Supporting Information

CSJ acting as a versatile highly efficient greener resource for organic transformations

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Contents

Materials and Methods

The substituted benzaldehydes (1a-q), substituted benzoic acids (3a-n) and all other reagents were purchased from Sigma–Aldrich, Merck and Fluka. Substituted cinnamic acids such as p-coumaric acid, caffeic acid, ferulic acid, sinapic acid and p-amino cinnamic acid were also purchased from Sigma–Aldrich and Fluka. α-phenylcinnamic acid derivatives (6o and 8j) were prepared by Knoevenagel–Doebner condensation or modified Perkin reaction. Acetyl protection of hydroxyl derivative of benzaldehydes, cinnamic acid derivatives, styrene derivatives and α-phenylcinnamic acid derivatives were synthesized. The structure and purity of the compounds were confirmed by nuclear magnetic resonance (NMR). TLC experiments were performed on EMD Merck F_{254}, 250 mm thickness. Column chromatography was performed with Merck silica gel (230–400 mesh). All solvents used throughout the experiments were purchased from Merck.

Synthesis of substituted cinnamic acids

Compounds 5c, 5f, 5g, 5i, 5j and 5k (in Scheme 3) were synthesized by Knoevenagel condensation reaction.[1] In each experiment, substituted benzaldehyde (30 mmol), malonic acid (60 mmol), pyridine (20 ml), and piperidine (0.5 ml) were mixed well, heated to 80–85 ºC for 1hr and finally refluxed (110–110 ^{o}C) for an additional 3hr. Then the reaction mixture was poured into water and acidified with concentrated hydrochloric acid. The precipitate obtained was filtered and washed with cold water repeatedly. The residue was dissolved in diluted sodium hydroxide (30 %), again acidified to obtain the precipitate and then washed with cold water. Then crude product was dried and recrystallized using ethyl methyl ketone. All structures were confirmed by NMR spectroscopy.

Synthesis of substituted 2, 3-Diphenyl-acrylic acids

Compounds (6o and 8j) were synthesized by Perkin Condensation.[2] Substituted phenyl acetic acid (20 mmol) was taken in a round bottom flask and then added triethylamine (5ml) and acetic anhydride (5 ml). The reaction mixture was stirred for 10 minutes at room temperature. After that, the corresponding substituted benzaldehyde (20 mmol) was added to the individual reaction mixture. Then, each reaction mixture was heated to 110 ºC for 3hr and finally 140 ^{o}C for 1hr. After cooling, the mixture was acidified with concentrated hydrochloric acid, poured into ice water, stirred, and stored for 4 hr. A fuscous yellowish solid was obtained, filtered, dissolved in 10% aqueous sodium hydroxide (40 ml), washed, and separated with ethyl acetate. Hydrochloric acid was added to the aqueous phase until pH 3–4. The precipitated solid was filtered and recrystallized from ethyl acetate to afford 6o and 8j compounds. The purity of compounds was confirmed by NMR spectroscopy.

Synthesis of substituted 2-Methyl-3-phenyl-acrylic acids

Substituted 2-Methyl-3-phenyl-acrylic acids were prepared by Knovenaegel condensation reaction where substituted benzaldehyde (10 mmol) condensed with propionic anhydride (10 mmol) in presence of sodium propionate (5 gm) at 110-120 ^{o}C for 24 hr.[3]After cooling, reaction mixture was poured into 20 % aqueous sodium hydroxide (30 ml). Then ethyl acetate was poured into the reaction mixture and shaken vigorously to separate organic and aqueous layer. Aqueous part was acidified with concentrated hydrochloric acid up to pH 3-4 and dichloromethane was added to it. Then the organic phase was dried over sodium sulphate and evaporated under reduced pressure. The products (5m and 5n) were recrystallized by using ethyl methyl ketone and structures were confirmed by NMR spectroscopy.

Acetylation of organic compounds

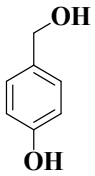
Acetyl protection of hydroxyl derivatives of benzaldehydes, cinnamic acids, styrenes and α-phenylcinnamic acids were synthesized by acetic anhydride in presence of pyridine either room temperature or refluxing condition.[4] All structures were confirmed by NMR spectroscopy.

Biotransformation by CSJ

In each experiment, substrate (1gm) separately was added to the freshly prepared cucumber juice (200ml). The reaction mixture was stirred at 30-35 ºC temperature maximum for 72 hr under inert atmosphere (scheme1-4). Each individual suspension was filtered, and the residue was washed with water, as well as with ethyl acetate. The filtrate was then extracted with ethyl acetate (3×100ml), and the organic phase was dried over sodium sulphate and evaporated under reduced pressure. After that, each reaction mixture was purified by column chromatography using ethyl acetate and n-hexane as eluent to afford the product. NMR spectra were recorded on Bruker 200 MHz spectrometer. All spectral data of obtained products agreed well the reported values. [2, 4-8]

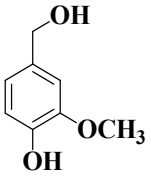
Characterization data of the products

4-Hydroxymethyl-phenol (2b):-



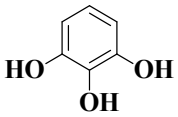
^{1}H NMR (200 MHz, D_4-MeOH) δ 7.13 (d, *J* = 8.4 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 4.44 ppm (s, 2H); Column chromatography on silica gel using n-hexane/ethyl acetate (4:1 v/v).

5-Hydroxymethyl-2-methoxy-phenol (2i):-



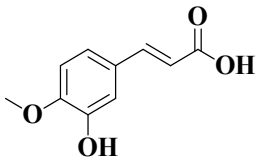
^{1}H NMR (200 MHz, $CDCl_3$) δ 6.87-6.77 (m, 3H), 5.61 (brs, 1H), 3.86 (s, 3H), 1.66 ppm (brs, 1H); Column chromatography on silica gel using n-hexane/ethyl acetate (4:1 v/v).

Benzene-1, 2, 3-triol (4m):-



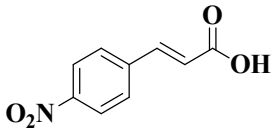
^{1}H NMR (200 MHz, DMSO-d_6) δ 8.75 (brs, 2H), 8.03 (brs, 1H), 6.44 (dd, *J* = 8.8Hz, 1H), 6.24 ppm (dd, *J* = 8.8Hz, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 146.70 (2xC) 133.53 (C), 118.86 (CH), 107.52 ppm (2xCH); Column chromatography was not required for product purification.

3-(3-Hydroxy-4-methoxy-phenyl)-acrylic acid (5f):-



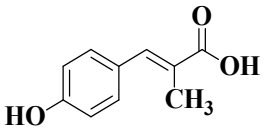
^{1}H NMR (200 MHz, DMSO-d_6) δ 12.17 (brs, 1H), 9.15 (brs, 1H), 7.43 (dd, *J* = 15.8, 6.6 Hz, 1H), 6.99 (m, 3H), 6.23 (dd, *J* = 15.8, 6.8 Hz, 1H), 3.79 ppm (s, 3H); ^{13}C NMR (50MHz, DMSO-d_6) 168.29 (C=O), 150.25 (C), 147.09 (C), 144.67 (C), 127.53 (C), 121.45 (CH), 116.70 (CH), 114.53 (CH), 112.33 (CH), 55.96 ppm (OCH_3); Column chromatography was not required for product purification.

(E)-3-(4-nitrophenyl) acrylic acid (5l):-



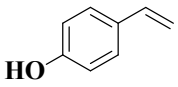
^{1}H NMR (200 MHz, DMSO-d_6) δ 8.18 (d, *J* = 8.4 Hz, 2H), 7.92 (d, *J* = 8.4Hz, 2H), 7.64 (d, *J* = 16 Hz, 1H), 6.69 ppm (d, *J* = 16Hz, 1H); ^{13}C NMR (50 MHz, DMSO- d_6) δ 167.51 (C=O), 148.37 (C), 141.65 (CH), 141.23 (C), 129.70 (2x CH), 124.19 (2x CH), 123.41 ppm (CH); Column chromatography was not required for product purification.

3-(4-Hydroxy-phenyl)-2-methyl-acrylic acid (5m):-



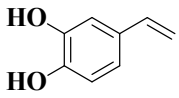
^{1}H NMR (200 MHz, $CDCl_3$) δ 11.98 (brs, 1H), 9.78 (brs, 1H), 7.54 (s, 1H), 7.29 (d, *J* = 8.8Hz, 2H), 6.82 (d, *J* = 8.8Hz, 2H), 2.01 ppm (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 190.95 (C=O), 172.71(C=O), 140.48 (CH), 131.06 (2xCH), 128.01 (C), 127.23 (C), 121.80 (2xCH), 14.18 ppm (CH_3); Column chromatography on silica gel using n-hexane/ethyl acetate (3:1 v/v).

4-Vinyl-phenol (6b):-



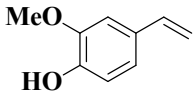
^{1}H NMR (200 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.8Hz, 2H), 6.90 (d, *J* = 8.8Hz, 2H),6.73 (dd, *J* = 10.8, 17.6Hz, 1H),5.68 (dd, *J* = 0.8, 17.6Hz, 1H),5.21 ppm (dd, *J* = 0.8, 10.8Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 155.58 (C), 136.48 (CH), 130.83 (CH), 127.91 (2xCH), 115.80 (2xCH), 111.85 ppm (CH_2); Column chromatography was not required for product purification.

4-Vinylbenzene-1, 2-diol (6d):-



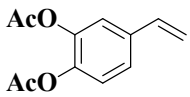
^{1}H NMR (200MHz, DMSO-d_6) δ 8.94 (brs, 2H), 6.83 (s, 1H), 6.68 (d, *J* = 8.2Hz, 2H), 6.48 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.45 (d, *J* = 17.6 Hz, 1H), 4.96 ppm (d, *J* = 10.8 Hz, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) 146.02 (C), 145.75 (C), 137.20 (CH), 129.33 (C), 118.54 (CH), 115.98 (CH), 113.34 (CH), 110.88 ppm (CH_2); Column chromatography was not required for product purification.

2-Methoxy-4-vinylphenol (6e):-



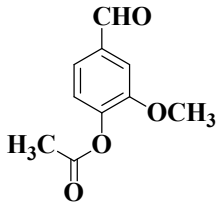
^{1}H NMR (200 MHz, $CDCl_3$) δ 6.90 (m, 3H), 6.65 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.60 (dd, *J* = 17.6, 0.8 Hz, 1H), 5.14 (dd, *J* = 10.8, 0.8 Hz, 1H), 3.90 ppm (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 146.77 (C), 145.78 (C), 136.78 (CH), 130.40 (C), 120.20 (CH), 114.55 (CH), 111.57 (CH_2), 108.21 (CH), 56.01 ppm (OCH_3); Column chromatography was not required for product purification.

