4 Experimental

4.1 Chemistry

4.1.1 Materials and Methods

Reagents were obtained from commercial suppliers and used without further purification. Solvents were procured from commercial source and used after distilling or drying according to the known methods. All the air and/or moisture sensitive reactions were carried out in dry solvents under nitrogen atmosphere. Melting points were recorded in open glass capillaries, using a scientific melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu FT IR 8300 spectrophotometer (ν_{max} in cm^{-1}, as film for liquids and as KBr pellets for solid compounds). The ^{1}H NMR spectra were recorded on a Bruker Avance-300 (300 MHz) or Bruker Avance-400 (400 MHz) spectrometer. The chemical shifts (δ) are reported in parts per million (ppm) relative to TMS,

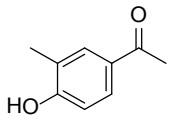
either in $CDCl_3$ or DMSO-d_6. Signal multiplicities are represented as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), bs (broad singlet), and m (multiplet). D_2O exchange experiments were carried out to confirm the exchangeable protons when present. ^{13}C NMR spectra were recorded on Bruker Avance-400 at 100 MHz either in $CDCl_3$ or DMSO-d_6. Mass spectra (ESI-MS) were obtained on Shimadzu LCMS 2010-A spectrometer. Elemental analyses were carried out using a Perkin-Elmer 2400 CHN analyzer. HPLC analyses were carried out at λ_{max} 220 nm using column ODS C-18, 150nm * 4.6 nm * 4 μ on AGILENT 1100. Progress of the reactions was monitored by TLC using precoated TLC plates (E. Merck Kieselgel 60 F254) and the spots were visualized by UV and/or iodine vapors. The chromatographic purification was performed on silica gel (230–400 mesh).

4.1.2 General procedure for the synthesis of Compounds 2a-f

1a-f **2a-f**

Anhydrous $AlCl_3$ (1 mole equivalent) was added in small portions to esters (**1a-f**) (1 mole equivalent) at 25 ^oC. The reaction temperature was slowly raised to 160 ^oC and stirred at the same temperature for 2 hours. The reaction mixture was poured in ice cold 6N HCl (20 fold) and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure to yield crude product. The crude product was purified by column chromatography (10-15% ethyl acetate in hexane) to give the compound **2a-f.**

4.1.2.1 4-Hydroxy-3-methylacetophenone (2a)



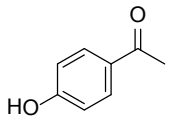
2a (7.0 gm, 28%) was prepared from **1a** (25.0 gm, 0.166 mol) following the general procedure described above as a yellow solid. mp: 99-100 ^{o}C; Purity by HPLC: 99.5%.

IR (KBr) : 3130, 2925, 1651, 1589, 1514, 1182 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.29 (s, 3H), 2.56 (s, 3H) , 5.92 (s, OH), 6.80 (d, *J* = 8.3 Hz, 1H), 7.74 (dd, *J* = 8.3 & 1.9 Hz, 1H), 7.79 (s, 1H)

ESI/MS (m/z) : 150.7 $(M+H)^{+}$

4.1.2.2 4-Hydroxyacetophenone (2b)



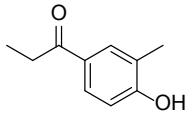
2b (8.0 gm, 40%) was prepared from **1b** (20.0 gm, 0.146 mol) following the general procedure described above as an off white solid. mp: 109-110 ^{o}C; Purity by HPLC: 97.8%.

IR (KBr) : 3309, 2968, 2424, 1662, 1602, 1577, 1357, 1278, 1219, 1165, 1107, 962, 848, 633, 567. cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.57 (s, 3H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.90 (d, *J* = 8.8 Hz, 2H)

ESI/MS (m/z) : 137.2 $(M+H)^{+}$

4.1.2.3 1-(4-Hydroxy-3-methylphenyl)propan-1-one (2c)



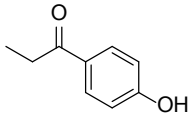
2c (8.7 gm, 58%) was prepared from **1c** (15.0 gm, 0.091 mol) following the general procedure described above as an off white solid. mp: 130-131 ^{o}C; Purity by HPLC: 95.3%.

IR (KBr) : 3365, 2980, 1664, 1593, 1514, 1465, 1352, 1257, 1170, 1132, 1082, 976, 910, 800, 675 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.20 (t, *J* = 7.4 Hz, 3H), 2.29 (s, 3H), 2.95 (q, *J* = 7.2 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 1H), 7.73 (dd, *J* = 8.4 & 2.4 Hz, 1H), 7.80 (d, *J* = 1.2 Hz, 1H)

ESI/MS (m/z) : 165.3 $(M+H)^+$

4.1.2.4 1-(4-Hydroxyphenyl)propan-1-one (2d)



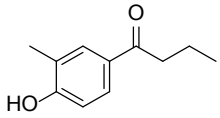
2d (7.8 gm, 58%) was prepared from **1d** (15.0 gm, 1.000 mol) following the general procedure described above as an off white solid. mp: 147-148 ^{o}C; Purity by HPLC: 97.4 %.

IR (KBr) : 3217, 2974, 2939, 2808, 1662, 1606, 1572, 1514, 1450, 1357, 1288, 1172, 1112, 1016, 952, 858, 802 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.22 (t, *J* = 7.2 Hz, 3H), 2.95 (q, *J* = 7.2 Hz, 2H), 6.86-6.90 (m, 2H), 7.90-7.93 (m, 2H)

ESI/MS (m/z) : 151.8 $(M+H)^+$

4.1.2.5 1-(4-Hydroxy-3-methylphenyl)butan-1-one (2e)



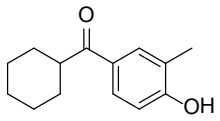
2e (4.05 gm, 27%) was prepared from **1e** (15.0 gm, 0.084 mol) following the general procedure described above as a yellow solid. mp: 129-130 ^{o}C; Purity by HPLC: 99.6%.

IR (KBr) : 3269, 3190, 2727, 2414, 1656, 1512, 1407, 1130 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.99 (t, *J* = 7.4 Hz, 3H), 1.66-1.81 (m, 2H), 2.29 (s, 3H), 2.89 (t, *J* = 7.3 Hz, 2H), 5.78 (s, OH), 6.81 (d, *J* = 8.3 Hz, 1H), 7.72-7.79 (m, 2H)

ESI/MS (m/z) : 178.7 $(M+H)^+$

4.1.2.6 Cyclohexyl(4-hydroxy-3-methylphenyl)methanone (2f)



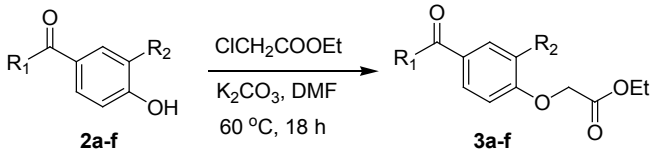
2f (3.90 gm, 26%) was prepared from **1f** (15.0 gm, 0.069 mol) following the general procedure described above as an off white solid. mp: 144-146 ^oC; Purity by HPLC: 98.7%.

IR (KBr) : 3348, 2858, 1899, 1652, 1589, 1512, 1456, 1269, 914, 827cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.21-1.63 (m, 5H), 1.72-1.74 (m, 1H), 1.80-1.91 (m, 4H), 2.30 (s, 3H), 3.11-3.31 (m, 1H), 6.82 (d, *J* = 8.3 Hz, 1H), 7.71-7.80 (m, 2H)

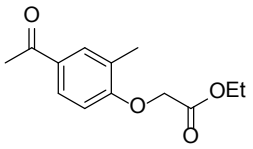
ESI/MS (m/z) : 240.9 $(M+Na)^+$

4.1.3 General procedure for the synthesis of Compounds 3a-f



To an ice cold solution of **2a-f** (1 mole equivalent) in DMF (5 fold), K_2CO_3 (2 mole equivalent) and ethyl chloroacetate (1.12 mole equivalent) was added and reaction mixture was stirred at 60 ^oC for 18 hours. The reaction mixture was poured in ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure to yield the compound **3a-f**.

4.1.3.1 Ethyl 2-(4-acetyl-2-methylphenoxy)acetate (3a)



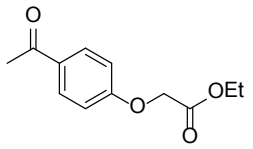
3a (10.79 gm, 98%) was prepared from **2a** (7.0 gm, 0.047 mol) following the general procedure described above as a thick oil. Purity by HPLC: 95.2%.

IR (Neat) : 3435, 3338, 2983, 2929, 1757, 1676, 1600, 1585, 1502, 1440, 1415, 1382, 1359, 1269, 1205, 1182, 1136, 1091, 1068, 1026, 970, 813 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.32 (t, *J* = 7.1 Hz, 3H), 2.32 (s, 3H), 2.54 (s, 3H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.73 (s, 2H), 6.70 (d, *J* = 8.2 Hz, 1H), 7.70-7.71 (m, 2H)

ESI/MS (m/z) : 236.8 $(M+H)^+$

4.1.3.2 Ethyl 2-(4-acetylphenoxy)acetate (3b)



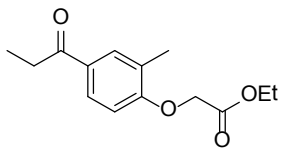
3b (10.85 gm, 95%) was prepared from **2b** (7.0 gm, 0.051 mol) following the general procedure described above as a thick oil. Purity by HPLC: 92.5%.

IR (Neat) : 3020, 2985, 1755, 1676, 1600, 1508, 1359, 1273, 1172, 1085, 1022, 958, 592 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.29 (t, *J* = 7.2 Hz, 3H), 2.56 (s, 3H), 4.26 (q, *J* = 7.2 Hz, 2H), 4.69 (s, 2H), 6.92-6.96 (m, 2H), 7.78-7.80 (m, 2H)

ESI/MS (m/z) : 223.3 $(M+H)^+$

4.1.3.3 Ethyl 2-(2-methyl-4-propionylphenoxy)acetate (3c)



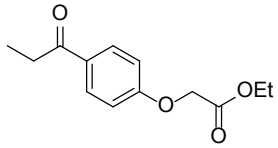
3c (11.94 gm, 90%) was prepared from **2c** (8.7 gm, 0.053 mol) following the general procedure described above as an off white solid. m.p. 55-57 ^{o}C; Purity by HPLC: 98.0%.

IR (KBr) : 2976, 1755, 1670, 1600, 1498, 1450, 1381, 1280, 1209, 1145, 1072, 798, 626 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.19 (t, *J* = 7.4 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 2.32 (s, 3H), 2.92 (q, *J* = 7.2 Hz, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.71 (s, 2H), 6.70 (d, *J* = 8.0 Hz, 1H), 7.78-7.80 (m, 2H)

ESI/MS (m/z) : 251.3 $(M+H)^{+}$

4.1.3.4 Ethyl 2-(4-propionylphenoxy)acetate (3d)



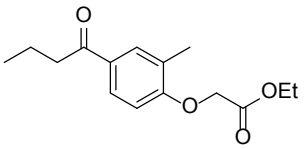
3d (11.66 gm, 95%) was prepared from **2d** (7.8 gm, 0.052 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 93.3%.

IR (Neat) : 3350, 3020, 2983, 2939, 1757, 1679, 1602, 1508, 1417, 1380, 1353, 1301, 1215, 1172, 1080, 1018, 842, 758, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.21 (t, *J* =7.2 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 2.91 (q, *J* = 7.2 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.68 (s, 2H), 6.89 (dd, *J* = 6.9 & 1.9 Hz, 2H), 7.92 (dd, *J* = 6.9 & 1.9 Hz, 2H)

ESI/MS (m/z) : 236.9 $(M+H)^{+}$

4.1.3.5 Ethyl 2-(4-butyryl-2-methylphenoxy)acetate (3e)



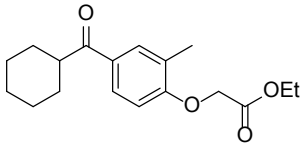
3e (5.81 gm, 98%) was prepared from **2e** (4.0 gm, 0.022 mol) following the general procedure described above as an off white solid. m.p. 70-71^{o}C; Purity by HPLC: 99.1%.

IR (KBr) : 3411, 3035, 2873, 1755, 1600, 1500, 1328, 1109 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.99 (t, *J* = 7.4 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.66-1.78 (m, 2H), 2.32 (s, 3H), 2.88 (t, *J* = 7.3 Hz, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.70 (s, 2H), 6.70 (d, *J* = 8.3 Hz, 1H), 7.72-7.79 (m, 2H)

ESI/MS (m/z) : 264.9 $(M+H)^+$

4.1.3.6 Ethyl 2-(4-(cyclohexanecarbonyl)-2-methylphenoxy)acetate (3f)



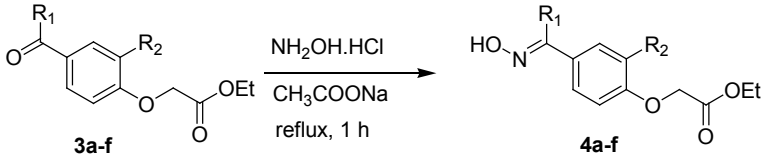
3f (5.27 gm, 97%) was prepared from **2f** (3.9 gm, 0.018 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.9%.

IR (Neat) : 3425, 2935, 1911, 1757, 1658, 1496, 1247, 1004, 916, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.21-1.49 (m, 8H), 1.71-1.72 (m, 1H), 1.82-1.84 (m, 4H), 2.33 (s, 3H), 3.11-3.26 (m, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.71 (s, 2H), 6.69 (d, *J* = 9.1 Hz, 1H), 7.74-7.80 (m, 2H)

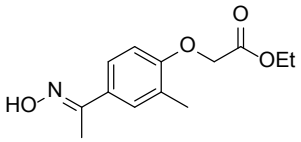
ESI/MS (m/z) : 304.9 $(M+H)^+$

4.1.4 General procedure for the synthesis of Compounds 4a-f



To a solution of **3a-f** (1 mole equivalent) in ethanol (6 fold), a solution of hydroxylammonium chloride (2 mole equivalent) and sodium acetate (2 mole equivalent) in water (2 fold) was added and the reaction mixture was heated to reflux for a period of about 1 hours. Rection mixture was cooled to room temperature and solvent was evapourated under reduced pressure. The residue was diluted with water, solid separated was filtered and dried over P_2O_5 under vaccum to yield compounds **4a-f**.

4.1.4.1 (*E*)-Ethyl 2-(4-(1-(hydroxyimino)ethyl)-2-methylphenoxy) acetate (4a)



4a (22.7 gm, 71%) was prepared from **3a** (15.0 gm, 0.064 mol) following the general procedure described above as a white soluid. m.p. 105-107 ^{o}C; Purity by HPLC: 98.3%.

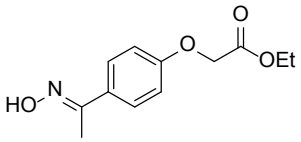
IR (KBr) : 3217, 3082, 2981, 2910, 1762, 1604, 1508, 1434, 1415, 1384, 1305, 1278, 1259, 1213, 1168, 1153, 1097, 1074, 945, 889, 813, 748 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.32 (t, *J* = 7.1 Hz, 3H), 2.25 (s, 3H), 2.31 (s, 3H), 4.22 (q, *J* = 7.1 Hz, 2H), 4.65 (s, 2H), 6.73 (d, *J* = 8.5 Hz, 1H), 7.37 (dd, *J* = 8.5 & 2.0 Hz, 1H), 7.45 (s, 1H)

^{13}C NMR (DMSO-*d*$_6$) : δ 11.4, 14.0, 16.1, 60.6, 64.9, 111.1, 124.3, 125.8, 127.8, 129.8, 152.4, 156.2, 168.7

ESI/MS (m/z) : 251.9 $(M+H)^{+}$

4.1.4.2 (*E*)-Ethyl 2-(4-(1-(hydroxyimino)ethyl)phenoxy)acetate (4b)



4b (8.65 gm, 81%) was prepared from **3b** (10.0 gm, 0.045 mol) following the general procedure described above as an off white soluid. m.p. 91-92 ^{o}C; Purity by HPLC: 98.1%.

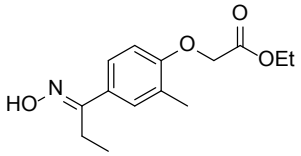
IR (KBr) : 3300, 2908, 1761, 1600, 1514, 1483, 1373, 1259, 1209, 1176, 1076, 1006, 927, 829, 765, 601 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.28 (t, *J* = 7.2 Hz, 3H), 2.26 (s, 3H), 4.25 (q, *J* = 7.2 Hz, 2H), 4.64 (s, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 7.57 (d, *J* = 8.8 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 11.4, 14.0, 60.7, 64.6, 114.3, 126.8, 130.1, 152.3, 158.0, 168.6

ESI/MS (m/z) : 238.3 $(M+H)^+$

4.1.4.3 (*E*)-Ethyl 2-(4-(1-(hydroxyimino)propyl)-2-methylphenoxy) acetate (4c)



4c (9.33 gm, 88%) was prepared from **3c** (10.0 gm, 0.040 mol) following the general procedure described above as an off white solid. m.p. 84-86 ^oC; Purity by HPLC: 98.7%.

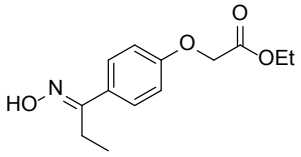
IR (KBr) : 3277, 2987, 2928, 1753, 1604, 1508, 1437, 1346, 1284, 1205, 1184, 1139, 1072, 1022, 956, 856, 754 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.14 (t, *J* = 7.6 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 2.31 (s, 3H), 2.75 (q, *J* = 7.6 Hz, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.66 (s, 2H), 6.68 (d, *J* = 8.4 Hz, 1H), 7.37 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.44 (s, 1H)

^{13}C NMR (DMSO-d_6) : δ 8.3, 14.0, 16.0, 30.8, 60.8, 64.9, 110.9, 126.1, 127.8, 129.7, 130.4, 159.5, 168.4, 199.0

ESI/MS (m/z) : 266.3 $(M+H)^+$

4.1.4.4 (*E*)-Ethyl 2-(4-(1-(hydroxyimino)propyl)phenoxy)acetate (4d)



4d (10.06 gm, 86%) was prepared from **3d** (11.0 gm, 0.047 mol) following the general procedure described above as a white solid. m.p. 70-72 ^oC; Purity by HPLC: 84.6%.

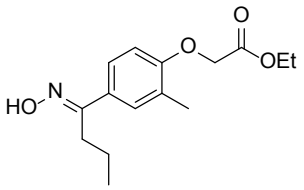
IR (KBr) : 3355, 2981, 2941, 2877, 1705, 1624, 1600, 1514, 1467, 1514, 1448, 1406, 1367, 1313, 1240, 1178, 1116, 1066, 1029, 970, 916, 825 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.16 (t, *J* = 7.5 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 2.82 (q, *J* = 7.6 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 4.64 (s, 2H), 6.92 (dd, *J* = 6.9 & 1.9 Hz, 2H), 7.54 (dd, *J* = 6.9 & 1.9 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 10.9, 14.0, 18.2, 60.7, 64.6, 114.4, 127.0, 128.9, 157.1, 157.9, 168.1

ESI/MS (m/z) : 252.0 $(M+H)^+$

4.1.4.5 (*E*)-Ethyl 2-(4-(1-(hydroxyimino)butyl)-2-methylphenoxy) acetate (4e)



4e (5.64 gm, 92%) was prepared from **3e** (5.8 gm, 0.022 mol) following the general procedure described above as an off white solid. m.p. 71-72 ^oC; Purity by HPLC: 97.7%.

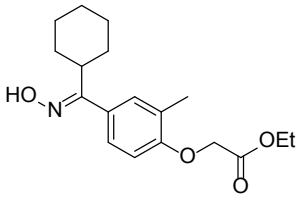
IR (KBr) : 3369, 3033, 2873, 1701, 1606, 1508, 1026 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.97 (t, *J* = 7.4 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.51-1.64 (m, 2H), 2.30 (s, 3H), 2.74 (t, *J* = 7.6 Hz, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.65 (s, 2H), 6.70 (d, *J* = 8.5 Hz, 1H), 7.37 (dd, J = 8.5 & 2.5 Hz, 1H), 7.43 (s, 1H)

^{13}C NMR (DMSO-d_6) : δ 14.0, 16.1, 19.5, 26.6, 60.6, 64.8, 111.1, 124.5, 125.9, 128.0, 128.9, 156.1, 168.7

ESI/MS (m/z) : 279.9 $(M+H)^+$

4.1.4.6 (*E*)-Ethyl 2-(4-(cyclohexyl(hydroxyimino)methyl)-2-methyl phenoxy)acetate (4f)



4f (3.46 gm, 66%) was prepared from **3f** (5.0 gm, 0.016 mol) following the general procedure described above as an off white solid. m.p. 100-103 ^{o}C; Purity by HPLC: 85.2%.

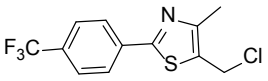
IR (KBr) : 3247, 3074, 2929, 1768, 1608, 1506, 1215, 1174, 956, 806 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.12-1.32 (m, 9H), 1.62-1.64 (m, 1H), 1.70-1.83 (m, 4H), 2.31 (s, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.62 (s, 2H), 6.71 (d, *J* = 8.1 Hz, 1H), 7.01-7.06 (m, 2H)

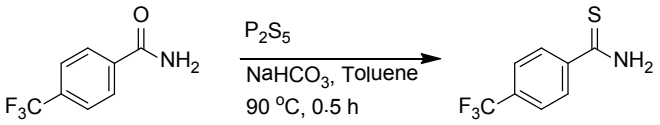
^{13}C NMR (DMSO-d_6) : δ 14.0, 16.0, 25.7, 25.8, 30.6, 43.2, 60.6, 64.8, 110.6, 125.2, 126.4, 127.2, 130.1, 155.2, 159.1, 168.8

ESI/MS (m/z) : 320.0 $(M+H)^{+}$

4.1.5 5-(Chloromethyl)-4-methyl-2-(4-trifluoromethylphenyl) thiazole (9)



Step I: 4-(Trifluoromethyl)benzothioamide (**6**)



5 **6**

Phosphorus pentasulfide (35.3 gm, 0.318 mol) and sodium bicarbonate (22.2 gm, 0.265 mol) were added to toluene (100 ml) under nitrogen. The resulting suspension was warmed to 90 °C and stirred for 30 minutes. To the resulting suspension were added a solution of 4-(trifluoromethyl)benzamide (**5**)

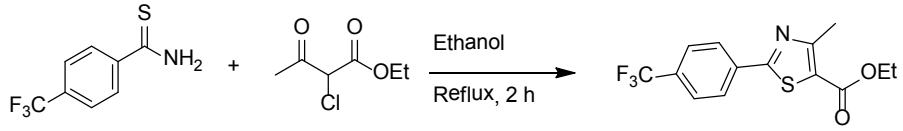
(25.0 gm, 0.132 mol) in toluene (100 ml) drop wise over 40 minutes. The resulting mixture was heated to reflux for 1 h. The heat was removed and 50 ml of tetrahydrofuran were added to the warm suspension. After the mixture had cooled to ambient temperature, 30 ml of water were added, and stirring was continued for three hours. The resulting suspension was filtered. The organic phase in the filtrate was separated, dried over sodium sulphate and evaporated under vacuum to yield the title compound as a white solid (27.0 gm, 99%). m.p. 140-142 ^{o}C; Purity by HPLC: 95.1%.

IR (KBr) : 3436, 3354, 3163, 1627, 1429, 1322, 1169, 1120, 1064, 1014, 896, 845 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 2H)

ESI/MS (m/z) : 204.0 $(M-H)^{+}$

Step II: Ethyl 4-methyl-2-(4-trifluoromethylphenyl)thiazole-5-carboxylate (**7**)



6 **7**

To a solution of **6** (5.0 gm, 0.0265 mol) in ethanol (25 ml), ethyl 2-chloroacetoacetate (3.38 ml, 0.0265 mol) was added and reaction mixture was refluxed for 2 h. The reaction mixture was cooled to ambient temperature and solvent was evaporated under vacuum. The residue was dissolved in ethyl acetate (50 ml), washed with water, dried over sodium sulphate and evaporated under vacuum to yield the title compound **7** as a pale brown solid (7.5 gm, 98%). m.p. 84-86 ^{o}C; Purity by HPLC: 99.1%.

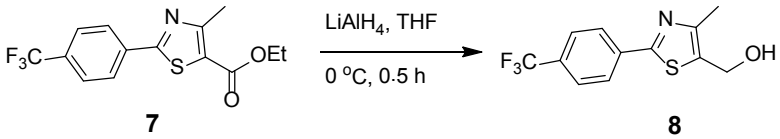
IR (KBr) : 3113, 2993, 1714, 1614, 1517, 1438, 1406, 1373, 1319, 1269, 1159, 1120, 1066, 1008, 846 cm^{-1}

^{1}H NMR : δ 1.42 (t, *J* = 7.1 Hz, 3H), 2.83 (s, 3H), 4.41 (q, *J* = 7.1 Hz, 2H),

($CDCl_3$) 7.74 (d, *J* = 8.2 Hz, 2H), 8.01 (d, *J* = 8.2 Hz, 2H)

ESI/MS (m/z) : 316.1 $(M+H)^+$

Step III: (4-Methyl-2-(4-trifluoromethylphenyl)thiazol-5-yl)methanol (**8**)



7 **8**

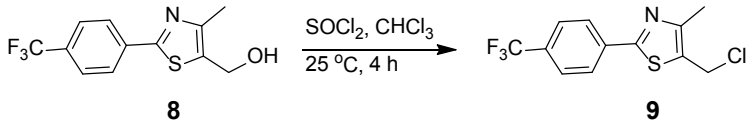
To a solution of **7** (7.0 gm, 0.022 mol) in THF (100 mL), $LiAlH_4$ (0.842 gm, 0.022 mol) was added in small portions at 0 °C over a period of 30 min. and stirred at 25 °C for 0.5 h. The excess $LiAlH_4$ was quenched by drop-wise addition of saturated aqueous Na_2SO_4 solution at 0-10 °C. Solid residue was filtered and washed with ethyl acetate. Filtrate was evaporated under reduced pressure to give the title compound **8** as a pale yellow solid. (3.1 gm, 51%). m.p. 122-124 °C; Purity by HPLC: 93.8%.

IR (KBr) : 3284, 3072, 2931, 1681, 1541, 1450, 1407, 1325, 1164, 1114, 1068, 1022, 846, 835 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.09 (bs, 1H), 2.45 (s, 3H), 4.84 (s, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 8.0 (d, *J* = 8.2 Hz, 2H)

ESI/MS (m/z) : 274.1 $(M+H)^+$

Step IV: 5-(Chloromethyl)-4-methyl-2-(4-trifluoromethylphenyl)thiazole (**9**)



8 **9**

To a solution of **8** (15.6 gm, 0.057 mol) in $CHCl_3$ (60 mL), $SOCl_2$ (5.0 ml, 0.069 mol) was added drop wise at 0 °C over a period of 10 min. and stirred at 25 °C for 4 h. The reaction mixture was diluted with $CHCl_3$ (200 ml), washed with water, $NaHCO_3$ solution and brine, dried over anhydrous $CaCl_2$ and evaporated

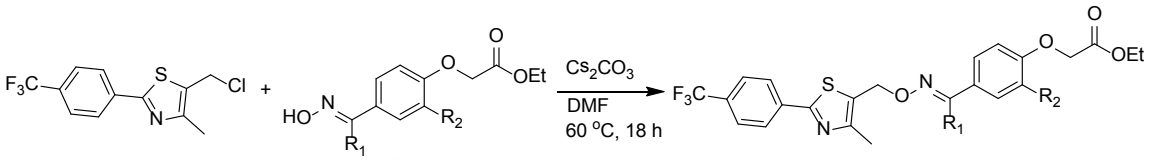
under vacuum to yield the title product **9** as a pale yellow solid. (17.2 gm, 99%). m.p. 62 - 64 ^{o}C; Purity by HPLC: 87.1%.

IR (KBr) : 3421, 2927, 1618, 1452, 1352, 1166, 1126, 1110, 1066, 848, 831 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.5 (s, 3H), 4.85 (s, 2H), 7.6 (d, *J* = 8.2 Hz, 2H), 8.0 (d, *J* = 8.1 Hz, 2H)

ESI/MS (m/z) : 292.0 $(M+H)^{+}$

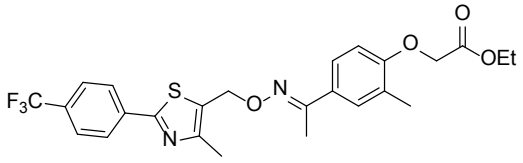
4.1.6 General procedure for the synthesis of Compounds 10a-f



9 **4a-f** **10a-f**

To a solution of **9** (1 mole equivalent) and **4a-f** (1 mole equivalent) in dry DMF (5 fold), Cs_2CO_3 (1.5 mole equivalent) was added and reaction mixture was stirred at 60 ^{O}C for 18 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (8 to 12% ethyl acetate in hexane) to yield the title compound **10a-f**.

4.1.6.1 (*E*)-Ethyl 2-(2-methyl-4-(1-(((4-methyl-2-(4-trifluoromethyl phenyl)thiazol-5-yl)methoxy)imino)ethyl)phenoxy)acetate (10a)



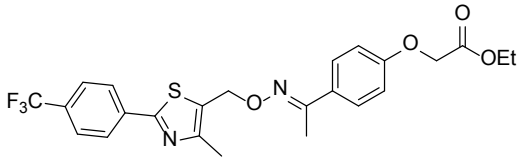
10a (1.72 gm, 66%) was prepared from **9** (1.5 gm, 5.14 mmol) and **4a** (1.29 gm, 5.14 mmol) following the general procedure described above as a white solid. m.p. 112-114 ^{o}C; Purity by HPLC: 98.9%.

IR (KBr) : 3433, 2989, 2935, 1764, 1726, 1616, 1500, 1508, 1452, 1325, 1271, 1240, 1172, 1149, 1114, 1068, 1031, 1001, 964, 918, 848, 810 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.30 (t, *J* = 7.1 Hz, 3H), 2.24 (s, 3H), 2.31 (s, 3H), 2.54 (s, 3H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.65 (s, 2H), 5.32 (s, 2H), 6.70 (d, *J* = 8.5 Hz, 1H), 7.41-7.44 (m, 1H), 7.44 (s, 1H), 7.65 (d, *J* = 8.2 Hz, 2H), 8.01 (d, *J* = 8.1 Hz, 2H)

ESI/MS (m/z) : 507.1 $(M+H)^+$

4.1.6.2 (*E*)-Ethyl 2-(4-(1-(((4-methyl-2-(4-trifluoromethylphenyl) thiazol-5-yl)methoxy)imino)ethyl)phenoxy)acetate (10b)



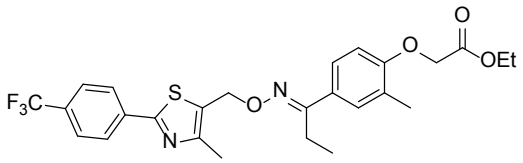
10b (1.22 gm, 72%) was prepared from **9** (1.0 gm, 3.43 mmol) and **4b** (0.81 gm, 3.43 mmol) following the general procedure described above as an off white solid. m.p. 100-102 ^oC; Purity by HPLC: 99.1%.

