Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information For:

Synthesis of chiral bis-oxazines: A preliminary assessment of helical conformational framework

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Contents:

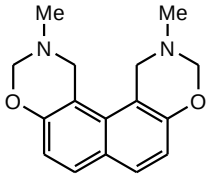
Experimental Section:

Reagents were purchased from Sigma-Aldrich Chemicals Limited, SD Fine, Sisco, Qualigens, Avara Chemicals Limited etc. Thin Layer Chromatography was performed on Merck 60 F254 Aluminium coated plates. The spots were visualized under UV light or with iodine vapour. All the compounds were purified by column chromatography using Sisco Research Laboratory silica gel (60-120 mesh). All reactions were carried out under an inert atmosphere (nitrogen) unless other conditions are specified. NMR Spectra were recorded on 400 MHz Bruker Avance 400 Spectrometer (400 MHz for ^{1}H-NMR & 100 MHz for ^{13}C-NMR) with $CDCl_3$ as solvent and TMS as internal standard. Signal multiplicity is denoted as singlet (s), doublet (d), doublet of doublets (dd), triplet (t), triplet of doublets (td), quartet (q), quartet of triplets (qt), septet (sept) and multiplet (m). Mass spectra were recorded on Thermo-Fischer DSQ II GCMS instrument. IR Spectra were recorded on a Perkin-Elmer FTIR RXI spectrometer as KBr pallets. Melting points were recorded in Thiele's tube using paraffin oil and are uncorrected. For the HPLC analysis chiral Diacel OD-H column was used on Waters 996 photodiode Array Detector and Waters 2690 Separation Module HPLC system.

General Procedure for the synthesis of 1,3-Bis-oxazines:

A solution of amine (2.5 eq.) and 37% formaldehyde solution (4.5 eq.) was stirred for 30 min. at room temperature under N_2 atmosphere. Then 2,7-dihydroxynaphthalene (1.0 g, 6.24 mmol, 1.0 eq.) was added and the reaction mixture was stirred for 24 h at 80 ^{o}C. After the completion of reaction absolute ethanol was added to precipitate out the crude product, which was filtered and recrystallized from ethylacetate:petroleum ether afford white solid. Yield = (~20-60%).

2,11-Dimethyl-2,3,11,12-tetrahydro-1H,10H,-4,9-dioxa-2,11-diaza-benzo[c]phenanthrene [9a]:



9a

Yield = 20%.

M.p. 180-182 ^{o}C. (Lit.[1] M.p. 171-173 °C).

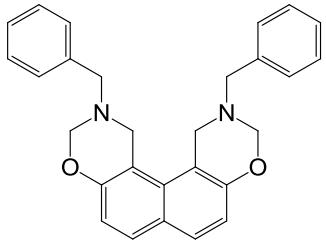
IR (KBr): 3058, 2986, 2952, 2886, 1605, 1510, 1468, 1445, 1417, 1390, 1358, 1304, 1239, 1193, 1158, 1117, 1055, 1026, 998, 973, 917, 864, 824, 768, 753, 681 cm.$^{-1}$

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 4.84 (s, 4H), 4.39 (s, 4H), 2.54 (s, 6H).

MS (EI): *m/z*, (%) 271 (11), 270 (64), 228 (08), 227 (48), 226 (09), 213 (14), 212 (99), 198 (07), 186 (12), 185 (17), 184 (100), 156 (27), 155 (14), 129 (06), 128 (40), 127 (15), 126 (06), 101 (06).

Anal. Calcd. for $C_{16}H_{18}N_2O_2$: C 71.09, H 6.71, N 10.36. Found: C 71.11, H 6.36, N 10.38.

***2,11-Dibenzyl-2,3,11,12-tetrahydro-1H,10H,-4,9-dioxa-2,11-diaza-benzo[c]phenanthrene [9b]*:**



9b

Yield = 54%.

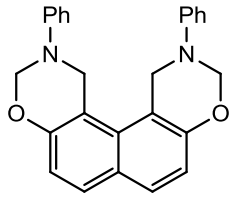
M.p. 123-124 °C. (Lit.[1] 123-124 °C).

IR (KBr): 3415, 3062, 3030, 2995, 2947, 2892, 2859, 1945, 1882, 1776, 1609, 1516, 1495, 1443, 1387, 1350, 1301, 1266, 1223, 1187, 1136, 1090, 1079, 1014, 985, 934, 872, 833, 777, 734, 696 cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.8 Hz, 2H), 7.27-7.17 (m, 10H), 6.81 (d, *J* = 8.76 Hz, 2H), 4.78 (s, 4H), 4.24 (s, 4H), 3.73 (s, 4H).

Anal. Calcd. for $C_{28}H_{26}N_2O_2$: C 79.59, H 6.20, N 6.63. Found: C 79.58, H 6.00, N 6.13.

***2,11-Diphenyl-2,3,11,12-tetrahydro-1H,10H,-4,9-dioxa-2,11-diaza-benzo[c]phenanthrene [9c]*:**



9c

Yield = 22%.

M.p. 164-165 °C. (Lit.[2] M.p. 138 °C).

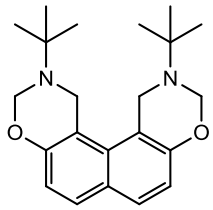
IR (KBr): 3433, 3011, 2900, 1924, 1607, 1494, 1447, 1363, 1222, 1165, 1111, 1029, 994, 940, 832, 786, 757, 693 $cm.^{-1}$

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.5 Hz, 2H), 7.25-7.22 (m, 4H), 7.08-7.07 (m, 4H), 6.95-6.92 (m, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 5.43 (s, 4H), 5.14 (s, 4H).

MS (EI): *m/z*, (%) 395 (05), 394 (08), 290 (06), 289 (27), 288 (10), 274 (17), 186 (12), 185 (09), 184 (42), 156 (08), 155 (05), 128 (18), 127 (07), 106 (29), 105 (100), 104 (57), 102 (06), 178 (06), 77 (32).

Anal. Calcd. for $C_{28}H_{26}N_2O_2$: C 79.16, H 5.62, N 7.10. Found: C 78.88, H 5.59, N 6.98.

2,11-Di-tert-butyl-2,3,11,12-tetrahydro-1H,10H-4,9-dioxa-2,11-diaza-benzo[c]phenanthrene(9d):



9d

Yield = 59%.

M.p. 160 ^{o}C.

IR (KBr): 3439, 3030, 3023, 2963, 2883, 2870, 2359, 1894, 1878, 1760, 1607, 1547, 1515, 1468, 1441, 1381, 1361, 1308, 1259, 1232, 1218, 1205, 1133, 1103, 1029, 1006, 923, 907, 827, 771 cm.$^{-1}$

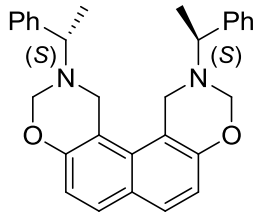
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H),), 5.07 (s, 4H), 4.61 (s, 4H), 1.20 (s, 18H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 154.25, 132.46, 129.11, 125.50, 116.23, 115.40, 77.65, 54.23, 46.97, 28.32.

MS (EI): *m/z*, (%) 355 (05)([M+1]$^{+}$), 354 (08), 270 (04), 269 (18), 254 (06), 213 (18), 212 (24), 198 (16), 186 (09), 185 (61), 184 (100), 182 (03), 157 (05), 156 (08), 155 (05), 128 (15), 127 (07), 86 (09), 70 (16), 57 (19).

Anal. Calcd. for $C_{22}H_{30}N_2O_2$: C 74.54, H 8.53, N 7.90. Found: C 74.35, H 8.62, N 7.60.

2,11-bis((S)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7-e']bis([1,3]oxazine)[10a]:



A solution of (*S*)-α-methylbenzylamine (0.416 g, 3.43 mmol) and 37% formaldehyde solution (0.608 mL, 7.48 mmol) in methanol (10 mL) was stirred for 30 min. at room temperature under N_2 atmosphere. Then 2,7-dihydroxynaphthalene (0.250 g, 1.56 mmol) was added and the reaction mixture was stirred for 48 h at room temperature. After the completion of reaction concentrated the reaction mixture under reduced pressure and the crude product was purified by column chromatography on silica gel and (only petroleum ether) to (80:20, petroleum ether:ethylacetate) as gradiant for the elution of the compound.

Yield = 0.141 g (20%); $[\alpha]_D^{34}$ = +175 (*c* 0.1 in $CHCl_3$)

M.p. 190-191°C (decomposed).

IR (KBr): 3443, 3024, 2977, 2887, 2844, 1883, 1611, 1517, 1491, 1461, 1450, 1440, 1386, 1359, 1320, 1235, 1198, 1165, 1129, 1065, 1016, 941, 836, 778, 753, 701 cm.$^{-1}$

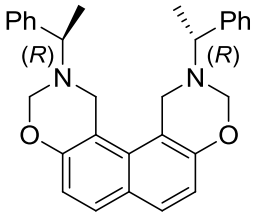
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.8 Hz, 2H), 7.34-7.23 (m, 10H), 6.88 (d, *J* = 8.8 Hz, 2H), 5.08 (dd, *J* = 1.2 Hz &10.0 Hz, 2H), 4.83 (d, *J* = 10.0, 2H), 4.18 (d, *J* = 16.4 Hz, 2H), 4.05 (d, *J* = 16.4 Hz, 2H), 3.85 (q, *J* = 6.4 Hz, 2H), 1.41 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 153.71, 144.23, 133.49, 129.33, 128.56, 127.33, 127.27, 125.63, 115.91, 112.53, 78.61, 56.99, 49.77, 21.32.

MS (EI): *m/z*, (%) 450 (07), 317 (20), 316 (04), 213 (20), 212 (33), 198 (07), 185 (22), 184 (33), 134 (05), 128 (09), 127 (05), 106 (08), 105 (100), 103 (10), 91 (07), 79 (13), 77 (13).

Anal. Calcd. for $C_{30}H_{30}N_2O_2$: C 79.97, H 6.71, N 6.22. Found: C 80.09, H 6.54, N 5.78.

2,11-bis((R)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7-e']bis([1,3]oxazine)[10b]:



A solution of (*R*)-α-methylbenzylamine (0.833 g, 6.86 mmol) and 37% formaldehyde solution (1.09 mL, 14.98 mmol) in methanol (10 mL) was stirred for 30 min. at room temperature under N_2 atmosphere. Then 2,7-dihydroxynaphthalene (0.500 g, 3.12 mmol) was added and the reaction mixture was stirred for 48 h at room temperature. After the completion of reaction concentrated the reaction mixture under reduced pressure and the crude product was purified by column chromatography on silica gel and (only petroleum ether) to (80:20, petroleum ether:ethylacetate) as gradiant for the elution of the compound.

Yield = 0.349 g (25%); $[\alpha]_D^{34}$ = -189 (*c* 0.11 in $CHCl_3$).

M.p. 188-190 °C (decomposed).

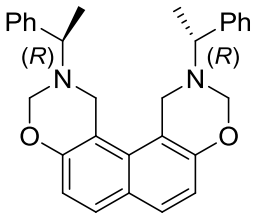
IR (KBr): 3440, 3055, 3024, 2977, 2886, 2844, 1952, 1883, 1760, 1610, 1517, 1491, 1451, 1440, 1386, 1367, 1359, 1320, 1305, 1235, 1198, 1165, 1128, 1117, 1065, 980, 940, 836, 770, 703 $cm.^{-1}$

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.51 (d, *J* = 8.8 Hz, 2H), 7.30-7.19 (m, 10H), 6.85 (d, *J* = 8.8 Hz, 2H), 5.05 (d, *J* = 10.0 Hz, 2H), 4.80 (d, *J* = 10.0 Hz, 2H), 4.14 (d, *J* = 16.0 Hz, 2H), 4.01 (d, *J* = 16.4 Hz, 2H), 3.83 (q, *J* = 6.8 Hz, 2H), 1.38 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 153.69, 144.19, 133.46, 129.33, 128.55, 127.33, 127.26, 125.63, 115.90, 112.50, 78.60, 57.00, 49.75, 21.29.

MS (EI): *m/z*, (%) 450 (05), 318 (04), 317 (18), 316 (04), 213 (19), 212 (31), 198 (08), 185 (24), 184 (35), 134 (05), 128 (10), 127 (05), 106 (08), 105 (100), 103 (11), 91 (07), 79 (12), 77 (13).

Anal. Calcd. for $C_{30}H_{30}N_2O_2$: C 79.97, H 6.71, N 6.22. Found: C 79.81, H 6.77, N 5.94.



Stepwise Synthesis of 10b:

2,11-bis((R)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7-e']bis([1,3]oxazine)[10b]:

A solution of (*R*)-α-methylbenzylamine (0.096 g, 0.79 mmol) and 37% formaldehyde solution (0.128 mL, 1.58 mmol) in methanol (10 mL) was stirred for 30 min. at room temperature under N_2 atmosphere. Then compound **12** [(R)-2-(1-phenylethyl)-2,3-dihydro-1H-naphtho[1,2-e][1,3]oxazin-9-ol] (0.20 g, 0.659 mmol) was added and the reaction mixture was stirred for 48 h at room temperature. After the completion of reaction concentrated the reaction mixture under reduced pressure and the crude product was purified by column chromatography on silica gel and (only petroleum ether) to (80:20, petroleum ether: ethylacetate) as gradiant for the elution of the compound.

Compound **10b** eluted with (80:20, petroleum ether:ethylacetate).

