.00, 27.54, 46.46, 116.34, 120.01, 133.59, 154.78, 169.34; HREIMS m/z (relative intensity) 221.1418 (26, calcd for $C_{13}H_{19}NO_2$ 221.1416), 206 (12), 193 (12), 179 (5), 165 (8), 139 (25), 110 (18), 95 (16), 84 (25), 55 (100).

***N*-(3,3-Dimethylacryloyl)-3-(1-bromo-1-methyl)ethyl-4-(2,2-dicyano)ethyl-2-pyrrolidone (39)** was isolated as a colorless oil. ^{1}H NMR δ 1.89 (s, 3H), 2.01 (d, J = 1.2 Hz, 3H), 2.07 (s, 3H), 2,19 (d, J = 1.2 Hz, 3H), 2.27 (ddd, J = 7.6, 8, 14 Hz, 1H), 2.41 (ddd, J = 6.4, 7.6, 14 Hz, 1H), 2.67 (d, J = 3.6 Hz, 1H), 2.82 (m, 1H), 3.60 (dd, J = 3.2, 12.4 Hz, 1H), 3.88 (t, J = 7.6 Hz, 1H), 4.08 (dd, J = 8.8, 12.4 Hz, 1H), 6.88 (m, 1H); ^{13}C NMR δ 20.95, 21.87, 28.40, 30.88, 32.15, 34.56, 37.51, 48.85, 63.33, 65.67, 111.91, 112.16, 117.12, 160.66, 165.99, 170.20; HREIMS m/z (relative intensity) 365.0733 (8, calcd for $C_{16}H_{20}N_3O_2{}^{79}Br$ 365.0739), 285 (58), 204 (28), 150 (11), 124 (32), 80 (100), 55 (78).

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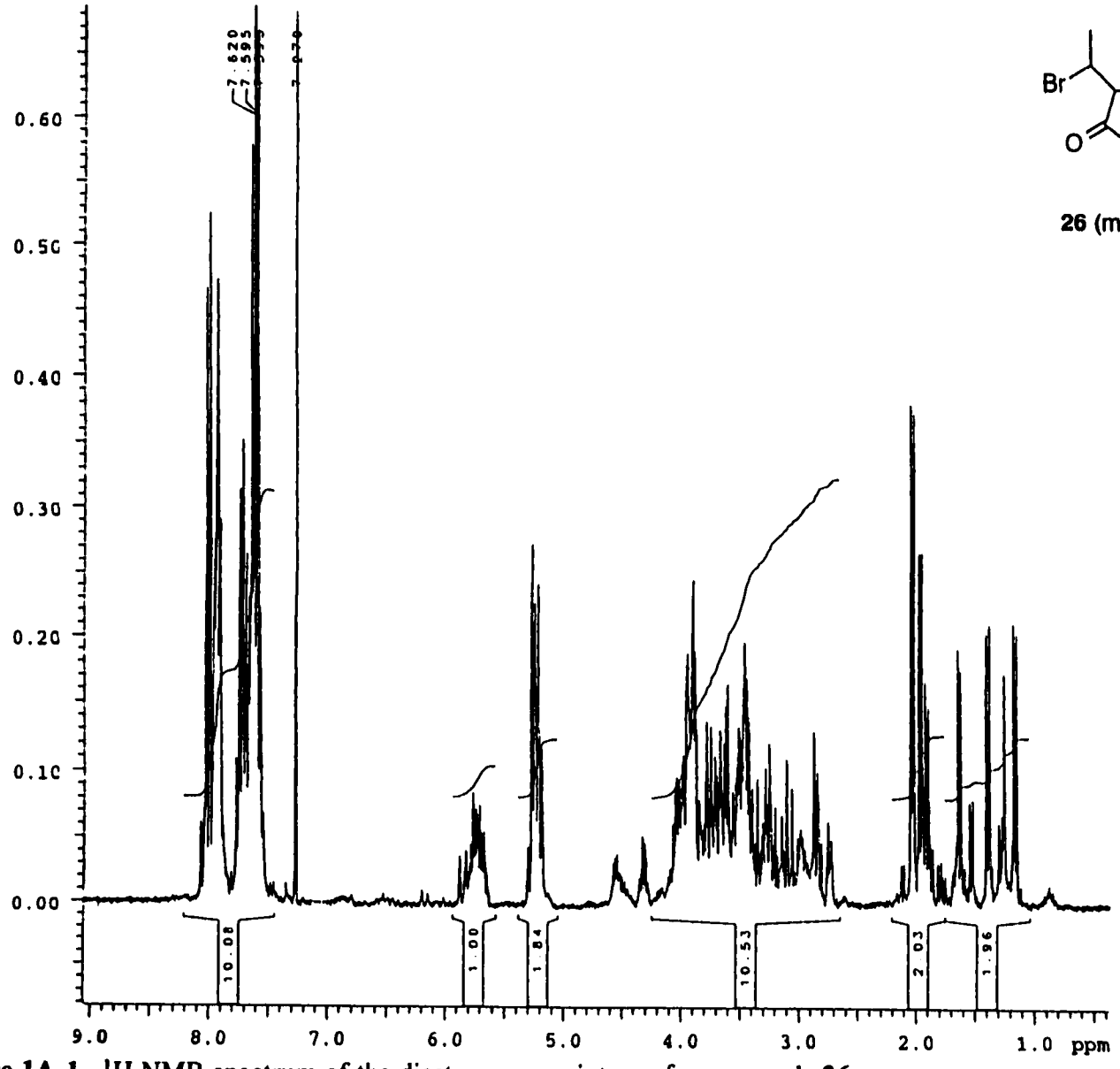
Appendix

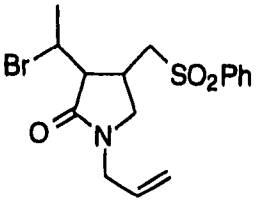
Spectra

NMR spectra were recorded in $CDCl_3$ or as stated otherwise (^1H at 400 MHz and ^{13}C at 100 MHz) with δ measured relative to $CHCl_3$ (7.27 ppm) or the central ^{13}C peak of $CDCl_3$ (77.23 ppm).

^1H and ^{13}C NMR spectra of compounds **9a-e**, **10c-f**, **12a-d**, **13a**, **13c-d**, **14**, **15**, **19**, **21**, **23**, **24**, **28**, **36**, and **37**, ^1H-^1H NOE spectra of compounds **9a-e**, **13a**, **13c-d**, **23**, **28**, and **37**, can be found in the supporting information accompanying the published paper, and are available via the Internet at http://pubs.acs.org.

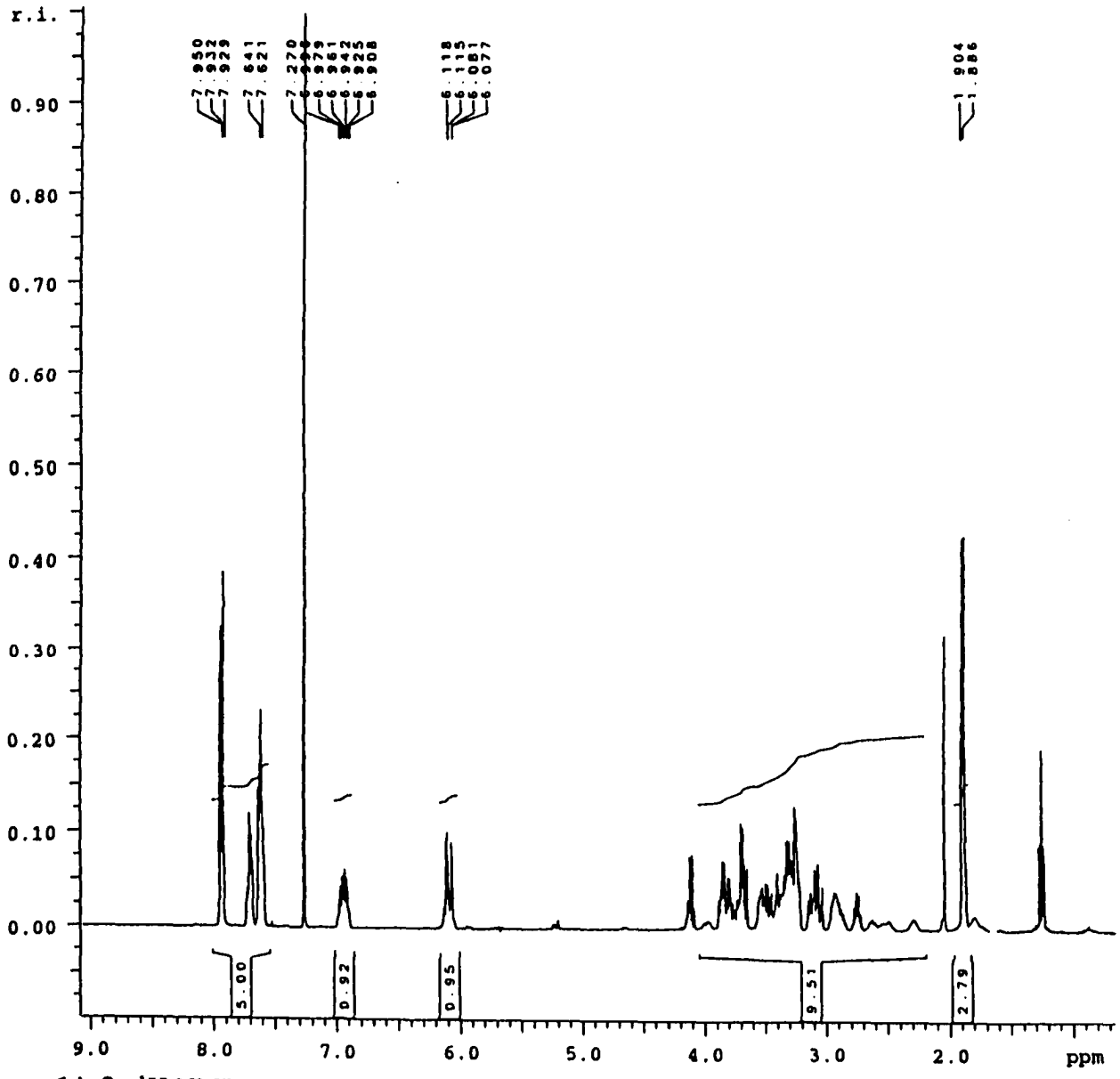
^1H spectra of compounds **26**, **27**, **29**, **33**, **38**, and **39**, ^{13}C NMR spectra of compounds **29**, **33**, **38**, and **39**, ^1H-^1H NOE spectra of compound **39**, are included in this appendix.

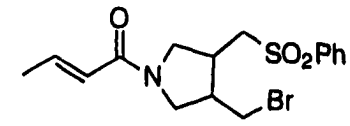




26 (mixture of diastereomers)

Figure 1A-1. ^{1}H NMR spectrum of the diastereomer mixture of compounds **26**.





27 (c/t = 1.6 or 1/1.6)

Figure 1A-2. ^{1}H NMR spectrum of the *cis/trans* isomer mixture of compounds **27**.

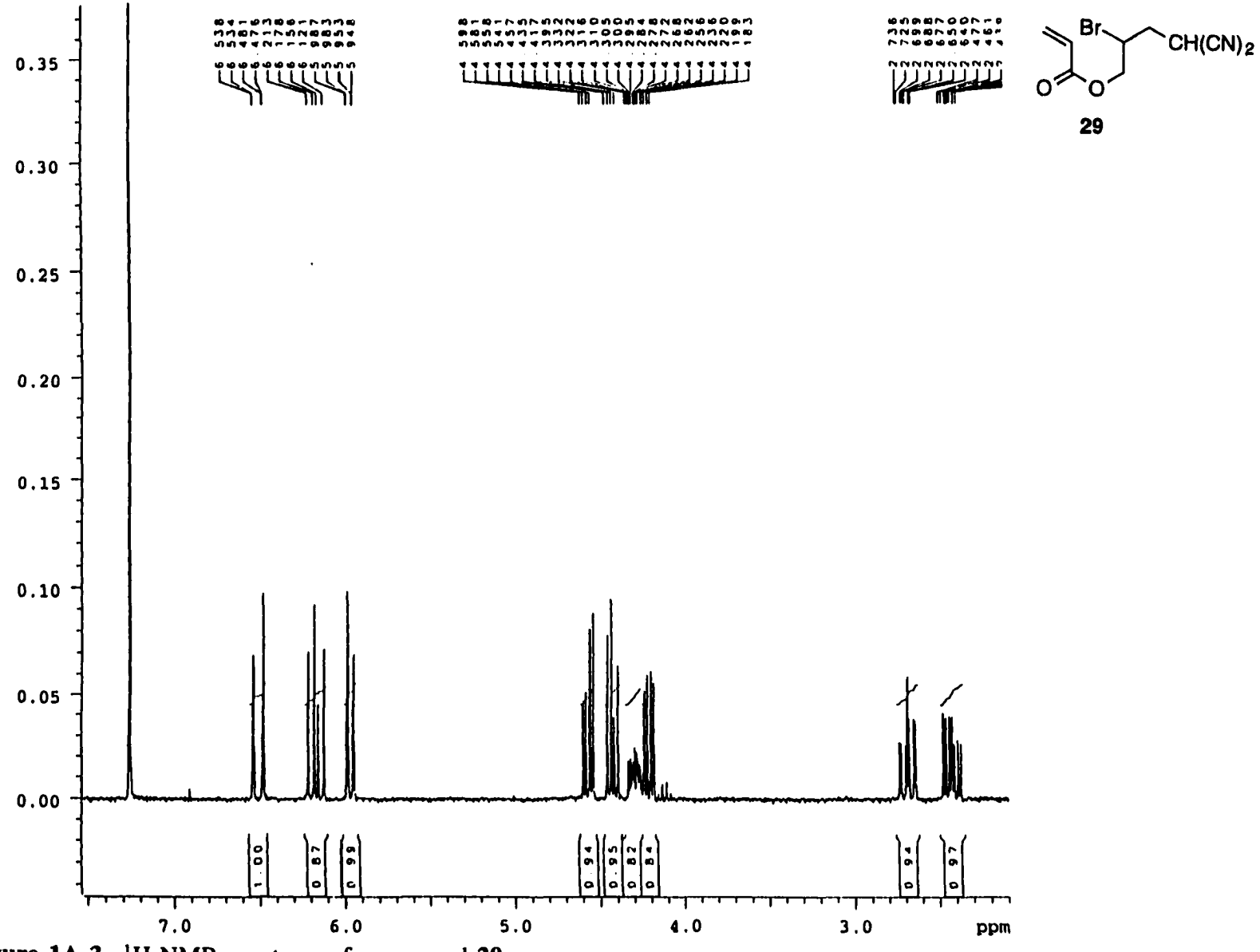


Figure 1A-3. ^{1}H NMR spectrum of compound **29**.

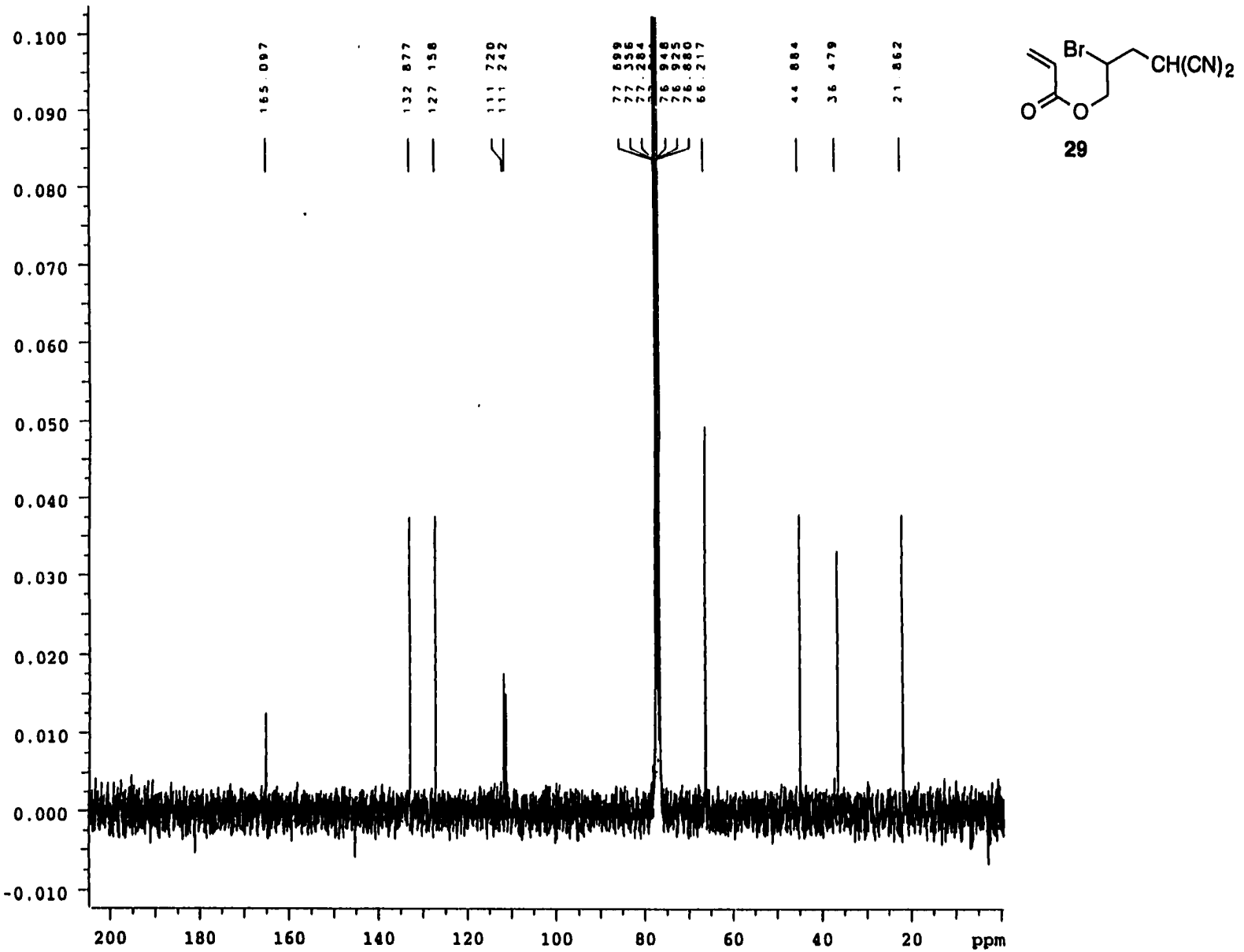
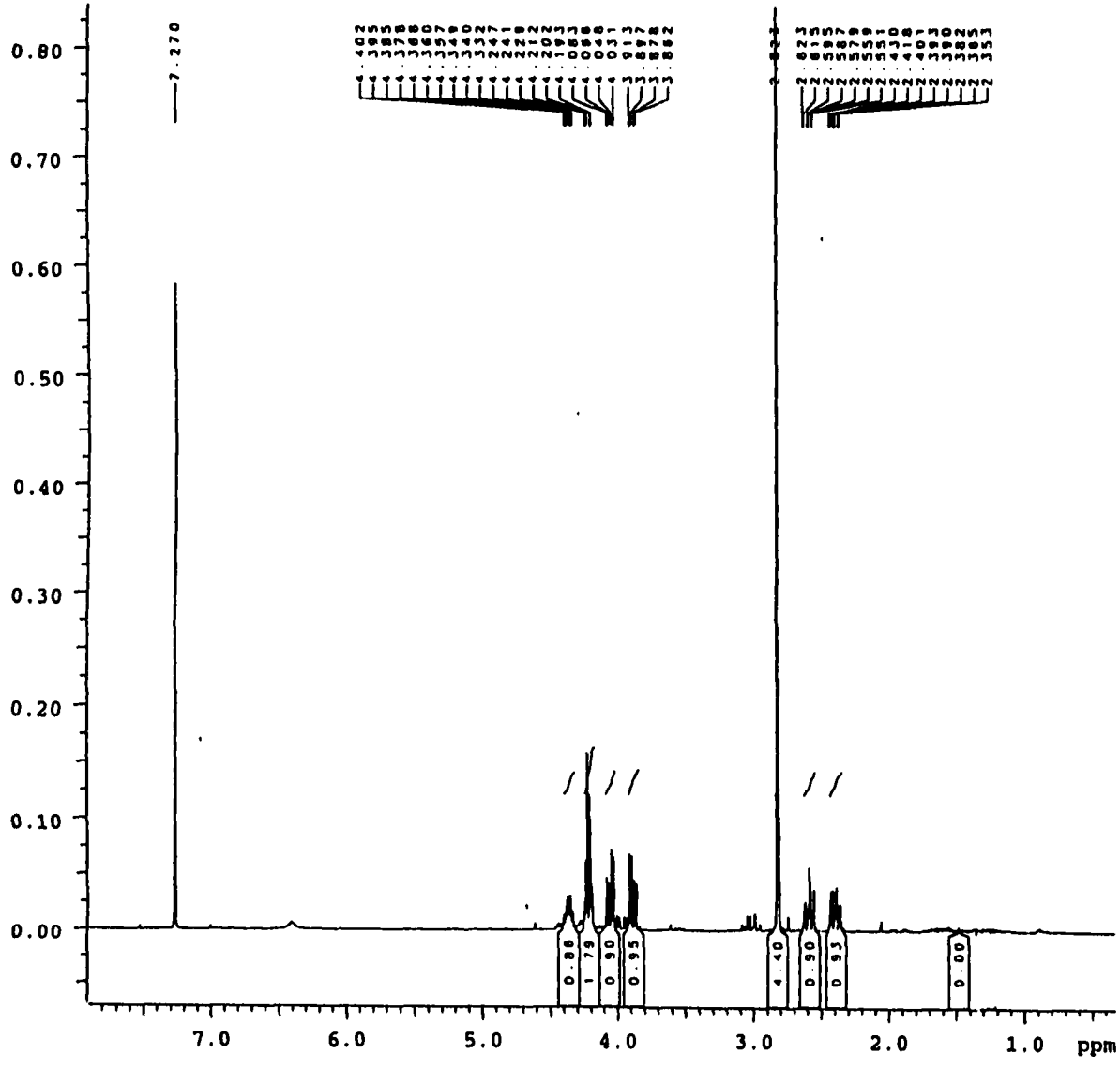


Figure 1A-4. ^{13}C NMR spectrum of compound **29**.



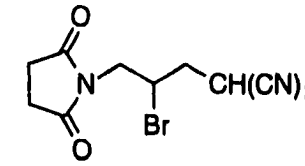


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Figure 1A-5. ^{1}H NMR spectrum of compound **33**.

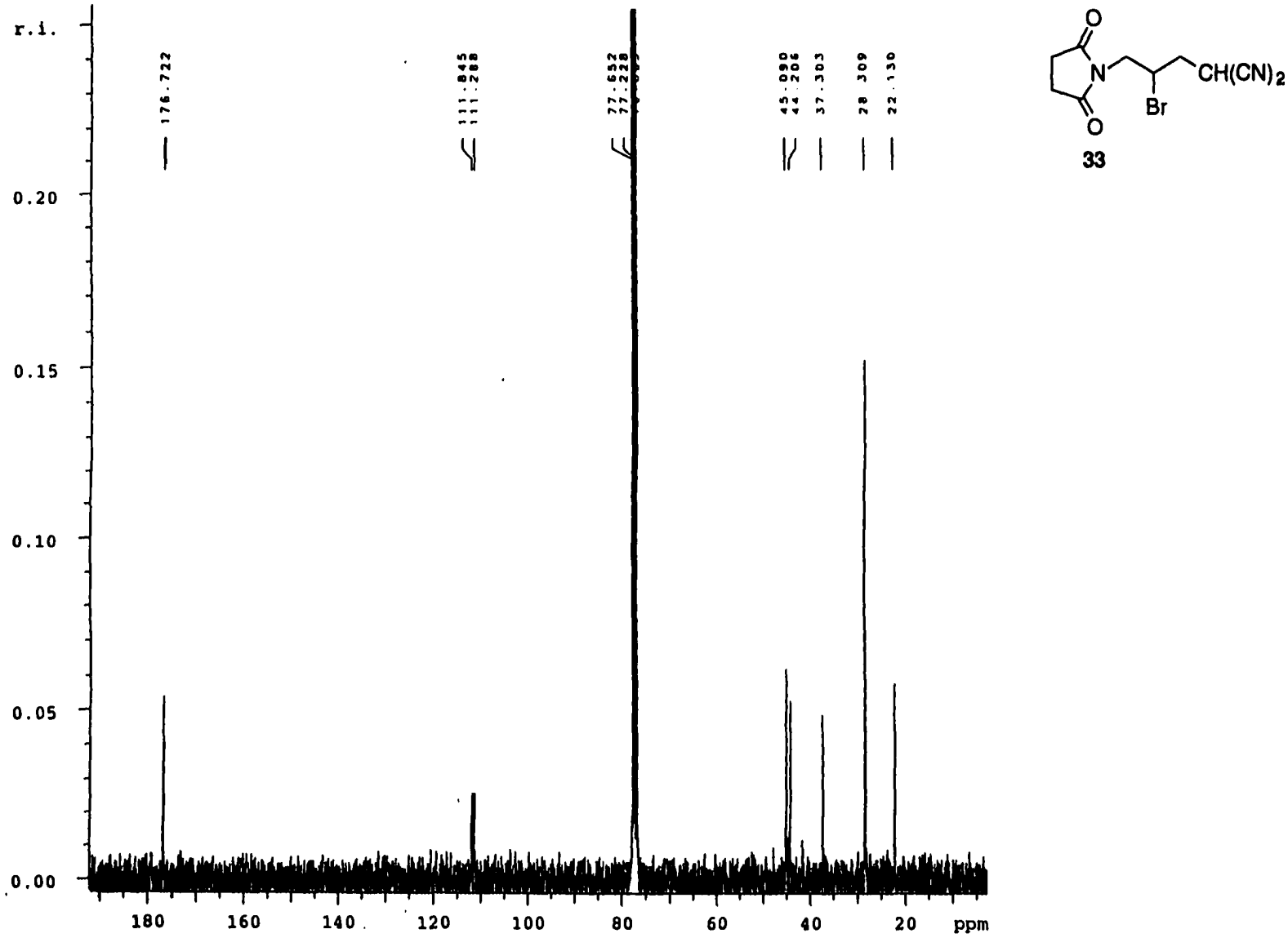
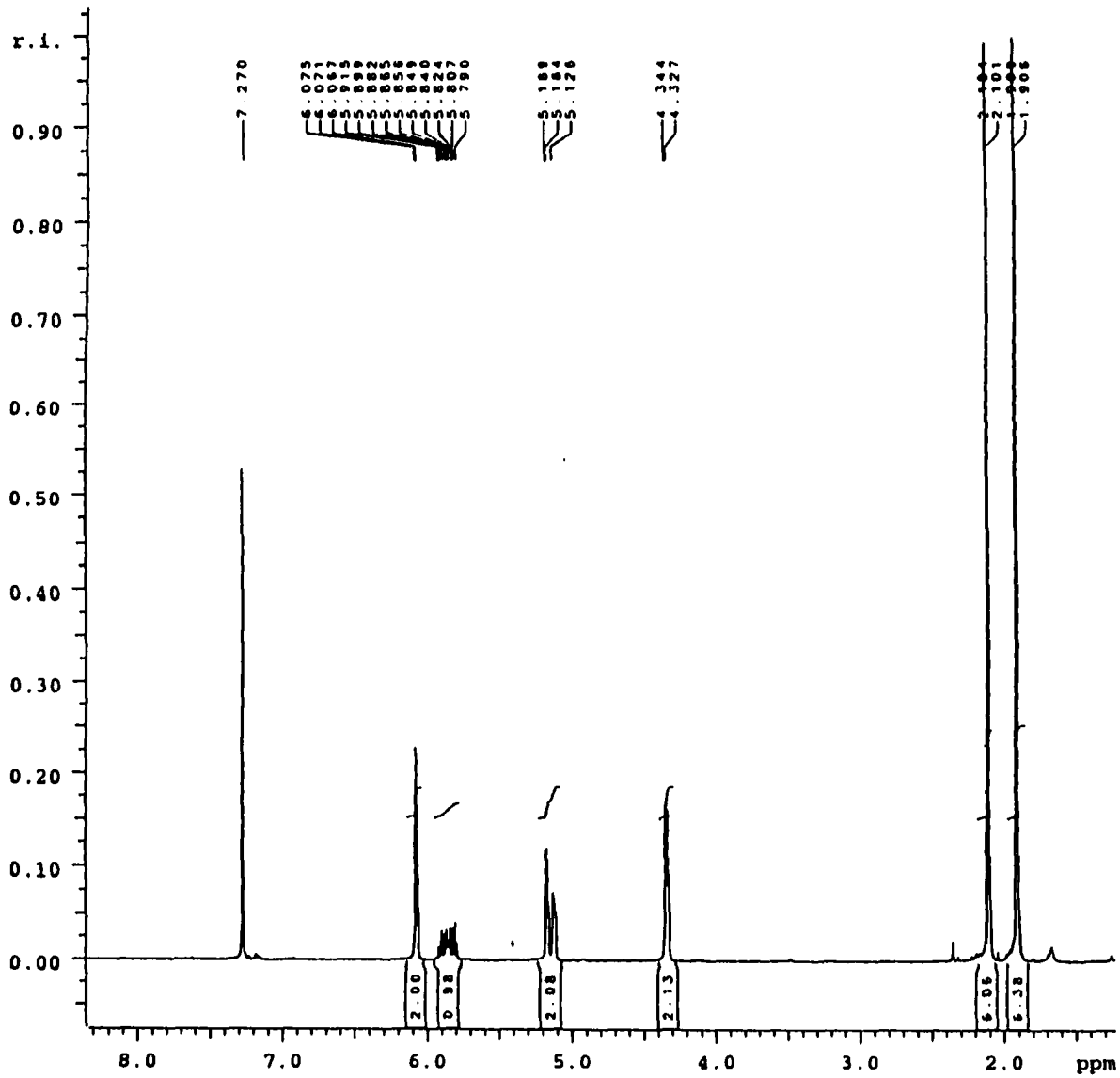


Figure 1A-6. ^{13}C NMR spectrum of compound **33**.



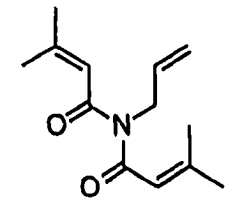


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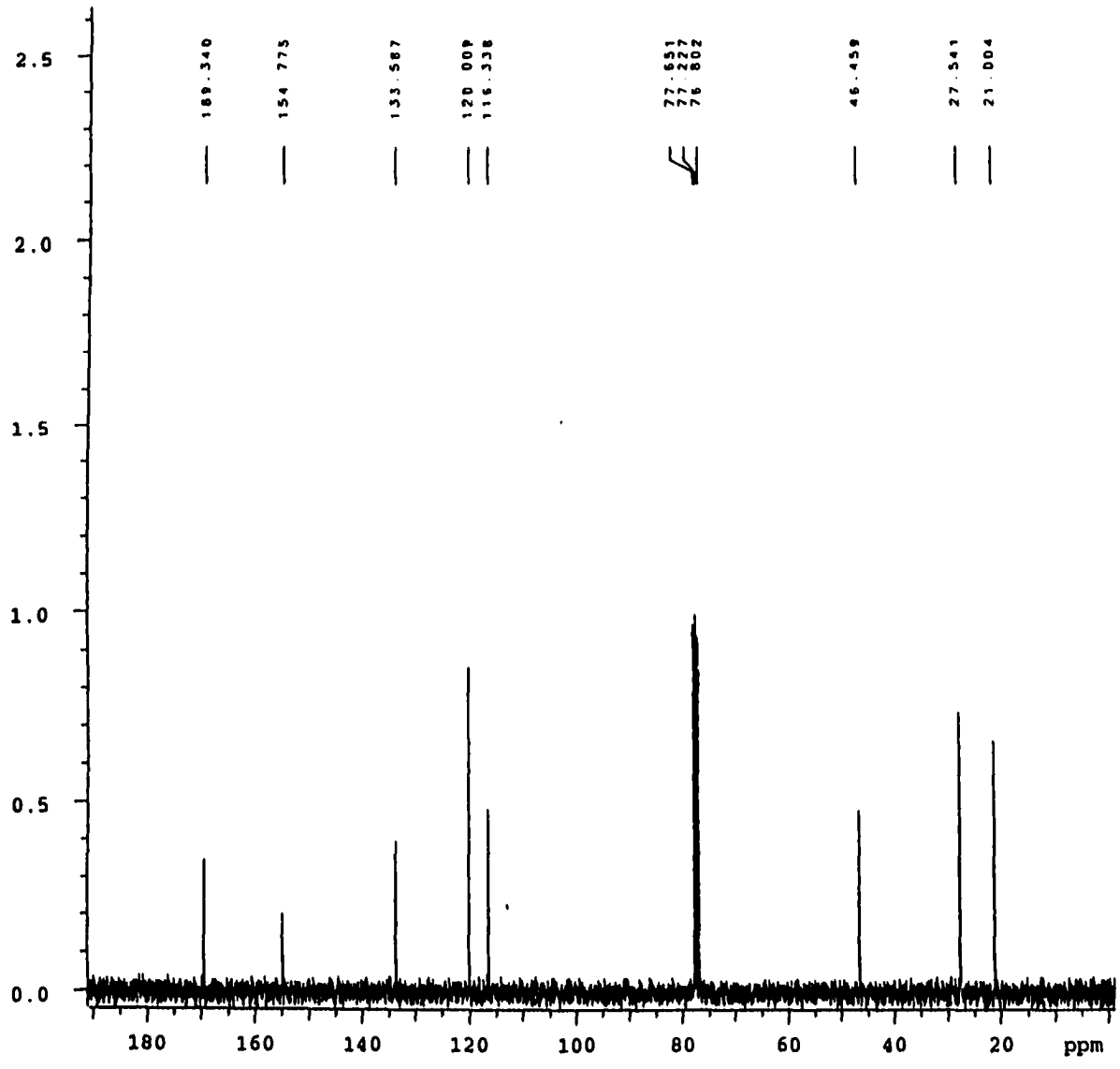
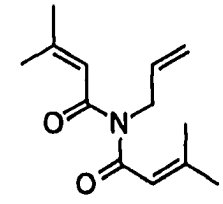
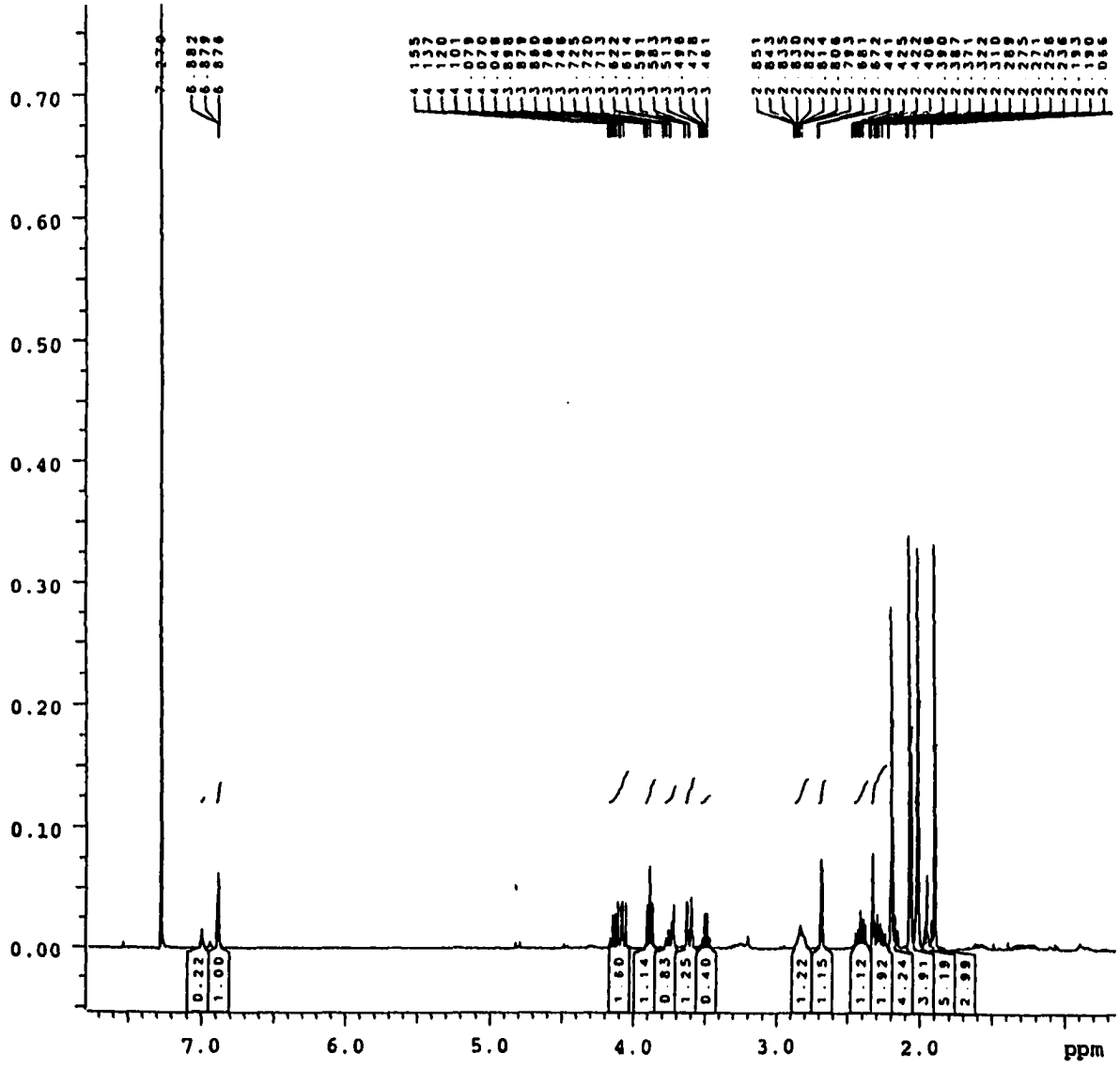
Figure 1A-7. ^{1}H NMR spectrum of compound **38**.

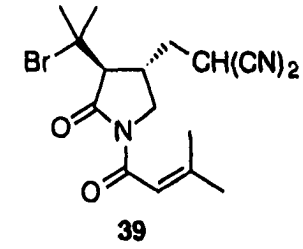




38

Figure 1A-8. ^{13}C NMR spectrum of compound **38**.





39

Figure 1A-9. ^{1}H NMR spectrum of compound **39**.

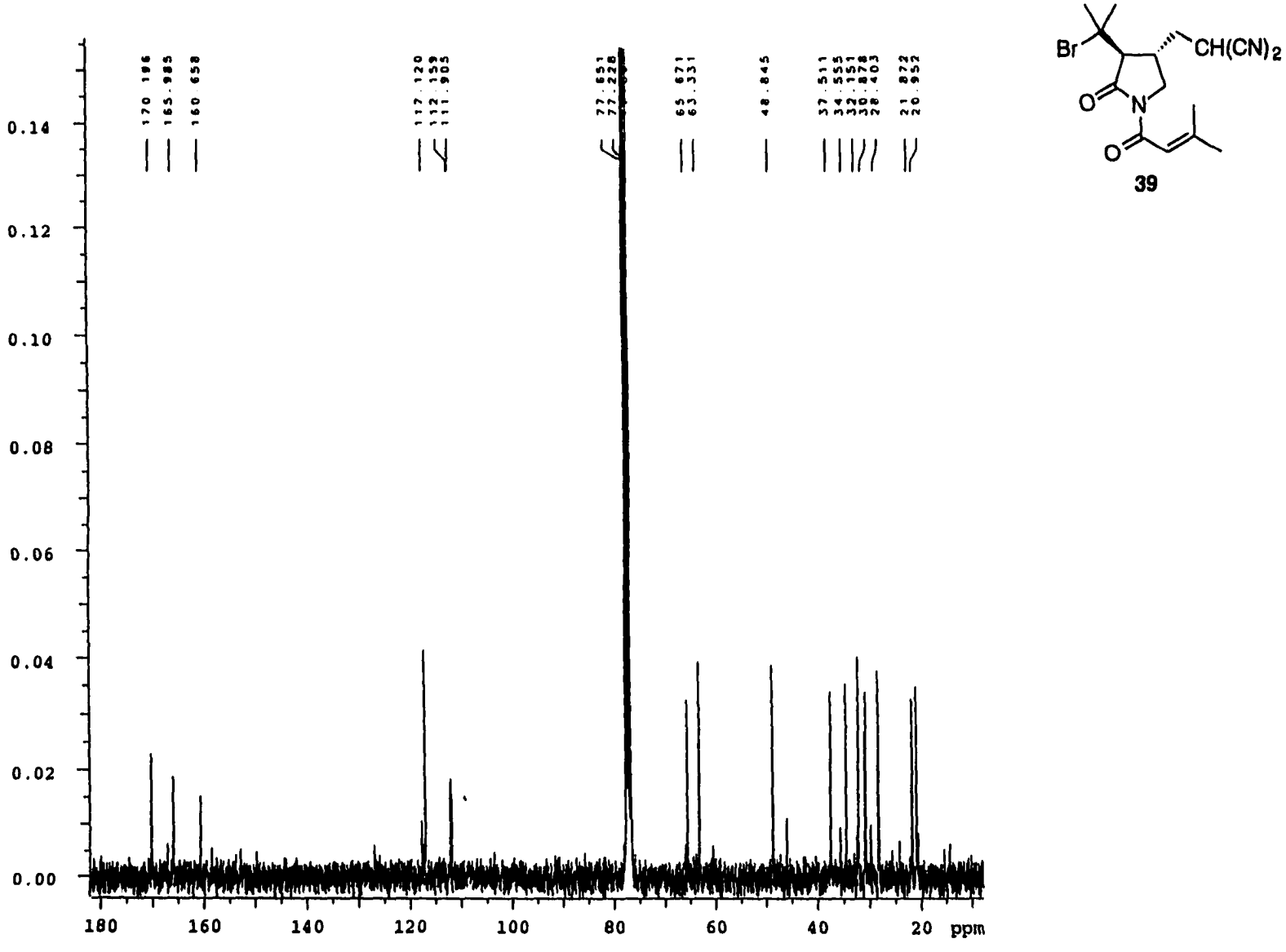


Figure 1A-10. ^{13}C NMR spectrum of compound **39**.

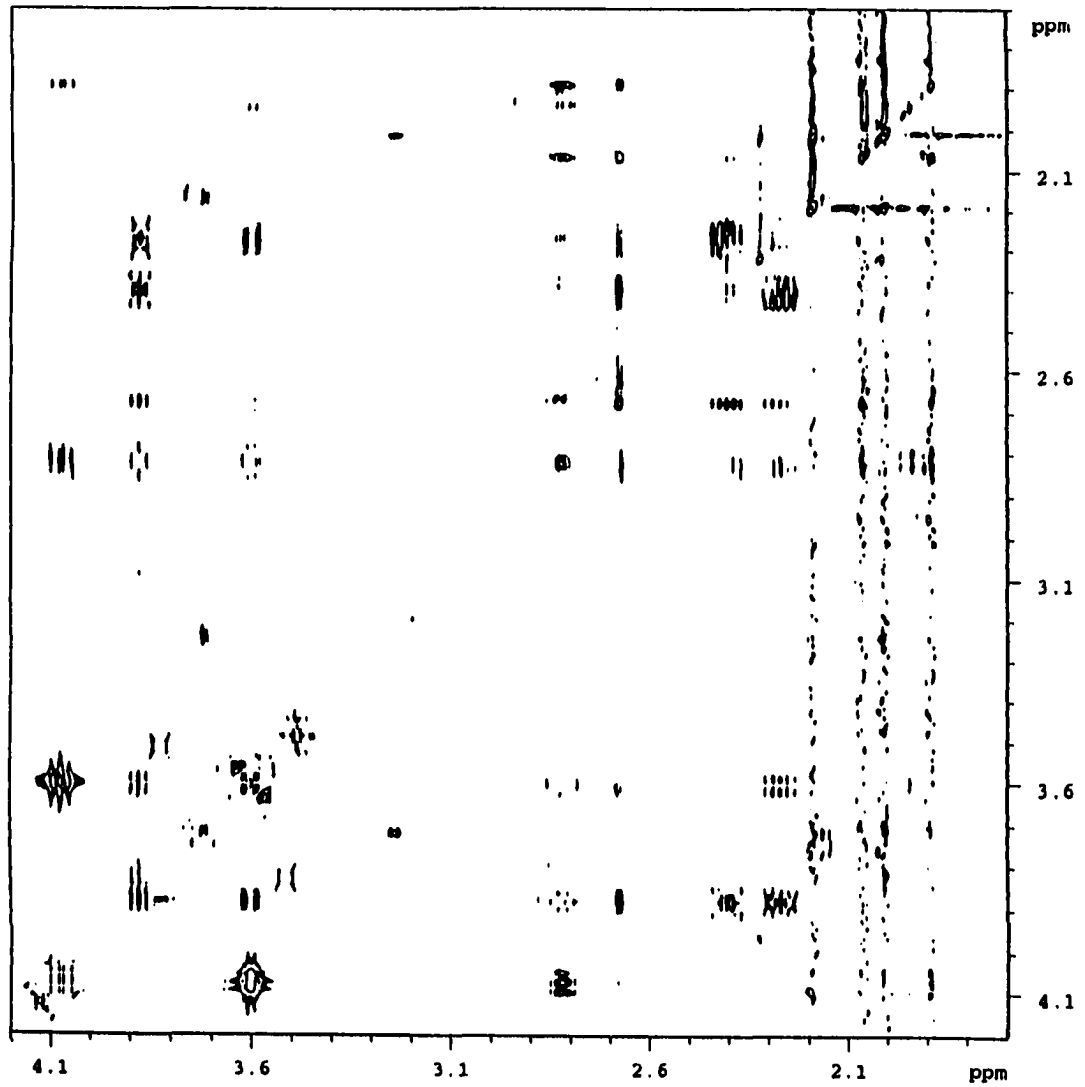
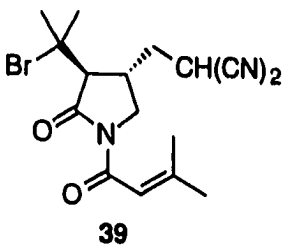


Figure 1A-11. ^{1}H-^{1}H NOE spectrum of compound **39**.



39

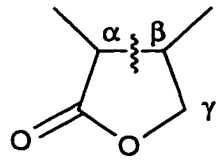
CHAPTER II. LACTONE FORMATION IN THE ADDITION OF BENZENESULFONYL BROMIDE TO DIENES AND ENYNE ESTERS

A paper, portions of which were published on the Journal of Organic Chemistry*

Chen Wang and Glen A. Russell

Introduction

The γ-lactone skeleton is present in a wide variety of bioactive natural products,[1] and functionalized lactones are versatile intermediates for the synthesis of stereo-defined acyclic compounds and other natural products.[2] The synthesis of γ-lactones can be achieved through many routes,[3] which include the lactonization of hydroxy acids, Baeyer-Villiger oxidation, the insertion of a carbonyl group by transition metals, etc.[4]



In recent years, assembly of γ-lactones by formation of the C_α - C_β (or C_3 - C_4) bond has drawn attention due to its potential advantage over other routes. Lu reported the Pd-catalyzed enyne cyclization as a convenient method to make α-alkylidene-γ-butyrolactone derivatives (Scheme 1).[5] Also, radical cyclization methodology has been explored in this field.[6] In most radical cyclization reports, a carbamoyl radical, generated from its α-derivatives under thermolysis, photolysis, or the mediation of Cu^+, Fe^o, Mn^{3+}, intramolecularly adds to a C=C or C≡C bond in a 5-exo mode (Scheme 2).

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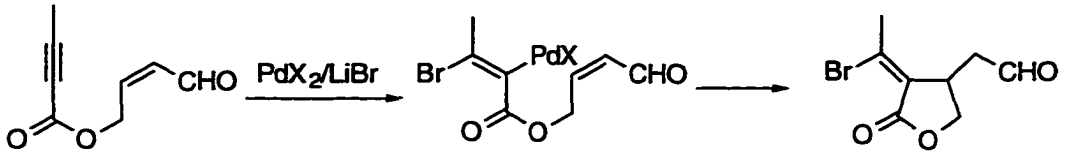
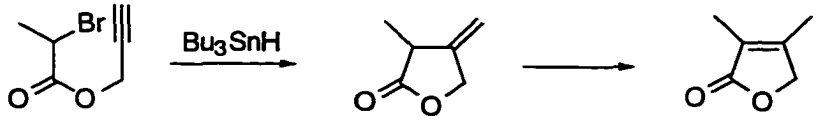
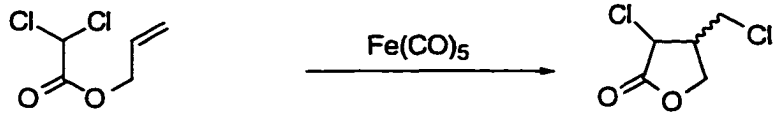
Scheme 1



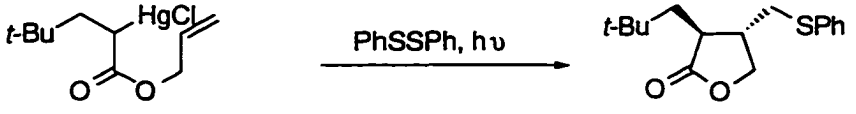
Scheme 2



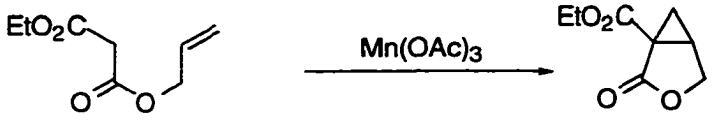
(ref. 6a)



(ref. 6b)



(ref. 6c)



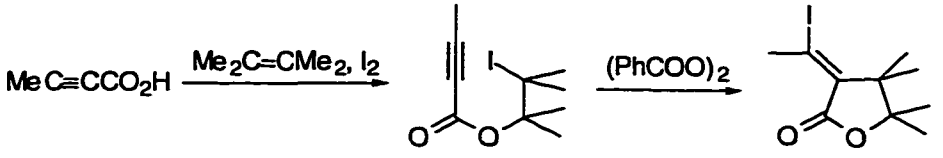
(ref. 6d)

It is interesting to notice one similarity among these reports in Scheme 1 and 2: the cyclizations proceed from C_α to C_β ($C_\alpha \rightarrow C_\beta$). We only found one example of a radical cyclization proceeding from C_β to C_α ($C_\beta \rightarrow C_\alpha$) to form lactones (Scheme 3).[7] We think this $C_\beta \rightarrow C_\alpha$ cyclization can provide a new approach to the γ-lactone skeleton with different functionality and therefore needs to be further explored.

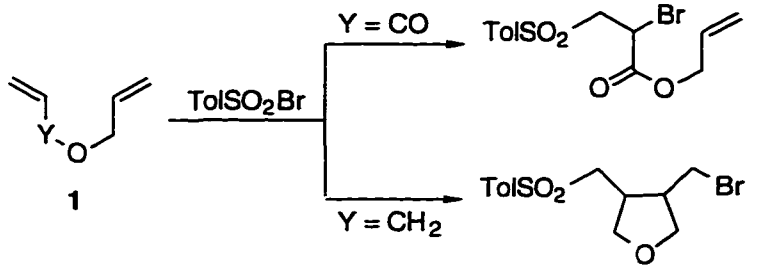
In Lu's report,[5] lactones are synthesized from enyne esters which can be conveniently made. While lactams can be made from unsymmetric diene amides like allylacrylamide through radical additions and cyclizations in one step,[8] similar attempts to make lactones from dienes like allylacrylates failed.[9] It was reported that the carbonyl group significantly slows down the

cyclization rate of the corresponding adduct radical of a diene ester (**1**, Y=CO) compared to that of a diene ether (**1**, $Y=CH_2$). The addition of tosyl bromide to allylacrylate gave only low yield of acrylic C=C monoadduct along with other telomers or polymer (Scheme 4).

Scheme 3



Scheme 4

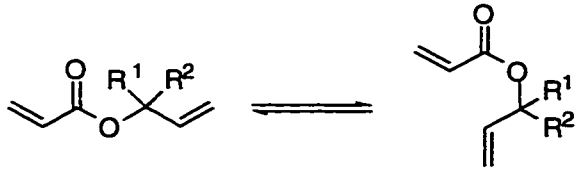


This observation is rationalized as the diene ester (**1**, Y = CO) exists primarily in an s-trans conformation at room temperature, while the cyclization process requires an s-cis conformer. It is estimated that for methyl acetate, its s-trans conformer is ~ 8.5 kcal/mol more stable than its s-cis conformer, and the interconversion barrier is about 10 to 15 kcal/mol.[10] Curran reported that in order to observe intramolecular cyclization from the α-carbamoyl radical to allyl C=C bond of allyl esters, reactions should be conducted in very low concentration (~0.003 M) and at high temperature (80 °C).[11]

It has been found that the additions of an arylsulfonyl halide to *N*-allyl acrylamides leads to γ-lactams as long as the second alkyl substituent on the amide N is bulky enough to ensure the cyclization-required s-cis conformer.[9] Conformer population of diene esters can be influenced by the gem-dialkyl effect or the Thorpe-Ingold effect.[12] Generally, this effect refers

to the acceleration of a cyclization due to the substitution of alkyl groups for the hydrogen atoms on the carbons in the chain that links the two reactive sites.[13] Russell reported that gem-dialkyl groups can increase the population of the s-cis conformer (**2** as R^1, R^2 are alkyl groups) and reduce the barrier of the s-trans to s-cis interconversion (Scheme 5).[6c]

Scheme 5



2, s-trans **2**, s-cis

We have explored the possibility of using the gem-dialkyl effect to promote γ-lactone formation from diene and enyne esters. Since the sulfonyl group is a versatile functional group in organic synthesis,[14] we investigated the addition of $PhSO_2Br$ to allyl ester **2** with appropriate R^1 and R^2 alkyl substitutents, so that both sulfonyl and bromide groups can be incorporated into the final lactones. Also, for ester **2**, the allyl C=C bond is more electron-rich than the acrylic C=C bond. Therefore we want to find out whether polar effects can control the chemoselectivity of attacking radicals between an acrylic C=C bond and an allyl C=C bond, so as to achieve both $C_\alpha \rightarrow C_\beta$ and $C_\beta \rightarrow C_\alpha$ cyclization processes.

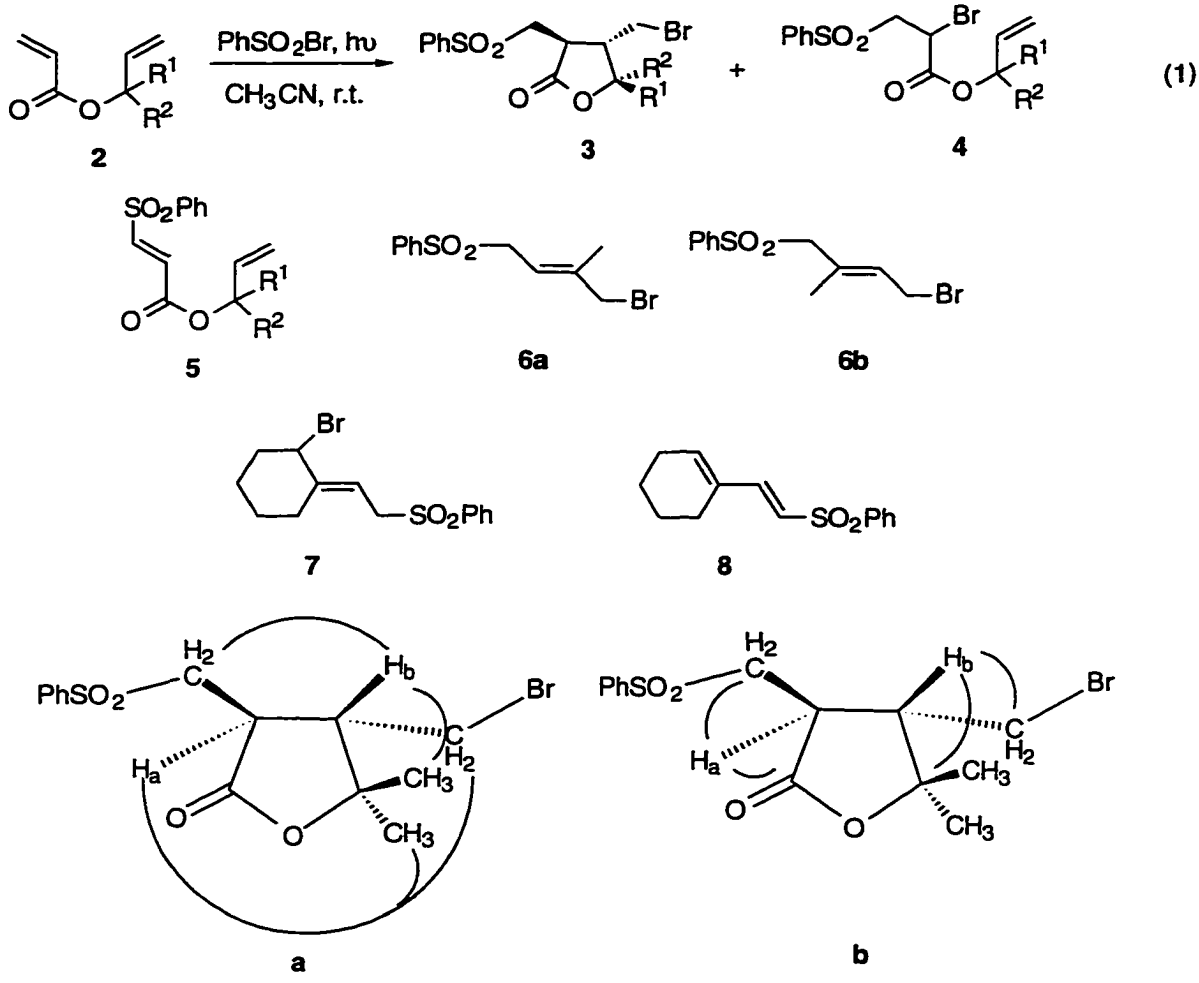
Results and Discussion

1. Addition of $PhSO_2Br$ to Acrylates

Table 1 summarizes the results of the addition of $PhSO_2Br$ to allyl aryllates **2** (eq 1). Reactions were conducted in acetonitrile under sunlamp irradiation at room temperature. The initial concentration of an ester was about 0.2 M with 1.1 equiv of $PhSO_2Br$.

The results in Table 1 show that with gem-dialkyl groups R^1 and R^2, γ-lactones can be formed stereoselectively from the diene esters. Only the *trans* $C_\alpha \rightarrow C_\beta$ cyclized lactones **3c-f** were isolated. The *trans* configurations of the lactones were determined by 2D COSY and

NOESY NMR spectroscopy. For example, the assignment of the *trans* configuration to **3c** is based on the observed NOE shown in Figure 1. No NOE was observed between $PhSO_2CH_2$ and $BrCH_2$. The NOE between H_a and H_b can not be used as a criterion because they are close in both *cis* and *trans* configurations. However, the trans isomer does have a weaker NOE between H_a and H_b than its *cis* isomer. Another possible structure with the $PhSO_2$ and Br groups reversed in **3c** was excluded by HMBC (Heteronuclear Multiple Bond Correlation) 2D spectroscopy. In the HMBC spectrum, H_a correlated to C=O (δ 173.00 ppm) and $PhSO_2CH_2$ (δ 56.63 ppm), while H_b correlates to $-C(Me)_2$ (δ 85.85 ppm) and $BrCH_2$ (δ 29.38 ppm).



(1)

Figure 1. 2D NOESY (**a**) and HMBC (**b**) spectra of lactone **3c**.

Table 1. Addition of $PhSO_2Br$ to Allyl Acrylates (2) under Sunlamp Irradiation in CH_3CN

2	R^1	R^2	products (yield %[a])			
2a	H	H	**5a** (15)			
2b	Me	H	**5b** (23)			
2c	Me	Me	**3c** (54, 74[b])		**6**[c] (31)	
2d	*i*-Pr	*i*-Pr	**3d** (30, 56[b])			
2e	$-(CH_2)_5-$		**3e** (26, 55[b])		**7** (24)	**8** (10)
2f	*t*-Bu	H	**3f** (18, 41[b])	**5f** (53, 15[d])		
2g	$-CH=CH_2$	H		**5g** (23)		

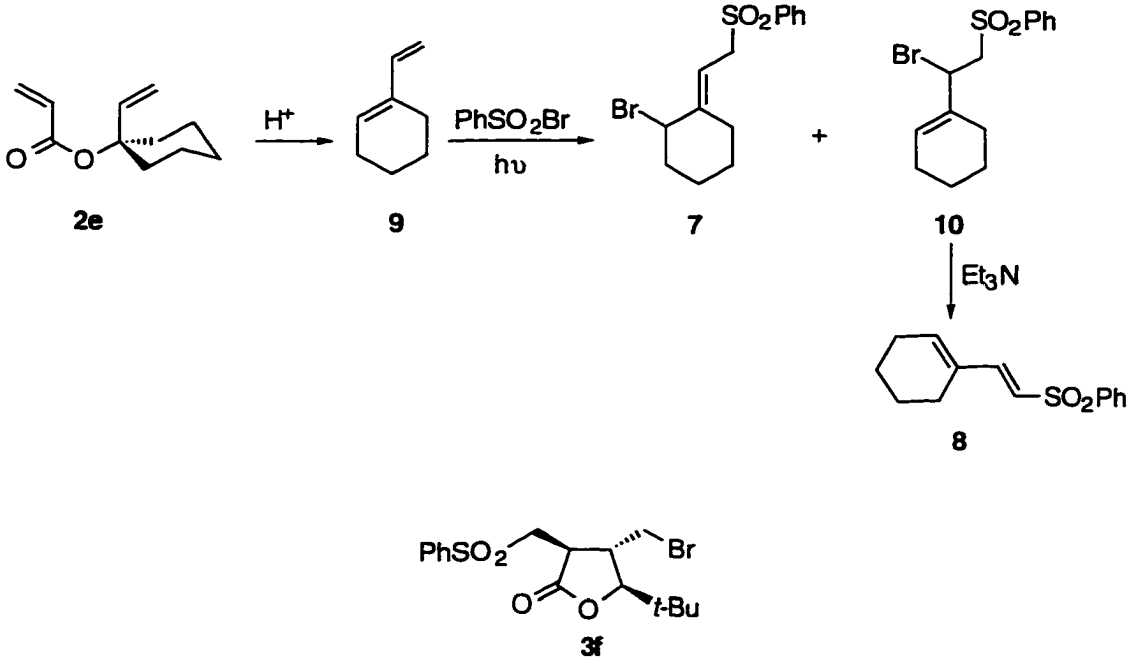
[a] Isolated yields based on the starting esters. [b] Yields of the reactions with 3 mol % of pyridine. [c] Compound **6** is an inseparable mixture of **6a** and **6b** in a ratio of 1/4.[15] [d] Yields of the reaction diluted to 0.05 M initially.

Uncyclized monoadducts **4** partially dehydrobromonated during TLC separation. Treatment of **4** with triethylamine (TEA) at room temperature yielded sulfone **5** quantitatively.

Products **6**, **7**, and **8** come from the addition of $PhSO_2Br$ to dienes liberated from the corresponding tertiary esters. Since the $PhSO_2Br$ sample inevitably contains a trace of acid, the R_1 and R_2 groups facilitate the acid-catalyzed hydrolysis and dehydration of the tertiary esters. We have found that adding 3 mol % of pyridine to the reaction mixture increases the yields of **3c-e** to 74%, 56%, and 55%, respectively, with decreased yields of **6**, **7**, and **8**, respectively. We have also confirmed that isoprene was generated when **2c** was mixed with $PhSO_2Br$ and kept in the dark at 40 °C for one hour. Authetic isoprene reacted with $PhSO_2Br$ under similar condition to yield **6** in 93% with the same ratio of **6a/6b**.[15] Similarly, **7** and **8** may come from the the addition of $PhSO_2Br$ to olefin **9**, which was liberated from **2e** as shown in Scheme 6. Since **10** and **3e** are inseparable on TLC, the mixture of **10** and **3e** was

treated with triethylamine for 1 h at r.t. and then **8** was isolated from **3e** by TLC. One interesting product is the lactone **3f** produced from **2f**. Only one diastereoisomer was found with the *tert*-Bu group trans to -CH_2Br and cis to -CH_2SO_2Ph. The stereogenic center at the γ-position induces the configurations of both α and β stereogenic centers in one step. Though the yield of **3f** was only 18%, it could be increased to 41% and the yield of **5f** was decreased to 15% when the concentration of the reaction mixture was diluted to one-fourth of that reported in Table 1. Obviously, a reaction conducted at low concentration favors intramolecular cyclization.

Scheme 6



2e **9** **7** **10** **8** **3f**

2. Competition Experiments

The chemoselectivity shown in Table 1 is another interesting point. The electrophilic $PhSO_2$• radical added to the acrylic C=C bond preferentially over the allyl C=C bond. No allyl C=C bond adduct was found. Similar chemoselectivity was also observed in reactions of arylsulfonyl halide with allylacrylamides. This suggests that polar effects cannot control the

chemoselectivity of the addition step. The relative reactivity of the acrylic C=C bond vs the allyl C=C bond towards the sulfonyl radical is the key to understand the chemoselectivity shown in eq 2. Similar to what we have done in Chapter 1, the relative reactivities for the addition of a sulfonyl radical to C=C bonds are quantitified by using eqs 2 - 4, where $[M_1]_0$, $[M_2]_0$ are the initial concentrations of olefins M_1 and M_2, and $[M_1]_t$, $[M_2]_t$ are the concentrations of olefins M_1 and M_2 at time t.[16]

$$PhSO_2^{\bullet} + \begin{cases} M_1 \xrightarrow{k_1} \text{Radical adduct 1} \\ M_2 \xrightarrow{k_2} \text{Radical adduct 2} \end{cases} \quad (2)$$

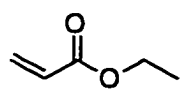
$$\alpha\,(M_1/M_2) = \{\log[M_1]_0 - \log[M_1]_t\} / \{\log[M_2]_0 - \log[M_2]_t\} \quad (3)$$

$$k_1/k_2 = \alpha\,(M_1/M_2) \quad (4)$$

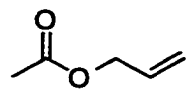
Several reactions were set up in NMR tubes with CD_3CN as the solvent and $(Me_3Si)_2O$ as the internal standard. Ethyl acrylate (**11**), allyl acetate (**12**), and 1,1-dimethyl-2-propenyl acetate (**13**) were selected as model compounds to measure α (**11/12**), α (**13/12**) (Table 2 and Figure 2).

Although the $PhSO_2^{\bullet}$ radical is characterized as an electrophilic radical,[16] it adds to the acrylic C=C bond of ester **11** 1.6 times faster than to the allyl C=C of ester **12**. This is contrary to what is expected from the consideration of polar effects. However, this difference is much smaller than that found from *N*-allyl acrylamide.

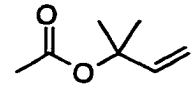
Ester **13** is less reactive than ester **12** in the presence of a trace of pyridine but more reactive without it. However, no constant relative reactivity ratio α can be obtained from the competition reaction of **13** vs **12**. This is probably because they react with $PhSO_2Br$ through different mechanisms. While **12** reacts with $PhSO_2Br$ to give the normal allyl C=C adduct, **13** is hydrolyzed and dehydrated in the presence of the trace of acid inevitably associated with $PhSO_2Br$. In fact, only **6** (**6a** and **6b**) was obtained from the reaction of **13**. The reactivity of **13** was decreased in the presence of 3 mol % of pyridine.



11



12



13

Table 2. Measurement of α (11/12) and α (13/12)

		reaction time (min)			
entry[a]	α (M_1/M_2)	15	30	45	60
1	α (**11/12**)	1.59	1.62	1.58	1.51
2	α (**13/12**)	1.27	1.22	1.43	1.58
3	α (**13/12**)	0.46	0.45	0.60	0.73

[a] One run for each entry. Initial molar ratio for entries (by ^{1}H NMR): (1) **11** : **12** : $PhSO_2Br$ = 1.00 : 1.16 : 1.22. (2) **13** : **12** : $PhSO_2Br$ = 1.00 : 1.33 : 1.86. (3) **13** : **12** : $PhSO_2Br$ = 1.00 : 1.34 : 1.78 with 3 mol % of pyridine. The concentration of **12** was 0.20 M initially for all entries.

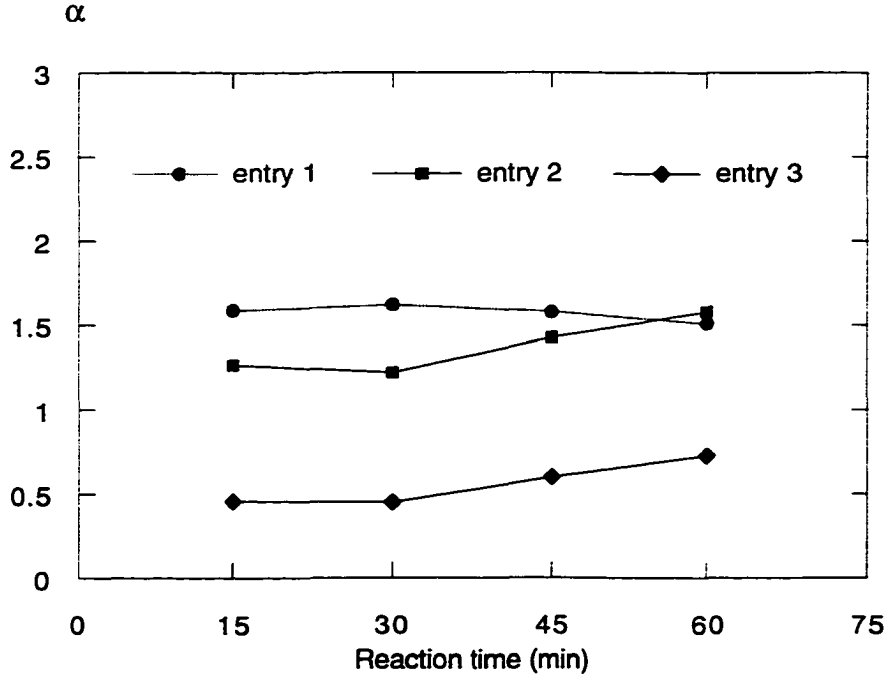
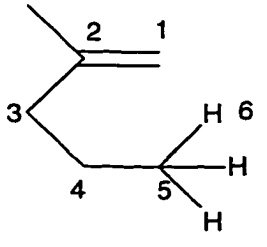


Figure 2. Relative reactivities of **11/12** and **13/12**.

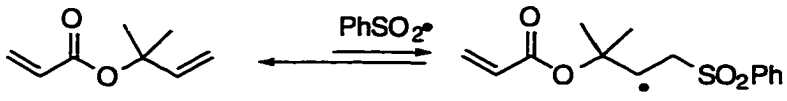
Overall, our competition experiments suggest that the allyl C=C of **2** is much less reactive than the acrylic C=C towards $PhSO_2$• when R_1 and R_2 are alkyl groups, and the acid-catalyzed hydrolysis and dehydration of the tertiary esters are inhibited by the presence of the trace of pyridine. The significant effect of the R^1 and R^2 groups on the rate of addition of $PhSO_2$• to allyl C=C bond is probably similarly to the steric effect introduced by remotely positioned groups reported before.[17] This remote steric effect was first postulated by Newman as the "rule of six",[17c] which means a reaction at an unsaturated linkage is sterically hindered by the atoms or groups positioned six atoms from the site at which the reaction is taking place. This rule is also known as the alkyl substituents at C-4 inhibit the addition of attacking radicals on the C=C bond at C-1 position.

