Supporting Information

Synthesis and anti-tubercular activity of conformationally-constrained and bisquinoline analogs of TMC207

Dimpy Kalia,[*ab] Anil Kumar K. S.,[b] Gajanand Meena,[b] Kashmir Prasad Sethi,[b] Rohit Sharma,[b] Priyanka Trivedi,[d] Shaheb Raj Khan,[c] Ajay Singh Verma,d Shyam Singh,[d] Sandeep Sharma,[c] Kuldeep K. Roy,[b] Ruchir Kant,[e] Manju Yasodha Krishnan,[c] Bhupendra N. Singh,[c] Sudhir Sinha,[d] Vinita Chaturvedi,[*d] Anil K. Saxenab and Dinesh K. Dikshit[*b]

[a]*Department of Chemistry, Savitribai Phule Pune University, Pune 411 007, Maharashtra, India. E-mail: dkalia@chem.unipune.ac.in,* [b]*Medicinal and Process Chemistry Division, CSIR–Central Drug Research Institute, B.S. 10/1, Sector 10, Jankipuram Extension, Sitapur Road, Lucknow 226031, India. E-mail: dk_dikshit@cdri.res.in,* [c]*Microbiology Division, CSIR–Central Drug Research Institute, B.S. 10/1, Sector 10, Jankipuram Extension, Sitapur Road, Lucknow 226031, India,* [d]*Biochemistry Division, CSIR–Central Drug Research Institute, B.S. 10/1, Sector 10, Jankipuram Extension, Sitapur Road, Lucknow 226031, India. E-mail: vinita_chaturvedi@cdri.res.in,* [e]*Molecular and Structural Biology Division, CSIR–Central Drug Research Institute, B.S. 10/1, Sector 10, Jankipuram Extension, Sitapur Road, Lucknow 226031, India*

Characterization of Mannich bases.

6-((dimethylamino)methyl)-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one hydrochloride (2a)[1]: Following procedure as described in the main text, compound **2a** was obtained from 1-benzosuberone (**1a**) in 86% yield.

4-((dimethylamino)methyl)-3,4-dihydrobenzo[b]oxepin-5(2H)-one hydrochloride (2b): Following procedure as described in the main text, compound **2b** was obtained from 2,3,4,5-tetrahydro-1-benzoxepin-5-one (**1b**) in 78% yield. IR (KBr, cm^{-1}) 3019, 2921, 2694, 2468, 1674, 1605, 1469, 1405, 1316, 1270, 1211, 1173; ^1H NMR (300 MHz, $CDCl_3$+CD_3OD) δ 7.77-7.81 (dd, 1H, *J* = 1.4 , 7.6 Hz), 7.48-7.54 (m, 1H), 7.11-7.17 (m, 1H), 4.62-4.69 (m, 1H), 3.79-3.95 (m, 2H), 3.63-3.69 (m, 1H), 3.24-3.29 (dd, 1H, *J* = 3.3, 12.9 Hz), 2.86 (s, 6H), 2.71-2.78 (m, 1H), 1.80-1.86 (m, 1H); MS (ESI) m/z 219, found 220 $[M+H]^+$; HRMS (ESI) *m/z* calcd. for $C_{13}H_{18}NO_2$ $[M+H]^+$ 220.1338, found 220.1326.

7-chloro-4-((dimethylamino)methyl)-3,4-dihydrobenzo[b]oxepin-5(2H)-one hydrochloride (2c)[2]: Following procedure as described in the main text, compound **2c** was obtained from 7-chloro-3,4-dihydrobenzo[*b*]oxepin-5(2H)-one (**1c**)[3] in 83% yield.

2-((dimethylamino)methyl)-3,4-dihydronaphthalen-1(2H)-one hydrochloride (2d)[4]: Following procedure as described in the main text, compound **2d** was obtained from 1-tetralone (**1d**) in 85% yield.

7-bromo-2-((dimethylamino)methyl)-3,4-dihydronaphthalen-1(2H)-one hydrochloride (2e): Following procedure as described in the main text, compound **2e** was obtained from 7-bromo-1-tetralone (**1e**) in 87 % yield; IR (KBr, cm^{-1}) 3023, 2944, 2854, 2689, 2480, 2366, 1677, 1588, 1481; ^1H NMR (300 MHz, $CDCl_3$+CD_3OD) δ 8.09-8.10 (d, 1H, *J* = 2.0 Hz), 7.61-7.64 (dd, 1H, *J* = 2.0, 8.2 Hz), 7.18-7.20 (d, 1H, *J* = 8.2 Hz), 3.70-3.77 (m, 1H), 3.13-3.23 (m, 3H), 3.02-3.04 (br, 1H), 2.94 (s, 6H), 2.62-2.68 (m, 1H), 1.92-2.06 (m, 1H); MS (ESI) m/z 281, found 282 $[M+H]^+$; HRMS (ESI) *m/z* calcd. for $C_{13}H_{17}BrNO$ $[M+H]^+$ 282.0494, found 282.0506.

3-((dimethylamino)methyl)chroman-4-one hydrochloride (2f): Following procedure as described in the main text, compound **2f** was obtained from 4-chromanone (**1f**) in 89% yield; IR (KBr, cm^{-1}) 3441, 3011, 2918, 2852, 2684, 2604, 2473, 2365, 1684, 1607; ^1H NMR (300 MHz, $CDCl_3$+CD_3OD) δ 7.82-7.85 (m, 1H), 7.50-7.55 (m, 1H), 6.97-7.06 (m, 2H), 4.97-5.03 (dd, 1H, *J* = 5.2, 11.3 Hz), 4.29-4.37 (m, 1H), 3.62-3.68 (dd, 1H, *J* = 4.9, 13.2 Hz), 3.46-3.55 (m, 1H), 3.18-3.24 (dd, 1H, *J* = 5.1, 13.1 Hz), 2.97 (s, 6H); MS (ESI) m/z 205, found 206 $[M+H]^+$; HRMS (ESI) *m/z* calcd. for $C_{12}H_{16}NO_2$ $[M+H]^+$ 206.1181, found 206.1162.

2-((dimethylamino)methyl)-2,3-dihydro-1H-inden-1-one hydrochloride (2g): Following procedure as described in the main text, compound **2g** was obtained from 1-indanone (**1g**) in 88 % yield; IR (KBr, cm^{-1}) 3458, 2955, 2681, 2481, 2363, 1714, 1655, 1610; ^1H NMR (300 MHz, $CDCl_3$+CD_3OD) δ 7.38-7.75 (m, 4H), 3.62-3.77 (m, 2H), 3.22-3.36 (m, 3H), 2.97 (s, 6H); MS (ESI) m/z 189, found 190 $[M+H]^+$; HRMS (ESI) *m/z* calcd. for $C_{12}H_{16}NO$ $[M+H]^+$ 190.1232, found 190.1223.

5-bromo-2-((dimethylamino)methyl)-2,3-dihydro-1H-inden-1-one hydrochloride (2h): Following procedure as described in the main text, compound **2h** was obtained from 5-bromo-1-indanone (**1h**) in 86 % yield; IR (KBr, cm^{-1}) 3420, 2931, 2576, 2473, 2364, 1704, 1595, 1469; ^1H NMR (300 MHz, $CDCl_3$+CD_3OD) δ 7.56-7.73 (m, 3H), 3.58-3.67 (m, 2H), 3.18-3.36 (m, 3H), 2.97 (s, 6H); MS (ESI) m/z 267, found 268 $[M+H]^+$; HRMS (ESI) *m/z* calcd. for $C_{12}H_{15}BrNO$ $[M+H]^+$ 268.0337, found 268.0345.

2-((dimethylamino)methyl)-6-methyl-2,3-dihydro-1H-inden-1-one hydrochloride (2i)[5]: Following procedure as described in the main text, compound **2i** was obtained from 6-methyl-1-indanone (**1i**) in 80% yield.

Characterization of conformationally-constrained diarylquinolines.

(±)-5-((6-bromo-2-methoxyquinolin-3-yl)(phenyl)methyl)-6-((dimethylamino)methyl)-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ol (5a): Following procedure as described in the main text, compound **5a** was obtained from **3** and **2a** as a mixture of two diastereomers (*de* 3:7) in 67% yield.

(Major isomer): R_f 0.25 (3:7 EtOAc/hexane); eluent for column chromatography (1:9 EtOAc/hexane); white solid; mp (HCl) 173-176 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.32 (s, 1H), 7.97 (s, 1H), 7.61-7.68 (m, 2H), 6.89-7.38 (m, 9H), 5.40 (s, 1H), 4.04 (s, 3H), 3.48-3.55 (m, 1H), 2.89-2.94 (dd, 1H, *J* = 3.6, 11.0 Hz), 2.47-2.50 (br m, 2H), 2.07 (s, 6H), 1.74-1.89 (m, 3H), 1.33-1.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 143.8, 137.8, 137.7,131.8, 130.7, 130.4, 129.7, 129.0, 128.5, 128.2, 127.4, 126.9, 126.8, 126.7, 126.5, 125.8, 125.6, 116.9, 84.7, 62.8, 54.1, 46.5, 44.9, 39.5, 38.5, 29.7, 22.7; MS (ESI) *m/z* 544, found 545 $[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{31}H_{34}Br_1N_2O_2$ $[M+H]^+$ 545.1804, found 545.1803.

(±)-5-((6-bromo-2-methoxyquinolin-3-yl)(phenyl)methyl)-4-((dimethylamino)methyl)-2,3,4,5-tetrahydrobenzo[b]oxepin-5-ol (5b): Following procedure as described in the main text, compound **5b** was obtained from **3** and **2b** as a mixture of two diastereomers (*de* 3:7) in 54% yield.

(Major isomer): R_f 0.3 (1:4 EtOAc/hexane); eluent for column chromatography (6:94 EtOAc/hexane); white solid; mp (HCl) 181-184 °C; IR (KBr, cm^{-1}) 3688, 3620, 3453, 3020, 2358, 1599, 1520; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.01-8.03 (d, 2H, *J* = 1.4 Hz), 7.78-7.79 (d, 1H, *J* = 1.4 Hz), 7.42-7.48 (m, 2H), 7.32-7.36 (m, 3H), 7.21-7.28 (m, 2H), 6.94-7.03 (m, 1H), 6.92-6.94 (m, 1H), 6.70-6.74 (m, 1H),5.69 (s, 1H), 4.26-4.30 (m, 1H), 3.62 (s, 3H), 3.54-3.61 (m, 1H), 2.48-2.66 (m, 3H), 2.14 (s, 6H), 1.87-1.90 (dd, 1H, *J*=1.3 Hz, 9.2 Hz), 1.20-1.23 (d, 1H, *J* =10.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 143.5, 142.2, 139.0, 138.0, 131.4, 130.7, 129.8, 129.6, 128.4, 128.2, 127.5, 126.6, 126.5, 123.4, 121.5, 116.3, 82.9, 67.4, 62.6, 53.3, 47.1, 45.4, 37.5, 30.9; MS (ESI) *m/z* 546, found 547 [M+H]; HRMS (DART) *m/z* calcd. for $C_{30}H_{32}Br_1N_2O_3$ [M+H] 547.1596, found 547.1596.

(±)-5-((6-bromo-2-methoxyquinolin-3-yl)(phenyl)methyl)-7-chloro-4-((dimethylamino)methyl)-2,3,4,5-tetrahydrobenzo[b]oxepin-5-ol (5c): Following procedure as described in the main text, compound **5c** was obtained from **3** and **2c** as a mixture of two diastereomers (*de* 1:2) in 65% yield.

(Minor isomer): R_f 0.5 (3:7 EtOAc/hexane); eluent for column chromatography (8:92 EtOAc/hexane); white solid; mp (HCl) 180-182 °C; IR (KBr, cm^{-1}) 3447, 2928, 2856, 2363, 1645, 1462, 1400, 1341; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.26 (s, 1H), 8.75 (br, 1H), 7.96 (d, 1H, *J* = 1.7 Hz), 7.61-7.68 (m, 2H), 6.91-7.24 (m, 8H), 5.54 (s, 1H), 4.24-4.29 (m, 1H), 4.04 (s, 3H), 3.50-3.59 (m, 1H), 2.51-2.62 (m, 2H), 2.17-2.40 (m, 1H), 1.96 (s, 6H), 1.93-1.96 (d, 1H, *J* = 10.6 Hz), 1.15-1.19 (d, 1H, *J* = 14.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 154.5, 143.8, 140.4, 139.0, 137.4, 131.9, 130.2, 129.7, 129.6, 129.3, 128.5, 128.1, 127.3, 126.9, 126.8, 126.0, 123.0, 116.9, 84.0, 67.7, 62.3, 54.0, 46.5, 37.2, 30.2; MS (ESI) *m/z* 580, found 581$[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{30}H_{31}Br_1Cl_1N_2O_3$ $[M+H]^+$ 581.1207, found 581.1206.

(Major isomer): R_f 0.48 (3:7 EtOAc/Hexane); eluent for column chromatography (8:92 EtOAc/hexane); mp (HCl) 186-188 °C; IR (neat, cm^{-1}) 3454, 2935, 2365, 1646, 1460, 1396, 1343, 1257, 1181, 1104, 1060, 1024; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (br, 1H), 8.28 (s, 1H), 7.96-7.99 (d, 2H, *J* = 7.3 Hz), 7.77-7.78 (d, 1H, *J* = 1.3 Hz), 7.43-7.50 (m, 2H), 6.84-7.35 (m, 6H), 5.63 (s, 1H), 4.23-4.28 (m, 1H), 3.64 (s, 3H), 3.47-3.56 (m, 1H), 2.44-2.63 (m, 3H), 2.14 (s, 6H), 1.87-1.91 (m, 1H), 1.17-1.23 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 155.6, 141.7, 140.1, 138.9, 131.5, 130.4, 129.6, 129.4, 128.7, 128.4, 128.1, 128.0, 126.7, 126.6, 126.4, 122.8, 116.3, 82.6, 67.5, 62.4, 53.1, 46.7, 37.2, 30.6; MS (ESI) *m/z* 580, found 581$[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{30}H_{31}Br_1Cl_1N_2O_3$ $[M+H]^+$ 581.1207, found 581.1206.

(±)-1-((6-bromo-2-methoxyquinolin-3-yl)(phenyl)methyl)-2-((dimethylamino)methyl)-1,2,3,4-tetrahydronaphthalen-1-ol (5d): Following procedure as described in the main text, compound **5d** was obtained from **3** and **2d** as a mixture of two diastereomers (*de* 2:3) in 69% yield.

(Minor isomer): R_f 0.3 (3:7 EtOAc/hexane); eluent for column chromatography (1:3 EtOAc/hexane); white solid; mp (HCl) 185-187 °C; IR (KBr, cm^{-1}) 3021, 2360, 1600, 1521, 1423, 1340, 1216, 1039, 928; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.26 (s, 1H), 7.95 (s, 1H), 7.63-7.64 (m, 2H), 7.04 (br s, 7H), 6.71-6.80 (m, 2H), 4.61 (s, 1H), 3.97 (s, 3H), 2.96-3.05 (m, 1H), 2.70-2.79 (m, 1H), 2.53-2.61 (m, 1H), 2.40-2.44 (br m, 1H), 2.02-2.12 (m, 8H), 1.25-1.31 (br m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3, 144.1, 142.2, 134.2, 133.8, 132.2, 131.7, 129.9, 129.1, 128.9, 127.8, 127.2, 126.6, 126.4, 124.9. 117.4, 79.9, 62.9, 54.2, 51.7, 45.4, 35.1, 24.5, 22.5; MS (ESI) *m/z* 530, found 531$[M+H]^+$; HRMS (ESI) *m/z* calcd. for $C_{30}H_{32}Br_1N_2O_2$ $[M+H]^+$ 531.1647, found. 531.1620

(Major isomer): R_f 0.25 (3/7 EtOAc/hexane); eluent for column chromatography (1:3 EtOAc/hexane); white solid; mp (HCl) 172-175 °C; IR (KBr, cm^{-1}) 3021, 2360, 1600, 1520, 1459, 1402, 1344, 1216, 1036, 928; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.94-7.96 (br d, 2H), 7.88 (s, 1H), 7.56 (s, 2H), 7.34-7.39 (m, 3H), 7.03 (br s, 2H), 6.73 (br s, 2H), 4.84 (s, 1H), 3.43 (s, 3H), 3.00-3.09 (m, 1H), 2.71-2.82 (m, 1H), 2.55-2.63 (m, 1H), 2.35-2.39 (br m, 2H), 2.13 (s, 6H), 2.01-2.05 (br d, 1H, *J* = 12.1 Hz), 1.39-1.43 (br m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 143.9, 142.5, 142.4, 139.0, 134.4, 131.8, 130.5, 130.0, 128.7, 128.5, 127.7, 127.6, 127.0, 126.9, 126.8, 126.6, 125.0, 116.7, 78.7, 62.9, 53.6, 50.8, 45.4, 34.8, 30.0, 24.4, 22.6; MS (ESI) *m/z* 530, found 531$[M+H]^+$; HRMS (ESI) *m/z* calcd. for $C_{30}H_{32}Br_1N_2O_2$ $[M+H]^+$ 531.1647, found 531.1569.

(±)-7-bromo-1-((6-bromo-2-methoxyquinolin-3-yl)(phenyl)methyl)-2-((dimethylamino)methyl)-1,2,3,4-tetrahydronaphthalen-1-ol (5e): Following procedure as described in the main text, compound **5e** was obtained from **3** and **2e** as a mixture of two diastereomers (*de* 1:1) in 71% yield.

(Minor isomer): R_f 0.6 (3/7 EtOAc/hexane); eluent for column chromatography (1:4 EtOAc/hexane); white solid; mp (HCl) 183-185 °C; IR (KBr, cm^{-1}) 3057, 2944, 2822, 1595, 1461, 1398, 1340, 1253, 1180; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.22 (s, 1H), 7.96-7.97 (d, 1H, *J* = 1.3 Hz), 7.61-7.68 (m, 2H), 6.78-7.20 (m, 8H), 4.56 (s, 1H), 3.97 (s, 3H), 2.71-2.97 (m, 1H), 2.54-2.68 (m, 2H), 2.39-2.43 (br m, 1H), 2.04-2.23 (m, 8H), 1.33-1.38 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 144.2, 143.9, 138.1, 136.9, 132.4, 132.3, 132.1, 131.3, 129.7, 129.5, 129.3, 128.6, 127.8,

127.1, 126.9, 126.6, 118.8, 117.2, 79.5, 62.4, 54.1, 51.6, 34.4, 23.8, 22.3; MS (ESI) *m/z* 608, found 609 $[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{30}H_{31}Br_2N_2O_2$ $[M+H]^+$ 609.0752; found 609.0712.

(Major isomer): R_f 0.53 (3:7 EtOAc/hexane); eluent for column chromatography (1:4 EtOAc/hexane); white solid; mp (HCl) 195-198 °C; IR (KBr, cm^{-1}) 3026, 2947, 2782, 1594, 1462, 1396, 1343, 1251, 1185, 1107, 1063, 1014; ^1H NMR (300 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.86-7.92 (m, 3H), 7.53-7.62 (m, 2H), 7.23-7.38 (m, 3H), 7.13-7.16 (dd, 1H, *J* = 1.9, 8.1 Hz), 6.89-6.92 (d, 1H, *J* = 8.1 Hz), 6.773-6.779 (d, 1H, *J* = 1.9Hz), 4.76 (s, 1H), 3.46 (s, 3H), 2.90-2.99 (m, 1H), 2.51-2.72 (m, 2H), 2.22-2.36 (m, 2H), 2.13 (s, 6H), 2.01-2.06 (dd, 1H, *J* = 1.6, 11.9 Hz), 1.38-1.45 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 144.6, 143.9, 141.8, 139.0, 133.2, 131.8, 130.2, 129.8, 129.4, 129.2, 128.6, 128.5, 126.9, 126.5, 125.8, 118.8, 78.2, 62.4, 53.6, 50.7, 34.1, 23.8, 22.3; MS (ESI)*m/z* 608, found 609$[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{30}H_{31}Br_2N_2O_2$ $[M+H]^+$ 609.0752; found 609.0740.

(±)-4-((6-bromo-2-methoxyquinolin-3-yl)(phenyl)methyl)-3-((dimethylamino)methyl)chroman-4-ol (5f): Following procedure as described in the main text, compound **5f** was obtained from **3** and **2f** as a mixture of two diastereomers (*de* 3:7) in 74% yield.

(Minor isomer): R_f 0.35 (1:4 EtOAc/hexane); eluent for column chromatography (1:4 EtOAc/hexane); white solid; mp (HCl) 198-200 °C; IR (KBr, cm^{-1}) 2948, 1600, 1459, 1398, 1342; ^1H NMR (300 MHz, $CDCl_3$) δ 9.23 (s, 1H), 8.85 (br, 1H), 7.97 (s, 1H), 7.67 (d, 2H, *J* = 1.8 Hz), 7.07-7.22 (m, 6H), 6.74-6.77 (d, 1H, *J* = 8.07 Hz), 6.57-6.58 (d, 2H, *J* = 4.1 Hz), 4.81(s, 1H), 4.56-4.61 (dd, 1H, *J* = 3.0, 11.9 Hz), 4.0 (s, 3H), 3.83-3.87 (d, 1H, *J* = 11.9 Hz), 2.80-2.88 (m, 1H), 2.18-2.37 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8, 151.5, 143.8, 137.9, 136.7, 132.2, 131.4, 129.7, 129.5, 128.5, 128.3, 127.5, 127.4, 127.1, 126.7, 126.4, 119.4, 117.2, 114.9, 66.6, 61.3, 54.0, 51.8, 45.0, 34.2; MS (ESI) *m/z* 532, found 533$[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{29}H_{30}Br_1N_2O_3$ $[M+H]^+$ 533.1440, found 533.1407.

(Major isomer): R_f 0.3 (1:4 EtOAc/hexane); eluent for column chromatography (1:4 EtOAc/hexane); white solid; mp (HCl) 195-197 °C; IR (KBr, cm^{-1}) 2923, 2853, 1599, 1456, 1398, 1377, 1245, 1184, 1112, 1061, 1019; ^1H NMR (300 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.90-7.93 (m, 3H), 7.56-7.67 (m, 2H), 7.36-7.41 (m, 2H), 7.26-7.31 (m, 1H), 7.03-7.08 (m, 1H), 6.74-6.77 (d, 1H, *J* = 8.07 Hz), 6.48-6.59 (m, 2H), 4.97 (s, 1H), 4.62-4.67 (dd, 1H, *J* = 3.1, 11.9 Hz), 3.88-3.92 (d, 1H, *J* = 11.9 Hz), 3.50 (s, 1H), 2.78-2.86 (t, 1H, *J* = 12.3 Hz), 2.18-2.33 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 151.8, 143.8, 141.0, 138.9, 131.7, 130.1, 129.7, 128.6, 128.3, 128.2, 128.0, 127.0, 126.4, 125.7, 119.6, 116.5, 114.9, 74.7, 66.7, 61.2, 53.4, 51.3, 45.0, 33.8; MS (ESI) *m/z* 532, found 533 $[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{29}H_{30}Br_1N_2O_3$ $[M+H]^+$ 533.1440, found 533.1412.

(±)-1-((6-bromo-2-methoxyquinolin-3-yl)(phenyl)methyl)-2-((dimethylamino)methyl)-2,3-dihydro-1H-inden-1-ol (5g): Following procedure as described in the main text, **5g** was obtained from compound **3** and **2g** as a mixture of two diastereomers (*de* 1:2) in 53% yield.

(Minor isomer): R_f 0.25 (3:7 EtOAc/hexane); eluent for column chromatography (1:9 EtOAc/hexane); white solid; mp (HCl) 158-160 °C; IR (KBr, cm^{-1}) 3018, 2951, 2856, 2787, 2362, 1598, 1460, 1399, 1342, 1252; ^1H NMR (300 MHz, $CDCl_3$) δ 8.96 (s, 1H) , 7.93 (s, 1H), 7.57-7.65 (m, 2H), 7.34-7.37 (m, 2H), 7.09-7.13 (m, 5H), 6.87-6.91 (m,

1H), 6.46-6.49 (d, 1H, *J* = 7.5 Hz), 4.41(s, 1H), 4.01(s, 3H), 3.25-3.33 (dd, 1H, *J* = 6.6,16.0 Hz), 2.28 -2.56 (m, 2H), 2.28-2.33 (br, 1H), 2.04-2.08 (br, 1H), 1.96 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 146.8, 143.6, 139.9, 138.7, 136.6, 131.9, 130.6, 129.5, 129.2, 128.5, 127.4, 127.3, 126.8, 126.4, 126.2, 125.7, 124.3, 117.0, 89.5, 62.2, 53.9, 49.5, 44.5, 42.0, 34.5; MS (ESI) *m/z* 516, found 517 $[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{29}H_{30}Br_1N_2O_2$ $[M+H]^+$ 517.149 found 517.1474.

(Major isomer): R_f 0.22 (3/7 EtOAc/hexane); eluent for column chromatography (1:9 EtOAc/hexane); white solid; mp (HCl) 178-181 °C; IR (KBr, cm^{-1}) 3020, 2856, 2788, 2362, 1598, 1461, 1400, 1342; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.63 (s, 1H), 7.60 (d, 2H), 7.37 (s, 2H), 7.09-7.34 (m, 5H), 6.87-6.93 (m, 1H), 6.63-6.64 (d, 1H, *J* = 9 Hz), 4.47 (s, 1H), 3.61 (s, 3H), 3.30-3.37 (dd, 1H, *J* = 6, 15 Hz), 2.54-2.61 (m, 2H), 2.32-2.37 (d, 1H, *J* = 15 Hz), 2.05-2.08 (d, 1H, *J* = 9 Hz), 1.98 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 147.0, 143.7, 142.1, 139.1, 137.1, 131.6, 130.4, 129.8, 128.33, 128.1, 127.2, 126.6, 126.0, 125.4, 124.4, 116.6, 88.4, 62.1, 53.4, 49.8, 44.5, 41.4, 34.2; MS (ESI) *m/z* 516, found 517 $[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{29}H_{30}Br_1N_2O_2$ $[M+H]^+$ 517.1491, found 517.1569.

(±)-5-bromo-1-((6-bromo-2-methoxyquinolin-3-yl)(phenyl)methyl)-2-((dimethylamino)methyl)-2,3-dihydro-1H-inden-1-ol (5h): Following procedure as described in the main text, compound **5h** was obtained from **3** and **2h** as a mixture of two diastereomers (*de* 2:3) in 51% yield.

(Minor isomer): R_f 0.45 (3/7 EtOAc/hexane); eluent for column chromatography (1:3 EtOAc/hexane); white solid; mp (HCl) 174-178 °C; IR (KBr, cm^{-1}) 3021, 2928, 2856, 1698, 1651, 1599, 1517, 1461; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.26 (br, 1H), 8.94 (s, 1H), 7.93 (d, 1H, *J* = 1.2 Hz), 7.62-7.67 (m, 2H), 7.15-7.37 (m, 6H), 7.02 (d, 1H, *J* = 7.9 Hz), 6.34 (d, 1H, *J* = 8.0 Hz), 4.37 (s, 1H), 4.02 (s, 3H), 3.24-3.32 (dd, 1H, *J* = 6.4 Hz,16.3 Hz), 2.40-2.57 (m, 2H), 2.25-2.30 (d, 1H, *J* = 16.3 Hz), 2.05-2.08 (d, 1H, *J* = 9.0 Hz), 1.96 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 146.1, 143.8, 141.2, 139.7, 136.7, 132.1, 130.7, 129.6, 129.14, 128.9, 128.6, 127.9, 127.7, 126.9, 126.7, 121.2, 117.2, 89.2, 62.2, 54.1, 49.5, 44.6, 42.1, 34.3; MS (ESI) *m/z* 594, found 595 $[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{29}H_{29}Br_2N_2O_2$ $[M+H]^+$ 595.0596, found 595.0550.

(Major isomer): R_f 0.42 (3:7 EtOAc/hexane); eluent for column chromatography (1:3 EtOAc/hexane); white solid; mp (HCl) 188-190 °C; IR (KBr, cm^{-1}) 3020, 2923, 2854, 2357, 1645, 1518, 1460, 1342; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (br, 1H), 8.83 (s, 1H), 7.95 (s, 1H), 7.75-7.77 (d, 2H, *J* = 7.1 Hz), 7.58-7.59 (d, 2H, *J* = 1.1 Hz), 7.23-7.34 (m, 4H), 6.98-7.01 (d, 1H, *J* = 8.1 Hz), 6.45-6.48 (d, 1H, *J* = 8.1 Hz), 4.41 (s, 1H), 3.63 (s, 3H), 3.27-3.34 (dd, 1H, *J* = 6.1, 16.3 Hz), 2.48-2.59 (m, 2H), 2.26-2.32 (d, 1H, *J* = 16.3 Hz), 2.03-2.06 (dd, 1H, *J* = 1.7,6.8 Hz), 1.95 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.8, 146.4, 143.8, 141.9, 141.6, 137.3, 131.9, 130.5, 129.9, 129.3, 128.5, 128.3, 127.7, 127.1, 126.9, 126.9, 126.6, 121.1, 116.8, 88.1, 62.1, 53.6, 49.6, 44.5, 41.58, 34.0; MS (ESI) *m/z* 594, found 595 $[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{29}H_{29}Br_2N_2O_2$ $[M+H]^+$ 595.0596, found 595.0542.

(±)-1-((6-bromo-2-methoxyquinolin-3-yl)(phenyl)methyl)-2-((dimethylamino)methyl)-6-methyl-2,3-dihydro-1H-inden-1-ol (5i): Following procedure as described in the main text, compound **5i** was obtained from **3** and **2i** as a mixture of two diastereomers (*de* 3:7) in 49% yield.

(Minor isomer): R_f 0.35 (3/8 EtOAc/hexane); eluent for column chromatography (1:3 EtOAc/hexane); white solid; mp (HCl) 165-167 °C; IR (KBr, cm^{-1}) 3023, 2920, 2789, 2361, 1597, 1451, 1393, 1337, 1253, 1120, 1060, 1019; ^{1}H

NMR (300 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.94-7.95 (d, 1H, *J* = 1.3 Hz), 7.58-7.67 (m, 2H), 7.14-7.32 (m, 5H), 7.02-7.04 (d, 1H, *J* = 7.5 Hz), 6.92-6.94 (d, 1H, *J* = 7.5 Hz), 6.20 (s, 1H), 4.37 (s, 1H), 4.01 (s, 3H), 3.19-3.27 (dd, 1H, *J* = 6.0, 16 Hz), 2.37-2.58 (m, 2H), 2.23-2.29 (d, 1H, *J* = 16 Hz), 2.05 (br s, 4H), 1.97 (s, 6H); ^{13}C NMR ($CDCl_3$) δ143.7, 136.6, 135.6, 132.1, 130.8, 129.6, 128.5, 127.4, 126.8, 126.5, 124.1, 117.2, 89.3, 62.2, 54.0, 49.7, 44.6, 42.3, 34.2, 21.2; MS (ESI) *m/z* 530, found 531$[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{30}H_{32}BrN_2O_2$ $[M+H]^+$ 531.1647, found 531.1653.

(Major isomer): R_f 0.33 (3:7 EtOAc/Hexane); eluent for column chromatography (1:3 EtOAc/hexane); white solid; mp (HCl) 170-172 °C; IR (KBr, cm^{-1}) 3020, 2923, 2855, 2357, 1600, 1458, 1401; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.95 (s, 1H), 7.75-7.78 (d, 2H, *J* = 7.1 Hz), 7.57-7.58 (d, 2H, *J* = 1.1 Hz), 7.19-7.34 (m, 3H), 7.00-7.03 (d, 1H, *J* = 7.5 Hz), 6.89-6.91 (d, 1h, *J* = 7.5 Hz), 6.35 (s, 1H), 4.43 (s, 1H), 3.56 (s, 3H), 3.21-3.28 (dd, 1H, *J* = 4.8, 15.8 Hz), 2.58 (br, 2H), 2.24-2.29 (d, 1H, *J* = 15.8 Hz), 1.95-1.99 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 143.8, 137.2, 136.2, 135.6, 131.7, 130.6, 129.9, 128.3, 128.2, 126.7, 126.6, 126.1, 124.2, 116.7, 88.4, 62.3, 53.5, 49.9, 44.6, 41.7, 33.9, 21.3; MS (ESI) *m/z* 530, found 531 $[M+H]^+$; HRMS (DART) *m/z* calcd. for $C_{30}H_{32}BrN_2O_2$ $[M+H]^+$ 531.1647, found 531.1645.

Synthesis of bisquinolines and their precursors.

Ethyl 2-((2-chloroquinolin-3-yl) (hydroxy) methyl) acrylate (7)[6]: To mixture of 2-chloroquinoline-3-carbaldehyde **6** (4 g, 20.87 mmol) and ethyl acrylate (10 mL) was added DABCO (2.34 g, 20.87 mmol) and MeOH (1 mL). The reaction mixture was stirred for 12h at room temperature and concentrated in vacuo. To the resultant residue was added brine (75 mL) and extracted with EtOAc (3 × 75 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated in vacuo to give a viscous liquid. Purification by flash chromatography (10:90 to 15:85 EtOAc/hexane) afforded **7** (5.78 g, 95%) as clear viscous oil. IR (neat, cm^{-1}) 3393, 3019, 2930, 1712, 1625, 1397, 1263, 1216, 1144, 1029; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.03-8.00 (d, 1H, *J* = 8.43 Hz), 7.86-7.84 (d, 1H, *J* = 8.13 Hz), 7.76-7.70 (m, 1H), 7.59-7.54 (t, 1H, *J* = 7.1 Hz), 6.40 (s, 1H), 6.06 (s, 1H), 5.64 (s, 1H), 4.27-4.20 (q, 2H, *J* = 7.1Hz), 3.66 (s, 1H), 1.31-1.26 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 149.4, 147.2, 140.5, 137.2, 132.8, 130.7, 128.3, 127.9, 127.6, 127.3, 127.3, 69.4, 61.5, 14.2; MS (ESI) *m/z* 291, found 292 $[M+H]^+$.