Acetic acid 2-acetoxy-5-vinyl-phenyl ester (7c):-



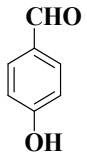
^{1}H NMR (200 MHz, DMSO-d_6) δ 7.30 (d, *J* = 2Hz, 1H), 7.26 (dd, *J* = 2, 6.8Hz, 1H), 7.12 (dd, *J* = 2, 6.8 Hz, 1H), 6.62 (dd, *J* = 11, 17.8Hz, 1H), 5.73 (dd, *J* = 0.8, 17.8Hz, 1H), 5.19 (dd, *J* = 0.8, 11Hz, 1H), 2.16 ppm (s, 6H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 168 (C=O), 142.72 (C), 142.06 (C), 136.51 (CH), 135.60 (C), 124.90 (CH), 124.20 (CH),121.37 (CH), 115.90 ppm.(CH_2); Column chromatography was not required for product purification.

Acetic acid 4-formyl-2-methoxy-phenyl ester (7b):-



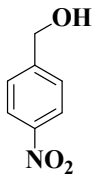
^{1}H NMR (200 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.45 (s, 1H), 7.41 (d, *J* = 7.6Hz,1H), 7.17 (d, *J* = 7.6Hz,1H), 3.85 (s, 3H), 2.30 ppm (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 191.08 (C=O), 168.36 (C=O), 152.03 (C), 145 (C), 135 (C), 124.65 (CH), 123.48 (CH), 111.00 (CH), 56.12 (OMe), 20.64 ppm (CH_3); Column chromatography was not required for product purification.

4-Hydroxy-benzaldehyde (8a):-



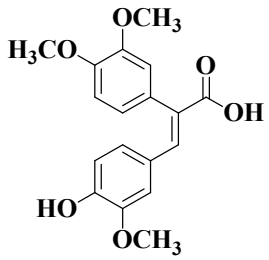
^{1}H NMR (200 MHz, $CDCl_3$) δ 9.84 (C=0), 7.80 (d, *J* = 7Hz, 1H), 6.93 ppm (d, *J* = 7Hz, 1H); Column chromatography was not required for product purification.

(4-Nitrophenyl)-methanol (8m):-



^{1}H NMR (200 MHz, DMSO-d_6) δ 8.22 (d, *J* = 8.8Hz, 2H), 7.54 (d, *J* = 8.8 Hz, 2H), 4.84 (s, 2H), 2.04 ppm (brs, 1H); Column chromatography on silica gel using n-hexane/ethyl acetate (4:1 v/v).

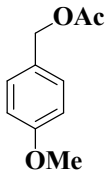
(E)-2-(3, 4-dimethoxyphenyl)-3-(4-hydroxy-3-methoxyphenyl) acrylic acid (8j):-



^{1}H NMR (200 MHz, DMSO-d_6) δ 12.31 (br s, 1H), 9.50 (br s, 1H), 7.65 (s, 1H), 7.02 (d, *J* = 8.2 Hz, 1H), 6.78 (s, 1H), 6.69 (m, 3H), 6.55 (s, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 3.40 ppm (s, 3H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.79 (C=O), 149.03 (C), 148.25 (C), 148.01 (C), 146.92 (C), 139.33 (CH), 129.58 (C), 129.40 (C), 125.81 (C), 125.18

(CH), 121.94 (CH), 115.17 (CH), 113.94 (CH), 113.48 (CH), 112.27 (CH), 55.66 (2x CH_3), 54.75 ppm (CH_3); Column chromatography on silica gel using n-hexane/ethyl acetate (3:1 v/v).

Acetic acid 4-methoxy-benzyl ester (7k):-



^{1}H NMR (200 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.4 Hz, 2H), 6.83 (d, 8.4 Hz, 2H), 4.99 (s, 2H), 3.71 (s, 3H), 1.96 ppm (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) 170.59 (C=O), 159.63 (C), 130.02 (2x CH), 128.18 (C), 113.85 (2x CH), 65.89 (CH_2), 54.99 (OCH_3), 20.74 ppm (CH_3); Column chromatography was not required for product purification.

References

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3. , E. Mincione, M. Barontini, G. Provenzano and L. Setti, *Tetrahedron*, 2007, **63**, 9663–9667. S. T. Hazeldine, L. Polin, J. Kushner, K. White, T. H. Corbett and J. P. Horwitz, *Bioorg. Med. Chem.*, 2005, **13**, 3910–3920.
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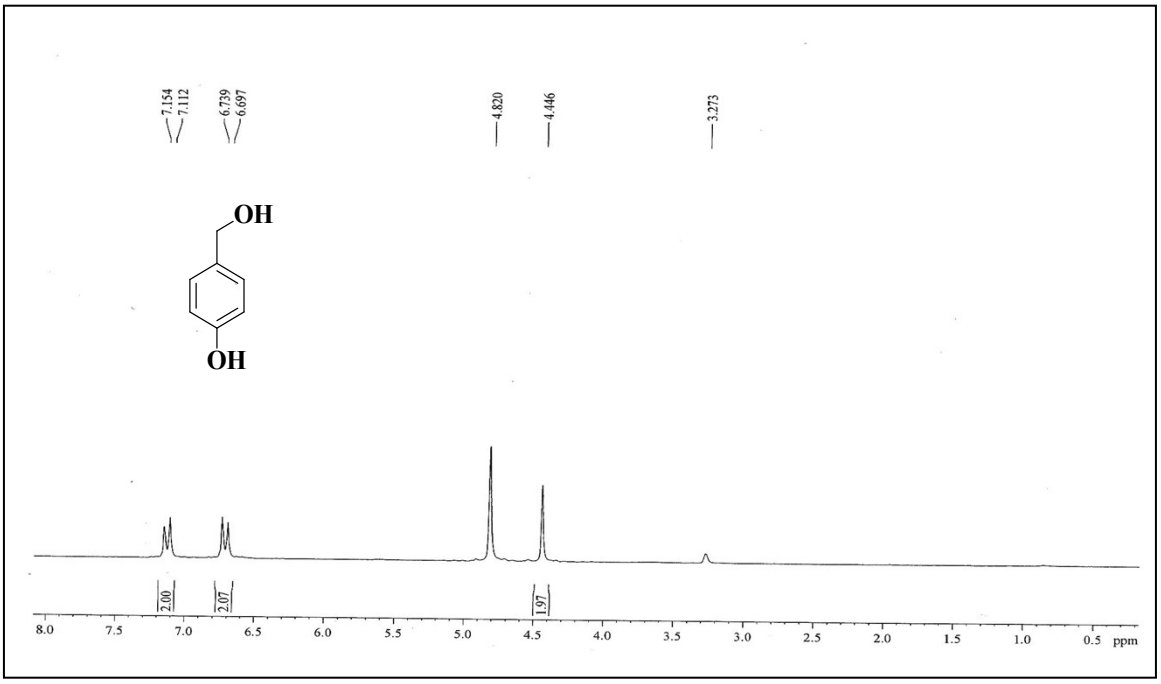
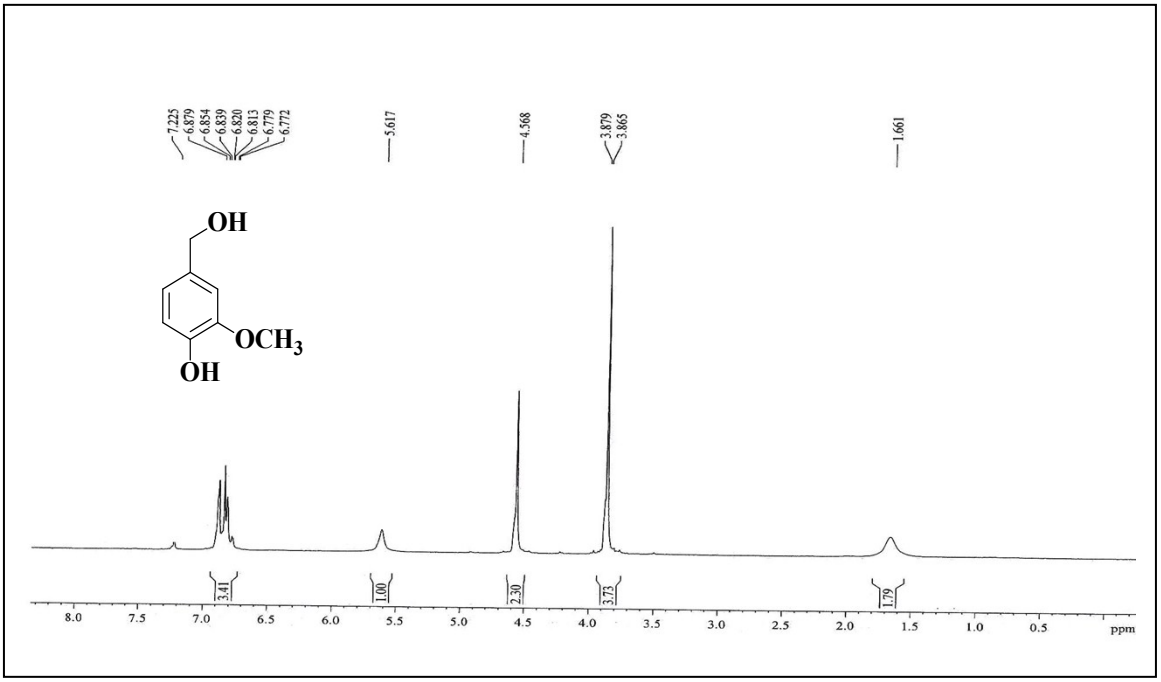
8. E. Nomura, A. Hosoda, H. Mori and H. Taniguchi, *Green Chem*., 2005, **7**, 863–866.