IR (KBr) : 3387, 2937, 2854, 1728, 1612, 1514, 1406, 1323, 1236, 1172, 1111, 1068, 1001, 898, 829 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.28 (t, *J* = 7.2 Hz, 3H), 2.21 (s, 3H), 2.55 (s, 3H), 4.25 (q, *J* = 7.0 Hz, 2H), 4.64 (s, 2H), 5.33 (s, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.60-7.64 (m, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 493.1 $(M+H)^+$

4.1.6.3 (*E*)-Ethyl 2-(2-methyl-4-(1-(((4-methyl-2-(4-trifluoromethyl phenyl)thiazol-5-yl) methoxy)imino)propyl)phenoxy)acetate (10c)



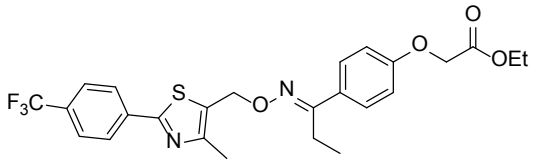
10c (1.20 gm, 67%) was prepared from **9** (1.0 gm, 3.43 mmol) and **4c** (0.91 gm, 3.43 mmol) following the general procedure described above as an off white solid. m.p. 105-107 ^{o}C; Purity by HPLC: 98.3%.

IR (KBr) : 2982, 2935, 1741, 1618, 1508, 1452, 1381, 1321, 1213, 1124, 1066, 1001, 962, 916, 839 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.08 (t, *J* = 7.6 Hz, 3H), 1.25 (t, *J* = 7.2 Hz, 3H), 2.31 (s, 3H), 2.55 (s, 3H), 2.68 (q, *J* = 7.6 Hz, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.66 (s, 2H), 5.32 (s, 2H), 6.68 (d, *J* = 8.4 Hz, 1H), 7.40 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.49 (d, *J* = 1.6 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 521.1 $(M+H)^{+}$

4.1.6.4 (*E*)-Ethyl 2-(4-(1-(((4-methyl-2-(4-trifluoromethylphenyl) thiazol-5-yl)methoxy)imino)propyl)phenoxy)acetate (10d)



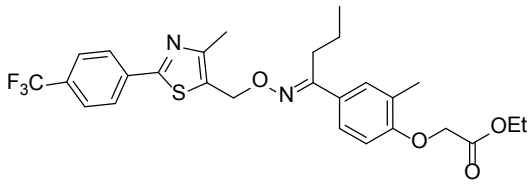
10d (1.15 gm, 66%) was prepared from **9** (1.0 gm, 3.43 mmol) and **4d** (0.86 gm, 3.43 mmol) following the general procedure described above as a pale yellow solid. m.p. 75 - 77 ^{o}C; Purity by HPLC: 98.7%.

IR (KBr) : 2985, 2966, 2937, 1741, 1612, 1569, 1542, 1512, 1467, 1454, 1406, 1380, 1350, 1321, 1271, 1240, 1211, 1174, 1120, 1066, 1033, 997, 964, 950, 891, 858, 840, 675 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.12 (t, *J* = 7.5 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 2.54 (s, 3H), 2.71 (q, *J* = 7.6 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.64 (s, 2H), 5.31 (s, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 7.59-7.67 (m, 4H), 7.5 (d, *J* = 8.2 Hz, 2H)

ESI/MS (m/z) : 507.0 $(M+H)^{+}$

4.1.6.5 (*E*)-Ethyl 2-(2-methyl-4-(1-(((4-methyl-2-(4-trifluoromethyl phenyl)thiazol-5-yl)methoxy)imino)butyl)phenoxy)acetate (10e)



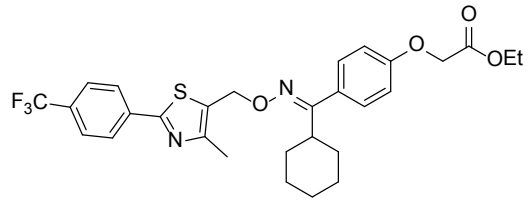
10e (1.01 gm, 55%) was prepared from **9** (1.0 gm, 3.43 mmol) and **4e** (0.96 gm, 3.43 mmol) following the general procedure described above as an off white solid. m.p. 90-92 ^{o}C; Purity by HPLC: 95.0%.

IR (KBr) : 2968, 2872, 1774, 1726, 1616, 1508, 1438, 1327, 1199, 1166, 1122, 1068, 1014, 964, 842 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 0.91 (t, *J* = 7.4 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.50-1.52 (m, 2H), 2.31 (s, 3H), 2.54 (s, 3H), 2.66 (t, *J* = 7.6 Hz, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.65 (s, 2H), 5.31 (s, 2H), 6.67 (d, *J* = 8.8 Hz, 1H), 7.34 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.48 (d, *J* = 1.2 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 8.02 (d, *J* = 8.4 Hz, 2H)

ESI/MS (m/z) : 535.7 (M+H)$^{+}$

4.1.6.6 (*E*)-Ethyl 2-(4-(cyclohexyl(((4-methyl-2-(4-trifluoromethyl phenyl)thiazol-5-yl)methoxy)imino)methyl)phenoxy)acetate (10f)



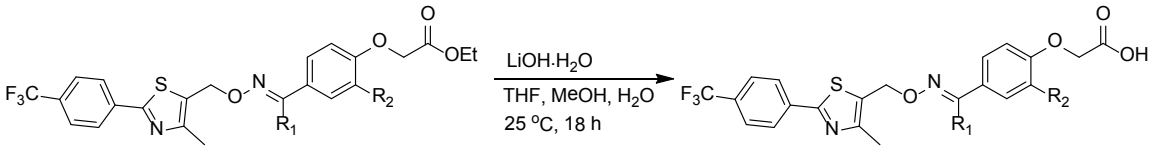
10f (0.61 gm, 31%) was prepared from **9** (1.0 gm, 3.43 mmol) and **4f** (1.09 gm, 3.43 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 95.5%.

IR (Neat) : 3435, 2929, 2854, 1739, 1502, 1450, 1325, 1128, 1066, 904, 675, 605 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.26-1.31 (m, 9H), 1.67-1.79 (m, 4H), 2.28 (s, 3H), 2.46 (s, 4H), 4.26 (q, J=7.1 Hz, 2H), 4.63 (s, 2H), 5.13 (s, 2H), 6.66 (d, *J* = 8.1 Hz, 1H), 6.99-7.02 (m, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 8.02 (d, *J* = 8.1 Hz, 2H)

ESI/MS (m/z) : 575.1 $(M+H)^+$

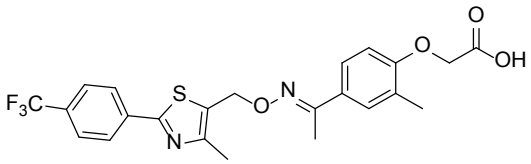
4.1.7 General procedure for the synthesis of Compounds 11a-f



10a-f **11a-f**

To a solution of **10a-f** (1 mole equivalent) in a mixture of tetrahydrofuran (15 fold) and methanol (5 fold) was added another solution of $LiOH.H_2O$ (2 mole equivalent) in water (5 fold) and the reaction mixture was stirred at ambient temperature for about 18 hours. Solvent was evaporated under reduced pressure, water was added to the residue, acidified with 1N HCl to pH 6 and extracted with ethyl acetate. The combined organic extracts were washed with water and brine solution, dried over sodium sulphate and evaporated under reduced pressure to yield the products **11a-f**.

4.1.7.1 (*E*)-2-(2-Methyl-4-(1-(((4-methyl-2-(4-trifluoromethylphenyl) thiazol-5-yl) methoxy)imino)ethyl)phenoxy)acetic acid (11a)



11a (0.87 gm, 92%) was prepared from **10a** (1.0 gm, 1.97 mmol) following the general procedure described above as an off white solid. m.p. 158-160 ^oC; Purity by HPLC: 99.8%.

IR (KBr) : 3435, 2925, 1718, 1618, 1508, 1450, 1406, 1355, 1325, 1274,

1226, 1174, 1114, 1068, 1010, 968, 920, 844, 819, 800 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.89 (s, 3H), 1.96 (s, 3H), 2.46 (s, 3H), 4.66 (s, 2H), 5.33 (s, 2H), 6.80 (d, *J* = 8.6 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.47 (s, 1H), 7.8 (d, *J* = 8.3 Hz, 2H), 8.0 (d, *J* = 8.1 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.4, 15.1, 16.2, 64.9, 66.5, 111.1, 124.9, 125.9, 126.1, 126.2, 126.6, 128.0, 128.1, 129.9, 136.5, 151.9, 154.9, 157.1, 163.3, 170.2

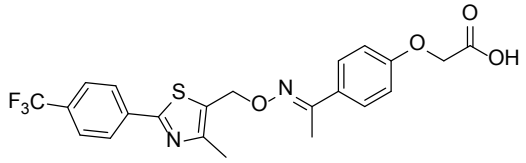
ESI/MS (m/z) : 479.0 $(M+H)^+$

Analysis **Mol.Formula:** $C_{23}H_{21}F_3N_2O_4S$

Calculated : C, 57.73%; H, 4.42%; N, 5.85%; S, 6.70%

Found : C, 56.69%; H, 4.55%; N, 5.50%; S, 6.75%

4.1.7.2 (*E*)-2-(4-(1-(((4-Methyl-2-(4-trifluoromethylphenyl)thiazol-5-yl) methoxy)imino)ethyl)phenoxy)acetic acid (11b)



11b (0.84 gm, 89%) was prepared from **10b** (1.0 gm, 2.03 mmol) following the general procedure described above as an off white solid. m.p. 150-152 ^oC; Purity by HPLC: 99.3%.

IR (KBr) : 2926, 2856, 1701, 1612, 1510, 1437, 1327, 1230, 1111, 1068, 999, 900, 825 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.16 (s, 3H), 2.49 (s, 3H), 4.65 (s, 2H), 5.36 (s, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.4, 15.2, 64.7, 66.5, 114.4, 125.6, 126.2, 127.3, 128.4, 129.9, 136.5, 151.9, 154.8, 158.9, 163.4, 170.1

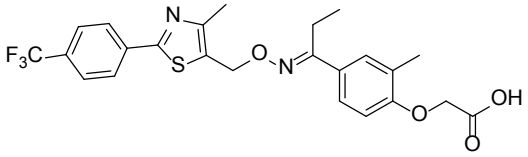
ESI/MS (m/z) : 465.5 $(M+H)^+$

Analysis **Mol.Formula:** $C_{22}H_{19}F_3N_2O_4S$

Calculated : C, 56.89%; H, 4.12%; N, 6.03%; S, 6.90%

Found : C, 56.58%; H, 4.22%; N, 5.95%; S, 6.84%

4.1.7.3 (*E*)-2-(2-Methyl-4-(1-(((4-methyl-2-(4-trifluoromethylphenyl) thiazol-5-yl) methoxy)imino)propyl)phenoxy)acetic acid (11c)



11c (0.75 gm, 80%) was prepared from **10c** (1.0 gm, 1.92 mmol) following the general procedure described above as an off white solid. m.p. 174-176 ^{o}C; Purity by HPLC: 99.3%.

IR (KBr) : 2982, 2926, 1701, 1616, 1502, 1325, 1228, 1170, 1116, 1068, 1003, 964, 914, 839 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.98 (t, *J* = 7.6 Hz, 3H), 2.20 (s, 3H), 2.49 (s, 3H), 2.63 (q, *J* = 7.4 Hz, 2H), 4.67 (s, 2H), 5.35 (s, 2H), 6.81 (d, *J* = 8.8 Hz, 1H), 7.41 (dd, *J* = 8.4 & 2.0 Hz, 1H), 4.48 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 8.08 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 11.2, 15.1, 16.2, 19.2, 65.0, 66.5, 111.2, 125.0, 126.1, 126.1, 126.6, 126.7, 128.3, 130.0, 136.5, 151.8, 157.2, 159.8, 163.3, 170.3

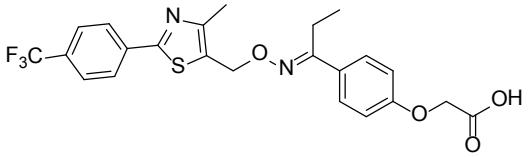
ESI/MS (m/z) : 493.1 $(M+H)^{+}$

Analysis **Mol.Formula**: $C_{24}H_{23}F_3N_2O_4S$

Calculated : C, 58.53%; H, 4.71%; N, 5.69%; S, 6.51%

Found : C, 57.94%; H, 4.78%; N, 5.60%; S, 6.36%

4.1.7.4 (*E*)-2-(4-(1-(((4-Methyl-2-(4-trifluoromethylphenyl)thiazol-5-yl) methoxy)imino)propyl)phenoxy)acetic acid (11d)



11d (0.83 gm, 80%) was prepared from **10d** (1.0 gm, 1.97 mmol) following the general procedure described above as an off white solid. m.p. 167-169 ^{o}C; Purity by HPLC: 99.5%.

IR (KBr) : 3411, 2983, 2935, 2883, 1701, 1610, 1510, 1452, 1352, 1325, 1230, 1184, 1170, 1112, 1068, 999, 966, 893, 846, 829, 675 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.00 (t, *J* = 7.4 Hz, 3H), 2.41 (s, 3H), 2.66 (q, *J* = 7.4 Hz, 2H), 4.70 (s, 2H), 5.35 (s, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 7.62 (d, *J* = 8.7 Hz, 2H), 7.83 (d, *J* = 8.3 Hz, 2H), 8.11 (d, *J* = 8.2 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 11.1, 15.2, 19.2, 64.5, 66.2, 114.6, 126.1, 126.2, 126.6, 127.2, 127.5, 129.9, 136.5, 151.9, 158.8, 159.7, 163.4, 170.0

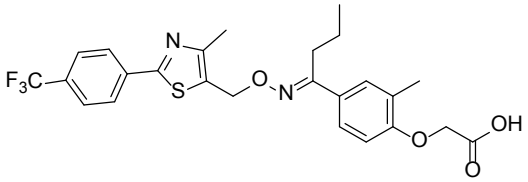
ESI/MS (m/z) : 479.0 $(M+H)^{+}$

Analysis **Mol.Formula:** $C_{23}H_{21}F_3N_2O_4S$

Calculated : C, 57.73%; H, 4.42%; N, 5.85%; S, 6.70%

Found : C, 57.73%; H, 4.51%; N, 5.98%; S, 6.76%

4.1.7.5 (*E*)-2-(2-Methyl-4-(1-(((4-methyl-2-(4-trifluoromethylphenyl) thiazol-5-yl)methoxy)imino)butyl)phenoxy)acetic acid (11e)



11e (0.58 gm, 61%) was prepared from **10e** (1.0 gm, 1.87 mmol) following the general procedure described above as an off white solid. m.p. 155-157 ^{o}C; Purity by HPLC: 95.8%.

IR (KBr) : 3433, 2966, 2872, 1747, 1616, 1506, 1431, 1327, 1242, 1166, 1122, 1068, 1014, 966, 806 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.90 (t, *J* = 7.4 Hz, 3H), 1.45-1.53 (m, 2H), 2.26 (s, 3H), 2.53 (s, 3H), 2.64 (t, *J* = 7.6 Hz, 2H), 4.60 (s, 2H), 5.29 (s, 2H), 6.67 (d, *J* = 8.4 Hz, 1H), 7.37 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.46 (d, *J* = 1.6 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 13.9, 15.1, 19.7, 27.5, 65.1, 66.5, 111.1, 125.1, 126.0, 126.1, 126.5, 127.0, 128.3, 129.9, 136.5, 151.8, 157.1, 158.7, 163.3, 170.3

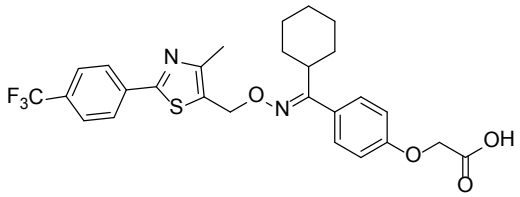
ESI/MS (m/z) : 507.6 $(M+H)^+$

Analysis **Mol.Formula**: $C_{25}H_{25}F_3N_2O_4S$

Calculated : C, 59.28%; H, 4.97%; N, 5.53%; S, 6.33%

Found : C, 58.55%; H, 5.37%; N, 5.68%; S, 5.85%

4.1.7.6 (*E*)-2-(4-(Cyclohexyl(((4-methyl-2-(4-trifluoromethylphenyl) thiazol-5-yl) methoxy)imino)methyl)phenoxy)acetic acid (11f)



11f (0.54 gm, 63%) was prepared from **10f** (0.9 gm, 1.57 mmol) following the general procedure described above as an off white solid. m.p. 52-55 ^oC; Purity by HPLC: 97.2%.

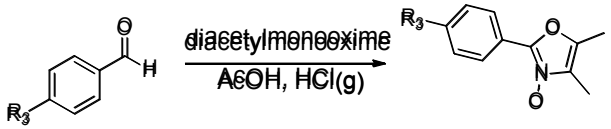
IR (KBr) : 3435, 2929, 2854, 1739, 1502, 1450, 1325, 1128, 1066, 904, 675, 605 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.25-1.29 (m, 6H), 1.71-1.73 (m, 4H), 2.22 (s, 3H), 2.47-2.48 (m, 4H), 4.57 (s, 2H), 5.10 (s, 2H), 6.67 (d, *J* = 8.3 Hz, 1H), 6.97 (s, 2H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.98 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 15.3, 16.4, 26.2, 29.6, 44.5, 65.8, 111.0, 126.0, 126.4, 126.7, 127.0, 127.4, 129.9, 130.4, 136.8, 152, 155.9, 163.2, 164.8

ESI/MS (m/z) : 547.1 $(M+H)^+$

4.1.8 General procedure for the synthesis of Compounds 14 and 15

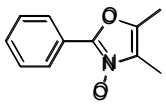


12; R_3 = H
13; R_3 = Me

14; R_3 = H
15; R_3 = Me

To an ice-cold solution of freshly distilled aldehyde (**12, 13)** 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 product (**14, 15**) as a white solid.

4.1.8.1 4,5-Dimethyl-2-phenyloxazole 3-oxide (16)



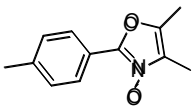
This compound (60.0 gm, 67%) was prepared from benzaldehyde (50gm, 0.471 mol) by means of a general procedure described above as an off white solid. mp: 172-173 °C; Purity by HPLC: 94.1%.

IR (KBr) : 3433, 3055, 2924, 1803, 1081, 1593, 1452, 1379, 1330, 1247, 1166, 1099, 964, 862, 788 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 2.15 (s, 3H), 2.40 (s, 3H), 7.56-7.64 (m, 3H), 8.29-8.34 (m, 2H)

ESI/MS (m/z) : 189.7 $(M+H)^+$

4.1.8.2 4,5-Dimethyl-2-(p-tolyl)oxazole 3-oxide (17)



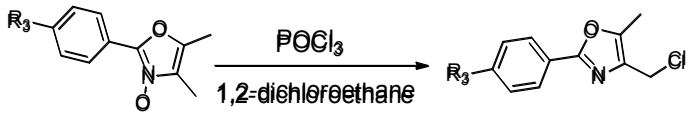
This compound (60 gm, 71%) was prepared from 4-methylbenzaldehyde (50 gm, 0.416 mol) by means of a general procedure described above as a white solid. mp: 180-181 °C; Purity by HPLC: 99.5%.

IR (KBr) : 3447, 2923, 1868, 1687, 1610, 1508, 1257, 1172, 1099, 833 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.46 (s, 9H), 7.38 (d, *J* = 8.1 Hz, 2H), 8.24 (d, *J* = 8.3 Hz, 2H)

ESI/MS (m/z) : 204.0 $(M+H)^+$

4.1.9 General procedure for the synthesis of Compounds 16 and 17

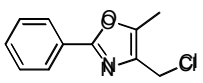


14; R_3 = H
15; R_3 = Me

16; R_3 = H
17; R_3 = Me

To an ice-cold suspension of *N*-oxide (**14, 15**) 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 extracts were washed with water, dried over $CaCl_2$ and concentrated under vacuum to furnish the products **16** and **17** which were further purified by recrystallization from hexane.

4.1.9.1 4-Chloromethyl-5-methyl-2-phenyloxazole (16)



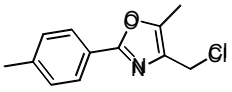
This compound (58.6 gm, 89%) was prepared from **14** (60 gm, 0.317 mol) by means of a general procedure described above as an off white solid. mp: 81-83 °C; Purity by HPLC: 99.1%.

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

^{1}H NMR ($CDCl_3$) **:** 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 $(M+H)^+$

4.1.9.2 4-Chloromethyl-5-methyl-2-(4-methylphenyl)-oxazole (17)



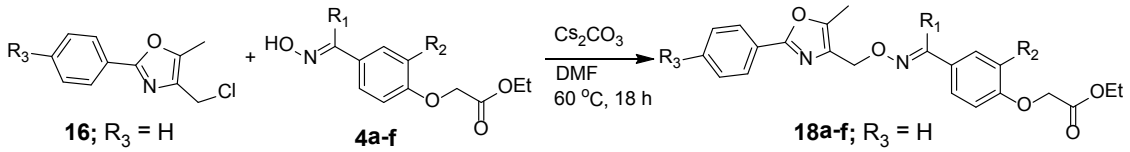
This compound (44.2 gm, 81%) was prepared from **15** (50 gm, 0.246 mol) by means of a general procedure described above as a white solid. mp: 87-88 °C; Purity by HPLC: 98.6%.

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

^{1}H NMR ($CDCl_3$) **:** 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 $(M+H)^+$

4.1.10 General procedure for the synthesis of Compounds 18a-f and 19a-f



16; R_3 = H
17; R_3 = CH_3

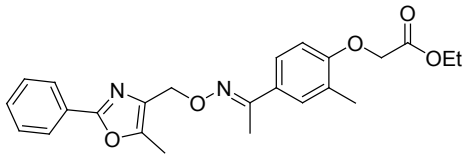
4a-f

18a-f; R_3 = H
19a-f; R_3 = CH_3

To a solution of **16** or **17** (1 mole equivalent) and **4a-f** (1 mole equivalent) in dry DMF (5 fold), Cs_2CO_3 (1.5 mole equivalent) was added and reaction mixture was stirred at 60 ^oC for 18 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced

pressure. The crude product was purified by column chromatography (10 to 12% ethyl acetate in hexane) to yield title compound **18a-f** or **19a-f**.

4.1.10.1 (*E*)-Ethyl 2-(2-methyl-4-(1-(((5-methyl-2-phenyloxazol-4-yl) methoxy)imino)ethyl)phenoxy)acetate (18a)



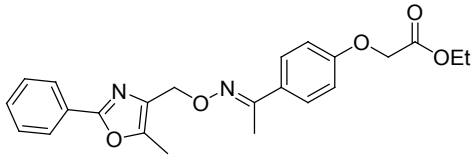
18a (0.64 gm, 52%) was prepared from **16** (0.50 gm, 2.41 mmol) and **4a** (0.6 gm, 2.41 mmol) following the general procedure described above as an off white solid. m.p. 86-88 ^{o}C; Purity by HPLC: 94.0%.

IR (KBr) : 3382, 2981, 2927, 2875, 1759, 1737, 1637, 1606, 1556, 1504, 1448, 1369, 1317, 1278, 1203, 1145, 1068, 1024,939, 891, 808, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.32 (t, *J* = 7.1 Hz, 3H), 2.11 (s, 3H), 2.34 (s, 3H), 2.48 (s, 3H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.64 (s, 2H), 5.12 (s, 2H), 6.68 (d, *J* = 8.5 Hz, 1H), 7.35-7.49 (m, 5H), 8.01-8.02 (m, 2H)

ESI/MS (m/z) : 423.0 $(M+H)^{+}$

4.1.10.2 (*E*)-Ethyl 2-(4-(1-(((5-methyl-2-phenyloxazol-4-yl)methoxy) imino)ethyl)phenoxy)acetate (18b)



18b (0.71 gm, 59%) was prepared from **16** (0.50 gm, 2.41 mmol) and **4b** (0.56 gm, 2.41 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.4%.

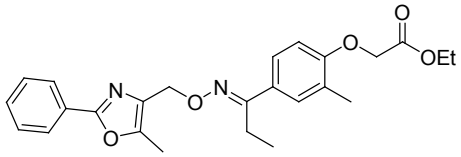
IR (Neat) : 3018, 2983, 2929, 1753, 1604, 1512, 1384, 1319, 1180, 1018, 923, 833, 669 cm^{-1}

^{1}H NMR : δ 1.28 (t, *J* = 7.0 Hz, 3H), 2.21 (s, 3H), 2.48 (s, 3H), 4.25 (q, *J* =

($CDCl_3$) 7.2 Hz, 2H), 4.63 (s, 2H), 5.12 (s, 2H), 6.88 (dd, *J* = 9.6 & 2.4 Hz, 2H), 7.39-7.45 (m, 3H), 7.58 (dd, *J* = 9.4 & 2.6 Hz, 2H), 8.00-8.03 (m, 2H)

ESI/MS (m/z) : 409.2 $(M+H)^+$

4.1.10.3 (*E*)-Ethyl 2-(2-methyl-4-(1-(((5-methyl-2-phenyloxazol-4-yl) methoxy)imino)propyl)phenoxy)acetate (18c)



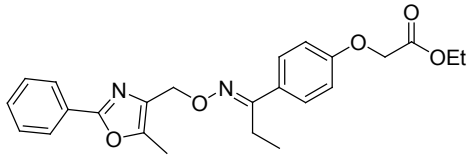
18c (0.69 gm, 55%) was prepared from **16** (0.50 gm, 2.41 mmol) and **4c** (0.64 gm, 2.41 mmol) following the general procedure described above as an off white solid. m.p. 95-97 ^oC; Purity by HPLC: 99.2%.

IR (KBr) : 2974, 2885, 1757, 1639, 1498, 1377, 1203, 1186, 1149, 1105, 1030, 937, 860, 700 cm^{-1}

^1H NMR ($CDCl_3$) : δ 1.07 (t, *J* = 7.6 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H), 2.30 (s, 3H), 2.48 (s, 3H), 2.69 (q, *J* = 7.6 Hz, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 4.64 (s, 2H), 5.11 (s, 2H), 6.66 (d, *J* = 8.4 Hz, 1H), 7.37-7.47 (m, 5H), 8.00-8.03 (m, 2H)

ESI/MS (m/z) : 437.2 $(M+H)^+$

4.1.10.4 (*E*)-Ethyl 2-(4-(1-(((5-methyl-2-phenyloxazol-4-yl)methoxy) imino)propyl)phenoxy)acetate (18d)



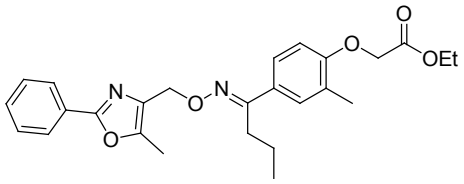
18d (0.75 gm, 59%) was prepared from **16** (0.50 gm, 2.41 mmol) and **4d** (0.60 gm, 2.41 mmol) following the general procedure described above as an off white solid. m.p. 84-86 ^oC; Purity by HPLC: 92.9%.

IR (KBr) : 2976, 2923, 1759, 1604, 1558, 1512, 1485, 1454, 1379, 1338, 1315, 1303, 1234, 1195, 1186, 1105, 1082, 1068, 1035, 1024, 954, 910, 833, 794, 781, 715, 700, 599 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.07 (t, *J* = 7.6 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 2.47 (s, 3H), 2.79 (q, *J* = 7.6 Hz, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.68 (s, 2H), 5.29 (s, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 7.41-7.44 (m, 3H), 7.60 (d, *J* = 8.7 Hz, 2H), 8.01-8.03 (m, 2H)

ESI/MS (m/z) : 423.1 $(M+H)^+$

4.1.10.5 (*E*)-Ethyl 2-(2-methyl-4-(1-(((5-methyl-2-phenyloxazol-4-yl) methoxy)imino)butyl)phenoxy)acetate (18e)



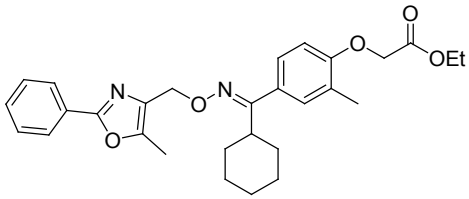
18e (0.66 gm, 51%) was prepared from **16** (0.50 gm, 2.41 mmol) and **4e** (0.67 gm, 2.41 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.4%.

IR (Neat) : 3018, 2968, 1753, 1508, 1384, 1145, 1026, 929 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.90 (t, *J* = 7.2 Hz, 3H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.47-1.57 (m, 2H), 2.30 (s, 3H), 2.48 (s, 3H), 2.67 (t, *J* = 7.4 Hz, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.64 (s, 2H), 5.11 (s, 2H), 6.65 (d, *J* = 8.4 Hz, 1H), 7.35-7.47 (m, 5H), 8.00-8.03 (m, 2H)

ESI/MS (m/z) : 451.2 $(M+H)^+$

4.1.10.6 (*E*)-Ethyl 2-(4-(cyclohexyl(((5-methyl-2-phenyloxazol-4-yl) methoxy)imino) methyl)-2-methylphenoxy)acetate (18f)



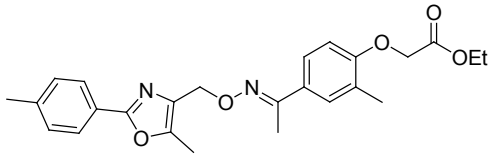
18f (0.77 gm, 55%) was prepared from **16** (0.50 gm, 2.41 mmol) and **4f** (0.77 gm, 2.41 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 94.1%.

IR (Neat) : 3018, 2931, 2854, 1757, 1500, 1448, 1384, 1149, 1035, 934 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.19-1.33 (m, 9H), 1.74-1.81 (m, 4H), 2.26 (s, 3H), 2.29 (s, 3H), 2.40-2.45 (m, 1H), 4.23 (q, *J* = 7.0 Hz, 2H), 4.62 (s, 2H), 4.95 (s, 2H), 6.64 (d, *J* = 8.4 Hz, 1H), 7.01-7.04 (m, 2H), 7.39-7.45 (m, 3H), 7.98-8.02 (m, 2H)

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

4.1.10.7 (*E*)-Ethyl 2-(2-methyl-4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy)imino) ethyl)phenoxy)acetate (19a)



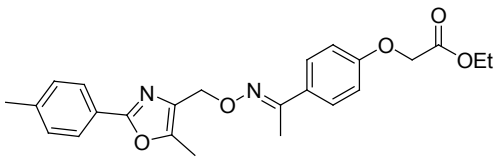
19a (0.60 gm, 55%) was prepared from **17** (0.50 gm, 2.26 mmol) and **4a** (0.57 gm, 2.26 mmol) following the general procedure described above as an off white solid. m.p. 114-116 ^oC; Purity by HPLC: 98.2%.

IR (KBr) : 3429, 2981, 2918, 2850, 1724, 1618, 1500, 1433, 1375, 1365, 1313, 1294, 1269, 1240, 1145, 1002, 981, 918, 858, 817, 794, 727 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.31 (t, *J* = 7.1 Hz, 3H), 2.23 (s, 3H), 2.30 (s, 3H), 2.41 (s, 3H), 2.47 (s, 3H) 4.27 (q, *J* = 7.1 Hz, 2H), 4.64 (s, 2H), 5.11 (s, 2H), 6.68 (d, *J* = 8.5 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.41 (dd, *J* = 8.5 & 2.0 Hz, 1H), 7.49 (d, *J* = 1.4 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 2H)

ESI/MS (m/z) : 437.2 $(M+H)^+$

4.1.10.8 (*E*)-Ethyl 2-(4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl)methoxy) imino)ethyl)phenoxy)acetate (19b).



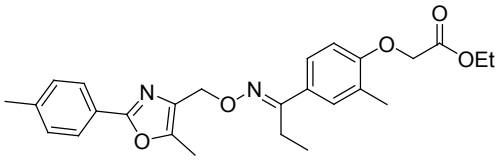
19b (0.65 gm, 68%) was prepared from **17** (0.50 gm, 2.26 mmol) and **4b** (0.54 gm, 2.26 mmol) following the general procedure described above as an off white solid; m.p. 112-113 ^{o}C; Purity by HPLC: 97.8%.

