Part 1. The Chemistry of A Planar Cyclooctatetraene Derivative Fused to Phenanthrene Ring.

Part 2. Regiospecific Synthesis of 2,3-Disubstituted and 2,3,5-Trisubstituted Furans from 2,4-Bis(trimethylsilyl)furan.

by

Chun-Yip Leung

A thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Philosophy
in
The Chinese University of Hong Kong
1993

Thesis committee:
Dr. Tony K. M. Shing (Chairman)
Dr. Kin-Shing Chan
Dr. Henry N. C. Wong
Prof. Ta Shue Chou (External Examiner)

Contents

Acknowledgements :

The author of this thesis is so grateful to express his thanks to his supervisor, Dr. Henry N. C. Wong, for giving him the privilege to pursue postgraduate study, for his guidance and advice in this research work.

Thanks are also given to Dr. Yu Li and Mr. Zhi-Zhong Song for their precious help and for measuring all the 250 MHz NMR spectra.

September 1993

Chun-Yip Leung
Department of Chemistry
The Chinese University of Hong Kong

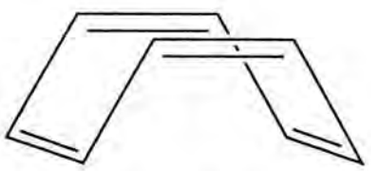
Part 1 : The Chemistry of A Planar Cyclooctatetraene Derivative Fused to Phenanthrene Ring.

(I). Abstract:

A benzo-phenanthro-fused planar cyclooctatetraene derivative, namely, 5,6,15,16-tetradehydrobenzo[*a*]phenanthro-[9,10-*e*]cyclooctene (**10**) was synthesized through the dehydrobromination (by potassium *tert*-butoxide) of the 5,6,15,16-tetrabromo-5,6,15,16-tetrahydrobenzo[*a*]phenanthro[9,-10-*e*]cyclooctene (**29**) generated from benzo[*a*]phenanthro[9,10-*e*]cyclooctene (**11**).

(II). Introduction :

Hückel, on the basis of molecular orbital theory, proposed that a monocyclic fully conjugated polyene will be aromatic if and only if it prossesses a closed shell of $[4n+2]\pi$ electrons,[1-3] where n is an integer greater than or equal to zero. Benzene, preferentially undergoes substitution rather than addition reactions, is a well known example of the $[4n+2]\pi$ systems. On the contrary, the $[4n]\pi$ systems are less stable than the $[4n+2]\pi$ systems and as a matter of fact, both systems behave differently. Later theoretical advancements have concluded that the $[4n]\pi$ systems are destabilized by delocalization and will be antiaromatic.[4-5] All the $[4n]\pi$ annulenes synthesized so far have fallen into this category. Cyclooctatetraene (COT) (1) has different properties from other larger $[4n]\pi$ members. COT is a nonplanar molecule with four conjugated double bonds. Its structure can be represented by a

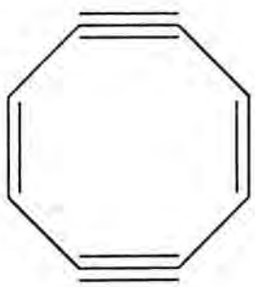


1

"tub" or "boat" conformation. It has the character of a normal polyene and belongs to the D_{2d} point group.[6-8] It is believed that the nonplanarity of COT arises not only from its geometrical strain caused by planar conformation but also, more importantly, from the pseudo Jahn-Teller effect.[9] A planar symmetrical COT is very unstable because there exist two degenerate nonbonding orbitals, and each is occupied by an unpair electron, thus forming an open

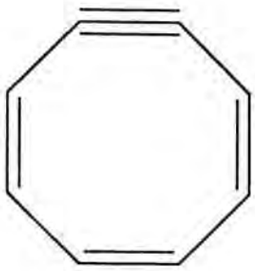
shell arrangement of triplet state. This electronic state may as well suffer from the pseudo Jahn-Teller distortion that results in a geometrical change of the molecule. As a result the orbital degeneracy is removed. The overall effect is a strainless tub shape molecule which is deprived of adjacent π bond overlap.

In order to convert COT to a planar conjugated 8-membered ring compound, the pseudo Jahn-Teller effect must be eliminated. One of the possible methods is to replace one or more of the double bonds by acetylenes, because linear sp-sp hybrid bonds would force the 8-membered carbocycle to become planar. This idea suggests that, a fully conjugated [8]-annulene such as cycloocta-1,5-diene-3,7-diyne (**2**) would presumably be planar, if it indeed exists despite its high angular strain.



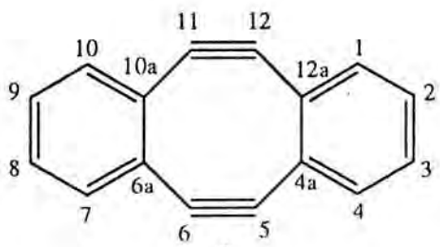
2

As a pioneer in this particular field, Krebs had synthesized cycloocta-1,3,5-triene-7-yne (**3**)[10] which was expected to possess planar conformation. Compound **3** was the first example in the dehydro[8]annulene family. Krebs showed that, dehydrobromination of bromocyclooctatetraene with potassium *tert*-butoxide (KO^tBu) gave **3**. However, due to its instability, **3** could not be isolated and its existence was only proved by trapping experiments.[11-13]

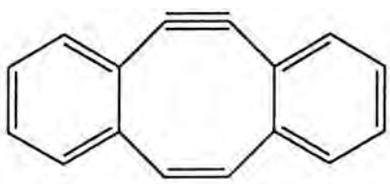


3

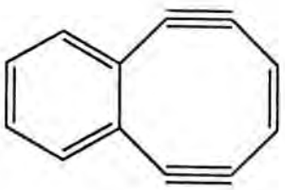
During the past two decades, many COT-derived compounds have been synthesized. Some of these COT derivatives were fused to aromatic rings to enhance stability of planar conformations. The unstable COT derivatives were usually confirmed by trapping reactions.[14] Some examples of aromatic fused COTs are: 5,6,11,12-tetradehydrodibenzo[*a*,*e*]cyclooctene (**4**),[15] 5,6-didehydrodibenzo-[*a*,*e*]cyclooctene (**5**),[15] 5,6,9,10-tetradehydrobenzocyclooctene (**6**),[14] 9,10-didehydrotribenzo[*a*,*c*,*e*]cyclooctene (**7**),[16] and 1,2,5,6-tetradehydro-3,4-benzo-7,8-naphtho[*b*]cyclooctene (**8**).[17-18]



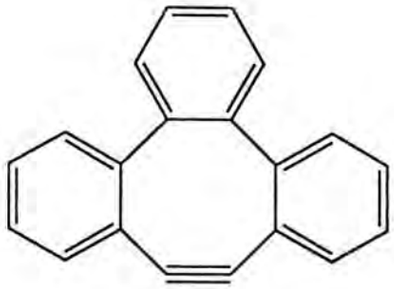
4



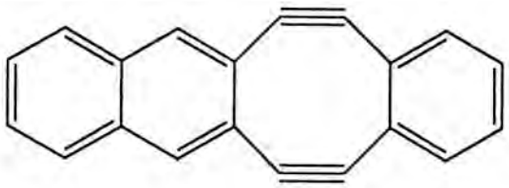
5



6

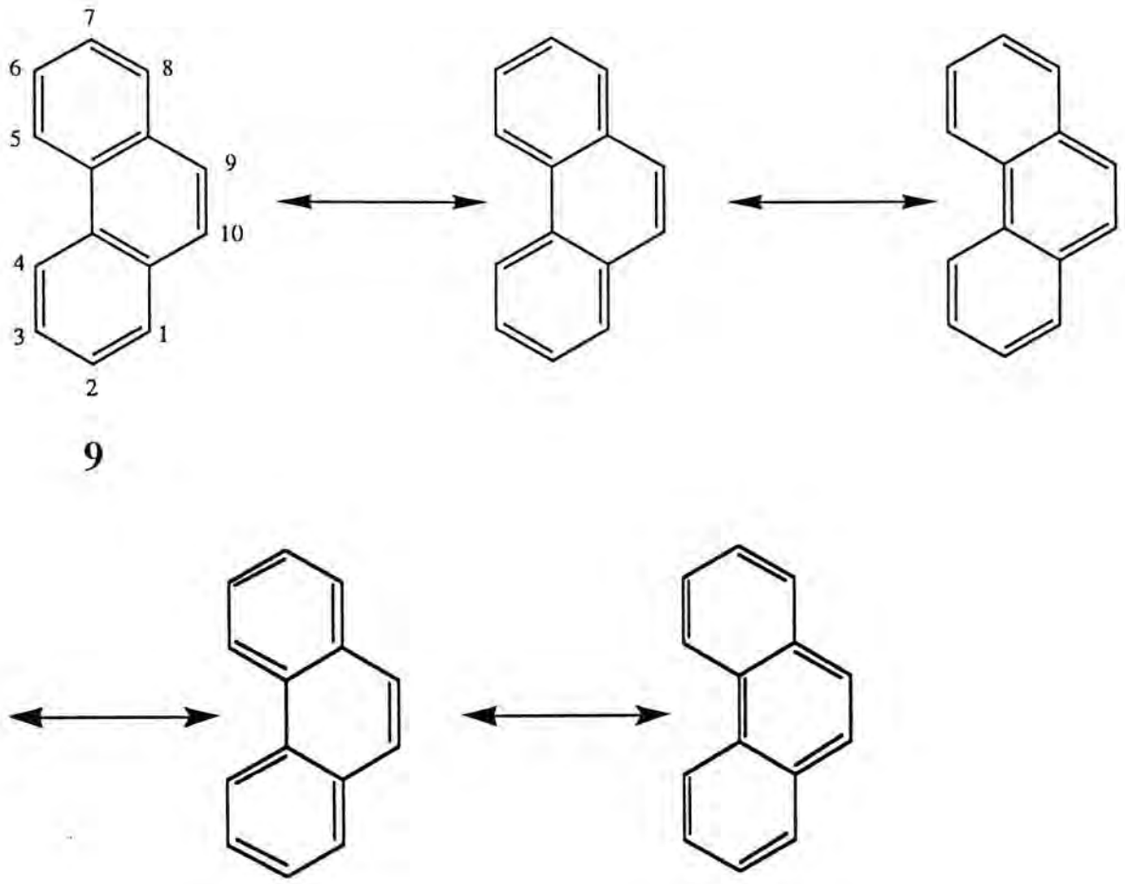


7



8

Many experimental data have shown that, in each of the benzo fused COT, the common bond shared by both rings is relatively longer compared with other bonds in the benzene moiety. Evidences from literature have confirmed that the C_{4a}-C_{12a} distances in compounds **4**[19] and **5**[20] are 1.422Å and 1.425Å, respectively, which are even longer than the bond length of benzene (1.39Å). It is therefore worthy to synthesize a planar [8]annulene derivative with a bond of fusion similar to the bond order of an ethylene double bond. To satisfy such criterion, the C_9-C_{10} bond of phenanthrene (**9**) was chosen to fuse with COT derivative. In phenanthrene, the C_9-C_{10} bond has been found to behave as a double bond (Figure 1).

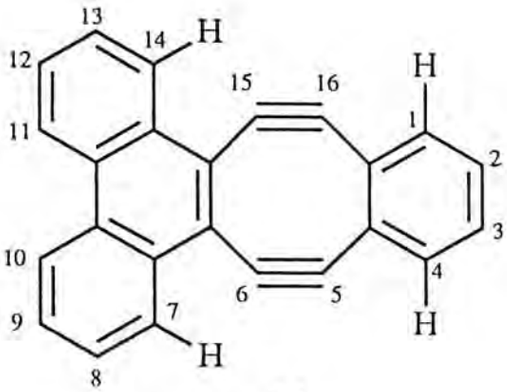


9

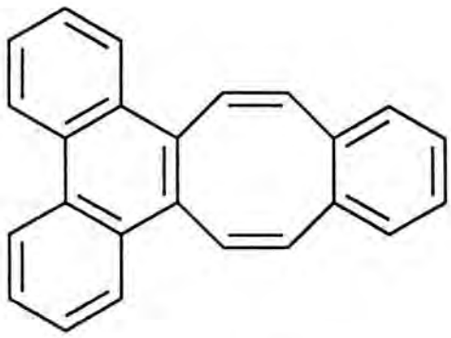
Figure 1.

The resonance structures depicted in Figure 1 show that in only one of five forms is C_9-C_{10} bond a single bond. In other words, C_9-C_{10} bond is a 4/5 π bond. In fact, the literature value of C_9-C_{10} distance is 1.341Å[21] which is almost equal to the length of an ethylene π bond (1.34Å).

Our target molecule is thus 5,6,15,16-tetradehydrobenzo[*a*]-phenanthro[9,10-*e*]cyclooctene (**10**). The aromatic rings, again, are responsible for the stability of the strained molecule. The two triple bonds are also kinetically protected by the protons at C_1, C_4, C_7, and C_{14} positions from nucleophilic attack.



10



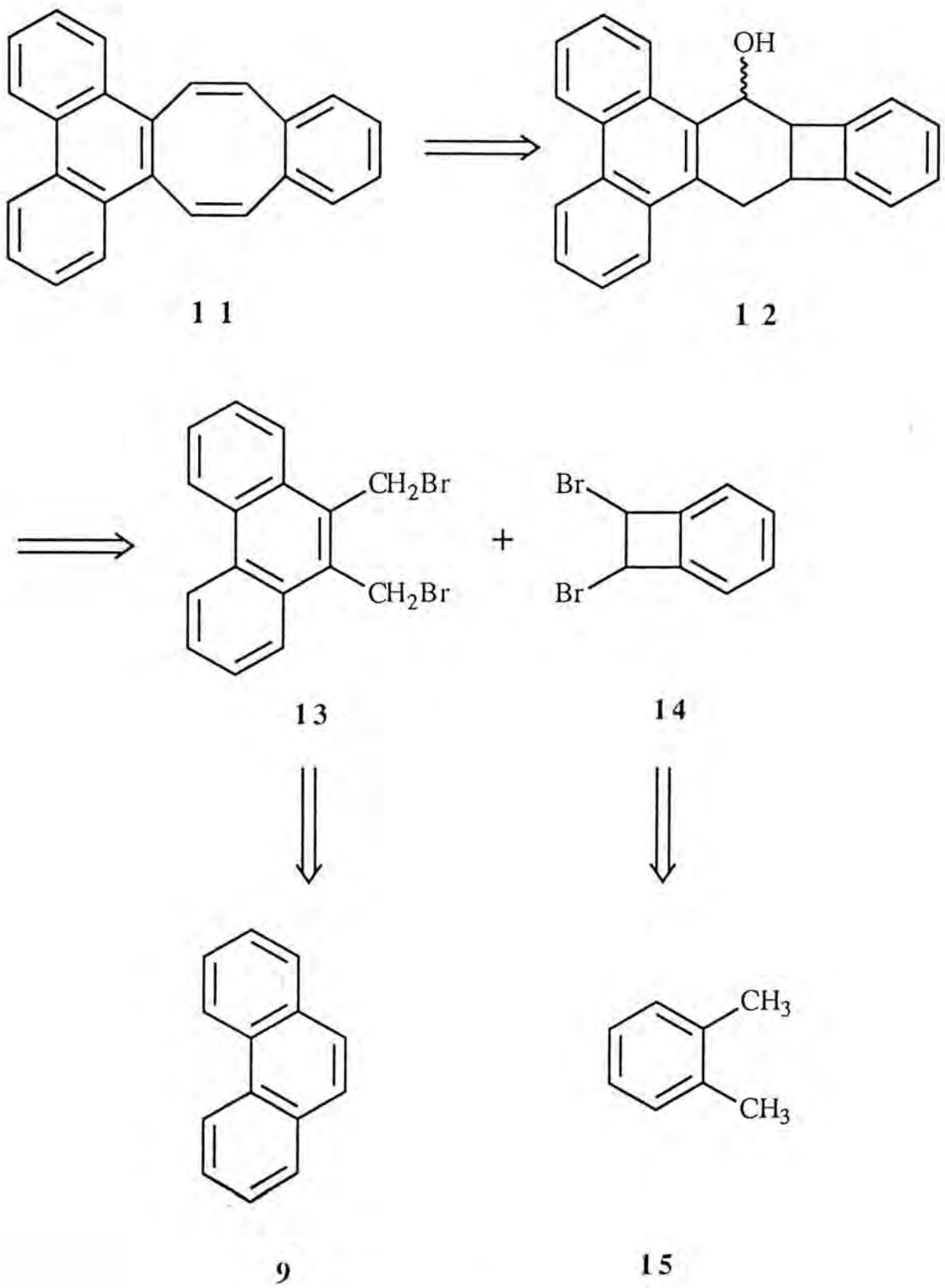
11

Benzo[*a*]phenanthro[9,10-*e*]cyclooctene (**11**) seems to be the only possible precursor of **10** and it has been synthesized earlier.[22] We report here the realization of **10** through the manipulation of **11**. It is also interesting to note that **10** can be regarded as a derivative of **6**, which has been found to be rather unstable.[14] The direct comparison of the stabilities of **6** and **10** should shed some light on the stability enhancement caused by the protons on C_7 and C_{14}.

(III). Results and Discussion :

The retrosynthetic pathway leading to **11** with phenanthrene (**9**) as the starting material is shown in Scheme 1.

Scheme 1



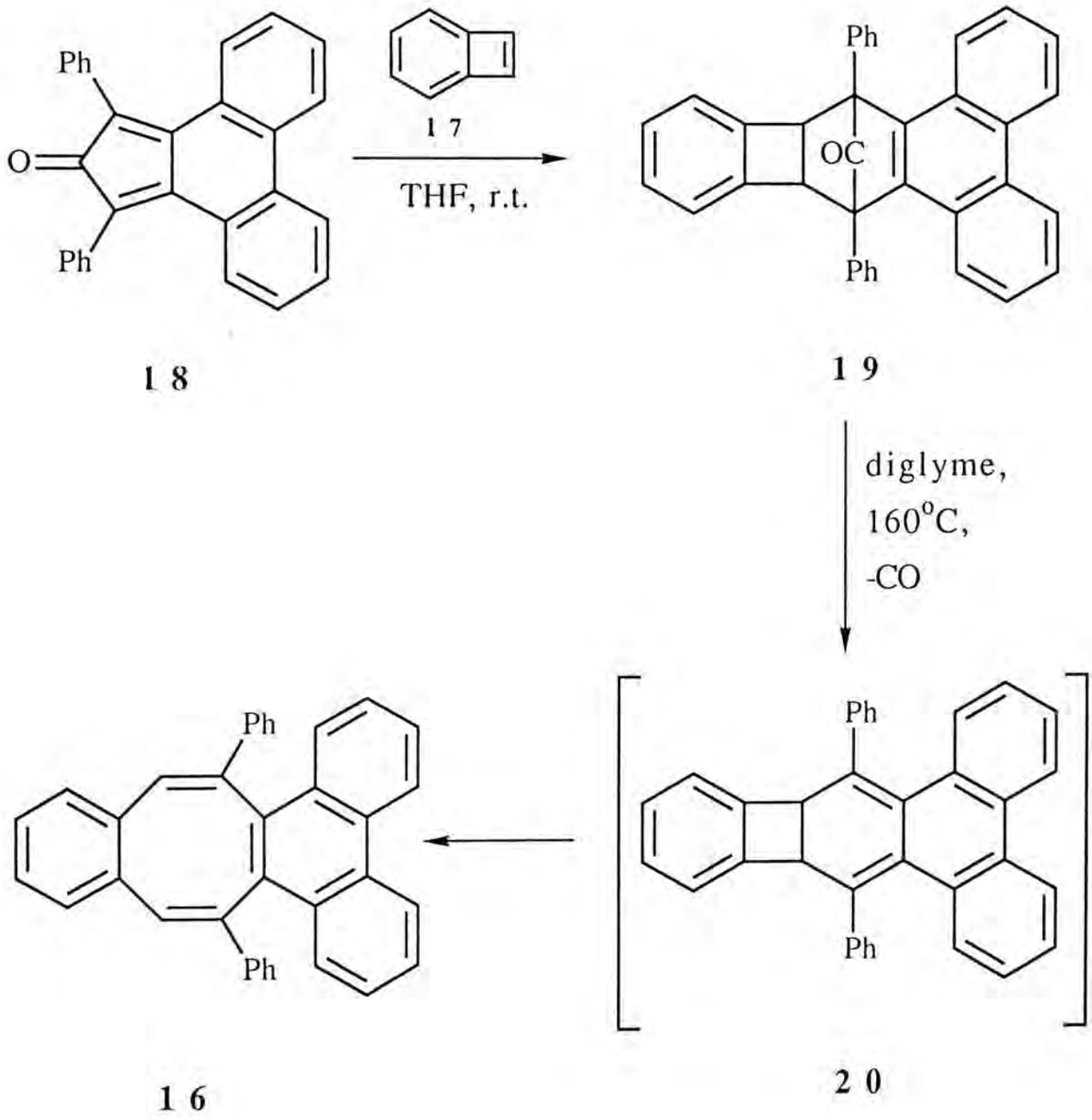
11 **12**

13 **14**

9 **15**

Coincidentally, Barton and coworkers have reported the synthesis of 6,15-diphenylbenzo[*a*]phenanthro[9,10-*e*]cyclooctene (**16**)[23] which is very similar to **11**. Their synthetic strategy is shown in Scheme 2.

Scheme 2



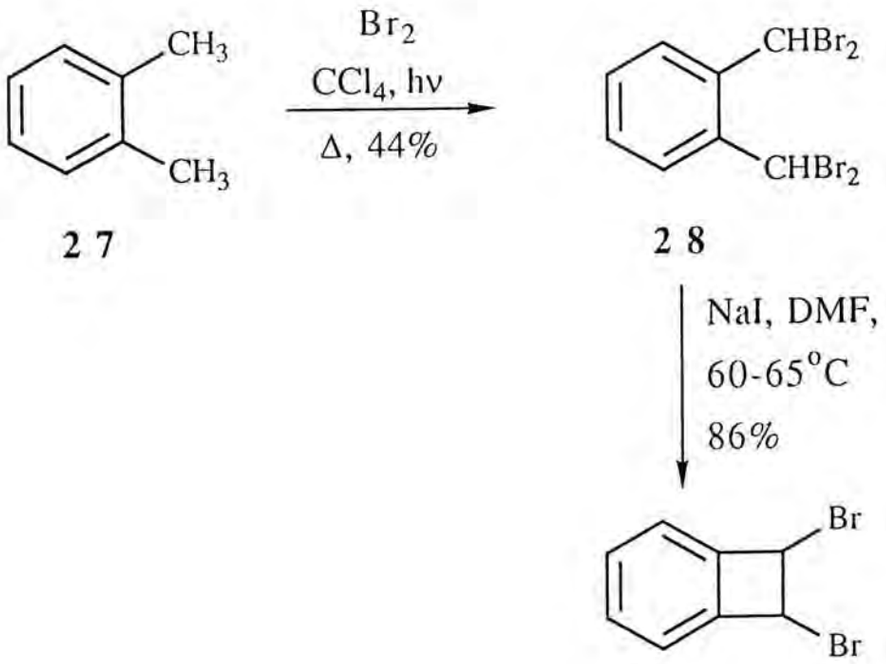
18 **19** **20** **16**

The room temperature cycloaddition between 1,3-diphenyl-2*H*-cyclopenta[*l*]phenanthrene-2-one (**18**)[24] and the reactive

intermediate benzocyclobutene (**17**), generated by debromination of 1,2-dibromobenzocyclobutane[25] with Zn, furnished a bridge ketone **19**. The annelated cyclooctene **16** was realized by the thermal decarbonylation of the cycloadduct **19** in diglyme at 160 °C, and was followed by disrotatory ring opening of the intermediate **20**.

The synthesis of **11** is somewhat similar to that of **16**. In our case, the phenanthro-benzo coupling was achieved by mixing 9,10-bis(bromomethyl)phenanthrene (**13**) and 1,2-dibromobenzocyclobutane (**14**) together in the presence of Zn in DMF. Compound **14**, in turn, can be prepared according to Cava's method[25] (Scheme 3).

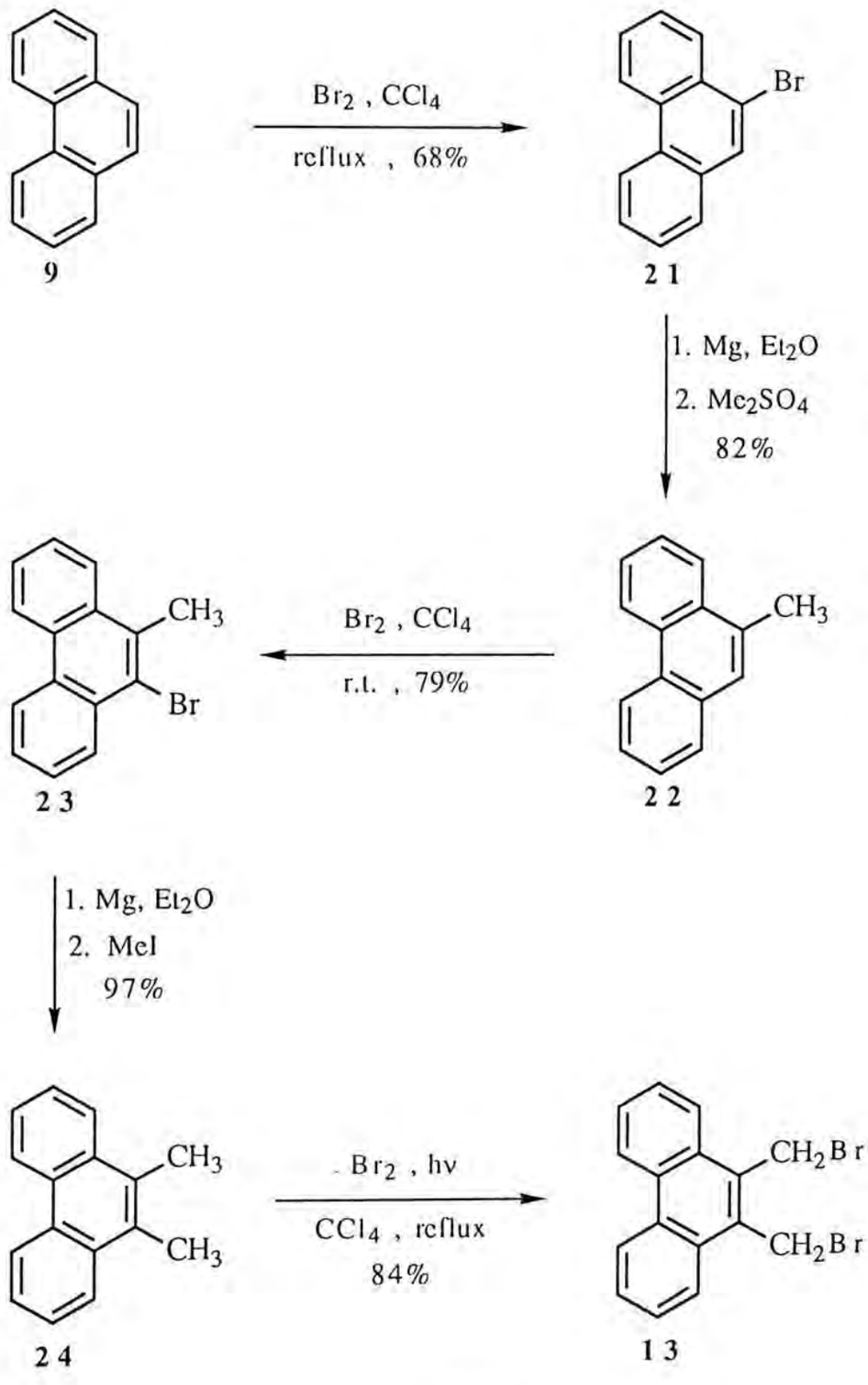
Scheme 3



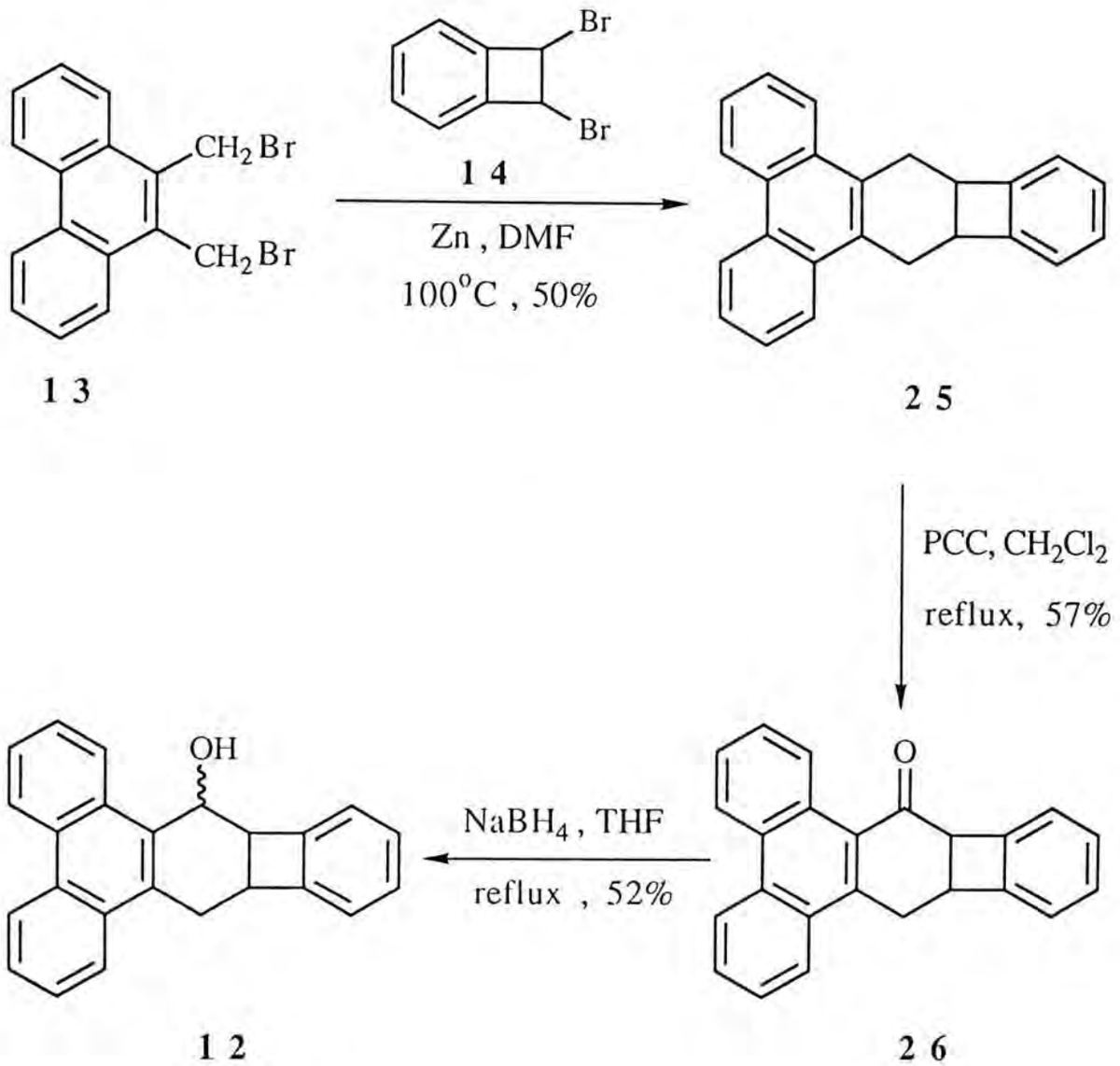
27 **28** **14**

The commercially available *o*-xylene (**27**) was treated with 4 equivalents of bromine through a radical mechanism to give the 1,2-bis(dibromomethyl)benzene (**28**). The debromination of **28** by sodium iodide in DMF at 60°C afforded the desired dibromide **14**. The synthesis of **11** is shown in Scheme 4.

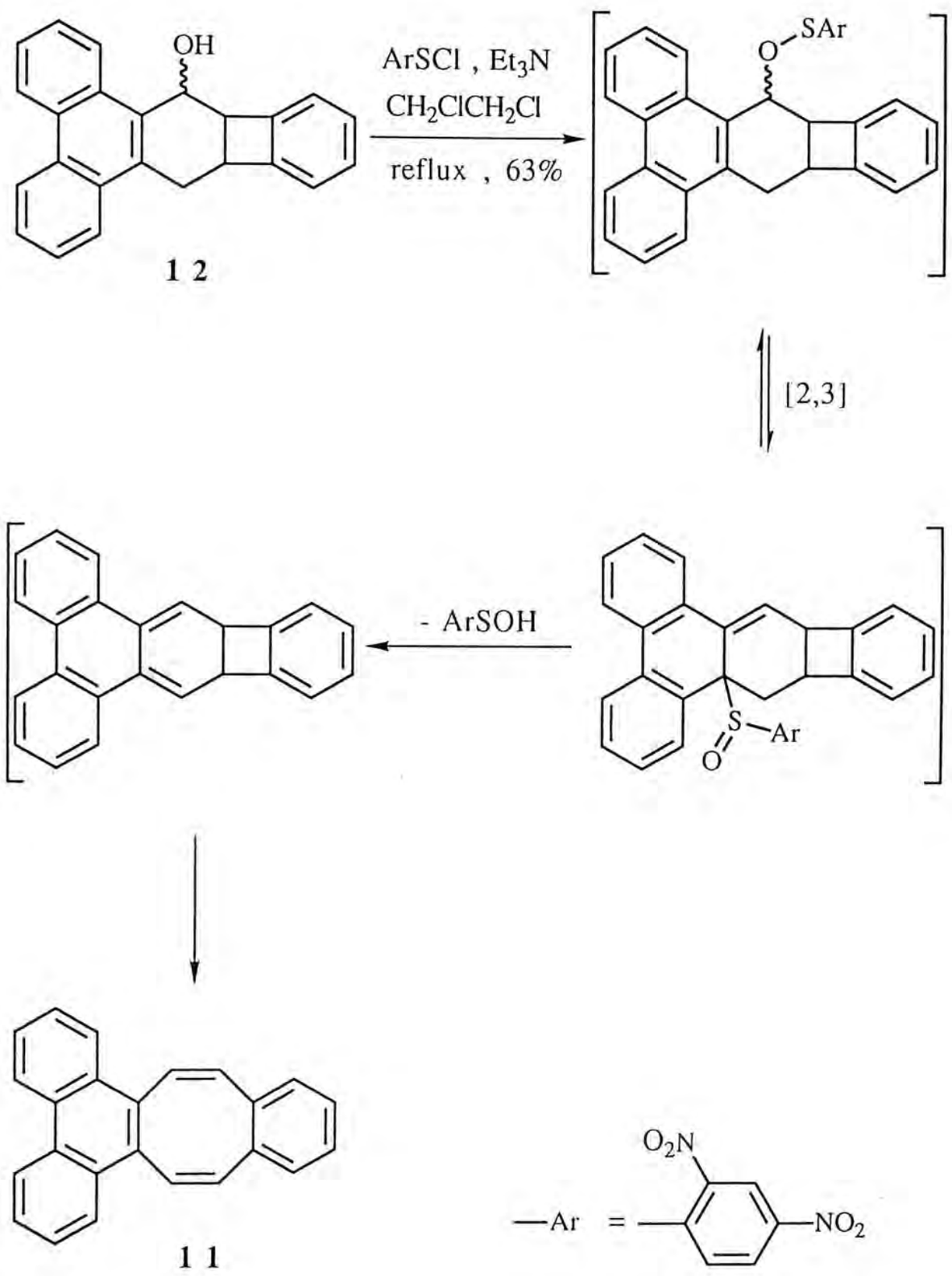
Scheme 4



Scheme 4 (continued)



Scheme 4 (continued)



1 2

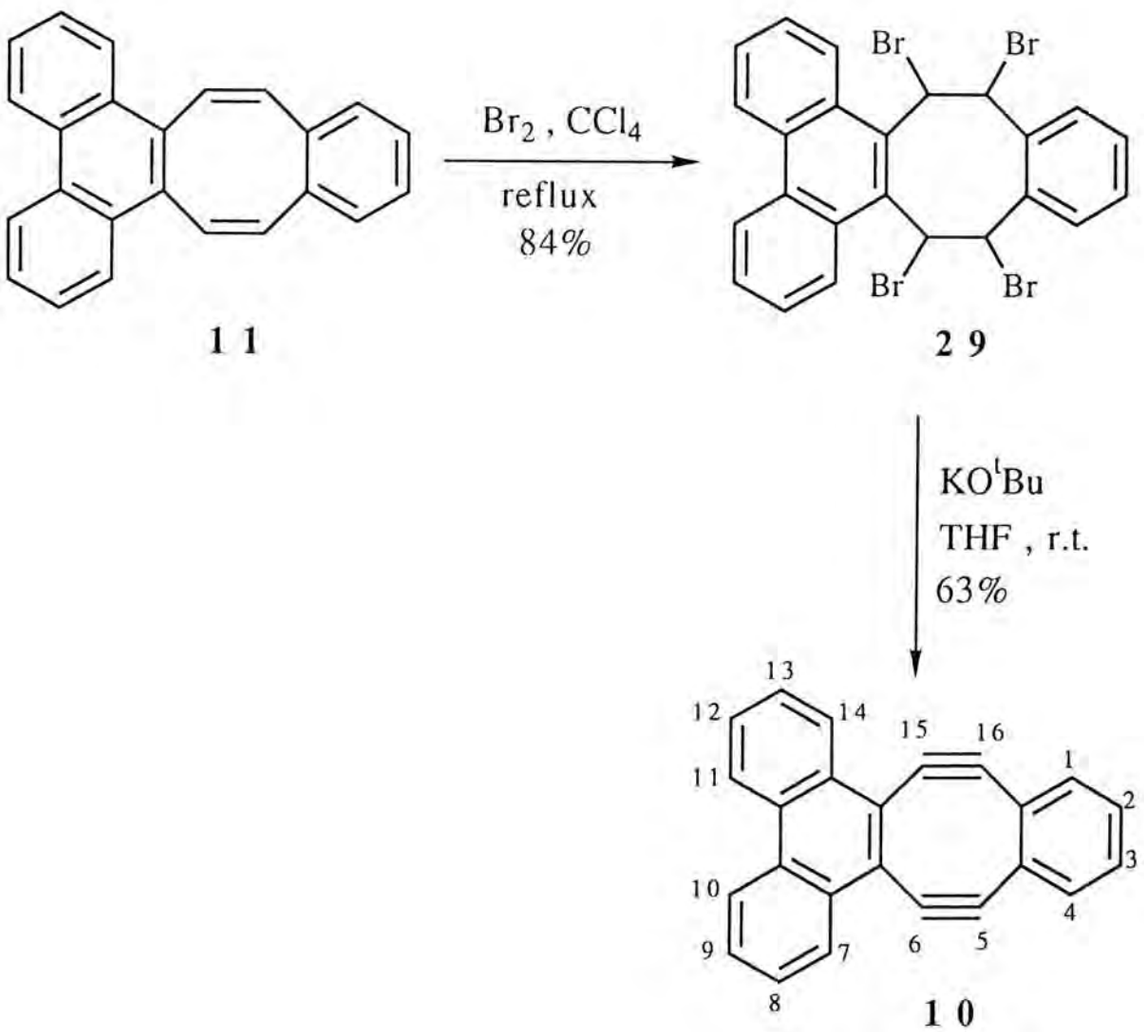
1 1

Phenanthrene (**9**) was allowed to react with bromine in refluxing temperature, giving 9-bromophenanthrene (**21**)[26] in fair yield. This electrophilic aromatic substitution released hydrogen

bromide to restore the aromaticity of the product. The bromide **21** was treated with magnesium to give the corresponding Grignard reagent which was then methylated by dimethyl sulfate to generate 9-methylphenanthrene (**22**).[27] The second bromination was performed on the C_9-C_{10} bond of **22** at room temperature. The simultaneous elimination of hydrogen bromide resulted in the formation of 9-bromo-10-methylphenanthrene (**23**).[28] The bromide **23**, after being converted to Grignard salt, was methylated by methyl iodide to furnish 9,10-dimethylphenanthrene (**24**).[28] Radical bromination on the dimethyl group of **24** with two equivalents of bromine afforded 9,10-bis(bromomethyl)phenanthrene (**13**).[22] 1,4,4a,8b-tetrahydro-2,3-phenanthro[*l*]biphenylene (**25**)[22] was prepared by coupling **13** and **14** in the presence of activated zinc in DMF at 100 °C. The benzylic position of biphenylene **25** was oxidized by pyridinium chlorochromate (PCC) in dichloromethane to provide 1,4,4a,8b-tetrahydro-2,3-phenanthro[*l*]biphenylene-1-one (**26**).[22] Reduction of the ketone **26** using sodium borohydride in THF yielded 1,4,4a,8b-tetrahydro-1-hydroxy-2,3-phenanthro[*l*]biphenylene (**12**).[22] The conversion of **12** to **11** was base on Wang and Paquette's method.[29] The "allylic" alcohol **12** was treated with 2,4-dinitrobenzenesulfenyl chloride and triethylamine in 1,2-dichloroethane, forming a sulfenate ester. It then underwent a [2,3] sigmatropic rearrangement followed by thermal *syn* elimination to give a diene which, through a disrotatory ring opening, afforded benzo[*a*]phenanthro[9,10-*e*]cyclooctene (**11**).

