EXPERIMENTAL

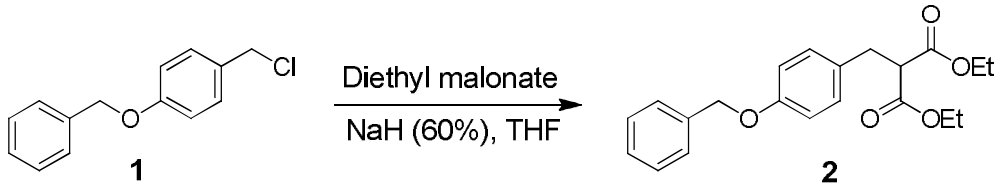
5 Experimental

5.1 Chemistry

5.1.1 Materials and Methods

Reagents were obtained from commercial suppliers and used without further purification. Solvents were procured from commercial source and used after distilling or drying according to the known methods. All the air and / or moisture sensitive reactions were carried out in dry solvents under nitrogen atmosphere. Melting points were recorded in open glass capillaries, using a scientific melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu FT IR 8300 spectrophotometer (νmax in cm^{-1}, as film for liquids and as KBr pellets for solid compounds). The ^{1}H NMR spectra were recorded on a Bruker Avance-300 (300 MHz) or Bruker Avance-400 (400 MHz) spectrometer. The chemical shifts (δ) are reported in parts per million (ppm) relative to TMS, either in $CDCl_3$ or DMSO-d_6. Signal multiplicities are represented as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), bs (broad singlet) and m (multiplet). D_2O exchange experiments were carried out to confirm the exchangeable protons when present. ^{13}C NMR spectra were recorded on Bruker Avance-400 at 100 MHz either in $CDCl_3$ or DMSO-d_6. Mass spectra (ESI-MS) were obtained on Shimadzu LCMS 2010-A spectrometer. Elemental analyses were carried out using a Perkin-Elmer 2400 CHN analyzer. HPLC analyses were carried out at λ_{max} 220 nm using column ODS C-18, 150nm * 4.6 nm * 4 μ on AGILENT 1100. Progress of the reactions was monitored by TLC using precoated TLC plates (E. Merck Kieselgel 60 F254) and the spots were visualized by UV and / or iodine vapors. The chromatographic purification was performed on silica gel (230–400 mesh).

5.1.2 Diethyl-2-(4-benzyloxybenzyl)-malonate (2)



1 2

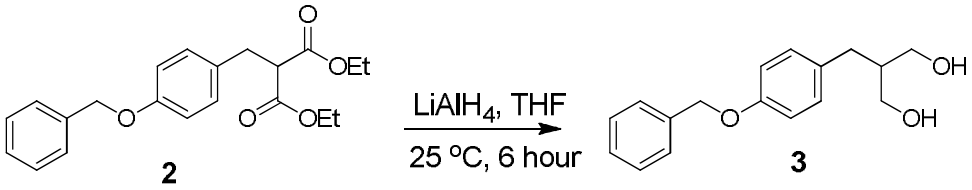
To an ice-cold suspension of NaH (60%, 178 gm, 3.7 mol) in THF (1000 ml), diethyl malonate (704 ml, 4.66 mol) was added dropwise over a period of 30 min at 0-10 °C and stirred at the same temperature for further 30 min. A solution of 4-benzyloxybenzyl chloride (434 gm, 1.864 mol) in THF (500 ml) was added to the reaction mixture at 0-10 °C and stirred at 25 °C for 14 hours. The reaction mixture was poured into ice cold water (2000 ml) and extracted with ethyl acetate (3 x 1000 ml). The combined organic layer was successively washed with water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum. Excess diethyl malonate was distilled out under vacuum to give title compound **2** (525 gm, 79%) as a thick liquid. Purity by HPLC: 90.0%.

IR (Neat) **:** 3020, 2983, 2939, 1728, 1610, 1512, 1371, 1217, 1153, 1033 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.20 (t, *J* = 7.1 Hz, 3H), 1.28 (t, *J* = 6.9 Hz, 3H), 3.15 (d, *J* = 7.7 Hz, 2H), 3.59 (t, *J* = 7.9 Hz, 1H), 4.08-4.24 (m, 4H), 5.03 (s, 2H), 6.88 (d, *J* = 8.55 Hz, 2H), 7.12 (d, *J* = 8.49 Hz, 2H), 7.31-7.43 (m, 5H)

ESI/MS (m/z) **:** 357.2 $(M+H)^+$

5.1.3 2-(4-Benzyloxybenzyl)-propane-1,3-diol (3)



2 3

To a solution of **2** (6.0 gm, 0.0175 mol) in THF (100 ml), $LiAlH_4$ (1.33 gm, 0.035 mol) was added in small portions at 0 °C over a period of 30 min. and stirred at 25 °C for 6 hours. The excess $LiAlH_4$ was quenched by dropwise addition of

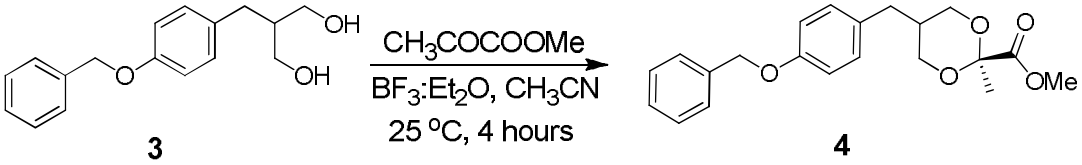
saturated aqueous Na_2SO_4 solution at 0-10 °C. Solid residue was filtered and washed with hot ethyl acetate. Filtrate was concentrated under vacuum. Crude product so obtained was triturated with diisopropyl ether to give title compound **3** (1.76 gm, 39.0%) as a white solid. m.p: 130-132 °C; Purity by HPLC: 98.3%.

IR (KBr) **:** 3381, 3064, 2922, 2868, 1635, 1514, 1442, 1386, 1245, 1174, 748 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.99-2.06 (m, 3H), 2.57 (d, *J* = 7.5 Hz, 2H), 3.67 (dd, *J* = 10.4 & 7.0 Hz, 2H), 3.74 (dd, *J* = 10.5 & 3.9 Hz, 2H), 5.04 (s, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 2H), 7.29-7.44 (m, 5H)

ESI/MS (m/z) **:** 273.2 $(M+H)^+$

5.1.4 Methyl-5-(4-benzyloxybenzyl)-2-methyl-1,3-dioxane-2-carboxylate (4)

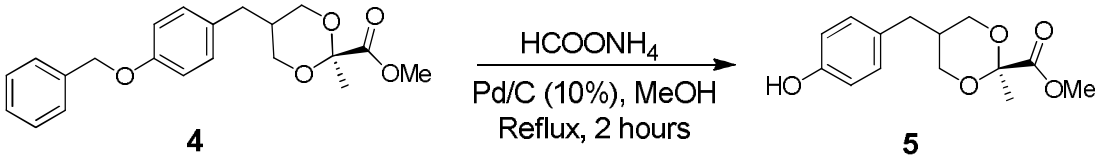


3 **4**

To a solution of **3** (1.05 gm, 3.86 mmol) and methyl pyruvate (1.14 ml, 15.5 mmol) in acetonitrile (15 ml), BF_3:OEt_2 (98%) (0.98 ml, 7.7 mmol) was added dropwise at 25 °C and stirred at the same temperature for 4 hours. The reaction mixture was poured into an ice-cold saturated aqueous sodium bicarbonate solution (50 ml) and extracted with ethyl acetate (3 X 20 ml). Combined organic extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to give thick liquid containing mixture of *cis* and *trans* isomers (1.04 gm, 76%). Separation of these isomers by column chromatography was unsuccessful and the mixture was subjected to debenzylation as described in the following procedure.

ESI/MS (m/z) **:** 357.2 $(M+H)^+$

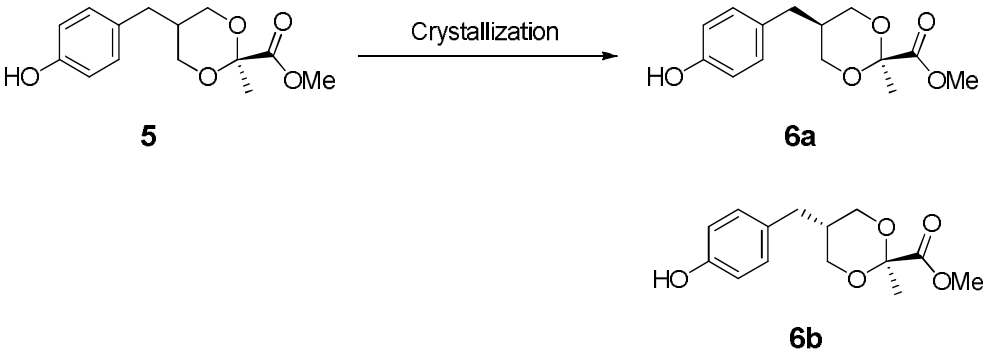
5.1.5 Methyl-5-(4-hydroxybenzyl)-2-methyl-1,3-dioxane-2-carboxylate. (5)



4 **5**

To a suspension of Pd/C (10%) (500 mg) in MeOH (25 ml), a solution of **4** (5.0 gm, 0.014 mol) in MeOH (100 ml) and ammonium formate (3.52 gm, 0.056 mol) was added and refluxed for 2 hours. The Reaction mixture was cooled to room temperature, filtered through celite and solvent was removed under vacuum. The residue was dissolved in ethyl acetate (50 ml), successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to give title product **5** (3.55 mg, 95%).

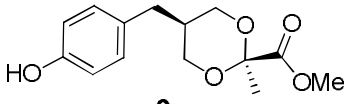
5.1.6 Preparation of the compounds 6a-b.



5 **6a**

6b

5.1.6.1 Methyl-*c*-5-(4-hydroxybenzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (6a)



6a

The mixture of isomers **5** (3.55 gm, 95.0 %) obtained in the previous experiment was subjected to crystallization from a mixture of ethyl acetate and hexane (1:2). The first crop yielded pure *cis* isomer **6a** (1.72 gm, 46%) as a white solid. m.p: 119-120 °C; Purity by HPLC: 99.7%.

IR (KBr) **:** 3402, 2933, 2866, 1722, 1612, 1514, 1373, 1244, 1186, 1035 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.50 (s, 3H), 2.27 (s, 3H), 3.46 (t, *J* = 10.9 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 11.8 & 3.3 Hz, 2H), 5.13 (s, 1H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 2.3 Hz, 2H)

^{13}C NMR (DMSO-d6) **:** δ 25.66, 32.79, 34.89, 52.29, 67.25, 97.76, 115.14, 128.28, 129.49, 155.62, 170.44

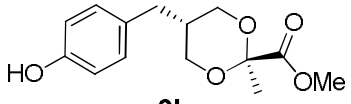
ESI/MS (m/z) **:** 288.9 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{14}H_{18}O_5$

Calculated **:** C, 63.15%; H, 6.81%

Found **:** C, 63.22%; H, 6.78%

5.1.6.2 Methyl-*t*-5-(4-hydroxybenzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (6b)



6b

The filtrate from crystallization experiment on subjecting to further crystallizations from a mixture of ethyl acetate and hexane (1:1) for two times, gave the *trans* isomer **13c** (1.12 gm, 30%) as a white solid. m.p: 62-64 °C; Purity by HPLC: 97.7%.

IR (KBr) **:** 3373, 2972, 2866, 1710, 1614, 1517, 1442, 1265, 1211, 1145, 1055, 956 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.51-1.57 (m, 1H), 1.59 (s, 3H), 2.93 (d, *J* = 8.0 Hz, 2H), 3.76 (d, *J* = 12.0 Hz, 2H), 3.84 (s, 3H), 3.93 (dd, *J* = 10.8 & 1.6 Hz, 2H), 5.02 (s, 1H), 6.77 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H)

^{13}C NMR (DMSO-d_6) **:** δ 25.64, 33.85, 34.39, 52.23, 65.06, 97.97, 115.15, 129.89, 130.16, 155.56, 170.59

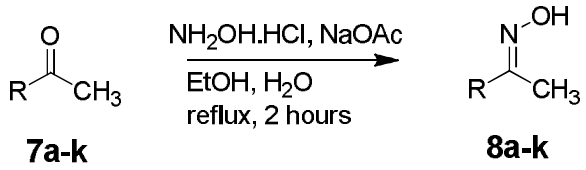
ESI/MS (m/z) **:** 288.9 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{14}H_{18}O_5$

Calculated : C, 63.15%; H, 6.81%

Found : C, 63.48%; H, 6.81%

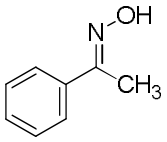
5.1.7 General procedure for the preparation of the compounds 8a-k.



7a-k **8a-k**

To a solution of **7a-k** (1 mole equivalent) in ethanol (10 fold) was added a mixed solution of hydroxylammonium chloride (2 mole equivalent) and sodium acetate (2 mole equivalent) in water (10 fold) and the reaction mixture was refluxed for 2 hours. Reaction mixture was cooled to 30 °C and ethanol was distilled out under vacuum. The residue was poured into water and extracted with ethyl acetate. Combined organic extracts were successively washed with water and brine, dried over sodium sulphate, filtered and concentrated under vacuum to yield the desired products **8a-k**.

5.1.7.1 (*E*)-Acetophenone oxime. (8a)



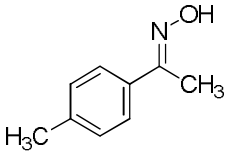
8a (5.29 gm, 94.0%) was prepared from **7a** (5.00 gm, 0.04126 mol) following the general procedure described above as a white solid. m.p: 56 °C; Purity by HPLC: 99.6%.

IR (KBr) : 3298, 3213, 3059, 2924, 1643, 1496, 1444, 1369, 1300, 1078, 1004 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.30 (s, 3H), 7.36-7.41 (m, 3H), 7.60-7.65 (m, 2H), 8.40 (s, 1H)

ESI/MS (m/z) : 135.8 $(M+H)^+$

5.1.7.2 (*E*)-1-(p-Tolyl)ethanone oxime. (8b)



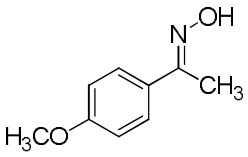
8b (5.45 gm, 98.0%) was prepared from **7b** (5.00 gm, 0.03726 mol) following the general procedure described above as a white solid. m.p: 71 °C; Purity by HPLC: 99.0%.

IR (KBr) **:** 3222, 3031, 2918, 1610, 1514, 1413, 1010, 748 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.27 (s, 3H), 2.36 (s, 3H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 8.51 (bs, 1H)

ESI/MS (m/z) **:** 149.9 $(M+H)^+$

5.1.7.3 (*E*)-1-(4-Methoxyphenyl)ethanone oxime. (8c)



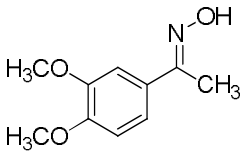
8c (5.17 gm, 94.0%) was prepared from **7c** (5.00 gm, 0.03129 mol) following the general procedure described above as a white solid. mp: 81-82 °C; Purity by HPLC: 99.4%.

IR (KBr) **:** 3242, 3072, 2908, 1606, 1512, 1460, 1311, 1249, 1118, 1012 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.27 (s, 3H), 3.83 (s, 3H), 6.89-6.92 (m, 2H), 7.55-7.60 (m, 2H), 8.43 (s, 1H)

ESI/MS (m/z) **:** 178.8 $(M+NH_4)^+$

5.1.7.4 (*E*)-1-(3,4-Dimethoxyphenyl)ethanone oxime. (8d)



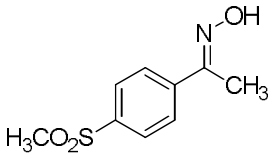
8d (2.87 gm, 88.3%) was prepared from **7d** (3.0 gm, 0.01665 mol) following the general procedure described above as a white solid. m.p: 79-80 °C; Purity by HPLC: 98.3%.

IR (KBr) **:** 3431, 3012, 2844, 1602, 1504, 1413, 1296, 1149, 1080 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 2.27 (s, 3H), 3.90 (s, 3H), 3.92 (s, 3H), 6.86 (d, *J* = 8.37 Hz, 1H), 7.15 (dd, *J* = 8.34 & 1.95 Hz, 2H), 8.24 (broad singlet, 1H)

ESI/MS (m/z) **:** 195.9 $(M+H)^+$

5.1.7.5 (*E*)-1-(4-(Methylsulfonyl) phenyl)ethanone oxime. (8e)



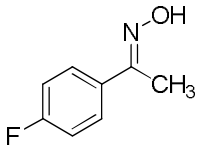
8e (4.98 gm, 93.0%) was prepared from **7e** (5.0 gm, 0.02334 mol) following the general procedure described above as a white solid. m.p: 139-140 °C; Purity by HPLC: 96.5%.

IR (KBr) **:** 3249, 3006, 2924, 1593, 1467, 1398, 1298, 1184, 1095, 929 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 2.31 (s, 3H), 3.07 (s, 3H), 7.82 (d, *J* = 8.6 Hz, 2H), 7.95 (d, *J* = 8.6 Hz, 2H), 8.25 (s, 1H)

ESI/MS (m/z) : 212.5 $(M-H)^+$

5.1.7.6 (*E*)-1-(4-Fluorophenyl)ethanone oxime. (8f)



8f (1.77 gm, 80.0%) was prepared from **7f** (2.0 gm, 0.01448 mol) following the general procedure described above as an off white solid. m.p: 64 °C; Purity by HPLC: 96.0%.

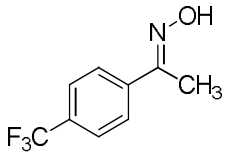
IR (KBr) **:** 3222, 3068, 2929, 1651, 1602, 1512, 1373, 1234, 1159, 1010 cm^{-1}

^{1}H NMR **:** δ 2.28 (s, 3H), 7.04-7.10 (m, 2H), 7.57-7.64 (m, 2H), 8.68 (s,

($CDCl_3$) 1H)

ESI/MS (m/z) **:** 175.5 $(M+ Na)^+$

5.1.7.7 (*E*)-1-(4-(Trifluoromethyl) phenyl)ethanone oxime. (8g)



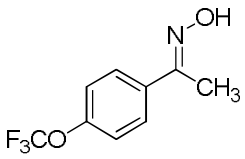
8g (4.54 gm, 84.0%) was prepared from **7g** (5.0 gm, 0.02658 mol) following the general procedure described above as an off white solid. m.p: 96 ^oC; Purity by HPLC: 99.1%.

IR (KBr) **:** 3267, 2931, 1618, 1407, 1326, 1159, 1114, 1062, 1008, 925, 844, 752 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 2.29 (s, 3H), 7.55 (s, 1H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H)

ESI/MS (m/z) **:** 202.0 $(M-H)^+$

5.1.7.8 (*E*)-1-(4-(Trifluoromethoxy) phenyl)ethanone oxime. (8h)



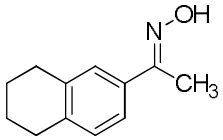
8h (4.83 gm, 90.0%) was prepared from **7h** (5.0 gm, 0.02449 mol) following the general procedure described above as an off white solid. m.p: 51-52 °C; Purity by HPLC: 99.5%.

IR (KBr) **:** 3250, 3136, 2929, 1602, 1508, 1373, 1311, 1174, 1008 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 2.29 (s, 3H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.64–7.68 (m, 2H), 8.43 (s, 1H)

ESI/MS (m/z) **:** 220.2 $(M+H)^+$

5.1.7.9 (*E*)-1-(5,6,7,8-Tetrahydronaphthalen-2-yl)ethanone oxime. (8i)



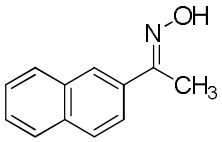
8i (3.0 gm, 92.0%) was prepared from **7i** (3.0 gm, 0.01722 mol) following the general procedure described above as an off white solid. m.p: 70 ^{o}C; Purity by HPLC: 96.6%.

IR (KBr) **:** 3199, 3058, 2835, 1635, 1568, 1504, 1284, 1136, 871 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.77-1.82 (m, 4H), 2.26 (s, 3H), 2.77-2.78 (m, 4H), 7.07 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 9.57 Hz, 2H), 7.95 (s, 1H)

ESI/MS (m/z) **:** 189.9 $(M+H)^{+}$

5.1.7.10 (*E*)-1-(Naphthalen-2-yl)ethanone oxime. (8j)



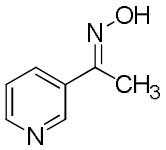
8j (5.39 gm, 99.0%) was prepared from **7j** (5.00 gm, 0.02938 mol) following the general procedure described above as an off white solid. m.p: 157-158 ^{o}C; Purity by HPLC: 99.0%.

IR (KBr) **:** 3209, 3055, 2904, 1502, 1415, 1384, 1197, 1018, 958 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 2.33 (s, 3H), 7.46-7.50 (m, 2H), 7.78-7.90 (m, 4H), 8.03 (s, 1H)

ESI/MS (m/z) **:** 185.9 $(M+H)^{+}$

5.1.7.11 (*E*)-1-(Pyridin-3-yl)ethanone oxime. (8k)



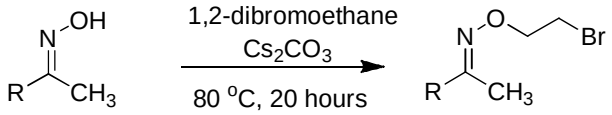
8k (4.32 gm, 48.0%) was prepared from **7k** (8.0 gm, 0.06658 mol) following the general procedure described above as an off white solid. m.p: 128-130 ^{o}C; Purity by HPLC: 99.0%.

IR (KBr) : 3165, 3055, 2786, 1647, 1510, 1407, 1363, 1309, 1190, 1128, 1049, 1008, 935 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.30 (s, 3H), 7.30-7.34 (m, 1H), 7.95 (dd, *J* = 8.01 & 2.1 Hz, 1H), 8.61 (dd, *J* = 4.83 & 1.59 Hz, 1H), 8.93 (d, *J* = 2.13 Hz, 1H), 9.03 (s, 1H)

ESI/MS (m/z) : 136.8 $(M+H)^+$

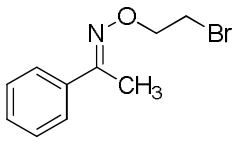
5.1.8 General procedure for the preparation of the compounds 9a-k.



8a-k **9a-k**

To a solution of **8a-k** (1 mole equivalent) in 1,2-dibromoethane (10 fold) was added cesium carbonate (3 mole equivalent) under nitrogen atmosphere and the reaction mixture was heated at 80 °C for 20 hours. Reaction mixture was filtered and the solvent was evaporated under vaccum. The residue was dissolved in ethyl acetate and successively washed with water and brine, dried over sodium sulfate, filtered and concentrated under vacuum to yield the desired product **9a-k**.

5.1.8.1 (*E*)-Acetophenone O- (2-bromoethyl) oxime. (9a)



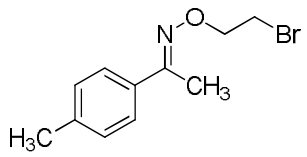
9a (1.02 gm, 19.0%) was prepared from **8a** (3.0 gm, 0.0220 mol) following the general procedure described above as a thick oil. Purity by HPLC: 97.9%.

IR (CHCl$_3$) : 3016, 2974, 1629, 1444, 1385, 1097, 1011, 889 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.27 (s, 3H), 3.62 (t, *J* = 6.4 Hz, 2H), 4.45 (t, *J* = 6.4 Hz, 2H), 7.35-7.39 (m, 3H), 7.62-7.65 (m, 2H)

ESI/MS (m/z) : 241.95 $(M+H)^+$

5.1.8.2 (*E*)-1-(p-Tolyl)ethanone O-(2-bromoethyl) oxime. (9b)



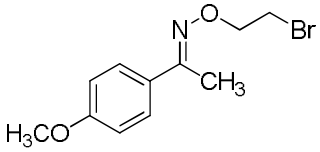
9b (1.46 gm, 34.0%) was prepared from **8b** (2.5 gm, 0.01676 mol) following the general procedure described above as a thick oil. Purity by HPLC: 98.1%.

IR ($CHCl_3$) **:** 3018, 2924, 2872, 1736, 1618, 1514, 1385, 1097, 1010, 887 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 2.24 (s, 3H), 2.36 (s, 3H), 3.61 (t, *J* = 6.4 Hz, 2H), 4.43 (t, *J* = 6.8 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H)

ESI/MS (m/z) **:** 256.17 $(M+H)^+$

5.1.8.3 (*E*)-1-(4-Methoxyphenyl)ethanone O-(2-bromoethyl) oxime. (9c)



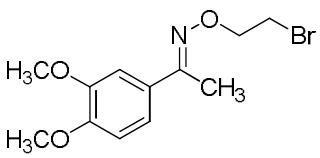
9c (1.19 gm, 29.1%) was prepared from **8c** (2.50 gm, 0.01513 mol) following the general procedure described above as an off white solid. m.p: 50-51 °C; Purity by HPLC: 99.7%.

IR (KBr) **:** 3012, 2935, 2839, 1606, 1514, 1463, 1369, 1319, 1178, 1031 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 2.24 (s, 3H), 3.61 (t, *J* = 6.36 Hz, 2H), 3.82 (s, 3H), 4.43 (t, *J* = 6.45 Hz, 2H), 6.87-6.91 (m, 2H), 7.57-7.61(m, 2H)

ESI/MS (m/z) **:** 273.7 $(M+H)^+$

5.1.8.4 (*E*)-1-(3,4-Dimethoxyphenyl)ethanone O-(2-bromoethyl) oxime. (9d)



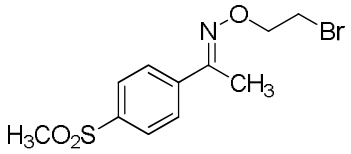
9d (2.21 gm, 95%) was prepared from **8d** (1.50 gm, 0.00768 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.1%.

IR ($CHCl_3$) **:** 3018, 2937, 1603, 1518, 1466, 1416, 1385, 1261, 1095, 1026, cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.24 (s, 3H), 3.62 (t, *J* = 6.4 Hz, 2H), 3.90 (s, 3H), 3.92 (s, 3H), 4.45 (t, *J* = 6.4 Hz, 2H), 6.86 (dd, *J* = 8.4 & 4.0 Hz, 1H), 7.15 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.27 (d, *J* = 2.0 Hz, 1H)

ESI/MS (m/z) **:** 302.1 $(M+H)^+$

5.1.8.5 (*E*)-1-(4-Methylsulfonylphenyl)ethanone O-(2-bromoethyl) oxime. (9e)



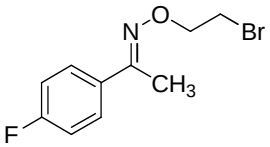
9e (1.53 gm, 34.0%) was prepared from **8e** (3.0 gm, 0.01407 mol) following the general procedure described above as a white solid. m.p: 87-88 °C; Purity by HPLC: 99.6%.

IR (KBr) **:** 3288, 2947, 2926, 1637, 1593, 1452, 1396, 1309, 1147, 1031, 893 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.30 (s, 3H), 3.06 (s, 3H), 3.62 (t, *J* = 6.4 Hz, 2H), 4.50 (t, *J* = 6.0 Hz, 2H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.94 (d, *J* = 8.4 Hz, 2H)

ESI/MS (m/z) **:** 320.15 $(M+H)^+$

5.1.8.6 (*E*)-1-(4-Fluorophenyl)ethanone O-(2-bromoethyl) oxime. (9f)



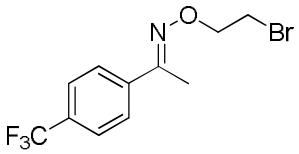
9f (2.14 gm, 84.0%) was prepared from **8f** (1.50 gm, 0.00979 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 89.6%.

IR ($CHCl_3$) **:** 3018, 2974, 2940, 1655, 1603, 1512, 1421, 1369, 1317, 1286, 1159, 1096, 1053, 1028, 930 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.25 (s, 3H), 3.61 (t, *J* = 6.4 Hz, 2H), 4.44 (t, *J* = 6.4 Hz, 2H), 7.03-7.08 (m, 2H), 7.61-7.65 (m, 2H)

ESI/MS (m/z) **:** 260.18 $(M+H)^+$

5.1.8.7 (*E*)-1-(4-Trifluoromethylphenyl)ethanone O-(2-bromoethyl) oxime. (9g)



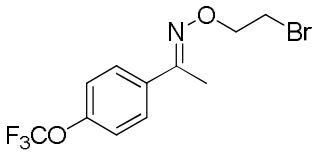
9g (1.77 gm, 58%) was prepared from **8g** (2.0 gm, 0.00984 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.2%.

IR ($CHCl_3$) **:** 3018, 2941, 2874, 1610, 1500, 1408, 1327, 1215, 1170, 1130, 1062, 1010, 895 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.28 (s, 3H), 3.62 (t, *J* = 6.4 Hz, 2H), 4.48 (t, *J* = 6.4 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) **:** 310.25 $(M+H)^+$

5.1.8.8 (*E*)-1-(4-Trifluoromethoxyphenyl) ethanone O-(2-bromoethyl) oxime. (9h)



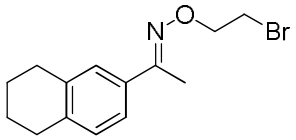
9h (1.37 gm, 46.0%) was prepared from **8h** (2.0 gm, 0.00913 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.7%.

IR ($CHCl_3$) **:** 3105, 3072, 2902, 1674, 1654, 1437, 1385, 1261, 1078, 850 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.26 (s, 3H), 3.61(t, *J* = 6.4 Hz, 2H), 4.45 (t, *J* = 6.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.66 - 7.69 (m, 2H)

ESI/MS (m/z) **:** 326.02 $(M+H)^+$

5.1.8.9 (*E*)-1-(5,6,7,8-Tetrahydronaphthalen-2-yl)ethanone O-(2-bromoethyl) oxime. (9i)



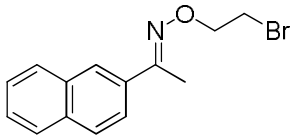
9i (1.49 gm, 38.0%) was prepared from **8i** (2.5 gm, 0.01321 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.2%.

IR ($CHCl_3$) **:** 3018, 2974, 2934, 1647, 1612, 1500, 1385, 1095, 1051, 939 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.78-1.81 (m, 4H), 2.23 (s, 3H), 2.77 (d, *J* = 6.0 Hz, 4H), 3.61 (t, *J* = 6.40 Hz, 2H), 4.43 (t, *J* = 6.4 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 2.8 Hz, 1H), 7.35 (s, 1H)

ESI/MS (m/z) **:** 296.17 $(M+H)^+$

5.1.8.10 (*E*)-1-(Naphthalen-2-yl)ethanone O-(2-bromoethyl) oxime.(9j)



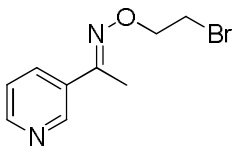
9j (1.00 gm, 26.0%) was prepared from **8j** (2.50 gm, 0.01321 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.5%.

IR ($CHCl_3$) **:** 3053, 2970, 2874, 1601, 1468, 1427, 1367, 1263, 1086, 1020, 928 cm^{-1}

^1HNMR ($CDCl_3$) **:** δ 2.38 (s, 3H), 3.66 (t, *J* = 6.4 Hz, 2H), 4.50 (t, *J* = 6.4 Hz, 2H), 7.47-7.51 (m, 2H), 7.80-7.91 (m, 4H), 8.00 (s, 1H)

ESI/MS (m/z) **:** 292.14 $(M+H)^+$

5.1.8.11 (*E*)-1-(Pyridin-3-yl)ethanone O-(2-bromoethyl) oxime. (9k)



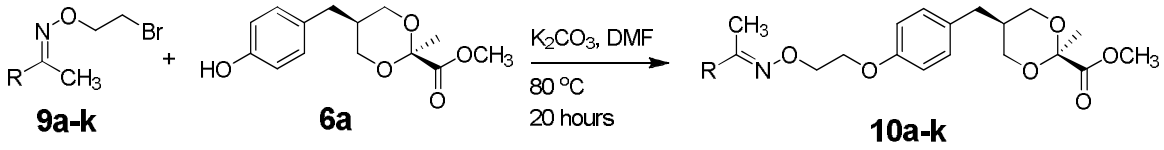
9k (1.37 gm, 22.0%) was prepared from **8k** (3.5 gm, 0.02571 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 86.7%.

IR ($CHCl_3$) : 3018, 2943, 1637, 1618, 1504, 1466, 1385, 1321, 1174, 1057, 927 cm^{-1}

^1H NMR ($CDCl_3$) : δ 2.28 (s, 3H), 3.62 (t, *J* = 6.4 Hz, 2H), 4.48 (t, *J* = 6.0 Hz, 2H), 7.31 (dd, *J* = 8.0 & 4.8 Hz, 1H), 7.94-7.97 (m, 1H), 8.60 (dd, *J* = 4.8 & 1.2 Hz, 1H), 8.87 (d, *J* = 2.4 Hz, 1H)

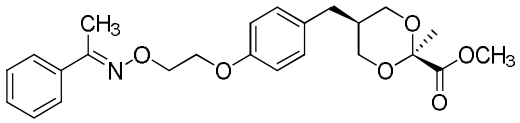
ESI/MS (m/z) : 244.0 $(M+H)^+$

5.1.9 General procedure for the preparation of the compounds 10a-k.



To a solution of 9a-**k** (1 mole equivalent) and **6a** (1 mole equivalent) in dry DMF (5 fold), K_2CO_3 (2 mole equivalent) was added and the reaction mixture was stirred at 80 °C for 20 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The combined organic extracts were successively washed with water and brine, dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography using 5-10% ethyl acetate in hexane as eleunt to furnish the pure compounds **10a-k**.

5.1.9.1 Methyl *c*-2-methyl-5-(4-(2-(((*E*)-(1-phenylethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (10a)



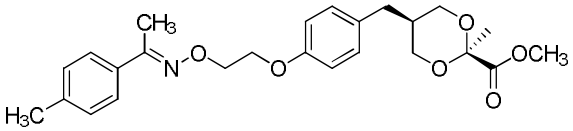
10a (918 mg, 52.0%) was prepared from **9a** (1.0 gm, 0.00413 mol) and **6a** (1.10 gm, 0.00413 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.4%.

IR ($CHCl_3$) **:** 3018, 2723, 1743, 1512, 1385, 1144, 1043, 929 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.24 (s, 3H), 2.27 (s, 3H), 3.46 (t, *J* = 10.8 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12 & 3.6 Hz, 2H), 4.25 (t, *J* = 5.2 Hz, 2H), 4.52 (t, *J* = 4.8 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.36 (dd, *J* = 4.0 & 2.0 Hz, 3H), 7.62 (dd, *J* = 7.6 & 3.6 Hz, 2H)

ESI/MS (m/z) **:** 428.29 $(M+H)^+$

5.1.9.2 Methyl *c*-2-methyl-5-(4-(2-(((*E*)-(1-phenylethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (10b)



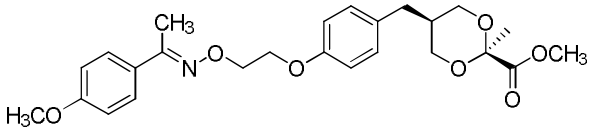
10b (1.14 gm, 66.0%) was prepared from **9b** (1.0 gm, 0.00390 mol) and **6a** (1.04 gm, 0.00390 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.0%.

IR ($CHCl_3$) **:** 3018, 2928, 1743, 1612, 1512, 1384, 1247, 1143, 1041, 929 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.22 (s, 3H), 2.24-2.30 (m, 3H), 2.35 (s, 3H), 3.46 (t, *J* = 10.8 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12 & 3.6 Hz, 2H), 4.24 (t, *J* = 5.2 Hz, 2H), 4.50 (t, *J* = 4.0 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) **:** 442.10 $(M+H)^+$

5.1.9.3 Methyl*c*-5-(4-(2-(((*E*)-(1-(4-methoxyphenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (10c)



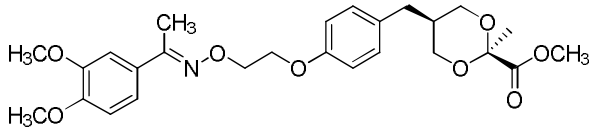
10c (1.56 gm, 93.0%) was prepared from **9c** (1.0 gm, 0.00367 mol) and **6a** (978.5 mg, 0.00367 mol) following the general procedure described above as a white solid; m.p: 71-72 ^{o}C; Purity by HPLC: 97.0%.

IR (KBr) **:** 2995, 2941, 2925, 2860, 1739, 1608, 1512, 1452, 1365, 1145, 1033 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.21 (s, 3H) , 2.27 (s, 3H), 3.46 (t, *J* = 10.9 Hz, 2H), 3.82 (s, 3H), 3.84 (s, 3H), 3.87 (dd, *J* =11.6 & 4.8 Hz, 2H), 4.24 (t, *J* = 5.04 Hz, 2H), 4.49 (t, *J* = 4.62 Hz, 2H), ,6.85-6.90 (m, 4H), 6.99 (d, *J* = 8.55 Hz, 2H), 7.58 (d, *J* = 8.82 Hz, 2H)

ESI/MS (m/z) **:** 458.1$(M+H)^{+}$

5.1.9.4 Methyl *c*-5-(4-(2-(((*E*)-(1-(3,4-dimethoxyphenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-2-*r*-carboxylate. (10d)



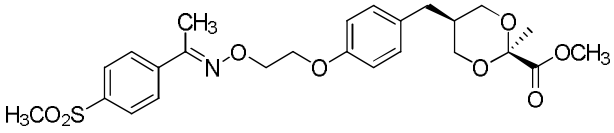
10d (984 mg, 61.0%) was prepared from **9d** (1.0 gm, 0.00331 mol) and **6a** (881 mg, 0.00331 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 99.0%.

