Supplementary Information

Direct Olefination of Benzaldehydes into Hydroxy Functionalized Oligo (*p*-phenylenevinylene)s via Pd-Catalyzed Heterodomino Knoevenagel-decarboxylation-Heck sequence and its Application for Fluoride Sensing π-Conjugated Units

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Experimental Section:

Materials

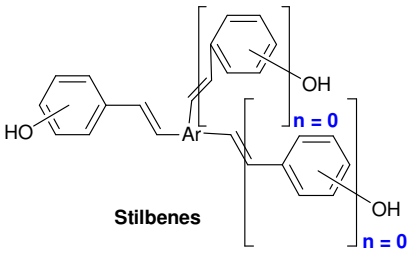
All the starting materials were reagent grade and purchased from Merck or Aldrich. The palladium catalysts were purchased from Acros, Aldrich and Merck and used as such. The aryl halides and all other reagents were obtained from commercial sources (Merck, Lancaster). All reactions were carried out in air. 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). Tetrabutyl ammonium salts were obtained from Lancaster. HPLC grade acetonitrile (J. T. Baker) was used as solvent for all UV-vis and Fluorescence experiments.

Apparatus:

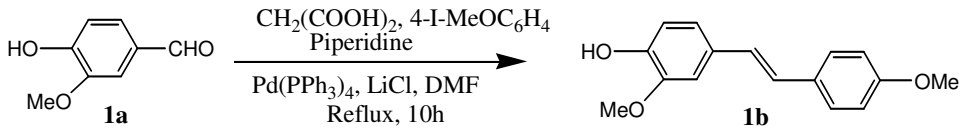
^{1}H (300 MHz) and ^{13}C (75.4 MHz) NMR spectra were recorded on a Bruker Avance-300 spectrometer. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet. The ^{13}C NMR spectra are proton decoupled. The melting points were determined on a digital Barnsted Electrothermal 9100 apparatus and are uncorrected. The U.V-vis absorption spectra were obtained on a Shimadzu UV-2450 PC spectrophotometer using a quartz cell of 1 cm path length. Fluorescence measurements were carried out on a Cary Eclipse fluorescence spectrophotometer with 5 nm slit for both excitation and emission. HPLC analysis was carried out on a Waters 600E system equipped with a photodiode array detector (Waters 2996) using a Merck Purosphere RP 18C (250 x 4.6 mm, 5µm) column at 25^{o}C using 0.05% TFA, MeOH: MeCN solvent gradient. HRMS-ESI spectra were determined using micromass Q-TOF ultima spectrometer and reported as m/z (relative intensity). The visualization of TLC especially in synthesis of Di and Tristyrylbenzenes was best monitored under U V chamber.

General procedure:

Representative procedure for domino olefination of benzaldehydes into hydroxy stilbenes:



Synthesis of 4-hydroxy- 3, 4′-dimethoxystilbene (Table 2, 1b):



Malonic acid (0.64 g, 6.15 mmol) was taken in a round bottom flask and piperidine (0.45 ml, 4.6 mmol) added gradually. The above mixture was stirred in DMF (15 ml) for 2 min. at room temperature. Thereafter, 4-hydroxy-3-methoxybenzaldehyde (1a, 0.23 g, 1.51 mmol), 4-iodoanisole (0.2 g, 0.85 mmol), $Pd(PPh_3)_4$ (0.029 g, 0.025 mmol), piperidine (0.26 ml, 3.1 mmol) and LiCl[1] (0.003 g, 0.07 mmol) were added, and the reaction mixture allowed to reflux for 10 hours. The above mixture was cooled to room temperature and filtered through celite. The filtrate was poured into water (100 ml, acidified with dil HCl, pH= 5-6) and extracted with ethyl acetate (2x40 ml). The combined organic layer was washed with water (1x30 ml), brine (1x10 ml), dried over Na_2SO_4 and vacuum evaporated. The obtained residue was subsequently purified by column chromatography on Silicagel (60-120 mesh size) using hexane-ethylacetate (9.5: 0.5) to give a solid which was further recrystallised in methanol to provide pure 4-hydroxy- 3, 4′-dimethoxystilbene **1b** as a white solid (0.123 g, 56 % yield),[2] m.p. 161-164 °C (lit. m.p. 163-166 °C)[3], R_f 0.34 (hexane:ethylacetate:: 8:2), ^{1}H NMR ($CDCl_3$, 300MHz), δ (ppm) 7.34 (2H, d, *J* = 8.2 Hz), 6.92-6.89 (2H, m), 6.80-6.78 (5H, m), 5.56 (1H, s), 3.84 (3H, s), 3.73 (3H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$), δ (ppm) 160.0, 147.6, 146.2, 131.2, 128.3, 127.6, 127.1, 121.1, 115.4, 115.1, 109.1, 56.2 and 56.0.

The above procedure was also followed for the synthesis of other stilbenes (Table 2, 2b-11b)

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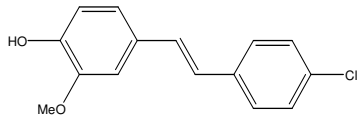
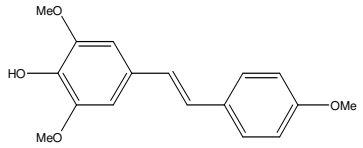
1. The use of LiCl as additive was found to improve the domino reaction as it significantly reduced the formation of regioisomeric α-arylated product. Similar findings have also been observed in several earlier reports; see Ebran, et al. *J. Am. Chem Soc.* 2007, **129**, 6931.
2. The corresponding two step-two pot approach- synthesis of styrene (60% yield) and its heck coupling with iodoanisole (40% yield) provided **1b** in overall 24% yield in our hands.
3. A. K. Sinha, V. Kumar, A. Sharma and A. Sharma, *Tetrahedron*, 2007, ***63***, 11070.

4-Chloro-4'-hydroxy-3'-methoxystilbene (2b, Table 2):



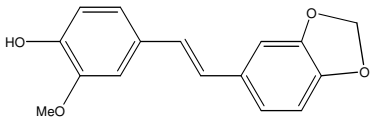
White solid, m.p. 119-122 °C (lit. m.p. 121-124)[3], R_f 0.35 (hexane:ethylacetate:: 8:2), ^{1}H NMR ($CDCl_3$, 300MHz), δ (ppm) 7.32 (2H, d, *J* = 8.4 Hz), 7.23 (2H, d, *J* = 8.4 Hz), 6.97-6.93 (3H, m), 6.86-6.82 (2H, m), 5.70 (1H, s), 3.86 (3H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$), δ (ppm) 147.0, 146.2, 136.7, 132.8, 129.8, 129.5, 128.8, 127.7, 125.7, 120.9, 114.9, 108.7 and 55.9.

4-Hydroxy-3,4',5-trimethoxy stilbene (3b, Table 2):



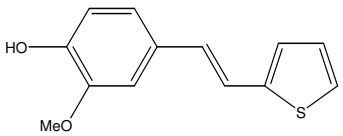
White solid, m.p. 96-98 °C, R_f 0.35 (hexane:ethylacetate:: 8:2), ^{1}H NMR ($CDCl_3$, 300MHz), δ (ppm) 7.46 (2H, d, *J* = 6.9 Hz), 6.98-6.90 (4H, m), 6.75 (2H, s), 5.60 (1H, s), 3.96 (6H, s), 3.85 (3H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$), δ (ppm) 159.2, 147.3, 134.6, 130.3, 129.4, 127.5, 126.9, 126.5, 114.2, 103.2, 56.4 and 55.4.

4-Hydroxy-3-methoxy, 3'4'-dioxymethylenestilbene (4b, Table 2):



White solid, m.p 153-156 °C, R_f 0.27 (hexane:ethylacetate:: 8:2), ^{1}H NMR (CD_3COCD_3, 300MHz), δ (ppm) 7.63 (1H, s), 7.10 (2H, d, *J* = 19.3 Hz), 6.97-6.91 (4H, m), 6.79 (2H, d, *J* = 8.0 Hz), 5.96 (2H, s), 3.85 (3H, s); ^{13}C NMR (75.4 MHz, CD_3COCD_3), δ (ppm) 148.3, 147.7, 147.0, 146.5, 132.5, 129.7, 127.1, 125.6, 120.9, 120.0, 115.0, 109.1, 108.2, 105.0, 100.8 and 55.3. HRMS-ESI: m/z $[M+H]^+$ for $C_{16}H_{14}O_4$, calculated 271.0965; observed 271.0951.

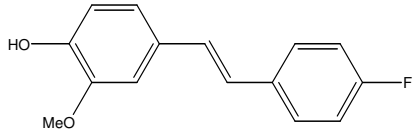
2-(4-hydroxy-3-methoxystyryl)thiophene (5b, Table 2):



Reddish yellow viscous solid, R_f 0.37 (hexane:ethylacetate:: 8:2), ^{1}H NMR ($CDCl_3$, 300MHz), δ (ppm) 7.19 (1H, s), 7.15 (1H, d, *J* = 14.2 Hz), 7.06-7.01 (4H, m), 6.95-6.86 (2H, m), 5.75 (1H, s), 3.95 (3H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$), δ (ppm)

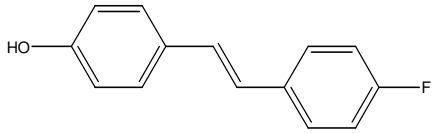
146.8, 145.7, 143.2, 129.7, 128.5, 127.7, 125.5, 123.9, 120.3, 119.8, 114.7, 108.2 and 56.0. HRMS-ESI: m/z $[M+H]^+$ for $C_{13}H_{12}O_2S$, calculated 233.0631; observed 233.0631.

4-Fluoro-4'-hydroxy-3'-methoxystilbene (6b, Table 2):



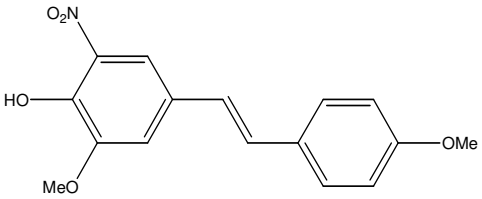
White solid, m.p. 128-130 °C, R_f 0.34 (hexane:ethylacetate:: 8:2), ^{1}H NMR ($CDCl_3$, 300MHz), δ (ppm) 7.47 (2H, t, *J* = 6.0 Hz), 7.07-7.03 (4H, m), 6.93-6.90 (3H, m), 5.70 (1H, s), 3.95 (3H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$), δ (ppm) 147.1, 146.1, 134.2, 130.2, 128.9, 127.6, 120.8, 116.1, 115.8, 115.0, 108.6 and 56.3. HRMS-ESI: m/z $[M+H]^+$ for $C_{15}H_{13}O_2F$, calculated 245.0972; observed 245.0945.

4-Fluoro-4'-hydroxystilbene (7b, Table 2):



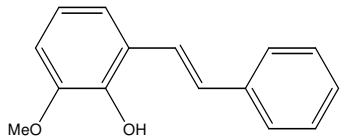
White solid, R_f 0.35 (hexane:ethylacetate:: 8:2), m.p. 195-196 °C, ^{1}H NMR ($CDCl_3$, 300MHz), 7.47-7.38, (4H, m), 7.27 (1H, s), 7.07-7.01 (2H, t, *J* = 8.9 Hz), 6.95 (2H, s), 6.83 (2H, d, *J* = 8.9 Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$), δ (ppm) 155.6, 130.6, 128.2, 125.9, 116.0 and 115.8, HRMS-ESI: m/z $[M+H]^+$ for $C_{14}H_{11}OF$, calculated 215.0867; observed 215.0836.

4-Hydroxy-3,4′-dimethoxy-5-nitrostilbene (8b, Table 2):



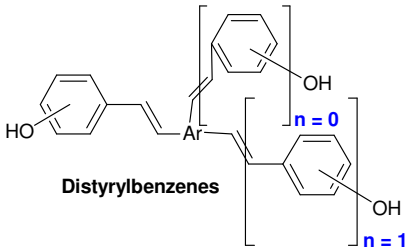
Orange solid, R_f 0.7 (hexane:ethylacetate:: 7:3), m.p. 139-142 °C ^{1}H NMR ($CDCl_3$, 300MHz), δ (ppm) 10.78 (1H, s), 7.77 (1H, s), 7.44 (2H, d, *J* = 8.0 Hz), 7.26(1H, s), 5.75 (1H, d, *J* = 16.2 Hz), 6.90-6.83 (3H, m), 4.0 (3H, S), 3.8 (3H, S); ^{13}C NMR (75.4 MHz, $CDCl_3$), δ (ppm) 160.8 151.2, 146.7, 135.1, 130.5, 130.3, 128.9, 125.1, 116.0, 115.3, 114.6, 57.8.2 and 56.4. HRMS-ESI: m/z $[M+H]^+$ for $C_{16}H_{15}O_5N$, calculated 302.1023; observed 302.0994.

2-Hydroxy-3-methoxystilbene (9b, Table 2):

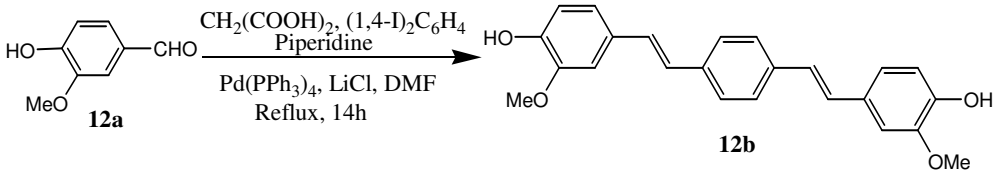


White solid, m.p. 88–91 °C (lit. m.p. 85-87 °C),[3] R_f 0.45 (hexane:ethylacetate:: 8:2), ^{1}H NMR ($CDCl_3$, 300MHz) δ (ppm) 7.50 (2H, d, *J* = 7.6 Hz), 7.42 (1H, d, *J* = 16.2 Hz), 7.33 (1H, d, *J* = 16.2 Hz), 7.28 (1H, t, *J* = 7.6 Hz), 7.25–7.18 (3H, m), 6.78 (1H, t, *J* =7.6 Hz), 6.71 (1H, d, *J* = 7.6 Hz), 5.93 (1H, s), 3.82 (3H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$), δ (ppm) 146.2, 143.0, 137.3, 128.7, 128.1, 126.8, 126.0, 123.2, 122.3, 119.1, 118.2, 108.9 and 55.9.

Representative procedure for palladium catalyzed one step olefination of hydroxy benzaldehydes into Di and Tri styrylbenzenes



i) Synthesis of ((*E*,*E*)-1,4-Bis(4-hydroxy-3-methoxy)styrylbenzene (Table 3, 12b) (*no requirement of column purification*):

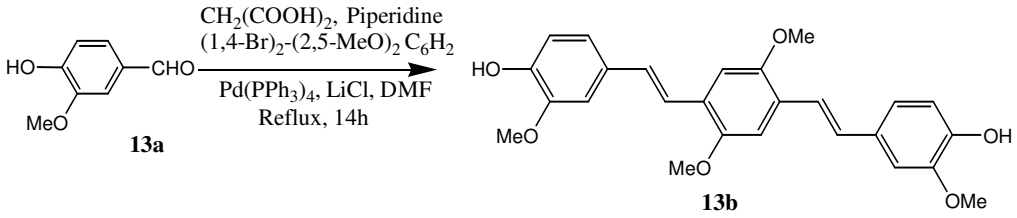


Malonic acid (4.5 g, 43.2 mmol) was taken in a round bottom flask and piperidine (3.2 ml, 32.9 mmol) added gradually. The above mixture was stirred in DMF (30 ml), for 2 min. at room temperature. Thereafter, 4-hydroxy-3-methoxy benzaldehyde (0.83 g, 5.4 mmol), 1,4-diiodobenzene (0.5 g, 1.51 mmol), $Pd(PPh_3)_4$ (0.105 g, 0.09 mmol), Piperidine (2.1 ml, 21.1 mmol) and LiCl (0.01 g, 0.24 mmol) were added and the reaction mixture allowed to reflux for 14 hours. The above mixture was cooled to room temperature and filtered through celite. The filtrate was poured into water (250ml, acidified with dil HCl, pH= 5) upon which the crude residue precipitated. The above residue was filtered under vacuum to give a solid which was washed with hot water (1x20 ml), hot hexane (2x10 ml) then diethylether (10ml). A suspension of this resultant solid was stirred in methanol (10 ml), for 30 min and filtered to provide pure ((*E*,*E*)-1,4-Bis(4-hydroxy-3-methoxy)styrylbenzene **12b** as grey solid (0.39 g, 68% yield), m.p 266-270 °C, ^{1}H NMR (DMSO, 300MHz), δ (ppm) 9.16 (2H, s), 7.52 (4H, s), 7.20 (2H, s), 7.18-7.02 (4H, d, *J* = 13.5 Hz), 7.01 (2H, d, *J* = 8.2 Hz), 6.79 (2H, d, *J* = 8.2 Hz), 3.83 (6H, s); ^{13}C NMR (75.4 MHz, DMSO), δ (ppm) 148.3,

147.1, 136.7, 129.2, 128.8, 127.4, 125.5, 120.6, 116.8, 110.2 and 55.3. HRMS-ESI: m/z $[M+H]^+$ for $C_{24}H_{22}O_4$, calculated 375.1591; observed 375.1591.

The above procedure was also followed for the synthesis of 14b, 17b and 19b.[4]

ii) Synthesis of (*E*,*E*)-1,4-Dimethoxy-2,5-bis(4-hydroxy-3-methoxy)styryl-benzene (Table 3, 13b) *(with column purification)*:



Malonic acid (5.0 g, 48 mmol) was taken in a round bottom flask and piperidine (3.6 ml, 36.2 mmol) added gradually. The above mixture was stirred in DMF (30 ml), for 2 min. at room temperature. Thereafter, 4-hydroxy-3-methoxy benzaldehyde (0.92 g, 6 mmol), 1,4-dibromro-2,5-dimethoxybenzene (0.5 g, 1.7 mmol), $Pd(PPh_3)_4$ (0.12 g, 0.10 mmol), Piperidine (2.4 ml, 24.2 mmol) and LiCl (0.012 g, 0.26 mmol) were added and the reaction mixture allowed to reflux for 14 hours. The above mixture was cooled to room temperature and filtered through celite. The filtrate was poured into water (250ml, acidified with dil HCl, pH= 5) and extracted with ethyl acetate (3x50 ml). The combined organic layer was washed with water (1x50 ml), brine (1x20 ml), dried over Na_2SO_4 and vacuum evaporated. The resultant residue was subsequently purified by column chromatography on Silicagel (60-120 mesh size) using hexane-ethylacetate (6:4) and obtained solid was washed with methanol to provide pure (*E*,*E*)-1,4-Dimethoxy-2,5-bis(4-hydroxy-3-methoxy)styryl-benzene **13b** as a yellowish green solid (0.365 g, 50 % yield), m.p 245-248 °C, ^{1}H NMR (DMSO, 300MHz), δ (ppm) 9.17 (2H, s), 7.24-7.21 (6H, d, *J* = 10.4 Hz), 7.13 (2H, s), 7.00 (2H, s), 6.79 (2H, s), 3.89 (6H, s), 3.84 (6H, s); ^{13}C NMR (75.4 MHz, DMSO), δ (ppm) 150.7, 147.7, 146.5, 129.1, 125.6, 119.6, 115.7, 110.0, 108.8, 56.0 and 55.5. HRMS-ESI: m/z $[M+H]^+$ for $C_{26}H_{26}O_6$, calculated 435.1802; observed 435.1800.

The above procedure was also followed for the synthesis of 15b, 16b and 18b

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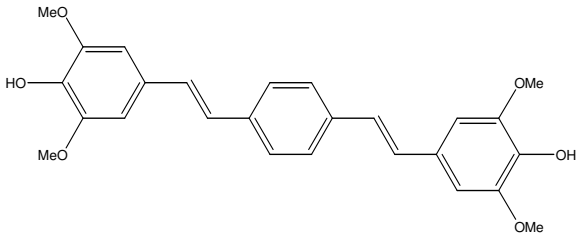
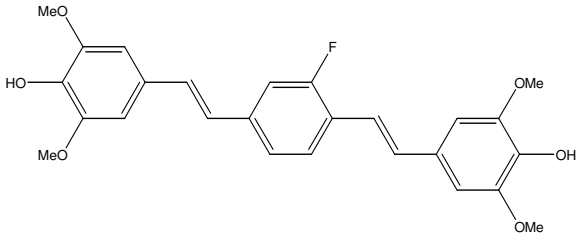
4. The 48 % yield in case of **19b** (Table 2, entry 19) compares well with the reported yield obtained via (a) two step protocol involving heck coupling of 1,4 dibromobenzene (32% yield) and deprotection (50% yield) see: Bayly *et al*, *J. Chem. Soc. Dalton Trans.*, 2001, 1401. (b) four step wittig approach comprising halogenation of xylene (58% yield), phosphonation (85% yield using Sato's method - *Eur. J. Med. Chem.* 2004, **39**, 573), wittig olefination (91% yield) and deprotection (68% yield)- (see Flaherty, et al *J. Med. Chem.* 2007, **50**, 4986).

((*E*,*E*)-1,4-Bis(4-hydroxy-3,5-dimethoxy)styrylbenzene (14b, Table 3):



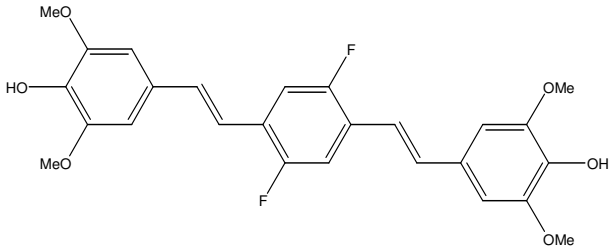
Greenish brown solid, m.p 246-250 °C, ^{1}H NMR (DMSO, 300MHz), δ (ppm) 8.45 (2H, s), 7.46 (4H, s), 7.06 (2H, d, *J* = 16.4 Hz), 7.05 (2H, d, *J* = 16.4 Hz), 6.82 (4H, s), 3.74 (12H, s); ^{13}C NMR (75.4 MHz, DMSO), δ (ppm) 148.6, 136.8, 136.3, 129.1, 128.1, 125.9, 124.6, 104.7 and 55.7. HRMS-ESI: m/z $[M+H]^+$ for $C_{26}H_{26}O_6$, calculated 435.1802; observed 435.1828.

(*E*,*E*)-2-Fluoro-1,4-bis(4-hydroxy-3,5-dimethoxy)styryl-benzene (15b, Table 3):



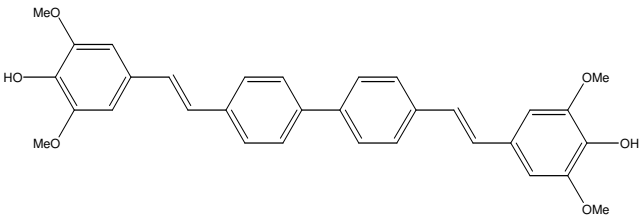
Yellow solid, m.p 225-227 °C, ^{1}H NMR (CD_3COCD_3, 300MHz), δ (ppm) 7.72 (1H, t, *J* = 8.0 Hz), 7.49 (2H, s), 7.38-7.32 (2H, m), 7.27-7.21 (3H, m), 7.15 (1H, s), 6.96 (4H, s), 3.89 (12H, s); ^{13}C NMR (75.4 MHz, CD_3COCD_3), δ (ppm) 148.8, 139.6, 139.5, 137.3, 132.0, 131.0, 129.0, 128.7, 127.7, 125.3, 124.7, 123.2, 118.4, 113.3, 113.0, 105.1 and 56.5. HRMS-ESI: m/z $[M+H]^+$ for $C_{26}H_{25}O_6F$, calculated 453.1708; observed 453.1708.