Finally, the generation of 5,6,15,16-tetradehydrobenzo[*a*]-phenanthro[9,10-*e*]cyclooctene (**10**) from **11** was carried out by dehydrobromination of the corresponding tetrabromide **9** which, in turn was obtained by bromination of the two ethylene double bonds of **11** (Scheme 5).

Scheme 5



11 **29** **10**

The ^{1}H-NMR spectrum of **10** includes an A_2B_2 system of H_1, H_2, H_3 and H_4 at δ 6.66-6.68 ppm with J = 3.3, 5.5 Hz. H_8, H_9, H_{12} and H_{13} exhibit adsorptions at δ 7.51-7.64 ppm centered at 7.57 ppm (m, 4H). H_7, H_{14} show adsorption at δ 7.69-7.72 ppm as a doublet of

doublets with J = 1.7, 7.32 Hz and H_{10}, H_{11} show adsorption at δ 8.50-8.53 ppm as a doublet having J = 8.65 Hz. The two pairs of symmetric acetylene carbons C_5, C_{16} and C_6, C_{15} gave two peaks in the ^{13}C-NMR spectrum at 109.67 and 113.04 ppm, respectively. The downfield shift of the acetylenic carbon adsorptions as compared with the chemical shifts of other ordinary linear sp-hybridized alkynes (eg. δ 80.3 for 4-octyne; δ 87 for 2,2,5,5-tetramethyl-3-hexyne) might be attributable to a hybridization change due to the angle strain in **10**.[30] The result of X-ray crystallography confirmed the bond length of C_{6a}-C_{14b} to be 1.343Å. The perspective view of **10** is shown in Figure 2.

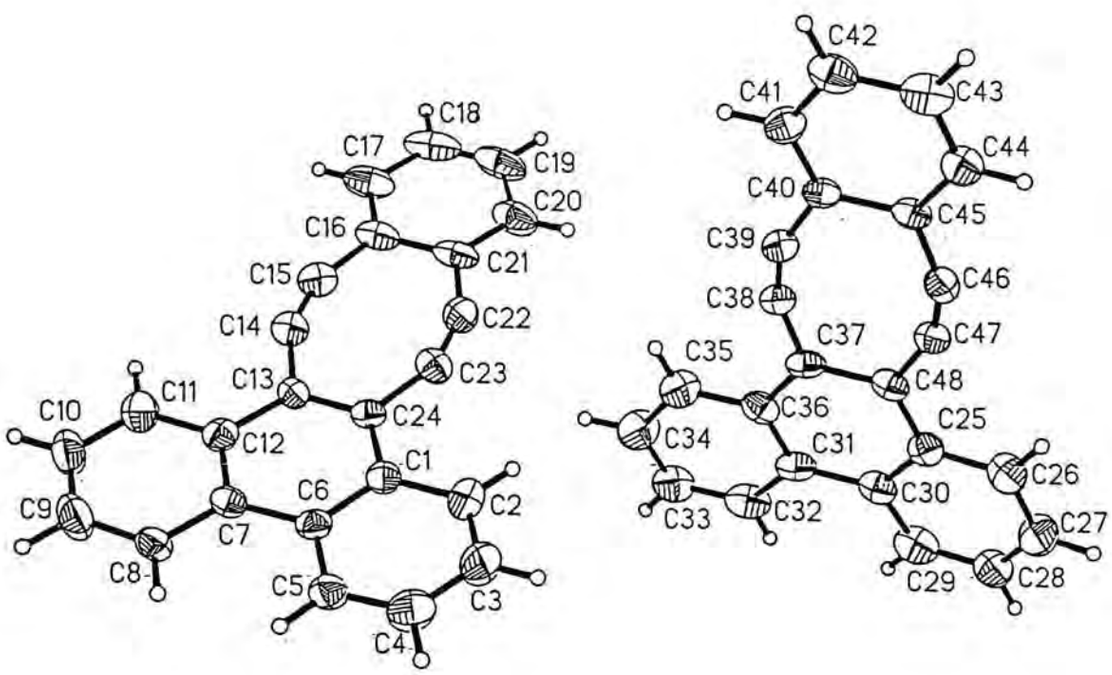


Figure 2. Perspective View of COT **10**

(IV). Conclusion :

5,6,15,16-Tetradehydrobenzo[*a*]phenanthro[9,10-*e*]cyclooctene (**10**) has been synthesized from phenanthrene. Compound **10** is confirmed to be a planar anti-aromatic [8]-annulene with the common double bond shared by the phenanthrene and the cyclooctatetraene being equal to 1.343 Å.

(V). Experimental Section :

All the ^{1}H-NMR and ^{13}C-NMR spectra were obtained from a Bruker Cryospec WM250 spectrometer. Samples were run in $CDCl_3$ solutions at ambient temperature and the chemical shifts were recorded downfield (δ scale) from the reference, TMS, at 0 ppm. Mass spectra were recorded on a VG Micromass 7070F spectrometer operated at 20 and 70eV. Melting points were determined on a hot-stage microscope apparatus and were uncorrected. E-Merk silica gel (70-230 mesh) was used for all column chromatography. Microanalyses were carried out by the Microanalysis Unit of the Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences and by MEDAC Ltd., Department of Chemistry, Brunel University.

9-Bromophenanthrene (21)[26]

Phenanthrene (**9**) (100 g, 0.56 mol) was dissolved in CCl_4 (100 mL) and was heated to reflux. Bromine (30 mL, 0.59 mol) in CCl_4 (30 mL) was added dropwise to the solution over a period of two hours. The HBr gas evolved was transferred through an inverted funnel (connected by a rubber tube to the reflux condenser) to a beaker (containing NaOH solution) to be neutralized. The resulting mixture was refluxed overnight, and then cooled to room temperature. The solution was washed by $Na_2S_2O_3$ (2 x 67 mL) and water (67 mL). The organic layer was separated, dried, and evaporated to give a brownish oil. The remaining solvent was removed under vacuum (0.01 mmHg) at room temperature to give crude brownish-yellow solids which were recrystallized from a mixture of 95% ethanol-acetone. The yellow crystals obtained were dried under vacuum at room temperature for 12 hours (98 g, 64%), mp 62-64 ^{o}C (lit.[26] 65-66 ^{o}C). ^{1}H NMR (NMR-1), δ 7.59-7.73 (m, 4H), 7.79-7.85 (m, 1H), 8.11 (s, 1H), 8.35-8.39 (m, 1H), 8.64-8.71 (m, 2H). MS m/e 258.0 (M^+ +2), 256.0 (M^+), 177.1 (M^+-Br).

9-Methylphenanthrene (22)[27]

9-Bromophenanthrene (**21**) (70 g, 0.27 mol) in dry diethyl ether (100 mL) and dry benzene (100 mL) was added dropwise to magnesium (7.2 g, 0.29 mol) in dry ether (50 mL). A catalytic amount of iodine was added to activate the reaction. After the

brown mixture had been refluxed for four hours, the flask was immersed in an ice bath. An excess amount of dimethyl sulfate (70 mL, 0.74 mol) in dry ether (70 mL) was added. The resulting yellow mixture was heated to reflux for another three hours and then left stirring overnight. The flask was again cooled in an ice bath, and HCl (10%, 100 mL) was added slowly. The organic layer was separated and NaOH (10%, 100 mL) was added. The resulting mixture was refluxed for one hour and was allowed to cool to room temperature. The organic layer was separated and washed with H_2O (3 x 200 mL), dried, and evaporated to give crude yellowish solids. Recrystallization from 95% ethanol gave light yellow crystals (43 g, 82%), mp 89-90 °C (lit.[31] 90-91 °C). ^1H NMR (NMR-2), δ 2.72 (s, 3H), 7.54-7.67 (m, 5H), 7.73-7.81 (m, 1H), 8.03-8.07 (m, 1H), 8.62-8.73 (m, 2H). MS m/e 192 (M^+,100%), 191 (M^+-H, 47%).

9-Bromo-10-methylphenanthrene (23)[28]

9-Methylphenanthrene (**22**) (45 g, 0.23 mol) was dissolved in dry CCl_4 (200 mL). Bromine (13 mL, 0.25 mol) in dry CCl_4 (30 mL) was added dropwise to the solution at room temperature. After the bromine was added, the solution turned dark brown. The resulting solution was stirred for 1.5 hour and was washed with saturated $Na_2S_2O_3$ (400 mL) and then with H_2O (2 x 400 mL). The organic layer was separated, dried and evaporated to give crude brownish-yellow solids which were recrystallized from 95% ethanol to afford yellow needle-like crystals (50 g, 79%), mp 118-120 °C (lit.[27] 119-120 °C, lit.[28]117-118 °C). ^1H NMR (NMR-3), δ

2.96 (s, 3H), 7.63-7.68 (m, 4H), 8.11-8.15 (m, 1H), 8.45-8.49 (m, 1H), 8.64-8.71 (m, 2H). MS m/e 272 (M^+ +2, 34%), 270 (M^+, 35%), 191 (M^+ -Br, 47%).

9,10-Dimethylphenanthrene (24)[28]

Oven-dried magnesium (8.4 g, 0.31 mol) was immersed in dry THF (20 mL). 9-Bromo-10-methylphenanthrene (**23**) (80 g, 0.29 mol) in dry THF (200 mL) was added dropwise during 3 hours to the magnesium. The solution was warmed to start the reaction. After all bromide had been added, the mixture was refluxed for 5 hours. The reaction flask was immersed in an ice bath. Excess methyl iodide (135 mL, 2.16 mol) was slowly added to the Grignard reagent and the reaction mixture was heated to reflux for 12 hours. The reaction flask was allowed to cool in an ice bath, and dilute HCl (10%, 200 mL) was added to the solution slowly with stirring to quench the reaction. The solution was washed with saturated NaCl solution (3 x 300 mL). The organic layer was separated, dried and evaporated to give yellow solids which were adsorbed on silica gel. Chromatography on silica gel (hexanes eluent) afforded white solids (59 g, 97%), mp 140-141 °C (lit.[28] 140.5-141 °C). ^{1}H NMR (NMR-4) δ 2.72 (s, 6H) 7.59-7.63 (m, 4H), 8.10-8.14 (m, 2H), 8.69-8.73 (m, 2H). MS m/e 206 (M^+, 85%), 191 (M^+-CH_3, 100%).

9,10-Bis(bromomethyl)phenanthrene (13)[22]

9,10-Dimethylphenanthrene (**24**) (15 g, 0.07 mol) in CCl_4 (300 mL) was illuminated with a 500W sunlamp until reflux. Bromine (7.5 mL, 0.15 mol) in CCl_4 (10 mL) was added dropwise to the refluxing solution under illumination. After all bromine had been added, the brown mixture was refluxed for 5.5 hours. The resulting solution was cooled to room temperature and part of the product precipitated as white solids. After filtering the solids the solution was washed with saturated $Na_2S_2O_3$ (300 mL) and water (2 x 300 mL). The organic layer was separated, dried and evaporated to give crude brownish solids which were combined with the filtered precipitates. Recrystallization of the crude products from $CHCl_3$ afforded white crystals (22 g, 84%), mp. 243.5-244 °C (lit.[22] 235.5-237.5 °C). ^{1}H NMR (NMR-5), δ 5.13 (s, 4H), 7.70-7.74 (m, 4H), 8.21-8.25 (m, 2H), 8.71-8.75 (m, 2H). MS m/e 366 (M^+ +4, 8%), 364 (M^+ +2, 17%), 362 (M^+, 10%), 285 (M^+ -Br+2, 51%), 283 (M^+ -Br, 49%), 204 (M^+ -2Br, 60%).

1,4,4a,8b-Tetrahydro-2,3-phenanthro[*l*]biphenylene (25)[22]

9,10-Bis(bromomethyl)phenanthrene (**13**) (19.46 g, 53.4 mmol) and 1,2-dibromo-1,2-dihydrobenzocyclobutene (**14**) (14 g, 53.4 mmol) were dissolved in DMF (300 mL) under nitrogen atmosphere. The resulting solution was heated at 100-110 °C, and activated zinc (20 g) was added to the solution in one portion. The heterogeneous solution was stirred at 100-110 °C for 6 hours. The

resulting solution was allowed to cool to room temperature and the excess zinc and zinc bromide were filtered. The filtrate was poured into ether (300 mL) and washed with water (4 x 500 mL). The organic layers were collected, dried and evaporated to give yellowish solids. The crude product was adsorbed on silica gel and purified by column chromatography on silica gel (EtOAc : hexanes = 1:30 eluent). The white solid obtained was recrystallized from $CHCl_3$: hexanes to yield white crystals (8 g, 50%), mp 215.5-217 °C (lit.[22] 216.5-217.5 °C). ^{1}H NMR (NMR-6), δ 3.21-3.29 (m, 2H), 3.57-3.64 (m, 2H), 3.93-3.96 (t, 2H, 3.5 Hz), 6.98 (s, 4H), 7.49-7.61 (m, 4H), 8.16-8.20 (dd, 2H, 2.1, 7.5 Hz), 8.60-8.64 (m, 2H). MS m/e 306 (M^+, 100%).

1,4,4a,8b-Tetrahydro-2,3-phenanthro[*l*]biphenylene-1-one (26)[22]

Biphenylene **25** (0.2 g, 0.7 mmol) was mixed with pyridinium chlorochromate (1.31 g, 6 mmol) in CH_2Cl_2 (20 mL). The mixture was refluxed for 20 hours. After cooling to room temperature, the dark brown mixture was extracted with dilute HCl (10%) and H_2O (50 mL). The organic layer was separated, dried and evaporated to give brown solids which were adsorbed on silica gel and chromatographed on a silica gel column (eluted with EtOAc : hexanes = 1:10) to give yellow solids. The product was recrystallized from CH_2Cl_2-hexanes to afford yellow crystals (0.12 g, 57%), mp 222.5-223 °C (lit.[22] 224-225 °C). ^{1}H NMR (NMR-7), δ 3.40-3.50 (dd, 1H, 6.9, 17 Hz), 3.94-4.02 (dd, 1H, 2.5, 17 Hz), 4.41-4.48 (m, 1H), 4.61-4.63 (d, 1H, 5.1 Hz), 7.05-7.25 (m, 4H),

7.56-7.71 (m, 4H), 8.20-8.25 (m, 1H), 8.46-8.50 (m, 1H), 8.56-8.66 (m, 2H). MS m/e 320 (M^+, 38%), 291 (M^+ -CO, 83%).

1,4,4a,8b-Tetrahydro-1-hydroxy-2,3-phenanthro[*l*]biphenylene (12)[22]

Sodium borohydride (0.1 g, 2.6 mmol) was mixed with the ketone **26** (0.2 g, 0.6 mmol) in THF (21 mL). The resulting solution was refluxed under N_2 for 20 hours. After cooling to room temperature, the solution was extracted with ether (35 mL) and washed with H_2O (50 mL). After layer separation, the aqueous layer was extracted with ether (2 x 50 mL). The organic layers were combined, dried and evaporated. The crude product was adsorbed on silica gel and purified by column chromatography on silica gel (EtOAc : hexanes = 1:5 eluent) to afford white solids (0.1 g, 52%), mp 214.5-215.5 °C (lit.[22] 218-219 °C). ^{1}H NMR (NMR-8), δ 1.64-1.65 (d, 1H, 2.3 Hz), 3.19-3.29 (dd, 1H, 11.2, 14.2 Hz), 3.69-3.71 (m, 1H), 3.94-3.99 (t, 1H, 5.7 Hz), 4.14-4.23 (dd, 1H, 7.7, 14.2 Hz), 6.41-6.44 (dd, 1H, 2, 5.5 Hz), 7.37- 7.40 (m, 4H), 7.66-7.73 (m, 4H), 8.35-8.44 (m, 2H), 8.78-8.82 (m, 2H). MS m/e 322 (M^+, 71%), 304 (M^+ -H_2O, 100%).

Benzo[*a*]phenanthro[9,10-*e*]cyclooctene (11)[22]

The alcohol **12** (0.79 g, 2.5 mmol) and 2,4-dinitrobenzenesulfenyl chloride[22] (3 g, 12.57 mmol) were dissolved in 1,2-dichloroethane (150 mL) at room temperature under N_2 atmosphere. To the solution was added triethylamine (2 mL) via a

syringe. The solution became turbid in one minute and was stirred at room temperature for 3.5 hours. It was then heated to reflux for 20 hours. The resulting mixture was allowed to cool to room temperature and evaporated. The crude product was adsorbed on silica gel and chromatographed on a silica gel column (CH_2Cl_2 : hexanes = 1:15 eluent) to give white solids which were recrystallized from benzene-hexanes to yield colorless needles (0.5 g, 63%), mp 231.5-232.5 °C (lit.[22] 238.5-239 °C). ^1H NMR (NMR-9), δ 7.06-7.26 (ABq, 4H, 11.8 Hz), 7.12 (s, 4 H), 7.59-7.63 (m, 4H), 8.06-8.10 (m, 2H), 8.61-8.65 (m, 2H). MS m/e 304 (M^+, 100%).

5,6,15,16-Tetrabromo-5,6,15,16-tetrahydrobenzo[*a*]phenanthro[9,10-*e*]cyclooctene (29)

To a stirring solution of **11** (0.47 g, 1.5 mmol) in dry CCl_4 (15 mL) was added Br_2 (0.18 mL, 3.6 mmol) through a syringe. The resulting solution was heated to reflux for 20 hours. The color of the solution became orange-red. The mixture was evaporated and adsorbed on silica gel. Purification by column chromatography on silica gel (CH_2Cl_2 : hexanes = 1:5 eluent) gave light yellow solids which were recrystallized from $CHCl_3$-hexanes to afford white crystals (0.8 g, 84%), mp 240.6-241.6 °C. ^1H NMR (NMR-10), δ 6.10-6.14 (d, 1H, J = 11 Hz), 6.20-6.23 (d, 1H, 9.2 Hz), 6.68-6.72 (d, 1H, J = 9.2 Hz), 6.78-6.83 (d, 1H, 10.9 Hz), 6.81-6.91 (m, 2H), 6.95-7.02 (m, 1H), 7.56-7.72 (m, 5H), 8.08-8.11 (m, 1H), 8.50-8.61 (m, 3H). MS m/e 624 (M^+ +4, 6%), 466 (M^+ -2Br+4, 5%), 464 (M^+ -2Br+2, 10%), 462 (M^+ -2Br, 4%), 385 (M^+ -3Br+2, 12%), 383 (M^+

-3Br, 16%), 304 (M^+ -4Br, 100%). Anal. Calcd. for $C_{24}H_{16}Br_4$: C, 46.20; H, 2.58. Found : C, 46.08; H, 2.06.

5,6,15,16-Tetradehydrobenzo[*a*]phenanthro[9,10-*e*]cyclooctene (10)

The tetrabromide **29** (98.4 mg, 0.16 mmol) was dissolved in dry THF (10 mL) at room temperature under N_2 atmosphere. Potassium *tetr*-butoxide (0.20 g, 1.7 mmol) in dry THF (6 mL) was added dropwise during 10 minutes to the solution. The mixture was left stirring for 30 minutes at room temperature. The resulting orange-red solution was poured into ether (15 mL) and washed with water (15 mL). After separating the organic fraction, the aqueous layer was extracted with ether (2 x 10 mL). The combined organic layers were dried and evaporated. The resulting crude brownish solids were adsorbed on silica gel and purified by column chromatography on silica gel (CH_2Cl_2 : hexanes = 1:10 eluent). The isolated orange product was recrystallized from benzene-hexanes, yielding red-orange crystals (29 mg, 63%). The crystals decomposed at 183 ^oC on an attempted melting point determination. Single crystals of **10** were obtained by recrystallization from cyclooctene. ^1H NMR (NMR-11), δ 6.66-6.88 (AA'BB', 4H, J = 3.3, 5.5 Hz), 7.51-7.64 (m, 4H), 7.69-7.72 (m, 2H), 8.50-8.53 (d, 2H, 8.6 Hz); $^{13}CNMR$ (CMR-1), δ 109.67, 113.04, 122.79, 126.93, 127.06, 127.32, 127.79, 128.96, 129.35, 130.28, 134.31. MS m/e 300 (M^+, 100%). Anal. Calcd. for $C_{24}H_{12}$: C, 95.97; H, 4.03 . Found : C, 95.07; H, 3.86.

Part 2 : The Syntheses of 2,3-Disubstituted and 2,3,5-Trisubstituted Furans from 2,4-Bis(trimethylsilyl)furan

(I). Abstract :

2-Benzyl-3-*m*-anisyl-5-*p*-tolyl-furan (**30**), 2-benzyl-3-*trans*-hexen-1-yl-5-*p*-tolyl-furan (**31**), 2-(3,5-dimethyl)benzyl-3-*p*-methoxylcarbonylbenzyl-5-hexyl-furan (**32**) and 2-benzyl-3-[3,4-(methylenedioxy)]benzylfuran (**33**) have been synthesized by utilizing a sequence of regiospecific iodination, Nickel catalyzed Grignard cross-coupling, Stille-type cross-coupling and Suzuki-type cross-coupling reactions.

(II). Introduction :

Polysubstituted furans commonly occurred as key structural units of a widespread natural substances.[32(a)-(e)] The furan derivatives (both saturated and unsaturated) have also made a tremendous contribution to the preparation of a wide range of cyclic and acyclic organic compounds[33] (eg. retro-isosenine,[32(b)] hallchondrin B,[34] and fusarin[35]) as well as some important pharmaceuticals.[36]

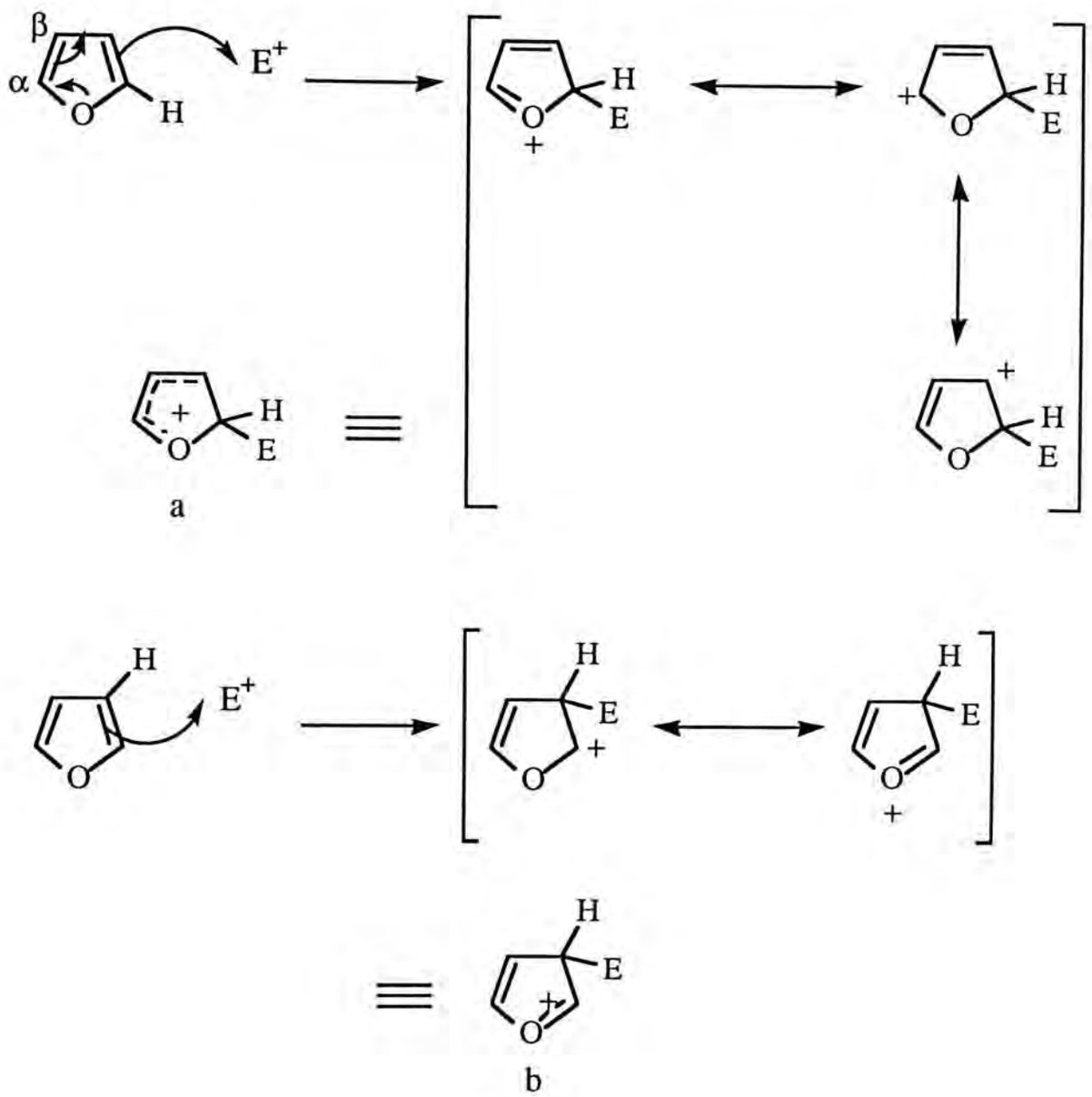
In connection with the studies on 3,4-disubstituted furans,[37(a)-(d)] we are also interested in developing new methodologies to the preparation of substituted furans of other kinds. We report herein a brief survey on the various reactions of furan.

(A). Reactions of Furan :

(1). Reaction with Electrophiles :

Furan is characterized as an electron rich heterocycle that contains six π-electrons distributed over the five-membered ring system. It undergoes electrophilic attack more readily at the α-position than the β-position. Such feature can be easily understood in terms of delocalization of a positive charge in the cationic intermediate[38] as shown in Scheme 6.

Scheme 6



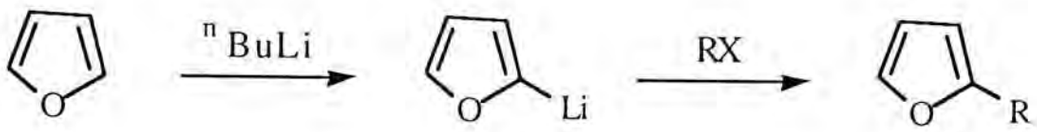
It is clear that the cation **a**, derived by α-addition, represents 3 resonance structures and as a result should have greater stability than cation **b**, which is derived by β-addition.

(2). Reactions with Nucleophilic Reagents :

Nucleophilic reagents do not react with furan and its alkyl derivatives by addition or by substitution. However, furan can be

treated with a strong base, resulting in the deprotonation at the α-carbon.[39(a)] In this manner, furan reacts effectively with n-butyllithium / TMEDA in refluxing hexane to give synthetically useful furyllithium.[40] (Scheme 7).

Scheme 7

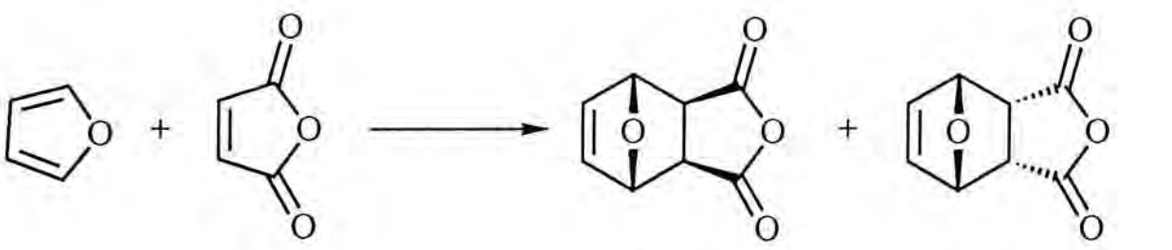


The 2-lithio species can immediately react with various electrophiles to produce 2-substituted furan.

(3). Cycloaddition reactions :

Furan, as a diene, undergoes Diels-Alder reaction[41] with dienophiles of high reactivity such as maleic anhydride[42] (Scheme 8).

Scheme 8

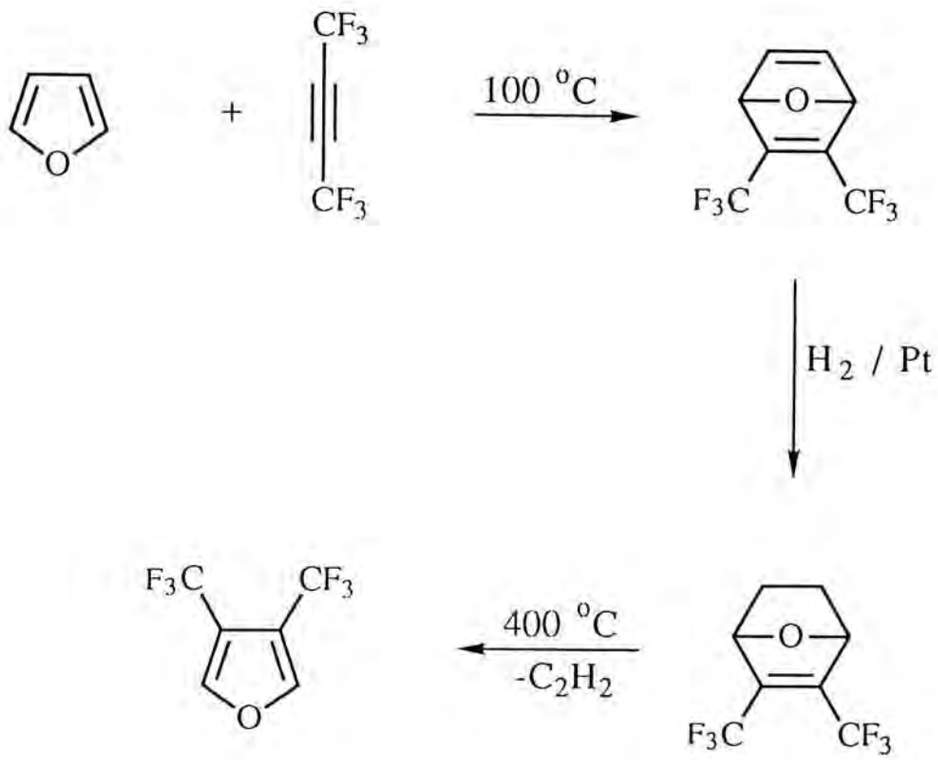


exo (thermodynamic product)

endo (kinetic product)

Equally important is the cycloaddition of furan to activated acetylenes (eg. 1,1,1,1,4,4,4,4-hexafluoro-2-butyne) in the generation of 3,4-disubstituted furans[43] (Scheme 9).

Scheme 9



(B). Syntheses of Polysubstituted Furans :

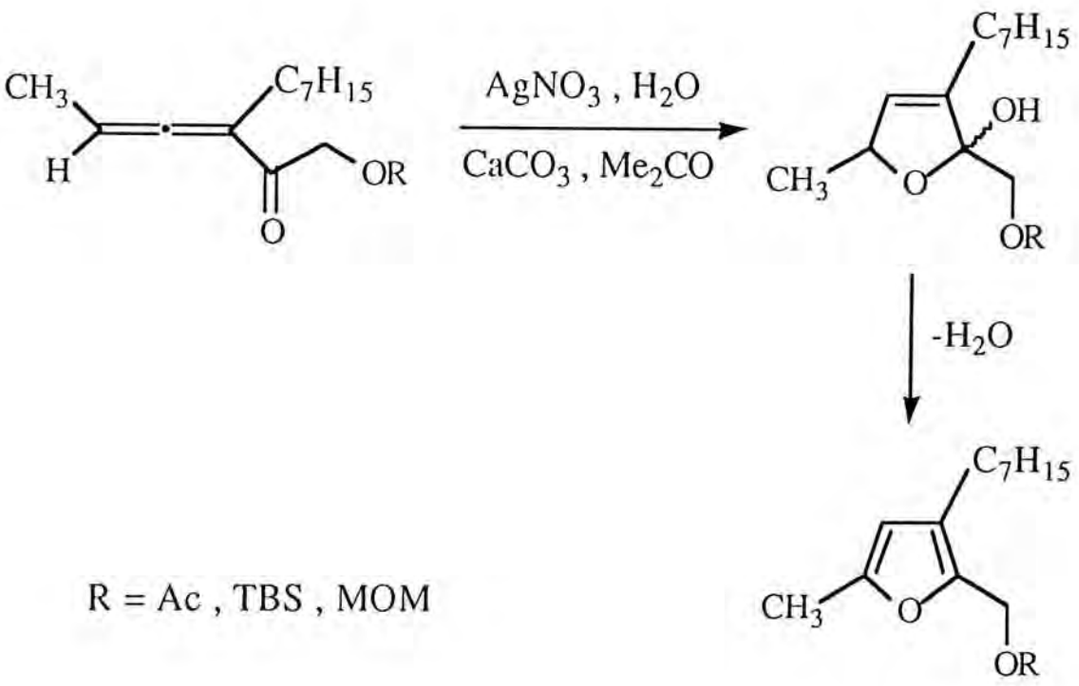
There is a resurgence in the literature of new and effective methodologies for furan synthesis in the last decade, due to the rapid development of organic chemistry, in particular organometallic chemistry. As a result of these activities, many new possibilities for furan synthesis have been recorded. In order to only focus our attention on the new synthetic methods, some old and not so frequently used methods are not discussed here

since they have been reviewed elsewhere.[39(b)-(e)] Some latest developments in furan synthesis are outlined below.