IR ($CHCl_3$) **:** 3020, 2968, 2937, 2843, 1743, 1610, 1512, 1464, 1417, 1385, 1250, 1146, 1117, 1028 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.50 (s, 3H), 2.23 (s, 3H), 2.28 (s, 3H), 3.47 (t, *J* = 11.2 Hz, 2H), 3.85 (s, 3H), 3.87 (d, *J* = 3.2 Hz, 1H), 3.91 (s, 4H), 3.93 (s, 3H), 4.26 (t, *J* = 5.2 Hz, 2H), 4.52 (t, *J* = 4.8 Hz, 2H), 6.87 (t, *J* = 7.6 Hz, 3H), 7.01 (d, *J* = 8.4 Hz, 2H), 7.15 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.28 (dd, *J* = 6.4 & 2.0 Hz, 1H)

ESI/MS (m/z) **:** 488.23 $(M+Na)^{+}$

5.1.9.5 Methyl *c*-2-methyl-5-(4-(2-(((*E*)-(1-(4-methylsulfonylphenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (10e)



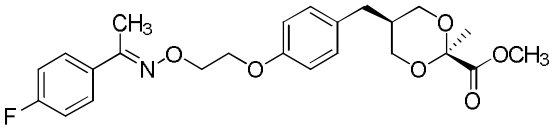
10e (1.15 mg, 73.0%) was prepared from **9e** (1.0 gm, 0.00312mol) and **6a** (831 mg, 0.00312 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 99.8%.

IR ($CHCl_3$) **:** 3020, 2930, 1743, 1595, 1512, 1385, 1317, 1153, 1041, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H) 2.24-2.29 (m, 6H), 3.05 (s, 3H), 3.43-3.49 (m, 2H), 3.84 (s, 3H), 3.87 (dd, *J* = 12.8 & 4.0 Hz, 2H), 4.26 (t, *J* = 4.8 Hz, 2H), 4.56 (t, *J* = 4.8 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.93 (dd, *J* = 8.4 & 2.0 Hz, 2H)

ESI/MS (m/z) **:** 528.1 $(M+Na)^+$

5.1.9.6 Methyl *c*-5-(4-(2-(((*E*)-(1-(4-fluorophenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (10f)



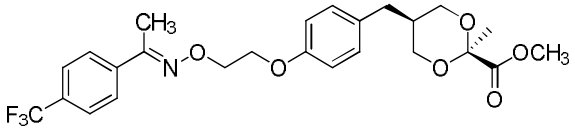
10f (1.34 mg, 78.0%) was prepared from **9f** (1.0 gm, 0.00384mol) and **6a** (1.02 gm, 0.00384 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 98.0%.

IR ($CHCl_3$) **:** 3018, 2928, 1743, 1600, 1512, 1385, 1144, 1041, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.22 (s, 3H), 2.27 (s, 3H), 3.46 (t, *J* = 11.2 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.4 & 4 Hz, 2H), 4.24 (t, *J* = 5.2 Hz, 2H), 4.51 (t, *J* = 4.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), 7.02-7.07 (m, 2H), 7.60-7.64 (m, 2H)

ESI/MS (m/z) **:** 464.9 $(M+K)^+$

5.1.9.7 Methyl-2-methyl-*c*-5-(4-(2-(((*E*)-(1-(4-trifluoromethylphenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (10g)



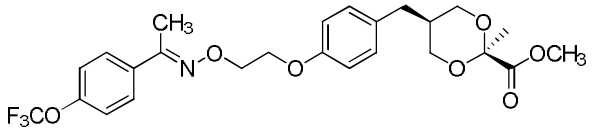
10g (782 mg, 49.0%) was prepared from **9g** (1.0 gm, 0.00322 mol) and **6a** (858 mg, 0.00322 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 99.5%.

IR ($CHCl_3$) **:** 3018, 2930, 1743, 1610, 1512, 1384, 1327, 1215, 1143, 1059, 929 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.25 (s, 3H), 2.27 (s, 3H), 3.43-3.48 (m, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.4 & 4.0 Hz, 2H), 4.25 (t, *J* = 5.2 Hz, 2H), 4.54 (t, *J* = 4.8 Hz, 2H), 6.87 (d, *J* = 9.2 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 6.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) **:** 518.16 $(M+Na)^+$

5.1.9.8 Methyl-2-methyl-*c*-5-(4-(2-(((*E*)-(1-(4-trifluoromethoxyphenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (10h)



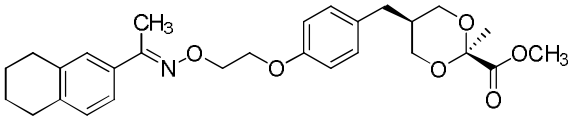
10h (1.14 gm, 73.0%) was prepared from **9h** (1.0 gm, 0.00307 mol) and **6a** (816 mg, 0.00307 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 98.5%.

IR ($CHCl_3$) **:** 3018, 2929, 2856, 1743, 1612, 1512, 1458, 1261, 1215, 1143, 1041, 927 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.49 (s, 3H), 2.23 (s, 3H), 2.27 (s, 3H), 3.43-3.49 (m, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.4 & 4.0 Hz, 2H), 4.24 (t, *J* = 5.2 Hz, 2H), 4.52 (t, *J* = 4.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.65-7.69 (m, 2H)

ESI/MS (m/z) **:** 512.20 $(M+H)^+$

5.1.9.9 Methyl-2-methyl-*c*-5-(4-(2-(((*E*)-(1-(5,6,7,8-tetrahydronaphthalen-2-yl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (10i)



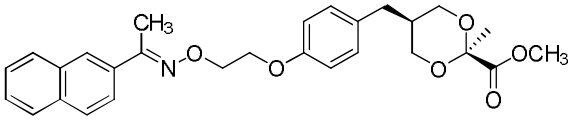
10i (1.14 gm, 70.0%) was prepared from **9i** (1.0 gm, 0.00338 mol) and **6a** (899.0 mg, 0.00338 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 99.0%.

IR (CHCl$_3$) **:** 3018, 2932, 1743, 1512, 1385, 1215, 1144, 1043 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.49 (s, 3H), 1.77-1.81 (m, 4H), 2.21 (s, 3H), 2.23-2.31 (m, 3H), 2.77 (d, *J* = 6.4 Hz, 4H), 3.46 (t, *J* = 11.2 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12 & 3.6 Hz, 2H), 4.24 (t, *J* = 4.8 Hz, 2H), 4.50 (t, *J* = 4.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 1H), 7.32-7.35 (m, 2H)

ESI/MS (m/z) **:** 504.22 $(M+Na)^+$

5.1.9.10 Methyl-2-methyl-*c*-5-(4-(2-(((*E*)-(1-(naphthalen-2-yl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (10j)



10j (1.13 gm, 69.0%) was prepared from **9j** (1.0 gm, 0.00342 mol) and **6a** (911.4 mg, 0.00342 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 95.2%.

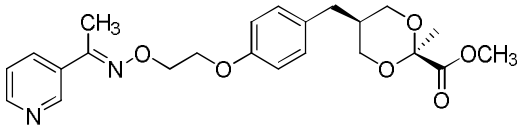
IR (CHCl$_3$) **:** 2943, 1749, 1605, 1514, 1450, 1363, 1275, 1244, 1188, 1111,

1058, 1031, 941 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.27 (s, 3H), 2.35 (s, 3H), 3.46 (t, *J* = 11.2 Hz, 2H), 3.83 (s, 3H), 3.88 (dd, *J* = 12 & 3.6 Hz, 2H), 4.29 (t, *J* = 4.8 Hz, 2H), 4.57 (t, *J* = 4.8 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.48-7.50 (m, 2H), 7.79-7.92 (m, 4H), 8.00 (s, 1H)

ESI/MS (m/z) : 500.18 $(M+Na)^+$

5.1.9.11 Methyl-2-methyl-*c*-5-(4-(2-(((*E*)-(1-(pyridin-3-yl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (10k)



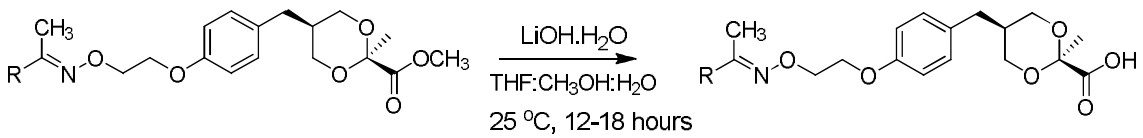
10k (1.06 gm, 60.0%) was prepared from **9k** (1.0 gm, 0.00411 mol) and **6a** (1.10 gm, 0.00411 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 99.0%.

IR ($CHCl_3$) : 3018, 2974, 2930, 1741, 1612, 1512, 1385, 1248, 1144, 1042, 928 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.26 (s, 3H), 2.27 (s, 3H), 3.43-3.49 (m, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.4 & 4.0 Hz, 2H), 4.25 (t, *J* = 4.8 Hz, 2H), 4.54 (t, *J* = 4.8 Hz, 2H), 6.86 (dd, *J* = 9.6 & 2.8 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.30 (dd, *J* = 8.0 & 4.8 Hz, 1H), 7.94-7.97 (m, 1H), 8.60 (d, *J* = 4.0 Hz, 1H), 8.87 (s, 1H)

ESI/MS (m/z) : 429.20 $(M+H)^+$

5.1.10 General procedure for the preparation of the compounds 11a-k.

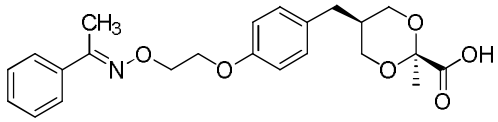


10a-k **11a-k**

To a solution of **10a-k** (1 mole equivalent) in THF (9 fold), MeOH (3 fold) and H_2O (3 fold), $LiOH.H_2O$ (2 mole equivalent) was added and stirred at 30 °C for 20

hours. The reaction mixture was concentrated under vacuum. Water was added to the reaction mixture, acidified by aq. HCl and extracted with ethyl acetate. The combined organic extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vaccum to yield the compounds **11a-k.**

5.1.10.1 2-Methyl-*c*-5-(4-(2-(((*E*)-(1-phenylethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (11a)



11a (783.42 mg, 90%) was prepared from **10a** (900 mg, 0.00211 mol) following the general procedure described above as a white solid. m.p: 82-84 °C; Purity by HPLC: 98.8%.

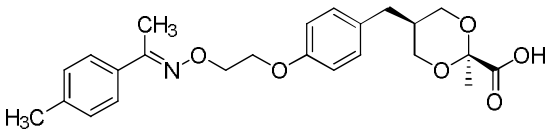
IR (KBr) **:** 3414, 3018, 2939, 2663, 2532, 1713, 1612, 1510, 1445, 1369, 1271, 1145, 959 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.55 (s, 3H), 2.24 (s, 3H), 2.27 -2.30 (m, 3H), 3.53 (t, *J* = 10.8 Hz, 2H), 3.93 (dd, *J* = 12.0 & 3.6 Hz, 2H), 4.25 (t, *J* = 5.2 Hz, 2H), 4.52 (t, *J* = 4.4 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 7.34-7.38 (m, 3H), 7.62-7.64 (m, 2H)

^{13}C NMR ($CDCl_3$) **:** δ 13.13, 25.93, 33.91, 35.21, 66.79, 68.30, 72.58, 98.22, 115.00, 126.24, 128.53, 129.29, 129.66, 130.13, 136.66, 155.77, 157.70, 175.21

ESI/MS (m/z) **:** 414.20 $(M+H)^+$

5.1.10.2 2-Methyl-*c*-5-(4-(2-(((*E*)-(1-(p-tolyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (11b)



11b (745 mg, 77.0%) was prepared from **10b** (1.0 gm, 0.00226 mol) following the general procedure described above as a white solid. m.p: 92-94 °C; Purity by HPLC: 99.7%.

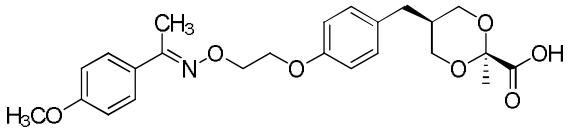
IR (KBr) : 3414, 3290, 2924, 2870, 1740, 1718, 1639, 1512, 1460, 1367, 1151, 1033, 655 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.55 (s, 3H), 2.22 (s, 3H), 2.30 (s, 3H), 2.35 (s, 3H), 3.52 (t, *J* = 10.4 Hz, 2H), 3.91 (d, *J* = 9.2 Hz, 2H), 4.24 (t, *J* = 4.8 Hz, 2H), 4.50 (t, *J* = 4.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (CDCl$_3$) : δ 13.08, 21.38, 25.91, 33.90, 35.19, 66.79, 68.27, 72.47, 98.23, 114.98, 126.12, 129.22, 129.64, 130.09, 133.80, 139.30, 155.73, 157.70, 174.83

ESI/MS (m/z) : 428.21 $(M+H)^+$

5.1.10.3 *c*-5-(4-(2-(((*E*)-(1-(4-Methoxyphenyl)ethylidene)amino)oxy)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (11c)



11c (1.35 gm, 93.0%) was prepared from **10c** (1.50 gm, 0.00328 mol) following the general procedure described above as an off white solid. m.p: 108-109 °C; Purity by HPLC: 98.8%.

IR (KBr) : 3348, 2995, 2852, 1764, 1720, 1606, 1512, 1369, 1190, 1035, 960 cm^{-1}

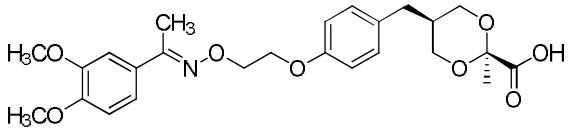
^{1}H NMR (CDCl$_3$) : δ 1.55 (s, 3H), 2.21 (s, 3H) , 2.26-2.30 (m, 3H), 3.52 (t, *J* = 10.56 Hz, 2H), 3.82 (s, 3H), 3.93 (dd, *J* = 12.35 & 5.2 Hz, 2H), 4.25 (t, *J* = 5.13 Hz, 2H), 4.49 (t, *J* = 4.71 Hz, 2H), 6.87 (dd, *J* = 8.82 & 5.25 Hz, 4H), 7.00 (d, *J* = 8.49 Hz, 2H), 7.59 (d, *J* = 8.85 Hz, 2H)

^{13}C NMR : δ 21.43, 21.58, 25.88, 29.83, 33.93, 35.34, 66.62, 68.20, 72.71,

($CDCl_3$) 98.22, 114.96, 128.04, 128.12, 128.25, 128.94, 129.07, 129.44, 129.63, 130.10, 130.24, 133.43, 133.73, 136.77, 139.06, 139.63, 157.64, 157.78, 175.00

ESI/MS (m/z) **:** 444.2 $(M+H)^+$

5.1.10.4 *c*-5-(4-(2-(((*E*)-(1-(3,4-Dimethoxyphenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (11d)



11d (562 mg, 61.0%) was prepared from **10d** (950 mg, 0.00195 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 99.0%.

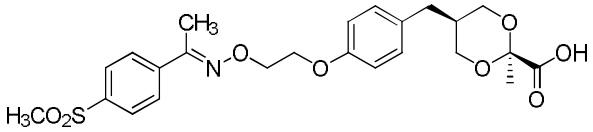
IR ($CHCl_3$) **:** 3385, 3018, 2937, 1739, 1610, 1512, 1406, 1249, 1147, 1057, 929, 869 cm^{-1}.

^{1}H NMR ($CDCl_3$) **:** δ 1.54 (s, 3H), 2.22 (s, 3H), 2.29 (s, 3H), 3.53 (t, *J* = 10.4 Hz, 2H), 3.90 (m, 8H), 4.24 (s, 2H), 4.50 (s, 2H), 6.83-6.87 (m, 3H), 6.99 (d, *J* = 7.2 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H)

^{13}C NMR ($CDCl_3$) **:** δ 12.98, 25.88, 33.90, 35.20, 56.02, 66.80, 68.22, 72.46, 98.30, 108.84, 110.70, 114.96, 119.37, 129.39, 129.64, 130.13, 148.91, 150.23, 155.33, 157.68, 174.81

ESI/MS (m/z) **:** 474.2 $(M+H)^+$

5.1.10.5 2-Methyl-*c*-5-(4-(2-(((*E*)-(1-(4-methylsulfonylphenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (11e)



11e (684 mg, 64.0%) was prepared from **10e** (1.10 gm, 0.00218 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.6%.

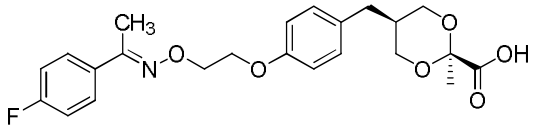
IR ($CHCl_3$) : 3450, 3020, 2976, 1724, 1610, 1512, 1385, 1317, 1246, 1153, 1041, 955 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.54 (s, 3H), 2.26 (s, 3H), 2.28-2.32 (m, 3H), 3.06 (s, 3H) 3.52 (t, *J* = 10.8 Hz, 2H), 3.89 (dd, *J* = 12.8 & 4.4 Hz, 2H), 4.26 (t, *J* = 4.8 Hz, 2H), 4.56 (t, *J* = 4.8 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 8.4 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 12.85, 25.89, 33.86, 35.20, 44.61, 66.65, 68.23, 73.09, 98.26, 114.94, 127.00, 127.60, 129.68, 130.29, 140.65, 141.81, 153.83, 157.54, 174.60

ESI/MS (m/z) : 491.73 $(M+H)^+$

5.1.10.6 *c*-5-(4-(2-(((*E*)-(1-(4-Fluorophenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (11f)



11f (836 mg, 72.0%) was prepared from **10f** (1.20 gm, 0.00269 mol) following the general procedure described above as a white solid; m.p: 80-81°C; Purity by HPLC: 97.9%.

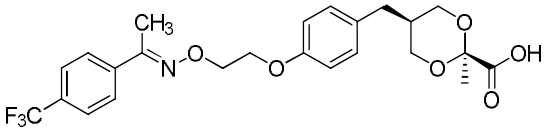
IR (KBr) : 3350, 3061, 2935, 2866, 1739, 1610, 1512, 1371, 1240, 1105, 935, 837 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.22 (s, 3H,), 2.24-2.32 (m, 3H), 3.53 (t, *J* = 10.8 Hz, 2H), 3.91 (dd, *J* = 12.4 & 4 Hz, 2H), 4.24 (t, *J* = 5.2 Hz, 2H), 4.51 (t, *J* = 4.4 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 7.02-7.07 (m, 2H), 7.60-7.65 (m, 2H)

^{13}C NMR ($CDCl_3$) : δ 13.08, 25.94, 33.90, 35.21, 66.75, 68.31, 72.62, 98.20, 114.98, 115.37, 115.59, 128.01, 129.67, 130.15, 132.75, 154.70, 157,68, 162.29, 164.76, 175.21

ESI/MS (m/z) : 432.26 $(M+H)^+$

5.1.10.7 2-Methyl-*c*-5-(4-(2-(((*E*)-(1-(4-trifluoromethylphenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (11g)



11g (476 mg, 70.0%) was prepared from **10g** (700 mg, 0.00141 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.5%.

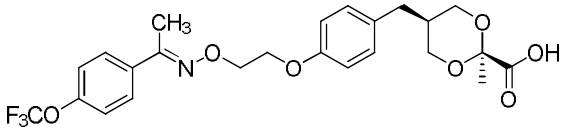
IR ($CHCl_3$) : 3580, 3018, 2976, 2930, 1724, 1610, 1512, 1458, 1385, 1327, 1215, 1130, 1059, 930 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.25 (s, 3H,), 2.30 (s, 3H), 3.53 (t, *J* = 10.8 Hz, 2H), 3.91 (dd, *J* = 9.6 & 4.0 Hz, 2H), 4.25 (t, *J* = 4.8 Hz, 2H), 4.54 (t, *J* = 4.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.8 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 12.92, 25.90, 33.92, 35.21, 66.71, 68.29, 72.92, 98.22, 114.97, 125.44, 126.48, 129.69, 130.22, 139.97, 154.34, 157.64, 174.38

ESI/MS (m/z) : 482.18 $(M+H)^+$

5.1.10.8 2-Methyl-*c*-5-(4-(2-(((*E*)-(1-(4-trifluoromethoxyphenyl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (11h)



11h (544 mg, 56.0%) was prepared from **10h** (1.0 gm, 0.00196 mol) following the general procedure described above as a white solid; m.p: 68-70 °C; Purity by HPLC: 98.5%.

IR (KBr) : 3550, 3149, 2934, 2868, 1736, 1610, 1512, 1452, 1371, 1249, 1157, 1103, 949, 748 cm^{-1}

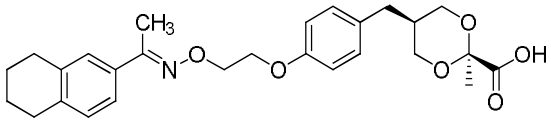
^{1}H NMR : δ 1.55 (s, 3H), 2.23 (s, 3H), 2.25-2.31 (m, 3H), 3.53 (t, *J* = 10.8

($CDCl_3$) Hz, 2H), 3.93 (dd, *J* = 14 & 4.0 Hz, 2H), 4.25 (t, *J* = 5.2 Hz, 2H), 4.52 (t, *J* = 4.8 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.8 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 12.99, 25.94, 33.88, 35.20, 66.71, 68.32, 72.75, 98.19, 114.97, 119.25, 120.87, 121.81, 127.70, 129.67, 130.19, 135.23, 149.91, 154.40, 157.64, 174.38

ESI/MS (m/z) : 498.18 $(M+H)^+$

5.1.10.9 2-Methyl-*c*-5-(4-(2-(((*E*)-(1-(5,6,7,8-tetrahydronaphthalen-2-yl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (11i)



11i (790 mg, 74.0%) was prepared from **10i** (1.10 gm, 0.00228 mol) following the general procedure described above as a thick oil. Purity by HPLC: 99.5%.

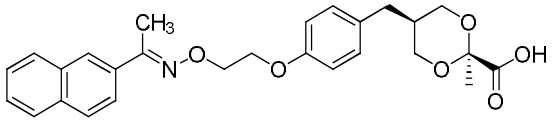
IR ($CHCl_3$) : 3448, 3300, 3018, 2932, 1724, 1512, 1385, 1246, 1145, 1041, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.55 (s, 3H), 1.77-1.80 (m, 4H), 2.21 (s, 3H), 2.26-2.30 (m, 3H), 2.76 (d, *J* = 6.0 Hz, 4H), 3.52 (t, *J* = 10.8 Hz, 2H), 3.92 (dd, *J* = 14.4 & 4.0 Hz, 2H), 4.24 (t, *J* = 4.8 Hz, 2H), 4.51 (t, *J* = 4.8 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 1H), 7.32-7.35 (m, 2H)

^{13}C NMR ($CDCl_3$) : δ 13.16, 23.25, 25.86, 29.37, 29.59, 33.93, 35.18, 60.82, 68.27, 72.43, 98.21, 114.99, 123.36, 126.85, 129.28, 129.63, 130.04, 133.85, 137.28, 137.47, 138.64, 155.96, 157.73, 174.81

ESI/MS (m/z) : 468.34 $(M+H)^+$

5.1.10.10 2-Methyl-*c*-5-(4-(2-(((*E*)-(1-(naphthalen-2-yl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (11j)



11j (514 mg, 53.0%) was prepared from **10j** (1.00 gm, 0.00208 mol) following the general procedure described above as a white solid; m.p: 136-137 °C; Purity by HPLC: 99.2%.

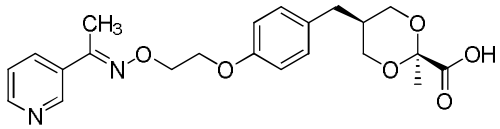
IR (KBr) **:** 3500, 3059, 2965, 2853, 1751, 1610, 1510, 1454, 1387, 1246, 1149, 1120, 1041, 964, 868 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.55 (s, 3H), 2.27-2.52 (m, 3H), 2.35 (s, 3H) 3.52 (t, *J* = 10.8 Hz, 2H), 3.93 (dd, *J* = 10.8 & 4.0 Hz, 2H), 4.29 (t, *J* = 5.2 Hz, 2H), 4.57 (t, *J* = 4.8 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.00 (dd, *J* = 8.4 & 2.8 Hz, 2H), 7.47-7.51 (m, 2H), 7.79-7.87 (m, 3H), 7.90 (dd, *J* = 8.8 & 1.6 Hz, 1H), 7.99 (s, 1H)

^{13}C NMR ($CDCl_3$) **:** δ 12.89, 25.94, 33.90, 35.18, 66.83, 68.34, 72.71, 98.13, 115.01, 123.60, 125.97, 126.46, 126.73, 127.77, 128.13, 128.60, 129.67, 130.12, 133.23, 133.80, 133.96, 155.52, 157.72, 174.81

ESI/MS (m/z) **:** 486.19 $(M+Na)^+$

5.1.10.11 2-Methyl-*c*-5-(4-(2-(((*E*)-(1-(pyridin-3-yl)-ethylidene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (11k)



11k (446 mg, 42.0%) was prepared from **10k** (1.10 gm, 0.00257 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.0%.

IR ($CHCl_3$) **:** 3387, 3018, 2976, 1739, 1612, 1512, 1385, 1246, 1151, 1043, 929 cm^{-1}

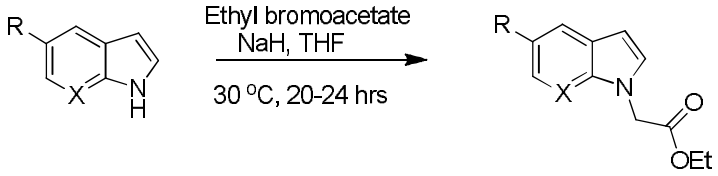
^{1}H NMR **:** δ 1.55 (s, 3H), 2.25 (s, 3H), 2.28-2.35 (m, 1H), 2.41 (d, *J* = 6.4

($CDCl_3$) Hz, 2H), 3.61 (t, *J* = 11.6 Hz, 2H), 3.90 (dd, *J* = 12.4 & 4.4 Hz, 2H), 4.31(t, *J* = 4.8 Hz, 2H), 4.55 (t, *J* = 4.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.98 (dd, *J* = 10.4 & 2.0 Hz, 2H), 7.40 (dd, *J* = 8.0 & 4.8 Hz, 1H), 7.96 (dd, *J* = 9.6 & 1.6 Hz, 1H), 8.57 (d, *J* = 4.0 Hz, 1H), 8.82 (s, 1H)

^{13}C NMR ($CDCl_3$) : δ 12.57, 26.06, 33.97, 35.21, 66.63, 68.07, 73.02, 98.64, 114.87, 124.09, 129.75, 130.48, 133.24, 135.05, 145.72, 148.00, 152.31, 157.45, 173.68

ESI/MS (m/z) : 415.21 $(M+H)^+$

5.1.11 General procedure for the preparation of the compounds 13a-g and 13i.

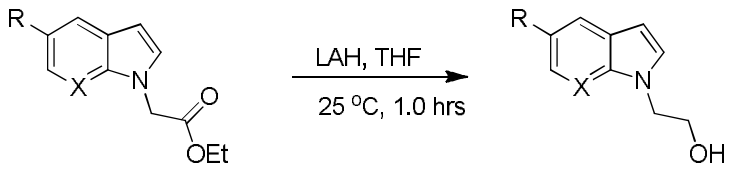


12a-g
12i

13a-g
13i

To an ice cold suspension of NaH (50%) (4 mole equivalent) in THF (10 fold), solution of indole (1 mole equivalent) in THF (25 fold) was added and the mixture was stirred for 30 min. To this ethyl bromoacetate (5 mole equivalent) was added and the reaction mixture was stirred for 20 to 24 hours at 30 °C. The reaction mixture was poured into ice cold water, extracted with ethyl acetate. The combined organic extracts were successively washed with water, brine, dried over sodium sulfate, filtered and concentrated under vaccum to give crude products. The compounds (**13a-g**, **13i**) obtained were used without purification for next step.

5.1.12 General procedure for the preparation of the compounds 14a-g and 14i.

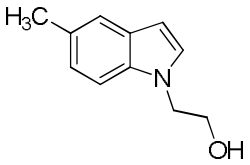


13a-g
13i

14a-g
14i

To a solution of the esters (**13a-g**, **13i**) (1 mole equivalent) in dry THF (25 fold), $LiAlH_4$ (1 mole equivalent) was added in small portion at 0 °C over period of 15 to 30 min and stirred at 25 °C for 1.0 hour. The excess $LiAlH_4$ was quenched by dropwise addition of saturated aqueous Na_2SO_4 solution at 0-10 °C. Solid seperated was filtered and washed with hot ethyl acetate. Filtrate was concentrated under reduced pressure to yield the crude products which were purified by column chromatography using 15-20% ethyl acetate in hexane as eleunt to give pure compounds (**14a-g**, **14i**).

5.1.12.1 2-(5-Methyl-1H-indol-1-yl) ethanol. (14a)



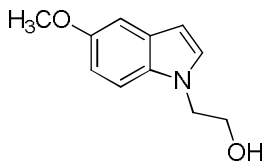
14a (290.0 mg, 12.0%) was prepared from **13a** (3.0 gm crude, 0.01381 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.9%.

IR ($CHCl_3$) : 3414, 3018, 2972, 2926, 2879, 1489, 1448, 1384, 1298, 1072, 1051, 857 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.47 (t, *J* = 6.0 Hz, 1H), 2.44 (s, 3H), 3.95 (q, *J* = 5.6 Hz, 2H), 4.26 (t, *J* = 5.2 Hz, 2H), 6.43 (d, *J* = 3.2 Hz, 1H), 7.04 (dd, *J* = 8.4 & 1.2 Hz, 1H), 7.12 (d, *J* = 3.2 Hz, 1H), 7.26 (d, *J* = 6.4 Hz, 1H), 7.42 (s, 1H)

ESI/MS (m/z) **:** 176.46 $(M+H)^+$

5.1.12.2 2-(5-Methoxy-indol-1-yl)-ethanol. (14b)



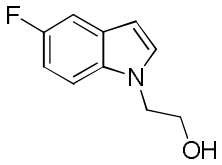
14b (1.20 gm, 54.0%) was prepared from **13b** (2.70 gm crude, 0.01157 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 95.8%.

IR ($CHCl_3$) **:** 3400, 3018, 2941, 2835, 1624, 1512, 1488, 1400, 1151, 1136, 1031, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (1H, exchangeble), 3.85 (s, 3H) , 3.94 (q, *J* = 7.18 Hz, 2H), 4.25 (t, *J* = 5.0 Hz, 2H), 6.44 (dd, *J* = 2.89 & 0.51 Hz, 1H), 6.88 (dd, *J* = 8.91 & 2.49 Hz, 1H), 7.12 (dd, *J* = 11.49 & 3.09 Hz, 2H), 7.25 (d, *J* = 8.88 Hz, 1H)

ESI/MS (m/z) **:** 214.7 $(M+Na)^+$

5.1.12.3 2-(5-Fluoro-1H-indol-1-yl) ethanol. (14c)



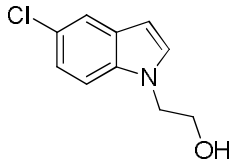
14c (419 mg, 13.0%) was prepared from **13c** (4.00 gm crude, 0.01808 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.2%.

IR ($CHCl_3$) **:** 3421, 3018, 2935, 2881, 1624, 1579, 1487, 1450, 1298, 1072, 864 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 3.95 (t, *J* = 5.2 Hz, 2H), 4.26 (t, *J* = 4.8 Hz, 2H), 6.47 (dd, *J* = 3.2 & 0.8 Hz, 1H), 6.93-6.98 (m, 1H), 7.19 (d, *J* = 2.8 Hz, 1H), 7.25-7.29 (m, 2H)

ESI/MS (m/z) **:** 180.49 $(M+H)^+$

5.1.12.4 2-(5-Chloro-1H-indol-1-yl) ethanol. (14d)



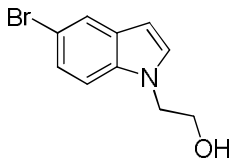
14d (493.0 mg, 10.0%) was prepared from **13d** (6.00 gm crude, 0.02524 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.8%.

IR ($CHCl_3$) **:** 3421, 3018, 2935, 2883, 1510, 1469, 1330, 1284, 1064, 1051, 871 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 3.93 (t, *J* = 5.2 Hz, 2H), 4.25 (t, *J* = 5.2 Hz, 2H), 6.45 (dd, *J* = 3.2 & 0.8 Hz, 1H), 7.15 (dd, *J* = 8.8 & 2.0 Hz, 2H), 7.27 (dd, *J* = 12.8 &3.6 Hz, 1H), 7.58 (d, *J* = 2.0 Hz, 1H)

ESI/MS (m/z) **:** 196.46 $(M+H)^+$

5.1.12.5 2-(5-Bromo-indol-1-yl)-ethanol. (14e)



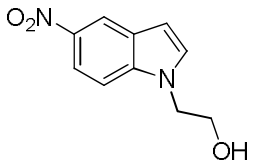
14e (2.72 gm, 64.0%) was prepared from **13e** (5.00 gm crude, 0.01772 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.0%.

IR ($CHCl_3$) **:** 3583, 3018, 2935, 2885, 1512, 1467, 1438, 1396, 1326, 1282, 1053, 929, 871, 771 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 3.94 (s, 2H), 4.25 (t, *J* = 5.1 Hz, 2H), 6.45 (d, *J* = 3.0 Hz, 1H), 7.16 (d, *J* = 3.1 Hz, 1H), 7.22-7.31 (m, 2H), 7.75 (s, 1H)

ESI/MS (m/z) **:** 256.9 $(M+NH_4)^+$

5.1.12.6 2-(5-Nitro-1H-indol-1-yl)ethanol. (14f)



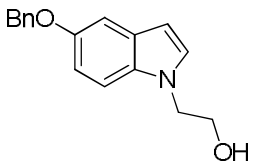
14f (1.69 gm, 58.0%) was prepared from **13f** (3.50 gm crude, 0.01410 mol) following the general procedure described above as a yellow solid; m.p: 69-70 °C; Purity by HPLC: 99.1%.

IR (KBr) **:** 3300, 2929, 2850, 1880, 1612, 1508, 1477, 1402, 1334, 1180, 1138, 889, 862 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.61 (t, *J* = 5.6 Hz, 1H), 4.01 (q, *J* = 5.2 Hz, 2H), 4.34 (t, *J* = 5.2 Hz, 2H), 6.71 (d, *J* = 3.2 Hz, 1H), 7.33 (d, *J* = 3.2 Hz, 1H), 7.40 (d, *J* = 9.2 Hz, 1H), 8.12 (dd, *J* = 9.2 & 2.4 Hz, 1H), 8.59 (d, *J* = 2.0 Hz, 1H)

ESI/MS (m/z) **:** 207.50 $(M+H)^+$

5.1.12.7 2-Benzyloxy-indol-1-yl)-ethanol. (14g)



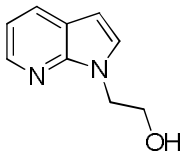
14g (1.19 gm, 39.6%) was prepared from **13g** (3.50 gm crude, 0.01131 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.5%.

IR (CHCl$_3$) **:** 3440, 3018, 2933, 2881, 1620, 1573, 1487, 1452, 1153, 1026 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.53 (t, *J* = 6.12 Hz, 1H exchangeble), 3.94 (q, *J* = 5.49 Hz, 2H), 4.24 (t, *J* = 5.1 Hz, 2H), 5.10 (s, 2H), 6.42 (d, *J* = 2.97 Hz, 1H), 6.96 (dd, *J* = 8.88 & 2.34 Hz, 1H) 7.15 (dd, *J* = 12.48 & 2.58 Hz, 2H), 7.25-7.41 (m, 4H), 7.47 (d, *J* = 6.78 Hz, 2H)

ESI/MS (m/z) **:** 268.7 $(M+H)^+$

5.1.12.8 2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)ethanol. (14i)



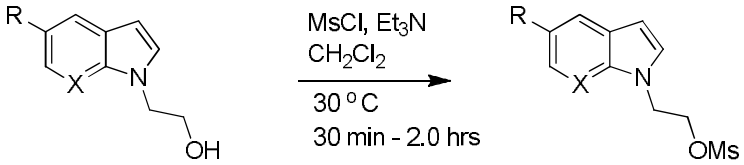
14i (1.18 gm, 55.0%) was prepared from **13i** (2.70 gm crude, 0.01323 mol) following the general procedure described above as a white solid; m.p: 53-54 °C; Purity by HPLC: 99.9%.

IR (KBr) : 3377, 3275, 3090, 2989, 1595, 1510, 1435, 1354, 1313, 1180, 1064, 1018, 796 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 4.03 (t, *J* = 4.8 Hz, 2H), 4.40 (t, *J* = 4.4 Hz, 2H), 5.35 (bs, 1H), 6.46 (d, *J* = 3.2 Hz, 1H), 7.08 (dd, *J* = 8.0 & 4.8 Hz, 1H), 7.19 (d, *J* = 3.6 Hz, 1H), 7.94 (dd, *J* = 7.6 & 1.2 Hz, 1H), 8.26 (dd, *J* = 4.8 & 1.2 Hz, 1H)

ESI/MS (m/z) : 163.21 $(M+H)^+$

5.1.13 General procedure for the preparation of the compounds 15a-g and 15i.

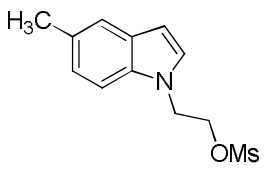


14a-g
14i

15a-g
15i

To an ice-cold solution of alcohol (**14a-g**, **14i**) (1 mole equivalent) in dry dichloromethane (10 fold), were added triethylamine (1.5 mole equivalent) and methanesulfonyl chloride (1.2 mole equivalent) and the reaction mixture was stirred for 30 min to 2 hours at 30 °C. Then the reaction mixture was diluted with excess dichloromethane and successively washed with water, brine and was concentrated under vacuum to yield the required product (**15a-g**, **15i**).

5.1.13.1 2-(5-Methyl-1H-indol-1-yl)ethyl methanesulfonate. (15a)



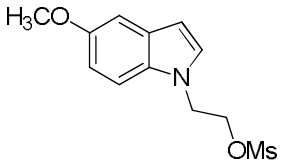
15a (263.0 mg, 65.0%) was prepared from **14a** (290.0 mg, 0.00160 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.7%.