^{1}H and ^{13}C NMR spectra of the products

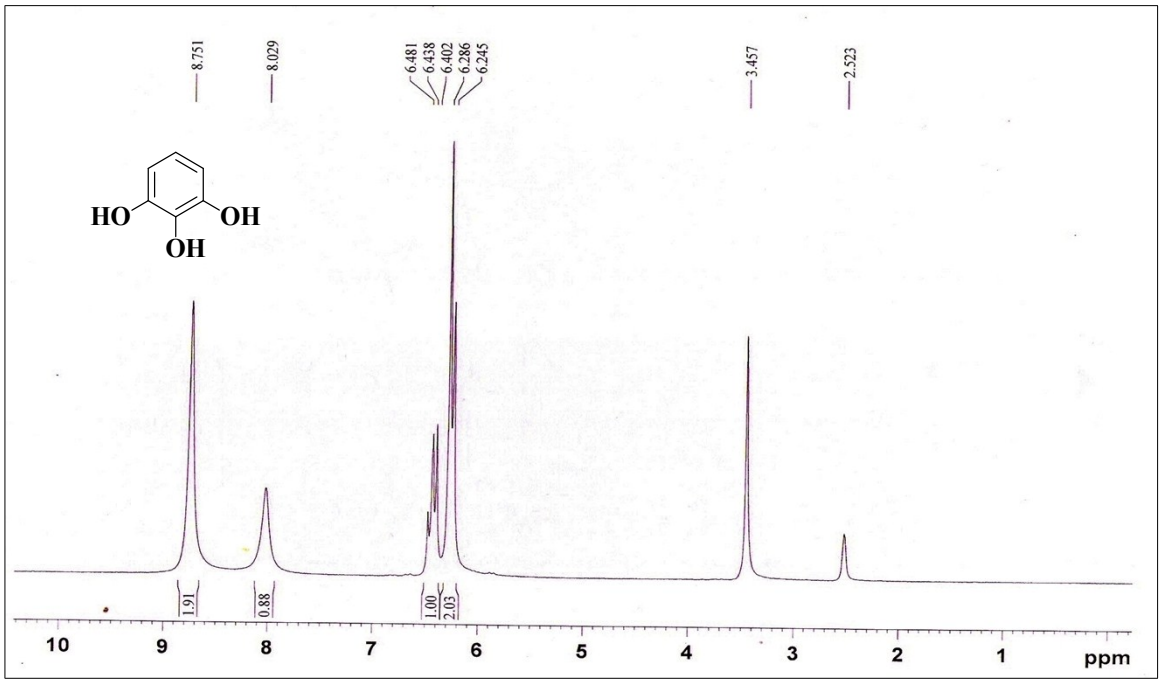
^{1}H NMR spectra of compound 2b



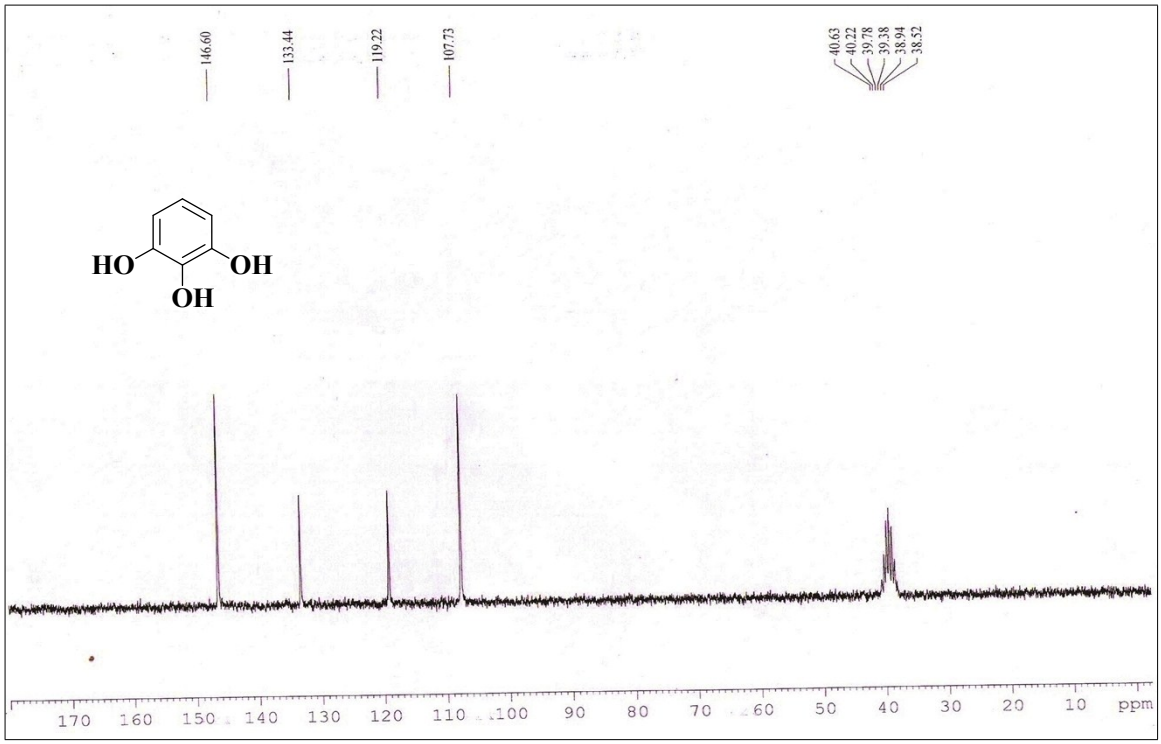
^{1}H NMR spectra of compound 2i



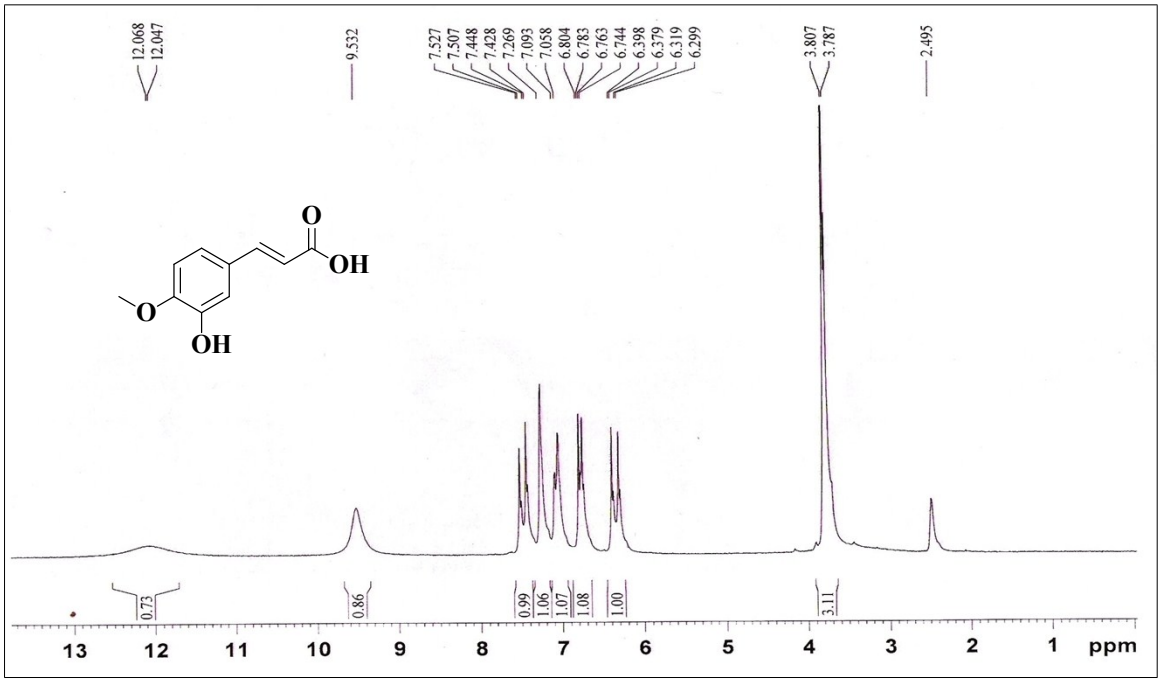
[1]H NMR spectra of compound 4m



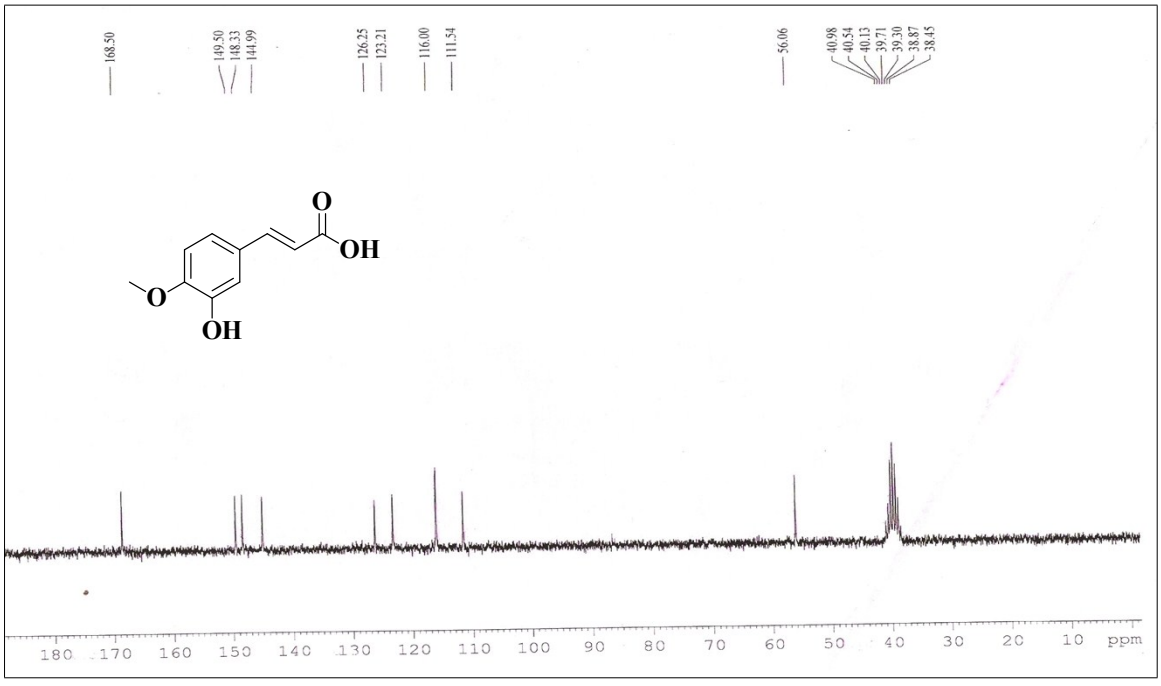
