Supporting Information

Novel, efficient and bio-based synthesis of secondary arylamines from (-)-shikimic acid

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Contents

I- Instrumentation and Chemicals

(-)-Shikimic acid was kindly provided by Guangxi WanShan Spice Co. Ltd. with chromatography grade as a natural product. Other reagents and chromatography grade solvents were purchased from commercial sources and used without any further purification unless indicated. Petroleum ether (PE) used in the experiments refers to the boiling fraction 60-90°C. The purity determination of the products and reactions monitoring were accomplished by thin layer chromatography (TLC) on silica-gel Polygram SILG/UV 254 plates.

(-)-Methyl-3-dehydroshikimate was readily prepared via IBX-mediated oxidation of easily accessible methyl shikimate in THF, starting from the renewable and biomass-based compound (-)-shikimic acid through an elegant and high-yielding strategy according to the effort of our laboratory.

Melting points of compounds were uncorrected and measured on Thiele apparatus. ^{1}H-NMR and ^{13}C-NMR spectra were performed on Brucker DRX-400 spectrometer for DMSO-d_6 or CD_3COCD_3 solutions, and chemical shifts were reported as δ values using tetramethylsilane (TMS) as an internal standard. Mass spectrometry was measured on a Shimadzu GCMSQP5050A and VG ZAB-HS mass spectrometer in electron ionization mode. IR spectra were recorded on a RFX-65A spectrometer. Specific rotation was measured on U.S. Rudolph's Autopol IV type polarimeter. Elemental analyses were carried out by Elementar Vario EL element analyzer.

II- Experimental Procedure

II-1 Typical procedure for the preparation of (-)-Methyl shikimate 2

A solution of (-)-shikimic acid (17.4 g, 0.10 mol) in MeOH (150 ml) was added $SOCl_2$ (15 ml, 0.20 mol) drop wise at 10-20°C over 1 h. The resulting mixture was heated to 40°C for 3h until completion of the reaction. The mixture was filtered and evaporated under reduced pressure to provide pale yellow oil. This was purified by recrystallizaion from EtOAc to give compound **2** as white powder solid.

II-2 Typical procedure for the preparation of (-)-Methyl-3-dehydroshikimate 3

To a mixture of compound **2** (9.4g, 0.05mol) and IBX (16.8g, 0.06mol) was added THF (220 ml).The resulting mixture was stirred at 10-20°C for the completion of the reaction. The IBA byproduct was filtered off and the filtrate was concentrated under reduced pressure to afford crude (-)-Methyl-3-dehydroshikimate **3** as white solid. The crude product was recrystallized from EtOAc to give compound **3** as white crystals.

II-3 Typical procedure for the preparation of compounds 5a-5v

To a stirred solution of (-)-methyl-3-dehydroshikimate (0.93g, 5.0mmol) and *p*-toluenesulfonic acid (0.05g, 0.25mmol) in MeOH (20 ml) was added aniline (5.0mmol). The resulting mixture was refluxed for the completion of the reaction (monitored by TLC). Then the reaction mixture was cooled to r.t., evaporated to dryness, and washed with 10% aqueous $NaHCO_3$ (20 ml). After that the aqueous layer was extracted with EtOAc (3 ×20 ml), the combined organic layers were dried (anhyd. $MgSO_4$), filtered, and then concentrated under reduced pressure to afford a crude oily product, which was subsequently crystallized from EtOAc-PE to give the product.

II-4 Typical procedure for the preparation of compounds 7a-7i

Aliphatic amine (5.0mmol) was added to a solution of (-)-methyl-3-dehydroshikimate (0.93g, 5.0mmol) and *p*-toluenesulfonic acid (0.05g, 0.25mmol) in CH_2Cl_2 (20 ml). The solution was stirred at ambient temperature for the completion of the reaction (monitored by TLC). Then the reaction mixture was evaporated to dryness, and washed with 10% aqueous $NaHCO_3$ (20 ml). Gathered aqueous phase was extracted with EtOAc (3 ×20 ml). Organic layers were gathered, dried over $MgSO_4$, filtered and concentrated under vacuum to furnish the crude product, which was subsequently crystallized from EtOAc-PE to give the product.

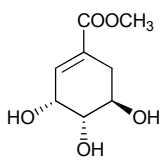
II-5 Procedure for the preparation of compounds 12

To a stirred solution of (-)-methyl-3-dehydroshikimate (0.93g, 5.0mmol) and $Cu(OAc)_2$ (0.05g, 0.25mmol) in MeOH (20 ml) was added aniline (5.0mmol). The resulting mixture was refluxed for the completion of the reaction (monitored by TLC). Then the reaction mixture was cooled to r.t., evaporated to dryness, and washed with 10% aqueous $NaHCO_3$ (20 ml). After that the aqueous layer was extracted with EtOAc (3 ×20 ml), the combined organic layers were dried (anhyd. $MgSO_4$), filtered, and then concentrated under reduced pressure to afford a crude oily product, which was subsequently crystallized from EtOAc-PE to give the product.

III- Characterization Data for Products

III-1 Characterization Data for Product 2

(-)-Methyl shikimate (2) m.p.112~113°C; $[a]_D^{20}$= -142° (c=0.2, MeOH); ^{1}H NMR (CD_3COCD_3, 400 MHz) δ: 6.73(m, 1H, 2-H), 4.38(m, 1H, 3-H), 4.02(s, 1H, 4-OH D_2O exchangeable), 4.00(brs, 2H, 3,5-OH D_2O exchangeable), 3.69(s, 3H, OCH_3), 3.85(m, 1H, 5-H), 3.68(m, 1H, 4-H), 2.64(dd, J_1=17.6Hz, J_2=4.4Hz, 1H, 6α-H), 2.18(dd, J_1=17.6Hz, J_2=6.8Hz, 1H, 6β-H); MS (EI): m/z=188 $[M]^+$, 170$[M-H_2O]^+$, 157$[M-OCH_3]^+$, 129 $[M-COOCH_3]^+$.



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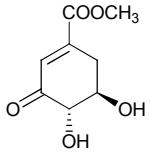
III-2 Characterization Data for Product 3

(-)-Methyl-3-dehydroshikimate (3) m.p.122~123°C; $[a]_D^{20}$= -55° (c=0.2, MeOH); ^{1}H NMR (CD_3COCD_3, 400 MHz) δ: 6.45(d, *J*=2.8Hz, 1H, 2-H), 4.57(d, *J*=3.6Hz, 1H, 4-OH D_2O exchangeable), 4.47(d, *J*=3.6Hz, 1H, 5-OH D_2O exchangeable), 4.57(dd, J_1=10.4Hz, J_2=3.6Hz, 1H, 4-H), 3.85(m, 1H, 5-H), 3.81(s, 3H, OCH_3), 3.06(dd, J_1=18.4Hz, J_2=5.2Hz, 1H, 6α-H), 2.18(ddd, J_1=18.4Hz, J_2=8.8Hz, J_3=3.2Hz, 1H, 6β-H); MS (EI): m/z= 186 $[M]^+$, 155$[M-OCH_3]^+$, 127 $[M-COOCH_3]^+$.



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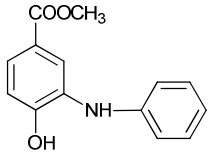
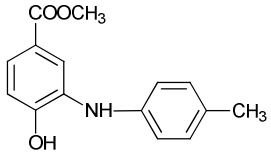
III-3 Characterization Data for Products 5a-5v

Methyl 4-hydroxy-3-(phenylamino) benzoate (5a) m.p.160～162°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.48 (s, 1H, 4-OH), 7.74 (d, *J*=2.0 Hz, 1H, 2-ArH), 7.40 (dd, J_1= 8.0 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.37 (s, 1H, NH), 7.22 (t, *J*= 7.6 Hz, 2H, 3′, 5′-ArH), 7.04 (d, *J*=7.6 Hz, 2H, 2′, 6′-ArH), 6.91(d, *J*=8.0 Hz, 1H, 5-ArH), 6.81 (t, *J*= 7.2 Hz, 1H, 4′-ArH), 3.74 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.2(C=O), 152.2, 143.5, 131.3, 129.0, 122.9, 120.4, 119.8, 117.5, 117.2, 114.8, 51.6(OCH_3); MS (EI): m/z=243$[M]^+$, 228$[M-CH_3]^+$,184$[M-COOCH_3]^+$, 166$[M-C_6H_5]^+$.



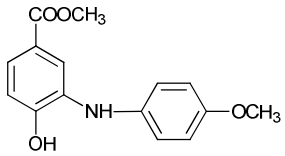
5a

Methyl 4-hydroxy-3-(p-tolylamino) benzoate (5b) m.p.152～153°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.45 (s, 1H, 4-OH), 7.66 (d, *J*=2.0 Hz, 1H, 2-ArH), 7.34 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.18 (s, 1H, NH), 7.05 (d, *J*=8.4 Hz, 2H, 2′, 6′-ArH), 6.98 (d, *J*=8.4 Hz, 2H, 3′, 5′-ArH), 6.88 (d, *J*= 8.4 Hz, 1H, 5-ArH), 3.73 (s, 3H, OCH_3), 2.22 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.3(C=O), 151.4, 140.5, 132.2, 129.5, 129.1, 122.1, 120.4, 118.3, 115.8, 114.5, 51.6(OCH_3), 20.3(CH_3); MS (EI): m/z=257$[M]^+$, 156, 141, 129, 126, 106. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 69.94; H, 5.76; N, 5.42. Found: C, 70.04; H, 5.84; N, 5.45.



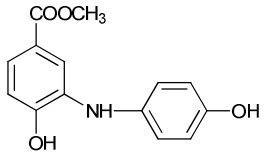
5b

Methyl 4-hydroxy-3-(4-methoxyphenylamino)benzoate (5c) m.p.153～154°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.42 (s, 1H, 4-OH), 7.51(d, *J*=2.0 Hz, 1H, 2-ArH), 7.28 (dd, J_1= 8.0 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.06 (d, *J*=6.8 Hz, 2H, 3′, 5′-ArH), 6.88 (d, *J*=8.0 Hz, 1H, 5-ArH), 6.85 (d, *J*= 6.8 Hz, 2H, 2′, 6′-ArH), 3.72 (s, 3H, $COOCH_3$), 3.71 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.4(C=O), 154.2, 150.5, 135.7, 133.6, 121.4, 121.1, 120.5, 114.5, 114.2, 113.8, 55.2($ArOCH_3$), 51.6(OCH_3); MS (EI): m/z=273$[M]^+$, 258$[M-CH_3]^+$, 170, 156, 141, 129.



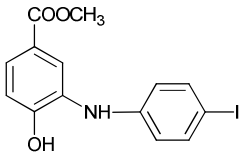
5c

Methyl 4-hydroxy-3-(4-hydroxyphenylamino)benzoate(5d) m.p.＞200°C; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 10.38 (s, 1H, 4-OH), 7.41 (d, J=2.0 Hz, 1H, 2-ArH), 7.24 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 6.96 (d, J=7.6 Hz, 2H, 3′, 5′-ArH), 6.82 (d, J=8.4 Hz, 1H, 5-ArH), 6.71 (d, J= 7.6 Hz, 2H, 2′, 6′-ArH), 3.71 (s, 3H, OCH_3)； ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.4(C=O), 152.6, 150.0, 145.4, 137.8, 134.3, 133.7, 128.1, 125.5, 122.7, 120.6, 120.4, 115.7, 113.9, 113.0, 51.5(OCH_3); MS (EI): m/z=259$[M]^+$, 244$[M\text{-}CH_3]^+$, 228, 200, 183, 172.



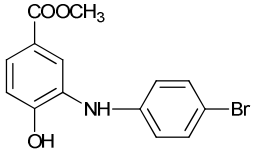
5d

Methyl 4-hydroxy-3-(4-iodophenylamino)benzoate(5e) m.p.156～157°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.52 (s, 1H, 4-OH), 7.71(d, *J*=2.0 Hz, 1H, 2-ArH), 7.49 (d, *J*= 8.8 Hz, 2H, 2′, 6′-ArH), 7.47 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 6.93 (d, *J*=8.4 Hz, 1H, 5-ArH), 6.82 (d, *J*=8.8 Hz, 2H, 3′, 5′-ArH), 3.75 (s, 3H, OCH_3)； MS (EI): m/z=369$[M]^+$, 228, 213, 195, 180.



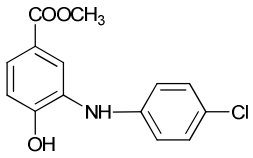
5e

Methyl 3-(4-bromophenylamino)-4-hydroxybenzoate(5f) m.p.178～180°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.52 (s, 1H, 4-OH), 7.71 (d, *J*=2.0 Hz, 1H, 2-ArH), 7.62 (s, 1H, NH), 7.46 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.33 (d, *J*= 8.4 Hz, 2H, 2′, 6′-ArH), 6.93 (d, *J*=8.4 Hz, 2H, 3′, 5′-ArH), 6.93 (d, *J*=8.4 Hz, 1H, 5-ArH), 3.75 (s, 3H, OCH_3)； ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.1(C=O), 153.0, 143.4, 131.6, 130.3, 124.0, 120.5, 119.3, 118.3, 115.2, 110.1, 51.7(OCH_3); MS (EI): m/z=321$[M]^+$, 292, 262, 241, 227, 210.



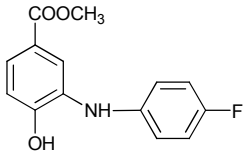
5f

Methyl 3-(4-chlorophenylamino)-4-hydroxybenzoate (5g) m.p.164～165°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.53 (s, 1H, 4-OH), 7.71 (d, *J*=2.0 Hz, 1H, 2-ArH), 7.61 (s, 1H, NH), 7.45 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.23 (d, *J*= 12.0 Hz, 2H, 3′, 5′-ArH), 6.99 (d, *J*=12.0 Hz, 2H, 2′, 6′-ArH), 6.93 (d, *J*=8.4 Hz, 1H, 5-ArH), 3.75 (s, 3H, OCH_3)； ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.1(C=O), 152.9, 142.9, 130.5, 128.8, 123.8, 122.6, 120.5, 119.0, 118.0, 115.1, 51.7(OCH_3); MS (EI): m/z=277$[M]^+$, 246, 218, 183, 154.



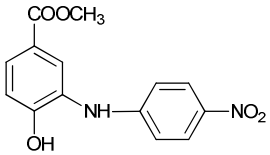
5g

Methyl 3-(4-fluorophenylamino)-4-hydroxybenzoate (5h) m.p.180～182°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.48 (s, 1H, 4-OH), 7.62 (d, J=2.0 Hz, 1H, 2-ArH), 7.38 (dd, J_1= 8.0 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.07 (d, J= 5.6 Hz, 2H, 3′, 5′-ArH), 7.05 (d, J=5.6 Hz, 2H, 2′, 6′-ArH), 6.90 (d, J=8.0 Hz, 1H, 5-ArH), 3.73 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.2(C=O), 157.7, 155.4, 151.8, 139.7, 132.0, 122.6, 120.5, 119.5(d, J= 40.0 Hz), 116.5, 115.7, 115.4, 114.7, 51.6(OCH_3); MS (EI): m/z=261[M]$^+$, 230, 202, 184, 172.



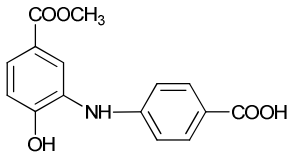
5h

Methyl 4-hydroxy-3-(4-nitrophenylamino)benzoate (5i) m.p.＞200°C;^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.77 (s, 1H, 4-OH), 8.83 (s, 1H, NH), 8.05 (d, J= 9.2 Hz, 2H, 3′, 5′-ArH), 7.77 (d, J=2.0 Hz, 1H, 2-ArH), 7.67 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.04 (d, J=8.4 Hz, 1H, 5-ArH), 6.85 (d, J=9.2 Hz, 2H, 2′, 6′-ArH), 3.78 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 165.7(C=O), 155.7, 151.7, 137.6, 127.4, 127.0, 125.9, 125.4, 120.7, 116.2, 113.2, 51.8(OCH_3); MS (EI): m/z=288 [M]$^+$, 258, 183, 167, 154.



5i

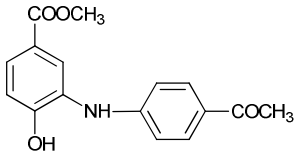
4-(2-hydroxy-5-(methoxycarbonyl)phenylamino)benzoic acid (5j) m.p. ＞ 200°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.63 (s, 1H, 4-OH), 8.13 (s, 1H, NH), 7.80 (d, J=2.0 Hz, 1H, 2-ArH), 7.76 (d, J= 8.0 Hz, 2H, 3′, 5′-ArH), 7.58 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.00 (d, J=8.4 Hz, 1H, 5-ArH), 6.91 (d, J=8.0 Hz, 2H, 2′, 6′-ArH), 3.78 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 167.3(COOH), 166.0(C=O), 154.6, 149.0, 131.0, 128.8, 125.7, 122.8, 120.6, 120.0, 115.8, 114.0, 51.8(OCH_3); MS (EI): m/z=287 [M]$^+$, 270, 256, 241, 228, 220. Anal. Calcd for $C_{15}H_{13}NO_5$: C, 62.71; H, 4.42; N, 4.88. Found: C, 62.72; H, 4.53; N, 4.88.



5j

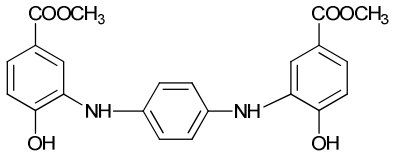
Methyl 3-(4-acetylphenylamino)-4-hydroxybenzoate (5k) m.p.166～167°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.65 (s, 1H, 4-OH), 8.23 (s, 1H, NH), 7.80 (d, J=2.0 Hz, 1H, 2-ArH), 7.78 (d, J=8.8Hz, 2H, 3′, 5′-ArH), 7.58 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 6.99 (d, J= 8.4 Hz, 1H, 5-ArH), 6.91(d, J=8.8 Hz, 2H, 2′, 6′-ArH), 3.77 (s, 3H, OCH_3), 2.49 (s, 3H, $COCH_3$); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 195.5, 166.0, 154.7, 149.3, 130.2, 128.5, 127.4, 125.9, 123.0, 120.6, 115.8, 113.8, 51.8(OCH_3),

26.1(CH_3); MS (EI): m/z=285$[M]^+$, 270$[M\text{-}CH_3]^+$, 254, 242, 227, 210, 183. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.16; H, 5.21; N, 4.84. Found: C, 67.37; H, 5.26; N, 4.91.



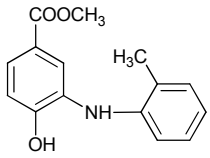
5k

Dimethyl 3,3'-(1,4-phenylenebis(azanediyl))bis(4-hydroxybenzoate) (5l) m.p.＞200°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.44 (s, 2H, 2′**,** 2′′-OH), 7.59 (d, *J*=2.0 Hz, 2H, 6′**,** 6′′-ArH), 7.30 (dd, J_1= 8.0 Hz, J_2=2.0 Hz, 2H, 4′**,** 4′′-ArH), 7.11 (s, 2H, NH), 7.04 (s, 4H, 2, 3**,** 5, 6-ArH), 6.86 (d, *J*=8.0 Hz, 2H, 3, 3′-ArH), 3.73 (s, 6H, OCH_3)； MS (EI): m/z=258, 115, 99, 97, 83, 70.



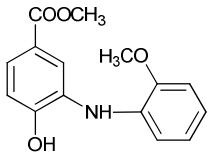
5l

Methyl 4-hydroxy-3-(o-tolylamino)benzoate (5m) m.p.＞200°C;^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.45 (s, 1H, 4-OH), 7.34 (dd, J_1= 8.0 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.26 (d, *J*=2.0 Hz, 1H, 2-ArH), 7.20 (d, *J*=7.6Hz, 1H, 6′ -ArH), 7.11 (t, *J*=7.2 Hz, 1H, 5′-ArH), 7.01 (d, *J*= 8.0 Hz, 1H, 3′-ArH), 6.93 (t, *J*=7.6 Hz, 1H, 4′-ArH), 6.88 (d, *J*= 8.0 Hz, 1H, 5 -ArH), 6.61 (s, 1H, NH), 3.71 (s, 3H, OCH_3), 2.16 (s, 3H, CH_3)； ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.3(C=O), 151.2, 141.0, 132.9, 130.7, 129.7, 126.6, 122.2, 121.9, 120.4, 116.0, 114.4, 51.6(OCH_3), 17.7(CH_3); MS (EI): m/z=257$[M]^+$, 242$[M\text{-}CH_3]^+$, 226, 224, 196, 180.



5m

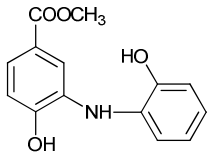
Methyl 4-hydroxy-3-(2-methoxyphenylamino)benzoate (5n) m.p.119～120°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.70 (s, 1H, 4-OH), 7.69 (d, *J*=2.0 Hz, 1H, 2-ArH), 7.38 (dd, J_1= 8.0 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.18 (d, *J*=7.6Hz, 1H, 6′ -ArH), 7.03 (t, *J*=7.2 Hz, 1H, 5′-ArH), 6.92 (d, *J*= 8.0 Hz, 1H, 3′-ArH), 6.90 (d, *J*= 8.0 Hz, 1H, 5 -ArH), 6.89 (t, *J*=7.6 Hz, 1H, 4′-ArH), 6.61 (s, 1H, NH), 3.83 (s, 3H, $COOCH_3$), 3.75 (s, 3H, OCH_3)； ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.3(C=O), 151.0, 148.9, 131.4, 131.2, 122.3, 120.8, 120.7, 120.5, 115.8, 115.4, 114.3, 111.2, 55.6, 51.7; MS (EI): m/z=273$[M]^+$, 258$[M\text{-}CH_3]^+$, 241, 226, 199, 170.



5n

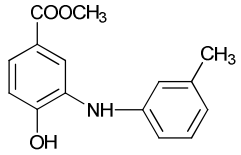
Methyl 4-hydroxy-3-(2-hydroxyphenylamino)benzoate (5o) m.p.＞200°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.67 (s, 1H, 4-OH), 9.72 (s, 1H, 2′-OH), 7.66 (d, *J*=2.0 Hz, 1H, 2-ArH), 7.34 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.18 (d, *J*=7.6Hz, 1H, 3′ -ArH), 6.90 (d, *J*= 8.4 Hz, 1H, 5 -ArH), 6.87 (d, *J*=8.4 Hz, 1H, 6′-ArH), 6.78 (t, *J*= 7.6 Hz, 1H, 4′-ArH), 6.77 (t, *J*=7.2 Hz, 1H, 5′-ArH), 6.59 (s, 1H, NH),

3.75 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.5(C=O), 150.6, 147.4, 132.1, 130.3, 121.7, 121.3, 120.6, 119.5, 117.2, 115.3, 114.1, 51.7(OCH_3); MS (EI): m/z=259$[M]^+$, 241, 227, 199, 183.



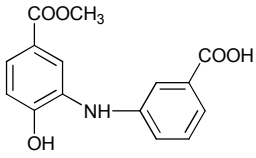
5o

Methyl 4-hydroxy-3-(m-tolylamino)benzoate (5p) m.p.149～150°C; ^1H NMR (DMSO-d_6, 400 MHz) δ: 10.44 (s, 1H, 4-OH), 7.71 (d, J=2.0 Hz, 1H, 2-ArH), 7.39 (dd, J_1= 8.0 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.24 (s, 1H, NH), 7.09 (t, J=7.6Hz, 1H, 5′-ArH), 6.90 (d, J= 8.0 Hz, 1H, 5-ArH), 6.84 (s, 1H, 2′-ArH), 6.83 (d, J= 8.0 Hz, 1H, 6′-ArH), 6.64 (d, J=7.6 Hz, 1H, 4′-ArH), 3.74 (s, 3H, OCH_3), 2.22 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.2(C=O), 152.2, 143.5, 138.2, 131.4, 128.8, 122.9, 120.6, 120.4, 118.0, 117.8, 114.8, 114.3, 51.6(OCH_3), 21.2(CH_3); MS (EI): m/z=257$[M]^+$, 226, 156, 141, 129, 106.



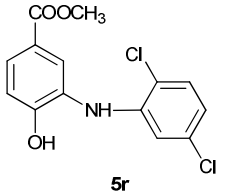
5p

3-(2-hydroxy-5-(methoxycarbonyl)phenylamino)benzoic acid (5q) m.p. ＞ 200°C; ^1H NMR (DMSO-d_6, 400 MHz) δ: 12.78 (s, 1H, 3′-COOH), 10.51 (s, 1H, 4-OH), 7.72 (d, J=2.0 Hz, 1H, 2-ArH), 7.70 (s, 1H, NH), 7.52 (s, 1H, 2′-ArH), 7.49 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.35 (d, J= 8.4 Hz, 1H, 6′-ArH), 7.30 (t, J=7.6Hz, 1H, 5′-ArH), 7.16 (d, J= 7.2 Hz, 1H, 4′-ArH), 6.95 (d, J=8.4 Hz, 1H, 5-ArH), 3.76 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 167.5(COOH), 166.1(C=O), 153.5, 144.5, 131.5, 130.3, 129.1, 124.3, 120.5, 120.4, 120.2, 120.0, 116.7, 115.3, 51.7(OCH_3); MS (EI): m/z=287$[M]^+$, 288$[M+1]^+$, 269, 255, 241, 227.



5q

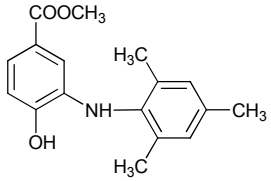
Methyl 3-(2,5-dichlorophenylamino)-4-hydroxybenzoate (5r) m.p.196 ～ 198°C; ^1H NMR (DMSO-d_6, 400 MHz) δ: 10.69 (s, 1H, 4-OH), 7.67 (d, J=2.0 Hz, 1H, 2-ArH), 7.63 (dd, J_1= 8.4 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.40 (d, J= 8.4 Hz, 1H, 3′-ArH), 7.33 (s, 1H, NH), 7.01 (d, J=8.4 Hz, 1H, 5-ArH), 6.83 (dd, J_1= 8.4 Hz, J_2=2.4 Hz, 1H, 4′-ArH), 6.61 (d, J= 2.4 Hz, 1H, 6′-ArH), 3.78 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 165.9(C=O), 154.8, 142.3, 132.0, 130.7, 128.1, 126.6, 124.4, 120.7, 119.2, 119.1, 115.8, 115.1, 51.7(OCH_3); MS (EI): m/z=311$[M]^+$, 280, 257, 241, 219, 217.



5r

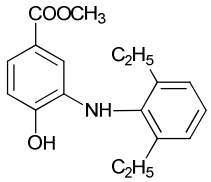
Methyl 4-hydroxy-3-(mesitylamino)benzoate (5s) ^1H NMR (DMSO-d_6, 400 MHz) δ: 10.32(s,1H, 4-OH), 7.17 (dd, J_1= 8.4 Hz, J_2=2.4 Hz, 1H, 6-ArH), 6.95(s, 2H, 3′, 5′-ArH), 6.83 (d, J= 8.4 Hz, 1H,

5-ArH), 6.46 (d, *J*=2.4 Hz, 1H, 3-ArH), 6.38 (s, 1H, NH), 3.30 (s, 3H, OCH_3), 2.26 (s, 3H, 4′-CH_3), 2.07(s, 6H, 2′, 6′-CH_3)；IR(KBr, ν/cm^{-1}): 3390, 2956, 2917, 1689, 1592, 1519, 1486, 1438, 1255, 1162, 1120, 856, 761, 605； MS (EI): m/z=285$[M]^+$, 119.



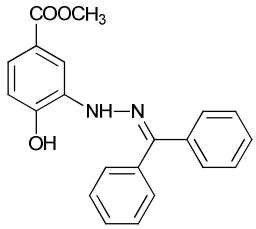
5s

Methyl 3-(2,6-diethylphenylamino)-4-hydroxybenzoate (5t) m.p.168～170°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.41 (s, 1H, 4-OH), 7.18 (t, *J*= 7.6 Hz, 1H, 4′-ArH), 7.16 (d, *J*= 7.6 Hz, 2H, 3′**,** 5′-ArH), 7.14 (dd, J_1= 8.0 Hz, J_2=2.0 Hz, 1H, 6-ArH), 7.81 (d, *J*=8.0 Hz, 1H, 5-ArH), 6.49 (s, 1H, NH), 6.45 (d, *J*=2.0 Hz, 1H, 2-ArH), 3.63 (s, 3H, OCH_3), 2.49 (q, 4H, CH_2), 1.04 (t, 6H, CH_3)； ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.5(C=O), 148.6, 142.2, 137.0, 136.3, 126.6, 126.4, 120.6, 119.1, 113.3, 110.4, 51.4(OCH_3), 24.1(CH_2), 14.7(CH_3); MS (EI): m/z=299$[M]^+$, 284 $[M-CH_3]^+$, 268, 266, 252, 238.



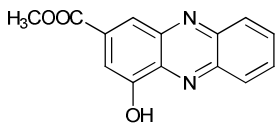
5t

Methyl 3-(2-(diphenylmethylene)hydrazinyl)-4-hydroxybenzoate (5u) m.p.197～198°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 10.54 (s, 1H, 4-OH), 8.00 (d, *J*=2.4 Hz, 1H, 2-ArH), 7.89 (s, 1H, NH), 7.67 (t, *J*= 7.6 Hz, 2H, 4′**,**4′′-ArH), 7.48 (dd, J_1= 7.2 Hz, J_2=1.2 Hz, 2H, 2′**,** 6′-ArH), 7.39 (dd, J_1= 8.0 Hz, J_2=2.4 Hz, 1H, 6-ArH), 7.38 (dd, J_1= 7.2 Hz, J_2=1.2 Hz, 2H, 2′′**,** 6′′-ArH), 7.36 (ddd, J_1= 12.0 Hz, J_2=8.0 Hz, J_3= 3.8 Hz, 4H, 3′**,** 3′′**,**5′**,** 5′′-ArH), 6.79 (d, *J*=8.0 Hz, 1H, 5-ArH), 3.81 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.4(C=O), 147.3, 145.4, 137.7, 132.6, 132.2, 129.9, 129.5, 128.6, 128.5, 128.3, 126.0, 121.7, 121.2, 113.9, 112.4, 51.7(OCH_3); MS (EI): m/z=346$[M]^+$, 180, 166, 138, 118.



5u

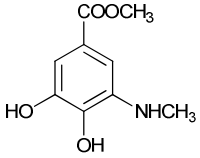
4-Hydroxy-phenazine-2-carboxylic acid methyl ester (5v) m.p.＞200°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.10 (s, 1H, 4-OH), 8.33 (m, 1H, 4′-ArH), 8.29 (d, *J* = 1.2 Hz, 1H, 3-ArH), 8.28 (m, 1H, 1′-ArH), 8.03 (m, 1H, 3′-ArH), 8.02 (m, 1H, 2′-ArH), 7.61 (d, *J*= 1.2 Hz, 1H, 1-ArH), 3.96 (s, 3H, OCH_3)； MS (EI): m/z=254$[M]^+$, 238, 223,197,195.



5v

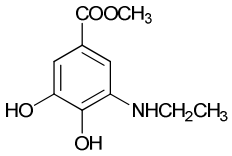
III-4 Characterization Data for Products 7a-7i

Methyl 3,4-dihydroxy-5-(methylamino)benzoate (7a) m.p.163～164°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.84 (d, *J*= 2.0 Hz, 1H, 2-ArH), 6.60 (d, *J*= 2.0 Hz, 1H, 6-ArH), 3.74 (s, 3H, OCH_3)，2.69(s, 3H, CH_3)；MS (EI): m/z=197[M]$^+$, 182 [M-CH_3]$^+$, 166, 154.



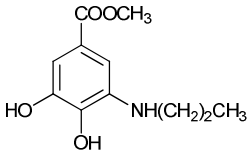
7a

Methyl 3,4-dihydroxy-5-(ethylamino)benzoate (7b) m.p.180～182°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.84 (d, *J*= 1.6 Hz, 1H, 2-ArH), 6.66 (d, *J*= 1.6 Hz, 1H, 6-ArH), 3.73 (s, 3H, OCH_3)，3.07(q, 2H, CH_2), 1.15 (t, J_1= 7.2 Hz , J_2= 6.8 Hz ,3H, CH_3)；^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.8(C=O), 143.7, 138.0, 136.2, 120.1, 106.2, 102.8, 51.5(OCH_3), 37.5, 14.6; MS (EI): m/z=211[M]$^+$, 196 [M-CH_3]$^+$, 180, 164. Anal. Calcd for $C_{10}H_{13}NO_4$: C, 57.14; H, 5.96; N, 6.54. Found: C, 56.87; H, 6.16; N, 6.64.



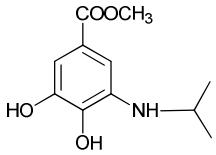
7b

Methyl 3,4-dihydroxy-5-(propylamino)benzoate (7c) m.p.159～160°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.34 (s, 1H, OH), 6.83 (d, *J*= 1.6 Hz, 1H, 2-ArH), 6.65 (d, *J*= 1.6 Hz, 1H, 6-ArH), 3.73 (s, 3H, OCH_3)，2.99 (t, J_1= 6.8 Hz , J_2= 7.2 Hz, 2H, CH_2), 1.56 (m, 2H, CH_2), 0.91 (t, J_1= 7.6 Hz , J_2= 7.2 Hz ,3H, CH_3)；MS (EI): m/z=225[M]$^+$, 196[M-C_2H_5]$^+$, 194, 151, 137.