(*E*,*E*)-2,5-Difluoro-1,4-bis(4-hydroxy-3,5-dimethoxy)styryl-benzene (16b, Table 3):



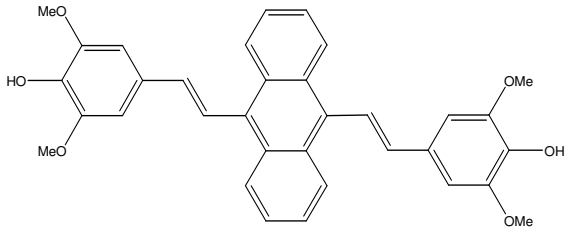
Yellowish green solid, m.p. 229-232 °C, R_f 0.33 (hexane:ethylacetate:: 6:4), ^{1}H NMR (DMSO, 300MHz), δ (ppm) 8.7 (2H, s), 7.59 (2H, t, *J* = 9.3 Hz), 7.29 (2H, d, *J* = 16.6 Hz), 7.08 (2H, d, *J* = 16.6 Hz), 6.91 (4H, s), 3.83 (12H, s); ^{13}C NMR (75.4 MHz, DMSO), δ (ppm) 148.1, 136.5, 132.8, 130.9, 127.1, 116.3, 112.7, 104.6 and 56.02. HRMS-ESI: m/z $[M+H]^+$ for $C_{26}H_{24}0_6F_2$, calculated 471.1614; observed 471.1613.

((*E*,*E*)-4,4'-Bis(4-hydroxy-3,5-dimethoxy)styrylbiphenyl (17b, Table 3):



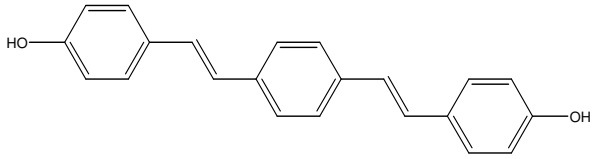
Yellowish brown solid, m.p 277-280 °C, ^{1}H NMR (DMSO, 300MHz), δ (ppm) 8.58 (2H, s), 7.74 (4H, d, *J*= 7.6 Hz), 7.65 (4H, d, *J* = 7.6 Hz), 7.19 (4H, s), 6.93 (4H, s), 3.83 (12H, s); ^{13}C NMR (75.4 MHz, DMSO), δ (ppm) 148.1, 138.0, 136.6, 135.8, 129.1, 127.5, 126.6, 125.1, 104.2 and 56.0. HRMS-ESI: m/z $[M+H]^+$ for $C_{32}H_{30}O_6$, calculated 511.2115; observed 511.2141.

(*E*,*E*)-9,10-Bis(4-hydroxy-3,5-dimethoxy)styrylanthracene (18b, Table 3):



Brown solid, m.p 212-216 °C, ^{1}H NMR (DMSO, 300MHz), δ (ppm) 8.62 (2H, s), 8.43 (4H, d, *J* = 6.4 Hz), 8.03 (2H, d, *J* = 16.2 Hz), 7.57-7.54 (4H, d, *J* = 7.3 Hz), 7.11 (4H, s), 6.84 (2H, d, *J* = 16.2 Hz), 3.87 (12H, s); ^{13}C NMR (75.4 MHz, DMSO), δ (ppm) 148.2, 137.7, 136.0, 132.3, 129.0, 127.4, 126.3, 125.3, 121.8, 104.5 and 56.1. HRMS-ESI: m/z $[M+H]^+$ for $C_{34}H_{30}O_6$, calculated 535.2115; observed 535.2123.

(*E*,*E*)-1,4-Bis(4-hydroxy)styrylbenzene (19b, Table 3):



Grey solid, m.p 362-366 °C (lit. m.p. 310-312),[5] ^{1}H NMR (DMSO, 300MHz), δ (ppm) 9.68 (2H, s), 7.51-7.45 (8H, m), 7.13-7.04 (4H, m), 6.78 (4H, s); ^{13}C NMR (75.4 MHz, DMSO), δ (ppm) 157.7, 136.7, 128.6, 128.5, 128.3, 126.8, 125.3, 116.0.

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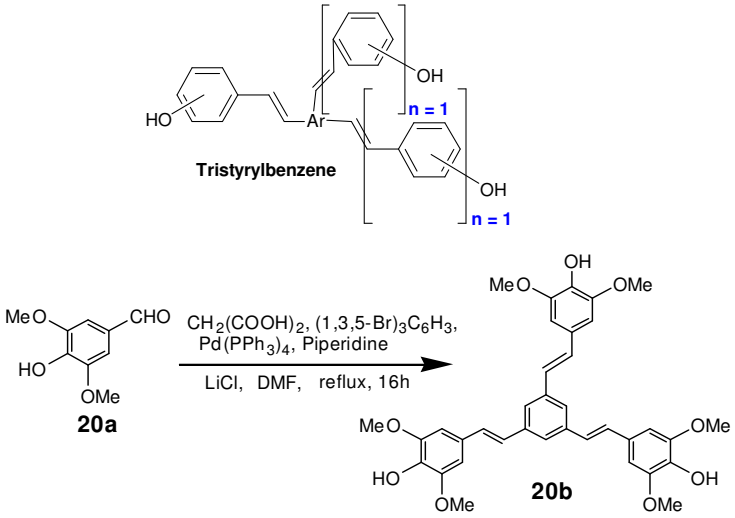
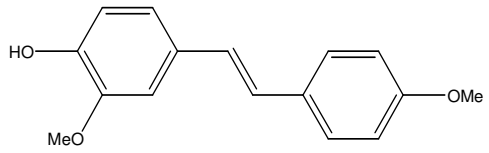
iii) Synthesis of ((*E*,*E*,*E*)-1,3,5-Tris(4-hydroxy-3,5-dimethoxy)styrylbenzene (20 b, Scheme 2)



Malonic acid (10.7 g, 102.8 mmol) was taken in a round bottom flask and piperidine (8.5 ml, 85.8 mmol) added gradually. The above mixture was stirred in DMF (30 ml), for 2 min. at room temperature. Thereafter, 4-hydroxy-3,5-dimethoxybenzaldehyde (1.56 g, 8.6 mmol), 1,3,5-tribomobenzene (0.5 g, 1.58 mmol), $Pd(PPh_3)_4$ (0.165 g, 0.14 mmol), Piperidine (4.25 ml, 42.5 mmol) and LiCl (0.016g, 0.038 mmol) were added, then reaction mixture allowed to reflux for 16 hours. The above mixture was cooled to room temperature and filtered through celite. The filtrate was poured into water (250ml, acidified with dil HCl, pH= 5) and extracted with ethyl acetate (3x50 ml). The combined organic layer was washed with water (1x50 ml), brine (1x20 ml), dried over Na_2SO_4 and vacuum evaporated. The resulting residue was subsequently purified by column chromatography on Silica gel (60-120 mesh size) using hexane-ethylacetate (6:4) and obtained solid was washed with methanol to provide pure ((*E*,*E*,*E*)-1,3,5-Tris(4-hydroxy-3,5-dimethoxy)styrylbenzene **20b** as a yellow solid (0.38 g, 39 % yield), m.p 223-225 °C, ^{1}H NMR ($CDCl_3$, 300MHz), δ (ppm) 7.53 (3H, s), 7.17 (3H, d, *J* = 15.7 Hz), 7.04 (3H, d, *J* = 15.7 Hz), 6.81 (6H, s), 5.62 (3H, s), 3.98 (18H, s); ^{13}C NMR (75.4 MHz, $CDCl_3$), δ (ppm) 147.4, 138.3, 135.1, 129.4, 129.0, 126.7, 123.4, 103.6 and 56.5. HRMS-ESI: m/z $[M+H]^+$ for $C_{36}H_{36}O_9$, calculated 613.2432; observed 613.2432.

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



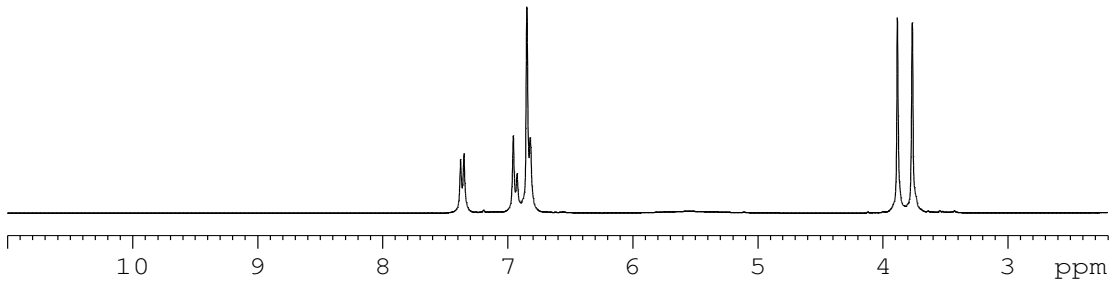
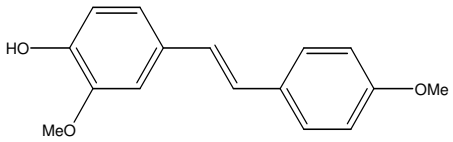


Table 2/Entry-1b, ^{13}C NMR (in $CDCl_3$)



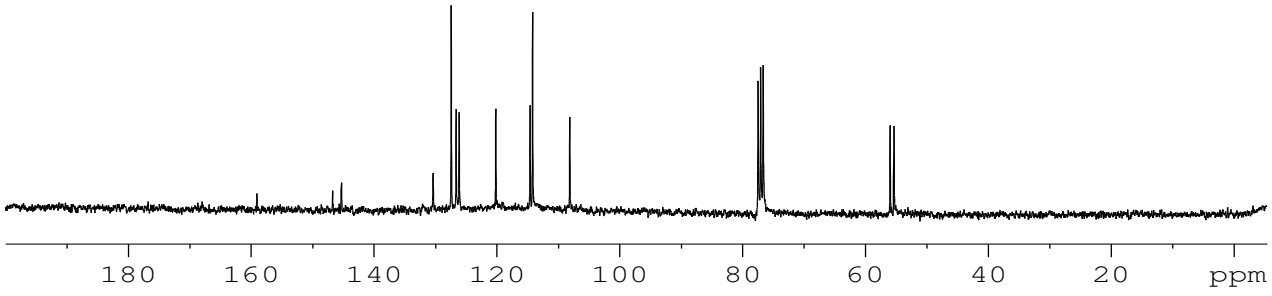
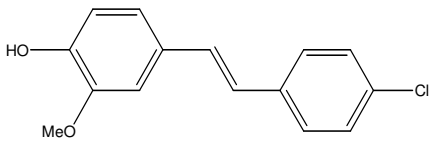


Table 2/Entry-2b, ^{1}H NMR (in $CDCl_3$)



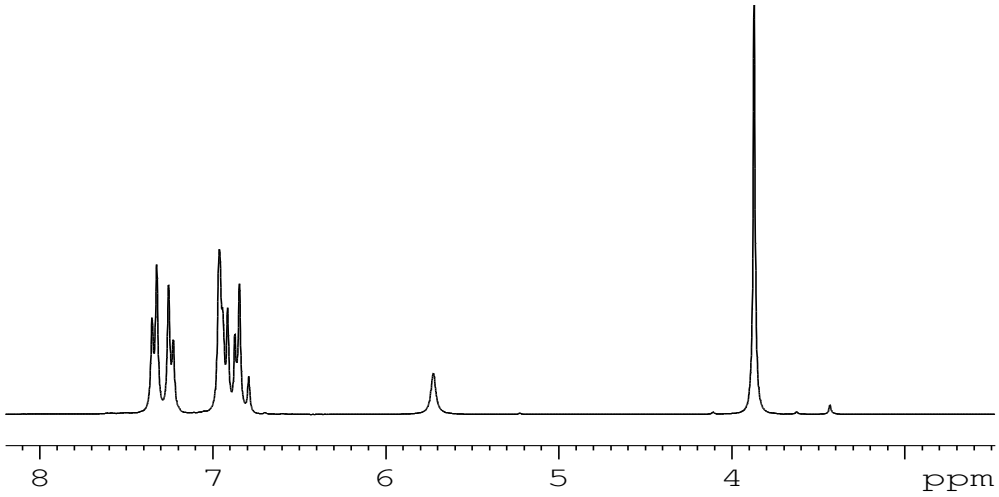
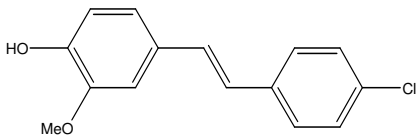


Table 2/Entry-2b, ^{13}C NMR (in $CDCl_3$)



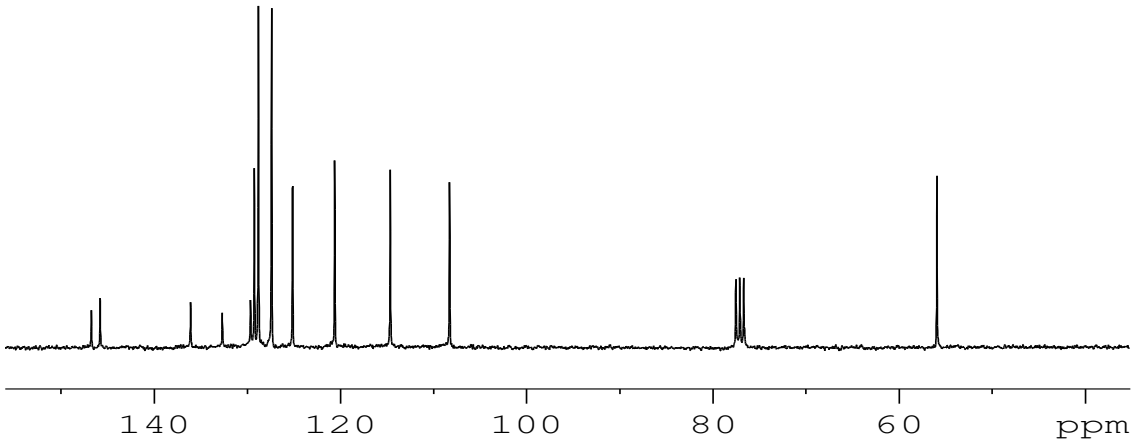
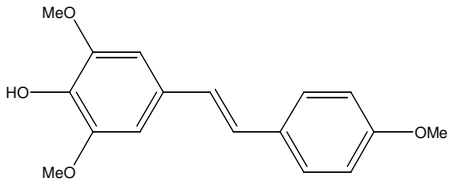


Table 2/Entry-3b, ^{1}H NMR (in $CDCl_3$



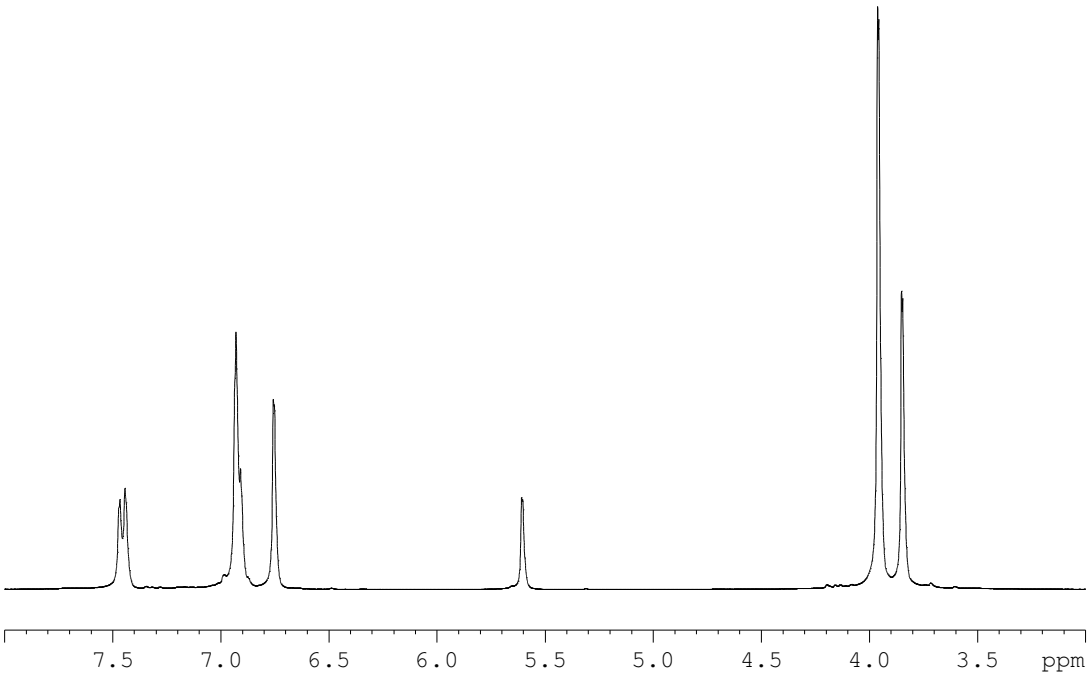


Table 2/Entry-3b, ^{13}C NMR (in $CDCl_3$)

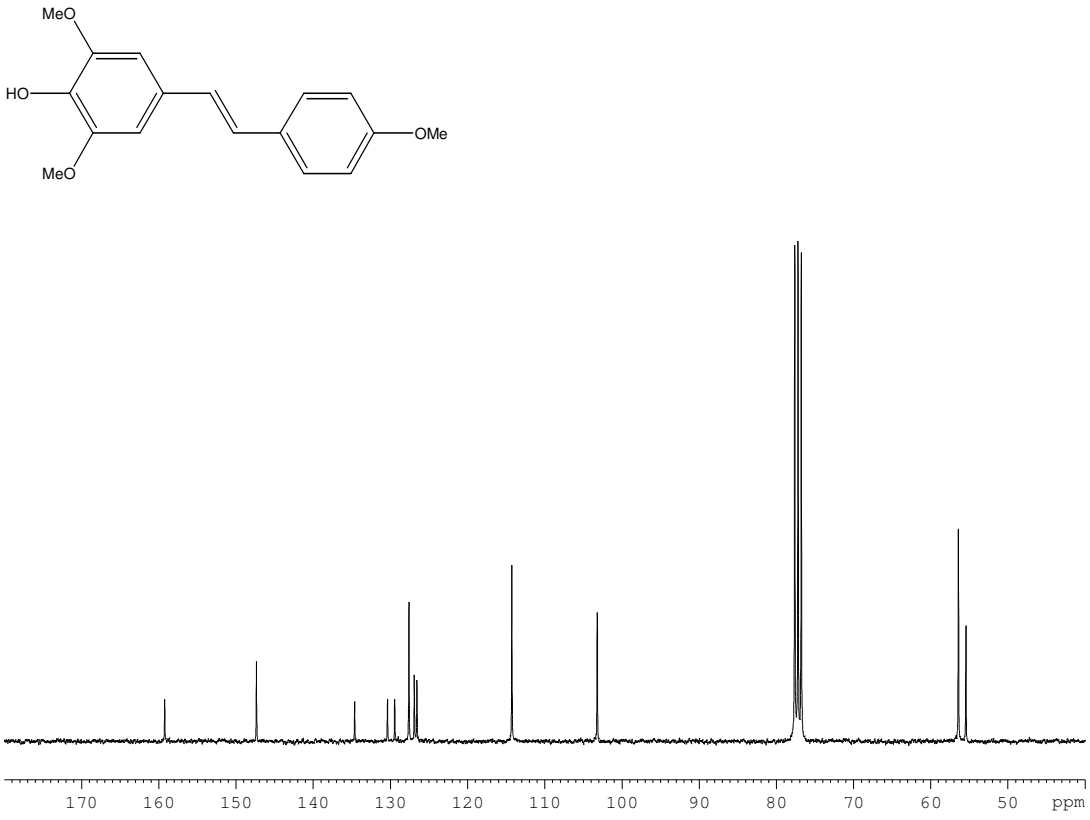
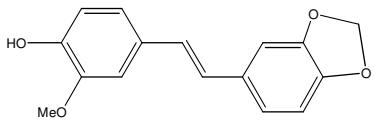


Table 2/Entry-4b, ^{1}H NMR (in CD_3COCD_3)



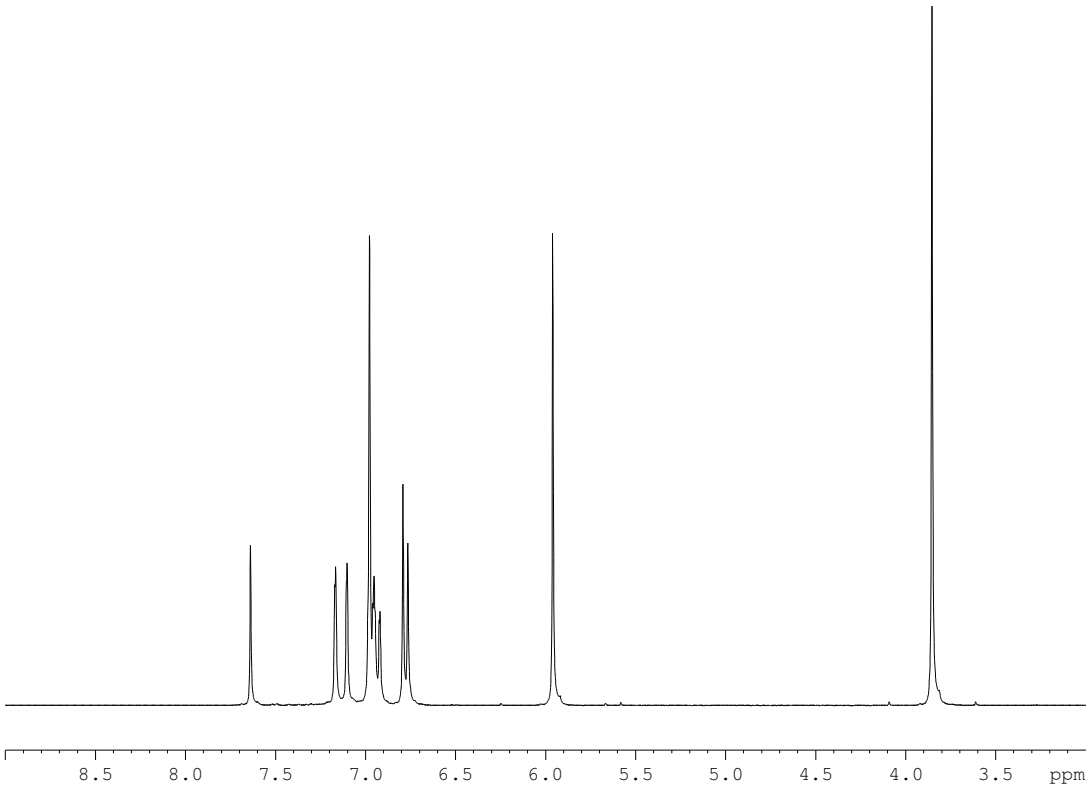
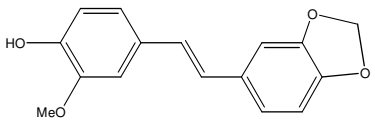


