

Highly stereo-selective synthesis of (Z)-2,3-diiodo-1,4-diarylbut-2-ene-1,4-diones via oxidative iodination of 1,4-diarylbuta-1,3-diyne

Raju Singha, Shubhendu Dhara and Jayanta K. Ray*

Department of Chemistry, Indian Institute of Technology, Kharagpur 721302, India

* Corresponding author. Tel.: +91 3222283326; fax: +91 3222282252.

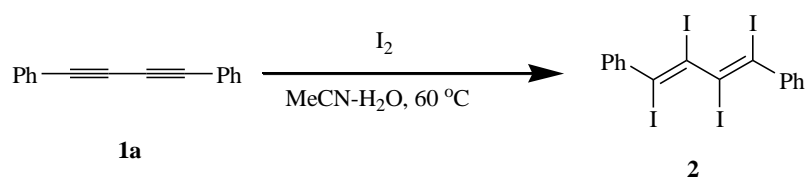
E-mail address: jkray@chem.iitkgp.ernet.in (J. K. Ray).

Supplementary Data

Table of contents	Page
General methods	2
General procedures for the experiments and analytical data	2-9
References	10
NMR spectra	11-26

General methods: High quality reagents were purchased from Sigma Aldrich. Analytical grade commercial reagents and solvents were purified by standard procedures prior to use. Chromatographic purification was done with 60-120 mesh silica gel (Merck). For reaction monitoring, pre-coated silica gel 60 F254 sheets (Merck) were used. ^1H NMR (200 MHz) spectra were recorded on a BRUCKER-AC 200 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuteriochloroform: 7.26 ppm). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = double doublet, brs = broad singlet), coupling constant (Hz). ^{13}C NMR (50 MHz) spectra were recorded on a BRUKER-AC 200 MHz. Spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuteriochloroform: 77.23 ppm). HRMS (ESI) spectra were taken using Waters Xevo G2 QToF mass spectrometer. ^{19}F NMR spectra were recorded on a BRUKER-AC 400 MHz. Spectrometer

General procedure for the synthesis of (1*E*, 3*E*)-1,2,3,4-tetraiodo-1,4-diphenylbuta-1,3-diene (2):

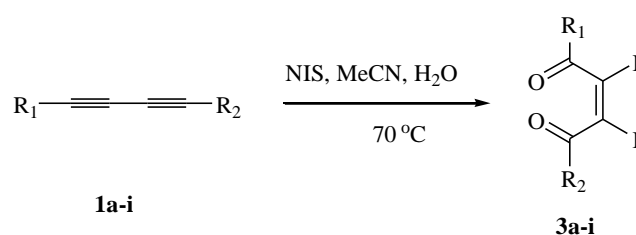


The compound 1,4-diphenylbuta-1,3-diyne (1a) (0.5 mmol) and iodine (1 mmol) were placed in a two-necked round bottomed flask fitted with a condenser. Then 4 mL of acetonitrile-water mixture (3:1 v/v) was added and stirred at 60 °C for 12 hour. Then the reaction mixture was allowed to cool to room temperature and diluted with sodium thiosulfate solution. The solution was extracted with EtOAc (3 x 20 mL) and washed with brine, dried over anhydrous

Na₂SO₄ and evaporated under reduced pressure. The crude product was purified by column chromatography using silica gel (60-120 mesh) and petroleum ether/EtOAc as eluent.

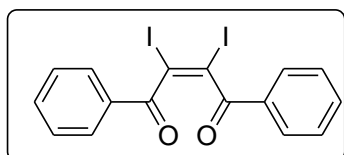
Light pink coloured solid; mp: 138-139 °C; Yield 58%; ¹H NMR (CDCl₃, 200 MHz) δ: 7.39 (10 H, brs); ¹³C NMR (CDCl₃, 50 MHz) δ: 100.9 (2 x C), 105.5 (2 x C), 128.4 (4 x CH), 128.6 (4 x CH), 129.2 (2 x CH), 145.6 (2 x C). Spectral data are in well agreement with the literature data.¹

General procedure for the synthesis of (Z)-2,3-diiodo-1,4-diarylbut-2-ene-1,4-dions (3a-i):



The compound 1,4-diarylbuta-1,3-diyne (0.5 mmol) and N-iodosuccinamide (1.5 mmol) were taken in a two-necked round bottomed flask fitted with a condenser. Then 4 mL of acetonitrile-water solvent mixture (3:1 v/v) was added and stirred at 70 °C for the required time. Then the reaction mixture was allowed to cool to room temperature and diluted with sodium thiosulfate solution. The mixture was extracted with EtOA (3 x 20 mL) and the combined organic layer was then washed with brine, dried over anhydrous Na₂SO₄ and evaporated under reduced pressure. The crude product was then purified by column chromatography using silica gel (60-120 mesh) and petroleum ether/EtOAc as eluent.

(Z) 2,3-diiodo-1,4-diphenylbut-2-ene-1,4-dione (3a)

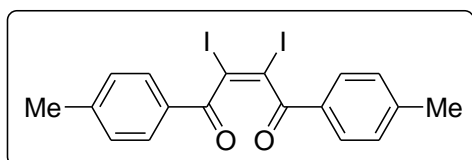


The title compound was prepared from **1a** in 72% yield as yellow solid; mp: 93-94 °C; ¹H NMR (CDCl₃, 200 MHz) δ: 7.38-7.45 (4H, m), 7.52-7.59 (2H, m), 7.82 (4H, d, *J* = 7.6 Hz);

¹³C NMR (CDCl₃, 50 MHz) δ: 115.5 (2 x C), 128.8 (4 x CH), 130.4 (4 x CH), 133.3 (2 x C),

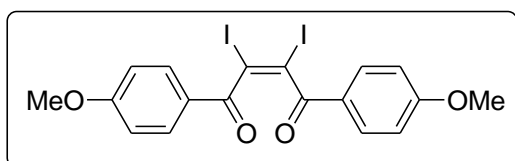
134.5 (2 x CH), 190.4 (2 x C). HRMS (ESI) calculated for $C_{16}H_{11}I_2O_2$ $[M + H]^+$: 488.8843; found: 488.8842; Crystal data: CCDC No 946434, unit cell parameters: $a = 15.590$, $b = 7.2248$, $c = 14.053$, $\alpha = 90$, $\beta = 92.501$, $\gamma = 90$; space group C 2/C.

(Z) 2,3-diiodo-1,4-di *p*-tolylbut-2-ene-1,4-dione (3b)



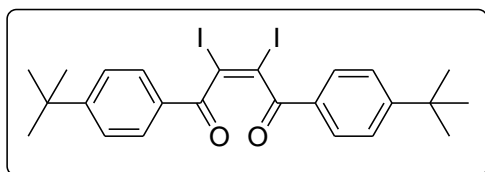
The title compound was prepared from **1b** in 75% yield as a yellow solid; mp: 103-105 °C; 1H NMR ($CDCl_3$, 200 MHz) δ : 2.39 (6H, s), 7.20 (4H, d, $J = 8.2$ Hz), 7.71 (4H, d, $J = 8.2$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ : 22.1 (2 x CH_3), 114.7 (2 x C), 129.5 (4 x CH), 130.6 (4 x CH), 130.7 (2 x CH), 145.8 (2 x C), 190.0 (2 x C). HRMS (ESI) calculated for $C_{18}H_{15}I_2O_2$ $[M + H]^+$: 516.9156; found: 516.9157.

(Z) 2,3-diiodo-1,4-bis(4-methoxyphenyl)but-2-ene-1,4-dione (3c)



The title compound was obtained from **1c** as a mixture of Z and E isomers (Z and E ratio = 100:16 by NMR ratio); Yield 65%; 1H NMR ($CDCl_3$, 200 MHz) (for Z isomer) δ : 3.85 (6H, s), 6.87 (4H, d, $J = 9.0$ Hz), 7.78 (4H, d, $J = 9.0$ Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) (for Z isomer) δ : 55.8 (2 x CH_3), 114.2 (4 x CH), 125.9 (2 x C), 132.5 (2 x C), 133.1 (4 x CH), 164.8 (2 x C), 190.0 (2 x C). HRMS (ESI) calculated for $C_{18}H_{15}I_2O_4$ $[M + H]^+$: 548.9054; found: 548.9051.

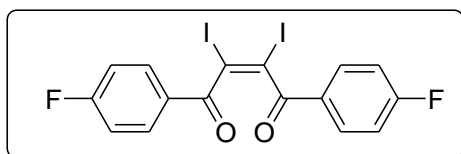
(Z)-1,4-bis(4-*tert*-butylphenyl)-2,3-diiodobut-2-ene-1,4-dione (3d)



The title compound was obtained from **1d** as a mixture with 10% E isomer; Yield 67%; 1H NMR ($CDCl_3$, 200 MHz) δ : 1.32 (18 H, s), 7.42 (4H, d, $J =$

8.6 Hz), 7.77 (4H, d, $J = 8.6$ Hz); ^{13}C NMR (CDCl_3 , 50 MHz) δ : 31.2 (6 x CH_3), 35.5 (2 x C), 114.9 (2 x C), 125.8 (4 x CH), 130.4 (4 x CH), 130.6 (2 x C), 158.5 (2 x C), 190.0 (2 x C). HRMS (ESI) calculated for $\text{C}_{24}\text{H}_{27}\text{I}_2\text{O}_2$ [$\text{M} + \text{H}$] $^+$: 601.0095; found: 601.0096.

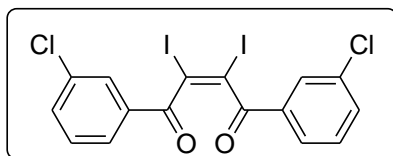
(Z) 2,3-diiodo-1,4-bis(4-fluorophenyl)but-2-ene-1,4-dione (3e)



The title compound was prepared from **1e** as a yellow solid; mp: 96-98 °C; Yield 59%; ^1H NMR (CDCl_3 , 200 MHz) δ : 7.06-7.15 (4H, m), 7.82-7.89 (4H, m); ^{13}C

NMR (CDCl_3 , 50 MHz) δ : 114.8 (2 x C), 116.3 (4 x CH, d, $J = 22$ Hz), 129.6 (2 x C, d, $J = 3.0$ Hz), 133.2 (4 x CH, d, $J = 9.5$ Hz), 166.6 (2 x C, d, $J = 256$ Hz), 189.1 (2 x C). ^{19}F NMR (CDCl_3 , 376 MHz) δ : -39.0 (s, 2F); HRMS (ESI) calculated for $\text{C}_{16}\text{H}_9\text{F}_2\text{I}_2\text{O}_2$ [$\text{M} + \text{H}$] $^+$: 524.8654; found: 524.8656.

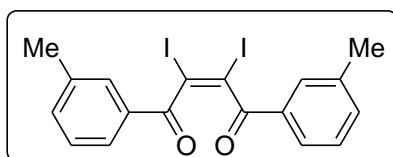
(Z)-1,4-bis(3-chlorophenyl)-2,3-diiodobut-2-ene-1,4-dione (3f)



The title compound was prepared from **1f** as a yellow solid; mp: 119-121 °C; Yield 61%; ^1H NMR (CDCl_3 , 200 MHz) δ : 7.37 (2H, d, $J = 8.0$ Hz), 7.53 (2H, d, $J = 8.0$ Hz), 7.70-

7.77 (4H, m); ^{13}C NMR (CDCl_3 , 50 MHz) δ : 115.8 (2 x C), 128.5 (2 x CH), 129.9 (2 x CH), 130.2 (2 x CH), 134.5 (2 x CH), 134.9 (2 x C), 135.2 (2 x C), 189.3 (2 x C). HRMS (ESI) calculated for $\text{C}_{16}\text{H}_9\text{Cl}_2\text{I}_2\text{O}_2$ [$\text{M} + \text{H}$] $^+$: 556.8063; found: 556.8062.

(Z) 2,3-diiodo-1,4-di *m*-tolylbut-2-ene-1,4-dione (3g)

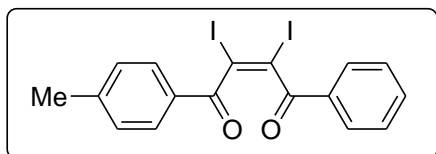


The title compound was obtained from **1g** as a yellow solid; mp: 107-109 °C; Yield 74%; ^1H NMR (CDCl_3 , 200 MHz) δ : 2.36 (6H, s), 7.29-7.33 (4H, m), 7.58-7.64 (4H, m); ^{13}C

NMR (CDCl_3 , 50 MHz) δ : 21.5 (2 x CH_3), 115.7 (2 x C), 127.8 (2 x CH), 128.6 (2 x CH),

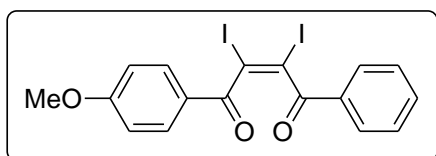
130.6 (2 x CH), 133.4 (2 x C), 135.3 (2 x CH), 138.7 (2 x C), 190.5 (2 x C). HRMS (ESI) calculated for $C_{18}H_{15}I_2O_2$ $[M + H]^+$: 516.9156; found: 516.9154.

(Z) 2,3-diiodo-1-phenyl-4-*p*-tolylbut-2-ene-1,4-dione (3h)



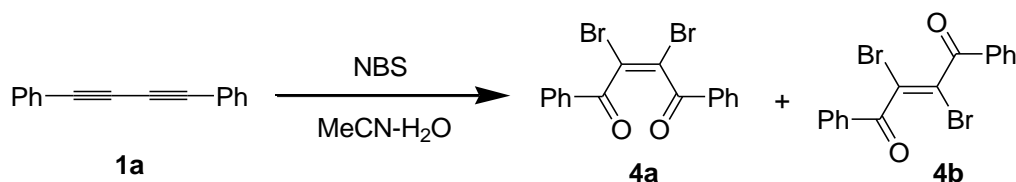
The title compound was prepared from **1h** as a yellow solid; mp: 100-102 °C; Yield 73%; 1H NMR ($CDCl_3$, 200 MHz) δ : 2.39 (3H, s), 7.21 (2H, d, $J = 8.0$ Hz), 7.37-7.45 (2H, m), 7.51-7.58 (1H, m), 7.71 (2H, d, $J = 8.0$ Hz), 7.79-7.83 (2H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ : 22.1 (CH₃), 114.8 (C), 115.5 (C), 128.8 (2 x CH), 129.6 (2 x CH), 130.4 (2 x CH), 130.6 (2 x CH), 130.7 (C), 133.3 (C), 134.5 (CH), 145.8 (C), 190.1 (C), 190.4 (C). HRMS (ESI) calculated for $C_{17}H_{13}I_2O_2$ $[M + H]^+$: 502.8999; found: 502.8998.