(1). By Ag(I) Catalyzed Cyclization ;

Conjugated allenones readily cyclized to 2,3,5-trisubstituted furans upon treatment with $AgNO_3$-$CaCO_3$ in aqueous acetone[44] (Scheme 10)

Scheme 10



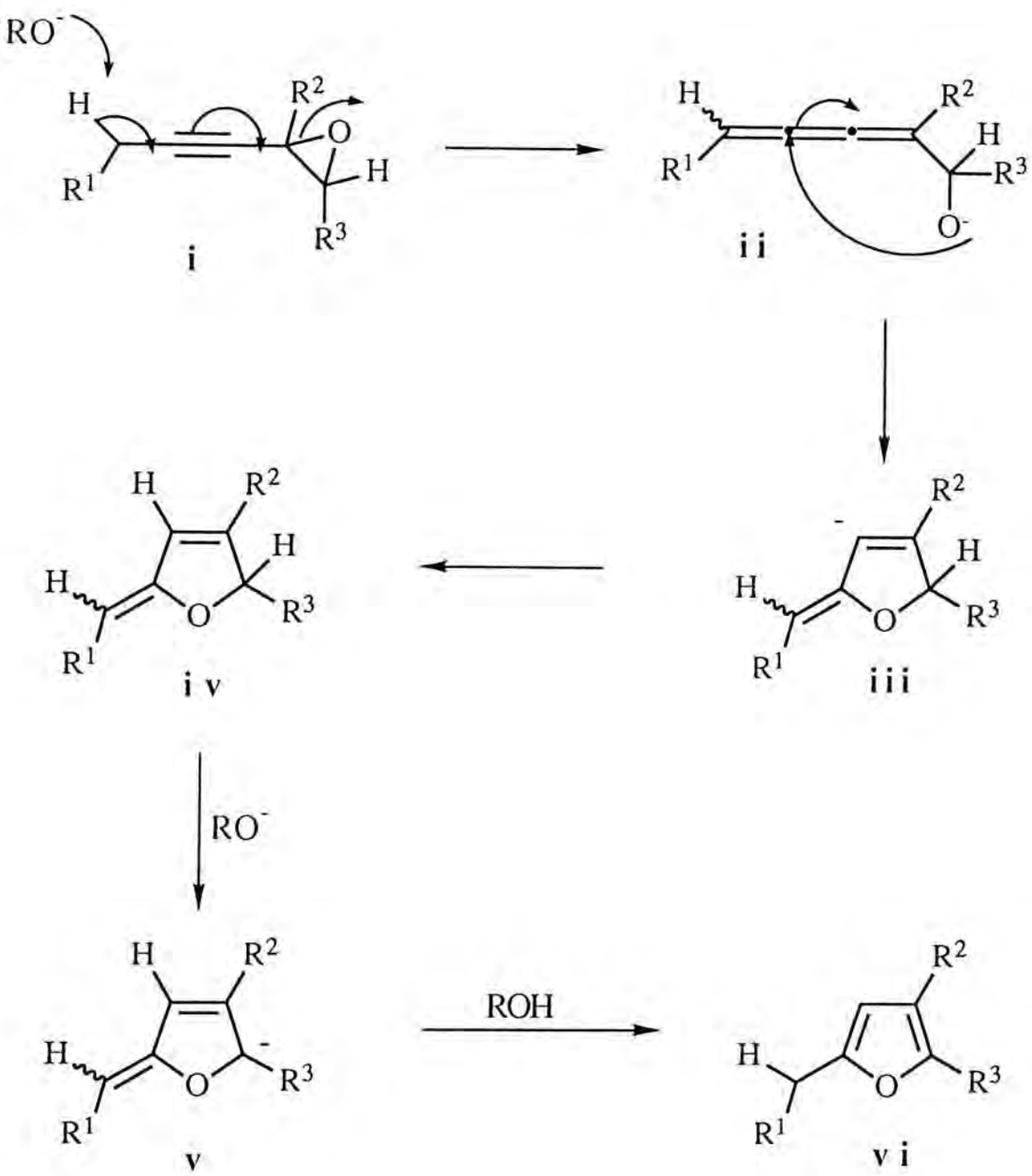
R = Ac , TBS , MOM

(2). By Base-Catalyzed Isomerization of Alkynyloxiranes ;

Alkynyloxiranes can isomerize to different substituted furans upon treatment with KO^tBu in ^tBuOH-18-crown-6. This is an unusual cyclization[45] (Scheme 11) which involves an initial 1,4-elimination of the alkynyloxirane **i** leading to the cumulene **ii**. Intramolecular cyclization of **ii** gives a vinylic anion **iii** which

undergoes proton transfer via **iv** and **v** followed by protonation to furnish **vi**.

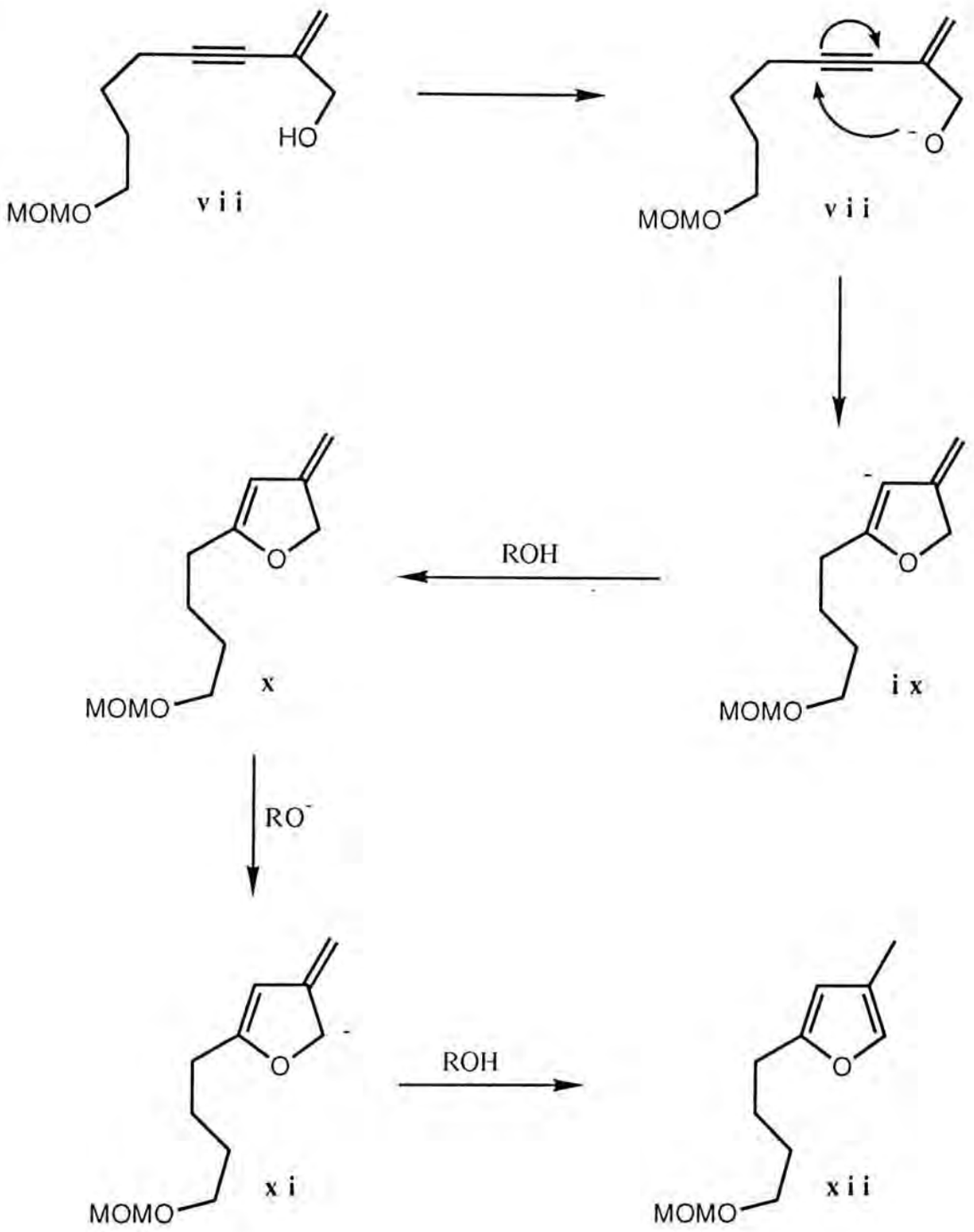
Scheme 11



This pathway can be further verified with the used of α-methylene homopropargylic alcohol **vii** as a starting material to provide a 2,4-disubstituted furan **xii** (Scheme 12). The anion **viii** generated from the alcohol **vii** in the presence of KO^{t}Bu undergoes

cyclization to give the vinylic anion **ix**, proton transfer through **x** and **xi** followed by protonation affords the furan **xii**.

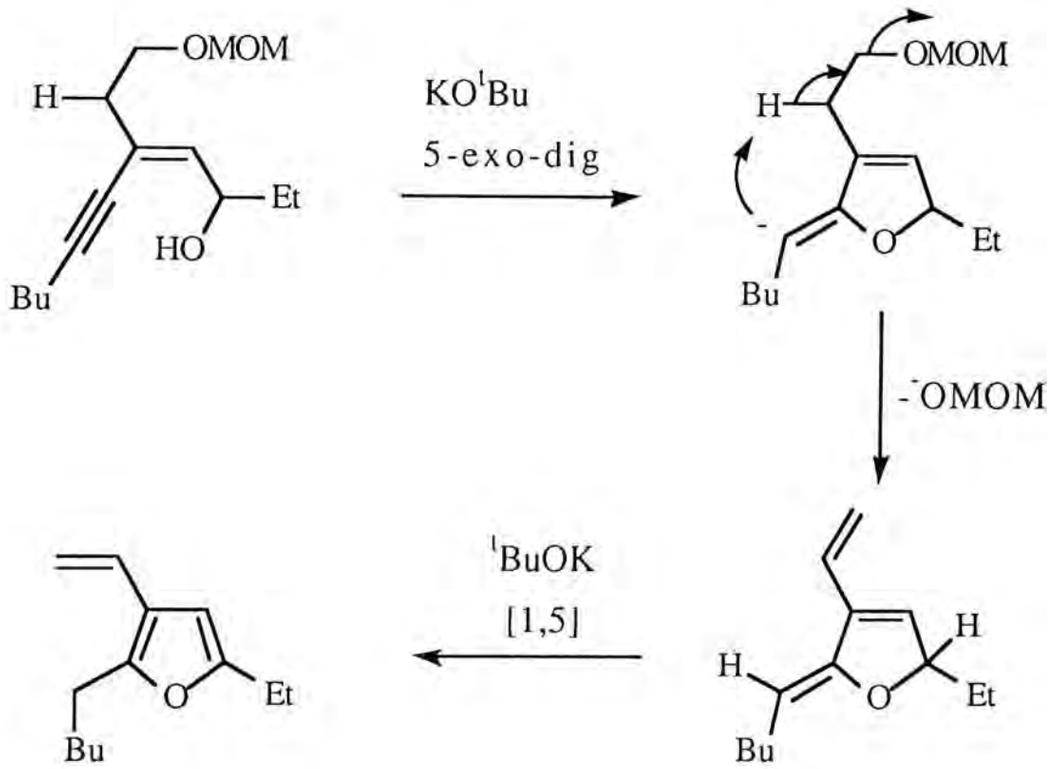
Scheme 12



(3). By Base-Catalyzed Cyclization-Isomerization of γ-Alkynyl Allylic Alcohol :

This methodology has been employed for the preparation of 2,3,5-trisubstituted furans via cyclization of γ-alkynyl allylic alcohol followed by a subsequent isomerization in KO^tBu.[46] An illustration of the mechanism is shown in Scheme 13.

Scheme 13

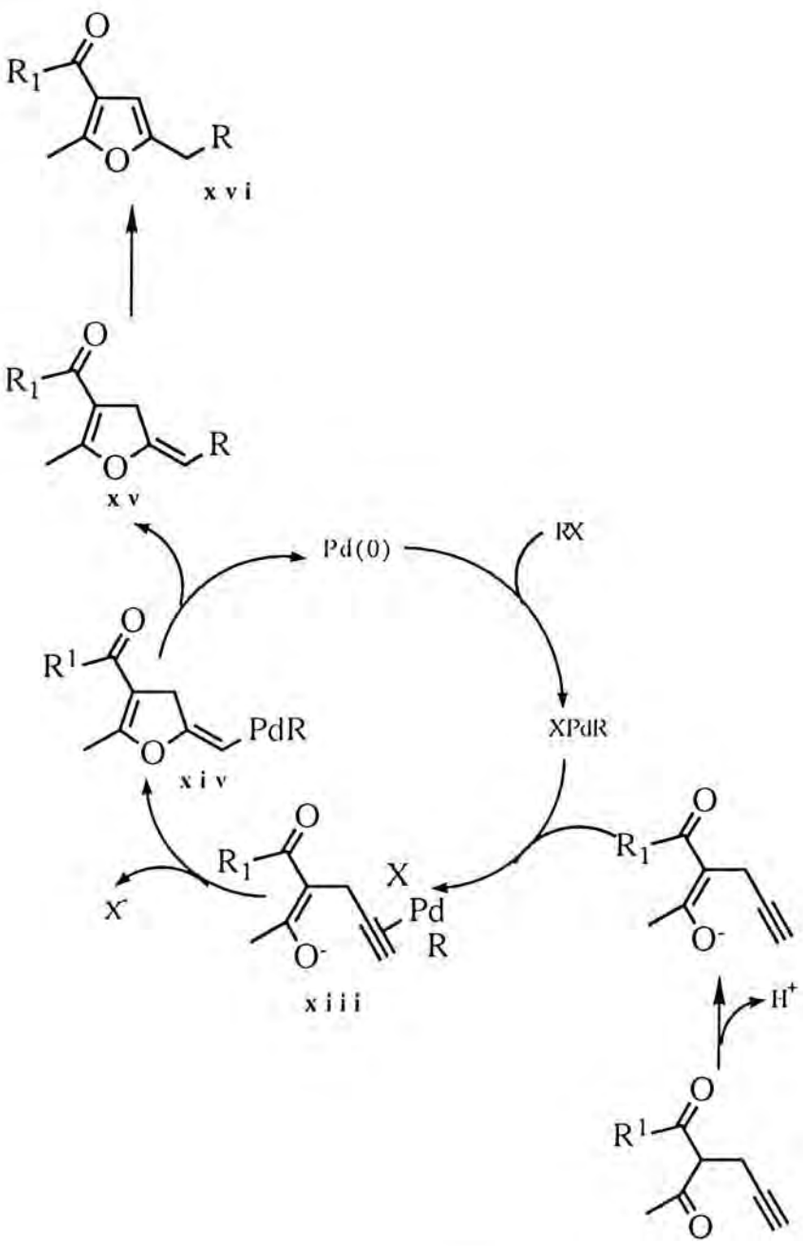


(4). By Palladium-Catalyzed Coupling of 2-Propargyl-1,3-dicarbonyl Compounds and Vinylic, Aryl Triflates or Halides :

2-Propargyl-1,3-dicarbonyl reacts as a functionalized alkyne with vinyl, aryl triflates or halides in the presence of $Pd(PPh_3)_4$

and K_2CO_3, providing 2,3,5-trisubstituted furans[47] (Scheme 14). The reaction proceeds through the formation of a π-palladium complex **xiii** and is followed by generation of the σ-vinyl-palladium complex **xiv** via regioselective *trans* addition of oxygen. The reductive elimination of Pd(0) gives hydrofuran **xv** which undergoes isomerization to afford the 2,3,5-trisubstituted furan **xvi**.

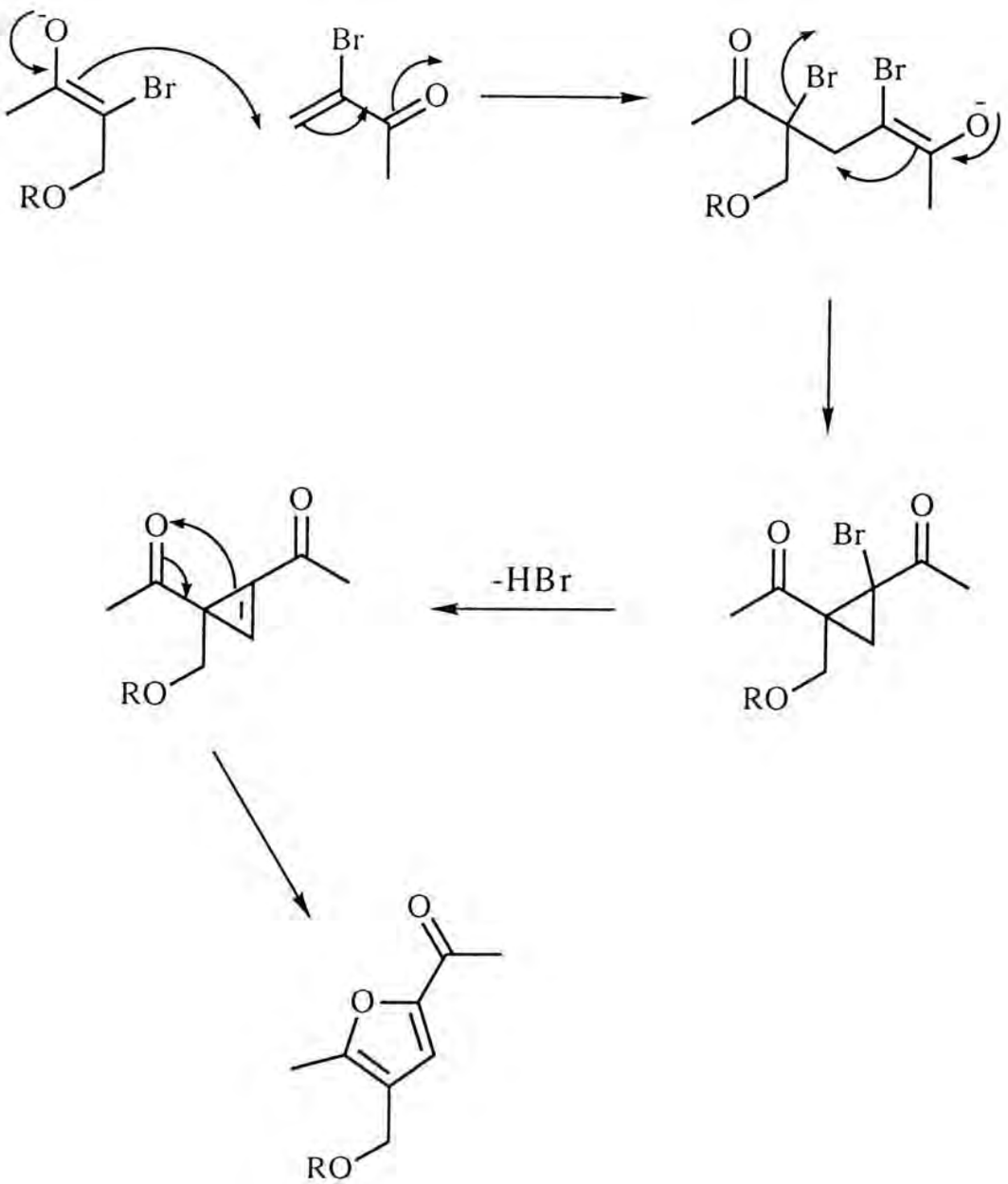
Scheme 14



(5). From α,β-Unsaturated Ketones :

α-Bromo-β-alkoxy ketone (in its enolated form) can be converted to 2-acetyl-4-alkoxymethyl-5-methylfurans in a one pot process by dehydrohalogenation with 1,8-diazabicyclo[5,4,0]-undec-7-ene (DBU)[48] (Scheme 15).

Scheme 15

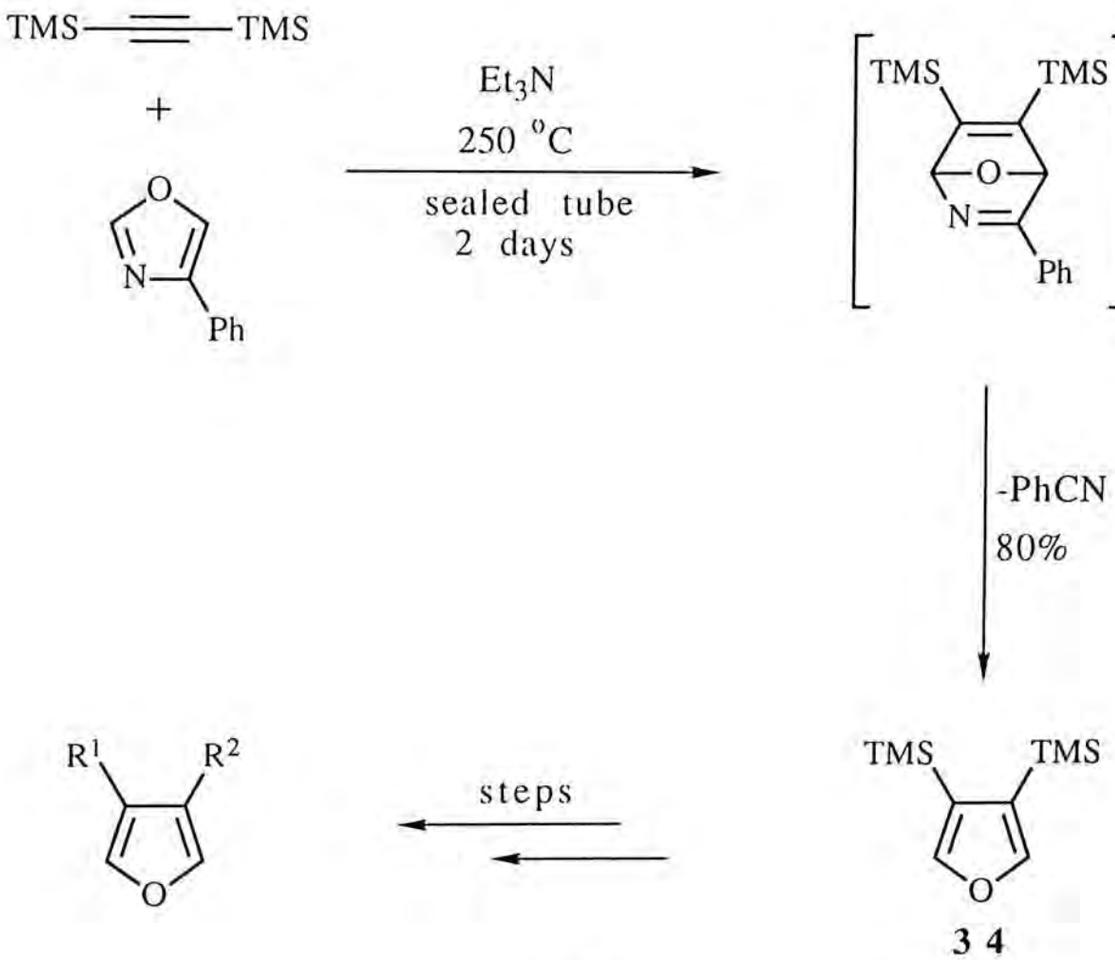


All the aforementioned methods are well established synthetic methodologies for the preparation of polysubstituted furans. However, a common shortcoming of these methods is that the availability of starting materials may be limited.

(C). Recent Achievement:

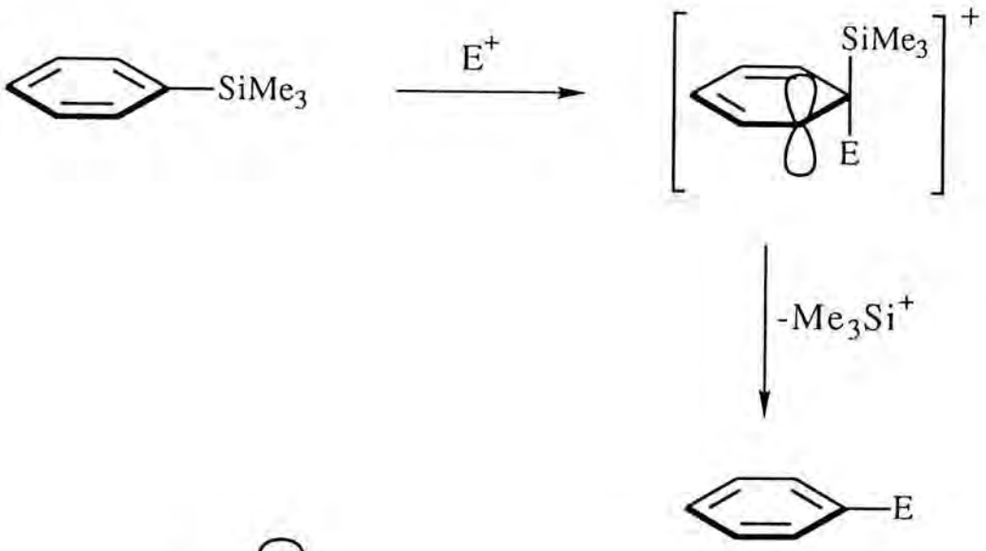
In previous works, we have demonstrated the use of Diels-Alder and retro Diels-Alder reactions to prepare 3,4-bis(trimethylsilyl)furan (**34**), which can be used as a building block for the synthesis of 3,4-disubstituted furans[37(a),(d)] (Scheme 16).

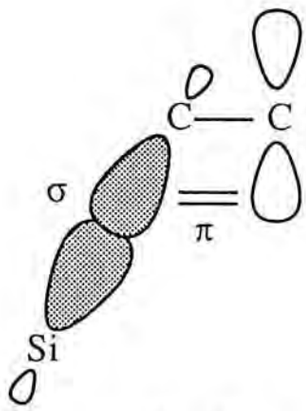
Scheme 16 :



It is known that the trimethylsilyl-substituted aromatic compounds would experience electrophilic substitution readily at the *ipso*-position.[49] The intermediate thus formed is stabilized by a β-effect as a result of the contribution from the carbon-silicon bond to the adjacent carbocation (Scheme 17).

Scheme 17



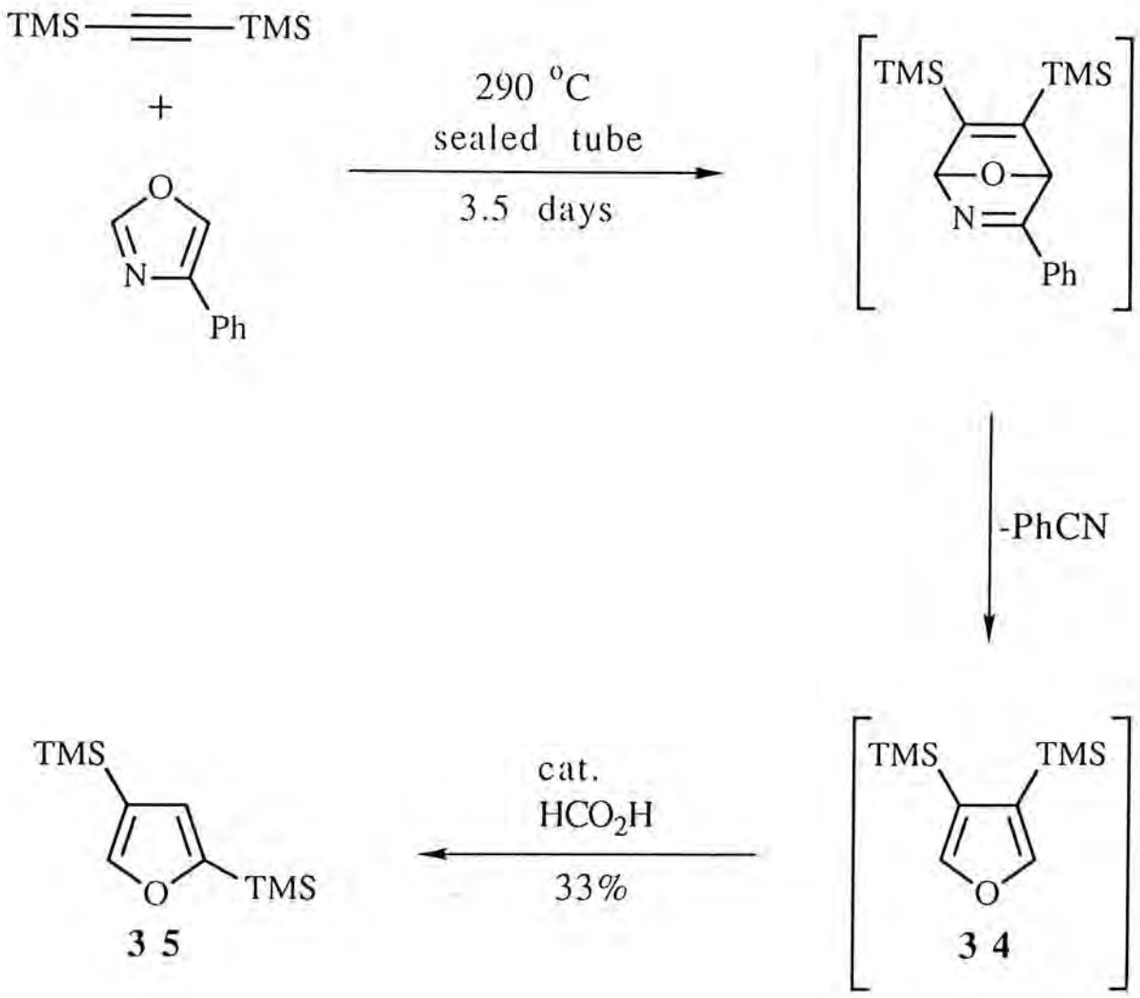


β-effect

The conjugation between the carbon-silicon σ-bond and the adjacent p-orbital is responsible for the intermediate's stability.[49] Experiments have shown that *ipso*-substitution of a proton on trimethylsilylated aromatic compounds would result in the rearrangement of the trimethylsilyl group.[50]

Based on these facts, we have successfully prepared 2,4-bis(trimethylsilyl)furan (**35**) from bis(trimethylsilyl)acetylene and 4-phenyloxazole[51] (Scheme 18). It is noteworthy that **35** has been previously prepared[52] in a small quantity by a photorearrangement of 2,5-bis(trimethylsilyl)furan.

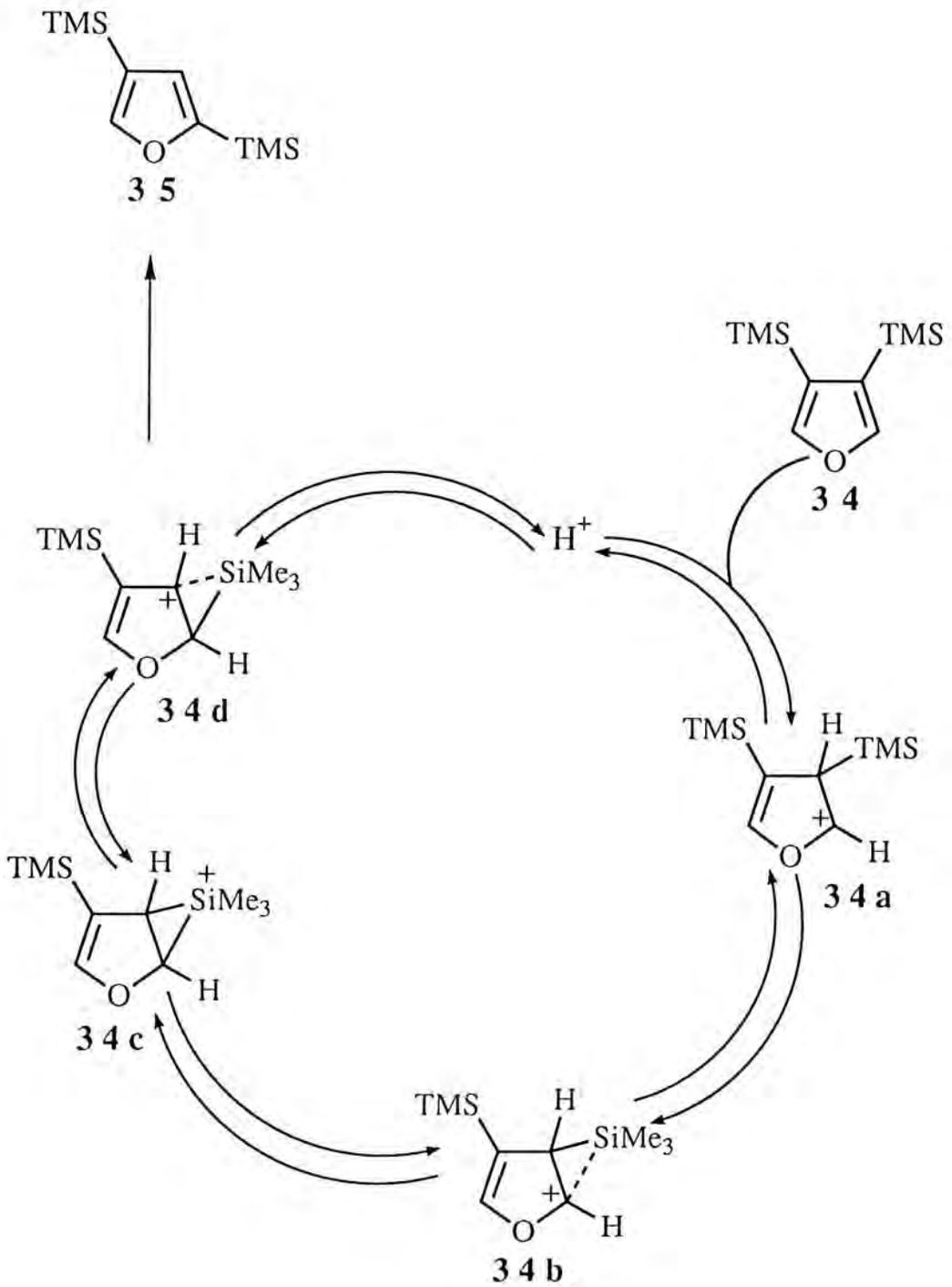
Scheme 18



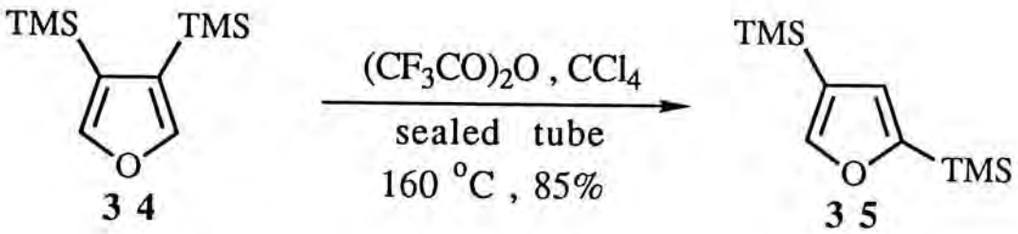
The rearrangement of a trimethylsilyl group occurs because of the sterically unfavorable orientation of the two trimethylsilyl groups at the C-3 and C-4 positions. The mechanism of the isomerization of **34** to **35** is shown in Scheme 9. It begins with the electrophilic attack of a proton on the *ipso*-position to form a cation **34a**. As

the rearrangement proceeds from **34b** to **34d**, it is likely that a pentavalent silicon cation intermediate **34c** is also involved.[53] The resulting 2,4-bis(trimethylsilyl)furan (**35**) is formed through the simultaneous elimination of a proton from the C-2 position.

Scheme 19



In a separate experiment, 3,4-bis(trimethylsilyl)furan (**34**) was converted efficiently to **35** on exposure to trifluoroacetic anhydride containing a catalytic amount of trifluoroacetic acid with CCl_4 as a solvent.