IR (KBr) : 2987, 2918, 1757, 1599, 1512, 1500, 1435, 1373, 1273, 1201, 1074, 1026, 927, 727, 599 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.28 (t, *J* = 7.2 Hz, 3H), 2.21 (s, 3H), 2.39 (s, 3H), 2.47 (s, 3H), 4.24 (q, *J* = 7.0 Hz, 2H), 4.63 (s, 2H), 5.11 (s, 2H), 6.87 (dd, *J* = 11.6 & 2.8 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.58-7.61 (m, 2H), 7.89 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 423.2 $(M+H)^{+}$

4.1.10.9 (*E*)-Ethyl 2-(2-methyl-4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy)imino) propyl)phenoxy)acetate (19c)



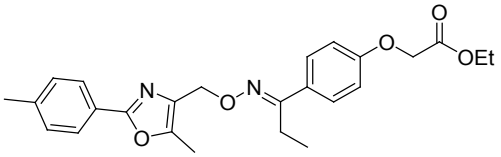
19c (0.69 gm, 68%) was prepared from **17** (0.50 gm, 2.26 mmol) and **4c** (0.60 gm, 2.26 mmol) following the general procedure described above as an off white solid. m.p. 116-118 ^{o}C; Purity by HPLC: 99.8%.

IR (KBr) : 2966, 2872, 1743, 1612, 1500, 1448, 1377, 1213, 1149, 1103, 1074, 993, 846, 729 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.07 (t, *J* = 7.6 Hz, 3H), 1.28 (t, *J* = 7.0 Hz, 3H), 2.30 (s, 3H), 2.38 (s, 3H), 2.47 (s, 3H), 2.69 (q, *J* = 7.6 Hz, 2H), 4.23 (q, *J* = 7.0 Hz, 2H), 4.64 (s, 2H), 5.10 (s, 2H), 6.65 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.37 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.47 (d, *J* = 1.6 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 451.2 $(M+H)^+$

4.1.10.10 (*E*)-Ethyl 2-(4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl)methoxy) imino)propyl)phenoxy)acetate (19d)



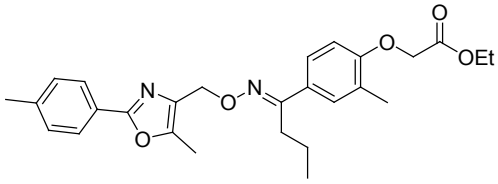
19d (0.44 gm, 45%) was prepared from **17** (0.50 gm, 2.26 mmol) and **4d** (0.57 gm, 2.26 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.9%.

IR (Neat) : 3018, 2981, 2937, 1757, 1610, 1512, 1500, 1442, 1299, 1215, 1180, 1078, 1018, 968, 827, 759, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.11 (t, *J* = 7.5 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 2.38 (s, 3H), 2.46 (s, 3H), 2.74 (q, *J* = 7.5 Hz, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 4.62 (s, 2H), 5.29 (s, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.91 (d, *J* = 8.1 Hz, 2H)

ESI/MS (m/z) : 437.1 $(M+H)^+$

4.1.10.11 (*E*)-Ethyl 2-(2-methyl-4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl)methoxy)imino)butyl)phenoxy)acetate (19e)



19e (0.46 gm, 45%) was prepared from **17** (0.50 gm, 2.26 mmol) and **4e** (0.60 gm, 2.26 mmol) following the general procedure described above as a white solid. m.p. 110-111 ^oC; Purity by HPLC: 99.1%.

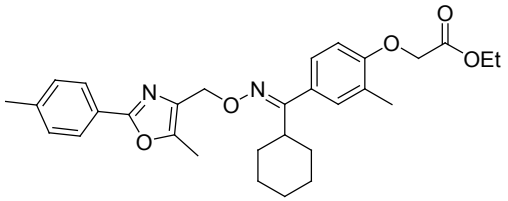
IR (KBr) : 3060, 2958, 2871, 1743, 1614, 1502, 1190 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.91 (t, *J* = 7.3 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.48-1.62 (m, 2H), 2.71 (s, 3H), 2.30 (s, 3H), 2.46 (s, 3H), 2.67 (t, *J* = 6.6 Hz, 2H), 4.26 (q, *J* = 7.2 Hz, 2H), 4.64 (s, 2H), 5.30 (s, 2H), 6.65 (d,

J = 8.5 Hz, 1H), 7.21-7.23 (m, 2H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.46 (s, 1H), 7.90 (d, *J* = 8.1 Hz, 2H)

ESI/MS (m/z) : 465.0 $(M+H)^+$

4.1.10.12 (*E*)-Ethyl 2-(4-(cyclohexyl(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy)imino)methyl)-2-methylphenoxy)acetate (19f)



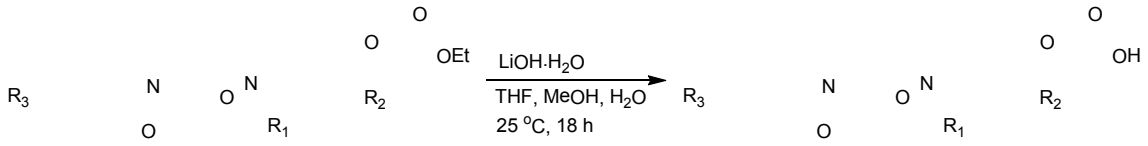
19f (0.49 gm, 22%) was prepared from **17** (1.0 gm, 4.52 mmol) and **4f** (1.34 gm, 4.52 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 94.2%;

IR (Neat) : 3130, 3020, 2029, 1732, 1633, 1502, 1215, 1145, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.21-1.35 (m, 9H), 1.69-1.72 (m, 5H), 2.24 (s, 3H), 2.30 (s, 3H), 2.32 (s, 3H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.61 (s, 2H), 4.90 (s, 2H), 6.64 (d, *J* = 8.1 Hz, 1H), 7.01-7.02 (m, 2H), 7.21 (s, 2H), 7.85 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 527.1 $(M+Na)^+$

4.1.11 General procedure for the synthesis of Compounds 20a-f and 21a-f



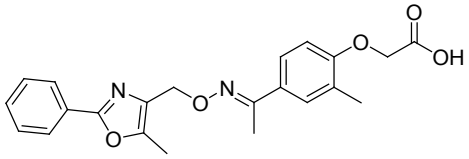
18a-f; R_3 = H
19a-f; R_3 = CH_3

20a-f; R_3 = H
21a-f; R_3 = CH_3

To a solution of **18a-f** or **19a-f** (1 mole equivalent) in a mixture of tetrahydrofuran (15 fold) and methanol (5 fold) was added solution of $LiOH.H_2O$ (2 mole equivalent) in water (5 fold) and the reaction mixture was stirred at ambient temperature for about 18 hours. Solvent was evaporated under reduced

pressure, water was added to the residue, acidified with 1N HCl to pH 6 and extracted with ethyl acetate. The combined organic extracts were washed with water and brine solution, dried over sodium sulphate and evaporated under reduced pressure to yield the products **20a-f** or **21a-f**.

4.1.11.1 (*E*)-2-(2-Methyl-4-(1-(((5-methyl-2-phenyloxazol-4-yl) methoxy) imino)ethyl)phenoxy)acetic acid (20a)



20a (0.44 gm, 94%) was prepared from **18a** (0.50 gm, 1.18 mmol) following the general procedure described above as an off white solid. m.p. 184-186 ^{o}C; Purity by HPLC: 99.7%.

IR (KBr) : 3429, 3049, 3049, 2949, 2916, 2852, 1724, 1632, 1618, 1556, 1508, 1488, 1448, 1436, 1315, 1265, 1242, 1195, 1159, 1145, 1062, 1020, 970, 870, 871, 800., 702 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 2.14 (s, 3H), 2.21 (s, 3H), 2.47 (s, 3H), 4.73 (s, 2H), 5.05 (s, 2H), 6.85 (d, *J* = 8.6 Hz, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.50-7.52 (m, 4H), 7.95 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 10.2, 12.4, 16.2, 64.7, 66.9, 111.0, 124.8, 125.6, 125.9, 127.0, 128.0, 128.3, 129.1, 130.3, 132.8, 147.8, 154, 156.9, 158.6, 170.2

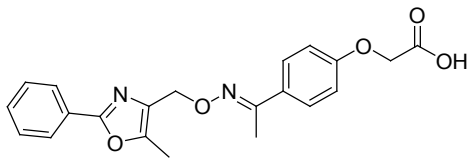
ESI/MS (m/z) : 395.0 $(M+H)^{+}$

Analysis **Mol.Formula**: $C_{22}H_{22}N_2O_5$

Calculated : C, 66.99%; H, 5.62%; N, 7.10%

Found : C, 66.39%; H, 5.52%; N, 7.28%

4.1.11.2 (*E*)-2-(4-(1-(((5-Methyl-2-phenyloxazol-4-yl)methoxy)imino) ethyl)phenoxy)acetic acid (20b)



20b (0.43 gm, 92%) was prepared from **18b** (0.50 gm, 1.22 mmol) following the general procedure described above as an off white solid. m.p. 186-188 ^{o}C; Purity by HPLC: 98.9%.

IR (KBr) : 3072, 2920, 1718, 1612, 1149, 1103, 1072, 1004, 970, 912 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.14 (s, 3H), 2.46 (s, 3H), 4.68 (s, 2H), 5.05 (s, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.46-7.53 (m, 3H), 7.58 (d, *J* = 8.8 Hz, 2H), 7.91-7.94 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 10.2, 12.3, 64.6, 67.0, 114.4, 125.6, 127, 127.2, 128.7, 129.1, 130.3, 132.8, 147.8, 153.9, 158.6, 158.7, 170.1

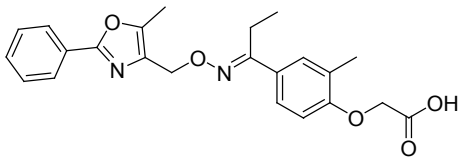
ESI/MS (m/z) : 381.1 $(M+H)^{+}$

Analysis **Mol.Formula**: $C_{21}H_{20}N_2O_5$

Calculated : C, 66.31%; H, 5.30%; N, 7.36%

Found : C, 65.82%; H, 5.18%; N, 7.50%

4.1.11.3 (*E*)-2-(2-Methyl-4-(1-(((5-methyl-2-phenyloxazol-4-yl) methoxy) imino)propyl)phenoxy)acetic acid (20c)



20c (0.40 gm, 85%) was prepared from **18c** (0.50 gm, 1.14 mmol) following the general procedure described above as an off white solid. m.p. 144-145 ^{o}C; Purity by HPLC: 99.3%.

IR (KBr) : 3387, 2968, 2875, 1726, 1647, 1597, 1550, 1504, 1446, 1344, 1215, 1149, 1103, 1072, 1004, 970, 912 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 0.96 (t, *J* = 7.6 Hz, 3H), 2.19 (s, 3H), 2.45 (s, 3H), 2.62 (q, *J* = 7.2 Hz, 2H), 4.71 (s, 2H), 5.04 (s, 2H), 6.81 (d, *J* = 8.4 Hz, 1H), 7.39 (d, *J* = 8.8 Hz, 1H), 7.46-7.52 (m, 4H), 7.91-7.93 (m, 2H)

^{13}C NMR (DMSO-*d*$_6$) : δ 10.1, 11.1, 16.2, 19.1, 64.8, 66.8, 111.1, 124.9, 125.5, 126.0, 127.0, 128.2, 129.1, 130.2, 132.9, 147.7, 156.9, 158.6, 159.0, 170.2

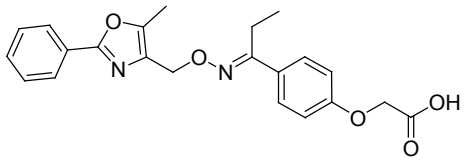
ESI/MS (m/z) : 409.2 $(M+H)^+$

Analysis **Mol.Formula**: $C_{23}H_{24}N_2O_5$

Calculated : C, 67.63%; H, 5.92%; N, 6.86%

Found : C, 66.81%; H, 5.84%; N, 6.99%

4.1.11.4 (*E*)-2-(4-(1-(((5-Methyl-2-phenyloxazol-4-yl)methoxy)imino) propyl)phenoxy) acetic acid (20d)



20d (0.37 gm, 80%) was prepared from **18d** (0.50 gm, 1.18 mmol) following the general procedure described above as an off white solid. m.p. 131-133 ^oC; Purity by HPLC: 98.0%.

IR (KBr) : 3070, 2956, 2875, 1741, 1651, 1606, 1587, 1558, 1512, 1487, 1467, 1415, 1350, 1321, 1296, 1249, 1215, 1182, 1120, 1105, 1080, 1026, 975, 956, 904, 835, 717, 700 cm^{-1}

^{1}H NMR (DMSO-*d*$_6$) : δ 1.05 (t, *J* = 7.4 Hz, 3H), 2.45 (s, 3H), 2.67 (q, *J* = 7.4 Hz, 2H), 4.69 (s, 2H), 5.04 (s, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 7.50-7.52 (m, 3H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.91-7.93 (m, 2H)

^{13}C NMR (DMSO-*d*$_6$) : δ 10.2, 11.1, 19.1, 64.5, 66.9, 114.5, 125.6, 127.0, 127.4, 127.5, 129.1, 130.3, 132.9, 147.7, 158.6, 158.6, 158.9, 170.0

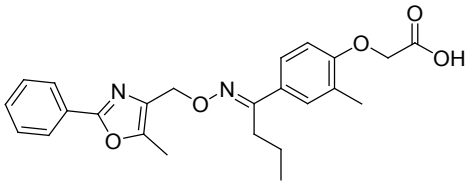
ESI/MS (m/z) : 395.0 $(M+H)^+$

Analysis **Mol.Formula**: $C_{23}H_{24}N_2O_5$

Calculated : C, 66.99%; H, 5.62%; N, 7.10%

Found : C, 66.68%; H, 5.58%; N, 7.36%

4.1.11.5 (*E*)-2-(2-Methyl-4-(1-(((5-methyl-2-phenyloxazol-4-yl) methoxy) imino)butyl) phenoxy)acetic acid (20e)



20e (0.37 gm, 80%) was prepared from **18e** (0.50 gm, 1.18 mmol) following the general procedure described above as an off white solid. m.p. 141-142 ^{o}C; Purity by HPLC: 99.9%;

IR (KBr) : 3389, 2935, 2812, 1728, 1728, 1647, 1597, 1504, 1448, 1419, 1342, 1269, 1207, 1149, 1070, 1001, 968, 864, 702 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 0.82 (t, *J* = 7.2 Hz, 3H), 1.38-1.44 (m, 2H), 2.18 (s, 3H), 2.45 (s, 3H), 2.62 (t, *J* = 7.6 Hz, 2H), 4.62 (s, 2H), 5.03 (s, 2H), 6.77 (d, *J* = 8.8 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 1H), 7.45 (s, 1H), 7.49-7.51 (m, 3H), 7.91-7.93 (m, 2H)

^{13}C NMR (DMSO-d_6) : δ 10.2, 13.9, 16.2, 19.6, 27.4, 65.2, 66.8, 111.0, 125.0, 125.5, 125.9, 127.0, 127.2, 128.2, 129.1, 130.3, 132.5, 147.7, 157.0, 157.9, 158.5, 170.3

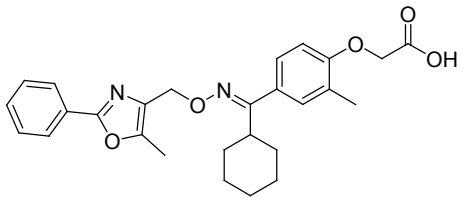
ESI/MS (m/z) : 423.2 $(M+H)^{+}$

Analysis **Mol.Formula**: $C_{24}H_{26}N_2O_5$

Calculated : C, 68.23%; H, 6.20%; N, 6.63%

Found : C, 66.12%; H, 5.98%; N, 6.73%

4.1.11.6 (*E*)-2-(4-(Cyclohexyl(((5-methyl-2-phenyloxazol-4-yl)methoxy) imino)methyl)-2-methylphenoxy)acetic acid (20f)



20f (0.41 gm, 88%) was prepared from **18f** (0.50 gm, 1.02 mmol) following the general procedure described above as a white solid. m.p. 84-86 ^{o}C; Purity by HPLC: 95.7%.

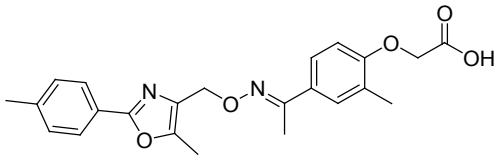
IR (KBr) : 3412, 2926, 2852, 1608, 1500, 1429, 1338, 1300, 1230, 1143, 989, 895, 798, 690 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 0.92-0.94 (m, 6H), 1.56-1.59 (m, 1H), 1.65-1.67 (m, 4H), 2.11 (s, 3H), 2.35 (s, 3H), 4.22 (s, 2H), 4.84 (s, 2H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.99 (s, 1H), 7.47-7.49 (m, 3H), 7.88-7.90 (m, 2H)

^{13}C NMR (DMSO-*d*$_6$) : δ 10.2, 16.2, 25.6, 25.7, 30.4, 43.2, 66.5, 99.5, 110.8, 124.9, 125.1, 125.5, 126.0, 127, 129.1, 129.6, 130.2, 132.9, 147.5, 158.4, 161.3

ESI/MS (m/z) : 463.2 $(M+H)^{+}$

4.1.11.7 (*E*)-2-(2-Methyl-4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy)imino)ethyl) phenoxy)acetic acid (21a)



21a (0.43 gm, 92%) was prepared from **19a** (0.50 gm, 1.15 mmol) following the general procedure described above as an off white solid. m.p. 194-196 ^{o}C; Purity by HPLC: 99.5%.

IR (KBr) : 3030, 2947, 2914, 2848, 1722, 1618, 1556, 1500, 1436, 1371, 1321, 1265, 1240, 1195, 1145, 1083, 1066, 1014, 970, 916, 873, 800, 729, 661 cm^{-1}

^{1}H NMR (DMSO-*d*$_6$) : δ 2.13 (s, 3H), 2.20 (s, 3H), 2.35 (s, 3H), 2.46 (s, 3H), 4.73 (s, 2H), 5.0 (s, 2H), 6.85 (d, *J* = 8.6 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 1H), 7.49 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-*d*$_6$) : δ 10.1, 12.3, 16.1, 21.0, 64.7, 66.9, 111.0, 124.3, 124.8, 125.6, 125.9, 128.0, 128.3, 129.6, 132.6, 140.1, 147.4, 154.0, 156.8,

158.8, 170.1

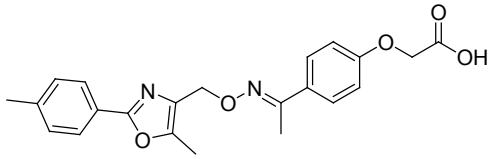
ESI/MS (m/z) : 409.0 $(M+H)^+$

Analysis **Mol.Formula**: $C_{23}H_{24}N_2O_5$

Calculated : C, 67.63%; H, 5.92%; N, 6.86%

Found : C, 67.16%; H, 5.81%; N, 6.81%

4.1.11.8 (*E*)-2-(4-(1-(((5-Methyl-2-(*p*-tolyl)oxazol-4-yl)methoxy)imino) ethyl)phenoxy)acetic acid (21b)



21b (0.42 gm, 90%) was prepared from **19b** (0.50 gm, 1.18 mmol) following the general procedure described above as an off white solid. m.p. 185-186 ^oC; Purity by HPLC: 99.5%.

IR (KBr) : 2920, 1720, 1612, 1514, 1500, 1371, 1240, 1182, 1066, 1010, 885, 825, 731 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 2.13 (s, 3H), 2.35 (s, 3H), 2.44 (s, 3H), 4.63 (s, 2H), 5.03 (s, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 10.2, 12.3, 21.0, 64.9, 66.9, 114.4, 124.3, 125.6, 127.2, 128.6, 129.7, 132.6, 140.1, 147.4, 153.9, 158.8, 158.8, 170.3

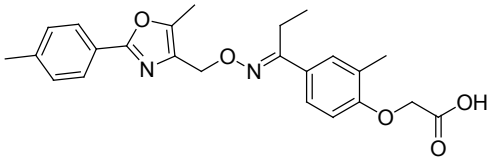
ESI/MS (m/z) : 395.2 $(M+H)^+$

Analysis **Mol.Formula**: $C_{22}H_{22}N_2O_5$

Calculated : C, 66.99%; H, 5.62%; N, 7.10%

Found : C, 65.57%; H, 5.47%; N, 7.37%

4.1.11.9 (*E*)-2-(2-Methyl-4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy)imino)propyl) phenoxy)acetic acid (21c)



21c (0.43 gm, 92%) was prepared from **19c** (0.50 gm, 1.11 mmol) following the general procedure described above as an off white solid. m.p. 190-191 ^{o}C; Purity by HPLC: 99.3%.

IR (KBr) : 3387, 2972, 2875, 1726, 1504, 1446, 1332, 1215, 1151, 1103, 1004, 970, 821, 732 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 0.96 (t, *J* = 7.6 Hz, 3H), 2.20 (s, 3H), 2.34 (s, 3H), 2.44 (s, 3H), 2.60 (q, *J* = 7.4 Hz, 2H), 4.72 (s, 2H), 5.02 (s, 2H), 7.39 (d, *J* = 8.8 Hz, 1H), 7.46 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 10.1, 11.1, 16.2, 19.1, 21.0, 64.7, 66.9, 111.1, 124.4, 124.9, 125.5, 126.1, 127.1, 128.2, 129.6, 132.7, 140.1, 147.3, 156.8, 158.8, 159.0, 170.1

ESI/MS (m/z) : 423.2 $(M+H)^{+}$

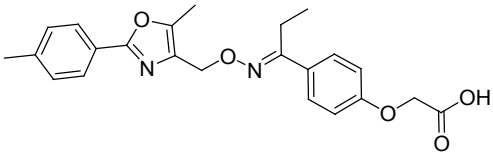
Analysis

Mol.Formula: $C_{24}H_{26}N_2O_5$

Calculated : C, 68.23%; H, 6.20%; N, 6.63%

Found : C, 66.70%; H, 6.34%; N, 6.71%

4.1.11.10 (*E*)-2-(4-(1-(((5-Methyl-2-(*p*-tolyl)oxazol-4-yl)methoxy)imino) propyl)phenoxy) acetic acid (21d)



21d (0.34 gm, 91%) was prepared from **19d** (0.40 gm, 0.92 mmol) following the general procedure described above as an off white solid. m.p. 155 - 157 ^{o}C; Purity by HPLC: 97.5%.

IR (KBr) : 3433, 2916, 2941, 2875, 2503, 1726, 1643, 1610, 1556, 1512, 1498, 1446, 1434, 1336, 1269, 1244, 1211, 1190, 1074, 987, 970, 871, 827, 731, 688 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 1.00 (t, *J* = 7.4 Hz, 3H), 2.34 (s, 3H), 2.43 (s, 3H), 2.67 (q, *J* = 7.4 Hz, 2H), 4.69 (s, 2H), 5.35 (s, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.82 (d, *J* = 8.1 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 10.1, 11.1, 19.1, 21.0, 64.5, 66.9, 114.5, 124.4, 125.6, 127.4, 127.5, 129.6, 132.7, 140.7, 147.3, 158.6, 158.8, 158.9, 170.0

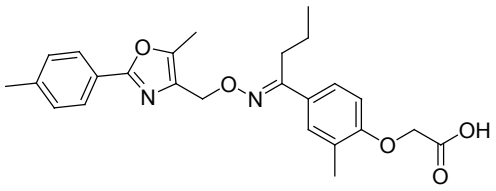
ESI/MS (m/z) : 409.0 $(M+H)^+$

Analysis **Mol.Formula**: $C_{23}H_{24}N_2O_5$

Calculated : C, 67.63%; H, 5.92%; N, 6.86%

Found : C, 67.32%; H, 5.95%; N, 6.75%

4.1.11.11 (*E*)-2-(2-Methyl-4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy)imino)butyl)phenoxy)acetic acid (21e)



21e (0.26 gm, 68%) was prepared from **19e** (0.40 gm, 0.86 mmol) following the general procedure described above as a white solid. m.p. 151-152 ^oC; Purity by HPLC: 99.4%.

IR (KBr) : 2964, 2873, 1728, 1645, 1558, 1338, 1001 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.91 (t, *J* = 7.3 Hz, 3H), 1.49-1.51 (m, 2H), 2.30 (s, 3H), 2.39 (s, 3H), 2.46 (s, 3H), 2.68 (t, *J* = 7.5 Hz, 2H), 4.66 (s, 2H), 5.11 (s, 2H), 6.67 (d, *J* = 8.5 Hz, 1H), 7.22 (s, 2H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.46 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 10.6, 14.4, 16.5, 20.2, 21.6, 28.6, 65.4, 67.2, 111.0, 124.6, 125.2, 126.3, 127.3, 129.1, 129.2, 129.6, 132.6, 140.7, 147.3, 156.9, 160.2, 172.2

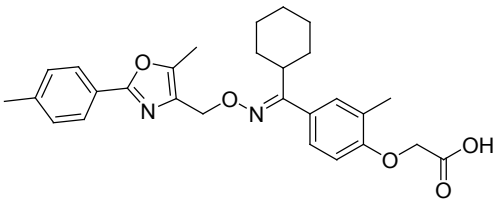
ESI/MS (m/z) : 437.0 $(M+H)^+$

Analysis **Mol.Formula:** $C_{25}H_{28}N_2O_5$

Calculated : C, 68.79%; H, 6.47%; N, 6.42%

Found : C, 67.86%; H, 6.55%; N, 6.61%

4.1.11.12 (*E*)-2-(4-(Cyclohexyl(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy) imino)methyl)-2-methylphenoxy)acetic acid (21f)



21f (0.30 gm, 80%) was prepared from **19f** (0.40 gm, 0.79 mmol) following the general procedure described above as a white solid. m.p. 58-60 ^oC; Purity by HPLC: 97.2%.

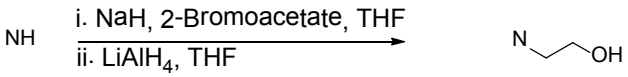
IR (KBr) : 3431, 2927, 2852, 1618, 1560, 1500, 1431, 1332, 1226, 1072, 985, 823, 731 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.20-1.23 (m, 8H), 2.16-2.17 (m, 3H), 2.32 (s, 3H), 2.34 (s, 3H), 2.36 (s, 3H), 4.88 (s, 2H), 5.01 (s, 2H), 6.66-6.67 (m, 1H), 6.89-6.91 (m, 1H), 7.04-7.09 (m, 1H), 7.11-7.14 (m, 2H), 7.78-7.80 (m, 1H), 7.88 (d, *J* = 7.6 Hz, 1H)

^{13}C NMR (DMSO-d_6) : δ 10.2, 16.3, 21, 22.8, 25.2, 25.6, 25.8, 25.9, 28.8, 29.3, 30.4, 43.2, 66.5, 66.7, 66.8, 99.6, 110.7, 124.4, 125, 125.2, 125.3, 125.5, 126.1, 127.2, 129.7, 132.8, 140.0, 147.0, 156.5, 157.0, 158.5, 161.3, 163.0, 171.2

ESI/MS (m/z) : 499.1 $(M+Na)^+$

4.1.12 General procedure for the preparation of the compounds 24a-c

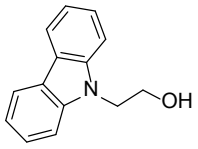


22a-c **24a-c**

Step I: To an ice cold suspension of sodium hydride (60%) (2 mole equivalent) in dry THF (10 fold) was added **22a-c** (1 mole equivalent) 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 ether extracts were successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was triturated with hexane to remove excess bromoacetate to yield the product **23a-c** as viscous liquid and that was subjected to reduction without any purification.

Step II: To an ice cold solution of the product **23a-c** 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 **24a-c.**

4.1.12.1 2-(*9H*-Carbazol-9-yl)ethanol (24a)



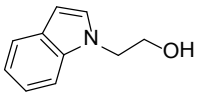
24a (5.37 gm, 85%) was prepared from carbazole (**22a**) (5 gm, 29.9 mmol) in 3 steps as described in the general procedure above as a thick liquid.

IR (Neat) : 3209, 2866, 1624, 1591, 1483, 1460, 1332, 1245, 1080, 1056, 894, 750 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 3.93-3.95 (m, 2H), 4.37 (t, *J* = 5.4, 2H), 7.19-7.25 (m, 2H), 7.39-7.46 (m, 4H), 8.05 (d, *J* = 7.8 Hz, 2H)

ESI/MS (m/z) : 211.9 $(M+H)^+$

4.1.12.2 2-(*1H*-Indol-1-yl)ethanol (24b)



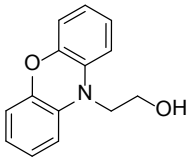
24b (5.16 gm, 75%) was prepared from indole (**22b**) (5 gm, 42.68 mmol) in 3 steps as described in the general procedure above as a thick liquid.

IR (Neat) :3431, 3018, 1512, 1463, 1398, 1315, 1215, 1053, 929, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 3.93-3.95 (m, 2H), 4.28 (t, *J* = 5.2 Hz, 2H), 6.51 (dd, *J* = 3.9 & 2.4 Hz, 1H), 7.11-7.26 (m, 3H), 7.35 (dd, *J* = 8.2 & 0.8 Hz, 1H), 7.62 (dd, *J* = 8.7 & 0.9 Hz, 1H)

ESI/MS (m/z) : 161.9 $(M+H)^+$

4.1.12.3 2-(*10H*-Phenoxazin-10-yl)ethanol (24c)



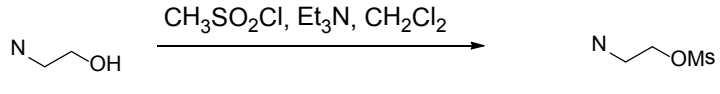
24c (11.1 gm, 80%) was prepared from phenoxazine (**22c**) (10 gm, 54.58 mmol) in 3 steps as described in the general procedure above as a brown solid. mp: 101-102 °C.

IR (KBr) : 3400, 3180, 3060, 2914, 1591, 1490, 1377, 1269, 1126, 1045, 736 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 3.72 (t, *J* = 6.2 Hz, 2H), 3.90-3.92 (m, 2H), 6.59-6.66 (m, 6H), 6.75-6.81 (m, 2H)

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

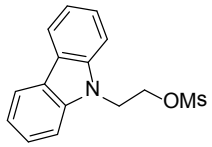
4.1.13 General procedure for the preparation of the compounds 34a-c



24a-c **34a-c**

To an ice cold solution of the product **24a-c** 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 **34a-c**.

4.1.13.1 2-(*9H*-Carbazol-9-yl)-ethyl methanesulfonate (34a)



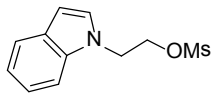
34a (5.48 gm, 80%) was prepared from **24a** (5.0 gm, 23.67 mmol) as described in the general procedure above as a white solid. mp: 148-150 °C; Purity by HPLC: 98%.

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

^{1}H NMR ($CDCl_3$) : 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 $(M+H)^+$

4.1.13.2 2-Indol-1-yl-ethyl methane sulfonate (34b)



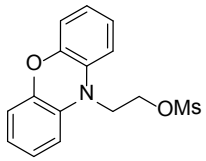
34b (4.45 gm, 60%) was prepared from **24b** (5.0 gm, 31.02 mmol) as described in the general procedure above as a yellow solid. mp: 80-82 °C; Purity by HPLC: 98.3%.

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

^{1}H NMR ($CDCl_3$) : 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 $(M+H)^+$

4.1.13.3 2-(Phenoxazin-10-yl)-ethyl methanesulfonate (34c)



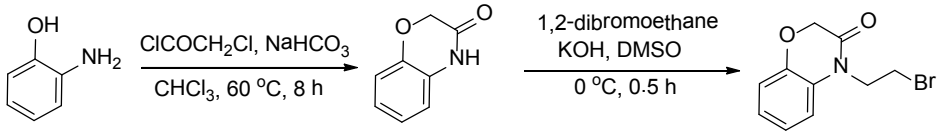
34c (10.8 gm, 80%) was prepared from **24c** (10 gm, 44.00 mmol) as described in the general procedure above as a white solid. mp: 79-80°C; Purity by HPLC: 97.3%.

