Supporting Information

Tandem allylic oxidation-condensation/esterification catalyzed by silica gel: An expeditious approach towards antimalarial diaryldienones and enones from natural methoxylated phenylpropenes

Abhishek Sharma[a‡], Naina Sharma[a], Amit Shard[a], Rakesh Kumar[a], Dinesh Mohanakrishnan[b], Saima,[a] Arun K. Sinha[a]* and Dinkar Sahal[b]

[a]*Natural Plant Products Division, Institute of Himalayan Bioresource Technology, Council of Scientific and Industrial Research (C.S.I.R), Palampur (H.P.)-176061, India*
[b]*Malaria Research Laboratory, International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi 110067, India*
[‡]*Present address: Department of Chemistry, Katholieke Universiteit Leuven, Celestijnenlaan 200F, B-3001, Leuven, Belgium*

aksinha08@rediffmail.com

Table of Contents

Experimental Section:

Materials

β-asarone (*cis*-2,4,5-trimethoxyphenylpropene) and isosafrole (*trans*-3,4 dioxymethylenephenylpropene) were purified from their respective natural essential oils following our earlier reported procedure.[1] The solvents used for isolation/purification of compounds were obtained from commercial sources (Merck) and used without further purification. DDQ, PDC and thionyl chloride were reagent grade (Merck) and used as supplied. The solvents used for isolation/purification of compounds were obtained from commercial sources (Merck) and used without further purification. The chromatographic solvents are mentioned as volume: volume ratios. Column chromatography was performed using silica gel (Merck, 60-120 mesh size).

Apparatus:

^{1}H (300 MHz) and ^{13}C (75.4 MHz) NMR spectra were recorded on a Bruker Avance-300 spectrometer. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. The ^{13}C NMR spectra are proton decoupled. The melting points were determined on a digital Barnsted Electrothermal 9100 apparatus and are uncorrected. CEM Discover© focused microwave (2450 MHz, 300W) was used wherever mentioned. The temperature of reactions in microwave experiments was measured by an inbuilt infrared temperature probe that determined the temperature on the surface of reaction flask. The sensor is attached in a feedback loop with an on-board microprocessor to control the temperature rise rate. In the case of conventional heating in oil bath, the temperature of reaction mixture was monitored by an inner thermometer. HRMS-ESI spectra were determined using micromass Q-TOF ultima spectrometer and reported as m/z (relative intensity).

---

1 A. K. Sinha, R. Acharya and B. P. Joshi, *J. Nat. Prod.*, 2002, **65**, 764-765.

General procedure:

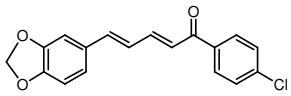
Representative procedure for one-pot two-step synthesis of diaryldienones from phenylpropenes via one-pot oxidation-condensation

Synthesis of (1-(4-bromophenyl)-5-(3,4-dioxymethylenephenyl)-penta-2,4-dien-1-one) (1b, Table 2):

To a stirred mixture of 3,4-dioxymethylene phenylpropene (1a, 0.1 g, 0.61 mmol), silica (0.2 g) and dioxane (6 mL), DDQ (0.32g, 1.41 mmol) was added and the reaction mixture irradiated under focused microwave system in parts (100W, 90°C) for 25 min. Subsequently, 4-bromoacetophenone (0.95 mmol), methanol (5 mL) and $SOCl_2$ (0.5 mL) were added to the above reaction mixture and further irradiated under focused microwave system (100W, 90°C) for 40 min. The reaction mixture was cooled, filtered and shaken well with methanol (5 mL) and vacuum evaporated. To the obtained solid, DCM (10 mL) was added and filtered the solution over alumina. The residue was purified by column chromatography on silica gel (60-120 mesh size) possessing a thin bed of alumina using hexane-ethylacetate (9.7:0.3) to give **1b** (0.113 g, 51% yield) as a yellow solid, m. p. 122-125°C, , IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1652, ^{1}H NMR δ (CD_3COCD_3, 300MHz), 7.98 (2H, d, *J*= 7.8 Hz), 7.82 (2H, d, *J*= 7.8 Hz), 7.62-7.55 (1H, m), 7.23-7.08 (5H, m), 6.91 (1H, d, *J*= 7.8 Hz), 6.07 (2H, s); ^{13}C NMR δ (75.4MHz, $CDC1_3$), 189.6, 149.3, 148.8, 146.0, 142.6, 137.5, 132.2, 131.0, 130.3, 128.0, 125.5, 124.4, 123.8, 109.0, 106.3 and 101.9. HRMS-ESI: m/z $[M+H]^+$ for $C_{18}H_{13}O_3Br$, calculated 357.0120; observed 357.0156.

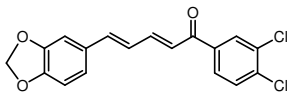
The above procedure was also followed for synthesis of various other diaryldienones (Table 2, entries 2-11).

1-(4-Chlorophenyl)-5-(3,4-dioxymethylenephenyl)-penta-2,4-dien-1-one (2b, Table 2)



Yellow solid, m. p. 139-142°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1652, ^{1}H NMR δ ($CDCl_3$, 300MHz), 7.93 (2H, d, *J*= 8.4 Hz), 7.63-7.55 (1H, m), 7.48 (2H, d, *J*=8.2 Hz), 7.03 (1H, s), 6.98 (1H, s), 6.97-6.80 (4H, m), 6.01 (2H, s); ^{13}C NMR δ (75.4MHz, $CDC1_3$), 189.4, 149.3, 148.7, 146.0, 142.6, 139.3, 137.0, 131.0, 130.1, 129.2, 125.5, 124.4, 123.7, 109.0, 106.3 and 101.9. HRMS-ESI: m/z $[M+H]^+$ for $C_{18}H_{13}O_3Cl$, calculated 313.0625; observed 313.0602.

1-(3,4-Dichlorophenyl)-5-(3,4-dioxymethylenephenyl)-penta-2,4-dien-1-one (3b, Table 2)



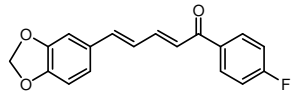
Yellow solid, m. p. 146-148°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1653, ^{1}H NMR δ (C_5D_5N[2], 300MHz), 8.29 (1H, s), 7.79 (1H, s), 7.59 (2H, s), 7.05-6.84 (6H, m), 6.02 (2H, s); ^{13}C NMR δ (75.4MHz, C_5D_5N), 189.7, 153.7, 152.1, 149.5, 148.9, 146.3, 142.9,

---

2. **3b** was found to display low solubility in majority of the common NMR solvents.

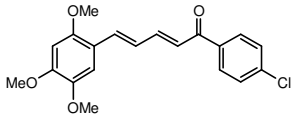
139.8, 137.7, 131.4, 130.6, 129.7, 125.9, 124.8, 124.0, 109.6, 106.8 and 102.4. HRMS-ESI: m/z $[M+H]^+$ for $C_{18}H_{12}O_3Cl_2$, calculated 347.0236; observed 347.0209.

1-(4-Fluorophenyl)-5-(3,4-dioxymethylenephenyl)-penta-2,4-dien-1-one (4b, Table 2)



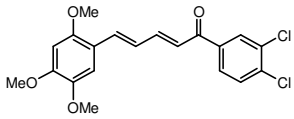
Light yellow solid, m. p. 176-178°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1657, ^{1}H NMR δ (CD_3COCD_3, 300MHz), 8.13 (2H, d, *J*= 8.8 Hz), 7.59-7.53 (1H, m), 7.34-7.26 (3H, m), 7.20 (1H, s), 7.13-7.08 (3H, m), 6.91 (1H, d, *J*= 7.9 Hz), 6.07 (2H, s); ^{13}C NMR δ (75.4MHz, $CDC1_3$), 189.1, 149.2, 148.8, 145.7, 142.4, 135.1, 131.3, 131.2, 131.0, 125.5, 124.5, 116.2, 115.9, 109.0, 106.3 and 101.8. HRMS-ESI: m/z $[M+H]^+$ for $C_{18}H_{13}O_3F$, calculated 297.0921; observed 297.0961.

1-(4-Chlorophenyl)-5-(2,4,5-trimethoxyphenyl)-penta-2,4-dien-1-one (5b, Table 2)



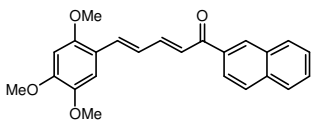
Yellow solid, m. p. 120-124°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1653, ^{1}H NMR δ ($CDCl_3$, 300MHz), 7.89 (2H, d, *J*= 6.0 Hz), 7.67 (1H, t, *J* = 8.0 Hz), 7.43 (2H, d, *J* = 6.0 Hz), 7.35 (1H, d, *J* =15.7 Hz), 7.02-6.94 (3H, m), 6.48 (1H, s), 3.91 (3H, s), 3.88 (3H, s), 3.86 (3H, s); ^{13}C NMR δ (75.4MHz, $CDC1_3$), 189.6, 153.6, 151.9, 147.3, 143.9, 139.1, 137.9, 137.3, 130.1, 129.2, 125.4, 123.6, 117.2, 110.5, 97.6, 56.9 and 56.5. HRMS-ESI: m/z $[M+H]^+$ for $C_{20}H_{19}O_4Cl$, calculated 359.1044; observed 359.1015.

1-(3,4-Dichlorophenyl)-5-(2,4,5-trimethoxyphenyl)-penta-2,4-dien-1-one (6b, Table 2)



Yellow solid, m. p. 190-194°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1656, ^{1}H NMR δ ($CDCl_3$, 300MHz), 8.05 (1H, s), 7.81 (1H, d, *J* =8.0 Hz), 7.71 (1H, q, *J* = 11.0 Hz), 7.58 (1H, d, *J* =9.7 Hz), 7.40 (1H, d, *J*=15.9 Hz), 7.04 (1H, s), 7.00-6.91 (2H, m), 6.50 (1H, s), 3.94 (3H, s), 3.91 (6H, s); ^{13}C NMR δ (75.4MHz, $CDC1_3$), 188.3, 153.7, 152.1, 147.9, 143.9, 138.6, 138.5, 137.1, 133.5, 131.0, 130.7, 127.7, 125.2, 122.9, 117.1, 110.3, 97.5, 56.9 and 56.8. HRMS-ESI: m/z $[M+H]^+$ for $C_{20}H_{18}O_4Cl_2$, calculated 393.0654; observed 393.0619.

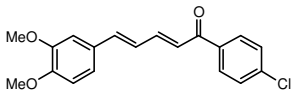
1-Naphthyl-5-(2,4,5-trimethoxyphenyl)-penta-2,4-dien-1-one (7b, Table 2)



Red solid, m. p. 142-144°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1647, ^{1}H NMR δ ($CDCl_3$, 300MHz), 8.50 (1H, s), 8.09 (1H, d, *J*=8.0 Hz), 7.98-7.87 (3H, m), 7.67 (1H, t, *J*=12.2 Hz), 7.59 (2H, s), 7.35 (1H, d, *J*=15.5 Hz), 7.25 (1H, d, *J*=15.5 Hz), 7.09-7.03 (2H, m),

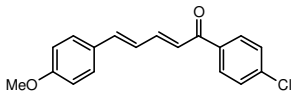
6.52 (1H, s), 3.93 (6H, s), 3.88 (3H, s); ^{13}C NMR δ (75.4MHz, CDC1$_3$), 190.7, 153.5, 151.8, 146.7, 143.9, 137.4, 136.3, 135.7, 133.0, 129.9, 128.7, 128.5, 128.2, 127.0, 125.6, 124.9, 124.3, 117.5, 110.5, 97.7, 56.9 and 56.5. HRMS-ESI: m/z $[M+H]^+$ for $C_{24}H_{22}O_4$, calculated 375.1590; observed 375.1558.

1-(4-Chlorophenyl)-5-(3,4-dimethoxyphenyl)-penta-2,4-dien-1-one (8b, Table 2)



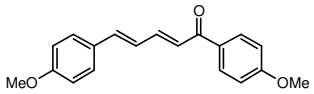
Yellow solid, m. p. 152-154°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1653, ^{1}H NMR δ ($CDCl_3$, 300MHz), 7.93 (2H, d, *J*=8.4 Hz), 7.65-7.57 (1H, q, *J* =9.8 Hz), 7.47 (2H, d, *J*=8.4 Hz), 7.05-6.82 (6H, m), 3.94 (6H, s); ^{13}C NMR δ (75.4MHz, CDC1$_3$), 189.2, 150.9, 149.7, 146.1, 142.8, 139.3, 137.1, 130.1, 129.5, 129.2, 125.3, 124.1, 121.9, 111.6, 109.7 and 56.4. HRMS-ESI: m/z $[M+H]^+$ for $C_{19}H_{17}O_3Cl$, calculated 329.0719; observed 329.0762.

1-(4-Chlorophenyl)-5-(4-methoxyphenyl)-penta-2,4-dien-1-one[3] (9b, Table 2)



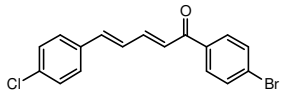
Yellow solid, m. p. 139-142°C, ^{1}H NMR δ ($CDCl_3$, 300MHz), 7.93 (2H, d, *J* =9.1 Hz), 7.66-7.57 (1H, q, *J* =9.8 Hz), 7.47 (4H, d, *J*=16.2 Hz), 7.03-6.85 (5H, m), 3.94 (3H, s); ^{13}C NMR δ (75.4MHz, CDC1$_3$), 189.5, 161.1, 146.3, 142.7, 139.3, 137.1, 130.1, 129.3, 129.2, 125.1, 124.0, 114.8, 55.7. HRMS-ESI: m/z $[M+H]^+$ for $C_{18}H_{15}O_2Cl$, calculated 299.0635; observed 299.0611.

1, 5-Di (4-methoxyphenyl)-penta-2,4-dien-1-one[4] (10b, Table 2)



Yellow solid, m. p. 145-147°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1652, ^{1}H NMR δ (1:9, $CDCl_3$: CD_3COCD_3, 300MHz), 8.04 (2H, d, *J*=8.6 Hz), 7.52 (3H, d, *J*=8.4 Hz), 7.25 (1H, d, *J*=14.7 Hz), 7.03-7.00 (4H, m), 6.94 (2H, d, *J*=8.6 Hz), 3.87 (3H, s), 3.81 (3H, s); ^{13}C NMR δ (75.4MHz, 1:9, $CDCl_3$: CD_3COCD_3), 189.6, 164.5, 161.8, 145.2, 142.1, 132.4, 131.5, 130.2, 129.9, 126.2, 125.2, 115.4, 114.9, 56.2 and 56.0.

1-(4-Chlorophenyl)-5-(4-bromophenyl)-penta-2,4-dien-1-one[5] (11b, Table 2)



---

3. F. Straus and H. Blankenhorn, *Justus Liebigs Annalender Chemie*, 1918, **415**, 232-256.
4.L. M. R. Valdez, A. M. Villafañe and D. G. Mitnik, *Journal of Molecular Structure*: *Theochem.*, 2004, **682**, 83-88.
5. Y. Cao, A. H. Yuan, X. P. Shen, W. J. Chen and C. Q. Liu, *Chinese Chemical Letters,* 1993, **4**, 719-720.

Yellow solid, m. p. 165-167°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1653, ^{1}H NMR δ [{(1:1) $CDCl_3$: CD_3OD}, 300MHz], 7.87 (2H, d, *J* = 8.2 Hz), 7.66 (2H, d, *J* = 8.03), 7.59-7.56 (1H, m), 7.46 (2H, d, *J* = 8.3 Hz), 7.37 (2H, d, *J* = 8.3 Hz), 7.09 (1H, d, *J* = 14.8 Hz), 7.00-6.98 (2H, m); ^{13}C NMR δ (75.4MHz, $CDC1_3$); 189.6, 145.3, 141.2, 137.2, 135.5, 134.9, 132.3, 130.3, 129.5, 128.9, 128.3, 127.7 and 125.5.

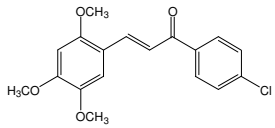
Representative procedure for synthesis of chalcones from phenylpropenes via one-pot oxidative cleavage-condensation

Synthesis of 1-(4-chlorophenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (12b) via one-pot oxidative cleavage-condensation of *β*-asarone 1a with (i) 4-chloroacetophenone or (ii) (1-(4-chlorophenyl) ethanol under MW (12b, Scheme 3)

(i) To a stirred mixture of 2,4,5-trimethoxy phenylpropene (5a, 0.1 g, 0.48 mmol), acetic acid (3 ml) and dioxane (6 ml), PDC (0.36 g, 0.95 mmol) was added and the reaction mixture irradiated under focused microwave (MW) system in parts (200W, 150°C) for 20 min. Subsequently, 4-chloroacetophenone (0.12 g, 0.86 mmol), methanol (5 ml) and $SOCl_2$ (0.5 ml) were added to the above reaction mixture and further irradiated under MW (100W, 90°C) for 40 min. The reaction mixture was cooled, filtered and shaken well with methanol (5 ml) and vacuum evaporated. The residue was purified by column chromatography on silica gel (60-120 mesh size) using hexane-ethylacetate (9.7:0.3) to give **12b** (0.055 g, 35% yield) as a yellow solid, m. p. 141-142°C.

(ii) In the second case (i.e use of 1-(4-chlorophenyl) ethanol in place of 1-chloroacetophenone), the procedure was same as above for the first step. However, after the initial oxidative cleavage of 5a, 1-(4-chlorophenyl)ethanol (0.15 g, 0.95 mmol), PDC (0.18 g, 0.47 mmol), acetic acid (3 mL), and dioxane (3 mL) were added to the same pot and the reaction mixture irradiated under MW in parts (200W, 150°C) for 20 min. Subsequently, methanol (5 mL) and $SOCl_2$ (0.5 mL) were added to the above reaction mixture and further irradiated under focused microwave system (100W, 90°C) for 40 min. The reaction mixture was cooled, filtered and shaken well with methanol (5 mL) and vacuum evaporated. The residue was purified by column chromatography on silica gel (60-120 mesh size) using hexane-ethylacetate (9.7:0.3) to give **12b** (0.047 g, 30% yield) whose spectral data (^{1}H and ^{13}C NMR) matched well with that obtained above.

1-(4-chlorophenyl)-3-(2, 4, 5-trimethoxyphenyl) prop-2-en-1-one[6](12b, Scheme 3)



Yellow solid , m. p. 141-142 °C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1653, ^{1}H NMR (300 MHz, CDCl3); δ 8.12 (1H, d, *J* = 15.9 Hz), 7.97

---

6. R. Kumar, D. Mohankrishnan, A. Sharma, N. Kaushik, K. Kalia, A. K. Sinha and D. Sahal, *Eur. J. Med. Chem.*, 2010, **45**, 5292-5301.

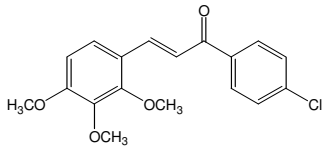
(2H, d, *J* = 8.6 Hz), 7.49 (2H, d, *J* = 8.4 Hz), 7.45 (1H, d, *J* = 16.2 Hz), 7.13 (1H, s), 6.54 (1H, s,) 3.96 (3H, s), 3.92 (6H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$); 190.18, 155.2, 155.1, 143.7, 141.0, 139.0, 137.5, 130.2, 129.1, 120.1, 115.7, 112.0, 97.2, 57.0, 56.7 and 56.4.

Representative procedure for synthesis of 1-(4-chlorophenyl)-3-(2,3, 4-trimethoxyphenyl) prop-2-en-1-one (13b, Scheme 4) via one-pot oxidation of (1-(2, 3, 4-trimethoxyphenyl) ethanol and condensation with 4-chloroacetophenone

Synthesis of 1-(4-chlorophenyl)-3-(2, 3, 4-trimethoxyphenyl) prop-2-en-1-one (13b, Scheme 4)

To a stirred mixture of (1-(2,3,4-trimethoxyphenyl)methanol) (0.1 g, 0.47 mmol), silica (0.2 g) and dioxane (6 ml), DDQ (0.139g, 0.61 mmol) was added and further the reaction mixture was irradiated under focused microwave system in parts (100W, 90^{o}C) for 25 min. Subsequently, 4-chloroacetophenone (0.087 g, 0.56 mmol), methanol (5 ml) and $SOCl_2$ (0.5 ml) were added to the above reaction mixture and further irradiated under MW (100W, 90^{o}C) for 40 min. The reaction mixture was cooled, filtered and shaken well with methanol (5 ml) and vacuum evaporated. The residue was purified by column chromatography on silica gel (60-120 mesh size) using hexane-ethylacetate (9.7:0.3) to give **13b** (0.062, 41%) as yellow solid.

1-(4-chlorophenyl)-3-(2, 3, 4-trimethoxyphenyl)prop-2-en-1-one[7] (13b, Scheme 4)



Yellow solid , m. p. 86-89°C, ^{1}H NMR (300 MHz, CD_3COCD_3); δ 8.13 (2H, d, *J* = 8.5 Hz), 8.07 (1H, d, *J* = 15.7 Hz), 7.76 (1H, d, *J* = 15.7 Hz), 7.65 (1H, d, *J* = 8.8 Hz), 7.58 (2H, d, *J* = 8.5 Hz), 6.88 (1H, d, *J* = 8.8 Hz), 3.94 (3H, s), 3.91 (3H, s), 3.84 (3H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$); δ 189.9, 156.5, 154.3, 142.9, 141.1, 139.3, 137.4, 130.3, 129.3, 124.1, 122.3, 121.2, 108.2, 61.8, 61.3 and 56.5. HRMS-ESI: m/z $[M+H]^+$ for $C_{18}H_{17}O_4Cl$, calculated 333.0888; observed 333.0886.

Representative procedure for synthesis of chalcones from corresponding alcohols via one pot oxidation-condensation

Synthesis of 1-(4-Methoxyphenyl)-3-(1-naphthyl) prop-2-en-1-one[8] (14b, Scheme 5)

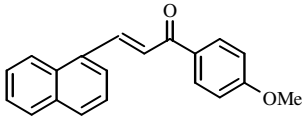
To a stirred mixture of (1-(napthyl) methanol) (0.1g, 0.63 mmol), 1-(4-methoxyphenyl) ethanol (0.14 g, 0.94 mmol), silica (0.2 g) and dioxane (6 ml), DDQ (0.46 g, 2.02 mmol), was added and the reaction mixture irradiated under focused microwave system in parts (100W, 90^{o}C) for 25 min. Subsequently, methanol (5 ml) and $SOCl_2$ (0.5 ml) were added to the reaction mixture and further irradiated under focused microwave system (100W, 90^{o}C) for 40 min. The reaction mixture was cooled, filtered and shaken well with methanol (5 ml) and vacuum evaporated. To the obtained solid, DCM (10 ml) was added and

---

7. Y. Han, M. Riwanto, M. L. Go and P. L. R. Ee, *Eur. J. Pharm. Sci*., 2008, **35** , 30–41.
8. J. A. Geyer, S. M. Keenan, C. L. Woodard, P. A. Thompson, L. Gerena, D. A. Nichols, C. E. Gutteridge and N. C. Waters, *Bioorg. & Med.l Chem.Lett.*, 2009, **19**, 1982–1985.

filtered the solution over alumina. The residue was purified by column chromatography on silica gel (60-120 mesh size) possessing a thin bed of alumina using hexane-ethylacetate (9.7:0.3) to give **14b** (0.07 g, 30% yield) as a light yellow solid.

1-(4-Methoxyphenyl)-3-(1-naphthyl)prop-2-en-1-one[8] (14b, Scheme -5)



Yellow solid, m. p. 127-133°C, IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1656, ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.72 (1H, d, *J* = 15.3 Hz), 8.31 (1H, d, *J* = 8.4 Hz), 8.14 (2H, d, *J* = 7.6 Hz), 7.95-7.90 (3H, m), 7.70 (1H, d, *J* = 15.3 Hz), 7.65-7.50 (3H, m), 7.05 (2H, d, *J* = 8.4 Hz), 3.92 (3H, s); ^{13}CNMR δ (75.4 MHz, $CDCl_3$); 188.9, 163.9, 140.9, 133.7, 132.6, 131.8, 131.0, 130.9, 130.6, 128.7, 127.3, 126.7, 125.9, 125.4, 124.9, 123.9, 114.3 and 55.9.

