2012

Synthesis of Benzofluorenyl Derivatives Bearing Thiophene Substituents

Doreen Makaya
West Virginia University

Synthesis of Benzofluorenyl Derivatives Bearing Thiophene Substituents

DOREEN MAKAYA

Thesis submitted to the

Eberly College of Arts and Sciences

At West Virginia University

in partial fulfillment of the requirements

for the degree of

Master of Science

in

Chemistry

Kung K. Wang, Ph.D., Chair

Jeffrey L. Petersen, Ph.D.

Björn C.G. Söderberg, Ph.D.

C. Eugene Bennett Department of Chemistry

Morgantown, West Virginia

2012

Keywords: Benzannulated enyne-allene, thiophene

ABSTRACT

Synthesis of Benzofluorenyl Derivatives Bearing Thiophene Substituents

Doreen Makaya

A four-step synthetic sequence was used to prepare 10-(1,1-dimethylethyl)-5-thienyl-11*H*-benzo[*b*]fluorene from pivalophenone. The key step of the synthetic sequence involved the Schmittel cascade cyclization reaction of the corresponding benzannulated enyne-allene having a thienyl substituent at the alkynyl terminus. The benzannulated enyne-allene was prepared by an initial condensation of pivalophenone with the lithium acetylide derived from 2-iodophenylethyne to form 3-(2-iodophenyl)-1-(1,1-dimethylethyl)-1-phenyl-2-propyn-1-ol. Reduction of the propagylic alcohol with triethylsilane in the presence of trifluoroacetic acid then furnished 1-(1,1-iodophenyl)-3-(1,1-dimethylethyl)-3-phenyl-1-propyne. The Sonogashira reaction with 2-ethynylthiophene then produced the corresponding 10-(1,1-dimethylethyl)-5-thienyl-11H-benzo[*b*]fluorene from pivalophenone. Similarly, starting from benzophenone, 10-phenyl-5-thienyl-11*H*-benzo[*b*]fluorene was obtained.

The X-ray crystallographic structure of 10-(1,1-dimethylethyl)-5-thienyl-11*H*-benzo[*b*]fluorene shows that the thienyl substituent has a perpendicular orientation relative to the backbone of the benzofluorenyl system. As a result, the hydrogen atom on carbon-4 is in the magnetically shielded region of the thienyl ring current and thus shows an upfield-shifted signal at δ 6.45.

The successful Sonogashira reaction between 2,6-bis[(4*R*)-4,5-dihydro-4-phenyl-2-oxazolyl]-4-ethynylpyridine and iodobenzene is a promising way of making benzannulated enediynes bearing pyridine-2,6-bisoxazoline (pybox) ligands at the acetylenic position leading to benzofluorenyl systems possessing pybox moieties. Such heteroaromatic compounds are potentially useful for enantioselective reactions and for asymmetric catalysis.

Dedicated to

my daughters Sithokozile and Christaan

ACKNOWLEDGEMENT

My utmost gratitude and appreciation goes to my research advisor, Dr. Kung. K. Wang for his advice, encouragement and kindness during the course of my research and in compilation of my thesis. Special thanks is due to my research committee members, Dr. Jeffrey L. Petersen and Dr. Björn C. G. Söderberg for their constructive comments and suggestions. Further appreciation is extended to Dr. Jeffrey L. Petersen for his help with X-ray structure analysis of my compounds.

I also wish to thank my daughters, Sithokozile and Christaan for their understanding, encouragement, happiness and joy. Many thanks go to my parents for their support. Above all, I thank my friend Barbara Linn for her helpful assistance in supporting my dreams and aspirations.

For financial support, I thank the C. Eugene Bennett Department of Chemistry and the National Science Foundation.

TABLE OF CONTENTS

LIST OF FIGURES

Appendix (^{1}H NMR and ^{13}C NMR Spectra)

1. INTRODUCTION

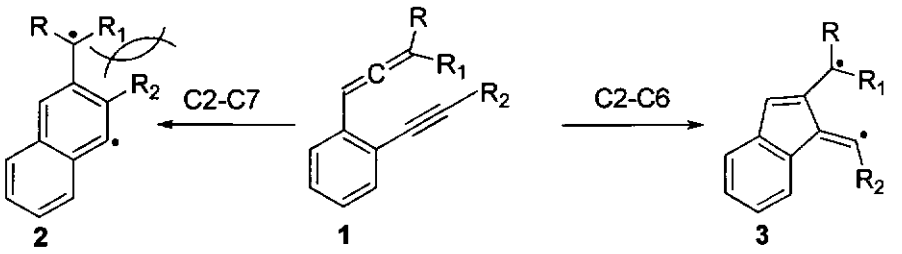
Over the past few decades, thiophene chemistry has been intensively investigated and many interesting applications have been discovered. Considerable attention has been given to the unique physical and chemical properties of thiophene compounds, notably their outstanding electronic, optical, redox,[1] charge transport and self-assembly properties.[2,3] Self-assembly is a versatile tool in constructing supramolecular organization of pi-conjugated molecules by formation of non-covalent bonds.[4] Pi-conjugation of polymer backbones increases the intermolecular interactions resulting in rigid structures. Thiophene rings have highly polarizable sulfur atoms which stabilize conjugated chains and provides exceptional charge transport properties. These self-organizing properties[5,6] are vital in manipulating new compounds for organic electronics.[7] Conjugate polymers can be structurally tailored to synthesize new electronic compounds by varying the position and character of side chains and the types of functional groups. These variations may affect solubility, ionic conductivity, band gap, morphology and miscibility.[8]

Structural variations of thiophene present great potential in tuning of their electrical properties.[6] Numerous methods have now been developed to modify thiophene systems. Conducting polymers have turned out to be of intense interest because of their favorable technological applications especially in the construction of electrochromic devices.[9,10] Conducting thiophene compounds are structurally versatile and easier to synthesize for solid state applications than inorganic materials.[11]

Our research group has reported several synthetic routes using benzanulated enyne-allenes to form benzofluorenes via the Schmittel cyclization reactions. The reaction is also

applicable to systems bearing nitrogen as a heteroatom. Intrigued by the vast applications of compounds bearing thiophene moieties, we envisioned that the chemistry developed in our group for making benzofluorenes could also provide opportunities to incorporate thiophenes in the aromatic systems.

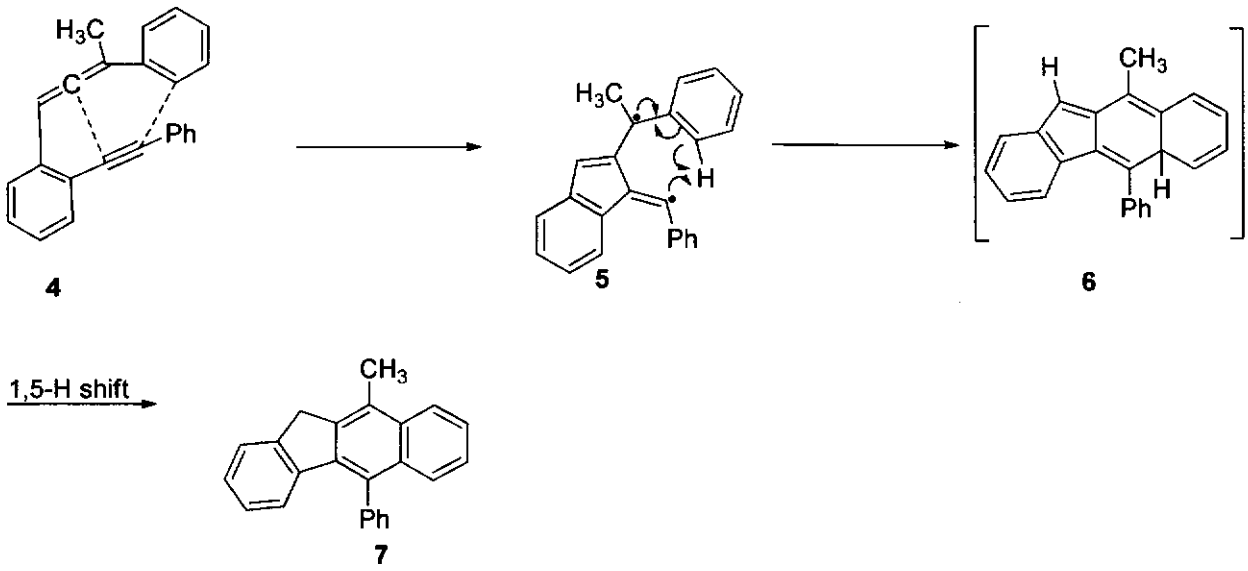
Understanding the mechanisms of the Schmittel cyclization reactions is pivotal in designing new synthetic methods for these aromatization reactions. Enyne-allenes will follow either the Myers-Saito (C2-C7)[12] pathway or the C2-C6 (Schmittel)[13] pathway depending on the substitution at the allenic or acetylenic terminus (Scheme 1).[14] Both steric and electronic effects play a role in determining whether a reaction will undergo the Schmittel or the Myers-Saito pathway. If R1 and R2 are sterically demanding, biradical **2** is not formed because steric interactions of the two groups will prevent it from forming. Instead, in the case where R2 is a sterically demanding *tert*-butyl or a trimethylsilyl group, the Schmittel cyclization reaction to form biradical **3** is favored.[15]



Scheme 1. Saito-Myers cyclization (**2**) and Schmittel cyclization (**3**)

If the R2 group is a hydrogen atom or a sterically non-demanding alkyl group, the Myers-Saito cyclization reaction is favored. This is due, in part, to the aromaticity gained when biradical **2** is formed.[16]

Electronic effects come into play when an aryl substituent occupies the acetylenic position because it stabilizes the alkenyl radical site in **5** (Scheme 2). A phenyl substituent at the allenic terminus allows the radical-radical coupling to occur, producing the formal Diels-Alder adduct **6**. Although the formation of the intermediate **6** from **4** can be viewed as a concerted Diels-Alder reaction, mechanistic studies indicate a step-wise route leading to the formation of **6** via the benzofulvenyl biradical **5.** A 1,5-prototropic rearrangement of the intermediate **6** results in generation of the benzofluorene system **7**.

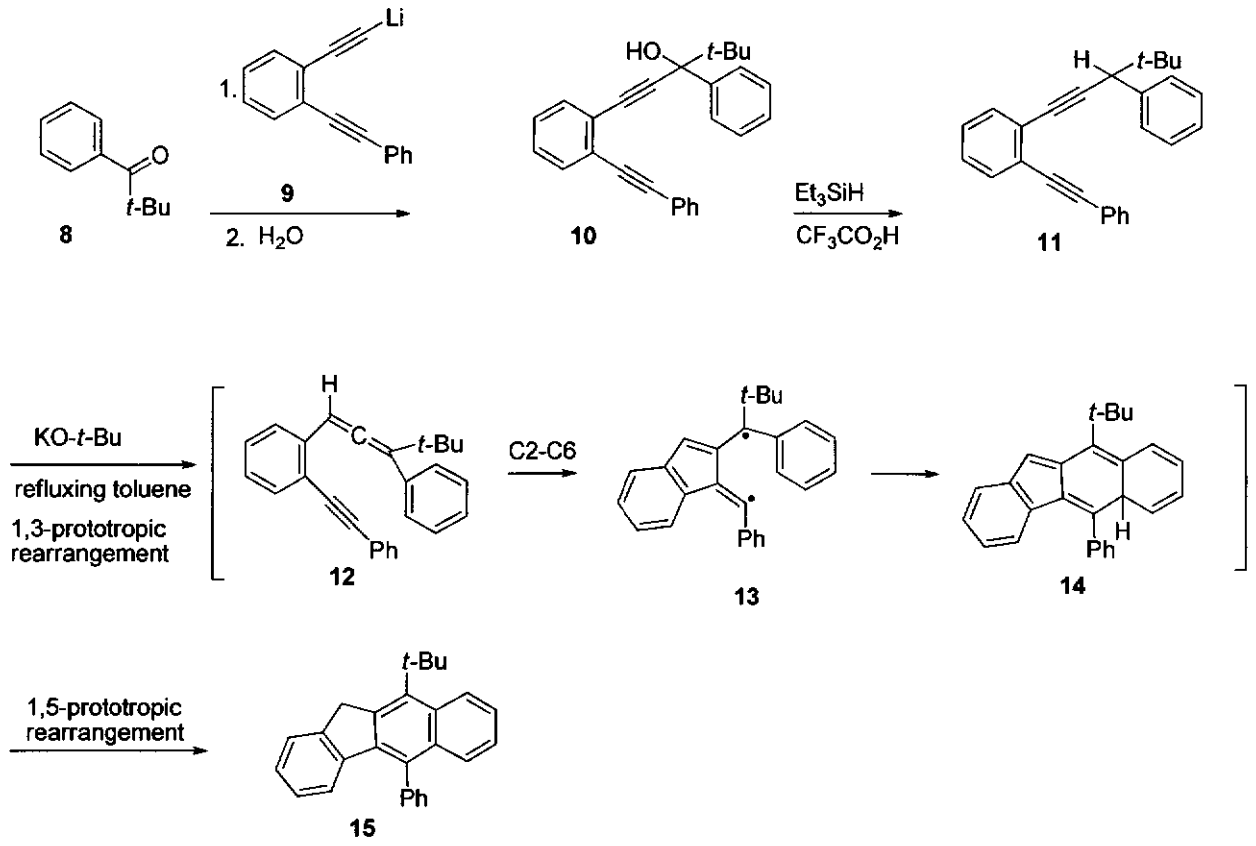


Scheme 2. Preparation of 11-H-benzo[*b*]fluorene **7**

Our research group has developed a variety of synthetic methods for benzannulated enyne-allenes bearing a phenyl substituent at the acetylenic and allenic termini leading to benzofluorenyl derivatives.

One of the methods involved condensation between a ketone, such as **8**, and a lithiated benzannulated endiyne such as **9**, to form a propagylic alcohol as depicted in **10** (Scheme 3).[17] Reduction of the propagylic alcohol with triethylsilane in the presence of trifluoroacetic acid led

to the reduced adduct **11**. On treatment with potassium *tert*-butoxide and *tert*-butyl alcohol, **11** was converted, in situ, to the benzannulated enyne-allene **12**, which then underwent the Schmittel cyclization reaction through **13** to form **14**. A 1,5-prototropic rearrangement to regain aromaticity then afforded 11-*H*-benzo[*b*]fluorene **15**.[18-22]

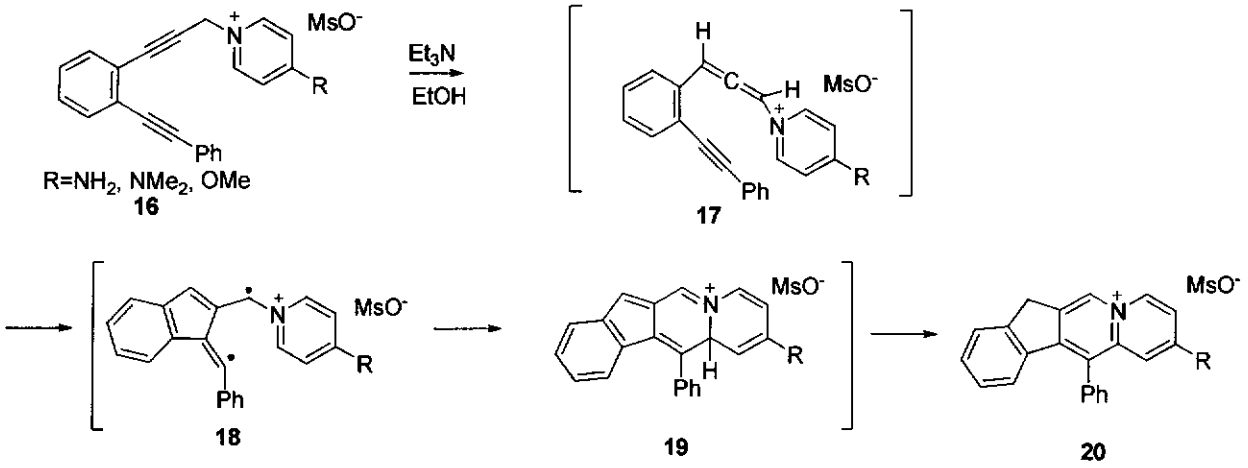


Scheme 3. Mechanism for formation of **15**

Placing a pyridine group as the heteroaromatic substituent at the allenic terminus of the enyne-allene system led to a benzofluorene system bearing a pyridine moiety. This synthetic strategy again utilized the 1,3-prototropic rearrangement to form the allenic moiety.