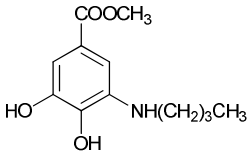
7c

Methyl 3,4-dihydroxy-5-(isopropylamino)benzoate (7d) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.37 (brs, 1H, OH), 6.85 (d, *J* = 1.2 Hz, 1H, 2-ArH), 6.82 (d, *J* = 1.2Hz, 1H, 6-ArH), 3.73 (s, 3H, OCH_3), 3.53(m, 1H, CH), 1.13(d, *J* = 6.0 Hz, 6H, CH_3)；IR(KBr, ν/cm^{-1}): 3397, 3268, 2966, 1702, 1604, 1459, 1317, 1234, 1006, 817, 763, 617；MS (EI): m/z=225[M]$^+$, 210 [M-OCH_3]$^+$, 183, 152.



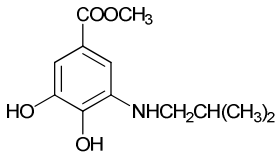
7d

Methyl 3-(butylamino)-4,5-dihydroxybenzoate (7e) m.p.162～163°C;^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.83 (d, *J*= 2.0 Hz, 1H, 2-ArH), 6.66 (d, *J*= 2.0 Hz, 1H, 6-ArH), 3.73 (s, 3H, OCH_3)，3.03 (t, J_1= 6.8 Hz , J_2= 7.2 Hz ,2H, CH_2), 1.53 (m, 2H, CH_2), 1.37 (m, 2H, CH_2), 0.91 (t, J_1= 7.2 Hz , J_2= 7.2 Hz ,3H, CH_3)；^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.8(C=O), 143.7, 138.1, 136.1, 120.1, 106.2, 102.8, 51.5(OCH_3), 42.7, 30.9, 19.8, 13.8; MS (EI): m/z=239[M]$^+$, 238, 197, 196, 164.



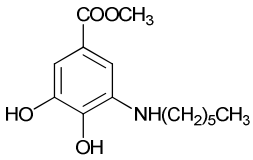
7e

Methyl 3,4-dihydroxy-5-(isobutylamino)benzoate (7f) m.p.161～162°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.82 (d, *J*= 2.0Hz, 1H, 2-ArH), 6.65 (d, *J*= 2.0 Hz, 1H, 6-ArH), 3.74 (s, 3H, OCH_3)，2.85 (d, *J*= 6.8 Hz, 2H, CH_2), 1.86 (m, 1H, CH)，0.91 (d, *J*= 6.8 Hz, 6H, $2CH_3$)； MS (EI): m/z=239[M]$^+$, 197, 196, 180.



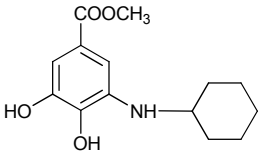
7f

Methyl 3-(hexylamino)-4,5-dihydroxybenzoate (7g) m.p.179～180°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.33 (s, 1H, OH), 6.83 (d, *J*= 2.0 Hz, 1H, 2-ArH), 6.65 (d, *J*= 2.0 Hz, 1H, 6-ArH), 3.73 (s, 3H, OCH_3)，3.01 (t, J_1= 7.2 Hz , J_2= 7.2 Hz, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.32 (m, 6H, $3\times CH_2$), 0.87 (t, J_1= 6.4 Hz , J_2= 7.2 Hz ,3H, CH_3)；^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.8(C=O), 143.6, 138.1, 136.1, 120.1, 106.1, 102.7, 51.5(OCH_3), 43.0, 31.1, 28.7, 26.3, 22.1, 13.9; MS (EI): m/z=267[M]$^+$, 266, 225, 197, 196.



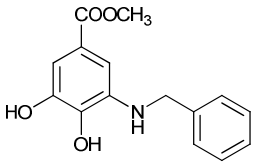
7g

Methyl 3-(cyclohexylamino)-4,5-dihydroxybenzoate (7h) m.p.186～188°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.37 (s, 1H, 4-OH), 6.81 (d, *J*= 1.2 Hz, 1H, 2-ArH), 6.68 (d, *J*= 1.2 Hz, 1H, 6-ArH), 3.73 (s, 3H, OCH_3)，3.18 (m, 1H, CH), 1.69 (d, *J*= 4.0 Hz, 2H, CH_2), 1.67 (d, *J*= 3.2 Hz, 2H, CH_2), 1.31 (m, 3H), 1.20 (m, 3H)； ^{13}C NMR (DMSO-d_6, 400 MHz) δ: 166.8(C=O), 143.9, 136.8, 136.2, 120.2, 105.9, 103.4, 51.5(OCH_3), 50.7, 32.8($2CH_2$), 25.5, 24.6($2CH_2$); MS (EI): m/z=265[M]$^+$, 249, 234, 222, 209, 183.



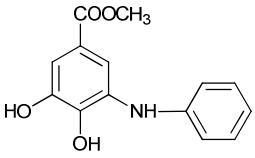
7h

Methyl 3-(benzylamino)-4, 5-dihydroxybenzoate (7i) m.p.190～192°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.40 (d, *J*= 7.6 Hz, 2H, 2′, 6′-ArH), 7.31 (t, *J* = 7.6 Hz, 2H, 3′, 5′-ArH), 7.21 (t, *J*= 7.2 Hz, 1H, 4′-ArH), 6.96 (d, *J* = 1.6Hz, 1H, 2-ArH), 6.84 (d, *J*= 1.6Hz, 1H, 6-ArH), 4.42 (s, 2H, CH_2), 3.71(s, 3H, OCH_3)； MS (EI): m/z=273[M]$^+$, 242, 91.



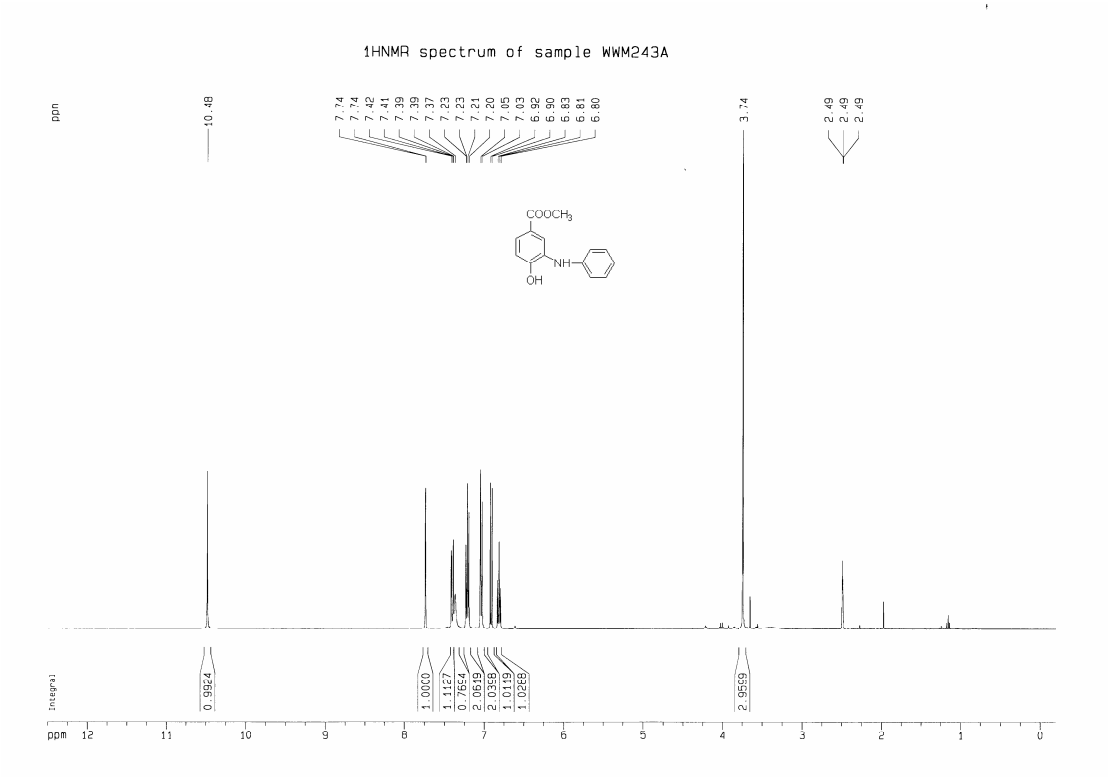
7i

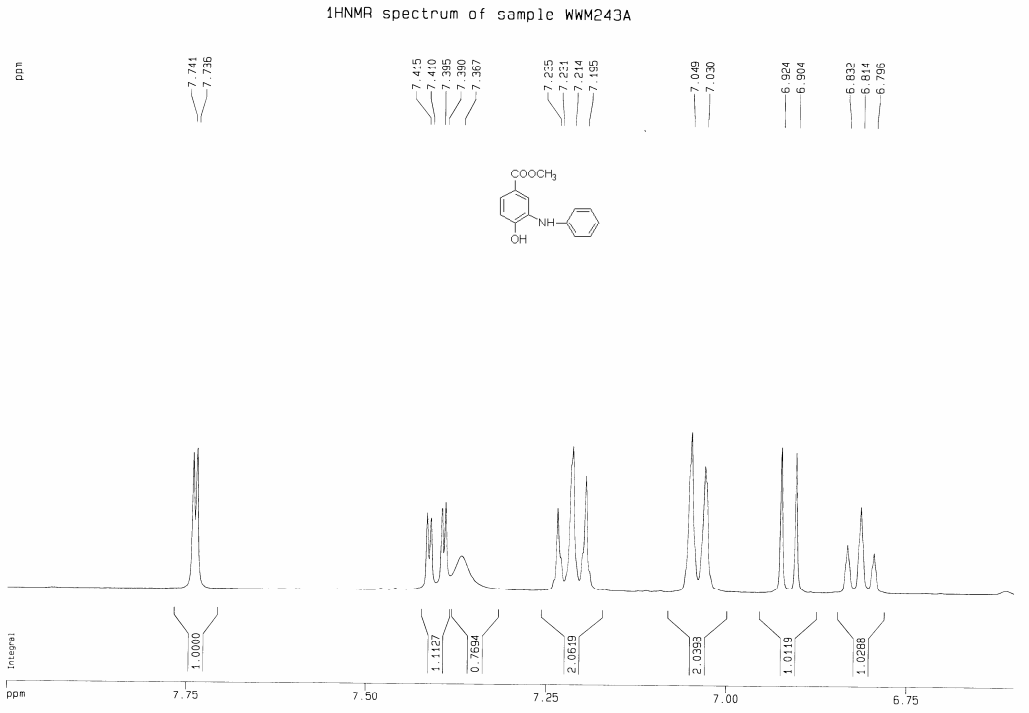
III-5 Characterization Data for Products 12 m.p.186～187°C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 9.68 (s, 1H, 4-OH), 9.34 (s, 1H, 3-OH), 7.32 (d, J= 2.0 Hz, 1H, 2-ArH), 7.31 (s, 1H, NH), 7.19 (t, J_1 = 8.4 Hz, J_2 = 7.6 Hz, 2H, 3′, 5′-ArH), 7.08 (d, J= 2.0Hz, 1H, 6-ArH), 7.00 (d, J= 7.6 Hz, 2H, 2′, 6′-ArH), 6.78 (t, J = 7.2 Hz, 1H, 4′-ArH), 3.74(s, 3H, CH_3)； MS (EI): m/z=259[M]$^+$, 184, 170.

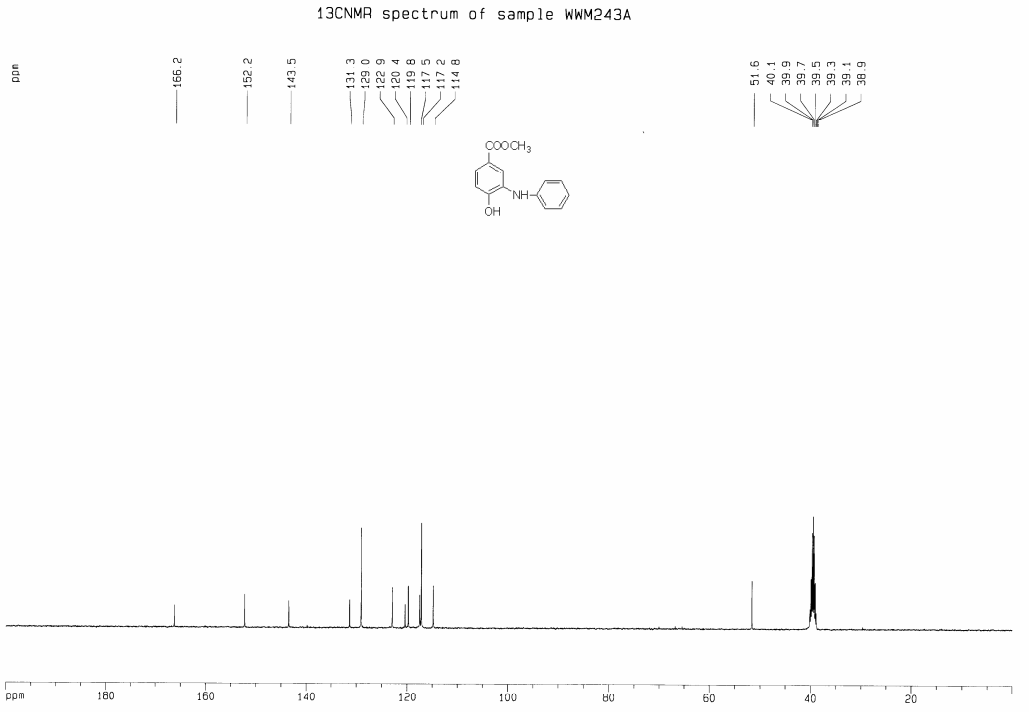


12

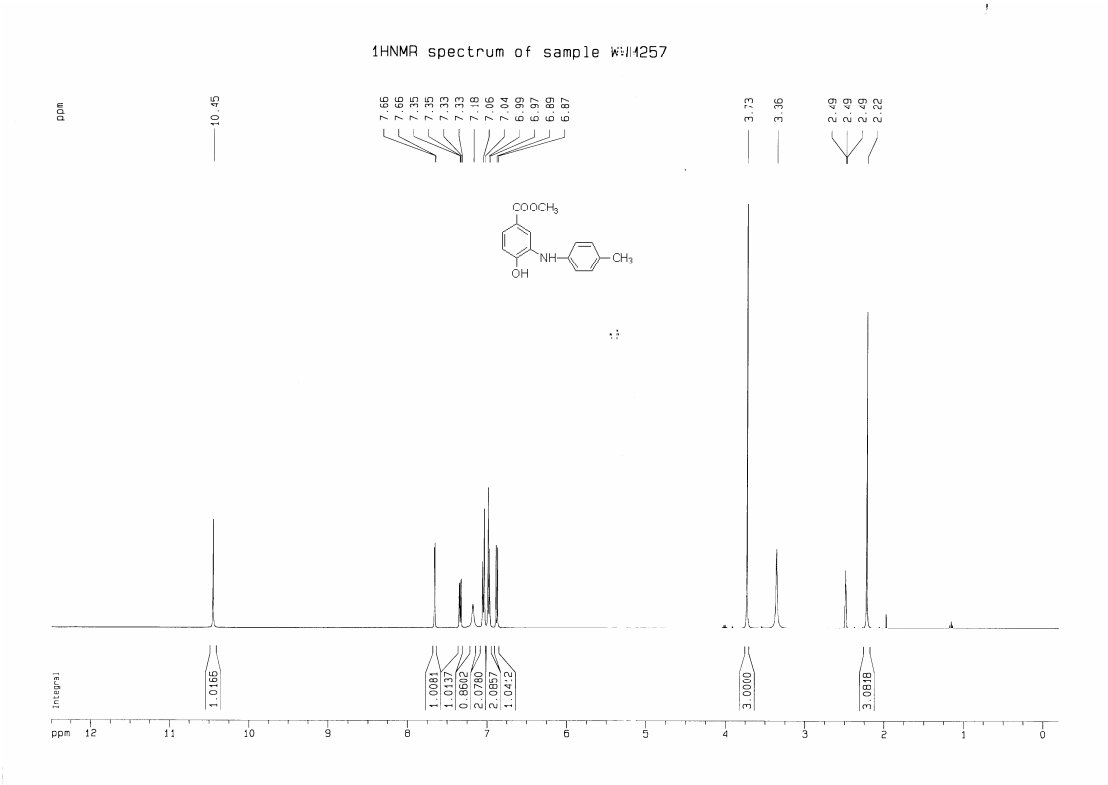
[^{1}H and ^{13}C NMR Spectra of 5a]

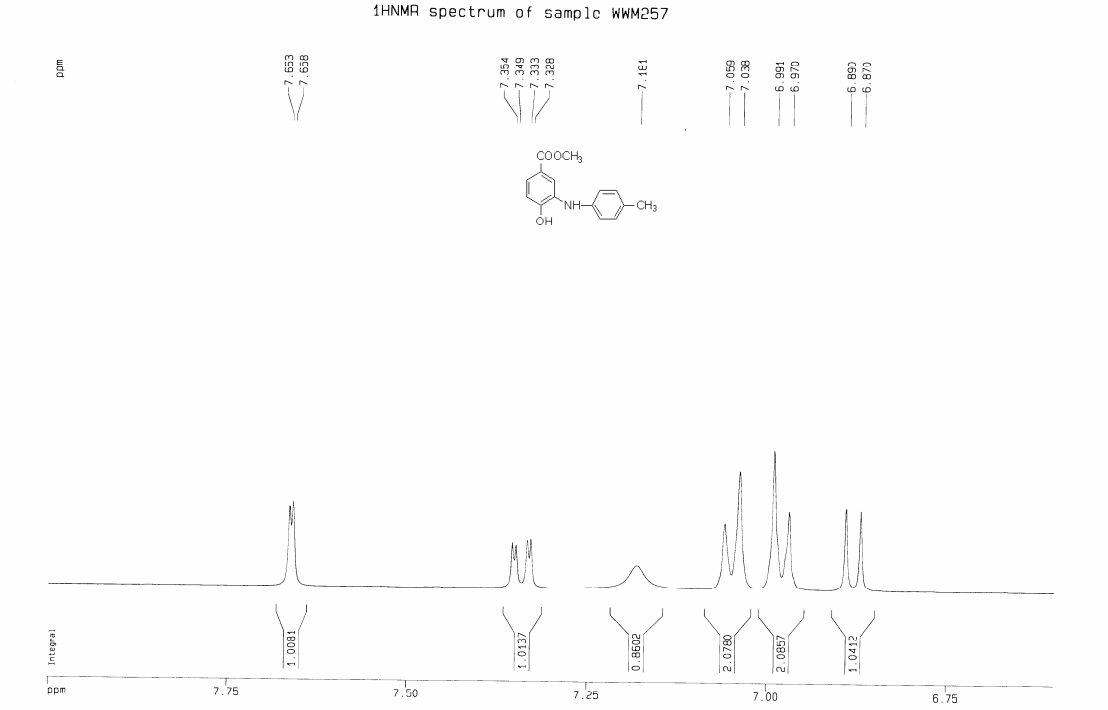


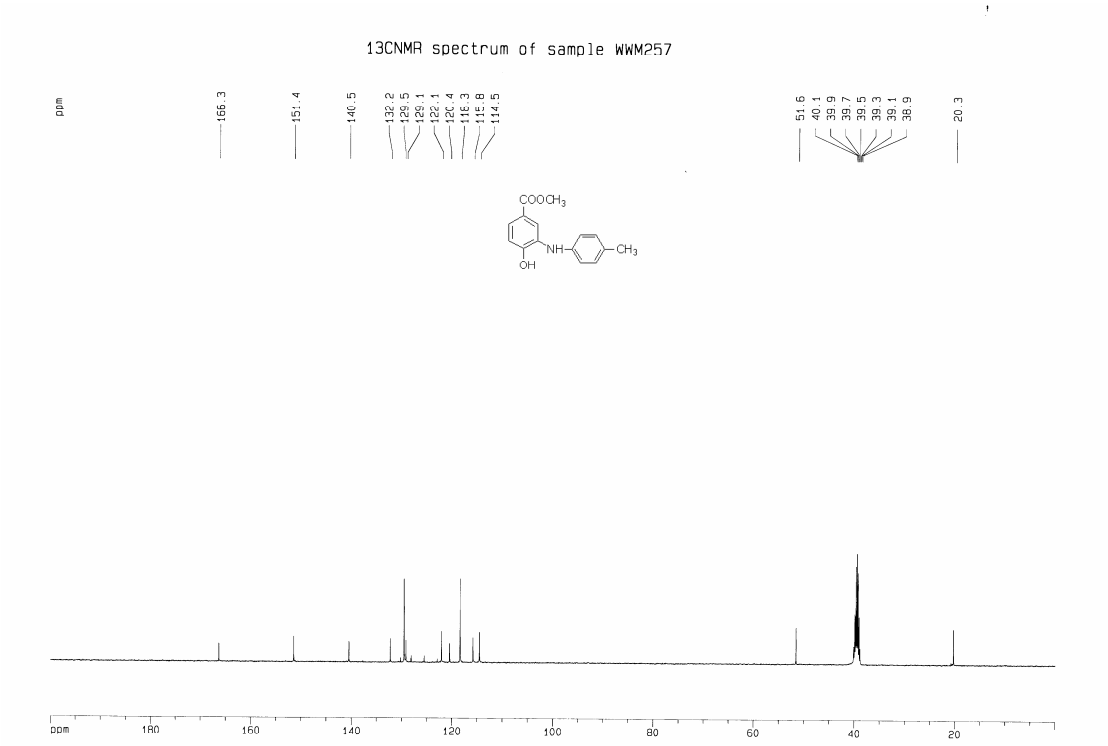

1HNMR spectrum of sample WWM243A
ppm
7.741
7.736
7.415
7.410
7.395
7.390
7.367
7.235
7.231
7.214
7.195
7.049
7.030
6.924
6.904
6.832
6.814
6.796
COOCH3
NH
OH
Integral
1.0000
1.1127
0.7694
2.0619
2.0393
1.0119
1.0288
ppm
7.75
7.50
7.25
7.00
6.75


13CNMR spectrum of sample WWM243A
ppm
166.2
152.2
143.5
131.3
129.0
122.9
120.4
119.8
117.5
117.2
114.8
51.6
40.1
39.9
39.7
39.5
39.3
39.1
38.9
COOCH3
NH
OH
ppm
180
160
140
120
100
80
60
40
20

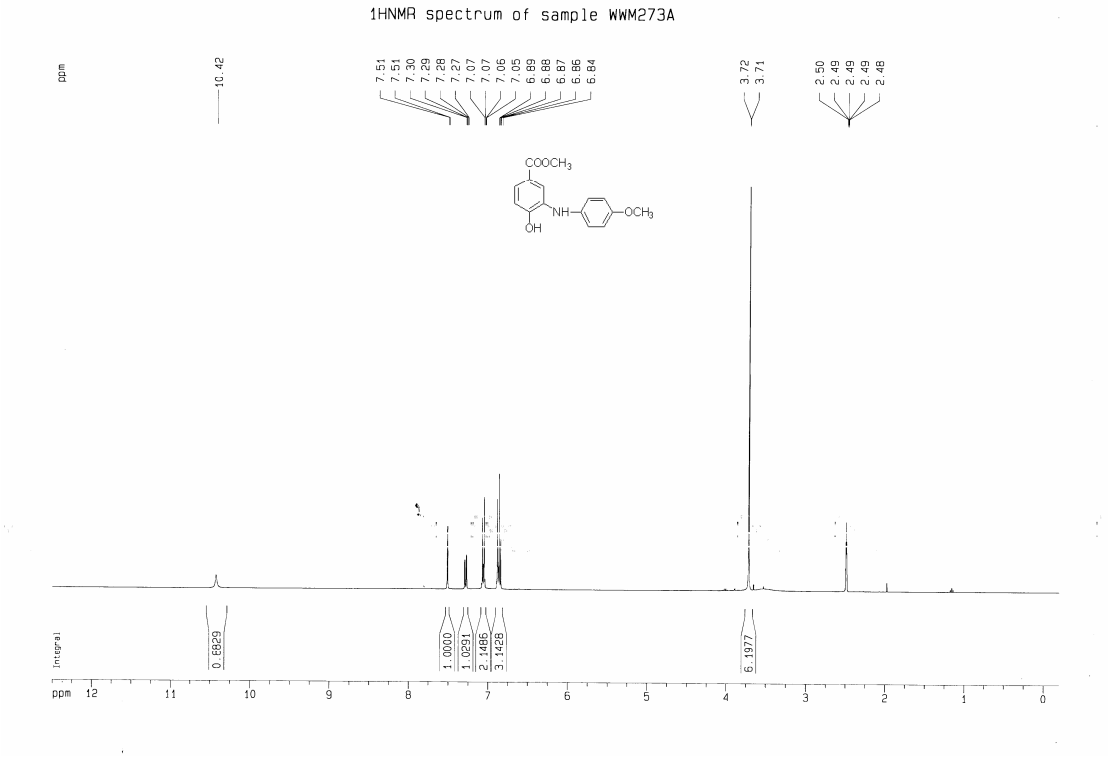
[^{1}H and ^{13}C NMR Spectra of 5b]



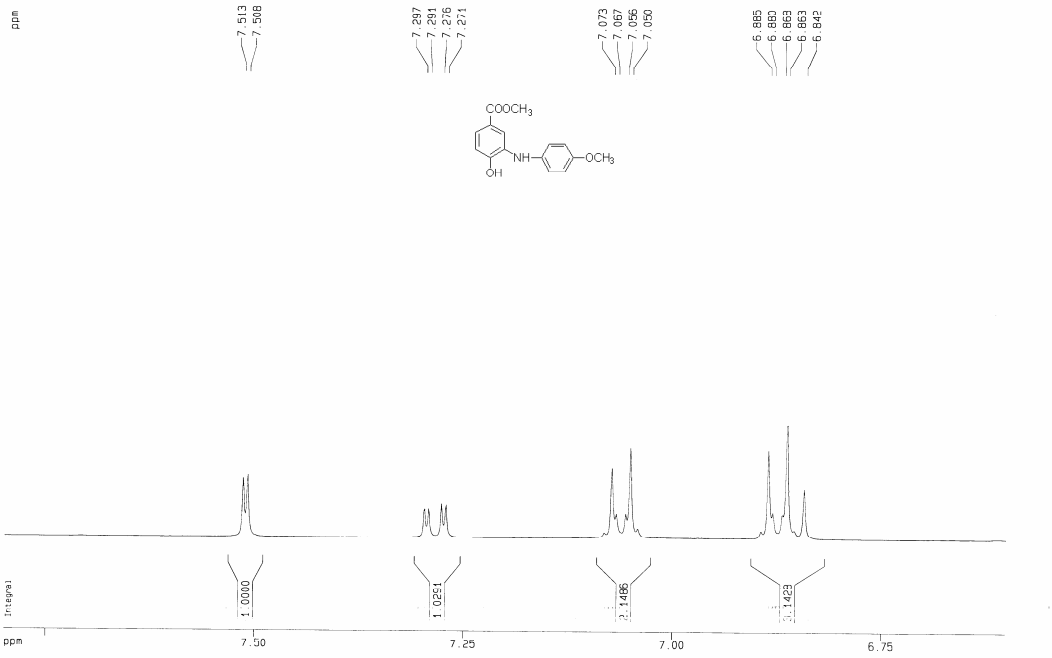




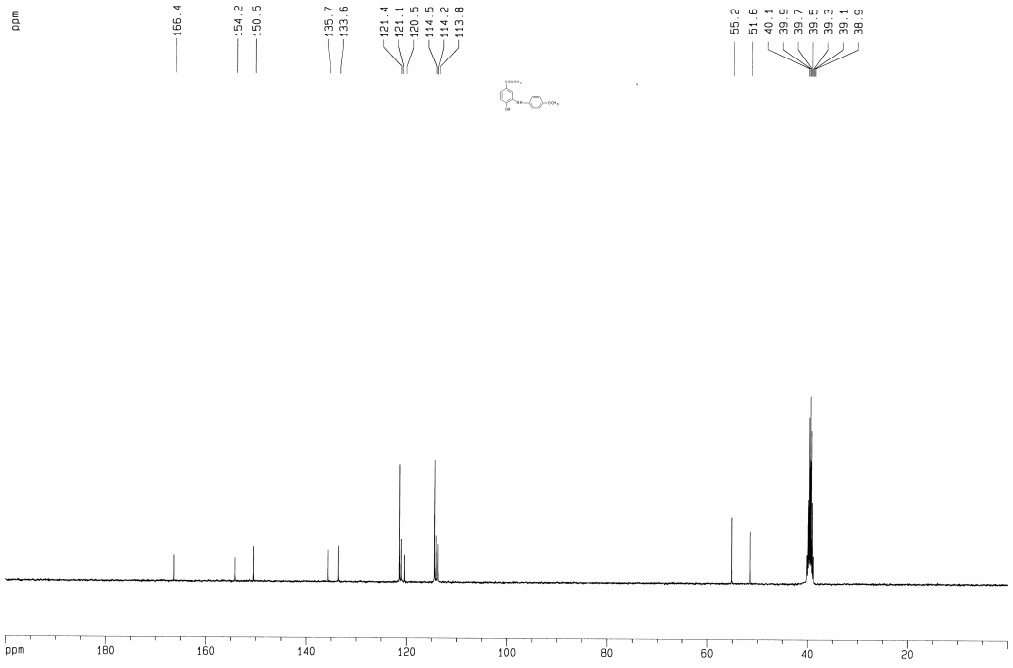
[^{1}H and ^{13}C NMR Spectra of 5c]