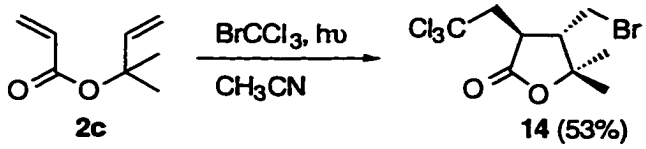
However, in **2c**, the two methyl groups are at C-3 instead of C-4 position. We think, first, the methyl groups still hinder the addition of $PhSO_2Br$ to the allyl C=C bond, and second, the methyl groups probably also hinder the abstraction of Br from $PhSO_2Br$ by the adduct radical, so the reversed step probably becomes significant (Scheme 7). The reversability of the addition of the arylsulfonyl radical to C=C bonds has been found in many cases.[18] Overall, reactivity of the allyl C=C bond in ester **2** is strongly decreased by the gem dialkyl groups R^1 and R^2.

Another electrophilic radical Cl_3C• has been tested in our work (eq 5). It gives the same chemoselectivity as $PhSO_2$• does. It is unlikely that the electrophilicity of the attacking radical itself can shift the chemoselectivity of addition from an acrylic C=C bond to an allyl C=C bond.



Scheme 7



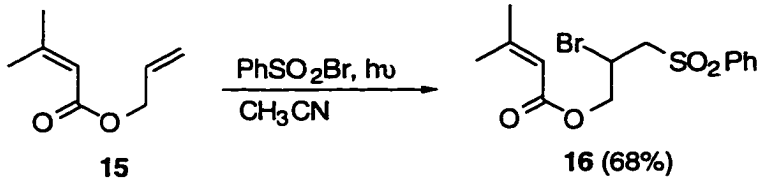


(5)

3. Addition of $PhSO_2Br$ to β-Substituted Allyl Acrylates

From the former results, we know that polar effects cannot control the chemoselectivity in the addition of electrophilic radicals towards the acrylic C=C bond and the allyl C=C bond of ester **2**. We tried to realize $C_\beta \rightarrow C_\alpha$ cyclization in the reactions of β-substituted allyl acrylates.

Reaction of ester **15** with $PhSO_2Br$ yielded only uncyclized allyl C=C adduct product **16** (eq 6), which means the bromine transfer from $PhSO_2Br$ to the allyl C=C bond adduct radical of **15** is much faster than the $C_\beta \rightarrow C_\alpha$ cyclization process. So, for the $C_\beta \rightarrow C_\alpha$ cyclization to be realized, either the $C_\beta \rightarrow C_\alpha$ cyclization of the allyl C=C bond adduct intremediate should be increased, or the halide transfer from arylsulfonyl halide should be decreased.

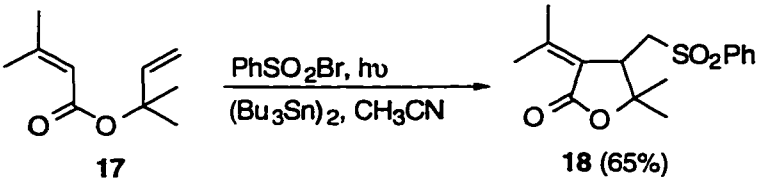


(6)

From the reaction of ester **17**, the $C_\beta \rightarrow C_\alpha$ cyclized product **18** was obtained in good yield (eq 7). Stereoselectivity of the $C_\beta \rightarrow C_\alpha$ cyclization cannot be measured because the initially formed lactone loses HBr readily to give **18**. Compared to the result given in eq 6, this result shows that the gem-dimethyl groups on the allyl chain accelerate the rate of the $C_\beta \rightarrow C_\alpha$ cyclization significantly. It was found that with the addition of 20 mol % of $(Bu_3Sn)_2$, the reaction proceeded faster and less amount of **6** was formed. This is probably

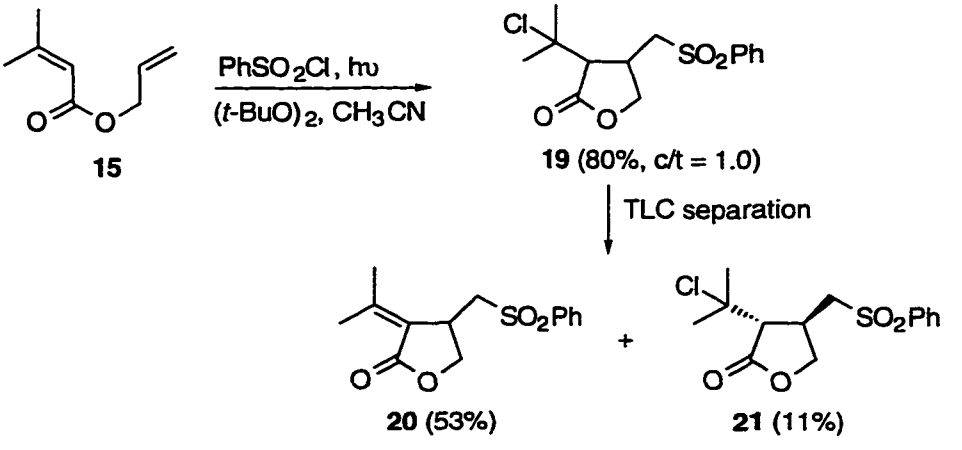
because, first, $(Bu_3Sn)_2$ is a radical initiator and the $C_\beta \rightarrow C_\alpha$ cyclized tertiary radical from **17** probably can not propagate the radical chain process efficiently. Second, $(Bu_3Sn)_2$ is a proton acceptor which inhibits the acid-catalyzed hydrolysis of the tertiary ester.

The bromine transfer from $PhSO_2Br$ is estimated to be about 190 times faster than the chlorine transfer from $PhSO_2Cl$[16b, 19] which accounts for the observation of a good yield of **19** from the reaction of **15** with $PhSO_2Cl$. However, the S-Cl bond is more difficult to be broken under photolysis, and a prolonged reaction time is needed. The *cis/trans* ratio of **19** is about 1/1 (by NMR), which is quite different from that of the $C_\alpha \rightarrow C_\beta$ cyclization where the trans product is predominant. However, **19** was very liable and lost HCl readily during TLC separation and finally an inseparatable mixture of compound **20** and **21** was obtained. Since the configuration of compound **21** was identified by NOESY as *trans*, *cis* **19** was probably more labile than *trans* **19** and lost HCl completely on TLC plates (Scheme 8).



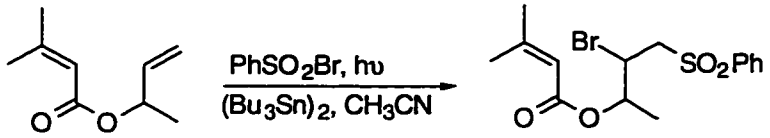
(7)

Scheme 8

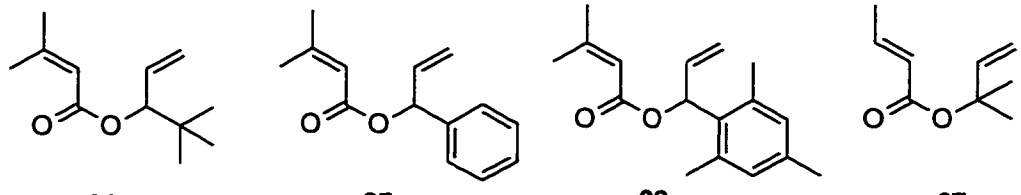


The effect of one alkyl group on the allyl part on the $C_\beta \rightarrow C_\alpha$ cyclization has also been investigated. We have observed that only uncyclized product **23** is obtained from the reaction of ester **22** in the presence of $(Bu_3Sn)_2$, which suggests that both of the two gem-dialkyl group are essential (eq 8). Also, no significant reaction was observed from esters **24**, **25** or **26**, which means a bulky group at the allyl part strongly hinderes the addition of $PhSO_2Br$ to the corresponding allyl C=C bond. This postulation is consistent with the chemoselectivity observed in the reaction of $PhSO_2Br$ with **2f** (Table 1). Both of the alkyl groups on the β position of the acrylic C=C bond of **17** are essential as indicated by the reaction of ester **27** with $PhSO_2Br$, which gave only messy products including a low yield of **6**.

Since reversibility of a $C_\beta \rightarrow C_\alpha$ cyclization process may be a reason for the nonexistence of cyclized products, we found the reaction of ester **28** with $PhSO_2Br$ formed only the uncyclized product **29**, even though the proposed cyclized intermediate **30** could undergo a facile elimination step (eqs 9 and 10).

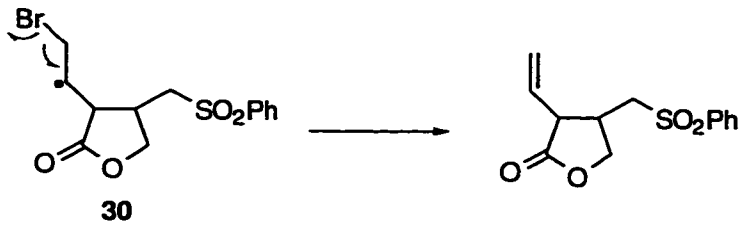


22 **23** (68%, syn/anti = 1) (8)



24 **25** **26** **27**

28 **29** (73%) (9)



30 (10)

The significant acceleration of the rate of the $C_\beta \rightarrow C_\alpha$ cyclization by two alkyl groups at the β position of the acrylic C=C bond may come from three reasons (Scheme 9). First, the two alkyl groups can make the cyclized radical thermodynamically more stable, which should favor the $C_\beta \rightarrow C_\alpha$ cyclization. Second, without the two alkyl substituents, the LUMO coefficient on the α-carbon of the acryl C=C bond is much smaller compared to that of the β-carbon due to the electron-withdrawing effect of carbonyl group.[20] The two alkyl groups can increase the LUMO coefficient on the α-carbon dramatically.[21] Third, without the two alkyl groups, the acrylic C=C bond is conjugated with the carbonyl group to achieve a planar conformation which makes the acrylic C=C bond less reactive. The two alkyl groups at β position can make the acrylic C=C bond out of the plane of the C=O bond, making the orbital interaction easier (Figure 3). It was estimated that in mesityl oxide, the C=C bond plane is about 38° out of the C=O bond plane.[22]

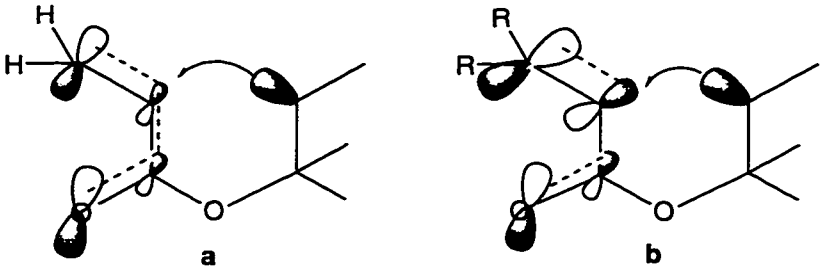
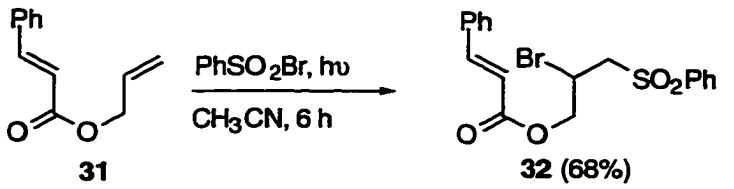
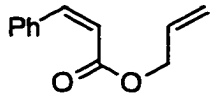


Figure 3. Conformation comparison of an acrylate (**a**) and a β-substituted acrylate (**b**).

Some interesting results are obtained from the reactions of β-phenyl acrylates. Eq 12 showed that one phenyl group is not enough to promote the $C_\beta \rightarrow C_\alpha$ cyclization. Even with $PhSO_2Cl$, only isomerization of **31** to **33** was observed with the ratio of 1.05/1 (**31/33**) after 5 days, and the rate of this isomeraization is about the same as that without $PhSO_2Cl$.

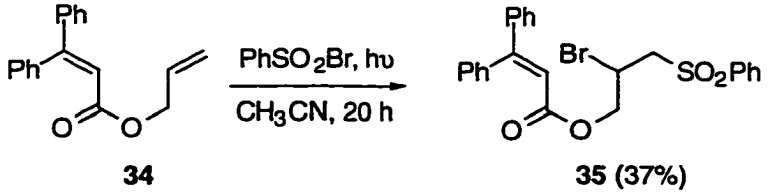


31 **32** (68%) (12)



33

However, the reaction of β,β-diphenyl allyl acrylate **34** with $PhSO_2Br$ generated only 37% yield of **35** in 20 h with 59% of **34** unreacted (eq 13). Doubling the reaction time only decreased the amount of **34** to 42% without increasing the amount of **35**. Compared to the fast well-behaved reactions of **15** and **31** with $PhSO_2Br$, the reaction of **34** is puzzling at first because the reactivities of the allyl C=C bonds in esters **15**, **31**, and **34** should be almost the same. We think that this puzzling observation can be understood as the initial adduct radical **36** undergoes a $C_\beta \rightarrow C_\alpha$ cyclization step efficiently to generate radical **37**. Radical **37** cannot abstract a bromine atom from $PhSO_2Br$ rapidly and is unlikely to continue a chain process (Scheme 10).[23] So, the reaction of **36** to **37** serves as a inhibition step for the formation of **35**. During the short reaction time, the concentration of $PhSO_2Br$ was relatively high so that the bromine abstraction by **36** can compete with the step of **36**→**37** and therefore **35** was formed. However, at a certain extent of the reaction, the concentration of $PhSO_2Br$ was so low that bromine abstraction by **36** is slower than the step of **36**→**37** and therefore **35** could not be formed further.

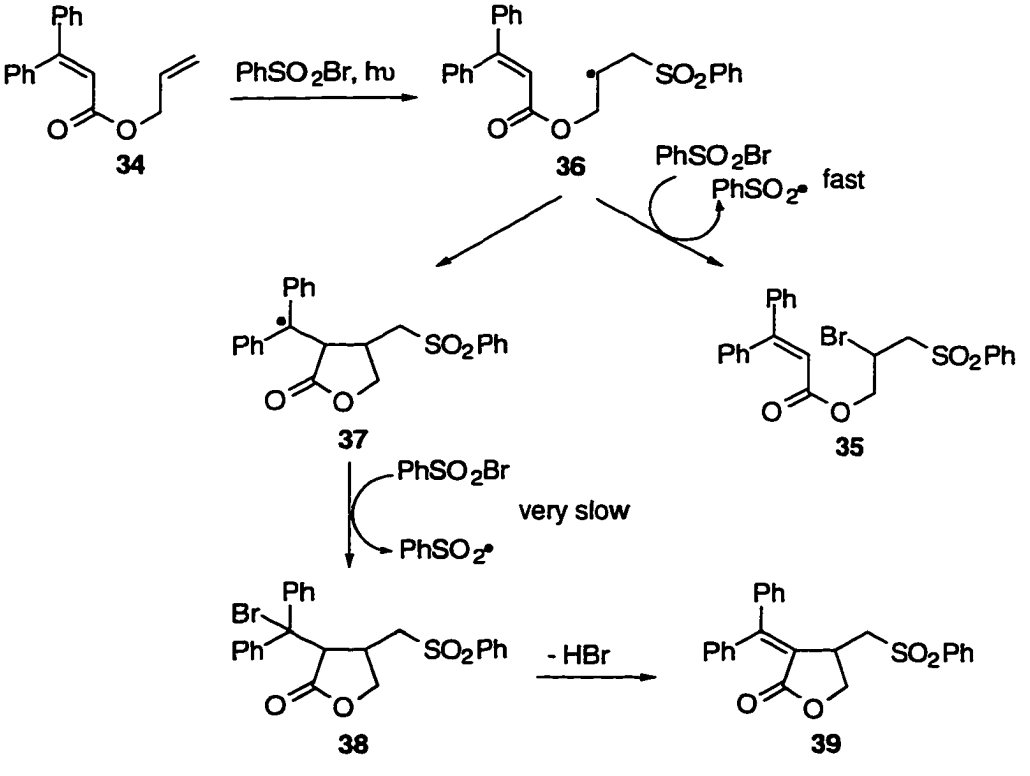


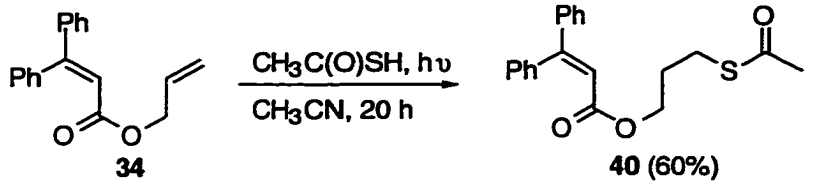
34 **35** (37%) (13)

Several reactions were conducted to confirm the proposal in Scheme 9. The reaction of **34** with $PhSO_2I$ could be useful because of the much faster iodine transfer than the bromine transfer from the corresponding benzenesulfonyl halides. However, $PhSO_2I$ is very labile and decomposes readily even when stored in the dark.[24] Another method to increase the rate of halide transfer step is to increase the concentration of $PhSO_2Br$. The reaction of **34** with 10 equiv of $PhSO_2Br$ under similar conditions yielded 83% of **35** (94% in NMR yield) in 4 h. In this case, the high concentration of $PhSO_2Br$ converted **36** to **37** rapidly.

The reaction of **34** with 1.0 equiv of $CH_3C(O)SH$ in 20 h yielded 60% of the uncyclized allyl C=C bond adduct **40** as well as 30% of the unreacted **34** (eq 14). This yield is higher than that of **35** in eq 13. Extending the reaction to 40 h did not increase the yield of **40**. This observation could be explained probably as the H-abstraction from $CH_3C(O)SH$ was a faster step than the bromine abstraction from $PhSO_2Br$ (see Chapter 1). However, for the same reason, this reaction failed to go to completion.

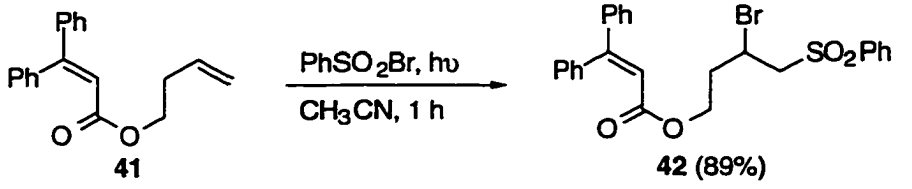
Scheme 9





(14)

Ester **41** was another good probe because a 6-exo cyclization is much slower than a 5-exo cyclization. The reaction of **41** with 1 equiv of $PhSO_2Br$ yielded 89% of **42** in only 1 h (eq 15). In this reaction, the initial adduct radical (similar to **36**) was expected to undergo the bromine abstraction step rather than the 6-exo cyclization step.

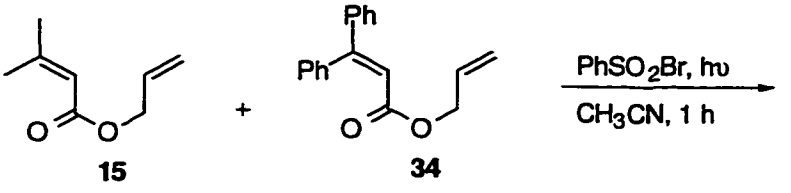


(15)

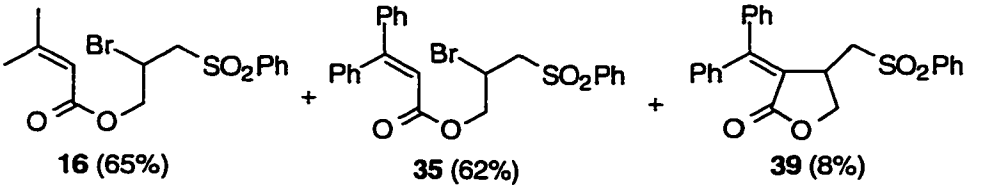
Compounds **38** and/or **39** are direct evidence for the $C_\beta \rightarrow C_\alpha$ cyclized intermediate **37**. However, they are not isolable from the reaction shown by eq 13 probably because of the low conversion of **34**. However, the reaction of the mixture of **15** and **34** with $PhSO_2Br$ in ratio of 0.5 : 0.5 : 1.0, where the concentration of $PhSO_2Br$ was the same as that in eq 6 or 13, yielded 8% of **39** as well as **16** and **35** (eq 16). Like compound **19**, compound **38** lost HBr during the TLC separation, therefore **39** was obtained. While $PhSO_2^\bullet$ can not be generated in a chain process from the reaction of **34** , it can be from the reaction of **15**. As for $PhSO_2^\bullet$, it adds to the allyl C=C bonds of **15** and **34** without preference, so the intermediate **37** can be generated and accumulate until it abstracts a bromine atom from $PhSO_2Br$. Since the yield of **39** is very low compared to **35**, we think there might be a reversible step like **37**→**36**. As we know, reversibility in a radical cyclization process has been observed in many systems.[25]

Another quantitative piece of evidence to support the mechanism shown in Scheme 10 is the initial kinetic chain length (KCL). KCL is the average number of reactant molecules

consumed or the product formed for every radical which initiates a chain reaction. It tells whether a reaction is a chain reaction or not, and can be caculated by using eq 17.



(16)



KCL = Initial reaction rate / Rate of initiation (17)

For eq 13, the initial reaction rate here was measured experimently as the rate of the formation of **35**. The rate of initiation is measured as the inhibition period in the presence of small known amount of a radical inhibitor, like di-*tert*-butyl nitroxide (DTBN). The progress can be conveniently monitored through ^1H NMR spectroscopy in CD_3CN with $(Me_3Si)_2O$ as the internal standard. Table 3 shows the results of eq 13 with or without DTBN.

In Figure 4, the initial reaction rate, or the slope of curve A at the beginning, is 0.0025 M/h. Since the inhibition period is 3.0 h with 20 mol % DTBN, the initiation rate is 0.0033 M/h. So its KCL is 0.75. The reaction shown in eq 13 is not a chain process. However, the KCL of the reaction shown in eq 5 is 8 as measured by the same method. So, the cyclization step involved for the formation of **39** indeed acts as a inhibition step for the consumption of **34**. Overall, we have confirmed the proposal shown in Scheme 9: the diphenyl groups at the β position of allyl acrylate greatly increase the rate of $C_\beta \rightarrow C_\alpha$ cyclizations. This effect is quite different from that of the dialkyl substituents in the 5-hexenyl cyclization. Newcomb and Curran reported that in 5-exo and 6-exo cylizations of all-carbon chains, terminal diphenyl groups can increase the cyclization rates by 2 orders of magnitude (Scheme 10).[26]

Table 3. Reaction of 34 with $PhSO_2Br$ for KCL Measurement[a]

reaction time	% yield of 35[b]	
(h)	without DTBN	with DTBN[c]
1.0	5.0	0.0
2.0	9.7	0.0
3.0	14.2	0.0
4.0	17.3	5.7
5.0	—	10.0

[a]-Photolysis of 0.05 M of **34** with 1.1 equiv of $PhSO_2Br$. [b] Yields in CD_3CN by ^1H NMR spectroscopy with $(Me_3Si)_2O$ as the internal standard. [c] 20 mol % of DTBN.

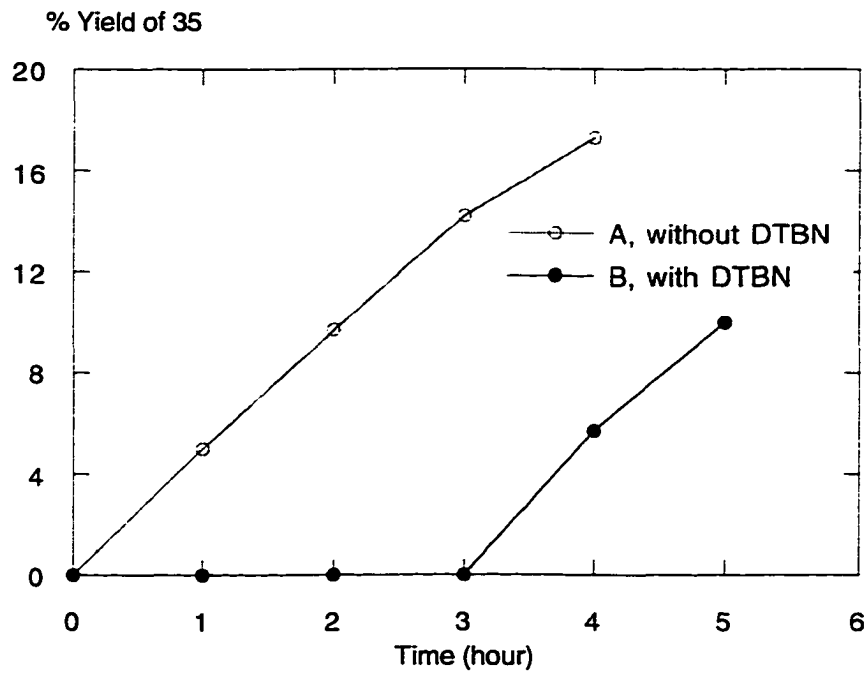
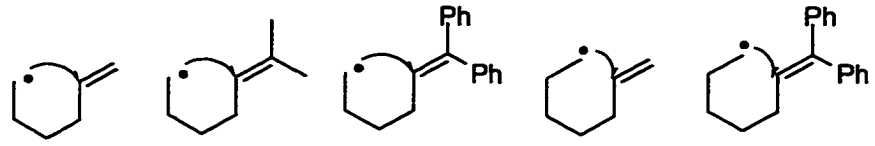


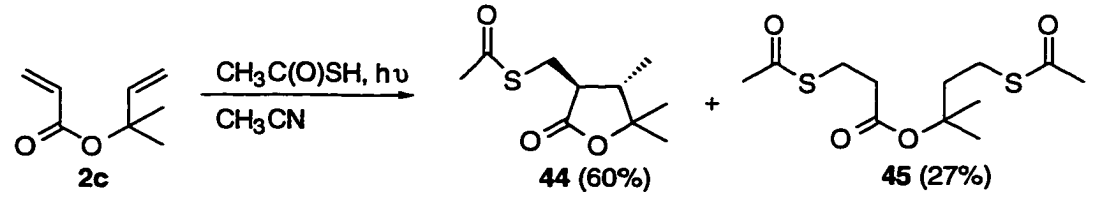
Figure 4. Measurement of the KCL of eq 13.

Scheme 10

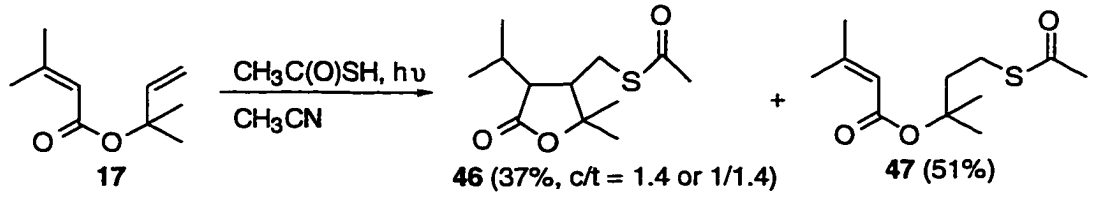


relative cyclization rates 1.0 2.4 200 0.05 4.5

In previous work, Russell estimated the rate constant $k_{\alpha\beta}$ of the $C_\alpha \rightarrow C_\beta$ cyclization from **2c** to be 5 x 10^5 /s.[6c] A comparison of cyclization rate constants $k_{\beta\alpha}$ and $k_{\alpha\beta}$ cannot be found. We think this comparison can be estimated from the reactions of **2c** and **17** with $CH_3C(O)SH$ (eqs 18 and 19). Both cyclized and uncyclized products were produced from the two reactions. The ratio of the yields of the cyclized to uncyclized products (**44/45**) of eq 18 is 2.2, and this same ratio (**46/47**) of eq 19 is 0.72. So it is concluded that the rate constant $k_{\alpha\beta}$ of **2c** is slightly greater than the rate constant $k_{\alpha\beta}$ of **17**. Also, the $C_\beta \rightarrow C_\alpha$ cyclization process shows less stereoselectivity than the $C_\alpha \rightarrow C_\beta$ cyclization process, which is also found for *N*-alkyl acrylamides.



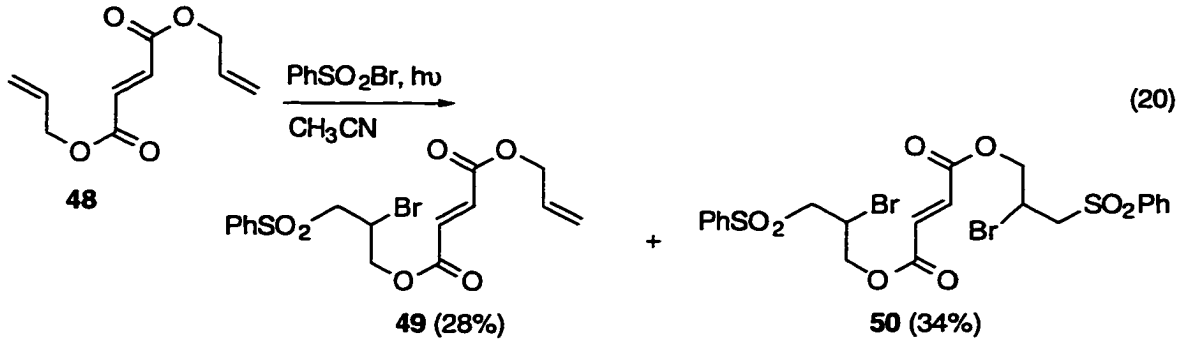
(18)



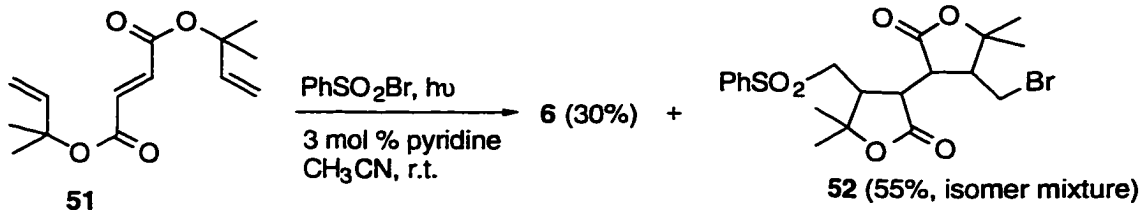
(19)

So far, both $C_\alpha \rightarrow C_\beta$ and $C_\beta \rightarrow C_\alpha$ cyclizations have been observed separately. They can proceed in sequence to make bicyclic compounds. While the reaction of fumarate **48** gave only uncyclized products **49** and **50** as expected (eq 20), the reaction of fumarate **51** yielded a

mixture of bicyclic product **52** (33%) as well as **6** (42%) (eq 21). Addition of 3 mol % pyridine increased the yield of **52** to 55% and decreased the yield of **6** to 30%. For **51**, gem-dimethyl groups accelerate both $C_\beta \rightarrow C_\alpha$ and $C_\alpha \rightarrow C_\beta$ cyclizations (Scheme 11).

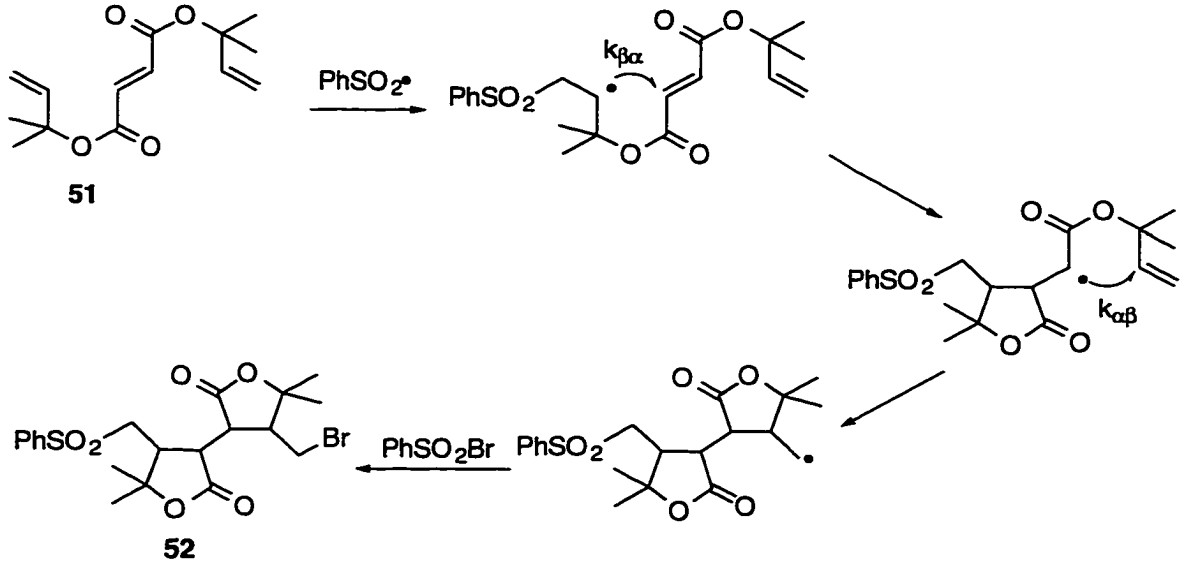


(20)



(21)

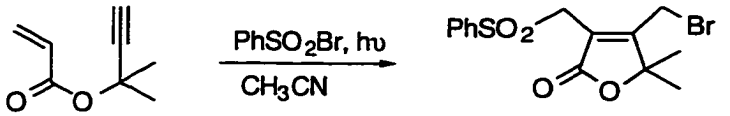
Scheme 11



4. Addition of $PhSO_2Br$ to Enynes

Lactones can be formed from the addition of $PhSO_2Br$ to propargyl acrylates or allyl propiolates in the presence of gem-dialkyl groups with lower yields than those of diene esters.

A $C_\alpha \rightarrow C_\beta$ cyclization was observed from the reaction of enyne ester **53** (eq 22). A further isomerization step of the C=C bond was involved to give the final product **54**.

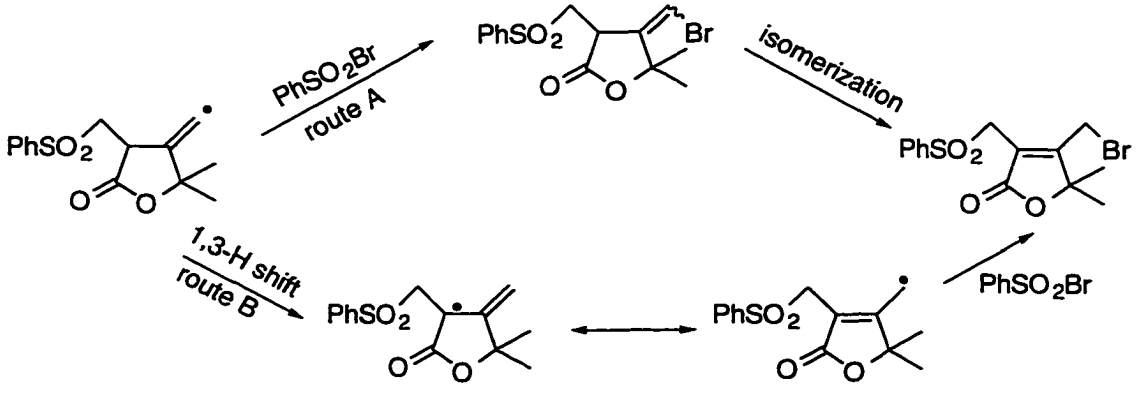


53 **54** (40%) (22)

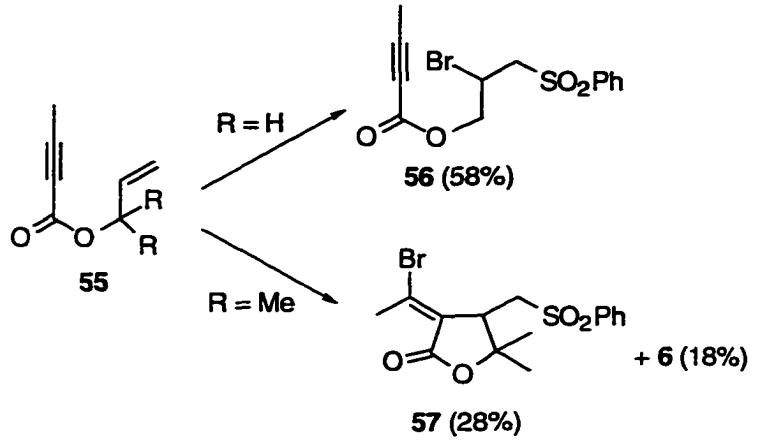
However, as shown in Scheme 12, the timing for the isomerization step is not clear. It can happen after the bromine transfer to the cyclized vinyl radical (route A), or the vinyl radical can rearrange first to give the allyl radical (route B). When the reaction was monitored by NMR spectroscopy with CD_3CN as the solvent, it was found that compound **54** was formed consistently from the start of the reaction and no detectable unrearranged product was found. While the isomerization in route A is unlikely to be that fast, the 1,3-H shift in route B is a well-documented fast step.[27] In this reaction, conjugation of the C=C bond with the C=O bond is the driving force for the rearrangement.

Schemes 13 and 14 show that the gem-dimethyl groups are also essential in the $C_\beta \rightarrow C_\alpha$ cyclization to make lactones from the enynes esters.

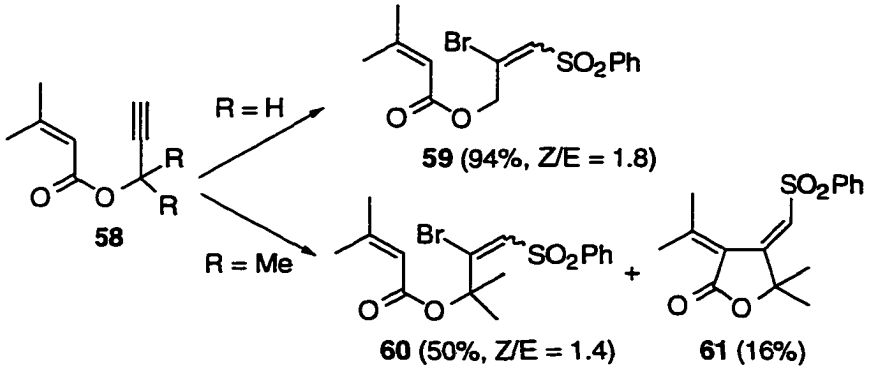
Scheme 12



Scheme 13

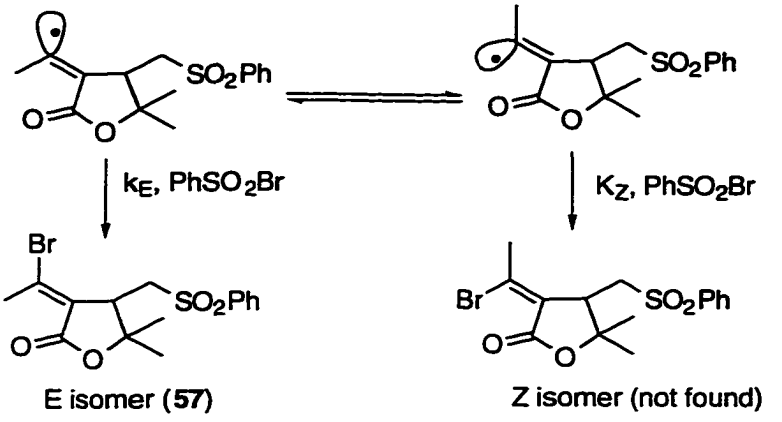


Scheme 14



The formation of compound **57** deserves attention. Compound **57** was inseparable with **6** by TLC. Since ^{1}H and ^{13}C peaks of this two compounds do not overlap and **6** has been fully characterzed, NMR peaks for **57** can be assigned undoubtedly. It was shown there there is ^{1}H-^{1}H NOE coupling between CH_2SO_2Ph and $C(CH_3)_2$, but not between CH_2SO_2Ph and CH_3CBr. So, orientation of the Br atom can be assigned. Since vinyl radicals are known to undergo rapid inversion ($k \sim 10^{8\sim10}$ /s),[28] and both of Z and E vinyl radicals can abstract iodine atoms competitively.[7, 29] We think this stereoselectivity can be explained as either the E-vinyl radical is more stable than the Z-vinyl raidcal, $K << 1$, and/or the bromine transfer has higher selectivity towards the E-vinyl radical than the Z-vinyl radical, $k_E >> k_Z$ (Scheme 15).

Scheme 15

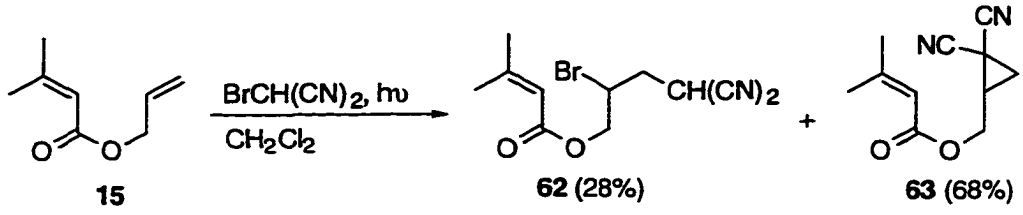


Unlike the formation of **54**, the formation of compound **57** does not involve an isomerization step. This is probably because the new-formed C=C bond of **57** is already conjugated with the C=O bond.

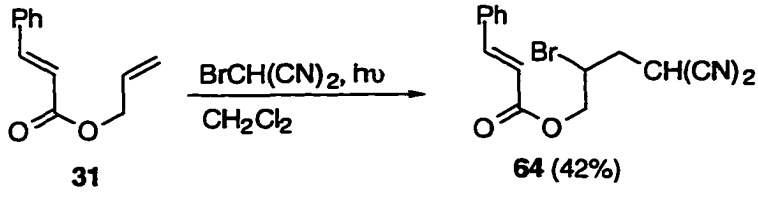
5. Lactone Formation Initiated by Other Radicals

Lactone formations initiated by $CH_3C(O)S\bullet$ have been presented in eqs 18 and 19. We tried to initiate lactone formations by using a much stronger electrophilic radical $(CN)_2CH\bullet$ which is generated from $BrCH(CN)_2$ under photolysis. It was found that $BrCH(CN)_2$ added only to the allyl C=C bond of **2a** in 58% yield (eq 9 in Chapter 1), showing the expected chemoselectivity for $C_\beta \rightarrow C_\alpha$ cyclization. However, no reaction was observed between **2c** and $BrCH(CN)_2$ under photolysis. Decomposition of $BrCH(CN)_2$ was observed after a prolonged reaction time. Also, $(NC)_2CHBr$ could add to ester **15** (eq 23), but not ester **11**. Compound **63** was formed from **62** during TLC separation. These results suggest that in the reaction of ester **2c**, the acrylic C=C bond inteferes with the electrophilic $(NC)_2CH\bullet$ radical in a non-chain process which is unknown, and the rate of the addition of $(NC)_2CH\bullet$ to the allyl C=C bond of **2c** is inhibited compared to that of **15**. We also found $(CN)_2CHBr$ can add to ester **31** (eq 24), but not **34** probably because of the same reason discussed for eqs 12 and 13. As for the reactions of enynes, $BrCH(CN)_2$ addes to esters **54** and **56** to form the unexpected dibromolactones **65** and **66**, respectively, in low yields. The stereo configuration of **66** and

67 were determined similarly as discussed for **57**. What is interesting is the formation of the lactones shows the same orientation of the vinyl bromine atom (Scheme 16).

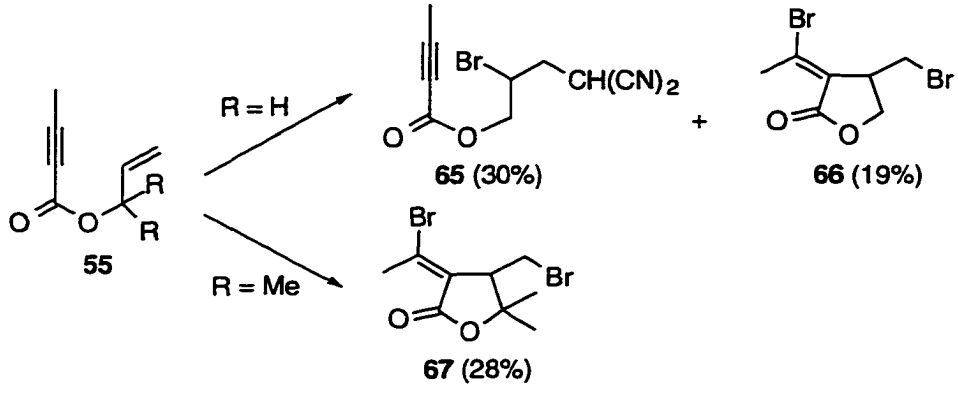


15 **62** (28%) **63** (68%) (23)



31 **64** (42%) (24)

Scheme 16

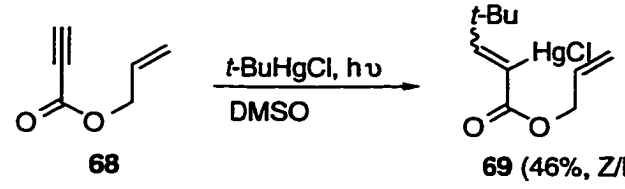


55 **65** (30%) **66** (19%) **67** (28%)

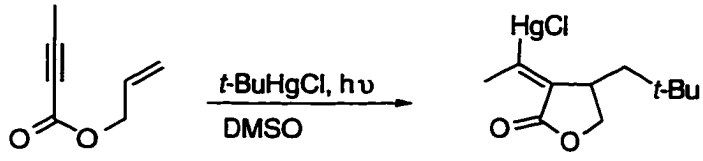
Nucleophilic radical *t*-Bu•, generated from *t*-BuHgCl under photolysis, was also investigated. *t*-BuHgCl added to ester **68** yielded only uncyclized adduct **69** whose chemoselectivity can be understood as the nucleophilic *t*-Bu• adds to the electrophilic C≡C bond preferentially over the allyl C=C bond (eq 25).

However, the reaction of *t*-BuHgCl with **55** (R = H) gave a low yield of lactone **70** (eq 26). The β-methyl group in **55** (R = H) forced the *t*-Bu• to add to the allyl C=C bond. The then-generated adduct radical has a stronger tendency to undergo $C_\beta \rightarrow C_\alpha$ cyclization even

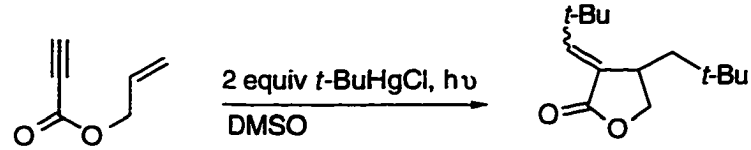
without the presence of gem-dialkyl groups. From the result of eqs 25 and 26, we think the addition of another equiv of *t*-BuHgCl to **69** may yield lactones. The reaction of ester **68** with 2 equiv of *t*-BuHgCl under similar conditions did yield dibutyllactone **71** (eq 27 and Scheme 17).



68 **69** (46%, Z/E = 1/1.6) (25)

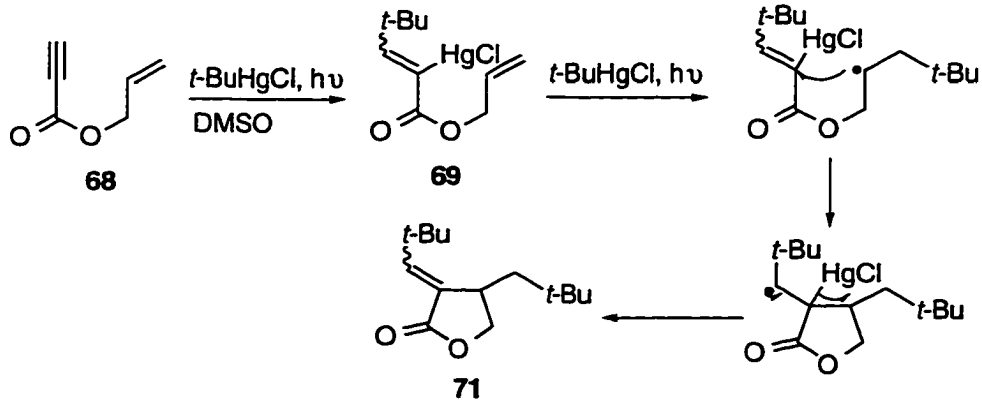


55 (R=H) **70** (18%) (26)



68 **71** (60%, Z/E = 1/1.7) (27)

Scheme 17



68 **69** **71**

Conclusions

A variety of lactones have been formed in one step from the addition of $PhSO_2Br$ to diene and enyne esters. Gem-dialkyl groups have been confirmed to significantly increase the cyclization rates of the corresponding adduct radicals in both the $C_\alpha \rightarrow C_\beta$ and $C_\beta \rightarrow C_\alpha$ cyclization processes. As for the chemoselectivity, an α,β unsaturated C=C bond or C≡C bond always have higher reactivities over an allyl C=C bond or propargyl C≡C bond for electrophilic $PhSO_2\bullet$. The $C_\beta \rightarrow C_\alpha$ cyclization can be observed only when the β position of the α,β unsaturated C=C bond or C≡C bond is substituted. Gem-dialkyl groups on the allyl part strongly inhibit the addition of $PhSO_2\bullet$ to the allyl C=C bond of allyl acrylates or allyl propiolates, and facilitate the hydrolysis and dehydration of tertiary esters.

Experimental Section

General Considerations

NMR spectra were recorded in $CDCl_3$ or as stated otherwise (^1H at 300 or 400 MHz and ^{13}C at 75 MHz or 100 MHz). 2D NMR spectra were obtained with a Bruker DRX400 spectrometer. CI, EIMS (70 ev) were obtained with Finnigan 4000 (GC mode) and Kratos MS-50 spectrometers. All mp's were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Most products were isolated by TLC on silica gel with hexanes-ethyl acetate as the eluent. Photostimulated reactions utilized a Sylvania 275 W fluorescent sunlamp and 5-mm NMR tubes at room temperature. Yields were based on the starting esters. Diene and enyne esters were made from the corresponding acylchloride and either a primary alcohol with triethylamine at room temperature, or a deprotonated secondary or tertiary alcohol (by ^{n}BuLi) at 0 °C in anhydrous ethyl ether.

General Preparative Procedures and Compound Characterization

General Procedure for the Addition of $PhSO_2Br$ to Diene or Enyne Esters. A mixture of an ester (0.20 mmol) and $PhSO_2Br$ (0.22 mmol) with or without 3 mol

% of pyridine in CH_3CN (1.0 mL) was irradiated in a 5-mm NMR tube at room temperature until the starting ester disappeared as indicated by TLC analysis. The products were obtained by TLC separation on 20 x 10 cm silica gel plates with hexanes-ethyl acetate as the eluent.

***trans*-3-Benzenesulfonylmethyl-4-bromomethyl-5,5-dimethyldihydro-2(3*H*)-furanone (3c)** was isolated as a white solid, mp 123-125 °C. IR (cm^{-1}) 1770, 1308, 1146; ^1H NMR δ 1.46 (s, 3H), 1.68 (s, 3H), 2.76 (ddd, *J* = 4.0, 11.0, 11.7 Hz, 1H), 3.09 (ddd, *J* = 3.0, 7.8, 11.7 Hz, 1H), 3.28 (dd, *J* = 7.8, 14.4 Hz, 1H), 3.45 (t, *J* = 11.0 Hz, 1H), 3.79 (dd, *J* = 3.0, 14.4 Hz, 1H), 4.18 (dd, *J* = 4.0, 11.0 Hz, 1H), 7.60-8.00 (m, 5H); ^{13}C NMR δ 21.93, 28.60, 29.55, 40.76, 52.37. 56.81, 86.03, 128.15, 129.82, 134.60, 139.24, 173.18; HREIMS m/z (relative intensity) 281.0848 [8, calcd for $C_{14}H_{17}O_2S$ (M - Br) 281.0848], 263 (27), 223 (19), 148 (100), 139 (34), 125 (59), 123 (46), 95 (93), 77 (49); CIMS m/z 380/378 ($M + NH_4^+$).

***trans*-3-Benzenesulfonylmethyl-4-bromomethyl-5,5-diisopropyldihydro-2(3*H*)-furanone (3d)** was isolated as a colorless oil. IR (cm^{-1}) 1770, 1319, 1152; ^1H NMR δ 0.97 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 2.22 (septet, *J* = 6.8 Hz, 1H), 2.38 (septet, *J* = 6.8 Hz, 1H), 3.16 (ddd, *J* = 5.2, 6.0, 7.2 Hz, 1H), 3.23 (ddd, *J* = 4.8, 5.2, 6.0 Hz, 1H), 3.52 (dd, *J* = 5.2, 14.4 Hz, 1H), 3.68 (dd, *J* = 5.2, 10.8 Hz, 1H), 3.80 (dd, *J* = 4.8, 14.4 Hz, 1H), 3.90 (dd, *J* = 7.2, 10.8 Hz, 1H), 7.50-8.10 (m, 5H); ^{13}C NMR δ 17.10, 17.12, 17.77, 19.44, 30.83, 31.17, 33.23, 43.71, 44.98, 57.06, 93.25, 128.22, 129.63, 134.31, 139.91, 174.41; HREIMS m/z (relative intensity) 373.0117 [8, calcd for $C_{15}H_{18}{}^{79}BrO_4S$ (M - C_3H_7) 373.0109], 293 (100), 275 (19), 223 (13), 151 (83), 125 (24), 77 (30), 41 (48); CIMS m/z 436/334 ($M + NH_4^+$).

***trans*-3-Benzenesulfonylmethyl-4-bromomethyl-1-oxaspiro[4,5]-2-decanone (3e)** was isolated as a white solid, mp 205-207 °C. IR (cm^{-1}) 1761, 1310, 1148; ^1H NMR δ 1.20-1.30 (m, 2H), 1.55-1.90 (m, 7H), 2.10-2.20 (m, 1H), 2.68 (ddd, *J* = 4.0, 10.0, 11.6 Hz, 1H), 3.11 (ddd, *J* = 3.2, 7.6, 11.6 Hz, 1H), 3.31 (dd, *J* = 7.6, 14.4 Hz, 1H),

3.52 (dd, J = 10.0, 11.2 Hz, 1H), 3.78 (dd, J = 3.2, 14.4 Hz, 1H), 4.09 (dd, J = 4.0, 11.2 Hz, 1H), 7.60-8.00 (m, 5H); ^{13}C NMR δ 21.55, 22.72, 25.16, 28.75, 30.80, 38.21, 40.55, 52.41, 56.90, 87.25, 128.17, 129.79, 134.55, 139.30, 173.49; HREIMS m/z (relative intensity) 321.1168 [58 , calcd for $C_{17}H_{21}O_4S$ (M - Br) 321.1161], 303(18), 259 (17), 223 (41), 179(100), 125 (51), 77 (69), 69 (81), 55 (43), 53 (46); CIMS m/z 420/418 (M + NH_4^+).

(3α, 4β, 5α)-(±)-3-Benzenesulfonylmethyl-4-bromomethyl-5-*tert*-butyldihydro-2(3*H*)-furanone (3f) was isolated as a white solid, mp 103-105 °C. IR (cm^{-1}) 1771, 1309, 1154; ^{1}H NMR δ 1.01 (s, 9H), 2.81-2.86 (m, 1H), 3.23 (dd, J = 10.8, 14.0 Hz, 1H), 3.37 (ddd, J = 2.4, 7.2, 10.8 Hz, 1H), 3.62 (dd, J = 2.8, 10.2 Hz, 1H), 3.72 (dd, J = 2.4, 14.0 Hz, 1H), 4.21 (dd, J = 2.8, 10.2 Hz, 1H), 4.25 (d, J = 6.4 Hz, 1H), 3.90 (dd, J = 7.2, 10.8 Hz, 1H), 7.60-8.00 (m, 5H); ^{13}C NMR δ 25.40, 34.78, 37.57, 39.69, 41.36, 56.99, 89.51, 128.26, 129.89, 134.68, 138.60, 174.95; HREIMS m/z (relative intensity) 331.9726 [62, calcd for $C_{12}H_{13}{}^{79}BrO_4S$ (M - C_4H_8) 331.9718], 225 (10), 197 (16), 151 (15), 143 (78), 125 (84), 109 (46), 77 (49), 57 (100); CIMS m/z 408/406 (M + NH_4^+).

Allyl (*E*)-3-Benzenesulfonylacrylate (5a) was isolated about 70% pure. ^{1}H NMR δ 4.69 (d, J = 6.0 Hz, 2H), 5.29 (dd, J = 0.8, 10.4 Hz, 1H), 5.35 (dd, J = 0.8, 17.2 Hz, 1H), 5.78-5.88 (m, 1H), 6.88 (d, J = 15.2 Hz, 1H), 7.36 (d, J = 15.2 Hz, 1H), 7.60-7.95 (m, 5H); ^{13}C NMR δ 66.76, 116.55, 128.58, 129.87, 130.85, 134.64, 135.48, 139.36, 143.72, 165.76; HREIMS m/z (relative intensity) 252.0461 (16, calcd for $C_{12}H_{12}O_4S$ 252.0456), 196 (12), 125 (100), 111 (24), 77 (48), 55 (19).

1-Methylallyl (*E*)-3-Benzenesulfonylacrylate (5b) was isolated about 70% pure. ^{1}H NMR δ 1.37 (d, J = 6.4 Hz, 3H), 5.19 (dd, J = 0.8, 10.0 Hz, 1H), 5.28 (dd, J = 0.8, 17.2 Hz, 1H), 5.42 (pentet, J = 6.4 Hz, 1H), 5.83 (ddd, J = 6.4, 10.0, 17.2 Hz, 1H), 6.84 (d, J = 15.2 Hz, 1H), 7.33 (d, J = 15.2 Hz, 1H), 7.50-7.95 (m, 5H); ^{13}C NMR δ

20.01, 73.40, 117.25, 128.59, 129.86, 131.44, 134.61, 136.76, 138.66, 143.39, 162.90; HREIMS m/z (relative intensity) 196.0199 [14, calcd for $C_9H_8O_3S$ (M - C_4H_6) 196.0194], 142 (14), 125 (100), 77 (21), 55 (36); CIMS m/z 284 (M + NH_4^+).

1-*tert*-Butyl-2-propenyl (*E*)-3-Benzenesulfonylacrylate (5f) was isolated as a colorless oil. IR (cm^{-1}) 1732, 1327, 1148; ^1H NMR δ 0.93 (s, 3H), 5.04 (d, *J* = 7.6 Hz, 1H), 5.22-5.29 (m, 2H), 5.4-5.81 (m, 1H), 6.88 (d, *J* = 15.2 Hz, 1H), 7.33 (d, *J* = 15.2 Hz, 1H), 7.50-7.95 (m, 5H); ^{13}C NMR δ 25.89, 34.47, 84.71, 119.70, 128.55, 129.86, 131.45, 132.74, 134.62, 138.66, 143.39, 162.95; HREIMS m/z (relative intensity) 293.0843 [2, calcd for $C_{15}H_{17}O_4S$ (M - CH_3) 293.0848], 252 (9), 196 (100), 125 (48), 77 (24), 55 (61); CIMS m/z 308 (M^+).

1-Ethenyl-2-propenyl (*E*)-3-Benzenesulfonylacrylate (5g) was isolated about 70% pure. ^1H NMR δ 5.29 (d, *J* = 10.4 Hz, 2H), 5.33 (d, *J* = 16.8 Hz, 2H), 5.78-5.80 (m, 1H), 5.81-5.89 (m, 2H), 6.88 (d, *J* = 15.2 Hz, 1H), 7.34 (d, *J* = 15.2 Hz, 1H), 7.50-7.95 (m, 5H); ^{13}C NMR δ 77.43, 118.89, 128.60, 129.87, 132.26, 134.21, 134.62, 138.61, 143.68, 162.59; HREIMS m/z (relative intensity) 196.0191 [15, calcd for $C_9H_8O_3S$ (M - C_5H_6O) 196.0194), 137 (14), 125 (100), 83 (11), 77 (36), 67 (41), 55 (23); CIMS m/z 296 (M + NH_4^+).

(*E*)-1-Benzenesulfonyl-2-methyl-4-bromo-2-butene (6a) and (*E*)-1-benzenesulfonyl-3-methyl-4-bromo-2-butene (6b) were isolated as an inseparable white solid mixture of **6a** and **6b** in a ratio of 1 : 4 (from ^1H NMR), mp 70-72 °C (lit.[15] 73-74 °C). The NMR data were obtained from mixture of sulfone **6**. **6a:** ^1H NMR δ 1.86 (s, 3H), 3.77 (s, 2H), 3.85 (d, *J* = 8.4 Hz, 2H), 5.39 (t, *J* = 8.4 Hz, 1H), 7.27-7.87 (m, 5H); ^{13}C NMR δ 16.92, 26.96, 65.74, 128.71, 129.38, 130.39, 130.65, 134.05, 138.24; **6b:** ^1H NMR δ 1.43 (s, 3H), 3.82 (d, *J* = 8.0 Hz, 2H), 3.88 (s, 2H), 5.62 (t, *J* = 8.4 Hz, 1H), 7.27-7.87 (m, 5H); ^{13}C NMR δ 14.94, 38.92, 56.18, 116.46, 128.67, 129.47, 134.05, 138.46,

141.89; HREIMS of **6** m/z (relative intensity) 209.0639 [100, calcd for $C_{11}H_{13}O_2S$ (M - Br) 209.0636], 145 (14), 125 (24), 77 (66), 53 (15); CIMS m/z 308/306 ($M + NH_4^+$).

(*E*)-1-Bromo-2-(2-benzenesulfonyl)ethylidenecyclohexane (7) was isolated as a colorless oil. IR (cm^{-1}) 1305, 1146; ^1H NMR δ 0.79-0.91 (m, 1H), 1.50-2.20 (m, 7H), 3.83 (d, J = 8.0 Hz, 2H), 4.86 (t, J = 3.0 Hz, 1H), 5.53 (t, J = 8.0 Hz, 1H), 7.54-7.87 (m, 5H); ^{13}C NMR δ 21.16, 24.06, 26.22, 36.63, 55.20, 58.30, 111.74, 128.83, 129.44, 133.98, 138.51, 148.16; HREIMS m/z (relative intensity) 248.0874 (100, calcd for $C_{14}H_{16}O_2S$ 248.0871), 215 (3), 179 (21), 125 (17), 107 (53), 77 (21), 67 (12), 51 (39).

(*E*)-[2-(1-Cyclohexenyl)ethenylsulfonyl]benzene (8) was isolated as a colorless oil. IR (cm^{-1}) 1306, 1146; ^1H NMR δ 1.55-1.70 (m, 4H), 2.00-2.10 (m, 2H), 2.20-2.30 (m, 2H), 6.20 (dd, J = 0.8, 14.8 Hz, 1H), 6.28-6.32 (m, 1H), 7.28 (d, J = 14.8 Hz, 1H), 7.54-8.00 (m, 5H); ^{13}C NMR δ 21.94, 22.00, 24.39, 26.76, 123.84, 127.66, 129.41, 133.24, 133.60, 141.59, 141.94, 146.16; HREIMS m/z (relative intensity) 248.0876 [4, calcd for $C_{14}H_{16}O_2S$ (M - HBr) 248.0871], 189 (13), 143 (9), 125 (4), 107 (100), 91 (21), 79 (48), 77 (30), 51 (16); CIMS m/z 348/346 ($M + NH_4^+$).

***trans*-4-Bromomethyl-3-(2,2,2-trichloroethyl)-5,5-diisopropyldihydro-2(3*H*)-furanone (14)** was isolated as a white solid, mp 119-121 °C. IR (cm^{-1}) 1770; ^1H NMR δ 1.49 (s, 3H), 1.68 (s, 3H), 2.62 (dt, J = 4.0, 11.2 Hz, 1H), 2.80 (dt, J = 11.2, 4.4 Hz, 1H), 2.91 (dd, J = 4.4, 15.2 Hz, 1H), 3.42 (t, J = 11.2 Hz, 1H), 3.50 (dd, J = 4.4, 15.2 Hz, 1H), 3.87 (dd, J = 4.0, 11.2 Hz, 1H); ^{13}C NMR δ 21.60, 28.53, 29.58, 43.93, 52.72. 54.42, 85.13, 97.84, 173.95; HREIMS m/z (relative intensity) 320.8843 [7, calcd for $C_8H_9{}^{79}Br^{35}Cl_3O_2S$ (M - CH_3) 320.8852), 267 (5), 201 (26), 199 (28), 135 (39), 117 (100), 75 (45); CIMS m/z 360/358/356/354 ($M + NH_4^+$).

Allyl 3-Methyl-2-butenoate (15) was isolated as a colorless liquid. ^1H NMR δ 1.88 (d, J = 1.2 Hz, 3H), 2.15 (d, J = 1.2 Hz, 3H), 4.58 (dt, J = 5.7, 1.5 Hz, 2H), 5.20 (dd, J = 1.5, 10.5 Hz, 1H), 5.32 (dd, J = 1.5, 17.1 Hz, 1H), 5.60-5.70 (m, 1H), 5.93 (ddt, J =

10.5, 17.1, 5.7 Hz, 1H); ^{13}C NMR δ 20.22, 27.41, 64.24, 115.80, 117.74, 132.72, 157.13, 166.24; HREIMS m/z (relative intensity) 140.0840 (5, calcd for $C_8H_{12}O_2$ 140.0837), 95 (14), 83 (100), 55 (29).

3-Benzenesulfonyl-2-bromopropyl 3-Methyl-2-butenoate (16) was isolated as a white solid, mp 84-85 °C. IR (cm^{-1}) 1726, 1308, 1148; ^{1}H NMR δ 1.92 (d, J = 1.2 Hz, 3H), 2.17 (d, J = 1.2 Hz, 3H), 3.65 (dd, J = 6.0, 14.8 Hz, 1H), 3.79 (dd, J = 6.4, 14.8 Hz, 1H), 4.42-4.45 (m, 2H), 4.45-4.53 (m, 1H), 5.67-5.70 (m, 1H); ^{13}C NMR δ 20.65, 27.74, 39.88, 60.75, 65.58, 115.05, 128.45, 129.71, 134.49, 139.17, 159.27, 165.54; HREIMS m/z (relative intensity) 360.0030 (4, calcd for $C_{14}H_{17}SO_4{}^{79}Br$ 360.0031), 207 (13), 178 (16), 141 (17), 125 (13), 83 (100), 77 (43).

1,1-Dimethyl-2-propenyl 3-Methyl-2-butenoate (17) was isolated as a colorless liquid. ^{1}H NMR δ 1.52 (s, 6H), 1.85 (d, J = 1.2 Hz, 3H), 2.12 (d, J = 1.2 Hz, 3H), 5.06 (dd, J = 0.6, 10.8 Hz, 1H), 5.15 (dd, J = 0.6, 17.4 Hz, 1H), 5.60-5.63 (m, 1H), 6.10 (dd, J = 10.8, 17.4 Hz, 1H); ^{13}C NMR δ 19.98, 26.72, 27.33, 79.80, 112.19, 117.28, 143.16, 155.55, 165.77; HREIMS m/z (relative intensity) 168.1149 (1, calcd for $C_{10}H_{16}O_2$ 168.1150), 123 (2), 100 (6), 83 (100), 69 (32), 55 (10).

4-Benzenesulfonylmethyl-3-isopropylidene-5,5-dimethyldihydro-2(3*H*)-furanone (18) was isolated as a white solid, mp 143-144 °C. IR (cm^{-1}) 1743, 1308, 1150; ^{1}H NMR δ (CD_3CN) 1.32 (s, 3H), 1.43 (s, 3H), 1.73 (s, 3H), 2.10 (s, 3H), 3.14 (dd, J = 3.2, 15.2 Hz, 3H), 3.38-3.41 (m, 1H), 3.63 (dd, J = 8.0, 15.2 Hz, 1H), 7.60-7.90 (m, 5H); ^{13}C NMR δ 20.76, 23.71, 24.01, 29.75, 43.11, 57.79, 81.78, 124.56, 128.02, 129.83, 134.34, 140.03, 153.66, 168.51; HREIMS m/z (relative intensity) 308.1080 (36, calcd for $C_{16}H_{20}SO_4$ 308.1082), 290 (9), 225 (7), 166 (63), 149 (62), 121 (80), 81 (100), 43 (35).

4-Benzenesulfonylmethyl-3-isopropylidenedihydro-2(3*H*)-furanone (20) was isolated as a white solid mixture with compound **21**. ^{1}H NMR δ 1.81 (s, 3H), 2.20 (s, 3H), 3.02 (dd, J = 1.6, 14.4 Hz, 1H), 3.27 (dd, J = 11.6, 14.4 Hz, 1H), 3.60-3.70 (m,

1H), 4.25 (dd, J = 6.8, 10 Hz, 1H), 4.46 (dd, J =2, 10 Hz, 1H), 7.60-7.90 (m, 5H); ^{13}C NMR δ 20.21, 23.79, 34.47, 58.73, 68.60, 120.69, 128.03, 129.75, 134.40, 139.08, 153.64, 169.11; HREIMS m/z (relative intensity) 280.0767 (74, calcd for $C_{14}H_{16}SO_4$ 280.0769), 216 (14), 143 (16), 138 (100), 125 (30), 111 (14), 81 (20), 77 (53), 41 (42).

4-Benzenesulfonylmethyl-3-(1-chloro-1-methyl)ethyldihydro-2(3*H*)-furanone (21) was isolated as a white solid mixture with **20**. ^1H NMR δ 1.68 (s, 3H), 1.79 (s, 3H), 2.68 (d, J = 5.7 Hz, 1H), 3.20-3.30 (m, 1H), 3.25 (dd, J = 2, 10 Hz, 1H), 3.58 (dd, J = 1, 10 Hz, 1H), 4.23 (dd, J = 5, 10 Hz, 1H), 4.67 (dd, J =7.8, 10 Hz, 1H), 7.60-7.90 (m, 5H); ^{13}C NMR δ 20.21, 23.79, 34.47, 58.73, 68.60, 120.69, 128.03, 129.75, 134.40, 139.08, 153.64, 169.11; HREIMS m/z (relative intensity) 280.0767 [74, calcd for $C_{14}H_{16}SO_4$ (M - HCl) 280.0769], 216 (14), 143 (16), 138 (100), 125 (30), 111 (14), 81 (20), 77 (53), 41 (42); CIMS m/e 336/334 ($M + NH_4^+$).

1-Methyl-2-propenyl 3-Methyl-2-butenoate (22) was isolated as a colorless liquid. ^1H NMR δ 1.31 (d, J = 6.6 Hz, 3H), 1.88 (d, J = 1.2 Hz, 3H), 2.16 (d, J = 1.2 Hz, 3H), 5.11 (d, J = 10.5 Hz, 1H), 5.23 (d, J = 17.4 Hz, 1H), 5.30-5.40 (m, 1H), 5.60-5.70 (m, 1H), 5.86 (ddd, J = 6.6, 10.5, 17.4 Hz, 1H); ^{13}C NMR δ 20.23, 20.36, 27.57, 70.10, 115.55, 116.43, 138.31, 156.87, 166.06; HREIMS m/z (relative intensity) 154.0994 (2, calcd for $C_9H_{14}O_2$ 154.0997), 141 (4), 109 (3), 100 (16), 83 (100), 69 (24), 55 (41).

3-Benzenesulfonyl-2-bromo-1-methylpropyl 3-Methyl-2-butenoate (23) was isolated as an oily mixture of two diastereoisomers (syn/anti = 1 : 1 by ^1H NMR). IR (cm^{-1}) 1715, 1308, 1148; ^1H NMR δ 1.32-1.36 (m, 3H), 1.90 (d, J = 1.2 Hz, 3H), 2.17 (d, J = 1.2 Hz, 3H), 3.60-3.80 (m, 2H), 4.38-4.48 (m, 1H), 5.10-5.30 (m, 1H), 5.60-5.70 (m, 1H), 7.57-8.10 (m, 5H); ^{13}C NMR δ (* for overlapping peaks), 16.83. 17.81, 20.61, 20.64, 27.71*, 46.12, 46.62, 60.65, 60.73, 69.96, 70.32, 115.36, 115.48, 128.49, 128.65, 129.61*, 134.33, 134.44, 139.11, 139.27, 158.94, 159.00, 165.18, 165.24; HREIMS m/z

(relative intensity) 374.0190 (2, calcd for $C_{15}H_{19}SO_4{}^{79}Br$ 374.0187), 277 (9), 235 (2), 195 (4), 125 (6), 83 (100), 69 (55), 55 (28).