3 4 **3 5**

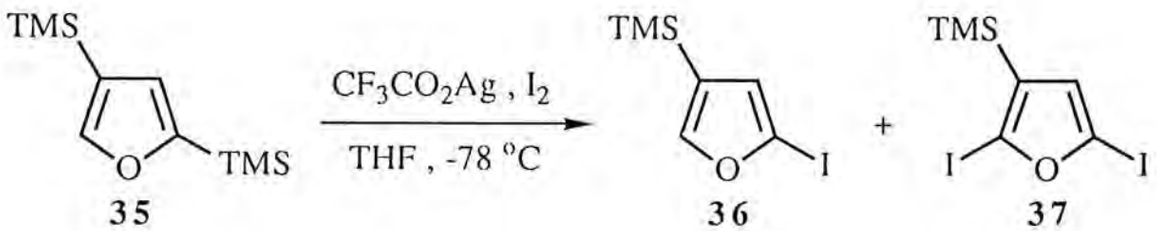
2,4-Bis(trimethylsilyl)furan (**35**) was used as a building block for the synthesis of polysubstituted furans. The synthetic utility of **35** is outlined in the following section.

(III). Results and Discussion :

(A). Attempted Synthesis of 2,4-disubstituted furans :

Our first attempt in the use of 2,4-bis(trimethylsily1)furan (**25**) was to prepare 2,4-disubstituted furans. It was known that aryltrimethylsilane can be iodinated easily at the *ipso*-position upon treatment with silver salt and iodine.[54] Therefore, our approach used as the key step was an iodination of the furan **35** with silver trifluoroacetate, iodine and THF at -78 °C. Unfortunately, the products turned out to be a mixture of non-separable mono- and di-iodo-furans (Scheme 20).

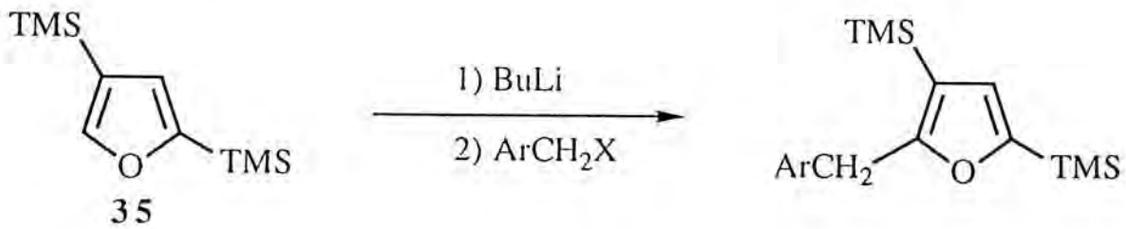
Scheme 20



The ^1H NMR spectrum of the non-polar fraction, separated by column chromatography on silica gel, indicates two peaks at δ 6.53 (s, 1H) and 7.44 (s, 1H) corresponding to the protons at C-3 and C-5 of iodofuran **36**, respectively. There also exists a singlet at δ 6.49 ppm which represents the C-4 proton of diiodofuran **37**. Both the mass peaks of **36** and **37** were found in the mass spectrum. In view of the results obtained in the direct iodination of **35**, further manipulation was not sought.

(B). Synthesis of 2,3,5-trisubstituted furans :

Since the direct iodination route had failed to give pure product, attention was drawn to the manipulation of C-2 position. It was well known that lithiation took place readily at C-2 position of furan.[55] Therefore, a blocking group could be added to the C-2 position of 2,4-bis(trimethylsilyl)furan (**35**) through ^{n}BuLi and alkyl or benzyl halides.

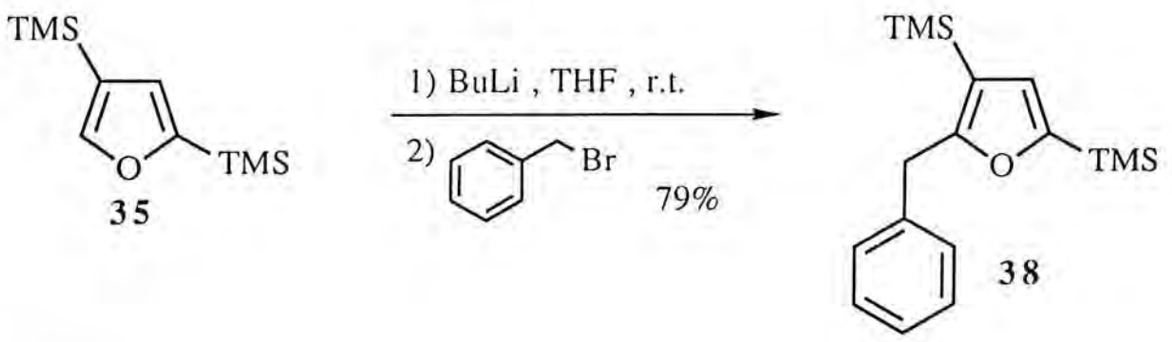


35

(1). Synthesis of 2-benzyl-3-*m*-anisyl-5-*p*-tolyl-furan (30) :

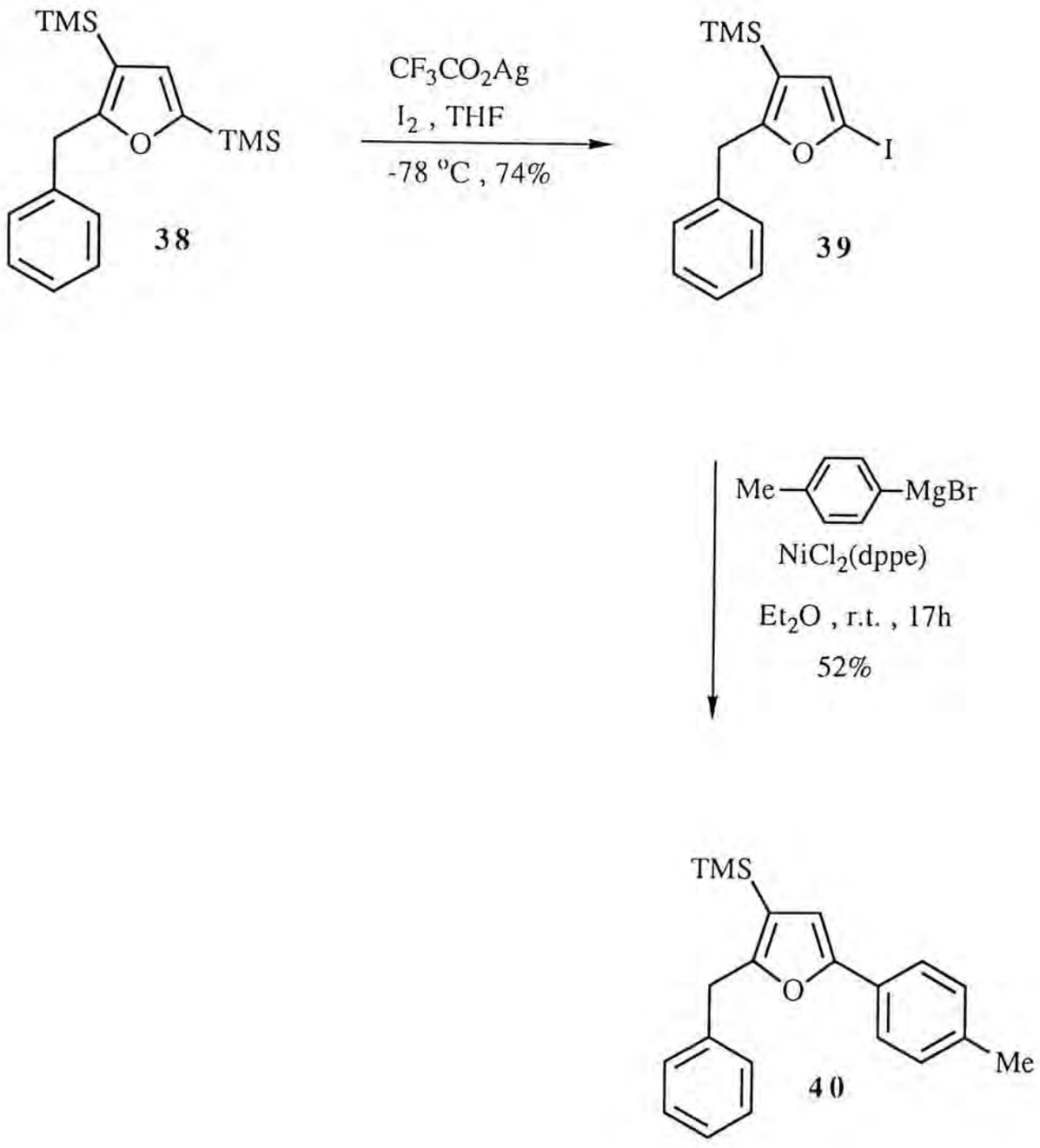
A benzyl group was chosen as a blocking substitutent to replace the C-2 proton of **35**, thus resulting in the generation of benzylfuran **38**. Subsequent *ipso*-iodination at C-5 provided the iodide **39**, which through a Ni-catalyzed cross-coupling yielded the diaryl-furan **40** (Scheme 21).

Scheme 21



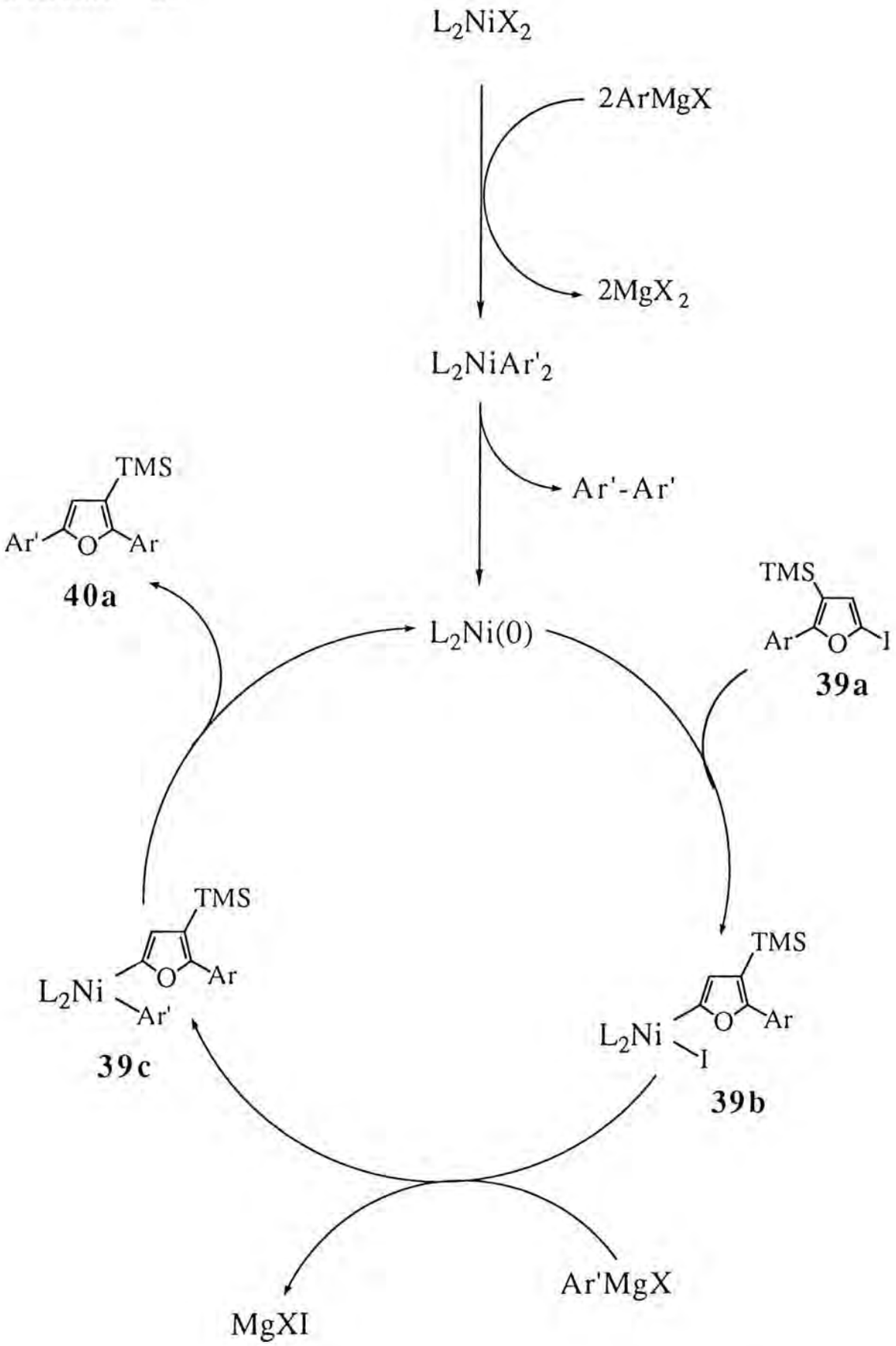
35 **38**

Scheme 21 (continued)



Nickel(II)-phosphine complexes are useful tools for the conversion of halofurans to arylfurans [56]. Here $NiCl_2$(dppe) was employed to catalytically convert the iodofuran **39** together with *p*-tolylmagnesium bromide to 2-benzyl-5-*p*-tolyl-3-trimethylsilyl-furan (**40**). The general mechanism of a Ni-catalyzed cross-coupling is shown in Scheme 22.

Scheme 22



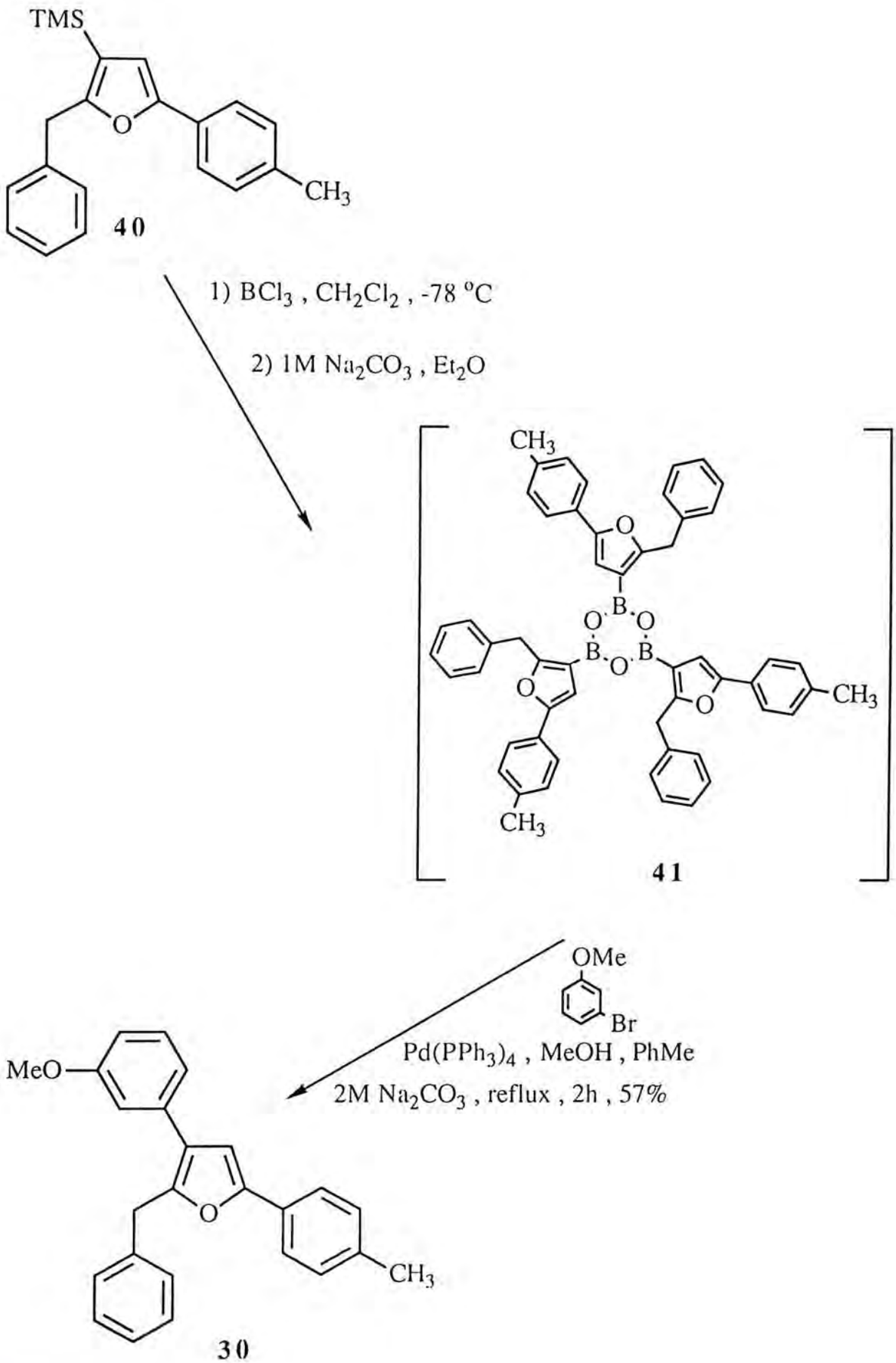
The dihalodiphosphine nickel reacted with a Grignard reagent to form an intermediate diorganonickel complex which, after

releasing an organo-dimer, was converted to an activated Ni(0) complex. An oxidative addition of the halofuran **39a** on Ni(0) followed by transmetallation with Ar'MgX furnished the diorgano complex **39c**. The reductive elimination of the coupling product **40a** resulted in the regeneration of the activated Ni(0) to complete the cycle.

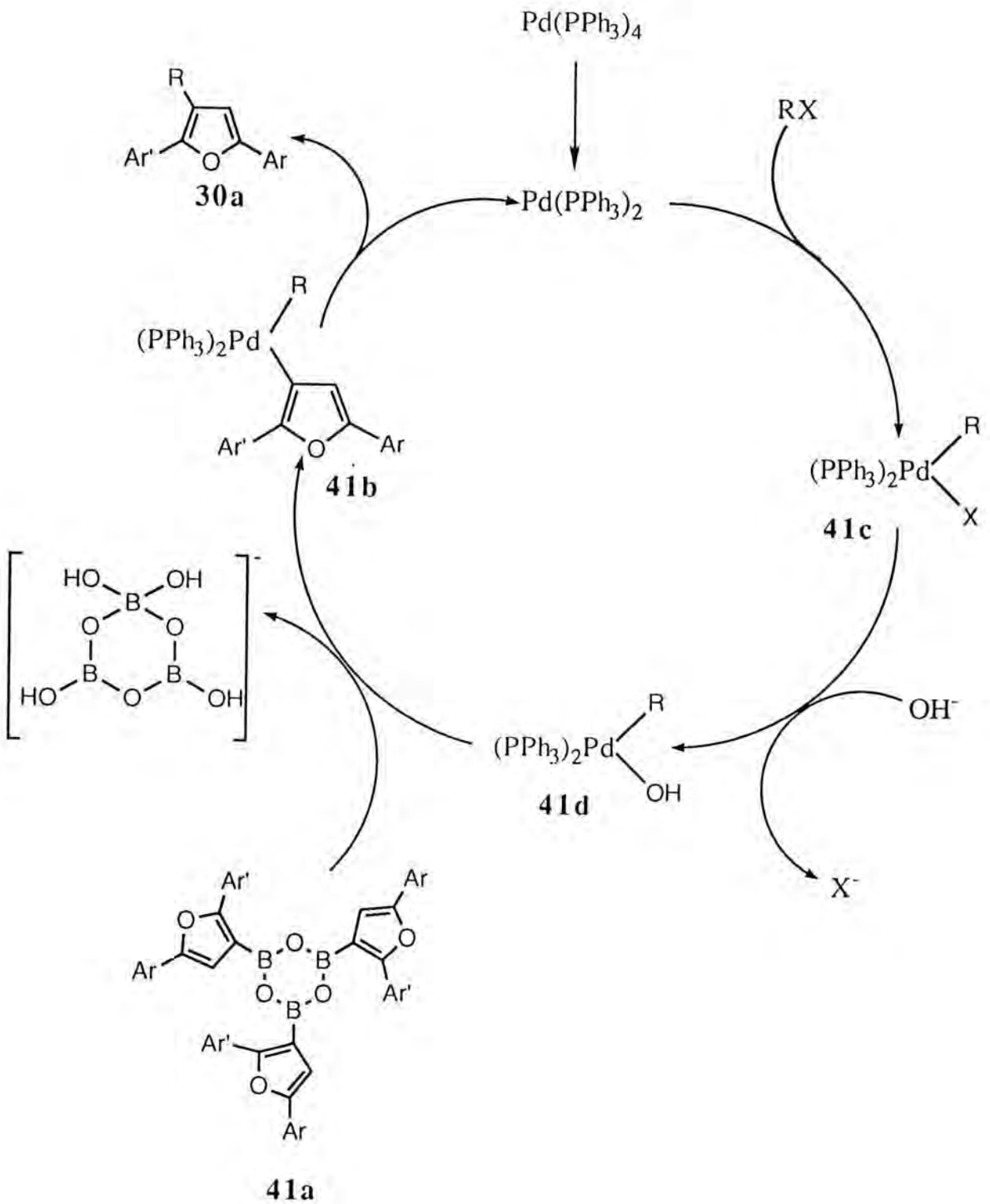
Treatment of **40** with one equivalent of boron trichloride at -78 ^{o}C and a subsequent work up with 1M Na_2CO_3 and ether afforded the boroxine **41** as an intermediate[37(d)] (Scheme 23). A palladium-catalyzed Suzuki-type cross-coupling[57] of the boroxine **41** and 3-bromoanisole using tetrakis(triphenylphosphine)-palladium(0) as a catalyst, in methanol, toluene and 2M Na_2CO_3 at refluxing temperature afforded **30**. Scheme 24 represents the general catalytic pathway of this Suzuki-type cross-coupling reaction.

The oxidative addition of RX on the activated $Pd(PPh_3)_2$, given by $Pd(PPh_3)_4$, generated an organo-halo-palladium complex **41c** which upon an anion exchanged provided an intermediate **41d**. The trimer **41a** then took part in the cycle, releasing the tetrahydroxyboroxine, and furnishing the diorgano-palladium **41b**. On completion of the cycle, the reductive elimination of the expected product [i.e. the 2,3,5-trisubstituted furan **30a**] and the simultaneous regeneration of the activated $Pd(PPh_3)_2$ took place.

Scheme 23


TMS
O
CH3
40
1) BCl3 , CH2Cl2 , -78 °C
2) 1M Na2CO3 , Et2O
CH3
O
B
O
O
B
O
B
O
O
CH3
CH3
41
OMe
Br
Pd(PPh3)4 , MeOH , PhMe
2M Na2CO3 , reflux , 2h , 57%
MeO
O
CH3
30

Scheme 24



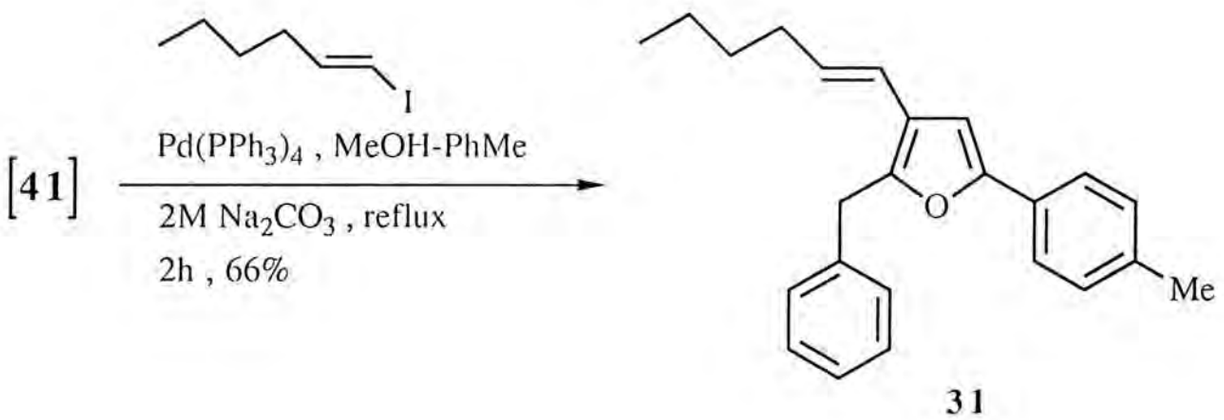
The ^{1}H NMR spectrum exhibits an AA'XX' system at δ 7.16-7.19 and 7.55-7.58 ppm (4H, J = 8.2 Hz) which corresponds to the two pairs of symmetrical protons of the tolyl group at the C-5 position. The methyl-protons of the tolyl group resonance as a singlet at δ

2.35 ppm (3H), so do the methoxy and the benzylic protons at δ 3.76 ppm (3H) and δ 4.20 ppm (2H), respectively. The C-4 proton shows a singlet at δ 6.76 ppm (1H). The rest of the 9 aromatic protons gave rise to the appearance of a multiplet at δ 6.81-7.33 ppm.

(2). Synthesis of 2-benzyl-3-*trans*-hexen-1-yl-5-*p*-tolyl-furan (31) :

Catalyzed by $Pd(PPh_3)_4$, the boroxine **41** reacted with *trans*-1-iodo-1-hexene at refluxing temperature to afford 2-benzyl-3-*trans*-hexen-1-yl-5-*p*-tolyl-furan (**31**) (Scheme 25).

Scheme 25



31

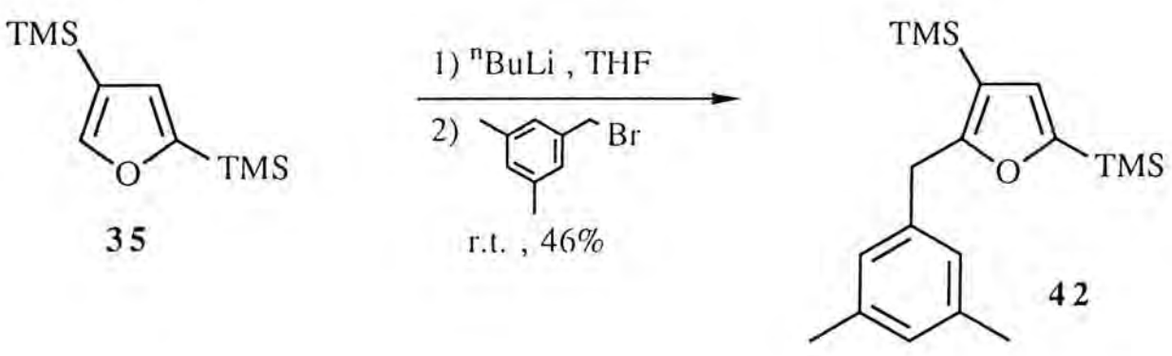
In the ^1H NMR spectrum of **31**, the terminal methyl-protons of the hexenyl group show a triplet at δ 0.89-0.95 ppm (3H, J = 7 Hz) and the aliphatic protons resonance at δ 1.26-1.46 ppm (4H) and δ 2.14-2.22 ppm (2H) as multiplets. The methyl protons of the tolyl group and the benzylic protons display two singlets at δ 2.34 ppm (3H) and δ 4.05 ppm (2H), respectively. The vinylic protons

resonance at δ 5.89-6.00 ppm (1H) and δ 6.20-6.27 ppm (1H) as two sets of multiplets. The C-4 proton provides a singlet at δ 6.69 ppm. There is also an AA'XX' system locating at δ 7.13-7.16 (2H, J = 8.2 Hz) and δ 7.49-7.53 (2H, J = 8.2 Hz). The rest of the aromatic protons afford a multiplet at δ 7.20-7.33 (5H).

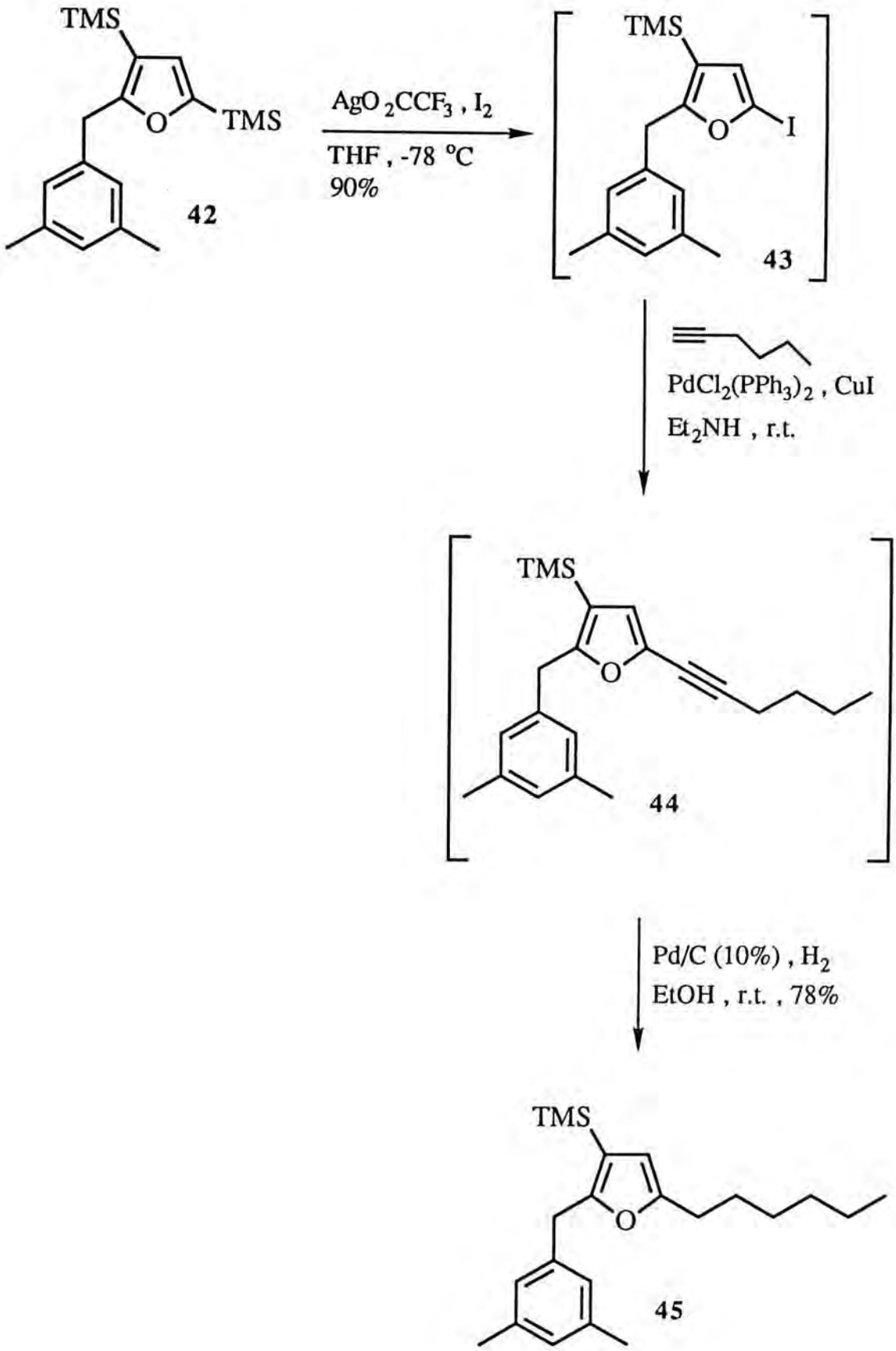
(3). Synthesis of 2-(3,5-dimethyl)benzyl-3-methoxycarbonylbenzyl-5-hexyl-furan (32) :

2,4-Bis(trimethylsilyl)furan (**35**) reacted with ^{n}BuLi and the resulting lithium salt was alkylated by 3,5-dimethylbenzyl bromide to give 2-(3,5-dimethyl)benzyl-3,5-bis(trimethylsilyl)furan (**42**). The usual iodination with AgO_2CCF_3 and I_2 in THF at -78 °C furnished the iodide **43**. Palladium-catalyzed cross-coupling reaction[58] was used to convert **43** to an alkynyl furan **44**. The triple bond was hydrogenated catalytically to generate a hexyl-furan **45** in good yield (Scheme 26). The general catalytic cycle of the Pd-catalyzed cross-coupling is shown in Scheme 27.

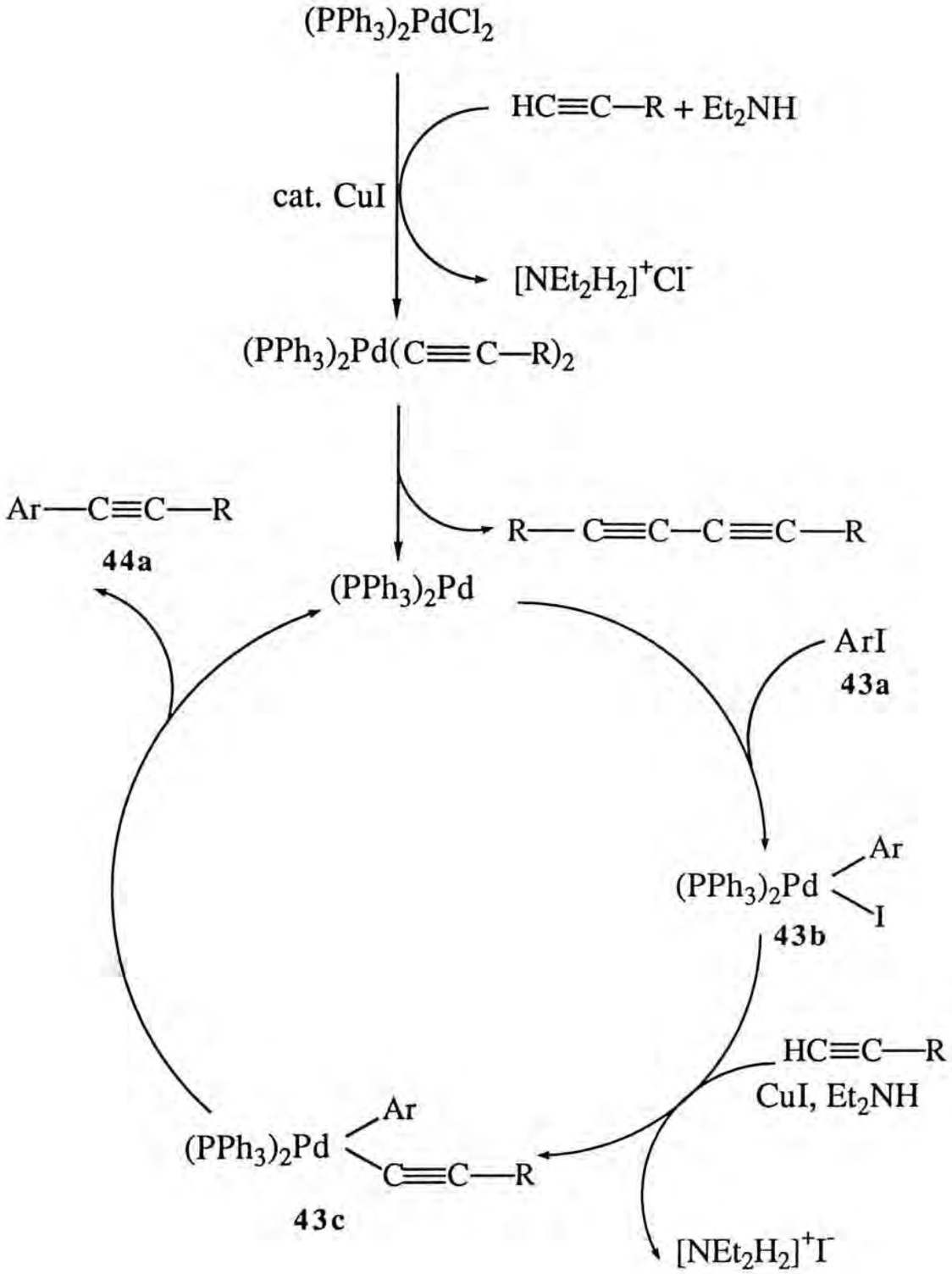
Scheme 26



Scheme 26 (continued)



Scheme 27



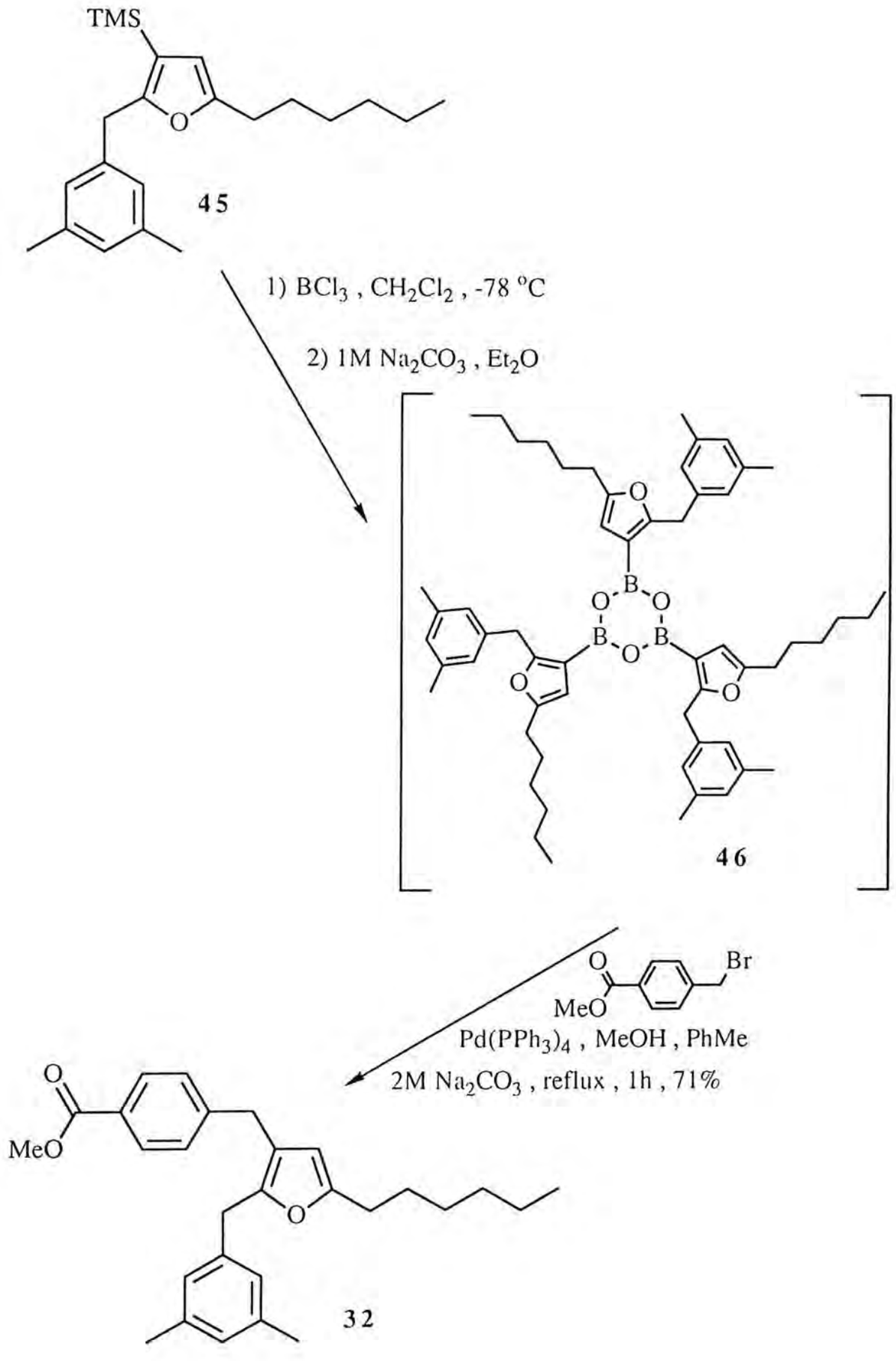
The mechanism was initiated when the Pd(II) complex reacted with a terminal acetylene in the presence of Et_2NH and CuI to form a dialkynylpalladium complex, which, through a reductive elimination of the diacetylene, became a reactive species of

$Pd(PPh_3)_2$. A subsequent oxidative addition of ArI to $Pd(PPh_3)_2$ gave the aryl-iodo-palladium complex **43b** on which alkynylation took place to form an aryl-alkynyl palladium **43c**. Subsequently, the cycle was completed by an reductive elimination of the coupling product **44a** and the regenerateion of the reactive $Pd(PPh_3)_2$.

