Supporting Information

Consecutive reactions between methyl 3-dehydroshikimiate, amines and 1, 2-dichloroalkanes under microwave conditions: A practical, one-pot construction of N-substituted dihydrobenzoxazines

Ensheng Zhang,[a,d] Tianlong Xu,[a,d] Dejian Wang, [a,d] Tongkun Huang,[a] Mu Yuan,[b]
Jun Li[c] and Yong Zou[a] *

[a]Guangzhou Institute of Chemistry, Chinese Academy of Sciences, Guangzhou 510650, P. R. China.
[b]Guangzhou Medical University, Guangzhou, 510182, P. R. China.
[c]Second Affiliated Hospital, College of Medicine, Zhejiang University, Zhejiang 310009, P. R. China.
[d]University of Chinese Academy of Sciences, Beijing, 100039, P. R. China.

*Corresponding Author E-mail: *zou_jinan@163.com;*

Contents

I- Instrumentation and Chemicals

(-)-Shikimic acid was kindly provided as a natural product by Guangxi Wan Shan Spice Co. Ltd. with chromatography grade. (-)-methyl 3-dehydroshikimate was readily prepared from (-)-shikimic acid through an improved method of our previously established procedure. Petroleum ether (PE) used in the experiments refers to the boiling fraction of 60-90 °C. Other reagents and solvents were purchased from commercial sources and used without further purification unless otherwise stated.

Reactions were monitored by thin-layer chromatography (TLC). Column chromatography was performed with silica gel (200-300 mesh) using EtOAc-PE system as the eluent. Melting points were measured on a Thiele apparatus and were uncorrected. Microwave experiments were carried out with a WBFY scientific microwave reactor in a flask connected with a condenser under atmosphere pressure. ^{1}H NMR and ^{13}C NMR spectra were measured on a 400 MHz spectrometer (^{1}H 400 MHz, ^{13}C 100 MHz) using $CDCl_3$ or DMSO-d_6 as the solvent at room temperature. Chemical shifts were reported in parts per million (ppm) and are calibrated using residual undeuterated solvent as an internal reference. HRMS spectras were recorded on a LC-Q-TOF (ESI) apparatus. Mass spectrometry were measured on a Shimadzu GC-MS QP5050A in electron ionization mode and a Thermo Finnigan LCQ DECA XP ion trap mass spectrometer in electrospray ionization mode.

II- Experimental Procedure

II-1 Synthesis of (-)-methyl 3-dehydroshikimate (3-MDHS)

Based on our previous studies, an improved method for the synthesis of (-)-methyl 3-

dehydroshikimate has been established as follows:

Step 1:

To a solution of (-)-shikimic acid (17.4 g, 100 mmol) in MeOH (150 ml) was added *p*-TsOH (1.90 g, 10 mmol). The resulting mixture was heated to reflux until completion of the reaction (monitored by TLC). The mixture was filtered and the filtrate was evaporated under reduced pressure to afford a pale yellow oil, which was purified by recrystallization from EtOAc to give (-)-methyl shikimate as a white powder**.**

Step 2:

To a mixture of (-)-methyl shikimate (9.40 g, 0.05 mol) in THF (220 ml) was added IBX (16.8 g, 0.06 mol). The resulting mixture was stirred at 10-20 °C for the completion of the reaction (monitored by TLC). The iodosylbenzoic acid (IBA) byproduct was filtered off and recycled via oxidation into IBX with oxone. The filtrate was concentrated under reduced pressure to afford crude (-)-methyl 3-dehydroshikimate as a white solid. The crude product was recrystallized from EtOAc to give methyl 3-dehydroshikimiate (3-MDHS) in pure form as white crystals.

II-2 General procedure for the preparation of compounds (4a-4u and 4w-4x)

To a flask (25 ml) were added (-)-methyl 3-dehydroshikimate (0.20 g, 1.1 mmol), arylamine (1.0 mmol) or benzophenone hydrazone (1.0 mmol), DCE (1.5 ml), *p*-TsOH (9.5 mg, 0.05 mmol) and DMSO (5 ml). The flask was then placed into the microwave reactor and the mixture was irradiated with stirring for indicated minutes (t_1) at 110 °C (240 W). After that, Cs_2CO_3 (0.98 g, 3 mmol) was added and stirred for indicated minutes (t_2) at 120 °C (240 W). Upon cooling, the mixture was quenched with water (15 ml), washed with brine (20 ml), extracted with ethyl acetate (3 × 20 ml), dried over anhydrous $MgSO_4$. The organic layer was concentrated under vacuum to furnish the crude product, which could be further purified by recrystallization from EtOAc-PE or by column chromatography on silica gel (200-300) using EtOAc-PE system as the eluent.

II-3 Procedure for the preparation of compound 4a under conventional heating (Table 1, entry 22)

To a flask (25 ml) were added (-)-methyl 3-dehydroshikimate (0.20 g, 1.1 mmol), aniline (93 mg, 1.0 mmol), DCE (1.5 ml), *p*-TsOH (0.95 mg, 0.05 mmol) and DMSO (5 ml). The mixture was stirred for 4 h at 110°C in an oil bath. After that, Cs_2CO_3 (0.98 g, 3 mmol) was added and stirred for 6 h at 120°C. Upon cooling, the mixture was quenched with water (15 mL), washed with brine (20 ml), extracted with ethyl acetate (3 × 20 ml) and dried over anhydrous $MgSO_4$. The organic layer was concentrated under vacuum to furnish the crude product, which could be further purified by column chromatography on silica gel (200-300) using EtOAc-PE system as the eluent.

II-4 Procedure for the preparation of compounds 4v (Scheme 1)

To a flask (25 ml) were added (-)-methyl 3-dehydroshikimate (0.41 g, 2.2 mmol), benzidine (184 mg, 1.0 mmol), DCE (2.0 ml), *p*-TsOH (19 mg, 0.10 mmol) and DMSO (5 ml). The flask was then placed into the microwave reactor and the mixture was irradiated with stirring for 10 minutes (t_1) at 110 °C (240 W). After that, Cs_2CO_3 (6 mmol) was added and stirred for 10 minutes (t_2) at 120 °C (240 W). Upon cooling, the mixture was quenched with water (15 mL), washed with brine (20 ml), extracted with ethyl acetate (3 × 20 ml), dried over anhydrous $MgSO_4$. The organic layer was concentrated under vacuum to furnish the crude product, which could be further purified

by recrystallization from EtOAc-PE.

II-5 General procedure for the preparation of compound (Table 3, 6a-6d)

To a flask (25 ml) were added (-)-methyl 3-dehydroshikimate (0.20 g, 1.1 mmol), alkylamine (1.0 mmol), DCE (1.5 ml), *p*-TsOH (9.5 mg, 0.05 mmol) and DMSO (5 ml). The flask was then placed into the microwave reactor and the mixture was irradiated with stirring for indicated minutes (t_1) at 110 °C (240 W). After that, Cs_2CO_3 (0.98 g, 3 mmol) was added and stirred for indicated minutes at 120 °C (240 W). Upon cooling, the mixture was quenched with water (15 mL), washed with brine (20 ml), extracted with ethyl acetate (3 × 20 ml), the organic layers were combined, dried over anhydrous $MgSO_4$ and filtered, the filtrate was concentrated under vacuum to furnish the crude product, which could be further purified by column chromatography on silica gel (200-300) using EtOAc-PE system as the eluent.

II-6 General procedure for the preparation of compounds (Table 4, compounds 7 and 8)

To a flask (25 ml) were added (-)-methyl 3-dehydroshikimate (0.20 g, 1.1 mmol), arylamine (1.0 mmol), 1, 2-dichloropropane (2.0 ml), *p*-TsOH (9.5 mg, 0.05 mmol) and DMSO (5 ml). The flask was then placed into the microwave reactor and the mixture was irradiated with stirring for indicated minutes (t_1) at 110°C (240 W). After that, Cs_2CO_3 (0.98 g, 3 mmol) was added and stirred for indicated minutes (t_2) at 120°C (240 W). Upon cooling, the mixture was quenched with water (15 mL), washed with brine (20 ml), extracted with ethyl acetate (3 × 20 ml) and dried over anhydrous $MgSO_4$. The organic layer was concentrated under vacuum to furnish the crude product, which could be further purified by column chromatography on silica gel (200-300) using EtOAc-PE (1:10) system as the eluent to afford the products **7** and **8** in regioisomeric mixture with the ratios of 0.9-1.50 (**7/8**).

II-7 General procedure for the preparation of compounds 9c-9e (Scheme 2).

To a flask (25 ml) were added (-)-methyl 3-dehydroshikimate (0.20 g, 1.1 mmol), aniline (1.0 mmol), *p*-TsOH (9.5 mg, 0.05 mmol) and DMSO (5 ml). The flask was then placed into the microwave reactor and the mixture was irradiated with stirring for 8 minutes at 110°C (240 W). After that, **3c-3e** (respectively, 1.0 ml) and Cs_2CO_3 (0.98 g, 3 mmol) was added and stirred for 15 minutes at 120°C (240 W). Upon cooling, the mixture was quenched with water (15 mL), washed with brine (20 ml), extracted with ethyl acetate (3 × 20 ml) and dried over anhydrous $MgSO_4$. The organic layer was concentrated under vacuum to furnish the crude product, which could be further purified by column chromatography on silica gel (200-300) using EtOAc-PE system as the eluent to afford the products **9c-9e.**

II-8 Preparation and isolation of methyl 3-(benzylamino)-4-(2-chloro-ethoxy)benzoate (Intermediate Ⅱ) from the reaction mixture of 3-MDHS (1), benzylamine (5a) and DCE (3a)

To a flask (25 ml) were added (-)-methyl 3-dehydroshikimate (0.20 g, 1.1 mmol), benzylamine (107 mg, 1.0 mmol), DCE (1.5 ml), *p*-TsOH (9.5 mg, 0.05 mmol) and DMSO (5 ml). The mixture was stirred for 5 minutes at 110°C (240 W). After that, Cs_2CO_3 (0.98 g, 3 mmol) was added and stirred for 2 minutes at 120°C (240 W). The mixture was cooled to rt. and washed with brine (20 ml), extracted with ethyl acetate (3 × 20 ml) and dried over anhydrous $MgSO_4$. The organic layer was concentrated under vacuum to furnish the crude product, which was purified by column chromatography on silica gel (200-300) using EtOAc-PE system as the eluent to afford a white solid.

II-9 Procedure for the ferric chloride test and Hinsberg reaction of intermediate (Ⅱ)

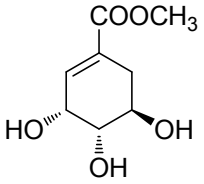
Ferric chloride test: To a test tube was added intermediate Ⅱ (0.01 g) and ethanol (1 ml), then a few drops of dilute ferric chloride solution was added to the solution and the tube was shaken. No precipitate in red, blue, green or purple color could be observed, indicating the absence of any phenolic hydroxyl group in the intermediate.

Hinsberg reaction test: To intermediate Ⅱ (0.01g in 1 ml ethanol) in a test tube, was added 3 mL of 10% NaOH solution and 1.0 ml para-toluensulfonyl chloride in ethanol. The mixture was shaken vigorously and kept alkaline with 10% NaOH solution. After all of the para-toluensulfonyl chloride has been reacted, an oil residue was separated. The residue was not dissolved when treated with 10% HCl solution, proving the existence of secondary amino group in intermediate Ⅱ.

Both of the above-mentioned experiments as well as the spectroscopy data proved the correctness of the structure for intermediate Ⅱ.

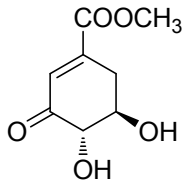
Ⅲ-Characterization Data for Products

III-1 Characterization Data for (-)-methyl shikimate and (-)-Methyl-3-dehydroshikimate



(-)-Methyl shikimate

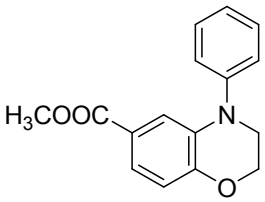
White solid, (yield: 16 g, 85 %). Mp 112~113 °C (lit. Mp 112-113 °C); $[\alpha]_D^{20}$ = -142° (c = 0.2, MeOH); ^{1}H NMR (CD_3COCD_3, 400 MHz) δ: 6.73 (m, 1H, 2-H)，4.38 (m, 1H, 3-H), 4.02 (s, 1H, 4-OH D_2O exchangeable), 4.00 (brs, 2H, 3,5-OH D_2O exchangeable), 3.69 (s, 3H, OCH_3), 3.85 (m, 1H, 5-H), 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 $[M-COOCH_3]^+$.



(-)-Methyl 3-dehydroshikimate

White solid, (yield: 6.70 g, 72 %). Mp 122~123 °C; (lit. Mp 124-125 °C) $[\alpha]_D^{20}$ = -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 $[M-COOCH_3]^+$.

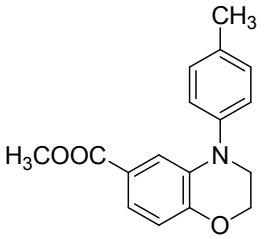
III-2 Characterization Data for Products (Table 2, 4a-4u)



6-methoxycarbonyl-4-phenyl-3, 4-dihydro-2H-1, 4-benzoxazine (4a)

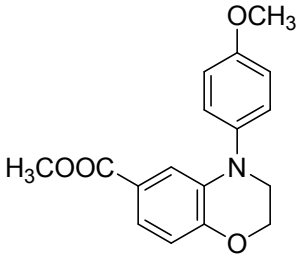
White solid. (yield: 247 mg, 92 %), Mp 87～89 ℃, R_f =0.45 (EtOAc:PE =1:9); ^{1}H NMR (400

MHz, $CDCl_3$) δ: ppm 7.59 (d, J = 2.00 Hz, 1H), 7.45 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.36 (m, 2H), 7.20 (m, 2H), 7.11 (t, J = 6.40 Hz, 1H), 6.87 (d, J = 8.40 Hz, 1H), 4.32 (t, J = 4.40 Hz, 2H), 3.78 (s, 3H), 3.70 (t, J = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.9(C=O), 148.8, 146.4, 132.2, 129.6, 124.0, 123.3, 122.8, 122.1, 118.1, 116.8, 64.7, 51.7, 48.1; IR (KBr) ν_{max}/cm^{-1} 3065, 3006, 2949, 2885, 2848, 1703, 1608, 1591, 1509, 1491, 1459, 1437, 1325, 1282, 1113, 1090, 761, 697; MS (EI): m/z =269 $[M]^+$, 238 $[M\text{-}OCH_3]^+$, 210 $[M\text{-}COOCH_3]^+$, 194, 164, 77; HRMS (ESI-TOF) calcd. for $C_{16}H_{16}NO_3$ $[M+H^+]$ 270.1125, found: 270.1125.



4-(4-methylphenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4b)

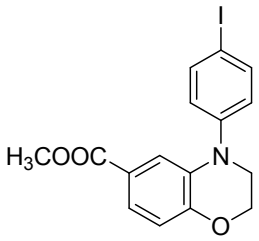
White solid (yield: 271 mg, 96 %), Mp 106～108 ℃, R_f = 0.50 (EtOAc:PE = 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.50 (d, J = 1.60 Hz, 1H), 7.41 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.17 (d, J = 8.40 Hz, 2H), 7.09 (d, J = 8.40 Hz, 2H), 6.85 (d, J = 8.40 Hz, 1H), 4.32 (t, J = 4.40 Hz, 2H), 3.77 (s, 3H), 3.67 (t, J = 4.40 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.0(C=O), 148.5, 143.9, 134.0, 132.8, 130.2, 123.7, 122.8, 121.6, 117.6, 116.7, 64.7, 51.7, 48.3, 20.8; IR (KBr) ν_{max}/cm^{-1} 3072, 3001, 2949, 2888, 2849, 1707, 1603, 1578, 1514, 1458, 1372, 818; MS (EI): m/z =283 $[M]^+$, 268 $[M\text{-}CH_3]^+$, 252 $[M\text{-}OCH_3]^+$, 224 $[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{17}H_{17}NNaO_3$ $[M+Na^+]$ 306.1101, found: 306.1108.



4-(4-methoxyphenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4c)

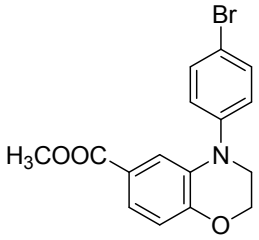
Pale yellow crystal, (yield: 284 mg, 95 %), Mp 107～109 ℃, R_f=0.41 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.38 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.32 (d, J = 2.00 Hz, 1H), 7.14 (dd, J_1 = 6.80 Hz, J_2 = 2.00 Hz, 2H), 6.92 (dd, J_1 = 6.80 Hz, J_2 = 1.60 Hz, 2H), 6.83 (d, J =

8.40 Hz, 1H), 4.34 (t, J = 4.40 Hz, 2H), 3.81 (s, 3H), 3.76 (s, 3H), 3.63 (t, J = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.0(C=O), 156.9, 148.3, 139.3, 133.9, 126.2, 122.9, 121.1, 116.7, 116.5, 115.0, 64.8, 55.4, 51.7, 48.8; MS (EI): m/z=299 $[M]^+$, 284 $[M\text{-}CH_3]^+$, 268 $[M\text{-}OCH_3]^+$, 240 $[M\text{-}COOCH_3]^+$, 77; IR (KBr) ν_{max}/cm^{-1} 3012, 2980, 2953, 2836, 1715, 1608, 1576, 1512, 1440, 1367, 1285, 1251, 1209, 839; HRMS (ESI-TOF) calcd. for $C_{17}H_{17}NNaO_4$ $[M+Na]^+$ 322.1050, found: 322.1051.



4-(4-iodophenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4d)

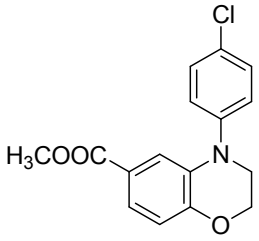
Grey white solid, (yield: 347 mg, 88 %), Mp 135～137 ℃, R_f = 0.51 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.63 (d, J = 8.80 Hz, 2H), 7.60 (d, J = 1.60 Hz, 1H), 7.47 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 6.96 (d, J = 8.80 Hz, 2H), 6.88 (d, J = 8.80 Hz, 1H), 4.32 (t, J = 4.40 Hz, 2H), 3.79 (s, 3H), 3.67 (t, J = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.8(C=O), 149.0, 146.2, 138.5, 131.1, 129.6, 124.8, 122.8, 122.7, 118.4, 117.1, 64.6, 51.8, 47.9; IR (KBr) ν_{max}/cm^{-1} 3051, 2989, 2946, 2914, 2819, 1706, 1578, 1509, 1482, 1457, 832; MS (EI): m/z =395 $[M]^+$, 280 $[M\text{-}CH_3]^+$, 264 $[M\text{-}OCH_3]^+$, 236 $[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{16}H_{14}INNaO_3$ $[M+Na]^+$ 417.9911, found: 417.9912.



4-(4-bromophenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4e)

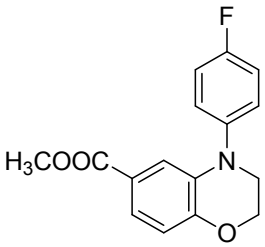
White crystal, (yield: 296 mg, 85 %), Mp 118～120 ℃, R_f=0.53 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.57 (d, J = 2.00 Hz, 1H), 7.46 (m, 3H), 7.07 (d, J = 8.80 Hz, 2H), 6.88 (d, J = 8.40 Hz, 1H), 4.31(t, J = 4.40 Hz, 2H), 3.79 (s, 3H), 3.66 (t, J = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.8(C=O), 148.9, 145.5, 132.6, 131.4, 124.6, 122.8, 122.6, 118.2, 117.0,

116.4, 64.6, 51.8, 48.0 ; IR (KBr) ν_{max}/cm^{-1} 3027, 2946, 2947, 2892, 2852, 1704, 1578, 1509, 1486, 1436, 1368, 1329, 834; MS (EI): m/z =349 $[M+2]^+$, 347 $[M]^+$, 332 $[M-CH_3]^+$, 316 $[M-OCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{16}H_{14}{}^{79}BrNNaO_3$ $[M+Na]^+$ 370.0049, found: 370.0051.



4-(4-chlorophenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4f)

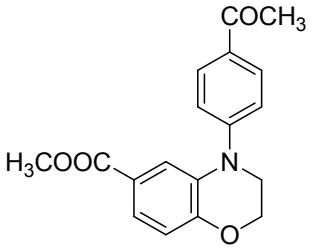
White solid, (yield: 252 mg, 83 %), Mp 87～89 ℃, R_f =0.62 (EtOAc:PE =1:6); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.54 (d, J = 1.60 Hz, 1H), 7.46 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.31 (d, J = 8.80 Hz, 2H), 7.13 (d, J = 8.80 Hz, 2H), 6.87 (d, J = 8.40 Hz, 1H), 4.31 (t, J = 4.40 Hz, 2H), 3.79 (s, 3H), 3.66 (t, J = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.9 (C=O), 148.9, 145.0, 131.7, 129.7, 129.0, 124.5, 122.9, 122.5, 118.2, 117.0, 64.6, 51.8, 48.1 ; MS (EI): m/z =305 $[M+2]^+$, 303 $[M]^+$, 288 $[M-CH_3]^+$, 272 $[M-OCH_3]^+$, 244 $[M-COOCH_3]^+$, 77; IR (KBr) ν_{max}/cm^{-1} 3064, 2981, 2958, 2938, 2886, 1718, 1606, 1576, 1507, 1486, 1448, 1369, 834: HRMS (ESI-TOF) calcd. for $C_{16}H_{14}{}^{35}ClNNaO_3$ $[M+Na]^+$ 326.0554, found: 326.0556.



4-(4-fluorophenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4g)

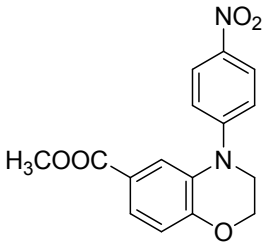
Pale yellow solid, (yield: 224 mg, 78 %), Mp 85～87 ℃, R_f =0.50 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.43 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.38 (d, J = 2.00 Hz, 1H), 7.17(m, 2H), 7.06 (m, 2H), 6.86 (d, J = 8.40 Hz, 1H), 4.33 (t, J = 4.40 Hz, 2H), 3.77 (s, 3H), 3.64 (t, J = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.8(C=O), 158.4, 148.5, 142.4, 132.8, 125.8, 122.8, 121.8, 117.2, 116.7, 116.6, 64.6, 51.7, 48.5; MS (EI): m/z =287 $[M]^+$, 272 $[M-CH_3]^+$, 256 $[M-OCH_3]^+$, 228 $[M-COOCH_3]^+$, 77; IR (KBr) ν_{max}/cm^{-1} 3074, 3028, 2991, 2949, 2897, 1705, 1609, 1581, 1513, 1465, 1369, 834; HRMS (ESI-TOF) calcd. for $C_{16}H_{14}FNNaO_3$ $[M+Na]^+$

310.0850, found: 310.0860.



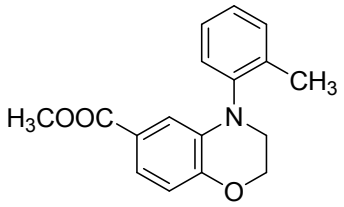
4-(4-acetylphenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4h)

Pale yellow solid, (yield: 255 mg, 82 %), Mp 102～104 ℃, R_f=0.38 (EtOAc:PE =1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.94 (dd, J_1 = 7.20 Hz, J_2 = 1.60 Hz, 2H), 7.84 (d, J = 2.00 Hz, 1H), 7.55 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.22 (dd, J_1 = 7.20 Hz, J_2 = 1.60 Hz, 2H), 6.92 (d, J = 8.40 Hz, 1H), 4.32 (t, J = 4.40 Hz, 2H), 3.80 (s, 3H), 3.78 (t, J = 4.40 Hz, 2H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 196.6 (C=O), 166.7 (C=O), 150.3, 149.5, 131.2, 130.3, 129.5, 124.0, 122.7, 120.2, 120.0, 117.4, 64.9, 51.9, 47.0, 26.4; MS (EI): m/z =311$[M]^+$, 296 $[M\text{-}CH_3]^+$, 280 $[M\text{-}OCH_3]^+$, 252 $[M\text{-}COOCH_3]^+$, 77. IR (KBr) ν_{max}/cm^{-1} 3058, 3022, 2976, 2940, 2884, 1705, 1678, 1593, 1502, 1439, 1378, 818: HRMS (ESI-TOF) calcd. for $C_{18}H_{17}NNaO_4$ $[M+Na]^+$ 334.1050, found: 334.1054.



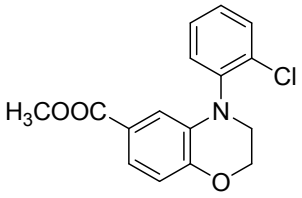
6-methoxycarbonyl-4-(4-nitrophenyl)-3, 4-dihydro-2H-1, 4-benzoxazine (4i)

Brown solid, (yield: 264 mg, 84 %), Mp 181～183 ℃, R_f=0.50 (EtOAc:PE =1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 8.18 (d, J = 8.40 Hz, 2H), 7.87 (d, J = 2.00 Hz, 1H), 7.62 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.23 (d, J = 8.40 Hz, 2H), 6.95 (d, J = 8.40 Hz, 1H), 4.34 (t, J = 4.40 Hz, 2H), 3.82 (t, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.4 (C=O), 151.5, 149.9, 141.5, 128.3, 125.7, 125.1, 122.8, 120.8, 119.2, 117.8, 65.0, 52.0, 46.8; IR (KBr) ν_{max}/cm^{-1} 3073, 2985, 2944, 2897, 2841, 1717, 1582, 1509, 1491, 1436, 1378, 838; MS (EI): m/z= 314 $[M]^+$, 299 $[M\text{-}CH_3]^+$, 283 $[M\text{-}OCH_3]^+$, 255 $[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{16}H_{14}N_2NaO_5$ $[M+Na]^+$ 337.0795, found: 337.0792.



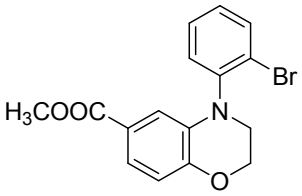
4-(2-methylphenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4j)

White needle-like crystal, (yield: 241 mg, 85 %), Mp 96～98℃, R_f =0.48 (EtOAc:PE =1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.35 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.30 (d, J = 6.80 Hz, 1H), 7.24 (m, 2H), 7.15 (d, J = 6.80 Hz, 1H), 6.87 (d, J = 2.00 Hz, 1H), 6.85 (d, J = 8.00 Hz, 1H), 4.38 (m, 2H), 3.74 (s, 3H), 3.60 (m, 2H), 2.21(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.1(C=O), 147.8, 144.1, 136.0, 134.0, 131.5, 127.6, 126.9, 126.7, 123.1, 120.5, 116.3, 115.7, 65.0, 51.7, 48.0, 17.9; MS (EI): m/z = 283 $[M]^+$, 268 $[M\text{-}CH_3]^+$, 252 $[M\text{-}OCH_3]^+$, 224 $[M\text{-}COOCH_3]^+$, 77; IR (KBr) ν_{max}/cm^{-1} 3066, 2998, 2948, 2882, 2837, 1710, 1608, 1578, 1510, 1490, 1462, 1438, 1370, 761; HRMS (ESI-TOF) calcd. for $C_{17}H_{17}NNaO_3$ $[M+Na^+]$ 306.1101, found: 306.1107.



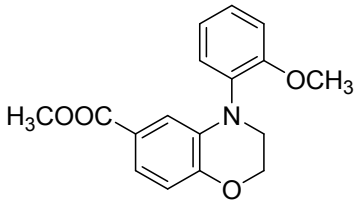
4-(2-chlorophenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4k)

Colourless needle-like crystal, (yield: 242 mg, 80 %), Mp 110～112℃, R_f=0.57 (EtOAc:PE =1:6); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.49 (d, J = 8.00 Hz, 1H), 7.40 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.29 (m, 2H), 7.21 (m, 1H), 7.03 (d, J = 2.00 Hz, 1H), 6.87 (d, J = 8.40 Hz, 1H), 4.36(s, 2H), 3.75(s, 3H), 3.65(s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.9 (C=O), 148.2, 142.9, 132.9, 132.5, 131.1, 128.9, 128.3, 127.6, 123.1, 121.3, 116.7, 116.7, 64.6, 51.7, 48.0; MS (EI): m/z = 305$[M+2]^+$, 303$[M]^+$, 288$[M\text{-}CH_3]^+$, 272$[M\text{-}OCH_3]^+$, 244$[M\text{-}COOCH_3]^+$, 77; IR (KBr) ν_{max}/cm^{-1} 3067, 3002, 2951, 2884, 2849, 1713, 1608, 1581, 1511, 1475, 1437, 1371, 762; HRMS (ESI-TOF) calcd. for $C_{16}H_{14}{}^{35}ClNNaO_3$ $[M+Na]^+$ 326.0554, found: 326.0557.



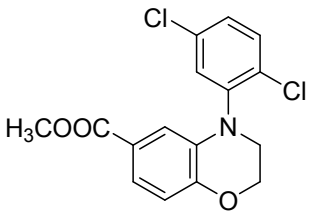
4-(2-bromophenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4l)

Colourless needle-like crystal, (yield: 285 mg, 82 %), Mp 106～108℃, R_f=0.56 (EtOAc:PE =1:6); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.68 (dd, J_1 = 8.00 Hz, J_2 = 1.20 Hz, 1H), 7.39 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.35 (m, 1H), 7.27 (m, 1H), 7.15 (m, 1H), 7.00 (d, J = 2.00 Hz, 1H), 6.87 (d, J = 8.00 Hz, 1H), 4.37 (d, J = 26.40 Hz, 2H), 3.75(s, 3H), 3.63(d, J = 31.60 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.9 (C=O), 148.1, 144.4, 134.3, 133.0, 129.3, 129.1, 129.1, 128.1, 123.1, 121.2, 116.7, 116.6, 64.6, 51.7, 48.2; MS (EI): m/z = 349 $[M+2]^+$, 347 $[M]^+$, 332 $[M-CH_3]^+$, 316 $[M-OCH_3]^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3067, 3004, 2950, 2883, 2848, 1712, 1608, 1580, 1512, 1471, 1437 ,1371, 762; HRMS (ESI-TOF) calcd. for $C_{16}H_{14}{}^{79}BrNNaO_3$ $[M+Na]^+$ 370.0049, found: 370.0050.



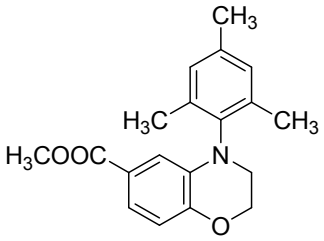
4-(2-methoxyphenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4m)

White soild, (yield: 260 mg, 87%), Mp 66～68 ℃, R_f =0.55 (EtOAc:PE =1:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.35 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.25-7.29 (m, 2H), 7.10 (d, J = 2.00 Hz, 1H), 6.94-7.00 (m, 2H), 6.84 (d, J = 8.40 Hz, 1H) , 4.34 (t, J = 4.40 Hz, 2H), 3.78 (s, 3H), 3.74 (s, 3H), 3.63 (t, J = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.1 (C=O), 155.3, 148.1, 134.0, 133.6, 127.8, 127.2, 122.8, 121.3, 120.5, 116.5, 116.3, 112.6, 64.7, 55.5, 51.6, 47.8; MS (EI): m/z= 299 $[M]^+$, 284 $[M-CH_3]^+$, 268 $[M-OCH_3]^+$, 240 $[M-COOCH_3]^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3079, 3054, 3003, 2945, 2838, 1711, 1610, 1579, 1500, 1439, 1370, 763; HRMS (ESI-TOF) calcd. for $C_{17}H_{17}NNaO_4$ $[M+Na]^+$ 322.1050, found: 322.1052.



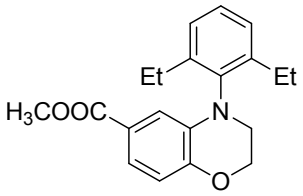
4-(2, 5-dichlorophenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4n)

White flake crystal, (yield: 253mg, 75 %), Mp 116～118 ℃, R_f=0.66(EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.44 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.42 (d, J = 8.80 Hz, 1H), 7.25 (d, J = 2.40 Hz, 1H), 7.18 (dd, J_1 = 8.80 Hz, J_2 = 2.40 Hz, 1H), 7.06 (d, J = 2.00 Hz, 1H) , 6.88 (d, J = 8.40 Hz, 1H), 4.35 (s, 2H), 3.78 (s, 3H), 3.63(s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.9(C=O), 148.5, 144.2, 133.5, 132.0, 131.9, 130.7, 128.7, 127.5, 123.3, 122.2, 117.5, 116.9, 64.6, 51.9, 48.1; MS (EI): m/z = 341[M+4]$^+$, 339 [M+2]$^+$, 337 [M]$^+$, 322 [M-CH_3]$^+$, 306 [M-OCH_3]$^+$, 278 [M-$COOCH_3$]$^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3064, 2999, 2950, 2893, 2854, 1713, 1611, 1581, 1509, 1470, 1438, 1395, 1324, 1294, 1272, 1239, 1093 ,1044, 878, 726; HRMS (ESI-TOF) calcd. for $C_{16}H_{13}{}^{35}Cl_2NNaO_3$ [M+Na]$^+$ 360.0165, found: 360.0167, calcd. for $C_{16}H_{13}{}^{37}Cl_2NNaO_3$ [M+Na]$^+$ 364.0116, found: 364.0115, calcd. for $C_{16}H_{13}{}^{37}Cl^{35}ClNNaO_3$ [M+Na]$^+$ 362.0138, found: 362.0139.



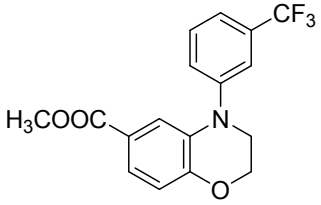
6-methoxycarbonyl-4-(2, 4, 6-trimethylphenyl)-3, 4-dihydro-2H-1, 4-benzoxazine (4o)

Yellow crystal, (yield: 202 mg, 65 %), Mp 134～136 ℃, R_f =0.70(EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.27 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 6.95 (s, 2H), 6.84 (d, J = 8.40 Hz, 1H), 6.66 (d, J = 2.00 Hz, 1H), 4.36 (t, J = 4.40 Hz, 2H), 3.74 (s, 3H), 3.55 (t, J = 4.40 Hz, 2H), 2.30 (s, 3H), 2.08(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.3(C=O), 146.6, 138.0, 137.3, 137.2, 133.9, 130.0, 123.8, 118.9, 116.2, 112.8, 64.6, 51.7, 46.6, 21.0, 18.1; IR (KBr) ν_{max} / cm^{-1} 3065, 3000, 2950, 2917, 2845, 1705, 1610, 1578, 1510, 1465, 1439, 1372, 1269, 1087, 897, 860, 766; MS (EI): m/z = 311 [M]$^+$, 296 [M-CH_3]$^+$, 280 [M-OCH_3]$^+$, 252 [M-$COOCH_3$]$^+$, 77; HRMS (ESI-TOF) calcd. for $C_{19}H_{21}NNaO_3$ [M+Na]$^+$ 334.1414, found: 334.1420.



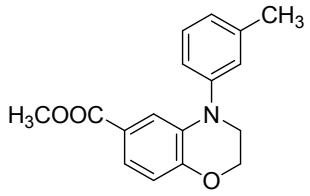
4-(2, 6-diethylphenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4p)

Yellow crystal, (yield: 198 mg, 61 %), Mp 93～95 ℃, R_f =0.64(EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.27 (m, 2H), 7.20 (d, *J* = 7.60 Hz, 2H), 6.85 (d, *J* = 8.40 Hz, 1H), 6.63 (d, *J* = 2.00 Hz, 1H), 4.38 (t, *J* = 4.40 Hz, 2H), 3.72 (s, 3H), 3.59 (t, *J* = 4.40 Hz, 2H), 2.43-2.50 (m, 4H), 1.27 (t, *J* = 7.60 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.2 (C=O), 146.4, 143.4, 139.6, 134.6, 128.1, 127.3, 123.7, 119.0, 116.2, 113.3, 64.5, 51.6, 47.7, 24.1, 14.6; MS (EI): m/z= 325 $[M]^+$, 310 $[M\text{-}CH_3]^+$, 294 $[M\text{-}OCH_3]^+$, 266 $[M\text{-}COOCH_3]^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3066, 3016, 2964, 2869, 1712, 1605, 1578, 1509, 1461, 1438, 1366, 1321, 1293, 1234, 764, 715; HRMS (ESI-TOF) calcd. for $C_{20}H_{23}NNaO_3$ $[M+Na]^+$ 348.1570, found: 348.1575.



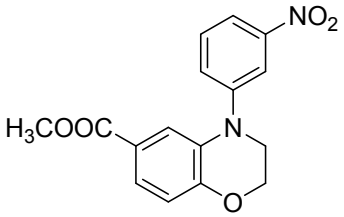
6-methoxycarbonyl-4-(3-(trifluoromethyl)phenyl)-3, 4-dihydro-2H-1, 4-benzoxazine (4r)

White solid, (yield: 242 mg, 72 %), Mp 119～121℃, R_f =0.58 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.64 (d, *J* = 1.60 Hz, 1H), 7.50 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.39-7.46 (m, 3H), 7.31 (d, *J* = 7.60 Hz, 1H), 6.91 (d, *J* = 8.40 Hz, 1H), 4.32 (t, *J* = 4.40 Hz, 2H), 3.79 (s, 3H), 3.73 (t, *J* = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.7(C=O), 149.1, 147.0, 132.2(q, J=32Hz, 1C) , 124.5(q, J=258.7Hz, 1C, CF_3), 122.9, 120.0, 119.6, 119.1, 118.6, 117.3, 64.6, 51.9, 47.9; IR (KBr) ν_{max}/cm^{-1} 3073, 3012, 2999, 2956, 2894, 1713, 1604, 1583, 1512, 1492, 1441, 1375, 884, 760, 704; MS (EI): m/z = 337 $[M]^+$, 322 $[M\text{-}CH_3]^+$, 306 $[M\text{-}OCH_3]^+$, 278 $[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{17}H_{14}F_3NNaO_3$ $[M+Na]^+$ 360.0818, found: 360.0826.



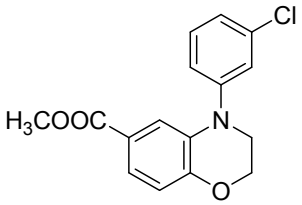
4-(3-methylphenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4s)

Colourless crystal, (yield: 260 mg, 92 %), Mp 70～72℃, R_f =0.48 (EtOAc:PE =1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.58 (d, J = 2.00 Hz, 1H), 7.43 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.24 (m, 1H), 7.00 (t, 2H), 6.93 (d, J = 7.60 Hz, 1H), 6.87 (t, J = 8.40 Hz, 1H), 4.31 (t, J = 4.40 Hz, 2H), 3.78 (s, 3H), 3.69 (t, J = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.0 (C=O), 148.7, 146.4, 139.6, 132.3, 129.4, 124.9, 124.0, 122.7, 121.9, 120.5, 118.2, 116.8, 64.7, 51.7, 48.2, 21.4; MS (EI): m/z = 283 $[M]^+$, 268 $[M\text{-}CH_3]^+$, 252 $[M\text{-}OCH_3]^+$, 224 $[M\text{-}COOCH_3]^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3073, 3039, 2987, 2951, 2907, 2880, 2853, 1708, 1599, 1578, 1509, 1491, 1435, 1375, 869, 763, 700; HRMS (ESI-TOF) calcd. for $C_{17}H_{17}NNaO_3$ $[M+Na^+]$ 306.1101, found: 306.1106.



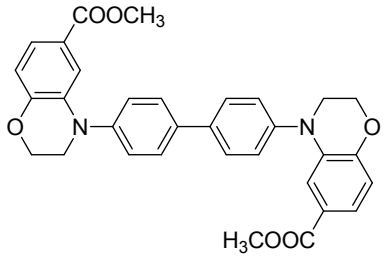
6-methoxycarbonyl-4-(3-nitrophenyl)-3, 4-dihydro-2H-1, 4-benzoxazine (4t)

Red crystal, (yield: 245 mg, 78 %), Mp 175～177 ℃, R_f =0.56 (EtOAc:PE =1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.98 (t, J = 2.00 Hz, 1H), 7.88 (dd, J_1 = 8.00 Hz, J_2 = 0.80 Hz, 1H), 7.67 (t, J = 2.00 Hz, 1H), 7.54 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 2H), 7.48 (t, J =8.00 Hz, 1H), 6.93 (d, J = 8.40 Hz, 1H), 4.33 (t, J = 4.40 Hz, 2H), 3.79 (s, 3H), 3.77 (t, J = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.6 (C=O), 149.4, 147.6, 130.2, 130.0, 127.8, 123.9, 122.9, 119.6, 119.1, 117.7, 117.5, 116.5, 64.6, 51.9, 47.7; MS (EI): m/z = 314 $[M]^+$, 299 $[M\text{-}CH_3]^+$, 283 $[M\text{-}OCH_3]^+$, 255 $[M\text{-}COOCH_3]^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3091, 3067, 2923, 2893, 2856, 1715, 1604, 1580, 1525, 1481, 1432, 1373, 875, 764, 734; HRMS (ESI-TOF) calcd. for $C_{16}H_{14}N_2NaO_5$ $[M+Na]^+$ 337.0795, found: 337.0793.



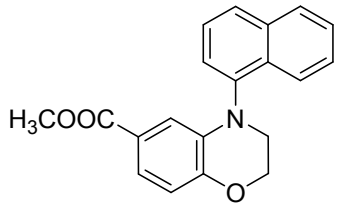
4-(3-chlorophenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4u)

Colourless crystal, (yield: 248 mg, 82 %), Mp 92～94 ℃, R_f =0.61 (EtOAc:PE =1:6); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.63 (d, *J* = 2.00 Hz, 1H), 7.50 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.25 (t, *J* = 8.40 Hz, 1H), 7.15 (t, *J* = 2.00 Hz, 1H), 7.08-7.11(m, 1H), 7.03-7.06 (m, 1H), 6.89 (d, *J* = 8.40 Hz, 1H), 4.30 (t, *J* = 4.40 Hz, 2H), 3.79 (s, 3H), 3.68 (t, *J* = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.7 (C=O), 149.0, 147.8, 135.1, 131.0, 130.5, 123.6, 122.9, 122.8, 122.7, 120.9, 118.9, 117.1, 64.5, 51.8, 47.9; IR (KBr) ν_{max} / cm^{-1} 3068, 3037, 2916, 2879, 2823, 1717, 1589, 1510, 1473, 1441, 1371, 879, 762, 693; MS(EI): m/z=305 $[M+2]^+$, 303 $[M]^+$, 288 $[M-CH_3]^+$, 272 $[M-OCH_3]^+$, 244 $[M-COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{16}H_{14}{}^{35}ClNNaO_3$ $[M+Na]^+$ 326.0554, found: 326.0559.



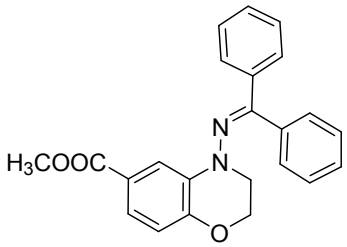
N,N'-biphenyl-bis-(6-methoxycarbonyl-3,4-dihydro-2H-1,4- benzoxazine (4v)

White solid, (yield: 429 mg, 80 %), Mp ＞200 ℃, R_f = 0.29 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, DMSO-d_6) δ: ppm 7.74 (d, *J* = 8.40 Hz, 4H), 7.50 (d, *J* = 2.00 Hz, 2H), 7.33-7.37 (m, 6H), 6.93 (d, *J* = 8.40 Hz, 2H), 4.34 (t, *J* = 4.00 Hz, 4H), 3.74(d, *J* = 4.00 Hz, 4H), 3.71 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: ppm 166.0 (C=O), 148.6, 144.9, 134.9, 132.2, 127.5, 123.5, 121.9, 121.5, 117.0, 116.6, 64.8, 51.8, 47.2; IR (KBr) ν_{max} / cm^{-1} 3060, 3035, 2981, 2950, 2896, 2852, 1713, 1600, 1579, 1508, 1494, 1437, 1371, 1336, 1297, 1244, 1210, 1113, 1049, 822, 762; MS (ESI): m/z = 537 $[M+H]^+$; HRMS (ESI-TOF) calcd. for $C_{32}H_{28}N_2NaO_6$ $[M+Na^+]$ 559.1840, found: 559.1835.



6-methoxycarbonyl-4-(1-naphthyl)-3, 4-dihydro-2H-1, 4-benzoxazine (4w)

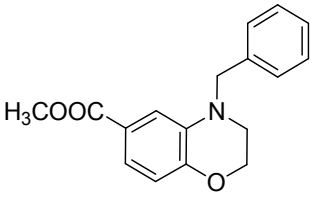
Pink solid, (yield: 249 mg, 78 %), Mp 130～132 ℃, R_f =0.59 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.98 (d, *J* = 8.00 Hz, 1H), 7.91 (d, *J* = 7.60 Hz, 1H), 7.79 (t, *J* = 8.40 Hz, 1H), 7.45-7.54 (m, 3H), 7.35-7.41(m, 2H), 6.96 (d, *J* = 2.00 Hz, 1H), 6.91 (d, *J* = 8.40 Hz, 1H), 4.50 (m, 1H), 4.40 (m, 1H), 3.71-3.77 (m, 2H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.9 (C=O), 148.3, 143.1, 135.1, 134.7, 130.5, 128.6, 126.9, 126.5, 126.4, 126.3, 124.1, 123.2, 123.1, 121.1, 117.3, 116.5, 64.9, 51.6, 49.2; MS(EI): m/z= 319 $[M]^+$, 304 $[M\text{-}CH_3]^+$, 288 $[M\text{-}OCH_3]^+$, 260 $[M\text{-}COOCH_3]^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3052, 2999, 2949, 2873, 2844, 1704, 1605, 1580, 1510, 1461, 1439, 1397, 1320, 1291, 1260, 1241, 1127, 1039, 850, 776, 716; HRMS (ESI-TOF) calcd. for $C_{20}H_{17}NNaO_3$ $[M+Na]^+$ 342.1101, found: 342.1101.