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

^{1}H NMR ($CDCl_3$) : 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, 3H)

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

4.1.14 4-(2-Bromoethyl)-*2H*-benzo[*b*][1,4]oxazin-3(*4H*)-one (34d)



25 **26** **34d**

Step I: To an ice cold suspension of sodium bicarbonate (30.8 gm, 0.367 mol) in chloroform (150 ml) was added **25** (10.0 gm, 0.092 mol) and benzyltrimethylammonium chloride (17.0 gm, 0.092 mol) followed by drop-wise

addition of chloroacetyl chloride (8.9 ml, 0.110 mol) at 0-10 ^{o}C over a period of 20 minutes under nitrogen atmosphere. The reaction mixture was stirred at 60 ^{o}C for 8 hours. The reaction mixture was cooled to room temperature, poured into ice cold water and extracted with chloroform. The combined organic extracts were washed with water and brine, dried over calcium chloride and concentrated to yield the product **26** as an off white solid. mp: 170-171 °C

IR (KBr) **:** 3150, 1680, 1500, 1400, 1220, 1050, 749 cm^{-1}

^{1}H NMR (DMSO-d_6) **:** δ 4.54 (s, 3H), 6.80-6.96 (m, 4H)

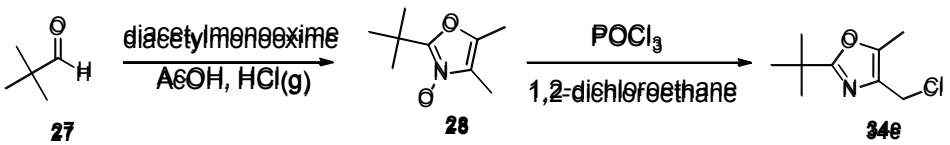
Step II: To an ice cold suspension of potassium hydroxide (7.52 gm, 0.13 mol) in dry DMSO (50 ml) was added **26** (10 gm, 0.067 mol) followed by drop-wise addition of 1,2-dibromoethane (37.79 gm, 0.201 mol) at 0 ^{o}C over a period of 10 minutes under nitrogen atmosphere and stirred for 30 minutes at the same temperature. The reaction mixture was poured into ice cold water and extracted with ethyl acetate. The ethyl acetate extract was successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography (Eluent: 15% Ethyl acetate in hexane) to yield 4.29 gm of product **34d** as a thick liquid.

IR (KBr) **:** 1689, 1500, 1402, 1274, 1215, 1056, 754 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 3.5 (t, *J* = 7.6 Hz, 2H), 4.3 (t, *J* = 7.5 Hz, 2H), 4.6 (s, 2H), 7.0 (m, 4H)

ESI/MS (m/z) **:** 150.7 $(M+H)^{+}$

4.1.1 2-*tert*-Butyl-4-chloromethyl-5-methyloxazole (34e)



Step I: To an ice-cold solution of freshly distilled pivalaldehyde (**27**) (15 gm, 0.174 mole) and diacetylmonoxime (17.6 gm, 0.174 mole) in AcOH (30 ml), dry HCl gas was passed for 3 h at 0 °C. The reaction mixture was diluted with diethyl ether (60 ml). Diethyl ether was decanted and resulted semisolid was dried under vacuum to obtain the product **28** as a thick oil (20 gm, 68%). Purity by HPLC: 97.95%.

IR (Neat) **:** 3392, 2976, 1689, 1485, 1433, 1392, 1259, 1217, 1124, 1039, 991, 754 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.58 (s, 9H), 2.38 (s, 6H)

ESI/MS (m/z) **:** 170.49 $(M+H)^+$

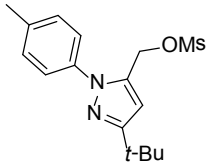
Step II: To an ice-cold suspension of *N*-oxide **28** (20.0 gm, 0.12 mole) in dichloroethane (150 ml) was added $POCl_3$ (19.9 gm, 0.13 mole) drop wise over a period of 2 hours at 10 °C. Reaction mixture was slowly heated to 60 °C and stirred at that temperature for 3 hours. Reaction mixture was cooled to room temperature, poured into ice-cold water and extracted with dicloroethane. The combined organic extracts were washed with water, dried over $CaCl_2$ and concentrated under vacuum to furnish title product **34e** as a white solid (18 gm, 80%). Purity by HPLC: 89.9%.

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

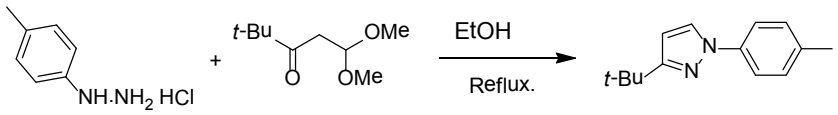
^{1}H NMR ($CDCl_3$) **:** δ 1.35 (s, 9H), 2.30 (s, 3H), 4.47 (s, 2H)

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

4.1.15 (3-(*tert*-Butyl)-1-(*p*-tolyl)-*1H*-pyrazol-5-yl)methyl methane sulfonate (34f)



Step I: 3-(*tert*-Butyl)-1-(*p*-tolyl)-*1H*-pyrazole (**31**)



29 **30** **31**

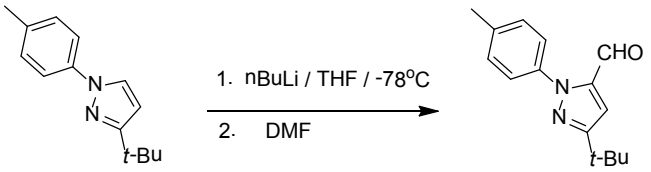
p-Tolylhydrazine hydrochloride (**29**) (9.1 gm, 0.058 mol) was added to a solution of 1,1-dimethoxy-4,4-dimethylpentan-3-one (**30**) (10.0 gm, 0.058 mol) in EtOH (100 ml) and reaction mixture was refluxed for 1 hour. The reaction mixture was cooled to room temperature and solvent was evaporated under vacuum. The residue was diluted with ice cold water and extracted with diethyl ether. The diethyl ether extract was washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography (Eluent: 1% Ethyl acetate in hexane) to yield title product **31** as a thick liquid (10 gm, 80%). Purity by HPLC: 97.7%.

IR (Neat) **:** 2960, 2927, 1693, 1612, 1531, 1365, 1269, 1168, 1045, 950, 813, 786, 759 cm^{-1}

^{1}H NMR (CDCl$_3$) **:** δ 1.36 (s, 9H), 2.35 (s, 3H), 6.28 (d, *J* = 2.4Hz, 1H), 7.2 (d, *J* = 8.2 Hz, 2H), 7.5 (d, *J* = 8.3 Hz, 2H), 7.75 (d, *J* = 2.4 Hz, 1H)

ESI/MS (m/z) **:** 215.0 $(M+H)^+$

Step II: 3-(*tert*-Butyl)-1-(*p*-tolyl)-*1H*-pyrazole-5-carbaldehyde (**32**)



31 **32**

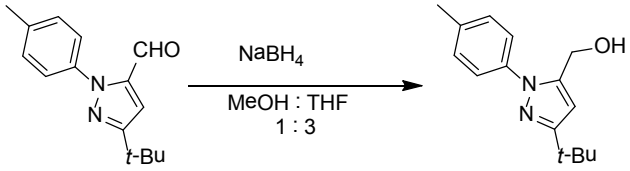
To a solution of **31** (8.0 gm, 0.037 mol) in dry THF (100 ml), *n*-BuLi (15% in hexane) (31 ml, 0.075 mol) was added drop-wise over a period of 30 minute at -78 °C under nitrogen atmosphere. The reaction mixture was allowed to come at room temperature, stirred for 30 min and then again cooled to -78 °C, DMF (6.0 ml, 0.075 mol) was added drop-wise and stirred at room temperature for 2 hours. The reaction mixture was poured into ice cold water and extracted with ethyl acetate. The ethyl acetate extract was successively washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography (Eluent: 5% Ethyl acetate in hexane) to yield title product **32** as a white solid (7.4 gm, 83%). m.p. 62-64 °C; Purity by HPLC: 95.9%.

IR (KBr) **:** 3070, 2958, 2289, 1919, 1691, 1527, 1514, 1479, 1431, 1379, 1336, 1236, 1147, 1109, 1037, 1014, 987, 827, 779, 721 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.37 (s, 9H), 2.42 (s, 3H), 6.94 (s, 1H), 7.2 (d, *J* =8.1 Hz, 2H), 7.36 (d, *J* = 8.3 Hz, 2H), 9.8 (s, 1H)

ESI/MS (m/z) **:** 275.0 $(M+H)^+$

Step III: (3-(*tert*-Butyl)-1-(*p*-tolyl)-*1H*-pyrazol-5-yl)methanol (**33**)



32 **33**

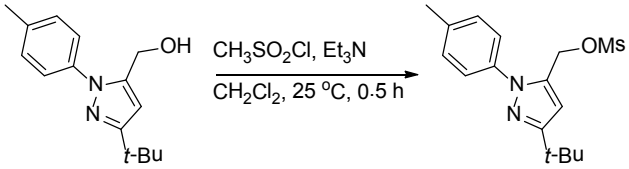
To an ice cold solution of **32** (7.0 gm, 0.029 mol) in a mixture of THF:MeOH (3:1) (60 ml), sodium borohydride (0.55 gm, 0.015 mol) was added in small portion over a period of 10 minute keeping the reaction temperature between 0 to 5 ^{o}C and reaction mixture was stirred at 30 ^{o}C for 2 hours. Solvents were removed from the reaction mixture under vacuum. The residue was diluted with ice cold water and extracted with ethyl acetate. The ethyl acetate extract was washed with water and brine, dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography (Eluent: 7% ethyl acetate in hexane) to yield title product **33** as a white solid (6.1 gm, 86%). m.p. 86-88 ^{o}C; Purity by HPLC: 96.9%.

IR (KBr) **:** 3238, 3080, 2906, 1612, 1548, 1519, 1460, 1442, 1371, 1359, 1242,1213, 1143, 1041, 1008, 937, 831, 813, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.34 (s, 9H), 2.01 (bs, 1H), 2.37 (s, 3H), 4.56 (s, 2H), 6.27 (s, 1H), 7.2 (d, *J* = 7.2 Hz, 2H), 7.40 (d, *J* = 7.5 Hz, 2H)

ESI/MS (m/z) **:** 245.0 $(M+H)^+$

Step IV: (3-(*tert*-Butyl)-1-(*p*-tolyl)-*1H*-pyrazol-5-yl)methyl methanesulfonate (**34f**)



33 **34f**

To an ice cold solution of **33** (6.0 gm, 0.025 mol) in dichloromethane (30 ml), Et_3N (4.10 ml, 0.030 mol) was added followed by drop-wise addition of methane sulfonyl chloride (2.17 ml, 0.028 mol) at 0 ^{o}C over a period of 10 minute under nitrogen atmosphere. The reaction mixture was stirred at 30 ^{o}C for 30 minute. The reaction mixture was poured into ice cold water and extracted with dichloromethane. The organic extracts were washed with water and brine, dried

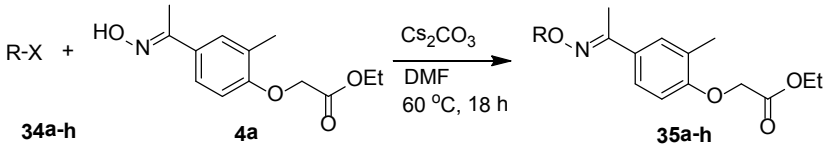
over $CaCl_2$, filtered and concentrated under vacuum. The product was triturated in hexane to yield title product **34f** as an off white solid (6.4 gm, 80%)..

IR (KBr) : 1519, 1483, 1371, 1317, 1240, 1176, 1039, 964, 785, 761 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.34 (s, 9H), 2.40 (s, 3H), 4.53 (s, 2H), 6.36 (s, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.41 (dd, *J* = 6.6 & 1.8 Hz, 2H)

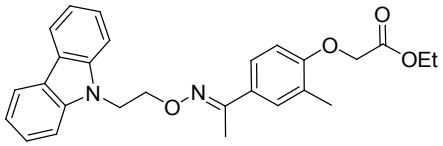
ESI/MS (m/z) : 328.2 $(M+H)^+$

4.1.16 General procedure for the synthesis of Compounds (35a-h)



To a solution of **34a-h** (1 mole equivalent) and **4a** (1 mole equivalent) in dry DMF (5 fold), Cs_2CO_3 (1.5 mole equivalent) was added and reaction mixture was stirred at 60 ^oC for 18 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (10 to 15% ethyl acetate in hexane) to yield title compound **35a-h**.

4.1.16.1 (*E*)-Ethyl 2-(4-(1-((2-(*9H*-carbazol-9-yl)ethoxy)imino)ethyl) -2-methylphenoxy) acetate (35a)



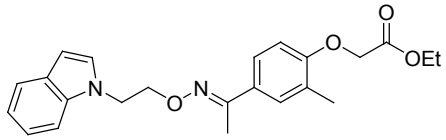
35a (0.35 gm, 45%) was prepared from **34a** (0.50 gm, 1.73 mmol) and **4a** (0.43 gm, 1.73 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.1%.

IR (Neat) : 3051, 2929, 2883, 1732, 1600,1502, 1238 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.30 (t, *J* = 7.1 Hz, 3H), 1.93 (s, 3H), 2.31 (s, 3H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.56 (t, *J* = 5.0 Hz, 2H), 4.64-4.68 (m, 4H), 6.67 (d, *J* = 8.5 Hz, 1H), 7.21-7.24 (m, 2H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.43-7.48 (m, 5H), 8.00 (d, *J* = 7.7 Hz, 2H)

ESI/MS (m/z) : 467.1 $(M+Na)^+$

4.1.16.2 (*E*)-Ethyl 2-(4-(1-((2-(*1H*-indol-1-yl)ethoxy)imino)ethyl)-2-methylphenoxy)acetate (35b)



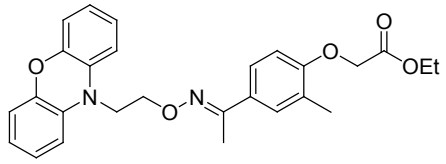
35b (0.45 gm, 52%) was prepared from **34b** (0.50 gm, 2.09 mmol) and **4a** (0.53 gm, 2.09 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.9%.

IR (Neat) : 3018, 2929, 1957, 1757, 1610, 1504, 1440, 1400, 1355, 1315, 1215, 1064, 869, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.30 (t, *J* = 7.1 Hz, 3H), 2.09 (s, 3H), 2.31 (s, 3H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.47 (s, 4H), 4.65 (s, 2H), 6.50 (d, *J* = 2.9 Hz, 1H), 6.67 (d, *J* = 8.5 Hz, 1H), 7.07-7.21 (m, 3H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.44 (s, 1H), 7.62 (d, *J* = 7.7 Hz, 1H)

ESI/MS (m/z) : 417.0 $(M+Na)^+$

4.1.16.3 (*E*)-Ethyl 2-(4-(1-((2-(*10H*-phenoxazin-10-yl)ethoxy)imino) ethyl)-2-methyl phenoxy)acetate (35c)



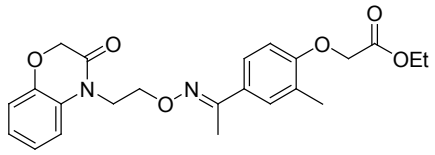
35c (0.32 gm, 43%) was prepared from **34c** (0.50 gm, 1.64 mmol) and **4a** (0.41 gm, 1.64 mmol) following the general procedure described above as a yellow solid. m.p. 62-64 ^{o}C; Purity by HPLC: 99.5%.

IR (KBr) : 3062, 2939, 2852, 1764, 1627, 1591, 1494, 1205 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.30 (t, *J* = 7.1 Hz, 3H), 2.13 (s, 3H), 2.32 (s, 3H), 3.83-3.89 (m, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.39 (t, *J* = 6.1 Hz, 2H), 4.66 (s, 2H), 6.62-6.76 (m, 9H), 7.39 (d, *J* = 9.0 Hz, 1H), 7.50 (s, 1H)

ESI/MS (m/z) : 461.1 $(M+H)^{+}$

4.1.16.4 (*E*)-Ethyl 2-(2-methyl-4-(1-((2-(3-oxo-2H-benzo[*b*][1,4] oxazin-4(*3H*)-yl)ethoxy)imino)ethyl)phenoxy)acetate (35d)



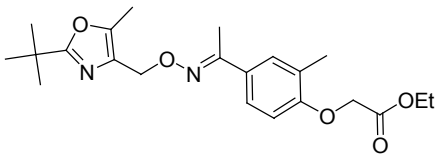
35d (0.70 gm, 84%) was prepared from **34d** (0.50 gm, 1.95 mmol) and **4a** (0.49 gm, 1.95 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.1%.

IR (Neat) : 3141, 3020, 2401, 1732, 1681, 1502, 1404, 1305, 1215, 758, 667 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.25 (t, J = 7.1 Hz, 3H), 2.02 (s, 3H), 2.34 (s, 3H), 4.21-4.24 (m, 4H), 4.41 (t, *J* = 5.4 Hz, 2H), 4.60 (s, 2H), 4.72 (s, 2H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.67 (s, 3H), 7.10-7.15 (m, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.50 (s, 1H)

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

4.1.16.5 (*E*)-Ethyl 2-(4-(1-((2-(2-(*tert*-butyl)-5-methyloxazol-4-yl)ethoxy) imino)ethyl)-2-methylphenoxy)acetate (35e)



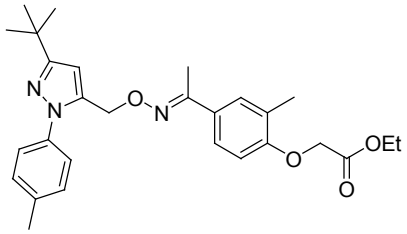
35e (0.71 gm, 66%) was prepared from **34e** (0.50 gm, 2.67 mmol) and **4a** (0.67 gm, 2.67 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.7%.

IR (Neat) : 3130, 2974, 2871, 1760, 1737, 1606, 1504, 1184 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.29 (t, *J* = 7.1 Hz, 3H), 1.36 (s, 9H), 2.19 (s, 3H), 2.30 (s, 3H), 2.36 (s, 3H), 4.26 (q, *J* = 7.2 Hz, 2H), 4.64 (s, 2H), 5.03 (s, 2H), 6.66 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* =8.3 Hz, 1H), 7.48 (s, 1H)

ESI/MS (m/z) : 403.0 $(M+H)^+$

4.1.16.6 (*E*)-Ethyl 2-(4-(1-(((3-(*tert*-butyl)-1-(*p*-tolyl)-*1H*-pyrazol-5-yl) methoxy)imino) ethyl)-2-methylphenoxy)acetate (35f)



35f (0.69 gm, 93%) was prepared from **34f** (0.50 gm, 1.55 mmol) and **4a** (0.39 gm, 1.55 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 93.5%.

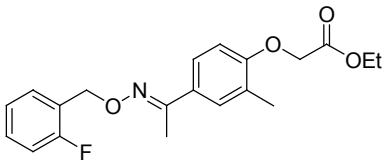
IR (Neat) : 1759, 1737, 1612, 1517, 1317, 1278, 1186, 1097, 995, 756 cm^{-1}

^{1}H NMR : δ 1.21 (t, *J* = 7.1 Hz, 3H), 1.30 (s, 9H), 2.23 (s, 3H), 2.32 (s,

($CDCl_3$) 3H), 2.39 (s, 3H), 4.22 (q, *J* = 7.1 Hz, 2H), 4.64 (s, 2H), 5.11 (s, 2H), 6.39 (s, 1H), 6.7 (d, *J* = 8.5 Hz, 1H), 7.21-7.23 (m, 2H), 7.40-7.44 (m, 4H)

ESI/MS (m/z) : 478.2 $(M+H)^+$

4.1.16.7 (*E*)-Ethyl 2-(4-(1-(((2-fluorobenzyl)oxy)imino)ethyl)-2-methyl phenoxy)acetate (35g)



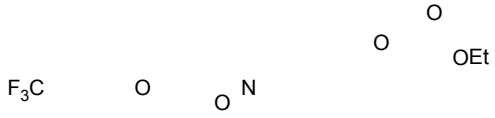
35g (0.69 gm, 73%) was prepared from **34g** (0.50 gm, 2.64 mmol) and **4a** (0.66 gm, 2.64 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 92.1%.

IR (Neat) : 3130, 3020, 2401, 1755, 1620, 1404, 1215, 1145, 758, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.29 (t, *J* = 7.1 Hz, 3H), 2.24 (s, 3H), 2.26 (s, 3H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.64 (s, 2H), 5.29 (s, 2H), 6.66 (d, *J* = 8.5 Hz, 1H), 7.02-7.15 (m, 2H), 7.29-7.42 (m, 2H), 7.46-7.49 (m, 2H)

ESI/MS (m/z) : 360.0 $(M+H)^+$

4.1.16.8 (*E*)-Ethyl 2-(2-methyl-4-(1-((2-(3-(trifluoromethyl) phenoxy) ethoxy)imino)ethyl)phenoxy)acetate (35h)



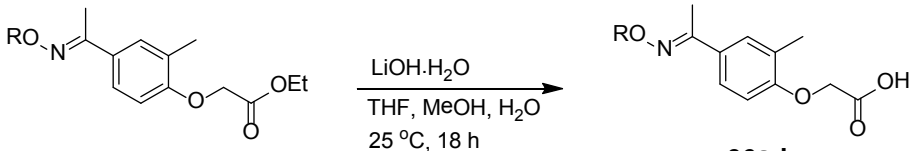
35h (0.53 gm, 54%) was prepared from **34h** (0.50 gm, 2.23 mmol) and **4a** (0.56 gm, 2.23 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.6%.

IR (Neat) : 3130, 3022, 2949, 1957, 1759, 1712, 1604, 1502, 1448, 1328, 1215, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.29 (t, *J* = 7.1 Hz, 3H), 2.19 (s, 3H), 2.30 (s, 3H), 4.20-4.35 (m, 4H), 4.50-4.54 (m, 2H), 4.62 (s, 2H), 6.67 (d, *J* = 8.6 Hz, 1H), 7.10-7.22 (m, 3H), 7.35-7.50 (m, 2H), 7.60 (s, 1H)

ESI/MS (m/z) : 462.0 $(M+Na)^+$

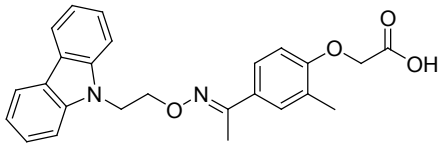
4.1.17 General procedure for the synthesis of Compounds (36a-h)



35a-h **36a-h**

To a solution of **35a-h** 9 (1 mole equivalent) in a mixture of tetrahydrofuran (15 fold) and methanol (5 fold) was added another solution of $LiOH.H_2O$ (2 mole equivalent) in water (5 fold) and the reaction mixture was stirred at ambient temperature for about 5 hours. Solvent was evaporated under reduced pressure, water was added to the residue, acidified with 1N HCl to pH 6 and extracted with ethyl acetate. The combined organic extracts were washed with water and brine solution, dried over sodium sulphate and evaporated under reduced pressure to yield title product **36a-h**.

4.1.17.1 (*E*)-2-(4-(1-((2-(*9H*-Carbazol-9-yl)ethoxy)imino)ethyl)-2-methylphenoxy)acetic acid (36a)



36a (0.20 gm, 61%) was prepared from **35a** (0.35 gm, 0.79 mmol) following the general procedure described above as a white solid. m.p. 182-183 ^{O}C; Purity by HPLC: 98.6%.

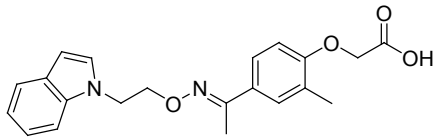
IR (KBr) : 3407, 2904, 2781, 1749, 1625, 1500, 1245 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.79 (s, 3H), 2.16 (s, 3H), 4.46 (t, *J* = 4.7 Hz, 2H), 4.70 (s, 4H), 6.77 (d, *J* = 8.5 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 2H), 7.27 (m, 2H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 8.13 (d, *J* = 7.7 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 13.7, 16.5, 42.8, 71.7, 100.1, 108.9, 119.1, 120.4, 123.1, 125.0, 125.7, 127.4, 129.0, 140.8, 170.2

ESI/MS (m/z) : 417.4 $(M+H)^+$

4.1.17.2 (*E*)-2-(4-(1-((2-(*1H*-Indol-1-yl)ethoxy)imino)ethyl)-2-methyl phenoxy)acetic acid (36b)



36b (0.25 gm, 60%) was prepared from **35b** (0.45 gm, 1.14 mmol) following the general procedure described above as an off white solid. m.p. 123-125 ^oC; Purity by HPLC: 96.4%.

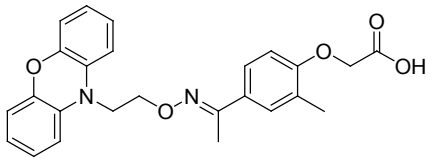
IR (KBr) : 3411, 2908, 2881, 2572, 1890, 1751, 1708, 1614, 1510, 1465, 1429, 1348, 1261, 1149, 1080, 968, 792, 742, 584 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.09 (s, 3H), 2.30 (s, 3H), 4.46 (s, 4H), 4.69 (s, 2H), 6.50 (d, *J* = 3.2 Hz, 1H), 6.71 (d, *J* = 8.6 Hz, 1H), 7.07-7.21 (m, 3H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.44 (s, 1H), 7.62 (d, *J* = 7.7 Hz, 1H)

^{13}C NMR ($CDCl_3$) : δ 13.1, 16.4, 65.2, 72.5, 101.5, 109.5, 110.9, 119.4, 121.0, 121.6, 125.0, 127.4, 128.4, 128.7, 129.0, 130.0, 136.4, 155.6, 156.8, 174.0

ESI/MS (m/z) : 389.0 $(M+Na)^+$

4.1.17.3 (*E*)-2-(4-(1-((2-(*10H*-Phenoxazin-10-yl)ethoxy)imino) ethyl)-2-methylphenoxy)acetic acid (36c)



36c (0.29 gm, 95%) was prepared from **35c** (0.32 gm, 0.70 mmol) following the general procedure described above as an off white solid. m.p. 136-138 ^{o}C; Purity by HPLC: 99.5%.

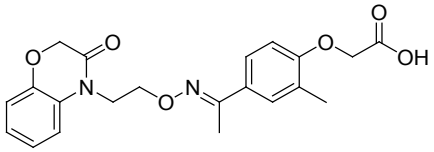
IR (KBr) : 3064, 2881, 2779, 1753, 1494, 1274, 1039 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.11 (s, 3H), 2.29 (s, 3H), 3.87 (t, *J* = 6.3 Hz, 2H), 4.38 (t, *J* = 6.3 Hz, 2H), 4.67 (s, 2H), 6.59-6.78 (m, 9H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.49 (s, 1H)

^{13}C NMR (CDCl$_3$) : δ 12.9, 16.5, 43.8, 65.4, 69.3, 111.0, 111.9, 115.5, 121.1, 123.6, 125.0, 127.4, 128.9, 129.9, 133.4, 145.0, 155.4, 156.8, 174.1

ESI/MS (m/z) : 433.1 (M+H)$^{+}$

4.1.17.4 (*E*)-2-(2-Methyl-4-(1-((2-(3-oxo-2H-benzo[b][1,4]oxazin-4(*3H*)-yl)ethoxy)imino)ethyl)phenoxy)acetic acid (36d)



36d (0.31 gm, 67%) was prepared from **35d** (0.50 gm, 1.17 mmol) following the general procedure described above as a white solid. m.p. 170-172 ^{o}C; Purity by HPLC: 96.9%.

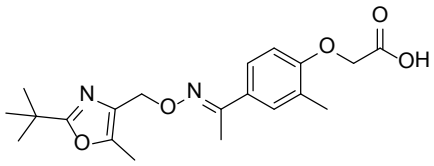
IR (KBr) : 3431, 2925, 1762, 1685, 1647, 1502, 1726, 1056, 918, 752, 522 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.07 (s, 3H), 2.21 (s, 3H), 4.25 (t, *J* = 6.3 Hz, 2H), 4.40 (t, *J* = 6.3 Hz, 2H), 4.50 (s, 2H), 4.62 (s, 2H), 6.60 (d, *J* = 8.5 Hz, 1H), 6.90 (s, 3H), 7.15 (m, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.50 (s, 1H)

^{13}C NMR (DMSO-*d*$_6$) : δ 12.5, 67.3, 74.2, 114.4, 125.2, 127.0, 127.5, 128.3, 143.3, 154.7, 159.8, 171.2

ESI/MS (m/z) : 399.0 $(M+H)^+$

4.1.17.5 (*E*)-2-(4-(1-(((2-(*tert*-Butyl)-5-methyloxazol-4-yl)methoxy) imino)ethyl)-2-methylphenoxy)acetic acid (36e)



36e (0.53 gm, 80%) was prepared from **35e** (0.71 gm, 1.71 mmol) following the general procedure described above as a white solid. m.p. 125-129 ^oC; Purity by HPLC: 99.1%.

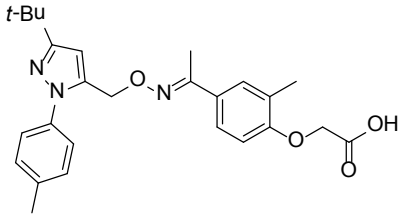
IR (KBr) : 3433, 2972, 2879, 1753, 1616, 1508, 1203 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.32 (s, 9H), 2.13 (s, 3H), 2.27 (s, 3H), 2.35 (s, 3H), 4.56 (s, 2H), 5.04 (s, 2H), 6.56 (d, *J* = 8.5 Hz, 1H), 7.29-7.33 (m, 1H), 7.45 (s, 1H)

^{13}C NMR (CDCl$_3$) : δ 10.4, 12.8, 1643, 28.6, 33.8, 16.5, 67.0, 110.9, 124.9, 127.2, 128.6, 129.5, 130.2, 146.7, 154.9, 157.0, 169.7, 171.7

ESI/MS (m/z) : 375.0 $(M+H)^+$

4.1.17.6 (*E*)-2-(4-(1-(((3-(*tert*-butyl)-1-(*p*-tolyl)-*1H*-pyrazol-5-yl) methoxy)imino)ethyl)-2-methylphenoxy)acetic acid (36f)



36f (0.57 gm, 88%) was prepared from **35f** (0.69 gm, 1.44 mmol) following the general procedure described above as a white solid. m.p. 157-159 ^{o}C; Purity by HPLC: 98.4%.

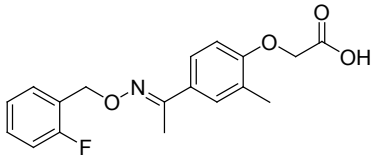
IR (KBr) : 1739, 1614, 1596, 1550, 1515, 1467, 1363, 1317, 1240, 1205, 1149, 1070, 1024, 941, 800 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.31 (s, 9H), 2.23 (s, 3H), 2.31 (s, 3H), 2.40 (s, 3H), 4.62 (s, 2H), 5.11 (s, 2H), 6.41 (s, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 7.21-7.26 (m, 2H), 7.41-7.44 (m, 4H)

^{13}C NMR ($CDCl_3$) : δ 13.1, 16.4, 21.2, 30.7, 32.3, 65.4, 66.5, 105.6, 111.0, 125.0, 125.1, 127.4, 129, 129.7, 129.8, 137.2, 137.6, 139.2, 155.2, 157.0, 162.2, 172.3

ESI/MS (m/z) : 450.2 (M+H)$^{+}$

4.1.17.7 (*E*)-2-(4-(1-(((2-Fluorobenzyl)oxy)imino)ethyl)-2-methyl phenoxy)acetic acid (36g)



36g (0.25 gm, 39%) was prepared from **35g** (0.69 gm, 1.92 mmol) following the general procedure described above as a white solid. m.p. 128-130 ^{o}C; Purity by HPLC: 99.9%.