The furan **45** was finally converted to **32**, via a boroxine intermediate **46**, by the usual consecutive treatment with BCl_3, Na_2CO_3-ether and Suzuki cross-coupling with methyl 4-bromomethylbenzoate (Scheme 28).

The ^1H NMR spectrum of **32** indicates the presence of the hexyl protons in between δ 0.83 and δ 2.54 ppm. The protons of the two methyl groups exhibit a singlet at δ 2.24 ppm (6H). The two sets of benzylic protons at C-2 and C-3 resonance as two singlets at δ 3.84 ppm (2H) and δ 3.72 ppm (2H), respectively. The benzoate methyl shows a singlet at δ 3.89 ppm (3H). The C-4 proton resonances at δ 5.72 ppm as a singlet (1H). The aromatic protons of the C-2 benzyl group show two singlets at δ 6.74 ppm (2H) and δ 6.82 ppm (1H). There is also an AA'XX' system (from the C-3 benzyl group) locating at δ 7.18-7.94 ppm (4H, J = 8.3 Hz).

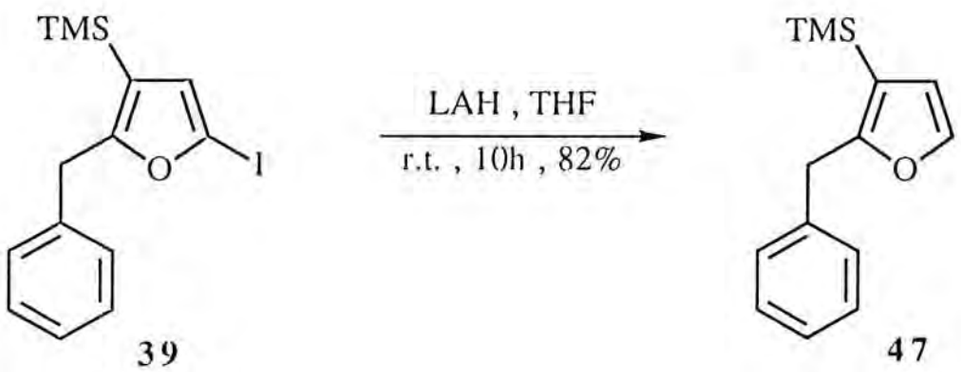
Scheme 28


TMS
O
45
1) BCl_3 , CH_2Cl_2 , -78 °C
2) 1M Na_2CO_3 , Et_2O
B
O
46
O
Br
MeO
$Pd(PPh_3)_4$, MeOH , PhMe
2M Na_2CO_3 , reflux , 1h , 71%
MeO
O
32

(4). Synthesis of 2-benzyl-3-[3,4-(methylenedioxy)]-benzylfuran (33) ;

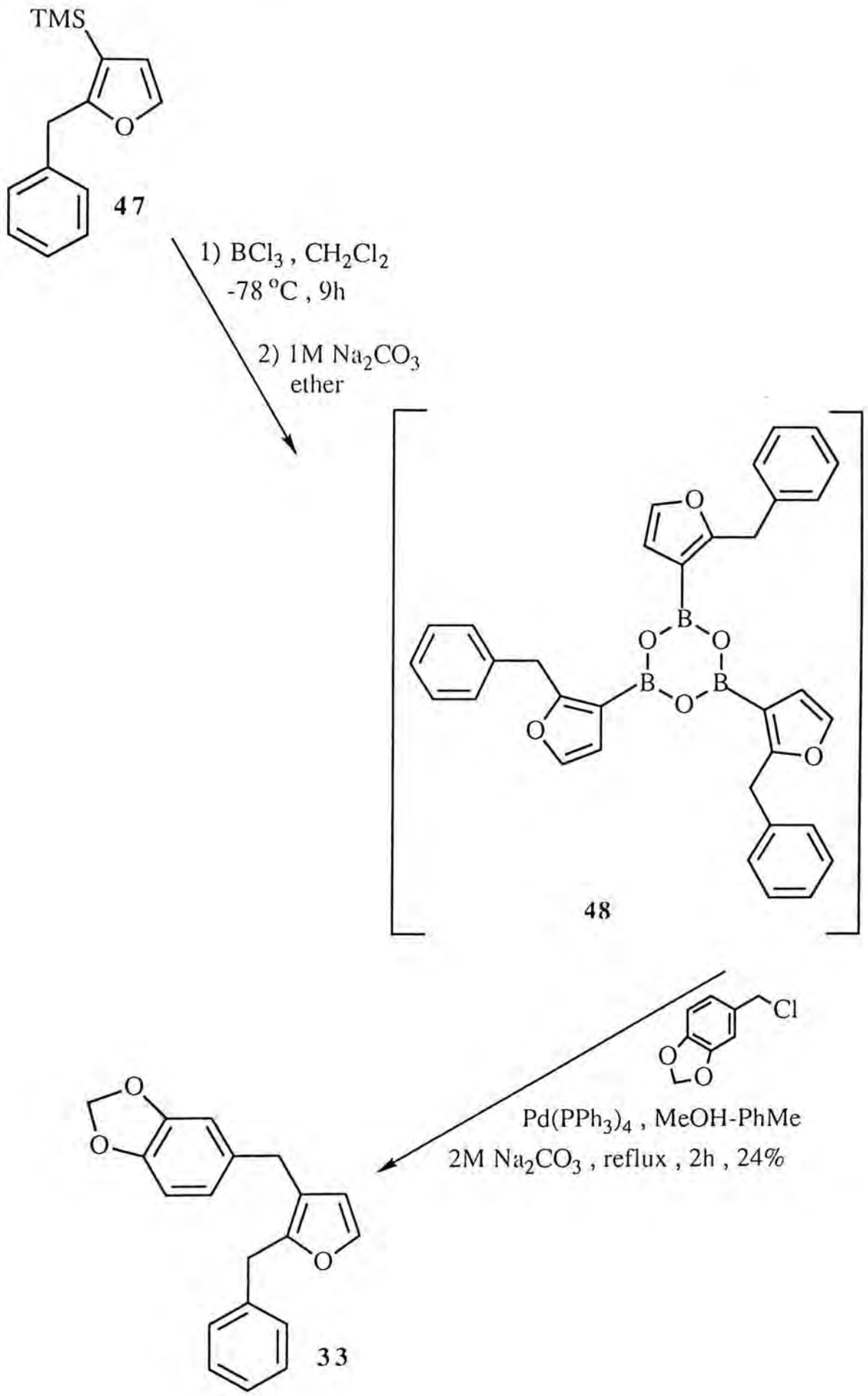
The previously prepared iodofuran **39** was reduced by LAH in THF at room temperature to furnish 2-benzyl-3-trimethylsilylfuran (**47**) which, upon treatment with BCl_3 and Na_2CO_3-ether, provided an intermediate boroxine **48**. A Pd(0)-catalyzed Suzuki-type cross-coupling reaction between **48** and 3,4-(methylenedioxy)benzyl chloride afforded the desired 2,3-disubstituted furan **33** (Scheme 29).

Scheme 29



39 **47**

Scheme 29 (continued)



In the ^{1}H NMR spectrum of **33**, there are three singlets locating at δ 3.58 ppm (2H), δ 3.88 ppm (2H) and δ 5.82 ppm (2H), which correspond to the benzylic protons at C-2, C-3, and the methylene protons respectively. The C-4 and C-5 protons show two doublets at δ 6.07 ppm (1H) and δ 7.18 ppm (1H), respectively. The multiplets of the aromatic protons appear in between δ 6.51 and δ 7.23 ppm (8H).

(IV). Conclusion :

The 2-benzyl-3-*m*-anisyl-5-*p*-tolyl-furan (**30**), 2-benzyl-3-*trans*-hexen-1-yl-5-*p*-tolyl-furan (**31**) and 2-(3,5-dimethyl)-benzyl-3-*p*-methoxycarbonylbenzyl-5-hexyl-furan (**32**) have been synthesized from 2,4-bis(trimethylsilyl)furan (**35**). The strategy used involved a C-2 lithiation-alkylation, a C-5 *ipso*-iodination, nickel-catalyzed cross-compling reaction and Pd(0)-catalyzed Suzuki-type cross-coupling reaction. 2-Benzyl-3-[3,4-(methylenedioxy)]benzylfuran (**33**) was synthesized through the reduction of iodofuran **39** and was followed by a Pd(0)-catalyzed Suzuki-type cross-coupling reaction.

These experimental series described above are expected to find important application in the synthesis of polysubstituted furans.

(V). Experimental Section :

4-Phenyloxazole[51]

A mixture of phenacyl bromide (255 g, 1.28 mol), ammonium formate (281 g, 4.4 mol) in anhydrous formic acid (1.3 L) was refluxed for 5.5 hours. The resulting dark-brown solution was poured into ice (1 kg). NaOH solution (8.3 M, 4 L) was added to the mixture with continuous stirring in order to neutralize the acid. When the pH reached 8, ether (1 L) was added to extract the product. The organic layer was separated, dried, and evaporated to give a crude dark-red liquid which was distilled under vacuum at 94-95 °C (10 mmHg) [lit.[51] bp. 57-60 °C (0.6 mmHg)] to furnish a light yellow liquid. Silica gel column chromatography (ether : hexanes = 1 :6 eluent) afforded a colorless oil (57 g, 30%). ^{1}H NMR (NMR-12), δ 7.27-7.43 (m, 3H), 7.73-7.77 (m, 2H), 7.91 (s, 1H). MS m/e 145 (M^+).

2,4-Bis(trimethylsilyl)furan (35)[52]

(a). Bis(trimethylsilyl)acetylene (2 g, 0.02 mol) and 4-phenyloxazole (2 g, 0.01 mol) were mixed in a sealed tube to which anhydrous HCOOH (0.1 mL, 2.6 mmol) was added. The sealed tube was heated at 290 °C for 3.5 days to give a dark mixture. Vacuum distillation of the resulting mixture gave a colorless liquid. Column chromatography on silica gel (hexanes eluent) afforded a colorless oil of **35** (1.63 g, 33%). ^{1}H NMR (NMR-13), δ 0.21 (s, 9H), 0.26 (s, 9H), 6.60 (s, 1H), 7.54 (s, 1H).

(b). From 3,4-bis(trimethylsilyl)furan (**34**) :

3,4-Bis(trimethylsilyl)furan (**34**) (0.1 g, 0.5 mmol) and CCl_4 (1 mL) were mixed in a sealed tube. To this solution $(CF_3CO)_2O$ (0.1 mL) was added through a syringe. The sealed tube was heated to 160 °C for 24 hours. The resulting mixture was evaporated to give a brown oil which was purified by chromatography on a silica gel column (hexanes eluent) to afford a colorless oil (85 mg, 85%). The physical and spectrometric data are identical with an authentic sample prepared previously.

Iodination of 2,4-bis(trimethylsilyl)furan (34)

2,4-Bis(trimethylsilyl)furan (**34**) (0.27 g, 1.3 mmol) was mixed with AgO_2CCF_3 (0.62 g, 2.8 mmol) in dry THF (10 mL). After all silver salt had been dissolved, the reaction flask was cooled in a dry ice-acetone bath (-78 °C). The mixture was stirred under N_2 for 5 minutes and I_2 (0.33 g, 1.3 mmol) in dry THF (10 mL) was added dropwise in a period of 20 minutes. The resulting suspension was stirred for 1 hour and was filtered to give a light yellow solution which was diluted with saturated $Na_2S_2O_5$ solution (20 mL) and ether (20 mL). The organic layer was separated, dried and evaporated to furnish a yellowish oil. Purification by silica gel column chromatography (hexanes eluent) afforded a mixture of **36** and **37** as a colorless oil (137.8 mg). The oil decomposed quickly on prolonged standing at room temperature. ^1H NMR (NMR-14) δ 0.29 (s, 11H), 6.49 (s, 0.5H), 6.53 (s, 1H), 7.44

(s, 1H). MS m/e 266 (M^+, mono-iodide, 29%), 392 (M^+, di-iodide, 76%).

2-Benzyl-3,4-bis(trimethylsilyl)furan (38)

To a stirred solution of 2,4-bis(trimethylsilyl)furan (**35**) (0.66 g, 3.1 mmol) in dry THF (12 mL) was added ^{n}BuLi (2 mL, 3.3 mmol) through a syringe. The mixture was stirred under N_2 for 30 minutes. Benzyl bromide (0.4 mL, 3.4 mmol) in dry THF (8 mL) was added dropwise to the orange mixture and it became light yellow immediately. The resulting mixture was left stirring for another 30 minutes, and then was poured into ether (20 mL) and washed with H_2O (20 mL). The organic fraction was separated, dried and evaporated to give a yellowish oil. The crude product was purified by silica gel column chromatography (hexanes eluent) to afford a colorless oil as product of **38** (0.75 g, 79%). ^{1}H NMR (NMR-15), δ 0.23 (s, 9H), 0.28 (s, 9H), 4.10 (s, 2H), 6.58 (s, 1H), 7.18-7.34 (m, 5H). MS m/e 302 (M^+, 10%), 73 (TMS, 100%). Anal. : Calcd for $C_{17}H_{26}OSi_2$: C, 67.48 ; H, 8.66. Found : C, 67.51 ; H, 8.48.

2-Benzyl-5-iodo-3-trimethylsilylfuran (39)

2-Benzyl-3,5-bis(trimethylsilyl)furan (**38**) (0.47 g, 1.6 mmol) was mixed with AgO_2CCF_3 (0.78 g, 3.5 mmol) in dry THF (10 mL). After all silver salt had been dissolved, the reaction flask was immersed in a dewar flask containing dry ice and acetone (-78 ^{o}C). The mixture was stirred under N_2 for 5 minutes and I_2

(0.40 g, 1.6 mmol) in THF (10 mL) was added dropwise in a period of 30 minutes. One hour later the resulting suspension was filtered through celite to give a light yellow solution which was diluted with saturated sodium metabisulfite ($Na_2S_2O_5$) solution (20 mL) and ether (20 mL). The organic portion was separated, dried and evaporated to yield a yellow oil. Purification by silica gel column chromatography (hexanes eluent) afforded a colorless oil of **39** (0.41 g, 74%). ^{1}H NMR (NMR-16), δ 0.25 (s, 9H), 4.07 (s, 2H), 6.46 (s, 1H), 7.18-7.35 (m, 5H). MS m/e 356 (M^+, 42%). Anal. : Calcd for $C_{14}H_{17}OSiI$: C, 47.20 ; H, 4.81. Found : C, 47.32 ; H, 4.63.

2-Benzyl-5-*p*-tolyl-3-trimethylsilylfuran (40)

The Grignard reagent was prepared by reacting 4-bromotoluene (2 g, 11.7 mmol) and a large excess of magnesium (1 g, 41.1 mmol) in dry ether (10 mL) at reflux temperature. The concentration of the Grignard salt formed was approximately 2.28 g per 10 mL. The iodide **39** (0.62 g, 1.7 mmol) was stirred with $NiCl_2$(dppe) (49.1 mg, 0.08 mmol) in dry ether (5 mL) under N_2 at room temperature. The Grignard reagent *p*-tolyl magnesium bromide (6 mL, 1.37 g, 7 mmol) was added to the solution through a syringe. After stirring for 17 hours, the resulting mixture was poured into saturated NH_4Cl solution (10 mL) and was extracted with ether (10 mL). The organic layer was separated, dried and evaporated to furnish a brownish oil. Column chromatography on silica gel (hexane eluent) afforded a colorless oil of **40** (0.29 g, 52%). ^{1}H NMR (NMR-17), δ 0.24 (s, 9H), 2.32 (s, 3H), 4.07 (s, 2H), 6.51 (s, 1H), 7.12-7.15 and 7.48-7.52 (AA'XX', 4H, 8.2 Hz), 7.21-

7.29 (m, 6H). MS m/e 320 (M^+, 100%). Anal. : Calcd. for $C_{21}H_{24}OSi$: C, 78.69 ; H, 7.55. Found : C, 78.80 ; H, 7.38.

2-Benzyl-3-*m*-anisyl-5-*p*-tolyl-furan (30)

Furan **40** (74 mg, 0.2 mmol) was stirred in CH_2Cl_2 (10 mL) under N_2 at -78 °C. 1 M BCl_3 in CH_2Cl_2 (0.27 mL, 0.3 mmol) was added via a syringe to the stirring solution. One hour later, the mixture was poured into 1 M Na_2CO_3 solution (10 mL) and was extracted with ether (15 mL). After layer separation, the organic fraction was dried and evaporated to give the crude yellowish boroxine **41**. Without purification, the boroxine **41** was mixed with 3-bromoanisole (0.06 mL, 0.5 mmol) and $Pd(PPh_3)_4$ (14.3 mg, 0.01 mmol) in MeOH (6 mL) and PhMe (6 mL). The solution was heated to dissolve all $Pd(PPh_3)_4$ and 2 M Na_2CO_3 (3 mL) was added. The mixture was heated to reflux for 1 hour. The resulting mixture was diluted with H_2O (10 mL) and ether (10 mL). The organic layer was separated, dried and evaporated to furnish a brownish oil which was chromatographed on a silica gel column (ether : hexanes = 1 : 20 eluent) to afford a colorless oil of **30** (46.7 mg, 57%). ^1H NMR (NMR-18), δ 2.35 (s, 3H), 3.76 (s, 3H), 4.20 (s, 2H), 6.76 (s, 1H), 6.81-7.03 (m, 3H), 7.16-7.19 and 7.55-7.58 (AA'XX', 4H, 8.2 Hz), 7.21-7.33 (m, 6H). MS m/e 354 (M^+, 100%). Anal. : Calcd. for $C_{25}H_{22}O_2$: C, 84.72 ; H, 6.26. Found : C, 84.56 ; H, 6.33.

2-Benzyl-3-*trans*-hexen-1-yl-5-*p*-tolyl-furan (31)

To a stirring solution of furan **40** (116.5 mg, 0.4 mmol) in CH_2Cl_2 (10 mL) at -78 °C under N_2 was added BCl_3 in CH_2Cl_2 (1M, 0.54 mL, 0.5 mmol). The mixture was stirred for 30 minutes. The resulting solution was poured into 1 M Na_2CO_3 solution (10 mL) and was extracted with ether (15 mL). The separated organic fraction was dried and evaporated to yield a yellow oil which was chromatographed on a silica gel column (ether : hexanes = 1 : 1 eluent) to furnish white solids. The solids obtained were immediately treated with *trans*-1-iodo-1-hexene, (supplied by Zhi-Zhong Song, Department of Chemistry, The Chinese University of Hong Kong), (147.7 mg, 0.7 mmol) and $Pd(PPh_3)_4$ (20 mg, 0.02 mmol) in MeOH (7 mL) and PhMe (7 mL). The solution was heated to dissolved all Pd(0) reagent and 2 M Na_2CO_3 (2 mL) was added in one portion. The resulting mixture was refluxed for 1 hour and was then diluted with H_2O (10 mL) and ether (10 mL). The organic layer was separated, dried and evaporated to furnish a brownish oil, which was purified by silica gel column chromatography (hexanes eluent) to afford a colorless oil of **31** (66.8 mg, 66%). ^1H NMR (NMR-19), δ 0.89-0.95 (t, 3H, 7 Hz), 1.26-1.46 (m, 4H), 2.14-2.22 (q, 2H, 6.7 Hz), 2.34 (s, 3H), 4.05 (s, 2H), 5.89-6.01 (m, 1H), 6.20-6.27 (d, 1H, 16.7 Hz), 6.69 (s, 1H), 7.13-7.16 and 7.49-7.52 (AA'XX', 4H, 8.2 Hz), 7.20-7.33 (m, 5H). MS m/e 330 (M^+, 18%). Anal. : Calcd. for $C_{24}H_{26}O$: C, 87.23 ; H, 7.93. Found : C, 87.36 ; H, 7.56.

3,5-Bis(trimethylsilyl)-2-(3,5-dimethyl)benzylfuran (42)

To a stirring solution of 2,4-bis(trimethylsilyl)furan (**35**) (0.59 g, 2.8 mmol) in THF (12 mL) at room temperature under N_2 was added ^nBuLi (1.7 mL, 2.8 mmol) through a syringe. After 30 minutes, 3,5-dimethylbenzyl bromide (393 mg, 2 mmol) in dry THF (5 mL) was added to the solution. The resulting solution was stirred for 30 minutes and was poured into ether (20 mL) and H_2O (20 mL). After layer separation, the organic fraction was dried and evaporated to give a brown oil. The crude product was chromatographed on a silica gel column (hexanes eluent) to afford a colorless oil of **42** (0.42 g, 46%). ^1H NMR (NMR-20), δ 0.32 (s, 9H), 0.35 (s, 9H), 2.37 (s, 6H), 4.10 (s, 2H), 6.65 (s, 1H), 6.90 (s, 2H), 6.92 (s, 1H). MS m/e 330 (M^+, 39%). Anal. : Calcd. for $C_{19}H_{30}OSi_2$: C, 69.02 ; H, 9.14. Found : C, 69.12 ; H, 9.00.

2-(3,5-dimethyl)benzyl-5-hexyl-3-trimethylsilylfuran (45)

(a) Formation of 2-(3,5-dimethyl)benzyl-5-iodo-3-trimethylsilylfuran (**43**) :

Furan **42** (404.5 mg, 1.2 mmol) was mixed with AgO_2CCF_3 (0.55 g, 2.5 mmol) in dry THF (10 mL) under N_2. After all the Ag salt had been dissolved, the reaction flask was cooled to -78 °C. Iodine (314.4 mg, 1.2 mmol) in dry THF (10 mL) was added to the solution dropwise in a period of 30 minutes. After stirring for 1 hour, the resulting suspension was filtered through celite to give a light yellow solution which was poured into a saturated $Na_2S_2O_5$

solution (20 mL) and was extracted by ether (20 mL). The organic layer was dried and evaporated to furnish a yellowish oil. Purification by silica gel column chromatography (hexanes eluent) afforded a colorless oil of **43** (426 mg, 91%) which decomposed gradually on prolonged standing at room temperature. ^{1}H NMR (NMR-21) δ 0.21 (s, 9H), 2.27 (s, 6H), 3.95 (s, 2H), 6.42 (s, 1H), 6.77 (s, 2H), 6.85 (s, 1H). Compound **43** was used in the following reaction without further purification.

(b) Formation of 2-(3,5-dimethyl)benzyl-5-hexynyl-3-trimethylsilylfuran (**44**)

Iodide **43** (180 mg, 0.5 mmol) was mixed with $PdCl_2(PPh_3)_2$ (128 mg, 0.2 mmol) and CuI (100 mg, 0.5 mmol) in Et_2NH (5 mL) and was stirred under N_2 at room temperature. After 1-hexyne (1 g, 12.7 mmol) had been added through a syringe, the mixture turned dark in a few minutes. The mixture was left stirring for 36 hours and was followed by evaporation of the organic solvent. The black residue was adsorbed on silica gel and column chromatography on silica gel using hexanes as eluent gave a colorless oil of **44**, which was used in the following reaction without further purification.

(c) Hydrogenation of **44**

The acetylene **44**, without further purification, was mixed with a catalytic amount of Pd/C (10%) in absolute ethanol (12 mL). The solution was then stirred under hydrogen atmosphere for 18 hours. The resulting mixture was filtered through celite and

evaporated. The crude product was purified by silica gel column chromatography (hexanes eluent) to afford a colorless oil of **45** (126 mg, 78%). ^{1}H NMR, (NMR-22) δ 0.20 (s, 9 H), 0.84-0.89 (t, 3H, 6.8 Hz), 1.26-1.59 (m, 8H), 2.26 (s, 6H), 2.52-2.58 (t, 2H, 7.6 Hz), 3.89 (s, 2H), 5.86 (s, 1H), 6.78 (s, 2H), 6.83 (s, 1H). Anal. : Calcd. for $C_{22}H_{34}OSi$: C, 77.13 ; H, 10.00. Found : C, 77.72 ; H, 10.07.

2-(3,5-dimethyl)benzyl-3-*p*-methoxycarbonylbenzyl-5-hexyl-furan (32)

Furan **45** (62 mg, 0.2 mmol) was stirred in CH_2Cl_2 (9 mL) at -78 °C under N_2. BCl_3 (1 M solution in CH_2Cl_2, 0.23 mL, 0.2 mmol) was added through a syringe. The solution was stirred for 30 minutes and was poured into 1 M Na_2CO_3 (15 mL) and ether (20 mL). The organic layer was separated, dried and evaporated to give a yellowish oil of **46**. The crude boroxine **46** was chromatographed on a silica gel column (ether : hexanes = 1 : 2 eluent) to furnish a yellowish oil as a pure boroxine **46**. It was immediately treated with $Pd(PPh_3)_4$ (15 mg, 0.01 mmol) and methyl 4-bromomethylbenzoate (44 mg, 0.2 mmol) in MeOH (5 mL) and PhMe (5 mL). The mixture was heated to dissolve all the $Pd(PPh_3)_4$. 2 M Na_2CO_3 (3 mL) was added to the stirring solution in one portion. The resulting mixture was refluxed for 1 hour and was then cooled to room temperature. It was diluted with H_2O (15 mL) and ether (15 mL). The organic layer was separated, dried and evaporated to give a brownish-yellow residue which was adsorbed on silica gel and purified by column chromatography on silica gel (ether : hexanes = 1 : 20 eluent) to yield a colorless oil of

32 (54 mg, 71%). ^{1}H NMR (NMR-23), δ 0.83-0.89 (t, 3H, 6.8 Hz), 1.26-1.61 (m, 8H), 2.24 (s, 6H), 2.48-2.54 (t, 2H, 7.6 Hz), 3.72 (s, 2H), 3.84 (s, 2H), 3.89 (s, 3H), 5.72 (s, 1H), 6.74 (s, 2H), 6.82 (s, 1H), 7.18-7.22 and 7.90-7.94 (AA'XX', 4H, 8.3 Hz). MS m/e 418 (M^+ ,100%). Anal. : Calcd. for $C_{28}H_{34}O_3$: C, 80.35 ; H, 8.19. Found : C, 80.35 ; H, 8.21.

2-Benzyl-3-trimethylsilylfuran (47)

Lithium aluminum hydride (49 mg, 1.3 mmol) was added in one portion to a stirred solution of 2-benzyl-5-iodo-3-trimethylsilylfuran (**39**) (0.83 g, 2.3 mmol) in THF (10 mL) under N_2 at room temperature. The suspension was stirred for 10 hours. The reaction flask was immersed in an ice bath and H_2O (5 mL) was added very slowly to destroy the unreacted LAH. The resulting solution was diluted with H_2O (10 mL) and ether (15 mL). The organic layer was separated, dried and evaporated. The crude product was purified by silica gel column chromatography (hexanes eluent) to afford a colorless oil of **47** (441 mg, 82%). ^{1}H NMR (NMR-24) δ 0.24 (s, 9H), 4.02 (s, 2H), 6.29-6.30 (t, 1H, 1.8 Hz), 7.14-7.27 (m, 5H), 7.34-7.35 (t, 1H, 1.8 Hz). Anal. : Calcd. for $C_{14}H_{18}OSi$: C, 72.99 ; H, 7.87. Found : C, 72.78 ; H, 7.65.

2-Benzyl-3-[3,4,-(methylenedioxy)]benzylfuran (33)

2-Benzyl-3-trimethylsilylfuran (**47**) (190 mg, 0.8 mmol) was stirred in CH_2Cl_2 (10 mL) at -78 °C under N_2. BCl_3 (1 M solution in CH_2Cl_2, 1.22 mL, 1.2 mmol) was added through a

syringe to the reaction flask. The solution was left stirring for 9 hours. The resulting mixture was poured into 1 M Na_2CO_3 (10 mL) and was extracted with ether (15 mL). After layer separation, the organic fraction was dried and evaporated. The crude boroxine **48** was chromatographed on a silica gel column (ether: hexanes = 1 : 2 eluent) to give yellowish solids. The amount of the starting **47** recovered was 96.6 mg (0.4 mmol) and the amount of starting material actually reacted was 93.3 mg (0.4 mmol). The yield of boroxine **48** was 46 mg (62%). Boroxine **48** was immediately treated with 3,4-(methylenedioxy)benzyl chloride (73 mg, 0.4 mmol) and $Pd(PPh_3)_4$ (20 mg, 17 mmol) in MeOH (6 mL) and PhMe (6 mL). The solution was heated to dissolve the palladium catalyst. 2 M Na_2CO_3 (2 mL) was added to the mixture in one portion. The mixture was refluxed for 2 hours. The resulting mixture was allowed to cool to room temperature and was poured into H_2O (15 mL). After extraction with ether (15 mL), the organic layer was separated, dried and evaporated. Purification of the crude product through silica gel column chromatography (hexanes eluent) afforded a yellowish oil of **33** (17 mg, 24%). ^1H NMR (NMR-25) δ 3.58 (s, 2H), 3.88 (s, 2H), 5.82 (s, 2H), 6.07-6.08 (d, 1H, 1.8 Hz), 7.19-7.20 (d, 1H, 1.8 Hz), 6.51-6.54 (m, 2H), 6.61-6.64 (m, 1H), 7.07-7.23 (m, 5H). Anal. : Calcd for $C_{19}H_{16}O_3$: C, 78.06 ; H, 5.52. Found : C, 77.81 ; H, 5.61.

References :

(1). Hückel, E., *Z. Phys.* **1931,** *70,* 204

(2). Hückel, E., *Z. Elektrochem.*, **1937,** *43,* 752.

(3). Hückel, E., *Grundzüge der Theorie ungesättigter und aromatischer Verbindungen*, Verlag Chemie: Berlin, 1938.

(4). Breslow, R., *Acc. Chem. Res.*, **1973,** *6,* 393

(5). Dewar, M. J. S., *Adv. Chem. Phys.*, **1965,** *8* 121.

(6). Rapheal, R. A., In *Non-Benzenoid Aromatic Compounds*; Ginsburg, D., Ed; Interscience: New York, 1959; Ch VIII.

(7). Schröder, G., *Cyclooctatetraen*; Verlag Chime: Weinheim, 1965.

(8). Paquette, L. A., *Tetrahedron,* **1975,** *31,* 2855.

(9). Salem, L. *The Molecular Orbital Theory of Conjugated Systems* ; W. A. Benjamin: New York, 1966, pp 122-125, pp 468-470.

(10). Krebs, A. *Angew. Chem. Int. Ed. Engl.* **1965,** *4,* 953.

(11). Krebs, A. ; Byrd, D. *Justus Liebigs Ann. Chem.* **1967,** *707,* 66.

(12). Elix, J. A.; Sargent, M. V.; Sondheimer, F.; *J. Am. Chem. Soc.* **1970,** *92,* 962.

(13). Lankey, A. S.; Ogliaruso, M. A.; *J. Org. Chem.* **1971,** *36,* 3339.

(14). Wong, H. N. C.; Sondheimer, F. *Angew. Chem. Int. Ed. Engl.* **1976,** *15,* 117.

(15). Wong, H. N. C.; Sondheimer, F. *Tetrahedron* **1981,** *37 (S1),* 99.

(16). Huang, N. Z.; Sondheimer, F. *Acc. Chem. Res.* **1982,** *15,* 96.

(17). Rynard, C. M. Thankachan, C.; Tidwell, T.T. *J. Am. Chem. Soc.* **1979,** *101,* 1196;
Naito, K.; Rickborn, B. *J. Org. Chem.* **1980,** *45,* 4061.
Rodrigo, R. *Tetrahedron* **1988,** *44,* 2093

(18). Man, Y. M.; Mak, T. C. W; Wong, H. N. C. *J. Org. Chem.* **1990,** *55,* 3214.

(19). Destro, R.; Pilati, T.; Simonetta, M. *J. Am. Chem. Soc.* **1975,** *97,* 658; *Acta Crystallogr.* **1977,** *B33,* 447.

(20). Graaf, R. A. G.; Gorter, S.; Romers, C.; Wong, H. N. C.; Sondheimer, F. *J. Chem. Soc. Perkin Trans. 2* **1980,** 478.

(21). Kay, M. I.; Okaya, Y.; Cox, D. E. *Acta Crystallogr.* **1971,** *27,* 26.

(22). Cheng, S. K. T.; Wong, H. N. C. *Synth. Comm.* **1990,** *20,* 3053.

(23). Barton, J. W.; Lee, D. V.; Shepherd, M. K. *J. Chem. Soc. Perkin. Trans. 1.* **1985,** 1407.

(24). Dilthey, W.; ter Horst, I.; Schommer, W. *J. Prakt. Chem.* **1935,** *143,* 189.

(25). Cava, M. P.; Napier, D. R. *J. Am. Chem. Soc.* **1957,** *79,* 1701.

(26). Dornfeld, C. A.; Callen, J. E.; Coleman, G. H. *Org. Syn. Coll. Vol.* **1960,** *3,* 134.

(27). Lambert, P.; Martin, R. H. *Bull. Soc. Chim. Belg.* **1952,** *61,* 124.

(28). DeRidder, R.; Martin, R. H. *Bull. Soc. Chim. Belg.* **1960,** *69,* 534.

(29). Wang, T.-Z.; Paquette, L. A. *Tetrahedron Lett.* **1988,** *29,* 41.

(30). Meier, H.; Peterson, H.; Kolshorn, H. *Chem. Ber.* **1980,** *113,* 2398.