Ethyl 2-(acetoxy(2-chloroquinolin-3-yl) methyl) acrylate (8): To a cooled (0-5 ^{o}C) solution of **7** (4 g, 13.71mmol) and pyridine (2.79 ml, 34.27 mmol) in CH_2Cl_2 (75 mL) was added drop wise acetyl chloride (1.16 mL, 16.45 mmol) with vigorous stirring. The reaction mixture was allowed to warm to room temperature and stirred for 8h. To the reaction mixture was then added water (75 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (50 mL). The combined organic extracts were washed with 1N HCl (2 × 75 mL), dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (1:4 to 1:3 EtOAc/hexane) on silica gel to give **8** as white solid (4.25 g, 93%). IR (KBr, $cm^{-1,}$) 2935, 2368, 1744,1704, 1629, 1373, 1233, 1161, 1047; mp 82-85 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.04-8.01 (d, 1H, *J* = 8.4 Hz), 7.83-7.81 (d, 1H, *J* = 8.0 Hz), 7.77-7.72 (m, 1H), 7.60-7.55 (m, 1H), 7.13 (s, 1H), 6.57 (s, 1H), 5.79-5.78 (d, 1H, *J* = 0.5 Hz), 4.23-4.15 (m, 2H), 2.17 (s, 3H), 1.25-1.21 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 164.7, 149.9, 147.4, 138.0,

137.5, 131.0, 130.0, 128.4, 128.2, 127.8, 127.5, 126.9, 70.1, 61.4, 20.9, 14.1; MS (ESI) *m/z* 333.7, found 334.1[M +H] $^{+}$.

Ethyl 2-((2-chloroquinolin-3-yl) (phenyl amino) methyl) acrylate (9): To a solution of **8** (3 g, 8.98 mmol), DABCO (1.51 g, 13.48 mmol) in THF/H_2O (1:1, 30 mL) was added aniline (1.47 mL, 16.17 mmol). The reaction mixture was stirred for 3h and then concentrated in vacuo. To the residue was added water (50 mL), and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (80:20 to 85:15 $CHCl_3$/hexane) on silica gel to give **9** (2.63 g, 80%) as white solid. IR (KBr, cm^{-1}) 3386, 3318, 2990, 2361, 1711, 1600, 1511, 1388, 1321, 1272, 1171, 1101, 1031; mp 150-152 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.03-8.00 (d, 1H, *J* = 8.4 Hz), 7.78-7.68 (m, 2H), 7.56-7.50 (m, 1H), 7.18-7.13 (m, 2H), 6.76-6.71 (t, 1H, *J* = 7.3 Hz), 6.61-6.59 (d, 2H, *J* = 7.7 Hz), 6.49 (s, 1H), 5.94 (s, 1H), 5.80 (s, 1H), 4.22-4.15 (br m, 3H), 1.24-1.19 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 150.7, 147.2, 146.3, 139.5, 137.0, 132.3, 130.6, 129.4, 128.3, 128.2, 127.8, 127.3, 127.3, 118.6, 113.5, 61.3, 55.9, 14.1; MS (ESI) *m/z* 366.8, found 367.0 [M^{+}+H].

Bis(2-chloroquinolin-3-yl) methane (10): A solution of **9** (2 g, 5.45 mmol) in TFA (7 mL) was refluxed at 70 °C for 16h with stirring. The reaction mixture was allowed to cool to room temperature and then concentrated in vacuo. The resultant yellow residue was dissolved in acetone (20 mL) followed by addition of anhydrous K_2CO_3 (1.5 g, 10.90 mmol). The reaction mixture was refluxed at 60 °C for 20 min and then concentrated in vacuo. The residue was diluted with water and the resultant suspension was filtered and dried under vacuum to give a yellow solid. To this yellow solid was added $POCl_3$ (10.14 mL, 108.49 mmol) and the reaction mixture was refluxed at 120 °C for 40 min. The reaction mixture was poured on crushed ice, basified to pH 8-8.5 with saturated aqueous $NaHCO_3$ and extracted with EtOAc (3 × 40 mL). The combined organic extracts were washed with brine (40 mL), dried (Na_2SO_4), and filtered and concentrated in vacuo. The residue was purified by flash chromatography (6:94 to 10:90 EtOAc/hexane) on silica gel to give **10** (1.47 g, 80%, three steps) as white solid. IR (KBr, cm^{-1}) 3755, 3037, 2925, 2364, 2053, 1709, 1559, 1484, 1397, 1327, 1179, 1129, 1028; mp 170-173 ºC; ^{1}H NMR (200 MHz, $CDCl_3$,) δ 8.06-8.02 (m, 2H), 7.82 (s, 2H), 7.76-7.68 (m, 4H), 7.57-7.49 (m, 2H), 4.46 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.2, 146.9, 138.5, 130.4, 130.3, 128.3, 127.4, 127.3, 127.3, 36.8; MS (ESI) *m/z* 339, found 339 [M+H] $^{+}$.

Bis(2-methoxyquinolin-3-yl) methane (11a): To a round bottom flask (100 mL) charged with methanol (30 mL) was added Na (2.67 g, 116.62 mmol) portion wise and the mixture was stirred at room temperature for additional 5 min. To the resultant sodium methoxide solution was added bis 2-chloroquinoline **10** (2 g, 5.9 mmol). The reaction mixture was refluxed at 80 °C for 12 h and then concentrated in vacuo. To the cooled (0 ^{o}C) residue was added water (40 mL) and extracted with EtOAc (3×50 mL). The combined organic extract was washed with brine (40 mL), dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by flash chromatography (2:98 to 5:95 EtOAc/hexane) on silica gel to afford **11a** (1.71 g, 88%) as white solid. IR (KBr, cm^{-1}) 3449, 3007, 2949, 2364, 1623, 1567, 1397, 1256, 1008; mp 167-169 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86-7.83 (d, 2H, *J* = 8.1 Hz), 7.65-7.53 (m, 6H), 7.34-7.29 (m, 2H), 4.10 (s, 2H), 4.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 145.7, 137.4, 128.9, 127.1, 126.9, 125.6, 124.0, 123.9, 53.7, 30.6; MS (ESI) *m/z* 330, found 331 [M+H] $^{+}$.

Bis(2-(allyloxy) quinolin-3-yl) methane (11b): Following the procedure as described above for **11a**, allyl alcohol (30 mL), Na (2.67 g, 116.62 mmol) and bis 2-chloroquinoline **10** (2 g, 5.9 mmol) at 100 °C afforded **11b** (2.2 g, 98%), as white solid, after flash chromatography (2:98 to 5:95 EtOAc/hexane) on silica gel. IR (KBr, cm^{-1}) 3446, 3016, 2938, 2368, 1621, 1573, 1500, 1415, 1341, 1263, 1148; mp 99 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90-7.95 (m, 4H), 7.58-7.60 (m, 4H), 7.28-7.39 (m, 2H), 6.10-6.23 (m, 2H), 5.40-5.46 (dd, 2H, *J* = 3, 18 Hz), 5.25-5.29 (dd, 2H, *J* = 3, 12 Hz); 5.05-5.07 (d, 4H, *J* = 6 Hz), 4.21 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.2, 145.6, 137.8, 133.7, 128.8, 127.0, 126.9, 125.5, 124.0, 123.8, 117.3, 66.7, 30.7; MS (ESI) *m/z* 382, found 383 $[M+H]^+$.

Bis(2-(but-3-enyloxy)quinolin-3-yl)methane (11c): Following the procedure as described above for **11a**, but-3-en-1-ol (20 mL), Na (2.67 g, 116.62 mmol) and bis 2-chloroquinoline **10** (2 g, 5.9 mmol) at 110 °C afforded **11c** (2.05 g, 85%), as an oil, after flash chromatography (2:98 to 5:95 EtOAc/hexane) on silica gel. IR (neat, cm^{-1}) 3432, 2959, 1736, 1624, 1527, 1500, 1464, 1426, 1375, 1346, 1260, 1156; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87-7.81 (m, 4H), 7.67-7.60 (m, 4H), 7.37-7.35 (m, 2H), 5.96-5.87 (m, 2H), 5.20-5.17 (m, 4H), 4.59-4.57 (m, 4H), 4.15 (s, 2H), 2.62-2.59 (m, 4H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 13.9, 14.6, 19.4, 30.9, 31.1, 33.4, 61.8, 65.2, 116.7, 123.9, 125.4, 126.9, 128.7, 14.9, 137.7, 145.5, 160.6; MS (ESI) *m/z* 410, found 411 $[M+H]^+$.

4-(dimethylamino)-1, 1-bis(2-methoxyquinolin-3-yl)-2-phenylbutan-2-ol (13). Following procedure as described above compound **13** was obtained from **11a** and **12a** in 82% yield as white solid, after flash chromatography (1:1 EtOAc/hexane); mp 60-62 °C; IR (KBr, cm^{-1}) 3058, 2949, 2823, 2367, 1616, 1469, 1443, 1399, 1257, 1017; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.30 (s, 1H), 7.84-7.81 (d, 1H, *J* = 8.3 Hz), 7.66-7.52 (m, 6H), 7.46-7.41 (m, 1H), 7.32-7.19 (m, 4H), 7.08-7.03 (t, 1H, *J* = 7.3 Hz), 5.56 (s, 1H), 4.24 (s, 3H), 3.77 (s, 3H), 2.28-1.82 (br m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 160.6, 147.0, 145.2, 144.8, 140.0, 138.8, 128.8, 128.4, 127.8, 127.7, 126.8, 126.6, 126.4, 126.2, 126.1, 125.5, 125.4, 123.7, 123.4, 81.6, 55.9, 53.9, 53.4, 44.8, 44.4, 35.7; MS (ESI) *m/z* 507.6, found 508.2 $[M+H]^+$; HRMS (ESI) m/z calcd. for $C_{32}H_{34}N_3O_3$ $[M+H]^+$ 508.2600; found 508.2594.

2-(3-bromophenyl)-4-(dimethylamino)-1,1-bis(2-methoxyquinolin-3-yl)butan-2-ol (14). Following procedure as described above compound **14** was obtained from **11a** and **12b** in 84% yield as white solid, after flash chromatography (1:1 EtOAc/hexane); mp 155-157 °C; IR (KBr, cm^{-1}) 3452, 2950, 2859, 2366, 1658, 1619, 1496, 1441, 1400, 1344, 1253, 1113, 1013; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.28 (s, 1H), 7.77-7.74 (d, 2H, *J* = 8.3 Hz), 7.41-7.32 (m, 6H), 7.22-7.10 (m, 2H), 7.08 (m, 1H), 6.97-6.92 (t, 1H, *J* = 7.3 Hz), 5.40 (s, 1H), 4.10 (s, 3H), 3.70 (s, 3H), 2.20 (br m, 1H); 1.93 (m, 8H), 1.79-1.74 (br m, 1H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 29.7, 35.5, 44.4, 53.9, 55.5, 80.5, 122.3, 123.5, 125.9, 126.6, 127.7, 128.9, 129.4, 138.7, 139.8, 144.8, 145.2, 160.3, 161.3 ppm; MS (ESI) *m/z* 585, found 586 $[M+H]^+$; HRMS (ESI) m/z calcd. for $C_{32}H_{33}BrN_3O_3$ $[M+H]^+$ 586.1705; found 586.5188.

1,1-bis(2-(allyloxy)quinolin-3-yl)-4-(dimethylamino)-2-phenylbutan-2-ol (15). Following procedure as described above compound **15** was obtained from **11b** and **12a** in 35% yield as clear oil, after flash chromatography (1:1 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.18 (s, 1H), 7.70-7.67 (d, 2H, *J* = 8.3 Hz), 7.70-7.49 (m, 7H), 7.32-7.13 (m, 4H), 6.18-6.13 (m, 1H), 5.84-5.78 (m, 1H), 5.61 (s, 1H), 5.50-5.44 (dd, 2H, *J* = 3, 18 Hz), 5.24-5.11 (m, 4H), 4.59-4.58 (m, 2H), 2.29 (br m, 1H), 1.95 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 138.9, 134.0, 133.7, 128.8, 128.4, 127.9, 127.7, 126.6, 126.3, 126.2, 123.7, 123.4, 117.05, 117.0, 116.7, 77.2, 66.9, 66.5,

55.5, 36.0, 33.4, 31.9, 26.7, 29.6, 29.5, 29.3, 23.1, 22.7, 17.8, 14.1; MS (ESI) *m/z* 559.7, found 560 $[M+H]^+$; HRMS (ESI) m/z calcd. for $C_{36}H_{38}N_3O_3$ $[M+H]^+$ 560.2913; found 560.2908.

1,1-bis(2-(allyloxy)quinolin-3-yl)-2-(3-bromophenyl)-4-(dimethylamino)butan-2-ol (16). Following procedure as described above compound **16** was obtained from **11b** and **12b** in 30% yield as white solid, after flash chromatography (1:1 EtOAc/hexane); mp 102-106 ^oC; IR (KBr, cm^{-1}) 3626, 3437, 3366, 3065, 2925, 2362, 1614, 1416, 1343, 1258, 1106, 996; ^1H NMR (300 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.39 (s, 1H), 7.85-7.82 (d, 2H, *J* = 8.3 Hz), 7.70-7.49 (m, 6H), 7.28-7.09 (m, 4H), 6.31-6.25 (m, 1H); 6.01-5.97 (m, 1H), 5.72 (s, 1H), 5.63-5.57 (d, 2H, *J* = 18 Hz), 5.32-5.14 (m, 4H), 4.77-4.71 (d, 2H, *J* = 18Hz), 2.27-2.23 (br m, 1H), 2.02 (m, 8H), 1.90-1.85 (br m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.7, 35.4, 43.7, 44.7, 55.7, 66.6, 81.3, 116.8, 122.3, 125.2, 126.2, 127.7, 129.3, 133.8, 140.0, 144.7, 159.5, 160.5; MS (ESI) *m/z* 637, found 638 $[M+H]^+$; HRMS (ESI) m/z calcd. for $C_{36}H_{37}BrN_3O_3$ $[M+H]^+$ 638.2018; found 638.2020.

1,1-bis(2-(allyloxy)quinolin-3-yl)-2-(4-bromophenyl)-4-(dimethylamino)butan-2-ol (17). Following procedure as described above compound **17** was obtained from **11b** and **12c** in 40 % yield as white solid, after flash chromatography (1:1 EtOAc/hexane); mp 105-110 ^oC; IR (KBr, cm^{-1}) 3049, 2928, 2823, 2779, 2365, 1683, 1622, 1569, 1465, 1418, 1343, 1264, 1205, 1144, 1101; ^1H NMR (300 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.42 (s, 1H), 7.82-7.79 (d, 2H, *J* = 8.3 Hz), 7.68-7.52 (m, 6H), 7.34-7.28 (m, 4H), 6.28-6.26 (m, 1H); 5.99-5.95 (m, 1H), 5.70 (s, 1H), 5.62-5.32 (dd, 2H, *J* = 3, 18 Hz), 5.31-5.16 (m, 4H); 4.76-4.71 (m, 2H), 2.25-2.21 (br m, 1H); 2.01 (m, 8H), 1.89-1.84 (br m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.1, 29.3, 29.7, 31.9, 66.7, 76.6, 77.0, 77.4, 117.0, 117.8, 124.3, 125.2, 126.8, 127.6, 129.4, 133.2, 136.1, 145.8; MS (ESI) m/z 637, found 638 $[M+H]^+$; HRMS (ESI) m/z calcd. for $C_{36}H_{37}BrN_3O_3$ $[M+H]^+$ 638.2018; found 639.2009.

2-(4-bromophenyl)-1,1-bis(2-(but-3-enyloxy)quinolin-3-yl)-4-(dimethylamino)butan-2-ol (18). Following procedure as described above compound **18** was obtained from **11c** and **12c** in 15% yield as sticky oil, after flash chromatography (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3425, 2919, 2851, 2365, 1618, 1464, 1423, 1346, 1218, 1008; ^1H NMR (300 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.10 (s, 1H), 7.70-7.67 (d, 2H, *J* = 8.3 Hz), 7.52-7.36 (m, 6H), 7.25-7.14 (m, 4H), 5.95-5.90 (m, 1H), 5.67-5.65 (m, 1H), 5.48 (s, 1H), 5.21-5.14 (dd, 2H, *J* = 3, 18 Hz), 5.06-4.46 (m, 4H), 4.19-4.13 (m, 2H), 2.65-2.63 (m, 2H), 2.33-2.30 (m, 2H), 2.17 (br m, 2H), 1.90 (m, 8H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 14.1, 17.8, 22.7, 23.1, 29.3, 31.9, 33.4, 44.5, 55.5, 65.0, 116.7, 123.7, 125.1, 126.4, 126.6, 127.6, 128.5, 131.0, 134.8, 145.2; MS (ESI) *m/z* 665, found 666 $[M+H]^+$; HRMS (ESI) m/z calcd. for $C_{38}H_{41}BrN_3O_3$ $[M+H]^+$ 666.2331; found 666.2236.

4-(dimethylamino)-1, 1-bis (2-methoxyquinolin-3-yl)-2-(naphthalen-2-yl) butan-2-ol (19). Following procedure as described above compound **19** was obtained from **11a** and **12d** in 62% yield as white solid, after flash chromatography (1:1 EtOAc/hexane); mp 170-172 ^oC; IR (KBr, cm^{-1}) 3058, 2951, 2857, 2367, 1619, 1468, 1443, 1401, 1262; ^1H NMR (500 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.28 (s, 1H), 8.06 (bs, 1H), 7.76-7.73 (m, 2H), 7.63-7.52 (m, 7H), 7.84-7.45 (m, 3H), 7.31-7.11 (m, 2H), 5.61 (s, 1H), 4.18 (s, 3H), 3.64 (s, 3H), 2.12-2.10 (m, 2H), 1.97-1.88 (br m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 160.5, 145.2, 144.6, 140.0, 138.7, 133.1, 132.1, 128.7, 128.3, 128.0, 127.7, 127.6, 127.3, 126.5, 126.3, 125.7, 125.4, 125.3, 123.6, 123.3, 81.7, 55.8, 53.6, 53.3, 44.8; MS (ESI) *m/z* 557, found 558 $[M+H]^+$; HRMS (ESI) m/z calcd. for $C_{36}H_{36}N_3O_3$ $[M+H]^+$ 558.2757; found 558.2745.

2-(4-bromophenyl)-4-(dimethylamino)-1,1-bis(2-methoxyquinolin-3-yl)butan-2-ol (20). Following procedure as described above compound **20** was obtained from **11a** and **12c** in 82 % yield as clear oil, after flash chromatography (1:1 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.81-1.85 (t, 2H, *J* = 12 Hz); 2.01 (s, 6H); 2.22-2.31 (t, 2H, *J* = 12 Hz); 3.82 (s, 3H), 4.25 (s, 3H); 5.54 (s, 1H); 7.28-7.87 (m, 12H); 8.39 (s, 1H); 8.69 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 29.7, 35.3, 44.1, 44.7, 53.4, 53.9, 55.8, 81.4, 120.1, 123.5, 123.7, 125.2, 125.4, 125.7, 126.3, 126.4, 126.6, 127.6, 127.7, 128.5, 128.8, 130.8, 138.7, 139.9, 144.8, 145.2, 146.3, 160.4, 161.5; MS (ESI) m/z 585, found 586 $[M+H]^+$; HRMS (ESI) m/z calcd. for $C_{32}H_{33}BrN_3O_3$ $[M+H]^+$ 586.1705, found 586.1712.

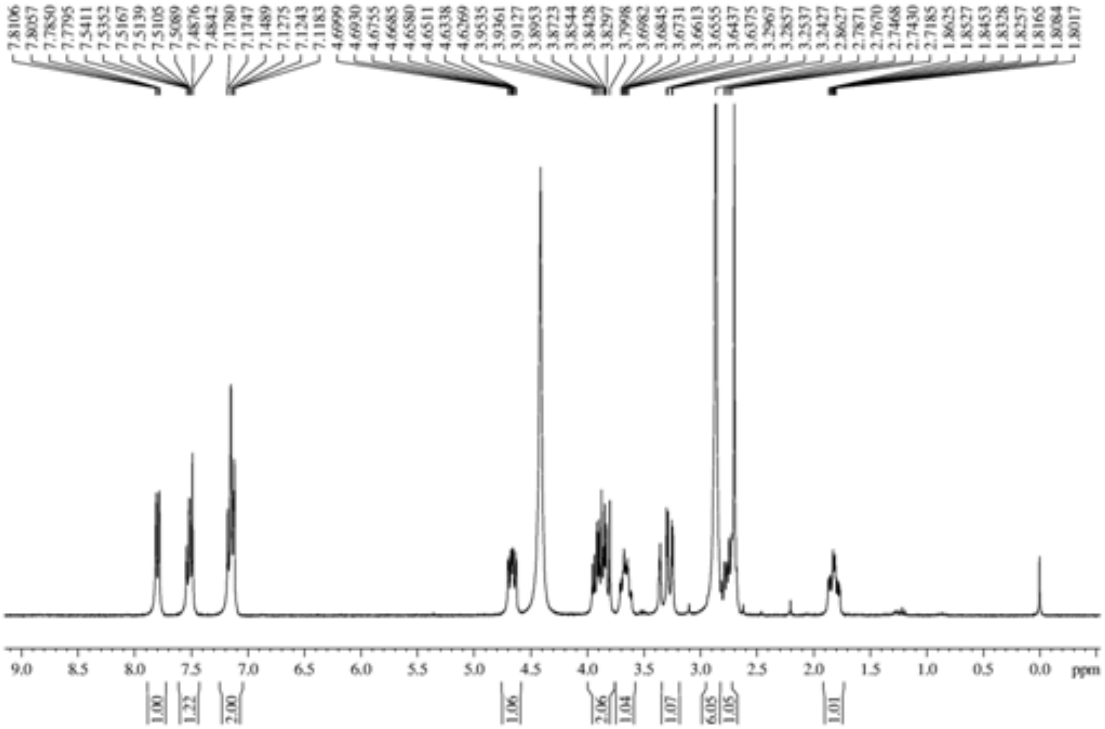
4-(dimethylamino)-1,1-bis(2-methoxyquinolin-3-yl)-2-(naphthalen-2-yl)butan-2-ol (21). Following procedure as described above compound **21** was obtained from **11a** and **12e** in 32 % yield as clear oil, after flash chromatography (1:1 EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.97-2.07 (m, 8H); 2.28-2.32 (t, 2H, *J* = 9 Hz); 3.45 (s, 3H), 4.37 (s, 3H); 6.50 (s, , 1H); 7.28-7.91 (m, 15H); 8.23 (s, 1H); 8.26 (s, 1H); ^{13}C NMR; (125 MHz, $CDCl_3$) *δ* 161.6, 160.5, 145.2, 144.6, 140.0, 138.7, 133.1, 132.1, 128.7, 128.3, 128.0, 127.7, 127.6, 127.3, 126.5, 126.3, 125.9, 125.7, 125.4, 125.3, 125.2, 123.6, 123.3, 81.7, 55.8, 53.9, 53.3, 44.8; MS (ESI) m/z 557, found 558 $[M+H]^+$; HRMS (ESI) m/z calcd. for $C_{36}H_{36}N_3O_3$ $[M+H]^+$ 558.2757; found 558.2812.

(Z)-8,11,12,20-tetrahydro-7H-diquinolin[2,3-b:2',3'-e][1,7]dioxacyclotridecine (22).

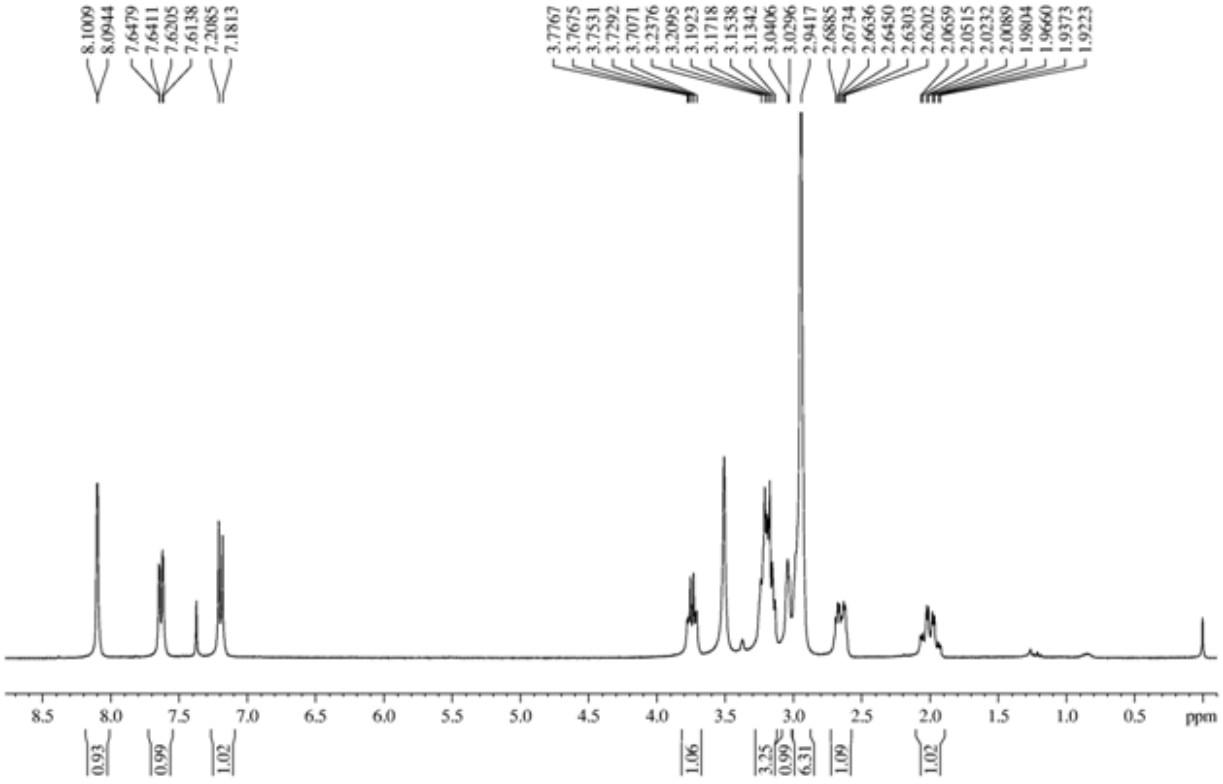
To a solution of compound **11c** (600 mg, 1.4616 mmol) in dry toluene (20 mL) was added Grubb's second generation catalyst (186.36 mg, 0.2192 mmol) at r.t. under nitrogen atmosphere. The color of the reaction mixture turned brick red. After stirring for 1h, the color changed from red to black and the solution was left stirring for an additional 24 h. The reaction mixture was then concentrated under vacuum and the resultant crude mixture was purified by flash column chromatography (2:3 benzene/hexane) on silica gel using to yield **22** in 61 % yield as white solid; mp 175-176 °C; IR (KBr, cm^{-1}) 3429, 2925, 2855, 1625, 1426, 1264, 1217, 1033; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (m, 2H), 7.75 (s, 1H), 7.65 (s, 1H), 7.48-7.46 (m, 4H),7.29-7.23 (m, 2H), 5.51 (t, 1H), 5.23 (t, 1H), 4.48 (m, 4H), 4.03 (bs, 2H), 2.48-2.38 (dd, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.2, 28.6, 29.6, 32.1, 48.8, 49.6, 64.5, 70.3, 124.9, 125.0, 126.9, 129.2, 137.8, 156.9; MS (ESI) m/z 382, found 383 $[M+H]^+$; HRMS (ESI) *m/z* calcd. for $C_{25}H_{23}N_2O_2$ $[M+H]^+$ 383.1760, found 383.1757.

(Z)-1-(3-bromophenyl)-3-(dimethylamino)-1-(7,8,11,12-tetrahydro-20H-[1,7]dioxacyclotridecino[2,3-b:5,6-b']diquinolin-20-yl)propan-1-ol (23). Following general procedure as described for compound **5** above, compound **23** was obtained from **22** and **12b** in 10% yield as colorless viscous oil, after flash chromatography (1:1 EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.39 (bs, 1H), 7.80-7.78 (d, 1H, *J* = 6 Hz), 7.72-7.67 (m, 3H), 7.61-7.53, (m, 4H), 7.49-7.44 (m, 2H) ,7.33-7.29 (t, 1H, *J* = 6 Hz), 7.19-7.00 (t, 1H, *J* = 6 Hz) ,5.72 (m, 1H), 5.65-5.48 (m, 1H), 5.01 (t, 1H), 4.43-4.41 (q, 1H, *J* = 3 Hz), 4.30-4.20 (m, 2H), 2.79-2.76 (m, 1H), 2.59-2.50 (m, 4H) , 2.08 (s, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 145.3, 144.8, 139.5, 129.9, 129.3, 129.0, 128.9, 128.5, 127.7, 126.5, 126.3, 125.2, 125.1, 123.6, 123.4, 64.5, 64.0, 43.1, 38.1, 32.3, 31.9, 31.8, 31.2, 29.7, 22.6, 14.1; MS (ESI) m/z 638, found 639 $[M+H]^+$.