IR ($CHCl_3$) : 3020, 2935, 1489, 1385, 1363, 1176, 1082, 972, 906 cm^{-1}

^1H NMR ($CDCl_3$) : δ 2.44 (s, 3H), 2.55 (s, 3H), 4.43 (t, *J* = 4.8 Hz, 2H), 4.49 (t, *J* = 5.2 Hz, 2H), 6.44 (d, *J* = 3.2 Hz, 1H), 7.05-7.09 (m, 2H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.41 (s, 1H)

ESI/MS (m/z) : 254.46 $(M+H)^+$

5.1.13.2 2-(5-Methoxy-indol-1-yl)-ethyl methanesulfonate. (15b)



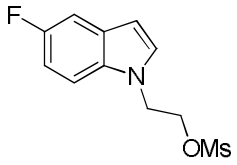
15b (1.41 gm, 100%) was prepared from **14b** (1.0 gm, 0.00523 mol) following the general procedure described above as a brown solid; m.p: 80-81°C; Purity by HPLC: 93.4%.

IR (KBr) : 3012, 2935, 2833, 1708, 1618, 1527, 1488, 1328, 1234, 1151, 921 cm^{-1}

^1H NMR ($CDCl_3$) : δ 2.57 (s, 3H), 3.85 (s, 3H), 4.42-4.52 (m, 4H), 6.45 (d, *J* = 2.79 Hz, 1H) 6.90 (dd, *J* = 8.88 & 2.43 Hz, 1H), 7.10 (dd, *J* = 7.11 & 3.06 Hz, 2H), 7.22 (s, 1H)

ESI/MS (m/z) : 270.6 $(M+H)^+$

5.1.13.3 2-(5-Fluoro-1H-indol-1-yl)ethyl methanesulfonate. (15c)



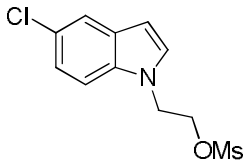
15c (229.0 mg, 40.0%) was prepared from **14c** (400 mg, 0.00223 mol) following the general procedure described above as a thick liquid; Purity by HPLC: 96.0%.

IR ($CHCl_3$) **:** 3020, 2939, 1624, 1579, 1516, 1487, 1361, 1215, 1174, 1039, 972 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 2.63 (s, 3H), 4.46 (t, *J* = 4.8 Hz, 2H), 4.50 (t, *J* = 5.2 Hz, 2H), 6.50 (dd, *J* = 2.8 & 0.4 Hz, 1H), 6.96-7.01 (m, 1H), 7.17 (d, *J* = 2.8 Hz, 1H), 7.24-7.28 (m, 2H)

ESI/MS (m/z) **:** 258.42 $(M+H)^+$

5.1.13.4 2-(5-Fluoro-1H-indol-1-yl)ethyl methanesulfonate. (15d)



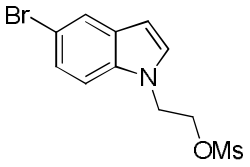
15d (510.0 mg, 76.0%) was prepared from **14d** (480 mg, 0.00245 mol) following the general procedure described above as a brown solid, m.p: 51-52 °C; Purity by HPLC: 97.5%.

IR (KBr) **:** 3020, 2939, 2897, 1514, 1469, 1384, 1363, 1176, 1041, 1004 970 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 2.64 (s, 3H), 4.45 (t, *J* = 7.2 Hz, 2H), 4.50 (t, *J* = 4.4 Hz, 2H), 6.48 (d, *J* = 3.2 & 0.4 Hz, 1H), 7.15 (d, *J* = 3.2 Hz, 1H), 7.19 (dd, *J* = 8.8 & 2.0 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.59 (d, *J* = 2.0 Hz, 1H)

ESI/MS (m/z) **:** 296.37 $(M+Na)^+$

5.1.13.5 2-(5-Bromo-indol-1-yl)-ethyl methanesulfonate. (15e)



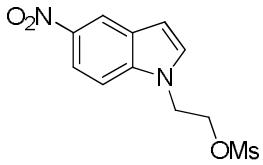
15e (1.31 gm, 99.0%) was prepared from **14e** (1.0 gm, 0.00416 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.3%.

IR ($CHCl_3$) : 3022, 2937, 1550, 1467, 1365, 1249, 1178, 1083, 1039, 1004, 970 cm^{-1}

^1H NMR ($CDCl_3$) : δ 2.64 (s, 3H), 4.43-4.52 (m, 4H), 6.48 (d, *J* = 3.2 Hz, 1H), 7.15 (d, *J* = 3.2 Hz, 1H), 7.23 (d, *J* = 8.73 Hz, 1H), 7.32 (dd, *J* = 8.7 & 1.8 Hz, 1H), 7.75 (d, *J* = 1.8 Hz, 1H)

ESI/MS (m/z) : 315.2 $(M+H)^+$

5.1.13.6 2-(5-Nitro-1H-indol-1-yl)ethyl methanesulfonate. (15f)



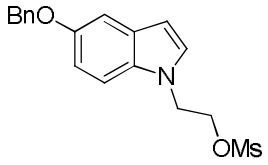
15f (1.38 gm, 100%) was prepared from **14f** (1.0 gm, 0.00485 mol) following the general procedure described above as a white solid, m.p: 119-120 °C. Purity by HPLC: 98.6%.

IR (KBr) : 3105, 3022, 2939, 1610, 1508, 1340, 1161, 929, 526 cm^{-1}

^1H NMR ($CDCl_3$) : δ 2.78 (s, 3H), 4.54 (s, 4H), 6.74 (d, *J* = 3.2 Hz, 1H), 7.31(d, *J* = 8.8 Hz, 1H), 7.39 (d, *J* = 8.8 Hz, 1H), 8.16 (dd, *J* = 8.8 & 2.0 Hz, 1H), 8.60 (d, *J* = 2.0 Hz, 1H)

ESI/MS (m/z) : 285.38 $(M+H)^+$

5.1.13.7 2-(5-Benzyloxy-indol-1-yl)-ethyl methanesulfonate. (15g)



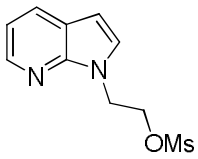
15g (1.22 gm, 96.4%) was prepared from **14g** (1.0 gm, 0.00374 mol) following the general procedure described above as a pink solid; m.p: 82-84 °C Purity by HPLC: 99.1%.

IR (KBr) **:** 3068, 3026, 2875, 2850, 2822, 1614, 1575, 1487, 1450, 1355, 1240, 1155, 1003 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 2.57 (s, 3H), 4.43 (t, *J* = 4.44 Hz, 2H), 4.49 (t, *J* = 5.07 Hz, 2H), 5.10 (s, 2H), 6.44 (d, *J* = 3.15 Hz, 1H), 6.97 (dd, *J* = 8.58 & 2.34 Hz, 1H), 7.10 (d, *J* = 3.01 Hz, 1H), 7.16 (d, *J* = 2.31 Hz, 1H), 7.23 (s, 1H), 7.31-7.41 (m, 3H), 7.46 (d, *J* = 7.26 Hz, 2H)

ESI/MS (m/z) **:** 345.1$(M+H)^+$

5.1.13.8 2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)ethyl methanesulfonate. (15i)



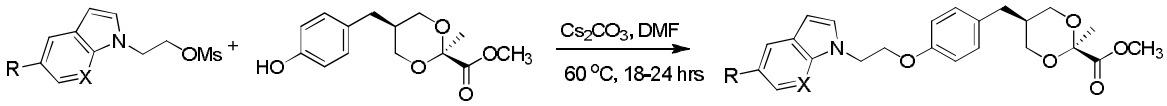
15i (1.35 gm, 91.0%) was prepared from **14i** (1.0 gm, 0.00617 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.6%.

IR (KBr) **:** 3020, 2974, 1595, 1573, 1512, 1429, 1176, 1043, 970 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 2.75 (s, 3H), 4.60-4.67 (m, 4H), 6.49 (d, *J* = 3.6 Hz, 1H), 7.10 (dd, *J* = 7.6 & 4.8 Hz, 1H), 7.28 (d, *J* = 3.6 Hz, 1H), 7.94 (dd, *J* = 7.6 & 1.2 Hz, 1H), 8.33 (dd, *J* = 4.8 & 1.2 Hz, 1H)

ESI/MS (m/z) **:** 241.26 $(M+H)^+$

5.1.14 General procedure for the preparation of the compounds 16a-g and 16i.



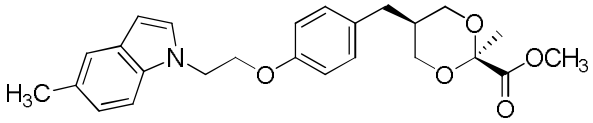
15a-g
15i

6a

16a-g
16i

To a solution of mesylates (**15a-g**, **15i**) (1 mole equivalent) and **6a** (1 mole equivalent) in dry DMF (5 fold), Cs_2CO_3 (2 mole equivalent) was added and the reaction mixture was stirred at 60 °C for 18-24 hours. Reaction mixture was poured into ice cold water and was extracted with ethyl acetate. The combined organic extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude products were purified by column chromatography using 10-15% ethyl acetate in hexane as eluent to furnish the pure compounds (**16a-g**, **16i**).

5.1.14.1 Methyl *c*-2-methyl-5-(4-(2-(5-methyl-1H-indol-1-yl)ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (16a)



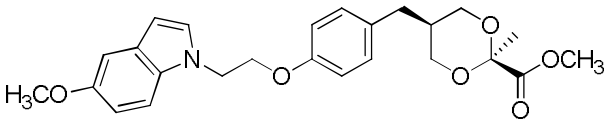
16a (250 mg, 60%) was prepared from **15a** (250 mg, 0.000986 mol) and **6a** (262.0 mg, 0.000986 mol) by means of a general procedure described above as a white solid. mp: 109-110 °C; Purity by HPLC: 99.7%.

IR (KBr) **:** 3001, 2933, 2854, 1741, 1608, 1512, 1442, 1296, 1236, 1143, 1116, 802 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.48 (s, 3H), 2.22-2.26 (m, 3H), 2.44 (s, 3H), 3.41-3.48 (m, 2H), 3.81-3.87 (m, 5H), 4.22 (t, *J* = 5.6 Hz, 2H), 4.47 (t, *J* = 6.0 Hz, 2H), 6.41 (d, *J* = 2.8 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 7.04 (dd, *J* = 8.4 & 0.8 Hz, 1H), 7.15 (d, *J* = 2.8 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.41 (s, 1H)

ESI/MS (m/z) **:** 424.56 $(M+H^+$

5.1.14.2 Methyl *c*-5-(4-(2-(5-methoxy-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (16b)



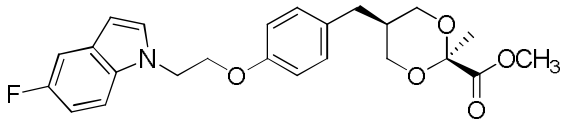
16b (1.20 gm, 73.5%) was prepared from **15b** (1.0 gm, 0.00371 mol) and **6a** (1.05 gm, 0.00371 mol) by means of a general procedure described above as a thick liquid. Purity by HPLC: 96.7%.

IR ($CHCl_3$) **:** 3018, 2929, 2856, 1743, 1612, 1512, 1448, 1369, 1144, 1033, 891 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.25 (s, 3H), 3.44 (t, *J* = 10.92 Hz, 2H), 3.83-3.87 (m, 8H), 4.22 (t, *J* = 5.61 Hz, 2H), 4.47 (t, *J* = 5.64 Hz, 2H), 6.43 (d, *J* = 3.09 Hz, 1H), 6.73 (d, *J* = 8.52 Hz, 2H), 6.87 (dd, *J* = 8.79 & 2.34 Hz, 1H), 6.96 (d, *J* = 8.58 Hz, 2H), 7.08 (d, *J* = 2.43 Hz, 1H), 7.17 (d, *J* = 3.06 Hz, 1H), 7.30 (s, 1H)

ESI/MS (m/z) **:** 440.7 $(M+H)^+$

5.1.14.3 Methyl *c*-5-(4-(2-(5-fluoro-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (16c)



16c (241 mg, 66.0%) was prepared from **15c** (220 mg, 0.000855 mol) and **6a** (227 mg, 0.000855 mol) by means of a general procedure described above as a thick liquid. Purity by HPLC: 97.5%.

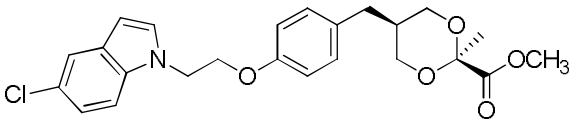
IR ($CHCl_3$) **:** 3018, 2900, 2810, 1743, 1599, 1512, 1487, 1384, 1143, 1122, 1051, 1043, 699 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.48 (s, 3H), 2.22-2.25 (m, 3H), 3.41-3.48 (m, 2H), 3.82-3.89 (m, 5H), 4.23 (t, *J* = 5.2 Hz, 2H), 4.48 (t, *J* = 5.6 Hz, 2H), 6.45 (dd, *J* = 2.8 & 0.4 Hz, 1H), 6.72-6.75 (m, 2H), 6.94-6.99 (m,

3H), 7.23-7.27 (m, 2H), 7.31 (dd, *J* = 9.2 & 4.4 Hz, 1H)

ESI/MS (m/z) **:** 428.59 $(M+H)^+$

5.1.14.4 Methyl *c*-5-(4-(2-(5-chloro-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (16d)



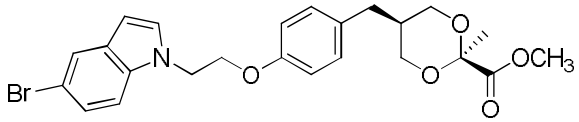
16d (600 mg, 74.0%) was prepared from **15d** (500 mg, 0.00183 mol) and **6a** (486 mg, 0.00183 mol) by means of a general procedure described above as a thick liquid. Purity by HPLC: 98.4%.

IR ($CHCl_3$) **:** 3018, 2928, 2856, 1743, 1610, 1512, 1471, 1444, 1265, 1143, 908 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.25 (s, 3H), 3.41-3.47 (m, 2H), 3.82-3.87 (m, 5H), 4.23 (t, *J* = 5.2 Hz, 2H), 4.48 (t, *J* = 5.6 Hz, 2H), 6.44 (dd, *J* = 3.2 & 0.4 Hz, 1H), 6.72-6.75 (m, 2H), 6.97 (dd, *J* = 6.8 & 1.6 Hz, 2H), 7.17 (dd, *J* = 8.8 & 2.0 Hz, 1H), 7.21 (d, *J* = 3.2 Hz, 1H), 7.32 (d, *J* = 8.8 Hz, 1H), 7.58 (d, *J* = 2.0 Hz, 1H)

ESI/MS (m/z) **:** 444.53 $(M+H)^+$

5.1.14.5 Methyl *c*-5-(4-(2-(5-bromo-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (16e)



16e (1.34 gm, 87.0%) was prepared from **15e** (1.0 gm, 0.00314 mol) and **6a** (837 mg, 0.00314 mol) by means of a general procedure described above as a thick liquid. Purity by HPLC: 98.9%.

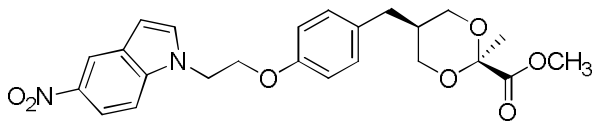
IR ($CHCl_3$) **:** 3018, 2927, 2858, 1743, 1610, 1512, 1469, 1367, 1244, 1215, 1143, 1055 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.48 (s, 3H), 2.21-2.27 (m, 3H), 3.44 (t, *J* = 11.3 Hz, 2H), 3.83-3.88 (m, 5H), 4.29 (t, *J* = 5.4 Hz, 2H), 4.48 (t, *J* = 5.4 Hz,

2H), 6.45 (d, *J* = 3.1 Hz, 1H), 6.73 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 3.2 Hz, 1H), 7.28 (s, 2H), 7.74 (s, 1H)

ESI/MS (m/z) **:** 512.1 $(M+Na)^+$

5.1.14.6 Methyl *c*-2-methyl-5-(4-(2-(5-nitro-1H-indol-1-yl)ethoxy)benzyl)-1,3-dioxane-*r*-2-carboxylate. (16f)



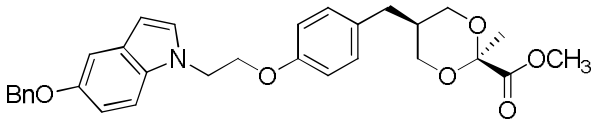
16f (1.17 gm, 73.0%) was prepared from **15f** (1.0 gm, 0.00352 mol) and **6a** (936 mg, 0.00352 mol) by means of a general procedure described above as a thick liquid. Purity by HPLC: 99.2%.

IR ($CHCl_3$) **:** 3020, 2928, 1743, 1612, 1512, 1385, 1336, 1143, 1043 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.48 (s, 3H), 2.22-2.26 (m, 3H), 3.41-3.46 (m, 2H), 3.82-3.87 (m, 5H), 4.27 (t, *J* = 5.2 Hz, 2H), 4.55 (t, *J* = 5.2 Hz, 2H), 6.69-6.74 (m, 3H), 6.97 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 3.6 Hz, 1H), 7.45 (d, *J* = 9.2 Hz, 1H), 8.14 (dd, *J* = 9.2 & 2.0 Hz, 1H), 8.58 (d, *J* = 2.4 Hz, 1H)

ESI/MS (m/z) **:** 477.59 $(M+Na)^+$

5.1.14.7 Methyl *c*-5-(4-(2-(5-(benzyloxy)-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (16g)



16g (895 mg, 60.0%) was prepared from **15g** (1.0 gm, 0.00290 mol) and **6a** (771 mg, 0.00290 mol) by means of a general procedure described above as a white solid; m.p: 109-110°C. Purity by HPLC: 96.5%.

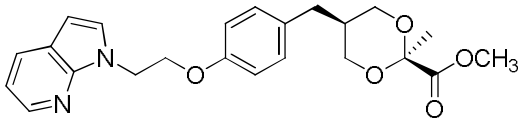
IR (KBr) **:** 2927, 2850, 1737, 1618, 1512, 1452, 1371, 1296, 1122, 1041 cm^{-1}

^{1}H NMR **:** δ 1.49 (s, 3H), 2.25 (s, 3H), 3.44 (t, *J* = 10.98 Hz, 2H), 3.83-

($CDCl_3$) 3.88 (m, 5H) 4.23 (t, *J* = 5.49 Hz, 2H), 4.47 (t, *J* = 5.61 Hz, 2H), 5.10 (s, 2H), 6.41 (d, *J* = 3.03 Hz, 1H), 6.74 (d, *J* = 8.61 Hz, 2H), 6.97 (dd, *J* = 8.88 & 2.22 Hz, 3H), 7.16 (t, *J* = 2.76 Hz, 2H), 7.28-7.40 (m, 4H), 7.47 (d, *J* = 6.90 Hz, 2H)

ESI/MS (m/z) **:** 516.2 $(M+H)^+$

5.1.14.8 Methyl *c*-5-(4-(2-(1H-pyrrolo[2,3-b]pyridin-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (16i)



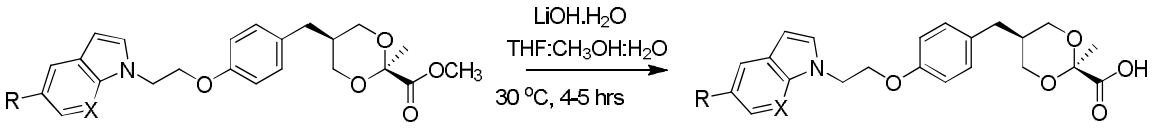
16i (1.42 gm, 83.0%) was prepared from **15i** (1.0 gm, 0.00416 mol) and **6a** (1.11 gm, 0.00416 mol) by means of a general procedure described above as a thick liquid. Purity by HPLC: 99.1%.

IR ($CHCl_3$) **:** 3018, 2929, 2856, 1743, 1512, 1429, 1384, 1246, 1143, 1116, 1041, 974 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.48 (s, 3H), 2.22 -2.27 (m, 3H), 3.41-3.46 (m, 2H), 3.81-3.87 (m, 5H), 4.30 (t, *J* = 5.2 Hz, 2H), 4.68 (t, *J* = 5.2 Hz, 2H), 6.45 (d, *J* = 3.2 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 7.06 (dd, *J* = 7.6 & 4.4 Hz, 1H), 7.38 (d, *J* = 3.6 Hz, 1H), 7.90 (dd, *J* = 7.6 & 1.6 Hz, 1H), 8.30 (dd, *J* = 4.8 & 1.2 Hz, 1H)

ESI/MS (m/z) **:** 411.54 $(M+H)^+$

5.1.15 General procedure for the preparation of the compounds 17a-g and 17i.



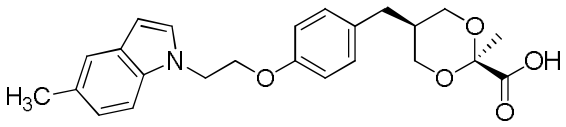
16a-g
16i

17a-g
17i

To a solution of esters (**16a-g**, **16i**) (1 mole equivalent) in THF (9 fold), MeOH (3 fold) and H_2O (3 fold), $LiOH.H_2O$ (2 mole equivalent) was added and was stirred at 30 °C for 4-5 hours. The reaction mixture was concentrated under vacuum.

Water was added to the reaction mixture, acidified with aq. HCl and was extracted with ethyl acetate. The organic extract was washed with water followed by brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield the products (**17a-g**, **17i**).

5.1.15.1 *c*-2-Methyl-5-(4-(2-(5-methyl-1H-indol-1-yl)ethoxy)benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (17a)



17a (197.0 mg, 85.0%) was prepared from **16a** (240.0 mg, 0.000566 mol) following the general procedure described above as a white solid. m.p: 109-110 °C; Purity by HPLC: 99.9%.

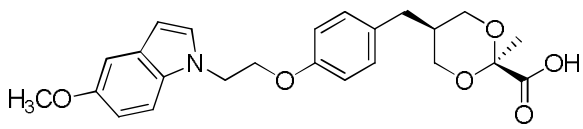
IR (KBr) **:** 3387, 3095, 3005, 2935, 2835, 1726, 1610, 1512, 1359, 1300, 1149, 1037, 802 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.54 (s, 3H), 2.23-2.27 (m, 3H), 2.44 (s, 3H), 3.50 (t, *J* = 10.8 Hz, 2H), 3.89 (dd, *J* = 10.4 & 4.0 Hz, 2H), 4.21 (t, *J* = 5.6 Hz, 2H), 4.47 (t, *J* = 5.6 Hz, 2H), 6.41 (d, *J* = 3.2 Hz, 1H), 6.73 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 2.8 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.41 (s, 1H)

^{13}C NMR (DMSO-d6) : δ 21.09, 25.54, 32.85, 34.85, 45.09, 66.86, 66.95, 97.65, 99.54, 100.17, 109.65, 114.28, 119.95, 122.60, 127.46, 128.36, 129.01, 129.65, 130.56, 134.38, 156.45, 171.34

ESI/MS (m/z) **:** 410.57 $(M+H)^+$

5.1.15.2 *c*-5-(4-(2-(5-Methoxy-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (17b)



17b (758.0 mg, 78.4%) was prepared from **16b** (1.0 gm, 0.00228 mol) following the general procedure described above as an off white solid. m.p: 180-181 °C; Purity by HPLC: 96.7%

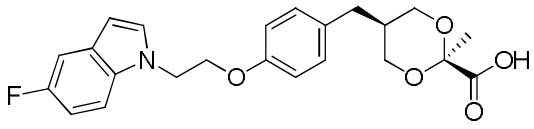
IR (KBr) : 3411, 2922, 2871, 2833, 1716, 1610, 1510, 1446, 1294, 1190, 1149, 1029, 891 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.28 (s, 3H), 3.49 (t, *J* = 11.4 Hz, 2H), 3.85 (s, 3H), 3.90 (dd, *J* = 13.48 & 5.28 Hz, 2H), 4.23 (t, *J* = 5.49 Hz, 2H), 4.47 (t, *J* = 5.61 Hz, 2H), 6.42 (d, *J* = 3.06 Hz, 1H), 6.73 (d, *J* = 8.49 Hz, 2H), 6.88 (dd, *J* = 8.91 & 2.43 Hz, 1H), 6.96 (d, *J* = 8.46 Hz, 2H), 7.09 (d, *J* = 2.37 Hz, 1H), 7.17 (d, *J* = 3.06 Hz, 1H), 7.30 (s, 1H)

^{13}C NMR (DMSO-d6) : δ 25.81, 33.39, 35.37, 45.24, 55.33, 66.62, 66.95, 99.44, 99.56 100.41, 102.10, 110.67, 111.13, 114.29, 128.52, 129.54, 131.09, 131.22, 153.48, 156.39, 165.57, 172.31

ESI/MS (m/z) : 448.7 $(M+Na)^+$

5.1.15.3 *c*-5-(4-(2-(5-Fluoro-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (17c)



17c (178.0 mg, 82.0%) was prepared from **16c** (225 mg, 0.000526 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.4%

IR ($CHCl_3$) : 3440, 3018, 2929, 2874, 1724, 1612, 1512, 1487, 1448, 1141, 1043, 929, 671 cm^{-1}

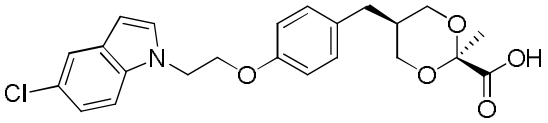
^{1}H NMR ($CDCl_3$) : δ 1.54 (s, 3H), 2.24-2.28 (m, 3H), 3.50 (t, *J* = 10.8 Hz, 2H), 3.88 (dd, *J* = 13.2 & 4.0 Hz, 2H), 4.23 (t, *J* = 5.6 Hz, 2H), 4.48 (t, *J* = 5.2 Hz, 2H), 6.45 (d, *J* = 3.2 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 2H), 6.97 (dd, *J* = 6.4 & 3.2 Hz, 3H), 7.23-7.32 (m, 3H)

^{13}C NMR (DMSO-d6) : δ 25.52, 32.84, 34.85, 45.35, 66.86, 66.98, 97.63, 99.53, 100.83, 104.73, 104.96, 108.96, 109.22, 111.01, 111.11,

114.28, 128.23, 128.34, 129.63, 130.61, 130.93, 132.72, 155.89, 156.40, 158.19, 171.32

ESI/MS (m/z) **:** 414.61 $(M+H)^+$

5.1.15.4 *c*-5-(4-(2-(5-Chloro-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (17d)



17d (406.0 mg, 73.0%) was prepared from **16d** (575 mg, 0.000130 mol) following the general procedure described above as an off white solid. m.p: 110-111 °C; Purity by HPLC: 99.3%

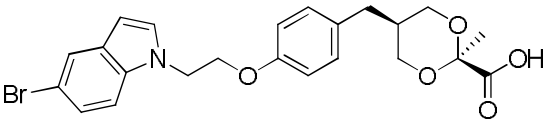
IR (KBr) **:** 3387, 3122, 2933, 2870, 1724, 1610, 1512, 1469, 1290, 1240, 1143, 1030, 891 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.54 (s, 3H), 2.23-2.29 (m, 3H), 3.50 (t, *J* = 10.8 Hz, 2H), 3.88 (dd, *J* = 12.4 & 4.0 Hz, 2H), 4.21 (t, *J* = 5.6 Hz, 2H), 4.47 (t, *J* = 5.6 Hz, 2H), 6.44 (dd, *J* = 2.8 & 0.4 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 7.16 (dd, *J* = 8.8 & 2.0 Hz, 1H), 7.21 (d, *J* = 2.8 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 1.6 Hz, 1H)

^{13}C NMR (DMSO-d6) **:** δ 25.53, 32.85, 34.85, 45.29, 66.86, 66.97, 97.65, 99.53, 100.56, 111.65, 114.28, 119.44, 120.90, 123.72, 129.19, 129.62, 130.64, 130.74, 134.52, 156.38, 171.39

ESI/MS (m/z) : 430.54 $(M+H)^+$

5.1.15.5 *c*-5-(4-(2-(5-Bromo-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (17e)



17e (767.0 mg, 79.0%) was prepared from **16e** (1.0 gm, 0.00205 mol) following the general procedure described above as a white solid. m.p: 153-154 °C; Purity by HPLC: 97.3%

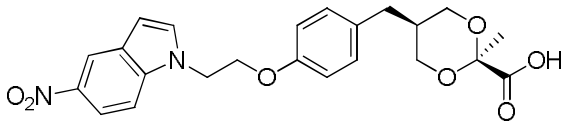
IR (KBr) **:** 3448, 3149, 2929, 2875, 1718, 1610, 1512, 1460, 1319, 1240, 1137, 1066, 1039, 912 cm^{-1}

^{1}H NMR (CD_3OD +$CDCl_3$) **:** δ 1.40 (s, 3H), 2.14-2.20 (m, 1H), 2.25 (d, *J* = 7.35 Hz, 2H), 3.46 (t, *J* = 11.7 Hz, 2H), 3.75 (dd, *J* = 12.06 & 4.35, 2H), 4.24 (t, *J* = 5.2 Hz, 2H), 4.49 (t, *J* = 5.1 Hz, 2H), 6.40 (d, *J* = 3.0 Hz, 1H), 6.73 (d, *J* = 8.6 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H), 7.22 (dd, *J* = 8.7 & 1.9 Hz, 1H), 7.28 (d, *J* = 3.1Hz, 1H), 7.38 (d, *J* = 8.8 Hz, 1H), 7.64 (d, *J* = 1.8 Hz, 1H)

^{13}C NMR (DMSO-d6) : δ 25.54, 32.82, 34.83, 45.30, 59.77, 66.87, 67.03, 97.56, 99.55, 100.51, 111.70, 112.17, 114.29, 115.13, 122.52, 123.46, 129.66, 129.94, 130.61, 134.77, 156.40, 171.32

ESI/MS (m/z) : 474.3 $(M+H)^+$

5.1.15.6 *c*-2-Methyl-5-(4-(2-(5-nitro-1H-indol-1-yl)ethoxy)benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (17f)



17f (503.0 mg, 52.0%) was prepared from **16f** (1.0 gm, 0.00220 mol) following the general procedure described above as a white solid. m.p: 49-50 °C; Purity by HPLC: 99.9%.

IR (KBr) **:** 3423, 3105, 2926, 2870, 1735, 1610, 1508, 1332, 1244, 1186, 1114, 891, 742 cm^{-1}

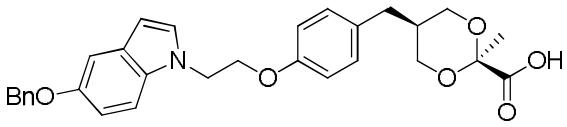
^{1}H NMR ($CDCl_3$) **:** δ 1.54 (s, 3H), 2.23-2.29 (m, 3H), 3.49 (t, *J* = 14.8 Hz, 2H), 3.87 (dd, *J* = 12.4 & 4.4 Hz, 2H), 4.27 (t, *J* = 5.2 Hz, 2H), 4.55 (t, *J* = 5.2 Hz, 2H), 6.70 (d, *J* = 3.2 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 3.2 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 1H), 8.13 (dd, *J* = 9.2 & 2.0 Hz, 1H), 8.58 (d, *J* = 2.0

Hz, 1H)

^{13}C NMR (CDCl$_3$) : δ 25.89, 33.82, 35.12, 46.42, 67.02, 68.22, 98.13, 104.53, 109.50, 114.69, 117.42, 118.35, 127.93, 129.77, 130.83, 131.62, 139.26, 141.77, 156.76, 175.00

ESI/MS (m/z) : 463.53 $(M+Na)^+$

5.1.15.7 *c*-5-(4-(2-(5-Methoxy-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (17g)



17g (417.0 mg, 49.0%) was prepared from **16g** (875 mg, 0.00170 mol) following the general procedure described above as an off white solid. m.p: 98-99 °C; Purity by HPLC: 98.7%.

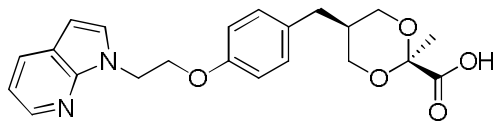
IR (KBr) : 3444, 2939, 2866, 1726, 1612, 1512, 1488, 1371, 1144, 1022, 914 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.54 (s, 3H), 2.24-2.28 (m, 3H), 3.50 (t, *J* = 10.47 Hz, 2H), 3.90 (dd,*J* = 13.23 & 4.17 Hz, 2H), 4.23 (t, *J* = 5.49 Hz, 2H), 4.46 (t, *J* = 5.61 Hz, 2H), 5.10 (s, 2H), 6.41 (d, *J* = 3.03 Hz, 1H), 6.73 (d, *J* = 8.58 Hz, 2H), 6.97 (dd,*J* = 8.46 & 1.95 Hz, 3H), 7.16 (d,*J* = 4.47 Hz, 2H), 7.26-7.40 (m, 4H), 7.47 (d, *J* = 7.05 Hz, 2H)

^{13}C NMR (DMSO-d6) : δ 25.56, 32.88, 34.88, 45.22, 66.91, 66.98, 69.74, 97.74, 100.42, 103.70, 110.69, 111.77, 114.29, 127.54, 128.46, 129.58, 130.60, 131.37, 137.80, 152.46, 156.45, 171.58

ESI/MS (m/z) : 502.4 $(M+H)^+$

5.1.15.8 *c*-5-(4-(2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (17i)



17i (841.0 mg, 67.0%) was prepared from **16i** (1.30 gm, 0.00317 mol) following the general procedure described above as a white solid. m.p: 50-52 °C; Purity by HPLC: 99.3%

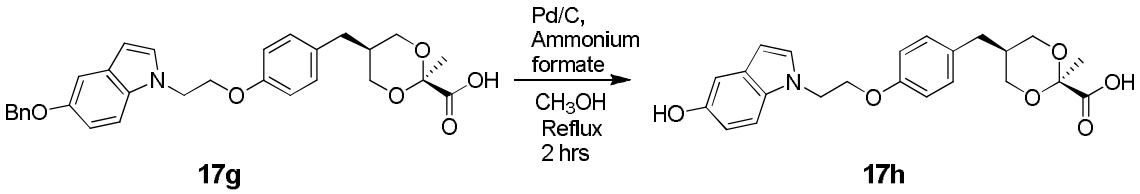
IR (KBr) **:** 3450, 3063, 2928, 2870, 1734, 1610, 1581, 1512, 1429, 1244, 1143, 1039 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.57 (s, 3H), 2.26 (s, 3H), 3.55 (t, *J* = 10.8 Hz, 2H), 3.88 (dd, *J* = 9.2 & 3.2 Hz, 2H), 4.28 (t, *J* = 4.8 Hz, 2H), 4.71 (t, *J* = 4.8 Hz, 2H), 6.48 (d, *J* = 3.2 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 7.11 (dd, *J* = 8.0 & 5.2 Hz, 1H), 7.39 (d, *J* = 3.6 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 8.39 (d, *J* = 4.4 Hz, 1H)

^{13}C NMR (DMSO-d6) : δ 24.86, 25.54, 32.83, 34.86, 43.34, 66.33, 67.02, 97.61, 99.11, 99.55, 114.36, 115.69, 120.12, 128.53, 129.66, 130.62, 136.89, 142.30, 147.06, 156.48, 171.33

ESI/MS (m/z) : 397.56 $(M+H)^+$

5.1.16 *c*-5-(4-(2-(5-Hydroxy-1H-indol-1-yl)ethoxy)benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (17h)



17g **17h**

To a suspension of Pd/C (10%) (20 mg) in MeOH (5 ml), a solution of **17g** (150 mg, 0.3 mmol) in MeOH (10 ml) and ammonium formate (941 mg, 1.5 mmol) was added and the mixture was refluxed for 2 hours. The reaction mixture was filtered through celite after cooling and filtrate was concentrated under vacuum. The residue was dissolved in ethyl acetate (50 ml) and successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield **17h** (64 mg, 49%) as a white solid. m.p: 75-76 °C; Purity by HPLC: 95.4%.

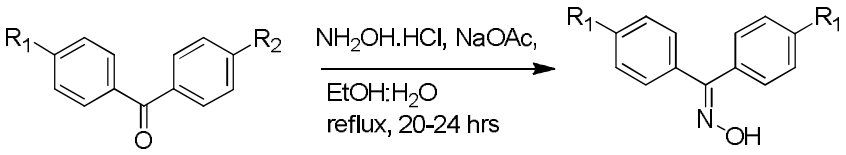
IR (KBr) **:** 3381, 2924, 2854, 1745, 1707, 1577, 1512, 1444, 1357, 1244, 1136, 1033, 887 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 1.29 (s, 3H), 2.01-2.06 (m, 1H), 2.22 (d, *J* = 7.2 Hz, 2H), 3.37 (t, *J* = 11.6 Hz, 2H), 3.66 (dd, *J* = 11.6 & 4.4 Hz, 2H), 4.19 (t. *J* = 5.2 Hz, 2H), 4.44 (t, *J* = 5.2 Hz, 2H), 6.22 (d, *J* = 2.8 Hz, 1H), 6.63 (dd, *J* = 8.8 & 2.0 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 2.04 Hz, 1H), 7.03 (d, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 2.8 Hz, 1H), 7.30 (d, *J* = 8.8 Hz, 1H), 8.66 (s, 1H), 13.10 (s, 1H)

^{13}C NMR (DMSO-d6) : δ 25.53, 32.84, 34.83, 45.15, 66.86, 67.00, 97.60, 99.55, 99.74, 104.23, 110.24, 111.28, 114.29, 128.87, 129.25, 129.67, 130.54, 130.60, 150.78, 156.47, 171.33

ESI/MS (m/z) : 412.17 $(M+H)^+$

5.1.17 General procedure for the preparation of the compounds 19a-c and 19e-j.

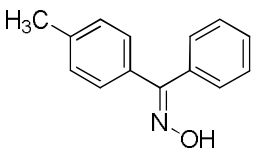


18a-c
18e-j

19a-c
19e-j

To a solution of ketones (**18a-c**, **18e-j**) (1 mole equivalent) in ethanol (10 fold) was added a solution of hydroxylammonium chloride (2 mole equivalent) and sodium acetate (2 mole equivalent) in water (10 fold) and the reaction mixture was refluxed for 20-24 hours as required. Ethanol was distilled out and residue was poured into water and was extracted with ethyl acetate. Combined organic extracts were successively washed with water and brine, dried over sodium sulfate, filtered and concentrated under vacuum to yield the desired products (**19a-c**, **19e-j**).