(31). Bachmann, W. E. *J. Am. Chem. Soc.* **1934,** *56,* 1365.

(32) (a). DeShong, P.; Ramesh, S.; Elango, V.; Perez, J. J. *J. Am. Chem. Soc.* **1985,** *107,* 5219.

(b). Klein, L. L. *J. Am. Chem. Soc.* **1985,** *107,* 2573.

(c). Danheiser, R. L.; Stoner, E. J.; Koyama, H.; Yamashita, D. S.; Klade, C. A. *J. Am. Chem. Soc.* **1989,** *111,* 4407.

(d). Takano, S.; Iwabuchi, Y.; Ogasawara, K. *J. Chem. Soc., Chem. Commum.* **1989,** 1371.

(e). Carney, J. R.; Scheuer, P.J.; Kelly-Borges, M. *J. Org. Chem.* **1993,** *58,* 3460.

(33). Lipshutz, B. H. *Chem. Rev.* **1986,** *86,* 795.

(34). Nicolaou, K. C.; Prasad, C. V. C.; Somers, P. K.; Hwang, C.-K. *J. Am. Chem. Soc.* **1989,** *111,* 5330.

(35). Williams, R. M.; Esslinger, C. S. *Tetrahedron Lett.* **1991,** *32,* 3635.

(36). Nakanishi, K. *Natural Products Chemistry* Kodansha, Ltd.: Tokyo, **1974**

(37) (a). Ho, M. S.; Wong, H. N. C. *J. Chem. Soc., Chem. Commun.* **1989,** 1238.

(b). Yang, Y.; Wong, H. N. C. *J. Chem. Soc., Chem. Commun.* **1992,** 656.

(c). Yang, Y.; Wong, H. N. C. *J. Chem. Soc., Chem. Commun,* **1992,** 1723.

(d). Song, Z. Z.; Zhou, Z. Y.; Mak, T. C. W.; Wong, H. N. C.; *Angew. Chem. Int. Ed. Engl.* **1993,** *32,* 432.

(38). Joule, J. A.; Smith, G. F. *Heterocyclic Chemistry;* ELBS : U. K., **1986.**

(39) (a). Gschwend, H. W.; Rodriguez, H. R. *Org. Reactions* **1979,** *26,* 1.

(b). Donnelly, D. M. X.; Meegan, M. J. In *Comprehensive Heterocyclic Chemistry;* Bird, C. W.; Cheeseman, G. W. H., Eds.; Pergamon Press: Oxford, 1984; Vol. 4, Part 3, pp 657-712.

(c). Dean, F. M. In *Advances in Heterocyclic Chemistry;* Katritzky, A. R., Ed.; Academic Press: New York, 1982; Vol. 30, pp 167-238.

(d). Dean, F. M. In *Advances in Heterocyclic Chemistry;* Katritzky, A. R., Ed.; Academic Press: New York, 1982; Vol. 31, pp 237-344.

(e). Yang, Y. Ph. D. Thesis, The Chinese University of Hong Kong, 1993.

(40). Chadwick, D. J.; Willbe, C. *J. Chem. Soc., Perkin Trans 1.* **1977,** 887.

(41). Bosshard, P.; Eugster, C. H. In *Advances in Heterocyclic Chemistry;* Katritzky, A. R., Ed.; Academic Press: New York, 1966; Vol. 7, pp 378-392.

(42). Lee, M. W.; Herndon, W. C. *J. Org. Chem.,* **1978,** *43,* 518.

(43). Weis, C. D. *J. Org. Chem.* **1962,** *27,* 3693.

(44). Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1991,** *56,* 960.

(45). Marshall, J. A.; DuBay, W. J. *J. Am. Chem. Soc.* **1992,** *114,* 1450.

(46). Marshall, J. A.; DuBay, W. J. *J. Org. Chem.* **1993,** *58,* 3435.

(47). Arcadi, A.; Cacchi, S.; Larock, R. C; Marinelli, F.; *Tetrahedron Lett.* **1993,** *34,* 2813.

(48). Dulcère, J.-P.; Faure, R.; Rodriguez, J. *Synlett.* **1992,** 737.

(49). Chan, T. H.; Fleming, I. *Synthesis* **1979,** 761.

(50). Seyferth, D.; White, D. L. *J. Am. Chem. Soc.* **1972,** *94,* 3132.

(51). Bredereck, H.; Gompper, R.; *Chem. Ber.* **1954,** *87,* 700.

(52). Barton, T. J.; Hussmann, G. P. *J. Am. Chem. Soc.* **1983,** *105,* 6316.

(53). Knölker, H.-J.; Jones, P. G.; Pannek, J.-B. *Synlett.* **1990,** 429.

(54). Wilson, S.R.; Jacob, L. A. *J. Org. Chem.* **1986,** *51,* 4833.

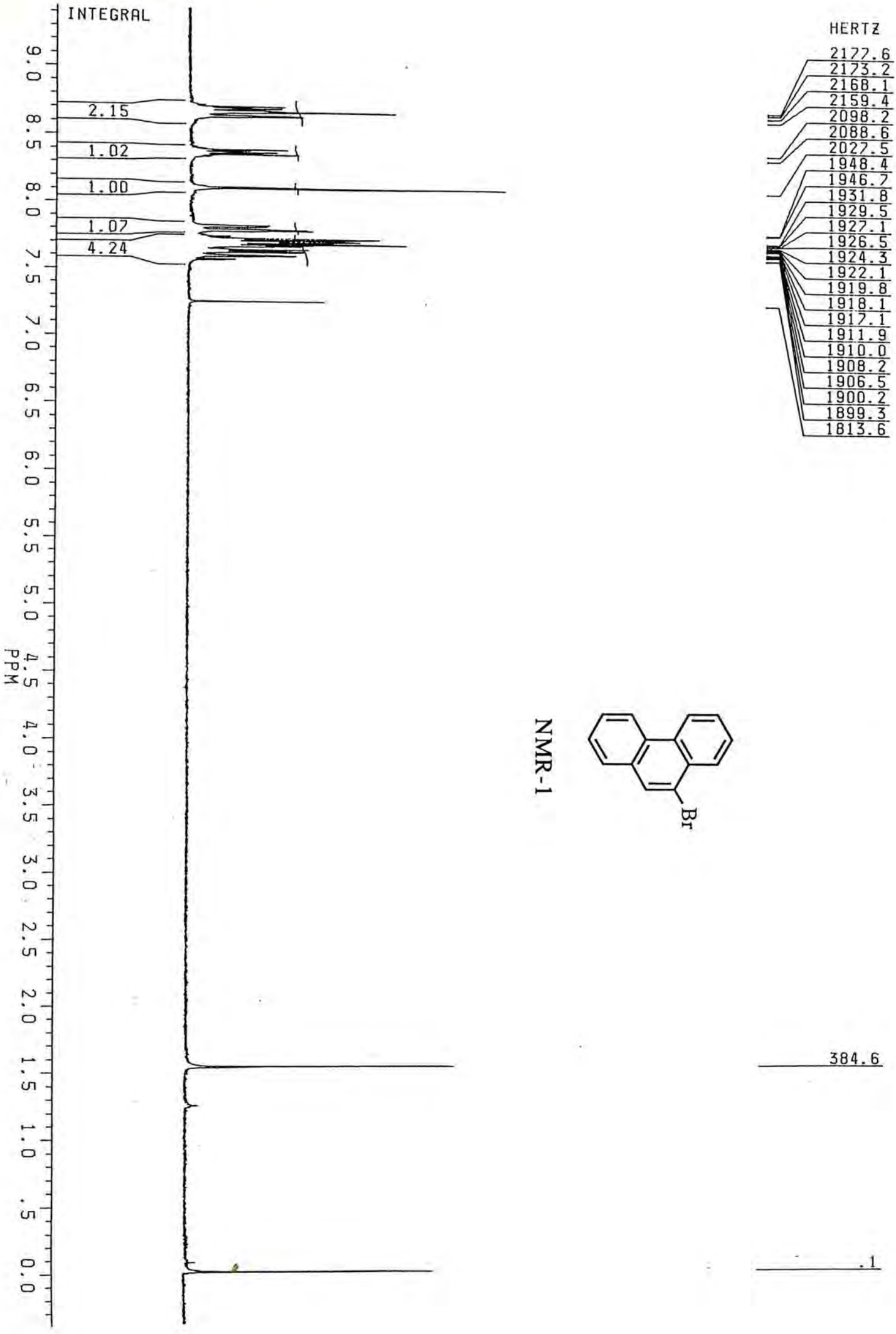
(55). Kuwajima, I.; Urabe, H. *Tetrahedron Lett.* **1981,** *22,* 5191.

(56). Pridgen, L. N.; Jones, S. S. *J. Org. Chem.* **1982,** *47,* 1590.

(57). Suzuki, A. *Pure and Appl. Chem.* **1991,** *63,* 419.
Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981,** *11,* 513.
Miyaura, N; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem.Soc.* **1985,** *107,* 972.

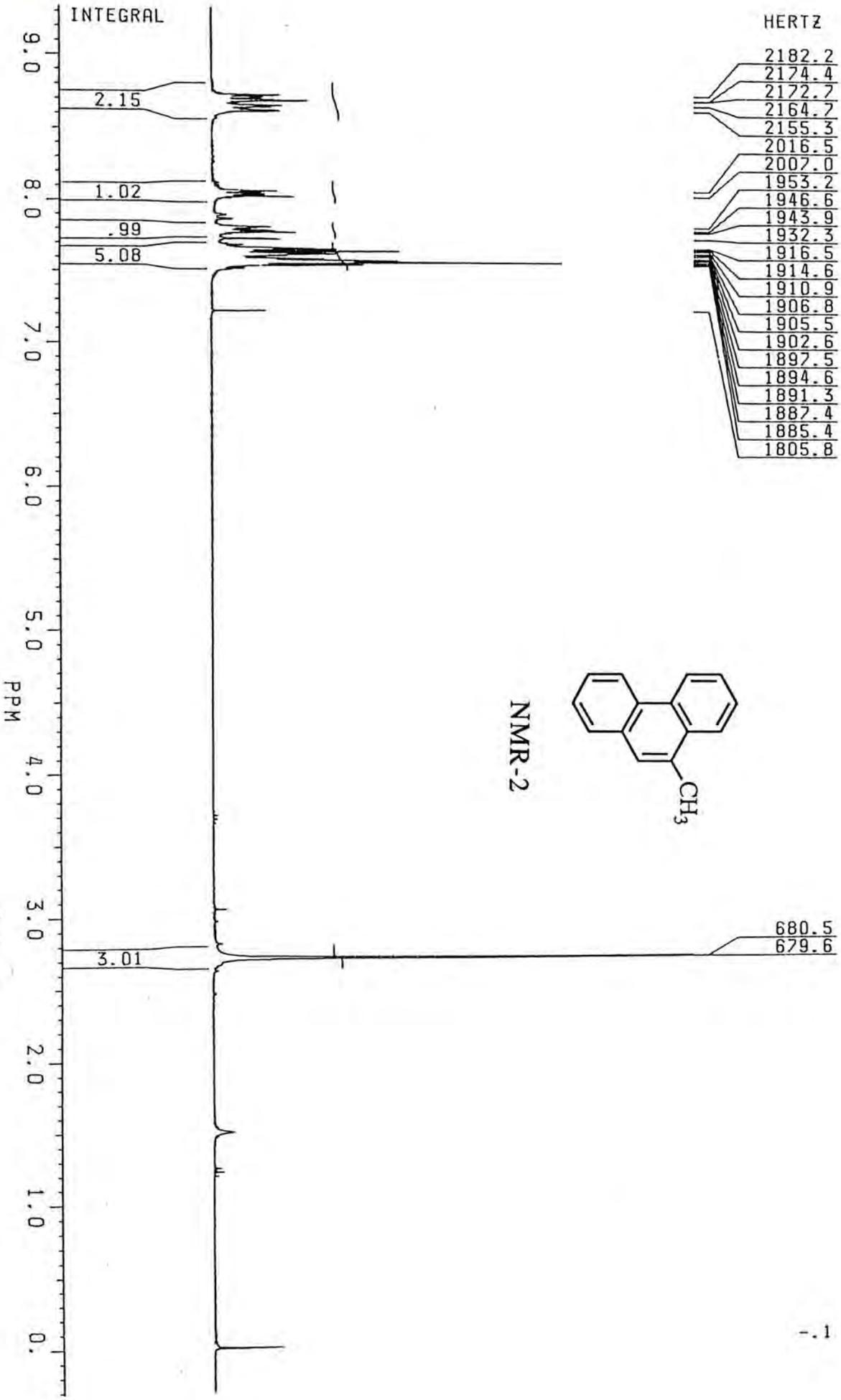
(58). Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975,** 4467.

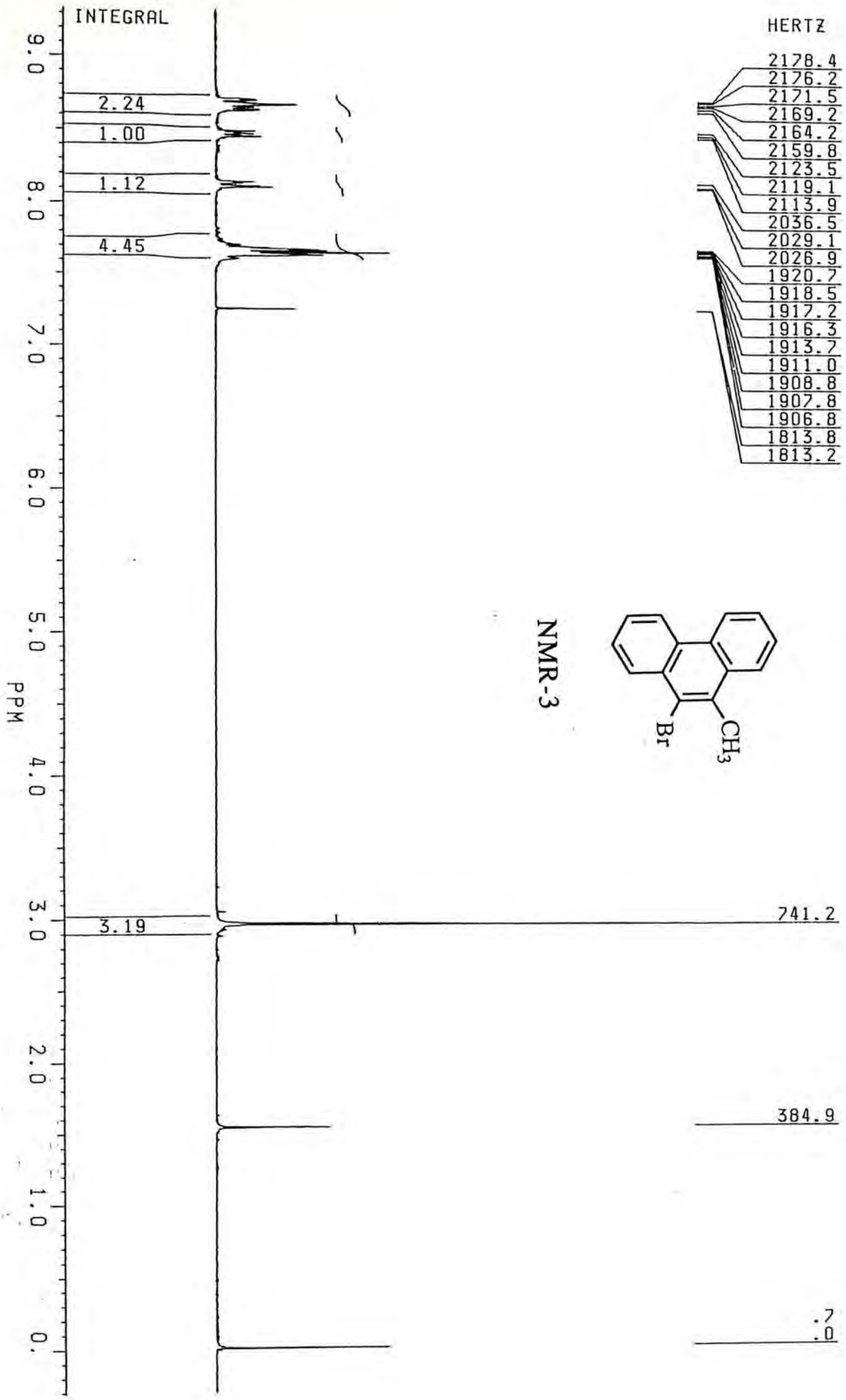
List of Spectra :


INTEGRAL
2.15
1.02
1.00
1.07
4.24
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
PPM
HERTZ
2177.6
2173.2
2168.1
2159.4
2098.2
2088.6
2027.5
1948.4
1946.7
1931.8
1929.5
1927.1
1926.5
1924.3
1922.1
1919.8
1918.1
1917.1
1911.9
1910.0
1908.2
1906.5
1900.2
1899.3
1813.6
384.6
.1

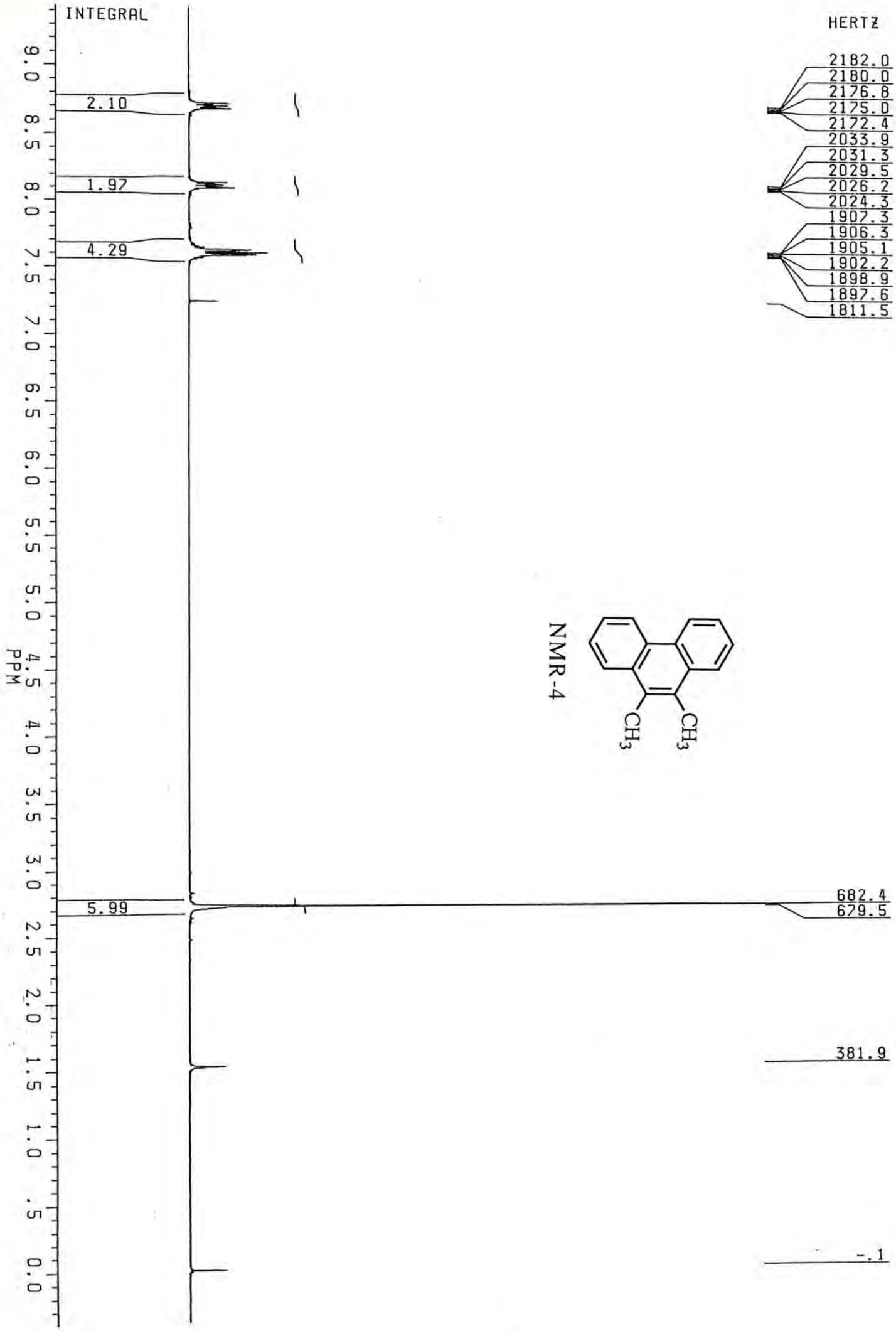
NMR-1

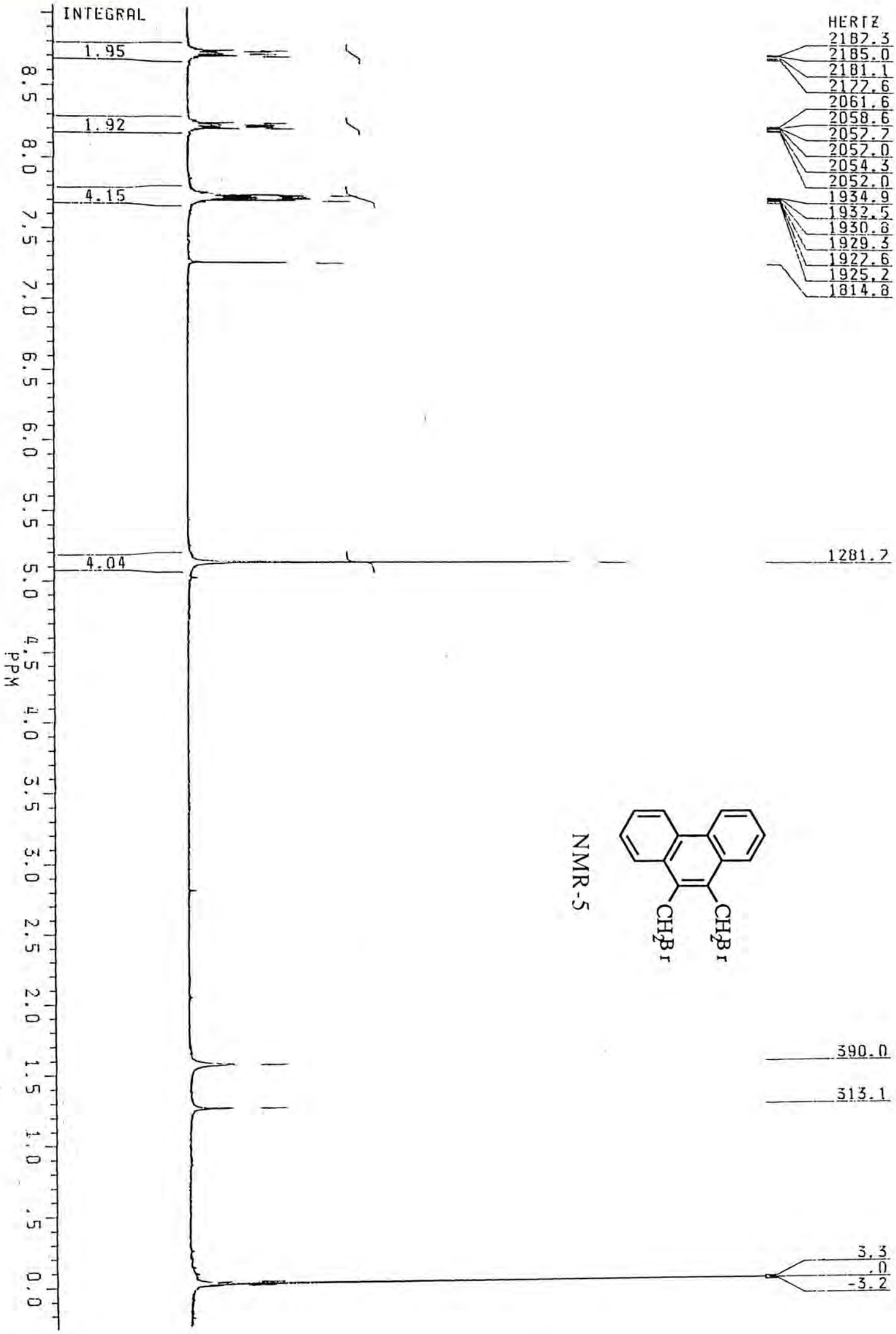
Br


INTEGRAL
HERTZ
2.15
1.02
.99
5.08
3.01
2182.2
2174.4
2172.7
2164.7
2155.3
2016.5
2007.0
1953.2
1946.6
1943.9
1932.3
1916.5
1914.6
1910.9
1906.8
1905.5
1902.6
1897.5
1894.6
1891.3
1887.4
1885.4
1805.8
680.5
679.6
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.
-.1
NMR-2
CH3

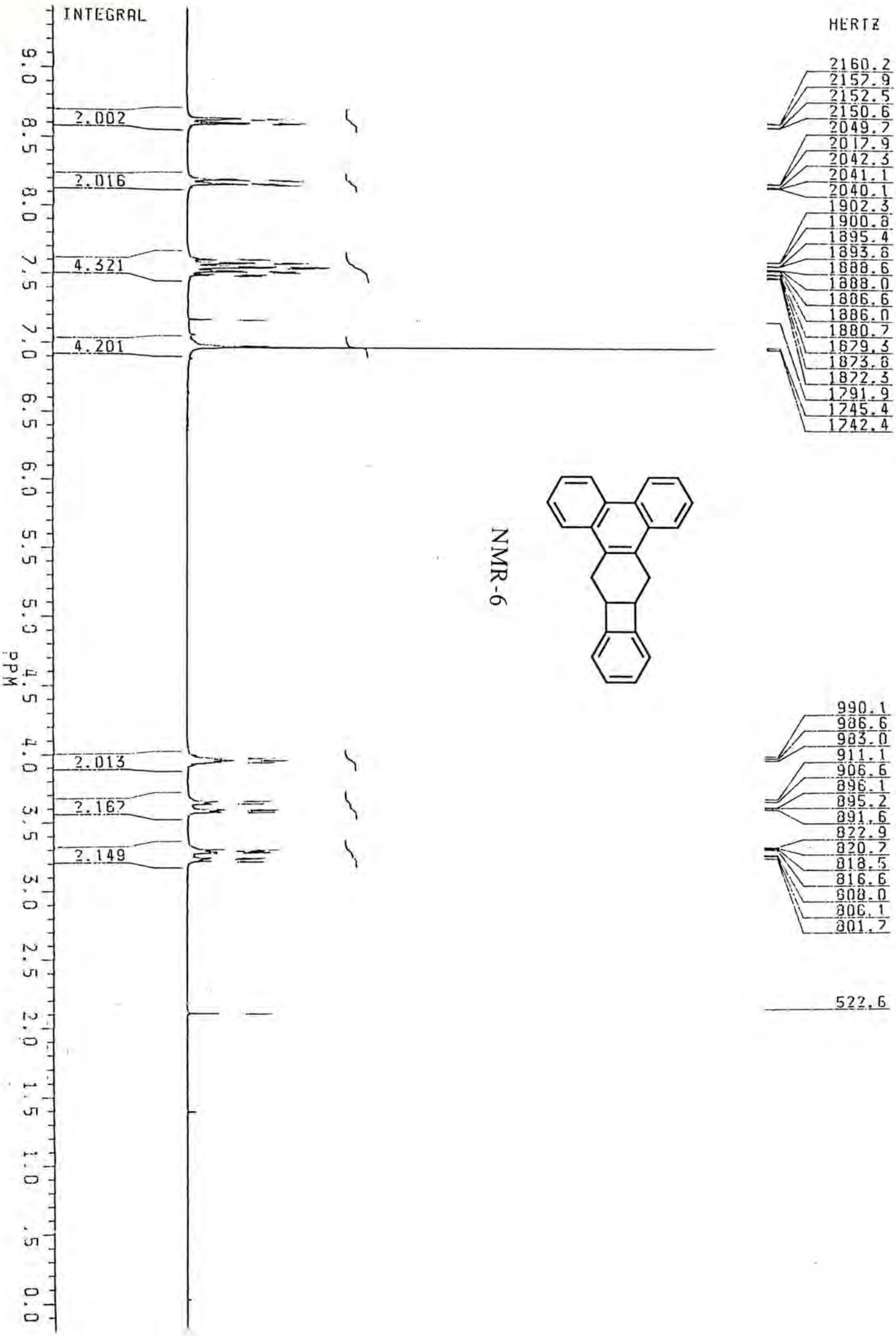

INTEGRAL
HERTZ
2178.4
2176.2
2171.5
2169.2
2164.2
2159.8
2123.5
2119.1
2113.9
2036.5
2029.1
2026.9
1920.7
1918.5
1917.2
1916.3
1913.7
1911.0
1908.8
1907.8
1906.8
1813.8
1813.2
2.24
1.00
1.12
4.45
3.19
741.2
384.9
.7
.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.
PPM
Br
CH3

NMR-3

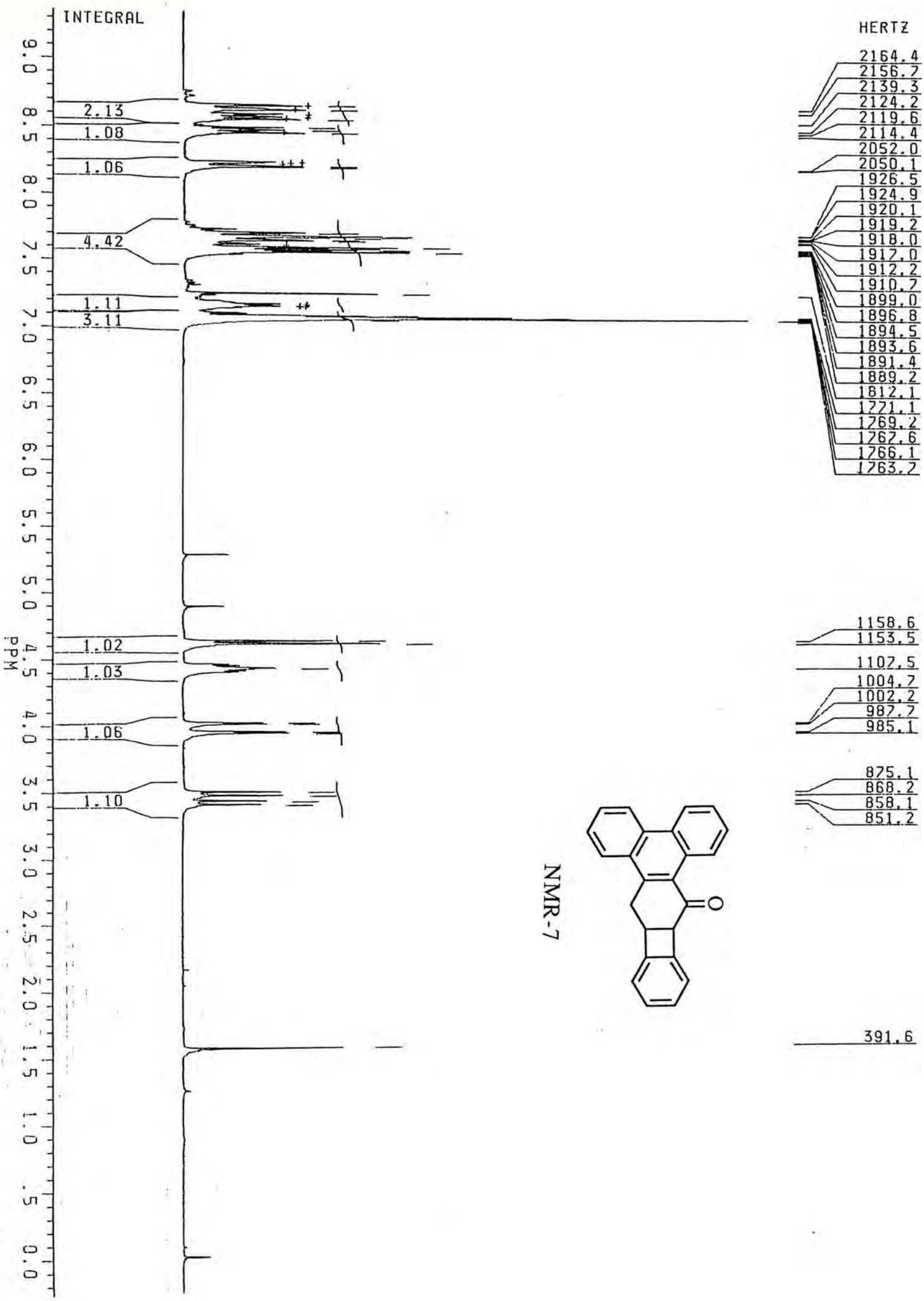

INTEGRAL
2.10
1.97
4.29
5.99
PPM
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
HERTZ
2182.0
2180.0
2176.8
2175.0
2172.4
2033.9
2031.3
2029.5
2026.2
2024.3
1907.3
1906.3
1905.1
1902.2
1898.9
1897.6
1811.5
682.4
679.5
381.9
-.1
NMR-4
CH3
CH3


INTEGRAL
1.95
1.92
4.15
4.04
HERTZ
2187.3
2185.0
2181.1
2177.6
2061.6
2058.6
2057.7
2057.0
2054.3
2052.0
1934.9
1932.5
1930.8
1929.3
1927.6
1925.2
1814.8
1281.7
390.0
313.1
3.3
.0
-3.2
PPM
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
CH2Br
CH2Br