1-*tert*-Butyl-2-propenyl 3-Methyl-2-butenoate (24) was isolated as a yellow liquid. ^1H NMR δ 0.92 (s, 9H), 1.90 (d, J = 1.2 Hz, 3H), 2.17 (d, J = 1.2 Hz, 3H), 5.01 (d, J = 6.6 Hz, 1H), 5.15-5.25 (m, 2H), 5.65-5.75 (m, 1H), 5.82 (ddd, J = 6.6, 10.5, 17.1 Hz, 1H); ^{13}C NMR δ 20.44, 26.04, 27.62, 34.37, 80.99, 116.45, 117.93, 134.21, 156.82, 166.20; HREIMS m/z (relative intensity) 196.1471 (1, calcd for $C_{12}H_{20}O_2$ 196.1463), 141 (45), 83 (100).

1-Phenyl-2-propenyl 3-Methyl-2-butenoate (25) was isolated a yellow liquid. ^1H NMR δ 1.88 (d, J = 0.8 Hz, 3H), 2.16 (d, J = 0.8 Hz, 3H), 5.22 (dd, J = 1.2, 10.4 Hz, 1H), 5.28 (dd, J = 1.2, 16.8 Hz, 1H), 5.70-5.80 (m, 1H), 6.01 (ddd, J = 5.6, 10.4, 16.8 Hz, 1H), 6.29 (d, J = 5.6 Hz, 1H), 7.30-7.50 (m, 5H); ^{13}C NMR δ 20.40, 27.57, 75.36, 116.05, 116.68, 127.22, 128.08, 128.63, 136.83, 139.47, 157.69, 165.58; EIMS m/z (relative intensity) M (not observed), 117 (53), 116 (53), 115 (39), 91 (10), 83 (100), 69(27), 55 (10); CIMS m/z 262 ($M + NH_4^+$).

1-Mesityl-2-propenyl 3-Methyl-2-butenoate (26) was isolated as a yellow liquid. ^1H NMR δ 1.94 (d, J = 1.2 Hz, 3H), 2.22 (d, J = 1.2 Hz, 3H), 2.31 (s, 3H), 2.48 (s, 6H), 5.14-5.26 (m, 2H), 5.80-5.82 (m, 1H), 6.78-6,81 (m, 1H), 6.91 (s, 2H); ^{13}C NMR δ 20.33, 20.70, 20.97, 27.52, 72.00, 115.79, 115.99, 129.88, 132.26, 135.95, 137.15, 137.43, 157.30, 165.70; HREIMS m/z (relative intensity) 258.1617 (9, calcd for $C_{17}H_{22}O_2$ 258.1620), 158 (53), 143 (100), 129 (29), 115 (11), 91 (11), 55 (21).

1,1-Dimethyl-2-propenyl 2-Butenoate (27) was isolated as a colorless liquid. ^1H NMR δ 1.52 (s, 6H), 1.82 (d, J = 7.7 Hz, 3H), 5.05 (d, J = 10.5 Hz, 1H), 5.15 (d, J = 17.4 Hz, 1H), 5.78 (d, J = 15.6 Hz, 1H), 6.10 (dd, J = 10.8, 17.4 Hz, 1H), 6.80-6.90 (m, 1H); ^{13}C NMR δ 17.98, 26.72, 80.53, 112.64, 124.23, 142.90, 143.83, 165.68; HREIMS

m/z (relative intensity) 154.0996 (3, calcd. for $C_9H_{14}O_2$ 154.0994), 139 (2), 84 (19), 69 (100), 49 (22).

Allyl 4-Bromocrotonate (28) was prepared in 4 steps from crotonic acid.[30]

Trimethylsilyl Crotonate: To 50 mL of dry Et_2O was added crotonic acid (8.6 g, 0.1 mol) and Me_3SiCl (13g, 0.12 mol). The solution was stirred and cooled to -78 °C. To the solution was added dry pyridine (8.3 g, 0.12 mol) dropwise. The solution was then heated to reflux for 30 min and cooled to 0 °C. The white precipitate (pyridinium chrolide) was filtered off, and the ethereal filtrate solution was concentrated and vacuum distilled (57 °C/11 mmHg) to give liquid trimethylsilyl crotonate (11.5 g, 73%). ^{1}H NMR δ 0.30 (s, 9H), 1.86 (dd, J = 1.8, 6.9 Hz, 3H), 5.80 (dq, J = 15.8, 1.6 Hz, 1H), 6.95 (dq, J = 15.8, 6.9 Hz, 1H); ^{13}C NMR δ 0.13, 17.89, 124.51, 145.28, 166.73.

4-Bromocrotonyl Acid: A CCl_4 solution (50 mL) of trimethylsilylcrotonate (6.32 g, 40 mmol), NBS (8.54 g, 48 mmol) and Bz_2O_2 (160 mg) was heated to reflux and irradiated by a sunlamp for 3 h. The solution was then cooled to 0 °C and the floating succinimide was filtered off. The filtered solution was concentrated and vacuum distilled (115 °C/11 mmHg). The distillate was stirred in water (20 mL) for 10 min. The aqueous solution was extracted with Et_2O. The ethereal extract was dried by anhydrous $MgSO_4$. After the MgSO4 was filtered off, the ethereal solution was concentrated until the white solid 4-bromocrotonyl acid (5.6 g, 85%) was obtained. ^{1}H NMR δ 4.03 (dd, J = 1.2, 7.5 Hz, 2H), 6.00 (dt, J = 15.6, 1.2 Hz, 1H), 6.95 (dt, J = 15.6, 7.5 Hz, 1H), 11.2 (b, 1H); ^{13}C NMR δ 28.71, 123.81, 144.58, 171.07.

4-Bromocrotonyl Chloride: 4-Bromocrotonic acid (4.8 g, 29 mmol) was dissolved in $SOCl_2$ (6.9 g) and the solution was heated to reflux for 2 h. Vacuum distillation gave liquid 4-bromocrotonyl chloride (3.7 g, 69%). ^{1}H NMR δ 4.04 (dd, J = 1.2, 7.2 Hz, 2H), 6.26 (dt, J = 14.8, 1.2 Hz, 1H), 7.20 (dt, J = 14.8, 7.5 Hz, 1H); ^{13}C NMR δ 27.72, 129.09, 147.84, 165.31.

Allyl 4-Bromocrotonate: To anhydrous Et_2O (1 mL) cooled at -78 °C was added allyl alcohol (320 mg, 5.5 mmol), Et_3N (1 mL), and 4-bromocrotonyl chloride (0.92 g, 5 mmol). the solution was stirred and warmed to r. t. over 2 h. A usual aqueous workup and column chromatography separation gave colorless liquid **28** (360 mg, 50%). ^1H NMR δ 4.01 (dd, *J* = 1.2, 7.2 Hz, 2H), 4.65 (dd, *J* = 1.5, 5.7 Hz, 2H), 5.26 (dd, *J* = 1.5, 10 Hz, 1H), 5.36 (dd, *J* = 1.5, 17.6 Hz, 1H), 5.90 (ddd, *J* = 5.7, 10, 17.6 Hz, 2H), 6.08 (dt, *J* = 15.3, 1.2 Hz, 1H), 7.05 (dt, *J* = 15.3, 7.2 Hz, 1H); ^{13}C NMR δ 29.13, 65.49, 118.61, 131.98, 124.40, 142.20, 165.20; HREIMS m/z (relative intensity) 203.9784 (1, calcd for $C_7H_9O_2{}^{79}Br$ 203.9786), 149 (98), 147 (100), 120 (12), 103 (95), 84 (20), 68 (50), 57 (18).

Allyl Cinnamate (31) was isolated as a light yellow liquid. ^1H NMR δ 4.72 (dt, *J* = 6.0, 1.5 Hz, 2H), 5.28 (dd, *J* = 1.5, 17.0 Hz, 1H), 5.40 (dd, *J* = 1.5, 10.5 Hz, 1H), 6.00 (ddt, *J* = 10.5, 17, 6 Hz, 1H), 6.46 (d, *J* = 16 Hz, 1H), 7.30-7.60 (m, 5H), 7.77 (d, *J* = 16 Hz, 1H); ^{13}C NMR δ 65.27, 117.95, 118.35, 128.98, 130.41, 132.37, 134.45, 145.14, 166.68; HREIMS m/z (relative intensity) 188.0839 (22, calcd for $C_7H_9O_2$ 188.0837), 173 (4), 143 (17), 131 (100), 103 (41), 77 (27).

3-Benzenesulfonyl-2-bromopropyl Cinnamate (32) was isolated as a white solid, mp 100-102 °C. ^1H NMR δ 3.71 (dd, *J* = 5.7, 14.7 Hz, 1H), 3.84 (dd, *J* = 6.6, 14.7 Hz, 1H), 4.50-4.60 (m, 3H), 6.46 (d, *J* = 16.0 Hz, 1H), 7.70 (d, *J* = 16 Hz, 1H), 7.50-8.0 (m, 10H); ^{13}C NMR δ 39.61, 60.67, 66.30, 116.83, 128.32, 129.05, 129.65, 130.76, 134.14, 134.44, 139.03, 146.29, 165.99; HREIMS m/z (relative intensity) 408.0030 (4, calcd for $C_{18}H_{17}SO_4{}^{79}Br$ 408.0031), 328 (3), 141 (16), 131 (100), 103 (38), 77 (58).

Allyl (Z)-Cinnamate (33) was isolated as a light yellow oil. ^1H NMR δ 4.62 (d, *J* = 6 Hz, 2H), 5.22 (dd, *J* = 1.6, 10.4 Hz, 1H), 5.28 (dd, *J* = 1.6, 17.2 Hz, 1H), 5.92 (ddt, *J* = 10.4, 17.2, 6 Hz, 1H), 6.00 (d, *J* = 12.6 Hz, 1H), 7.00 (d, *J* = 12.6 Hz, 1H), 7.30-7.60 (m, 5H); ^{13}C NMR δ 65.23, 118.57, 119.59, 128.24, 129.30, 129.96, 132.23, 134.96,

143.94, 165.97; HREIMS m/z (relative intensity) 188.0842 (18, calcd for $C_7H_9O_2$ 188.0837), 143 (17), 131 (100), 103 (42), 77 (32).

Allyl 4-Phenylcinnmate (34) was prepared from 4-cinnamic acid and allyl alcohol in 96% yield. ^{1}H NMR δ 4.51 (dt, J = 5.6, 1.2 Hz, 2H), 5.20 (m, 2H), 5.80 (m, 1H), 6.39 (s, 1H), 7.10-7.50 (m, 10H); ^{13}C NMR δ 64.90, 117.00, 118.09, 127.98, 128.27, 128.39, 128.45, 129.19, 129.56, 132.23, 138.92, 140.84, 157.25, 165.69. HREIMS m/z (relative intensity) 264.1150 (34, calcd. for $C_{18}H_{16}O_2$ 264.1148), 219 (27), 207 (100), 192 (39), 178 (86), 165 (20), 152 (14), 105 (16), 77 (11).

4-Cinnamic Acid: An anhydrous THF solution (10 mL) of $(Et)_2P(O)CH_2CO_2Et$ (2.24 g, 10 mmol), *t*-BuOK (1.12 g, 12 mmol) and diphenyl ketone (1.82 g, 10 mmol) was heated to reflux for 30 min. Then 20% KOH solution (10 mL) was added to the reaction solution. The reaction solution was further kept at 80 °C overnight. This reaction solution was extracted by Et_2O (discard this ethereal solution), and then acidified by conc. HCl until pH < 1, and then the acidified solution was extracted again with Et_2O. This ethreal extract was further dried and concentrated to give a light yellow solid, 4-Cinnamic acid (1.1 g, 50%), mp 158-160 °C. ^{1}H NMR δ 6.31 (s, 1H), 7.10-7.50 (m, 10H), 11.18 (b, 1H); ^{13}C NMR δ 116.48, 128.02, 128.49, 128.55, 128.61, 129.35, 129.82, 138.47, 140.92, 159.10, 170.98. HREIMS m/z (relative intensity) 224.0834 (100, calcd for $C_{15}H_{12}O_2$ 224.0837), 207 (13), 178 (47), 165 (11).

3-Benzenesulfonyl-2-bromopropyl 4-Phenylcinnamate (35) was isolated as a colorless oil. ^{1}H NMR δ 3.40 (d, J = 6.0 Hz, 2H), 4.34-4.42 (m, 2H), 6.37 (s, 1H), 7.21-7.36 (m, 10H), 7.60-7.93 (m, 5H); ^{13}C NMR δ 39.30, 60.32, 66.34, 116.24, 128.33, 128.46, 128.60 (2), 128.66, 129.30, 129.67, 130.00, 134.47, 139.03, 139.23, 140.68, 158.31, 165.21. HREIMS m/z (relative intensity) 483.0273 [15, calcd for $C_{24}H_{21}SO_4{}^{79}Br$ (M-H) 483.0266], 344 (5), 207 (5), 178 (100), 152 (34), 140 (17), 77 (32); CIMS m/z 504/502 ($M + NH_4^+$).

4-Benzenesulfonylmethyl-3-diphenylmethylenedihydro-2(3*H*)-furanone (39) was isolated as a white solid, mp 217-218 °C. ^{1}H NMR δ 2.30 (dd, *J* = 2.0, 14.0 Hz, 1H), 3.13 (dd, *J* = 11.6, 14.0 Hz, 1H), 3.87-3.93 (m, 1H), 4.56-4.63 (m, 2H), 7.03-7.70 (m, 15H); ^{13}C NMR δ 35.18, 57.47, 68.76, 122.58, 128.05, 128.08, 128.14, 129.20, 129.32, 129.39, 129.44, 129.72, 134.24, 138.40, 138.55, 140.08, 156.92, 168.08; HREIMS m/z (relative intensity) 404.1084 (3, calcd for $C_{24}H_{20}SO_4$ 404.1082), 263 (58), 217 (100), 203 (95), 189 (34), 178 (44), 165 (47), 141 (34), 115 (36), 91 (35), 77 (92); CIMS m/z 504/502 (M + NH_4^+).

3-Acetylthiopropyl 4-Phenylcinnamate (40) was isolated as a colorless oil. ^{1}H NMR δ 1.70-1.80 (m, 2H), 2.33 (s, 3H), 2.69 (t, *J* = 7.2 Hz, 2H), 4.04 (t, *J* = 6.0 Hz, 2H), 6.38 (s, 1H), 7.20-7.59 (m, 10H); ^{13}C NMR δ 25.85, 28.70, 30.82, 62.76, 117.40, 128.14, 128.38, 128.51, 128.59, 129.26, 129.69, 139.27, 140.87, 156.91, 166.28, 195.83; HREIMS m/z (relative intensity) 340.1134 (6, calcd for $C_{20}H_{20}SO_3$ 340.1133), 281 (2), 264 (22), 224 (18), 207 (100), 178 (33), 152 (5), 105 (6), 77 (3).

3-Butenyl 4-Phenylcinnamate (41) was isolated as a colorless oil. ^{1}H NMR δ 2.29 (tq, *J* = 1.0, 6.8 Hz, 2H), 4.08 (t, *J* = 6.8 Hz, 3H), 5.03-5.10 (m, 2H), 5.68 (ddt, *J* = 10.4, 17.2, 6.8 Hz, 1H), 6.40 (s, 1H), 7.20-7.45 (m, 10H); ^{13}C NMR δ 33.04, 63.47, 117.16, 117.43, 128.07, 128.32, 128.47, 128.54, 129.29, 129.60, 134.30, 139.13, 140.94, 156.88, 166.23; HREIMS m/z (relative intensity) 278.1308 (18, calcd for $C_{19}H_{18}O_2$ 278.1307), 250 (3), 224 (83), 207 (100), 178 (78), 152 (11), 105 (16), 77 (8).

4-Benzenesulfonyl-3-bromobutyl 4-Phenylcinnamate (42) was isolated as a white solid, mp 112-114 °C. ^{1}H NMR δ 2.01-2.07 (m, 1H), 2.38-2.39 (m, 1H), 3.59 (dd, *J* = 8.0, 14.8 Hz, 1H), 3.70 (d, *J* = 5.6, 14.8 Hz, 1H), 4.13-4.16 (m, 1H), 4.24-4.30 (m, 2H), 6.38 (s, 1H), 7.20-7.45 (m, 10H), 7.60-8.00 (m, 5H); ^{13}C NMR δ 37.02, 41.37, 61.44, 63.86, 116.84, 128.22, 128.36, 128.47, 128.53, 128.62, 129.25, 129.68, 129.82, 134.41, 138.99, 139.41, 140.78, 157.63, 165.82; HREIMS m/z (relative intensity) 498.0506

(8, calcd for $C_{25}H_{23}O_4{}^{79}Br$ 498.0500), 359 (10), 357 (10), 277 (6), 225 (9), 207 (100), 178 (66), 152 (8), 105 (15), 77 (30).

***trans*-5,5-Dimethyl-4-methyl-3-acetylthiomethyldihydro-2(3*H*)-furanone (44)** was isolated as a white solid, mp 65-67 °C. ^{1}H NMR δ 1.13 (d, J = 6.8 Hz, 3H), 1.23 (s, 3H), 1.41 (s, 3H), 2.03 (dq, J = 12.4, 6.8 Hz, 1H), 2.36 (s, 3H), 2.61 (dt, J = 4.8, 12.4 Hz, 1H), 3.22 (d, J = 4.8 Hz, 2H); ^{13}C NMR δ 13.09, 22.02, 26.82, 27.12, 30.69, 44.43, 47.21, 85.60, 176.06, 195.69; HREIMS m/z (relative intensity) 216.0821 (7, calcd for $C_{10}H_{16}SO_3$ 216.0820), 201 (3), 174 (88), 159 (32), 141 (6), 127 (48), 113 (11), 88 (21), 70 (28), 55 (24), 43 (100).

1,1-Dimethyl-3-acetylthiopropyl 3-Acetylthiopropionate (45) was isolated as a colorless oil. ^{1}H NMR δ 1.49 (s, 6H), 1.97-2.01 (m, 2H), 2.33 (s, 3H), 2.34 (s, 3H), 2.58 (t, J = 7.2 Hz, 2H), 2.86-2.90 (m, 2H), 3.09 (t, J = 7.2 Hz, 2H); ^{13}C NMR δ 24.09, 24.55, 26.04, 30.77, 30.78, 35.64, 40.95, 82.51, 171.00, 195.80, 195.91; EIMS m/z (relative intensity) M (not observed), 144 (42), 131 (22), 102 (30), 69 (69), 43 (100); CIMS m/z 310 ($M + NH_4^+$).

3-Isopropyl-5,5-Dimethyl-4-acetylthiomethyldihydro-2(3*H*)-furanone (46) was isolated as an inseparable *cis/trans* isomer mixture (1/1.4 or 1.4 by NMR). ^{1}H NMR δ all the H peaks are in the range of 1.0-3.4 ppm and cannot be assigned specifically due to serious overlap; ^{13}C NMR δ (the *cis/trans* mixture) 18.68, 19.91, 20.86, 22.96, 23.01, 25.34, 25.57, 25.75, 27.67, 28.15, 28.92, 29.31, 30.76, 30.84, 46.88, 47.90, 50.21, 51.69, 83.23, 83.63, 175.66, 175.94, 194.83, 194.86; HREIMS m/z (relative intensity) 244.1136 (2, calcd. for $C_{12}H_{20}SO_3$ 244.1133), 229 (2), 202 (59), 187 (17), 155 (24), 143 (9), 126 (44), 113 (25), 102 (51), 82 (29), 69 (45), 55 (20), 43 (100).

(1,1-Dimethyl-3-acetylthio)propyl 3-Methyl-2-butenoate (47) was isolated as a colorless oil. ^{1}H NMR δ 1.50 (s, 6H), 1.86 (s, 3H), 2.13 (s, 3H), 2.32 (s, 3H), 1.99-2.03 (m, 2H), 2.87-2.92 (m,2H), 5.60-5.62 (m, 1H); ^{13}C NMR δ 20.20, 24.23, 26.26,

27.54, 30.76, 41.03, 80.83, 117.58, 155.75, 166.28, 196.06; EIMS m/z (relative intensity) M (not observed), 144 (64), 111 (3), 102 (27), 83 (100), 69 (66), 43 (35); CIMS m/z 262 (M + NH_4^+)

Diallyl Fumarate (48) was isolated as a colorless oil. ^{1}H NMR δ 4.70 (d, *J* = 5.7 Hz, 4H), 5.28 (dd, *J* = 1.5, 10.5 Hz, 2H), 5.35 (dd, *J* = 1.5, 17.4 Hz, 2H), 5.95 (ddt, *J* = 10.5, 17.4, 5.7 Hz, 2H), 6.90 (s, 2H); ^{13}C NMR δ 66.09, 119.07, 131.65, 133.82, 164.71; HREIMS m/z (relative intensity) 196.0737 (2, calcd. for $C_{10}H_{12}O_4$ 196.0736), 136 (100), 111 (29), 99 (24), 83 (8), 67 (6), 55 (20), 41 (26).

Allyl (3-Benzenesulfonyl-2-bromo)propyl Fumarate (49) was isolated as a colorless oil. ^{1}H NMR δ 3.69 (dd, *J* = 5.1, 14.7 Hz, 1H), 3.78 (dd, *J* = 7.5, 14.7 Hz), 4.57-4.65 (m, 3H), 4.71 (d, *J* = 5.1 Hz, 2H), 5.30 (dd, *J* = 1.2, 10.5 Hz, 1H), 5.40 (dd, *J* = 1.2, 17.1 Hz, 1H), 5.98 (ddt, *J* = 10.5, 17.1, 5.1 Hz, 1H), 6.90 (s, 1H), 6.91 (s, 1H); ^{13}C NMR δ 39.19, 60.60, 66.30, 67.07, 119.36, 128.38, 129.86, 131.57, 132.82, 134.69, 139.04, 164.11, 164.50; HREIMS m/z (relative intensity) 415.9917 (7, calcd for $C_{16}H_{17}SO_4{}^{79}Br$ 415.9929), 337 (8), 277 (70), 181 (17), 139 (100), 125 (33), 99 (24), 77 (40), 55 (17).

Di(3-benzenesulfonyl-2-bromo)propyl Fumarate (50) was isolated as a white solid, mp 145-147 °C. ^{1}H NMR (CD_3CN) δ 3.83 (dd, *J* = 6.3, 15.6 Hz, 2H), 3.93 (dd, *J* = 6.3, 15.6 Hz, 2H), 4.50-4.60 (m, 6H), 6.81 (s, 2H); ^{13}C NMR (CD_3CN) δ 41.16, 60.64, 68.45, 129.47, 130.96, 134.57, 135.77, 140.54, 165.14; HREIMS m/z (relative intensity) 496.9099 [31, calcd for $C_{16}H_{17}SO_6{}^{79}Br_2$ (M - $PhSO_2$) 496.9093], 361 (133), 359 (28), 228 (16), 181 (28), 125 (94), 77 (100).

Di(1,1-dimethyl-2-propenyl) Fumarate (51) was isolated as a yellow liquid. ^{1}H NMR δ 1.56 (s, 12H), 5.11 (dd, *J* = 0.8, 10.8 Hz, 2H), 5.20 (dd, *J* = 0.8, 17.6 Hz, 2H), 6.09 (dd, *J* = 10.8, 17.6, 2H), 6.71 (s, 2H); ^{13}C NMR δ 26.54, 82.17, 113.47, 134.64, 142.00, 164.10; HREIMS m/z (relative intensity) 167.0706 [14, calcd for $C_7H_{11}O_3$ (M - C_5H_9O) 167.0708], 140 (9), 99 (88), 85 (68), 69 (100); CIMS m/z 270 (M + NH_4^+).

4-Benzenesulfonylmethyl-3-[4'-bromomethyl-5',5'-dimethyldihydro-2'(3'*H*)-furanone-3'-yl)]-5,5-dimethyldihydro-2(3*H*)-furanone (52) was isolated as a mixture of stereoisomers. Only one isomer can be isolated partially pure as a white solid, mp 165-167 °C. IR (cm^{-1}) 1766, 1307, 1109; ^1H NMR (one isomer) δ 1.29 (s, 3H), 1.40 (s, 3H), 1.46 (s, 3H), 1.68 (s, 3H), 3.14-3.58 (m, 8H), 7.60-8.00 (m, 5H); ^{13}C NMR (one isomer) δ 21.90, 23.09, 27.13, 28.34, 29.56, 41.19, 44.51, 44.62, 48.73, 56.40, 84.49, 85.49, 128.35, 129.92, 134.69, 138.70, 174.53, 174.63; HREIMS m/z (relative intensity) 472.0554 [8, calcd for $C_{20}H_{25}SO_6{}^{79}Br$ 472.0555], 393 (100), 251 (40), 233 (32), 193 (17), 125 (20), 77 (60), 69 (75), 43 (65); CIMS m/z 490 ($M + NH_4^+$).

1,1-Dimethyl-2-propynyl Acrylate (53) was isolated as a colorless liquid. ^1H NMR δ 1.72 (s, 6H), 2.56 (s, 1H), 5.80 (dd, J = 0.8, 10.4 Hz, 1H), 6.07 (dd, J = 10.4, 17.6 Hz, 1H), 6.37 (dd, J = 0.8, 17.6 Hz, 1H); ^{13}C NMR δ 29.10, 72.04, 72.62, 84.75, 129.29, 130.89, 164.71; HREIMS m/z (relative intensity) 138.0675 (3, calcd for $C_8H_{10}O_2$ 138.0680), 123 (8), 95 (18), 83 (17), 67 (100), 55 (98).

3-Benzenesulfonylmethyl-4-bromomethyl-5,5-dimethyl-2(5*H*)-furanone (54) was isolated as a white solid, mp 162-164 °C. IR (cm^{-1}) 1758, 1310, 1144; ^1H NMR δ 1.56 (s, 6H), 4.25 (s, 2H), 4.38 (s, 2H), 7.50-7.90 (m, 5H); ^{13}C NMR δ 18.87, 25.46, 51.48, 86.92, 119.59, 128.62, 129.60, 134.83, 138.06, 168.87, 169.59; HREIMS m/z (relative intensity) 279.0687 [75, calcd for $C_{14}H_{15}SO_4$ (M-Br) 279.0691), 215 (48), 125 (18), 123 (64), 121 (47), 95 (20), 77 (82), 67 (20), 51 (41), 42 (100).

Allyl 2-Butynoate (55, R = H) was isolated as a colorless liquid. ^1H NMR δ 1.99 (s, 3H), 4.64 (dt, J = 5.8, 1.2 Hz, 2H), 5.28 (dd, J = 1.2, 10.5 Hz, 1H), 5.35 (dd, J = 1.2, 17.1 Hz, 1H), 5.80-5.90 (m, 1H); ^{13}C NMR δ 3.87, 66.35, 72.30, 85.92, 119.25, 131.32, 153.45; EIMS m/z (relative intensity) 123 (2, M - H), 95 (8), 79 (17), 67 (100), 57 (5), 49 (6); CIMS m/z 142 ($M + NH_4^+$).

1,1-Dimethyl-2-propenyl 2-Butynoate (55, R = Me) was isolated as a colorless liquid. ^{1}H NMR δ 1.52 (s, 6H), 1.92 (s, 3H), 6.02 (d, J = 10.8 Hz, 1H), 6.06 (dd, J = 10.8, 17.6 Hz, 1H), 6.07 (d, J = 17.6 Hz, 1H); ^{13}C NMR δ 3.77, 26.42, 73.05, 83.06, 83.48, 113.54, 141.60, 152.40; EIMS m/z (relative intensity) 152 (M, 2), 137 (6), 109 (10), 69 (100); CIMS m/z 170 (M + NH_4^+).

3-Benzenesulfonyl-2-bromopropyl 2-Butynoate (56) was isolated as an inseparable mixture with its elimination product (M - HBr). ^{1}H NMR δ 2.01 (s, 3H), 3.65 (dd, J = 5.7, 15.3 Hz, 1H), 3.82 (dd, J = 7.2, 15.3 Hz, 1H), 4.40-4.55 (m, 3H), 7.60-7.90 (m, 5H); ^{13}C NMR δ 4.00, 38.81, 60.33, 67.11, 68.13, 87.55, 128.29, 129.67, 134.49, 139.21, 152.64; HREIMS m/z (relative intensity) 265.0533 [26, calcd for $C_{13}H_{13}SO_4$ (M - Br) 265.0534], 203 (33, M - H), 181 (8), 125 (17), 77 (48), 67 (100), 51 (12); CIMS m/z 364/362 (M + NH_4^+).

4-Benzenesulfonylmethyl-3-(1-*E*-bromoethylene)-5,5-dimethydihydro-2(3*H*)-furanone (57) was isolated as a inseparable mixture with **6**. ^{1}H NMR δ 1.50 (s, 3H), 1.70 (s, 3H), 2.80 (s, 3H), 3.31 (dd, J = 1.0, 14.8 Hz, 1H), 3.51 (d, J = 10.0 Hz, 1H), 3.59 (dd, J = 10.0, 14.8 Hz, 1H), 7.60-7.90 (m, 5H); ^{13}C NMR δ 24.13, 26.20, 30.22, 48.38, 56.22, 82.76, 128.35, 129.70, 129.73, 134.30, 142.00, 142.76, 165.21; HREIMS m/z (relative intensity) 293.0845 [100, calcd for $C_{15}H_{17}SO_4$ (M - Br) 293.0848], 209 (3), 175 (14), 125 (17), 107 (17), 77 (23); CIMS m/z 392/390 (M + NH_4^+).

Propargyl 3-Methyl-2-butenoate (58, R = H) was isolated as a colorless liquid. ^{1}H NMR δ 1.91 (d, J = 1.2 Hz, 3H), 2.18 (d, J = 1.2 Hz, 3H), 2.45 (t, J = 2.4 Hz, 1H), 4.68 (d, J = 2.4 Hz, 2H), 5.65-5.72 (m, 1H); ^{13}C NMR δ 20.42, 27.57, 51.11, 74.45, 78.26, 115.06, 158.74, 165.63; HREIMS m/z (relative intensity) 138.0678 (6, calcd for $C_8H_{10}O_2$ 138.0681), 123 (8), 93 (30), 83 (100), 55 (54), 40 (63).

1,1-Dimethyl-2-propynyl 3-Methyl-2-butenoate (58, R = Me) was isolated as a colorless liquid. ^{1}H NMR δ 1.68 (s, 6H), 1.87 (d, J = 1.5 Hz, 3H), 2.16 (d, J = 1.2 Hz,

3H), 2.53 (s, 1H), 5.65-5.72 (m, 1H); ^{13}C NMR δ 20.23, 27.48, 29.17, 70.76, 72.05, 85.27, 116.48, 157.14, 165.11; HREIMS m/z (relative intensity) 166.0992 (6, calcd for $C_{10}H_{14}O_2$ 166.0994), 151 (2), 123 (4), 100 (13), 83 (100), 67 (28), 55 (15), 41 (14).

3-Benzenesulfonyl-2-bromo-2-propenyl 3-Methyl-2-butenoate (59). The Z isomer was isolated as a white solid, mp 80-82 °C. IR (cm^{-1}) 1727, 1325, 1137; ^{1}H NMR δ 1.94 (d, *J* = 1.2 Hz, 3H), 2.17 (d, *J* = 1.2 Hz, 3H), 4.78 (d, *J* = 1.8 Hz, 2H), 5.70-5.75 (m, 1H), 7.16 (t, *J* = 1.8 Hz, 1H); ^{13}C NMR δ 20.62, 27.69, 66.18, 114.33, 128.24, 129.23, 130.36, 133.98, 135.06, 140.35, 160.72, 164.41; HREIMS m/z (relative intensity) 279.0689 [97, calcd for $C_{14}H_{15}SO_4$ (M - Br) 279.0691), 197 (93), 125 (18), 83 (100), 77 (35), 51 (12). The E isomer was isolated as a colorless oil. IR (cm^{-1}) 1724, 1322, 1138; ^{1}H NMR δ 1.93 (d, *J* = 1.2 Hz, 3H), 2.19 (d, *J* = 1.2 Hz, 3H), 5.43 (d, *J* = 1.2 Hz, 2H), 5.70-5.75 (m, 1H), 6.88 (t, *J* = 1.2 Hz, 1H); ^{13}C NMR δ 20.55, 27.65, 60.96, 114.83, 127.88, 129.64, 133.98, 134.02, 139.54, 140.10, 159.44, 165.29; HREIMS m/z (relative intensity) 279.0688 [38, calcd for $C_{14}H_{15}SO_4$ (M - Br) 279.0691), 197 (45), 125 (8), 83 (100), 77 (25), 51 (15).

3-Benzenesulfonyl-2-bromo-1,1-dimethyl-2-propenyl 3-Methyl-2-butenoate (60). The Z isomer was isoalted as a white solid, mp 87-89 °C. IR (cm^{-1}) 1721, 1320, 1146; ^{1}H NMR δ 1.61 (s, 6H), 1.85 (d, *J* = 1.2 Hz, 3H), 2.03 (d, *J* = 1.2 Hz, 3H), 5.55-5.62 (m, 1H), 7.14 (s, 1H), 7.50-7.90 (m, 5H); ^{13}C NMR δ 20.23, 26.59, 27.53, 80.57, 115.77, 128.01, 128.96, 130.03, 133.57, 140.56, 147.34, 158.42, 164.53; HREIMS m/z (relative intensity) 307.1007 [70, calcd for $C_{16}H_{19}SO_4$ (M - Br) 307.1004], 225 (63), 166 (20), 125 (22), 83 (100), 77 (25), 55 (15); CIMS m/z 406/404 (M + NH_4^+). The E isomer was isoalted as a colorless oil. IR (cm^{-1}) 1719, 1322, 1147; ^{1}H NMR δ 1.87 (s, 6H), 1.91 (d, *J* = 1.2 Hz, 3H), 2.16 (d, *J* = 1.2 Hz, 3H), 5.80-5.82 (m, 1H), 6.82 (s, 1H), 7.50-7.90 (m, 5H); ^{13}C NMR δ 20.46, 27.26, 27.77, 80.88, 116.79, 127.65, 129.50, 131.76, 133.88, 136.81, 146.48, 157.30, 165.45; HREIMS m/z (relative intensity) 307.1008 [30,

calcd. for $C_{16}H_{19}SO_4$ (M - Br) 307.1004), 225 (26), 166 (12), 125 (25), 83 (100), 77 (35), 55 (52); CIMS m/z 406/404 ($M + NH_4^+$).

4-(*E*)-Benzenesulfonylmethylene-3-isopropylidene-5,5-dimethyldihydro-2-(3*H*)-furanone (61) was isolated as a white solid, mp 135-137 °C. IR (cm^{-1}) 1756, 1307, 1150; ^1H NMR δ 1.40 (s, 6H), 2.37 (s, 3H), 2.51 (s, 3H), 6.04 (s, 1H), 7.50-7.90 (m, 5H); ^{13}C NMR δ 22.67, 26.60, 28.40, 82.84, 121.43, 127.50, 129.52, 131.59, 133.78, 141.26, 152.63, 165.88, 167.80; HREIMS m/z (relative intensity) 306.0923 [24, calcd for $C_{16}H_{18}SO_4$ 306.0926), 288 (14), 165 (100), 147 (15), 119 (23), 77 (59), 43 (36).

(2-Bromo-4,4-dicyano)butyl 3-Methyl-2-butenoate (62) was isolated as a colorless oil. ^1H NMR δ 1.95 (s, 3H), 2.19 (s, 3H), 2.45 (ddd, *J* = 4.8, 11.1, 14.8 Hz, 1H), 2.70 (ddd, *J* = 3.3, 11.1, 14.8 Hz, 1H), 4.20 (dd, *J* = 4.8, 11.1 Hz, 1H), 4.20-4.30 (m, 1H), 4.31 (dd, *J* = 6.4, 12 Hz, 1H), 4.50 (dd, *J* = 4.8, 12 Hz, 1H), 5.70-5.78 (m, 1H); ^{13}C NMR δ 20.60, 21.86, 27.68, 36.55, 45.29, 65.34, 111.34, 111.83, 114.55, 160.20, 165.33; EIMS m/z (relative intensity) 286/284 (8, M^+), 187/185 (8), 121/119 (18), 100 (64), 83 (100), 55 (26).

(2,2-Dicyanocyclopropyl)methyl 3-Methyl-2-butenoate (63) was isolated as a colorless oil. ^1H NMR δ 1.92 (s, 3H), 2.17 (s, 3H), 2.95 (dd, *J* = 8.4, 15.2 Hz, 1H), 3.06 (dd, *J* = 3.6, 15.2 Hz, 1H), 4.27 (dd, *J* = 7.6, 11.2 Hz, 1H), 4.28-4.35 (m, 1H), 4.47 (dd, *J* = 4.0, 11.2 Hz, 1H), 5.65-5.75 (m, 1H); ^{13}C NMR δ 20.60, 22.08, 27.68, 42.29, 46.79, 65.44, 111.39, 111.94, 114.55, 160.21, 165.24; CIMS m/z 222 ($M + NH_4^+$).

2-Bromo-4,4-dicyanobutyl Cinnamate (64) was isolated as a colorless oil. ^1H NMR δ 2.45 (ddd, *J* = 4.8, 11.2, 14.4 Hz, 1H), 2.71 (ddd, *J* = 3.2, 11.2, 14.4 Hz, 1H), 4.20 (dd, *J* = 4.8, 11.2 Hz, 1H), 4.25-4.35 (m, 1H), 4.45 (dd, *J* = 6.8, 12 Hz, 1H), 4.60 (dd, *J* = 4.8, 12 Hz, 1H), 6.46 (d, J = 16 Hz, 1H), 7.30-7.60 (m, 5H), 7.75 (d, J = 16 Hz, 1H); ^{13}C NMR δ 22.02, 36.61, 45.27, 66.34, 111.44, 111.92, 116.50, 128.53, 129.22,

131.10, 134.09, 147.04, 166.10; HREIMS m/z (relative intensity) 332.0153 (15, calcd for $C_{15}H_{13}N_2O_2{}^{79}Br$ 332.0160), 252 (7), 148 (51), 131 (100), 103 (27), 77 (14), 51 (6).

(2-Bromo-4,4-dicyano)butyl 2-Butynoate (65) was isolated as a colorless oil. ^1H NMR δ 2.04 (s, 3H), 2.40 (ddd, *J* = 4.8, 11.1, 14.7 Hz, 1H), 2.70 (ddd, *J* = 3.0, 11.1, 14.4 Hz, 1H), 4.20 (dd, *J* = 4.8, 11.1 Hz, 1H), 4.25-4.35 (m, 1H), 4.40 (dd, *J* = 7.2, 12 Hz, 1H), 4.55 (dd, *J* = 5.1, 12 Hz, 1H); ^{13}C NMR δ 4.00, 21.85, 36.36, 44.17, 66.97, 71.46, 88.30, 111.19, 111.66, 152.35; CIMS m/z 286/284 ($M + NH_4^+$).

4-Bromomethyl-3-(1-*E*-bromoethylidene)dihydro-2(3*H*)-furanone (66) was isolated as colorless oil. ^1H NMR δ 2.89 (d, *J* = 1.5 Hz, 3H), 3.45 (t, *J* = 9.9 Hz, 1H), 3.50-3.60 (m, 1H), 3.70 (ddd, *J* = 0.9, 3.3, 9.9 Hz, 1H), 4.35 (ddd, *J* = 0.9, 6.6, 9.6 Hz, 1H), 4.42 (dd, *J* = 1.5, 9.6 Hz, 1H); ^{13}C NMR δ 26.06, 32.23, 45.84, 68.36, 127.41, 143.42, 166.33; HREIMS m/z (relative intensity) 281.8888 (15, calcd for $C_7H_8N_2O_2{}^{79}Br_2$ 281.8891), 203 (100), 145(7), 80 (33), 65 (32), 53 (29).

4-Bromomethyl-3-(1-*E*-bromoethylidene)-5,5-dimethyldihydro-2(3*H*)-furanone (67) was isolated as a colorless oil. ^1H NMR δ 1.40 (s, 3H), 1.63 (s, 3H), 2.90 (d, *J* = 1.2 Hz, 3H), 3.20-3.30 (m, 1H), 3.53 (dd, *J* = 2.4, 11 Hz, 1H), 3.66 (dd, *J* = 7.2, 11 Hz, 1H); ^{13}C NMR δ 22.08, 25.99, 29.13, 30.58, 54.16, 82.13, 130.04, 142.68, 165.37; HREIMS m/z (relative intensity) 309.9193 (6, calcd for $C_9H_{12}O_2{}^{79}Br_2$ 309.9204), 233 (100), 217 (10), 175 (78), 173 (80), 151(60), 107 (23), 91 (34), 65 (65).

Allyl Propynoate (68) was isolated as a colorless liquid. ^1H NMR δ 2.88 (s, 1H), 4.66 (d, *J* = 6.0 Hz, 2H), 5.28 (dd, *J* = 1.0, 10.4 Hz, 1H), 5.35 (dd, *J* = 1, 17.2 Hz, 1H), 5.80-5.90 (m, 1H); ^{13}C NMR δ 66.79, 74.52, 74.99, 119.65, 130.83, 152.44; EIMS m/z (relative intensity) 110 (M, not observed), 81 (13), 66 (8), 53 (100), 41 (16).

Allyl 4,4-Dimethyl-2-chloromercurio-2-pentenoate (69). The Z isomer was isolated as a colorless oil. ^1H NMR δ 1.22 (s, 9H), 4.65 (dt, *J* = 5.6, 1.2 Hz, 2H), 5.25 (dd, *J* = 1.2, 9.2 Hz, 1H), 5.30 (dd, *J* = 1.2, 16.4 Hz, 1H), 5.85-5.95 (m, 1H), 7.73 (s, 1H);

^{13}C NMR δ 30.03, 34.32, 66.50, 118.86, 131.93, 137.54, 167.17, 168.98; HREIMS m/z (relative intensity) 167.1071 [35, calcd for $C_{10}H_{15}O_2$ (M-HgCl) 167.1072], 153 (15), 121 (30), 109 (72), 81 (100), 67 (45), 57 (40); CIMS m/z 418 ($M + NH_4^+$). The E isomer was isolated as a colorless oil. ^1H NMR δ 1.12 (s, 9H), 4.60 (dt, J = 6.0, 1.2 Hz, 2H), 5.27 (dd, J = 1.2, 10.4 Hz, 1H), 5.36 (dd, J = 1.2, 16.0 Hz, 1H), 5.85 (s, 1H), 5.86-5.95 (m, 1H); ^{13}C NMR δ 29.69, 37.45, 66.15, 119.54, 131.61, 139.60, 158.42, 168.86; HREIMS m/z (relative intensity) 167.1070 [28, calcd. for $C_{10}H_{15}O_2$ (M - HgCl) 167.1072], 153 (21), 121 (39), 109 (89), 81 (100), 67 (51), 57 (56); CIMS m/z 418 ($M + NH_4^+$).

4-*tert*-Butyl-3-(1-*E*-chloromercurioethylidene)-5,5-dimethyldihydro-2(3*H*)-furanone (70) was isolated as a white solid, mp 117-119 °C. ^1H NMR δ 0.97 (s, 9H), 1.46 (dd, J = 1.2, 14.4 Hz, 1H), 1.84 (dd, J = 11.6, 14.4 Hz, 1H), 2.62 (d, J = 1.2 Hz, 3H), 2.85-2.93 (m, 1H), 4.13 (dd, J = 2.0, 9.2 Hz, 1H), 4.41 (ddd, J = 1.2, 7.2, 8.8 Hz, 1H); ^{13}C NMR δ 23.75, 30.09, 31.60, 41.73, 53.34, 71.41, 137.45, 167.44, 168.16; HREIMS m/z (relative intensity) 181.1229 [100, calcd for $C_{11}H_{17}O_2$ (M - HgCl) 181.1228], 165 (4), 125 (8), 109 (12), 57 (68), 43 (32); CIMS m/z 436 ($M + NH_4^+$).

4-*tert*-Butyl-3-(2,2-dimethylpropylene)-5,5-dimethyldihydro-2(3*H*)-furanone (71). The Z isomer was isolated as a colorless oil. ^1H NMR δ 0.94 (s, 9H), 1.27 (s, 9H), 1.43-1.49 (m, 2H), 2.95-2.99 (m,1H), 3.92 (dd, J = 6.6, 8.7 Hz, 1H), 4.57 (t, J = 8.7 Hz, 1H), 6.09 (d, J = 2.4 Hz, 1H); ^{13}C NMR δ 29.93 (6), 30.92, 33.42, 38.88, 49.63, 72.58, 129.27, 153.58, 168.82; HREIMS m/z (relative intensity) 224.1777 (12, calcd for $C_{14}H_{24}O_2$ 224.1776), 209 (9), 153 (100), 125 (7), 107 (15). The E isomer was isolated a white solid, mp 63-64 °C. ^1H NMR δ 0.98 (s, 9H), 1.19 (s, 9H), 1.43 (dt, J = 14.4, 1.2, Hz, 1H), 1.59 (dd, J = 11.4, 14.4 Hz, 1H), 3.33-3.39 (m, 1H), 4.20 (ddd, J = 1.5, 3.3, 8.7 Hz, 1H), 4.28 (dd, J = 0.6, 8.7 Hz, 1H), 6.65 (d, J = 2.4 Hz, 1H); ^{13}C NMR δ 29.84, 30.36, 31.70, 34.35, 34.39, 48.54, 71.39, 127.61, 149.83, 173.32; HREIMS m/z (relative

intensity) 224.1776 (14, calcd for $C_{14}H_{24}O_2$ 224.1776), 209 (8), 153 (100), 125 (7), 107 (15).

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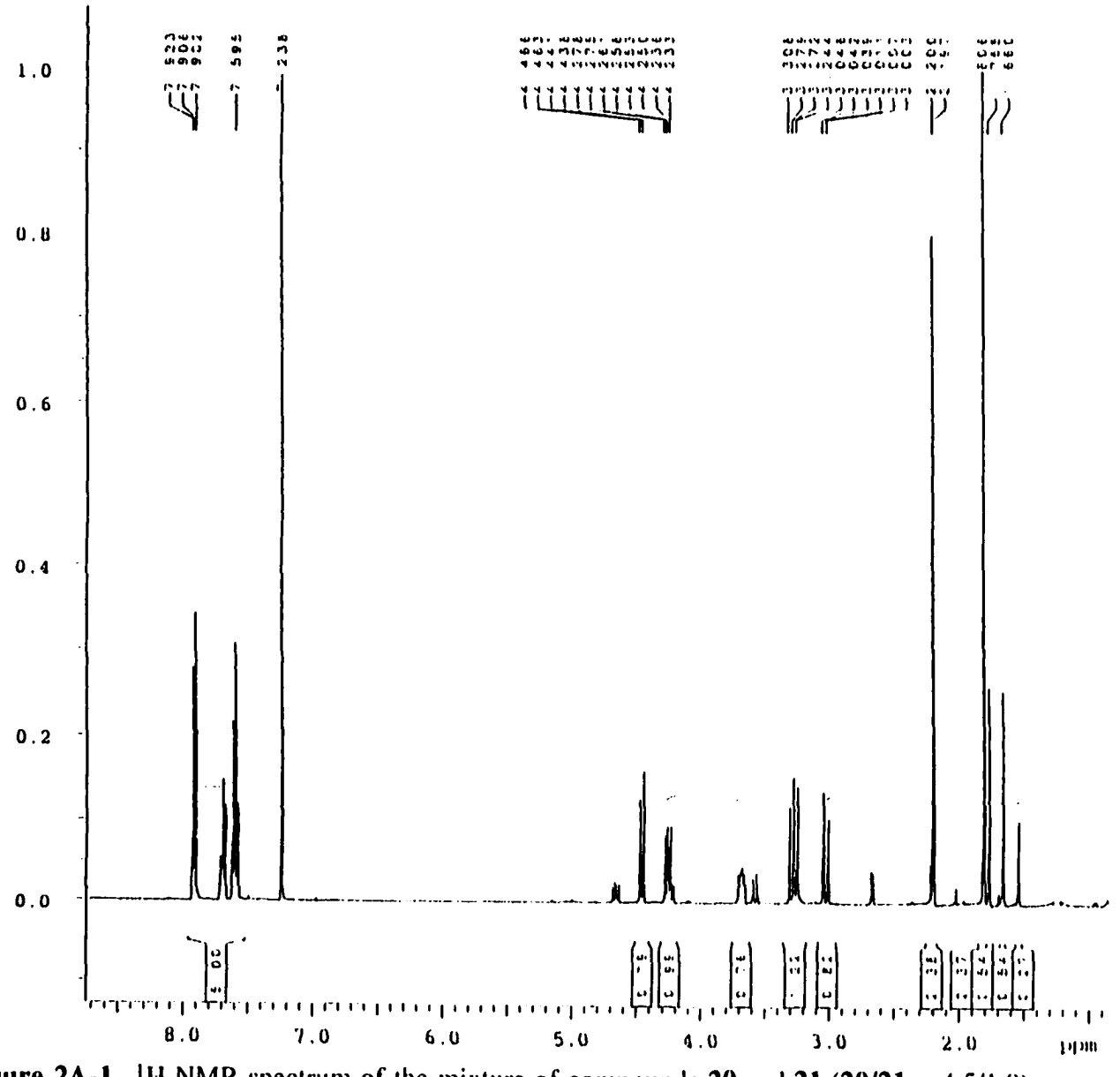
Appendix

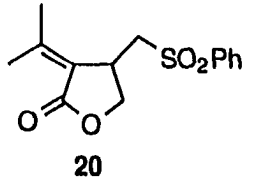
Spectra

NMR spectra were recorded in $CDCl_3$ or as stated otherwise (^1H at 400 MHz and ^{13}C at 100 MHz) with δ measured relative to $CHCl_3$ (7.27 ppm) or the central ^{13}C peak of $CDCl_3$ (77.23 ppm)

^1H and ^{13}C NMR spectra for compounds **3c-f**, **5a-b**, **5f-g**, **6-8**, **14**, **16**, **18**, **23**, **52**, **54**, **56**, **57**, and **59-61**, ^1H-^1H NOE spectra of compounds **3c-f**, **14**, and **61**, can be found in the supporting information accompanying the published paper, and are available via the Internet at http://pubs.acs.org.

^1H and ^{13}C NMR spectra for compounds **20/21** mixture, **29**, **32**, **33**, **35**, **39**, **40**, **42**, **44-47**, **62-67**, **70**, and **71**, ^1H-^1H NOE spectra of compounds **44**, **66**, **67**, and **71**, are included in this appendix.





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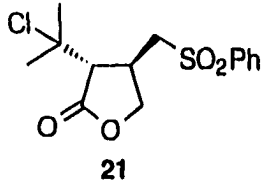
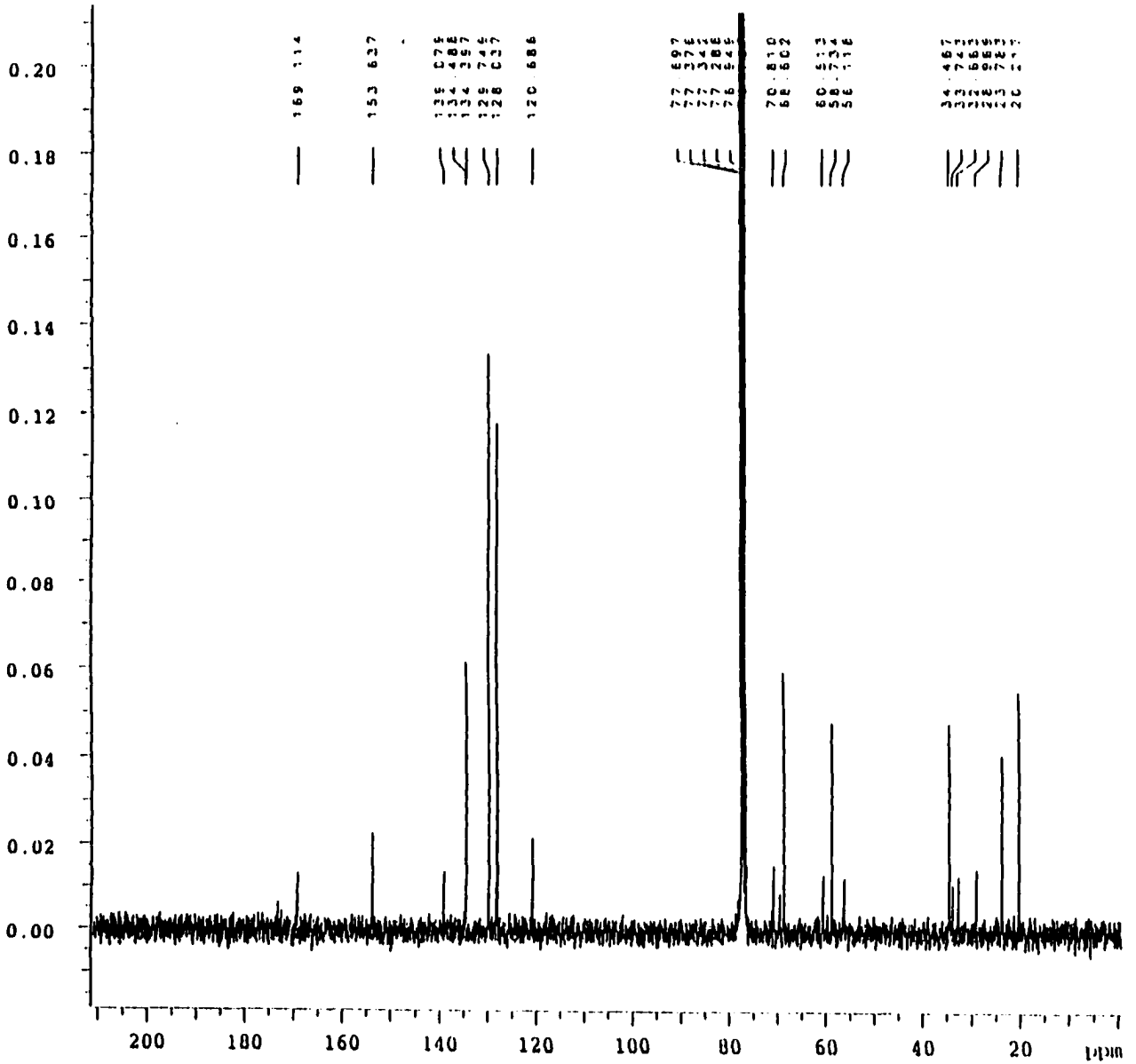
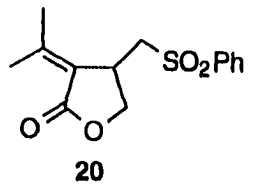


21

Figure 2A-1. ^{1}H NMR spectrum of the mixture of compounds **20** and **21** (**20/21** = 4.5/1.0).





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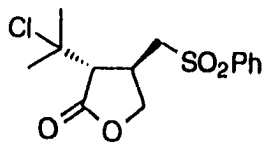
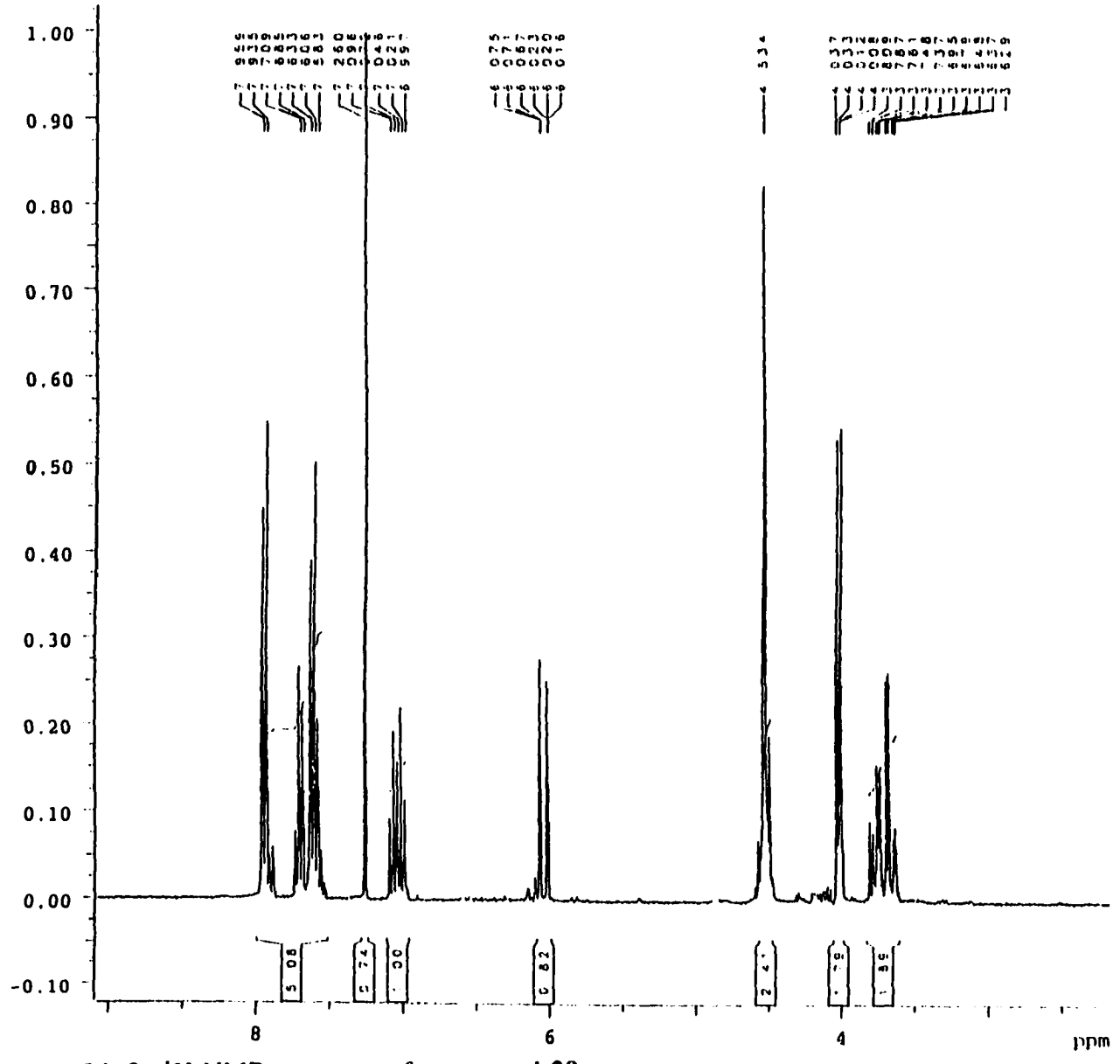
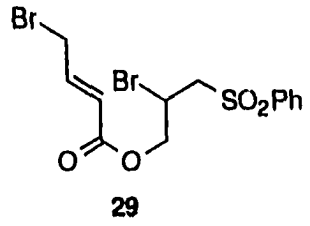


21

Figure 2A-2. ^{13}C NMR spectrum of the mixture of compounds **20** and **21** (**20/21** = 4.5/1.0).





29

Figure 2A-3. ^{1}H NMR spectrum of compound **29**.

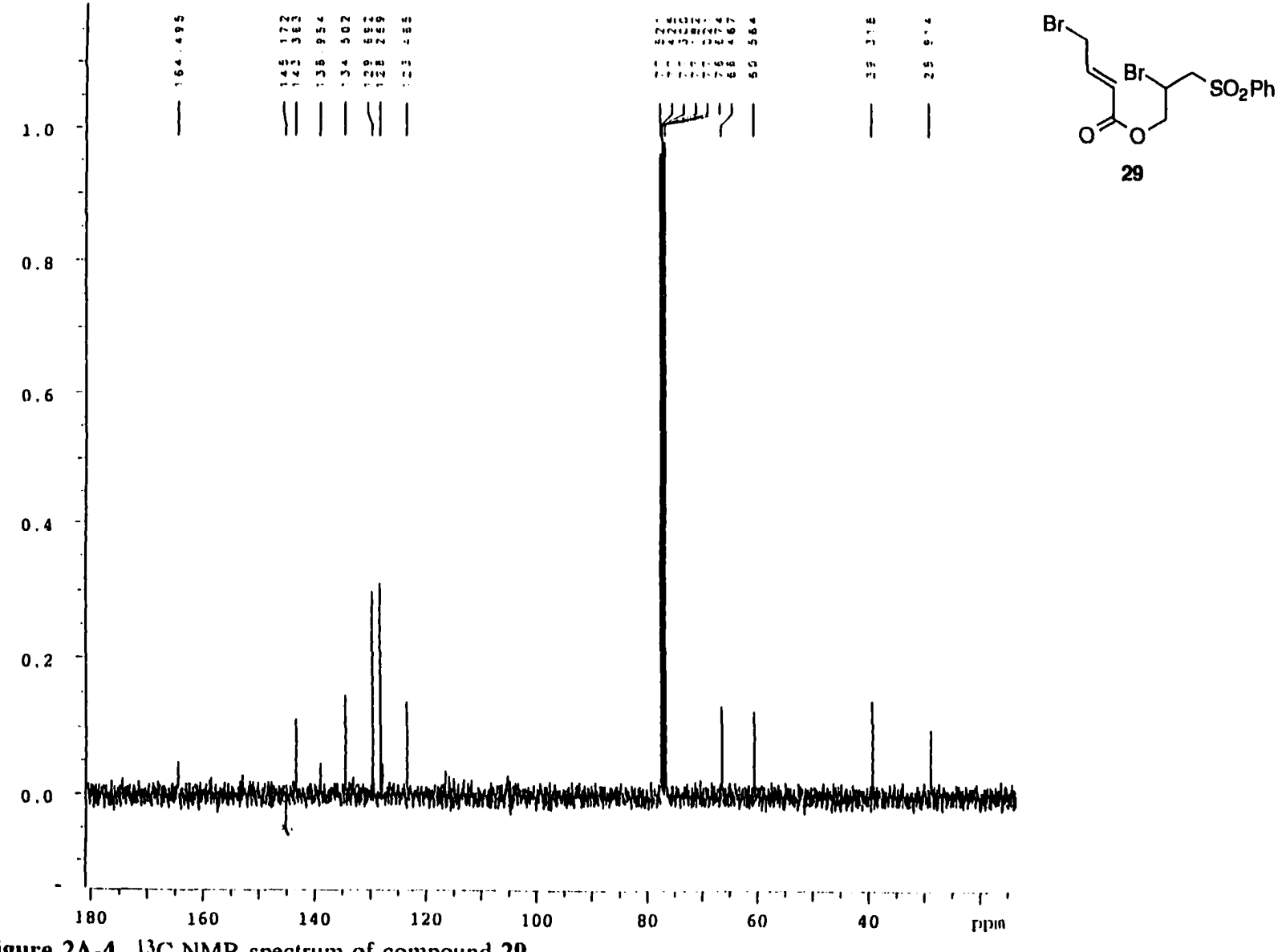
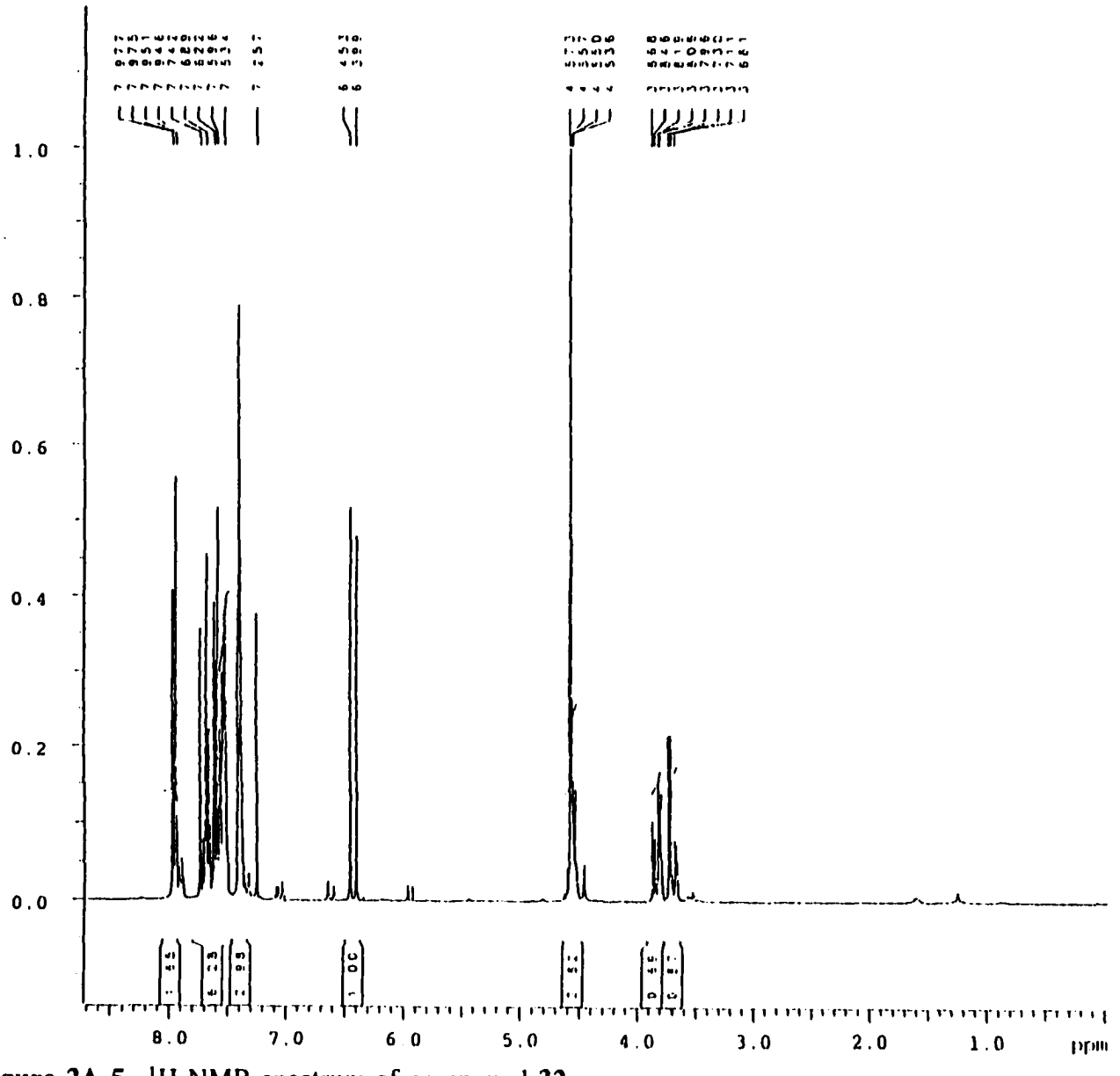
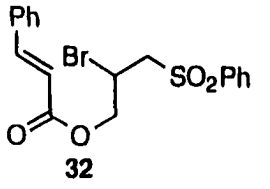


Figure 2A-4. ^{13}C NMR spectrum of compound **29**.





32

Figure 2A-5. ^{1}H NMR spectrum of compound **32**.