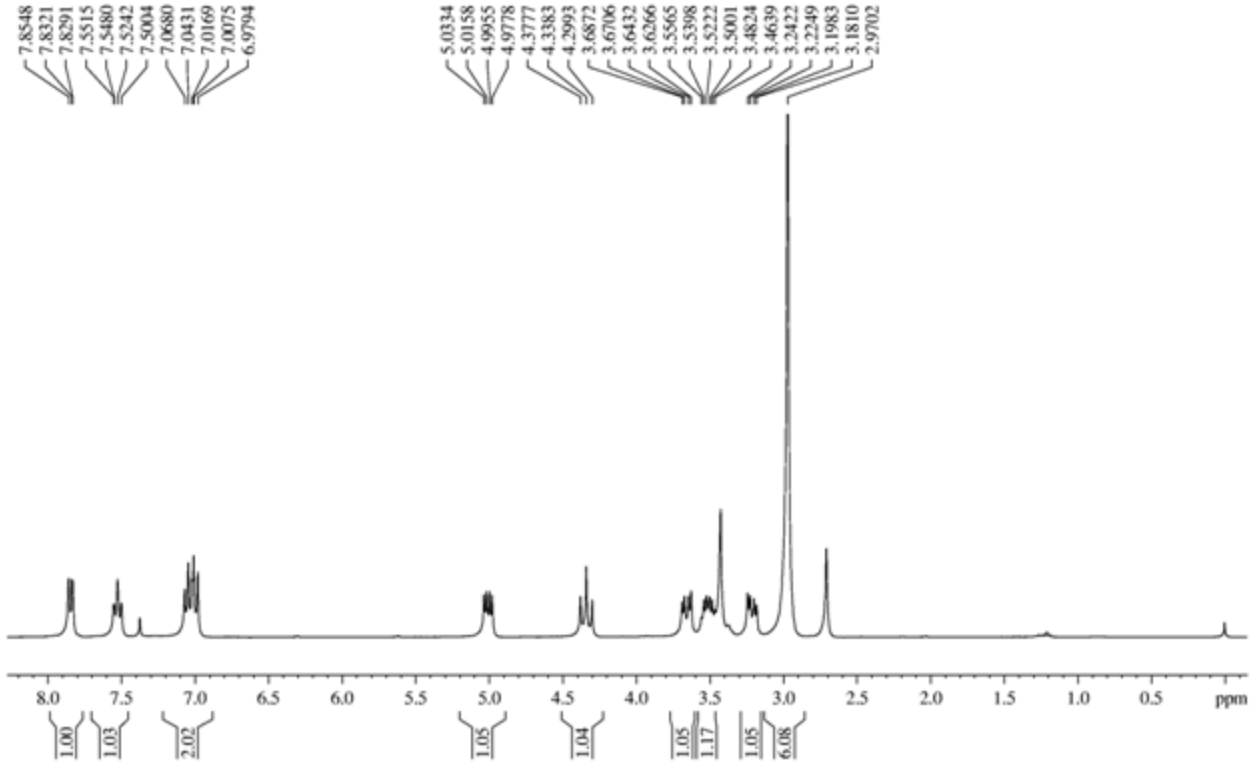
Compound 2b, ^{1}H NMR, $CDCl_3$+MeOD, 300 MHz



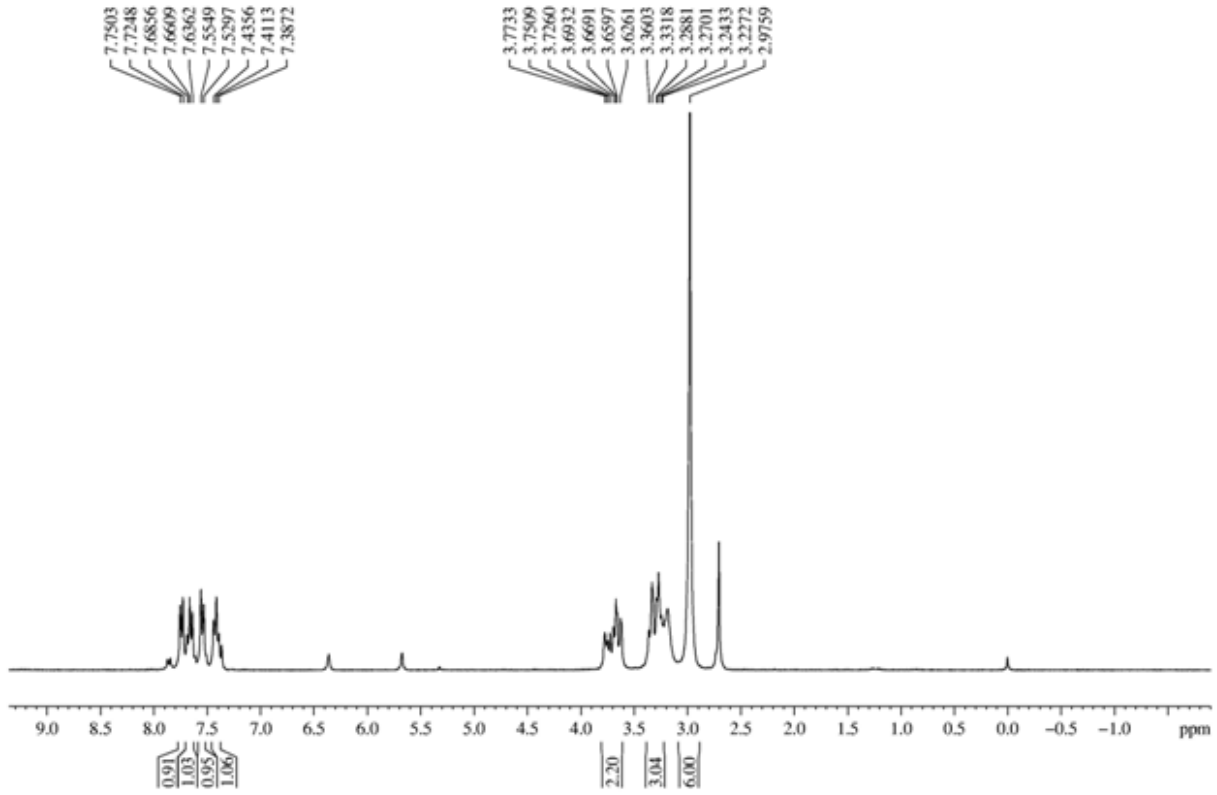
Compound 2e, ^{1}H NMR, $CDCl_3$+MeOD, 300 MHz



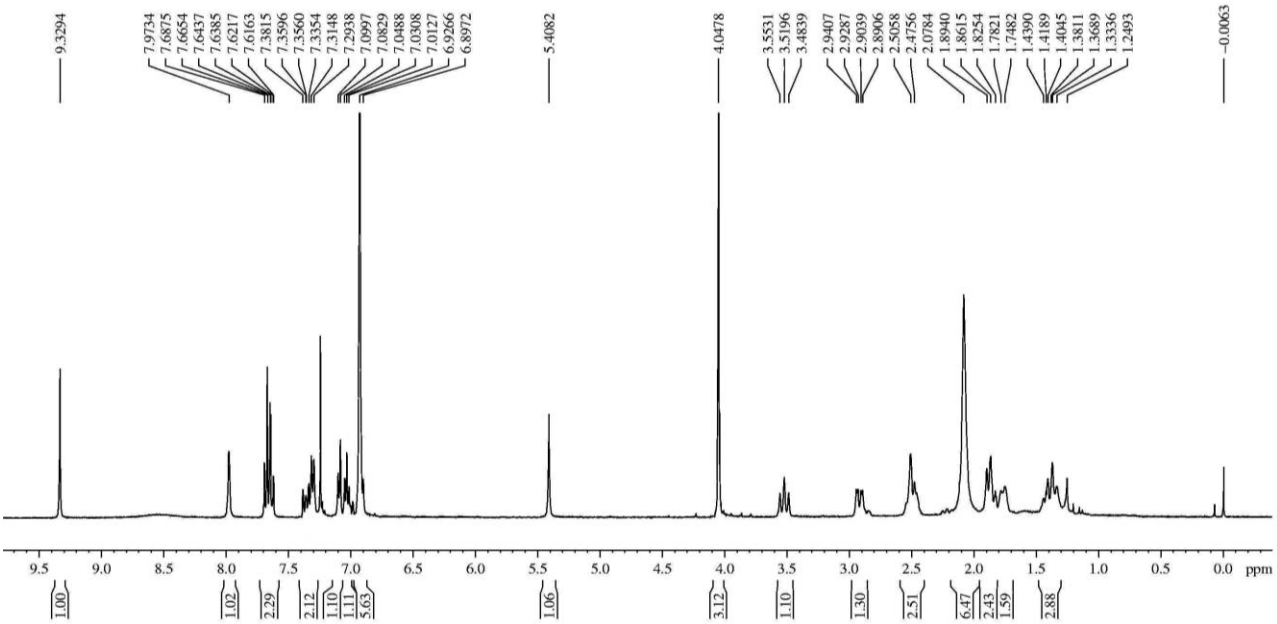
Compound 2f, ^{1}H NMR, $CDCl_3$+MeOD, 300 MHz



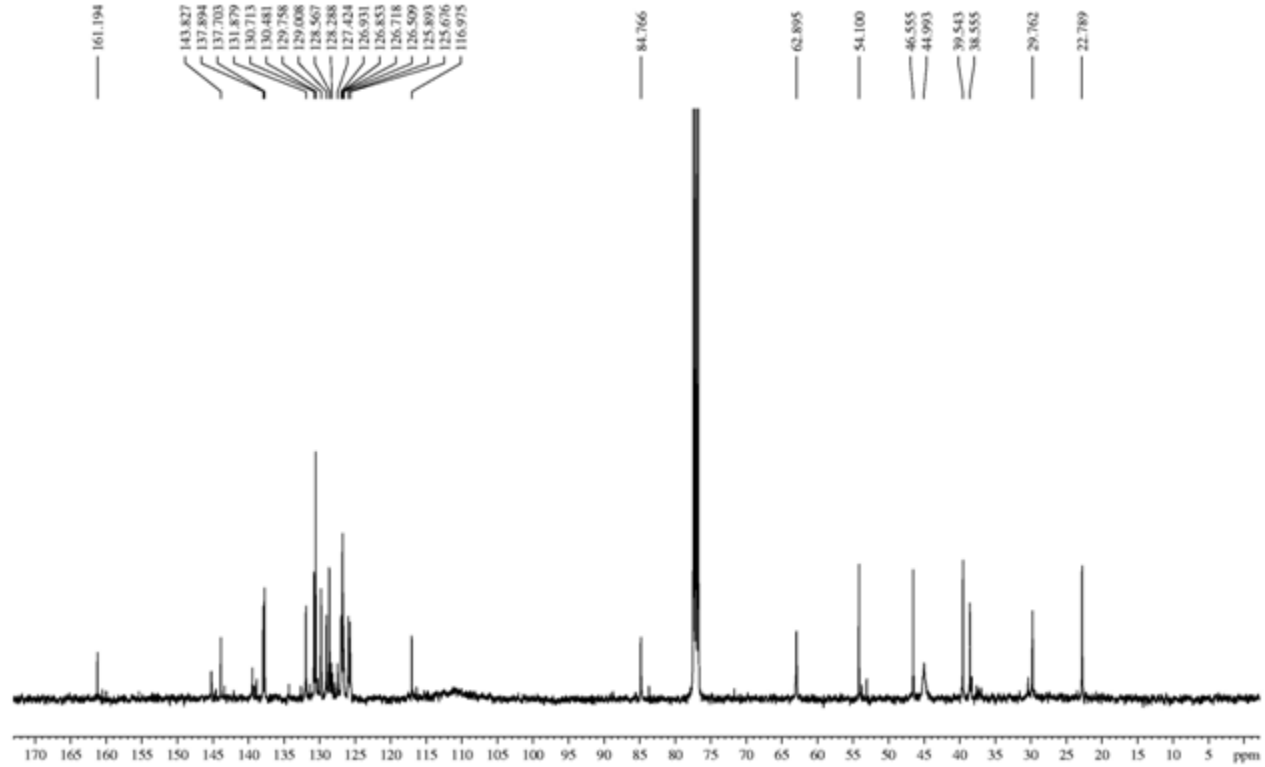
Compound 2g, ^{1}H NMR, $CDCl_3$+MeOD, 300 MHz



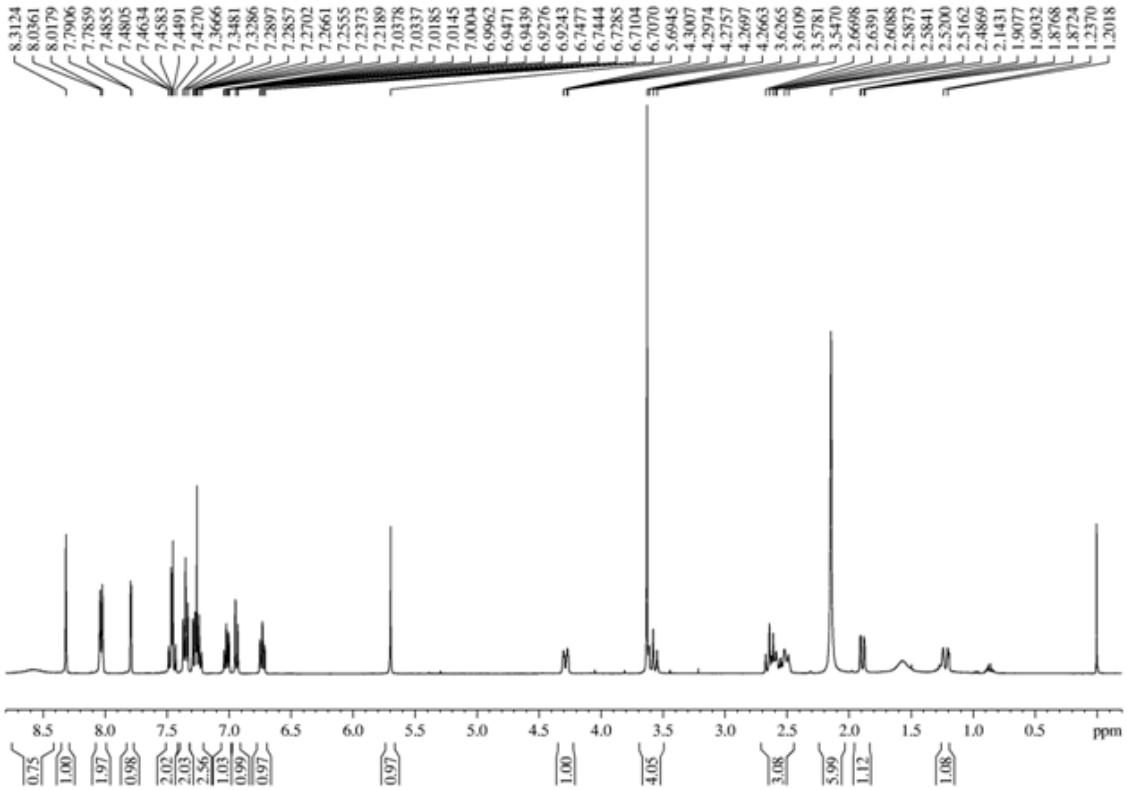
Compound 5a (major), ^{1}H NMR, $CDCl_3$, 300 MHz



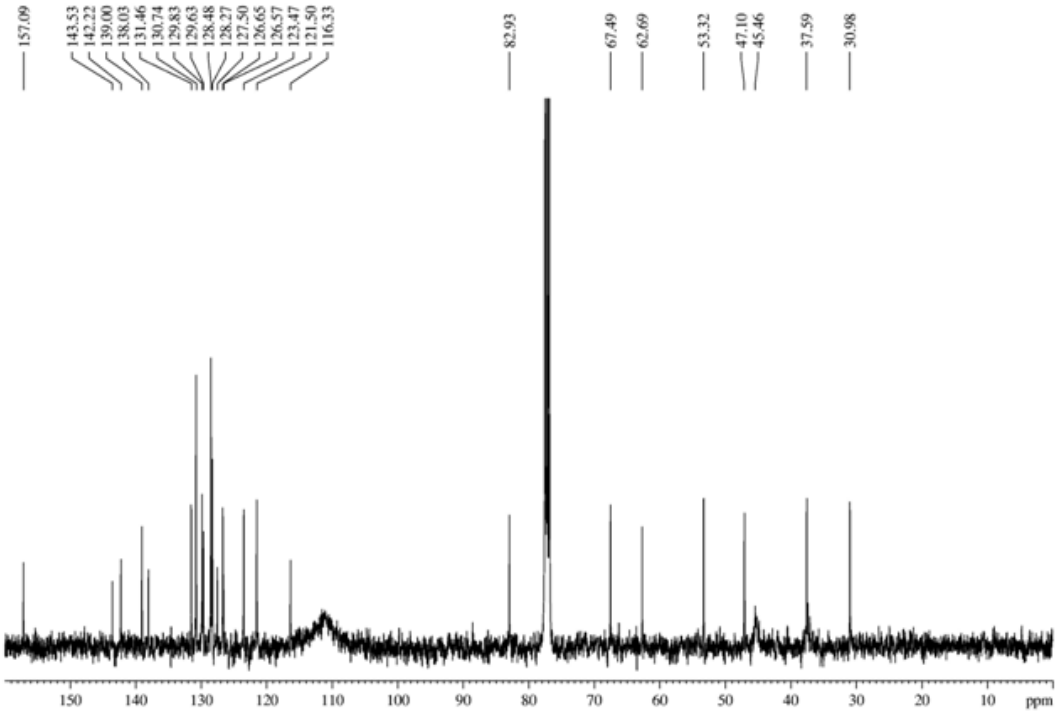
Compound 5a (major), ^{13}C NMR, $CDCl_3$, 75 MHz



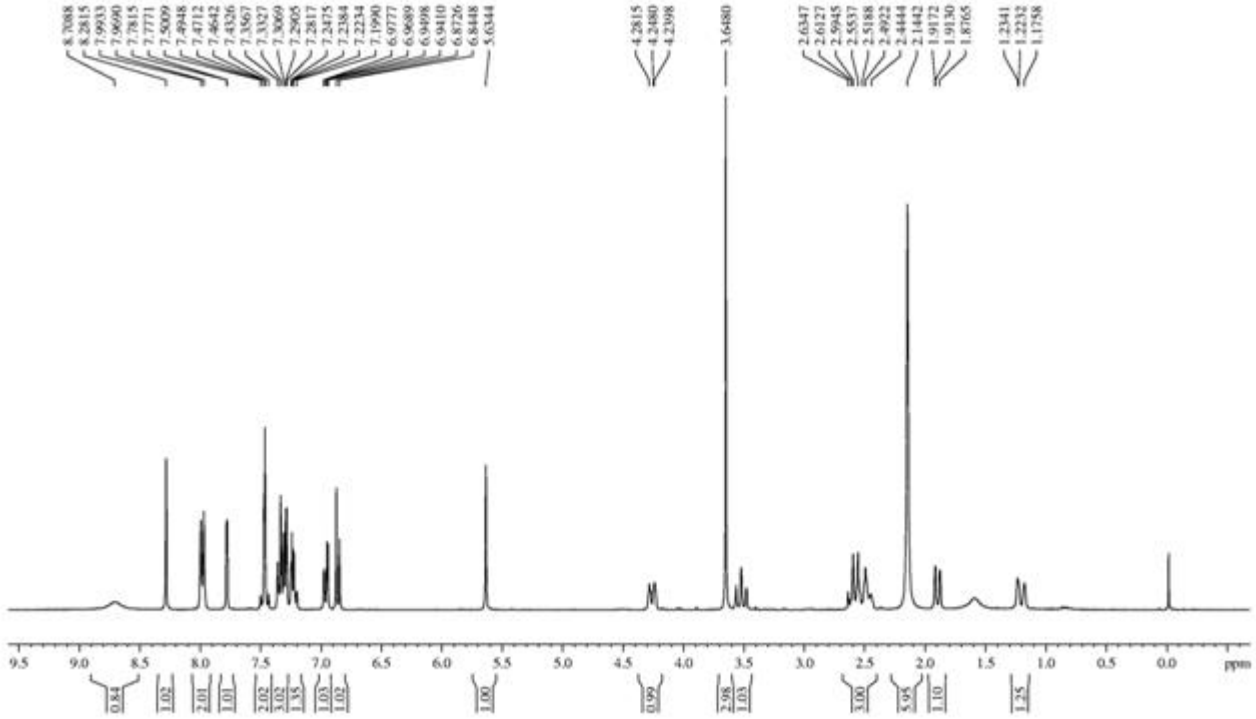
Compound 5b (major), ^{1}H NMR, $CDCl_3$, 300 MHz



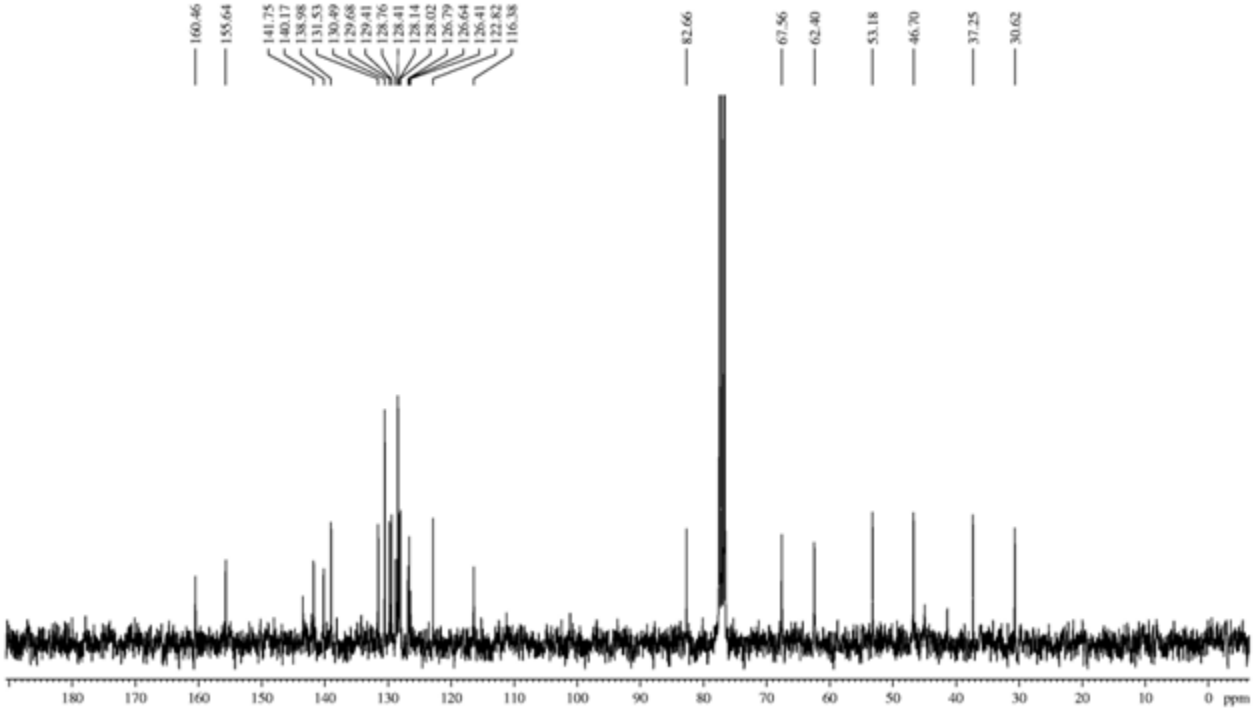
Compound 5b (major), ^{13}C NMR, $CDCl_3$, 75 MHz



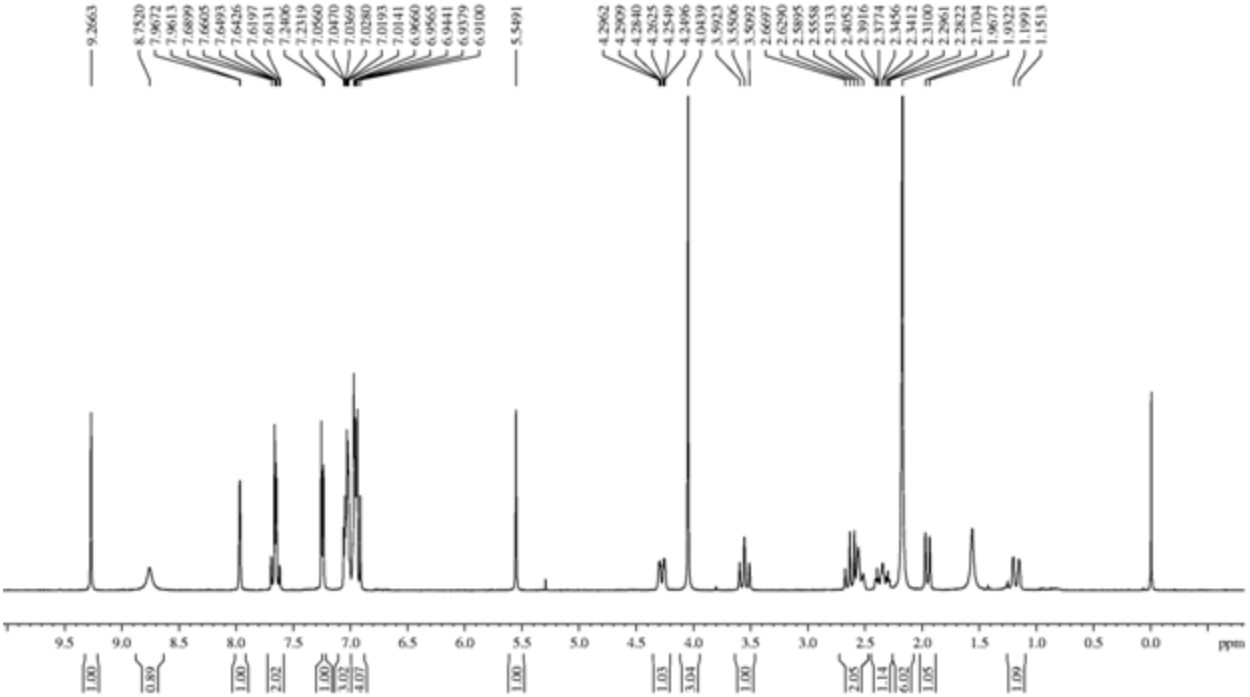
Compound 5c (major), ^{1}H NMR, $CDCl_3$, 300 MHz



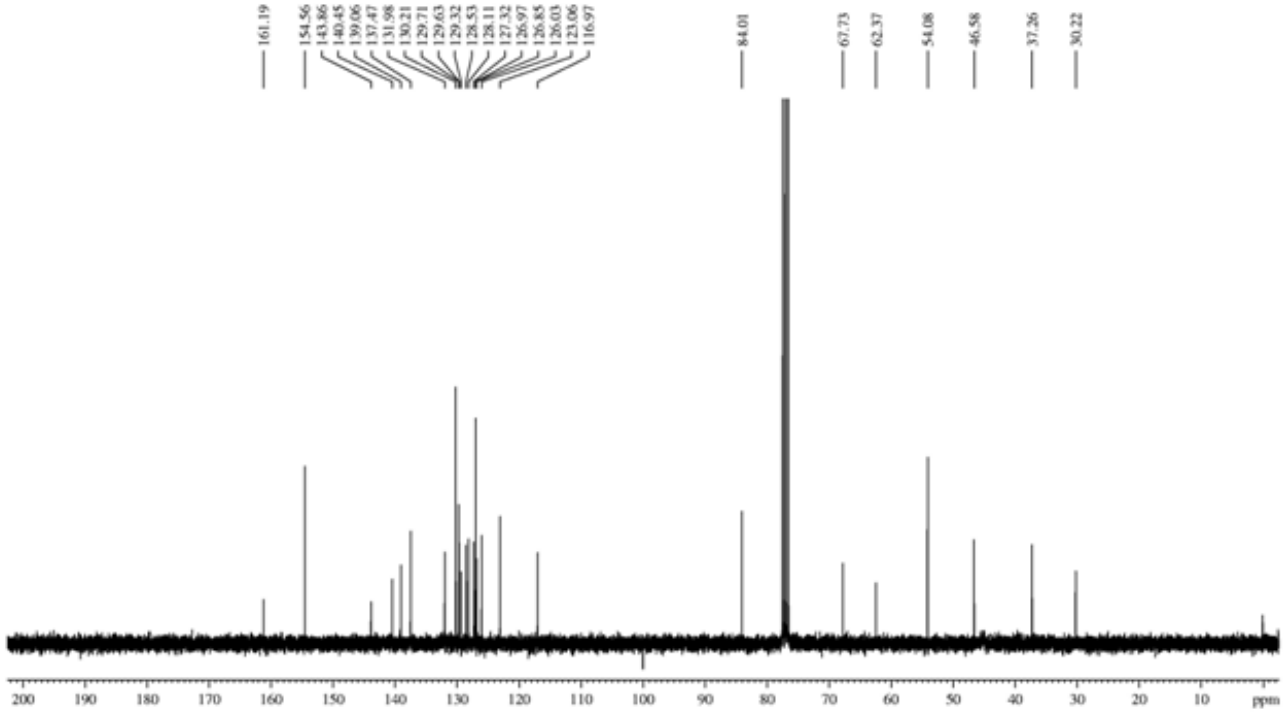
Compound 5c (major), ^{13}C NMR, $CDCl_3$, 75 MHz



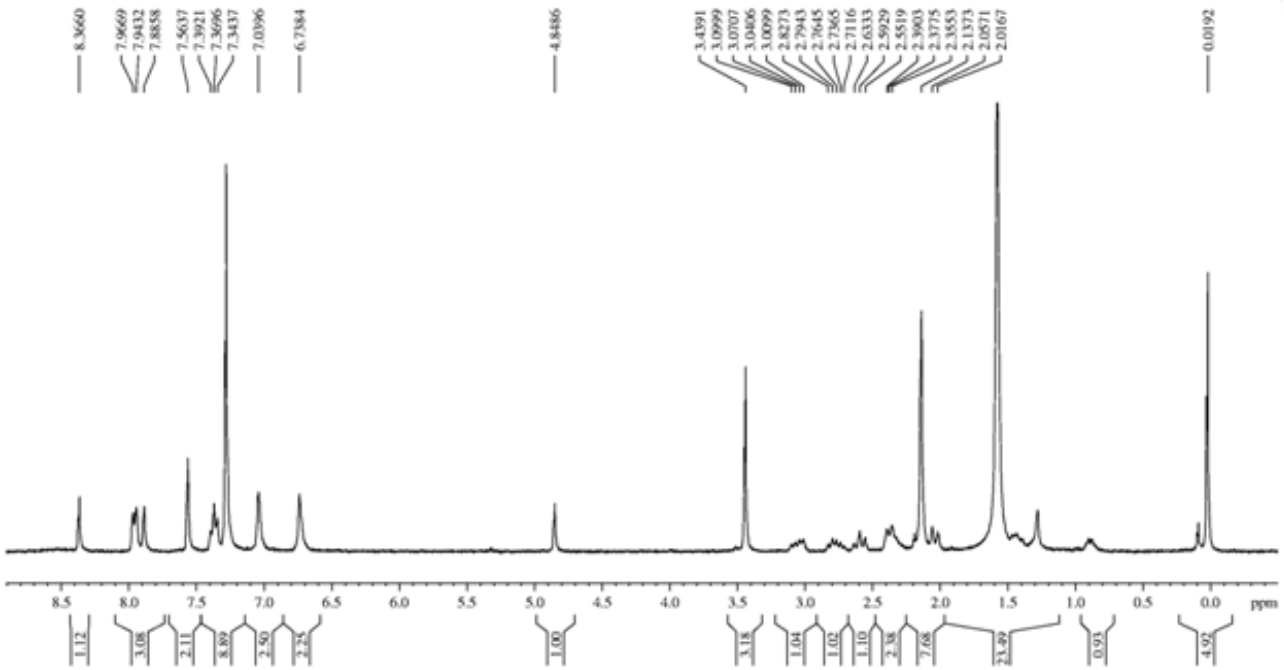
Compound 5c (minor), ^{1}H NMR, $CDCl_3$, 300 MHz



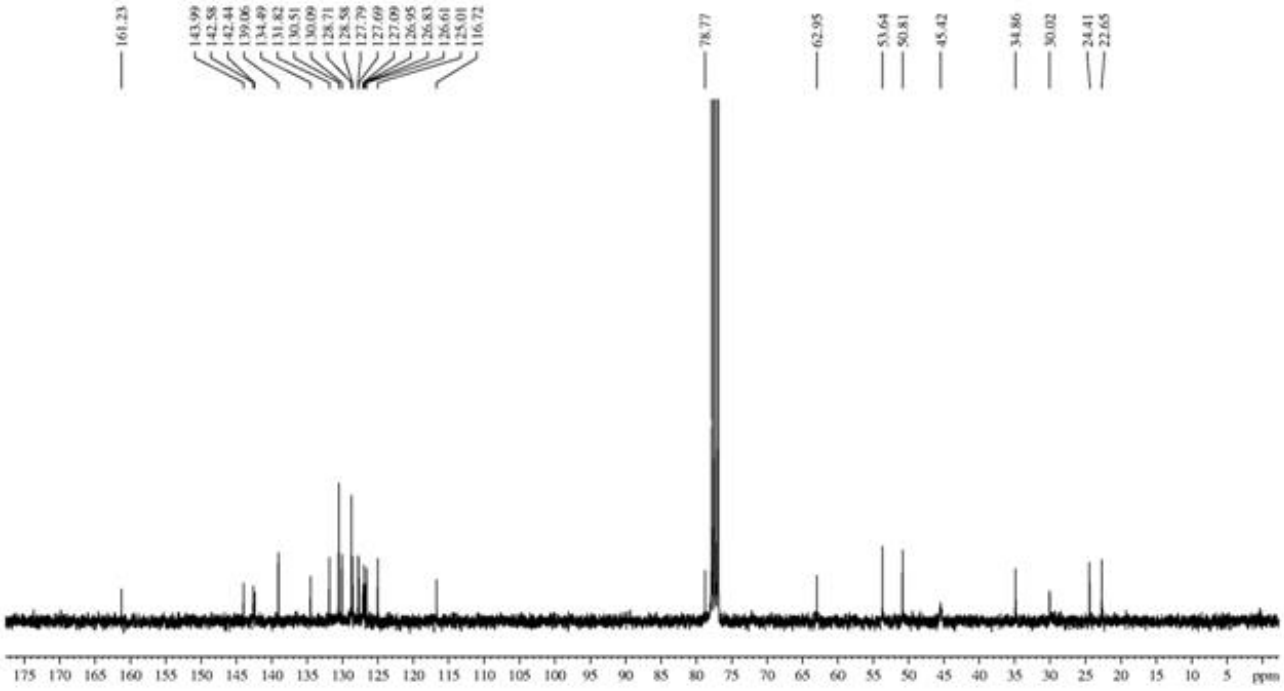
Compound 5c (minor), ^{13}C NMR, $CDCl_3$, 75 MHz



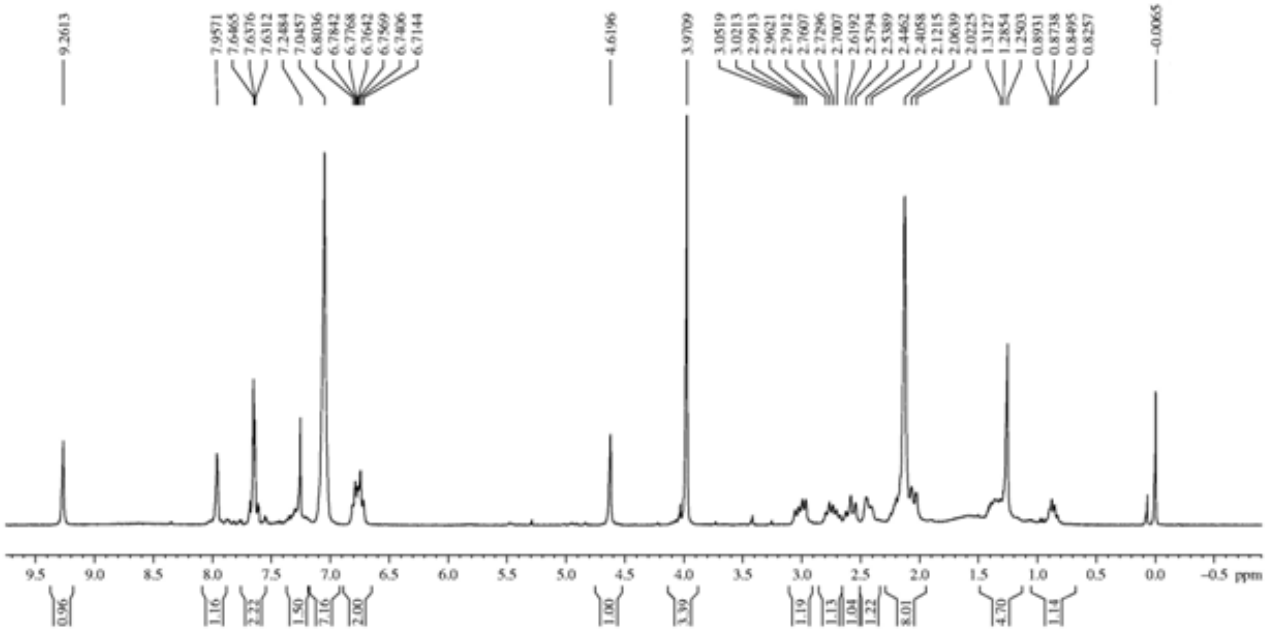
Compound 5d (major), ^{1}H NMR, $CDCl_3$, 300 MHz



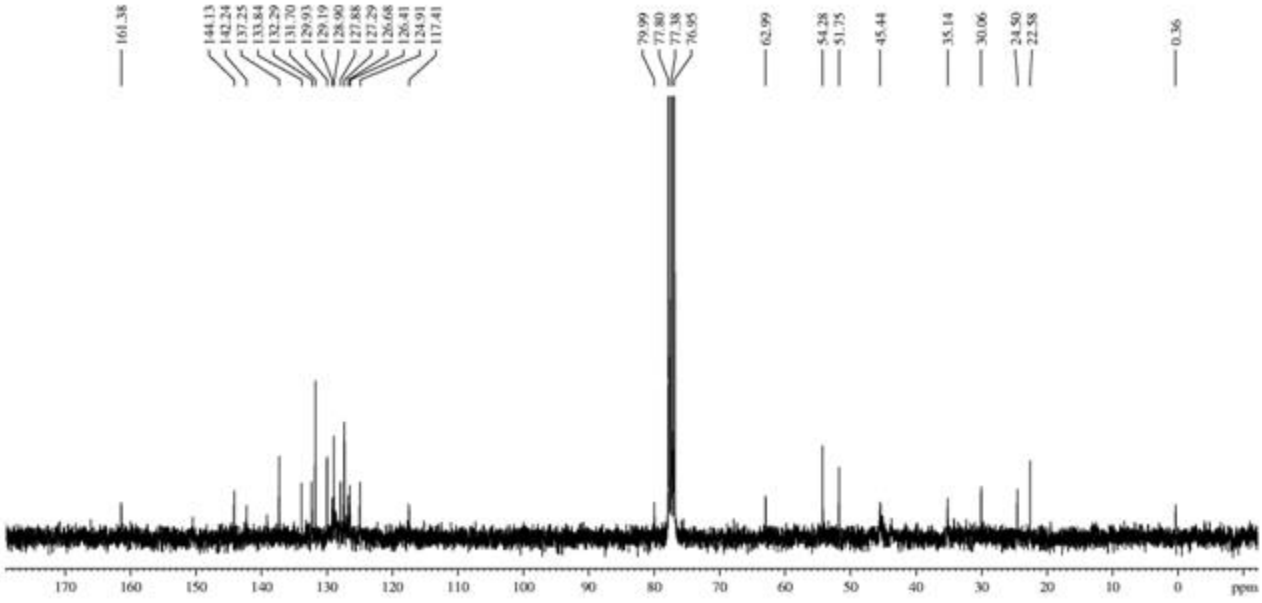
Compound 5d (major), ^{13}C NMR, $CDCl_3$, 75 MHz