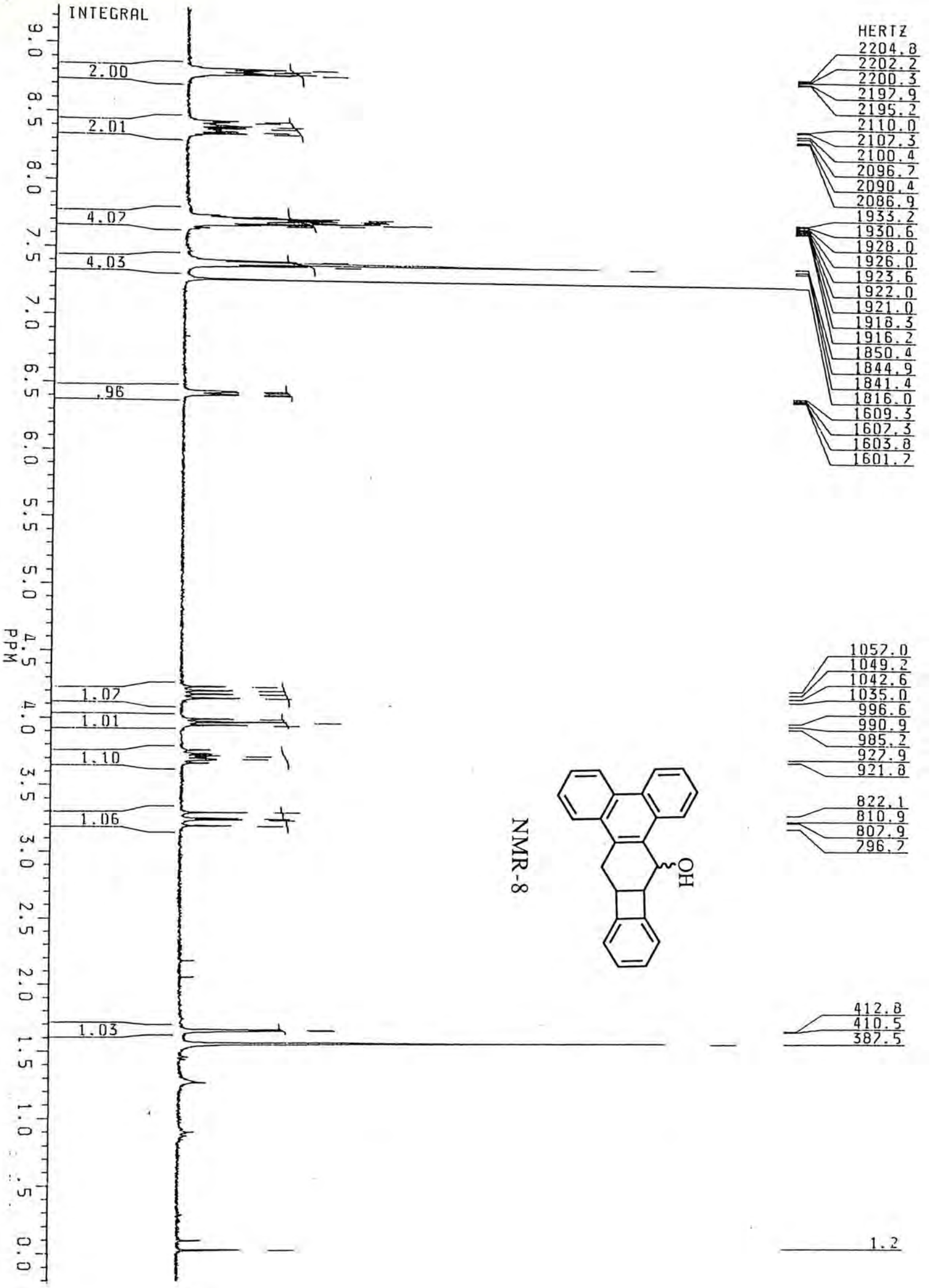
NMR-5

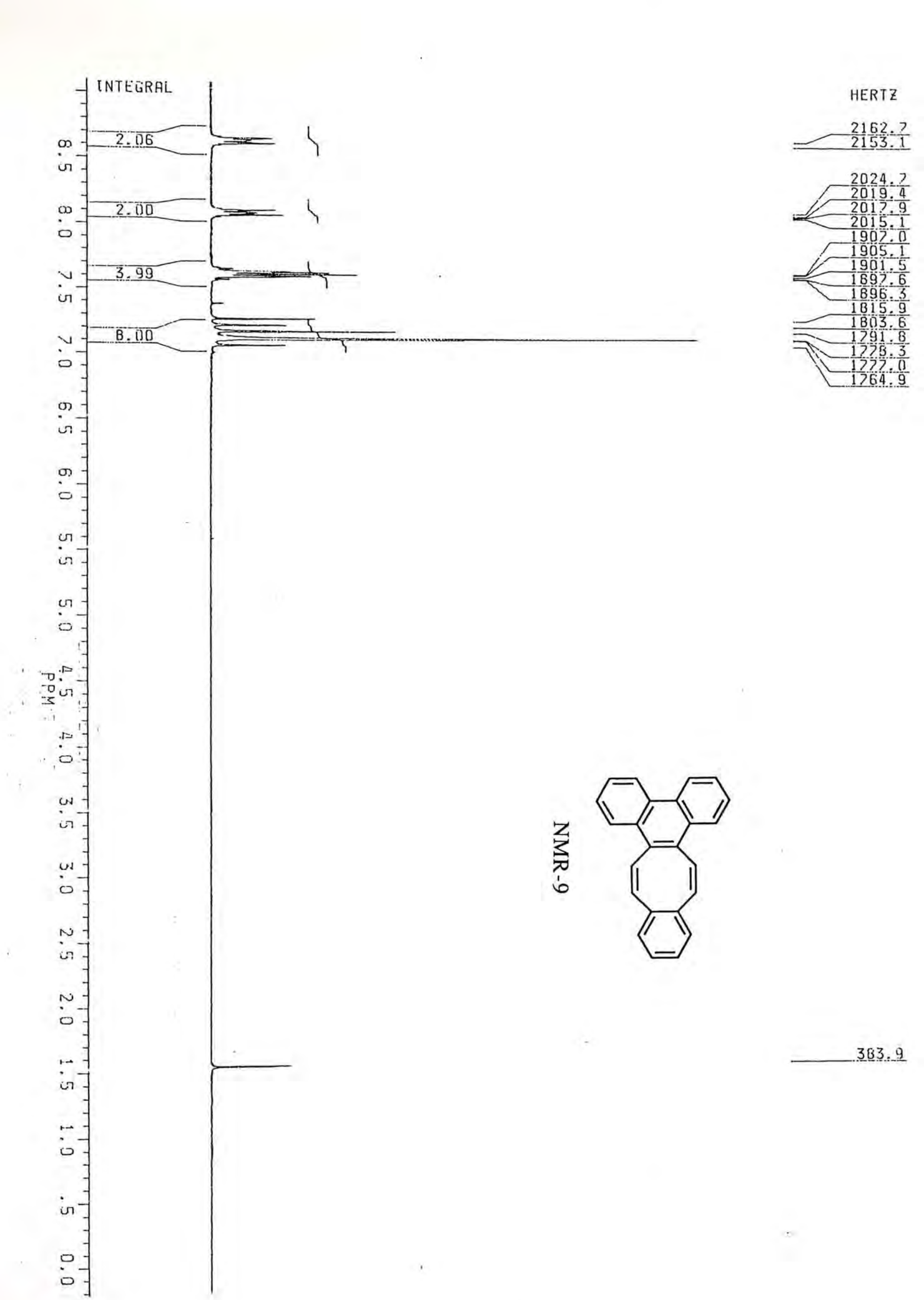

INTEGRAL
HERTZ
2.002
2.016
4.321
4.201
2.013
2.167
2.149
PPM
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
2160.2
2157.9
2152.5
2150.6
2049.7
2017.9
2042.3
2041.1
2040.1
1902.3
1900.8
1895.4
1893.8
1888.6
1888.0
1886.6
1886.0
1880.7
1879.3
1873.8
1872.3
1791.9
1745.4
1742.4
990.1
986.6
983.0
911.1
906.6
896.1
895.2
891.6
822.9
820.7
818.5
816.6
808.0
806.1
801.7
522.6

NMR-6

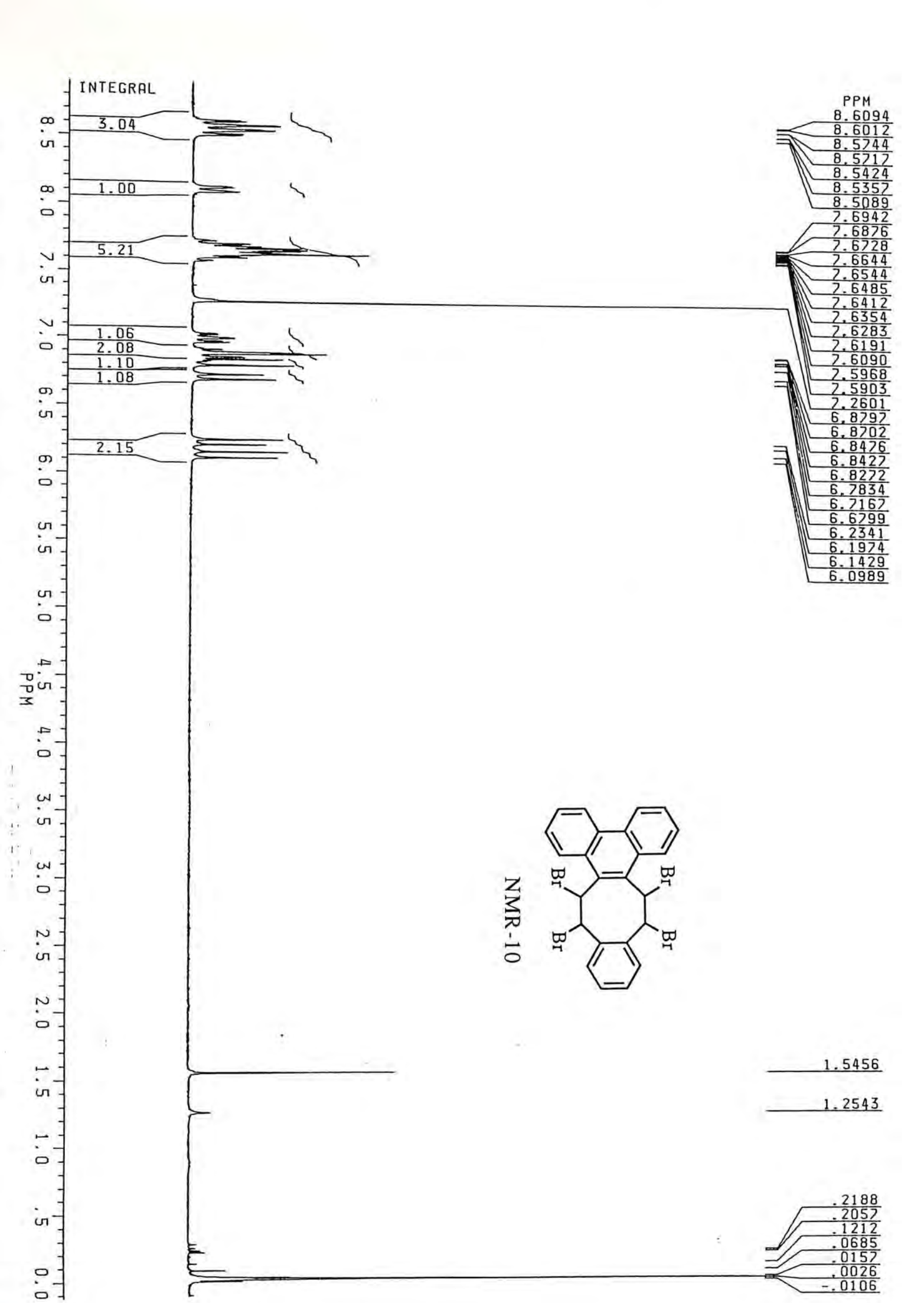

INTEGRAL
HERTZ
2.13
1.08
1.06
4.42
1.11
3.11
1.02
1.03
1.06
1.10
2164.4
2156.7
2139.3
2124.2
2119.6
2114.4
2052.0
2050.1
1926.5
1924.9
1920.1
1919.2
1918.0
1917.0
1912.2
1910.7
1899.0
1896.8
1894.5
1893.6
1891.4
1889.2
1812.1
1771.1
1769.2
1767.6
1766.1
1763.2
1158.6
1153.5
1107.5
1004.7
1002.2
987.7
985.1
875.1
868.2
858.1
851.2
391.6
PPM
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
O

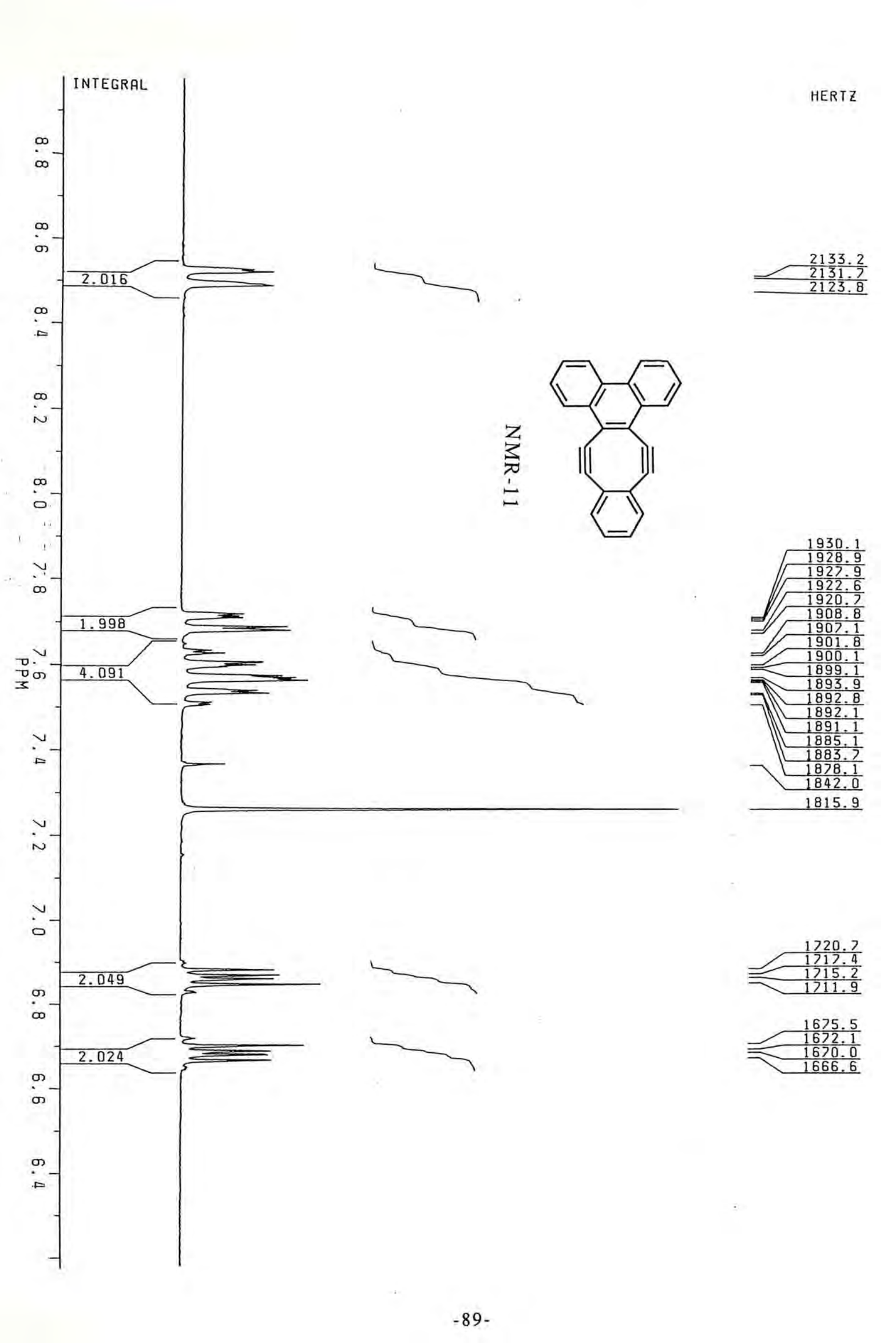
NMR-7


INTEGRAL
2.00
2.01
4.07
4.03
.96
1.07
1.01
1.10
1.06
1.03
PPM
HERTZ
2204.8
2202.2
2200.3
2197.9
2195.2
2110.0
2107.3
2100.4
2096.7
2090.4
2086.9
1933.2
1930.6
1928.0
1926.0
1923.6
1922.0
1921.0
1918.3
1916.2
1850.4
1844.9
1841.4
1816.0
1609.3
1607.3
1603.8
1601.7
1057.0
1049.2
1042.6
1035.0
996.6
990.9
985.2
927.9
921.8
822.1
810.9
807.9
796.2
412.8
410.5
387.5
1.2
OH
NMR-8

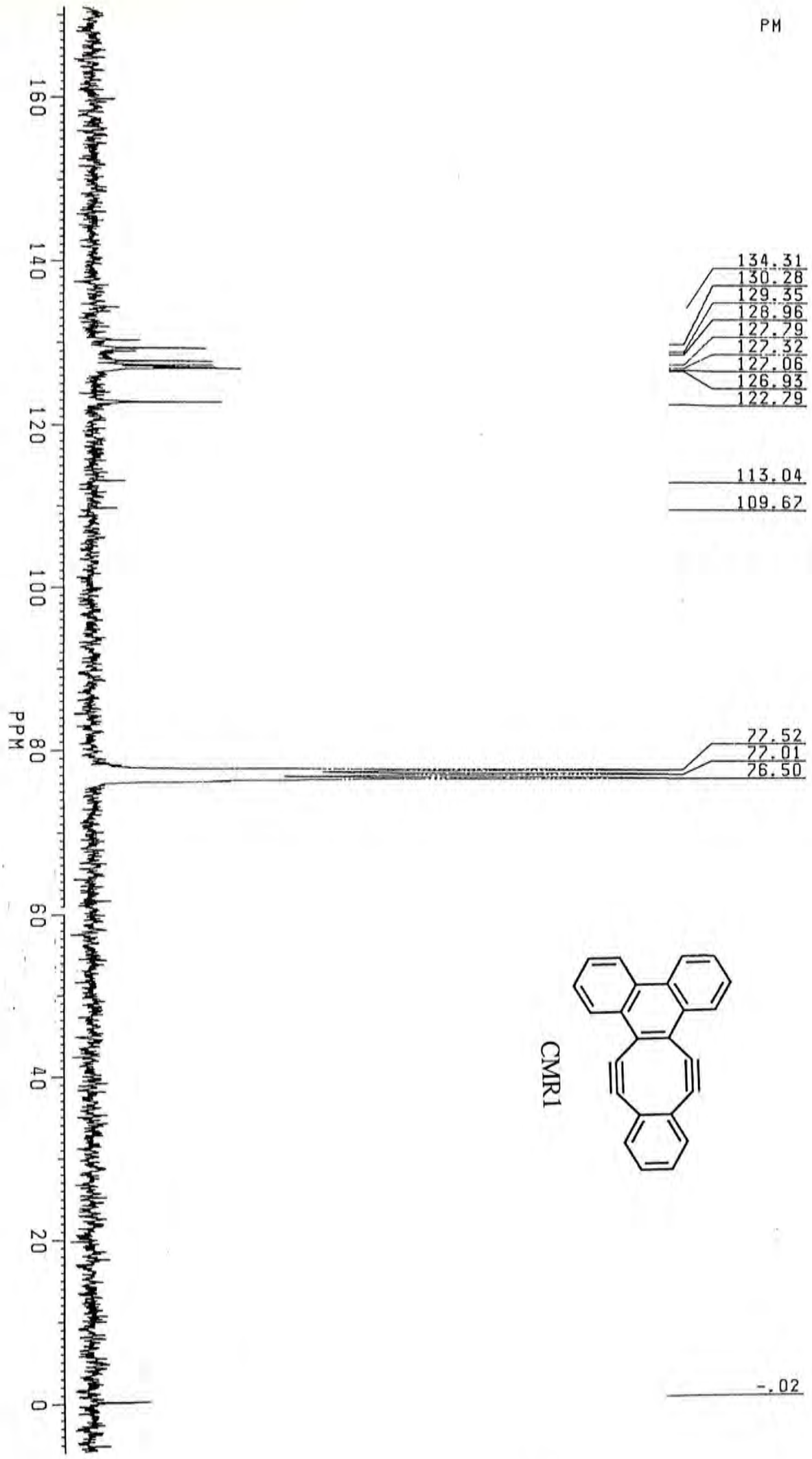

INTEGRAL
2.06
2.00
3.99
8.00
HERTZ
2162.7
2153.1
2024.7
2019.4
2017.9
2015.1
1907.0
1905.1
1901.5
1897.6
1896.3
1815.9
1803.6
1791.8
1778.3
1777.0
1764.9
383.9
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 .5 0.0
PPM

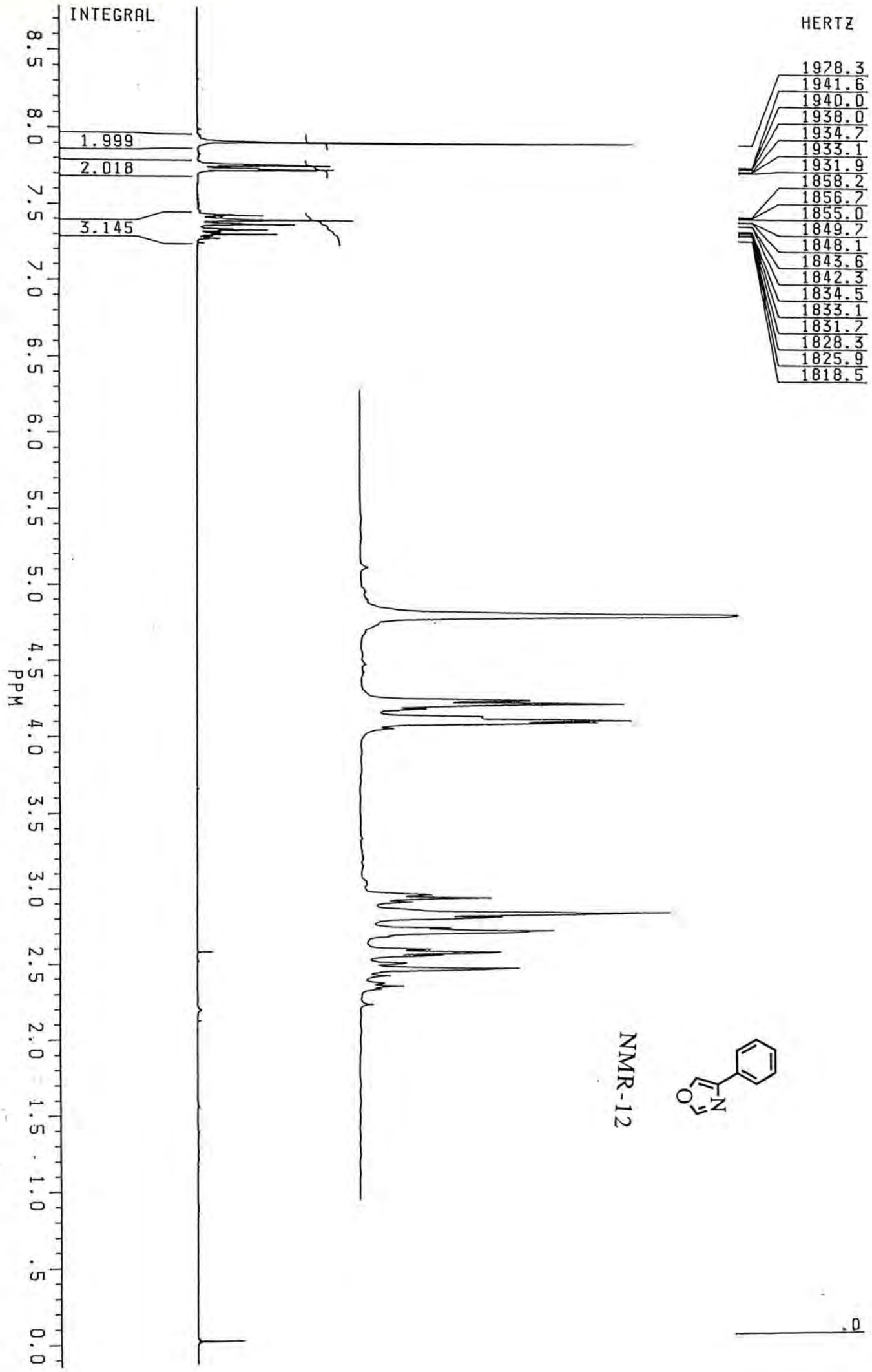
NMR-9


INTEGRAL
3.04
1.00
5.21
1.06
2.08
1.10
1.08
2.15
PPM
8.6094
8.6012
8.5744
8.5717
8.5424
8.5357
8.5089
7.6942
7.6876
7.6728
7.6644
7.6544
7.6485
7.6412
7.6354
7.6283
7.6191
7.6090
7.5968
7.5903
2.2601
6.8797
6.8702
6.8476
6.8427
6.8272
6.7834
6.7167
6.6799
6.2341
6.1974
6.1429
6.0989
PPM
Br
Br
Br
Br
NMR-10
1.5456
1.2543
.2188
.2057
.1212
.0685
.0157
.0026
-.0106

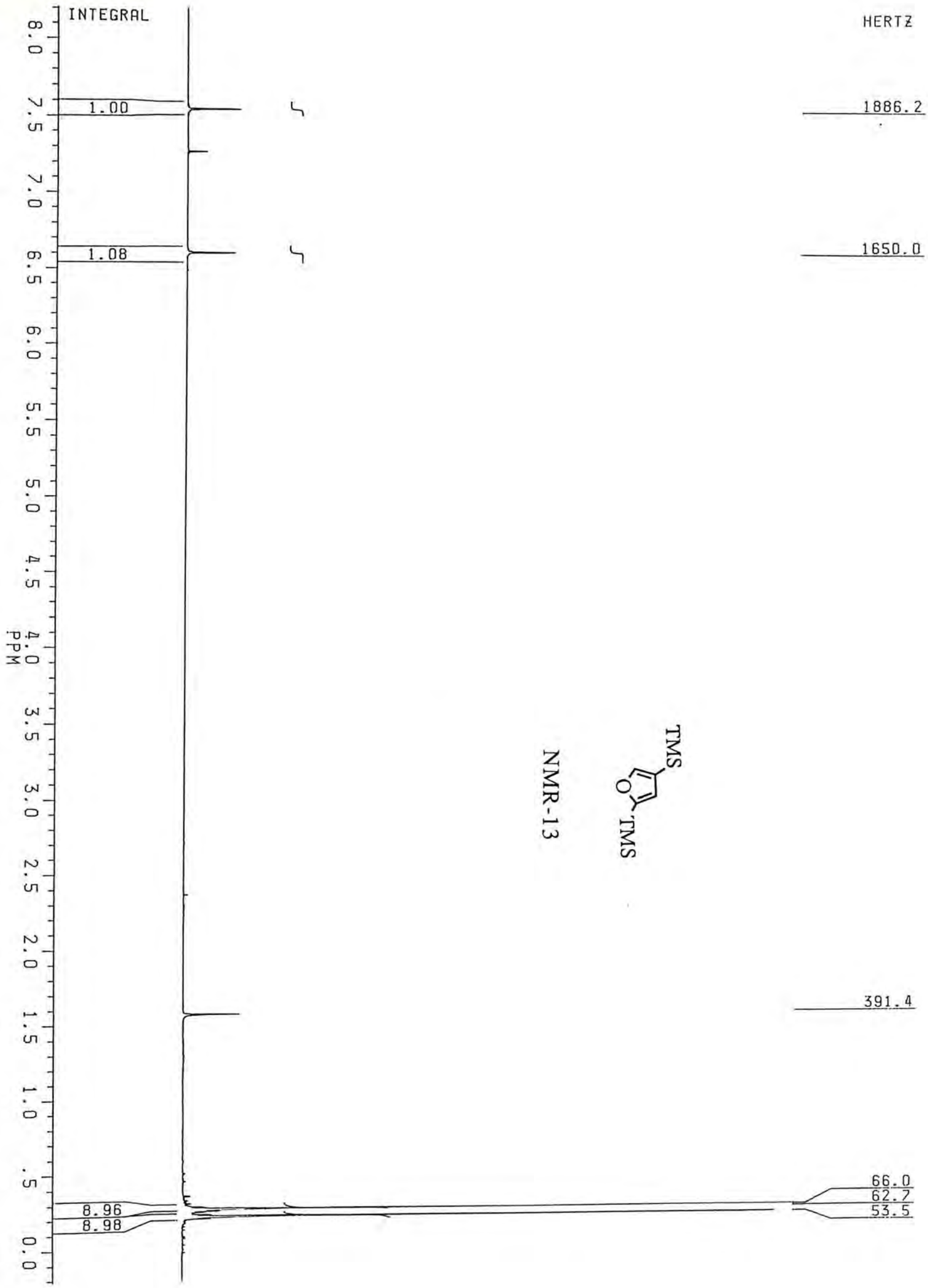

INTEGRAL
HERTZ
2.016
1.998
4.091
2.049
2.024
PPM
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
2133.2
2131.7
2123.8
1930.1
1928.9
1927.9
1922.6
1920.7
1908.8
1907.1
1901.8
1900.1
1899.1
1893.9
1892.8
1892.1
1891.1
1885.1
1883.7
1878.1
1842.0
1815.9
1720.7
1717.4
1715.2
1711.9
1675.5
1672.1
1670.0
1666.6

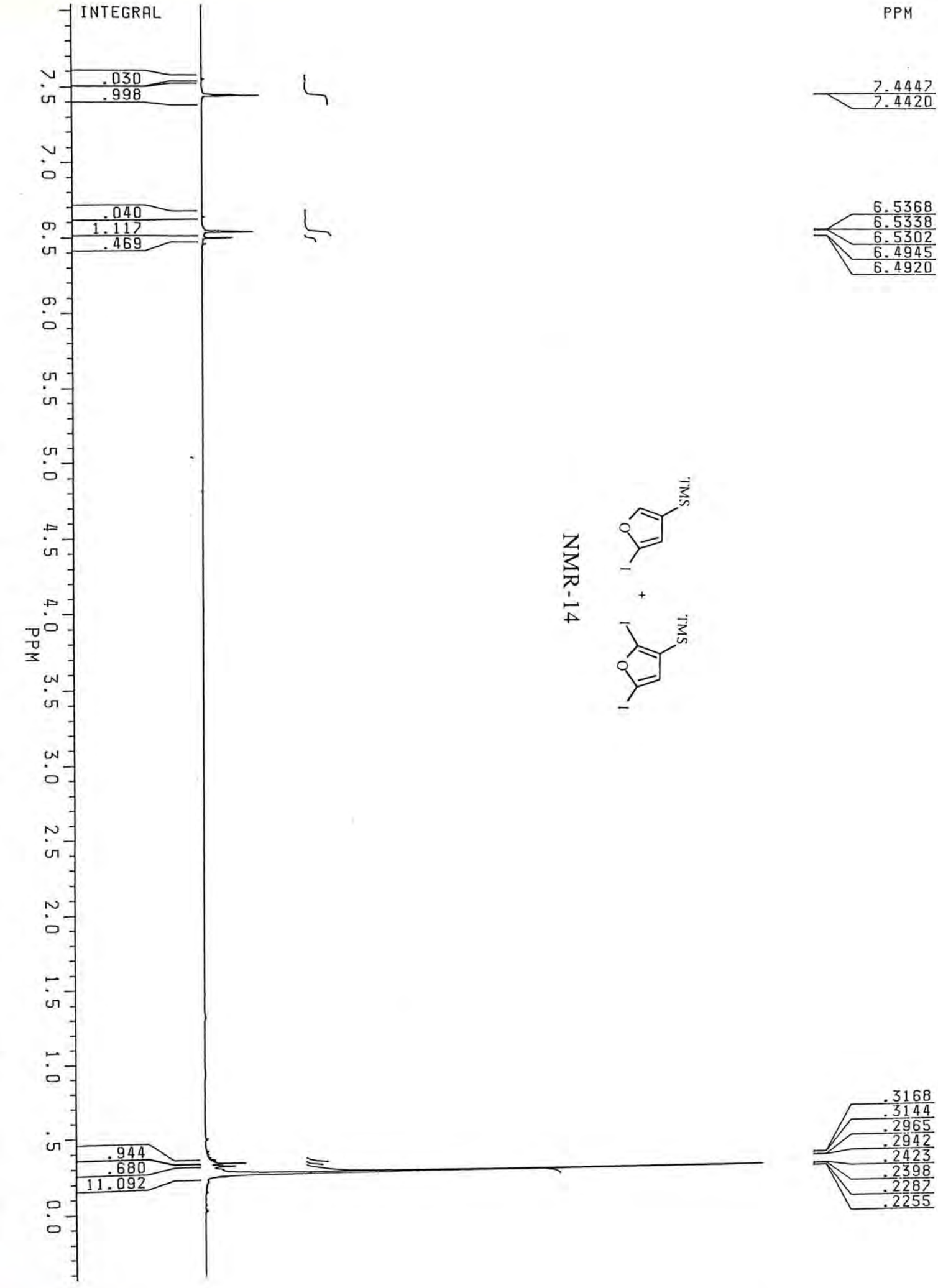
NMR-11


PM
134.31
130.28
129.35
128.96
127.79
127.32
127.06
126.93
122.79
113.04
109.67
77.52
77.01
76.50
-.02
160
140
120
100
80
60
40
20
0
PPM
CMR1


INTEGRAL
1.999
2.018
3.145
HERTZ
1978.3
1941.6
1940.0
1938.0
1934.7
1933.1
1931.9
1858.2
1856.7
1855.0
1849.7
1848.1
1843.6
1842.3
1834.5
1833.1
1831.7
1828.3
1825.9
1818.5
PPM
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 .5 0.0
.0
N
O

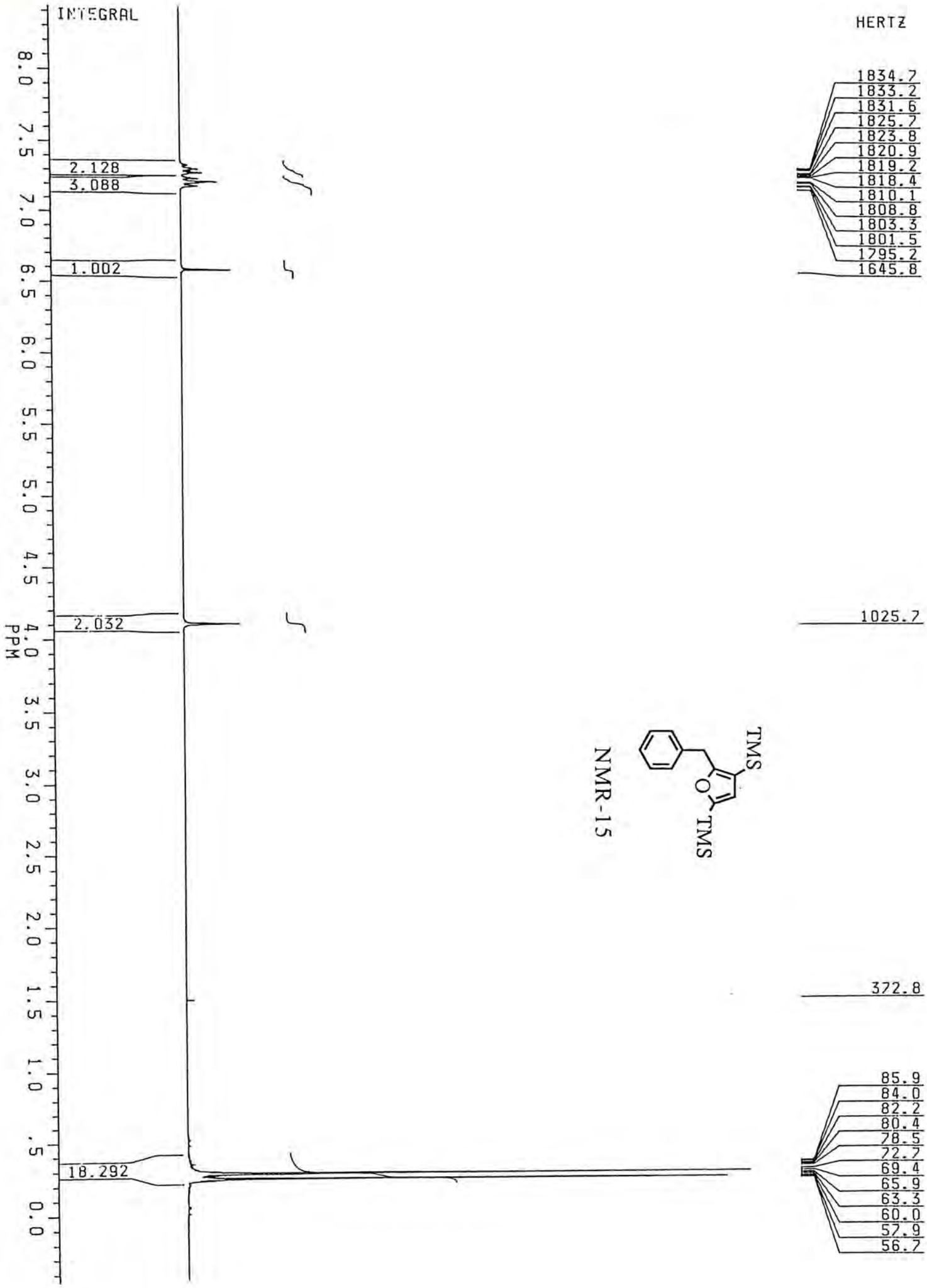
NMR-12

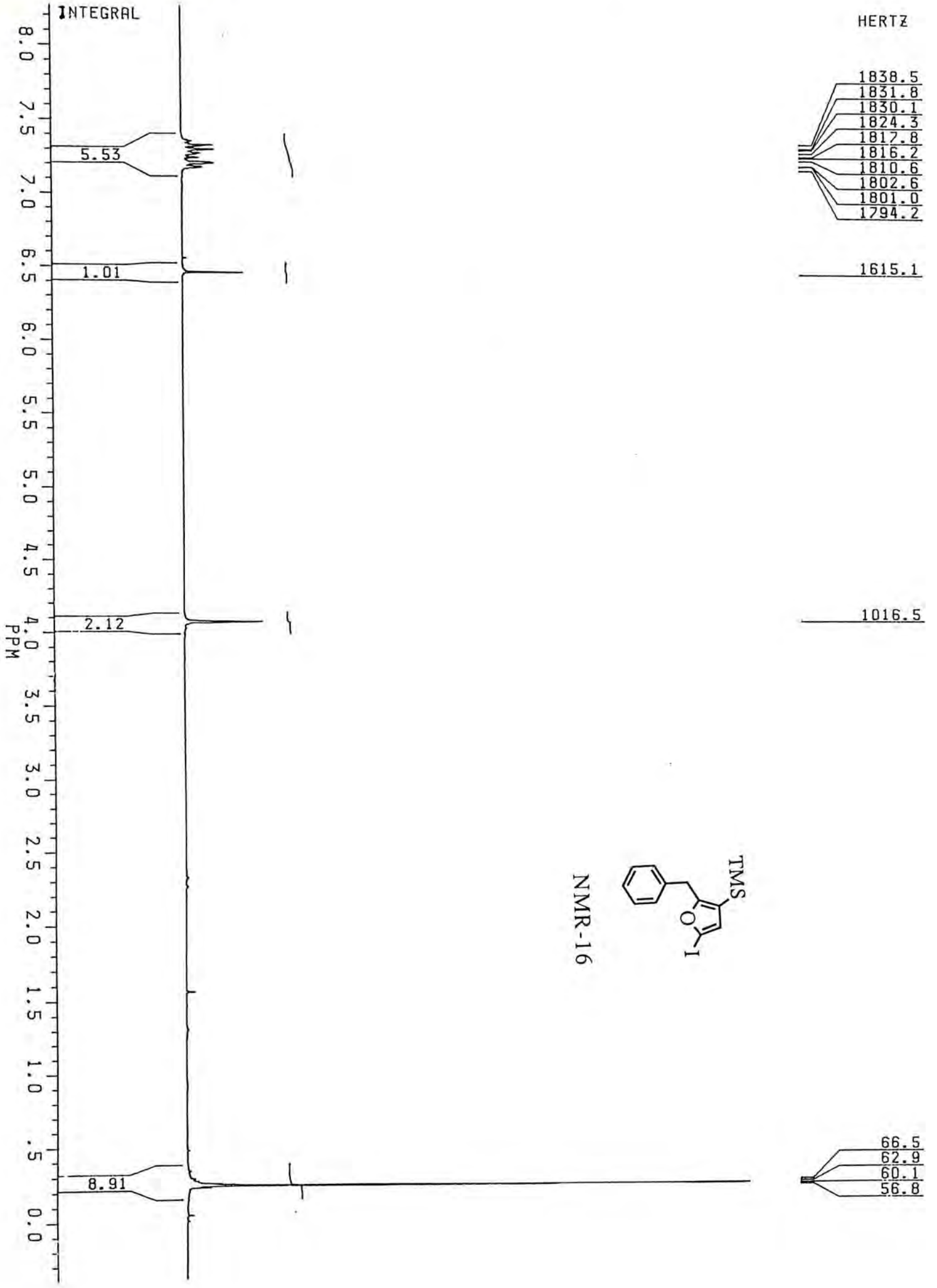

INTEGRAL
HERTZ
1.00
1.08
1886.2
1650.0
391.4
66.0
62.7
53.5
8.96
8.98
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
PPM
NMR-13
TMS
TMS
O