Apart from using potassium *tert*-butoxide and *tert*-butyl alcohol as a way of making benzannulated enyne-allenes, our research group has also utilized triethylamine and ethanol to

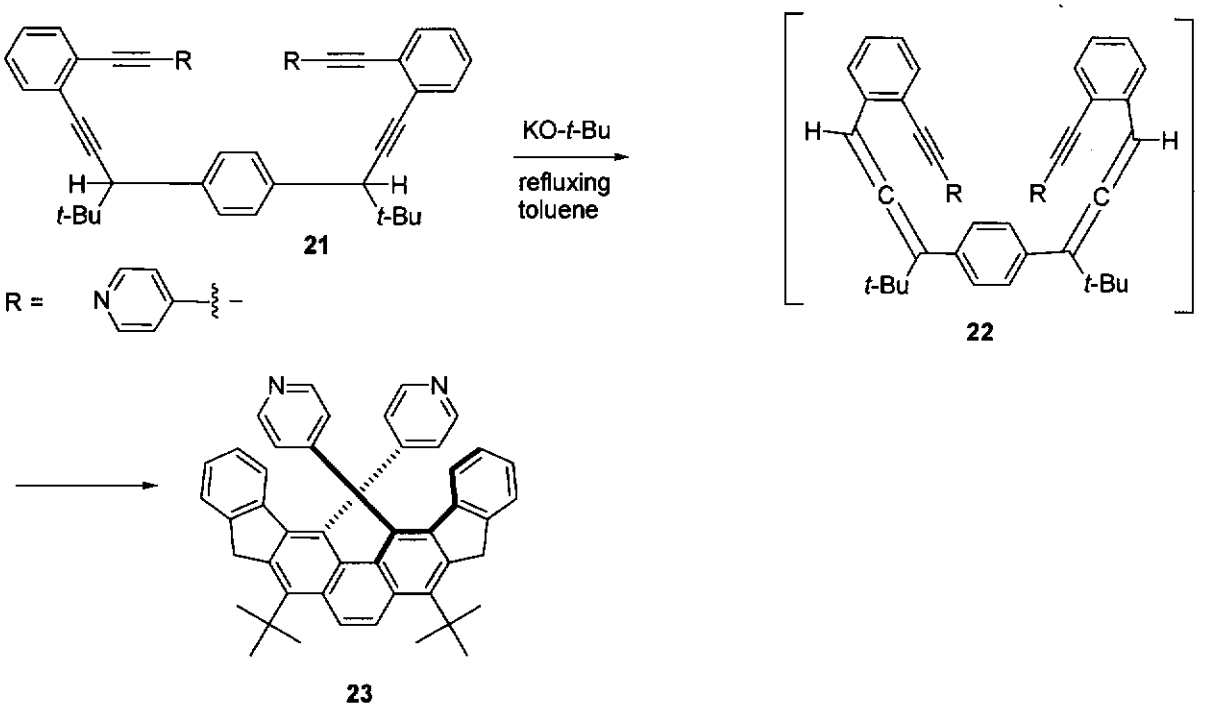
effect such transformations. The pyridinium methanesulfonate **16** gave enyne-allene **17** after treatment with triethylamine in refluxing ethanol (Scheme 4).[23] Similarly to what has been described about the mechanism for the formation of benzofluorenyl systems, enyne-allene **17** underwent a C2-C6 cyclization reaction to form biradical **18** by the Schmittel cyclization pathway. Radical-radical coupling of **18** to afford **19** was followed by prototropic rearrangement to produce the fused quilizinium methanesulfonate **20**. This reaction demonstrates another approach, leading to the generation of benzofulvene biradical **18**, using the Schmittel protocol to form benzofluorenyl systems with pyridine as a heteroaromatic substituent at the allenic terminus. Similar transformations of pyridine systems to enyne- allenes using *tert*-butoxide, for example, and *tert*-butyl alcohol have also been successfully demonstrated.



Scheme 4. Preparation of quilizinium methanesulfonate **20**

The Schmittel cyclization reaction has been extended to the synthesis of compounds with helical twists. Our research group has successfully applied the Schmittel cyclization reaction to

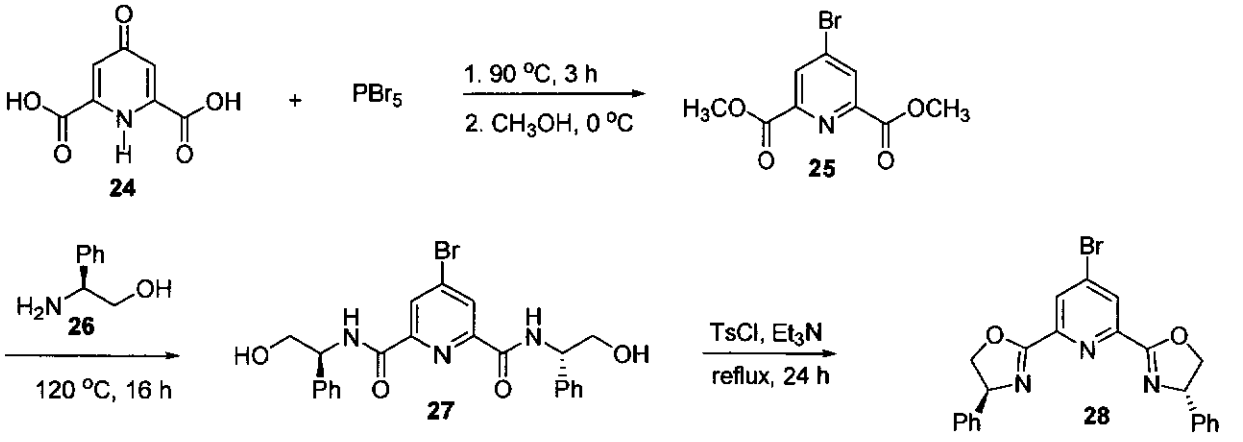
synthesize benzannulated enyne-allene systems with a pyridine substituent at the acetylenic terminus (Scheme 5).[24]



Scheme 5. Formation of benzofluorene **23**

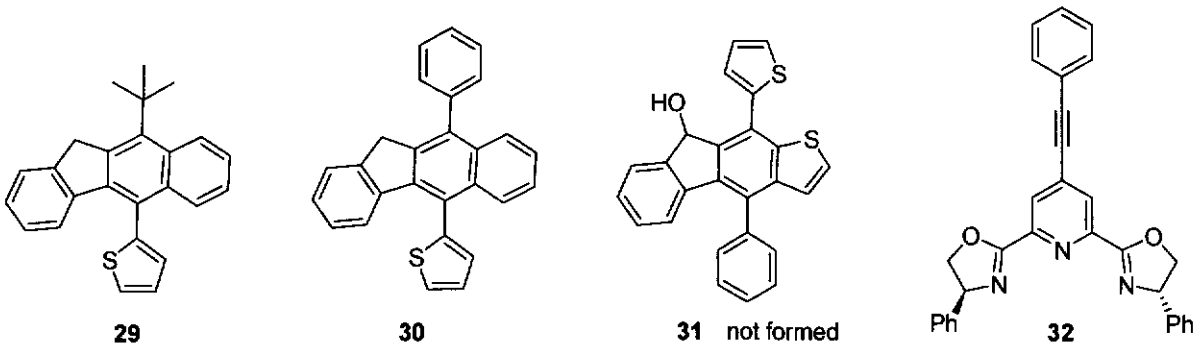
In addition to synthesizing enyne-allenes bearing thiophene moieties, attempts to apply a similar synthetic route in synthesizing enyne-allenes bearing pyridine-2,6-bisoxazolines, pybox[25] as a substituent were also made. Our research group has successfully applied the Schmittel cyclization reactions for synthesis of benzofluorenyl systems bearing terpyridine ligands as substituents. We envisioned that a similar chemistry could be applied in making benzofluorenyl systems bearing pybox ligands as substituents. Pybox ligands contain two oxazolines and a pyridine ring. Pybox ligands are versatile compounds due to the wide variety of asymmetric catalysis reactions they offer.[26]

Various methods for the synthesis of pybox ligands have been reported by many groups. The synthetic route for making pybox **28** is outlined in Scheme 6.[27] This method involves heating a mixture of one equivalent of chelidamic acid (**24**) and nine equivalents of phosphorus pentabromide at 90 °C for 3 hours. The product obtained was treated with methanol at 0 °C to generate dimethyl 4-bromopyridine-2,6-dicarboxylate (**25**). (*R*)-Phenylglycinol (**26**) was then mixed with **25** and heated at 120 °C for 16 hours to give diamide **27**. para-Toluenesulfonyl chloride (TsCl) was mixed with **28** and refluxed with triethylamine for 24 hours to yield the pybox ligand **28**.



Scheme 6. Formation of pybox ligand **28**

In this project, the C2-C6 cyclization synthetic sequence also found success in the synthesis of **29** and **30** shown in Figure 1. However, attempts to synthesize **31** containing two thiophene units were unsuccessful. Preliminary studies using **32** as a model to try to introduce the heterocyclic pyridine bisoxazoline onto the benzofluorenyl system were conducted.



29 **30** **31** not formed **32**

Figure 1. Structures of an oxazoline system and benzofluorenyl systems bearing thienyl substituents.

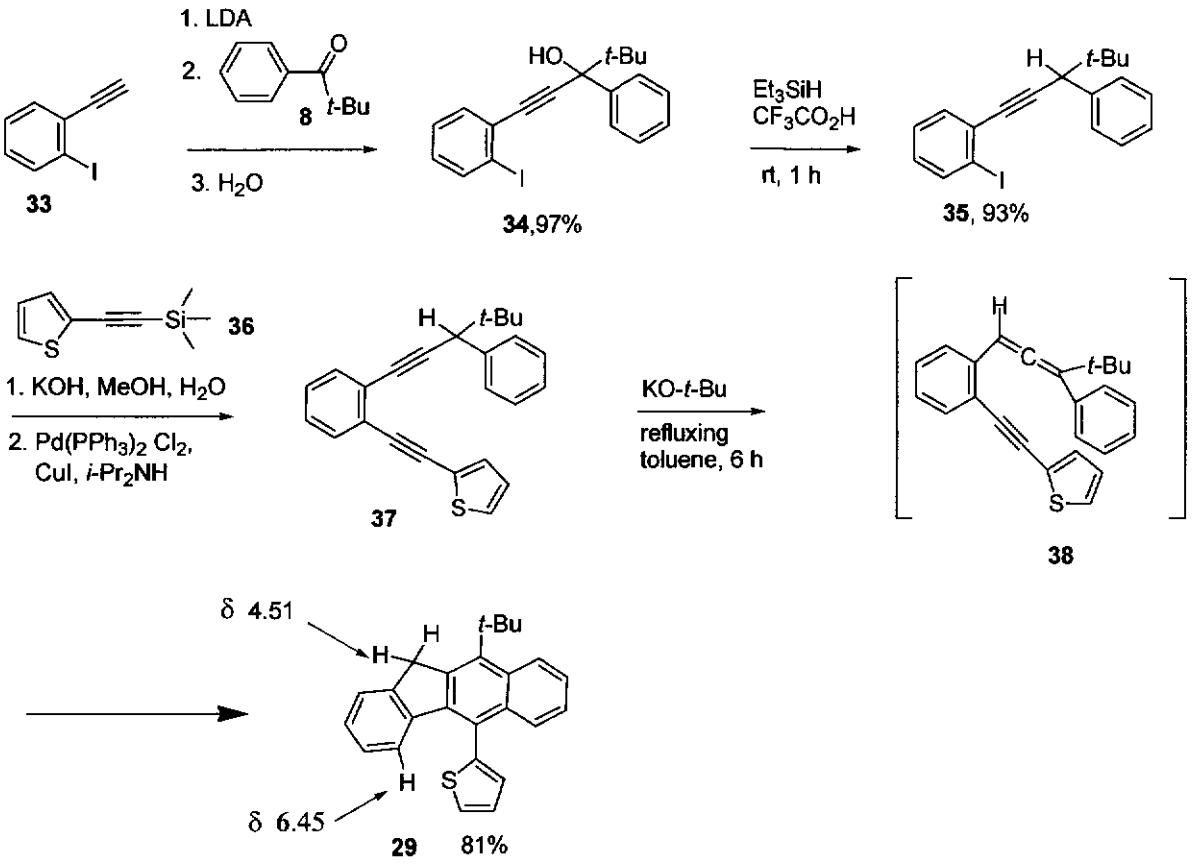
2. RESULTS AND DISCUSSION

2.1. Development of a synthetic route for 29

Benzofluorenes **29** and **30** contain a thiophene group at the C5 position of the benzofluorenyl system. The synthetic sequence outlined in Scheme 7 for **29** involved condensation of **8** and one equivalent of the lithium acetylide of **33** to afford alcohol **34** in excellent yield. Reduction of **34** with triethylsilane in the presence trifluoroacetic acid furnished **35**. Treatment of **36** with potassium hydroxide in the presence of methanol and water allowed an efficient in-situ generation of 2-ethynylthiophene. The subsequent Sonogashira coupling of 2-ethynylthiophene with **35** produced **37**. Exposure of **37** to potassium *tert*-butoxide in refluxing toluene for 6 hours promoted a prototropic rearrangement to form, in situ, the corresponding benzannulated enyne-allene **38**, which in turn underwent the cascade Schmittel cyclization reaction leading to benzo[*b*]fluorene **29** in 81% yield.

The ^{1}H NMR spectrum of **29** in $CDCl_3$ showed a singlet at δ 4.51 attributable to the methylene hydrogens on the five-membered ring of the benzofluorenyl system. The upfield shifted aromatic hydrogen at the C5 position indicates that the thiophene substituent is oriented

perpendicular to the benzofluorenyl system. As a result, the hydrogen on the C5 position is located in the magnetically shielded region of the thiophene ring current, causing an upfield shift. The ^{1}H NMR analysis of the thienyl hydrogens showed that their δ values are 7.62 (dd, J =5.2, 1.0 Hz), 7.37 (multiplet) and 7.10 (multiplet).



Scheme 7. Synthesis of benzofluorene **29**

The structure of **29** was established by X-ray structure analysis. The ORTEP drawing of the crystal structure of **29** is given in Figure 2. The crystallographic asymmetric unit contains two independent molecules of $C_{25}H_{22}S$. The planar five-membered thiophene ring containing atoms C(43), C(44), C(43), C(46), and S(2) suffers from two-site rotational disorder. The X-ray

structure also shows that the thiophene unit is oriented essentially perpendicular to the benzofluorenyl system, placing the hydrogen on the C4 carbon in the magnetically shielded region of the thiophene ring current as indicated in the ^{1}H NMR spectrum.

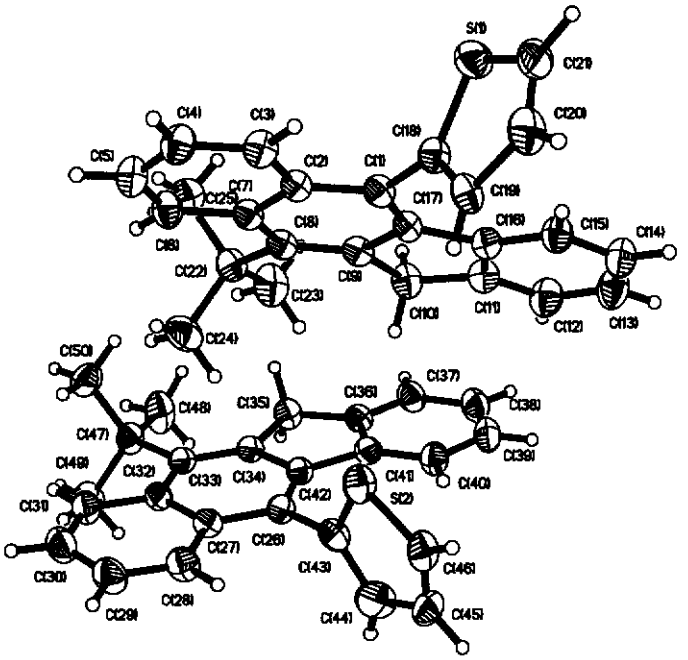
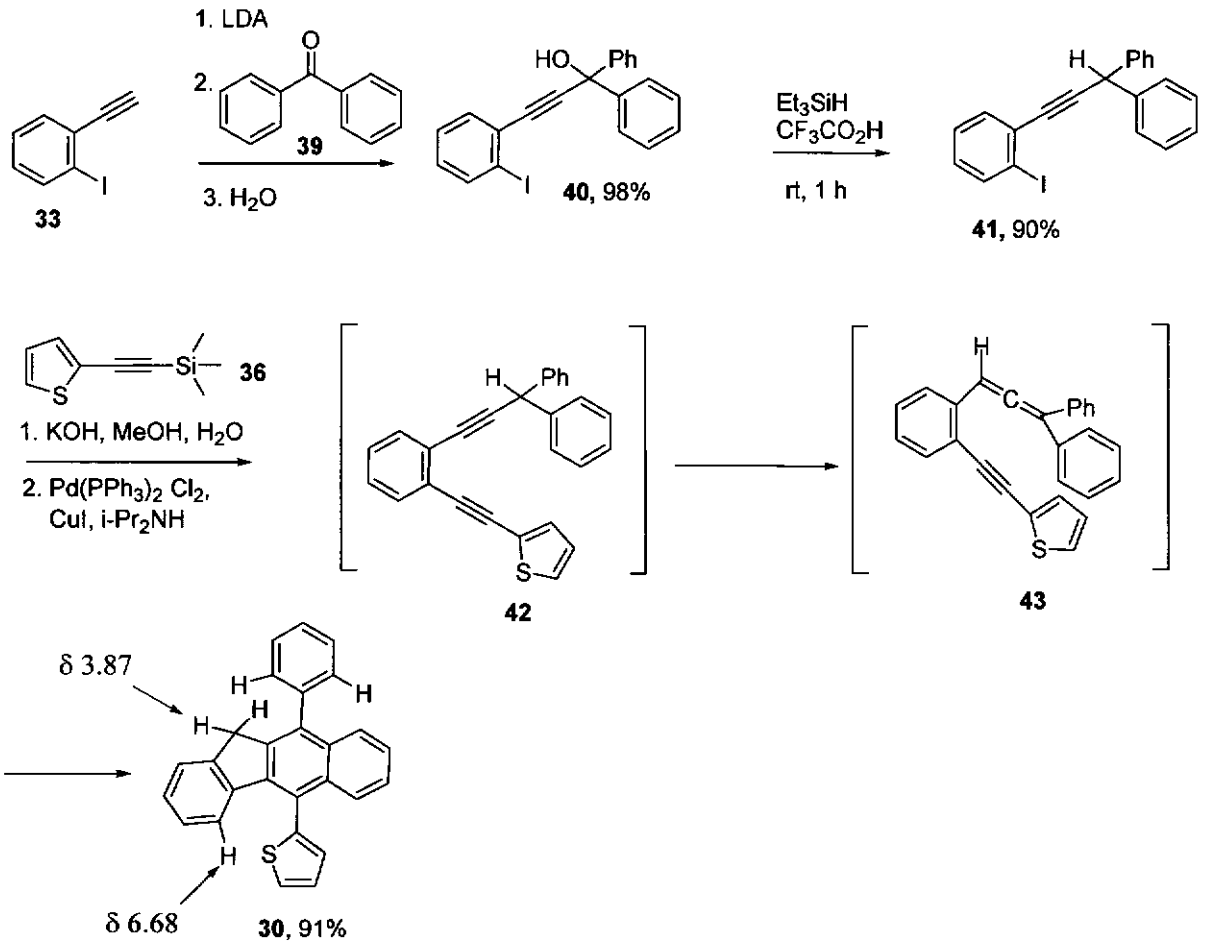


Figure 2. ORTEP drawing of the crystal structure of **29** containing two independent molecules. The thermal ellipsoids are scaled to enclose 30% probability.