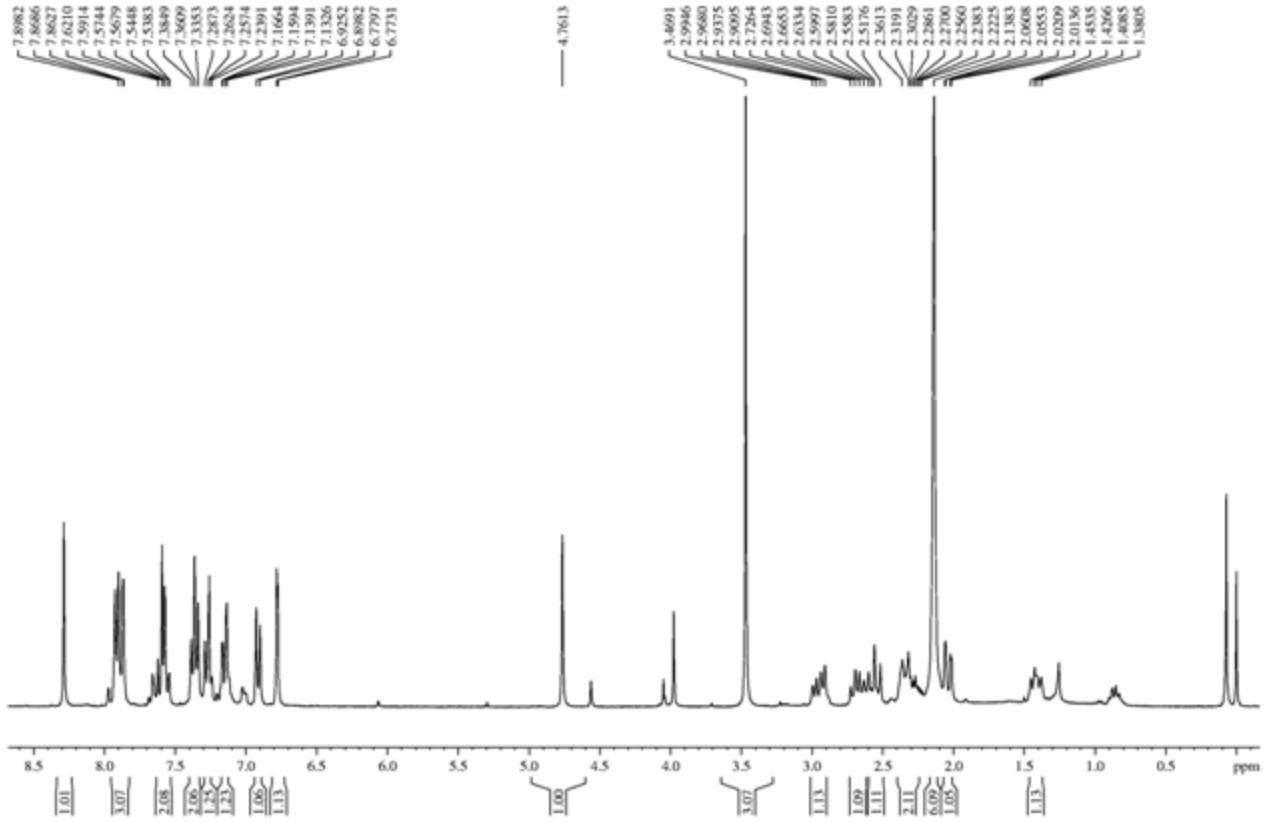
Compound 5d (minor), ^{1}H NMR, $CDCl_3$, 300 MHz



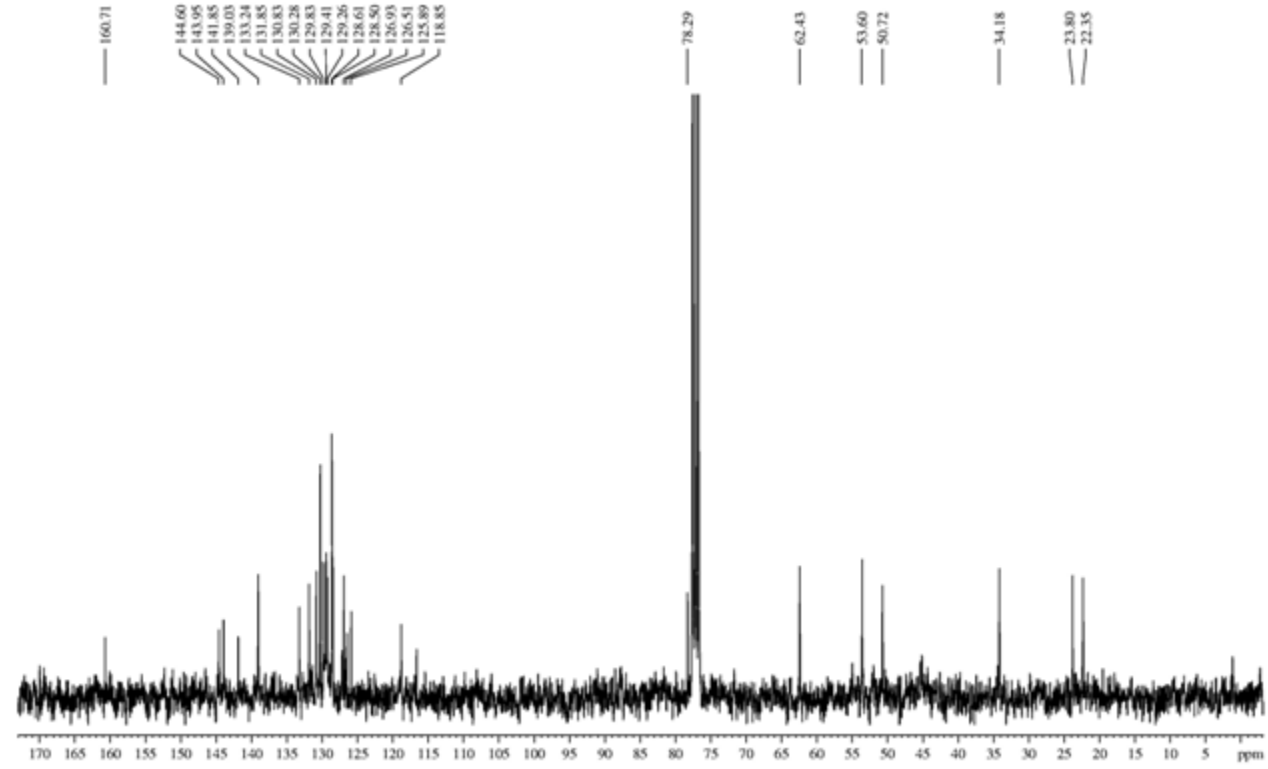
Compound 5d (minor), ^{13}C NMR, $CDCl_3$, 75 MHz



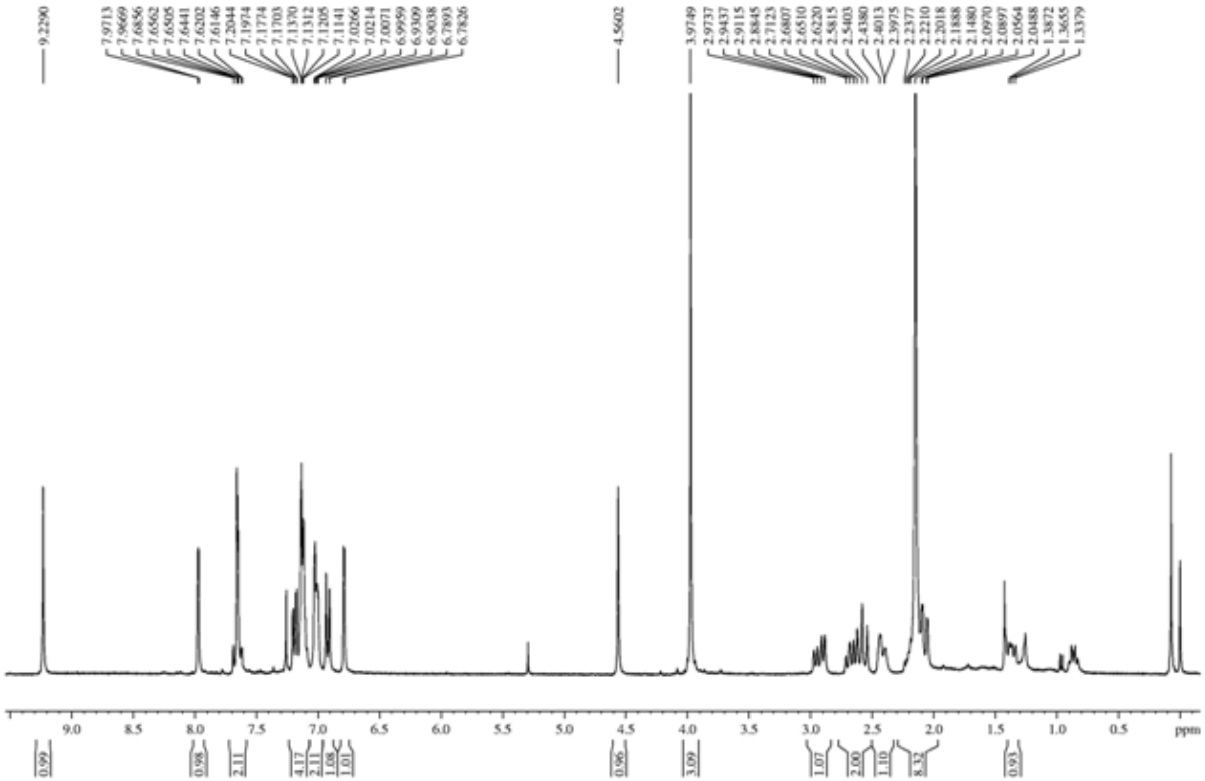
Compound 5e (major), ^{1}H NMR, $CDCl_3$, 300 MHz



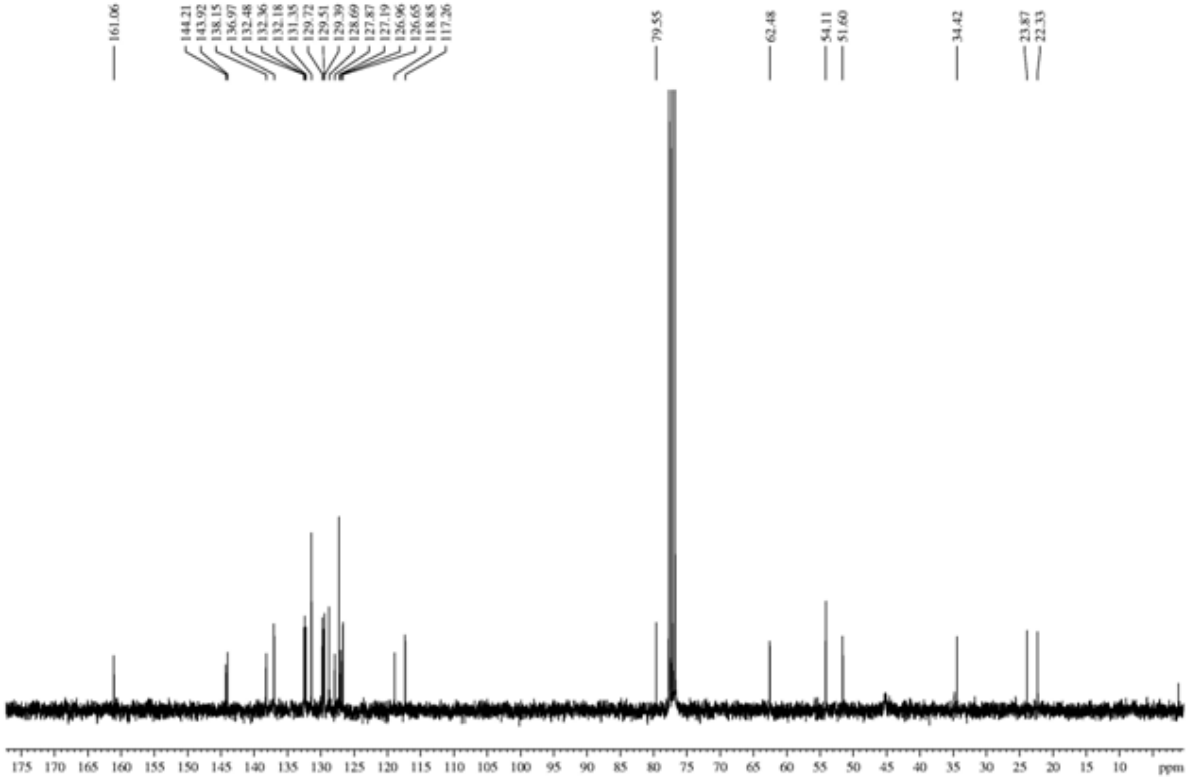
Compound 5e (major), ^{13}C NMR, $CDCl_3$, 75 MHz



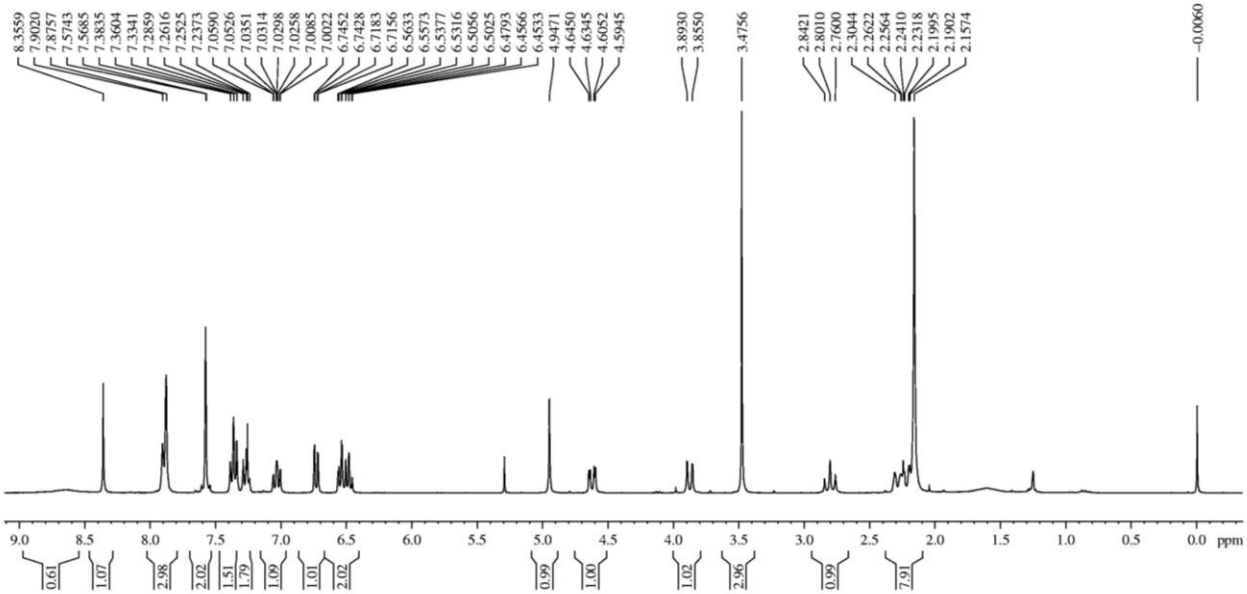
Compound 5e (minor), ^{1}H NMR, $CDCl_3$, 300 MHz



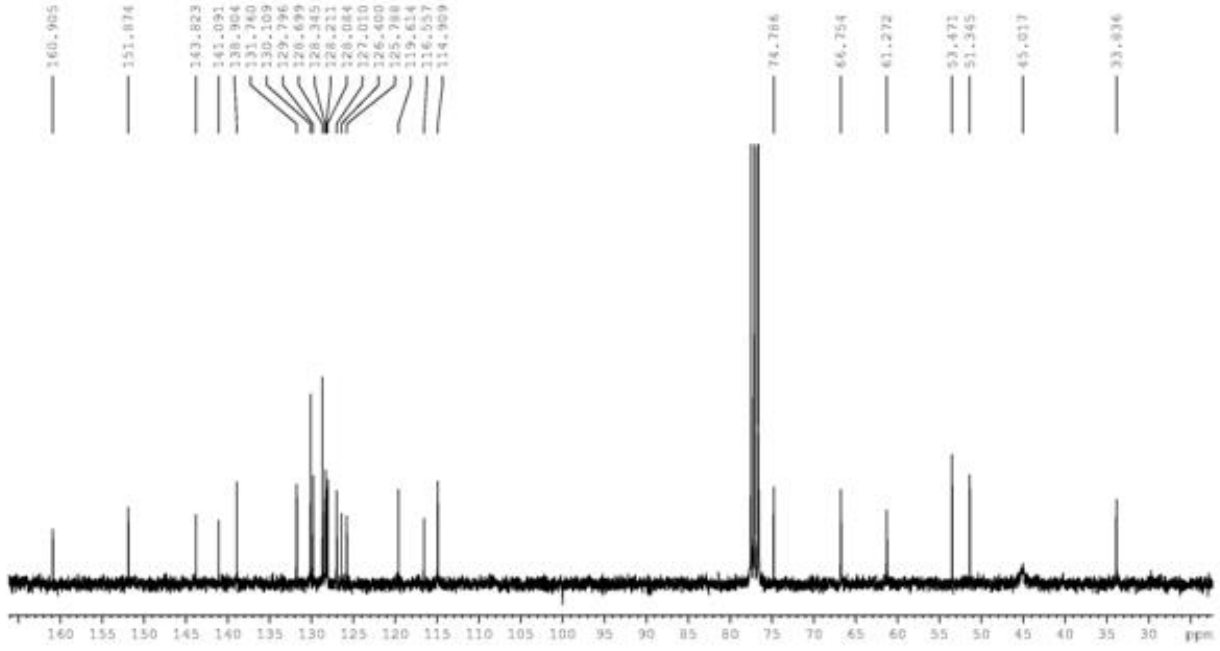
Compound 5e (minor), ^{13}C NMR, $CDCl_3$, 75 MHz



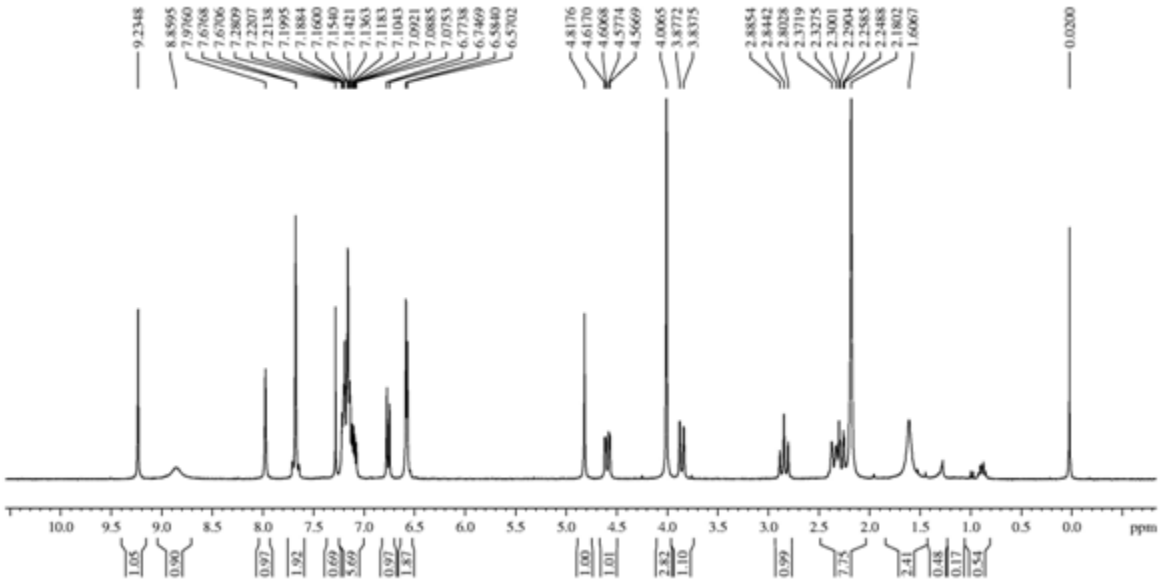
Compound 5f (major), ^{1}H NMR, $CDCl_3$, 300 MHz



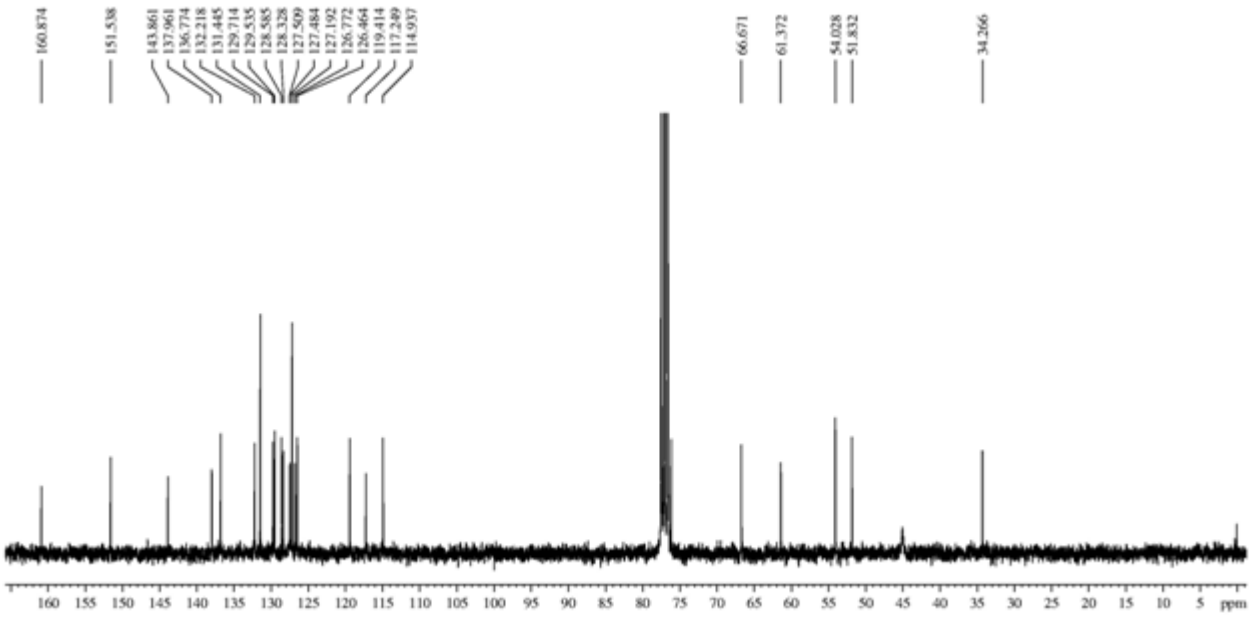
Compound 5f (major), ^{13}C NMR, $CDCl_3$, 75 MHz



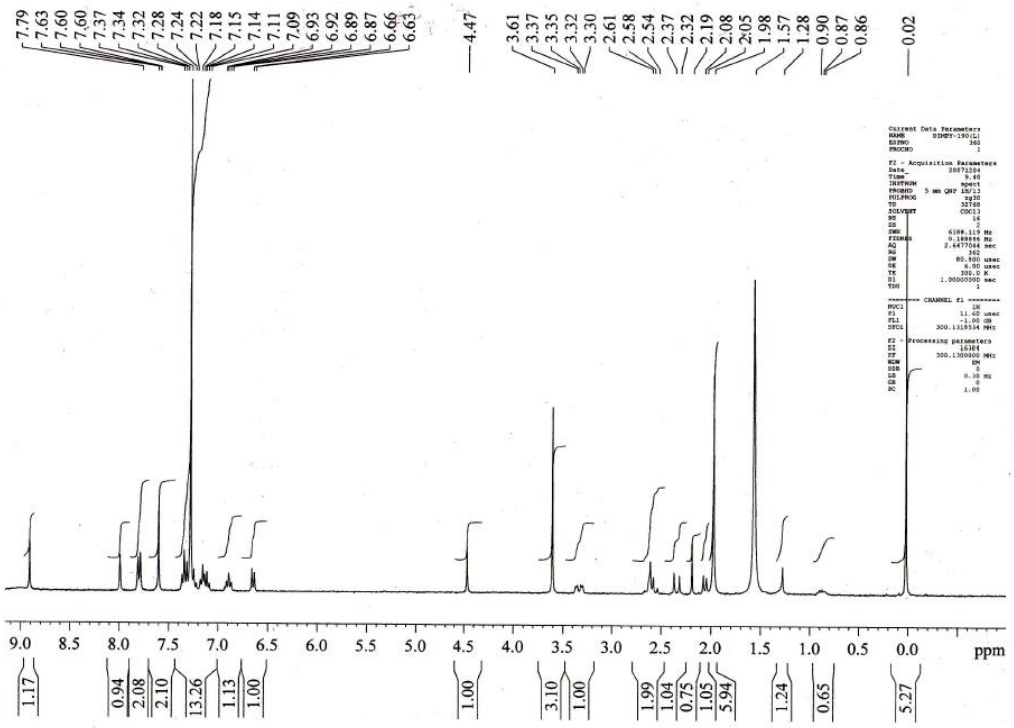
Compound 5f (minor), ^{1}H NMR, $CDCl_3$, 300 MHz



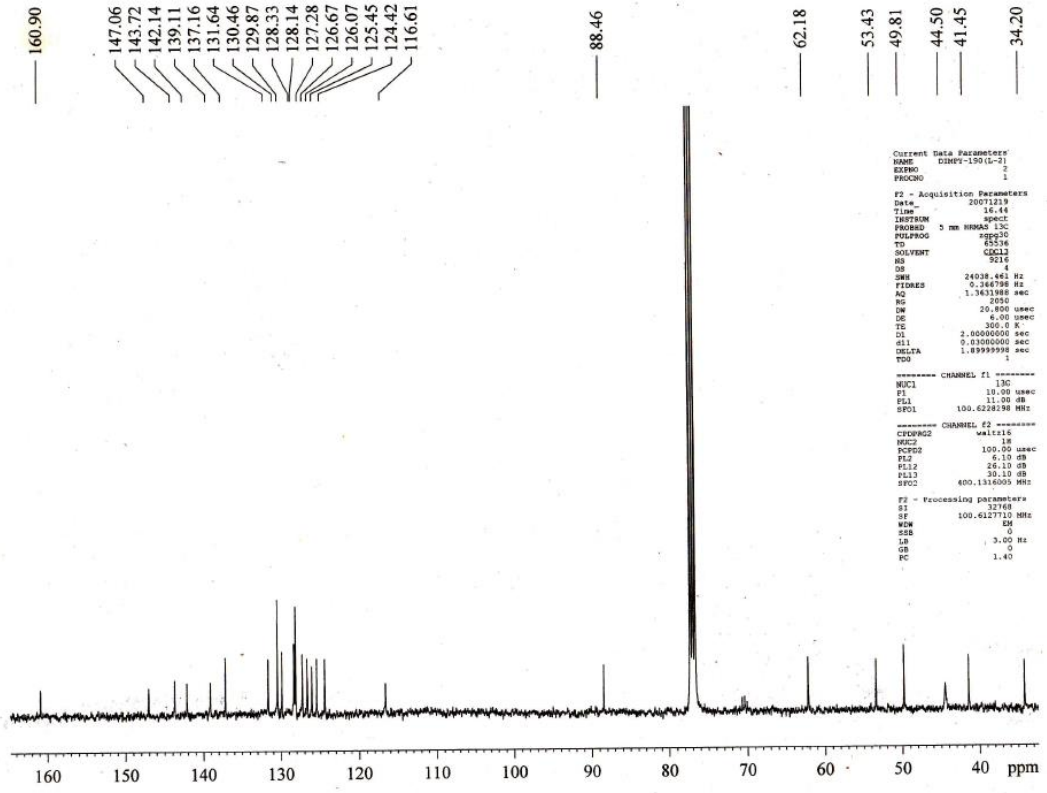
Compound 5f (minor), ^{13}C NMR, $CDCl_3$, 75 MHz



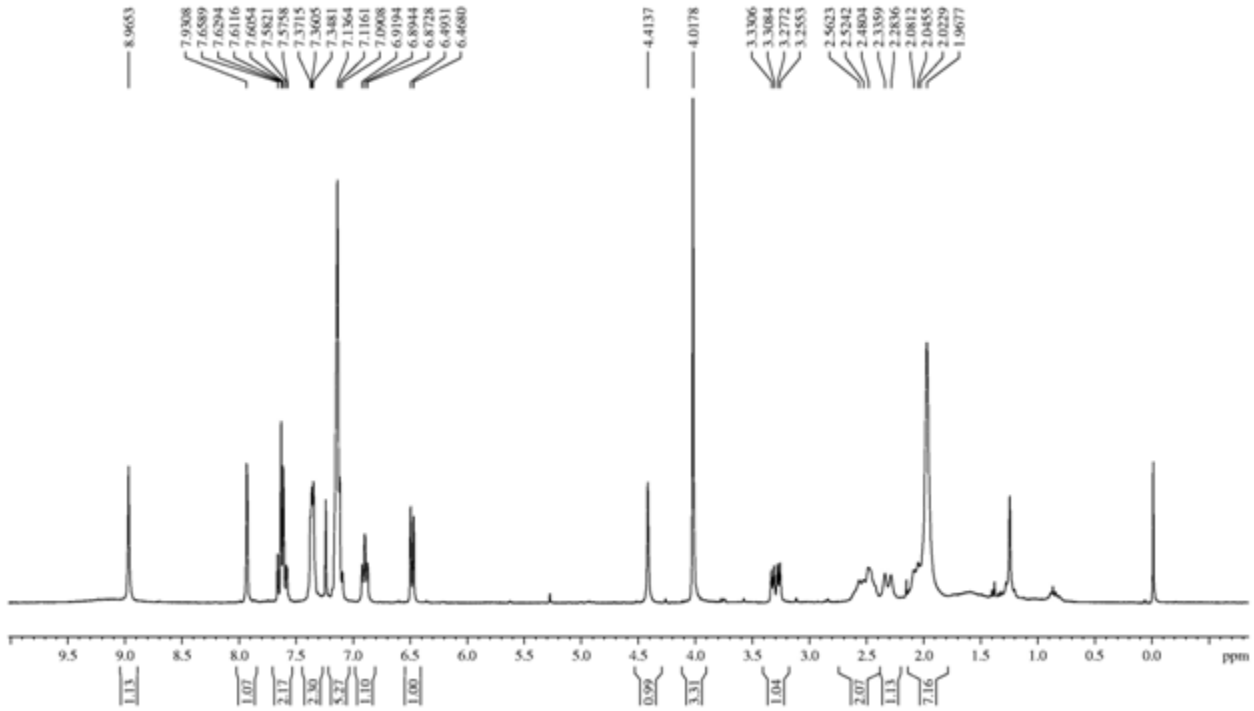
Compound 5g (major), ^{1}H NMR, $CDCl_3$, 300 MHz



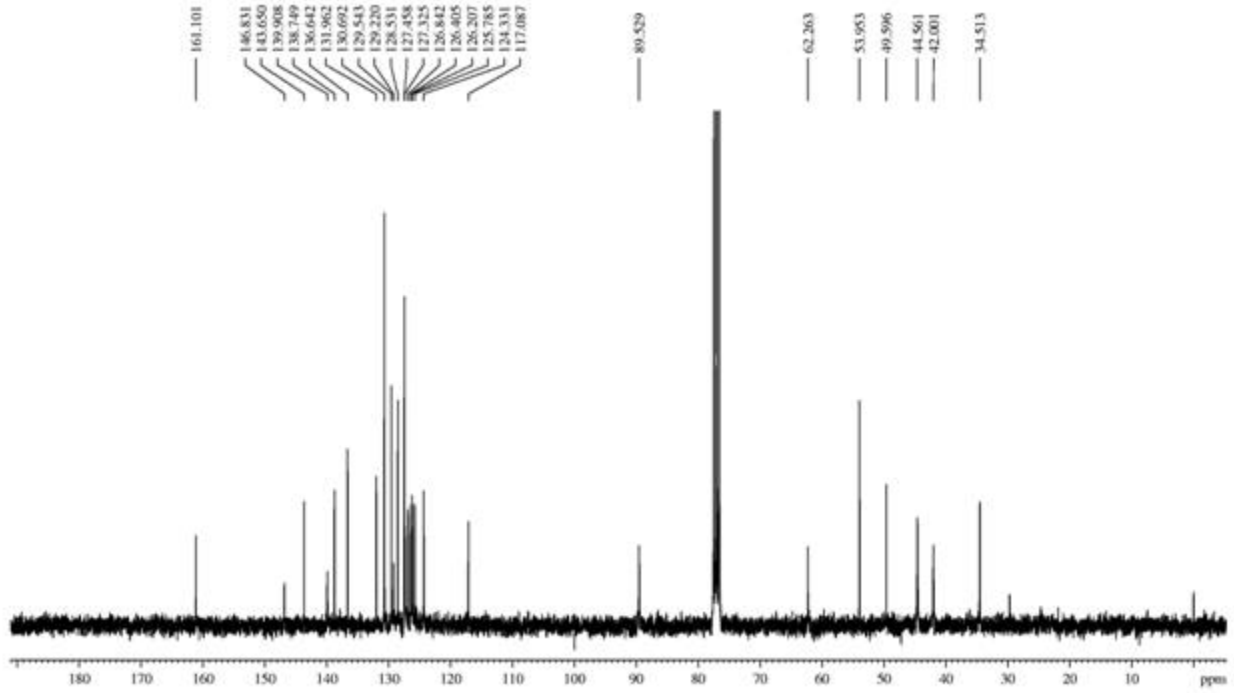
Compound 5g (major), ^{13}C NMR, $CDCl_3$, 100 MHz



