Experimental

"It is true of every scientific discovery that the road means more than the goal"

Erwin Chargaff

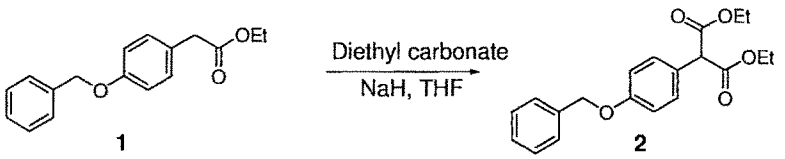
5. EXPERIMENTAL

5.1. CHEMISTRY

5.1.1. Materials and Methods

Reagents were obtained from Sigma Aldrich 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 (vmax in cm^{-1}, as film for liquids and as KBr pellets for solid compounds). The ^{1}HNMR 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}CNMR 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. Single crystal X-ray data was collected on Bruker Smart Apex CCD X-ray diffractometer and images were generated using Mercury software 2.3 version. 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-benzyloxyphenyl)-malonate (2)



1 2

To an ice-cold suspension of NaH (60%) (4.4 g, 0.111 mol) in THF (30 mL), a solution of **1** (10.0 g, 0.037 mol) in THF (50 mL) was added drop wise over a period of 30 min at 0-10 °C and stirred at the same temperature for 30 min. Diethyl carbonate (18 mL, 0.148 mol) was added to the reaction mixture at 0-10 °C and stirred at 25 °C for 18 hours. The reaction mixture was poured into ice cold water (200 mL) and extracted with ethyl acetate (3 X 100 mL). The combined organic layer was successively washed with water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum to get the crude product which was purified by column chromatography using 10% ethyl acetate in hexane as eluent to furnish title compound **2** (6.5 g, 51%) as a white solid. mp: 58-60 °C; Purity by HPLC: 90%.

IR (KBr) : 2936, 2879, 1743, 1609, 1512, 1247, 1226, 1177, 1010, 750 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, J = 7.1 Hz, 6H), 4.15-4.55 (m, 4H), 4.55 (s, 1H), 5.05 (s, 2H), 6.91 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 7.35-7.45 (m, 5H).

ESI/MS (m/z) : 343.2 $(M+H)^+$.

5.1.3. 2-(4-Benzyloxyphenyl)-propane-1,3-diol (3)

2 3

To a solution of **2** (6.0 g, 0.0175 mol) in THF (100 mL), $LiAlH_4$ (1.33 g, 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 drop-wise addition of saturated aqueous Na_2SO_4 solution at 0-10 °C. Solid residue was filtered and washed with

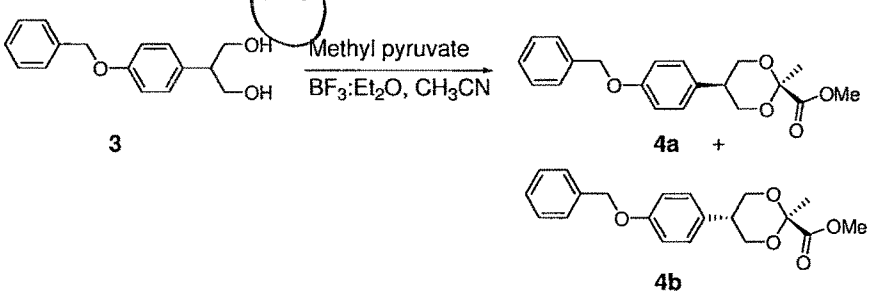
hot ethyl acetate. Filtrate was concentrated under vacuum. Crude product so obtained was triturated with diisopropyl ether to give title compound **3** (1.76 g, 39%) as white solid. mp: 130-132 °C; Purity by HPLC: 93%.

IR (KBr) : 3278, 2943, 2868, 1614, 1514, 1226, 1026, 740 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.01 (bs, 2H, OH), 3.02-3.11 (m, 1H), 3.93-3.97 (m, 4H), 5.05 (s, 2H), 6.95 (d, J = 8.6 Hz, 2H), 7.16 (d, J = 8.6 Hz, 2H), 7.32-7.44 (m, 5H)

ESI/MS (m/z) : 276.2 $(M+NH_4)^+$

5.1.4. Methyl-*c*-5-(4-benzyloxyphenyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate (4a) and the trans isomer (4b)



3 4a + 4b

To a solution of **3** (1 g, 3.87 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 drop-wise 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). The combined organic layer was successively washed with water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum to give mixture of *cis* and *trans* isomers which were separated by means of flash chromatography on a silicagel column using 10% ethyl acetate in hexane as eluent to yield the title compound **4a** (0.55g, 41%) (mp: 84-86 °C; Purity by HPLC: 98%) and *trans* isomer **4b** (0.52g, 39%) (mp: 110-112 °C; Purity by HPLC: 97%) as white solids.

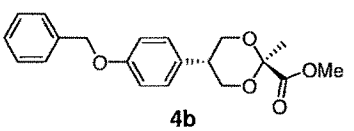
IR (KBr) : 1739, 1514, 1236, 1218, 1195, 1139, 1043, 748 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.58 (s, 3H), 3.15-3.24 (m, 1H), 3.82 (d, J = 11.8 Hz, 2H), 3.87 (s, 3H), 4.05 (dd, J = 11.8 & 4.7 Hz, 2H), 5.03 (s, 2H),

6.91 (d, J = 8.6 Hz, 2H), 7.03 (d, J = 8.6 Hz, 2H), 7.32-7.42 (m, 5H)

ESI/MS (m/z) : 360.3 $(M+NH_4)^+$

5.1.5. Methyl-*t*-5-(4-benzyloxyphenyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate (4b)



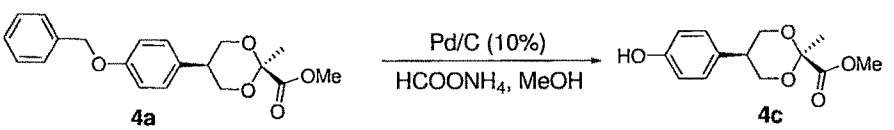
4b

IR (KBr) : 3000, 2890, 1739, 1514, 1236, 1218, 1195, 1139, 1043, 748 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ1.60 (s, 3H), 2.69-2.71 (m, 1H), 3.86 (s, 3H), 4.07 (dd, J = 11.9 & 2.3 Hz, 2H), 4.23 (dd, J = 12 & 3.6 Hz, 2H), 5.06 (s, 2H), 6.94 (d, J = 8.6 Hz, 2H), 7.29-7.44 (m, 7H)

ESI/MS (m/z) : 360.3 $(M+NH_4)^+$

5.1.6. Methyl-*c*-5-(4-hydroxyphenyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate (4c)



4a 4c

To a suspension of Pd/C (10%) (55 mg) in MeOH (5 mL), a solution of **4a** (550 mg, 1.6 mmol) in MeOH (10 mL) and ammonium formate (405 mg, 6.4 mmol) 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 the title compound **4c** (0.4 g, 99%) as white solid. mp: 110-112 °C; Purity by HPLC: 99%.

IR (KBr) : 3400, 2945, 2869, 1716, 1614, 1517, 1271, 1028, 827 cm^{-1}

^{1}HNMR : δ1.40 (s, 3H), 2.97-3.06 (m, 1H), 3.66 (d, J = 11.8 Hz, 2H),

(DMSO-d_6) 3.78 (s, 3H), 3.89 (dd, J = 11.9 & 4.8 Hz, 2H), 6.66 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 8.4 Hz; 2H), 9.32 (bs, 1H, OH)

^{13}C NMR (DMSO-d_6) : δ 25.72, 38.43, 52.39, 67.48, 97.51, 115.39, 127.44, 128.56, 156.59, 170.43

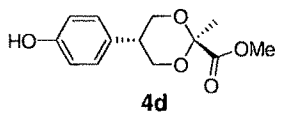
ESI/MS (m/z) : 274.8 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{13}H_{16}O_5$

Calculated : C, 61.90%; H, 6.39%

Found : C, 61.74%; H, 6.42%

5.1.7. Methyl-*t*-5-(4-hydroxyphenyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate (4d)



4d

4d (0.36 g, 99%) was prepared from **4b** (0.5 g, 1.61 mmol) by means of a procedure similar to that reported for **4c** as white solid. mp: 144-146 °C; Purity by HPLC: 99.6%.

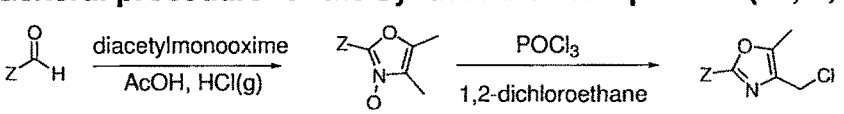
IR (KBr) : 3429, 2908, 2841, 1726, 1616, 1519, 1436, 1276, 810 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 1.41 (s, 3H), 2.63 (m, 1H), 3.74 (s, 3H), 3.90 (d, J = 12.0 Hz, 2H), 4.06 (dd, J = 3.2 & 12.0 Hz, 2H), 6.48 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.8 Hz, 2H), 9.20 (bs, 1H, OH)

^{13}C NMR (DMSO-d_6) : δ 24.78, 36.57, 52.28, 66.64, 97.69, 114.92, 192.02, 132.50, 155.85, 170.36

ESI/MS (m/z) : 274.8 $(M+Na)^+$

5.1.8. General procedure for the synthesis of Compounds (7a, b, f, h)



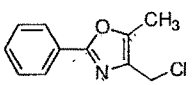
5 **6** **7a, b, f, h**

Step I: To an ice-cold solution of freshly distilled aldehyde **5** and diacetylmonoxime (1 mole equivalent) in AcOH (3 fold), dry HCl gas was passed for 3 h at 0 °C. The reaction mixture was diluted with diethyl ether (6 fold).

Separated solid was filtered, washed with diethylether and dried under vacuum to obtain the title product **6** as white solid. The product was directly used for the next reaction.

Step II: To an ice-cold suspension of *N*-oxide **6** prepared in step I above in dichloroethane (5 fold) was added $POCl_3$ (1.1 mole equivalent) dropwise over a period of 2 hours at 10 °C. Reaction mixture was slowly heated to 60 °C and stirred at that temperature for 3 hours. Reaction mixture was cooled to room temperature, poured into ice-cold water and extracted with dicloroethane. The combined organic extract was washed with water, dried over $CaCl_2$ and concentrated under vacuum to furnish title product.

5.1.8.1. 4-Chloromethyl-5-methyl-2-phenyloxazole (7a)



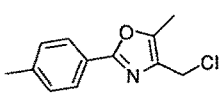
7a (58.7 g, 60%) was prepared from benzaldehyde (50g, 471 mmol) in two steps by means of a general procedure described above as off white solid. mp: 81-83 °C; Purity by HPLC: 99.1%.

IR (KBr) : 3041, 2923, 1631, 1556, 1487, 1444, 110, 775 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.43 (s, 3H), 4.56 (s, 2H), 7.42-7.47 (m, 3H), 7.98-8.02 (m, 2H)

ESI/MS (m/z) : 207.8 $(M+H)^+$

5.1.8.2. 4-Chloromethyl-5-methyl-2-(4-methylphenyl)-oxazole (7b)



7b (73.8 g, 81%) was prepared from 4-methylbenzaldehyde (50 g, 461 mmol) in two steps by means of a general procedure described above as white solid. mp: 87-88 °C; Purity by HPLC: 98.6%.

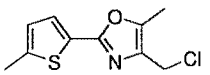
IR (KBr) : 3033, 2972, 2852, 1639, 1539, 1498, 1112, 827 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.39 (s, 3H), 2.41 (s, 3H), 4.54 (s, 2H), 7.22 (d, J = 8.2

Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H)

ESI/MS (m/z) : 222.1 $(M+H)^+$

5.1.8.3. 4-Chloromethyl-5-methyl-2-(5-methylthiophen-2-yl)-oxazole (7f)



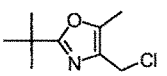
7f (15.5 g, 86%) was prepared from 5-methylthiophene-2-carboxaldehyde (10 g, 79.2 mmol) in two steps by means of a general procedure described above as yellow solid. mp: 79-80 °C; Purity by HPLC: 98.7%.

IR (KBr) : 3080, 2852, 1633, 1593, 1521, 1433, 1257, 1222, 1056, 804 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ2.38 (s, 3H), 2.51 (s, 3H), 4.51 (s, 2H), 6.73-6.75 (m, 1H), 7.42 (d, J = 3.6 Hz, 1H)

ESI/MS (m/z) : 228.1 $(M+H)^+$

5.1.8.4. 2-*tert*-Butyl-4-chloromethyl-5-methyloxazole (7h)



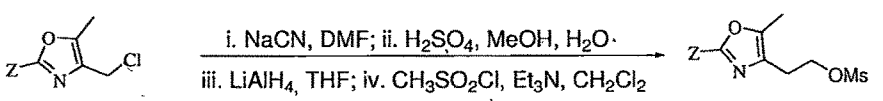
7h (9.37 g, 43%) was prepared from 2,2-dimethyl-propionaldehyde (10 g, 116 mmol) in two steps by means of the general procedure described above as white solid. mp:; Purity by HPLC: 88.9%

IR (KBr) : 3010, 2906, 1641, 1569, 1458, 1269, 1143, 717 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ1.35 (s, 9H), 2.30 (s, 3H), 4.47 (s, 2H)

ESI/MS (m/z) : 187.8 $(M+H)^+$

5.1.9. General procedure for the synthesis of Compounds (7c, d, g, i)



7a, b, f, h **7c, d, g, i**

Step I: To a solution of chloromethyloxazole **7a** or **7b** or **7f** or **7h** in DMF (5 fold), NaCN (1.2 mole equivalent) was added and the reaction mixture was stirred at ambient temperature for 8 hours. Reaction mixture was poured in water (15 fold),

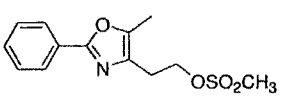
solid separated was filtered, washed with excess water and dried under vacuum to furnish the corresponding cyanomethyloxazole derivative. The product was directly taken for next step.

Step II: To a suspension of cyano compound prepared in step I above in a mixture of ethanol (2 fold) and water (catalytic) was added H_2SO_4 (0.8 fold) drop wise and the reaction mixture was refluxed for 36 hours. Solvents were evaporated under vacuum. The residue was poured into water and extracted with ethyl acetate. The combined organic extract was successively washed with water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum to furnish corresponding ester derivative which was used further without purification.

Step III: To an ice-cold solution of the ester from step II in THF (5 fold), $LiAlH_4$ (1 mole equivalent) was added in portions over a period of 30 minutes and the reaction mixture was stirred below 20 °C for one hour. Reaction mixture was quenched with saturated aqueous solution of Na_2SO_4 till solid separated out. The solids were filtered and washed with hot ethyl acetate. The combined filtrate was concentrated under vacuum to yield corresponding hydroxy compound, which was directly taken for the next step.

Step IV: To an ice-cold solution of the hydroxy compound of step III in dichloromethane (5 fold) were added triethylamine (1.2 mole equivalent) followed by dropwise addition of methanesulfonylchloride (1.1 mole equivalent) at 10 °C and the reaction mixture was stirred at ambient temperature for 4 hours. The reaction mixture was diluted with chloroform and successively washed with water, 1N HCl, again water and finally with sodium bicarbonate solution. The organic extract was dried over $CaCl_2$ and concentrated under vacuum. The crude syrup so obtained was triturated with methanol to obtain corresponding mesylate derivative.

5.1.9.1. 2-(5-Methyl-2-phenyloxazol-4-yl)-ethyl methanesulfonate (7c)



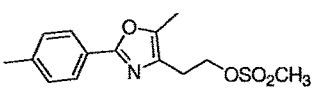
7c (9 g, 67%) was prepared from **7a** (10 g, 48.1 mmol) in four steps by means of a general procedure described above as white solid. mp: 135-137 °C; Purity by HPLC: 99.5%.

IR (KBr) : 3031, 2935, 1635, 1552, 1340, 1163, 867, 713 cm^{-1}1

^{1}HNMR ($CDCl_3$) : δ2.36 (s, 3H), 2.92-2.97 (m, 5H), 4.52 (t, J = 6.6 Hz, 2H), 7.42-7.45 (m, 3H), 7.94-7.98 (m, 2H)

ESI/MS (m/z) : 282.0 $(M+H)^+$

5.1.9.2. 2-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-ethyl methanesulfonate (7d)



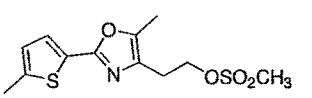
7d (7 g, 53%) was prepared from **7b** (10 g, 45.1 mmol) in four steps by means of a general procedure described above as off white solid. mp: 109-110 °C; Purity by HPLC: 97.2%.

IR (KBr) : 3033, 2929, 1635, 1500, 1161, 975, 866 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ2.35 (s, 3H), 2.39 (s, 3H), 2.93-2.97 (m, 5H), 4.52 (t, J = 6.57 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H)

ESI/MS (m/z) : 296.2 $(M+H)^+$

5.1.9.3. 2-[5-Methyl-2-(5-methylthiophen-2-yl)-oxazol-4-yl]-ethyl methanesulfonate (7g)



7g (5.56 g, 84%) was prepared from **7f** (5 g, 21.9 mmol) in four steps by means of a general procedure described above as white solid. mp: 108-109 °C; Purity by HPLC: 97.8%.

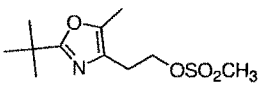
IR (KBr) : 3078, 2918, 2856, 1639, 1589, 1519, 1456, 1338, 1161, 977, 867 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ2.31 (s, 3H), 2.51 (s, 3H), 2.90 (t, J = 6.5 Hz, 2H), 2.95 (s,

3H), 4.49 (t, J = 6.5 Hz, 2H), 6.73-6.75 (m, 1H), 7.36 (d, J = 3.6 Hz, 1H)

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

5.1.9.4. 2-(2-*tert*-Butyl-5-methyloxazol-4-yl)-ethyl methanesulfonate (7i)



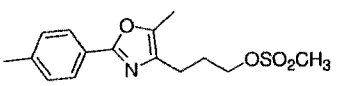
7i (4.87 g, 70%) was prepared from **7h** (5 g, 26.6 mmol) in four steps by means of a general procedure described above as a liquid. Purity by HPLC: 96.8%.

IR (Neat) : 2974, 2904, 1566, 1460, 1363, 1178, 785 cm^{-1}

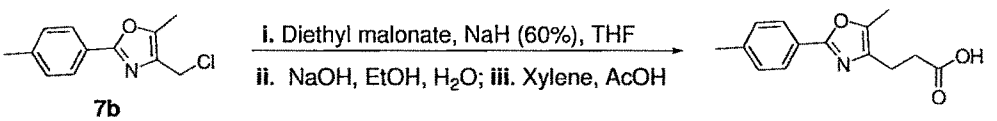
^{1}HNMR ($CDCl_3$) : δ 1.33 (s, 9H), 2.24 (s, 3H), 2.86 (t, J = 6.5 Hz, 2H), 2.93 (s, 3H), 4.44 (t, J = 6.6 Hz, 2H)

ESI/MS (m/z) : 262.0 $(M+H)^+$

5.1.10. 3-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-propyl methanesulfonate (7e)



Step I: Preparation of 3-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-propanoic acid



7b

To an ice-cold suspension of NaH (50%, 16.3 g, 0.339 mol) in THF (150 mL), diethyl malonate (108 mL, 0.677 mol) was added drop wise at 0-10 °C over a period of 30 min and stirred at the same temperature for further 30 min. A solution **7b** (50 g, 0.226 mol) in THF (150 mL) was added to the reaction mixture at 0-10 °C and stirred at 25 °C for 18 h. The reaction mixture was poured into ice cold water (500 mL) and extracted with ethyl acetate (3 X 200 mL). The combined organic layer was successively washed with water, brine, dried over Na_2SO_4 and concentrated under vacuum to yield 140 g crude product as viscous liquid which was dissolved in EtOH (600 mL) and a solution of NaOH (65 g, 1.62 mol) in H_2O (200 mL) was added. The mixture was stirred at 25 °C for 15 min.

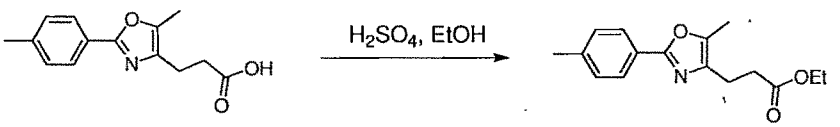
The reaction mixture was concentrated under vacuum, diluted with water, neutralized with HCl. Solid separated out was filtered and dried to yield 60 g of dicarboxylic acid as white solid. The solid was dissolved in a mixture of xylene (200 mL) and AcOH (100 mL) and refluxed for 5 h. Solvent was evaporated under vacuum to give 48 g (58%) of title compound as white solid. mp: 113-115 °C.

IR (KBr) : 3411, 2922, 1710, 1498, 1257, 1234, 817 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.33 (s, 3H), 2.39 (s, 3H), 2.76-2.79 (m, 4H), 7.24 (d, J = 9.6 Hz, 2H), 7.83 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 246.1 $(M+H)^+$

Step II: Preparation of Ethyl-3-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-propionate.



To a solution of 3-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-propanoic acid (48 g, 0.196 mol) obtained from Step I in EtOH (500 mL), H_2SO_4 (10 mL) was added and refluxed for 24 h. Reaction mixture was concentrated under vacuum. The residue was dissolved in EtOAc (300 mL), successively washed with water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum to give 30g (57%) of title compound as viscous liquid.

IR (Neat) : 2981, 2923, 1728, 1643, 1500, 1215, 1188, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.23 (t, J = 7.1 Hz, 3H), 2.33 (s, 3H), 2.38 (s, 3H), 2.66-2.67 (m, 2H), 2.77-2.81 (m, 2H), 4.13 (q, J = 7.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.83 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 274.0 $(M+H)^+$

Step III: Preparation of 3-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-propan-1-ol.

To a solution of ethyl-3-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-propionate (30 g, 0.1 mol) obtained from Step II in THF (200 mL), $LiAlH_4$ (4.18 g, 0.10 mol) was

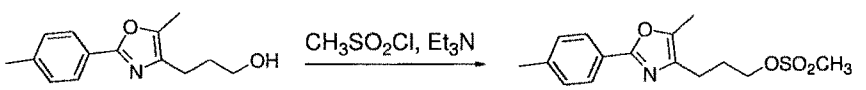
added in small portions at 0 °C over a period of 30 min and stirred at 25 °C for further 30 min. Reaction mixture was quenched by drop-wise addition of saturated aqueous Na_2SO_4 solution at 0-10 °C. Solid separated was filtered and washed with hot ethyl acetate. Filtrate was concentrated under vacuum to give 24g (95%) title compound as white solid. mp: 72-74 °C; Purity by HPLC: 95.2%.

IR (KBr) : 3313, 2923, 1645, 1498, 1161, 1120, 825 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.85-1.93 (m, 2H), 2.31 (s, 3H), 2.38 (s, 3H), 2.63 (t, J = 6.6 Hz, 2H), 3.58 (bs, 1H, OH), 3.75 (t, J = 5.5 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.83 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 232.0 $(M+H)^+$

Step IV: Preparation of 3-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-propyl methanesulfonate (**7e**).



7e

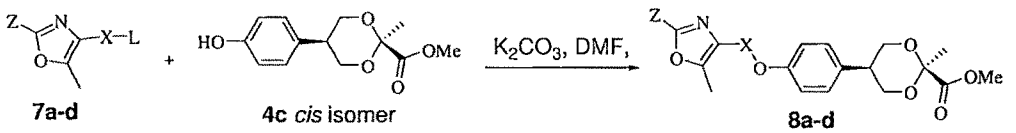
To a solution of 3-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-propan-1-ol (24 g, 0.104 mol) obtained from Step III in CH_2Cl_2 (150 mL), Et_3N (22 mL, 0.150 mol) was added followed by drop-wise addition of CH_3SO_2Cl (9.7 mL, 0.125 mol) at 0-10 °C and stirred at the same temperature for 15 min. The reaction mixture was diluted with CH_2Cl_2 (150 mL), successively washed with water, $NaHCO_3$ solution, dil HCl & brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was triturated with hexane to give 29.4 g (92%) of title compound **7e** as off-white solid. mp: 57-58 °C.

IR (KBr) : 3028, 2920, 1647, 1500, 1342, 1338, 1196, 1176, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.11-2.15 (m, 2H), 2.31 (s, 3H), 2.38 (s, 3H), 2.62 (t, J = 7.0 Hz, 2H), 3.02 (s, 3H), 4.28 (t, J = 6.1 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 310.0 $(M+H)^+$

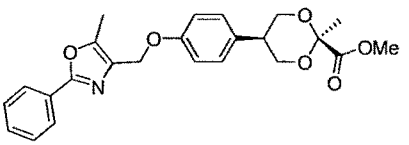
5.1.11. General procedure for the preparation of the compounds 8a-d



7a-d **4c** *cis* isomer **8a-d**

To a solution of **4c** and **7a-d** (1 mole equivalent) in dry DMF (5 fold), K_2CO_3 (2 mole equivalent) was added and reaction mixture was stirred at 60 °C for 18-24 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The combined organic extract was successively washed with water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography using 5-10% ethyl acetate in hexane as eluent to furnish pure compound.

5.1.11.1. Methyl-2-methyl-*c*-5-[4-(5-methyl-2-phenyloxazol-4-ylmethoxy)-phenyl]-1,3-dioxane-*r*-2-carboxylate (8a).



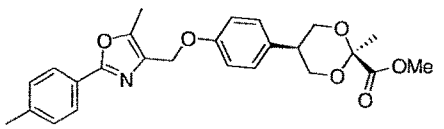
8a (1.71 g, 84%) was prepared from **7a** (1 g, 4.82 mmol) and **4c** (1.21 g, 4.82 mmol) following the general procedure described above as white solid. mp: 82-84 °C; Purity by HPLC: 96%.

IR (KBr) : 2929, 2875, 1739, 1610, 1585, 1269, 1234, 1218, 1147, 700 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.58 (s, 3H), 2.42 (s, 3H), 3.16-3.25 (m, 1H), 3.83 (d, J = 11.8 Hz, 2H), 3.88 (s, 3H), 4.08 (dd, J = 11.8 & 4.6 Hz, 2H), 4.96 (s, 2H), 6.96 (d, J = 8.6 Hz, 2H), 7.05 (d, J = 8.6 Hz, 2H), 7.42-7.44 (m, 3H), 7.99-8.02 (m, 2H)

ESI/MS (m/z) : 424.2 $(M+H)^+$

5.1.11.2. Methyl-{2-Methyl-*c*-5-[4-(5-methyl-2-(4-methylphenyl)-oxazol-4-ylmethoxy)-phenyl]}-1,3-dioxane-*r*-2-carboxylate (8b).



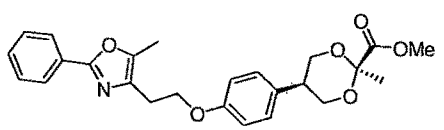
8b (1.78 g, 90%) was prepared from **7b** (1 g, 4.51 mmol) and **4c** (1.14 g, 4.51 mmol) following the general procedure described above as white solid. mp: 145-147 °C; Purity by HPLC: 96%.

IR (KBr) : 2908, 2852, 1741, 1612, 1515, 1267, 1242, 1215, 1141, 1045, 1012, 732 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.58 (s, 3H), 2.40 (s, 3H), 2.42 (s, 3H), 3.18-3.21 (m, 1H), 3.82 (d, J = 11.6 Hz, 2H), 3.88 (s, 3H), 4.05 (dd, J = 11.8 & 4.6 Hz, 2H), 5.00 (s, 2H), 6.96 (d, J = 8.6 Hz, 2H), 7.05 (d, J = 8.6 Hz, 2H), 7.26 (d, J = 7.65 Hz, 2H), 7.95 (d, J = 8.0 Hz, 2H)

ESI/MS (m/z) : 438.2 $(M+H)^+$

5.1.11.3. Methyl-{2-Methyl-*c*-5-[4-(2-(5-methyl-2-phenyloxazol-4-yl)-ethoxy)-phenyl]}-1,3-dioxane-*r*-2-carboxylate (8c).



8c (0.886 g, 57%) was prepared from **7c** (1g. 3.55 mmol) and **4c** (0.896 g, 3.55 mmol) following the general procedure described above as Viscous liquid. Purity by HPLC: 91%.

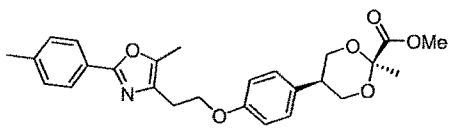
IR (Neat) : 2952, 2927, 1745, 1612, 1514, 1218, 1260, 1143, 1049 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.57 (s, 3H), 2.36 (s, 3H), 2.95 (t, J = 9.2 Hz, 2H), 3.13-3.21 (m, 1H), 3.81 (d, J = 11.8 Hz, 2H), 3.87 (s, 3H), 4.06 (dd, J = 11.8 & 4.7 Hz, 2H), 4.20 (t, J = 6.6 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 8.6 Hz, 2H), 7.40-7.42 (m,

3H), 7.94-7.98 (m, 2H)

ESI/MS (m/z) : 438.2 $(M+H)^+$

5.1.11.4. Methyl-2-Methyl-*c*-5-{4-[2-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-ethoxy]-phenyl}-1,3-dioxane-*r*-2-carboxylate (8d).



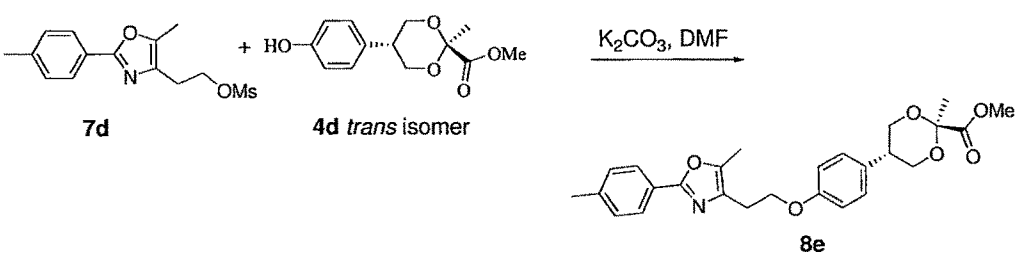
8d (0.642 g, 42%) was prepared from **7d** (1 g, 3.39 mmol) and **4c** (0.854 g, 3.39 mmol) following the general procedure described above as white solid. mp: 121-123 °C; Purity by HPLC: 98%.

IR (KBr) : 2923, 2869, 1718, 1610, 1515, 1269, 1244, 1045, 823 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.58 (s, 3H), 2.35 (s, 3H), 2.38 (s, 3H), 2.95 (t, J = 6.6 Hz, 2H), 3.16-3.21 (m, 1H), 3.80 (t, J = 11.9 Hz, 2H), 3.88 (s, 3H), 4.04 (dd, J = 12.0 & 4.7 Hz, 2H), 4.20 (t, J = 6.7 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 8.6 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 8.16 Hz, 2H)

ESI/MS (m/z) : 452.2 $(M+H)^+$

5.1.12. Methyl-2-methyl-*t*-5-{4-[2-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-ethoxy]-phenyl}-[1,3]dioxane-*r*-2-carboxylate (8e)



7d **4d** *trans* isomer **8e**

8e (0.947 g, 62%) was prepared from **7d** (1 g, 3.39 mmol) and **4d** (0.854 g, 3.39 mmol) by means of the general procedure given for **8a-d** as a Liquid. Purity by HPLC: 87%.

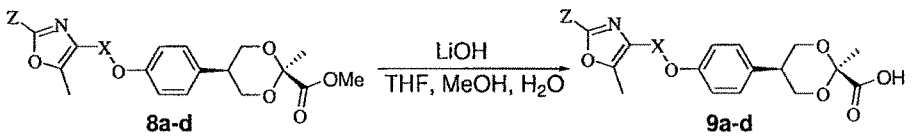
IR (Neat) : 2923, 2869, 1749, 1672, 1514, 1245, 128, 1031, 785 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.62 (s, 3H), 2.35 (s, 3H), 2.37 (s, 3H), 2.69 (bs, 1H),

2.89 (t, J = 6.4 Hz, 2H), 3.86 (s, 3H), 4.04 (d, J = 10.4 Hz, 2H), 4.17 (t, J = 6.4 Hz, 4H), 6.85 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 7.6 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.7 (d, J = 7.6 Hz, 2H)

ESI/MS (m/z) : 452.2 $(M+H)^+$

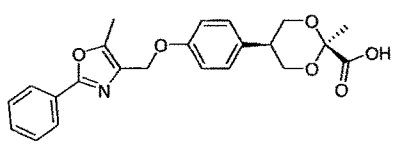
5.1.13. General procedure for the preparation of the compounds 9a-d



8a-d **9a-d**

To a solution **8a-d** in THF (9 fold), MeOH (3 fold) and H_2O (3 fold), $LiOH.H_2O$ (2 mole equivalent) was added and stirred at 25 °C for 12-18 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 & brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by flash column chromatography using 12-20% ethyl acetate in hexane as eluent to give pure compounds **9.**

5.1.13.1. 2-Methyl-*c*-5-[4-(5-methyl-2-phenyloxazol-4-ylmethoxy)-phenyl]-1,3-dioxane-*r*-2 carboxylic acid (9a)



9a (0.493 g, 51%) was prepared from **8a** (1 g, 3.36 mmol) following the general procedure described above as white solid. mp: 172-174 °C; Purity by HPLC: 99%.

IR (KBr) : 3448, 2860, 1710, 1637, 1554, 1355, 1271, 1240, 1215, 1151 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.61 (s, 3H), 2.46 (s, 3H), 3.02-3.10 (m, 1H), 3.65 (t, J = 11.5 Hz, 2H), 3.74 (dd, J = 11.7 & 4.8 Hz, 2H), 5.05 (s, 2H,

s), 6.88-6.96 (m, 4H), 7.46-7.48 (m, 3H), 8.04-8.07 (m, 2H)

^{13}C NMR ($CDCl_3$) : δ 10.46, 26.13, 39.74, 60.75, 68.15, 98.04, 114.83, 126.44, 126.66, 129.11, 129.94, 131.05, 131.26, 147.74, 157.80, 160.89, 172.9

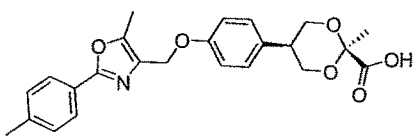
ESI/MS (m/z) : 410.1 $(M+H)^+$

Analysis **Mol.Formula:** $C_{23}H_{23}NO_6$

Calculated : C, 67.47%; H, 5.66%; N, 3.42%

Found : C, 67.09%; H, 5.66%; N, 3.40%

5.1.13.2. {2-Methyl-*c*-5-[4-(5-methyl-2-(4-methylphenyl)-oxazol-4-ylmethoxy)-phenyl]}-1,3-dioxane-*r*-2-carboxylic acid (9b)



9b (0.871 g, 90%) was prepared from **8b** (1 g, 2.29 mmol) following the general procedure described above as white solid. mp: 193-195 °C; Purity by HPLC: 98%.

IR (KBr) : 3450, 2922, 2754, 1735, 1612, 1514, 1244, 1222, 1145, 1049 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.61 (s, 3H), 2.40 (s, 3H), 2.45 (s, 3H), 3.03-3.08 (m, 1H), 3.62 (t, J = 11.5 Hz, 2H), 3.71 (dd, J = 11.6 & 4.0 Hz, 2H), 5.05 (s, 2H), 6.87 (d, J = 8.6 Hz, 2H), 6.94 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.94 (d, J = 8.0 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 10.40, 21.14, 26.11, 39.74, 60.67, 68.11, 98.02, 114.79, 123.67, 126.63, 129.10, 129.49, 129.80, 130.37, 141.49, 147.36, 157.79, 161.14, 172.89

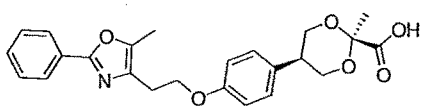
ESI/MS (m/z) : 424.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{24}H_{25}NO_6$

Calculated : C, 68.07%; H, 5.95%; N, 3.31%

Found : C, 67.53%; H, 5.79%; N, 3.21%

5.1.13.3. {2-Methyl-*c*-5-[4-(2-(5-methyl-2-phenyloxazol-4-yl)-ethoxy)-phenyl]}-1,3-dioxane-*r*-2-carboxylic acid (9c)



9c (0.392 g, 81%) was prepared from **8c** (0.5 g, 1.14 mmol) following the general procedure described above as off white solid. mp: 145-147 °C; Purity by HPLC: 98%.