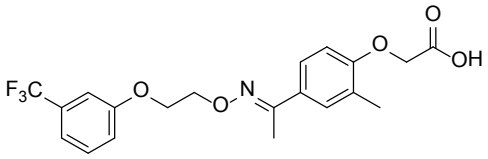
IR (KBr) : 3433, 2881, 1739, 1718, 1606, 1589, 1508, 1249, 1186, 1139, 937, 767, 497 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.22 (s, 3H), 2.30 (s, 3H), 4.70 (s, 2H), 5.29 (s, 2H), 6.71 (d, *J* = 8.6 Hz, 1H), 7.03-7.15 (m, 2H), 7.41-7.48 (m, 3H), 7.49 (s, 1H)

^{13}C NMR ($CDCl_3$) : δ 13.0, 16.4, 65.1, 69.7, 69.7, 110.8, 115.2, 115.5, 124.0, 124.1, 125, 125.3, 125.4, 127.3, 129.0, 129.5, 129.6, 130.1, 130.5, 130.6, 155.1, 156.7, 159.7, 162.2, 174.2

ESI/MS (m/z) : 331.8 $(M+H)^+$

4.1.17.8 (*E*)-2-(2-Methyl-4-(1-((2-(3-(trifluoromethyl)phenoxy)ethoxy) imino)ethyl)phenoxy)acetic acid (36h)



36h (0.26 gm, 53%) was prepared from **35h** (0.53 gm, 1.21 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 93.6%.

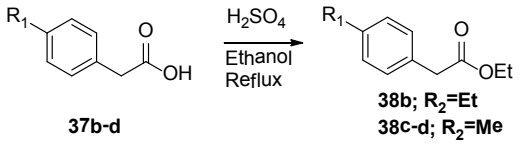
IR (KBr) : 3138, 3020, 2029, 1612, 1502, 1404, 1215, 1066, 758 cm^{-1}

^{1}H NMR (DMSO-*d*$_6$) : δ 2.10 (s, 3H), 2.12 (s, 3H), 4.25-4.40 (m, 6H), 6.68 (s, 1H), 7.26 (s, 3H), 7.40-7.50 (m, 3H)

^{13}C NMR (DMSO-*d*$_6$) : δ 12.4, 16.4, 62.2, 66.8, 71.9, 99.6, 111.1, 117.2, 119.0, 124.7, 125.5, 127.1, 127.7, 130.5, 130.7, 154.6, 158.1, 158.9

ESI/MS (m/z) : 433.9 $(M+H)^+$

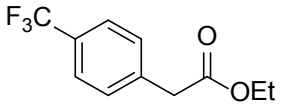
4.1.18 General procedure for the preparation of the compounds 38b-d



37b-d **38b; R_2=Et** **38c-d; R_2=Me**

To an ice cold solution of substituted phenyl acetic acid **37b-d** in ethanol/methanol (10 fold), H_2SO_4 (0.1 fold) was added and the reaction mixture was refluxed for 5 hours. Solvent was evaporated from the reaction mixture in rotavapour under vacuum. The residue was poured into ice cold water and extracted with diethylether. The ether extract was successively washed with water and brine, dried over Na_2SO_4 and concentrated under vacuum to yield the product **38a-d** as viscous liquid and this was subjected to reduction without any purification.

4.1.18.1 Ethyl 2-(4-trifluoromethylphenyl)acetate (38b)



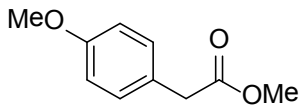
38b (5.6 gm, 98%) was prepared from 2-(4-trifluoromethylphenyl)acetic acid (**37b**) (5.00 gm, 24.57 mmol) as described in the general procedure above as a thick liquid. Purity by HPLC: 97.87%.

IR (Neat) **:** 3020, 2983, 2908, 1732, 1620, 1421, 1371, 1326, 1217, 1166, 1128, 1068, 1020, 823, 756, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.26 (t, *J* = 7.2 Hz, 3H), 3.67 (s, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 8.1 Hz, 2H)

ESI/MS (m/z) **:** 237.0

4.1.18.2 Methyl 2-(4-methoxyphenyl)acetate (38c)



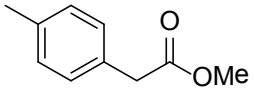
38c (10.0 gm, 93%) was prepared from 2-(4-methoxyphenyl)acetic acid (**37c**) (9.4 gm, 0.166 mol) as described in the general procedure above as a thick liquid. Purity by HPLC: 99.38%.

IR (Neat) : 3001, 2952, 2910, 2837, 1739, 1612, 1585, 1514, 1463, 1436, 1301, 1247, 1178, 1159, 1107, 1033, 1016, 891, 819, 788, 763 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 3.57 (s, 2H), 3.68 (s, 3H), 3.79 (s, 3H), 6.83-6.88 (m, 2H), 7.17-7.22 (m, 2H)

ESI/MS (m/z) : 202.8 $(M+H)^+$

4.1.18.3 Methyl 2-(*p*-tolyl)acetate (38d)



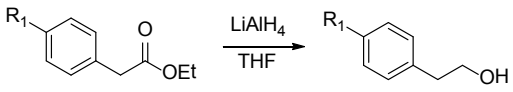
38d (5.5 gm, 98%) was prepared from 2-(4-methylphenyl)acetic acid (**37d**) (5.00 gm, 33.33 mmol) in 3 steps as described in the general procedure above as a thick liquid. Purity by HPLC: 99.05%.

IR (KBr) : 3022, 2952, 2923, 2866, 1735, 1651, 1515, 1436, 1417, 1382, 1342, 1301, 1259, 1217, 1191, 1157, 1016, 925, 842, 808, 756, 723, 667 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.33 (s, 3H), 3.58 (s, 3H), 3.68 (s, 3H), 7.11-7.25 (m, 4H).

ESI/MS (m/z) : 182.9 $(M+H)^+$

4.1.19 General procedure for the preparation of the compounds 39b-d

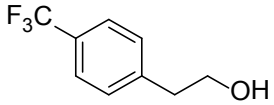


38b; R_2=Et
38c-d; R_2=Me

39b-d

To an ice cold solution of **38b-d** 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 hexane to obtain pure product **39b-d** which was directly subjected to the next step.

4.1.19.1 2-(4-trifluoromethylphenyl)ethanol (39b)



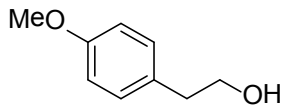
39b (3.6 gm, 80%) was prepared from **38b** (5.5 gm, 23.70 mmol) as described in the general procedure above as a thick liquid. Purity by HPLC: 68%.

IR (KBr) : 3616, 3415, 3018, 2952, 2883, 1732, 1620, 1517, 1475, 1417, 1326, 1215, 1166, 1128, 1068, 1045, 1020, 844, 825, 769, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.92 (t, *J* = 6.5 Hz, 2H), 3.88 (t, *J* = 6.5 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 196.9

4.1.19.2 2-(4-Methoxyphenyl)ethanol (39c)



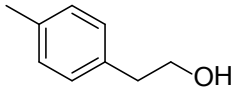
39c (8.3 gm, 98%) was prepared from **38c** (10 gm, 55.55 mmol) as described in the general procedure above as a thick liquid. Purity by HPLC: 82%.

IR (KBr) : 3411, 3014, 2937, 2912, 2879, 2837, 1730, 1612, 1586, 1512, 1465, 1442, 1384, 1299, 1247, 1217, 1178, 1110, 1039, 823, 810, 765, 667 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.80 (t, *J* = 6.5 Hz, 2H), 3.39-3.82 (m, 5H), 6.83-6.87 (m, 2H), 7.13 (d, *J* = 8.5 Hz, 2H)

ESI/MS (m/z) : 153.0 $(M+Na)^+$

4.1.19.3 2-(*p*-Tolyl)ethanol (39d)



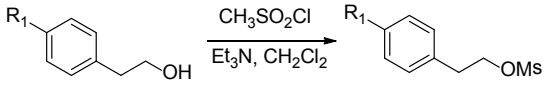
39d (4.3 gm, 99%) was prepared from **37d** (5.3 gm, 32.32 mmol) as described in the general procedure above as a thick liquid. Purity by HPLC: 77%.

IR (KBr) : 3359, 3047, 3020, 2923, 2871, 1739, 1515, 1434, 1417, 1384, 1240, 1166, 1047, 842, 808 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.33 (s, 3H), 2.81 (t, *J* = 6.5 Hz, 2H), 3.81 (t, *J* = 6.5 Hz, 2H), 7.06-7.12 (m, 4H).

ESI/MS (m/z) : 231.9 $(M+NH_4)^+$

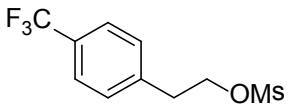
4.1.20 General procedure for the preparation of the compounds 42b-d



39b-d **42b-d**

To an ice cold solution of **39b-d** in dichloromathane (10 fold) were added triethylamine (1.5 mole equivalent) and methane sulfonyl 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 and successively washed with water and 1N HCl. The dichloromethane extract was dried over $CaCl_2$ and concentrated under vacuum to yield required product **42b-d**.

4.1.20.1 4-(Trifluoromethyl)phenethyl methanesulfonate (42b)

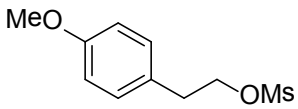


42b (2.8 gm, 99%) was prepared from **39b** (2.0 gm, 10.52 mmol) as described in the general procedure above as a thick liquid. Purity by HPLC: 59%.

^{1}H NMR ($CDCl_3$) : δ 2.91 (s, 3H), 3.14 (t, *J* = 6.0 Hz, 2H), 4.44 (t, *J* = 6.0 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H).

ESI/MS (m/z) : 239.0 $(M+H)^+$

4.1.20.2 4-Methoxyphenethyl methanesulfonate (42c)



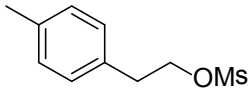
42c (10.5 gm, 84%) was prepared from **39c** (8.2 gm, 53.95 mmol) as described in the general procedure above as a thick liquid. Purity by HPLC: 82%.

IR (KBr) : 3024, 2939, 2912, 2912, 1733, 1583, 1514, 1465, 1355, 1301, 1249, 1217, 1174, 1112, 1035, 972, 954, 931, 864, 829, 813, 758, 667 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.84 (s, 3H), 3.01 (t, *J* = 6.9 Hz, 2H), 3.80 (s, 3H), 4.37 (t, *J* = 6.9 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 2H).

ESI/MS (m/z) : 252.9 $(M+Na)^+$

4.1.20.3 4-Methylphenethyl methanesulfonate (42d)



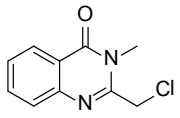
42d (6.3 gm, 93%) was prepared from **39d** (4.3 gm, 31.62 mmol) in 3 steps as described in the general procedure above as a thick liquid. Purity by HPLC: 76%.

IR (KBr) : 3024, 2923, 2869, 1732, 1515, 1467, 1382, 1357, 1217, 1172, 1049, 972, 956, 906, 813, 758, 667 cm^{-1}

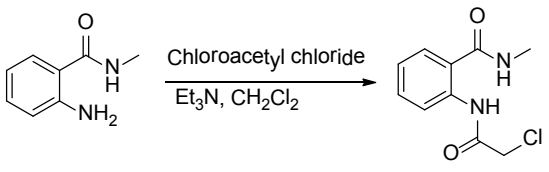
^{1}H NMR ($CDCl_3$) : δ 2.32 (s, 3H), 2.84 (s, 3H), 3.01 (t, *J* = 6.9 Hz, 2H), 4.42 (t, *J* = 6.9 Hz, 2H), 7.10-7.13 (m, 4H).

ESI/MS (m/z) : 231.9 $(M+NH_4)^+$

4.1.21 2-Chloromethyl-3-methyl-*3H*-quinazolin-4-one (42e)



Step I: 2-(2-Chloroacetamido)-*N*-methylbenzamide (**41**)



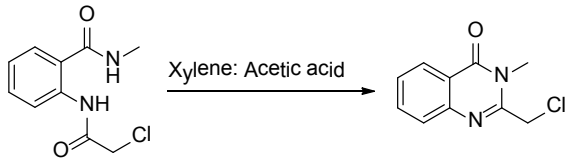
To an ice-cold solution of 2-amino-*N*-methylbenzamide (**40**) (2.25 gm, 12.1 mmoles) in dichloromethane were added triethylamine (3.36 mL, 24.2 mmoles) followed by chloroaceylchloride (0.97 mL, 12.1 mmoles) and the reaction mixture was stirred at ambient temperature for 3 hours. Reaction mixture was diluted with chloroform, washed with water, dried over calcium chloride, filtered and concentrated under vacuum to yield 2.14 g (78%) of compound **41** as a brown solid. mp: 144-146 °C; Purity by HPLC: 98%.

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

^{1}H NMR ($CDCl_3$) **:** δ 3.0 (t, *J* = 4.9 Hz,3H), 4.1 (s, 2H), 6.4 (bs, NH), 7.2 (m, 2H), 7.5 (m, 2H), 11.9 (bs, NH)

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

Step II: 2-Chloromethyl-3-methyl-*3H*-quinazolin-4-one (**42e**)



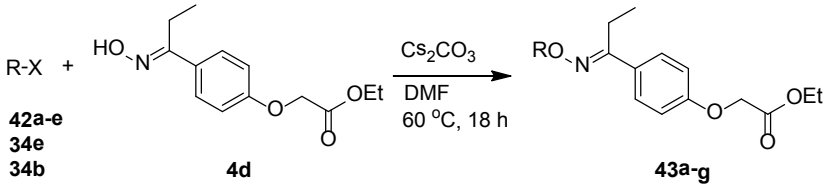
2-(2-Chloroacetamido)-*N*-methylbenzamide (**41**) (2.14 gm, 9.4 mmoles) was added to a 1:1 mixture of xylene and acetic acid (20 mL) and refluxed for 15 hours. Solvents were evaporated under vacuum and the residue was triturated with methanol to obtain 1.46 g (74%) of title product **42e** as off-white solid. mp: 181-183 °C; Purity by HPLC: 98.3%.

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

^{1}H NMR ($CDCl_3$) **:** 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)

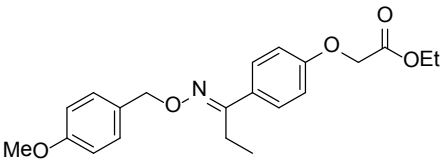
ESI/MS (m/z) **:** 209.0 $(M+H)^+$

4.1.22 General procedure for the synthesis of Compounds 43a-g



To a solution of **42a-e**, **34b** or **34e** (1 mole equivalent) and **4d** (1 mole equivalent) in dry DMF (5 fold), Cs_2CO_3 (1.5 mole equivalent) was added and reaction mixture was stirred at 60 ^oC for 18 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (12 to 15% ethyl acetate in hexane) to yield the compounds **43a-g**.

4.1.22.1 (*E*)-Ethyl 2-(4-(1-(((4-methoxybenzyl)oxy)imino)propyl) phenoxy)acetate (43a)



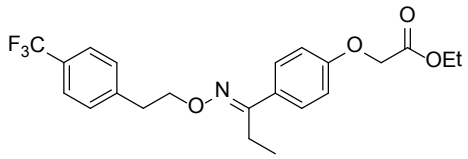
43a (0.69 gm, 58%) was prepared from 4-methoxybenzyl chloride (**42a**) (0.50 gm, 3.19 mmol) and **4d** (0.80 gm, 3.19 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 95.4%.

IR (Neat) : 3018, 2937, 2877, 2839, 1755, 1610, 1514, 1442, 1384, 1301, 1245, 1215, 1180, 1082, 1033, 833, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.09 (t, *J* = 7.5 Hz, 3H), 1.29 (t, *J* =7.2 Hz, 3H), 2.73 (q, *J* =7.4 Hz, 2H), 3.81 (s, 3H), 4.26 (q, *J* = 7.7 Hz, 2H), 4.63 (s, 2H), 5.12 (s, 2H), 6.89 (d, *J* = 8.5 Hz, 4H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H)

ESI/MS (m/z) : 394.0 $(M+Na)^+$

4.1.22.2 (*E*)-Ethyl 2-(4-(1-((4-(trifluoromethyl)phenethoxy)imino) propyl)phenoxy) acetate (43b)



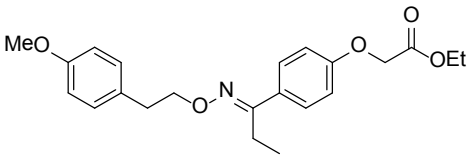
43b (0.65 gm, 82%) was prepared from **42b** (0.50 gm, 1.86 mmol) and **4d** (0.47 gm, 1.86 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 85.06%.

IR (Neat) : 3436, 3020, 2981, 2937, 2877, 1757, 1610, 1512, 1465, 1442, 1415, 1379, 1326, 1217, 1166, 1126, 1068, 1020, 958, 927, 862, 835, 758, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.05 (t, *J* = 7.6 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 2.65 (q, *J* = 7.6 Hz, 2H), 3.09 (t, *J* = 6.6 Hz, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.38 (t, *J* = 6.8 Hz, 2H), 4.63 (s, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.53-7.59 (m, 4H)

ESI/MS (m/z) : 446.1 $(M+Na)^+$

4.1.22.3 (*E*)-Ethyl 2-(4-(1-((4-(methoxy)phenethoxy)imino)propyl) phenoxy)acetate (43c)



43c (0.55 gm, 33%) was prepared from **42c** (1.00 gm, 4.34 mmol) and **4d** (1.09 gm, 4.34 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 94.30%.

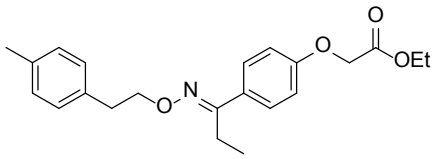
IR (Neat) : 3018, 2981, 2937, 2877, 1755, 1610, 1512, 1382, 1299, 1245, 1215, 1180, 1076, 1031, 960, 927, 835, 769, 669 cm^{-1}

^{1}H NMR : δ 1.08 (t, *J* = 7.6 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 2.70 (q, *J* =

($CDCl_3$) 7.6 Hz, 2H), 2.97 (t, *J* = 6.9 Hz, 2H), 3.79 (s, 3H), 4.24-4.34 (m, 4H), 4.63 (s, 2H), 6.82 - 6.92 (m, 4H), 7.16 (d, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 8.6 Hz, 2H)

ESI/MS (m/z) : 386.0 $(M+H)^+$

4.1.22.4 (*E*)-Ethyl 2-(4-(1-((4-(methyl)phenethoxy)imino)propyl) phenoxy)acetate (43d)



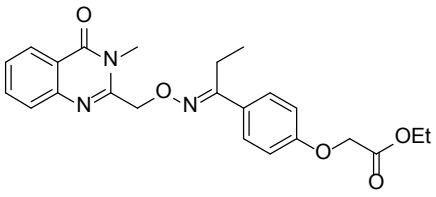
43d (0.58 gm, 68%) was prepared from **42d** (0.50 gm, 2.33 mmol) and **4d** (0.58 gm, 2.33 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 84.2%.

IR (Neat) : 3018, 2981, 2937, 2877, 1757, 1608, 1514, 1465, 1442, 1413, 1382, 1336, 1301, 1215, 1180, 1078, 1028, 960, 925, 835, 761, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.08 (t, *J* = 7.5 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 2.32 (s, 3H), 2.70 (q, *J* = 7.6 Hz, 2H), 2.99 (t, *J* = 7.0 Hz, 2H), 4.24-4.36 (m, 4H), 4.63 (s, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.09-7.16 (m, 4H), 7.58 (d, *J* = 8.8 Hz, 2H)

ESI/MS (m/z) : 391.9 $(M+Na)^+$

4.1.22.5 (*E*)-Ethyl 2-(4-(1-(((3-methyl-4-oxo-3,4-dihydroquinazolin-2-yl) methoxy)imino)propyl)phenoxy)acetate (43e)



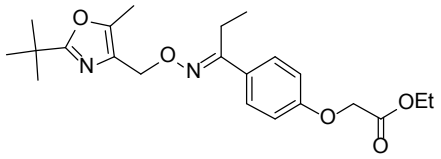
43e (0.83 gm, 41%) was prepared from **42e** (1.00 gm, 4.79 mmol) and **4d** (1.20 gm, 4.79 mmol) following the general procedure described above as a pale yellow solid. m.p. 115-117 ^{o}C; Purity by HPLC: 98.9%.

IR (KBr) : 3423, 2970, 2973, 1760, 1679, 1606, 1514, 1465, 1421, 1373, 1330, 1396, 1247, 1053, 1014, 952, 908, 840, 779,744, 698, 596 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.13 (t, *J* = 7.6 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 2.77 (q, *J* = 7.6 Hz, 2H), 3.75 (s, 3H), 4.27 (q, J = 7.1 Hz, 2H), 4.62 (s, 2H), 5.31 (s, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 7.47-7.52 (m, 1H), 7.57 (d, *J* = 8.7 Hz, 2H), 7.71-7.78 (m, 2H), 8.30 (1H, d, *J* = 7.9 Hz)

ESI/MS (m/z) : 424.1 $(M+H)^{+}$

4.1.22.6 (*E*)-Ethyl 2-(4-(1-(((2-(*tert*-butyl)-5-methyloxazol-4-yl)methoxy) imino)propyl)phenoxy)acetate (43f)



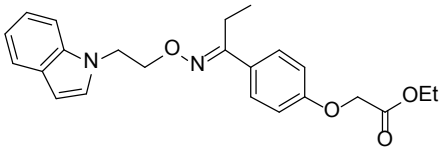
43f (0.57 gm, 44%) was prepared from **34e** (0.60 gm, 3.20 mmol) and **4d** (0.80 gm, 3.20 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 94.36%.

IR (KBr) : 3415, 3018, 2974, 2935, 1759, 1608, 1512, 1463, 1442, 1382, 1215, 1180, 1118, 1082, 1020, 979, 958, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.07 (t, *J* = 7.3 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.36 (s, 9H), 2.35 (s, 3H), 2.73 (q, *J* = 7.6 Hz, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.63 (s, 2H), 5.01 (s, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.58 (d, *J* = 8.8 Hz, 2H)

ESI/MS (m/z) : 403.1 $(M+H)^{+}$

4.1.22.7 (*E*)-Ethyl 2-(4-(1-((2-(*1H*-indol-1-yl)ethoxy)imino)propyl) phenoxy)acetate (43g)



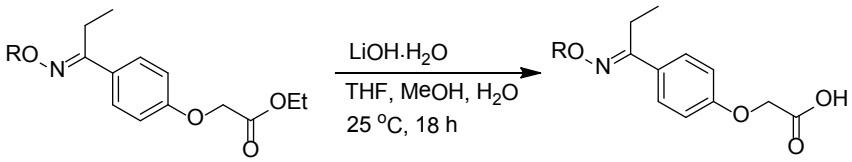
43g (0.77 gm, 47%) was prepared from **34b** (1.00 gm, 4.18 mmol) and **4d** (1.05 gm, 4.18 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 87.2%.

IR (KBr) : 3018, 2981, 2937, 1755, 1679, 1602, 1512, 1463, 1442, 1380, 1315, 1215, 1180, 1082, 1028, 927, 835, 756, 667 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.00 (t, *J* = 7.6 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 2.63 (q, *J* = 7.6 Hz, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.46 (s, 4H), 4.64 (s, 2H), 6.50 (d, *J* = 3.0 Hz, 1H), 6.89 (dd, *J* = 6.9 & 2.0 Hz, 2H), 7.09-7.12 (m, 2H), 7.12-7.19 (m, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.55 (dd, *J* = 6.9 & 2.0 Hz, 2H), 7.61 (d, *J* = 7.9 Hz, 1H)

ESI/MS (m/z) : 417.1 $(M+Na)^+$

4.1.23 General procedure for the synthesis of Compounds 44a-g

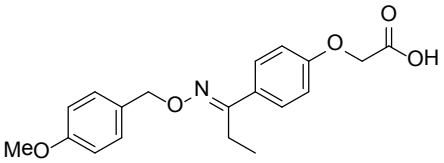


43a-g **44a-g**

To a solution of **43a-g** (1 mole equivalent) in a mixture of tetrahydrofuran (15 fold) and methanol (5 fold) was added another solution of $LiOH.H_2O$ (2 mole equivalent) in water (5 fold) and the reaction mixture was stirred at ambient temperature for about 5 hours. Solvent was evaporated under reduced pressure, water was added to the residue, acidified with 1N HCl to pH 6 and extracted with ethyl acetate. The combined organic extracts were washed with water and brine

solution, dried over sodium sulphate and evaporated under reduced pressure to yield the products **44a-g**.

4.1.23.1 (*E*)-2-(4-(1-(((4-Methoxybenzyl)oxy)imino)propyl) phenoxy) acetic acid (44a)



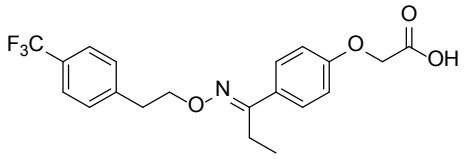
44a (0.44 gm, 95%) was prepared from **43a** (0.50 gm, 1.35 mmol) following the general procedure described above as an off white solid. m.p. 92-94 ^{o}C; Purity by HPLC: 98.5%.

IR (KBr) : 3500, 3384, 2937, 2875, 2844, 1718, 1685, 1647, 1608, 1498, 1458, 1438, 1425, 1369, 1299, 1245, 1203, 1176, 1091, 1031, 1018, 956, 910, 829, 815, 607 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.97 (t, *J* = 7.4 Hz, 3H), 2.65 (q, *J* = 7.4 Hz, 2H), 3.72 (s, 3H), 4.30 (s, 2H), 5.04 (s, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.6 Hz, 2H), 7.3 (d, *J* = 8.6 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H)

ESI/MS (m/z) : 344.2 $(M+H)^{+}$

4.1.23.2 (*E*)-2-(4-(1-((4-(Trifluoromethyl)phenethoxy)imino) propyl) phenoxy)acetic acid (44b)



44b (0.40 gm, 86%) was prepared from **43b** (0.50 gm, 1.22 mmol) following the general procedure described above as an off white solid. m.p. 90-92 ^{o}C; Purity by HPLC: 94.08%.

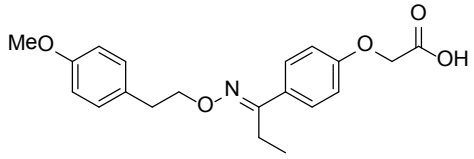
IR (KBr) : 3435, 2943, 2883, 1745, 1708, 1606, 1512, 1469, 1413, 1323,

1305, 1265, 1236, 1172, 1110, 1066, 1018, 970, 835, 740 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 0.91 (t, *J* = 7.4 Hz, 3H), 2.60 (q, *J* = 7.4 Hz, 2H), 3.06 (t, *J* = 6.3 Hz, 2H), 4.32 (t, *J* = 6.4 Hz, 2H), 4.61 (s, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 7.46-7.54 (m, 4H), 7.65 (d, *J* = 8.0 Hz, 2H)

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

4.1.23.3 (*E*)-2-(4-(1-((4-(Methoxy)phenethoxy)imino)propyl) phenoxy) acetic acid (44c)



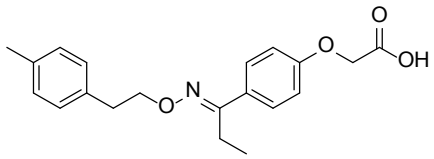
44c (0.42 gm, 92%) was prepared from **43c** (0.50 gm, 1.35 mmol) following the general procedure described above as an off white solid. m.p. 73-75 ^oC; Purity by HPLC: 99.6%.

IR (KBr) : 3554, 3433, 3066, 2966, 2937, 2920, 2841, 1720, 1685, 1654, 1610, 1514, 1467, 1440, 1369, 1334, 1301, 1249, 1178, 1116, 1055, 1035, 960, 935, 889, 837, 813, 756, 696 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.95 (t, *J* = 7.4 Hz, 3H), 2.59 (q, *J* = 7.5 Hz, 2H), 2.87 (t, J = 6.7 Hz, 2H), 3.69 (s, 3H), 4.21 (t, *J* = 6.7 Hz, 2H), 4.38 (s, 2H), 6.84-6.87 (m, 4H), 7.16 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.8 Hz, 2H)

ESI/MS (m/z) : 358.1 $(M+H)^+$

4.1.23.4 (*E*)-2-(4-(1-((4-(Methyl)phenethoxy)imino)propyl) phenoxy) acetic acid (44d).



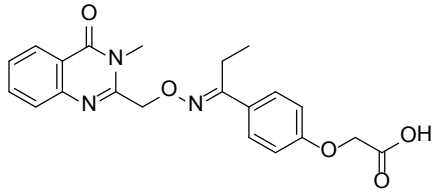
44d (0.42 gm, 91%) was prepared from **43d** (0.50 gm, 1.41 mmol) following the general procedure described above as an off white solid. m.p. 97-99 ^{o}C; Purity by HPLC: 95.2%.

IR (KBr) : 3435, 2981, 2960, 2931, 2580, 1739, 1708, 1608, 1514, 1467, 1433, 1413, 1317, 1305, 1267, 1240, 1184, 1089, 1056, 1035, 1024, 956, 925, 889, 833, 806 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.07 (t, *J* = 7.6 Hz, 3H), 2.32 (s, 3H), 2.70 (q, *J* = 7.6 Hz, 2H), 2.99 (t, *J* = 7.0 Hz, 2H), 4.34 (t, *J* = 7.0 Hz, 2H), 4.68 (s, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 7.06-7.15 (m, 4H), 7.58 (d, *J* = 8.8 Hz, 2H)

ESI/MS (m/z) : 342.0 $(M+H)^{+}$

4.1.23.5 (*E*)-2-(4-(1-(((3-Methyl-4-oxo-3,4-dihydroquinazolin-2-yl) methoxy)imino)propyl)phenoxy)acetic acid (44e)



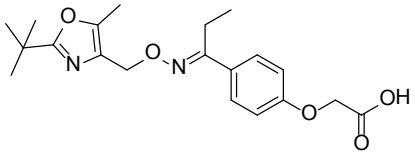
44e (0.23 gm, 50%) was prepared from **43e** (0.50 gm, 1.18 mmol) following the general procedure described above as a white solid. m.p. 134-135 ^{o}C; Purity by HPLC: 96.4%.

IR (KBr) : 3414, 2978, 2897, 1708, 1681, 1608, 1570, 1512, 1465, 1427, 1379, 1329, 1238, 1184, 1074, 1014, 906, 833, 779 cm^{-1}

^{1}H NMR (DMSO-*d*$_6$) : δ 1.06 (t, *J* = 7.4 Hz, 3H), 2.77 (q, *J* = 7.2 Hz, 2H), 3.62 (s, 3H), 4.62 (s, 2H), 5.32 (s, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.52-7.55 (m, 3H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.79-7.83 (m, 1H), 8.12 (dd, *J* = 7.8 & 1.0 Hz, 1H)

ESI/MS (m/z) : 395.9 $(M+H)^+$

4.1.23.6 (*E*)-2-(4-(1-(((2-(*tert*-Butyl)-5-methyloxazol-4-yl)methoxy) imino)propyl)phenoxy)acetic acid (44f)



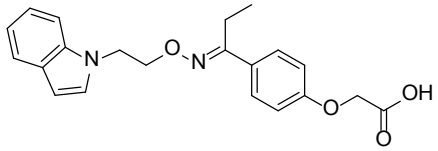
44f (0.33 gm, 71%) was prepared from **43f** (0.50 gm, 1.24 mmol) following the general procedure described above as a white solid. m.p. 120-122 ^oC; Purity by HPLC: 97.4%.