(Z) 2,3-diiodo-1-(4-methoxyphenyl)-4-phenylbut-2-ene-1,4-dione (3i)



The title compound was obtained from **1i** with trace amount of its E isomer; Yield 68%; 1H NMR ($CDCl_3$, 200 MHz) δ : 3.86 (3H, s), 6.87 (2H, d, $J = 8.8$ Hz), 7.37-7.58 (4H, m), 7.76-7.83 (3H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ : 55.8 (CH₃), 114.2 (2 x CH + C) (two picks merged with each other), 115.3 (C), 126.0 (CH), 128.8 (2 x CH), 130.4 (2 x CH), 133.0 (2 x CH), 133.3 (C), 134.5 (CH), 164.8 (C), 188.9 (C), 190.4 (C). HRMS (ESI) calculated for $C_{17}H_{13}I_2O_3$ $[M + H]^+$: 518.8949; found: 518.8952.

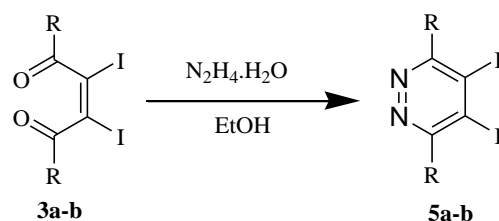
Procedure for the preparation of (Z) 2,3-dibromo-1,4-diphenylbut-2-ene-1,4-dione and (E) 2,3-dibromo-1,4-diphenylbut-2-ene-1,4-dione: (4a and 4b)



The compound 1,4-diarylbuta-1,3-diyne (0.5 mmol) and N-bromosuccinamide (1 mmol) were taken in a two-necked round bottomed flask fitted with a condenser. Then 4 mL of acetonitrile-water solvent mixture (3:1 v/v) was added and stirred at room temperature for the 12 h. Then the reaction mixture was diluted with sodium thiosulfate solution. The mixture was extracted with EtOA (3 x 20 mL) and the combined organic layer was then washed with brine, dried over anhydrous Na₂SO₄ and evaporated under reduced pressure. The crude product was then purified by column chromatography using silica gel (60-120 mesh) and petroleum ether/EtOAc as eluent.

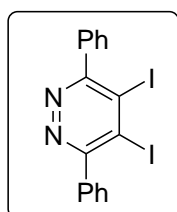
The title compounds were Obtained as mixture of Z:E isomers, ratio = 100:16; Yield (37+14) %; ¹H NMR (CDCl₃, 200 MHz) (for only Z isomer) δ: 7.37-7.45 (4H, m), 7.52-7.60 (2H, m), 7.81-7.85 (4H, m); ¹³C NMR (CDCl₃, 50 MHz) (for Z and E isomer) δ: 128.5 (c), 128.8 (CH), 129.4 (CH), 130.2(CH), 130.3 (CH), 132.4 (C), 133.9 (C), 134.5 (CH), 135.2 (CH), 188.3 (C), 188.7 (C). HRMS (ESI) calculated for C₁₆H₁₁Br₂O₂ [M + H]⁺ : 392.9120; found: 392.9120. (Presence of two Br are also confirmed from the mass ratio of 392.9120, 394.9111, 396.9112 and the intensity ratio is 1:2:1).

General procedure for the synthesis of 4,5-diiodo-3,6-diarylpyridazines:



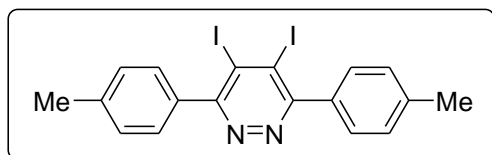
The compound 3a or 3b (0.5 mmol) was taken in a round bottom flask and then 2 mL ethanol was added to it. Then hydrazine hydrate (0.75 mmol) was added and the reaction mixture was stirred at room temperature for two minutes. The reaction mixture was diluted with water and extracted with ethyl acetate (3 x 20 mL). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄ and evaporated under reduced pressure. The crude product was purified by column chromatography using silica gel (60-120 mesh) and petroleum ether/EtOAc as eluent.

4,5-diiodo-3,6-diphenylpyridazine (5a)



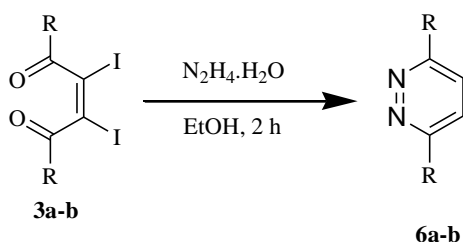
Light yellow solid; mp: 243-245 °C; Yield 91%; ¹H NMR (CDCl₃, 200 MHz) δ: 7.50-7.52 (6H, m), 7.58-7.61 (4H, m); ¹³C NMR (CDCl₃, 50 MHz) δ: 121.2 (2 x C), 128.3 (4 x CH), 129.5 (4 x CH), 129.8 (2 x CH), 141.1 (2 x C), 164.1 (2 x C). HRMS (ESI) calculated for C₁₆H₁₁I₂N₂ [M + H]⁺ : 484.9006; found: 484.9003.

4,5-diiodo-3,6-dip-tolylpyridazine (5b)



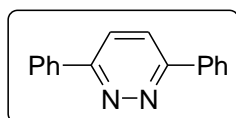
Yellow solid; mp: 252-254 °C; Yield 90%; ¹H NMR (CDCl₃, 200 MHz) δ: 2.46 (6H, s), 7.31 (4H, d, *J* = 8.2 Hz), 7.51 (4H, d, *J* = 8.2 Hz); ¹³C NMR (CDCl₃, 50 MHz) δ: 21.6 (2 x CH₃), 120.9 (2 x C), 128.9 (4 x CH), 129.5 (4 x CH), 138.5 (2 x C), 139.8 (2 x C), 163.9 (2 x C). HRMS (ESI) calculated for C₁₈H₁₅I₂N₂ [M + H]⁺ : 512.9319; found: 512.9321.

General procedure for the synthesis of 3,6-diarylpyridazines:



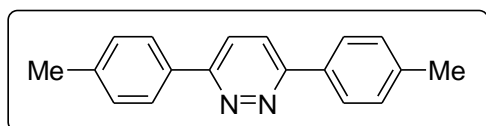
The compound 3a or 3b (0.5 mmol) was taken in a round bottom flask and then 2 mL ethanol was added to it. Then excess amount of hydrazine hydrate (about 5 mmol) was added and the reaction mixture was stirred at room temperature for two hours. The reaction mixture was diluted with water and extracted with ethyl acetate (3 x 20 mL). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄ and evaporated under reduced pressure. The crude product was purified by column chromatography using silica gel (60-120 mesh) and petroleum ether/EtOAc as eluent.

3,6-diphenylpyridazine (6a)



White solid; mp: 220-222 °C; Yield 93%; ¹H NMR (CDCl₃, 200 MHz) δ: 7.49-7.58 (6H, m), 7.94 (2H, s), 8.14-8.19 (4H, m); ¹³C NMR (CDCl₃, 50 MHz) δ: 124.4 (2 x CH), 127.2 (4 x CH), 129.3 (4 x CH), 130.3 (2 x CH), 134.4 (2 x C), 157.9 (2 x C). Spectral data are in well agreement with the literature reported data.²

3,6-dip-tolylpyridazine (6b)

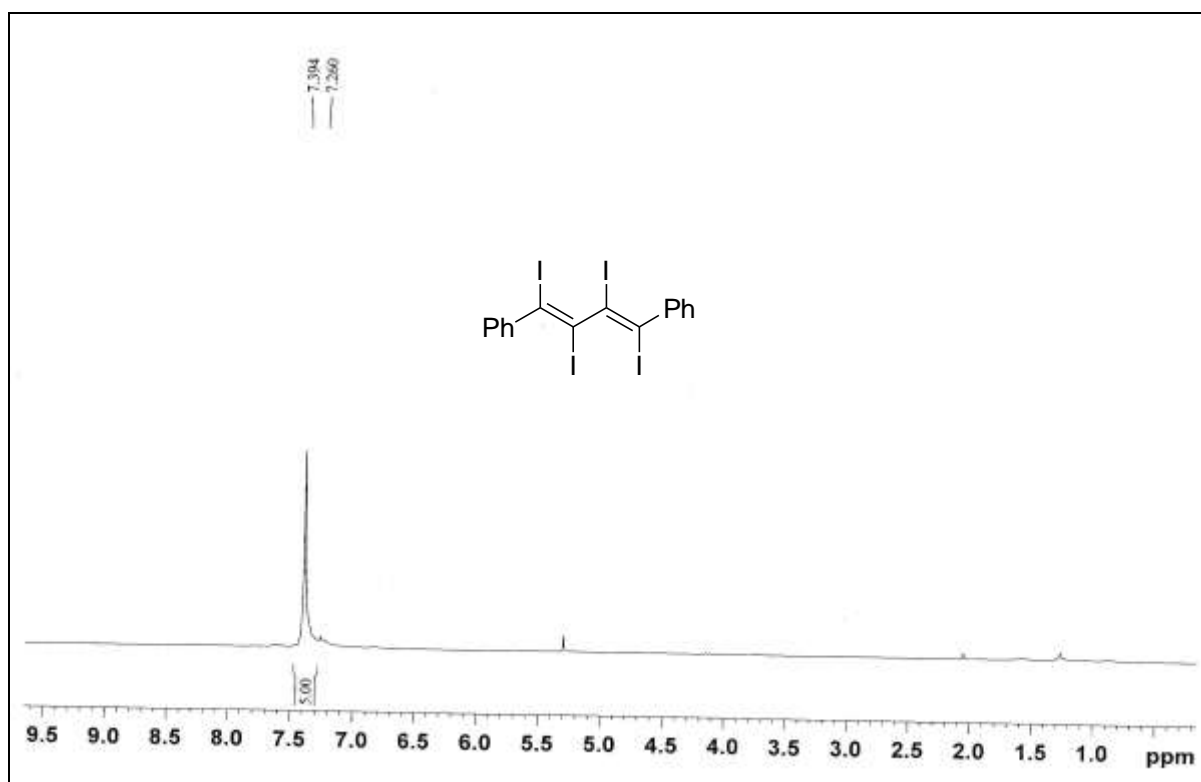


Yellow solid; mp: 228-230 °C; Yield 94%; ¹H NMR (CDCl₃, 200 MHz) δ: 2.44 (6H, s), 7.34 (4H, d, *J* = 8.0 Hz), 7.87 (2H, s), 8.05 (4H, d, *J* = 8.0 Hz); ¹³C NMR (CDCl₃, 50 MHz) δ: 21.6 (2 x CH₃), 124.1 (2 x CH), 126.9 (4 x CH), 129.9 (4 x CH), 133.6 (2 x C), 140.3 (2 x C), 157.5 (2 x C). Spectral data are in well agreement with the literature reported data.³

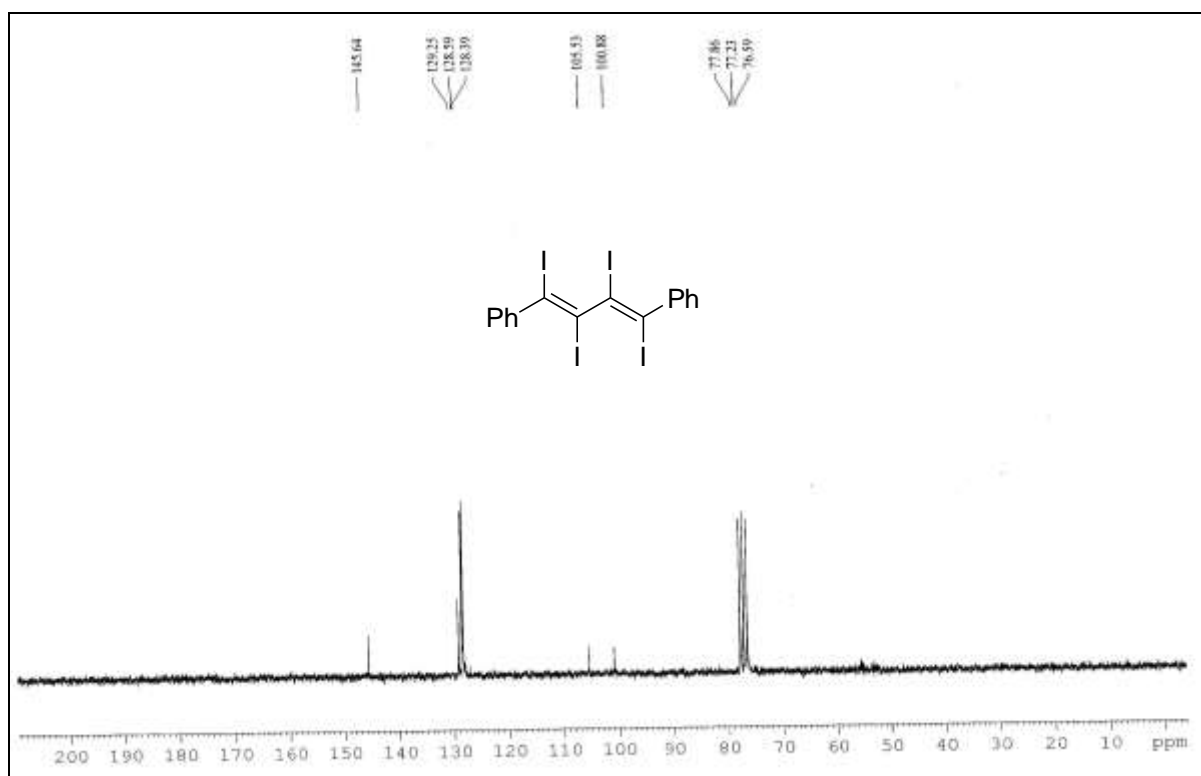
References:

1. R. A. Hollins and M. P. A. Campos, *J. Org. Chem.*, 1979, **44**, 3931.
2. Q. Gao, Y. Zhu, M. Lian, M. Liu, J. Yuan, G. Yin and A. Wu, *J. Org. Chem.* 2012, **77**, 9865.
3. M. Gnanadeepam, S. Selvaraj, S. Perumal and S. Renuga, *Tetrahedron*, 2002, **58**, 2227.