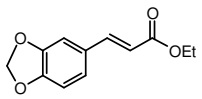
Representative procedure for one-pot synthesis of cinnamic esters from phenylpropenes via one-pot oxidation-esterification

Synthesis of Methyl 3-(3, 4-dioxymethylene phenyl) propenoate (15b, Table 3)

To a stirred mixture of 3, 4-dioxymethylenephenylpropene (1a, 0.1 g, 0.61 mmol), silica (0.2 g) and dioxane (6 ml), DDQ (0.27g, 1.18 mmol) was added and the reaction mixture irradiated under focused microwave system in parts (100W, 90°C) for 25 min. To the above reaction mixture methanol (5 ml) and DDQ (0.25 g, 1.10 mmol) were added and further irradiated under focused microwave system (110W, 100°C) for 30 min. The reaction mixture was cooled, filtered and vacuum evaporated. To the obtained solid, DCM (10 ml) was added and the solution filtered over alumina. The residue was purified by column chromatography on silica gel (60-120 mesh size) possessing a thin bed of alumina using hexane-ethylacetate (9.7:0.3) to give methyl 3-(3,4-dioxymethylenephenyl)propenoate[9] (15b, 0.081g, 64% yield) as a white solid, m. p. 67-68°C, ^{1}H NMR δ ($CDCl_3$, 300MHz), 7.59 (1H, d, *J*=15.9 Hz), 6.99 (1H, s), 6.95 (1H, d, *J* = 8.0 Hz), 6.78 (1H, d, *J* = 8.0 Hz), 6.26 (1H, d, *J*=15.9 Hz), 5.97 (2H, s), 3.77 (3H, s); ^{13}C NMR δ (75.4MHz, $CDC1_3$), 167.9, 150.0, 148.7, 144.9, 129.2, 124.8, 116.1, 108.9, 106.9, 101.9 and 51.9. HRMS-ESI: m/z $[M+H]^+$ for $C_{11}H_{10}O_4$, calculated 207.0651; observed 207.0673.

The above procedure was also followed for synthesis of various other cinnamic esters (16b-21b, Table 3).

Ethyl-3-(3,4-dioxymethylenephenyl)propenoate[10] (16b, Table 3)



Light yellow solid, m. p. 57-60°C, ^{1}H NMR δ ($CDCl_3$, 300MHz), 7.55 (1H, d, *J*=15.9 Hz), 6.96 (1H, s), 6.94 (1H, d, *J* =8.0

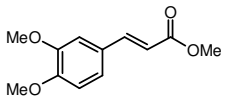
---

9. D. K. Barma, A. Kundu, A. Bandyopadhyay, A. Kundu, B. Sangras, A. Briot, C. Mioskowski and J. R. Falck, *Tetrahedron Letters* , 2004, **45**, 5917–5920.

10. P. S. W. Leung, Y. Teng and P. H. Toy, *Org. Lett.*, 2010, **12**, 4996-4999.

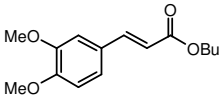
Hz), 6.74 (1H, d, *J*=8.0 Hz), 6.22 (1H, d, *J*=15.9 Hz), 5.93 (2H, s), 4.3 (2H, q, *J* = 7.1 Hz), 1.3 (3H, t, *J* =7.1 Hz),; ^{13}C NMR δ (75.4MHz, CDC1$_3$), 167.9, 149.9, 148.7, 144.6, 129.3, 124.7, 116.6, 108.9, 106.9, 101.9, 60.7 and 14.7. HRMS-ESI: m/z $[M+H]^+$ for $C_{12}H_{12}O_4$, calculated 221.0808; observed 221.0836.

Methyl-3-(3,4-dimethoxyphenyl)propenoate[11] **(17b, Table 3)**



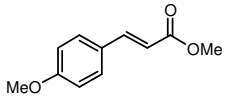
Light yellow solid, m. p. 56-58°C, ^{1}H NMR δ ($CDCl_3$, 300MHz), 7.55 (1H, d, *J*=15.9 Hz), 6.99 (2H, t, *J*=6.8 Hz), 6.75 (1H, d, *J* =8.2 Hz), 6.24 (1H, d, *J*=15.9 Hz), 3.79 (6H, s), 3.69 (3H, s); ^{13}C NMR δ (75.4MHz, CDC1$_3$), 168.0, 151.5, 149.6, 145.2, 127.8, 122.9, 119.7, 115.9, 111.4, 110.1, 56.2 and 51.8. HRMS-ESI: m/z $[M+H]^+$ for $C_{12}H_{14}O_4$, calculated 223.0964; observed 223.0987.

Butyl-3-(3,4-dimethoxyphenyl)propenoate[12] **(18b, Table 3)**



Colourless liquid; IR (KBr, cm^{-1}) $\upsilon_{c=o}$ = 1706, ^{1}H NMR ($CDCl_3$, 300 MHz) 7.64 (1H, d, *J* =16.2 Hz), 7.11(1H, d, *J* =6.1 Hz), 7.06 (1H, s), 6.87 (1H, d, *J* =6.1 Hz), 6.34 (1H, d, *J*=16.2 Hz), 4.22 (2H, t, *J* =7.3Hz), 3.90 (6H, s), 1.71-1.63 (2H, m), 1.47-1.40 (2H, m), 0.98 (3H, t, *J* =7.7 Hz); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz) 171.6, 151.0, 149.1, 144.3, 127.4, 122.5, 115.8, 110.9, 109.5, 64.6, 56.3, 56.2, 31.2, 19.6 and 14.1.

Methyl-3-(4-methoxyphenyl)propenoate[13] **(19b, Table 3)**

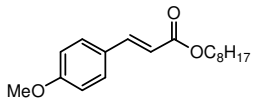


White solid, m. p. 76-80°C, ^{1}H NMR δ ($CDCl_3$, 300MHz), 7.63 (1H, d, *J*=16.8 Hz), 7.41 (2H, d, *J* =9.9 Hz), 6.85 (2H, d, *J* =9.9 Hz), 6.28 (1H, d, *J* =16.8), 3.75 (3H, s), 3.74 (3H, s); ^{13}C NMR δ (75.4MHz, CDC1$_3$), 168.1, 161.8, 144.9, 130.1, 127.5, 115.7, 114.7, 55.7 and 51.9. HRMS-ESI: m/z $[M+H]^+$ for $C_{11}H_{12}O_3$, calculated 193.0859; observed 193.0841.

---

11. S. A. Snyder and F. Kontes, *J. Am. Chem. Soc*., 2009, **131**, 1745–1752.
12. A. K. Chatterjee, T. L. Choi, D. P. Sanders, and R. H. Grubbs, *J. Am. Chem. Soc.*, 2003, **125**, 11360-11370.
13. C. Diebold, S. Schweizer, J. M. Becht and C. L. Drian, *Org. Biomol. Chem*., 2010, **8**, 4834–4836.

Octyl-3-(4-methoxyphenyl)propenoate[14] **(20b, Table 3)**



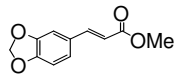
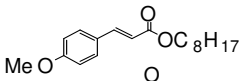
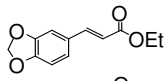
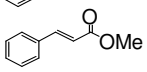
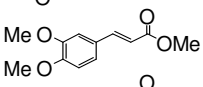
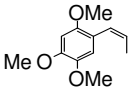
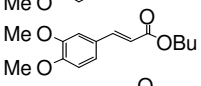
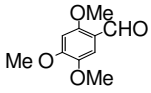
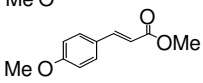
Light yellow viscous liquid; IR (KBr, cm^{-1})$\upsilon_{c=o}$ = 1709, ^{1}H NMR δ ($CDCl_3$, 300MHz), 7.67 (1H, d, *J* =15.9 Hz), 7.50 (2H, d, *J* =8.7 Hz), 6.92 (2H, d, *J* =8.7 Hz), 6.35 (1H, d, *J* =15.9 Hz), 4.13-4.09 (2H, m), 3.84 (3H, s), 1.41-1.26 (8H, m), 0.96-0.87 (7H, m); ^{13}C NMR δ (75.4MHz, $CDC1_3$); 171.7, 167.9, 161.7, 144.5, 130.1, 127.6, 116.3, 114.7, 67.2, 55.7, 39.3, 31.3, 29.5, 24.3, 14.4 and 11.4.

Methyl 3-(3, 4-dioxymethylene phenyl) propenoate (21b, Table 3)

White solid, yield 66%, spectra matches well with **15b**.

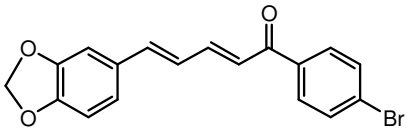
14. F. Xu, R. D. Tillyer, D. M. Tschaen, E. J. J. Grabowski and P. J. Reider, *Tet. Asymm.,* 1998, **9**, 1651-1655.

Table S1: Antimalarial activity of enones (15b-21b), methoxylated phenylpropene (22b) and asaronaldehyde (23b) against *P. falciparum* (3D7 strain)

Compound No.	Compound	IC_{50} µM	Compound No.	Compound	IC_{50} µM
15b		-	**20b**		>100.0
16b		>100.0	**22b**		-
17b		>100.0	**23b**		>100.0
18b		-	**24b**		>100.0
19b		-	**Chloroquine**		40.0 nm

Compound 21b and 15b are same synthesized from α/β and γ–isomer of phenylpropene respectively , Table 3)

Table 2, 1b/Entry-1, ^{1}H NMR (in CD_3COCD_3)



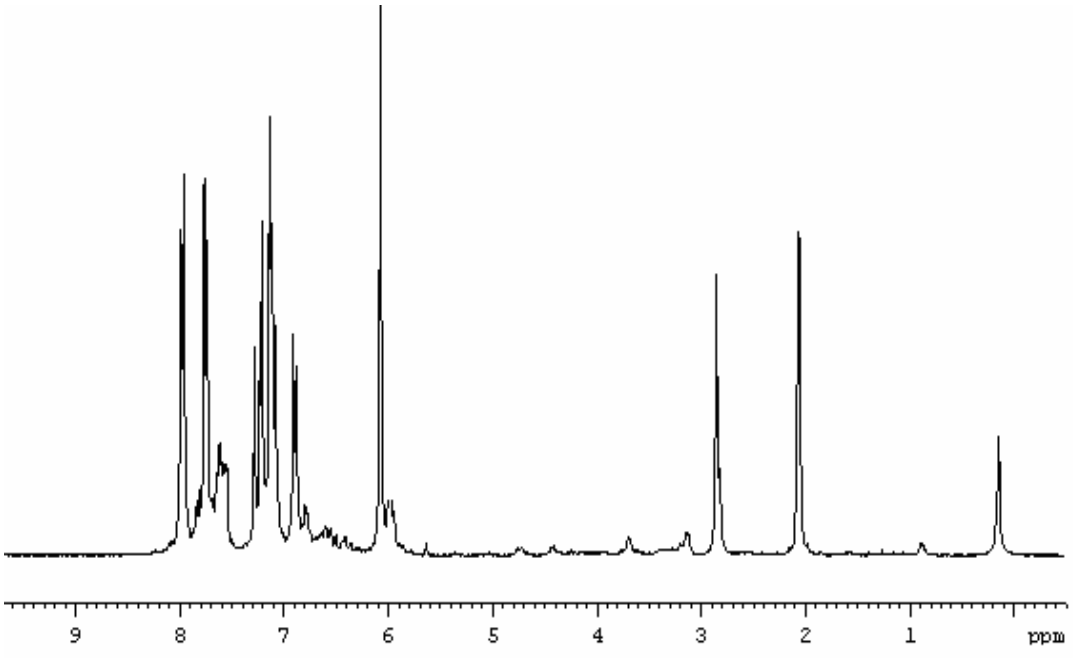
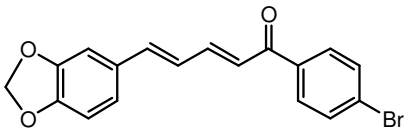


Table 2, 1b/Entry-1, ^{13}C NMR (in $CDCl_3$)



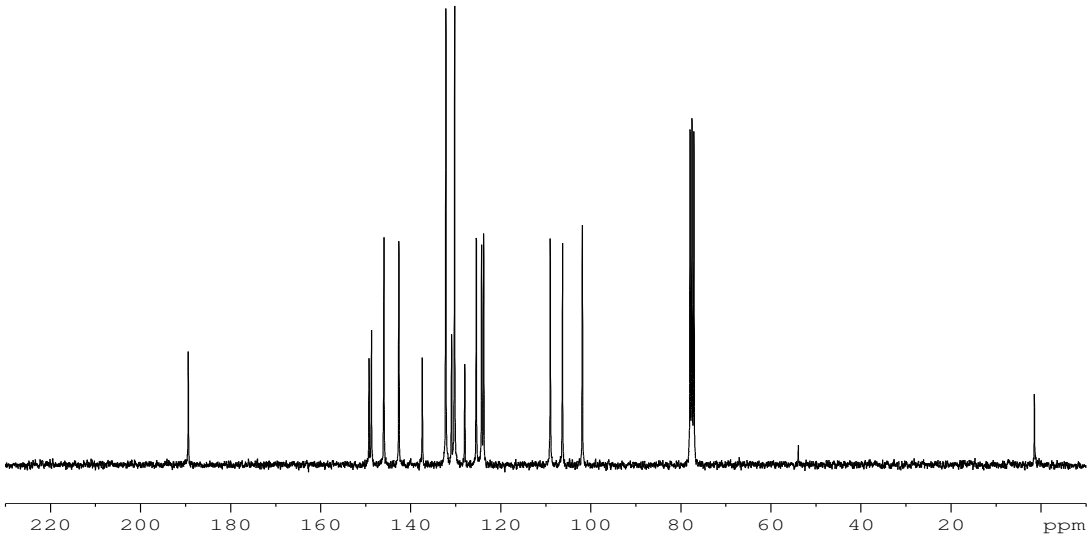
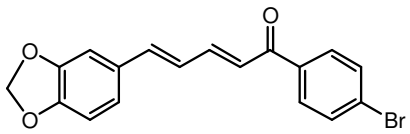


Table 2, 1b/Entry-1, HRMS spectrum



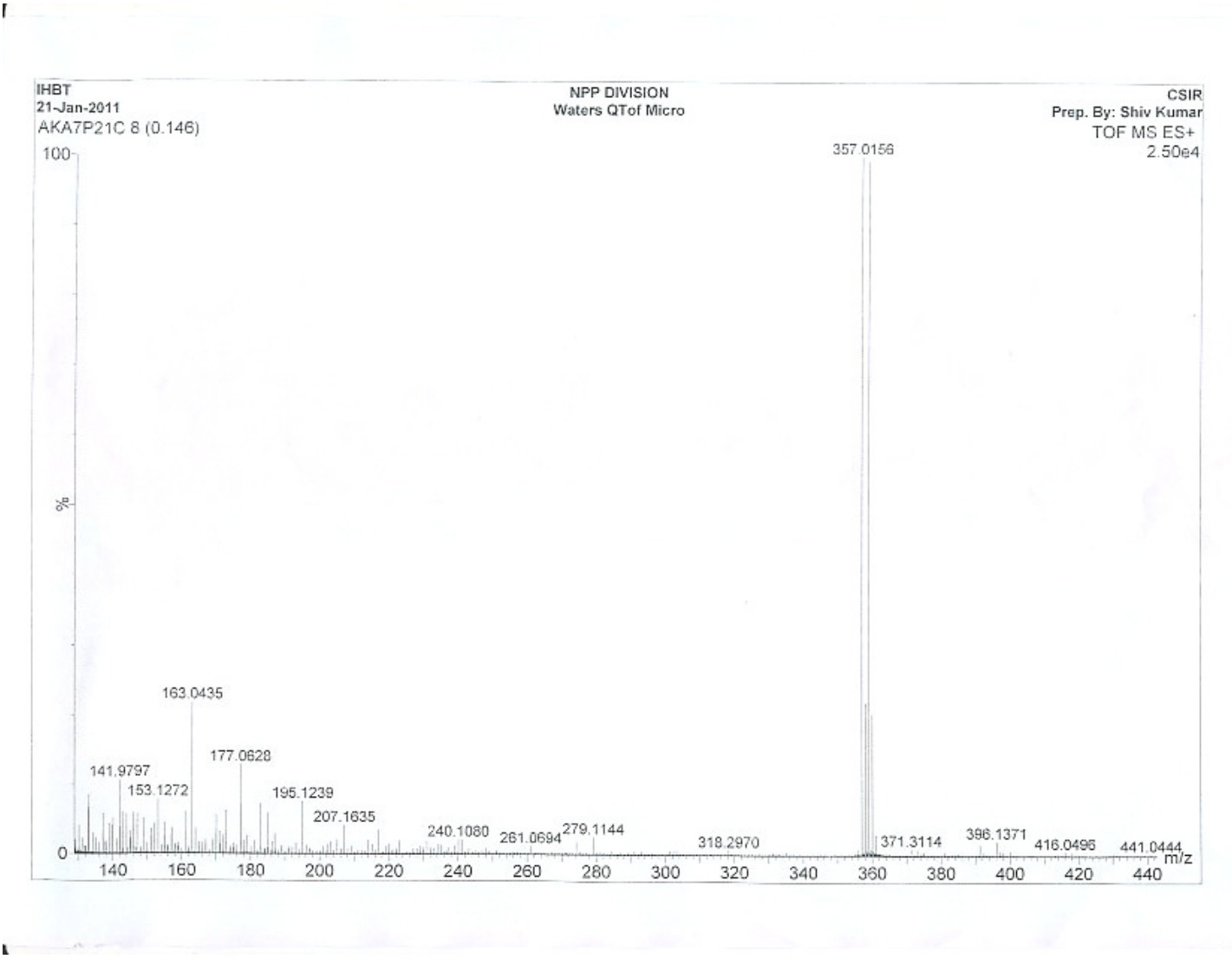
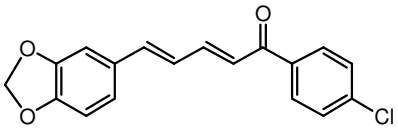


Table 2, 2b /Entry-2, ^{1}H NMR (in $CDCl_3$)



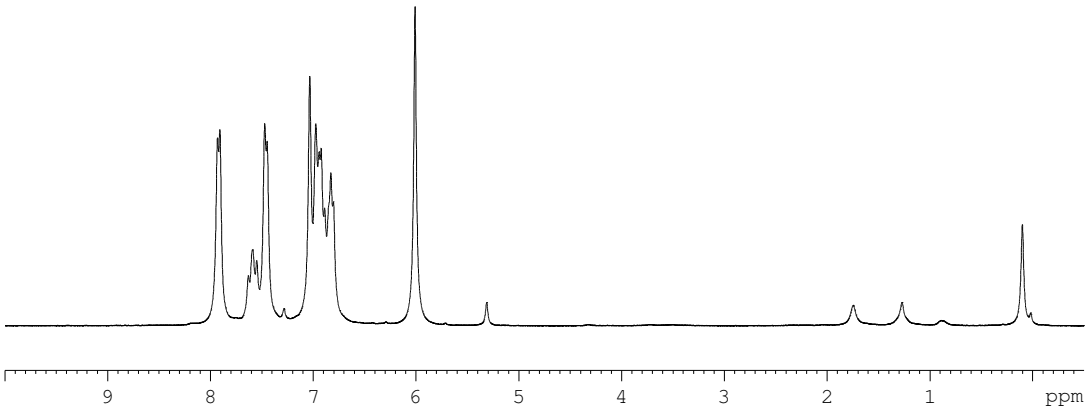
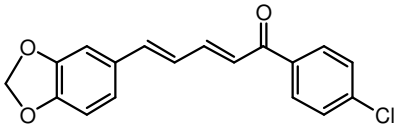


Table 2, 2b /Entry-2, ^{13}C NMR (in $CDCl_3$)



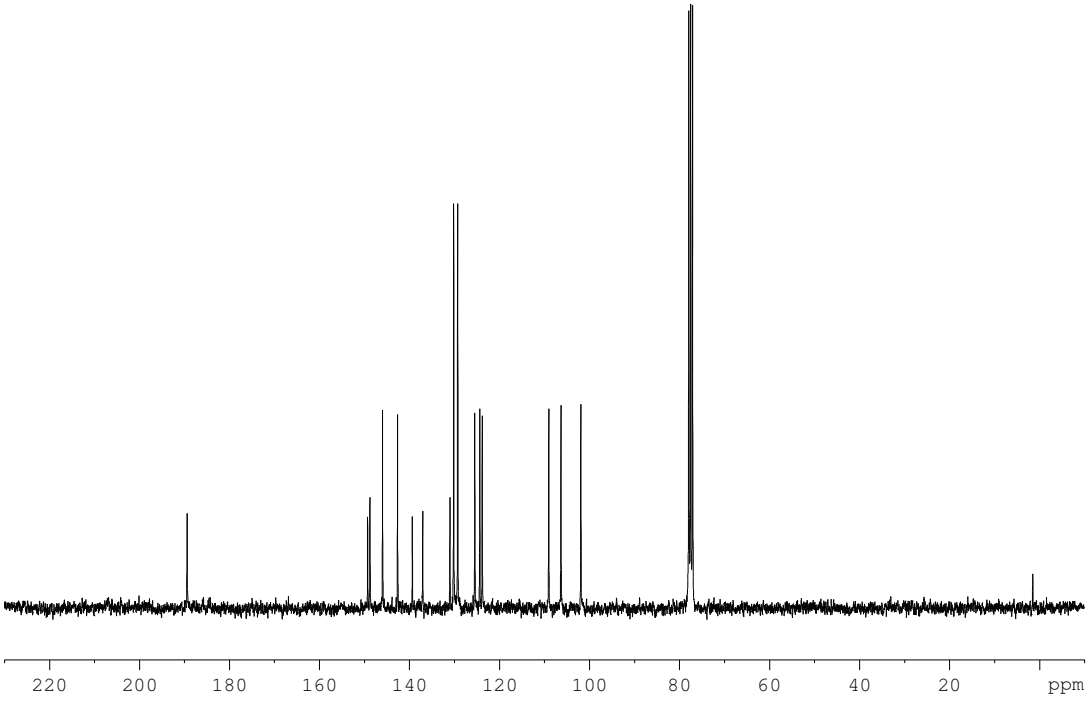
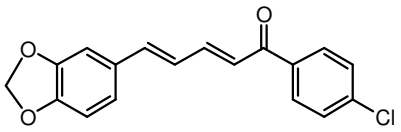


Table 2, 2b /Entry-2, HRMS spectrum



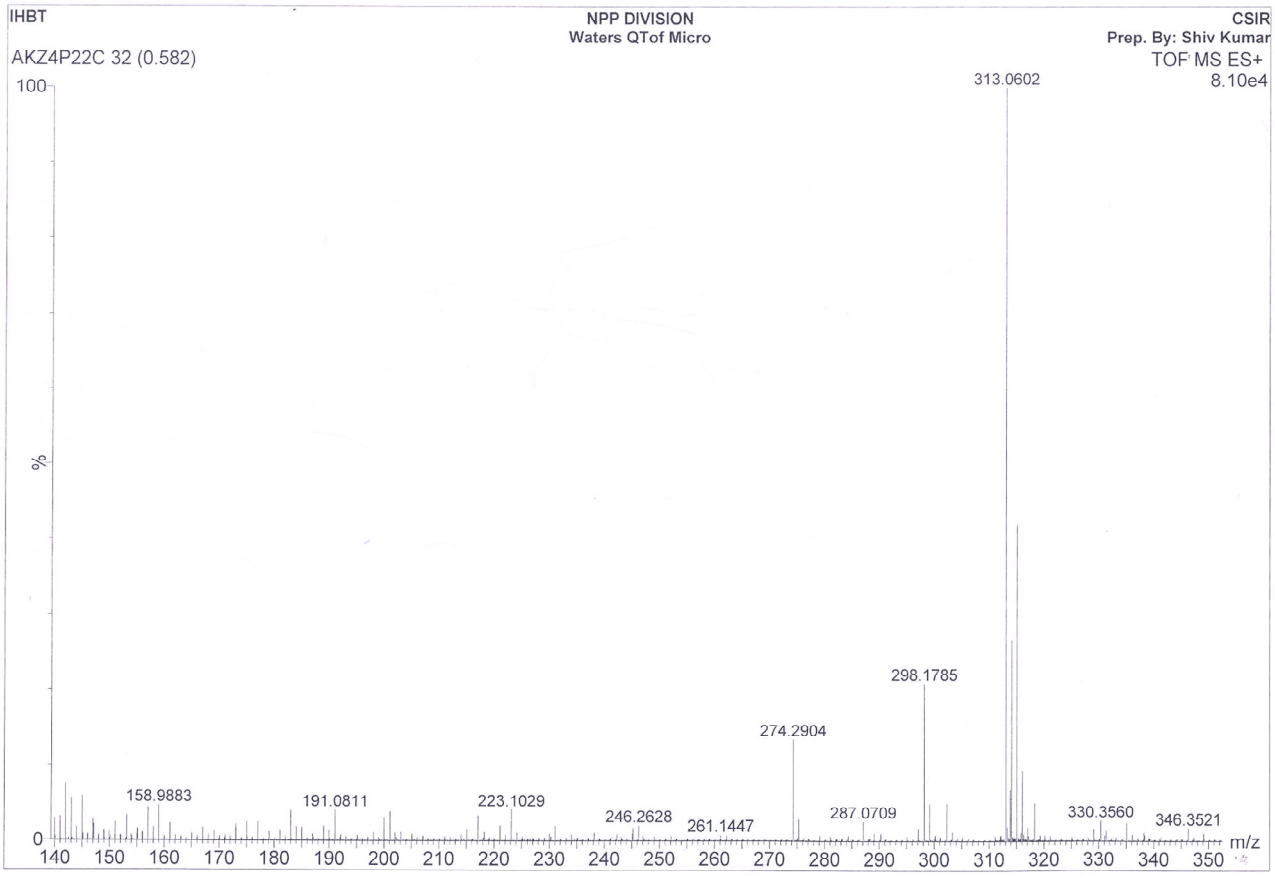
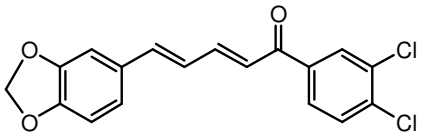