4-((diphenylmethylene)amino)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (4x)

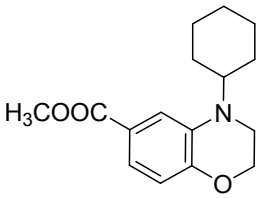
Yellow solid, (yield: 316 mg, 85 %), Mp 117～119 ℃, R_f =0.44 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.93 (d, *J* = 2.00 Hz, 1H), 7.62 (d, *J* = 7.20 Hz, 2H), 7.51 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.33-7.44 (m, 8H), 6.80 (d, *J* = 8.40 Hz, 1H), 4.02 (t, *J* = 4.40 Hz, 2H), 3.84 (s, 3H), 3.14 (t, *J* = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.2(C=O), 161.4, 148.3, 138.4, 136.3, 135.1, 129.8, 129.2, 128.7, 128.6, 128.5, 128.1, 123.6, 122.7, 117.7, 115.9, 64.5, 51.8, 48.1; MS(EI): m/z=372$[M]^+$, 341$[M\text{-}OCH_3]^+$, 313$[M\text{-}COOCH_3]^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3056, 3029, 2992, 2954, 2886, 1705, 1592, 1505, 1459, 1440, 1312, 1268, 1228, 782, 765, 694; HRMS (ESI-TOF) calcd. for $C_{23}H_{20}N_2NaO_3$ $[M+Na]^+$ 395.1366, found: 395.1366.

III-3 Characterization Data for Products (Table 3, 6a-6d)



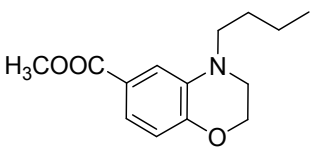
4-benzyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (6a)

Faint yellow oil, (yield: 232 mg, 82 %), R_f=0.62 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.44 (d, *J* = 1.60 Hz, 1H), 7.26-7.37 (m, 6H), 6.80 (d, *J* = 8.40 Hz, 1H), 4.47 (s, 2H), 4.26 (t, *J* = 4.40 Hz, 2H), 3.84(s, 3H), 3.29 (t, *J* = 4.40 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.2(C=O), 148.0, 137.3, 135.2, 128.7, 127.4, 127.3, 123.2, 120.1, 116.1, 113.6, 64.9, 54.6, 51.8, 46.1; MS(EI): m/z=283 $[M]^+$, 252 $[M\text{-}OCH_3]^+$, 224 $[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{17}H_{17}NNaO_3$ $[M+Na]^+$ 306.1101, found: 306.1099.



4-cyclohexyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (6b)

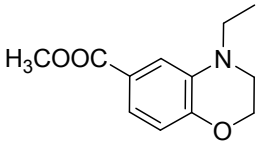
Faint yellow oil, (yield: 165 mg, 60 %), R_f=0.38 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.39 (d, *J* = 1.20 Hz, 1H), 7.28 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 6.74 (d, *J* = 8.40 Hz, 1H), 4.22 (t, *J* = 4.40 Hz, 2H), 3.85 (s, 3H), 3.64(m, 1H), 3.26 (t, *J* = 4.40 Hz, 2H), 1.38-1.85 (m, 10H); MS(EI): m/z=275$[M]^+$, 244$[M\text{-}OCH_3]^+$, 216$[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{16}H_{22}NO_3$ $[M+H]^+$ 276.1594, found: 276.1590.



4-butyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (6c)

Colourless oil, (yield: 154 mg, 62 %), R_f=0.64 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ:

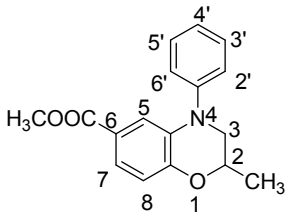
ppm 7.32 (d, J = 1.60 Hz, 1H), 7.29 (dd, J_1 = 8.00 Hz, J_2 = 2.00 Hz, 1H), 6.74 (d, J = 8.00 Hz, 1H), 4.25 (t, J = 4.40 Hz, 2H), 3.84 (s, 3H), 3.30 (t, J = 4.40 Hz, 2H), 3.26 (t, J = 7.20 Hz, 2H), 1.56(m, 2H), 1.37 (m, 2H), 0.94 (t, J = 7.20 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.4 (C=O), 148.0, 134.9, 123.2, 119.3, 115.8, 113.1, 64.8, 51.7, 50.5, 46.3, 29.6, 28.0, 20.3, 13.9; MS(EI): m/z= 249 $[M]^+$, 218 $[M\text{-}OCH_3]^+$, 190 $[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{14}H_{19}NNaO_3$ $[M+Na]^+$ 272.1257, found: 272.1264.



4-ethyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (6d)

Colourless oil, (yield: 144 mg, 65 %), R_f=0.56 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.33 (d, J = 1.60 Hz, 1H), 7.29 (dd, J_1 = 8.00 Hz, J_2 = 2.00 Hz, 1H), 6.74 (d, J = 8.00 Hz, 1H), 4.26 (t, J = 4.40 Hz, 2H), 3.83 (s, 3H), 3.36(q, J = 7.20 Hz, 2H), 3.28 (t, J = 4.40 Hz, 2H), 1.38 (t, J = 7.40 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.4(C=O), 148.3, 134.5, 123.2, 119.7, 115.9, 113.3, 64.8, 51.8, 45.3, 44.8, 10.3; MS(EI): m/z=221 $[M]^+$, 206 $[M\text{-}CH_3]^+$, 190 $[M\text{-}OCH_3]^+$, 162 $[M\text{-}COOCH_3]^+$, 77.

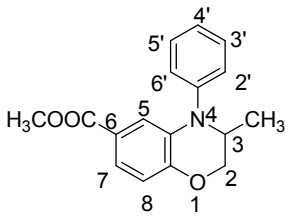
III-4 Characterization Data for Products Table 4 (7 and 8)



6-methoxycarbonyl-2-methyl-4-phenyl-3, 4-dihydro-2H-1, 4-benzoxazine (7a)

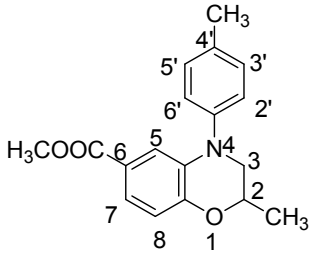
Colourless oil, (yield: 7a+8a, 85 %), ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.61 (d, J = 1.20 Hz, 1H, 5-H), 7.42-7.46 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H, 7-H), 7.07-7.38 (m, 5H, Ar-H′), 6.87 (d, J = 8.40 Hz, 1H, 8-H), 4.34 (m, 1H, 2-H), 3.77 (s, 3H, $COOCH_3$), 3.67 (m, 1H, 3-H), 3.37 (m, 1H, 3-H), 1.37 (d, J = 6.40 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.0(C=O), 116.6-148.9 (Ar-C, 10C), 70.0 (OCH_3, C), 53.8, 51.7, 18.2; MS (EI): m/z =283$[M]^+$, 268$[M\text{-}CH_3]^+$, 252$[M\text{-}OCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{17}H_{17}NNaO_3$ $[M+Na]^+$ 306.1101, found:

306.1104.



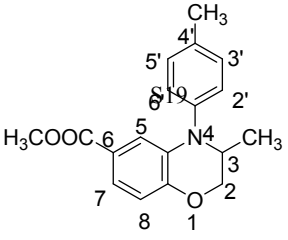
6-methoxycarbonyl-3-methyl-4-phenyl-3, 4-dihydro-2H-1, 4-benzoxazine (8a)

Colourless oil, (yield: 7a+8a, 85%), ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.40-7.46 (m, 2H, 5-H and 7-H), 7.07-7.38 (m, 5H, Ar-H′), 6.88 (d, J = 8.80 Hz, 1H, 8-H), 4.17(m, 1H, 2-H), 4.14(m, 1H, 2-H) 3.84 (m, 1H, 3-H), 3.76 (s, 3H, $COOCH_3$), 1.21 (d, J = 6.80 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.0(C=O), 116.6-148.9 (Ar-C, 10C), 68.9(OCH_3, C), 52.6, 51.7, 16.6; MS (EI): m/z =283$[M]^+$, 268$[M\text{-}CH_3]^+$, 252$[M\text{-}OCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{17}H_{17}NNaO_3$ $[M+Na]^+$ 306.1101, found: 306.1104.



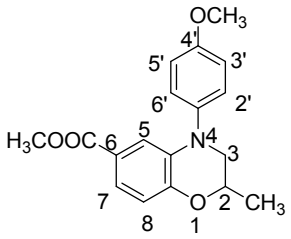
2-methyl-4-(4-methylphenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (7b)

Colourless oil, (yield: 7b+8b, 86%), ^{1}H NMR (400 MHz, DMSO-d_6) δ: ppm 7.33 (d, J = 2.00 Hz, 1H, 5-H), 7.28-7.30 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H, 7-H), 7.10-7.25 (m, 4H, Ar-H′), 6.87-6.89 (d, J = 8.40 Hz, 1H, 8-H), 4.35(m, 1H, 2-H), 3.68 (s, 3H, $COOCH_3$), 3.63(m, 1H, 3-H) 3.31 (m, 1H, 3-H), 2.29(s, 3H, Ar-CH_3), 1.30 (d, J = 6.40 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ: ppm 166.0 (C=O), 115.5-148.2 (Ar-C, 10C), 68.9 (OCH_3, 1C), 52.9, 51.7, 20.5, 17.9; MS (EI): m/z =297$[M]^+$, 282$[M\text{-}CH_3]^+$, 266$[M\text{-}OCH_3]^+$, 238$[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{18}H_{19}NNaO_3$ $[M+Na]^+$ 320.1257, found: 320.1257.



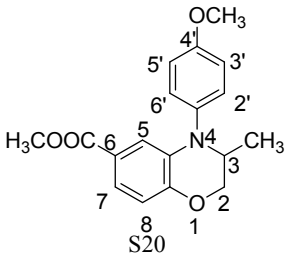
3-methyl-4-(4-methylphenyl)-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (8b)

Colourless oil, (yield: 7b+8b, 86%),^{1}H NMR (400 MHz, DMSO-d_6) δ: ppm 7.23-7.27 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H, 7-H), 7.10-7.25 (m, 4H, Ar-H′), 7.10 (d, J = 1.60 Hz, 1H, 5-H), 6.86-6.88 (d, J = 8.40 Hz, 1H, 8-H), 4.18 (m, 1H, 2-H), 4.13 (m, 1H, 2-H), 3.84 (m, 1H, 3-H), 3.67 (s, 3H, $COOCH_3$), 2.30 (s, 3H, Ar-CH_3), 1.06 (d, J = 6.40 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ: ppm 166.0 (C=O), 115.5-148.2 (Ar-C, 10C), 70.2 (OCH_3, 1C), 51.8, 51.7, 20.4, 16.1; MS (EI): m/z =297$[M]^+$, 282$[M\text{-}CH_3]^+$, 266$[M\text{-}OCH_3]^+$, 238$[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{18}H_{19}NNaO_3$ $[M+Na]^+$ 320.1257, found: 320.1257.



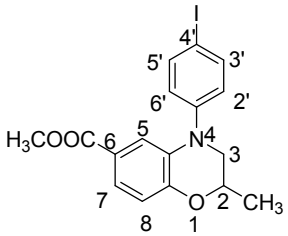
4-(4-methoxyphenyl)-2-methyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (7c)

Colourless oil, (yield: 7c+8c, 86%),^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.37-7.40 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H, 7-H), 7.33-7.36 (1H, 5-H), 6.90-6.93(m, 4H, Ar-H′), 6.83-6.85 (d, J = 8.00 Hz, 1H, 8-H), 4.36 (m, 1H, 2-H), 3.80 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.56 (m, 1H, 3-H), 3.38(m, 1H, 3-H), 1.37 (d, J = 6.00 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.0 (C=O), 114.9-157.5 (Ar-C, 10C), 70.0 (OCH_3, 1C), 55.3, 54.4, 51.6, 18.2; MS (EI): m/z =313$[M]^+$, 298$[M\text{-}CH_3]^+$, 282$[M\text{-}OCH_3]^+$, 254$[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{18}H_{19}NNaO_4$ $[M+Na]^+$ 336.1206, found:336.1209.



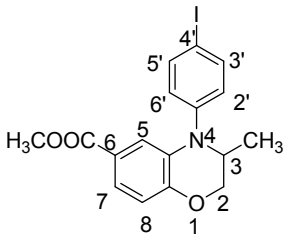
4-(4-methoxyphenyl)-3-methyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (8c)

Colourless oil, (yield: 7c+8c, 86%), ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.33-7.36 (1H, 7-H), 7.10-7.14 (1H, 5-H), 7.10-7.14 (m, 4H, Ar- H′), 6.83-6.85 (d, *J* = 8.00 Hz, 1H, 8-H), 4.23 (m, 1H, 2-H), 4.10 (m, 1H, 2-H), 3.80 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.72-3.81 (m, 1H, 3-H), 1.12 (d, *J* = 6.40 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 167.0 (C=O), 114.9-157.5 (Ar-C, 10C), 69.5 (OCH_3, 1C), 55.3, 52.4, 51.6, 16.4; MS (EI): m/z =313$[M]^+$, 298$[M\text{-}CH_3]^+$, 282$[M\text{-}OCH_3]^+$, 254$[M\text{-}COOCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{18}H_{19}NNaO_4$ $[M+Na]^+$ 336.1206, found: 336.1209.



4-(4-iodophenyl)-2-methyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (7d)

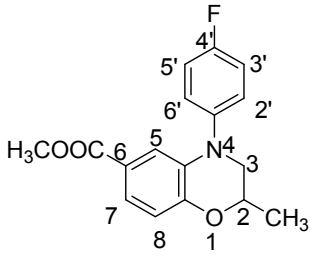
Brown oil, (yield: 7d+8d, 74%),^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.61-7.65 (2H, Ar-H′), 7.61-7.65 (1H, 5-H), 7.44-7.49 (1H, 7-H), 6.93-6.96 (2H, Ar-H′), 6.87-6.99 (d, *J* = 8.40 Hz, 1H, 8-H), 4.30 (m, 1H, 2-H), 3.78 (s, 3H, OCH_3), 3.61-3.65 (m, 1H, 3-H), 3.33-3.36 (m, 1H, 3-H), 1.36 (d, *J* = 6.00 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.8 (C=O), 116.8-149.1 (Ar-C, 10C), 70.0, 53.4, 51.8, 16.5; MS(EI): m/z=409$[M]^+$, 394$[M\text{-}CH_3]^+$, 378$[M\text{-}OCH_3]^+$, 77; HRMS (ESI-TOF) calcd. for $C_{17}H_{16}INNaO_3$ $[M+Na]^+$ 432.0067, found: 432.0062.



4-(4-iodophenyl)-3-methyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (8d)

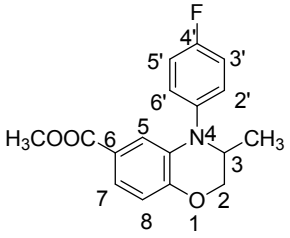
Brown oil, (yield: 7d+8d, 74%),^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.61-7.65 (2H, Ar-H′), 7.44-7.49 (2H, 7-H and 5-H), 6.93-6.96 (2H, Ar-H′), 6.86-6.98 (d, *J* = 8.40 Hz, 1H, 8-H), 4.12-4.14(m, 2H, 2-H), 3.83 (m, 1H, 3-H), 3.77 (s, 3H, OCH_3), 1.22 (d, *J* = 6.80 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.8 (C=O), 116.8-149.1 (Ar-C, 10C), 68.7, 52.6, 51.8, 18.1; MS(EI):

m/z=409[M]$^+$, 394[M-CH_3]$^+$, 378[M-OCH_3]$^+$, 77; HRMS (ESI-TOF) calcd. for $C_{17}H_{16}INNaO_3$ [M+Na]$^+$ 432.0067, found: 432.0062.



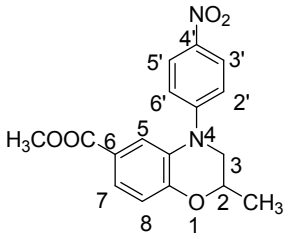
4-(4-fluorophenyl)-2-methyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (7g)

Faint yellow oil, (yield: 7g+8g, 70%), ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.38-7.44 (1H, 7-H), 7.19 (d, *J* = 2.00 Hz, 1H, 5-H), 7.13-7.17 (2H, Ar-H′), 7.03-7.09 (2H, Ar-H′), 6.86(d, *J* = 8.00 Hz, 1H, 8-H), 4.34 (m, 1H, 2-H), 3.76 (s, 3H, OCH_3), 3.56-3.59 (m, 1H, 3-H), 3.34-3.38 (m, 1H, 3-H), 1.37 (d, *J* = 6.00 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.9 (C=O), 121.2-161.4 (Ar-C, 9C), 116.2-116.9 (4′Ar-C), 70.0, 54.3, 51.7, 18.2; MS(EI): m/z=301[M]$^+$, 286[M-CH_3]$^+$, 270[M-OCH_3]$^+$, 77; HRMS (ESI-TOF) calcd. for $C_{17}H_{16}FNNaO_3$ [M+Na]$^+$ 324.1006, found: 324.1004.



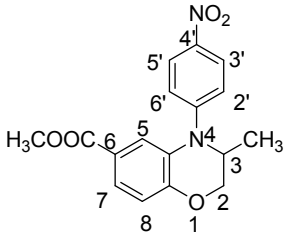
4-(4-fluorophenyl)-3-methyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (8g)

Faint yellow oil, (yield: 7g+8g, 70%),^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.38-7.44 (2H, 7-H and 8-H), 7.13-7.17 (2H, Ar-H′), 7.03-7.09 (2H, Ar-H′), 6.86 (d, *J* = 8.00 Hz, 1H, 8-H), 4.19-4.22 (m, 1H, 2-H), 4.08-4.12 (m, 1H, 2-H), 3.75-3.82 (m, 1H, 3-H), 3.76 (s, 3H, OCH_3), 1.15 (d, *J* = 6.40 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.9 (C=O), 121.2-161.4 (Ar-C, 9C), 116.2-116.9 (4′Ar-C), 69.2, 52.7, 51.7, 16.4; MS(EI): m/z=301[M]$^+$, 286[M-CH_3]$^+$, 270[M-OCH_3]$^+$, 77; HRMS (ESI-TOF) calcd. for $C_{17}H_{16}FNNaO_3$ [M+Na]$^+$ 324.1006, found: 324.1004.



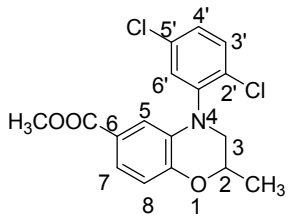
6-methoxycarbonyl-2-methyl-4-(4-nitrophenyl)-3, 4-dihydro-2H-1, 4-benzoxazine (7i)

Yellow oil，(yield: 7i+8i, 68%), ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 8.15-8.17 (d, J = 9.20 Hz, 2H, 3-H′ and 5-H′), 7.87 (d, J = 2.00 Hz, 1H, 5-H), 7.60-7.62 (dd, J_1 = 8.40 Hz, J_2 = 1.60 Hz, 1H, 7-H 1H), 7.20-7.23 (d, J = 9.20 Hz, 2H, 2-H′ and 6-H′), 6.95-6.97 (d, J = 8.40 Hz, 1H, 8-H) 4.33-4.36(m, 1H, 2-H), 3.87 (m, 1H, 3-H), 3.83 (s, 3H, OCH_3), 3.37-3.43 (m, 1H, 3-H), 1.38 (d, J = 6.40 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.4 (C=O), 117.5-151.6 (Ar-C, 10C), 70.7, 52.3, 51.9, 18.1; MS(EI): m/z=328$[M]^+$, 313$[M\text{-}CH_3]^+$, 297$[M\text{-}OCH_3]^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3109, 3074, 2985, 2943, 2840, 1718, 1587, 1493, 1436, 1385, 1332, 1257, 1153, 1110, 1072, 842, 761; HRMS (ESI-TOF) calcd. for $C_{17}H_{16}N_2NaO_5$ $[M+Na]^+$ 351.0951, found: 351.0950.



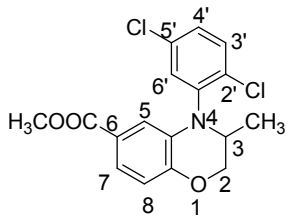
6-methoxycarbonyl-3-methyl-4-(4-nitrophenyl)-3, 4-dihydro-2H-1, 4-benzoxazine (8i)

Yellow oil，(yield: 7i+8i, 68%), ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 8.14-8.16 (d, J = 9.20 Hz, 2H, 3-H′ and 5-H′), 7.86 (d, J = 1.60 Hz, 1H, 5-H), 7.60-7.62 (dd, J_1 = 8.40 Hz, J_2 = 1.60 Hz, 1H, 7-H 1H), 7.20-7.23 (d, J = 9.20 Hz, 2H, 2-H′ and 6-H′), 6.92-6.95 (d, J = 8.40 Hz, 1H, 8-H), 4.18-4.21(m, 2H, 2-H), 4.09-4.11 (m, 1H, 3-H), 3.83 (s, 3H, OCH_3), 1.36 (d, J = 7.60 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: ppm 166.4 (C=O), 117.5-151.6 (Ar-C, 10C), 68.7, 52.0, 51.9, 16.0; MS(EI): m/z=328$[M]^+$, 313$[M\text{-}CH_3]^+$, 297$[M\text{-}OCH_3]^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3109, 3074, 2985, 2943, 2840, 1718, 1587, 1493, 1436, 1385, 1332, 1257, 1153, 1110, 1072, 842, 761; HRMS (ESI-TOF) calcd. for $C_{17}H_{16}N_2NaO_5$ $[M+Na]^+$ 351.0951, found: 351.0950.



4-(2, 5-dichlorophenyl)-2-methyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (7n)

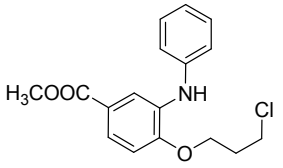
Brown oil, (yield: 7n+8n, 61%), ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.39-7.46 (m, 2H, 5-H and 7-H), 7.17(d, J = 8.40 Hz, 1H, 8-H), 6.88 (d, J = 8.40 Hz, 1H, 3-H′), 6.74 (d, J = 2.0 Hz, 1H, 6-H′), 6.62-6.65 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H, 4-H′), 4.31 (m, 1H, 2-H), 3.77 (s, 3H, $COOCH_3$), 3.48 (m, 1H, 3-H), 3.39 (m, 1H, 3-H), 1.40 (d, J = 6.40 Hz, 3H, CH_3); MS(EI): m/z=353[M+2] $^+$, 351[M]$^+$, 336[M-CH_3]$^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3076, 2973, 1708, 1620, 1580, 1512, 1433, 1347, 1300, 1255, 1209, 1096, 1048, 871, 763; HRMS (ESI-TOF) calcd. for $C_{17}H_{15}Cl_2NNaO_3$ [M+Na]$^+$ 374.0321, found: 374.0323.



4-(2, 5-dichlorophenyl)-3-methyl-6-methoxycarbonyl-3, 4-dihydro-2H-1, 4-benzoxazine (8n)

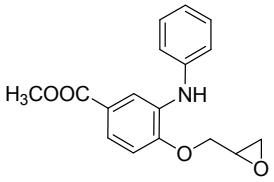
Brown oil, (yield: 7n+8n, 61%), ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.39-7.46 (1H, 5-H), 7.26-7.32(1H, 7-H), 7.11-7.13 (2H, 8-H and 3-H′), 7.02 (1H, 6-H′), 6.87-6.89 (1H, 4-H′), 4.09-4.14 (m, 2H, 2-H), 3.88 (m, 1H, 3-H), 3.77 (s, 3H, $COOCH_3$), 1.16 (d, J = 6.40 Hz, 3H, CH_3); MS(EI): m/z=353 [M+2]$^+$, 351 [M]$^+$, 336 [M-CH_3]$^+$, 77; IR (KBr) ν_{max} / cm^{-1} 3076, 2973, 1708, 1620, 1580, 1512, 1433, 1347, 1300, 1255, 1209, 1096, 1048, 871, 763; HRMS (ESI-TOF) calcd. for $C_{17}H_{15}Cl_2NNaO_3$ [M+Na]$^+$ 374.0321, found: 374.0323.

Ⅲ-5 Characterization Data for Products 9c-9e(Scheme 2) and intermediate (Ⅱ)



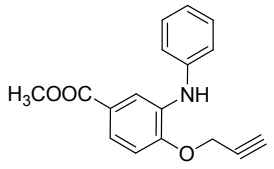
methyl 4-(3-chloropropoxy)-3-(phenylamino)benzoate (9c)

Colourless oil, (yield: 287 mg, 90 %), ^{1}H NMR (400 MHz, DMSO-d_6) δ: ppm 7.73 (d, J = 2.00 Hz, 1H), 7.47-7.49 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.46 (s, 1H, NH), 7.24-7.28 (t, J = 8.00 Hz, 2H), 7.09 (d, J = 8.00 Hz, 2H), 7.06 (d, J = 8.80 Hz, 1H), 6.89 (t, J = 7.60 Hz, 1H), 4.17 (t, J = 6.00 Hz, 2H), 3.82 (t, J = 6.40 Hz, 2H), 3.77 (s, 3H), 2.16-2.22 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: ppm 166.2 (C=O), 152.0, 142.8, 133.0, 129.1, 122.2, 121.9, 120.8, 118.8, 115.8, 111.4, 65.1, 51.8, 42.2, 31.7; MS(EI): m/z=319 $[M]^+$, 288 $[M\text{-}OCH_3]^+$, 242 $[M\text{-}C_3H_6Cl]^+$, 77. HRMS (ESI-TOF) calcd. for $C_{17}H_{18}ClNNaO_3$ $[M+Na]^+$ 342.0867, found 342.0867,



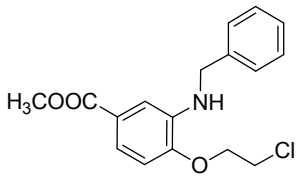
methyl 4-(2,3-epoxypropoxyl)-3-(phenylamino)benzoate (9d)

Colourless oil, (yield: 278 mg, 93 %), ^{1}H NMR (400 MHz, DMSO-d_6) δ: ppm 7.76 (d, J = 2.00 Hz, 1H), 7.46-7.48 (dd, J_1 = 8.40 Hz, J_2 = 2.00 Hz, 1H), 7.48 (s, 1H, NH), 7.25 (t, J = 8.00 Hz, 2H), 7.11 (d, J = 7.60 Hz, 2H), 7.07 (d, J = 8.80 Hz, 1H), 6.88 (t, J = 7.60 Hz, 1H), 4.41-4.45 (dd, J_1 = 11.60 Hz, J_2 = 2.00 Hz, 1H), 3.95-3.99 (q, J = 6.40 Hz, 1H), 3.75 (s, 3H), 3.37-3.41 (m, 1H), 2.83 (t, J = 4.80 Hz, 1H), 2.72-2.72 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: ppm 166.2 (C=O), 152.0, 142.8, 133.1, 129.2, 129.2, 122.3, 120.8, 118.5, 116.0, 112.1, 69.8, 51.9, 49.8, 43.9; MS(EI): m/z=299 $[M]^+$, 268 $[M\text{-}OCH_3]^+$, 242 $[M\text{-}C_3H_5O]^+$, 77.



methyl 3-(phenylamino)-4-(propynoxyl)benzoate (9e)

Colourless oil, (yield: 267 mg, 95 %), ^{1}H NMR (400 MHz, DMSO-d_6) δ: ppm 7.75 (d, J = 2.00 Hz, 1H), 7.54 (s, 1H, NH), 7.48-7.51 (dd, J_1 = 8.80 Hz, J_2 = 2.00 Hz, 1H), 7.25 (t, J = 8.00 Hz, 2H), 7.16 (d, J = 8.80 Hz, 1H), 7.09 (d, J = 7.60 Hz, 2H), 6.88 (t, J = 7.60 Hz, 1H), 4.95 (d, J = 2.40 Hz, 2H), 3.76 (s, 3H), 3.65 (t, J = 2.40 Hz, 1H); MS(EI): m/z=281 $[M]^+$, 242 $[M\text{-}C_3H_3]^+$, 77.



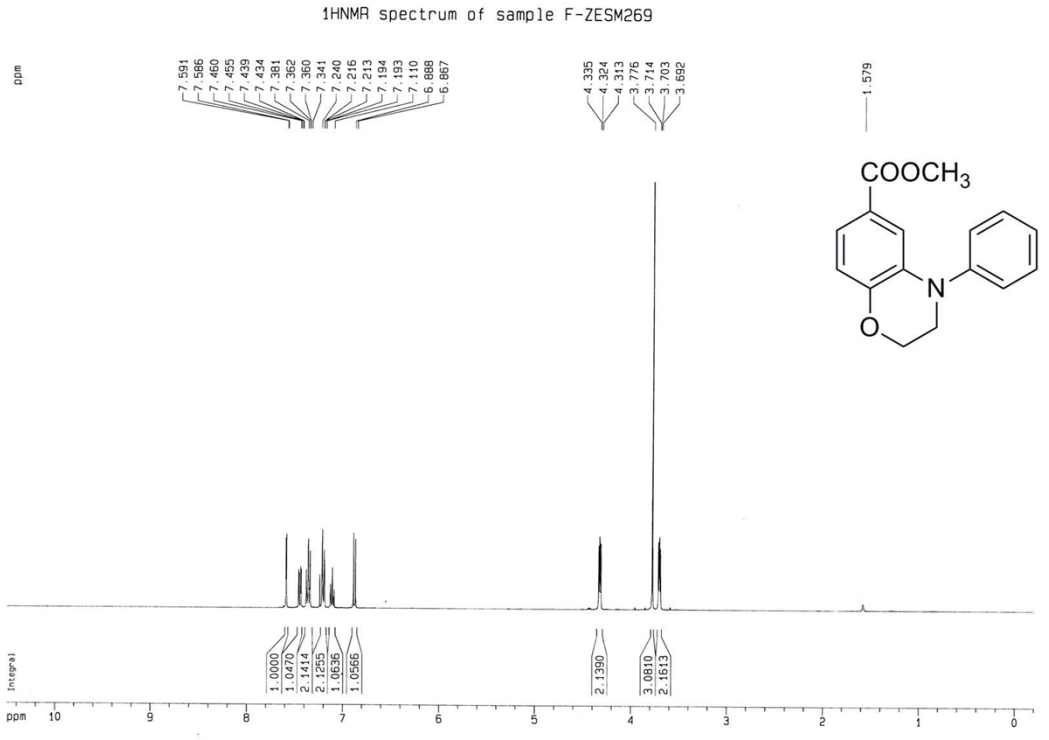
Methyl 3-(benzylamino)-4-(2-chloroethoxy)benzoate (intermediate Ⅱ)

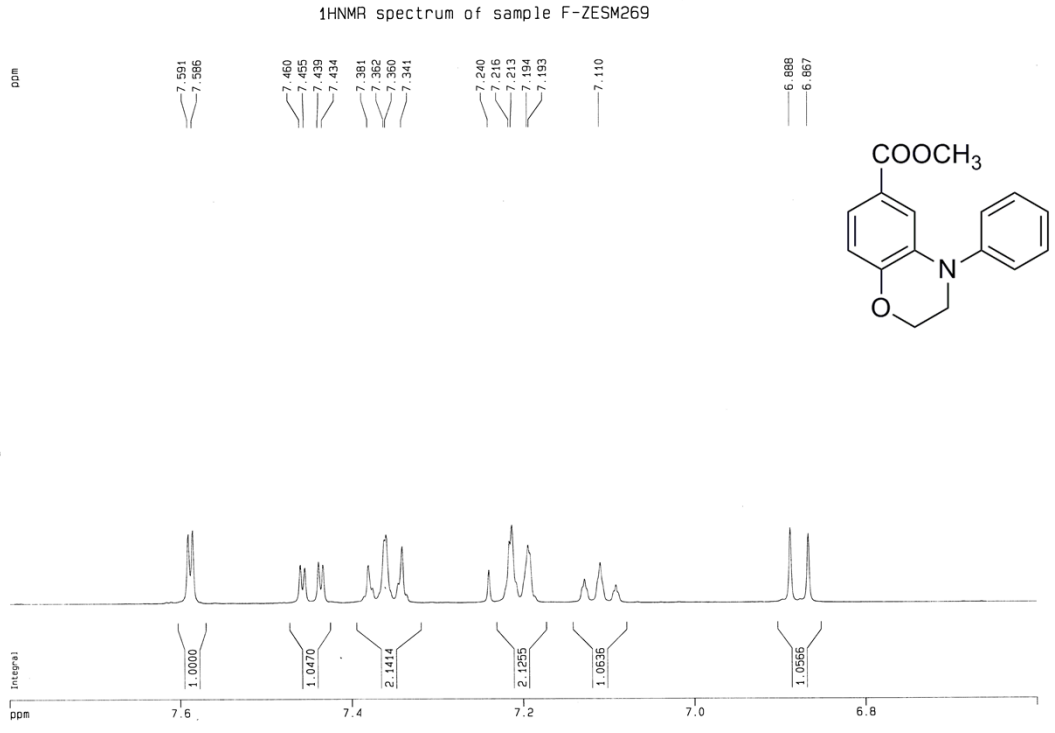
White solid, Mp 68～70℃, R_f=0.42 (EtOAc:PE =1:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ: ppm 7.29-7.34 (m, 4H), 7.16-7.24 (m, 2H), 7.01 (d, *J* = 1.20 Hz, 1H), 6.94 (d, *J* = 8.40 Hz, 1H), 5.62 (s, 1H), 4.50 (s, 2H), 4.35 (t, *J* = 5.20 Hz, 2H), 4.01 (t, *J* = 5.20 Hz, 2H), 3.72 (s, 3H); MS(EI): m/z=319$[M]^+$, 321$[M+2]^+$, 178, 91, 79. IR (KBr) ν_{max} / cm^{-1} 3435, 3027, 2945, 1712,1596, 1523, 1450, 1286, 1243, 763, 726. HRMS (ESI-TOF) calcd. for $C_{17}H_{18}ClNNaO_3$ $[M+Na]^+$ 342.0867, found 342.0867, calcd. for $C_{17}H_{18}Cl^{37}NNaO_3$ $[M+Na]^+$ 344.0844, found: 344.0842.

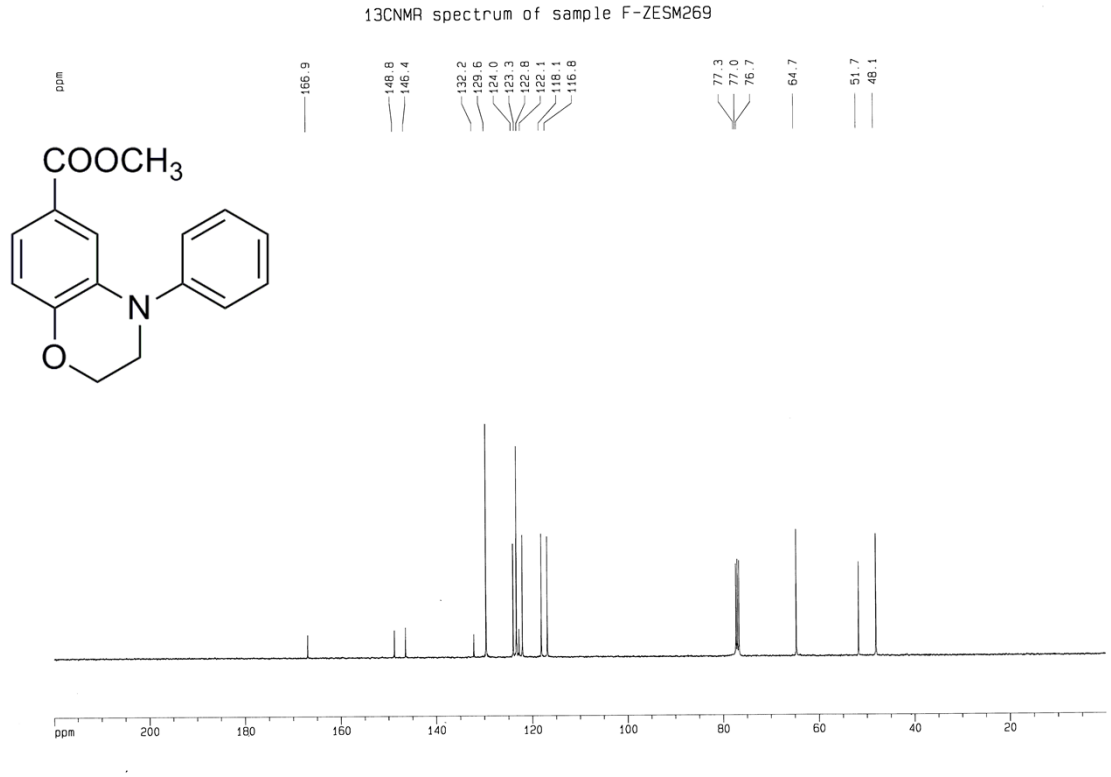
Ⅳ- ^{1}H-NMR and ^{13}C-NMR spectra of compounds

Ⅳ-1 ^{1}H-NMR and ^{13}C-NMR spectra of compounds 4a-4x

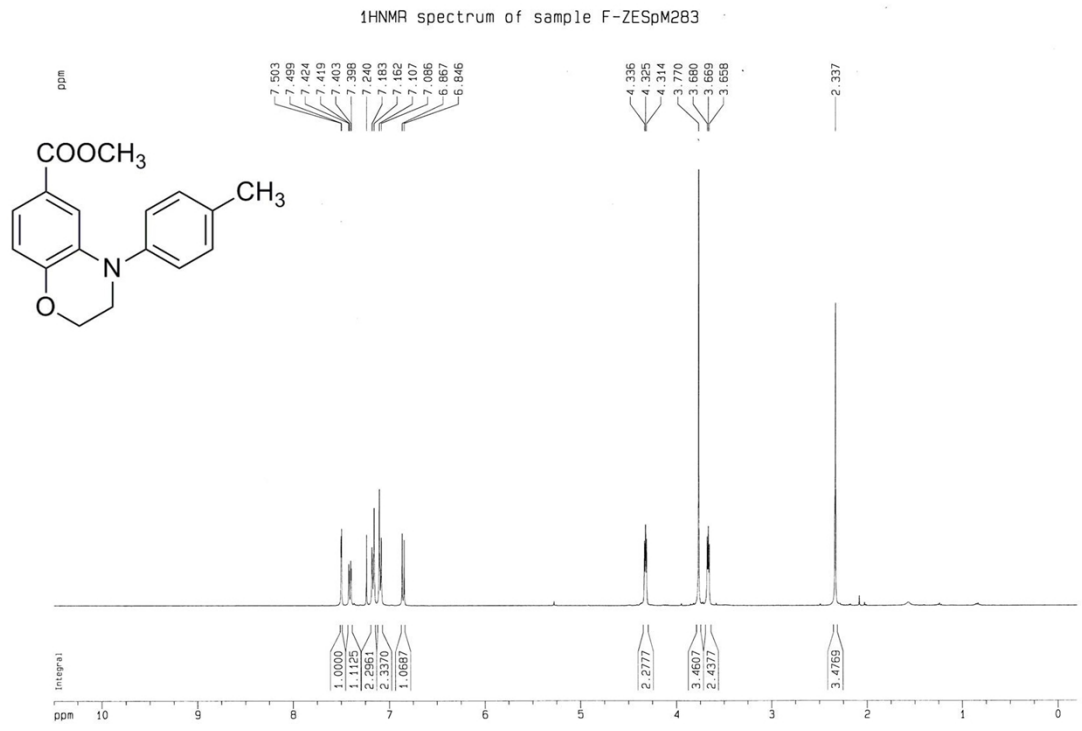
[^{1}H NMR and ^{13}C NMR spectrum of 4a in $CDCl_3$]

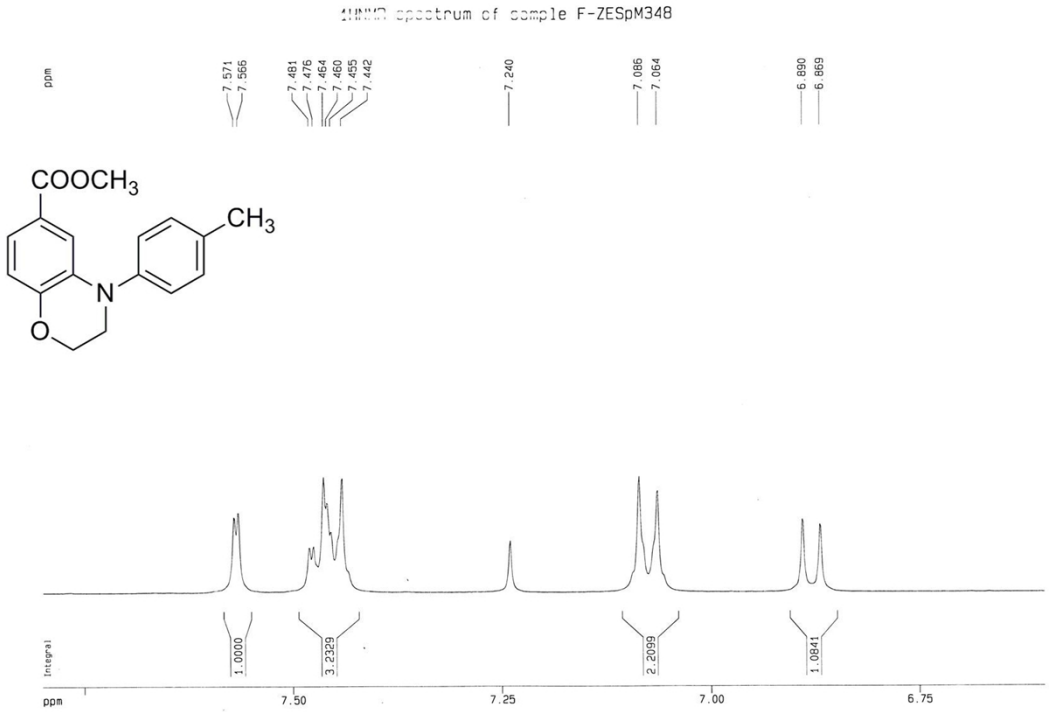

1HNMR spectrum of sample F-ZESM269
ppm
7.591
7.586
7.460
7.455
7.439
7.434
7.381
7.362
7.360
7.341
7.240
7.216
7.213
7.194
7.193
7.110
6.888
6.867
4.335
4.324
4.313
3.776
3.714
3.703
3.692
1.579
COOCH3
N
O
Integral
1.0000
1.0470
2.1414
2.1255
1.0636
1.0566
2.1390
3.0810
2.1613
ppm
10
9
8
7
6
5
4
3
2
1
0

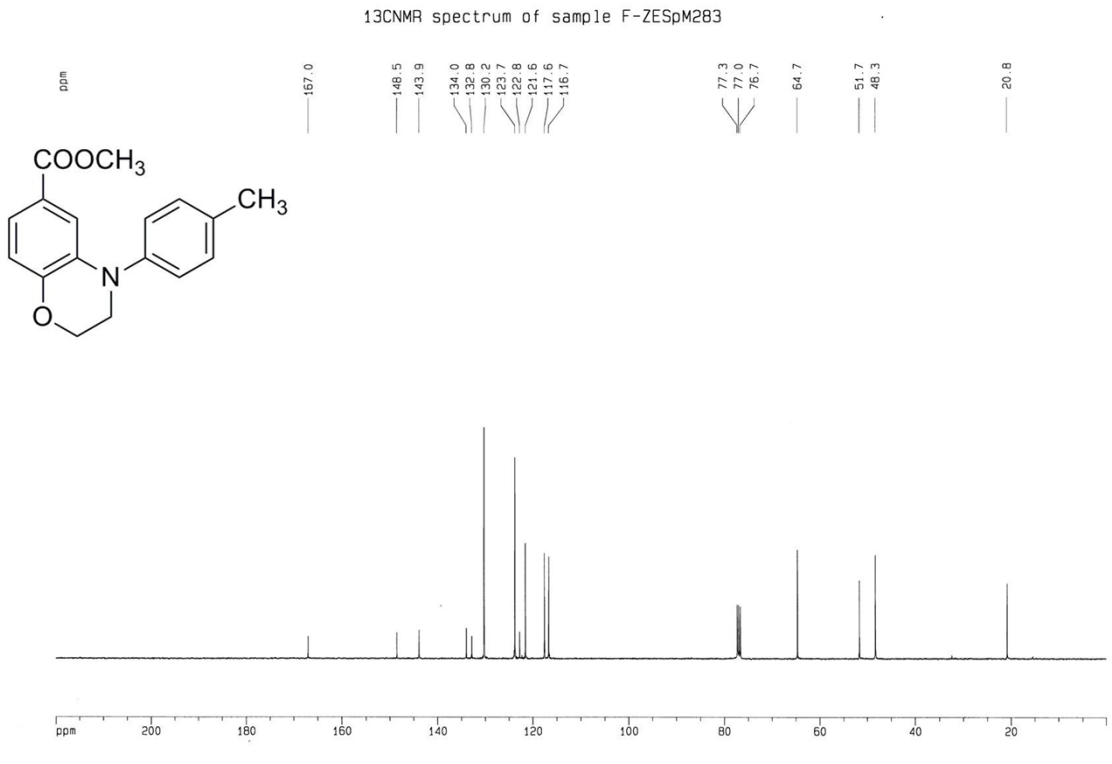

1HNMR spectrum of sample F-ZESM269
ppm
7.591
7.586
7.460
7.455
7.439
7.434
7.381
7.362
7.360
7.341
7.240
7.216
7.213
7.194
7.193
7.110
6.888
6.867
COOCH3
N
O
Integral
1.0000
1.0470
2.1414
2.1255
1.0636
1.0566
ppm
7.6
7.4
7.2
7.0
6.8