1.2. Development of a synthetic route for 30. The synthetic sequence leading to **30** involved reaction of 1-ethynyl-2-iodobenzene (**33**) with lithium diisopropylamide to generate the corresponding lithium acetylide followed by condensation with benzophenone (**39**) to produce propagylic alcohol **40** (Scheme 8). Subsequent reduction of **40** with triethylsilane in the presence of trifluoroacetic acid afforded **41**. An in-situ generation of 2-ethynylthiophene from **36** occurred after treatment with potassium hydroxide in the presence of methanol and water as described

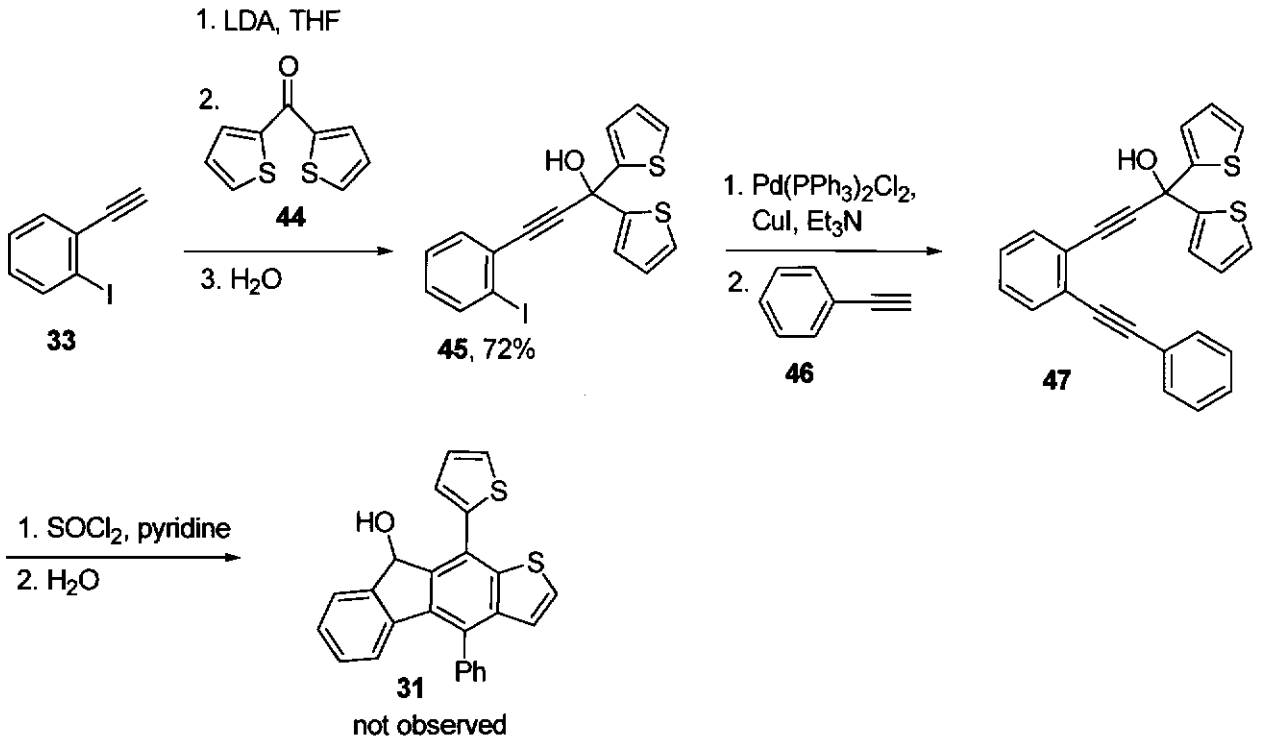
earlier for the synthesis of **29**. The subsequent Sonogashira coupling reaction of **41** with 2-ethynylthiophene at room temperature for 24 hours produced **30** in a single operation. An initial formation of **42**, which in the presence of potassium hydroxide was transformed to the benzannulated enyne-allene **43,** occurred at room temperature. The subsequent Schmittel cyclization reaction then led to **30**. The ^{1}H NMR spectrum of **30** in $CDCl_3$ showed a singlet at δ 3.87 which is indicative of the methylene hydrogens on the five-membered ring of the benzofluorenyl molecule. Again, the hydrogen at the C4 position, which experiences the shielding effect of the thienyl group appears at δ 6.68. The observation of a relatively broad aromatic hydrogen signal at δ 7.47 suggests that the rates of rotations around the C-C bonds attaching to the phenyl and the thiophene groups to the benzofluorenyl system are relatively slow on the NMR scale. As a result, the ^{1}H NMR signal of the ortho hydrogens on the phenyl substituents is broadened.



Scheme 8. Synthesis of benzofluorene **30**

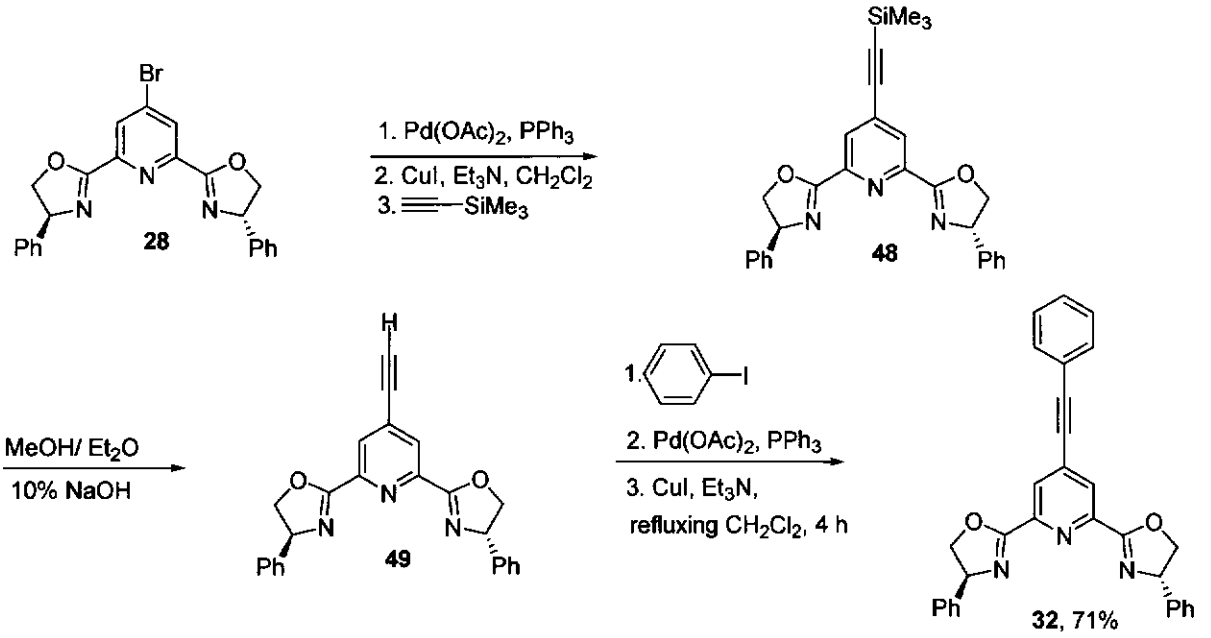
2.3. Development of a synthetic route for 31

Attempted development of **31** using a similar procedure as described for **29** was unsuccessful (Scheme 9). However, the first two steps of the synthetic scheme were successful. The synthetic sequence outlined in Scheme 9 involved condensation of the acetylide generated from **33** with di-2-thienyl ketone (**44**), to give the corresponding propagylic alcohol **45** in good yields. Attempts to reduce **45** with triethylsilane in the presence of trifluoroacetic acid was unable to produce the expected product. Coupling **45** with phenylacetylene (**46**) using the Sonogashira protocol was successful. Unfortunately, treatment of **47** with thionyl chloride failed to produce **31** in contrast to what was observed in other related systems.



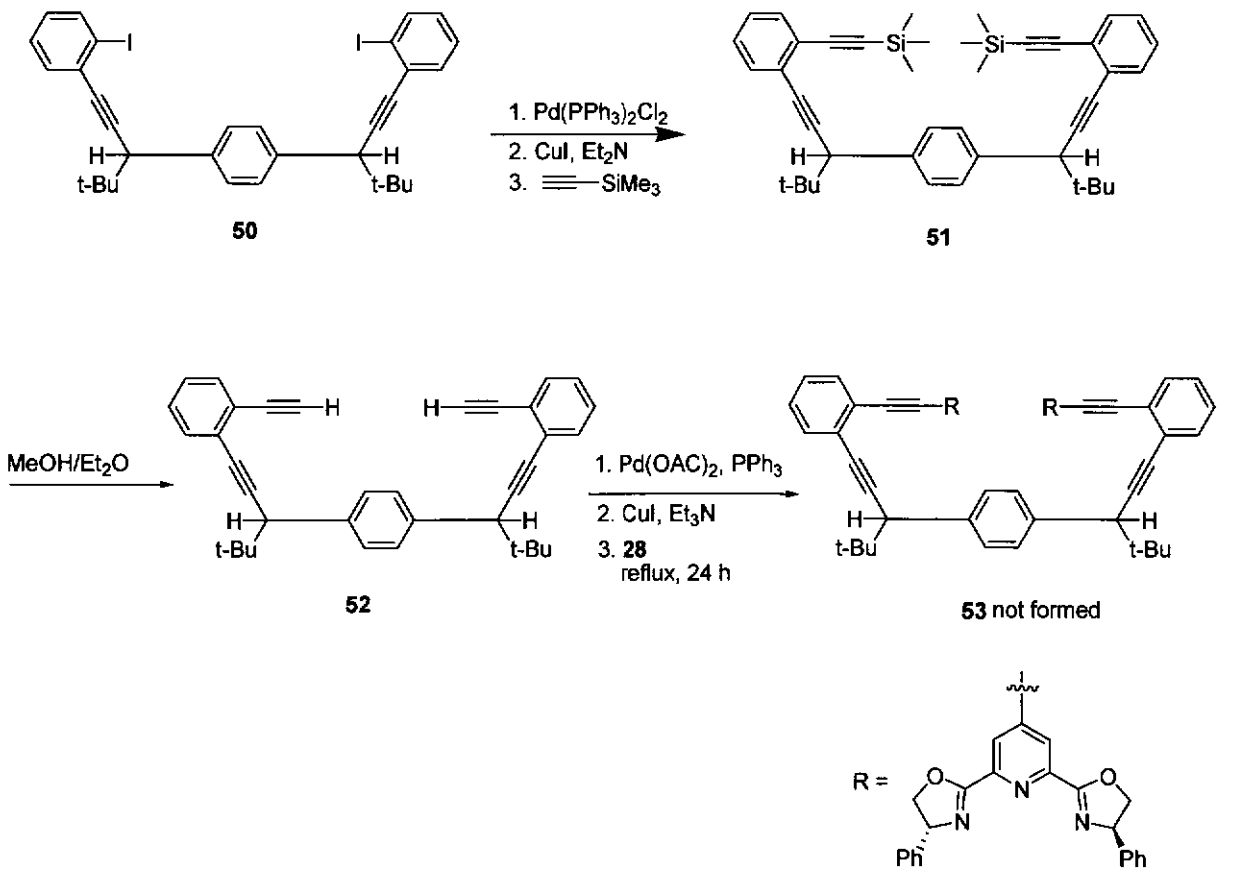
Scheme 9. Proposed synthetic route for **31**

We first tested the feasibility of the Sonogashira reaction of **28** with phenylacetylene to give **32** and it was successful. Alternatively, the Sonogashira reaction of **28** to form **48** followed by a second Sonogashira reaction of **49**[28] and iodobenzene was also successful in producing **32** (Scheme 10).



Scheme 10. Synthesis of a derivative of a pybox ligand **32**

We then investigated the possibility of using pybox as substituents at the alkyne termini of **52** for the cascade cyclization reaction as shown in Scheme 11. However an attempt to synthesize **53** using **28** for the Sonogashira reaction was unsuccessful.



Scheme 11. Preparation of pybox **28**

3. CONCLUSION

Two benzofluorenes, 10-(1,1-dimethylethyl)-5-thienyl-11H-benzo[b]fluorene and 10-phenyl-5-thienyl-11H-benzo[*b*]fluorene, bearing thienyl substituents were synthesized via the corresponding benzannulated enyne-allenes. The structure of **29** was established by X-ray crystallographic structure analysis. The Schmittel cyclization protocol was found to be efficient in producing benzofluorenyl systems bearing thienyl substituents. Success in the Sonogashira reaction between 2,6-bis[(4*R*)-4,5-dihydro-4-phenyl-2-oxazolyl]-4-ethynylpyridine and iodobenzene forms the basis of including pybox moieties in benzofluorenyl systems.

Thiophene compounds have many useful applications in various areas, including solid

state systems. Pybox compounds have also found applications in asymmetric catalysis. Applications of benzofluorenyl compounds bearing a thiophene substituent as well as pybox bearing compounds await further investigation.

EXPERIMENTAL SECTION

Glassware used for all reactions was dried in an oven (120 °C) for at least 5 hours. All reactions were conducted under a dry nitrogen atmosphere. Anhydrous tetrahydrofuran (THF ≥ 99.9%), diethyl ether (≥ 99.7 %,), potassium *tert*-butoxide, *tert*-butanol, *tert*-butyllithium (1.7 M) in pentane, and lithium diisopropylamine (1.8 M) in THF were purchased from Aldrich. Anhydrous triethylamine (99.7 %), trifluoroacetic acid (99 %), anhydrous dichloromethane (99.9 %), and triethylsilane were purchased from Acros. Di-2-thienyl ketone and 2-iodothiophene were purchased from Alfa Aesar. $Pd(PPh_3)_2Cl_2$ was purchased from Oakwood Products, Inc. Silica gel used for flash column chromatography was purchased from Dynamic Adsorbents. Melting points were uncorrected. ^1H (600 MHz) and ^{13}C NMR (150 MHz) spectra were recorded using $CDCl_3$ as solvent.

Synthesis of propagylic alcohol 34

To a mixture of 1-ethynyl-2-iodobenzene (1.10 g, 4.80 mmol) in 20 mL of THF under a nitrogen atmosphere at 0 °C was added 3.2 mL of a 1.8 M solution of lithium diisopropylamide (LDA) (5.78 mmol). After 30 min of stirring, a solution of pivalophenone (0.78 g, 4.80 mmol) in 40 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 2 h, 50 mL of water was introduced and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over Na_2SO_4, and concentrated. The residue was purified by flash column

chromatography (silica gel/10% THF in hexanes) to produce 1.82 g of **34** (4.6 mmol, 97%) as a yellow oil: IR 3451, 1464, 750 cm^{-1};^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.84 (1 H, dd, *J* = 7.8, 1.2 Hz), 7.44 (3 H, m), 7.32 (2 H, t, *J* = 7.2 Hz), 7.28-7.25 (2 H, m), 6.96 (1 H, ddd, *J* = 7.8, 1.8 Hz), 3.69 (1 H, s), 1.09 (9 H, s); ^{13}C NMR ($CDCl_3$, 150 MHz)δ 142.0, 138.9, 133.3, 129.6, 128.0, 127.9, 127.6, 100.5, 96.3, 87.7, 79.7, 40.1, 25.8; HRMS *m/z* calcd for $C_{19}H_{19}IONa$ (MNa^+) 413.0373, found 413.0379.

Synthesis of compound 35

To a mixture of **34** (0.996 g, 2.55 mmol) and triethylsilane (0.889 g, 7.66 mmol) in 50 mL of dichloromethane was added trifluoroacetic acid (2.619 g, 23.0 mmol). After 1 h of stirring at room temperature, sodium carbonate (1.086 g, 10.2 mmol) was added followed by 25 mL of water. The organic layer was separated, washed with brine and water, dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel/10% diethyl ether in hexanes, R_f = 0.60) to provide 0.887 g (2.37 mmol, 93%) of **35** as a yellow oil: IR 1583, 1264, 737, 704 cm^{-1} ; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.83 (1 H, dd *J* = Hz), 7.43 (3 H, ddd, *J* =), 7.32 (2 H, ddd, *J* =), 7.27-7.24 (2 H, m), 6.96 (1 H, td, *J* =) ^{13}C NMR ($CDCl_3$, 150 MHz); HRMS *m/z* calcd for $C_{19}H_{19}INa$ (MNa^+) 397.0424, found 397.0430.