Table 2/Entry-4b, ^{13}C NMR (in CD_3COCD_3)



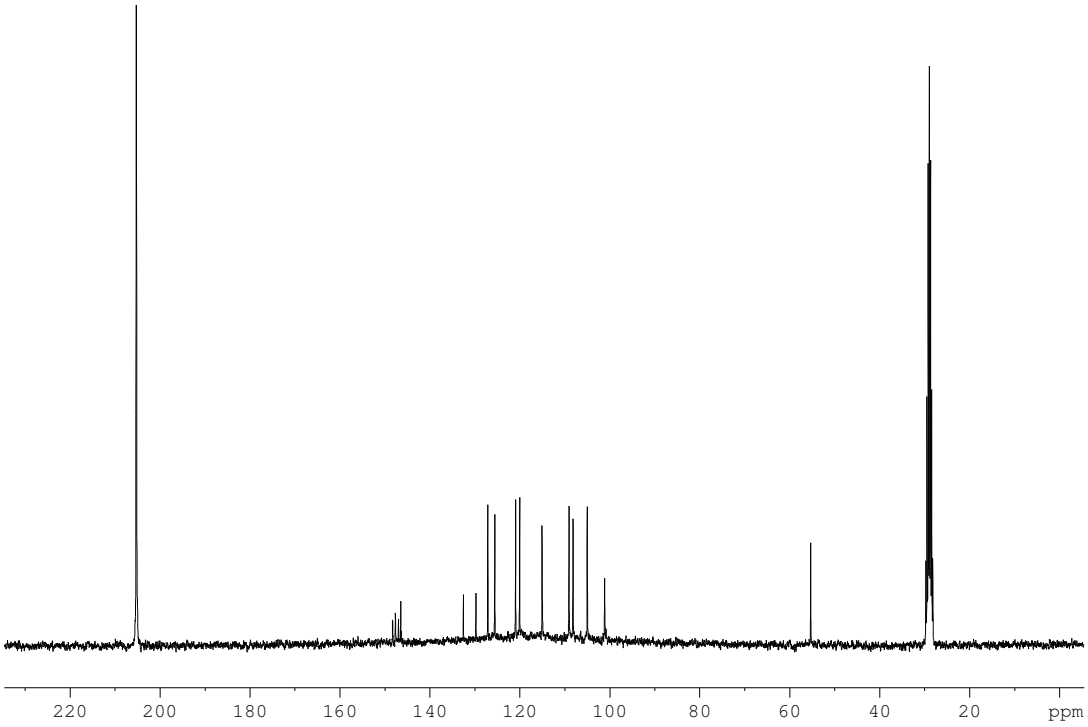
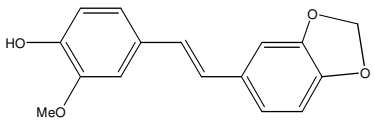


Table 2/Entry-4b, HRMS Spectrum



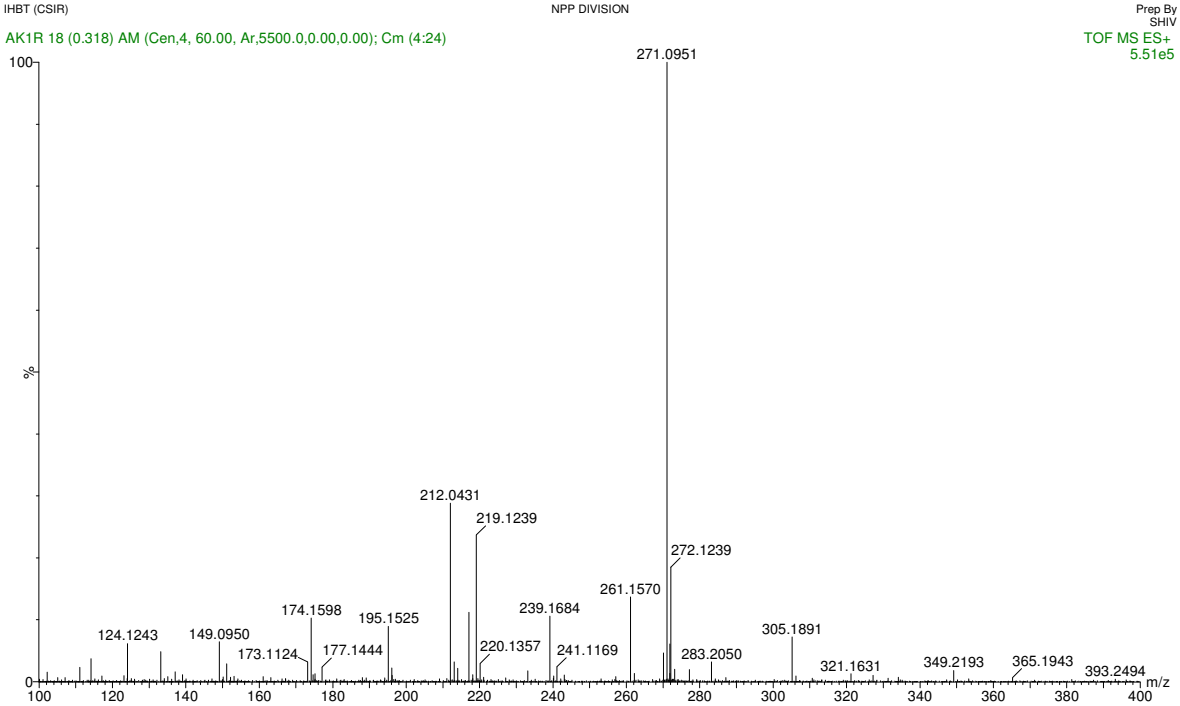
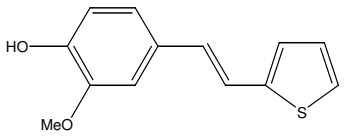


Table 2/Entry-5b, ^{1}H NMR (in $CDCl_3$)



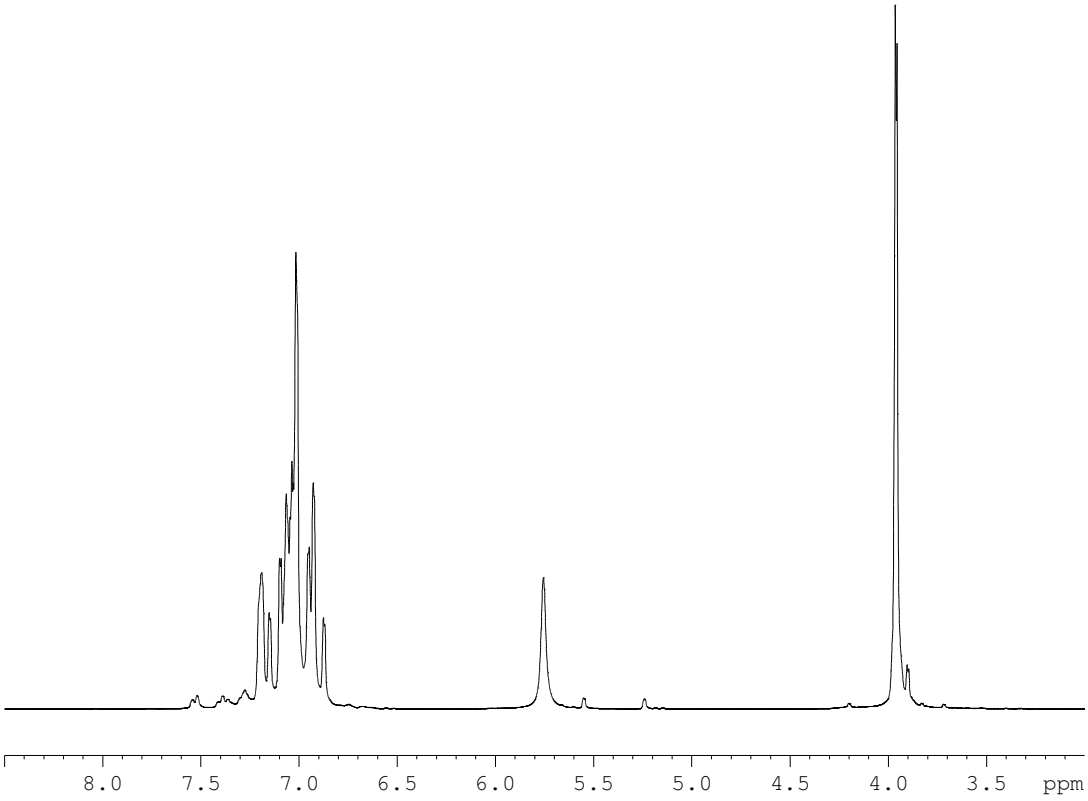
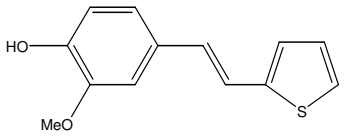


Table 2/Entry-5b, ^{13}C NMR (in $CDCl_3$)



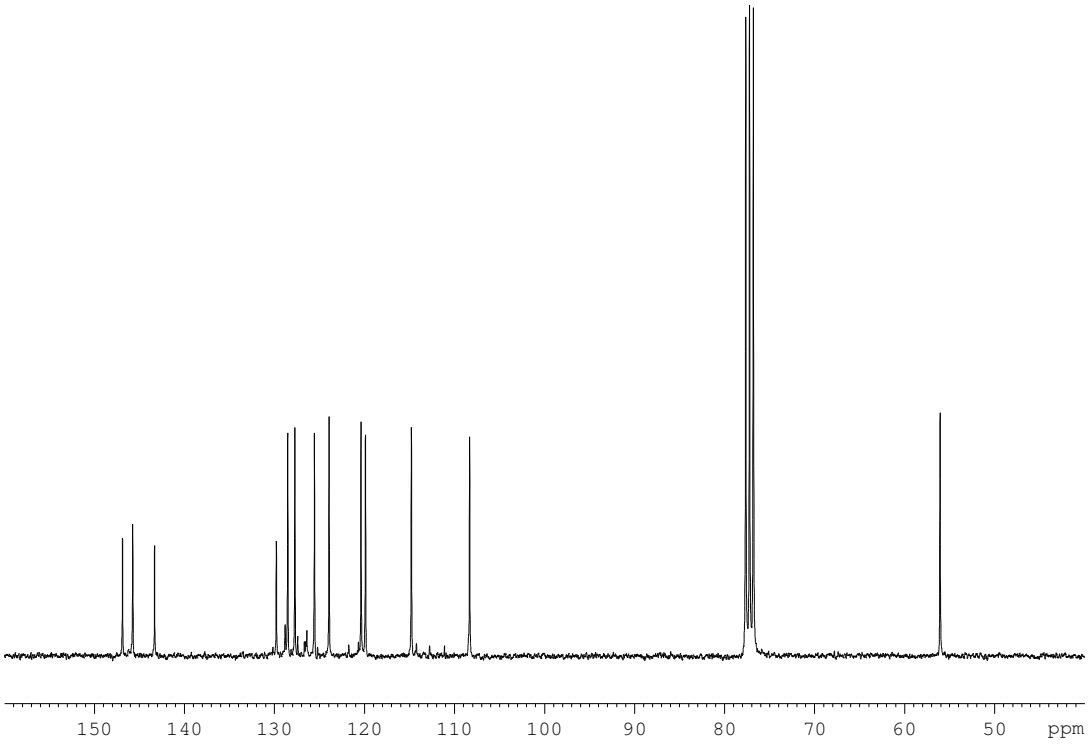
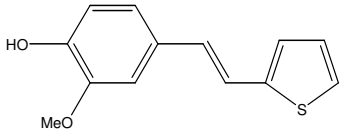


Table 2/Entry-5b, HRMS Spectrum



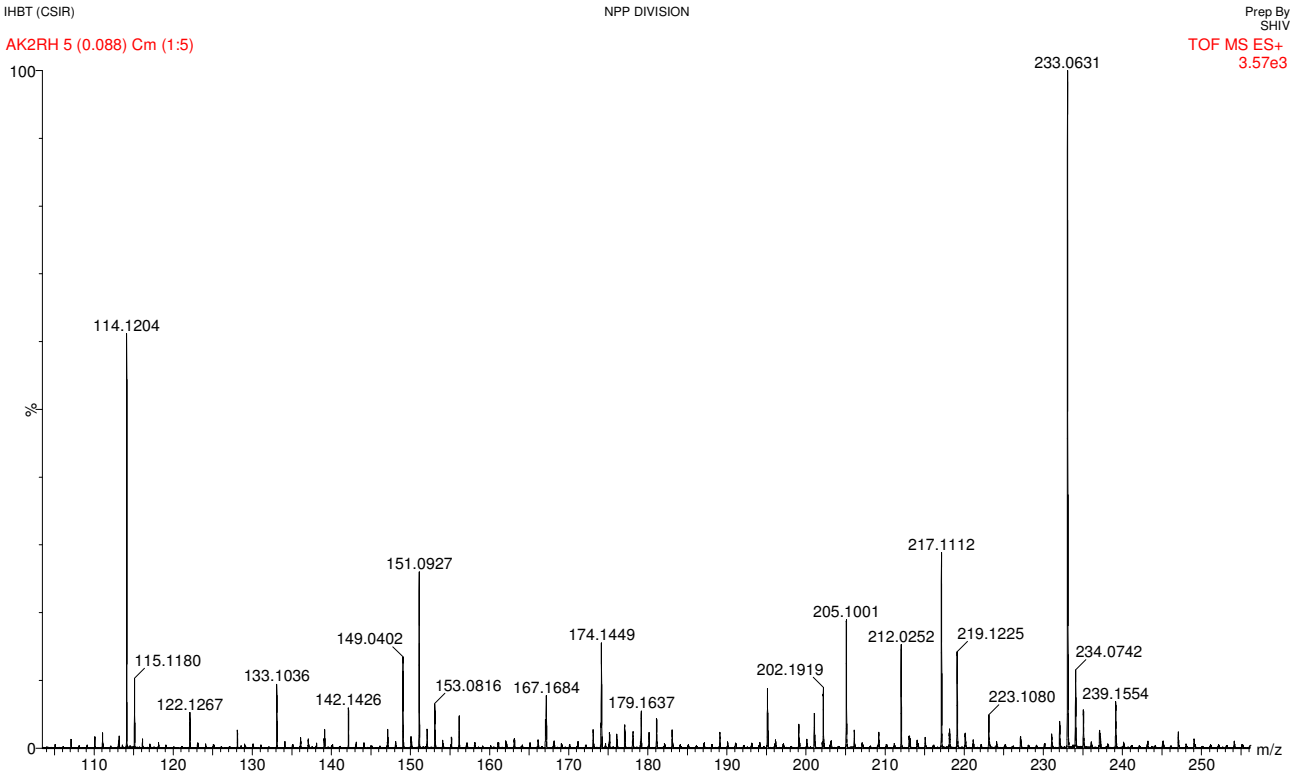
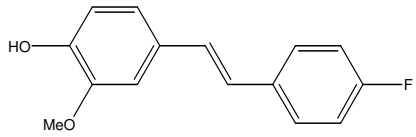


Table 2/Entry-6b, ^{1}H NMR (in $CDCl_3$)



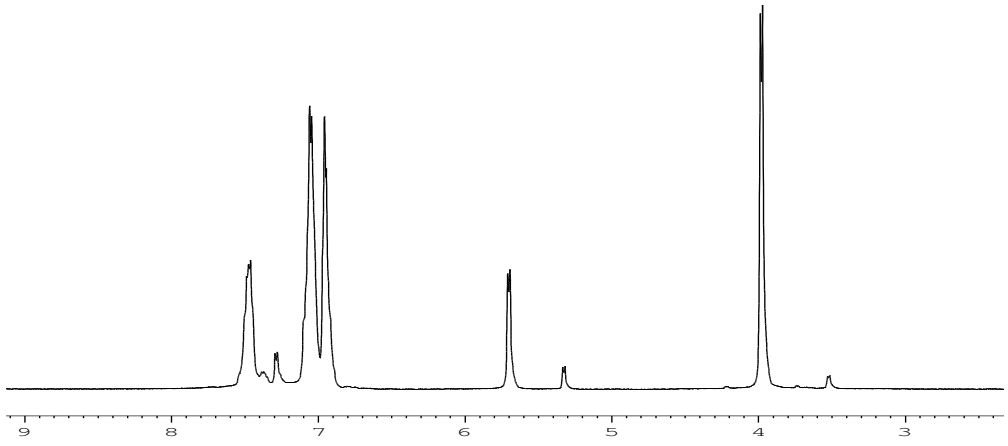
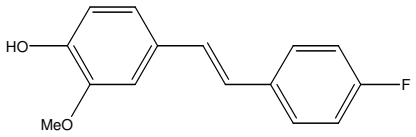


Table 2/Entry-6b, ^{13}C NMR (in $CDCl_3$)



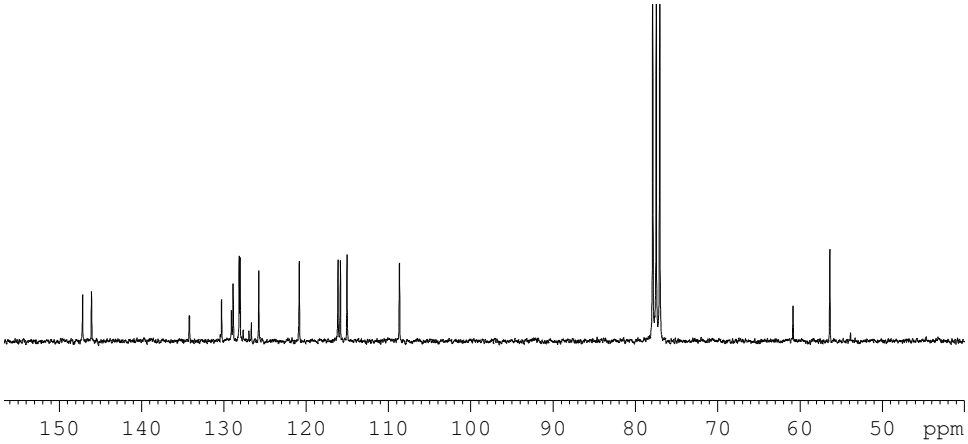
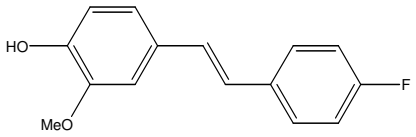


Table 2/Entry-6b, HRMS Spectrum



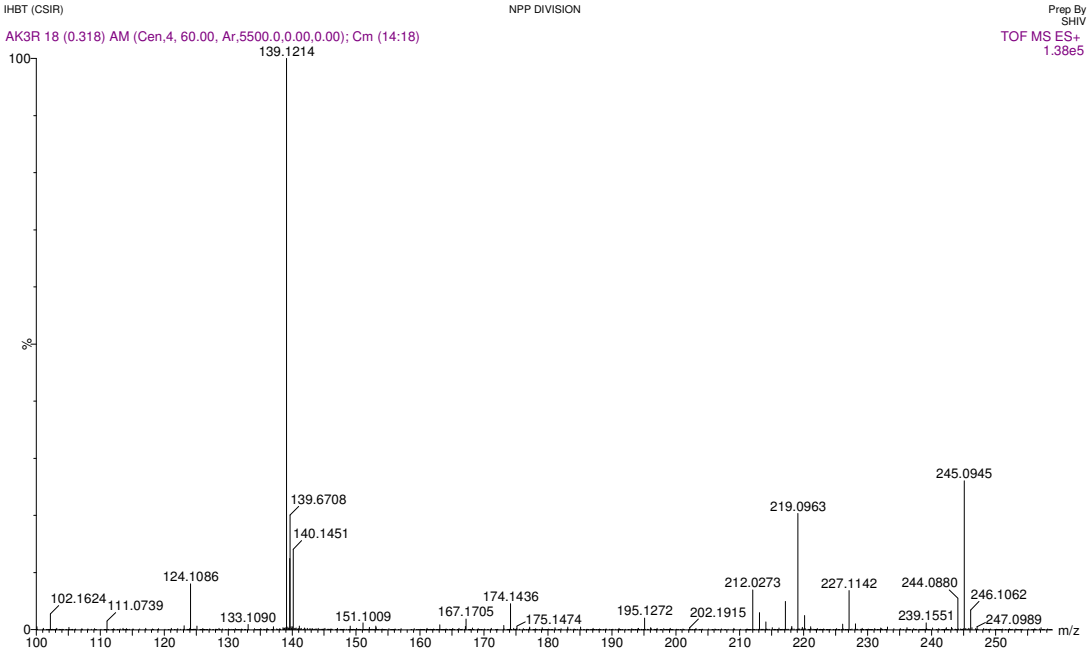
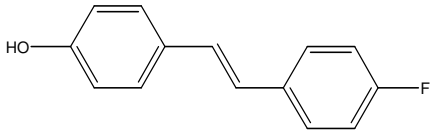


Table 2/Entry-7b, ^{1}H NMR (in $CDCl_3$)



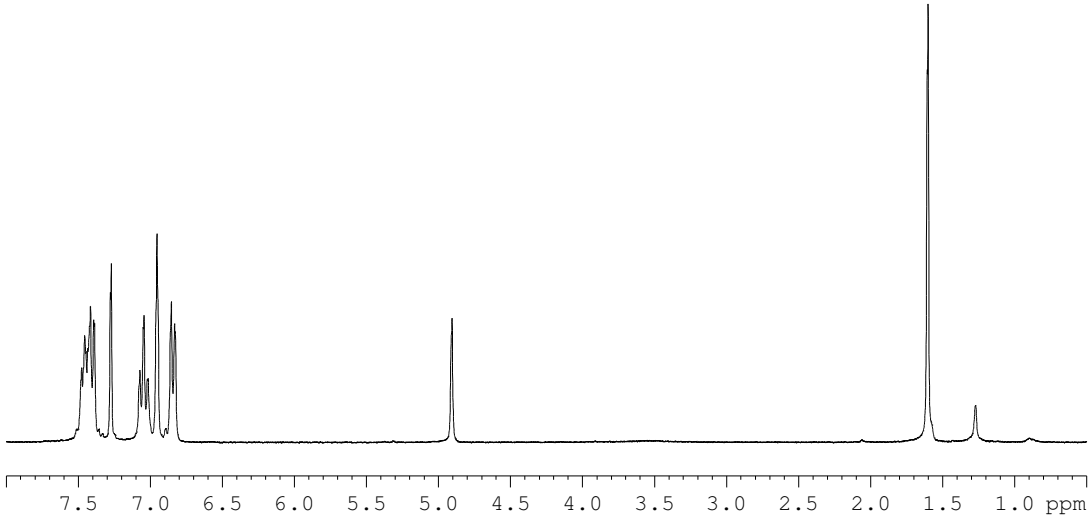
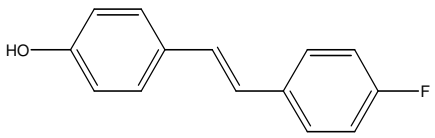