IR (KBr) : 3435, 2964, 2927, 1720, 1550, 1269, 1441, 1218, 1110, 1024, 759 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.63 (s, 3H), 2.40 (s, 3H), 3.06 (t, J = 6.5 Hz, 2H), 3.12-3.21 (m, 1H), 3.89 (t, J = 11.5 Hz, 2H), 3.97 (dd, J = 11.6 & 4.8 Hz, 2H), 4.17 (t, J = 6.6 Hz, 2H), 6.77 (d, J = 8.5 Hz, 2H), 6.95 (d, J = 8.5 Hz, 2H), 7.42-7.44 (m, 3H), 7.97-8.00 (m, 2H)

^{13}C NMR ($CDCl_3$) : δ 10.26, 21.58, 26.03, 39.37, 66.72, 68.36, 98.13, 114.85, 124.12, 126.34, 128.64, 129.59, 131.81, 140.92, 145.25, 158.05, 160.33, 173.13

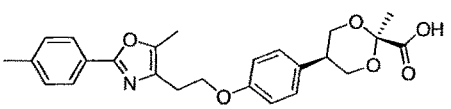
ESI/MS (m/z) : 424.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{24}H_{25}NO_6$

Calculated : C, 68.07%; H, 5.95%; N, 3.31%

Found : C, 67.83%; H, 5.77%; N, 3.24%

5.1.13.4. 2-Methyl-*c*-5-{4-[2-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-ethoxy]-phenyl}-1,3-dioxane-*r*-2-carboxylic acid (9d)



9d (0.455 g, 94%) was prepared from **8d** (0.5 g, 1.11 mmol) following the general procedure described above as white solid. mp: 184-186 °C; Purity by HPLC: 99%.

IR (KBr) : 3492, 3033, 2925, 1724, 1651, 1515, 1269, 1244, 1218,

759 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 1.39 (s, 3H), 2.31 (s, 3H), 2.32 (s, 3H), 2.87 (t, J = 6.5 Hz, 2H), 3.02-3.10 (m, 1H), 3.74 (t, J = 11.5 Hz, 2H), 3.89 (dd, J = 11.7 & 4.8 Hz, 2H), 4.14 (t, J = 6.6 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.5 Hz, 2H), 7.27 (d, J = 9.96 Hz, 2H), 7.75 (d, J = 8.1 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 10.26, 21.58, 25.87, 26.03, 39.37, 66.72, 68.36, 98.13, 114.85, 124.12, 126.34, 128.64, 129.59, 131.81, 140.92, 145.25, 158.05, 160.33, 173.13

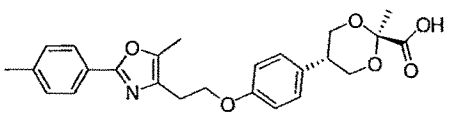
ESI/MS (m/z) : 437.9 $(M+H)^+$

Analysis **Mol.Formula:** $C_{25}H_{27}NO_6$

Calculated : C, 68.63%; H, 6.22%; N, 3.20%

Found : C, 68.41%; H, 6.23%; N, 3.53%

5.1.14. 2-Methyl-*t*-5-{4-[2-(5-methyl-2-(4-methylyphenyl)-oxazol-4-yl)-ethoxy]-phenyl}-[1,3]dioxane-*r*-2-carboxylic acid (9e)



9e (0.406 g, 84%) was prepared from **8e** (0.5 g, 1.11 mmol) following the general procedure described above as off white solid. mp: 124-126 °C; Purity by HPLC: 98.9%.

IR (KBr) : 3411, 2920, 1701, 1583, 1514, 1467, 1247, 1145 Cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 1.42 (s, 3H), 2.33 (s, 6H), 2.69 (bs, 1H), 2.89 (t, J = 6.4 Hz, 2H), 3.79 (d, J = 10.4 Hz, 2H), 4.15-4.18 (m, 4H), 6.85 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 7.6 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 7.6 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.84, 20.98, 25.71, 37.17, 66.14, 66.19, 98.27, 114.16, 124.57, 125.45, 128.75, 129.18, 132.54, 139.81, 144.64, 156.91, 158.59, 172.23

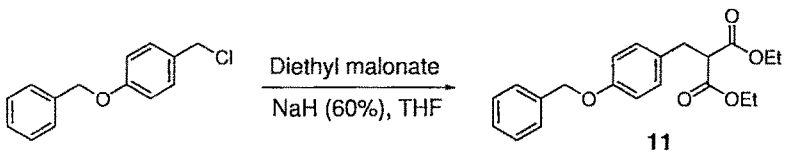
ESI/MS (m/z) : 438.1 $(M+H)^+$

Analysis **Mol.Formula:** $C_{25}H_{27}NO_6$

Calculated : C, 68.63%; H, 6.22%; N, 3.20%

Found : C, 68.46%; H, 6.22%; N, 3.56%

5.1.15. Diethyl-2-(4-benzyloxybenzyl)-malonate (11)



11

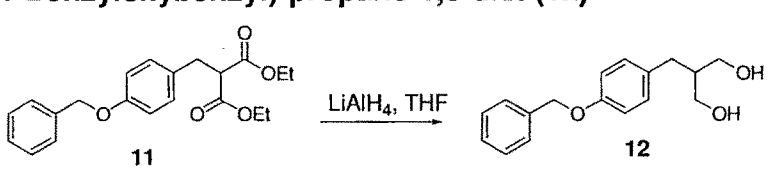
To an ice-cold suspension of NaH (60%, 178g, 3.7 mol) in THF (1000 mL), diethyl malonate (704 mL, 4.66 mol) was added drop wise over a period of 30 min at 0-10 °C and stirred at the same temperature for further 30 min. A solution of 4-benzyloxybenzyl chloride (434 g, 1.864 mol) in THF (500 mL) was added 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 (2 L) 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 tittle compound **11**(525g, 79%) as viscous liquid. Purity by HPLC: 90%.

IR (Neat) : 3020, 2939, 1728, 1512, 1217, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ1.20 (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 $(M+H)^+$

5.1.16. 2-(4-Benzyloxybenzyl)-propane-1,3-diol (12)



11 12

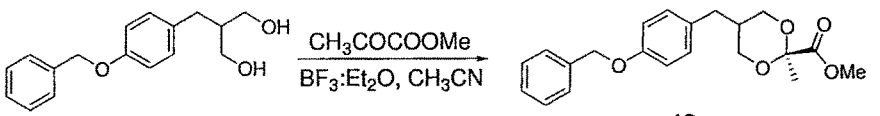
12 (179.5 g, 47%) was prepared from **11** (500 g, 1.4 mol) by means of a procedure similar to that reported for **3** as white solid. mp: 81-82 °C; Purity by HPLC: 98%.

IR (KBr) : 3381, 3064, 2922, 1635, 1514, 1245, 748 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.99-2.05 (m, 1H), 2.06 (bs, 2H, OH), 2.57 (d, J = 7.5 Hz, 2H), 3.67 (dd, J = 10.4 & 7.0 Hz, 2H), 3.78 (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 $(M+H)^+$

5.1.17. Methyl-5-(4-benzyloxybenzyl)-2-methyl-1,3-dioxane-2-carboxylate (13a)

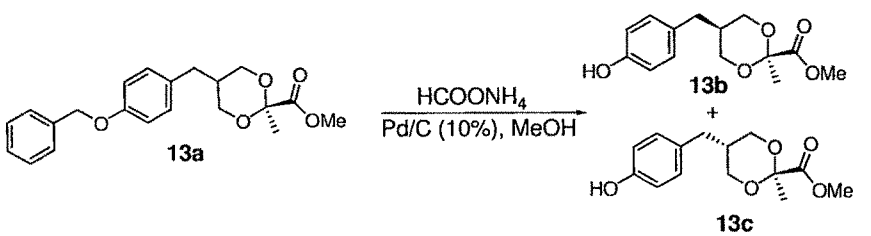


12 **13a**

13a (169 g, 76%) was prepared from **12** (170 g, 624.2 mmol) by means of a procedure similar to that described for **4a** as a viscous liquid containing mixture of *cis* and *trans* isomers. Separation of these isomers by column chromatography was unsuccessful and the mixture was subjected to debenzylation as described in the following experiment.

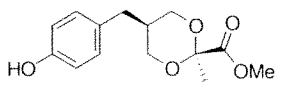
ESI/MS (m/z) : 357.2 $(M+H)^+$

5.1.18. Preparation of the compounds 13b-c



13a **13b** **13c**

5.1.18.1. Methyl-*c*-5-(4-hydroxybenzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate (13b)



The mixture of isomers **13a** (5 g, 14 mmol) obtained in the previous experiment was subjected to debenzylation by a method similar to that used for **4c**. The crude product (3.55 g, 95%) was recrystalized from a mixture of ethyl acetate and hexane (1:2). The first crop yielded pure *cis* isomer **13b** (1.72 g, 46%) as white solid. mp: 119-120 °C; Purity by HPLC: 99%.

IR (KBr) : 3402, 2933, 2866, 1722, 1612, 1514, 1267,1244, 1184, 1035 cm^{-1}

^{1}HNMR ($CDCl_3$) : 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, OH), 6.74 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 2.3 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 25.64, 32.81, 35.27, 52.23, 67.08, 97.40, 115.15, 127.90, 129.17, 155.64, 170.43

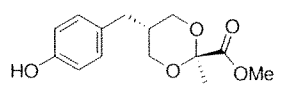
ESI/MS (m/z) : 288.9 $(M+Na)^+$

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

Calculated : C, 63.15%; H, 6.81%

Found : C, 63.22%; H, 6.78%

5.1.18.2. Methyl-*t*-5-(4-hydroxybenzyl)-2-methyl-1,3-dioxane-*r*-2-carboxylate (13c)



The filtrate from the previous experiment on subjecting to repeated crystalizations from a mixture of ethyl acetate and hexane (1:1) for 2 times gave the *trans* isomer **13c** (1.12 g, 30%) as white solid. mp: 62-64 °C; Purity by HPLC: 98%.

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

^{1}HNMR ($CDCl_3$) : 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, OH), 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

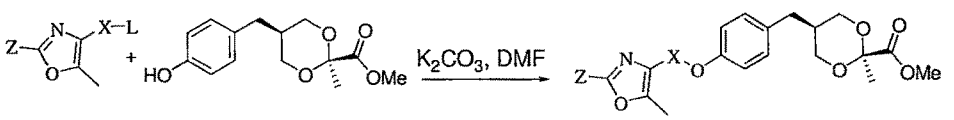
ESI/MS (m/z) : 288.9 $(M+Na)^+$

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

Calculated : C, 63.15%; H, 6.81%

Found : C, 63.48%; H, 6.81%

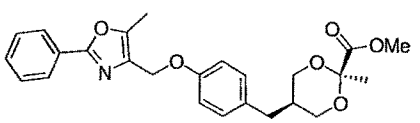
5.1.19. Preparation of the compounds 14a-i



7a-i **13b** *cis* isomer **14a-i**

Compounds **14a-i** were prepared by following the general procedure given for compounds **8**.

5.1.19.1. Methyl-2-methyl-*c*-5-[4-(5-methyl-2-phenyloxazol-4-ylmethoxy)-benzyl]-1,3-dioxane-*r*-2-carboxylate (14a)



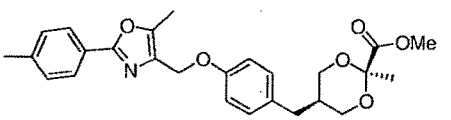
14a (1.31 g, 62%) was prepared from **7a** (1 g, 4.82 mmol) and **13c** (1.28 g, 4.82 mmol) by following the general procedure given for compounds **8** as a viscous liquid. Purity by HPLC: 95%.

IR (Neat) : 3018, 2955, 2856, 1741, 1508, 1262,116, 754 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.51 (s, 3H), 2.26-2.28 (m, 3H), 2.42 (s, 3H), 3.46 (t, J = 10.8 Hz, 2H), 3.7-3.95 (m, 5H), 4.96 (s, 2H), 6.93 (d, J = 8.5 Hz, 2H), 7.00 (d, J = 8.5 Hz, 2H), 7.43-7.45 (m, 3H), 8.00-8.03 (m, 2H)

ESI/MS (m/z) : 438.2 $(M+H)^+$

5.1.19.2. Methyl-2-methyl-*c*-5-[4-(5-methyl-2-(4-methylphenyl)-oxazol-4-ylmethoxy)-benzyl]-1,3-dioxane-*r*-2-carboxylate (14b)



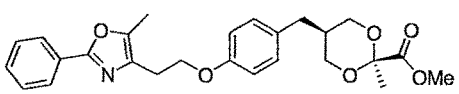
14b (1.98 g, 97%) was prepared from **7b** (1 g, 4.51 mmol) and **13c** (1.2 g, 4.51 mmol) by following the general procedure given for compounds **8** as a viscous liquid. Purity by HPLC: 97%.

IR (Neat) : 2925, 2856, 1745, 1647, 1500, 1244, 1141, 1116, 1022 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ1.49 (s, 3H), 2.20-2.22 (m, 3H), 2.39 (s, 3H), 2.41 (s, 3H), 3.46 (t, J = 10.9 Hz, 2H), 3.84 (s, 3H), 3.86-3.90 (m, 2H), 4.95 (s, 2H), 6.92 (d, J = 8.5 Hz, 2H), 7.02 (d, J = 8.5 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 7.90 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 452.4 $(M+H)^+$

5.1.19.3. Methyl-2-methyl-*c*-5-[4-{2-(5-methyl-2-phenyloxazol-4-yl)ethoxy}-benzyl]-1,3-dioxane-*r*-2-carboxylate (14c)



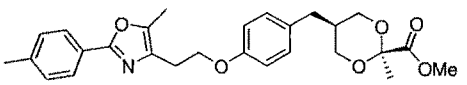
14c (1.22 g, 76%) was prepared from **7c** (1 g, 3.55 mmol) and **13c** (0.946 g, 3.55 mmol) by following the general procedure given for compounds **8** as a viscous liquid. Purity by HPLC: 96%.

IR (Neat) : 2925, 2852, 1732, 1614, 1537, 1217, 1188, 1143, 785 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ1.49 (s, 3H), 2.27 (s, 3H), 2.32 (s, 3H), 2.96 (t, J = 6.7 Hz, 2H), 3.45 (t, J = 10.4 Hz, 2H), 3.83-3.90 (m, 5H), 4.21 (t, J = 6.7 Hz, 2H), 6.74 (d, J = 8.5 Hz, 3H), 6.97 (d, J = 8.5 Hz, 3H), 7.39-7.44 (m, 2H), 7.97 (m, 1H)

ESI/MS (m/z) : 452.0 $(M+H)^+$

5.1.19.4. Methyl-2-methyl-*c*-5-{4-[2-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-ethoxy]-benzyl}-1,3-dioxane-*r*-2-carboxylate (14d)



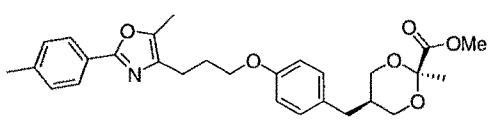
14d (1.25 g, 79%) was prepared from **7d** (1 g, 3.39 mmol) and **13c** (0.901 g, 3.39 mmol) by following the general procedure given for compounds **8** as a viscous liquid. Purity by HPLC: 95%.

IR (Neat) : 2925, 2854, 1747, 1645, 1514, 1245, 1217, 1190, 1167, 785 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ1.49 (s, 3H), 2.04 (s, 3H), 2.35 (s, 3H), 2.38 (s, 3H), 2.95 (t, J = 6.7 Hz, 2H), 3.45 (t, J = 9.0 Hz, 2H), 3.84-3.90 (m, 5H), 4.20 (t, J = 13.5 Hz, 2H), 6.74 (d, J = 8.4 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 466.1 $(M+H)^+$

5.1.19.5. Methyl-2-methyl-*c*-5-{4-[3-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-propoxy]-benzyl}-1,3-dioxane-*r*-2-carboxylate (14e)



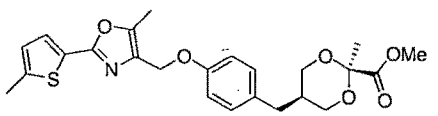
14e (1.29 g, 83%) was prepared from **7e** (1 g, 3.23 mmol) and **13c** (0.86 g, 3.23 mmol) by following the general procedure given for compounds **8** as a viscous liquid. Purity by HPLC: 92%.

IR (Neat) : 2950, 2923, 1747, 1612, 1512, 1245, 1217, 1143, 1116, 786 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ1.50 (s, 3H), 2.09-2.18 (m, 2H), 2.25 (s, 3H), 2.27 (s, 3H), 2.38 (s, 3H), 2.68 (t, J = 7.2 Hz, 2H), 3.46 (t, J = 11.3 Hz, 2H), 3.84 (s, 3H), 3.86-3.96 (m, 4H), 6.81 (d, J = 8.5 Hz, 2H), 6.99 (d, J = 8.5 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 480.2 $(M+H)^+$

5.1.19.6. Methyl-2-Methyl-*c*-5-{4-[5-methyl-2-(5-methylthiophen-2-yl)-oxazol-4-ylmethoxy]-benzyl}-1,3-dioxane-*r*-2-carboxylate (14f)



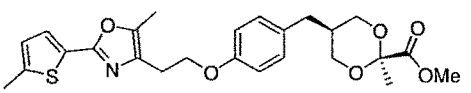
14f (1.29 g, 80%) was prepared from **7f** (0.8 g, 3.51 mmol) and **13c** (0.935 g, 3.51 mmol) by following the general procedure given for compounds **8** as a viscous liquid. Purity by HPLC: 95%.

IR (Neat) : 2927, 2864, 1747, 1610, 1591, 1508, 1234, 1213, 1087 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.62 (s, 3H), 2.22-2.28 (m, 3H), 2.38 (s, 3H), 2.52 (s, 3H), 3.46 (t, J = 11.0 Hz, 2H), 3.84 (s, 3H), 3.88 (dd, J = 12.0 & 3.6 Hz, 2H), 4.92 (s, 2H), 6.74 (d, J = 2.8 Hz, 1H), 6.90 (d, J = 8.6 Hz, 2H), 7.01 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 3.5 Hz, 1H)

ESI/MS (m/z) : 458.3 $(M+H)^+$

5.1.19.7. Methyl-2-Methyl-*c*-5-{4-[2-(5-methyl-2-(5-methylthiophen-2-yl)-oxazol-4-yl)ethoxy]-benzyl}-1,3-dioxane-*r*-2-carboxylate (14g)



14g (0.774 g, 55%) was prepared from **7g** (0.9 g, 2.99 mmol) and **13c** (0.795 g, 2.99 mmol) by following the general procedure given for compounds **8** as a viscous liquid. Purity by HPLC: 94%.

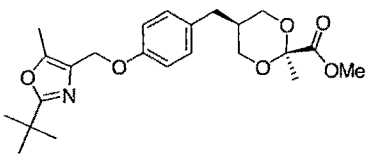
IR (Neat) : 2923, 2854, 1747, 1614, 1512, 1245, 1218, 1116, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.21-2.26 (m, 3H), 2.32 (s, 3H), 2.51 (s, 3H), 2.92 (t, J = 6.5 Hz, 2H), 3.42-3.48 (m, 2H), 3.82-3.90 (m, 5H), 4.17 (t, J = 6.6 Hz, 2H), 6.74 (d, J = 2.8 Hz, 1H), 6.90 (d, J = 8.6 Hz, 2H), 7.01 (d, J = 8.6 Hz, 2H), 7.42 (d, J =

3.5 Hz, 1H)

ESI/MS (m/z) : 472.1 $(M+H)^+$

5.1.19.8. Methyl-*c*-5-[4-(2-*tert*-Butyl-5-methyloxazol-4-ylmethoxy)-benzyl]-2-methyl-1,3-dioxane-*r*-2-carboxylate (14h)



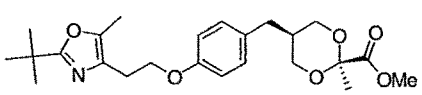
14h (2.11 g, 95%) was prepared from **7h** (1 g, 5.33 mmol) and **13c** (1.42 g, 5.33 mmol) by following the general procedure given for compounds **8** as a viscous liquid. Purity by HPLC: 95%.

IR (Neat) : 3025, 2989, 1743, 1612, 1566, 1238, 1217, 1118, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ1.38 (s, 9H), 1.57 (s, 3H), 2.22-2.28 (m, 3H), 2.31 (s, 3H), 3.46-3.48 (m, 2H), 3.84-3.90 (m, 5H), 4.85 (s, 2H), 6.88 (d, J = 8.3 Hz, 2H), 7.00 (d, J = 8.0 Hz, 2H)

ESI/MS (m/z) : 418.1 $(M+H)^+$

5.1.19.9. Methyl-*c*-5-[4-{2-(2-*tert*-Butyl-5-methyloxazol-4-yl)ethoxy}-benzyl]-2-methyl-1,3-dioxane-*r*-2-carboxylate (14i)



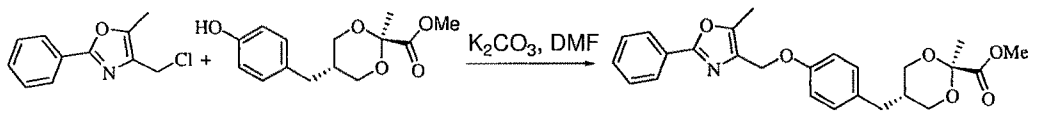
14i (1.6 g, 97%) was prepared from **7i** (1 g, 3.83 mmol) and **13c** (1.02 g, 3.83 mmol) by following the general procedure given for compounds **8** as a viscous liquid. Purity by HPLC: 94%.

IR (Neat) : 3052, 2975, 1735, 1512, 1251, 1143, 1109, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ1.35 (s, 9H), 1.54 (s, 3H), 2.24 (s, 3H), 2.27 (s, 3H), 2.91 (dd, J = 15.0 & 8.1 Hz, 2H), 3.50 (t, J = 9.5 Hz, 2H), 3.84-3.89 (m, 5H), 4.12 (t, J = 6.7 Hz, 2H), 6.78 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 432.2 $(M+H)^+$

5.1.20. Methyl-2-methyl-*t*-5-[4-(5-methyl-2-phenyloxazol-4-ylmethoxy)-benzyl]-[1,3]dioxane-*r*-2-carboxylate(14j)



7a **13c** *trans* isomer **14j**

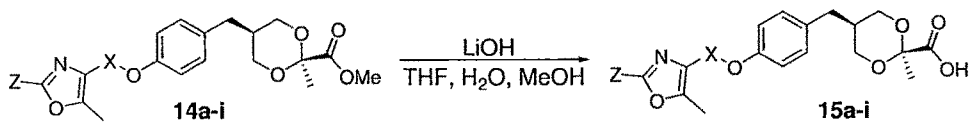
14j (1.96 g, 93%) was prepared from **7a** (1 g, 4.82 mmol) and **13c** (1.28 g, 4.82 mmol) by means of a general procedure similar to that reported for compounds **8** as a liquid. Purity by HPLC: 99.4%.

IR (Neat) : 3064, 2873, 1741, 1643, 1512, 1269, 1182, 1018, 713 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.57-1.59 (m, 4H), 2.43 (s, 3H), 2.94 (d, J = 7.6 Hz, 2H), 3.75 (d, J = 11.2 Hz, 2H), 3.82 (s, 3H), 3.93 (dd, J = 10.8 & 1.6 Hz, 2H), 4.97 (s, 2H), 6.94 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 7.42-7.46 (m, 3H), 8.00-8.02 (m, 2H)

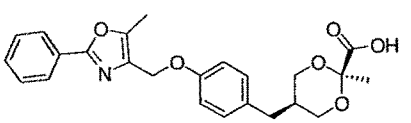
ESI/MS (m/z) : 460.0 $(M+Na)^+$

5.1.21. Preparation of the compounds 15a-i



14a-i **15a-i**

5.1.21.1. 2-Methyl-*c*-5-[4-(5-methyl-2-phenyloxazol-4-ylmethoxy)-benzyl]-1,3-dioxane-*r*-2-carboxylic acid (15a)



15a (0.905 g, 85%) was prepared from **14a** (1.1 g, 2.51 mmol) by following the general procedure given for compounds **9** as off white solid. mp: 170-171 °C; Purity by HPLC: 98%.

IR (KBr) : 3421, 2995, 2862, 1720, 1608, 1558, 1363, 1122, 1024, 833 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.52 (s, 3H), 2.16-2.28 (m, 3H), 2.43 (s, 3H), 3.49 (t, J =

10.8 Hz, 2H), 3.84 (dd, *J* = 11.8 & 3.6 Hz, 2H), 5.01 (s, 2H), 6.93 (d, *J* = 8.5 Hz, 2H), 7.00 (d, *J* = 8.5 Hz, 2H), 7.44-7.45 (m, 3H), 8.00-8.03 (m, 2H), 10.98 (bs, 1H, COOH)

^{13}C NMR (DMSO-d_6) : δ 9.96, 25.54, 32.89, 34.38, 61.38, 67.09, 97.78, 114.98, 125.59, 126.87, 129.05, 129.63, 129.99, 130.30, 132.04, 147.36, 156.56, 158.82, 171.32

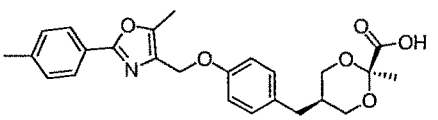
ESI/MS (m/z) : 424.3 $(M+H)^+$

Analysis **Mol.Formula:** $C_{24}H_{25}NO_6$

Calculated : C, 68.07%; H, 5.95%; N, 3.31%

Found : C, 67.61%; H, 5.96%; N, 3.27%

5.1.21.2. 2-Methyl-*c*-5-[4-(5-methyl-2-(4-methylphenyl)-oxazol-4-ylmethoxy)-benzyl]-1,3-dioxane-*r*-2-carboxylic acid (15b)



15b (1.38 g, 95%) was prepared from **14b** (1.5 g, 3.32 mmol) by following the general procedure given for compounds **9** as white solid. mp: 197-198 °C; Purity by HPLC: 99%.

IR (KBr) :3435, 2929, 2856, 1759, 1610, 1502,1286, 1226, 1182, 827 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 1.32 (s, 3H), 2.09-2.13 (m, 1H), 2.27 (d, *J* = 6.9 Hz, 2H), 2.36 (s, 3H), 2.42 (s, 3H), 3.42 (t, *J* = 11.4 Hz, 2H), 3.71 (dd, *J* = 11.6 & 4.1 Hz, 2H), 4.94 (s, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.83 (d, *J* = 8.1 Hz, 2H), 13.08 (bs, 1H, COOH)

^{13}C NMR (DMSO-d_6) : δ 9.93, 20.96, 25.52, 32.87, 34.86, 61.38, 67.07, 97.56, 114.64, 124.24, 125.57, 129.62, 130.58, 131.85, 140.15, 146.95, 156.65, 158.98, 171.31

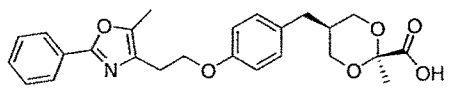
ESI/MS (m/z) : 438.4 $(M+H)^+$

Analysis **Mol.Formula:** $C_{25}H_{27}NO_6$

Calculated : C, 68.63%; H, 6.22%; N, 3.20%

Found : C, 68.16%; H, 6.23%; N, 3.02%

5.1.21.3. 2-Methyl-*c*-5-[4-{2-(5-methyl-2-phenyloxazol-4-yl)ethoxy}-benzyl]-1,3-dioxane-*r*-2-carboxylic acid (15c)



15c (0.31 g, 32%) was prepared from **14c** (1 g, 2.21 mmol) by following the general procedure given for compounds **9** as viscous liquid. Purity by HPLC: 97%.

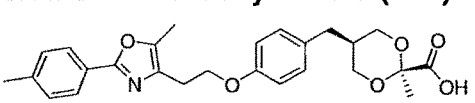
IR (Neat) :3450, 2925, 2854, 1732, 1614, 1512, 1367, 1245, 1217, 1145 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.54 (s, 3H), 2.29 (bs, 3H), 2.37 (s, 3H), 2.97 (t, J = 6.7 Hz, 2H), 3.51-3.55 (m, 2H), 3.91 (dd, J = 12.6 & 4.2 Hz, 2H), 4.21 (t, J = 6.7 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 6.99 (d, J = 8.5 Hz, 2H), 7.40-7.43 (m, 3H), 7.95-7.99 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.78, 25.54, 32.88, 34.88, 66.07, 67.09, 97.79, 114.33, 125.43, 126.92, 128.69, 129.60, 129.96, 130.27, 132.95, 145.01, 156.72, 158.38, 171.49

ESI/MS (m/z) : 438.2 $(M+H)^+$

5.1.21.4. 2-Methyl-*c*-5-{4-[2-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-ethoxy]-benzyl}-1,3-dioxane-*r*-2-carboxylic acid (15d)



15d (0.3 g, 31%) was prepared from **14d** (1 g, 2.15 mmol) by following the general procedure given for compounds **9** as off-white solid. mp: 129-131 °C; Purity by HPLC: 99%.

IR (KBr) : 3411, 2923, 2871, 1718, 1612, 1500, 1247, 1217, 1143 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.54 (s, 3H), 2.27 (bs, 3H), 2.36 (s, 3H), 2.38 (s, 3H), 2.98 (t, J = 6.7 Hz, 2H), 3.52 (t, J = 10.7 Hz, 2H), 3.91 (dd, J = 12.6 & 4.2 Hz, 2H), 4.20 (t, J = 6.7 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 6.95 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 7.85 (d, J = 8.1 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.78, 20.94, 25.51, 32.84, 34.88, 66.08, 67.01, 97.56, 114.33, 124.56, 125.41, 129.60, 129.97, 130.26, 132.50, 139.76, 144.59, 156.65, 158.54, 171.32

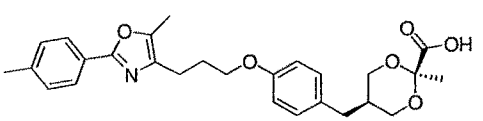
ESI/MS (m/z) : 452.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{26}H_{29}NO_6$

Calculated : C, 69.16%; H, 6.47%; N, 3.10%

Found : C, 68.85%; H, 6.51%; N, 3.01%

5.1.21.5. 2-Methyl-*c*-5-{4-[3-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-propoxy]-benzyl}-1,3-dioxane-*r*-2-carboxylic acid (15e)



15e (0.779 g, 73%) was prepared from **14e** (1.1 g, 2.29 mmol) by following the general procedure given for compounds **9** as white solid. mp: 126-128 °C; Purity by HPLC: 97%.

IR (KBr) : 3431, 2989, 2922, 2489, 1716, 1556, 1469, 1244, 1215, 1120, 1035 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.56 (s, 3H), 2.05-2.15 (m, 2H), 2.27-2.29 (m, 6H), 2.38 (s, 3H), 2.72 (t, J = 7.2 Hz, 2H), 3.55 (t, J = 10.8 Hz, 2H), 3.89-3.97 (m, 4H), 6.80 (d, J = 8.5 Hz, 2H), 6.98 (d, J = 8.5 Hz, 2H), 7.22-7.26 (m, 2H), 7.86 (d, J = 8.2 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.62, 20.93, 21.42, 25.53, 27.98, 32.87, 34.89, 66.33, 67.09, 97.56, 114.29, 124.65, 125.38, 129.52, 130.12, 134.89, 139.66, 143.39, 157.02, 158.50, 171.31

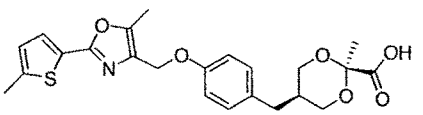
ESI/MS (m/z) : 466.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{27}H_{31}NO_6$

Calculated : C, 69.66%; H, 6.71%; N, 3.01%

Found : C, 69.13%; H, 6.84%; N, 2.89%

5.1.21.6. 2-Methyl-*c*-5-{4-[5-methyl-2-(5-methylthiophen-2-yl)-oxazol-4-ylmethoxy]-benzyl}-1,3-dioxane-*r*-2-carboxylic acid (15f)



15f (0.682 g, 64%) was prepared from **14f** (1.1 g, 2.4 mmol) by following the general procedure given for compounds **9** as pale yellow solid. mp: 172-173 °C; Purity by HPLC: 99%.

IR (KBr) : 3413, 2923, 2763, 1718, 1608, 1508, 1350, 1259, 1224, 1122 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.54 (s, 3H), 2.19-2.28 (m, 3H), 2.39 (s, 3H), 2.52 (s, 3H), 3.49 (t, J = 11.1 Hz, 2H), 3.85 (dd, J = 12.6 & 4.2 Hz, 2H), 4.96 (s, 2H), 6.75 (d, J = 2.8 Hz, 1H), 6.91 (d, J = 8.6 Hz, 2H), 7.00 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 3.6 Hz, 1H)

^{13}C NMR (DMSO-d_6) : δ 9.86, 14.95, 25.53, 32.89, 34.86, 61.23, 67.08, 97.56, 114.64, 126.74, 127.54, 129.62, 130.61, 131.68, 142.95, 146.49, 155.13, 156.61, 171.31

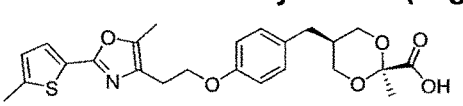
ESI/MS (m/z) : 444.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{23}H_{25}NO_6S$

Calculated : C, 62.29%; H, 5.68%; N, 3.16%

Found : C, 62.14%; H, 5.72%; N, 3.13%

5.1.21.7. 2-Methyl-*c*-5-{4-[2-(5-methyl-2-(5-methylthiophen-2-yl)-oxazol-4-yl)ethoxy]-benzyl}-1,3-dioxane-*r*-2-carboxylic acid (15g)



15g (0.267 g, 46%) was prepared from **14g** (0.6 g, 1.27 mmol) by following the general procedure given for compounds **9** as off white solid. mp: 122-124 °C; Purity by HPLC: 96%.

IR (KBr) : 3435, 2922, 2856, 1718, 1610, 1514, 1249, 1118 cm^{-1}

^{1}HNMR (CDCl$_3$) : δ 1.55 (s, 3H), 2.26 (bs, 3H), 2.34 (s, 3H), 2.51 (s, 3H), 2.95 (t, J = 6.7 Hz, 2H), 3.53 (t, J = 10.7 Hz, 2H), 3.90 (d, J = 9.9 Hz, 2H), 4.18 (t, J = 6.3 Hz, 2H), 6.73 (d, J = 2.8 Hz, 1H), 6.80 (d, J = 8.2 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 3.6 Hz, 1H)

^{13}C NMR (DMSO-d_6) : δ 9.71, 14.93, 25.55, 32.90, 34.89, 66.01, 67.10, 97.58, 114.33, 126.72, 127.01, 127.20, 129.60, 130.27, 132.40, 142.41, 144.17, 154.73, 156.71, 171.35

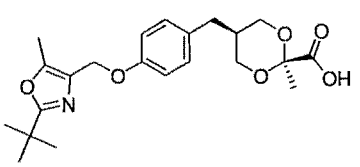
ESI/MS (m/z) : 458.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{24}H_{27}NO_6S$

Calculated : C, 63.00%; H, 5.95%; N, 3.06%

Found : C, 62.67%; H, 5.98%; N, 3.08%

5.1.21.8. *c*-5-[4-(2-*tert*-Butyl-5-methyloxazol-4-ylmethoxy)-benzyl]-2-methyl-1,3-dioxane-*r*-2-carboxylic acid (15h)



15h (0.784 g, 49%) was prepared from **14h** (1.6 g, 3.97 mmol) by following the general procedure given for compounds **9** as white solid. mp: 117-118 °C; Purity by HPLC: 99%.

IR (KBr) : 3450, 2968, 2871, 1735, 1610, 1514, 1375, 1217, 1120, 1029 cm^{-1}

^{1}HNMR (CDCl$_3$) : δ 1.39 (s, 9H), 1.51 (s, 3H), 2.07 (d, J = 7.2 Hz, 2H), 2.19-2.25 (m, 1H), 2.33 (s, 3H), 3.43 (t, J = 11.3 Hz, 2H), 3.78 (dd, J = 11.8 & 4.1 Hz, 2H), 4.92 (s, 2H), 6.88 (d, J = 8.3

Hz, 2H), 6.94 (d, J = 8.7 Hz, 2H), 11.20 (bs, 1H, COOH)

^{13}C NMR (DMSO-d_6) : δ 10.35, 25.84, 28.53, 33.69, 33.86, 34.77, 61.63, 68.10, 98.24, 114.97, 129.39, 129.64, 130.66, 146.63, 157.28, 170.17, 173.09

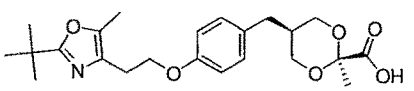
ESI/MS (m/z) : 404.1 $(M+H)^+$

Analysis **Mol.Formula:** $C_{22}H_{29}NO_6$

Calculated : C, 65.49%; H, 7.24%; N, 3.47%

Found : C, 65.31%; H, 7.27%; N, 3.41%

5.1.21.9. *c*-5-[4-{2-(2-*tert*-Butyl-5-methyloxazol-4-yl)ethoxy}-benzyl]-2-methyl-1,3-dioxane-*r*-2-carboxylic acid (15i)



15i (1.04 g, 60%) was prepared from **14i** (1.8 g, 4.17 mmol) by following the general procedure given for compounds **9** as off white solid. mp: 140-141 °C; Purity by HPLC: 98.9%.