Table 2, 3b/Entry-3, ^{1}H NMR (in C_5D_5N)



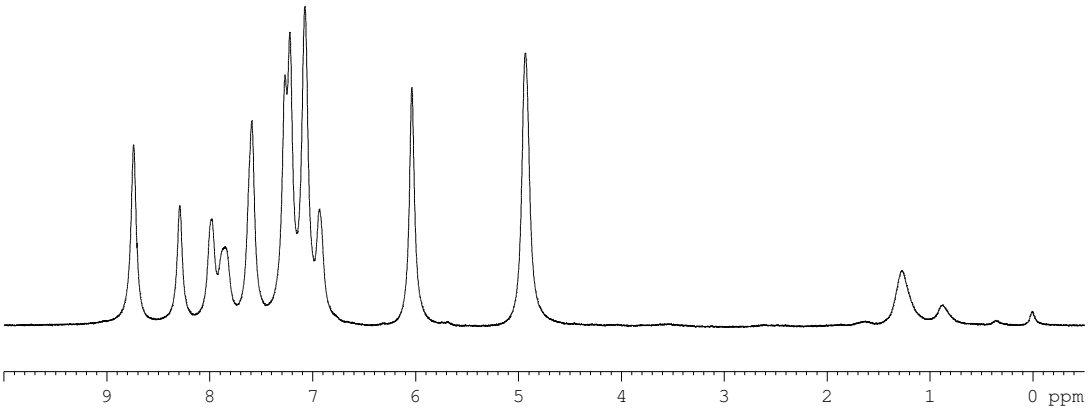
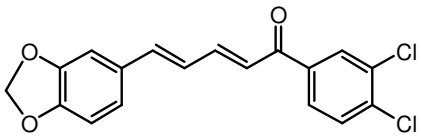


Table 2, 3b/Entry-3, ^{13}C NMR (in C_5D_5N)



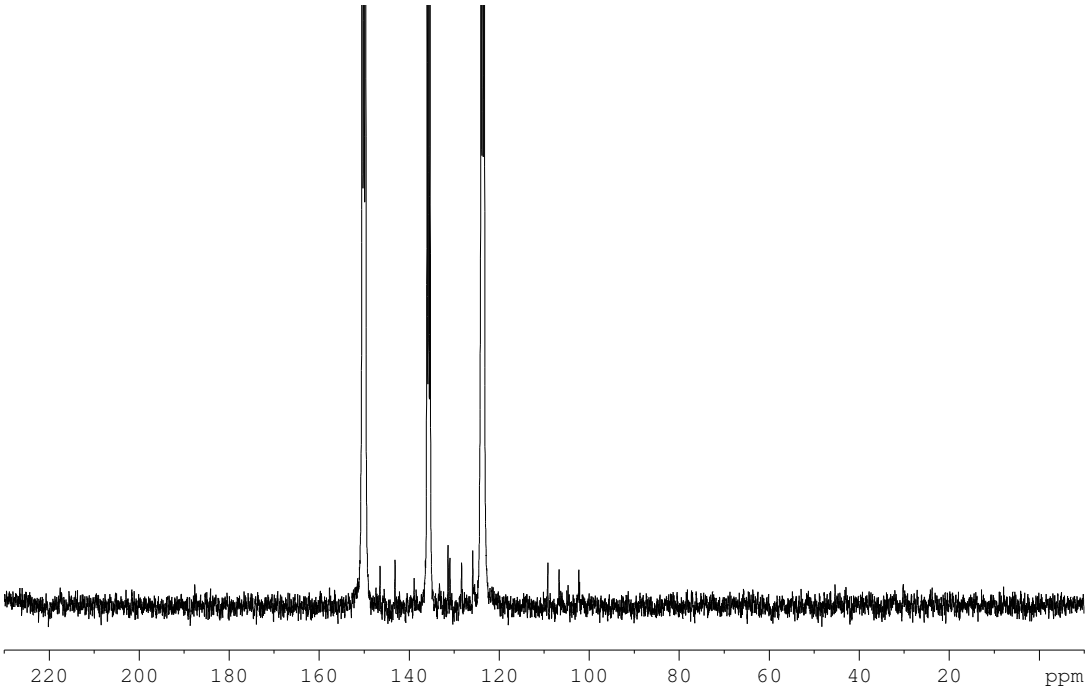
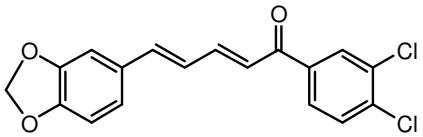


Table 2, 3b/Entry-3, HRMS spectrum



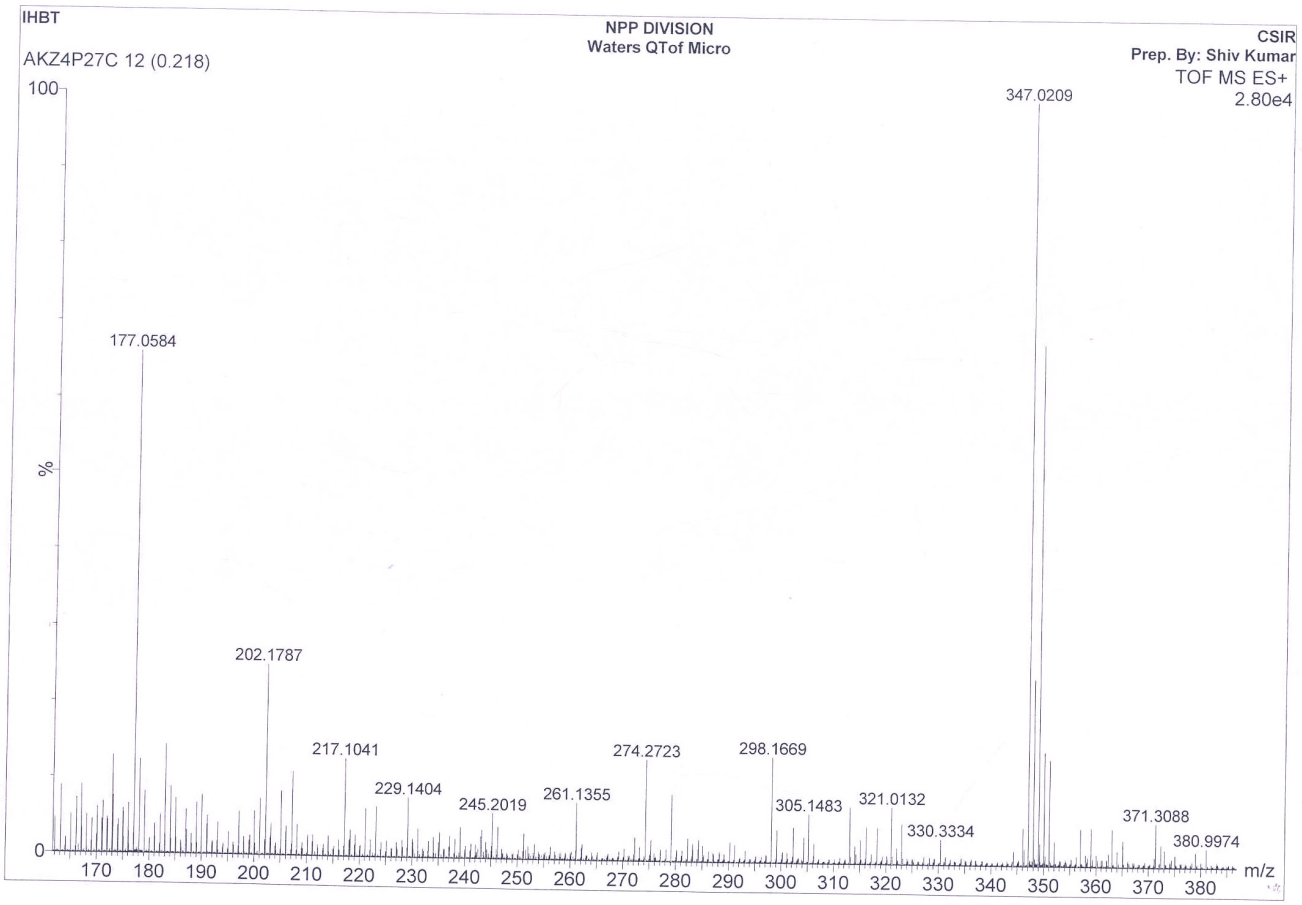
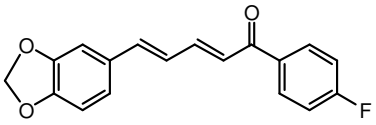


Table 2, 4b/Entry-4, ^{1}H NMR (in CD_3COCD_3)



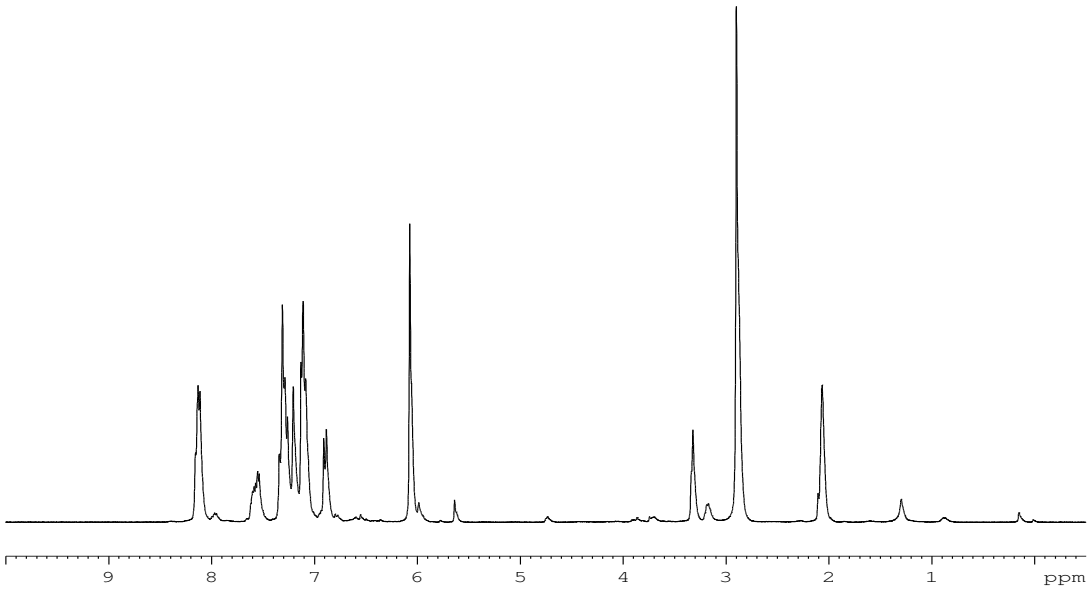
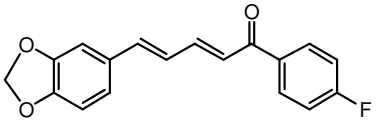


Table 2, 4b/Entry-4, ^{13}C NMR (in $CDCl_3$)



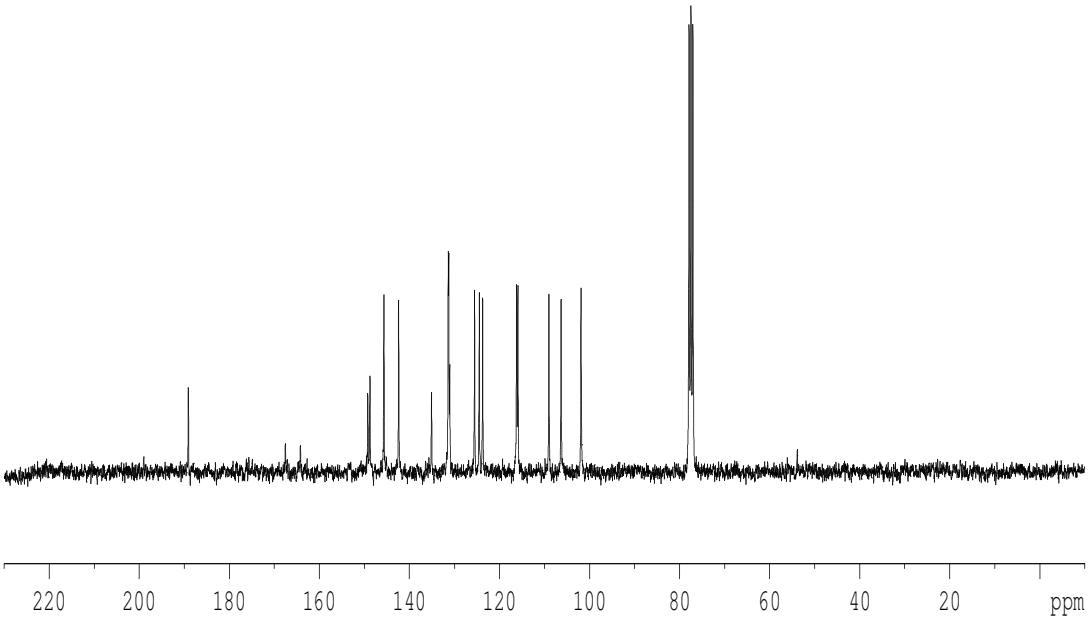
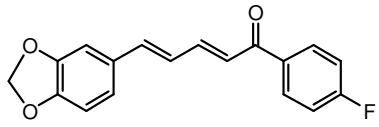


Table 2, 4b/Entry-4, HRMS spectrum



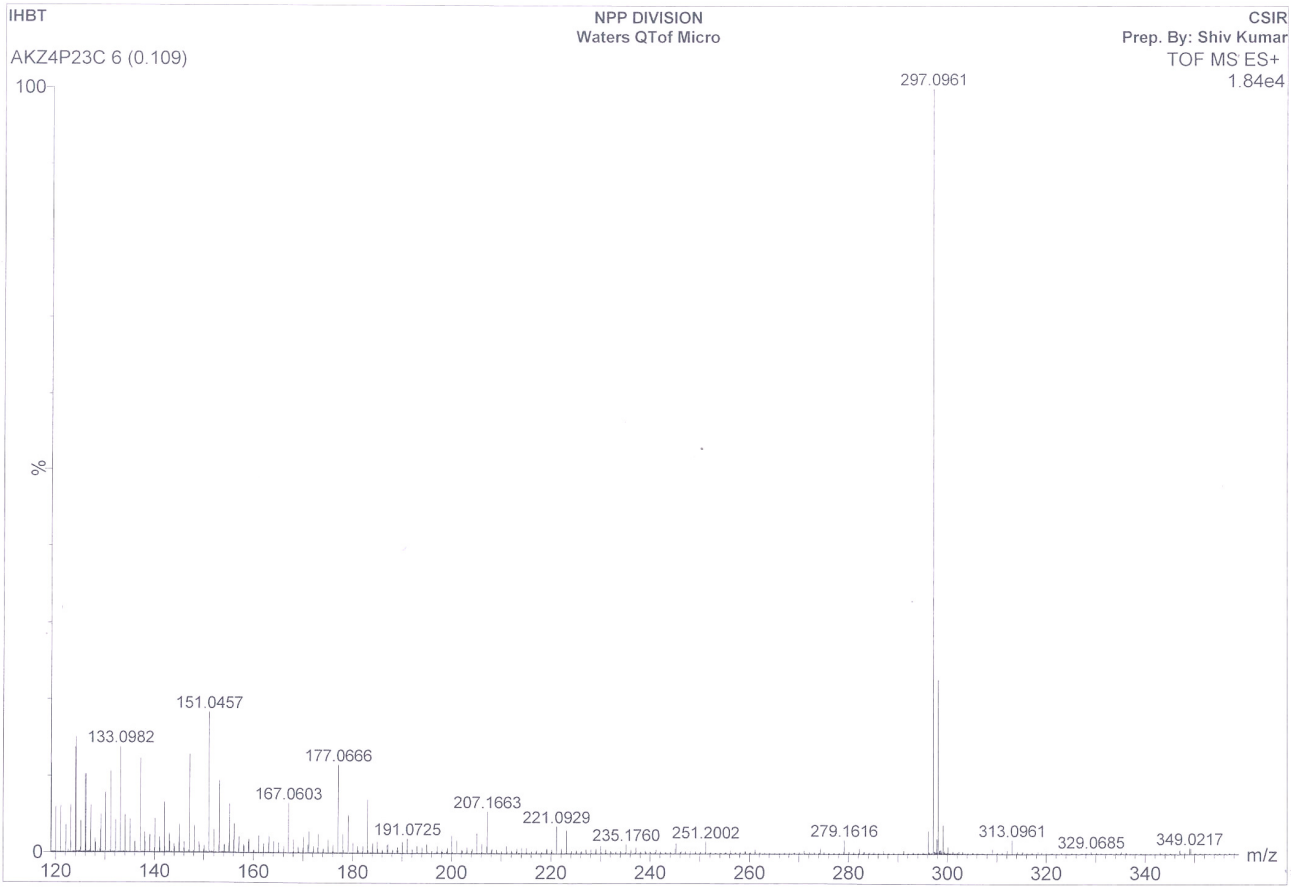
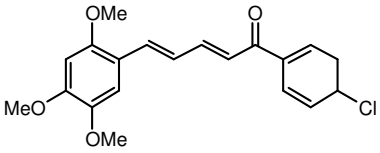


Table 2, 5b/Entry-5, ^{1}H NMR (in $CDCl_3$)



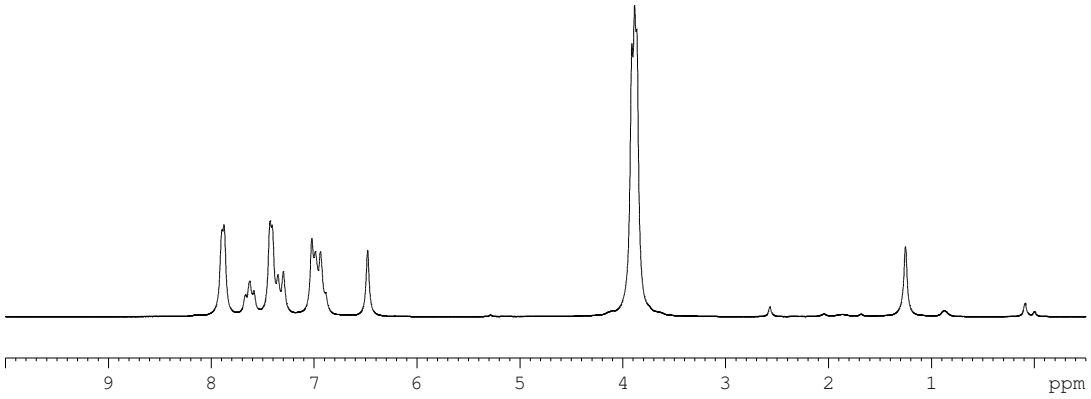
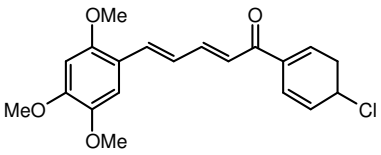


Table 2, 5b/Entry-5,^{13}C NMR (in $CDCl_3$)



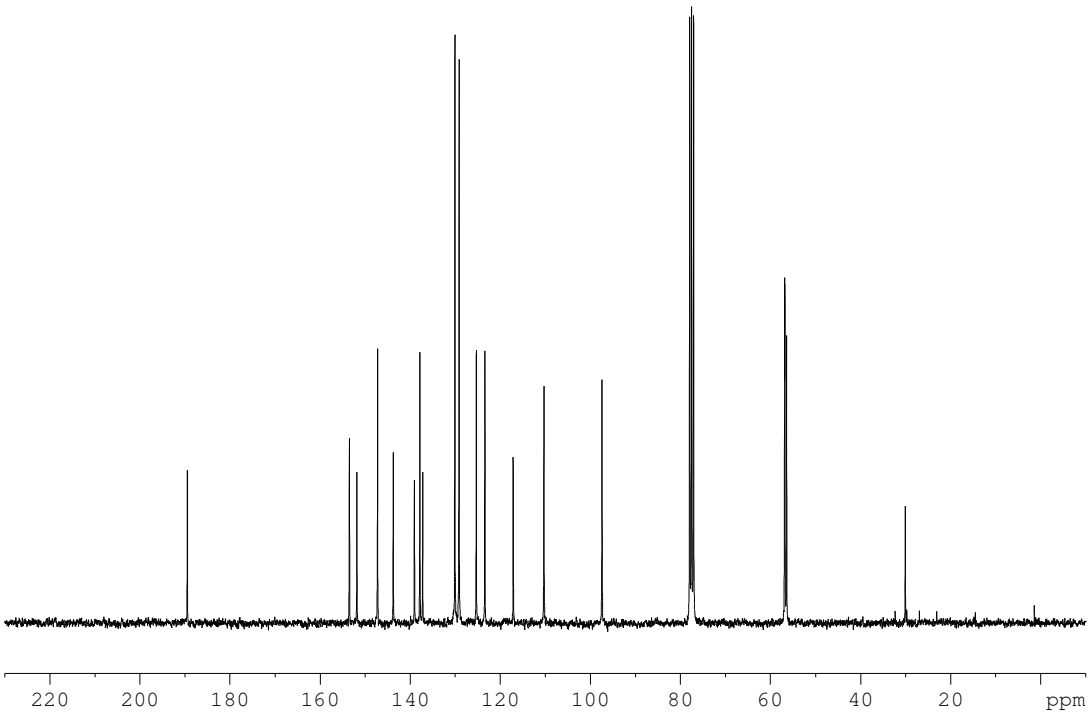
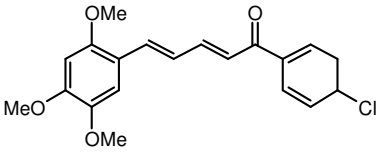