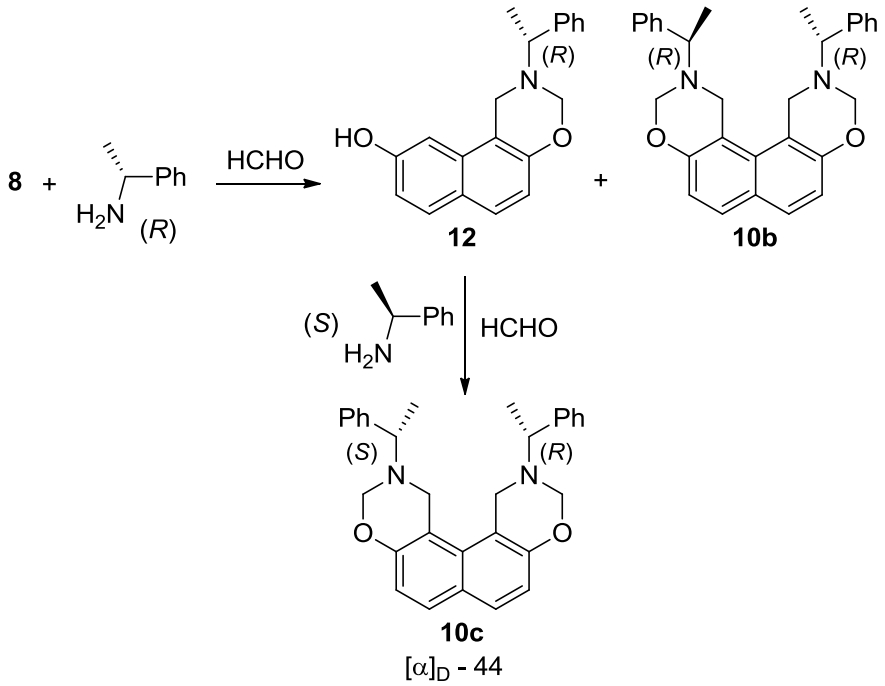
Yield = 0.036 g (30%); $[\alpha]_D^{34}$ = -190 (*c* 0.1 in $CHCl_3$).

M.p. 189-190 °C (decomposed).

(R)-2-(1-phenylethyl)-2,3-dihydro-1H-naphtho[1,2-e][1,3]oxazin-9-ol [12]:

2,11-bis((R)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7-e']bis([1,3]oxazine) [10b]:

2-((R)-1-phenylethyl)-11-((S)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7 e']bis([1,3]oxazine) [10c]:



A solution of (*R*)-α-methylbenzylamine (0.726 g, 5.99 mmol) and 37% formaldehyde solution (0.972 mL, 11.98 mmol) in methanol (15 mL) was stirred for 30 min. at room temperature under N_2 atmosphere. Then 2,7-dihydroxynaphthalene (0.800 g, 4.94 mmol) was added and the reaction mixture was stirred for 48 h at room temperature. After the completion of reaction concentrated the reaction mixture under reduced pressure and the crude product was purified by column chromatography on silica gel and (only petroleum ether) to (80:20, petroleum ether:ethylacetate) as gradiant for the elution of the compound.

2,11-bis((R)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7-e']bis([1,3]oxazine) [10b]:

Eluted with (80:20, petroleum ether:ethylacetate).

Yield = 0.268 g (18%);

M.p. 188-190 °C (decomposed).

(R)-2-(1-phenylethyl)-2,3-dihydro-1H-naphtho[1,2-e][1,3]oxazin-9-ol [12]:

Eluted with (70:30, petroleum ether:ethylacetate).

Yield = 0.957 g (63%);

M.p. 118-119 °C (decomposed).

IR (KBr): 3440, 3055, 3024, 2977, 2886, 2844, 1952, 1883, 1760, 1610, 1517, 1491, 1451, 1440, 1386, 1367, 1359, 1320, 1305, 1235, 1198, 1165, 1128, 1117, 1065, 980, 940, 836, 770, 703 $cm.^{-1}$

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.8 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.39-7.28 (m, 5H), 6.94 (dd, *J* = 2.4 Hz & 8.8 Hz, 1H), 6.93 (d, *J* = 9.2 Hz, 1H), 6.75 (d, *J* = 2.4 Hz, 1H), 5.17 (dd, *J* = 1.2 Hz & 10.4 Hz, 1H), 4.93 (d, *J* = 10.0 Hz, 1H), 4.31 (d, *J* = 16.8 Hz, 1H), 4.05 (m, 2H), 1.53 (d, *J* = 6.4 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 154.35, 153.13, 144.48, 133.25, 130.54, 128.62 (2 x CH), 127.77, 127.39 (2 x CH), 127.36, 124.17, 115.98, 114.95, 110.68, 103.81, 79.83, 58.25, 46.19, 21.52.

Anal. Calcd. for $C_{30}H_{30}N_2O_2$: C 78.66, H 6.27, N 4.59. Found: C 77.93, H 6.42, N 4.42.

Synthesis of *2-((R)-1-phenylethyl)-11-((S)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7 e']bis([1,3]oxazine) [10c]:*

A solution of (*S*)-α-methylbenzylamine (0.238 g, 1.96 mmol) and 37% formaldehyde solution (0.318 mL, 3.93 mmol) in methanol (10 mL) was stirred for 30 min. at room temperature under N_2 atmosphere. Then Compound A [(R)-2-(1-phenylethyl)-2,3-dihydro-1H-naphtho[1,2-e][1,3]oxazin-9-ol] (0.500 g, 1.64 mmol) was added and the reaction mixture was stirred for 48 h at room temperature. After the completion of reaction concentrated the reaction mixture under reduced pressure and the crude product was purified by column chromatography on silica gel and (only petroleum ether) to (80:20, petroleum ether:ethylacetate) as gradiant for the elution of the compound.

Compound **10c** eluted with (80:20, petroleum ether:ethylacetate).

Yield = 0.305 g (41%); $[\alpha]_D^{34}$ = -44 (*c* 0.1 in $CHCl_3$).

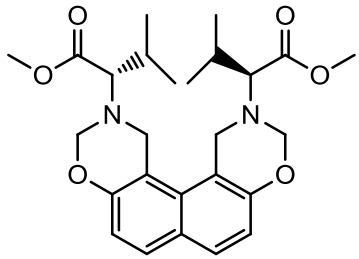
M.p. 188-190 °C (decomposed).

IR (KBr): 3436, 2977, 2886, 2844, 1883, 1611, 1516, 1491, 1461, 1450, 1440, 1371, 1359, 1235, 1198, 1165, 1129, 1065, 1016, 991, 980, 941, 931, 836, 779, 770, 753, 702 $cm.^{-1}$

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 8.8 Hz, 2H), 7.35-7.19 (m, 10H), 6.84 (d, *J* = 8.8 Hz, 2H), 5.0 (dd, *J* =1.6 Hz & 10.4 Hz, 2H), 4.79 (d, *J* = 10.0 Hz, 2H), 4.14 (d, *J* = 16.4 Hz, 2H), 4.01 (d, *J* = 16.0 Hz, 2H), 3.82 (q, *J* = 6.4 Hz, 2H), 1.38 (d, *J* = 6.8 Hz, 6H).

Anal. Calcd. for $C_{30}H_{30}N_2O_2$: C 79.97, H 6.71, N 6.22. Found: C 79.77, H 6.44, N 5.84.

(2S,2'S)-dimethyl 2,2'-(naphtho[1,2-e:8,7-e']bis([1,3]oxazine)-2,11(1H,3H,10H,12H)-diyl)bis(3-methylbutanoate)[11]:



A solution of *L*-valinemethylester hydrochloride (1.152 g, 6.86 mmol), 37% formaldehyde solution (1.22 mL, 14.98 mmol) and triethylamine (1.04 mL, 7.49 mmol) in methanol (10 mL) was stirred for 30 min. at room temperature under N_2 atmosphere. Then 2,7-dihydroxynaphthalene (0.50 g, 3.12 mmol) was added and the reaction mixture was stirred for 48 h at room temperature. After the completion of reaction concentrated the reaction mixture under reduced pressure and the crude product was purified by column chromatography on silica gel and (only petroleum ether) to (80:05, petroleum ether:ethylacetate) as gradiant for the elution of the compound.

Yield = 0.955 g (65%); $[\alpha]_D^{34}$ = +231 (*c* 0.1 in $CHCl_3$)

M.p. 121-122 °C.

IR (KBr): 2962, 2930, 2874, 1740, 1674, 1610, 1516, 1441, 1370, 1286, 1237, 1193, 1122, 1043, 1027, 938, 9831, 759, 685 cm.$^{-1}$

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 4.75 (d, J = 10.00 Hz, 2H), 4.94 (dd, J = 1.6 Hz & 9.6 Hz, 2H), 4.64 (d, J = 15.6 Hz, 2H), 4.37 (broad d, J = 15.6 Hz, 2H), 3.34 (s, 6H), 3.17 (d, J = 9.2 Hz, 2H), 2.23-2.16 (m, 2H), 1.05 (d, J = 6.8 Hz, 6H), 0.93 (d, J = 6.8 Hz, 6H).

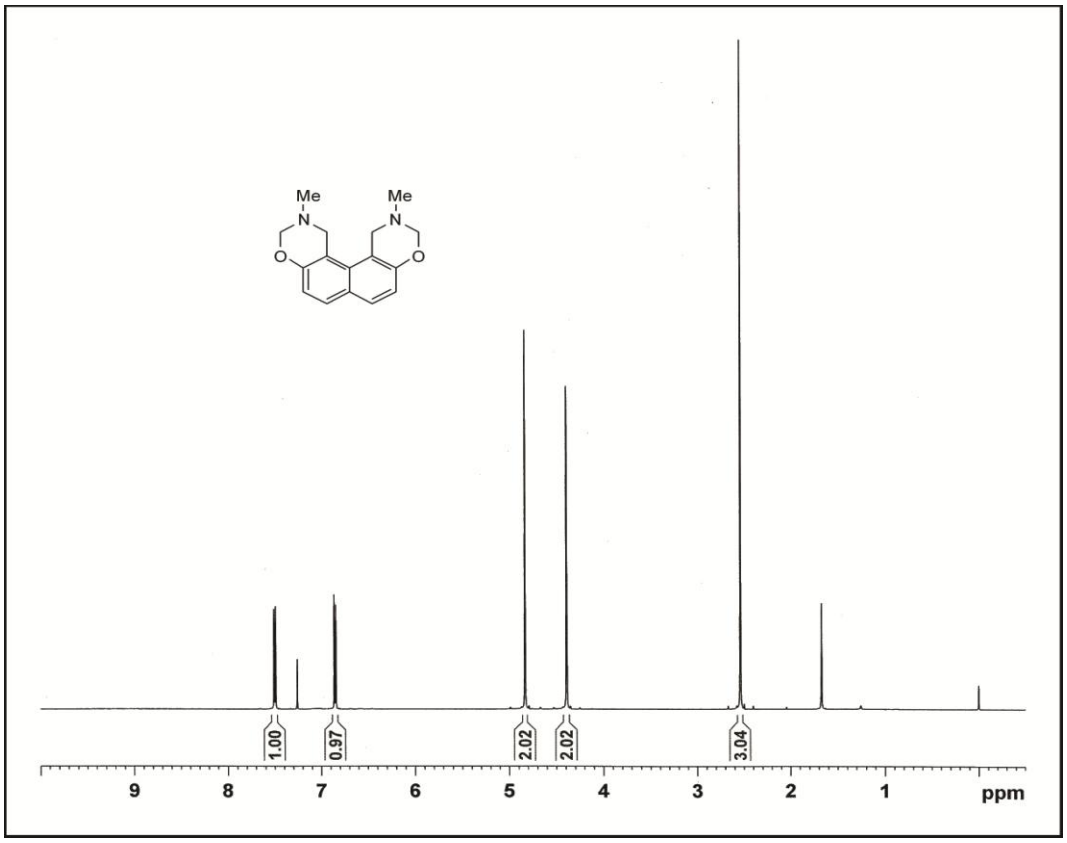
^{13}C-NMR (100 MHz, $CDCl_3$): δ 172.97, 153.38, 132.81, 129.23, 125.48, 116.19, 113.52, 80.25, 70.61, 51.30, 49.00, 28.01, 19.72, 18.75.

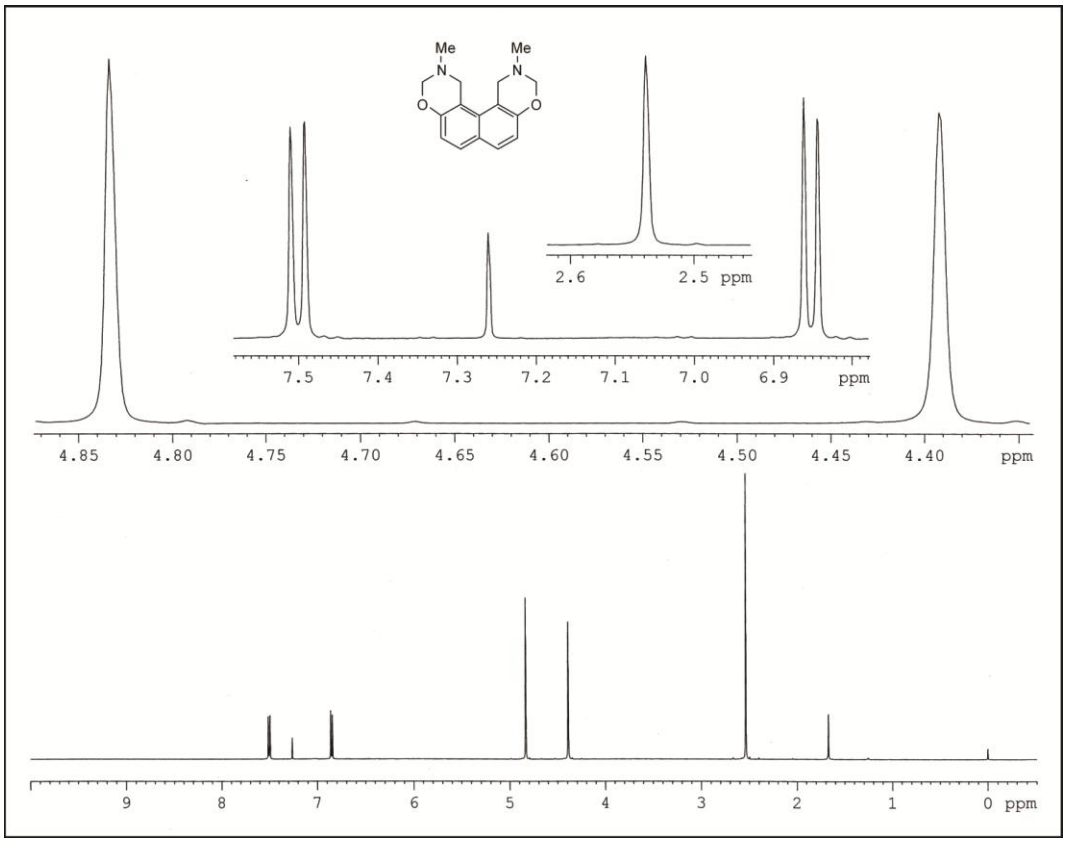
MS (EI): *m/z*, (%) 470 (06), 354 (12), 311 (19), 268 (37), 213 (16), 212 (100), 198 (33), 197 (09), 185 (13), 184 (46), 156 (15), 155 (10), 144 (25), 128 (28), 127 (09),116 (10), 100 (17), 84 (55).