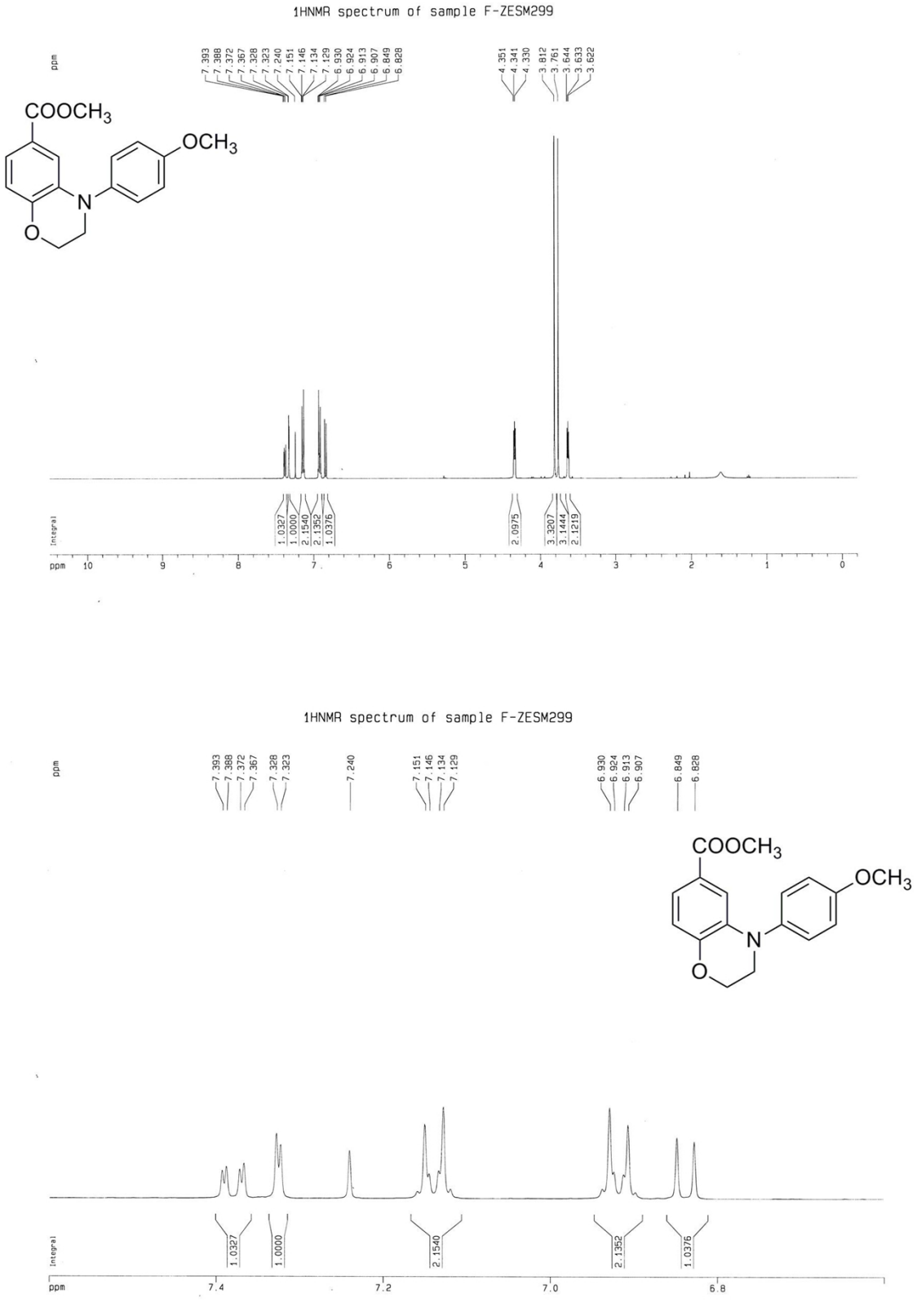
[^{1}H NMR and ^{13}C NMR spectrum of 4b in $CDCl_3$]

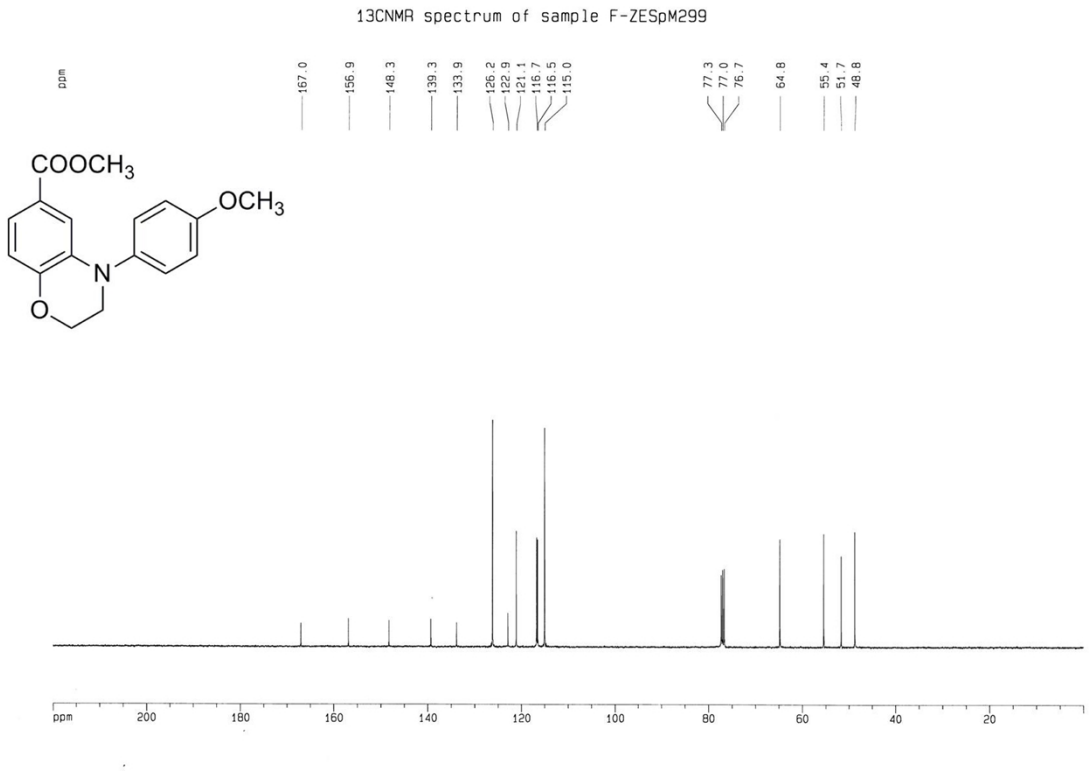



1HNMR spectrum of sample F-ZESpM348
ppm
7.571
7.566
7.481
7.476
7.464
7.460
7.455
7.442
7.240
7.086
7.064
6.890
6.869
COOCH3
CH3
N
O
Integral
1.0000
3.2329
2.2099
1.0841
ppm
7.50
7.25
7.00
6.75

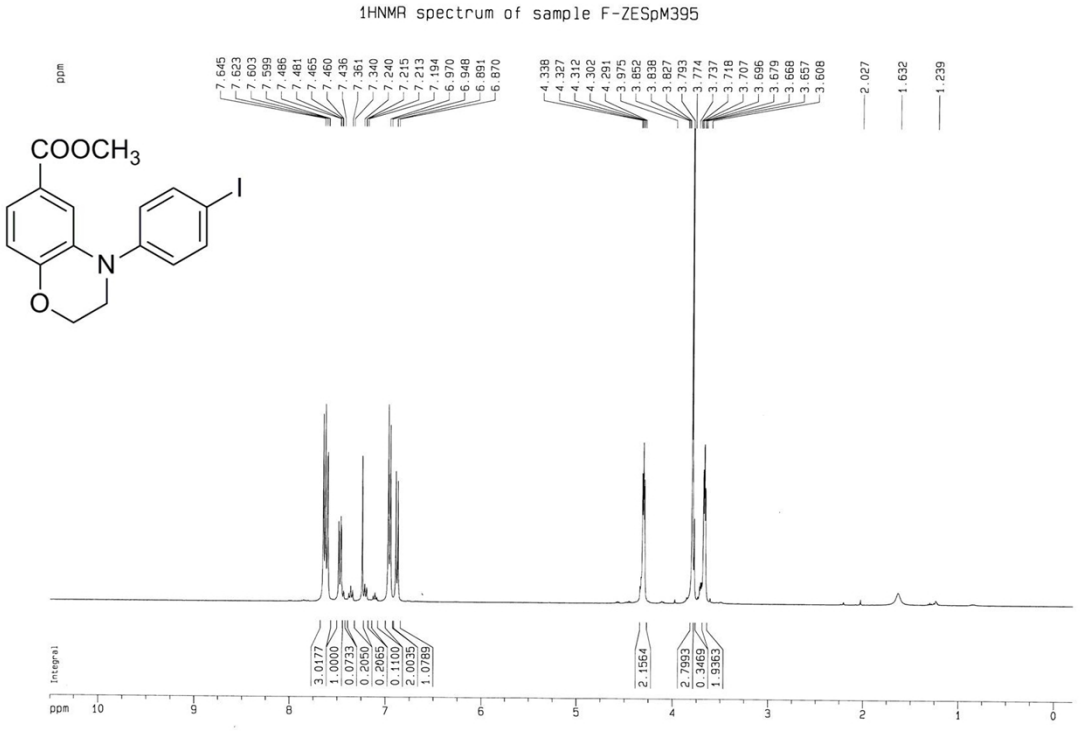

13CNMR spectrum of sample F-ZESpM283
ppm
167.0
148.5
143.9
134.0
132.8
130.2
123.7
122.8
121.6
117.6
116.7
77.3
77.0
76.7
64.7
51.7
48.3
20.8
COOCH3
CH3
N
O
ppm
200
180
160
140
120
100
80
60
40
20

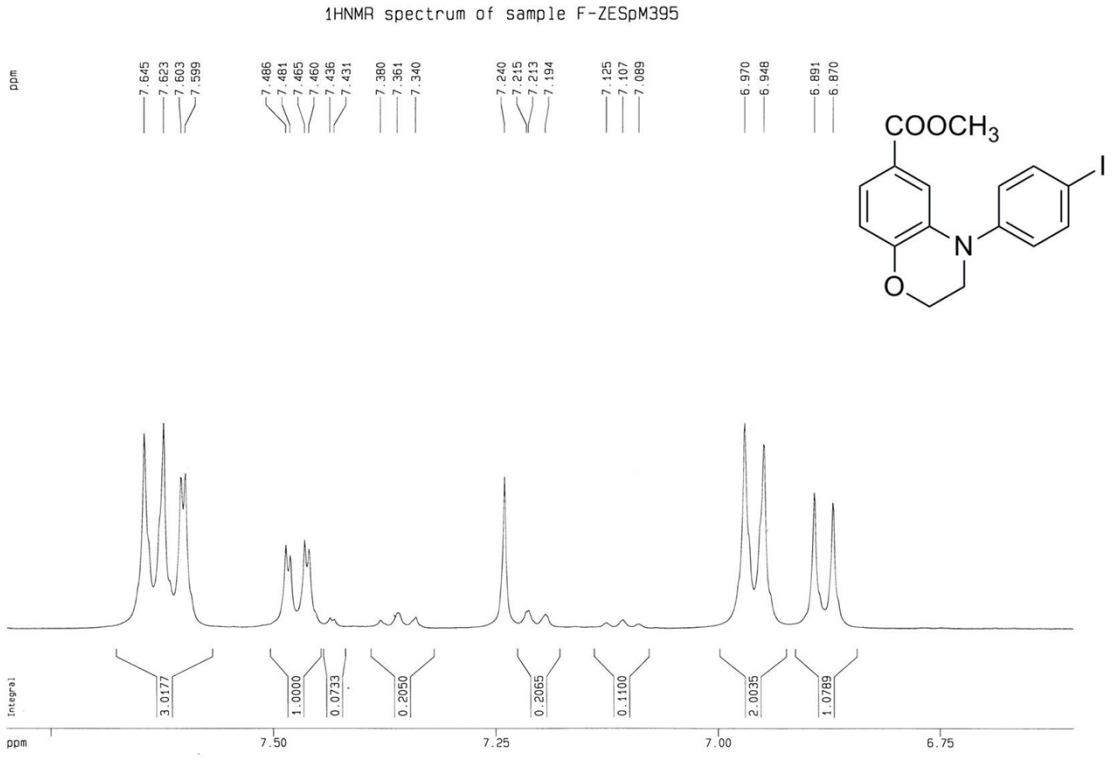
[^{1}H NMR and ^{13}C NMR spectrum of 4c in $CDCl_3$]

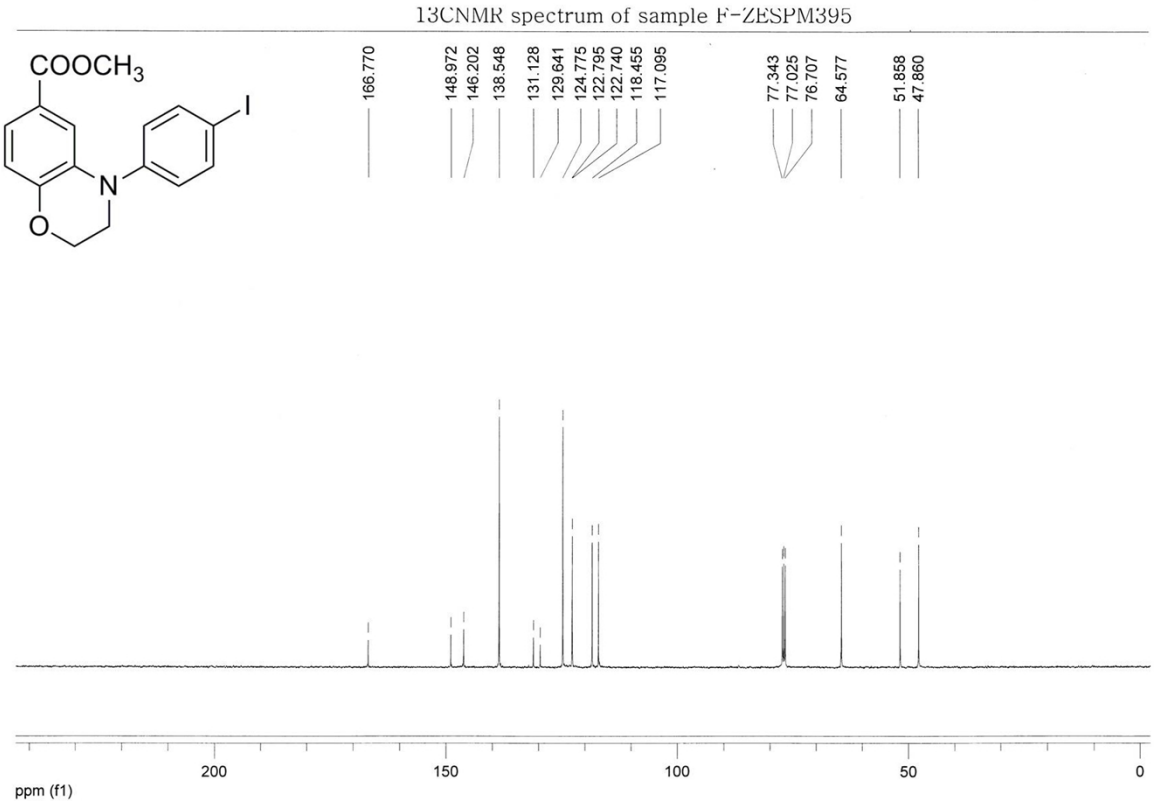




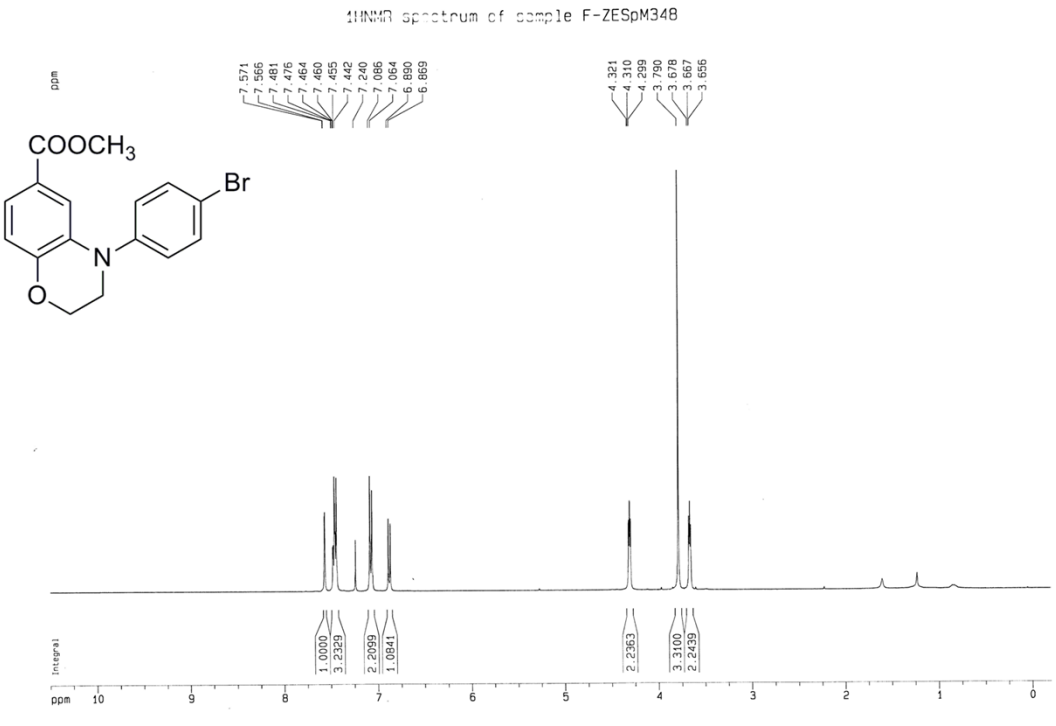
[^{1}H NMR and ^{13}C NMR spectrum of 4d in $CDCl_3$]

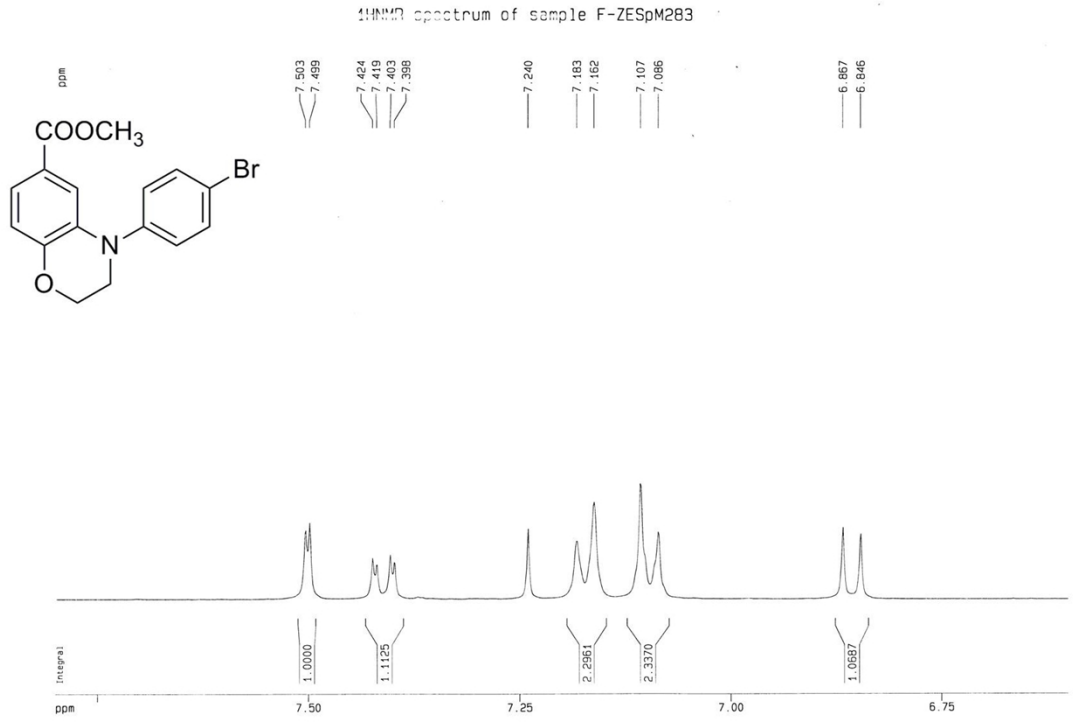

1HNMR spectrum of sample F-ZESpM395
ppm
7.645
7.623
7.603
7.599
7.486
7.481
7.465
7.460
7.436
7.361
7.340
7.240
7.215
7.213
7.194
6.970
6.948
6.891
6.870
4.338
4.327
4.312
4.302
4.291
3.975
3.852
3.838
3.827
3.793
3.774
3.737
3.718
3.707
3.696
3.679
3.668
3.657
3.608
2.027
1.632
1.239
COOCH3
I
N
O
Integral
3.0177
1.0000
0.0733
0.2050
0.2065
0.1100
2.0035
1.0789
2.1564
2.7993
0.3469
1.9363
ppm
10
9
8
7
6
5
4
3
2
1
0

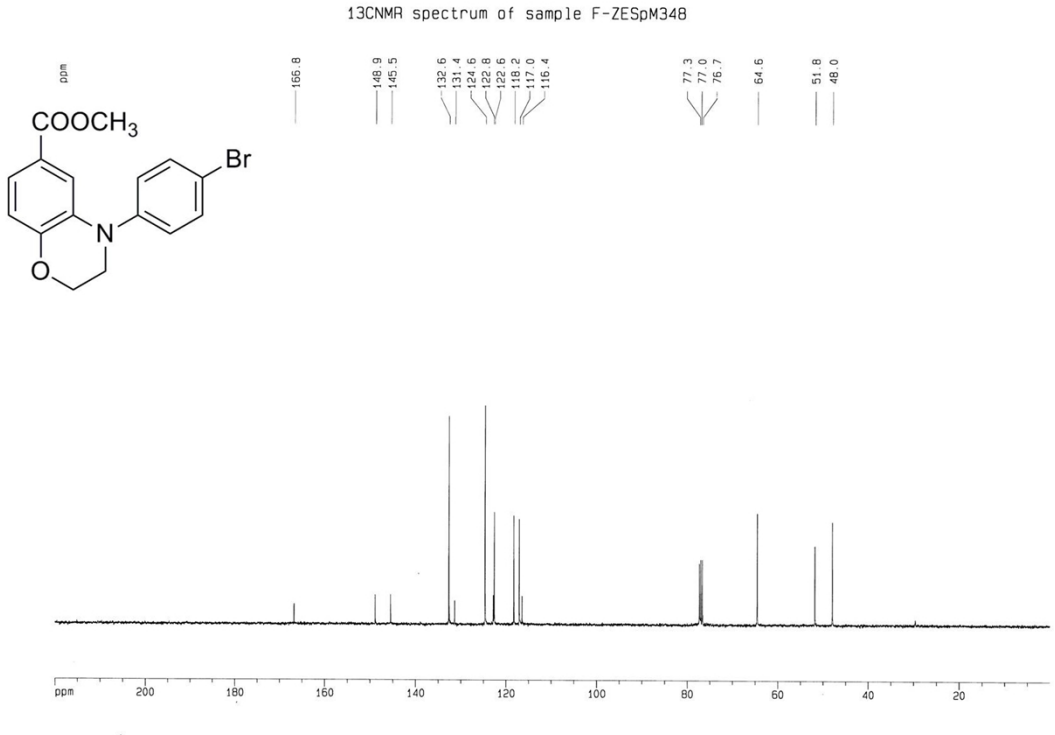

1HNMR spectrum of sample F-ZESpM395
ppm
7.645
7.623
7.603
7.599
7.486
7.481
7.465
7.460
7.436
7.431
7.380
7.361
7.340
7.240
7.215
7.213
7.194
7.125
7.107
7.089
6.970
6.948
6.891
6.870
COOCH3
I
N
O
Integral
3.0177
1.0000
0.0733
0.2050
0.2065
0.1100
2.0035
1.0789
ppm
7.50
7.25
7.00
6.75



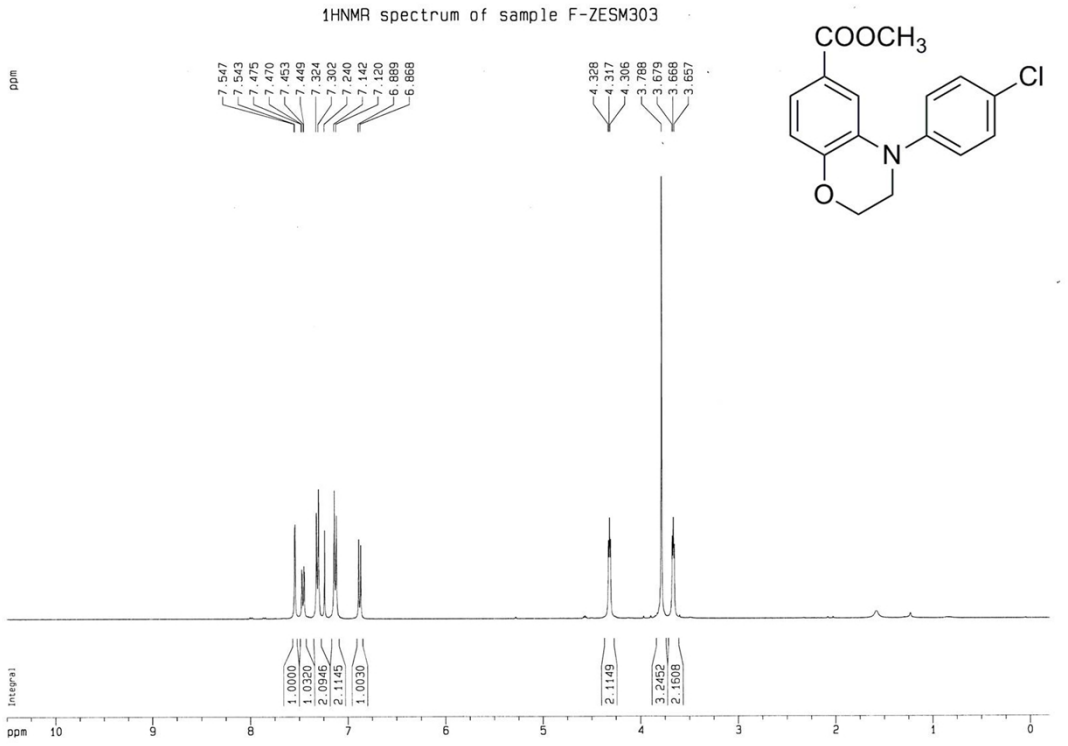
[^{1}H NMR and ^{13}C NMR spectrum of 4e in $CDCl_3$]

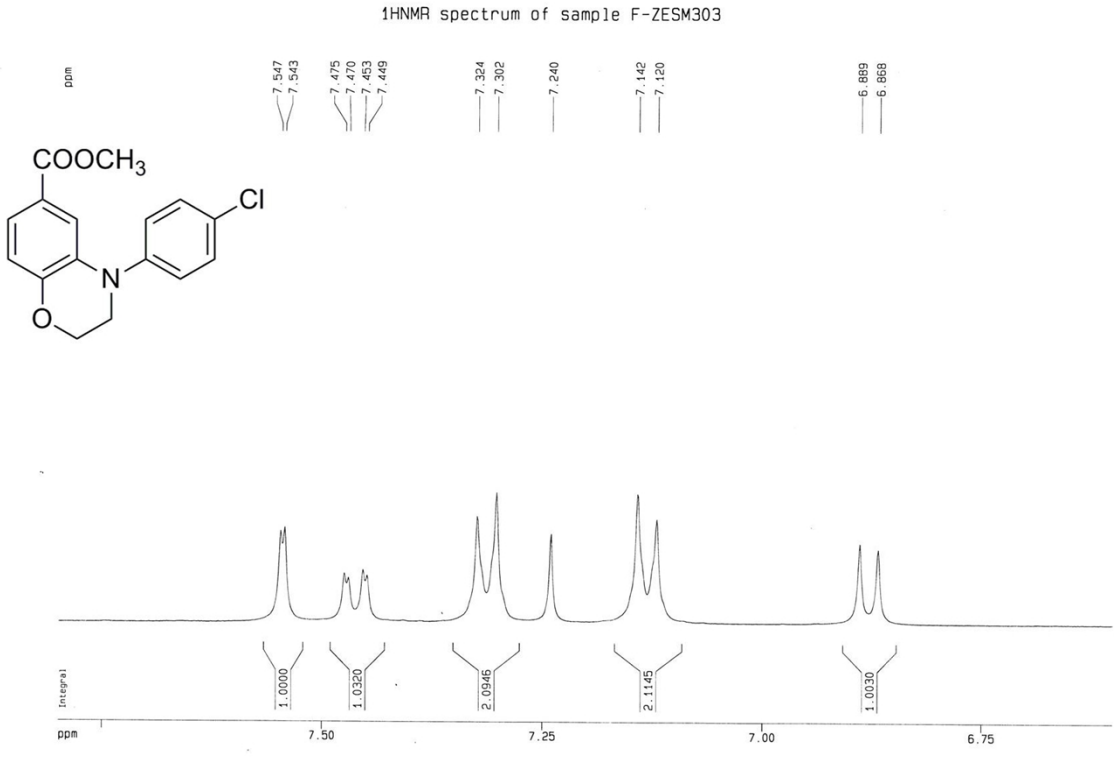


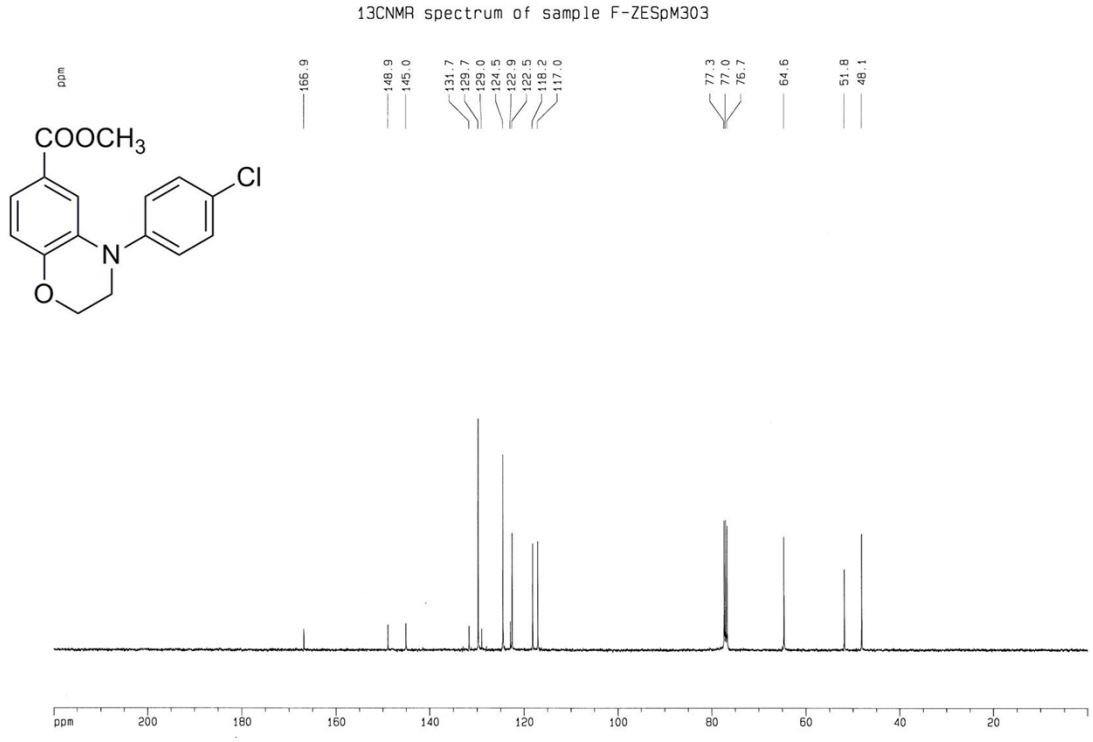




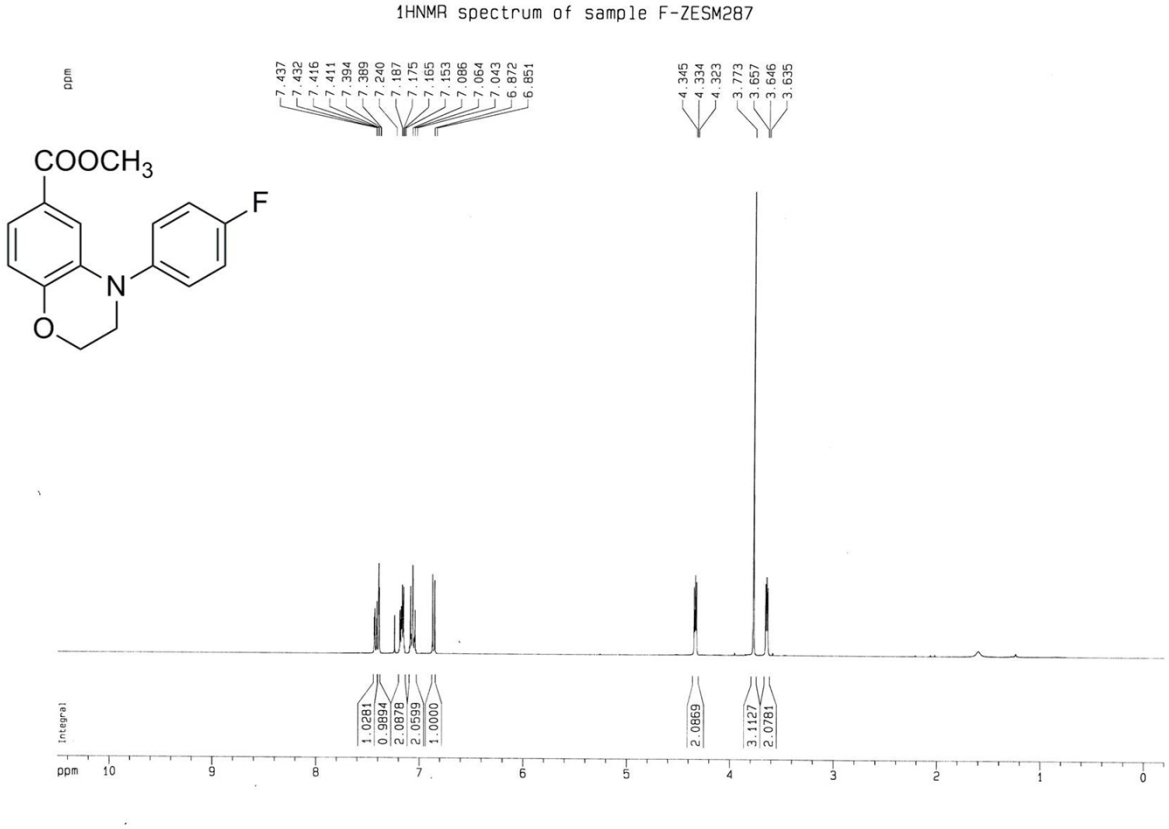
[^{1}H NMR and ^{13}C NMR spectrum of 4f in $CDCl_3$]


1HNMR spectrum of sample F-ZESM303
ppm
7.547
7.543
7.475
7.470
7.453
7.449
7.324
7.302
7.240
7.142
7.120
6.889
6.868
4.328
4.317
4.306
3.788
3.679
3.668
3.657
COOCH3
Cl
N
O
Integral
1.0000
1.0320
2.0946
2.1145
1.0030
2.1149
3.2452
2.1608
ppm
10
9
8
7
6
5
4
3
2
1
0

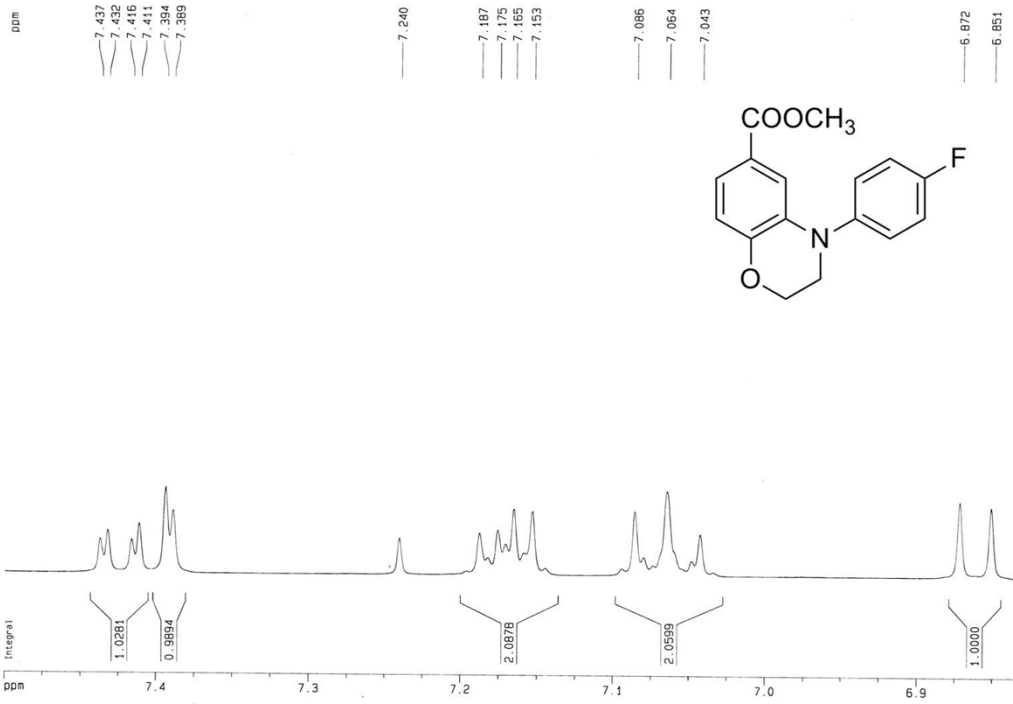

1HNMR spectrum of sample F-ZESM303
ppm
7.547
7.543
7.475
7.470
7.453
7.449
7.324
7.302
7.240
7.142
7.120
6.889
6.868
COOCH3
Cl
N
O
Integral
1.0000
1.0320
2.0946
2.1145
1.0030
ppm
7.50
7.25
7.00
6.75



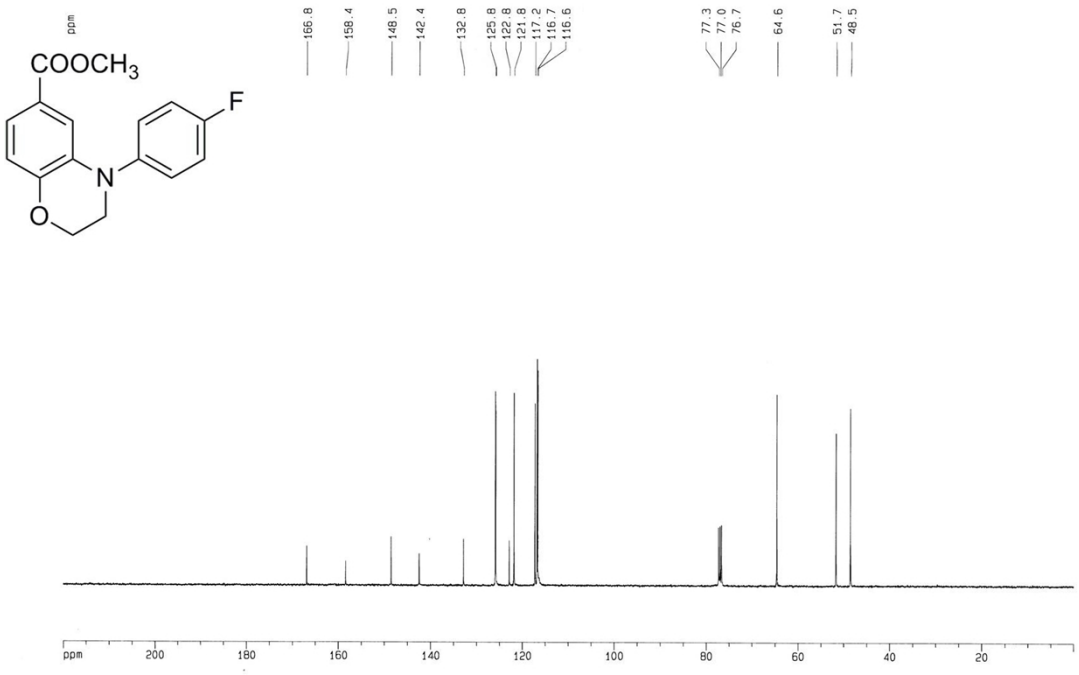
[^{1}H NMR and ^{13}C NMR spectrum of 4g in $CDCl_3$]