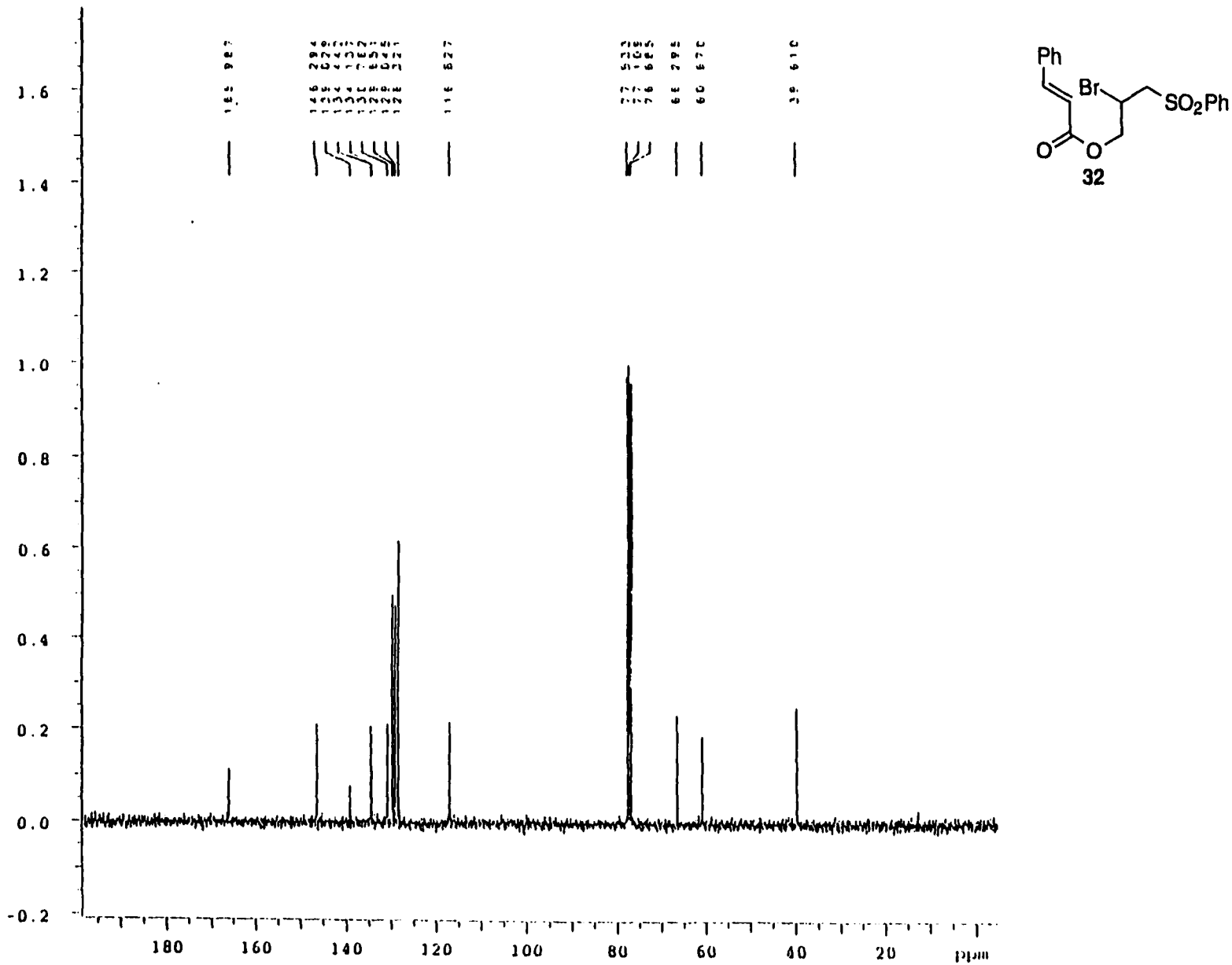
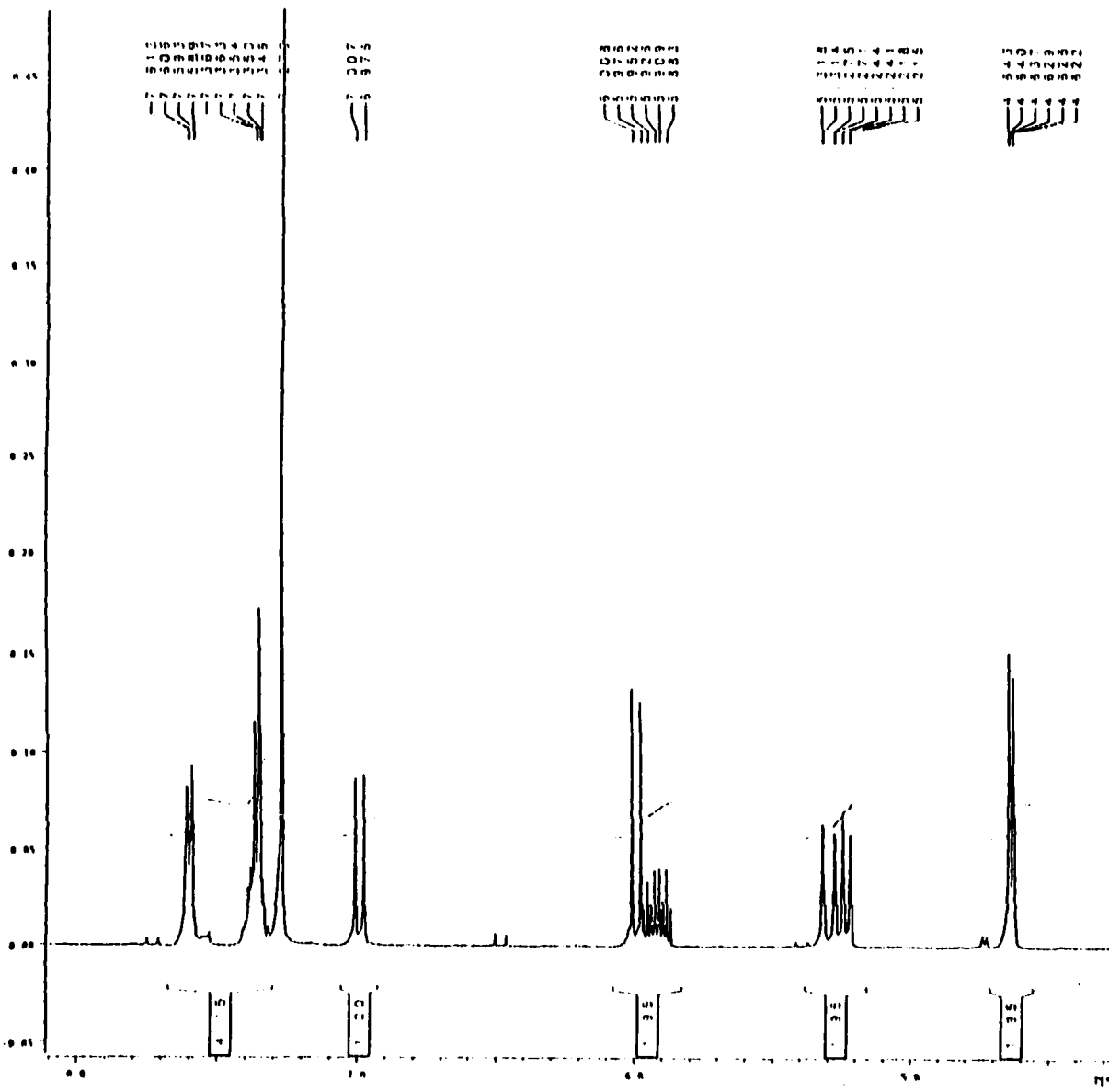
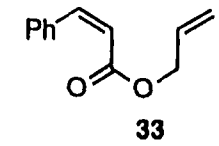


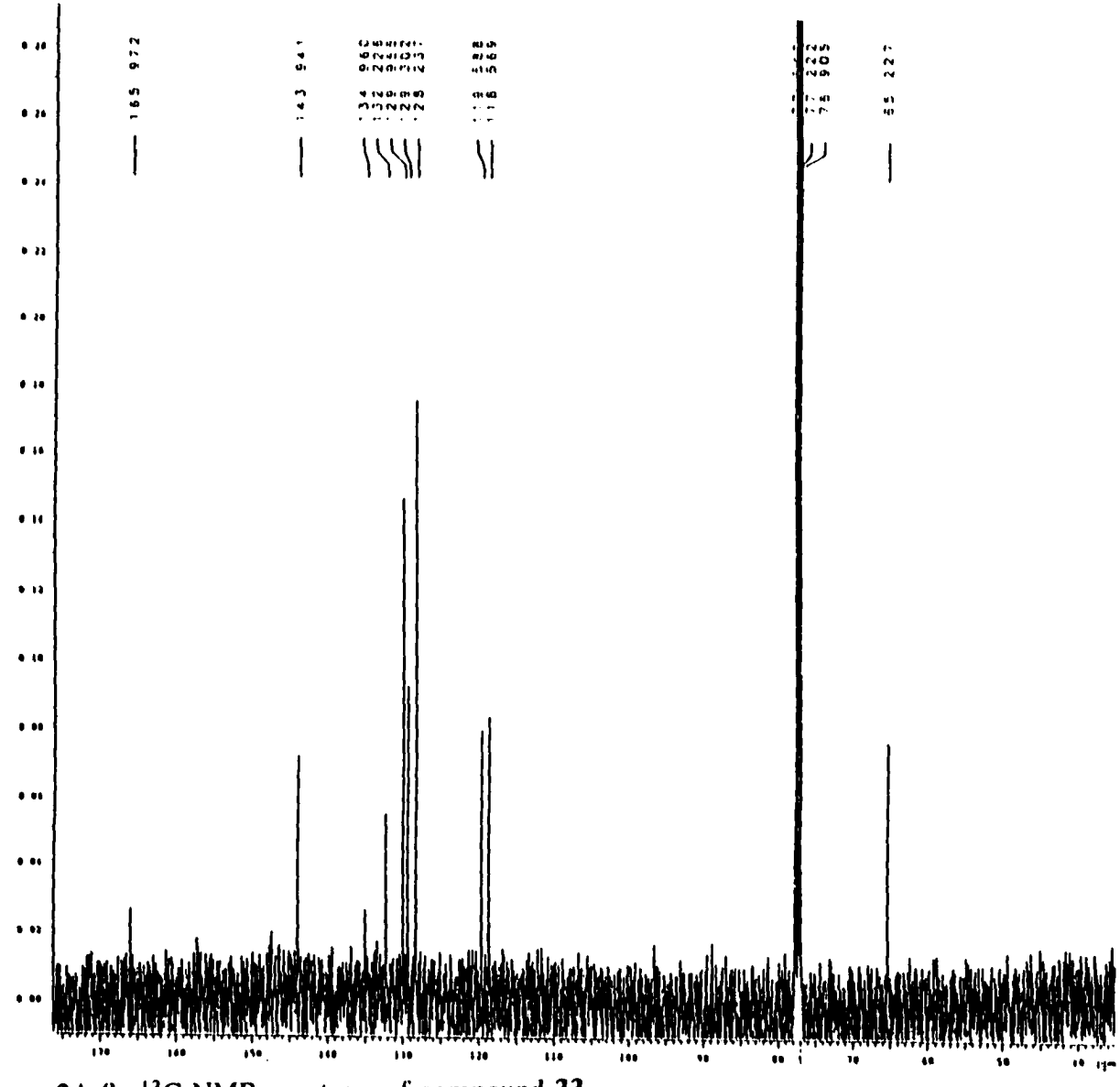
Figure 2A-6. ^{13}C NMR spectrum of compound **32**.

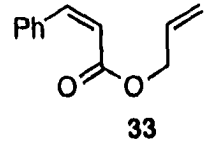




33

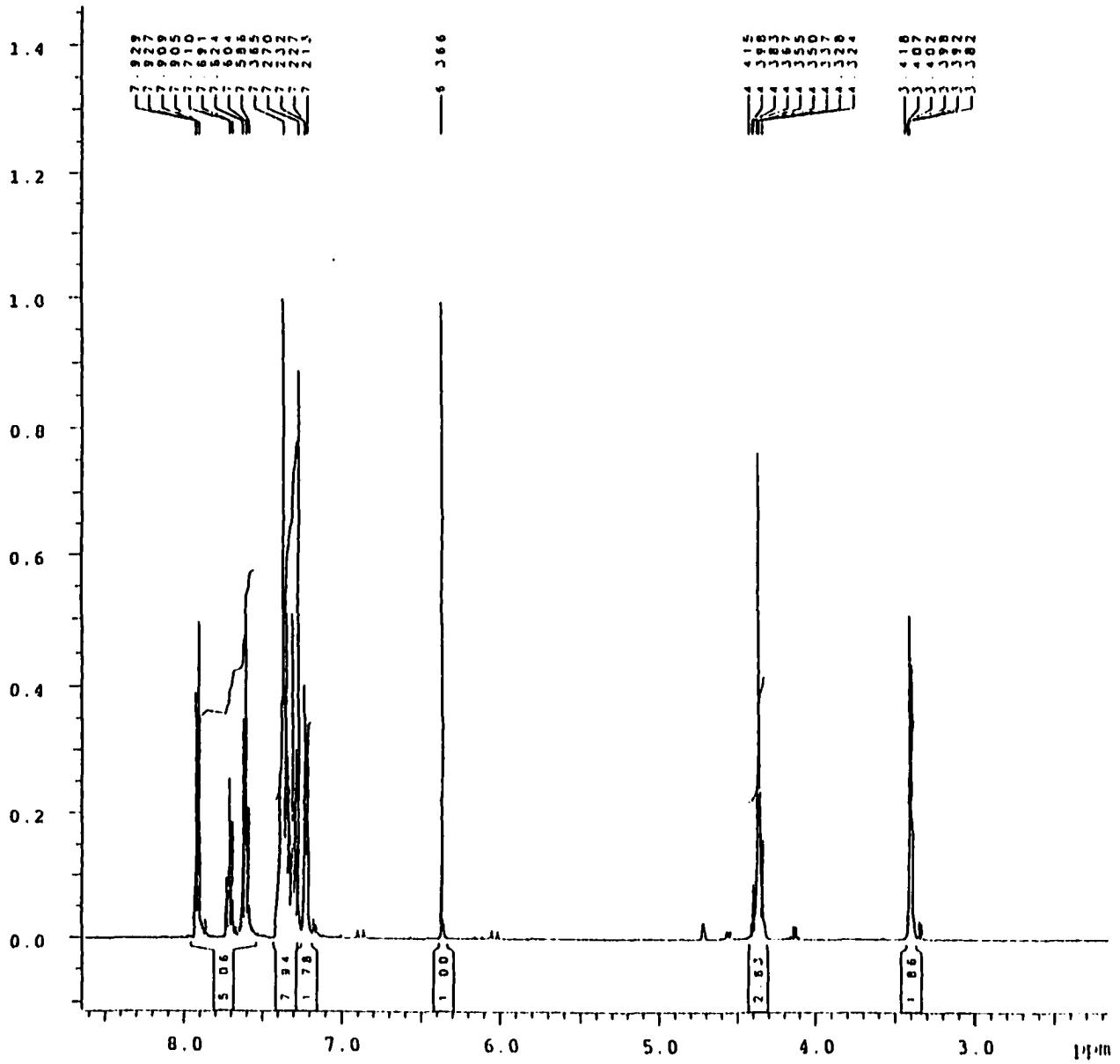
Figure 2A-7. ^{1}H NMR spectrum of compound **33**.

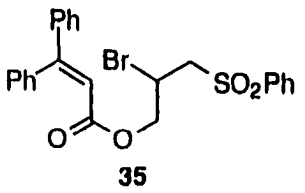




33

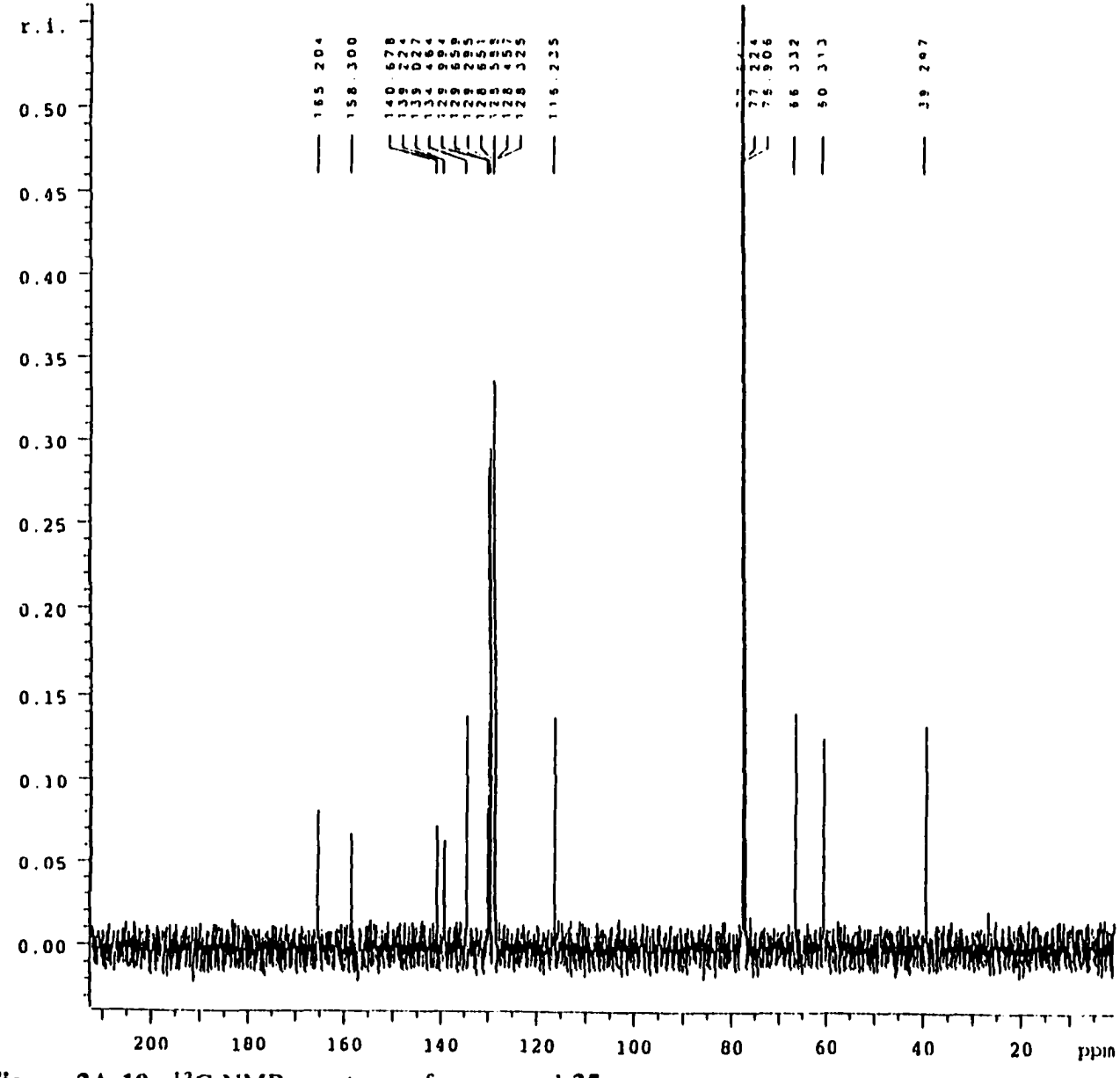
Figure 2A-8. ^{13}C NMR spectrum of compound **33**.

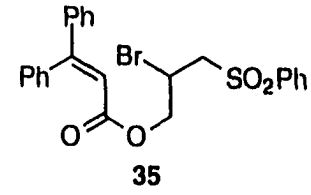




35

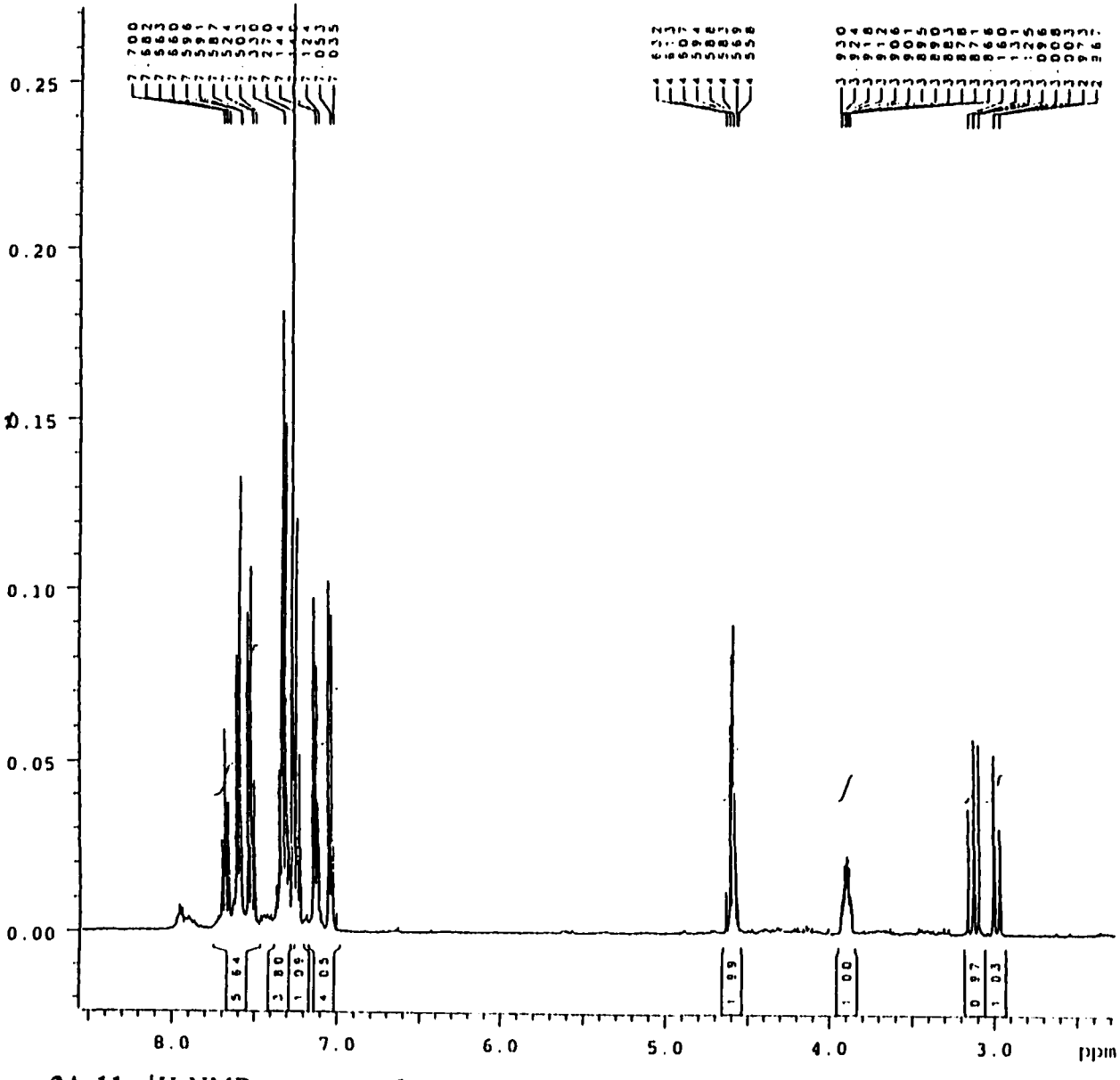
Figure 2A-9. ^{1}H NMR spectrum of compound **35**.

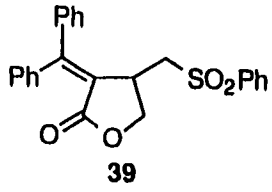




35

Figure 2A-10. ^{13}C NMR spectrum of compound **35**.





39

Figure 2A-11. ^{1}H NMR spectrum of compound **39**.

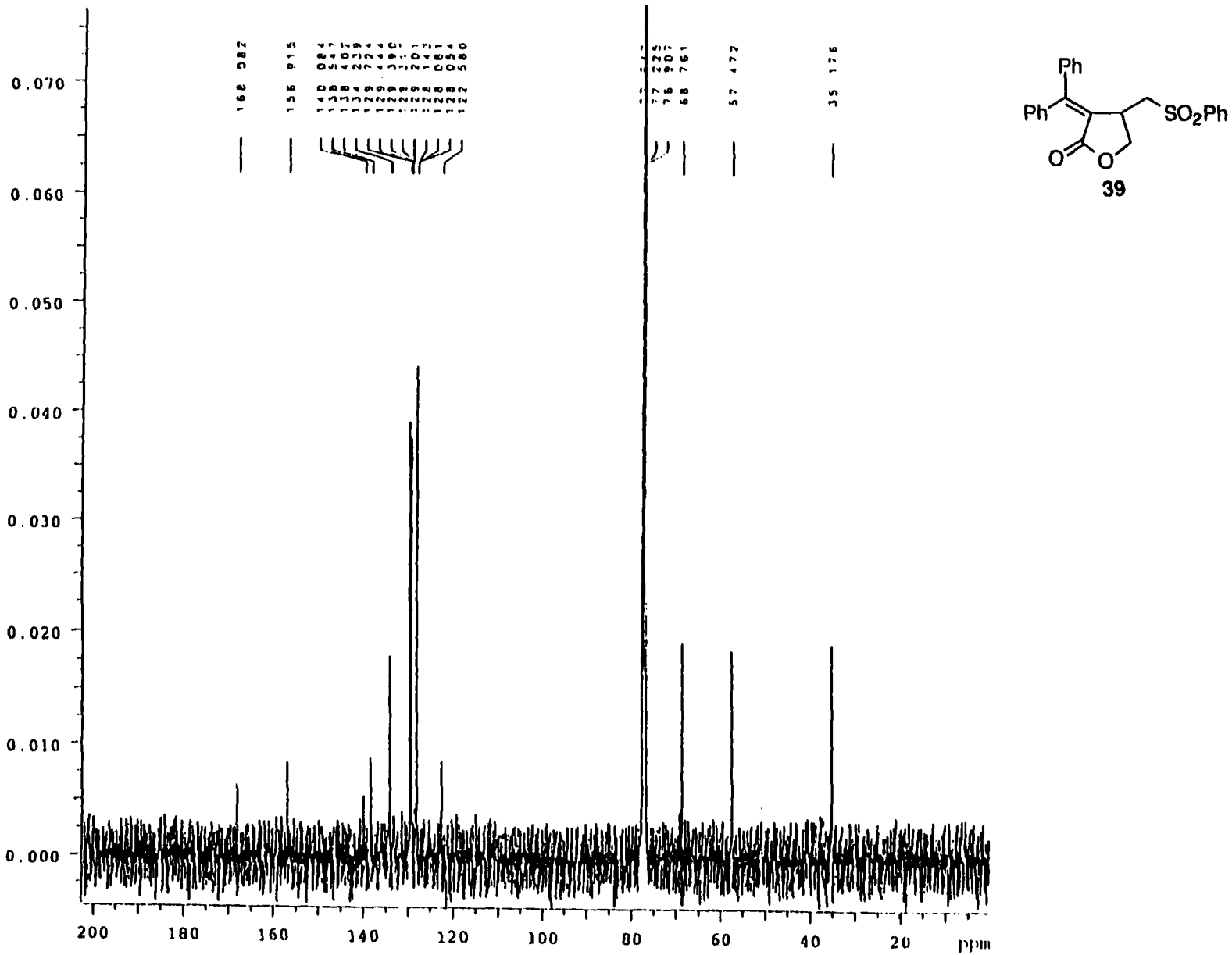
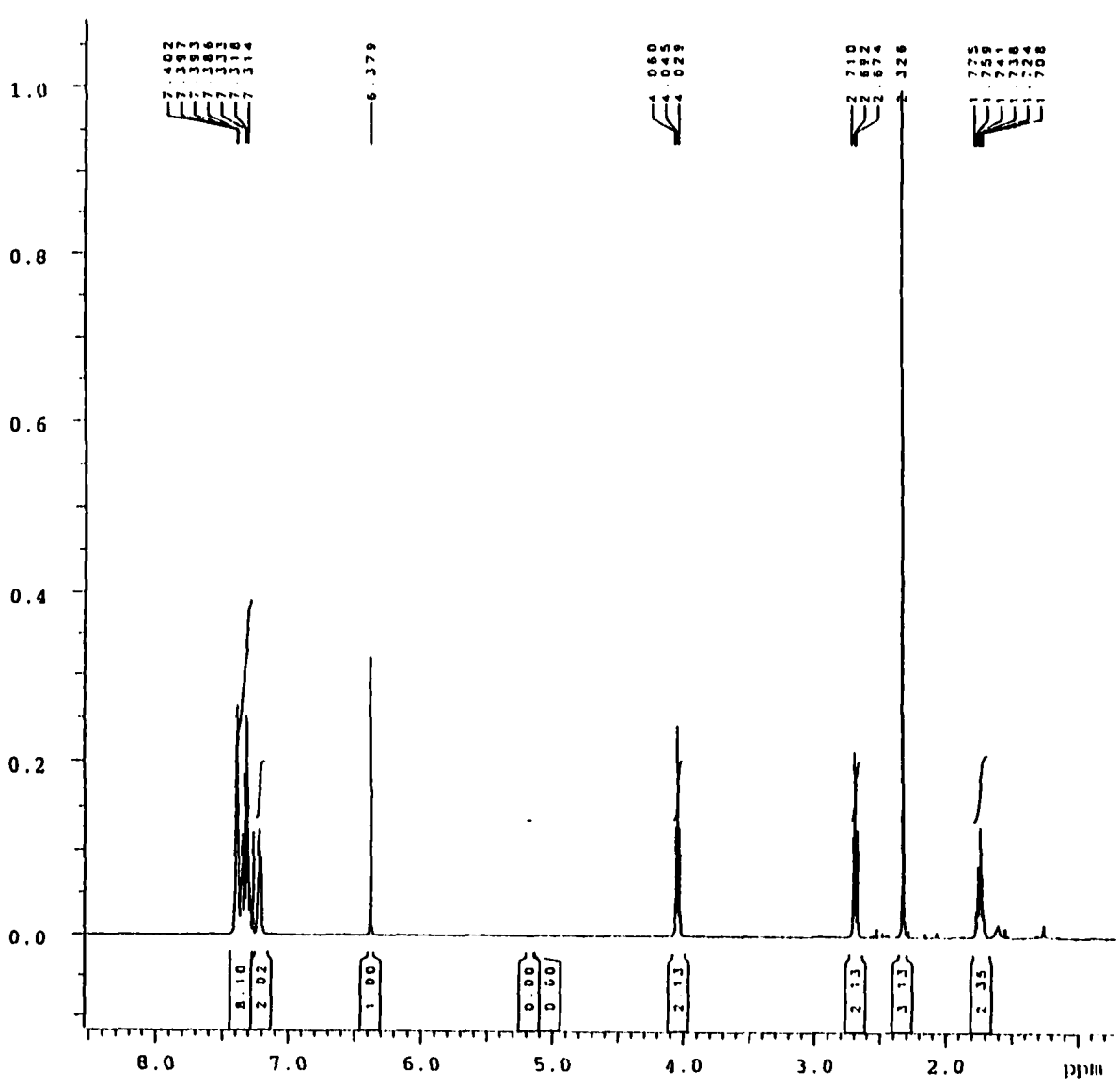
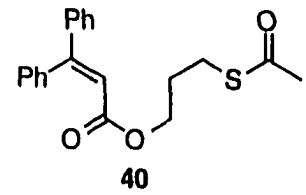


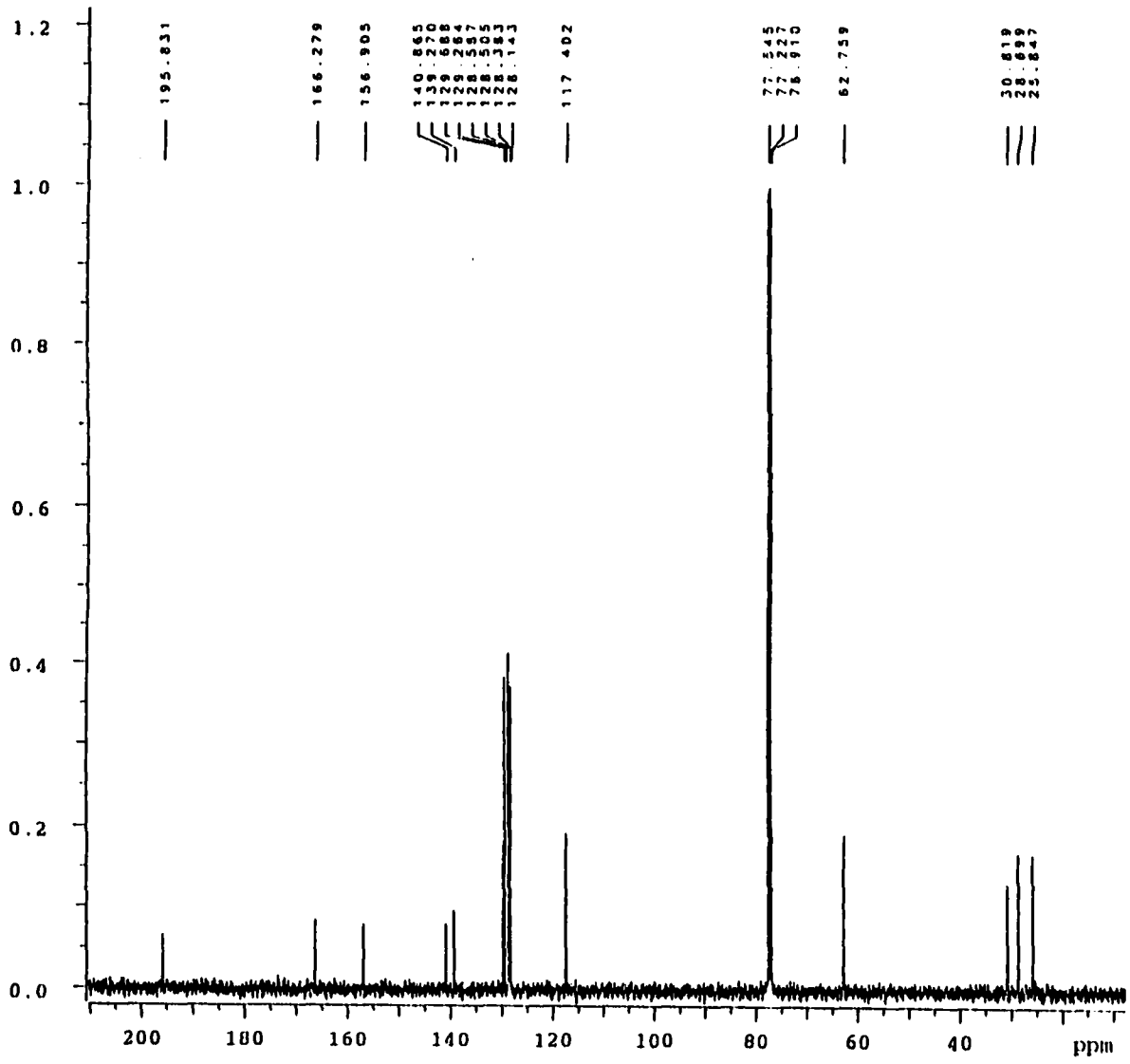
Figure 2A-12. ^{13}C NMR spectrum of compound **39**.

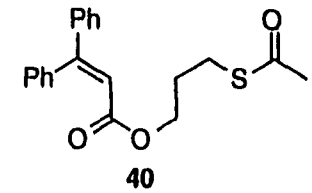




40

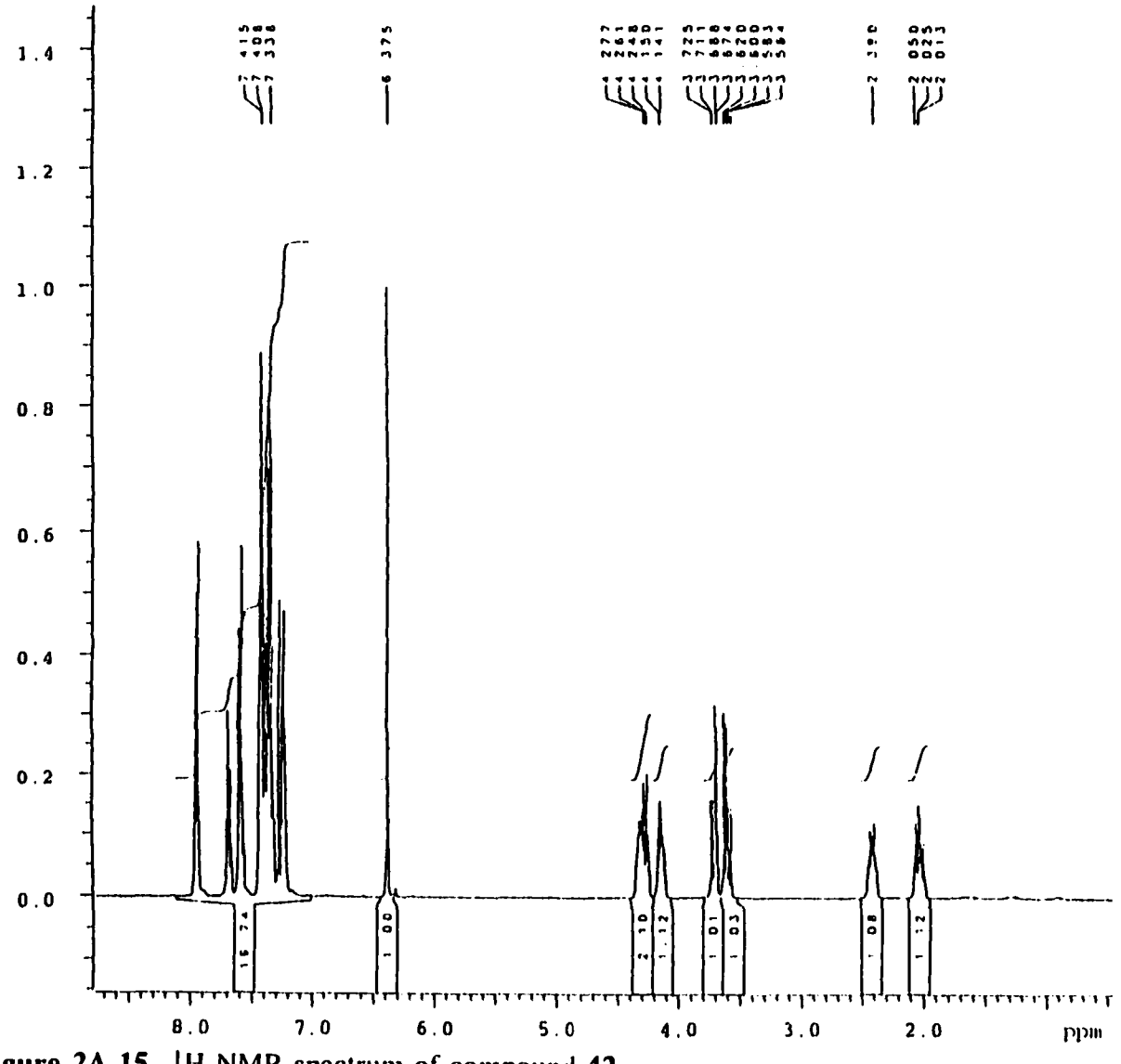
Figure 2A-13. ^{1}H NMR spectrum of compound **40**.

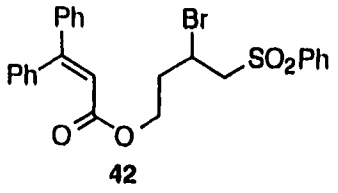




40

Figure 2A-14. ^{13}C NMR spectrum of compound **40**.





42

Figure 2A-15. ^{1}H NMR spectrum of compound **42**.

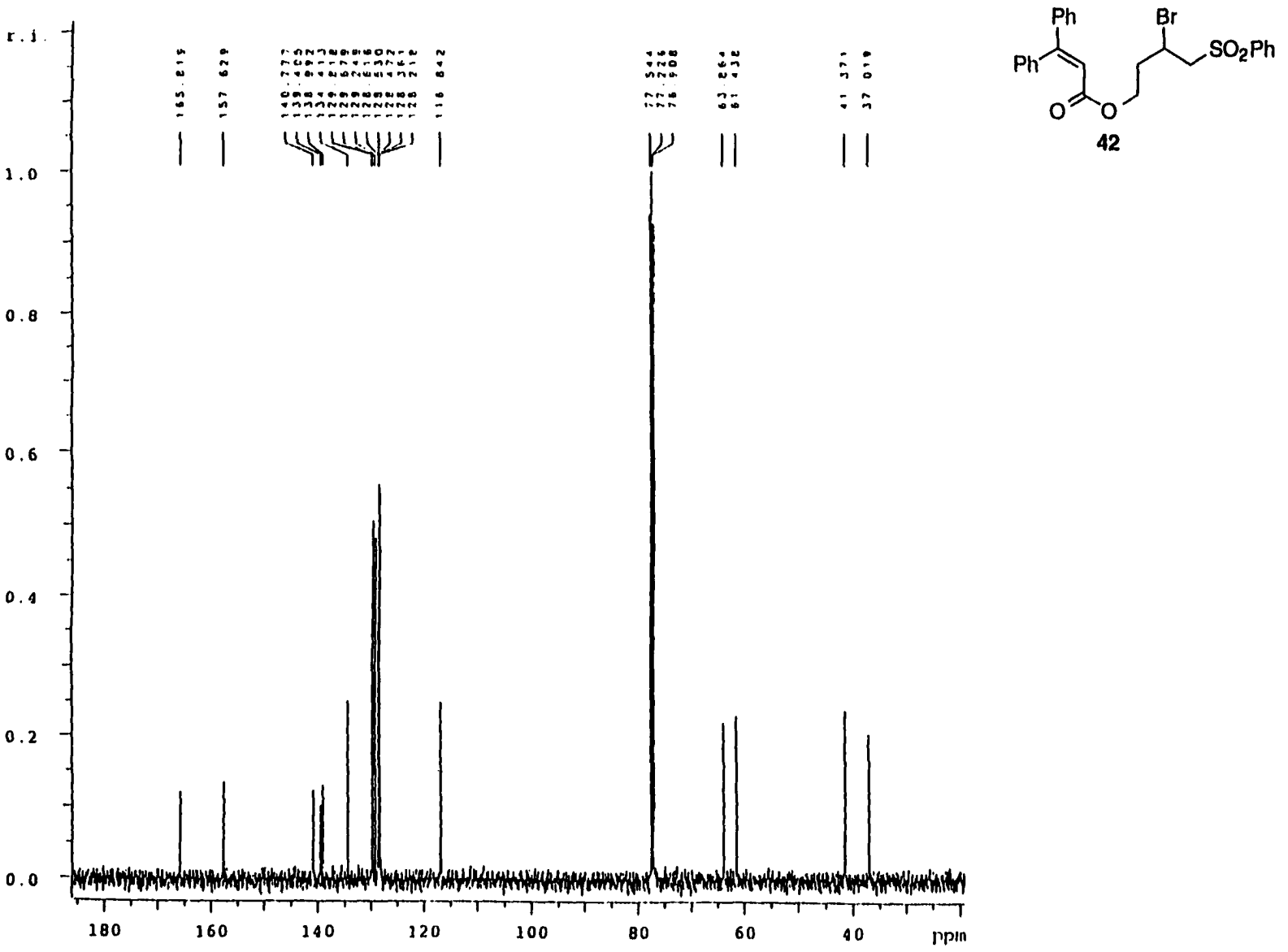
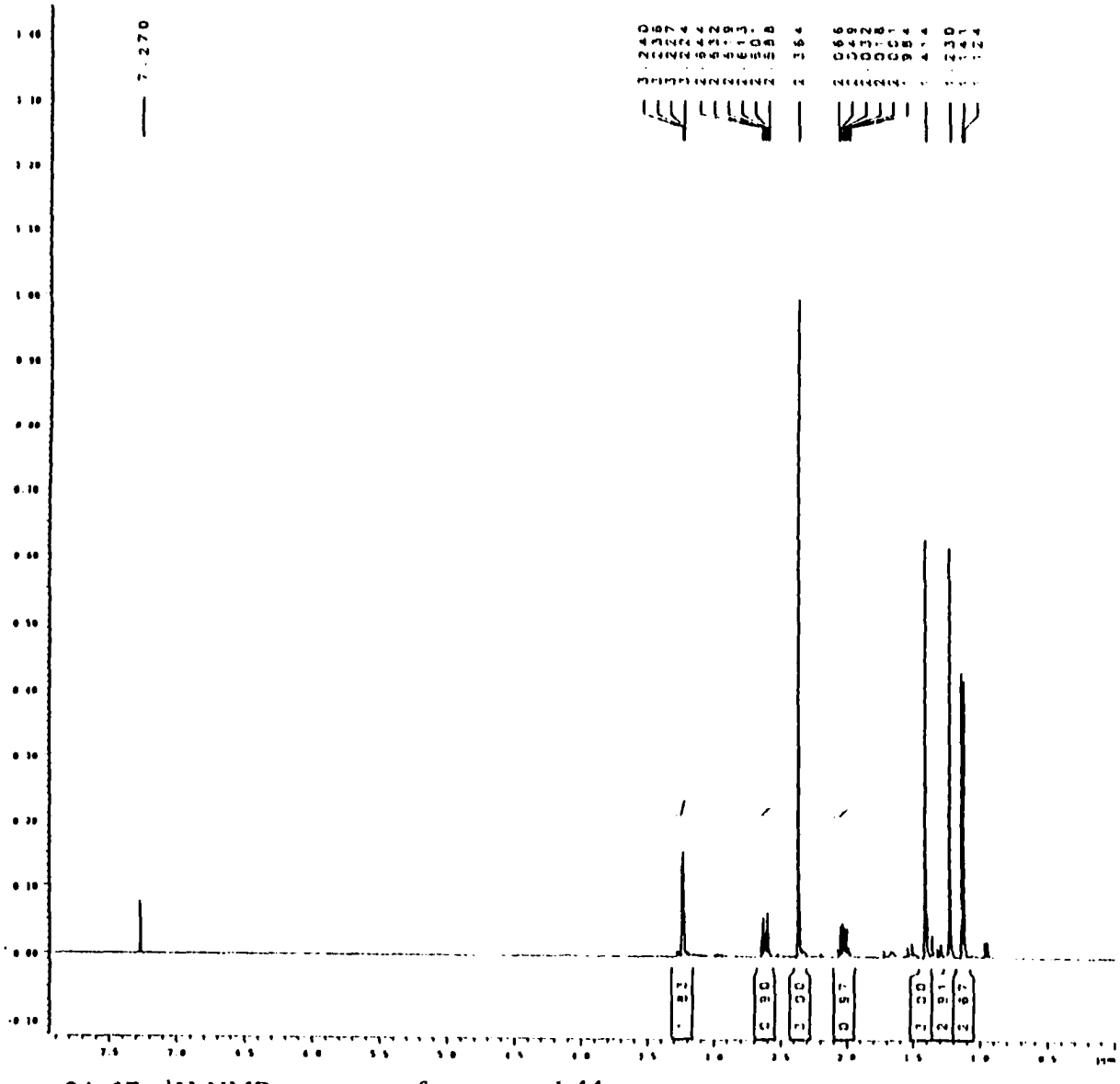
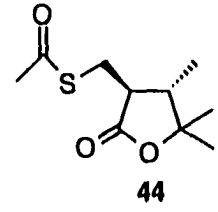


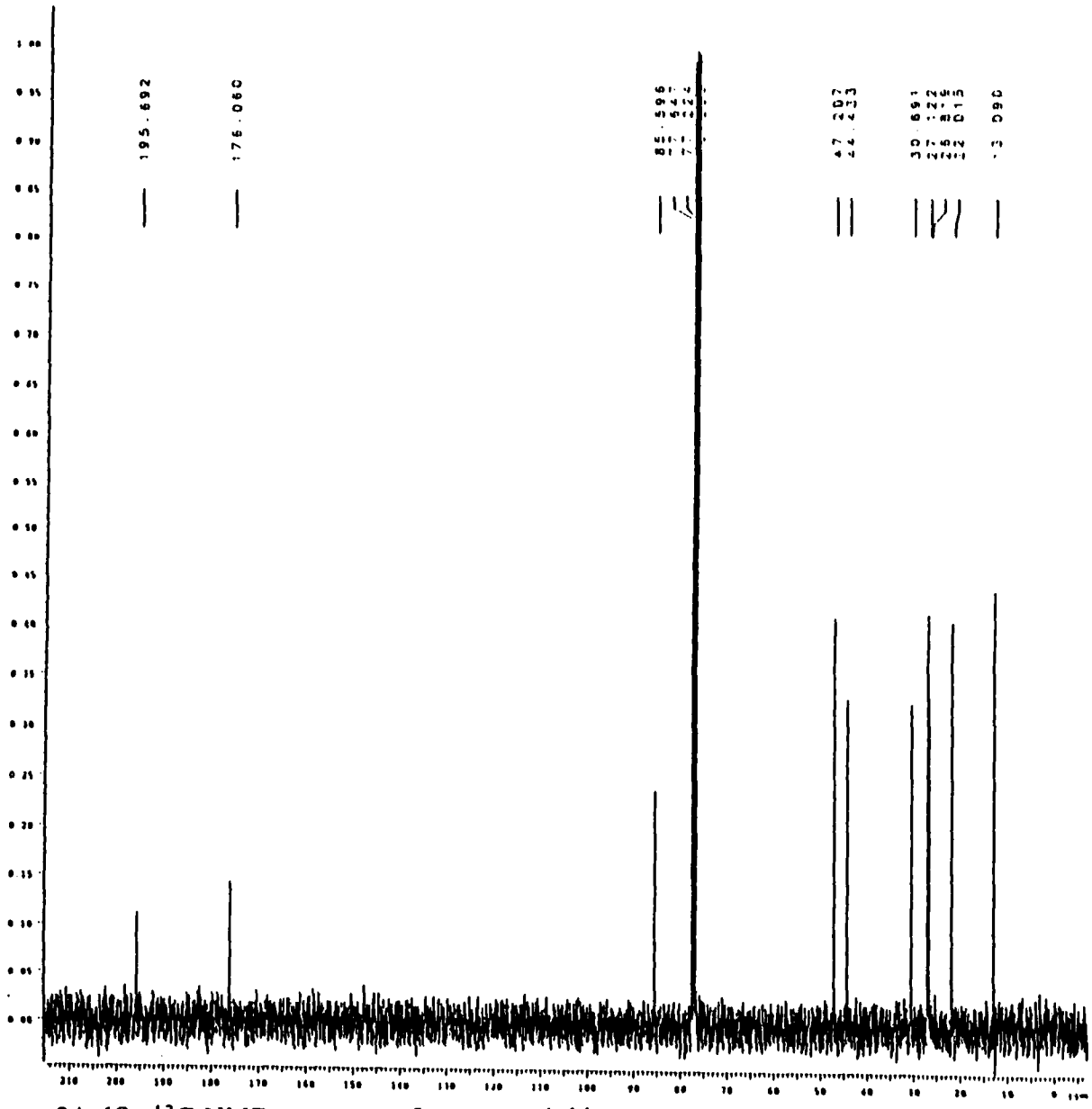
Figure 2A-16. ^{13}C NMR spectrum of compound **42**.

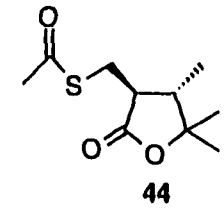




44

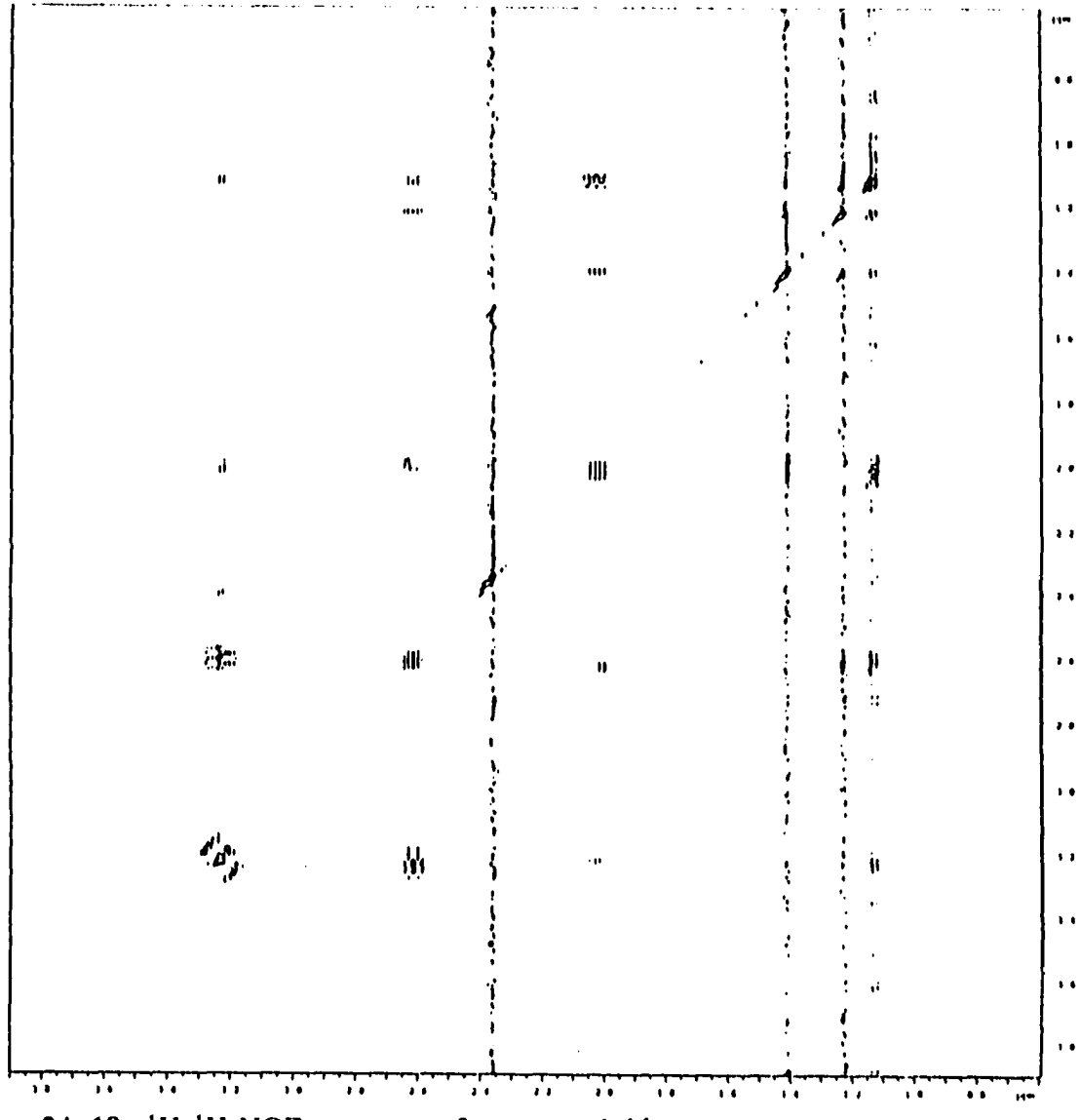
Figure 2A-17. ^{1}H NMR spectrum of compound **44**.

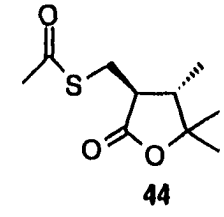




44

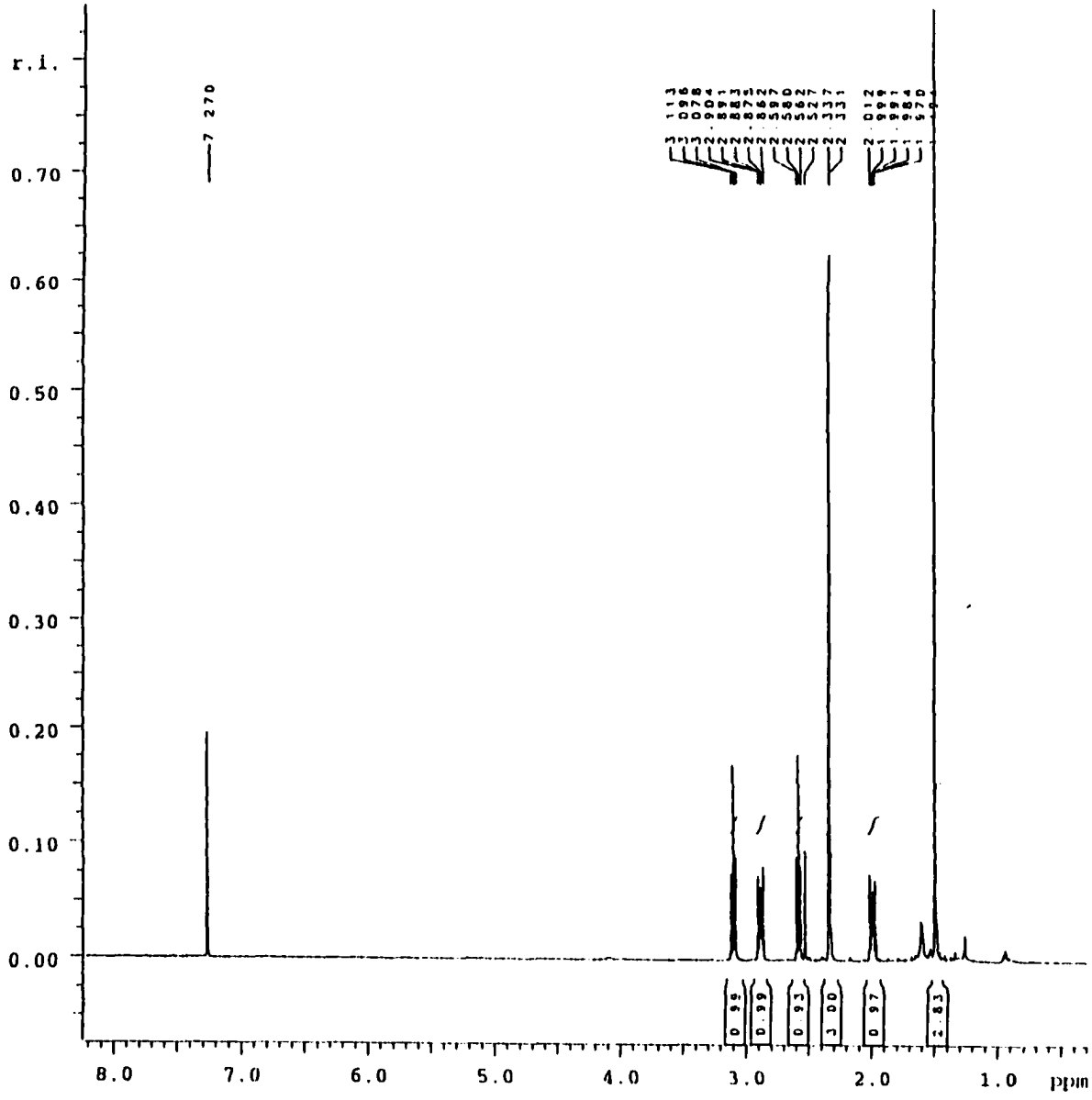
Figure 2A-18. ^{13}C NMR spectrum of compound **44**.

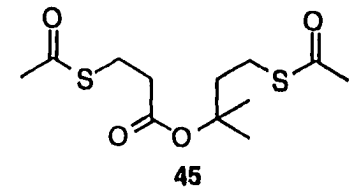




44

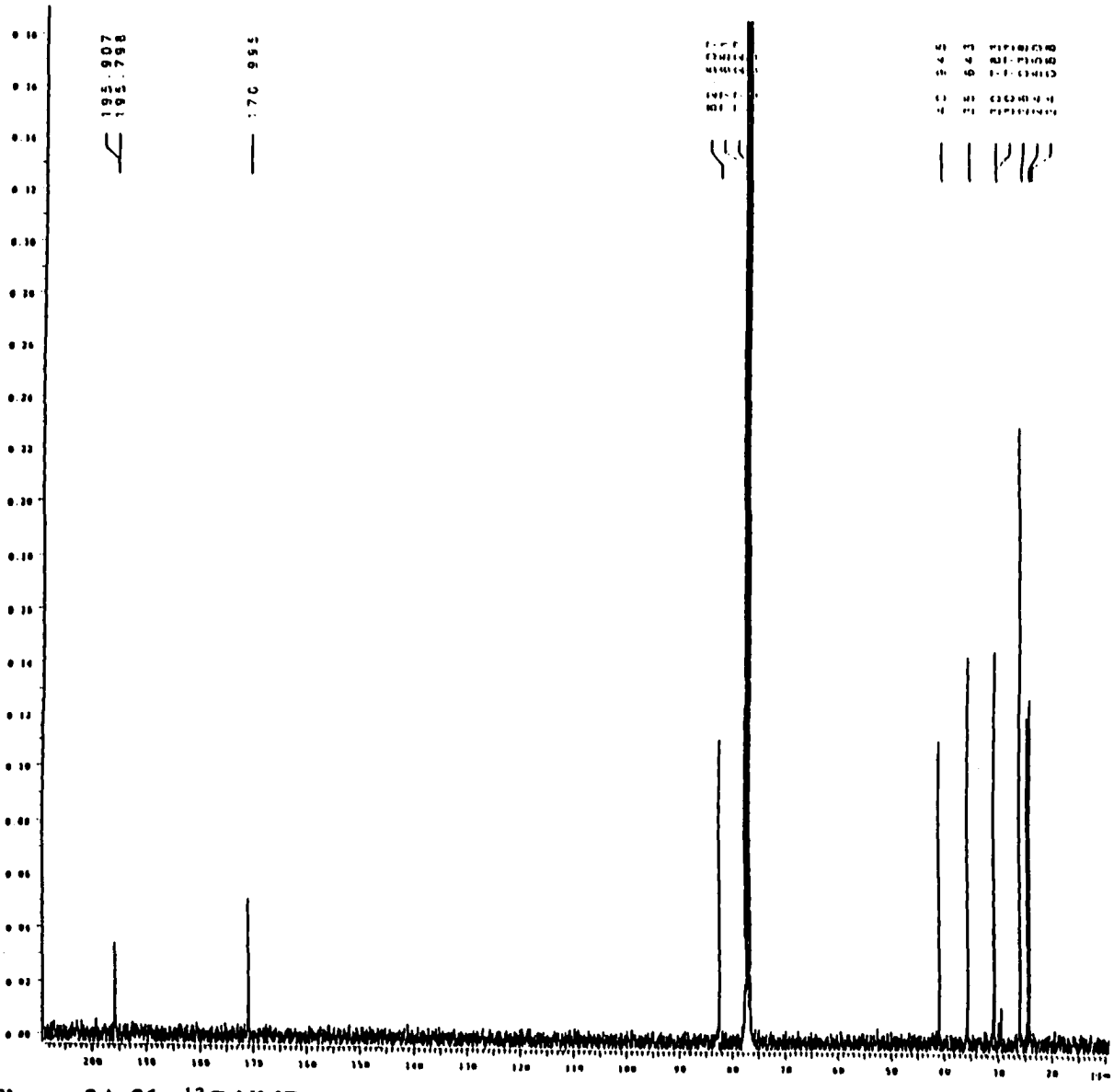
Figure 2A-19. ^{1}H-^{1}H NOE spectrum of compound **44**.

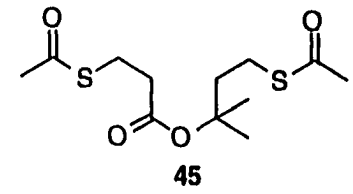




45

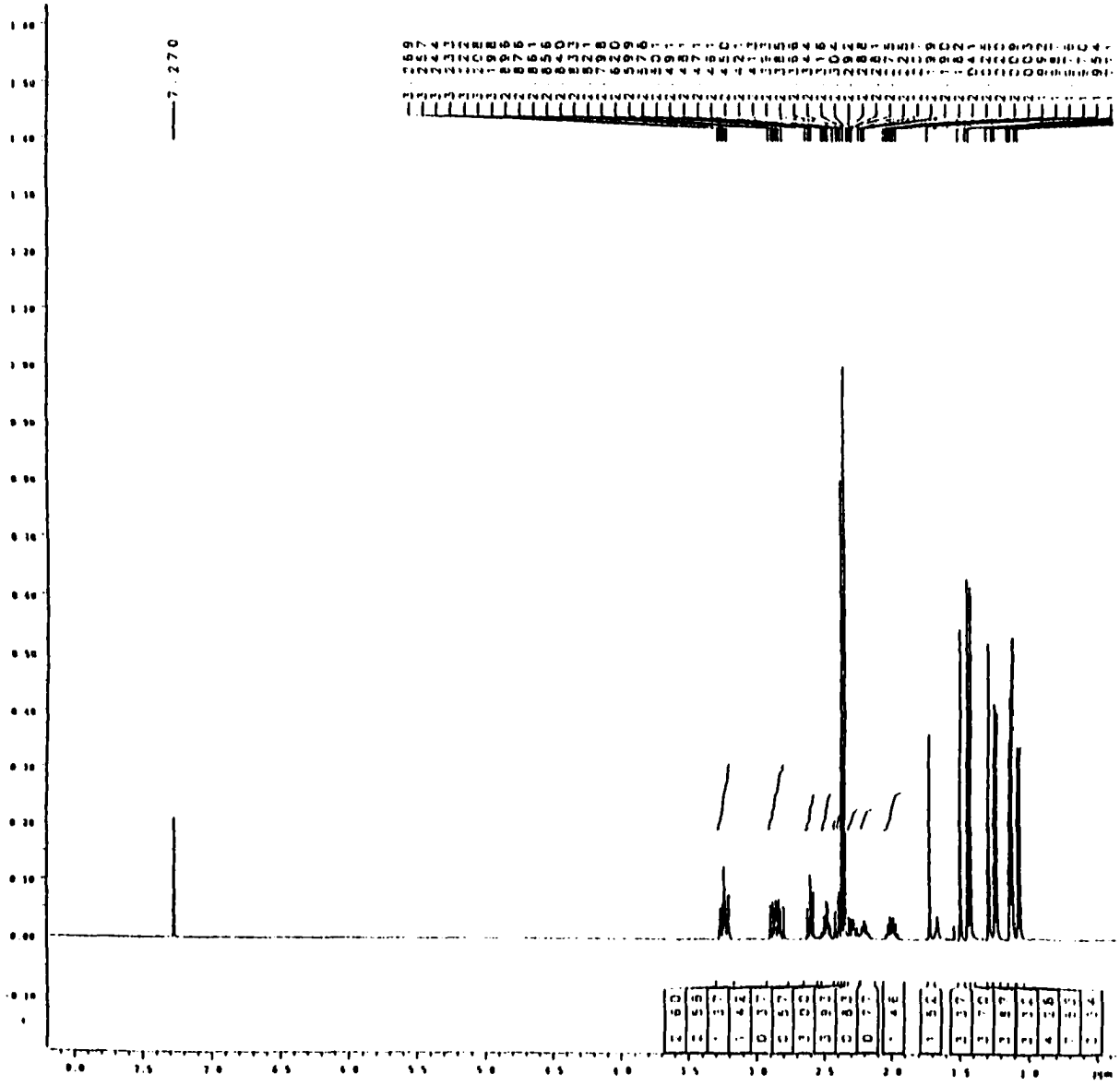
Figure 2A-20. ^{1}H NMR spectrum of compound **45**.

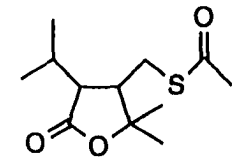




45

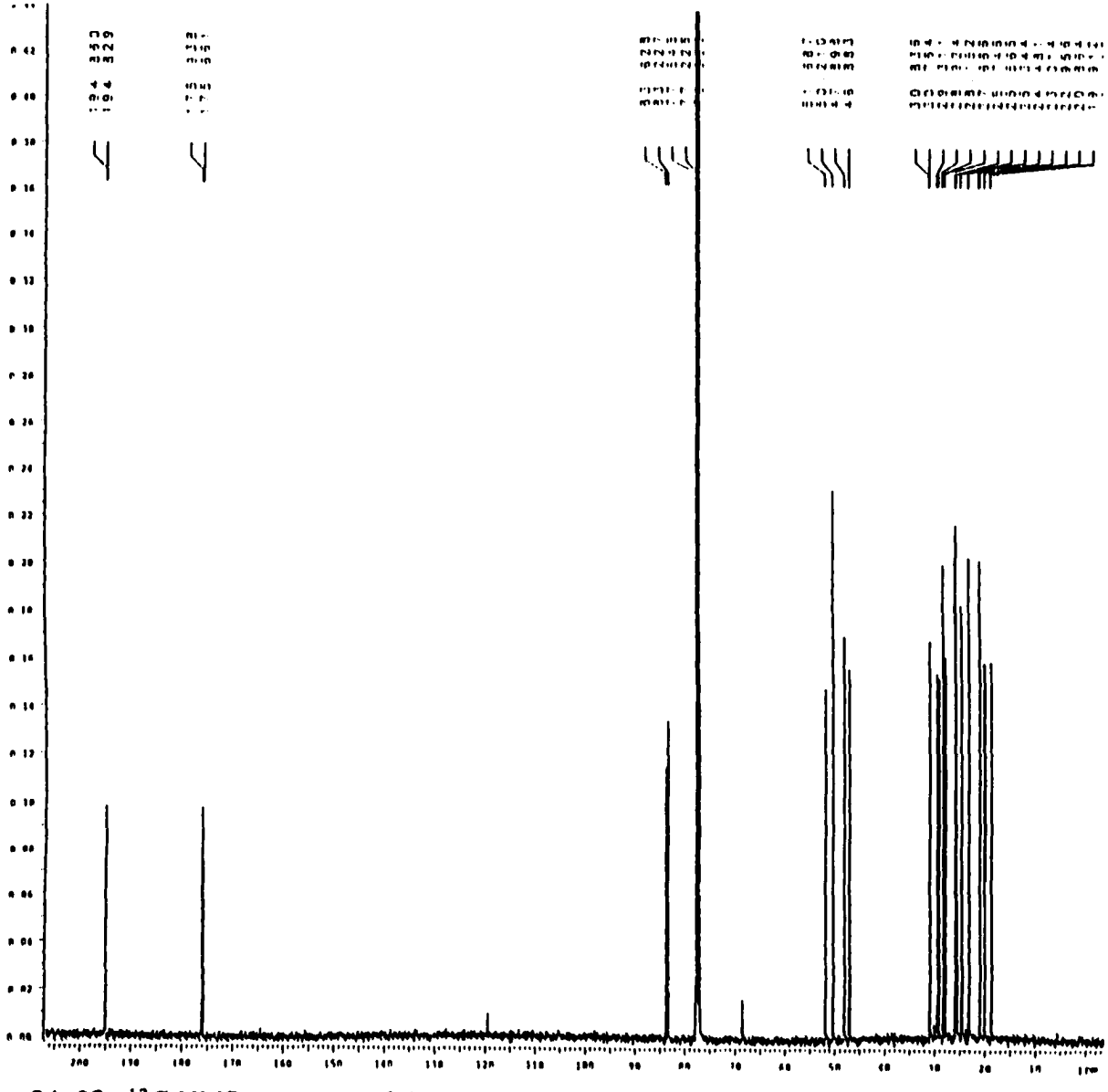
Figure 2A-21. ^{13}C NMR spectrum of compound **45**.

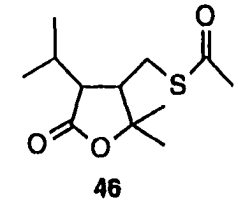




46

Figure 2A-22. ^{1}H NMR spectrum of the *cis/trans* mixture of compound **46** (c/t = 1.4 or 1/1.4).





46

Figure 2A-23. ^{13}C NMR spectrum of the *cis/trans* mixture of compound **46** (c/t = 1.4 or 1/1.4).

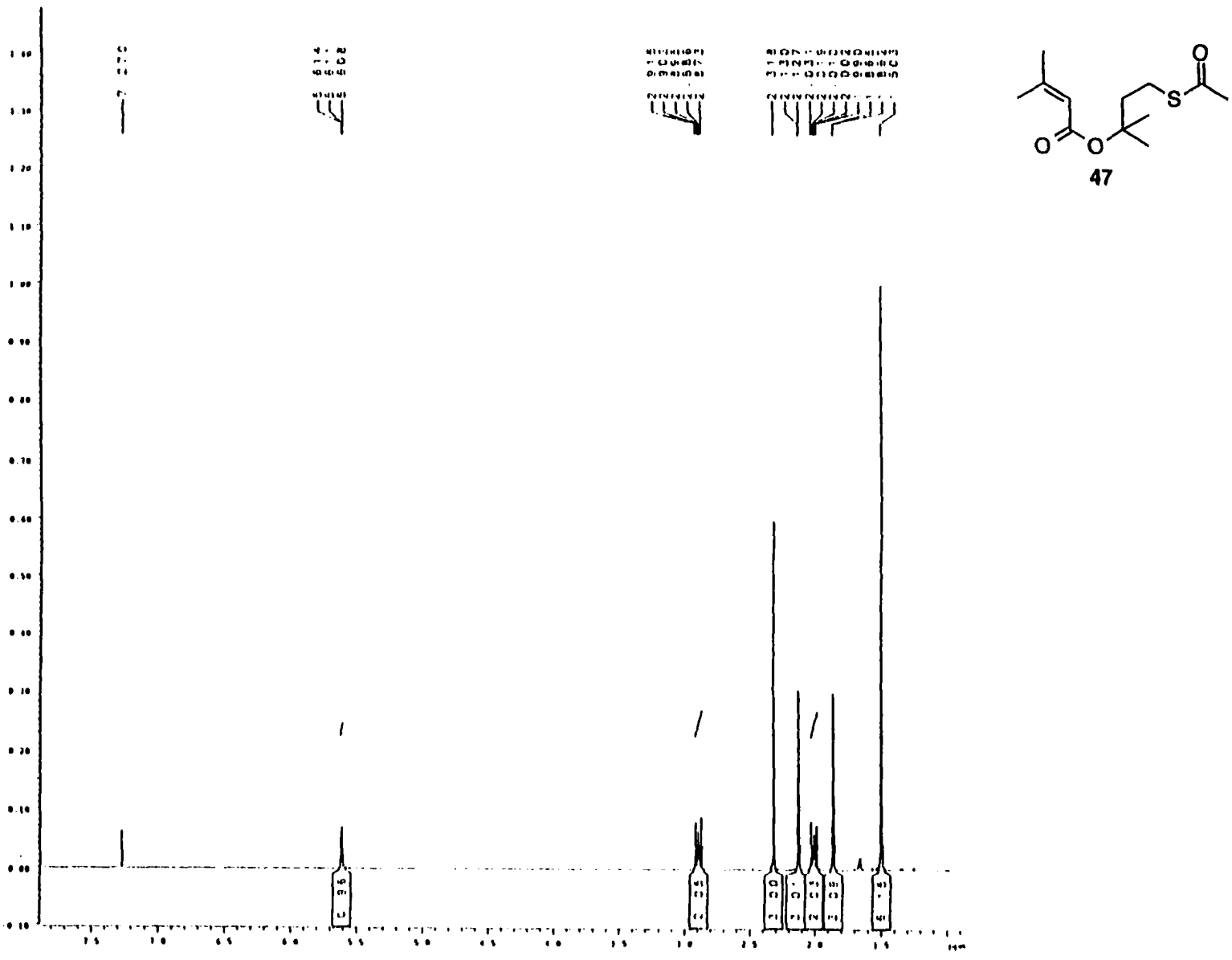
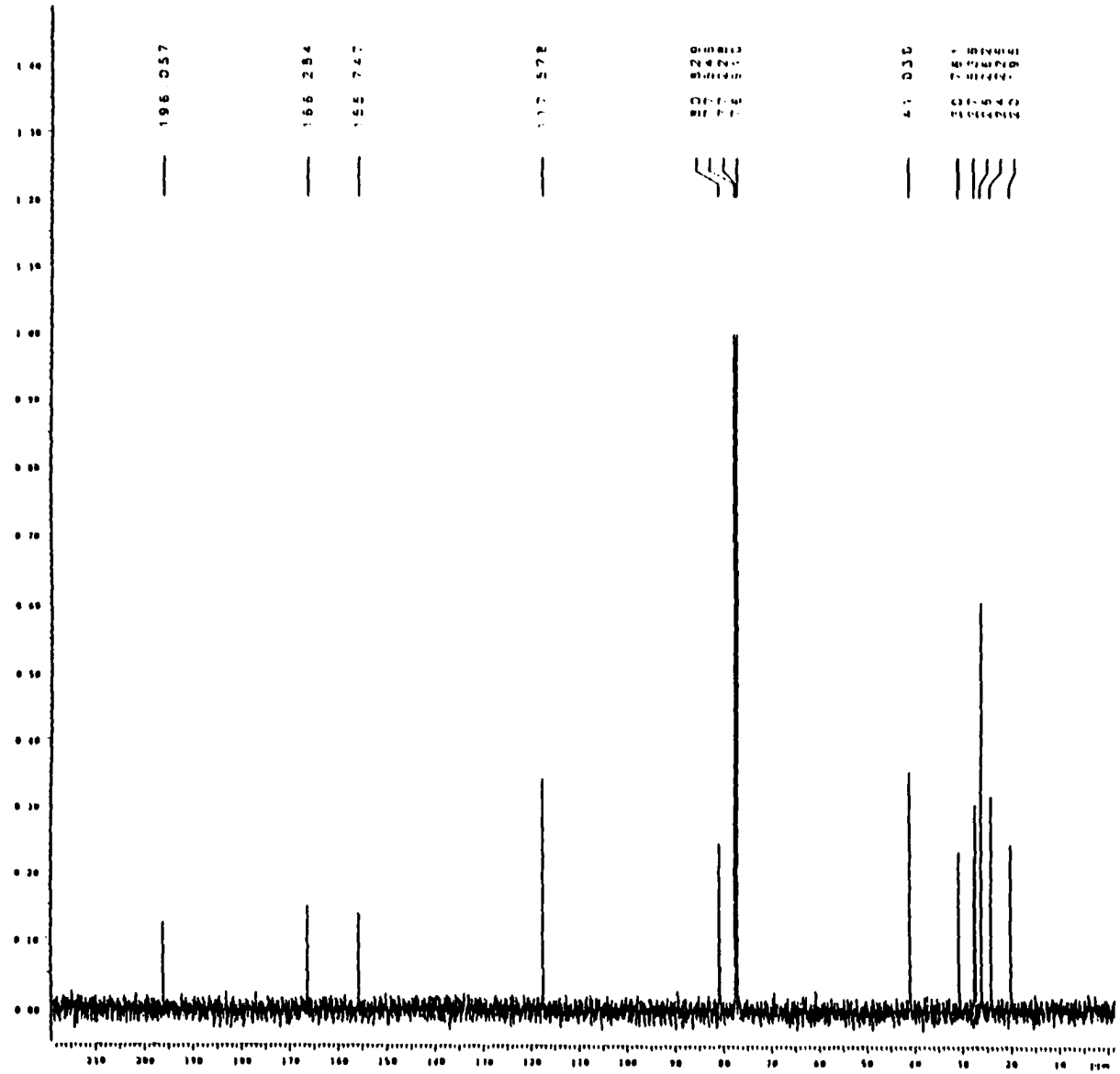


Figure 2A-24. ^{1}H NMR spectrum of compound **47**.