IR (KBr) : 3431, 2960, 2856, 1718, 1610, 1514, 1249, 1120, 767 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.35 (s, 9H), 1.54 (s, 3H), 2.24 (s, 3H), 2.27 (s, 3H), 2.89-2.96 (m, 2H), 3.50 (t, J = 13.2 Hz, 2H), 3.84 (dd, J = 13.0 & 3.8 Hz, 2H), 4.12 (t, J = 6.7 Hz, 2H), 6.77 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.1 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 10.45, 25.84, 28.83, 33.69, 33.86, 34.87, 61.43, 68.10, 98.24, 114.97, 129.39, 129.64, 130.66, 146.63, 157.28, 170.17, 173.09

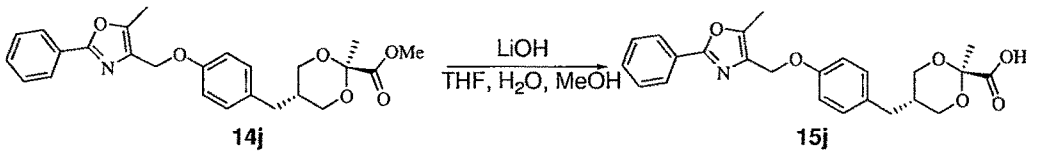
ESI/MS (m/z) : 418.1 $(M+H)^+$

Analysis **Mol.Formula:** $C_{23}H_{31}NO_6$

Calculated : C, 66.17%; H, 7.48%; N, 3.35%

Found : C, 66.28%; H, 7.53%; N, 3.31%

5.1.22. 2-Methyl-*t*-5-[4-(5-methyl-2-phenyloxazol-4-ylmethoxy)-benzyl]-[1,3]dioxane-*r*-2-carboxylic acid (15j)



14j **15j**

15j (1.5 g, 91%) was prepared from **14j** (1.7 g, 3.89 mmol) by following the general procedure reported for compounds **9** as white solid. mp: 114-116 °C; Purity by HPLC: 99.5%.

IR (KBr) : 3433, 2927, 2871, 1720, 1610, 1510, 1236, 1053 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 1.28 (s, 3H), 1.45-1.48 (m, 1H), 2.42 (s, 3H), 2.80 (d, J = 7.6 Hz, 2H), 3.41 (d, J = 11.2 Hz, 2H), 3.94 (d, J = 10.0 Hz, 2H), 4.94 (s, 2H), 6.94 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H), 7.46-7.53 (m, 3H), 7.91-7.93 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.9, 25.24, 33.88, 34.81, 61.37, 64.46, 98.93, 114.61, 125.55, 126.83, 129.03, 129.93, 130.27, 132.04, 132.80, 147.32, 156.45, 158.76, 172.42

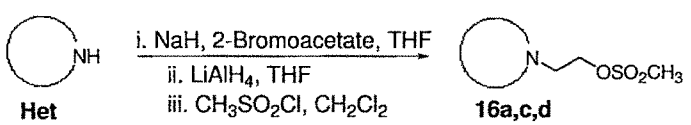
ESI/MS (m/z) : 445.9 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{24}H_{25}NO_6$

Calculated : C, 68.07%; H, 5.95%; N, 3.31%

Found : C, 67.93%; H, 6.00%; N, 3.28%

5.1.23. General procedure for the preparation of the compounds 16a,c,d



Het **16a,c,d**

a: Het = indole; **c**: Het = phenoxazine; **d**: Het = carbazole

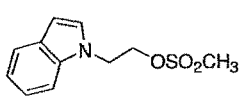
Step I: To an ice cold suspension of sodium hydride (60%) (2 mole equivalent) in dry THF (10 fold) was added Het and stirred for 30 minutes. To this was added ethyl-2-bromoacetate (4 mole equivalent) and the reaction mixture was stirred at ambient temperature for 8 hours. The reaction mixture was poured into ice cold water and extracted with diethylether. The etherial extract was successively

washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was triturated with hexane to get rid of excess bromoacetate to yield the product as viscous liquid and this was subjected to reduction without any purification.

Step II: To an ice cold solution of the product obtained in the above step in dry THF (10 fold) was added $LiAlH_4$ (1.2 mole equivalent) in portions over a period of 30 minutes at 0-10 °C and the reaction mixture was stirred for 2 hours at ambient temperature. The reaction mixture was cooled in an ice bath and quenched with a saturated solution of sodium acetate till the solid separated out. The solid was filtered and washed with hot ethyl acetate. The combined filtrate was dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was triturated with 10 % ethyl acetate in hexane to obtain pure product which was directly subjected to the next step.

Step III: To an ice cold solution of the product obtained from step II in dichloromathane (10 fold w/v) were added triethylamine (15 mole equivalent) and methanesulfonyl chloride (1.2 mole equivalent) at 10 °C under N_2 atmosphere and the reaction mixture was stirred at ambient temperature for 3 hours. The reaction mixture was diluted with dichloromethane, successively washed with water and 1N HCl. The dichloromethane extract was dried over $CaCl_2$ and concentrated under vacuum to yield required product **16a, c, d**.

5.1.23.1. 2-indol-1-yl-ethyl methane sulfonate (16a)



16a (6.13 g, 60%) was prepared from **indole** (5 g, 42.68 mmol) in 3 steps as described in the general procedure above as yellow solid. mp: 80-82 °C; Purity by HPLC: 98.3%.

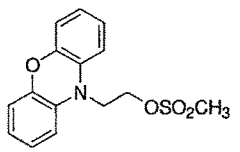
IR (KBr) : 3006, 2868, 1604, 1514, 1483, 1350, 1209, 979, 808, 742 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.57 (s, 3H), 4.45-4.54 (m, 4H), 6.53 (d, J = 8.9 Hz, 1H),

7.13-7.24 (m, 2H), 7.25-7.27 (m, 1H), 7.36 (d, J = 8.9 Hz, 1H), 7.63 (d, J = 8.7 Hz, 1H)

ESI/MS (m/z) : 239.8 $(M+H)^+$

5.1.23.2. 2-(phenoxazin-10-yl)-ethyl methanesulfonate (16c)



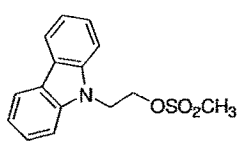
16c (13.3 g, 80%) was prepared from phenoxazine (10 g, 54.58 mmol) in 3 steps as described in the general procedure above as white solid. mp: 79-80°C; Purity by HPLC: 97.3%.

IR (KBr) : 1271, 1174, 736, 522 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 3.02 (s, 3H), 3.92 (t, J = 7.5 Hz, 2H), 4.40 (t, J = 6.2 Hz, 2H), 6.55 (d, J = 7.8 Hz, 2H), 6.64-6.73 (m, 4H), 6.79-6.85 (m, 2H)

ESI/MS (m/z) : 306.1 $(M+H)^+$

5.1.23.3. 2-(*9H*-carbazol-9-yl)-ethyl methanesulfonate (16d)



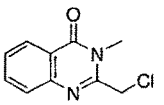
16d (6.92 g, 80%) was prepared from **carbazole** (5 g, 29.9 mmol) in 3 steps as described in the general procedure above as white solid. mp: 148-150 °C; Purity by HPLC: 98%.

IR (KBr) : 3004, 2931, 1625, 1596, 1487, 1463, 1454, 1336, 1247, 1215, 1168, 1012, 918 cm^{-1}

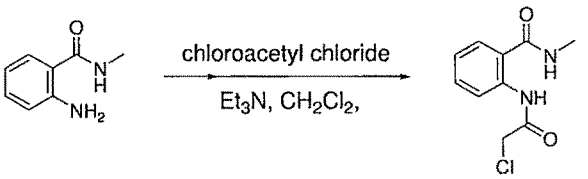
^{1}HNMR ($CDCl_3$) : δ 2.52 (s, 3H), 4.57-4.61 (m, 2H), 4.65-4.69 (m, 2H), 7.24-7.29 (m, 2H), 7.43-7.52 (m, 4H), 8.10 (d, J = 7.7 Hz, 2H)

ESI/MS (m/z) : 289.8 $(M+H)^+$

5.1.24. 2-Chloromethyl-3-methyl-*3H*-quinazolin-4-one (16b)



Step I: Preparation of 2-(2-chloroacetamido)-*N*-methylbenzamide



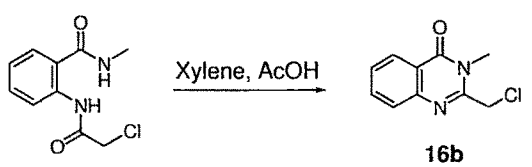
To an ice-cold solution of 2-amino-*N*-methylbenzamide (2.25 g, 12.1 mmoles) in dichloromethane were added triethylamine (3.36 mL, 24.2 mmoles) followed by chloroaceylchloride (0.97 mL, 12.1 mmoles) and the reaction mixture was stirred at ambient temperature for 3 hours. Reaction mixture was diluted with chloroform, washed with water, dried over calcium chloride, filtered and concentrated under vacuum to yield 2.14 g (78%) of compound as brown solid. mp: 144-146 °C; Purity by HPLC: 98%.

IR (KBr) : 3373,1657, 1516, 1405, 1264, 1160, 760cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 3.0 (t, J = 4.89 Hz,3H), 4.1 (s, 2H), 6.4 (bs, 1H, NH), 7.2 (m, 2H) 7.5 (m, 2H), 11.9 (bs, 1H, NH)

ESI/MS (m/z) : 226.9 $(M+H)^+$

Step II: preparation of 2-Chloromethyl-3-methyl-*3H*-quinazolin-4-one (**16b**)



16b

2-(2-chloroacetamido)-*N*-methylbenzamide (2.14 g, 9.4 mmoles) was added to a 1:1 mixture of xylene and acetic acid (20 mL) and refluxed for 15 hours. Solvents were evaporated under vacuum and the residue was triturated with methanol to obtain 1.46 g (74%) of product as off-white solid. mp: 181-183 °C; Purity by HPLC: 98.3%.

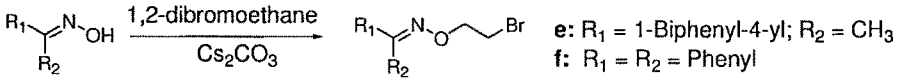
IR (KBr) : 3039, 2989, 1672, 1596, 1471, 1419, 1257, 1125, 777 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 3.76 (s, 3H), 4.64 (s, 2H), 7.51 (t, J = 7.9 Hz, 1H), 7.68

(d, J = 7.7 Hz, 1H), 7.76 (t, J = 8.2 Hz, 1H), 8.29 (d, J = 7.9 Hz, 1H)

ESI/MS (m/z) : 209.0 $(M+H)^+$

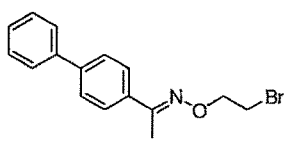
5.1.25. General procedure for the preparation of the compounds 16e-f.



16e & 16f

To a solution of oxime in 1,2-dibromoethane (10 fold) was added cesium carbonate (3 mole equivalent) under nitrogen atmosphere and the reaction mixture was heated at 95 °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, brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield required product **16a-f**;

5.1.25.1. 1-Biphenyl-4-yl-ethanone O-(2-bromoethyl)-oxime (16e)



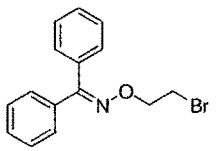
16e (1.99 g, 66%) was prepared from1-biphenyl-4-yl-ethanone oxime (2 g, 9.47 mmol) according to the general procedure described above as white solid. mp: 90-91 °C; Purity by HPLC: 97.4%.

IR (KBr) : 3425, 3055, 2869, 1612, 1487, 1404, 1263, 1093 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ2.30 (s, 3H), 3.64 (t, J = 6.3 Hz, 2H), 4.47 (t, J = 6.3 Hz, 2H), 7.36 (t, J = 7.1 Hz, 1H), 7.45 (t, J = 7.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 4H), 7.72 (d, J = 8.3 Hz, 2H)

ESI/MS (m/z) : 317.9 $(M+H)^+$

5.1.25.2. Diphenyl-methanone O-(2-bromoethyl)-oxime (16f)



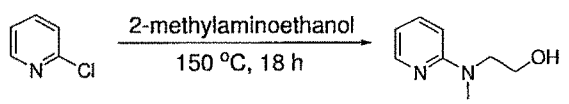
16f (1.05 g, 34%) was prepared from diphenyl-methanone oxime (2 g, 10.14 mmol) according to the general procedure described above as liquid. Purity by HPLC: 99.2%.

IR (Neat) : 3018, 1641, 1512, 1413, 1008 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 3.63 (t, J = 6.45 Hz, 2H), 4.43 (t, J = 6.51 Hz, 2H), 7.33-7.48 (m, 10H)

ESI/MS (m/z) : 304.0 $(M+H)^+$

5.1.26. 2-(Methylpyridin-2-yl-amino)-ethanol (16g)



16g

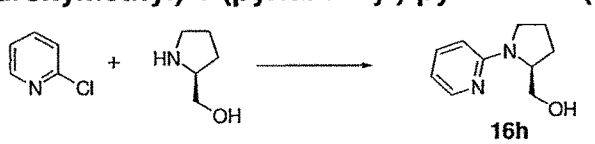
A mixture of 2-chloropyridine (50 g, 0.44 mol) and 2-methylaminoethanol (300 mL) was stirred at 150 °C 18 hours. Excess 2-methylaminoethanol was evaporated and the product was distilled under vacuum to yield 65 g (97%) of product as viscous liquid. Purity by HPLC: 97.8%.

IR (Neat) : 3286, 1616, 1480, 1432, 1370, 1018, 729 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 3.04 (s, 3H), 3.66 (t, J = 5.1 Hz, 2H), 3.79 (t, J = 4.5 Hz, 2H), 6.50-6.57 (m, 2H), 7.42-7.48 (m, 1H), 8.02-8.04 (m, 1H)

ESI/MS (m/z) : 153.1 $(m+H)^+$

5.1.27. (*S*)-2-(Hydroxymethyl)-1-(pyridin-2-yl)-pyrrolidine (16h)



16h

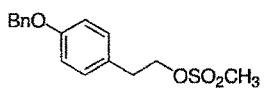
A mixture of 2-chloropyridine (33.7 g, 297 mmol) and L-prolinol (20 g, 198 mmol) was heated under nitrogen atmosphere at 160 °C with stirring for 4 h. The mixture was cooled to room temperature and poured into water (100 mL), and the solution was extracted with CH_2Cl_2 (3 X 150 mL). The combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated to dryness under vacuum. The crude product was chromatographed over silica gel using 2% methanol in chloroform to afford 19.4 g (55%) of the title compound as a liquid. Purity by HPLC: 94.0%.

IR (Neat) : 3372, 1600, 1491, 1442, 1377 cm-1

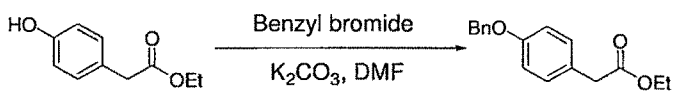
^{1}HNMR ($CDCl_3$) : δ 1.72-1.74 (m, 1H), 1.97-2.09 (m, 3H), 3.30-3.35 (m, 1H), 3.42-3.48 (m, 2H), 3.58-3.62 (m, 1H), 4.26-4.27 (m, 1H), 6.43 (d, J = 8.4 Hz, 1 H), 6.58 (t, J = 6.0 Hz, 1H), 7.42-7.50 (m, 1H), 8.02 (dd, J = 5.1 & 1.2 Hz, 1H)

ESI/MS (m/z) : 179.0 $(M+H)^+$

5.1.28. 2-(4-Benzyloxyphenyl)-ethylmethanesulfonate (16i)



Step I: preparation of ethyl-(4-benzyloxy-phenyl)-acetate



To a stirred mixture of ethyl-(4-hydroxyphenyl)-acetate (25 g, 0.138 mol) and potassium carbonate (38.35 g, 0.277 mol) in dry DMF was added benzylbromide (24.91 g, 0.146 moles) and the reaction mixture was stirred at ambient temperature for 6 hours. Reaction mixture was poured into ice-cold water and extracted with ethyl acetate (3 X 150 mL). The organic extract was successively washed with water, brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield 34.9 g (93%) of product as a liquid. Purity by HPLC: 96.0 %.

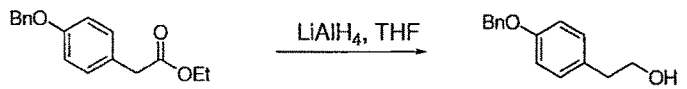
IR (Neat) : 1733, 1612, 1512, 1456, 1298, 1242, 1029 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.21 (t, J = 7.1 Hz, 3H), 3.54 (s, 2H), 4.09 (q, J = 7.1 Hz, 2H), 5.03 (s, 2H), 6.91 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 8.6

Hz, 2H), 7.34-7.43 (m, 5H)

ESI/MS (m/z) : 288.0 $(M+NH_4)^+$

Step II: preparation of 2-(4-benzyloxyphenyl)-ethanol



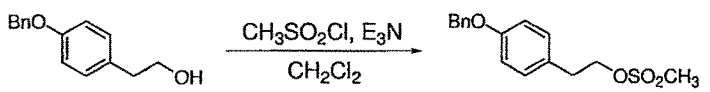
To an ice-cold solution of ethyl-(4-benzyloxy-phenyl)-acetate (34 g, 0.125 moles) in dry THF (250 mL) was added $LiAlH_4$ (5.25 g, 0.138 moles) in portions over a period of 30 minutes and the reaction mixture was stirred for 2 hours. Reaction mixture was quenched with saturated solution of Na_2SO_4 till free flowing solid was separated. Solid was filtered and washed with hot ethyl acetate and the combined filtrate was concentrated under vacuum. The residue was dissolved in ethyl acetate, successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield 27.3 g (95%) of product as white solid. mp: 90-92 °C; Purity by HPLC: 99.0%.

IR (KBr) : 3284, 2935, 1608, 1514, 1238, 1053 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.36 (t, J=5.7 Hz, 1H, OH), 2.79 (t, J=6.5 Hz, 2H), 3.79 (q, J = 6.4 Hz, 2H), 5.05 (s, 2H), 6.91 (d, J = 8.5 Hz, 2H), 7.13 (d, J = 8.5Hz, 2H), 7.34-7.44 (m, 5H)

ESI/MS (m/z) : 246.2 $(M+NH_4)^+$

Step III: preparation of 2-(4-Benzyloxyphenyl)-ethylmethanesulfonate (**16i**)



16i

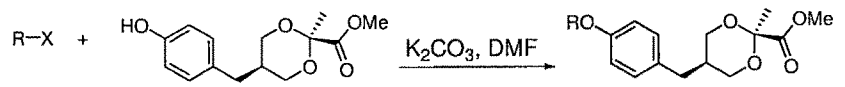
To an ice-cold solution of 2-(4-benzyloxy-phenyl)-ethanol (27 g, 0.188 moles) in dry dichloromethane (250 mL) were added triethylamine (24.7 mL, 0.177 moles) and methanesulphonylchloride (11 mL, 0.141 moles) and the reaction mixture was stirred at 25 °C for half an hour. Reaction mixture was diluted with chloroform (500 mL) and successively washed with dil.HCl, water and then with $NaHCO_3$ solution. Organic extract was dried over $CaCl_2$ and concentrated under vacuum. The syrup so obtained was tritutared with 200 mL of methanol to furnish 23 g (65%) of pure product as White solid. mp: 78-80 °C; Purity by HPLC: 98.6%.

IR (KBr) : 3018, 2846, 1612, 1514, 1460, 1350, 1172 cm^{-1}

^{1}HNMR (CDCl$_3$) : δ 2.83 (s, 3H), 2.99 (t, J = 6.8 Hz, 2H), 4.37 (t, J = 6.9 Hz, 2H), 5.05 (s, 2H), 6.91 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 8.5 Hz, 2H), 7.32-7.44 (m, 5H)

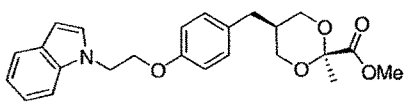
ESI/MS (m/z) : 324.2 $(M+NH_4)^+$

5.1.29. Preparation of the compounds 17a-f.



16a-f **13b** **17a-f**

5.1.29.1. Methyl-*c*-5-[4-(2-indol-1-yl-ethoxy)-benzyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (17a)



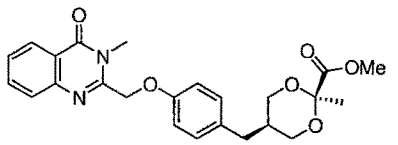
17a (0.741 g, 55%) was prepared from **16a** (1 g, 4.18 mmol) and **13b** (1.11 g, 4.18 mmol) according to the general procedure described for the synthesis of compounds **8** as a liquid. Purity by HPLC: 96.8%.

IR (Neat) : 3018, 2927, 1743, 1614, 1514, 1461, 1373, 1244, 1188, 1143, 1116, 1041, 808 cm^{-1}

^{1}HNMR (CDCl$_3$) : δ 1.48 (s, 3H), 2.24-2.28 (m, 3H), 3.42-3.48 (m, 2H), 3.84-3.98 (m, 5H), 4.23 (t, J = 5.57 Hz, 2H), 4.49 (t, J = 5.66 Hz, 2H), 6.50 (d, J = 2.5 Hz, 1H), 6.73 (d, J = 7.1 Hz, 2H), 6.95 (d, J = 8.3 Hz, 2H), 7.08 (t, J = 7.4 Hz, 1H), 7.20 (d, J = 3.3 Hz, 2H), 7.36-7.41 (m, 1H), 7.61 (d, J = 7.8 Hz, 1H)

ESI/MS (m/z) : 410.2 $(M+H)^+$

5.1.29.2. Methyl-2-methyl-*c*-5-[4-(3-methyl-4-oxo-3,4-dihydroquinazolin-2-ylmethoxy)-benzyl]-[1,3]-dioxane-*r*-2-carboxylate (17b)



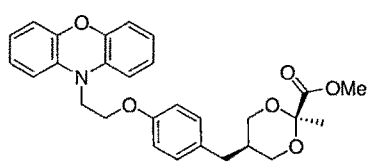
17b (1.2 g, 57%) was prepared from **16b** (1 g, 4.79 mmol) and **13b** (1.28 g, 4.79 mmol) according to the general procedure described for the synthesis of compounds **8** as a liquid. Purity by HPLC: 90.2%.

IR (Neat) : 1743, 1678,1606, 1510, 929 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.2-2.28 (m, 3H), 3.46 (t, J = 12.39 Hz, 2H), 3.74 (s, 3H), 3.82-3.94 (m, 5H) 5.15 (s, 2H), 6.95-6.70 (m, 3H), 7.14 (d, J = 8.46 Hz, 1H), 7.51 (t, J = 6.75 Hz, 1H), 7.69-7.79 (m, 2H), 8.30 (d, J = 7.92 Hz, 1H)

ESI/MS (m/z) : 439.2 $(M+H)^+$

5.1.29.3. Methyl-2-methyl-*c*-5-[4-(2-phenoxazin-10-yl-ethoxy)-benzyl]-[1,3]-dioxane-*r*-2-carboxylate (17c)



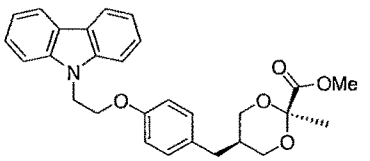
17c (1.35 g, 87%) was prepared from **16c** (1 g, 3.27 mmol) and **13b** (0.872 g, 3.27 mmol) according to the general procedure described for the synthesis of compounds **8** as a liquid. Purity by HPLC: 96.5%.

IR (Neat) : 1870, 1718, 1865, 1654, 1510, 1490, 1377, 1215, 1145, 1043, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.27-2.31 (m, 3H), 3.49 (t, J = 10.7 Hz, 2H), 3.83-3.98 (m, 7H), 4.13 (t, J = 6.6 Hz, 2H), 6.58-6.67 (m, 4H), 6.75-6.81 (m, 4H), 6.98 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.5 Hz, 2H)

ESI/MS (m/z) : 476.2$(M+H)^+$

5.1.29.4. Methyl-*c*-5-[4-(2-carbazol-9-yl-ethoxy)-benzyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (17d)



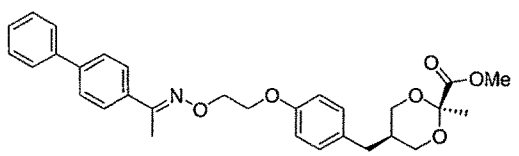
17d (1.22 g, 77%) was prepared from **16d** (1 g, 3.46 mmol) and **13b** (0.92 g, 3.46 mmol) according to the general procedure described for the synthesis of compounds **8** as white solid. mp: 95-97 °C Purity by HPLC: 95%.

IR (KBr) : 1747, 1724, 1610, 1512, 1485, 1458, 1352, 1326, 1242, 1217, 1188, 1141, 1110, 837, 754 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.5 (s, 3H), 2.2 (m, 3H), 3.4 (t, J = 10.2 Hz, 2H), 3.8 (s, 3H), 3.9 (m, 2H), 4.3 (t, J = 6.0 Hz, 2H), 4.7 (t, J = 6.0 Hz, 2H), 6.7 (d, J = 8.4 Hz, 2H), 6.9 (d, J = 8.4 Hz, 2H), 7.2 (m, 2H), 7.5 (m, 4H), 8.1 (d, J = 7.7 Hz, 2H)

ESI/MS (m/z) : 460.3 $(M+H)^+$

5.1.29.5. Methyl-*c*-5-{4-[2-(1-biphenyl-4-yl-ethylideneaminooxy)-ethoxy]-benzyl}-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (17e)



17e (1.11 g, 70%) was prepared from **16e** (1 g, 3.14 mmol) and **13b** (0.836 g, 3.14 mmol) according to the general procedure described for the synthesis of compounds **8** as white solid. mp: 89-90 °C Purity by HPLC: 99.7%.

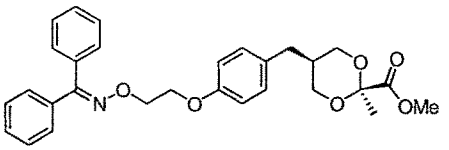
IR (KBr) : 2977, 2856, 1745, 1610, 1514, 1247 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.27-2.32 (m, 6H), 3.46 (t, J = 10.68 Hz, 2H,), 3.84 (s, 3H), 3.90 (dd, J = 12.03 & 3.66 Hz, 2H), 4.27 (t, J = 4.98 Hz, 2H), 4.54 (t, J = 4.71 Hz, 2H), 6.87 (d, J = 8.58 Hz, 2H), 7.01 (d, J = 8.55 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.08 Hz, 2H), 7.62 (dd, J = 8.34 & 1.8 Hz,

4H), 7.71 (d, J = 8.37 Hz, 2H)

ESI/MS (m/z) : 504.1 $(M+H)^+$

5.1.29.6. Methyl-*c*-5-[4-(2-benzhydrylideneaminooxyethoxy)-benzyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (17f)



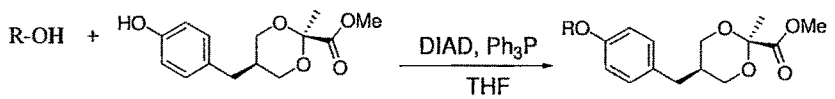
17f (1.79 g, 74%) was prepared from **16f** (1.5 g, 4.93 mmol) and **13b** (1.31 g, 4.93 mmol) according to the general procedure described for the synthesis of compounds **8** as a liquid. Purity by HPLC: 93.4%.

IR (Neat) : 3018, 2929, 1743, 1612, 1512, 1444, 1215 cm-1

^{1}HNMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.27 (s, 3H), 3.46 (t, J = 10.74 Hz, 2H), 3.82-3.90 (m, 5H), 4.24 (t, J = 5.04 Hz, 2H), 4.50 (t, J = 4.90 Hz, 2H), 6.83 (d, J = 8.52 Hz, 2H), 6.99 (d, J = 8.55 Hz, 2H), 7.29-7.47 (m, 10H)

ESI/MS (m/z) : 490.0 $(M+H)^+$

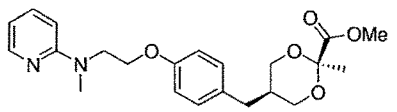
5.1.30. General procedure for the preparation of the compounds 17g-h



16g-h **13b** **17g-h**

To an ice-cold solution of triphenylphosphine (2.8 mole equivalent) in dry THF was added diethylazadicarboxylate (2 mole equivalent) and the reaction mixture was stirred for 10 minutes. To this were added **13b** followed by **16g-h** (1 mole equivalent) and stirred for 16 hours at ambient temperature. Reaction mixture was poured into ice-cold water and extracted with ethyl acetate. The combined organic extract was washed with water followed by brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield product **17g-h**. Crude product was chromatographed over silicagel to obtained pure product.

5.1.30.1. Methyl-2-methyl-*c*-5-{4-[2-(methylpyridin-2-yl-amino)-ethoxy]-benzyl}-[1,3]-dioxane-*r*-2-carboxylate (17g)



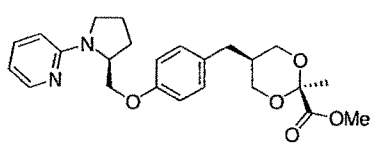
17g (2 g, 76%) was prepared from **16g** (1 g, 6.57 mmol) and **13b** (1.75 g, 6.57 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 96.8%.

IR (Neat) : 3018, 2927, 1743, 1596, 1510, 1425, 1215, 1143, 1039, 977, 754 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.26-2.31 (m, 3H), 3.14 (s, 3H), 3.45 (t, J = 11.4 Hz, 2H), 3.77-3.82 (m, 2H), 3.83 (s, 3H), 3.94 (t, J = 5.6 Hz, 2H), 4.13 (t, J = 5.5 Hz, 2H), 6.50-6.57 (m, 2H), 6.81 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 7.42-7.48 (m, 1H), 8.14 (d, J = 4.3 Hz, 1H)

ESI/MS (m/z) : 401.2 $(M+Na)^+$

5.1.30.2. Methyl-2-methyl-*c*-5-[4-(1-pyridin-2-yl-pyrrolidin-(2*S*)-ylmethoxy)-benzyl]-[1,3]-dioxane-*r*-2-carboxylate (17h)



17h (1.05 g, 44%) was prepared from **16h** (1 g, 5.61 mmol) and **13b** (4.41 g, 5.61 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 95%.

IR (Neat) : 3020, 2930, 1743, 1598, 1512, 1477, 1442, 1377, 1244, 1215, 1143, 1037 cm^{-1}

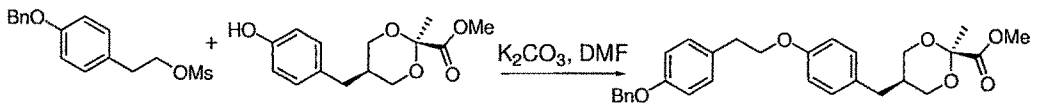
^{1}HNMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.14-2.16 (m, 2H), 2.23-2.26 (m, 2H), 2.24-2.28 (m, 3H), 3.30-3.32 (m, 2H), 3.52-3.55 (m, 3H), 3.81 (s, 3H), 3.90-3.93 (m, 2H), 4.21 (dd, J = 9.1 & 3.1 Hz, 1H), 4.54-4.56 (m, 1H), 6.43 (d, J = 8.5 Hz, 1H), 6.51 (t, J = 5.9

Hz, 1H), 6.90 (d, J = 8.5 Hz, 2H), 7.01 (d, J = 8.5 Hz, 2H), 7.39-7.42 (m, 1H), 8.11 (d, J = 4.0 Hz, 1H)

ESI/MS (m/z) : 427.0 $(M+H)^+$

5.1.31. Methyl-*c*-5-{4-[2-(4-methanesulfonyloxyphenyl)-ethoxy]-benzyl}-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (17i)

Step I: Methyl-*c*-5-{4-[2-(4-benzyloxy-phenyl)-ethoxy]-benzyl}-2-methyl-[1,3]dioxane-*r*-2 carboxylate



16i **13b**

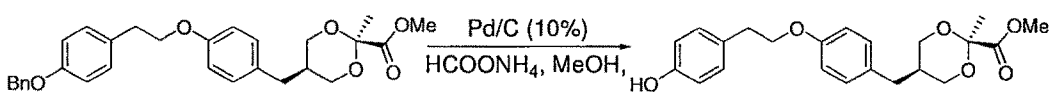
This compound (1.24 g, 80%) was prepared from **13b** (0.869 g, 3.26 mmol) and **16i** (1 g, 3.26 mmol) according to the general procedure reported for **8** as a liquid. Purity by HPLC: 97.2%.

IR (Neat) : 3032, 2924, 2854, 1748,1611,1510,1243 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.27 (s, 3H), 3.02 (t, J = 7.1 Hz, 2H), 3.49 (t, J = 10.68 Hz, 2H), 3.82-3.90 (m, 5H), 4.09 (t, J = 7.11 Hz, 2H), 5.05 (s, 2H), 6.79 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 9.18 Hz, 2H), 6.99 (d, J = 8.49 Hz, 2H), 7.19 (d, J = 8.46 Hz, 2H), 7.32-7.44 (m, 5H)

ESI/MS (m/z) : 477.3 $(M+NH_4)^+$

Step II: Methyl-*c*-5-{4-[2-(4-hydroxyphenyl)-ethoxy]-benzyl}-2-methyl-[1,3]-dioxane-*r*-2-carboxylate



This compound (0.651 g, 73%) was prepared from the compound prepared in **step I** above (1.1 g, 2.31 mmol) by means of a procedure similar to that reported for **4c** as white solid. mp: 94-96 °C; Purity by HPLC: 98.0%.

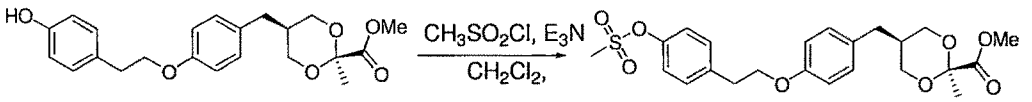
IR (KBr) : 3415, 2927, 2869, 1724, 1616, 1515, 1247 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.27 (s, 3H), 3.01 (t, J = 7.05 Hz, 2H), 3.45 (t, J = 10.68 Hz, 2H), 3.84-3.90 (m, 5H), 4.09 (t, J = 7.11

Hz, 2H), 4.70 (bs, 1H, OH), 6.79 (dd, J = 7.83 & 4.74 Hz, 4H), 6.98 (d, J = 8.37 Hz, 2H), 7.00 (d, J = 8.28 Hz, 2H)

ESI/MS (m/z) : 404.3 $(M+NH_4)^+$

Step III: Methyl-*c*-5-{4-[2-(4-methanesulfonyloxyphenyl)-ethoxy]-benzyl}-2-methyl-[1,3]-dioxane-*r*-2-carboxylate **17i**



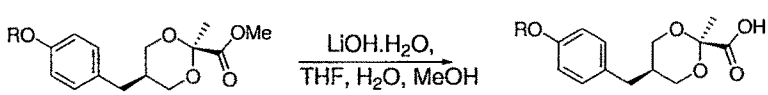
To an ice-cold solution of the product obtained from **step II** (0.59 g, 1.53 mmol) in dichloromethane (5 mL) were added triethylamine (0.319 mL, 2.29 mmol) and methanesulphonyl chloride (0.141 mL, 1.83 mmol) and the reaction mixture was stirred for 2 hours at ambient temperature. Reaction mixture was diluted with chloroform and washed with water, dried over $CaCl_2$ and concentrated under vacuum to yield 0.695 g (98%) of product as a liquid. Purity by HPLC: 98.5%.

IR (Neat) : 3033, 2950, 1747, 1612, 1512, 1244 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.49 (s, 3H), 2.27 (s, 3H), 3.09 (t, J = 6.57 Hz, 2H), 3.13 (s, 3H), 3.45 (t, J = 11.73 Hz, 2H) 3.82-3.92 (m, 5H), 4.13 (t, J = 6.75 Hz, 2H), 6.79 (d, J = 8.46 Hz, 2H), 7.00 (d, J = 8.46 Hz, 2H), 7.23 (d, J = 8.55 Hz, 2H), 7.33 (d, J=8.43 Hz, 2H)

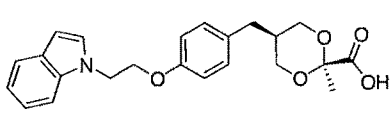
ESI/MS (m/z) : 487.4 $(M+Na)^+$

5.1.32. Preparation of the compounds 18a-i.



17a-i **18a-i**

5.1.32.1. *c*-5-[4-(2-Indol-1-yl-ethoxy)-benzyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (18a)



18a (0.231 g, 40%) was prepared from **17a** (0.6 g, 1.47 mmol) following the general procedure described for compounds **9** as white solid. mp: 105-107 °C; Purity by HPLC: 99%.