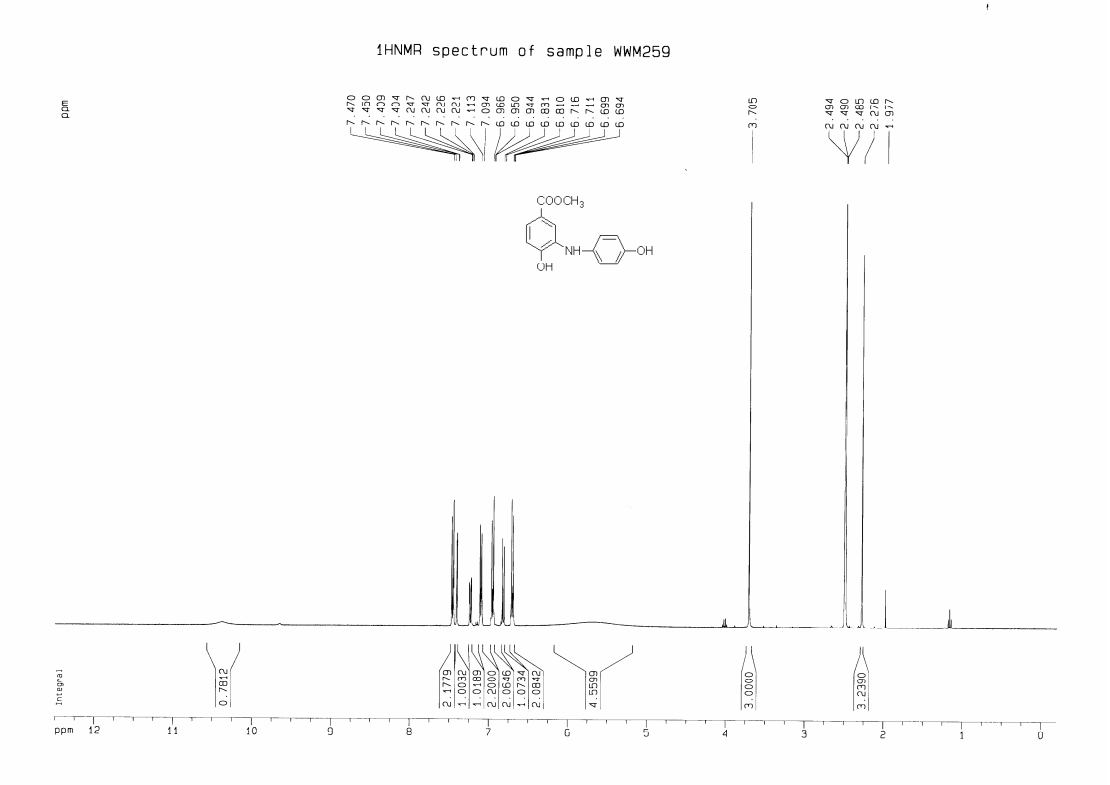
1HNMR spectrum of sample WWM273A

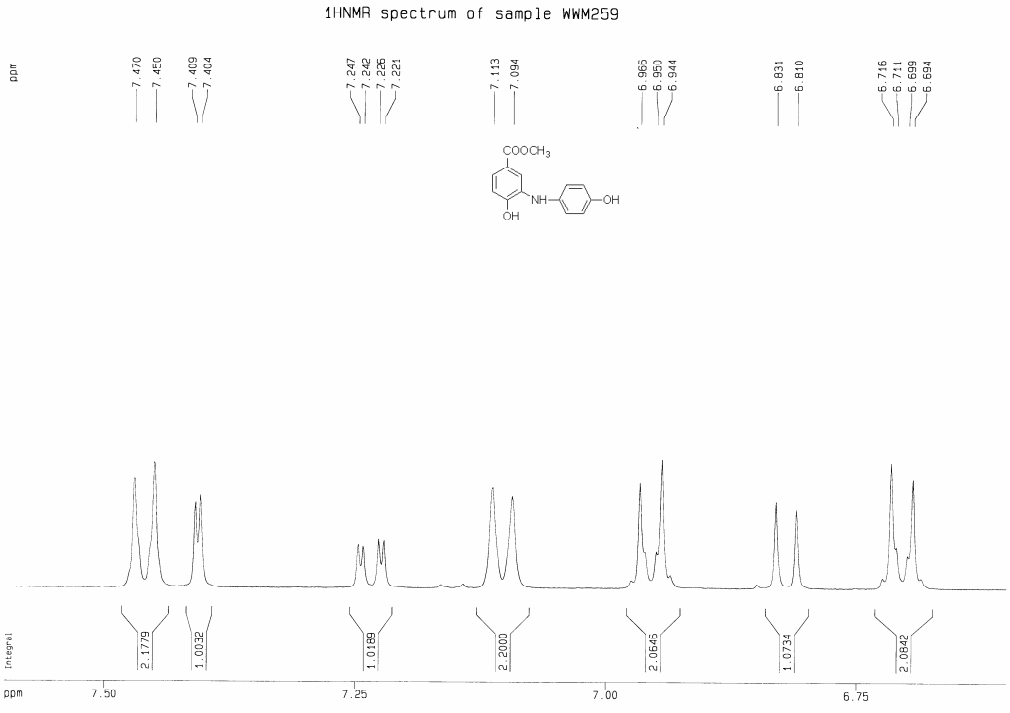


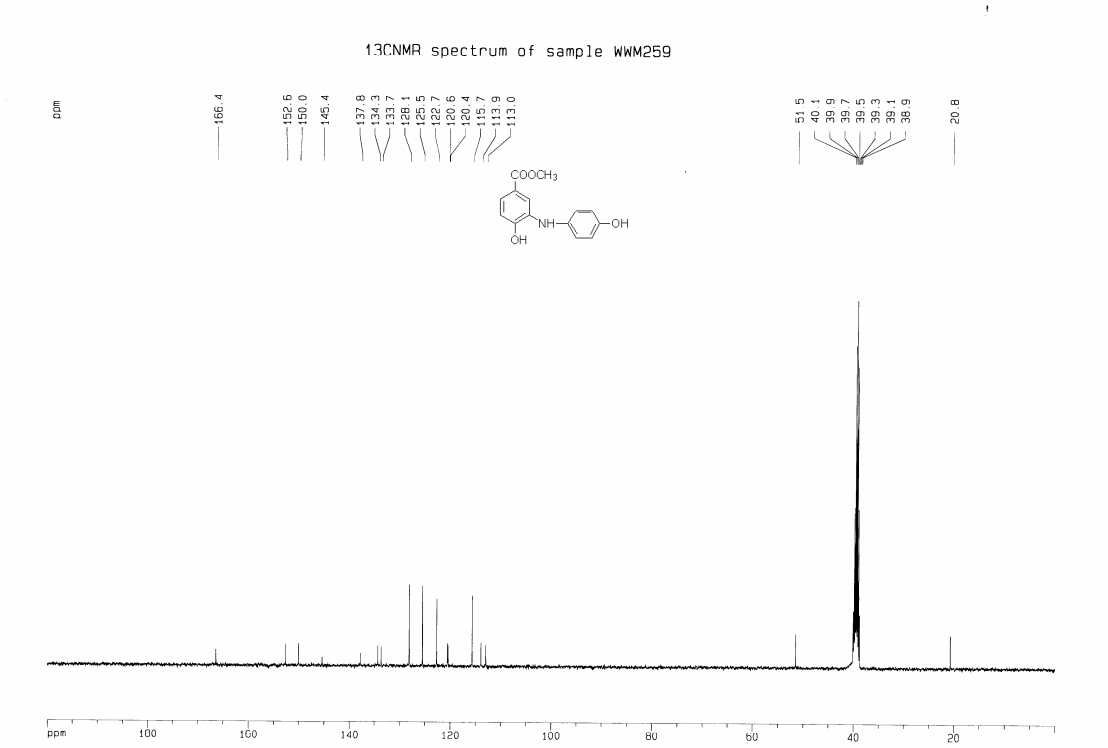
13CNMR spectrum of sample WWM273A



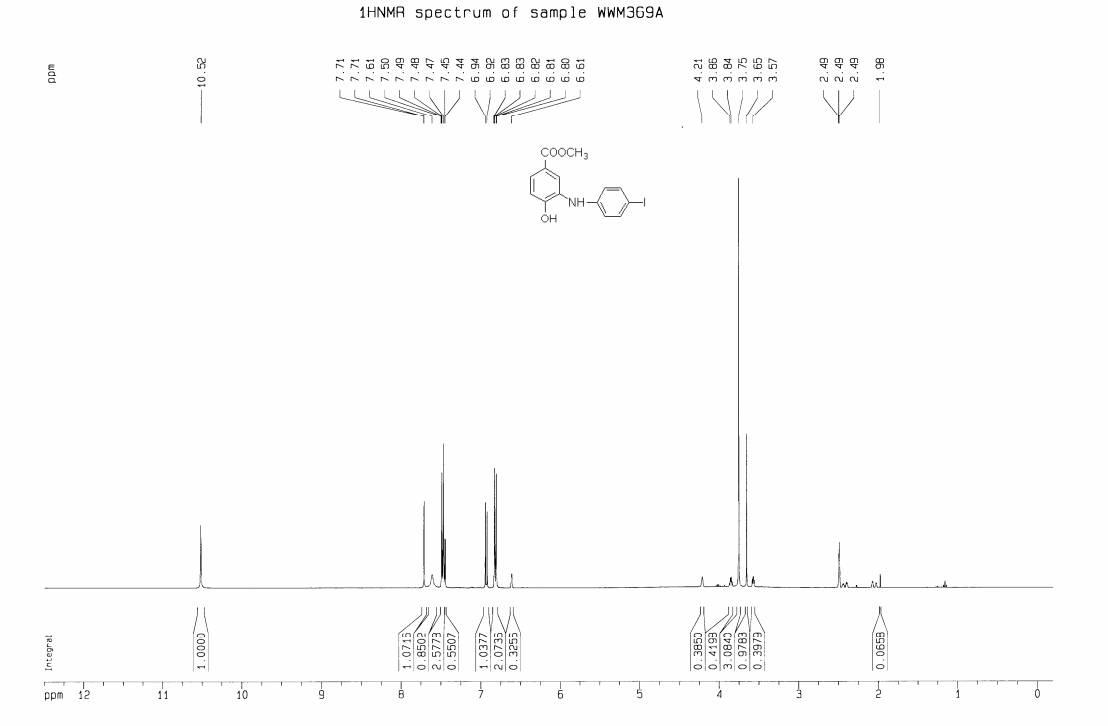
[^{1}H and ^{13}C NMR Spectra of 5d]

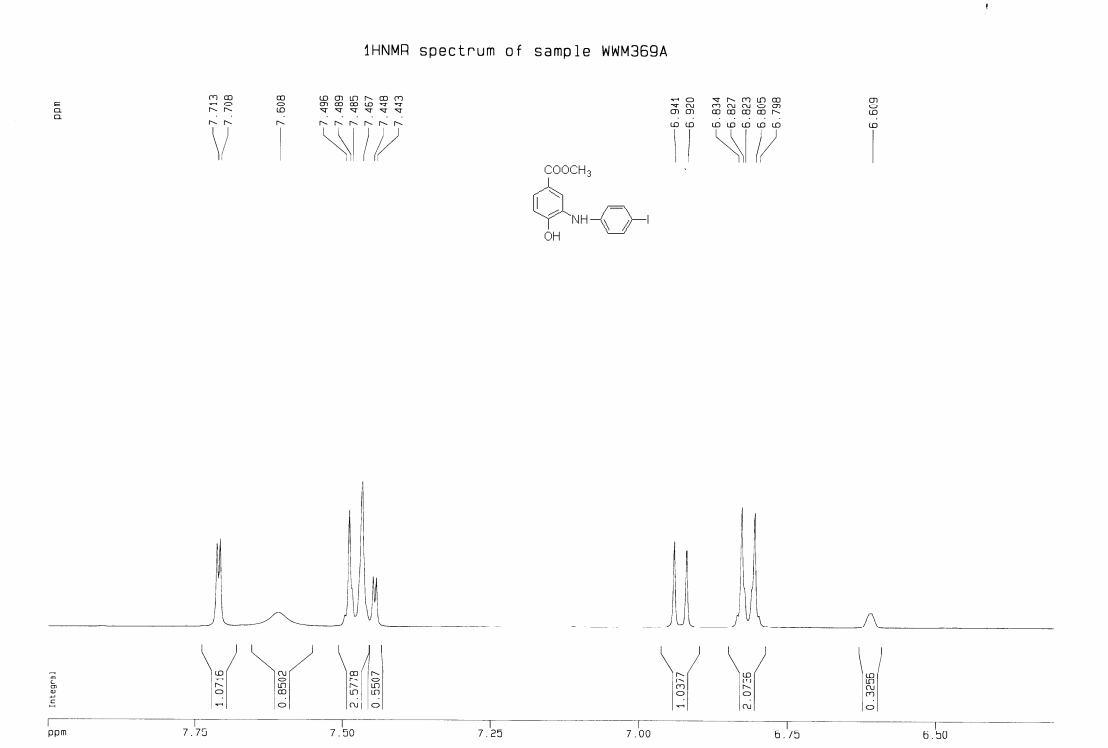




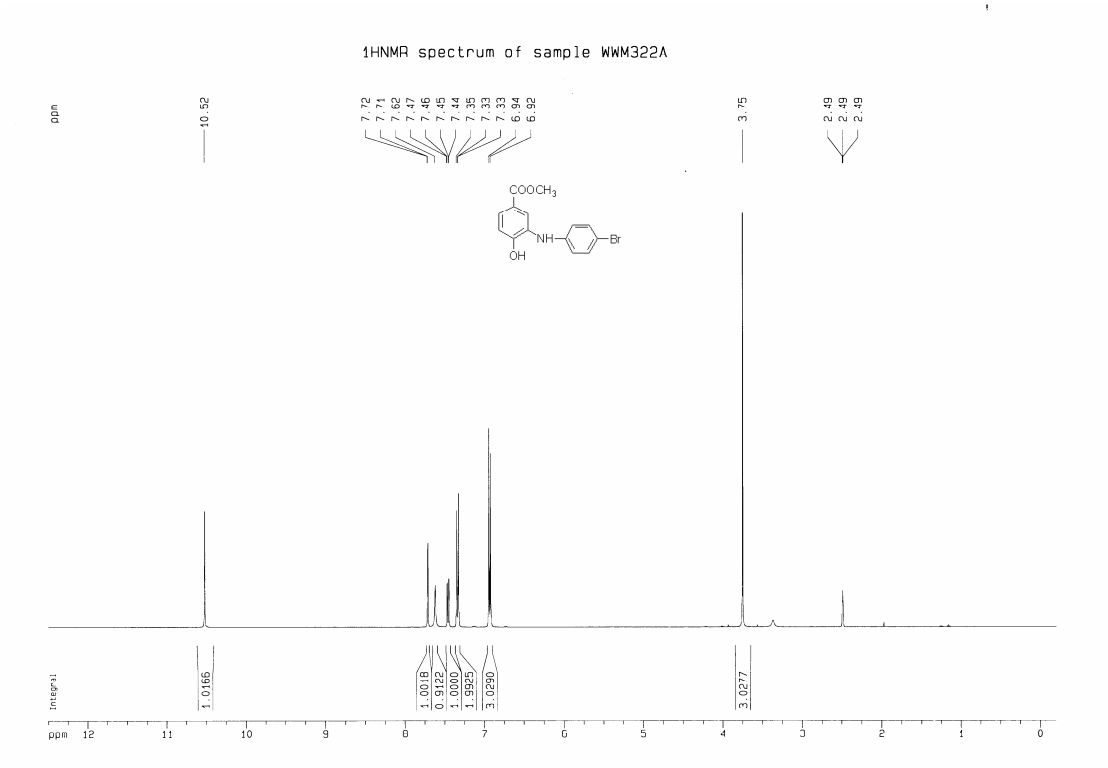


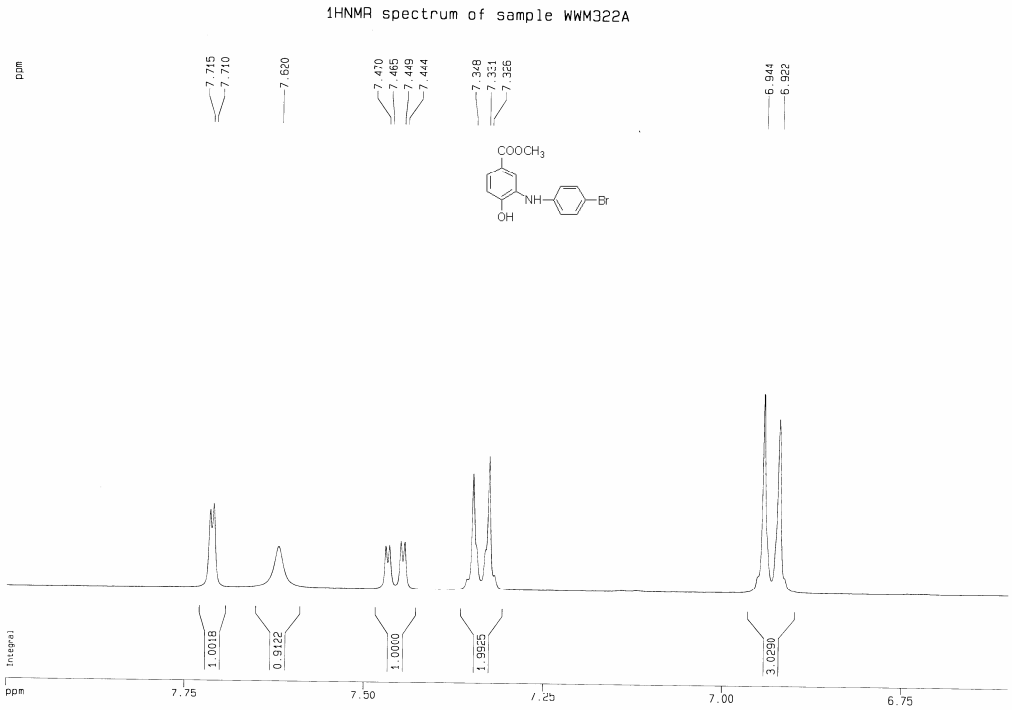
[^{1}H NMR Spectra of 5e]

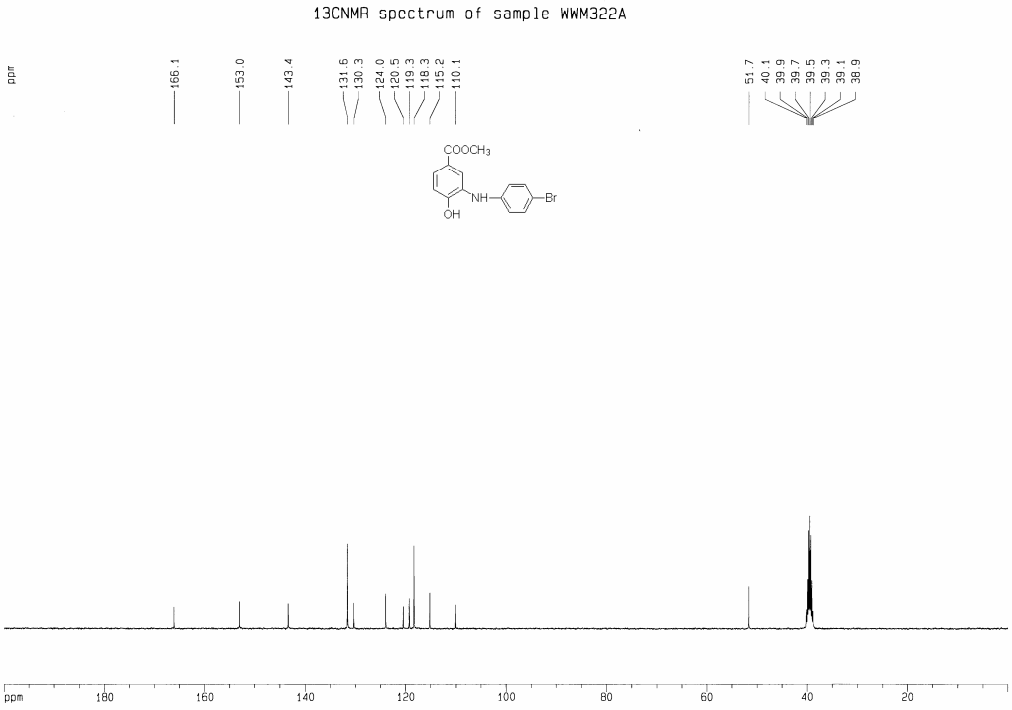




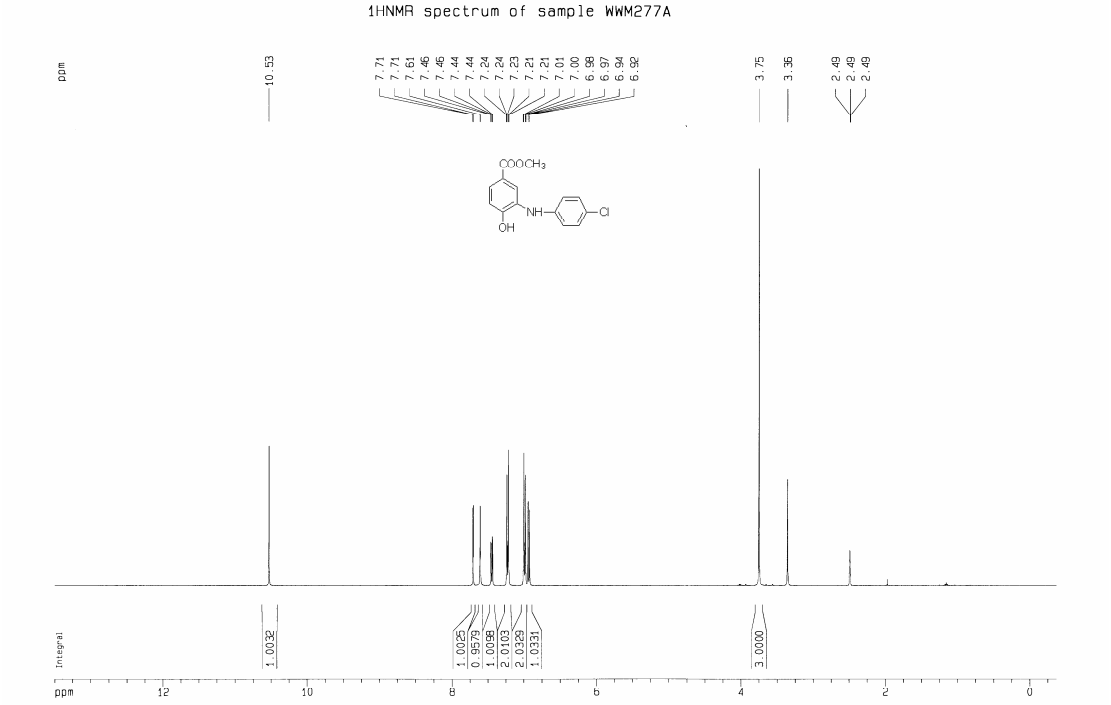
[^{1}H and ^{13}C NMR Spectra of 5f]

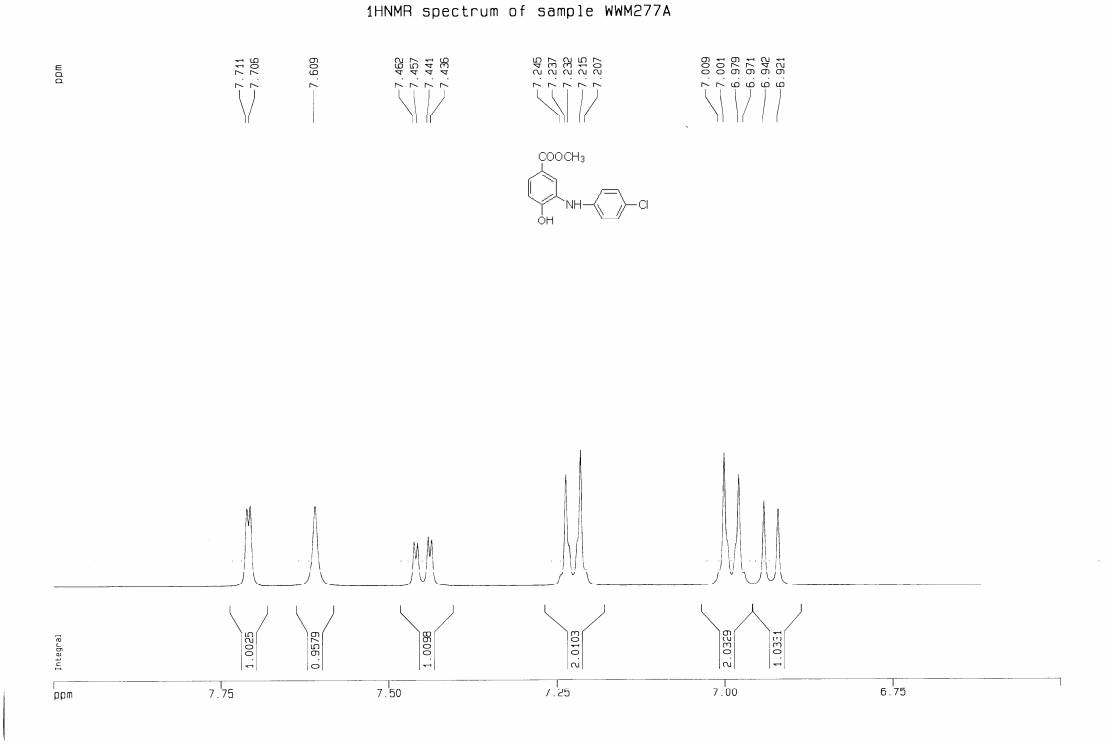


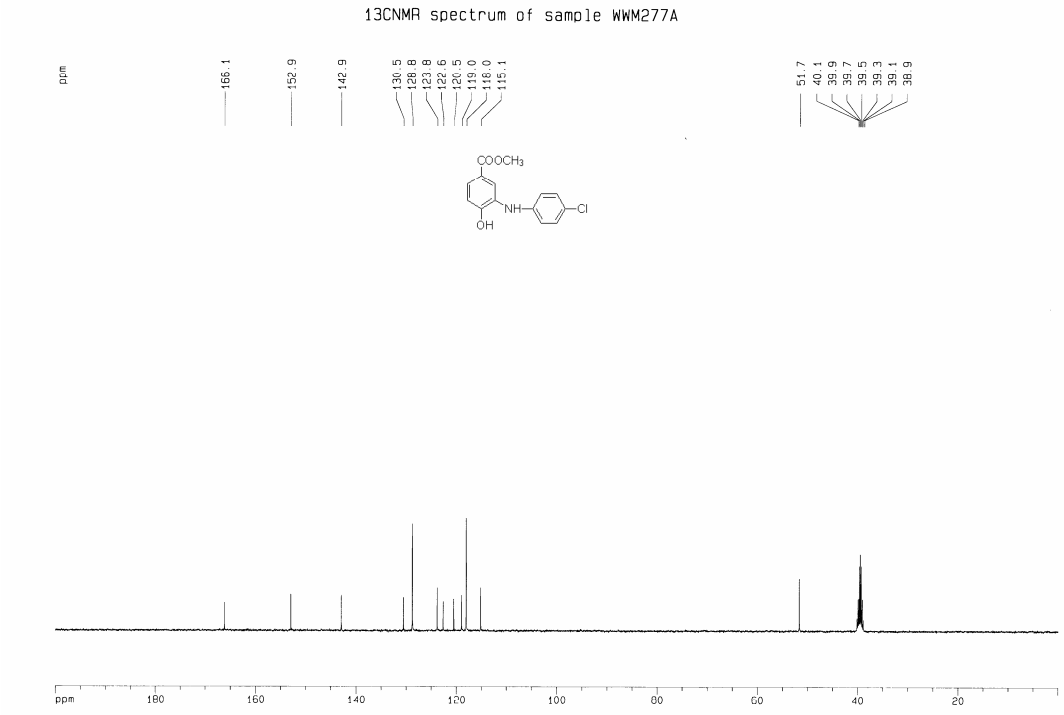




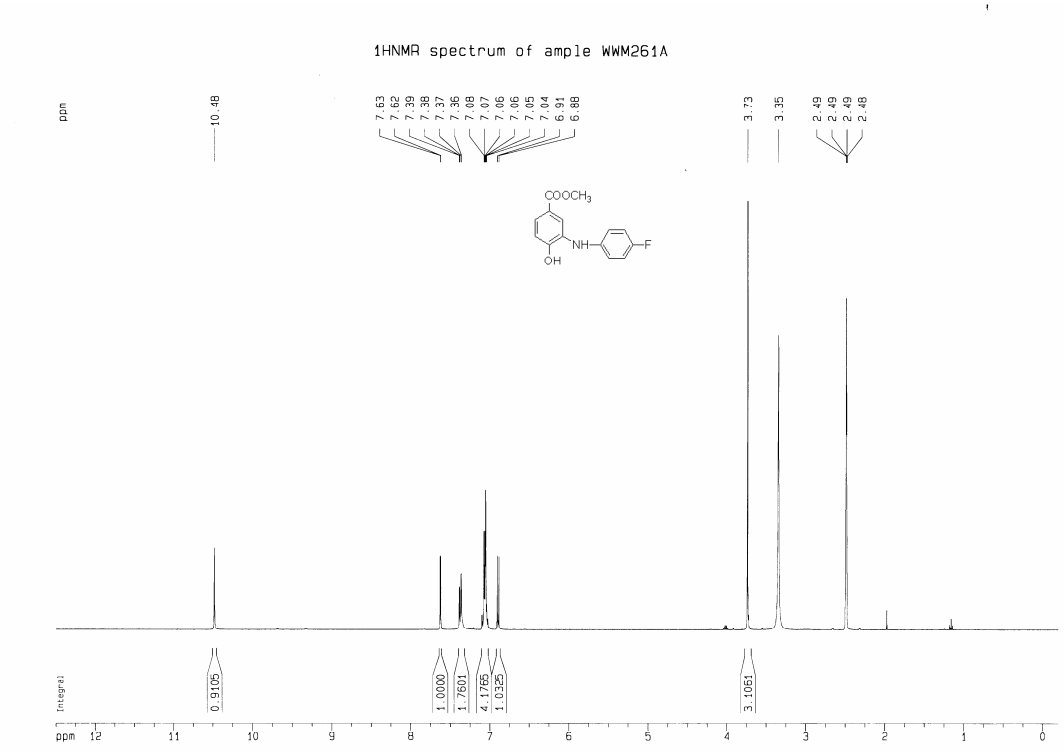
[^{1}H and ^{13}C NMR Spectra of 5g]

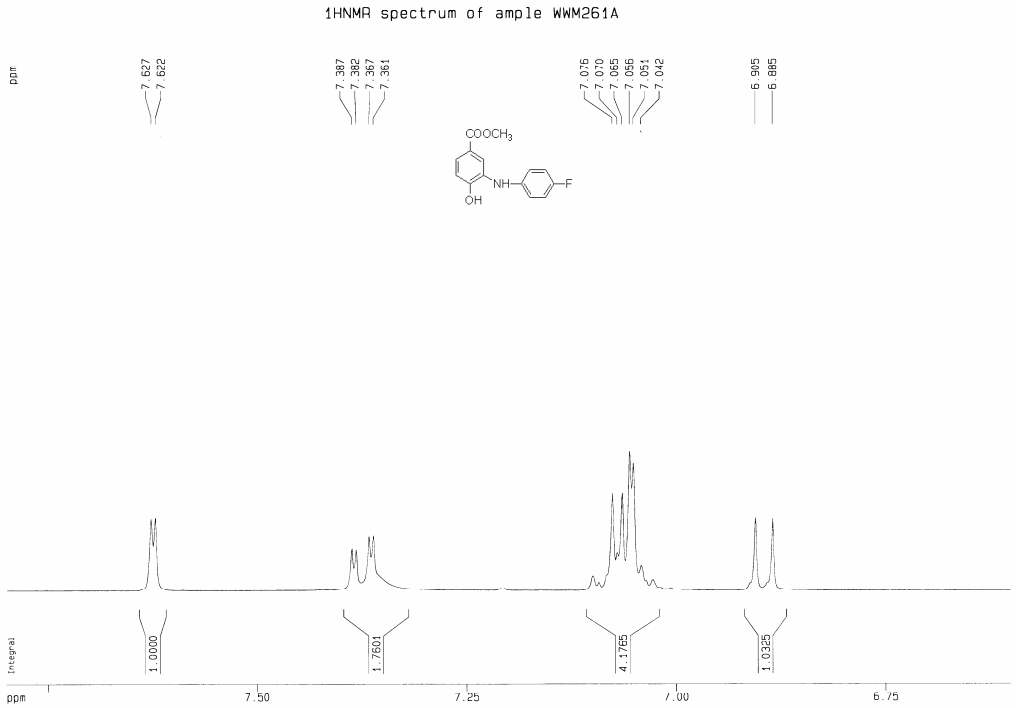

1HNMR spectrum of sample WWM277A
ppm
10.53
7.71
7.71
7.61
7.46
7.45
7.44
7.24
7.24
7.23
7.21
7.21
7.01
7.00
6.98
6.97
6.94
6.92
3.75
3.36
2.49
2.49
2.49
COOCH3
NH
Cl
OH
Integral
1.0032
1.0025
0.9579
1.0098
2.0103
2.0329
1.0331
3.0000
ppm
12
10
8
6
4
2
0

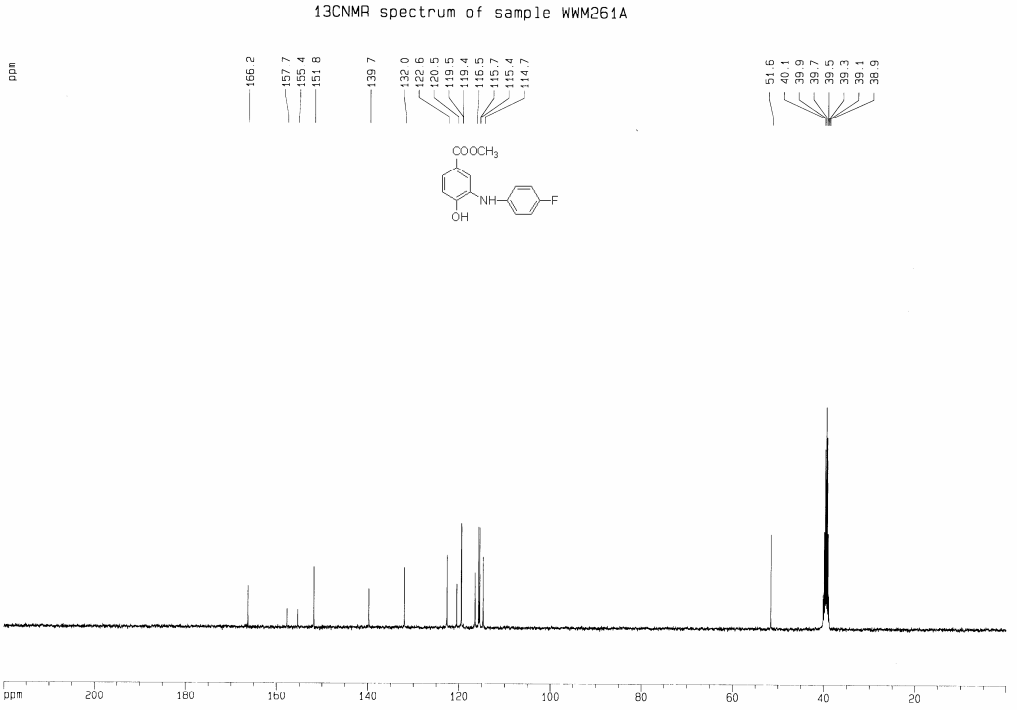

1HNMR spectrum of sample WWM277A
ppm
7.711
7.706
7.609
7.462
7.457
7.441
7.436
7.245
7.237
7.232
7.215
7.207
7.009
7.001
6.979
6.971
6.942
6.921
COOCH3
NH
Cl
OH
Integral
1.0025
0.9579
1.0098
2.0103
2.0329
1.0331
ppm
7.75
7.50
7.25
7.00
6.75