5.1.17.1 (*Z*/*E*)-Phenyl (p-tolyl)methanone oxime. (19a)



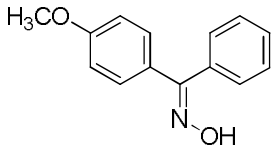
19a (3.28 gm, 61.0%) was prepared from **18a** (5.0 gm, 0.02548 mol) following the general procedure described above as a white solid; m.p: 124-125 °C; Purity by HPLC: 99.0%.

IR (KBr) **:** 3231, 3024, 2918, 1608, 1500, 1443, 1327, 999 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.35 (s, 3H, *E* isomer) & 2.41 (s, 3H, *Z* isomer), 7.13 (d, *J* = 5.2 Hz, 1H), 7.28-7.41 (m, 6H), 7.43-7.48 (m, 2H), 7.72 & 7.78 (s, 1H, =N-OH, *Z* & *E* isomer, exchangeable)

ESI/MS (m/z) **:** 212.31$(M+H)^+$

5.1.17.2 (*Z*/*E*)-(4-Methoxy-phenyl)-phenyl-methanone oxime. (19b)



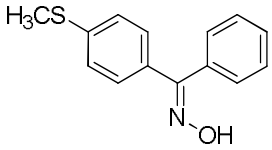
19b (4.18 gm, 78.0%) was prepared from **18b** (5.0 gm, 0.02356 mol) following the general procedure described above as a white solid; m.p: 135-136 °C; Purity by HPLC: 99.8% (*Z* isomer: *E* isomer, 1:0.64, 60.78 & 38.98%).

IR (KBr) **:** 3196, 3060, 2927, 2833, 1608, 1512, 1251, 1159, 997 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 3.81 (s, 3H, *E* isomer), 3.85 (s, 3H, Z isomer), 6.85 (d, *J* = 8.55 Hz, 1H), 6.97 (d, *J* = 8.79 Hz, 2H), 7.32-7.48 (m, 6H), 8.75 (s, 1H, =N-OH, exchangeable)

ESI/MS (m/z) **:** 228.0 $(M+H)^+$

5.1.17.3 (*Z*/*E*)-(4-Methylsulfanyl-phenyl)-phenyl-methanone oxime. (19c)



19c (5.33 gm, 100%) was prepared from **18c** (5.0 gm, 0.02190 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.8% (*Z* isomer: *E* isomer, 1:1.09).

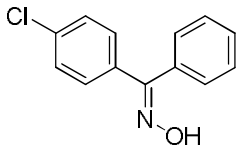
IR ($CHCl_3$) **:** 3178, 3053, 2920, 1593, 1491, 1438, 1326, 1091, 997 cm^{-1}

^{1}H NMR **:** δ 2.48 (s, 3H, *E* isomer), 2.52 (s, 3H, *Z* isomer), 7.18 (d, *J* =

($CDCl_3$) 8.55 Hz, 1H), 7.30-7.40 (m, 6H), 7.45-7.60 (m, 2H), 8.10 & 8.22 (s, 1H, =N-OH, *Z* & *E* isomer, exchangeable)

ESI/MS (m/z) **:** 242.1 $(M-H)^+$

5.1.17.4 (*Z*/*E*)-(4-Methylsulfanyl-phenyl)-phenyl-methanone oxime. (19e)



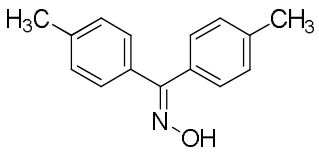
19e (3.05 gm, 95.0%) was prepared from **18e** (3.0 gm, 0.01385 mol) following the general procedure described above as a white solid; m.p: 126-128 °C; Purity by HPLC: 99.2% (54.72 & 44.49%).

IR (KBr) **:** 3205, 3059, 2912, 1593, 1452 1325, 1161, 1091, 1016 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 7.28-7.60 (m, 9H), 7.96 & 8.08 (s, 1H, =N-OH, *Z* & *E* isomer, exchangeable)

ESI/MS (m/z) **:** 231.7 $(M+H)^+$

5.1.17.5 Di-p-tolylmethanone oxime. (19f)



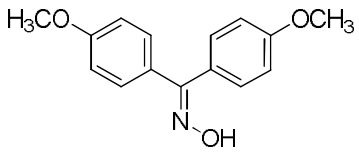
19f (4.29 gm, 80.0%) was prepared from **18f** (5.0 gm, 0.02378 mol) following the general procedure described above as a white solid; m.p: 162-163 °C; Purity by HPLC: 99.58%.

IR (KBr) **:** 3223, 3051, 2916, 1608, 1508, 1325, 1159, 1113, 1003, 925, 819 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.35 (s, 3H), 2.41 (s, 3H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.25-7.31 (m, 4H), 7.35 (d, *J* = 8.0 Hz, 2H), 8.10 (s, 1H, =N-OH, exchangeable)

ESI/MS (m/z) **:** 226.31 $(M+H)^+$

5.1.17.6 Bis (4-methoxyphenyl)methanone oxime. (19g)



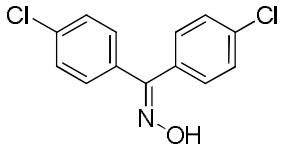
19g (4.99 gm, 94.0%) was prepared from **18g** (5.0 gm, 0.02064 mol) following the general procedure described above as an off white solid; m.p: 118-119 °C; Purity by HPLC: 98.8%.

IR (KBr) **:** 3227, 3063, 2962, 2837, 1606, 1512, 1456, 1327, 1251, 1172, 1033, 924 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 3.81 (s, 3H), 3.85 (s, 3H), 6.83-6.87 (m, 2H), 6.95-6.99 (m, 2H), 7.36-7.42 (m, 4H)

ESI/MS (m/z) **:** 257.8 $(M+H)^+$

5.1.17.7 Bis (4-chlorophenyl)methanone O-(2-bromoethyl) oxime. (19h)



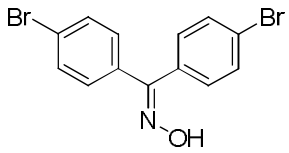
19h (3.34 gm, 63.0%) was prepared from **18h** (5.0 gm, 0.01991 mol) following the general procedure described above as a white solid; m.p: 120-122 °C; Purity by HPLC: 99.4%.

IR (KBr) **:** 3400, 3215, 2916, 1591, 1491, 1396, 1319, 1161, 1093, 999, 831 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 7.30-7.34 (m, 4H), 7.37-7.40 (m, 2H), 7.43-7.48 (m, 2H), 7.74 (s, 1H)

ESI/MS (m/z) **:** 266.03 $(M+H)^+$

5.1.17.8 Bis(4-bromophenyl)methanone oxime. (19i)



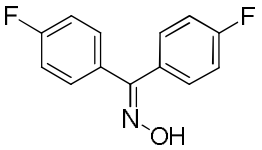
19i (4.96 gm, 95.0%) was prepared from **18i** (5.0 gm, 0.01471 mol) following the general procedure described above as a white solid; m.p: 138-140 °C; Purity by HPLC: 98.9%.

IR (KBr) **:** 3211, 3051, 2901, 1585, 1489, 1390, 1319, 1070, 993 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 7.25-7.29 (m, 2H), 7.30-7.33 (m, 2H), 7.45-7.49 (m, 2H), 7.59-7.62 (m, 2H), 8.04 (s, 1H)

ESI/MS (m/z) : 355.9 $(M+H)^+$

5.1.17.9 Bis-(4-fluoro-phenyl)-methanone oxime. (19j)



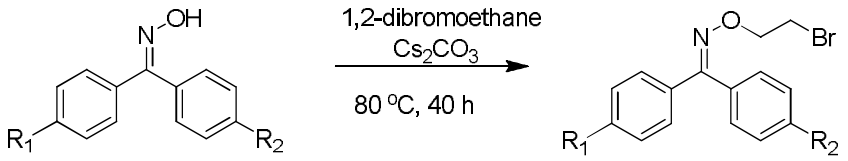
19j (5.34 gm, 100%) was prepared from **18j** (5.0 gm, 0.02291 mol) following the general procedure described above as an off white solid; m.p: 119-120 °C; Purity by HPLC: 99.9%.

IR (KBr) **:** 3373, 3049, 2864, 2802, 1629, 1602, 1508, 1407,1155, 1001, 929 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 7.00-7.06 (m, 2H), 7.13-7.18 (m, 2H), 7.39-7.45 (m, 4H), 8.41 (s, 1H)

ESI/MS (m/z) **:** 234.2 $(M+H)^+$

5.1.18 General procedure for the preparation of the compounds 20a-c and 20e-j.



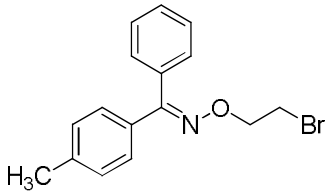
19a-c
19e-j

20a-c
20e-j

To a solution of oximes (**19a-c**, **19e-j**) (1 mole equivalent) in 1,2-dibromoethane (10 fold), cesium carbonate (3 mole equivalent) was added under nitrogen atmosphere and the reaction mixture was heated at 80 °C for 40 hours. Reaction

mixture was filtered and the solvent was concentrated under vacuum. The residue was dissolved in ethyl acetate and successively washed with water, brine, dried over sodium sulfate and concentrated under vacuum. The crude products were purified by column chromatography using 100% hexane to 12.0% ethyl acetate in hexane as eleunt to yield the desired pure products (**20a-c**, **20e-j**).

5.1.18.1 (*Z*/*E*)-Phenyl (p-tolyl)methanone O-(2-bromoethyl) oxime. (20a)



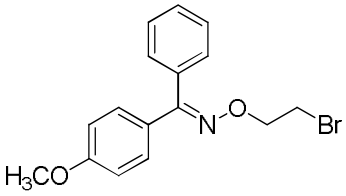
20a (2.49 gm, 55.0%) was prepared from **19a** (3.0 gm, 0.01420 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 94.3% (*Z* isomer: *E* isomer, 1: 0.80).

IR ($CHCl_3$) **:** 3018, 2924, 1510, 1444, 1385, 1088, 1009, 974 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.36 (s, 3H, *E* isomer), 2.40 (s, 3H, *Z* isomer), 3.61-3.65 (m, 2H), 4.39-4.44 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.23 (s, 1H), 7.29-7.43 (m, 6H), 7.46-7.48 (m, 1H)

ESI/MS (m/z) **:** 318.10 $(M+H)^+$

5.1.18.2 (*Z*/*E*)-(4-Methoxy-phenyl)-phenyl-methanone O-(2-bromo-ethyl)-oxime. (20b)



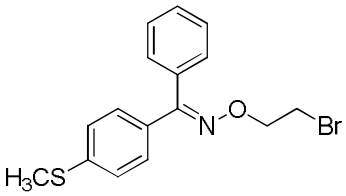
20b (4.24 gm, 96.0%) was prepared from **19b** (3.0 gm, 0.01320 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.9% (*Z* isomer: *E* isomer, 1: 1.22, 44.93 & 55.04%).

IR ($CHCl_3$) **:** 3016, 2937, 2839, 1608, 1510, 1442, 1251, 1008, 837 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 3.60-3.67 (m, 2H), 3.81 (s, 3H, *E* isomer), 3.85 (s, 3H, *Z* isomer), 4.37-4.46 (m, 2H), 6.84 (d, *J* = 8.94 Hz, 1H), 6.95 (d, *J* = 8.91 Hz, 1H), 7.35-7.46 (m, 7H)

ESI/MS (m/z) : 334.1 $(M+H)^+$

5.1.18.3 (*Z*/*E*)-(4-Methylsulfanyl-phenyl)-phenyl-methanone O-(2-bromo-ethyl)-oxime. (20c)



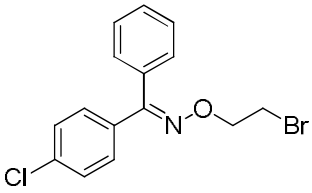
20c (3.37 gm, 78.0%) was prepared from **19c** (3.0 gm, 0.01233 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.6% (*Z* isomer: *E* isomer, 1: 1.12).

IR (CHCl$_3$) : 3013, 2922, 2868, 1597, 1493, 1215, 1093, 1006, 974 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.48 (s, 3H, *E* isomer), 2.52 (s, 3H, *Z* isomer), 3.60-3.66 (m, 2H), 4.39-4.46 (m, 2H), 7.18 (d, *J* = 8.43 Hz, 1H), 7.29-7.48 (m, 8H)

ESI/MS (m/z) : 350.1 $(M+H)^+$

5.1.18.4 (*Z*/*E*)-4-Chlorophenyl)(phenyl)methanone O-(2-bromoethyl) oxime. (20e)



20e (2.74 gm, 75.0%) was prepared from **19e** (2.5 gm, 0.01097 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 91.5% (*Z* isomer: *E* isomer, 81.47 & 10.06%).

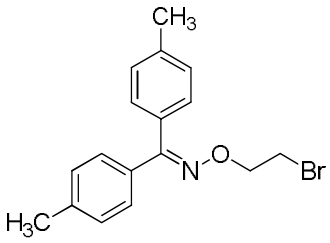
IR (CHCl$_3$) : 3018, 1655, 1597, 1489, 1385, 1090, 1008, 974 cm^{-1}

^{1}H NMR : δ 3.62 (t, *J* = 6.00 Hz, 2H), 4.43 (t, *J* = 6.4 Hz, 2H), 7.32-7.51

($CDCl_3$) (m, 9H)

ESI/MS (m/z) **:** 338.08 $(M+H)^+$

5.1.18.5 Di-p-tolylmethanone O-(2-bromoethyl) oxime. (20f)



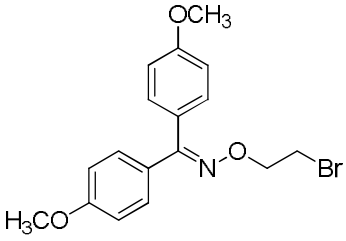
20f (1.81 gm, 41.0%) was prepared from **19f** (3.0 gm, 0.01332 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 92.6%.

IR ($CHCl_3$) **:** 3018, 2922, 1610, 1508, 1384, 1087, 1047, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.35 (s, 3H), 2.39 (s, 3H), 3.62 (t, *J* = 6.8 Hz, 2H), 4.40 (t, *J* = 6.4 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.22-7.29 (m, 4H), 7.35 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) **:** 332.0 $(M+H)^+$

5.1.18.6 Bis-(4-methoxy-phenyl)-methanone O-(2-bromo-ethyl)-oxime. (20g)



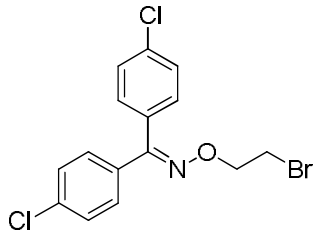
20g (2.63 gm, 62.0%) was prepared from **19g** (3.0 gm, 0.01166 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.5%.

IR ($CHCl_3$) **:** 3018, 2937, 2910, 2839, 1608, 1510, 1326, 1250, 1032, 931, cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 3.64 (t, *J* = 6.42 Hz, 2H), 3.82 (s, 3H), 3.85 (s, 3H), 4.41 (t, *J* = 6.45 Hz, 2H), 6.84-6.88 (m, 2H), 6.92-6.96 (m, 2H), 7.35-7.42 (m, 4H)

ESI/MS (m/z) **:** 364.2 $(M+H)^+$

5.1.18.7 Bis(4-chlorophenyl)methanone O-(2-bromoethyl) oxime. (20h)



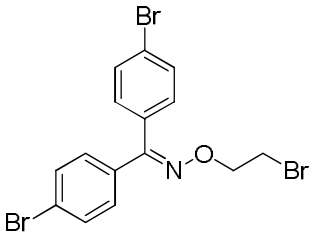
20h (2.65 gm, 63.0%) was prepared from **19h** (3.00 gm, 0.01127 mol) following the general procedure described above as a white solid; m.p: 42-44 °C; Purity by HPLC: 97.5%

IR (KBr) **:** 3018, 2976, 1600, 1491, 1384, 1091, 976 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 3.61 (t, *J* = 6.4 Hz, 2H), 4.43 (t, *J* = 6.4 Hz, 2H), 7.29-7.34 (m, 4H), 7.38-7.44 (m, 4H).

ESI/MS (m/z) **:** 374.05 $(M+H)^+$

5.1.18.8 Bis(4-bromophenyl)methanone O-(2-bromoethyl) oxime. (20i)



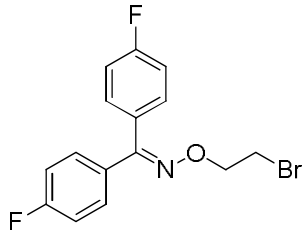
20i (2.73 gm, 70.0%) was prepared from **19i** (3.00 gm, 0.00845 mol) following the general procedure described above as a white solid; m.p: 65-66 °C; Purity by HPLC: 98.4%

IR (KBr) **:** 3018, 2976, 1597, 1489, 1384, 1008, 974 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 3.61 (t, *J* = 6.4 Hz, 2H), 4.43 (t, *J* = 6.0 Hz, 2H), 7.24-7.27 (m, 2H), 7.30-7.34 (m, 2H), 7.45-7.48 (m, 2H), 7.56-7.59 (m, 2H)

ESI/MS (m/z) **:** 459.9 $(M+H)^+$

5.1.18.9 Bis-(4-fluoro-phenyl)-methanone O-(2-bromo-ethyl)-oxime. (20j)



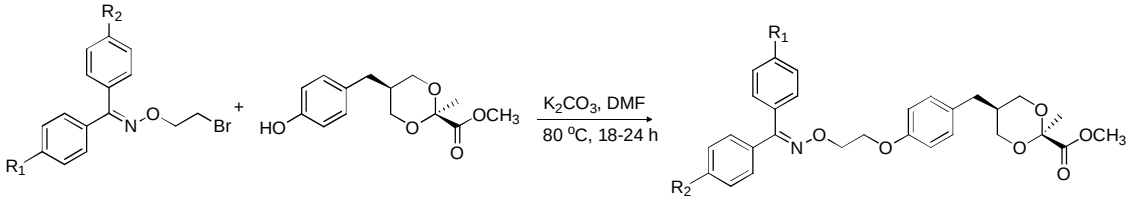
20j (2.82 gm, 77.3%) was prepared from **19j** (2.50 gm, 0.01072 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.4%.

IR ($CHCl_3$) **:** 3018, 2976, 2872, 1693, 1604, 1508, 1421, 1369, 1321, 1155, 1008 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 3.62 (t, *J* = 6.24 Hz, 2H), 4.43 (t, *J* = 6.27 Hz, 2H), 7.00-7.06 (m, 2H) 7.10-7.16 (m, 2H), 7.37-7.47 (m, 4H)

ESI/MS (m/z) **:** 341.0 $(M+H)^+$

5.1.19 General procedure for the synthesis of compounds 21a-c and 21e-j.



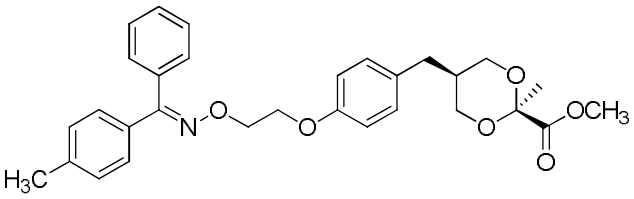
20a-c
20e-j

6a

21a-c
21e-j

To a solution of the halides (**20a-c**, **20e-j**) (1 mole equivalent) and **6a** (1 mole equivalent) in dry DMF (5 fold), K_2CO_3 (2 mole equivalent) was added and the reaction mixture was stirred at 80 °C for 18-24 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The combined organic extracts were successively washed with water and brine and were dried over Na_2SO_4, filtered and concentrated under vacuum. The crude products were purified by column chromatography using 5-10% ethyl acetate in hexane as eleunt to furnish pure required compounds (**21a-c**, **21e-j**).

5.1.19.1 Methyl-2-methyl-*c*-5-(4-(2-(((*Z*/*E*)-(phenyl(p-tolyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (21a)



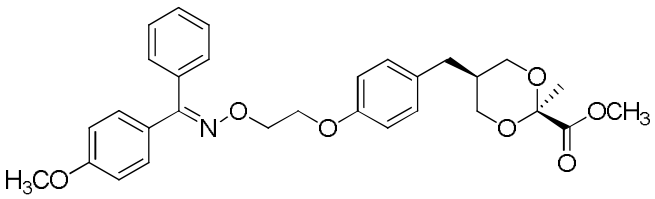
21a (1.38 gm, 58.0%) was prepared from **20a** (1.50 gm, 4.7 mmol) and **6a** (1.26 gm, 4.7 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.2% (*Z* isomer: *E* isomer, 1: 0.76).

IR ($CHCl_3$) **:** 3018, 2955, 2928, 2858, 1743, 1612, 1512, 1444, 1384, 1248, 1143, 1041, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.24-2.30 (m, 3H), 2.35(s, 3H, *E* isomer), 2.39 (s, 3H, *Z* isomer), 3.46 (t, *J* = 11.2 Hz, 2H), 3.82 (s, 3H), 3.88 (dd, *J* = 12.0 & 3.6 Hz, 2H), 4.22-4.26 (m, 2H), 4.47-4.51 (m, 2H), 6.83 (dd, *J* = 8.4 7 3.2 Hz, 2H), 6.99 (dd, *J* = 7.6 & 2.4 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.25-7.39 (m, 5H), 7.46 (, dd, *J* = 8.4 & 1.6 Hz, 1H)

ESI/MS (m/z) **:** 526.2 $(M+Na)^+$

5.1.19.2 Methyl-*c*-5-(4-(2-(((*Z*/*E*)-((4-methoxyphenyl)-(phenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (21b)



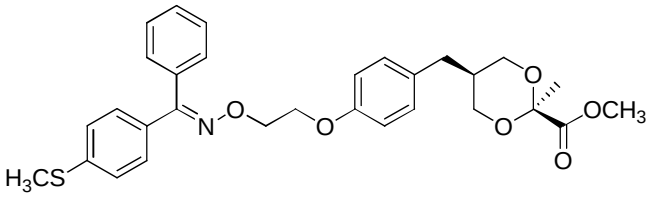
21b (1.35 gm, 86.9%) was prepared from **20b** (1.00 gm, 3.0 mmol) and **6a** (796 mg, 3.0 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 94.8 % (*Z* isomer: *E* isomer, 1: 1.08, 45.39 & 49.44%).

IR ($CHCl_3$) **:** 2928, 2839, 1747, 1610, 1512, 1250, 1143, 1037, 835 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.49 (s, 3H), 2.20-2.35 (m, 3H), 3.46-3.50 (m, 5H), 3.81(s, 3H, *E* isomer), 3.84 (s, 3H, *Z* isomer), 3.88 (dd, *J* = 16.08 & 4.92 Hz, 2H), 4.23-4.27 (m, 2H), 4.45-4.51 (m, 2H), 6.83-6.86 (m, 3H), 6.91 (d, *J* = 8.91 Hz, 1H), 6.99 (dd, *J* = 6.27 & 2.37, 2H), 7.32-7.41 (m, 6H), 7.44-7.48 (m, 1H)

ESI/MS (m/z) : 520.3 $(M+H)^+$

5.1.19.3 Methyl-2-methyl-*c*-5-(4-(2-(((*Z*/*E*)-((4-methylthiophenyl)-(phenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (21c)



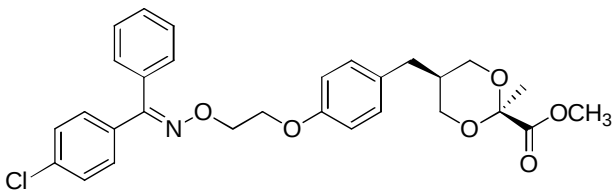
21c (1.38 gm, 90.0%) was prepared from **20c** (1.00 gm, 2.8 mmol) and **6a** (760 mg, 2.8 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 91.4% (*Z* isomer: *E* isomer, 1: 1.13).

IR (CHCl$_3$) : 2926, 2852, 1747, 1597, 1493, 1248, 1116, 1016, 979 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.49 (s, 3H), 2.23-2.31 (m, 3H), 2.48 (s, 3H, *E* isomer) & 2.51 (s, 3H, *Z* isomer), 3.46 (t, *J* = 11.37 Hz, 2H), 3.84 (s, 3H), 3.90 (dd, *J* = 12.0 & 3.61 Hz, 2H), 4.23-4.27 (m, 2H), 4.47-4.52 (m, 2H), 6.84 (dd, *J* = 8.64 & 2.31 Hz, 2H), 6.99 (d, *J* = 7.62 Hz, 2H), 7.17 (d, *J* = 8.64 Hz, 1H), 7.29-7.47 (m, 8H)

ESI/MS (m/z) : 536.2 $(M+H)^+$

5.1.19.4 Methyl-*c*-5-(4-(2-(((*Z*/*E*)-((4-chlorophenyl)-(phenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-r-2-carboxylate. (21e)



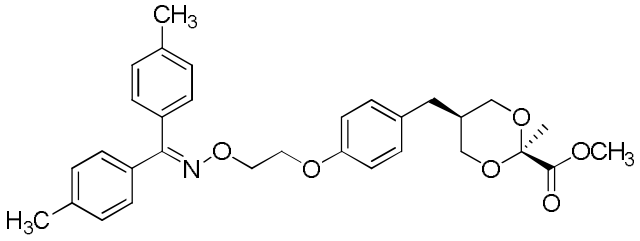
21e (1.16 gm, 50.0%) was prepared from **20e** (1.50 gm, 4.4 mmol) and **6a** (1.18 gm, 4.4 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.5 % (85.86 & 10.62%).

IR ($CHCl_3$) **:** 3018, 2928, 2872, 1743,1610, 1512, 1385, 1248, 1144, 980 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.24-2.29 (m, 3H), 3.46 (t, *J* = 11.2 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12 & 3.6 Hz, 2H), 4.23 (t, *J* = 5.2 Hz, 2H), 4.50 (t, *J* = 4.8 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.28-7.34 (m, 3H), 7.36-7.41 (m, 4H), 7.43-7.45 (m, 2H)

ESI/MS (m/z) **:** 524.22 $(M+H)^+$

5.1.19.5 Methyl-*c*-5-(4-(2-(((di-p-tolylmethylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (21f)



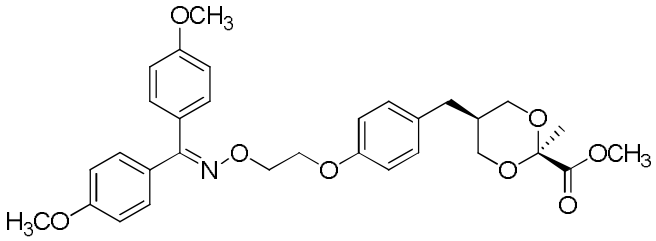
21f (1.52 gm, 65.0%) was prepared from **20f** (1.50 gm, 4.5 mmol) and **6a** (1.20 gm, 4.5 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 94.1%.

IR ($CHCl_3$) **:** 3018, 2926, 2872, 1743, 1612, 1512, 1446, 1384, 1247, 1041, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.27-2.31 (m, 3H), 2.35 (s, 3H), 2.39 (s, 3H), 3.46 (t, *J* = 11.2 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.0& 4.0 Hz, 2H), 4.24 (t, *J* = 5.2 Hz, 2H), 4.48 (t, *J* = 5.2 Hz, 2H), 6.83 (dd, *J* = 8.8 & 2.0 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.19-7.24 (m, 4H), 7.35 (d, *J* = 8.4 Hz, 2H)

ESI/MS (m/z) **:** 518.19 $(M+H)^+$

5.1.19.6 Methyl-*c*-5-(4-(2-(((bis(4-methoxyphenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (21g)



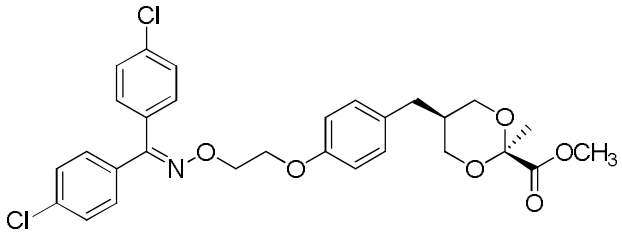
21g (1.40 gm, 62.0%) was prepared from **20g** (1.50 gm, 4.1 mmol) and **6a** (1.10 gm, 4.1 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.9%.

IR ($CHCl_3$) : 3020, 2935, 1741, 1608, 1512, 1425, 1278, 1141, 1093, 1018 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.19-2.33 (m, 3H), 3.46 (t, *J* = 10.89 Hz, 2H), 3.82 (s, 3H), 3.84 (s, 6H), 3.88 (dd, *J* = 12.27 & 5.0 Hz, 2H), 4.24 (t, *J* = 5.13 Hz, 2H), 4.48 (t, *J* = 4.49 Hz, 2H), 6.83-6.86 (m, 4H), 6.90 (dd, *J* = 9.16 & 2.68 Hz, 2H), 6.99 (d, *J* = 8.61 Hz, 2H) 7.33 (dd, *J* = 12.0 & 2.8 Hz, 2H), 7.40 (dd, *J* = 11.6 & 2.8 Hz, 2H)

ESI/MS (m/z) : 550.2 $(M+H)^+$

5.1.19.7 Methyl-*c*-(4-(2-(((bis(4-chlorophenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-r-2-carboxylate. (21h)



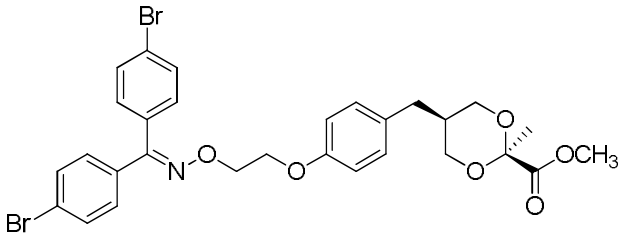
21h (1.29 gm, 86.0%) was prepared from **20h** (1.00 gm, 2.7 mmol) and **6a** (713.8 mg, 2.7 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.1%.

IR ($CHCl_3$) **:** 2939, 2856, 1749, 1602, 1512, 1489, 1367, 1232, 1141, 935 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.24-2.31 (m, 3H), 3.46 (t, *J* = 10.8 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.4 & 4.0 Hz, 2H), 4.22 (t, *J* = 5.2 Hz, 2H), 4.49 (t, *J* = 4.4 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), 7.27-7.31 (m, 4H), 7.38 (d, *J* = 8.8 Hz, 4H)

ESI/MS (m/z) **:** 580.17 $(M+Na)^+$

5.1.19.8 Methyl-*c*-5-(4-(2-(((bis(4-bromophenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (21i)



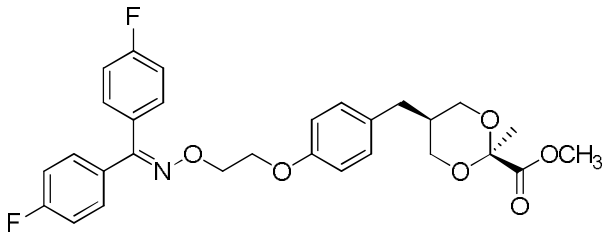
21i (1.13 gm, 67.0%) was prepared from **20i** (1.20 gm, 2.6 mmol) and **6a** (691 mg, 2.6 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.8%.

IR ($CHCl_3$) **:** 3018, 2976, 2928, 1743, 1512, 1384, 1246, 1143, 1072, 929 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.23-2.29 (m, 3H), 3.46 (t, *J* = 10.8 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.0 & 3.6 Hz, 2H), 4.22 (t, *J* = 4.8 Hz, 2H), 4.49 (t, *J* = 4.4 Hz, 2H), 6.81 (, d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H), 7.20 (dd, *J* = 6.8 & 2.0 Hz, 2H), 7.31 (dd, *J* = 6.8 & 2.0 Hz, 2H), 7.44-7.47 (m, 2H), 7.52-7.55 (m, 2H)

ESI/MS (m/z) **:** 647.95 $(M+H)^+$

5.1.19.9 Methyl-*c*-5-(4-(2-(((bis(4-fluorophenyl)methylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-carboxylate. (21j)



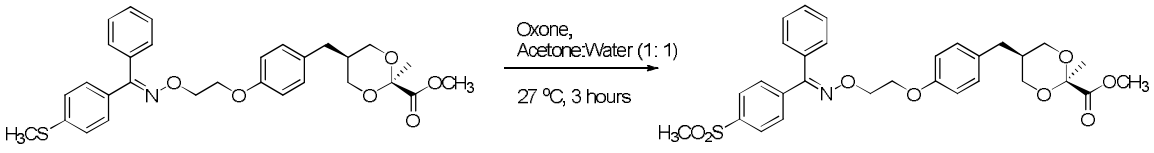
21j (1.34 gm, 86.8%) was prepared from **20j** (1.00 gm, 2.9 mmol) and **6a** (782 mg, 2.9 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 93.7%.

IR ($CHCl_3$) : 3020, 2929, 2881, 1745, 1606, 1510, 1427, 1371, 1143, 1041 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.23-2.29 (m, 3H), 3.46 (t, *J* = 10.8 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.15 & 3.75 Hz, 2H), 4.23 (t, *J* = 4.98 Hz, 2H), 4.49 (t, *J* = 4.71 Hz, 2H), 6.83 (d, *J* = 8.52 Hz, 2H), 6.98-7.06 (m, 4H), 7.11 (d, *J* = 8.67 Hz, 2H), 7.33 (dd, *J* = 8.71 & 5.40 Hz, 2H), 7.44 (dd, *J* = 8.76 & 5.46 Hz, 2H)

ESI/MS (m/z) : 548.2 $(M+Na)^+$

5.1.20 Methyl-2-methyl-*c*-5-(4-(2-(((*Z*/*E*)-((4-methylsulfonylphenyl)-(phenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate.(21d)



21c **21d**

To a solution of methyl 2-methyl-*c*-5-(4-(2-(*Z*/*E*)-((4-methylthiophenyl)-(phenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate **(21c)** (500 mg, 0.93 mmol) in acetone (20 ml), solution of oxone (1.2 gm, 1.86 mmol) in water (20 ml) was added and reaction mixture was stirred for an 3 hrs at 27 °C. The reaction mixture was concentrated under vacuum and residue was dissolved

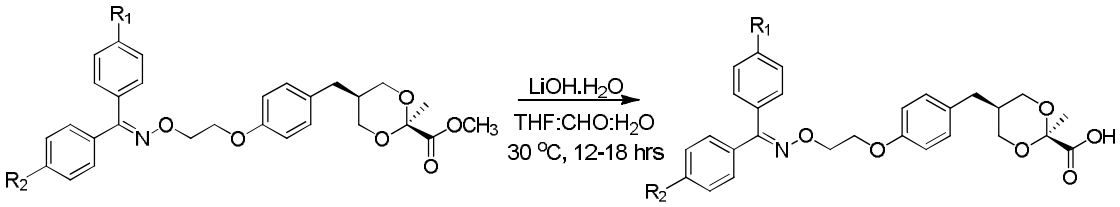
in water and extracted with ethyl acetate, the organic extracts were washed with water, brine, dried over sodium sulfate and concentrated under vacuum to yield **21d** (440 mg, 83%) as a thick liquid. Purity by HPLC: 91.2% (*Z* isomer: *E* isomer, 1: 1.05, 43.86 & 47.29%).

IR ($CHCl_3$) **:** 3020, 1743, 1630, 1512, 1385, 1319, 1150, 1043, 985 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.27 (s, 3H), 3.05 (s, 3H, *E* isomer), 3.11 (s, 3H, *Z* isomer), 3.46 (t, *J* = 10.4 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 13.8 & 3.4, 2H), 4.22-4.26 (m, 2H), 4.50-4.55 (m, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.98-7.01 (m, 2H), 7.31-7.36 (m, 3H), 7.40-7.45 (m, 2H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.8 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H)

ESI/MS (m/z) **:** 568.15 $M+H)^+$

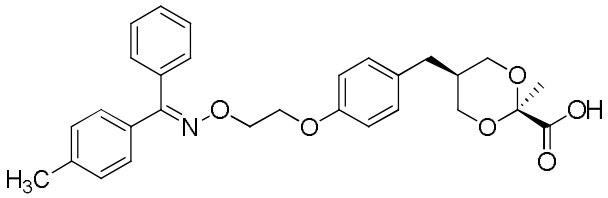
5.1.21 General procedure for the preparation of the compounds 22a-j.



21a-j **22a-j**

To a solution of **21a-j** (1 mole equivalent) in THF (9 fold), MeOH (3 fold) and H_2O (3 fold), $LiOH.H_2O$ (2 mole equivalent) was added and stirred at 30 °C for 12-18 hours. The reaction mixture was concentrated under vacuum. Water was added to the reaction mixture, acidified with aq. HCl and was extracted with ethyl acetate. The organic extract was washed with water followed by brine, dried over Na_2SO_4, filtered and concentrated under vacuum to give pure products **22a-j**.

5.1.21.1 2-Methyl-*c*-5-(4-(2-(((*Z*/*E*)-(phenyl-(p-tolyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (22a)



22a (1.25 gm, 86.0%) was prepared from **21a** (1.50 gm, 3.0 mmol) following the general procedure described above as a thick liquid; Purity by HPLC: 99.4% (*Z* isomer: *E* isomer, 1: 0.78).