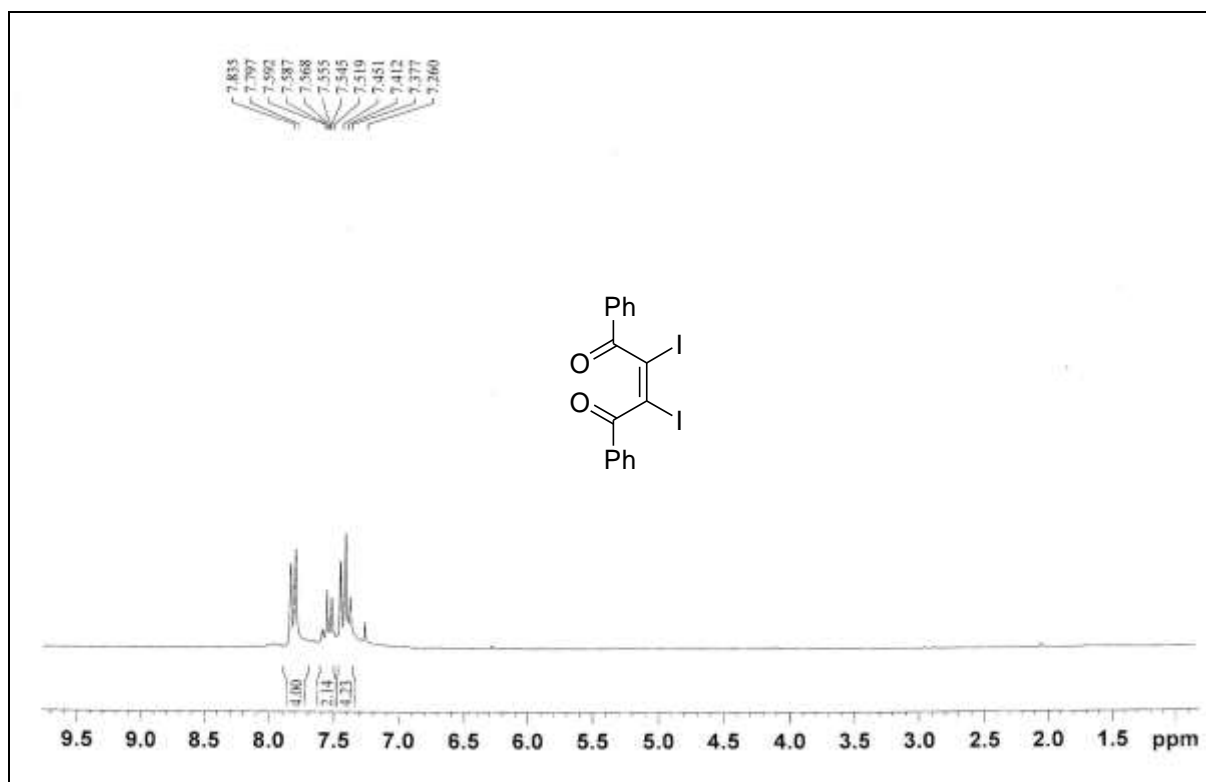
^1H NMR (CDCl_3 , 200 MHz) spectra of compound **2**



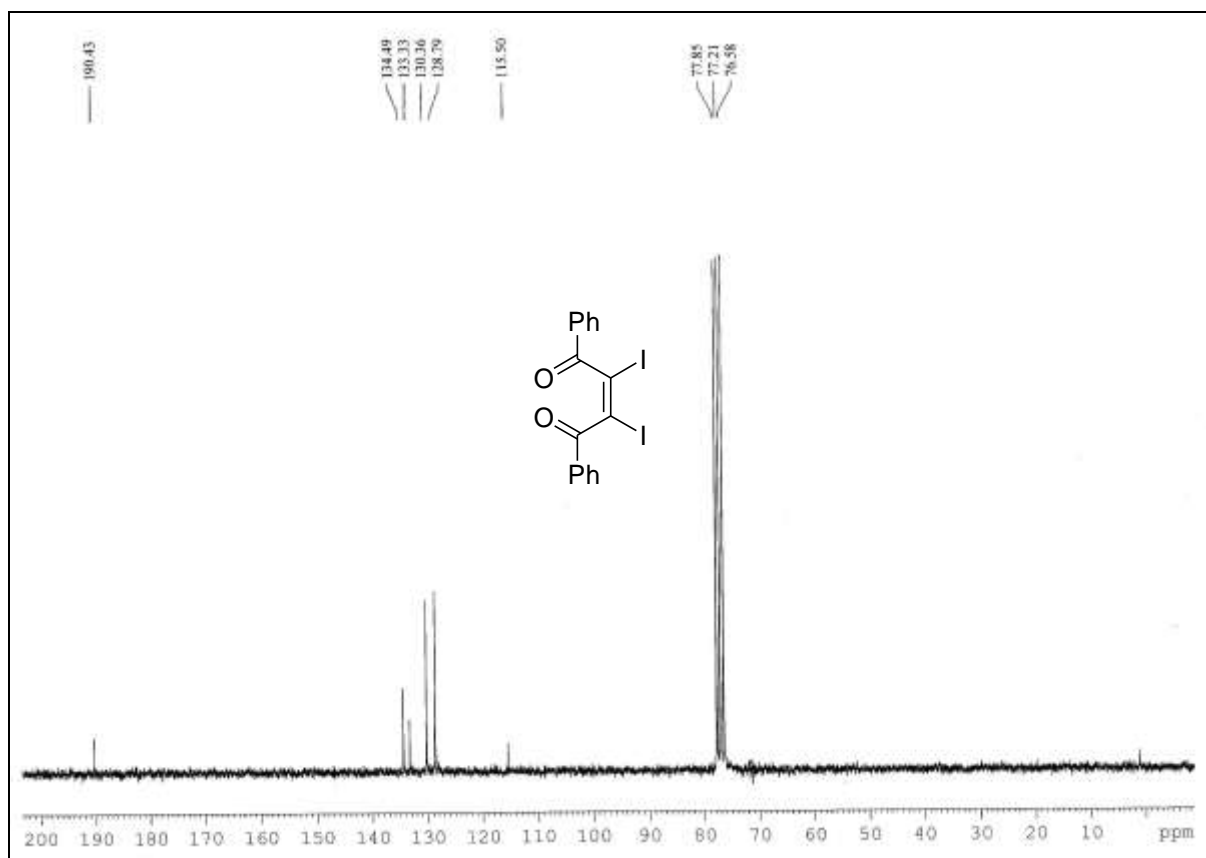
^{13}C NMR (CDCl_3 , 50 MHz) of compound **2**



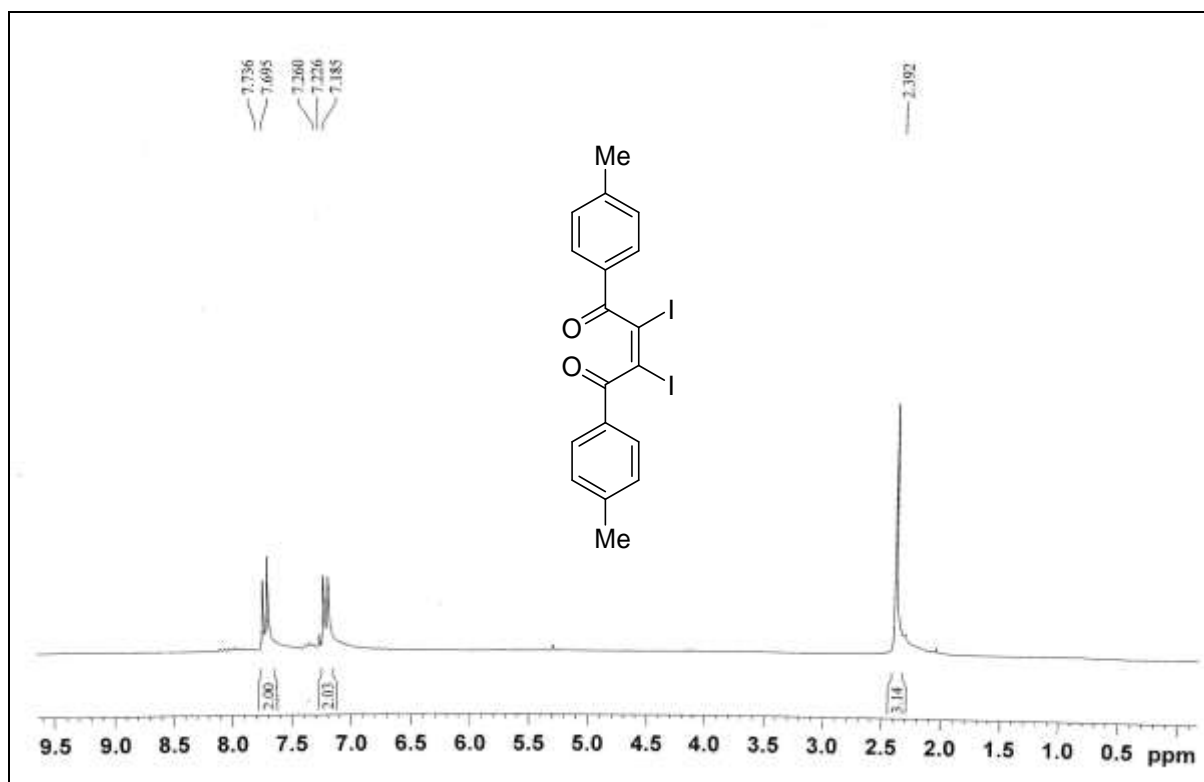
^1H NMR (CDCl_3 , 200 MHz) of compound **3a**



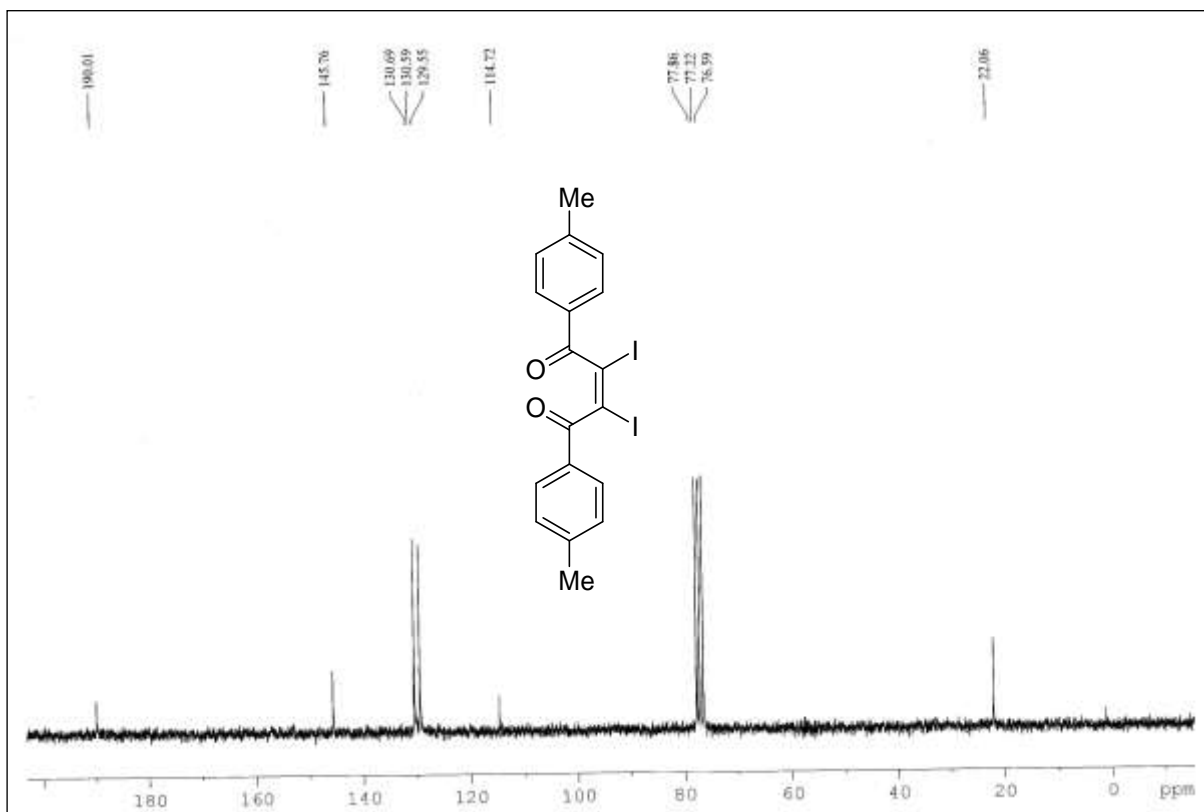
^{13}C NMR (CDCl_3 , 50 MHz) of compound **3a**



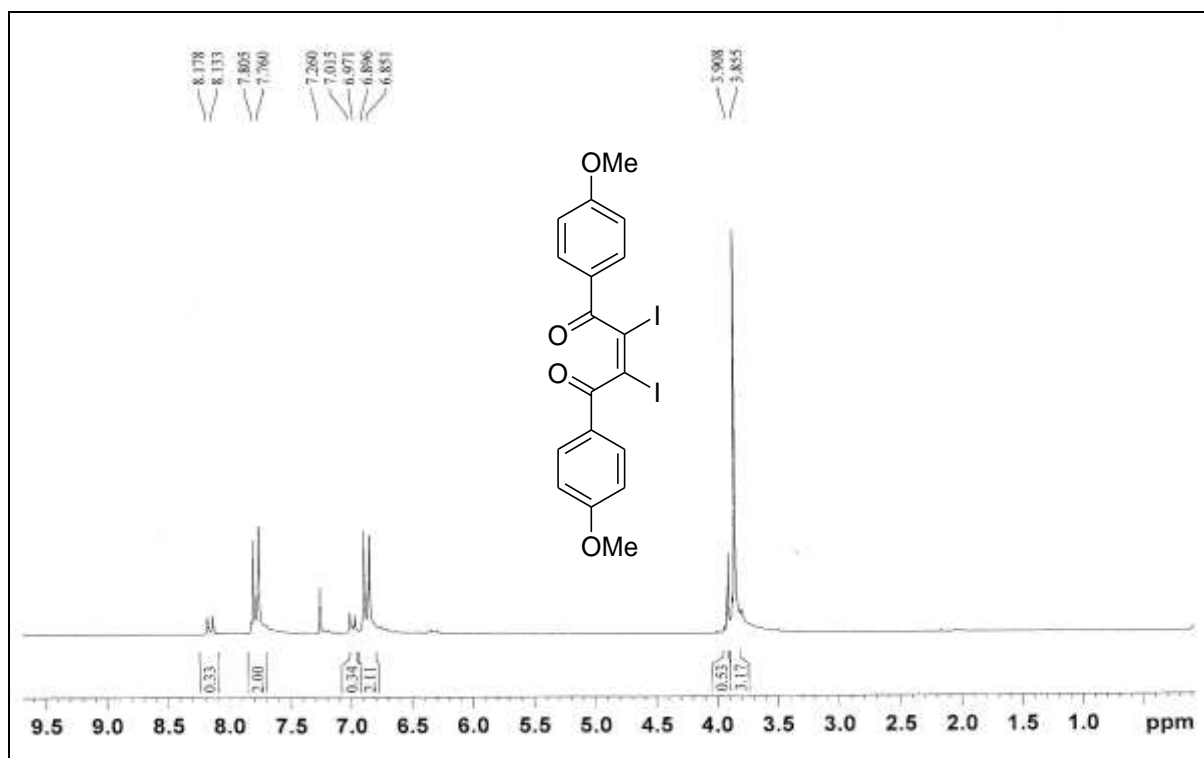
^1H NMR (CDCl_3 , 200 MHz) of compound **3b**