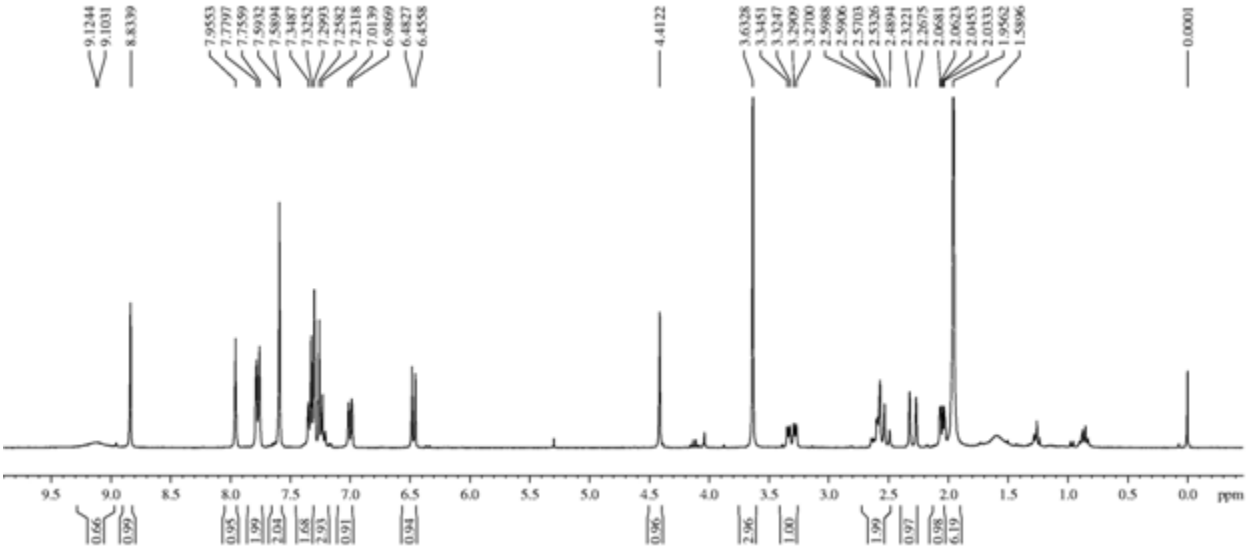
Compound 5g (minor), ^{1}H NMR, $CDCl_3$, 300 MHz



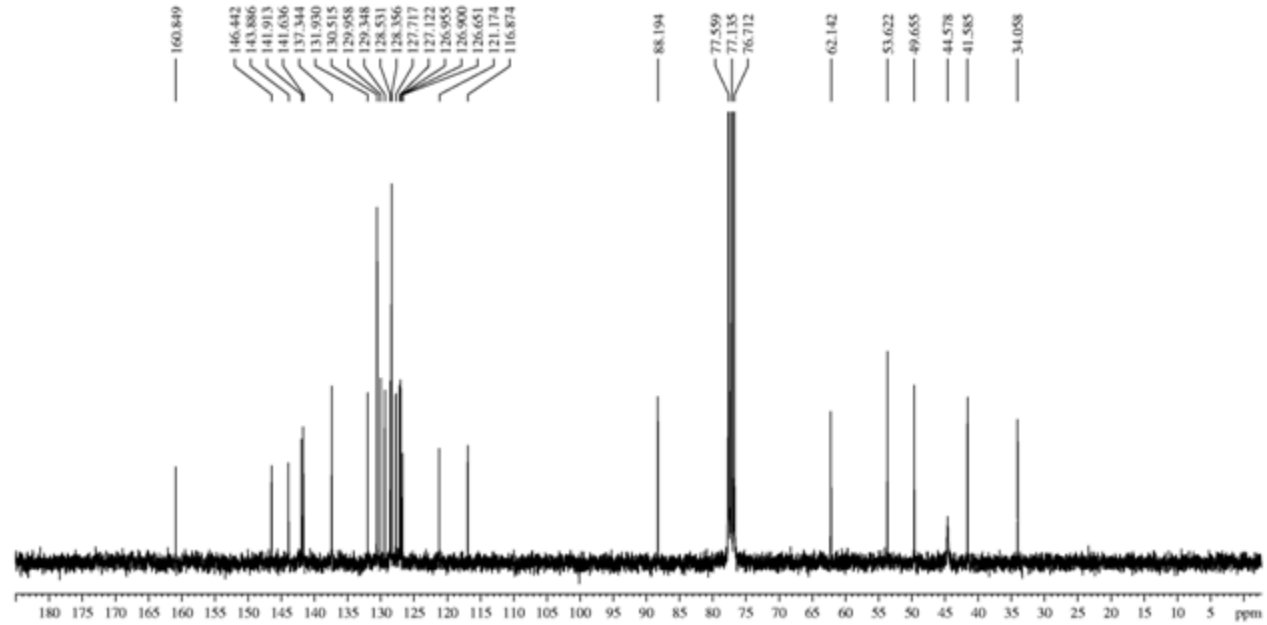
Compound 5g (minor), ^{13}C NMR, $CDCl_3$, 75 MHz



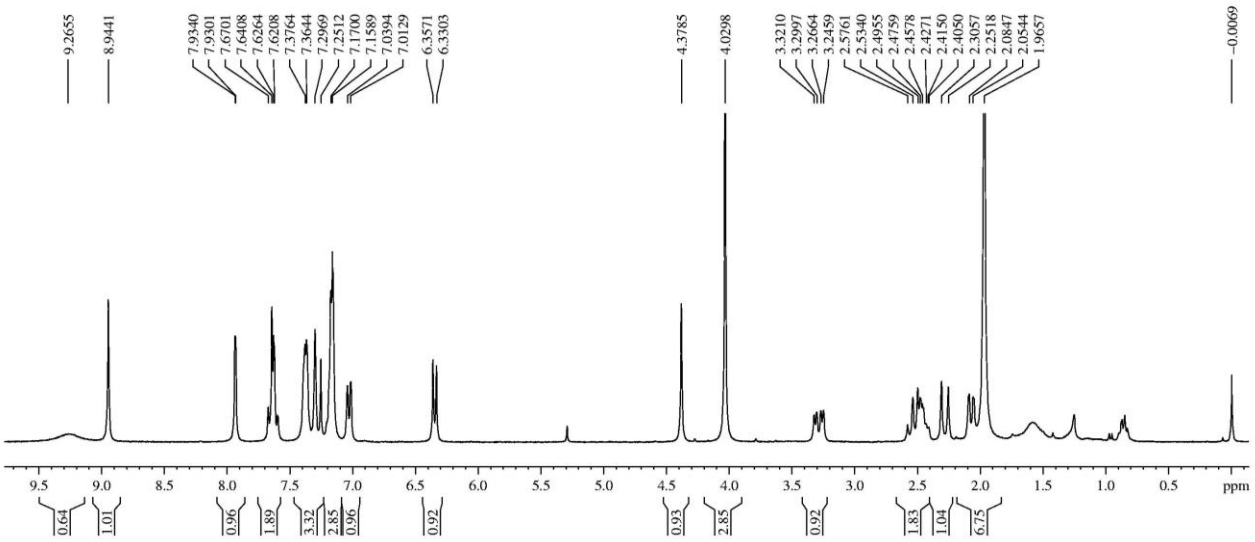
Compound 5h (major), ^{1}H NMR, $CDCl_3$, 300 MHz



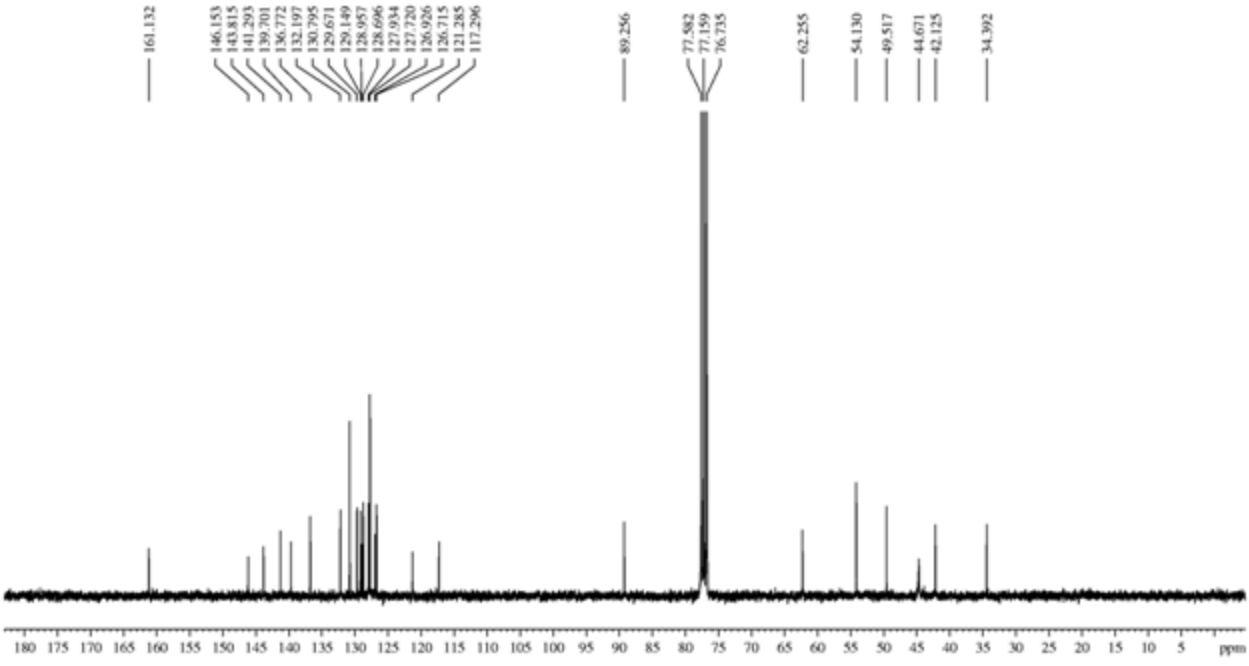
Compound 5h (major), ^{13}C NMR, $CDCl_3$, 75 MHz



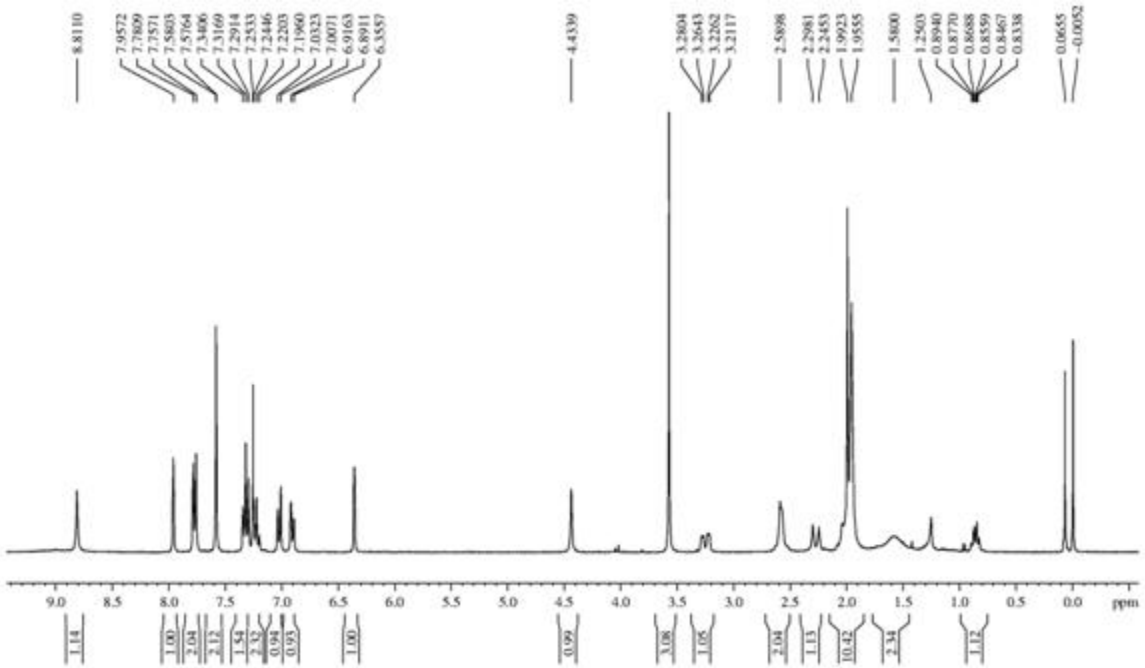
Compound 5h (minor), ^{1}H NMR, $CDCl_3$, 300 MHz



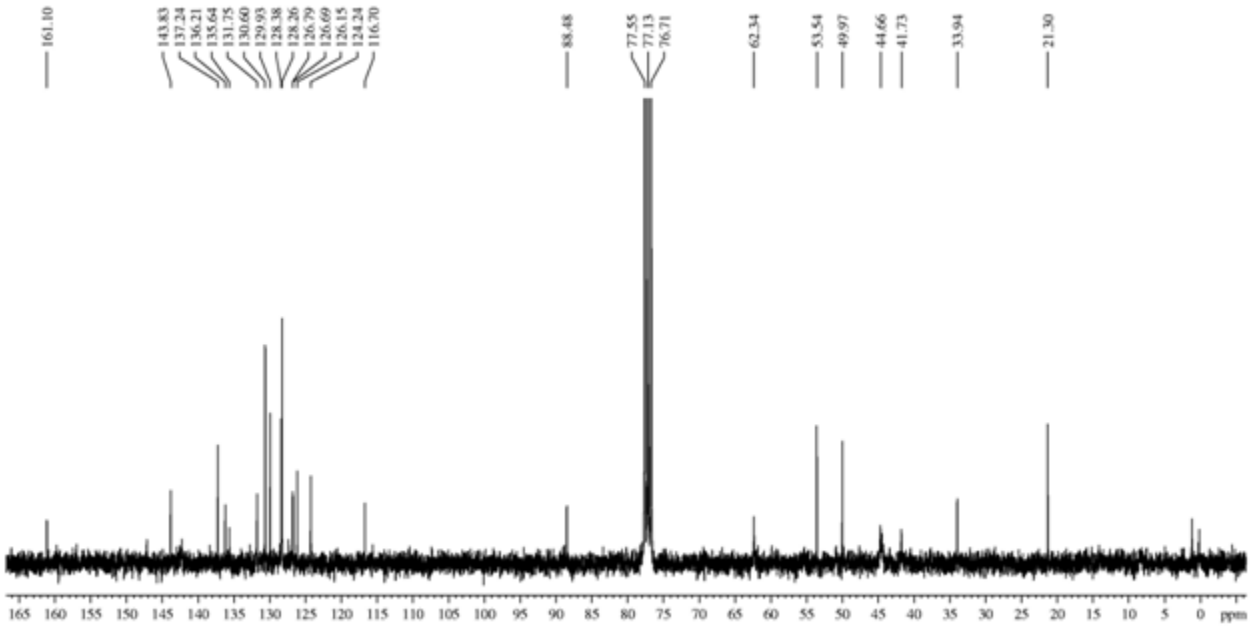
Compound 5h (minor), ^{13}C NMR, $CDCl_3$, 75 MHz



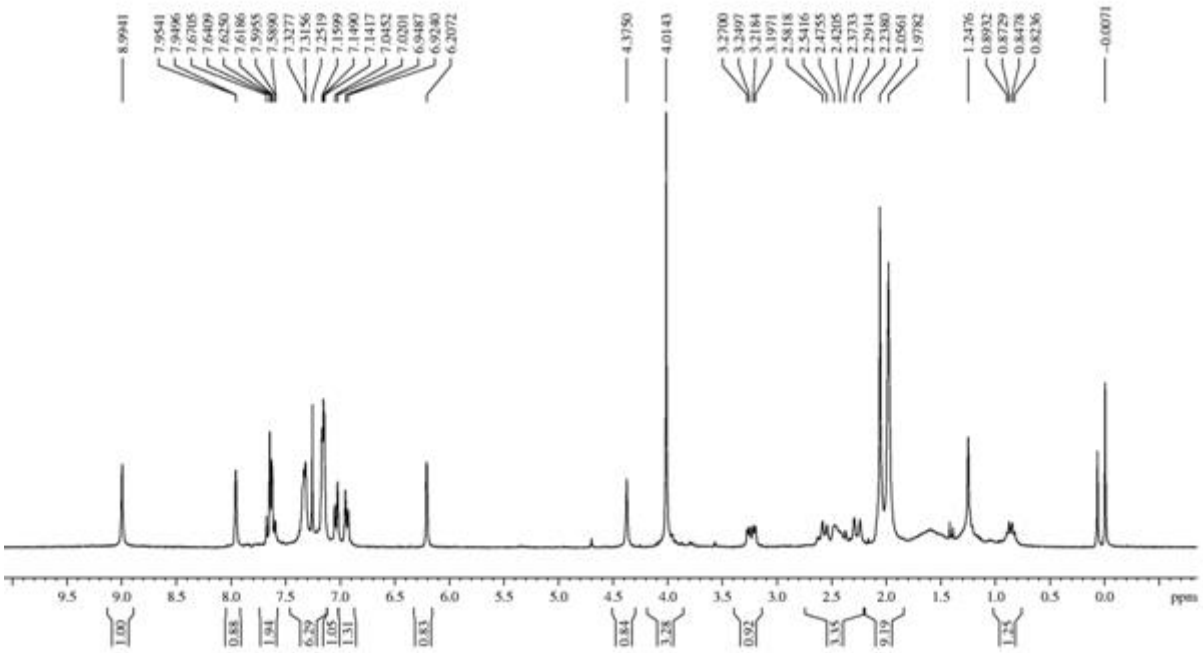
Compound 5i (major), ^{1}H NMR, $CDCl_3$, 300 MHz



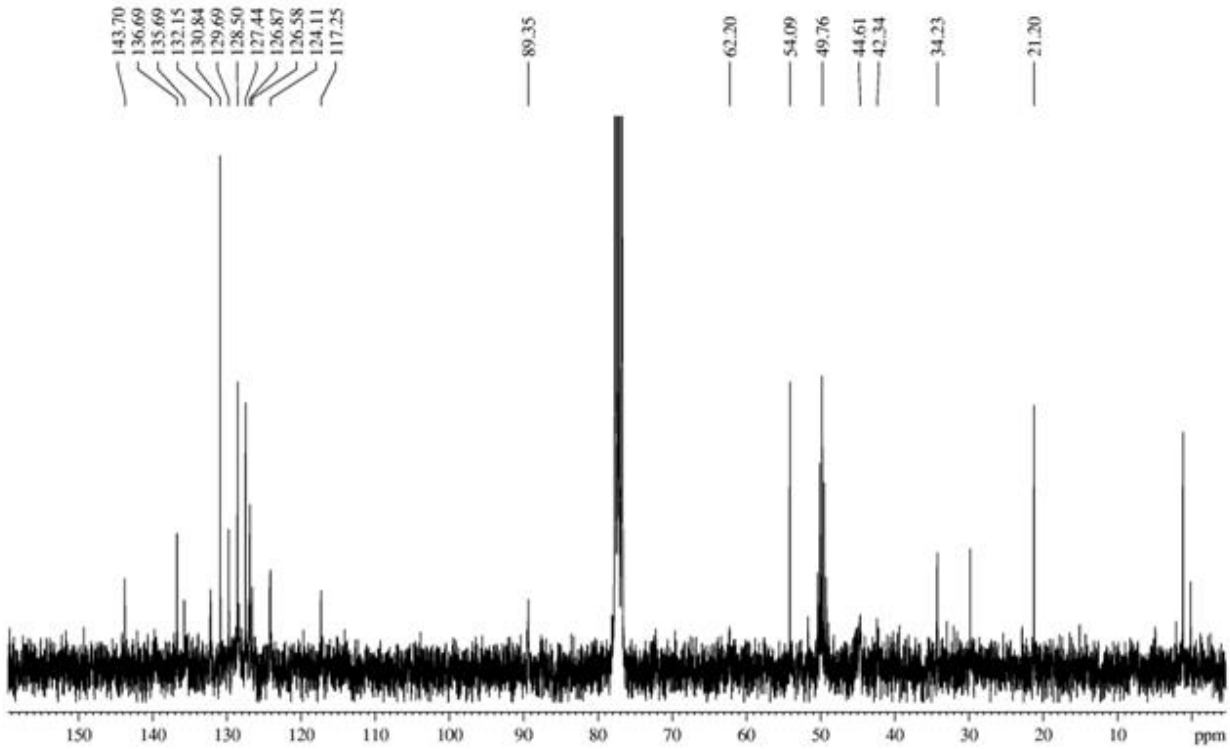
Compound 5i (major), ^{13}C NMR, $CDCl_3$, 75 MHz



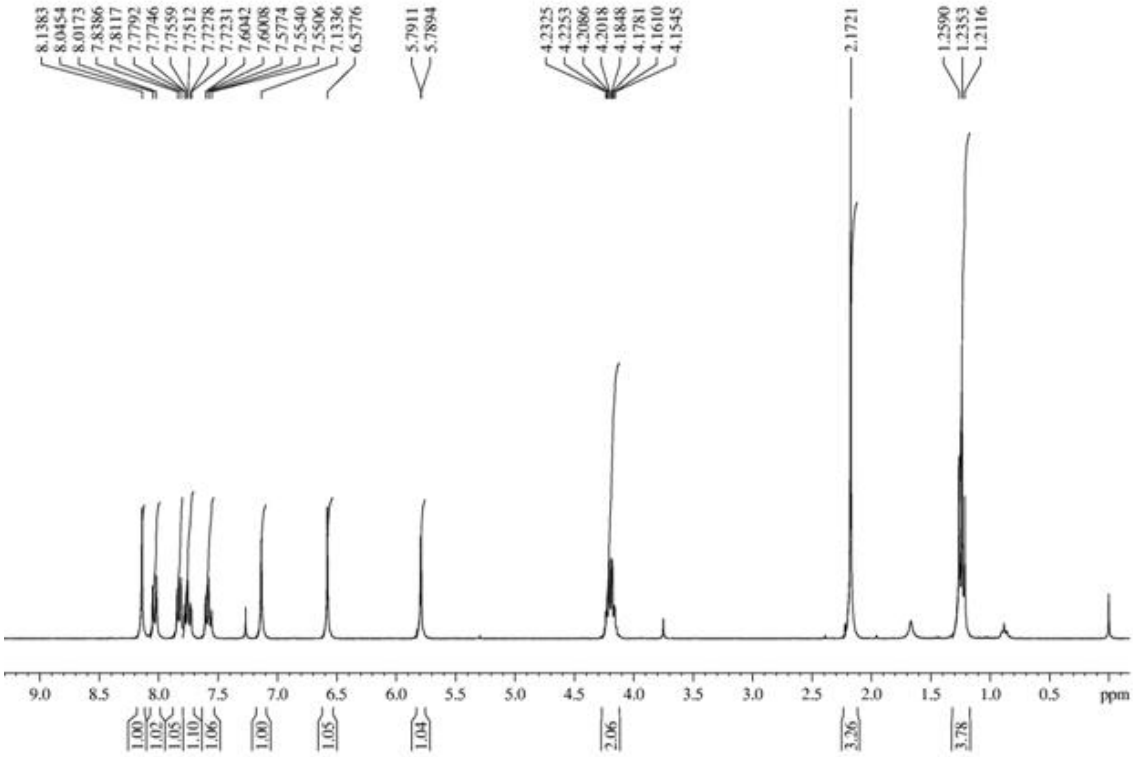
Compound 5i (minor), ^{1}H NMR, $CDCl_3$, 300 MHz



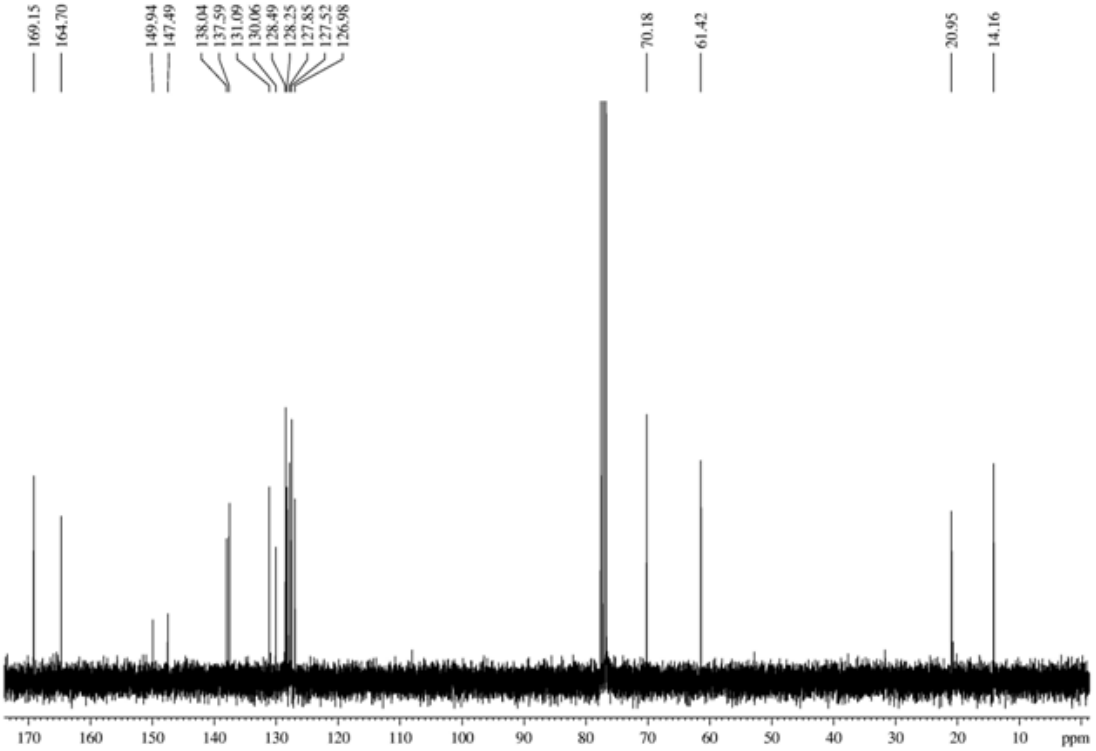
Compound 5i (minor), ^{13}C NMR, $CDCl_3$, 75 MHz



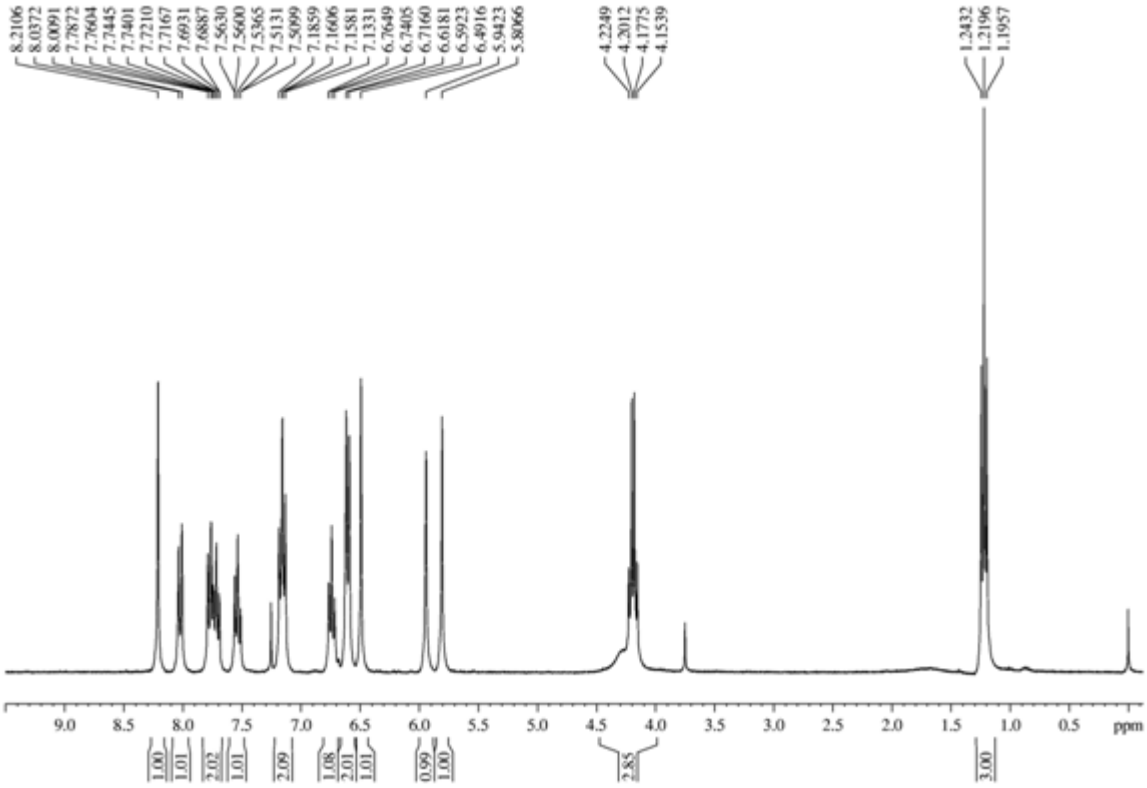
Compound 8, ^{1}H NMR, $CDCl_3$, 300 MHz



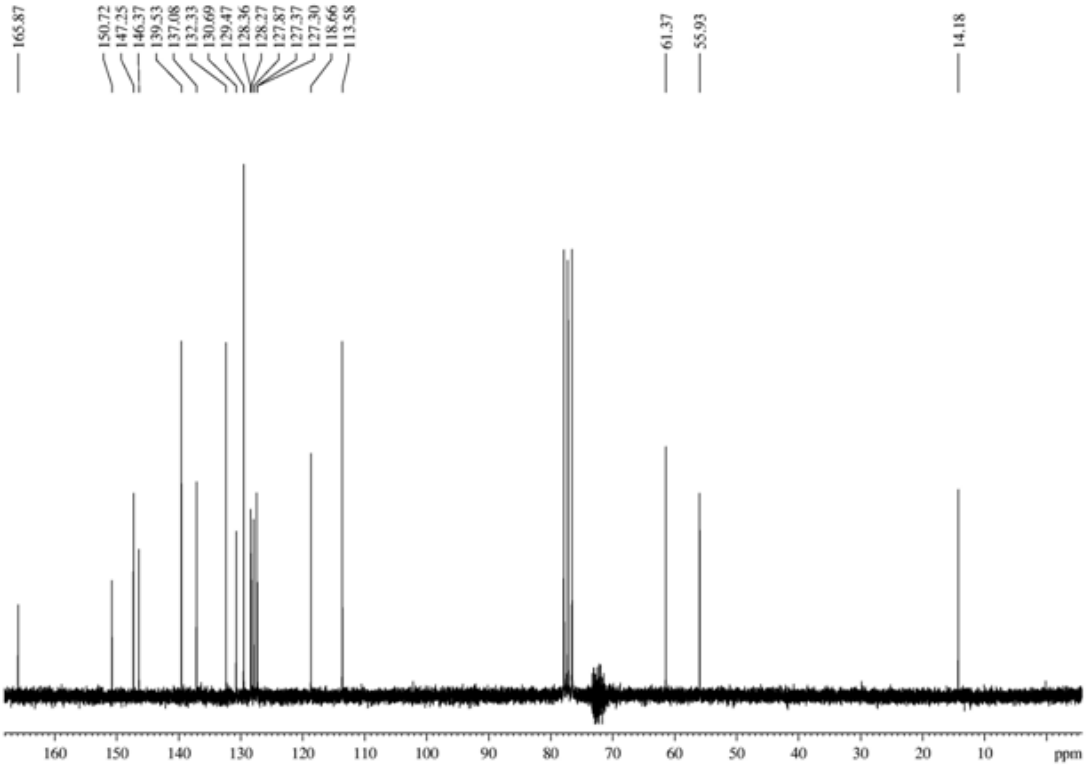
Compound 8, ^{13}C NMR, $CDCl_3$, 75 MHz



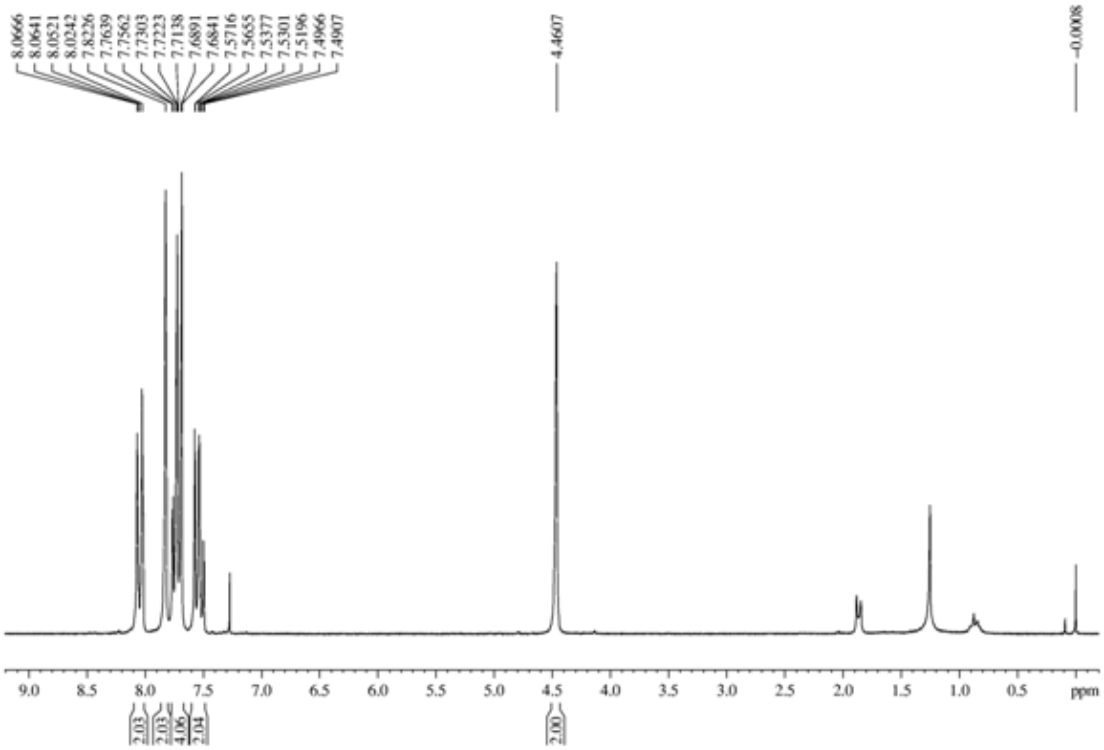
Compound 9, ^{1}H NMR, $CDCl_3$, 300 MHz