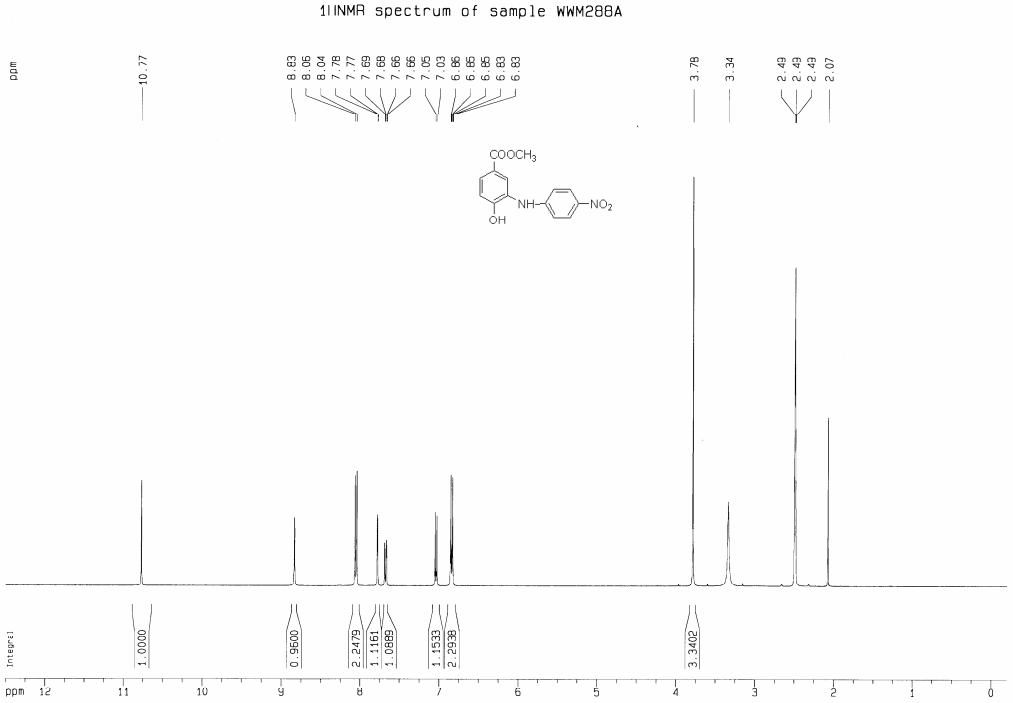
[^{1}H and ^{13}C NMR Spectra of 5h]

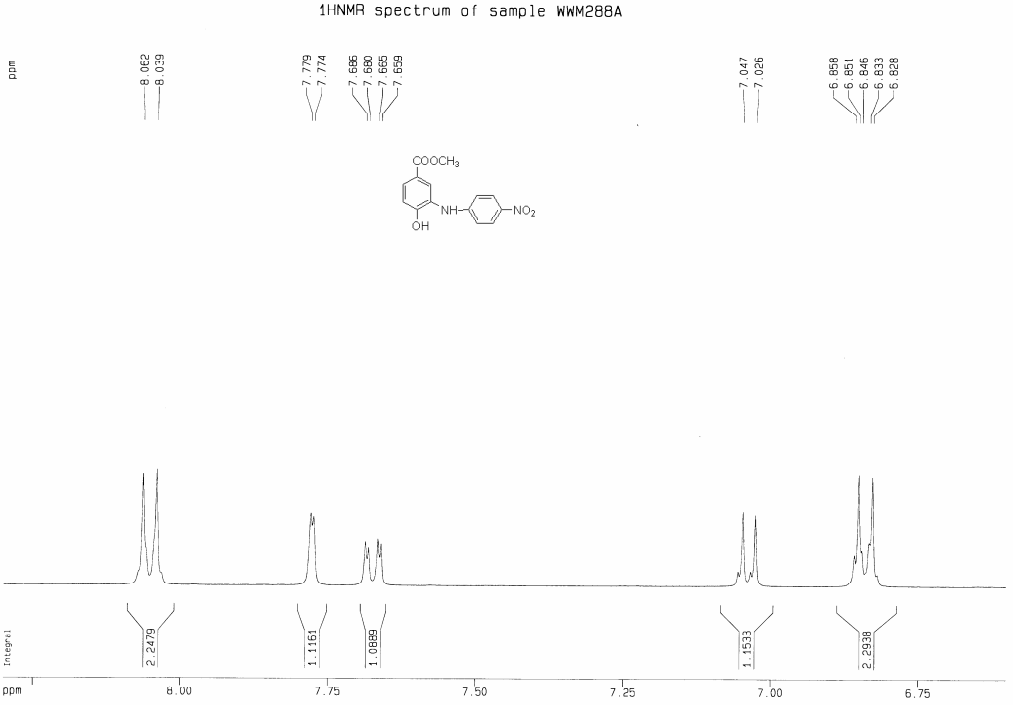


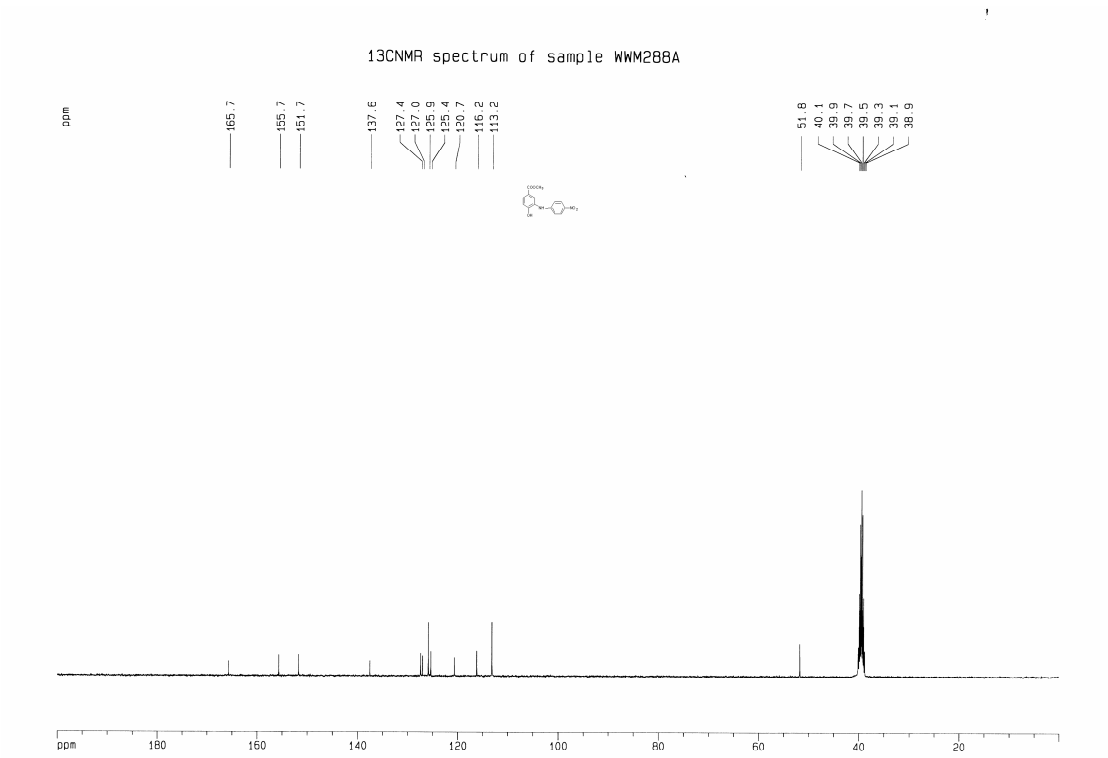




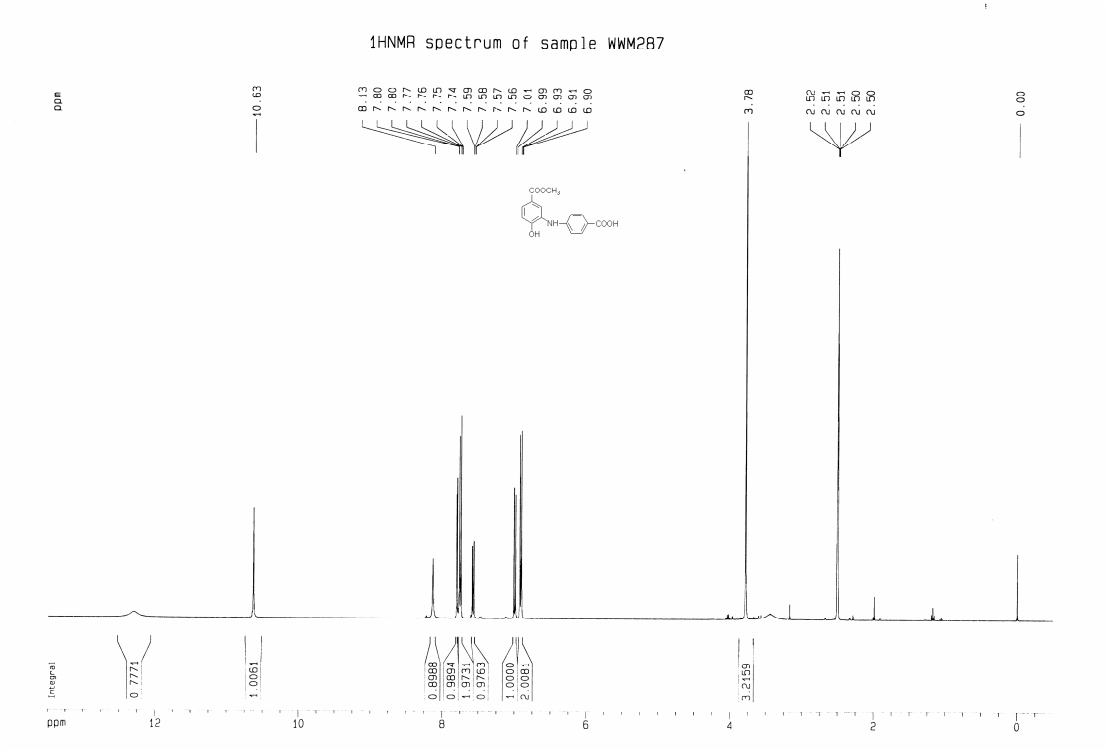
[^{1}H and ^{13}C NMR Spectra of 5i]

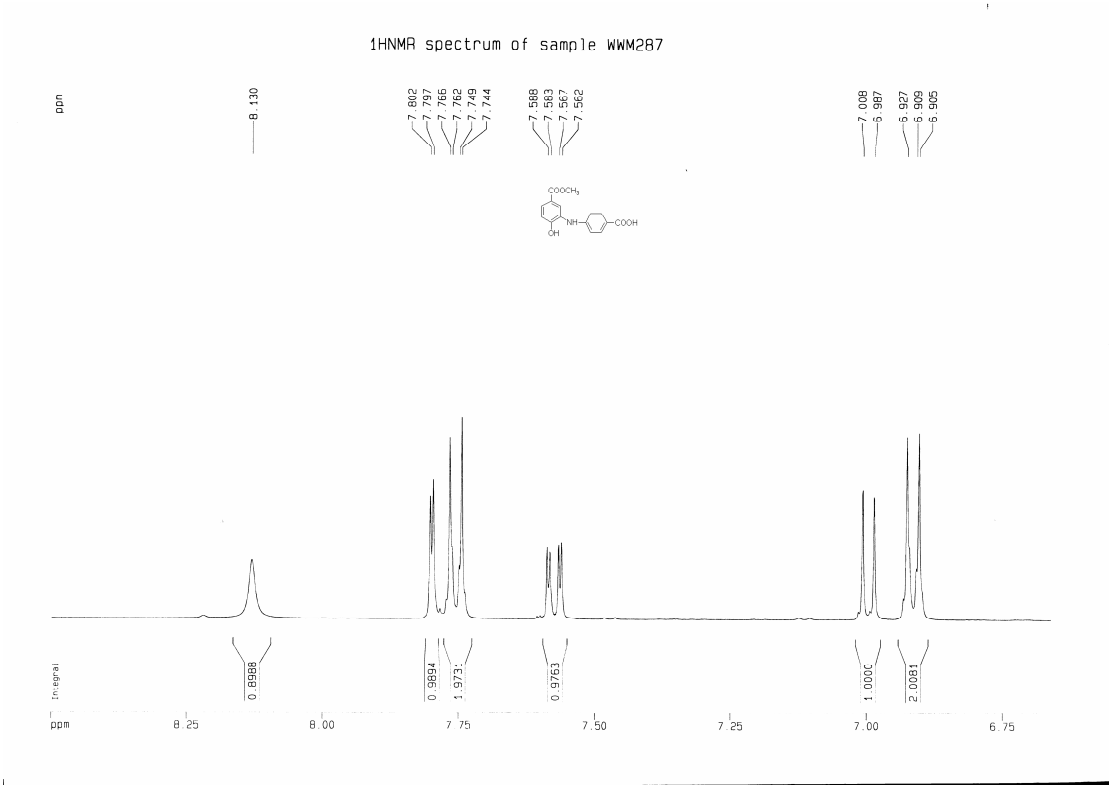

1HNMR spectrum of sample WWM288A
ppm
10.77
8.83
8.05
8.04
7.78
7.77
7.69
7.68
7.66
7.66
7.05
7.03
6.86
6.85
6.85
6.83
6.83
3.78
3.34
2.49
2.49
2.49
2.07
COOCH3
NH
NO2
OH
Integral
1.0000
0.9600
2.2479
1.1161
1.0889
1.1533
2.2938
3.3402
ppm

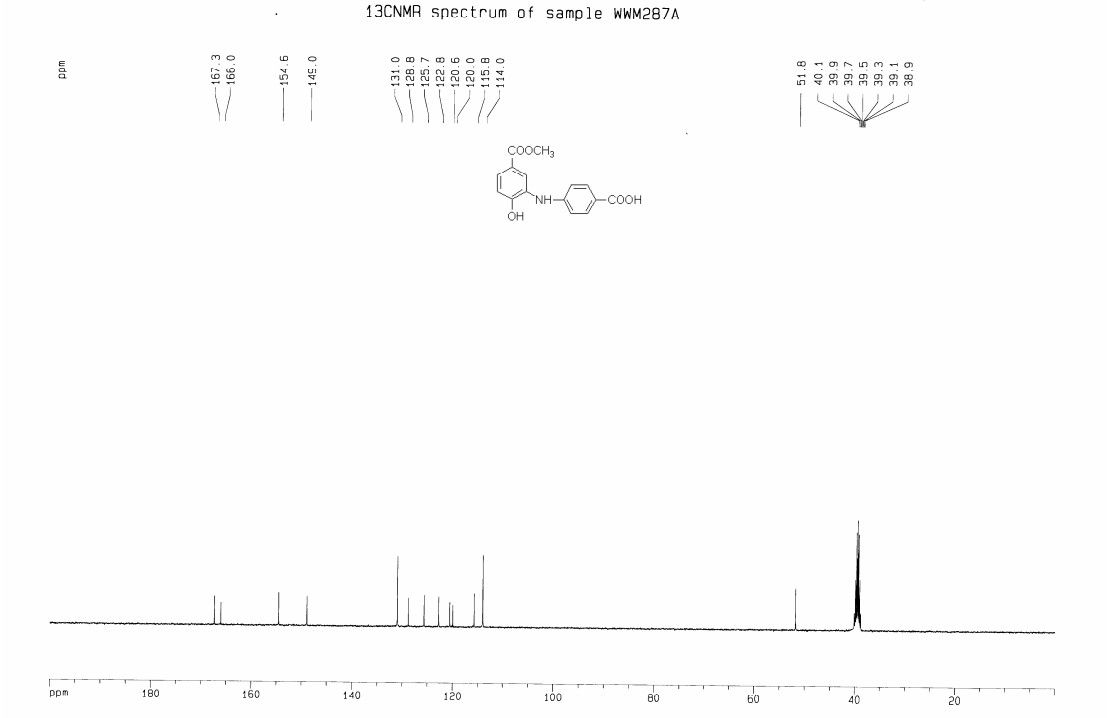

1HNMR spectrum of sample WWM288A
ppm
8.062
8.039
7.779
7.774
7.686
7.680
7.665
7.659
7.047
7.026
6.858
6.851
6.846
6.833
6.828
COOCH3
NH
NO2
OH
Integral
2.2479
1.1161
1.0889
1.1533
2.2938
ppm
8.00
7.75
7.50
7.25
7.00
6.75



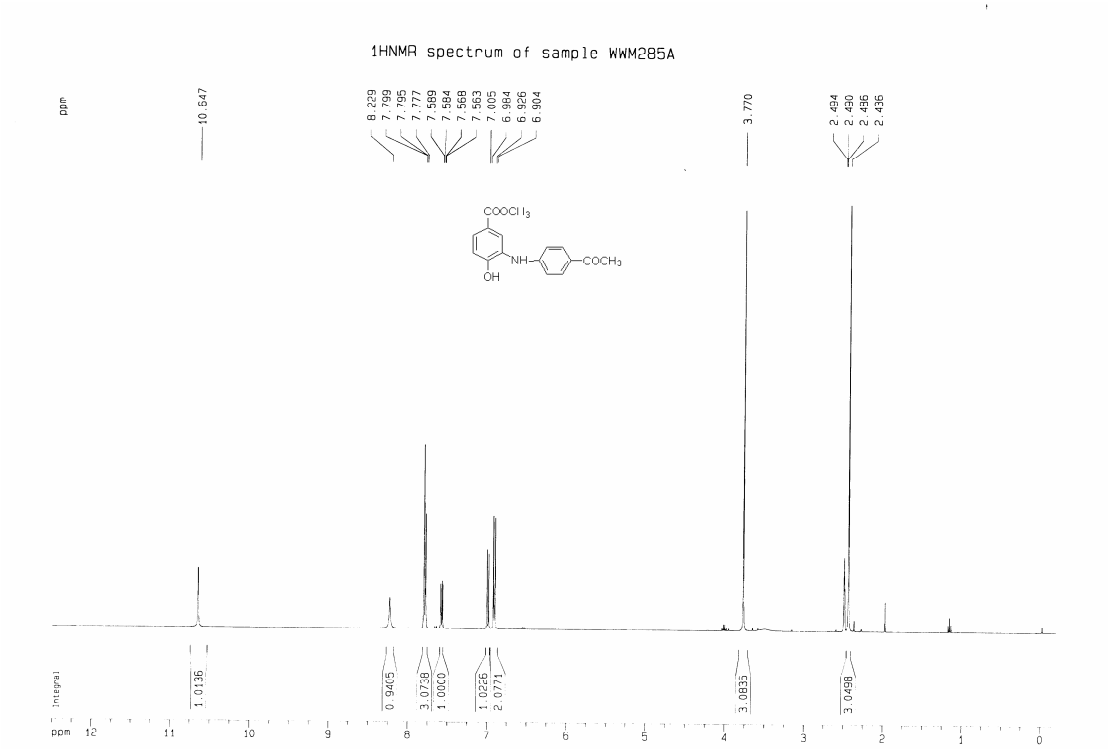
[^{1}H and ^{13}C NMR Spectra of 5j]

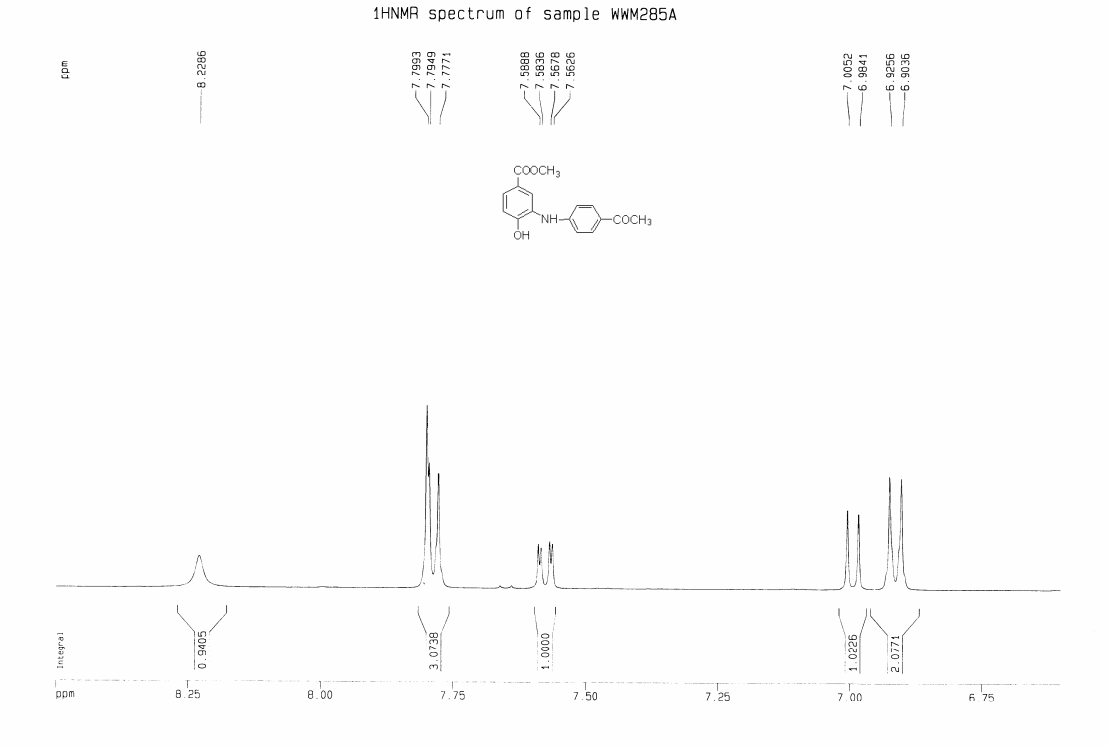


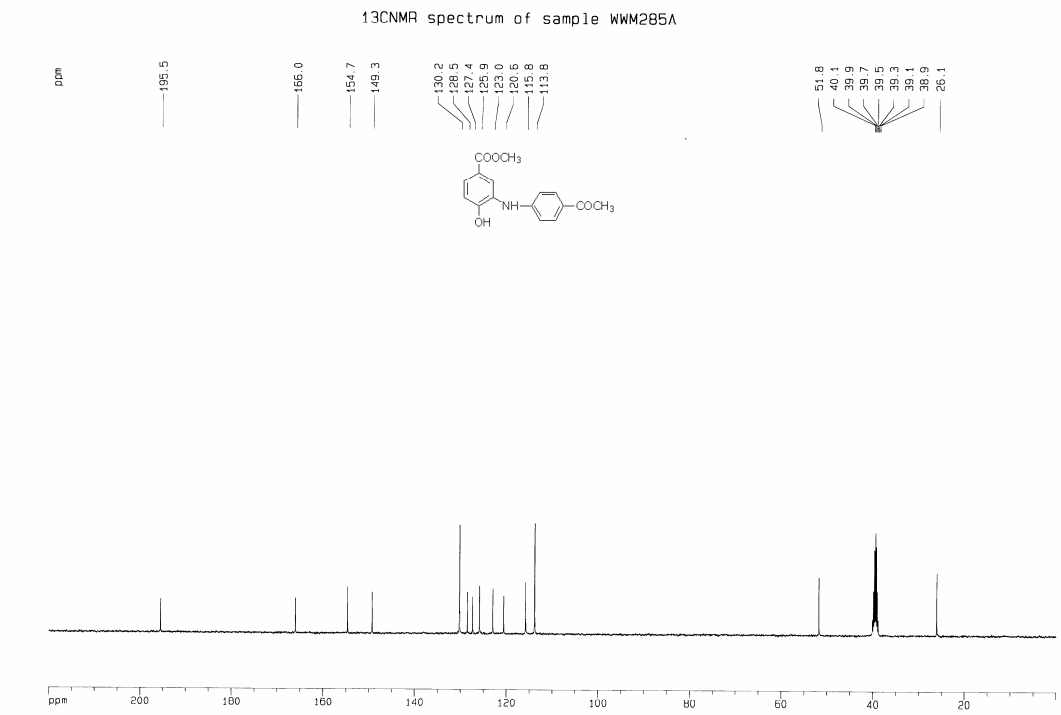

1HNMR spectrum of sample WWM287
ppm
8.130
7.802
7.797
7.766
7.762
7.749
7.744
7.588
7.583
7.567
7.562
7.008
6.987
6.927
6.909
6.905
COOCH3
NH
COOH
OH
Integral
0.8988
0.9894
1.973:
0.9763
1.000C
2.0081
ppm
8.25
8.00
7.75
7.50
7.25
7.00
6.75


13CNMR spectrum of sample WWM287A
ppm
167.3
166.0
154.6
145.0
131.0
128.8
125.7
122.8
120.6
120.0
115.8
114.0
51.8
40.1
39.9
39.7
39.5
39.3
39.1
38.9
COOCH3
NH
COOH
OH
ppm
180
160
140
120
100
80
60
40
20

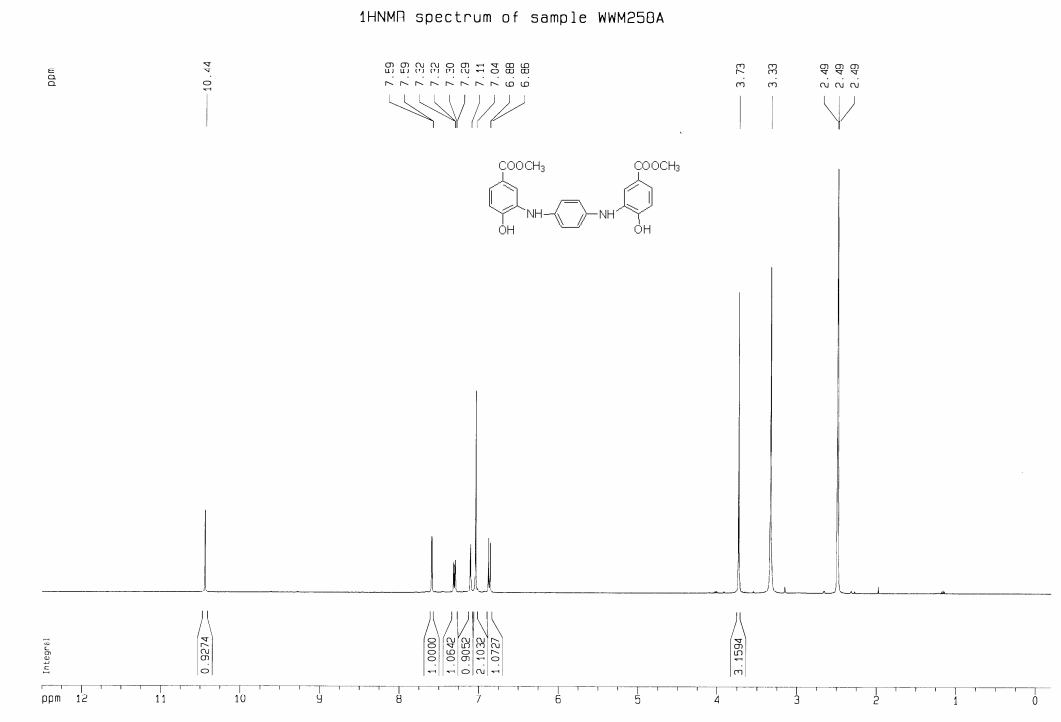
[^{1}H and ^{13}C NMR Spectra of 5k]

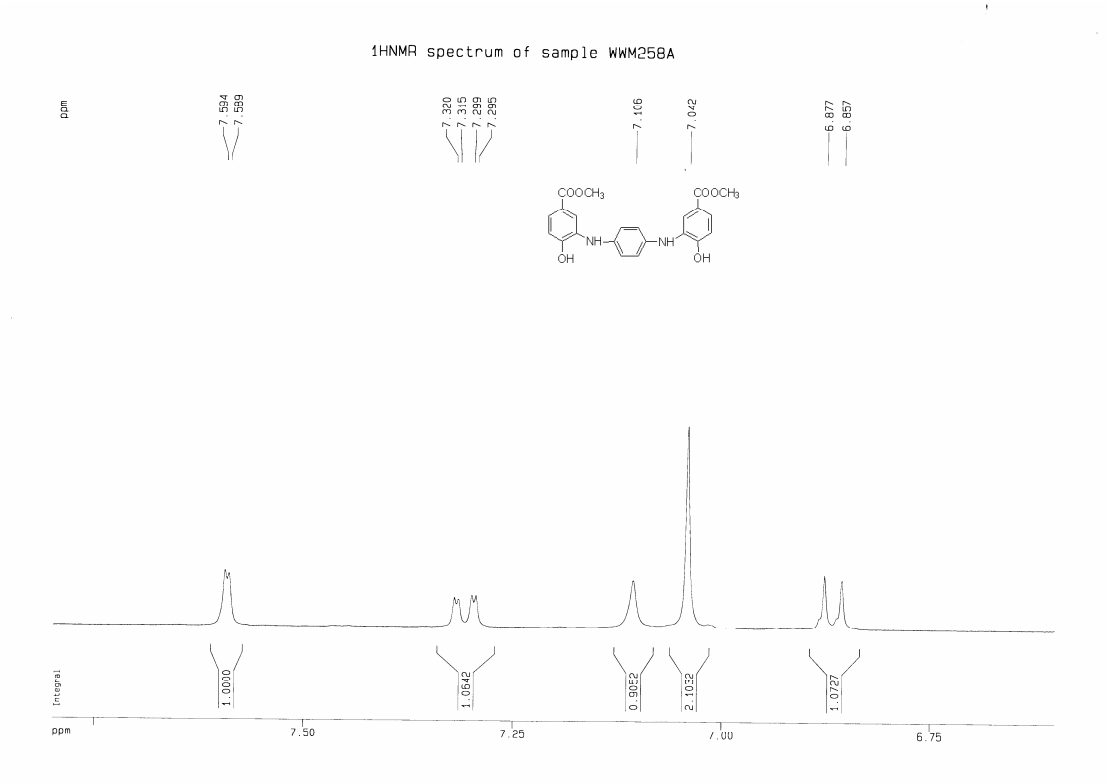




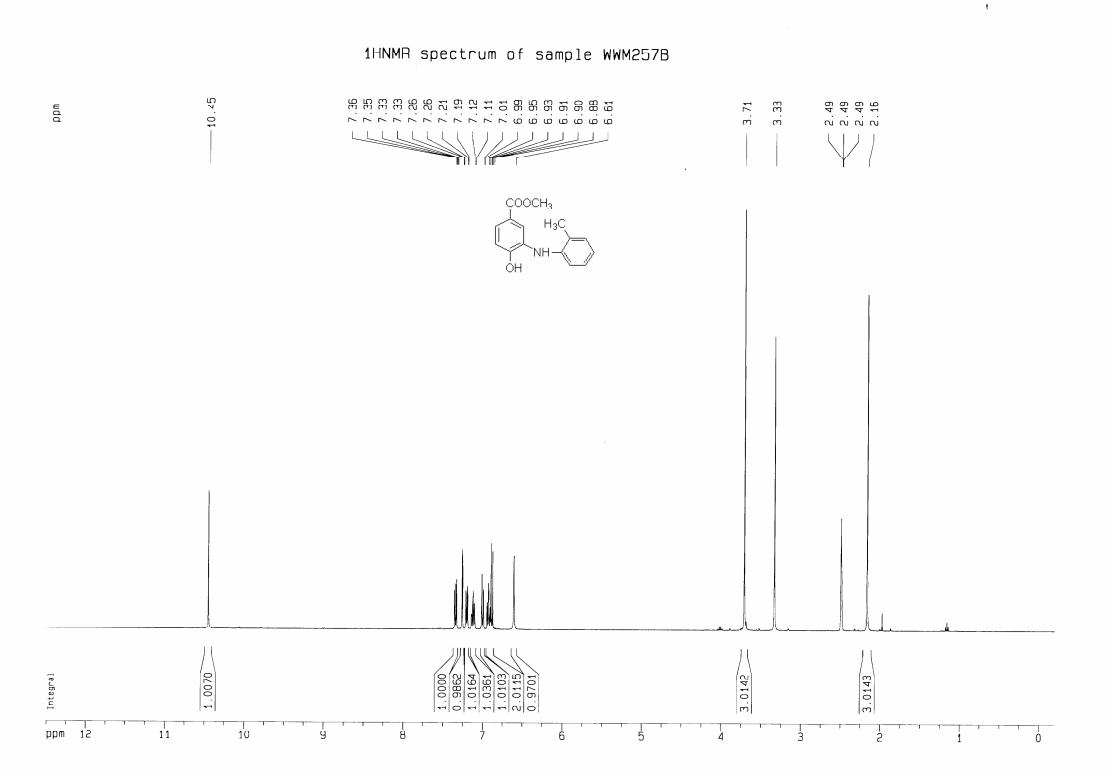


[^{1}H NMR Spectra of 5l]