IR (KBr) : 3413, 2972, 2939, 2906, 1751, 1606, 1560, 1535, 1512, 1460, 1438, 1332, 1299, 1215, 1182, 1134, 1083, 1072, 1008, 974, 873, 831, 785 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 0.97 (t, *J* = 7.4 Hz, 3H), 1.27 (s, 9H), 2.30 (s, 3H), 2.65 (q, *J* = 7.4 Hz, 2H), 4.68 (s, 2H), 4.91 (s, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 7.58 (d, *J* = 8.8 Hz, 2H)

ESI/MS (m/z) : 375.0 $(M+H)^+$

4.1.23.7 (*E*)-2-(4-(1-((2-(*1H*-indol-1-yl)ethoxy)imino)propyl) phenoxy) acetic acid (44g)



44g (0.32 gm, 70%) was prepared from **43g** (0.50 gm, 1.27 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 87.2%.

IR (KBr) : 3018, 2978, 2879, 1735, 1610, 1512, 1464, 1215, 1180, 1076, 985, 927, 758 cm^{-1}

^{1}H NMR : δ 1.00 (t, *J* = 7.6 Hz, 3H), 2.62 (q, *J* = 7.6 Hz, 2H), 4.46 (s, 4H),

($CDCl_3$) 4.70 (s, 2H), 6.49 (d, *J* = 3.0 Hz, 1H), 6.90-6.93 (m, 2H), 7.09-7.12 (m, 2H), 7.19-7.21 (m, 1H), 7.36-7.39 (m, 1H), 7.55-7.59 (m, 2H), 7.61 (d, *J* = 7.9 Hz, 1H)

ESI/MS (m/z) : 367.1 $(M+H)^+$

4.1.24 Ethyl 2-(4-aceltylphenyl)acetate (46)

45 46

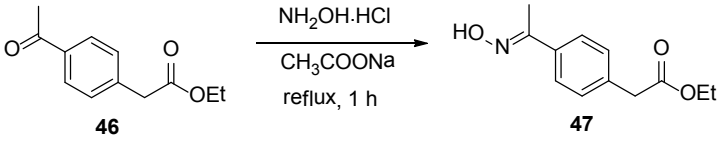
Anhydrous $AlCl_3$ (266 gm, 1.99 mol) was added in small portions to a solution of ethyl 2-phenylacetate (**45**) (165 gm, 0.99 mol) in CS_2 (1.5 lit) followed by drop wise addition of acetyl chloride (113.2 ml, 1.59 mol) at 0 ^oC. The reaction temperature was slowly raised to 30 ^oC and stirred at the same temperature for 22 hours. The reaction mixture was poured in ice cold 6N HCl (2 lit) and extracted with ethyl acetate (500 ml x 3). The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure to yield crude product. The crude product was purified by column chromatography (12% ethyl acetate in hexane) to give title compound **46** as an off white solid. (13.8 gm, 7%). m.p. 51-53 ^oC; Purity by HPLC: 98.9%.

IR (KBr) : 3442, 3342, 3091, 2871, 1733, 1608, 1473, 1269 cm^{-1}

^1H NMR ($CDCl_3$) : δ 1.25 (t, *J*=7.2 Hz, 3H), 2.59 (s, 3H), 3.67 (s, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.92 (d, *J* = 8.2 Hz, 2H)

ESI/MS (m/z) : 206.8 $(M+H)^+$

4.1.25 (*E*)-Ethyl 2-(4-(1-(hydroxyimino)ethyl)phenyl)acetate (47)



46 47

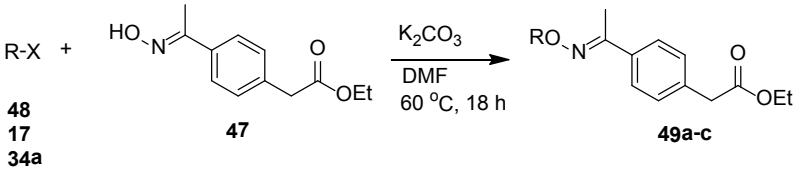
To a solution of **46** (10.00 gm, 0.049 mol) in ethanol (50 ml), a solution of hydroxylammonium chloride (6.74 gm, 0.097 mol) and sodium acetate (8.00 gm, 0.097 mol) in water (50 ml) was added and the reaction mixture was heated to reflux for a period of about 1 hours. Rection mixture was cooled to room temperature and solvent was evapourated under reduced pressure. The residue was diluted with water, solid separated was filtered and dried over P_2O_5 under vaccum to yield compound **47** (10.19 gm, 95%). m.p. 69-70 ^oC; Purity by HPLC: 98.2%.

IR (KBr) **:** 3247, 3134, 2906, 1733, 1608, 1512, 1348 cm^{-1}

^{1}H NMR ($CDCl_3$) **:** δ 1.25 (t, *J* = 7.2 Hz, 3H), 2.28 (s, 3H), 3.62 (s, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H)

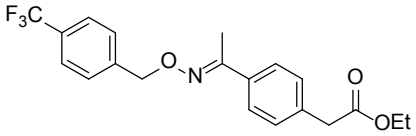
ESI/MS (m/z) **:** 221.8 $(M+H)^+$

4.1.26 General procedure for the synthesis of Compounds 49a-c



To a solution of **48**, **17** or **34a** (1 mole equivalent) and **47** (1 mole equivalent) in dry DMF (5 fold), K_2CO_3 (2 mole equivalent) was added and reaction mixture was stirred at 60 ^oC for 18 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (82 to 10% ethyl acetate in hexane) to yield title compound **49a-c**.

4.1.26.1 (*E*)-ethyl 2-(4-(1-(((4-trifluoromethylbenzyl)oxy)imino)ethyl) phenyl)acetate (49a)



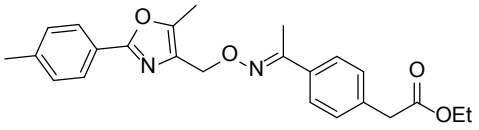
49a (0.28 gm, 38%) was prepared from 4-trifluoromethylbenzyl methanesulfonate (**48**) (0.50 gm, 1.97 mmol) and **47** (0.43 gm, 1.97 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.6%.

IR (KBr) : 3444, 2993, 1932, 1732, 1620, 1566, 1371, 1139, 923, 758, 563 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.24 (t, *J* = 7.2 Hz, 3H), 2.27 (s, 3H), 3.61 (s, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 5.27 (s, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.57-7.63 (m, 4H)

ESI/MS (m/z) : 379.9 $(M+H)^+$

4.1.26.2 (*E*)-Ethyl 2-(4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy) imino)ethyl)phenyl)acetate (49b)



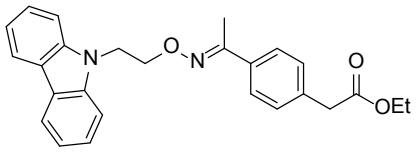
49b (0.23 gm, 16%) was prepared from **17** (0.75 gm, 3.38 mmol) and **47** (0.75 gm, 3.38 mmol) following the general procedure described above as a white solid. Purity by HPLC: 95.4%.

IR (KBr) : 3032, 2943, 2851, 1736, 1618, 1501, 1221 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.24 (t, *J* = 7.0 Hz, 3H), 2.23 (s, 3H), 2.38 (s, 3H), 2.47 (s, 3H), 3.61 (s, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 5.13 (s, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 2H)

ESI/MS (m/z) : 407.1 $(M+H)^+$

4.1.26.3 (*E*)-Ethyl 2-(4-(1-((2-(*9H*-carbazol-9-yl)ethoxy)imino)ethyl) phenyl)acetate (49c)



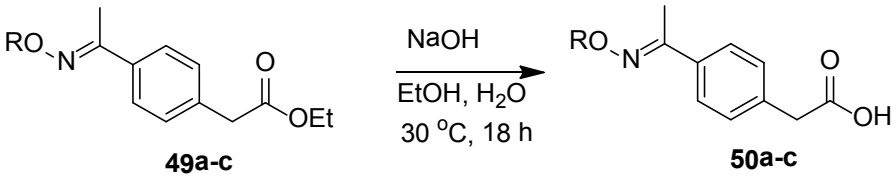
49c (0.59 gm, 50%) was prepared from **34a** (0.75 gm, 2.89 mmol) and **47** (0.57 gm, 2.89 mmol) following the general procedure described above as a white solid. Purity by HPLC: 99.1%.

IR (KBr) : 3018, 2936, 2876, 1730, 1514, 1404, 1215 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.26 (t, *J* = 7.2 Hz, 3H), 1.94 (s, 3H), 3.63 (s, 2H), 4.15 (q, *J* = 7.0 Hz, 2H), 4.57 (t, *J* = 5.4 Hz, 2H), 4.65 (t, *J* = 5.2 Hz, 2H), 7.20-7.24 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.40-7.45 (m, 4H), 7.54 (d, *J* = 8.4 Hz, 2H), 8.10 (d, *J* = 7.6 Hz, 2H)

ESI/MS (m/z) : 415.0 $(M+H)^+$

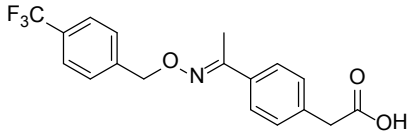
4.1.27 General procedure for the synthesis of Compounds 50a-c



49a-c **50a-c**

To a solution of **23a-b** (1 mole equivalent) in ethanol (15 fold) was added another solution of NaOH (2 mole equivalent) in water (5 fold) and the reaction mixture was stirred at ambient temperature for about 18 hours. Solvent was evaporated under reduced pressure, water was added to the residue and acidified with 1N HCl to pH 6. Solid separated was filtered, washed with water and dried over P_2O_5 under vacuum to yield the product **24a-b**.

4.1.27.1 (*E*)- 2-(4-(1-(((4-trifluoromethylbenzyl)oxy)imino)ethyl) phenyl)acetic acid (50a)



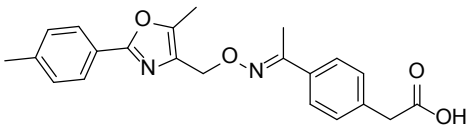
50a (0.19 gm, 73%) was prepared from **49a** (0.28 gm, 0.74 mmol) following the general procedure described above as a white solid. m.p. 94-96 ^{o}C; Purity by HPLC: 97.2%.

IR (KBr) : 3037, 2862, 2655, 1689, 1622, 1514, 1413, 1367, 1126, 1058, 935, 823 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.26 (s, 3H), 3.62 (s, 2H), 5.27 (s, 2H), 7.24 (d, *J* = 7.6 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.57-7.61 (m, 4H)

ESI/MS (m/z) : 351.9 $(M+H)^{+}$

4.1.27.2 (*E*)-2-(4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl)methoxy) imino) ethyl)phenyl)acetic acid (50b)



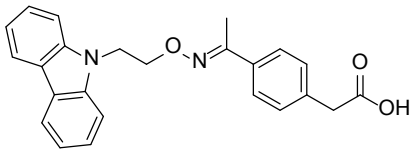
50b (0.30 gm, 80%) was prepared from **49b** (0.40 gm, 0.98 mmol) following the general procedure described above as an off white solid. m.p. 179-180 ^{o}C; Purity by HPLC: 99.3%.

IR (KBr) : 2887, 2856, 2521, 1724, 1651, 1558, 1121 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.20 (s, 3H), 2.38 (s, 3H), 2.46 (s, 3H), 3.64 (s, 2H), 5.12 (s, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H)

ESI/MS (m/z) : 379.0 $(M+H)^{+}$

4.1.27.3 (*E*)- 2-(4-(1-((2-(*9H*-carbazol-9-yl)ethoxy)imino)ethyl)phenyl) acetic acid (50c)



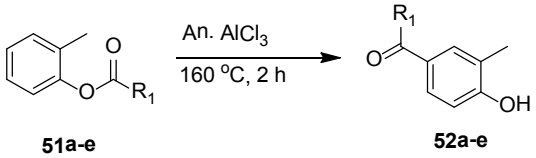
50c (0.28 gm, 51%) was prepared from **49c** (0.59 gm, 1.43 mmol) following the general procedure described above as a white solid. m.p. 173-174 ^{o}C; Purity by HPLC: 99.3%.

IR (KBr) : 3022, 2870, 2646, 1705, 1560, 1485, 1244 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.96 (s, 3H), 3.68 (s, 2H), 4.57 (t, *J* = 5.0 Hz, 2H), 4.65 (t, *J* = 5.0 Hz, 2H), 7.20-7.24 (m, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.41-7.44 (m, 4H), 7.56 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 387.0 $(M+H)^{+}$

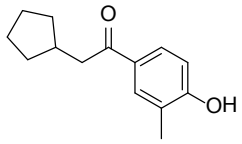
4.1.28 General procedure for the synthesis of Compounds 52a-e



51a-e **52a-e**

Anhydrous $AlCl_3$ (1 mole equivalent) was added in small portions to phenol (**51a-e**) (1 mole equivalent) at 25 ^{o}C. The reaction temperature was slowly raised to 160 ^{o}C and stirred at the same temperature for 2 hours. The reaction mixture was poured in ice cold 6N HCl (20 fold) and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure to yield crude product. The crude product was purified by column chromatography (10-15% ethyl acetate in hexane) to give the compounds **52a-e**.

4.1.28.1 2-Cyclopentyl-1-(4-hydroxy-3-methylphenyl)ethanone (52a)



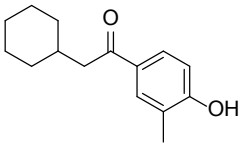
52a (14.6 gm, 73%) was prepared from **51a** (20.0 gm, 0.092 mol) following the general procedure described above as a white solid. mp: 114-116 ^{o}C; Purity by HPLC: 96.6%.

IR (KBr) : 3176, 1649, 1591, 1512, 1371, 1336, 1288, 1174, 1120, 1028, 991, 821, 725 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.14-1.20 (m, 2H), 1.55-1.61 (m, 4H), 1.64-1.86 (m, 2H), 2.29 (s, 3H), 2.34-2.39 (m, 1H), 2.90 (d, *J* = 7.1 Hz, 2H), 6.82 (d, *J* = 8.3 Hz, 1H), 7.72-7.78 (m, 2H)

ESI/MS (m/z) : 218.9 $(M+H)^{+}$

4.1.28.2 2-Cyclohexyl-1-(4-hydroxy-3-methylphenyl)ethanone (52b)



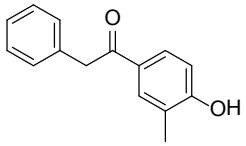
52b (8.0 gm, 16%) was prepared from **51b** (50.0 gm, 0.215 mol) following the general procedure described above as a white solid. mp: 122-123 ^{o}C; Purity by HPLC: 96.3%.

IR (KBr) : 3159, 2850, 2611, 1639, 1585, 1450, 1350, 1136, 1031, 827 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 0.94-1.06 (m, 2H), 1.12-1.30 (m, 4H), 1.61-1.76 (m, 4H), 1.91-1.95 (m, 1H), 2.29 (s, 3H), 2.74 (d, *J* = 6.8 Hz, 2H), 6.79 (d, *J* = 8.3 Hz, 1H), 7.72-7.79 (m, 2H)

ESI/MS (m/z) : 254.9 $(M+Na)^+$

4.1.28.3 1-(4-Hydroxy-3-methylphenyl)-2-phenylethanone (52c)



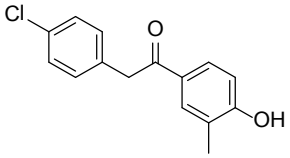
52c (9.0 gm, 30%) was prepared from **51c** (30.0 gm, 0.133 mol) following the general procedure described above as a thick liquid.

IR (Neat) : 3284, 1656, 1604, 1514, 1454, 1400, 1332, 1255, 1178, 1112, 1018, 837 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.26 (s, 3H), 4.22 (s, 2H), 6.75 (d, *J* = 8.4 Hz, 1H), 7.24-7.33 (m, 5H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.83 (s, 1H)

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

4.1.28.4 2-(4-Chlorophenyl)-1-(4-hydroxy-3-methylphenyl)ethanone (52d)



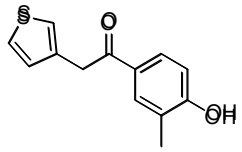
52d (8.6 gm, 43%) was prepared from **51d** (20.0 gm, 0.077 mol) following the general procedure described above as a yellow solid. mp: 129-132 ^oC; Purity by HPLC: 84.4%.

IR (KBr) : 3359, 2908, 1747, 1666, 1589, 1494, 1409, 1280, 1126, 817 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.28 (s, 3H), 4.19 (s, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 7.17-7.20 (m, 2H), 7.27-7.33 (m, 2H), 7.74 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.82 (d, *J* = 1.6 Hz, 1H)

ESI/MS (m/z) : 282.9 $(M+Na)^+$

4.1.28.5 1-(4-Hydroxy-3-methylphenyl)-2-(thiophen-3-yl)ethanone (52e)



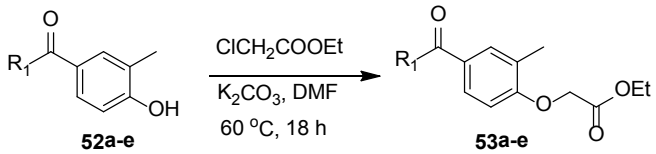
52e (6.4 gm, 32%) was prepared from **51e** (20.0 gm, 0.086 mol) following the general procedure described above as a white solid. mp: 183-184 ^oC; Purity by HPLC: 96.2%.

IR (KBr) : 3240, 1651, 1587, 1456, 1400, 1334, 1282, 1257, 1226, 1178, 1112, 1018, 835, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.28 (s, 3H), 4.24 (s, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 7.00-7.02 (m, 1H), 7.10-7.11 (m, 1H), 7.26-7.29 (m, 1H), 7.76 (dd, *J* = 8.4 & 2.4 Hz, 1H), 7.83 (d, *J* = 1.6 Hz, 1H)

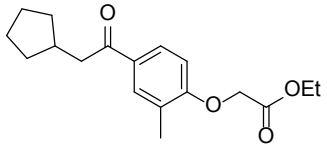
ESI/MS (m/z) : 232.8 $(M+H)^+$

4.1.29 General procedure for the synthesis of Compounds (53a-e)



To an ice cold solution of **52a-e** (1 mole equivalent) in DMF (5 fold), K_2CO_3 (2 mole equivalent) and ethyl chloroacetate (1.12 mole equivalent) was added and reaction mixture was stirred at 60 ^oC for 18 hours. The reaction mixture was poured in ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure to yield title compound **53a-e**.

4.1.29.1 Ethyl 2-(4-(2-cyclopentylacetyl)-2-methylphenoxy)acetate (53a)



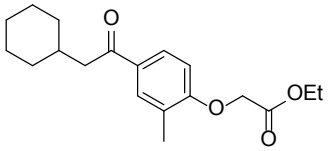
53a (13.8 gm, 99%) was prepared from **52a** (10.0 gm, 0.046 mol) following the general procedure described above as an off-white solid. mp: 82-86 ^{o}C;

IR (KBr) : 1759, 1666, 1600, 1498, 1448, 1379, 1284, 1217, 1134, 1039, 808, 750 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.16-1.20 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.55-1.64 (m, 4H), 1.84-1.88 (m, 2H), 2.32 (s, 3H), 2.33-2.36 (m, 1H), 2.91 (d, *J* = 7.1 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.72 (s, 2H), 6.69 (d, *J* = 8.4 Hz, 1H), 7.77-7.79 (m, 2H)

ESI/MS (m/z) : 304.9 $(M+H)^{+}$

4.1.29.2 Ethyl 2-(4-(2-cyclohexylacetyl)-2-methylphenoxy)acetate (53b)



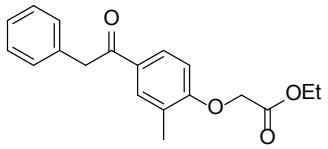
53b (10.8 gm, 99%) was prepared from **52b** (8.0 gm, 0.034 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 95.8%.

IR (Neat) : 3141, 3020, 2029, 1759, 1672, 1502, 1384, 1124, 1076, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.97-1.05 (m, 2H), 1.16-1.33 (m, 6H), 1.67-1.76 (m, 5H), 1.91-2.02 (m, 1H), 2.32 (s, 3H), 2.74 (d, *J* = 6.8 Hz, 2H), 4.25 (q, *J* = 4.7 Hz, 2H), 4.70 (s, 2H), 6.68 (d, *J* = 8.2 Hz, 1H), 7.76-7.79 (m, 2H)

ESI/MS (m/z) : 341.0 $(M+Na)^{+}$

4.1.29.3 Ethyl 2-(2-methyl-4-(2-phenylacetyl)phenoxy)acetate (53c)



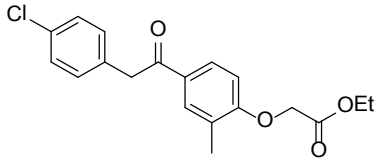
53c (11.2 gm, 90%) was prepared from **52c** (9.0 gm, 0.040 mol) following the general procedure described above as a thick liquid.

IR (Neat) : 1757, 1737, 1674, 1600, 1500, 1440, 1411, 1379, 1274, 1234, 1205, 136, 1074, 1031, 808, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.27 (t, *J* = 7.1 Hz, 3H), 2.31 (s, 3H), 4.23-4.30 (m, 4H), 4.64 (s, 2H), 6.67 (d, *J* = 8.2 Hz, 1H), 7.24-7.34 (m, 5H), 7.82-7.85 (m, 2H)

ESI/MS (m/z) : 312.9 $(M+H)^+$

4.1.29.4 Ethyl 2-(4-(2-(4-chlorophenyl)acetyl)-2-methylphenoxy) acetate (53d)



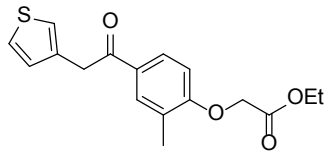
53d (5.52 gm, 52%) was prepared from **52d** (8.0 gm, 0.031 mol) following the general procedure described above as a yellow solid. mp: 78-80 ^oC; Purity by HPLC: 92.2%.

IR (KBr) : 3485, 2987, 2131, 1753, 1708, 1676, 1581, 1494, 1222, 831 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.25 (t, *J* = 7.1 Hz, 3H), 2.32 (s, 3H), 4.19 (s, 2H), 4.24 (q, *J* = 5.8 Hz, 2H), 4.70 (s, 2H), 6.69 (d, *J* = 8 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.27-7.29 (m, 2H), 7.80-7.83 (m, 2H)

ESI/MS (m/z) : 346.9 $(M+H)^+$

4.1.29.5 Ethyl 2-(2-methyl-4-(2-(thiophen-3-yl)acetyl)phenoxy)acetate (53e)



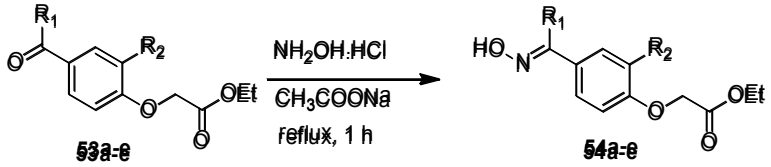
53e (5.26 gm, 64%) was prepared from **52e** (6.0 gm, 0.026 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 87.4%.

IR (KBr) : 3020, 2928, 1959, 1755, 1674, 1600, 1500, 1404, 1384, 1217, 1128, 1097, 1041, 756 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.28 (t, *J* = 7.2 Hz, 3H), 2.32 (s, 3H), 4.23-4.29 (m, 4H), 4.70 (s, 2H), 6.69 (d, *J* = 8.4 Hz, 1H), 7.00 (dd, *J* = 4.8 & 1.2 Hz, 1H), 7.10-7.11 (m, 1H), 7.27-7.29 (m, 1H), 7.82-7.84 (m, 2H)

ESI/MS (m/z) : 318.8 $(M+H)^+$

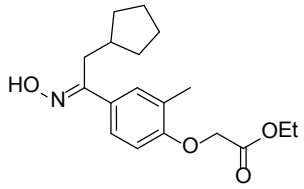
4.1.30 General procedure for the synthesis of Compounds (54a-e)



53a-e 54a-e

To a solution of **53a-e** (1 mole equivalent) in ethanol (6 fold), a solution of hydroxylammonium chloride (2 mole equivalent) and sodium acetate (2 mole equivalent) in water (2 fold) was added and the reaction mixture was heated to reflux for a period of about 1 hours. Rection mixture was cooled to room temperature and solvent was evapourated under reduced pressure. The residue was diluted with water, solid separated was filtered and dried over P_2O_5 under vaccum to yield the compounds **54a-e**.

4.1.30.1 (*E*)-Ethyl 2-(4-(2-cyclopentyl-1-(hydroxyimino)ethyl)-2-methyl phenoxy)acetate (54a)



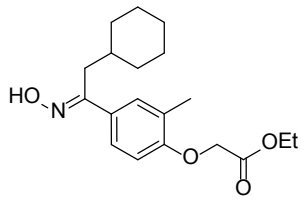
54a (8.69 gm, 69%) was prepared from **53e** (12.0 gm, 0.039 mol) following the general procedure described above as a white solid. mp: 112-114 ^{o}C; Purity by HPLC: 96.7%.

IR (KBr) : 3215, 1753, 1604, 1504, 1456, 1419, 1307, 1211, 1143, 1091, 1018, 962 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.24-1.27 (m, 2H), 1.34-1.37 (t, *J* = 7.1 Hz, 3H), 1.47-1.48 (m, 2H), 1.59-1.68 (m, 4H), 2.04-2.10 (m, 1H), 2.31 (s, 3H), 2.80 (dd, *J* = 7.4 & 2.2 Hz, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 4.64 (s, 2H), 6.66 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.40 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.55 (s, 1H)

ESI/MS (m/z) : 319.9 $(M+H)^{+}$

4.1.30.2 (*E*)-Ethyl 2-(4-(2-cyclohexyl-1-(hydroxyimino)ethyl)-2-methyl phenoxy)acetate (54b)



54b (8.06 gm, 77%) was prepared from **53b** (10.0 gm, 0.031 mol) following the general procedure described above as a thick liquid. Purity by HPLC: 87.3%.

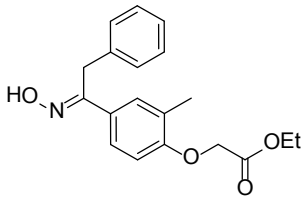
IR (Neat) : 3238, 2925 1957, 1757, 1604, 1504, 1215, 1145, 758 cm^{-1}

^{1}H NMR : δ 1.00-1.14 (m, 6H), 1.30 (t, *J* = 6.6 Hz, 3H), 1.61-1.68 (m, 5H),

($CDCl_3$) 2.31 (s, 3H), 2.68 (d, *J* = 7.0 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.66 (s, 2H), 6.66 (d, *J* = 8.5 Hz, 1H), 7.32 (dd, *J* = 8.5 & 2.5 Hz, 1H), 7.41 (s, 1H)

ESI/MS (m/z) : 334.0 $(M+H)^+$

4.1.30.3 (*E*)-Ethyl 2-(4-(1-(hydroxyimino)-2-phenylethyl)-2-methyl phenoxy)acetate (54c)



54c (10.38 gm, 90%) was prepared from **53c** (11.0 gm, 0.035 mol) following the general procedure described above as a white solid. m.p. 70-73 ^oC; Purity by HPLC: 93.6%.

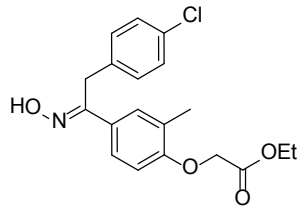
IR (KBr) : 3190, 1728, 1604, 1504, 1444, 1307, 1392, 1240, 1143, 1031, 808 cm^{-1}

^1H NMR ($CDCl_3$) : δ 1.29 (t, *J* = 7.1 Hz, 3H), 2.26 (s, 3H), 4.17 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.62 (s, 2H), 6.61 (d, *J* = 8.8 Hz, 2H), 7.16-7.20 (m, 2H), 7.35 (d, *J* = 8.5 Hz, 2H), 7.47 (s, 2H)

^{13}C NMR (DMSO-d_6) : δ 14.0, 16.2, 30.4, 60.6, 64.8, 111.1, 124.9, 125.9, 128.4, 128.4, 128.6, 130.3, 130.6, 136.6, 154.1, 156.4, 168.7

ESI/MS (m/z) : 328.0 $(M+H)^+$

4.1.30.4 (*E*)-Ethyl 2-(4-(2-(4-chlorophenyl)-1-(hydroxyimino)ethyl)-2-methylphenoxy) acetate (54d)



54d (4.12 gm, 79%) was prepared from **53d** (5.0 gm, 0.014 mol) following the general procedure described above as a white solid. m.p. 100-102 ^{o}C; Purity by HPLC: 86.2%.

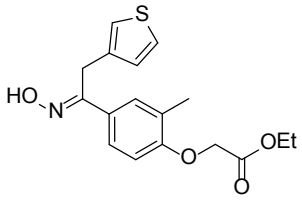
IR (KBr) : 3436, 3172, 2985, 1730, 1685, 1602, 1504, 1242, 1166, 1089, 975, 804 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.24 (t, *J* = 6.6 Hz, 3H), 2.27 (s, 3H), 4.11 (s, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.62 (s, 2H), 6.62 (d, *J* = 4.8 Hz, 1H), 7.16-7.19 (m, 2H), 7.21-7.23 (m, 2H), 7.32 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.46 (d, *J* = 1.6 Hz, 1H)

^{13}C NMR (DMSO-d_6) : δ 14.0, 16.1, 29.8, 60.6, 64.8, 111.2, 124.9, 126.0, 128.3, 128.3, 128.6, 130.3, 130.6, 136.6, 154.1, 156.4, 168.7

ESI/MS (m/z) : 361.9 $(M+H)^{+}$

4.1.30.5 (*E*)-Ethyl 2-(4-(1-(hydroxyimino)-2-(thiophen-3-yl)ethyl)-2-methylphenoxy)acetate (54e)



54e (3.14 gm, 50%) was prepared from **53e** (6.0 gm, 0.019 mol) following the general procedure described above as a white solid. m.p. 91-92 ^{o}C; Purity by HPLC: 98.3%.

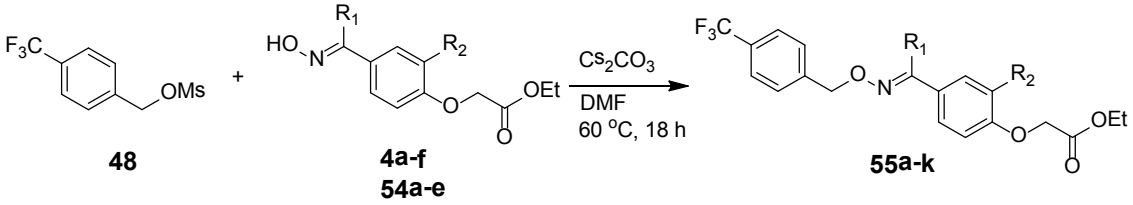
IR (Neat) : 1755, 1604, 1504, 1402, 1309, 1215, 1139, 1085, 1031, 964, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.28 (t, *J* = 7.1 Hz, 3H), 2.27 (s, 3H), 4.12 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.63 (s, 2H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.98-7.01 (m, 2H), 7.21-7.24 (m, 1H), 7.37-7.40 (m, 1H), 7.49 (s, 1H)

^{13}C NMR (CDCl$_3$) : δ 14.3, 16.5, 27.3, 61.5, 65.7, 111.0, 121.8, 125.3, 125.6, 127.6, 128.5, 128.7, 129.2, 136.5, 157, 157.3, 169.0

ESI/MS (m/z) : 334.0 $(M+H)^+$

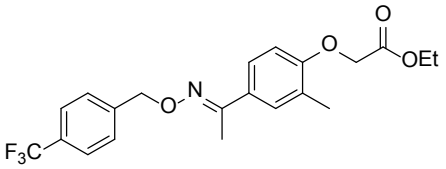
4.1.31 General procedure for the synthesis of Compounds (55a-K)



48 **4a-f** **54a-e** **55a-k**

To a solution of **48** (1 mole equivalent) and **4a-f** or **54a-e** (1 mole equivalent) in dry DMF (5 fold), Cs_2CO_3 (1.5 mole equivalent) was added and reaction mixture was stirred at 40 ^{O}C for 18 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (8 to 10% ethyl acetate in hexane) to yield the compounds **55a-k**.