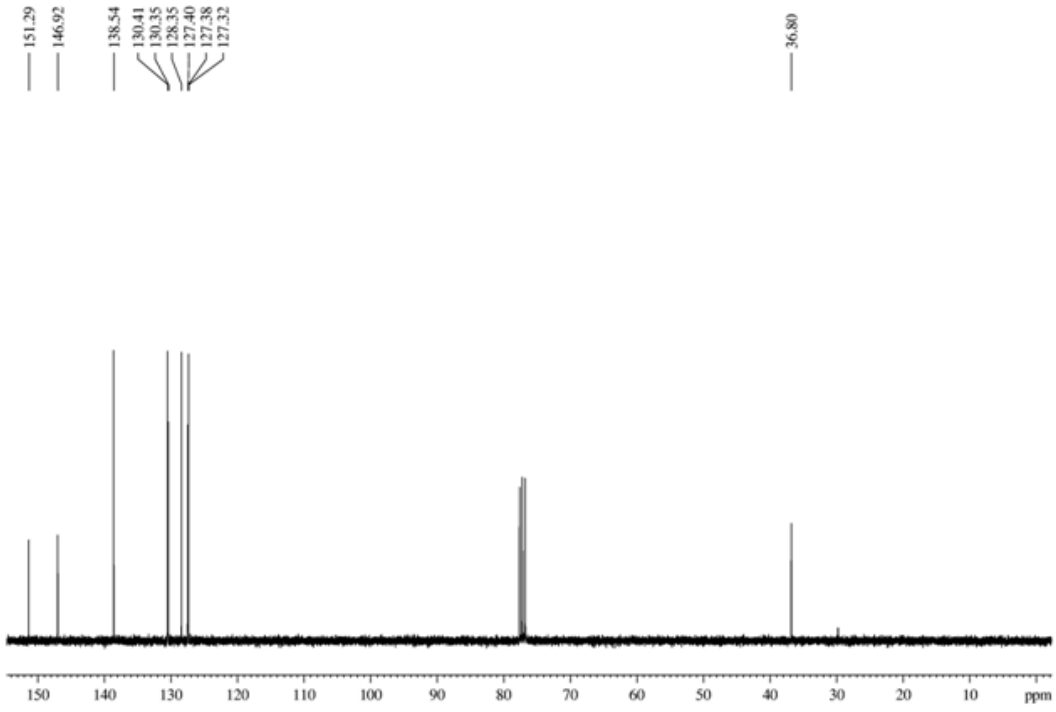
Compound 9, ^{13}C NMR, $CDCl_3$, 75 MHz



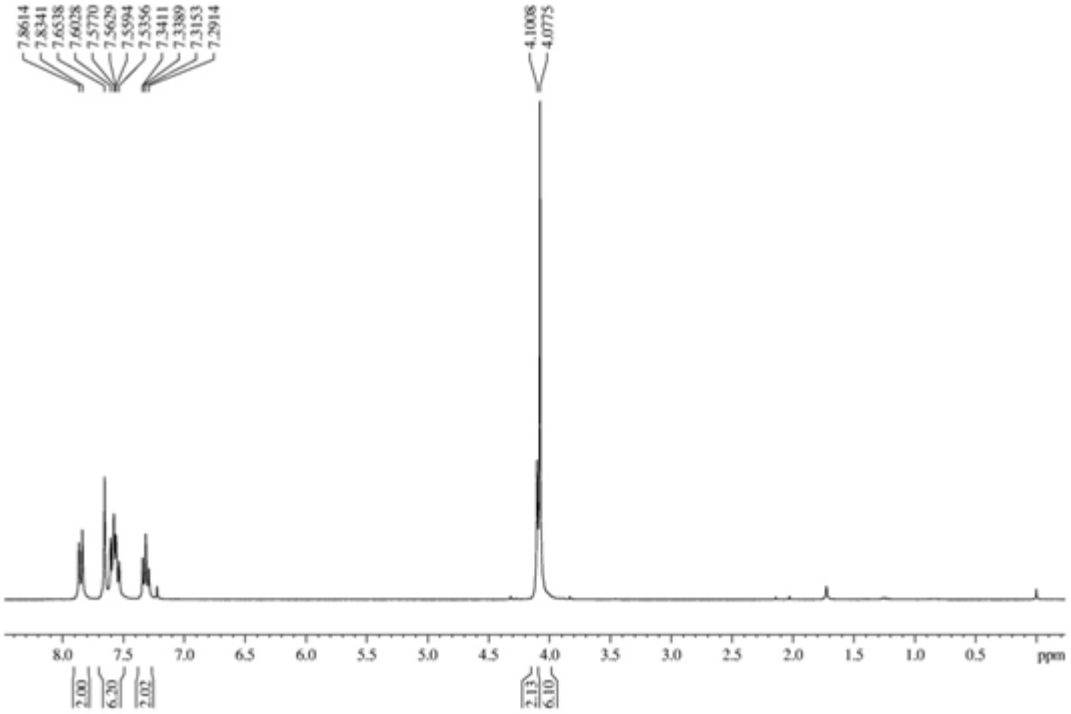
Compound 10, ^{1}H NMR, $CDCl_3$, 200 MHz



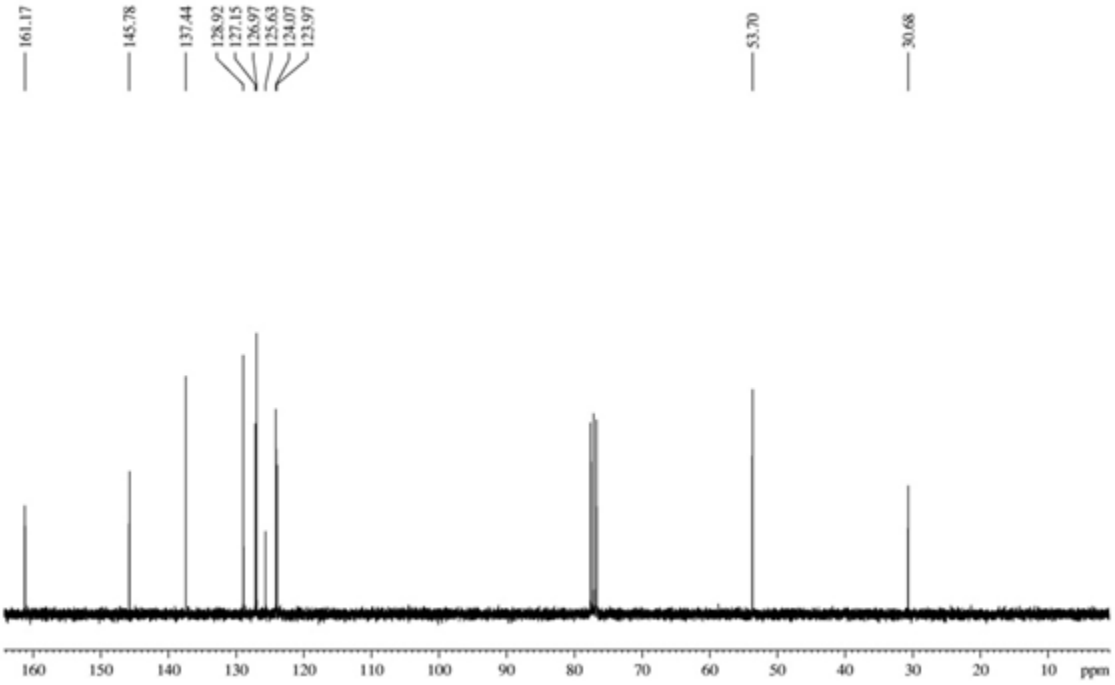
Compound 10, ^{13}C NMR, $CDCl_3$, 75 MHz



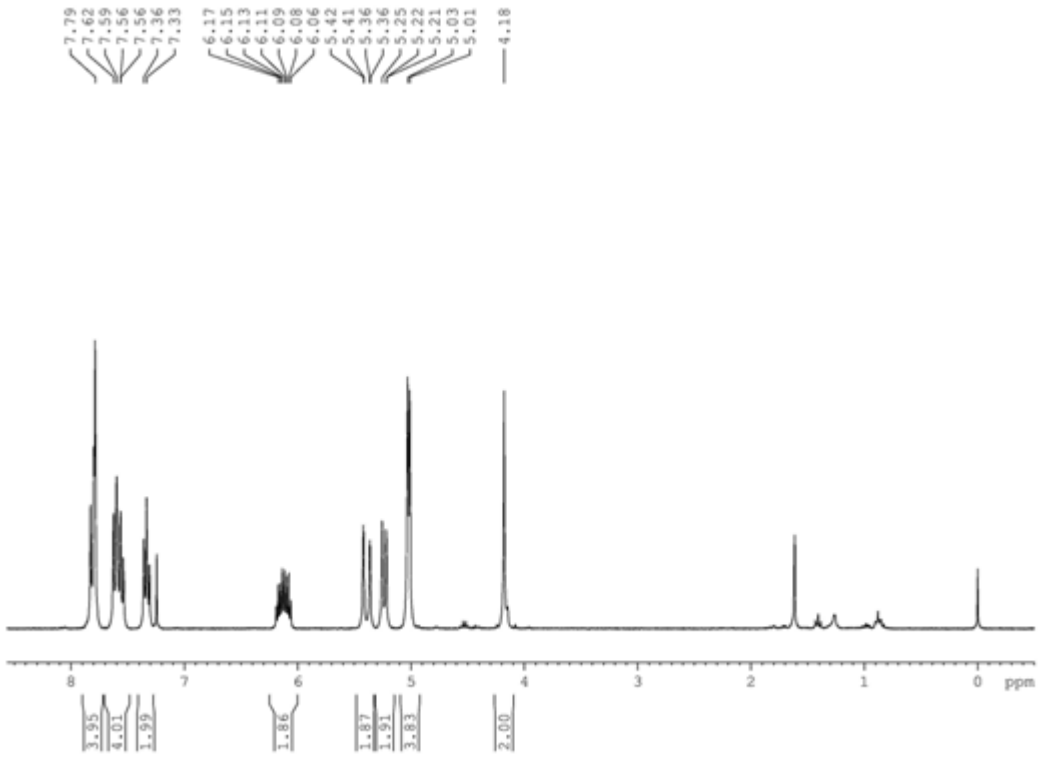
Compound 11a, ^{1}H NMR, $CDCl_3$, 300 MHz



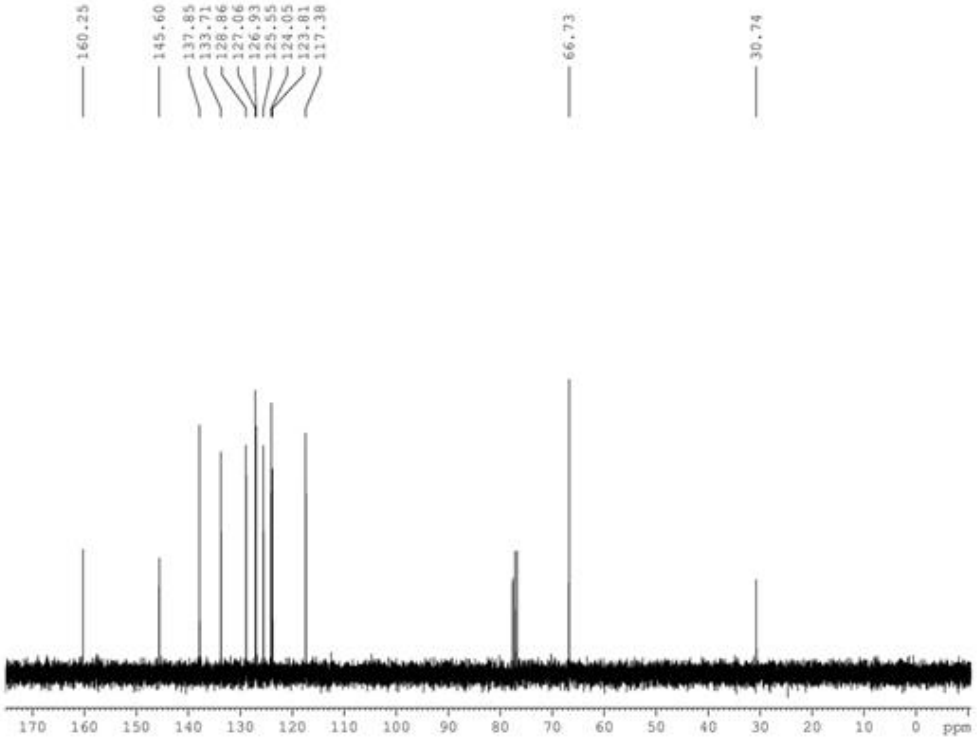
Compound 11a, ^{13}C NMR, $CDCl_3$, 75 MHz



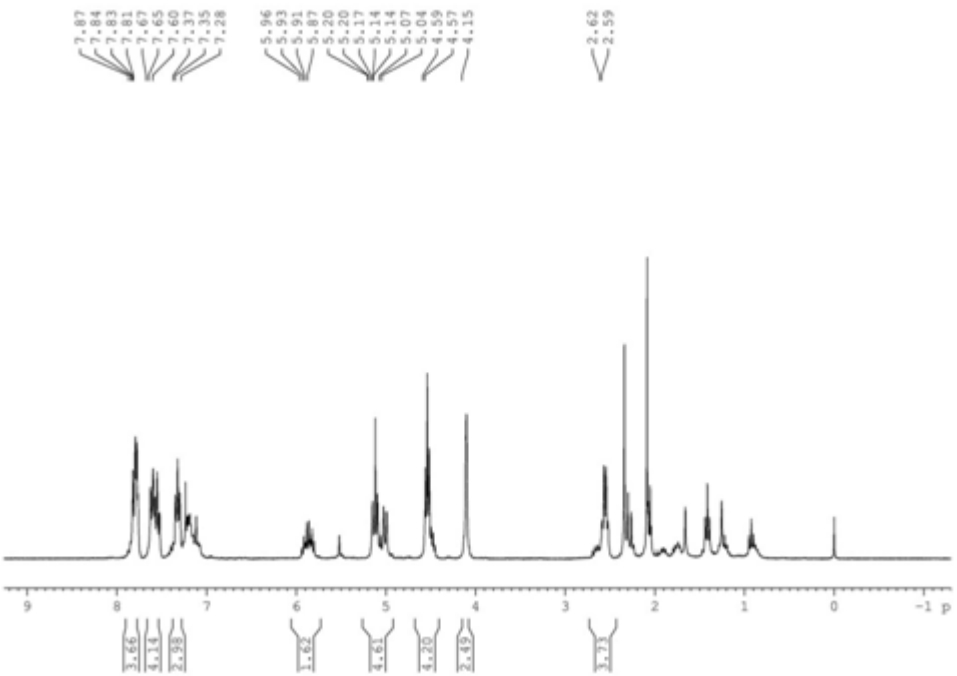
Compound 11b, ^{1}H NMR, $CDCl_3$, 300 MHz



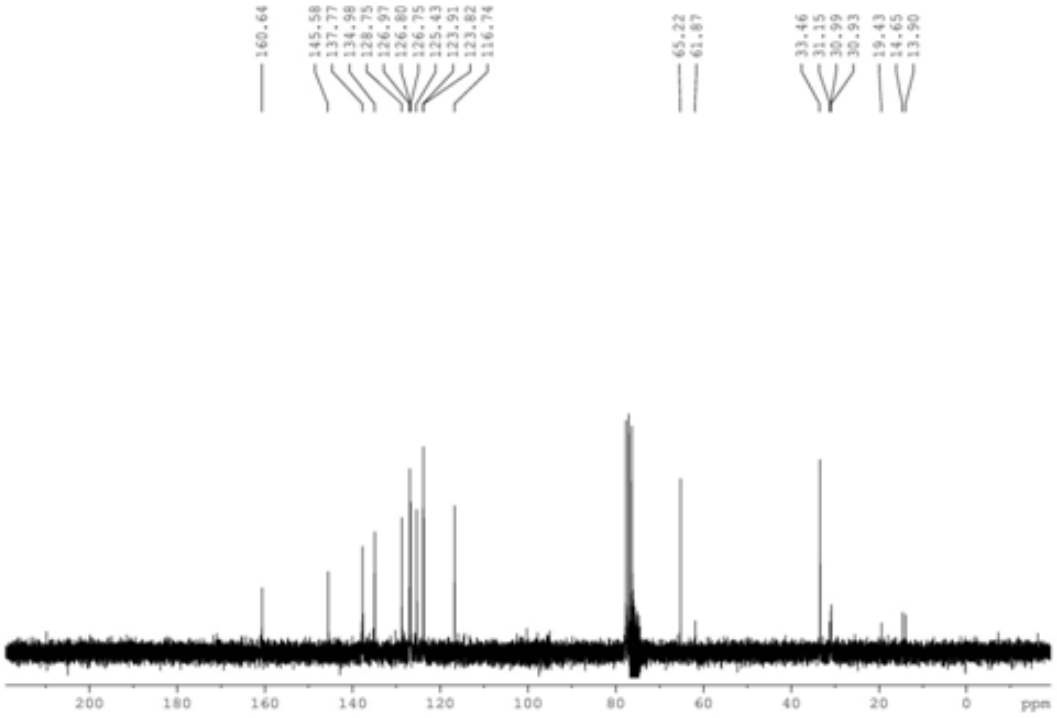
Compound 11b, ^{13}C NMR, $CDCl_3$, 75 MHz



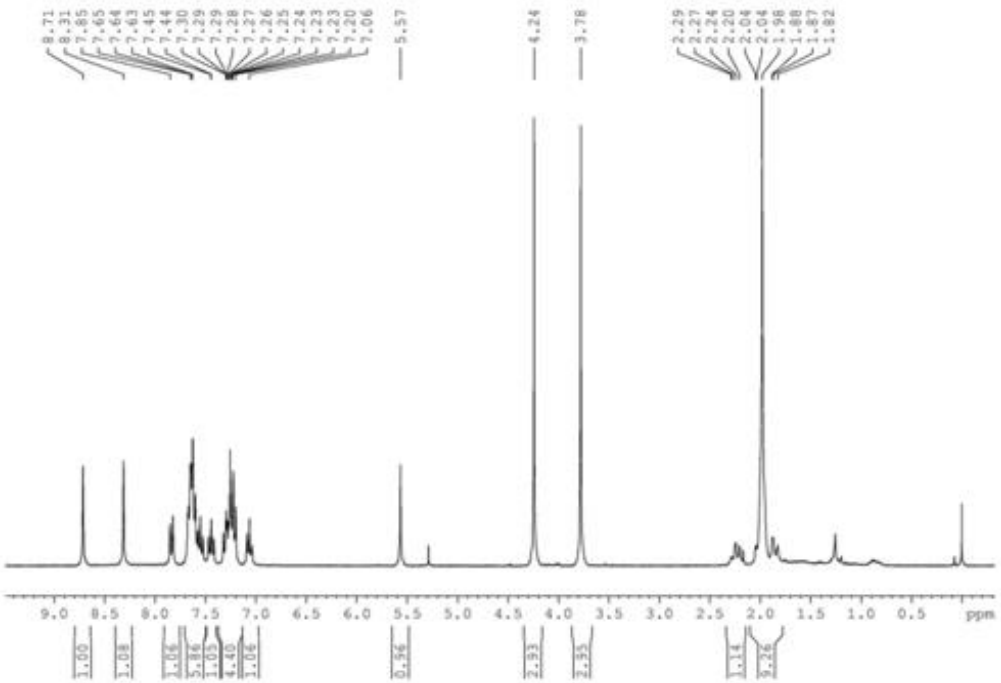
Compound 11c, ^{1}H NMR, $CDCl_3$, 300 MHz



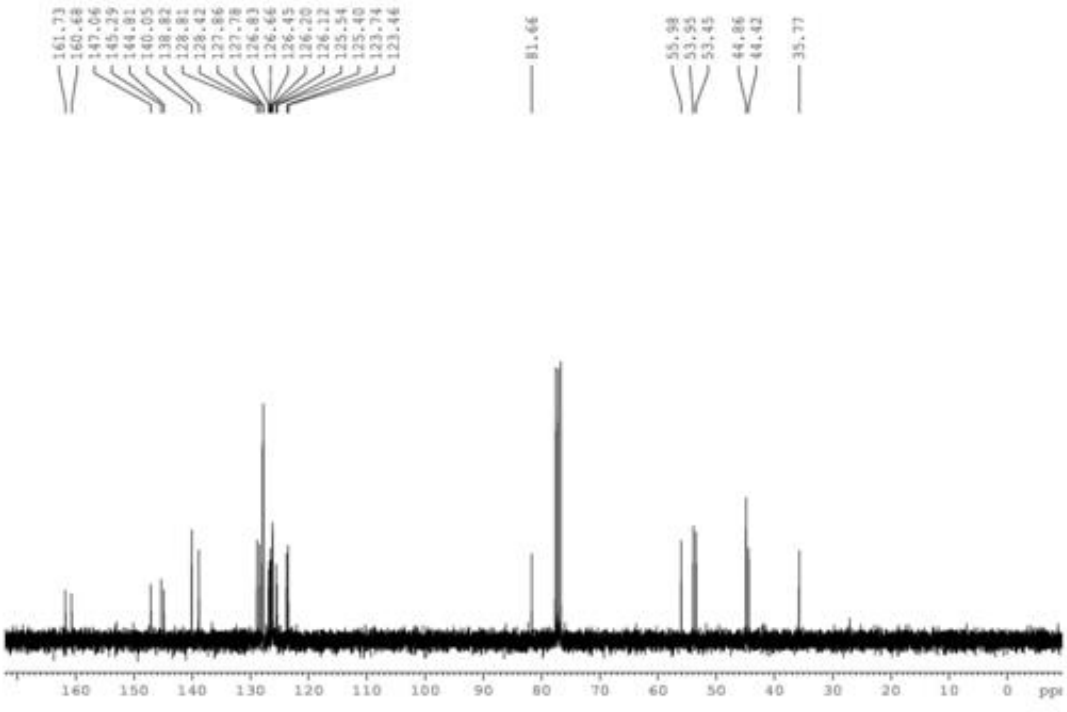
Compound 11c, ^{13}C NMR, $CDCl_3$, 75 MHz



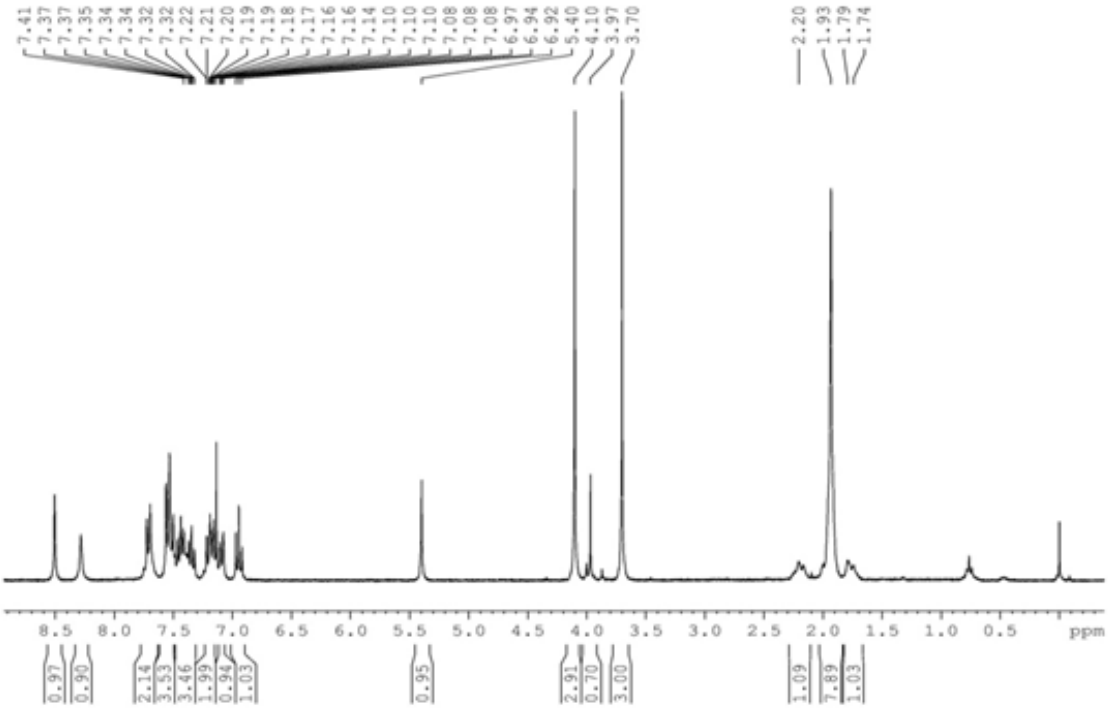
Compound 13, ^{1}H NMR, $CDCl_3$, 300 MHz



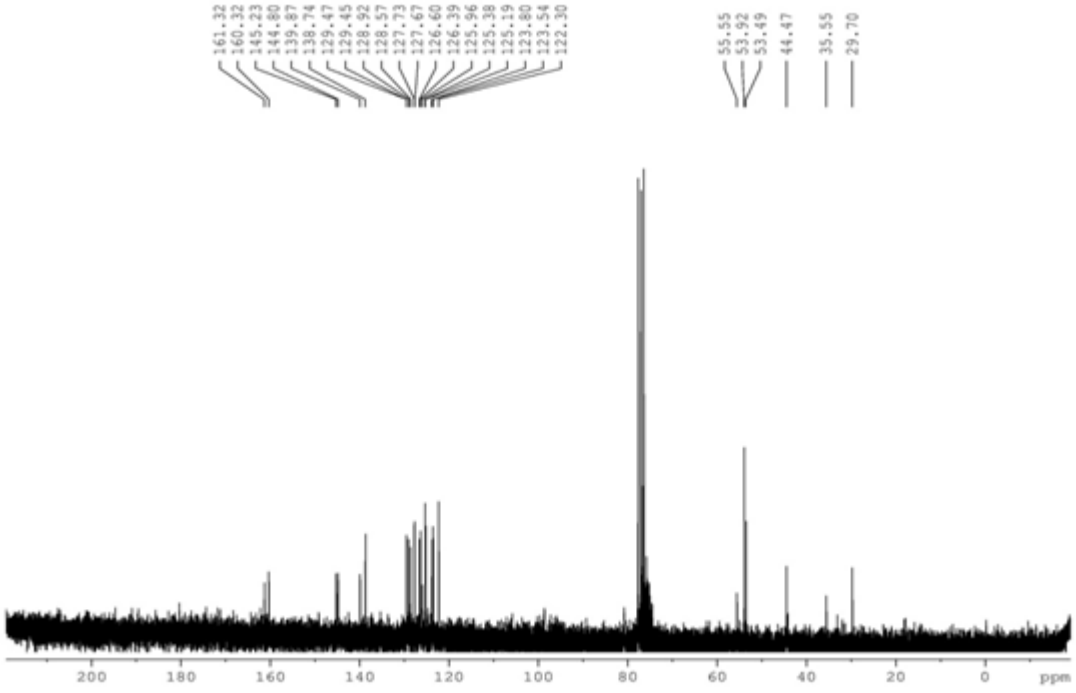
Compound 13, ^{13}C NMR, $CDCl_3$, 75 MHz



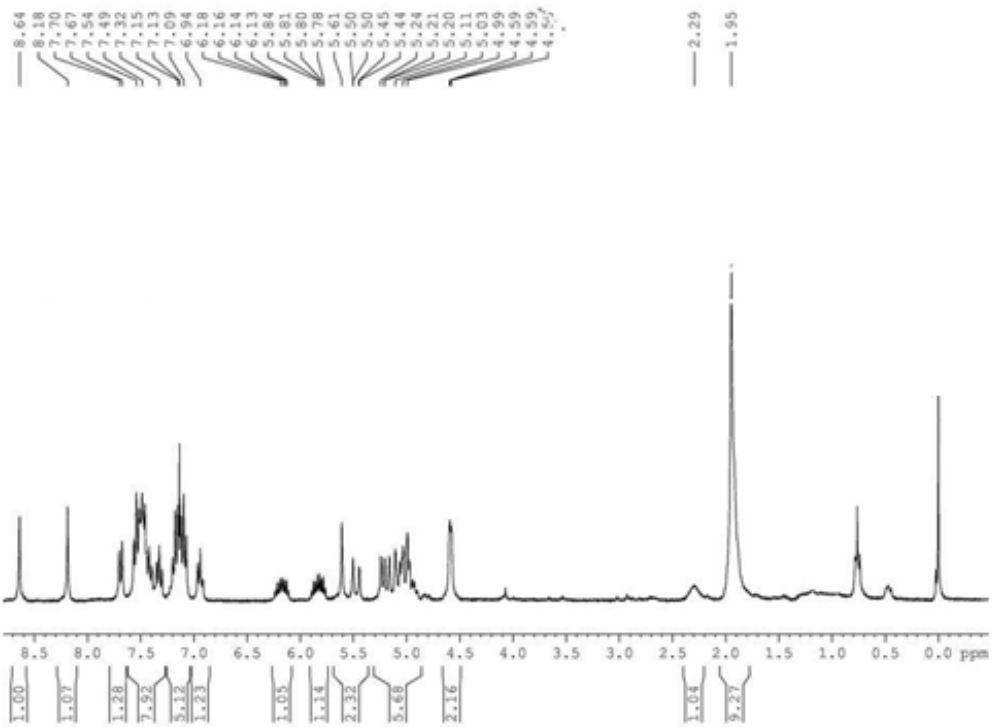
Compound 14, ^{1}H NMR, $CDCl_3$, 300 MHz



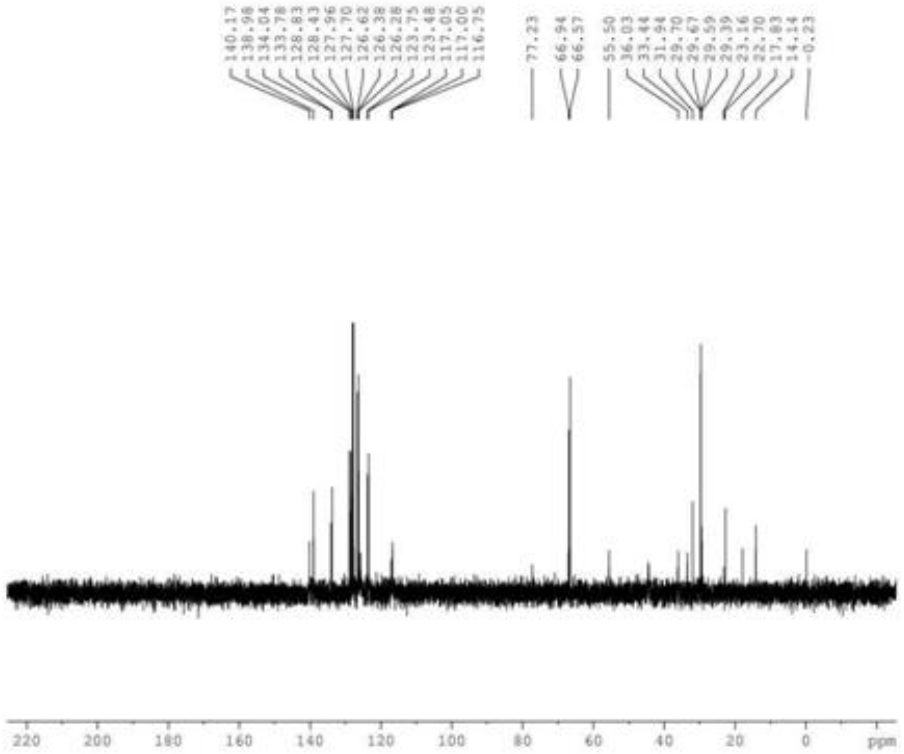
Compound 14, ^{13}C NMR, $CDCl_3$, 75 MHz