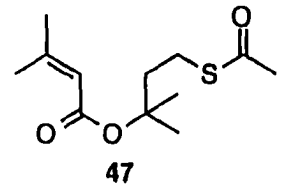
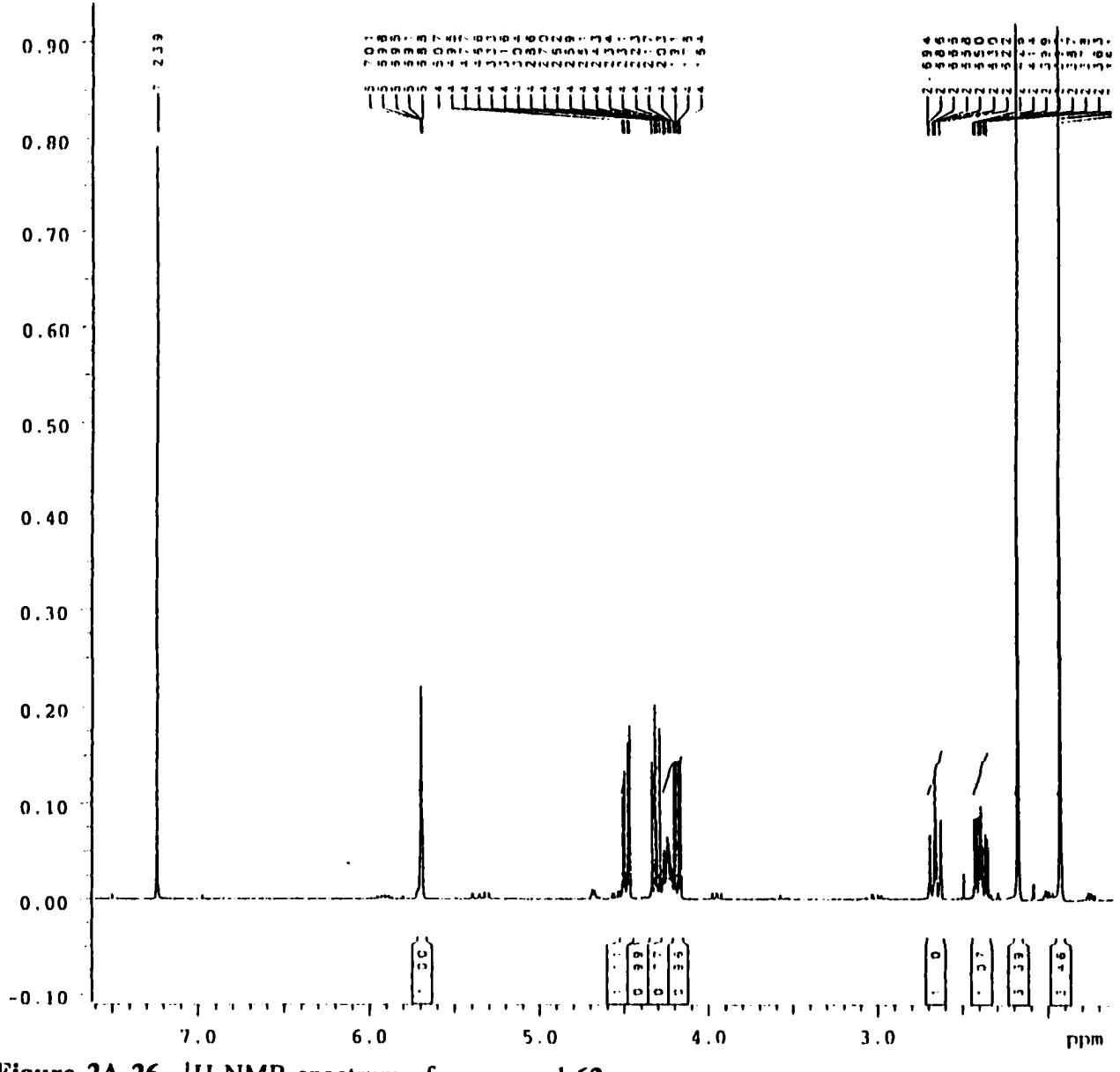
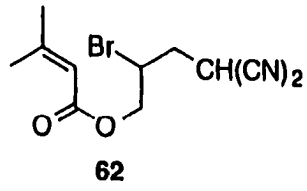


Figure 2A-25. ^{13}C NMR spectrum of compound **47**.





62

Figure 2A-26. ^{1}H NMR spectrum of compound **62**.

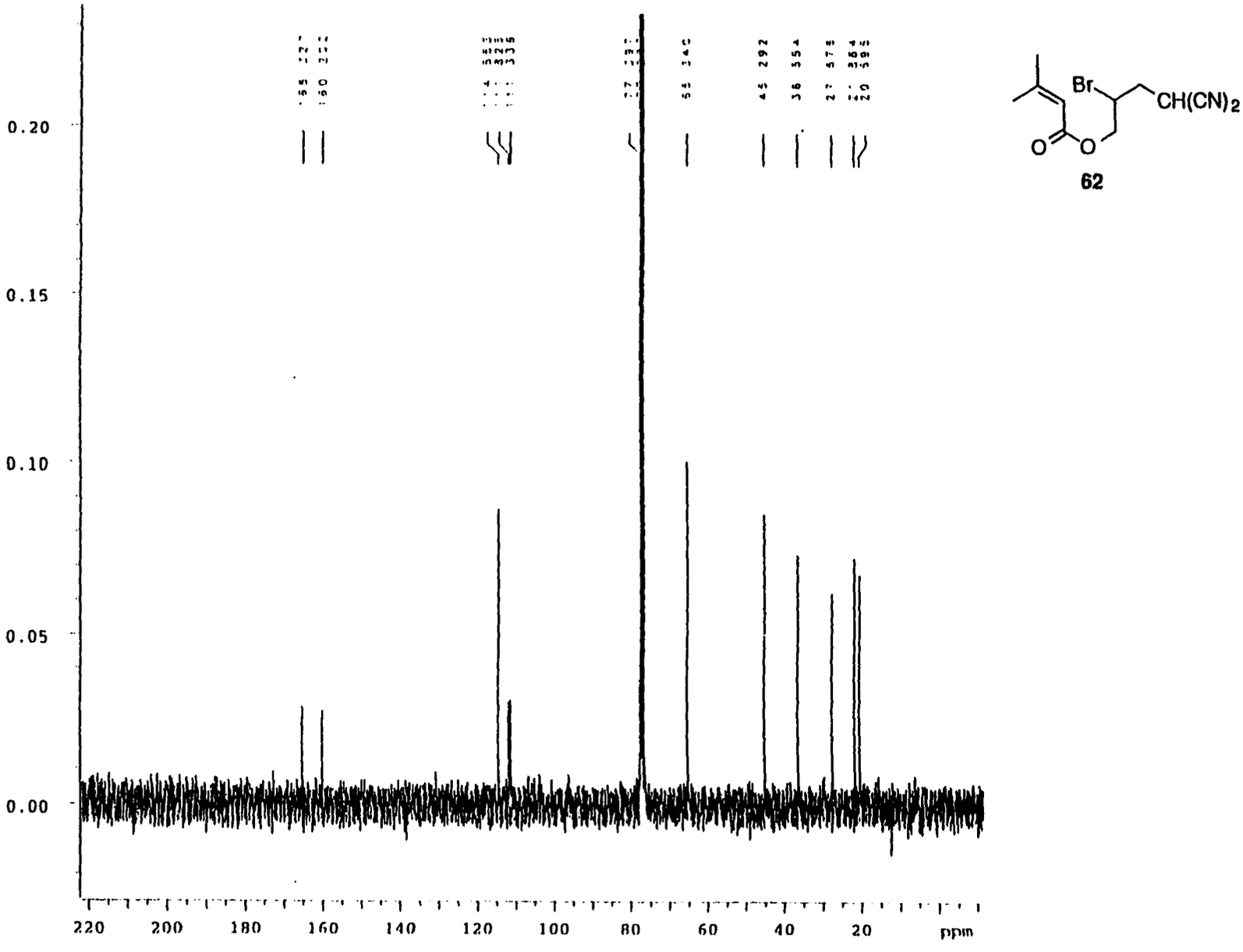
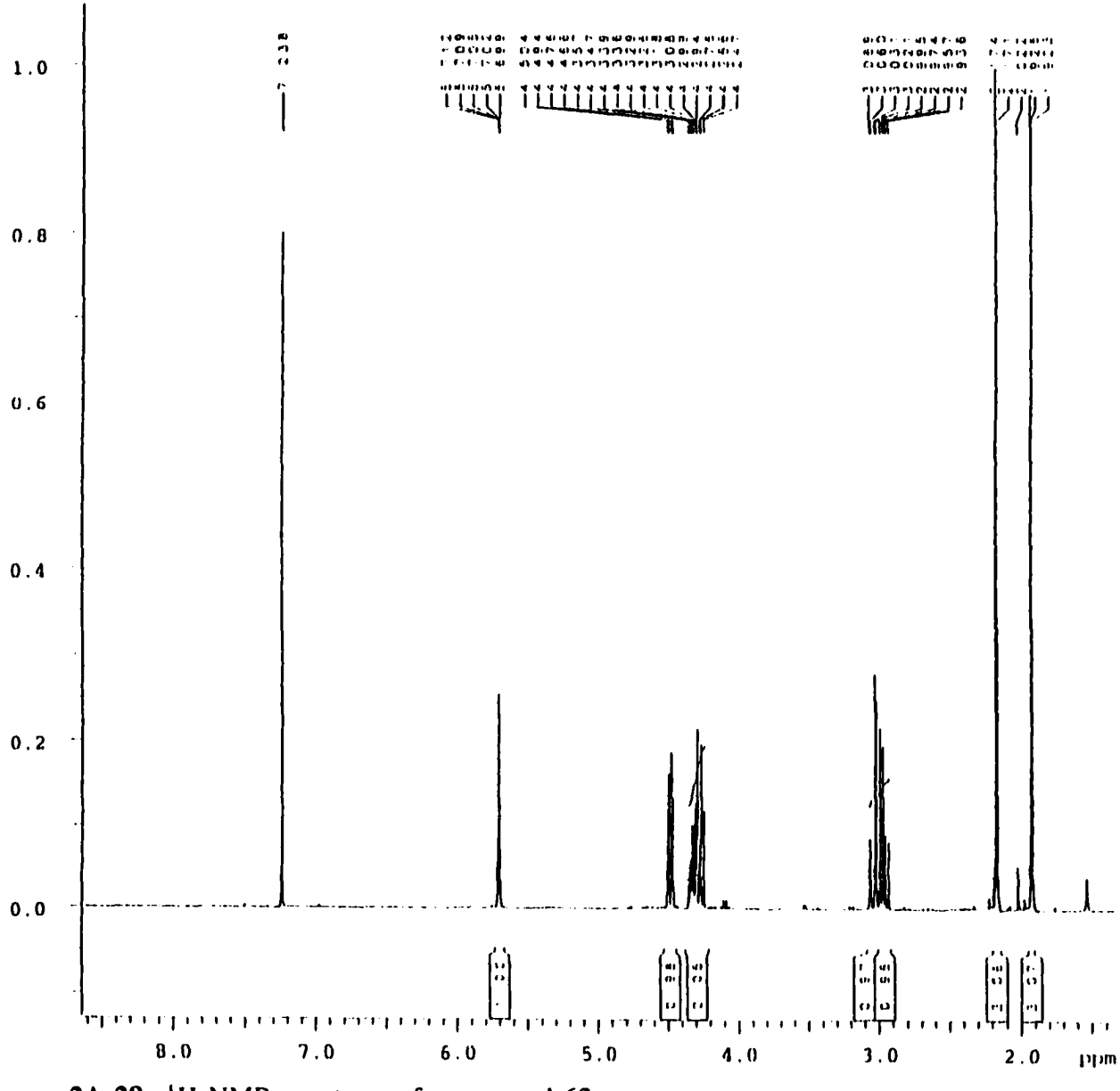
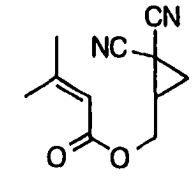


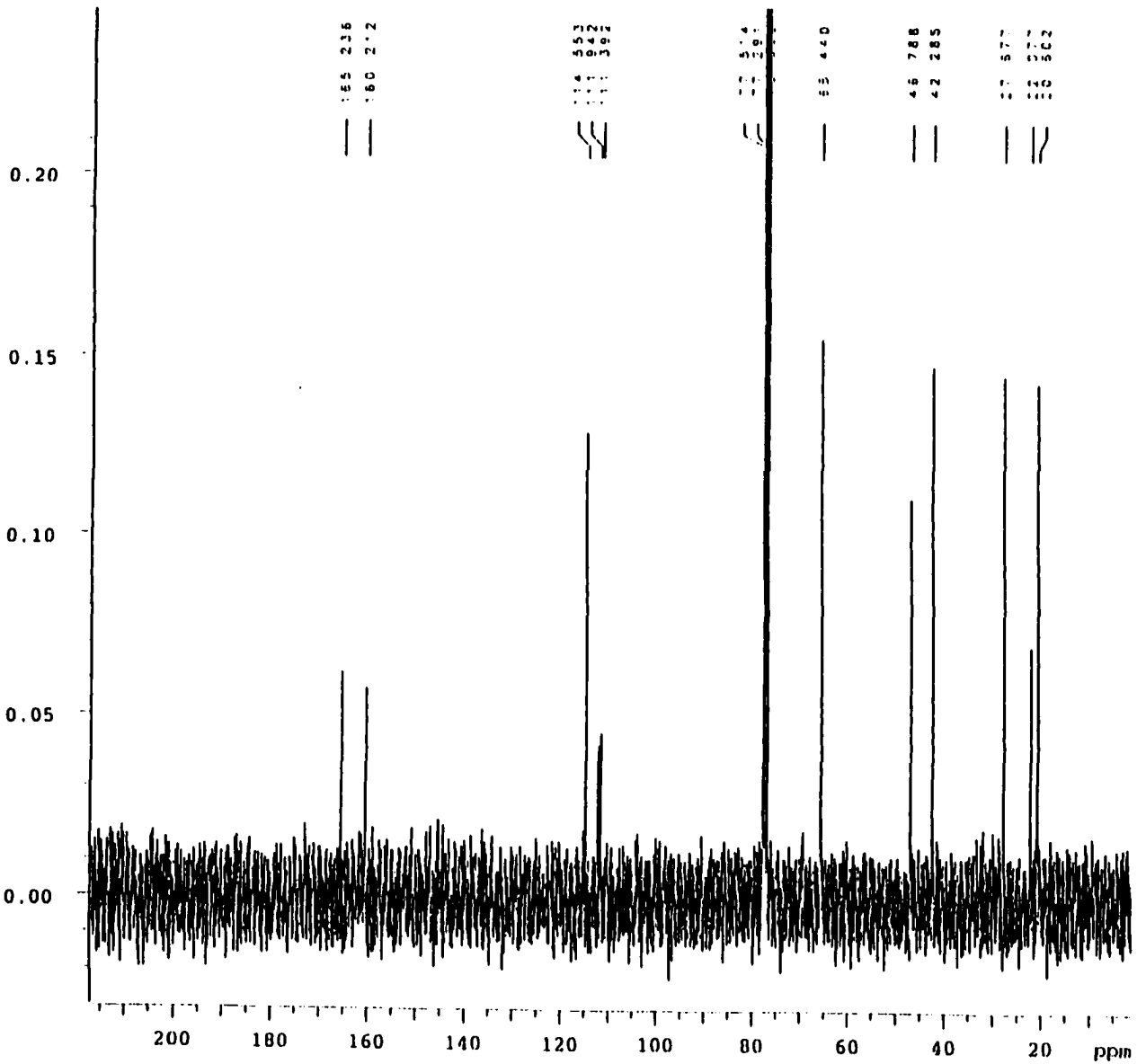
Figure 2A-27. ^{13}C NMR spectrum of compound **62**.

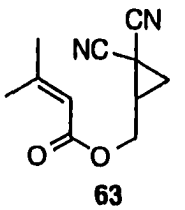




63

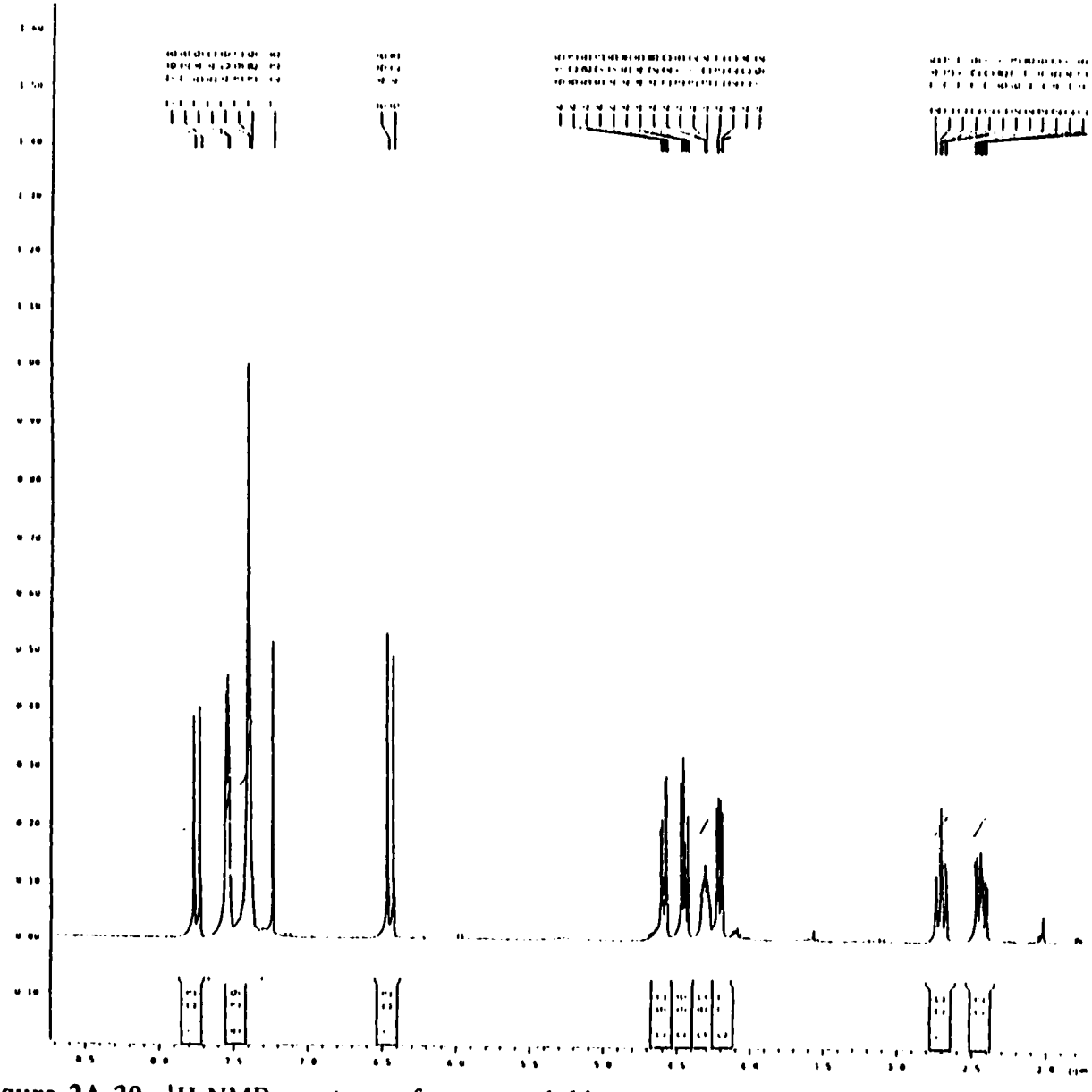
Figure 2A-28. ^{1}H NMR spectrum of compound **63**.

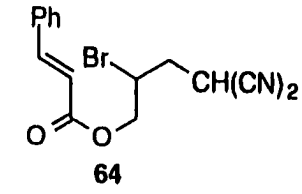




63

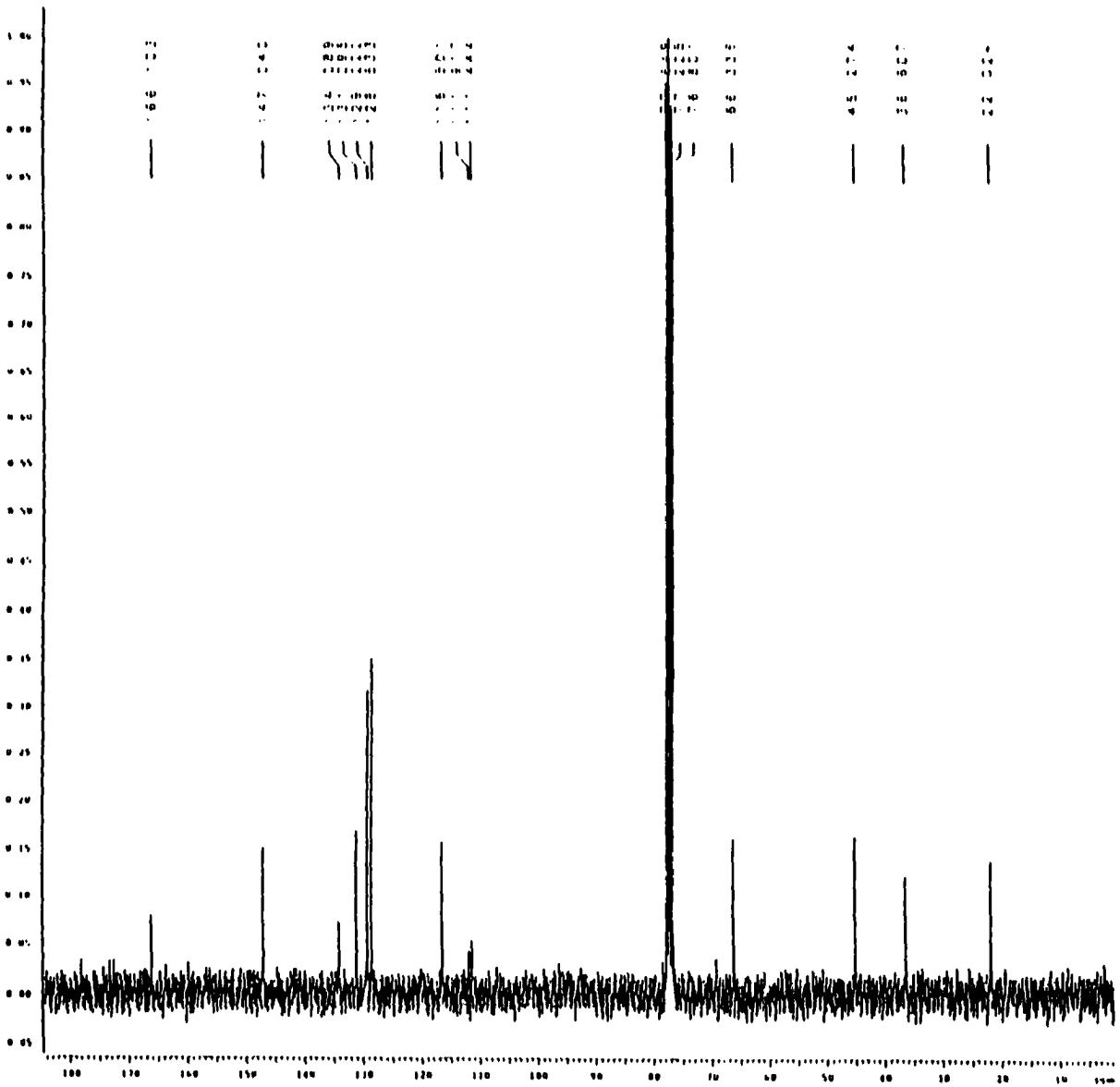
Figure 2A-29. ^{13}C NMR spectrum of compound **63**.

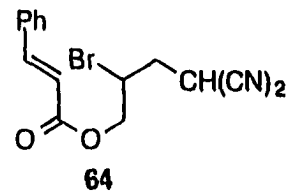




64

Figure 2A-30. ^{1}H NMR spectrum of compound **64**.





64

Figure 2A-31. ^{13}C NMR spectrum of compound **64**.

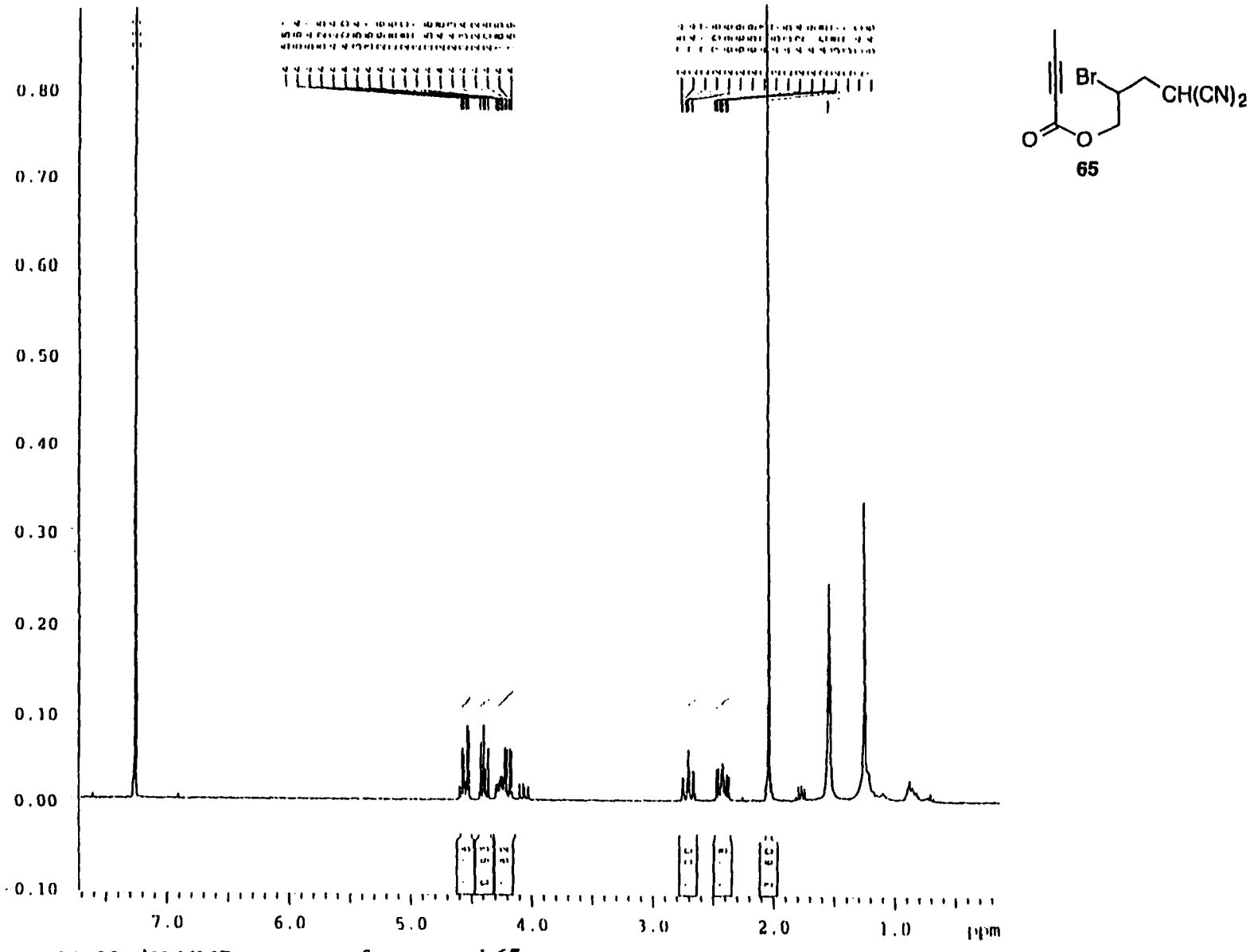
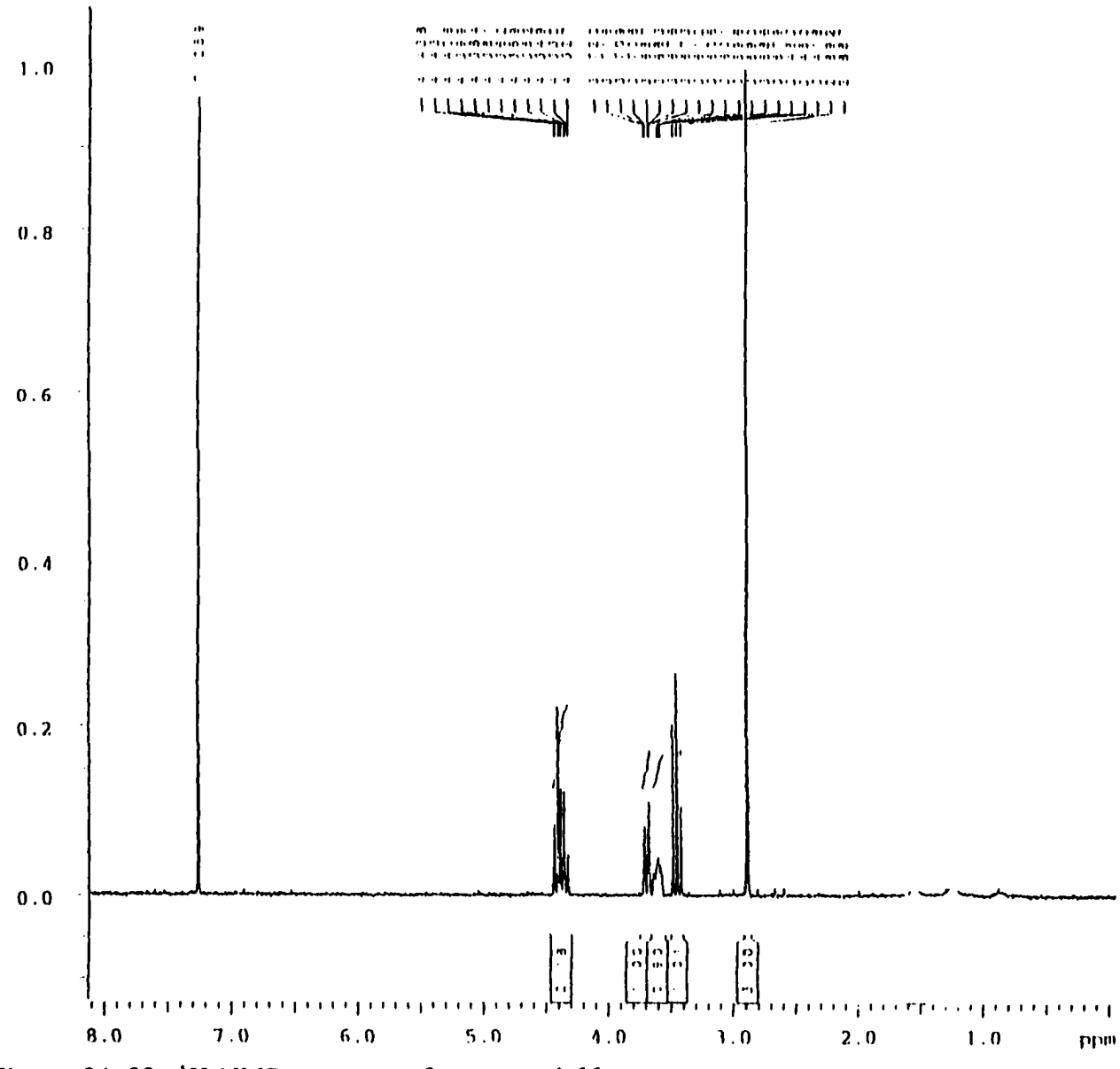
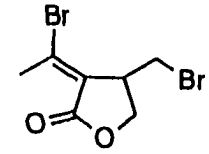


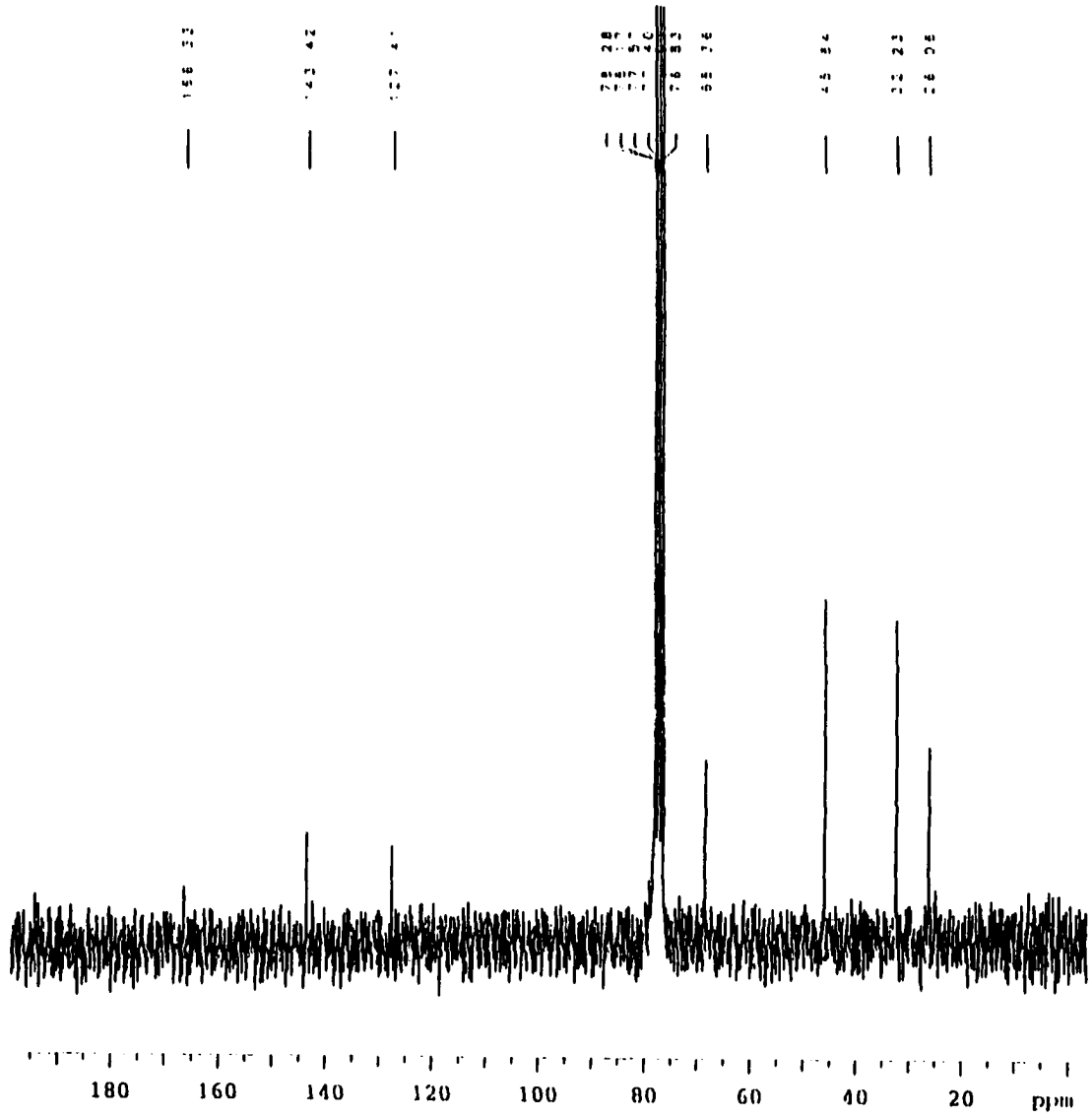
Figure 2A-32. ^{1}H NMR spectrum of compound **65**.

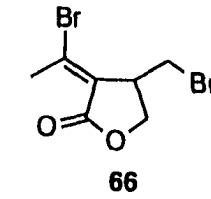




66

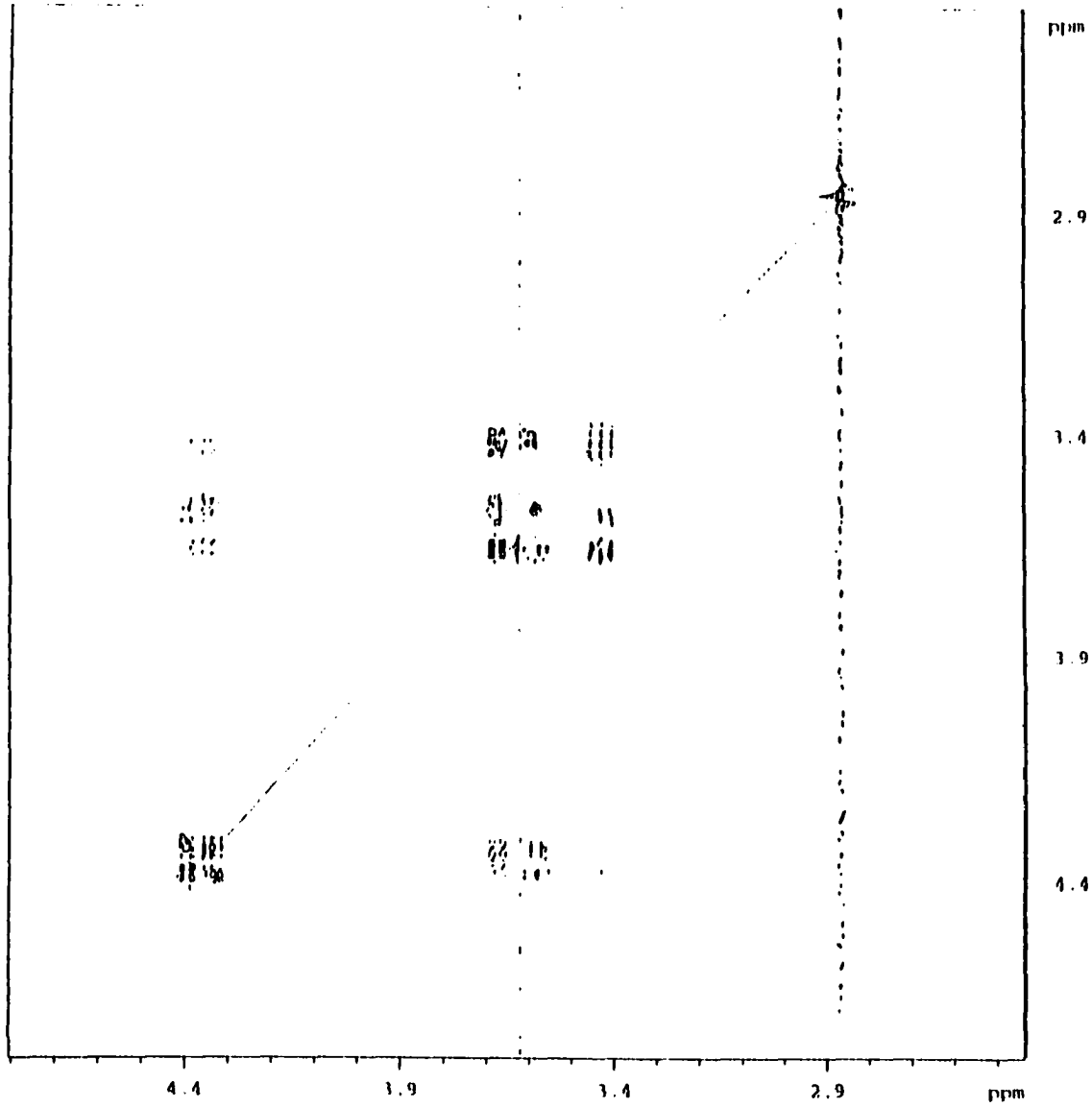
Figure 2A-33. ^{1}H NMR spectrum of compound **66**.

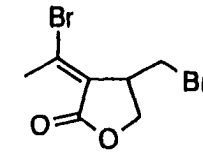




66

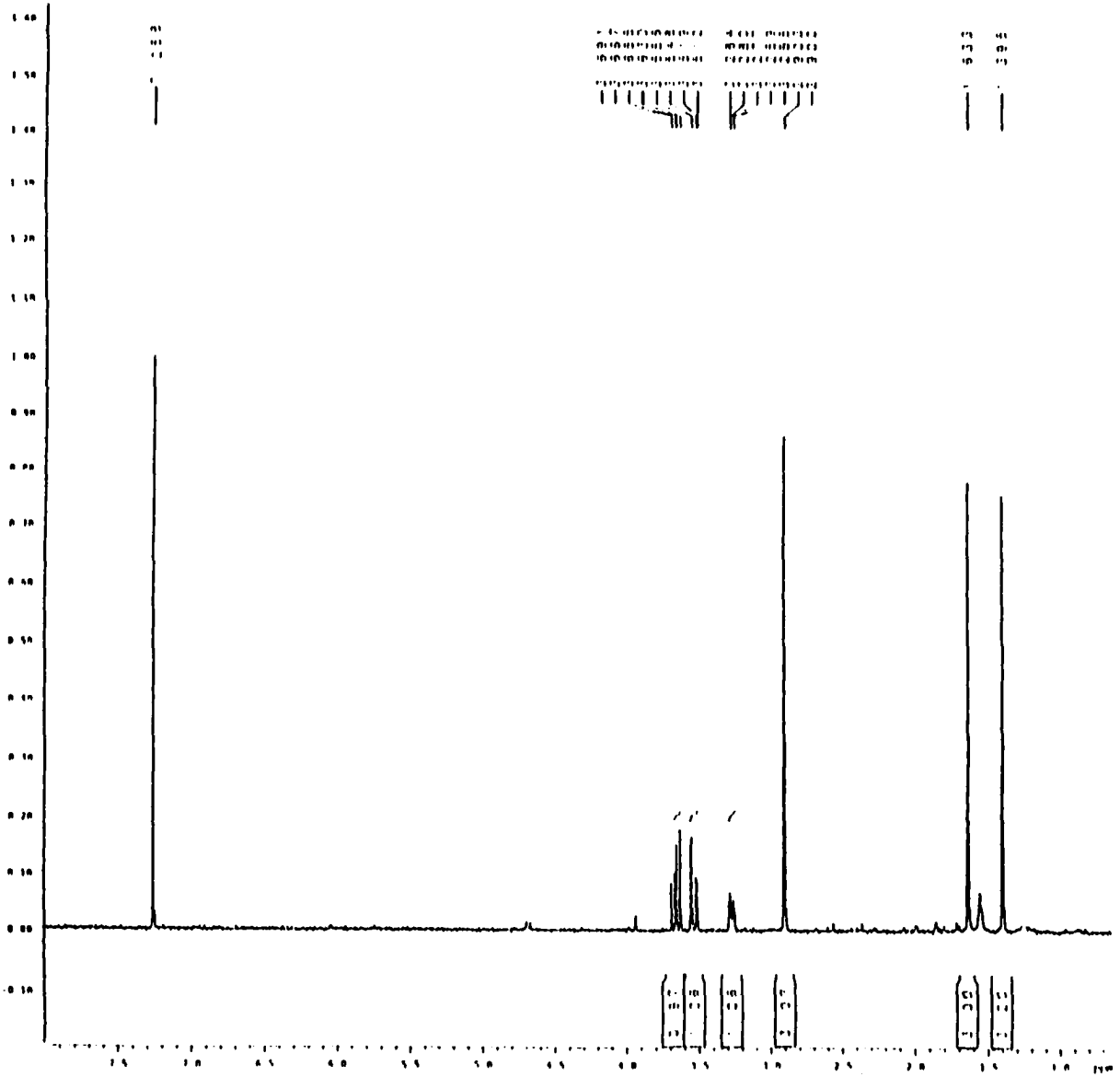
Figure 2A-34. ^{13}C NMR spectrum of compound **66**.

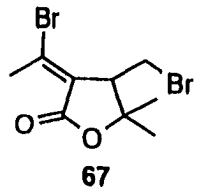




66

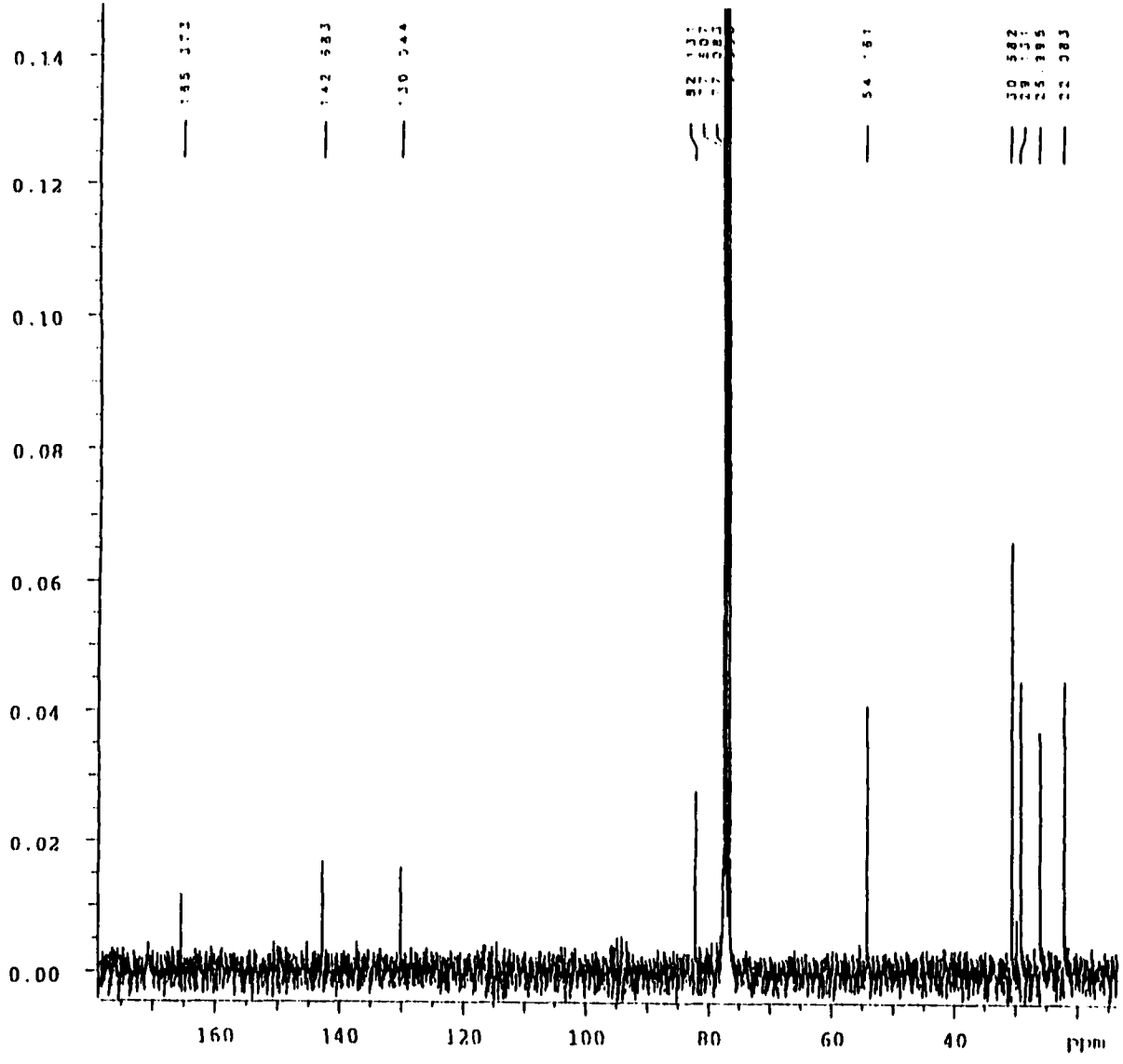
Figure 2A-35. ^{1}H-^{1}H NOE spectrum of compound **66**.

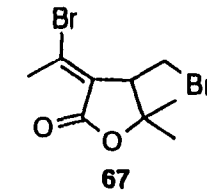




67

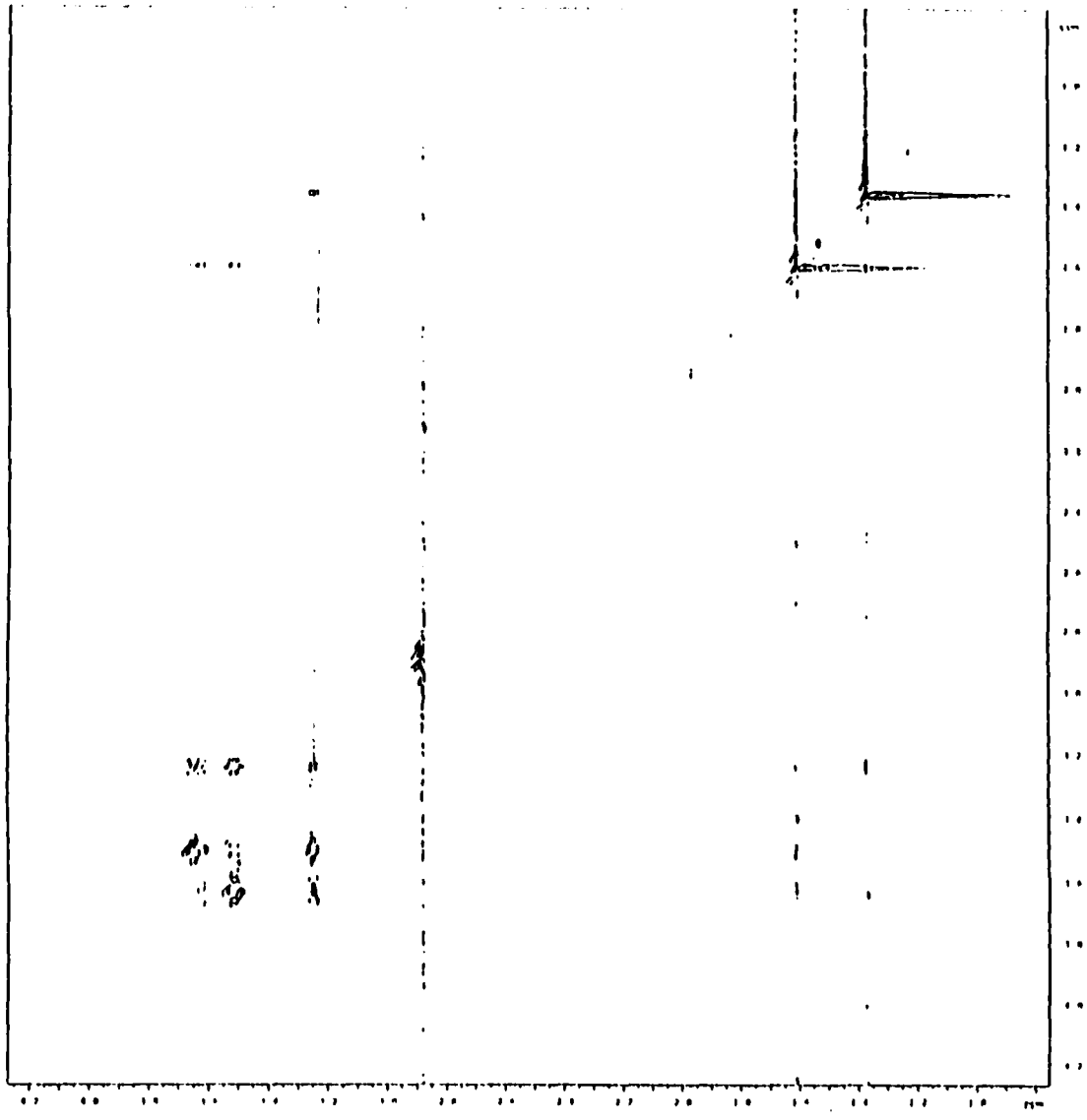
Figure 2A-36. ^{1}H NMR spectrum of compound **67**.

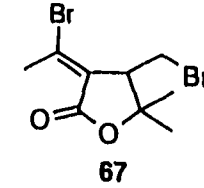




67

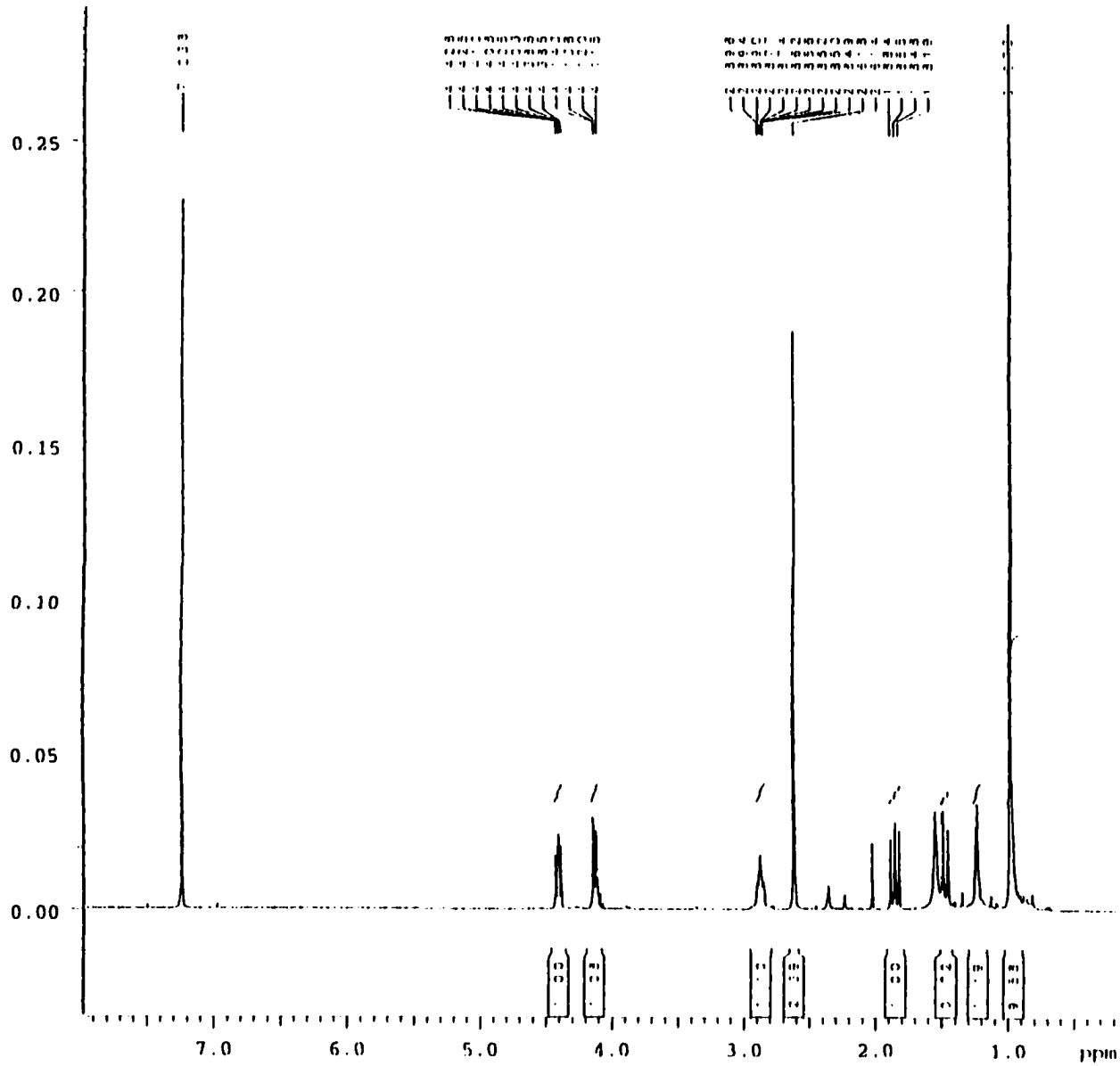
Figure 2A-37. ^{13}C NMR spectrum of compound **67**.

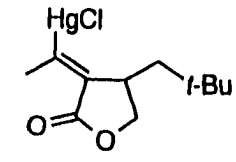




67

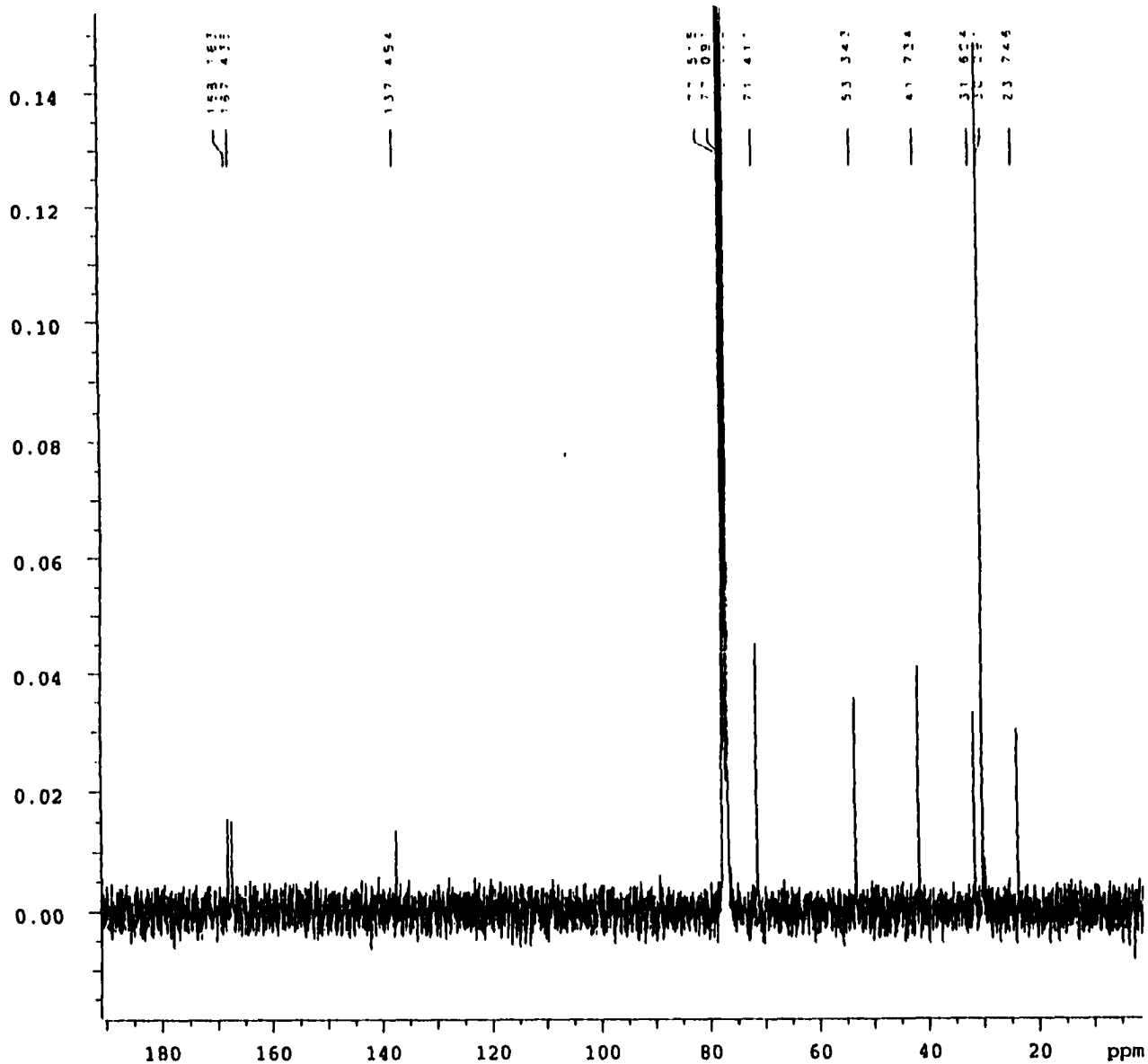
Figure 2A-38. ^{1}H-^{1}H NOE spectrum of compound **67**.

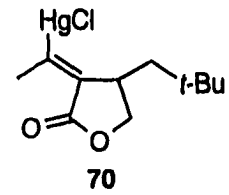




70

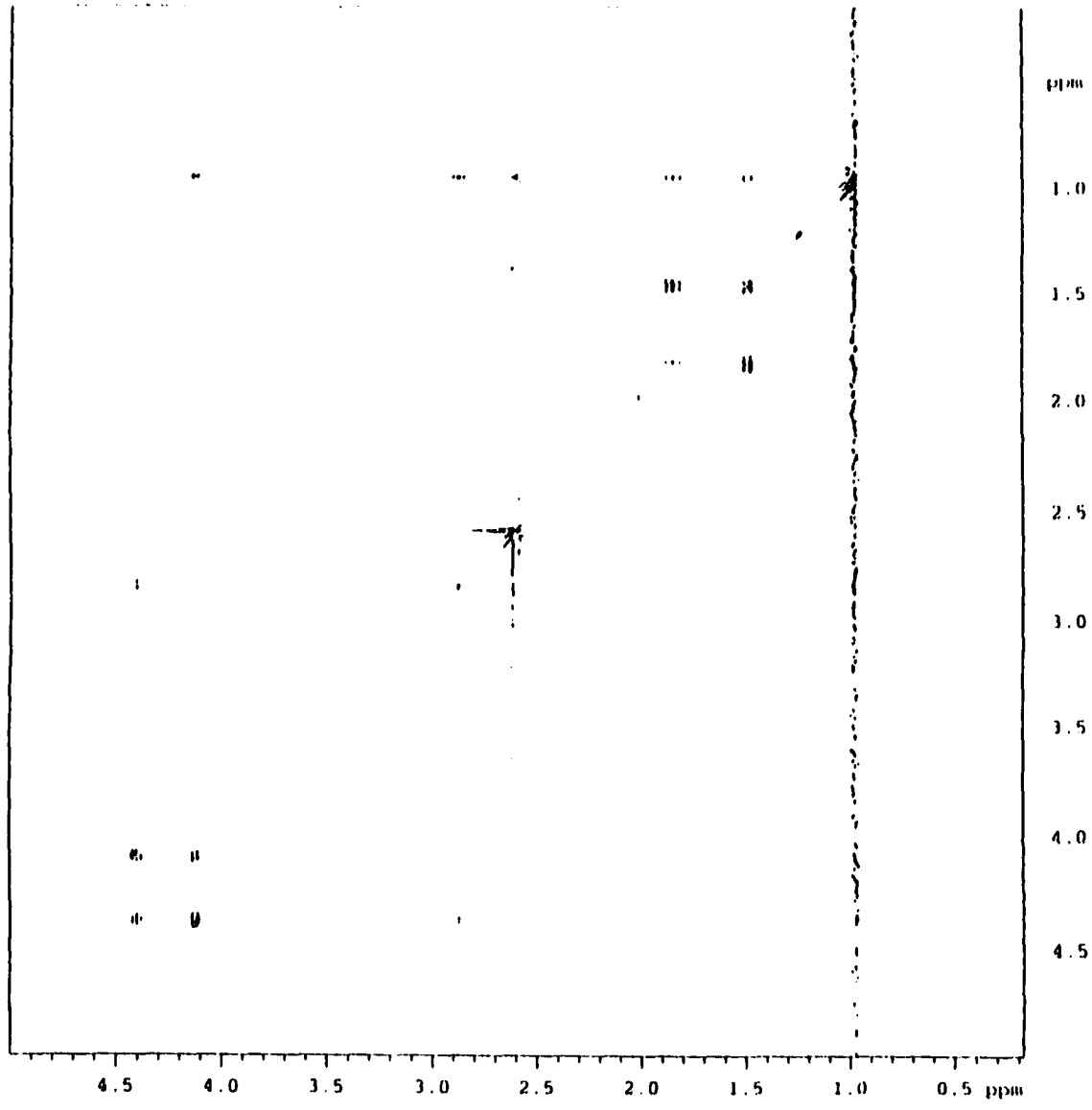
Figure 2A-39. ^{1}H NMR spectrum of compound **70**.

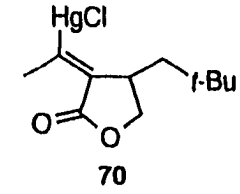




70

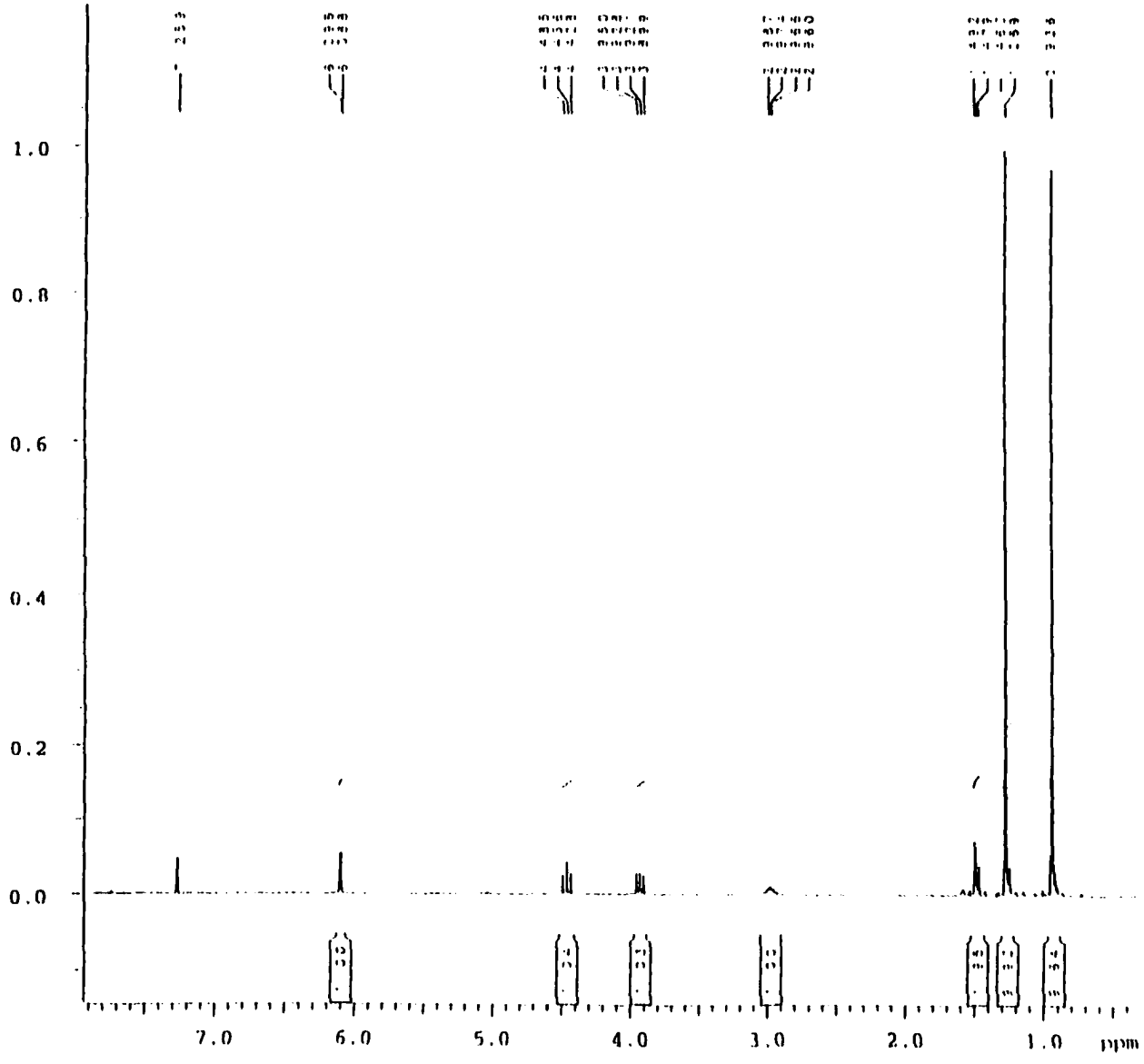
Figure 2A-40. ^{13}C NMR spectrum of compound **70**.

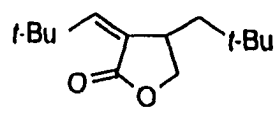




70

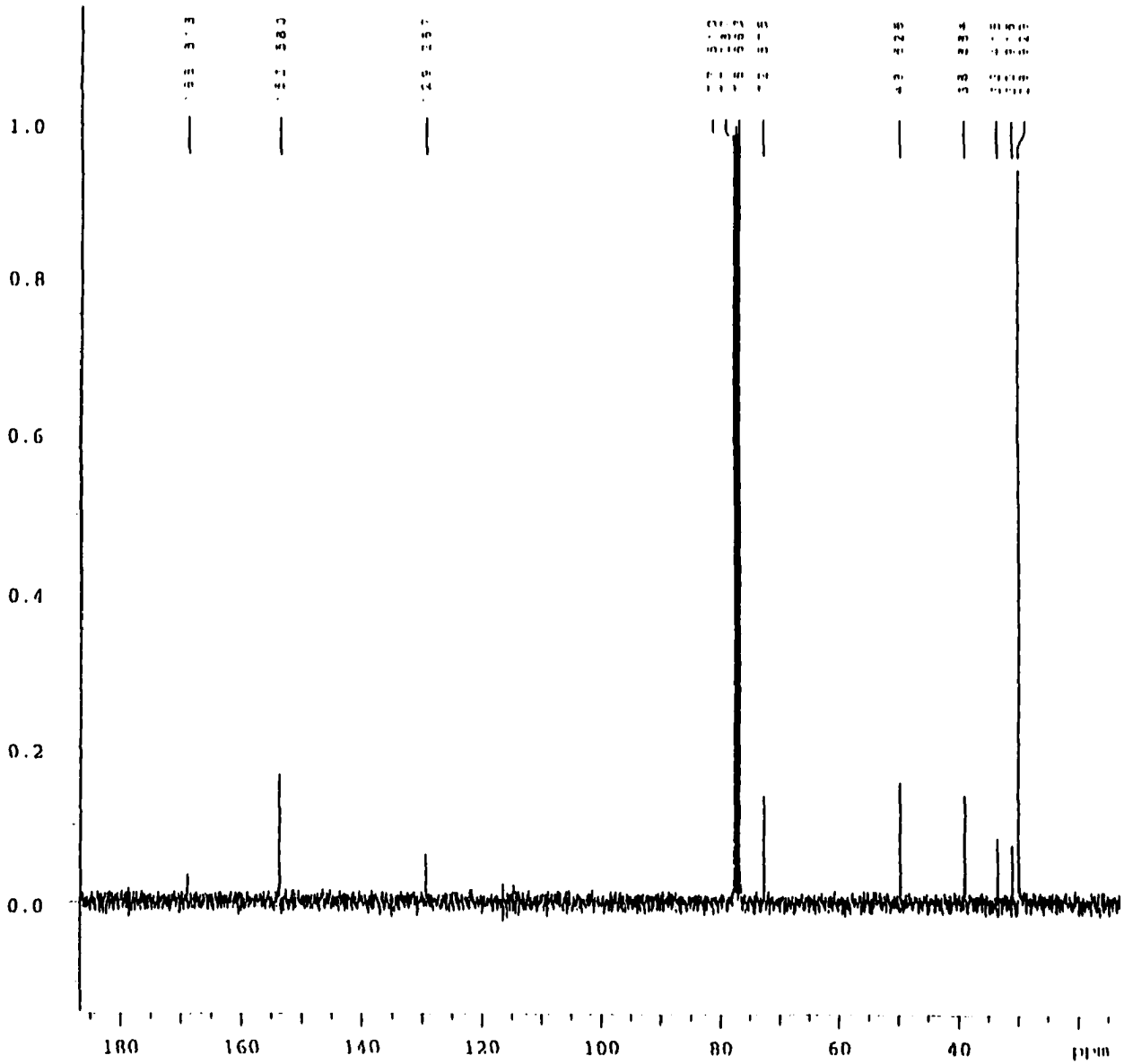
Figure 2A-41. ^{1}H-^{1}H NOE spectrum of compound **70**.