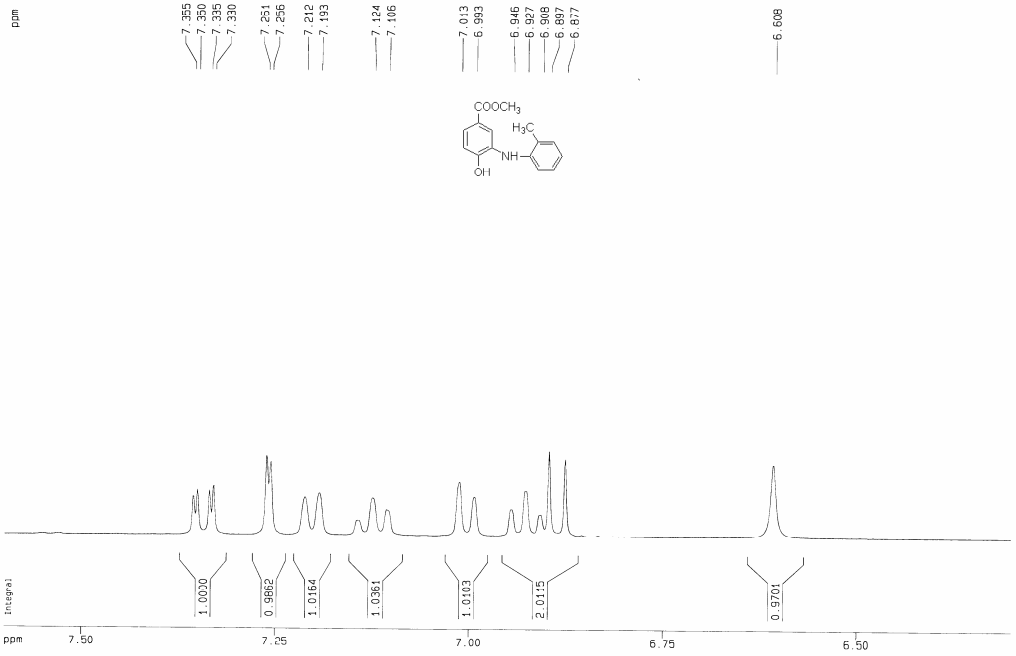




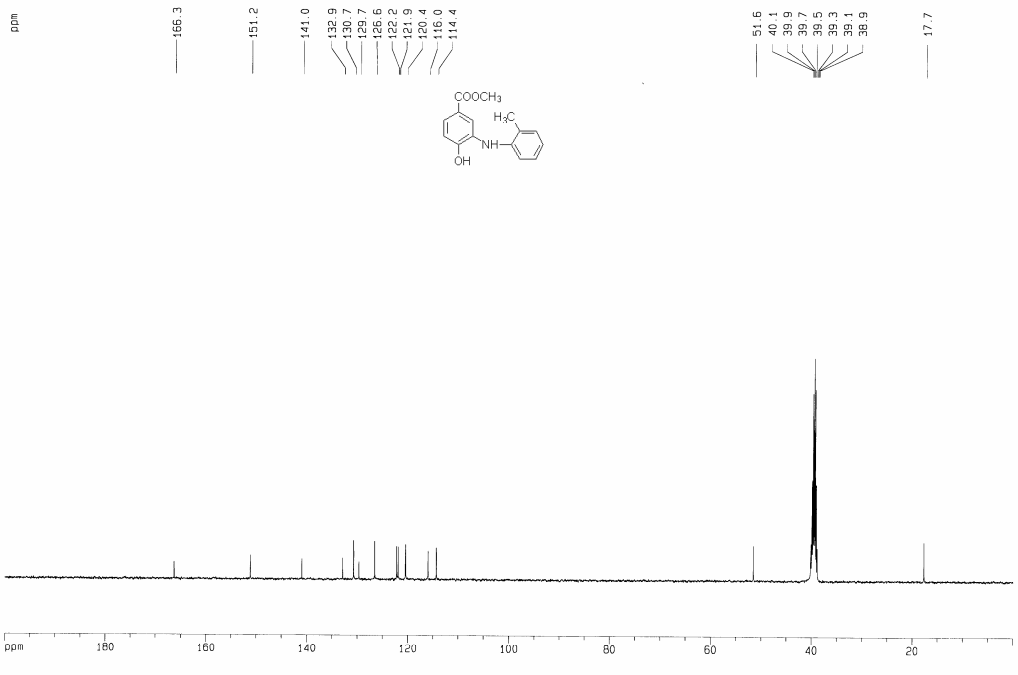
[^{1}H and ^{13}C NMR Spectra of 5m]



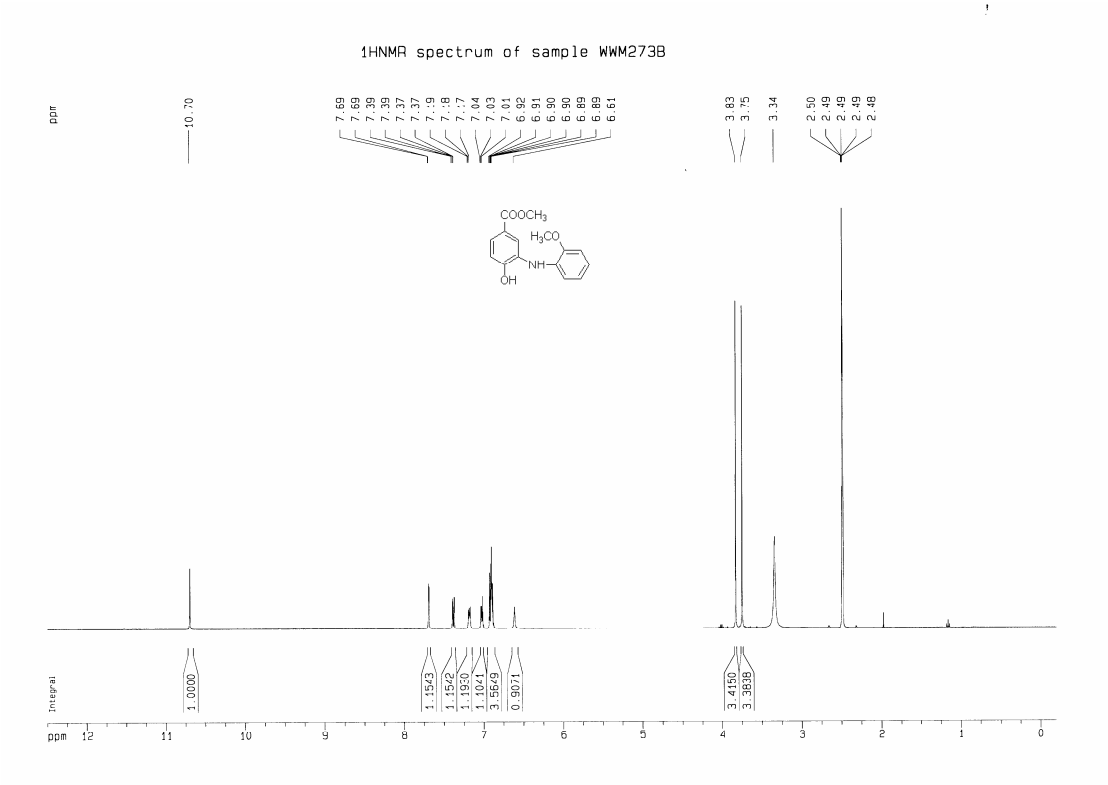
1HNMR spectrum of sample WWM257B

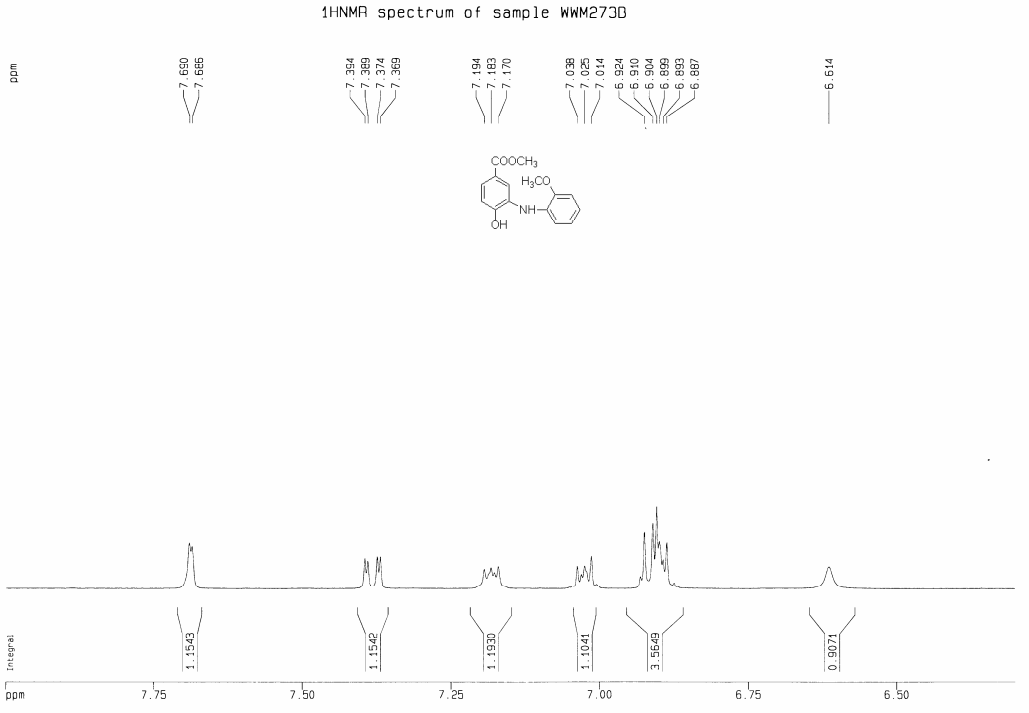


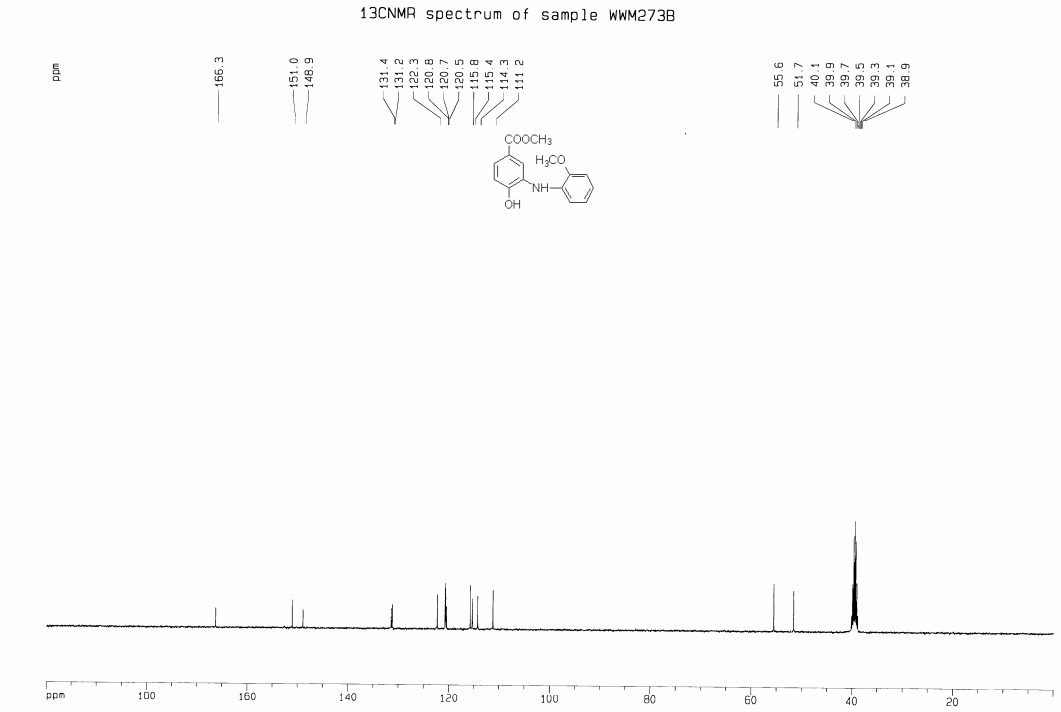
13CNMR spectrum of sample WWM257B



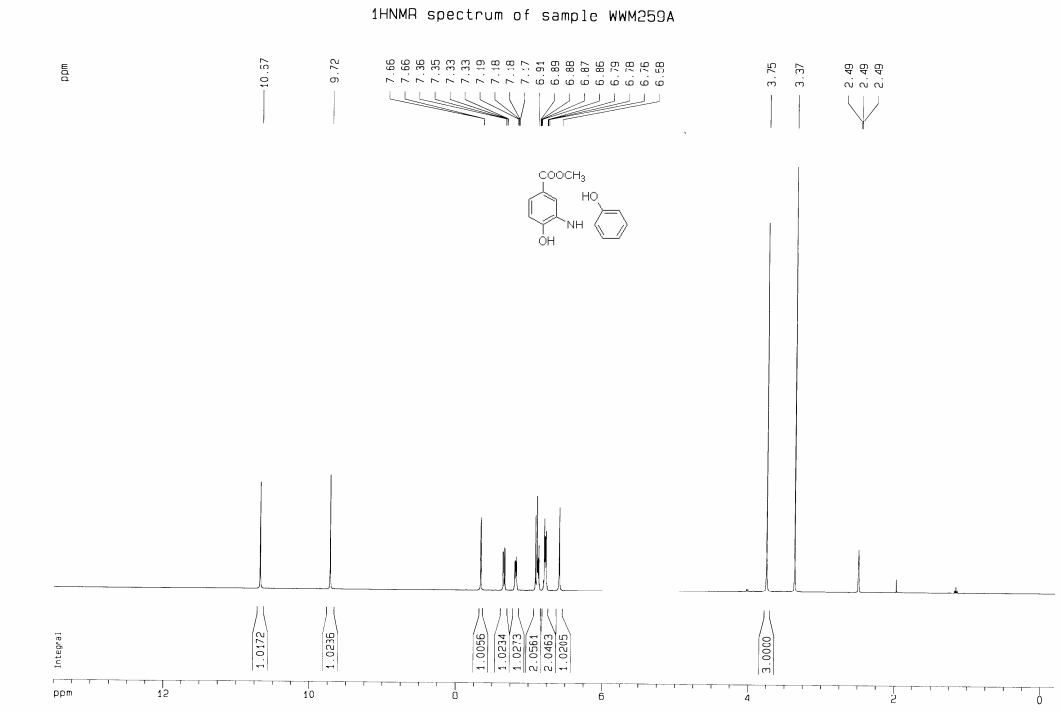
[^{1}H and ^{13}C NMR Spectra of 5n]

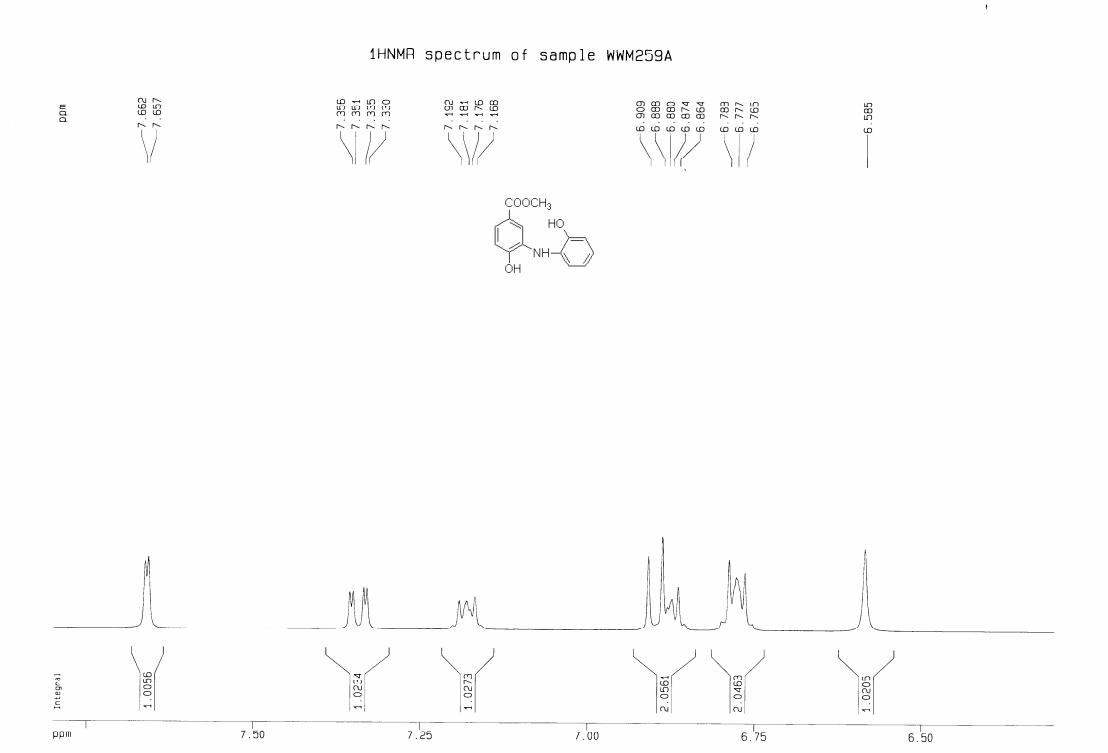


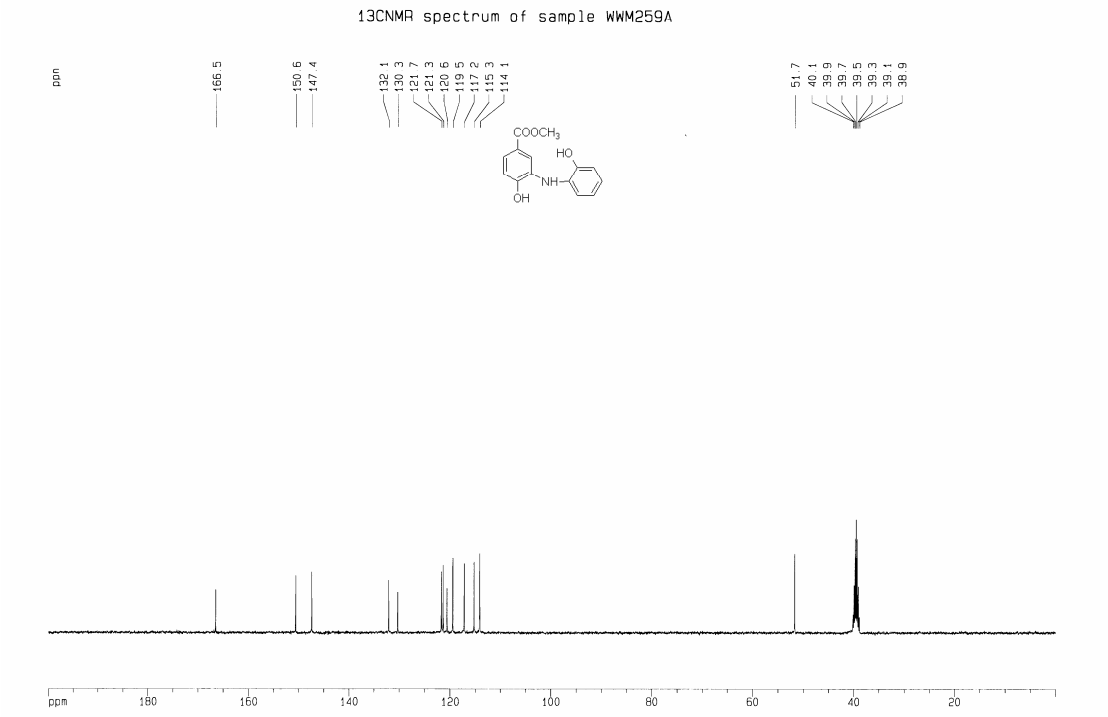




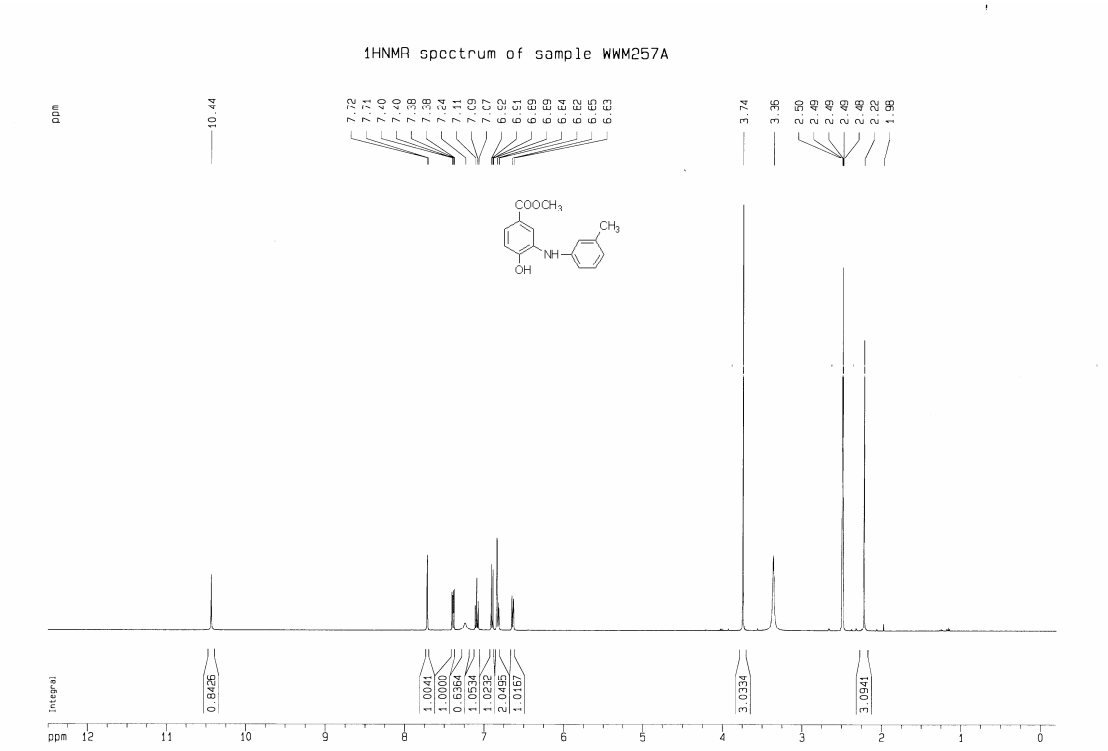
[^{1}H and ^{13}C NMR Spectra of 5o]

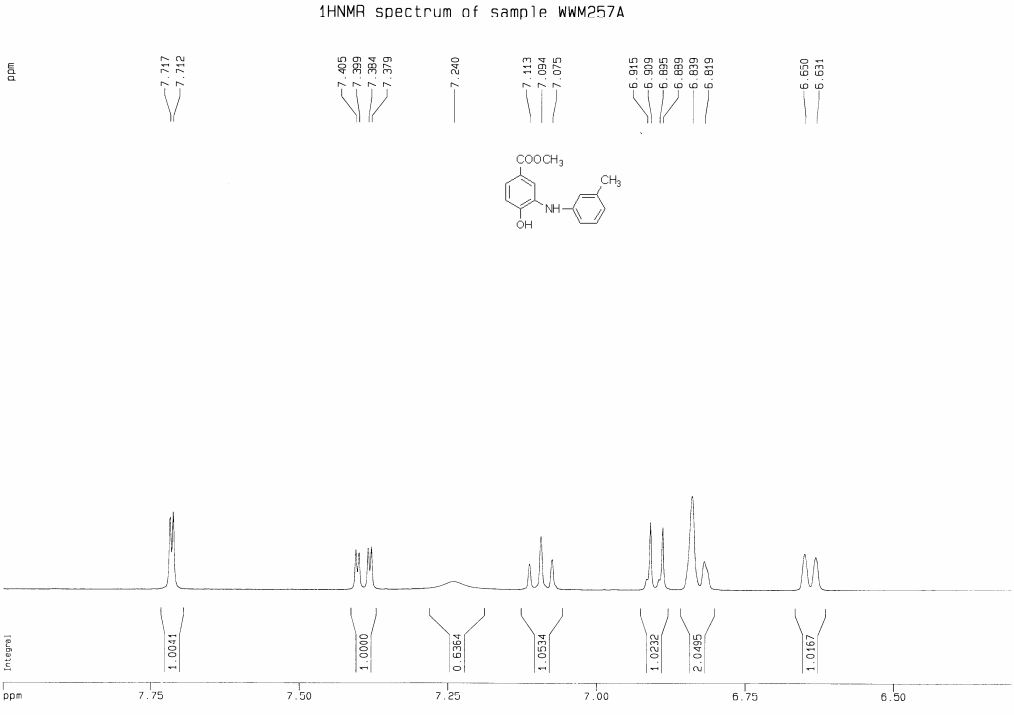


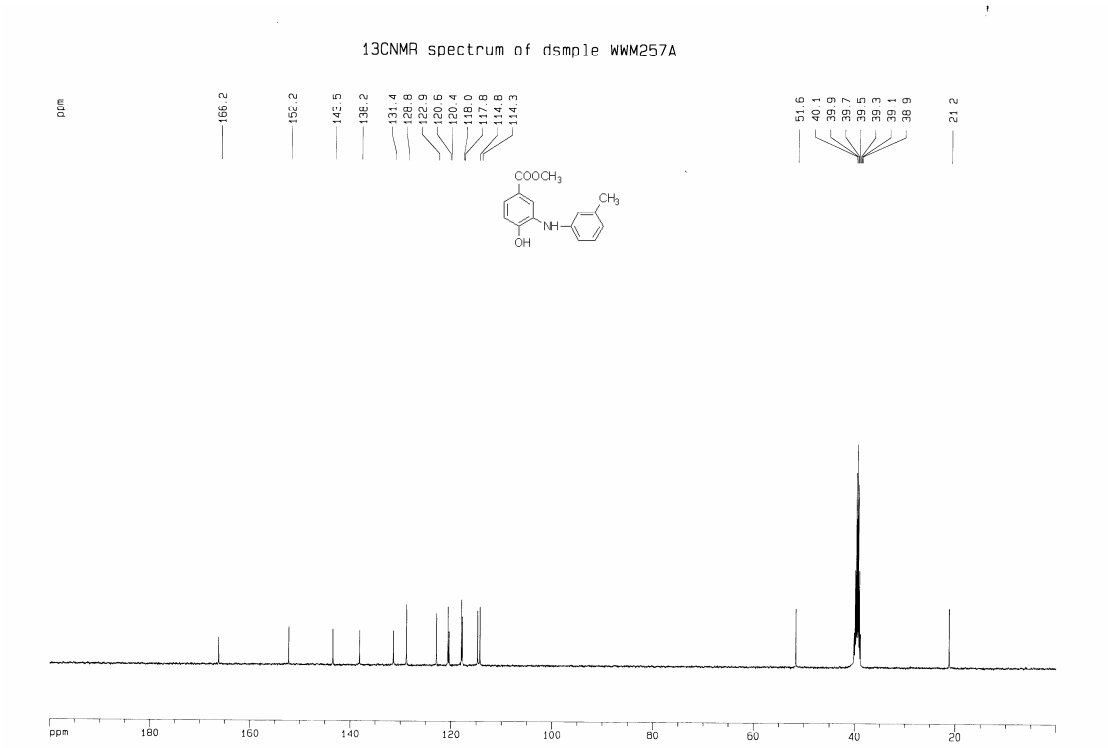

1HNMR spectrum of sample WWM259A
ppm
7.662
7.657
7.356
7.351
7.335
7.330
7.192
7.181
7.176
7.168
6.909
6.888
6.880
6.874
6.864
6.783
6.777
6.765
6.585
COOCH3
HO
NH
OH
Integral
1.0056
1.0234
1.0273
2.0561
2.0463
1.0205
ppm
7.50
7.25
7.00
6.75
6.50


13CNMR spectrum of sample WWM259A
ppm
166.5
150.6
147.4
132.1
130.3
121.7
121.3
120.6
119.5
117.2
115.3
114.1
51.7
40.1
39.9
39.7
39.5
39.3
39.1
38.9
COOCH3
HO
NH
OH
ppm
180
160
140
120
100
80
60
40
20

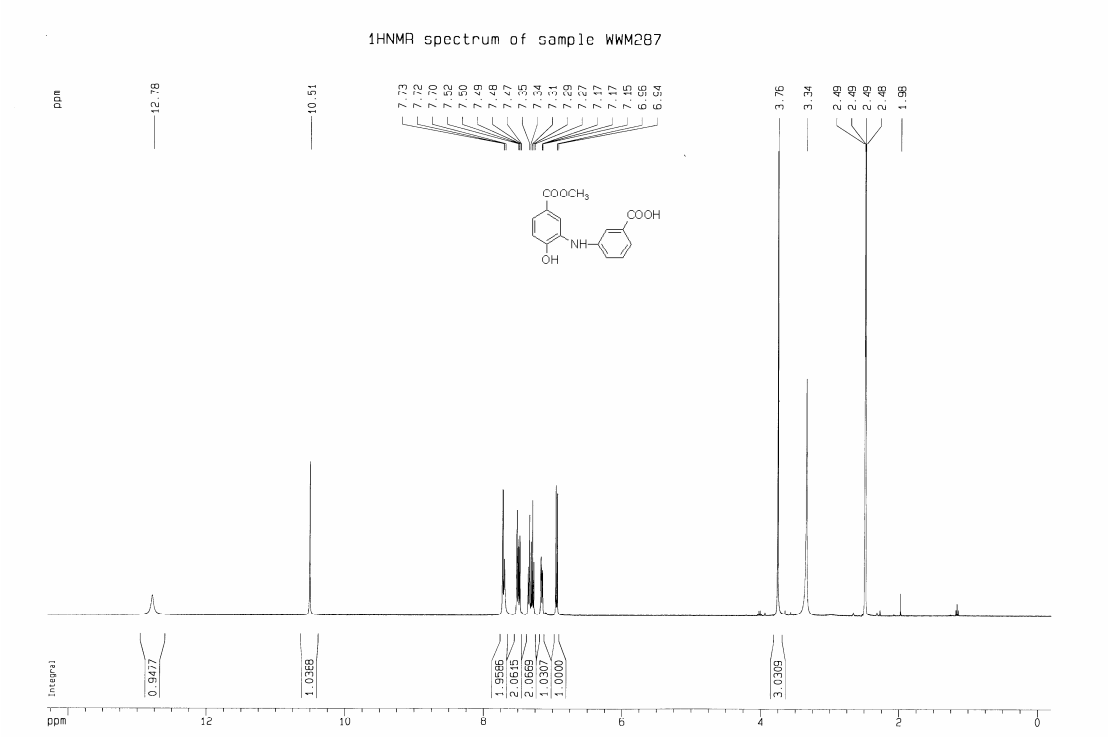
[^{1}H and ^{13}C NMR Spectra of 5p]