Synthesis of benzannulated enediyne 37

To 2-[(2-trimethylsilylethynyl)]-thiophene (0.36 g, 2.0 mmol) were added KOH (0.45 g, 8.0 mmol), MeOH (2 mL) and H_2O (0.5 mL). The reaction mixture was stirred for 3 h at room temperature. A mixture of **35** (0.705 g, 1.88 mmol) in THF (6 mL), $Pd(PPh_3)_2Cl_2$ (0.014 g, 0.02 mmol), PPh_3 (0.010 g, 0.04 mmol), CuI (0.004 g, 0.019 mmol), and diisopropylamine (1.0 mL)

in 6 mL of THF and 5.0 mL of toluene was then added via cannula and refluxed for 16 hours. The reaction mixture was then quenched with NH_4Cl solution (20 mL) and extracted with methylene chloride (3x10 mL). The organic layer was separated, washed with a 2 M solution of HCl (20 mL), water and brine, and then dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatograph (silica gel/20% EtOAc in hexanes, $R_f = 0.33$) to produce **37** (1.53 mmol, 81%) as a viscous, dark yellow oil: IR 1264, 736, 704 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.53-7.51 (1 H, m), 7.46-7.43 (3 H, m) 7.29 (1 H, dd, $J = 5.1$, 1.1 Hz), 7.25-7.21 (6 H, m), 7.19 (1 H, dd, $J = 3.7$, 1.1 Hz), 3.70 (1 H, s), 1.06 (9 H, s); ^{13}C NMR ($CDCl_3$, 150 MHz) δ139.1, 132.1, 132.1, 131.9, 129.8, 128.0, 127.6, 127.3, 127.0, 126.6, 126.2, 125.3, 123.4, 119.5, 95.9, 92.3, 85.9, 82.3, 50.6, 35.5, 27.8; HRMS *m/z* calcd for $C_{25}H_{22}S$ (MNa^+), 377.1336 found 377.1339.

Synthesis of 10-(1,1-dimethylethyl)-5-thienyl-11*H*-benzo[*b*]fluorene 29

To **37** (0.400 g, 1.13 mmol) in 20 mL of anhydrous toluene under an argon atmosphere was added potassium *tert*-butoxide (0.281 g, 2.50 mmol) followed by 2-methyl-2-propanol (0.038 g, 0.51 mmol). The reaction mixture was heated under reflux for 6 h. The reaction mixture was then allowed to cool to room temperature, and 10 mL of water and 50 mL of dichloromethane were introduced. The organic layer was separated, dried over sodium sulfate, and concentrated. The crude product was recrystallized from ethanol to yield 0.324 g of **29** (0.91 mmol, 81%) as brown crystals: mp 204-206 ^0C , IR 2955, 764, 730, 701 cm^{-1} ;^1H NMR ($CDCl_3$, 600 MHz) δ 8.61 (1 H, d, $J = 8.9$ Hz), 7.77 (1 H, dd, $J = 8.3$ Hz), 7.50 (1 H, d, $J = 7.5$ Hz), 7.45 (1 H, ddd, $J = 8.2$, 1.5 Hz), 7.37 (1 H, dd, $J = 8.1$, 0.9 Hz), 7.32 (1 H, dd, $J = 5.2$, 5.2 Hz), 7.24 (1 H, dd, $J = 7.5$, 0.9 Hz), 7.09-7.08 (2 H, m), 6.44 (1 H, d, $J = 8.1$ Hz) 4.51 (1 H, s), 1.91 (9 H, s) ^{13}C NMR ($CDCl_3$, 150 MHz) δ 144.3, 142.4, 140.6, 140.2, 139.8, 137.5, 135.7, 131.2, 127.9, 127.8, 127.6,

127.3,127.1 126.6, 126.4, 124.6, 124.5, 123.9, 123.7, 123.5, 40.2,38.9,34.3, 25.9; HRMS *m/z* calcd for $C_{25}H_{23}S$ (MH^+), 355.1514 found 355.1519.

Synthesis of propagylic alcohol 40

To a mixture of 1-ethynyl-2-iodobenzene (0.701 g, 3.07 mmol) in 20 mL of THF under a nitrogen atmosphere at 0 °C was added 2.00 mL of a 1.8 M solution of LDA (3.68 mmol). After 30 min of stirring, a solution of benzophenone (0.56 g, 3.07 mmol) in 40 mL THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 2 h, 50 mL of water was introduced, and the reaction was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography (silica gel/10% THF in hexanes, R_f= 0.33) to produce **40** (1.236 g; 98%) as a yellow oil: IR 7.02 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.87 (1 H, dd, *J* = 7.8, 0.6 Hz), 7.76-7.74 (4 H, m), 7.50 (1 H, dd, *J* = 7.7, 1.6 Hz), 7.35-7.34 (4 H, m) 7.32-7.27 (3 H, m), 7.02 (1H, ddd, *J* = 7.6, 1.7 Hz), 2.94 (1 H, s); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 144.6, 138.3, 133.0, 129.8, 129.0, 128.3, 127.8, 127.7, 126.2, 100.7, 95.2, 89.0, 75.0; HRMS *m/z* calcd for $C_{21}H_{15}IONa$ (MNa^+) 433.0060, found 433.0063.

Synthesis of compound 41

To a mixture of **40** (1.234 g, 3.00 mmol) and triethylsilane (1.52 g, 13.1 mmol) in 50 mL of dichloromethane was added trifluoroacetic acid (3.27 g, 29.0 mmol). After 1 h of stirring at room temperature, sodium carbonate (1.086 g, 10.2 mmol) was added followed by 25 mL of water. The organic layer was separated, washed with brine and water, dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by flash column chromatography

(silica gel/10% diethyl ether in hexanes, R_f = 0.60) to provide 1.06 g of **41** (2.70 mmol, 90%) as a yellow oil: IR 1658, 1492, 1463, 1277, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.84 (1 H, dd, *J* = 8.4, 0.6 Hz), 7.82-7.80 (1 H, m), 7.60 (1 H, tt, *J* = 7.5, 1.3 Hz), 7.61-7.45 (4 H, m), 7.46 (1 H, dd, *J* = 7.7, 1.6 Hz), 7.35-7.32 (3 H, m), 7.28 (1 H, ddd, *J* = 7.6, 1.3 Hz), 7.24 (2 H, tt, *J* = 7.4, 1.2 Hz), 6.98 (1 H, ddd, *J* = 7.2, 1.8 Hz), 5.22 (1 H, s); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 141.3, 138.6, 132.8, 130.1, 129.1, 128.6, 128.1, 127.7, 126.9, 100.9, 94.1, 86.9, 44.0; HRMS *m/z* calcd for $C_{21}H_{16}I$ (MH^+) 395.0291, found 395.0287.

Synthesis of 10-phenyl-5-thienyl-11*H*-benzo[*b*]fluorene 30

To 2-[2-(trimethylsilyl)ethynyl]-thiophene (0.32 g, 1.8 mmol) were added KOH (0.404 g, 7.2 mmol), water (0.5 mL) and methanol (2 mL). After 3 h at room temperature, a mixture of degassed **41**, $Pd(PPh_3)_2Cl_2$ (0.014 g, 0.020 mmol), PPh_3 (0.010 g, 0.040 mmol), CuI (0.036 g, 0.019 mmol), diisopropylamine (1.0 mL) and toluene (5.0 mL) was added via cannula. After 16 h at room temperature, saturated ammonium chloride solution (20 mL) was then added. The organic layer was separated and extracted with methylene chloride (3x10 mL), washed with a 2 M solution of HCl (20 mL), water and brine and, dried over $Na_2SO_4$and concentrated. The crude product was recrystallized from ethanol to yield 0.511 g of **30** (1.36 mmol, 91%) as brown crystals: IR 1369, 1029, 762, 725, 701 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.82 (1 H, dd, *J* = 8.3, 0.7 Hz), 7.67-7.65 (2 H, m), 7.60-7.57 (2 H, m), 7.52 (1 H, tt, *J*= 7.4, 1.3 Hz), 7.47 (2 H, d, 3.3), 7.45-7.43 (2 H, m), 7.4-7.38 (1 H, m), 7.36 (1 H, dd, *J* = 5.3, 3.4 Hz), 7.25 (2 H, ddd, *J* = 7.3, 1.0 Hz) 7.19 (1 H, dd, *J* = 3.4, 2.0 Hz), 7.14 (1 H, ddd, *J* = 7.9, 0.8 Hz), 6.68 (1 H, d, *J* = 7.9 Hz), 3.87 (2 H, s); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 144.4, 141.0, 139.4, 139.3, 139.0, 136.4,

134.3, 131.4, 129.8, 128.7, 127.9, 127.4, 126.7, 126.7, 126.1, 125.7, 125.5,125.4, 124.8, 124.7, 123.8, 36.6; HRMS *m/z* calcd for $C_{27}H_{18}S(MNa^{+})$ 397.1021, found 397.1023.

Synthesis of propagylic alcohol 45

To a mixture of 1-ethynyl-2-iodobenzene (0.775 g, 3.34 mmol) in 20 mL of THF under a nitrogen atmosphere at 0 °C was added 2.26 mL of a 1.8 M solution of LDA (4.08 mmol). After 30 min of stirring, a solution of di-2-thithienyl ketone (0.66 g, 3.40 mmol) in 40 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 2 h, 50 mL of water was introduced, and the reaction mixture was extracted with dichloromethane. The combined organic extracts were washed with brine and water, dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography (silica gel/20% THF in hexanes) to produce 0.688 g **45** (1.63 mmol; 72 %) as a dark oil: IR 1462, 1230, 1015, 837 735, 753, 697 cm^{-1}; ^{1} H NMR ($CDCl_3$, 600 MHz) 7.86 (1 H, d, J =7.9 Hz), 7.52 (1 H, dd, J = 7.6, 1.5 Hz), 7.35-7.30 (5 H, m), 7.04 (1 H, ddd, J = 7.9, 1.6 Hz), 6.98 (2 H, dd, J = 5.0, 3.7 Hz), 3.31 (1 H, s); ^{13}C NMR ($CDCl_3$, 150 MHz)δ 148.8, 138.8, 133.1, 130.1, 128.5, 127.8, 126.5, 126.1, 125.8, 100.6, 93.6, 88.0, 70.1; HRMS *m/z* calcd for $C_{17}H_{11}IOS_2Na$ (MNa^{+}) 444.9188, found 444.9191.

Synthesis of benzannulated enediynyl alcohol 47

To a mixture of **45** (0.300 g, 0.71 mmol), $Pd(PPh_3)_2Cl_2$ (0.03g, mmol), and CuI (0.003 g, mmol) in 20 mL of triethylamine under a nitrogen atmosphere was added via cannula a solution of phenylacetylene (0.075 g, 0.71 mmol) in 10 mL of triethylamine. The resulting mixture was allowed to react for 12 h at room temperature and washed with water, then brine and extracted with dichloromethane (3x10 mL). The organic layer was separated, dried over sodium sulfate,

and concentrated. The residue was purified by flash column chromatography (silica gel/20% EtOAc in hexanes, R_f = 0.53), to provide **47** as a dark solution: IR 3526, 1494, 1231, 1024, 756, 702, 691 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.57-7.54 (2 H, m), 7.43-7.41 (2 H, m), 7.36-7.28 (2 H, m), 7.25 (2 H, dd, *J* = 5.1, 1.3 Hz), 7.84 (2 H, dd, *J* = 5.1, 3.7 Hz), 3.28 (1 H, s); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 149.1, 132.3, 132.0, 131.8, 128.7, 128.5, 128,3, 128.0, 126.5, 126.1, 126.0, 125.8, 124.3,123.0, 94.0, 88.0, 85.0, 70.1; HRMS *m/z* calcd for $C_{25}H_{16}OS_2Na$ (MNa^+) 419.0535, found 419.0535.

Synthesis of 2,6-bis[(4R)-4,5-dihydro-4-phenyl-2-oxazolyl]-4-ethynylpyridine, 32. To a mixture of iodobenzene (0.150 g, 0.735 mmol), $Pd(OAc)_2$ (0.013 g, mmol), PPh_3 (0.030 g, 0.114 mmol), and CuI (0.003 g, 0.016 mmol) in 3 mL of triethylamine under a nitrogen atmosphere were added via cannula a solution of **49** (0.300 g, 0.668 mmol) in 10 mL of dichloromethane. The resulting mixture was refluxed for 4 h and washed with water and brine and, extracted with dichloromethane (3x10 mL). The combined organic layers were dried over sodium sulfate and concentrated. The residue was recrystallized from hexanes to yield 0.259 g of **32** (0.553 mmol, 83 %) as brown crystals: IR 1265, 736, 705 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 8.44 (2 H, s), 7.52 (2 H, d, J = 6.6 Hz), 7.40-7.30 (13 H, m), 5.48 (2 H, t, *J* = 9.1 Hz), 4.95 (2 H, dd, *J* = 8.8 Hz), 4.45 (2 H, t, *J* = 8.6 Hz); ^{13}C NMR ($CDCl_3$,150 MHz) δ 163.2, 163.0, 147.0, 141.6, 133.4, 132.0, 129.6, 128.8, 128.6, 128.0, 127.8, 126.8, 121.6, 96.0, 85.6, 75.6, 70.3; HRMS *m/z* calcd for $C_{31}H_{24}N_3O_2$ (MH^+) 470.1868, found 470.1860.

REFERENCES

1. Ho, C.-L.; Wong, W.-Y. *Coordination Chemistry Reviews* **2011**, *255*, 2469– 2502.

2. Halik, M.; Klauk, H.; Zschieschang, U.; Schmid, G.; Ponomarenko, S.; Kirchmeyer, S.; Weber, W. *Adv. Mater.*, **2003**, *15*, 917.

3. Breslow, R.; Foss, F. W. Jr. *J. Phys Condens. Matter* **2008**, *20*, 374104

4. Lecle`re, Ph.; Surin, M.; Brocorens, P.; Cavallini,M.; Biscarini, F.; Lazzaroni, R. *Materials Science and Engineering* R **2006**, *55*, 1–56

5. Shaytan, A. K.; Schillinger, E. –K.; Mena-Osteritz, E.; Schmid, S.; Khalatur, P. G.; Bäuerle, P.; Khokhlov, A. R.; *Beilstein J. Nanotechnol.* **2011**, *2*, 525–544

6. Hoofman, R. J. O. M; de Haas, M.; Siebbeles, D. A.; Warmann, J. M. *Nature* **1998**, *392*, 54

7. Perepichka, I. F.; Perepichka, D. F.; Zade, S. S.; Bendikov; M. **2009**

8. Brunetti, F. G.; Kumarb, R.; Wudl, F. *J. Mater. Chem.*, **2010**, 20, 2934–2948

9. Zmija, J.; Malachowski, M. J. *Journal of Acheivements in Materials and Manufacturing Engineering* **2011**, *48*, 14-21

10. Loveday, D. C.; Hmyene, M.; Ferraris, J. P.; *Synthetic Metals* **1997**, *84* 245-246

11. Shiota, N.; Kinuta, T.; Sato, T.; Tajima, N.; Kuroda, R.; Matsubara, Y.; Imai; Y. *Crystal Growth & Design*, **2010**, *10*, 1341–1345

12. (a) Myers, A. G.; Kuo, E. Y.; Finney, N. S. *J. Am. Chem. Soc.***1989**, *111*, 8057-8059. (b) Nagata, R.; Yamanaka, H.; Okazaki, E.; Saito, I. *Tetrahedron Lett.* **1989**, *30*, 4995-4998.

13. Schmittel, M.; Vavilala, C. *J. Org. Chem.* **2005**, *70*, 4865-4868.

14. a) Schmittel, M.; Strittmatter, M.; Kiau, S. *Tetrahedron Lett.* **1995**, *36*, 4975-4978. (b) Schmittel, M.; Strittmatter, M.; Vollmann, K.; Kiau, S. *Tetrahedron Lett.* **1996**, *37*, 99-1002.

15. Li, H.; Yang, H.; Petersen, J. L.; Wang, K. K.; *J. Org. Chem.* **2004**, *69*, 4500-4508.

16. (a) Engels, B.; Lennartz, C.; Hanrath, M.; Schmittel, M.;Strittmatter, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1960-1963. (b) Schmittel, M.; Kiau, S.; Siebert, T.; Strittmatter, M. *Tetrahedron Lett.* **1996**, *37*, 7691-7694.