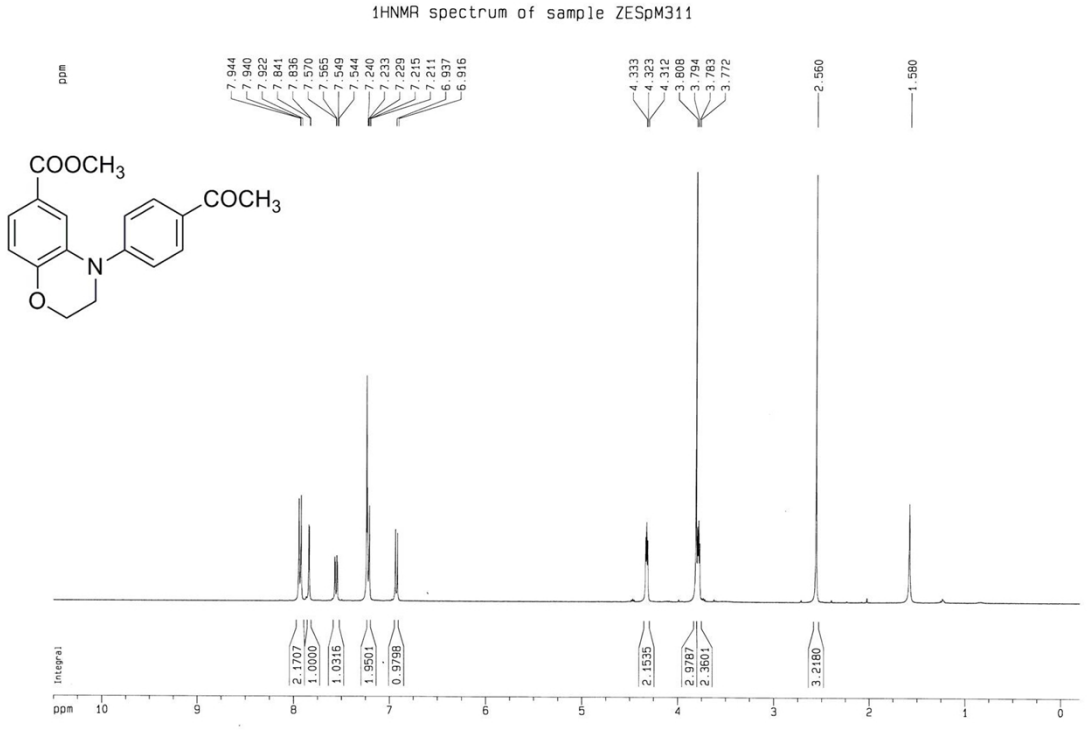
1HNMR spectrum of sample F-ZESM287

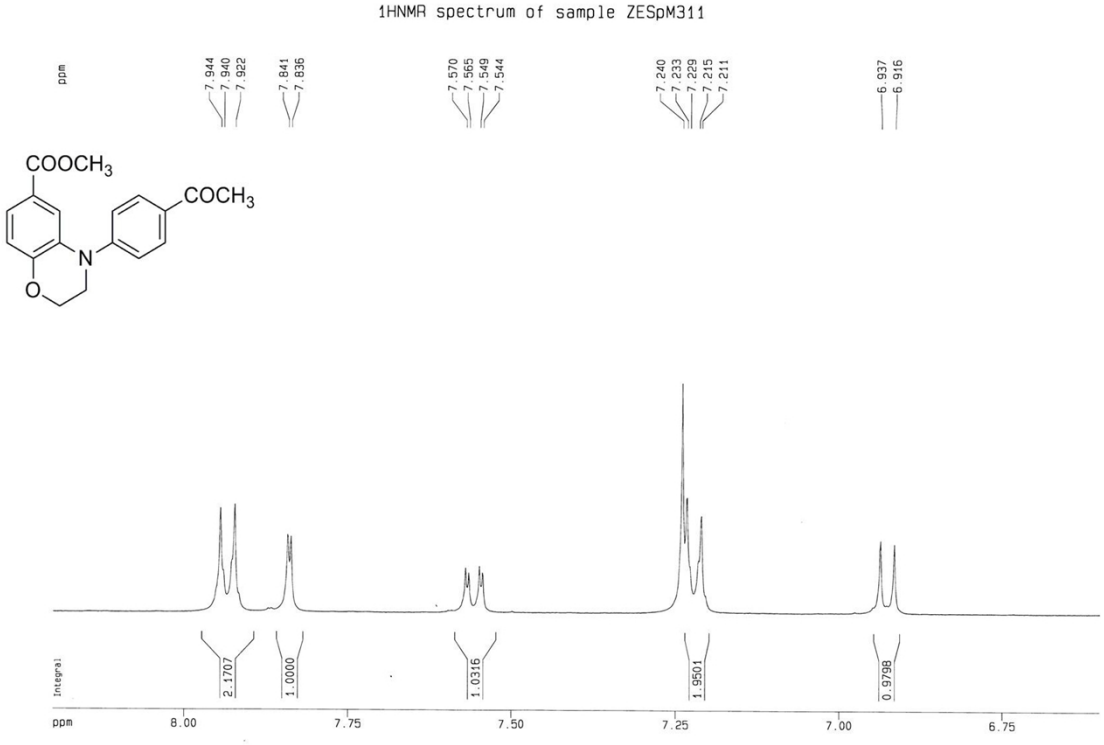


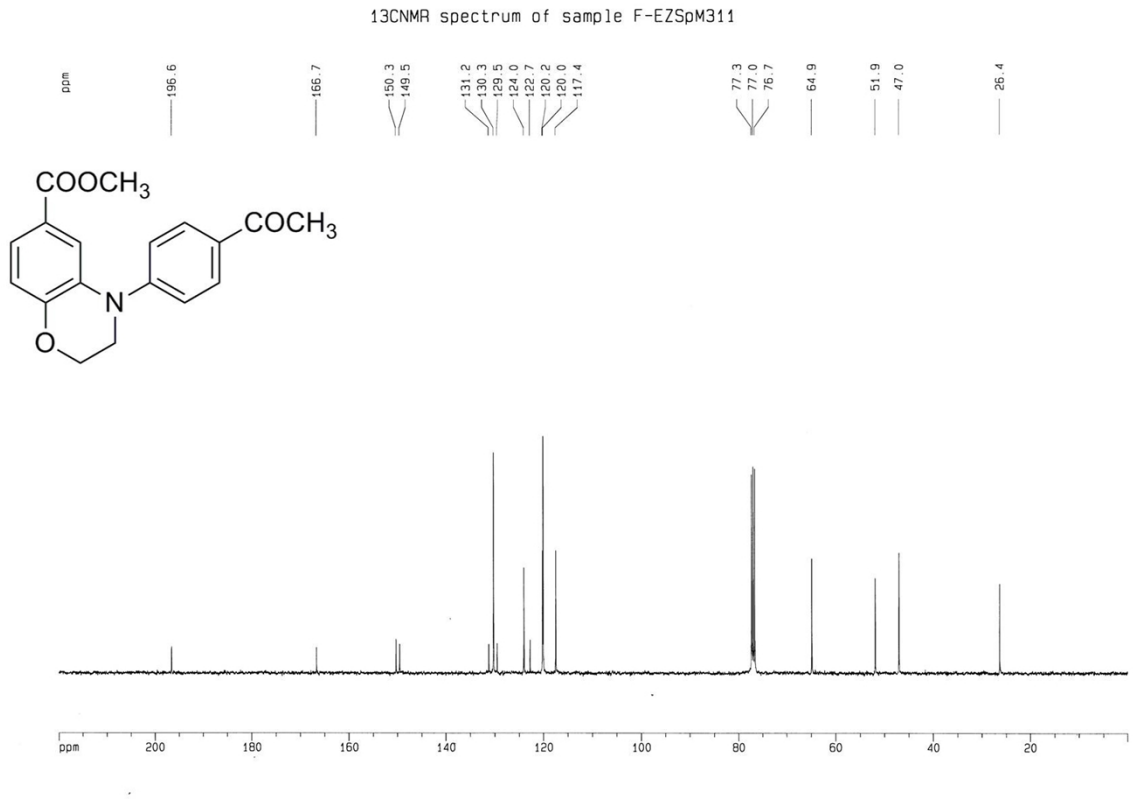
13CNMR spectrum of sample F-ZESpM287



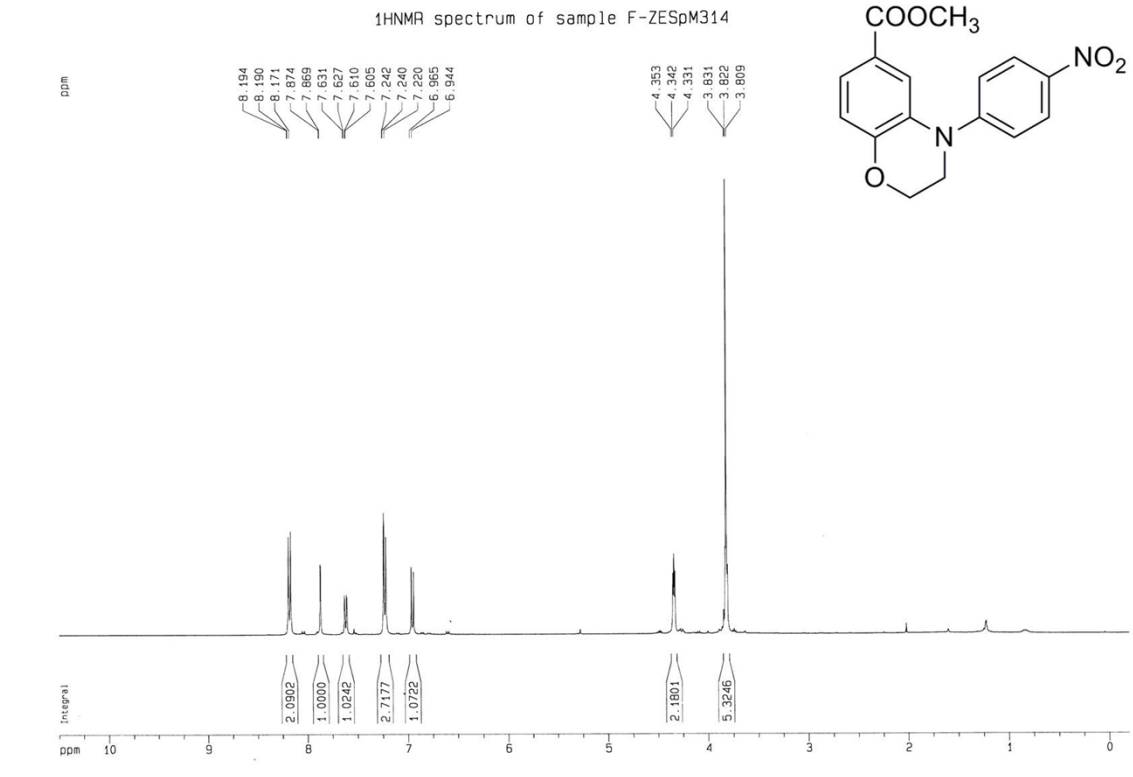
[^{1}H NMR and ^{13}C NMR spectrum of 4h in $CDCl_3$]



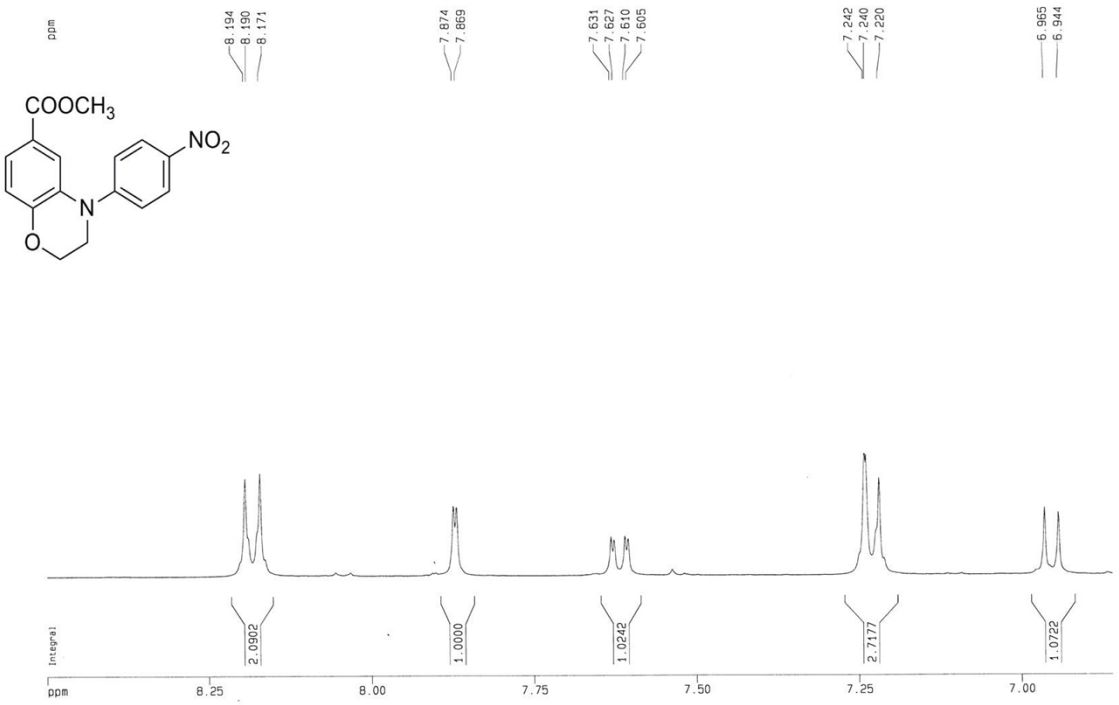




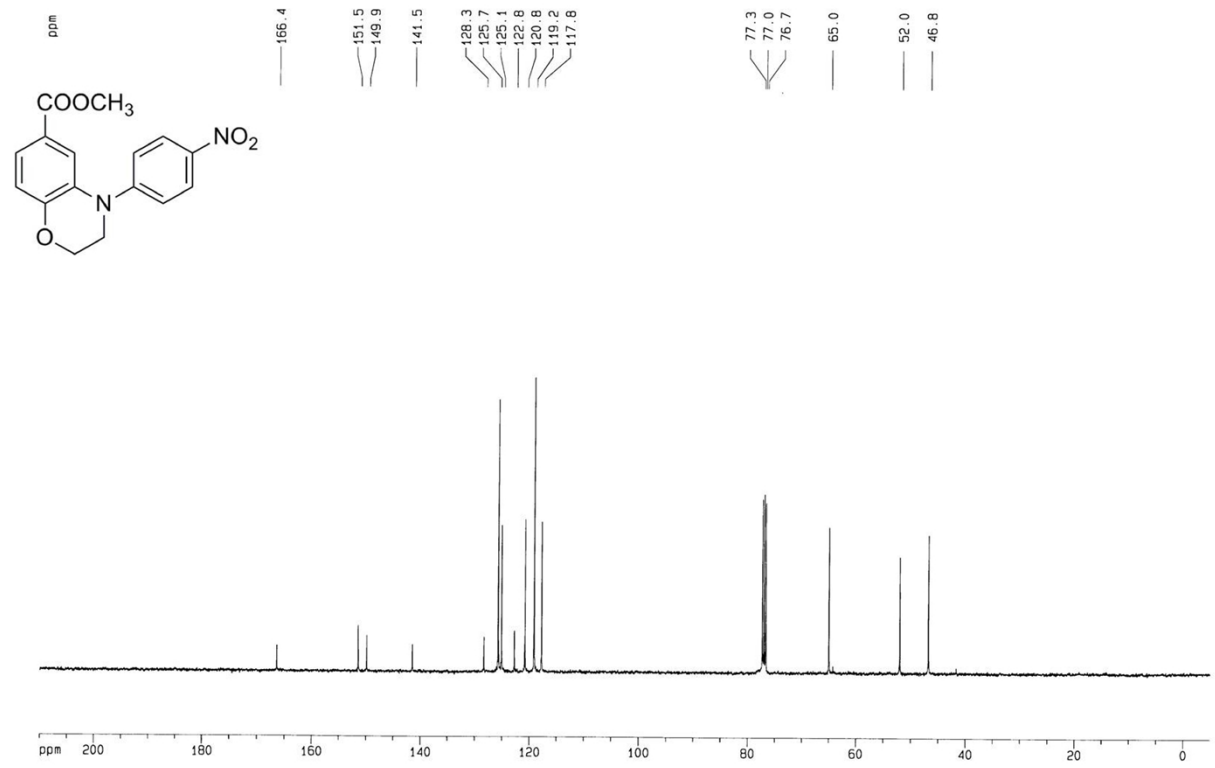
[^{1}H NMR and ^{13}C NMR spectrum of 4i in $CDCl_3$]



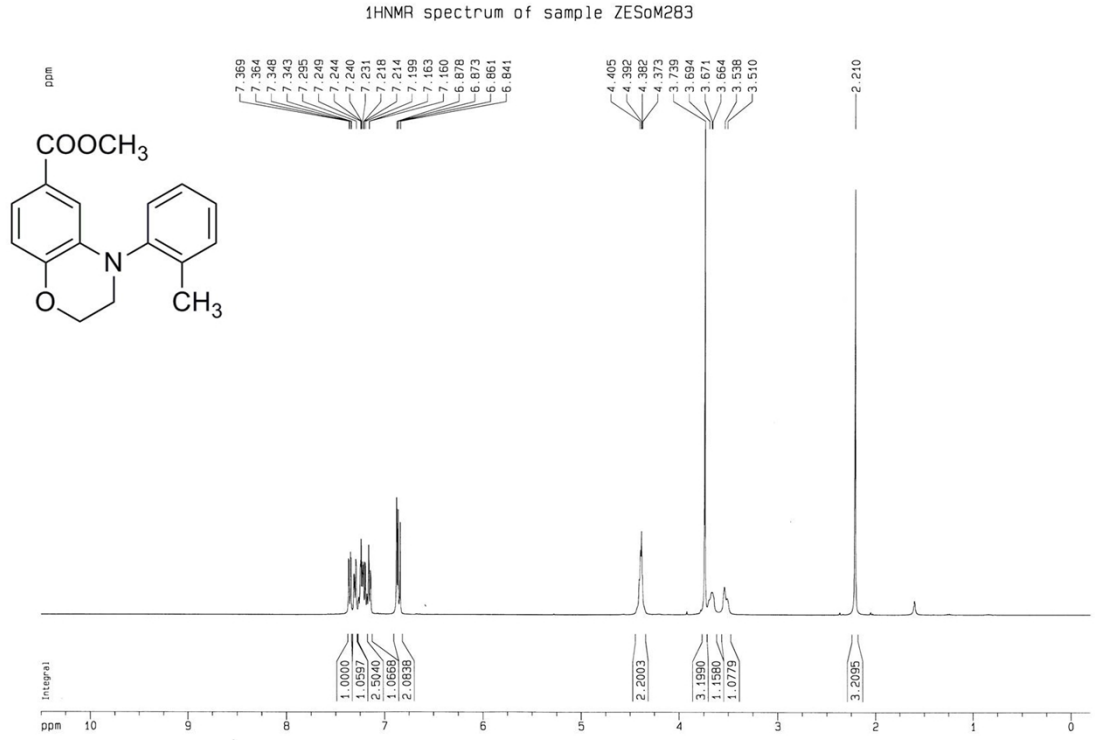
1HNMR spectrum of sample F-ZESpM314

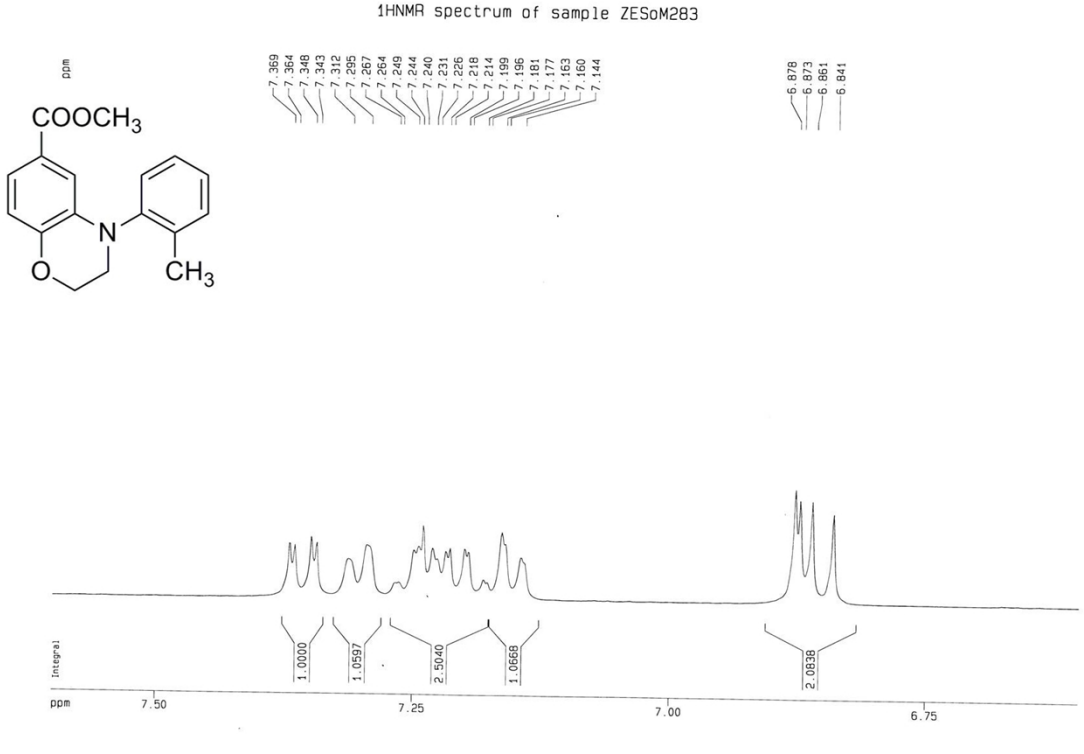


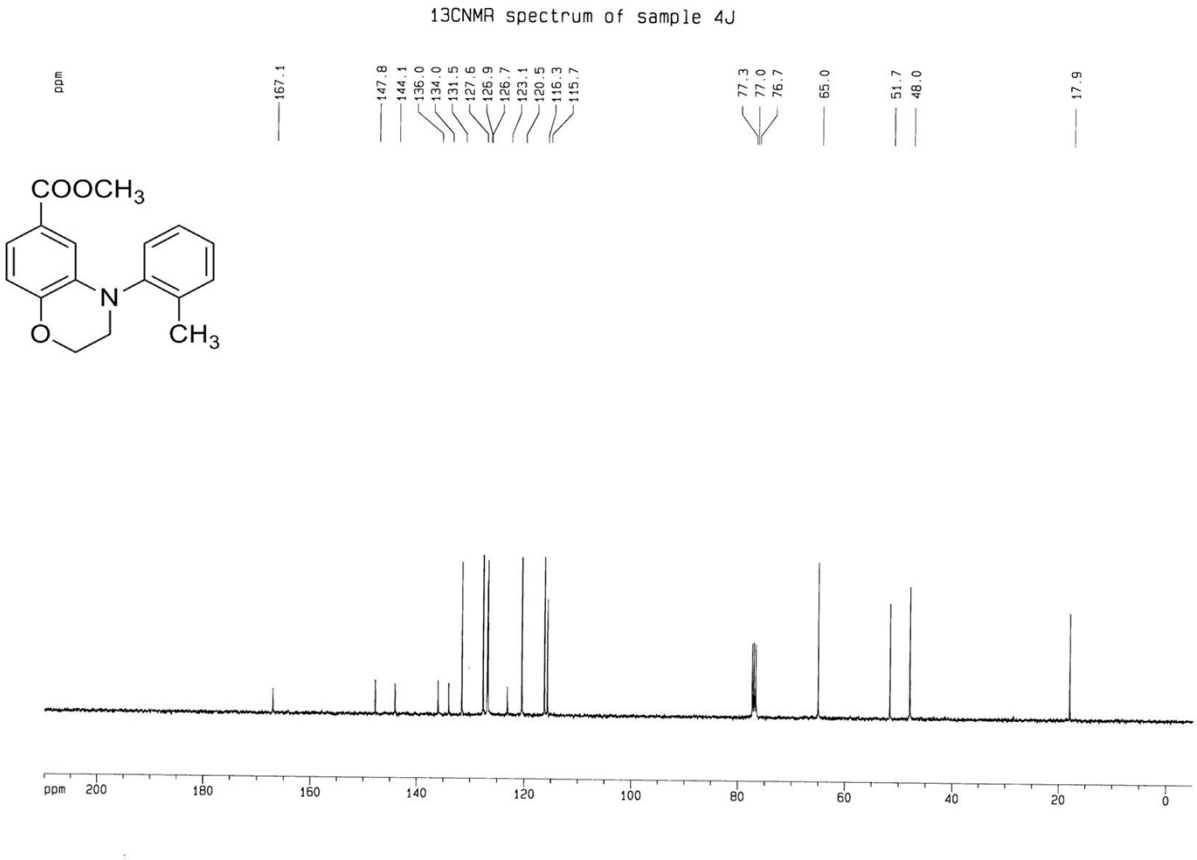
13CNMR spectrum of sample 4I



[^{1}H NMR and ^{13}C NMR spectrum of 4j in $CDCl_3$]

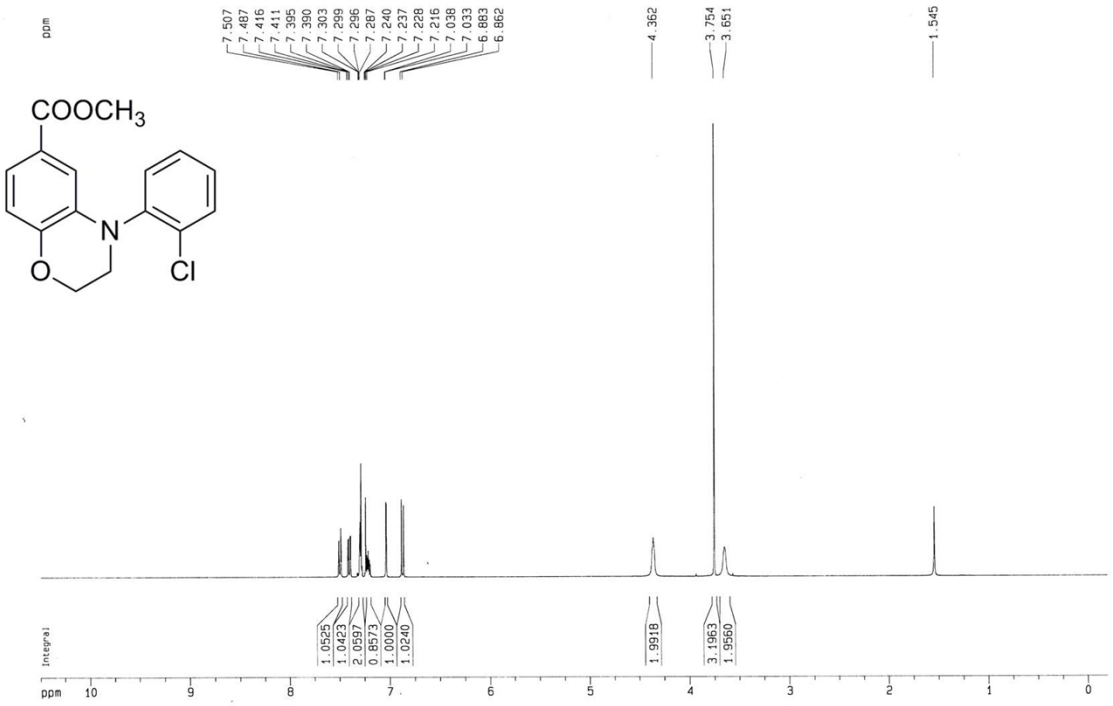




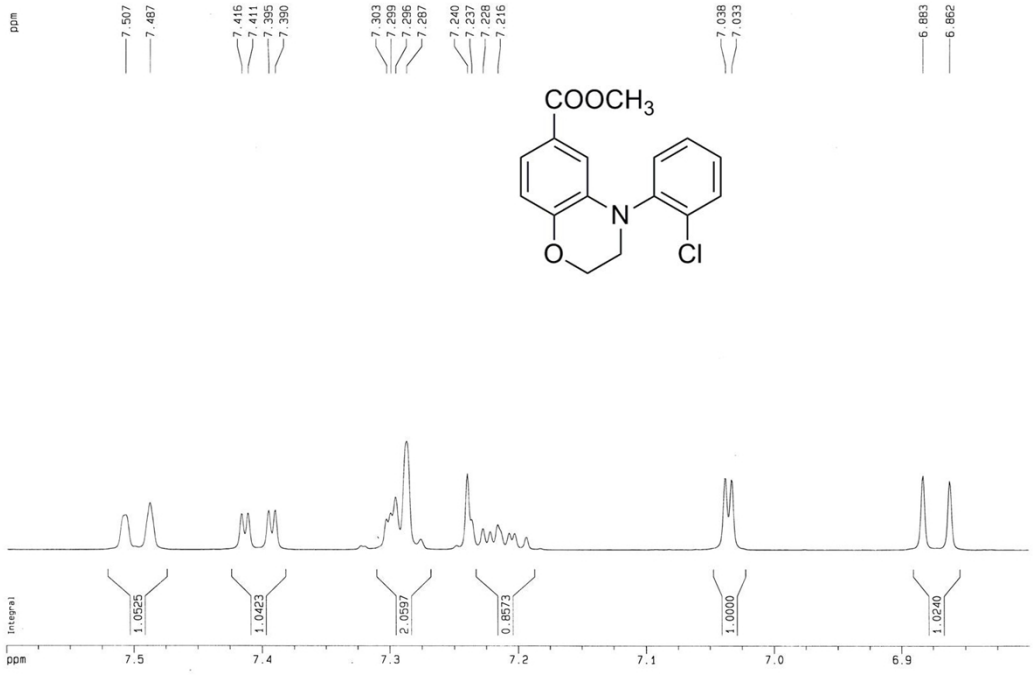


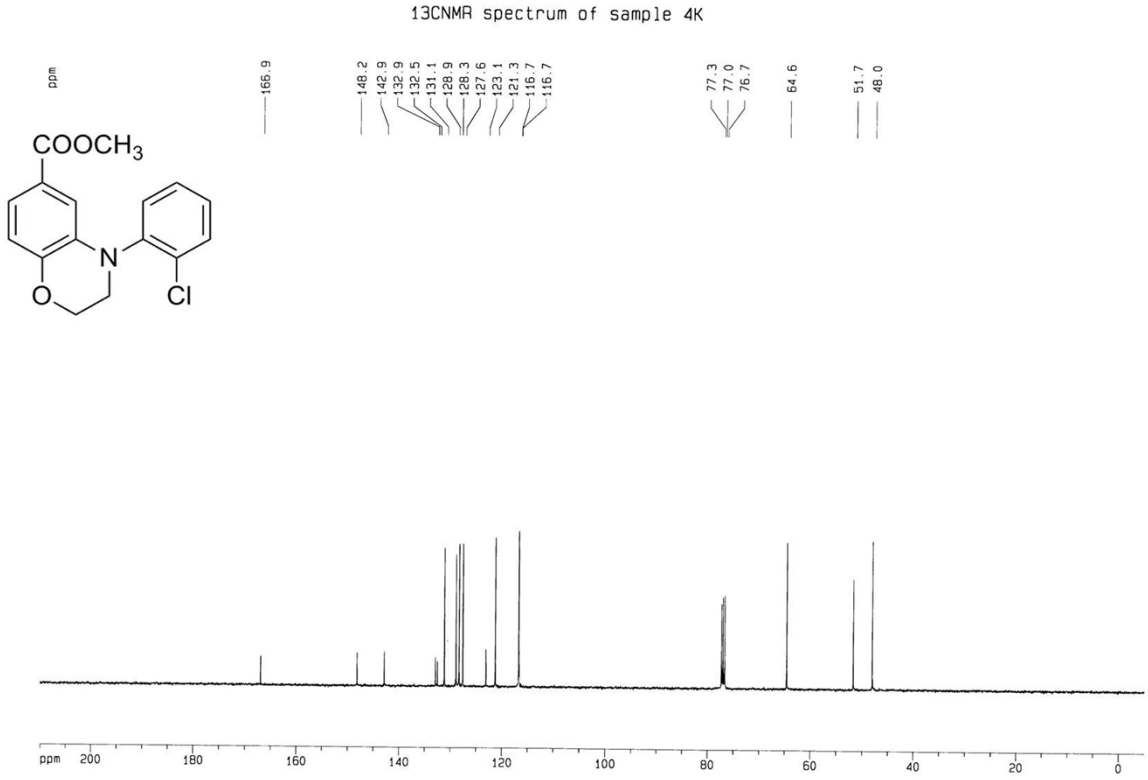
[^{1}H NMR and ^{13}C NMR spectrum of 4k in $CDCl_3$]

1HNMR spectrum of sample F-ZESM303

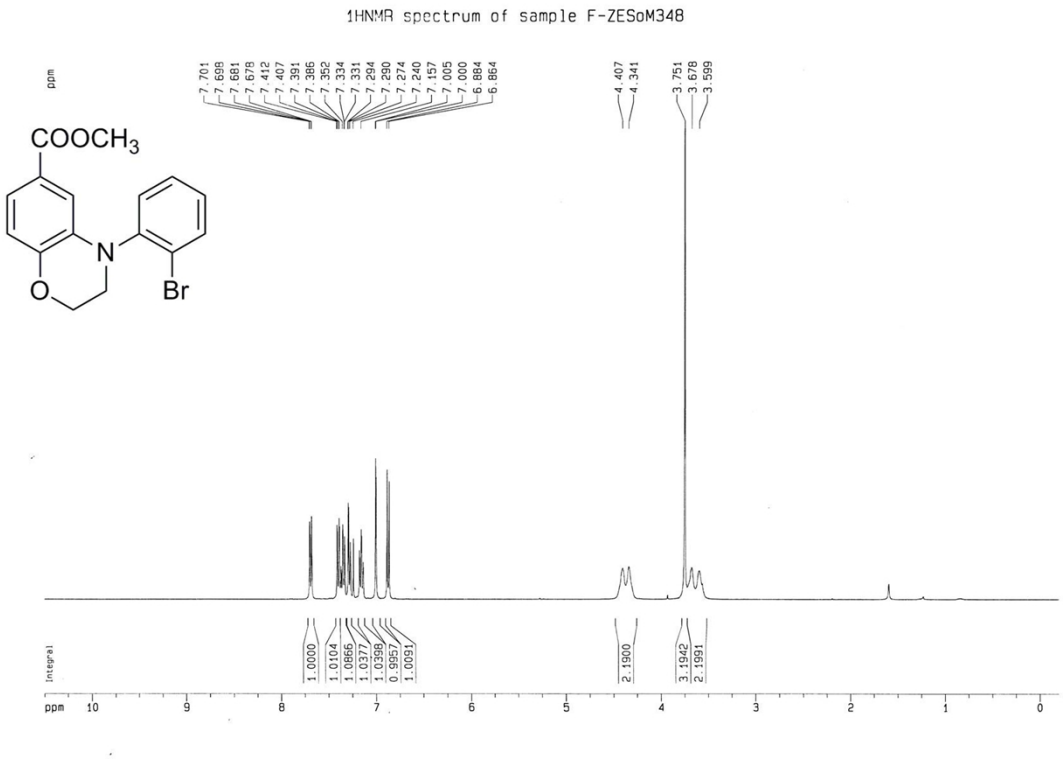


1HNMR spectrum of sample F-ZESM303

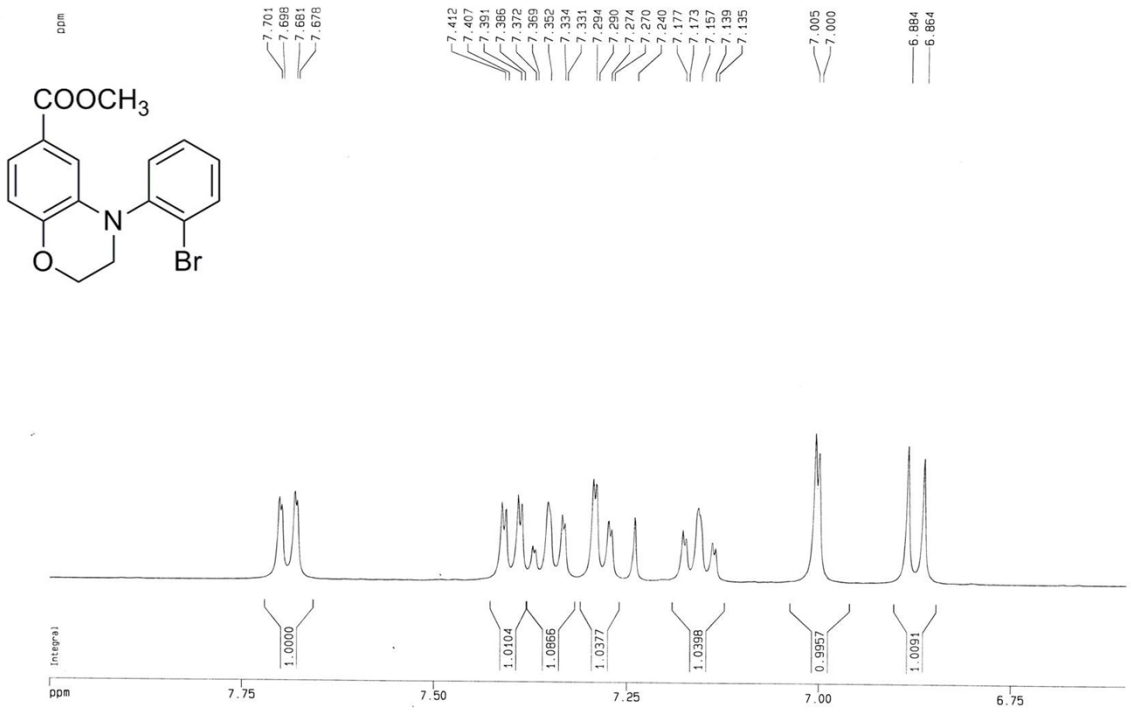




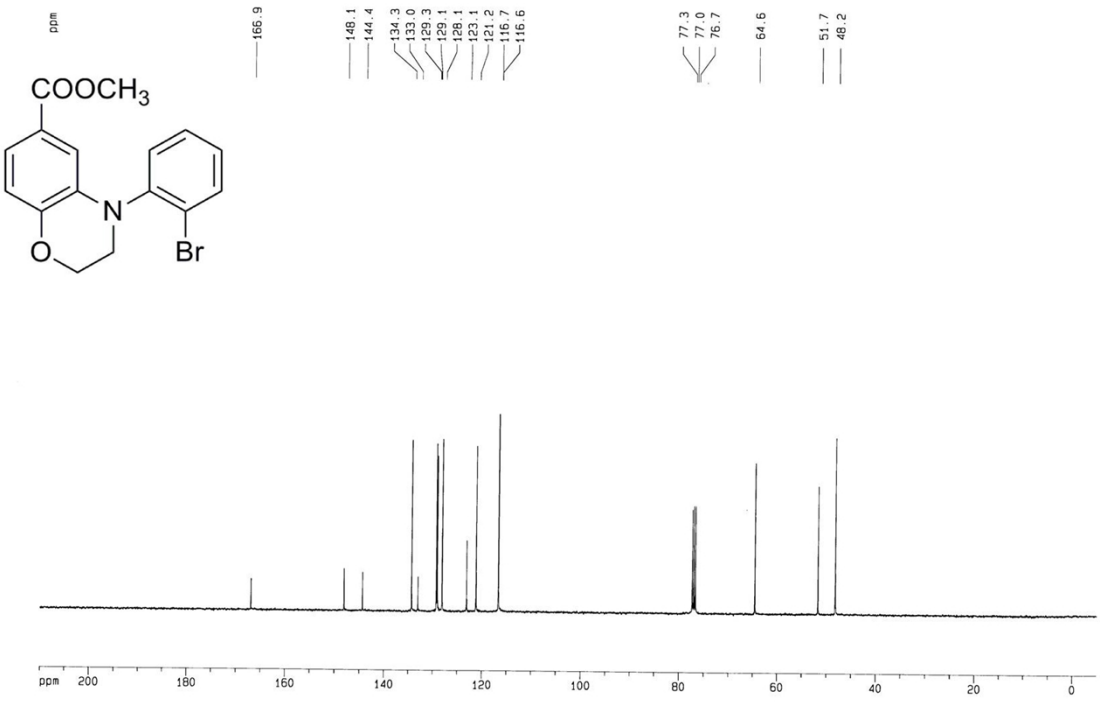
[^{1}H NMR and ^{13}C NMR spectrum of 4l in $CDCl_3$]



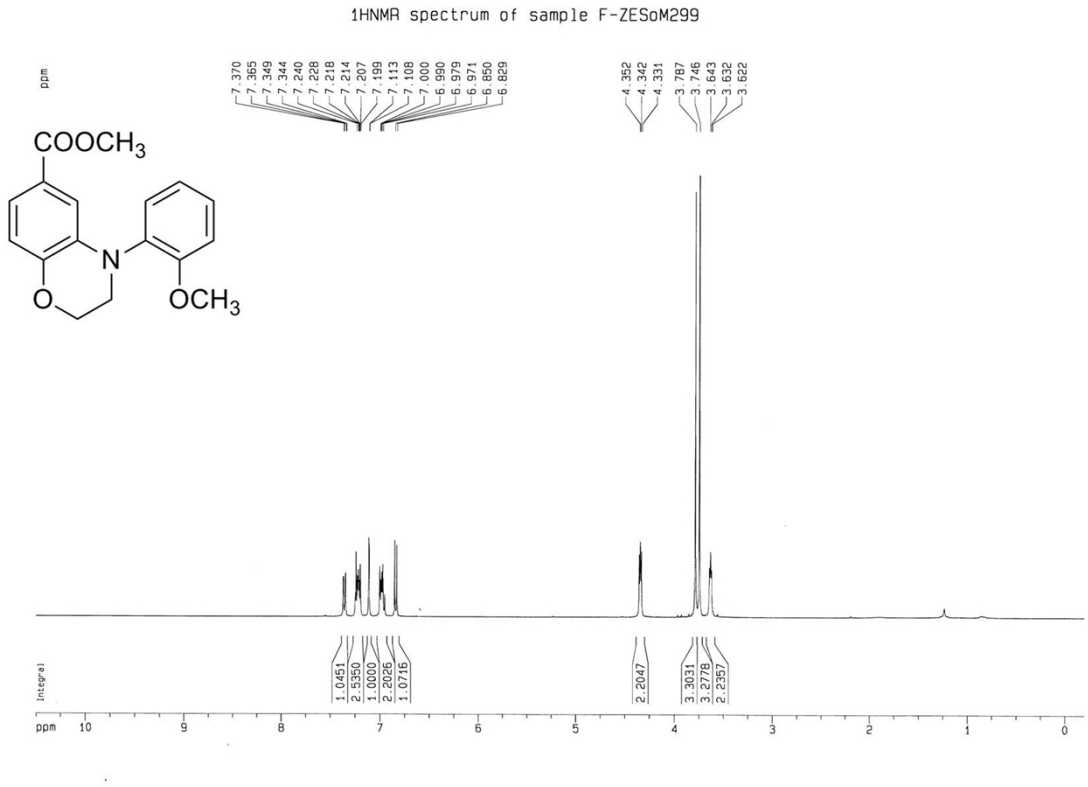
1HNMR spectrum of sample F-ZESoM348

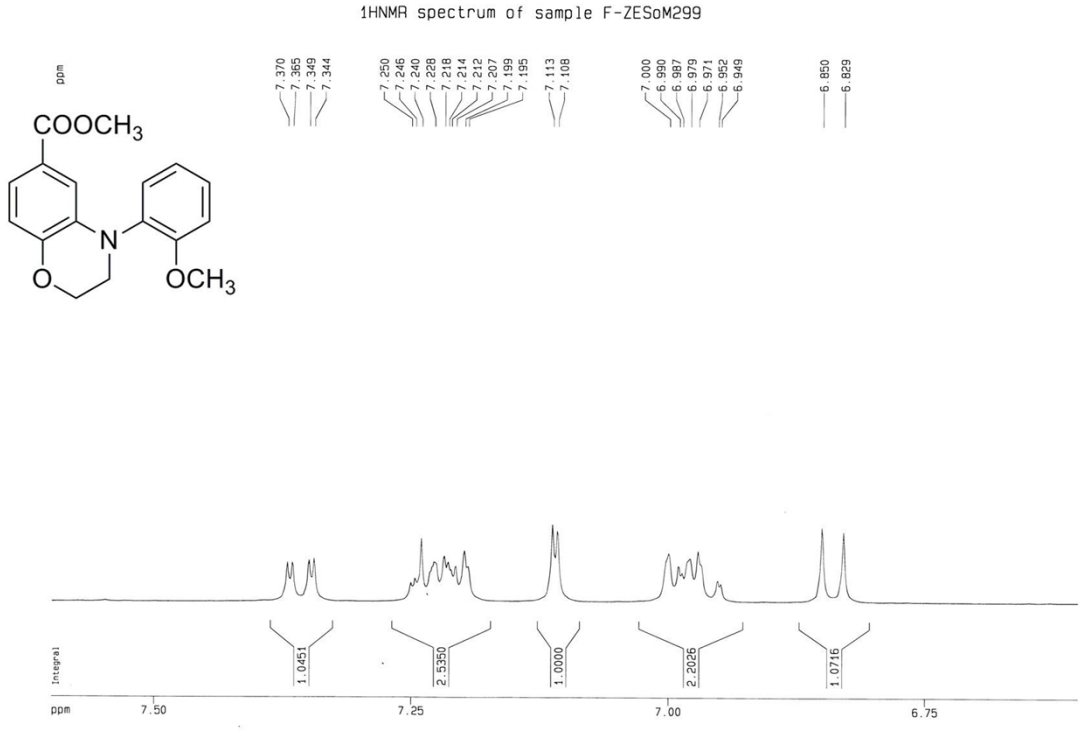


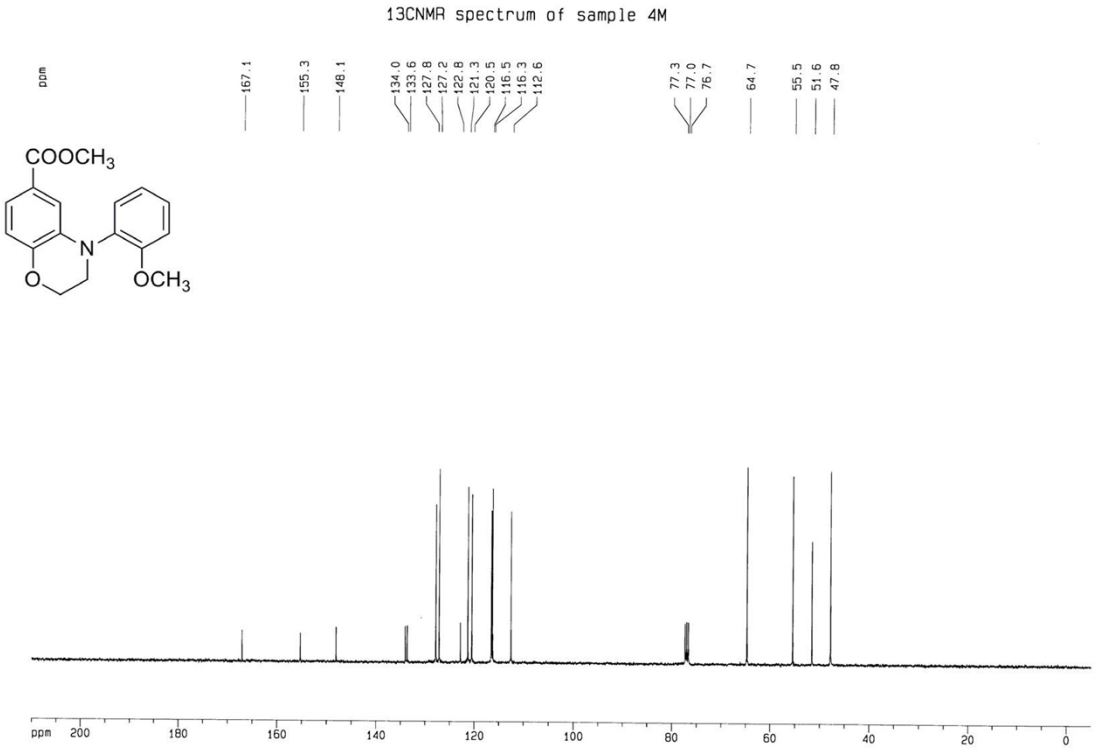
13CNMR spectrum of sample 4L



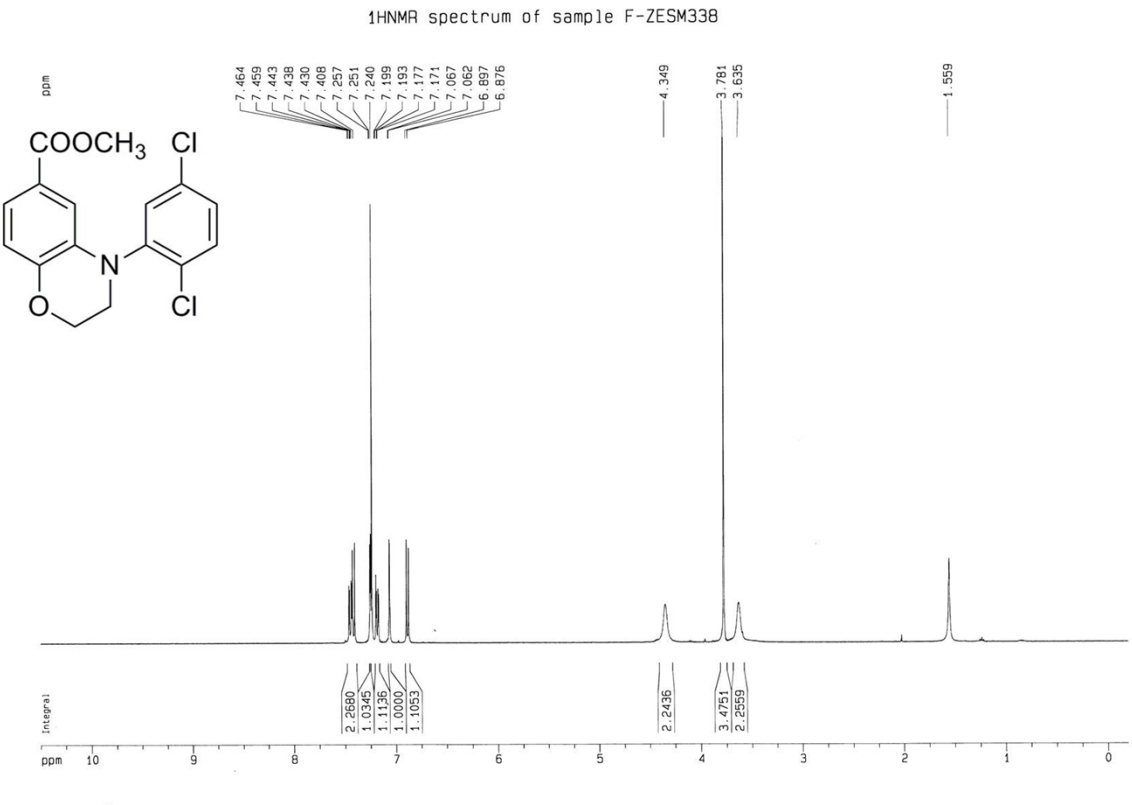
[^{1}H NMR and ^{13}C NMR spectrum of 4m in $CDCl_3$]