IR (KBr) : 3450, 2925, 2854, 1716, 1510, 1463, 1315, 1143, 1028, 783, 761 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.22-2.25 (m, 3H), 3.47 (t, J = 10.7 Hz, 2H), 3.94 (dd, J = 17.9 & 4.6 Hz, 2H), 4.22 (t, J = 5.6 Hz, 2H), 4.49 (t, J = 5.6 Hz, 2H), 6.50 (d, J = 3.3 Hz, 1H), 6.73 (d, J = 8.6 Hz, 2H), 6.95 (d, J = 8.5 Hz, 2H), 7.11 (t, J = 7.4 Hz, 1H), 7.20-7.22 (m, 2H), 7.39 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H)

^{13}C NMR (DMSO-d_6) : δ 25.50, 32.81, 34.77, 45.04, 66.84, 66.99, 97.51, 100.73, 109.87, 114.29, 118.97, 120.32, 120.98, 128.11, 128.96, 129.47, 130.53, 135.91, 156.44, 171.26

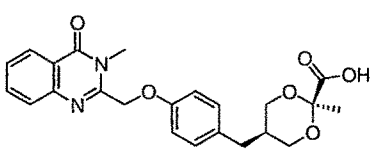
ESI/MS (m/z) : 396.1 $(M+H)^+$

Analysis **Mol.Formula:** $C_{23}H_{25}NO_5$

Calculated : C, 69.86%; H, 6.37%; N, 3.54%

Found : C, 69.24%; H, 6.48%; N, 3.51%

5.1.32.2. 2-Methyl-*c*-5-[4-(3-methyl-4-oxo-3,4-dihydroquinazolin-2-ylmethoxy)-benzyl]-[1,3]-dioxane-*r*-2-carboxylic acid (18b)



18b (0.919 g, 95%) was prepared from **17b** (1 g, 2.28 mmol) follwing the general procedure described for compounds **9** as white solid. mp: 210-211 °C; Purity by HPLC: 98.4%.

IR (KBr) : 3431, 2927, 2858, 1679, 1608, 1512, 1467, 1371, 1336, 1240, 1184, 1145, 1037, 754 cm^{-1}

^{1}HNMR : δ 1.31 (s, 3H), 2.09-2.12 (m, 1H), 2.26 (d, J = 6.9 Hz, 2H),

(DMSO-d_6) 3.38 (t, J = 11.3 Hz, 2H), 3.61 (s, 3H), 3.70 (dd, J = 11.7 & 4.2 Hz, 2H,), 5.24 (s, 2H), 7.00 (d, J = 8.5 Hz, 2H), 7.11 (d, J = 8.3 Hz, 2H), 7.54 (t, J = 7.5 Hz, 1H), 7.65 (d, J = 8.04 Hz, 1H), 7.81 (t, J = 7.1 Hz, 1H), 8.14 (d, J = 7.8 Hz, 1H)

^{13}C NMR (DMSO-d_6) : δ 25.52, 30.07, 32.84, 34.83, 67.05, 69.10, 97.56, 114.90, 120.30, 126.20, 127.14, 127.28, 129.72, 131.43, 134.38, 146.45, 152.53, 1256.01, 161.29, 171.30

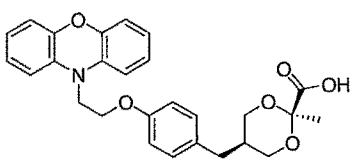
ESI/MS (m/z) : 425.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{23}H_{24}N_2O_6$

Calculated : C, 65.08%; H, 5.70%; N, 6.60%

Found : C, 64.42%; H, 5.52%; N, 5.87%

5.1.32.3. 2-Methyl-*c*-5-[4-(2-phenoxazin-10-yl-ethoxy)-benzyl]-[1,3]-dioxane-*r*-2-carboxylic acid (18c)



18c (0.663 g, 57%) was prepared from **17c** (1.2 g, 2.52 mmol) following the general procedure described for compounds **9** as white solid. mp: 54-56 °C; Purity by HPLC: 98.5%.

IR (KBr) : 3018, 1726, 1627, 1510, 1490, 1377, 1274, 1245, 1149, 1043, 925, 754 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.26-2.30 (m, 3H), 3.49 (t, J = 10.4 Hz, 2H), 3.89-4.00 (m, 4H), 4.13 (t, J = 6.5 Hz, 2H), 6.61-6.69 (m, 4H), 6.74-6.90 (m, 4H), 6.99 (d, J = 8.5 Hz, 2H), 7.10 (d, J = 8.5 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 24.27, 30.74, 32.90, 33.81, 34.89, 35.73, 43.41, 54.85, 64.15, 64.77, 66.95, 99.51, 112.56, 114.34, 114.99, 121.08, 123.88, 129.60, 129.95, 130.65, 132.93, 143.99, 156.52, 162.25, 171.47

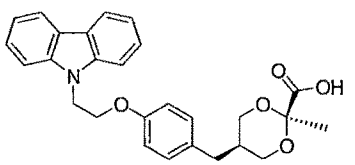
ESI/MS (m/z) : 462.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{27}H_{27}NO_6$

Calculated : C, 70.27%; H, 5.90%; N, 3.03%

Found : C, 69.97%; H, 6.04%; N, 2.89%

5.1.32.4. *c*-5-[4-(2-Carbazol-9-yl-ethoxy)-benzyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (18d)



18d (0.339 g, 35%) was prepared from **17d** (1 g, 2.18 mmol) following the general procedure described for compounds **9** as white solid. mp: 125-127 °C; Purity by HPLC: 99.8%.

IR (KBr) : 3423, 1747, 1596, 1512, 1460, 1325, 1247, 1137, 1118, 1033, 885, 827, 746 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.5 (s, 3H), 2.2 (m, 3H), 3.5 (t, J = 10.7 Hz, 2H), 3.9 (m, 2H), 4.3 (t, J = 5.9 Hz, 2H), 4.7 (t, J = 5.9 Hz, 2H), 6.7 (d, J = 8.5 Hz, 2H), 6.9 (d, J = 8.5 Hz, 2H), 7.2 (m, 2H), 7.5 (m, 4H), 8.12 (d, J = 7.8 Hz, 2H)

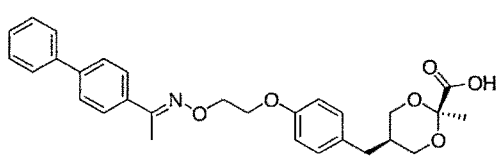
ESI/MS (m/z) : 446.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{27}H_{27}NO_5$

Calculated : C, 72.79%; H, 6.11%; N, 3.14%

Found : C, 72.37%; H, 6.36%; N, 3.02%

5.1.32.5. *c*-5-{4-[2-(1-Biphenyl-4-yl-ethylideneaminooxy)-ethoxy]-benzyl}-2-methyl-[1,3]dioxane-*r*-2-carboxylic acid (18e)



18e (0.544 g, 56%) was prepared from **17e** (1 g, 1.99 mmol) following the general procedure described for compounds **9** as white solid. mp: 122-123 °C; Purity by HPLC: 99.8%.

IR (KBr) : 3436, 2923, 1722, 1610, 1369, 1269, 1215, 1070, 943, 721 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.27 (s, 3H), 2.31 (s, 3H), 3.52 (t, J = 11.4 Hz, 2H), 3.94 (dd, J =13.3 & 4.0 Hz, 2H), 4.27 (t, J = 4.9 Hz, 2H), 4.54 (t, J = 4.7 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 7.01 (d, J = 8.5 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.0 Hz, 2H), 7.59 (dd, J = 8.3 & 1.8 Hz, 4H), 7.71 (d, J = 8.3 Hz, 2H)

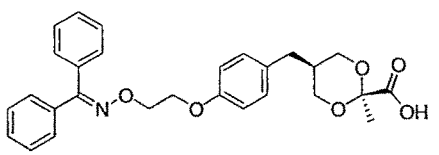
ESI/MS (m/z) : 512.1 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{29}H_{31}NO_6$

Calculated : C, 71.15%; H, 6.38%; N, 2.86%

Found : C, 70.95%; H, 6.47%; N, 2.58%

5.1.32.6. *c*-5-[4-(2-Benzhydrylideneaminooxyethoxy)-benzyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (18f)



18f (1.17 g, 80%) was prepared from **17f** (1.5 g, 3.06 mmol) following the general procedure described for compounds **9** as white solid. mp: 117-119 °C; Purity by HPLC: 99.6%.

IR (KBr) : 3431, 2976, 2900, 1708, 1610, 1510, 1363, 1272 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.56 (s, 3H), 2.26-2.30 (m, 3H), 3.53 (t, J = 10.8 Hz, 2H), 3.93 (d, J = 12.4 Hz, 2H), 4.24 (t, J = 5.2 Hz, 2H), 4.49 (t, J = 5.2 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 6.98 (d, J = 8.8 Hz, 2H), 7.29-7.36 (m, 5H), 7.37-7.40 (m, 3H), 7.45 (d, J = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 26.32, 32.88, 64.89, 67.06, 72.52, 97.60, 114.14, 127.46, 128.16, 128.56, 128.86, 129.47, 129.61, 130.43, 132.56, 135.82, 156.67, 156.83, 171.37

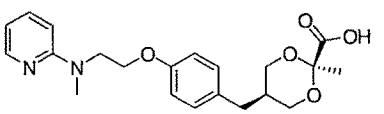
ESI/MS (m/z) : 498.1(M+Na)$^+$

Analysis **Mol.Formula:** $C_{28}H_{29}NO_6$

Calculated : C, 70.72%; H, 6.15%; N, 2.95%

Found : C, 70.45%; H, 6.16%; N, 3.17%

5.1.32.7. 2-Methyl-*c*-5-{4-[2-(methylpyridin-2-yl-amino)-ethoxy]-benzyl}-[1,3]-dioxane-*r*-2-carboxylic acid (18g)



18g (0.796 g, 55%) was prepared from **17g** (1.5 g, 3.75 mmol) following the general procedure described for compounds **9** as off white solid. mp: 88-90 °C; Purity by HPLC: 98.3%.

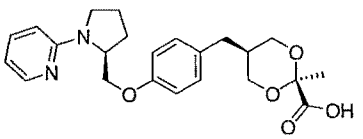
IR (KBr) : 3377, 1647, 1608, 1510, 1400, 1245, 1215, 1159, 1055, 769 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.53 (s, 3H), 2.24-2.28 (m, 3H), 3.18 (s, 3H), 3.53 (t, J = 10.52 Hz, 2H), 3.86-3.89 (m, 2H), 4.00 (t, J = 5.0 Hz, 2H), 4.16-4.20 (m, 2H), 6.57-6.62 (m, 2H), 6.75 (d, J = 8.28 Hz, 2H), 6.93 (d, J = 8.4 Hz, 2H), 7.51-7.56 (m, 1H), 8.18-8.23 (m, 1H)

^{13}C NMR (DMSO-d_6) : δ 25.59, 32.96, 34.97, 37.06, 48.57, 64.84, 65.35, 67.01, 97.86, 105.74, 111.51, 114.28, 129.64, 130.02, 130.40, 137.31, 147.57, 156.76, 158.06, 171.46

ESI/MS (m/z) : 387.2 (M+H)$^+$

5.1.32.8. 2-Methyl-*c*-5-[4-(1-pyridin-2-yl-pyrrolidin-(2S)-ylmethoxy)-benzyl]-[1,3]-dioxane-*r*-2-carboxylic acid (18h)



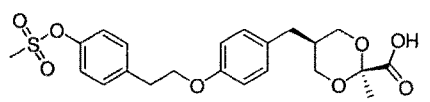
18h (0.502 g, 65%) was prepared from **17h** (0.8 g, 1.88 mmol) following the general procedure described for compounds **9** as off white solid. mp: 81-83 °C; Purity by HPLC: 97%.

IR (KBr) : 3429, 1733, 1647, 1558, 1512, 1440, 1363, 1244, 1035, 769 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.54 (s, 3H), 2.13 (m, 3H), 2.22 (m, 4H), 3.30-3.32 (m, 2H), 3.64 (m, 2H), 3.83 (m, 2H), 3.91 (t, J = 5.1 Hz, 1H), 4.14 (m, 1H), 4.53 (m, 1H), 6.54 (d, J = 8.5 Hz, 1H), 6.63 (t, J = 5.9 Hz, 1H), 6.82 (d, J = 8.31 Hz, 2H), 6.91 (d, J = 8.22 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 8.22 (m, 1H)

ESI/MS (m/z) : 413.4 $(M+H)^+$

5.1.32.9. *c*-5-{4-[2-(4-Methanesulfonyloxyphenyl)-ethoxy]-benzyl}-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (18i)



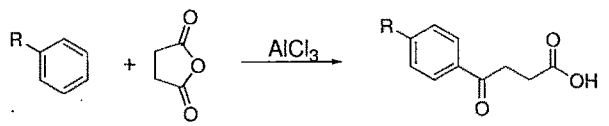
18i (0.353 g, 73%) was prepared from **17i** (0.5 g, 1.08 mmol) follwing the general procedure described for compounds 9 as white solid. mp: 118-120 °C; Purity by HPLC: 97%.

IR (KBr) : 3400, 3018, 2927, 1718, 1610, 1510, 1215 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.55 (s, 3H), 2.27 (s, 3H), 3.09 (t, J = 6.72 Hz, 2H), 3.13 (s, 3H), 3.44-3.55 (m, 2H), 3.90 (dd, J = 13.7 & 4.2 Hz, 2H), 4.16 (t, J = 6.69 Hz, 2H), 6.80 (d, J = 8.49 Hz, 2H), 6.99 (d, J = 8.49 Hz, 2H), 7.23 (d, J = 8.61 Hz, 2H), 7.33 (d, J = 8.49 Hz, 2H)

^{13}C NMR (DMSO-d_6)	: δ 25.60, 32.90, 34.33, 34.44, 34.94, 37.32, 67.13, 67.78, 97.65, 114.38, 122.14, 129.71, 130.38, 130.62, 137.93, 147.69, 156.78, 171.43
ESI/MS (m/z)	: 473.3 $(M+Na)^+$
Analysis	**Mol.Formula:** $C_{22}H_{26}O_8S$
	Calculated : C, 58.65%; H, 5.82%
	Found : C, 58.21%; H, 6.01%

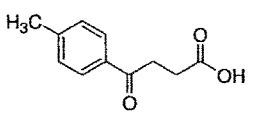
5.1.33. General procedure for the preparation of the compounds 19a-e.



19a-e

To an ice-cold solution of succinic anhydride in corresponding benzene derivatives (5 fold) anhydrous $AlCl_3$ (2.05 mole equivalent) was added portionwise at 10 °C over a period of 0.5 hour. The reaction mixture was allowed to warm upto ambient temperature and then heated to reflux for 4 hours. Contents of the reaction mixture were poured into an ice cold solution of 5N HCl and extracted with ethyl acetate. Combined organic extract was successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum to obtain required product.

5.1.33.1. 4-(4-Methylphenyl)-4-oxobutanoic acid (19a)

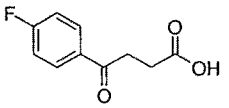


19a (13.45 g, 70%) was prepared from toluene (50 mL) and succinic anhydride (10 g, 99.93 mmol) according to the general procedure described above as white solid. mp: 125-127 °C; Purity by HPLC: 93%.

IR (KBr)	: 3350, 3066, 2966, 1681, 1606, 810 cm^{-1}
^{1}HNMR ($CDCl_3$)	: δ 2.41 (s, 3H), 2.80 (t, J = 6.6 Hz, 2H), 3.29 (t, J = 6.6 Hz, 2H), 7.25 (d, J = 7.9 Hz, 2H), 7.87 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 215.1 $(M+Na)^+$

5.1.33.2. 4-(4-Fluorophenyl)-4-oxobutanoic acid (19b)



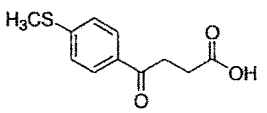
19b (7.84 g, 40%) was prepared from fluorobenzene (50 mL) and succinic anhydride (10 g, 99.93 mmol) according to the general procedure described above as white solid. mp: 105-107 °C; Purity by HPLC: 98%.

IR (KBr) : 3352, 3076, 2950, 1697, 1678, 1595, 1234, 941, 827 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.81 (t, J = 6.5 Hz, 2H), 3.28 (t, J = 6.5 Hz, 2H), 7.14 (t, J = 8.5 Hz, 2H), 7.99-8.03 (m, 2H)

ESI/MS (m/z) : 197.1 $(M+H)^+$

5.1.33.3. 4-(4-(Methylthio)phenyl)-4-oxobutanoic acid (19c)



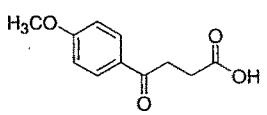
19c (13.9 g, 62%) was prepared from thioanisole (50 mL) and succinic anhydride (10 g, 99.93 mmol) according to the general procedure described above as white solid. mp: 95-97 °C; Purity by HPLC: 93%.

IR (KBr) : 3411, 3030, 2574, 1712, 1678, 1589, 1433, 1242, 1093, 950 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 2.48-2.57 (m, 5H), 3.19 (t, J = 6.1 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 7.89 (d, J = 8.4 Hz, 2H), 12.11 (bs, 1H, COOH)

ESI/MS (m/z) : 225.0 $(M+H)^+$

5.1.33.4. 4-(4-Methoxyphenyl)-4-oxobutanoic acid (19d)



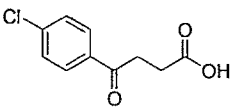
19d (17.06 g, 82%) was prepared from anisole (50 mL) and succinic anhydride (10 g, 99.93 mmol) according to the general procedure described above as white solid. mp: 113-115 °C; Purity by HPLC: 98%.

IR (KBr) : 3409, 3029, 1710, 1668, 1591, 1422, 1240, 1082, 951 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ2.81 (t, J = 6.5 Hz, 2H), 3.20 (t, J = 6.5 Hz, 2H), 3.77 (s, 3H), 6.84 (d, J = 8.2 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H)

ESI/MS (m/z) : 209.1 $(M+H)^+$

5.1.33.5. 4-(4-Chlorophenyl)-4-oxobutanoic acid (19e)



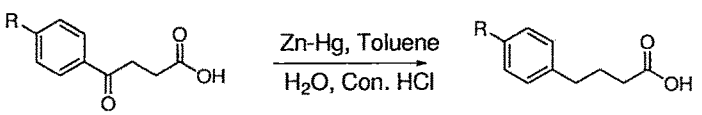
19e (15.94 g, 75%) was prepared from chlorobenzene (50 mL) and succinic anhydride (10 g, 99.93 mmol) according to the general procedure described above as white solid. mp: 116-118 °C; Purity by HPLC: 96%.

IR (KBr) : 3410, 1690, 1681, 1590, 1229, 928, 821 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ2.83 (t, J = 6.6 Hz, 2H), 3.21 (t, J = 6.6 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 214.0 $(M+H)^+$

5.1.34. General procedure for the preparation of the compounds 20a-e

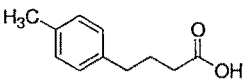


19a-e **20a-e**

Amalgamated zinc was prepared by stirring Zn powder (7 mole equivalent) and $HgCl_2$ (0.17 mole equivalent) in a mixture of water (4 fold) and Conc. HCl (0.11 fold) for 5 minutes. Supernatant was decanted and to the residue was added **19** in tolune (2-fold), water (1.5 fold) and conc.HCl (3.5 fold). The reaction mixture was stirred under reflux for 24 hours. Organic layer was separated and the aqueous layer was extracted with diethylether. Combined organic extracts were

successively washed with water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield product **20a-e**.

5.1.34.1. 4-(4-Methylphenyl)-butanoic acid (20a)



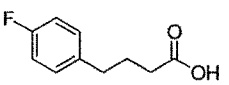
20a (8.44 g, 70%) was prepared from **19a** (13 g, 67.63 mmol) by following the general procedure described above as white solid. mp: 72-74 °C; Purity by HPLC: 98.7%.

IR (KBr) : 3043, 2923, 2871, 1691, 1515, 1280, 1209, 914 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.89-1.99 (m, 2H), 2.31 (s, 3H), 2.36 (t, J = 7.4 Hz, 2H), 2.63 (t, J = 7.4 Hz, 2H), 7.05-7.11 (m, 4H)

ESI/MS (m/z) : 217.1 $(M+K)^+$

5.1.34.2. 4-(4-Fluorophenyl)-butanoic acid (20b)



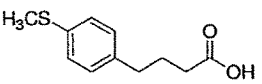
20b (1.95 g, 30%) was prepared from **19b** (7 g, 35.68 mmol) by following the general procedure described above as a liquid. Purity by HPLC: 95%.

IR (Neat) : 3020, 2929, 1708, 1600, 1510, 1217, 1112, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.89-1.99 (m, 2H), 2.36 (t, J = 7.4 Hz, 2H), 2.64 (t, J = 7.4 Hz, 2H), 6.96 (t, J = 8.7 Hz, 2H), 7.11-7.15 (m, 2H)

ESI/MS (m/z) : 200.0 $(M+NH_4)^+$

5.1.34.3. 4-(4-(Methylthio)phenyl)-butanoic acid (20c)



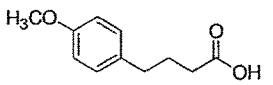
20c (7.68 g, 63%) was prepared from **19c** (13 g, 57.96 mmol) by following the general procedure described above as white solid. mp: 126-128 °C; Purity by HPLC: 94%.

IR (KBr) : 3020, 2930, 1712, 1251, 1194, 1188, 1020, 929 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.87-1.90 (m, 2H), 2.36 (t, J = 6.7 Hz, 2H), 2.47 (s, 3H), 2.73 (t, J = Hz, 2H), 7.01 (d, J = Hz, 2H), 7.21 (d, J = Hz, 2H)

ESI/MS (m/z) : 233.1 $(M+Na)^+$

5.1.34.4. 4-(4-Methoxyphenyl)-butanoic acid (20d)



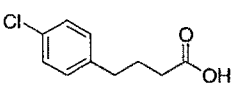
20d (13.85 g, 90%) was prepared from **19d** (16.5 g, 79.25 mmol) by follwing the general procedure described above as white solid. mp: 65-67 °C; Purity by HPLC: 95%.

IR (KBr) : 3018, 2914, 1697, 1610, 1512, 1299, 1245, 1180, 1029, 929 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.90-1.98 (m, 2H), 2.35 (t, J = 7.4 Hz, 2H), 2.61 (t, J = 7.4 Hz, 2H), 3.78 (s, 3H), 6.82 (d, J = 8.5 Hz, 2H), 7.09 (d, J = 8.5 Hz, 2H)

ESI/MS (m/z) : 217.2 $(M+Na)^+$

5.1.34.5. 4-(4-Chlorophenyl)-butanoic acid (20e)



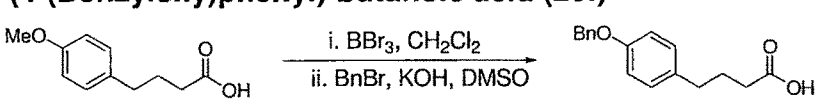
20e (10.72 g, 74%) was prepared from **19e** (15.5 g, 72.9 mmol) by following the general procedure described above as a liquid. Purity by HPLC: 96%.

IR (Neat) : 3068, 1681, 1592, 1231, 924, 819 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.89-1.93 (m, 2H), 2.29 (t, J = Hz, 2H), 2.80 (t, J = Hz, 2H), 7.29 (d, J = Hz, 2H), 7.82 (d, J = Hz, 2H)

ESI/MS (m/z) : 222.1 $(M+Na)^+$

5.1.35. 4-(4-(Benzyloxy)phenyl)-butanoic acid (20f)



20f

Step I: A solution of **20d** (10 g, 0.052 mol) in dichloromethane (100 ml) was cooled to –40 °C and BBr_3 (25.8 g, 0.103 mol) was added drop wise and the reaction mixture was stirred at ambient temperature for 4 hours. Reaction mixture was poured into ice cold water (200 ml) and the organic layer was separated. Aqueous layer was extracted with dichloromethane (2 x 100 ml). The combined organic extract was washed with water (100 ml), dried over $CaCl_2$, filtered and concentrated under vacuum. The crude product was purified through column chromatography using 15 % ethyl acetate in hexane as eluent to obtain 9.0 g of product as white solid which was directly taken for the next step.

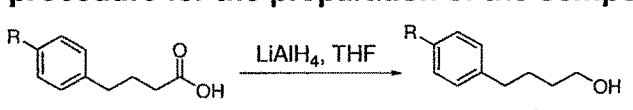
Step II: A solution of the product of **step I** (9.0 g, 0.05 mol) in DMSO (50 mL) was cooled to 0 °C and KOH (22.42 g, 0.40 mol) was added followed by drop wise addition of BnBr (20.50 g, 0.12 mole) and the reaction mixture was stirred at ambient temperature for 2 hours. Reaction mixture was poured into water (250 ml), stirred at 25 °C for 30 min and extracted with ethyl acetate (3 x 100 ml). The combined organic extract was successively washed with water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield 11.7 g (87%) product **20f** as white solid. mp: 146-148 °C; Purity by HPLC: 98.8%.

IR (Neat) : 3429, 3058, 2912, 1706, 1608, 1512, 1409, 1380, 1211, 1022, 910 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ1.62-1.72 (m, 2H), 1.99 (t, J = 7.3 Hz, 2H), 2.45 (t, J = 7.7 Hz, 2H), 5.03 (s, 2H), 6.88 (d, J = 8.4 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 7.27-7.43 (m, 5H)

ESI/MS (m/z) : 309.1 $(M+K)^+$

5.1.36. General procedure for the preparation of the compounds 21a-f

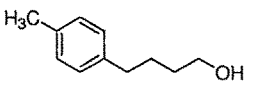


20a-f **21a-f**

To an ice-cold solution of **20a-f** in dry THF (10 fold) was added $LiAlH_4$ (2 mole equivalent) in small portions over a period of 30 minutes and the reaction mixture was stirred for 4 hours at 25 °C. The reaction mixture was quenched with

saturated solution of Na_2SO_4 till white solids were separated. The solids were filtered and washed with hot ethyl acetate. The combined filtrate was dried over Na_2SO_4, filtered and concentrated on rotavapor under vacuum to yield product **21a-f**.

5.1.36.1. 4-(4-Methylphenyl)-butanol (21a)



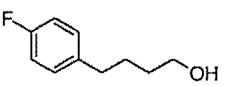
21a (6.56 g, 89%) was prepared from **20a** (8 g, 44.89 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 93.3%.

IR (Neat) : 3354, 3051, 2933, 2860, 1645, 1515, 1454, 1112, 617 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.32 (bs, 1H, OH), 1.55-1.72 (m, 4H), 2.31 (s, 3H), 2.60 (t, J = 7.2 Hz, 2H), 3.64 (t, J = 5.9 Hz, 2H), 7.05-7.14 (m, 4H)

ESI/MS (m/z) : 182.0 $(M+NH_4)^+$

5.1.36.2. 4-(4-Fluorophenyl)-butanol (21b)



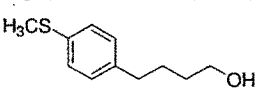
21b (1.48 g, 89%) was prepared from **20b** (1.8 g, 9.88 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 96%.

IR (Neat) : 3352, 2935, 1510, 1220, 1101, 1066, 833 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (bs, 1H, OH), 1.59-1.70 (m, 4H), 2.61 (t, J = 7.2 Hz, 2H), 3.66 (t, J = 6.1 Hz, 2H), 6.95 (t, J = 8.7 Hz, 2H), 7.10-7.15 (m, 2H)

ESI/MS (m/z) : 169.1.2$(M+H)^+$

5.1.36.3. 4-(4-Methylthiophenyl)-butanol (21c)



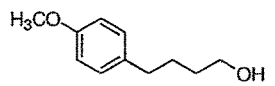
21c (5.39 g, 77%) was prepared from **20c** (7.5 g, 35.66 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 96%.

IR (Neat) : 3346, 2933, 2858, 1633,1497, 1434, 1095, 1031 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.27 (bs, 1H, OH), 1.55-1.72 (m, 4H), 2.46 (s, 3H), 2.60 (t, J = 7.2 Hz, 2H), 3.65 (t, J= 5.8 Hz, 2H), 7.10 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 214.2 $(M+NH_4)^+$

5.1.36.4. 4-(4-Methoxyphenyl)-butanol (21d)



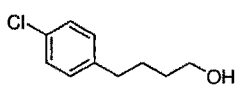
21d (2.27 g, 70%) was prepared from **20d** (3.5 g, 18.02 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 96%.

IR (Neat) : 3381, 3031, 2960, 1508, 1430, 1085, 1036, 929 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.60-1.65 (m, 4H), 2.59 (t, J = Hz, 2H), 3.62 (t, J = Hz, 2H), 3.74 (s, 3H), 6.80 (d, J = Hz, 2H), 7.01 (d, J = Hz, 2H)

ESI/MS (m/z) : 181.1 $(M+H)^+$

5.1.36.5. 4-(4-Chlorophenyl)-butanol (21e)



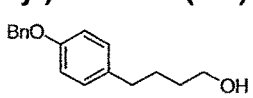
21e (6.93 g, 71%) was prepared from **20e** (10.5 g, 52.86 mmol) according to the general procedure described above as a liquid.

IR (Neat) : 3348, 2934, 1490, 1401, 1209, 1169, 969, 930 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.56-1.60 (m, 4H), 2.60 (t, J = Hz, 2H), 3.64 (t, J = Hz, 2H), 7.23 (d, J = Hz, 2H), 7.78 (d, J = Hz, 2H)

ESI/MS (m/z) : 202.1 $(M+NH_4)^+$

5.1.36.6. 4-(4-Benzyloxyphenyl)-butanol (21f)



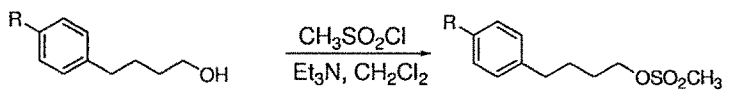
21f (8.94 g, 82%) was prepared from **20f** (11.5 g, 42.54 mmol) according to the general procedure described above as white solid. mp 66-68 °C; Purity by HPLC: 96%.

IR (KBr) : 3381, 2928, 1612, 1512, 1454, 1379, 1247, 1174, 1012, 738 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.55-1.68 (m, 4H), 2.57 (t, J = 6.9 Hz, 2H), 3.63 (t, J = 6.0 Hz, 2H), 5.04 (s, 2H), 6.89 (d, J = 8.5 Hz, 2H), 7.10 (d, J = 8.4 Hz, 2H), 7.26-7.43 (m, 5H)

ESI/MS (m/z) : 274.2 $(M+NH_4)^+$

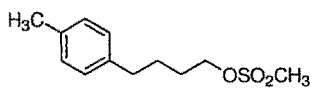
5.1.37. General procedure for the preparation of the compounds 22a-f



21a-f **22a-f**

To an ice-cold solution of **21a-f** in dichloromethane (5 fold) were added triethylamine (1.2 mole equivalent) followed by dropwise addition of methanesulfonylchloride (1.1 mole equivalent) at 10 °C and the reaction mixture was stirred at ambient temperature for 4 hours. The reaction mixture was diluted with chloroform and successively washed with water, 1N HCl, again water and finally with sodium bicarbonate solution. The organic extract was dried over $CaCl_2$ and concentrated under vacuum to obtain the title products **22a-f**.

5.1.37.1. 4-(4-Methylphenyl)-butyl methanesulfonate (22a)



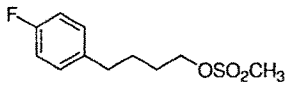
22a (9.02 g, 97%) was prepared from **21a** (6.3 g, 38.36 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 92%.

IR (Neat) : 2939, 1515, 1460, 1353, 1174, 1114, 974, 933, 771 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.60-1.75 (m, 4H), 2.32 (s, 3H), 2.61 (t, J = 6.9 Hz, 2H), 2.98 (s, 3H), 4.23 (t, J = 5.9 Hz, 2H), 7.04-7.15 (m, 4H)

ESI/MS (m/z) : 260.1 $(M+NH_4)^+$

5.1.37.2. 4-(4-Fluorophenyl)-butyl methanesulfonate (22b)



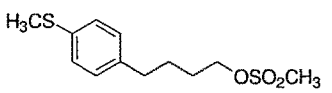
22b (1.71 g, 90%) was prepared from **21b** (1.3 g, 7.73 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 98%.

IR (Neat) : 3033, 2941, 2864, 1600, 1510, 1353, 1218, 1174, 974, 933 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.69-1.75 (m, 4H), 2.63 (t, J = 6.9 Hz, 2H), 2.99 (s, 3H), 4.23 (t, J = 5.9 Hz, 2H), 6.97 (t, J = 8.7 Hz, 2H), 7.10-7.14 (m, 2H)

ESI/MS (m/z) : 264.0 $(M+NH_4)^+$

5.1.37.3. 4-(4-Methylthiophenyl)-butyl methanesulfonate (22c)



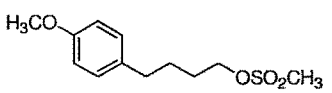
22c (6.71 g, 96%) was prepared from **21c** (5 g, 25.47 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 96%.

IR (Neat) : 3020, 2923, 2860, 1494, 1352, 1174, 1093, 933 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.70-1.79 (m, 4H), 2.47 (s, 3H), 2.62 (t, J = 6.9 Hz, 2H), 2.98 (s, 3H), 4.23 (t, J = 5.9 Hz, 2H), 7.10 (d, J = 8.1 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 297.1 $(M+Na)^+$

5.1.37.4. 4-(4-Methoxyphenyl)-butyl methanesulfonate (22d)



22d (2.59 g, 86%) was prepared from **21d** (2.1 g, 11.65 mmol) according to the general procedure described above as a liquid.

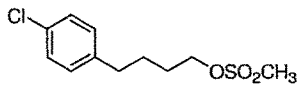
IR (Neat) : 2919, 1490, 1368, 1170, 1089, 937 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.63-1.70 (m, 4H), 2.63 (t, J = 6.9 Hz, 2H), 2.99 (s, 3H), 3.74 (s, 3H), 4.22 (t, J = 6.0 Hz, 2H), 6.80 (d, J = 8.5 Hz,

2H), 7.02 (d, J = 8.4 Hz, 2H)

ESI/MS (m/z) : 259.1 $(M+H)^+$

5.1.37.5. 4-(4-Chlorophenyl)-butyl methanesulfonate (22e)



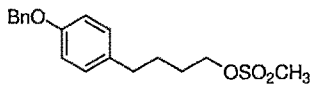
22e (8.32 g, 90%) was prepared from **21e** (6.5 g, 35.2 mmol) according to the general procedure described above as a liquid.

IR (Neat) : 2939, 1512, 1369, 1211, 1178, 971, 931 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.64-1.70 (m, 4H), 2.64 (t, J = 6.8 Hz, 2H), 3.0 (s, 3H), 4.23 (t, J = 6.2 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 263.1 $(M+H)^+$

5.1.37.6. 4-(4-Benzyloxyphenyl)-butyl methanesulfonate (22f)



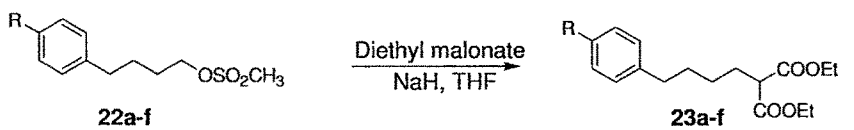
22f (9.43 g, 85%) was prepared from **21f** (8.5 g, 33.16 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 93%.

IR (Neat) : 3028, 2868, 2993, 1610, 1510, 1355, 1217, 1174, 935, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.65-1.79 (m, 4H), 2.60 (t, J = 6.9 Hz, 2H), 2.97 (s, 3H), 4.22 (t, J = 6.0 Hz, 2H), 5.04 (s, 2H), 6.89 (d, J = 8.5 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 7.31-7.44 (m, 5H)

ESI/MS (m/z) : 352.2 $(M+NH_4)^+$

5.1.38. General procedure for the preparation of the compounds 23a-f

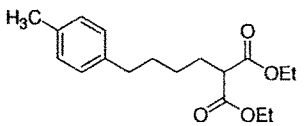


22a-f **23a-f**

To an ice-cold suspension of NaH (1.5 mole equivalent) in THF (2 fold), diethyl malonate (3 mole equivalent) was added drop wise over a period of 30 min at 0-

10 °C and stirred at the same temperature for 30 min. A solution of **22a-f** in THF (3 fold) was added to the reaction mixture at 25 °C and stirred at 60 °C under nitrogen atmosphere for 72 hours. The reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic layer was successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. Excess diethyl malonate was distilled out under vacuum to give the tittle compounds **23a-f**.

5.1.38.1. Diethyl-2-(4-(4-methylphenyl)-butyl)-malonate (23a)



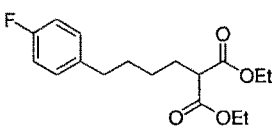
23a (9.89 g, 92%) was prepared from **22a** (8.5 g, 35.08 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 93.8%.

IR (Neat) : 2927, 2856, 1733, 1514, 1463, 1141 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, J = 7.0 Hz, 6H), 1.34-1.40 (m, 2H), 1.59-1.66 (m, 2H), 1.87-1.95 (m, 2H), 2.30 (s, 3H), 2.56 (t, J = 7.5 Hz, 2H), 3.31 (t, J = 7.5 Hz, 1H), 4.18 (q, J = 7.2 Hz, 4H), 7.03-7.09 (m, 4H)

ESI/MS (m/z) : 307.2 $(M+H)^+$

5.1.38.2. Diethyl-2-[4-(4-fluorophenyl)-butyl]-malonate (23b)



23b (1.63 g, 86%) was prepared from **22b** (1.5 g, 6.09 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 96%.