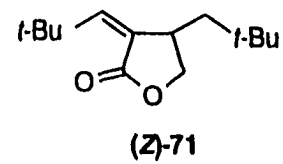




(Z)-71

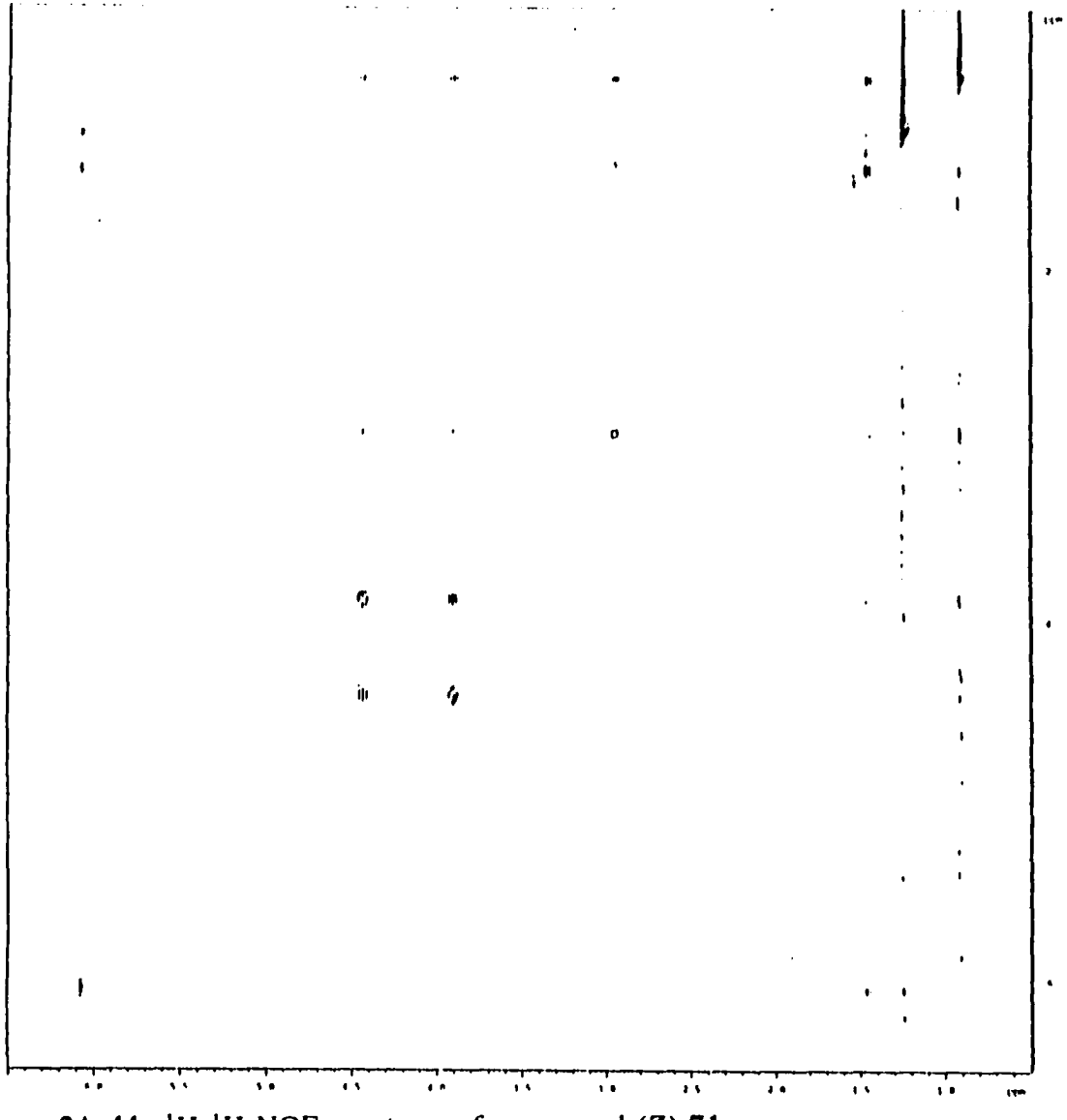
Figure 2A-42. ^{1}H NMR spectrum of compound (Z)-71.

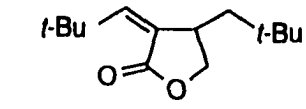




(Z)-71

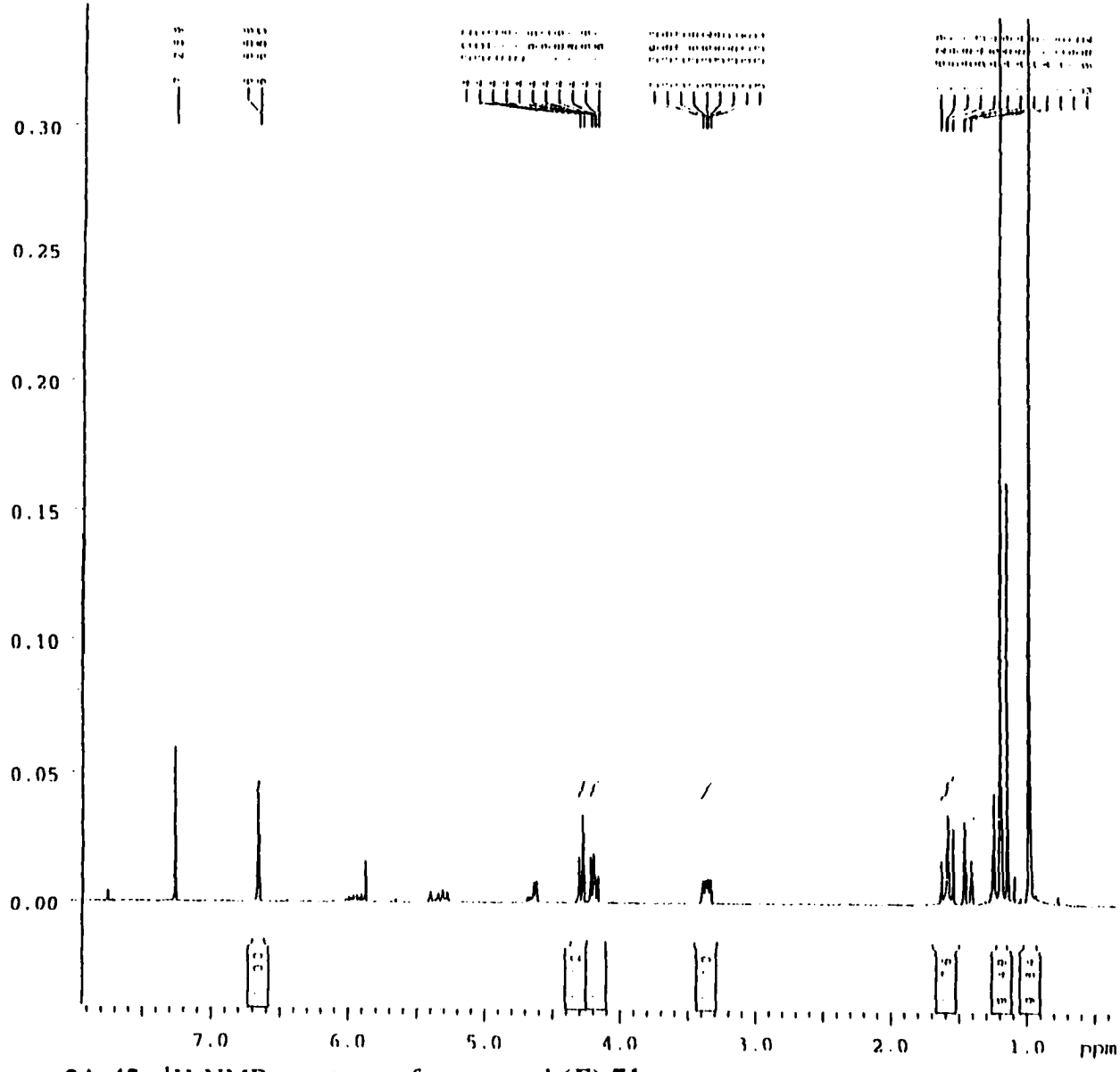
Figure 2A-43. ^{13}C NMR spectrum of compound (Z)-71.

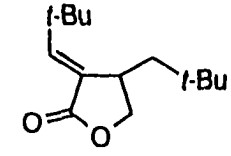




(Z)-71

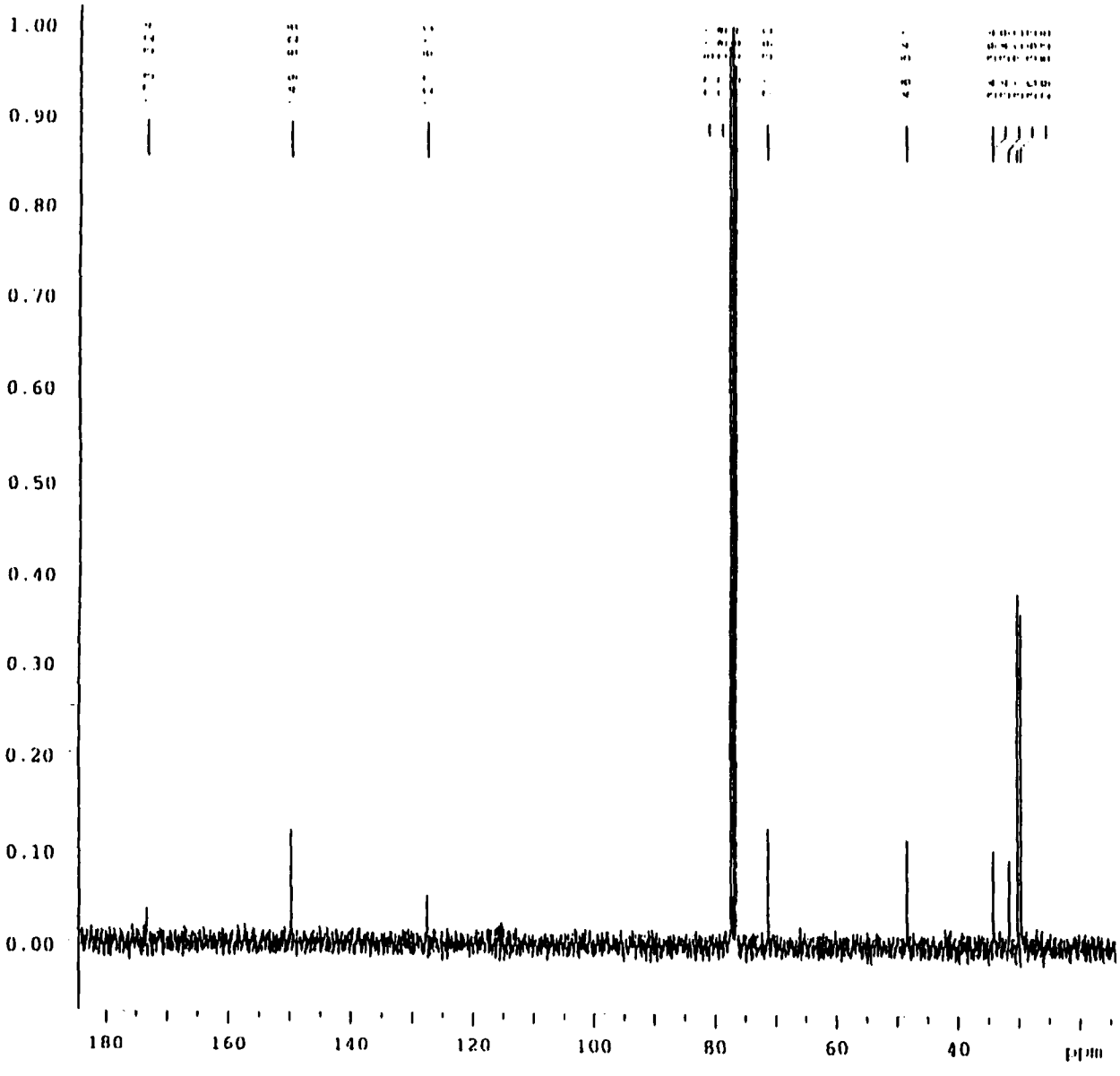
Figure 2A-44. ^{1}H-^{1}H NOE spectrum of compound (Z)-71.

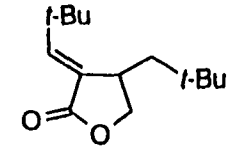




(*E*)-71

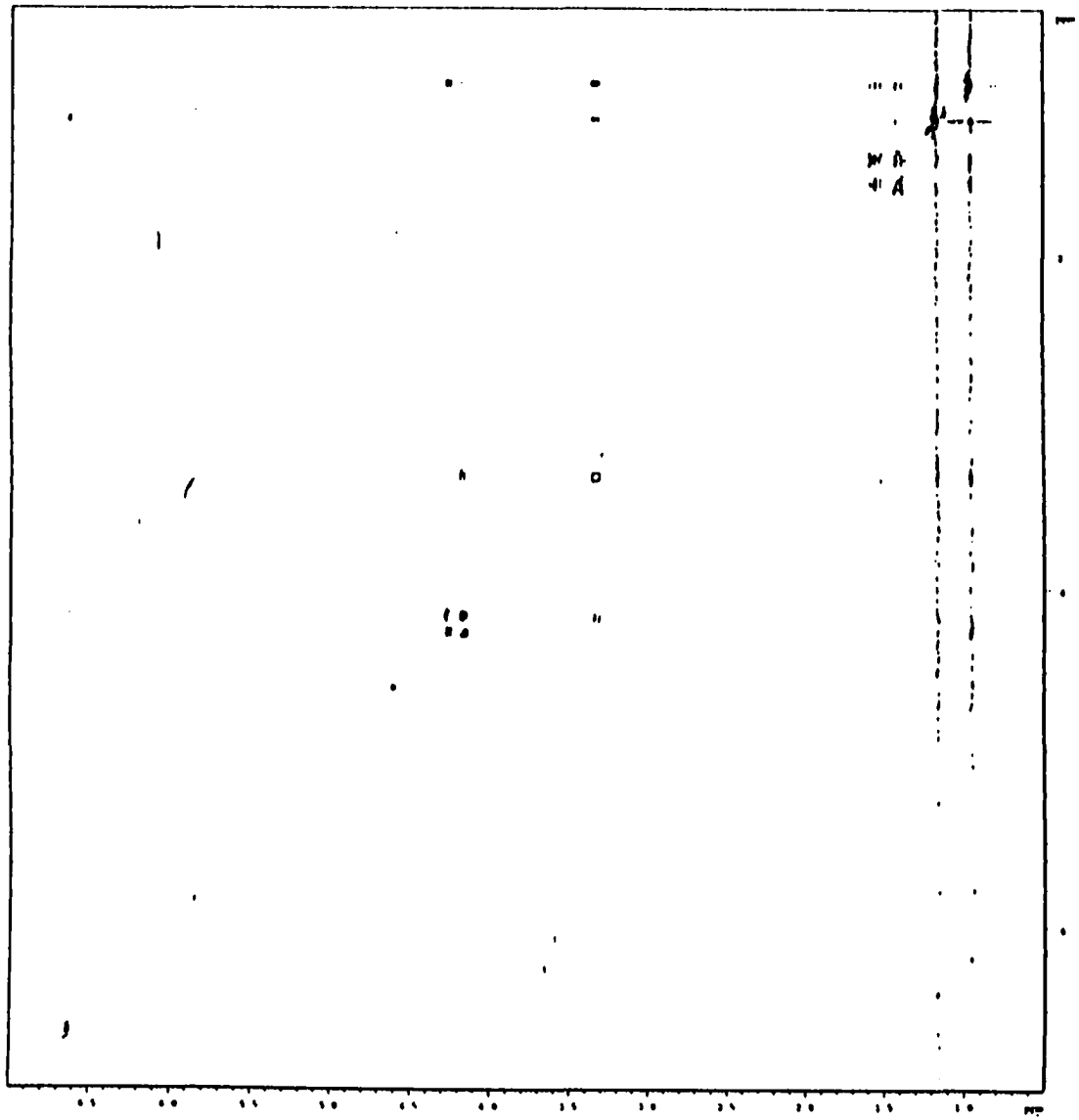
Figure 2A-45. ^{1}H NMR spectrum of compound (*E*)-71.

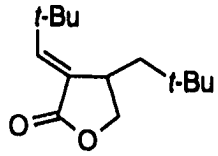




(*E*)-71

Figure 2A-46. ^{13}C NMR spectrum of compound (*E*)-71.





(*E*)-71

Figure 2A-47. ^{1}H-^{1}H NOE spectrum of compound (*E*)-71.

CHAPTER III. HOMOLYTIC BASE-PROMOTED AROMATIC ALKYLATIONS BY ALKYL HALIDES

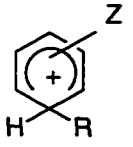
A paper, portions of which were published on the Journal of Organic Chemistry*

Chen Wang, Glen A. Russell and Walter S. Trahanovsky

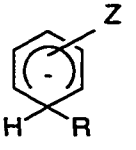
Introduction

Alkylation of aromatic compounds is a long-investigated topic in organic chemistry. It is known that the Friedel-Crafts reaction can be used to alkylate aromatic compounds bearing electron-donating groups through a electrophilic substitution mechanism.[1] This reaction involves the attack of an alkyl cation on the aromatic ring to form the cyclohexadienyl cation **1**, and the loss of a proton (H^+) from cation **1** to give the alkylated product. However, for aromatic compounds bearing electron-withdrawing groups, this reaction often gives unsatisfactory results. This is because the formation of the cation adduct **1** is favored by electron-donating groups, but not by electron-withdrawing groups.

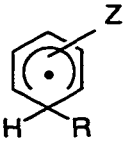
Although it might be proposed that aromatic compounds bearing electron-withdrawing groups could be alkylated by an alkyl anion through a nucleophilic substitution mechanism, because the proposed anion adduct **2** could be stabilized by an electron-withdrawing substitutent Z, this proposal has never been reported successful. One reason is probably that the loss of a hydride (H^-) from the anion adduct **2** is a very unfavored process.



1



2



3

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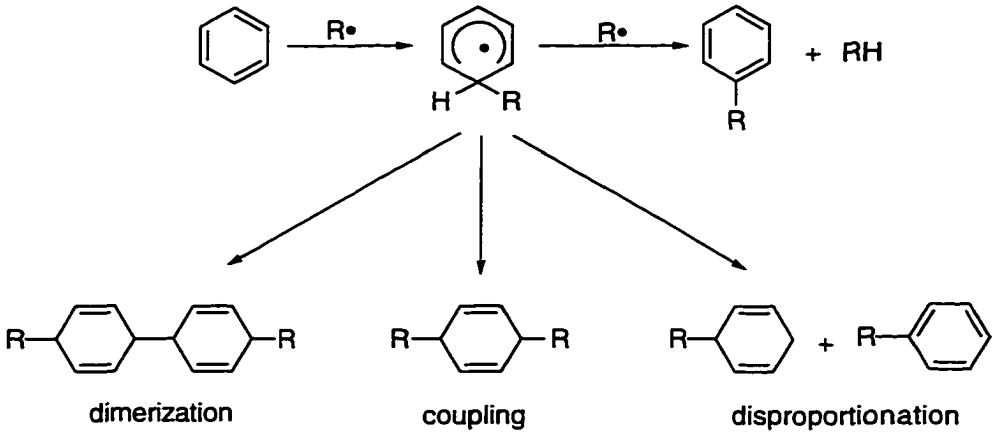
The next intriguing question is whether the aromatic alkylation can proceed through an adduct radical **3**. As known, alkyl radicals are quite compatible with many functional groups, such as alcohols, aldehydes, ketones, amides, and nitriles.[2] However, most early research found that homolytic alkylations of aromatic compounds formed only low yields of products with poor regioselectivity (Scheme 1).[3] The loss of a hydrogen atom (H•) from **3** is facilitated by the attack of another alkyl radical. However, radical side reactions like dimerization, disproportion, and coupling with other radicals interfere with the substitution process.[4] So, the overall yields are still low even although a large excess of a radical source is used. The radical sources typically used include: 1) $RCO_2H/Ag^+/S_2O_8^{2-}$. 2) RI/H_2O_2-Fe(II). 3) $RCO_2H/Pb(OAc)_2$. Homolytic aromatic alkylation was once considered only of theoretical interest.

Scheme 1

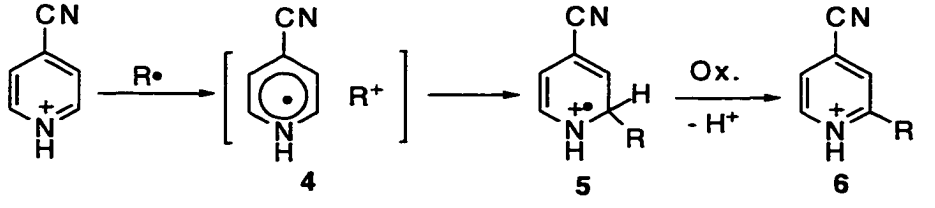


In 1970's, Minisci found that homolytic alkylation is more efficient for pyridines, quinolines, and other heteroaromatic compounds.[5] This alkylation reaction is accelerated significantly by protonating the substrates (Scheme 2).[6a]

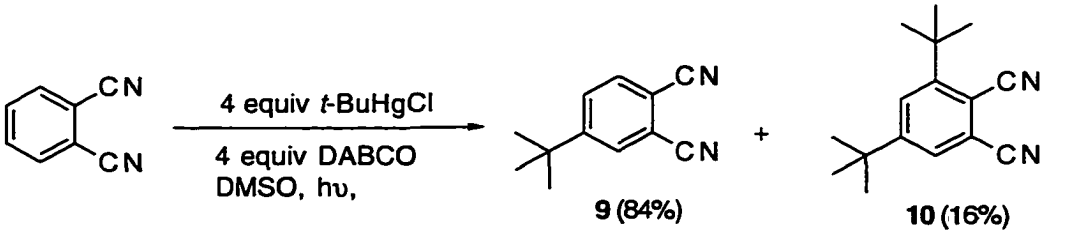
The higher reactivity of heteroaromatc compounds over benzene derivatives in this homolytic process was explained by the relative lower activation energy needed to reach the electron-transfer transition state **4**. Also, the polar effect appears to be a dominant factor

favoring higher regioselectivity and reactivity.[7] Also, a further oxidative step by Ag^{2+}, Fe^{3+}, or other oxidation reagent is introduced in this process so that it is the loss of a proton rather than H atom in going from **5** to **6** to complete the final transformation . However, the conversion of heteroaromatic compounds is usually low when only one equiv of a radical source is used and the reaction is not a chain process.[6b] Overall, Minisci's work shows that formation of a radical ion intermediate and incorporation of an electron-transfer step may make homolytic alkylation process more efficient and synthetically important.

Scheme 2



During the past decade, Russell developed a series of radical chain reactions using alkylmercury halides. Alkylmercury halides can undergo oxidative homolytic reactions with various unsaturated compounds in the presence of a base, such as 1,4-diazabicyclo[2.2.2] octane (DABCO).[8] Recently, Russell reported that benzenes bearing an electron-withdrawing group Z (Z = CN, CHO, CO_2Et) can be alkylated by RHgX/DABCO (R = *t*-Bu, *i*-Pr) in a chain process (eq 1).[9]

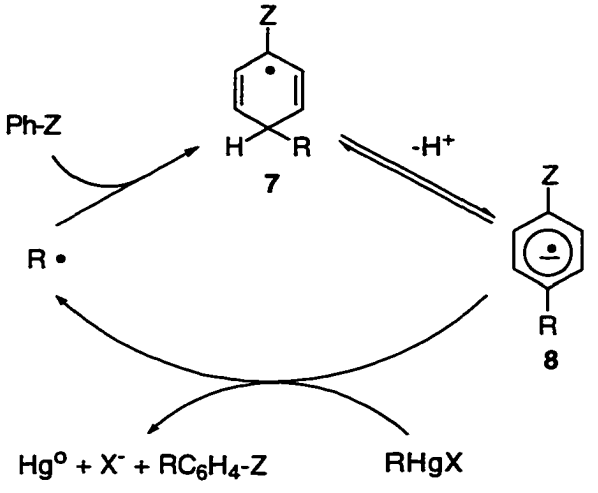


(1)

In Russell's reaction (Scheme 3), it also involves the loss of a proton, not a hydrogen atom from the radical adduct **7**. A proton is a much better leaving group than a hydrogen atom,

or a hydride, especially in the presence of an base. Although **7** may undergo radical side reactions mentioned in Scheme 1, it is converted rapidly to radical anion **8** which will not undergo those side reactions, so the yields are usually higher than those of former reports. Most importantly, Russell's process is a chain process. RHgX is a very good radical precursor. In the initial step, it decomposes to generate R• upon photolysis. In the propagation step it participates in electron transfer with **8** to form the very reactive $[RHgX]^{-\bullet}$ which then decomposes to generate R•,[10] forming a chain process is. So, this sequence of reactions is a novel type of homolytic aromatic alkylation.

Scheme 3

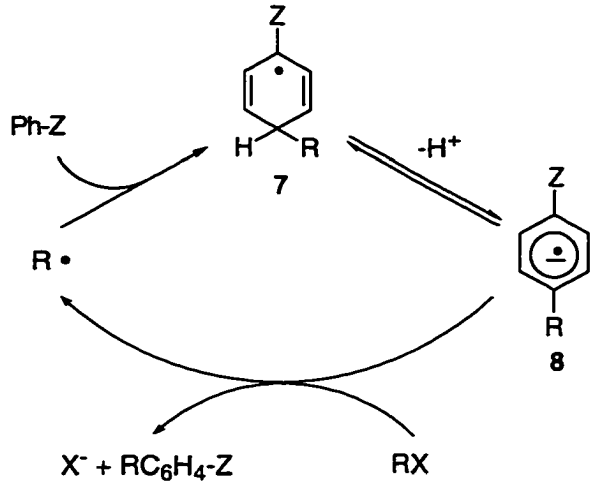


It is known that alkyl halides are also good precusors of alkyl radicals in the presence of appropriate radical initiators like $(Bu_3Sn)_2$. We were interested in replacing RHgX by RX to realize a similar process (Scheme 4). This modification, although simple, is mechanistically and synthetically important.

It has been found that RX can also participate in electron transfer with many anion species to form $[RX]^{-\bullet}$ which can decompose readily to give R•.[11] Estimated E^o-values of *t*-BuX suggest that RX can participate in electron transfer with dicyanobenzene radical anions. Estimated E^o-values (NHE) in DMSO and DMF are *t*-BuBr, -0.73, -0.92; *t*-BuI, -0.56,

-0.77V.[12] Observed irreversible E^o-values (NHE) are also in the range of that for *t*-BuHgX, e.g., *t*-BuHgBr, $E^{1/2}$ (CH_3CN) = -1.08 V (SCE); *t*-BuI, $E^{1/2}$ (DMF) = -1.84 V (SCE), where the reduction potentials of the dicyanobenzenes are in the range of -1.5 to -1.6 V (E^o, SCE).[13] So the replacement of RHgX by RX is probably feasible theoretically. Besides, RX is more conveniently available and less toxic than RHgX.

Scheme 4



However, early attempts failed completely when *t*-BuBr or *t*-BuI was substituted for *t*-BuHgX.[9] No reaction is observed when the mixture of *t*-BuX and dicyanobenzene is photolyzed in the presence of 4 equiv of DABCO and 10 mol % of AIBN, Bz_2O_2, or $(Bu_3Sn)_2$ at 35-70 °C in DMF, DMSO, or C_6H_6. An attempt to initiate the reaction by using 20 mol % *t*-BuHgX in DMSO was also unsuccessful. The reactions stopped after the *t*-BuHgX was consumed.

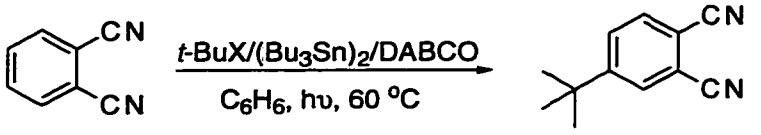
Reminded by the earlier report that 4 equiv of *t*-BuHgX were used for the alkylations of one equiv of disubstituted benzenes even though the reactions were good chain processes, we thought that the alkylations by *t*-BuX might be achieved if more than one equiv of *t*-Bu• is generated from *t*-BuX. Minisci also reported that when only one equiv of the radical source was used the conversions of heteroaromatic compounds were as low as 15 to 50% in many

cases while the yields based on the converted heteroaromatic compounds were as high as 82 to 98%.[6] We reinvestigated the alkylation reactions with 4 equiv of alkyl halides in the presence of 2 equiv of $(Bu_3Sn)_2$ and 4 equiv of DABCO.

Results and Discussion

1. 1,2-Disubstituted Benzenes

We have found that 1,2-dicyanobenzene can be *tert*-butylated upon photolysis with 4 equiv of *t*-BuX, 2 equiv of $(Bu_3Sn)_2$, and 4 equiv of DABCO at 60 °C (eq 2 and Table 1).



9 (2)

Table 1. *tert*-Bulylation of 1,2-Dicyanobenzene[a]

BuX (X)	DABCO (equiv)	yield% of **9** at the time of[b] 20 h	40 h
Br, I	0	none	none
Br	0.5	63	88
Br	4	75	97
I	4	90	

[a] Photolysis of 0.05 M substrate by a 275 W fluorescent sunlamp with 4 equiv of *t*-BuX and 2 equiv of $(Bu_3Sn)_2$. [b] Yield in C_6D_6 by ^1H NMR with $(Me_3Si)_2O$ as an internal standard.

A higher yield of **9** was formed at a faster rate when *t*-BuX was *t*-BuI rather than *t*-BuBr. This observation is accounted for by the different rates of formation of the *t*-Bu• from the two *t*-butyl halides. Alkylation by RX gives comparable yields of alkylated products to that by RHgX but requires a much longer reaction time. The dibutylated product **10** which is

formed by the *t*-BuHgX method was not found. Without DABCO, no alkylated product was found. This shows that without a base the corresponding adduct radical which is probably formed reversibly, is converted to **9** slowly. Also, no reaction was observed when AIBN or Bz_2O_2 was used instead of $(Bu_3Sn)_2$, or when DBU was used instead of DABCO.

Kinetic chain length (KCL) is a very important index for radical chain reactions, telling whether a reaction is an efficient chain process or not.[14] It measures the average number of reactant molecule consumed for every radical which initiates a chain reaction (eq 3).

$$\text{KCL} = \text{Initial reaction rate} / \text{Rate of initiation} \qquad (3)$$

Table 2 shows the results of reaction 2 with and without DTBN.

Table 2. *tert*-Butylation of 1,2-Dicyanobenzene in KCL measurement[a]

time	% yield of **9**[b]	
(h)	without DTBN	with DTBN[c]
0.5	9.1	0.0
1.0	19.8	0.0
1.5	29.4	0.0
2.0	38.1	0.0
3.0	47.4	0.0
5.0	68.5	0.0
7.0	75.0	0.5
8.0	---	16.6
9.0	82.9	26.8
10.0		32.9

a. Photolysis of 0.05 M 1,3-dicyanobenzene by a 275 W fluorescent sunlamp with 4 equiv of *t*-BuI and 2 equiv of $(Bu_3Sn)_2$. *b*. Yields in C_6D_6 by ^1H NMR spectroscopy with $(Me_3Si)_2O$ as the internal standard. *c*. 20 mol % DTBN.

The initial reaction rate can be measured experimently as the consumption rate of the substrate or the formation rate of the product(s). The rate of initiation is measured as the inhibition period in the presence of small amount of a radical inhibitor, like di-*tert*-butyl nitroxide (DTBN). The reaction progress can be conveniently monitored through ^{1}H NMR spectroscopy in an appropriate deuterium solvent with an internal standard.

From Figure 1, the initial reaction rate, or the slope of curve A at t = 0 h, is 0.010 M/h. Since the inhibition period is 7.0 h in the presence of 20 mol % DTBN, the initiation rate is 0.00143 M/h. Therefore the KCL is about 7.0, confirming that the eq 2 is a chain reaction.

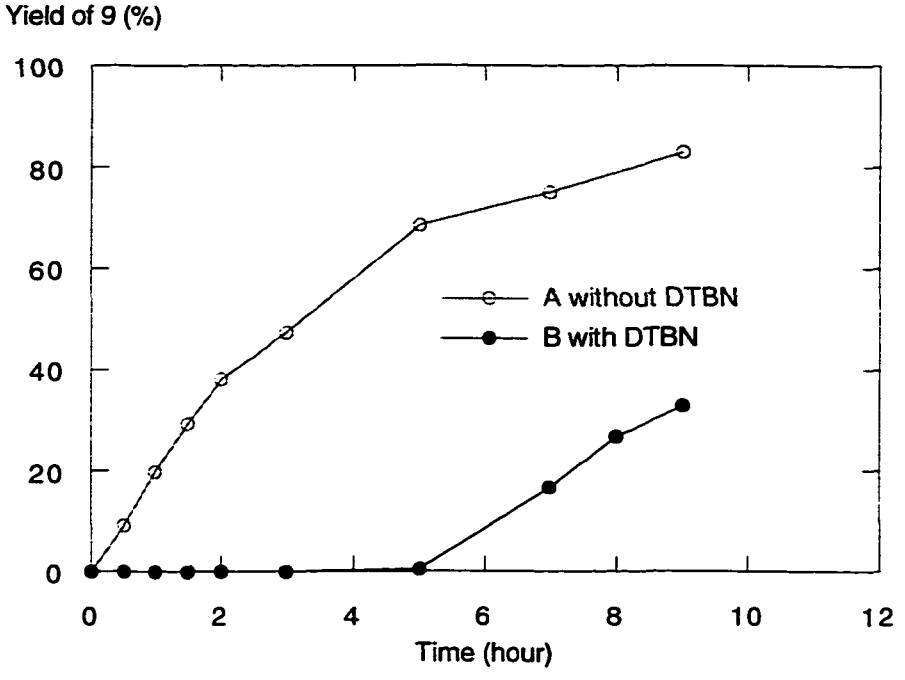
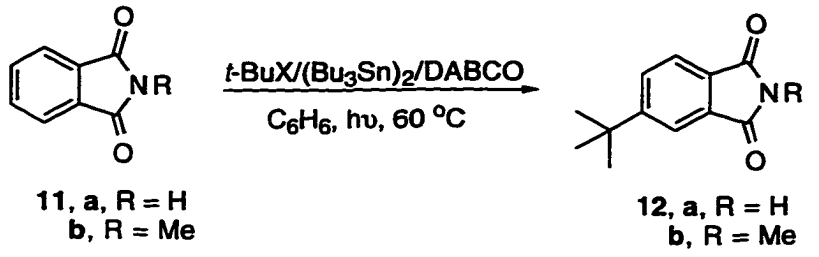


Figure 1. Plot of yield of **9** vs time for KCL measurement

Phthalimides also can be alkylated slowly by *t*-BuX (eq 4 and Table 3). Compound **11b** is more reactive than **11a**, and both are less reactive than 1,2-dicyanobenzene. Higher yields of products (**12a**, **12b**) were obtained with *t*-BuBr than with *t*-BuI. With *t*-BuI, it is likely that the *t*-Bu• was generated so rapidly that most of it went to disproportionation, leaving most of the starting material unreacted.



11, **a**, R = H
b, R = Me

12, **a**, R = H
b, R = Me

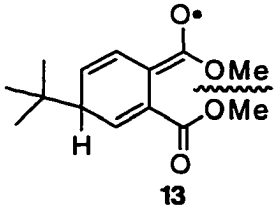
(4)

Table 3. *tert*-Butylation of Phthalimides[a]

substrate	X	product	yield% of product at the time of[b]		
			20 h	60 h	100 h
11a	Br	**12a**	14	28	
11a	I	**12a**	15		
11b	Br	**12b**	27	57	75
11b	I	**12b**	31		

[a] See footnote *a* of Table 1. [b] See footnote *b* of Table 1.

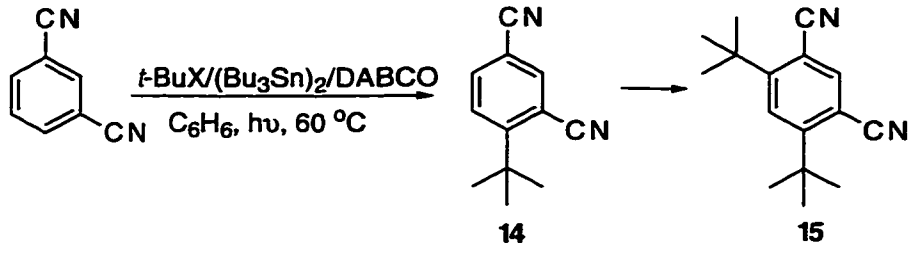
Surprisingly, dimethyl phthalate and phthalic anhydride failed to undergo reaction under the same conditions. For the dimethyl phthalate, the steric hindrance of the resonance in the adduct radical **13** may be involved. For the phthalic anhydride probably because it has a more negative reduction potential than phthalimide (-1.16 vs -0.70 V, SCE, in H_2O)[15]. As Minisci pointed out,[7] the transition state for attack of the nucleophilic *t*-Bu• upon an aromatic ring should be stablized by $t\text{-Bu}^{+}\text{Ar}^{\bullet -}$, and this is unfavored for phthalic anhydride which has the more negative reduction potential.



13

2. 1,3-Disubstituted Benzenes

Table 4 summarizes results for the formation of the mono and di-*tert*-butylated products **14** and **15** from 1,3-dicyanobenzene (eq 5).



14 **15** (5)

Even though for 1,3-disubstituted benzenes the adduct radical **16** can be stabilized by both electron-withdrawing substituents Z^1 and Z^2, 1,3-dicyanobenzene is less reactive than 1,2-dicyanobenzene as shown by the comparison of their alkylation yields at 20 h. We think the steric effect is more important than the resonance stablization effect because in compound **9**, the *t*-Bu is meta and para to the two cyano groupss, and in compound **14**, it is ortho and para to the two cyano groups.

From Table 5 and Figure 2, the KCL is only 4.7, shorter than that with *t*-BuHgX.[9]

Diethyl isophthalate cannot be *tert*-butylated by *t*-BuBr or *t*-BuI in the presence of $(Bu_3Sn)_2$ and DABCO. However, with *i*-Pr•, which is less sterically demanding than *t*-Bu•, the alkylation could happen. Compound **17** was produced in a yield of 18% in 20 h with 4 equiv of *i*-PrI, and in a yield of 35% in 100 h with 4 equiv *i*-PrBr (eq 6). In contrast to the dialkylation observed with *t*-BuHgX, no dialkylated product was found.

16

Table 4. *tert*-Butylation of 1,3-Dicyanobenzene[a]

t-BuX (X)	DABCO (equiv)	time (h)	**14** (%)[b]	**15** (%)[b]
Br, I	0	20	none	none
Br	0.5	20	23	
Br	0.5	60	38	
Br	4	20	33	
Br	4	60	65	15
I	4	4	49	3.3
I	4	20	66	18

[a] See footnote a of Table 1. [b] See footnote *b* of Table 1.

Table 5. *tert*-Butylation of 1,3-Dicyanobenzene in KCL measurement[a]

time	% yield without DTBN[b]		% yield with DTBN[c]	
(h)	**14**	**15**	**14**	**15**
0.5	4.6	0.0	0.0	0.0
1.0	14.7	0.0	0.0	0.0
2.0	28.4	0.0	0.0	0.0
3.0	38.5	1.9	0.0	0.0
4.0	49.4	3.3	0.0	0.0
5.0	56.6	4.3	0.0	0.0
6.5	---	---	0.0	0.0
7.0	66.4	7.6	8.4	0.0
7.5	---	---	20.0	0.0
8.5	---	---	32.0	0.0
11.0	69.0	15.0	52.8	0.0

[a] See footnote *a* of Table 2. [b] See footnote *b* of Table 2. [c] See footnote *c* of Table 2.

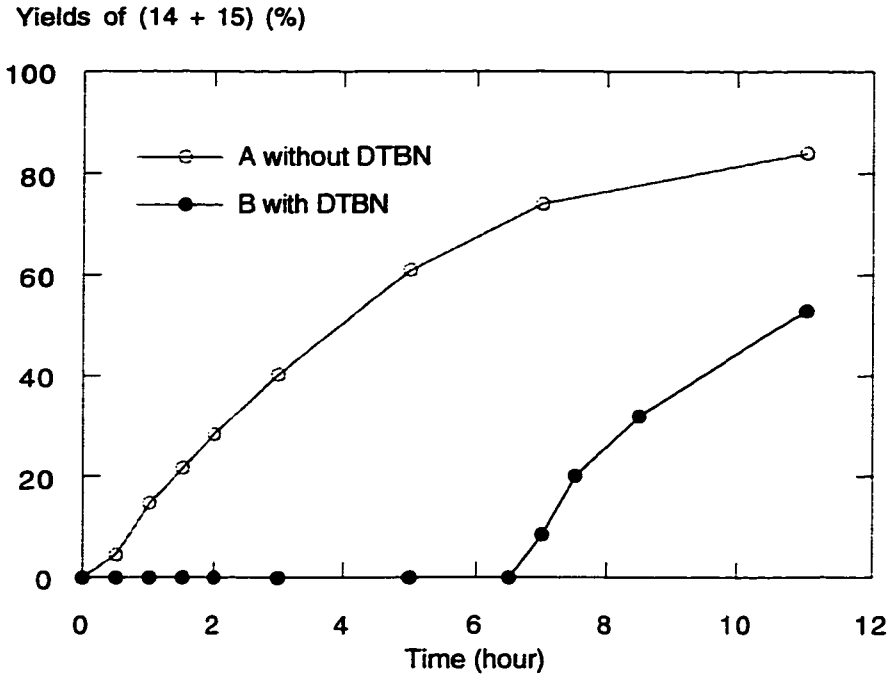
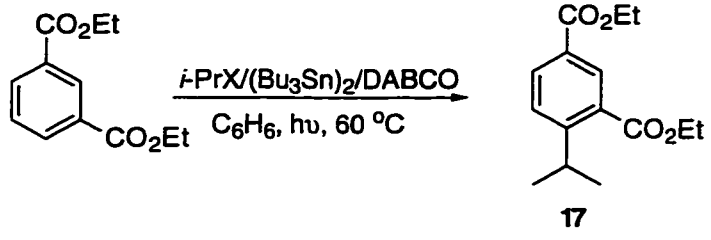
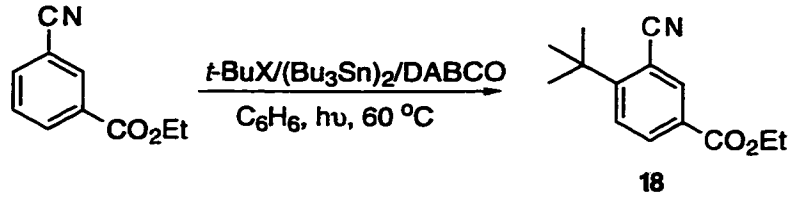


Figure 2. Plot of yield of (**14** + **15**) vs time for KCL measurement



17 (6)

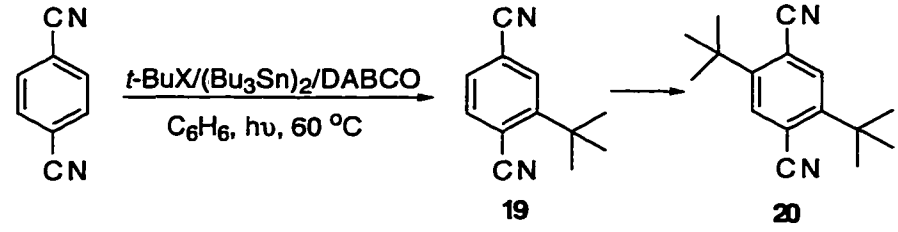
Ethyl 3-cyanobenzoate reacted slowly with 4 equiv of *t*-BuBr, 2 equiv of $(Bu_3Sn)_2$, and 4 equiv of DABCO. Compound **18** was formed in yields of 25, 82% upon photolysis in 20, 100 h, respectively. The *t*-butyl group is always introduced ortho to the -CN group, which is less sterically hindered than the position ortho to $-CO_2Et$. Replacement of *t*-BuBr by *t*-BuI yielded only a trace of **18** (eq 7).



18 (7)

3. 1,4-Disubstituted Benzenes

Table 6 summarizes the results for the alkylations of 1,4-dicyanobenzene (eq 8). The dialkylated product **19** was also formed as well as the monoalkylated product **20**. The initial KCL was only 1.3 with *t*-BuI as measured by 20 mol % DTBN (Table 7 and Figure 3). Obviously, this reaction did not proceed by an efficient chain process.



19 20 (8)

Table 6. *tert*-Butylation of 1,4-Dicyanobenzene[a]

t-BuX (X)	DABCO (equiv)	time (h)	**19** (%)[b]	**20** (%)[b]
Br, I	0	100	none	none
Br	0.5	20	6	
Br	0.5	100	27	
Br	4	20	17	
Br	4	100	74	10
I	4	20	38	
I	8	20	51	3

[a] See footnote *a* of Table 1. [b] See footnote *b* of Table 1.

Table 7. *tert*-Butylation of 1,4-Dicyanobenzene in KCL Measurement[a]

Time	% yield without DTBN[b]		% yield with DTBN[c]	
(h)	**19**	**20**	**19**	**20**
1.0	1.3	0.0	0.0	0.0
2.0	4.2	0.0	0.0	0.0
3.0	7.2	0.0	0.0	0.0
4.0	10.1	0.0	0.0	0.0
6.0	15.4	0.0	0.0	0.0
9.0	21.9	7.6	0.0	0.0
10.5	---	---	3.0	0.0
11.5	24.9	---	4.9	0.0
12.5	---	---	6.8	0.0

[a] See footnote *a* of Table 2. [b] See footnote *b* of Table 2. [c] See footnote *c* of Table 2.

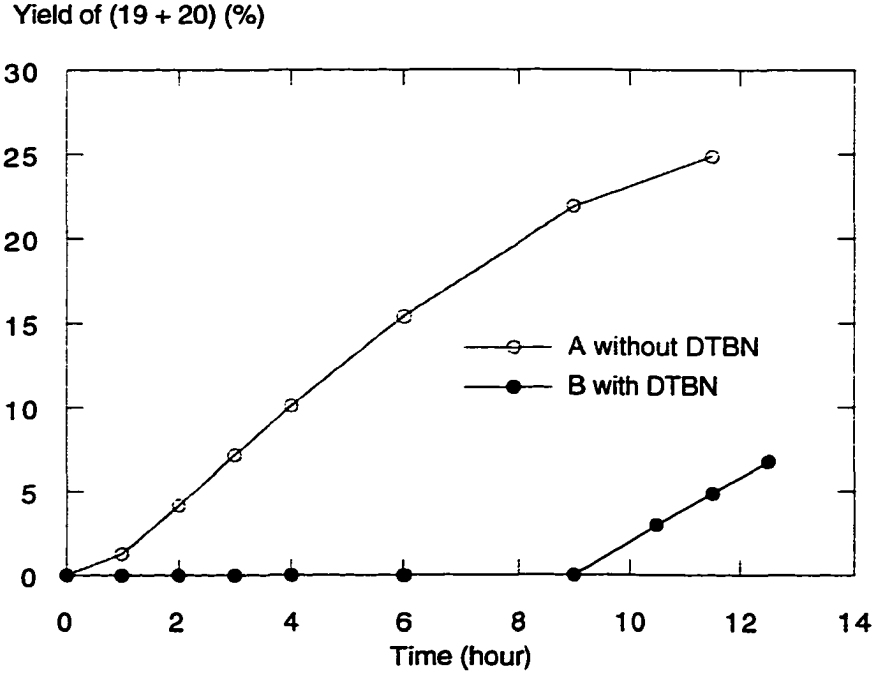
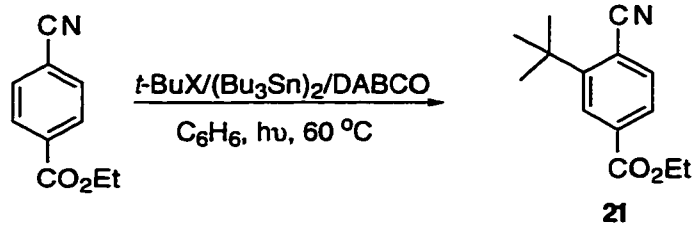


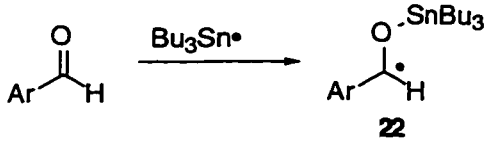
Figure 3. Plot of yield of (**19** + **20**) vs time for KCL measurement

Ethyl 4-cyanobenzoate yielded only a trace of **21** with *t*-BuI. However, with *t*-BuBr, **21** was formed in yields of 39, 57, and 70% upon photolysis for 20, 60, and 100 h, respectively (eq 9). The *t*-butyl groups were always introduced ortho to the -CN group instead of the $-CO_2Et$ group. Unlike the significant reactivity difference between 1,3- and 1,4-dicyanobenzenes, the reactivity difference between ethyl 3- and 4- benzoates is small.



21 (9)

Although former alkylation results show that *t*-Bu• does not attack a cyano or an ester group, aldehyde-substituted benzenes gave complicated results when reacted with $RX/(Bu_3Sn)_2$/DABCO. It is not likely that *t*-Bu• attacks the aldehyde carbonyl group or abstracts the aldehyde H because alkylations proceed smoothly when *t*-BuHgX was used as the *t*-Bu• precusor.[9] However, the initiator radical Bu_3Sn• can react with aldehyde group to form an O-stannyl ketyl radical intermediate **22** leading to other side reactions.[16] So, no aromatic alkylation product was found.

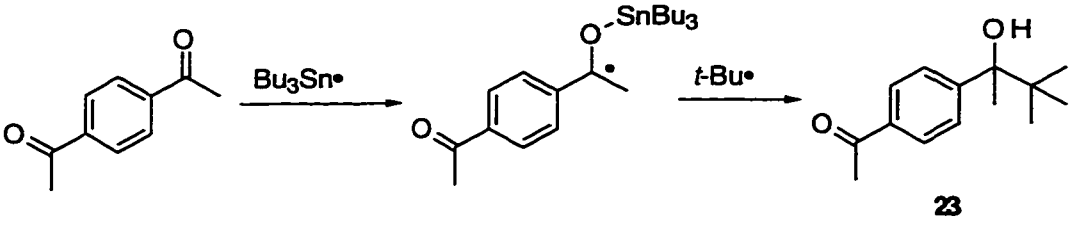


22

As for acetyl substituted benzene, 1,2- and 1,3-diacetyl benzenes showed no reaction with $RX/(Bu_3Sn)_2$/DABCO. However, for 1,4-diacetylbenzene, unexpected product **23** was obtained in a yield of 48% in 20 hr with *t*-BuI, and 72% in 60 hr with *t*-BuBr. Its formation

was probably initiated by the attack of $Bu_3Sn\bullet$ on the carbonyl oxygen atom (Scheme 5). The reason for the lack of reaction of 1,2- and 1,3-diacetyl benzenes is not clear.

Scheme 5



23

Conclusions

Overall, we find that homolytic base-promoted aromatic alkylations can be observed with alkyl halides, $(Bu_3Sn)_2$, and DABCO in C_6H_6 at 60 °C. These results suggest that base-promoted homolytic aromatic substitutions may be a rather general process for aromatic compounds with electron-withdrawing substituents. This alkylation method can to some extent serve as a complementary methodology to the well-known Friedel-Crafts reaction which can alkylate benzene derivatives bearing electron-donating substituents. Alkylations by alkyl halides have a much shorter kinetic chain length than those involving alkylmercury halides[9] and usually need a longer reaction time. Yields vary from low to high depending on the substrates and are much higher if recovered starting benzene derivatives are taken into account. In most reactions unreacted aromatic compounds remained after the RX was consumed. The lower reactivity of *t*-BuX compared to *t*-BuHgX, is probably due to the slower electron transfer rate from the radical anions to *t*-BuX. Lund has reported that the rate of electron transfer from aromatic radical anion to RX is only 10 L/(mol·s) at 25 °C.[17] This rate is not enough to sustain a good chain process.

Usually the reactivity and initial kinetic chain length decrease from 1,2- to 1,3- to 1,4-disubstituted benzenes. For reactive substrates like 1,2-dicyanobenzene, alkylations by *t*-BuI

give higher yields of products than those by *t*-BuBr. Otherwise, alkylations by *t*-BuBr give higher yields of the products.

In comparison to the CO_2Et group, the CN group is a much better activating group with less steric requirement. The introduction of alkyl substituents is very regioselective and usually monoalkylated products are the major products.

Dialkylated products were formed from the less reactive 1,3- and 1,4-dicyanobenzenes but not from the more reactive 1,2-dicyanobenzene. This observation shows that the formation of dialkylated products is not strongly related to the reactivity of the starting benzene derivatives but to the reactivity difference between the starting aromatic compounds and the corresponding monoalkylated products.

Because $Bu_3Sn^{\bullet}$ is incompatible with the CHO group, no aldehyde-substituted benzenes can be alkylated by this method. Acetyl-substituted benzene derivatives showed different reaction results.

Even though there are many literature methods available for removal of the tin compounds from the desired products,[18] the use of excess $(Bu_3Sn)_2$ is still a drawback in preparative applications. Further work on replacing the tin radical initiator is highly desired.

Experimental Section

General Considerations

^1H and ^{13}C NMR spectra were recorded on a DRX 400 spectrometer. Chemical shifts are reported in ppm for ^1H NMR measured relative to internal trace $CHCl_3$ (7.27 ppm), or for ^{13}C NMR measured relative to the central line of internal $CDCl_3$ (77.23 ppm). GC-MS spectra were recorded on a Finnegan 4000 spectrometer with Incos data system or a Varian Magnum spectrometer. High resolution mass spectra were recorded on a Kratos MS-50 spectrometer. Infrared spectra were recorded on an IBM IR-98 FT spectrometer. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected.

Most chemical reagents were purchased from Aldrich. In most cases, the reagents were used without further purification. Most products were isolated either by flash column chromatography on silica gel (Merck, 230-400 mesh, purchased from Aldrich) with mixed solvents (hexanes-ethyl acetate) as eluents, or by TLC on 20 cm x 10 cm silica gel plates. ^1H NMR spectroscopic yields were determined by integration with a known amount of an internal standard $Me_3SiOSiMe_3$ (bp. 101 °C).

General Preparative Procedures and Compound Characterization

General aromatic alkylation procedure: The aromatic substrates (0.5 mmol), DABCO (2 mmol) and $(Bu_3Sn)_2$ (1 mmol) were dissolved in C_6H_6 (10 mL) under a nitrogen atmosphere in a Pyrex test tube and irradiated with a 275 W Sylvania fluorescent sunlamp which was approximately 20 cm away from the reation tube. After the reaction stopped, the solution was concentrated to about 4 mL, cooled to 0 °C, and some precipitate was removed by filtration. Then 1 M NaOH solution (2 mL) was added to the filtered solution and the mixture solution was stirred for 30 min at room temperature for further removal of the tin compounds.[18a] After the ethereal extract was dried by $MgSO_4$ and concentrated, the reaction products were isolated by TLC using hexanes-ethyl acetate as the eluent.

For reactions monitored by ^1H NMR spectrum, the substrate (0.05 mmol) and added reagents (with or without 20 mol % DTBN) were dissolved in 0.6 mL of C_6D_6 in a 5-mm NMR tube with 2 μL of $(Me_3Si)_2O$ (bp ~ 101 °C) as the internal standard.

Ethyl 3-Cyanobenzoate was prepared as a white solid in 95% yield by the reaction of 3-cyanobenzoyl chloride with ethanol in the presence of triethylamine in CH_2Cl_2 at 0-25 °C. mp 48-50 °C. ^1H NMR δ 8.26 (t, J = 1.2 Hz, 1H), 8.22 (dd, J = 8.0, 1.2 Hz, 1H), 7.79 (dd, J = 8.0, 1.2 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 4.37 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H). ^{13}C NMR δ 164.55, 135.88, 133.63, 133.20, 131.74, 129.46, 117.94, 112.85, 61.79, 14.25; HREIMS m/z (rel intensity) 175.0637 (29, calcd for $C_{10}H_9NO_2$ 175.0633), 147 (44), 130 (100), 102 (40), 75 (12), 69 (40).

Diethyl Isophthalate was prepared by the reaction of isophthaloyl dichloride with ethanol in the presence of triethylamine in CH_2Cl_2 at 0-25 °C ^{1}H NMR δ 8.69-8.68 (m, 1H), 8.23 (dd, J = 7.8, 1.8 Hz, 2H), 7.53 (t, J = 7.5 Hz, 1H), 4.42 (q, J = 7.2 Hz, 4H), 1.42 (t, J = 7.2 Hz, 6H); ^{13}C NMR δ 165.72, 133.58, 130.81, 130.52, 128.42, 61.23, 14.23.

1,2-Dicyano-4-(1,1-dimethylethyl)benzene (9) was isolated as a white solid, mp 57-59 °C. FTIR (cm^{-1}) 3103, 2962, 2874, 2234, 1596; ^{1}H NMR δ 7.82 (t, J = 1.2 Hz, 1H), 7.75 (d, J = 1.2 Hz, 2H), 1.37 (s, 9H); ^{13}C NMR δ 157.91, 133.57, 131.11, 130.60, 116.02, 115.94, 115.79, 113.03, 35.82, 30.91; HREIMS m/z (rel intensity) 184.1002 (20, calcd for $C_{12}H_{12}N_2$ 184.1001), 169 (100), 141 (51), 114 (7).

4-(1,1-Dimethylethyl)phthalimide (12a) was isolated as a white solid, mp 130-132 °C. FTIR (cm^{-1}) 3250, 3050, 2868, 1748, 1700; ^{1}H NMR δ 7.91 (s, 1H), 7.85 (b, 1H), 7.79-7.78 (m, 2H), 1.39 (s, 9H); ^{13}C NMR δ 168.73, 168.31, 159.26, 133.03, 131.62, 130.13, 123.65, 120.95, 36.00, 31.35; HREIMS m/z (rel intensity) 203.0947 (23, calcd for $C_{12}H_{13}NO_2$ 203.0946), 188 (100), 169 (39), 145 (12), 115 (6).

4-(1,1-Dimethylethyl)-*N*-methylphthalimide (12b) was isolated as a white solid, mp 87-89 °C. FTIR (cm^{-1}) 2968, 2871, 1765, 1709, 1602; ^{1}H NMR δ 7.87 (d, J = 1.6 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.71 (d, J = 1.6 Hz, 1H), 3.16 (s, 3H), 1.37 (s, 9H); ^{13}C NMR δ 169.16, 168.76, 158.64, 132.60, 131.00, 129.70, 123.17, 120.60, 35.98, 31.33, 24.08; HREIMS m/z (rel intensity) 217.1105 (30, calcd for $C_{13}H_{15}NO_2$ 217.1103), 202 (100), 174 (20), 145 (20), 115 (8).

2,4-Dicyano-1-(1,1-dimethylethyl)benzene (14) was isolated as a white solid, mp 56-58 °C. FTIR (cm^{-1}) 3119, 3044, 2988, 2878, 2237, 2230, 1602; ^{1}H NMR δ 7.96 (d, J = 2.0 Hz, 1H), 7.80 (dd, J = 8.4, 2.0 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 1.55 (s, 9H); ^{13}C NMR δ 159.07, 138.77, 135.95, 127.88, 118.29, 116.97, 112.76, 112.24, 36.57, 30.02; HREIMS m/z (rel intensity) 184.1002 (21, calcd for $C_{12}H_{12}N_2$ 184.1001), 169 (100), 141 (26), 114 (5), 57 (4).

2,4-Dicyano-1,5-bis(1,1-dimethylethyl)benzene (15) was isolated as a white solid, mp 176-178 °C. FTIR (cm^{-1}) 2959, 2873, 2224, 1593; ^1H NMR δ 7.94 (s, 1H), 7.64 (s, 1H), 1.54 (s, 18H); ^{13}C NMR δ 158.37, 141.83, 125.10, 118.45, 109.57, 36.77, 30.03; HREIMS m/z (rel intensity) 240.1626 (13, calcd for $C_{16}H_{20}N_2$ 240.1627), 225 (100), 210 (4), 197 (6), 57 (5).

Diethyl 4-(1-Methylethyl)isophthalate (17) was isolated as a colorless liquid. FTIR (cm^{-1}) 2990, 2906, 2872, 1731, 1717, 1305, 1229; ^1H NMR δ 8.36 (d, J = 2.0 Hz, 1H), 8.09 (dd, J = 8.4, 2.0 Hz, 1H), 7.48 (d, J = 8.4 Hz, 1H), 4.39 (q, J = 7.2 Hz, 2H), 4.38 (q, J = 7.2 Hz, 2H), 3.74 (septet, J = 6.8 Hz, 1H), 1.41 (t, J = 7.2 Hz, 3H), 1.38 (t, J = 7.2 Hz, 3H), 1.26 (d, J = 6.8 Hz, 6H); ^{13}C NMR δ 167.90, 166.04, 154.62, 132.47, 131.10, 130.80, 128.07, 126.60, 61.42, 61.24, 30.01, 23.87, 14.49, 14.42; HREIMS m/z (rel intensity) 264.1364 (71, calcd for $C_{15}H_{20}O_4$ 264.1362), 235 (23), 218 (100), 203 (39), 189 (13), 145 (13), 117 (11), 91 (7). [lit.[9] ^1H NMR ($CDCl_3$, 300 MHz) δ 8.38 (d, J = 2.1 Hz, 1H), 8.10 (dd, J = 8.4, 2.1 Hz, 1H), 7.48 (d, J = 8.4 Hz, 1H), 4.39 (q, J = 7.2 Hz, 2H), 4.38 (q, J = 7.2 Hz, 2H), 3.76 (septet, J = 6.9 Hz, 1H), 1.41 (t, J = 7.2 Hz, 3H), 1.40 (t, J = 7.2 Hz, 3H), 1.28 (d, J = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.6, 165.8, 154.4, 132.2, 130.8, 130.5, 127.8, 126.3, 61.1, 61.0, 29.7, 23.6, 14.2, 14.15.]

Ethyl 3-Cyano-4-(1,1-dimethylethyl)benzoate (18) was isolated as a colorless liquid. FTIR (cm^{-1}) 2990, 2910, 2225, 1731, 1607, 1298, 1129; ^1H NMR δ 8.33 (d, J = 2.0 Hz, 1H), 8.14 (dd, J = 8.4, 2.0 Hz, 1H), 7.57 (d, J = 8.4Hz, 1H), 4.39 (q, J = 7.2 Hz, 2H), 1.54 (s, 9H), 1.41 (t, J = 7.2Hz, 3H); ^{13}C NMR δ 164.86, 158.50, 136.82, 133.69, 128.99, 126.83, 119.64, 111.31, 61.72, 36.22, 30.16, 14.46; HREIMS m/z (rel intensity) 231.1258 (25, calcd for $C_{14}H_{17}NO_2$ 231.1259), 216 (100), 188 (34), 144 (13), 116 (4). [lit.[9] ^1H NMR ($CDCl_3$, 300 MHz) δ 8.34 (d, J = 2.1 Hz, 1H), 8.15 (dd, J = 8.4, 2.1 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 1.55 (s, 9H), 1.41 (t, J = 7.2 Hz,

3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6, 158.2, 136.6, 133.4, 128.8, 126.6, 119.4, 111.1, 61.5, 36.0, 29.9, 14.2.]

1,4-Dicyano-2-(1,1-dimethylethyl)benzene (19) was isolated as a white solid, mp 150-152 °C. FTIR (cm^{-1}) 3115, 2988, 2875, 2231, 2226, 1558; ^1H NMR δ 7.80-7.78 (m, 2H), 7.60 (dd, J = 7.6, 1.6 Hz, 1H), 1.55 (s, 9H); ^{13}C NMR δ 155.36, 136.22, 130.44, 129.78, 118.73, 117.82, 116.58, 115.42, 36.20, 30.04; HREIMS m/z (rel intensity) 184.1002 (19, calcd for $C_{12}H_{12}N_2$ 184.1001), 169 (100), 141 (27), 114 (6), 57 (6). [lit.[9] ^1H NMR ($CDCl_3$, 300 MHz) δ 7.81-7.78 (m, 2H), 7.60 (dd, J = 7.8, 1.5 Hz, 1H), 1.55 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.1, 136.0, 130.2, 129.5, 118.5, 117.5, 116.3, 115.1, 35.9, 29.8.]

Ethyl 4-Cyano-3-(1,1-dimethylethyl)benzoate (20) was isolated as a white solid, mp 44-46 °C. FTIR (cm^{-1}) 2970, 2873, 2223, 1733; ^1H NMR δ 8.16 (d, J = 1.2 Hz, 1H), 7.93 (dd, J = 8.0, 1.2 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 4.41 (q, J = 7.2Hz, 2 H), 1.55 (s, 9H), 1.42 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 165.66, 154.34, 135.78, 134.07, 127.54, 127.15, 119.73, 114.82, 61.89, 35.99, 30.26, 14.46; HREIMS m/z (rel intensity) 231.1259 (18, calcd for $C_{14}H_{17}NO_2$ 231.1259), 216 (100), 188 (26), 144 (12), 115 (5), 57 (4). [lit.[9] ^1H NMR ($CDCl_3$, 300 MHz) δ 8.16 (d, J = 1.5 Hz, 1H), 7.94 (dd, J = 7.8, 1.5 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 4.42 (q, J = 7.2Hz, 2 H), 1.56 (s, 9H), 1.42 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.4, 154.1, 135.5, 133.8, 127.3, 126.9, 119.5, 114.6, 61.6, 35.7, 30.0, 14.2.]

1,4-Dicyano-2,5-bis(1,1-dimethylethyl)benzene (21) was isolated as a white solid, mp 172-174 °C. FTIR (cm^{-1}) 2959, 2874, 2223; ^1H NMR δ 7.48 (s, 2H), 1.52 (s, 18H); ^{13}C NMR δ 151.80, 133.60, 119.30, 114.93, 35.57, 30.05; HREIMS m/z (rel intensity) 240.1626 (12, calcd for $C_{16}H_{20}N_2$ 240.1627), 225 (100), 210 (4), 197 (9), 182 (5), 57 (5).

4-Acetyl-α-(1,1-dimethyl)ethylbenzyl Alcohol (23) was isolated as a white solid, mp 75-77 °C (lit[19] 66-69 °C). FTIR (cm^{-1}) 3506 (b), 2975, 2922, 2857, 1674, 1605, 1273; ^1H NMR δ 7.90 (d, J = 8.8, 2H), 7.56 (d, J = 8.8, 2H), 2.62 (s, 3H), 1.63 (s, 3H), 1.80-1.50 (b, 1H), 0.94 (s, 9H); ^{13}C NMR δ 198.25, 151.88, 135.52, 127.58, 127.39, 78.85, 38.28, 26.84, 25.85, 25.32; HREIMS m/z (rel intensity) 163.0760 [100, calcd for (M - C_4H_9), 163.0759], 121 (31), 43 (28); CIMS m/z 221 ($M + H^+$).

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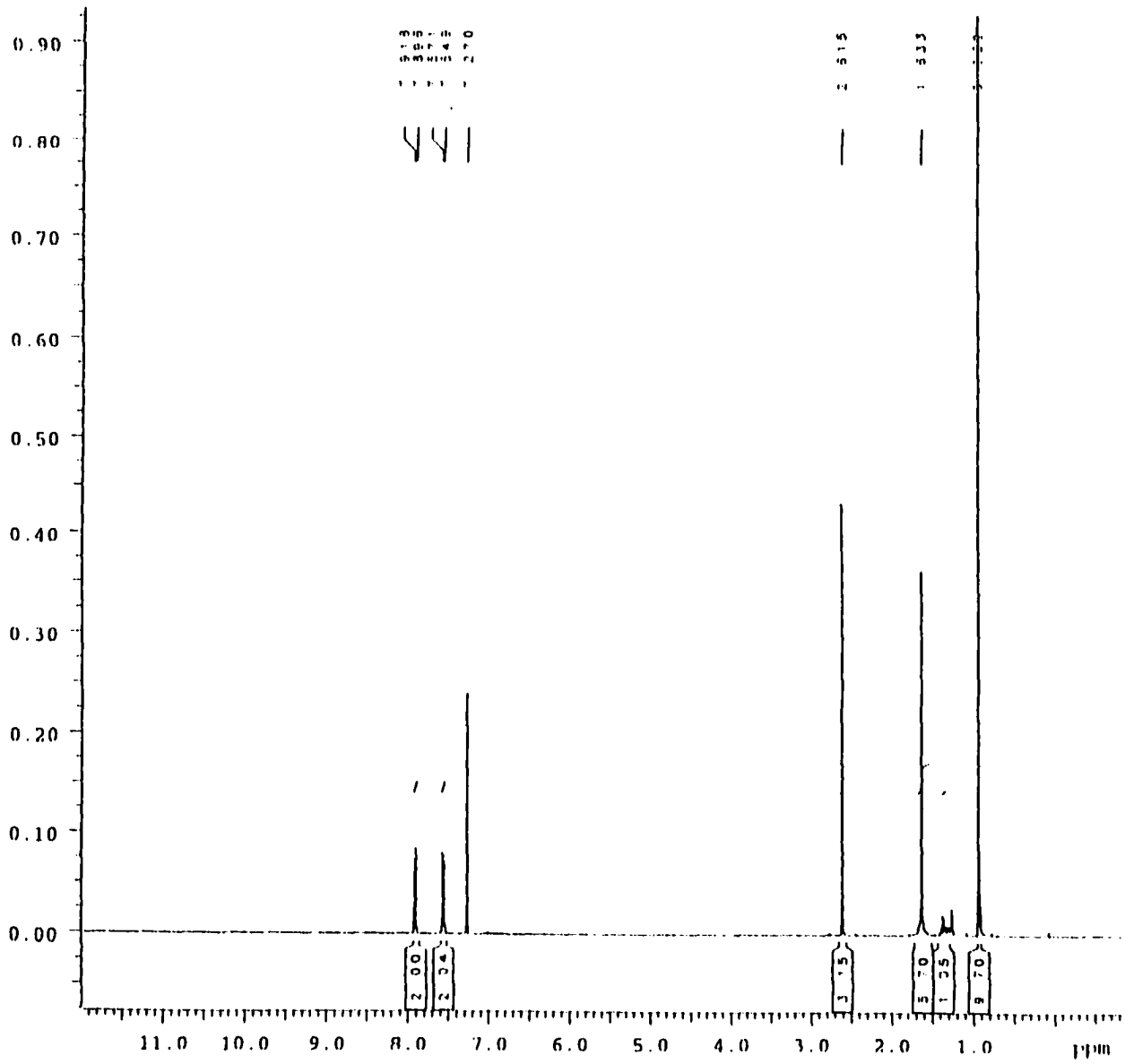
Appendix

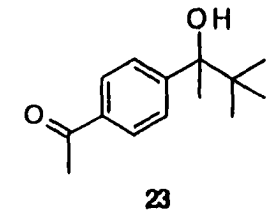
Spectra

NMR spectra were recorded in $CDCl_3$ (^1H at 400 MHz and ^{13}C at 100 MHz) with δ measured relative to $CHCl_3$ (7.27 ppm) or the central ^{13}C peak of $CDCl_3$ (77.23 ppm).