[13] C NMR spectra of compound 4m



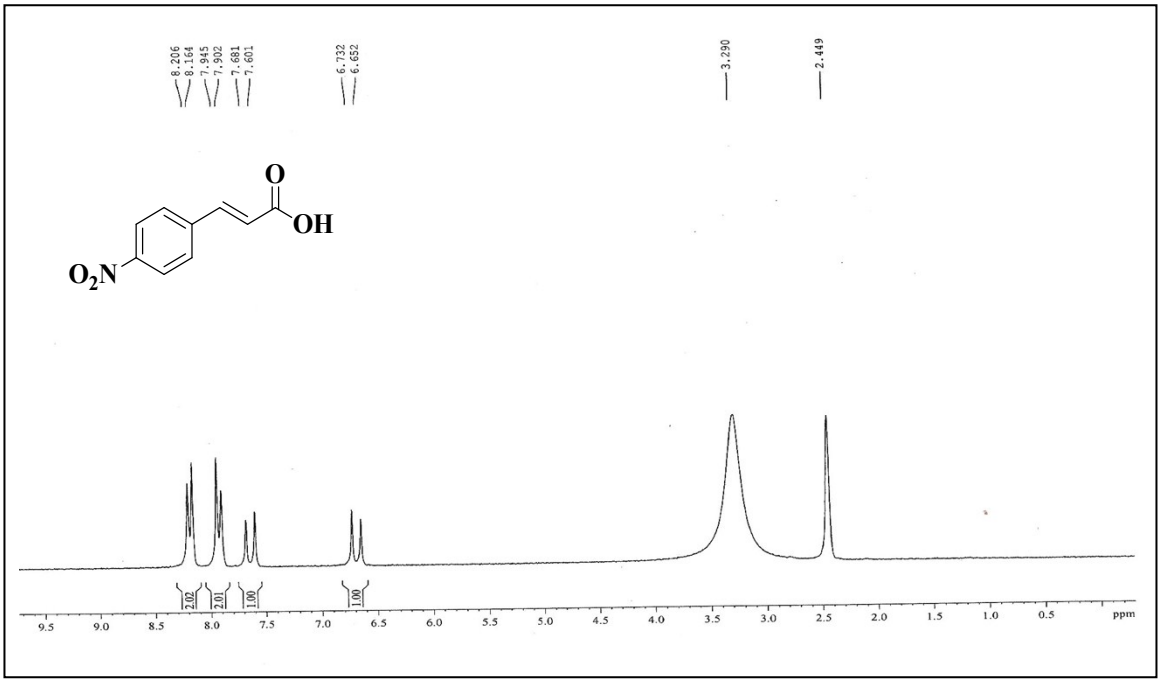
[1]H NMR spectra of compound 5f



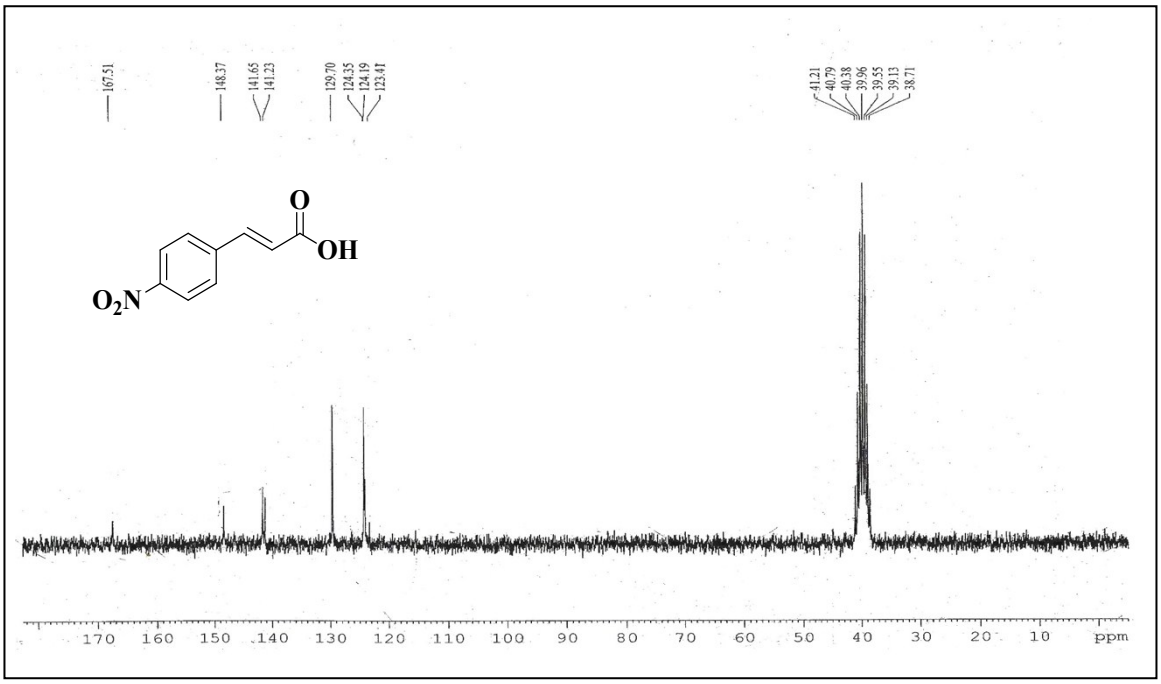
[13] C NMR spectra of compound 5f



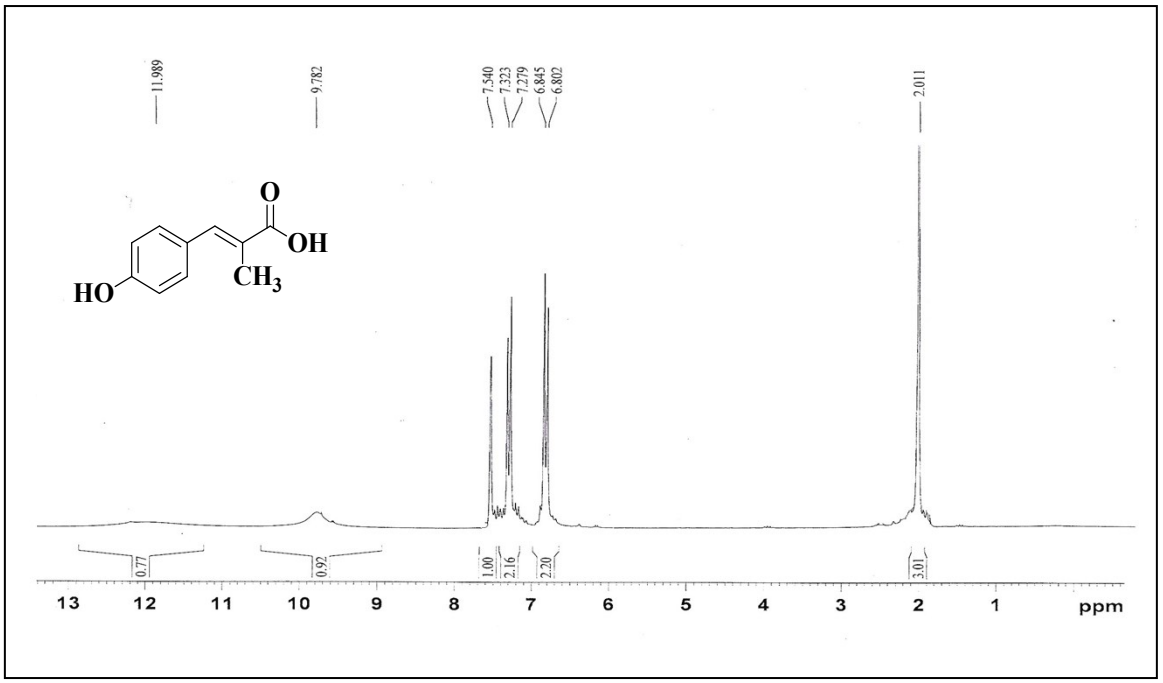
[1]H NMR spectra of compound 5l



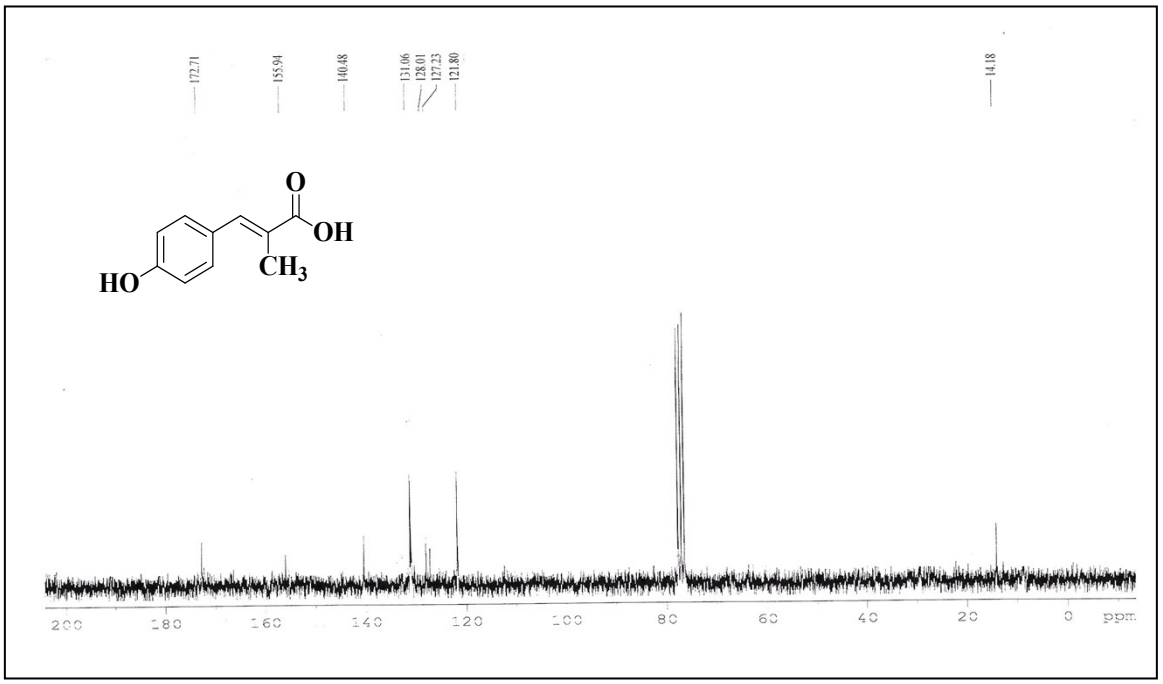
[13] C NMR spectra of compound 5l