Table 2/Entry-7b, ^{13}C NMR (in $CDCl_3$)



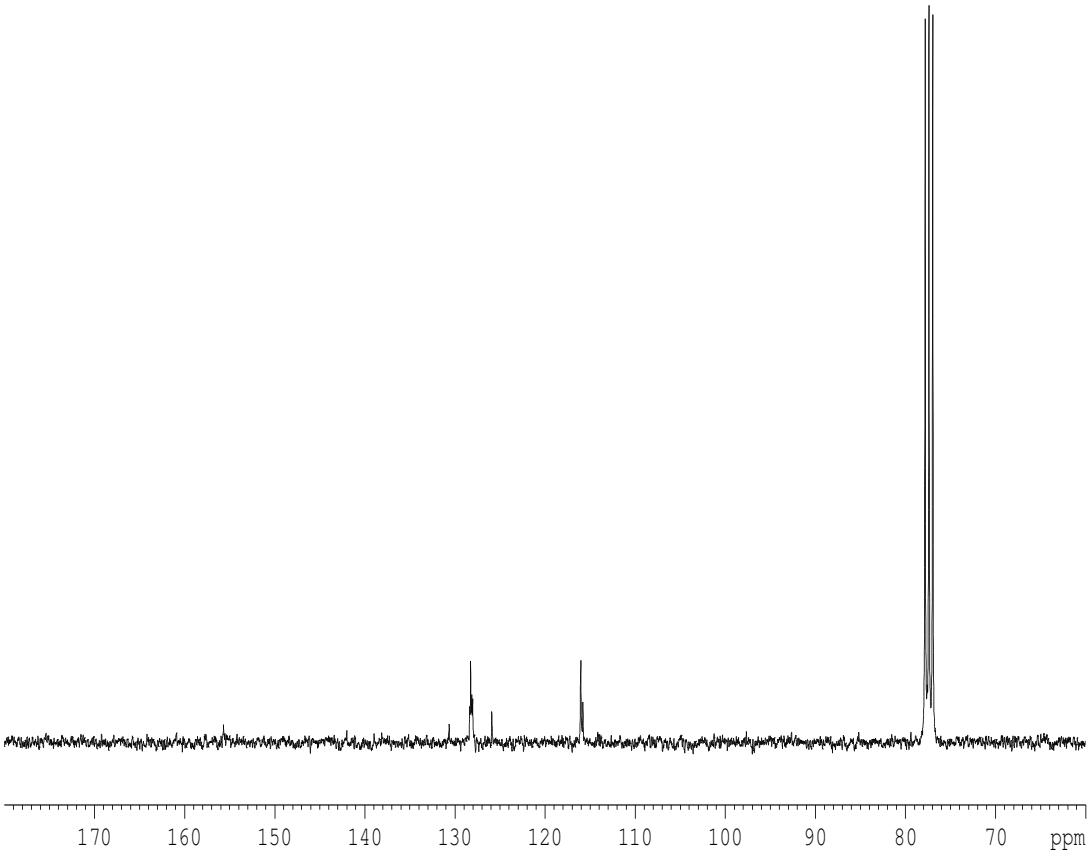
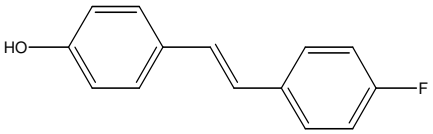


Table 2/Entry-7b, HRMS Spectrum



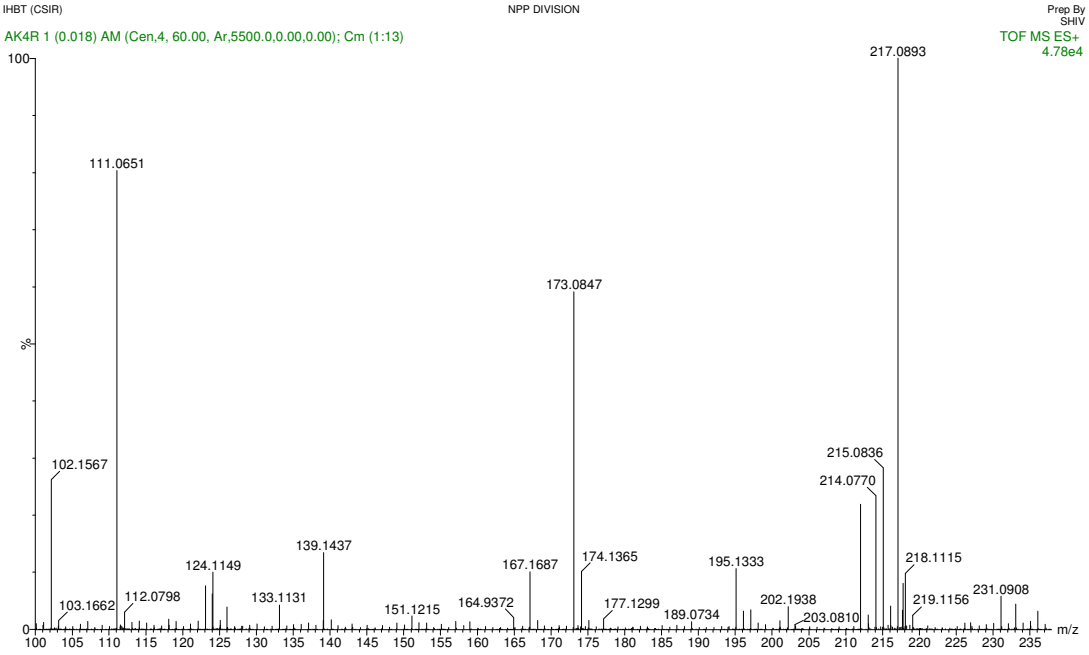
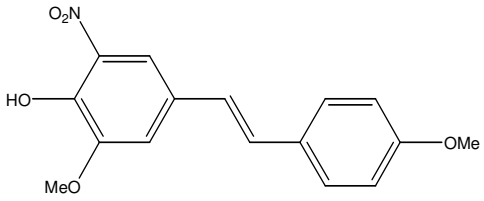


Table 2/Entry-8b, ^{1}H NMR (in $CDCl_3$)



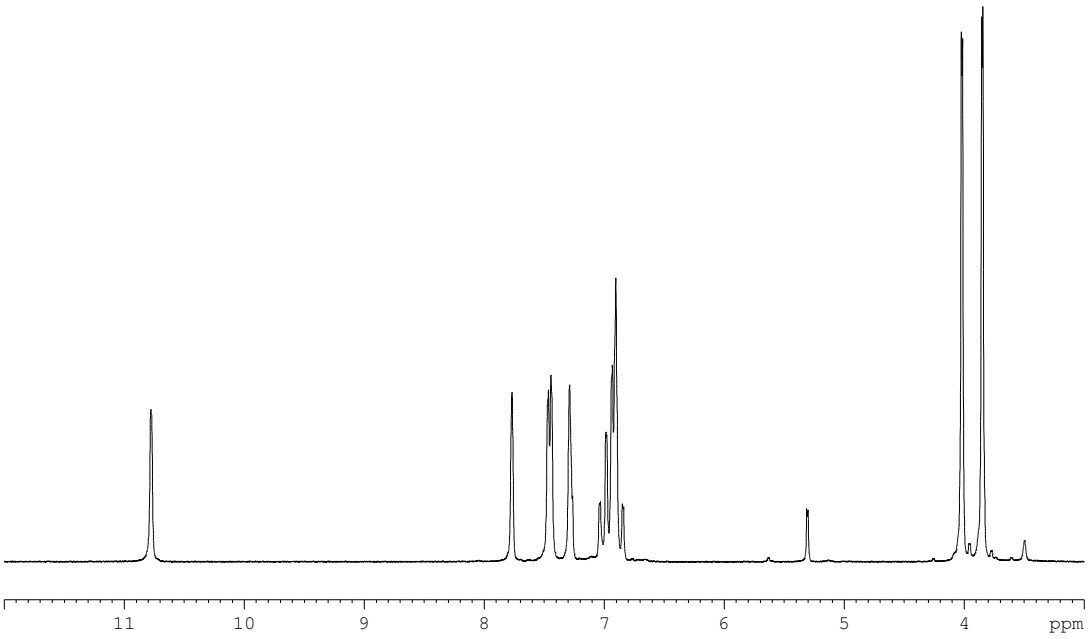
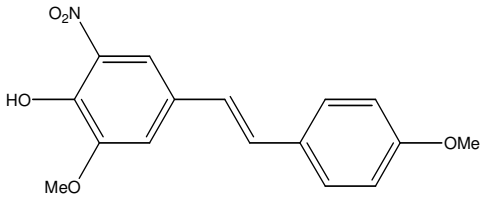


Table 2/Entry-8b, ^{13}C NMR (in $CDCl_3$)



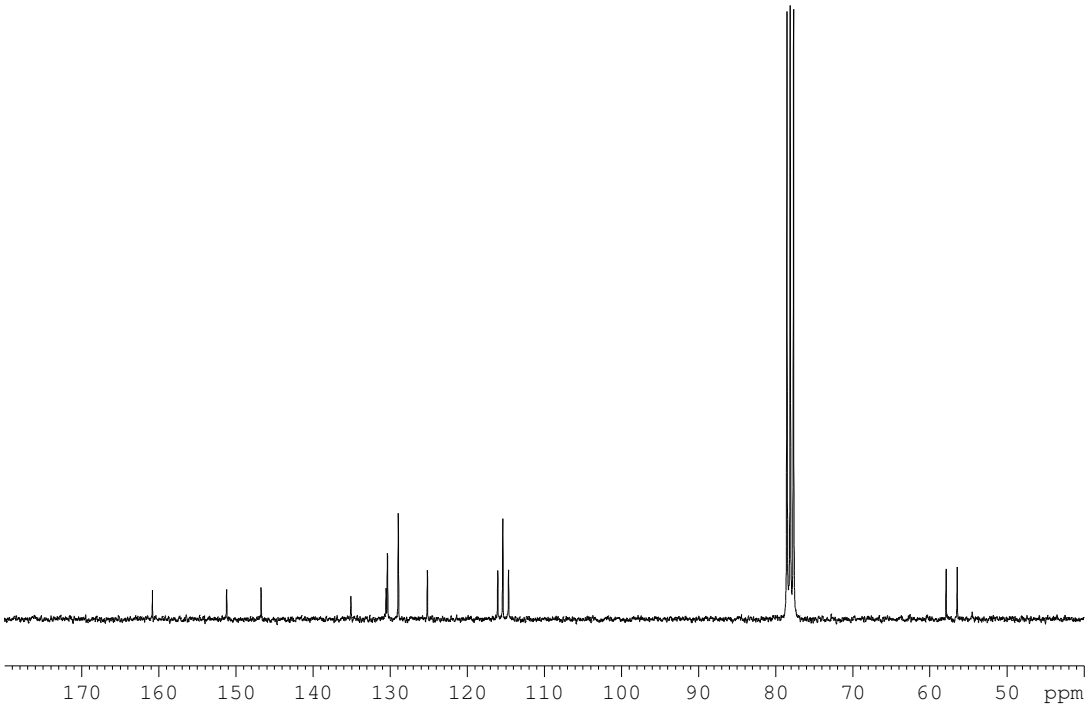
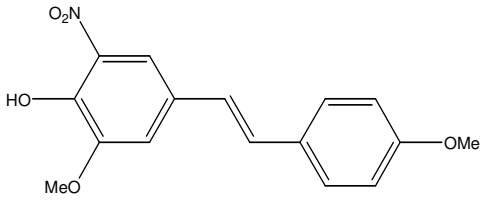


Table2/Entry-8b, HRMS Spectrum



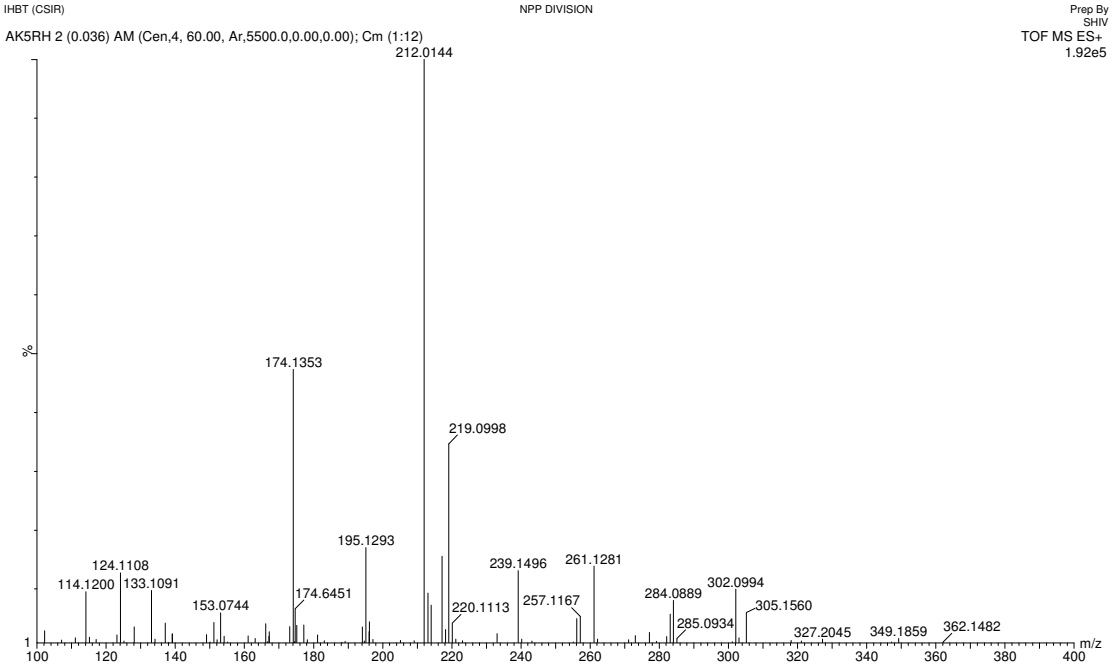
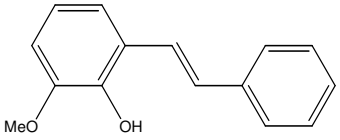


Table 2/Entry-9b, ^{1}H NMR (in $CDCl_3$)



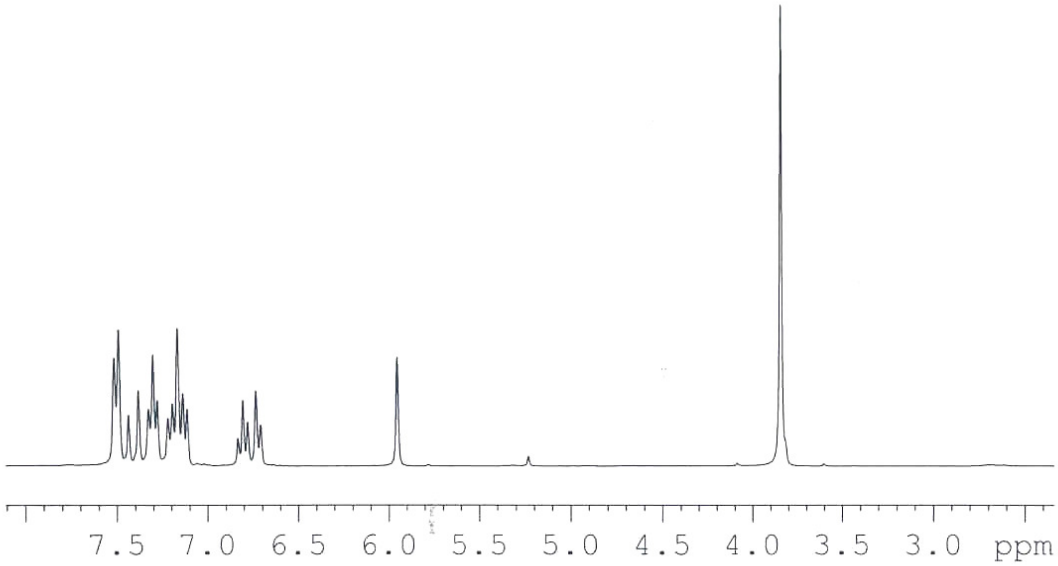
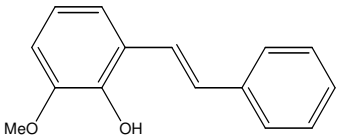


Table 2/Entry-9b, ^{13}C NMR (in $CDCl_3$)



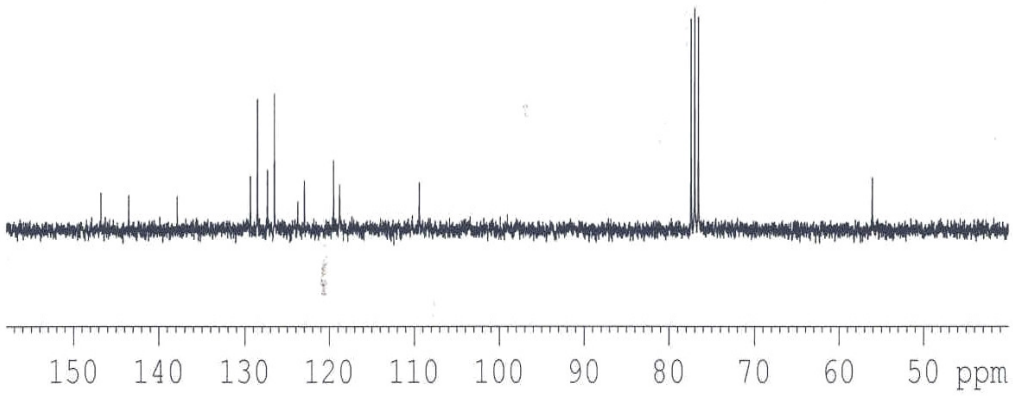
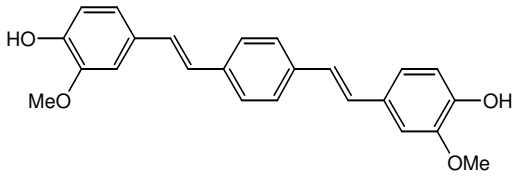


Table 3/Entry-12b, ^{1}H NMR (in DMSO)



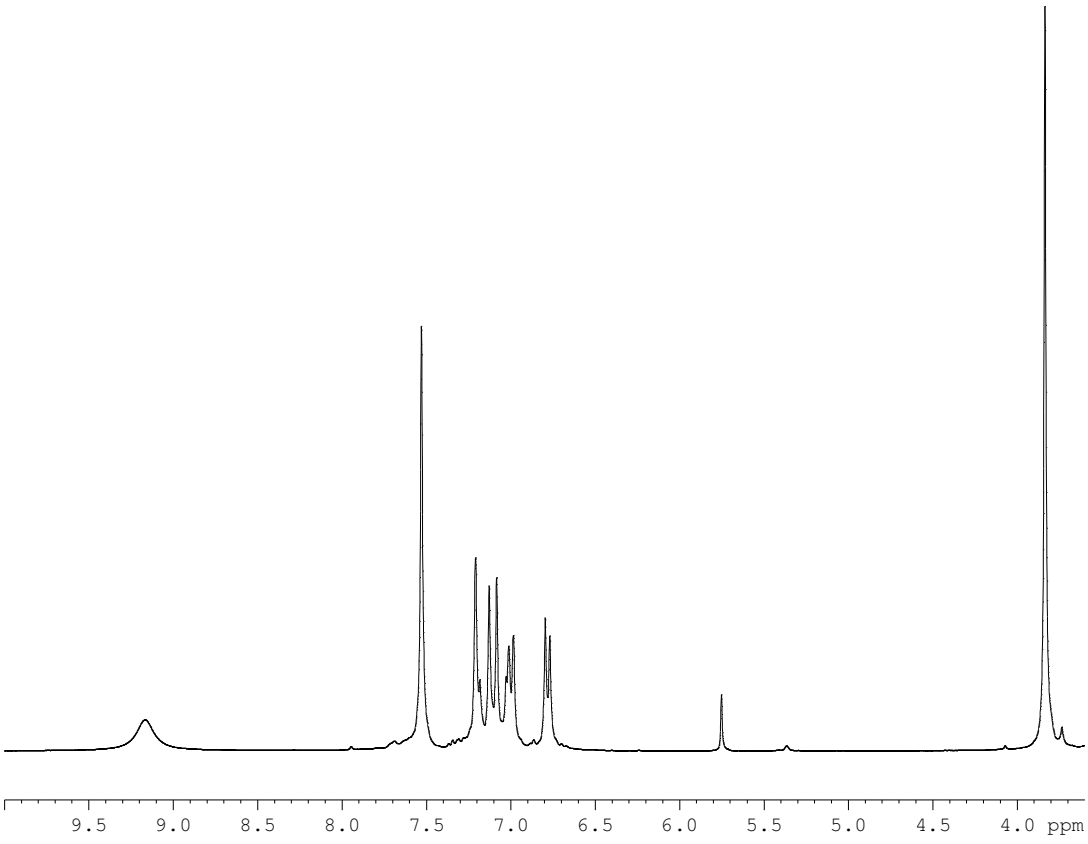
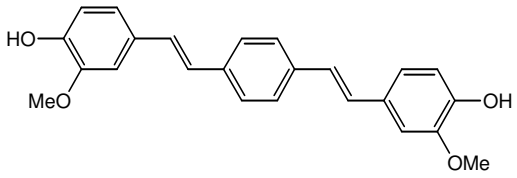


Table 3/Entry-12b, ^{13}C NMR (in DMSO)



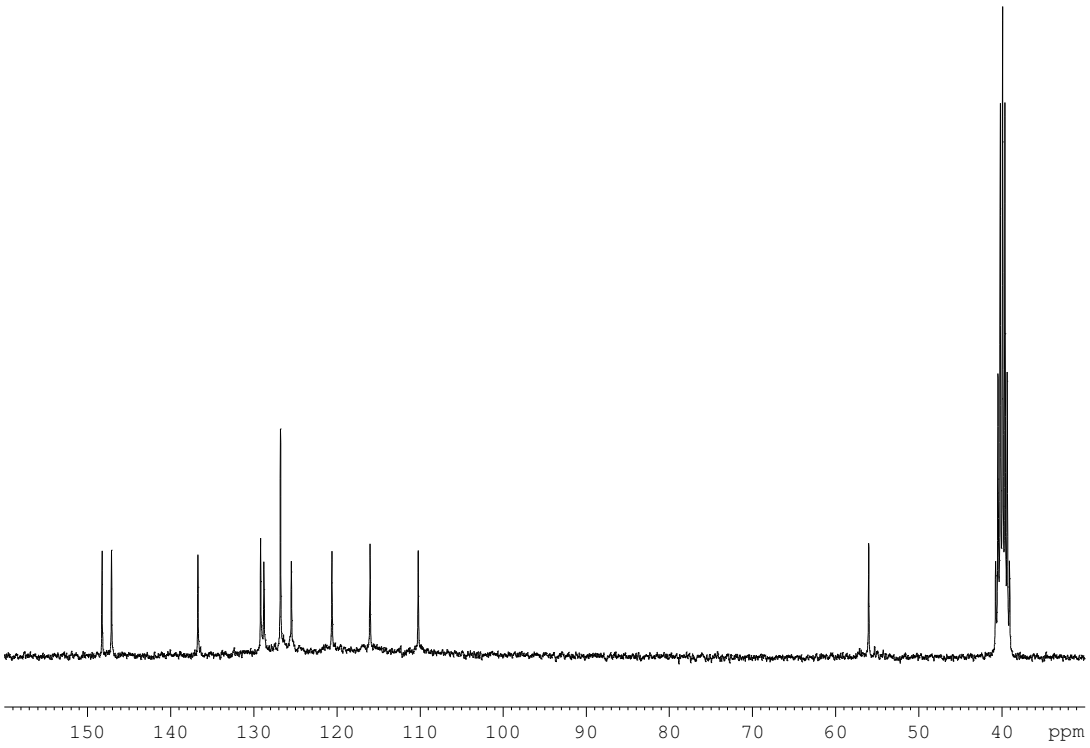
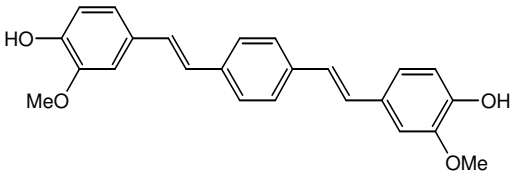