^1H and ^{13}C NMR spectra for compounds **9**, **10**, **12a-b**, **14**, **15**, **17**, and **18-21** can be found in the supporting information accompanying the published paper, and available via the Internet at http://pubs.acs.org.

^1H and ^{13}C NMR spectra for compound **23** are included in this appendix.





23

Figure 3A-1. ^{1}H NMR spectrum of compound **23**.

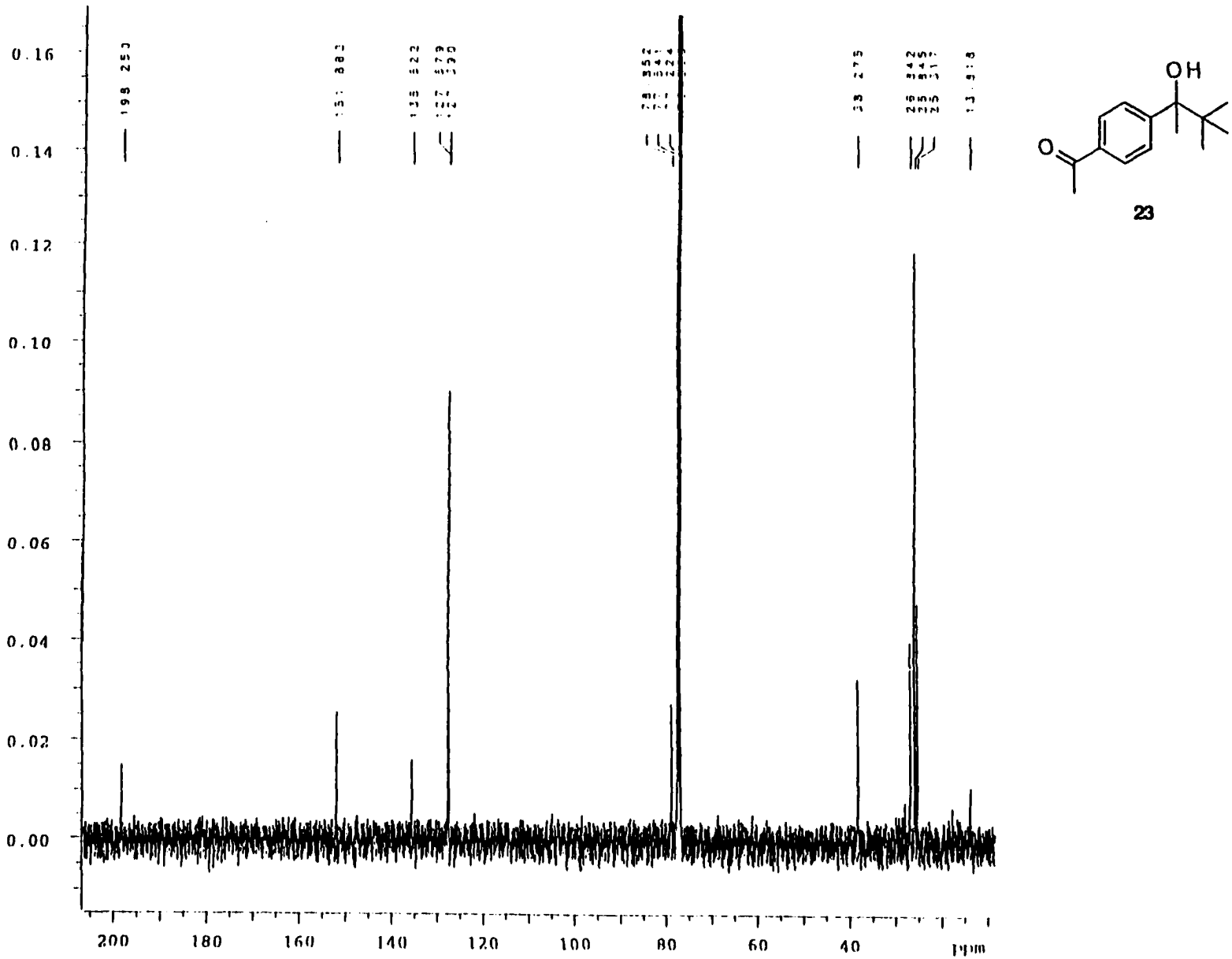


Figure 3A-2. ^{13}C NMR spectrum of compound **23**.

CHAPTER IV. PREPARATION OF LEVOGLUCOSENONE AND ITS CHIRAL DERIVATIVES

A paper to be submitted to the Journal of Organic Chemistry

Walter S. Trahanovsky and Chen Wang

Introduction

Practical methods for deriving economically useful fuels and chemicals from renewable plant material, biomass, are desirable since they make it possible to use biomass instead of petroleum as the source of fuels and chemicals. Though there has been considerable effort focused on developing methods to convert biomass to useful fuels, the conversion of biomass to valuable chemicals is underdeveloped.[1]

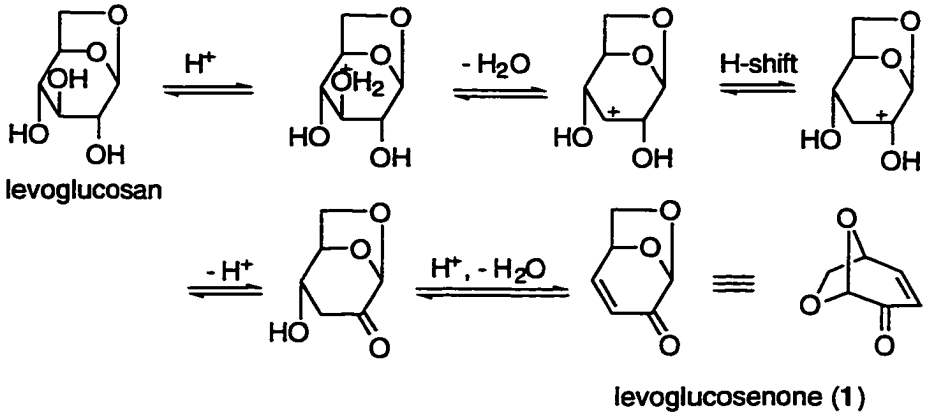
As known, most biomass is composed of nonracemic chiral molecules. For example, starch and cellulose are composed of the chiral carbohydrate unit D-glucose. The chirality associated with biomass is wasted when it is used as or converted to fuels. Also, the enantioselective synthesis of chiral molecules, such as drugs and other bioactive natural products, is usually difficult and high-cost, but can be significantly facilitated if proper chiral starting materials are available and cheap.[2]

In the 1970's, 1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose, or levoglucosenone (**1**), was first reported to be a major pyrolysis product of acidified cellulose and related carbohydrates.[3] A mechanism for the formation of levoglucosenone (**1**) from levoglucosan was also proposed (Scheme 1). Since then, the procedure for preparation of levoglucosenone (**1**) has been refined by many groups and the yield is in the range of 2 to 5%.[4] Although levoglucosenone (**1**) can be synthesized from D-galactose, anhydrous D-glucose, or furfural in several steps,[5] the pyrolysis procedure is still the most straightforward

and economical way to prepare this chiral compound. Currently it is sold as only 1-gram samples for over $ 50/g.[6]

A close look at levoglucosenone (**1**) shows that it is a small (six carbon atoms), enantiomerically pure, and rigid molecule with several important functional groups, including a ketone, an α,β-unsaturated C=C bond, an acetal, and two protected hydroxyl groups. Obviously, levoglucosenone (**1**) is a very versatile synthon for the synthesis of carbohydrates and other natural products.[7]

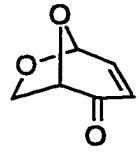
Scheme 1



In the early preparative methods, vacuum pyrolysis of acidified cellulose powder at or above 300 °C yields water, levoglucosenone (**1**) and other volatile compounds as the pyrolysate, and most of the cellulose is converted directly to charcoal.[4] Usually, 0.5 to 5.0 wt % of phosphoric acid is used to preacidify the cellulose. Early work on the optimization of this procedure shows that phosphoric acid is better than sulfuric acid, hydrochloric acid, and other mineral acids.[8]

As a comparison, fast pyrolysis of neutral cellulose, starch, or ligocellulose around 400-550 °C in a fluidized bed reactor yields another potentially useful chiral molecule, levoglucosan, at a yield of around 30-40%.[9] At this high temperature, traces of alkaline cations which originally reside within the cellulose can catalyze cracking reactions of cellulose,

and therefore need to be washed out at first with diluted acids. Under these conditions most of the cellulose in a pyrolysis process goes through depolymerization steps giving a high yield of levoglucosan.[10] However, it is not sure whether levoglucosan is the precursor of levoglucosenone (**1**) during the pyrolysis of acidified cellulose, although levoglucosan can be converted to levoglucosenone (**1**) upon pyrolysis.[3] Also, isolevoglucosenone, which is not a pyrolysis product of cellulose, can be converted to levoglucosenone (**1**) in several steps.[5b, 11]



isolevoglucosenone

Most of the past research of cellulose pyrolysis used cellulose powder and did not pay enough attention to its detailed specifications. Cellulose exists in various forms in the nature with different degrees of crystallinity, degrees of polymerization, and crystal structures. For example, pure cellulose can be amorphrous, in Cellulose I structure (parallel chain packing), or in Cellulose II (antiparallel chain packing) structure.[12] How these specifications affect the yields of pyrolysates is still an unanswered question.

In studying the pyrolysis of cellulose in the presence of hydrogen-rich materials, the Trahanovsky group made an unexpected observation that the use of soybean oil during the pyrolysis of cellulose can increase the yield of levoglucosenone (**1**) to *ca* 10 wt %.[13] We tried to further investigate this novel procedure, to identify some varibles in this method, and to prepare some potentially valuable chiral derivatives from levoglucosenone (**1**).

Results and Discussion

1. Preparation of Levoglucosenone (1) from Cellulose

The cellulose used in this research is microcrystalline white power prepared by milling of amorphrous cellulose. Its size is about 75 μm with less than 0.1% of residue on ignition.[14]

The amount of acid is very important in the preparation of levoglucosenone (1) from pyrolysis of acidified cellulose.[8] While the trace of acid promotes the formation of levoglucosenone (1), it also catalyzes the formation of charcoal. We tried to optimize the amount of H_3PO_4 used in this pyrolysis procedure with respect to the weight of cellulose. Table 1 shows the yields of levoglucosenone (1) from the pyrolysis of cellulose in the presence of various amounts of H_3PO_4 using LoSat soybean oil. LoSat is the trademark of a vegetable oil which has a lower content of saturated fatty acids than a regular soybean oil.[15]

Table 1. Pyrolysis of Cellulose With Various Amounts of H_3PO_4[a]

amount of cellulose (g)	wt % of H_3PO_4	yield of 1 (wt %)[b]
5.0	0.0	1.4
5.0	0.1	5.6
5.0 (0.5% preacidified)	0.0	9.3
5.0	0.5	9.6, 9.5, 8.0,[c] 7.4[c]
5.0	1.0	8.1, 8.1
5.0	3.0	7.6
5.0 (used oil)[d]	0.5	8.7
5.0	0.5	5.1, 6.2
5.0 (slow heating)[e]	0.5	7.9
20.0	0.5	6.7, 6.8
20.0	1.0	6.8

[a] LoSat soybean oil was used with its weight 3 times that of the cellulose. [b] GC yields with octyl alcohol as the internal standard. Each yield value is for one run. [c] Runs using a different bottle of LoSat soybean oil of the same brand; all other runs used the same bottle of LoSat soybean oil. [d] Oil recovered from a previous run after filtration of charcoal. [e] The reaction temperature reached 270 °C in 15 min, compared to 7 min in other runs.

In a typical procedure, under reduced pressure (20-30 mm Hg), the temperature of the reaction mixture is raised to 270 °C in 7 min. The formation of levoglucosenone (**1**) starts at this temperature, as indicated by the appearance of a yellow distillate. When the rate of the distillation decreases, the temperature of the reaction is slowly increased to 310 °C. The total reaction time is about 30 min for a reaction of 5-grams of cellulose. The purity of levoglucosenone (**1**) prepared by this procedure is about 70 wt % estimated by GC analysis, 75% pure estimated by ^{1}H NMR after crude levoglucosenone (**1**) is extracted with CH_2Cl_2 and dried over $MgSO_4$.

From the data in Table 1, it can be found that 0.5 wt % of H_3PO_4 is the optimum percent of acid used for the formation of levoglucosenone (**1**). When LoSat soybean oil is used, the yield from the pyrolysis of H_3PO_4 (0.5 wt %)-preacidified cellulose and that of cellulose and H_3PO_4 (0.5 wt %) are comparable. So the pretreatment of cellulose with H_3PO_4 is not necessary and H_3PO_4 can be added to the cellulose immediately before the pyrolysis. This is probably because the vegetable oil serves as a medium for thorough mixing of cellulose and the acid. Also, at the end of one run, the charcoal can be removed by filtration and the LoSat soybean oil can be used again giving a comparable yield of levoglucosenone (**1**). When the reaction was scaled up from 5 grams to 20 grams, the yield decreased slightly.

The heating rate may be an important factor. When the pyrolysis temperature (~ 270 °C) was reached in 15 min instead of 7 min, the yield of levoglucosenone (**1**) was 7.9 % instead of 9.5 %. This can be understood as when being pyrolyzed at a temperature lower than 270 °C, cellulose is converted mainly to charcoal. However, at a higher temperature, further pyrolysis of the *in situ* generated levoglucosenone (**1**) and other side reactions may lower the yield of levoglucosenone (**1**).[16] Further repeated runs are needed to confirm the effect of the heating rate. Also, we found that vacuum distillation (20-25 mmHg/ 280-300 °C) of the mixture of an vegetable oil (15 g) and levoglucosenone (**1**, 400 mg) gave only 34% of

levoglucosenone (**1**) recovered with less than 0.01% of levoglucosenone (**1**) left in the vegetable oil. This mean levoglucosenone (**1**) is not quite stable at the pyrolysis temperature.[16]

Other cellulose sources were also tested for the pyrolysis. Cotton is over 99% pure of cellulose in Cellulose I form, and paper also have a high content of cellulose.[12] However, pyrolysis of 0.5 wt % H_3PO_4-preacidified cotton or paper using the same procedure yielded only less than 3 wt % of levoglucosenone (**1**). The reason for the low yield of levoglucosenone (**1**) from cotton and paper is not clear, and may be pertinent to the size and crystal structure of the cellulose in cotton and paper. Switchgrass, corn stover, and wood chips, which are mainly composed of cellulose and lignocellulose, yielded only a trace of levoglucosenone (**1**) upon being pyrolysed with 0.5 to 3 wt % of H_3PO_4-preacidification.

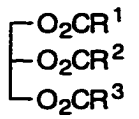
The yield of levoglucosenone (**1**) seems to vary when different vegetable oils are used (Table 2). However, since there is only one or two runs for most vegetable oils, one should be cautious to draw any conclusion about the relative yields using different vegetable oils.

Table 2. Yields of Levoglucosenone (1) Using Various Vegetable Oils[a]

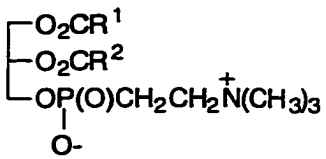
vegetable oil	yield of **1** (wt %)[b]
peanut	5.1
safflower	6.0
soybean (regular)	6.2, 5.5, 5.1
corn	6.9, 6.6
olive	7.3
sunflower	7.6
canola	8.6, 8.4

[a] All the reaction were conducted at the same scale: cellulose (5 g), vegetable oil (15 g), and H_3PO_4 (25 mg). [b] GC yields with octyl alcohol as the internal standard. Each yield is for one run.

Usually, crude vegetable oils are composed mainly of triglycerides (95-97%), phosphatides (2-3%), unsaponifiables (1.5%), and free fatty acids (0.3-0.7%).[17] After being refined, vegetable oils are about 100 % of triglycerides. The main difference between one vegetable oil and another is the composition of R^1, R^2, and R^3 in the triglyceride part. Table 3 shows the typical major fatty acid compositions of several vegetable oils after these oils are hydrolyzed. However, the fatty acid composition of a vegetable oil varies depending not only on the plant species, but also within the same species, due to variations in season, geographical location, and so forth.[17]



triglycerides



phosphatidylcholine

From data in Table 3, no general conclusion can be drawn about the composition of the fatty acids and the yield of levoglucosenone (**1**). Also, we found that the yield of levoglucosenone (**1**) varies when different bottles of vegetable oil of the same brand are used (footnote c of Table 1). In addition to the physical properties of a vegetable oil, such as viscosity and thermal conductivity, minor constituents of a vegetable oil may also affect the yield of levoglucosenone (**1**). Although our NMR study finds no observable difference between the fresh LoSat soybean oil and used LoSat soybean oil, minor constituents of a vegetable oil may react with levoglucosenone (**1**) at high temperatures (around 300 °C).

The role of soybean oil in this procedure is an interesting point. At least the soybean oil serves as a medium facilitating heat and mass transfer during the pyrolysis. This facilitation is absent from the previous procedures where cellulose is subjected to pyrolysis directly, especially since levoglucosenone (**1**) is unstable at high temperatures. In view of this point, our soybean oil procedure should be easily scaled up.

Table 3. Major Fatty Acid Compositions of Vegetable Oils.

vegetable oil	palmitic 16:0[a]	stearic 18:0	oleic 18:1	linoleic 18:2	linolenic 18.3	iodine value[b]
peanut	11.6	3.1	46.5	31.4	0.0	188-196
safflower	6.5	2.4	13.1	77.7	0.0	122-139
soybean (regular)	11.0	4.0	23.4	53.2	7.8	125-138
corn	12.2	2.2	27.5	57.0	0.9	110-128
olive	13.7	2.5	71.1	10.0	0.6	76 - 90
sunflower	6.8	4.7	18.6	68.2	0.5	122-139
canola	3.9	1.9	64.1	18.7	9.2	110-115
soybean (LoSat)[c]	4.0	3.4	19.0	65.5	8.3	not available

[a] The first number refers to the number of carbon atoms in the fatty acid molecule, and the second number refers to the number of C=C bonds in it. [b] Iodine value refers to the weight of iodine absorbed under standard conditions by 100 g of lipid. [c] Data of LoSat soybean oil are provided by Professor Walter Fehr in Iowa State University, Ames, Iowa 50010.

Overall, the yield of the levoglucosenone (**1**) from the pyrolysis of a mixture of cellulose, a trace of H_3PO_4 and a vegetable oil is in the range of 5-10 wt %. The purity of levoglucosenone (**1**) prepared by this procedure is about 70 wt %.

2. Preparation of Chiral Derivatives of Levoglucosenone (1)

In addition to the preparation of carbohydrate derivatives,[7a-c] levoglucosenone (**1**) has also be used for the preparation of other chiral natural products, such as (-)-Hongconin and (+)-Grandisol.[7d-f]

We used Michael addition[18] and Baeyer-Villiger oxidation[19] reactions to prepare some potentially useful chiral compounds of levoglucosenone (**1**). Previous research reported only exo-addition products from the Michael addition of methyl and *n*-pentyl cuprates[7f-g], and other

Michael donors[20a] to levoglucoseneone (**1**). Diels-Alder reactions using levoglucosenone (**1**) as a dienophile always have a high exo-face selectivity.[20b] The exo/endo selectivity of 1,3-dipole addition can be as high as 100.[20c] When the adduct from the addition of pentyl cuprate to levoglucosenone (**1**) was oxidized by hydrogen peroxide, and followed by hydrolysis, a γ-lactone product was reported.[7f] We investigated the Michael addition of *n*-hexyl cuprate to levoglucosenone (**1**) and the Baeyer-Villiger oxidation of the Michael adduct (**2**) using 3-chloroperoxybenzoic acid (mCPBA) as shown in Scheme 2.

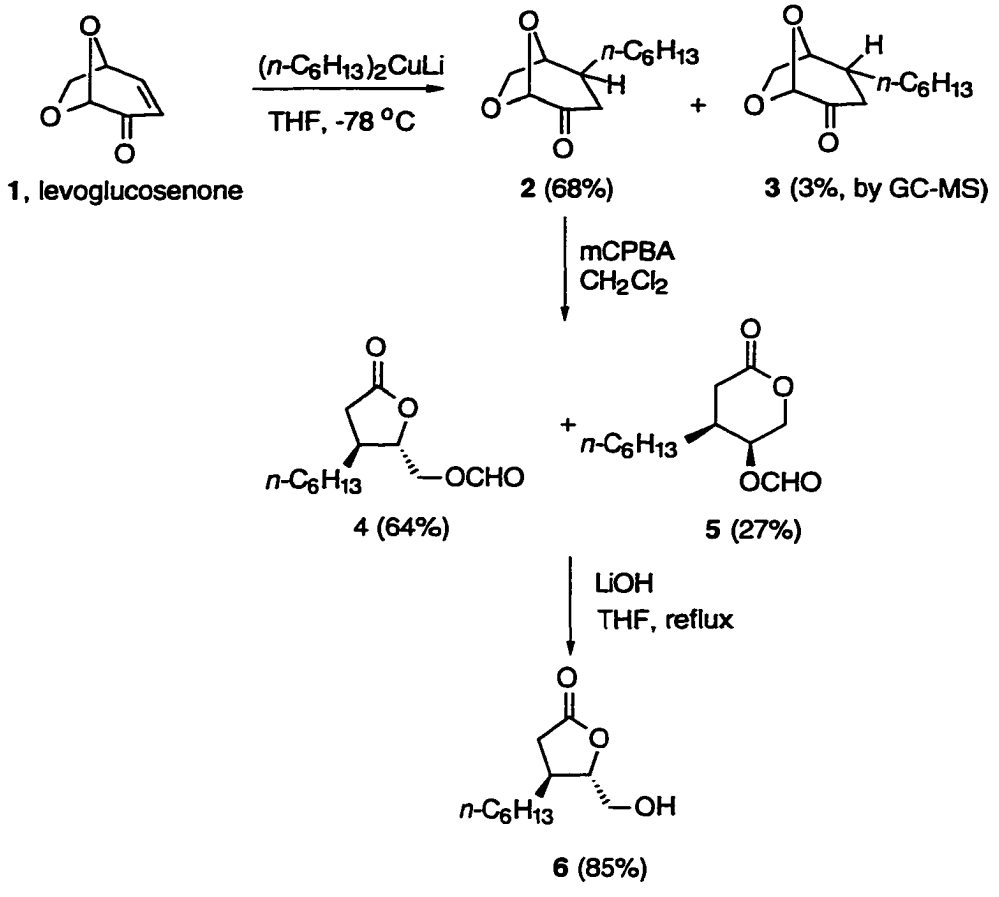
We found that from the Michael addition reaction of *n*-hexyl cuprate, a trace of the endo-addition product **3** was also formed as an inseparable mixture with **2** (**2/3** = 23 as detected by GC-MS) in addition to the major exo-addition product **2**. This exo/endo mixture of **2** and **3**, when subjected to the oxidation by mCPBA, yielded a mixture of **4** and **5** with the ratio of 2.4/1.0. No product from **3** was detectable. The mixture of **4** and **5** was converted to γ-lactone **6** through hydrolysis catalyzed by LiOH. The stereoconfigurations of the isolated products shown in Scheme 2 were assigned by NOE spectroscopy. The final nonracemic chiral γ-lactone **6** is a potentially valuable compound. A similar nonracemic chiral compound with the hexyl group in **6** replaced by a hydrogen atom sells as 1-gram samples for around $ 80/g.[21] Compound **6** and its analogous compounds may be used as chiral synthons in the synthesis of natural products,[22] and can be used as resolving agents for the separation of racemic acid or alcohol mixtures by forming diastereomers with them.[23]

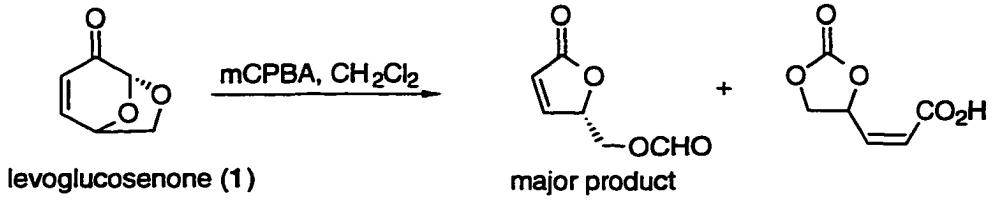
Usually, Baeyer-Villiger oxidation of a cyclic ketone yields a ring-expanded lactone by incorporating one oxygen atom from the oxidizing reagent.[19] However, two formates, **4** and **5**, were found from the Baeyer-Villiger oxidation of **2**. This unexpected observation is probably due to the unique structure of levoglucosenone (**1**); specifically, a ketal group is located α to the carbonyl group. It was reported that the Baeyer-Villiger oxidation of levoglucosenone (**1**) yielded a formate as a major product (eq 1).[7f] Several possible routes for the formation of **4** and **5** are shown in Scheme 3. It is still not clear whether each of the two

adduct intermediates goes to a specific product **4** or **5**, or whether both of the intermediates are converted to another intermediate, which is highly strained and then undergoes rearrangement (indicated by a and b) to give products **4** and **5**.

Acetal **7**, converted from compound **2** (eq 2) in one step,[24] may be a useful chiral ligand for metal ions.

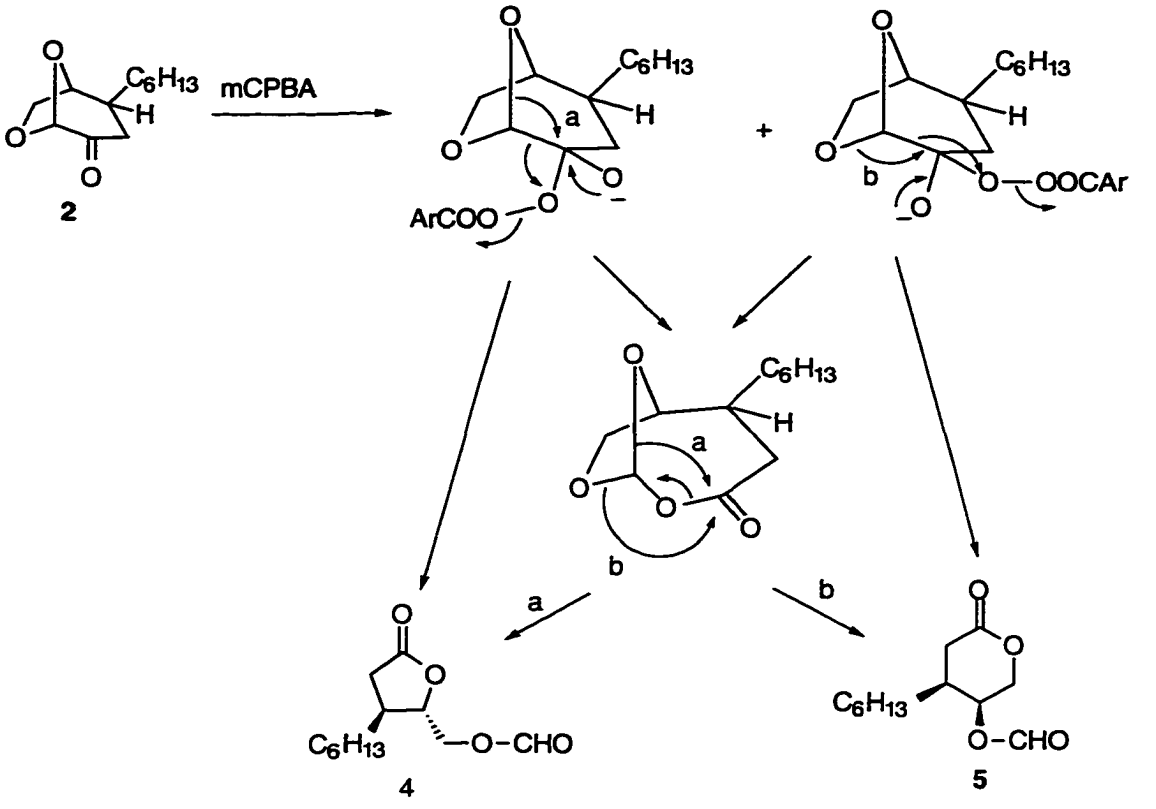
Scheme 2

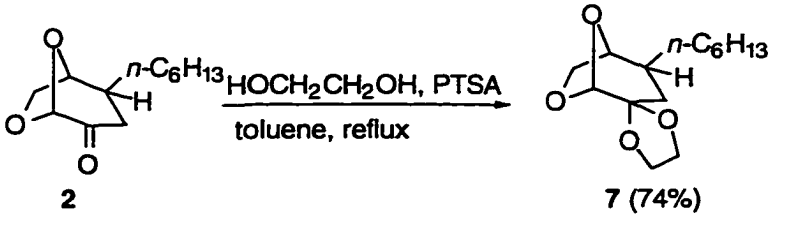




(1)

Scheme 3

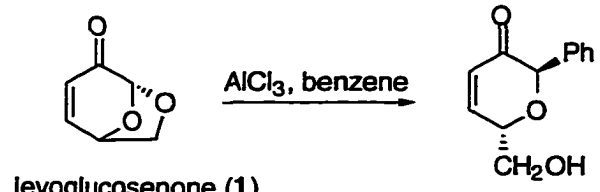




(2)

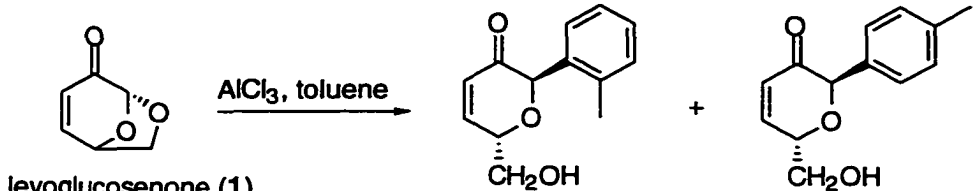
Since levoglucosenone (**1**) is a bicyclic compound, we investigated the selective ring-opening of levoglucosenone (**1**) through libration of the ketal group by Lewis acids. In the presence of $AlCl_3$, levoglucosenone (**1**) opens one ring in benzene at room temperature to give 7.4% of product **8** (eq 3). When toluene was used as the solvent, two inseparable products **9** and **10** were obtained in a higher total yield (eq 4). The reaction in *p*-xylene is not feasible because *p*-xylene is difficult to be removed after the reaction due to its high boiling point (b.p. 135 °C). Also, the yield was not increased when $TiCl_4$, $SnCl_4$, or BF_3•Et_2O was used instead

of $AlCl_3$. This is probably because levoglucosenone (**1**) or its ring-opened cation intermediate has a strong tendancy to polymerize under the reaction conditions. Selectivity in the ring opening process favors the formation of the six-membered ring, instead of the seven-membered ring (Scheme 4). The stereoconfiguration of products **8**, **9**, and **10** were assigned by NOE spectroscopy.



levoglucosenone (**1**)

8 (7.4%) (3)

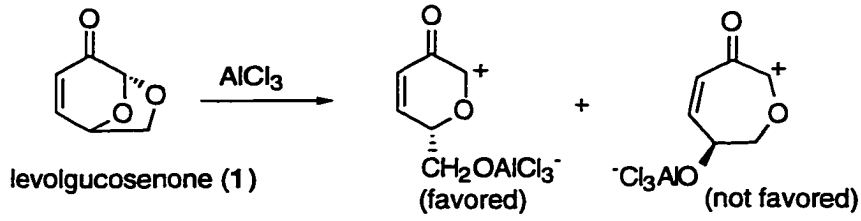


levoglucosenone (**1**)

9 **10**

(28%, **9**/**10** = 1/2.8) (4)

Scheme 4



levolgucosenone (**1**) (favored) (not favored)

Conclusions

A convenient procedure for the preparation of levoglucosenone (**1**) has been investigated using vegetable oil as a medium for the pyrolysis of cellulose in the presence of H_3PO_4. The yield of levoglucosenone (**1**) is in the range of 5-10 wt % with its purity up to 70 wt %. The amount of H_3PO_4, heating rate, and kind of vegetable oil have been identified as important variables in this pyrolysis procedure.

The Michael addition of *n*-hexyl cuprate shows a highly exo/endo selectivity (exo/endo = 23). The Baeyer-Villger oxidation of the hexyl adduct from the Michael addition gives two formates. The preparation of chiral derivatives of levoglucosenone (**1**) should be further explored.

Experimental Section

General Considerations

The NMR spectra were recorded in $CDCl_3$ or as stated otherwise (^1H at 400 MHz and ^{13}C at 100 MHz). 2D NMR spectra were obtained with a Bruker DRX400 spectrometer. CI, EIMS (70ev) were obtained with Finnigan 4000 (GC mode). GC analysis was performed on Hewlett Packard 5890 Series II. Most products were isolated either by column chromatography or by TLC on silica gel with hexanes-ethyl acetate as the eluent. Vegetable oils were purchased from the local HyVee Food Store. Cellulose (microcrystalline powder) was purchased from Aldrich.

General Preparative Procedures and Compound Characterization

Preparation of Levoglucosenone (1): To a 50 mL round bottom flask with a distillation apparatus was added H_3PO_4 (25 mg, 0.5 wt %), cellulose (5 g) and vegetable oil (15 g). The slurry was stirred for about 5 min under the reduced pressure (20-30 mm Hg), and then heated by an appropriate heating mantle to 270 °C in 7 min, as indicated by the internal thermometer. The reaction mixture began to turn black and water distillate appeared at about 140 °C. Yellow distillate containing water and levoglucosenone (**1**) appeared on the flask wall around 270 °C, and the temperature in the distillation head reached around 110-120 °C. The reaction temperature was increased to 300-310 °C over 15 min until no more distillate came over. The yellow distillate was further extracted by methylene chloride, and dried over $MgSO_4$. After rotatory evaporation of the solvent, levoglucosenone (**1**) can be used directly, or further purified by silica gel column chromatography. ^1H NMR δ 3.67 (d, J = 6.8 Hz,

1H), 3.80 (dd, J = 4.8, 6.8 Hz, 1H), 4.95 (t, J = 4.8 Hz, 1H), 5.25 (d, J = 4.0 Hz, 1H), 6.01 (dd, J = 4.0, 10.0 Hz, 1H), 7.22 (dd, J = 4.8, 10.0 Hz, 1H); ^{13}C NMR δ 66.60, 71.82, 101.64, 126.76, 148.45, 189.01.

For the pyrolysis of preacidified cellulose, no H_3PO_4 was added. The preacidified cellulose was prepared by mixing cellulose throughly with a certain amount of H_3PO_4 (0.1 to 3 wt %) and enough methanol to cover the cellulose, and then removing the methanol on a rotary evaporator under reduced pressure until dry.

Procedure for the Yield Measurement of Levoglucosenone (1) by GC: All of the yellow distillate from the pyrolysis of cellulose was dissolved in THF until the total volume reached 10 mL. Then 2 mL of this solution was transferred to a 10 mL flask containing an accurately known amount of octyl alcohol (~130 mg). This mixture was subjected to GC analysis using a DB-1 capillary chromatographic column. The temperature is initially set up at 45 °C for 5 min, then increased at the rate of 10 °C/min until 250 °C. The response factor, 2.2 favoring the weight of levoglucosenone (**1**), was measured by GC analysis of known amounts of pure levoglucosenone and octyl alcohol.

Procedure for the Yield Measurement of Levoglucosenone (1) by ^{1}H NMR: All of the yellow distillate from the pyrolysis of cellulose was extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with water, aqueous 5% $NaHCO_3$ solution, and water in sequence. After the extract was dried over anhydrous $MgSO_4$ and concentrated with rotatory evaporator, brown crude levoglucosenone (**1**) was obtained. In a 2-mL vial, accurately known amounts of the crude levoglucosenone (**1**) and durene (internal standard) were dissolved in $CDCl_3$ (0.7 mL), and this $CDCl_3$ solution was transferred to a 5-mm NMR tube for ^{1}H NMR measurement. The yield of pure levoglucosenone (**1**) was calculated from the ratio of integral areas of ^{1}H peaks of levoglucosenone (**1**) and durene.

Michael Addition of Levoglucosenone:[18e] To 20 mL of anhydrous THF solution containing CuBr•Me_2S (2.73 g, 13 mmol) cooled to -78 °C was added slowly 2.5 M

n-hexyl lithium solution in hexane (10.7 mL, 26 mmol). The solution turned black and was stirred for another 30 min. Then levoglucosenone (0.42 g, 3.3 mmol) was added. The reaction mixture was stirred for another 4 h at room temperature, then hydrolyzed with saturated aqueous NH_4Cl solution, and extracted with ethyl ether. After the ethereal extract was dried and concentrated, the crude product was subjected to silica gel column chromatography using hexanes-ethyl acetate (10:1) as the eluent, followed by isolation of compound **2** with a trace of inseparable **3** as a light yellow liquid (0.50 g, 71%).

(1S,4R,5S)-4-Hexyl-7,8-dioxabicyclo[3.2.1]octan-2-one (2) was isolated as a light yellow liquid. IR (cm^{-1}) 2958, 2857, 1734, 1457, 1112, 912; ^1H NMR δ 0.88 (t, J = 6.8 Hz, 3H), 1.28-1.36 (m, 8H), 1.41-1.49 (m, 1H), 1.59-1.68 (m, 1H), 2.07 (q, J = 7.6 Hz, 1H), 2.16 (dd, J = 1.2, 16.0 Hz, 1H), 2.77 (dd, J = 7.6, 16.0 Hz, 1H), 3.97-4.03 (m, 2H), 4.53-4.55 (m, 1H), 5.06 (s, 1H); ^{13}C NMR δ 14.23, 22.76, 27.21, 29.35, 31.87, 32.64, 37.32, 41.43, 68.20, 76.34, 101.77, 200.91; HREIMS m/z (relative intensity) 212.1410 (2, calcd for $C_{12}H_{20}O_3$ 212.1413), 166 (54), 138 (42), 124 (24), 110 (37), 97 (100), 81 (82), 68 (82), 55 (80); Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H 9.50. Found C, 67.76; H 9.85.

(1S,4S,5S)-4-Hexyl-7,8-dioxabicyclo[3.2.1]octan-2-one (3) was detected by GC-MS only as a trace amount inseparable with **2**. EIMS m/z (relative intensity) 213 (M+1, 50), 185 (17), 166 (28), 138 (20), 123 (48), 109 (55), 96 (100), 81 (82), 67 (72).

Baeyer-Villiger Oxidation of 2:[19e] To a stirred solution of methylene chroride (20 mL) at room temperature was added **2** (106 mg, 0.5 mmol) and mCPBA (86 mg, 0.5 mmol). Another portion of mCPBA was added at 10 h and 20 h respectively. After a total of 30 h, the reaction mixture was washed with 10% $Na_2S_2O_3$, 5% $NaHCO_3$, and saturated NaCl solution in sequence. The methylene solution was further dried over $MgSO_4$, and concentrated under reduced pressure. Column chromatography using hexanes-ethyl acetate (8/2) as the

eluent gave an inseparable mixture of **4** and **5** (103 mg, 90%, **4/5** = 2.5/1 molar ratio). TLC separation gave partially separated **4** (10/1 with **5**) and **5** (10/1 with **4**).

(4S,5S)-5-Formyloxymethyl-4-hexyl-4,5-dihydro-2(3*H*)-furanone (4) was isolated as a colorless liquid. IR (cm^{-1}) 2955, 2928, 2857, 1788, 1730, 1160; ^1H NMR δ 0.88 (t, *J* = 6.4 Hz, 3H), 1.20-1.35 (m, 8H), 1.35-1.45 (m, 1H), 1.50-1.62 (m, 1H), 2.24 (dd, *J* = 8.4, 16.8 Hz, 1H), 2.28-2.36 (m, 1H), 2.73 (dd, *J* = 8.4, 16.8 Hz, 1H), 4.21 (ddd, *J* = 0.8, 6.8, 12.4 Hz, 1H), 4.32-4.36 (m, 1H), 4.42 (ddd, *J* = 0.8, 5.6, 12.4 Hz, 1H), 8.09 (d, *J* = 0.4 Hz, 1H); ^{13}C NMR δ 14.16, 22.66, 27.49, 29.21, 31.71, 33.42, 34.91, 37.35, 63.93, 82.32, 160.53, 175.86; HREIMS m/z (relative intensity) 229.1440 [4, calcd for $C_{12}H_{21}O_3$ (M + 1) 229.1440], 169 (48), 151 (20), 109 (100), 81 (21), 55 (22).

(4S,5R)-5-Formyloxy-4-hexyltetrahydro-2-pyranone (5) was isolated as a colorless liquid. IR (cm^{-1}) 2957, 2929, 2857, 1727, 1171; ^1H NMR δ 0.89 (t, *J* = 7.2 Hz, 3H), 1.20-1.45 (m, 10H), 2.14-2.18 (m, 1H), 2.47 (dd, *J* = 12.8, 18.4 Hz, 1H), 2.69 (ddd, *J* = 0.8, 6.4, 18.4 Hz, 1H), 4.41 (ddd, *J* = 0.4, 2.0, 13.2 Hz, 1H), 4.52 (dd, *J* = 2.0, 13.2 Hz, 1H), 5.30 (bs, 1H), 8.16 (d, *J* = 0.4 Hz, 1H); ^{13}C NMR δ 14.23, 22.74, 26.31, 29.26, 31.41, 31.77, 32.38, 35.20, 66.60, 71.76, 160.32, 169.29; HREIMS m/z (relative intensity) 229.1447 [4, calcd for $C_{12}H_{21}O_3$ (M + 1) 229.1440], 169 (36), 156 (42), 140 (48), 109 (100), 97 (75), 81 (66), 57 (60).

Hydrolysis of 4 and 5: $LiOH{\bullet}H_2O$ (50 mg) and the mixture of **4** and **5** (103 mg) was dissolved in 10 mL of THF and refluxed for 4 h. TLC separation gave **(6)** (76 mg, 85%)

(4S,5S)-4-Hexyl-5-hydroxylmethyl-4,5-dihydro-2(3*H*)-furanone (6): IR (cm^{-1}) 3443, 2957, 2856, 1781; ^1H NMR δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.20-1.35 (m, 8H), 1.38-1.45 (m, 1H), 1.53-1.58 (m, 1H), 2.06 (bs, 1H), 2.24 (dd, *J* = 8.8, 17.6 Hz, 1H), 2.37-2.46 (m, 1H), 2.74 (dd, *J* = 8.8, 17.6 Hz, 1H), 3.66 (dd, *J* = 4.8, 12.4 Hz, 1H), 3.91 (dd, *J* = 2.8, 12.4 Hz, 1H), 4.20 (ddd, *J* = 2.8, 4.8, 6.4 Hz, 1H); ^{13}C NMR δ 14.22, 22.73, 27.62, 29.33, 31.81, 33.55, 35.51, 36.45, 63.42, 86.23, 176.98; HREIMS m/z (relative

intensity) 201.1490 [2, calcd for $C_{11}H_{21}O_3$ (M + 1) 201.1491], 169 (47), 151 (17), 109 (100), 81 (21), 55 (16).

Ethylene Glycol Acetal of (1S,4R,5S)-4-Hexyl-7,8-dioxabicyclo[3.2.1] octan-2-one (7) was isolated as a colorless liquid. Toluene solution (5 mL) containing **2** (21 mg, 0.1 mmol), PTSA•H_2O (19 mg, 0.1 mmol), and ethylene glycol (0.25 mL) was refluxed for 10 h. Routine work-up and TLC separation gave **7** (19 mg, 74%). IR (cm^{-1}) 2980, 2850, 1457, 1099; ^1H NMR δ 0.89 (t, J = 6.4 Hz, 3H), 1.25-1.35 (m, 8H), 1.54-1.66 (m, 3H), 1.71-1.78 (m, 1H), 2.09 (dd, J = 6.4, 14.4 Hz, 1H), 3.85-4.00 (m, 5H), 4.04-4.06 (m, 1H), 4.40-4.41 (m, 1H), 4.99 (s, 1H); ^{13}C NMR δ 14.30, 22.84, 27.81, 29.47, 31.05, 31.52, 32.01, 38.21, 64.75, 65.72, 68.37, 75.85, 101.15, 104.99; HREIMS m/z (relative intensity) 256.1671 (18, calcd for $C_{14}H_{24}O_4$ 256.1675), 239 (12), 211 (20), 183 (98), 99 (20), 87 (100), 73 (18).

(2R,6R)-2-Hydroxymethyl-6-phenyl-5,6-dihydro(2*H*)-5-pyranone (8) was isolated as a colorless oil. To 5 mL of anhydrous benzene under N_2 was added **1** (126 mg, 1 mmol), $AlCl_3$ (266 mg, 2 mmol). The solution was stirred at room temperature for 2 h. Routine work-up and TLC separation gave **8** (15 mg, 7.4%). IR (cm^{-1}) 3500, 2926, 1684, 1088; ^1H NMR δ 1.90-2.20 (bs, 1H), 3.80-3.89 (m, 2H), 4.36-4.39 (m, 1H), 5.35 (s, 1H), 6.34 (dd, J = 2.8, 10.4 Hz, 1H), 6.97 (dd, J = 2.0, 10.4 Hz, 1H), 7.33-7.40 (m, 5H); ^{13}C NMR δ 64.43, 70.31, 80.12, 127.44, 128.36, 128.90, 128.94, 133.99, 148.40, 194.42; HREIMS m/z (relative intensity) 205.0860 [4, calcd for $C_{12}H_{13}O_3$ (M + 1) 205.0865], 187 (6), 173 (10), 115 (28), 98 (100), 70 (68).

(2R,6R)-2-Hydroxymethyl-6-(2-methylphenyl)-5,6-dihydro(2*H*)-5-pyranone (9) was prepared similar to **8**, except using toluene instead of benzene as the reaction solvent, and isolated by TLC as an inseparable mixture with **10** (**9/10** = 1/2.8 molar ratio). ^1H NMR δ 2.28 (bs, 1H), 2.44 (s, 3H), 3.76-3.85 (m, 2H), 4.14-4.19 (m, 1H), 5.48 (s, 1H), 6.40 (dd, J = 2.4, 10.4 Hz, 1H), 7.06 (dd, J = 2.0, 10.4 Hz, 1H), 7.10-7.28 (m,

4H); ^{13}C NMR δ 19.59, 63.99, 70.52, 78.35, 125.72, 127.27, 129.00, 129.29, 131.35, 132.73, 139.03, 148.89, 195.87; EIMS m/z (relative intensity) 219 (9, M + 1), 201 (40), 171 (100), 119 (47), 98 (63).

(2R,6R)-2-Hydroxymethyl-6-(4-methylphenyl)-5,6-dihydro(2*H*)-5-pyranone (10) was isolated as an inseparable mixture with **9** (**9/10** = 1/2.8 molar ratio). ^{1}H NMR δ 2.28 (bs, 1H), 2.35 (s, 3H), 3.76-3.85 (m, 2H), 4.33-4.36 (m, 1H), 5.30 (s, 1H), 6.31 (dd, *J* = 1.2, 10.4 Hz, 1H), 6.95 (dd, *J* = 1.2, 10.4 Hz, 1H), 7.16-7.22 (AB, 4H); ^{13}C NMR δ 21.31, 64.30, 70.19, 79.97, 127.38, 128.24, 129.56, 130.87, 138.74, 148.55, 194.74; EIMS m/z (relative intensity) 219 (8, M + 1), 201 (37), 171 (100), 119 (20), 105 (12).

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Appendix

Spectra

NMR spectra were recorded in $CDCl_3$ (^1H at 400 MHz and ^{13}C at 100 MHz) with δ measured relative to $CHCl_3$ (7.27 ppm) or the central ^{13}C peak of $CDCl_3$ (77.23 ppm).

^1H NMR spectrum of a pyrolysate containing levoglucosenone (**1**), GC spectrum of a pyrolysate containing levoglucosenone (**1**) and octyl alcohol, ^1H and ^{13}C NMR spectra of compounds **2**, **4-6**, **7**, **8**, mixture of **9** and **10**, ^1H-^1H NOE spectra of compounds **2**, **4-6**, **8**, mixture of **9** and **10**, are included in this appendix.

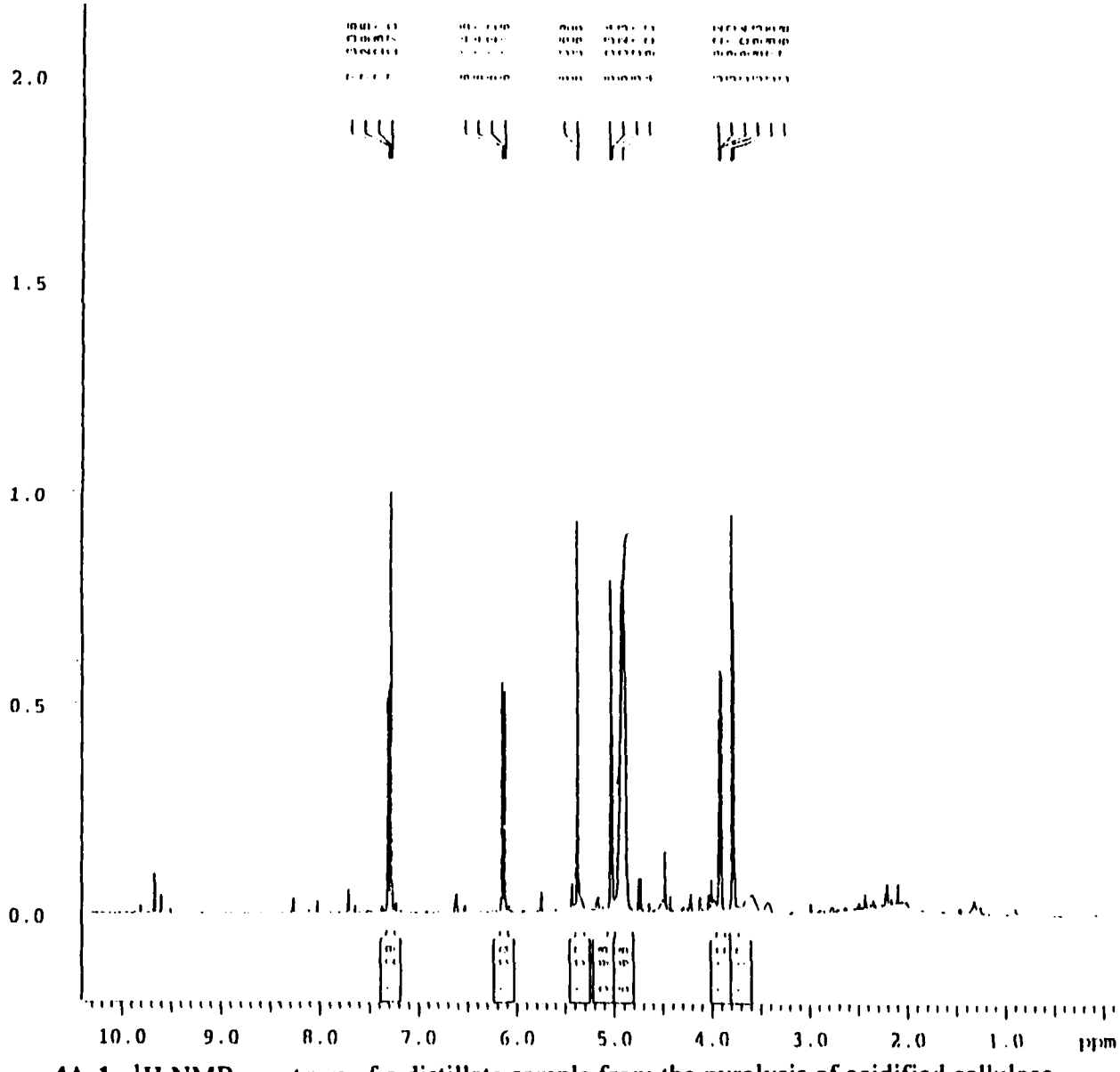


Figure 4A-1. ^{1}H NMR spectrum of a distillate sample from the pyrolysis of acidified cellulose.

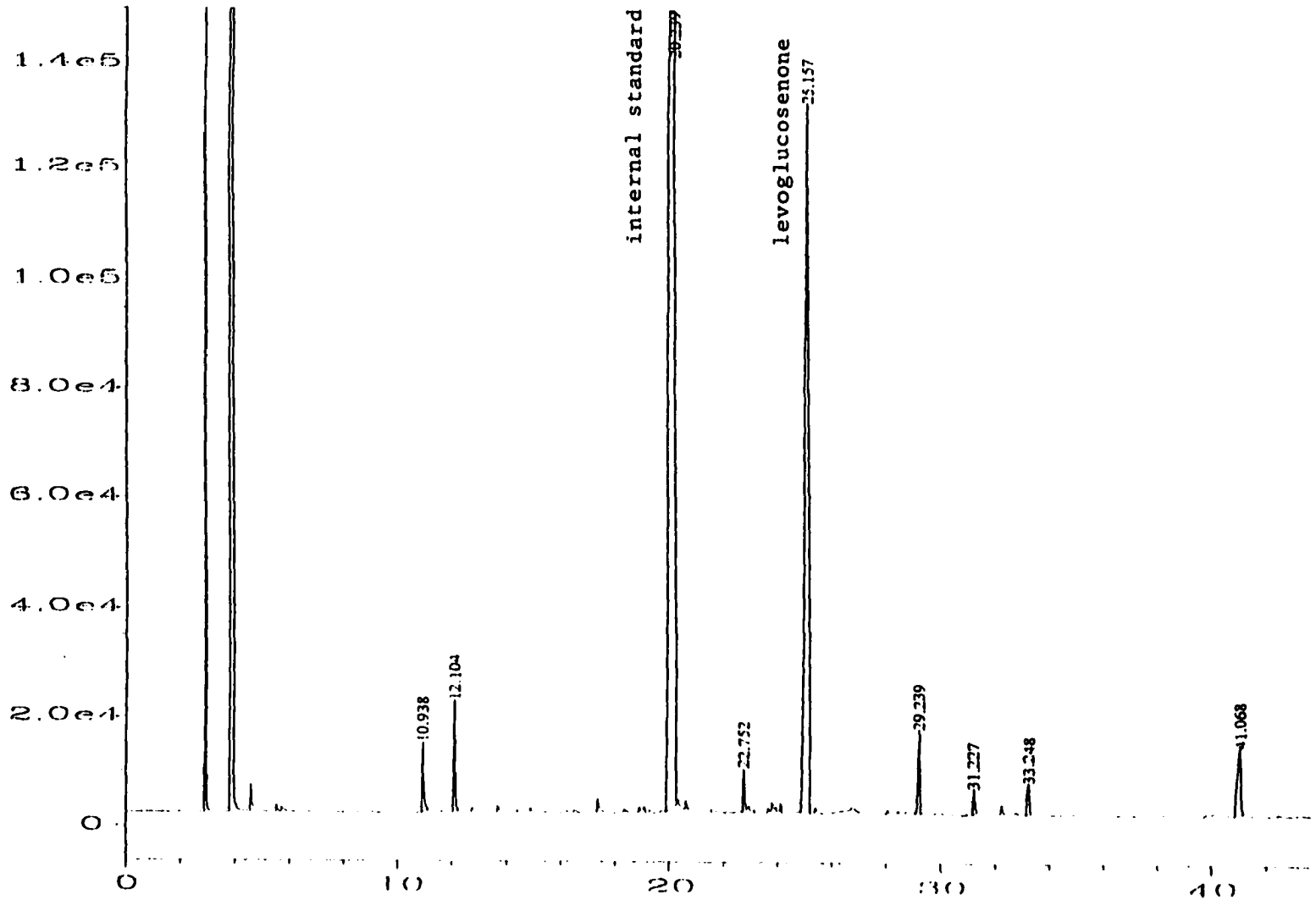
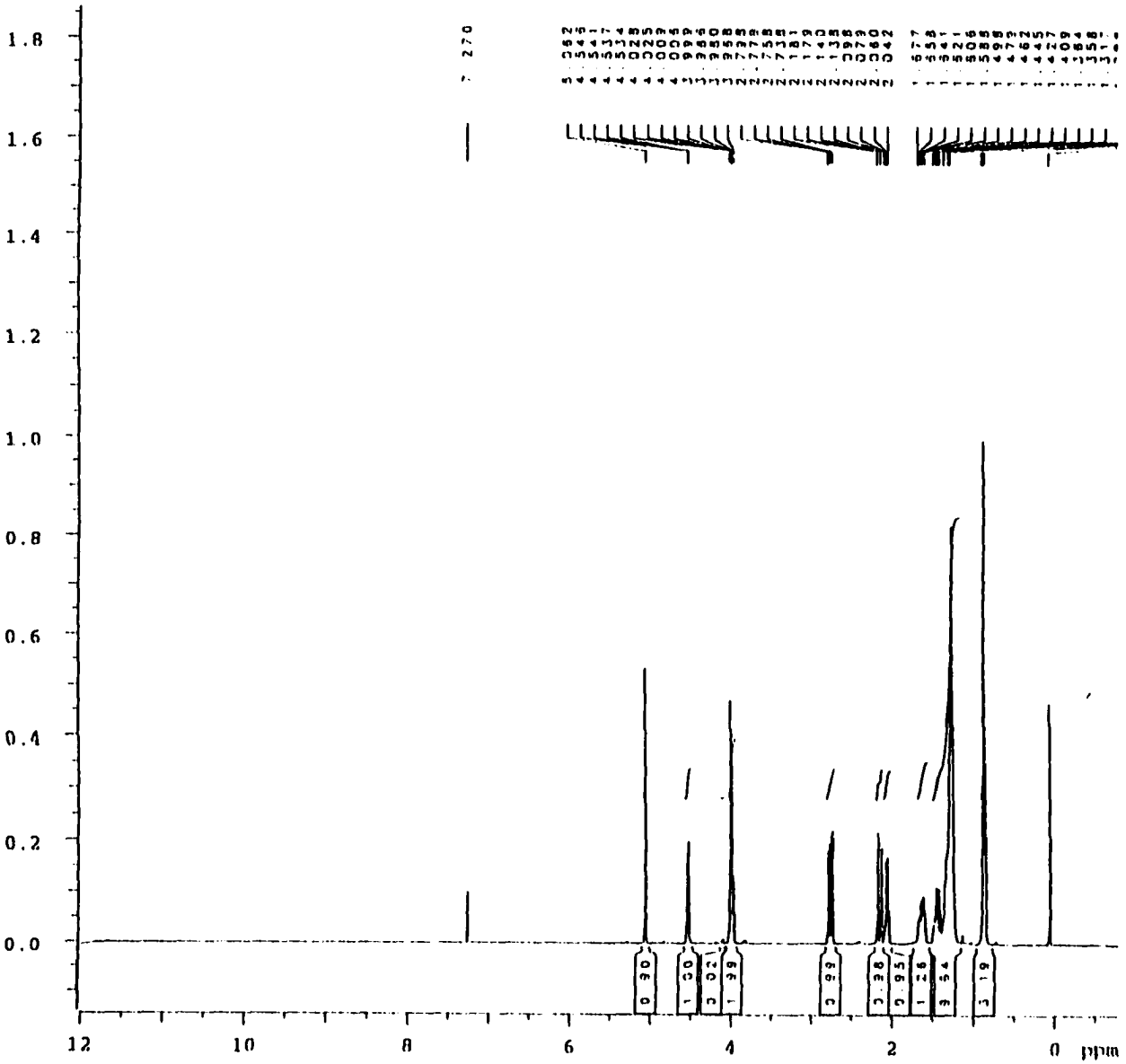
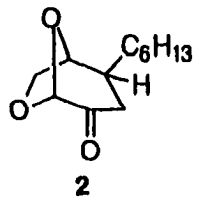


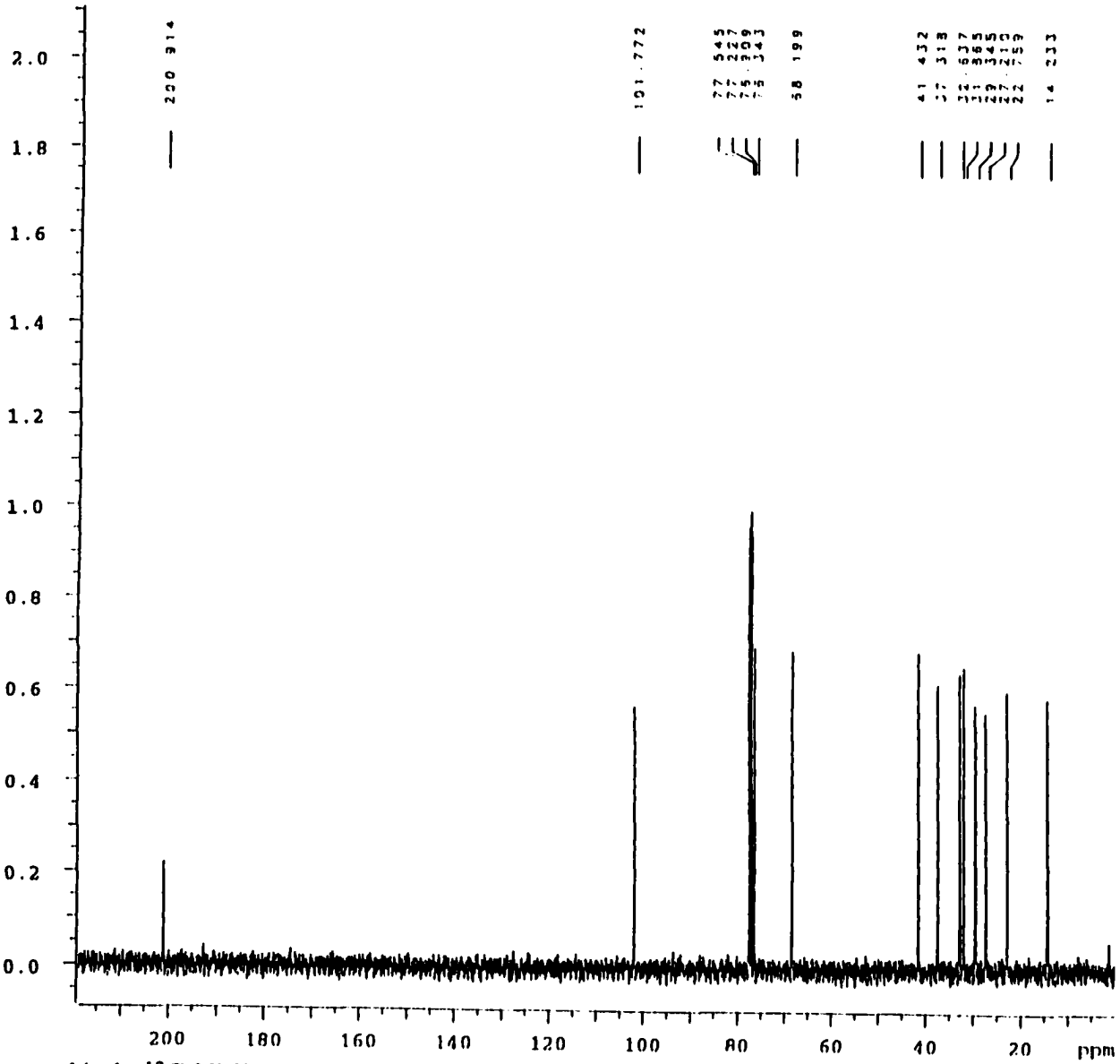
Figure 4A-2. GC spectrum of a distillate sample from the pyrolysis of acidified cellulose.

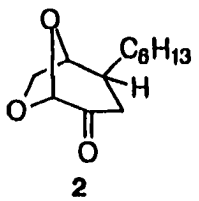




2

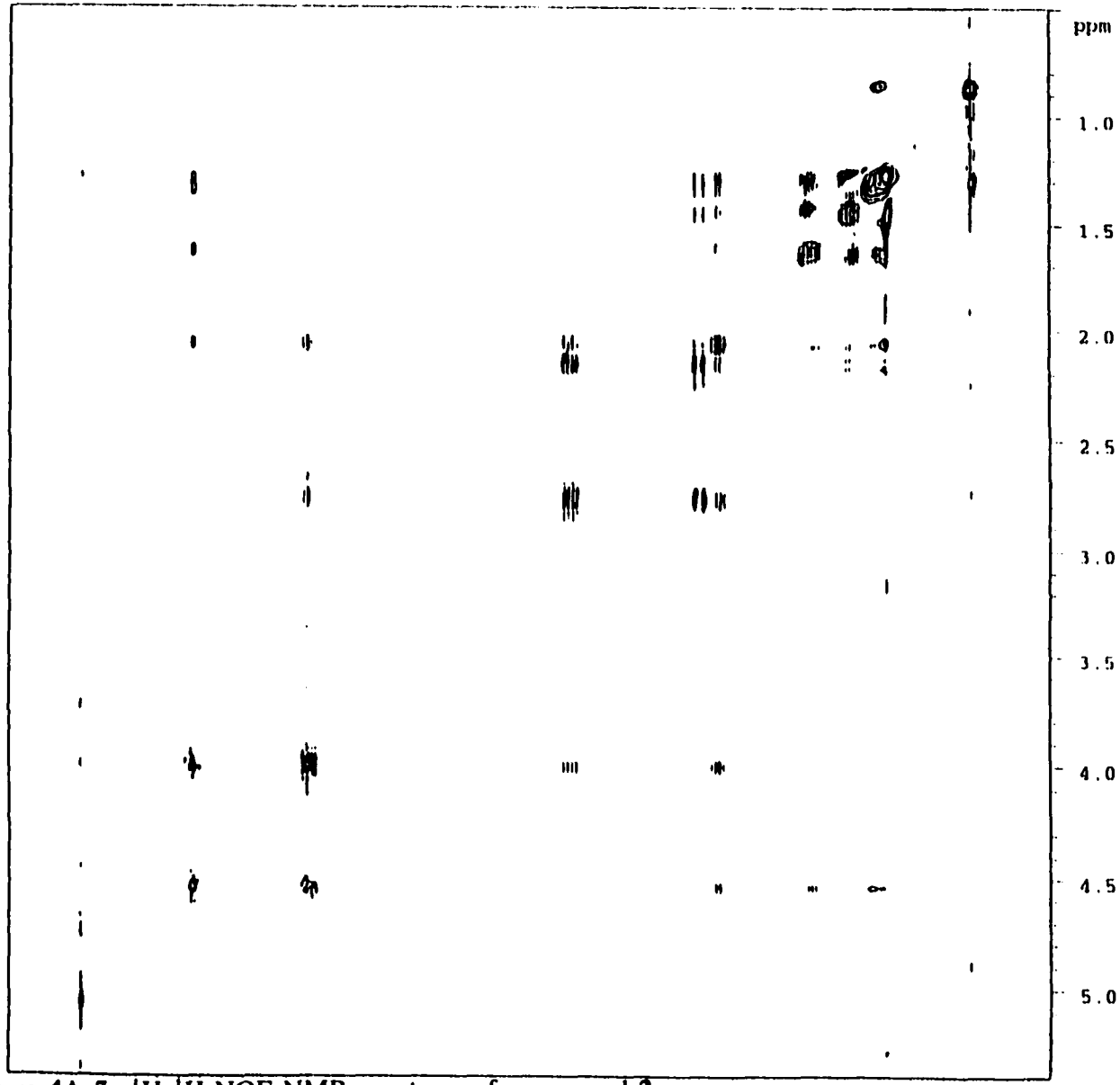
Figure 4A-3. ^{1}H NMR spectrum of compound **2**.

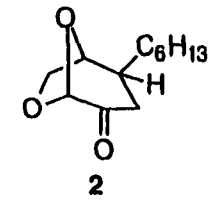




2

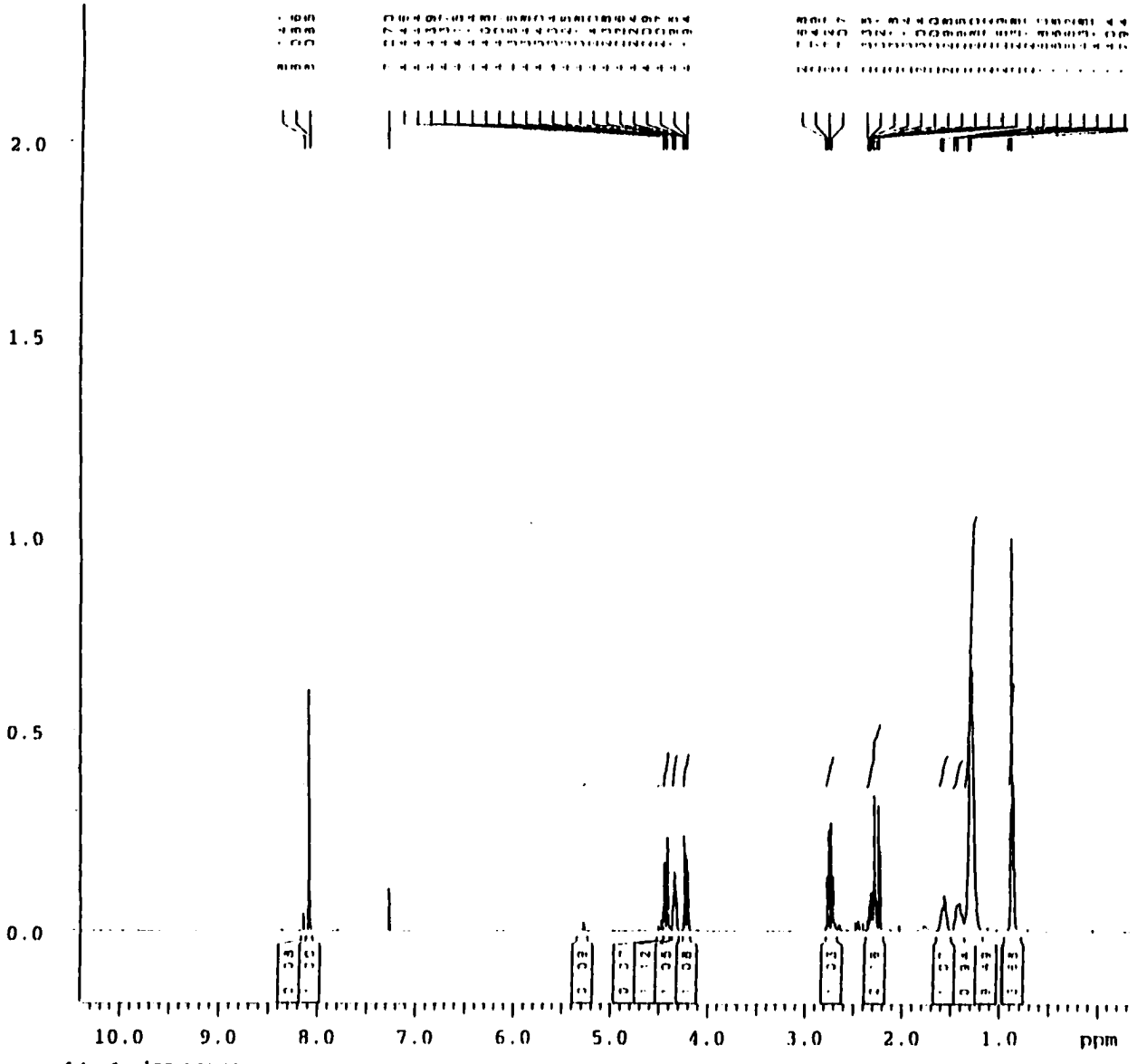
Figure 4A-4. ^{13}C NMR spectrum of compound **2**.