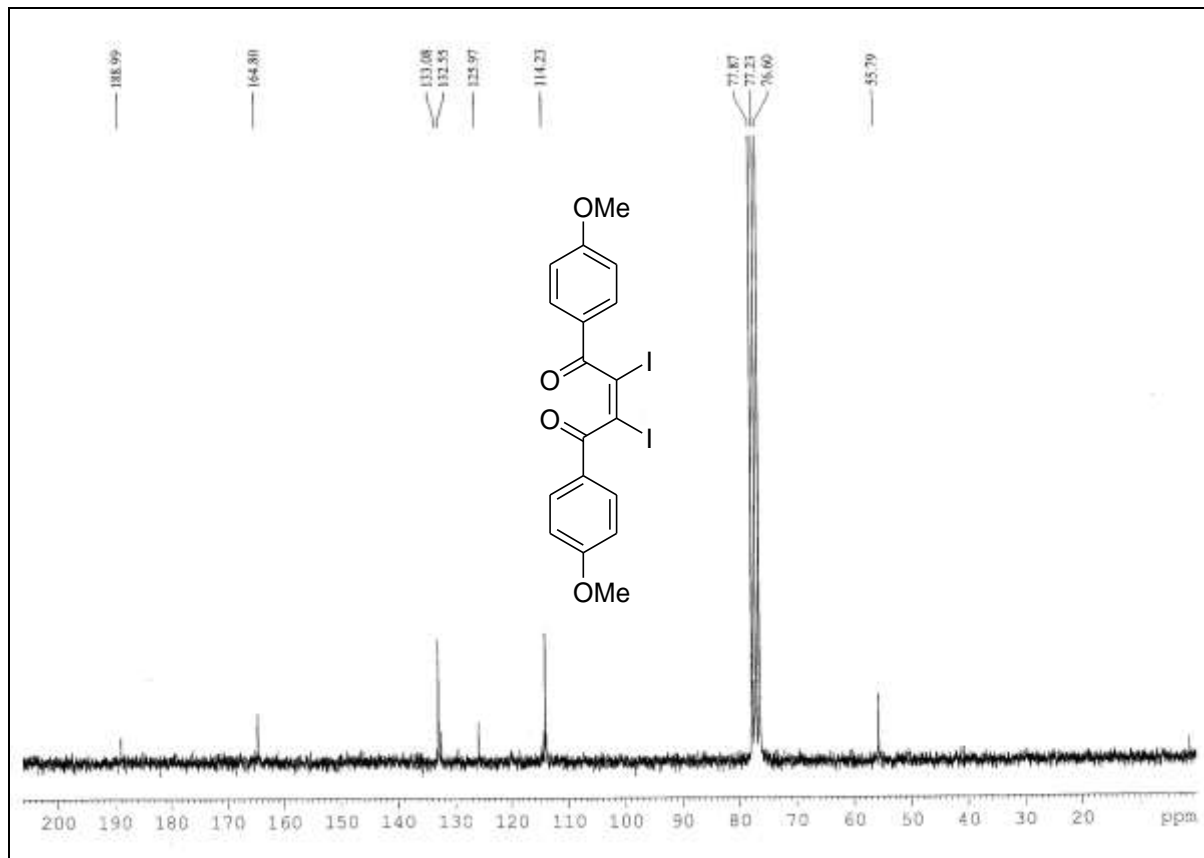
^{13}C NMR (CDCl_3 , 50 MHz) of compound **3b**



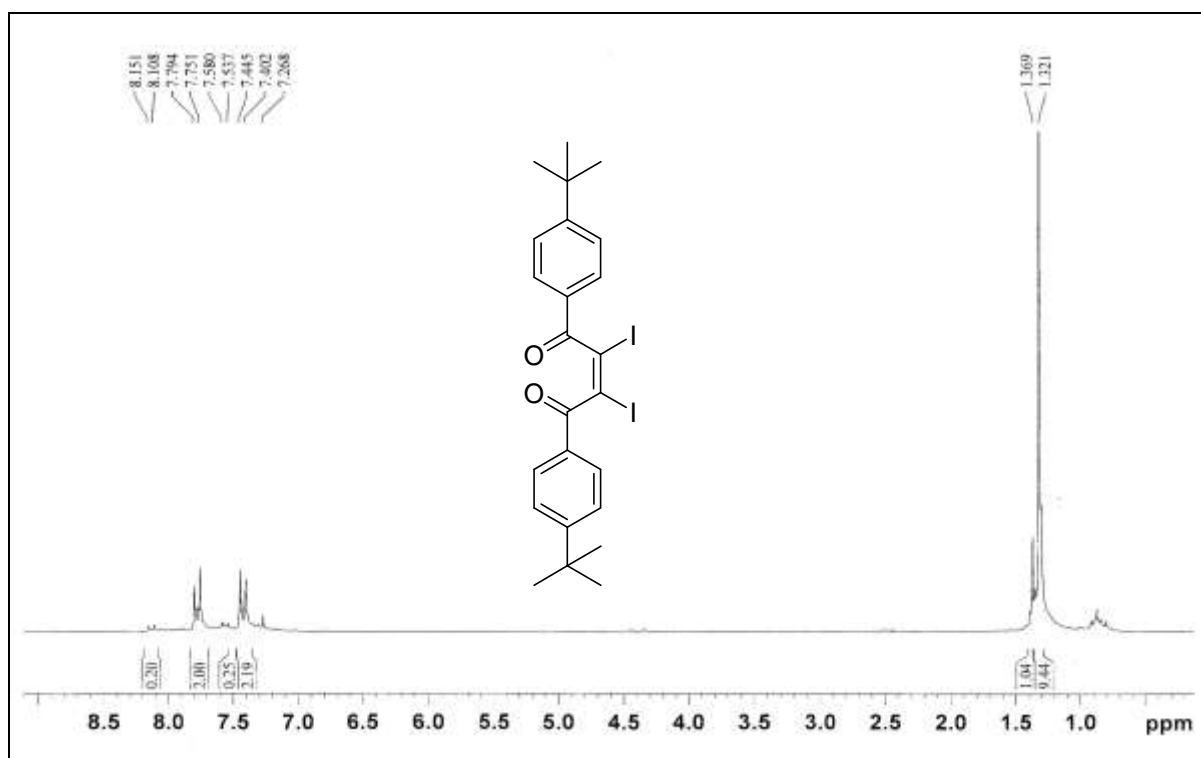
^1H NMR (CDCl_3 , 200 MHz) of compound **3c**



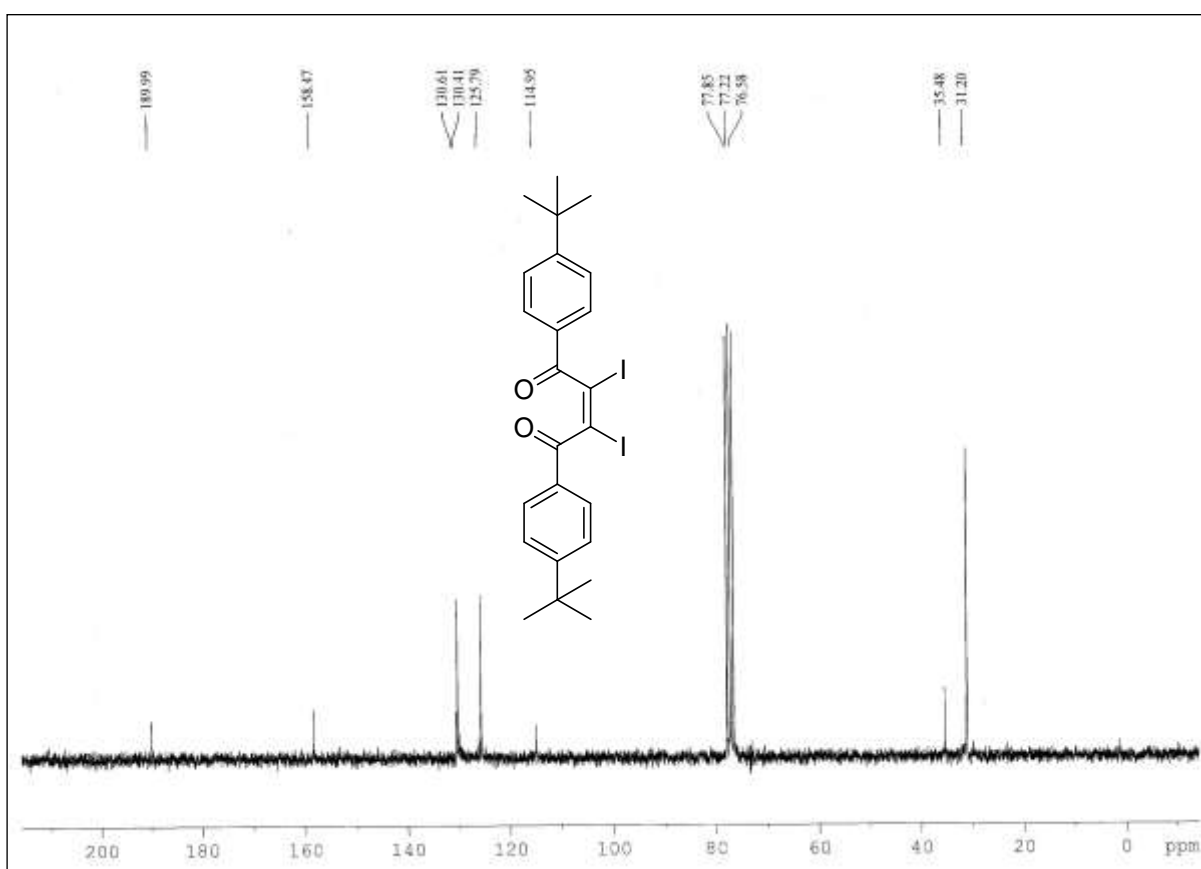
^{13}C NMR (CDCl_3 , 50 MHz) of compound **3c**



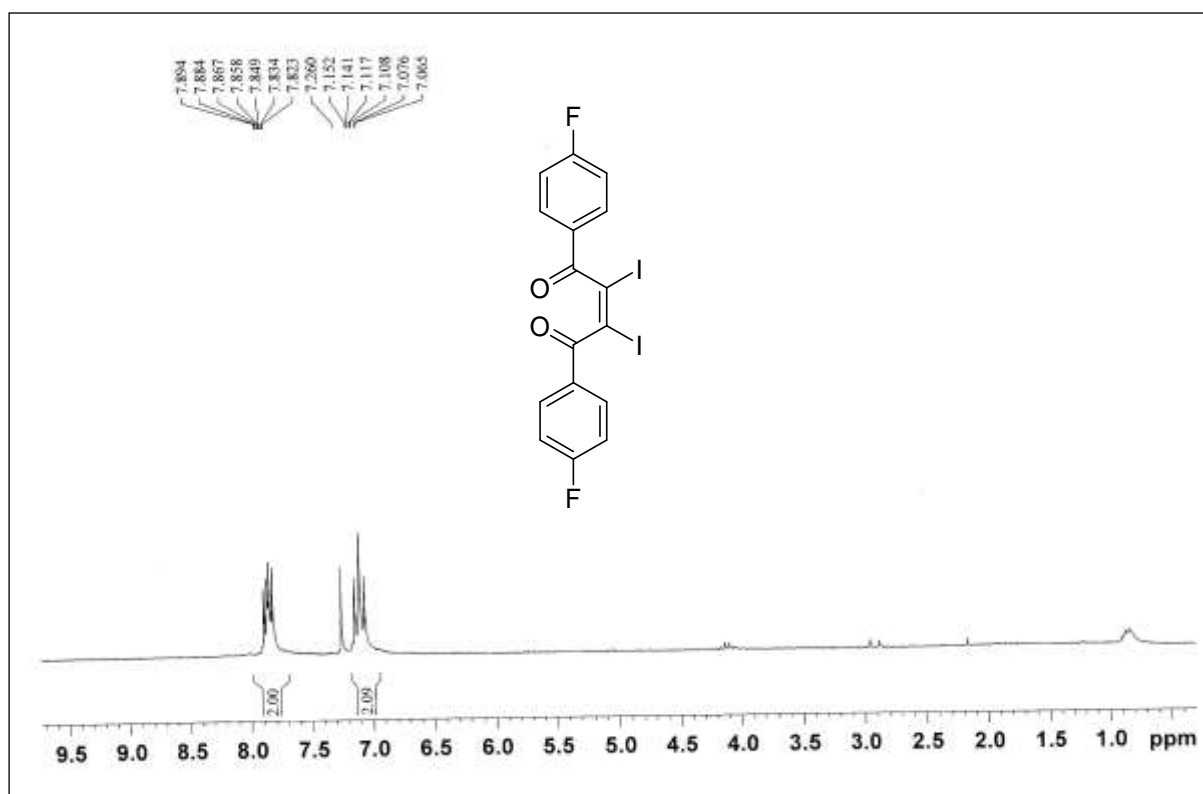
^1H NMR (CDCl_3 , 200 MHz) of compound **3d**



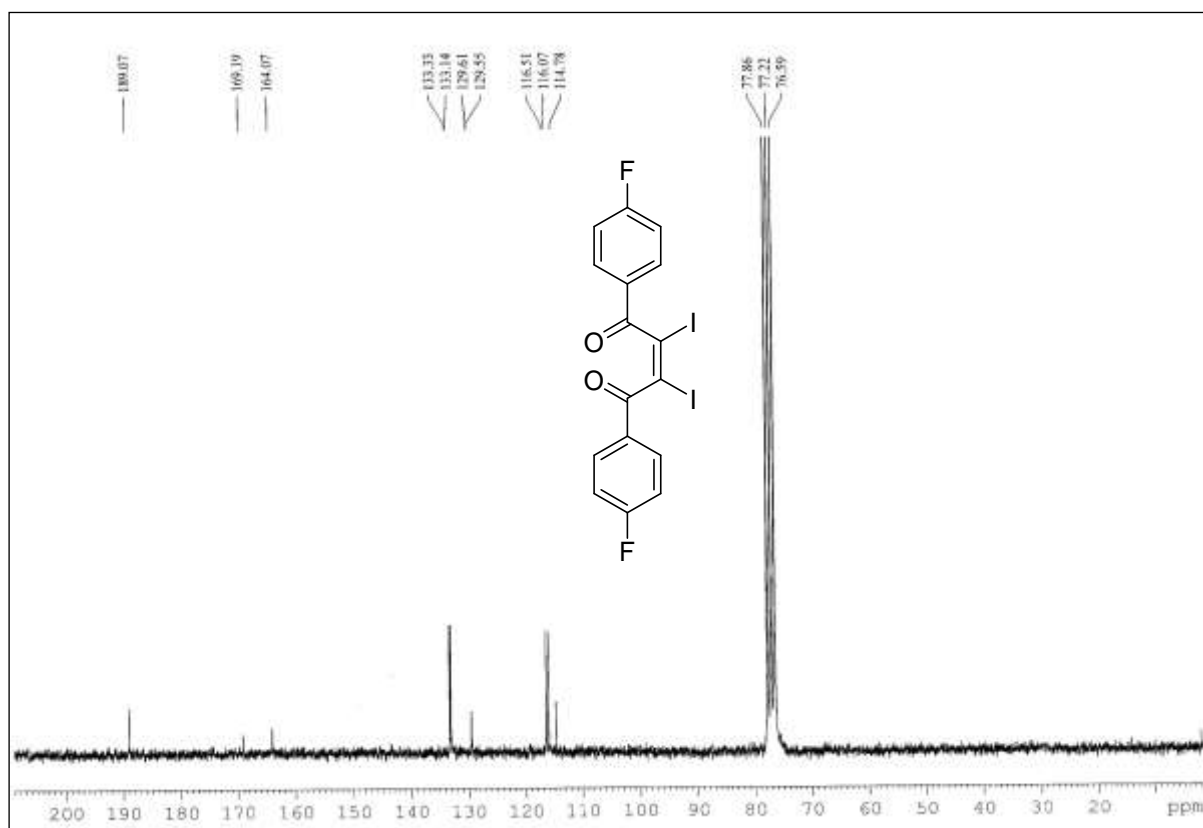
^{13}C NMR (CDCl_3 , 50 MHz) of compound **3d**