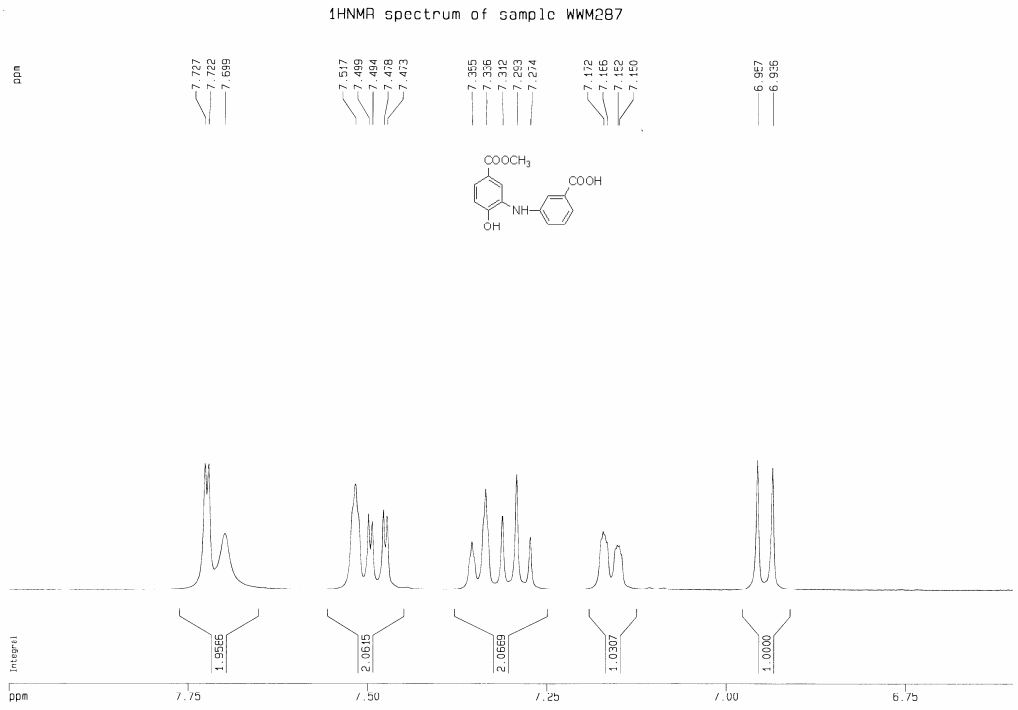


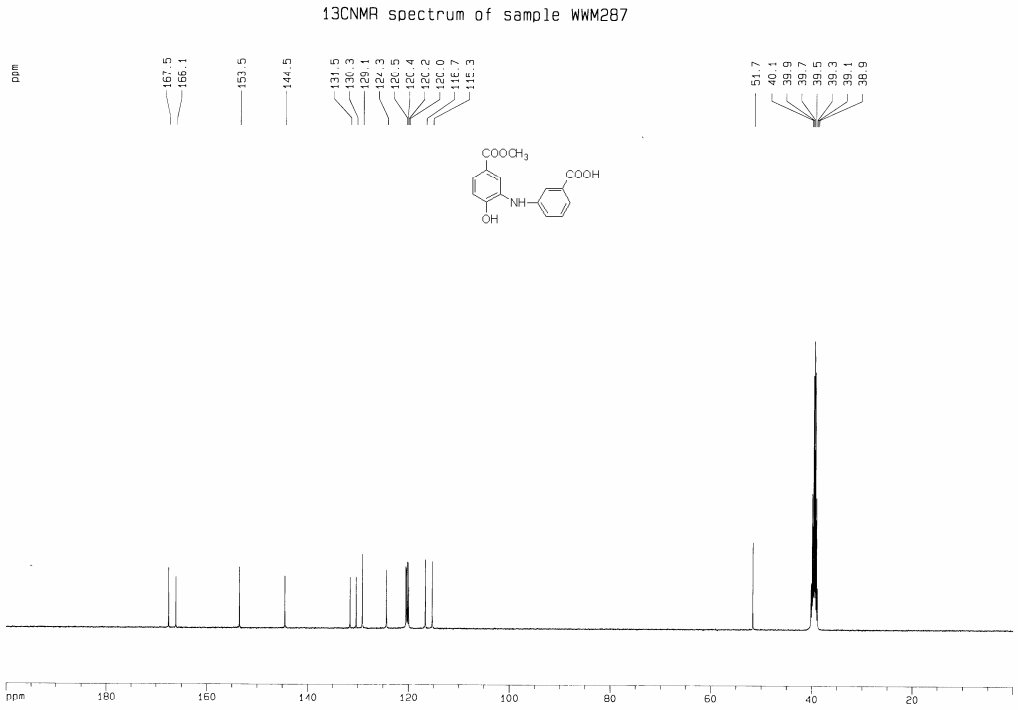




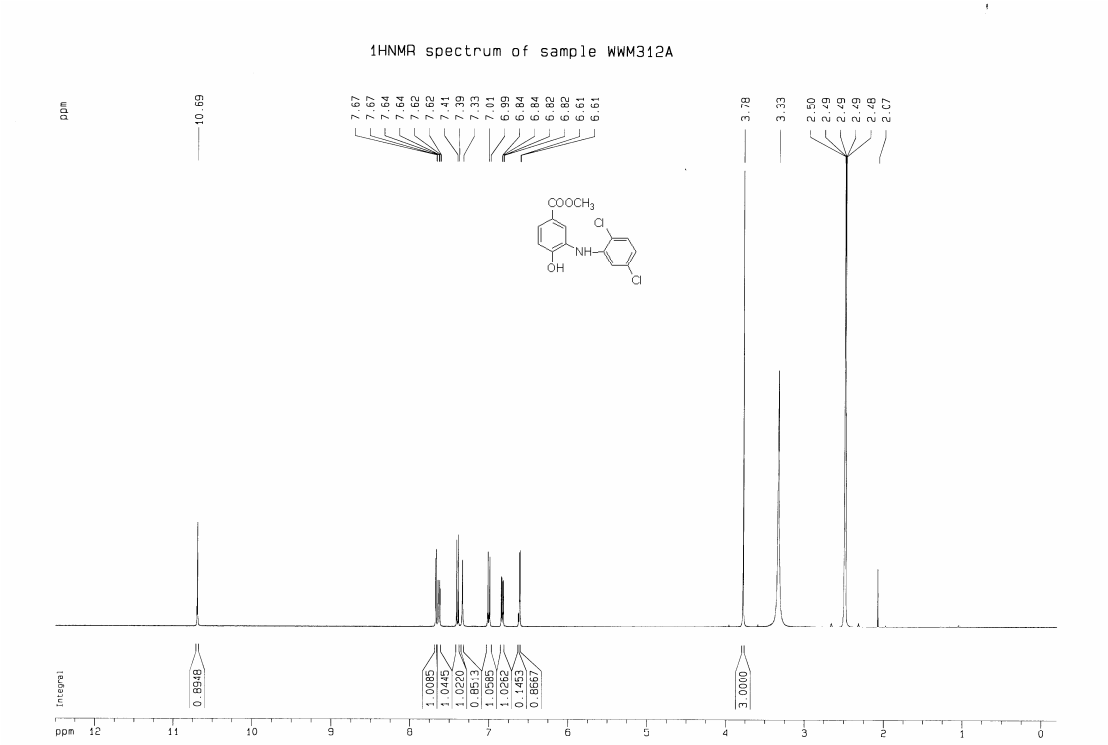
[^{1}H and ^{13}C NMR Spectra of 5q]

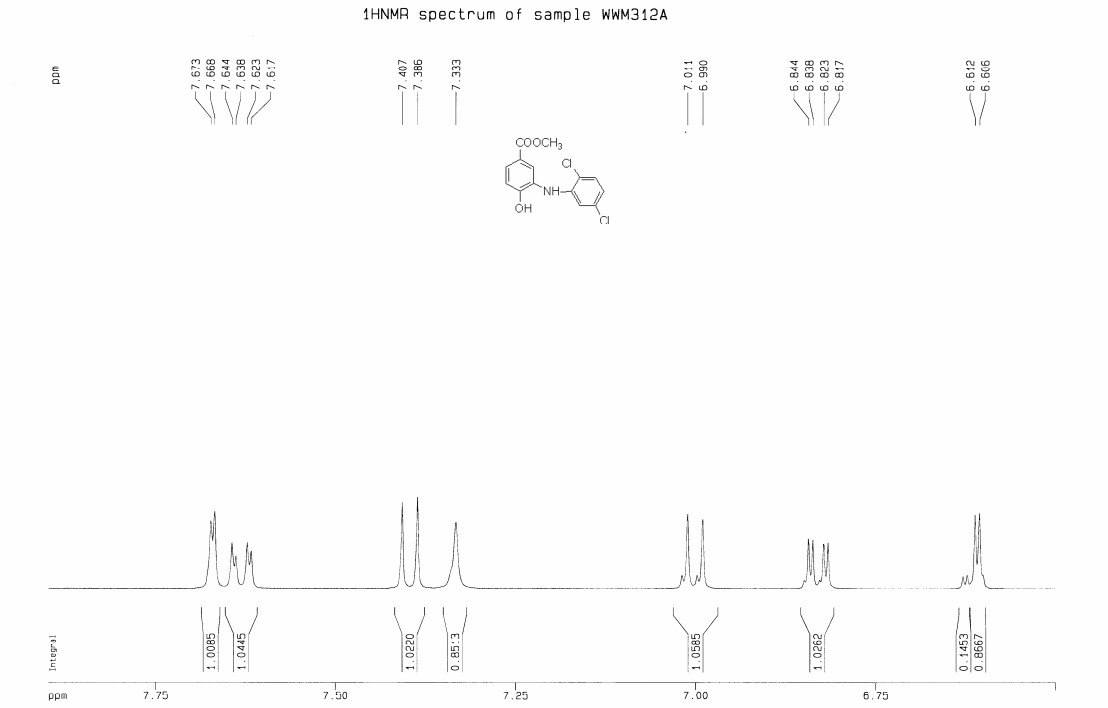


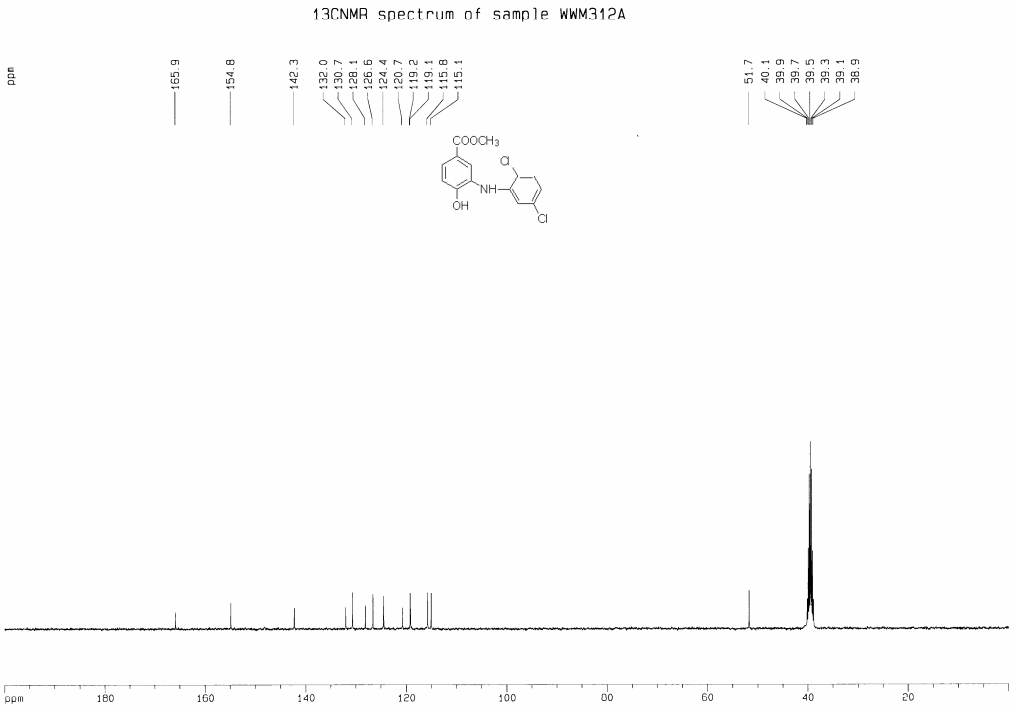

1HNMR spectrum of sample WWM287
ppm
7.727
7.722
7.699
7.517
7.499
7.494
7.478
7.473
7.365
7.336
7.312
7.293
7.274
7.172
7.166
7.152
7.150
6.967
6.936
COOCH3
COOH
NH
OH
Integral
1.9565
2.0615
2.0669
1.0307
1.0000
ppm
7.75
7.50
7.25
7.00
6.75


13CNMR spectrum of sample WWM287
ppm
167.5
166.1
153.5
144.5
131.5
130.3
129.1
124.3
120.5
120.4
120.2
120.0
116.7
115.3
51.7
40.1
39.9
39.7
39.5
39.3
39.1
38.9
COOCH3
COOH
NH
OH
ppm
180
160
140
120
100
80
60
40
20

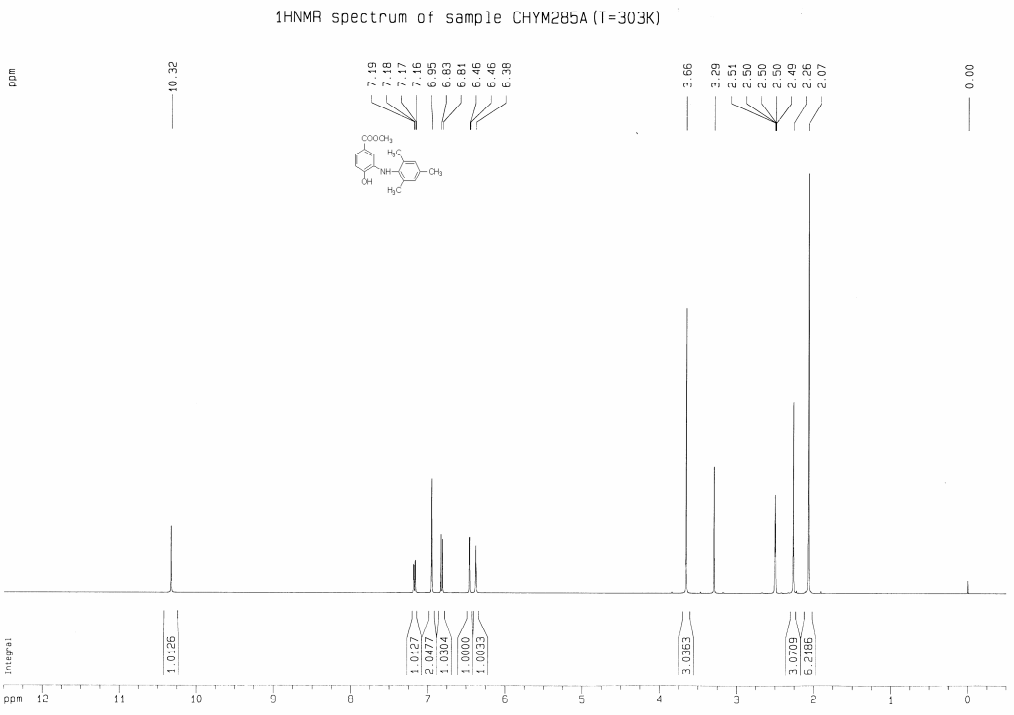
[^{1}H and ^{13}C NMR Spectra of 5r]

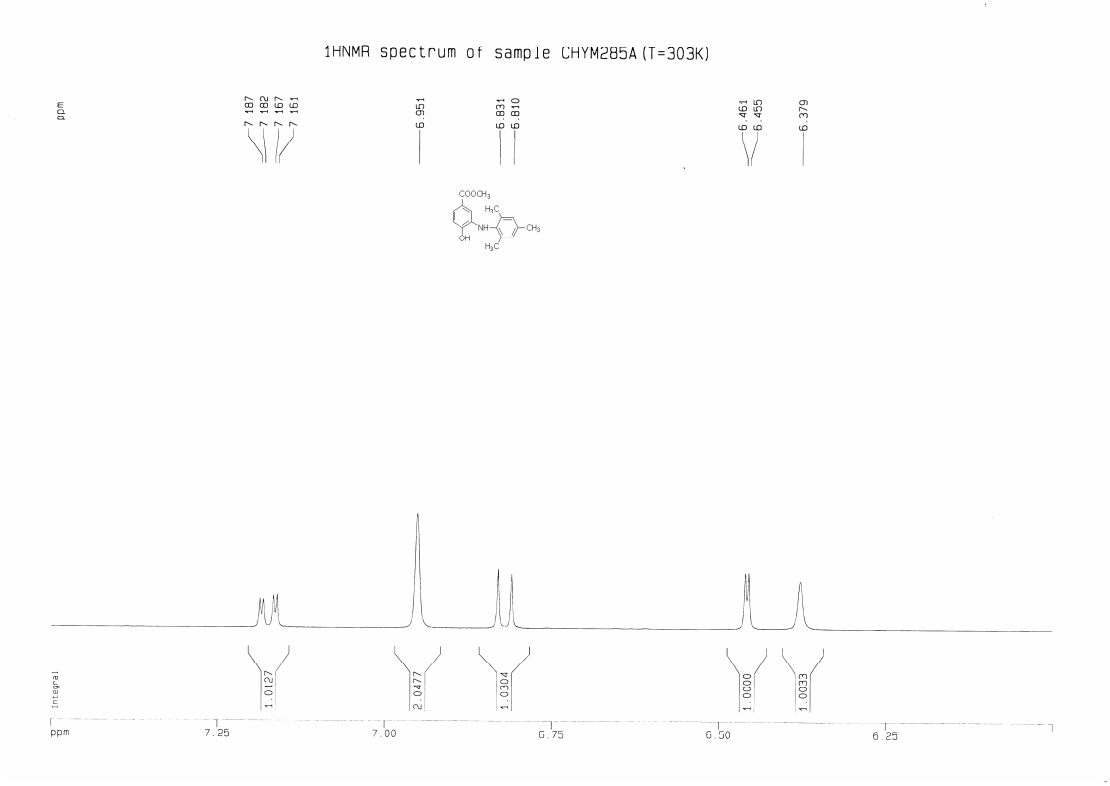




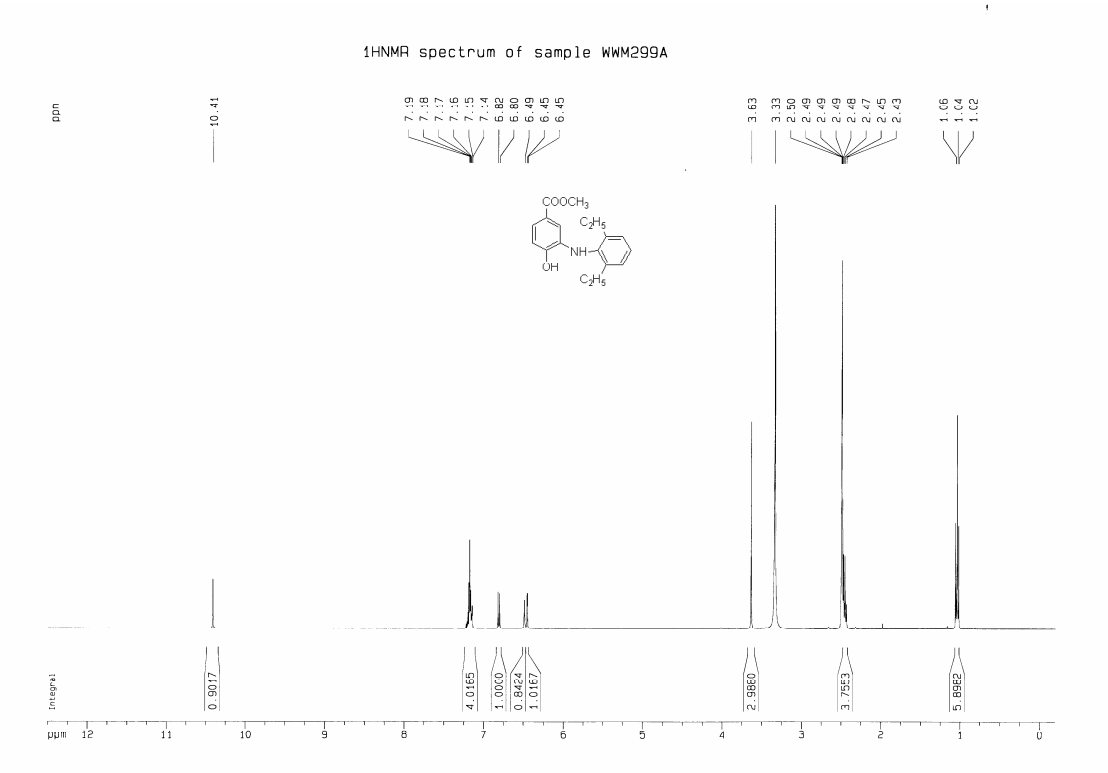


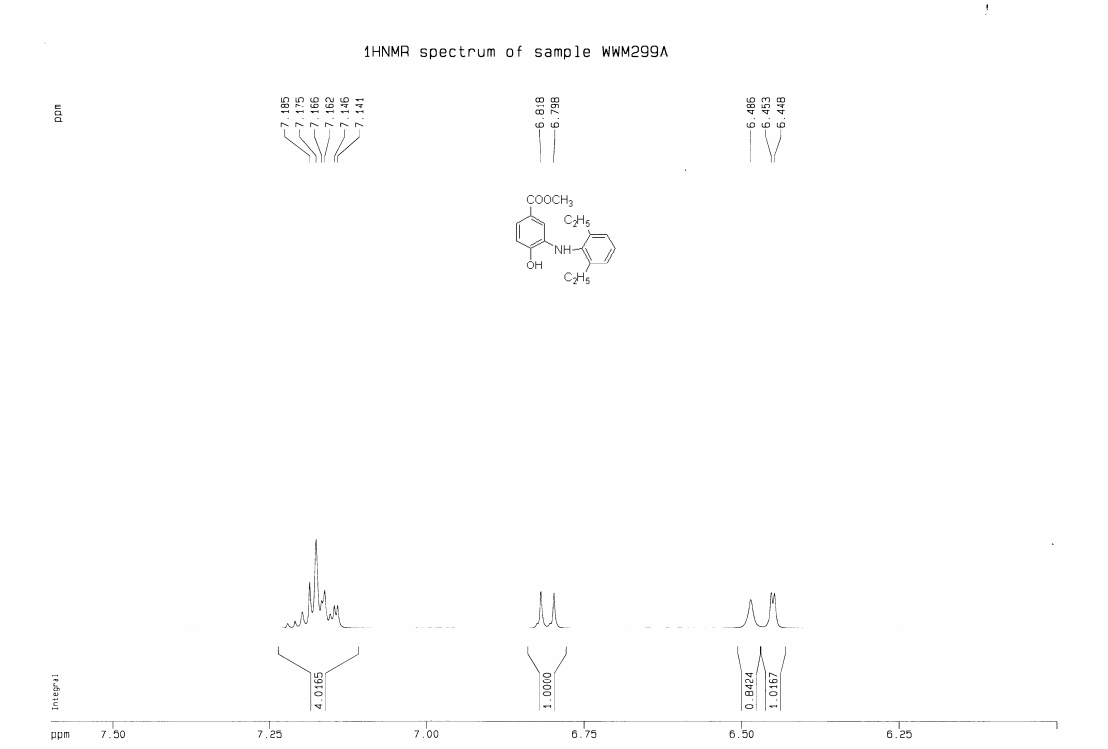
[^{1}H NMR Spectra of 5s]

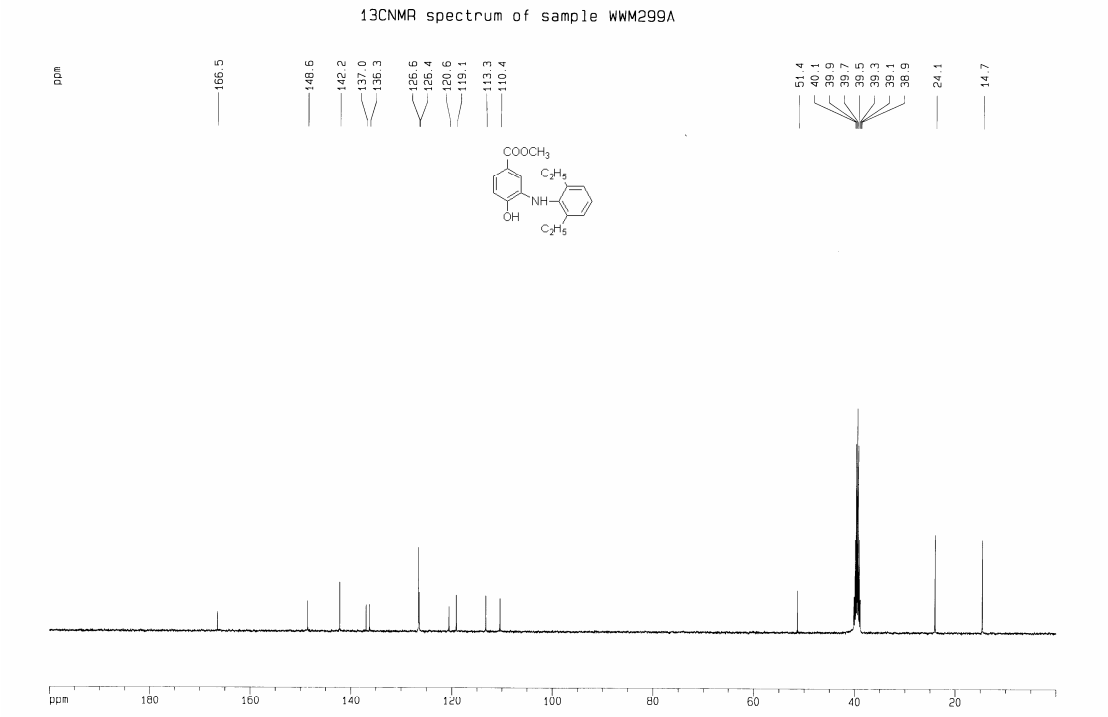




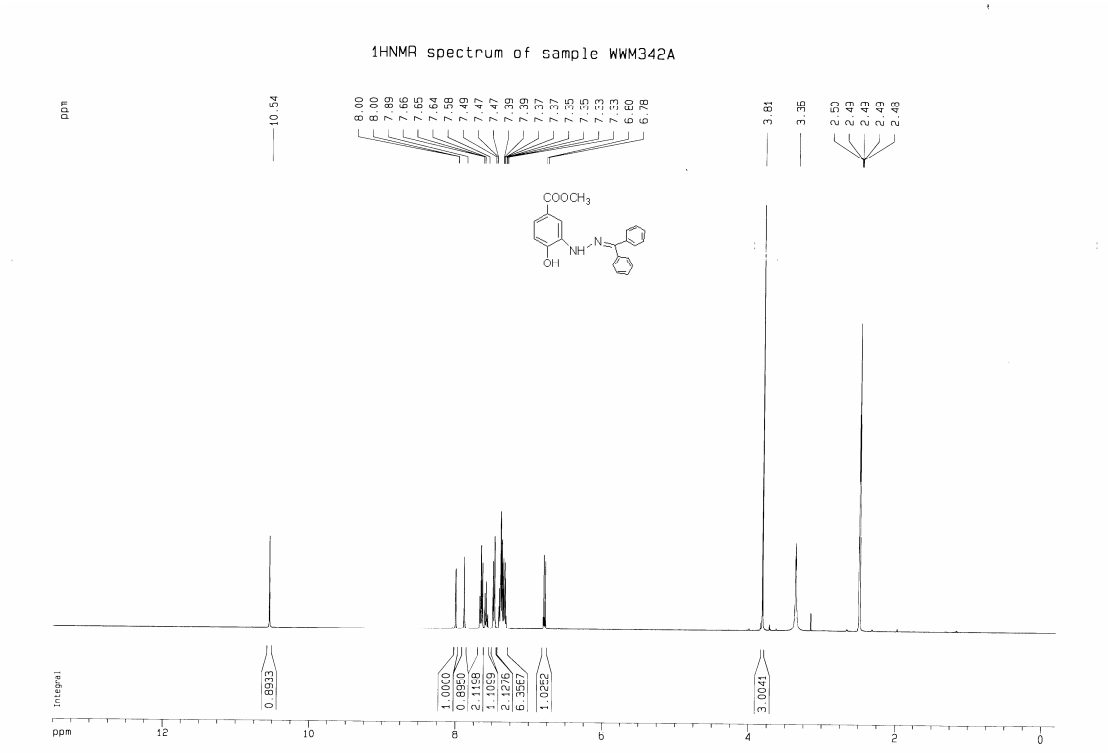
[^{1}H and ^{13}C NMR Spectra of 5t]

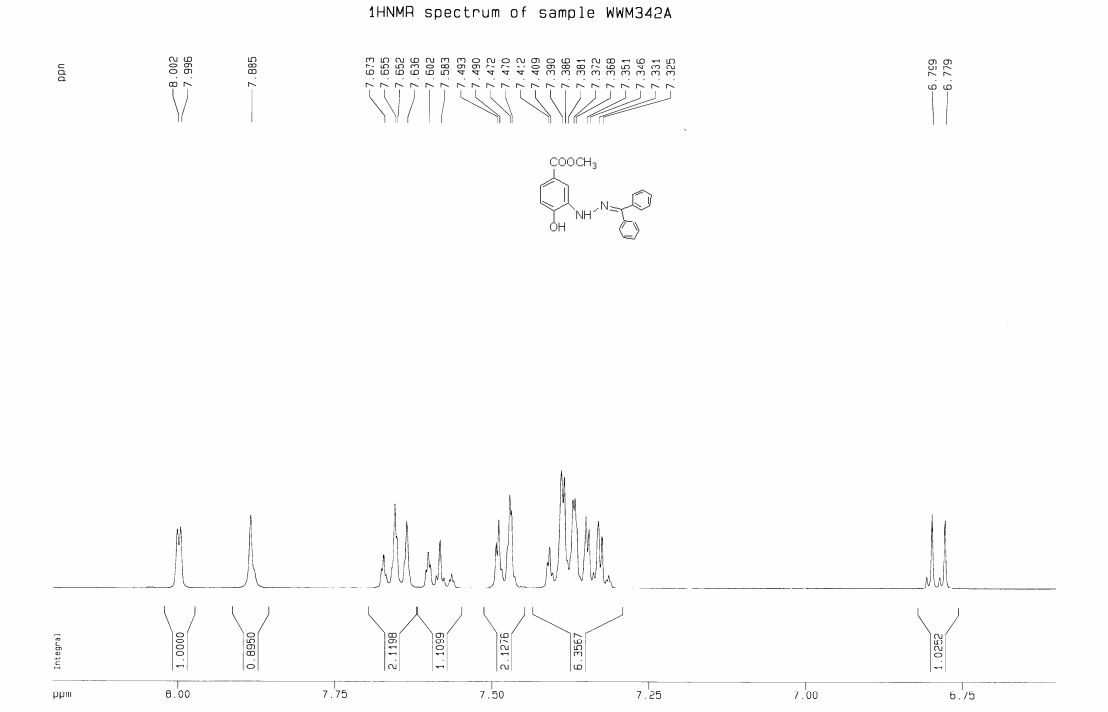


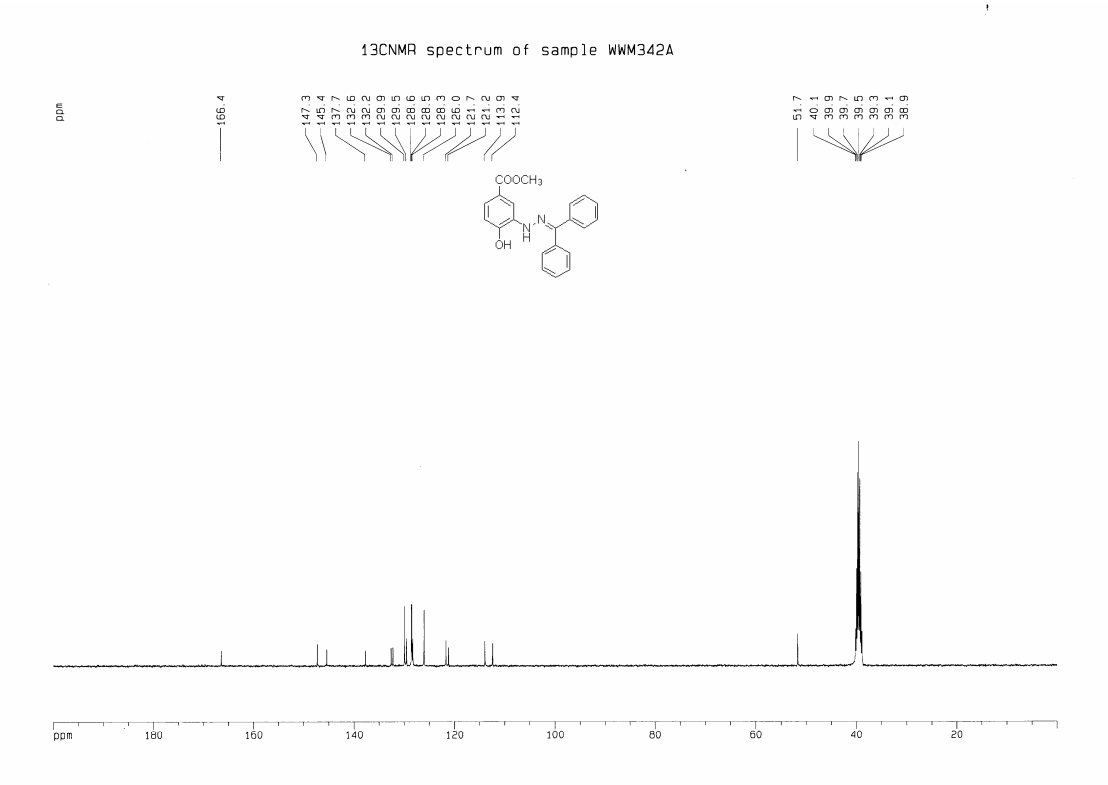

1HNMR spectrum of sample WWM299A
ppm
7.185
7.175
7.166
7.162
7.146
7.141
6.818
6.798
6.486
6.453
6.448
COOCH3
C2H5
NH
OH
C2H5
Integral
4.0165
1.0000
0.8424
1.0167
ppm
7.50
7.25
7.00
6.75
6.50
6.25


13CNMR spectrum of sample WWM299A
ppm
166.5
148.6
142.2
137.0
136.3
125.6
125.4
120.6
119.1
113.3
110.4
51.4
40.1
39.9
39.7
39.5
39.3
39.1
38.9
24.1
14.7
COOCH3
C2H5
NH
OH
C2H5
ppm
180
160
140
120
100
80
60
40
20

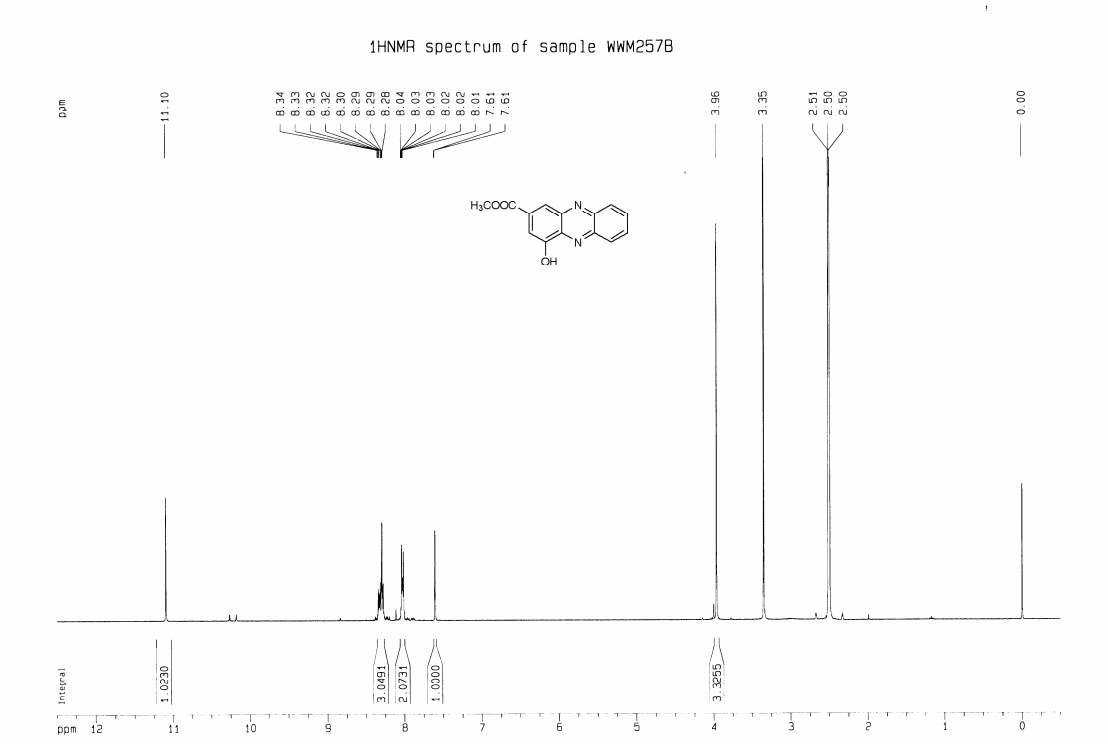
[^{1}H and ^{13}C NMR Spectra of 5u]