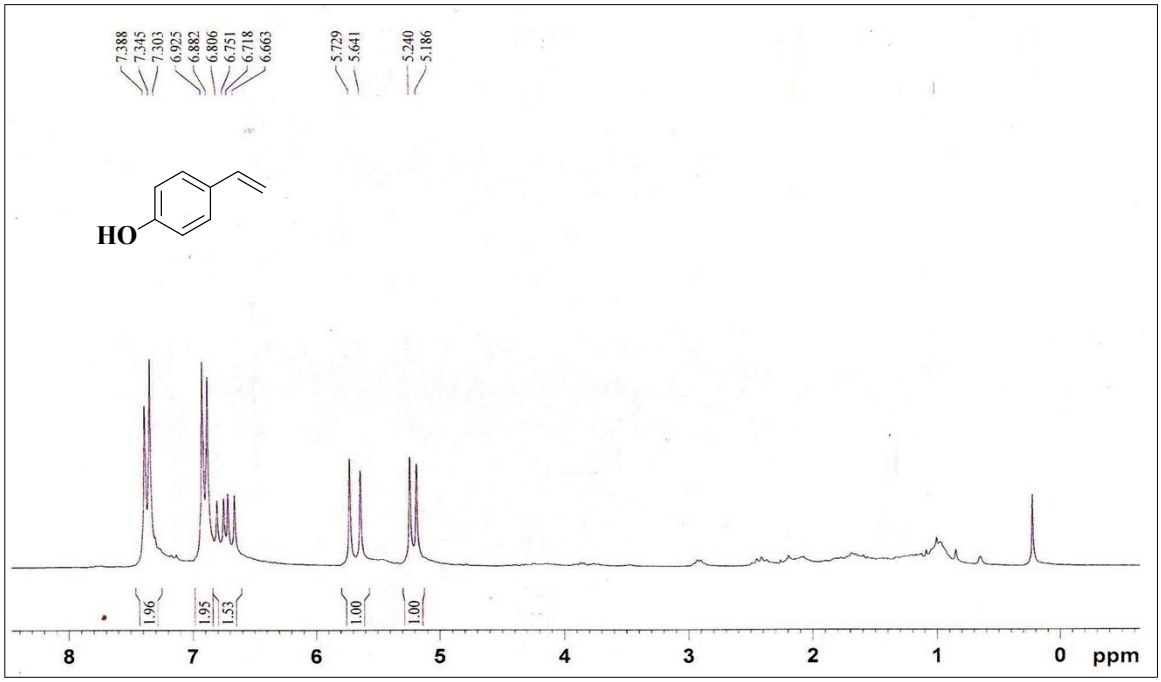
[1]H NMR spectra of compound 5m



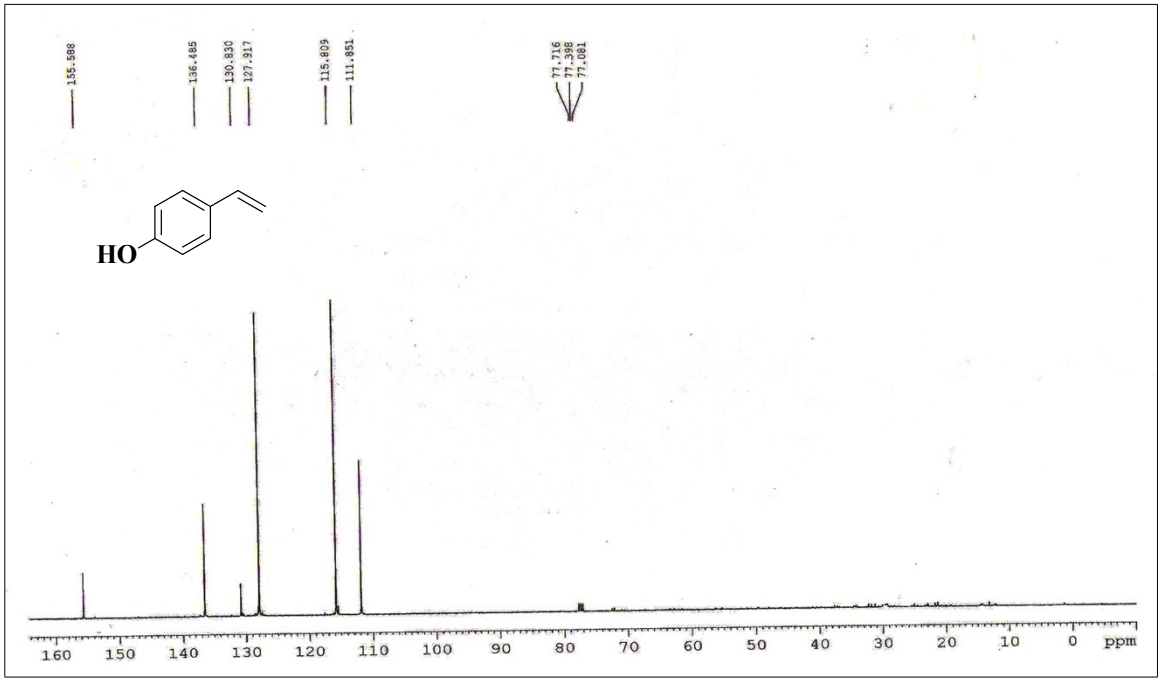
[13] C NMR spectra of compound 5m



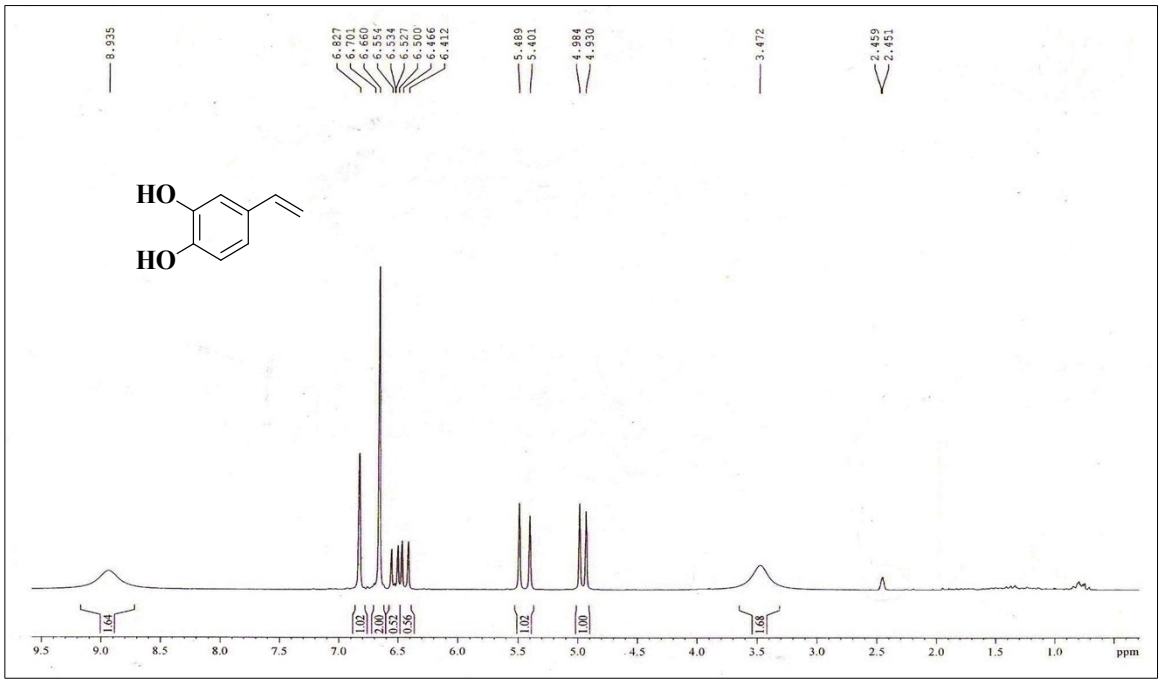
^{1}H NMR spectra of compound 6b



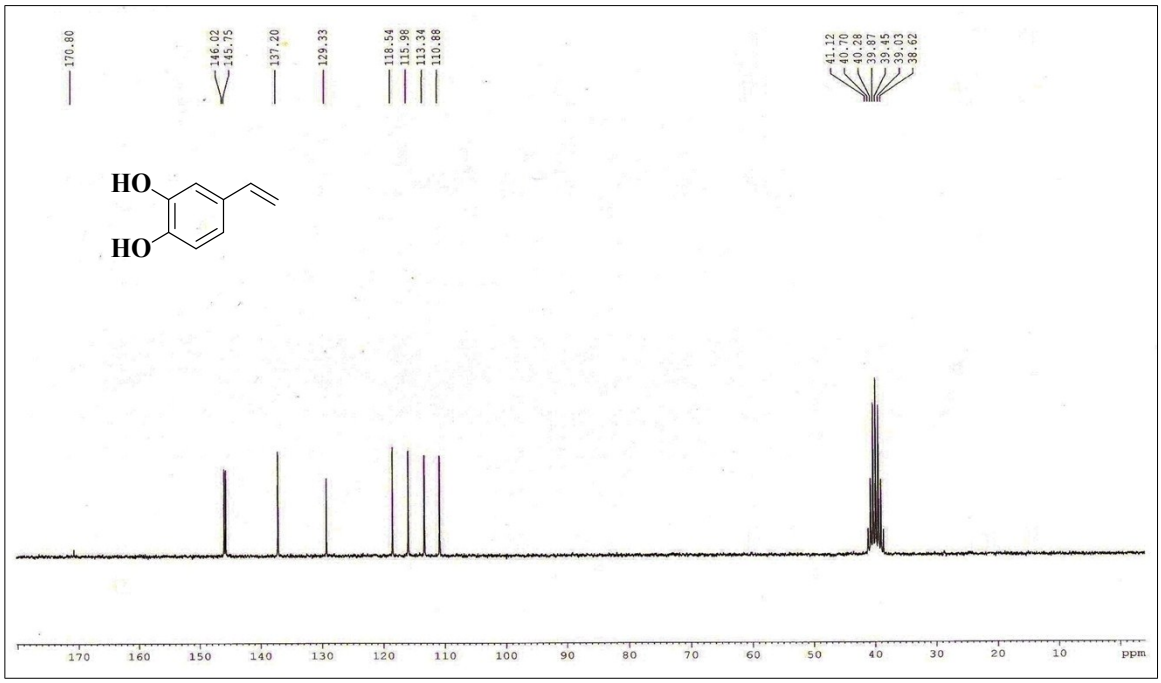
^{13}C NMR spectra of compound 6b



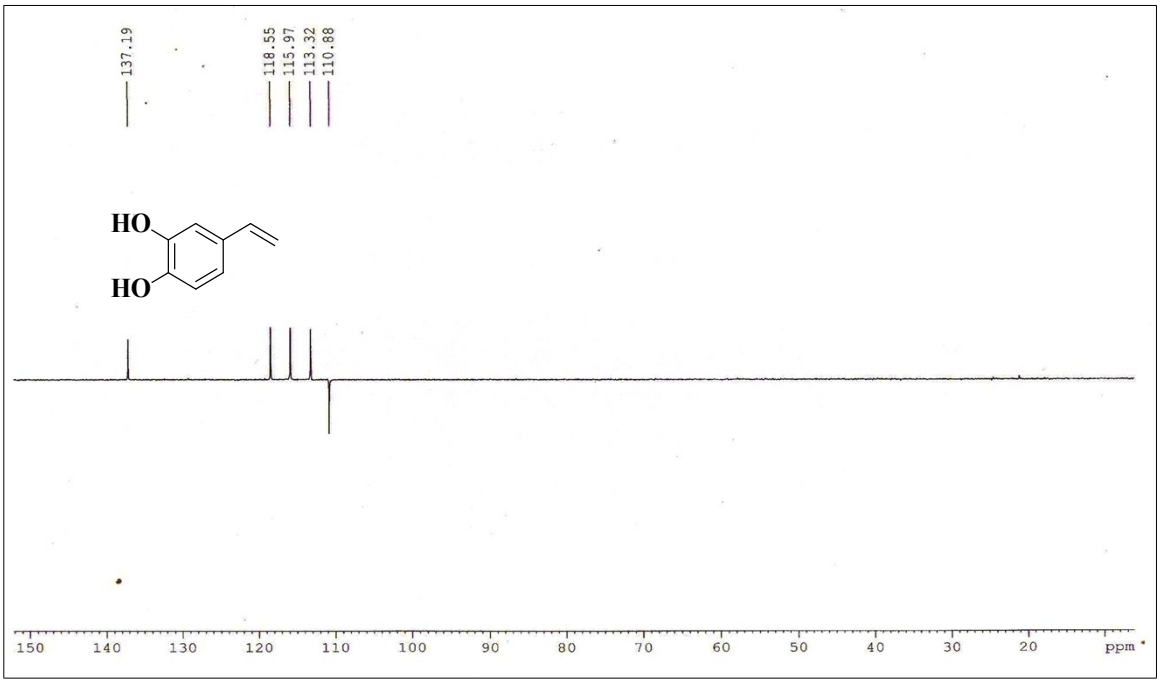