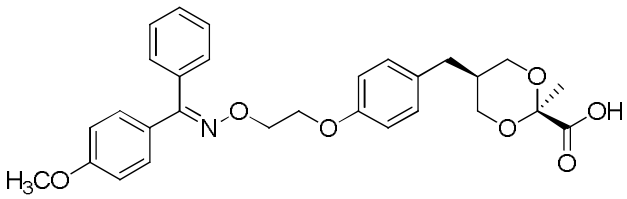
IR ($CHCl_3$) **:** 3358, 3018, 2928, 1724, 1610, 1512, 1384, 1043, 981, 929 cm^{-1}

^1H NMR (DMSO-*d6*) **:** δ 1.26 (s, 3H), 1.98-2.11 (m, 1H), 2.22 (d, *J* = 7.2 Hz, 2H), 2.29 (s, 3H, *E* isomer), 2.34 (s, 3H, *Z* isomer), 3.43 (t, *J* = 11.6 Hz, 2H), 3.62 (dd, *J* = 11.2 & 3.6 Hz, 2H), 4.19 (s, 2H), 4.38-4.39 (m, 2H), 6.84 (dd, *J* = 8.8 & 2.4 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.23-7.26 (m, 3H), 7.35-7.43 (m, 4H)

^{13}C NMR ($CDCl_3$) **:** δ 13.03, 25.96, 33.89, 35.20, 55.44, 66.79, 68.25, 72.42, 98.30, 113.89, 114.97, 127.57, 129.17, 129.64, 130.11, 155.34, 157.69, 160.54, 174.76

ESI/MS (m/z) **:** 512.21 $(M+Na)^+$

5.1.21.2 5-(4-(2-(((*Z*/*E*)-((4-methoxyphenyl)-(phenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-2-carboxylic acid. (22b)



22b (948 mg, 75.0%) was prepared from **21b** (1.30 gm, 2.5 mmol) following the general procedure described above as a thick liquid; Purity by HPLC: 98.7% (*Z* isomer: *E* isomer, 1: 1.13, 46.32 & 52.35%).

IR ($CHCl_3$) **:** 3450, 3018, 2931, 2841, 1724, 1610, 1512, 1444, 1301, 1217, 1145, 1033, 837 cm^{-1}

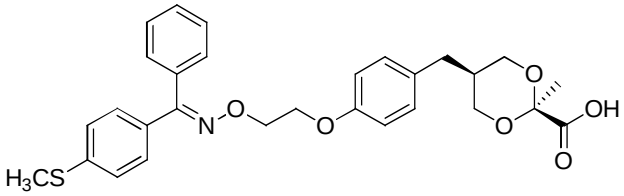
^1H NMR ($CDCl_3$) **:** δ 1.55 (s, 3H), 2.28-2.30 (m, 3H), 3.52 (t, *J* = 10.59 Hz, 2H), 3.81(s, 3H, *E* isomer), 3.84 (s, 3H, *Z* isomer), 3.93 (dd, *J* = 13.17 & 3.96 Hz, 2H), 4.22-4.27 (m, 2H), 4.45-4.53 (m, 2H),

6.83-6.86 (m, 3H), 6.90 (d, *J* = 8.85 Hz, 1H), 6.99 (dd, *J* = 7.62 & 1.92 Hz, 2H), 7.33-7.41 (m, 7H)

^{13}C NMR ($CDCl_3$) : δ 25.93, 33.90, 35.17, 55.39, 55.45, 66.69, 68.32, 72.61, 72.76, 98.15, 113.47, 113.77, 114.99, 125.35, 128.13, 128.31, 128.46, 129.06, 129.44, 129.50, 129.66, 130.08, 131.50, 133.50, 137.01, 157.45, 157.50, 157.67, 160.06, 160.78, 174.50

ESI/MS (m/z) : 506.2 $(M+H)^+$

5.1.21.3 2-Methyl-*c*-5-(4-(2-(((*Z*/*E*)-(4-methylthiophenyl)-(phenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (22c)



22c (670 gm, 80.0%) was prepared from **21c** (860 mg, 1.6 mmol) following the general procedure described above as a yellow solid; m.p: 65-66 °C; Purity by HPLC: 98.6% (*Z* isomer: *E* isomer, 1:1.11).

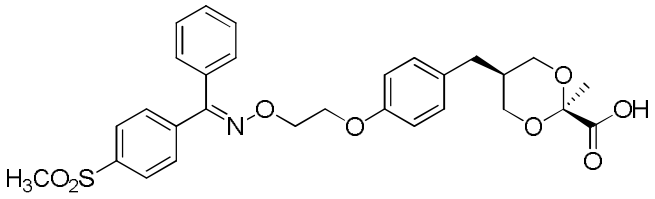
IR (KBr) : 3450, 3018, 2872, 1724, 1596, 1512, 1444, 1118, 1039, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.26-2.30 (m, 3H), 2.48 (s, 3H, *E* isomer), 2.51 (s, 3H, *Z* isomer), 3.52 (t, *J* = 10.59 Hz, 2H), 3.93 (dd, *J* = 13.17 & 3.96 Hz, 2H), 4.22-4.26 (m, 2H), 4.47-4.52 (m, 2H), 6.84 (dd, *J* = 8.64 & 2.31 Hz, 2H), 6.99 (d, *J* = 7.62 Hz, 2H), 7.17 (d, *J* = 8.49 Hz, 1H), 7.29-7.40 (m, 7H), 7.44-7.47 (m, 1H)

^{13}C NMR ($CDCl_3$) : δ 15.38, 15.51, 25.94, 33.89, 35.18, 66.66, 68.32, 72.76, 72.86, 98.14, 114.99, 125.52, 125.84, 128.30, 128.30, 128.36, 129.05, 129.49, 129.55, 129.65, 130.08, 130.11, 130.20, 133.09, 133.13, 136.55, 140.09, 140.59, 157.32, 157.64, 174.85

ESI/MS (m/z) : 522.1 $(M+H)^+$

5.1.21.4 2-Methyl-*c*-5-(4-(2-(((*Z*/*E*)-((4-methylsulfonylphenyl)-(phenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (22d)



22d (304 mg, 71.0%) was prepared from **21d** (440 mg, 0.78mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 90.5% (Z isomer: *E* isomer, 1:1.14, 42.11 & 48.43%).

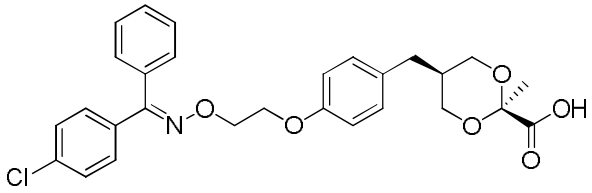
IR ($CHCl_3$) : 3358, 3020, 2930, 1724, 1610, 1512, 1385, 1151, 1043 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.26-2.34 (m, 3H), 3.06 (s, 3H, *E* isomer), 3.12 (s, 3H, *Z* isomer), 3.52 (t, *J* = 9.2 Hz, 2H), 3.90 (dd, *J* = 12.4 & 4.2 Hz, 2H), 4.22-4.26 (m, 2H), 4.51-4.55 (m, 2H), 6.83 (dd, *J* = 8.8 & 2.8 Hz, 2H), 6.98-7.01 (m, 2H), 7.31-7.45 (m, 5H), 7.52 (dd, *J* = 10.4 & 2 Hz, 1H), 7.67 (dd, *J* = 10.4 & 2.0 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H)

^{13}C NMR ($CDCl_3$) : δ 25.73, 33.48, 33.70, 35.01, 35.05, 44.39, 44.43, 66.35, 66.45, 67.93, 68.13, 73.10, 73.21, 98.05, 114.73, 114.83, 115.44, 116.38, 119.90, 127.20, 127.26, 127.72, 128.49, 128.62, 128.77, 128.95, 129.22, 129.46, 129.56, 129.63, 129.94, 130.16, 130.21, 130.37, 130.91, 131.94, 135.14, 137.31, 138.80, 140.47, 140.66, 141.74, 150.04, 155.84, 155.96, 157.32, 174.17

ESI/MS (m/z) : 554.16 $(M+H)^+$

5.1.21.5 *c*-5-(4-(2-(((*Z/E*)-((4-Chlorophenyl)-(phenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (22e)



22e (778 mg, 80.0%) was prepared from **21e** (1.0 gm, 1.91 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.6% (89.06 & 8.51%).

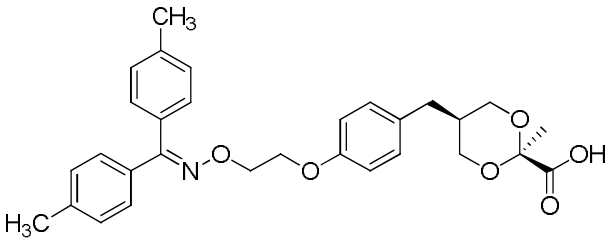
IR ($CHCl_3$) **:** 3379, 3018, 2930, 2876, 1724, 1610, 1512, 1385, 1248, 1146, 1042 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.56 (s, 3H), 2.27-2.31 (m, 3H), 3.53 (t, *J* = 10.8 Hz, 2H), 3.93 (dd, *J* = 13.6 & 4.0 Hz, 2H), 4.23 (t, *J* = 5.2 Hz, 2H), 4.50 (t, *J* = 4.0 Hz, 2H), 6.83 (t, *J* = 8.4 Hz, 2H), 7.00 (t, *J* = 8.8 Hz, 2H), 7.25-7.41 (m, 7H), 7.44 (dd,*J* = 8.4 & 1.6 Hz, 2H)

^{13}C NMR ($CDCl_3$) **:** δ 25.94, 33.88, 35.18, 66.60, 68.32, 72.96, 98.15, 114.96, 128.09, 128.28, 129.48, 128.57, 129.24, 129.36, 129.68, 129.73, 130.18, 131.06, 131.52, 135.01, 136.10, 156.72, 157.59, 175.11

ESI/MS (m/z) **:** 533.04 $(M+Na)^+$

5.1.21.6 *c*-5-(4-(2-(((bis-p-tolylmethylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (22f)



22f (990 mg, 67.0%) was prepared from **21f** (1.50 gm, 2.9 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 95.6%.

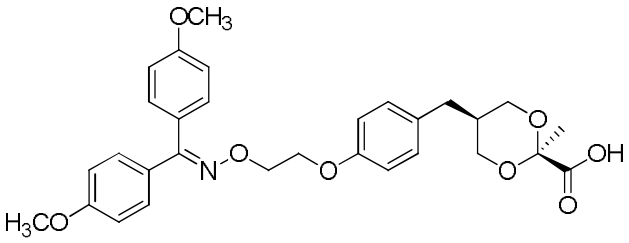
IR ($CHCl_3$) : 3400, 3018, 1718, 1610, 1512, 1384, 1145, 1043, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.27 (s, 3H), 2.35 (s, 3H), 2.39 (s, 3H), 3.52 (t, *J* = 10.4 Hz, 2H), 3.93 (dd, *J* = 14.0 & 4.0 Hz, 2H), 4.24 (t, *J* = 5.2 Hz, 2H), 4.48 (t, *J* = 5.2 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 6.4 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.19-7.24 (m, 4H), 7.35 (d, *J* = 8.4 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 20.81, 21.43, 21.58, 25.93, 33.92, 35.18, 66.68, 68.33, 72.62, 98.15, 114.99, 128.15, 128.81, 129.03, 129.55, 129.64, 130.03, 130.43, 133.96, 138.95, 139.55, 157.70, 157.82, 174.70

ESI/MS (m/z) : 504.22 $(M+H)^+$

5.1.21.7 *c*-5-(4-(2-(((Bis-(4-methoxyphenyl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (22g)



22g (1.17 gm, 62.0%) was prepared from **21g** (1.30 gm, 2.4 mmol) following the general procedure described above as an off white solid; m.p: 59-60 °C; Purity by HPLC: 98.0%.

IR (KBr) : 3433, 2926, 2856, 1750, 1610, 1508, 1458, 1217, 1172, 1116, 1031, 979 cm^{-1}

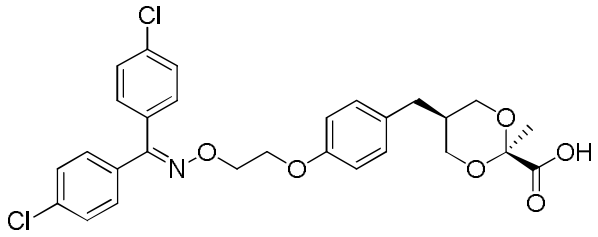
^{1}H NMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.30 (s, 3H), 3.47-3.55 (m, 2H), 3.82 (s, 3H), 3.84 (s, 3H), 3.93 (dd, *J* = 12.99 & 4.08 Hz, 2H), 4.25 (t, *J* = 5.04 Hz, 2H), 4.48 (t, *J* = 4.89 Hz, 2H), 6.85 (d, *J* = 8.76 Hz, 4H), 6.90 (d, *J* = 8.79 Hz, 2H), 6.99 (d, *J* = 8.58 Hz, 2H), 7.33 (d, *J* = 8.79 Hz, 2H), 7.40 (d, *J* = 8.79 Hz, 2H).

^{13}C NMR : δ 25.57, 32.89, 34.93, 55.16, 55.24, 55.52, 66.12, 67.10, 72.27,

(DMSO-d6) 97.64, 113.47, 113.80, 114.26, 114.45, 124.99, 128.68, 129.21, 129.68, 130.00, 130.44, 130.85, 131.87, 132.97, 156.03, 156.88, 159.52, 160.30, 171.40

ESI/MS (m/z) **:** 536.1 $(M+H)^+$

5.1.21.8 *c*-5-(4-(2-(((Bis(4-chlorophenyl)methylene)amino)oxy)ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (22h)



22h (997 mg, 93.0%) was prepared from **21h** (1.10 gm, 1.97 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.0%.

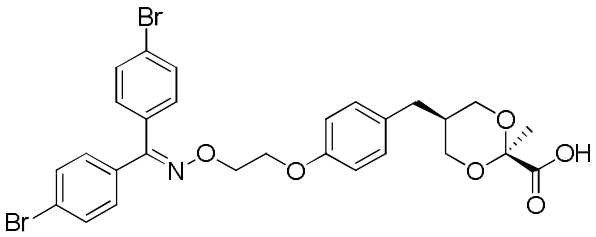
IR ($CHCl_3$) **:** 3420, 3018, 2976, 1724, 1600, 1512, 1384, 1247, 1143, 1091, 1043, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.54 (s, 3H), 2.25-2.29 (m, 3H), 3.52 (t, *J* = 10.8 Hz, 2H), 3.91 (dd, *J* = 14.0 & 4.0 Hz, 2H), 4.21 (t, *J* = 4.4 Hz, 2H), 4.48 (t, *J* = 4.8 Hz, 2H), 6.81 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 12.0 Hz, 2H), 7.26-7.30 (m, 4H), 7.38 (d, *J* = 8.4 Hz, 4H).

^{13}C NMR ($CDCl_3$) **:** δ 25.89, 33.90, 35.21, 66.52, 68.23, 73.09, 98.31, 114.92, 128.62, 128.69, 129.31, 129.69, 130.25, 130.96, 134.56, 135.24, 135.81, 155.65, 157.53, 175.17

ESI/MS (m/z) **:** 566.25 $(M+Na)^+$

5.1.21.9 *c*-5-(4-(2-(((Bis(4-bromophenyl)methylene)amino)oxy)ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (22i)



22i (636 mg, 93.0%) was prepared from **21i** (1.00 gm, 1.54 mmol) following the general procedure described above as a white solid; m.p: 90-91 °C; Purity by HPLC: 99.3%.

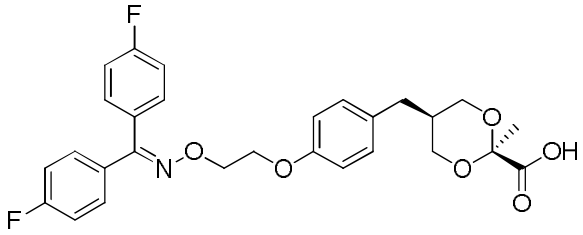
IR (KBr) **:** 3389, 2926, 2854, 1743, 1718, 1581, 1510, 1483, 1394, 1365, 1246, 1070 cm^{-1}

^{1}H NMR (CD_3OD) **:** δ 1.39 (s, 3H), 2.10-2.21 (m, 1H), 2.27 (d, *J* = 7.2 Hz, 2H), 3.53 -3.56 (m, 2H), 3.75 (dd, *J* = 11.2 & 4.0 Hz, 2H), 4.23 (t, *J* = 4.8 Hz, 2H), 4.46 (t, *J* = 4.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.35 (dd, *J* = 8.4 & 1.2 Hz, 2H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.59 (dd, *J* = 8.8 & 1.6 Hz, 2H).

^{13}C NMR (DMSO-d6) **:** δ 25.65, 33.19, 35.21, 65.99, 66.83, 72.88, 98.45, 114.46, 122.64, 123.29, 129.40, 129.58, 130.78, 131.12, 131.36, 131.41, 131.56, 134.52, 154.88, 156.72, 172.35

ESI/MS (m/z) **:** 634.12 $(M+H)^+$

5.1.21.10 *c*-5-(4-(2-(((Bis(4-fluorophenyl)methylene)amino)oxy)ethoxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (22j)



22j (887 mg, 76.0%) was prepared from **21j** (1.20 gm, 2.3mmol) following the general procedure described above as an off white solid; m.p: < 35 °C; Purity by HPLC: 98.4%.

IR (KBr) **:** 3450, 3074, 2929, 2868, 1751, 1720, 1610, 1510, 1225, 1143, 1039, 983 cm^{-1}

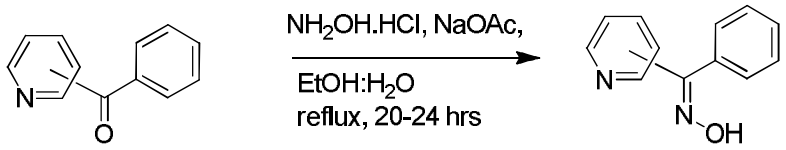
^{1}H NMR ($CDCl_3$) **:** δ 1.56 (s, 3H), 2.31 (s, 3H), 3.52 (t, *J* = 10.65 Hz, 2H), 3.93 (dd, *J* = 13.23 & 4.17 Hz, 2H), 4.23 (t, *J* = 5.49 Hz, 2H), 4.50 (t, *J* = 5.61 Hz, 2H), 6.83 (d, *J* = 8.55 Hz, 2H), 7.00 (dd, *J* = 8.34 &

1.32 Hz, 2H), 7.05-7.12 (m, 4H), 7.34 (dd, *J* = 8.76 & 5.88 Hz, 2H), 7.43 (dd, *J* = 8.85 & 5.43 Hz, 2H)

^{13}C NMR (DMSO-d6) **:** δ 25.55, 32.86, 34.92, 66.03, 67.09, 72.65, 97.62, 114.47, 115.25, 115.42, 115.46, 128.80, 129.68, 129.79, 130.50, 131.40, 131.48, 132.23, 154.88, 156.81, 160.97, 161.73, 163.42, 164.19, 171.37

ESI/MS (m/z) **:** 534.3 $(M+Na)^+$

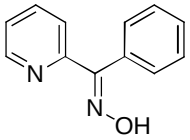
5.1.22 General procedure for the preparation of the compounds 24a-c.



23a-c **24a-c**

To a solution of **23a-c** (1 mole equivalent) in ethanol (10 fold) was added another solution of hydroxylammonium chloride (2 mole equivalent) and sodium acetate (2 mole equivalent) in water (10 fold) and the reaction mixture was refluxed for 20-24 hours. Ethanol was distilled out and the residue was poured into water and extracted with ethyl acetate. Combined organic extract were successively washed with water and brine, dried over sodium sulfate and concentrated under vacuum to yield desired products **24a-c**.

5.1.22.1 (*Z*/*E*)-Phenyl (pyridin-2-yl)methanone oxime. (24a)



24a (4.92 gm, 92.0%) was prepared from **23a** (5.0 gm, 0.028 mol) following the general procedure described above as a pink solid; m.p: 116-145 °C; Purity by HPLC: 99.7% (*Z* isomer: *E* isomer, 1: 1.06, 48.26 & 51.40%).

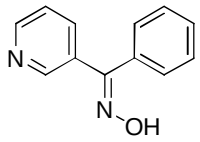
IR (KBr) **:** 3153, 3057, 2852, 1585, 1568, 1467, 1427, 1327, 1282, 1008, 941 cm^{-1}

^{1}H NMR **:** δ 7.27-7.39 (m, 1H, *E* isomer), 7.39-7.52 (m, 7H, *Z* isomer &

($CDCl_3$) 5H, *E* isomer), 7.60 (d, *J* = 10.8 Hz, 1H, *E* isomer), 7.67-6.81 (m, 1H, *E* isomer), 7.81-7.85 (m, 1H, *Z* isomer), 8.61 (dd, *J* = 4.4 Hz, 1H, *E* isomer), 8.67 (dd, *J* = 4.8 & 0.8 Hz, 1H, *Z* isomer), 14.75 (s, 1H, =N-OH, exchangeable)

ESI/MS (m/z) **:** 199.3 $(M+H)^+$

5.1.22.2 (*Z*/*E*)-Phenyl (pyridin-3-yl)methanone oxime. (24b)



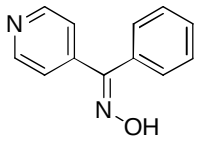
24b (3.25 gm, 100%) was prepared from **23b** (5.0 gm, 0.016 mol) following the general procedure described above as a white solid; m.p: 120-160 °C; Purity by HPLC: 99.6%, (*Z* isomer: *E* isomer, 1:1.07).

IR (KBr) **:** 3134, 3024, 2758, 1589, 1570, 1471, 1443, 1342, 1302, 1192, 1049, 1006, 945 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 7.28-7.51 (m, 6H), 7.51-7.81 (m, 1H), 8.60-8.77 (m, 2H)

ESI/MS (m/z) **:** 199.28 $(M+H)^+$

5.1.22.3 (*Z*/*E*)-Phenyl (pyridin-3-yl)methanone oxime. (24c)



24c (2.53 gm, 78.0%) was prepared from **23c** (5.0 gm, 0.016 mol) following the general procedure described above as a white solid; m.p: 110-140 °C; Purity by HPLC: 96.40% (*Z* isomer: *E* isomer, 1:1.53).

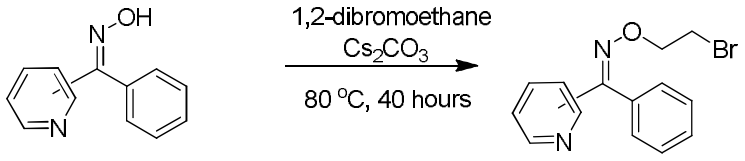
IR (KBr) **:** 3150, 2993, 2756, 1600, 1551, 1413, 1329, 1213, 1168, 1005, 825 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 7.33 (dd, *J* = 4.4 & 1.2 Hz, 2H, *Z* isomer), 7.35 -7.52 (m, 5H, *Z* isomer & 8H *E* isomer), 8.59 (dd, *J* = 4.8 & 1.6 Hz, 2H, *Z* isomer), 8.75 (dd, *J* = 4.4 & 1.6 Hz, 1H, *E* isomer), 8.95 (s, 1H,

=N-OH, exchangeable)

ESI/MS (m/z) : 199.28 $(M+H)^+$

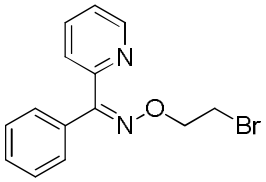
5.1.23 General procedure for the preparation of the compounds 25a-e.



24a-c **25a-e**

To a solution of **24a-c** (1 mole equivalent) in 1,2-dibromoethane (10 fold) was added cesium carbonate (3 mole equivalent) under nitrogen atmosphere and the reaction mixture was heated at 80 °C for 40 hours. Reaction mixture was filtered and the solvent was evaporated under vacuum. The residue was dissolved in ethyl acetate and successively washed with water and brine, dried over sodium sulfate, filtered and concentrated under vacuum to yield the required products. The crude products were purified by column chromatography using 12% ethyl acetate in hexane as eleunt to yield pure desired products **25a-e**.

5.1.23.1 (*Z*)-Phenyl-pyridin-2-yl-methanone O-(2-bromo-ethyl)-oxime. (25a)



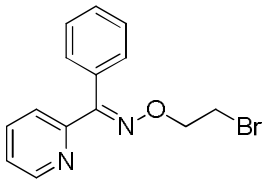
25a (1.62 gm, 35.0%) was prepared from **24a** (3.0 gm, 0.015 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.8%.

IR ($CHCl_3$) : 3060, 3012, 2939, 1585, 1444, 1369, 1330, 1236, 1087, 877 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 3.62 (t, *J* = 6.39 Hz, 2H), 4.43 (t, *J* = 6.42 Hz, 2H), 7.31-7.37 (m, 4H), 7.45 (dd, *J* = 7.44 & 1.38 Hz, 2H), 7.60 (d, *J* = 7.77 Hz, 1H), 7.78-7.83 (m, 1H), 8.72 (d, *J* = 4.74 Hz, 1H)

ESI/MS (m/z) **:** 305.0 $(M+H)^+$

5.1.23.2 (*E*)-Phenyl-pyridin-2-yl-methanone O-(2-bromo-ethyl)-oxime. (25b)



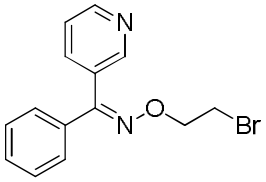
25b (1.39 gm, 30.0%) was prepared from **24a** (3.0 gm, 0.015 mol) following the general procedure described above as an off white solid; m.p: 64-65 °C, Purity by HPLC: 98.6%.

IR (KBr) **:** 3060, 3010, 2939, 1735, 1577, 1566, 1286, 1197, 993, 937 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 3.64 (t, *J* = 6.42 Hz, 2H), 4.50 (t, *J* = 6.42 Hz, 2H), 7.26-7.30 (m, 1H), 7.40-7.48 (m, 5H), 7.66-7.71 (m, 2H), 8.62 (d, *J* = 4.68 Hz, 1H)

ESI/MS (m/z) **:** 305.01 $(M+H)^+$

5.1.23.3 (*Z*)-Phenyl(pyridin-3-yl)methanone O-(2-bromoethyl) oxime. (25c)



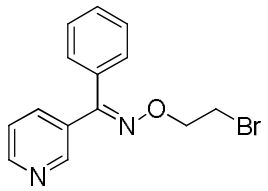
25c (690 mg, 14.0%) was prepared from **24b** (3.20 gm, 0.016 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.2%.

IR ($CHCl_3$) **:** 3018, 2974, 1597, 1475, 1414, 1385, 1086, 1009, 930 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 3.63 (t, *J* = 6.4 Hz, 2H), 4.45 (t, *J* = 6.0 Hz, 2H), 7.34-7.43 (m, 4H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.75-7.78 (m, 1H), 8.66 (dd, *J* = 6.8 & 1.2 Hz, 2H)

ESI/MS (m/z) **:** 305.13 $(M+H)^+$

5.1.23.4 (*E*)-Phenyl(pyridin-3-yl)methanone O-(2-bromoethyl) oxime. (25d)



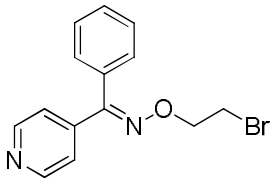
25d (492 mg, 10.0%) was prepared from **24b** (3.20 gm, 0.016 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.5%.

IR ($CHCl_3$) : 3018, 2974, 1597, 1475, 1414, 1385, 1088, 1009, 930 cm^{-1}

^1H NMR ($CDCl_3$) : δ 3.64 (t, *J* = 6.4 Hz, 2H), 4.46 (t, *J* = 6.4 Hz, 2H), 7.27-7.29 (m, 1H), 7.36-7.43 (m, 2H), 7.45-7.49 (m, 3H), 7.77-7.80 (m, 1H), 8.60 (dd, *J* = 4.8 & 1.2 Hz, 1H), 8.70 (d, *J* = 2.0 Hz, 1H)

ESI/MS (m/z) : 305.10 $(M+H)^+$

5.1.23.5 (*E*/*Z*)-Phenyl(pyridin-4-yl)methanone O-(2-bromoethyl) oxime. (25e)



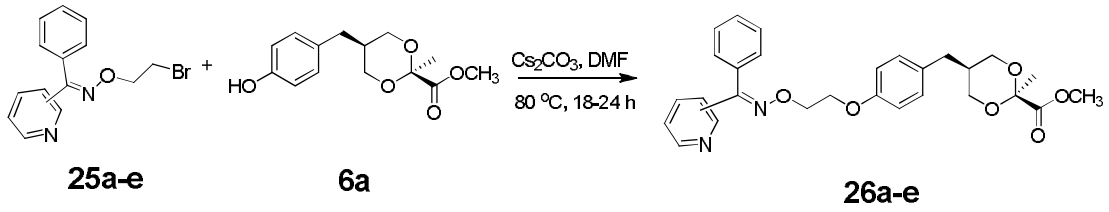
25e (1.92 mg, 50.0%) was prepared from **24c** (2.50 gm, 0.012 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 91.9% (*Z* isomer: *E* isomer, 1:2.04, 30.24 & 61.71%).

IR ($CHCl_3$) : 3018, 2974, 1601, 1384, 1215, 1086, 1009 cm^{-1}

^1H NMR ($CDCl_3$) : δ 3.60 -3.64 (m, 2H), 4.43-4.49 (m, 2H), 7.29 (dd, *J* = 4.4 & 1.4 Hz, 2H, *Z* isomer), 7.33-7.47 (m, 5H, *Z* isomer & 8H, *E* isomer), 8.59 (d, *J* = 6.0 Hz, 1H, *E* isomer) & 8.72 (d, *J* = 6.0 Hz, 2H, *Z* isomer)

ESI/MS (m/z) : 305.10 $(M+H)^+$

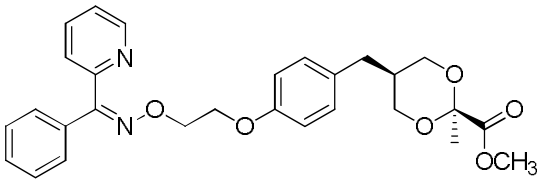
5.1.24 General procedure for the preparation of the compounds 26a-e.



25a-e **6a** **26a-e**

To a solution of **25a-e** (1 mole equivalent) and **6a** (1 mole equivalent) in dry DMF (5 fold), Cs_2CO_3 (2 mole equivalent) was added and reaction mixture was stirred at 80 °C for 18-24 hours. The reaction mixture was poured into ice cold water and extracted with ethyl acetate. The combined organic extracts were successively washed with water, brine and dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography using 8-30% ethyl acetate in hexane as eleunt to furnish pure compounds **26a-e**.

5.1.24.1 Methyl-*c*-2-methyl-5-(4-(2-(((*Z*)-(phenyl-(pyridin-2-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (26a)



26a (1.06 gm, 66.1%) was prepared from **25a** (1.0 gm, 3.3 mmol) and **6a** (872.0 mg, 3.3 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.5%.

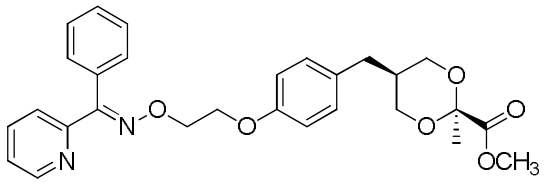
IR ($CHCl_3$) : 3018, 2928, 2856, 1743, 1585, 1512, 1332, 1247, 1043, 987 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.23-2.31 (m, 3H), 3.46 (t, *J* = 10.65 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 11.7 & 3.27 Hz, 2H), 4.23 (t, *J* = 5.10 Hz, 2H), 4.50 (t, *J* = 4.86 Hz, 2H), 6.83 (d, *J* = 8.58 Hz, 2H), 6.99 (d, *J* = 8.55 Hz, 2H), 7.29-7.36 (m, 4H), 7.45 (dd, *J* = 7.44 & 1.56 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.72-7.78 (m,

1H), 8.70 (d, *J* = 4.8 Hz, 1H)

ESI/MS (m/z) **:** 491.2 $(M+H)^+$

5.1.24.2 Methyl-2-methyl-*c*-5-(4-(2-(((*E*)-(phenyl-(pyridin-2-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (26b)



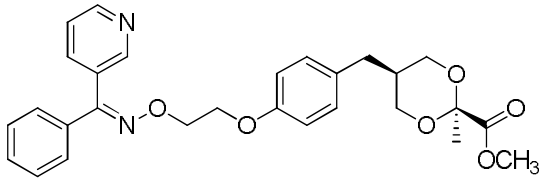
26b (1.17 gm, 72.50%) was prepared from **25b** (1.0 gm, 3.3 mmol) and **6a** (872.0 mg, 3.3 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.9%.

IR ($CHCl_3$) **:** 3018, 2929, 1743, 1612, 1512, 1371, 1247, 1043, 989, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.23-2.31 (m, 3H), 3.46 (t, *J* = 10.65 Hz, 2H), 3.84 (s, 3H) 3.88 (dd, *J* = 11.7 & 3.27 Hz, 2H), 4.25 (t, *J* = 5.07 Hz, 2H), 4.57 (t, *J* = 4.62 Hz, 2H), 6.83 (d, *J* = 8.58 Hz, 2H), 6.99 (d, *J* = 8.55 Hz, 2H), 7.27-7.29 (m, 1H), 7.33-7.40 (m, 5H), 7.66-7.73 (m, 2H), 8.61 (d, *J* = 4.59 Hz, 1H)

ESI/MS (m/z) **:** 513.2 $(M+Na)^+$

5.1.24.3 Methyl-2-methyl-*c*-5-(4-(2-(((*Z*)-(phenyl-(pyridin-3-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate.(26c)



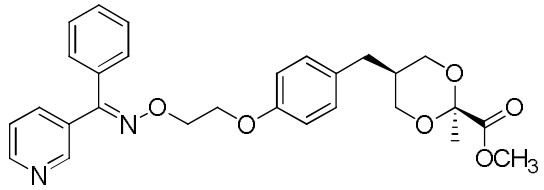
26c (658 mg, 63.0%) was prepared from **25c** (650 mg, 2.1 mmol) and **6a** (567.0 mg, 2.1 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.5%.

IR ($CHCl_3$) **:** 3018, 2976, 2930, 1743, 1610, 1512, 1385, 1144, 1042, 984 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.23-2.31 (m, 3H), 3.46 (t, *J* = 10.8 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.0 & 3.6 Hz, 2H), 4.24 (t, *J* = 4.8 Hz, 2H), 4.52 (t, *J* = 4.8 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.34-7.42 (m, 4H), 7.45 (d, *J* = 6.8 Hz, 2H), 7.69 (dd, *J* = 8.0 & 1.6 Hz, 1H), 8.61 (s, 1H), 8.63 (d, *J* = 4.8 Hz, 1H)

ESI/MS (m/z) **:** 491.23 $(M+H)^+$

5.1.24.4 Methyl-2-methyl-*c*-5-(4-(2-(((*E*)-(phenyl-(pyridin-3-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (26d)



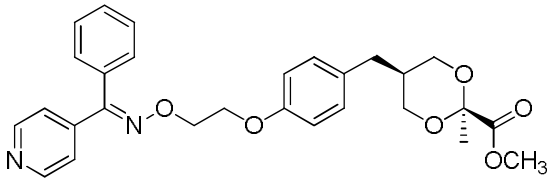
26d (311 mg, 43.0%) was prepared from **25c** (450 mg, 1.47 mmol) and **6a** (392.6 mg, 1.47 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.1%.

IR ($CHCl_3$) **:** 2993, 2924, 2868, 1739, 1610, 1512, 1468, 1362, 1251, 1146, 1073, 808 cm^{-1}

^1H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.23-2.31 (m, 3H), 3.46 (t, *J* = 10.8 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12.0 & 3.6 Hz, 2H), 4.25 (t, *J* = 4.8 Hz, 2H), 4.53 (t, *J* = 4.8 Hz, 2H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 7.26-7.28 (m, 1H), 7.35-7.36 (m, 2H), 7.42-7.43 (m, 3H), 7.76 (d, *J* = 8.0 Hz, 1H), 8.59 (d, *J* = 4.4 Hz, 1H), 8.70 (s, 1H)

ESI/MS (m/z) **:** 491.22 $(M+H)^+$

5.1.24.5 Methyl-2-methyl-*c*-5-(4-(2-(((*Z*/*E*)-(phenyl-(pyridin-4-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (26e)



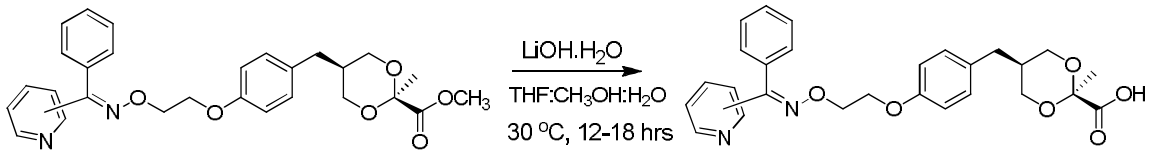
26e (1.21 gm, 50.0%) was prepared from **25e** (1.50 gm, 4.9 mmol) and **6a** (1.31 gm, 4.9 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.7% (*Z* isomer: *E* isomer, 1:2.39, 28.44 & 68.24%).

IR ($CHCl_3$) **:** 3018, 1743, 1512, 1385, 1248, 1045, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.21-2.31 (m, 3H), 3.46 (t, *J* = 11.2 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, *J* = 12 & 3.6 Hz, 2H), 4.21-4.25 (m, 2H), 4.49-4.55 (m, 2H), 6.83 (dd, *J* = 8.8 & 3.6 Hz, 2H), 6.99 (d, *J* = 9.2 Hz, 2H), 7.23 (d, *J* = 5.6 Hz, 2H, *Z* isomer), 7.31-7.44 (m, 5H, *Z* isomer & 8H, *E* isomer), 8.58 (d, *J* = 5.6 Hz, 1H, *E* isomer), 8.68 (d, *J* = 5.6 Hz, 2H, *Z* isomer)

ESI/MS (m/z) **:** 491.20 $(M+H)^+$

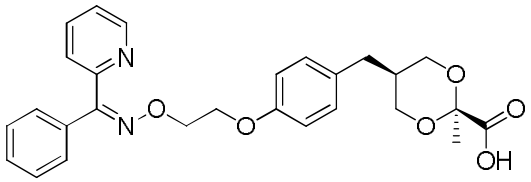
5.1.25 General procedure for the preparation of the compounds 27a-e.



26a-e **27a-e**

To a solution of **26a-e** (1 mole equivalent) in THF (9 fold), MeOH (3 fold) and water (3 fold), $LiOH.H_2O$ (2 mole equivalent) was added and stirred at 30 °C for 12-18 hours. The reaction mixture was concentrated under vacuum and water was added to the reaction mixture, acidified by aq. HCl and extracted with ethyl acetate. The combined organic extract was successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield pure compounds **27a-e**.