Table 3/Entry-12b, HRMS Spectrum



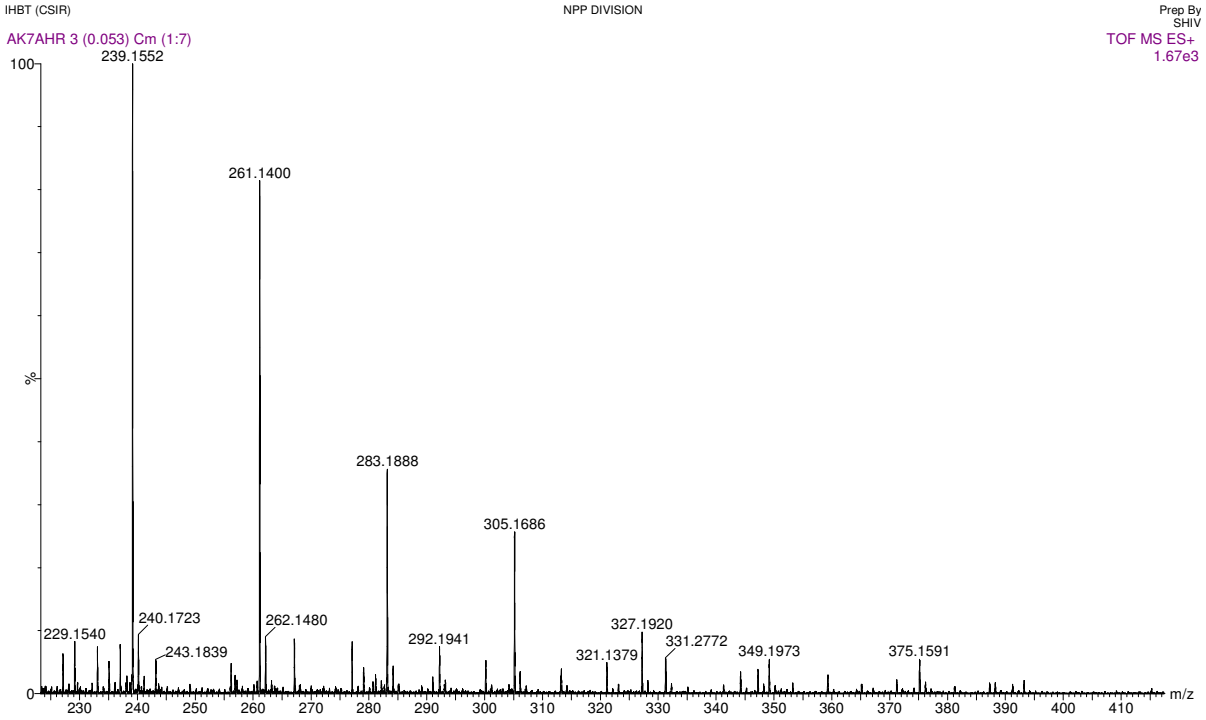
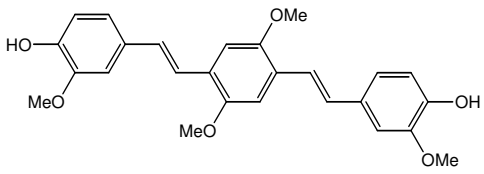


Table 3/Entry-13b, ^{1}H NMR (in DMSO)



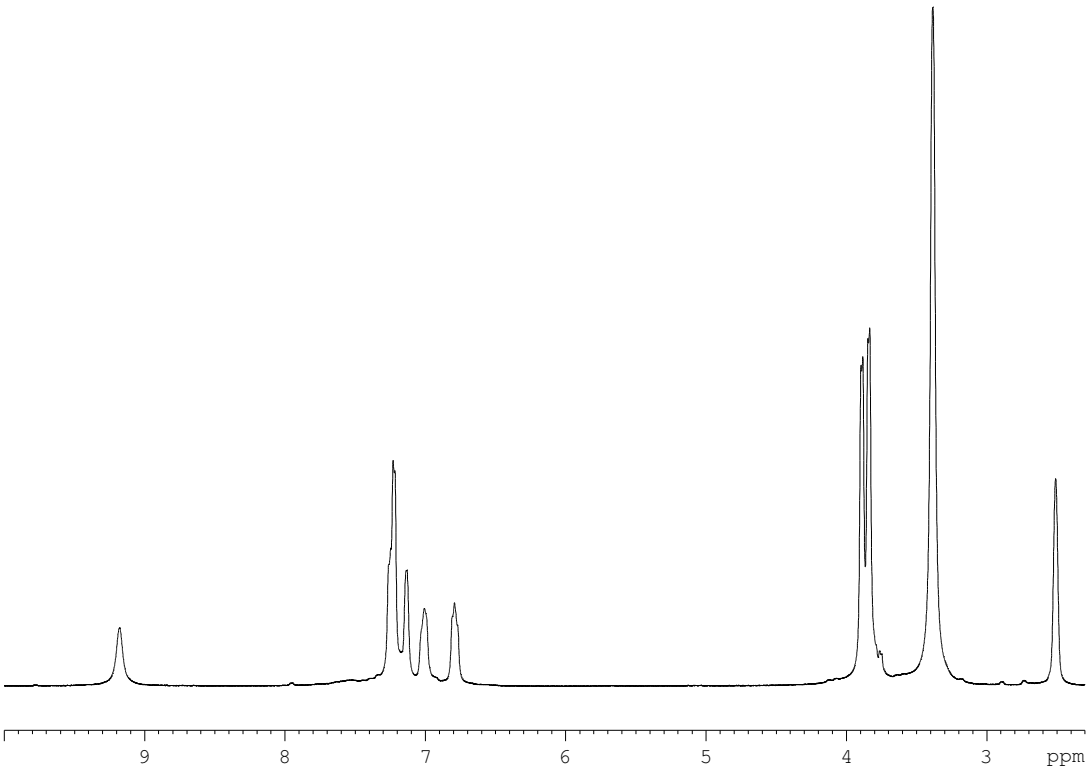
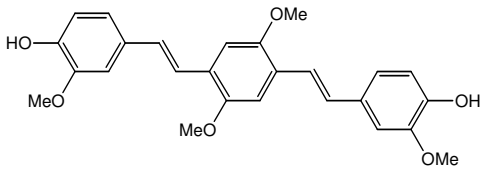


Table 3/Entry-13b, ^{13}C NMR (in DMSO)



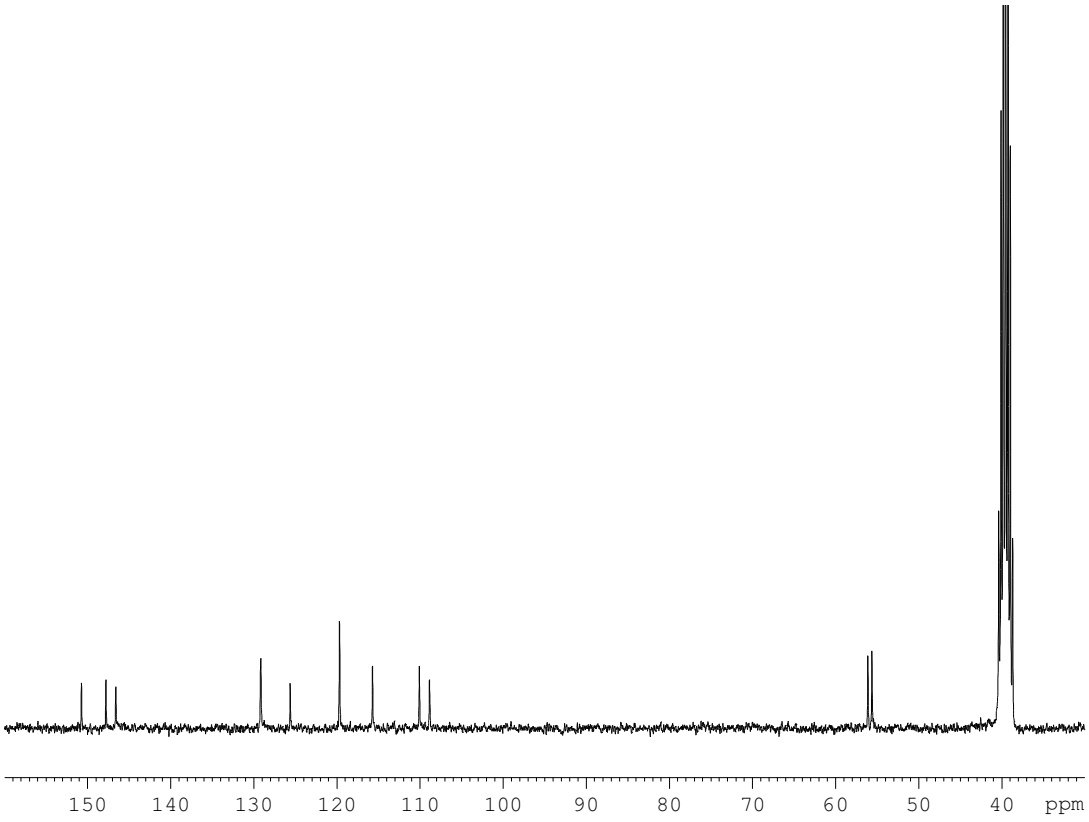
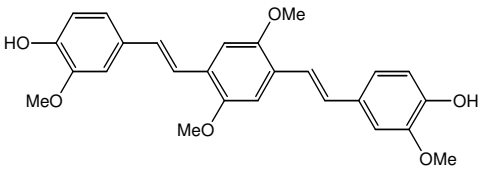


Table 3/Entry-13b, HRMS Spectrum



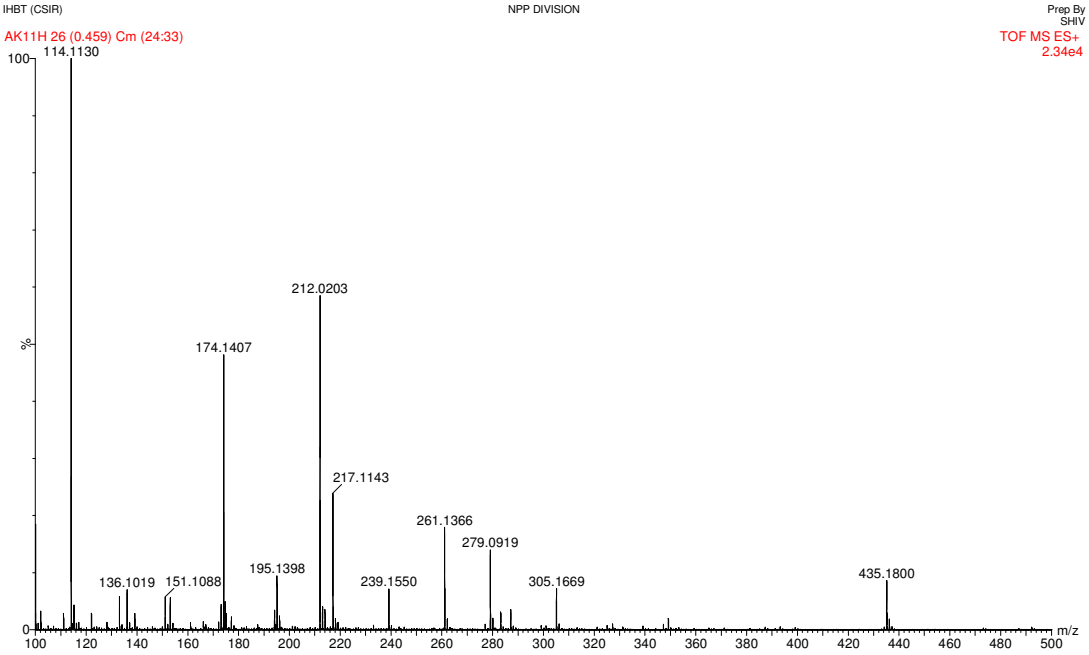
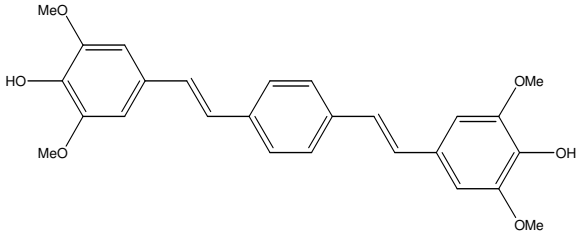


Table 3/Entry-14b, ^{1}H NMR (in DMSO)



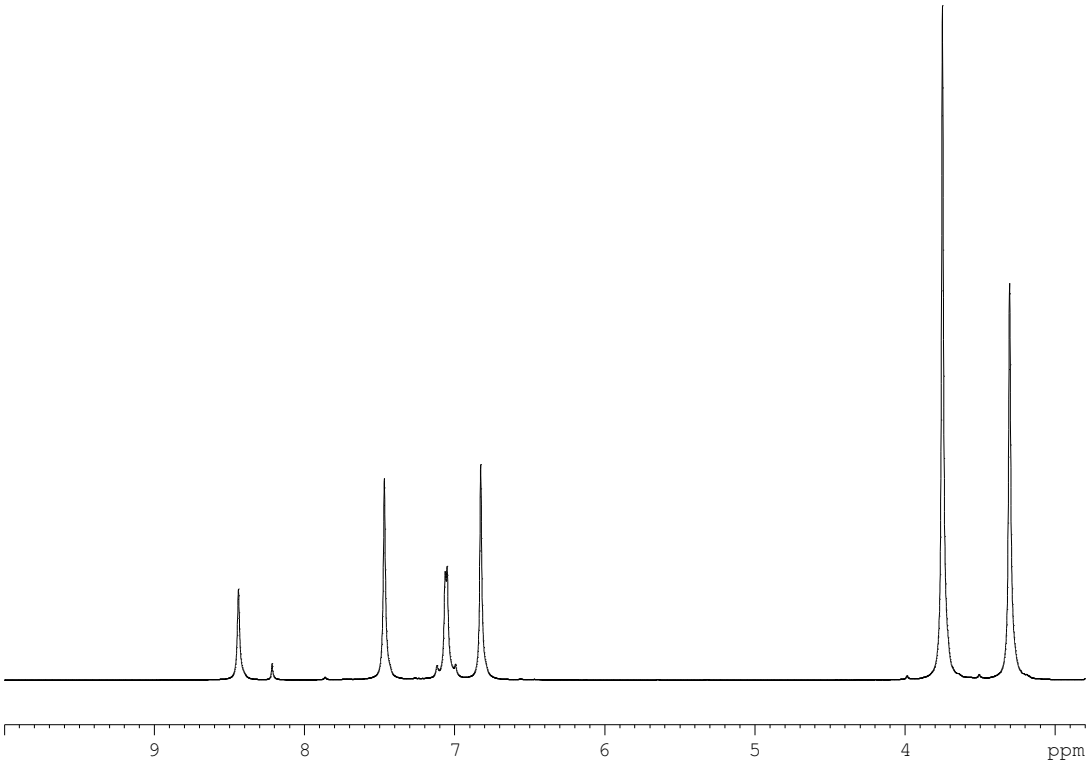
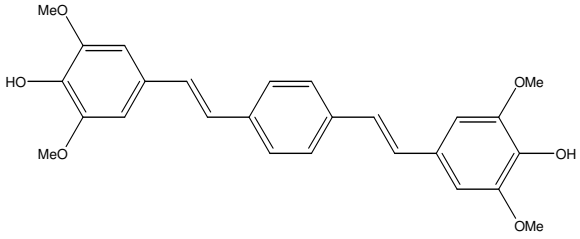


Table 3/Entry-14b, ^{13}C NMR (in DMSO)



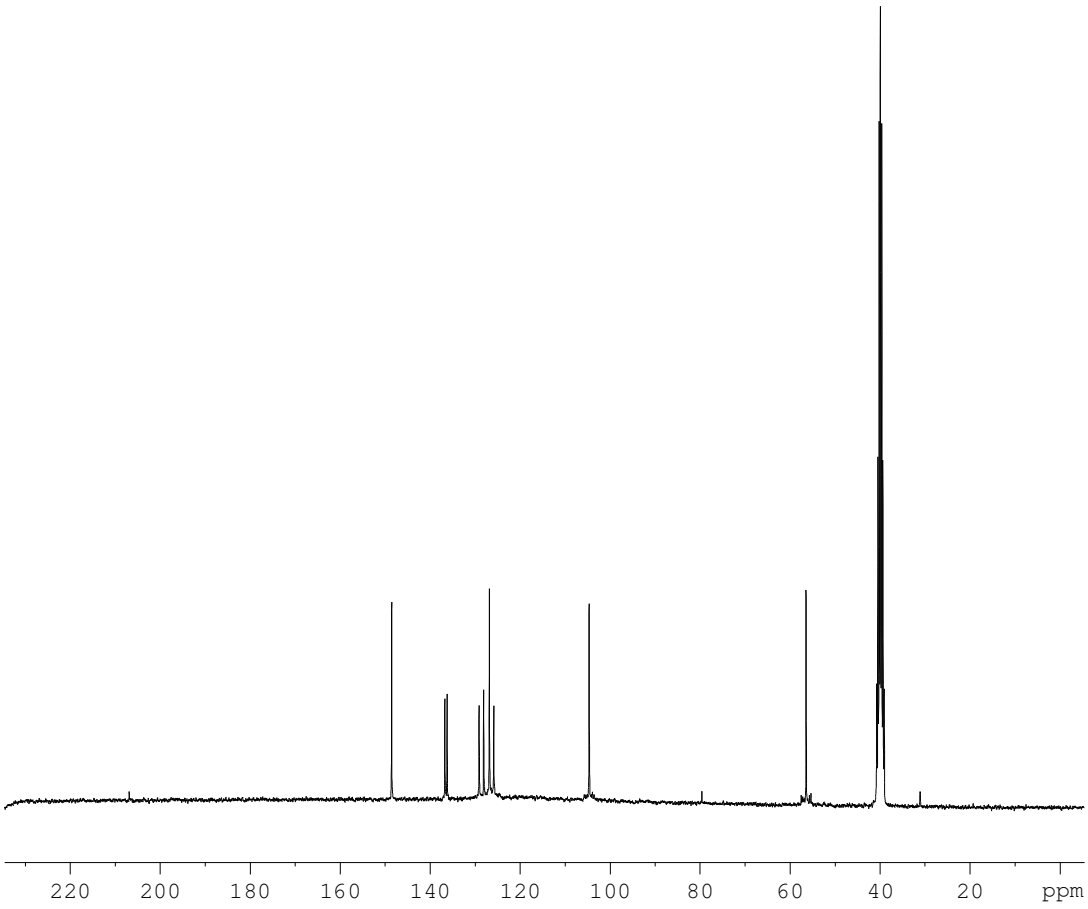
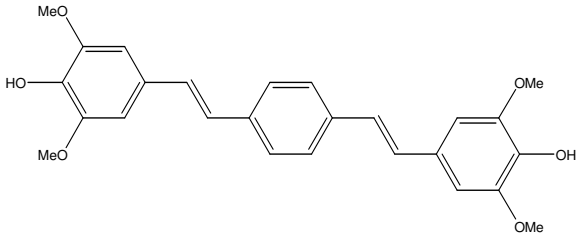


Table 3/Entry-14b, HRMS Spectrum



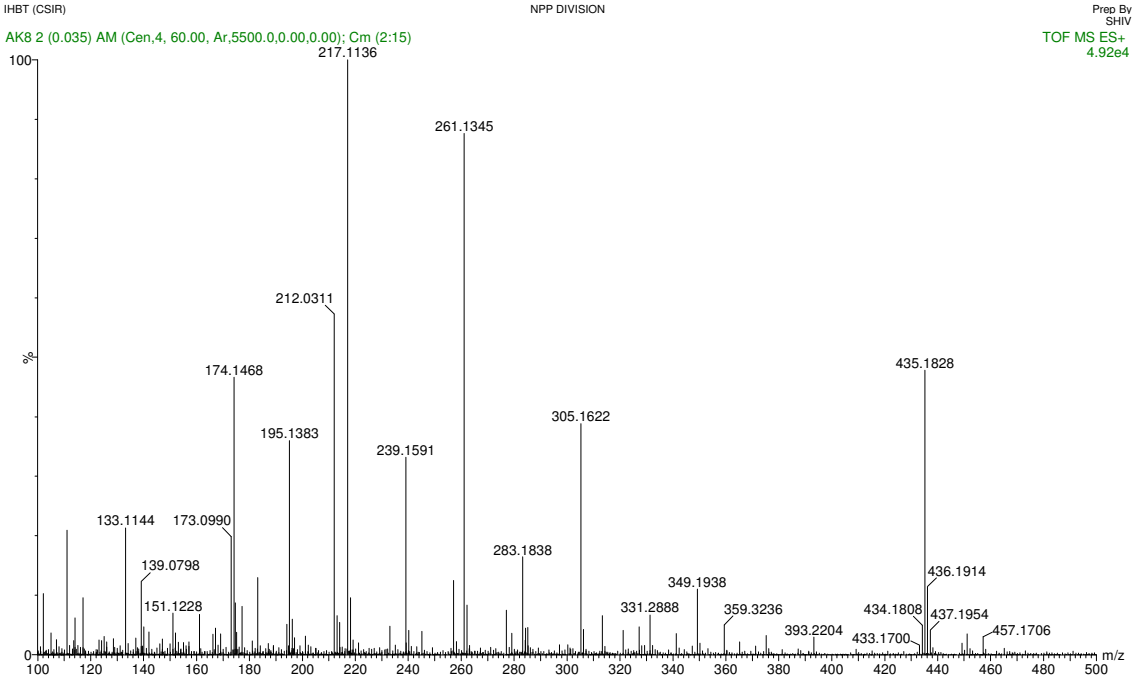
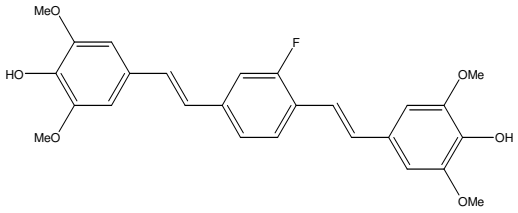