Anal. Calcd. for $C_{30}H_{30}N_2O_2$: C 66.36, H 7.28, N 5.95. Found: C 66.48, H 6.79, N 5.68.

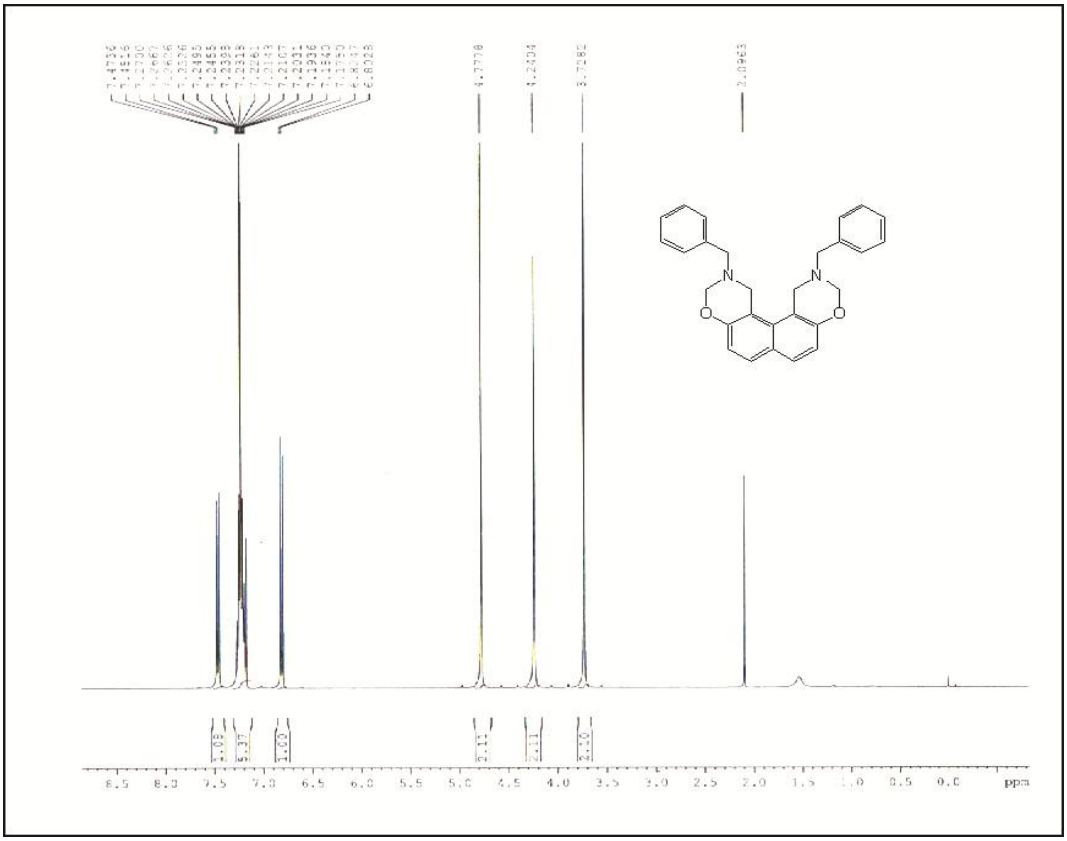
Reproduction of the Spectra

2,11-Dimethyl-2,3,11,12-tetrahydro-1H,10H,-4,9-dioxa-2,11-diaza-benzo[c]phenanthrene[9a]:

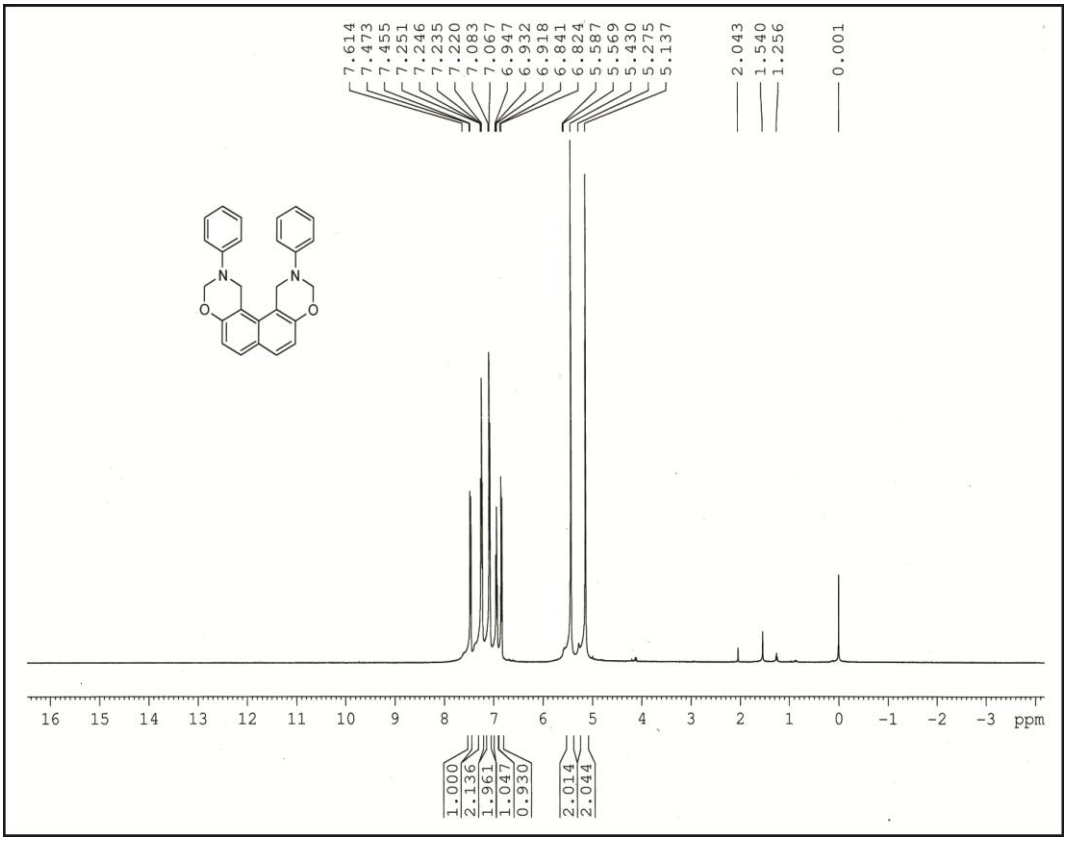


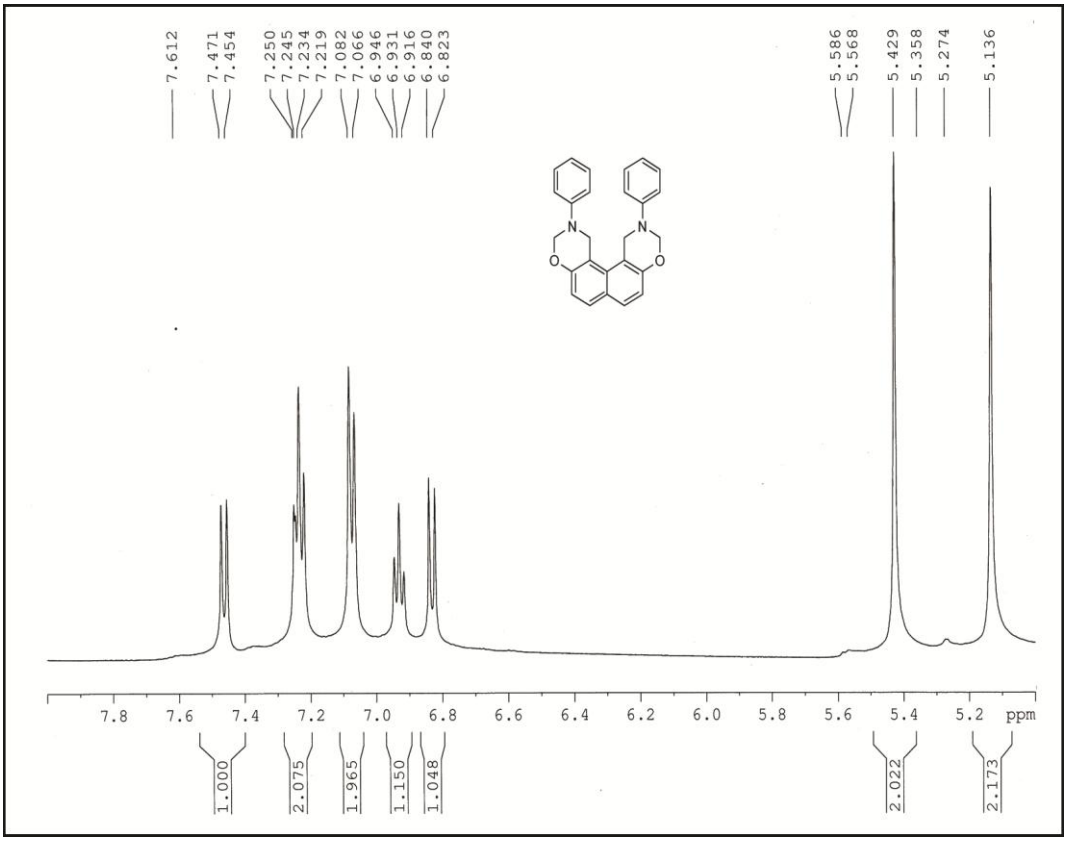


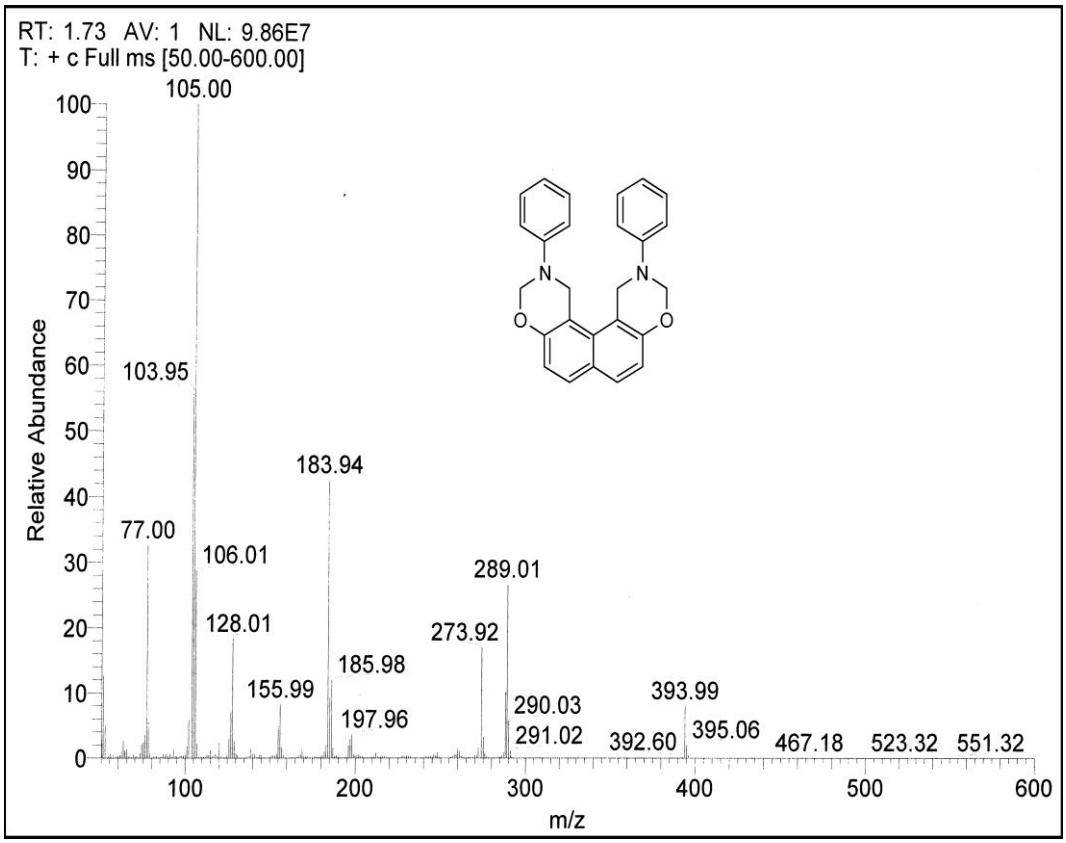
***2,11-Dibenzyl-2,3,11,12-tetrahydro-1H,10H,-4,9-dioxa-2,11-diaza-benzo[c]phenanthrene [9b]*:**