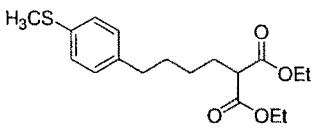
IR (Neat) : 2985, 2862, 1728, 1510, 1446, 1215, 759 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, J=7.0 Hz, 6H), 1.33-1.36 (m, 2H), 1.59-1.64 (m, 2H), 1.87-1.95 (m, 2H), 2.57 (t, J = 7.5 Hz, 2H), 3.30 (t, J = 11.6 Hz, 1H), 4.18 (q, J = 7.2 Hz, 4H), 6.94 (t, J = 8.7 Hz,

2H), 7.08-7.12 (m, 2H)

ESI/MS (m/z) : 333.2 $(M+Na)^+$

5.1.38.3. Diethyl 2-(4-(4-(methylthio)-phenyl)-butyl)-malonate (23c)



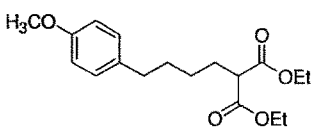
23c (6.41 g, 80%) was prepared from **22c** (6.5 g, 23.69 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 95.7%.

IR (Neat) : 2927, 2856, 1732, 1494, 1369, 1274, 1176, 1028 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, *J* = 7.0 Hz, 6H), 1.33-1.39 (m, 2H), 1.55-1.65 (m, 2H), 1.73-1.93 (m, 2H), 2.46 (s, 3H), 2.54 (t, *J* = 8.5 Hz, 2H), 2.88 (t, *J* = 7.5 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 4H), 7.08 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H)

ESI/MS (m/z) : 339.2 $(M+H)^+$

5.1.38.4. Diethyl 2-(4-(4-methoxyphenyl)-butyl)-malonate (23d)



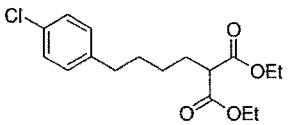
23d (2.85 g, 95%) was prepared from **22d** (2.4 g, 9.29 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 96.7%.

IR (Neat) : 2929, 2858, 1732, 1612, 1512, 1299, 1247, 1033, 827 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, *J* = 7.0 Hz, 6H), 1.34-1.40 (m, 2H), 1.56-1.66 (m, 2H), 1.91 (q, *J* = 8.0 Hz, 2H), 2.54 (t, *J* = 8.5 Hz, 2H), 3.30 (t, *J* = 7.5 Hz, 1H), 3.78 (s, 3H), 4.18 (q, *J* = 7.1 Hz, 4H), 6.81 (d, *J* = 8.5 Hz, 2H), 7.07 (d, *J* = 8.5 Hz, 2H)

ESI/MS (m/z) : 323.3 $(M+H)^+$

5.1.38.5. Diethyl 2-(4-(4-chlorophenyl)-butyl)-malonate (23e)



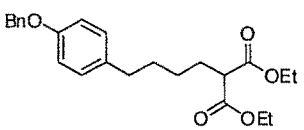
23e (9.05 g, 91%) was prepared from **22e** (8 g, 30.45 mmol) according to the general procedure described above as a liquid.

IR (Neat) : 2990, 1729, 1220, 759 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, J = 7.0 Hz, 6H), 1.33-1.36 (m, 2H), 1.60-1.65 (m, 2H), 1.91 (q, J = 8.0 Hz, 2H), 2.57 (t, J = 7.5 Hz, 2H), 3.35 (t, J = 7.5 Hz, 1H), 4.19 (q, J = 7.2 Hz, 4H), 6.99-7.10 (m, 4H)

ESI/MS (m/z) : 327.1 $(M+H)^+$

5.1.38.6. Diethyl 2-(4-(4-benzyloxyphenyl)-butyl)-malonate (23f)



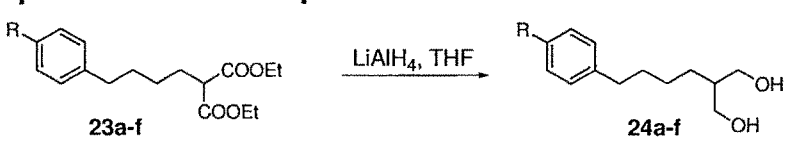
23f (9.54 g, 89%) was prepared from **22f** (9 g, 26.91 mmol) according to the general procedure described above as a liquid.

IR (Neat) : 2930, 1740, 1500, 1430, 1275, 1177, 1028, 828 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, J = 7.0 Hz, 6H), 1.33-1.40 (m, 2H), 1.55-1.66 (m, 2H), 1.91 (q, J = 8.0 Hz, 2H), 2.54 (t, J = 8.5 Hz, 2H), 3.31 (t, J = 7.5 Hz, 1H), 4.18 (q, J = 7.1 Hz, 4H), 5.01 (s, 2H), 6.78-6.83 (m, 2H), 6.87 (dd, J = 8.8 & 2.0 Hz, 2H), 7.29-7.43 (m, 5H)

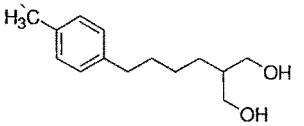
ESI/MS (m/z) : 399.2 $(M+H)^+$

5.1.39. Preparation of the compounds 24a-f



23a-f **24a-f**

5.1.39.1. 2-(4-(4-Methylphenyl)-butyl)-propane-1,3-diol (24a)



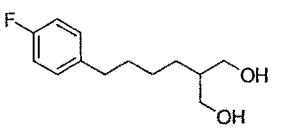
24a (0.899 g, 62%) was prepared from **23a** (2 g, 6.53 mmol) according to the general procedure described for compound **3** as white solid. mp : 71-73 °C; Purity by HPLC: 98.8%.

IR (KBr) : 3298, 2927, 2856, 1514, 1463, 1242, 1001, 763 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25-1.39 (m, 4H), 1.55-1.64 (m, 2H), 1.74-1.76 (m, 1H), 2.26 (bs, 2H, OH), 2.31 (s, 3H), 2.55 (t, J = 7.5 Hz, 2H), 3.64 (t, J = 11.6 Hz, 2H), 3.80 (d, J = 13.6 Hz, 2H), 7.03-7.10 (m, 4H)

ESI/MS (m/z) : 245.2 $(M+Na)^+$

5.1.39.2. 2-[4-(4-Fluorophenyl)-butyl]-propane-1,3-diol (24b)



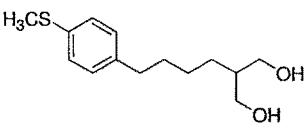
24b (0.612 g, 56%) was prepared from **23b** (1.5 g, 4.83 mmol) according to the general procedure described for compound **3** as a liquid. Purity by HPLC: 93.4%.

IR (Neat) : 3357, 2931, 2858, 1510, 1218, 1110, 1037, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25-1.31 (m, 2H), 1.33-1.36 (m, 2H), 1.55-1.64 (m, 2H), 1.65-1.75 (m, 1H), 2.57 (t, J = 7.5 Hz, 2H), 3.64 (dd, J = 11.6 Hz, 2H), 3.81 (dd, J = 11.8 & 4.6 Hz, 2H), 6.95 (t, J = 10 & 7.5 Hz, 2H), 7.08-7.13 (m, 2H)

ESI/MS (m/z) : 249.1 $(M+Na)^+$

5.1.39.3. 2-[4-(4-Methylsulfanylphenyl)-butyl]-propane-1,3-diol (24c)



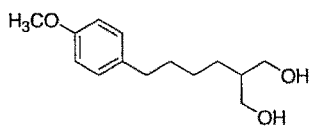
24c (1.13 g, 50%) was prepared from **23c** (3 g, 8.86 mmol) according to the general procedure described for compound **3** as a liquid. Purity by HPLC: 94.8%.

IR (Neat) : 3357, 1741, 1492, 1218, 1110, 1037, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.99-1.06 (m, 2H), 1.22-1.32 (m, 2H), 1.53-1.62 (m, 2H), 1.98-2.02 (m, 1H), 2.46 (s, 3H), 2.51 (t, J = 7.6 Hz, 2H), 3.33 (t, J = 11.6 Hz, 2H), 3.89 (dd, J = 11.9 & 4.5 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 277.2 $(M+Na)^+$

5.1.39.4. 2-[4-(4-Methoxyphenyl)-butyl]-propane-1,3-diol (24d)



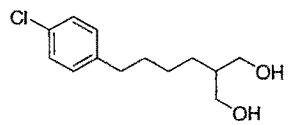
24d (1.66 g, 90%) was prepared from **23d** (2.5 g, 7.75 mmol) according to the general procedure described for compound **3** as white solid. mp: 59-60 °C; Purity by HPLC: 94.6%.

IR (KBr) : 3282, 2929, 2852, 1610, 1512, 1299, 1245, 1035, 827 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25-1.36 (m, 4H), 1.53-1.59 (m, 2H), 1.62-1.75 (m, 1H), 2.21 (t, J = 4.5 Hz, 2H, OH), 2.55 (t, J = 7.5 Hz, 2H), 3.60-3.68 (m, 2H), 3.68 (s, 3H), 3.80-3.83 (m, 2H), 6.81 (d, J = 8.5 Hz, 2H), 7.08 (d, J = 8.5 Hz, 2H)

ESI/MS (m/z) : 261.0 $(M+Na)^+$

5.1.39.5. 2-[4-(4-Chlorophenyl)-butyl]-propane-1,3-diol (24e)



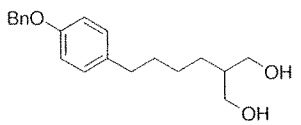
24e (1.34 g, 75%) was prepared from **23e** (2 g, 6.12 mmol) according to the general procedure described for compound **3** as a liquid. Purity by HPLC: 95.8%.

IR (Neat) : 3357, 1741, 1492, 1218, 1110, 1037, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.99-1.06 (m, 2H), 1.22-1.32 (m, 2H), 1.58-1.62 (m, 2H), 1.98-2.02 (m, 1H), 2.20 (bs, 2H, OH), 2.51 (t, J = 7.6 Hz, 2H), 3.33 (t, J = 11.6 Hz, 2H), 3.89 (dd, J = 11.9 & 4.5 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 265.2 $(M+Na)^+$

5.1.39.6. 2-[4-(4-Benzyloxyphenyl)-butyl]-propane-1,3-diol (24f)



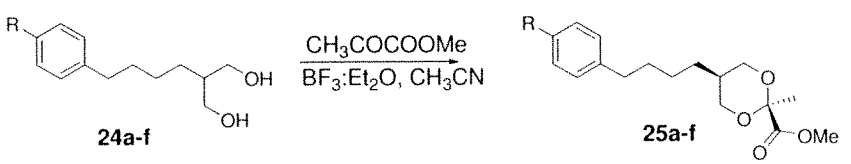
24f (1.12 g, 71%) was prepared from **23f** (2 g, 5.02 mmol) according to the general procedure described for compound **3** as a liquid.

IR (Neat) : 3282, 3062, 2854, 1608, 1512, 1247, 1002, 964 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.23-1.36 (m, 4H), 1.53-1.56 (m, 2H), 1.73-1.78 (m, 1H), 2.18 (bs, 2H, OH), 2.55 (t, J = 7.6 Hz, 2H), 3.64 (t, J = 11.6 Hz, 2H), 3.80 (dd, J = 12 & 5.2 Hz, 2H), 5.03 (s, 2H), 6.89 (d, J=11.2 Hz, 2H), 7.07 (d, J=8.4 Hz, 2H), 7.29-7.44 (m, 5H)

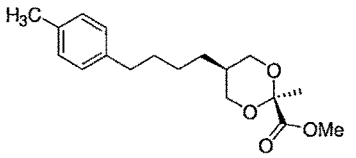
ESI/MS (m/z) : 337.0$(M+Na)^+$

5.1.40. Preparation of the compounds 25a-f



Compounds **25a-f** were prepared by means of a procedure similar to that reported for compound **4a.**

5.1.40.1. Methyl-2-methyl-*c*-5-(4-(4-methylphenyl)-butyl)-[1,3]-dioxane-*r*-2-carboxylate (25a)



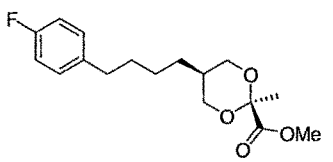
25a (0.816 g, 79%) was prepared from **24a** (0.75 g, 3.37 mmol) according to the procedure described for the preparation of the compound **4a** as a liquid. Purity by HPLC: 92%.

IR (Neat) : 3020, 2931, 2858, 1743, 1514, 1215, 1143, 1118, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.02-1.09 (m, 2H), 1.23-1.31 (m, 2H), 1.51-1.64 (m, 5H), 1.95-2.05 (m, 1H), 2.31 (s, 3H), 2.54 (t, J = 7.5 Hz, 2H), 3.44 (t, J = 11.6 Hz, 2H), 3.82 (s, 3H), 3.96 (dd, J = 11.8 & 4.6 Hz, 2H), 7.01-7.09 (m, 4H)

ESI/MS (m/z) : 329.2 $(M+Na)^+$

5.1.40.2. Methyl-*c*-5-[4-(4-fluorophenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (25b)



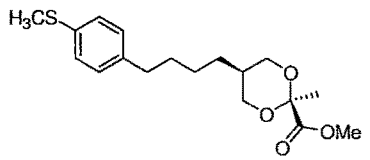
25b (0.55 g, 81%) was prepared from **24b** (0.5 g, 2.21 mmol) according to the procedure described for the preparation of the compound **4a** as a liquid. Purity by HPLC: 98.6%.

IR (Neat) : 3020, 2933, 1743, 1600, 1500, 1215, 1145, 1120, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.01-1.06 (m, 2H), 1.25-1.33 (m, 2H), 1.50 (s, 3H), 1.58-1.63 (m, 2H), 1.95-2.05 (m, 1H), 2.53 (t, J = 7.5 Hz, 2H), 3.37 (t, J = 11.6 Hz, 2H), 3.82 (s, 3H), 3.93 (dd, J = 11.8 & 4.7 Hz, 2H), 6.95 (t, J = 8.6 Hz, 2H), 7.06-7.11 (m, 2H)

ESI/MS (m/z) : 328.2 $(M+NH_4)^+$

5.1.40.3. Methyl-2-methyl-*c*-5-[4-(4-methylsulfanylphenyl)-butyl]-[1,3]-dioxane-*r*-2-carboxylate (25c)



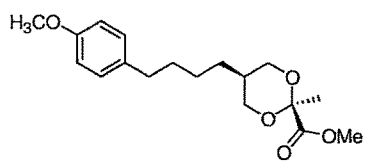
25c (0.665 g, 50%) was prepared from **24c** (1 g, 3.93 mmol) according to the procedure described for the preparation of **4a** as white solid. **mp:** 54-55 °C; Purity by HPLC: 96.6%.

IR (KBr) : 2925, 2889, 2854, 1741, 1629, 1492, 1271, 1022 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.99-1.06 (m, 2H), 1.22-1.32 (m, 2H), 1.50 (s, 3H), 1.53-1.62 (m, 2H), 1.98-2.02 (m, 1H), 2.46 (s, 3H), 2.51 (t, J = 7.6 Hz, 2H), 3.33 (t, J = 11.6 Hz, 2H), 3.82 (s, 3H), 3.89 (dd, J = 11.9 & 4.5 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 361.3 $(M+Na)^+$

5.1.40.4. Methyl-*c*-5-[4-(4-methoxyphenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (25d)



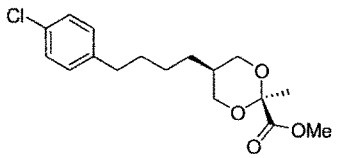
25d (1.44 g, 71%) was prepared from **24d** (1.5 g, 6.29 mmol) according to the procedure described for the preparation of **4a** as a liquid. Purity by HPLC: 97.8%.

IR (Neat) : 2929, 2880, 2850, 1727, 1556, 1228, 1136, 823 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.02-1.09 (m, 2H), 1.23-1.30 (m, 2H), 1.50-1.52 (m, 2H), 1.60 (s, 3H), 1.98-2.0 (m, 1H), 2.52 (t, J = 7.56 Hz, 2H), 3.44 (t, J = 11.56 Hz, 2H), 3.78 (s, 3H), 3.82 (s, 3H), 3.96 (dd, J = 11.91& 4.42 Hz, 2H), 6.83 (d, J = 8.47 Hz, 2H), 7.07 (d, J = 8.42Hz, 2H)

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

5.1.40.5. Methyl-*c*-5-[4-(4-chlorophenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (25e)



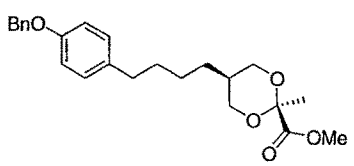
25e (1.1 g, 68%) was prepared from **24e** (1.2 g, 4.94 mmol) according to the procedure described for the preparation of **4a** as a liquid. Purity by HPLC: 96.5%.

IR (Neat) : 2936, 1741, 1516, 1238, 1136, 813 $cm^{-1}cm^{-1}$

^{1}HNMR ($CDCl_3$) : δ 0.94-1.00 (m, 2H), 1.15-1.21 (m, 2H), 1.29 (s, 3H), 1.36-1.47 (m, 2H), 1.75-1.83 (m, 1H), 2.37 (t, J = 7.5 Hz, 2H), 3.22 (t, J = 11.5 Hz, 2H), 3.82 (s, 3H), 3.86 (dd, J = 11.7 & 4.4 Hz, 2H), 6.61 (d, J = 8.3 Hz, 2H), 6.91 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 349.1 $(M+Na)^+$

5.1.40.6. Methyl-c-5-[4-(4-benzyloxyphenyl)-butyl]-2-methyl-[1,3]-dioxane-r-2-carboxylate (25f)



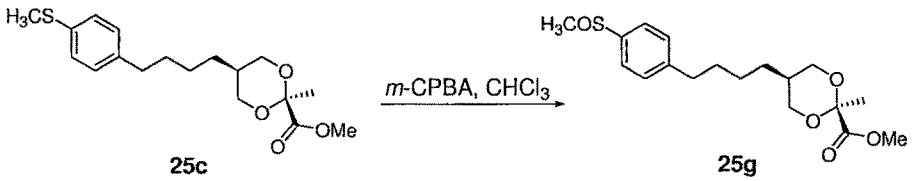
25f (0.583 g, 46%) was prepared from **24f** (1 g, 3.18 mmol) according to the procedure described for the preparation of **4a** as white solid. mp: 54-55 °C; Purity by HPLC: 98.7%.

IR (KBr) : 3001, 2852, 1739, 1608, 1510, 1236, 1047, 808 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.99-1.06 (m, 2H), 1.22-1.32 (m, 2H), 1.50 (s, 3H), 1.55-1.61 (m, 2H), 1.96-2.02 (m, 1H), 2.49 (t, J = 7.6 Hz, 2H), 3.33 (t, J = 11.6 Hz, 2H), 3.82 (s, 3H), 3.93 (dd, J = 11.9 & 4.5 Hz, 2H), 5.06 (s, 2H), 6.87 (d, J = 8.1 Hz, 2H), 7.04 (d, J = 8.1 Hz, 2H), 7.29-7.44 (m, 5H)

ESI/MS (m/z) : 416.2 $(M+NH_4)^+$

5.1.41. Methyl-2-methyl-*c*-5-[4-(4-methylsulfinylphenyl)-butyl]-[1,3]-dioxane-*r*-2-carboxylate (25g)



25c 25g

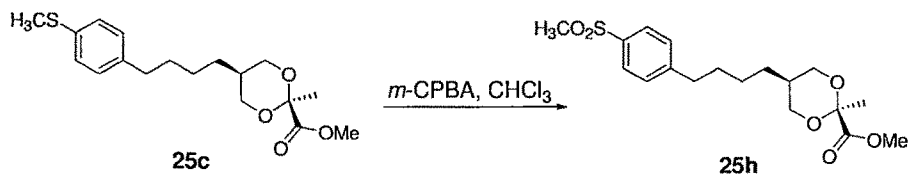
To an ice-cold solution of **25c** (1.0 g, 2.95 mmol) in chloroform (10 ml) was added *m*-CPBA (0.48 g, 2.81 mmol) at 10 °C and the reaction mixture was stirred at the same temperature for 30 min. The reaction mixture was diluted with chloroform (40 mL) and successively washed with water and sodium bicarbonate solution. The organic phase was dried over $CaCl_2$, filtered and concentrated under vacuum. The crude product was purified by column chromatography using 15% ethyl acetate in hexane as eluent to obtain 860mg (64%) of title product **25g** as a liquid. Purity by HPLC: 98.4%.

IR (Neat) : 3010, 2832, 1741, 1492, 1271, 1022 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.99-1.06 (m, 2H), 1.22-1.32 (m, 2H), 1.50 (s, 3H), 1.53-1.62 (m, 2H), 1.98-2.02 (m, 1H), 2.72 (s, 3H), 2.51 (t, J = 7.6 Hz, 2H), 3.33 (t, J = 11.6 Hz, 2H), 3.82 (s, 3H), 3.89 (dd, J = 11.9 & 4.5 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 377.3 $(M+Na)^+$

5.1.42. Methyl-2-methyl-*c*-5-[4-(4-methylsulfonylphenyl)-butyl]-[1,3]-dioxane-*r*-2-carboxylate (25h)



25c 25h

To an ice-cold solution of **25c** (1.0 g, 2.95 mmol) in chloroform (10 ml) was added *m*-CPBA (1.53 g, 8.86 mmol) at 25 °C and the reaction mixture was stirred at the same temperature for 2 hours. The reaction mixture was diluted with chloroform and successively washed with water and sodium bicarbonate

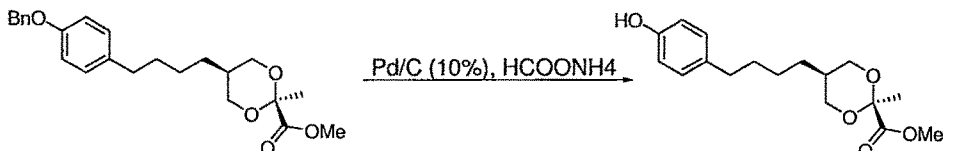
solution. The organic phase was dried over $CaCl_2$, filtered and concentrated under vacuum. The crude product was purified by column chromatography using 9% ethyl acetate in hexane as eluent to obtain 630 mg (58%) of title product **25h** as a liquid. Purity by HPLC: 96.8%.

IR (Neat) : 3020, 2910, 1741, 1492, 1271, 1022 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.99-1.06 (m, 2H), 1.22-1.32 (m, 2H), 1.50 (s, 3H), 1.53-1.62 (m, 2H), 1.98-2.02 (m, 1H), 3.05 (s, 3H), 2.51 (t, J = 7.6 Hz, 2H), 3.33 (t, J = 11.6 Hz, 2H), 3.82 (s, 3H), 3.89 (dd, J = 11.9 & 4.5 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 393.3 $(M+Na)^+$

5.1.43. Methyl-*c*-5-[4-(4-hydroxyphenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (25i)



25f 25i

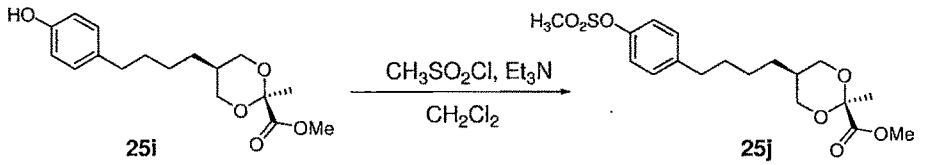
25i (0.588 g, 76%) was prepared from **25f** (1 g, 2.51 mmol) by means of a procedure similar to that reported for compound **4c** as a liquid. Purity by HPLC: 98.5%.

IR (Neat) : 3015, 2911, 1730, 1524, 1232, 1140, 813 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.92-1.00 (m, 2H), 1.13-1.22 (m, 2H), 1.31 (s, 3H), 1.38-1.52 (m, 2H), 1.75-1.83 (m, 1H), 2.37 (t, J = 7.5 Hz, 2H), 3.22 (t, J = 11.5 Hz, 2H), 3.76 (dd, J = 11.7 & 4.4 Hz, 2H), 3.86 (s, 3H), 6.61 (d, J = 8.3 Hz, 2H), 6.91 (d, J = 8.2 Hz, 2H), 9.06 (bs, 1H, OH)

ESI/MS (m/z) : 309.1 $(M+H)^+$

5.1.44. Methyl-*c*-5-[4-(4-methanesulfonyloxyphenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (25j)



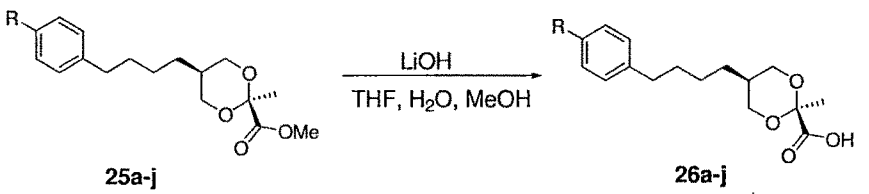
25j (0.5 g, 80%) was prepared from **25i** (0.5 g, 1.62 mmol) by means of a procedure similar to that reported for compound **17i** as a liquid. Purity by HPLC: 98.2%.

IR (Neat) : 3020, 2937, 1743, 1602, 1504, 1371, 1215, 758 cm^{-1}

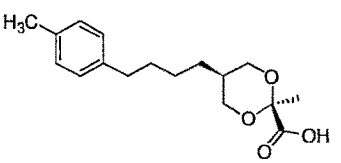
^{1}HNMR ($CDCl_3$) : δ 1.00-1.05 (q, J = 7.5 Hz, 2H), 1.29-1.34 (m, 2H), 1.50 (s, 3H), 1.57-1.63 (m, 2H), 1.98-2.03 (m, 1H), 2.59 (t, J = 7.6 Hz, 2H), 3.12 (s, 3H), 3.34 (t, J = 11.6 Hz, 2H), 3.82 (s, 3H), 3.89 (dd, J = 4.7 & 11.9 Hz, 2H), 7.18 (bs, 4H)

ESI/MS (m/z) : 409.2 $(M+Na)^+$

5.1.45. Preparation of the compounds 26a-j



5.1.45.1. 2-Methyl-*c*-5-(4-(4-methylphenyl)-butyl)-[1,3]-dioxane-*r*-2-carboxylic acid (26a)



26a (0.547 g, 86%) was prepared from **25a** (0.7 g, 2.26 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 111-113 °C; Purity by HPLC: 99%.

IR (KBr) : 3377, 2927, 2871, 1647, 1608, 1510, 1284, 1207, 1159

1047 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.02-1.09 (m, 2H), 1.23-1.31 (m, 2H), 1.51-1.64 (m, 5H), 1.95-2.05 (m, 1H), 2.31 (s, 3H), 2.54 (t, J = 7.5 Hz, 2H), 3.44 (t, J = 11.6 Hz, 2H), 3.97 (dd, J = 11.8 & 4.6 Hz, 2H), 7.01-7.09 (m, 4H)

^{13}C NMR (DMSO-d_6) : δ 20.63, 25.34, 25.63, 27.38, 31.24, 32.92, 34.54, 67.32, 97.76, 128.11, 128.61, 134.44, 139.04, 171.46

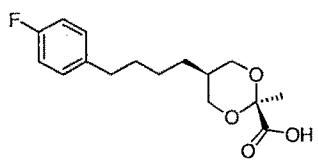
ESI/MS (m/z) : 310.2 $(M+NH_4)^+$

Analysis **Mol.Formula:** $C_{17}H_{24}O_4$

Calculated : C, 69.84%; H, 8.27%

Found : C, 69.47%; H, 8.32%

5.1.45.2. *c*-5-[4-(4-Fluorophenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (26b)



26b (0.378 g, 88%) was prepared from **25b** (0.45 g, 1.45 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 90-92 °C; Purity by HPLC: 98%.

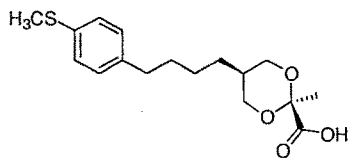
IR (KBr) : 3435, 2933, 2858, 1718, 1600, 1508, 1284, 1170 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.02-1.10 (m, 2H), 1.23-1.33 (m, 2H), 1.51-1.67 (m, 5H), 1.95-2.05 (m, 1H), 2.55 (t, J = 7.5 Hz, 2H), 3.44 (t, J = 11.5 Hz, 2H), 3.97 (dd, J = 11.8 & 4.6 Hz, 2H), 6.95 (t, J = 8.6 Hz, 2H), 7.06-7.14 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 25.33, 25.65, 27.47, 31.41, 33.05, 33.93, 67.07, 98.07, 115.01, 128.64, 132.14, 155.25, 171.60

ESI/MS (m/z) : 313.6 $(M+NH_4)^+$

5.1.45.3. 2-Methyl-*c*-5-[4-(4-methylsulfanylphenyl)-butyl]-[1,3]-dioxane-*r*-2-carboxylic acid (26c)



26c (0.431 g, 90%) was prepared from **25c** (0.5 g, 1.48 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 103-105 °C; Purity by HPLC: 97.8%.

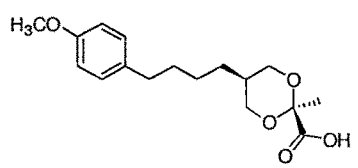
IR (KBr) : 3416, 2931, 2858, 1720, 1492, 1406, 1284, 1149 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.02-1.09 (m, 2H), 1.23-1.33 (m, 2H), 1.51-1.61 (m, 5H), 1.98-2.03 (m, 1H), 2.46 (s, 3H), 2.51 (t, J = 7.6 Hz, 2H), 3.44 (t, J = 11.8 Hz, 2H), 3.98 (dd, J = 11.8 & 4.4 Hz, 2H), 7.06 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 15.09, 25.14, 25.57, 27.27, 31.03, 32.82, 34.27, 67.26, 97.50, 126.30, 128.87, 134.72, 139.07, 171.35

ESI/MS (m/z) : 342.2 $(M+NH_4)^+$

5.1.45.4. *c*-5-[4-(4-Methoxyphenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (26d)



26d (0.765 g, 80%) was prepared from **25d** (1 g, 3.1 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 84-85 °C; Purity by HPLC: 98%.

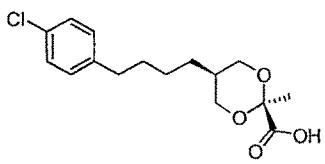
IR (KBr) : 3020, 2938, 1727, 1556, 1228, 1136, 823 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.02-1.09 (m, 2H), 1.23-1.30 (m, 2H), 1.50-1.52 (m, 2H), 1.60 (s, 3H), 1.98-2.0 (m, 1H), 2.52 (t, J = 7.5 Hz, 2H), 3.44 (t, J = 11.56 Hz, 2H), 3.78 (s, 3H), 3.97 (dd, J = 11.9 & 4.4 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 25.09, 25.54, 27.26, 31.29, 32.80, 33.93, 54.90, 67.24, 97.48, 113.90, 129.07, 133.98, 157.27, 171.32

ESI/MS (m/z) : 309.3 $(M+H)^+$

5.1.45.5. *c*-5-[4-(4-Chlorophenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (26e)



26e (0.74 g, 86%) was prepared from **25e** (0.9 g, 2.75 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 94-96 °C; Purity by HPLC: 99%.

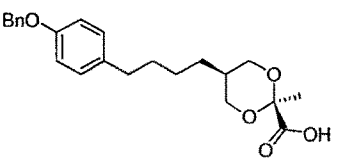
IR (KBr) : 3030, 2936, 1723, 1516, 1228, 1136, 813 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 0.92-1.00 (m, 2H), 1.13-1.21 (m, 2H), 1.31 (s, 3H), 1.38-1.49 (m, 2H), 1.75-1.83 (m, 1H), 2.37 (t, J = 7.5 Hz, 2H), 3.22 (t, J = 11.5 Hz, 2H), 3.79 (dd, J = 11.7 & 4.4 Hz, 2H), 6.61 (d, J = 8.3 Hz, 2H), 6.91 (d, J = 8.2 Hz, 2H), 9.06 (bs, 1H, COOH)

^{13}C NMR (DMSO-d_6) : δ 25.33, 25.66, 27.47, 31.39, 32.99, 34.03, 67.07, 98.07, 114.97, 128.60, 132.10, 155.24, 171.60

ESI/MS (m/z) : 335.1 $(M+Na)^+$

5.1.45.6. c-5-[4-(4-Benzyloxyphenyl)-butyl]-2-methyl-[1,3]-dioxane-r-2-carboxylic acid (26f)



26f (0.45 g, 84%) was prepared from **25f** (0.5 g, 1.25 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 102-104 °C; Purity by HPLC: 99%.

IR (KBr) : 3417, 2929, 2856, 1728, 1610, 1510, 1236, 1172, 1020 810 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 1.04-1.09 (m, 2H), 1.23-1.33 (m, 2H), 1.50-1.62 (m, 5H), 1.97-2.03 (m, 1H), 2.52 (t, J = 7.5 Hz, 2H), 3.43 (t, J = 11.5 Hz, 2H), 3.97 (dd, J = 11.8 & 4.4 Hz, 2H), 5.03 (s, 2H), 6.88 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 7.29-7.44 (m, 5H)

^{13}C NMR (DMSO-d_6) : δ 25.17, 25.61, 27.32, 31.36, 32.85, 34.02, 67.31, 69.13, 97.56, 114.56, 127.66, 128.42, 129.18, 134.34, 137.30, 156.43, 171.42, 185.15

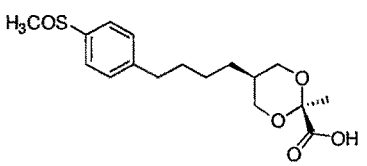
ESI/MS (m/z) : 402.3 $(M+NH_4)^+$

Analysis **Mol.Formula:** $C_{23}H_{28}O_5$

Calculated : C, 71.85%; H, 7.34%

Found : C, 71.36%; H, 7.48%

5.1.45.7. 2-Methyl-*c*-5-[4-(4-methylsulfinylphenyl)-butyl]-[1,3]-dioxane-*r*-2-carboxylic acid (26g)



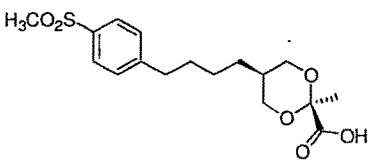
26g (0.423 g, 63%) was prepared from **25g** (0.7 g, 1.97 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 147-149 °C; Purity by HPLC: 99%.

IR (KBr) : 3435, 2939, 1730, 1595, 1490, 1363, 1265, 1215, 1197, 1147, 1001 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 0.98-1.06 (m, 2H), 1.21-1.32 (m, 2H), 1.53 (s, 3H), 1.57-1.65 (m, 2H), 1.98 - 2.04 (m, 1H), 2.63 (t, J = 7.4 Hz, 2H), 2.77 (s, 3H), 3.39 (t, J = 11.5 Hz, 2H), 3.90 (dd, J = 11.6 & 4.2 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.60 (d, J = 8.0 Hz, 2H)

^{13}C NMR	: δ 25.18, 25.55, 27.22, 30.86, 32.77, 34.59, 43.20, 67.24,
(DMSO-d_6)	97.48, 123.60, 129.10, 143.46, 145.26, 171.33
ESI/MS (m/z)	: 341.1 $(M+H)^+$
Analysis	**Mol.Formula:** $C_{17}H_{24}O_5S$
	Calculated : C, 59.98%; H, 7.11%
	Found : C, 59.44%; H, 7.32%

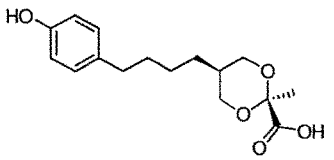
5.1.45.8. 2-Methyl-*c*-5-[4-(4-methylsulfonylphenyl)-butyl]-[1,3]-dioxane-*r*-2-carboxylic acid (26h)



26h (0.423 g, 88%) was prepared from **25h** (0.5 g, 1.35 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 152-154 °C; Purity by HPLC: 97.5%.

IR (KBr)	: 3450, 2933, 1743, 1596, 1461, 1299, 1134, 1118, 763 cm^{-1}
^{1}HNMR	: δ 1.04 -1.11 (m, 2H), 1.26- 1.36 (m, 2H), 1.56 (s, 3H), 1.59-
(DMSO-d_6)	1.67 (m, 2H), 2.01 - 2.06 (m, 1H), 2.68 (t, J = 7.6 Hz, 2H), 3.05 (s, 3H), 3.45 (t, J = 11.5 Hz, 2H), 3.96 (dd, J =11.9 & 4.4 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H)
^{13}C NMR	: δ 25.22, 25.60, 27.25, 30.72, 32.81, 34.72, 67.28, 97.58,
(DMSO-d_6)	127.01, 129.21, 138.31, 148.59, 171.43
ESI/MS (m/z)	: 379.2 $(M+Na)^+$
Analysis	**Mol.Formula:** $C_{17}H_{24}O_6S$
	Calculated : C, 57.28%; H, 6.79%
	Found : C, 56.97%; H, 6.95%

5.1.45.9. *c*-5-[4-(4-Hydroxyphenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (26i)



26i (0.41 g, 86%) was prepared from **25i** (0.5 g, 1.62 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 157-159 °C; Purity by HPLC: 99%.