17. Li, H.; Zhang, H.-R.; Petersen, J. L.; Wang, K. K. *J. Org. Chem.* **2001**, 66, 6662-6668

18. Schmittel, M.; Strittmatter, M.; Vollmann, K.; Kiau, S. *Tetrahedron Lett.* **1996**, *37*, 999-1002.

19. Schmittel, M.; Strittmatter, M.; Kiau, S. *Angew. Chem., Int. Ed.* **1996**, *35*, 1843-1845.

20. Schmittel, M.; Keller, M.; Kiau, S.; Strittmatter, M. *Chem. Eur. J.* **1997**, *3*, 807-816.

21. Schmittel, M.; Maywald, M. *Chem. Commun.* **2001**, 155-156.

22. Wang, K. K. *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany, **2004**; Vol. 2, pp 1091-1126.

23. Dai, W.; Petersen, J. L. and Wang, K. K *J. Org. Chem.* **2005**, *70*, 6647-6652

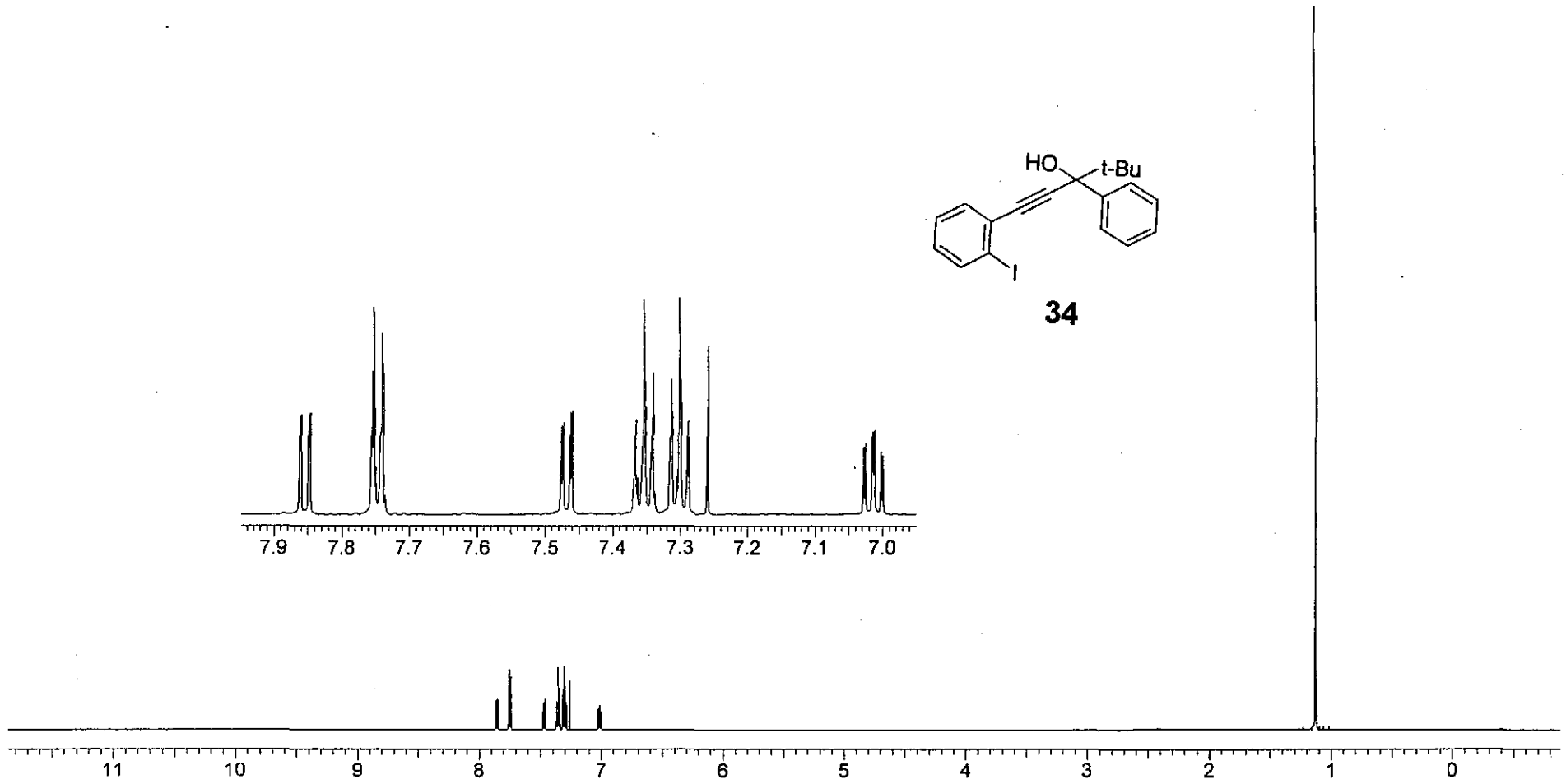
24. Wen, B.; Petersen, J. L. and Wang; K. K *Chem. Commun.* **2010**, *46*, 1938-1940

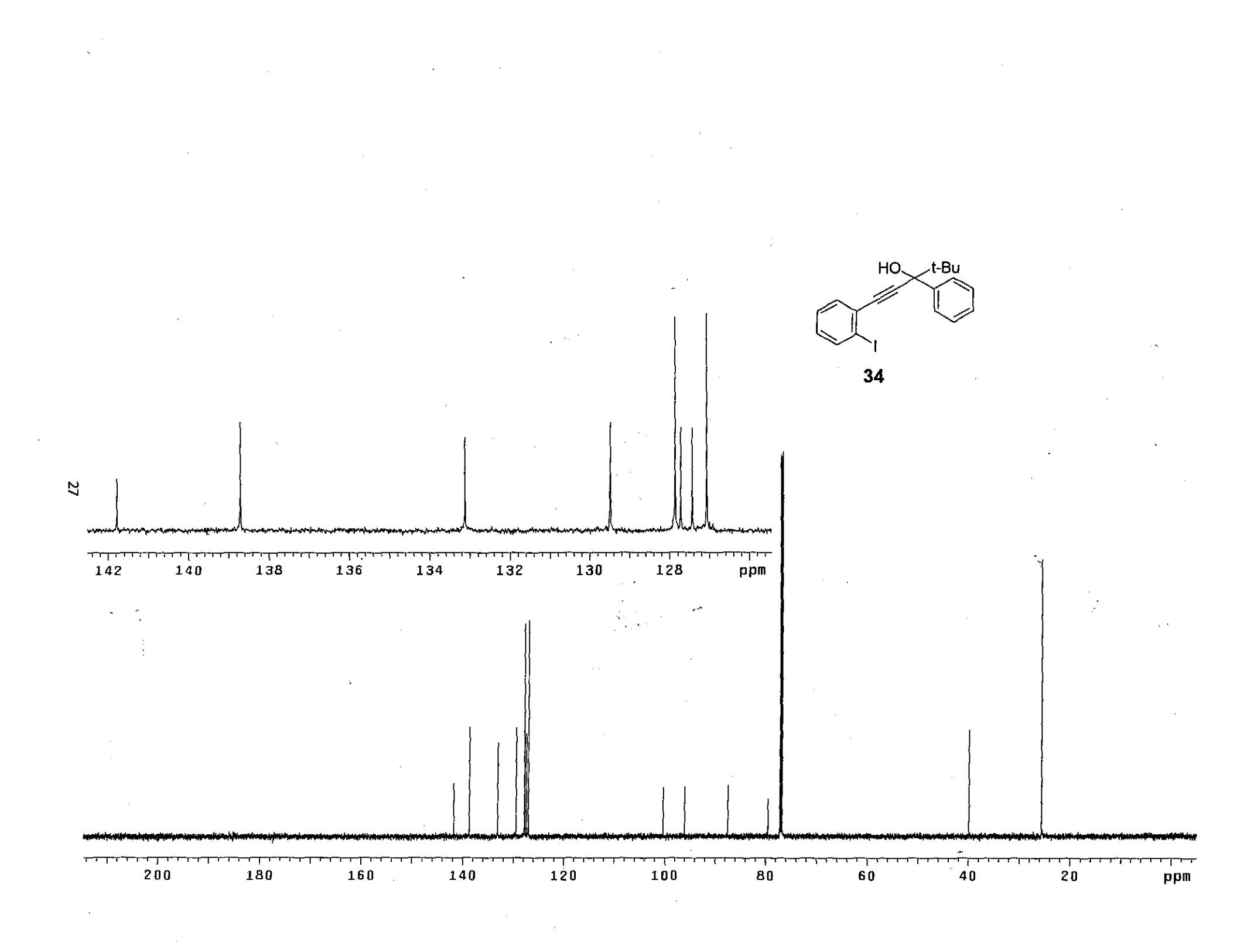
25. Nishiyama, H. *Adv. Catal. Proc.* **1997**, *2*, 153−188. (b) Desimoni, G.; Faita, G.; Quadrelli, P. Chem. Rev. **2003**, *103*, 3119−3154.

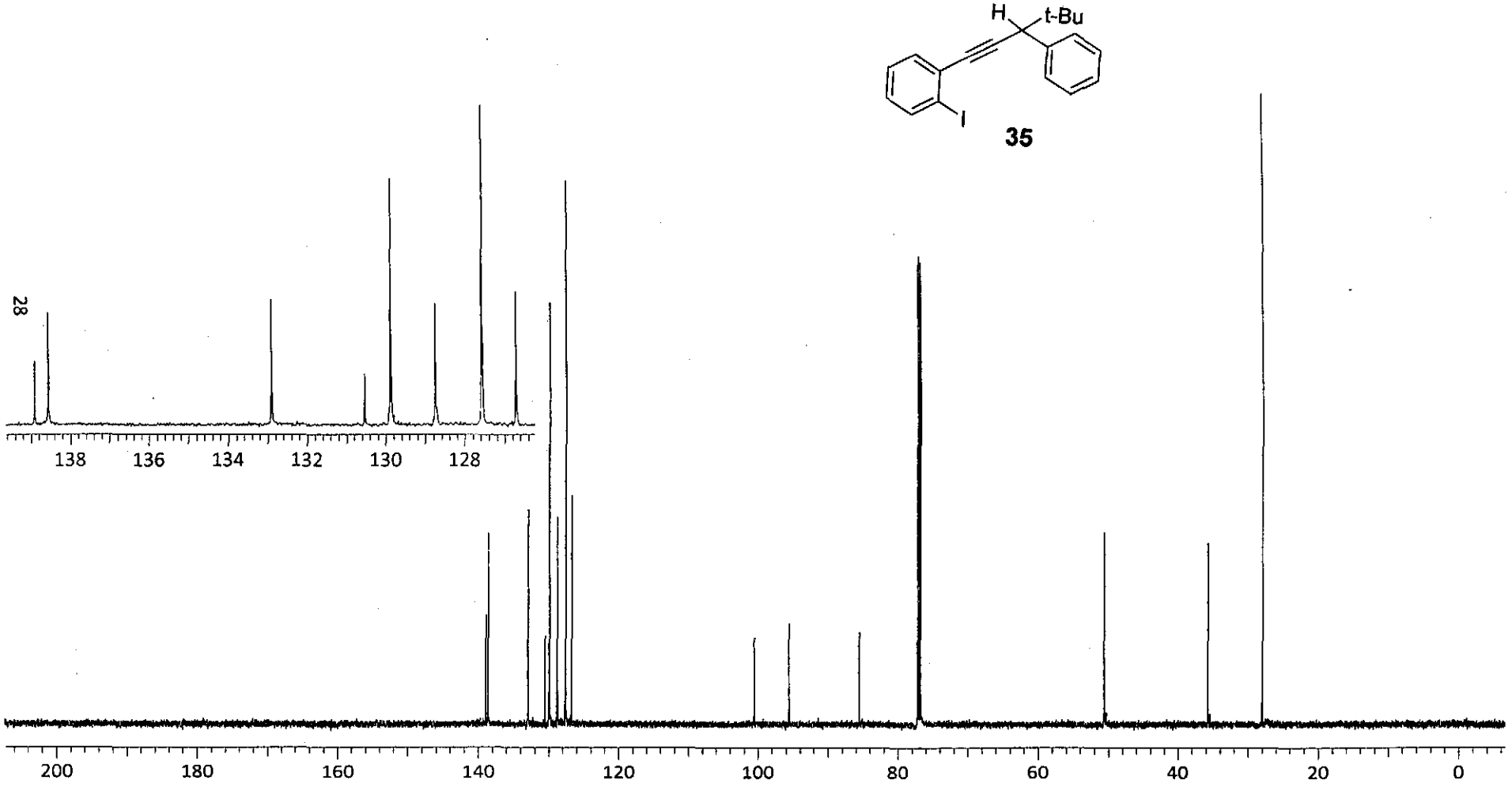
26. (a) Ojima, I. *Catalytic Asymmetric Synthesis*; John Wiley & Sons:New York, 2000. (b) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley & Sons: New York, 1994. (c) Seyden-Penne, J. *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; John Wiley & Sons: New York, 1995

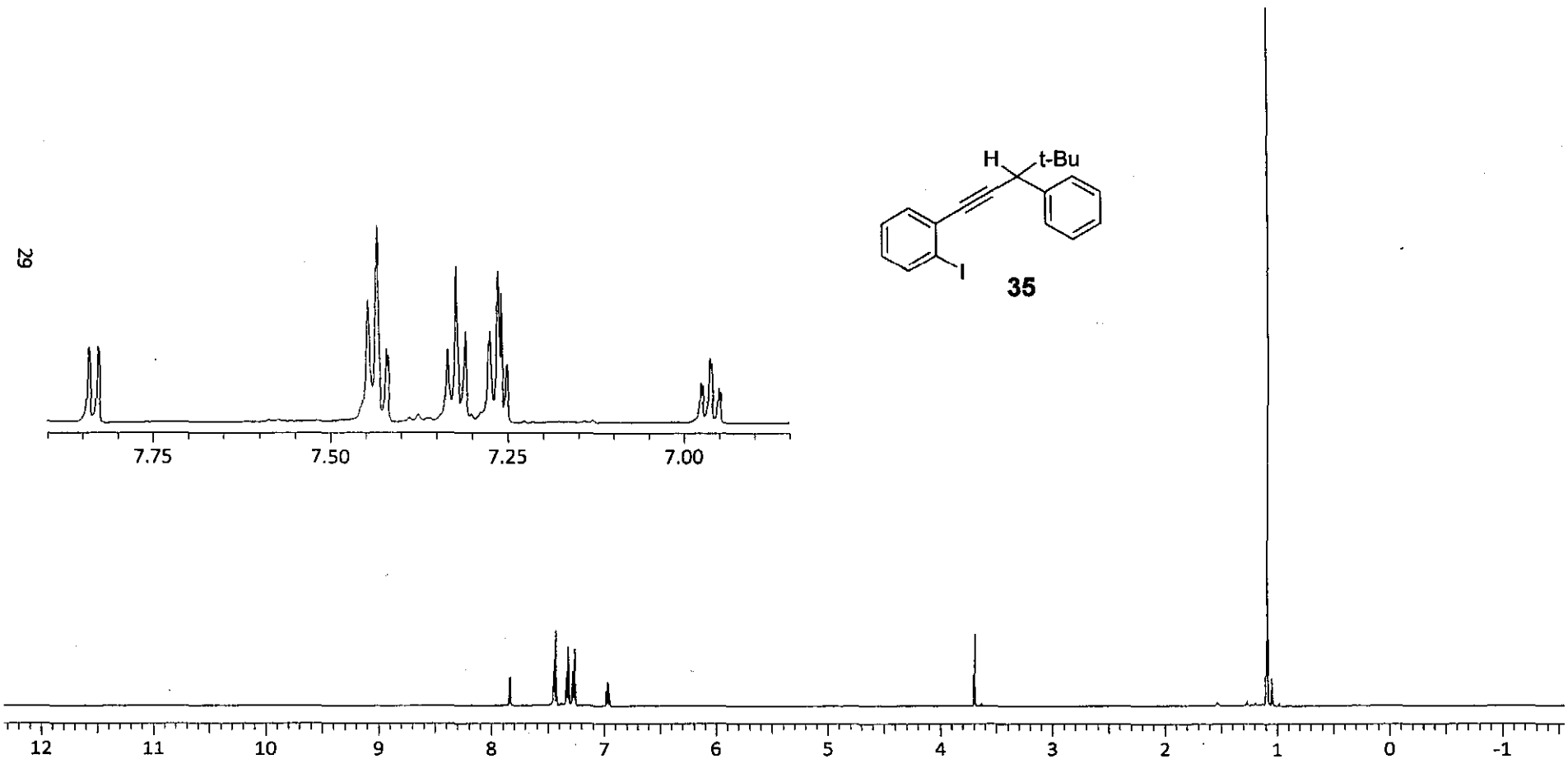
27. Pryor, K. E.; Shipps, G. W., Jr.; Skyler, D. A.; Rebek, J., Jr. *Tetrahedron* **1998**, *54*, 4107-4124.

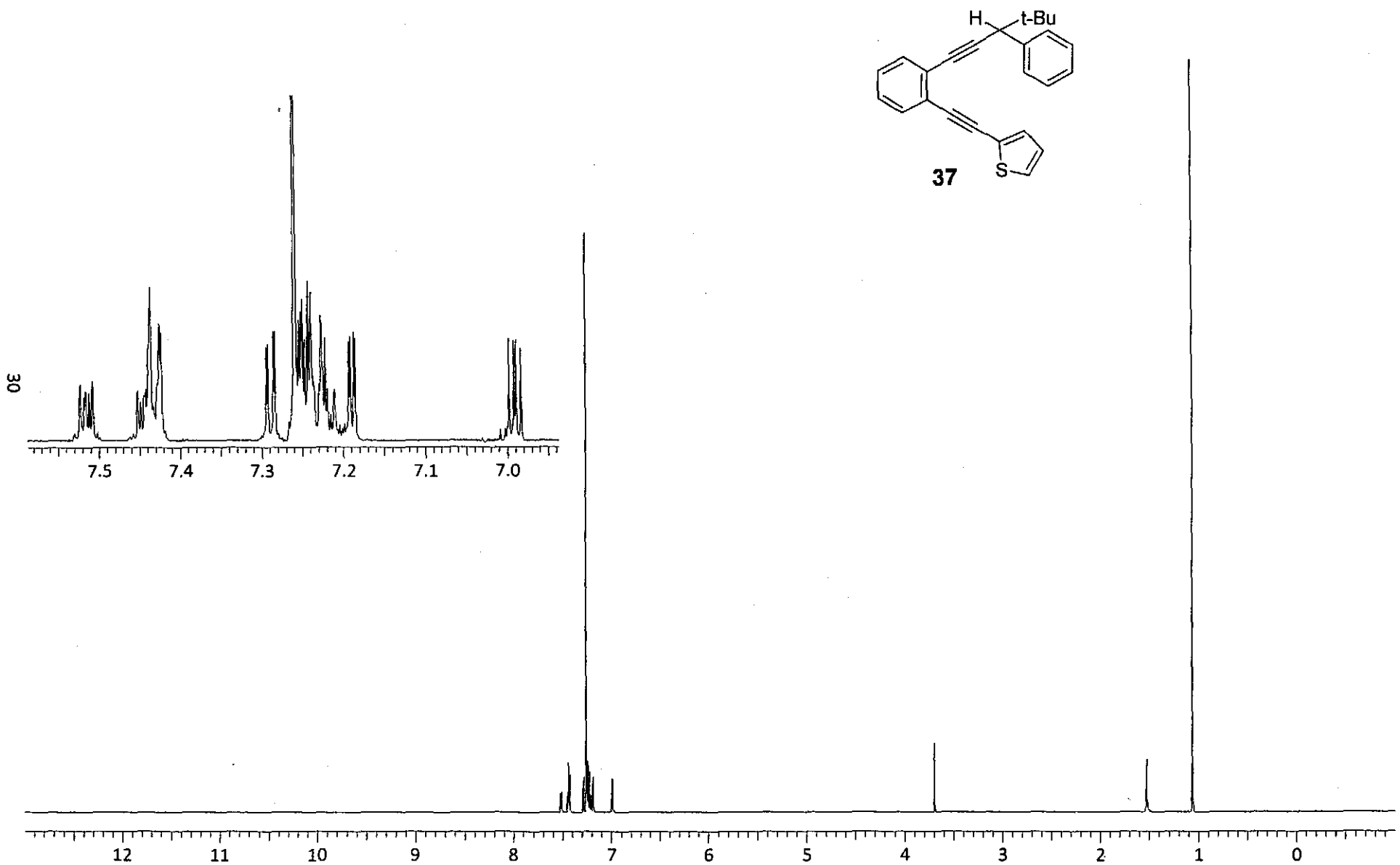
28. Tilliet, M.; Lundgren, S.; Moberg, C.; Levacher, V. *Advanced Synthesis & Catalysis* **2007**, *349*, 2079-2084.