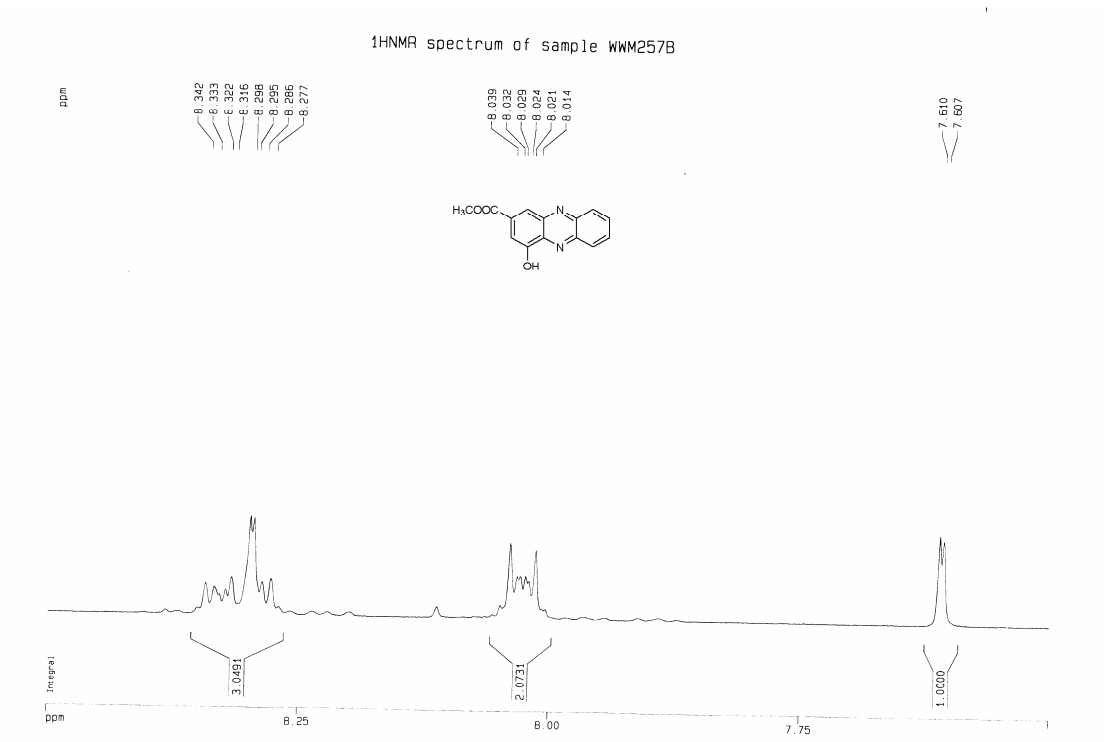




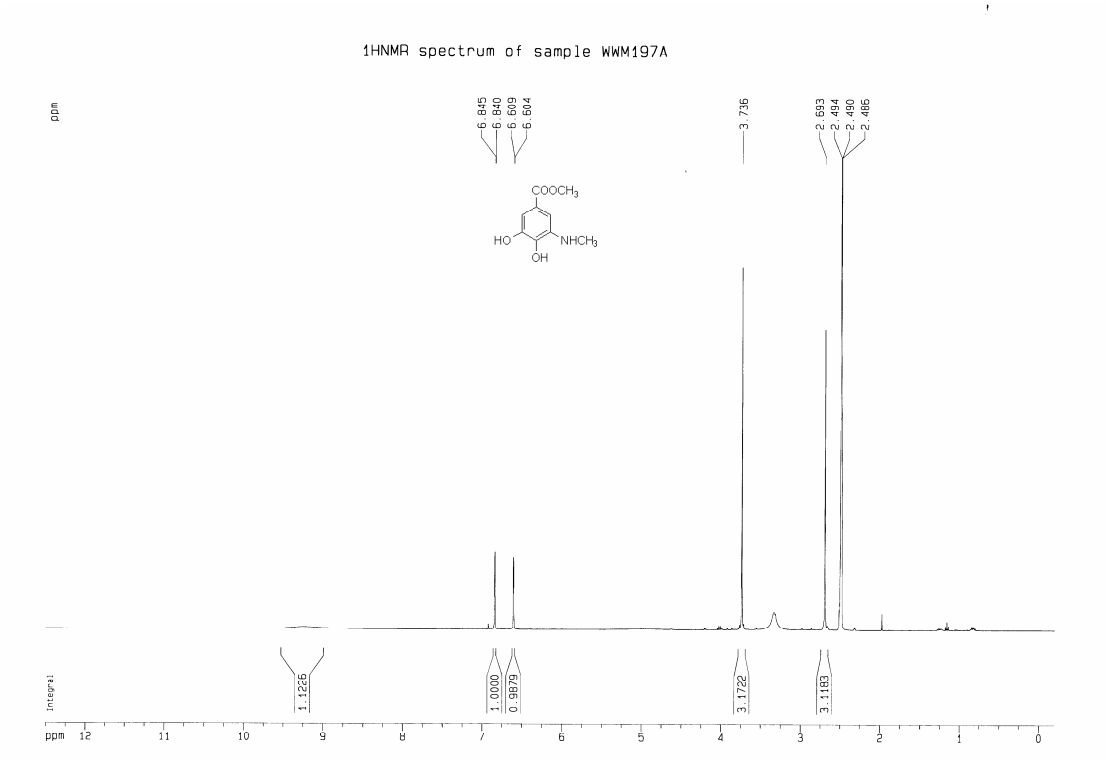


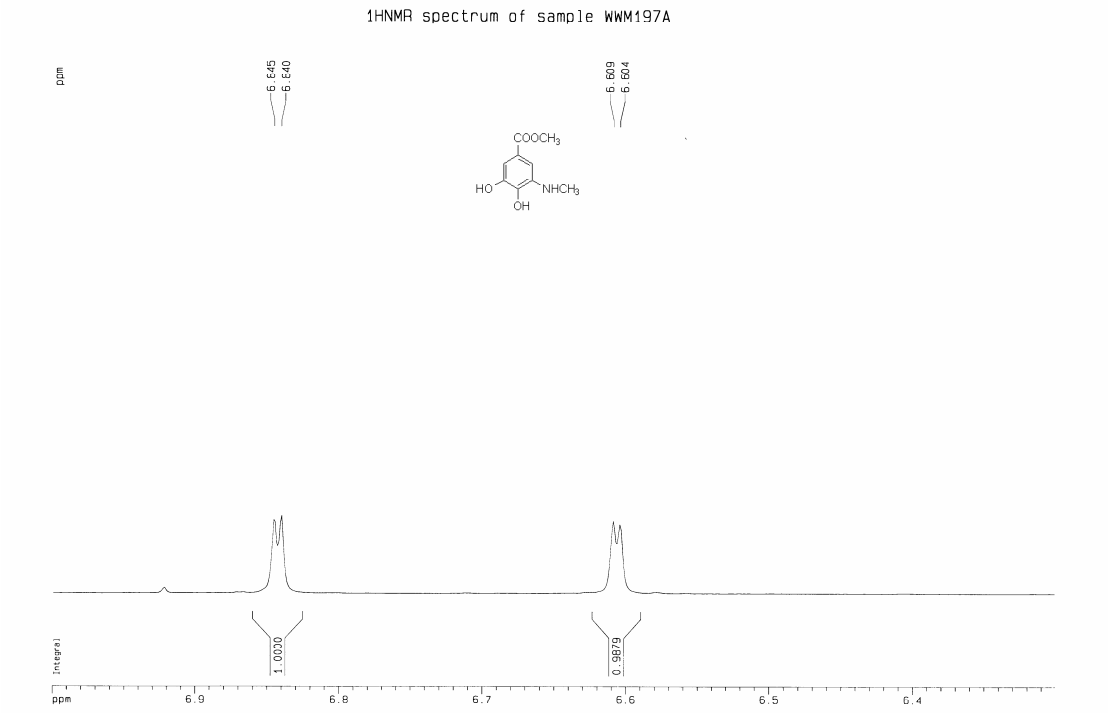
[^{1}H NMR Spectra of 5v]



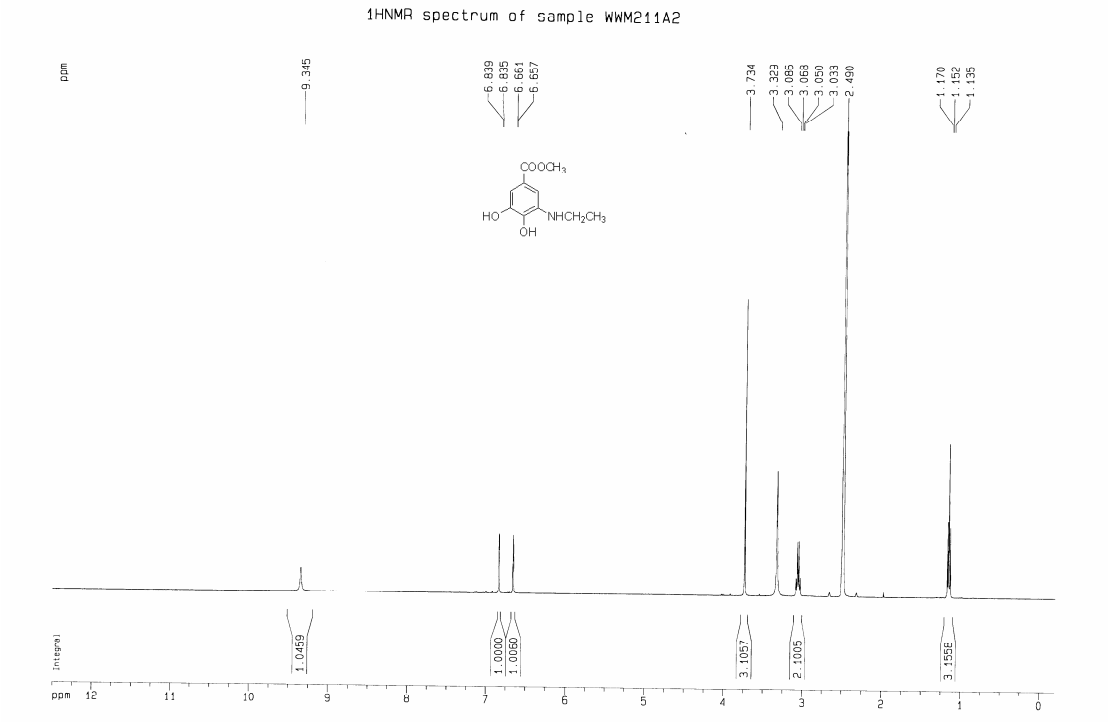


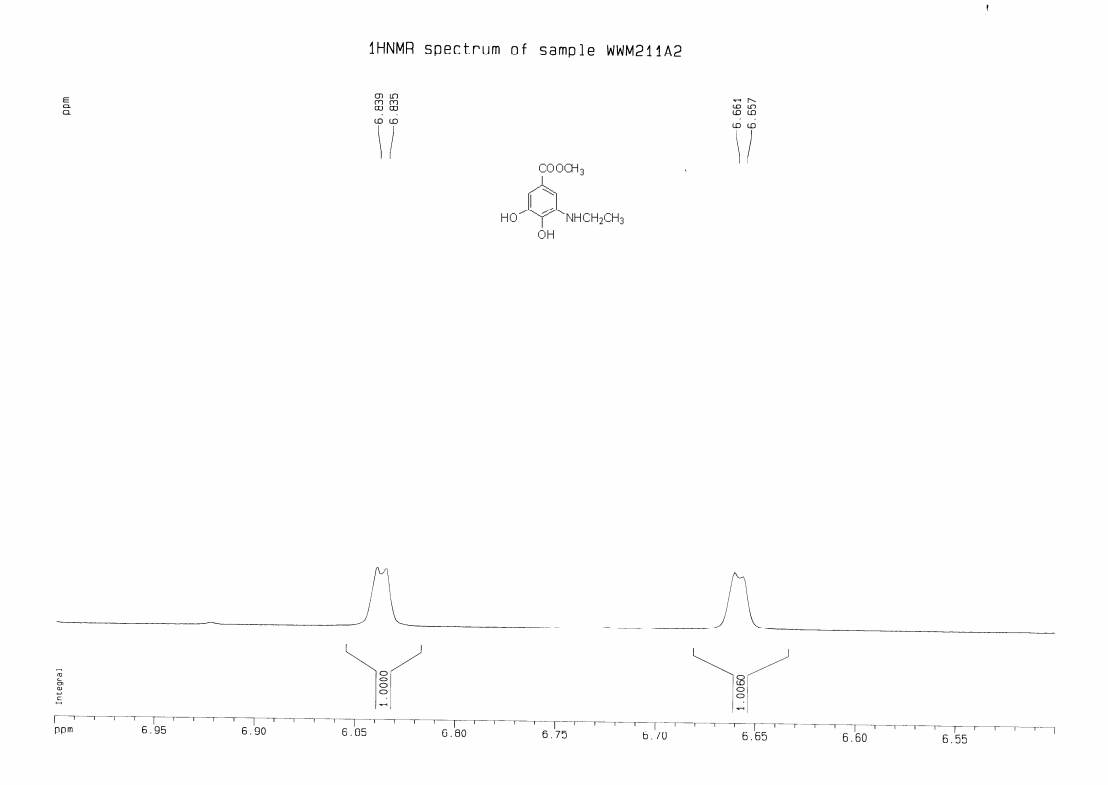
[^{1}H NMR Spectra of 7a]

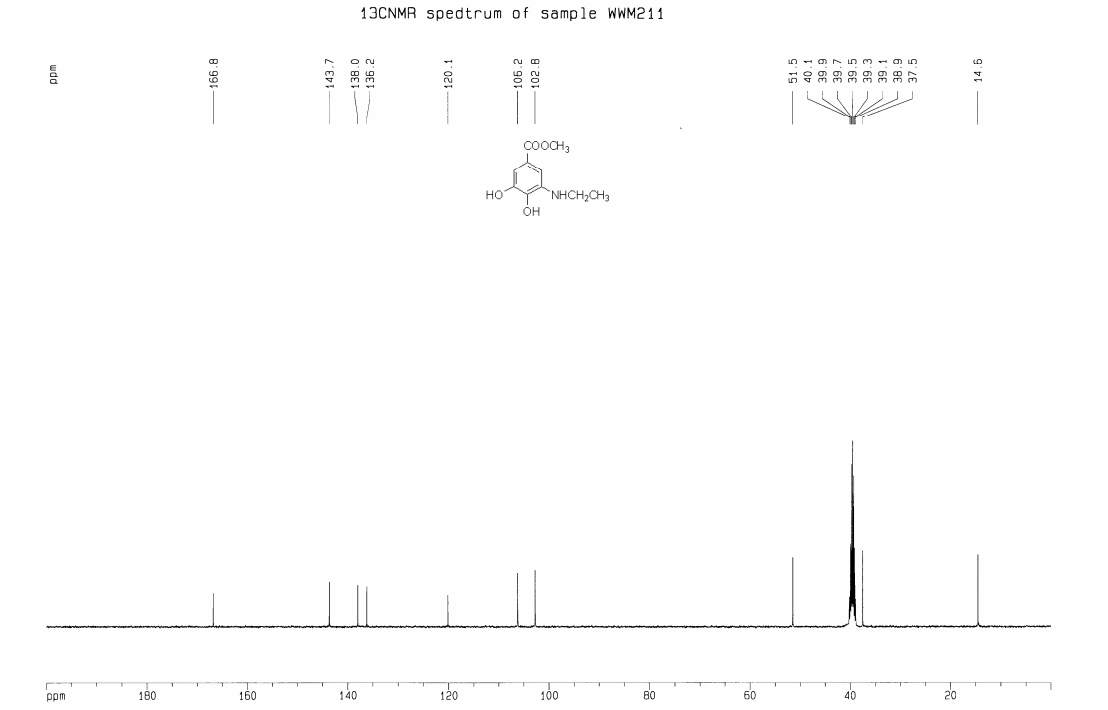




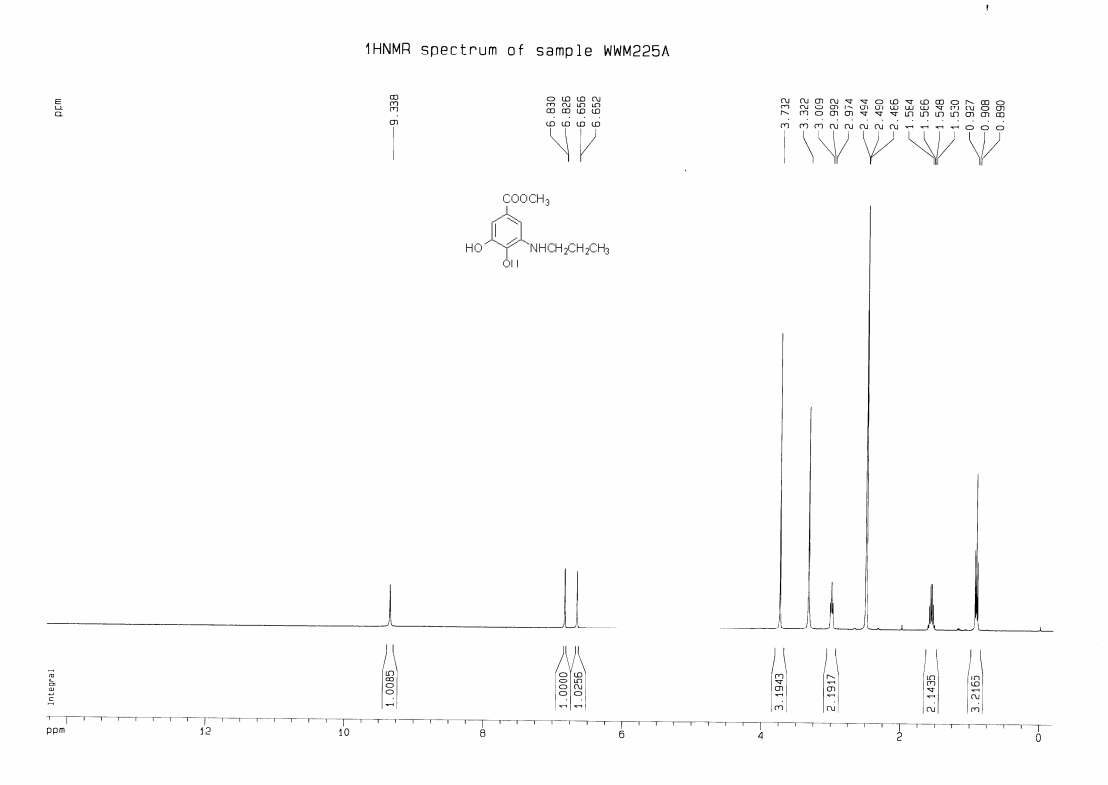
[^{1}H and ^{13}C NMR Spectra of 7b]

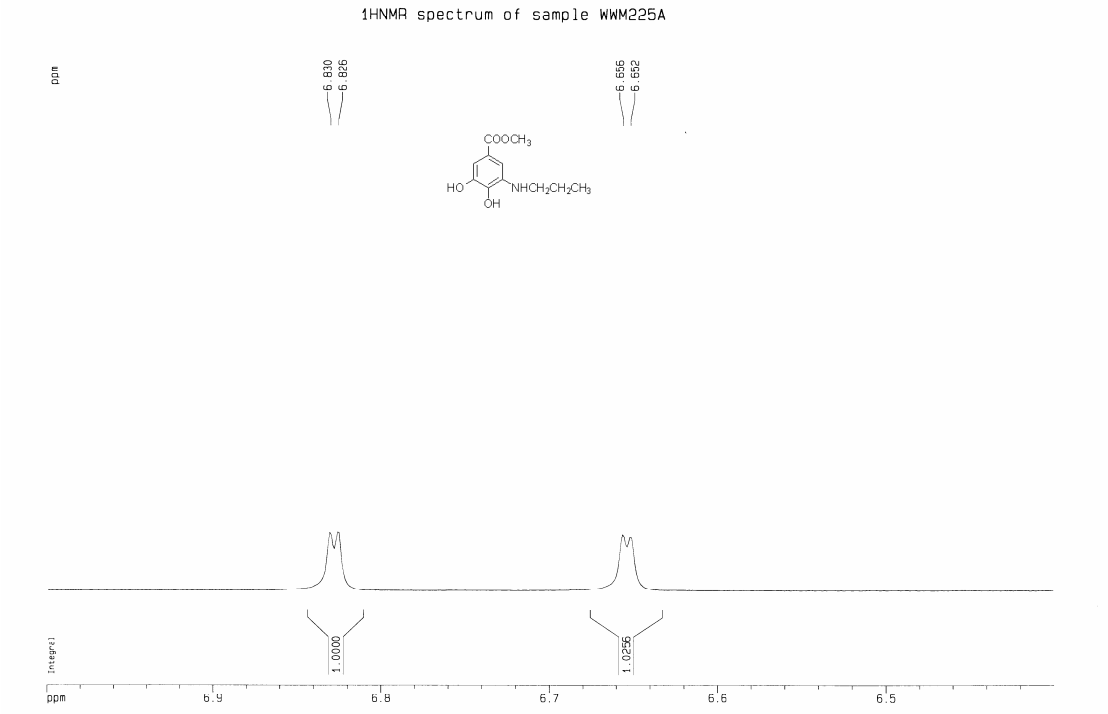



1HNMR spectrum of sample WWM211A2
ppm
6.839
6.835
6.661
6.657
COOCH3
HO
NHCH2CH3
OH
integral
1.0000
1.0060
6.95
6.90
6.85
6.80
6.75
6.70
6.65
6.60
6.55

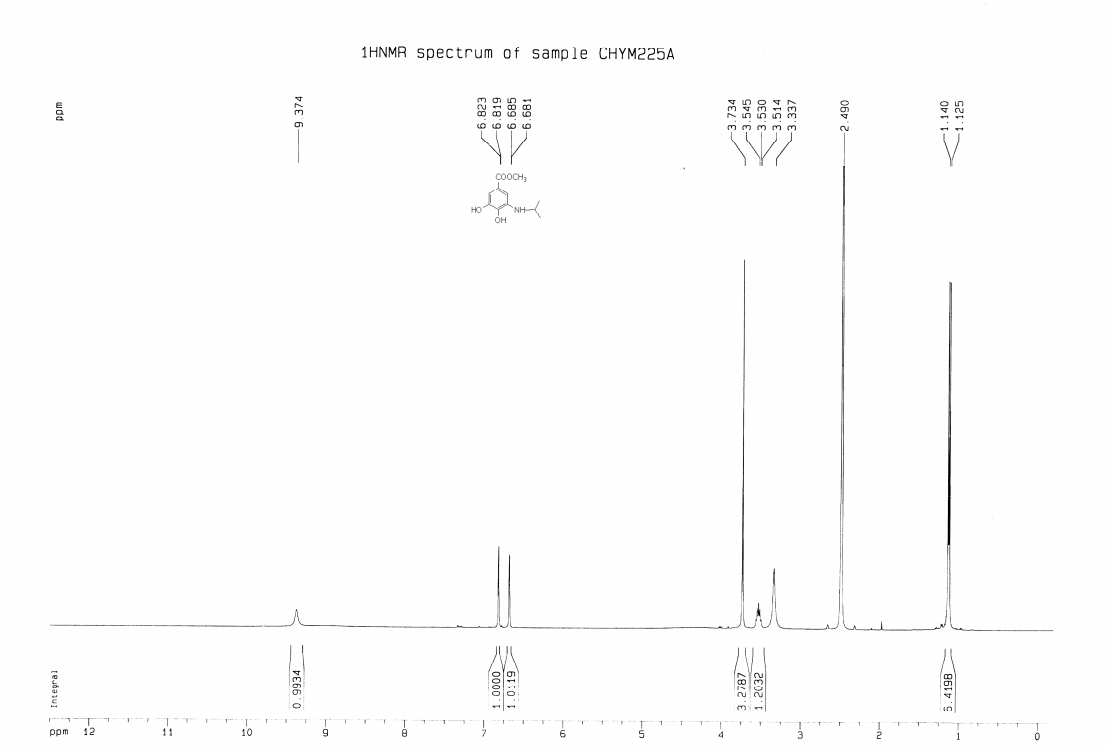

13CNMR spedtrum of sample WWM211
ppm
166.8
143.7
138.0
136.2
120.1
106.2
102.8
51.5
40.1
39.9
39.7
39.5
39.3
39.1
38.9
37.5
14.6
COOCH3
HO
NHCH2CH3
OH
180
160
140
120
100
80
60
40
20

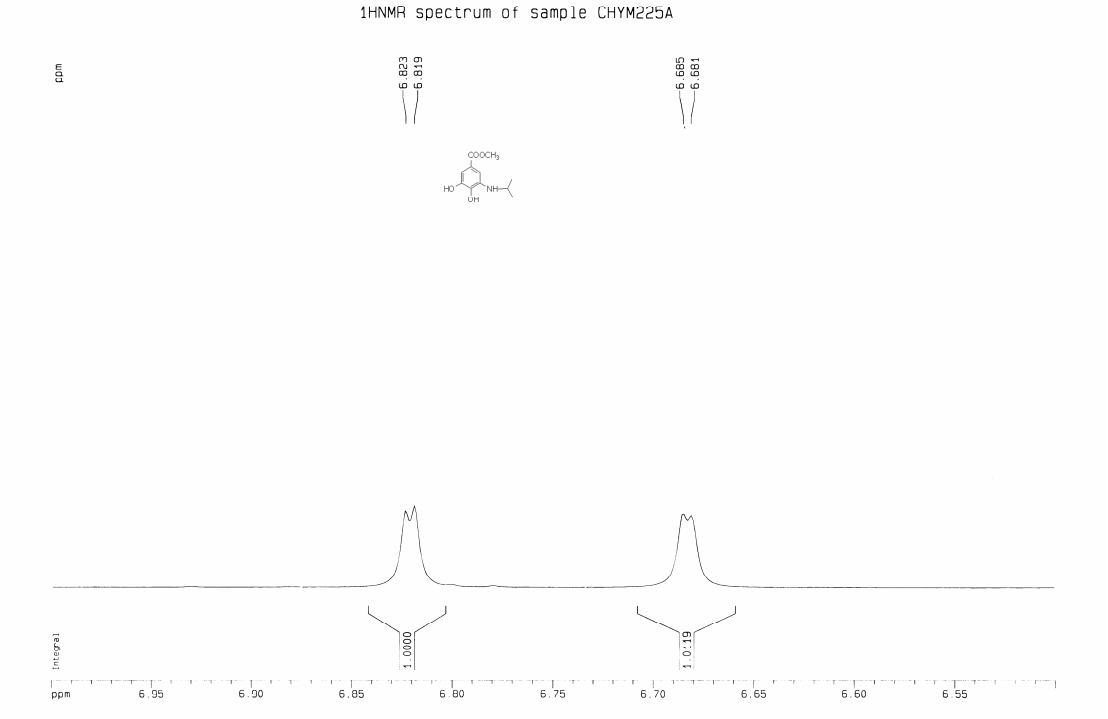
[^{1}H NMR Spectra of 7c]



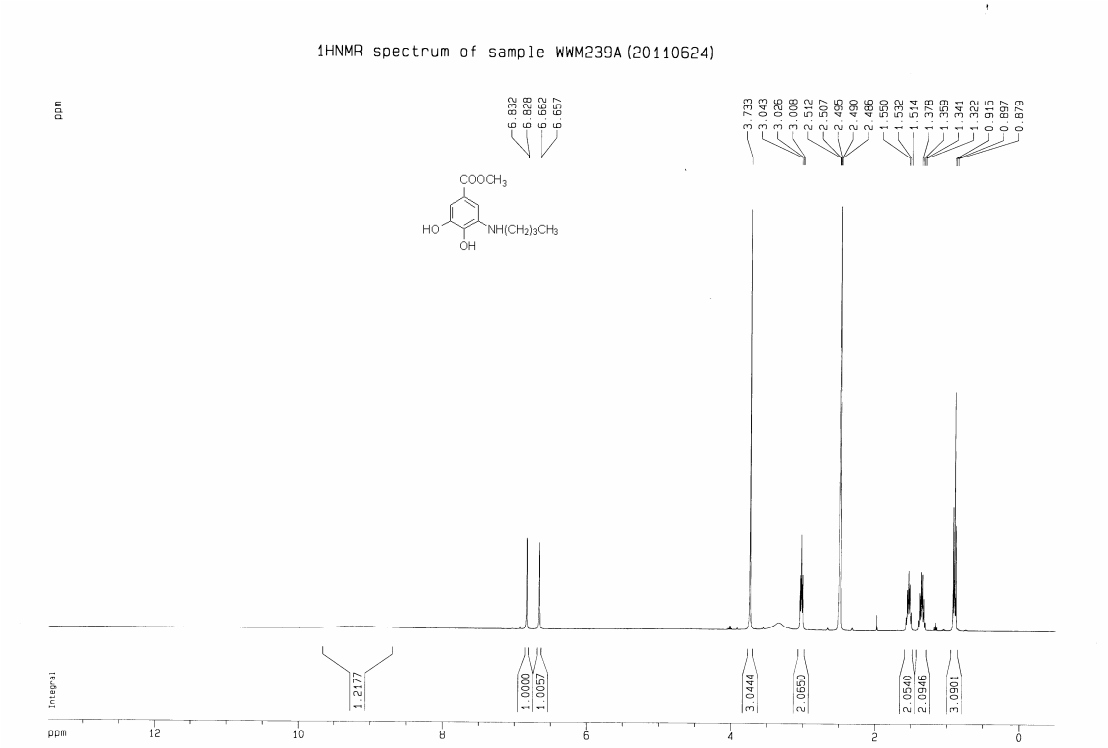


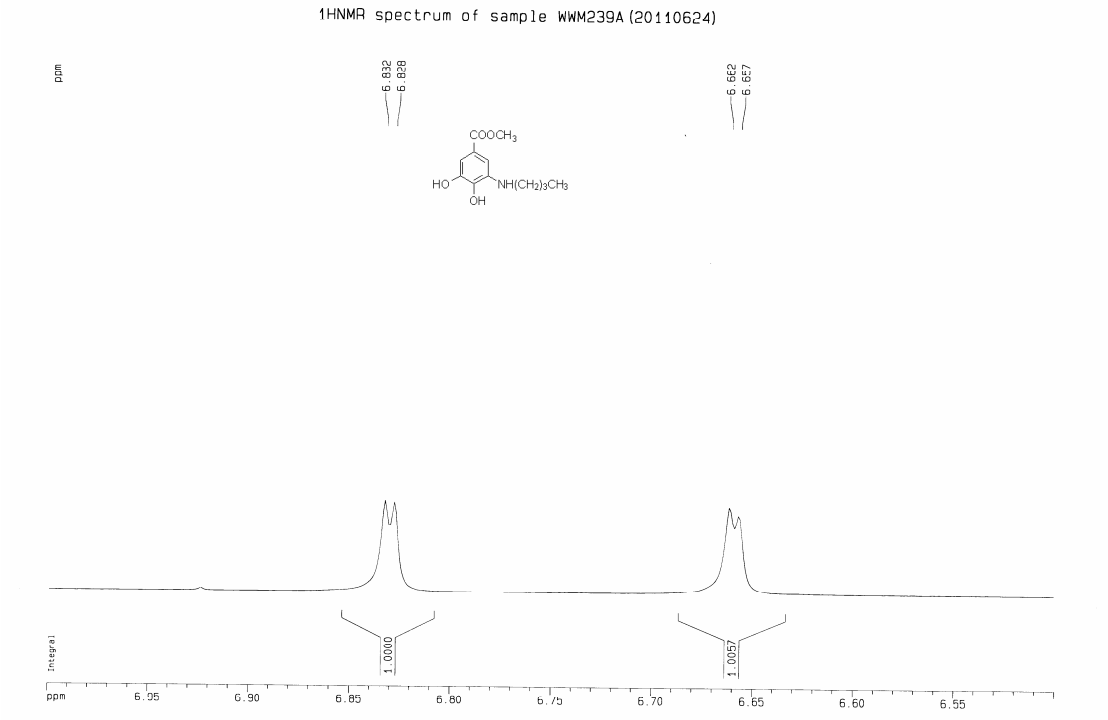
[^{1}H NMR Spectra of 7d]