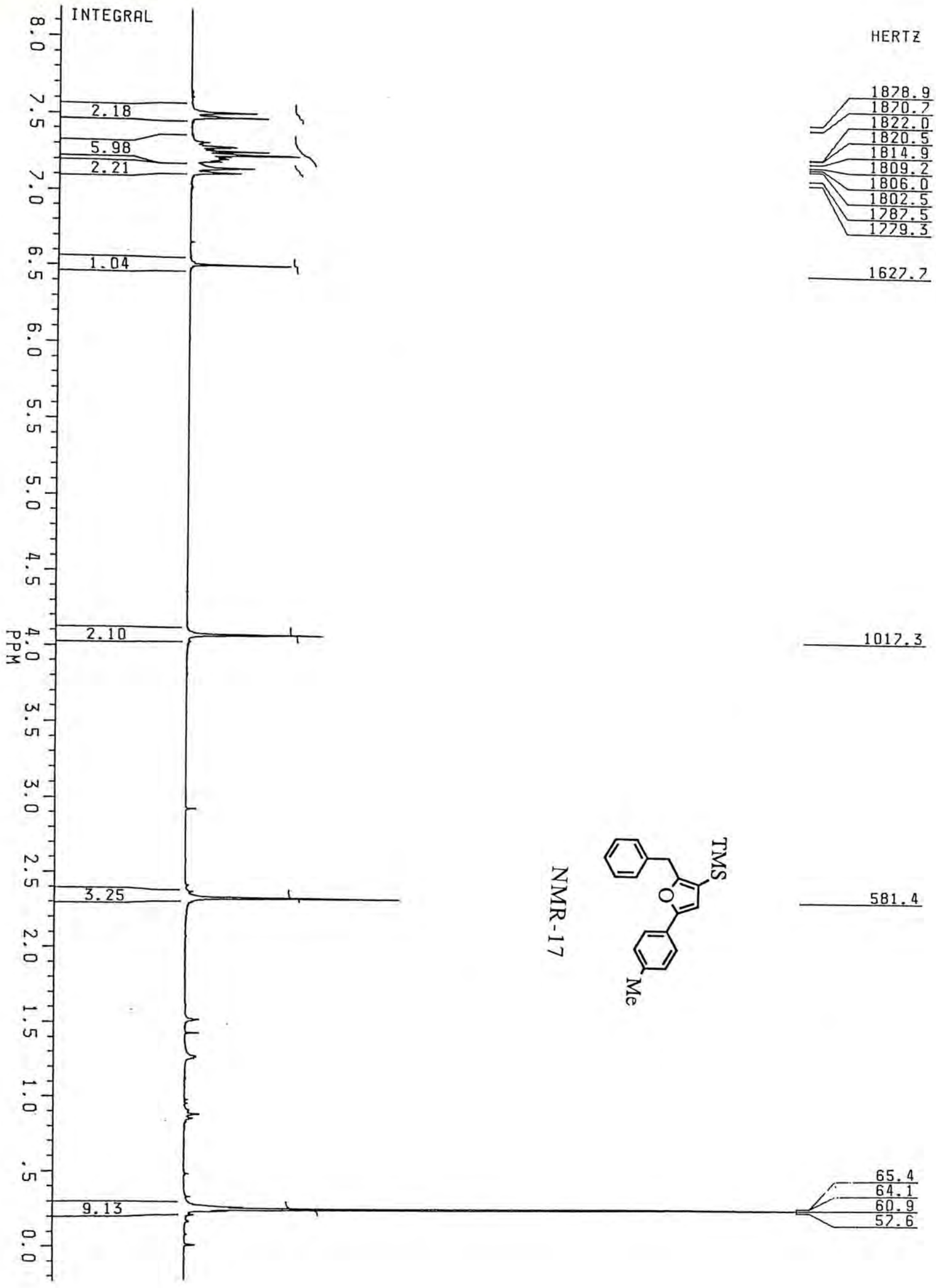

INTEGRAL
.030
.998
.040
1.117
.469
.944
.680
11.092
PPM
7.4447
7.4420
6.5368
6.5338
6.5302
6.4945
6.4920
.3168
.3144
.2965
.2942
.2423
.2398
.2287
.2255
PPM
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0

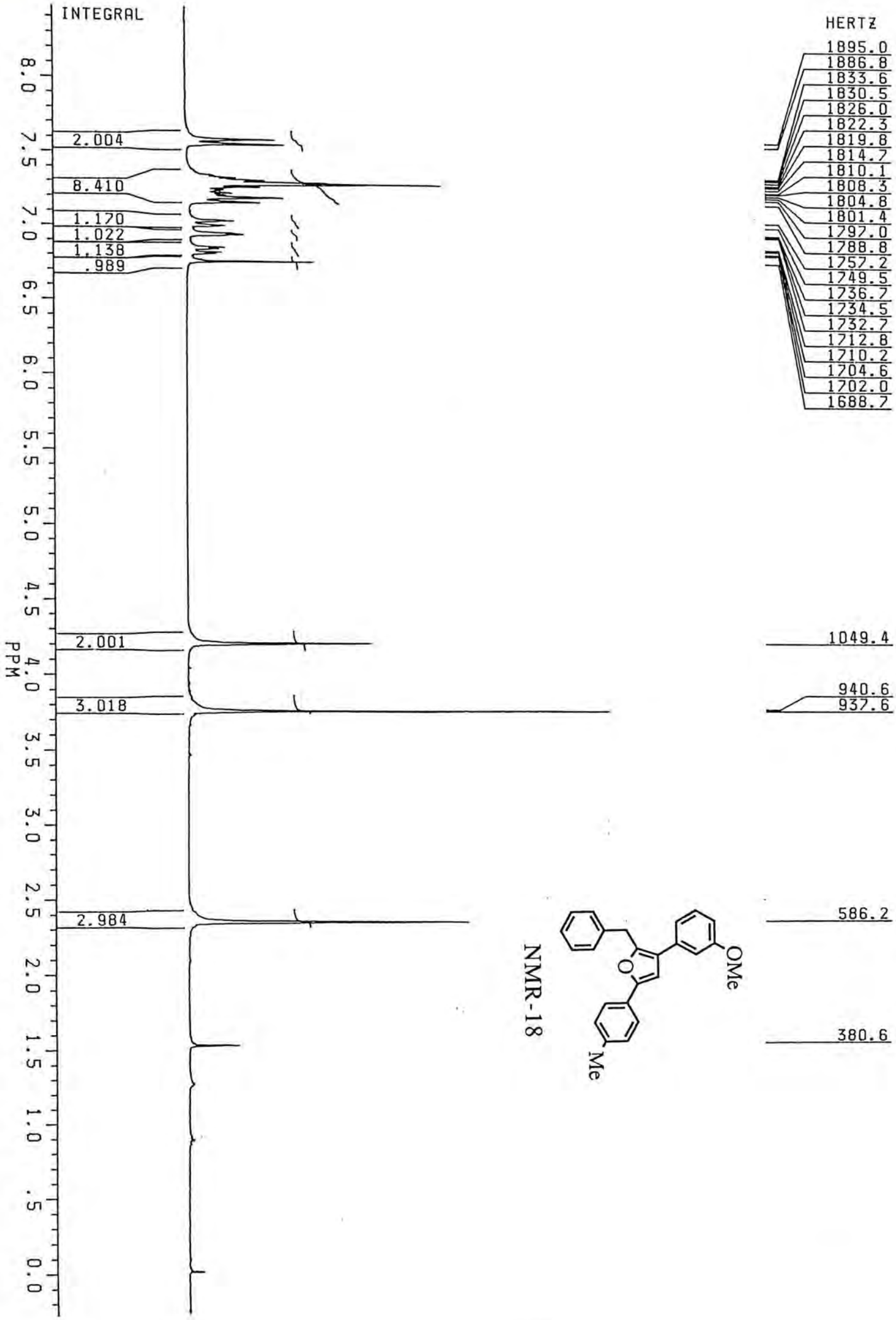
NMR-14

TMS
O
I
+
I
TMS
O
I

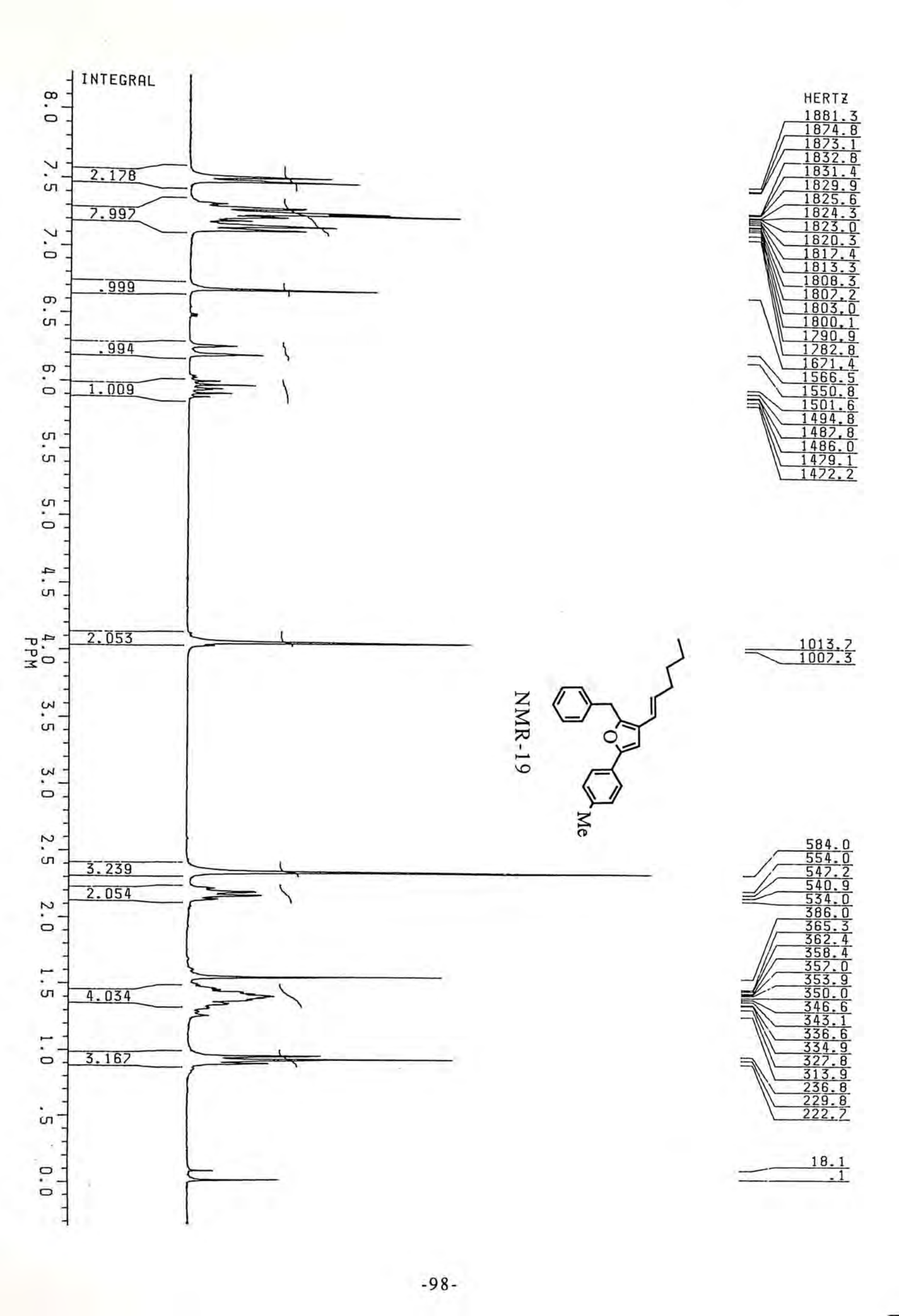

INTEGRAL
HERTZ
2.128
3.088
1.002
2.032
18.292
PPM
1834.7
1833.2
1831.6
1825.7
1823.8
1820.9
1819.2
1818.4
1810.1
1808.8
1803.3
1801.5
1795.2
1645.8
1025.7
372.8
85.9
84.0
82.2
80.4
78.5
72.7
69.4
65.9
63.3
60.0
57.9
56.7
TMS
TMS
NMR-15

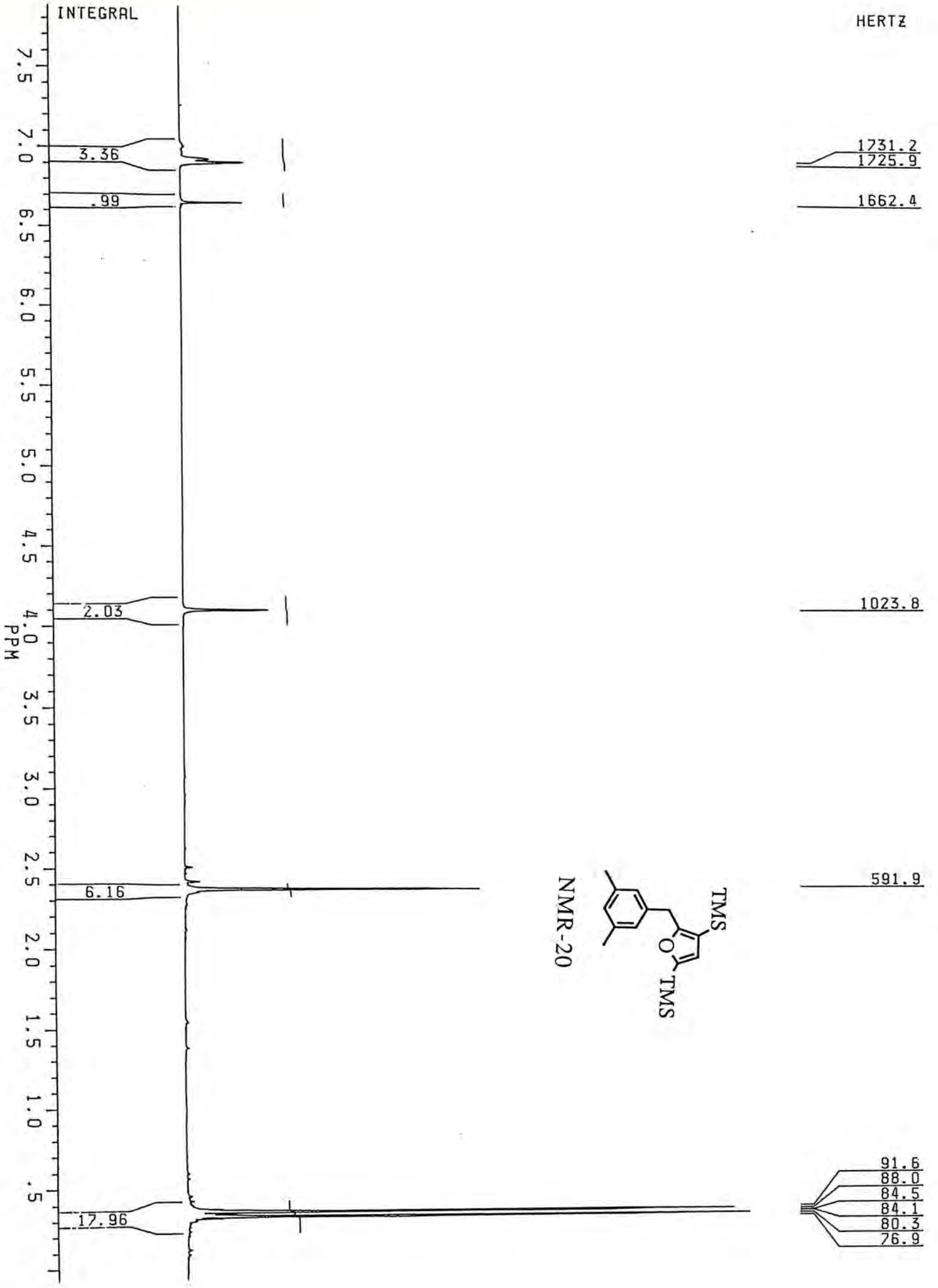

INTEGRAL
HERTZ
1838.5
1831.8
1830.1
1824.3
1817.8
1816.2
1810.6
1802.6
1801.0
1794.2
5.53
1.01
1615.1
2.12
1016.5
PPM
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
8.91
66.5
62.9
60.1
56.8
TMS
O
I
NMR-16

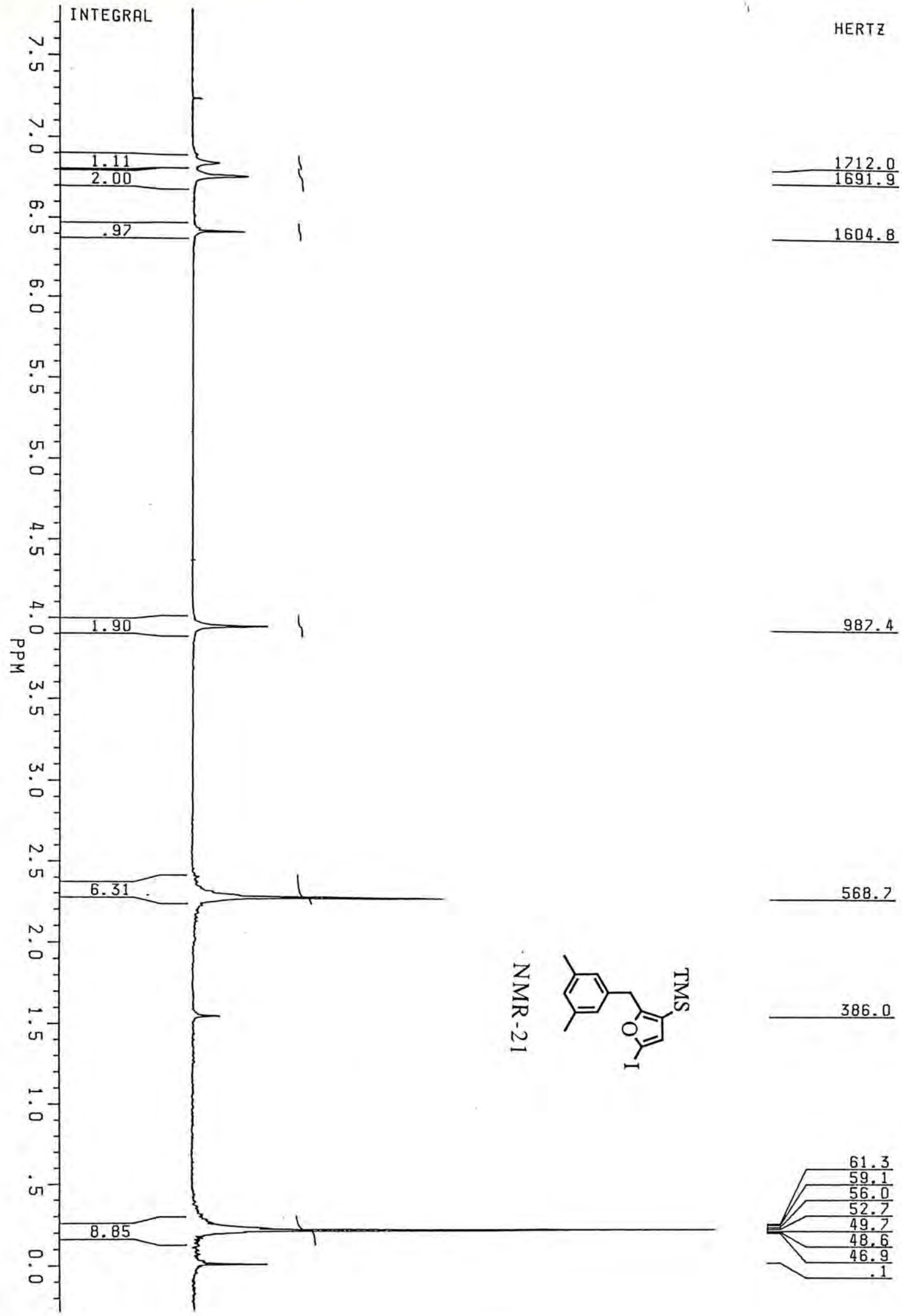

INTEGRAL
HERTz
2.18
5.98
2.21
1.04
2.10
3.25
9.13
PPM
1878.9
1870.7
1822.0
1820.5
1814.9
1809.2
1806.0
1802.5
1787.5
1779.3
1627.7
1017.3
581.4
65.4
64.1
60.9
57.6
TMS
Me
NMR-17

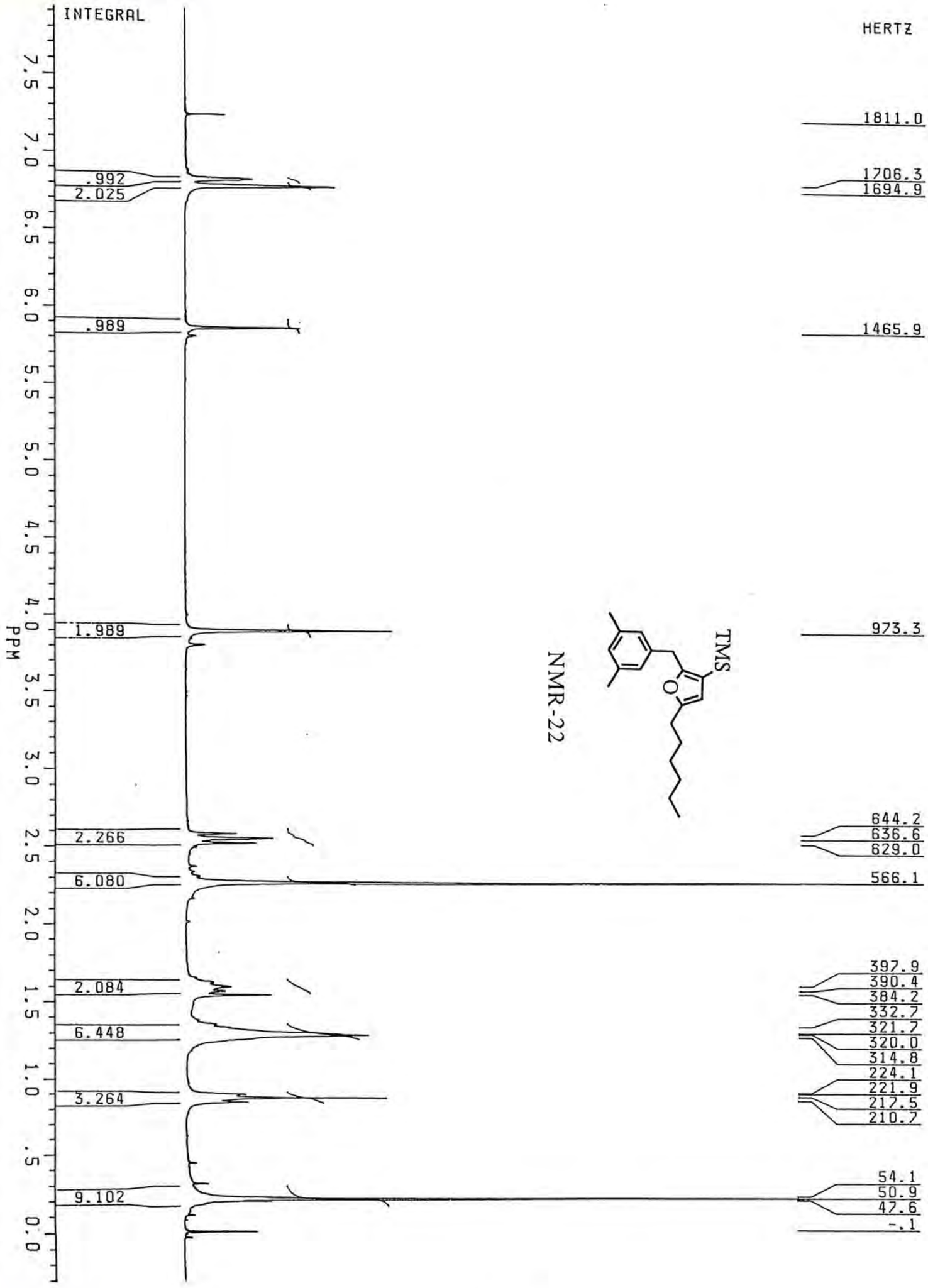

INTEGRAL
2.004
8.410
1.170
1.022
1.138
.989
2.001
3.018
2.984
PPM
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
HERTZ
1895.0
1886.8
1833.6
1830.5
1826.0
1822.3
1819.8
1814.7
1810.1
1808.3
1804.8
1801.4
1797.0
1788.8
1757.2
1749.5
1736.7
1734.5
1732.7
1712.8
1710.2
1704.6
1702.0
1688.7
1049.4
940.6
937.6
586.2
380.6
OMe
Me
O

NMR-18

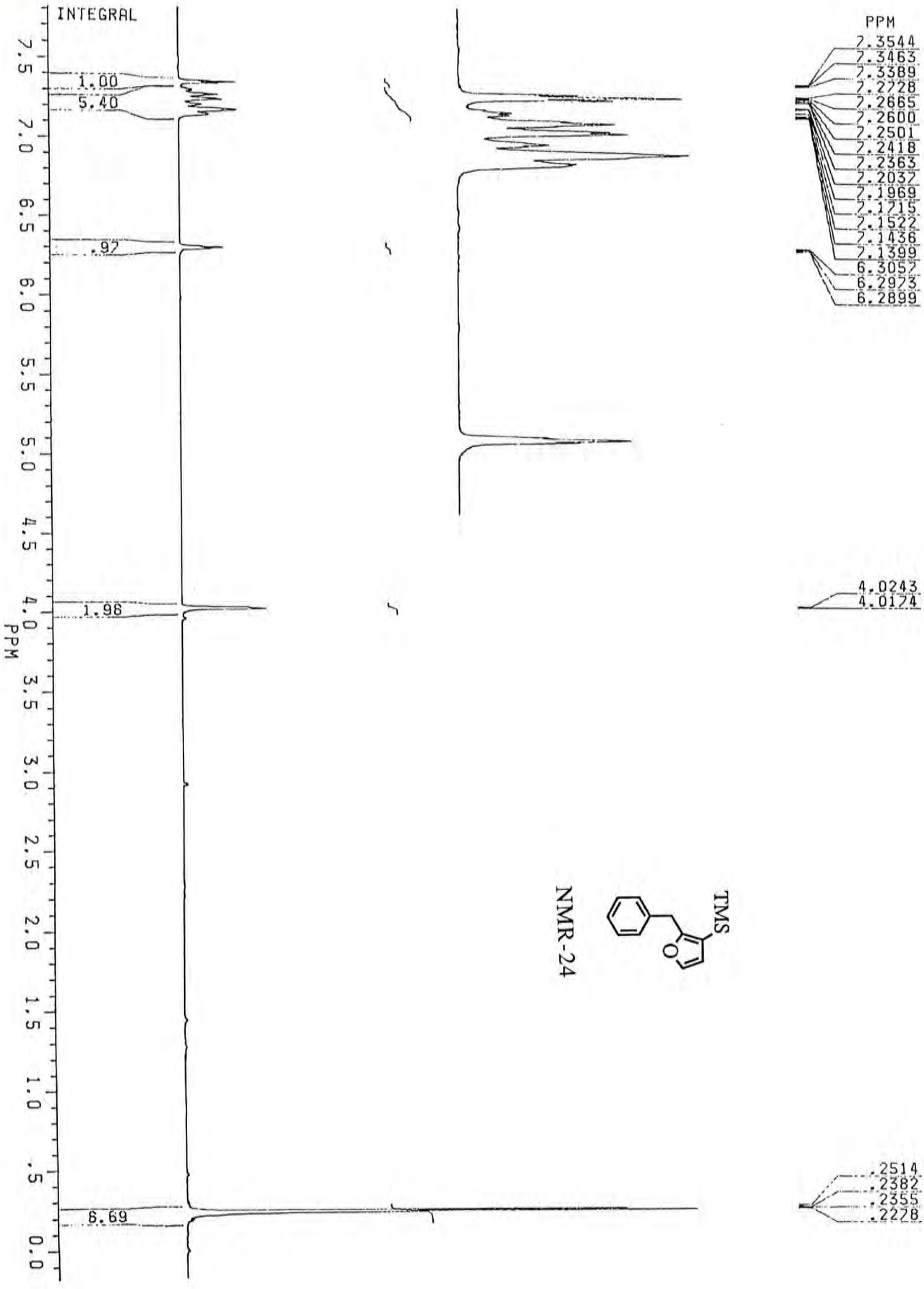

INTEGRAL
2.178
7.997
.999
.994
1.009
2.053
3.239
2.054
4.034
3.167
PPM
HERTZ
1881.3
1874.8
1873.1
1832.8
1831.4
1829.9
1825.6
1824.3
1823.0
1820.3
1817.4
1813.3
1808.3
1807.2
1803.0
1800.1
1790.9
1782.8
1671.4
1566.5
1550.8
1501.6
1494.8
1487.8
1486.0
1479.1
1472.2
1013.7
1007.3
584.0
554.0
547.2
540.9
534.0
386.0
365.3
362.4
358.4
357.0
353.9
350.0
346.6
343.1
336.6
334.9
327.8
313.9
236.8
229.8
222.7
18.1
.1
NMR-19
O
Me


INTEGRAL
HERTZ
3.36
.99
2.03
6.16
17.96
PPM
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
1731.2
1725.9
1662.4
1023.8
591.9
91.6
88.0
84.5
84.1
80.3
76.9
NMR-20
TMS
TMS
O

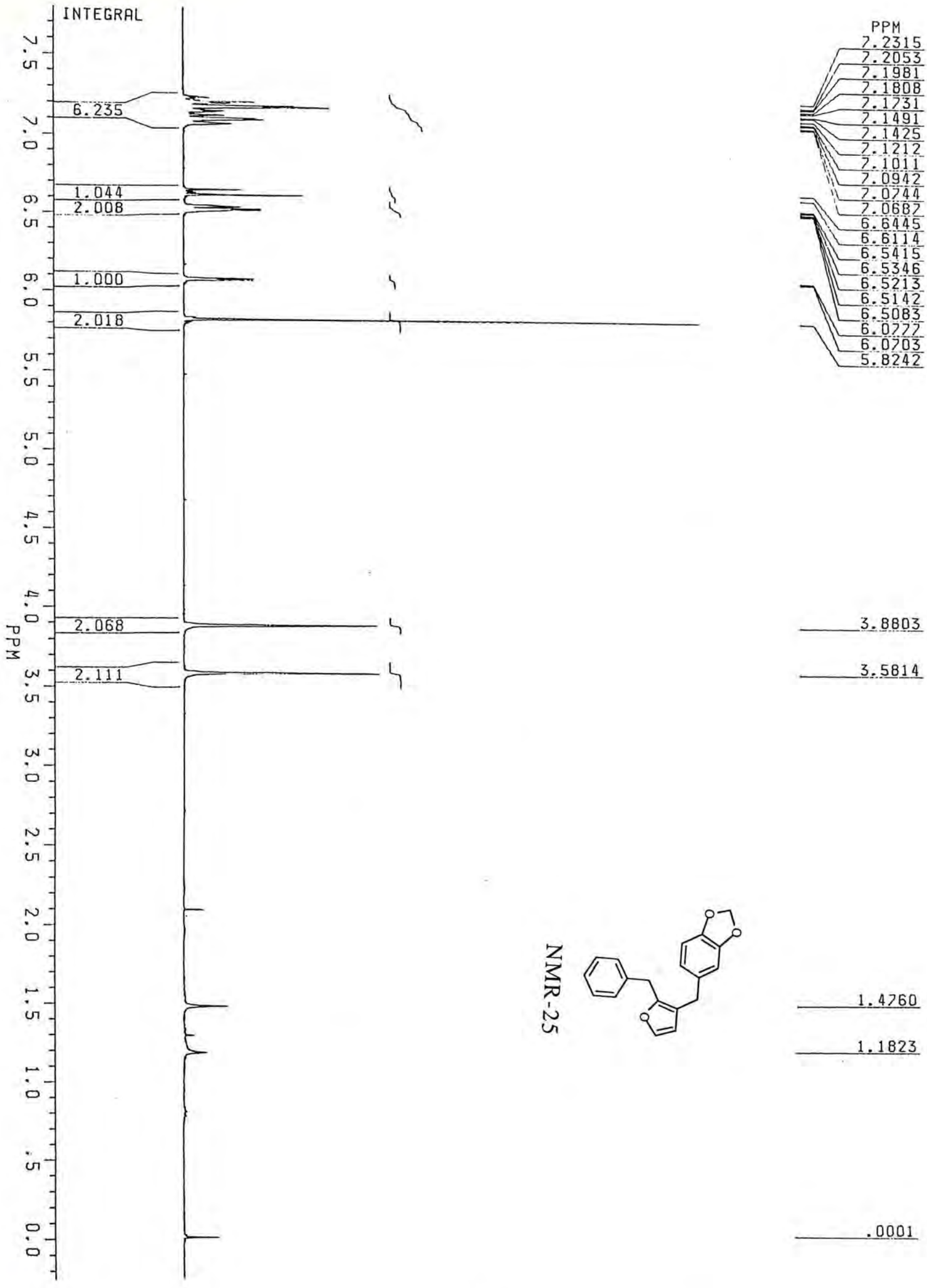

INTEGRAL
HERTZ
1.11
2.00
.97
1.90
6.31
8.85
1712.0
1691.9
1604.8
987.4
568.7
386.0
61.3
59.1
56.0
52.7
49.7
48.6
46.9
.1
PPM
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
NMR-21
TMS
O
I


INTEGRAL
HERTZ
1811.0
1706.3
1694.9
1465.9
973.3
644.2
636.6
629.0
566.1
397.9
390.4
384.2
332.7
321.7
320.0
314.8
224.1
221.9
217.5
210.7
54.1
50.9
47.6
-.1
.992
2.025
.989
1.989
2.266
6.080
2.084
6.448
3.264
9.102
PPM
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
NMR-22
TMS
O


INTEGRAL
2.02
1.94
1.03
1.94
.98
2.99
2.05
2.07
2.05
6.01
1.91
6.25
3.01
PPM
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
HERTZ
1984.9
1983.1
1978.5
1976.6
1810.6
1802.9
1796.2
1794.7
1794.3
1705.6
1685.3
1430.4
972.8
960.3
929.7
635.4
627.8
620.3
559.3
402.8
391.3
320.1
317.6
315.9
221.8
219.3
215.2
208.4
19.1
.0
NMR-23
MeO
O
O


INTEGRAL
1.00
5.40
.97
1.96
6.69
PPM
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
PPM
7.3544
7.3463
7.3389
7.2728
7.2665
7.2600
7.2501
7.2418
7.2363
7.2032
7.1969
7.1715
7.1522
7.1436
7.1399
6.3057
6.2973
6.2899
4.0243
4.0174
.2514
.2382
.2355
.2228
TMS
O

NMR-24


INTEGRAL
6.235
1.044
2.008
1.000
2.018
2.068
2.111
PPM
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0.0
PPM
7.2315
7.2053
7.1981
7.1808
7.1731
7.1491
7.1425
7.1212
7.1011
7.0942
7.0744
7.0687
6.6445
6.6114
6.5415
6.5346
6.5213
6.5142
6.5083
6.0727
6.0703
5.8242
3.8803
3.5814
1.4760
1.1823
.0001

NMR-25