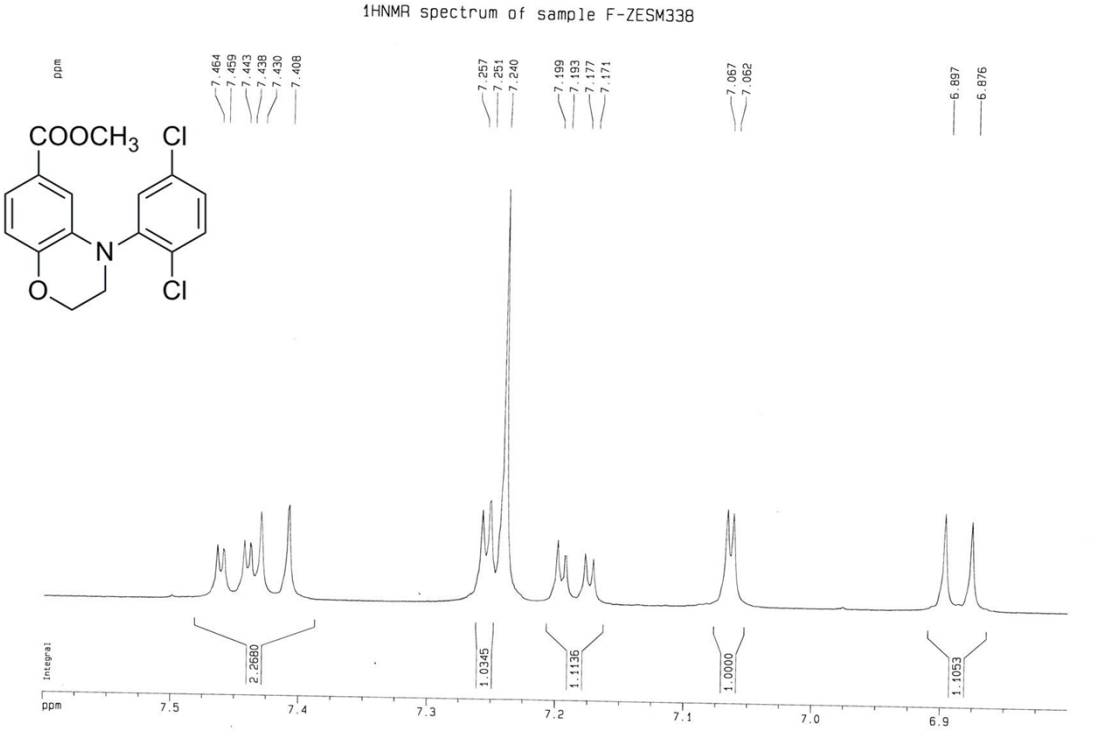


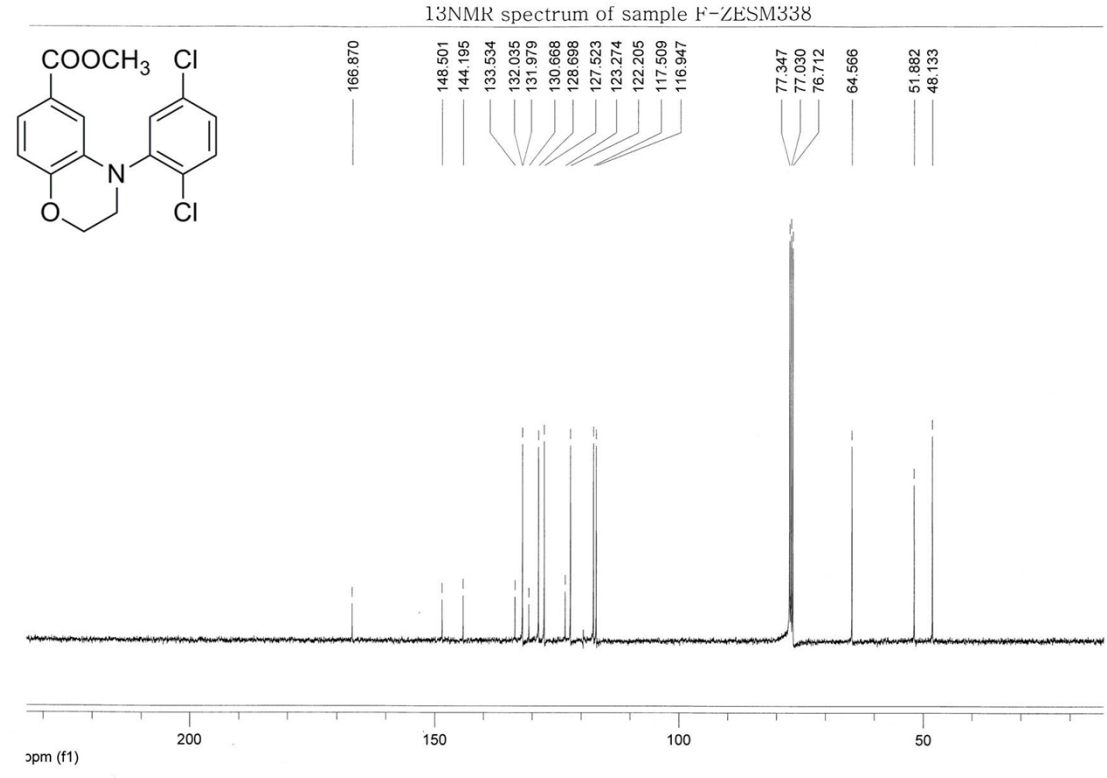




[^{1}H NMR and ^{13}C NMR spectrum of 4n in $CDCl_3$]

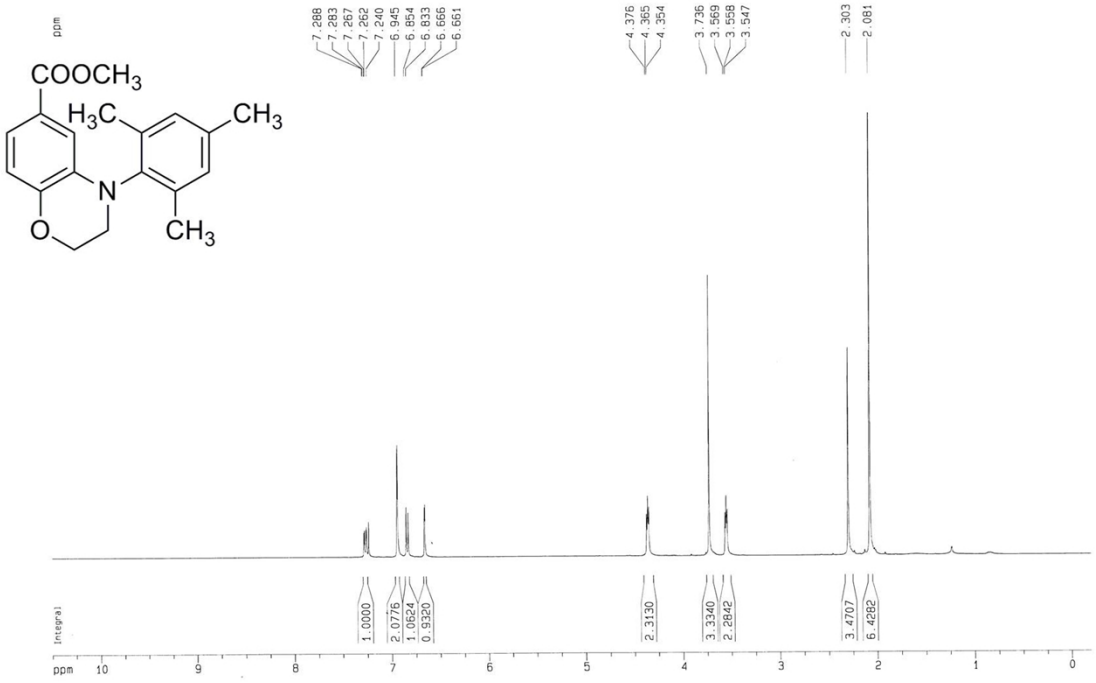




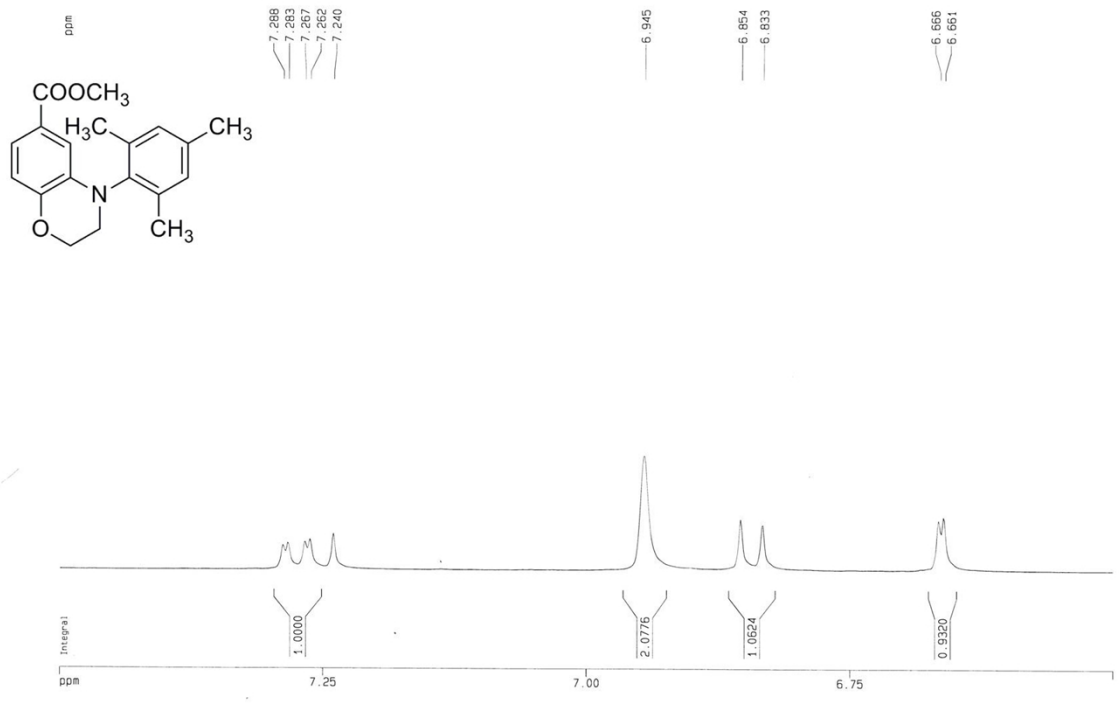


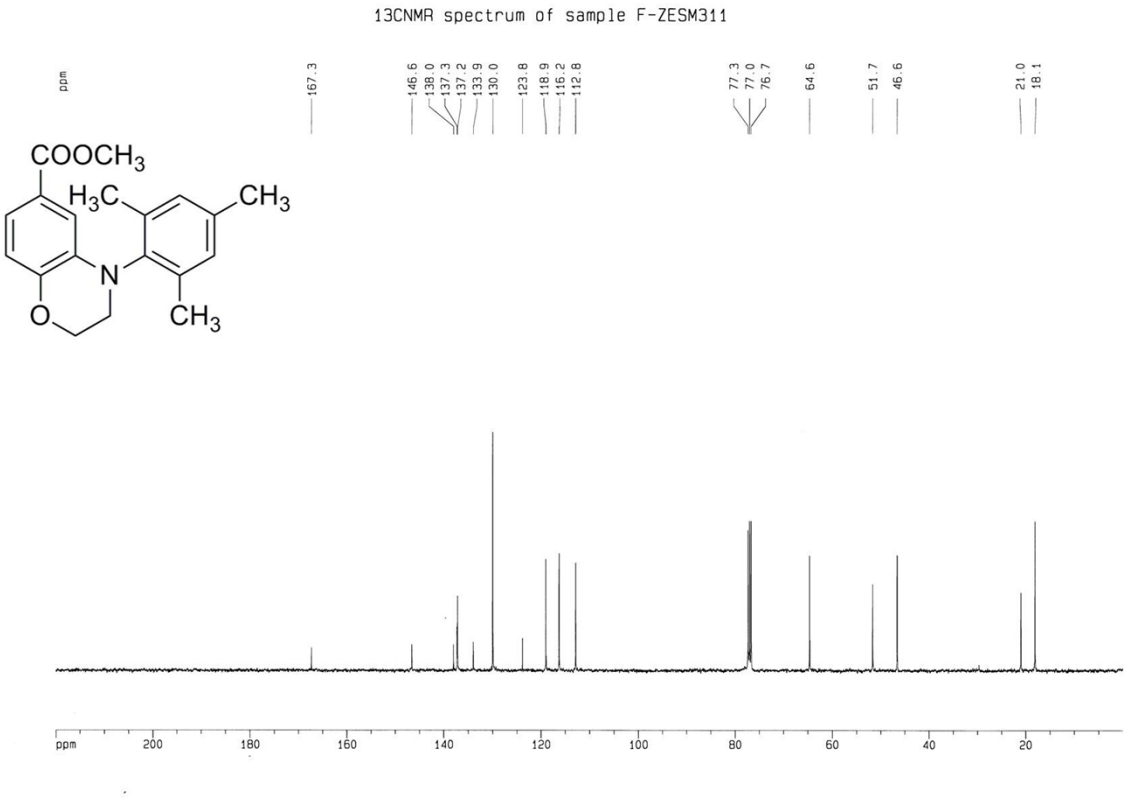
[^{1}H NMR and ^{13}C NMR spectrum of 4o in $CDCl_3$]

1HNMR spectrum of sample F-ZESM311

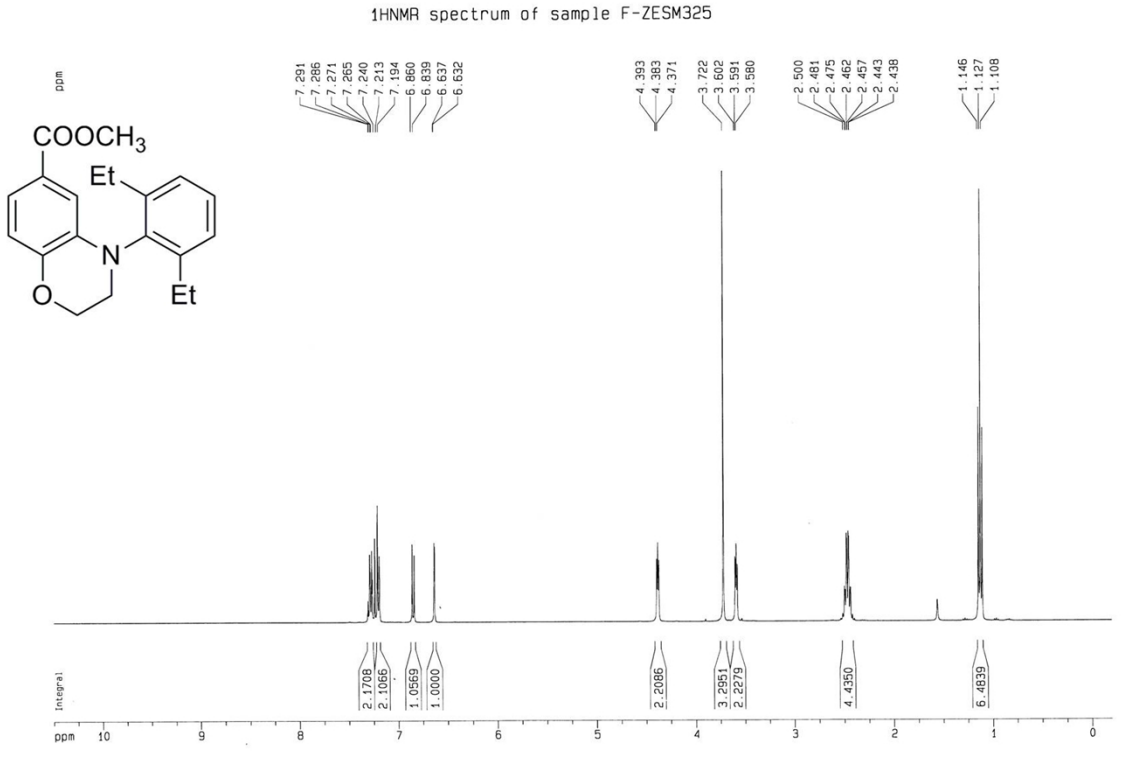


1HNMR spectrum of sample F-ZESM311

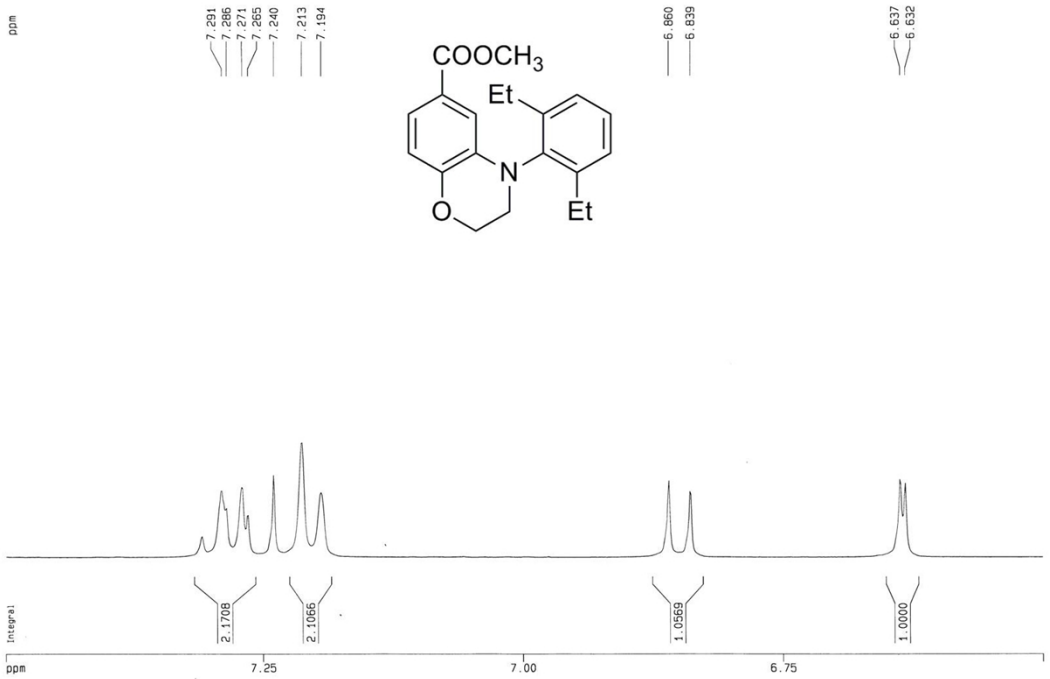




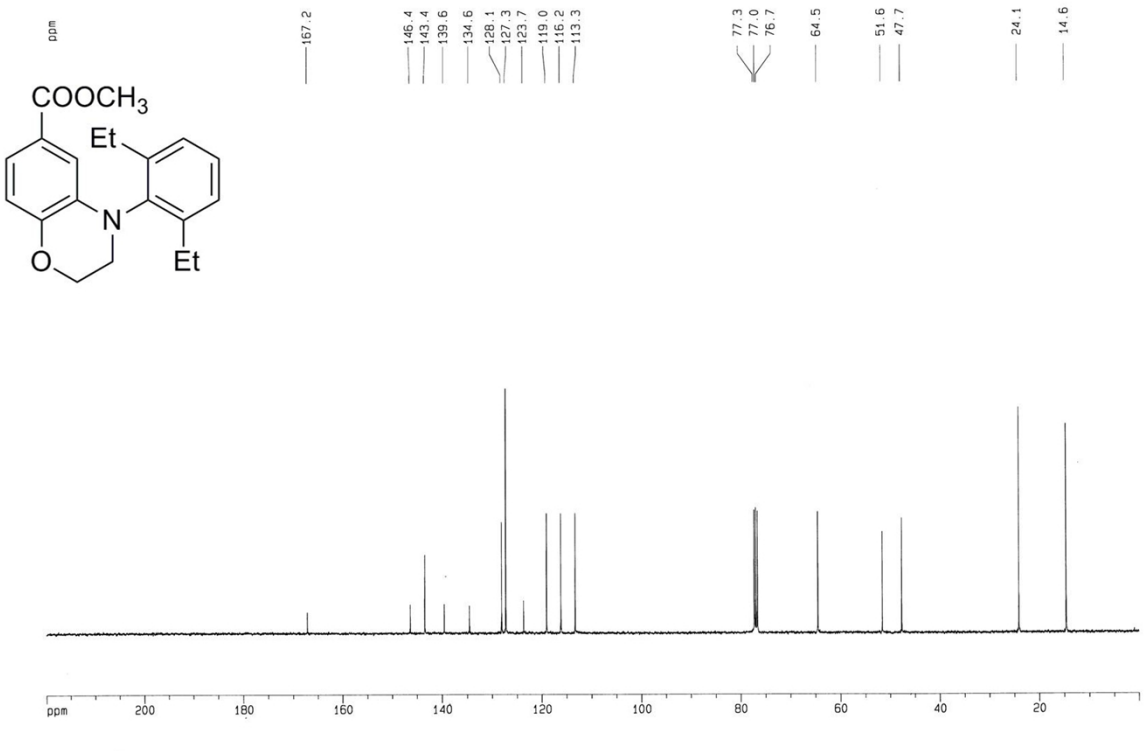
[^{1}H NMR and ^{13}C NMR spectrum of 4p in $CDCl_3$]



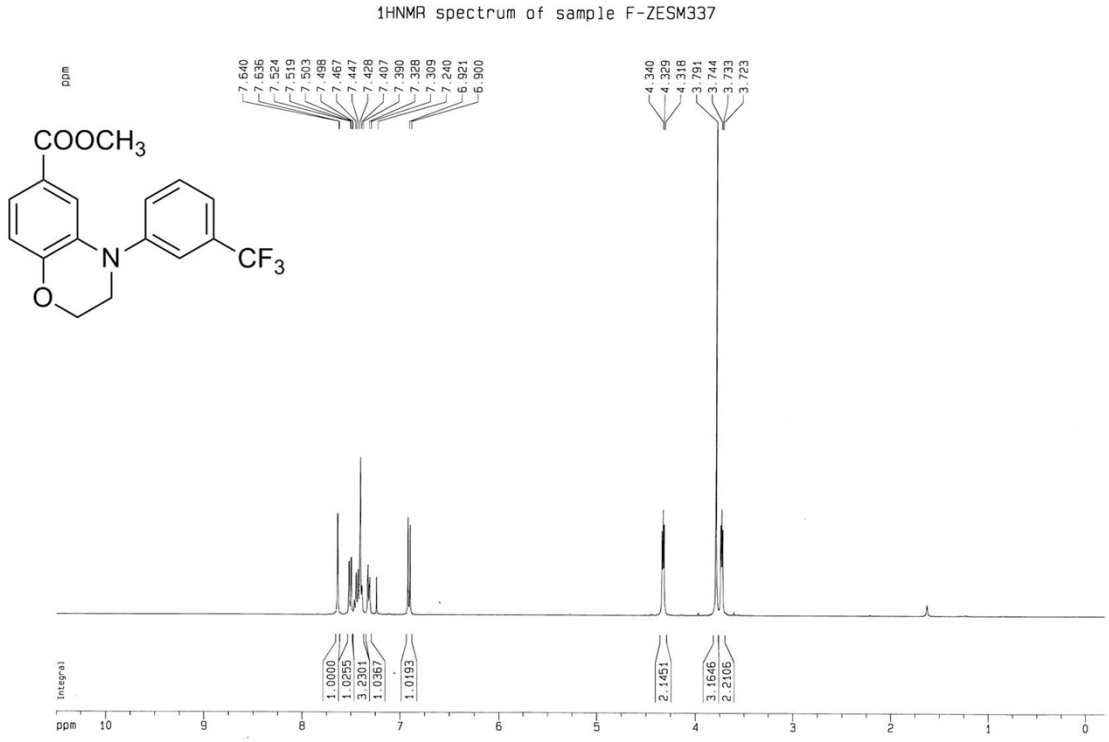
1HNMR spectrum of sample F-ZESM325

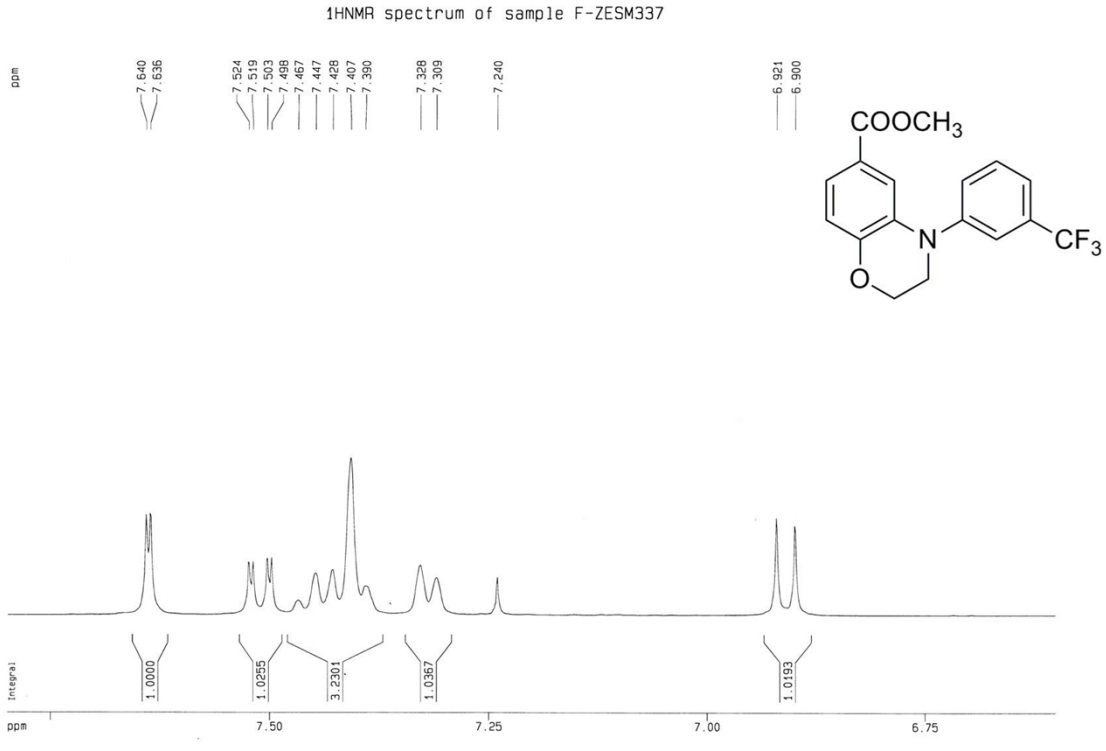


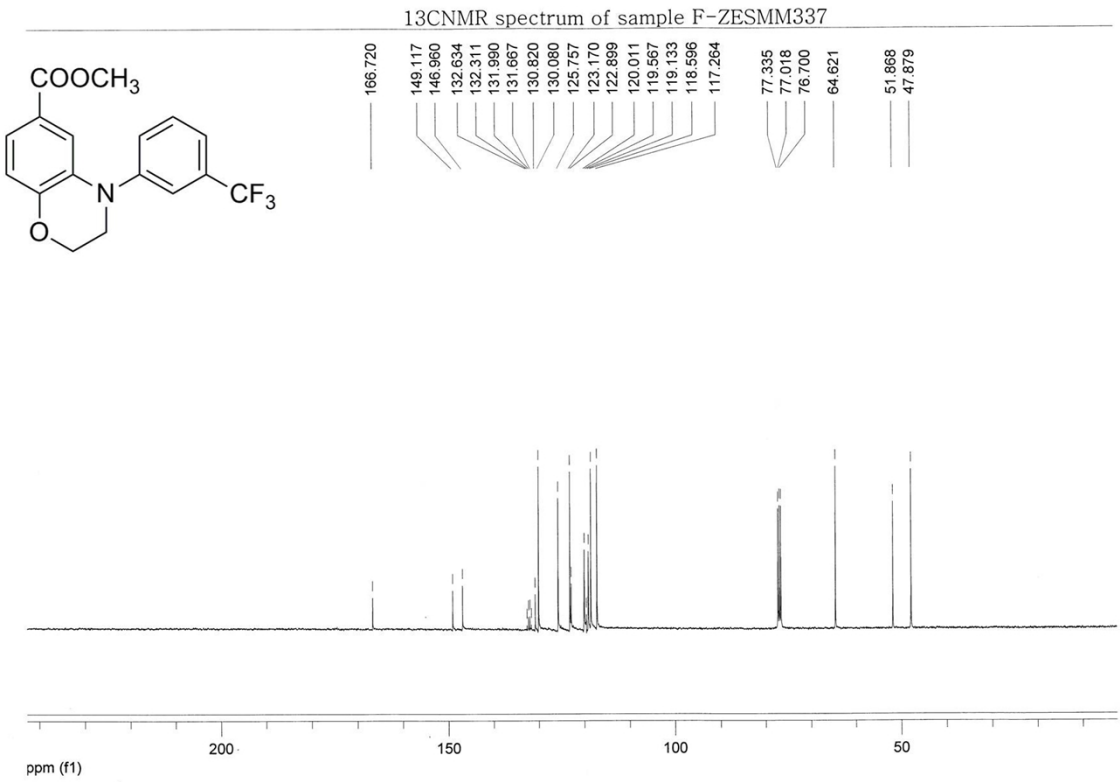
13CNMR spectrum of sample F-ZESM325



[^{1}H NMR and ^{13}C NMR spectrum of 4r in $CDCl_3$]

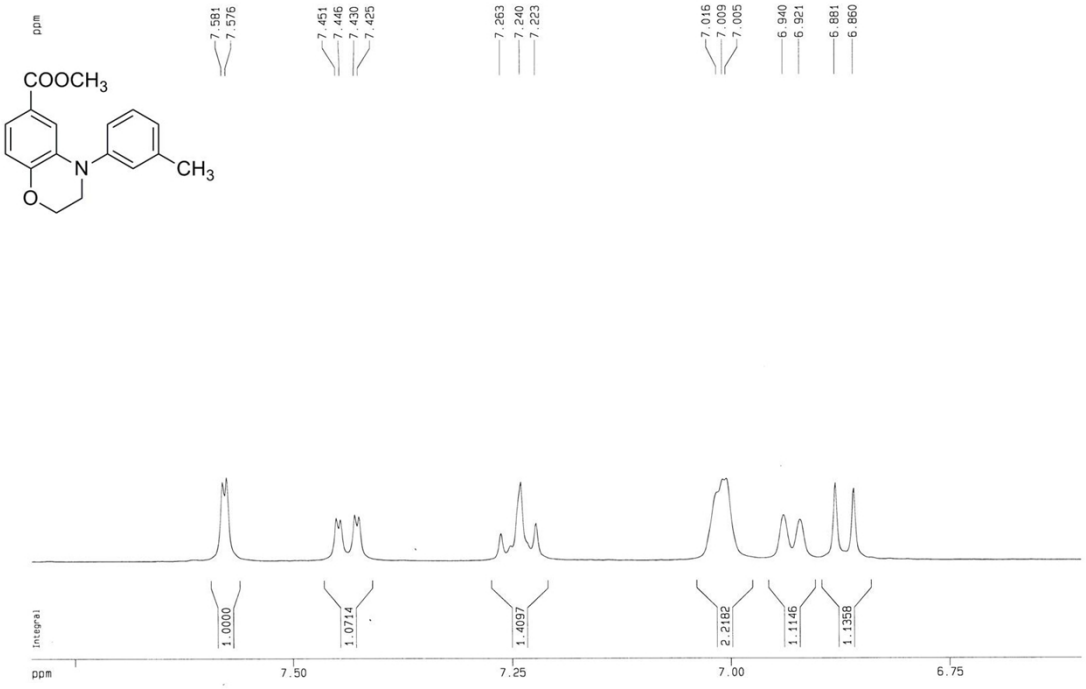




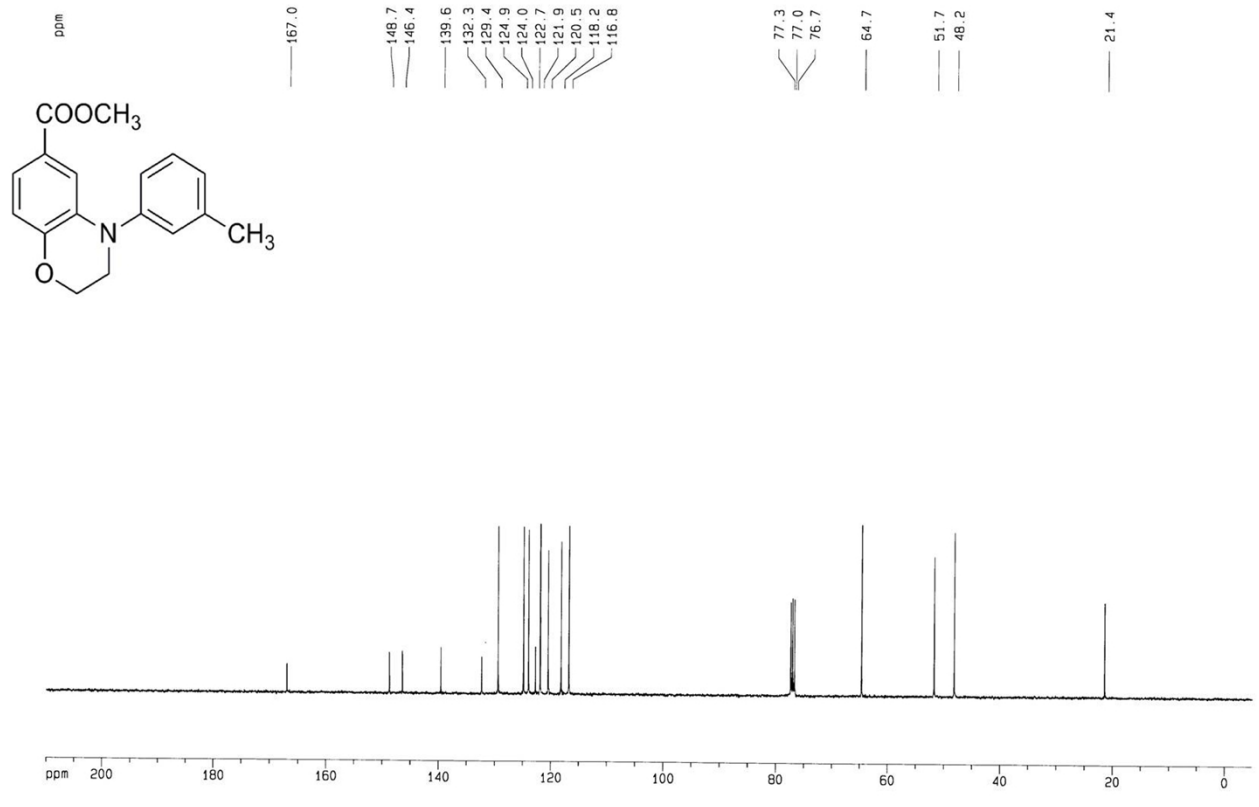


[^{1}H NMR ^{13}C NMR spectrum of 4s in $CDCl_3$]

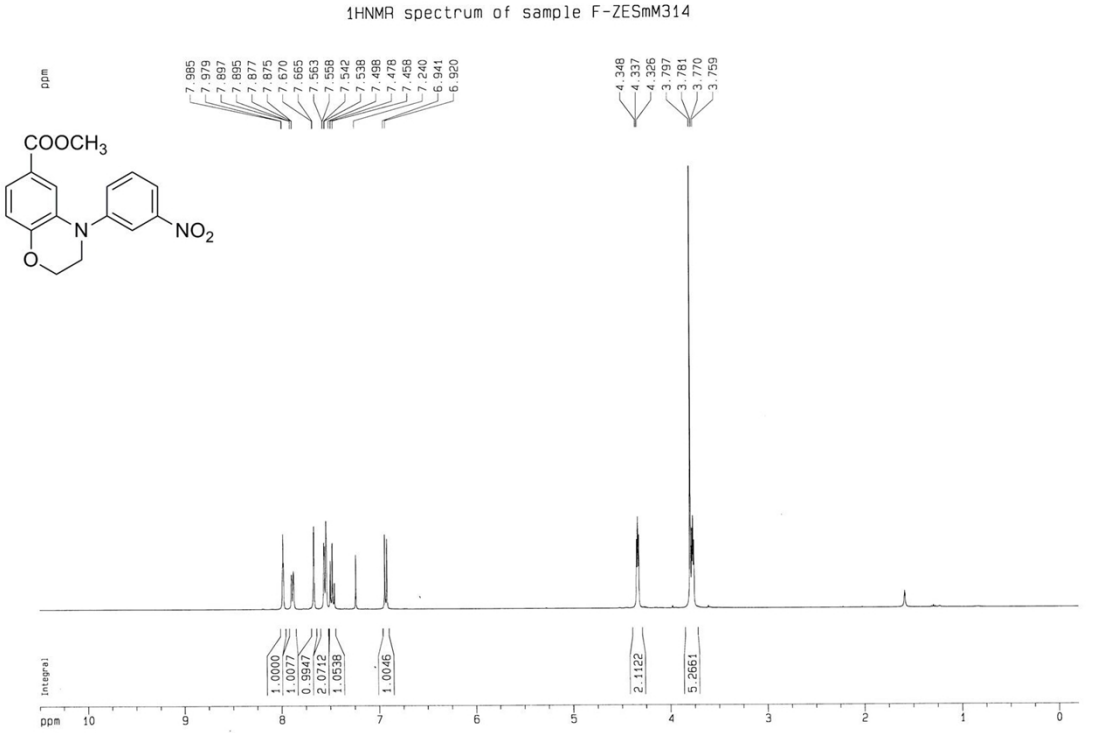
1HNMR spectrum of sample F-ZESmM283

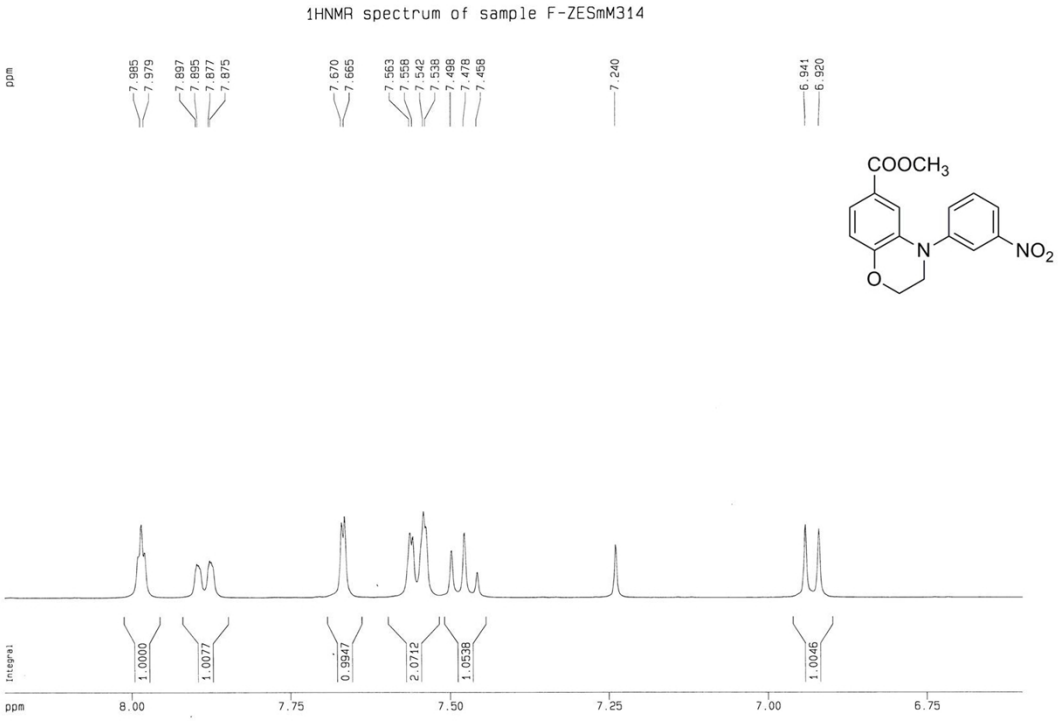


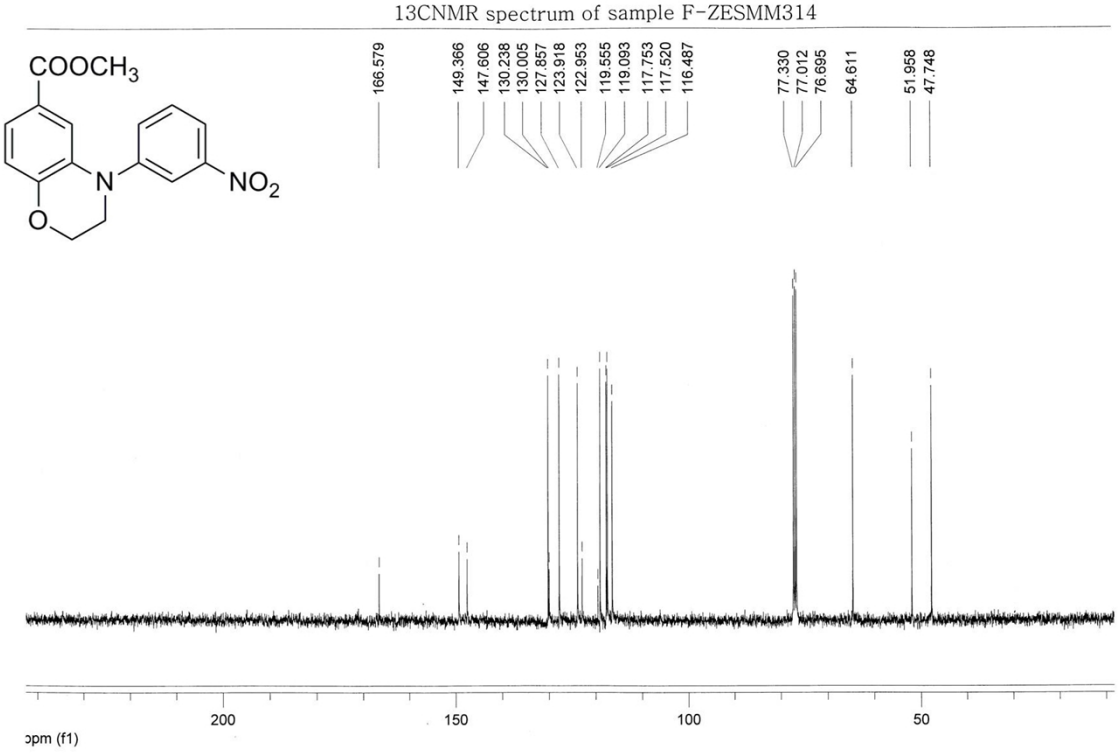
13CNMR spectrum of sample 4S



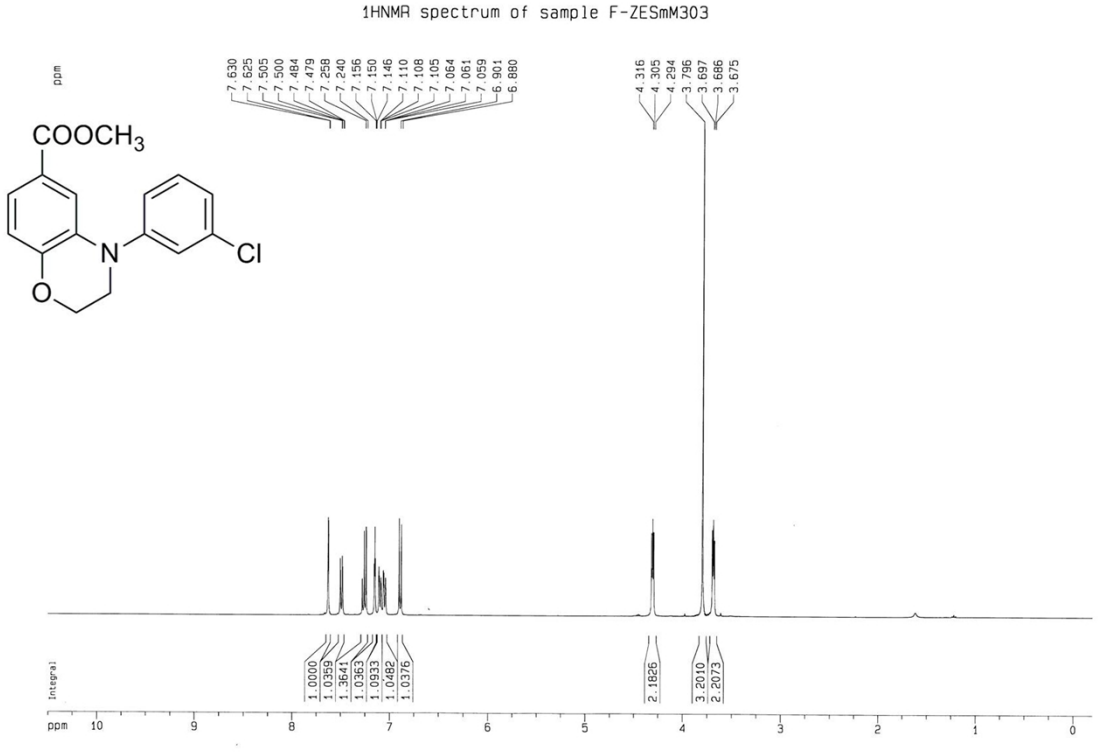
[^{1}H NMR and ^{13}C NMR spectrum of 4t in $CDCl_3$]