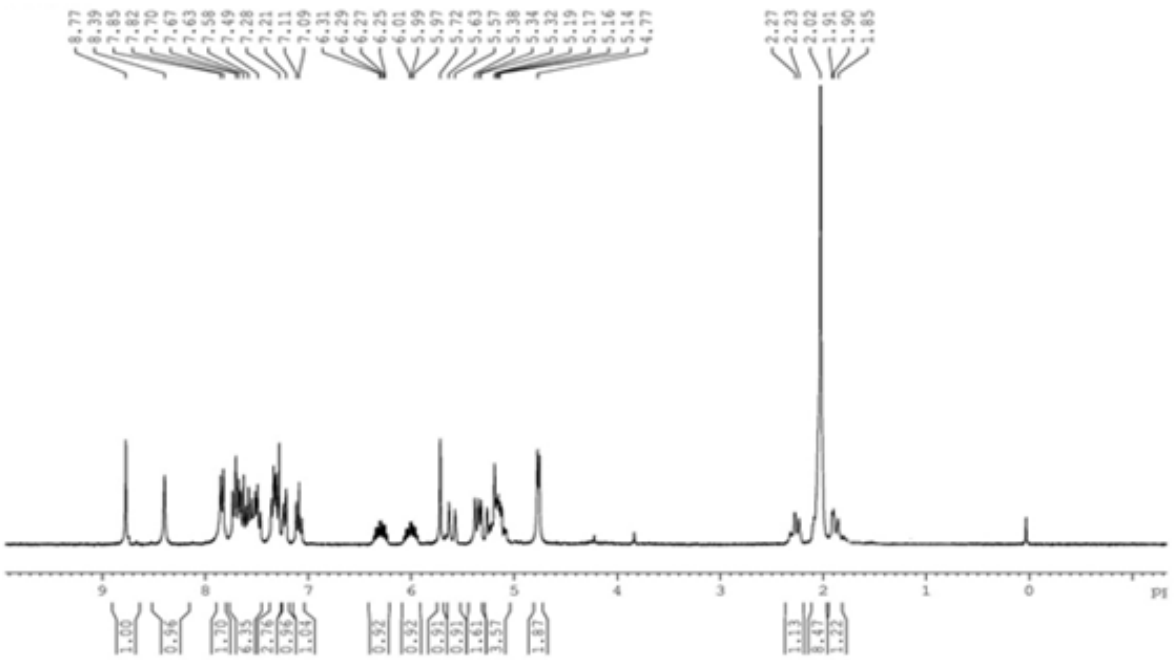
Compound 15, ^{1}H NMR, $CDCl_3$, 300 MHz



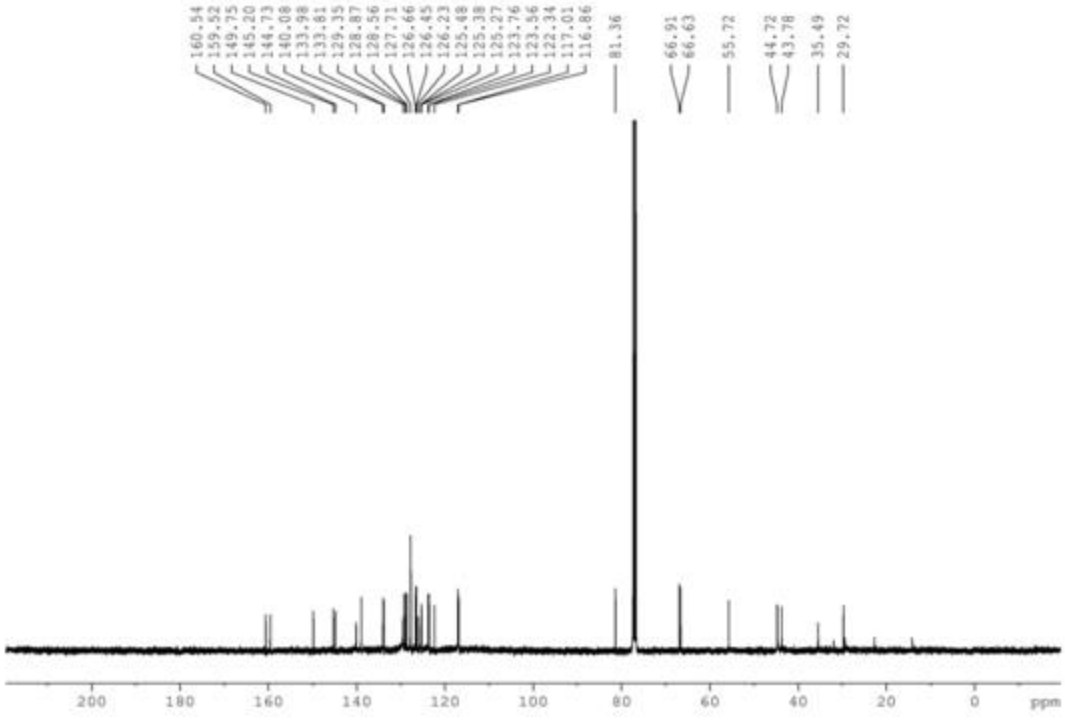
Compound 15, ^{13}C NMR, $CDCl_3$, 100 MHz



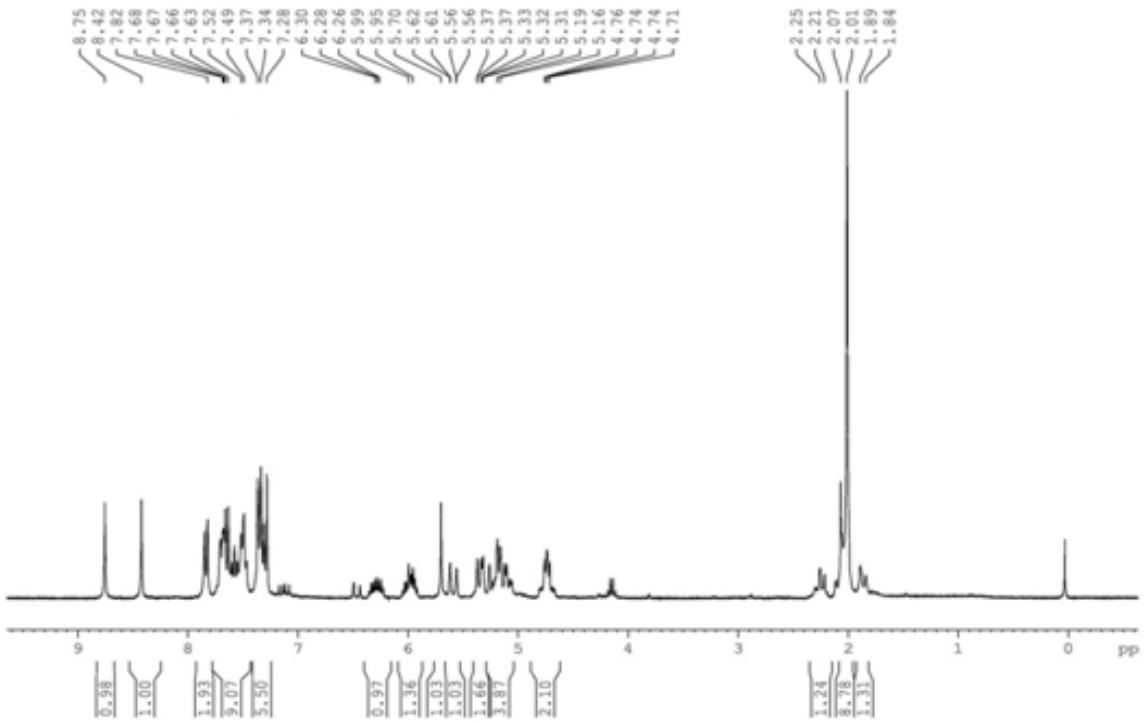
Compound 16, ^{1}H NMR, $CDCl_3$, 300 MHz



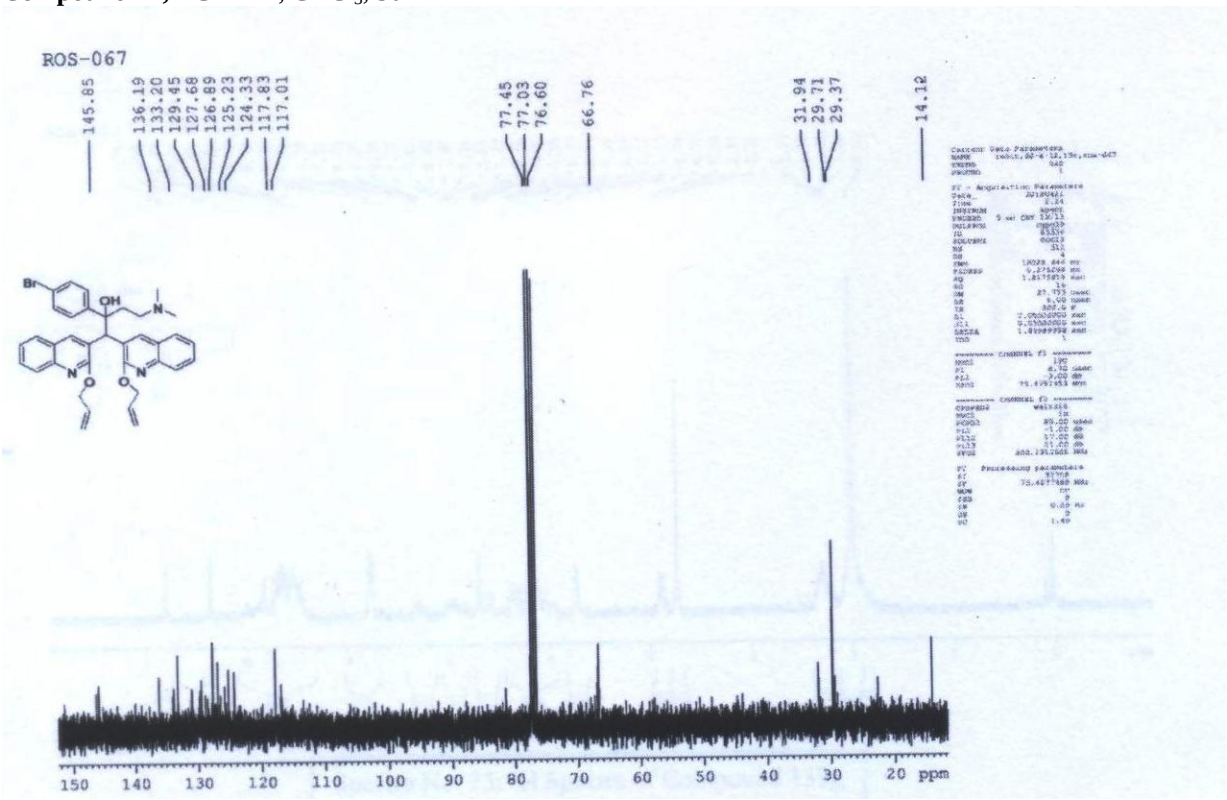
Compound 16, ^{13}C NMR, $CDCl_3$, 75 MHz



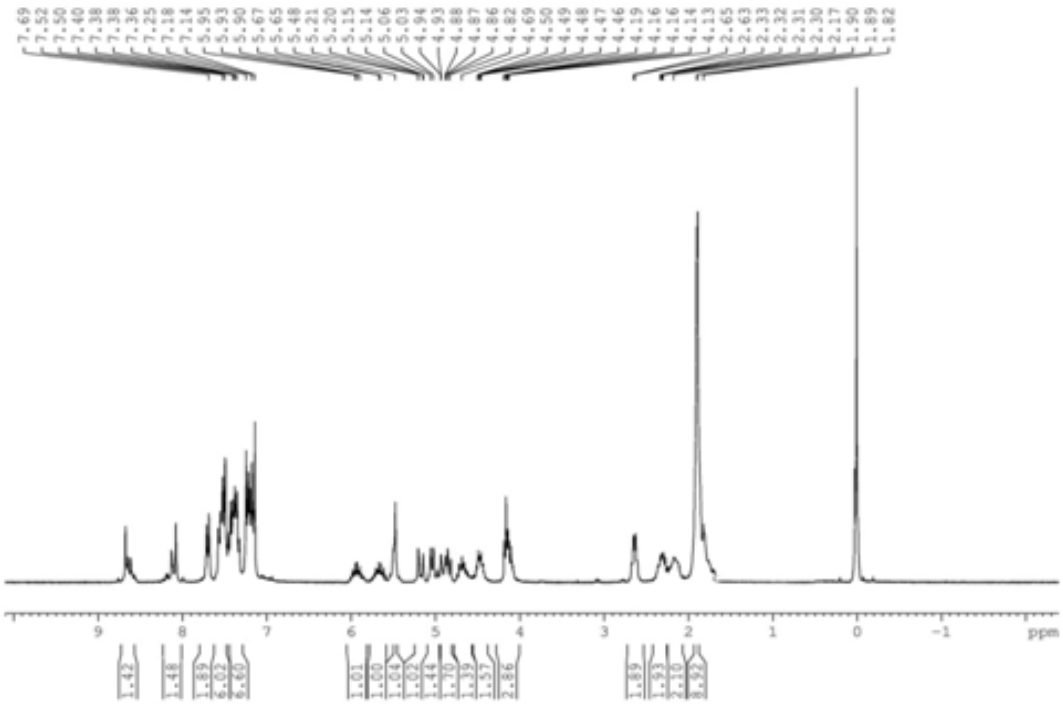
Compound 17, ^{1}H NMR, $CDCl_3$, 300 MHz



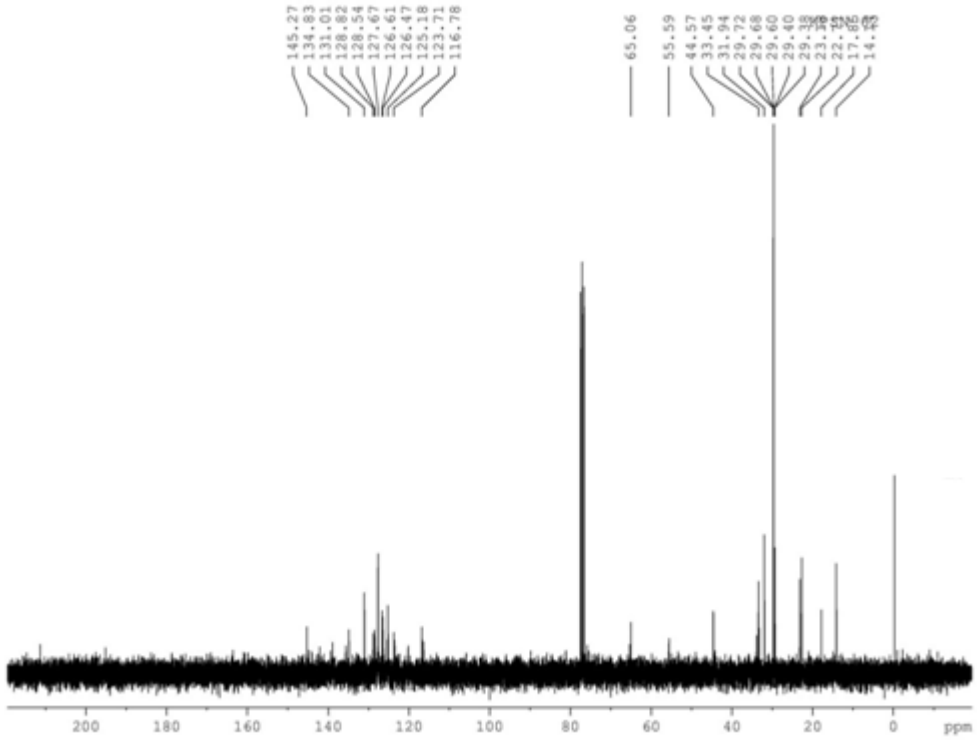
Compound 17, ^{13}C NMR, $CDCl_3$, 50 MHz



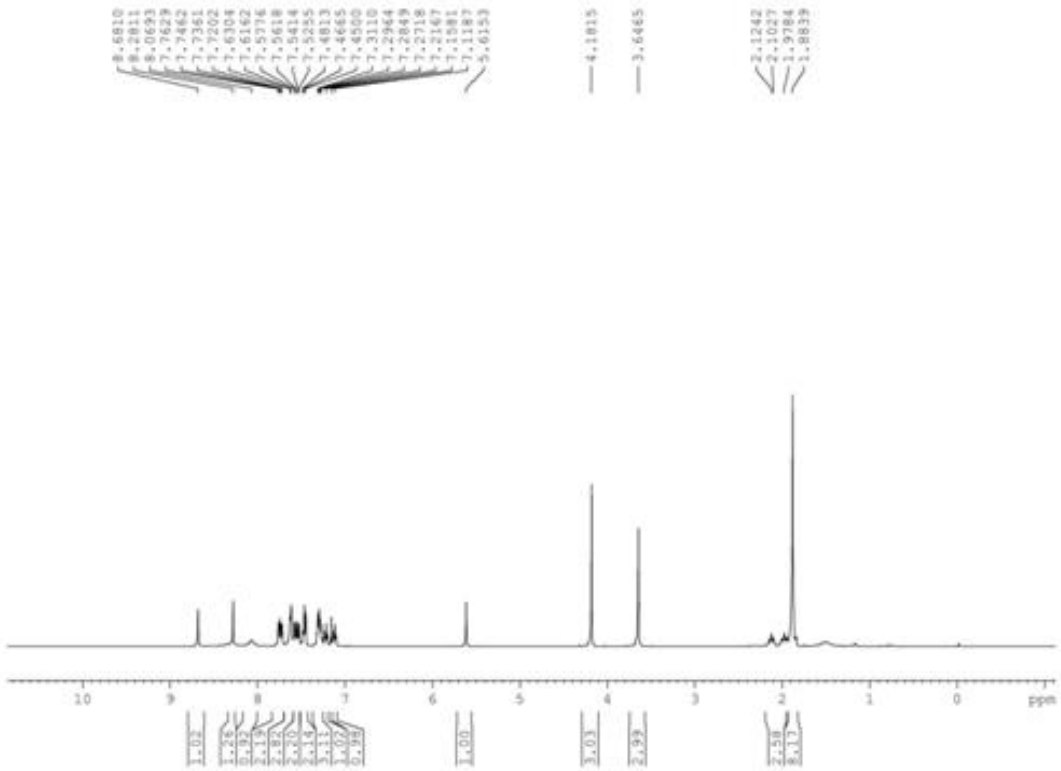
Compound 18, ^{1}H NMR, $CDCl_3$, 300 MHz



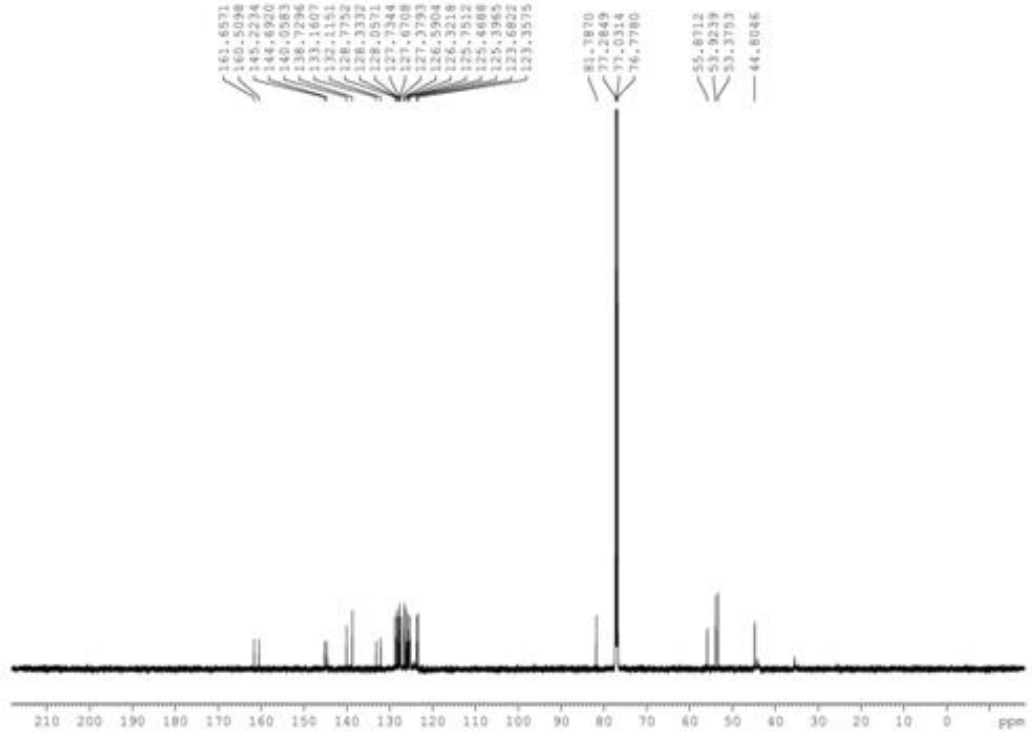
Compound 18, ^{13}C NMR, $CDCl_3$, 75 MHz



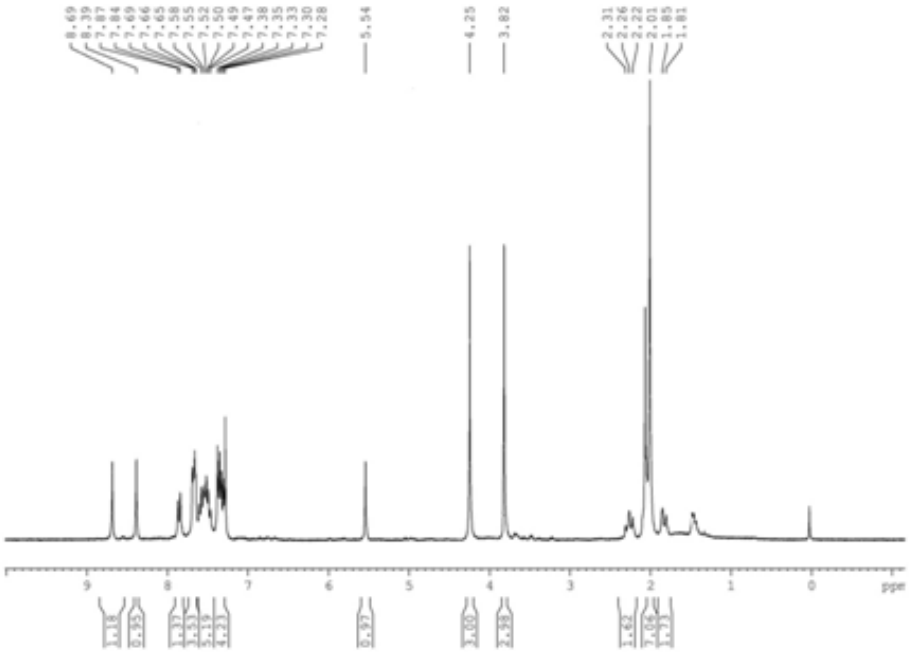
Compound 19, ^{1}H NMR, $CDCl_3$, 500 MHz



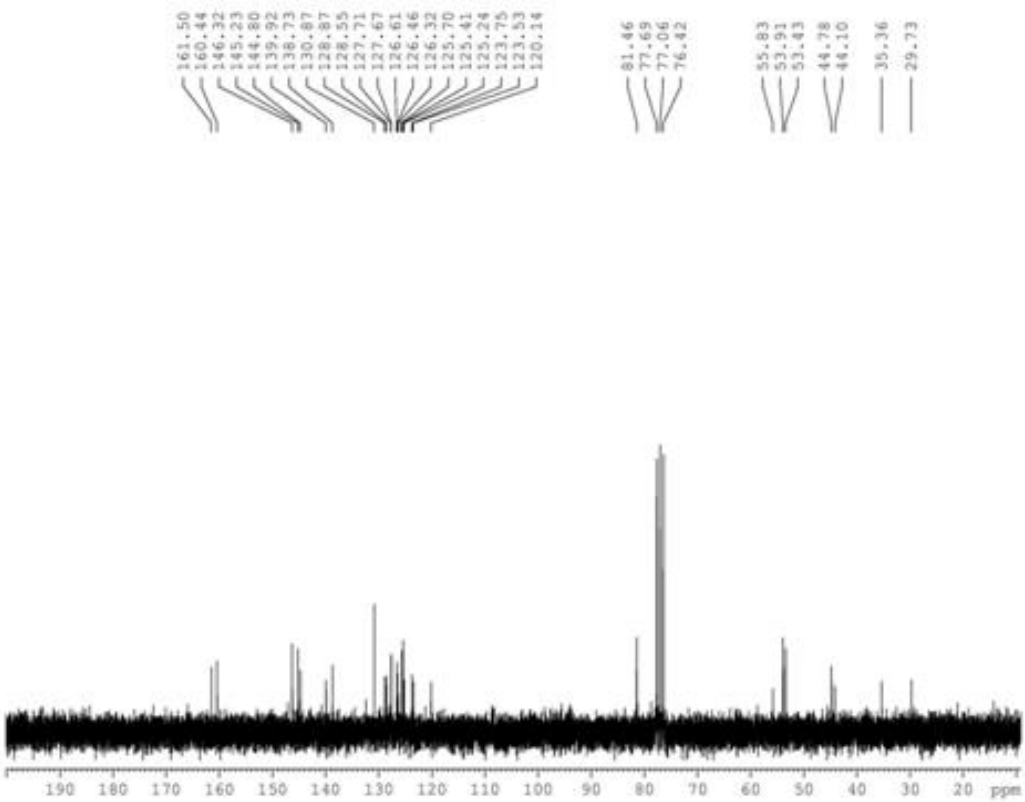
Compound 19, ^{13}C NMR, $CDCl_3$, 125 MHz



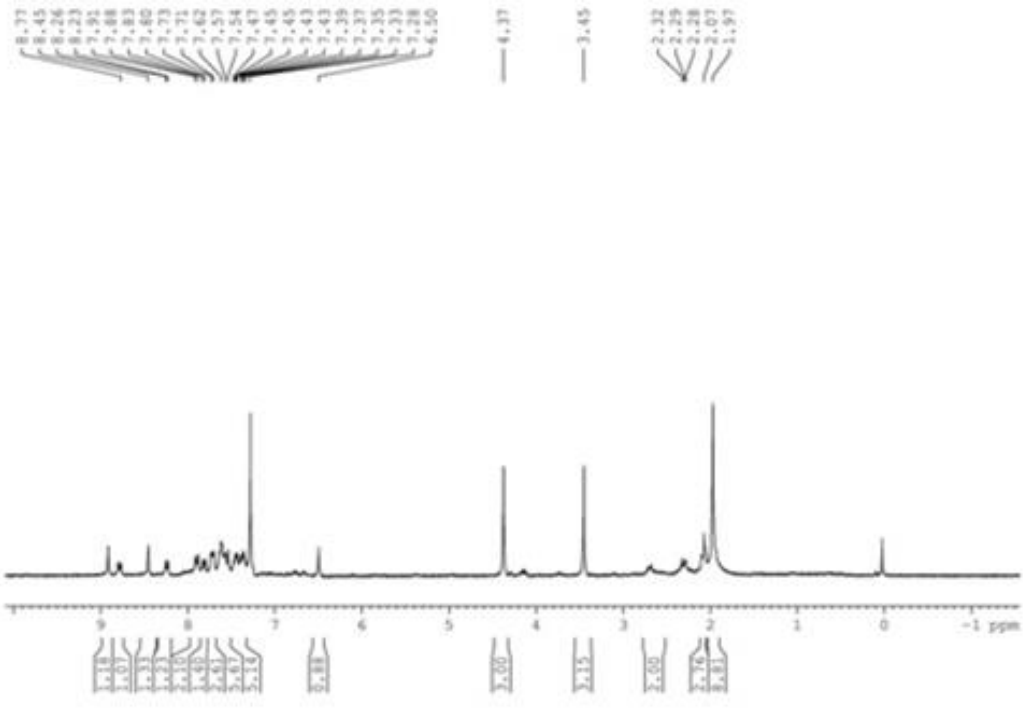
Compound 20, ^{1}H NMR, $CDCl_3$, 300 MHz



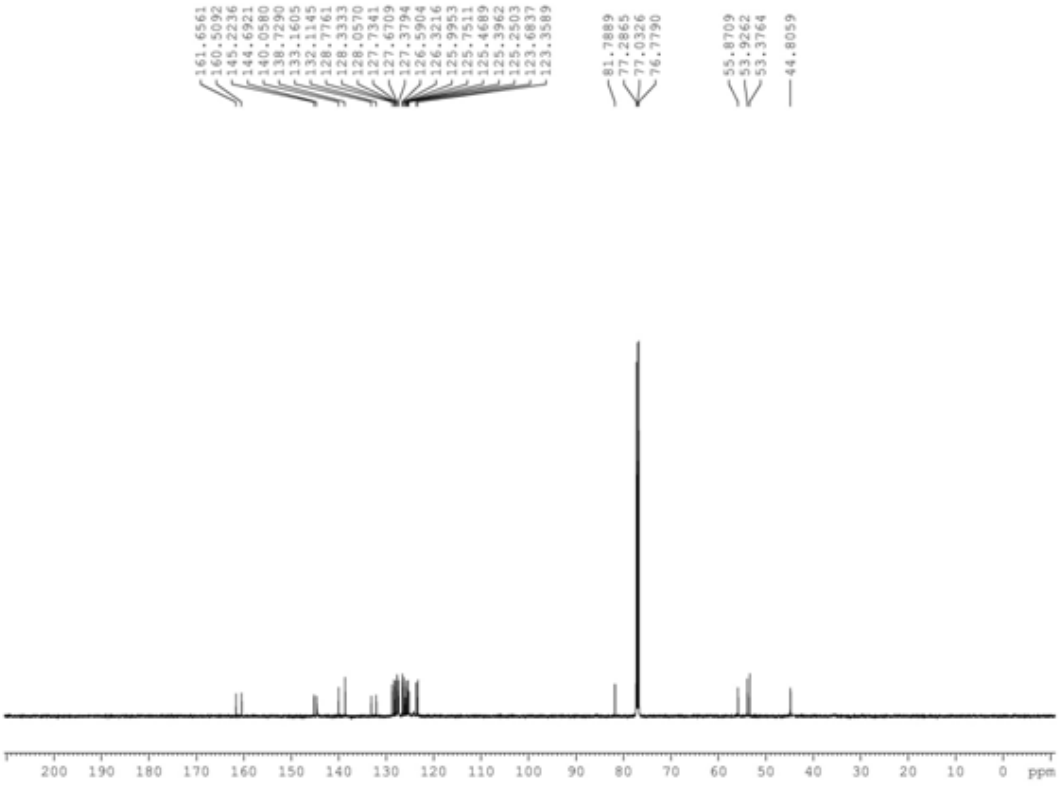
Compound 20, ^{13}C NMR, $CDCl_3$, 50 MHz



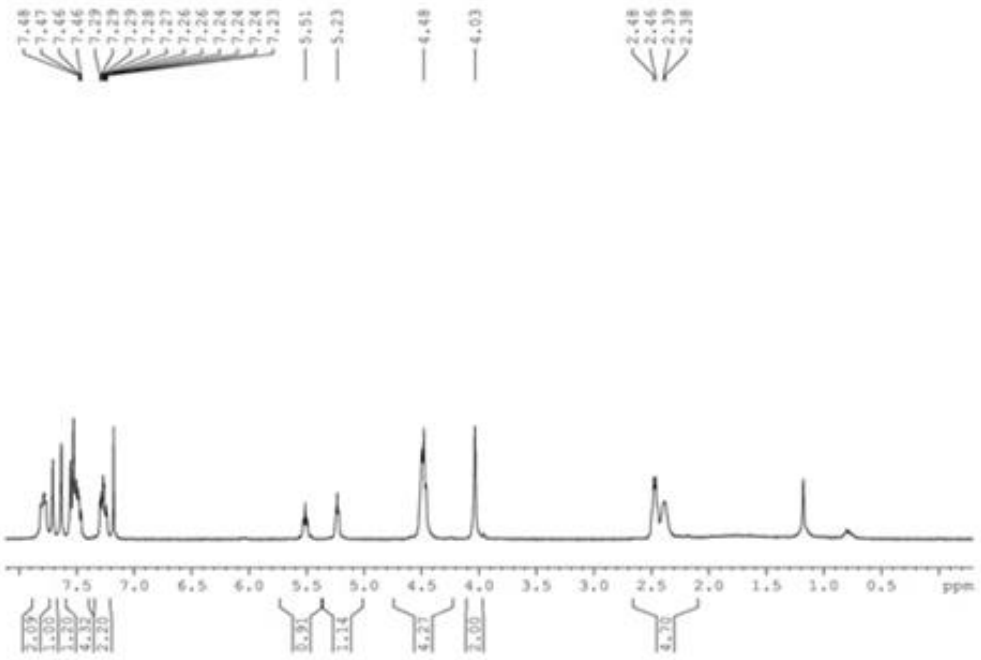
Compound 21, ^{1}H NMR, $CDCl_3$, 300 MHz



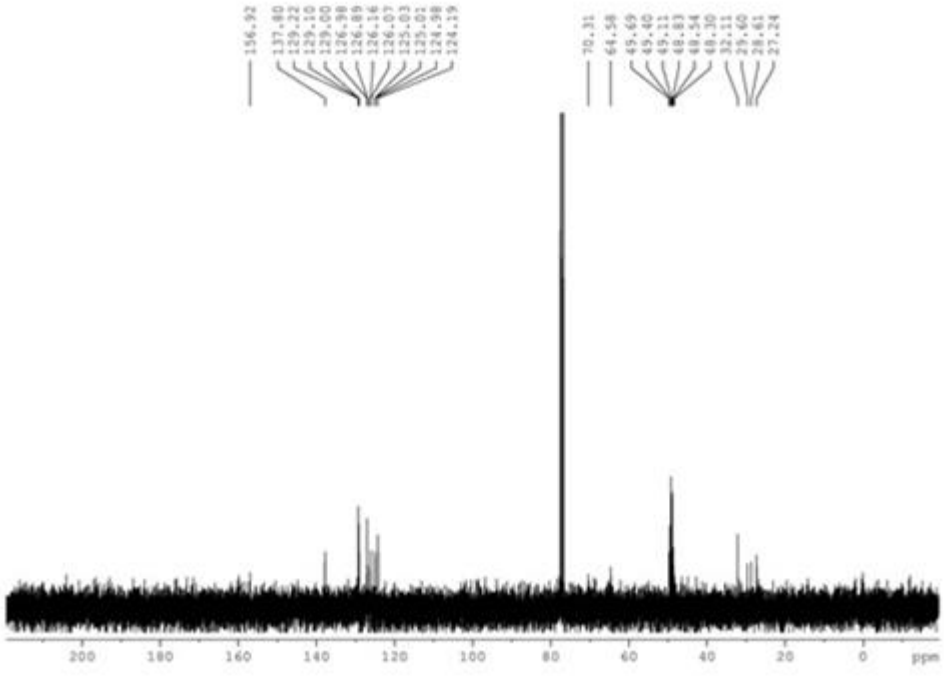
Compound 21, ^{13}C NMR, $CDCl_3$, 125 MHz