IR (KBr) : 3373, 3073, 2933, 1720, 1616, 1514, 1228, 1136, 813 cm^{-1}

^{1}HNMR (DMSO-d_6) : δ 0.92-1.00 (m, 2H), 1.13-1.22 (m, 2H), 1.31 (s, 3H), 1.38-1.46 (m, 2H), 1.75-1.83 (m, 1H), 2.40 (t, J = 7.5 Hz, 2H), 3.29 (t, J = 11.5 Hz, 2H), 3.80 (dd, J = 11.7 & 4.4 Hz, 2H), 6.62 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.2 Hz, 2H), 9.06 (bs, 1H, OH), 13.03 (bs, 1H, COOH)

^{13}C NMR (DMSO-d_6) : δ 25.32, 25.63, 27.42, 31.39, 32.99, 34.03, 67.07, 98.07, 114.97, 128.60, 132.10, 155.24, 171.60

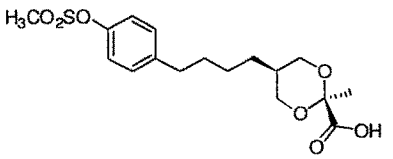
ESI/MS (m/z) : 317.1 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{16}H_{22}O_5$

Calculated : C, 65.29%; H, 7.53%

Found : C, 64.91%; H, 7.69%

5.1.45.10. *c*-5-[4-(4-Methanesulfonyloxyphenyl)-butyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (26j)



26j (0.323 g, 84%) was prepared from **25j** (0.4 g, 1.04 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 140-142 °C; Purity by HPLC: 98.7 %.

IR (KBr) : 3438, 3020, 2927, 1753, 1612, 1506, 1346, 1261, 1170,

987 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.03-1.11 (m, 2H), 1.27-1.32 (m, 2H), 1.53-1.63 (m, 5H), 2.02-2.04 (m, 1H), 2.59 (t, J = 7.5 Hz, 2H), 3.13 (s, 3H), 3.44 (t, J = 11.6 Hz, 2H), 3.96 (dd, J = 4.6 & 11.9 Hz, 2H), 7.18 (s, 4H)

^{13}C NMR (DMSO-d_6) : δ 25.20, 25.56, 27.25, 30.94, 32.80, 34.19, 37.23, 67.26, 97.50, 121.91, 129.72, 141.51, 147.15, 171.34

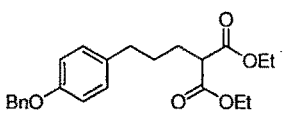
ESI/MS (m/z) : 395.0 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{17}H_{24}O_7S$

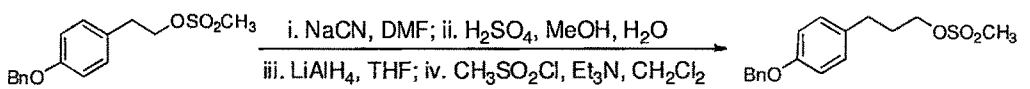
Calculated : C, 54.82%; H, 6.50%

Found : C, 54.34%; H, 6.83%

5.1.46. Diethyl 2-(3-(4-(benzyloxy)-phenyl)-propyl)-malonate (27)



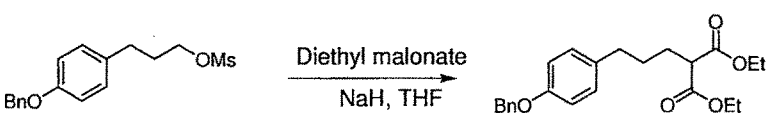
Step I: Preparation of 3-(4-(benzyloxy)phenyl)propyl methanesulfonate



16i

Title compound (5.23 g, 50%) was prepared from **16i** (10 g, 32.64 mmol) by means of a general procedure similar to that reported for compounds **7c,d,g,i.**

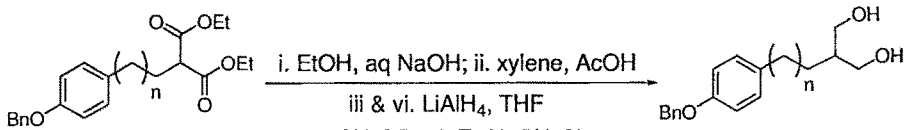
Step II: Preparation of Diethyl 2-(3-(4-(benzyloxy)-phenyl)-propyl)-malonate **(27)**



27

Compounds **27** (4.8 g, 80%) was prepared from the product of **step I** (5 g, 15.6 mmol) by means of a procedure similar to that reported for compounds **23.**

5.1.47. General procedure for the preparation of the compounds 28a-b.



27; n=2
23f; n=3

28a; n=4
28b; n=5

Step I: The crude product (**27** and **23f**) was dissolved in EtOH (9 fold) and a solution of NaOH (4 mole equivalent) in H_2O (3 fold) was added. The mixture was stirred at 25 °C for 15 min. The reaction mixture was concentrated under vacuum, diluted with water, neutralized with HCl. Solid separated out was filtered and dried to yield dicarboxylic acid as white solid.

Step II: The solid obtained in Step I was dissolved in a mixture of xylene (3 fold) and AcOH (3 fold) and refluxed for 5 h. Solvent was evaporated in vacuum to mono carboxylic acid as white solid.

Step III: To a solution of carboxylic acid obtained from Step II in THF (10 fold), $LiAlH_4$ (2 mole equivalent) was added in small portions at 0 °C over a period of 30 min and stirred at 25 °C for 4 hours. Excess $LiAlH_4$ was quenched by drop-wise addition of saturated aqueous Na_2SO_4 solution at 0-10 °C till solid separated out. Solid residue was filtered and successively washed with hot ethyl acetate. Filtrate was concentrated in vacuum to give alcohol compound.

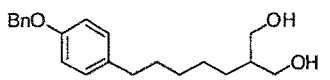
Step IV: To a solution of alcohol obtained from Step III in CH_2Cl_2 (5 fold), Et_3N (1.5 mole equivalent) was added followed by drop-wise addition of CH_3SO_2Cl (1.2 mole equivalent) at 0-10 °C and stirred at the same temperature for 15 min. The reaction mixture was diluted with CH_2Cl_2, successively washed with water, $NaHCO_3$ solution, dil HCl and brine, dried over $CaCl_2$, filtered and concentrated in vacuum to give mesylate compound.

Step V: To an ice-cold suspension of NaH (60%, 1.5 mole equivalent) in THF (2 fold), diethyl malonate (3 mole equivalent) was added drop wise over a period of 30 min at 0-10 °C and stirred at the same temperature for 30 min. A solution of the mesylate obtained from step V in THF (3 fold) was added to the reaction mixture at 25 °C and stirred at 60 °C for 72 hours. The reaction mixture was poured into ice cold water 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. Excess diethyl malonate was distilled out under vacuum to give crude diester which was directly used in next step.

Step VI: The diester obtained in previous step was subjected to the reduction according to the procedure reported in step III to obtain compound **28a-b**.

5.1.47.1. 2-[5-(4-Benzyloxyphenyl)-pentyl]-propane-1,3-diol (28a)



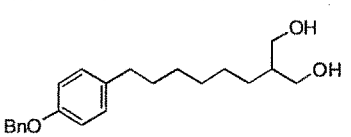
28a (7.48 g, 47%) was prepared from **27** (20 g, 48.48 mmol) in six steps as described in the general procedure described above as off-white solid. mp: 120-122 °C; Purity by HPLC: 97.5%.

IR (KBr) : 3317, 2877, 2850, 1610, 1583, 1514, 1452, 1247, 1028, 732 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.21-1.25 (m, 2H), 1.32-1.34 (m, 2H), 1.58-1.62 (m, 2H), 1.73-1.79 (m, 3H), 2.31 (bs, 2H, OH), 2.53 (t, J = 7.4 Hz, 2H), 3.64 (t, J = 11.7 Hz, 2H), 3.82 (dd, J = 12.0 & 4.6 Hz, 2H), 5.03 (s, 2H), 6.87 (d, J = 8.2 Hz, 2H), 7.06 (d, J = 8.2 Hz, 2H), 7.31-7.44 (m, 5H)

ESI/MS (m/z) : 351.0 $(M+Na)^+$

5.1.47.2. 2-[6-(4-Benzyloxyphenyl)-hexyl]-propane-1,3-diol (28b)



28b (11.56 g, 72%) was prepared from **23f** (20 g, 46.89 mmol) in six steps as described above as white solid. mp: 127-129 °C; Purity by HPLC: 97.8%.

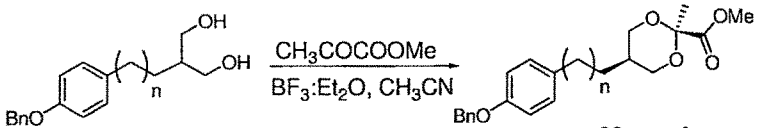
IR (KBr) : 3296, 2925, 2852, 1610, 1510, 1382, 1215, 1143, 1024, 929, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.22-1.28 (m, 8H), 1.54-1.58 (m, 2H), 1.72-1.77 (m, 1H), 2.30 (bs, 2H, OH), 2.53 (t, J = 7.4 Hz, 2H), 3.60-6.63 (m,

2H), 3.80 (dd, J = 10.8 & 4.8 Hz, 2H), 5.03 (s, 2H), 6.88 (d, J = 8.4 Hz, 2H), 7.07 (J = 8.4 Hz, 2H), 7.32-7.45 (m, 5H)

ESI/MS (m/z) : 365.0 $(M+Na)^+$

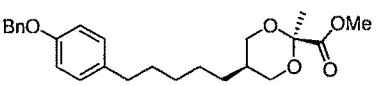
5.1.48. General procedure for the preparation of the compounds 29a-b



28a; n=4
28b; n=5

29a; n=4
29b; n=5

5.1.48.1. Methyl-*c*-5-[5-(4-benzyloxyphenyl)-pentyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (29a)



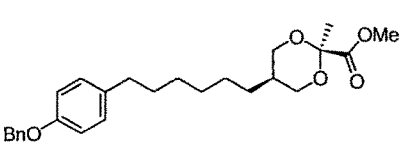
29a (6.24 g, 71%) was prepared from **28a** (7 g, 21.31 mmol) according to the procedure described for the synthesis of **4a** as a liquid. Purity by HPLC: 96.3%.

IR (Neat) : 3018, 2929, 2856, 1743, 1610, 1510, 1454, 1217, 1143, 1118, 1026, 974, 889, 771 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.98-1.01 (m, 2H), 1.25-1.28 (m, 4H), 1.51-1.57 (m, 5H), 1.96-2.03 (m, 1H), 2.52 (t, J = 7.5 Hz, 2H), 3.37 (t, J = 11.7 Hz, 2H), 3.83 (s, 3H), 3.94 (dd, J = 12.0 & 4.6 Hz, 2H), 5.03 (s, 2H), 6.87 (d, J = 8.2 Hz, 2H), 7.05 (d, J = 8.2 Hz, 2H), 7.31-7.44 (m, 5H)

ESI/MS (m/z) : 435.1 $(M+Na)^+$

5.1.48.2. Methyl-*c*-5-[6-(4-benzyloxyphenyl)-hexyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (29b)



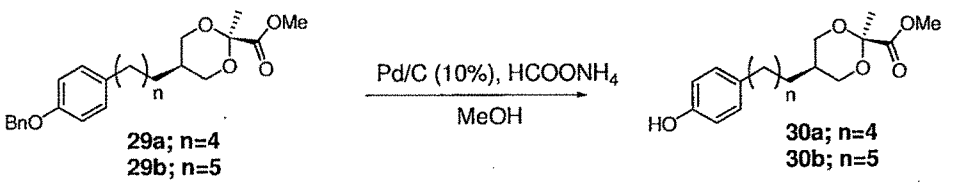
29b (9.86 g, 72%) was prepared from **28b** (11 g, 32.12 mmol) according to the procedure described for the synthesis of **4a** as a liquid. Purity by HPLC: 96.9 %.

IR (Neat) : 3020, 2930, 2858, 1743, 1658, 1566, 1510, 1382, 1215, 1143, 1024, 929, 758 cm^{-1}

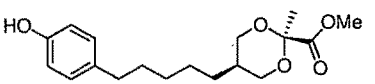
^{1}HNMR ($CDCl_3$) : δ 0.97-1.02 (m, 2H), 1.23-1.33 (m, 6H), 1.49-1.54 (m, 5H), 1.96-2.03 (m, 1H), 2.52 (t, J = 7.4 Hz, 2H), 3.37 (t, J = 11.8 Hz, 2H), 3.83 (s, 3H), 3.94 (dd, J = 12.0 & 4.6 Hz, 2H), 5.03 (s, 2H), 6.87 (d, J = 8.4 Hz, 2H), 7.06 (J = 8.4 Hz, 2H), 7.31-7.44 (m, 5H)

ESI/MS (m/z) : 449.3. $(M+Na)^+$

5.1.49. Preparation of the compounds 30a-b



5.1.49.1. Methyl-*c*-5-[5-(4-hydroxyphenyl)-pentyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (30a)



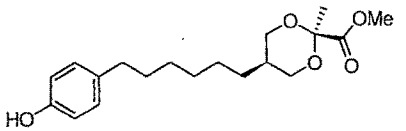
30a (4 g, 86%) was prepared from **29a** (6 g, 14.54 mmol) by debenzylating according to the procedure described for **4c** as off-white solid. mp: 95-97 °C; Purity by HPLC: 95.6%.

IR (KBr) : 3415, 3018, 2850, 1728, 1614, 1595, 1515, 1440, 1367, 1284, 1209, 1190, 1168, 1137, 1020, 964, 831, 680 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.98-1.04 (m, 2H), 1.25-1.27 (m, 4H), 1.48-1.54 (m, 5H), 1.96-2.05 (m, 1H), 2.50 (t, J = 7.5 Hz, 2H), 3.37 (t, J = 11.7 Hz, 2H), 3.83 (s, 3H), 3.94 (dd, J = 12.0 & 4.6 Hz, 2H), 6.70 (d, J = 8.2 Hz, 2H), 7.00 (d, J = 8.2 Hz, 2H), 9.12 (bs, 1H, OH)

ESI/MS (m/z) : 345.0 $(M+Na)^+$

5.1.49.2. Methyl-*c*-5-[6-(4-hydroxyphenyl)-hexyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (30b)



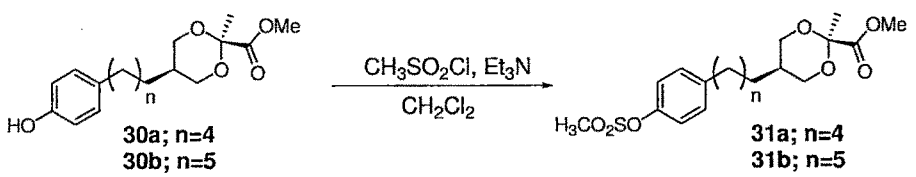
30b (6.89 g, 97%) was prepared from **29b** (9 g, 21.1 mmol) by debenzylating according to the procedure described for **4c** as a liquid. Purity by HPLC: 97.4%.

IR (Neat) : 3411, 3020, 2929, 2856, 1743, 1612, 1514, 1444, 1375, 1215, 1143, 1051, 758 cm^{-1}

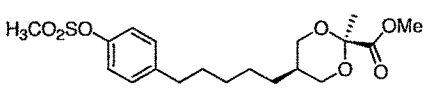
^{1}HNMR ($CDCl_3$) : δ 0.97-1.02 (m, 2H), 1.23-1.33 (m, 6H), 1.49-1.54 (m, 5H), 1.98-2.04 (m, 1H), 2.51 (t, J = 7.4 Hz, 2H), 3.37 (t, J = 11.8 Hz, 2H), 3.81 (s, 3H), 3.94 (dd, J = 12.0 & 4.6 Hz, 2H), 6.73 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 9.02 (bs, 1H, OH)

ESI/MS (m/z) : 359.0. $(M+Na)^+$

5.1.50. Preparation of the compounds 31a-b



5.1.50.1. Methyl-*c*-5-[5-(4-methanesulfonyloxyphenyl)-pentyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (31a)



31a (3.58 g, 96%) was prepared from **30a** (3 g, 19.31 mmol) by means of a procedure similar to that described for **17i** as a liquid. Purity by HPLC: 95.6%.

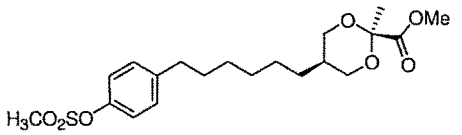
IR (Neat) : 3020, 2931, 1743, 1631, 1502, 1371, 1330, 1271, 1215, 1020, 970, 873, cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.99-1.04 (m, 2H), 1.26-1.29 (m, 4H), 1.49 (s, 3H), 1.51-1.58 (m, 2H), 1.98-2.02 (m, 1H), 2.59 (t, J = 7.5 Hz, 2H),

3.13 (s, 3H), 3.38 (t, J = 11.7 Hz, 2H), 3.83 (s, 3H), 3.94 (dd, J = 12.0 & 4.6 Hz, 2H), 7.16-7.21 (m, 4H)

ESI/MS (m/z) : 423.0 $(M+Na)^+$

5.1.50.2. Methyl-*c*-5-[6-(4-methanesulfonyloxyphenyl)-hexyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylate (31b)



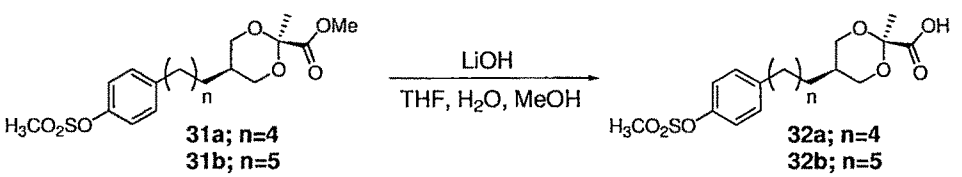
31b (3.47 g, 94%) was prepared from **30b** (3 g, 8.92 mmol) by means of a procedure similar to that described for **17i** as a liquid. Purity by HPLC: 95.4 %.

IR (Neat) : 3018, 2929, 1743, 1502, 1463, 1371, 1271, 1215, 1174, 1147, 1020, 970, 871, 759, 667, 528 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.98-1.03 (m, 2H), 1.24-1.34 (m, 6H), 1.55 (s, 3H), 1.57-1.67 (m, 2H), 1.98-2.04 (m, 1H), 2.59 (t, J = 7.5 Hz, 2H), 3.13 (s, 3H), 3.38 (t, J = 11.7 Hz, 2H), 3.83 (s, 3H), 3.94 (dd, J = 12.0 & 4.6 Hz, 2H), 7.16-7.22 (m, 4H)

ESI/MS (m/z) : 437.0. $(M+Na)^+$

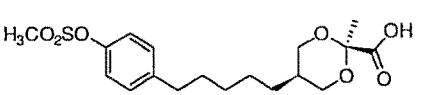
5.1.51. Preparation of the compounds 32a-b



31a; n=4
31b; n=5

32a; n=4
32b; n=5

5.1.51.1. *c*-5-[5-(4-Methanesulfonyloxyphenyl)-pentyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (32a)



32a (0.936 g, 97%) was prepared from **31a** (1 g, 2.5 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 102-104 °C; Purity by HPLC: 98.1%.

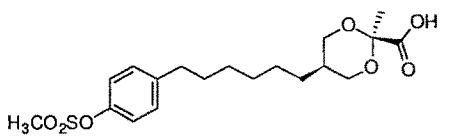
IR (KBr) : 2933, 1720, 1498, 1363, 1290, 1211, 1168, 1145 cm^{-1}.

^{1}HNMR ($CDCl_3$) : δ 1.02-1.07 (m, 2H), 1.23-1.30 (m, 4H), 1.57-1.61 (m, 5H), 1.98-2.05 (m, 1H), 2.59 (t, J = 7.4 Hz, 2H), 3.13 (s, 3H), 3.44 (t, J = 11.6 Hz, 2H), 3.96 (dd, J = 12.0 & 4.5 Hz, 2H), 7.18 (s, 4H)

^{13}C NMR (DMSO-d_6) : δ 25.34, 25.54, 27.41, 28.71, 30.54, 32.86, 34.33, 37.22, 67.27, 97.49, 121.86, 129.70, 141.54, 147.12, 171.32

ESI/MS (m/z) : 409.0 $(M+Na)^+$

5.1.51.2. *c*-5-[6-(4-Methanesulfonyloxyphenyl)-hexyl]-2-methyl-[1,3]-dioxane-*r*-2-carboxylic acid (32b)



32b (0.898 g, 93%) was prepared from **31b** (1 g, 2.41 mmol) by following the procedure described for the synthesis of **9** as white solid. mp: 105-106 °C; Purity by HPLC: 97.5 %.

IR (KBr) : 2922, 2850, 1755, 1602, 1504, 1467, 1415, 1346, 1259, 867, cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.02-1.05 (m, 2H), 1.25-1.29 (m, 6H), 1.56-1.59 (m, 5H), 1.98-2.06 (m, 1H), 2.59 (t, J = 7.6 Hz, 2H), 3.12 (s, 3H), 3.46 (t, J = 11.6 Hz, 2H), 3.98 (dd, J = 12.0 & 4.4 Hz, 2H), 7.16-7.21 (m, 4H), 10.12 (bs, 1H, COOH)

^{13}C NMR (DMSO-d_6) : δ 25.60, 26.72, 28.46, 29.02, 32.47, 33.06, 34.46, 37.23, 67.35, 97.13, 121.64, 129.47, 141.35, 147.50, 171.40

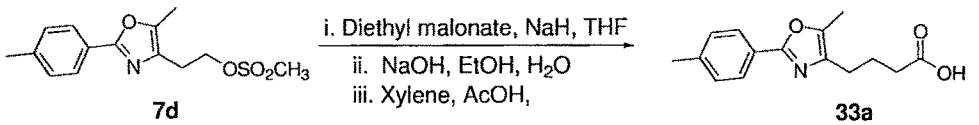
ESI/MS (m/z) : 423.0 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{19}H_{28}O_7S$

Calculated : C, 56.98%; H, 7.05%

Found : C, 57.22%; H, 7.09%

5.1.52. 4-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-butyric acid (33a).



7d 33a

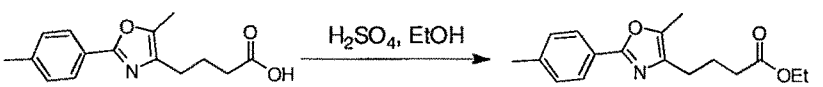
33a (11.41 g, 65%) was prepared from **7d** (20 g, 67.72 mmol) following the procedure of step I described for compound **7e** as yellow solid. mp: 80-82 °C; Purity by HPLC: 95.5 %.

IR (KBr) : 3419, 2866, 1708, 1619, 1556, 1448, 1257, 1234, 958, 829 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.95-2.05 (m, 2H), 2.31 (s, 3H), 2.38 (s, 3H), 2.41 (t, J = 7.0 Hz, 2H), 2.59 (t, J = 7.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 260.1 $(M+H)^+$

5.1.53. Ethyl-4-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-butyrate (33b).



33a 33b

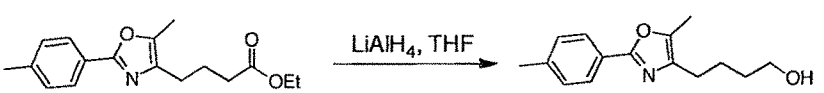
33b (11.82 g, 97%) was prepared from **33a** (11 g, 42.42 mmol) following the procedure of step II described for compound **7e** as viscous liquid.

IR (Neat) : 2981, 2873, 1726, 1618, 1500, 1298, 1215, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, J = 7.1 Hz, 3H), 1.97-2.04 (m, 2H), 2.30 (s, 3H), 2.32-2.35 (m, 2H), 2.38 (s, 3H), 2.53 (t, J = 7.2 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 288.1 $(M+H)^+$

5.1.54. 4-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-butan-1-ol (34a).



33b 34a

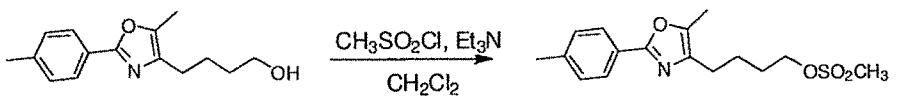
34a (8.83 g, 94%) was prepared from **33b** (11 g, 38.28 mmol) following the procedure of step III described for compound **7e** as viscous liquid.

IR (Neat) : 3357, 2923, 2964, 1639, 1620, 1500, 1334, 825 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.61-1.70 (m, 2H), 1.73-1.80 (m, 2H), 2.30 (s, 3H), 2.38 (s, 3H), 2.52 (t, J = 6.9 Hz, 2H), 3.68 (t, J = 6.3 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 7.85 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 246.2 $(M+H)^+$

5.1.55. 4-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-butyl methanesulfonate (34b).



34a **34b**

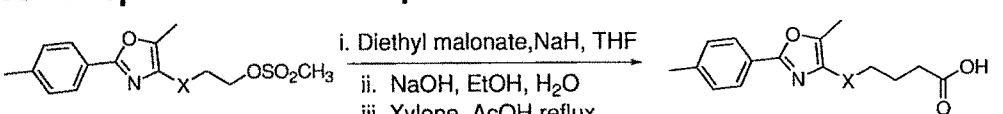
34b (9.91 g, 94%) was prepared from **34a** (8 g, 32.61 mmol) following the procedure of step IV described for compound **7e** as viscous liquid.

IR (Neat) : 3020, 2958, 1614, 1500, 1355, 1197, 1176, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.75-1.81 (m, 4H), 2.31 (s, 3H), 2.35 (s, 3H), 2.52 (t, J = 6.9 Hz, 2H), 2.99 (s, 3H), 4.26 (t, J = 6.3 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 7.86 (d, J = 8.0 Hz, 2H)

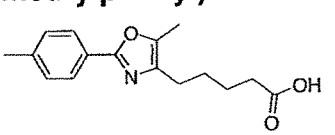
ESI/MS (m/z) : 324.2 $(M+H)^+$

5.1.56. Preparation of the compounds 35a-b



7e **34b** **35a** **35b**

5.1.56.1. 5-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-pentanoic acid (35a)



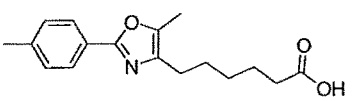
35a (7.86 g, 89%) was prepared from **7e** (10 g, 32.32 mmol) in three steps following the procedure of step I-III described for compound **7e** as viscous liquid. Purity by HPLC: 97.5 %.

IR (Neat) : 2923, 2862, 1732, 1620, 1500, 1157, 1020 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.69-1.78 (m, 4H), 2.32 (s, 3H), 2.37-2.44 (m, 5H), 2.48-2.56 (m, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 274.1 $(M+H)^+$

5.1.56.2. 6-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-hexanoic acid (35b)



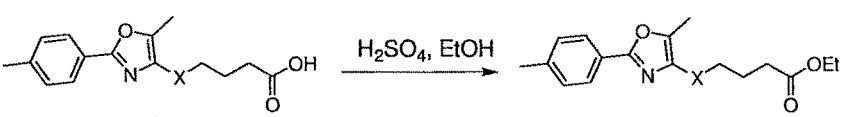
35b (7.36 g, 92%) was prepared from **34b** (9 g, 27.83 mmol) in three steps following the procedure of step I-III described for compound **7e** as viscous liquid. Purity by HPLC: 97.5 %.

IR (Neat) : 3018, 2927, 1710, 1643, 1500, 1217, 1180, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.38-1.43 (m, 2H), 1.65-1.71 (m, 4H), 2.26 - 2.37 (m, 8H), 2.48 (t, J = 7.5 Hz, 2H), 7.30 (d, J = 7.9 Hz, 2H), 7.87 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 288.1 $(M+H)^+$

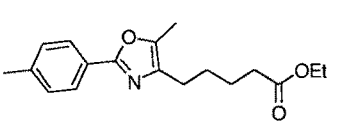
5.1.57. Preparation of the compounds 35c-d



35a
35b

35c
35d

5.1.57.1. Ethyl-5-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-pentanoate (35c)



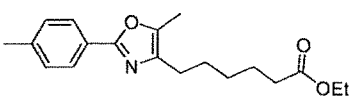
35c (6.86 g, 83%) was prepared from **35a** (7.5 g, 27.44 mmol) following the procedure of step II described for compound **7e** as viscous liquid.

IR (Neat) : 2981, 2925, 1735, 1639, 1500, 1238, 1157, 785 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.24 (t, J = 7.1 Hz, 3H), 1.66-1.71 (m, 4H), 2.27-2.33 (m, 5H), 2.38 (s, 3H), 2.49-2.52 (m, 2H), 4.12 (q, J = 7.1 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.2 Hz, 2H)

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

5.1.57.2. Ethyl-6-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-hexanoate (35d)



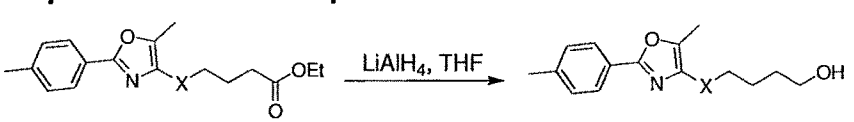
35d (7.15 g, 93%) was prepared from **35b** (7 g, 24.36 mmol) following the procedure of step II described for compound **7e** as viscous liquid.

IR (Neat) : 2925, 2860, 1735, 1637, 1500, 1251, 1178, 794 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.24 (t, J = 7.1 Hz, 3H), 1.35-1.40 (m, 2H), 1.61-1.72 (m, 4H), 2.27-2.37 (m, 5H), 2.38 (s, 3H), 2.47 (t, J = 7.5 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 316.2 $(M+H)^+$

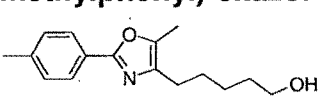
5.1.58. Preparation of the compounds 36a-b



35c
35d

36a
36b

5.1.58.1. 5-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-pentan-1-ol (36a)



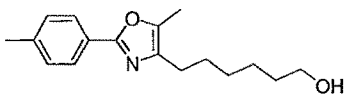
36a (5.54 g, 99%) was prepared from **35c** (6.5 g, 21.57 mmol) by following the procedure of step III described for compound **7e** as viscous liquid.

IR (Neat) : 3357, 2925, 2858, 1637, 1500, 1083, 785 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.39-1.46 (m, 2H), 1.59-1.71 (m, 4H), 2.30 (s, 3H), 2.38 (s, 3H), 2.48 (t, J = 7.3 Hz, 2H), 3.64 (t, J = 6.4 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.2 Hz, 2H)

ESI/MS (m/z) : 260.1 $(M+H)^+$

5.1.58.2. 6-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-hexan-1-ol (36b)



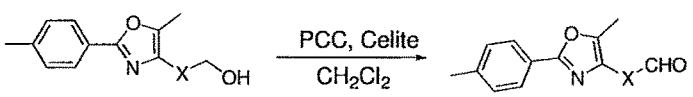
36b (5.28 g, 87%) was prepared from **35d** (7 g, 22.19 mmol) by following the procedure of step III described for compound **7e** as off white solid. mp: 60-62 °C.

IR (KBr) : 3359, 3016, 2933, 1620, 1500, 1215, 754 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.37-1.40 (m, 4H), 1.59-1.71 (m, 4H), 2.30 (s, 3H), 2.38 (s, 3H), 2.47 (t, J = 7.38 Hz, 2H), 3.64 (t, J = 6.45 Hz, 2H), 7.22 (d, J = 8.1 Hz, 2H), 7.85 (d, J = 8.19 Hz, 2H)

ESI/MS (m/z) : 274.1 $(M+H)^+$

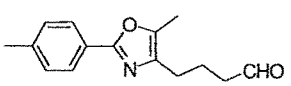
5.1.59. General procedure for the preparation of the compounds 37a-c



34a, 36a-b **37a-c**

To a solution of alcohol (**34a, 36a-b**) in CH_2Cl_2 (10 fold), a mixture of pyridinium chlorochromate (PCC) (1 mole equivalent) and celite (1 fold of PCC) at 0 °C and stirred at 25 °C for 2 h. Solvent was evaporated in vacuum and residue was purified by column chromatography to give title compound **37a-c**.

5.1.59.1. 4-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-butyraldehyde (37a)



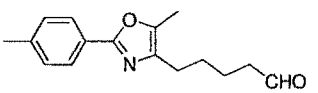
37a (1.65 g, 83%) was prepared from **34a** (2 g, 8.15 mmol) according to the general procedure given above as viscous liquid.

IR (Neat) : 2923, 2864, 2817, 2717, 1726, 1639, 1500, 1166, 761 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.99-2.06 (m, 2H), 2.30 (s, 3H), 2.38 (s, 3H), 2.47-2.55 (m, 4H), 7.22 (d, J = 7.9 Hz, 2H), 7.85 (d, J = 8.1 Hz, 2H), 9.76 (s, 1H)

ESI/MS (m/z) : 244.1 $(M+H)^+$

5.1.59.2. 5-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-pentanal (37b)



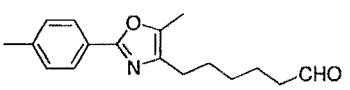
37b (1.17 g, 59%) was prepared from **36a** (2 g, 7.71 mmol) according to the general procedure given above as viscous liquid.

IR (Neat) : 2923, 2817, 2717, 1726, 1637, 1500, 1180, 788 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.67-1.72 (m, 4H), 2.31 (s, 3H), 2.38 (s, 3H), 2.44-2.52 (m, 4H), 7.22 (d, J= 8.0 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H), 9.77 (s, 1H)

ESI/MS (m/z) : 258.1 $(M+H)^+$

5.1.59.3. 6-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-hexanal (37c)



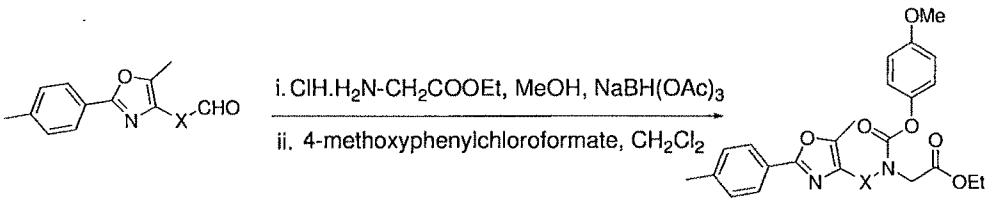
37c (1.87 g, 94%) was prepared from **36b** (2 g, 7.32 mmol) according to the general procedure given above as viscous liquid.

IR (Neat) : 3020, 2860, 2727, 1722, 1639, 1500, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.36-1.41 (m, 2H), 1.62-1.72 (m, 4H), 2.30 (s, 3H), 2.38 (s, 3H), 2.40-2.49 (m, 4H), 7.23 (d, J= 7.8 Hz, 2H), 7.85 (d, J = 8.0 Hz, 2H), 9.76 (s, 1H)

ESI/MS (m/z) : 272.1 $(M+H)^+$

5.1.60. General procedure for the preparation of the compounds 38a-c

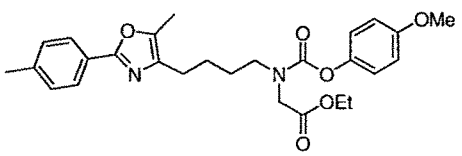


37a-c

38a-c

To a solution of **37a-c** and glycine ethylester hydrochloride (1.2 mole equivalent) in MeOH (10 fold), Et_3N (1.2 mole equivalent) was added followed by addition of sodium triacetoxyborohydride (1.5 mole equivalent) in small portions at 0 °C and stirred at the same temperature for 90 min. 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. Resulting viscous liquid was dissolved in CH_2Cl_2 (10 fold) and a solution of 4-Methoxyphenyl chloroformate (1.4 mole equivalent) in CH_2Cl_2 (2 fold) was added drop wise at 0 °C and stirred at 25 °C for 2 h. The reaction mixture was diluted with CH_2Cl_2, 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 title compounds **38a-c**.

5.1.60.1. Ethyl-{(4-methoxyphenoxycarbonyl)-[4-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-butyl]-amino}-acetate (38a)



38a (0.691 g, 35%) was prepared from **37a** (1 g, 4.11 mmol) according to the general procedure described above as viscous liquid. Purity by HPLC: 97%.

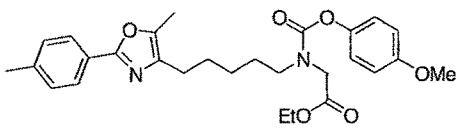
IR (Neat) : 3016, 3941, 1749, 1722, 1614, 1508, 1195, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.24 (t, J = 7.8 Hz, 3H), 1.71-1.73 (m, 4H), 2.32 (s, 3H), 2.38 (s, 3H), 2.49-2.53 (m, 2H), 3.43-3.50 (m, 2H), 3.72 (s, 3H), 4.03 (d, J = 12.0 Hz, 2H), 4.18 (q, J = 7.1 Hz, 2H),

6.80-6.87 (m, 2H), 6.97-7.03 (m, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 503.2 $(M+Na)^+$

5.1.60.2. Ethyl-{(4-methoxyphenoxycarbonyl)-[5-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-pentyl]-amino}-acetate (38b)



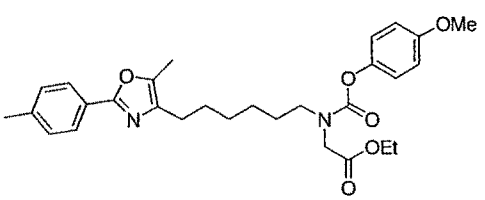
38b (0.307 g, 16%) was prepared from **37b** (1 g, 3.89 mmol) according to the general procedure described above as viscous liquid. Purity by HPLC: 94%.