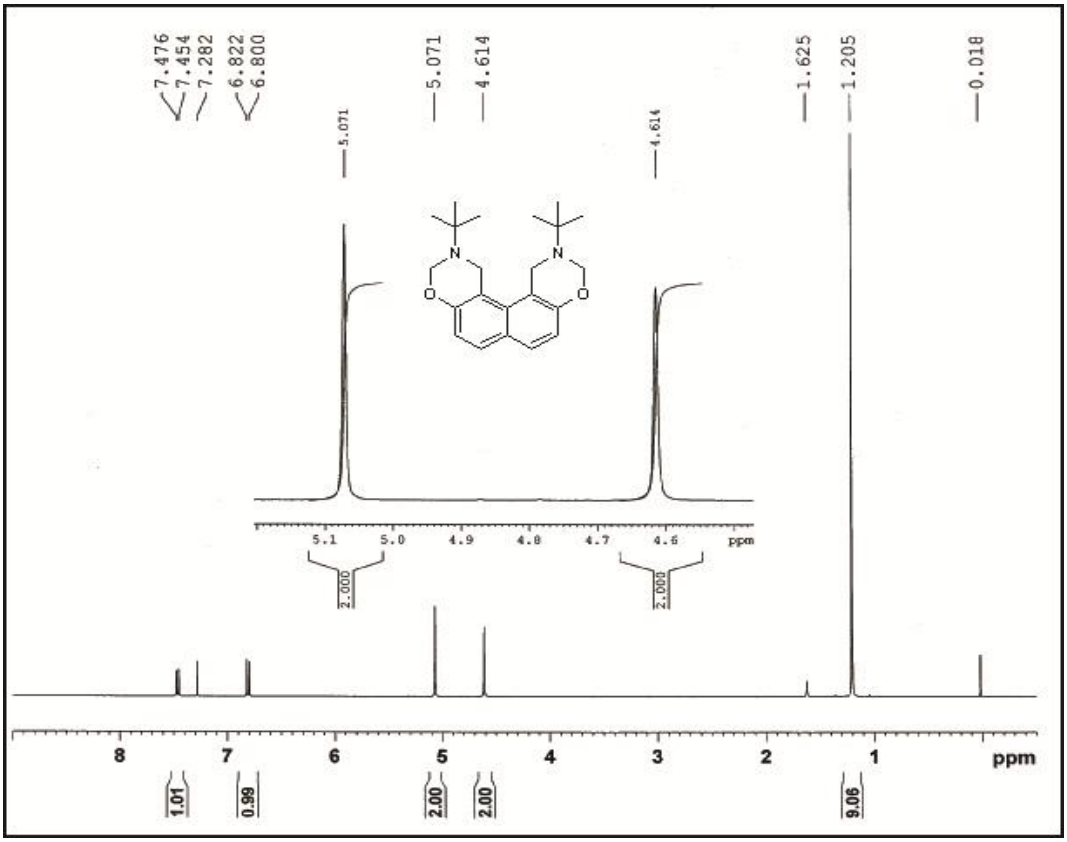
***2,11-Diphenyl-2,3,11,12-tetrahydro-1H,10H,-4,9-dioxa-2,11-diaza-benzo[c]phenanthrene [9c]*:**

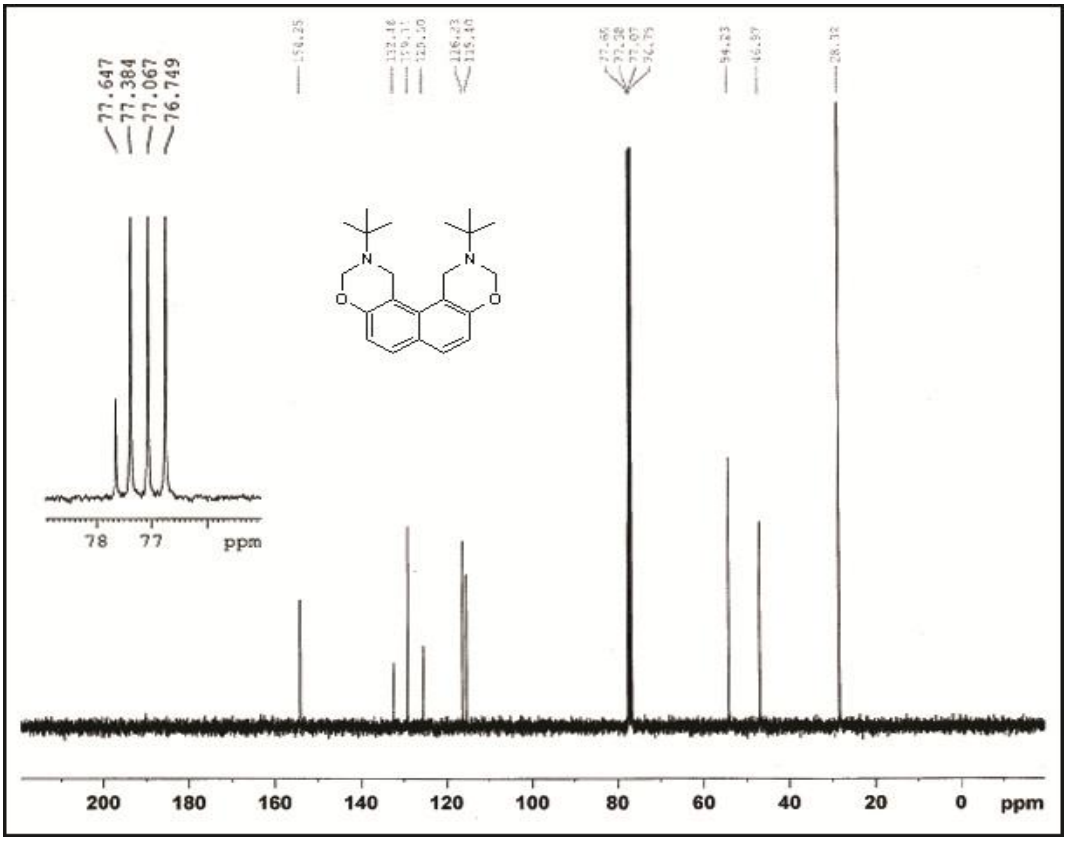


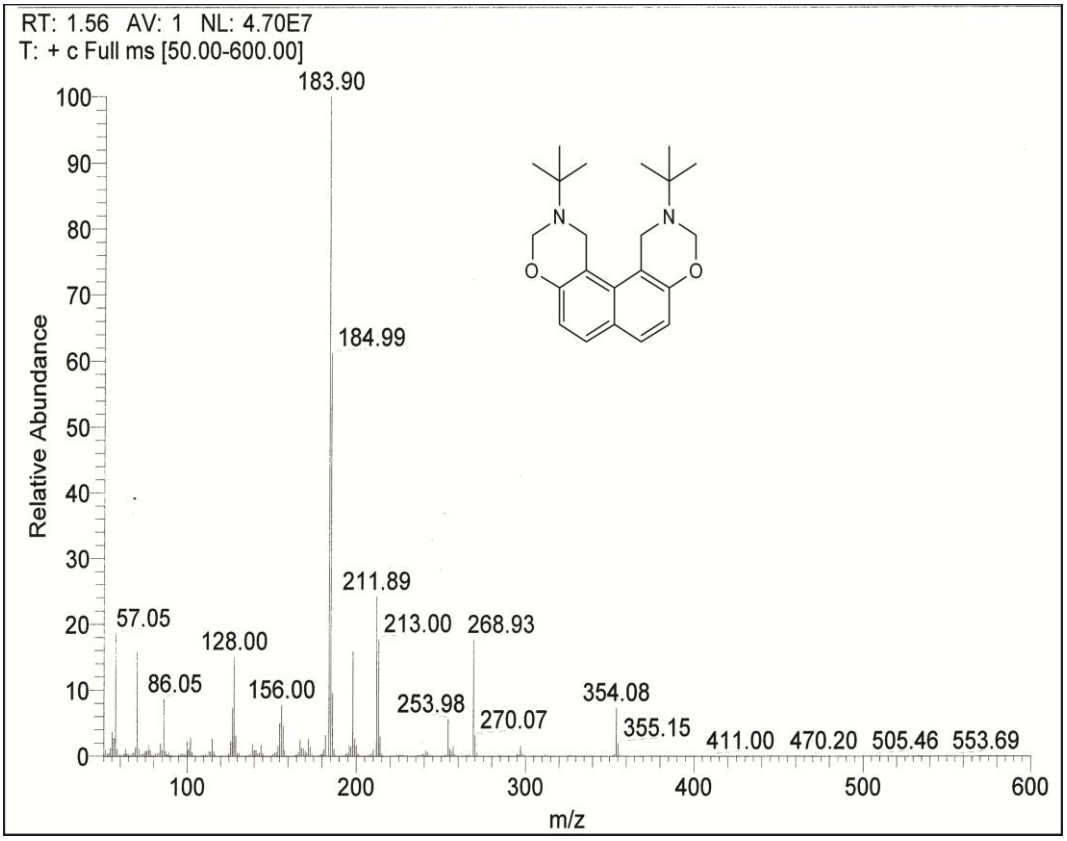




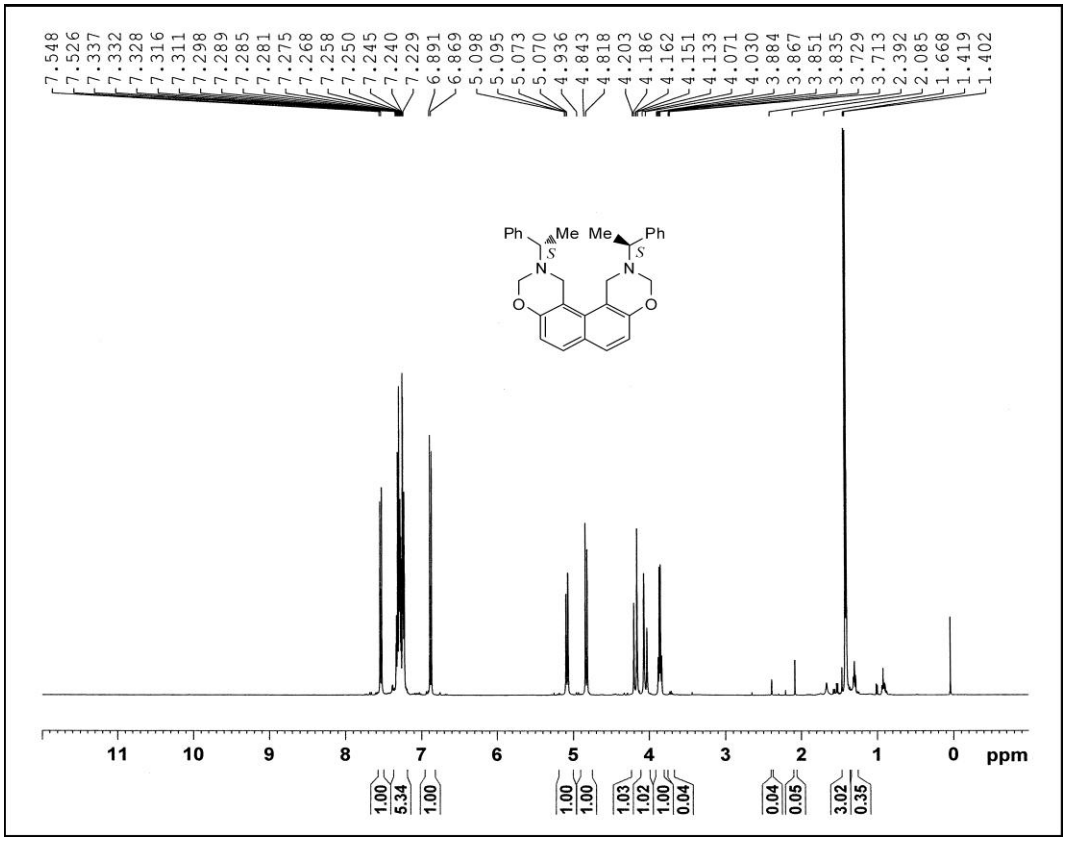
2,11-Di-tert-butyl-2,3,11,12-tetrahydro-1H,10H-4,9-dioxa-2,11-diaza-benzo[c]phenanthrene(9d):