Table 2, 5b/Entry-5,HRMS spectrum



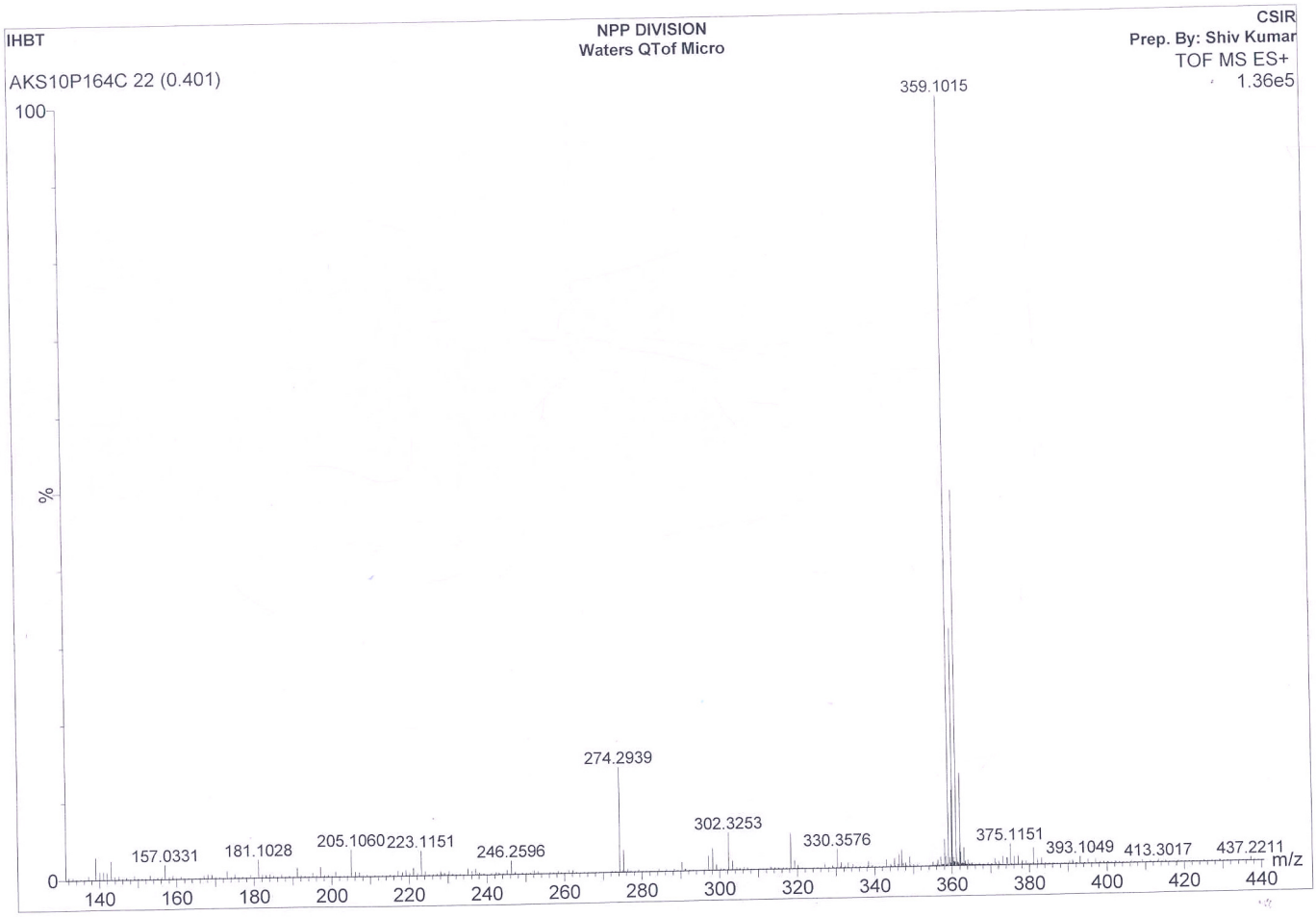
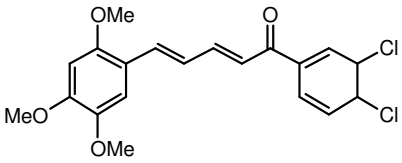


Table 2, 6b/Entry-6, ^{1}H NMR (in $CDCl_3$)



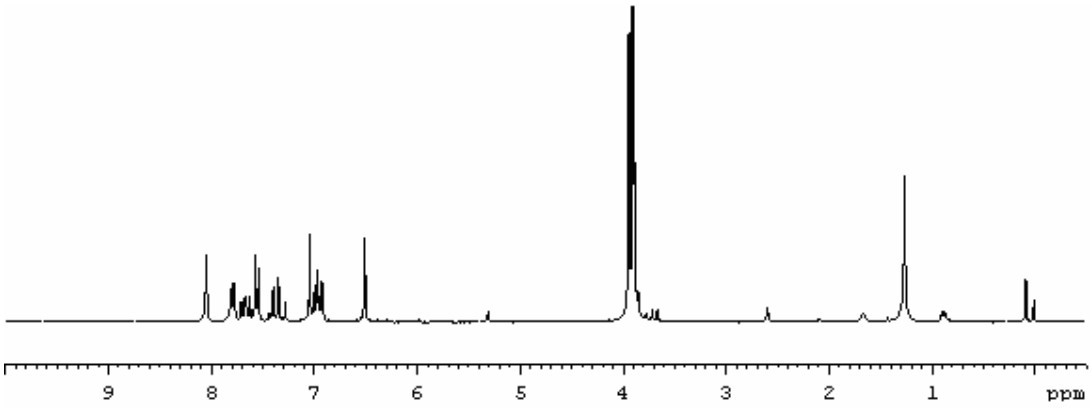
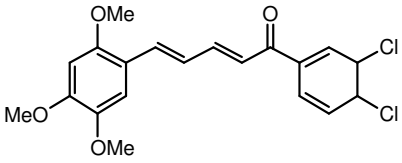


Table 2, 6b/Entry-6, ^{13}C NMR (in $CDCl_3$)



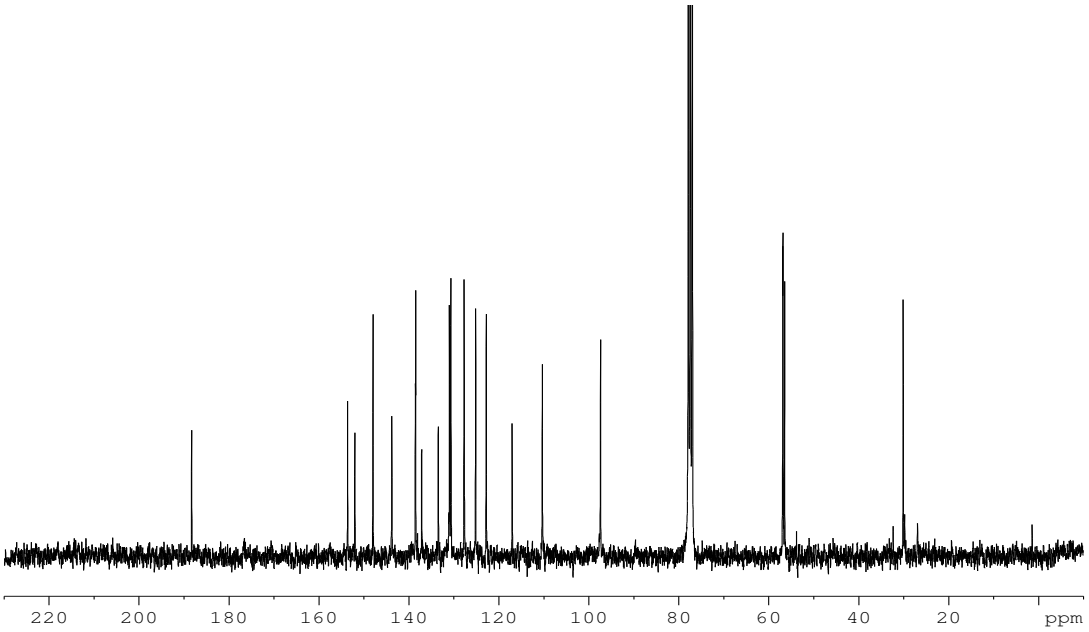
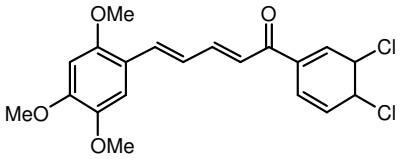


Table 2, 6b/Entry-6, HRMS spectrum



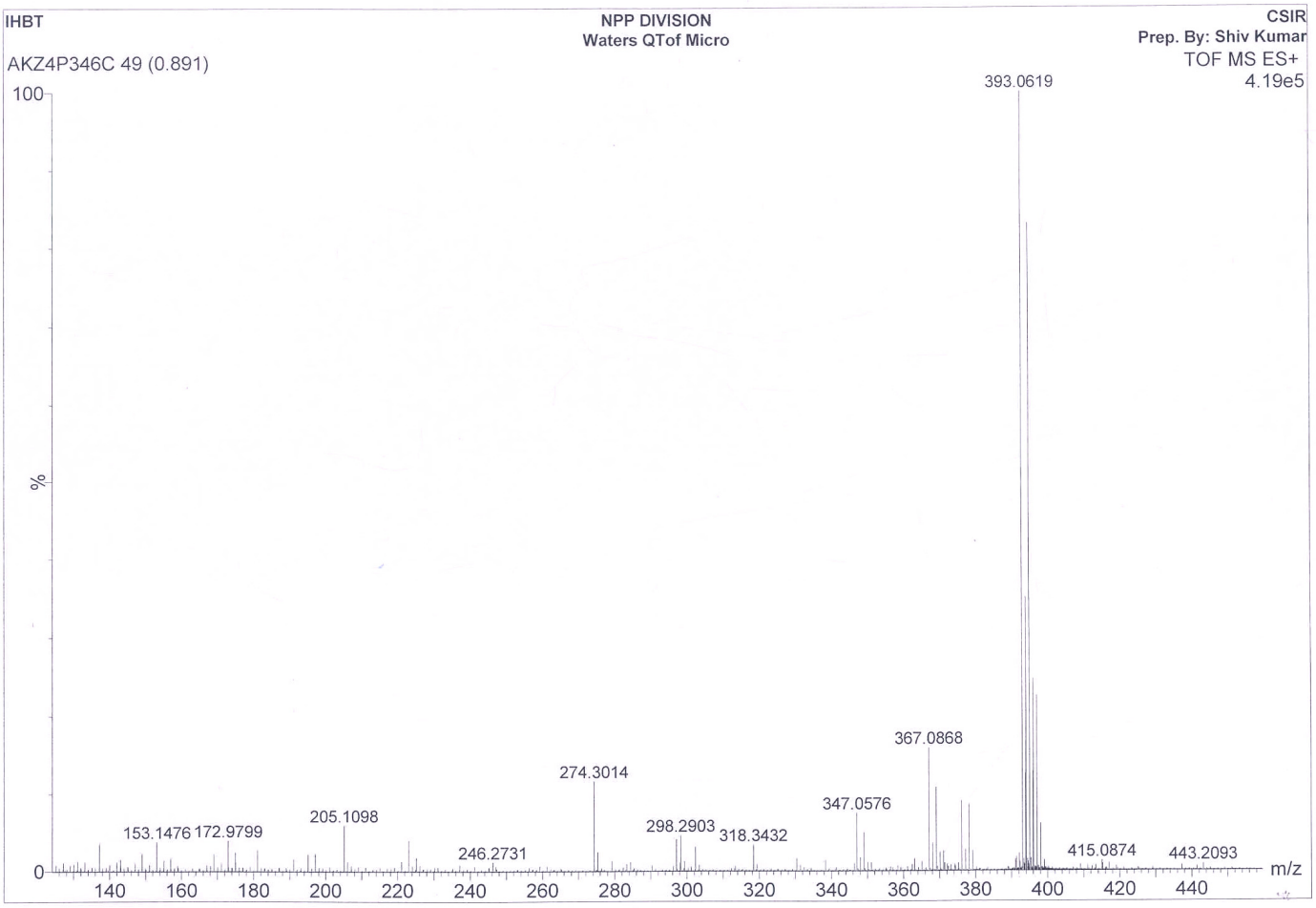
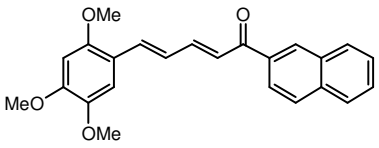


Table 2, 7b/Entry-7, ^{1}H NMR (in $CDCl_3$)



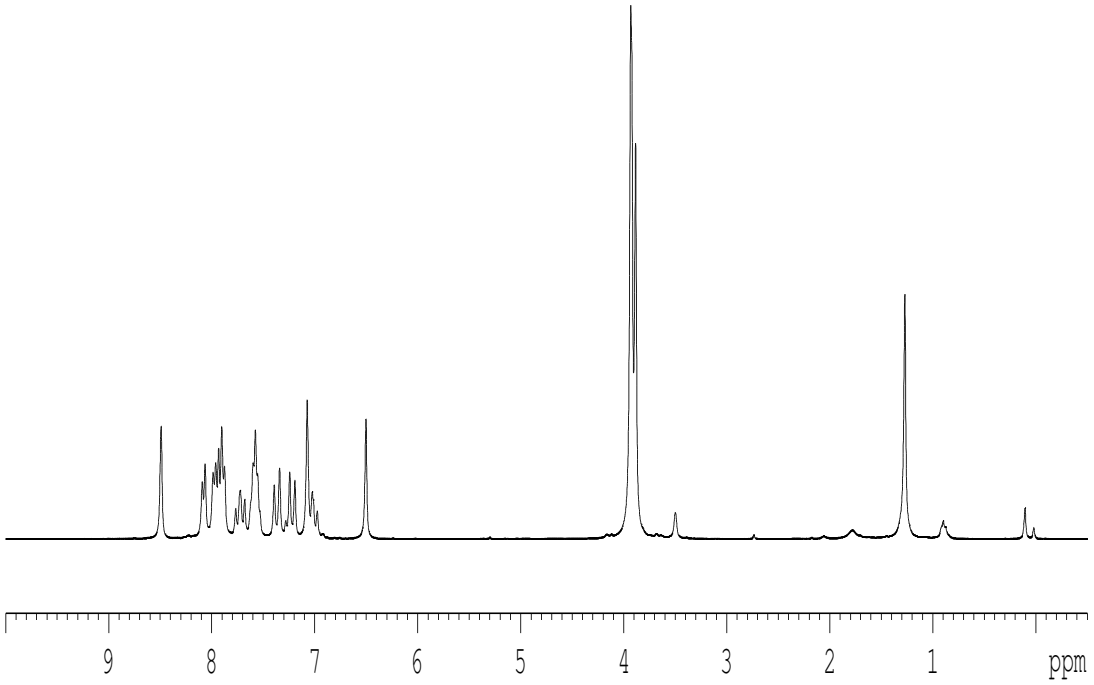
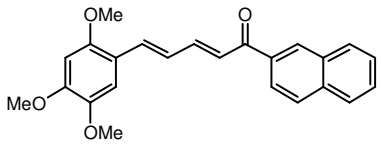


Table 2, 7b/Entry-7, ^{13}C NMR (in $CDCl_3$)



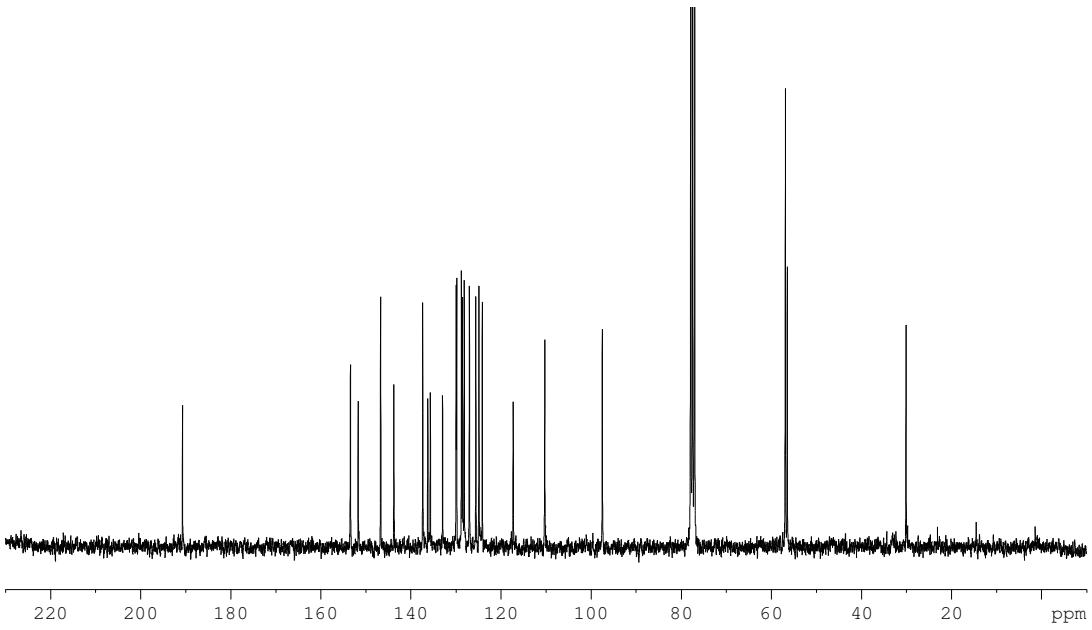
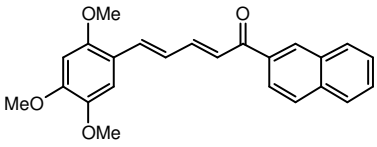


Table 2, 7b/Entry-7, HRMS spectrum



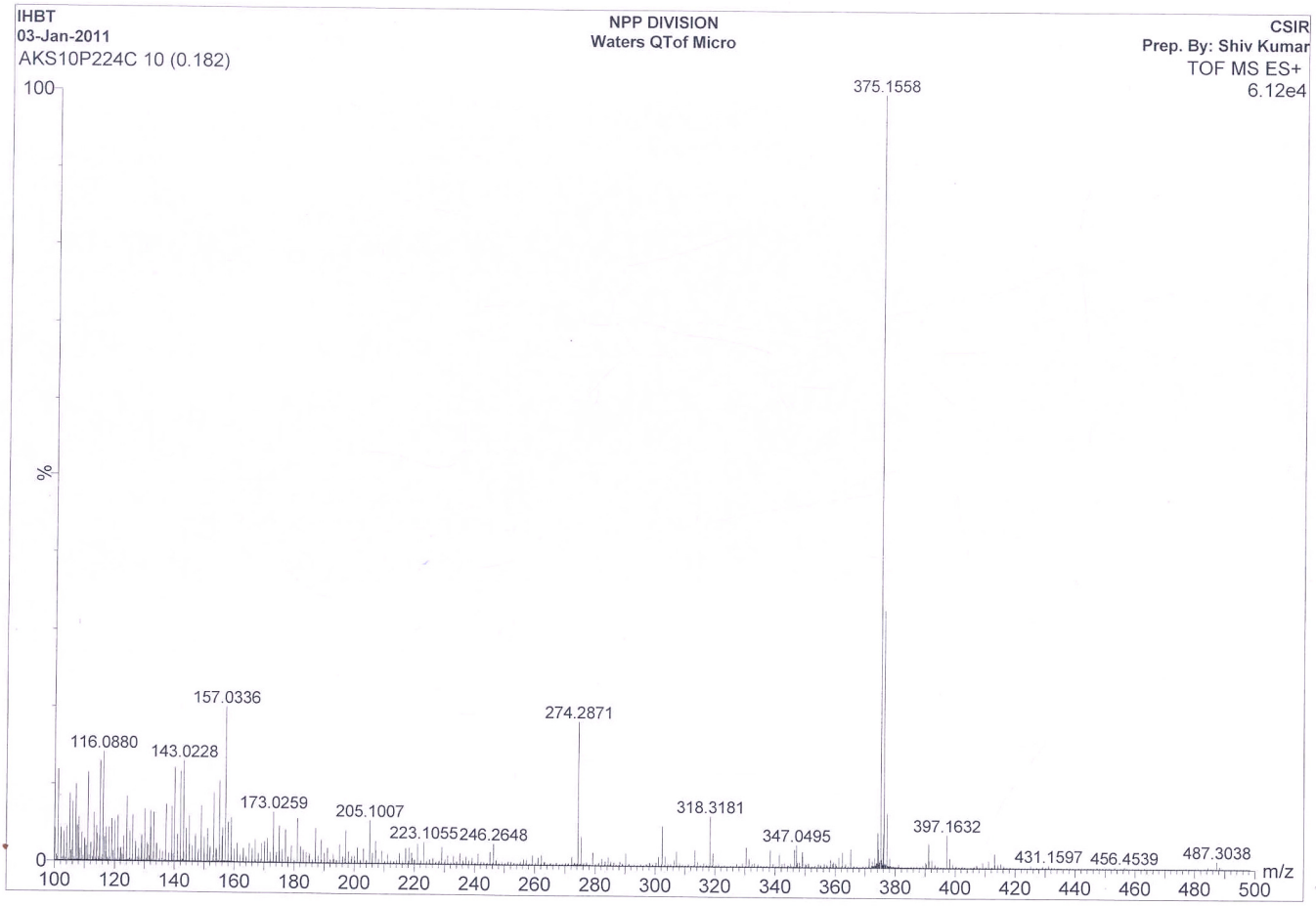
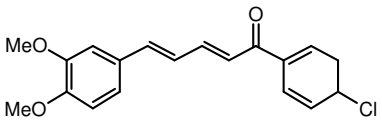


Table 2, 8b/Entry-8, ^{1}H NMR (in $CDCl_3$)



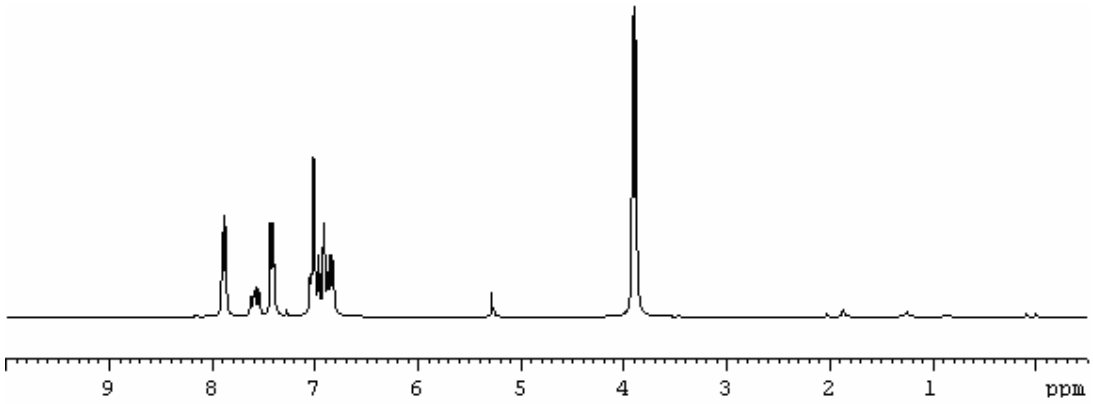
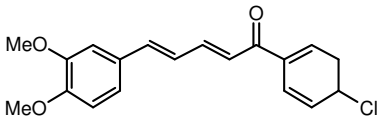


Table 2, 8b/Entry-8, ^{13}C NMR (in $CDCl_3$)



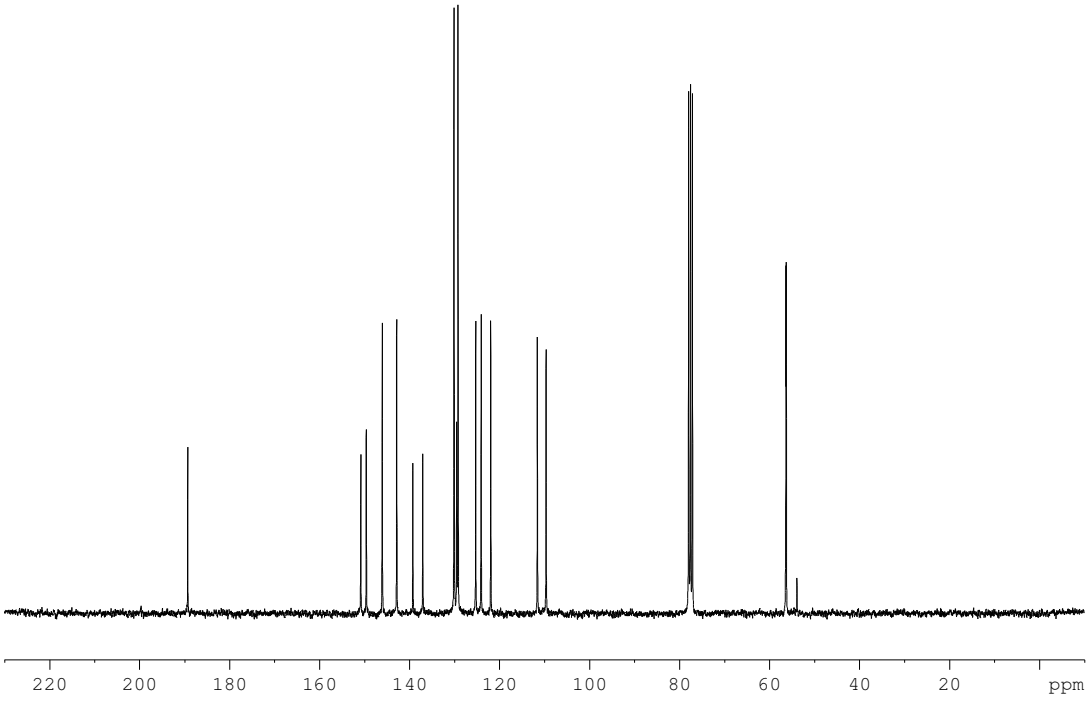
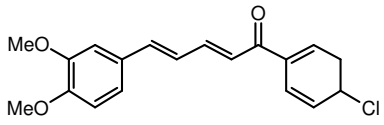