IR (Neat) : 3018, 2939, 1749, 1714, 1614, 1508, 1215, 756

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, J = 7.1 Hz, 3H), 1.38-1.41 (m, 2H), 1.68-1.71 (m, 4H), 2.23 (s, 3H), 2.38 (s, 3H), 2.46-2.49 (m, 2H), 3.36-3.47 (m, 2H), 3.78 (s, 3H), 4.02 (d, J = 12.2 Hz, 2H), 4.2 (q, J = 7.1 Hz, 2H), 6.81 (d, J = 8.9 Hz, 2H), 7.02-7.06 (m, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 7.8 Hz, 2H)

ESI/MS (m/z) : 495.0 $(M+H)^+$

5.1.60.3. Ethyl-{(4-methoxyphenoxycarbonyl)-[6-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-hexyl]-amino}-acetate (38c)



38c (0.88 g, 47%) was prepared from **37c** (1 g, 3.69 mmol) according to the general procedure described above as viscous liquid. Purity by HPLC: 96.4%.

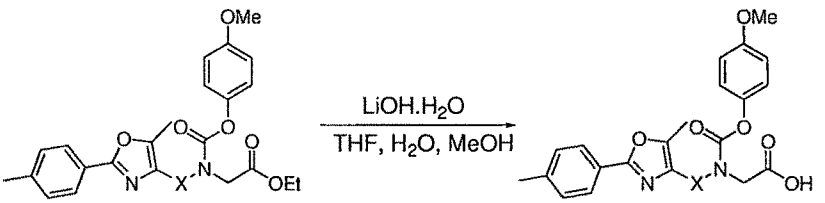
IR (Neat) : 3018, 2937, 1749, 1716, 1612, 1508, 1215, 1197, 769 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25 (t, J = 7.1 Hz, 3H), 1.37-1.39 (m, 4H), 1.59-1.62 (m, 4H), 2.28 (s, 3H), 2.38 (s, 3H), 2.45 (t, J = 7.1 Hz, 2H), 3.35-3.48 (m, 2H), 3.77 (s, 3H), 4.04 (d, J = 12.2 Hz, 2H),

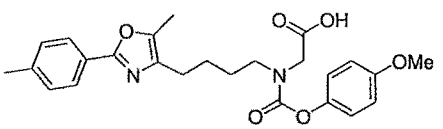
4.23 (q, J = 7.1 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 7.02-7.06 (m, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.84 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 509.3 $(M+H)^+$

5.1.61. Preparation of the compounds 39a-c



5.1.61.1. {(4-Methoxyphenoxycarbonyl)-[4-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-butyl]-amino}-acetic acid (39a)



39a (0.451 g, 96%) was prepared from **38a** (0.5 g, 1.04 mmol) by means of general procedure given for compounds **9** as viscous liquid. Purity by HPLC: 99%.

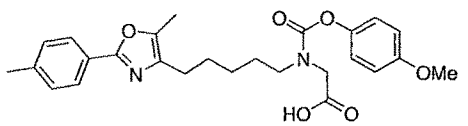
IR (Neat) : 3416, 2939, 2839, 1716, 1612, 1458, 1180, 761 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.68-1.73 (m, 4H), 2.29 (s, 3H), 2.38 (s, 3H), 2.49-2.52 (m, 2H), 3.43-3.50 (m, 2H), 3.77 (s, 3H), 4.07 (d, J = 8.0 Hz, 2H), 6.80-6.87 (m, 2H), 6.97-7.00 (m, 2H), 7.22 (d, J = 6.4 Hz, 2H), 7.85 (d, J = 7.8 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.70, 20.94, 23.68, 24.24, 24.65, 25.80, 26.66, 28.23, 47.80, 53.40, 55.31, 62.96, 113.96, 122.5, 124.69, 125.39, 129.53, 135.52, 139.61, 143.17, 145.14, 155.07, 156.16, 157.76, 158.37

ESI/MS (m/z) : 453.1 $(M+H)^+$

5.1.61.2. {(4-Methoxyphenoxycarbonyl)-[5-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-pentyl]-amino}-acetic acid (39b)



39b (0.3 g, 32%) was prepared from **38b** (1 g, 2.02 mmol) by means of general procedure given for compounds **9** as white solid. mp: 140-141 °C; Purity by HPLC: 96%.

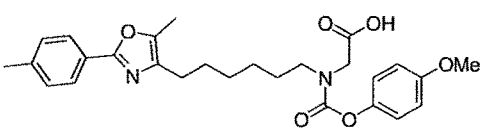
IR (KBr) : 3431, 2925, 2835, 1720, 1610, 1450, 1182, 827 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.38-1.41 (m, 2H), 1.66-1.73 (m, 4H), 2.28 (d, J=4.5 Hz, 3H), 2.38 (s, 3H), 2.46-2.49 (m, 2H), 3.36 (t, *J*=7.2 Hz, 1H),3.47 (t, *J*=7.2 Hz, 1H), 3.78 (s, 3H), 4.06 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 7.00-7.04 (m, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.71, 20.97, 24.90, 25.64, 27.15, 28.23, 48.48, 59.78, 114.16, 122.56, 124.71, 125.39, 129.56, 135.63, 139.64, 143.13, 144.62, 154.57, 156.48, 158.37

ESI/MS (m/z) : 467.3 $(M+H)^+$

5.1.61.3. {(4-Methoxyphenoxycarbonyl)-[6-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-hexyl]-amino}-acetic acid (39c)



39c (0.387 g, 82%) was prepared from **38c** (0.5 g, 0.983 mmol) by means of general procedure given for compounds **9** as viscous liquid. Purity by HPLC: 98%.

IR (Neat) : 3600, 3016, 2935, 2858, 1720,1612, 1508, 1199, 1180, 756 cm^{-1}

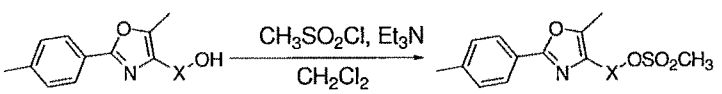
^{1}HNMR ($CDCl_3$) : δ 1.37-1.39 (m, 4H), 1.62-1.65 (m, 4H), 2.28 (d, *J*=3.1 Hz, 3H), 2.38 (s, 3H), 2.45 (t, *J* = 7.3 Hz, 2H), 3.38 (t, *J*=7.2 Hz,

1H), 3.46 (t, *J*=7.2 Hz, 1H), 3.77 (s, 3H), 4.06 (d, *J* = 12.5 Hz, 2H), 6.82 (d, *J* = 8.1 Hz, 2H), 7.00-7.04 (m, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.85 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.69, 20.93, 24.93, 26.10, 27.25, 27.69, 28.42, 48.16, 50.22, 55.30, 113.90, 114.08, 122.45, 122.84, 124.70, 125.35, 129.49, 135.69, 139.57, 142.95, 145.03, 154.44, 154.82, 156.23, 158.32

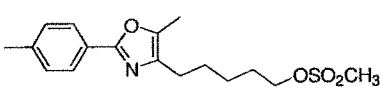
ESI/MS (m/z) : 481.3 $(M+H)^+$

5.1.62. Preparation of the compounds 40a-b



36a-b **40a-b**

5.1.62.1. 5-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-pentyl methanesulfonate (40a)



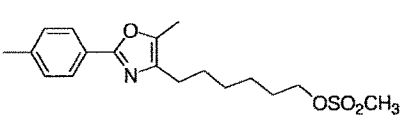
40a (5.99 g, 92%) was prepared from **36a** (5 g, 9.28 mmol) following the procedure of step IV described for compound **7e** as viscous liquid.

IR (Neat) : 2933, 2860, 1637, 1460, 1352, 1193, 1172, 823 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.25-1.50 (m, 2H), 1.71-1.82 (m, 4H), 2.33 (s, 3H), 2.39 (s, 3H), 2.53 (t, *J* = 7.3 Hz, 2H), 2.99 (s, 3H), 4.23 (t, *J* = 6.5 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.91 (d, *J* = 8.1 Hz, 2H)

ESI/MS (m/z) : 338.1 $(M+H)^+$

5.1.62.2. 6-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-hexyl methanesulfonate (40b)



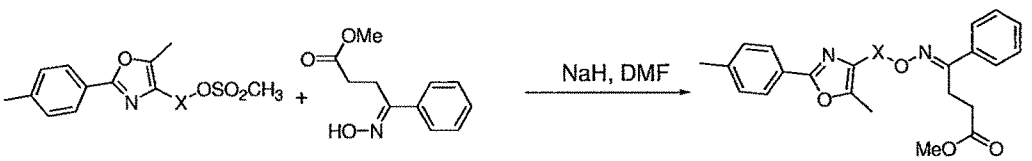
40b (5.09 g, 99%) was prepared from **36b** (4 g, 14.63 mmol) following the procedure of step IV described for compound **7e** viscous liquid.

IR (Neat) : 3020, 2862, 1676, 1591, 1506, 1373, 1193, 1174, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.42-1.44 (m, 4H), 1.71-1.76 (m, 4H), 2.34 (s, 3H), 2.40 (s, 3H), 2.54 (t, J = 7.3 Hz, 2H), 2.99 (s, 3H), 4.22 (t, J = 6.5 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.95 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 352.0 $(M+H)^+$

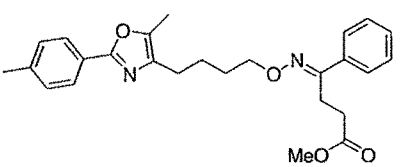
5.1.63. General procedure for the preparation of the compounds 41a-c



34b, 40a-b **44** **41a-c**

To a solution of mesylate compound (**34b, 40a-b**) and **44** in DMF (3 fold), NaH (50%) (1.5 mole equivalent) was added in small portions at 0-10 °C and stirred at 25 °C for 24 h. The reaction mixture was poured to ice cold water and extracted by ethyl acetate. The organic extract was successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by column chromatography to give title compound **41a-c**.

5.1.63.1. (*E*)-Methyl-4-[4-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-butoxyimino]-4-phenyl-butyrate (41a)



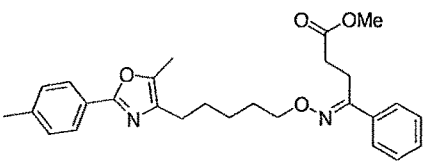
41a (1.63 g, 81%) was prepared from **34b** (1.5 g, 4.64 mmol) and **44** (0.961 g, 4.64 mmol) according to the general procedure described above as viscous liquid. Purity by HPLC: 95.9%.

IR (Neat) : 2950, 2868, 1741, 1637, 1500, 1284, 1244, 1197, 763 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.75-1.78 (m, 4H), 2.32 (s, 3H), 2.37 (s, 3H), 2.53-2.59 (m, 4H), 3.02-3.07 (m, 2H), 3.63 (s, 3H), 4.21 (t, J = 6.0 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.32-7.36 (m, 3H), 7.60-7.63 (m, 2H), 7.85 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 435.2 $(M+H)^+$

5.1.63.2. (*E*)-Methyl-4-[5-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-pentyloxyimino]-4-phenyl-butyrate (41b)



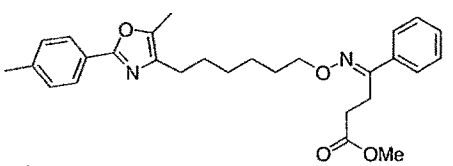
41b (1.41 g, 53%) was prepared from **40a** (2 g, 5.93 mmol) and **44** (1.23, 5.93 mmol) according to the general procedure described above as viscous liquid. Purity by HPLC: 94.7%.

IR (Neat) : 2943, 2860, 1735, 1637, 1500, 1438, 1217, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.45-1.47 (m, 2H), 1.69-1.78 (m, 4H), 2.30 (s, 3H), 2.38 (s, 3H), 2.46-2.58 (m, 4H), 3.01-3.06 (m, 2H), 3.64 (s, 3H), 4.18 (t, J = 6.6 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.33-7.38 (m, 3H), 7.60-7.63 (m, 2H), 7.85 (d, J = 8.1 Hz, 2H)

ESI/MS (m/z) : 449.1 $(M+H)^+$

5.1.63.3. (*E*)-Methyl-4-[6-(5-methyl-2-(4-methylphenyl)-oxazol-4-yl)-hexyloxyimino]-4-phenyl-butyrate (41c)



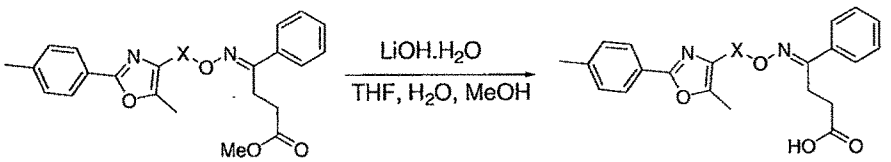
41c (0.342 g, 26%) was prepared from **40b** (1 g, 2.85 mmol) and **44** (0.589 g, 2.85 mmol) according to the general procedure described above as viscous liquid. Purity by HPLC: 93.8%.

IR (Neat) : 3020, 2935, 2858, 1733, 1637, 1500, 1438, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.40-1.43 (m, 4H), 1.67-1.74 (m, 4H), 2.30 (s, 3H), 2.38 (s, 3H), 2.47 (t, J = 7.6 Hz, 2H), 2.57 (t, J = 7.5 Hz, 2H), 3.01 (t, J = 7.6 Hz, 2H), 3.65 (s, 3H), 4.15 (t, J = 6.6 Hz, 2H), 7.21 (d, J = 8.1 Hz, 2H), 7.333-7.37 (m, 3H), 7.59-7.64 (m, 2H), 7.88 (d, J = 8.1 Hz, 2H)

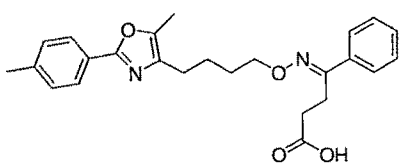
ESI/MS (m/z) : 463.4 $(M+H)^+$

5.1.64. Preparation of the compounds 42a-c



41a-c **42a-c**

5.1.64.1. (*E*)-4-[4-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-butoxyimino]-4-phenylbutyric acid (42a)



42a (1.07 g, 85%) was prepared from **41a** (1.3 g, 2.99 mmol) following the procedure described for compounds **9** as white solid. mp: 102-104 °C; Purity by HPLC: 99%.

IR (KBr) : 3404, 2922, 2858, 1649, 1596, 1307, 1265, 1147 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.76-1.82 (m, 4H), 2.31 (s, 3H), 2.36 (s, 3H), 2.47-2.54 (m, 4H), 3.17 (t, J = 6.8 Hz, 2H), 4.26 (t, J=6.0 Hz, 2H), 7.19-7.25 (m, 2H), 7.32-7.38 (m, 3H), 7.60-7.66 (m, 2H), 7.84 (d, J = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.94, 20.93, 21.93, 24.76, 24.97, 28.49, 30.46, 73.41, 124.75, 125.39, 126.08, 128.44, 129.08, 129.46, 135.00, 135.57, 139.81, 143.09, 154.93, 158.40, 173.51

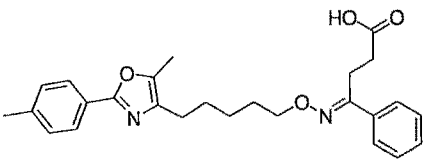
ESI/MS (m/z) : 421.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{25}H_{28}N_2O_4$

Calculated : C, 71.41%; H, 6.71%; N, 6.66%

Found : C, 71.19%; H, 6.71%; N, 6.59%

5.1.64.2. (*E*)-4-[5-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-pentyloxyimino]-4-phenylbutyric acid (42b)



42b (1 g, 86%) was prepared from **41b** (1.2 g, 2.68 mmol) following the procedure described for compounds **9** as off white solid. mp: 91-93 °C; Purity by HPLC: 97%.

IR (KBr) : 3413, 2931, 2860, 1718, 1610, 1500, 1269, 1163, 732 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.47-1.54 (m, 2H), 1.64-1.69 (m, 2H), 1.72-1.79 (m, 2H), 2.30 (s, 3H), 2.36 (s, 3H), 2.52 (t, J = 7.5 Hz, 2H), 2.58 (t, J = 7.5 Hz, 2H), 3.11 (t, J = 7.5 Hz, 2H), 4.20 (t, J = 6.0 Hz, 2H), 7.21 (d, J = 8.1 Hz, 2H), 7.34-7.36 (m, 3H), 7.60-7.63 (m, 2H), 7.84 (d, J = 8.1 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.67, 20.92, 21.90, 24.90, 28.25, 28.56, 30.40, 73.55, 124.72, 125.36, 126.05, 128.40, 129.08, 129.47, 133.88, 134.97, 135.61, 139.54, 143.02, 156.33, 158.36, 173.33

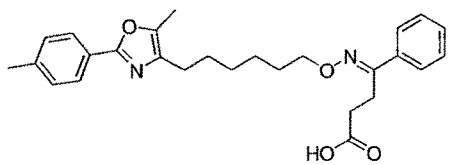
ESI/MS (m/z) : 435.1 $(M+H)^+$

Analysis **Mol.Formula:** $C_{26}H_{30}N_2O_4$

Calculated : C, 71.87%; H, 6.96%; N, 6.45%

Found : C, 71.42%; H, 6.76%; N, 5.96%

5.1.64.3. (*E*)-4-[6-(5-Methyl-2-(4-methylphenyl)-oxazol-4-yl)-hexyloxyimino]-4-phenylbutyric acid (42c)



42c (0.61 g, 63%) was prepared from **41c** (1 g, 2.16 mmol) following the procedure described for compounds **9** as off white solid. mp: 79-81 °C; Purity by HPLC: 99%.

IR (KBr) : 3020, 2862, 1714, 1625, 1492, 1402, 1217, 771 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.43-1.45 (m, 2H), 1.59-1.64 (m, 4H), 1.71-1.74 (m, 2H), 2.31 (s, 3H), 2.38 (s, 3H), 2.53 (t, J = 7.5 Hz, 2H), 2.64 (t, J = 7.5 Hz, 2H), 3.09 (t, J = 7.4 Hz, 2H), 4.22 (t, J = 5.7 Hz, 2H), 7.21-7.25 (m, 2H), 7.35-7.37 (m, 3H), 7.61-7.63 (m, 2H), 7.85 (d, J = 8.1 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 9.65, 20.89, 21.86, 24.84, 25.18, 28.26, 28.65, 73.56, 124.70, 125.32, 126.02, 128.40, 129.04, 129.44, 134.95, 135.67, 139.51, 142.94, 156.29, 158.29, 173.27

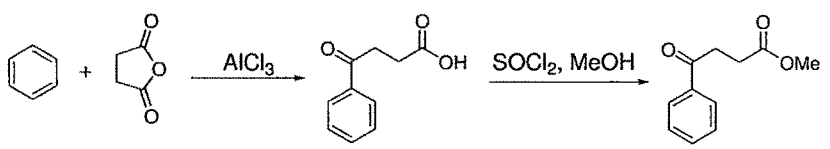
ESI/MS (m/z) : 449.1 $(M+H)^+$

Analysis **Mol.Formula:** $C_{27}H_{32}N_2O_4$

Calculated : C, 72.30%; H, 7.19%; N, 6.25%

Found : C, 72.12%; H, 7.34%; N, 5.93%

5.1.65. Methyl-(4-Oxo-4-phenyl)-butyrate (43)



43

Step 1: To a stirred suspension of $AlCl_3$ (293 g, 2.2 moles) in benzene (500 mL) was added succinic anhydride (100 g, 1.0 moles) portion wise 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. Solid separated was filtered, washed with excess water and dried under vacuum to yield 96 g (53%) of 4-oxo-4-phenyl-butyric acid as white solid. mp: 110-112 °C.

IR (KBr) : 3400, 2972, 1720, 1683, 1595, 1448, 1431, 1400, 1348, 1259, 1240, 1207, 1170, 1058, 947, 763, 688 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ2.80 (t, J = 6.7 Hz, 2H), 3.32 (t, J = 6.7 Hz, 2H), 7.44-7.50 (m, 2H), 7.55-7.59 (m, 1H), 7.97-8.00 (m, 2H)

ESI/MS (m/z) : 201 $(M+Na)^+$

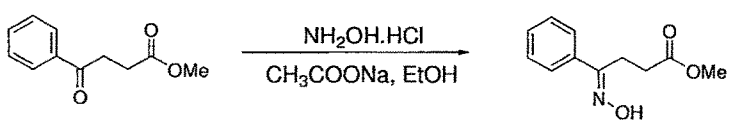
Step II :To an ice cold suspension of 4-oxo-4-phenylbutyric acid (94 g, 0.528 mol) in methanol was added thionyl chloride (42.5 mL, 0.59 mol) drop wise over a period of 2 hours and then the reaction mixture was slowly heated to reflux over a period of 1 hour and continued to reflux for further 2 hours. Solvents were distilled out, residue was poured into ice cold water and extracted with diethyl ether (3X 250 mL). The combined ether extract was successively washed with excess water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum to yield 100 g (98%) of product as liquid.

IR (Neat) : 2952, 2920, 1735, 1685, 1596, 1581, 1448, 1438, 1409, 1357, 1326, 1220, 1164, 1066, 750 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ2.77 (t, J = 6.6 Hz, 2H), 3.33 (t, J = 6.6 Hz, 2H), 3.70 (s, 3H), 7.45-7.49 (m, 2H), 7.55-7.58 (m, 1H), 7.97-8.00 (m, 2H)

ESI/MS (m/z) : 215 $(M+Na)^+$

5.1.66. (*E*)-Methyl (*E*)-4-hydroxyimino-4-phenylbutyrate (44)



43 44

To a solution of **43** (55g, 0.286 mol) in ethanol (450 mL) was added the solution of hydroxylammonium chloride (40 g, 0.572 mol) and sodiumacetate (47 g, 0.572 mol) in water (200 mL) and the reaction mixture was refluxed for 4 hours.

Ethanol was distilled out, residue was poured into water and extracted with ethyl acetate (3 X 200 mL). Combined organic extract was successively washed with water & brine, dried over Na_2SO_4, filtered and concentrated under vacuum. Crude product was purified by flash column chromatography using 5 % ethyl acetate in hexane as eluent to yield 40 g (78%) of pure product as a liquid. Purity by HPLC: 96.7 %

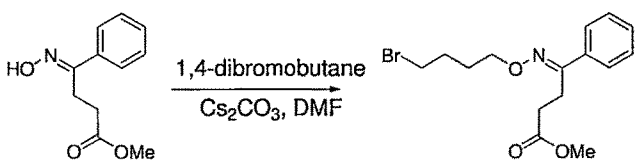
IR (Neat) : 3569, 3284, 3020, 2954, 1733, 1631, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.62 (t, J = 7.2 Hz, 2H), 3.12 (t, J = 7.4 Hz, 2H), 3.64 (s, 3H), 7.38-7.40 (m, 3H), 7.59-7.64 (m, 2H), 9.05 (bs, 1H, OH)

^{13}C NMR ($CDCl_3$) : δ 22.13, 30.44, 51.83, 126.22, 128.70, 129.48, 135.12, 157.96, 173.25

ESI/MS (m/z) : 229.7 $(M+Na)^+$

5.1.67. (*E*)-Methyl-4-(4-bromobutoxyimino)-4-phenylbutyrate (45)



44 **45**

To a solution of **44** (5 g, 0.024 mol) in DMF (30 mL) was added cesium carbonate (15.6 g, 0.028 mol) followed by 1,4-dibromobutane (17.3 mL, 0.145 mol) and the reaction mixture was stirred at 60 °C for 18 hours. Reaction mixture was cooled to ambient temperature, poured into water (200 mL) and extracted with ethyl acetate (3 X 50 mL). The combined organic extract was washed with water, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product so obtained was flash chromatographed over silicagel using 5% ethyl acetate in hexane to yield 6.8 g (72%) of pure product as a liquid. Purity by HPLC: 98.3%.

IR (Neat) : 3018, 2950, 1735, 1693, 1610, 1550, 1477, 1217, 785 cm^{-1}

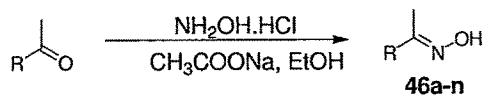
^{1}HNMR : δ 1.84-1.91 (m, 2H), 1.96-2.03 (m, 2H), 2.57 (t, J = 6.8 Hz,

(CDCl3) 2H), 3.05 (t, J = 7.6 Hz, 2H), 3.47 (t, J = 6.8 Hz, 2H), 3.66 (s, 3H), 4.22 (t, J = 6.0 Hz, 2H), 7.35-7.38 (m, 3H), 7.60-7.65 (m, 2H)

^{13}C NMR ($CDCl_3$) : δ 22.5, 28.01, 29.59, 30.75, 33.72, 51.88, 73.34, 76.84, 77.36, 77.48, 126.31, 128.67, 129.36, 135.27, 156.73, 173.13

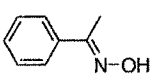
ESI/MS (m/z) : 363.9 $(M+Na)^+$

5.1.68. Preparation of the compounds 46a-n



46a-n

5.1.68.1. (*E*)-1-Phenylethanone oxime (46a)



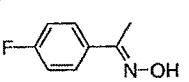
46a (2.11 g, 94%) was prepared from acetophenone (2 g, 16.65 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 56-58 °C; Purity by HPLC: 99%.

IR (KBr) : 3298, 3217, 1645, 1496, 1446, 1369, 1301, 1080, 1006, 925, 759 cm^{-1}

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

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

5.1.68.2. (*E*)-1-(4-flourophenyl)-ethanone oxime (46b)



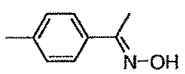
46b (1.77 g, 80%) was prepared from 4-flouroacetophenone (2 g, 14.48 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 62-64 °C; Purity by HPLC: 96%.

IR (KBr) : 3068, 2929, 1602, 1512, 1372, 1234, 1159, 835 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.28 (s, 3H), 7.04-7.10 (m, 2H), 7.57-7.64 (m, 2H), 8.68 (bs, 1H, OH)

ESI/MS (m/z) : 153.9 $(M+H)^+$

5.1.68.3. (*E*)-1-(4-Methylphenyl)-ethanone oxime (46c)



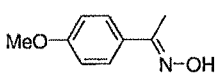
46c (2.18 g, 98%) was prepared from 4-methylacetophenone (2 g, 14.91 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 69-71 °C; Purity by HPLC: 97%.

IR (KBr) : 3242, 3072, 2908, 1606, 1512, 1249, 921 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.27 (s, 3H), 2.36 (s, 3H), 7.21 (d, J= 8.0 Hz, 2H), 7.51 (d, J= 8.2 Hz, 2H), 8.51 (bs, 1H, OH)

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

5.1.68.4. (*E*)-1-(4-Methoxyphenyl)-ethanone oxime (46d)



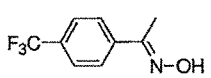
46d (2.07 g, 94%) was prepared from 4-methoxyacetophenone (2 g, 13.32 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 80-82 °C; Purity by HPLC: 99.4 %.

IR (KBr) : 3242, 3072, 2908, 1606, 1512, 1249, 921 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.27 (s, 3H), 3.83 (s, 3H), 6.89 (d, J = 8.6 Hz, 2H), 7.57 (d, J = 8.8 Hz, 2H), 8.43 (bs, 1H, OH)

ESI/MS (m/z) : 165.8 $(M+NH_4)^+$

5.1.68.5. (*E*)-1-(4-(trifluoromethyl)-phenyl)-ethanone oxime (46e)



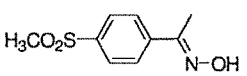
46e (1.81 g, 84%) was prepared from 4- trifluoromethylacetophenone (2 g, 10.63 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 94-96 °C; Purity by HPLC: 99.2 %.

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

^{1}HNMR ($CDCl_3$) : δ 2.29 (s, 3H), 7.56 (d, J = 8.5 Hz, 2H), 7.74 (d, J = 8.2 Hz, 2H), 8.25 (bs, 1H, OH)

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

5.1.68.6. (*E*)-1-(4-(methylsulfonyl)phenyl)-ethanone oxime (46f)



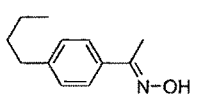
46f (2 g, 93%) was prepared from 4-methylsulfonylacetophenone (2 g, 10.09 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 138-140 °C; Purity by HPLC: 96.5 %.

IR (KBr) : 3006, 2923, 1593, 1467, 1398, 1375, 1298, 1184, 1147, 1095, 108, 974, 929, 765 cm^{-1}

^{1}HNMR ($CDCl_3$) : 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), 8.21 (bs, 1H, OH)

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

5.1.68.7. (*E*)-1-(4-Butylphenyl)-ethanone oxime (46g)



46g (2.06 g, 95%) was prepared from 4-*n*-butylacetophenone (2 g, 11.35 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 40-42 °C; Purity by HPLC: 92.5%.

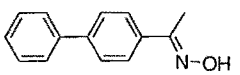
IR (KBr) : 3296, 3028, 2858, 1712, 1610, 1514, 1309, 1082, 923, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.92 (t, J = 7.3 Hz, 3H), 1.25-1.41 (m, 2H), 1.54-1.65 (m, 2H), 2.27 (s, 3H), 2.62 (t, J = 7.56 Hz, 2H), 7.18 (d, J = 8.2

Hz, 2H), 7.53 (d, J = 8.2 Hz, 2H), 8.13 (bs, 1H, OH)

ESI/MS (m/z) : 191.8 $(M+H)^+$

5.1.68.8. (*E*)-1-Biphenyl-4-yl-ethanone oxime (46h)



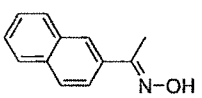
46h (1.72 g, 80%) was prepared from **4-phenylacetophenone** (2 g, 10.19 mmol) according to the procedure described for the preparation of 44 as off white solid. mp: 82-84 °C; Purity by HPLC: 99%.

IR (KBr) : 3263, 2906, 1672, 1487, 1369, 1267, 1002, 837 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.33 (s, 3H), 7.36-7.39 (m, 1H), 7.43-7.48 (m, 2H), 7.60-7.63 (m, 4H), 7.73 (d, J = 8.2 Hz, 2H), 8.05 (bs, 1H, OH)

ESI/MS (m/z) : 233.7 $(M+Na)^+$

5.1.68.9. (*E*)-1-Naphthalen-2-yl-ethanone oxime (46i)



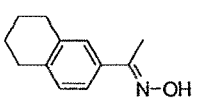
46i (1.96 g, 90%) was prepared from 1-Naphthalen-2-yl-ethanone (2 g, 11.75 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 156-158 °C; Purity by HPLC: 99%.

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

^{1}HNMR ($CDCl_3$) : δ 2.33 (s, 3H), 7.46-7.50 (m, 2H), 7.78-7.90 (m, 5H), 8.03 (bs, 1H, OH)

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

5.1.68.10. (*E*)-1-(5,6,7,8-Tetrahydronaphthalen-2-yl)-ethanone oxime (46j)



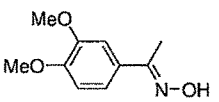
46j (2 g, 92%) was prepared from 1-(5,6,7,8-tetrahydro-naphthalen-2-yl)-ethanone (2 g, 11.48 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 68-70 °C; Purity by HPLC: 96.6%.

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

^{1}HNMR ($CDCl_3$) : 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), 7.32-7.35 (m, 2H), 7.95 (bs, 1H, OH)

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

5.1.68.11. (*E*)-1-(3,4-Dimethoxyphenyl)-ethanone oxime (46k)



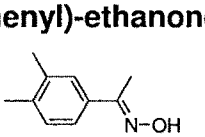
46k (1.91 g, 88%) was prepared from 3,4-dimethoxyacetophenone (2 g, 11.1 mmol) according to the procedure described for the preparation of **44** as off white solid. mp: 77-79 °C; Purity by HPLC: 98.2%.

IR (KBr) : 3431, 3012, 2844, 1602, 1504, 1296, 1149, 1016, 868, 765 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.27 (s, 3H), 3.90 (s, 3H), 3.92 (s, 3H), 6.86 (d, J = 8.3 Hz, 1H), 7.15 (dd, J = 8.3 & 1.9 Hz, 1H), 7.26 (s, 1H), 8.24 (bs, 1H, OH)

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

5.1.68.12. (*E*)-1-(3,4-Dimethylphenyl)-ethanone oxime (46l)



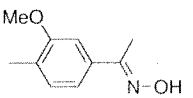
46l (2.04 g, 94%) was prepared from 3,4-dimethylacetophenone (2 g, 13.5 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 76-78 °C; Purity by HPLC: 98.5%.

IR (KBr) : 3203, 3057, 2864,1608, 1568,1508, 1026, 941, 815 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.27 (s, 6H), 2.28 (s, 3H), 7.14 (d, J = 7.8 Hz, 1H), 7.35 (dd, J = 7.8 & 1.6 Hz, 1H), 7.60 (s, 1H), 8.40 (bs, 1H, OH)

ESI/MS (m/z) : 163.9 $(M+H)^+$

5.1.68.13. (*E*)-1-(3-Methoxy-4-methylphenyl)-ethanone oxime (46m)



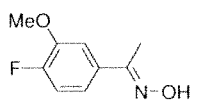
46m (2.14 g, 98%) was prepared from 3-methoxy-4-methylacetophenone (2 g, 12.18 mmol) according to the procedure described for the preparation of **44** as yellow solid. mp: 78-80 °C; Purity by HPLC: 98.3 %.

IR (KBr) : 3211, 3016, 1606, 1510, 1326, 1008, 877, 744 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.23 (s, 3H), 2.26 (s, 3H), 3.85 (s, 3H), 6.81 (d, J = 9.1 Hz, 1H), 7.41 (m, 2H), 8.20 (bs, 1H, OH)

ESI/MS (m/z) : 179.9 $(M+H)^+$

5.1.68.14. (*E*)-1-(4-Fluoro-3-methoxyphenyl)-ethanone oxime (46n)



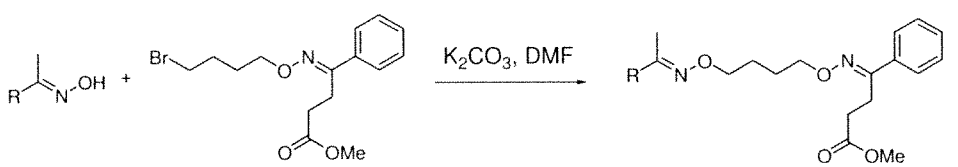
46n (1.92 g, 88%) was prepared from 4-Fluoro-3-methoxyacetophenone (2 g, 11.89 mmol) according to the procedure described for the preparation of **44** as white solid. mp: 125-127 °C; Purity by HPLC: 98%.

IR (KBr) : 3240, 3082, 2844, 1622, 1521, 1317, 1072, 950, 867 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 2.25 (s, 3H), 3.91 (s, 3H), 6.95 (t, J = 8.6 Hz, 1H), 7.33-7.39 (m, 1H), 7.43 (d, J = 2.1 Hz, 1H), 8.20 (bs, 1H, OH)

ESI/MS (m/z) : 183.8 $(M+H)^+$

5.1.69. General procedure for the preparation of the compounds 47a-n

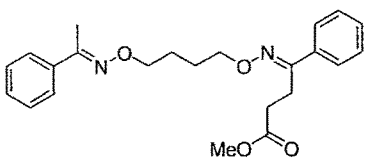


46a-n **45** **47a-n**

A mixture of **46**, **45** (1 mole equivalent) and potassium carbonate (2 mole equivalent) in DMF (5 fold) was stirred at 60 °C for 8 hours under nitrogen atmosphere. The reaction mixture was poured into ice-cold water 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. The crude product obtained was flash chromatographed to yield title product **47**.

5.1.69.1. (*E*,*E*)-Methyl-4-phenyl-4-[4-(1-phenylethylideneaminooxy)-butoxyimino]-butyrate (47a)



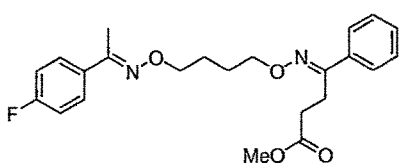
47a (90%) was prepared from **46a** (1 g, 7.4 mmol) and **45** (2.43, 7.4 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 99%.

IR (Neat) : 3020, 2953, 1735, 1608, 1514, 1219 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.81-1.88 (m, 4H), 2.22 (s, 3H), 2.55-2.59 (m, 2H), 3.03-3.07 (m, 2H), 3.64 (s, 3H), 4.22-4.26 (m, 4H), 7.33-7.39 (m, 6H), 7.60-7.65 (m, 4H)

ESI/MS (m/z) : 418.9 $(M+Na)^+$

5.1.69.2. (*E*,*E*)-Methyl-4-{4-[1-(4-fluorophenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyrate (47b)



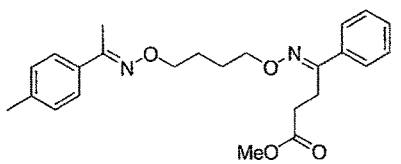
47b (2.57 g, 95%) was prepared from **46b** (1 g, 6.53 mmol) and **45** (2.14 g, 6.53 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 93%.