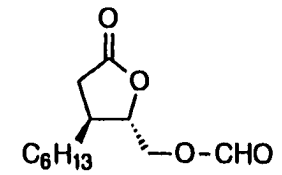




2

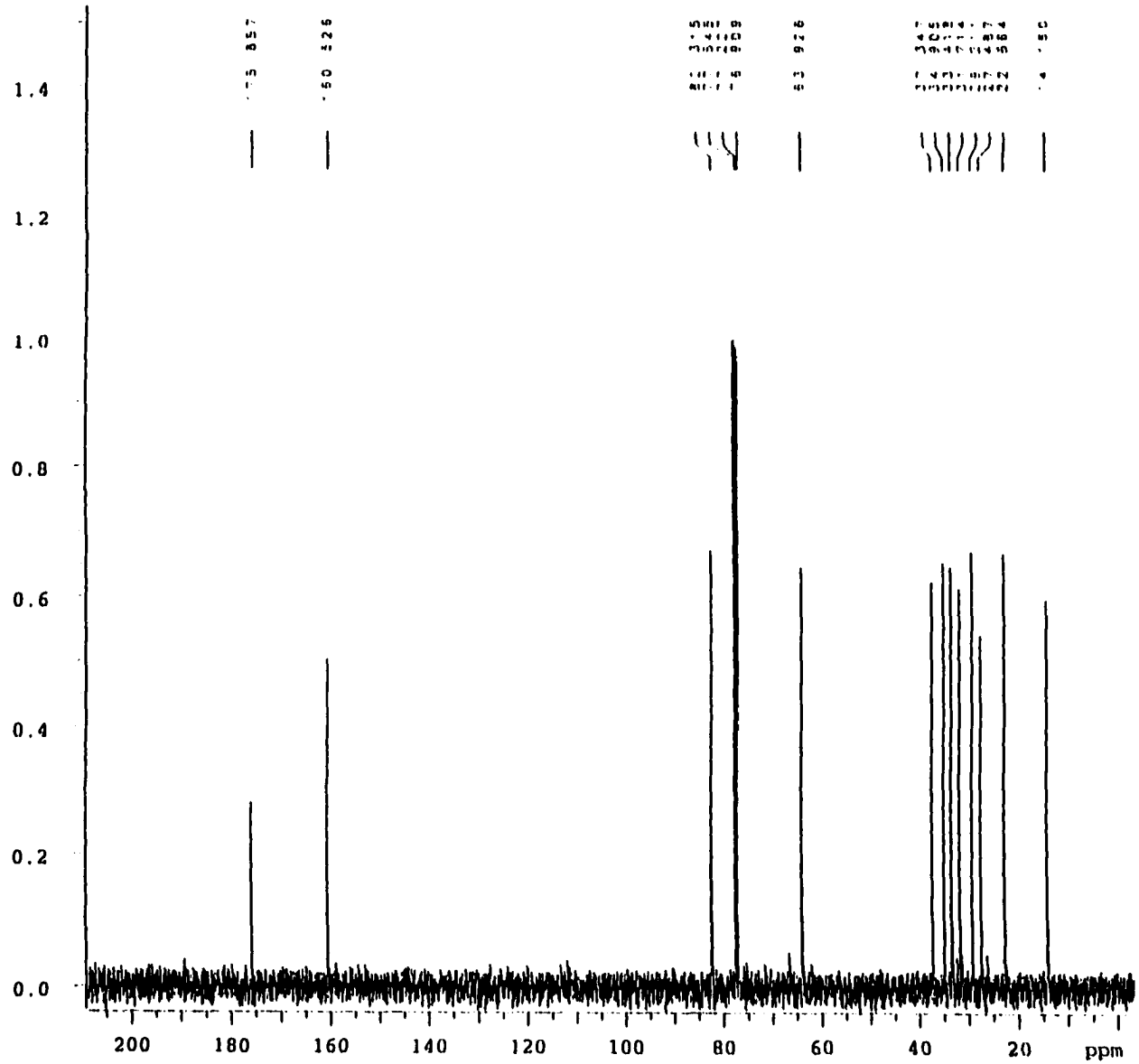
Figure 4A-5. ^1H-^1H NOE NMR spectrum of compound **2**.

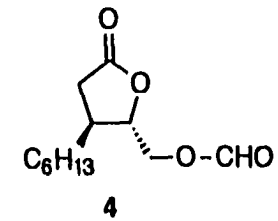




4

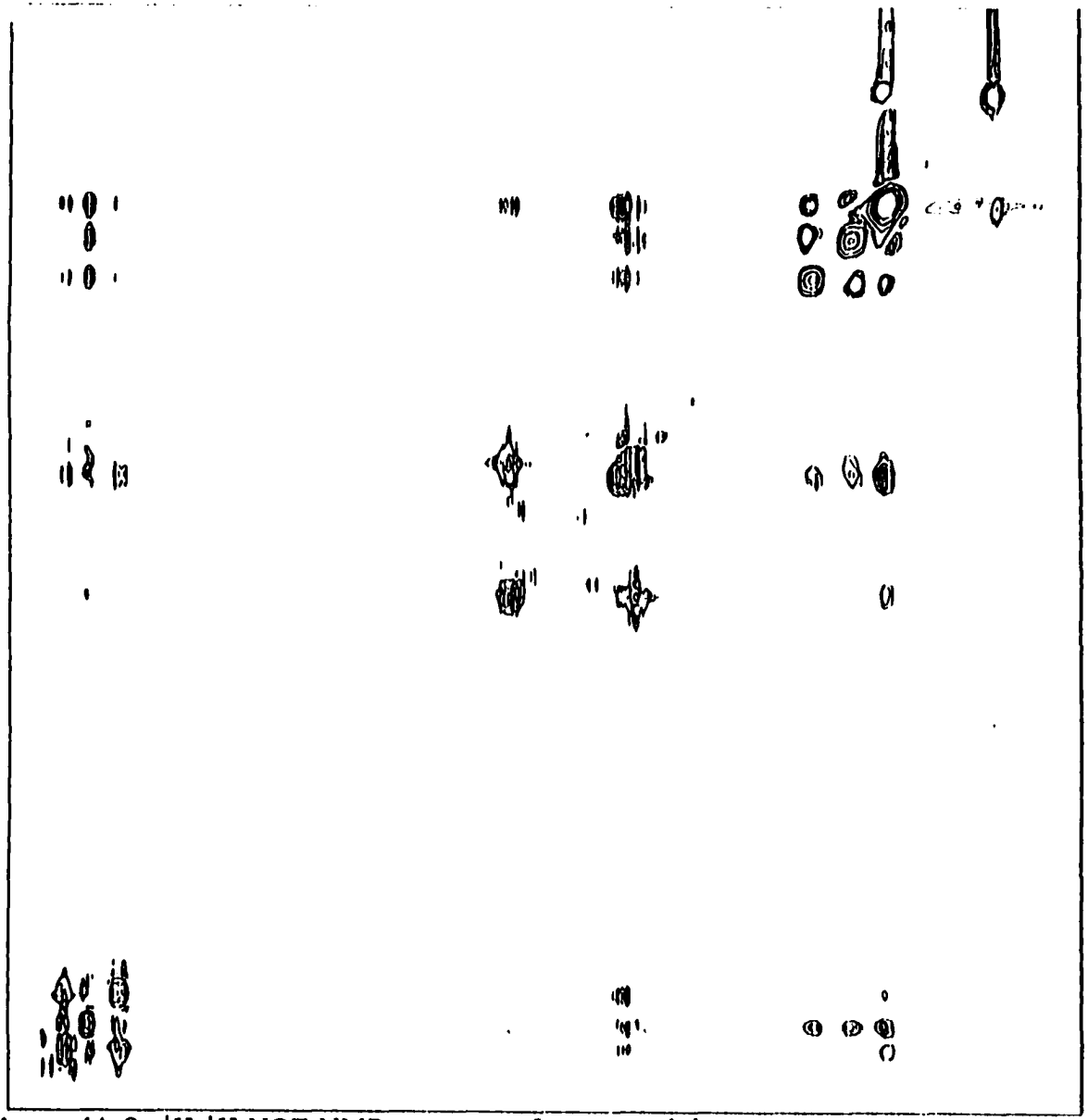
Figure 4A-6. ^{1}H NMR spectrum of compound **4**.

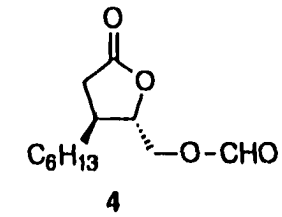




4

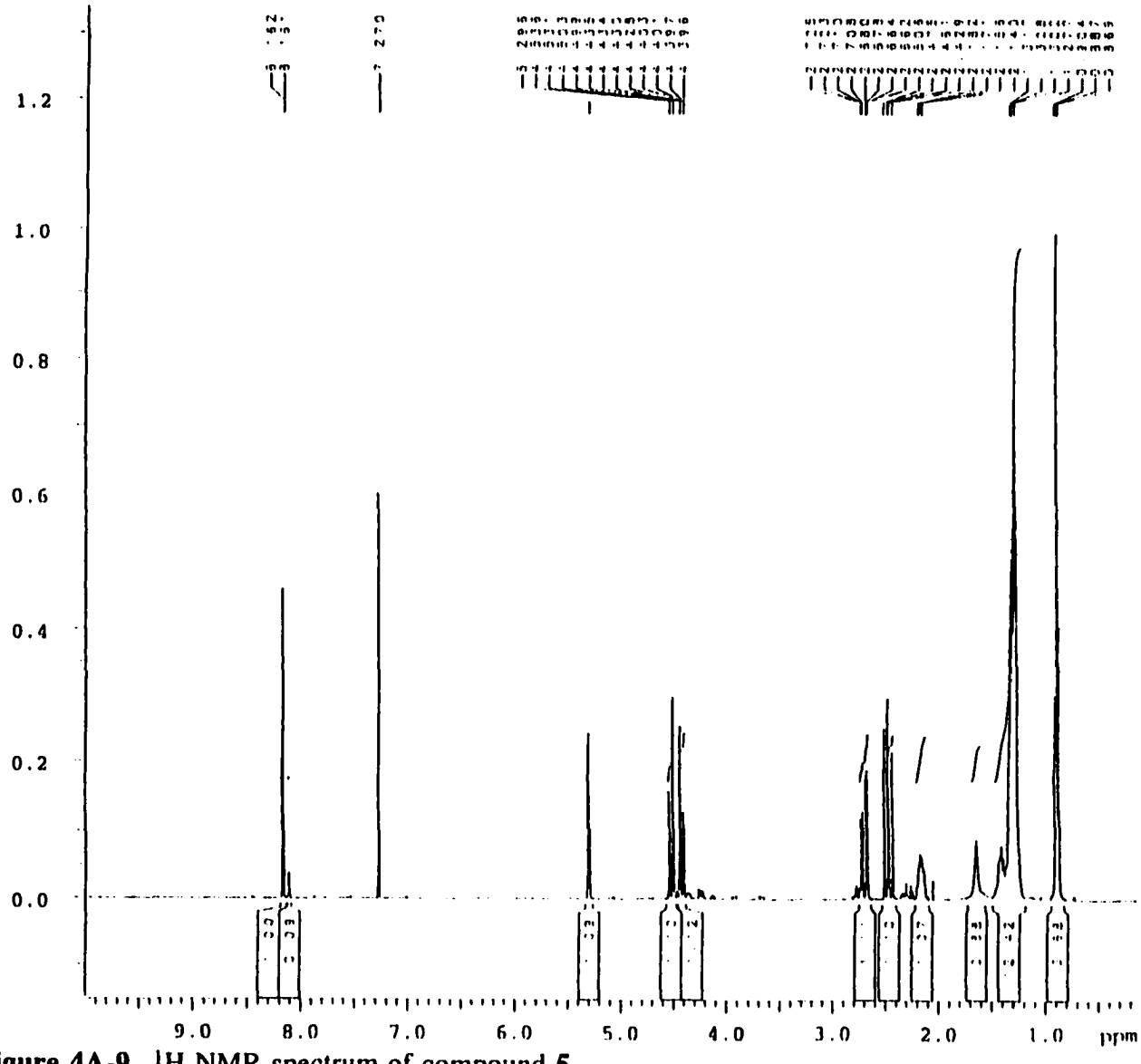
Figure 4A-7. ^{13}C NMR spectrum of compound **4**.

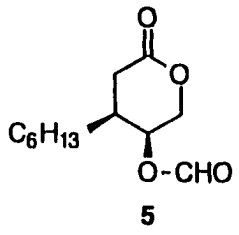




4

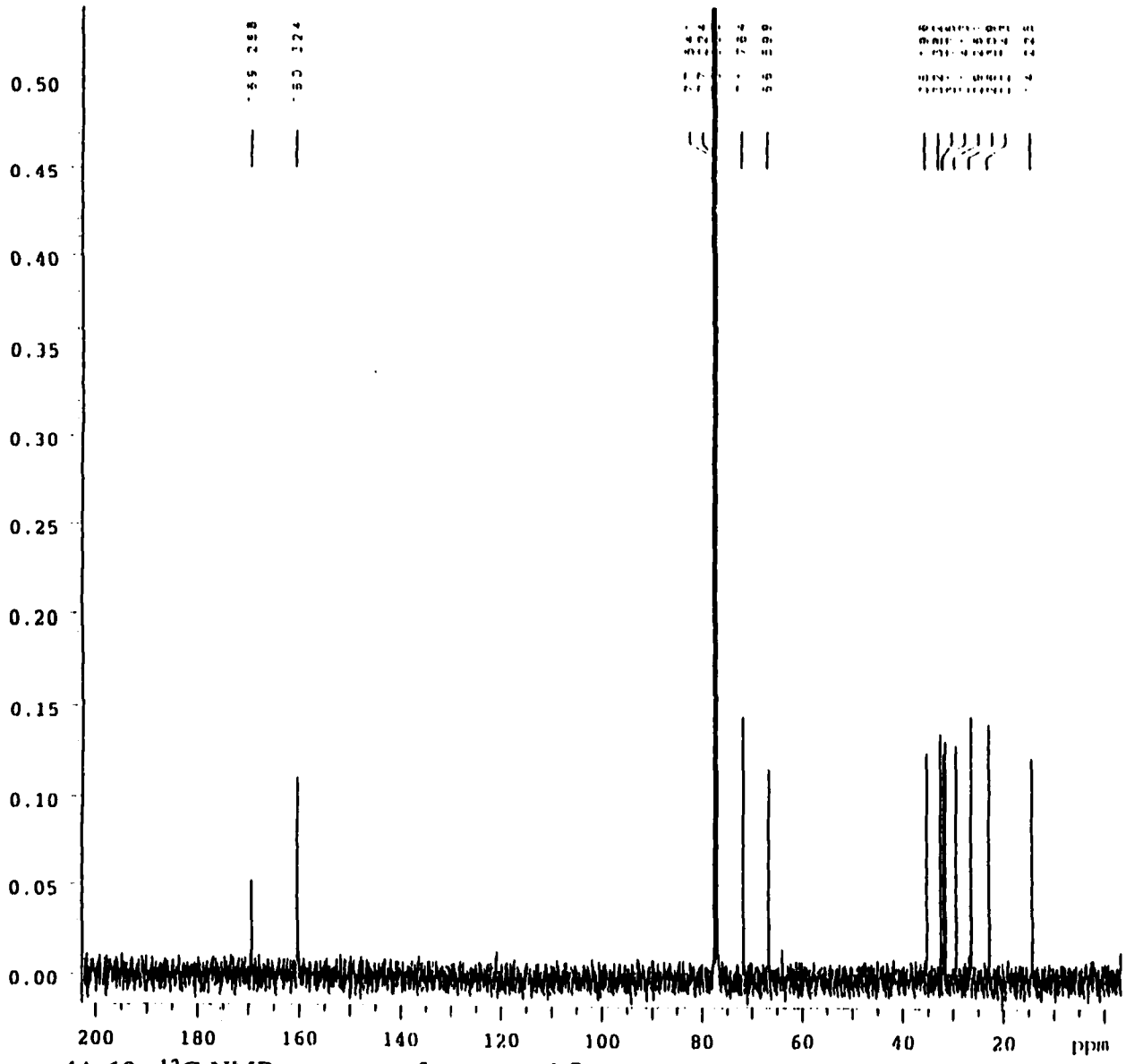
Figure 4A-8. ^{1}H-^{1}H NOE NMR spectrum of compound **4**.

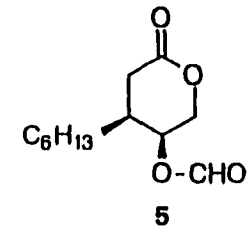




5

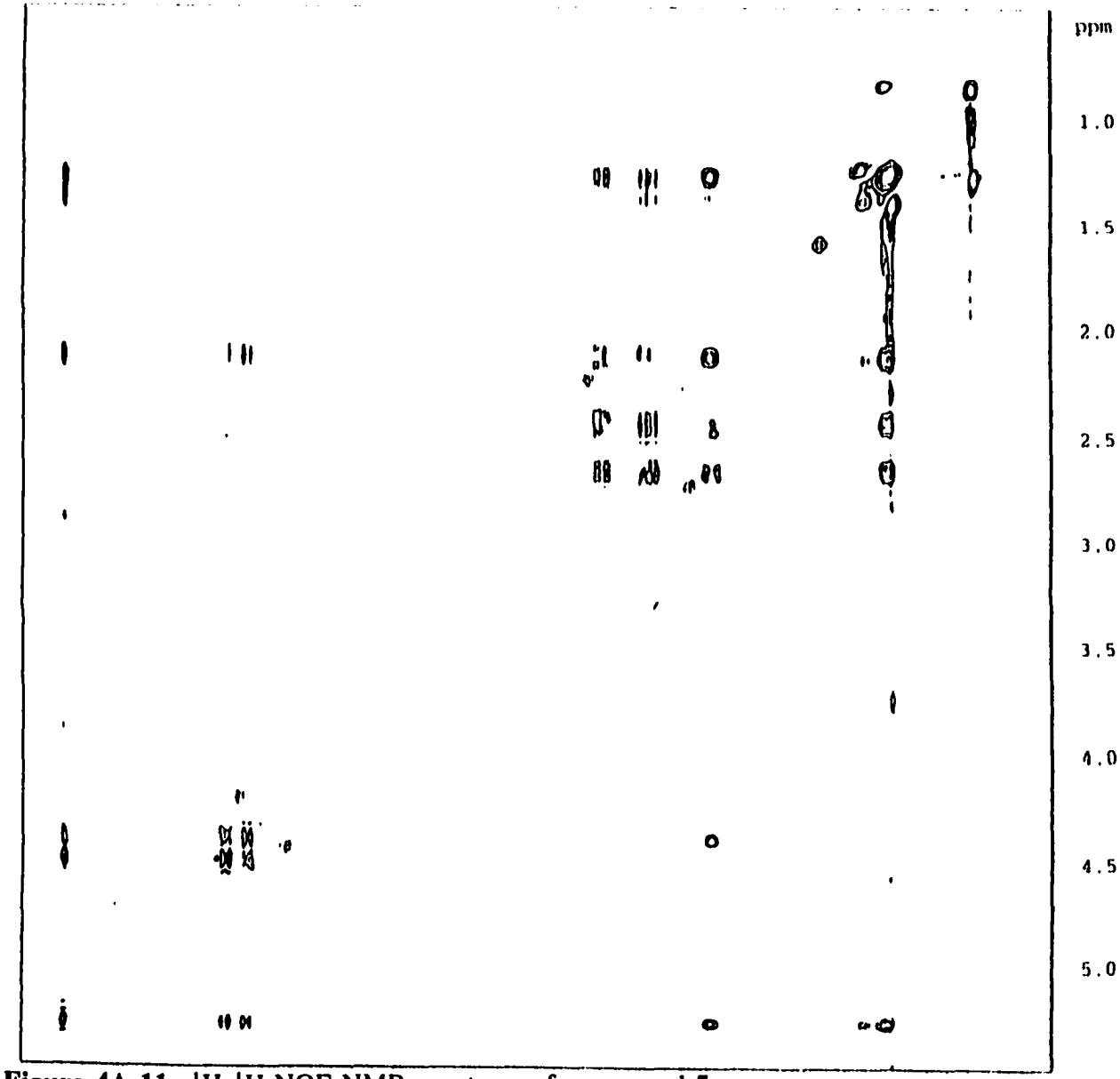
Figure 4A-9. ^{1}H NMR spectrum of compound **5**.

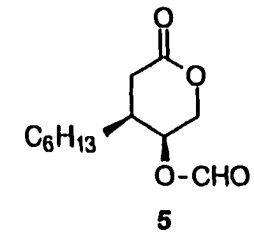




5

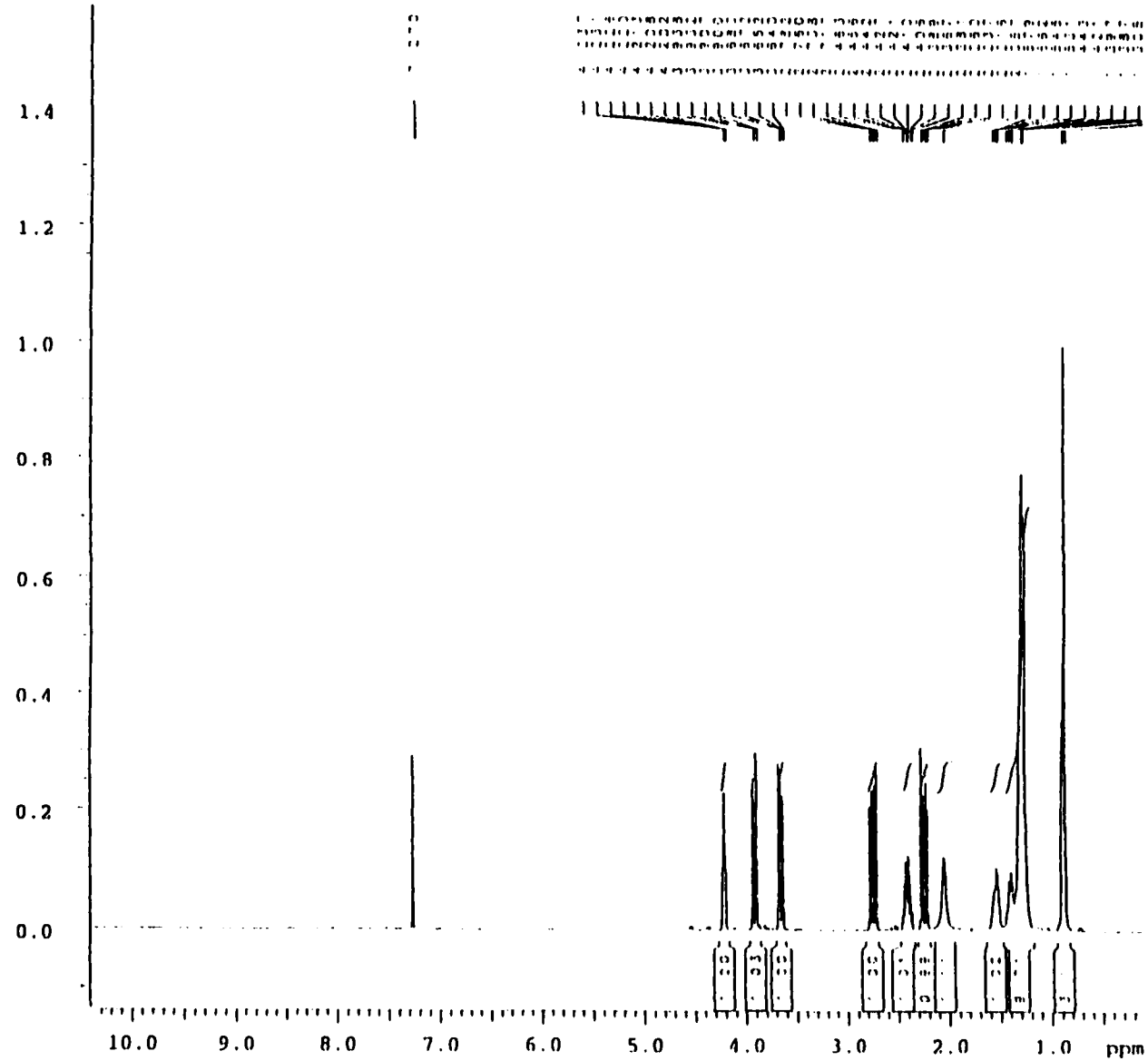
Figure 4A-10. ^{13}C NMR spectrum of compound **5**.

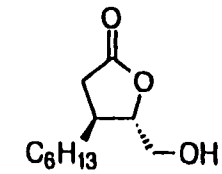




5

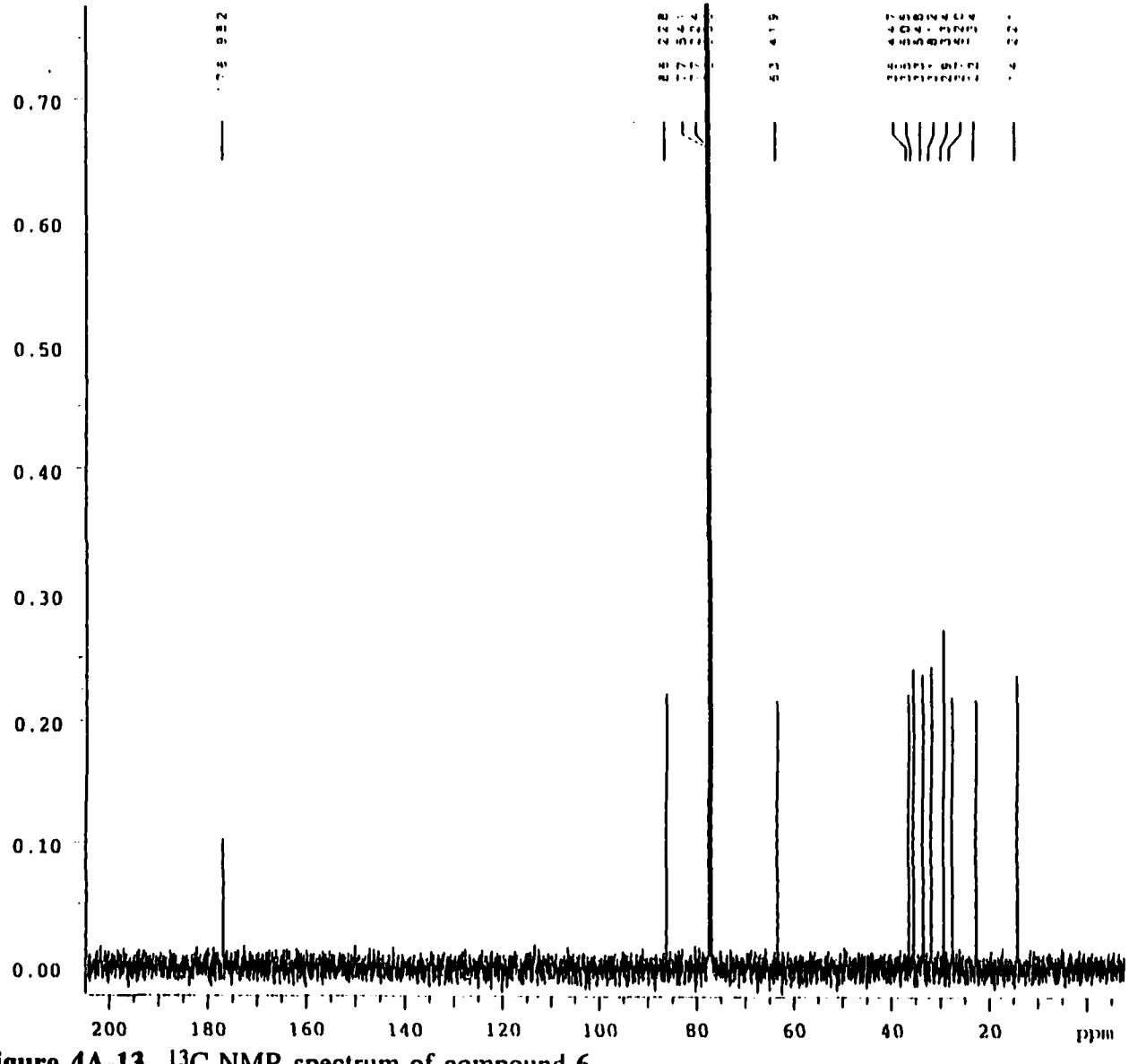
Figure 4A-11. ^{1}H-^{1}H NOE NMR spectrum of compound **5**.

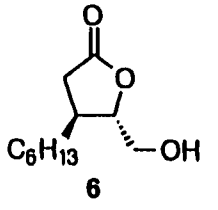




6

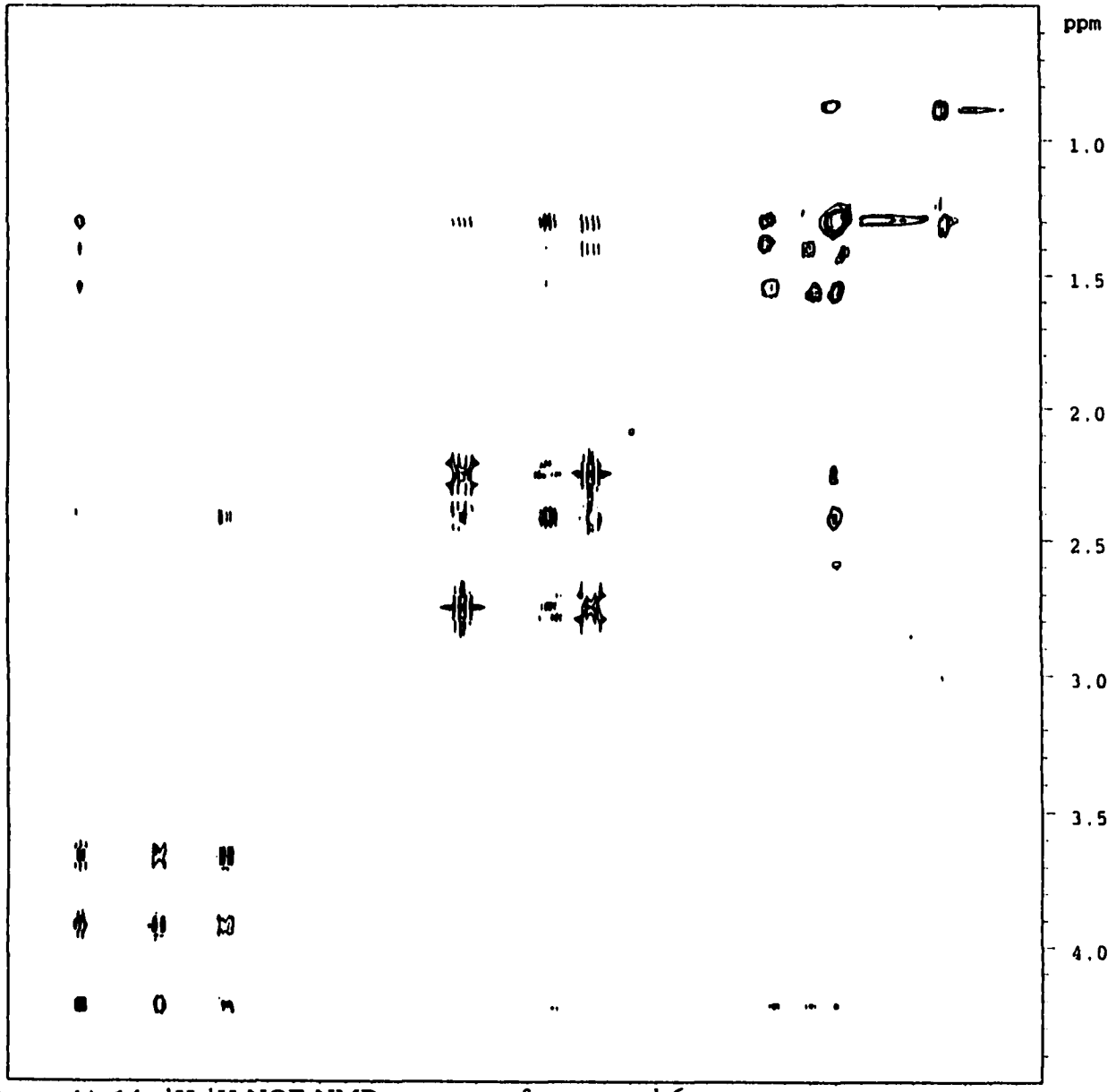
Figure 4A-12. ^{1}H NMR spectrum of compound **6**.

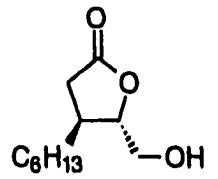




6

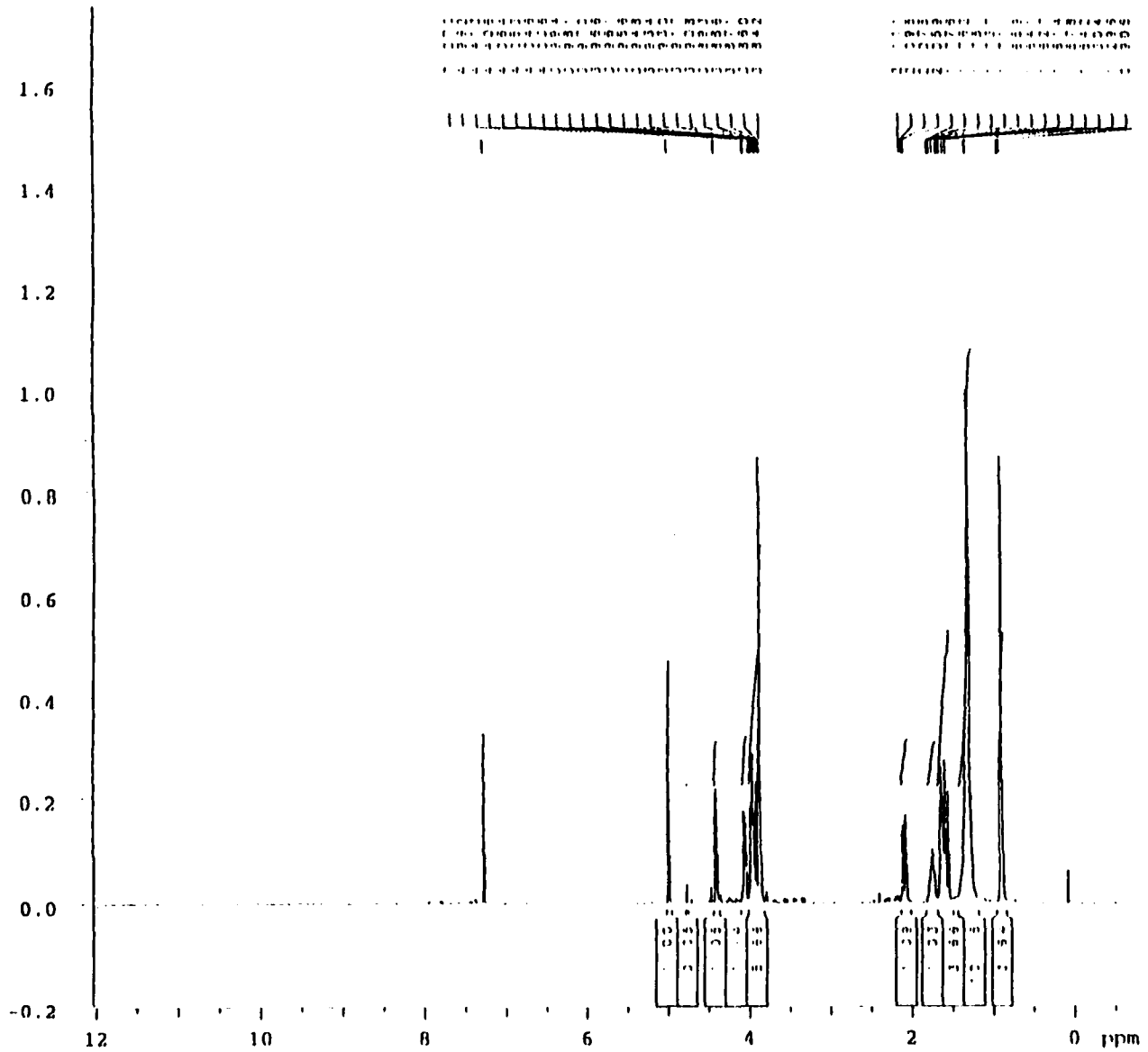
Figure 4A-13. ^{13}C NMR spectrum of compound **6**.

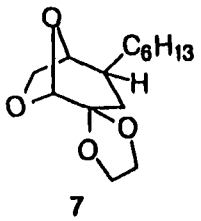




6

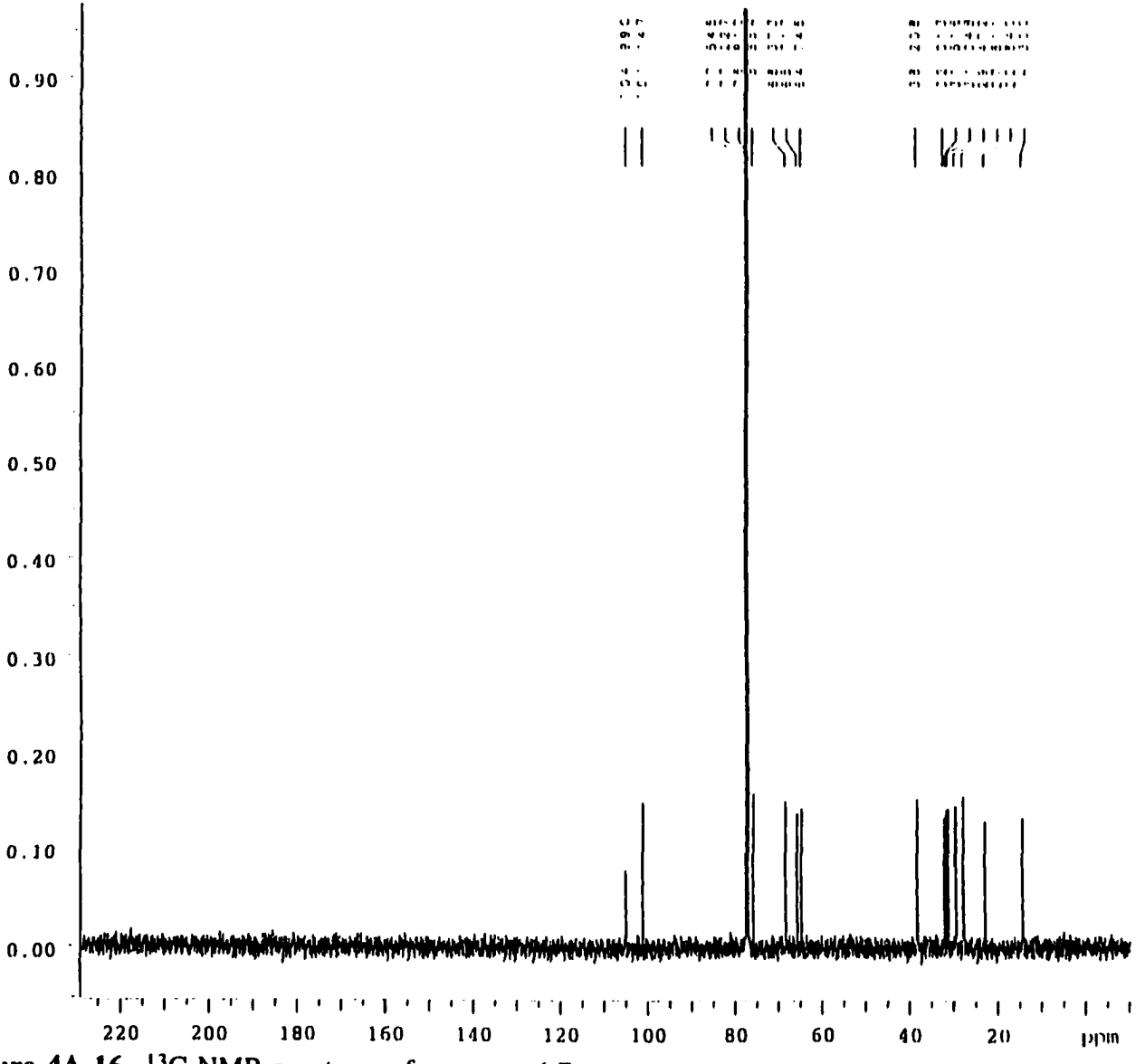
Figure 4A-14. ^{1}H-^{1}H NOE NMR spectrum of compound **6**.

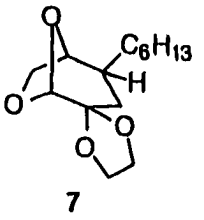




7

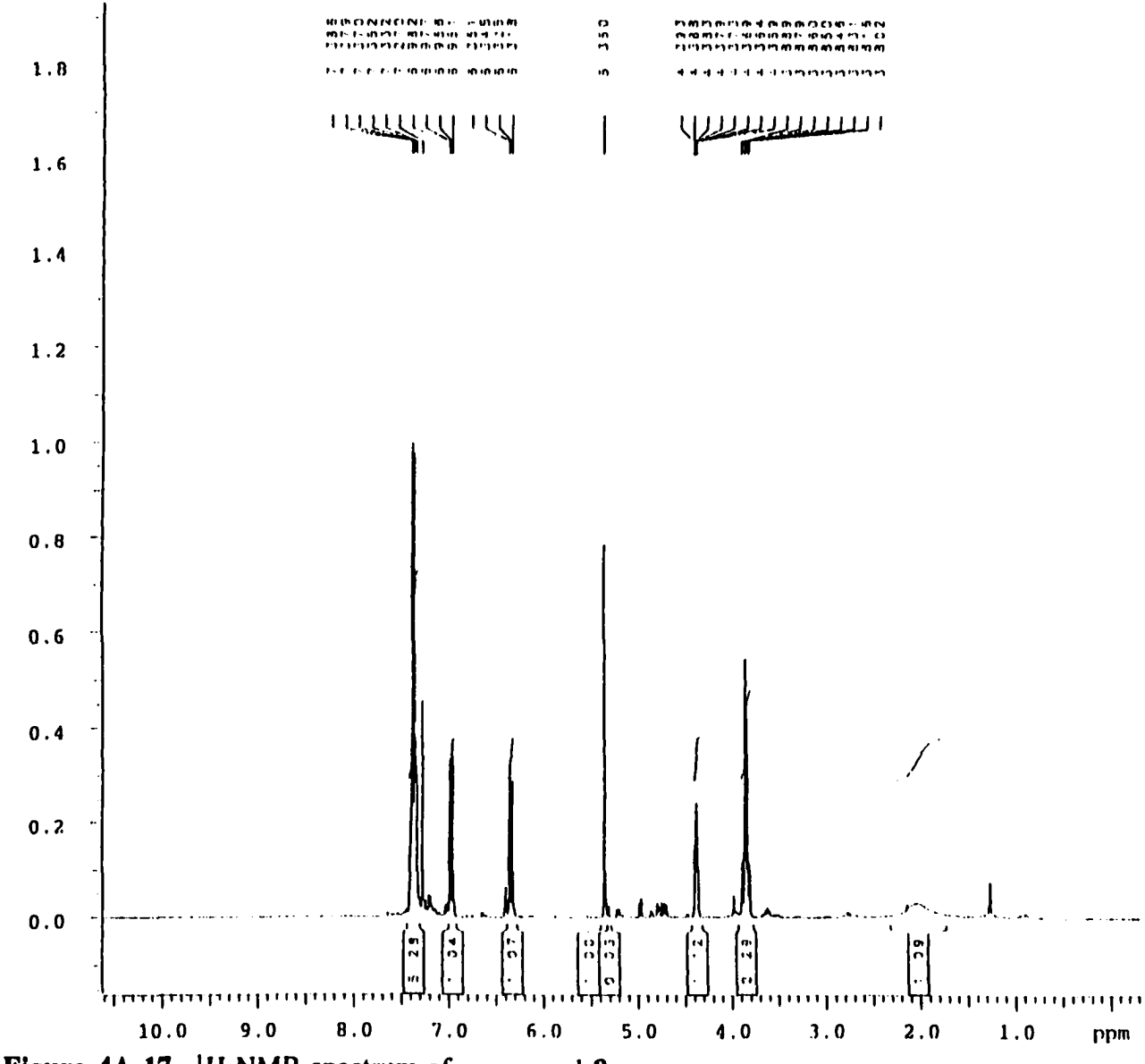
Figure 4A-15. ^{1}H NMR spectrum of compound 7.

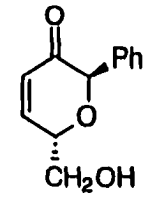




7

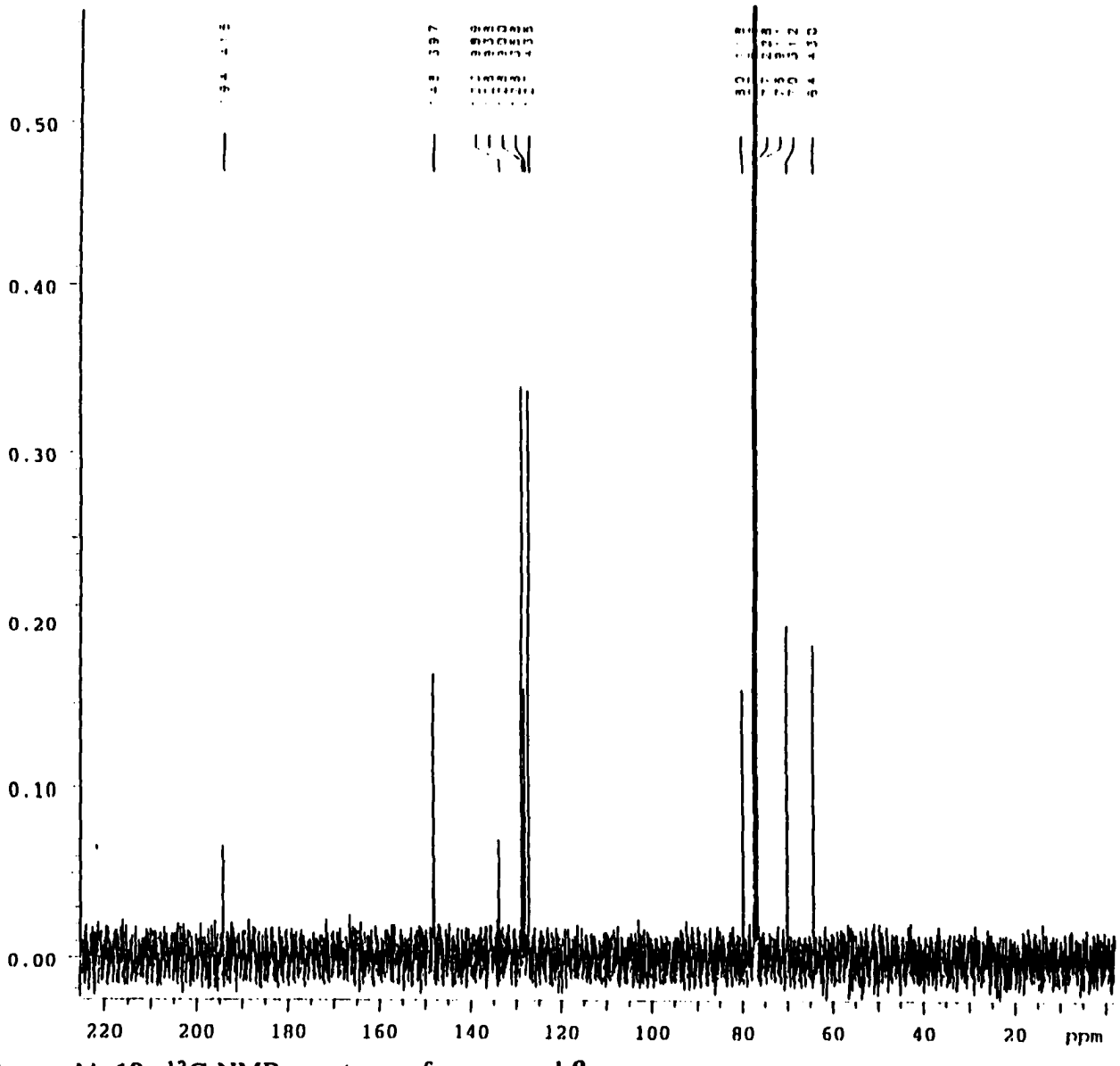
Figure 4A-16. ^{13}C NMR spectrum of compound 7.

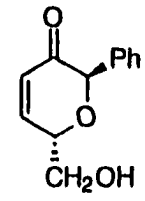




8

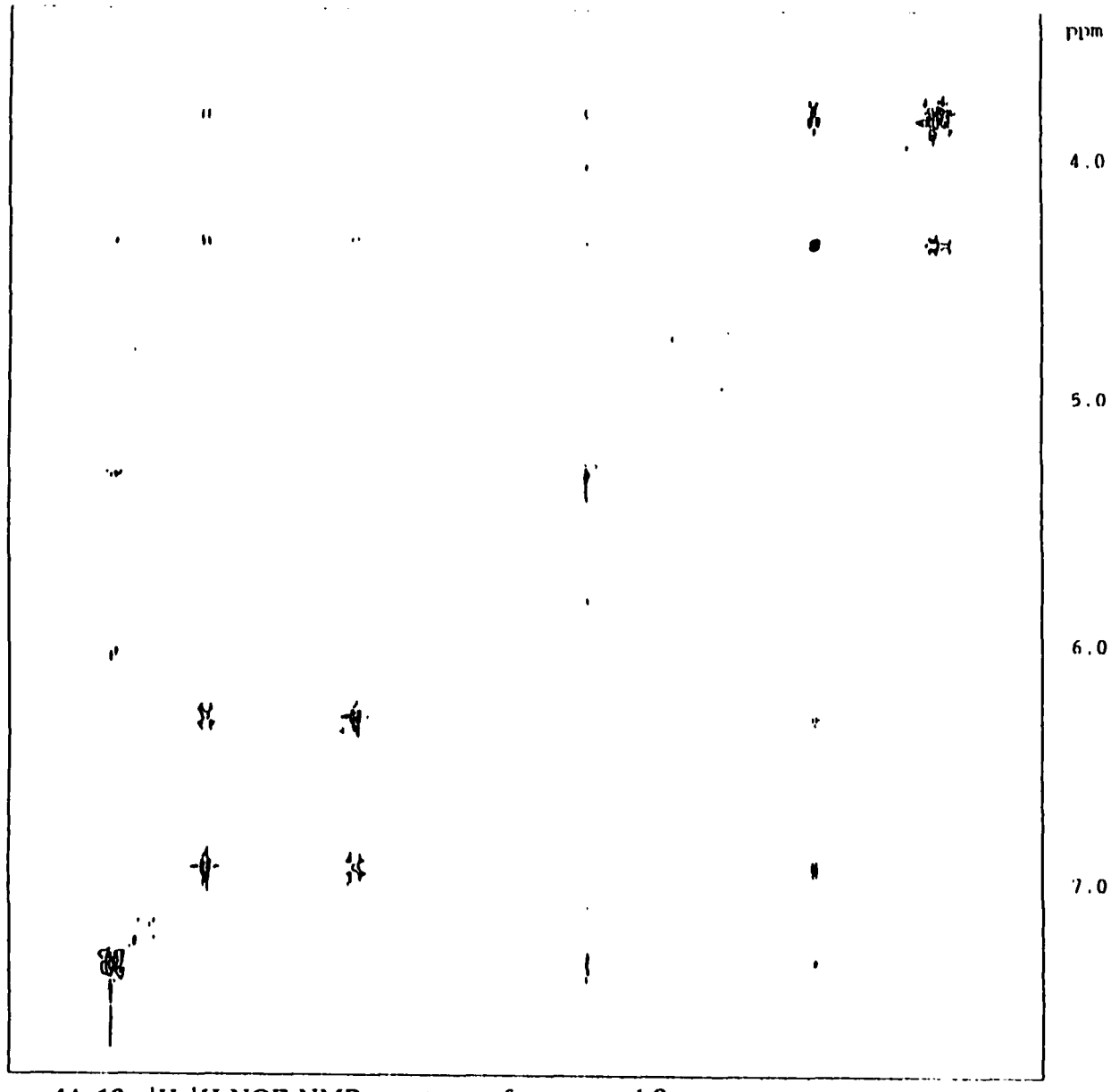
Figure 4A-17. ^{1}H NMR spectrum of compound **8**.

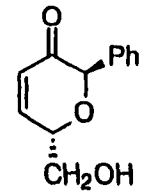




8

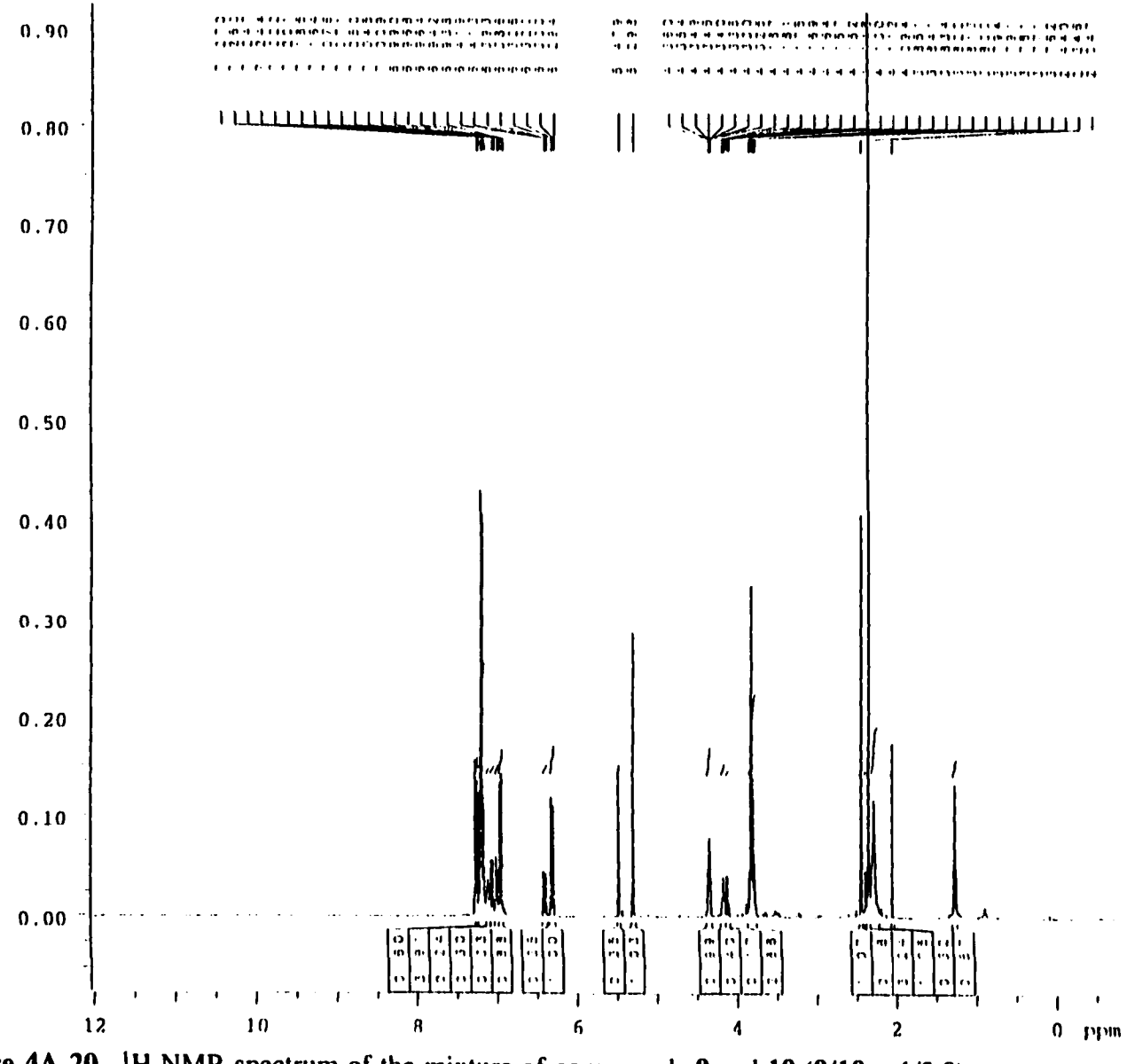
Figure 4A-18. ^{13}C NMR spectrum of compound **8**.

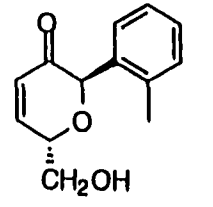




8

Figure 4A-19. ^{1}H-^{1}H NOE NMR spectrum of compound **8**.





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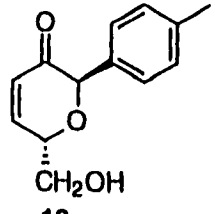

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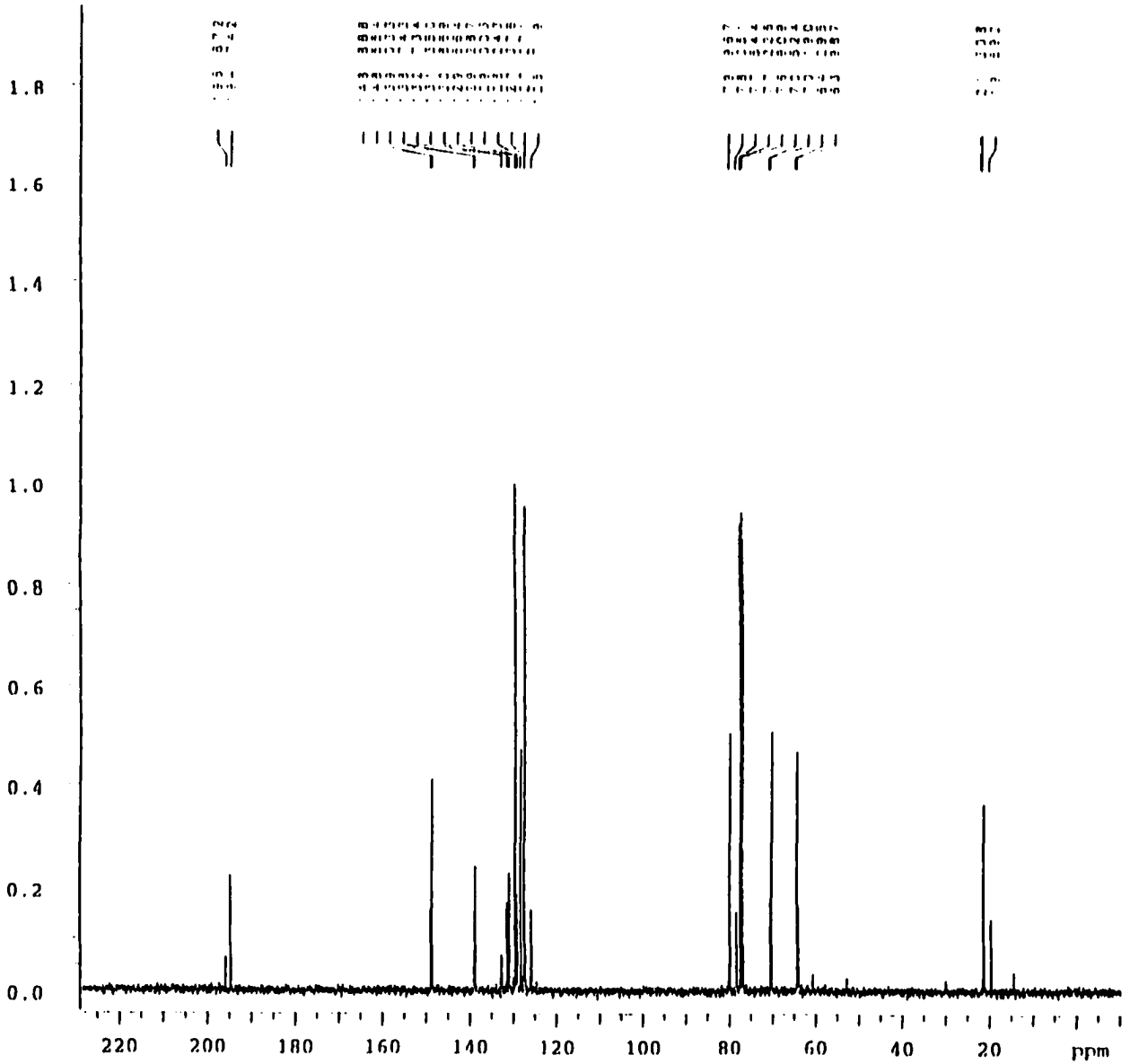
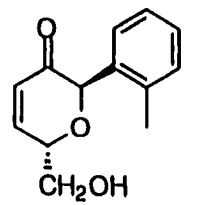
Figure 4A-20. ^{1}H NMR spectrum of the mixture of compounds **9** and **10** (**9/10** = 1/2.8).





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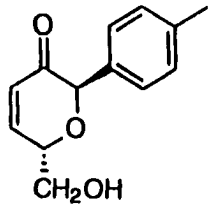

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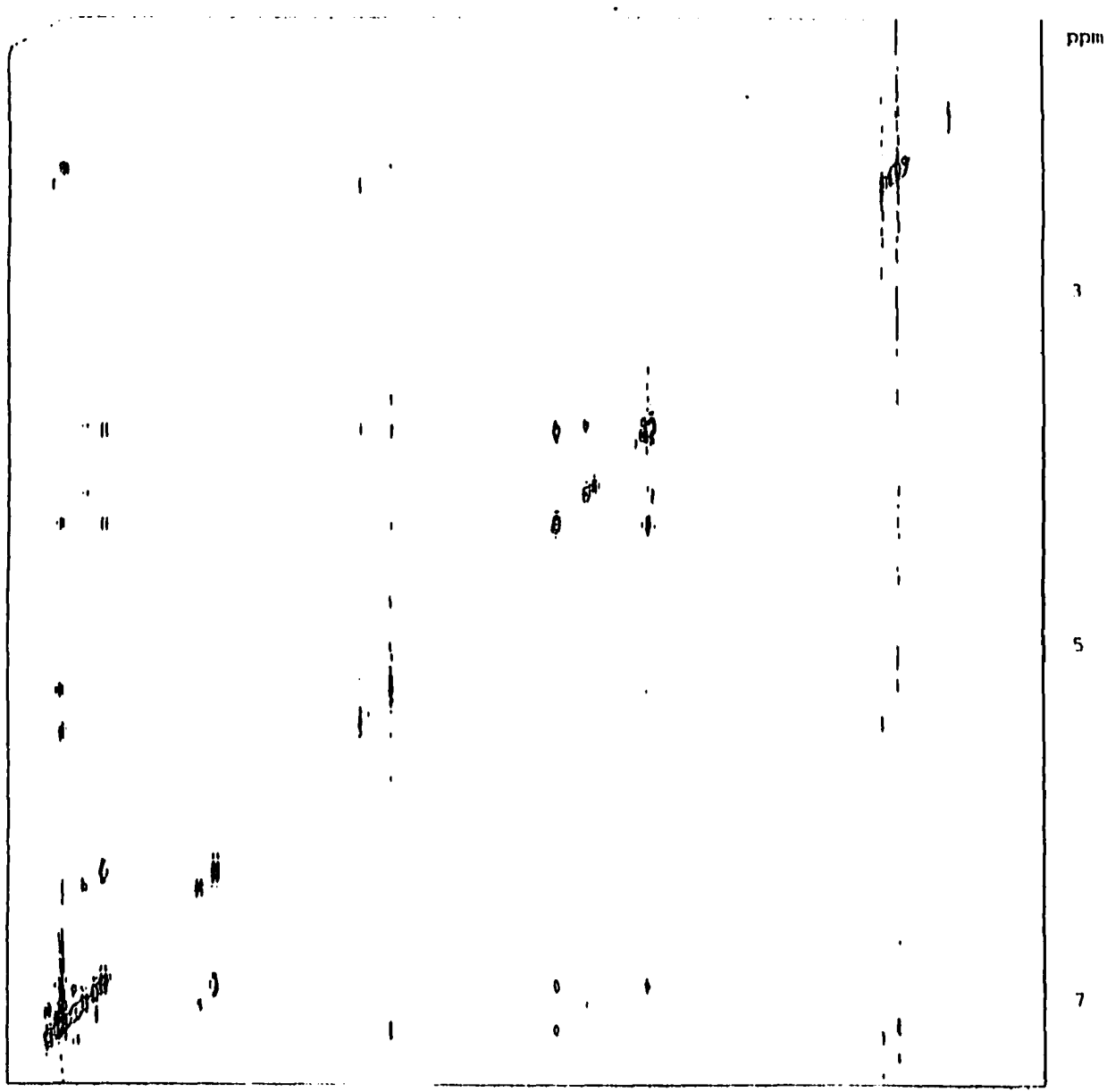
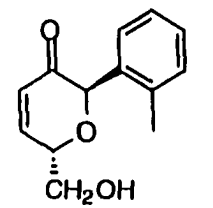
Figure 4A-21. ^{13}C NMR spectrum of the mixture of compounds **9** and **10** (**9/10** = 1/2.8).





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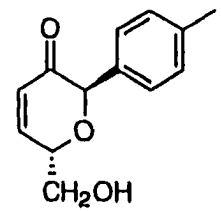

10

Figure 4A-22. ^{1}H-^{1}H NOE NMR spectrum of the mixture of compounds **9** and **10** (**9/10** = 1/2.8).

GENERAL CONCLUSIONS

Our work shows that radical cyclization methodology is a very powerful tool for the synthesis of functionalized lactams and lactones.

In the addition of $PhSO_2Br$ to *N*-allyl acrylamides, the trans lactams are obtained from the $C_\alpha \rightarrow C_\beta$ radical cyclization process where $PhSO_2\bullet$ adds only to the acrylic C=C bond, and then the adduct radical intramolecularly cyclizes by adding into the allyl C=C bond by a 5-exo mode. This chemoselectivity is confirmed due to the higher reactivity of the acrylic C=C bond towards the sulfonyl radical than the allyl C=C bond. So, the $C_\beta \rightarrow C_\alpha$ cyclization is observed only with *N*-allyl 3,3-dimethylacrylamides where the chemoselectivity is forced by steric effects. The third substituted group in the amides controls the conformation population of the amides, and thus the yields of lactams.

The trans γ-lactones can be formed in the addition of $PhSO_2Br$ to allyl acrylates with the promotion of the gem-dialkyl groups. The gem-dialkyl groups control the conformation population of the esters, and thus the yields of the lactones. The introduction of trace amounts of pyridine to the reactions to increase the yields of lactones is a important technical improvement. The gem-dialkyl effect can also be used to promote the formation of lactones from propargyl acrylates and allyl propiolates. Reactions of β-substituted acrylates and propiolates yield the lactones with different functionality.

Homolytic base-promoted aromatic alkylations can be observed with alkyl halides, $(Bu_3Sn)_2$, and DABCO in C_6H_6 at 60 °C. These results suggest that base-promoted homolytic aromatic substitutions may be a rather general process for aromatic compounds with electron-withdrawing substituents. This alkylation method is both mechanistically and synthetically interesting, and can serve as a complementary methodology to the well-known Friedel-Crafts reaction which can alkylate aromatic compounds bearing electron-donating substituents. Alkylations by alkyl halides have a much shorter kinetic chain length than those involving

alkylmercury halides and usually need a longer reaction time. Yields vary from low to high depending on the substrates and are much higher if the recovered starting benzene derivatives are taken into account. Though there are many literature methods available for the removal of the tin compounds from the desired products, further work on finding an environmentally friendly initiator is highly desired.

Levoglucosenone is a very versatile chiral chemical in organic synthesis. The use of vegetable oil in the pyrolysis of cellulose is an important advance for the preparation of levoglucosenone. The yield of levoglucosenone varies depending on types of vegetable oil, heating rate, and amounts of H_3PO_4. The relationship between the composition of the vegetable oil and the yield of levoglucosenone is not clear, and more variables need to be identified for this pyrolysis procedure. Further mechanistic study of this procedure leading to an improvement of its yield is highly desired. Preparation of chiral derivatives and other bioactive natural products from levoglucosenone is a broad research topic.

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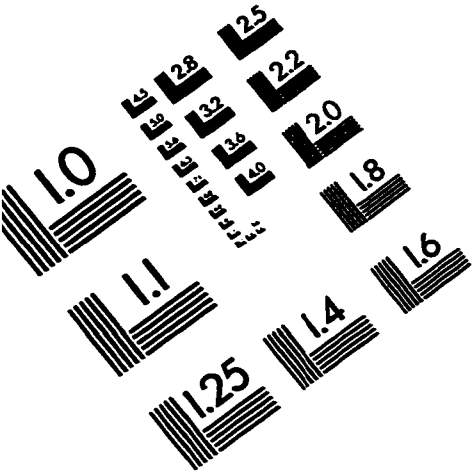
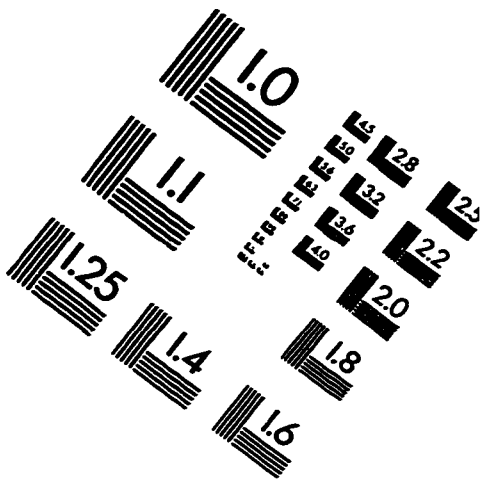
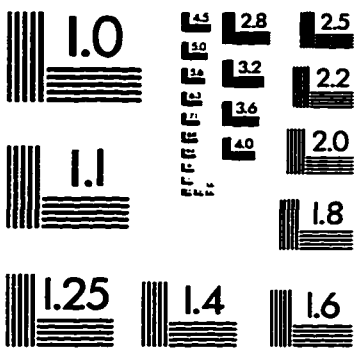
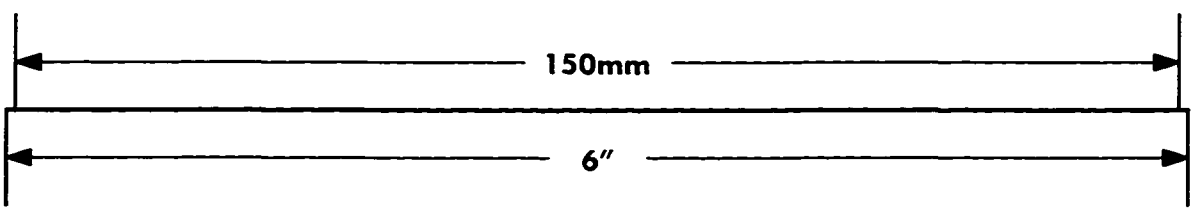
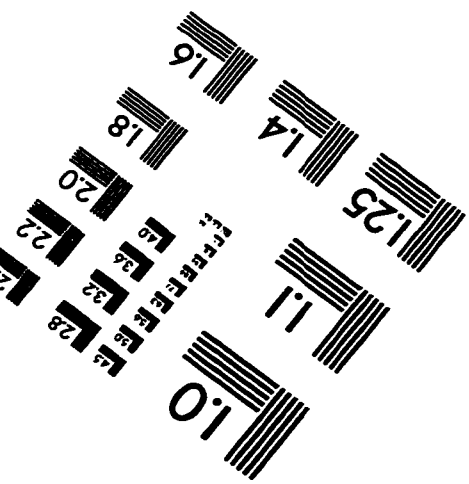
IMAGE EVALUATION
TEST TARGET (QA-3)

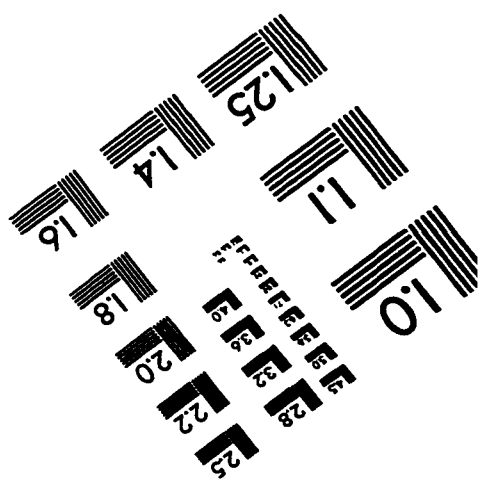












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