Table 2, 8b/Entry-8, HRMS spectrum



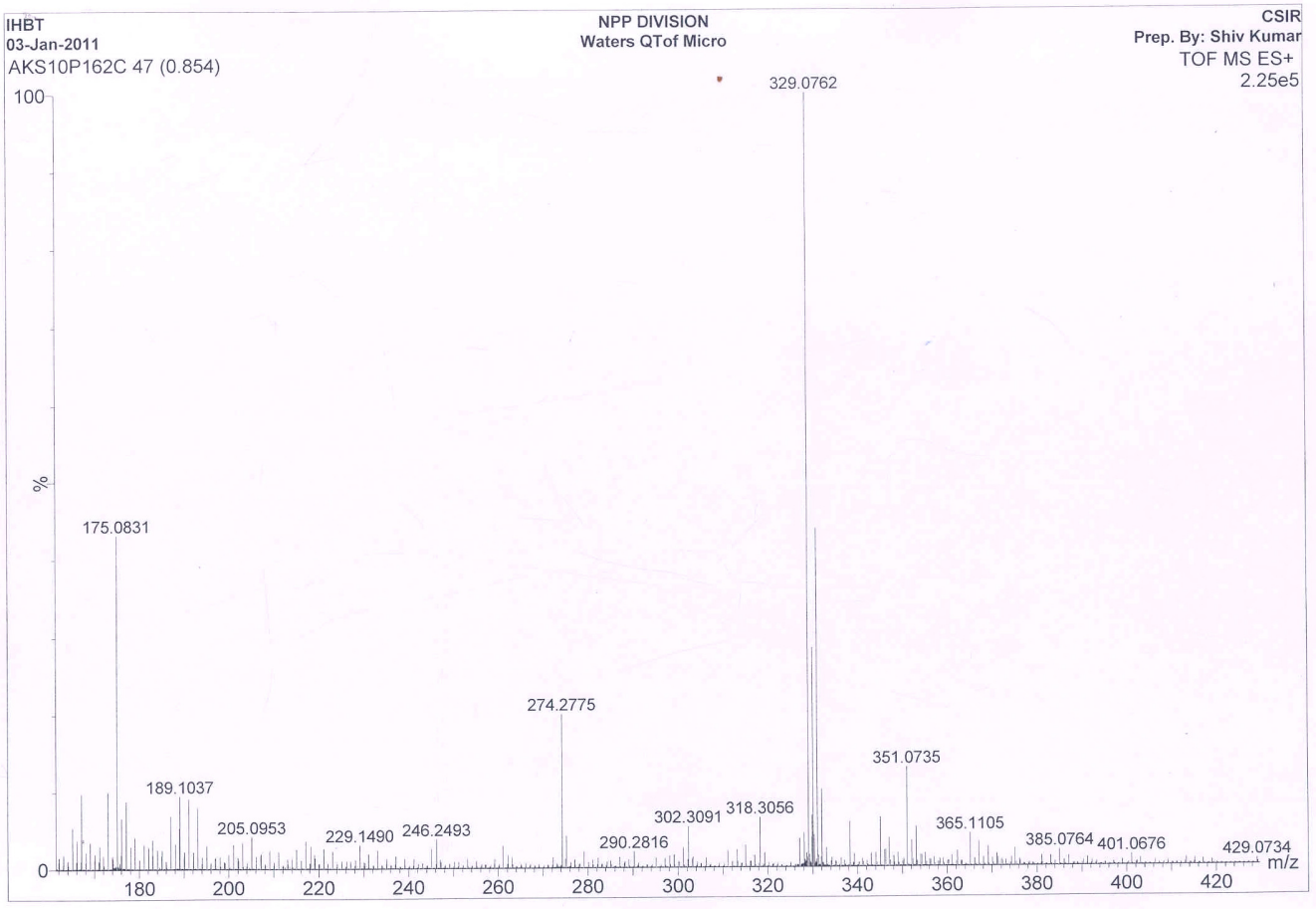
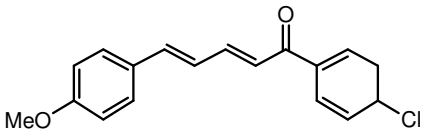


Table 2, 9b/Entry-9, ^{1}H NMR (in $CDCl_3$)



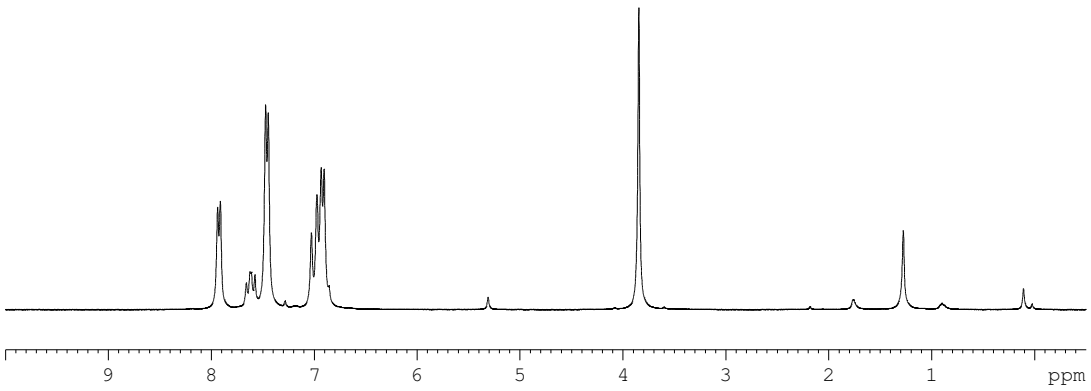
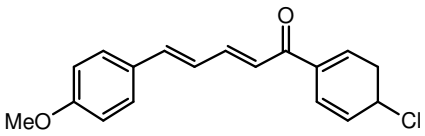


Table 2, 9b/Entry-9, ^{13}C NMR (in $CDCl_3$)



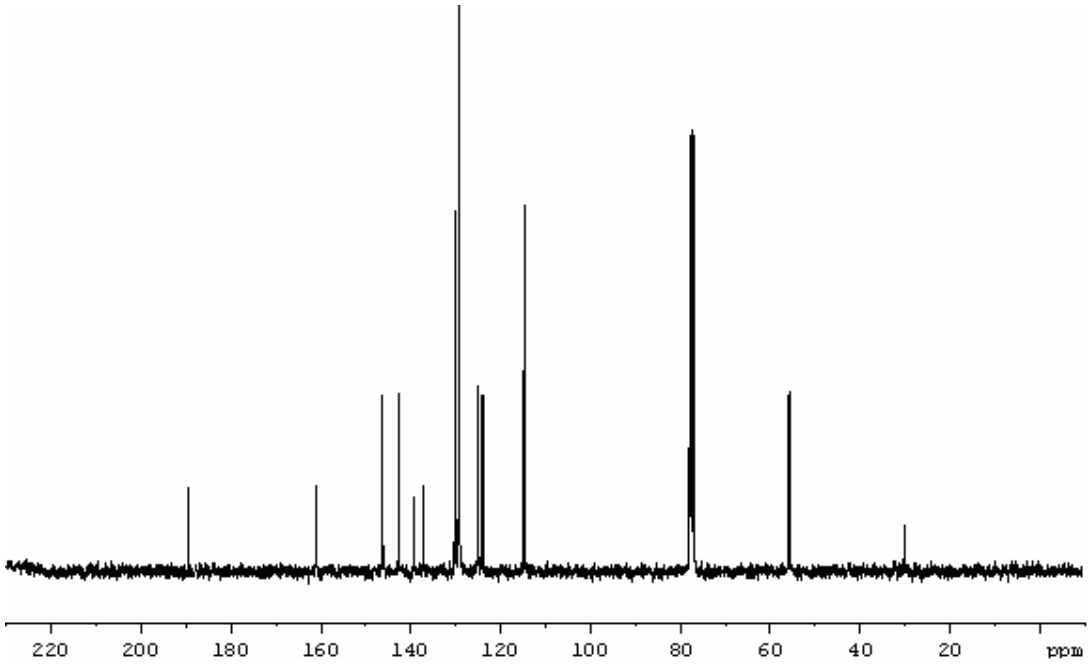
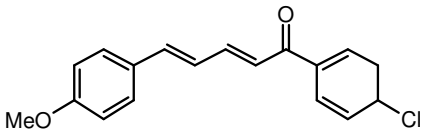


Table 2, 9b/Entry-9, HRMS spectrum



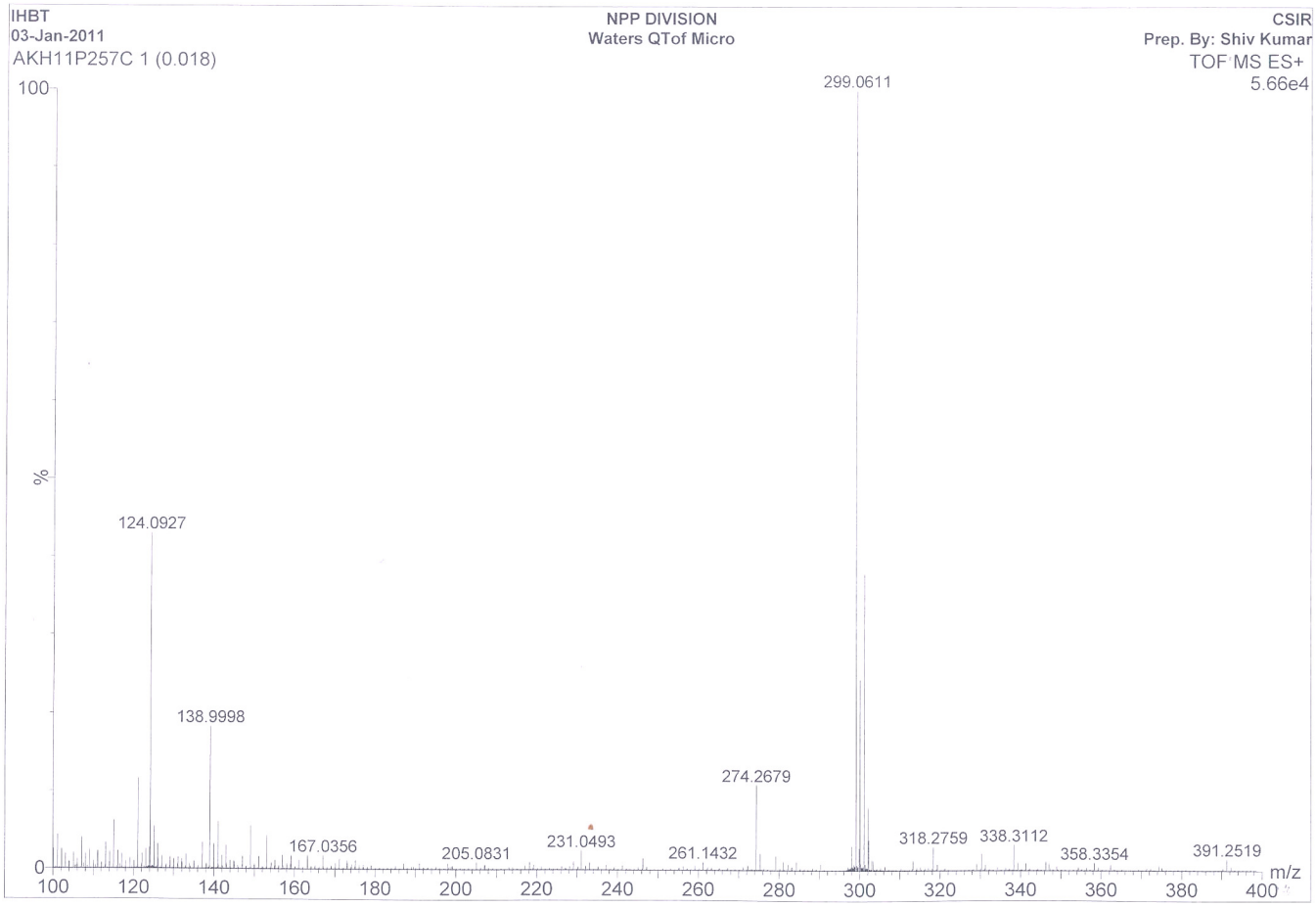
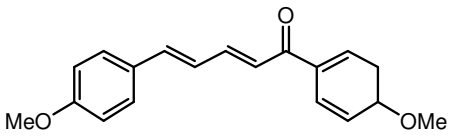


Table 2, 10b/Entry-10, ^{1}H NMR [in (1:9) $CDCl_3$: CD_3COCD_3]



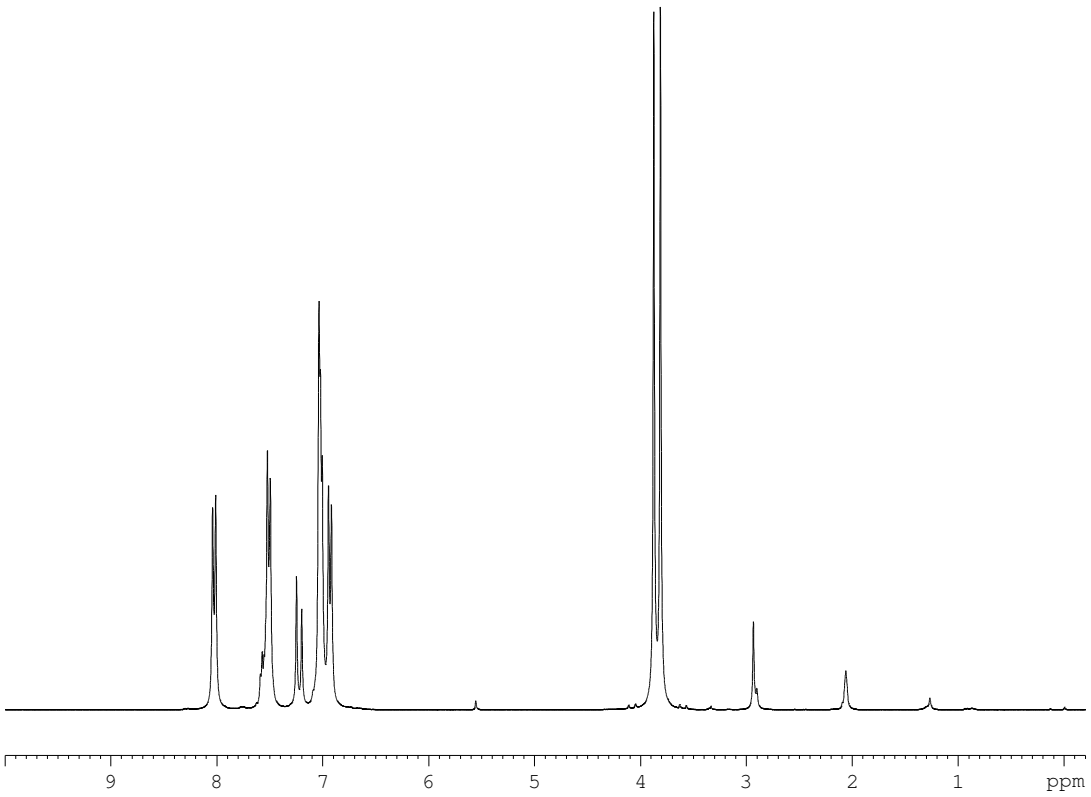
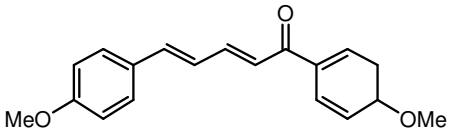


Table 2, 10b/Entry-10, ^{13}C NMR [in (1:9) $CDCl_3$: CD_3COCD_3]



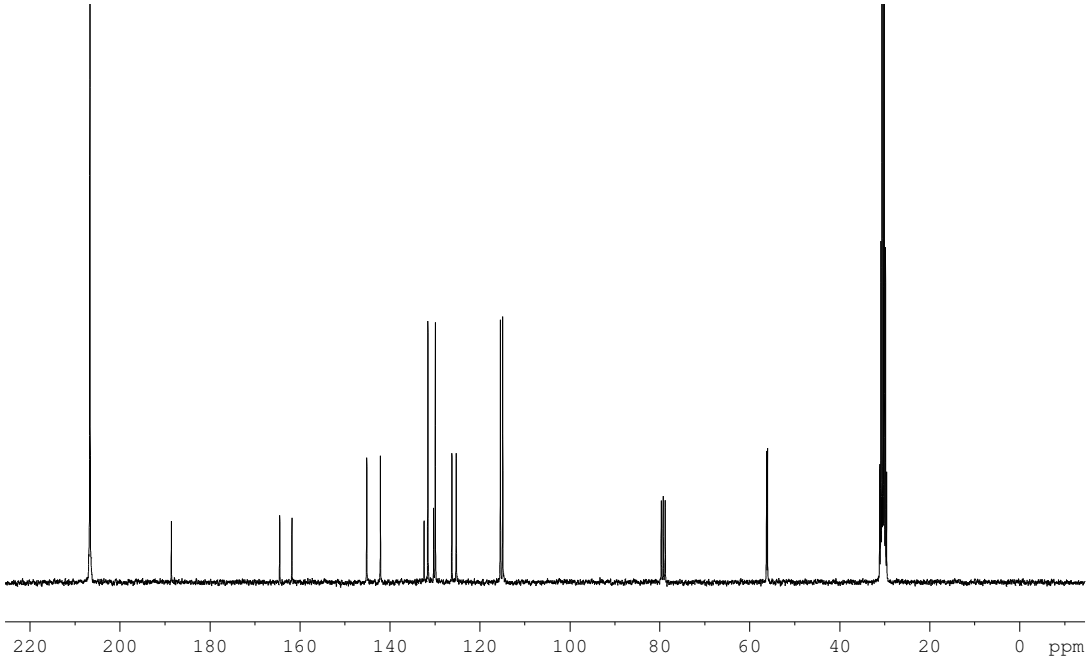
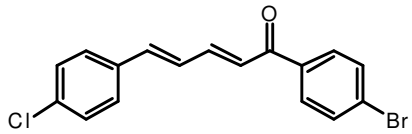


Table 2, 11b/Entry-11, ^{1}H NMR [in (1:1) $CDCl_3$:CD_3OD]



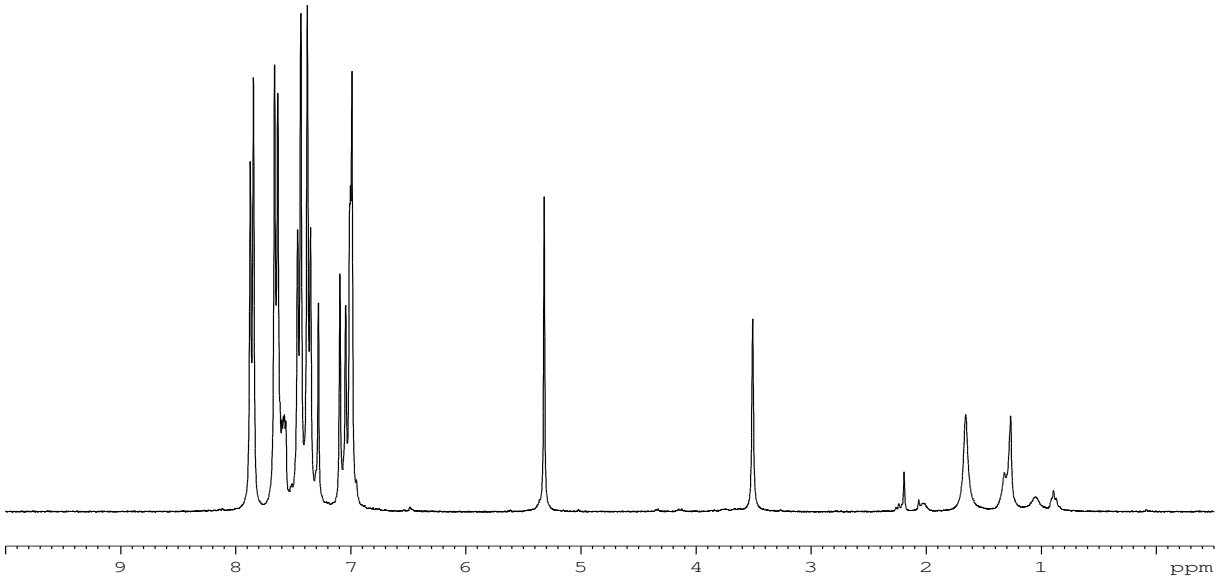
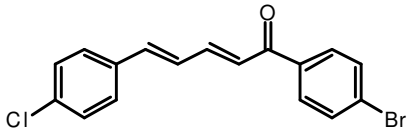
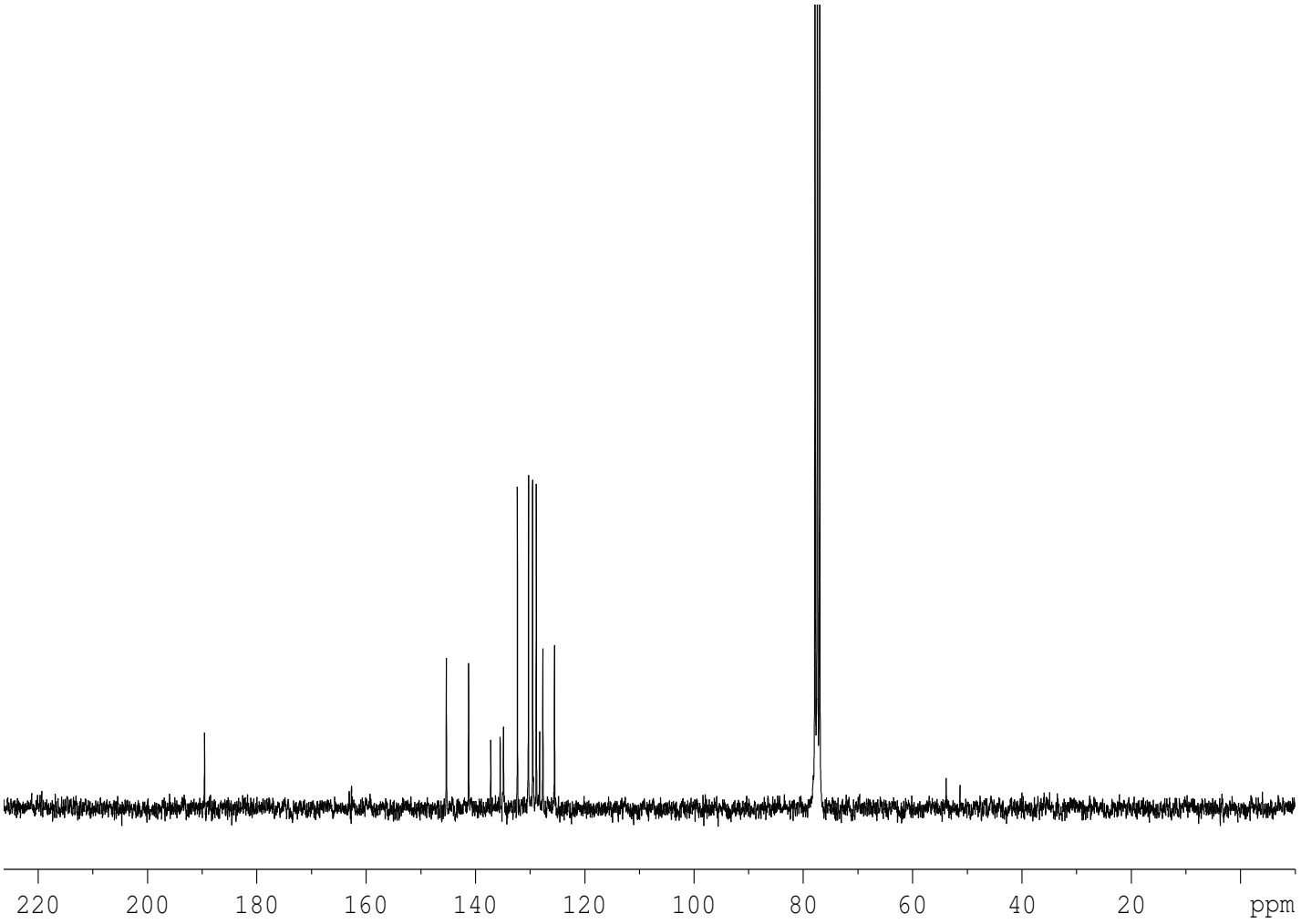
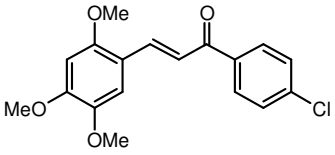