[1]H NMR spectra of compound 6d



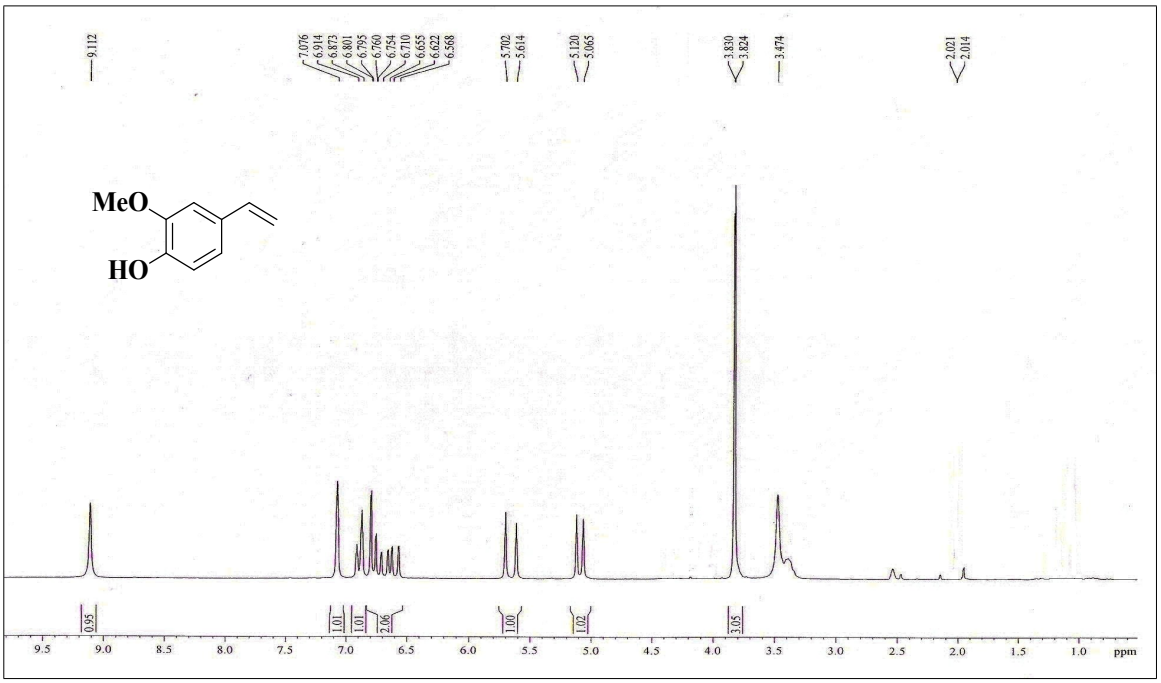
[13] C NMR spectra of compound 6d



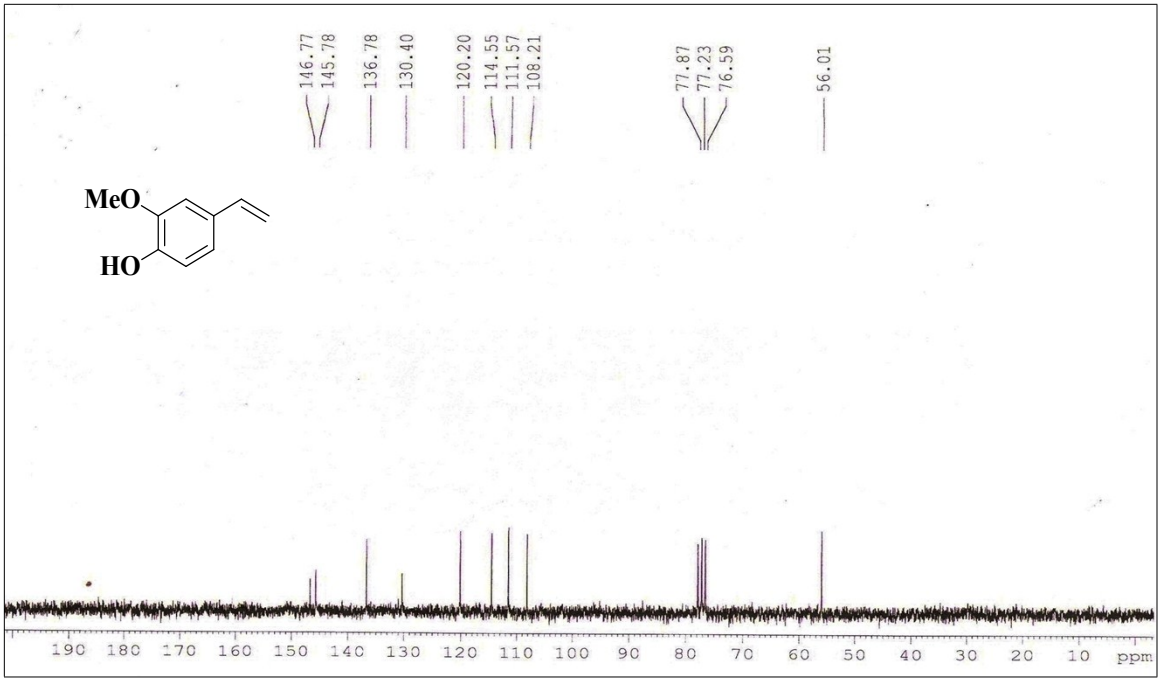
DEPT spectrum of compound 6d



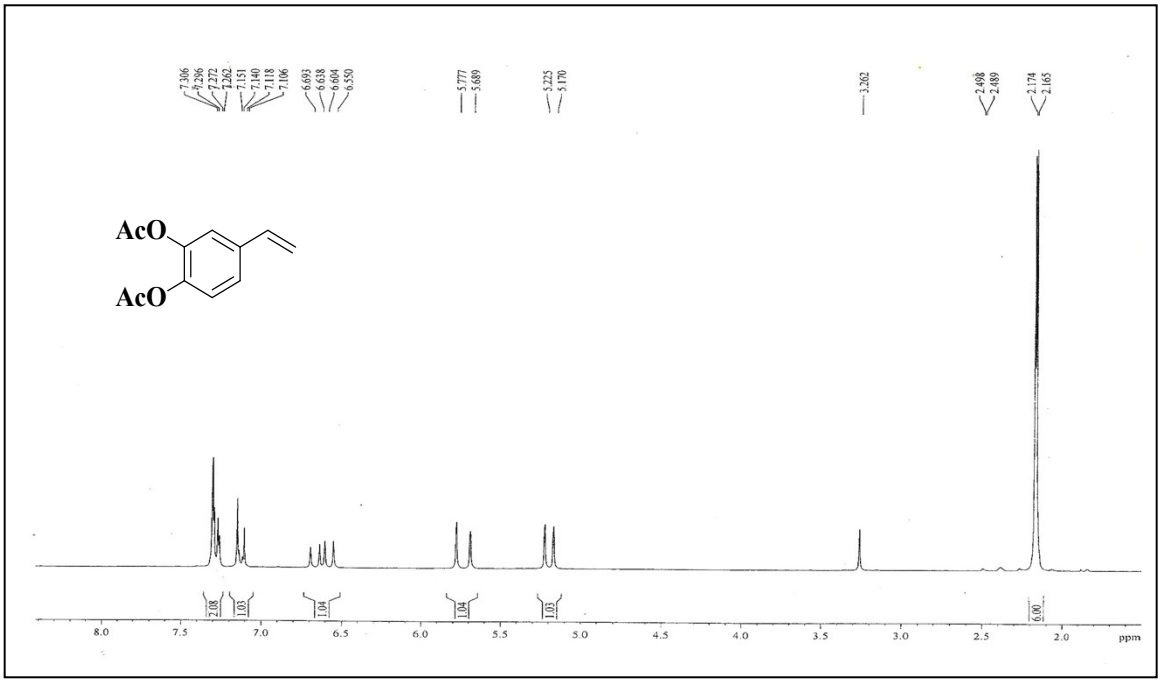
^{1}H NMR spectra of compound 6e



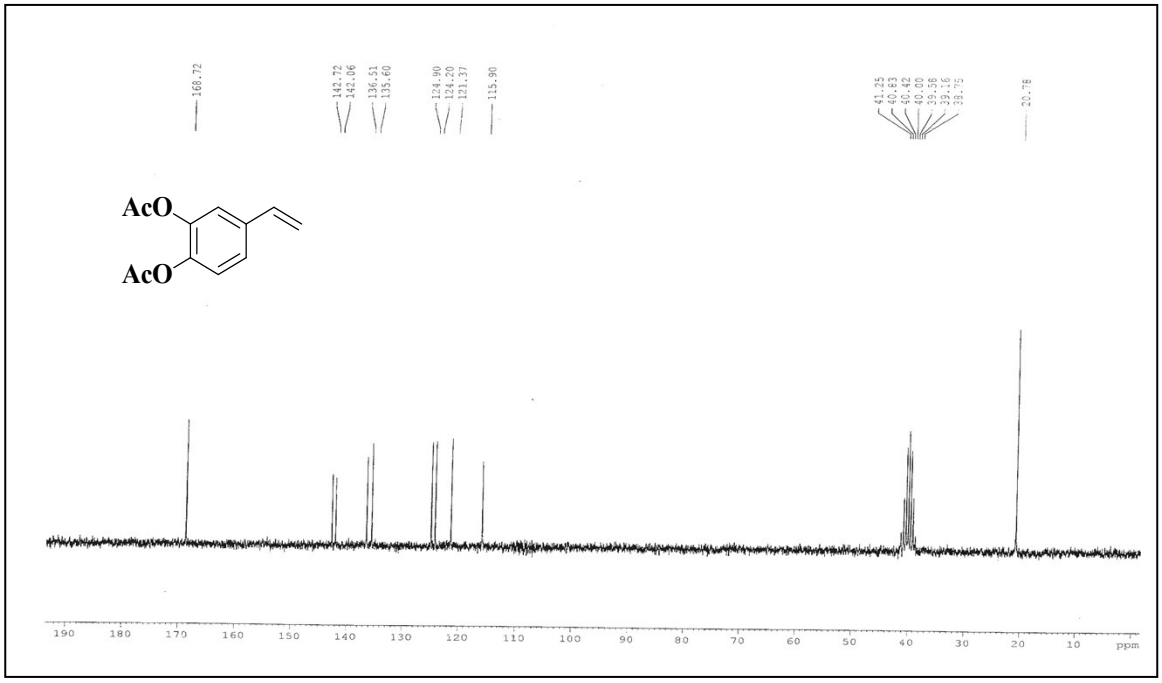