Table 3/Entry-15b, ^{1}H NMR (in CD_3COCD_3)



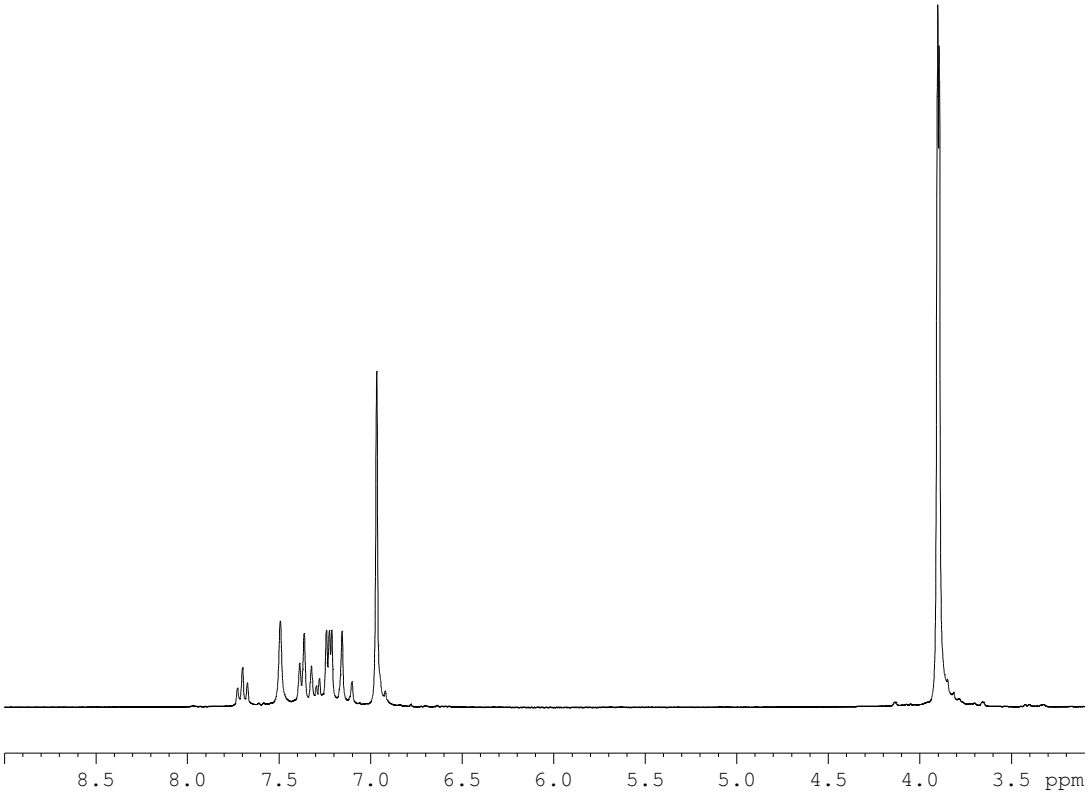
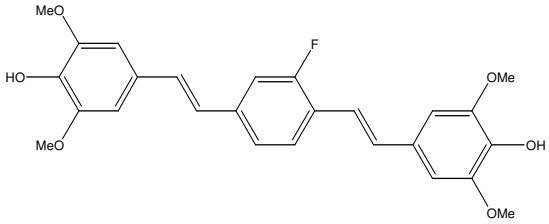


Table 3/Entry-15b, ^{13}C NMR (in CD_3COCD_3)



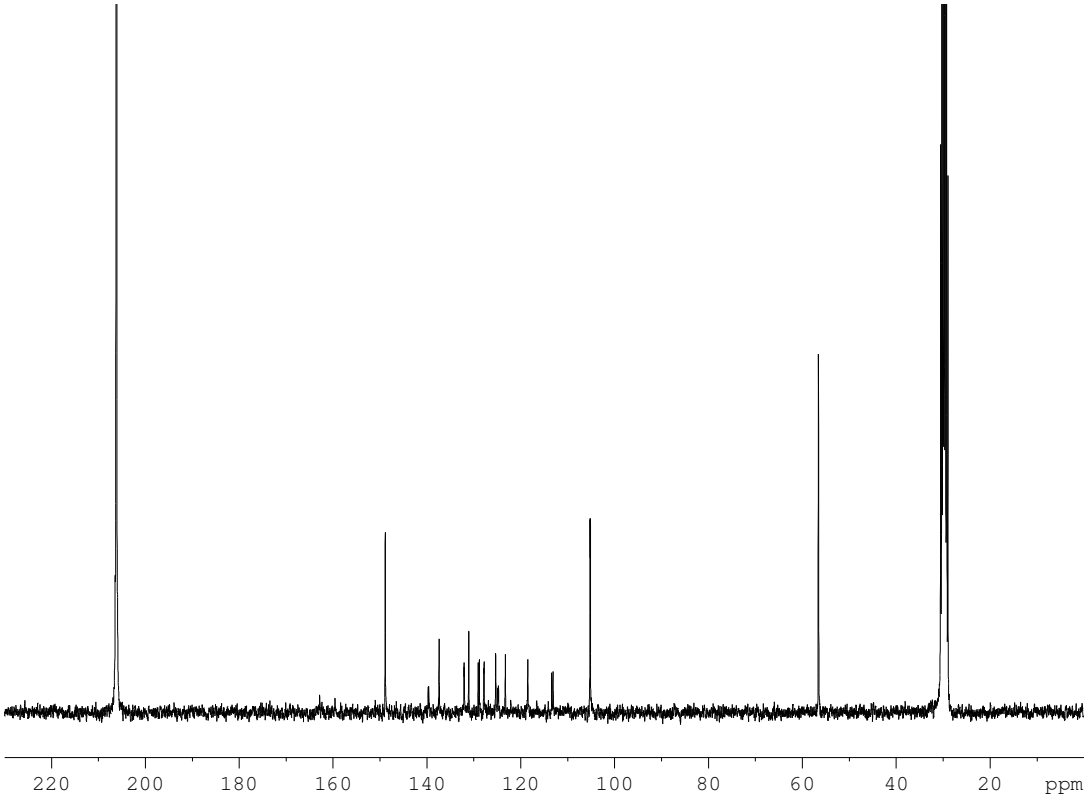
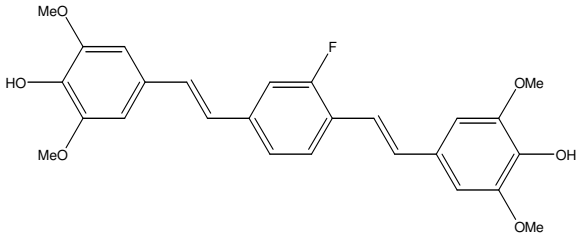


Table 3/Entry-15b, HRMS Spectrum



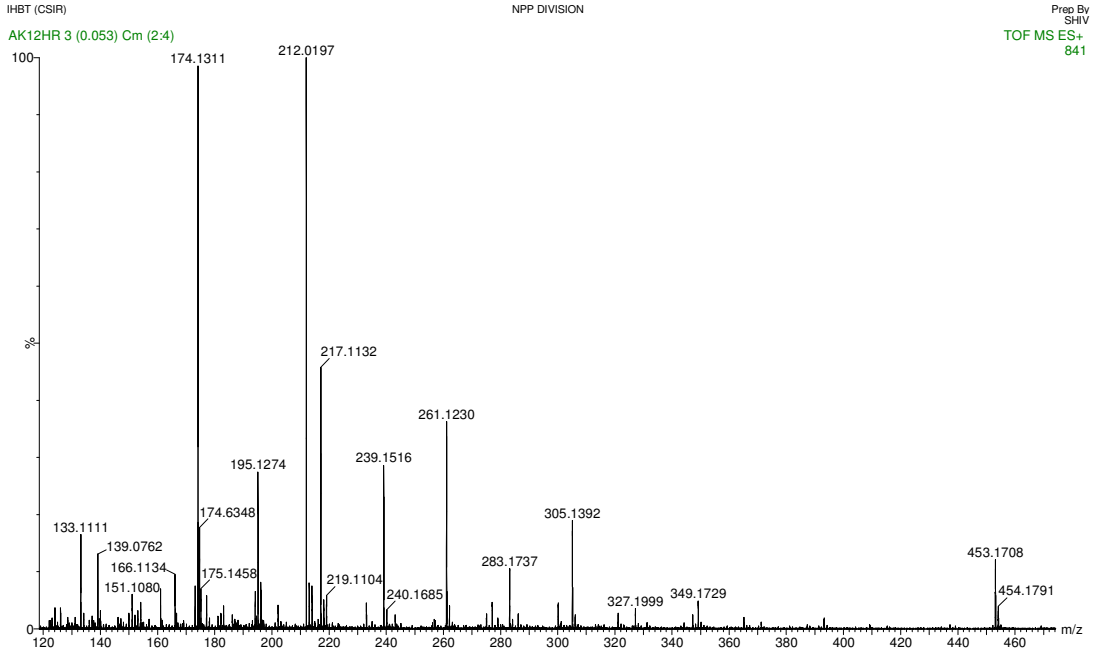
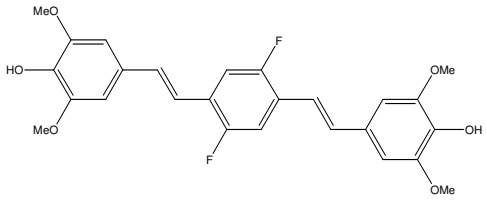


Table 3/Entry-16b, ^{1}H NMR (in DMSO)



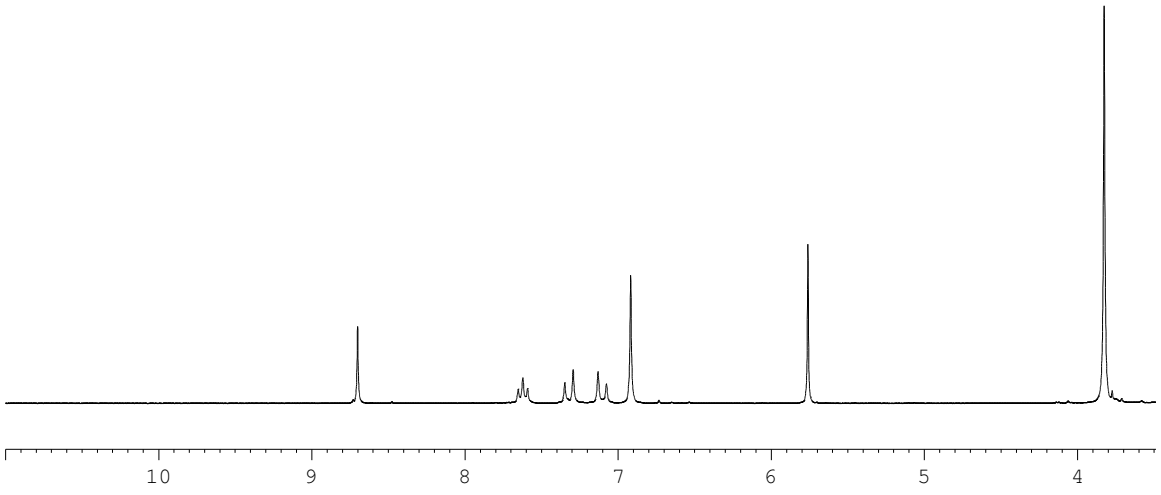
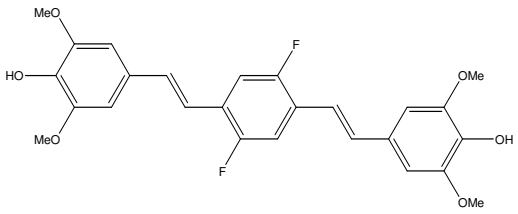


Table 3/Entry-16b, ^{13}C NMR (in DMSO)



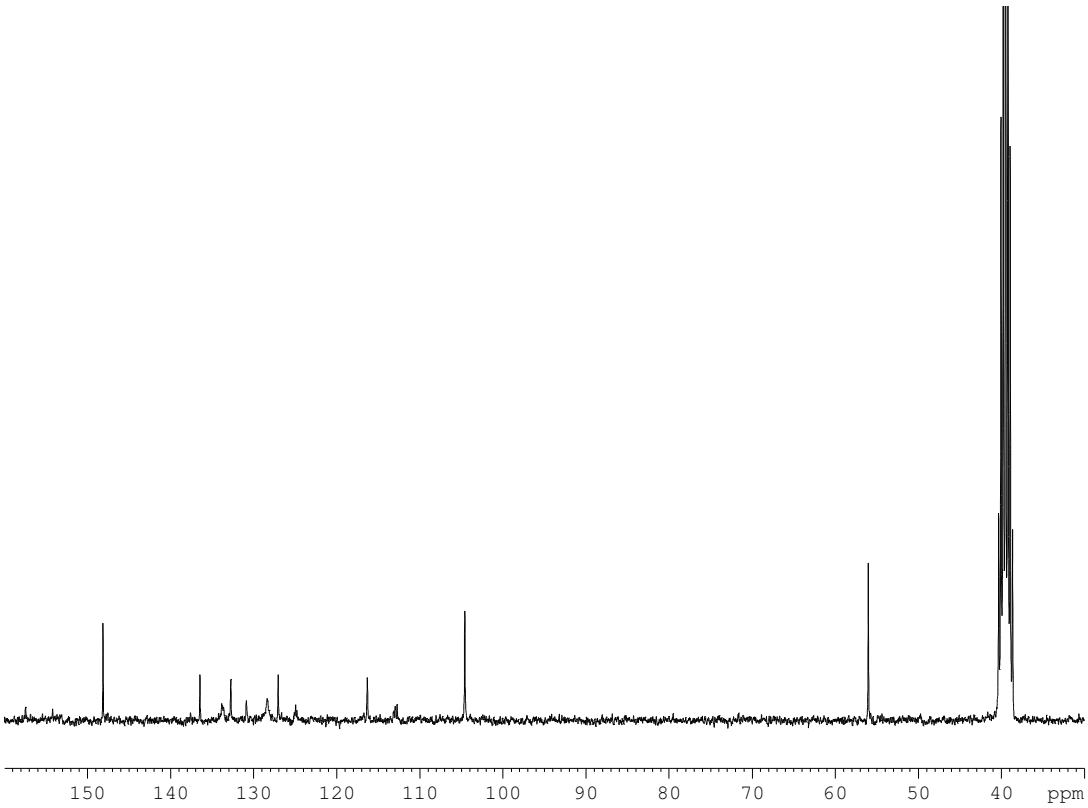
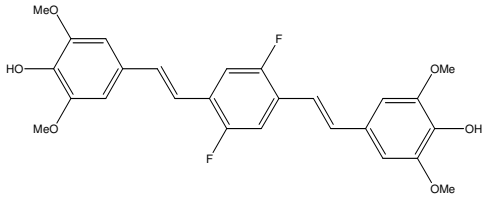


Table 3/Entry-16b, HRMS Spectrum



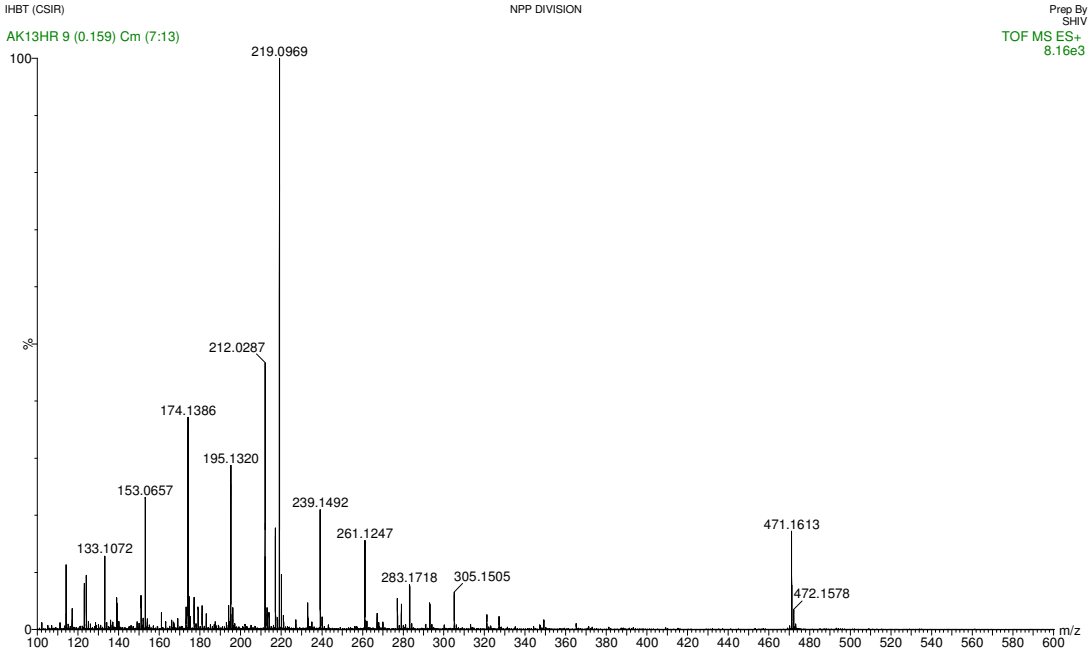
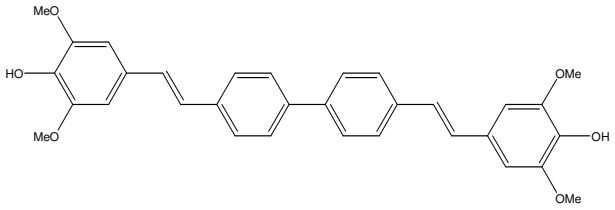


Table 3/Entry-17b, ^{1}H NMR (in DMSO)



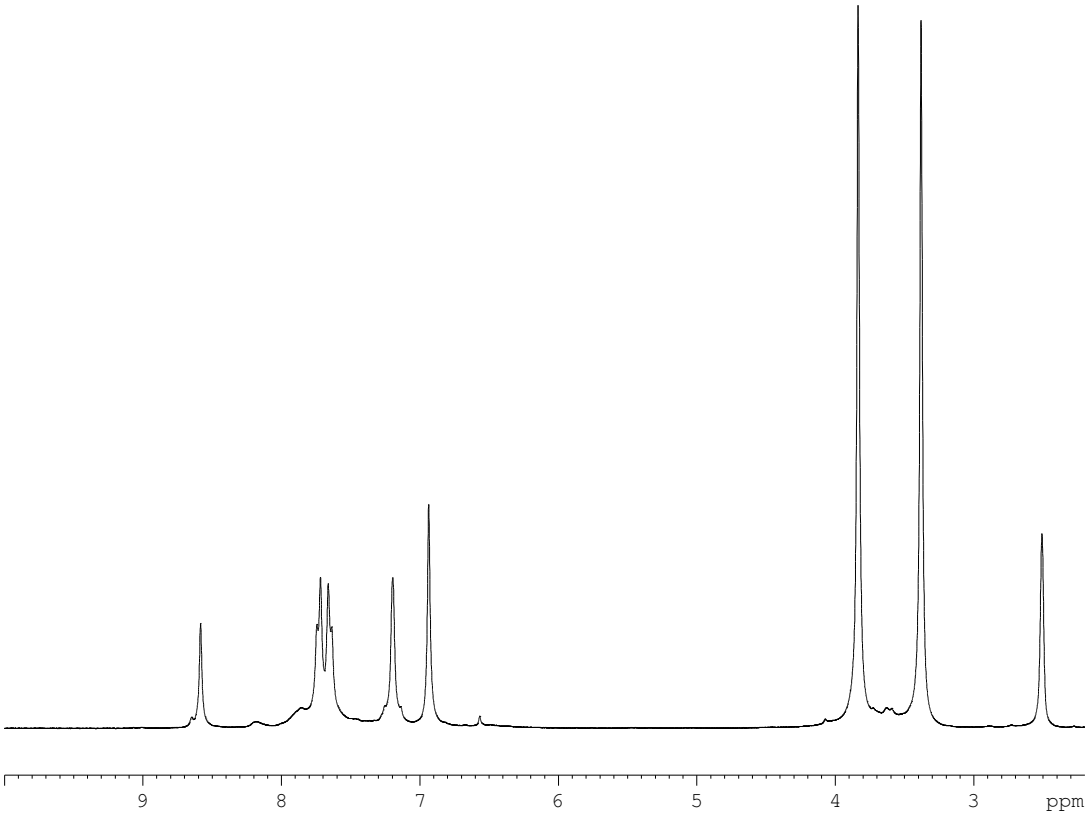
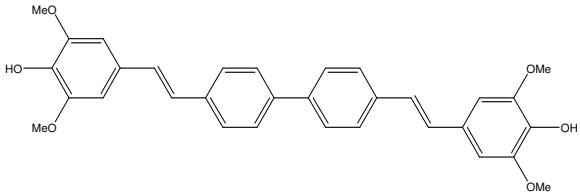


Table 3/Entry-17b, ^{13}C NMR (in DMSO)



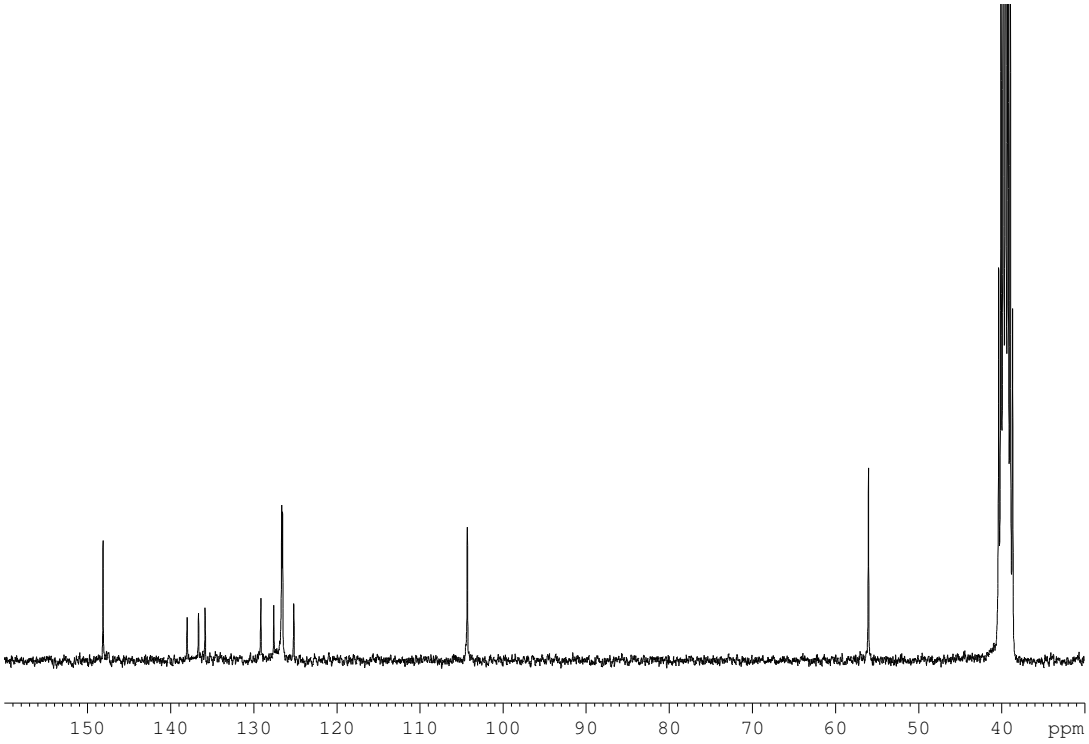
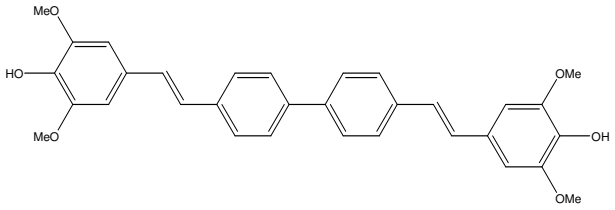