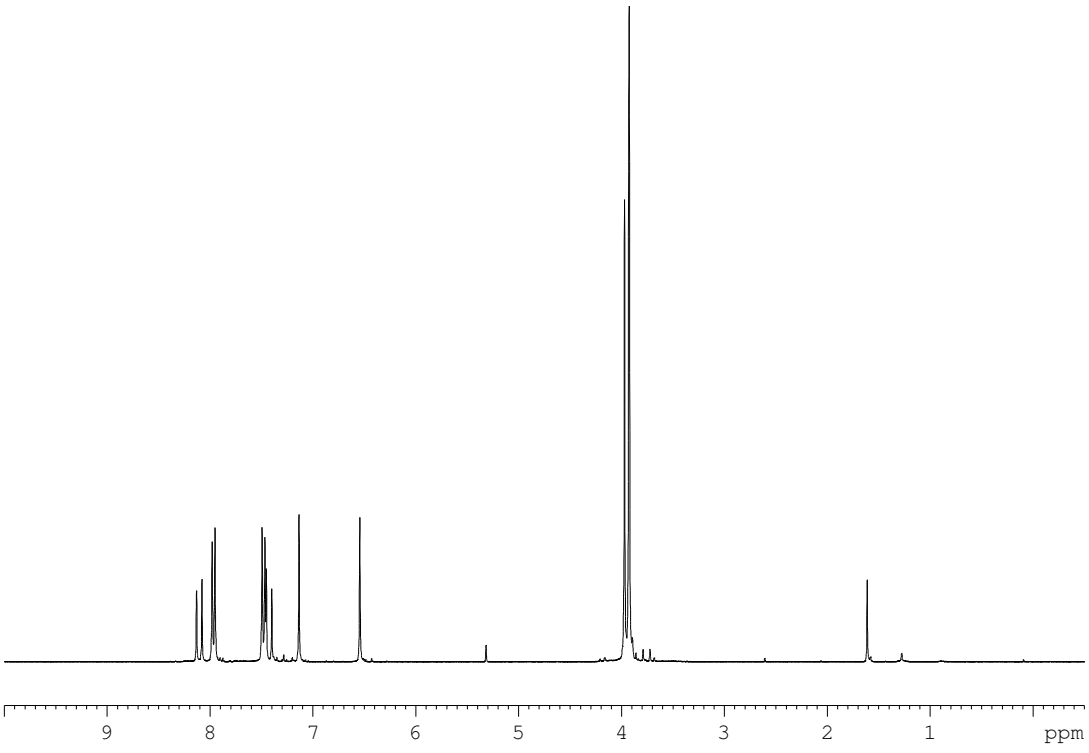
Table 2, 11b/Entry-11, ^{13}C NMR (in $CDCl_3$)



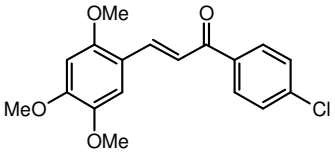


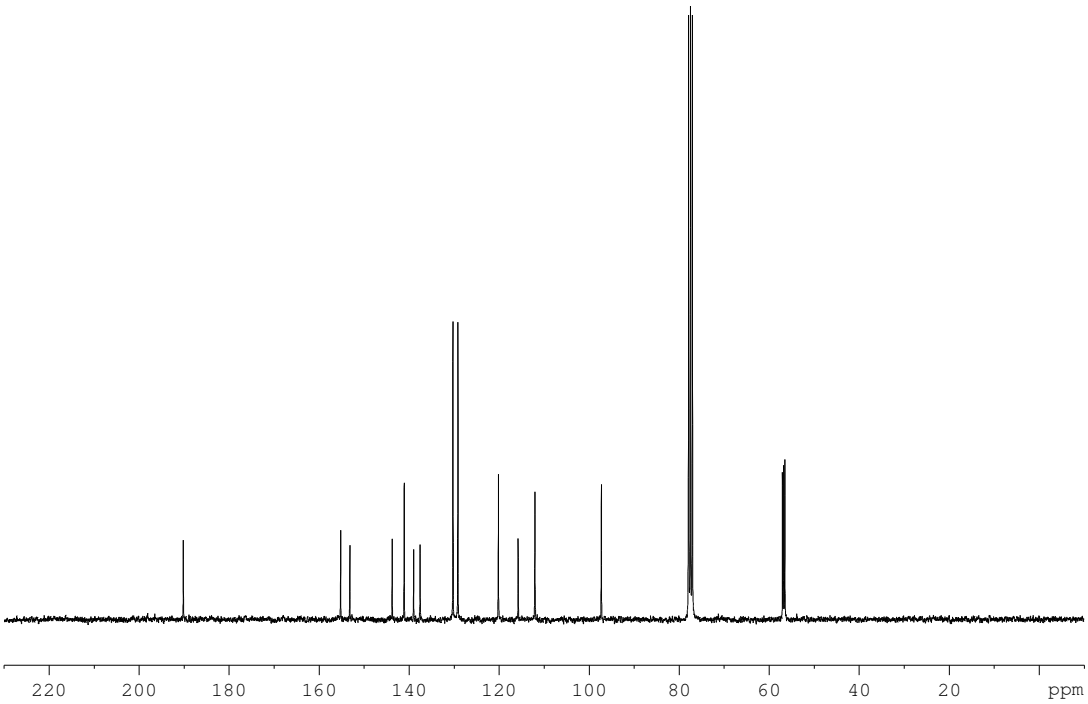
12b /Scheme -3, ^{1}HNMR (in $CDCl_3$)



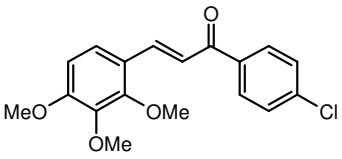


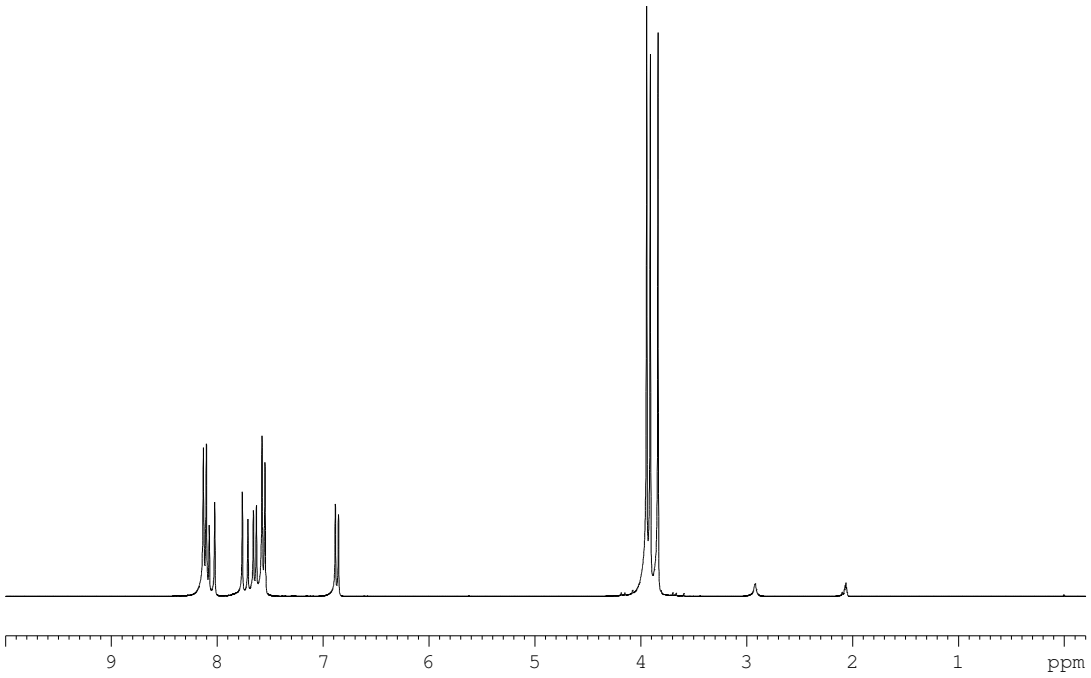
12b /Scheme-3, ^{13}C NMR (in $CDCl_3$)



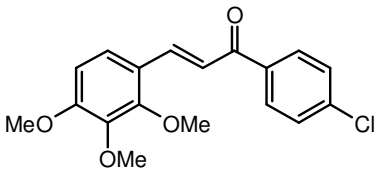


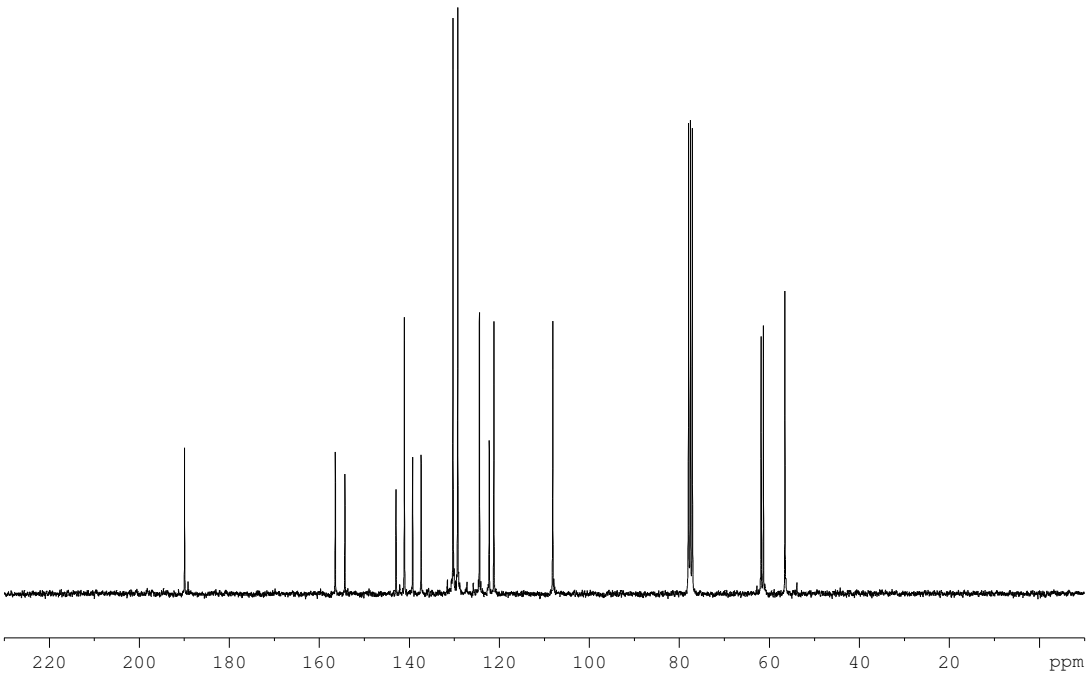
13b /Scheme-4, ^{1}H NMR (in CD_3COCD_3)



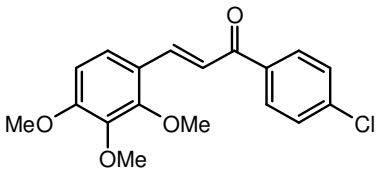


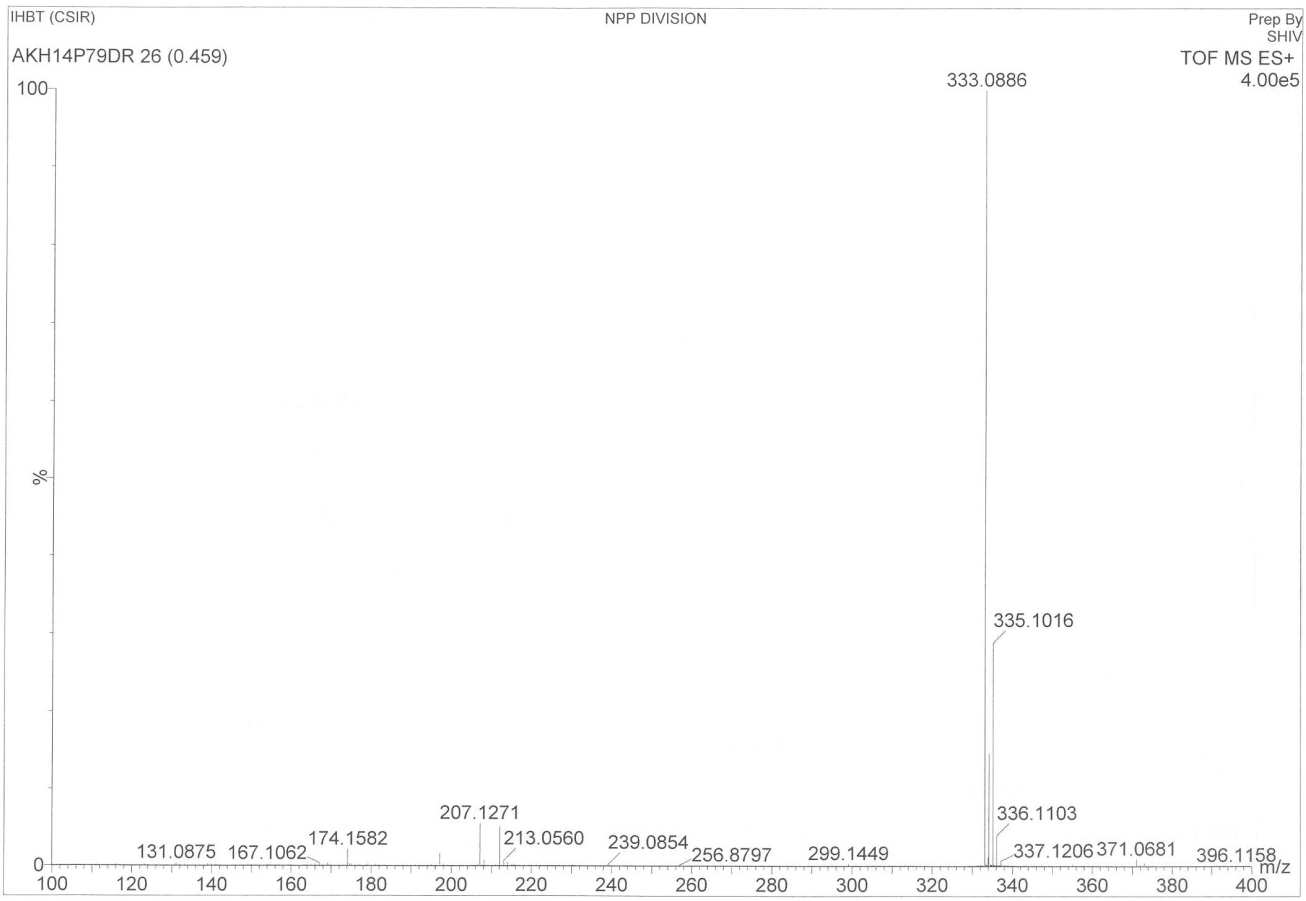
13b /Scheme-4, ^{13}C NMR (in $CDCl_3$)



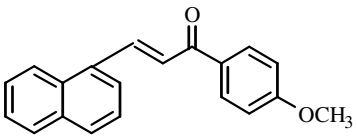


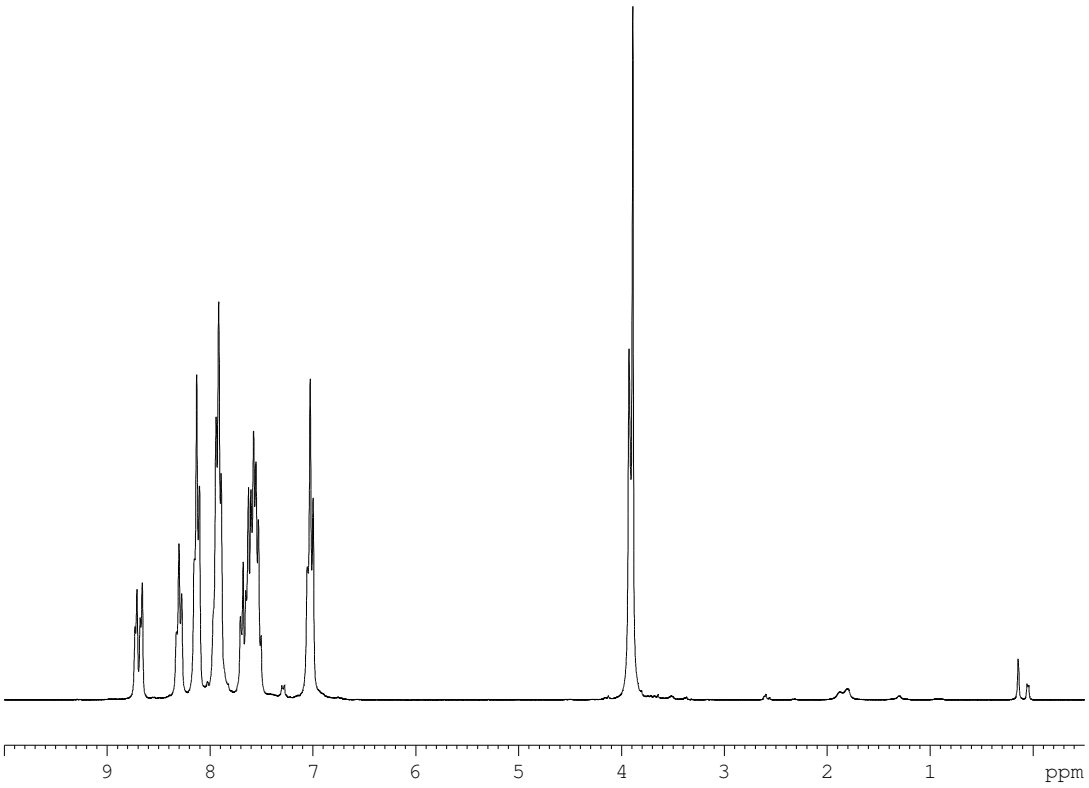
13b /Scheme-4, HRMS spectrum



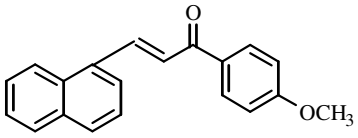


14b/Scheme-5, ^{1}H NMR (in $CDCl_3$)





14b/Scheme -5, ^{13}C NMR (in $CDCl_3$)



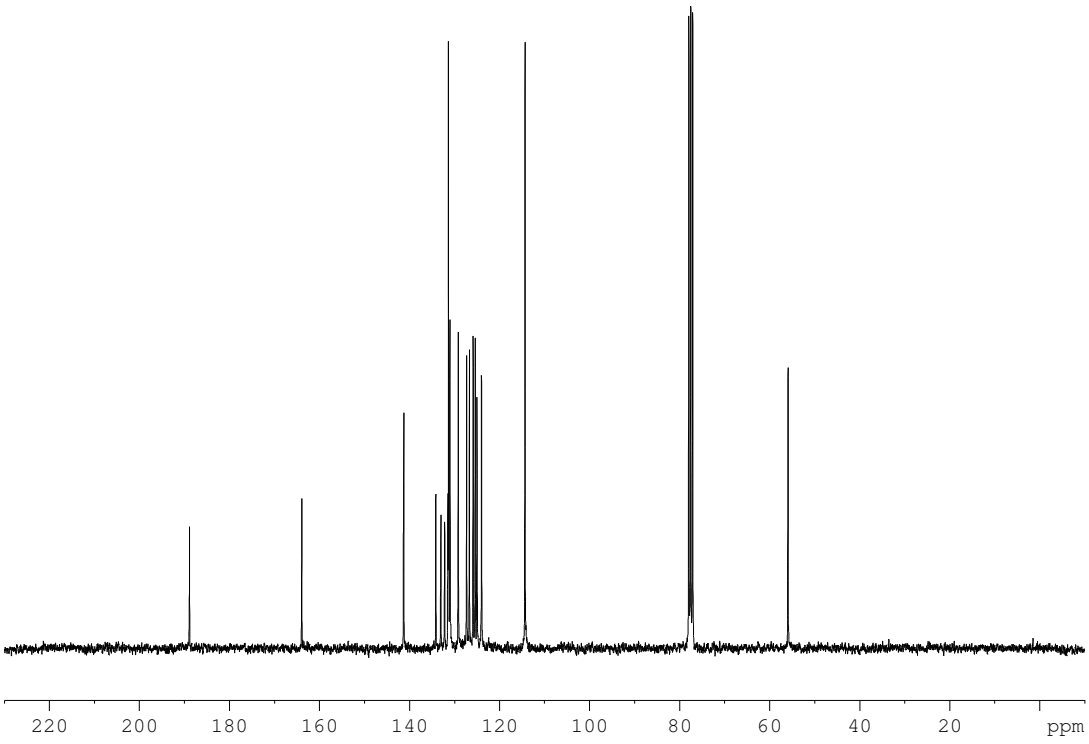
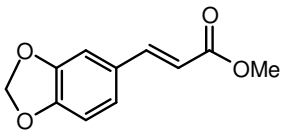


Table 3, 15b/Entry-15, ^{1}H NMR (in $CDCl_3$)



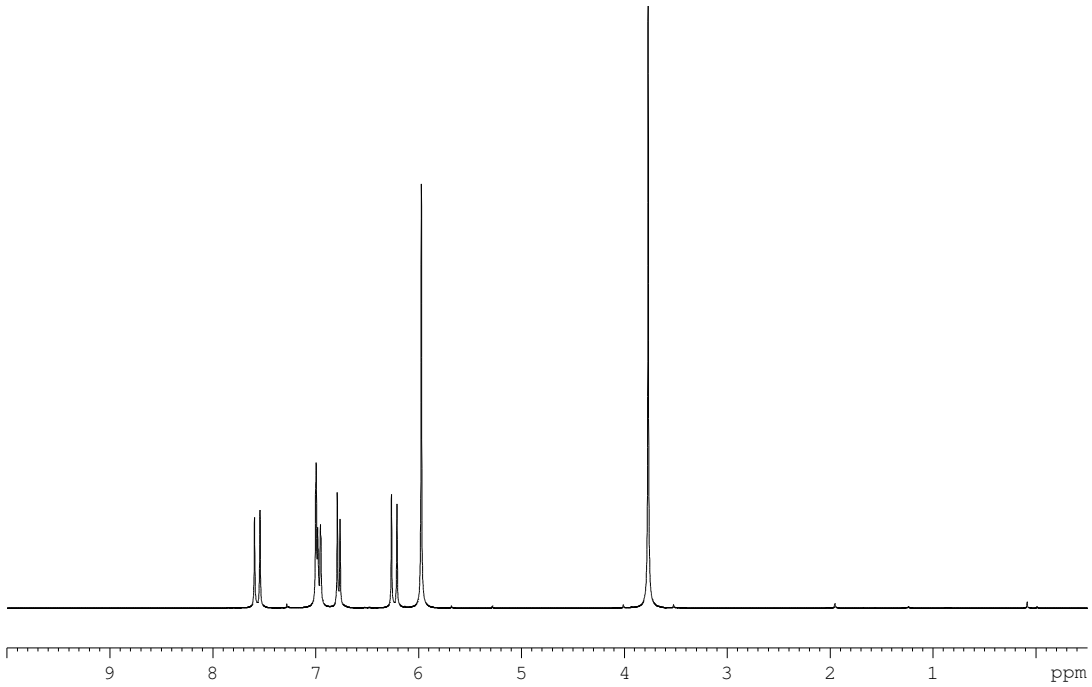
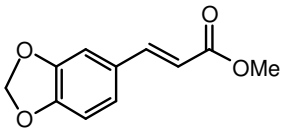


Table 3, 15b/Entry-15, ^{13}C NMR (in $CDCl_3$)