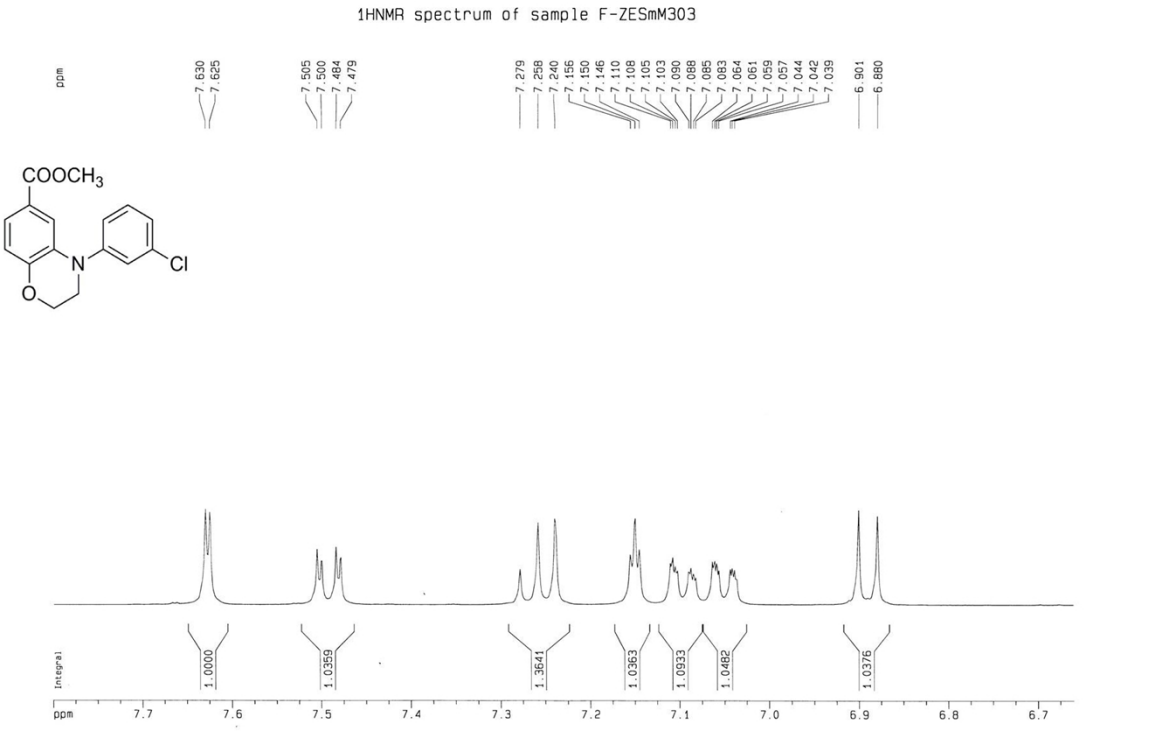


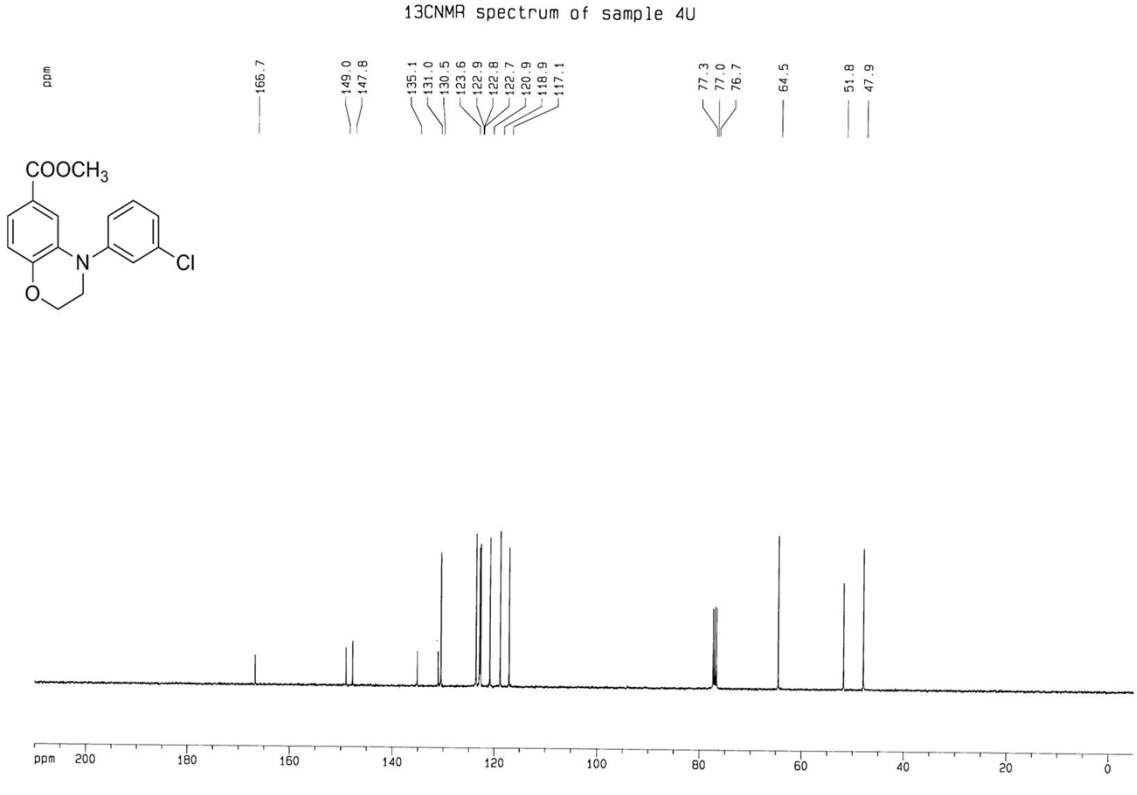




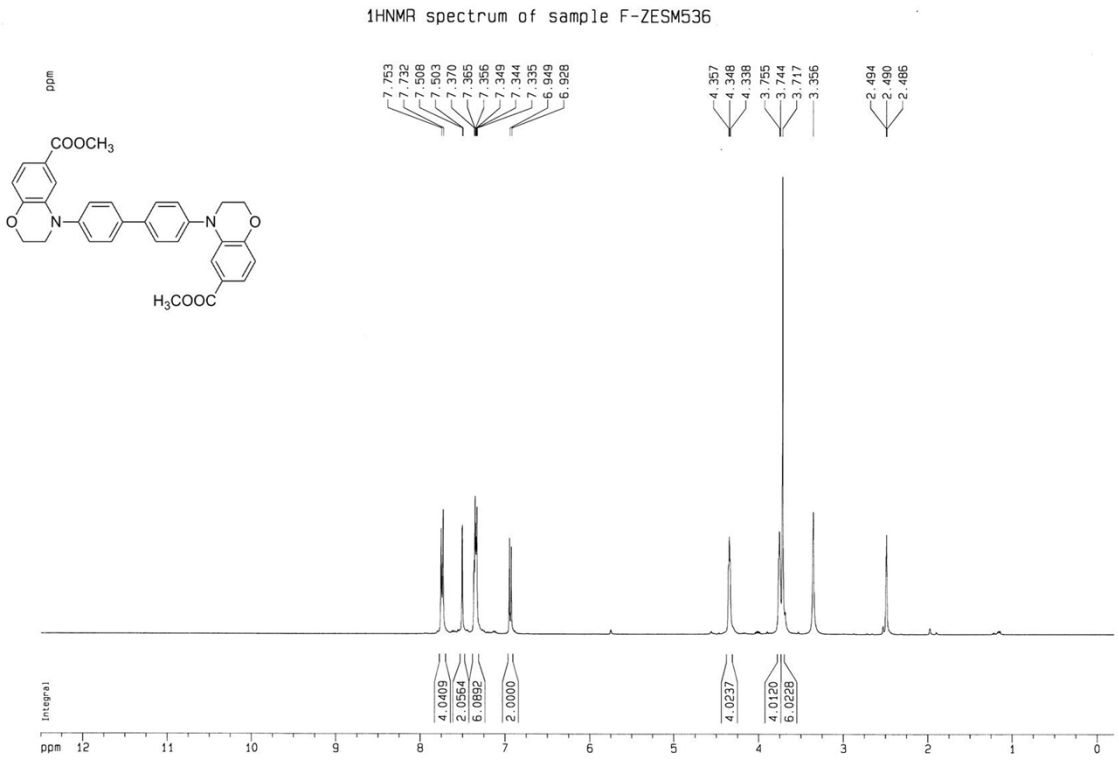
[^{1}H NMR and ^{13}C NMR spectrum of 4u in $CDCl_3$]

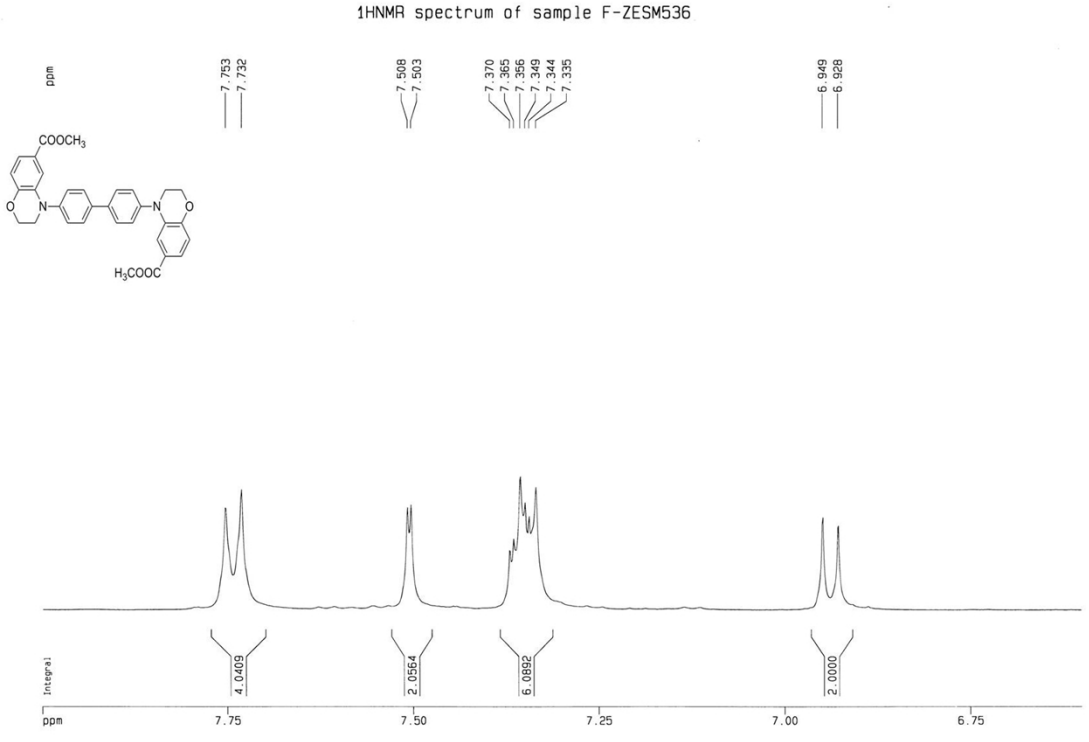


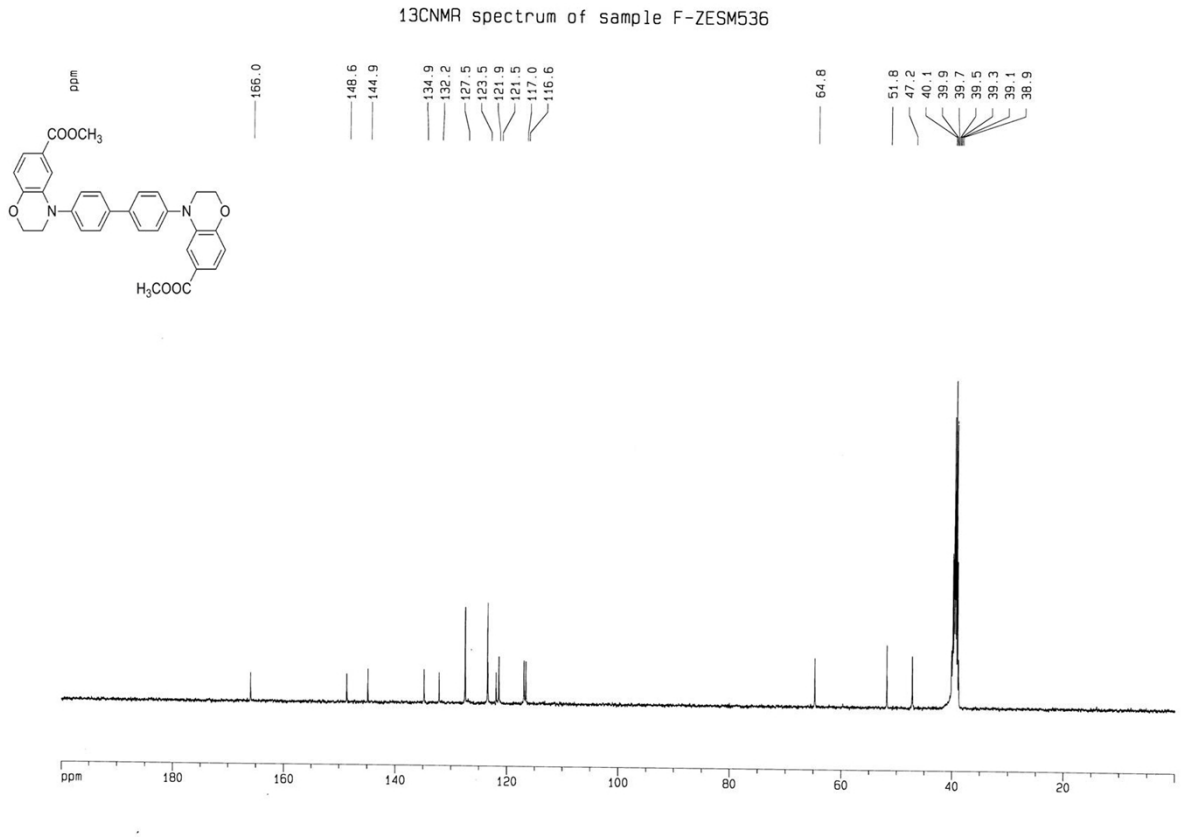




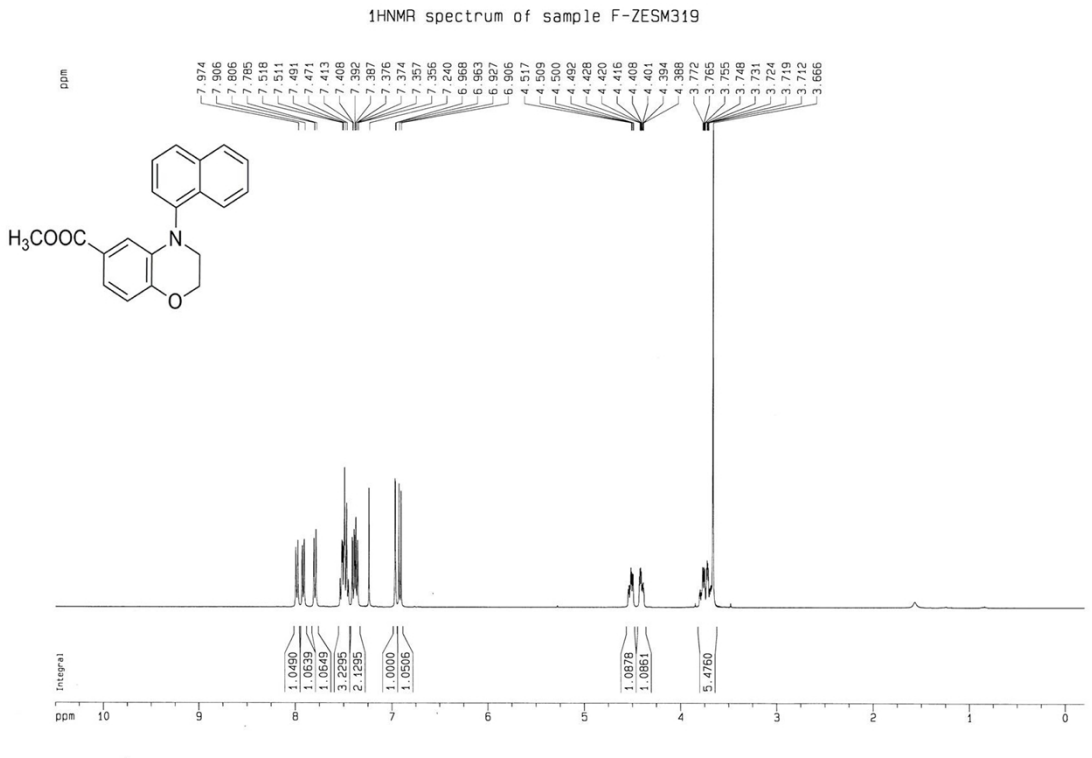
[^{1}H NMR and ^{13}C NMR spectrum of 4v in DMSO-d_6]


1HNMR spectrum of sample F-ZESM536
ppm
7.753
7.732
7.508
7.503
7.370
7.365
7.356
7.349
7.344
7.335
6.949
6.928
4.357
4.348
4.338
3.755
3.744
3.717
3.356
2.494
2.490
2.486
COOCH3
H3COOC
Integral
4.0409
2.0564
6.0892
2.0000
4.0237
4.0120
5.0228
ppm 12 11 10 9 8 7 6 5 4 3 2 1 0

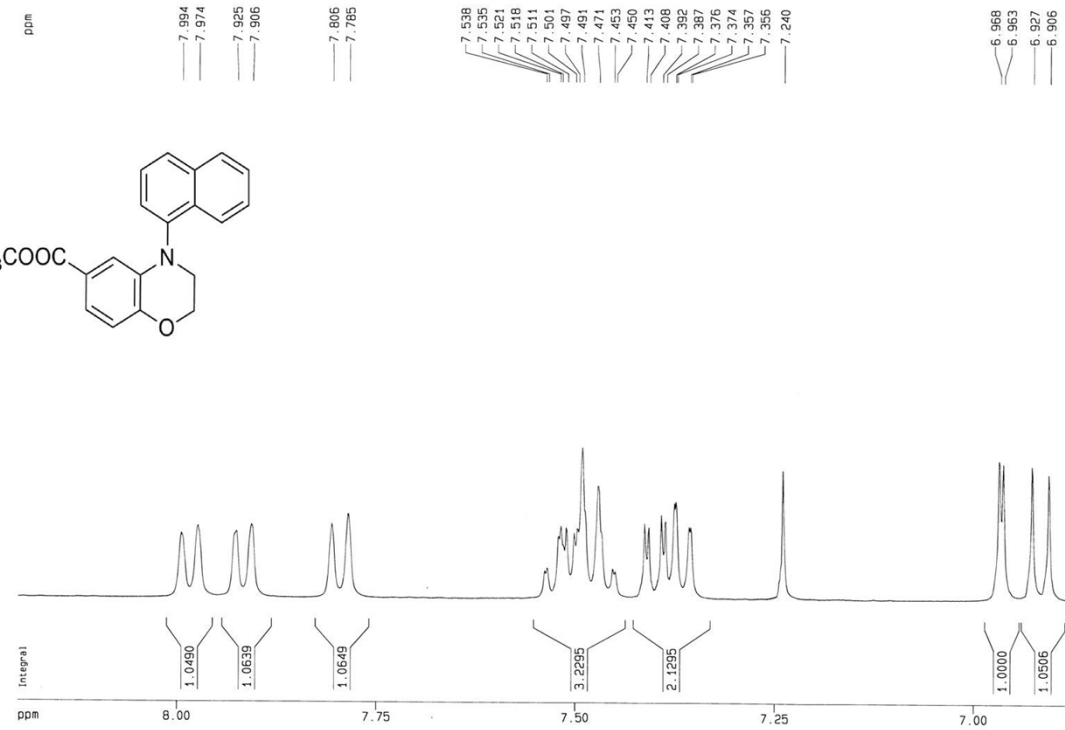

1HNMR spectrum of sample F-ZESM536
ppm
7.753
7.732
7.508
7.503
7.370
7.365
7.356
7.349
7.344
7.335
6.949
6.928
COOCH3
H3COOC
Integral
4.0409
2.0564
6.0892
2.0000
ppm 7.75 7.50 7.25 7.00 6.75



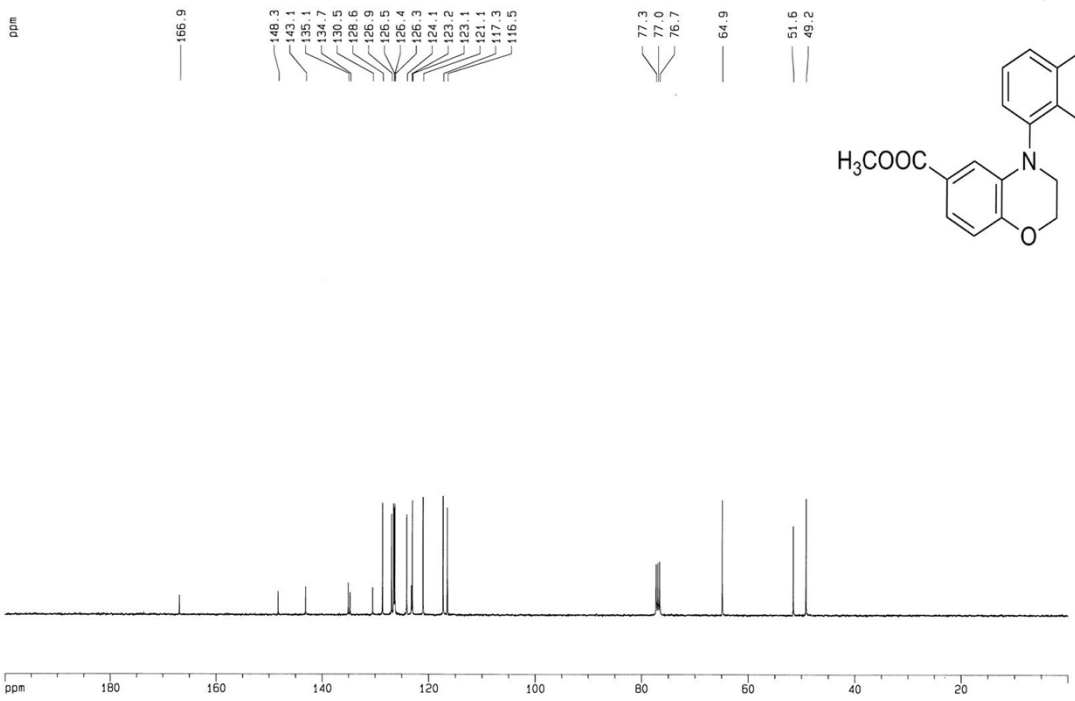
[^{1}H NMR and ^{13}C NMR spectrum of 4w in $CDCl_3$]



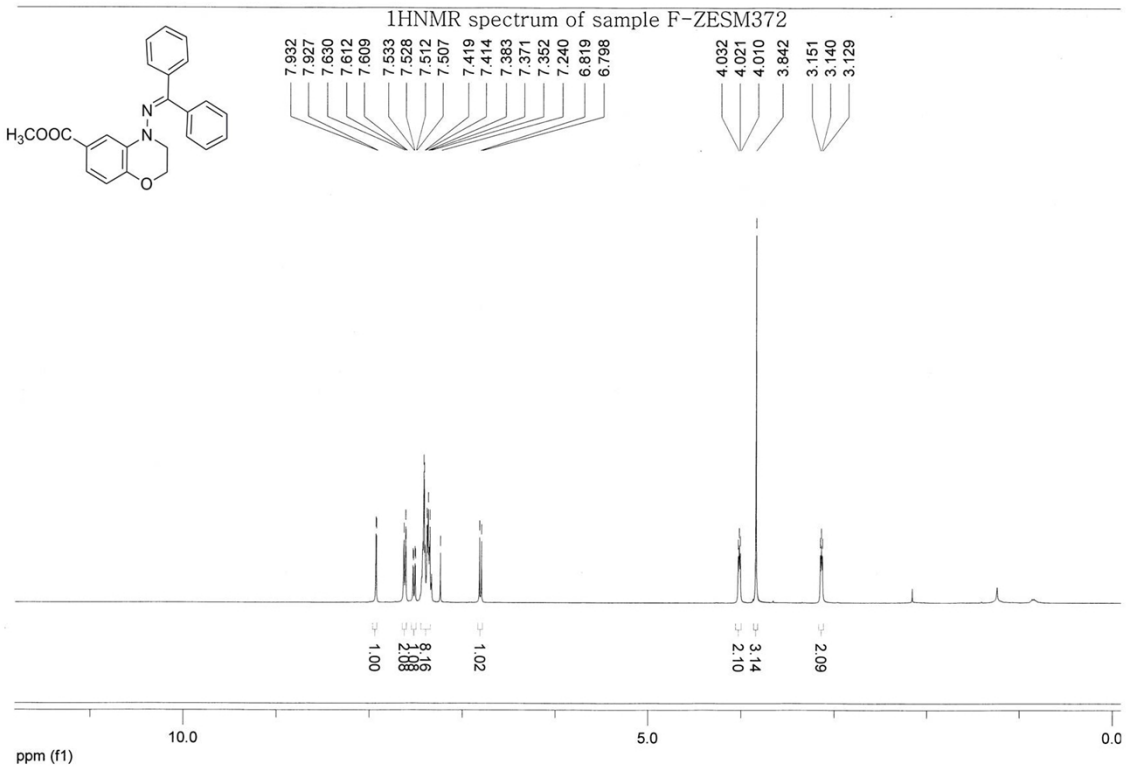
1HNMR spectrum of sample F-ZESM319

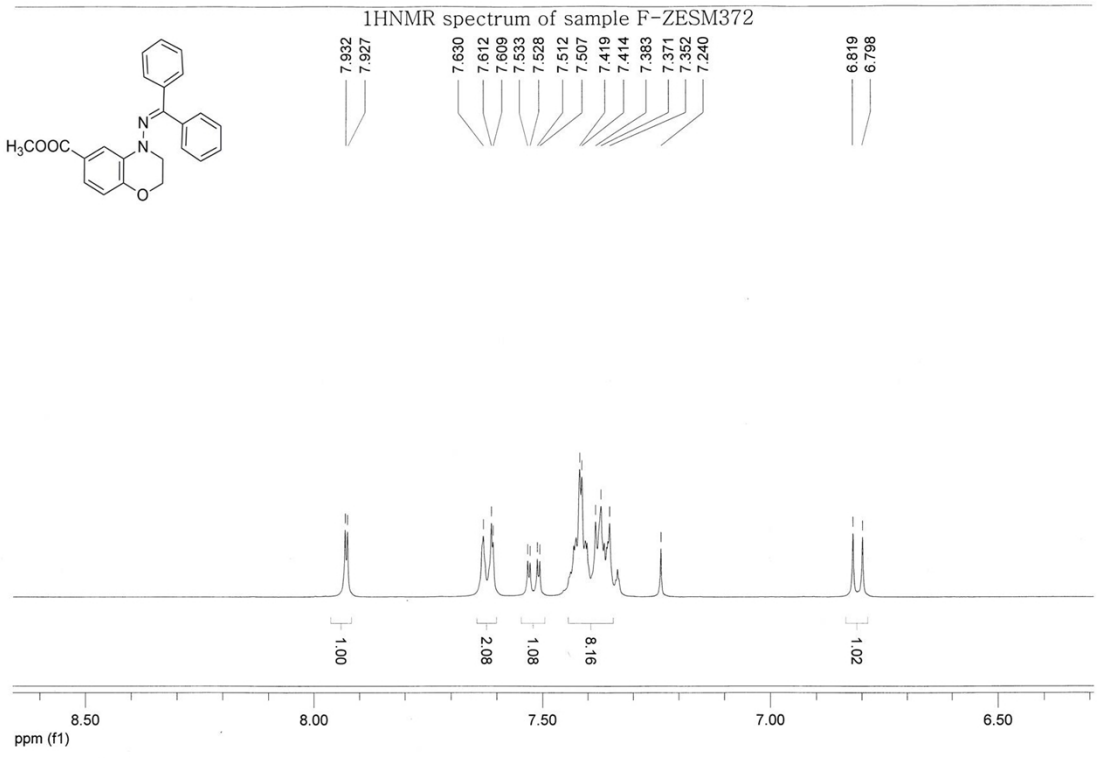


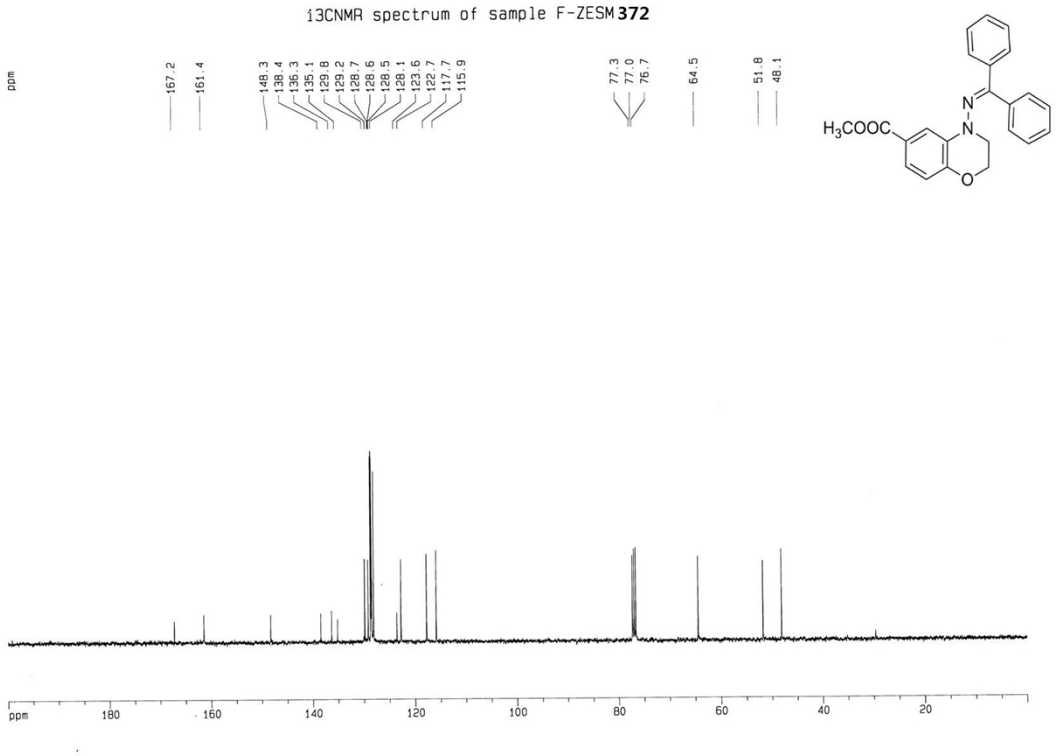
13CNMR spectrum of sample F-ZESM319



[^{1}H NMR and ^{13}C NMR spectrum of 4x in $CDCl_3$]

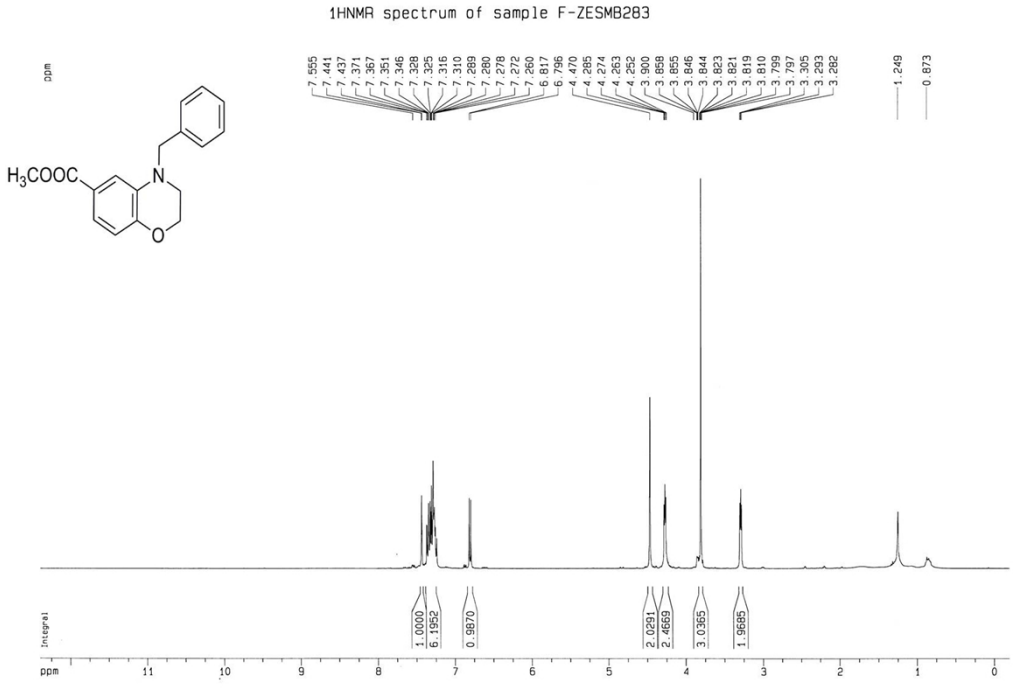




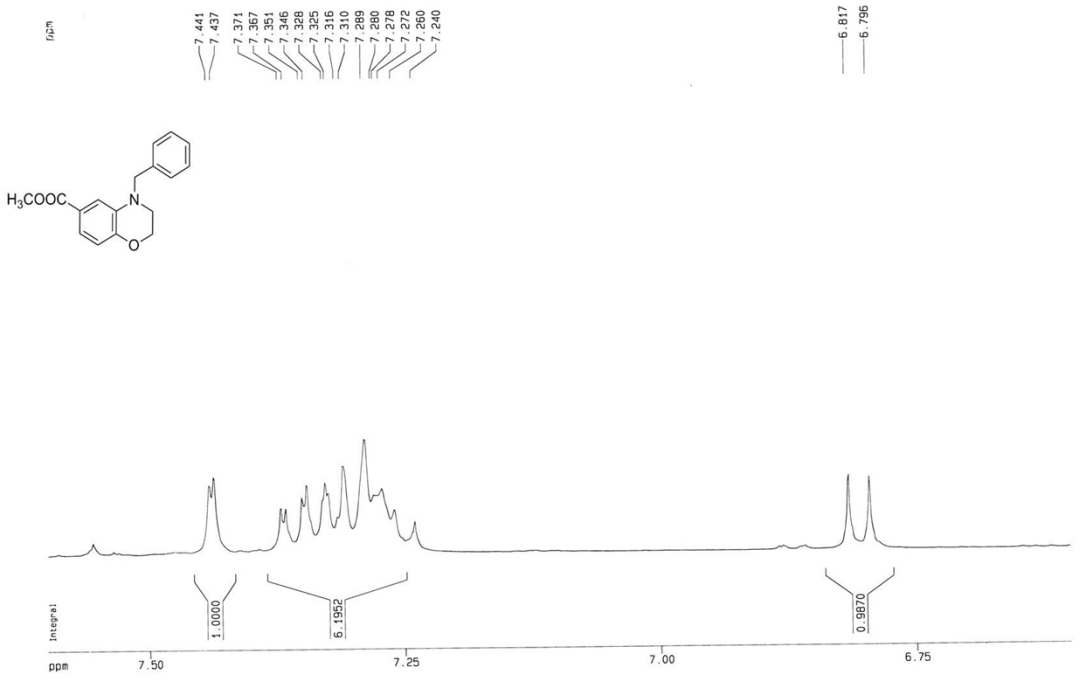


Ⅳ-2 ^{1}H-NMR and ^{13}C-NMR spectra of compounds 6a-6d

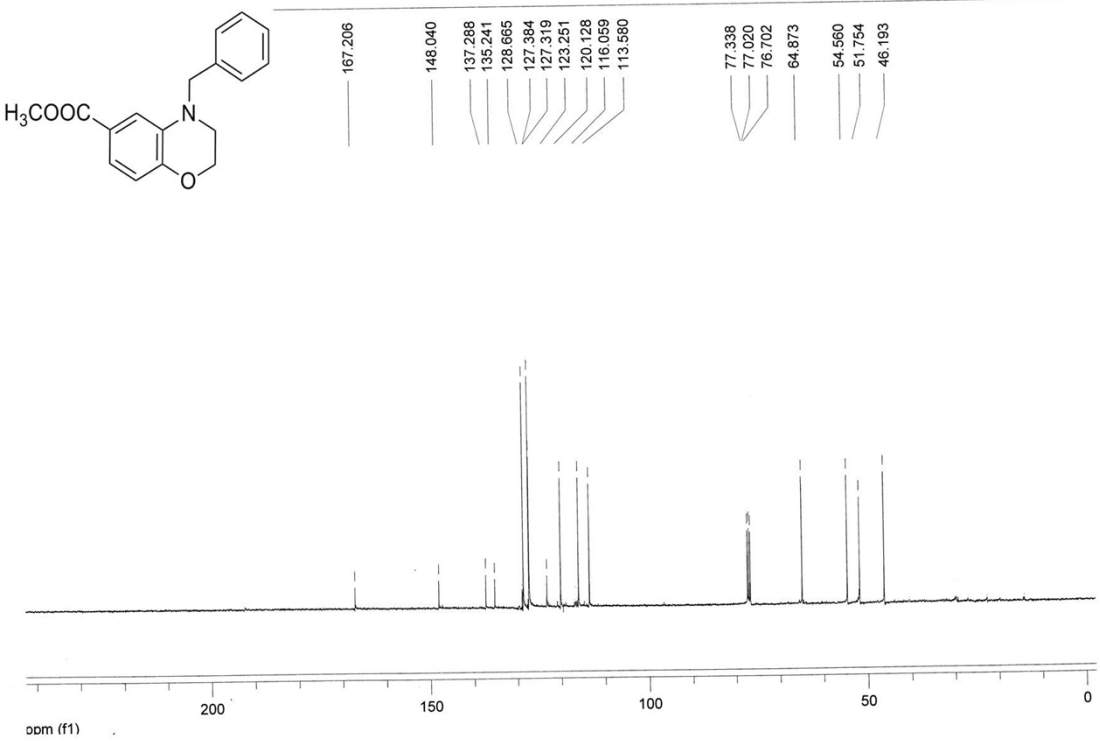
[^{1}H NMR and ^{13}C NMR spectrum of 6a in $CDCl_3$]



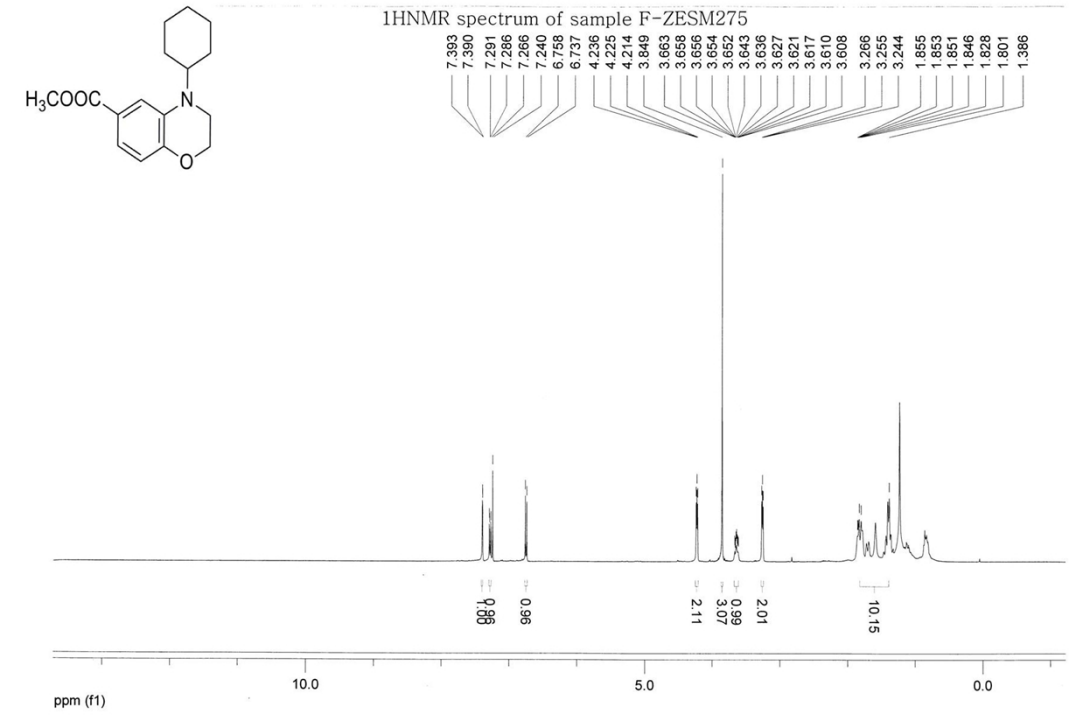
1HNMR spectrum of sample F-ZESMB283

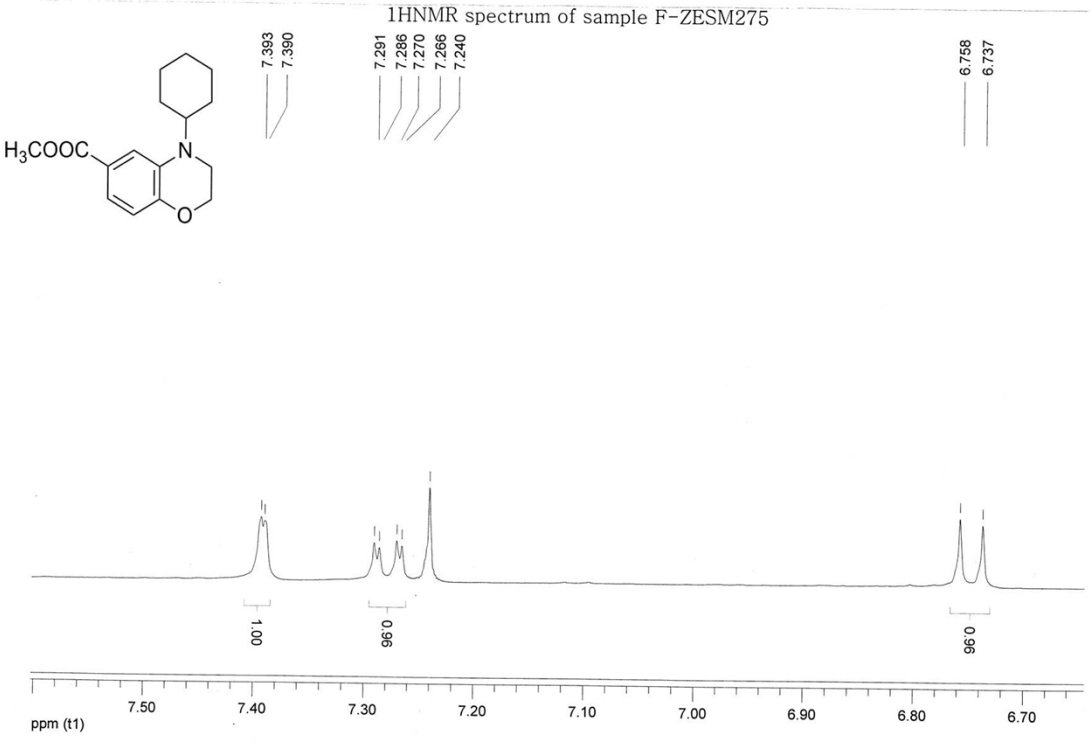


13CNMR spectrum of sample F-ZESMB283

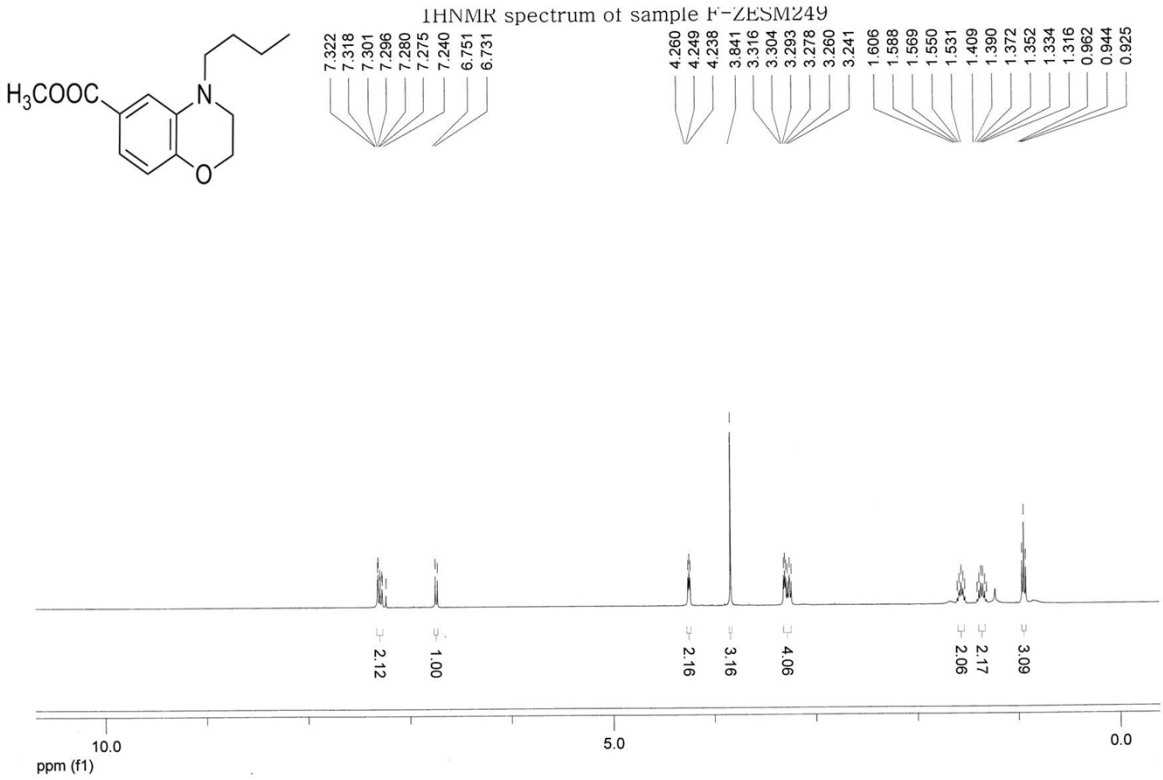


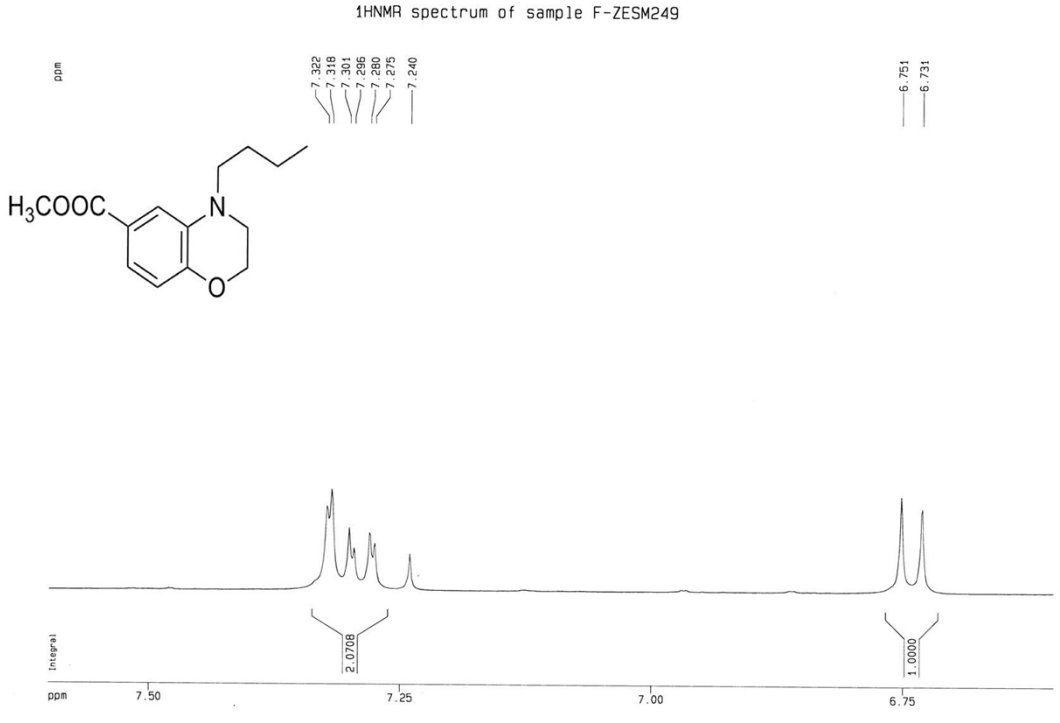
[^{1}H NMR and ^{13}C NMR spectrum of 6b in $CDCl_3$]