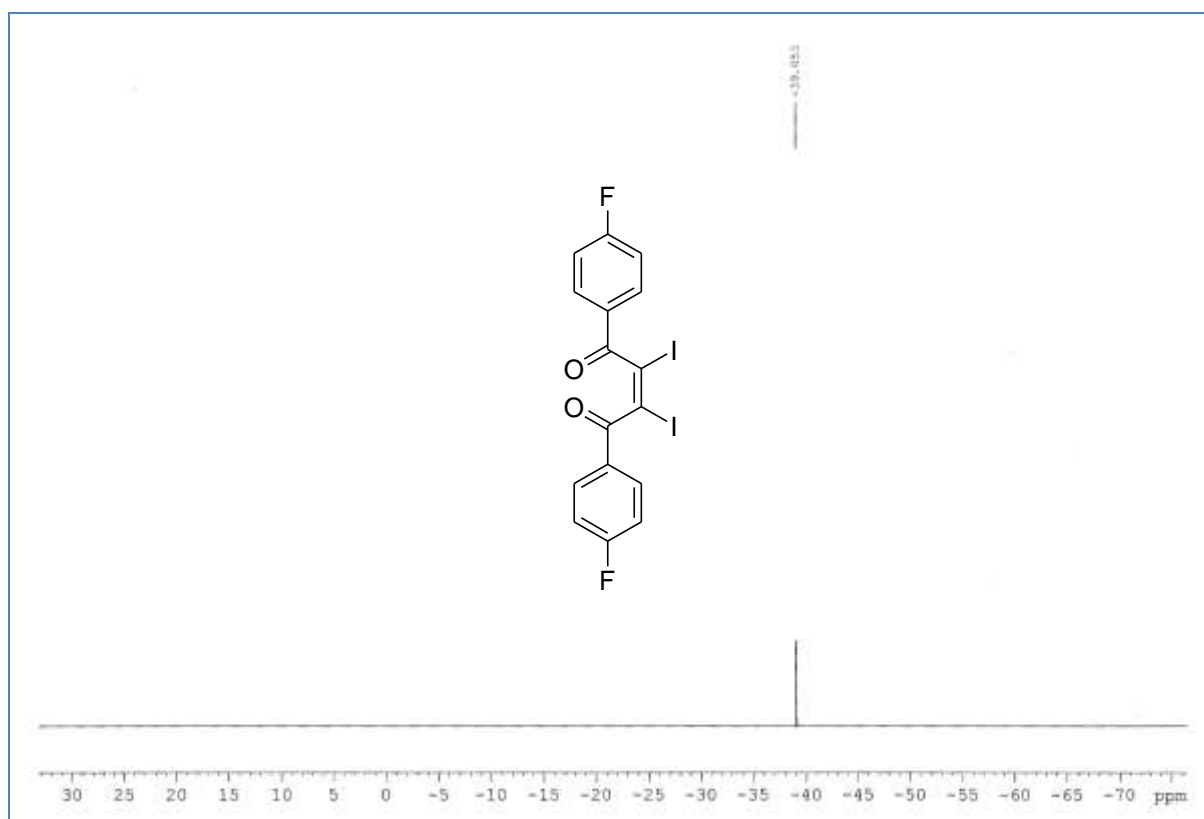
^1H NMR (CDCl_3 , 200 MHz) of compound **3e**



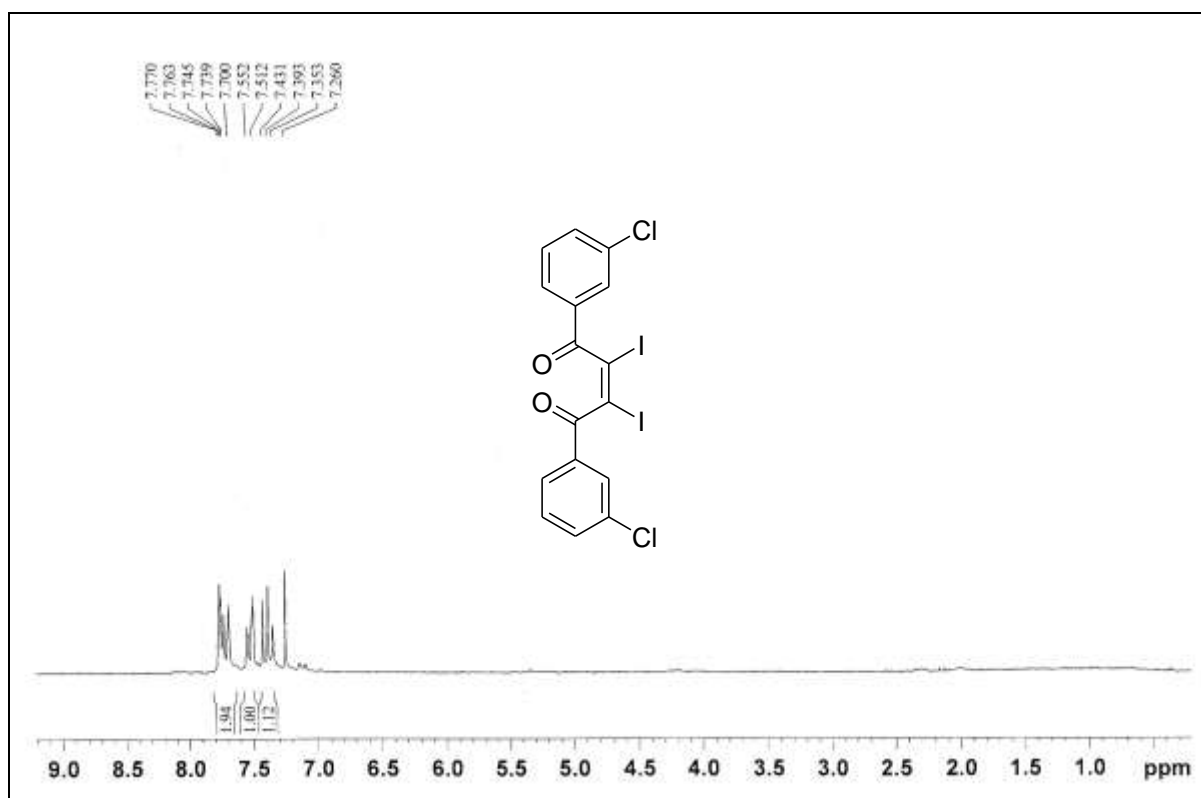
^{13}C NMR (CDCl_3 , 50 MHz) of compound **3e**



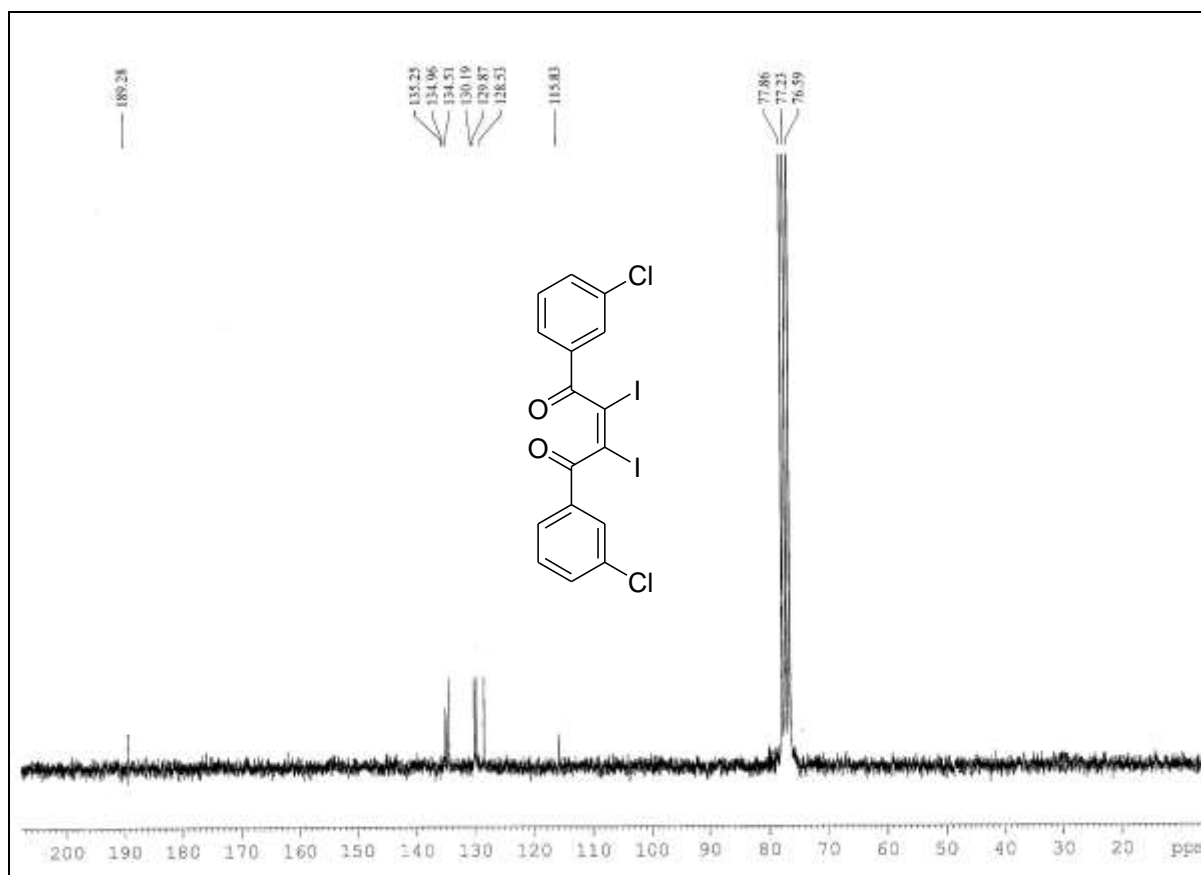
^{19}F NMR of compound **3e**



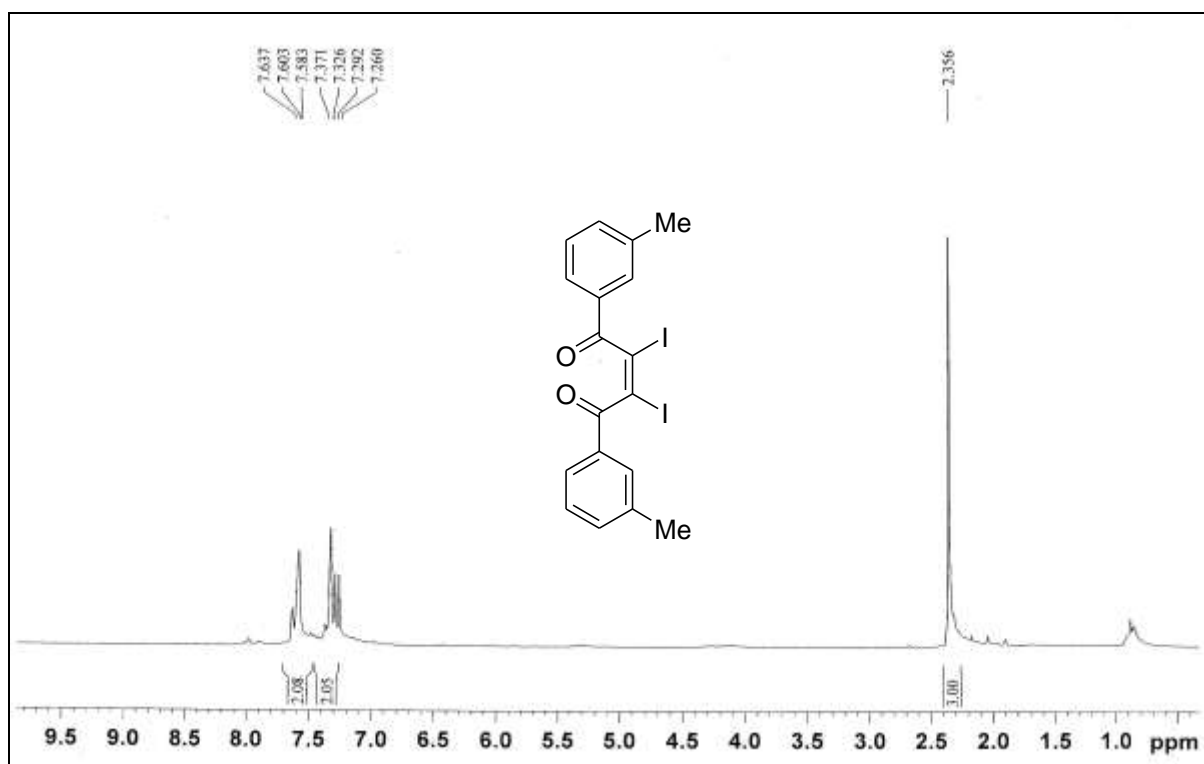
^1H NMR (CDCl_3 , 200 MHz) of compound **3f**