Table 3/Entry-17b, HRMS Spectrum



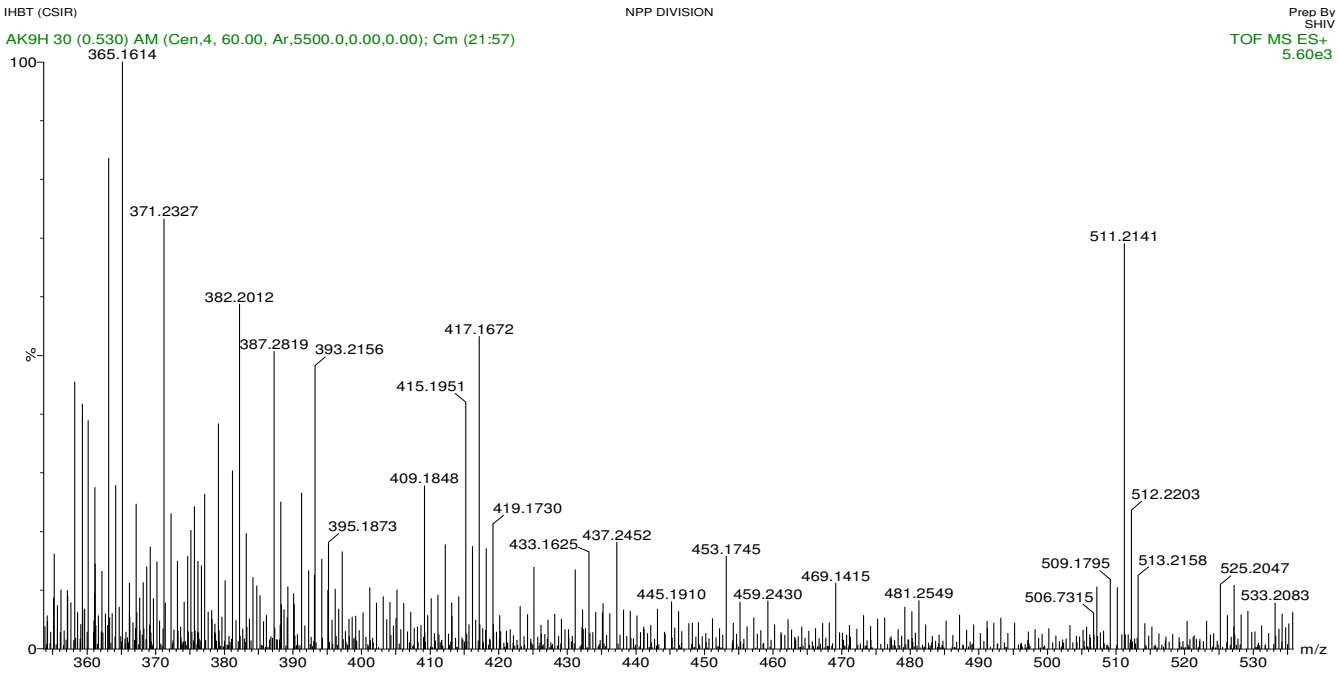
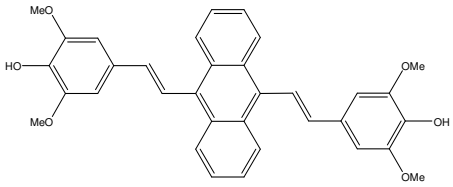


Table 3/Entry-18b, ^{1}H NMR (in DMSO)



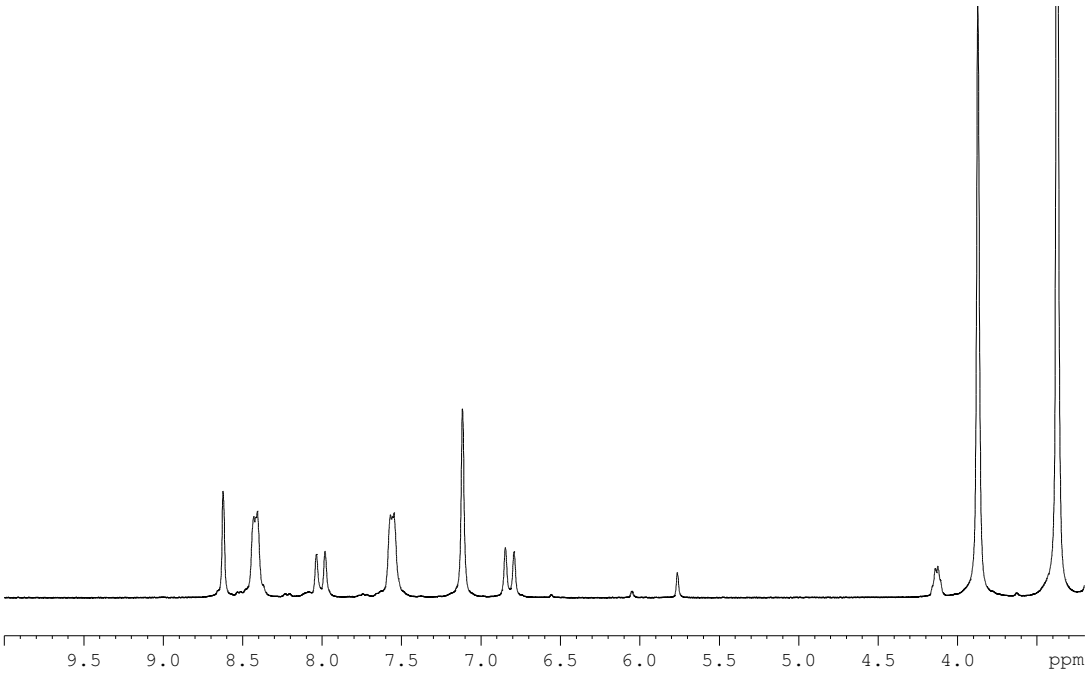
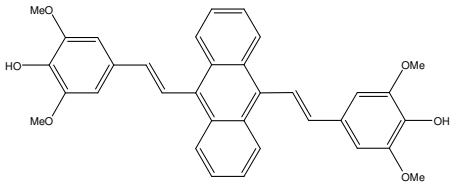


Table 3/Entry-18b, ^{13}C NMR (in DMSO)



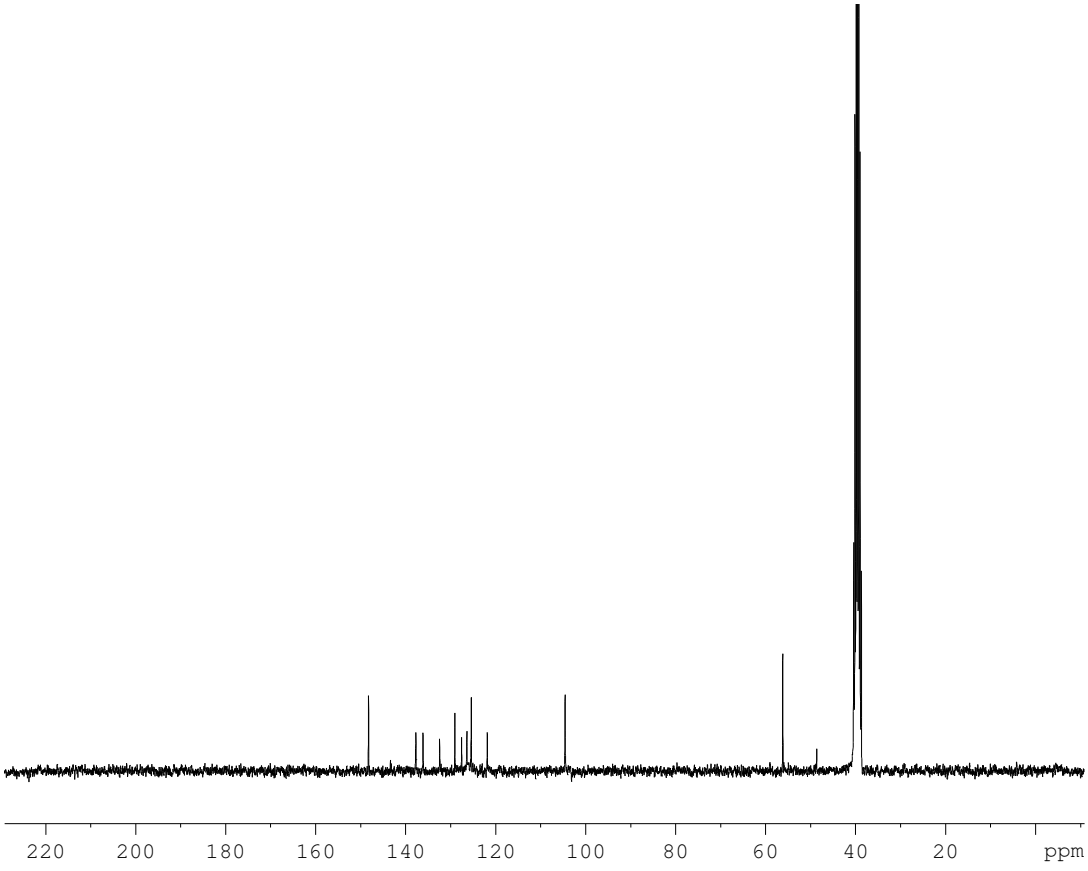
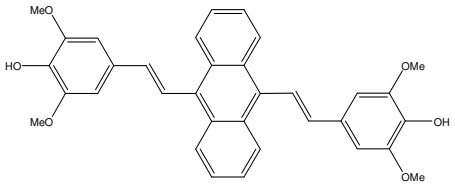


Table 3/Entry-18b, HRMS Spectrum



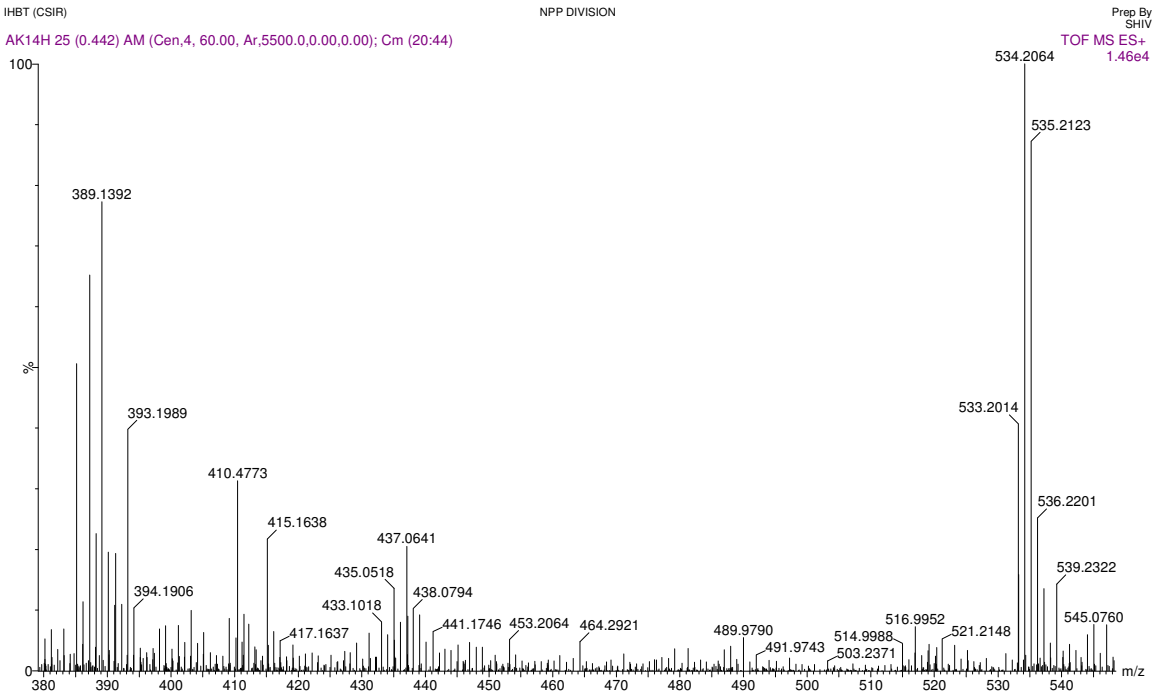
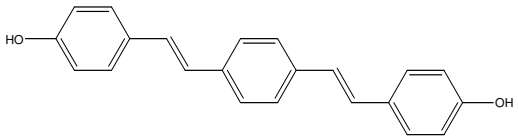


Table 3/Entry-19b, ^{1}H NMR (in DMSO)



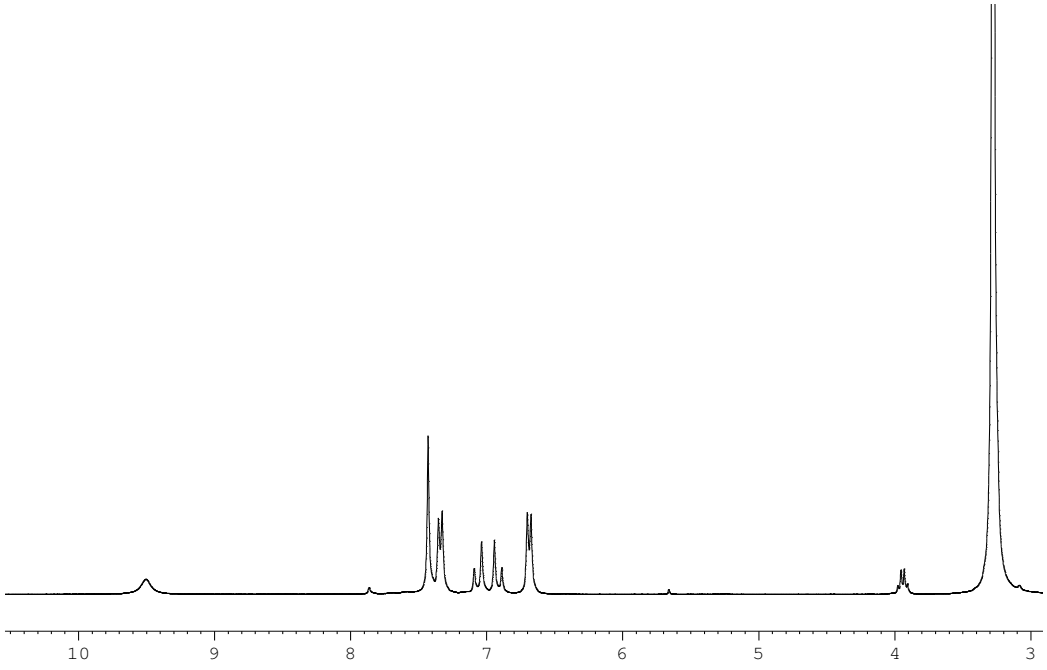
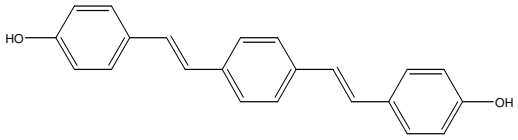
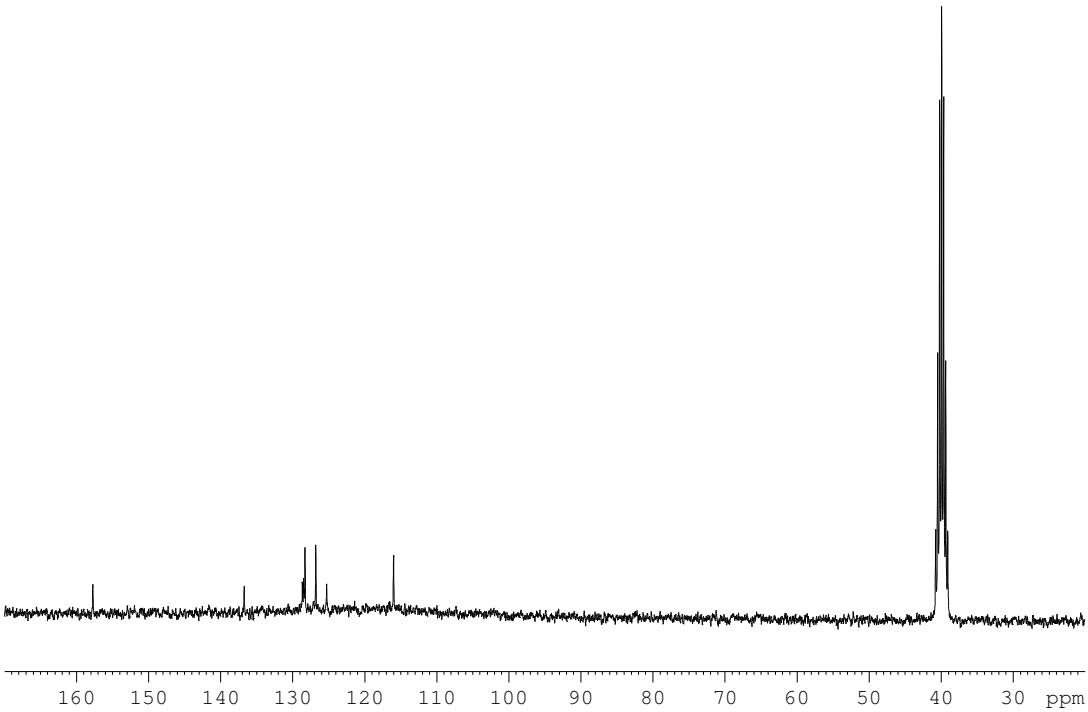
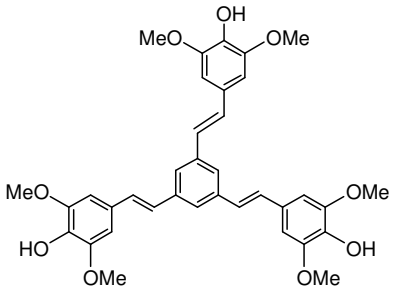


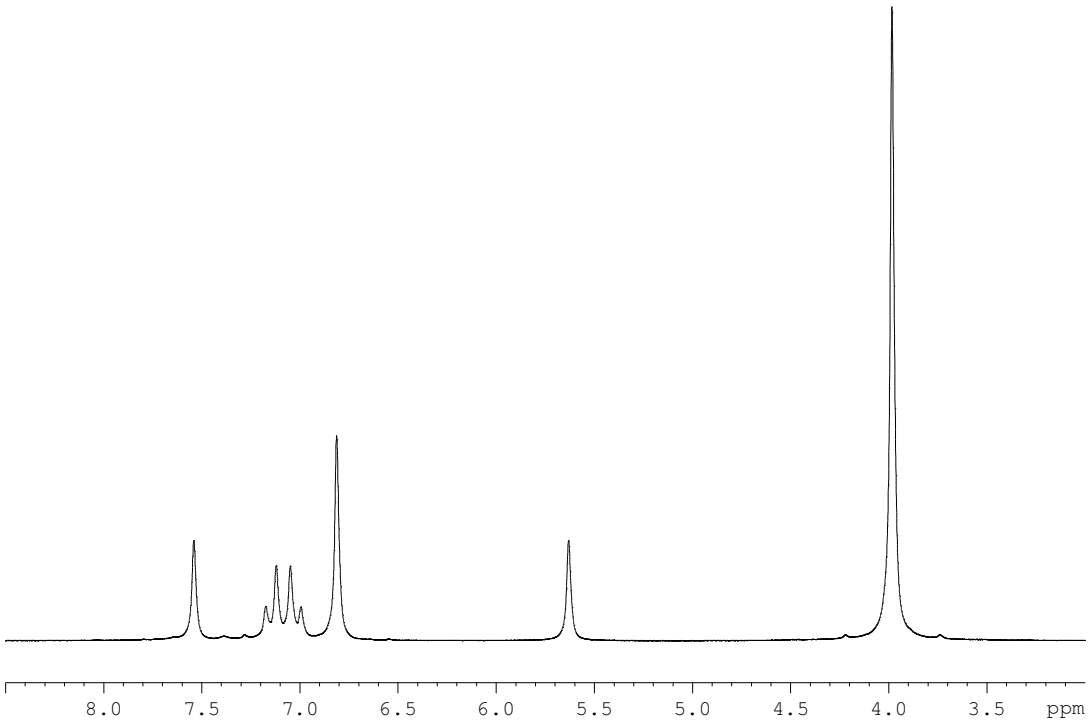
Table 3/Entry-19b, ^{13}C NMR (in DMSO)



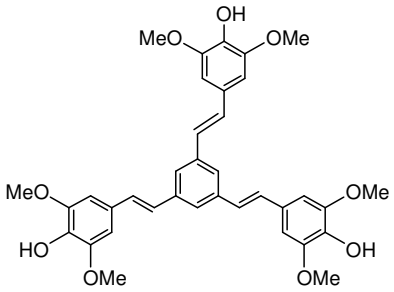


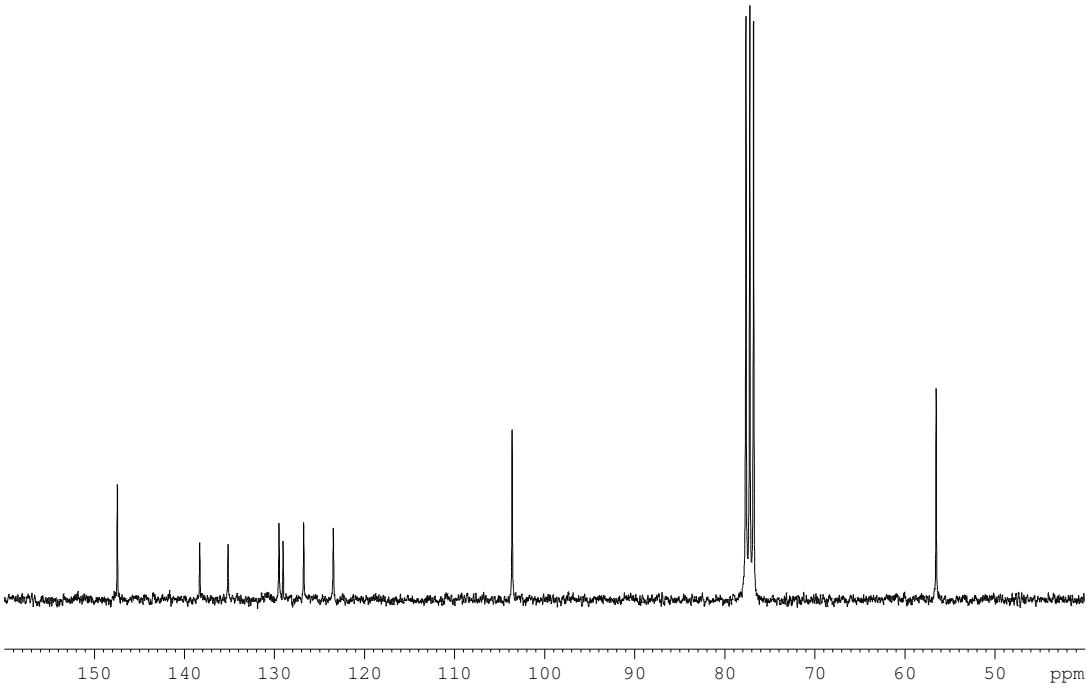
Scheme 2/20b, ^{1}H NMR (in $CDCl_3$)