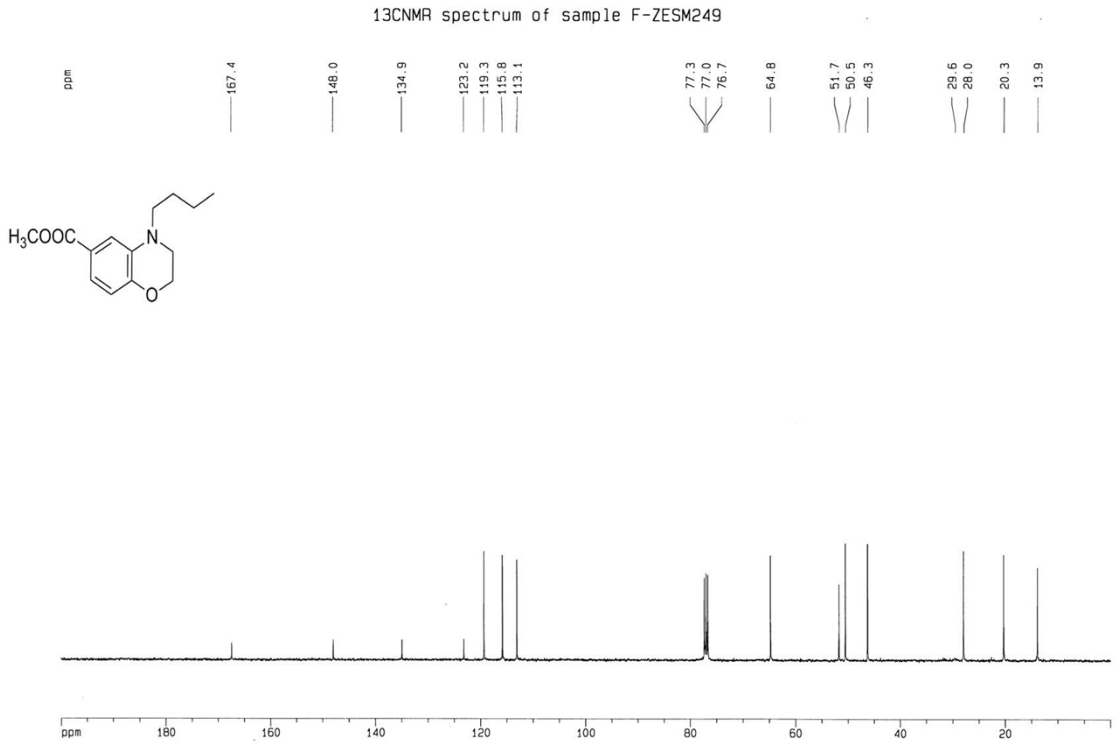




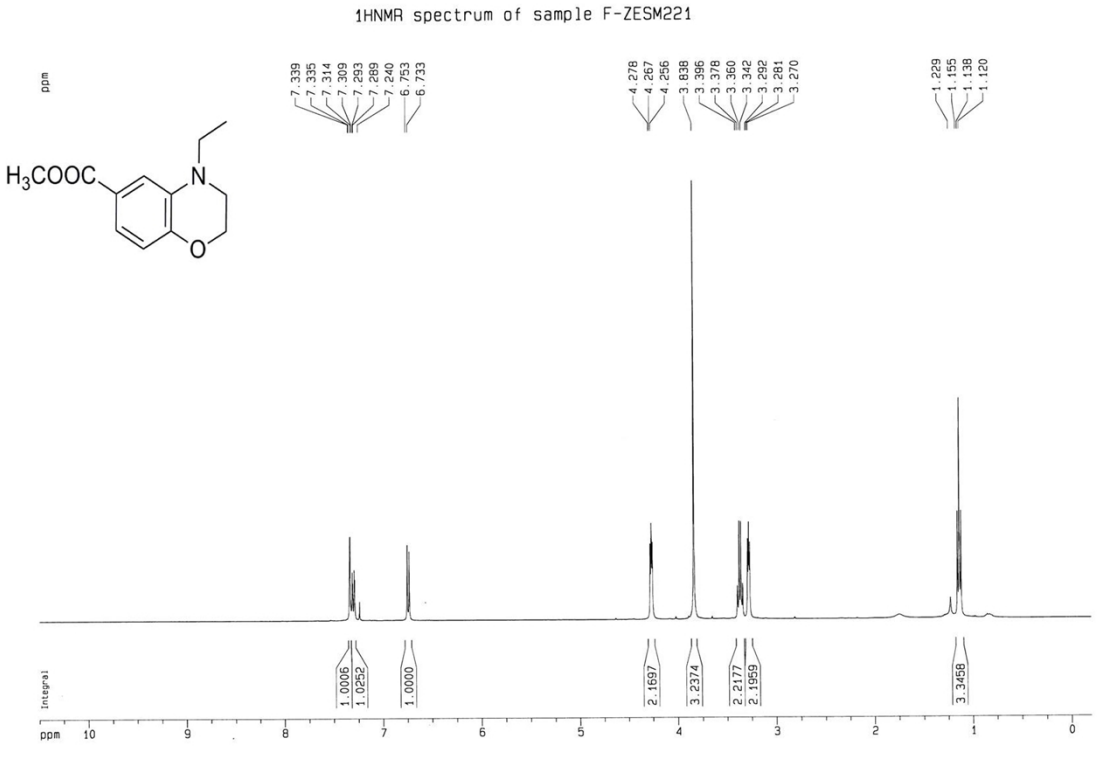
[^{1}H NMR and ^{13}C NMR spectrum of 6c in $CDCl_3$]



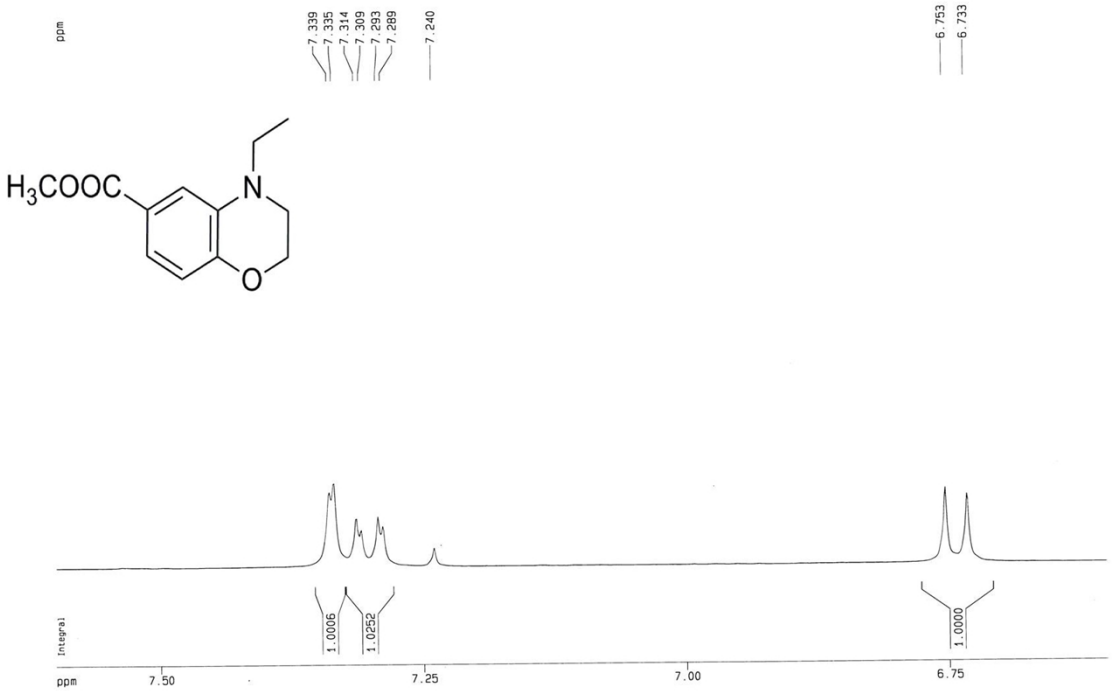




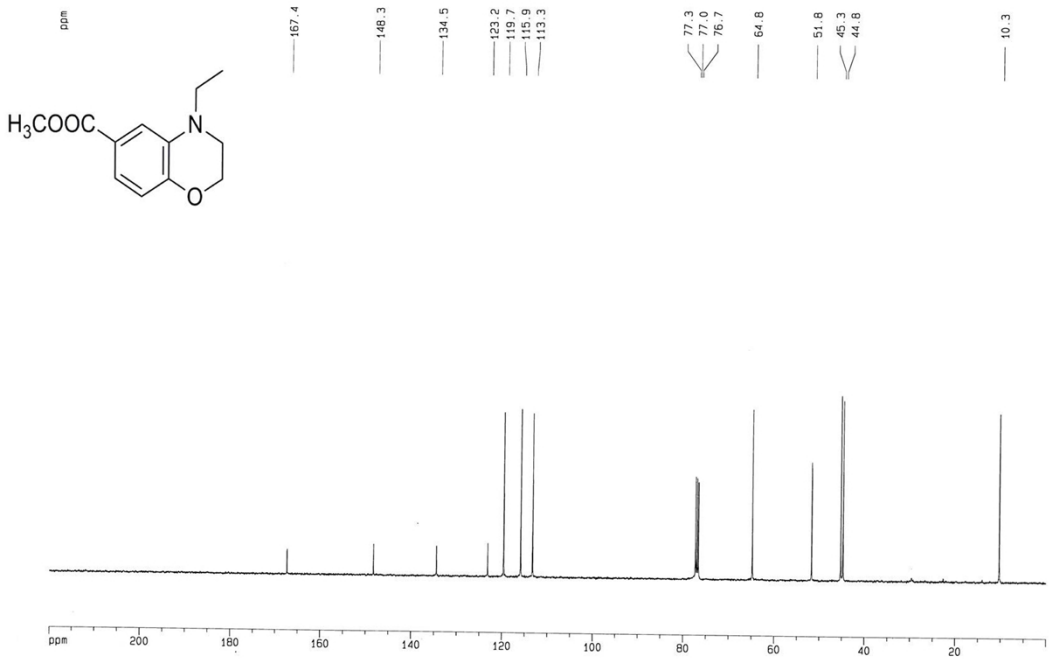
[^{1}H NMR and ^{13}C NMR spectrum of 6d in $CDCl_3$]



1HNMR spectrum of sample F-ZESM221

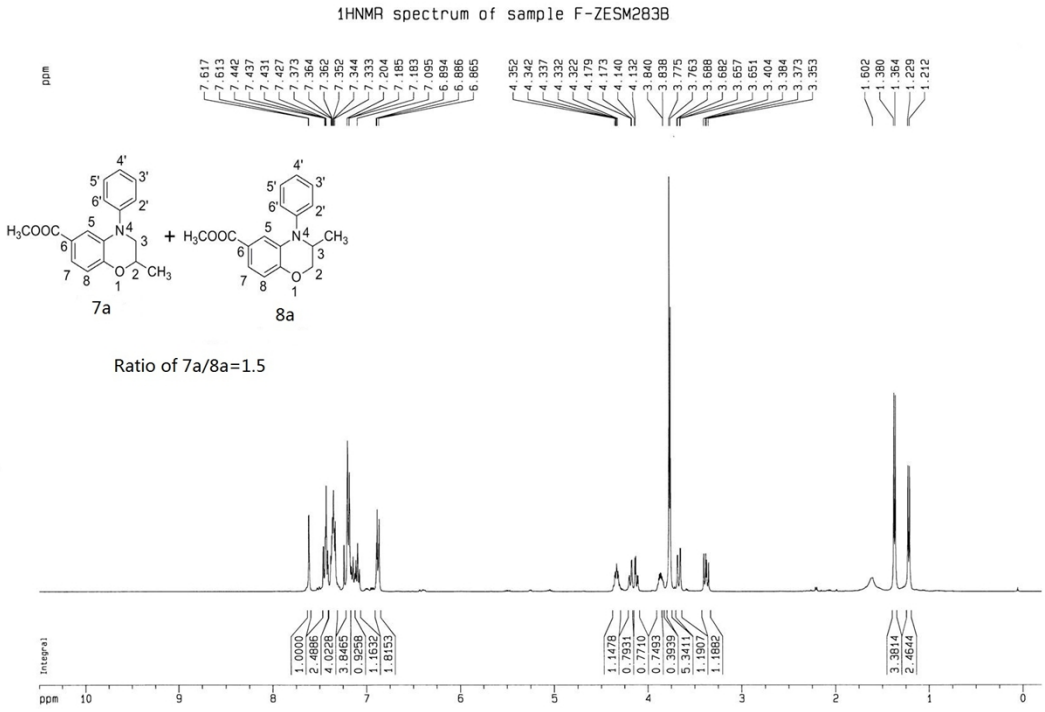


13CNMR spectrum of sample F-ZESM221

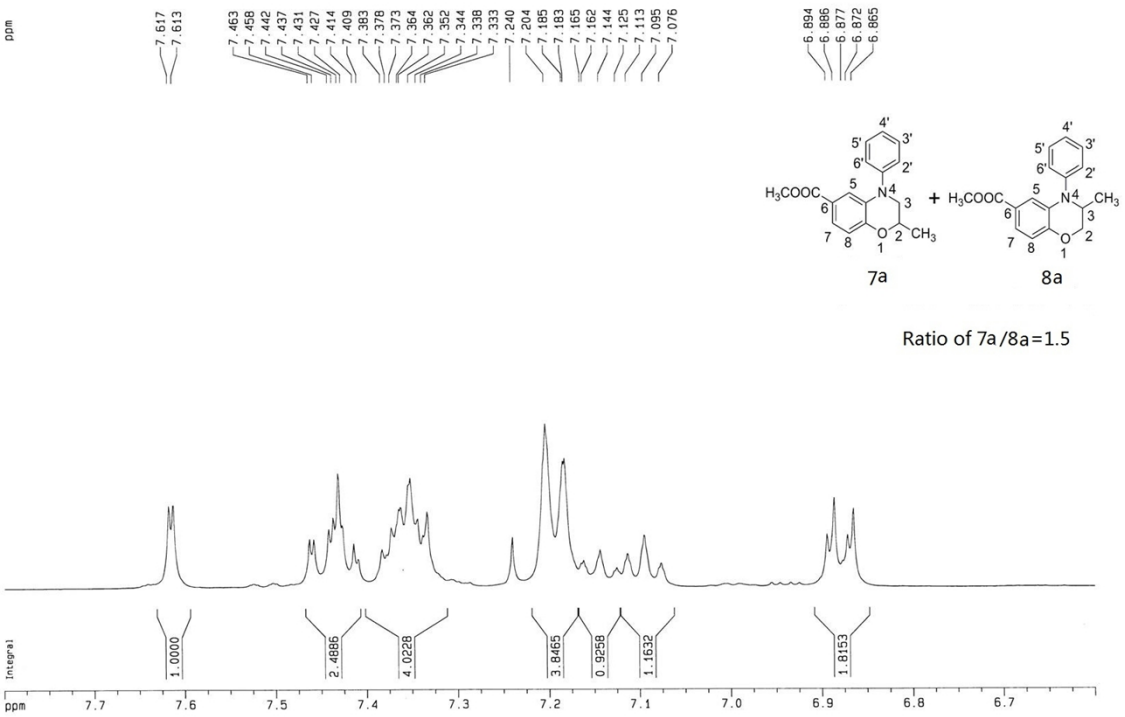


Ⅳ-2 ^{1}H-NMR and ^{13}C-NMR spectra of compounds table 4 (7 and 8)

^{1}H-NMR and ^{13}C-NMR spectra of compounds 7a and 8a

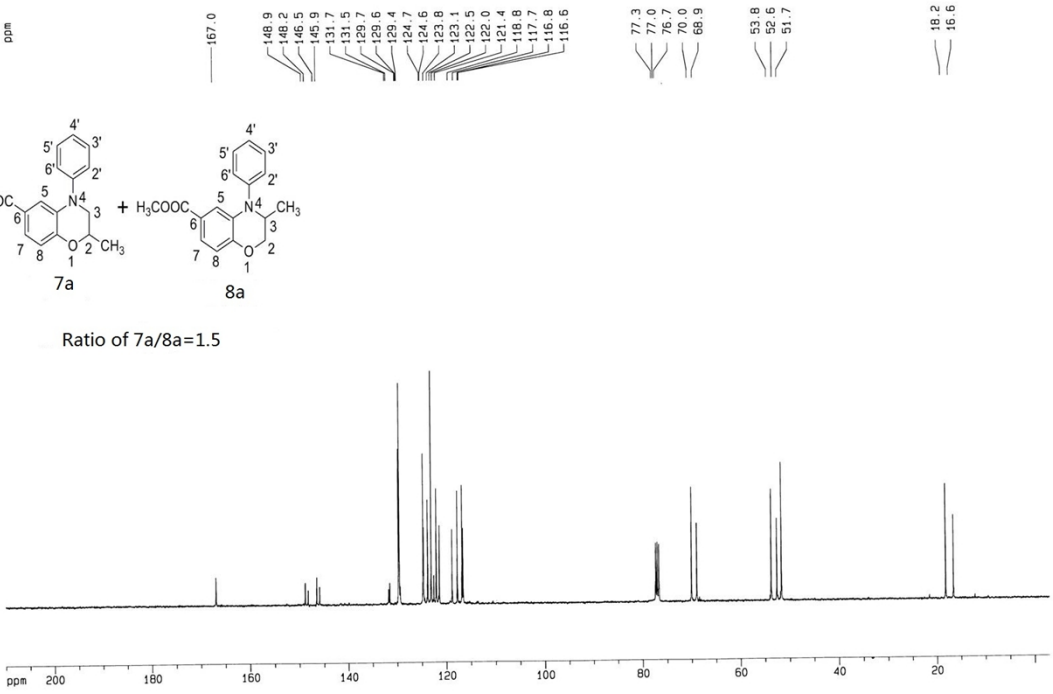


1HNMR spectrum of sample F-ZESM283B



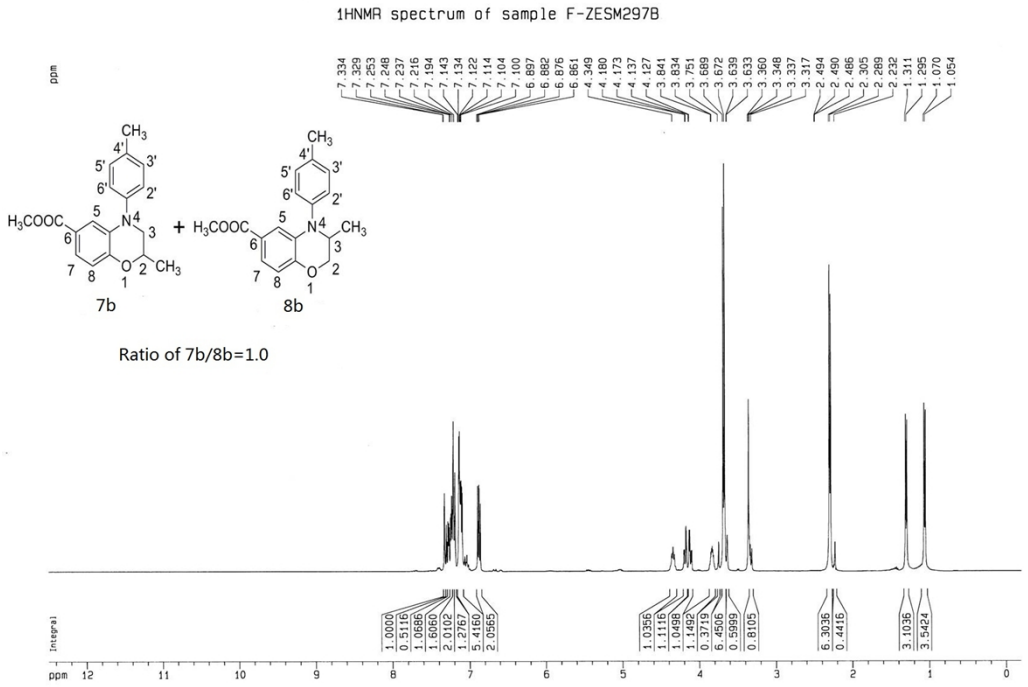
Ratio of 7a/8a=1.5

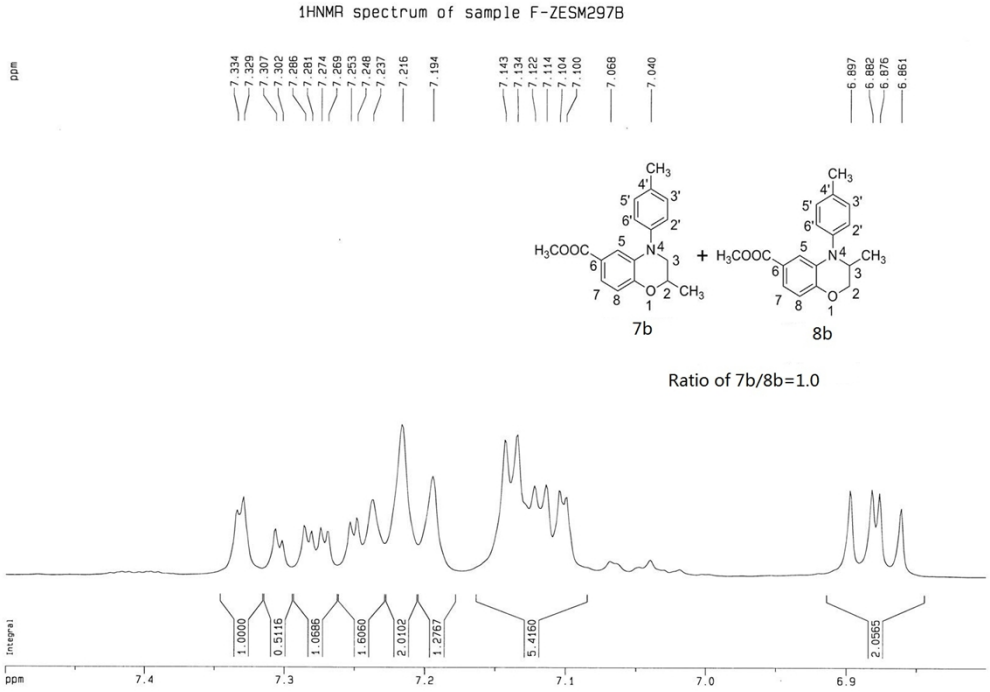
13CNMR spectrum of sample F-ZESM283B

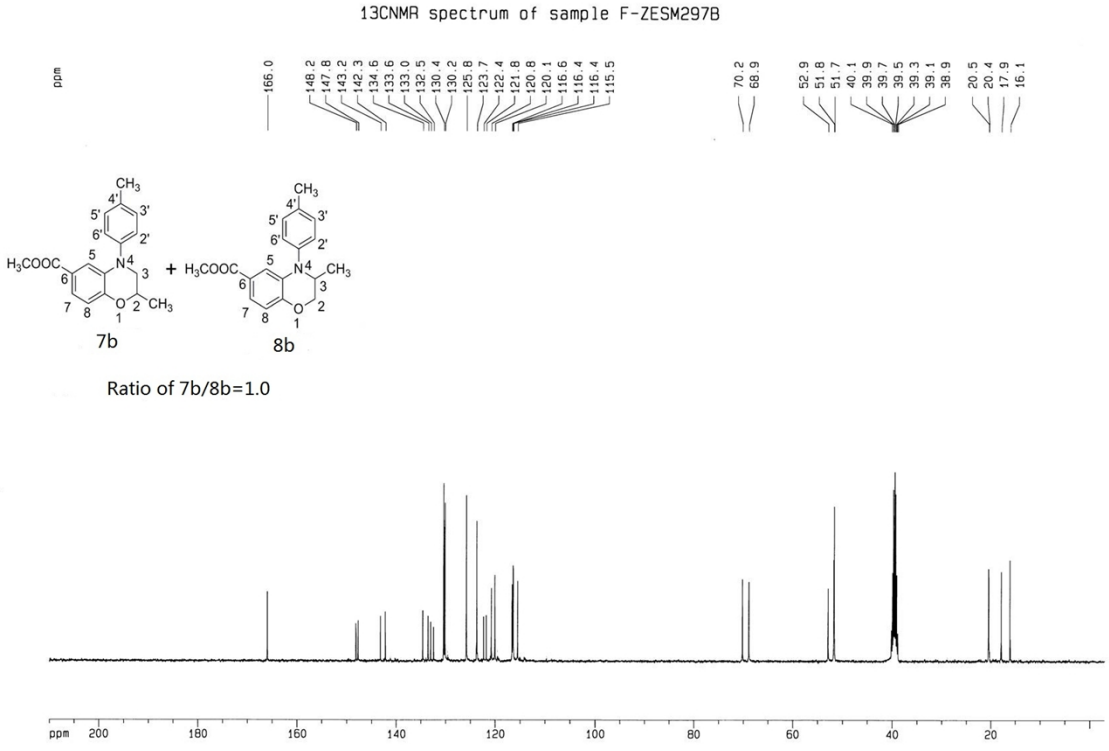


Ratio of 7a/8a=1.5

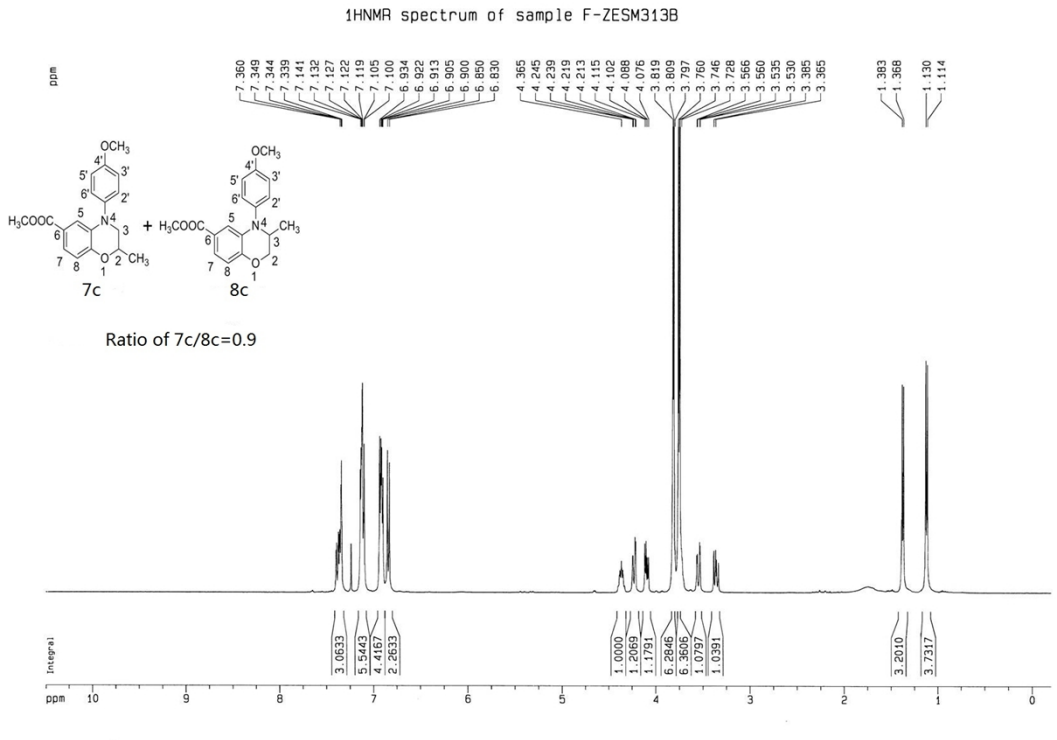
^{1}H-NMR and ^{13}C-NMR spectra of compounds 7b and 8b

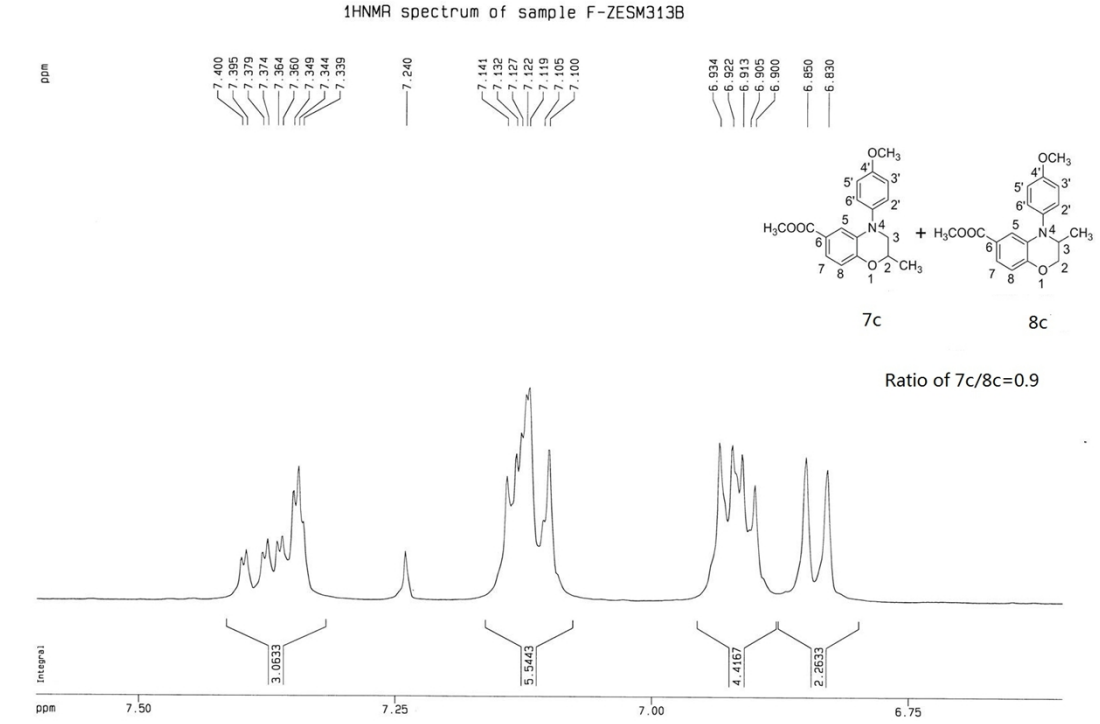


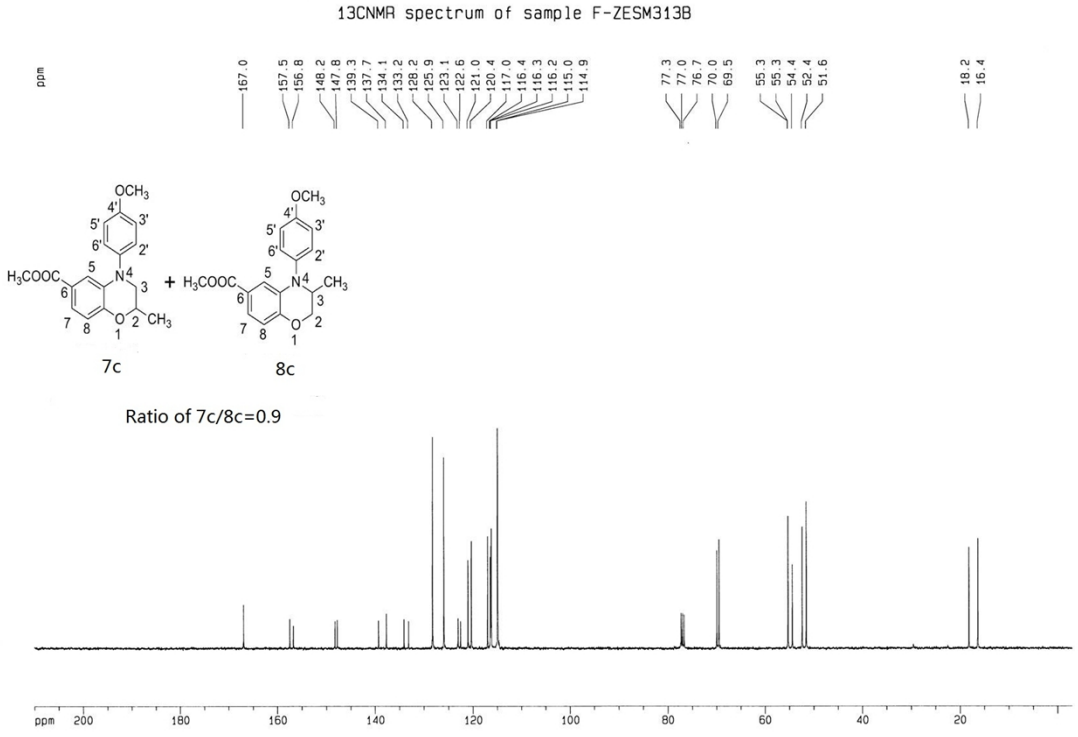




^{1}H-NMR and ^{13}C-NMR spectra of compounds 7c and 8c

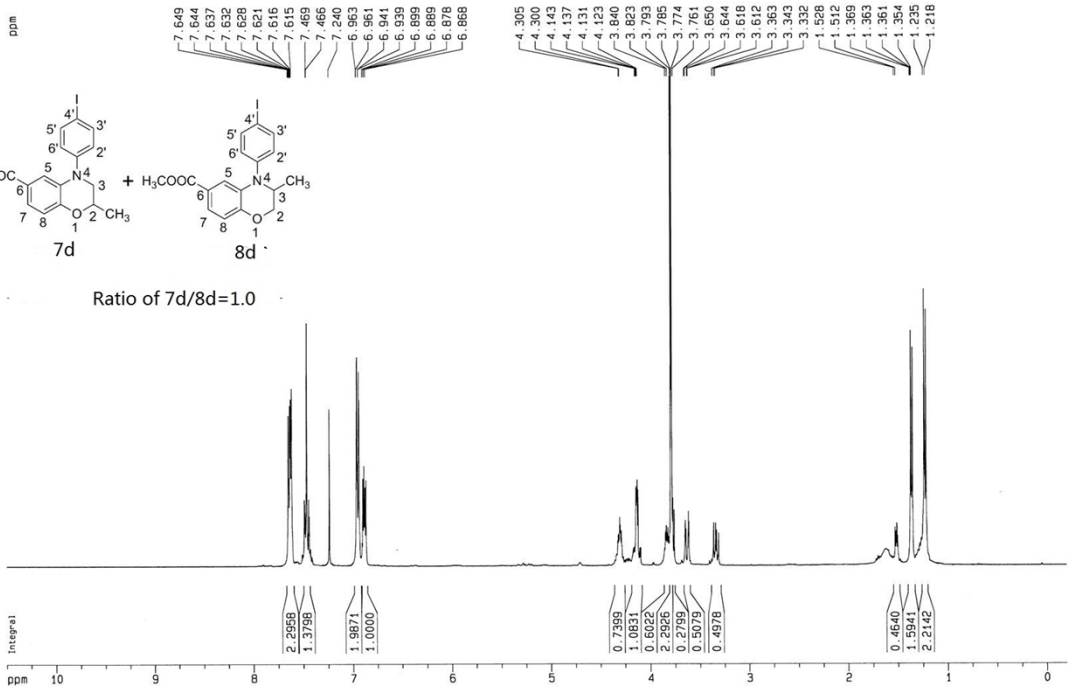




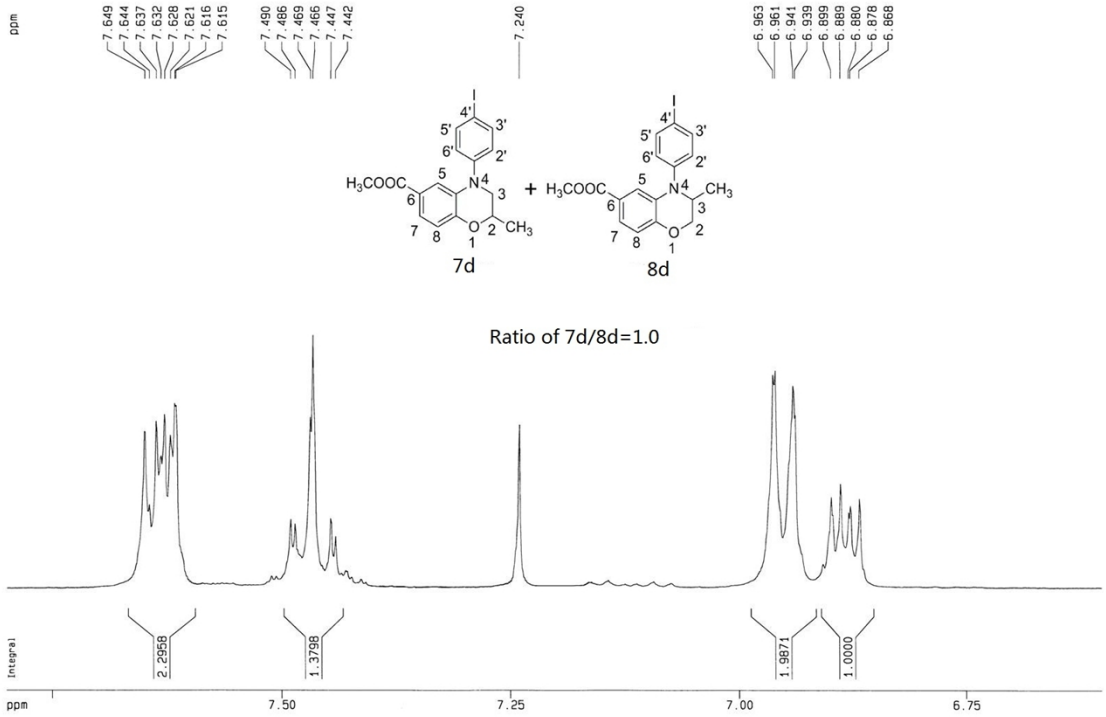


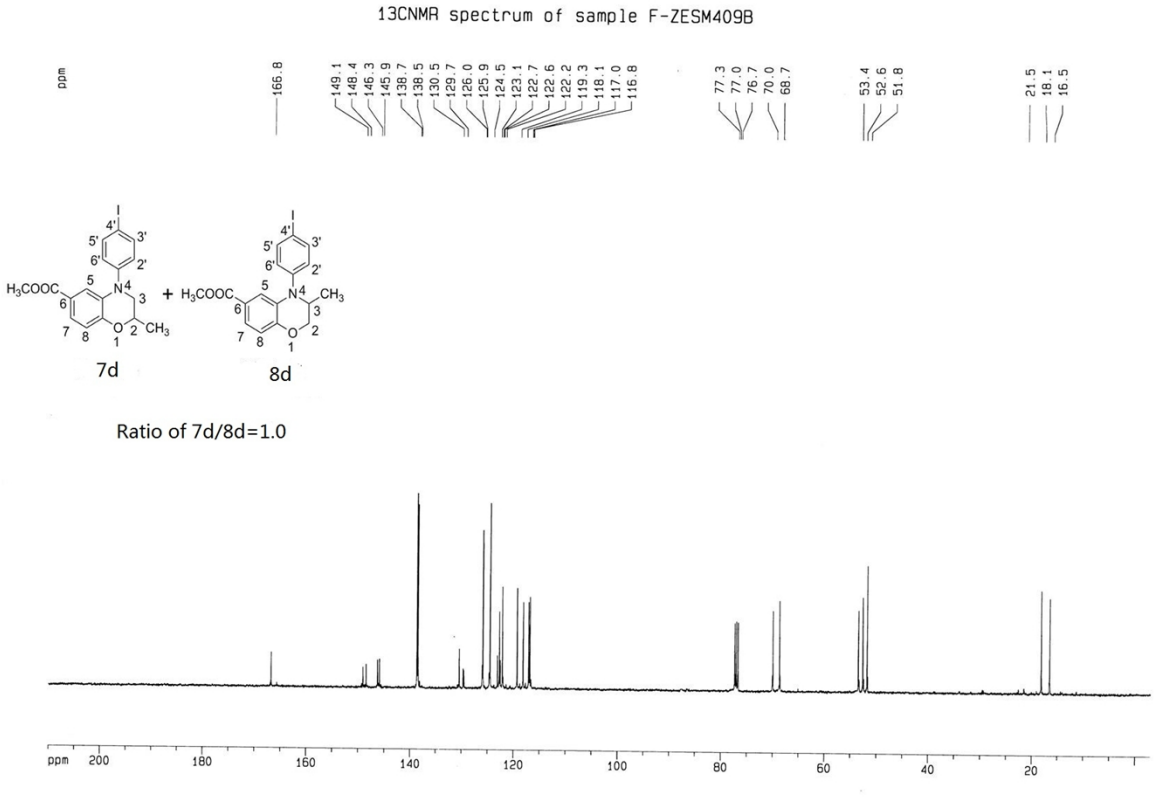
^{1}H-NMR and ^{13}C-NMR spectra of compounds 7d and 8d