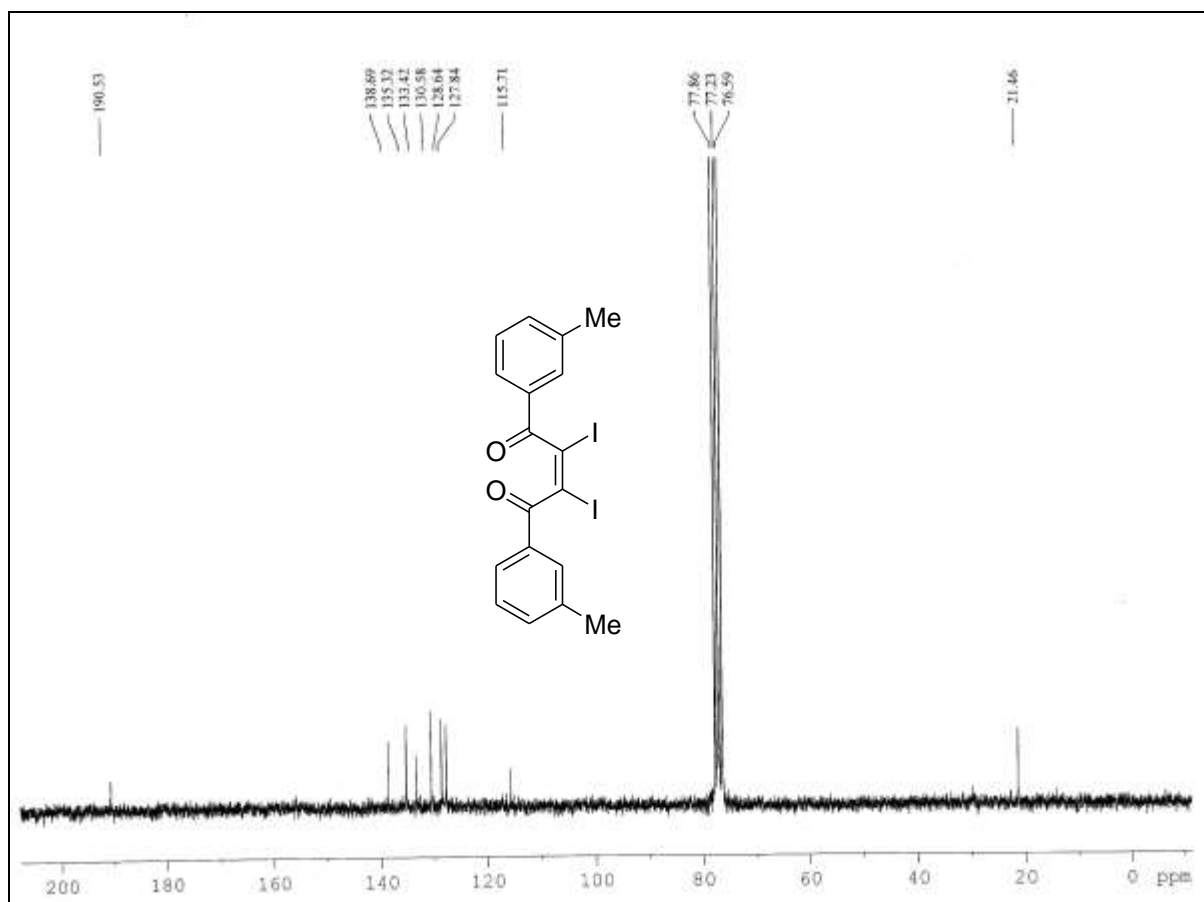
^{13}C NMR (CDCl_3 , 200 MHz) of compound **3f**



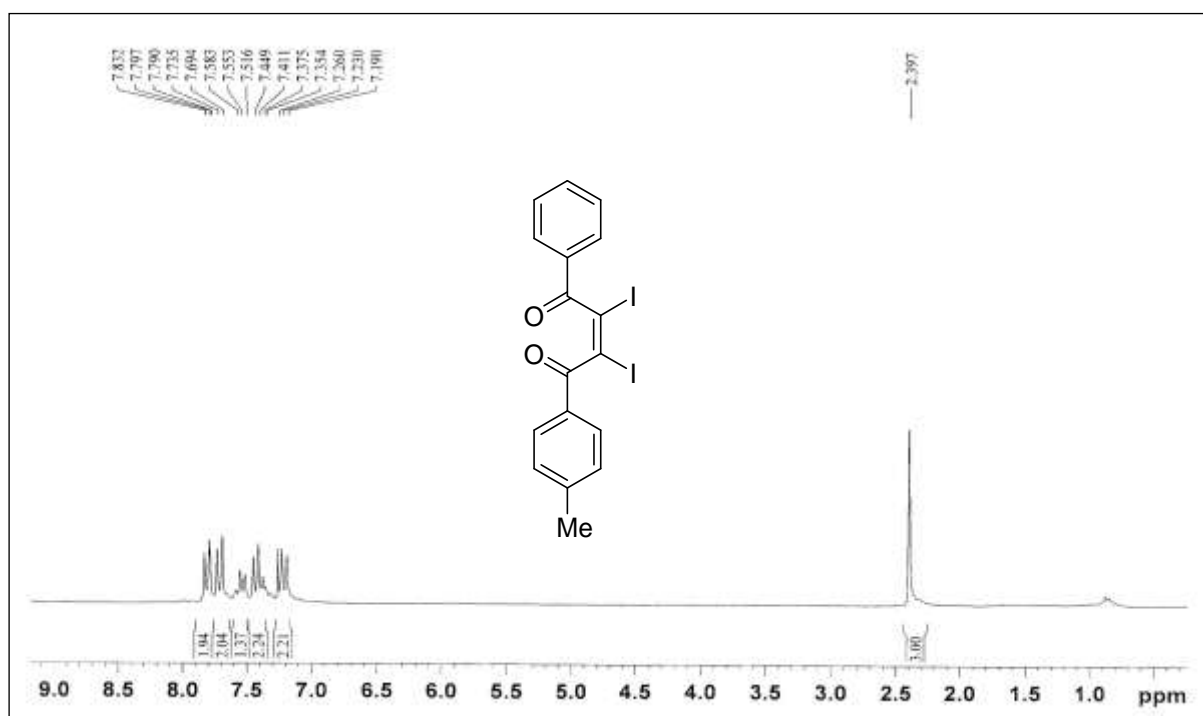
^1H NMR (CDCl_3 , 200 MHz) of compound **3g**



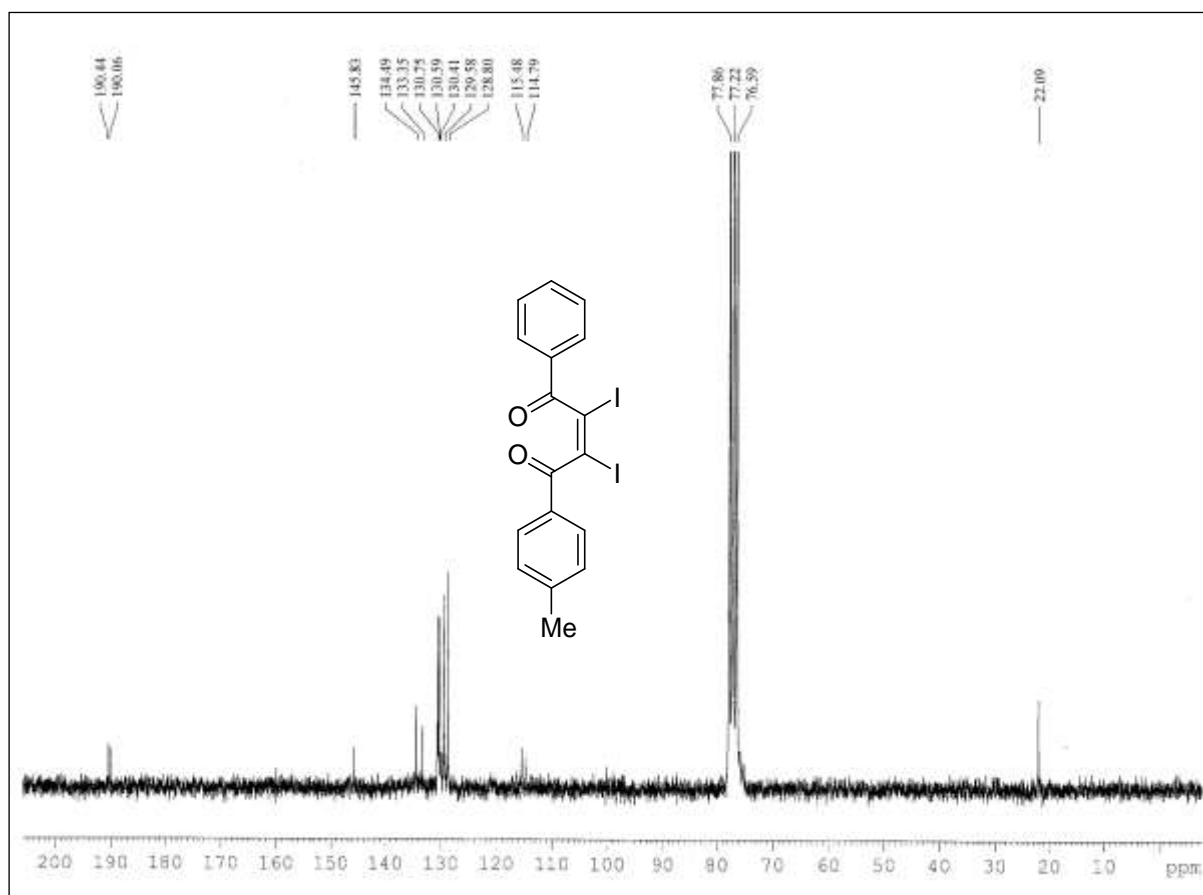
^{13}C NMR (CDCl_3 , 50 MHz) of compound **3g**



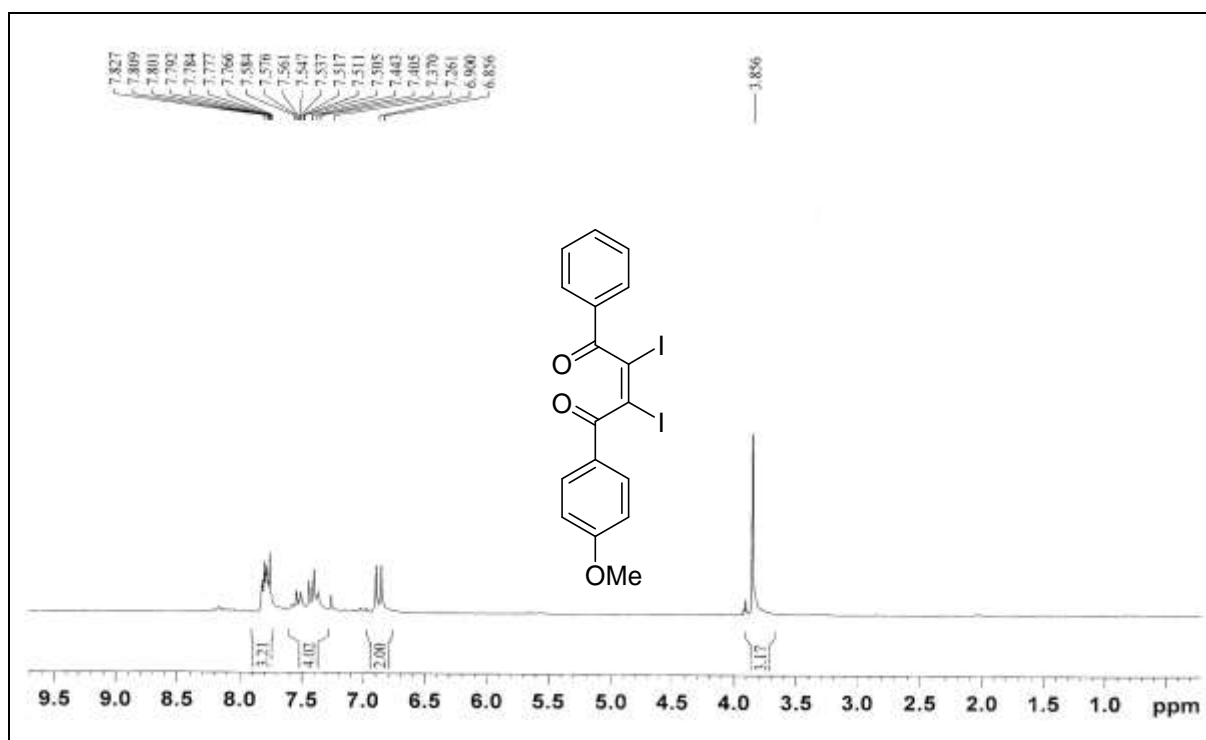
^1H NMR (CDCl_3 , 200 MHz) of compound **3h**



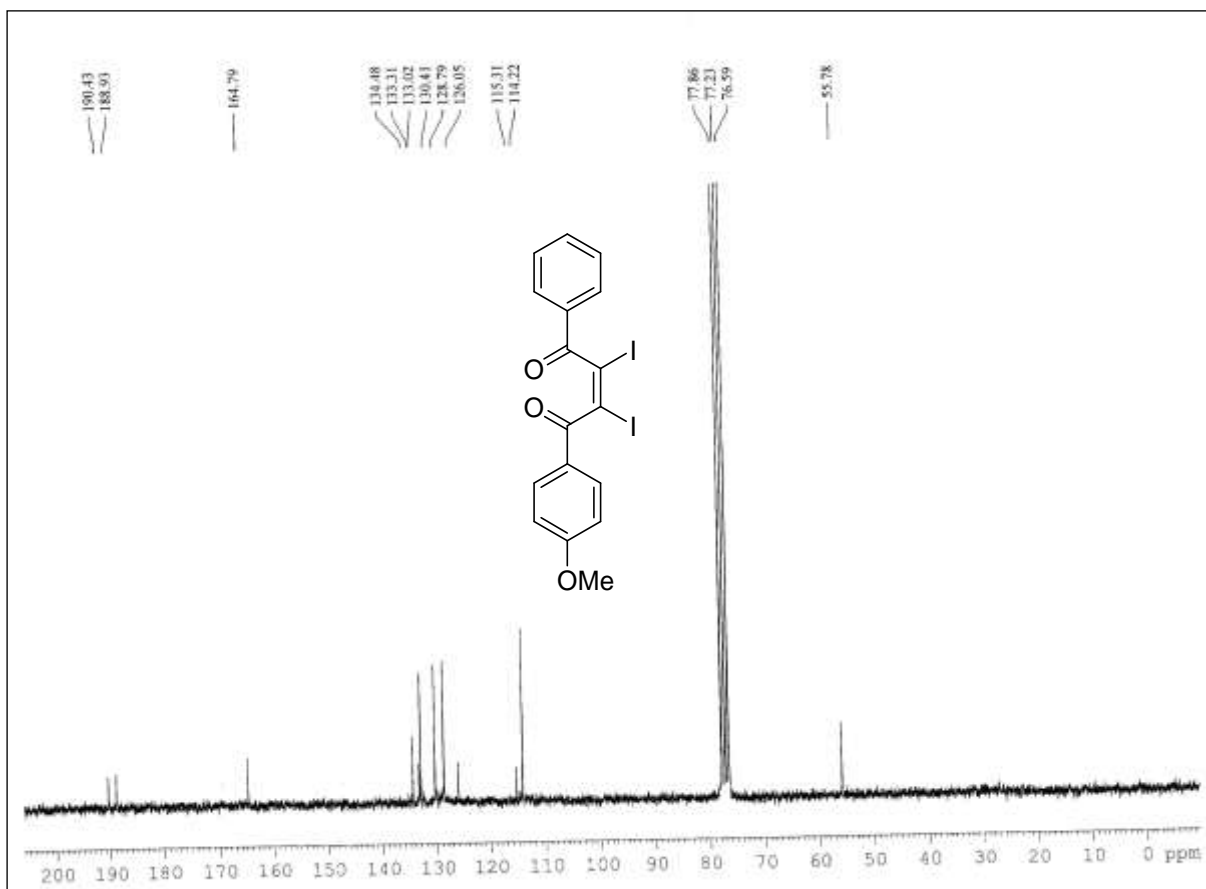
^{13}C NMR (CDCl_3 , 50 MHz) of compound **3h**