5.1.25.1 2-Methyl-*c*-5-(4-(2-(((*Z*)-(phenyl-(pyridin-2-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (27a)



27a (544 mg, 56.0%) was prepared from **26a** (1.00 gm, 2.0 mmol) following the general procedure described above as a white solid. m.p: 74-75 °C; Purity by HPLC: 99.0%.

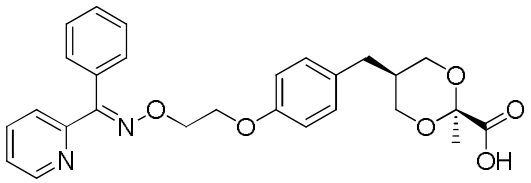
IR (KBr) **:** 3150, 2931, 2866, 1720, 1610, 1512, 1444, 1248, 1147, 987 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.49 (s, 3H), 2.24-2.27 (m, 3H), 3.48 (t, *J* = 10.8 Hz, 2H), 3.86 (dd, *J* = 12.8 & 4.0 Hz, 2H) 4.24 (t, *J* = 5.20 Hz, 2H), 4.50 (t, *J* = 4.80 Hz, 2H), 6.82 (dd, *J* = 9.6 & 2.8 Hz, 2H), 6.96 (d, *J* = 8.40 Hz, 2H), 7.29-7.37 (m, 4H) 7.43-7.45 (m, 2H), 7.52 (d, *J* = 8.00 Hz, 1H), 7.78-7.82 (m,1H), 8.74 (dd, *J* = 1.6 & 0.8 Hz, 1H)

^{13}C NMR (CDCl$_3$) **:** δ 25.76, 33.71, 35.04, 66.32, 67.96, 73.02 98.14, 114.74, 123.92, 125.78, 127.60, 128.33, 129.52, 129.67, 130.24, 134.69, 137.11, 148.76, 151.51, 155.46, 157.32, 173.26

ESI/MS (m/z) **:** 477.2 $(M+H)^+$

5.1.25.2 2-Methyl-*c*-5-(4-(2-(((*E*)-(phenyl-(pyridin-2-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (27b)



27b (703 mg, 72.4%) was prepared from **26b** (1.00 gm, 2.0 mmol) following the general procedure described above as a white solid. m.p: 71-72 °C; Purity by HPLC: 98.3%.

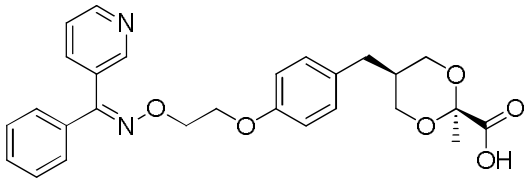
IR (KBr) **:** 3435, 2927, 2870, 1734, 1610, 1512, 1246, 1149, 1045, 993 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.51 (s, 3H), 2.24-2.30 (m, 1H), 2.36 (d, *J* = 6.8 Hz, 2H), 3.50 (t, *J* = 11.20 Hz, 2H), 3.88 (dd, *J* = 12.4 & 4.4 Hz, 2H), 4.29 (t, *J* = 4.8 Hz, 2H), 4.55 (t, *J* = 4.4 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 7.28-7.33 (m, 3H), 7.37-7.40 (m, 3H) 7.68 (d, *J* = 7.6 Hz, 1H), 7.72-7.76 (m, 1H), 8.63 (d, *J* = 5.2 Hz, 1H)

^{13}C NMR ($CDCl_3$) **:** δ 26.03, 33.86, 35.18, 66.64, 68.03, 73.46, 98.59, 114.97, 123.70, 124.14, 128.18, 129.40, 129.68, 129.74, 130.36, 131.95, 137.15, 149.11, 154.29, 156.50, 157.51, 173.91

ESI/MS (m/z) **:** 477.2 $(M+H)^+$

5.1.25.3 2-Methyl-*c*-5-(4-(2-(((*Z*)-(phenyl-(pyridin-3-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (27c)



27c (413 mg, 71.0%) was prepared from **26c** (0.600 gm, 1.22 mmol) following the general procedure described above as a white solid. m.p: 150-152 °C; Purity by HPLC: 99.6%.

IR (KBr) **:** 3433, 2974, 2926, 2876, 1708, 1610, 1510, 1460, 1412, 1279, 1186, 1053, 946 cm^{-1}

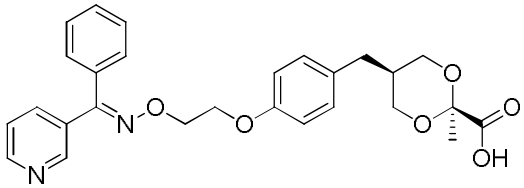
^{1}HNMR ($CDCl_3$) **:** δ 1.51 (s, 3H), 2.16-2.29 (m, 1H), 2.49 (s, 2H), 3.59 (t, *J* = 11.6 Hz, 2H), 3.88 (dd, *J* = 12.0 & 4.4 Hz, 2H), 4.18 (t, *J* = 4.0 Hz, 2H), 4.55 (s, 2H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz,

2H), 7.34-7.41 (m, 3H), 7.45-7.49 (m, 3H), 7.73 (d, *J* = 8.0 Hz, 1H), 8.45 (s, 1H), 8.60 (d, *J* = 4.8 Hz, 1H)

^{13}C NMR ($CDCl_3$) : δ 25.99, 33.93, 34.64, 66.52, 67.74, 73.47, 98.50, 114.64, 123.96, 127.85, 128.72, 129.96, 130.18, 135.21, 138.82, 147.96, 148.37, 154.22, 157.48, 173.27

ESI/MS (m/z) : 477.25 $(M+H)^+$

5.1.25.4 2-Methyl-*c*-5-(4-(2-(((*E*)-(phenyl-(pyridin-3-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (27d)



27d (148.6 mg, 51.0%) was prepared from **26d** (0.300 gm, 0.6 mmol) following the general procedure described above as a white solid. m.p: 70-72 °C; Purity by HPLC: 97.8%.

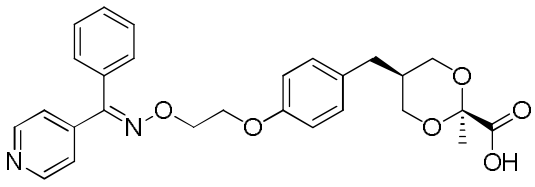
IR (KBr) : 3430, 2926, 2856, 1720, 1609, 1510, 1446, 1365, 1246, 1147, 1039, 939 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.52 (s, 3H), 2.25 (broad s, 1H), 2.48 (s, 2H), 3.60 (t, *J* = 11.2 Hz, 2H), 3.88 (d, *J* = 8.4 Hz, 2H), 4.27 (s, 2H), 4.51 (s, 2H), 6.80 (d, *J* = 7.6 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 7.28-7.31 (m, 1H), 7.35 (t, *J* = 6.0 Hz, 2H) 7.42 (s, 3H), 7.69 (d, *J* = 8.0 Hz, 1H), 8.55 (d, *J* = 4.0 Hz, 1H), 8.71 (s, 1H)

^{13}C NMR ($CDCl_3$) : δ 25.94, 34.80, 35.17, 66.54, 67.93, 73.18, 98.70, 114.89, 123.74, 128.55, 129.38, 129.78, 130.40, 131.77, 133.21, 136.52, 147.22, 148.69, 154.57, 157.45, 174.00

ESI/MS (m/z) : 477.18 $(M+H)^+$

5.1.25.5 2-Methyl-*c*-5-(4-(2-(((*E*/*Z*)-(phenyl-(pyridin-4-yl)-methylene)-amino)-oxy)-ethoxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (27e)



27e (893.0 mg, 92.0%) was prepared from **26e** (1.0 gm, 2.0 mmol) following the general procedure described above as a white solid. m.p: 49-50 °C; Purity by HPLC: 97.1% (*Z* isomer: *E* isomer, 1:2.38, 28.73 & 68.39%).

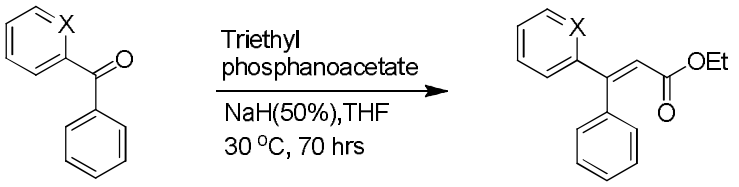
IR (KBr) : 3450, 3018, 2976, 2931, 1724, 1610, 1512, 1385, 1246, 1151, 1043, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.56 (s, 3H), 2.27-2.35 (m, 1H), 2.46 (d, *J* = 6.4 Hz, 2H), 3.60 (t, *J* = 11.6 Hz, 2H, *Z* & *E* isomer), 3.89 -3.93 (m, 2H, *Z* & *E* isomer), 4.15 (t, *J* = 4.4 Hz, 2H, *E* isomer), 4.27 (t, *J* =5.2 Hz, 2H, *Z* isomer), 4.50 (t, *J* = 2.0 Hz, 2H, *E* isomer), 4.53 (t, *J* = 5.2 Hz, 2H, *Z* isomer), 6.75 (d, *J* = 8.4 Hz, 2H, *E* isomer), 6.83 (d, *J* = 8.4 Hz, 2H, *Z* isomer), 6.94 (d, *J* = 8.4 Hz, 2H, *E* isomer), 6.99 (d, *J* = 8.4 Hz, 2H, Z isomer), 7.28-7.46 (m, 7H, *Z* isomer & 8H, *E* isomer), 8.60-8.63 (m, 2H, *Z* isomer & 1H, *E* isomer)

^{13}C NMR ($CDCl_3$) : δ 24.00, 26.08, 29.27, 33.98, 34.98, 35.35, 66.37, 66.58, 67.99, 68.20, 73.38, 73.58, 98.60, 114.72, 114.92, 122.81, 124.85, 127.65, 128.61, 128.74, 129.22, 129.73, 129.77, 129.93, 130.28, 130.42, 130.64, 134.33, 143.37, 147.86, 155.05, 157.38, 173.44

ESI/MS (m/z) : 477.19 $(M+H)^+$

5.1.26 General procedure for the preparation of 29a-c.

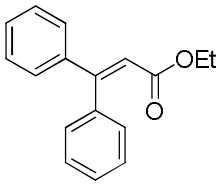


28; X = CH
23a; X = N

29a; X =CH
29b; X= N, *E* isomer
29c; X= N, Z isomer

To an ice cold suspension of sodium hydride (50%) (3 mole equivalent) in THF (5 fold), solution of triethyl phosphanoacetate (2 mole equivalent) in THF (5 fold) was added at 0 °C and stirred for five minute. Then in this, solution of ketone (**23a**, **28**) (1 mole equivalent) in THF (3 fold) was added at 0 °C and the reaction mixture was stirred for 70 hrs at 30 °C. The reaction mixture was poured to ice cold water and extracted with ethyl acetate.The combined organic extract was successively washed with water and brine, dried over sodium sulfate, filtered and concentrated under vacuum to yield title product. The crude product was purified column chromatography using ethyl acetate in hexane as eleunt to give pure product **29a-c**.

5.1.26.1 Ethyl 3,3-diphenylacrylate. (29a)



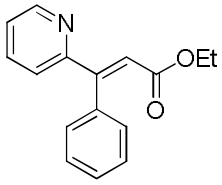
29a (3.88 gm, 56.0%) was prepared from **28** (5.0 gm, 0.027 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.4%.

IR (CCl_4) **:** 3026, 2981, 1726, 1706, 1618, 1550, 1446, 1369, 1263, 1161, 1095, 1039 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.11 (t, *J* = 7.14 Hz, 3H), 4.05 (q, *J* = 7.11 Hz, 2H), 6.36 (s, 1H), 7.19-7.22 (m, 2H), 7.28-7.34 (m, 5H), 7.37-7.40 (m, 3H)

ESI/MS (m/z) **:** 253.1 $(M+H)^+$

5.1.26.2 (*E*)-Ethyl 3-phenyl-3-(pyridin-2-yl)acrylate. (29b)



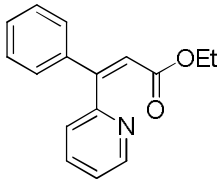
29b (3.00 gm, 43.4%) was prepared from **23a** (5.0 gm, 0.027 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.6%.

IR (CCl_4) : 3060, 2983, 2854, 1724, 1629, 1581, 1508, 1400, 1369, 1272, 1039 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.10 (t, *J* = 7.11 Hz, 3H), 4.05 (q, *J* = 7.15 Hz, 2H), 6.99 (d, *J* = 7.95 Hz, 1H), 7.17 (s, 1H), 7.23-7.25 (m, 3H), 7.40-7.44 (m, 3H), 7.55-7.61 (m, 1H), 8.66 (d, *J* = 4.5 Hz, 1H)

ESI/MS (m/z) : 254.0 $(M+H)^+$

5.1.26.3 (*Z*)-Ethyl 3-phenyl-3-(pyridin-2-yl)acrylate. (29c)



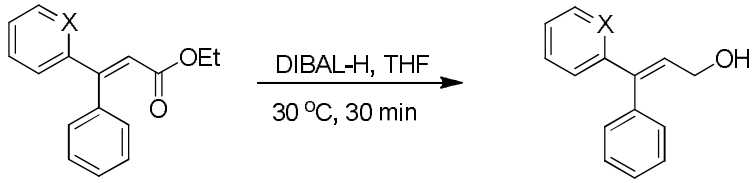
29c (1.94 gm, 28.0%) was prepared from **23a** (5.0 gm, 0.027 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.8%.

IR (CCl_4) : 3064, 2983, 2904, 1724, 1626, 1541, 1400, 1271, 1163, 1037 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.12 (t, *J* = 7.2 Hz, 3H), 4.05 (q, *J* = 7.17 Hz, 2H), 6.48 (s, 1H), 7.24-7.35 (m, 7H), 7.70-7.76 (m, 1H), 8.68 (d, *J* = 4.72 Hz, 1H)

ESI/MS (m/z) : 254.0 $(M+H)^+$

5.1.27 General procedure for the preparation of the compounds 30a-b.

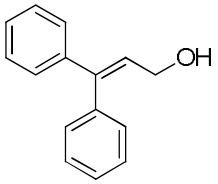


29a; X = CH
29b; X = N, *E*, isomer

30a; X = CH
30b; X = N, *E*, isomer

A 1 M solution of DIBAL-H in toluene (3 mole equivalent) was added dropwise at -70 °C over 1 hour to a solution of acrylic esters (**29a-b**) (1 mole equivalent) in dry THF (20 fold) and the mixture was stirred for 30 min. Saturated aqueous ammonium chloride was carefully added to quench the reaction mixture and the resulting mixture was extracted with ethyl acetate. The combined organic phase was successively washed with water and brine, dried over sodium sulfate, filtered and concentrated under vacuum. The crude residue was purified by column chromatography using 12-40% ethyl acetate in hexane as eleunt to give the desired alcohols (**30a-b**).

5.1.27.1 3,3-Diphenyl-prop-2-en-1-ol. (30a)



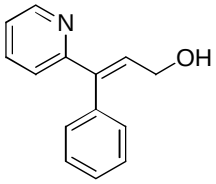
30a (2.50 gm, 91.3%) was prepared from **29a** (3.5 gm, 0.02729 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.1%.

IR (CCl_4) **:** 3411, 3060, 2875, 1550, 1492, 1444, 1253, 1014 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 4.23 (d, *J* = 6.78 Hz, 2H), 6.25 (t, *J* = 6.81 Hz, 1H), 7.17 (dd, *J* = 7.86 & 2.01 Hz, 2H), 7.26-7.29 (m, 5H), 7.33-7.38 (m, 3H)

ESI/MS (m/z) **:** 193.1 $(M+H)^+$

5.1.27.2 (*E*)-3-Phenyl-3-pyridin-2-yl-prop-2-en-1-ol. (30b)



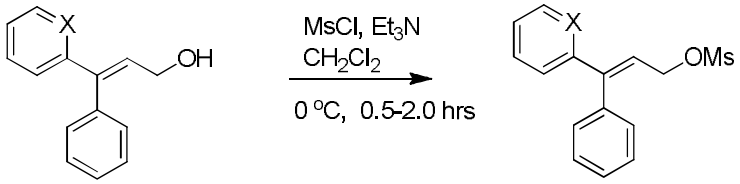
30b (2.18 gm, 87.0%) was prepared from **29b** (3.0 gm, 0.01184 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.7%.

IR (CCl_4) : 3417, 3062, 2929, 2875, 1583, 1494, 1429, 1253, 1215, 1151, 1024 cm^{-1}.

^{1}H NMR ($CDCl_3$) : δ 4.24 (d, *J* = 6.78 Hz, 2H), 6.96 (t, *J* = 7.02 Hz, 2H), 7.14-7.22 (m, 3H), 7.36-7.43 (m, 3H), 7.53-7.56 (m, 1H), 8.62 (d, *J* = 4.08 Hz, 1H)

ESI/MS (m/z) : 212.0 $(M+H)^+$

5.1.28 General procedure for the preparation of the compounds 31a-b.

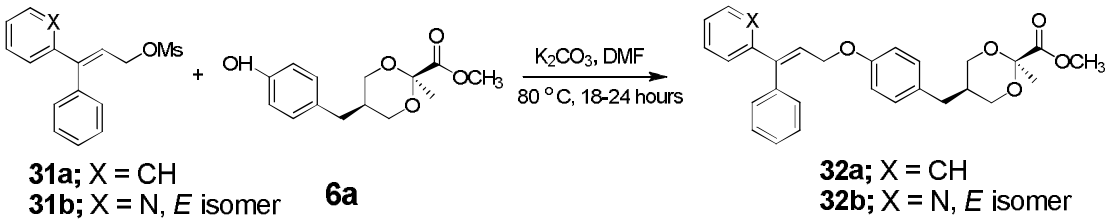


30a; X = CH
30b; X = N, *E* isomer

31a; X = CH
31b; X = N, *E* isomer

To a solution of **30a-b** (1 mole equivalent) in dichloromethane (10 fold), triethylamine (1.5 mole equivalent) was added with followed by the addition of methanesulfonyl chloride (1.2 mole equivalent) at 0 °C and the reaction mixture was stirred at 30 °C for 0.5 to 2.0 hours. Then reaction mixture was diluted with excess dichloromethane and washed with water followed by brine, dried over sodium sulfate, filtered and concentrated under vacuum to give the desired mesylates (**31a-b**).

5.1.29 General procedure for the preparation of the compounds 32a-b.



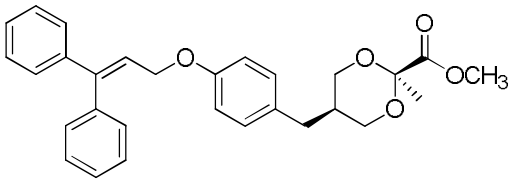
31a; X = CH
31b; X = N, *E* isomer

6a

32a; X = CH
32b; X = N, *E* isomer

To a solution of **31a-b** (1 mole equivalent) and **6a** (1 mole equivalent) in dry DMF (5 fold), K_2CO_3 (2 mole equivalent) was added and reaction mixture was stirred at 80 °C for 18-24 hours. The reaction mixture was poured into ice cold water and was extracted with ethyl acetate. The combined organic extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude products were purified by column chromatography using 12-15% ethyl acetate in hexane as eluent to yield the pure compounds **32a-b**.

5.1.29.1 Methyl-*c*-5-(4-((3,3-diphenylallyl)-oxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (32a)



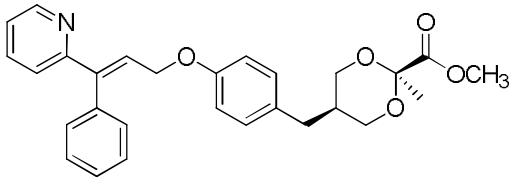
32a (819 mg, 51.5%) was prepared from **31a** (1.0 gm, 3.5 mmol) and **6a** (923.6 mg, 3.5 mmol) following the general procedure described above as a white solid. m.p: 81-82 °C; Purity by HPLC: 99.5%.

IR (KBr) **:** 3053, 2910, 2864, 1735, 1608, 1512, 1450,1375, 1219, 1190, 1019, 970 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.17-2.32 (m, 3H), 3.45 (t, *J* = 10.92 Hz, 2H), 3.83 (s, 3H), 3.87 (dd, *J* = 11.97 & 3.48 Hz, 2H), 4.56 (d, *J* = 6.57 Hz, 2H), 6.30 (t, *J* = 6.57 Hz, 1H), 6.75 (d, *J* = 8.49 Hz, 2H), 6.96 (d, *J* = 8.52 Hz, 2H), 7.21 (dd, *J* = 7.74 & 1.98 Hz, 2H), 7.26-7.27 (m, 5H), 7.35-7.41 (m, 3H)

ESI/MS (m/z) **:** 481.0 $(M+Na)^+$

5.1.29.2 Methyl-2-methyl-*c*-5-(4-(((*E*)-3-phenyl-3-(pyridin-2-yl)-allyl)-oxy)-benzyl)-1,3-dioxane-*r*-2-carboxylate. (32b)



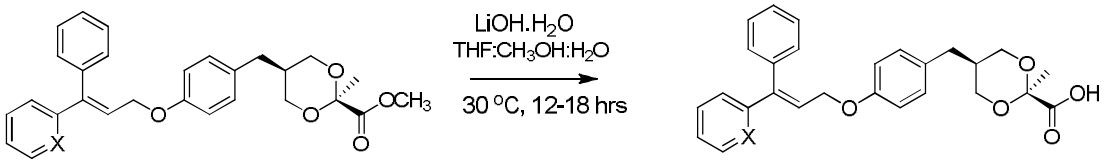
32b (690 mg, 29%) was prepared from **31b** (1.50 gm, 5.2 mmol) and **6a** (1.38 gm, 5.2 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.7%.

IR (CCl_4) **:** 2925, 2852 1749, 1614, 1510, 1444, 1371, 1143, 1037 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.49 (s, 3H), 2.17-2.31 (m, 3H), 3.44 (t, *J* = 10.92 Hz, 2H), 3.82-3.90 (m, 5H) 4.56 (d, *J* = 6.57 Hz, 2H), 6.75 (d, *J* = 8.49 Hz, 2H), 6.94-7.09 (m, 4H), 7.18-7.19 (m, 1H) 7.24-7.27 (m, 2H), 7.38-7.45 (m, 3H), 7.51-7.62 (m, 1H), 8.63 (d, *J* = 3.9 Hz, 1H).

ESI/MS (m/z) **:** 460.0 $M+H)^+$

5.1.30 General procedure for the preparation of the compounds 33a-b.

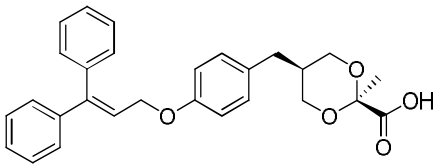


32a; X = CH
32b; X = N, *E* isomer

33a; X = CH
33b; X = N, *E* isomer

To a solution of **32a-b** (1 mole equivalent) in THF (9 fold), MeOH (3 fold) and H_2O (3 fold), $LiOH.H_2O$ (2 mole equivalent) was added and stirred at 30 °C for 12-18 hours. The reaction mixture was concentrated under vacuum and water was added to the reaction mixture, acidified by aq.HCl and extracted with ethyl acetate. The organic extract was washed with water followed by brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield the desired products **33a-b**.

5.1.30.1 *c*-5-(4-((3,3-Diphenylallyl)-oxy)-benzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (33a)



33a (736.0 mg, 95%) was prepared from **32a** (1.0 gm, 2.0 mmol) following the general procedure described above as a white solid. m.p: 120-121 °C; Purity by HPLC: 99.2%.

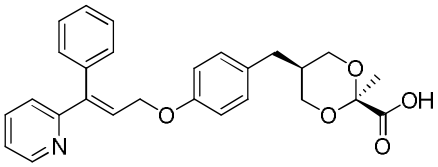
IR (KBr) **:** 3500, 3030, 2900, 2870, 1712, 1608, 1510, 1288, 1192, 1032 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.55 (s, 3H), 2.29 (s, 3H), 3.51 (t, *J* = 10.5 Hz, 2H), 3.90 (dd, *J* = 13.02 & 4.02 Hz, 2H), 4.57 (d, *J* = 6.57 Hz, 2H), 6.30 (t, *J* = 6.6 Hz, 1H), 6.75 (d, *J* = 8.58 Hz, 2H), 6.96 (d, *J* = 8.52 Hz, 2H), 7.21 (dd, *J* = 7.74 & 1.98 Hz, 2H), 7.26-7.27 (m, 5H), 7.38-7.41 (m, 3H)

^{13}C NMR ($CDCl_3$) **:** δ 25.94, 33.88, 34.18, 66.17, 68.33, 98.16, 115.02, 123.99, 127.89, 127.92, 128.32, 128.47, 129.63, 129.80, 129.98, 130.23, 139.04, 141.69, 145.67, 157.30, 175.18

ESI/MS (m/z) **:** 467.0 $(M+Na)^+$

5.1.30.2 2-Methyl-*c*-5-(4-(((*E*)-3-phenyl-3-(pyridin-2-yl)-allyl)-oxy)-benzyl)-1,3-dioxane-*r*-2-carboxylic acid. (33b)



33b (428.0 mg, 68.0%) was prepared from **32b** (650 gm, 1.4 mmol) following the general procedure described above as a white solid. m.p: 119-120 °C; Purity by HPLC: 98.8%.

IR (KBr) **:** 3550, 2995, 2862, 1741, 1610, 1512, 1429, 1215, 1149, 1036

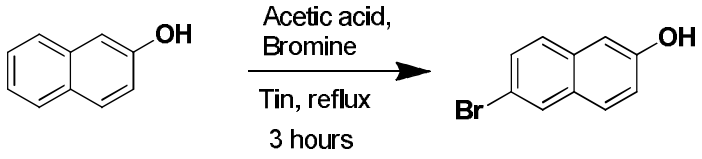
cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.55 (s, 3H), 2.26 (s, 3H), 3.54 (t, *J* = 10.95 Hz, 2H), 3.88 (dd, *J* = 12.33 & 3.84 Hz, 2H), 4.58 (d, *J* = 6.6 Hz, 2H), 6.72 (d, *J* = 8.58 Hz, 2H), 6.91 (d, *J* = 8.58 Hz, 2H), 6.95-7.03 (m, 2H), 7.23-7.27 (m, 3H), 7.38-7.46 (m, 3H), 7.63 (t, *J* = 7.06 Hz, 1H) 8.71 (d, *J* = 4.08 Hz, 1H)

^{13}C NMR (CDCl$_3$) : δ 25.87, 33.73, 34.99, 65.91, 68.01, 98.32, 114.73, 122.94, 123.61, 128.20, 128.69, 129.02, 129.46, 129.64, 130.19, 137.21, 137.58, 142.67, 148.31, 157.03, 157.56, 173.34

ESI/MS (m/z) : 446.1 $M+H)^+$

5.1.31 Preparation of 6-bromo-naphthalen-2-ol. (35)



34 **35**

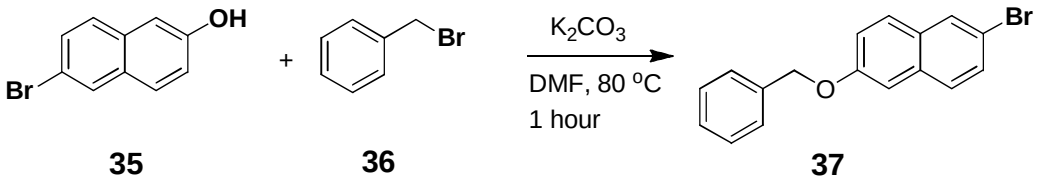
To a soution of β-naphthol (**34**) (36 gm, 0.250 mol) in acetic acid (100 ml), bromine (80 gm, 0.500 mol) was added dropwise over a period of 30 minute. Then it was heated at 60 °C and to it was an added tin granule (6.25 gm). After 15 minute, 6.2 gm tin granules was added and reaction mixture was refluxed for 30 minute. Then 25 gm more tin was added and reflux was continued for 3 hours, 25 ml water was added in the middle. The reaction mixture was cooled to 50 °C and tin salt was filtered. Filtrate was poured in to ice cold water, seperated solid product was filtered and dried over P_2O_5 to yield title product **35** (100 gm, 90%) as an off white solid. m.p: 110-111 °C; Purity by HPLC: 97.1%.

IR (KBr) : 3245, 3063, 1761, 1624, 1587, 1502, 1435, 1388, 1202, 1127, 1062, 884 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 5.15 (s, 1H), 7.10-7.14 (m, 2H), 7.46-7.57 (m, 2H), 7.66 (d, *J* = 6.16 Hz, 1H), 7.92 (s, 1H)

ESI/MS (m/z) : 223.2 $(M+H)^+$

5.1.32 2-Benzyloxy-6-bromo-naphthalene. (37)



35 **36** **37**

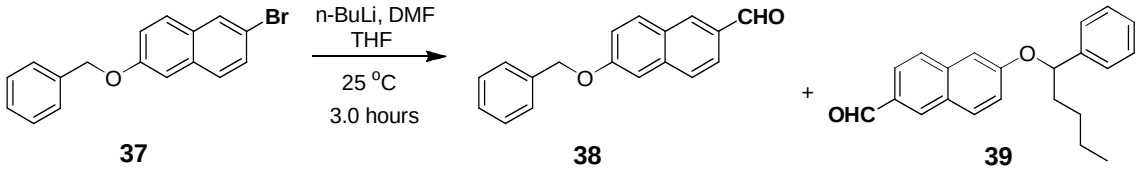
To a solution of 6-bromo-naphthalen-2-ol (**35**) (30 gm, 0.1349 mol), in dimethyl formamide (150 ml), K_2CO_3 (36.98 gm, 0.268 mol) was added and the reaction mixture was stirred for 10 minute at 30 °C. Then benzyl bromide (**36**) (23 gm, 0.1349 mol) was added and the reaction mixture was stirred at 80 °C for 1 hour. The reaction mixture was cooled to 30 °C and poured into ice cold water (800 ml). Seperated solid product was filtered and dried over P_2O_5 to yield the desired product (40 gm, 95%) as a white solid. m.p: 94-95 °C; Purity by HPLC: 98.6%.

IR (KBr) **:** 3037, 2939, 2881, 1623, 1585, 1495, 1453, 1374, 1257, 1203, 1164, 1063, 885 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 5.16 (s, 2H), 7.17 (d, *J* = 3.04 Hz, 1H), 7.25 (dd, *J* = 9.06 & 3.12 Hz, 1H), 7.37-7.51 (m, 6H), 7.57 (d, *J* = 11.90 Hz, 1H), 7.65 (d, *J* = 11.92 Hz, 1H), 7.91 (d, *J* = 2.16 Hz, 1H)

ESI/MS (m/z) **:** 314.0 $(M+H)^+$

5.1.33 Preparation of the compounds 38 and 39.

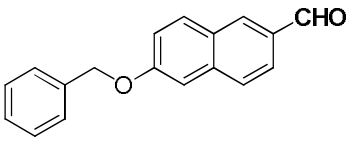


37 **38** **39**

To solution of 2-benzyloxy-6-bromo-naphthalene (**37**) (20.0 gm, 0.095 mol) in THF (200 ml), 78 ml n-BuLi (0.8 M solution in hexane) was added dropwise for 30 min at -78 °C. Then reaction mixture was stirred for 1 hour at -30 °C and dimethyl formamide (10 ml) was added with cooling the reaction mixture at -78 °C and the reaction mixture was allowed to rise the temperature upto 25 °C and the reaction mixture was stirred for 3.0 hours at 25 °C. The reaction mixture was quenched with methanol and poured to ice cold water and extracted with ethyl

acetate. The combined organic extract was washed successively with water and brine, dried over sodium sulfate, filtered and concentrated under vacuum to yield mixture of products as an oil. Then crude product was purified by column chromatography using 4.0% ethyl acetate in hexane to yield desired product **38** (3.5 gm, 13%) as a white solid. m.p: 90-91 °C; % Purity by HPLC: 93.1% and **39** (9.0 gm, 28%) as a thick liquid.

5.1.33.1 6-Benzyloxy-naphthalene-2-carbaldehyde. (38)

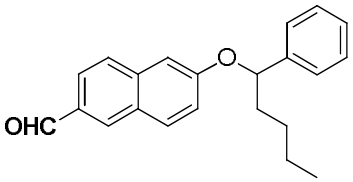


IR (KBr) **:** 3369, 3049, 3030, 2939, 2829, 2812, 2719, 1691, 1614, 1473, 1456, 1382, 1261, 1224, 1149, 1002 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 5.21 (s, 2H), 7.25-7.45 (m, 5H), 7.49 (d, *J* = 7.11 Hz, 2H), 7.80 (d, *J* = 8.55 Hz, 1H), 7.92 (dd, *J* = 11.9 & 1.95 Hz, 2H), 8.26 (s, 1H), 11.09 (s, 1H, -CHO)

ESI/MS (m/z) **:** 263.2 $(M+H)^+$

5.1.33.2 6-(1-Phenyl-pentyloxy)-naphthalene-2-carbaldehyde. (39)

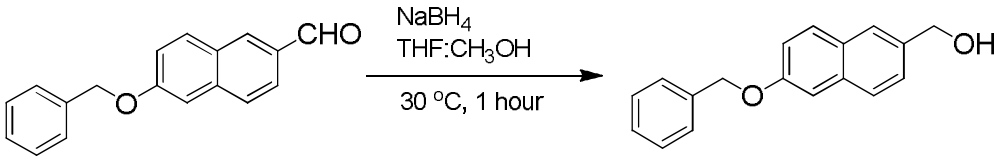


IR ($CHCl_3$) **:** 3019, 2932, 2861, 1691, 1623, 1475, 1392, 1267, 1216, 1174, 1015 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 0.91 (t, *J* = 7.05 Hz, 3H), 1.34-1.44 (m, 3H), 1.52-1.59 (m, 1H), 1.89-1.92 (m, 1H), 2.00-2.10 (m, 1H), 5.27 (q, *J* = 5.20 Hz, 1H), 7.04 (d, *J* = 2.10 Hz, 1H), 7.25-7.41 (m, 6H), 7.64 (d, *J* = 1.62 Hz, 1H), 7.82 (dd, *J* = 13.68 & 8.94 Hz, 2H), 8.19 (s, 1H), 10.04 (s, 1H)

ESI/MS (m/z) **:** 319.0 $(M+H)^+$

5.1.34 (6-(benzyloxy)naphthalen-2-yl)methanol. (40)



38 **40**

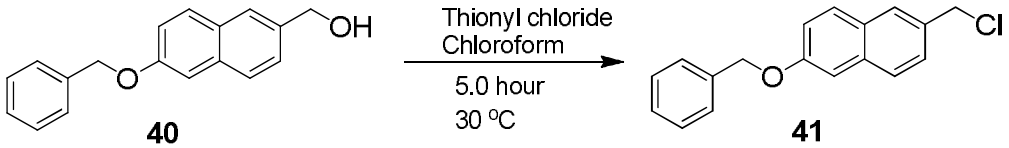
To a solution of **38** (2.0 gm, 7.6 mmol) in mixture of THF: MeOH (25 ml: 5 ml), sodium borohydride (144 mg, 3.8 mmol) was added portionwise at 0°C. The reaction mixture was stirred for 1 hour at 30 °C. The reaction mixture was concentrated under vacuum and the residue was dissolved in water, acidified (PH = 4-5) and extracted with ethyl acetate. The organic layer was washed with water followed by brine, dried over sodium sulfate, filtered and concentrated under vacuum to yield desired product **40** (1.98 gm, 98%) as an off white solid. m.p: 112-114°C; Purity by HPLC: 98.6%.

IR (KBr) **:** 3267, 3033, 2918, 2854, 1629, 1604, 1481, 1379, 1234, 1005, 855 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.71 (t, *J* = 5.9 Hz, 1H), 4.82 (d, *J* = 5.9 Hz, 2H), 5.18 (s, 2H), 7.23 (dd, *J* = 7.8 & 2.1 Hz, 1H), 7.36-7.50 (m, 7H), 7.71-7.76 (m, 3H)

ESI/MS (m/z) **:** 265.20 $(M+H)^+$

5.1.35 2-(Benzyloxy)-6-(chloromethyl) naphthalene. (41)



40 **41**

To an ice-cold solution of **40** (1.0 gm, 3.8 mmol) in chloroform (20 ml), thionyl chloride (0.303 ml, 4.1 mmol) was added. The reaction mixture was stirred at 30 °C for 5 hours. The reaction mixture was diluted with chloroform and successively washed with saturated aqueous sodium bicarbonate solution, water,

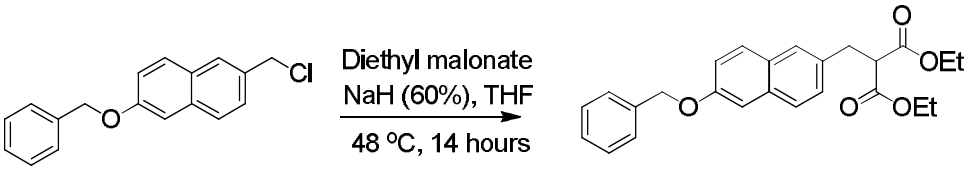
dried over calcium chloride, filtered and concentrated under vacuum to yield desired product **41** (995 mg, 93%) as an off white solid. m.p: 142-144 °C.