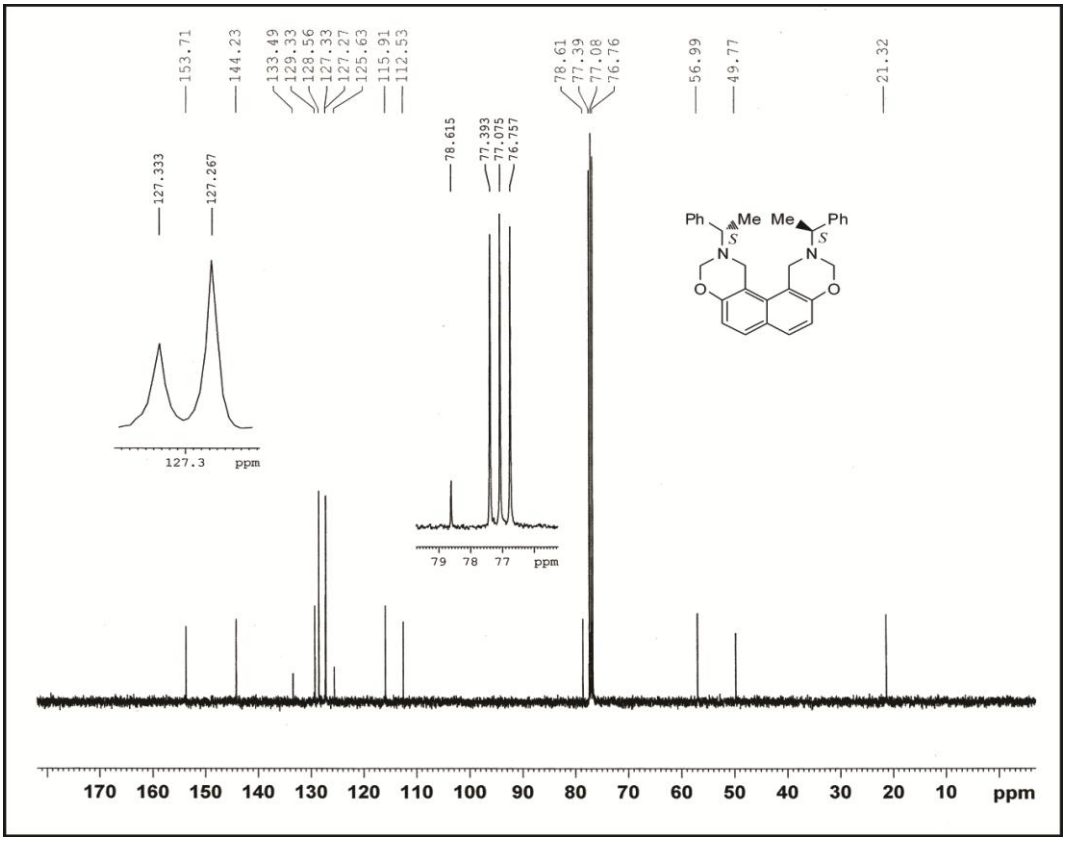


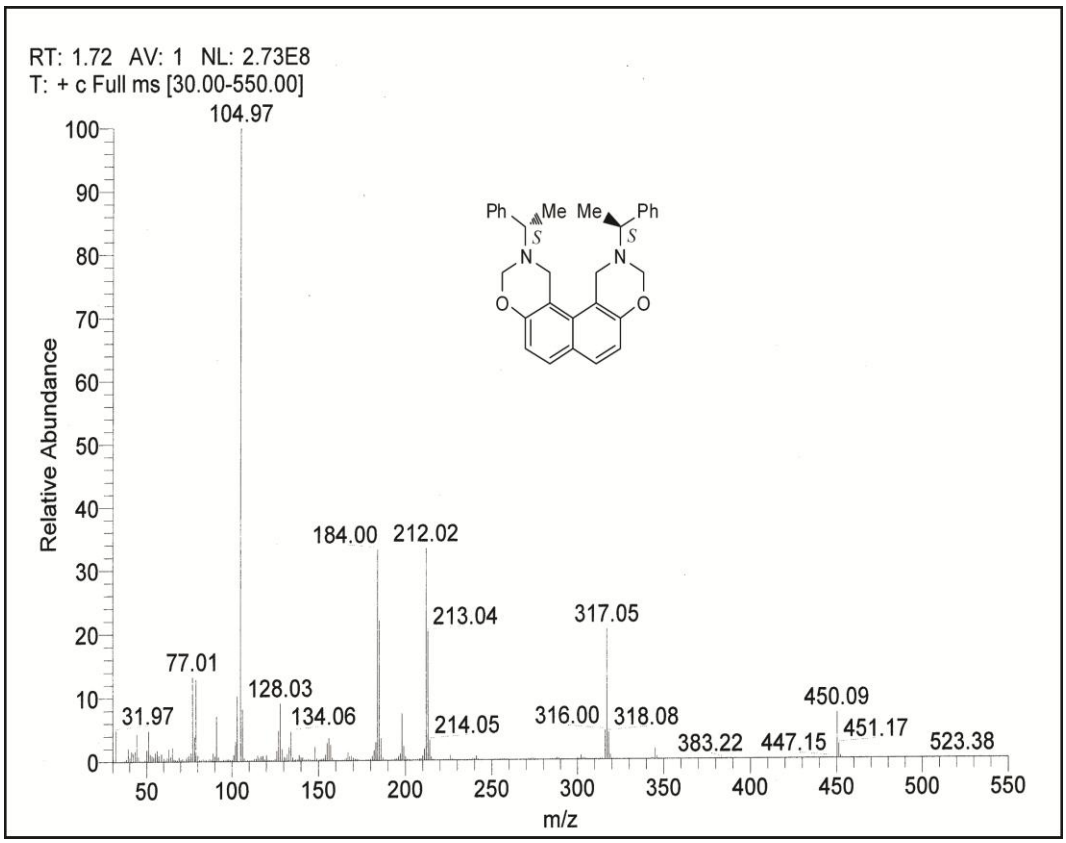


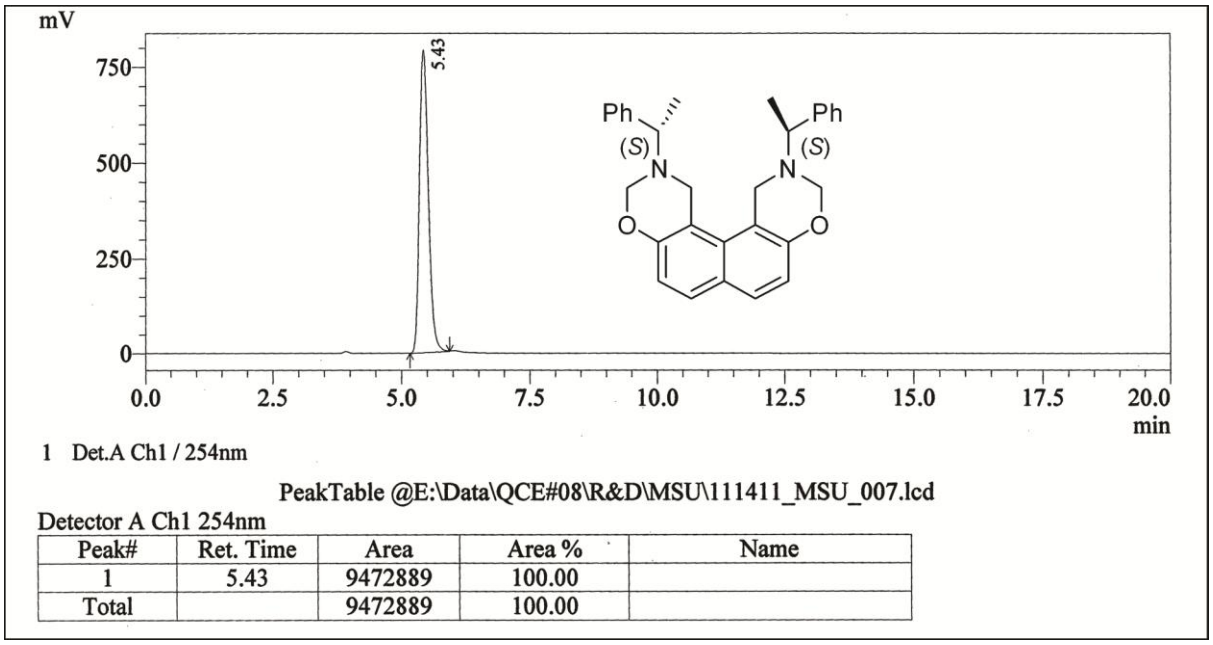


2,11-bis((S)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7-e']bis([1,3]oxazine [10a):









PeakTable @E:\Data\QCE#08\R&D\MSU\111411_MSU_007.lcd

Detector A Ch1 254nm

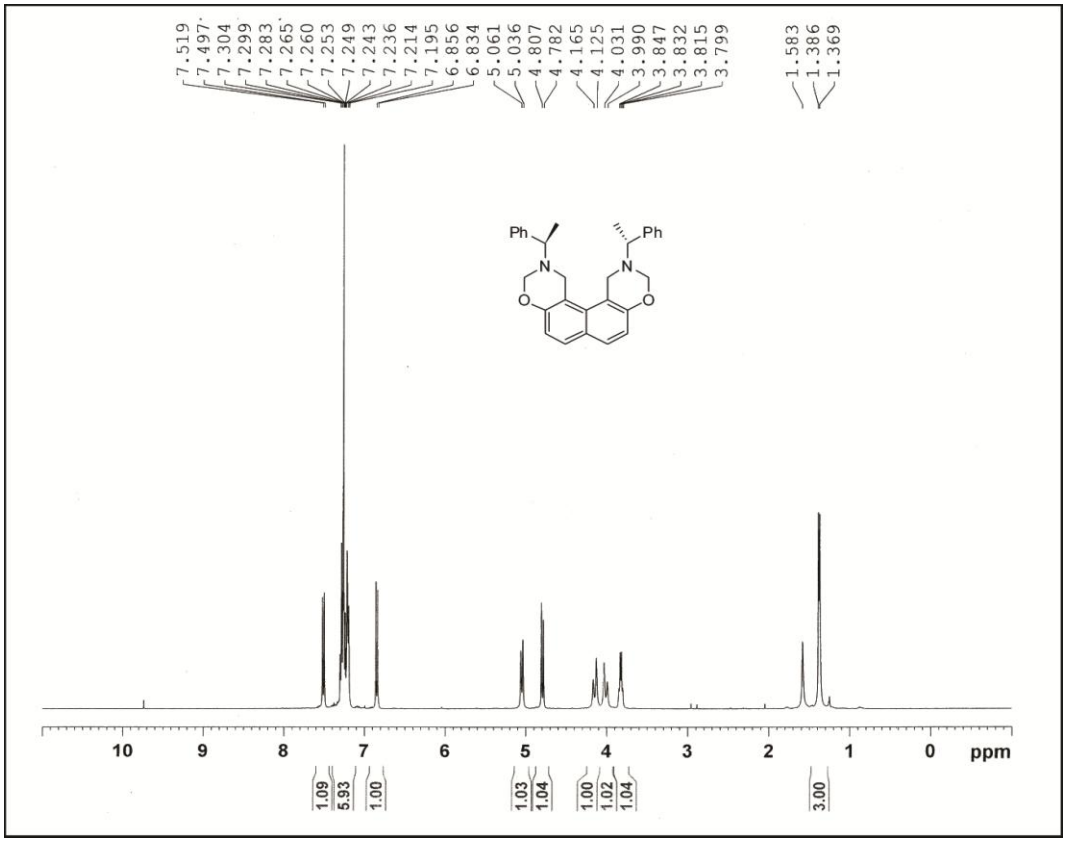
Peak#	Ret. Time	Area	Area %	Name
1	5.43	9472889	100.00	
Total		9472889	100.00	