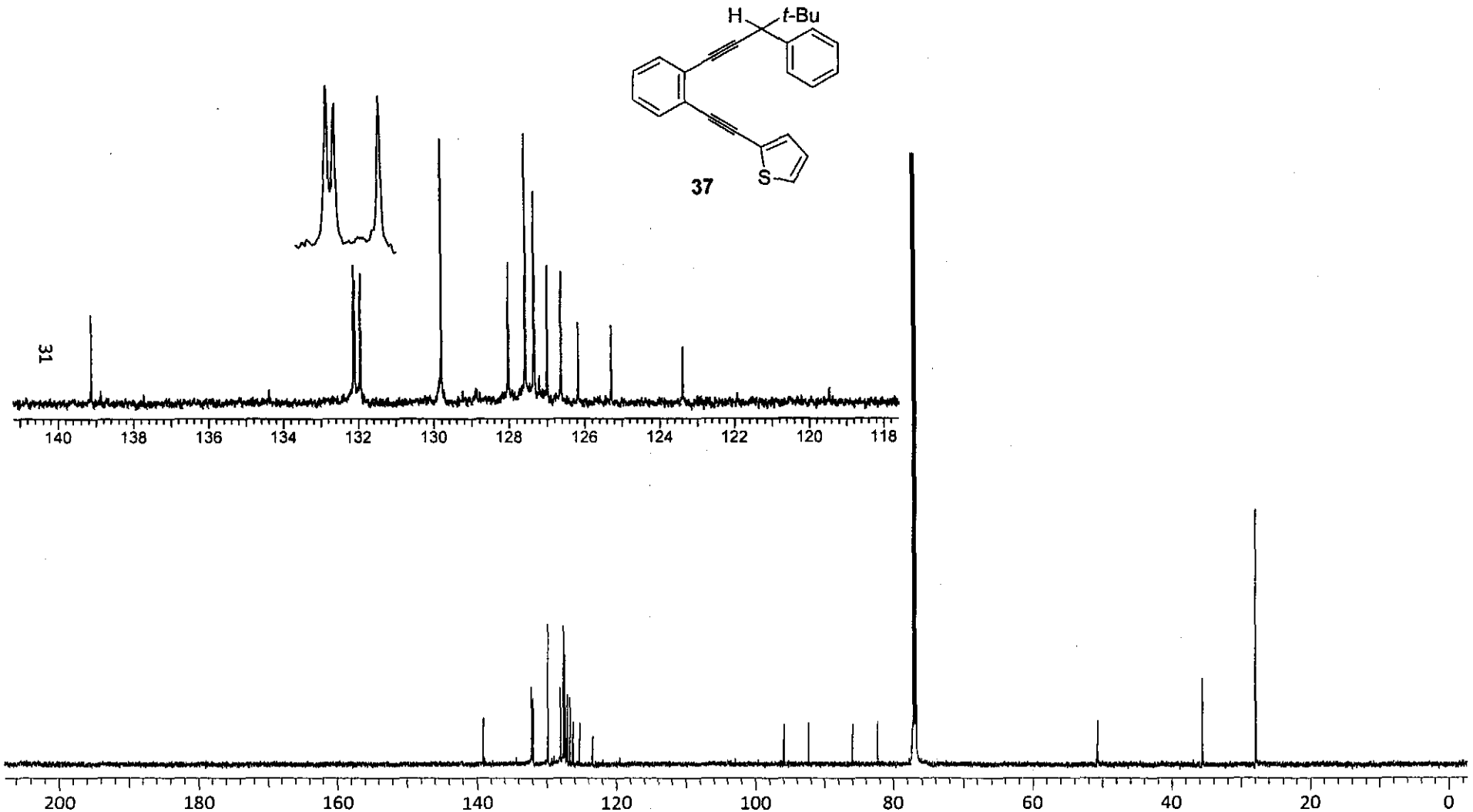

HO
t-Bu
I
34
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
11
10
9
8
7
6
5
4
3
2
1
0

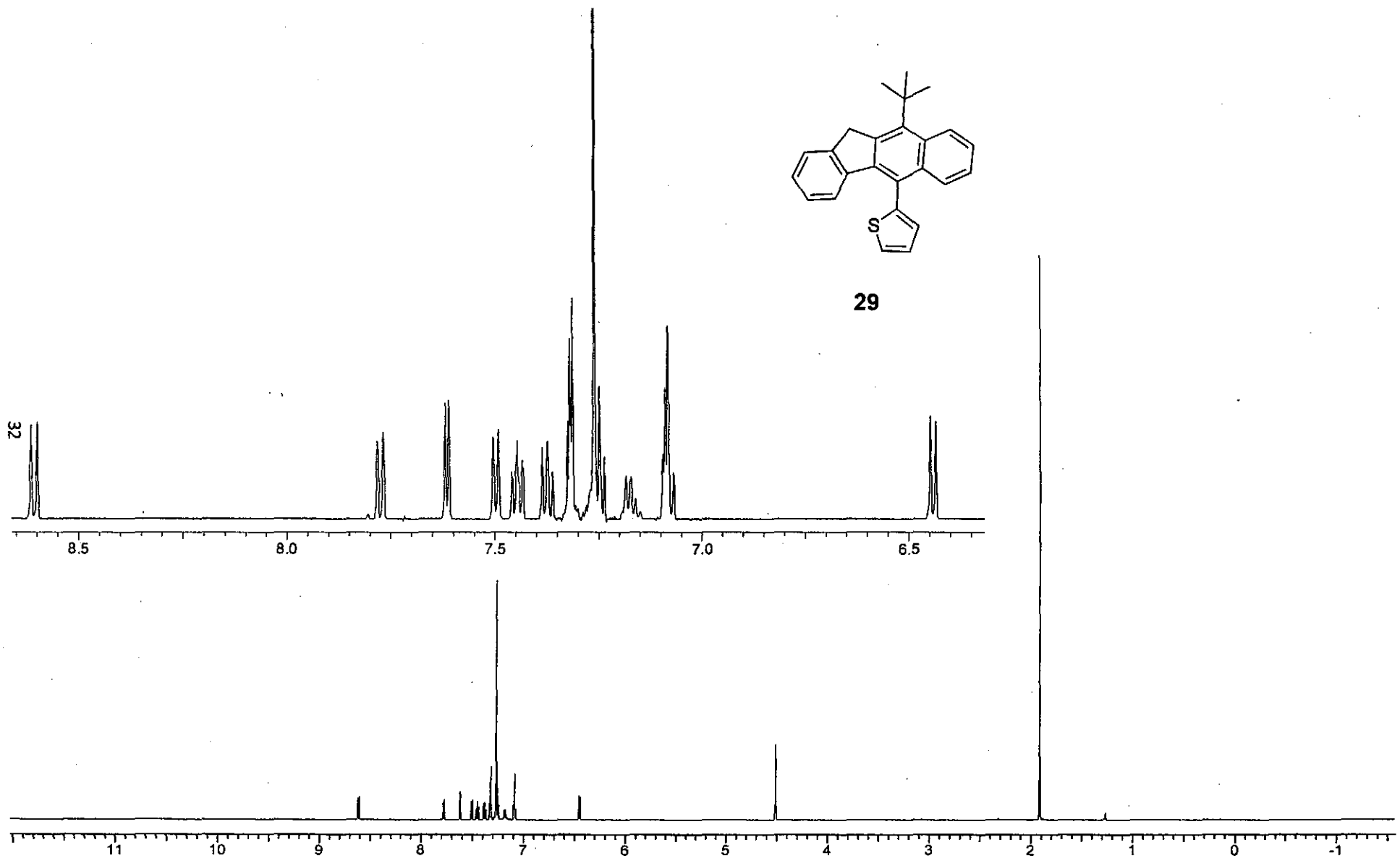

HO
t-Bu
I
34
27
142
140
138
136
134
132
130
128
ppm
200
180
160
140
120
100
80
60
40
20
ppm

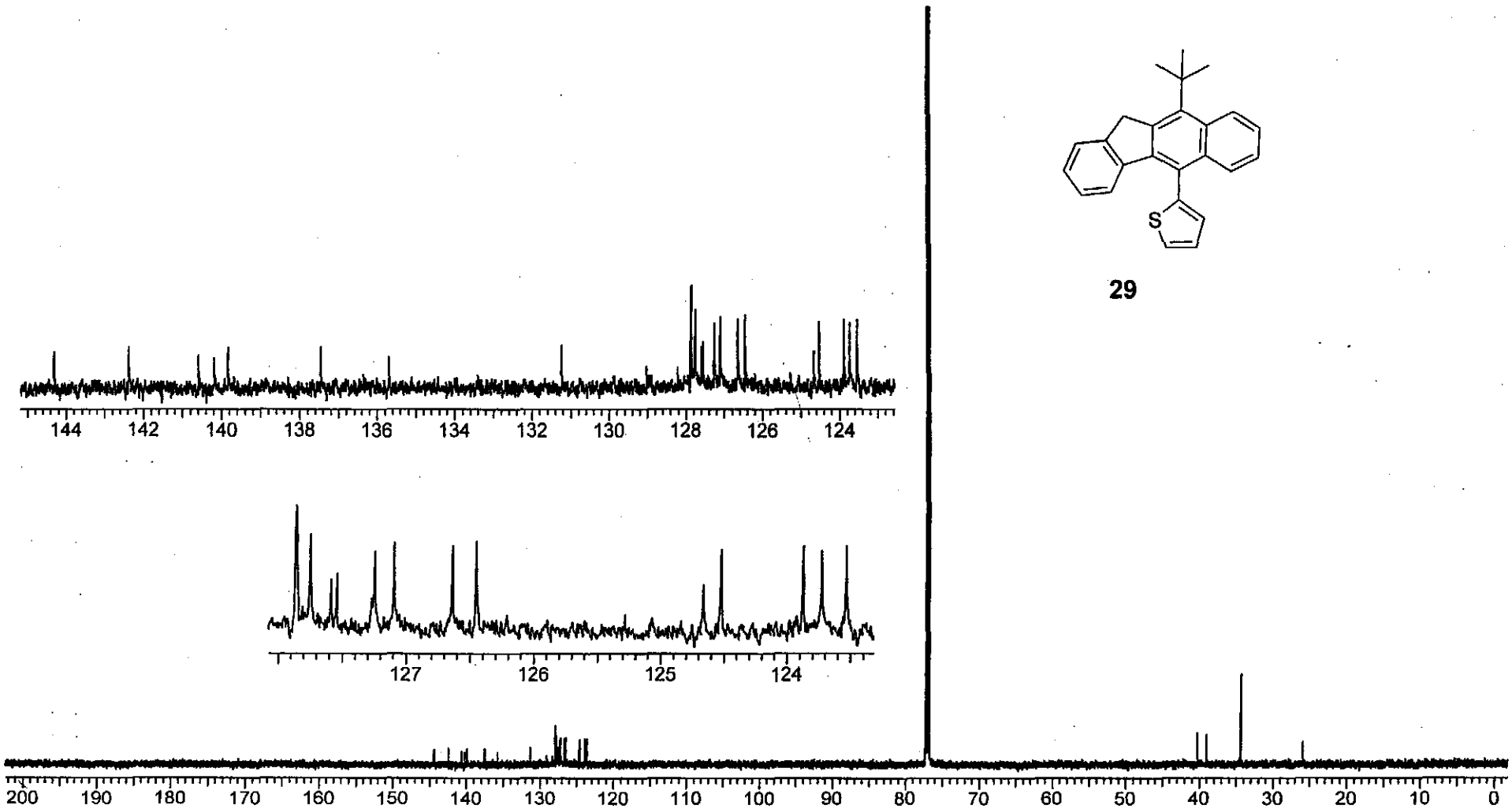

H
t-Bu
I
35
28
138
136
134
132
130
128
200
180
160
140
120
100
80
60
40
20
0


H
t-Bu
I
35
29
7.75
7.50
7.25
7.00
12
11
10
9
8
7
6
5
4
3
2
1
0
-1

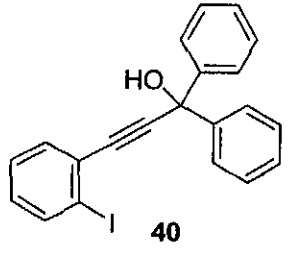

H
t-Bu
S
37
30
7.5
7.4
7.3
7.2
7.1
7.0
12
11
10
9
8
7
6
5
4
3
2
1
0


H
t-Bu
S
37
31
140
138
136
134
132
130
128
126
124
122
120
118
200
180
160
140
120
100
80
60
40
20
0

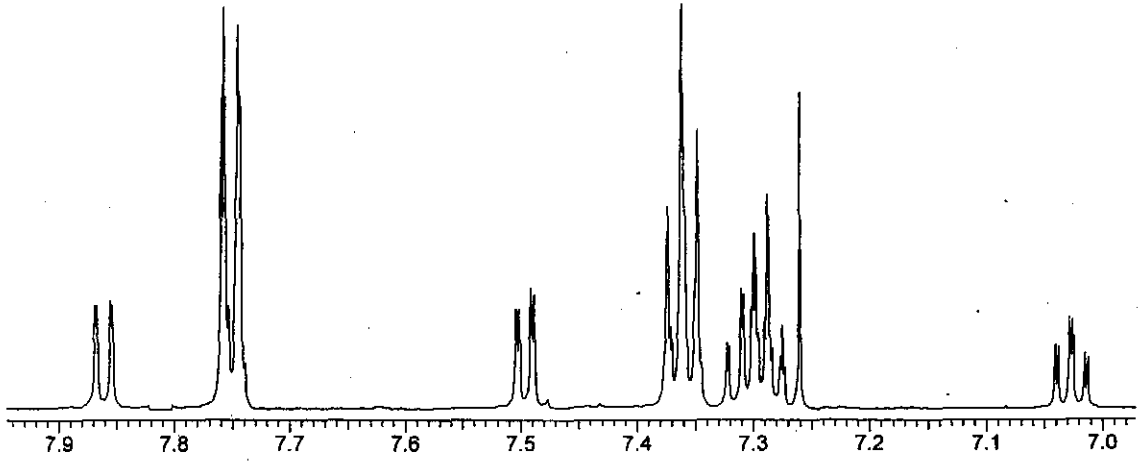

S
29
32
8.5
8.0
7.5
7.0
6.5
11
10
9
8
7
6
5
4
3
2
1
0
-1

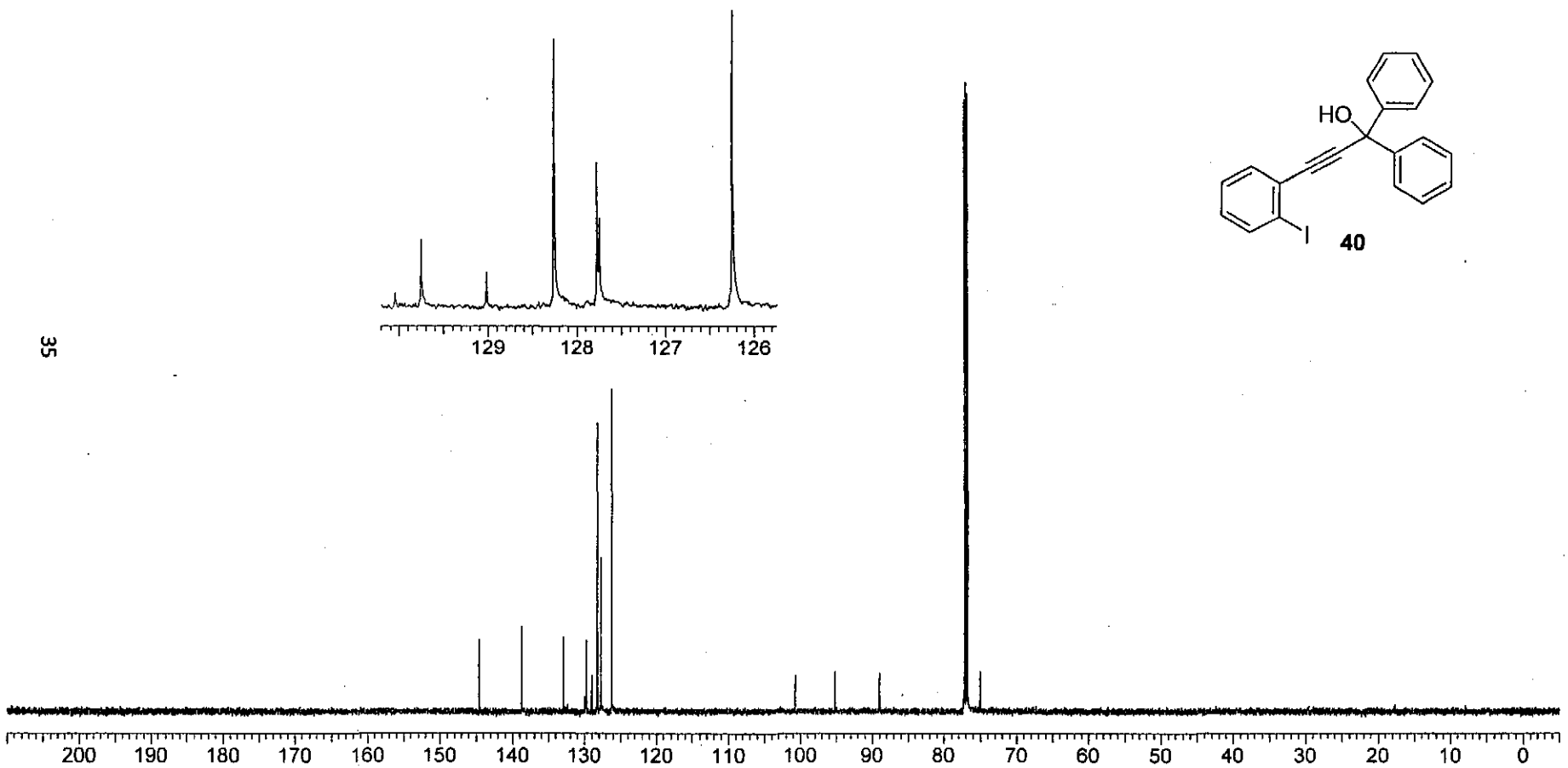

S
144
142
140
138
136
134
132
130
128
126
124
127
126
125
124
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