4.1.31.1 (*E*)-Ethyl 2-(2-methyl-4-(1-(((4-trifluoromethylbenzyl)oxy) imino)ethyl)phenoxy)acetate (55a)



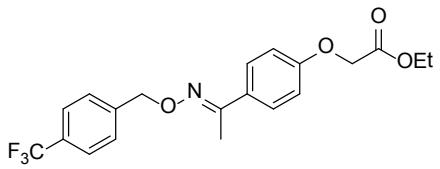
55a (0.40 gm, 25%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (1.0 gm, 3.94 mmol) and **4a** (0.98 gm, 3.94 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.7%.

IR (Neat) : 3141, 2931, 2875, 1757, 1620, 1404, 1325, 1167, 1067, 937, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.27 (t, *J* = 7.1 Hz, 3H), 2.24 (s, 3H), 2.30 (s, 3H), 4.22 (q, *J* = 7.1 Hz, 2H), 4.65 (s, 2H), 5.26 (s, 2H), 6.65 (d, *J* = 8.5 Hz, 1H), 7.36 (d, *J* = 1.9 Hz, 1H), 7.46-7.51 (m, 3H), 7.60 (d, *J* = 8.1 Hz, 2H)

ESI/MS (m/z) : 410.0 $(M+H)^+$

4.1.31.2 (*E*)-Ethyl 2-(4-(1-(((4-trifluoromethylbenzyl)oxy)imino)ethyl) phenoxy)acetate (55b)



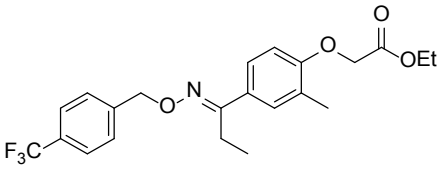
55b (0.45 gm, 48%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.6 gm, 2.36 mmol) and **4b** (0.56 gm, 2.36 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 94.6%.

IR (Neat) : 3020, 1757, 1735, 1610, 1514, 1327, 1168, 1128, 1066, 1018, 927, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.27 (t, *J* = 7.2 Hz, 3H), 2.25 (s, 3H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.63 (s, 2H), 5.26 (s, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.57-7.62 (m, 4H)

ESI/MS (m/z) : 396.2 $(M+H)^+$

4.1.31.3 (*E*)-Ethyl 2-(2-methyl-4-(1-(((4-trifluoromethylbenzyl)oxy) imino)propyl)phenoxy)acetate (55c)



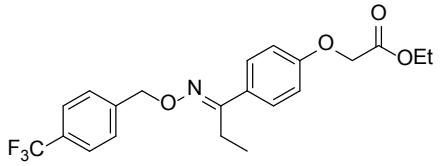
55c (0.45 gm, 49%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.6 gm, 2.36 mmol) and **4c** (0.63 gm, 2.36 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.9%.

IR (Neat) : 3416, 3020, 2983, 1757, 1620, 1504, 1327, 1166, 1128, 1066, 1018, 759 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.11 (t, *J* = 7.6 Hz, 3H), 1.28 (t, *J* = 7.0 Hz, 3H), 2.30 (s, 3H), 2.73 (q, *J* = 7.6 Hz, 2H), 4.23 (q, *J* = 7.0 Hz, 2H), 4.64 (s, 2H), 5.25 (s, 2H), 6.66 (d, *J* = 8.4 Hz, 1H), 7.36 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.44 (d, *J* = 1.2 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H)

ESI/MS (m/z) : 424.1 $(M+H)^+$

4.1.31.4 (*E*)-Ethyl 2-(4-(1-(((4-trifluoromethylbenzyl)oxy)imino)propyl) phenoxy)acetate (55d)



55d (0.19 gm, 20%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.6 gm, 2.36 mmol) and **4d** (0.59 gm, 2.36 mmol) following the general procedure described above as an off white solid. Yield: 20%; m.p. 112-114 ^oC; Purity by HPLC: 97.8%.

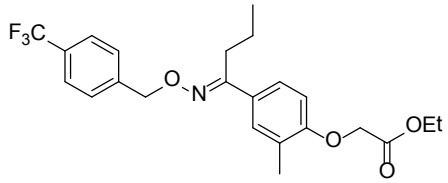
IR (KBr) : 2981, 2939, 2877, 1759, 1737, 1608, 1514, 1465, 1444, 1415, 1379, 1326, 1201, 1180, 1164, 1124, 1066, 1016, 958, 910, 873, 833, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.14 (t, *J* = 7.6 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 2.78 (q, *J* = 7.6 Hz, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.63 (s, 2H), 5.25 (s, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.61-7.65 (m,

4H)

ESI/MS (m/z) : 410.0 $(M+H)^+$

4.1.31.5 (*E*)-Ethyl 2-(2-methyl-4-(1-(((4-trifluoromethylbenzyl)oxy) imino)butyl)phenoxy)acetate (55e)



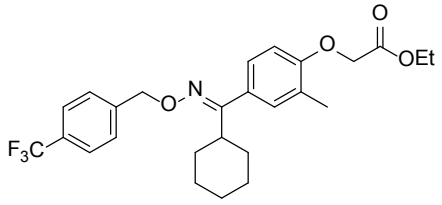
55e (0.93 gm, 90%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.6 gm, 2.36 mmol) and **4e** (0.66 gm, 2.36 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.8%.

IR (Neat) : 3126, 2873, 1759, 1620, 1504, 1203 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.95 (t, *J* = 7.5 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.50-1.60 (m, 2H), 2.29 (s, 3H), 2.73 (t, *J* = 7.5 Hz, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.64 (s, 2H), 5.24 (s, 2H), 6.64 (d, *J* = 8.5 Hz, 1H), 7.36 (dd, *J* = 8.5 & 2.1 Hz, 1H), 7.43-7.50 (m, 3H), 7.61 (d, *J* = 8.16 Hz, 2H)

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

4.1.31.6 (*E*)-Ethyl 2-(4-(cyclohexyl(((4-trifluoromethylbenzyl)oxy)imino) methyl)-2-methylphenoxy)acetate (55f)



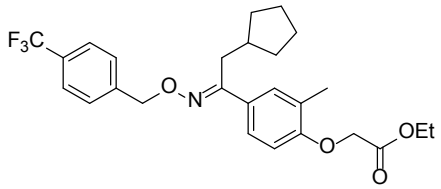
55f (0.51 gm, 45%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.6 gm, 2.36 mmol) and **4f** (0.75 gm, 2.36 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.5%.

IR (Neat) : 3134, 2931, 1759, 1620, 1505, 1402, 1326, 1164, 1066, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.08-1.32 (m, 9H), 1.75-1.76 (m, 4H), 2.29 (s, 3H), 2.40-2.41 (m, 1H), 4.27 (q, *J* = 7.12 Hz, 2H), 4.64 (s, 2H), 5.08 (s, 2H), 6.68 (d, *J* = 8.92 Hz, 1H), 7.01-7.03 (m, 2H), 7.36 (d, *J* = 8.03 Hz, 2H), 7.56 (d, *J* = 8.09 Hz, 2H)

ESI/MS (m/z) : 578.1 $(M+H)^+$

4.1.31.7 (*E*)-Ethyl 2-(4-(2-cyclopentyl-1-(((4-trifluoromethyl benzyl)oxy) imino)ethyl)-2-methylphenoxy)acetate (55g)



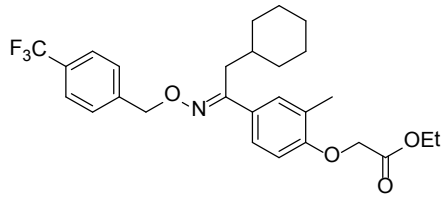
55g (0.58 gm, 78%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.4 gm, 1.57 mmol) and **54a** (0.50 gm, 1.57 mmol) following the general procedure described above as a thick liquid.

IR (Neat) : 1760, 1504, 1402, 1326, 1128, 1066, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.16-1.22 (m, 2H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.43-1.47 (m, 2H), 1.58-1.65 (m, 4H), 2.02-2.06 (m, 1H), 2.29 (s, 3H), 2.81 (d, *J* = 7.6 Hz, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 4.63 (s, 2H), 5.23 (s, 2H), 6.64 (d, *J* = 8.8 Hz, 1H), 7.33 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H)

ESI/MS (m/z) : 478.1 $(M+H)^+$

4.1.31.8 (*E*)-Ethyl 2-(4-(2-cyclohexyl-1-(((4-trifluoromethylbenzyl)oxy) imino)ethyl)-2-methylphenoxy)acetate (55h)



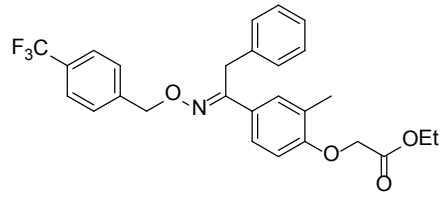
55h (0.68 gm, 70%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.50 gm, 1.97 mmol) and **54b** (0.66 gm, 1.97 mmol) following the general procedure described above as a thick liquid.

IR (Neat) : 1755, 1620, 1504, 1402, 1384, 1325,. 1215, 1128, 1066, 1051, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.97-1.00 (m, 2H), 1.10-1.14 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.59-1.64 (m, 7H), 2.30 (s, 3H), 2.67 (d, *J* = 7.2 Hz, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 4.64 (s, 2H), 5.23 (s, 2H), 6.64 (d, *J* = 8.8 Hz, 1H), 7.33 (dd, *J* = 8.8 & 2.4 Hz, 1H), 7.43-7.50 (m, 3H), 7.60 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 492.2 $(M+H)^+$

4.1.31.9 (*E*)-Ethyl 2-(2-methyl-4-(2-phenyl-1-(((4-trifluoromethylbenzyl) oxy)imino)ethyl)phenoxy)acetate (55i)



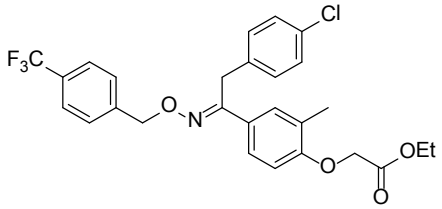
55i (0.55 gm, 58%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.50 gm, 1.97 mmol) and **54c** (0.64 gm, 1.97 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 90.1%.

IR (Neat) : 1957, 1735, 1602, 1504, 1325, 1215, 1066, 1018, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.27 (t, *J* = 7.1 Hz, 3H), 2.26 (s, 3H), 4.13 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 4.61 (s, 2H), 5.27 (s, 2H), 6.60 (d, *J* = 8.5 Hz, 1H), 7.15-7.19 (m, 5H), 7.21-7.25 (m, 3H), 7.49 (s, 1H), 7.54 (d, *J* = 7.9 Hz, 2H);

ESI/MS (m/z) : 486.1 $(M+H)^+$

4.1.31.10 (*E*)-Ethyl 2-(4-(2-(4-chlorophenyl)-1-(((4-trifluoromethylbenzyl) oxy)imino)ethyl)-2-methylphenoxy)acetate (55j)



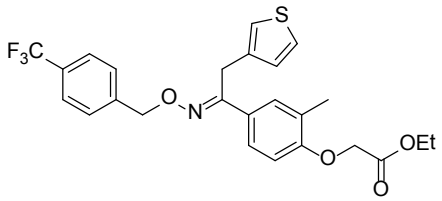
55j (0.50 gm, 41%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.60 gm, 2.36 mmol) and **54d** (0.85 gm, 2.36 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.7%.

IR (Neat) : 3138, 3020, 2929, 1759, 1743, 1612, 1504, 1325, 1215, 1066 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.28 (t, *J* = 7.0 Hz, 3H), 2.26 (s, 3H), 4.08 (s, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.62 (s, 2H), 5.26 (s, 2H), 6.60 (d, *J* = 8.8 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.17-7.21 (m, 2H), 7.32 (dd, *J* = 8.6 & 2.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 1.6 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 520.1 $(M+H)^+$

4.1.31.11 (*E*)-Ethyl 2-(2-methyl-4-(2-(thiophen-3-yl)-1-(((4-(trifluoro methyl)benzyl)oxy)imino)ethyl)phenoxy)acetate (55k)



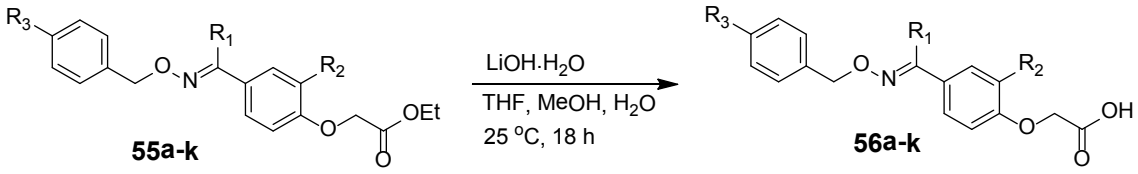
55k (0.66 gm, 68%) was prepared from 4-trifluoromethylbenzyl methanesulfonate **48** (0.50 gm, 1.97 mmol) and **54e** (0.66 gm, 1.97 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 98.7%.

IR (Neat) : 1759, 1612, 1502, 1382, 1325, 1215, 1130, 1066, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.26 (t, *J* = 7.2 Hz, 3H), 2.27 (s, 3H), 4.09 (s, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.62 (s, 2H), 5.28 (s, 2H), 6.62 (d, *J* = 8.8 Hz, 1H), 6.91-6.93 (m, 2H), 7.20-7.22 (m, 1H), 7.37-7.41 (m, 3H), 7.50 (d, *J* = 1.6 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 492.0 $(M+H)^+$

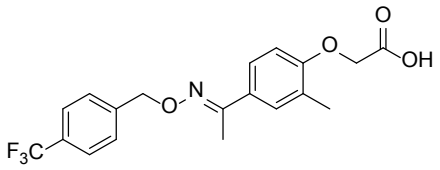
4.1.32 General procedure for the synthesis of Compounds (56a-k)



55a-k **56a-k**

To a solution of **55a-k** (1 mole equivalent) in a mixture of tetrahydrofuran (15 fold) and methanol (5 fold) was added a solution of $LiOH.H_2O$ (2 mole equivalent) in water (5 fold) and the reaction mixture was stirred at ambient temperature for about 5 hours. Solvent was evaporated under reduced pressure. Water was added to the residue, acidified with 1N HCl to pH 6 and extracted with ethyl acetate. The combined organic extracts were washed with water and brine solution, dried over sodium sulphate and evaporated under reduced pressure to yield the products **56a-k**.

4.1.32.1 (*E*)-2-(2-Methyl-4-(1-(((4-trifluoromethylbenzyl)oxy) imino) ethyl)phenoxy)acetic acid (56a)



56a (0.17 gm, 46%) was prepared from **55a** (0.40 gm, 0.98 mmol) following the general procedure described above as a white solid. Yield: 20%; m.p. 109-110 ^{o}C; Purity by HPLC: 99.9%.

IR (KBr) : 3419, 2929, 2873, 1759, 1620, 1506, 1326, 1164, 1066, 939, 806 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.15 (s, 3H), 2.17 (s, 3H), 4.46 (s, 2H), 5.21 (s, 2H), 6.58 (d, *J* = 8.8 Hz, 1H), 7.38 (s, 1H), 7.44 (d, *J* = 10.4 Hz, 2H), 7.56 (d, *J* = 11.1 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 12.8, 16.3, 75.1, 111.7, 125, 125.3, 125.4, 125.4, 127.3, 128.0, 128.8, 129.7, 142.4, 155.2, 157.0

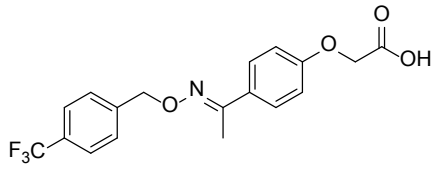
ESI/MS (m/z) : 382.0 $(M+H)^{+}$

Analysis **Mol.Formula:** $C_{19}H_{18}F_3NO_4$

Calculated : C, 59.84%; H, 4.76%; N, 3.67%

Found : C, 56.45%; H, 3.97%; N, 3.24%

4.1.32.2 (*E*)-2-(4-(1-(((4-trifluoromethylbenzyl)oxy)imino)ethyl) phenoxy)acetic acid (56b)



56b (0.35 gm, 96%) was prepared from **55b** (0.40 gm, 1.01 mmol) following the general procedure described above as an off white solid. m.p. 208-209 ^{o}C; Purity by HPLC: 98.8%.

IR (KBr) : 3518, 3410, 2901, 2858, 1718, 1631, 1618, 1597, 1518, 1413, 1338, 1238, 1180, 1132, 1058, 1018, 947, 825 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 2.19 (s, 3H), 4.17 (s, 2H), 5.24 (s, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 12.4, 16.2, 65.3, 67.1, 70.1, 110.9, 115.8, 116.6, 122.5, 123.5, 124.8, 125.8, 128.0, 128.8, 145, 154.6, 157.1, 164.1, 170.4

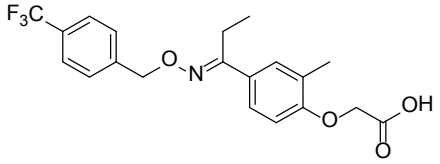
ESI/MS (m/z) : 368.1 $(M+H)^{+}$

Analysis **Mol.Formula:** $C_{18}H_{16}F_3NO_4$

Calculated : C, 58.86%; H, 4.39%; N, 3.81%

Found : C, 55.42%; H, 3.97%; N, 3.52%

4.1.32.3 (*E*)-2-(2-Methyl-4-(1-(((4-trifluoromethylbenzyl)oxy) imino) propyl)phenoxy)acetic acid (56c)



56c (0.37 gm, 99%) was prepared from **55c** (0.4 gm, 0.95 mmol) following the general procedure described above as an off white solid. m.p. 118-119 ^{o}C; Purity by HPLC: 99.4%.

IR (KBr) : 3385, 2983, 2868, 2584, 1749, 1707, 1622, 1506, 1327, 1247, 1168, 1151, 1111, 1066, 945, 798 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 1.01 (t, *J* = 7.6 Hz, 3H), 2.18 (s, 3H), 2.69 (q, *J* = 7.4 Hz, 2H), 4.70 (s, 2H), 5.25 (s, 2H), 6.80 (d, *J* = 8.8 Hz, 1H), 7.36 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.43 (s, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 11.11, 16.13, 19.33, 64.81, 74.21, 111.11, 125.04, 125.16, 125.19, 125.23, 126.13, 126.95, 128.02, 128.34, 143.32, 157.01, 159.57, 170.22

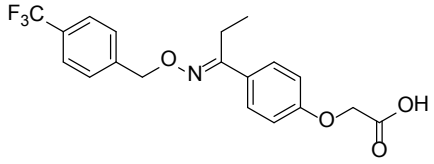
ESI/MS (m/z) : 396.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{20}H_{20}F_3NO_4$

Calculated : C, 60.76%; H, 5.10%; N, 3.54%

Found : C, 58.76%; H, 3.98%; N, 3.38%

4.1.32.4 (*E*)-2-(4-(1-(((4-trifluoromethylbenzyl)oxy)imino) propyl) phenoxy)acetic acid (56d)



56d (0.31 gm, 95%) was prepared from **55d** (0.35 gm, 0.86 mmol) following the general procedure described above as an off white solid. m.p. 125-127 ^oC; Purity by HPLC: 99.4%.

IR (KBr) : 3413, 2977, 2941, 2881, 1747, 1718, 1608, 1514, 1465, 1436, 1417, 1328, 1236, 1180, 1163, 1130, 1110, 1064, 1020, 962, 914, 831 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 1.01 (t, *J* = 7.48 Hz, 3H), 2.76 (q, *J* = 7.48 Hz, 2H), 4.67 (s, 2H), 5.25 (s, 2H), 6.92 (d, *J* = 8.78 Hz, 2H), 7.53-7.60 (m, 4H), 7.74 (d, *J* = 8.1 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 11.1, 19.3, 65.0, 74.2, 114.5, 125.2, 127.1, 127.4, 128.2, 143.3, 159, 159.4, 170.2

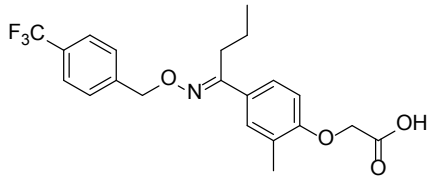
ESI/MS (m/z) : 382.0 $(M+H)^+$

Analysis **Mol.Formula:** $C_{19}H_{18}F_3NO_4$

Calculated : C, 59.84%; H, 4.76%; N, 3.67%

Found : C, 59.62%; H, 4.34%; N, 3.43%

4.1.32.5 (*E*)-2-(2-Methyl-4-(1-(((4-trifluoromethylbenzyl)oxy)imino) butyl)phenoxy)acetic acid (56e)



56e (0.32 gm, 83%) was prepared from **55e** (0.40 gm, 0.91 mmol) following the general procedure described above as a white solid. m.p. 129-130 ^oC; Purity by HPLC: 99.7%.

IR (KBr) : 2966, 2873, 2580, 1747, 1706, 1598,1506, 1149 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.95 (t, *J* = 7.05 Hz, 3H), 1.49-1.62 (m, 2H), 2.29 (s, 3H), 2.73 (t, *J* = 7.53 Hz, 2H), 4.69 (s, 2H), 5.24 (s, 2H), 6.69 (d, *J* = 8.5 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.48-7.50 (m, 3H), 7.61 (d, *J* = 8.1 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 14.4, 16.4, 20.1, 28.8, 65.0, 75.1, 110.9, 125.3, 125.3, 125.4, 125.4, 127.4, 128.0, 129.2, 129.3, 142.6, 156.7, 159.4, 174.2

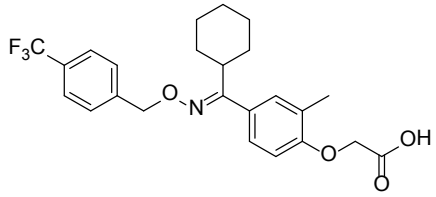
ESI/MS (m/z) : 409.9 $(M+H)^+$

Analysis **Mol.Formula:** $C_{21}H_{22}F_3NO_4$

Calculated : C, 61.61%; H, 5.42%; N, 3.42%

Found : C, 61.51%; H, 4.86%; N, 3.25%

4.1.32.6 (*E*)-2-(4-(Cyclohexyl(((4-trifluoromethylbenzyl)oxy)imino) methyl)-2-methylphenoxy)acetic acid (56f)



56f (0.37 gm, 98%) was prepared from **55f** (0.40 gm, 0.84 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 97.5%.

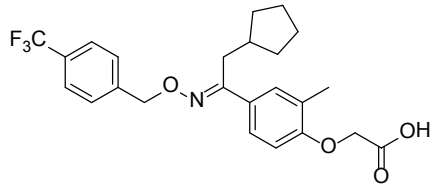
IR (Neat) : 3128, 3020, 2931, 1957, 1732, 1622, 1500, 1402, 1215, 1066, 758 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.11-1.24 (m, 6H), 1.61-1.87 (m, 4H), 2.28 (s, 3H), 2.40-2.48 (m, 1H), 4.68 (s, 2H), 5.07 (s, 2H), 6.71 (d, *J* = 8.9 Hz, 1H), 7.00-7.04 (m, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-*d*$_6$) : δ 16.1, 25.5, 25.6, 43.3, 65.0, 73.7, 99.6, 110.7, 125, 125.1, 125.4, 125.7, 126.0, 126.2, 127.7, 128.0, 129.6, 143.5, 155.9, 162.0, 170.5

ESI/MS (m/z) : 450.1 $(M+H)^+$

4.1.32.7 (*E*)-2-(4-(2-Cyclopentyl-1-(((4-trifluoromethylbenzyl)oxy)imino) ethyl)-2-methylphenoxy)acetic acid (56g)



56g (0.34 gm, 73%) was prepared from **55g** (0.50 gm, 1.05 mmol) following the general procedure described above as a white solid. m.p. 130-131 ^{o}C; Purity by HPLC: 99.9%.

IR (KBr) : 1722, 1604, 1504, 1448, 1334, 1245, 1159, 1114, 1070, 1056, 1018, 999, 819 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.18-1.95 (m, 2H), 1.44-1.46 (m, 2H), 1.58-1.65 (m, 4H), 2.01-2.09 (m, 1H), 2.30 (m, 3H), 2.80 (d, *J* = 7.6 Hz, 2H), 4.70 (s, 2H), 5.23 (s, 2H), 6.68 (d, *J* = 8.4 Hz, 1H), 7.36 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.44 (d, *J* = 1.6 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 16.1, 24.2, 30.8, 32.0, 37.5, 64.7, 74.2, 111.0, 125.1, 125.3, 126.0, 127.7, 128.2, 128.3, 128.5, 128.6, 143.2, 156.8, 158.4, 170.1

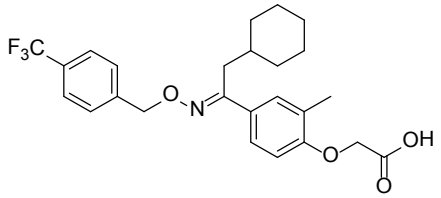
ESI/MS (m/z) : 450.1 $(M+H)^{+}$

Analysis **Mol.Formula:** $C_{24}H_{26}F_3NO_4$

Calculated : C, 64.13%; H, 5.83%; N, 3.12%

Found : C, 64.18%; H, 5.23%; N, 3.01%

4.1.32.8 (*E*)-2-(4-(2-Cyclohexyl-1-(((4-trifluoromethylbenzyl)oxy)imino) ethyl)-2-methylphenoxy)acetic acid (56h)



56h (0.28 gm, 59%) was prepared from **55h** (0.50 gm, 1.02 mmol) following the general procedure described above as a white solid. m.p. 132-133 ^{o}C; Purity by HPLC: 97.5%.

IR (KBr) : 1728, 1602, 1506, 1446, 1417, 1400, 1332, 1245, 1220, 1168, 1114, 1068, 1033, 887, 821 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 0.98-1.03 (m, 2H), 1.10-1.12 (m, 3H), 1.57-1.64 (m, 6H), 2.29 (m, 3H), 2.67 (d, *J* = 6.8 Hz, 2H), 4.69 (s, 2H), 5.23 (s, 2H), 6.68 (d, *J* = 8.4 Hz, 1H), 7.35 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.45 (d, *J* = 1.6 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 16.2, 25.6, 25.8, 32.8, 35.5, 64.7, 74.2, 111.0, 125.1, 125.2, 126.0, 127.8, 128.3, 128.3, 128.4, 143.3, 156.9, 157.8, 170.2

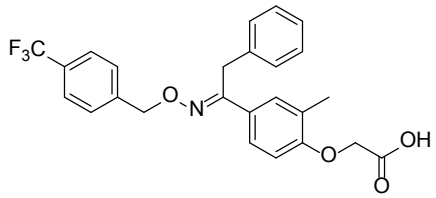
ESI/MS (m/z) : 464.1 $(M+H)^+$

Analysis **Mol.Formula:** $C_{25}H_{28}F_3NO_4$

Calculated : C, 64.78%; H, 6.09%; N, 3.02%

Found : C, 64.78%; H, 5.50%; N, 2.90%

4.1.32.9 (*E*)-2-(2-Methyl-4-(2-phenyl-1-(((4-trifluoromethylbenzyl)oxy) imino)ethyl)phenoxy)acetic acid (56i)



56i (0.25 gm, 53%) was prepared from **55i** (0.50 gm, 1.03 mmol) following the general procedure described above as a white solid. m.p. 135-136 ^oC; Purity by HPLC: 97.3%.

IR (KBr) : 1751, 1706, 1620, 1504, 1433, 1326, 1242, 1164, 1147, 1107, 1066, 1014, 943, 827, 806 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.15 (s, 3H), 4.16 (s, 2H), 4.68 (s, 2H), 5.31 (s, 2H), 6.76 (d, *J* = 8.8 Hz, 1H), 7.15-7.25 (m, 5H), 7.41 (dd, *J* = 8.4 & 2.4 Hz,

1H), 7.50 (d, *J* = 1.6 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 16.1, 31.4, 64.6, 71.4, 111.0, 125.1, 125.2, 125.5, 126.1, 126.2, 127.0, 128.3, 128.5, 136.8, 143.0, 156.4, 157.0, 170.1

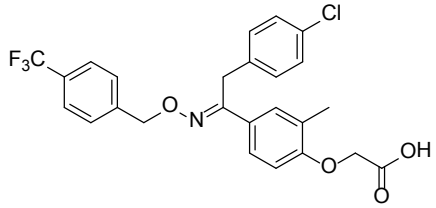
ESI/MS (m/z) : 452.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{25}H_{22}F_3NO_4$

Calculated : C, 65.64%; H, 4.85%; N, 3.06%

Found : C, 65.20%; H, 4.32%; N, 3.01%

4.1.32.10 (*E*)-2-(4-(2-(4-Chlorophenyl)-1-(((4-trifluoromethyl benzyl)oxy) imino)ethyl)-2-methylphenoxy)acetic acid (56j)



56j (0.38 gm, 81%) was prepared from **55j** (0.50 gm, 0.96 mmol) following the general procedure described above as an off white solid. m.p. 136-138 ^oC; Purity by HPLC: 97.8%.

IR (KBr) : 3411, 2916, 2584, 1706, 1618, 1506, 1433, 1326, 1056, 812 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ2.25 (s, 3H), 4.08 (s, 2H), 4.65 (s, 2H), 5.26 (s, 2H), 6.64 (d, *J* = 8.8 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.33 (dd, *J* = 8.4 & 2.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 1.6 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 16.1, 30.7, 64.8, 74.5, 111.1, 125.1, 125.5, 126.1, 126.7, 128.3, 128.4, 128.4, 130.2, 130.9, 135.8, 142.9, 156.1, 157.1, 170.1

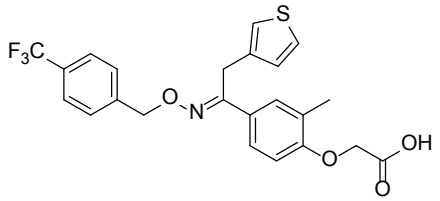
ESI/MS (m/z) : 492.1 $(M-H)^+$

Analysis **Mol.Formula:** $C_{25}H_{21}ClF_3NO_4$

Calculated : C, 61.04%; H, 4.30%; N, 2.85%

Found : C, 60.87%; H, 3.82%; N, 2.80%

4.1.32.11 (*E*)-2-(2-Methyl-4-(2-(thiophen-3-yl)-1-(((4-(trifluoro methyl) benzyl)oxy)imino)ethyl)phenoxy)acetic acid (56k)



56k (0.28 gm, 60%) was prepared from **55k** (0.50 gm, 1.02 mmol) following the general procedure described above as a white solid. m.p. 143-145 ^oC; Purity by HPLC: 98.4%.