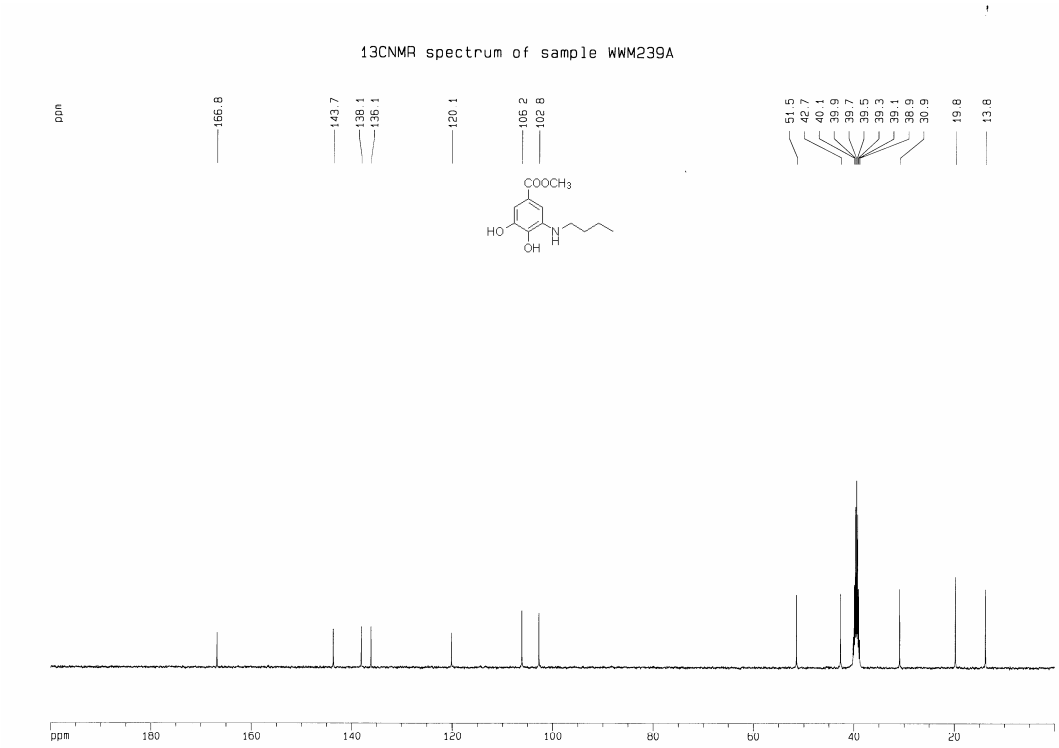




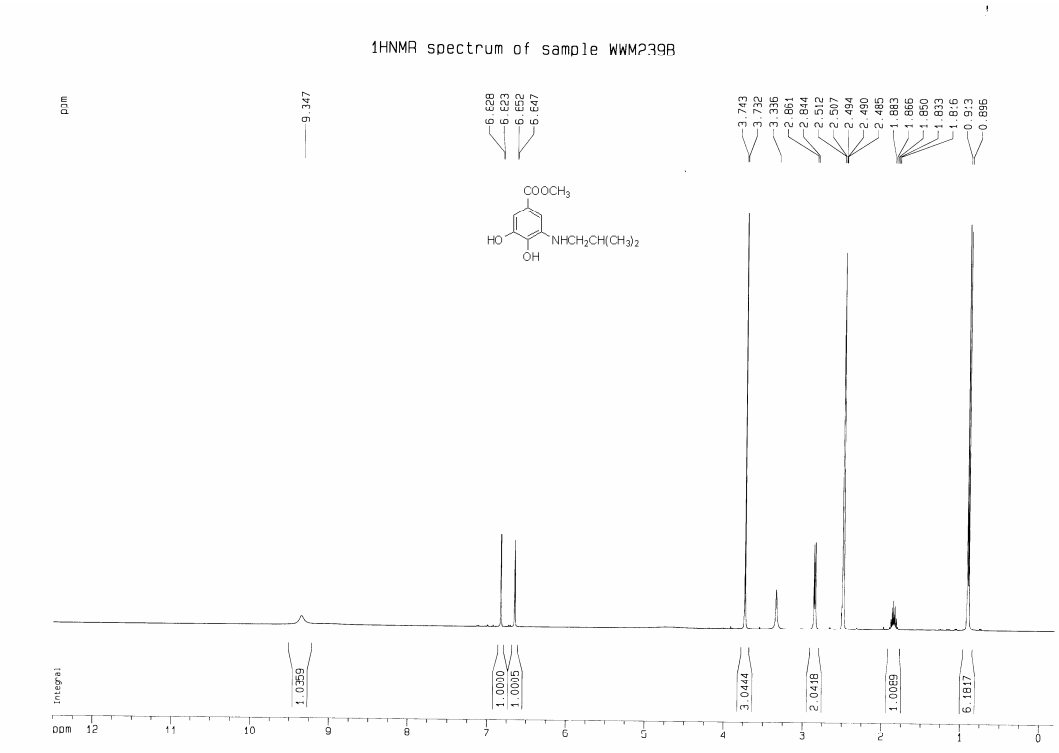
[^{1}H and ^{13}C NMR Spectra of 7e]

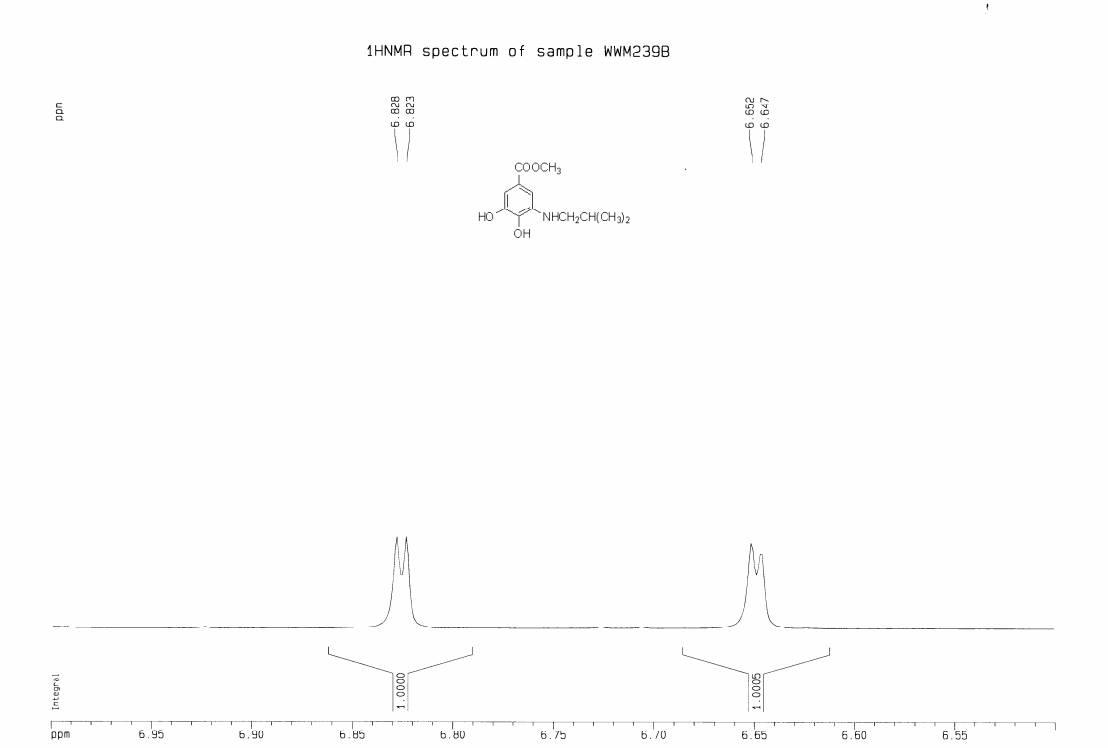




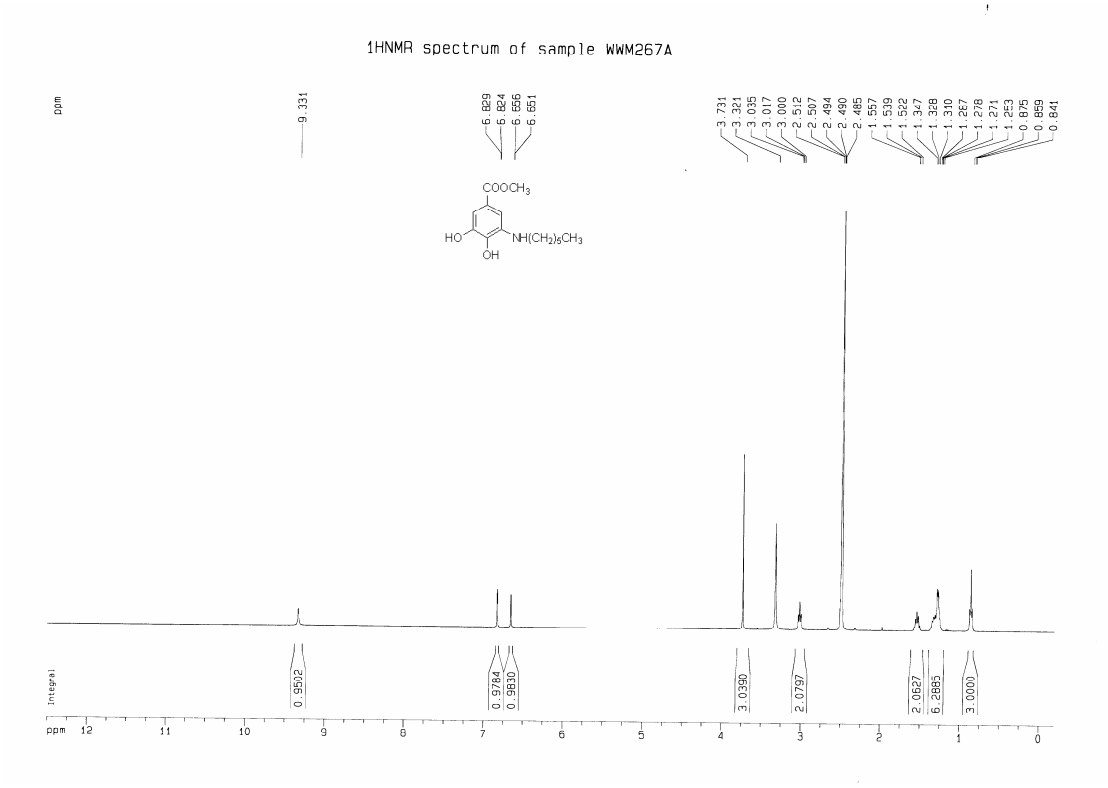


[^{1}H NMR Spectra of 7f]

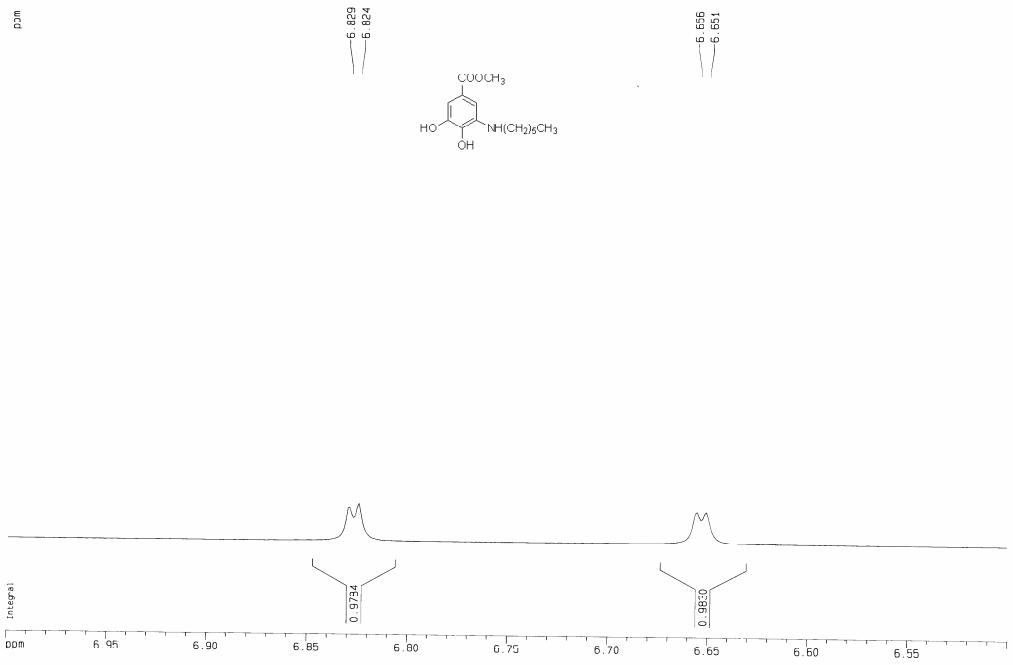




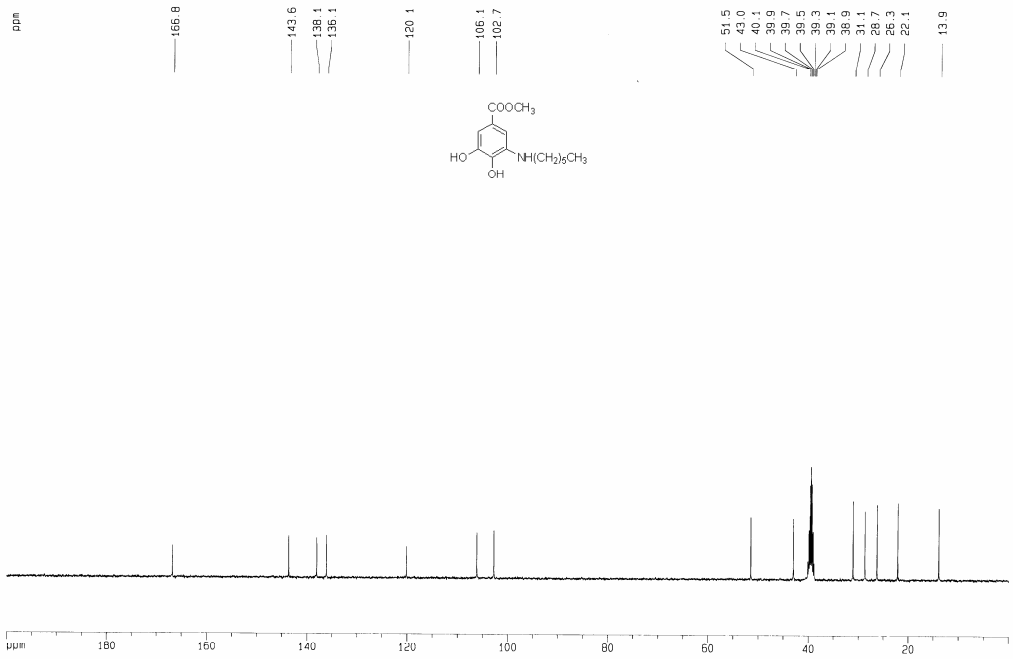
^{1}H and ^{13}C NMR Spectra of 7g]



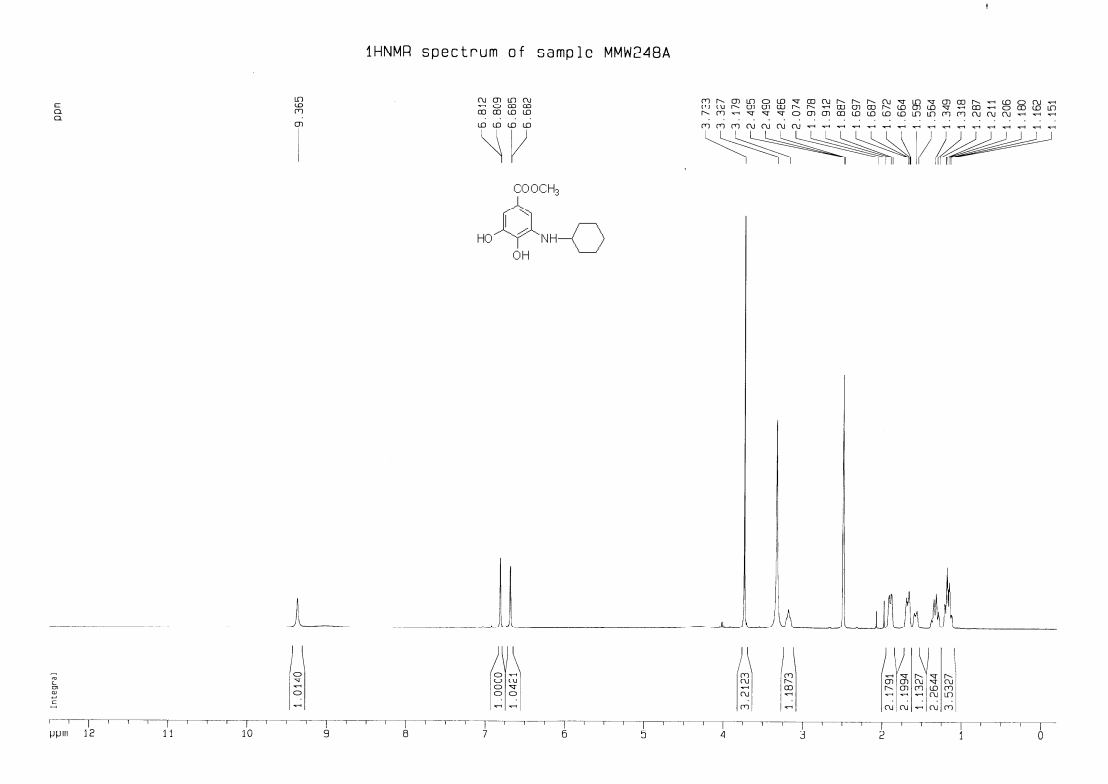
1HNMR spectrum of sample WWM267A

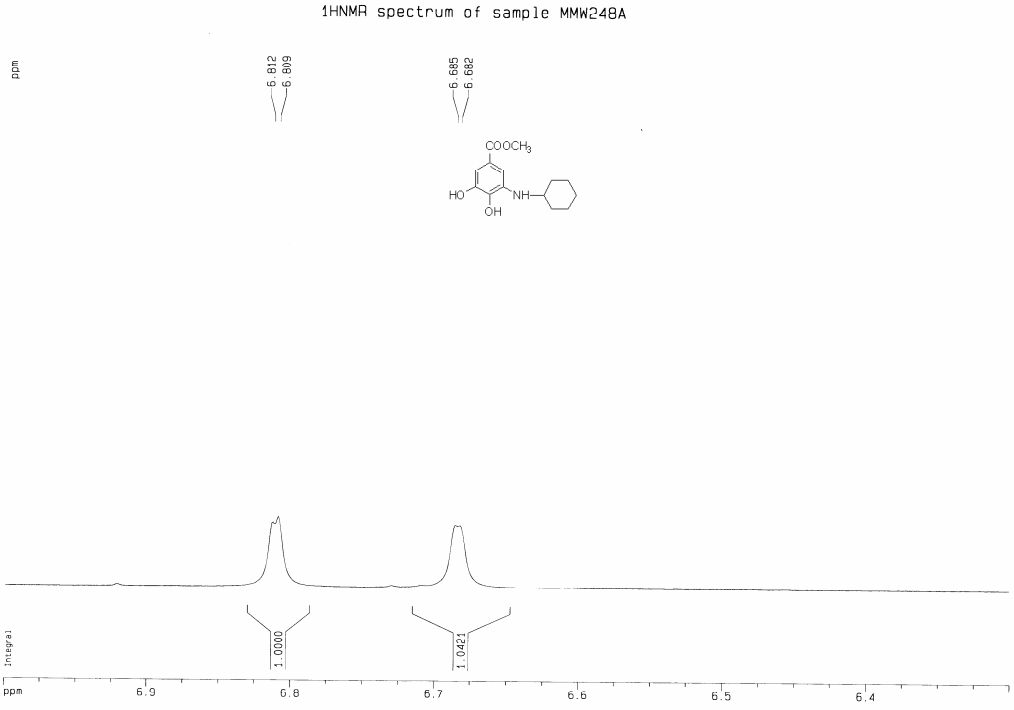


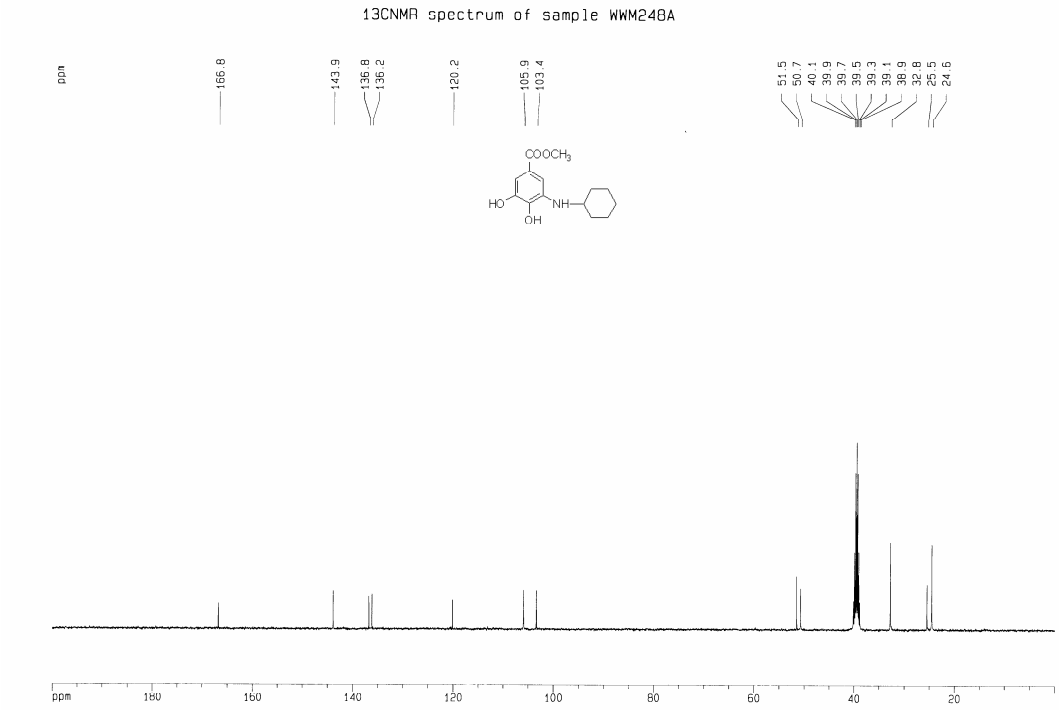
13CNMR spectrum of sample WWM267A



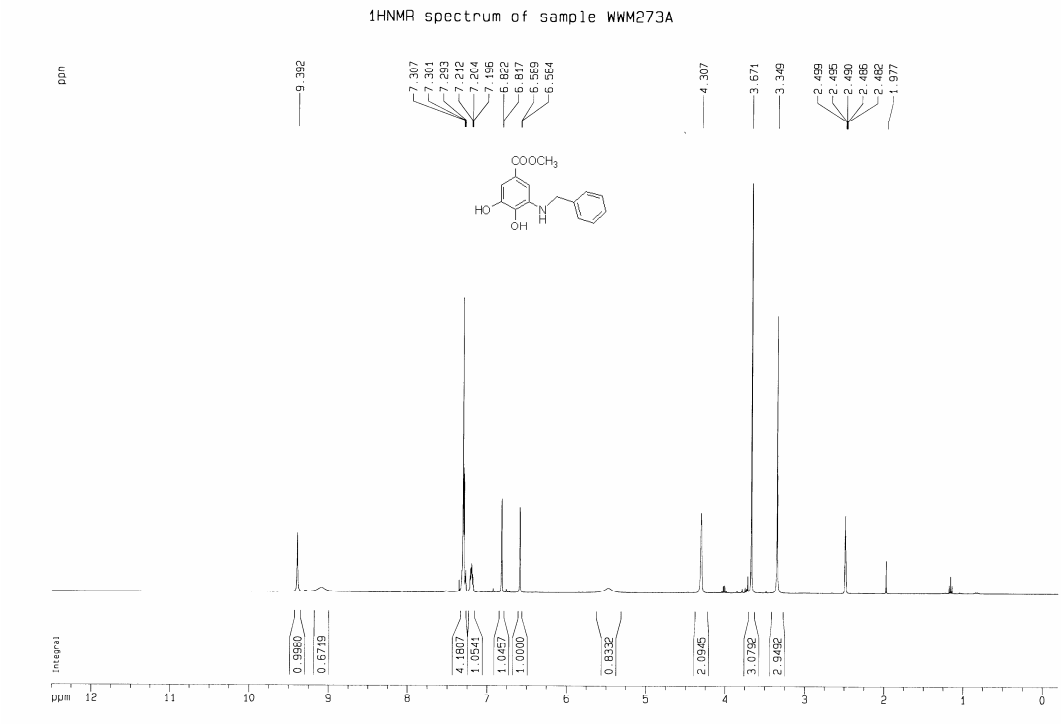
[^{1}H and ^{13}C NMR Spectra of 7h]

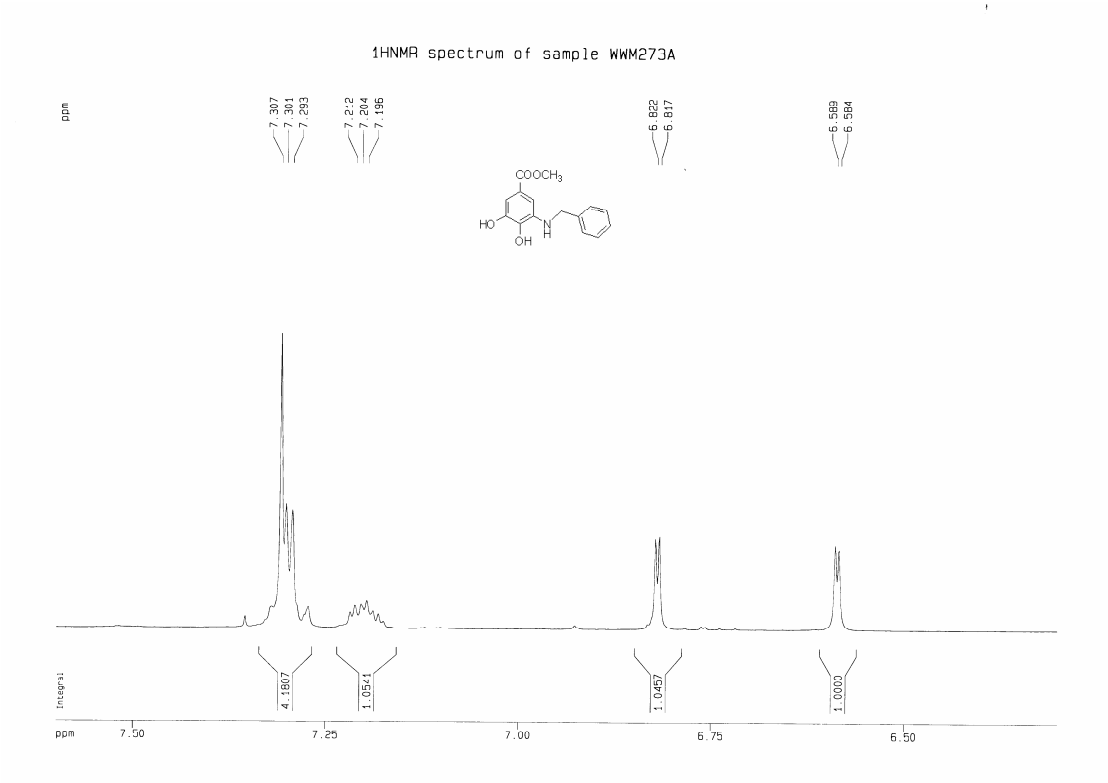




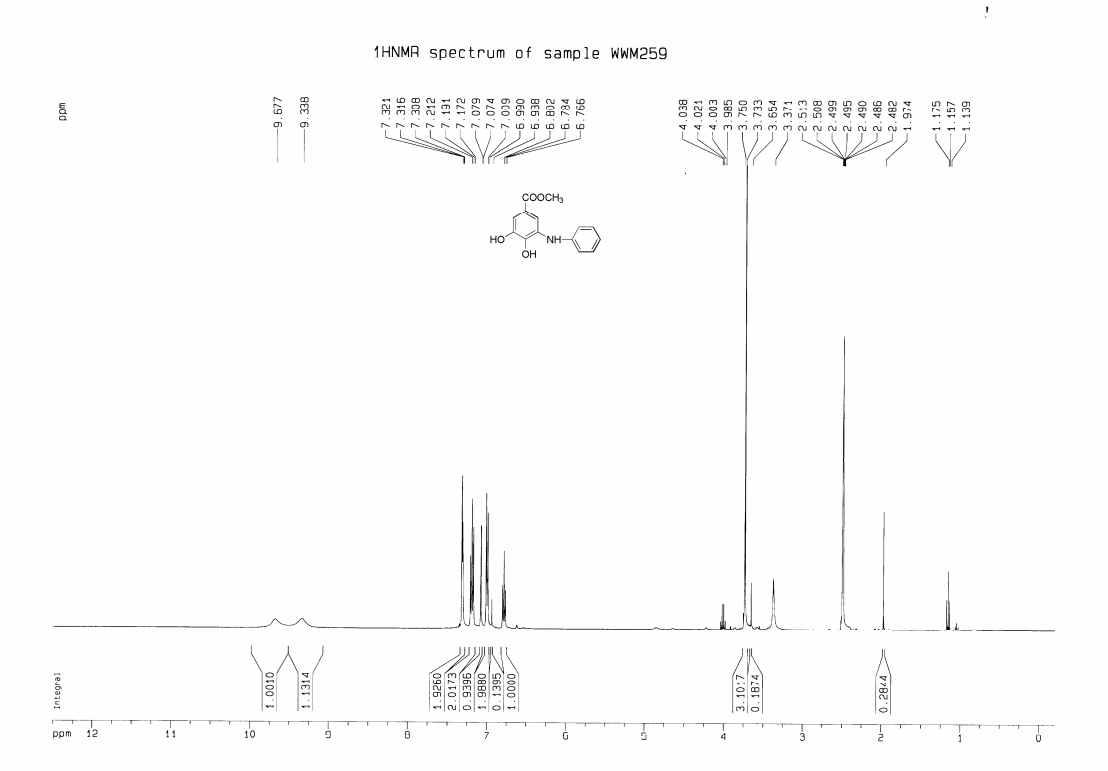


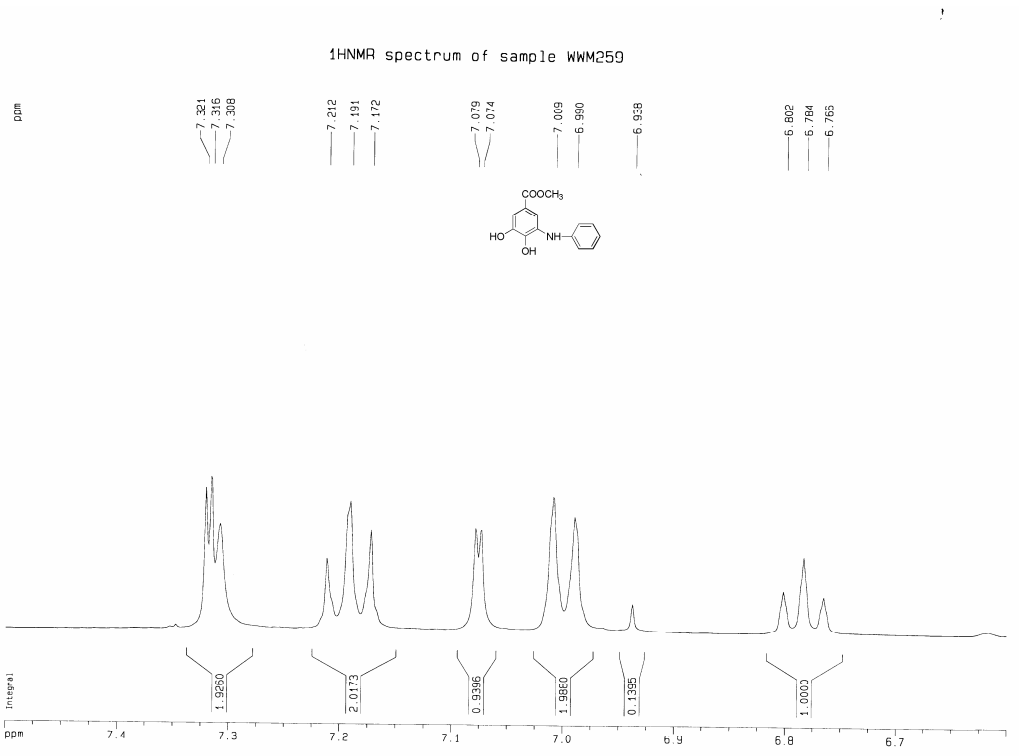
[^{1}H NMR Spectra of 7i]





[^{1}H NMR Spectra of 12]




1HNMR spectrum of sample WWM259
ppm
7.321
7.316
7.308
7.212
7.191
7.172
7.079
7.074
7.009
6.990
6.938
6.802
6.784
6.765
COOCH3
HO
NH
OH
Integral
1.9260
2.0173
0.9396
1.9860
0.1395
1.0000
ppm
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7