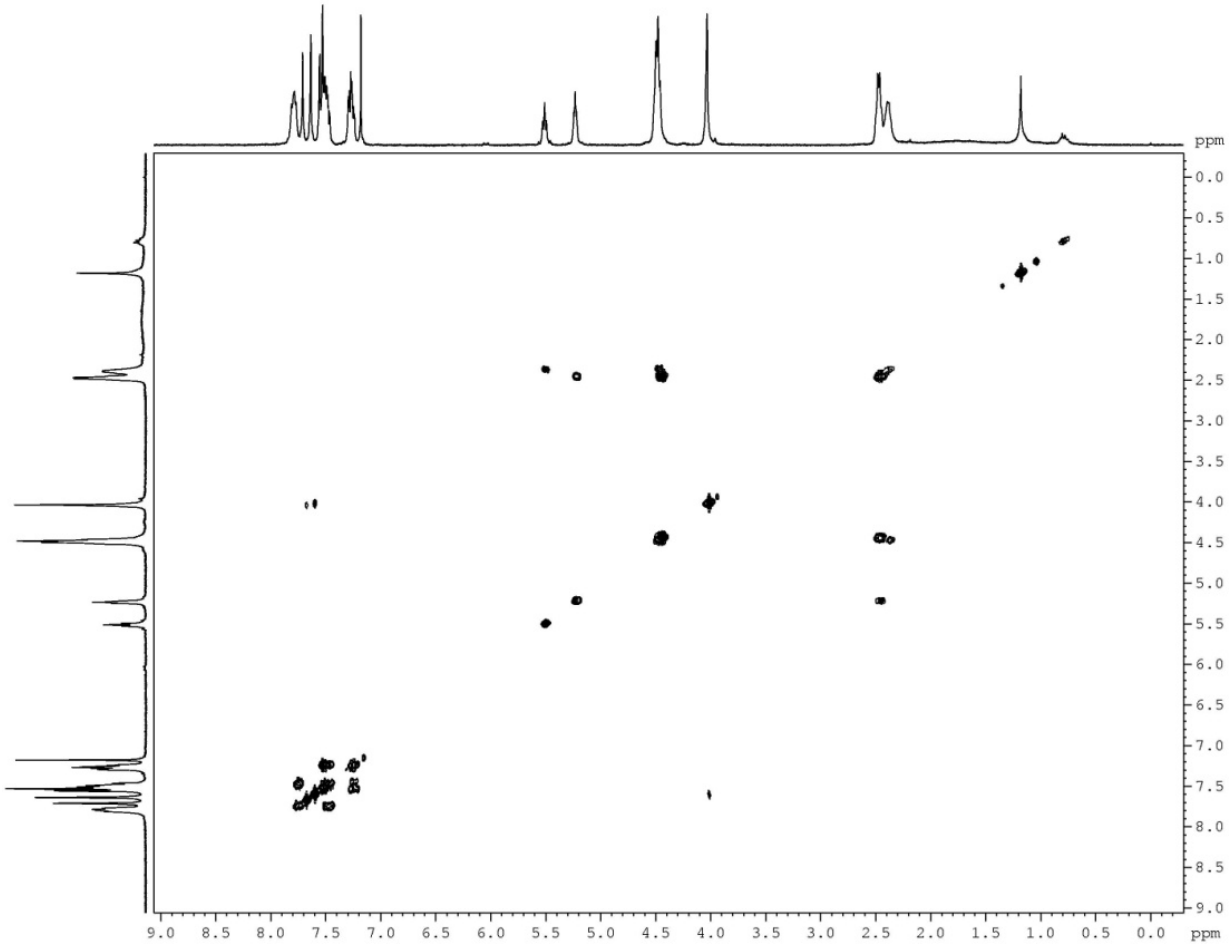
Compound 22, ^{1}H NMR, $CDCl_3$, 300 MHz



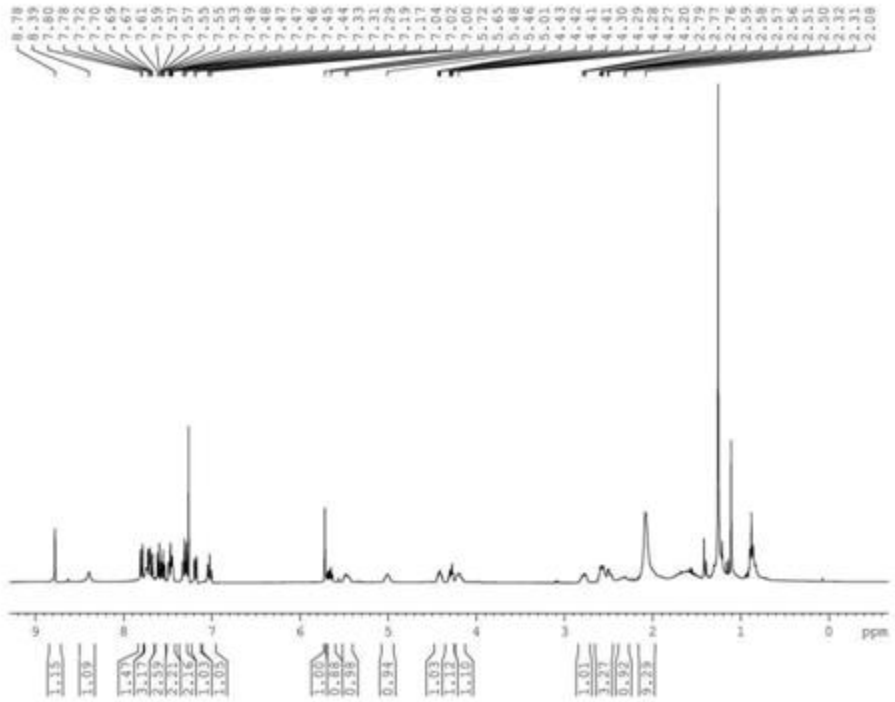
Compound 22, ^{13}C NMR, $CDCl_3$, 75 MHz



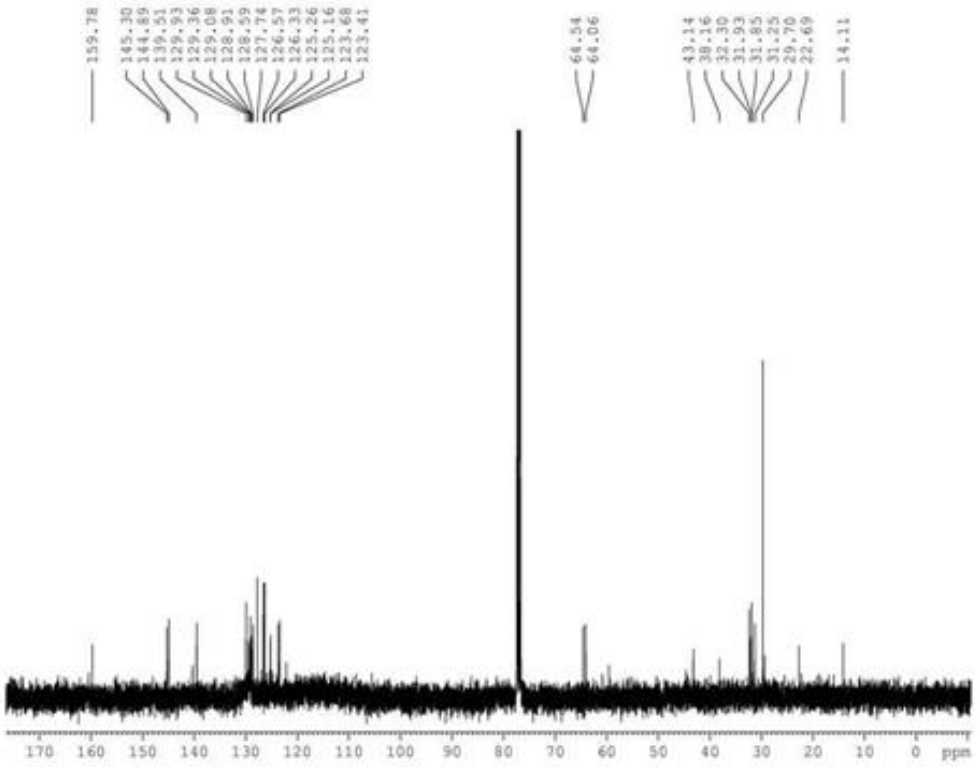
Compound 22, ^{1}H-^{1}H COSY



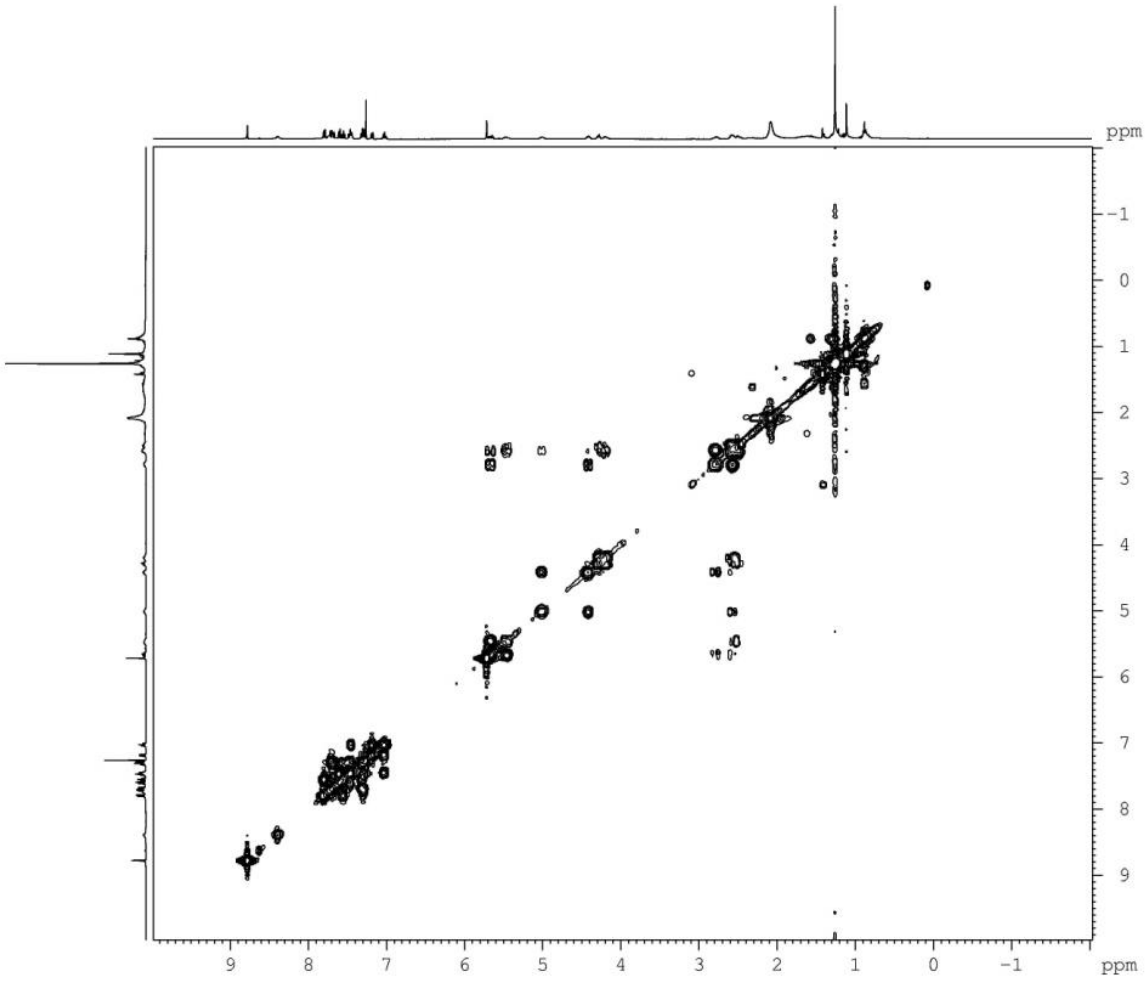
Compound 23, ^{1}H NMR, $CDCl_3$, 300 MHz



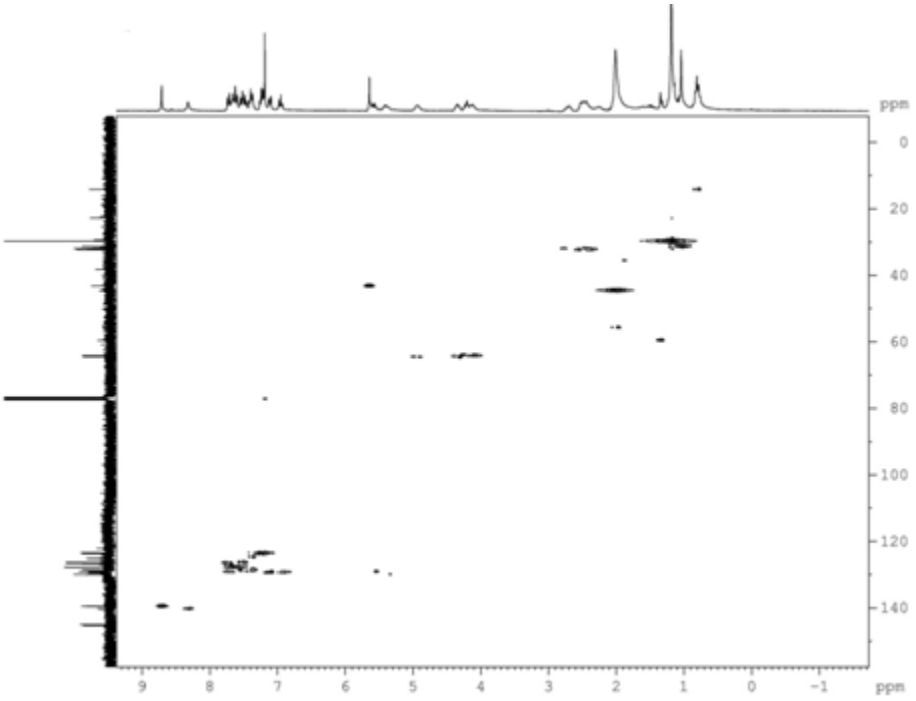
Compound 23, ^{13}C NMR, $CDCl_3$, 75 MHz



Compound 23, ^{1}H-^{1}H COSY



Compound 23, ^{1}H-^{13}C HSQC



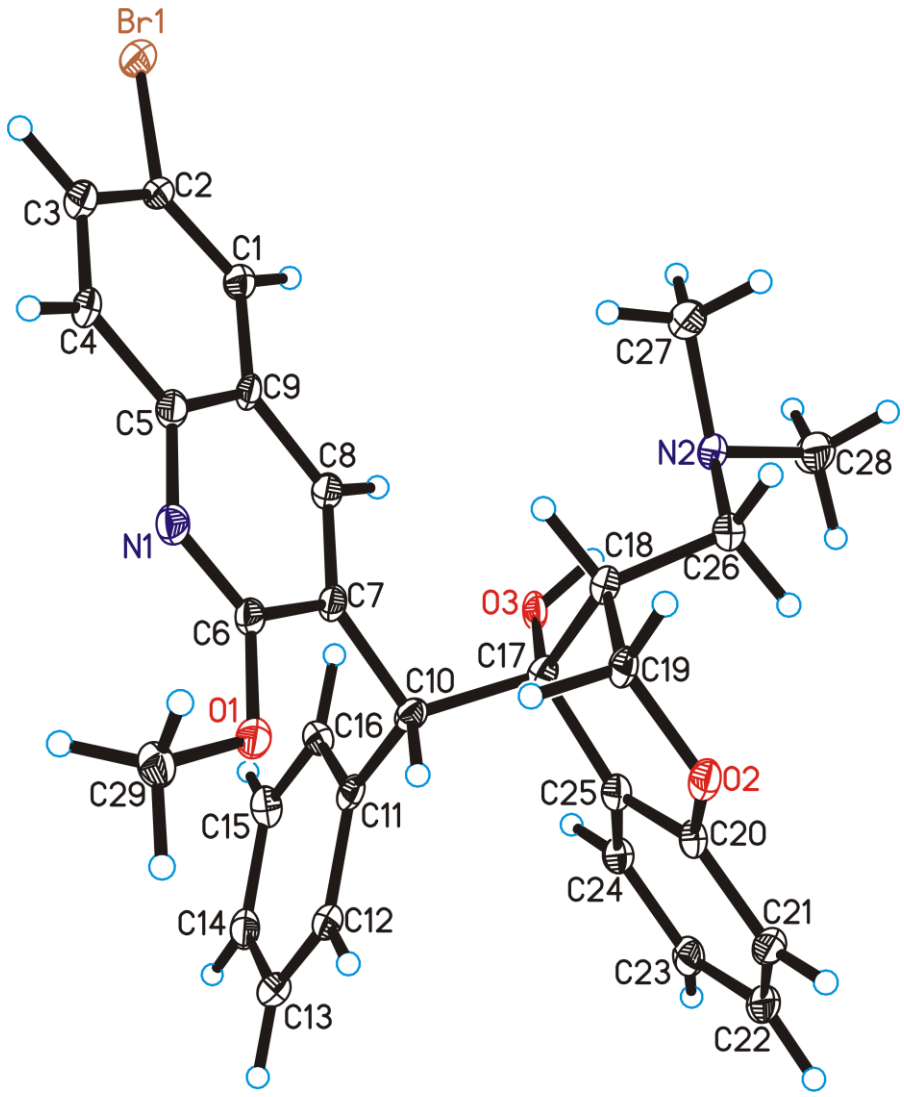


Figure S1. ORTEP diagram drawn with 30% ellipsoid probability for non-H atoms of the crystal structure of compound **5f (minor isomer)** determined at 293 K**.**

The crystal data of **5f (minor isomer)**: $C_{29}H_{29}BrN_2O_3$, M = 533.45, Monoclinic, P2(1)/c , a = 10.747(3)Å **,** b = 10.565(4)Å, c = 23.940(6) Å, β = 111.837(11)°, V = 2523.2(13) Å^3, Z = 4, D_c = 1.404 g cm^{-3}, μ (Mo-Kα) = 1.663 mm^{-1}, F(000) = 1104, rectangular block, 16158 reflections measured (R_{int} = 0.0647), 6176 unique, wR_2 = 0.2093 for all data, conventional $R1$ = 0.0599 for 4218 Fo > 4σ(Fo) and 0.0980 for all 6176 data, S = 1.111 for all data and 319 parameters.Unit cell determination and intensity data collection was performed on a Bruker SMART APEX CCD area-detector at 100(2) K. Structure solutions by direct methods and refinements by full-matrix least-squares methods on F^2. Programs: SMART 32(Bruker), SAINT (Bruker, 2001) ,SHELXTL-NT [Bruker AXS Inc.: Madison, Wisconsin, USA 1997].

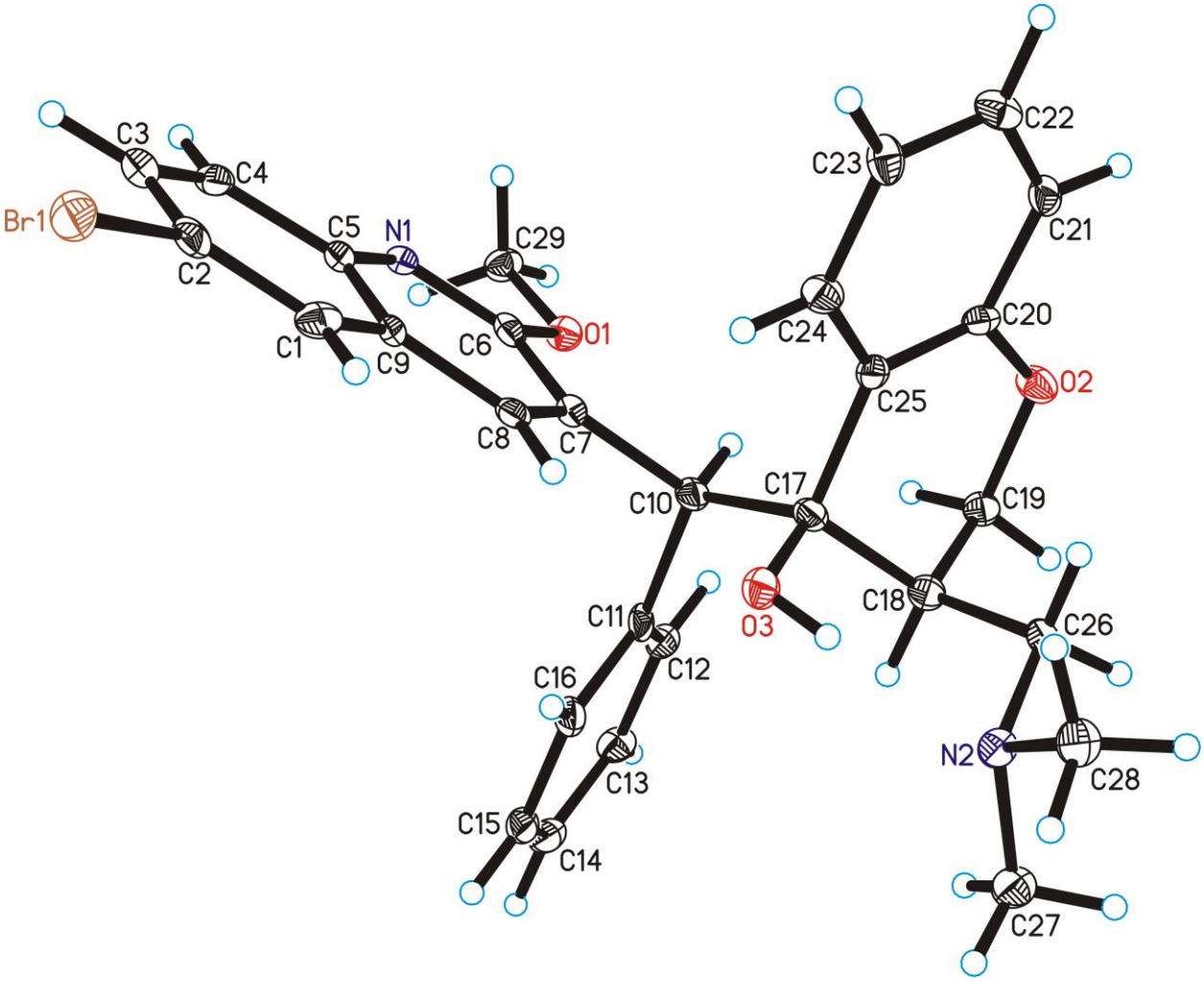


Figure S2. ORTEP diagram drawn with 30% ellipsoid probability for non-H atoms of the crystal structure of compound **5f (major isomer)** determined at 293 K**.**

The crystal data of **5f (major isomer)**: $C_{29}H_{29}BrN_2O_3$, M = 533.45, Monoclinic, P2(1)/, a = 13.077(4)Å **,** b = 12.197(4)Å, c = 16.687(4) Å, β = 114.690(18)°, V = 2418.3(12) Å^3, Z = 4, D_c = 1.465 g cm^{-3}, μ (Mo-Kα) = 1.735 mm^{-1}, F(000) = 1104, rectangular block, 15729 reflections measured (R_{int} = 0.1007), 5932 unique, wR_2 = 0.2595 for all data, conventional $R1$ = 0.0698 for 3738 Fo > 4σ(Fo) and 0.1117 for all 5932 data, S = 1.128 for all data and 320 parameters.Unit cell determination and intensity data collection was performed on a Bruker SMART APEX CCD area-detector at 100(2) K. Structure solutions by direct methods and refinements by full-matrix least-squares methods on F^2. Programs: SMART 32(Bruker), SAINT (Bruker, 2001) ,SHELXTL-NT [Bruker AXS Inc.: Madison, Wisconsin, USA 1997].

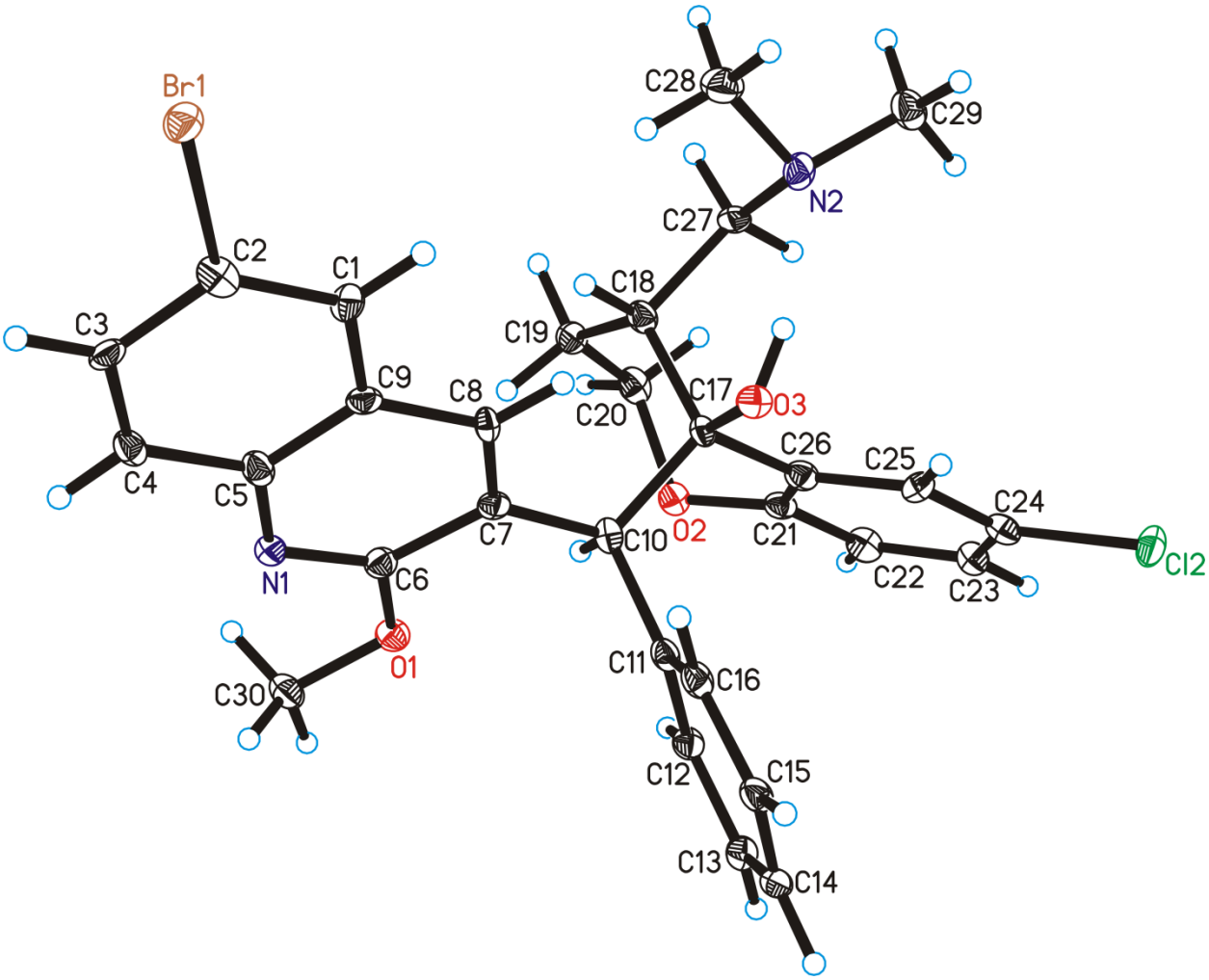


Figure S3. ORTEP diagram drawn with 30% ellipsoid probability for non-H atoms of the crystal structure of compound **5c (minor isomer)** determined at 293 K**.**

The crystal data of **5c (minor isomer)**: $C_{30}H_{30}BrClN_2O_3$, M = 581.92, triclinic, P -1 , a = 7.799(3) Å , b = 13.077(5) Å, c = 14.674(6) Å, α = 102.019(6)°, β = 102.584(7)°, γ = 105.196(6)°, V = 1352.6(9) Å^3, Z = 2, D_c = 1.429 g cm^{-3}, μ (Mo-Kα) = 1.653 mm^{-1}, F(000) = 600, rectangular block, 8938 reflections measured (R_{int} = 0.0337), 6414 unique, wR_2 = 0.2572 for all data, conventional $R1$ = 0.0695 for 4796 Fo > 4σ(Fo) and 0.1044 for all 6414 data, S = 1.103 for all data and 339 parameters.Unit cell determination and intensity data collection was performed on a Bruker SMART APEX CCD area-detector at 100(2) K. Structure solutions by direct methods and refinements by full-matrix least-squares methods on F^2. Programs: SMART 32(Bruker), SAINT (Bruker, 2001) ,SHELXTL-NT [Bruker AXS Inc.: Madison, Wisconsin, USA 1997].

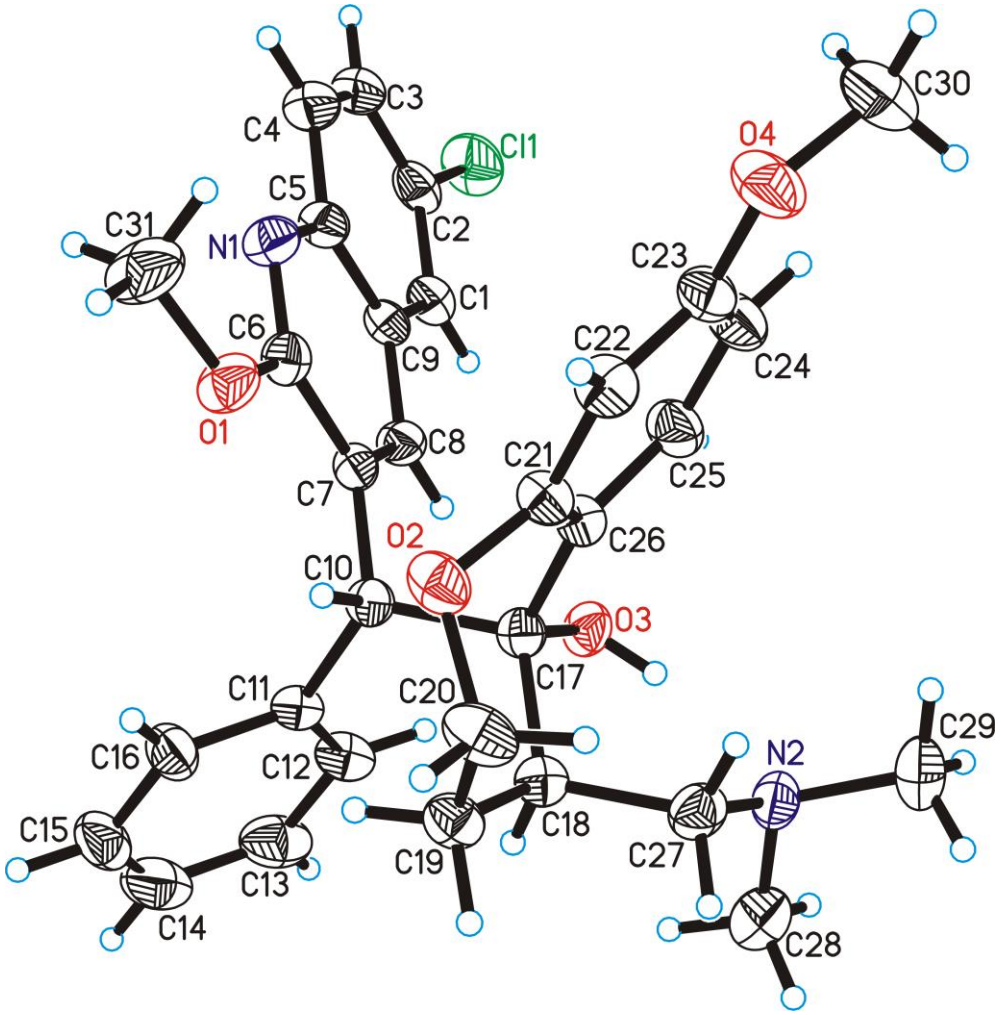


Figure S4. ORTEP diagram drawn with 30% ellipsoid probability for non-H atoms of the crystal structure of compound **S1** determined at 293 K**.**

The crystal data of compound **S1**: $C_{31}H_{33}ClN_2O_4$, M = 533.04, triclinic, P -1, a = 10.198(2) Å **,** b = 12.405(2) Å, c = 12.423(2) Å, α = 79.72(2) °, β = 70.82(2)°, γ = 72.77(2)°, V = 1412.0(4) Å^3, Z = 2, D_c = 1.254 gcm^{-3}, μ (Mo-Kα) = 0.173 mm^{-1}, F(000) = 564, rectangular block, 3023 reflections measured (R_{int} = 0.0173), 2114 unique, wR_2 = 0.1131 for all data, conventional R = 0.0383 [$(\Delta/\sigma)_{max}$ = 000)] on F-values of 1623 reflections with $I>2\sigma(I)$, S = 1.083 for all data and 348 parameters. Unit cell determination and intensity data collection (2θ= 50°) was performed on a Bruker P4 diffractometer at 293(2) K. Structure solutions by direct methods and refinements by full-matrix least-squares methods on F^2. Programs: XSCANS [Siemens Analytical X-ray Instrument Inc.: Madison, Wisconsin, USA 1996], SHELXTL-NT [Bruker AXS Inc.: Madison, Wisconsin, USA 1997].

References

(1) van Eis, M. J.; de Kanter, F. J. J.; de Wolf, W. H.; Bickelhaupt, F. *J Am Chem Soc* **1998**, *120*, 3371.

(2) Gawad, N. M. A.; Hassan, G. S.; Georgey, H. H.; El-Zorba, H. Y.*Med Chem Res* **2012**, *21*, 747.

(3) Khanna, J. M.; Tandon, V. K.; Kar, K.; Sur, R. N. *Indian J Chem B* **1985**, *24*, 71.

(4) Bhandari, K.; Srivastava, S.; Shankar, G.; Nath, C. *Bioorg Med Chem* **2006**, *14*, 2535.

(5) Ohkata, K.; Akiyama, M.; Wada, K.; Sakaue, S.; Toda, Y.; Hanafusa, T. *J Org Chem* **1984**, *49*, 2517.

(6) Rodrigues Jr., M. T.; Gomes, J. C.; Smith, J.; Coelho, F. *Tetrahedron Lett* **2010**, *51*, 4988.