IR (Neat) : 3018, 2935, 1735, 1602, 1562, 1384, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.83-1.85 (m, 4H), 2.21 (s, 3H), 2.54-2.58 (m, 2H), 3.03-3.07 (m, 2H), 3.64 (s, 3H), 4.24-4.26 (m, 4H), 7.03 (t, J = 8.8 Hz, 2H), 7.34-7.36 (m, 3H), 7.60-7.64 (m, 4H)

ESI/MS (m/z) : 437.1 $(M+Na)^+$

5.1.69.3. (*E,E*)-Methyl-4-{4-[1-(4-methylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyrate (47c)



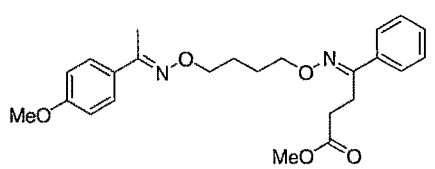
47c (1.93 g, 70%) was prepared from **46c** (1 g, 6.7 mmol) and **45** (2.2 g, 6.7 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 89.4%.

IR (Neat) : 3018, 2939, 1735, 1614, 1514, 1382, 1217, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.83-1.85 (m, 4H), 2.21 (s, 3H), 2.35 (s, 3H), 2.55-2.58 (m, 2H), 3.03-3.07 (m, 2H), 3.64 (s, 3H), 4.22-4.25 (m, 4H), 7.15 (d, J = 7.6 Hz, 2H), 7.33-7.39 (m, 3H), 7.52 (d, J = 8.4 Hz, 2H), 7.60-7.64 (m, 2H)

ESI/MS (m/z) : 411.1 $(M+H)^+$

5.1.69.4. (*E,E*)-Methyl-4-{4-[1-(4-methoxyphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenyl-butyrate (47d)



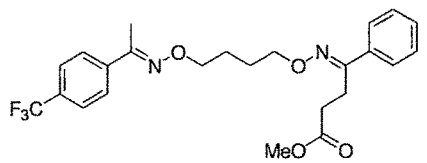
47d (2.14 g, 83%) was prepared from **46d** (1 g, 6.05 mmol) and **45** (1.99 g, 6.05 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 94.2%.

IR (Neat) : 3018, 2937, 1735, 1608, 1514, 1217 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.83-1.85 (m, 4H), 2.20 (s, 3H), 2.54-2.59 (m, 2H), 3.02-3.07 (m, 2H), 3.64 (s, 3H), 3.81 (s, 3H), 4.20-4.26 (m, 4H), 6.86 (dd, J = 6.9 & 2.1 Hz, 2H), 7.34-7.36 (m, 3H), 7.57-7.64 (m, 4H)

ESI/MS (m/z) : 449.1 $(M+Na)^+$

5.1.69.5. (*E,E*)-Methyl-4-{4-[1-(4-trifluromethylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyrate (47e)



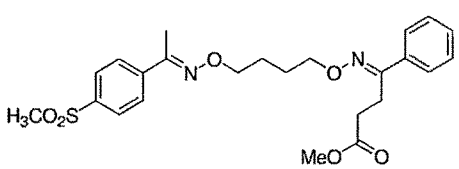
47e (1.94 g, 85%) was prepared from **46e** (1 g, 4.92 mmol) and **45** (1.62 g, 4.92 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 85.8%.

IR (Neat) : 3020, 2955, 1734, 1608, 1438, 1408, 1384, 1215, 1153, 769 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.81-1.87 (m, 4H), 2.23 (s, 3H), 2.55-2.65 (m, 2H), 3.03-3.07 (m, 2H), 3.64 (s, 3H), 4.20-4.28 (m, 4H), 7.34-7.37 (m, 3H), 7.58-7.63 (m, 4H), 7.63 (d, J = 8.8 Hz, 2H)

ESI/MS (m/z) : 486.8 $(M+Na)^+$

5.1.69.6. (*E,E*)-Methyl-4-{4-[1-(4-methylsulfonylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyrate (47f)



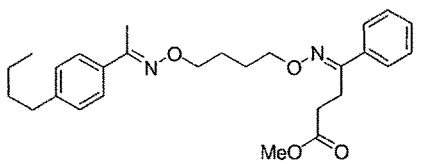
47f (2.21 g, 89%) was prepared from **46f** (1 g, 5.23 mmol) and **45** (1.72 g, 5.23 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 84.8%.

IR (Neat) : 3020, 2955, 1734, 1595, 1438, 1317, 1215, 1153, 769 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.81-1.88 (m, 4H), 2.25 (s, 3H), 2.54-2.58 (m, 2H), 3.03-3.07 (m, 5H), 3.64 (s, 3H), 4.22-4.30 (m, 4H), 7.34-7.37 (m, 3H), 7.61-7.63 (m, 2H), 7.82-7.85 (m, 2H), 7.90-7.94 (m, 2H)

ESI/MS (m/z) : 496.8 $(M+Na)^+$

5.1.69.7. (*E,E*)-Methyl-4-{4-[1-(4-butylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyrate (47g)



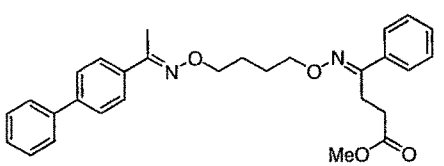
47g (1.75 g, 74%) was prepared from **46g** (1 g, 5.23 mmol) and **45** (1.72 g, 5.23 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 93%.

IR (Neat) : 3018, 2931, 1733, 1614, 1384, 1215, 1049, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.91 (t, J = 7.4 Hz, 3H), 1.33-1.37 (m, 2H), 1.55-1.60 (m, 2H), 1.83-1.85 (m, 4H), 2.21 (s, 3H), 2.55-2.62 (m, 4H), 3.03-3.07 (m, 2H), 3.64 (s, 3H), 4.21-4.25 (m, 4H), 7.15 (d, J = 8.4 Hz, 2H), 7.34-7.37 (m, 3H), 7.53 (d, J = 8.2 Hz, 2H), 7.61-7.63 (m, 2H)

ESI/MS (m/z) : 475.1 $(M+Na)^+$

5.1.69.8. (*E,E*)-Methyl-4-[4-(1-biphenyl-4-yl-ethylideneaminooxy)-butoxyimino]-4-phenylbutyrate (47h)



47h (1.79 g, 80%) was prepared from **46h** (1 g, 4.73 mmol) and **45** (1.55 g, 4.73 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 95.1%.

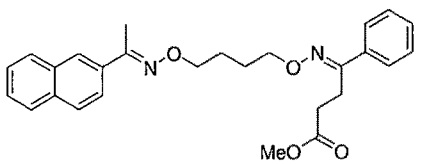
IR (Neat) : 3018, 2933, 1735, 1487, 1371, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.86-1.87 (m, 4H), 2.26 (s, 3H), 2.55-2.59 (m, 2H), 3.03-3.08 (m, 2H), 3.64 (s, 3H), 4.24-4.27 (m, 4H), 7.33-7.37 (m, 4H), 7.44 (t, J = 7.6 Hz, 2H), 7.59-7.64 (m, 6H), 7.71 (d, J =

8.0 Hz, 2H)

ESI/MS (m/z) : 473.1 $(M+H)^+$

5.1.69.9. (*E,E*)-Methyl-4-[4-(1-naphthalen-2-yl-ethylideneaminooxy)-butoxyimino]-4-phenylbutyrate (47i)



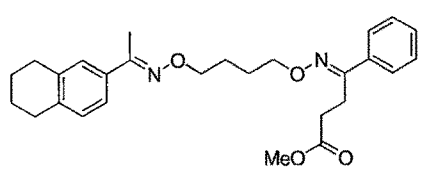
47i (1.69 g, 70%) was prepared from **46i** (1 g, 5.4 mmol) and **45** (1.77 g, 5.4 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 93.1%.

IR (Neat) : 3020, 2954, 1733, 1600, 1510, 1438, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.86-1.89 (m, 4H), 2.34 (s, 3H), 2.54-2.59 (m, 2H), 3.03-3.08 (m, 2H), 3.63 (s, 3H), 4.24-4.32 (m, 4H), 7.34-7.36 (m, 3H), 7.46-7.49 (m, 2H), 7.61-7.64 (m, 2H), 7.78-7.86 (m, 3H), 7.91 (dd, J = 8.7 & 1.8 Hz, 1H), 7.98 (s, 1H)

ESI/MS (m/z) : 469.0 $(M+Na)^+$

5.1.69.10. (*E,E*)-Methyl-4-phenyl-4-{4-[1-(5,6,7,8-tetrahydronaphthalen-2-yl)-ethylideneaminooxy]-butoxyimino}-butyrate (47j)



47j (1.55 g, 65%) was prepared from **46j** (1 g, 5.28 mmol) and **45** (1.73 g, 5.28 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 87.1%.

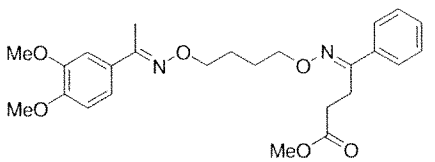
IR (Neat) : 3020, 2959, 1735, 1604, 1517, 1384, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.77-1.79 (m, 4H), 1.81-1.84 (m, 4H), 2.19 (s, 3H), 2.54-2.59 (m, 2H), 2.75-2.77 (m, 4H), 3.03-3.07 (m, 2H), 3.64 (s, 3H), 4.21-4.25 (m, 4H), 7.02 (d, J = 8.0 Hz, 1H), 7.32-7.38

(m, 5H), 7.60-7.63 (m, 2H)

ESI/MS (m/z) : 473.1 $(M+Na)^+$

5.1.69.11. (*E*,*E*)-Methyl-4-{4-[1-(3,4-dimethoxyphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyrate (47k)



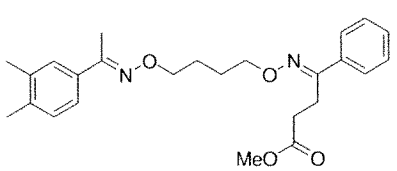
47k (1.92 g, 82%) was prepared from **46k** (1 g, 5.12 mmol) and **45** (1.68 g, 5.12 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 92.3%.

IR (Neat) : 3020, 2873, 1735, 1604, 1517, 1371, 1217, 756 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.84-1.87 (m, 4H), 2.21 (s, 3H), 2.55-2.59 (m, 2H), 3.03-3.07 (m, 2H), 3.64 (s, 3H), 3.89 (s, 3H), 3.91 (s, 3H), 4.22-4.26 (m, 4H), 6.82 (d, J = 8.4 Hz, 1H), 7.13 (dd, J = 8.4 & 2.0 Hz, 1H), 7.28 (d, J = 2.0 Hz, 1H), 7.34-7.37 (m, 3H), 7.60-7.63 (m, 2H)

ESI/MS (m/z) : 457.1 $(M+H)^+$

5.1.69.12. (*E*,*E*)-Methyl-4-{4-[1-(3,4-dimethylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyrate (47l)



47l (1.98 g, 76%) was prepared from **46l** (1 g, 6.13 mmol) and **45** (2 g, 6.13 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 93.1%.

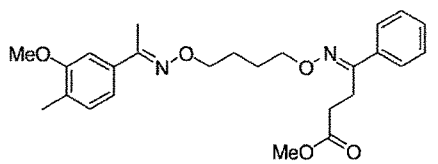
IR (Neat) : 3018, 2910, 1735, 1610, 1500, 1438, 1369, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.83-1.85 (m, 4H), 2.20 (s, 3H), 2.26 (s, 3H), 2.27 (s, 3H), 2.54-2.59 (m, 2H), 3.03-3.07 (m, 2H), 3.64 (s, 3H), 4.20-

4.23 (m, 4H), 7.09 (d, J = 7.7 Hz, 1H), 7.33-7.35 (m, 4H), 7.42 (s, 1H), 7.60-7.63 (m, 2H)

ESI/MS (m/z) : 425.1 $(M+H)^+$

5.1.69.13. (*E,E*)-Methyl-4-{4-[1-(3-methoxy-4-methylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyrate (47m)



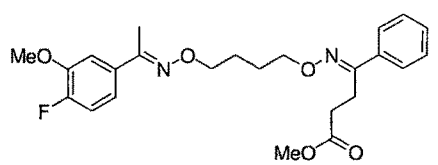
47m (1.77 g, 72%) was prepared from **46m** (1 g, 5.58 mmol) and **45** (1.83 g, 5.58 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 93.8%.

IR (Neat) : 3015, 2900, 1735, 1610, 1500, 1382, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.83-1.86 (m, 4H), 2.19 (s, 3H), 2.22 (s, 3H), 2.55-2.59 (m, 2H), 3.03-3.07 (m, 2H), 3.64 (s, 3H), 3.83 (s, 3H), 4.20-4.25 (m, 4H), 6.77 (d, J = 8.4 Hz, 1H), 7.34-7.36 (m, 3H), 7.41 (dd, J = 8.4 & 2.0 Hz, 1H), 7.44 (s, 1H), 7.62-7.64 (m, 2H)

ESI/MS (m/z) : 441.1 $(M+H)^+$

5.1.69.14. (*E,E*)-Methyl-4-{4-[1-(4-Fluoro-3-methoxyphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyrate (47n)



47n (1.18 g, 81%) was prepared from **46m** (0.6 g, 3.28 mmol) and **45** (1 g, 3.28 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 94.6%.

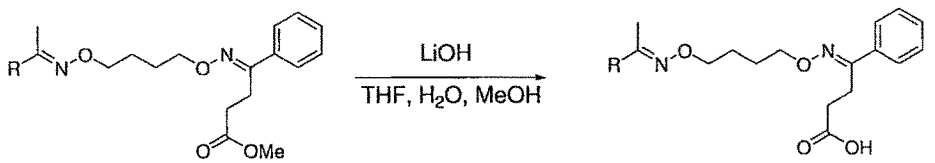
IR (Neat) : 3020, 2937, 1735, 1620, 1594, 1400, 1384, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.80-1.84 (m, 4H), 2.18 (s, 3H), 2.55-2.59 (m, 2H), 3.03-

3.07 (m, 2H), 3.64 (s, 3H), 3.90 (s, 3H), 4.21-4.25 (m, 4H), 6.91 (t, J = 8.8 Hz, 1H), 7.32-7.37 (m, 4H), 7.45 (dd, J = 12.8 & 2.0 Hz, 1H), 7.60-7.63 (m, 2H)

ESI/MS (m/z) : 467.1 $(M+Na)^+$

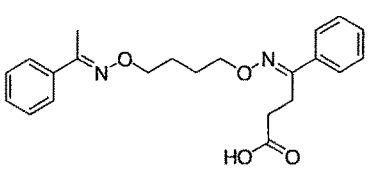
5.1.70. General procedure for the preparation of the compounds 48a-n



47a-n **47a-n**

To a solution of **47** in methanol (9 fold) was added another solution of sodium hydroxide (2 mole equivalent) in water (3 fold) was added and the reaction mixture was stirred at ambient temperature for 10 hours. Solvents were evaporated, the residue was dissolved in water and washed with ethyl acetate. The aqueous layer was acidified with 1N HCl to PH~3 and extracted with ethyl acetate. The organic extract was washed with water, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was flash chromatographed over silicagel to yield title product **48.**

5.1.70.1. (*E,E*)-4-Phenyl-4-[4-(1-phenylethylideneaminooxy)-butoxyimino]-butyric acid (48a)



48a (0.58 g, 60%) was prepared from **47a** (1 g, 2.52 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 97 %.

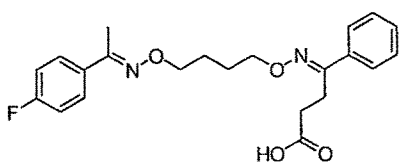
IR (Neat) : 3462, 3020, 1712, 1600, 1444, 1215, 754 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.84-1.88 (m, 4H), 2.23 (s, 3H), 2.58-2.62 (m, 2H), 3.03-3.07 (m, 2H), 4.19-4.26 (m, 4H), 7.32-7.43 (m, 6H), 7.61-7.65 (m, 4H)

^{13}C NMR (DMSO-d_6) : δ 12.90, 21.17, 25.98, 30.78, 73.90, 74.23, 125.14, 125.31, 127.89, 128.28, 129.35, 128.82, 135.31, 136.88, 154.65, 156.26, 178.57

ESI/MS (m/z) : 404.9 $(M+Na)^+$

5.1.70.2. (*E,E*)-4-{4-[1-(4-Fluorophenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48b)



48b (0.87 g, 90%) was prepared from **47b** (1 g, 2.41 mmol) according to the general procedure described above as white solid. mp: 51-53 °C; Purity by HPLC: 95.4 %.

IR (KBr) : 3411, 3018, 2875, 1712, 1602, 1510, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.83-1.85 (m, 4H), 2.21 (s, 3H), 2.58-2.62 (m, 2H), 3.03-3.07 (m, 2H), 4.22-4.26 (m, 4H), 7.05 (t, J = 8.8 Hz, 2H), 7.35-7.37 (m, 3H), 7.59-7.63 (m, 4H)

^{13}C NMR (DMSO-d_6) : δ 12.24, 22.06, 25.42, 30.46, 73.23, 73.37, 115.10, 115.32, 126.32, 128.15, 128.43, 128.57, 132.55, 134.94, 152.83, 156.43, 161.41, 163.85, 173.47

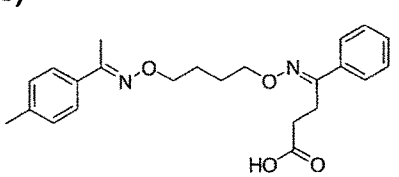
ESI/MS (m/z) : 422.9 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{22}H_{25}FN_2O_4$

Calculated : C, 65.99%; H, 6.29%; N, 7.00%

Found : C, 65.63%; H, 6.34%; N, 6.87%

5.1.70.3. (*E,E*)-4-{4-[1-(4-Methylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48c)



48c (1 g, 86%) was prepared from **47c** (1.2g, 2.92 mmol) according to the general procedure described above as white solid. mp: 64-66 °C; Purity by HPLC: 95.6 %.

IR (KBr) : 3408, 3018, 2875, 1710, 1560, 1384, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.83-1.85 (m, 4H), 2.21 (s, 3H), 2.34 (s, 3H), 2.57-2.61 (m, 2H), 3.04-3.08 (m, 2H), 4.19-4.24 (m, 4H), 7.15 (d, J = 7.6 Hz, 2H), 7.33-7.43 (m, 3H), 7.52 (d, J = 8.0 Hz, 2H), 7.60-7.63 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.22, 21.02, 21.92, 25.49, 25.58, 30.19, 72.98, 73.14, 125.72, 126.11, 128.49, 128.96, 129.25, 133.06, 134.69, 138.56, 153.54, 156.30, 173.40

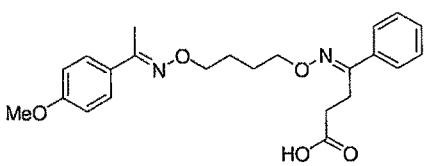
ESI/MS (m/z) : 419.0 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{23}H_{28}N_2O_4$

Calculated : C, 69.67%; H, 7.12%; N, 7.07%

Found : C, 69.25%; H, 7.01%; N, 6.92%

5.1.70.4. (*E,E*)-4-{4-[1-(4-Methoxyphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48d)



48d (1 g, 80%) was prepared from **47d** (1.3 g, 3.05 mmol) according to the general procedure described above as white solid. mp: 54-56 °C; Purity by HPLC: 97.5%.

IR (KBr) : 3400, 3049, 2941, 1701,1608, 1512, 1230, 1051 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.81-1.84 (m, 4H), 2.20 (s, 3H), 2.57-2.61 (m, 2H), 3.03-3.07 (m, 2H), 3.81 (s, 3H), 4.22-4.24 (m, 4H), 6.85 (d, J = 8.8 Hz, 2H), 7.34-7.36 (m, 3H), 7.56-7.60 (m, 4H)

^{13}C NMR (DMSO-d_6) : δ 12.16, 21.91, 25.56, 30.96, 55.12, 73.02, 73.42, 113.73, 126.09, 127.16, 128.46, 129.10, 134.97, 153.22, 156.45,

160.00, 173.34

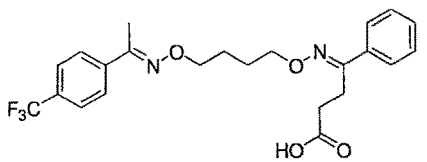
ESI/MS (m/z) : 435.1 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{23}H_{28}N_2O_5$

Calculated : C, 66.97%; H, 6.84%; N, 6.79%

Found : C, 67.19%; H, 6.83%; N, 7.25%

5.1.70.5. (*E,E*)-4-{4-[1-(4-trifluromethylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48e)



48e (1.27 g, 87%) was prepared from **47e** (1.5 g, 3.23 mmol) according to the general procedure described above as white solid. mp: 50-52 °C; Purity by HPLC: 97%.

IR (KBr) : 3412, 3018, 2875, 1710, 1560, 1408, 1327, 1215 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.82-1.87 (m, 4H), 2.24 (s, 3H), 2.58-2.62 (m, 2H), 3.03-3.07 (m, 2H), 4.21-4.28 (m, 4H), 7.34-7.38 (m, 3H), 7.58-7.64 (m, 4H), 7.73 (d, J = 8.4 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.67, 22.20, 25.99, 30.86, 74.28, 125.55, 126.36, 128.71, 129.03, 131.26, 140.23, 153.23, 156.23, 178.80

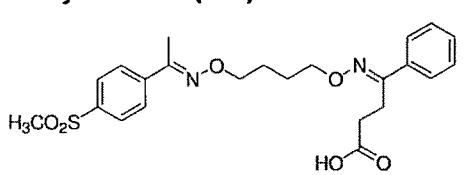
ESI/MS (m/z) : 472.8 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{23}H_{25}F_3N_2O_4$

Calculated : C, 61.33%; H, 5.59%; N, 6.22%

Found : C, 60.98%; H, 5.61%; N, 5.89%

5.1.70.6. (*E,E*)-4-{4-[1-(4-Methylsulfonylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48f)



48f (0.95 g, 49%) was prepared from **47f** (2 g, 4.21 mmol) according to the general procedure described above as white solid. mp: 88-90 °C; Purity by HPLC: 99%.

IR (KBr) : 3412, 2929, 2858, 1708, 1591, 1454, 1400, 1315, 1151, 970 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.77-1.87 (m, 4H), 2.25 (s, 3H), 2.59-2.63 (m, 2H), 3.03-3.07 (m, 5H), 4.22-4.30 (m, 4H), 7.34-7.39 (m, 3H), 7.59-7.63 (m, 2H), 7.82 (dd, J = 6.8 & 1.8 Hz, 2H), 7.91 (dd, J = 6.8 & 1.6 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 12.61, 22.16, 25.94, 30.60, 44.58, 74.10, 74.45, 126.24, 126.86, 127.53, 128.68, 129.37, 133.71, 140.38, 142.05, 152.75, 156.21, 178.28

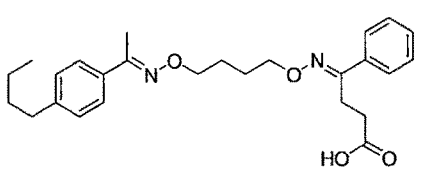
ESI/MS (m/z) : 460.9 $(M+H)^+$

Analysis **Mol.Formula:** $C_{23}H_{28}N_2O_6S$

Calculated : C, 59.98%; H, 6.13%; N, 6.08%

Found : C, 59.58%; H, 6.27%; N, 5.89%

5.1.70.7. (*E*,*E*)-4-{4-[1-(4-Butylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48g)



48g (1 g, 71%) was prepared from **47g** (1.5 g, 3.31 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 96.8%.

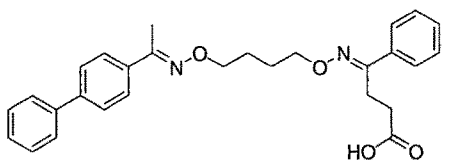
IR (Neat) : 3398, 3018, 2875, 1712, 1614, 1500, 1382, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 0.91 (t, J = 7.2 Hz, 3H), 1.29-1.38 (m, 2H), 1.56-1.62 (m, 2H), 1.83-1.85 (m, 4H), 2.21 (s, 3H), 2.58-2.66 (m, 4H), 3.03-3.07 (m, 2H), 4.21-4.25 (m, 4H), 7.15 (d, J = 8.4 Hz, 2H), 7.32-7.36 (m, 3H), 7.54 (d, J = 8.4 Hz, 2H), 7.60-7.63 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.59, 14.28, 21.95, 22.13, 25.73, 25.89, 29.44, 33.18, 34.98, 73.53, 125.80, 126.12, 128.19, 128.41, 129.30, 132.55, 133.99, 139.06, 143.79, 153.94, 153.98, 173.73

ESI/MS (m/z) : 461.0 $(M+Na)^+$

5.1.70.8. (*E,E*)-4-[4-(1-Biphenyl-4-yl-ethylideneaminooxy)-butoxyimino]-4-phenylbutyric acid (48h)



48h (0.93, 64%) was prepared from **47h** (1.6 g, 3.9 mmol) according to the general procedure described above as white solid. mp: 77-79 °C; Purity by HPLC: 97.4%.

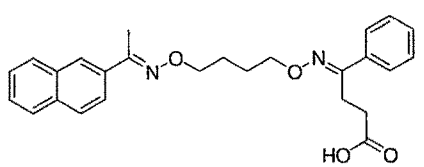
IR (KBr) : 3398, 3018, 2877, 1710, 1564, 1384, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.86-1.87 (m, 4H), 2.26 (s, 3H), 2.58-2.62 (m, 2H), 3.04-3.08 (m, 2H), 4.24-4.27 (m, 4H), 7.35-7.37 (m, 4H), 7.44 (t, J = 7.6 Hz, 2H), 7.57-7.63 (m, 6H), 7.71 (d, J = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.38, 21.93, 25.50, 31.53, 73.31, 73.44, 126.00, 126.37, 126.61, 127.70, 128.50, 129.09, 129.15, 134.97, 135.09, 138.71, 140.66, 153.36, 156.30, 173.41

ESI/MS (m/z) : 481.0 $(M+Na)^+$

5.1.70.9. (*E,E*)-4-[4-(1-Naphthalen-2-yl-ethylideneaminooxy)-butoxyimino]-4-phenylbutyric acid (48i)



48i (0.87 g, 71%) was prepared from **47i** (1 g, 2.24 mmol) according to the general procedure described above as white solid. mp: 72-74 °C; Purity by HPLC: 96.8%.

IR (KBr) : 3409, 2929, 2869, 1699, 1600, 1452, 1051 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.86-1.90 (m, 4H), 2.34 (s, 3H), 2.58-2.62 (m, 2H), 3.02-3.06 (m, 2H), 4.24-4.31 (m, 4H), 7.34-7.36 (m, 3H), 7.46-7.49 (m, 2H), 7.61-7.64 (m, 2H), 7.78-7.86 (m, 3H), 7.91 (dd, J = 8.7 & 1.8 Hz, 1H), 7.98 (s, 1H)

^{13}C NMR (DMSO-d_6) : δ 11.97, 21.94, 25.43, 30.55, 73.33, 123.07, 125.53, 126.03, 126.33, 126.56, 127.39, 127.67, 128.33, 128.37, 129.01, 132.72, 133.08, 133.42, 134.94, 153.53, 156.47, 173.35

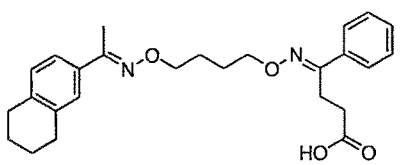
ESI/MS (m/z) : 455.0 $(M+Na)^+$

Analysis **Mol.Formula:** $C_{26}H_{28}N_2O_4$

Calculated : C, 72.20%; H, 6.53%; N, 6.48%

Found : C, 71.94%; H, 6.63%; N, 6.12%

5.1.70.10. (*E*,*E*)-4-Phenyl-4-{4-[1-(5,6,7,8-tetrahydronaphthalen-2-yl)-ethylideneaminooxy]-butoxyimino}-butyric acid (48j)



48j (1.13 g, 90%) was prepared from **47j** (1.3 g, 2.89 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 95.4%.

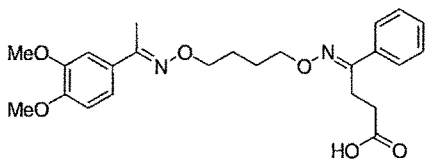
IR (Neat) : 3411, 3018, 1710, 1500, 1384, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.76-1.80 (m, 4H), 1.86-1.89 (m, 4H), 2.20 (s, 3H), 2.58-2.62 (m, 2H), 2.75-2.77 (m, 4H), 3.04-3.08 (m, 2H), 4.21-4.25 (m, 4H), 7.02 (d, J = 8.0 Hz, 1H), 7.32-7.43 (m, 5H), 7.61-7.63 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.19, 21.08, 22.64, 25.52, 28.56, 28.77, 30.44, 72.91, 73.02, 122.89, 126.04, 126.23, 128.41, 128.83, 129.00, 129.06, 133.83, 134.92, 136.08, 136.48, 153.64, 156.40, 173.42

ESI/MS (m/z) : 459.1 $(M+Na)^+$

5.1.70.11. (*E*,*E*)-4-{4-[1-(3,4-Dimethoxyphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48k)



48k (0.68, 72%) was prepared from **47k** (1.4 g, 3.07 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 95.3%.

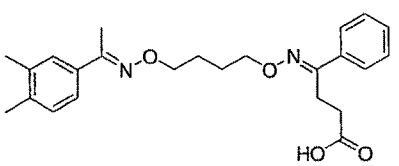
IR (Neat) : 3411, 3020,2875, 1712, 1579, 1518, 1384, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.84-1.87 (m, 4H), 2.21 (s, 3H), 2.57-2.61 (m, 2H), 3.03-3.07 (m, 2H), 3.88 (s, 3H), 3.90 (s, 3H), 4.22-4.26 (m, 4H), 6.82 (d, J = 8.4 Hz, 1H), 7.12 (dd, J = 8.4 & 2.0 Hz, 1H), 7.28 (d, J = 2.0 Hz, 1H), 7.34-7.36 (m, 3H), 7.60-7.63 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.27, 21.95, 25.51, 25.62, 30.21, 55.41, 72.99, 73.09, 108.80, 111.49, 118.98, 126.01, 128.51, 128.73, 133.92, 147.83, 148.81, 153.41, 156.50, 173.45

ESI/MS (m/z) : 465.1 $(M+Na)^+$

5.1.70.12. (*E*,*E*)-4-{4-[1-(3,4-Dimethylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48l)



48l (1.18 g, 76%) was prepared from **47l** (1.6 g, 3.77 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 95.5%.

IR (Neat) : 3124, 3018, 2875, 1712, 1610, 1498, 1404, 1215, 758 cm^{-1}

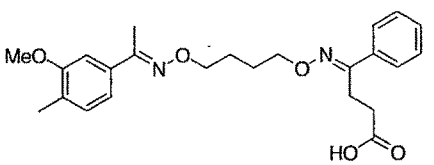
^{1}HNMR ($CDCl_3$) : δ 1.83-1.85 (m, 4H), 2.21 (s, 3H), 2.25 (s, 3H), 2.26 (s, 3H), 2.57-2.62 (m, 2H), 3.03-3.07 (m, 2H), 4.20-4.23 (m, 4H),

7.09 (d, J = 7.7 Hz, 1H), 7.33-7.35 (m, 4H), 7.42 (s, 1H), 7.60-7.63 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.24, 19.18, 19.41, 21.93, 25.36, 30.45, 73.11, 73.46, 123.33, 126.10, 126.75, 128.48, 129.12, 129.44, 133.70, 134.99, 136.11, 137.30, 153.63, 156.43, 173.41

ESI/MS (m/z) : 411.1 $(M+H)^+$

5.1.70.13. (*E*,*E*)-4-{4-[1-(3-Methoxy-4-methylphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48m)



48m (0.726 g, 50%) was prepared from **47m** (1.5 g, 3.4 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 96.5%.

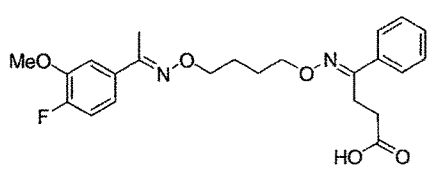
IR (Neat) : 3411, 3018, 2875, 1710, 1610, 1508, 1384, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.83-1.86 (m, 4H), 2.20 (s, 3H), 2.21 (s, 3H), 2.58-2.62 (m, 2H), 3.04-3.08 (m, 2H), 3.83 (s, 3H), 4.21-4.26 (m, 4H), 6.77 (d, J = 8.4 Hz, 1H), 7.34-7.36 (m, 3H), 7.41 (dd, J = 8.4 & 2.0 Hz, 1H), 7.44 (s, 1H), 7.61-7.63 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.18, 16.06, 21.90, 25.32, 25.45, 30.47, 55.28, 72.96, 73.41, 109.87, 124.90, 125.77, 126.09, 127.63, 128.04, 128.48, 129.13, 134.95, 153.31, 156.29, 158.14, 173.37

ESI/MS (m/z) : 449.1 $(M+Na)^+$

5.1.70.14. (*E*,*E*)-4-{4-[1-(4-Fluoro-3-methoxyphenyl)-ethylideneaminooxy]-butoxyimino}-4-phenylbutyric acid (48n)



48n (0.714 g, 82%) was prepared from **47n** (0.9 g, 2.02 mmol) according to the general procedure described above as a liquid. Purity by HPLC: 95.5%.

IR (Neat) : 3411, 3018, 2937, 1710, 1562, 1502, 1384, 1215, 758 cm^{-1}

^{1}HNMR ($CDCl_3$) : δ 1.83-1.86 (m, 4H), 2.18 (s, 3H), 2.58-2.62 (m, 2H), 3.04-3.08 (m, 2H), 3.89 (s, 3H), 4.21-4.26 (m, 4H), 6.91 (t, J = 8.8 Hz, 1H), 7.32-7.37 (m, 4H), 7.45 (dd, J = 12.8 & 2.0 Hz, 1H), 7.60-7.63 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.46, 21.26, 25.83, 25.93, 30.90, 56.45, 73.63, 73.78, 113.48, 113.86, 113.87, 122.85, 126.39, 128.45, 129.54, 134.29, 148.25, 150.46, 152.90, 156.93, 173.85

ESI/MS (m/z) : 453.0 $(M+Na)^+$

5.2. Biology

5.2.1. *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 the 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 β- galactosidase 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 PPARγ or PPARδ and 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 the supernatant was 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 [Promega] instructions in white 96-well plate [Nunc]. β-Galactosidase activity was determined in ELISA reader at 415 nm. The ratio of luciferase versus β-galactosidase 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 test compounds were calculated by nonlinear regression analysis using graph pad prism software. Each concentration point represents values in duplicates.

5.2.2. *in vivo* experiments

All the animals were bred at animal breeding facility of Zydus research centre, registered under Rule 5(a) for the "Breeding and Experiments on Animals (control and supervision) rules 1998, [Registration no.77/1999 (CPCSEA)]. All the study protocols were approved by Institutional Animal Ethics Committee.

5.2.2.1. Pharmacokinetics experiment

Pharmacokinetic behavior 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 carbomethoxy cellulose (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 (ethyl acetate: 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.

5.2.2.2. 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.

5.2.2.3. Glucose and triglyceride (TG) lowering activity in *db/db* mice

Male *db/db* mice of 8-12 weeks age and 30-45 g of body weight were selected for the study. The animals having serum glucose in the range 300-550 mg/dl on day 0 were randomized according to their non fasted serum glucose levels and divided into different groups having 6 animals in each group. All animals then were orally dosed once daily with vehicle (10 % PEG400 and 90% (0.5%) sodium carboxymethyl cellulose in water) and the test compounds for 6 days. All animals were fed *ad libitum* throughout the study. On day 6 exactly one hour after the last dose, the animals were bled and the serum was analyzed for glucose and triglycerides to calculate percent change due to drug treatment versus control group of animals using the formula mentioned in the previous experiment (This takes into account any changes that may have occurred in the vehicle-treated animals during the study).

5.2.2.4. Hypolipidemic & *anti*-hyperglycemic activity in Zucker *fa/fa* rats

Male Zucker *fa/fa* rats of 13-15 weeks age and 450-550 g of body weight were selected for the study. The animals were weighed and bled for pretreatment (day 0) non fasted serum triglyceride (TG), glucose, and cholesterol (TC) measurement. Animal were randomized and grouped with 6 animals per group based on day 0 mean glucose, TG and TC levels. All animals then were orally dosed once daily with vehicle (10 % PEG400 and 90% (0.5%) sodium carboxymethyl cellulose in water) and test compounds for 14 days. All the animals were fed *ad libitum* throughout the study. On day 14 exactly one hour after the last dose, the animals were bled and the serum was analyzed for glucose, triglycerides and total cholesterol (TC) to calculate percent change due to drug treatment versus control group of animals. (This takes into account any changes that may have occurred in the vehicle-treated animals during the study).

5.2.2.4.1. Oral Glucose tolerance test (OGTT) in *Zucker fa/fa* rats

On day 15, 16-18 hour fasted Zucker *fa/fa* rats were subjected to oral glucose challenge. Animals were treated with the test compounds and or vehicle as per group and exactly one hour after, 0 min blood collection was done and glucose load at 3g/kg was administered orally. After 30, 60 and 120 min of glucose load animals were bled for serum glucose. The glucose area-under-the-curve (AUC) was calculated over 0 to 120 min using the trapezoidal method in Graphpad prism software and the results are reported as percent improvement in glucose AUC versus vehicle treated control group.

5.2.2.5. 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 weight were 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.