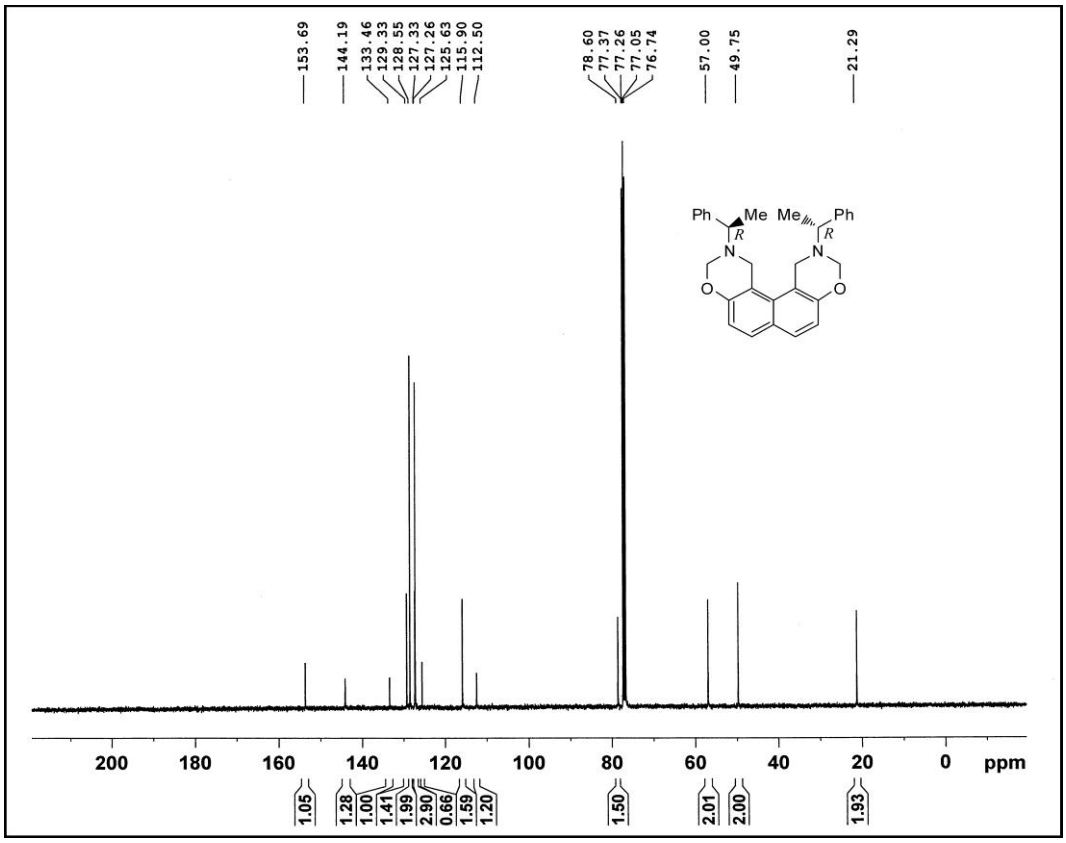
Method For HPLC Analysis

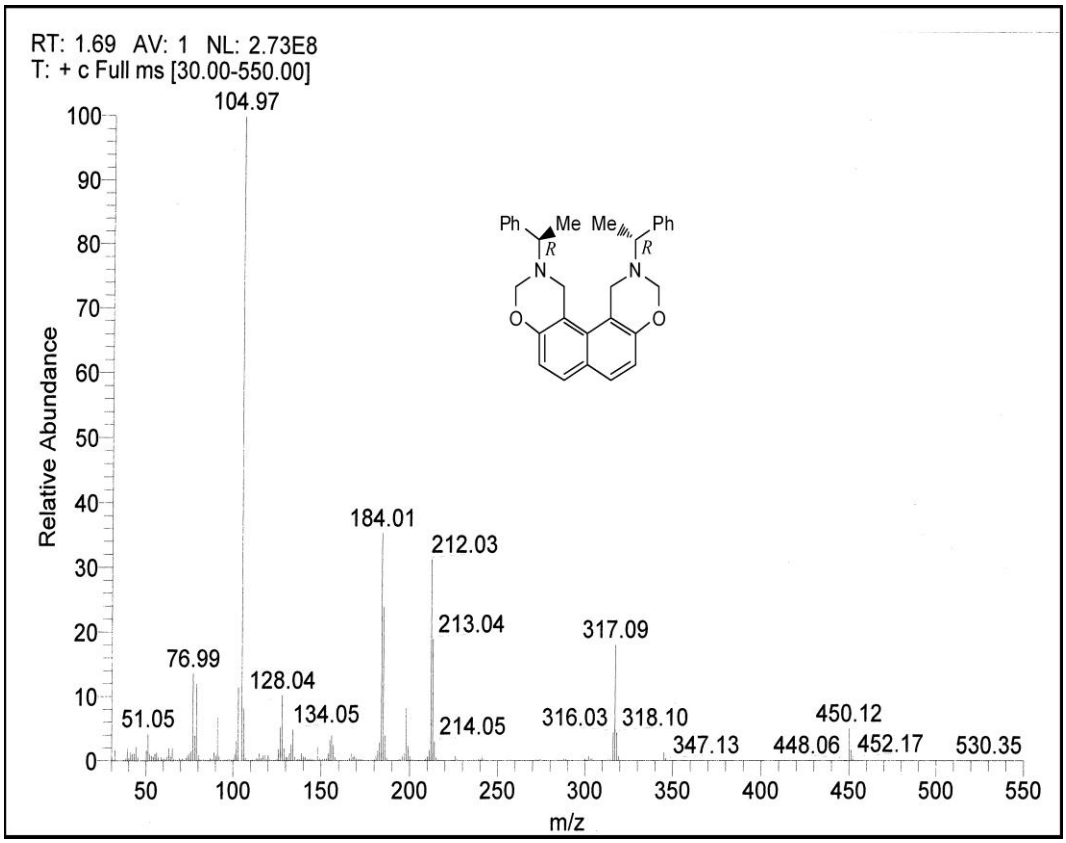
Solvent System: n-Hexane: *Iso*-propanol (60:40), Flow rate: 1ml/min., Injection vol.: 10 μL, Detector: UV-Vis (λ max – 254 nm), Oven Temperature: 27 °C

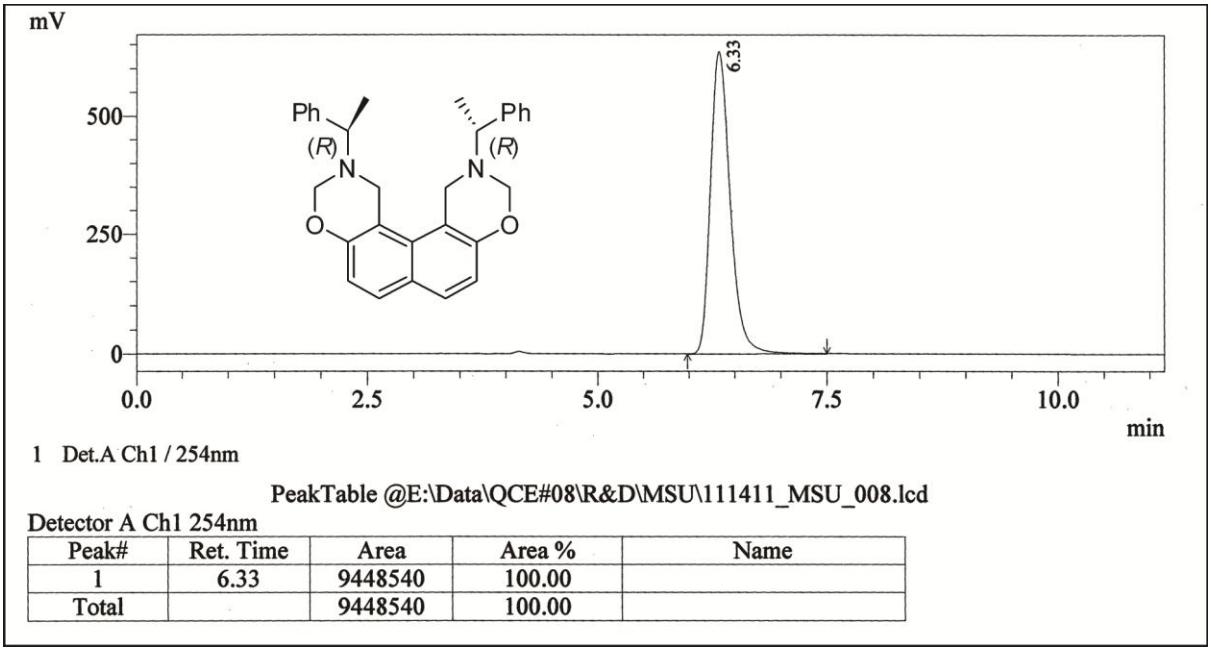
Chiral Column: Diacel OD-H

2,11-bis((R)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7-e']bis([1,3]oxazine [10b]:









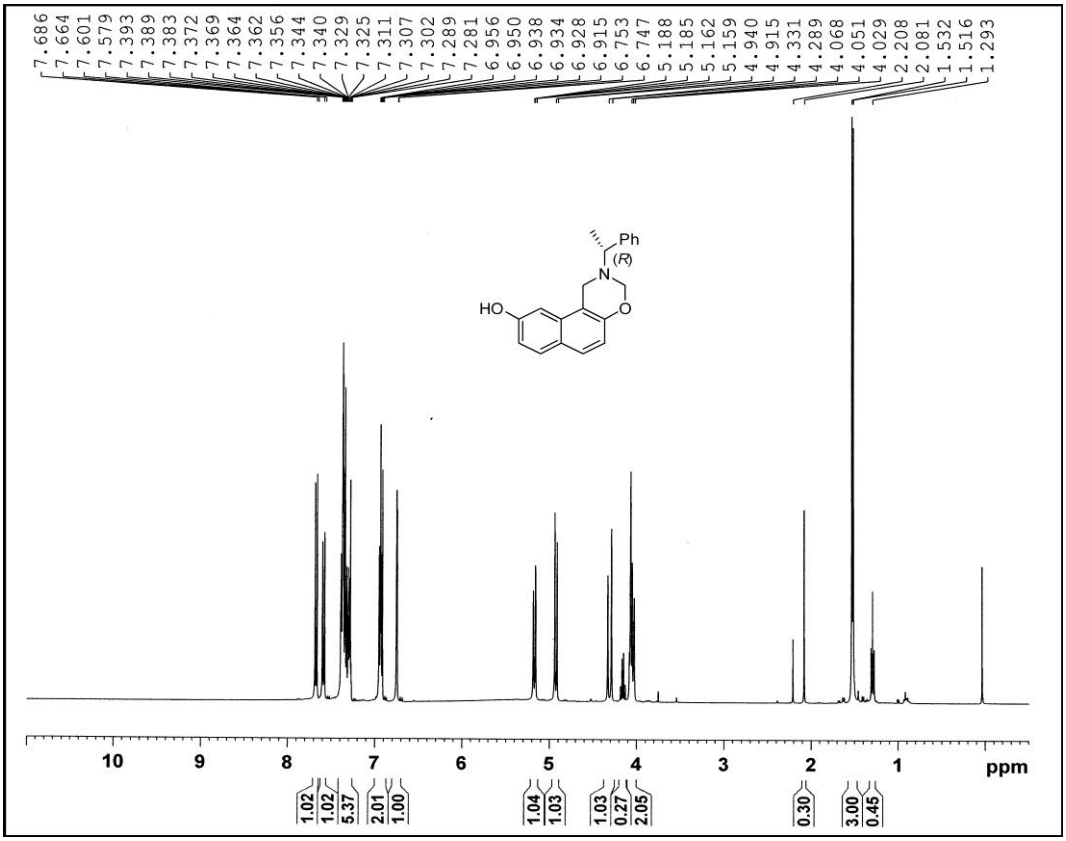
Peak#	Ret. Time	Area	Area %	Name
1	6.33	9448540	100.00	
Total		9448540	100.00	

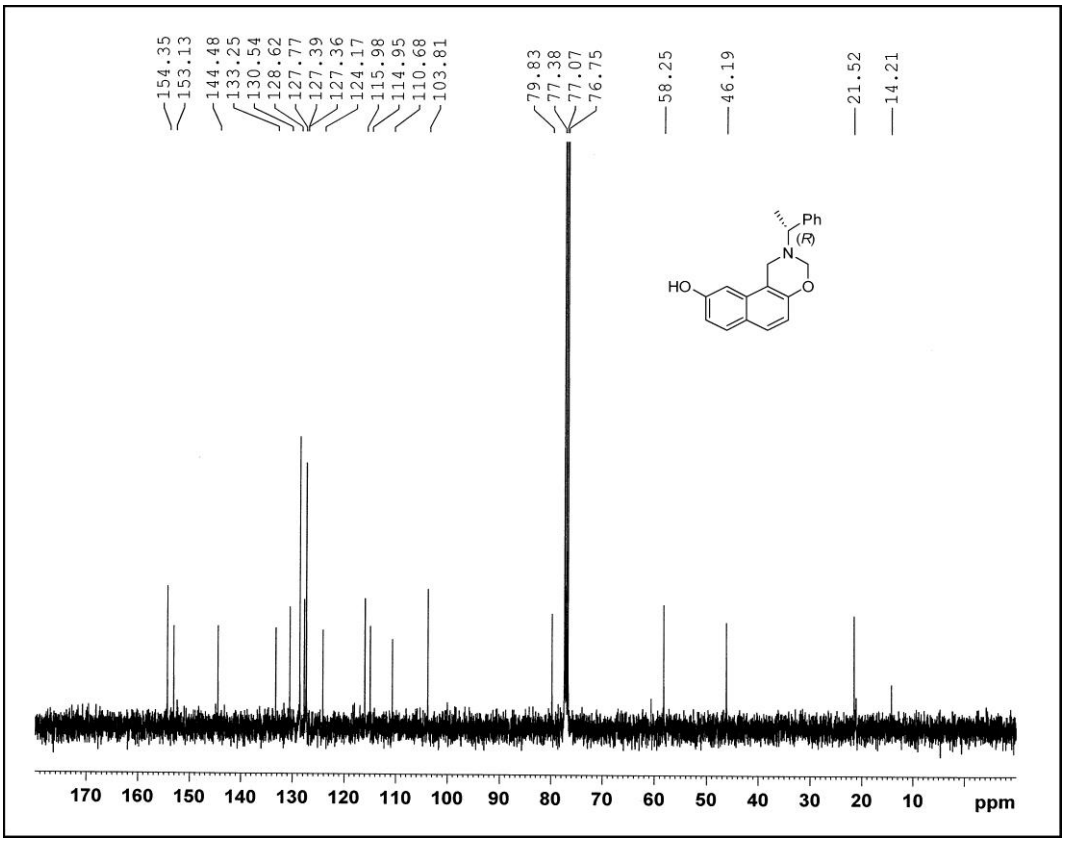
Method For HPLC Analysis

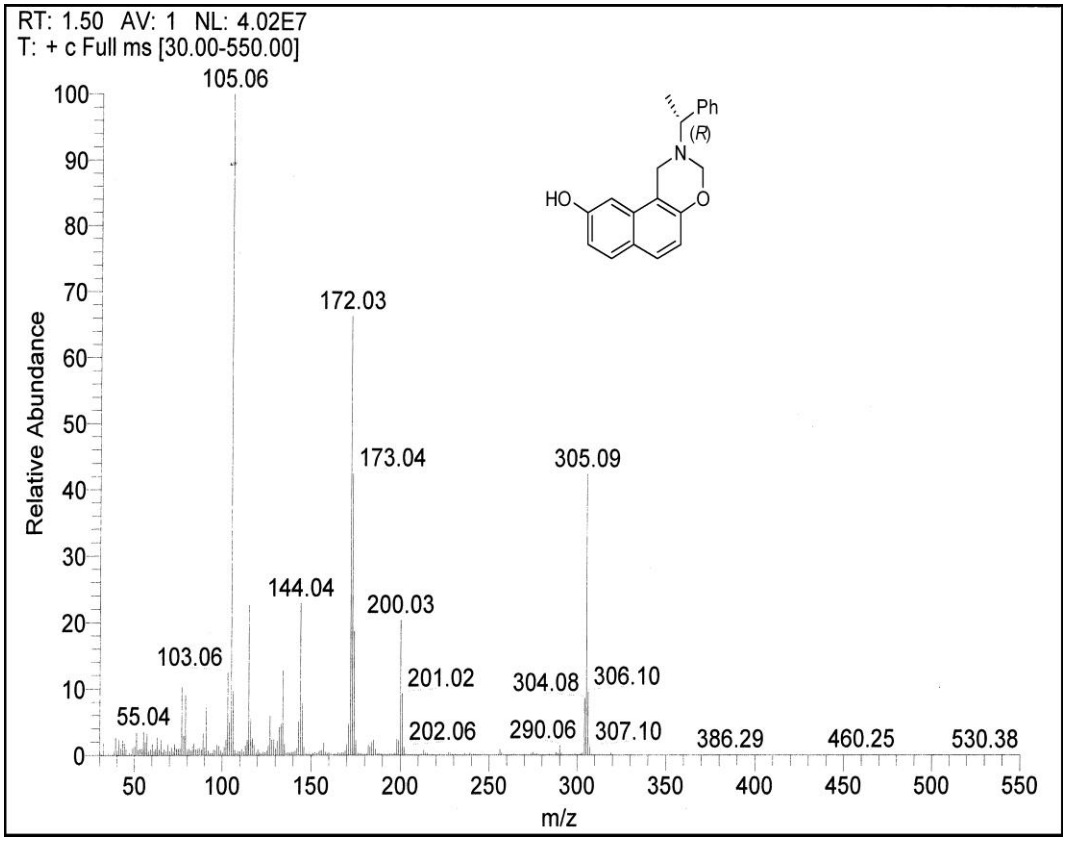
Solvent System: n-Hexane: *Iso*-propanol (60:40), Flow rate: 1ml/min., Injection vol.: 10 μL, Detector: UV-Vis (λ max – 254 nm), Oven Temperature: 27 °C