^{13}C NMR spectra of compound 6e



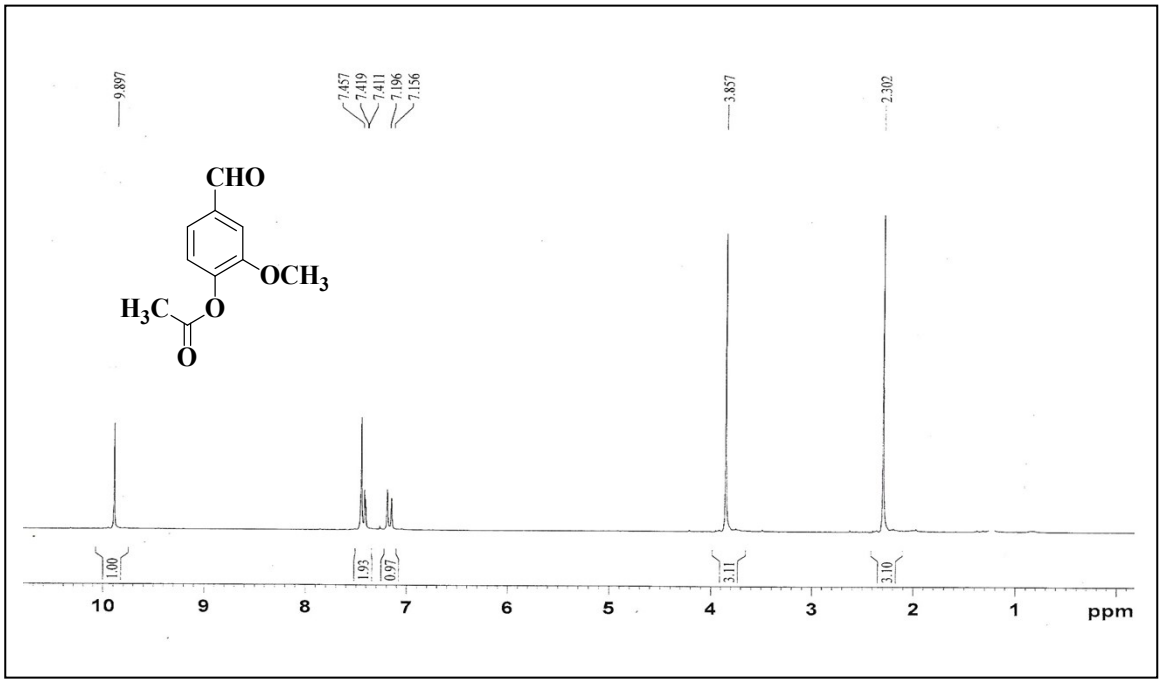
^{1}H NMR spectra of compound 7c



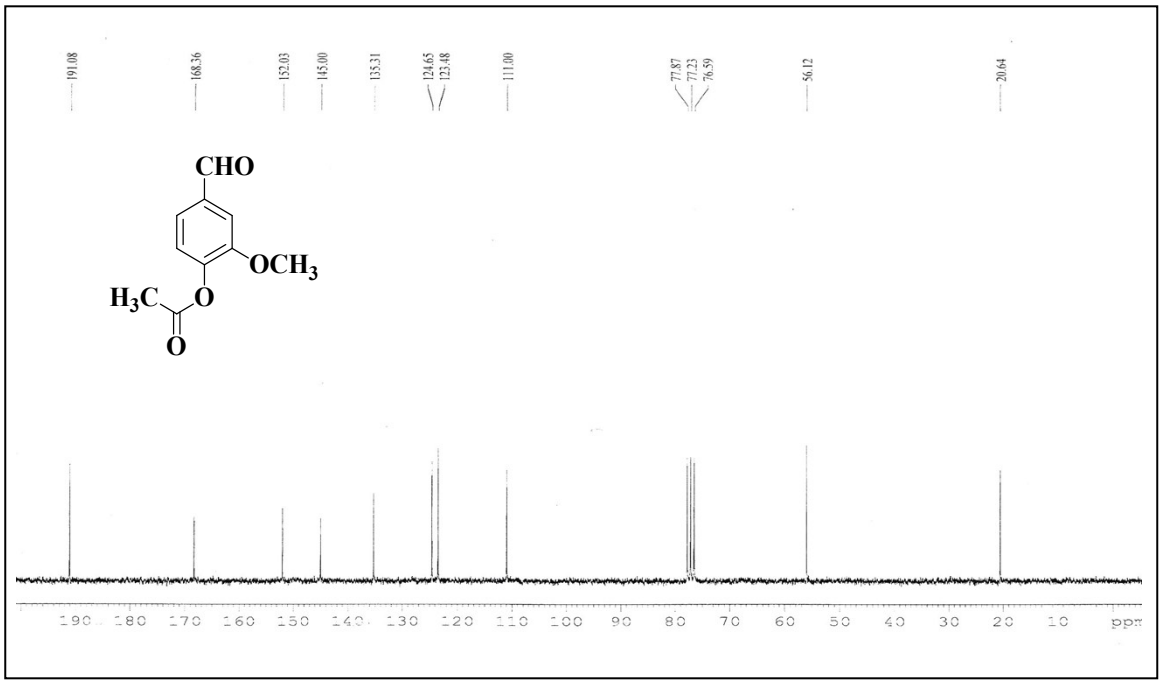
[13] C NMR spectra of compound 7c



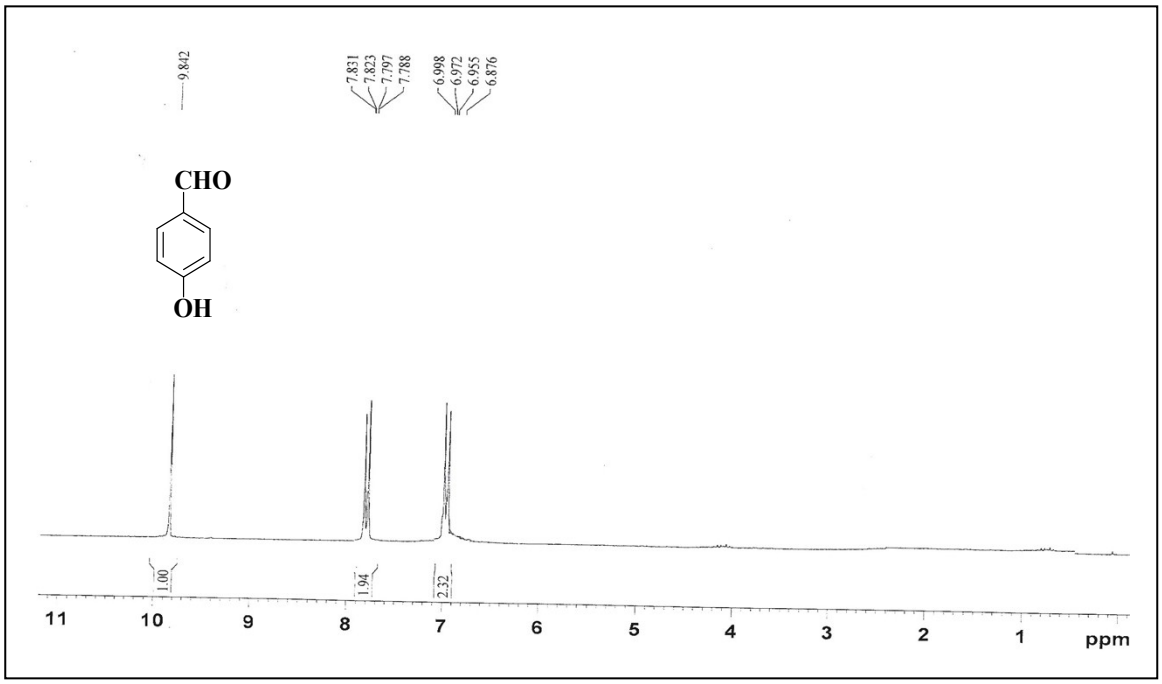
[1]H NMR spectra of compound 7b



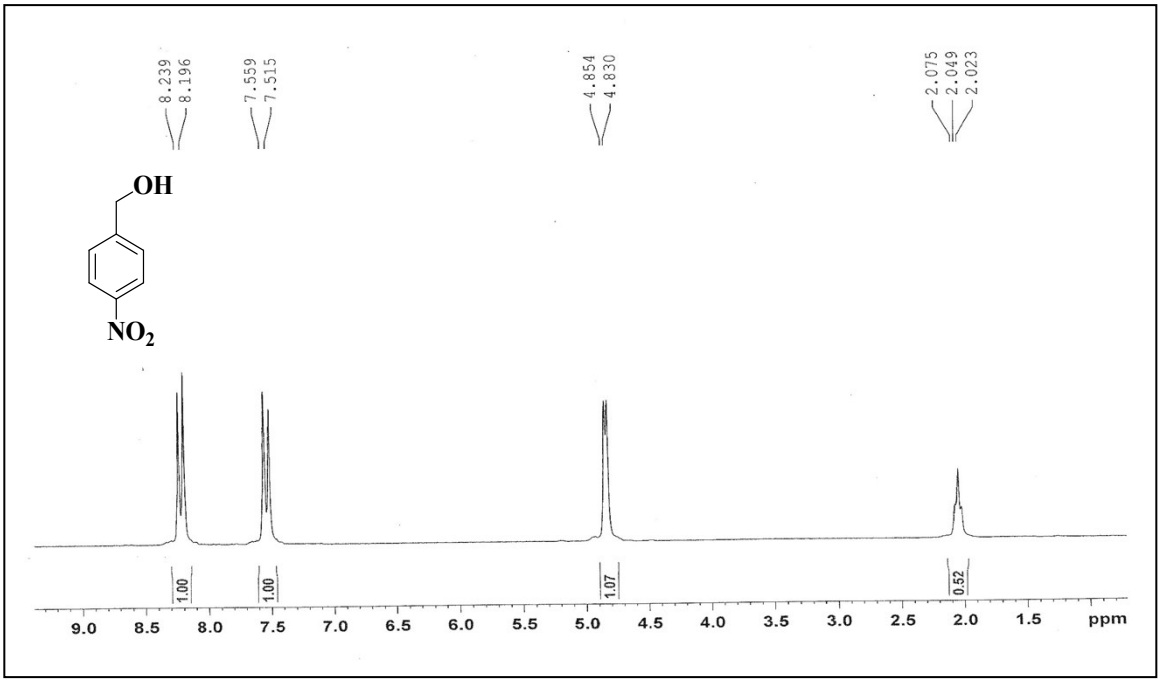
^{13}C NMR spectra of compound 7b