29



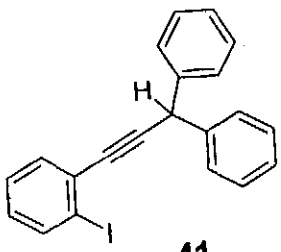
40



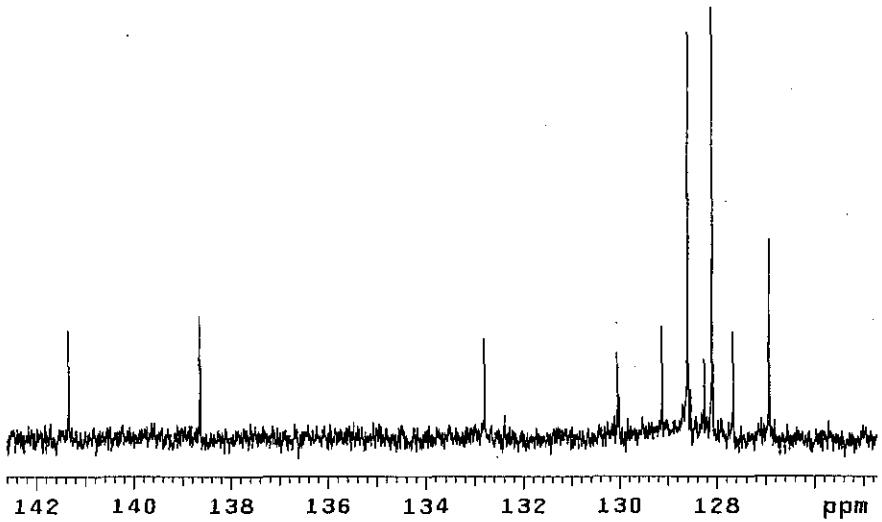

35
129
128
127
126
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

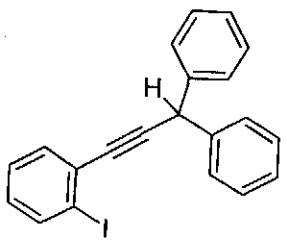
HO
I

40

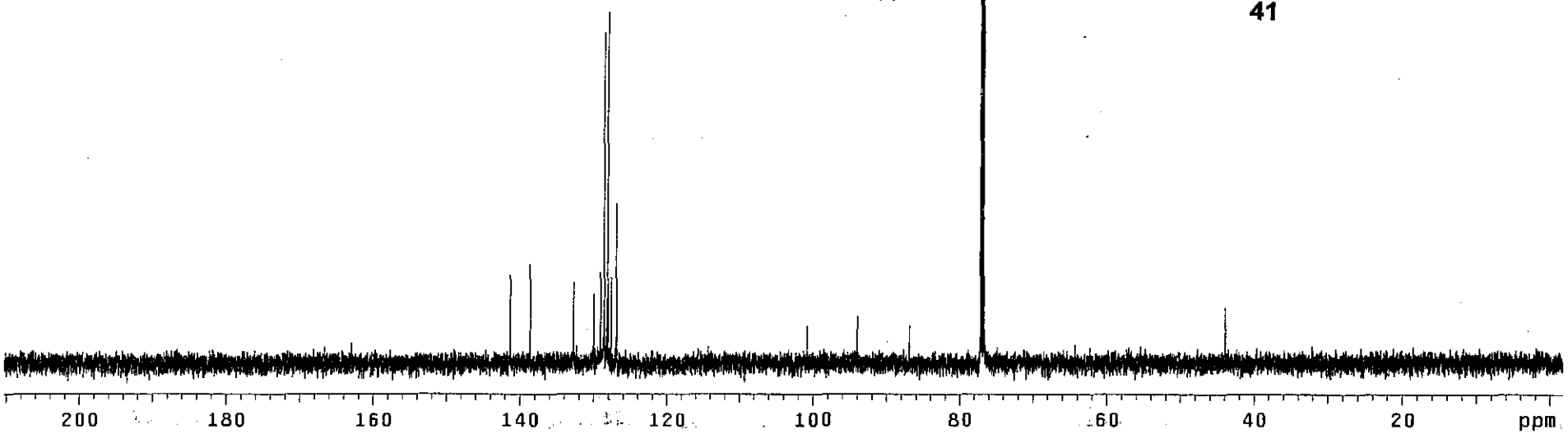


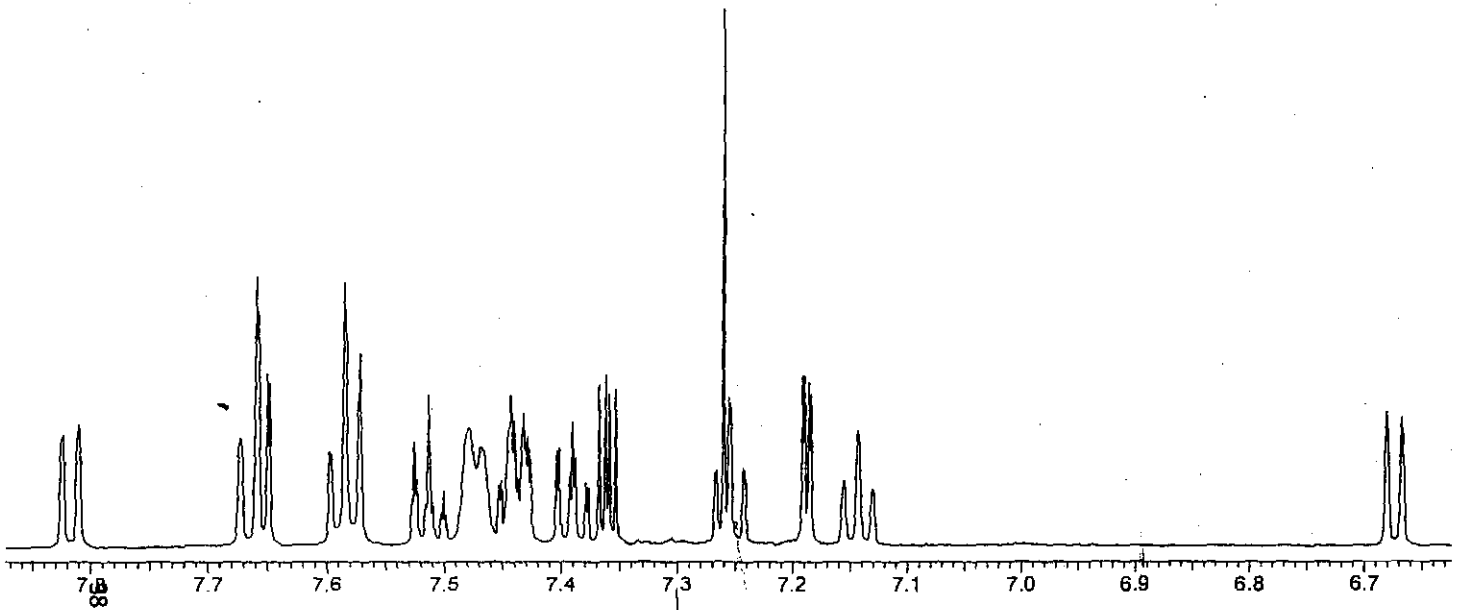
41

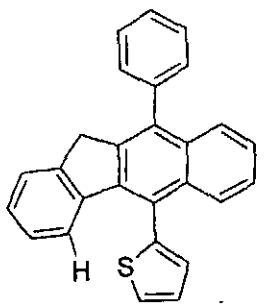

142
140
138
136
134
132
130
128
ppm


H
I

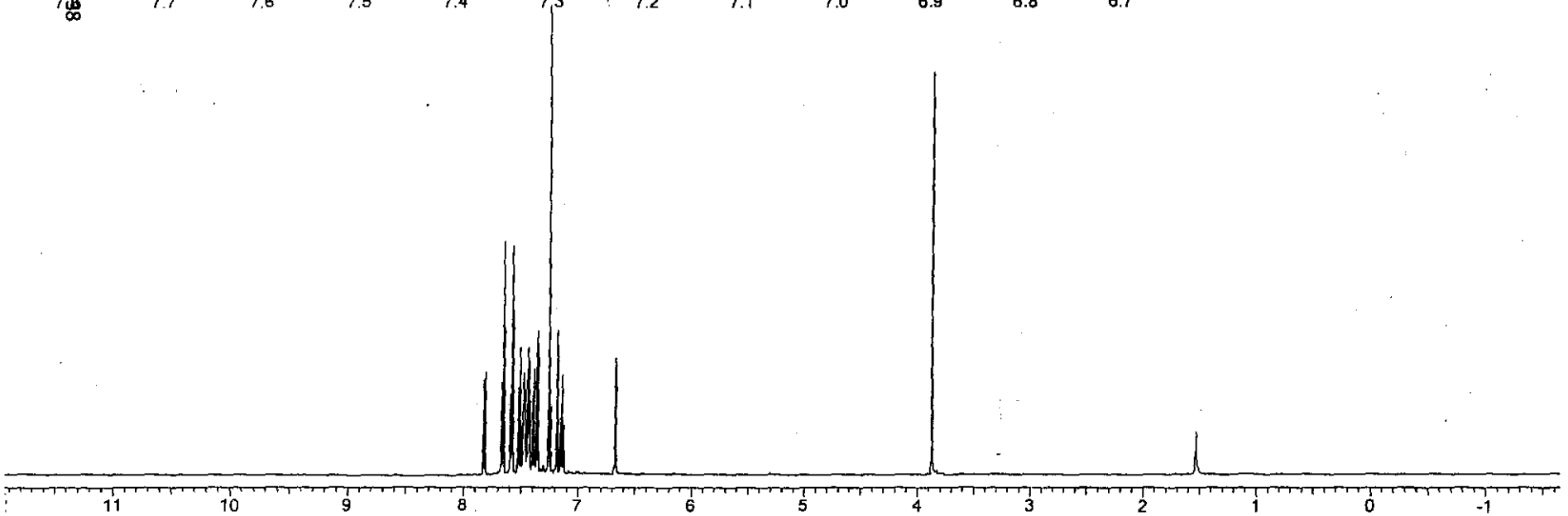
41

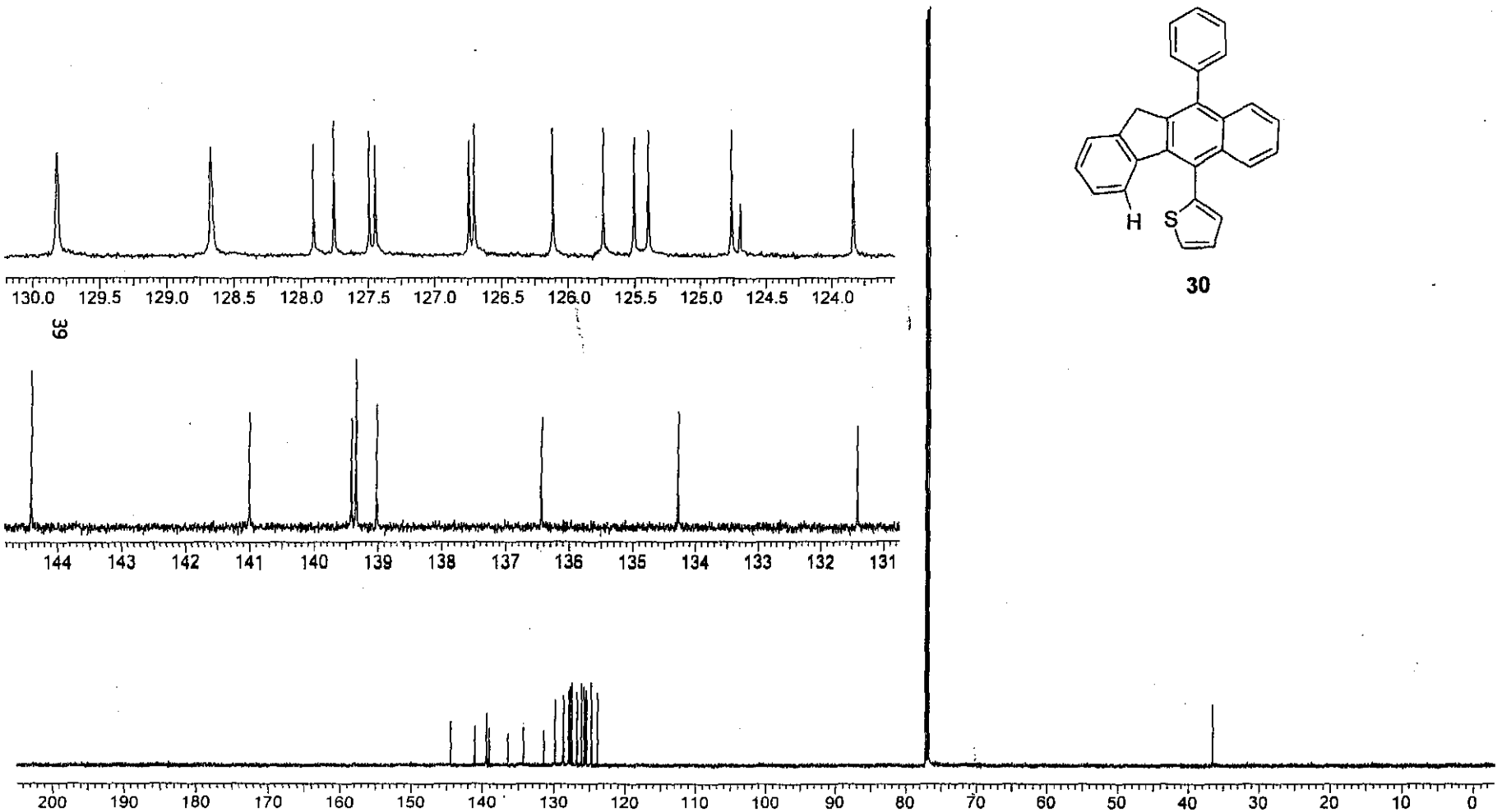

200
180
160
140
120
100
80
60
40
20
ppm

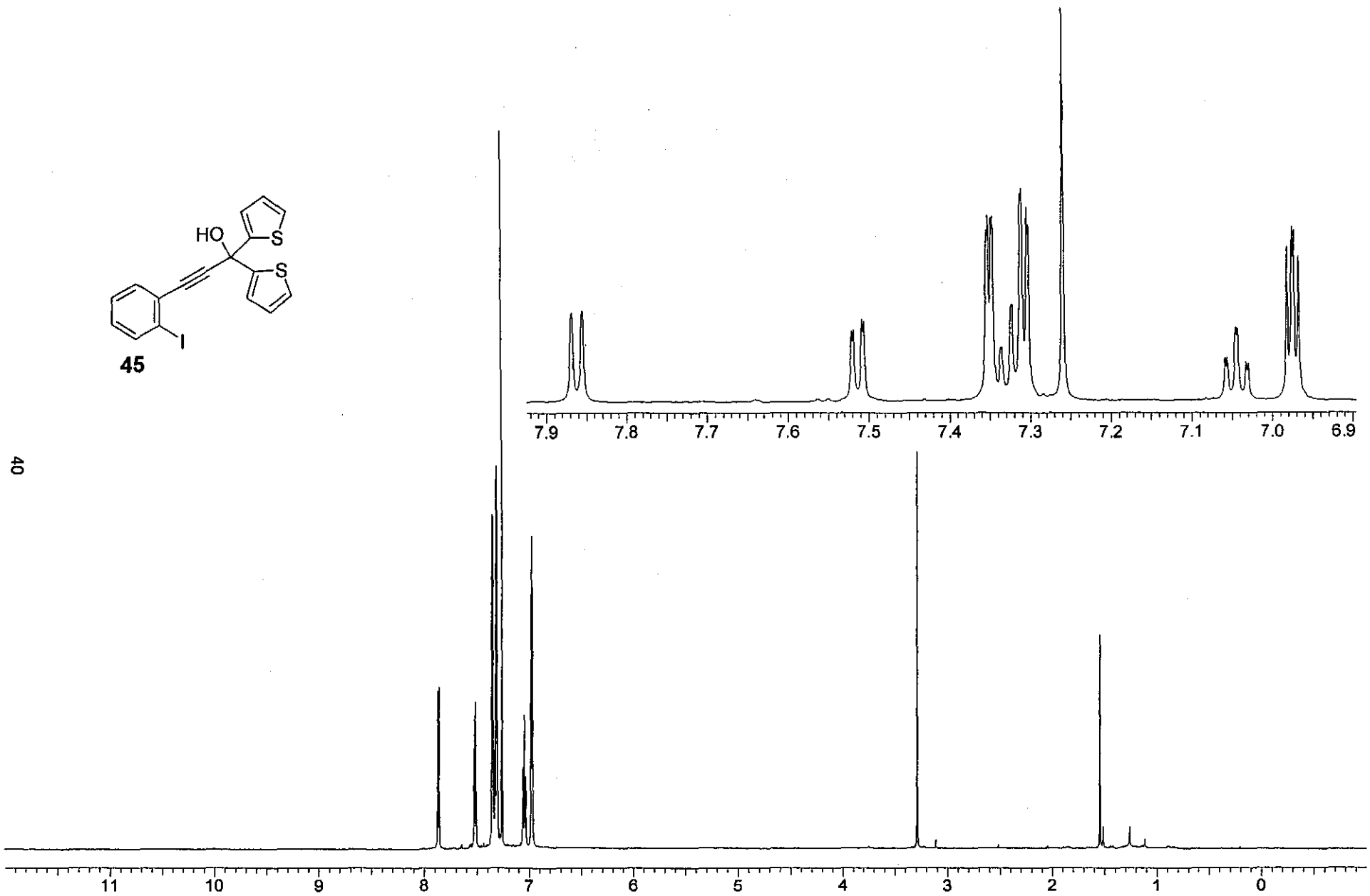


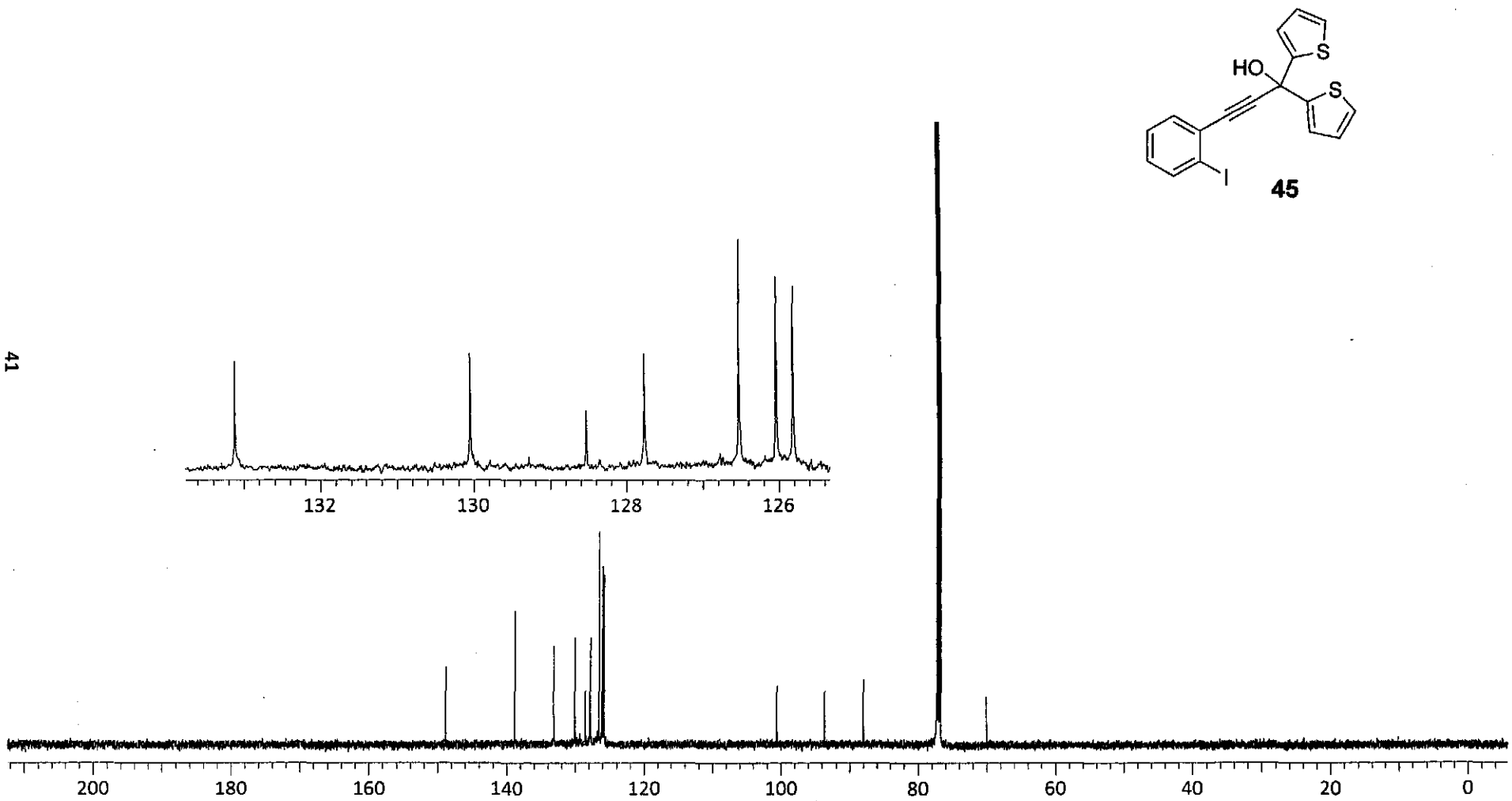


30

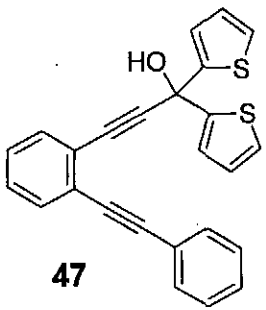



H
S
30