1HNMR spectrum of sample F-ZESM409B

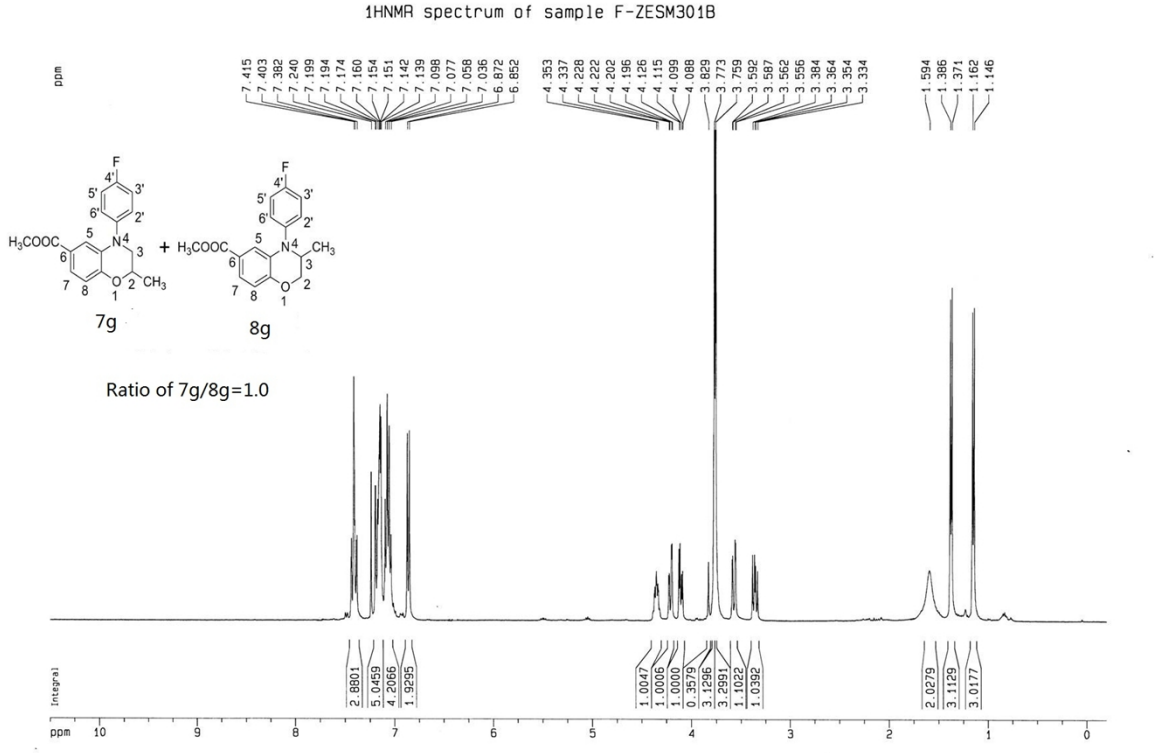


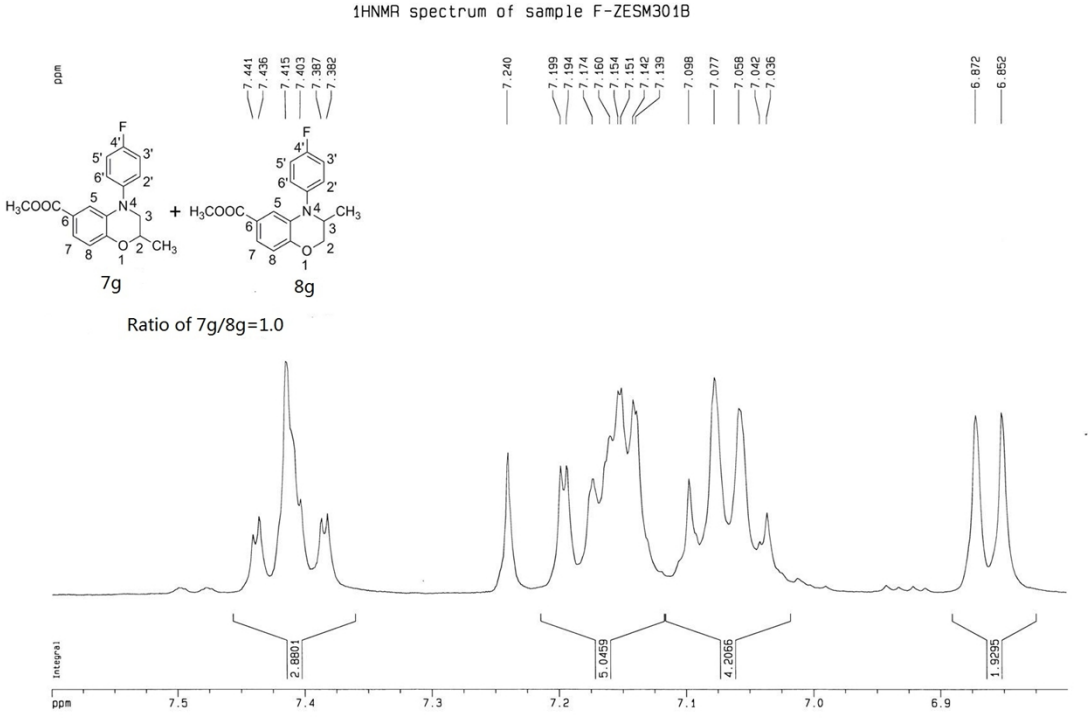
1HNMR spectrum of sample F-ZESM409B

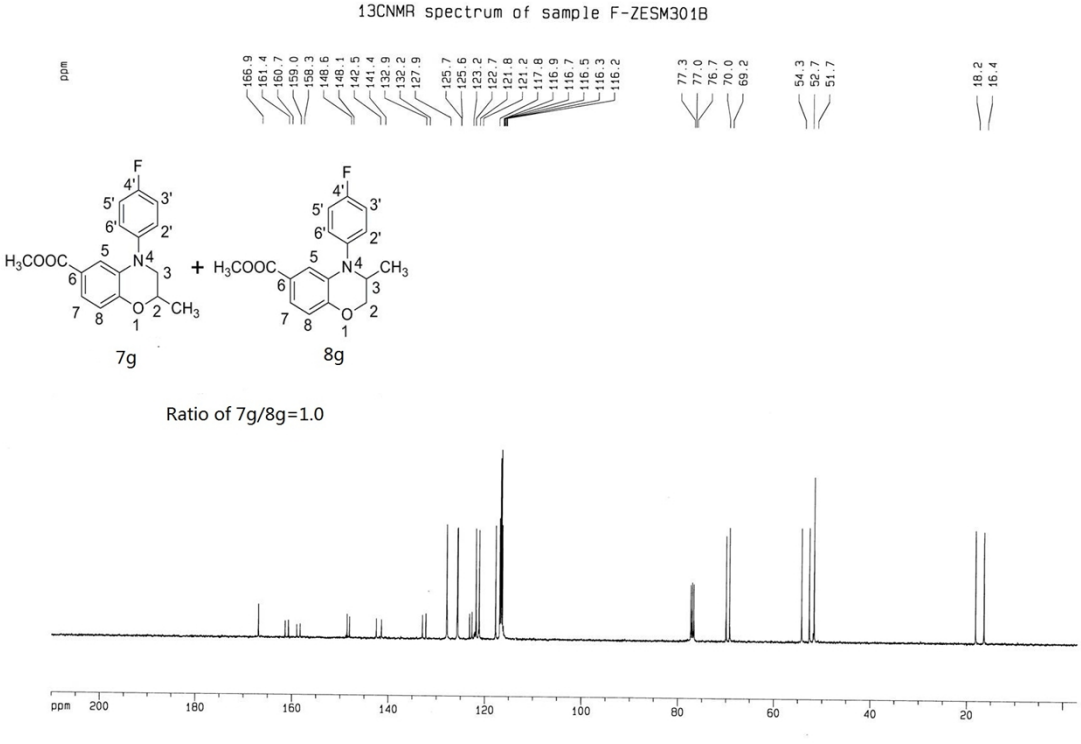




^{1}H-NMR and ^{13}C-NMR spectra of compounds 7g and 8g

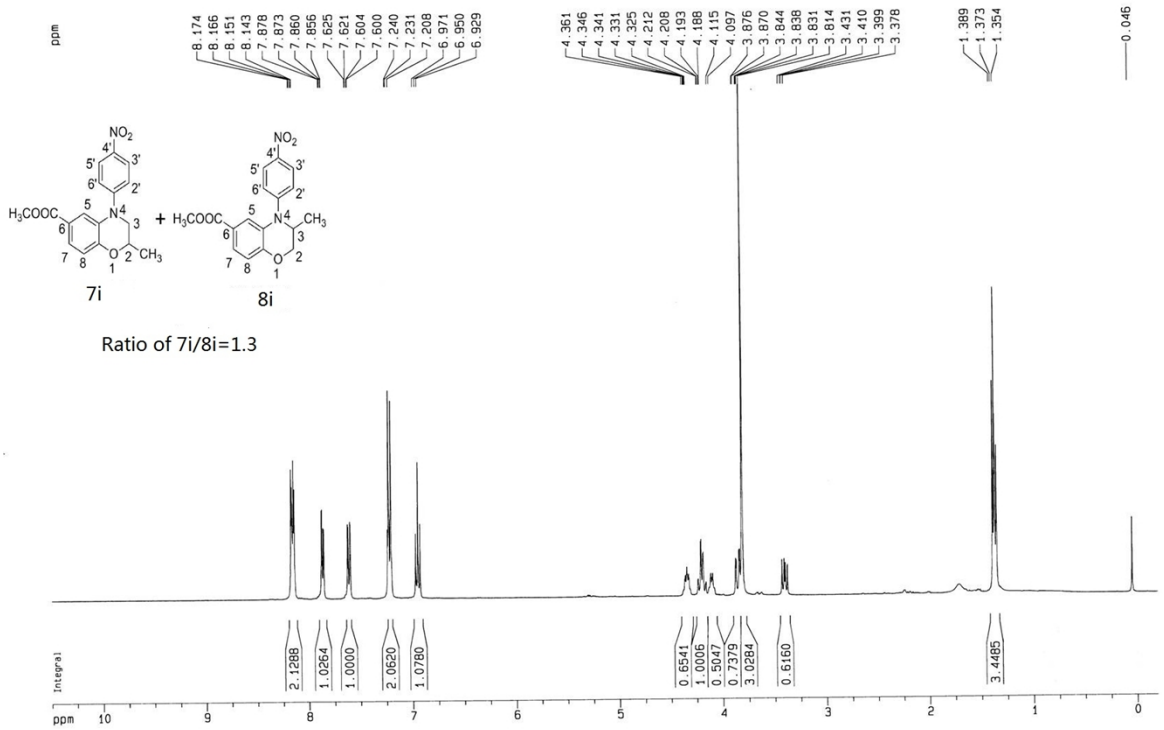






^{1}H-NMR and ^{13}C-NMR spectra of compounds 7i and 8i

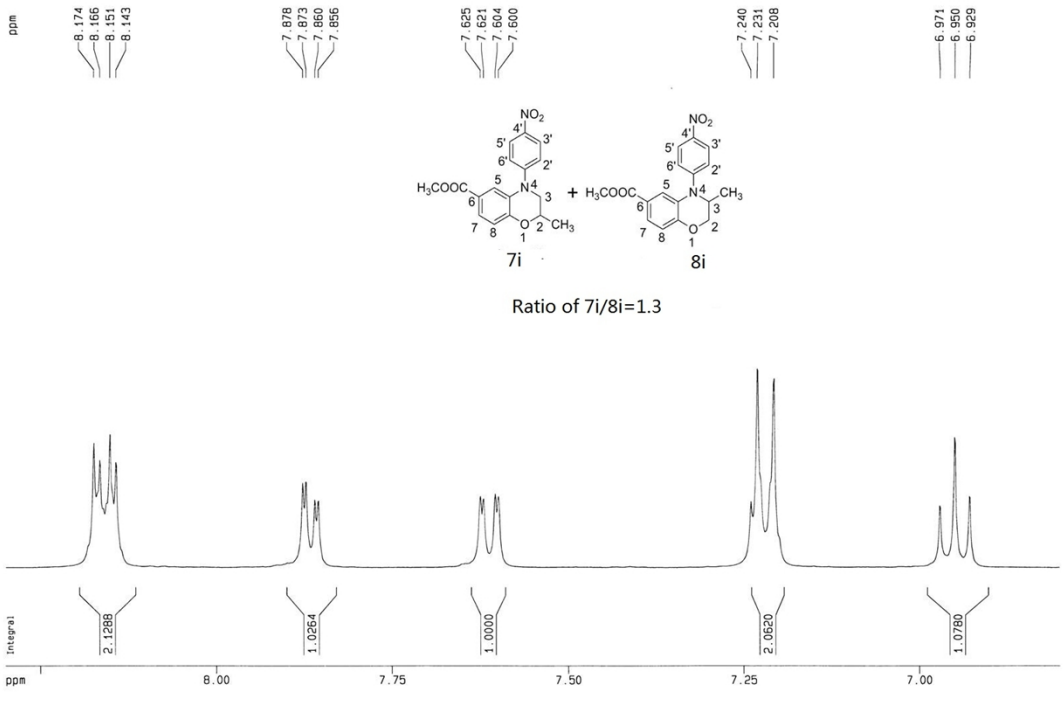
1HNMR spectrum of sample F-ZESM328B



7i + 8i

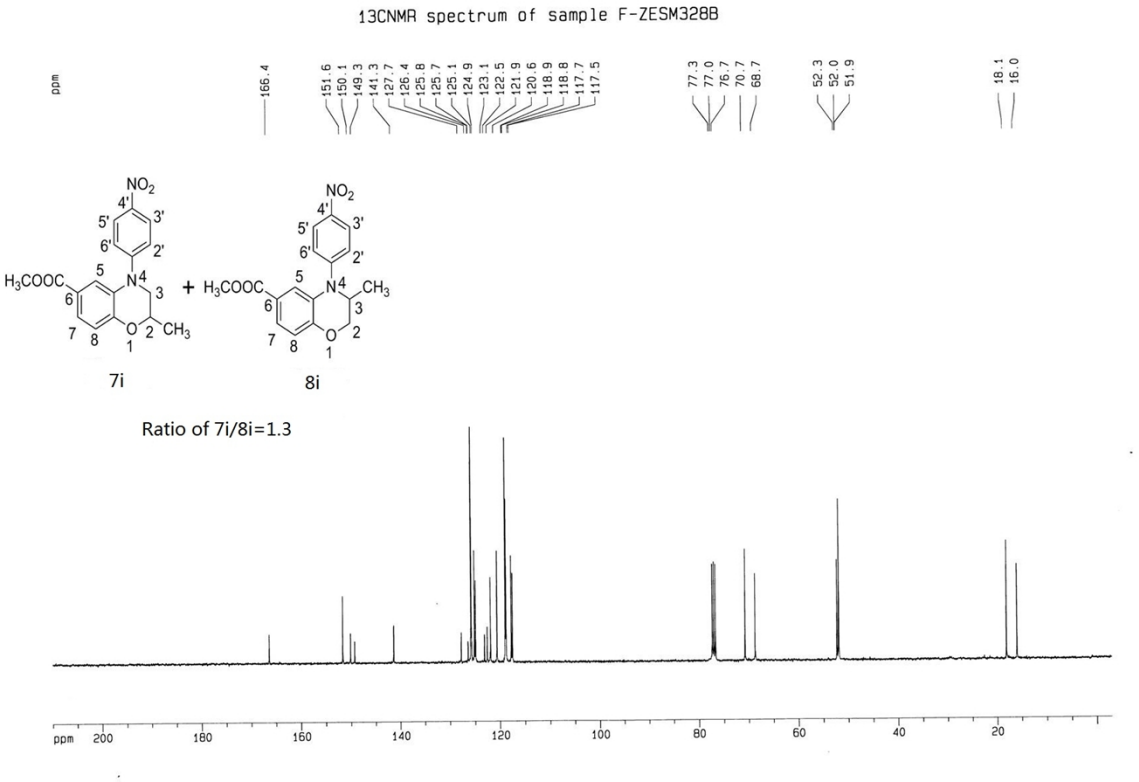
Ratio of 7i/8i=1.3

1HNMR spectrum of sample F-ZESM328B

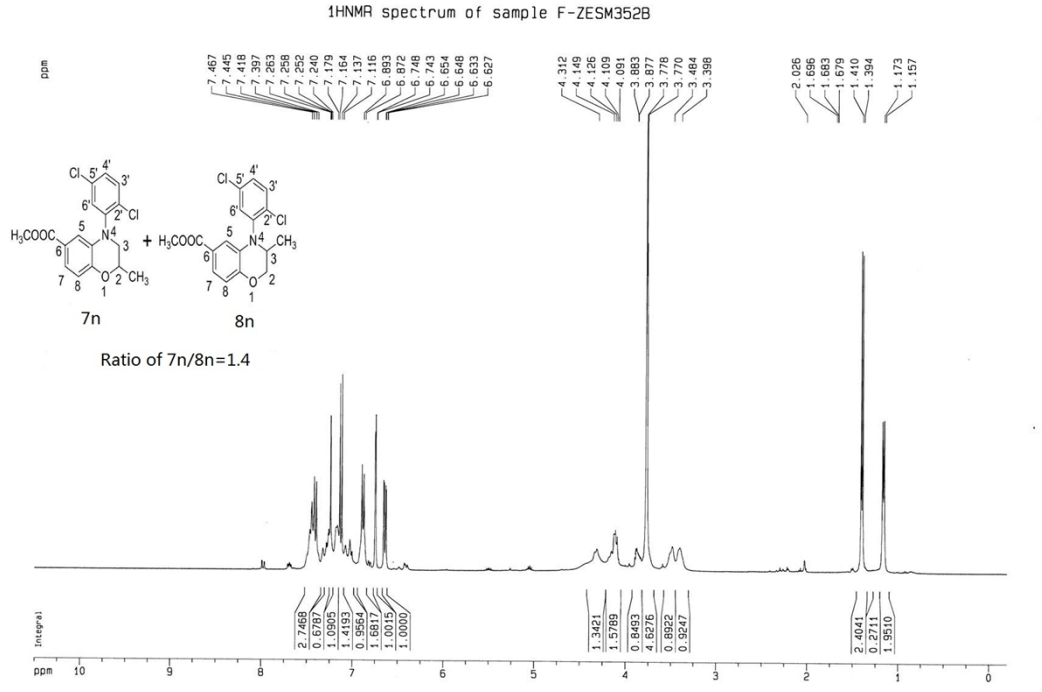


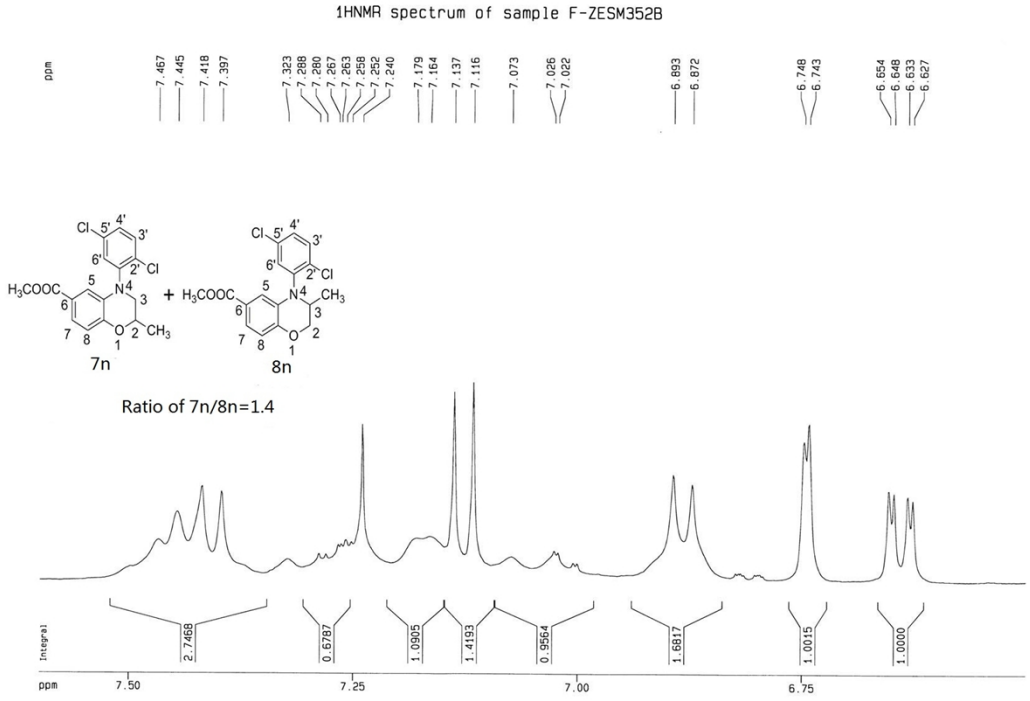
7i + 8i

Ratio of 7i/8i=1.3



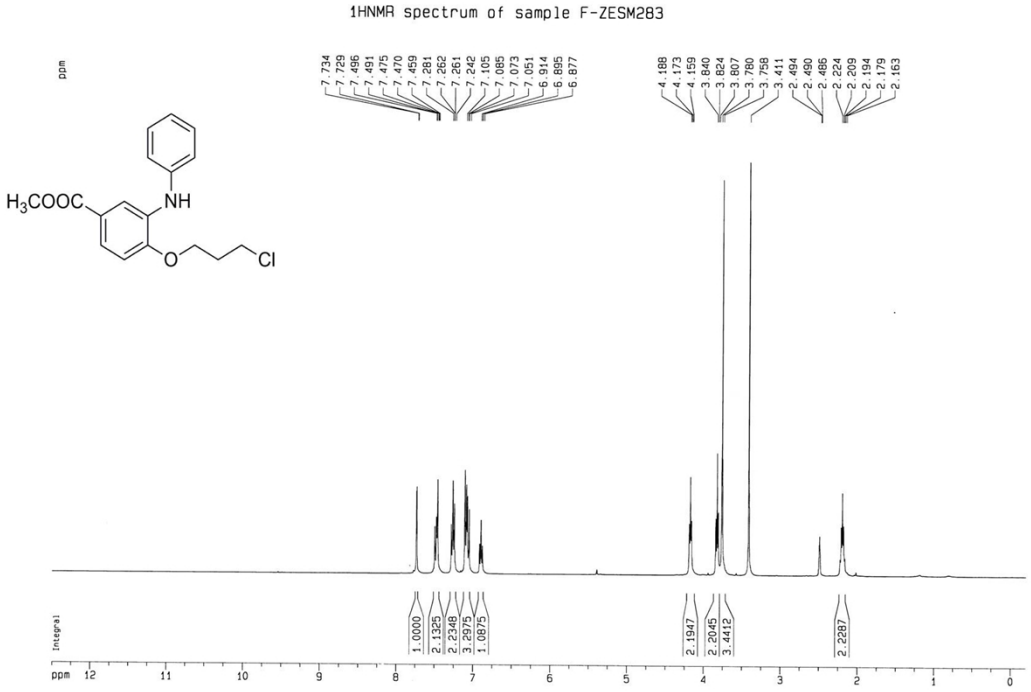
^{1}H-NMR and ^{13}C-NMR spectra of compounds 7n and 8n



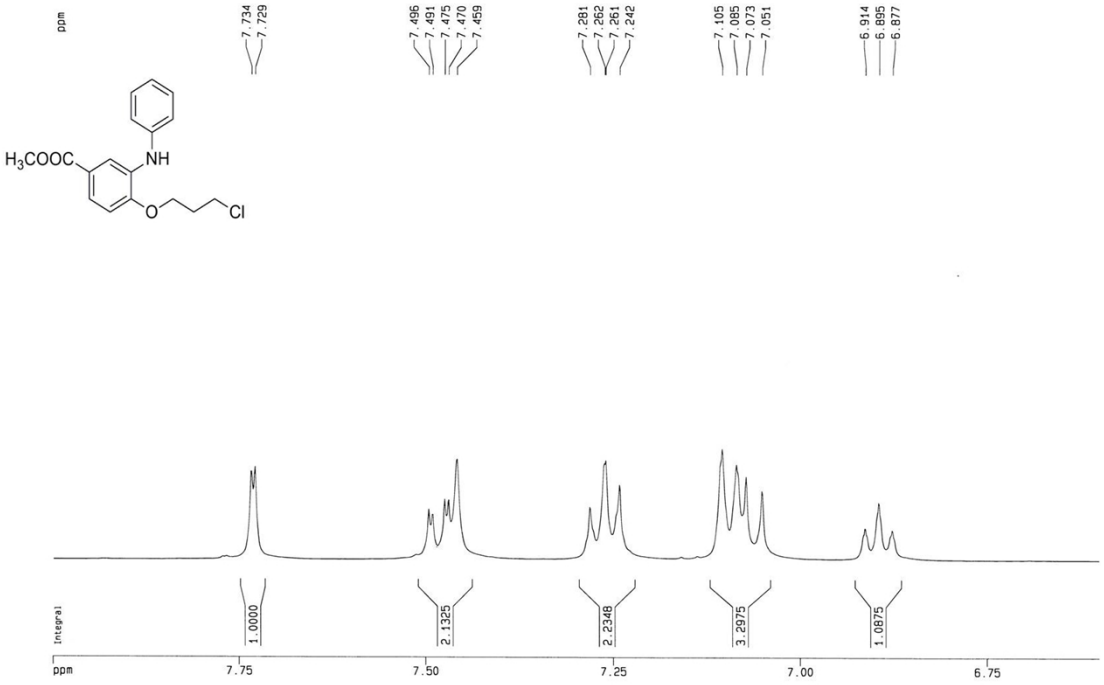


Ⅳ-3 ^{1}H-NMR and ^{13}C-NMR spectra of compounds 9c-9e and intermediate Ⅱ

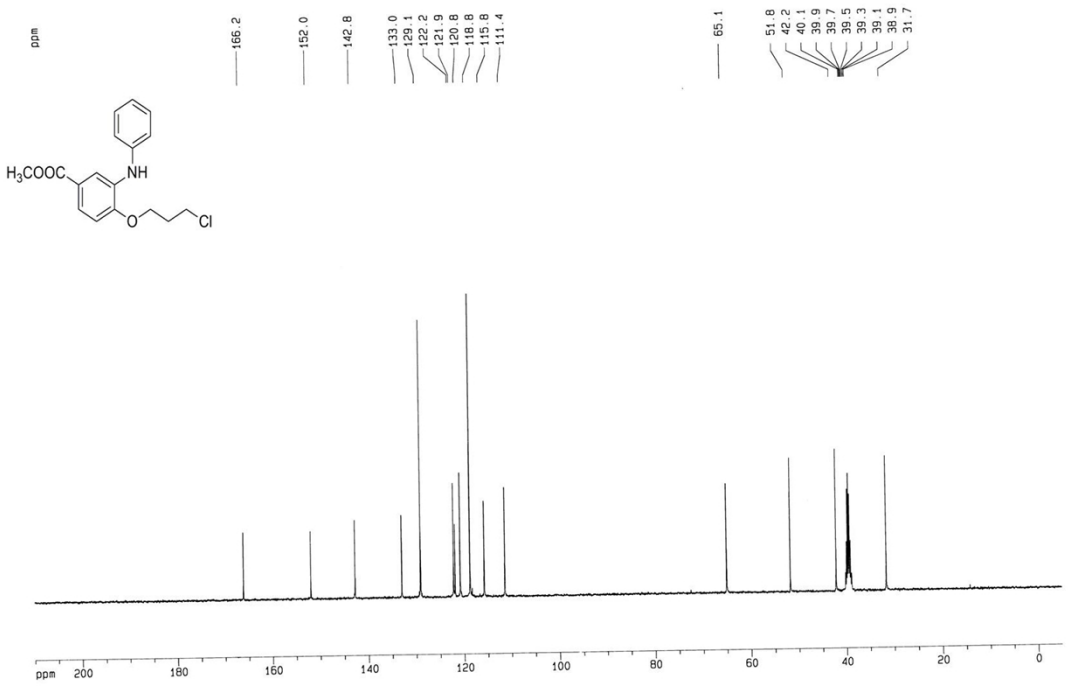
^{1}H-NMR and ^{13}C-NMR spectra of compounds 9c



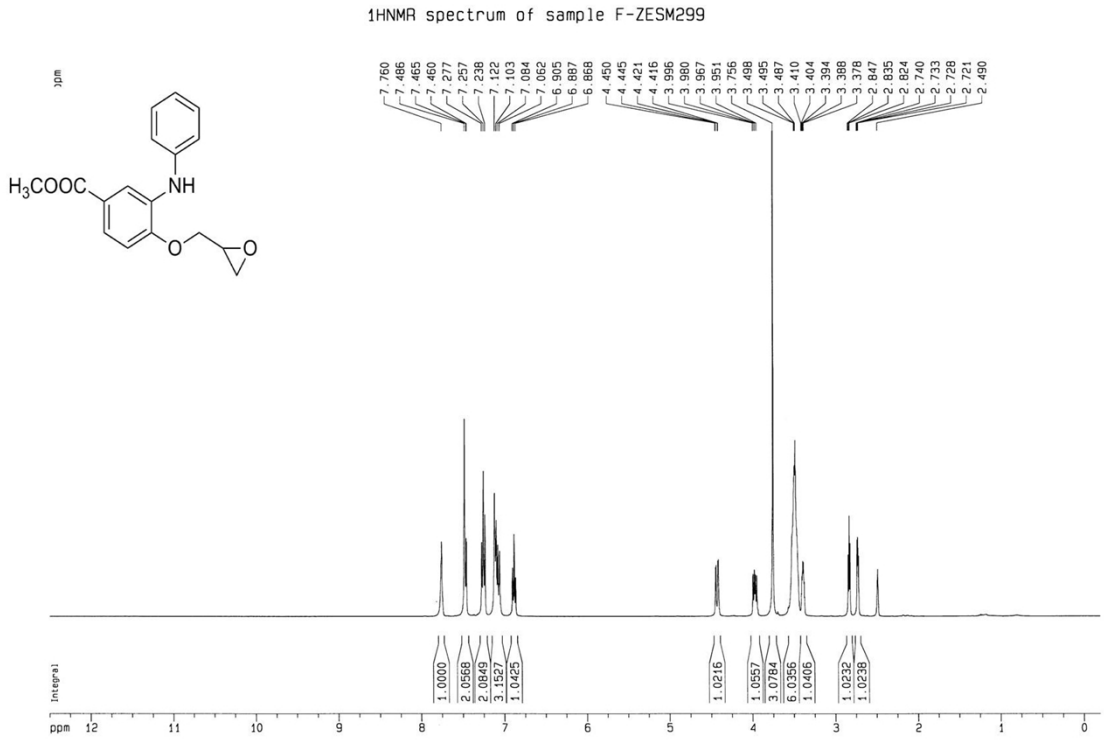
1HNMR spectrum of sample F-ZESM283

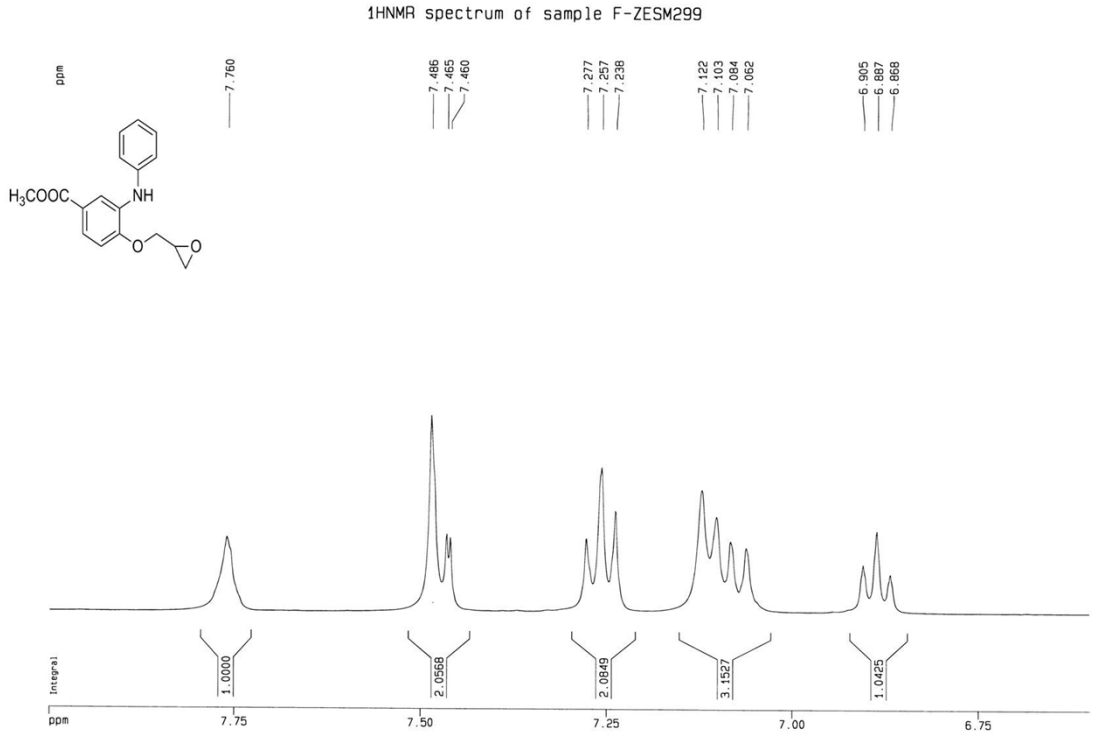


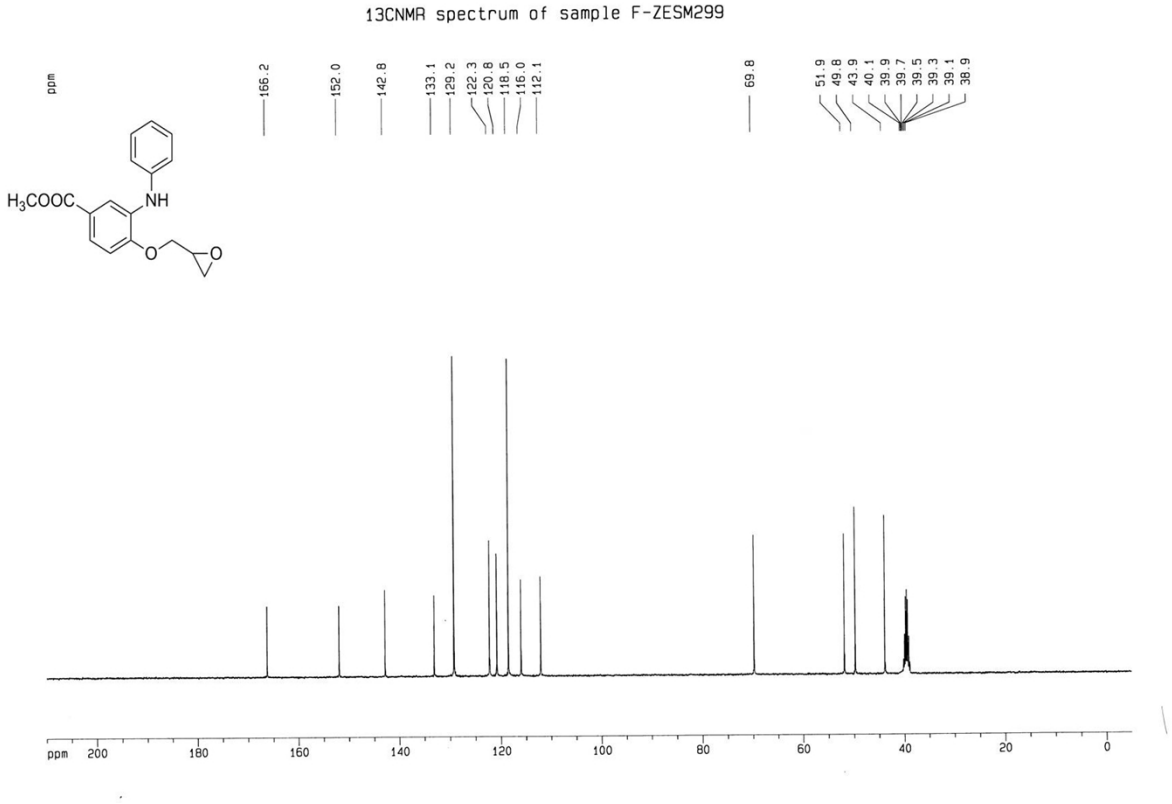
13CNMR spectrum of sample F-ZESM283 319



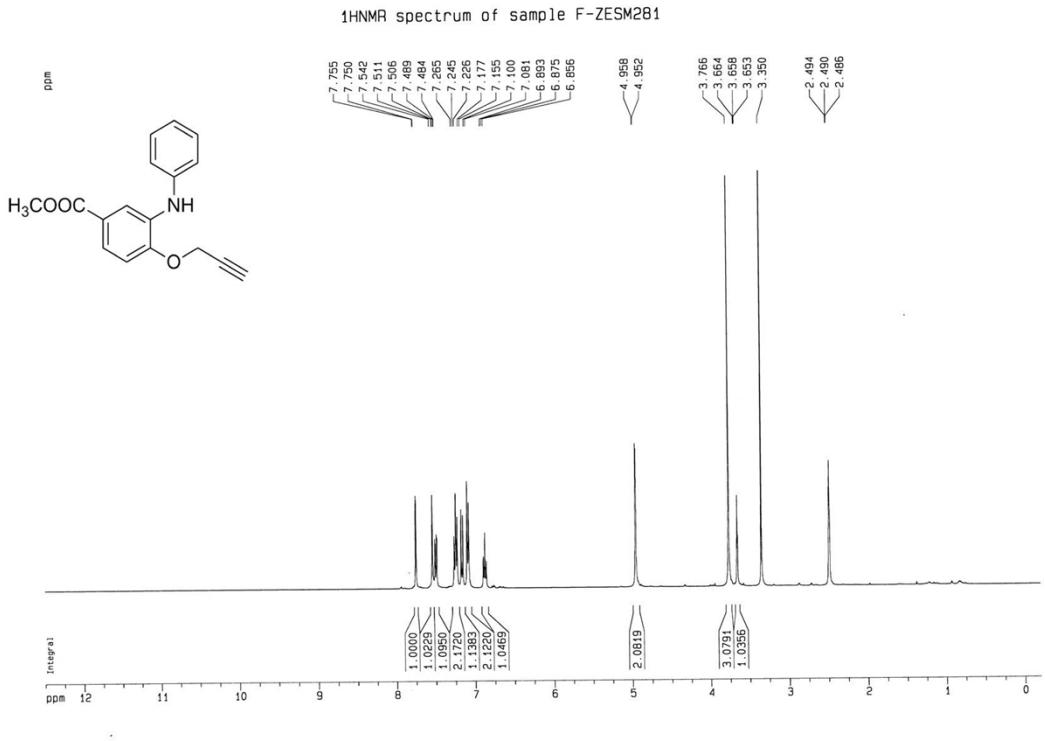
^{1}H-NMR and ^{13}C-NMR spectra of compounds 9d

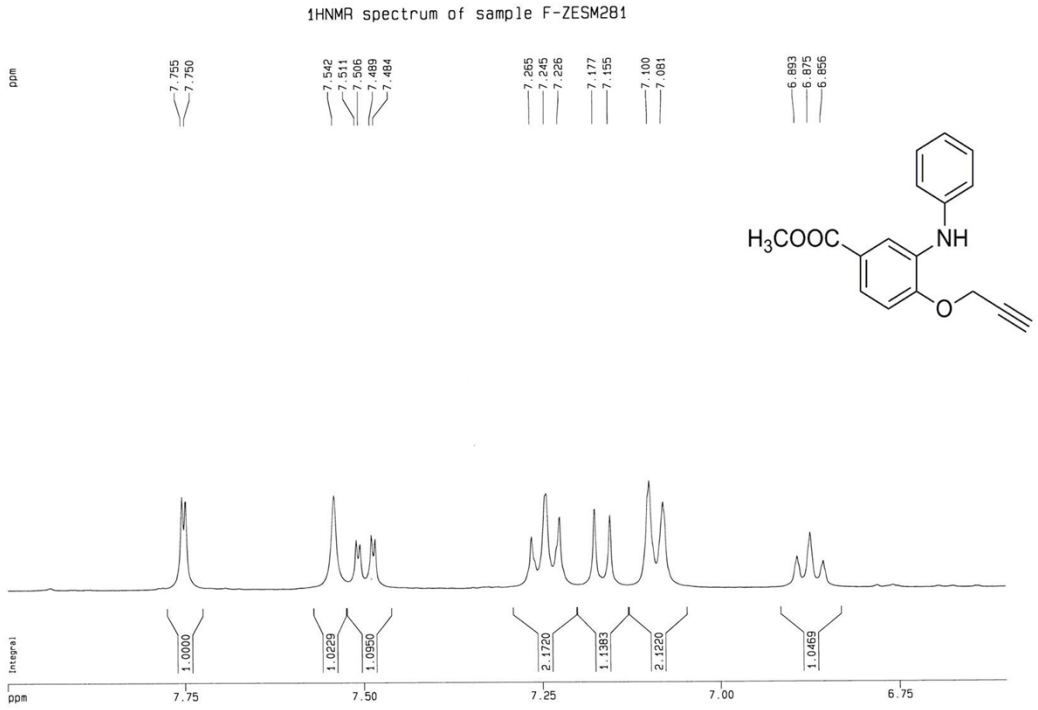




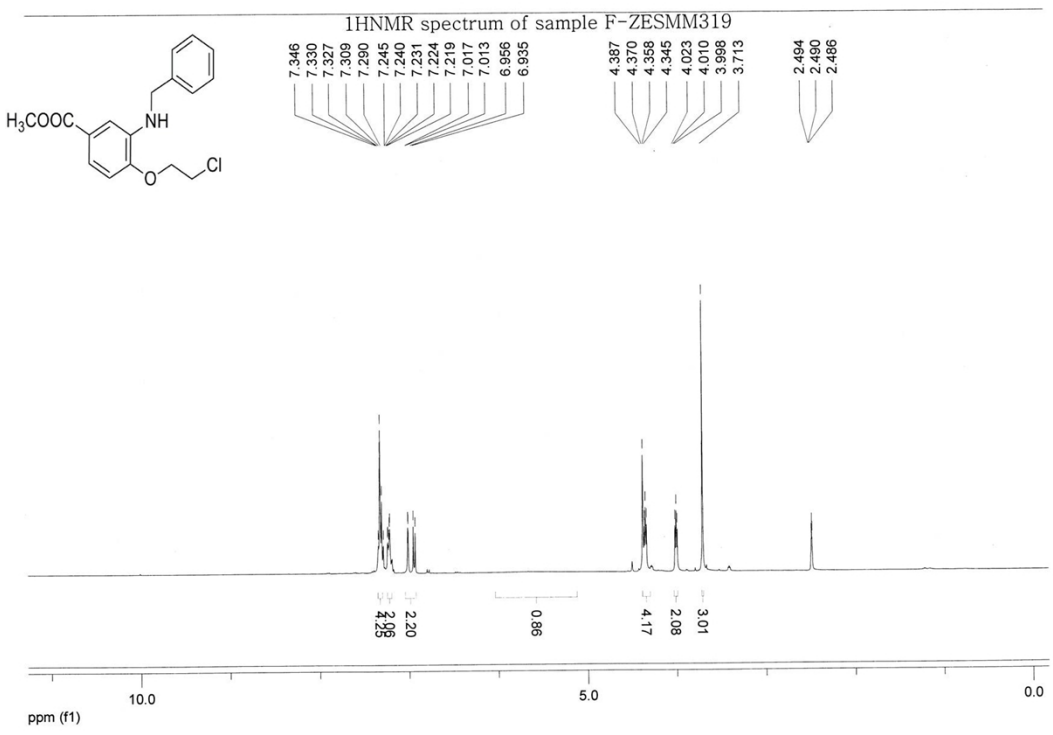


[1]H-NMR spectra of compounds 9e

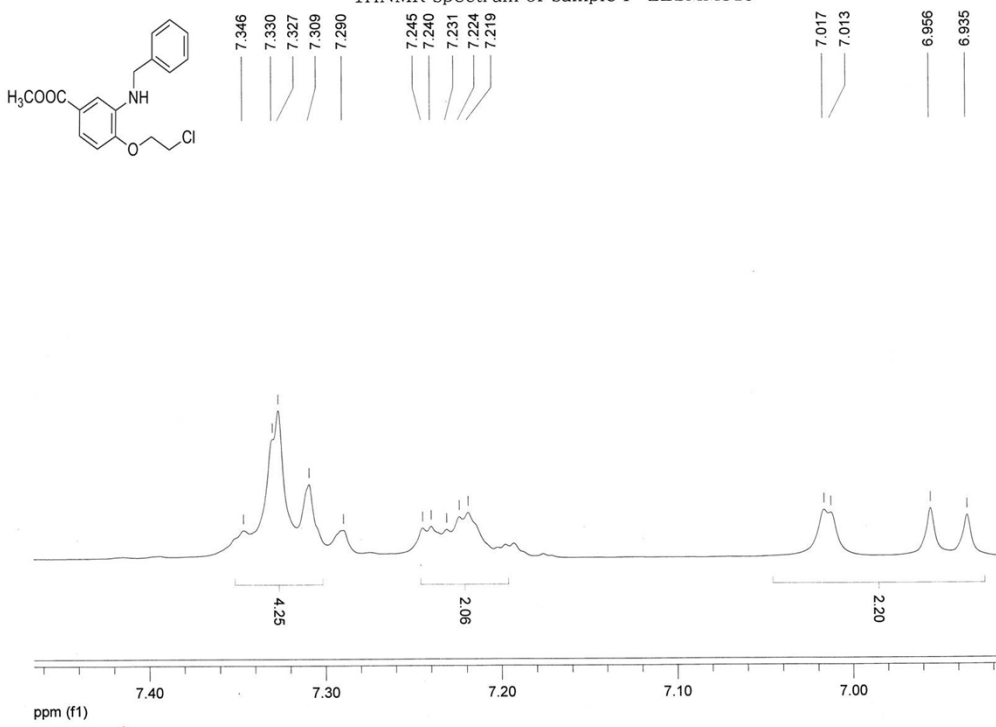




^{1}H NMR spectrum of intermediate Ⅱ in DMSO-d_6



1HNMR spectrum of sample F-ZESMM319



1HNMR spectrum of sample F-ZESMM319