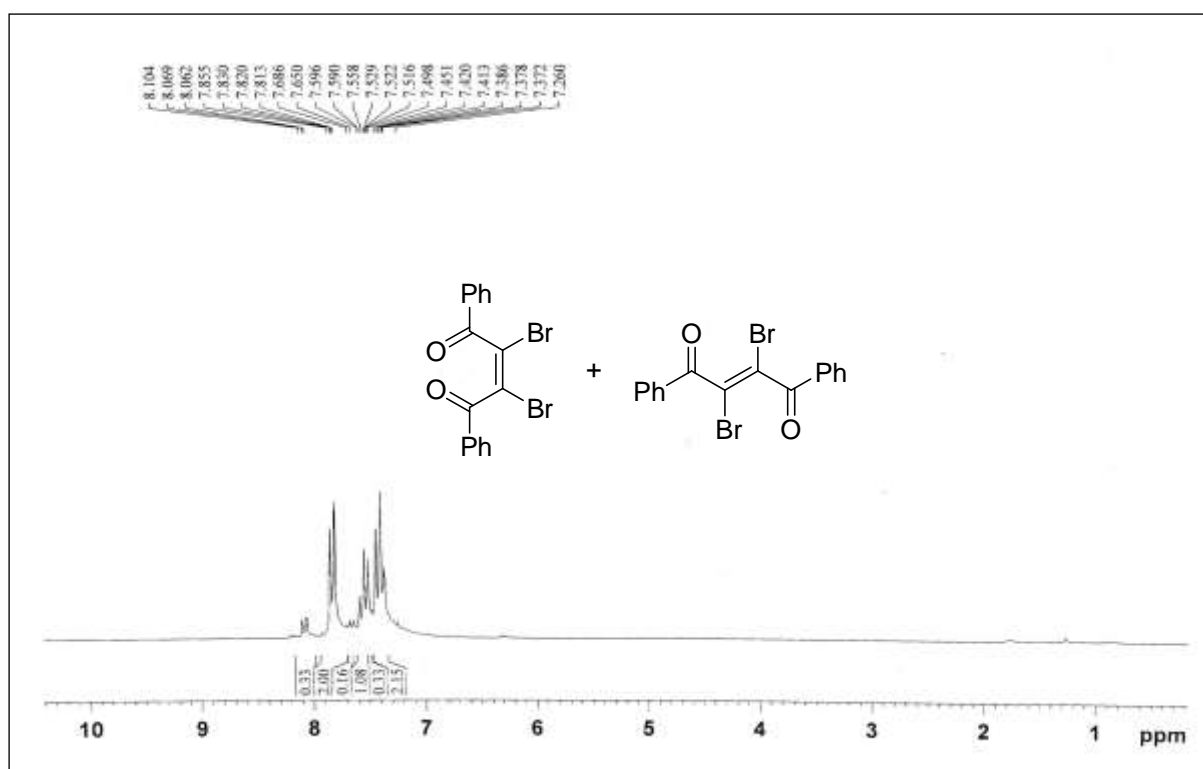
^1H NMR (CDCl_3 , 200 MHz) of compound **3i**



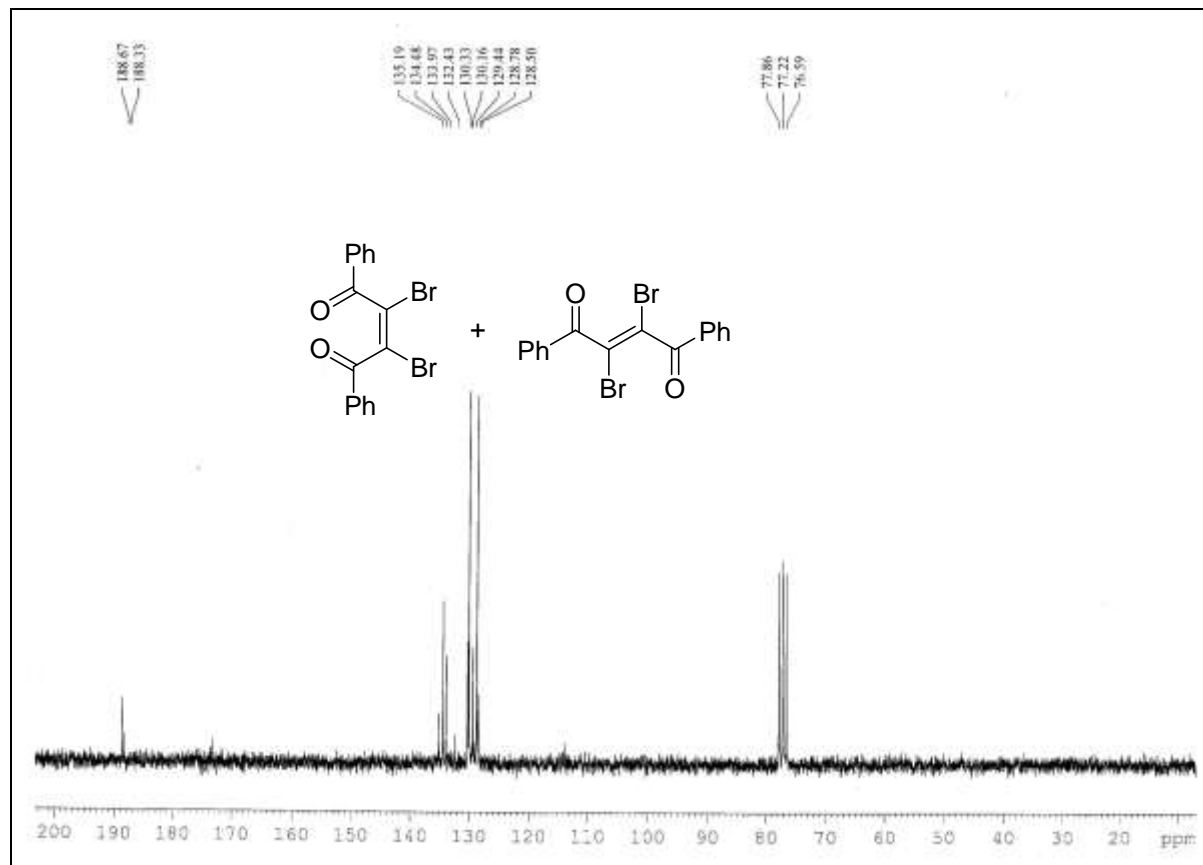
^{13}C NMR (CDCl_3 , 50 MHz) of compound **3i**



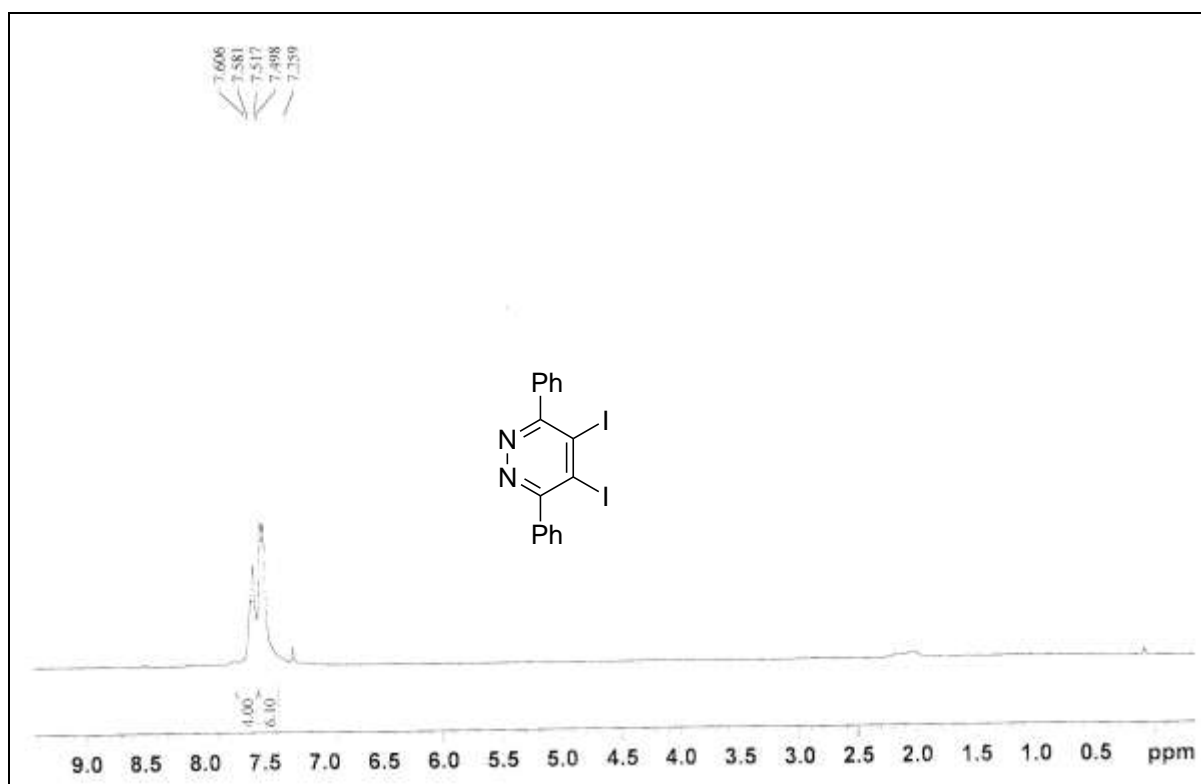
^1H NMR (CDCl_3 , 200 MHz) of compound **4a** and **4b**



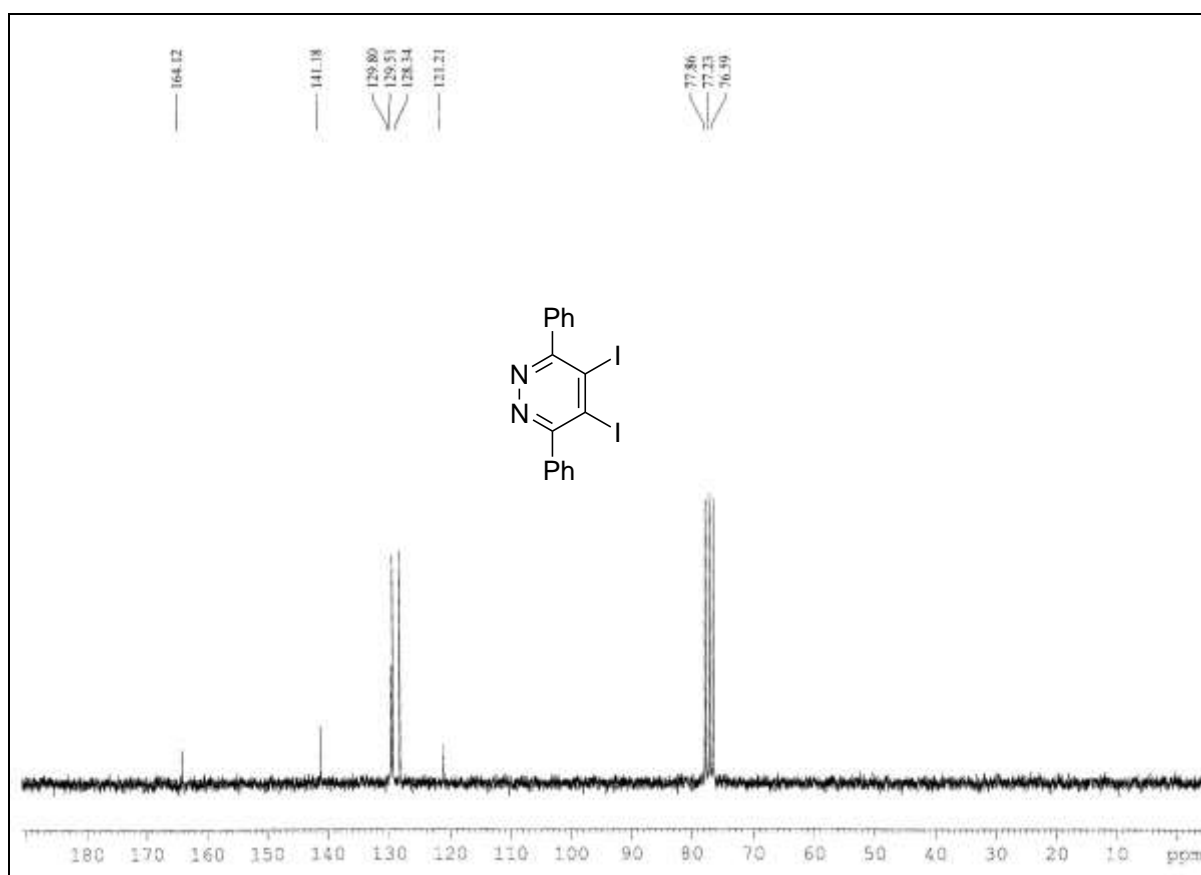
^{13}C NMR (CDCl_3 , 50 MHz) of compound **4a** and **4b**