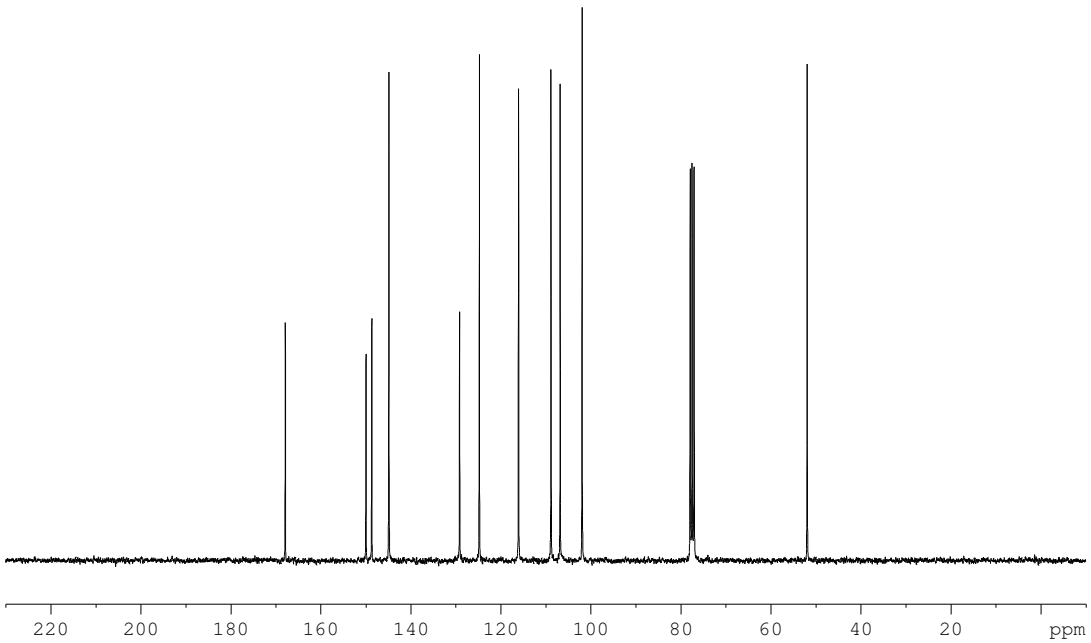
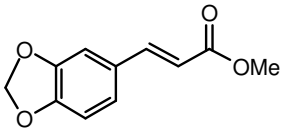


Table 3, 15b/Entry-15, HRMS spectrum



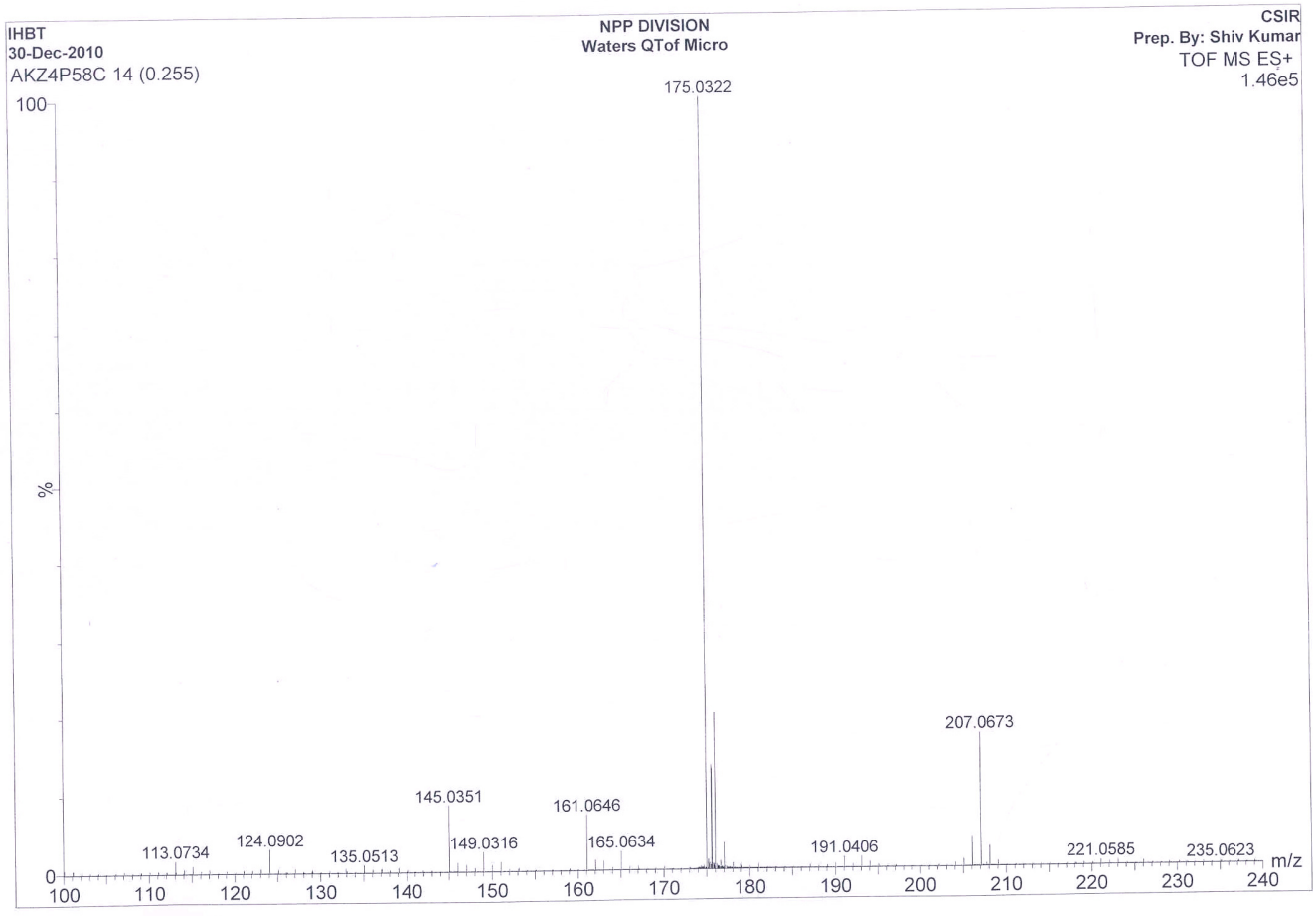
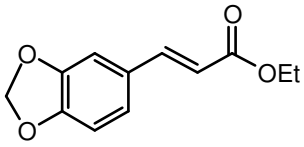


Table 3, 16b/Entry-16, ^{1}H NMR (in $CDCl_3$)



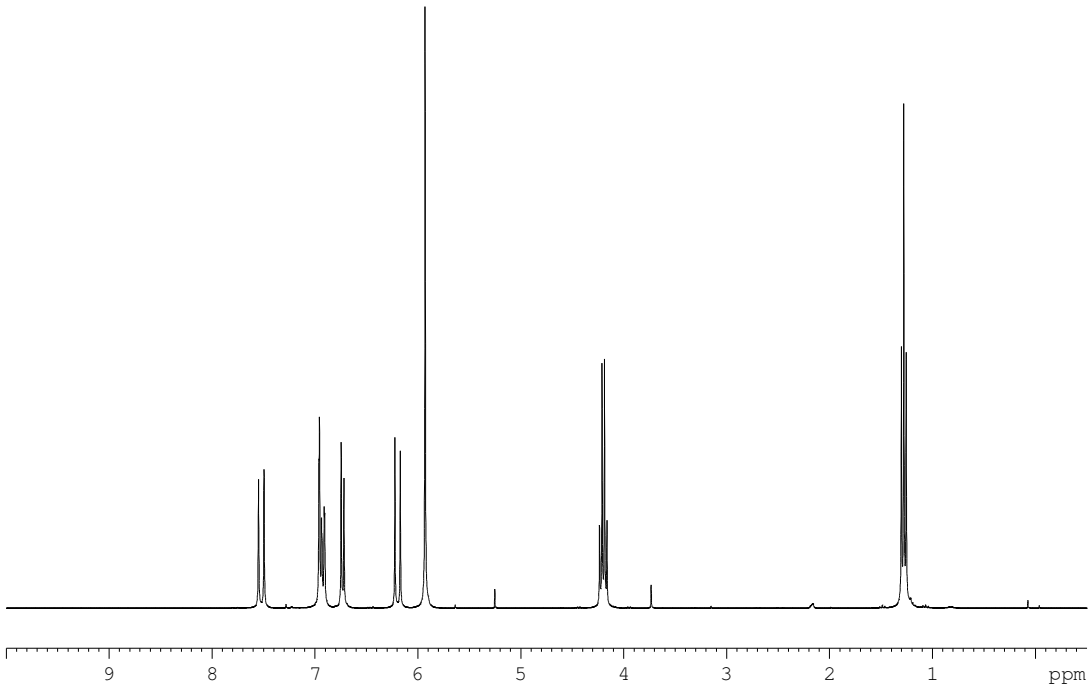
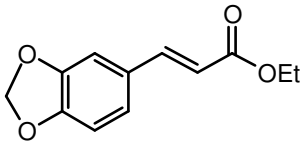


Table 3, 16b/Entry-16, ^{13}C NMR (in $CDCl_3$)



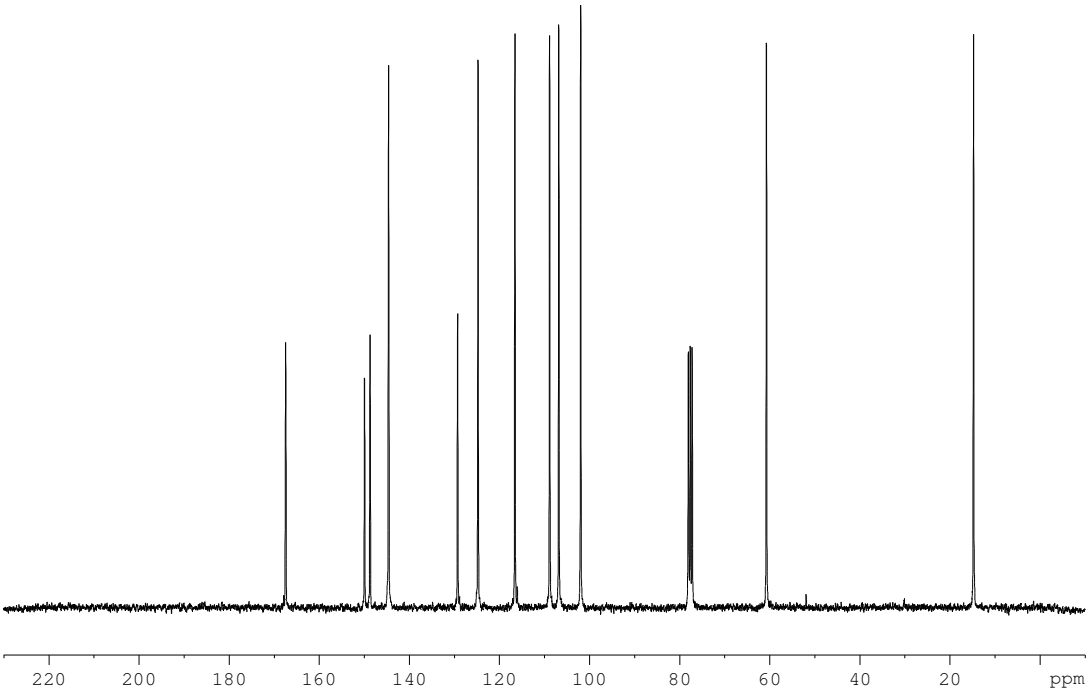
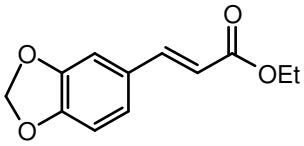


Table 3, 16b/Entry-16, HRMS spectrum



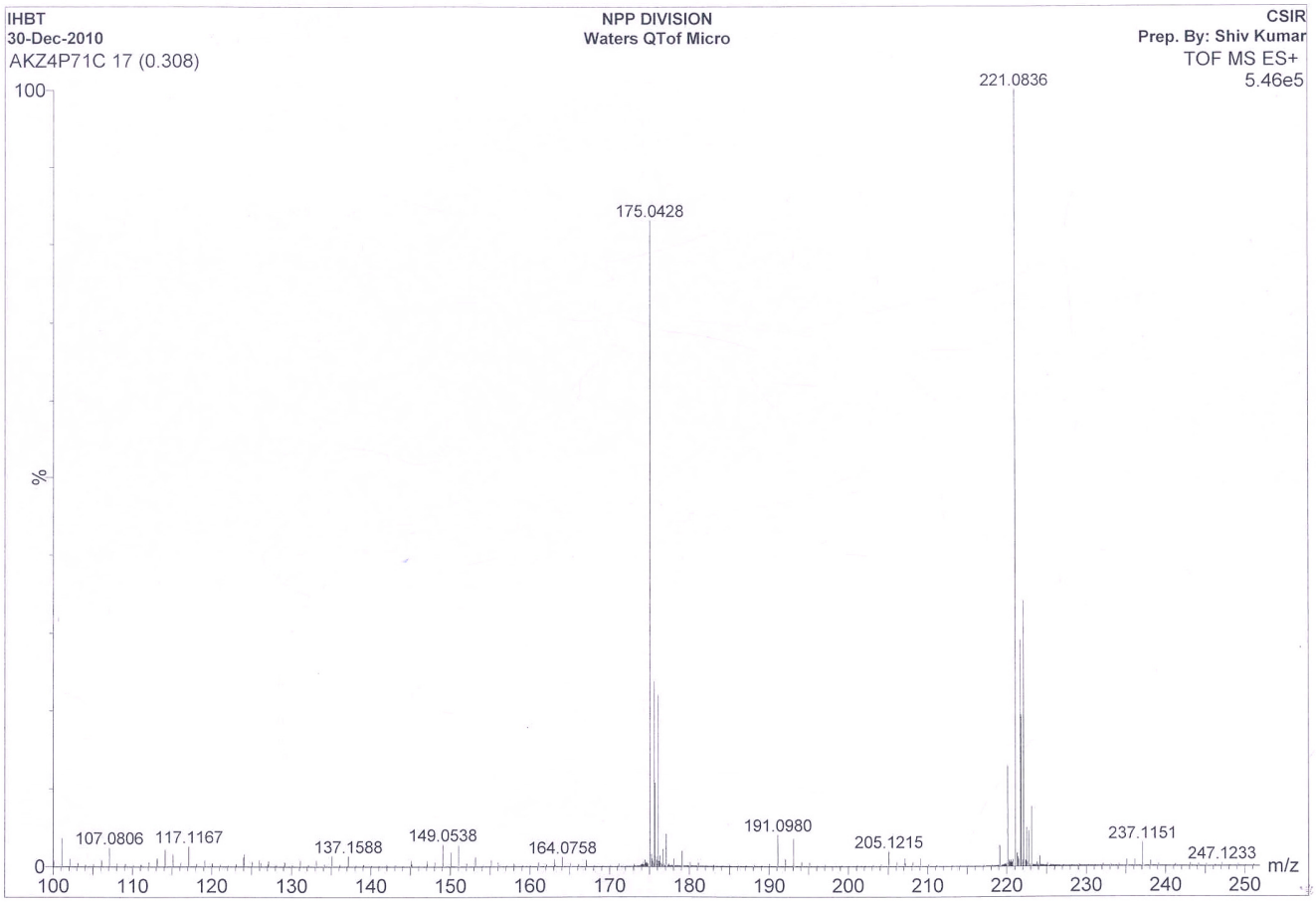
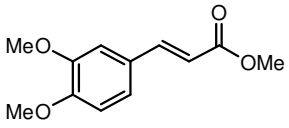


Table 3, 17b/Entry-17, ^{1}H NMR (in $CDCl_3$)



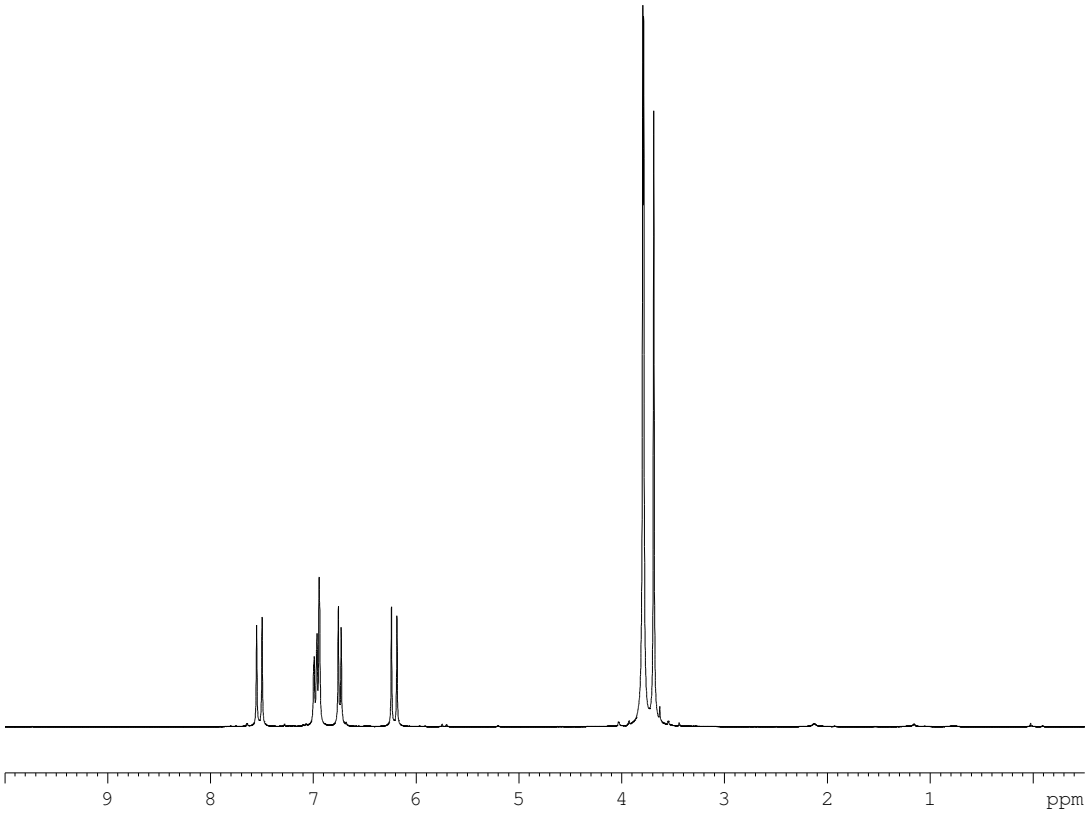
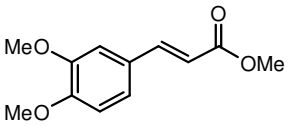


Table 3, 17b/Entry-17, ^{13}C NMR (in $CDCl_3$)



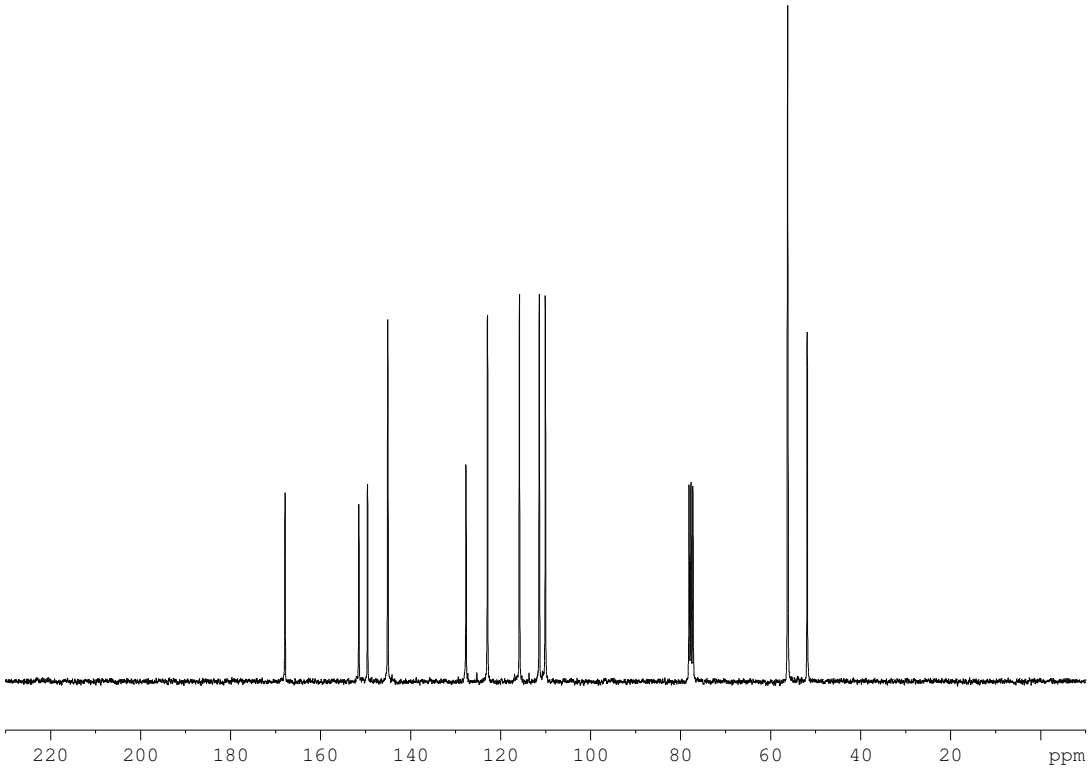
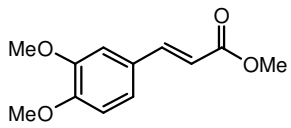


Table 3, 17b/Entry-17, HRMS spectrum



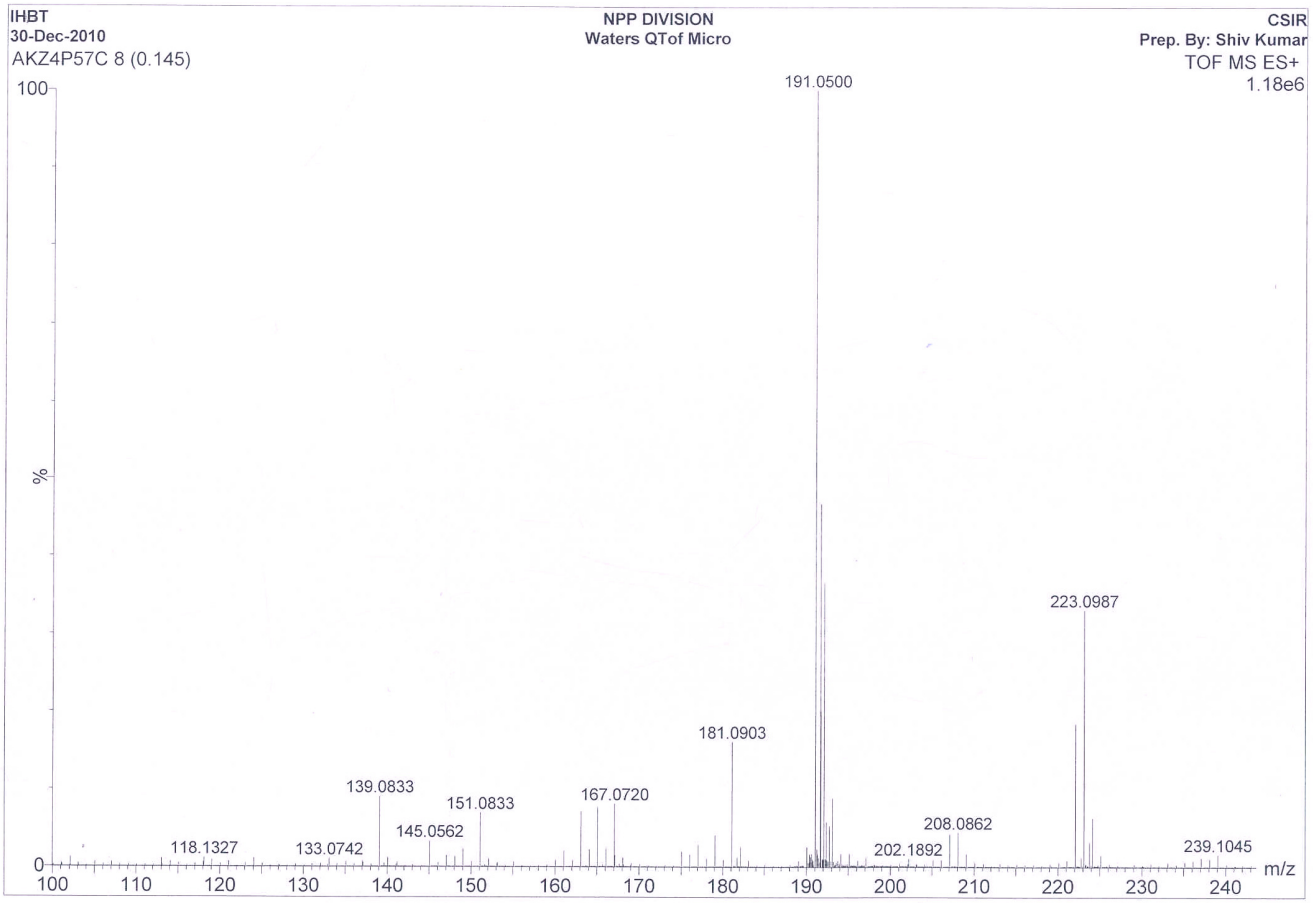
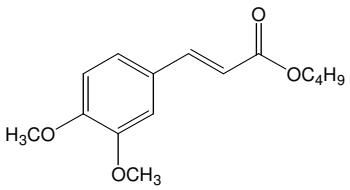