IR (KBr) **:** 3100, 2972, 2871, 1629, 1607, 1477, 1232, 1180, 1008, 852 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 4.74 (s, 2H), 5.18 (s, 2H), 7.24 (dd, *J* = 10.53 & 1.62 Hz, 2H), 7.34-7.50 (m, 6H), 7.71-7.75 (m, 3H)

ESI/MS (m/z) **:** 283.0 $(M+H)^+$

5.1.36 Diethyl 2-(6-benzyloxy-naphthalen-2-ylmethyl)-malonate. (42)



41 **42**

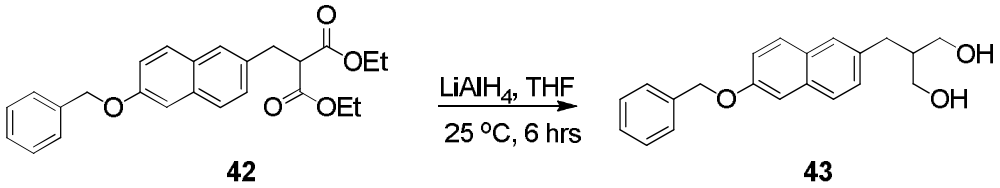
To an ice-cold suspension of NaH (60%, 6.0 gm, 0.126 mol) in THF (150 ml), diethyl malonate (32.18 ml, 0.211 mol) was added dropwise over a period of 30 min at 0-10 °C and stirred at the same temperature for further 30 min. A solution of **41** (23.9 gm, 0.0845 mol) in THF (100 ml) was added to the reaction mixture at 0-10 °C and stirred at 48 °C for 14 hours. The reaction mixture was poured into ice-cold water (500 ml) and was extracted with ethyl acetate (3 x 100 ml). The combined organic layers were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to give crude product. The crude product was purified by column chromatography using 12-15% ethyl acetate in hexane as eleunt to furnish title compound **42** (23.9 gm, 90%) as a white solid. m.p: 67-68 °C.

IR (KBr) **:** 3055, 2979, 2871, 1745, 1726, 1604, 1506, 1388, 1328, 1261, 1151, 752 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.19 (t, *J* = 7.14 Hz, 6H), 3.35 (dd, *J* = 8.79 & 5.64 Hz, 2H), 3.72 (t, *J* = 7.68 Hz, 1H), 4.11-4.19 (m, 4H), 5.17 (s, 2H), 7.18-7.43 (m, 6H), 7.48 (d, *J* = 6.57 Hz, 2H), 7.57 (d, *J* = 7.83 Hz, 1H), 7.66 (t, *J* = 9.57 Hz, 2H)

ESI/MS (m/z) **:** 407.1 $(M+H)^+$

5.1.37 2-(6-Benzyloxy-naphthalen-2-ylmethyl)-propane-1, 3-diol. (43)



42 **43**

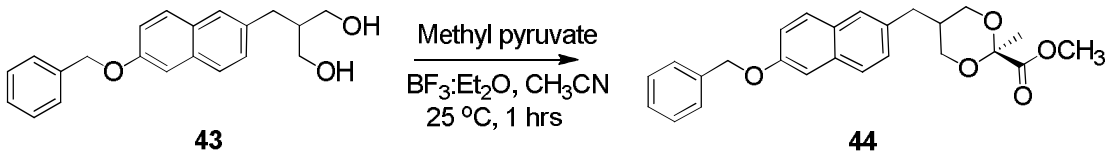
To a solution of **42** (18.7 gm, 0.040 mol) in THF (200 mL), $LiAlH_4$ (6.9 gm, 0.18 mol) was added in small portions at 0 °C over a period of 30 min. and stirred at 25 °C for 6 hours. The excess $LiAlH_4$ was quenched by dropwise addition of saturated aqueous Na_2SO_4 solution at 0-10 °C. Solid residue was filtered and washed with hot ethyl acetate. Filtrate was concentrated under vacuum to yield crude product. Crude product so obtained was triturated with diisopropyl ether to give title compound **43** (10.38 gm, 70%) as an off white solid. m.p: 119-120 °C; Purity by HPLC: 95.5%.

IR (KBr) **:** 3313, 3062, 2854, 1633, 1602, 1506, 1154, 1390, 1185, 1041, 893 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.04 (s, 2H), 2.14-2.17 (m, 1H), 2.77 (d, *J* = 7.5 Hz, 2H), 3.72-7.34 (m, 2H), 3.83-3.87 (m, 2H), 5.17 (s, 2H), 7.20-7.43 (m, 6H), 7.49 (d, *J* = 6.57 Hz, 2H), 7.56 (s, 1H), 7.68 (t, *J* = 7.62 Hz, 2H)

ESI/MS (m/z) **:** 345.1 $(M+Na)^+$

5.1.38 Methyl 5-(6-benzyloxy-naphthalen-2-ylmethyl)-2-methyl-1,3-dioxane-2-carboxylate. (44)



43 **44**

To a solution of **43** (6.0 gm, 0.018 mol) and methyl pyruvate (6.76 ml, 0.074 mol) in acetonitrile (30 ml), BF_3:OEt_2 (98%) (4.67 ml, 0.0372 mol) was added dropwise

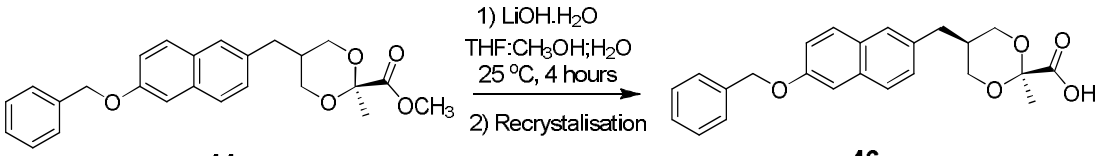
at 25 °C and stirred at the same temperature for 1.0 hours. The reaction mixture was poured into an ice-cold saturated aqueous sodium bicarbonate solution (250 ml) and extracted with ethyl acetate (3 X 100 ml). The combined organic extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to give mixture of *cis* and *trans* isomers **44** (5.37 gm, Yield: 71%) as a thick liquid. Separation of these isomers by column chromatography was unsuccessful.

IR ($CHCl_3$) **:** 3031, 2927, 2860, 1739, 1604, 1506, 1394, 1215, 1120, 858 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.50 (s, 3H, *cis* isomer), 1.61 (s, 3H, *trans* isomer), 1.62-1.65 (m, 1H, *trans* isomer), 2.46-2.49 (m, 3H, *cis* isomer), 3.14 (d, *J* = 7.8 Hz, 2H, *trans* isomer), 3.53 (t, *J* = 10.77 Hz, 2H, *cis* isomer), 3.80 (s, 2H, *trans* isomer), 3.83 (s, 3H, *cis* isomer), 3.85 (s, 3H, *trans* isomer), 3.90-3.97 (m,2H, *cis* isomer & m, 2H, *trans* isomer), 5.17 (s, 2H), 7.20-7.23 (m, 2H), 7.34-7.50 (m, 5H), 7.48 (d, *J* = 7.8 Hz, 2H), 7.64-7.68 (m, 2H)

ESI/MS (m/z) **:** 429.1 $(M+Na)^+$

5.1.39 *c*-5-(6-Benzyloxy-naphthalen-2-ylmethyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate. (46)



44 **46**

To a solution **44** (1.0 gm, 2.5 mmol) in THF (15 ml), MeOH (5 ml) and H_2O (5 ml), $LiOH.H_2O$ (206 mg, 4.9 mmol) was added and stirred at 25 °C for 4 hours. The reaction mixture was concentrated under vacuum. Water was added to the reaction mixture, acidified by HCl and extracted with ethyl acetate. The organic extract was successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product **45** (900 mg) was recrystallized from a mixture of ethyl acetate and hexane (1:2). The first crop

yielded title product **46** (436 mg, 46%) as a white solid. m.p: 151-152 °C; Purity by HPLC: 94.9%.

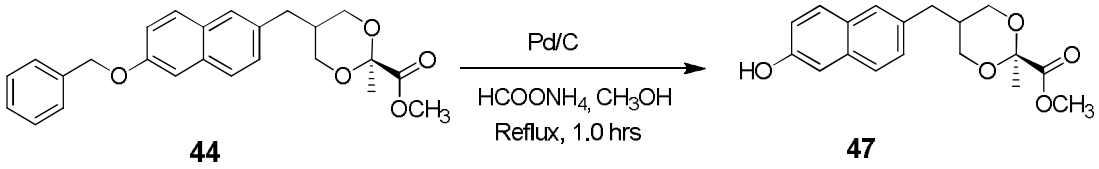
IR (KBr) **:** 3433, 3028, 2858, 1741, 1631, 1504, 1483, 1394, 1233, 1120, 1039, 852 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.56 (s, 3H), 2.41-2.52 (m, 3H), 3.60 (t, *J* = 10.95 Hz, 2H), 3.96 (dd, *J* = 12.39 & 4.35 Hz, 2H), 5.17 (s, 2H), 7.20-7.24 (m, 3H), 7.34-7.43 (m, 3H) 7.49 (d, *J* = 7.23 Hz, 3H), 7.66 (dd, *J* = 8.67 & 4.17 Hz, 2H).

^{13}C NMR ($CDCl_3$) **:** δ 25.96, 34.72, 34.98, 68.40, 70.16, 98.17, 107.16, 119.50, 126.98, 127.35, 127.55, 127.70, 128.16, 128.74, 129.09, 129.17, 133.08, 133.33, 136.94, 156.70, 175.60

ESI/MS (m/z) **:** 415.10 $(M+Na)^+$

5.1.40 Methyl 5-(6-hydroxy-naphthalen-2-ylmethyl)-2-methyl-1,3-dioxane-2-carboxylate. (47)



44 **47**

To a suspension of Pd/C (10%) (1.0 gm) in MeOH (30 ml), a solution of **44** (3.0 gm, 7.3 mmol) in MeOH (30 ml) and ammonium formate (1.86 gm, 0.029 mol) was added and refluxed for 1.0 hours. The reaction mixture was cooled to room temperature, filtered through celite and solvent was concentrated under vacuum. The residue was dissolved in ethyl acetate (100 ml), successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to get the title compound **47** (1.63 gm, 71%) as a yellow solid containing mixture of *cis* and *trans* isomers. m.p: 94-95 °C.

IR (KBr) **:** 3411, 3018, 2954, 2860, 1743, 1608, 1510, 1271, 1143, 1058, 975 cm^{-1}

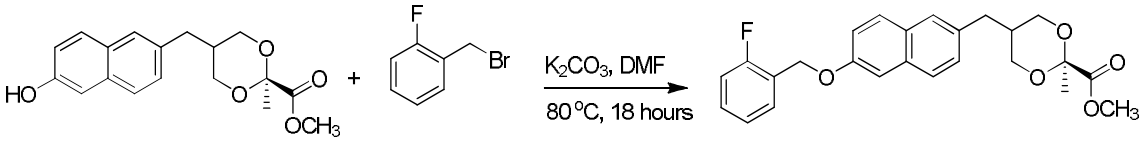
^{1}H NMR ($CDCl_3$) **:** δ 1.51 (s, 3H *cis* isomer), 1.62 (s, 3H, *trans* isomer), 1.69 (s, 1H, *trans* isomer), 2.39-2.45 (m, 3H, *cis* isomer), 3.13 (d, *J* =

7.68 Hz, 2H, *trans* isomer), 3.53 (t, *J* = 10.11 Hz, 2H, *cis* isomer), 3.80 (s, 2H, *trans* isomer), 3.84 (s, 3H, *cis* isomer), 3.86 (s, 3H, *trans* isomer), 3.91-3.97 (m, 2H, *cis* isomer & m, 2H, *trans* isomer), 5.40 (s, 1H, exchangeable), 7.07-7.17 (m, 3H, *cis* isomer), 7.17 (dd, *J* = 8.40 & 1.59 Hz, 3H, *trans* isomer), 7.26 (d, *J* = 8.37 Hz, 1H, *trans* isomer), 7.45 (s, 2H, *trans* isomer), 7.57-7.68 (m, 3H, *cis* isomer)

^{13}C NMR (DMSO-d6) : δ 25.66, 33.54, 34.15, 34.67, 52.30, 65.15, 67.28, 97.80, 98.04, 108.52, 118.67, 126.18, 126.58, 126.99, 127.72, 127.79, 127.91, 128.84, 132.44, 133.20, 134.27, 154.88, 170.44, 170.58

ESI/MS (m/z) : 339.1 $(M+Na)^+$

5.1.41 Methyl 5-[6-(2-fluoro-benzyloxy)-naphthalen-2-ylmethyl]-2-methyl-1,3-dioxane-2-carboxylate. (49)



47 **48** **49**

To a solution of **47** (597 mg, 3.2 mmol) and **48** (1 gm, 3.2 mmol) in dry DMF (12 ml), K_2CO_3 (872 mg, 6.3 mmol) was added and reaction mixture was stirred at 80 °C for 18 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The combined organic extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography using 15% ethyl acetate in hexane as eluent to furnish compound **49** (798 mg, 59%) as a thick liquid containing mixture of *cis* and *trans* isomers.

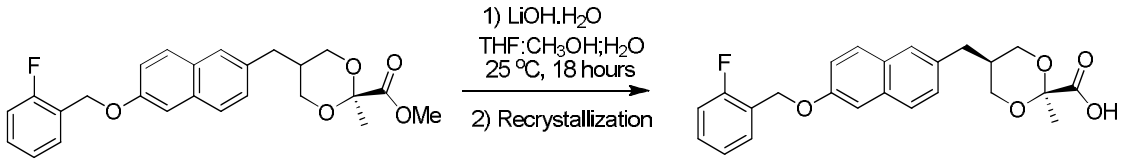
IR ($CHCl_3$) : 3018, 2927, 2858, 1743, 1606, 1493, 1215, 1143, 1120, 1039, 852 cm^{-1}

^{1}H NMR : δ 1.50 (s, 3H, *cis* isomer), 1.61 (s, 3H, *trans* isomer), 1.62-1.70

($CDCl_3$) (m, 1H, *trans* isomer), 2.44-2.46 (m, 3H, *cis* isomer), 3.14 (d, 2H, *J* = 7.95 Hz, *trans* isomer), 3.53 (t, *J* = 10.92 Hz, 2H, *cis* isomer), 3.80 (s, 3H,*trans* isomer), 3.83 (s, 3H, *cis* isomer), 3.85 (s, 3H, *trans* isomer), 3.90-3.97 (m, 2H, *cis* isomer & m, 2H, *trans* isomer), 5.24 (s, 2H), 7.08-7.34 (m, 6H), 7.47 (s, 1H) 7.53-7.61 (m, 1H), 7.66 -7.69 (m, 2H)

ESI/MS (m/z) **:** 447.20 $(M+Na)^+$

5.1.42 *c*-5-[6-(2-Fluoro-benzyloxy)-naphthalen-2-ylmethyl]-2-methyl-1,3-dioxane-*r*-2-carboxylic acid. (51)



49 **51**

To a solution **49** (708 mg, 1.9 mmol) in THF (15 ml), MeOH (5 ml) and H_2O (5 ml), $LiOH.H_2O$ (157.0 mg, 3.8 mmol) was added and stirred at 25 °C for 18 hours. The reaction mixture was concentrated under vacuum. Water was added to the reaction mixture, acidified by aq. HCl and extracted with ethyl acetate. The organic extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product **50** (675 mg) was recrystallized from a mixture of ethyl acetate and hexane (1:2). The first crop yielded title product **51** (300 mg, 38%) as a white solid. m.p: 163-164 °C; Purity by HPLC: 88.7%.

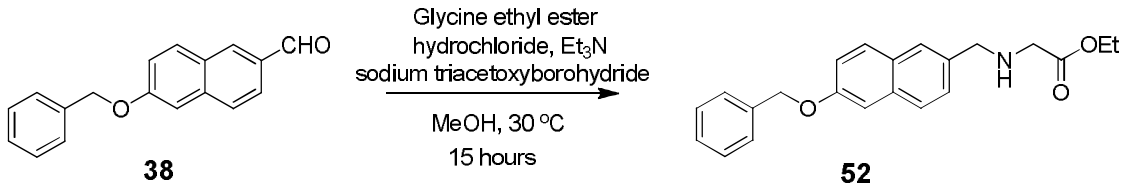
IR (KBr) **:** 3400, 3055, 2862, 1741, 1670, 1606, 1504, 1452, 1392, 1265, 1107, 1039 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.57 (s, 3H), 2.40-2.47 (m, 1H), 2.51 (d, *J* = 7.14 Hz, 2H), 3.60 (t, *J* = 10.95 Hz, 2H), 3.96 (dd, *J* = 12.39 & 4.35 Hz, 2H), 5.24 (s, 2H), 7.11-7.18 (m, 2H), 7.21 (dd, *J* = 4.32 & 1.56 Hz, 3H), 7.31-7.34 (m, 1H), 7.48 (s, 1H), 7.52-7.59 (m, 1H), 7.69 (d, *J* = 8.25 Hz, 2H)

^{13}C NMR (CDCl$_3$) : δ 25.97, 34.77, 35.00, 63.82, 63.86, 68.40, 98.18, 107.19, 115.41, 115.62, 119.39, 124.09, 124.23, 124.41, 124.45, 126.99, 127.43, 127.61, 129.16, 129.28, 129.89, 133.20, 133.33, 156.47, 159.41, 161.86, 175.15

ESI/MS (m/z) : 433.10 $(M+Na)^+$

5.1.43 Ethyl-{[6-Benyloxy-naphthalen-2-ylmethyl]-amino}-acetate. (52)



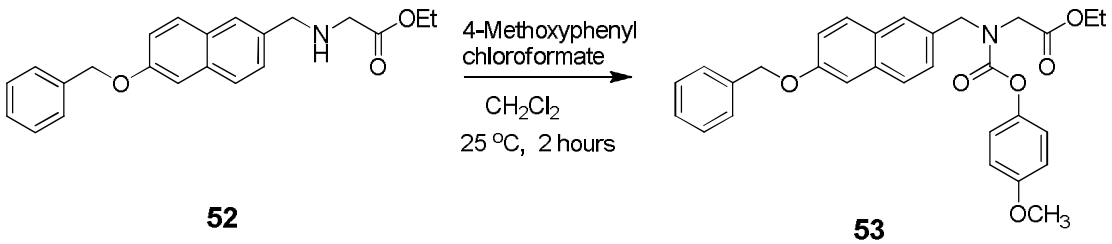
To a solution of **38** (3.25 gm, 0.0124 mol) and glycine ethyl ester hydrochloride (2.0 gm, 0.0148 mol) in MeOH (30 ml), Et_3N (2.06 ml, 0.0148 mole equivalent) was added followed by addition of sodium triacetoxyborohydride (3.94 gm, 0.0185 mole) in small portions at 0 °C and stirred at 30 °C for 15 hours. The reaction mixture was concentrated in vacuum. Water was added to reaction mixture and extracted with ethyl acetate. The organic extract was successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated in vacuum to yield desired product **52** (1.08 gm, 25%) as a pale yellow solid. m.p: 140-150 °C; % Purity by HPLC: 84.6%.

IR (KBr) : 3350, 3018, 2983, 2937, 2873, 1732, 1633, 1483, 1382, 1215, 1151, 1118, 1026, 852 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.25 (t, *J* = 7.14 Hz, 3H), 3.43 (s, 2H), 3.93 (s, 2H), 4.20 (q, *J* = 7.14 Hz, 2H), 5.17 (s, 2H), 7.21-7.25 (m, 2H), 7.34-7.44 (m, 4H), 7.48 (d, *J* = 7.1 Hz, 2H), 7.68-7.74 (m, 3H)

ESI/MS (m/z) : 349.9 $(M+H)^+$

5.1.44 Ethyl-[(6-Benzyloxy-naphthalen-2-ylmethyl)-(4-methoxy-phenoxycarbonyl)-amino]-acetate. (53)



52 **53**

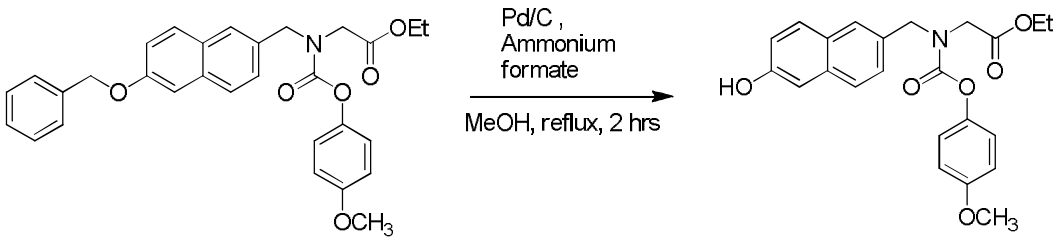
To a solution of **52** (1.00 gm, 2.9 mmol) in dichloromethane (20 ml), solution of 4-methoxyphenyl chloroformate (0.6 ml, 4.0 mmol) in dichloromethane (2 ml) was added dropwise at 0 °C and stirred at 25 °C for 2 hours. The reaction mixture was diluted with dichloromethane and successively washed with water and brine, dried over $CaCl_2$, filtered and concentrated in vacuum. The crude product was purified by column chromatography to give the desired product **53** (991 mg, 69%) as a thick liquid. % Purity by HPLC: 98.5%.

IR ($CHCl_3$) : 3018, 2837, 1747, 1720, 1633, 1608, 1508, 1454, 1392, 1197, 1026, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.25 (q, *J* = 14.25 Hz, 3H), 3.79 (s, 3H), 4.03 (s, 2H), 4.08-4.22 (m, 2H), 4.76 (s, 1H), 4.87 (s, 1H), 5.18 (s, 2H), 6.89 (d, *J* = 8.76 Hz, 2H), 7.04-7.10 (m, 2H), 7.22-7.25 (m, 2H), 7.32-7.43 (m, 4H), 7.50 (d, *J* = 7.13 Hz, 2H), 7.66 (s, 1H), 7.72 (t, *J* = 7.36 Hz, 2H)

ESI/MS (m/z) : 499.9 $(M+H)^+$

5.1.45 Ethyl-2-(((6-hydroxynaphthalen-2-yl)-methyl)-((4-methoxyphenoxy)-carbonyl)-amino)-acetate. (55)



53 **55**

To a suspension of Pd/C (10%) (120 mg) in MeOH (15 ml), a solution of **53** (1.2 gm, 2.4 mmol) in MeOH (10 ml) and ammonium formate (757 mg, 0.012 mol) was added and refluxed for 2 hours. The reaction mixture was cooled to room temperature, filtered through celite and solvent was concentrated under vacuum. The residue was dissolved in ethyl acetate (50 ml), successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to give the title compound **55** (750 mg, 76%) as an off white solid. m.p: 141-142 °C; % Purity by HPLC: 96.3%.

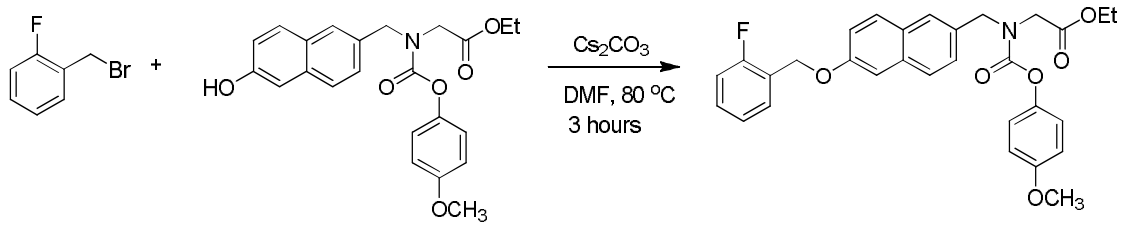
IR (KBr) **:** 3373, 2980, 2839, 1753, 1711, 1632, 1606, 1508, 1411, 1303, 1180, 1033, 866 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.23 (q, *J* = 14.8 Hz, 3H), 3.79 (s, 3H), 4.05 (s, 2H), 4.14-4.21 (m, 2H), 4.75 (s, 1H), 4.86 (s, 1H), 6.88 (dd, *J* = 8.8 & 2.0 Hz, 2H), 7.05-7.14 (m, 4H), 7.39-7.42 (m, 1H), 7.64-7.67 (m, 2H), 7.69-7.73 (m, 1H)

^{13}C NMR (DMSO-d6) **:** δ 14.01, 48.60, 48.88, 51.64, 51.70, 55.39, 60.65, 60.77, 108.61, 114.26, 118.82, 122.49, 122.56, 126.05, 126.09, 126.43, 126.50, 126.61, 127.43, 127.50, 129.23, 131.09, 131.33, 133.95, 134.00, 144.47, 154.62, 154.78, 155.39, 156.61, 169.06, 169.69

ESI/MS (m/z) **:** 432.07 $(M+Na)^+$

5.1.46 Ethyl-2-(((6-((2-fluorobenzyl)-oxy)-naphthalen-2-yl)-methyl)-((4-methoxyphenoxy)-carbonyl)-amino) acetate. (56)



48 **55** **56**

To a solution of **48** (199 mg, 0.00097 mol) and **55** (400 mg, 0.00097 mol) in dimethylformamide (15 ml), Cs_2CO_3 (478 mg, 0.00146 mol), was added and the reaction mixture was stirred for 3 hours at 80 °C. Reaction mixture was cooled to

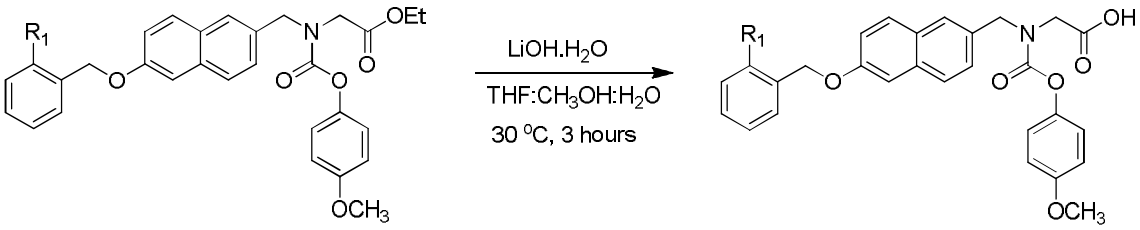
30 °C and poured into ice-cold water (20 ml) and was extracted with ethyl acetate. The organic extract was successively washed with water and brine, dried over sodium sulfate, filtered and concentrated under vacuum to yield crude product as a thick liquid. The crude product was purified by column chromatography using 15% ethyl acetate in hexane as eluent to give the required product **56** (419 mg, 83.0%) as a thick liquid. % Purity by HPLC: 96.8%.

IR ($CHCl_3$) **:** 3018, 1751, 1718, 1605, 1508, 1384, 1039 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.20-1.28 (m, 3H), 3.79 (s, 3H), 4.04 (s, 2H), 4.13-4.21 (m, 2H), 4.76 (s, 1H), 4.87 (s, 1H), 5.26 (s, 2H), 6.87 (dd, *J* = 8.8 & 1.2 Hz, 2H), 7.04-7.25 (m, 4H), 7.31-7.36 (m, 1H), 7.41-7.45 (m, 1H), 7.54-7.58 (m, 1H), 7.66 (d, *J*=4.0 Hz, 1H), 7.72-7.76 (m, 2H)

ESI/MS (m/z) **:** 540.12 $(M+Na)^+$

5.1.47 General procedure for the preparation of the compounds 54 and 57.

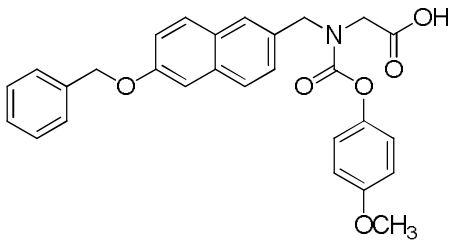


53; R_1 = H
56; R_1 = F

54; R_1 = H
57; R_1 = F

To a solution of ester (1.0 mole equivalent) in mixture of THF (9 fold), MeOH (3 fold) and H_2O (3 fold), $LiOH.H_2O$ (2 mole equivalent) was added and the reaction mixture was stirred for 3 hours at 30 °C. The reaction mixture was concentrated under vacuum and the residue was dissolved in water, acidified and extracted with ethyl acetate. The organic extract was washed with water followed by brine, dried over sodium sulfate, filtered and concentrated under vacuum to the yield required products.

5.1.47.1 [(6-Benzyloxy-naphthalen-2-ylmethyl)-(4-methoxy-phenoxycarbonyl)-amino]-acetic acid. (54)



54 (224 mg, 25%) was prepared from **53** (950 mg, 0.00190 mol) following the general procedure described above as a white solid. m.p: 169-171 °C; % Purity by HPLC: 97.0%.

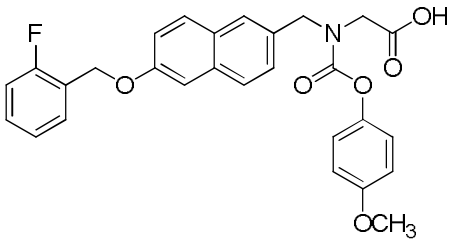
IR (KBr) : 3433, 3003, 2873, 2833, 2725, 1735,1683, 1608, 1508, 1454, 1390, 1238, 1199, 1008 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 3.79 (s, 3H), 4.09 (s, 2H), 4.77 (s, 1H), 4.87 (s, 1H), 5.18 (s, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 7.08 (t, *J* = 8.9 Hz, 2H), 7.23-7.26 (m, 2H), 7.34-7.43 (m, 4H), 7.50 (d, *J* = 7.3 Hz, 2H), 7.63 (s, 1H), 7.73 (t, *J* = 8.0 Hz, 2H)

^{13}C NMR (CDCl$_3$) : δ 48.56, 48.75, 51.52, 51.63, 55.40, 69.31, 99.54, 107.23, 114.24, 119.04, 122.53, 122.61, 125.88, 126.35, 126.74, 127.13, 127.17, 127.80, 127.91, 128.35, 128.47, 129.30, 132.40, 132.64, 133.55, 133.60, 136.95, 144.50, 144.95, 154.64, 154.99, 156.32, 156.59, 170.79

ESI/MS (m/z) : 471.8 $(M+H)^+$

5.1.47.2 2-(((6-((2-fluorobenzyl)-oxy)-naphthalen-2-yl)-methyl)-((4-methoxyphenoxy)-carbonyl)-amino)-acetic acid. (57)



57 (253 mg, 67%) was prepared from **56** (400 mg, 0.77 mmol) following the general procedure described above as a white solid. m.p: 169-171 °C; % Purity by HPLC: 94.3%.

IR (KBr) **:** 3448, 2955, 2935, 1736, 1685, 1608, 1508, 1390, 1238, 1199, 1031, 877, 857, 854 cm^{-1}

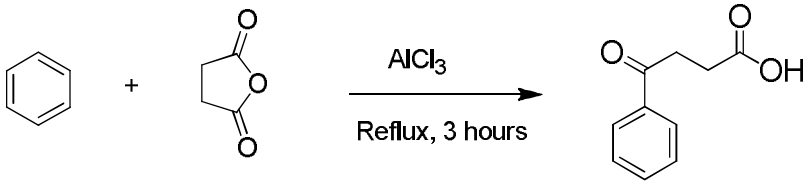
^{1}H NMR (DMSO-d6) **:** δ 3.72 (s, 3H), 3.93 (d, *J* = 18.0 Hz, 2H), 4.61 (s, 1H), 4.75 (s, 1H), 5.24 (s, 2H), 6.89-6.92 (m, 2H), 6.99-7.02 (m, 2H), 7.20-7.29 (m, 3H), 7.40-7.47 (m, 3H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.75-7.85 (m, 3H)

^{13}C NMR (DMSO-d6) **:** δ 48.96, 51.38, 51.55, 55.39, 62.20, 63.62, 107.16, 114.18, 114.25, 115.32, 115.53, 118.88, 122.54, 122.66, 123.67, 123.81, 124.58, 125.82, 126.34, 126.75, 127.18, 128.45, 128.52, 129.34, 130.41, 130.50, 130.77, 130.81, 132.66, 132.87, 133.50, 133.54, 144.58, 144.72, 154.61, 155.16, 156.13, 156.52, 159.24, 161.69, 170.92

ESI/MS (m/z) **:** 512.12 $(M+Na)^+$

5.1.48 (*E*)-Ethyl (*E*)-4-hydroxyimino-4-phenylbutyrate. (60)

5.1.48.1 4-Oxo-4-phenyl-butyric acid. (58)



To a stirred suspension of $AlCl_3$ (293 g, 2.2 mol) in benzene (500 ml) was added succinic anhydride (100 g, 1.0 mol) portionwise while keeping the temperature below 40 °C over a period of 1 hour and then the reaction mixture was refluxed for 3 hours. Solvent was distilled out and the residue was poured into ice-cold water. Separated solid product was filtered, washed with excess water and dried over P_2O_5 to yield the title product **58** (96 gm, 53%) as a white solid. m.p: 110-112 °C; % Purity by HPLC: 98.8%.

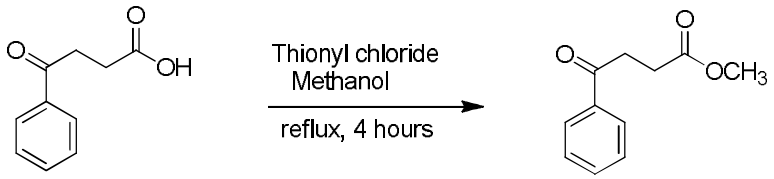
IR (KBr) **:** 3400, 2972, 2923, 2663, 1683, 1595, 1431, 1348, 1240, 1170,

947 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.76 (t, *J* = 6.7 Hz, 2H), 3.32 (t, *J* = 6.7 Hz, 2H), 7.43-7.49 (m, 2H), 7.54-7.59 (m, 1H), 7.97-8.00 (m, 2H)

ESI/MS (m/z) : 201.0 $(M+Na)^+$

5.1.48.2 Methyl 4-oxo-4-phenylbutanoate. (59)



58 **59**

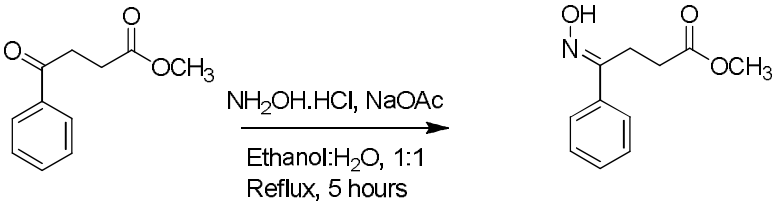
To an ice-cold suspension of **58** (98.62 gm, 0.258 mol) in methanol was added thionyl chloride (20.59 ml, 0.2838 mol) dropwise over a period of 2 hours and then the reaction mixture was slowly heated to reflux over a period of 1 hour and continued for further 4 hours. Solvents were distilled out; residue was poured into ice-cold water and was extracted with diethyl ether (3 X 250 ml). The combined ethereal extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield desired product **59** (100 gm, 98.6%) as a pale brown liquid; % Purity by HPLC: 96.4%.

IR (CHCl$_3$) : 3060, 2952, 2848, 1735, 1685, 1597, 1448, 1358, 1066 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.77 (t, *J* = 6.6 Hz, 2H), 3.33 (t, *J* = 6.6 Hz, 2H), 3.70 (s, 3H), 7.44-7.49 (m, 2H), 7.54-7.57 (m, 1H), 7.79-8.00 (m, 2H)

ESI/MS (m/z) : 215 $(M+Na)^+$

5.1.48.3 (*E*)-methyl 4-(hydroxyimino)-4-phenylbutanoate. (60)



59 **60**

To solution of **59** (33.0 gm, 0.286 mol) in ethanol (300 ml) was added a solution of hydroxylammonium chloride (39.72 gm, 0.572 mol) and sodium acetate (46.92 gm, 0.572 mol) in water (300 ml) and the reaction mixture was refluxed for 5 hours. Ethanol was distilled out; residue was poured into water and extracted with ethyl acetate. Combined organic extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. Crude product was purified by flash column chromatography using 5-6% ethyl acetate in hexane as eluent to yield the desired product **60** (55.0 gm, 76%) as a pale yellow liquid; % Purity by HPLC: 96.7%.

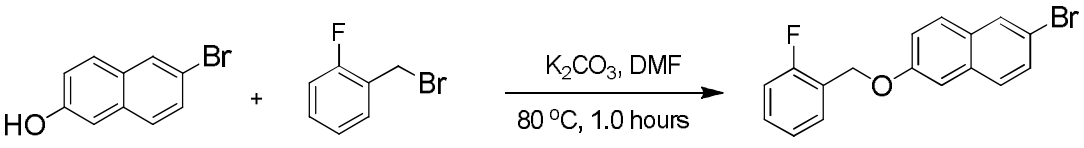
IR ($CHCl_3$) **:** 3284, 3020, 2954, 1734, 1601, 1499, 1439, 1321, 1072, 935 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.61-2.65 (m, 2H), 3.11-3.15 (m, 2H), 3.64 (s, 3H), 7.35-7.39 (m, 3H), 7.58-7.62 (m, 2H), 9.87 (s, 1H, =N-OH)

^{13}C NMR ($CDCl_3$) **:** δ 22.13, 30.44, 51.83, 126.22, 126.32, 128.70, 129.48, 135.12, 157.96, 173.25

ESI/MS (m/z) **:** 207.8 $(M+H)^+$

5.1.49 2-bromo-6-((2-fluorobenzyl)-oxy)-naphthalene. (61)



35 **48** **61**

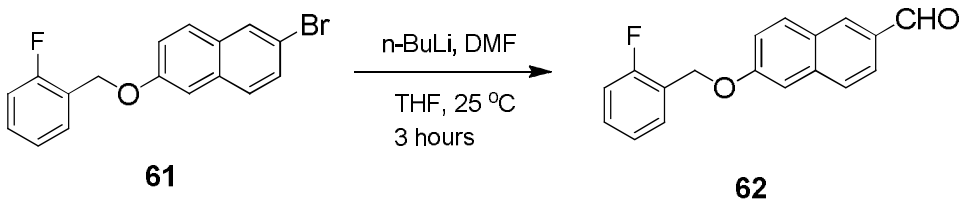
61 (5.49 gm, 74%) was prepared from **35** (5.0 gm, 0.022 mol) and **48** (4.03 gm, 0.021mol) according to the procedure described for the preparation of **37** as a white solid. m.p: 93-94 °C; % Purity by HPLC: 95.1%.