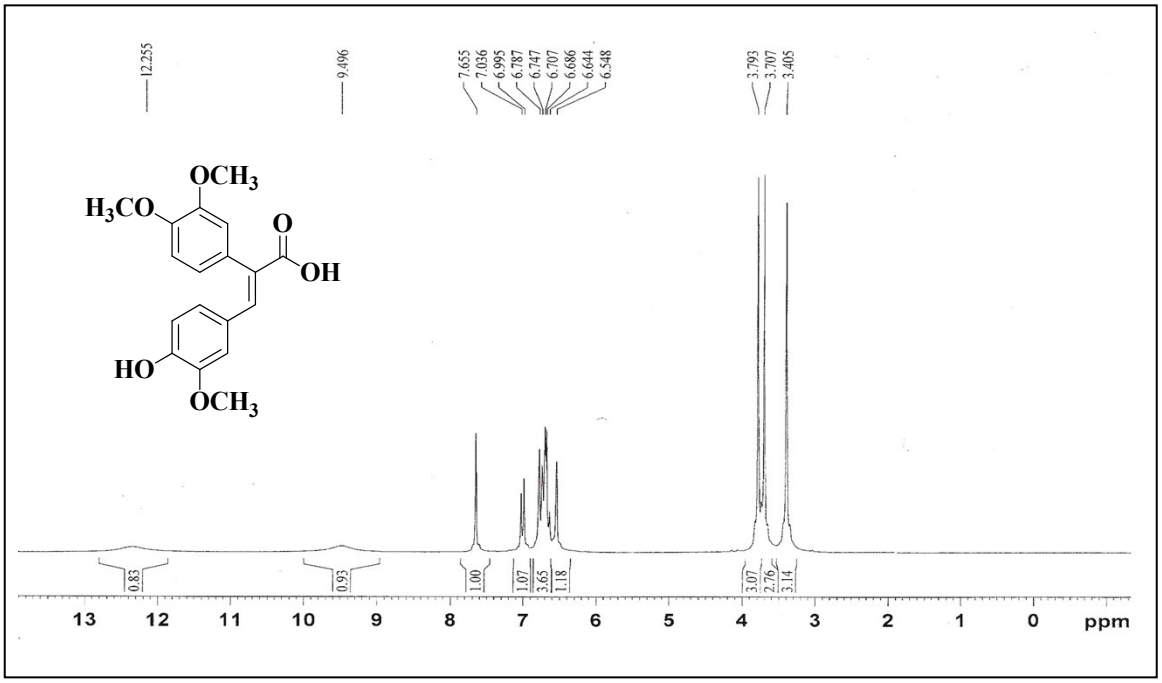
^{1}H NMR spectra of compound 8a



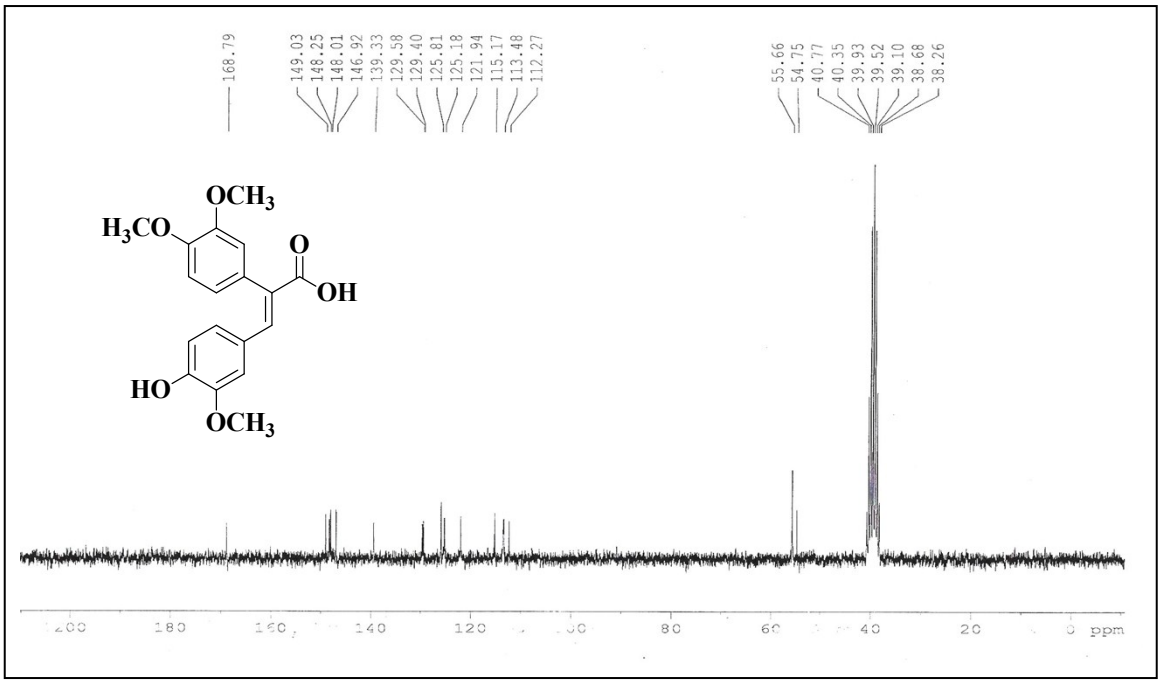
[1]H NMR spectra of compound 8m



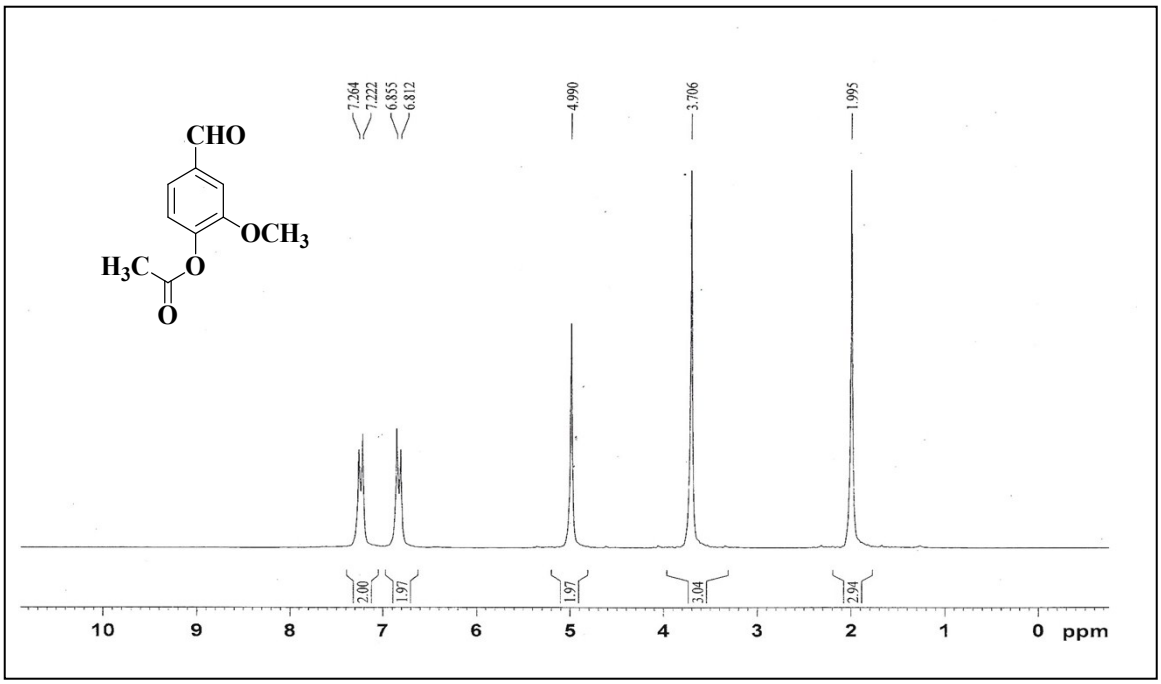
[1]H NMR spectra of compound 8j



^{13}C NMR spectra of compound 8j



^{1}H NMR spectra of compound 7k



^{13}C NMR spectra of compound 7k