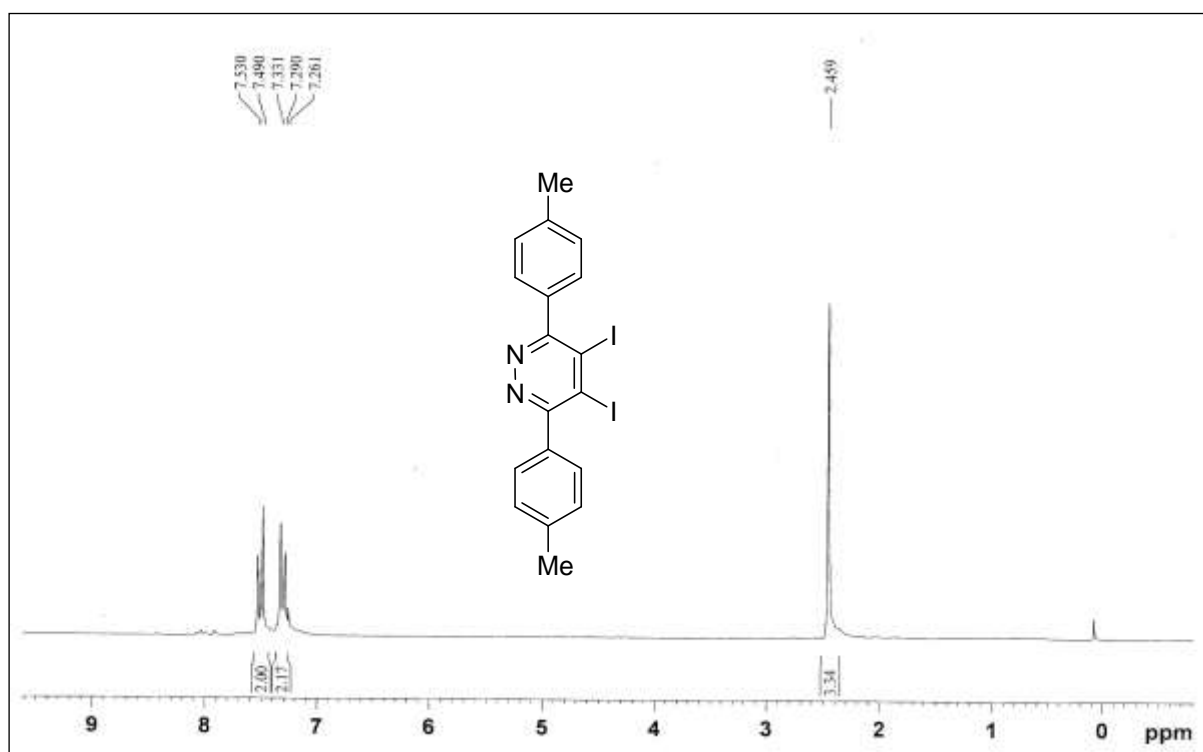
^1H NMR (CDCl_3 , 200 MHz) of compound **5a**



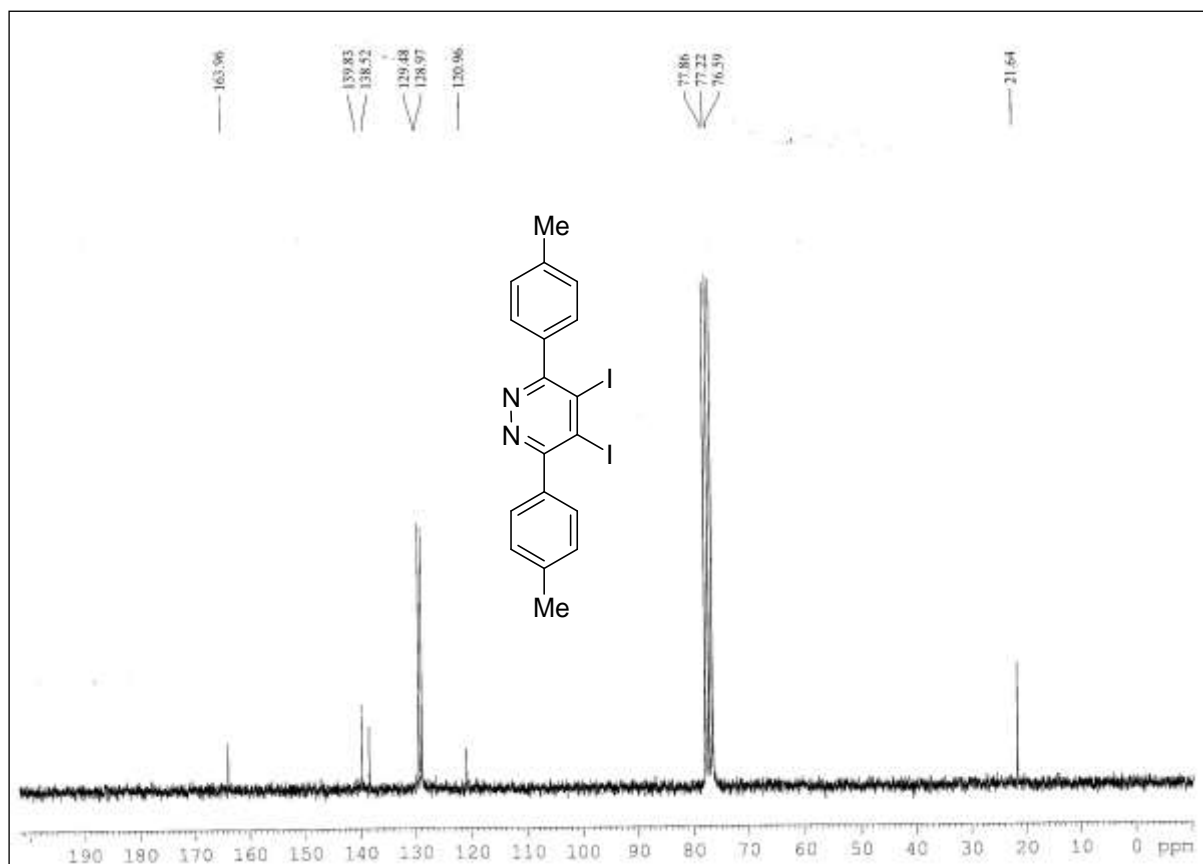
^{13}C NMR (CDCl_3 , 50 MHz) of compound **5a**



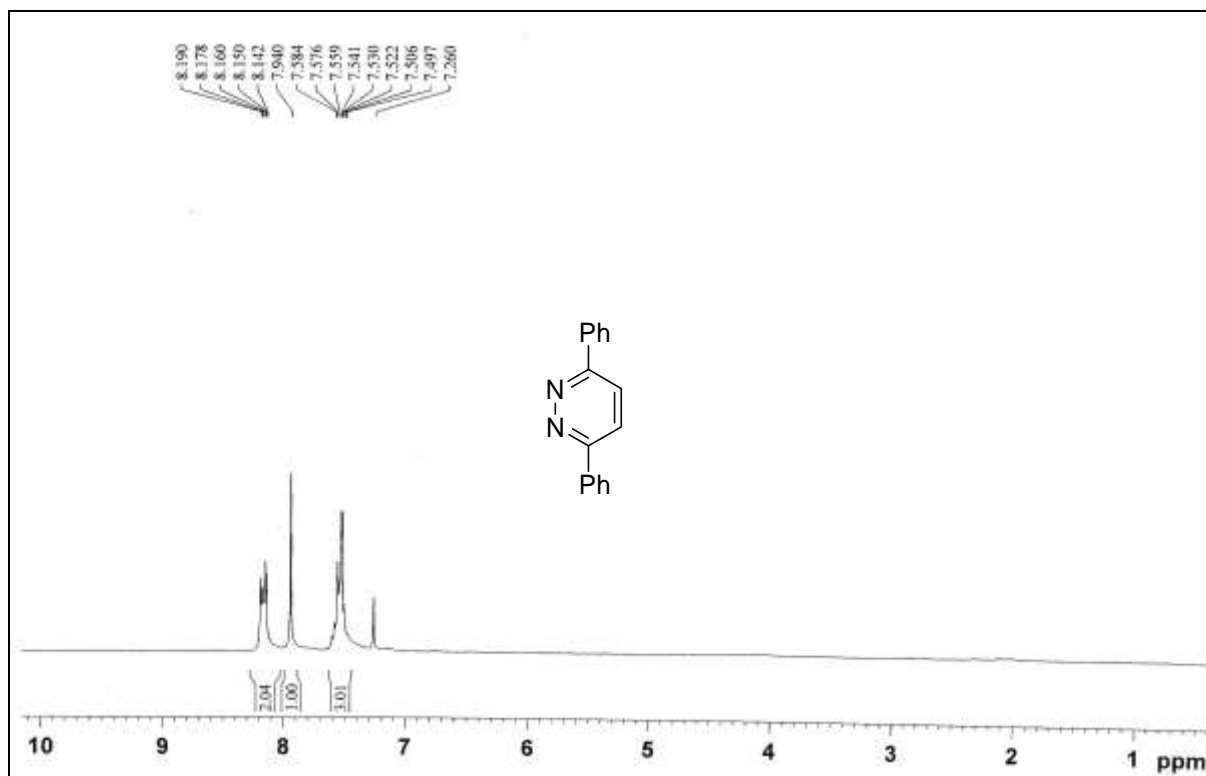
^1H NMR (CDCl_3 , 200 MHz) of compound **5b**



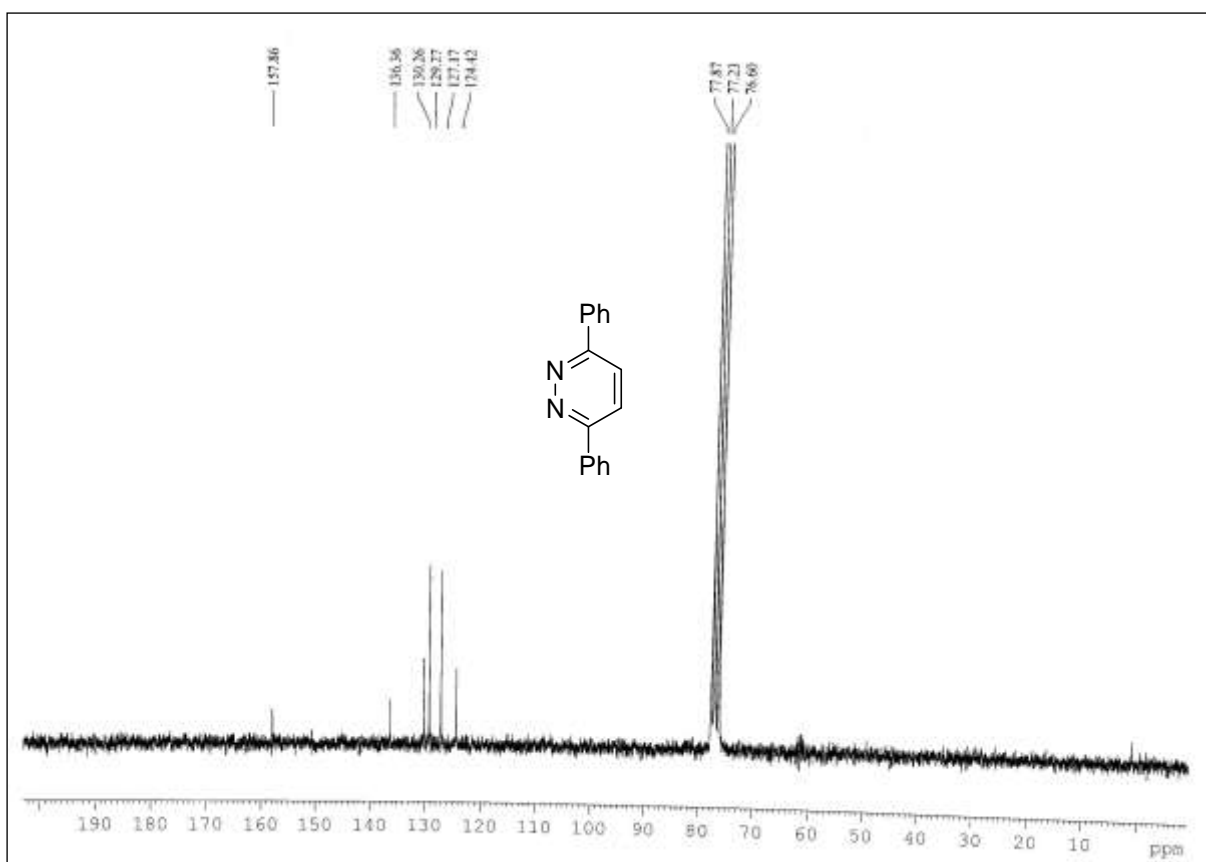
^{13}C NMR (CDCl_3 , 50 MHz) of compound **5b**



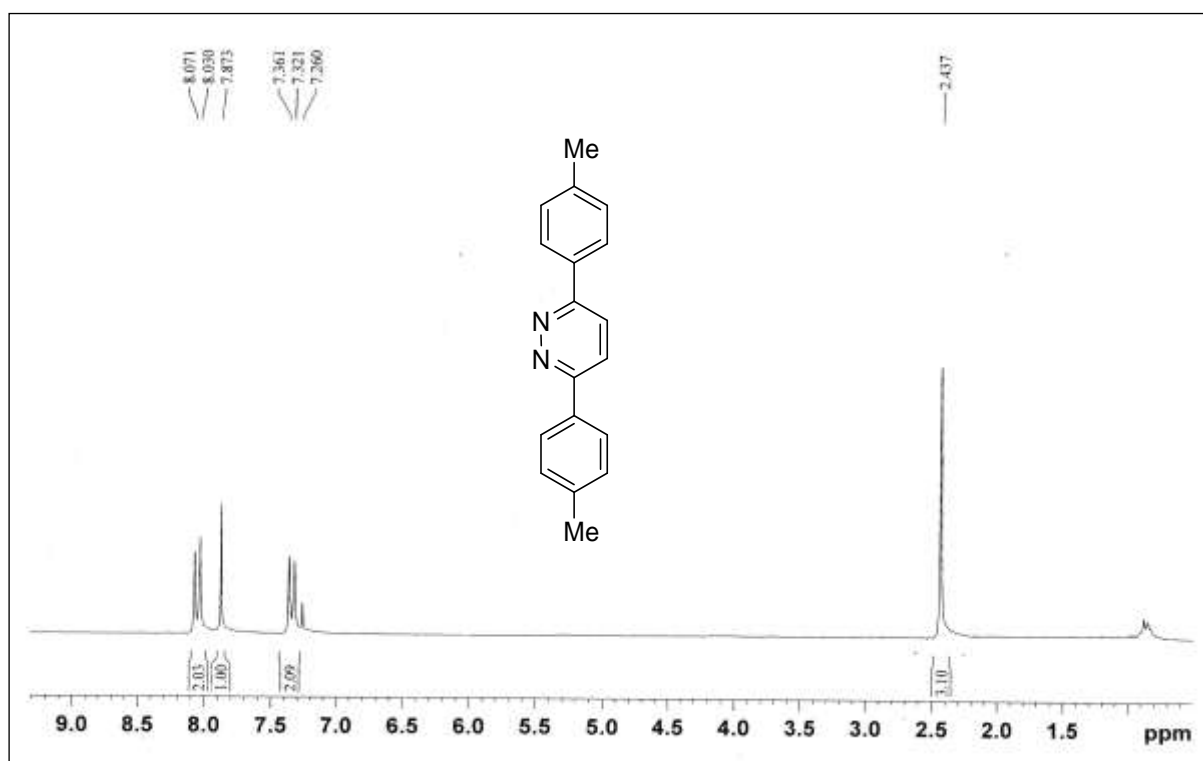
^1H NMR (CDCl_3 , 200 MHz) of compound **6a**



^{13}C NMR (CDCl_3 , 50 MHz) of compound **6a**



^1H NMR (CDCl_3 , 200 MHz) of compound **6b**



^{13}C NMR (CDCl_3 , 50 MHz) of compound **6b**