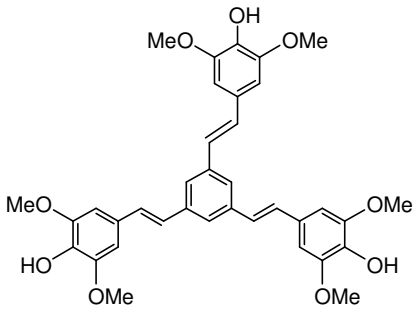


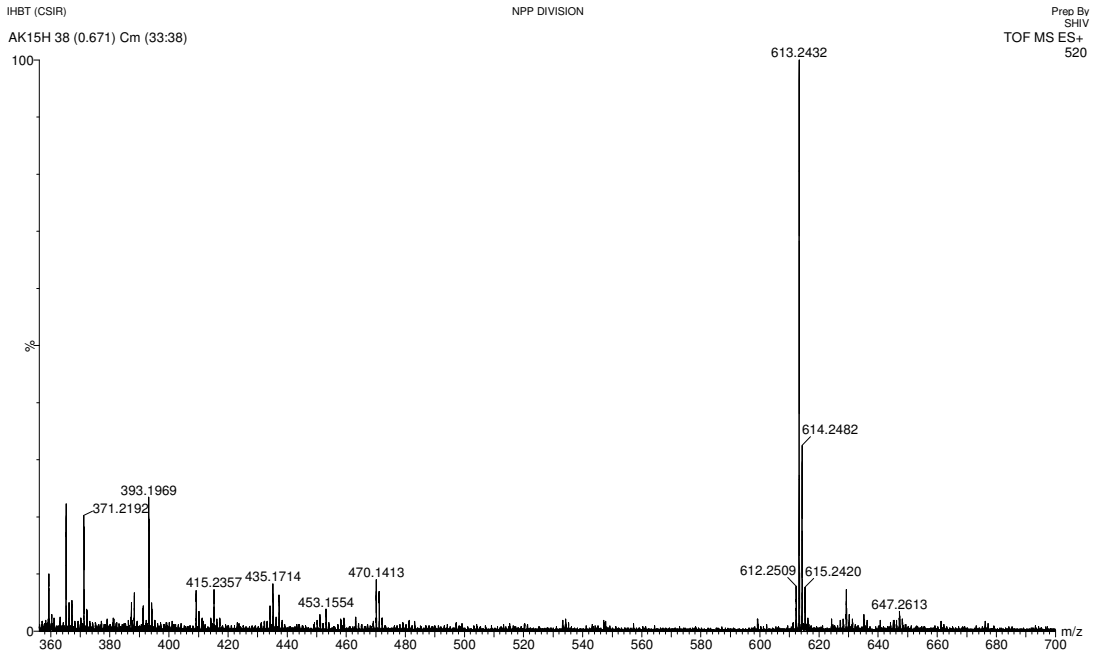
Scheme 2/20b, ^{13}C NMR (in $CDCl_3$)





Scheme 2/20b, HRMS Spectrum





Spectrophotometric and Spectrofluorimetric Studies

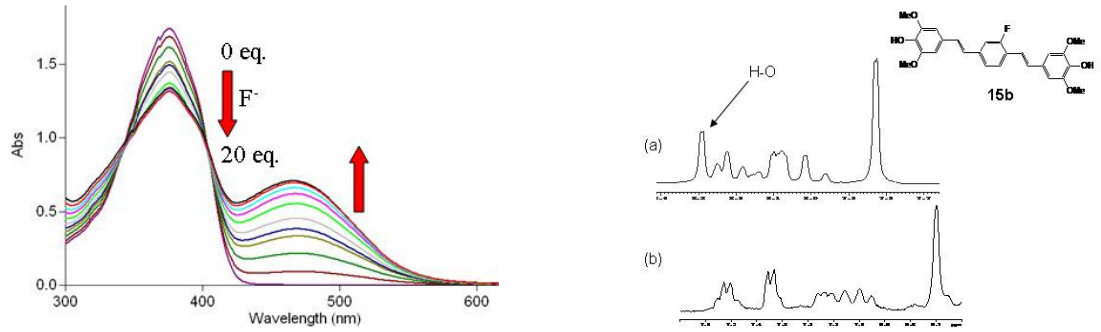
General:

The stock solutions of receptor **15b** ($8.4x10^{-4}$ M), in HPLC grade acetonitrile (J T Baker) were prepared and stored under refrigeration. These solutions were subsequently diluted to prepare test solutions ($2x10^{-5}$M) which were passed through syringe filters (0.45µm, Millipore) before use in all UV-vis and Fluorescence experiments. All the fluorescence studies of the receptor compound (15b) was conducted at an excitation wavelength of 375 nm. The Luminescence quantum yield of **15b** was measured through standard procedure[6] (equation 1) using quinine sulfate (0.5M H_2SO_4, Φ_f =0.54) as the reference standard. Absorbance of **15b** and reference (quinine sulfate) at their excitation wavelengths was controlled to be lower than 0.1.

$$\Phi_X = \Phi_{ST} \left(\frac{Grad_X}{Grad_{ST}}\right) \left(\frac{\eta^2_X}{\eta^2_{ST}}\right) \quad \text{--- Equation 1}$$

Where subscripts X and ST refer to the standard and sample respectively, Φ is the fluorescence quantum yield,
Grad is the gradient from the plot of integrated fluorescence intensity vs absorbance, η refers to the refractive index of solvent

UV-Vis and Fluorescence Titrations: The titrations of test solution of receptor **15b** (5 ml, $2x10^{-5}$M) in acetonitrile were carried out by sequential addition of microlitre amounts of F^- (TBAF). All the experiments were carried out at room temperature and the measurements were carried within 1 min. after the addition of anion.[7]
Thus, the addition of F^- aliquots progressively intensified the band at 455 nm in lieu of 373 nm (Figure 1a), while corresponding fluorescence titration (Figure 2a) revealed a gradual decrease in emission band at 455 nm.



(a) **(b)**

Fig. 1 (a) Changes in UV-vis spectra of **15b** in MeCN upon addition of TBAF; (b) Partial ^{1}H NMR spectra of **15b** in CD_3COCD_3 showing effect of F^- addition: a) before, b) after addition of F^- (20 eq)

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6. "A Guide to Recording Fluorescence Quantum Yields." Horiba Jobin Yvon Ltd.
Available online: http://www.jobinyvon.co.uk/ukdivisions/Fluorescence/plqy.htm

7. The initially colorless receptor (15b) solution upon addition of fluoride anion immediately turned orange. This solution slowly assumed pink coloration after prolonged period.

^{1}H NMR investigation of interaction of 15b with F^-

All the ^{1}H NMR experiments (300 Mhz) were conducted using 6.6 x10^{-3} M solution of receptor **15b** in CD_3COCD_3. Initially, the identity of phenolic H-O peak at 8.2 ppm was confirmed by D_2O exchange experiments. Thereafter, to a receptor solution of **15b**, F^- (TBAF) was added which resulted in the disappearance of the above phenolic peak at 8.2 ppm (Fig. 1b) with the concomitant upfield shift of aromatic protons thereby indicating redistribution and enhancement of aryl electron density.

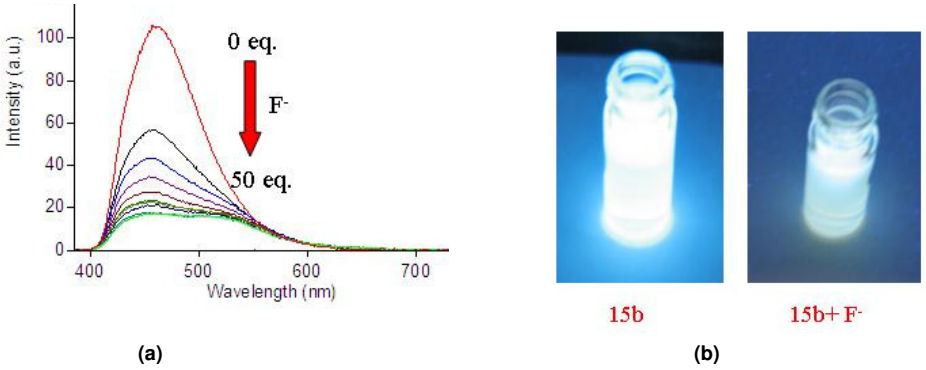


Fig. 2 (a) Changes in fluorescence spectra of **15b** in MeCN upon addition of TBAF (λ_{exc} = 375 nm) (b) Visual fluorescence change (in UV chamber) of a solution of **15b** (2x10^{-5}M) in acetonitrile following the addition of TBAF (365 nm) indicating slight quenching

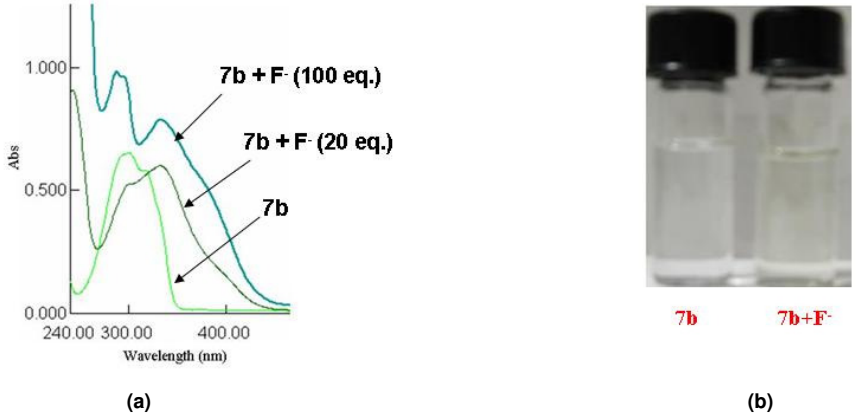


Fig. 3 (a) UV-vis spectra of *monomeric* **7b** (2x10^{-5}M) in acetonitrile showing the effect of addition of TBAF (only marginal red shift of the main absorption band was observed); (b) Visible effect of addition of TBAF (20 eq.) to receptor solution of **7b** (2x10^{-5}M) in acetonitrile indicating no apparent change in color

Sensory potential of 15b towards bases

In order to evaluate the effect of bases on OPV sensor **15b,** a $2x10^{-5}$M solution of **15b** in MeCN was exposed to various representative amines like Triethylamine, Piperidine, 1-Methylimidazole, however, none of these induced any appreciable response. Interestingly, the presence of a strong base like DBU (2 eq.) changed the solution from colorless to orange while the UV spectrum showed red shift as the λ_{max} shifted from 374 to 459 nm (Figure 4). On the other hand, the addition of even a large excess (30 eq.) of other amines (Triethylamine, Piperidine, Methylimidazole etc.) didn't elicit any appreciable response.

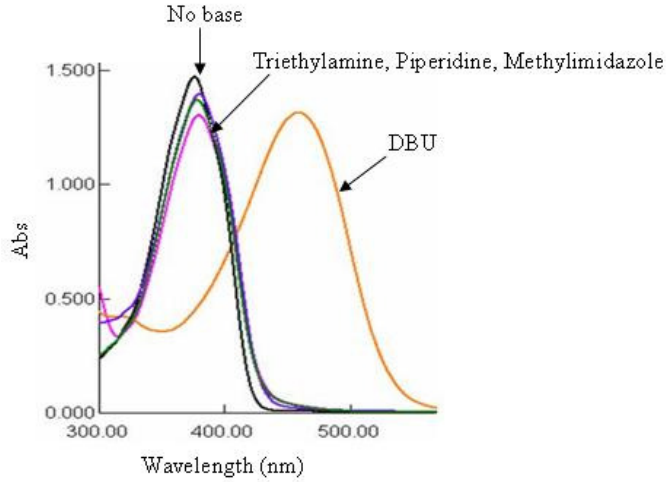


Fig. 4 UV-visible spectrum of **15b** ($2x10^{-5}$M) in MeCN and upon addition of various bases (amines)

Similarly, the addition of a hydroxide base like Tetrabutylammonium hydroxide (20 eq.) to a test solution of **15b** ($2x10^{-5}$M) in MeCN also changed the solution from colorless to orange while the λ_{max} (UV) shifted from 374 to 466 nm (Figure 5). The above result further reiterates that the colour changes and UV/Fluorescence response of **15b** to F^- might also be due to abstraction of phenolic proton. Analogous mechanistic rationale has also been disclosed in some other reports.[8]

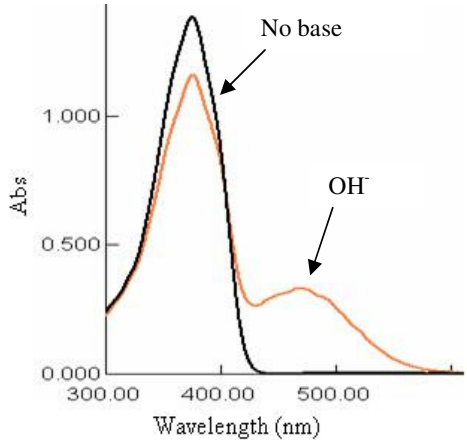


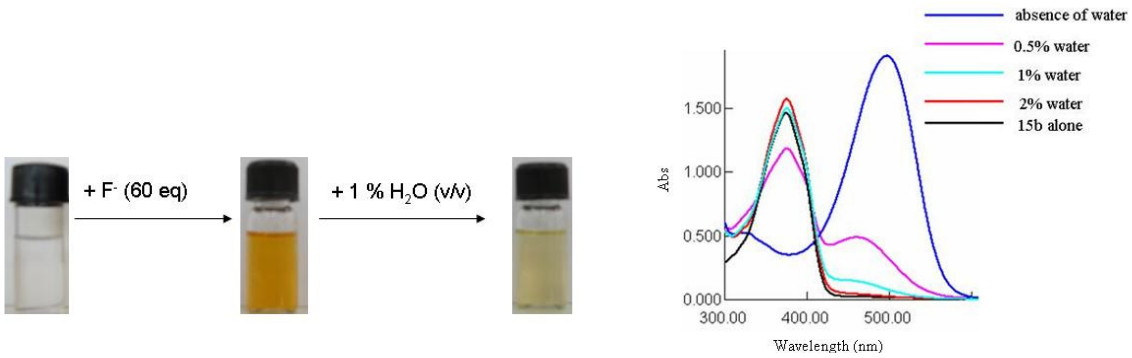
Fig. 5 UV-visible spectrum of **15b** ($2x10^{-5}$M) in MeCN and upon addition of Tetrabutylammonium hydroxide (20 eq.)

8. M. Cametti and K. Rissanen, *Chem. Commun*., 2009, 2809.

Fluoride sensing studies in aqueous conditions

Fluoride ion recognition from aqueous medium has been widely known to be a challenging but highly important domain.[9-10] Consequently, we were motivated to explore if the above developed oligomeric fluoride sensor (15b) can also be potentially used in aqueous conditions.

Initially, the role of aqueous medium was evaluated by introducing varying amount of water to the orange colored solution of **15b**-F^- complex in MeCN, wherein, a pale color was found to persist upon addition of upto 1% (v/v) H_2O (Figure 6a) while a further increase in water content disrupted any interaction between **15b** and F^-. The corresponding UV-visible spectrum (Figure 6b) also indicated a gradual blue shift with increasing concentration of water.



(a) (b)

Fig. 6 (a) Color changes of **15b** in MeCN upon sequential addition of Fluoride and 1% water; (b) Corresponding UV-vis spectra showing progressive blue shifts with increasing amount of water (v/v)

Analogous results have also been observed earlier as an efficient binding of receptor to fluoride *in presence of water* is generally difficult due to the extreme competition from solvation effect of water.[9-10] Consequently, some conceptually new approaches have sought to address this challenge by either excluding water from immediate environment of receptor-anion complex using micelles[11a] or test paper techniques[11b] or by using special Lewis acidic triarylborane[11c] receptors.

In the course of our efforts for fluoride sensing in aqueous solutions, the micellar approach[11a] didn't prove to be compatible using the OPV sensor **15b**. However, our initial investigations have revealed that **15b** can sense fluoride from even aqueous solutions through two separate but complementary approaches:

1) Test Paper approach:

Encouraged by a recent report,[11b] a test paper was obtained by dipping a filter paper in acetonitrile solution of **15b** ($2x10^{-3}$M) and drying. Subsequently, this strip was immersed in aqueous fluoride solution and then dried under a stream of hot air, wherein, the test paper showed a distinct colour change from colorless to red or yellow depending upon the concentration of fluoride solution (Figure 7). On the other hand, no such color change was observed when the above test paper was dipped in other anion solutions (Cl, I, Br, AcO, HPO_4), thereby, clearly highlighting the compatibility of OPV sensor **15b** for *fluoride detection in even aqueous solutions.*

9. P. Anzenbacher, K. Jursikova and J. L. Sessler, *J. Am. Chem. Soc*. 2000, **122**, 9350.
10. M. Melaimi, F. P. Gabbai, *J. Am. Chem. Soc*. 2005, **127**, 9680.
11. (*a*) M. Kametti, A. D. Cort and K. Bartik, *Chem Phys. Chem*, 2008, **9**, 2168. (*b*) Z. H. Lin, S. J. Ou, C. Y. Duan, B. G. Zhang and Z. P. Bai, *Chem. Commun*. 2006, 624. (*c*) C. W. Chiu and F. P. Gabbai, *J. Am. Chem. Soc*. 2006, **128**, 14248.

Fig. 7. (a) Detection of fluoride from its water:acetonitrile (1:1, v/v) solutions of different concentrations through colour changes in test papers coated with **15b**

Representative Procedure for fluoride detection using the test paper technique:

A 3x0.5 cm filter paper was immersed in the acetonitrile solution of **15b** ($2x10^{-3}$M) for 2 min followed by drying under stream of hot air. Thereafter, the above sensor paper was immersed in a test 50% (v/v) aqueous fluoride solution for 5 min and then dried under stream of hot air. The exposure to hot air was found to be necessary for the color change in test paper while this paper gradually reverted back to colorless state when exposure to hot air was removed.

2) <u>Additive approach:</u>

The above reversible anion sensing behavior by test paper motivated us to explore other alternatives for shielding the **15b-F**$^-$ complex from solvation by water while simultaneously providing a more persistent F^- responsive color signal. In this context various complementary approaches using additives like silica, activated alumina, PPh_3, DCC (N, N'-Dicyclohexylcarbodiimide) etc were initially explored. Subsequently, the use of molecular sieves (MS) as an additive was found to provide a *convenient and new approach for fluoride recognition by **15b** from aqueous conditions.*

Thus, the addition of MS (3A) to an otherwise colorless 1:1 water:MeCN (v/v) solution of **15b** ($2x10^{-5}$ M) in the presence of F^- led to a yellow colored solution in 15-30 min at room temperature (Figure 8). This yellow color underwent further intensification upon retaining the molecular sieves for prolonged duration. The above changes were also monitored by UV-vis spectroscopy (Figure 9) which indicated red shifts of the main absorption band from λ_{max}= 374 to 420-427 nm at different intervals of time.

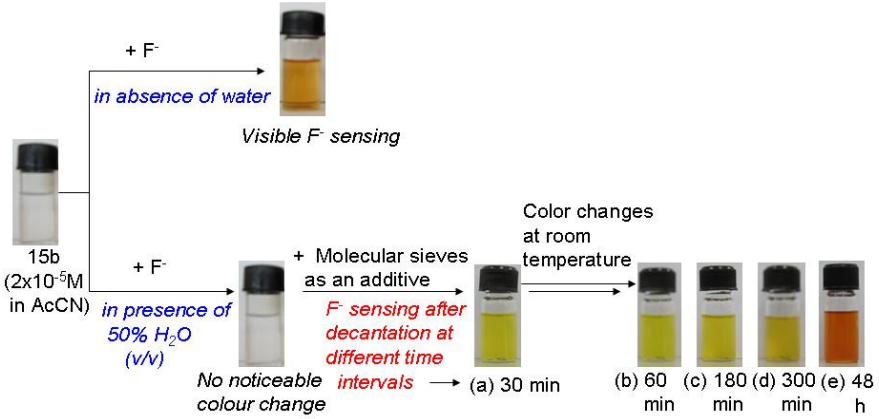


Fig. 8. Visible fluoride sensing by **15b** in water:acetonitrile (1:1, v/v) solution containing molecular sieves after decantation at different time intervals (30, 60, 180, 300 min and 48 h)

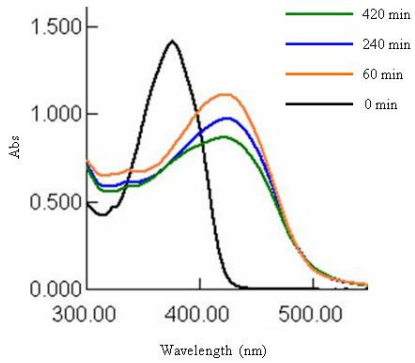


Fig. 9 (a) UV-Vis spectra of **15b** ($2x10^{-5}$ M) in water:acetonitrile (1:1, v/v) obtained using molecular sieves as additive which upon decantation at different intervals (0, 60, 240 and 420 min) showed red shift

The above convenient strategy employing inexpensive and recyclable molecular sieves as an additive could be used with upto 1:1 (v/v) water:MeCN solutions as the sensor **15b** underwent precipitation at higher water contents (> 50%). Moreover, the use of 3A molecular sieves at room temperature was optimum as an increase in pore size (>3A) or sonication didn't lead to a rapid visual response. Further investigations regarding various other aqueous fluoride sensing approaches using **15b** are currently under progress in our laboratory.

Representative procedure for visual detection of F^- from aqueous conditions:

In a typical example, a test solution of **15b** ($2x10^{-5}$ M) was prepared in 5 ml of 1:1 (v/v) water/acetonitrile mixture followed by addition of TBAF (60 eq). To the above colorless solution, molecular sieves (3A, 1.2 g) were added and the solution was allowed to stand still, whereupon, instantaneous colour changes were observed. Thus, after only 30 min, the solution completely changed from colorless to yellow (the solution was decanted from molecular sieves for recording the UV spectra) followed by a progressive deepening of the colour to eventually provide a orange-red colored solution after several hours (24-48h).