Chiral Column: Diacel OD-H

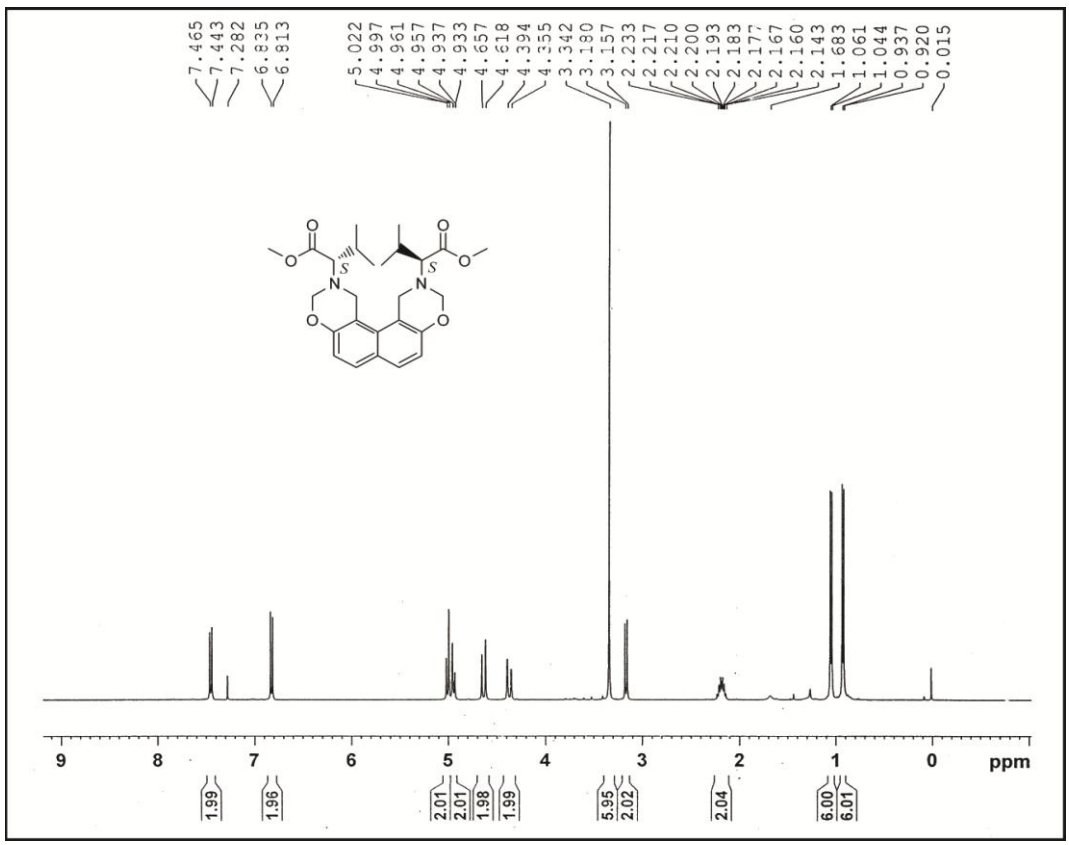
(R)-2-(1-phenylethyl)-2,3-dihydro-1H-naphtho[1,2-e][1,3]oxazin-9-ol [12]:

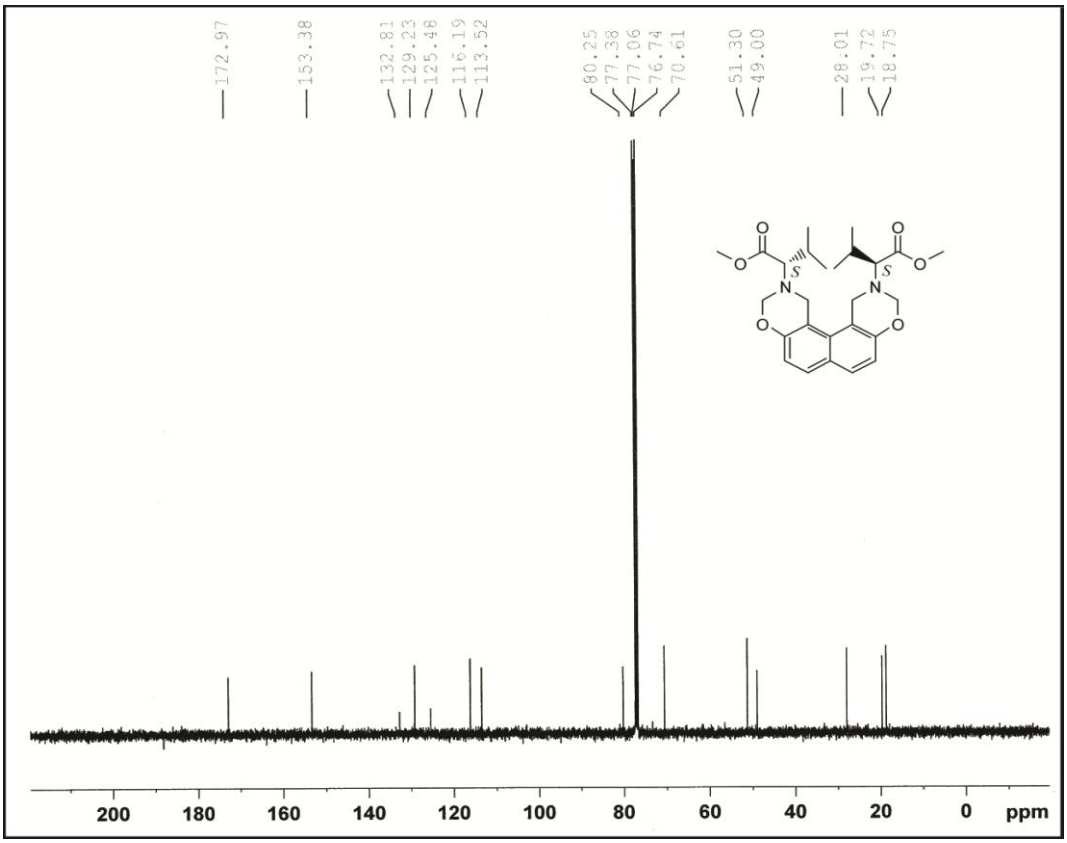


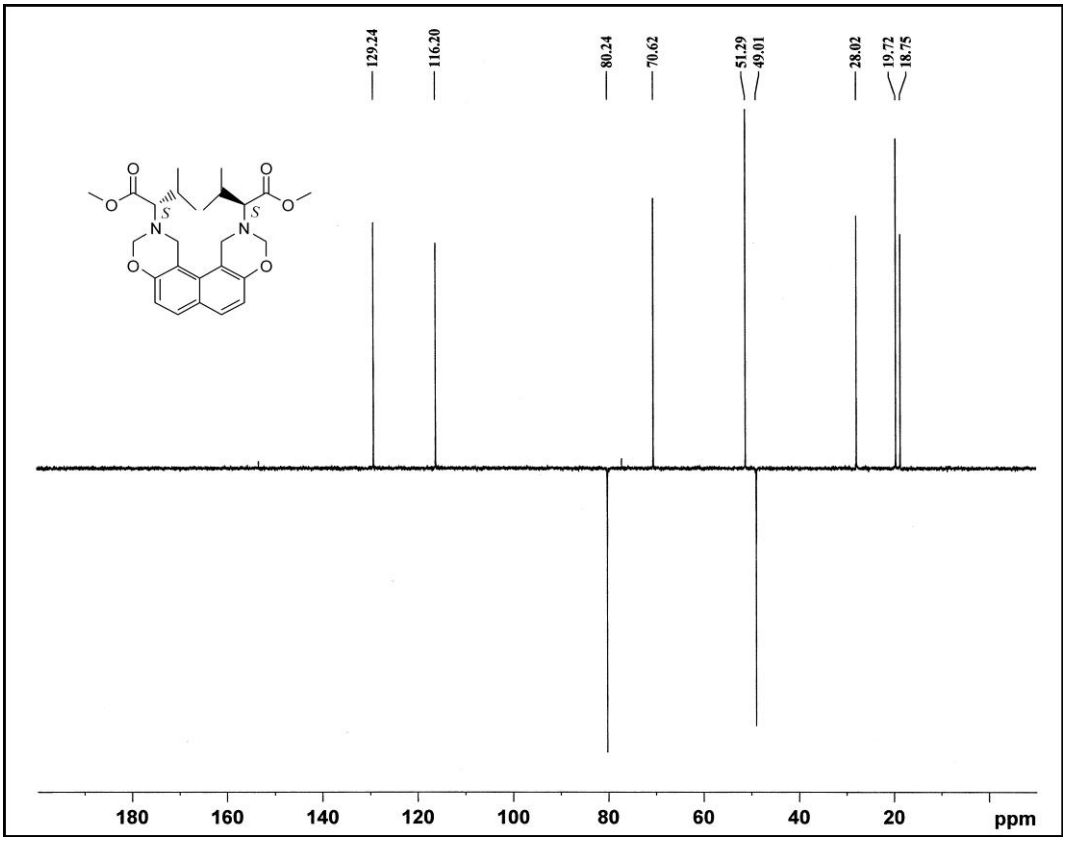




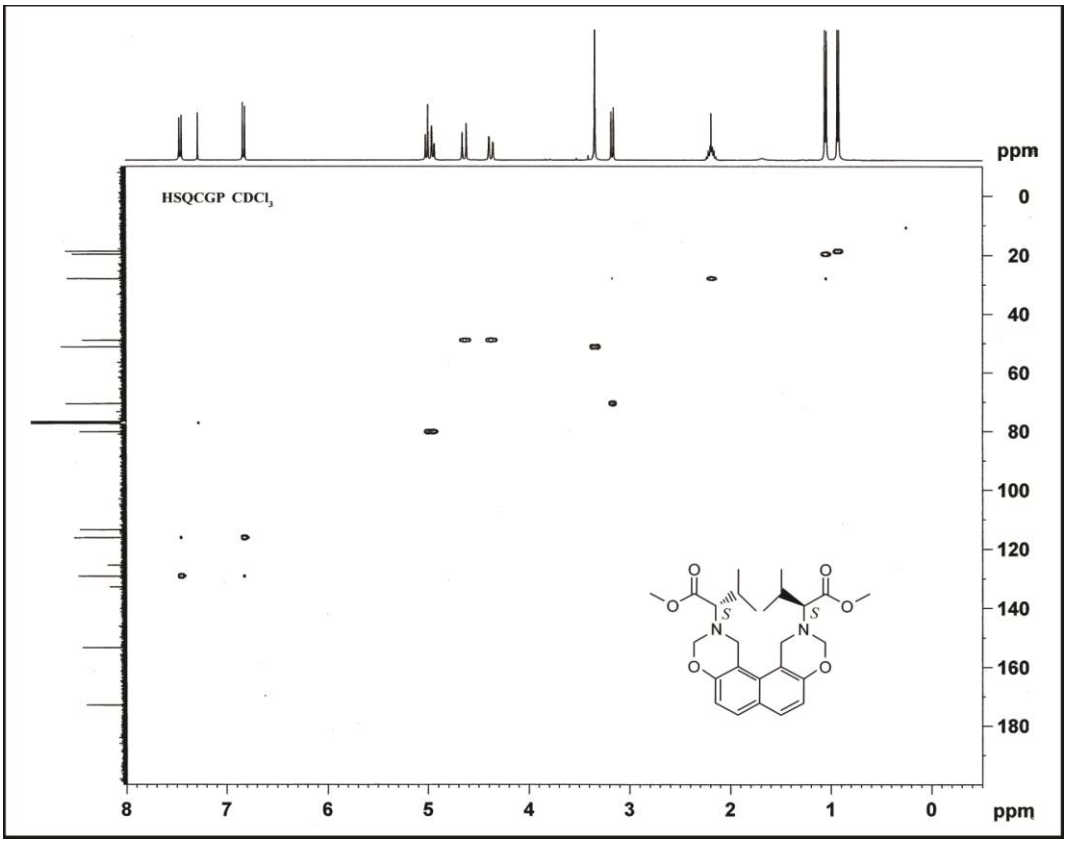
(2S,2'S)-dimethyl 2,2'-(naphtho[1,2-e:8,7-e']bis([1,3]oxazine)-2,11(1H,3H,10H,12H)-diyl)bis(3-methylbutanoate)[11]:

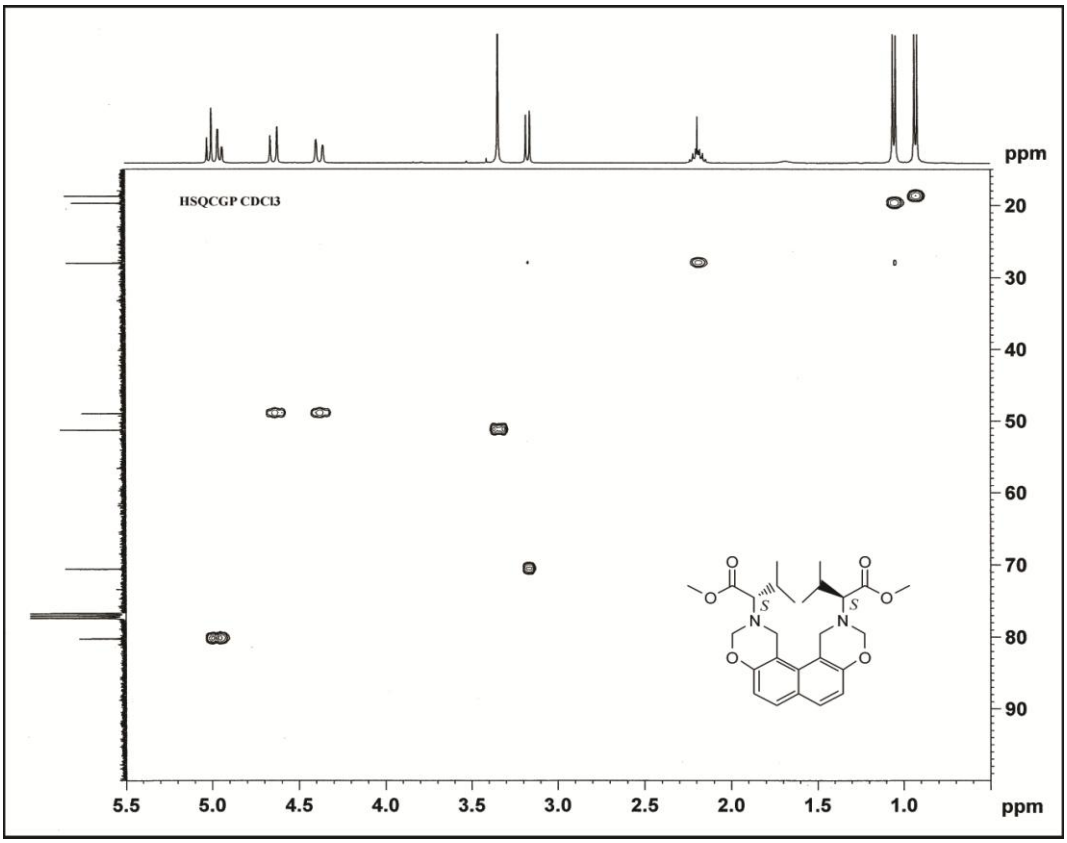


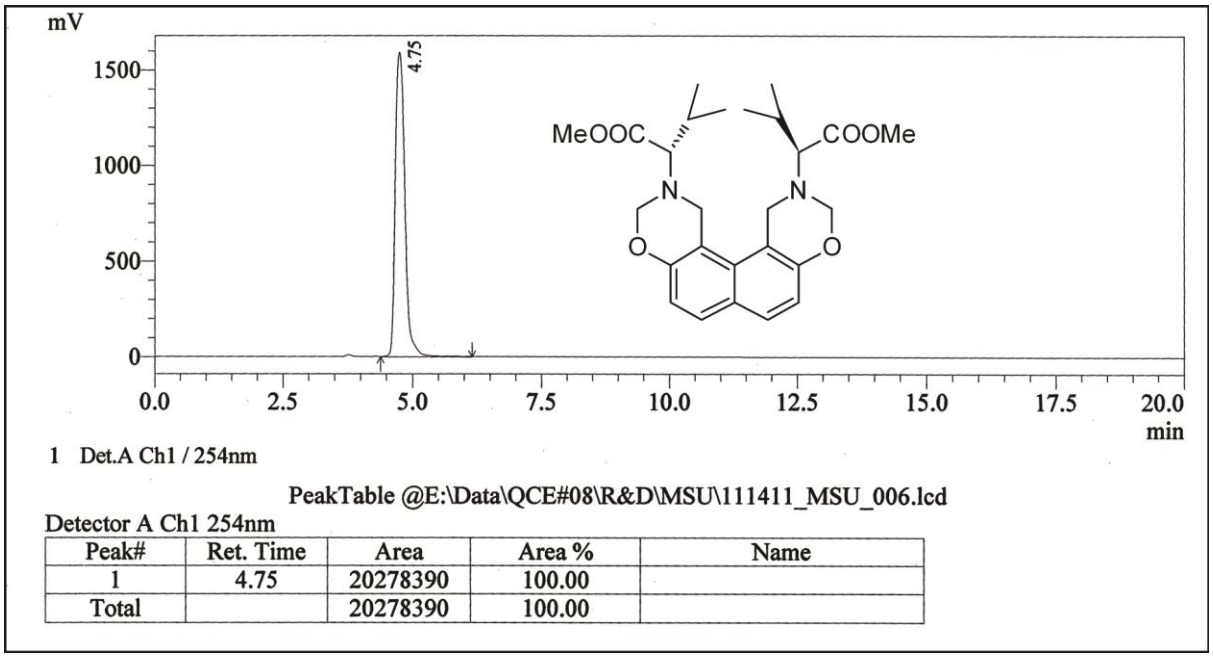




HSQCGP NMR spectrum for compound 11.







PeakTable @E:\Data\QCE#08\R&D\MSU\111411_MSU_006.lcd

Detector A Ch1 254nm

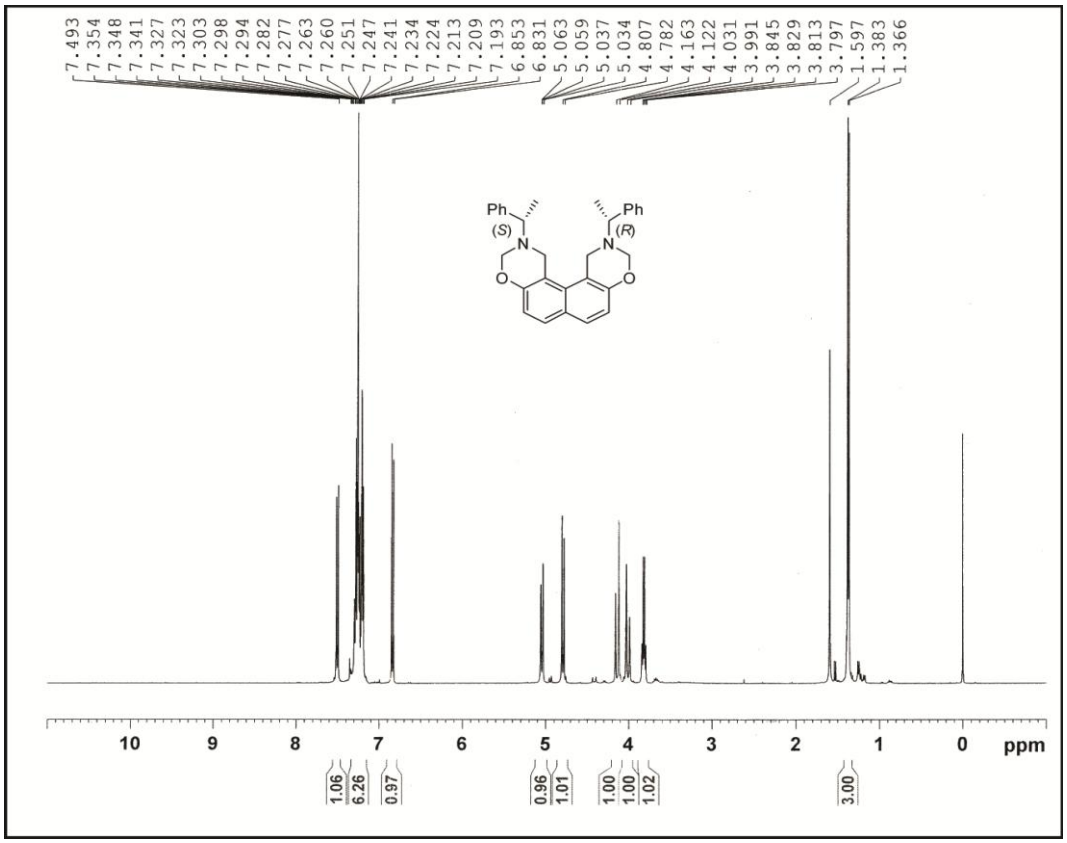
Peak#	Ret. Time	Area	Area %	Name
1	4.75	20278390	100.00	
Total		20278390	100.00	

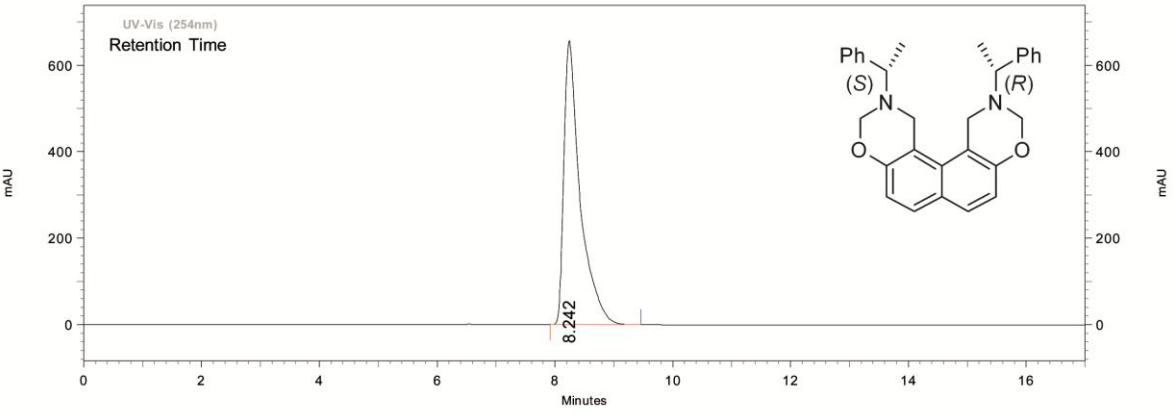
Method For HPLC Analysis

Solvent System: n-Hexane: *Iso*-propanol (60:40), Flow rate: 1ml/min., Injection vol.: 10 μL, Detector: UV-Vis (λ max – 254 nm), Oven Temperature: 27 °C

Chiral Column: Diacel OD-H

2-((R)-1-phenylethyl)-11-((S)-1-phenylethyl)-1,2,3,10,11,12-hexahydronaphtho[1,2-e:8,7 e']bis([1,3]oxazine)[10c]:





UV-Vis (254nm)

Name	Retention Time	Area	Theoretical plates	Resolution	Area Percent
	8.242	12587054	0.00	0.00	100.00
Totals		12587054			100.00

Method For HPLC Analysis

Solvent System: n-Hexane: *Iso*-propanol (98:2), Flow rate: 1ml/min., Injection vol.: 20 μL, Detector: UV-Vis (λ max – 254 nm), Oven Temperature: 27 °C

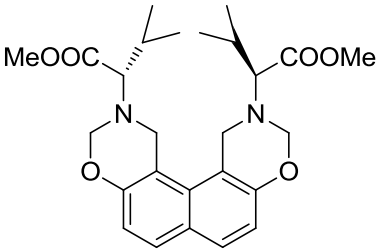
Chiral Column: Diacel AD-H (Instrument - Shimadzu CLASS-VP V 6.14)

X-ray Crystal Data

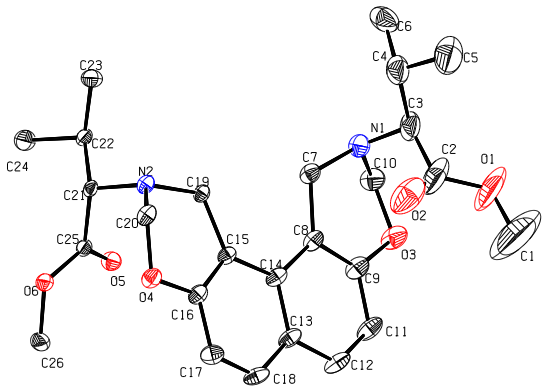
Crystal Data for Compound 11 (CCDC-882285)

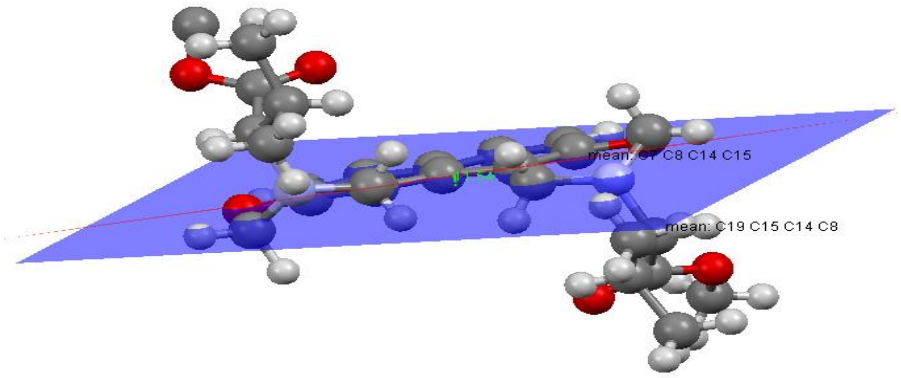
Details	**Compound 11**
Empirical formula	$C_{26}H_{31}N_2O_6$
Formula weight	467.53
Temperature	110(2) K
Wavelength	0.71073 Å
Crystal system	Tetragonal
Space group	P43
Unit cell dimensions	a = 17.0527(7) Å b = 17.0527(7) Å c = 8.4671(7) Å α = 90° β = 90° γ = 90°
Volume	2462.2(2) $Å^3$
Z	4
Density (calculated)	1.261 Mg/m^3
Absorption coefficient (μ)	0.090 mm^{-1}
F(000)	996
Crystal Size	0.43x0.37x0.29 mm
θ range for data collection	1.69-28.28º
Reflections collected	14632
Independent reflections	5685 [R(int) = 0.0294]
Max. and Min. transmission	0.9744 and 0.9624
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5685 / 1 / 409
Goodness-of-fit on F^2	1.081
Final R indices [I>2sigma(I)]	R1 = 0.0669 wR2 = 0.1597
R indices (all data)	R1 = 0.0751 wR2 = 0.1650
Largest difference peak and hole	0.624 and - 0.217 e/ $Å^3$

Structure of the compound **11**.



ORTEP Diagram of compound **11** with the atomic numbering scheme. Ellipsoids are drawn at the 30% probability level for non-H atoms, and the H atoms are omitted for clarity.





The measurement of the plane showing the twist in the conformations of oxazines, angle between the planes passing through the C7-C8-C14-C15 and C19-C15-C14-C8 is near about 11.54°.

References

1. Chylinska, J. B., Urbanski, T., Mordarski, M., *J. Med. Chem.* **1963**, *6*, 484
2. Shen, S. B., Ishida, H., *J. Appl. Poly. Sci.*, **1996**, 61, 1595.