IR (KBr) **:** 3059, 2929, 2883, 1622, 1589, 1492, 1454, 1381, 1209, 1166, 1012, 850 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 5.23 (s, 2H), 7.09-7.25 (m, 4H), 7.30-7.36 (m, 1H), 7.48-7.61 (m, 3H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.91 (s, 1H)

ESI/MS (m/z) **:** 354.00 $(M+Na)^+$

5.1.50 6-((2-Fluorobenzyl) oxy)-2-naphthaldehyde. (62)



61 **62**

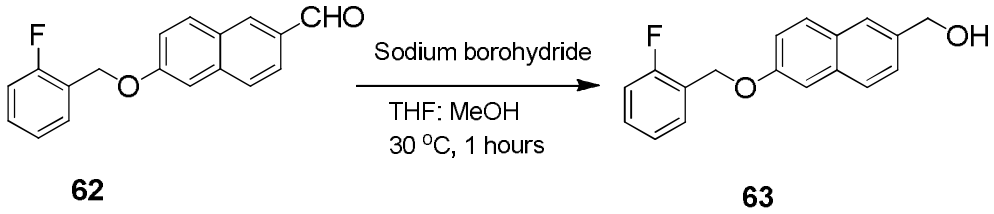
62 (1.96 gm, 35%) was prepared from **61** (6.60 gm, 0.02 mol) according to the procedure described for the preparation of **38** as a white solid. m.p: 78-79 °C, Purity by HPLC: 96.4%.

IR (KBr) **:** 2926, 2800, 2713, 2698, 1697, 1624, 1500, 1450, 1392, 1381, 1267, 1224, 1037, 850, 732 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 5.28 (s, 2H), 7.10-7.25 (m, 2H), 7.29-7.38 (m, 3H), 7.53-7.56 (m, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.90-7.93 (m, 2H), 8.26 (s, 1H), 10.09 (s, 1H, -CHO)

ESI/MS (m/z) **:** 281.21 $(M+H)^+$

5.1.51 (6-((2-fluorobenzyl) oxy) naphthalen-2-yl) methanol. (63)



62 **63**

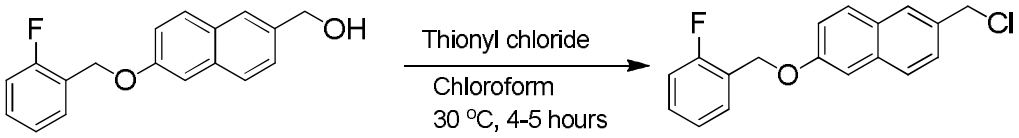
63 (1.98 gm, 98%) was prepared from **62** (1.0 gm, 3.5 mmol) according to the procedure described for the preparation of **40** as a white solid. m.p: 107-108 °C; % Purity by HPLC: 98.4%.

IR (KBr) **:** 3254, 3244, 2914, 2858, 1606, 1587, 1452, 1394, 1267, 1232, 1168, 1045, 852 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.71 (t, *J* = 6.0 Hz, 1H), 4.82 (d, *J* = 6.0 Hz, 2H), 5.25 (s, 2H), 7.09-7.25 (m, 4H), 7.30-7.36 (m, 1H), 7.45 (dd, *J* = 8.4 & 1.2 Hz, 1H), 7.54-7.58 (m, 1H), 7.73-7.76 (m, 3H)

ESI/MS (m/z) **:** 265.23 $(M-18)^+$

5.1.52 2-(Chloromethyl)-6-((2-fluorobenzyl) oxy) naphthalene. (64)



63 **64**

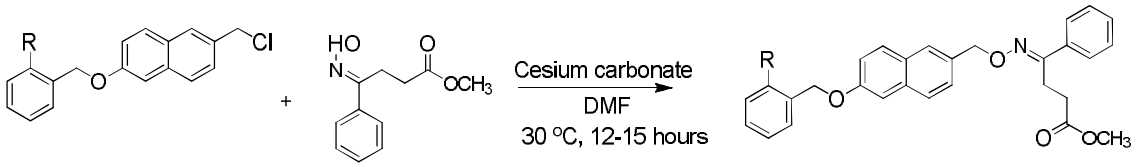
64 (522 mg, 70%) was prepared from **63** (700 mg, 2.5 mmol) according to the procedure described for the preparation of **41** as a white solid. m.p: 106-107°C.

IR (KBr) **:** 2929, 2875, 1919, 1604, 1587, 1494, 1394, 1271, 1180, 1109, 1014 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 4.73 (s, 2H), 5.25 (s, 2H), 7.09-7.19 (m, 2H), 7.22-7.25 (m, 2H), 7.30-7.36 (m, 1H), 7.47 (dd, *J* = 10.0 & 1.6 Hz, 1H), 7.53-7.57 (m, 1H), 7.74 (d, *J* = 10.0 Hz, 3H)

ESI/MS (m/z) **:** 301.51 $(M+H)^+$

5.1.53 General procedure for the preparation of the compounds 65a-b.



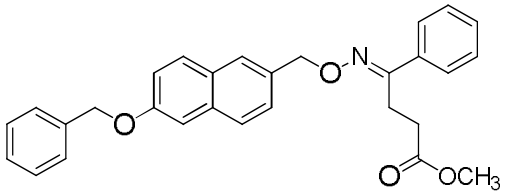
41; R = H
64; R = F

60

65a; R = H
65b; R = F

To a solution of chloride (**41**, **64**) (1.0 mole equivalent) and **60** (1.0 mole equivalent) in dimethylformamide (5 fold), cesium carbonate (1.5 mole equivalent) was added and the reaction mixture stirred for 30 °C for 12-15 hours. The reaction mixture was poured to ice-cold water and was extracted with ethyl acetate. The combined organic extracts were washed with water followed by brine and dried over sodium sulfate, filtered and concentrated under vacuum to yield crude product. Then crude product was purified by column chromatography using 3-5 % ethyl acetate in hexane to obtained pure products, (**65a-b**).

5.1.53.1 (*E*)-Ethyl-4-(((6-(benzyloxy)-naphthalen-2-yl)-methoxy)-imino)-4-phenylbutanoate. (65a)



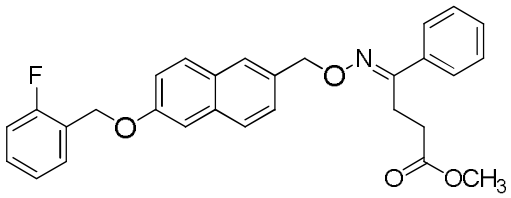
65a (1.09 gm, 70%) was prepared from **41** (975 mg, 3.4 mmol) and **60** (714 mg, 3.4 mmol) following the general procedure described above as a white solid. m.p: 115 °C.

IR (KBr) **:** 3018, 2873, 1728, 1608, 1483, 1377, 1265, 1215, 1176, 1018, cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.57 (t, *J* = 8.0 Hz, 2H), 3.09 (t, *J* = 8.0 Hz, 2H), 3.61 (s, 3H), 5.18 (s, 2H), 5.35 (s, 2H), 7.23 (dd, *J* = 1.8 & 0.4 Hz, 2H), 7.34-7.40 (m, 6H), 7.48-7.50 (m, 3H), 7.61-7.63 (m, 2H), 7.71-7.78 (m, 3H)

ESI/MS (m/z) **:** 454.3 $(M+H)^+$

5.1.53.2 (*E*)-methyl 4-(((6-((2-fluorobenzyl)oxy)naphthalen-2-yl)methoxy)imino)-4-phenylbutanoate. (65b)



65b (379 mg, 47%) was prepared from **64** (500 mg, 1.7 mmol) and **60** (367 mg, 1.7 mmol) following the general procedure described above as a thick liquid. % Purity by HPLC: 96.5%.

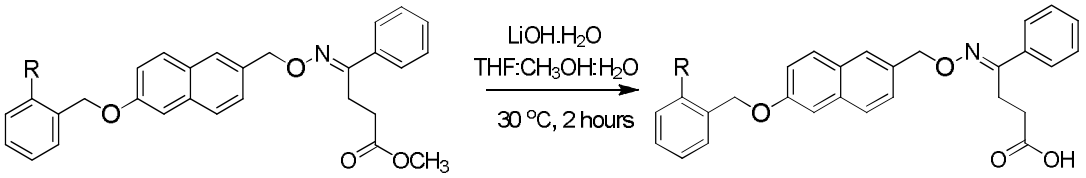
IR ($CHCl_3$) **:** 3018, 2929, 1735, 1608, 1500, 1384, 1265, 1174, 1045 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 2.57 (t, *J* = 8.4 Hz, 2H), 3.09 (t, *J* = 7.6 Hz, 2H), 3.61 (s, 3H), 5.25 (s, 2H), 5.35 (s, 2H), 7.08-7.25 (m, 4H), 7.29-7.36 (m, 4H), 7.50 (dd, *J* = 8.4 & 1.2 Hz, 1H), 7.54-7.57 (m, 1H), 7.61-7.64

(m, 2H), 7.72-7.75 (m, 1H), 7.78 (s, 2H)

ESI/MS (m/z) **:** 472.58 $(M+H)^+$

5.1.54 General procedure for the preparation of the compounds 66a-b.

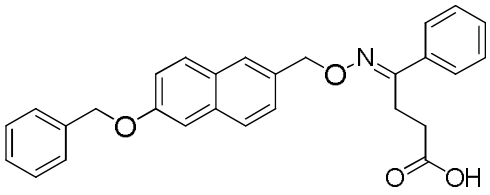


65a; R = H
65b; R = F

66a; R = H
66b; R = F

To a solution of **65a-b** (1.0 mole equivalent) in mixture of THF (9 fold), MeOH (3 fold) and H_2O (3 fold), $LiOH.H_2O$ (2 mole equivalent) was added and reaction mixture was stirred for 2.0 hours at 30 °C. The reaction mixture was concentrated under vacuum and residue was dissolved in water, acidified and was extracted with ethyl acetate. The extracted organic layer was washed with water followed by brine, dried over sodium sulfate, filtered and concentrated under vacuum to yield the crude product as oil. The crude product was purified by column chromatography using 0.5-1.0% methanol in chloroform to yield the desired product **66a-b**.

5.1.54.1 (*E*)-4-(((6-(benzyloxy)-naphthalen-2-yl)-methoxy)-imino)-4-phenylbutanoic acid. (66a)



66a (625 mg, 70%) was prepared from **65a** (950 mg, 2.03 mmol) following the general procedure described above as a white solid. m.p: 123-124 °C, % Purity by HPLC: 99.5%.

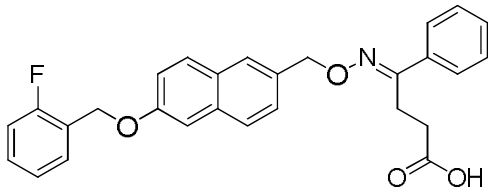
IR (KBr) **:** 3450, 3050, 2882, 1697, 1660, 1634, 1606, 1437, 1335, 1293, 1224, 1177, 1028, 932, 851 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.60 (t, *J* = 8.1 Hz, 2H), 3.09 (t, *J* = 8.1 Hz, 2H), 5.17 (s, 2H), 5.35 (s, 2H), 7.23 (d, *J* = 7.8 Hz, 2H), 7.35-7.40 (m, 6H), 7.47-7.50 (m, 3H), 7.61-7.63 (m, 2H), 7.73 (d, *J* = 10.5 Hz, 2H), 7.78 (s, 1H)

^{13}C NMR (CDCl$_3$) : δ 2.31, 30.41, 30.70, 62.75, 70.16, 76.39, 100.09, 107.23, 119.25, 119.38, 126.41, 127.17, 127.28, 128.13, 128.33, 128.74, 128.95, 129.08, 129.46, 129.58, 129.70, 133.20, 133.57, 134.29, 135.14, 136.97, 155.39, 156.92, 157.07, 178.54

ESI/MS (m/z) : 440.30 $(M+H)^+$

5.1.54.2 (*E*)-4-(((6-((2-fluorobenzyl)-oxy)-naphthalen-2-yl)-methoxy)-imino)-4-phenylbutanoic acid. (66b)



66b (244 mg, 70%) was prepared from **65b** (360 mg, 0.76 mmol) following the general procedure described above as a white solid. m.p: 78-79 °C, % Purity by HPLC: 97.9 %.

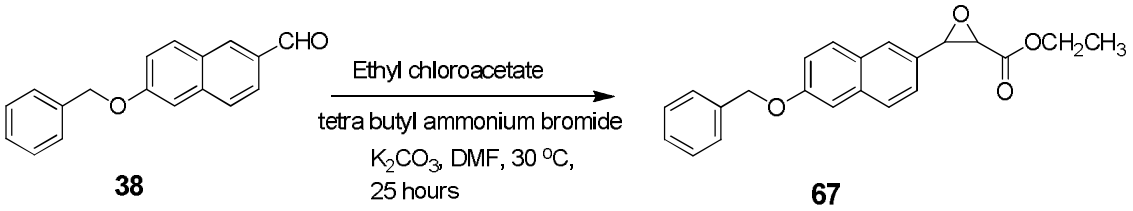
IR (KBr) : 3450, 3036, 2933, 2877, 1708, 1610, 1492, 1456, 1307, 1267, 1238, 1043, 937, 852 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.61 (t, *J* = 5.2 Hz, 2H), 3.09 (t, *J* = 8.0 Hz, 2H), 5.24 (s, 2H), 5.35 (s, 2H), 7.08-7.25 (m, 4H), 7.29-7.43 (m, 4H), 7.49-7.57 (m, 2H), 7.61-7.63 (m, 2H), 7.68-7.75 (m, 3H)

^{13}C NMR (DMSO-d6) : δ 22.03, 30.47, 63.64, 75.68, 107.16, 115.32, 115.53, 118.92, 123.65, 123.79, 124.54, 124.58, 126.20, 126.70, 126.75, 126.83, 126.95, 128.38, 128.55, 129.32, 129.50, 130.42, 130.50, 130.77, 130.81, 133.31, 133.77, 134.75, 156.28, 157.25, 159.24, 161.69, 173.34

ESI/MS (m/z) : 480.52 $(M+Na)^+$

5.1.55 Ethyl 3-(6-(benzyloxy)-naphthalen-2-yl)-oxirane-2-carboxylate. (67)



38 **67**

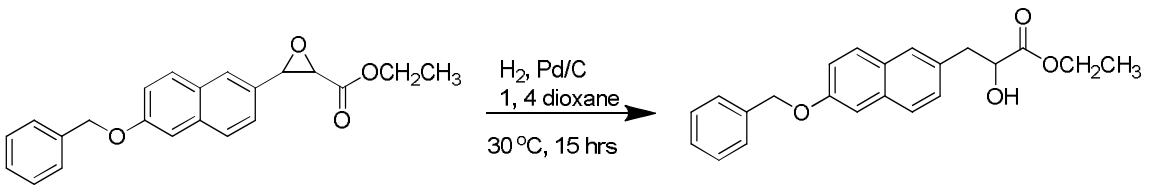
To solution of **38** (5.0 gm, 0.0196 mol) in dimethyl formamide (20 ml), potassium carbonate (9.46 gm, 0.0686 mol), ethyl chloroacetate (3.56 ml, 0.0333 mol) and tetra butyl ammonium bromide (1% respective to aldehyde) was added and reaction mixture was stirred at 30 °C for 25 hours. The reaction mixture was poured to ice cold water and stirred for 10-15 minutes. The solid product was filtered, washed with water and dried over P_2O_5 to yield the desired product **67** (5.45 gm, 82%) as an off white solid. m.p: 80-82 °C; % Purity by HPLC: 59.1 & 33.0%.

IR (KBr) **:** 2906, 2875, 1747, 1629, 1604, 1508, 1483, 1454, 1384, 1328, 1253, 1178, 1120, 1055, 1006 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.00 (t, *J* = 9.6 Hz, 3H, *cis* isomer), 1.34 (t, *J* = 9.6 Hz, 3H, *trans* isomer), 3.60 (d, *J* = 2.4 Hz, 1H, *trans* isomer), 3.87 (d, *J* = 6.0 Hz, 1H, *cis* isomer), 3.91-4.01 (m, 2H *cis* isomer), 4.22 (d, *J* = 2.12 Hz, 1H *trans* isomer), 4.28-4.32 (m, 2H, *cis* isomer), 4.39 (d, *J* = 6.0 Hz, 1H, *cis* isomer), 5.17 (s, 2H), 7.20-7.26 (m, 3H), 7.34-7.43 (m, 3H), 7.47-7.49 (m, 2H), 7.67-7.83 (m, 3H)

ESI/MS (m/z) **:** 349.0 $(M+H)^+$

5.1.56 Ethyl 3-(6-(benzyloxy)naphthalen-2-yl)-2-hydroxypropanoate. (68)



67 **68**

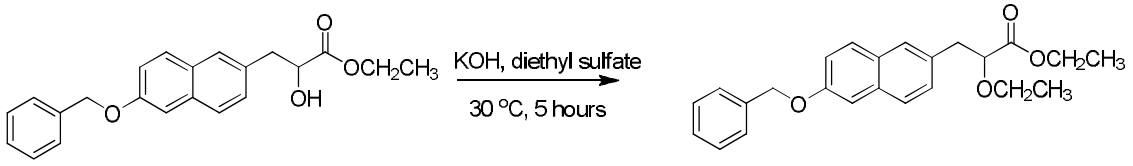
To a solution of **67** (25.0 gm, 0.071mol) in 1,4-dioxane (250 ml), Pd/C (10%) (2.50 gm) was added and was hydrogenated at 30 °C (5-10 psi of hydrogen pressure) for 15 hours. The reaction mixture was filtered through celite and filtrate was concentrated under vacuum to yield the crude product which was purified by column chromatography using ethyl acetate in hexane as an eleunt to yield the desired pure product **68** (12.07 gm, 48%) as a white solid. m.p: 68-69°C; % Purity by HPLC: 86.1%.

IR (KBr) **:** 3458, 2980, 2906, 2858, 1726, 1604, 1508, 1261, 1224, 1095, 1012, 850 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.28 (t, *J* = 9.6 Hz, 3H), 2.77 (d, *J* = 8.0 Hz, 1H), 3.10 (dd, *J* = 18.8 & 8.8 Hz, 1H), 3.25 (dd, *J* = 18.6 & 5.9 Hz, 1H), 4.22 (q, *J* = 9.4 Hz, 2H), 4.47-4.53 (m, 1H), 5.17 (s, 2H), 7.19-7.25 (m, 2H), 7.30-7.43 (m, 4H), 7.48 (d, *J* = 10.0 Hz, 2H), 7.60-7.67 (m, 3H)

ESI/MS (m/z) **:** 351.16 $(M+H)^+$

5.1.57 Ethyl 3-(6-(benzyloxy)naphthalen-2-yl)-2-ethoxypropanoate. (69)



68 **69**

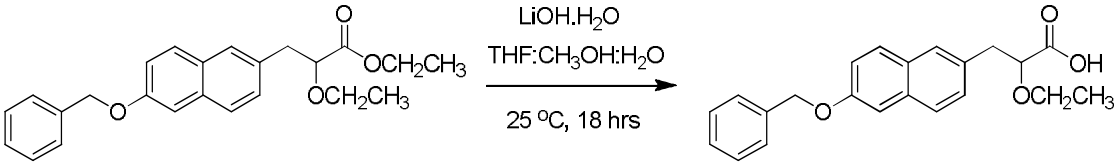
To a solution of **68** (12.0 gm, 0.034 mol) in dimethyl sulfoxide (60 ml), KOH (7.67 gm, 0.137 mol) was added followed by dropwise addition of diethyl sulfate (17.60 ml, 0.137 mol) over a peroid of 15 minute at 0 °C and the reaction mixture was stirred at 30 °C for 5 hours. Reaction mixture was poured in to ice-cold water and was extracted with ethyl acetate. Then organic extract was washed with water followed by brine, dried over sodium sulfate, filtered and concentrate under vacuum to yield the crude product which was purified on column chromatography using 8-10% ethyl acetate in hexane to yield the pure product **69** (12.83 gm, 99%) as a liquid. % Purity by HPLC: 99.3%.

IR ($CHCl_3$) **:** 3018, 2982, 1735,1606, 1508, 1385, 1263, 1120, 1028, 852 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.13-1.27 (m, 6H), 3.12-3.14 (m, 2H), 3.31-3.38 (m, 1H), 3.57-3.63 (m, 1H), 4.07 (dd, *J* = 7.6 & 4.2 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 5.17 (s, 2H), 7.19-7.22 (m, 2H), 7.32-7.37 (m, 2H), 7.40 (t, *J* = 6.8 Hz, 2H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.61 (s, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 1H)

ESI/MS (m/z) **:** 379.19 $(M+H)^+$

5.1.58 3-(6-(benzyloxy)naphthalen-2-yl)-2-ethoxypropanoic acid. (70)



69 **70**

To a solution of **69** (500 mg, 1.3 mmol) in mixture of THF (9 ml), MeOH (3 ml) and H_2O (3 ml), $LiOH.H_2O$ (110 mg, 2.6 mmol) was added and stirred at 25 °C for 18 hours. The reaction mixture was concentrated under vacuum. Water was added to the reaction mixture, acidified with hydrochloric acid and was extracted with ethyl acetate. The organic extract was successively washed with water and brine, dried over Na_2SO_4, filtered and was concentrated under vacuum to give the desired product **70** (230 mg, 50%) as an off white solid. m.p: 107-110 °C; % Purity by HPLC: 96.8%.

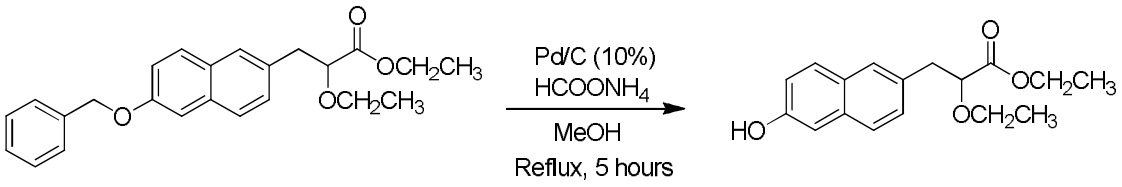
IR (KBr) **:** 3448, 3034, 2980, 2887, 2876, 1728, 1701, 1606, 1508, 1396, 1265, 1144, 1041, 852 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.16 (t, *J* = 6.8 Hz, 3H), 3.12 (dd, *J* = 14.0 & 7.6 Hz, 1H), 3.28 (dd, *J* = 14.0 & 4.0 Hz, 1H), 3.41-3.49 (m, 1H), 3.55-3.62 (m, 1H), 4.15 (dd, *J* = 7.6 & 4.0 Hz, 1H), 5.17 (s, 2H), 7.20-7.25 (m, 2H), 7.32-7.35 (m, 2H), 7.40 (t, *J* = 6.8 Hz, 2H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.62 (s, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.8 Hz, 1H)

^{13}C NMR (CDCl$_3$) : δ 15.14, 39.94, 67.00, 70.15, 79.89, 107.12, 119.29, 126.97, 127.55, 127.68, 128.05, 128.14, 128.35, 128.66, 128.73, 129.16, 129.22, 129.33, 132.18, 133.54, 137.00, 156.75, 176.41

ESI/MS (m/z) : 351.23 $(M+H)^+$

5.1.59 Ethyl 2-ethoxy-3-(6-hydroxynaphthalen-2-yl)propanoate. (71)



69 **71**

To a suspension of Pd/C (10%) (1.1 gm) in MeOH (50 ml), a solution of **69** (11.0 gm, 0.029 mol) in MeOH (200 ml) and ammonium formate (7.32 gm, 0.116 mol) was added and was refluxed for 5 hours. The reaction mixture was cooled to room temperature, filtered through celite and solvent was evaporated under vacuum. The residue was dissolved in ethyl acetate, successively washed with water and brine, dried over Na_2SO_4, filtered and was concentrated under vacuum to give the crude product. The crude product was purified by column chromatography using 10-15% ethyl acetate in hexane as an eluent to yield the desired product **71** (3.60 gm, 43%) as a white solid. m.p: 69-70°C; % Purity by HPLC: 93.6%.

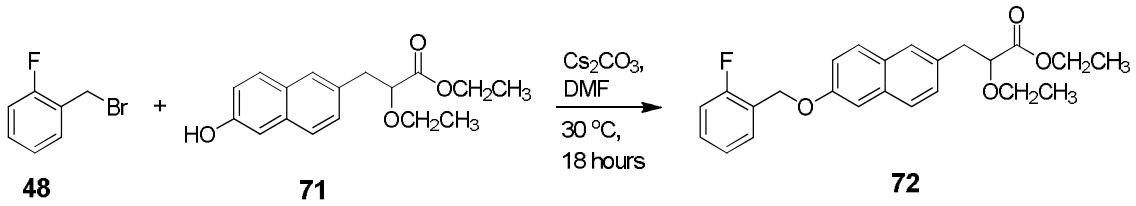
IR (KBr) : 3558, 2976, 2901, 1720, 1606, 1521, 1383, 1276, 1113, 866 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.14-1.21 (m, 6H,), 3.09-3.15 (m, 2H), 3.32-3.40 (m, 1H), 3.58-3.66 (m, 1H), 4.09 (t, *J* = 1.2 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 5.24 (s, 1H), 7.04-7.09 (m, 2H), 7.33 (dd, *J* = 8.4 & 1.6 Hz, 1H), 7.57 (s, 1H), 7.59 (d, *J* = 4.0 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 1H)

^{13}C NMR (CDCl$_3$) : δ 14.01, 15.06, 38.52, 51.53, 60.19, 65.02, 79.30, 108.47, 118.61, 125.79, 127.45, 127.64, 128.02, 128.93, 131.04, 133.38, 155.01, 171.75

ESI/MS (m/z) : 289.27 $(M+H)^+$

5.1.60 Ethyl 2-ethoxy-3-(6-((2-fluorobenzyl)-oxy)naphthalen-2-yl)-propanoate. (72)



48 **71** **72**

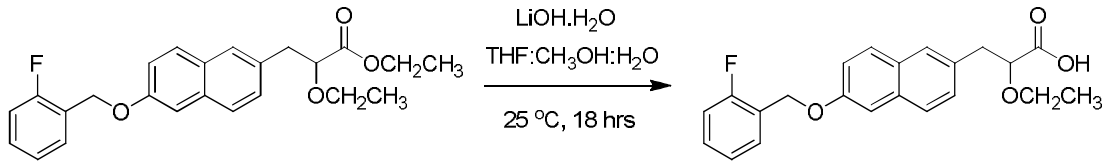
To a solution of **71** (600 mg, 2.1 mmol) and **48** (393.4 mg, 2.1 mmol) in dimethylformamide (8 ml), cesium carbonate (1.35 gm, 4.2 mmol) was added and the reaction mixture was stirred for 18 hours at 30°C. The reaction mixture was poured in to ice-cold water and extracted with ethyl acetate. The extracted organic extract was washed with water followed by brine, dried over sodium sulfate, filtered and concentrated under vacuum to yield title product **72** (478 mg, 58%) as a thick liquid. % Purity by HPLC: 97.3%.

IR (CHCl$_3$) : 3018, 2980, 2899, 1735, 1606, 1508, 1494, 1384, 1263, 1112, 1035, 852 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.15 (t, *J* = 6.8 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H), 3.09-3.17 (m, 2H), 3.31-3.38 (m, 1H), 3.57-3.65 (m, 1H), 4.08 (dd, *J* = 7.6 & 5.6 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 5.24 (s, 2H), 7.08-7.13 (m, 1H), 7.15-7.21 (m, 3H), 7.31-7.33 (m, 1H), 7.36 (dd, *J* = 8.4 & 1.6 Hz, 1H), 7.54-7.56 (m, 1H), 7.62 (s, 1H), 7.68 (dd, *J* = 13.6 & 8.4 Hz, 2H)

ESI/MS (m/z) : 397.21 $(M+H)^+$

5.1.61 2-ethoxy-3-(6-((2-fluorobenzyl)oxy)naphthalen-2-yl)propanoic acid. (73)



72 **73**

To a solution of **72** (450 mg, 1.14 mmol) in mixture of THF (9 ml), MeOH (3 ml) and H_2O (3 ml), $LiOH.H_2O$ (96 mg, 2.28 mmol) was added and stirred at 25 °C for 18 hours. The reaction mixture was concentrated under vacuum. Water was added to the reaction mixture, acidified with hydrochloric acid and was extracted with ethyl acetate. The organic extract was successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to obtain the title product **73** (225 mg, 54%) as a white solid. m.p: 66-67 °C %; Purity by HPLC: 99.4%.

IR (KBr) **:** 3520, 2978, 2929, 2879, 1718, 1604, 1494, 1390, 1226, 1111, 1014, 856 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.14 (t, *J* = 6.8 Hz, 3H), 3.11 (dd, *J* = 14 & 8.0 Hz, 1H), 3.26 (dd, *J* = 14.0 & 3.6 Hz, 1H), 3.39-3.46 (m, 1H), 3.53-3.60 (m, 1H), 4.14 (dd, *J* = 8.0 & 4.4 Hz, 1H), 5.23 (s, 2H), 7.08-7.21 (m, 4H), 7.30-7.36 (m, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.62 (s, 1H), 7.65-7.71 (m, 2H)

^{13}C NMR ($CDCl_3$) **:** δ 15.14, 39.00, 63.77, 66.94, 80.01, 107.10, 115.39, 115.60, 119.14, 124.12, 124.26, 124.39, 124.43, 127.01, 128.05, 128.43, 129.25, 129.40, 129.81, 129.84, 132.44, 133.50, 156.48, 159.39, 161.85, 176.41

ESI/MS (m/z) **:** 391.09 $(M+Na)^+$

5.2 *In vitro* PPAR transactivation assay

Principle: HepG2 cells are transfected with human full length PPARα, PPARβ (or δ) and PPARγ cloned in pSG5 expression vector. In presence of ligands, the PPAR will bind to PPAR response element (PPRE) cloned with the luciferase reporter vector that will lead to transactivation. The binding of ligand to the receptor would trigger the luciferin production in a dose dependent manner. Luciferin in presence of Mg^{2+} and luciferase will be converted to oxyluciferin and will emit light which can be detected and quantified in luminometer. The luciferase values were normalized with Bgal values and the values were obtained in terms of relative luciferase units (RLU)

Cell Culture: HepG2 cells (ATCC, USA) were maintained in growth medium composed of MEM (Sigma) supplemented with 10% FBS (Hyclone), 1 x MEM non essential amino acid (Sigma) and 1mM Sodium Pyruvate and 1% Penicillin /Streptomycin (Sigma).

Transient Transfection: HepG2 cells were seeded in 24 well plates at a density of 400000 cells / well in 1mL of medium per well. Cells were transfected using the transfection reagent Superfect (Qiagen). Cells were transfected with 0.08 μg of the pSG5 expression vector containing the *c*DNA of PPARα or 0.08 μg of the pSG5 expression vector containing the *c*DNA of PPARγ was cotransfected with PPRE3-TK-luc. Cells were incubated at 37 °C, 5% CO_2 for 3hours. After this, 1.0 mL of the medium containing the respective ligands to the respective wells were added. The cells were then incubated at 37 °C, 5% CO_2 for 20-22 hours. After the incubation period, cells were first washed with PBS, lysed and supernatant collected. Supernatant was then assayed for luciferase and β-galactosidase activity. The Luciferase activity was determined using commercial fire-fly luciferase assay according to the suppliers's instructions [Promega] in white 96-well plate [Nunc]. β-Galactosidase activity was determined in ELISA reader at 415 nm. The ratio of luciferase versus β-galactosidase l was calculated and fold induction was calculated with respect to DMSO. Fold inductions of the standard compounds were also calculated with respect to DMSO. EC_{50} values for the

NCEs were calculated by nonlinear regression analysis using graphpad prism software. Each concentration point represents values in duplicates.

5.3 *In vivo* experiments

All the animal were breed at animal breeding facility of Zydus research centre, registered under rule 5(a) for the " Breeding and Experiments on animals (control and supervision) rule 1998, (Registration number 77/1999 (CPCSEA))". The study protocols were approved by institutional animal ethics committee.

5.3.1 Triglyceride lowering activity in *Swiss albino mice* (SAM).

Male *Swiss albino* mice (SAM) of 6-8 week age and 20-30 g body weight with serum triglyceride levels in the range of 80-120 mg/dl have been used for screening the compounds. Animals were randomized based on pre-treatment (day 0) serum triglyceride levels and the test compounds were administered orally at an indicated dose for 6 days. On day 6 non-fasted blood samples were collected one hour after drug administration and serum triglyceride levels were measured. Reduction in serum triglycerides was calculated according to formula given below.

% Reduction = 1- {(TT/OT)/(TC/OC)}TT X 100, where,

TT= Serum TG level on test day of treated group.

OT= Serum TG level on day 0 of treatment of treated group.

TC= Serum TG level on test day of control group.

OC= Serum TG level on day 0 of treatment of control group.

5.3.2 Antihyperlipidemic and antihyperglycemic activity in *db/db* mice and *Zucker fa/fa* rats.

Male *db/db* mice of 6-8 weeks age and 30-40 g body weight and male Zucker *fa/fa* rats of 13-15 weeks age and body weight of 450-470 g were selected for the study. The animals were weighed and tail-bled prior to the start of study. Plasma was analyzed for glucose (PG), triglyceride (TG) levels in *db/db* mice and PG, TG and cholesterol (TC) levels in Zucker *fa/fa* rats. The animals

were arranged into the appropriate number of groups with each group having 6 animals of the same mean PG, TG and TC levels prior to dosing. All animals then were orally dosed once daily with vehicle (0.5% methylcellulose in water) and test compounds for 7 days in *db/db* mice and for 14 days in Zucker *fa/fa* rats. All animals were fed ad libitum throughout the study. Approximately 1 hour after the last dose, the animals were bled and the plasma analyzed for glucose and triglycerides (also cholesterol in Zucker *fa/fa* rats) to calculate percent change due to drug treatment.

5.3.2.1 Oral Glucose tolerance experiment *Zucker fa/fa* rats.

On day 15, Zucker *fa/fa* rats were fasted overnight, insulin levels were measured and given a 2 g/kg oral glucose load. Blood glucose was measured just prior to the glucose load and after 30, 60 and 120 min by collecting blood from tail tip. The glucose area-under-the-curve (AUC) was calculated over 0 to 120 min using the trapezoidal method and result was reported as percent improvement in glucose AUC verses vehicle treated control group.

5.3.3 Hypolipidemic activity in High cholesterol fed *Sprague Dawley* (HC-SD) rats.

Male *Sprague dawley* (SD) rats of 6-8 weeks age and 250-350 g of body weightwere selected for the study. The animals were fed with high cholesterol diet (HC diet), formulated by adding 1% cholesterol and 0.5% sodium cholate to rodent chow diet (National Institute of Nutrition, Hyderabad). HC diet was offered *ad libitum* for 15 days. After 15 days of modified diet animals were bled after 16 hour fasting and serum triglycerides (TG), total cholesterol (TC), LDL-cholesterol (LDL-C) and HDL-cholesterol (HDL-C) were measured and animals having total cholesterol (TC), between (180- 300 mg./dl) were randomized and grouped with 6 animals in each group. Animals were dosed with vehicle or the indicated dose of test compound daily for 4 days by oral gavage. Serum triglycerides (TG), total cholesterol (TC), LDL-cholesterol (LDL-C) and HDL-cholesterol (HDL-C) were measured one hour after the last dose on day 4 of overnight fasted animals. Values reported are % change versus control group.

5.3.4 Antihyperlipidemic activity in Hamsters.

Female *Hamsters* of 8-12 weeks age (80-150 gm body weight) were taken for study. Six animals whose average bodyweight was not significantly different from the rest of the animals were selected for normal NIN diet. Other animals were put on HF-HC-Sucrose (High fat, high cholesterol and Sucrose) diet for 14 days. On day 14 all the HF-HC-Sucrose diet fed animals were selected which had gained their body weight significantly more than the normal diet group animals. The selected animals were divided into different groups in such a way that the average bodyweight of the animals in each group was not significantly different from the other groups. Each animal received a single dose of the test compounds at 3.0 mg/kg and carbomethoxy cellulose or polyethylene glycol in the evening administered as an oral gavage daily for 14 days. On day 7 and 14, after 1 hour of dose administration fasted blood samples were collected from animals for determination of triglycerides, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) in serum and fasted insulin.

5.3.5 Pharmacokinetics experiment.

Pharmacokinetic behaviour of the test compounds was studied *via* per-oral route of administration in *wistar* rats of 8 to 10 weeks of age. Animals were fasted for 18 hours and food was supplied after 4 hours of administration of the test compound. There was free access to water throughout the study. A homogenous suspension of the test substance was prepared in 0.5 % w/v CMC in normal saline and a per-oral dose of 30 mg/kg was administered. After the administration of the test compounds, blood samples were withdrawn at various time intervals through retro-orbital plexus and collected into heparinized micro centrifuge tubes. Plasma was separated by centrifugation at 4000 rpm for 5 min at ambient temperature and analyzed immediately. Remaining samples were stored at -20 °C until analyzed.

Analysis was carried out by taking an aliquots of 180 μL plasma and 20 μL of internal standard (Atorvastatin) and was extracted with 2.5 mL of extracting solvent (ethylacetate: acetonitrile 80:20, v/v) in glass test-tube by vortexing with

spinix vortex mixture for a minute. This was then centrifuged at 2000 rpm for 2.0 min. The supernatant was transferred to another glass test-tube and the solvent was evaporated under nitrogen using Zymark evaporator at 40 °C. Finally, the tubes were reconstituted with 0.1 mL diluent (acetonitrile: methanol: water 40:40:20, v/v/v). The reconstituted samples were analyzed on Agilent 1100 Series HPLC system with a mobile phase of 0.05 % v/v trifluoroacetic acid in water: acetonitrile (32:68, v/v); flowing at a flow rate of 1.0 mL/min through a Kromasil 250 mm x 4.6 mm x 5 μ column maintained at 30 °C. Chromatographic separation was achieved within 15 min. Agilent software version Chemstation Rev.A.09.01. (1206) was used to acquire and process all chromatographic data. Quantification was based on a series of calibrators ranging from 0.031 to 32 μg/mL, prepared by adding test compound to drug free rat plasma. Quality control samples were analyzed in parallel to verify that the system performs in control. Pharmacokinetic parameters namely; maximum plasma concentration (C_{max}), time point of maximum plasma concentration (t_{max}), area under the plasma concentration–time curve from 0 hour to infinity ($AUC_{0-\infty}$) and half-life of drug elimination during the terminal phase ($t_{1/2}$) were calculated from plasma concentration *versus* time data, by standard non-compartmental methods, using the WinNonLin software version 4.0.1 procured from Pharsight Corporation, USA.