130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5 126.0 125.5 125.0 124.5 124.0
39
144 143 142 141 140 139 138 137 136 135 134 133 132 131
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

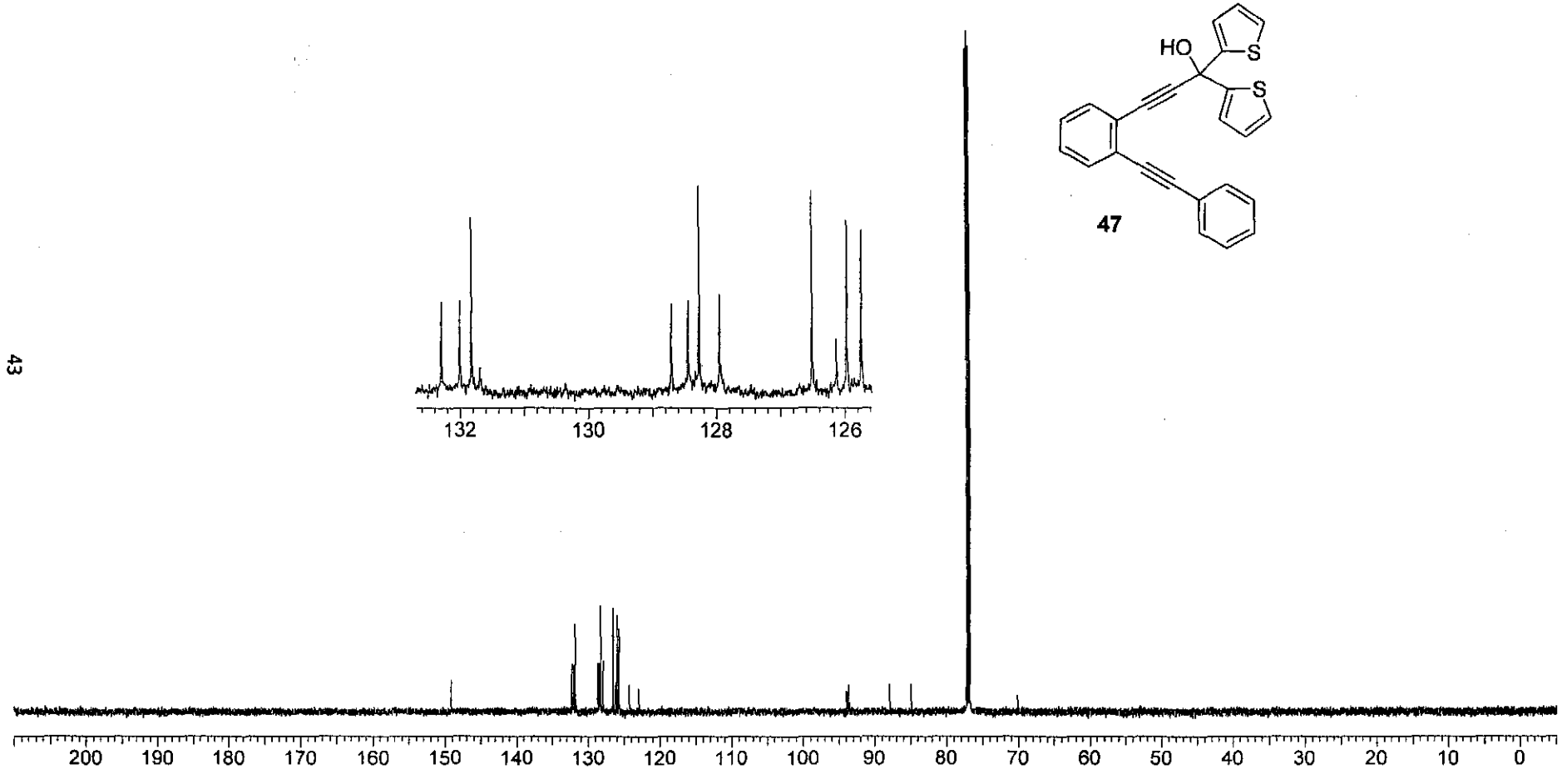

HO
S
S
I
45
40
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
11
10
9
8
7
6
5
4
3
2
1
0

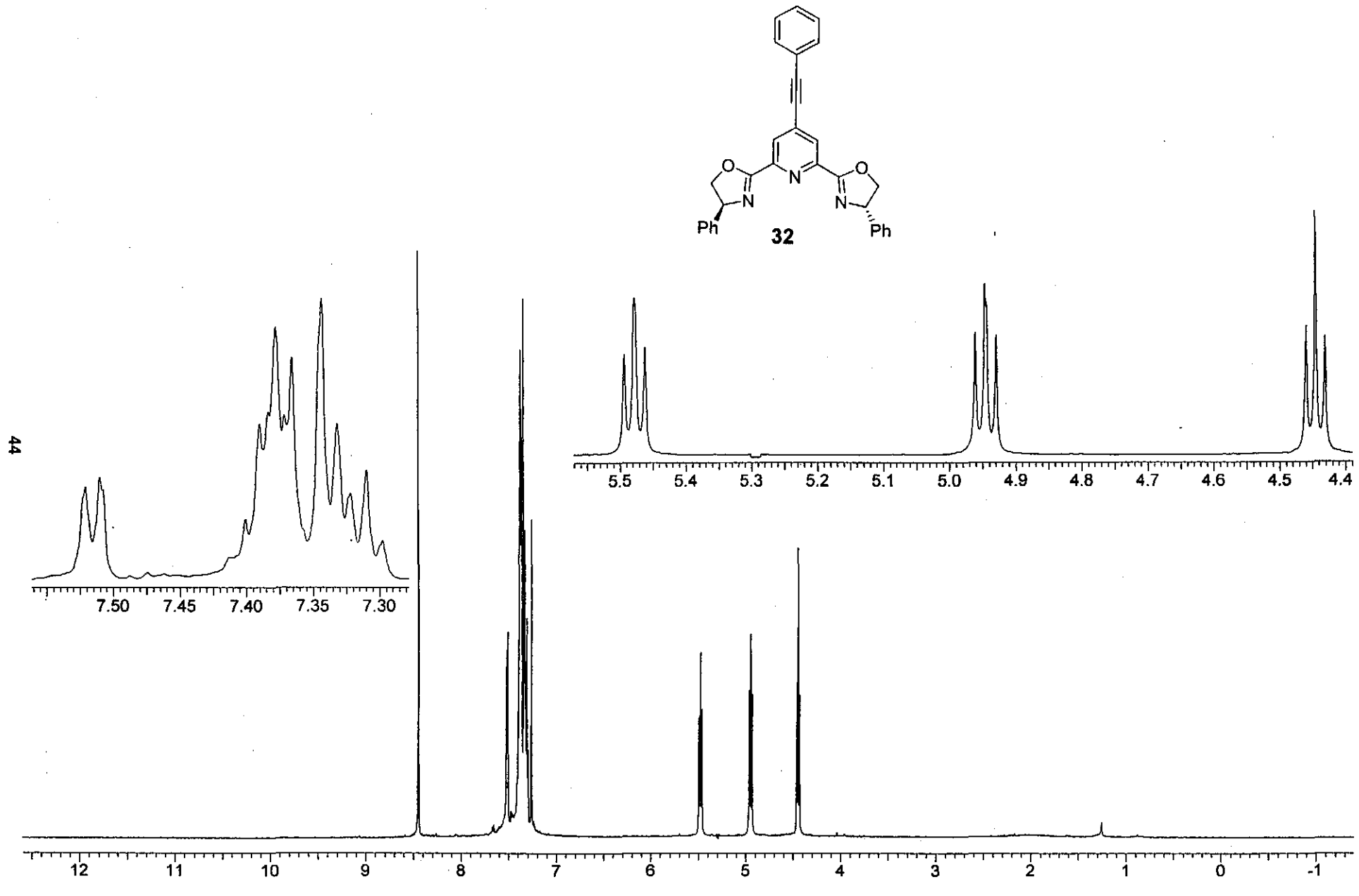


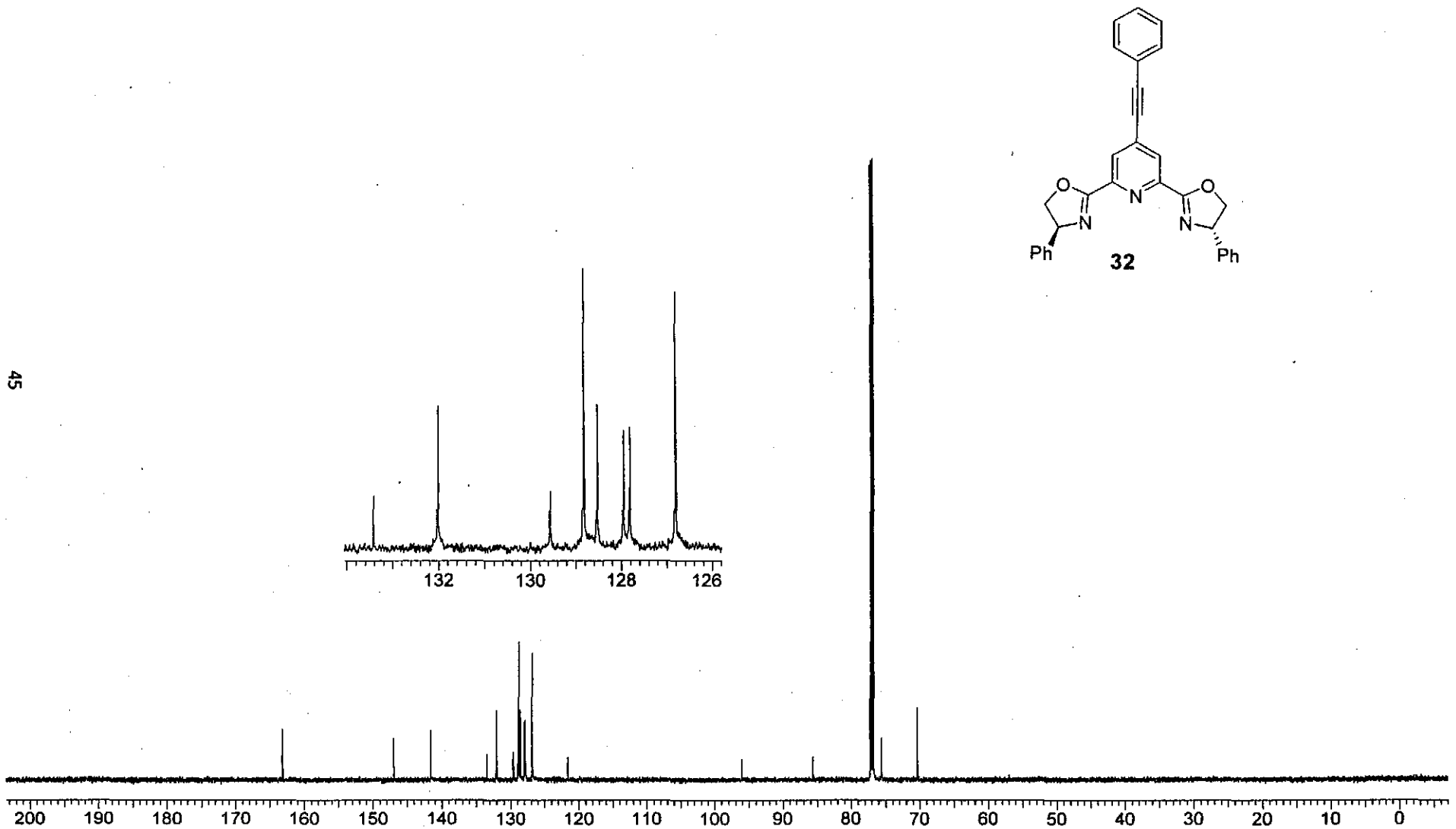
41



47


HO
S
S
47
132
130
128
126
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


Ph
Ph
32
44
7.50
7.45
7.40
7.35
7.30
5.5
5.4
5.3
5.2
5.1
5.0
4.9
4.8
4.7
4.6
4.5
4.4
12
11
10
9
8
7
6
5
4
3
2
1
0
-1


O
N
O
N
N
Ph
Ph
32
132
130
128
126
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0