Table 3, 18b/Entry-18, ^{1}H NMR (in $CDCl_3$)



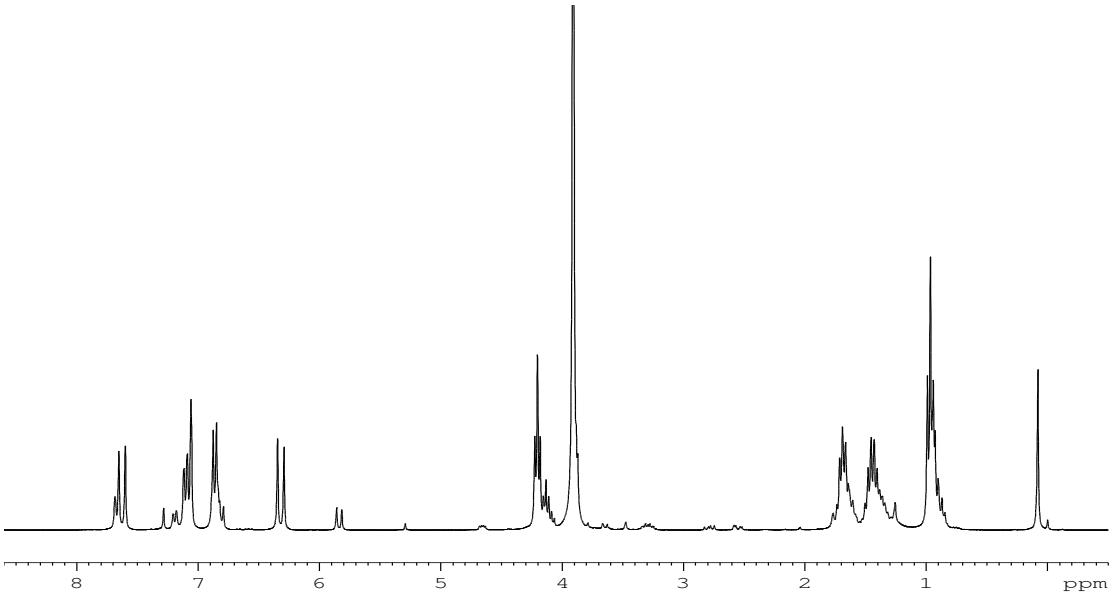
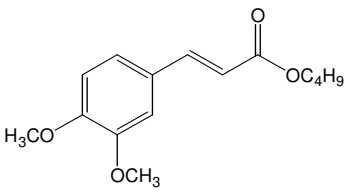


Table 3, 18b/Entry-18, ^{13}C NMR (in $CDCl_3$)



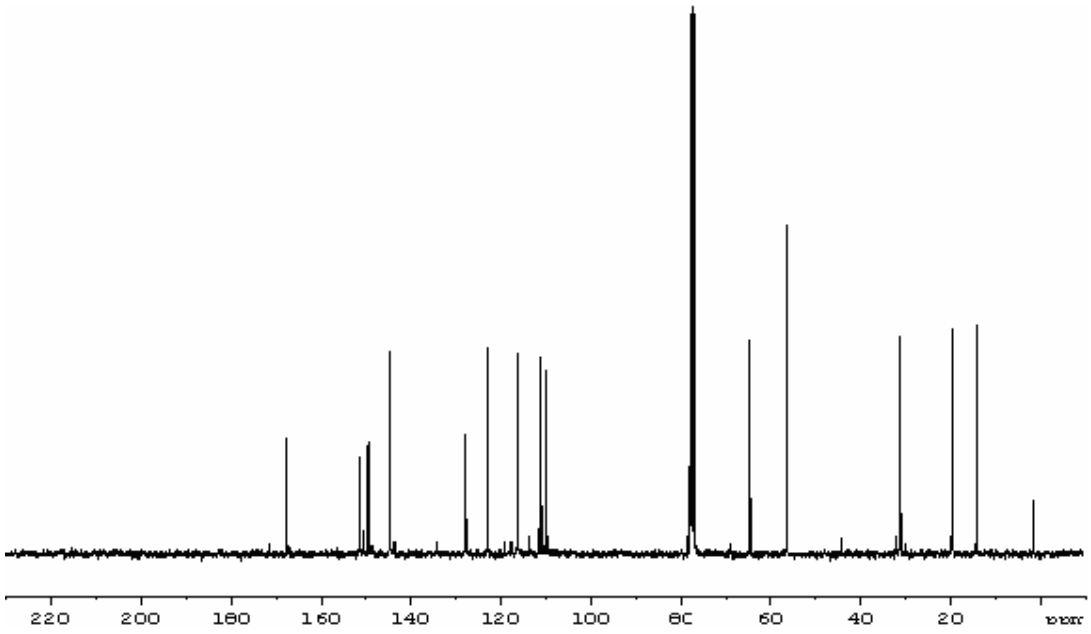
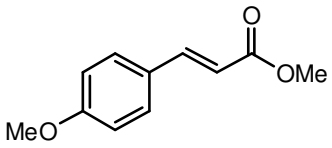


Table 3, 19b/Entry-19, ^{1}H NMR (in $CDCl_3$)



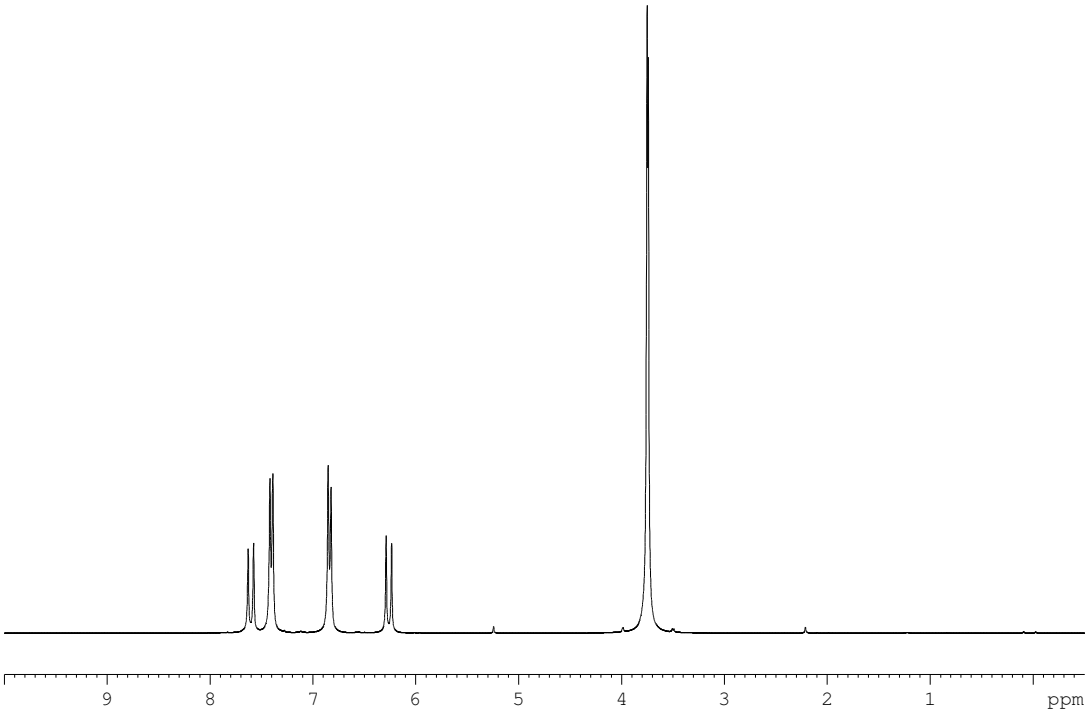
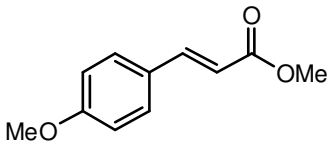


Table 3, 19b/Entry-19, ^{13}C NMR (in $CDCl_3$)



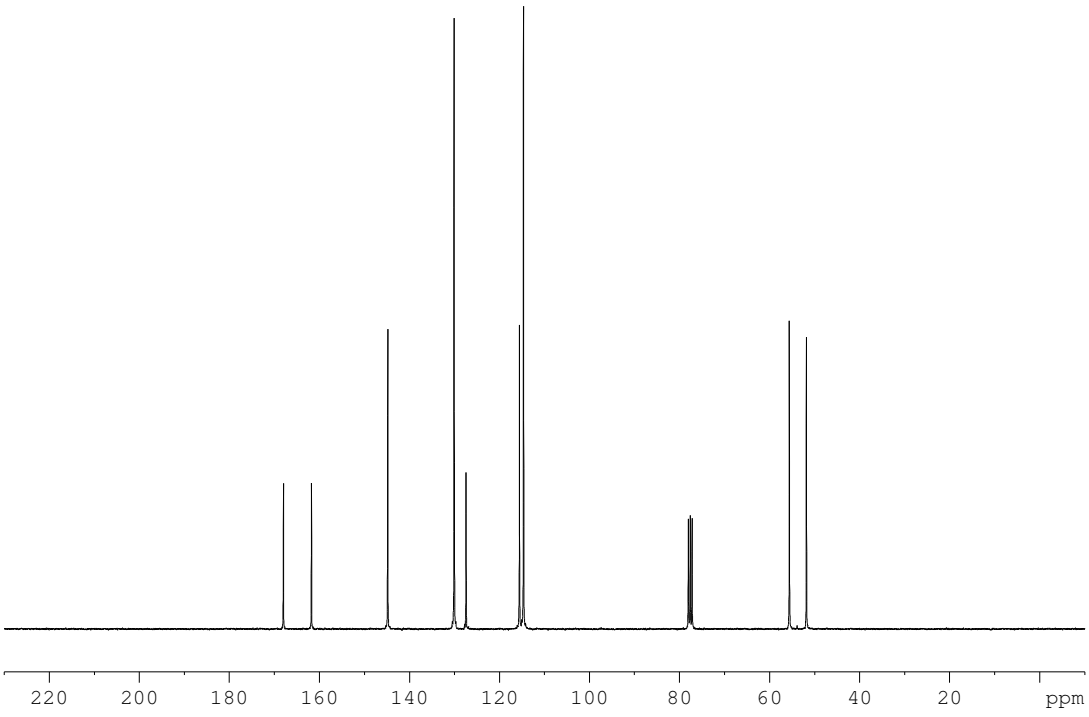
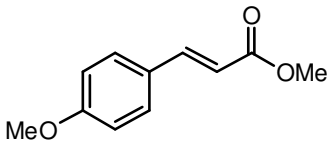


Table 3, 19b/Entry-19, HRMS spectrum



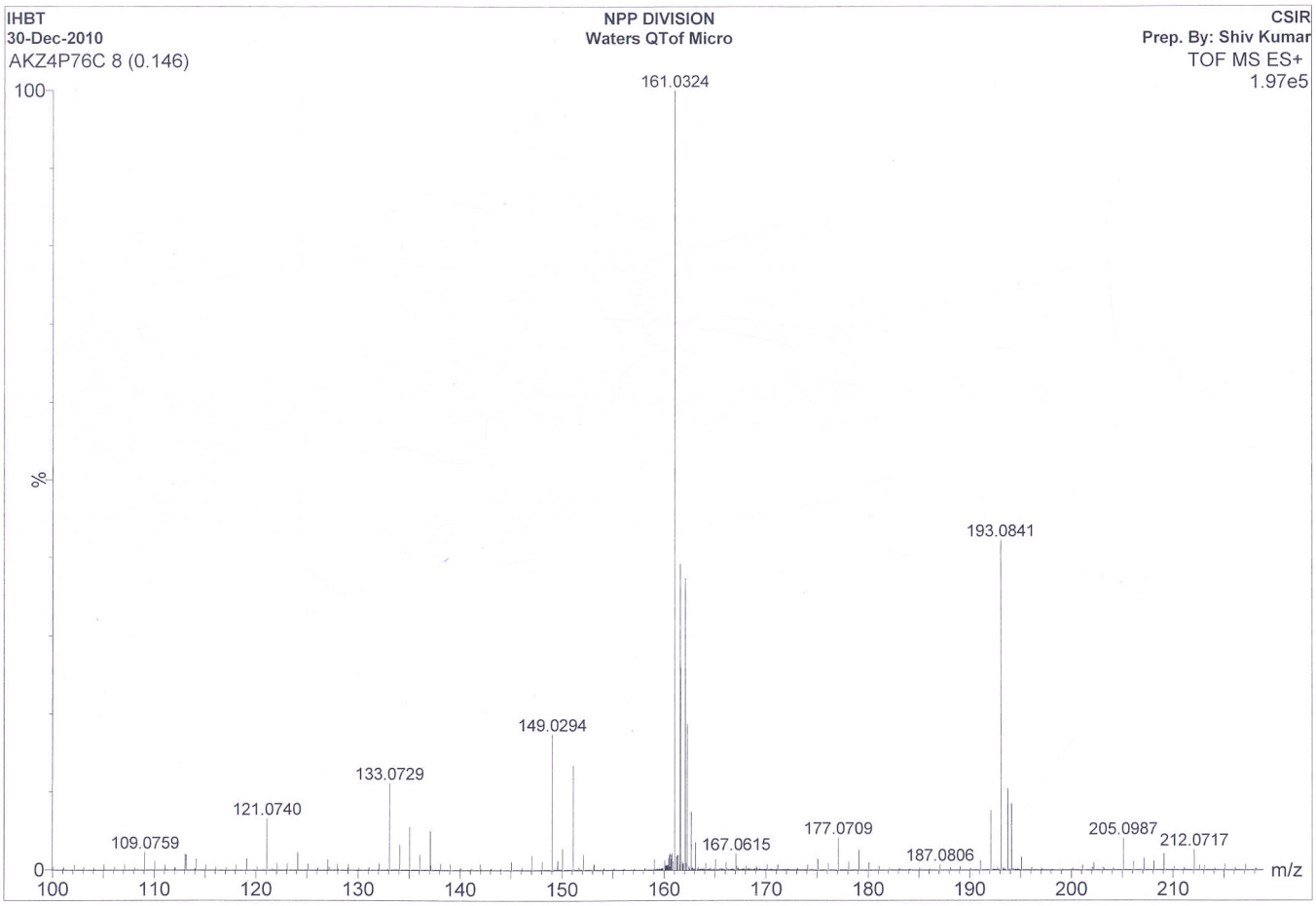
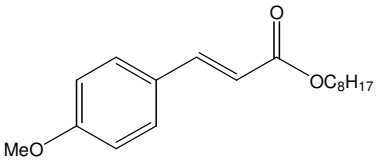


Table 3, 20b/Entry-20, ^{1}H NMR (in $CDCl_3$)



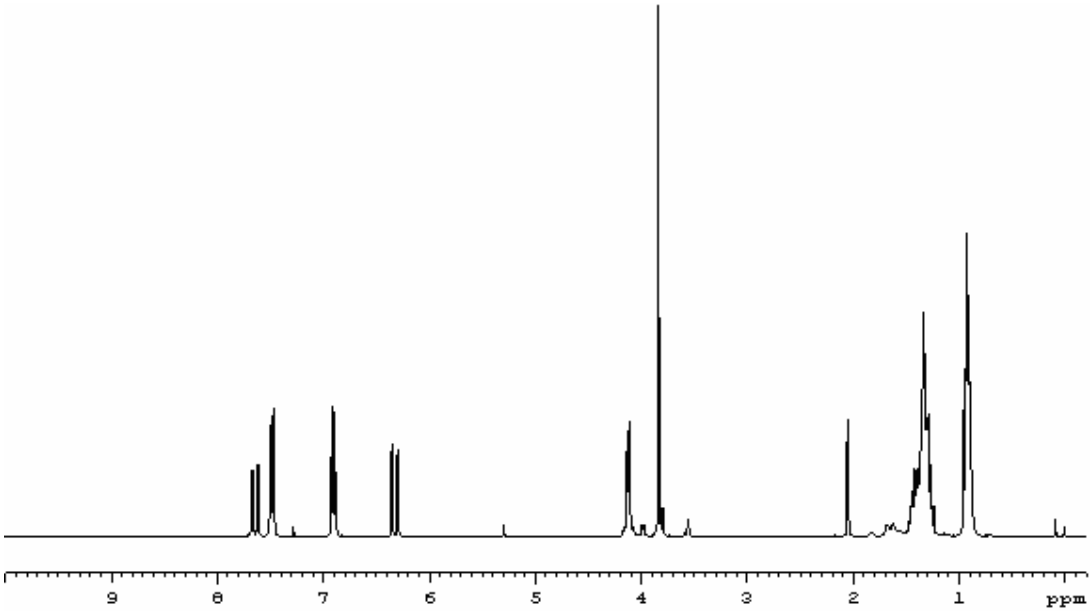
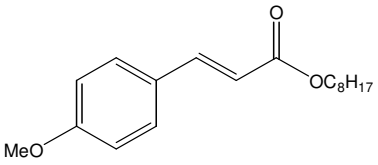
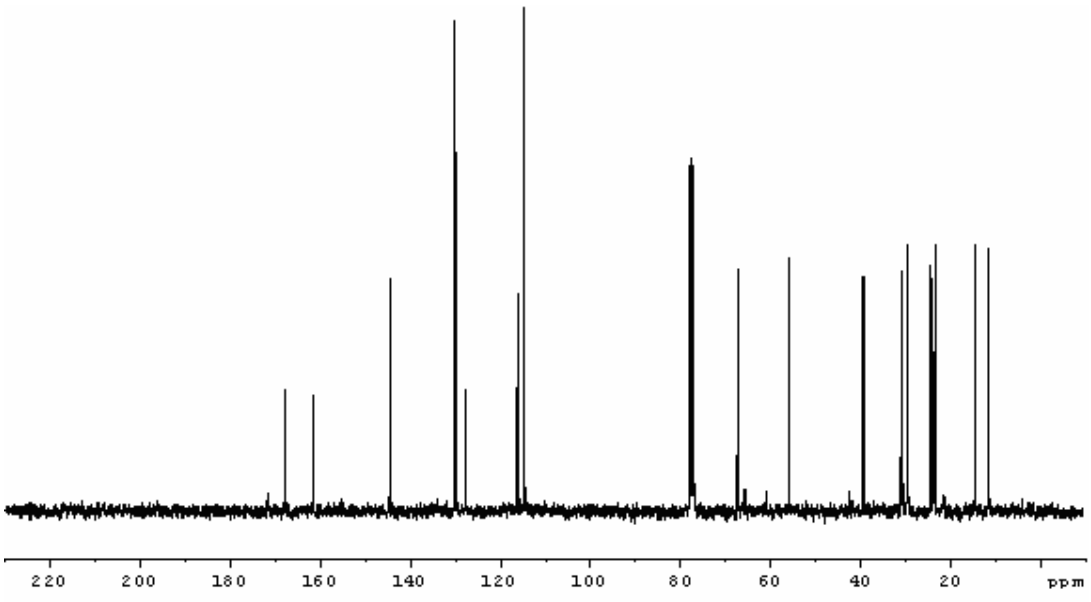
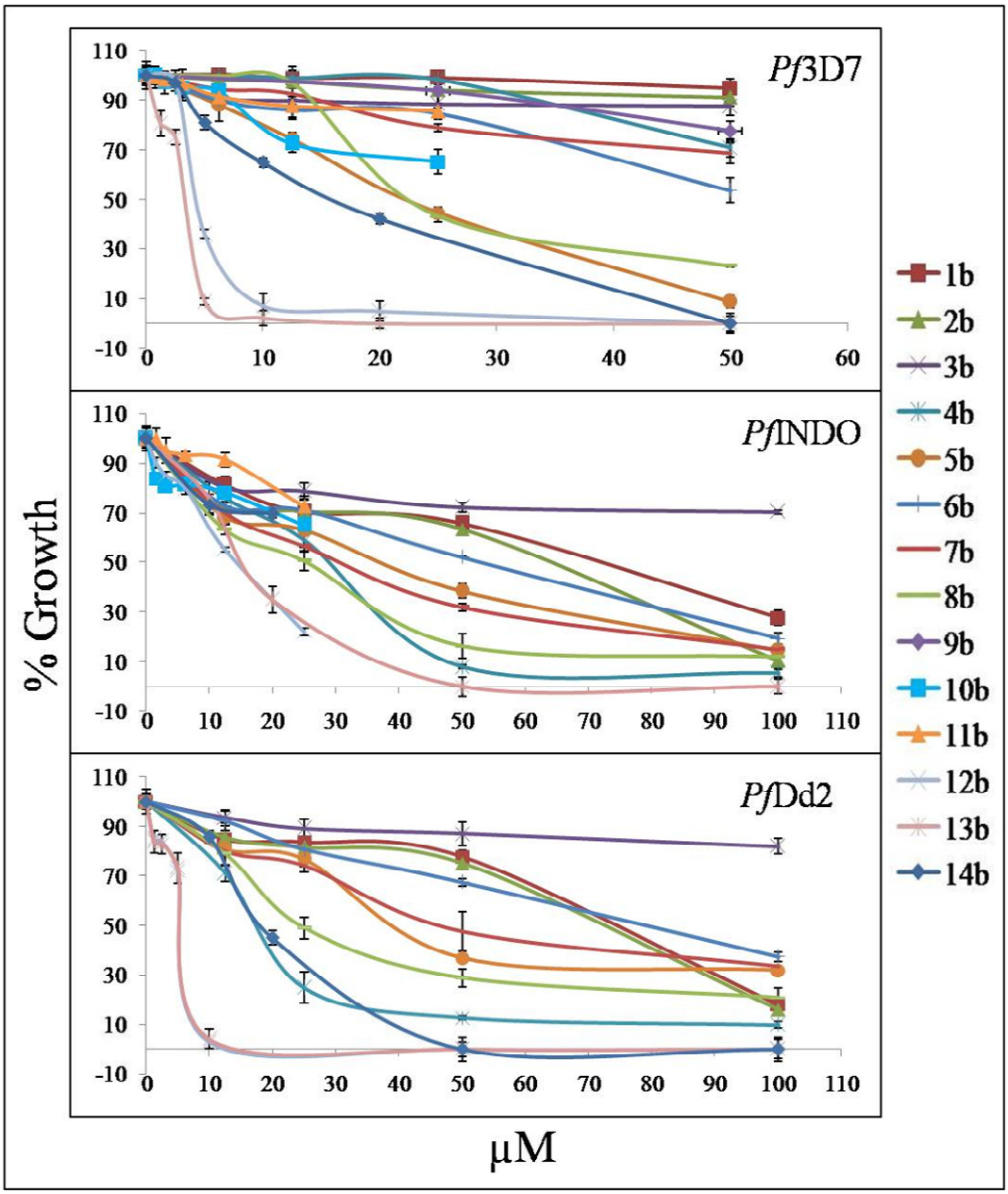


Table 3, 20b/Entry-20, ^{13}C NMR (in $CDCl_3$)







Supplementary Fig: Dose dependent inhibition by diaryldienone and enone compounds of the growth of malaria parasite in red blood cell culture as measured by SYBR Green fluorescence assay. Compound numbers and the corresponding color codes are indicated in the strip on the right. Standard deviation bars at each data point have been calculated from triplicate observations. *Pf*3D7 is Chloroquine sensitive while *Pf*Indo & *Pf*Dd2 are Chloroquine resistant strains of *Plasmodium falciparum.*