IR (KBr) : 1751, 1618, 1502, 1431, 1323, 1240, 1163, 1143, 1066, 1053, 941, 808 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.25 (s, 3H), 4.10 (s, 2H), 4.68 (s, 2H), 5.28 (s, 2H), 6.66 (d, *J* = 8.4 Hz, 2H), 6.90-6.93 (m, 2H), 7.20-7.22 (m, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 1.2 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H)

^{13}C NMR ($CDCl_3$) : δ 16.4, 28.0, 65.2, 75.3, 110.9, 121.7, 125.4, 125.4, 125.4, 127.5, 128.1, 128.4, 128.6, 129.2, 136.5, 142.3, 156.7, 157.2, 171.6

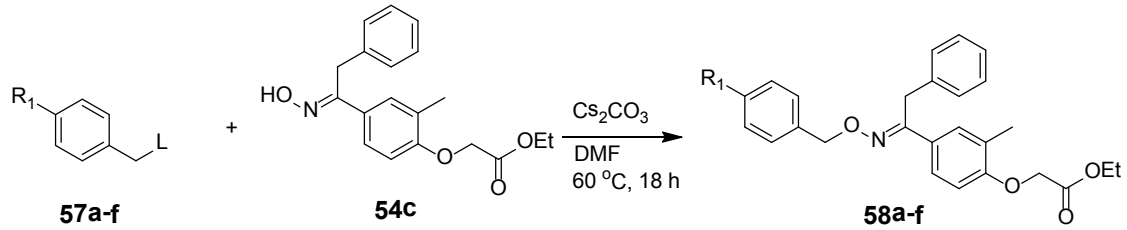
ESI/MS (m/z) : 463.9 $(M+H)^+$

Analysis **Mol.Formula:** $C_{23}H_{20}F_3NO_4S$

Calculated : C, 59.60%; H, 4.35%; N, 3.02%; S, 6.92%

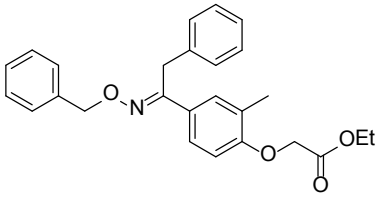
Found : C, 59.62%; H, 3.89%; N, 2.89%; S, 6.89%

4.1.33 General procedure for the synthesis of Compounds (58a-f)



To a solution of **57a-f** (1 mole equivalent) and **54c** (1 mole equivalent) in dry DMF (5 fold), Cs_2CO_3 (1.5 mole equivalent) was added and reaction mixture was stirred at 40 ^{O}C for 18 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (8 to 10% ethyl acetate in hexane) to yield the compounds **58a-f**.

4.1.33.1 (*E*)-Ethyl 2-(4-(1-((benzyloxy)imino)-2-phenylethyl)-2-methyl phenoxy)acetate (58a)



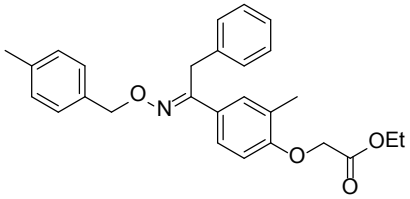
58a (0.57 gm, 58%) was prepared from benzyl chloride **57a** (0.30 gm, 2.37 mmol) and **54c** (0.78 gm, 2.37 mmol) following the general procedure described above as a white solid. m.p. 58-60 ^{o}C; Purity by HPLC: 97.2%.

IR (KBr) : 3032, 2933, 2874, 1747, 1602, 1500, 1448, 1381, 1348, 1280, 1213, 1134, 1028, 952, 819, 715 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.25 (t, *J* = 7.2 Hz, 3H), 2.25 (s, 3H), 4.13 (s, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.60 (s, 2H), 5.25 (s, 2H), 6.59 (d, *J* = 8.8 Hz, 1H), 7.14-7.25 (m, 5H), 7.27-7.38 (m, 6H), 7.51 (d, *J* = 1.6 Hz, 1H)

ESI/MS (m/z) : 418.0 $(M+H)^+$

4.1.33.2 (*E*)-Ethyl 2-(2-methyl-4-(1-((4-methylbenzyloxy)imino)-2-phenylethyl)phenoxy)acetate (58b)



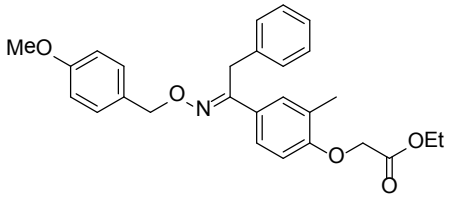
58b (0.60 gm, 93%) was prepared from 4-methylbenzyl methanesulfonate **57b** (0.30 gm, 1.50 mmol) and **54c** (0.49 gm, 1.50 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 90.7%.

IR (Neat) : 2983, 1753, 1502, 1384, 1215, 1030, 939 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.25 (t, *J* = 7.0 Hz, 3H), 2.25 (s, 3H), 2.34 (s, 3H), 4.11 (s, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.60 (s, 2H), 5.20 (s, 2H), 6.59 (d, *J* = 8.8 Hz, 1H), 7.13-7.25 (m, 9H), 7.35 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.51 (d, *J* = 1.2 Hz, 1H)

ESI/MS (m/z) : 432.1 $(M+H)^+$

4.1.33.3 (*E*)-Ethyl 2-(4-(1-((4-methoxybenzyloxy)imino)-2-phenylethyl) -2-methylphenoxy)acetate (58c)



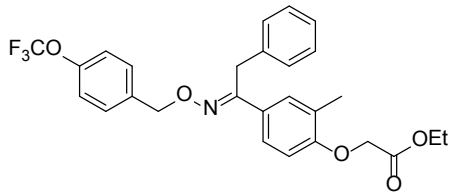
58c (0.53 gm, 86%) was prepared from 4-methoxybenzyl methanesulfonate **57c** (0.30 gm, 1.39 mmol) and **54c** (0.45 gm, 1.39 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 90.7%.

IR (Neat) :3018, 2935, 2874, 1757, 1612, 1514, 1440, 1301, 931, 669 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.25 (t, *J* = 7.0 Hz, 3H), 2.26 (s, 3H), 2.79 (s, 3H), 4.10 (s, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.60 (s, 2H), 5.17 (s, 2H), 6.59 (d, *J* = 8.4 Hz, 1H), 6.84-6.87 (m, 2H), 7.12-7.29 (m, 7H), 7.35 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.51 (d, *J* = 2.0 Hz, 1H)

ESI/MS (m/z) : 448.6 $(M+H)^+$

4.1.33.4 (*E*)-Ethyl 2-(2-methyl-4-(2-phenyl-1-((4-trifluoromethoxy benzyloxy)imino) ethyl)phenoxy)acetate (58d)



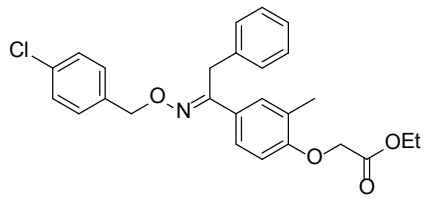
58d (0.66 gm, 84%) was prepared from 4-(trifluoromethoxy)benzyl bromide **57d** (0.40 gm, 1.57 mmol) and **54c** (0.51 gm, 1.57 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 99.4%.

IR (Neat) : 3387, 3020, 1757, 1508, 1261, 1018, 931 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.25 (t, *J* = 7.0 Hz, 3H), 2.26 (s, 3H), 4.12 (s, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.61 (s, 2H), 5.22 (s, 2H), 6.60 (d, *J* = 8.4 Hz, 1H), 7.14-7.25 (m, 7H), 7.31 (d, *J* = 8.8 Hz, 2H), 7.35 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.50 (d, *J* = 1.6 Hz, 1H)

ESI/MS (m/z) : 502.1 $(M+H)^+$

4.1.33.5 (*E*)-Ethyl 2-(4-(1-((4-chlorobenzyloxy)imino)-2-phenyl ethyl)-2-methylphenoxy)acetate (58e)



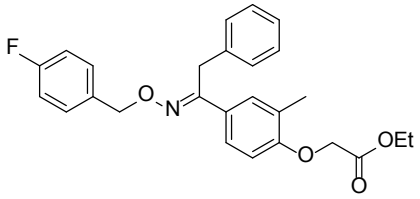
58e (0.56 gm, 85%) was prepared from 4-chlorobenzyl chloride **57e** (0.30 gm, 1.46 mmol) and **54c** (0.48 gm, 1.46 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 95.5%.

IR (Neat) : 2916, 1747, 1600, 1429, 1012, 943 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.25 (t, *J* = 7.2 Hz, 3H), 2.24 (s, 3H), 4.11 (s, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.61 (s, 2H), 5.16 (s, 2H), 6.59 (d, *J* = 8.8 Hz, 1H), 7.14-7.18 (m, 3H), 7.20-7.30 (m, 7H), 7.34 (dd, *J* = 8.6 & 1.8 Hz, 1H), 7.49 (d, *J* = 1.2 Hz, 1H)

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

4.1.33.6 (*E*)-Ethyl 2-(4-(1-((4-fluorobenzyloxy)imino)-2-phenyl ethyl)-2-methylphenoxy)acetate (58f)



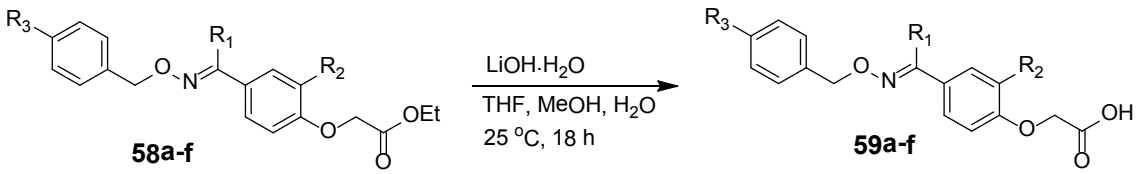
58f (0.56 gm, 41%) was prepared from 4-fluorobenzyl chloride **57f** (0.60 gm, 3.17 mmol) and **54c** (1.04 gm, 3.17 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 96.4%.

IR (Neat) : 3018, 2929, 1753, 1604, 1508, 1384, 1215, 1143, 1031, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.26 (t, *J* = 7.0 Hz, 3H), 2.26 (s, 3H), 4.11 (s, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.61 (s, 2H), 5.19 (s, 2H), 6.60 (d, *J* = 8.8 Hz, 1H), 6.98-7.02 (m, 2H), 7.14-7.30 (m, 7H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.50 (s, 1H)

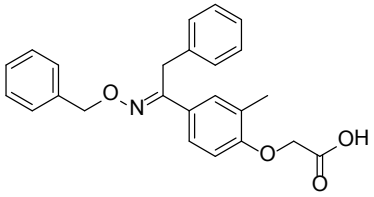
ESI/MS (m/z) : 436.2 $(M+H)^+$

4.1.34 General procedure for the synthesis of Compounds (59a-f)



To a solution of **58a-f** (1 mole equivalent) in a mixture of tetrahydrofuran (15 fold) and methanol (5 fold) was added another solution of $LiOH.H_2O$ (2 mole equivalent) in water (5 fold) and the reaction mixture was stirred at ambient temperature for about 5 hours. Solvent was evaporated under reduced pressure. Water was added to the residue, acidified with 1N HCl to pH 6 and extracted with ethyl acetate. The combined organic extracts were washed with water and brine solution, dried over sodium sulphate and evaporated under reduced pressure to yield the products **59a-f**.

4.1.34.1 (*E*)-2-(4-(1-(Benzyloxy)imino)-2-phenylethyl)-2-methyl phenoxy)acetic acid (59a)



59a (0.43 gm, 92%) was prepared from **58a** (0.50 gm, 1.20 mmol) following the general procedure described above as a white solid. m.p. 90-92 °C; Purity by HPLC: 99.8%.

IR (KBr) : 2914, 1751, 1602, 1504, 1431, 1348, 1249, 1138, 1041, 954, 908, 802, 715 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 2.14 (s, 3H), 4.12 (s, 2H), 4.64 (s, 2H), 5.21 (s, 2H), 6.74 (d, *J* = 8.8 Hz, 1H), 7.11-7.16 (m, 3H), 7.19-7.22 (m, 2H), 7.27-7.37 (m, 5H), 7.39 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.50 (d, *J* = 1.6 Hz, 1H)

^{13}C NMR (DMSO-d_6) : δ 16.2, 31.3, 64.9, 75.4, 111.0, 125.4, 126.0, 126.1, 127.0, 127.7, 128.0, 128.3, 128.4, 128.5, 136.9, 138, 155.8, 157.0, 170.3

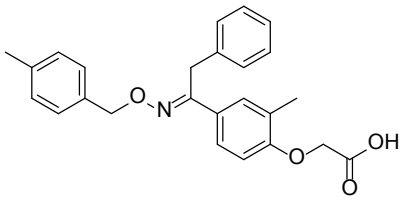
ESI/MS (m/z) : 390.0 $(M+H)^+$

Analysis **Mol.Formula:** $C_{24}H_{23}NO_4$

Calculated : C, 74.02%; H, 5.95%; N, 3.60%

Found : C, 73.24%; H, 4.98%; N, 3.51%

4.1.34.2 (*E*)-2-(2-Methyl-4-(1-((4-methylbenzyloxy)imino)-2-phenyl ethyl)phenoxy)acetic acid (59b)



59b (0.42 gm, 90%) was prepared from **58b** (0.50 gm, 1.16 mmol) following the general procedure described above as a white solid. m.p. 136-138 ^oC; Purity by HPLC: 98.2%.

IR (KBr) : 2916, 1753, 1506, 1433, 1251, 1089, 958 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 2.14 (s, 3H), 2.28 (s, 3H), 4.10 (s, 2H), 4.67 (s, 2H), 5.15 (s, 2H), 6.74 (d, *J* = 8.8 Hz, 1H), 7.10-7.16 (m, 5H), 7.18-7.26 (m, 4H), 7.39 (dd, *J* = 8.8 & 2.0 Hz, 1H), 7.50 (d, *J* = 1.2 Hz, 1H)

^{13}C NMR (DMSO-d_6) : δ 16.1, 20.8, 31.3, 64.8, 75.3, 111.0, 125.3, 126.0, 126.1, 127.1, 128.2, 128.4, 128.4, 128.9, 134.9, 136.9, 137.0, 155.7, 156.9, 170.1

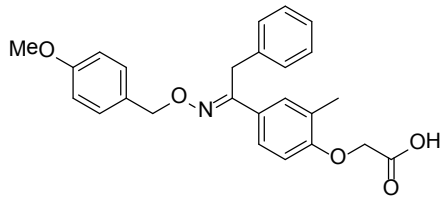
ESI/MS (m/z) : 404.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{25}H_{25}NO_4$

Calculated : C, 74.42%; H, 6.25%; N, 3.47%

Found : C, 73.97%; H, 5.24%; N, 3.37%

4.1.34.3 (*E*)-2-(4-(1-((4-Methoxybenzyloxy)imino)-2-phenylethyl)-2-methylphenoxy)acetic acid (59c)



59c (0.42 gm, 89%) was prepared from **58c** (0.50 gm, 1.12 mmol) following the general procedure described above as a white solid. m.p. 117-119 °C; Purity by HPLC: 99.5%.

IR (KBr) : 2928, 2872, 1724, 1612, 1512, 1469, 1365, 1290, 1242, 1030, 937, 889, 823 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ 2.15 (s, 3H), 3.73 (s, 3H), 4.08 (s, 2H), 4.61 (s, 2H), 5.12 (s, 2H), 6.73 (d, *J* = 8.8 Hz, 1H), 6.89-6.92 (m, 2H), 7.10-7.13 (m, 3H), 7.17-7.21 (m, 2H), 7.29-7.32 (m, 2H), 7.39 (dd, *J* = 8.6 & 2.2 Hz, 1H), 7.50 (d, *J* = 2.0 Hz, 1H)

^{13}C NMR (DMSO-d_6) : δ 16.2, 31.2, 55.0, 62.2, 65.1, 75.2, 111.0, 113.7, 125.3, 125.9, 126.1, 128.3, 128.4, 128.4, 129.8, 129.9, 136.9, 155.6, 157.1, 159.0, 170.4

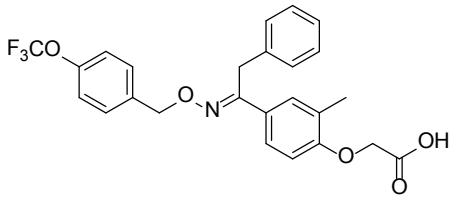
ESI/MS (m/z) : 420.6 $(M+H)^+$

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

Calculated : C, 71.58%; H, 6.01%; N, 3.34%

Found : C, 70.59%; H, 4.96%; N, 3.15%

4.1.34.4 (*E*)-2-(2-Methyl-4-(2-phenyl-1-((4-trifluoromethoxybenzyloxy) imino)ethyl)phenoxy)acetic acid (59d)



59d (0.42 gm, 89%) was prepared from **58d** (0.50 gm, 1.12 mmol) following the general procedure described above as a white solid. m.p. 123-125 ^{o}C; Purity by HPLC: 99.4%.

IR (KBr) : 3387, 3066, 2918, 2870, 1751, 1614, 1502, 1433, 1265, 1166, 1055, 947 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.23 (s, 3H), 4.10 (s, 2H), 4.60 (s, 2H), 5.21 (s, 2H), 6.60 (d, *J* = 8.4 Hz, 1H), 7.13-7.22 (m, 8H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.49 (s, 1H)

^{13}C NMR (DMSO-d_6) : δ 16.1, 31.3, 64.9, 74.4, 111, 120.9, 125.4, 126, 126.1, 126.9, 128.3, 128.4, 128.5, 129.8, 136.8, 137.5, 147.8, 156.2, 157.1, 170.2

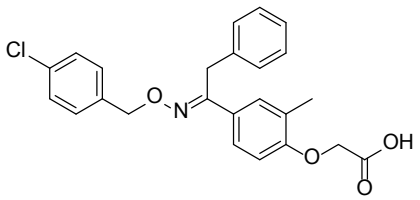
ESI/MS (m/z) : 474.2 $(M+H)^{+}$

Analysis **Mol.Formula:** $C_{25}H_{22}F_3NO_5$

Calculated : C, 63.42%; H, 4.68%; N, 2.96%

Found : C, 62.74%; H, 4.09%; N, 2.87%

4.1.34.5 (*E*)-2-(4-(1-((4-Chlorobenzyloxy)imino)-2-phenylethyl)-2-methylphenoxy)acetic acid (59e)



59e (0.42 gm, 89%) was prepared from **58e** (0.50 gm, 1.11 mmol) following the general procedure described above as a white solid. m.p. 118-120 ^{o}C; Purity by HPLC: 99.3%.

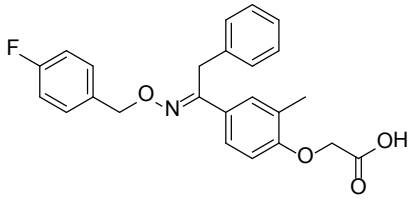
IR (KBr) : 3387, 2916, 1751, 1600, 1492, 1240, 1012, 943 cm^{-1}

^{1}H NMR (DMSO-d_6) : δ2.13 (s, 3H), 4.11 (s, 2H), 4.56 (s, 2H), 5.19 (s, 2H), 6.71 (d, *J* = 8.8 Hz, 1H), 7.11-7.14 (m, 3H), 7.19-7.22 (m, 2H), 7.35-7.41 (m, 5H), 7.48 (s, 1H)

^{13}C NMR (DMSO-d_6) : δ 16.2, 31.4, 65.3, 74.5, 111.0, 125.4, 126.0, 126.2, 126.8, 128.3, 128.4, 128.5, 129.9, 132.3, 136.8, 137.1, 156.2, 157.3, 170.4

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

4.1.34.6 (*E*)-2-(4-(1-((4-Fluorobenzyloxy)imino)-2-phenylethyl)-2-methylphenoxy)acetic acid (59f)



59f (0.44 gm, 93%) was prepared from **58f** (0.50 gm, 1.15 mmol) following the general procedure described above as a white solid. m.p. 127-128 ^{o}C; Purity by HPLC: 98.0%.

IR (KBr) : 3030, 2922, 2850, 1751, 1604, 1508, 1431, 1348, 1244, 1219, 1139, 1089, 1051, 1016, 923, 804, 719 cm^{-1}

^{1}H NMR : δ2.25 (s, 3H), 4.10 (s, 2H), 4.64 (s, 2H), 5.19 (s, 2H), 6.63 (d, *J*

($CDCl_3$) = 8.8 Hz, 1H), 6.98 (t, *J* = 8.6 Hz, 2H), 7.13-7.24 (m, 5H), 7.27-7.31 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.51 (s, 1H)

^{13}C NMR (DMSO-d_6) : δ 16.1, 31.3, 64.7, 74.6, 111.0, 115.0, 115.2, 125.4, 126.0, 127.1, 128.3, 128.4, 128.5, 130.2, 130.3, 134.2, 136.8, 156.0, 160.6, 162.6, 170.1

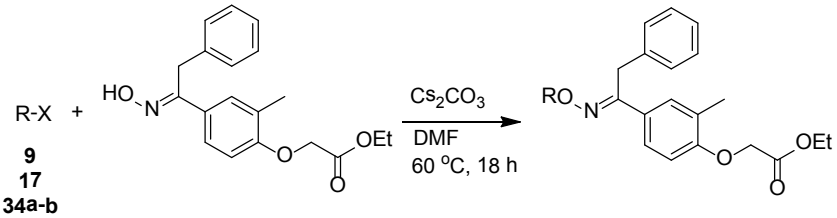
ESI/MS (m/z) : 408.2 $(M+H)^+$

Analysis **Mol.Formula:** $C_{24}H_{22}FNO_4$

Calculated : C, 70.75%; H, 5.44%; N, 3.44%

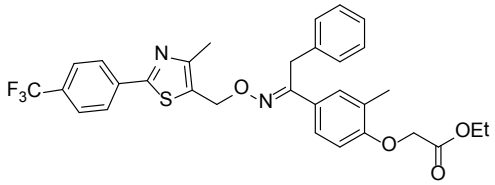
Found : C, 70.32%; H, 4.71%; N, 3.41%

4.1.35 General procedure for the synthesis of Compounds (60a-e)



To a solution of **9**, **17**, **34a-b** or **34g** (1 mole equivalent) and **54c** (1 mole equivalent) in dry DMF (5 fold), Cs_2CO_3 (1.5 mole equivalent) was added and reaction mixture was stirred at 60 ^{O}C for 18 hours. Reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extracts were washed with water and brine, dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by column chromatography (12 to 15% ethyl acetate in hexane) to yield the compounds **60a-e**.

4.1.35.1 (*E*)-Ethyl 2-(2-methyl-4-(1-(((4-methyl-2-(4-trifluoromethyl phenyl)thiazol-5-yl)methoxy)imino)-2-phenylethyl)phenoxy) acetate (60a)



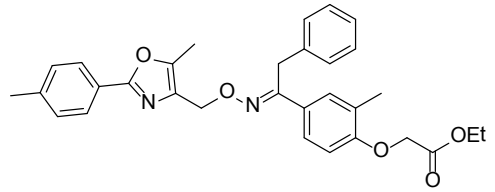
60a (1.72 gm, 73%) was prepared from **9** (1.00 gm, 3.43 mmol) and **54c** (1.12 gm, 3.43 mmol) following the general procedure described above as a thick liquid.

IR (Neat) : 3136, 1735, 1710, 1604, 1502, 1404, 1325, 1215, 1170, 1134, 1066, 1018, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.28 (t, *J* = 7.1 Hz, 3H), 2.27 (s, 3H), 2.51 (s, 3H), 4.09 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.62 (s, 2H), 5.35 (s, 2H), 6.62 (d, *J* = 8.5 Hz, 1H), 7.15-7.20 (m, 5H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.54 (s, 1H), 7.66 (d, *J* = 8.1 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H)

ESI/MS (m/z) : 583.1 $(M+H)^+$

4.1.35.2 (*E*)-Ethyl 2-(2-methyl-4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy)imino)-2-phenylethyl)phenoxy)acetate (60b)



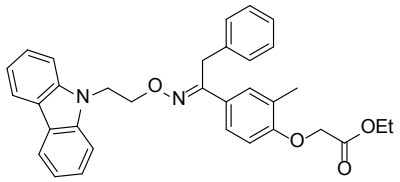
60b (0.78 gm, 86%) was prepared from **17** (0.50 gm, 1.78 mmol) and **54c** (0.58 gm, 1.78 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 92.2%.

IR (Neat) : 3020, 2985, 2929, 1957, 1757, 1602, 1502, 1438, 1404, 1380, 1215, 1018, 825, 669 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.28 (t, *J* = 7.1 Hz, 3H), 2.25 (s, 3H), 2.39 (s, 3H), 2.41 (s, 3H), 4.09 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.61 (s, 2H), 5.35 (s, 2H), 6.60 (d, *J* = 8.5 Hz, 1H), 7.11-7.22 (m, 7H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.51 (s, 1H), 7.90 (d, *J* = 7.9 Hz, 2H)

ESI/MS (m/z) : 513.1 $(M+H)^+$

4.1.35.3 (*E*)-Ethyl 2-(4-(1-((2-(*9H*-carbazol-9-yl)ethoxy)imino)-2-phenyl ethyl)-2-methylphenoxy)acetate (60c)



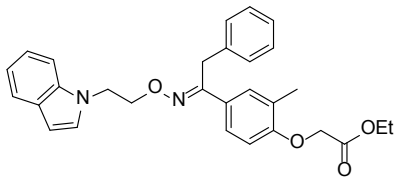
60c (0.44 gm, 35%) was prepared from **34a** (0.70 gm, 2.42 mmol) and **54c** (0.79 gm, 2.42 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 93.2%.

IR (Neat) : 1759, 1600, 1502, 1485, 1460, 1402, 1325, 1215, 1143, 1074, 750 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 1.28 (t, *J* = 7.1 Hz, 3H), 2.26 (s, 3H), 3.84 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.59-4.65 (m, 6H), 6.59 (d, *J* = 8.5 Hz, 1H), 6.98-7.01 (m, 2H), 7.10-7.11 (m, 3H), 7.19-7.31 (m, 3H), 7.36-7.43 (m, 5H), 8.08 (d, *J* = 7.7 Hz, 2H)

ESI/MS (m/z) : 521.1 $(M+H)^+$

4.1.35.4 (*E*)-Ethyl 2-(4-(1-((2-(*1H*-indol-1-yl)ethoxy)imino)-2-phenyl ethyl)-2-methylphenoxy)acetate (60d)



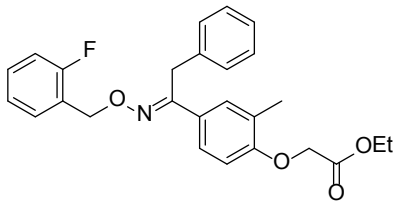
60d (0.44 gm, 60%) was prepared from **34b** (0.50 gm, 2.09 mmol) and **54c** (0.68 gm, 2.09 mmol) following the general procedure described above as a thick liquid.

IR (Neat) : 3020, 2808, 1602, 1504, 1402,1215, 1055, 929, 758, 669 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.28 (t, *J* = 7.1 Hz, 3H), 2.29 (s, 3H), 4.01 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.45-4.51 (m, 4H), 4.62 (s, 2H), 6.45 (d, *J* = 2.8 Hz, 1H), 6.62 (d, *J* = 8.5 Hz, 1H), 7.02 (d, *J* = 3.0 Hz, 1H), 7.09-7.22 (m, 7H), 7.34-7.36 (m, 2H), 7.46 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H)

ESI/MS (m/z) : 471.1 $(M+H)^+$

4.1.35.5 (*E*)-Ethyl 2-(4-(1-((2-fluorobenzyloxy)imino)-2-phenyl ethyl)-2-methylphenoxy)acetate (60e)



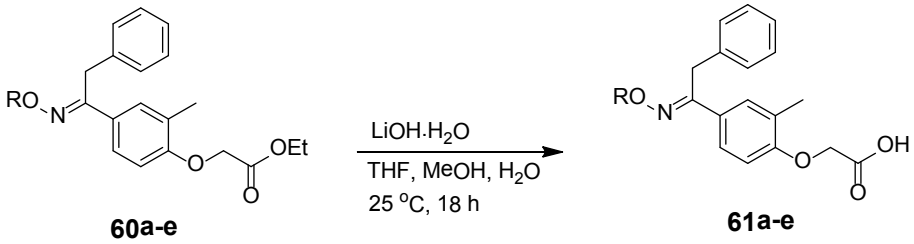
60e (1.06 gm, 65%) was prepared from **34g** (0.50 gm, 3.46 mmol) and **54c** (1.13 gm, 3.46 mmol) following the general procedure described above as a thick liquid. Purity by HPLC: 92.6%.

IR (Neat) : 3130, 3020, 2029, 1757, 1732, 1589, 1404, 1215, 1031, 758 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 1.27 (t, *J* = 7.1 Hz, 3H), 2.25 (s, 3H), 4.12 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.61 (s, 2H), 5.31 (s, 2H), 6.60 (d, *J* = 8.5 Hz, 1H), 7.04-7.11 (m, 2H), 7.15-7.26 (m, 5H), 7.28-7.39 (m, 3H), 7.51 (s, 1H)

ESI/MS (m/z) : 458.0 $(M+Na)^+$

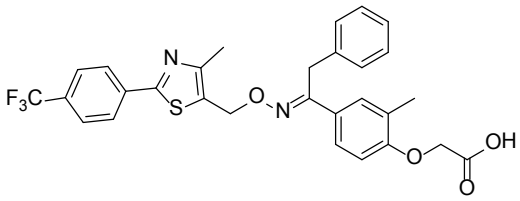
4.1.36 General procedure for the synthesis of Compounds (61a-e)



60a-e **61a-e**

To a solution of **60a-e** (1 mole equivalent) in a mixture of tetrahydrofuran (15 fold) and methanol (5 fold) was added a solution of $LiOH.H_2O$ (2 mole equivalent) in water (5 fold) and the reaction mixture was stirred at ambient temperature for about 5 hours. Solvent was evaporated under reduced pressure, water was added to the residue, acidified with 1N HCl to pH 6 and extracted with ethyl acetate. The combined organic extracts were washed with water and brine solution, dried over sodium sulphate and evaporated under reduced pressure to yield the products **61a-f**.

4.1.36.1 (*E*)-2-(2-Methyl-4-(1-(((4-methyl-2-(4-trifluoromethyl phenyl)thiazol-5-yl)methoxy)imino)-2-phenylethyl)phenoxy) acetic acid (61a)



61a (0.87 gm, 91%) was prepared from **60a** (1.00 gm, 1.72 mmol) following the general procedure described above as a white solid. m.p. 159-161 °C; Purity by HPLC: 98.2%.

IR (KBr) : 3400, 3028, 2935, 1712, 1614, 1502, 1440, 1325, 1222, 1168, 1145, 1083, 1066, 1014, 846 cm^{-1}

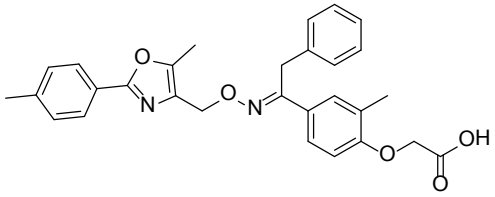
^{1}H NMR : δ 2.27 (s, 3H), 2.51 (s, 3H), 4.09 (s, 2H), 4.66 (s, 2H), 5.35 (s, 2H), 6.64 (d, *J* = 8.5 Hz, 1H), 7.13-7.20 (m, 5H), 7.42 (d, *J* = 8.4

($CDCl_3$) Hz, 1H), 7.54 (s, 1H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.99 (d, *J* = 8.1 Hz, 2H)

^{13}C NMR ($DMSO$-d_6) : δ 15.1, 16.2, 31.2, 64.8, 66.6, 111.1, 125.5, 126.1, 126.1, 126.5, 126.8, 128.3, 128.5, 129.7, 136.6, 152.1, 156.6, 157.2, 163.4, 170.2

ESI/MS (m/z) : 555.0 $(M+H)^+$

4.1.36.2 (*E*)-2-(2-Methyl-4-(1-(((5-methyl-2-(*p*-tolyl)oxazol-4-yl) methoxy)imino)-2-phenylethyl)phenoxy)acetic acid (61b)



61b (0.27 gm, 58%) was prepared from **60b** (0.5 gm, 0.97 mmol) following the general procedure described above as a white solid. m.p. 166-167 ^oC; Purity by HPLC: 97.8%.

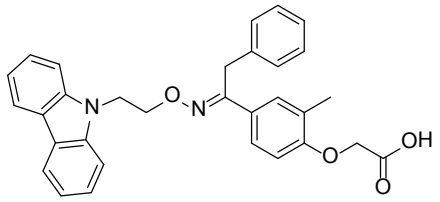
IR (KBr) : 3062, 2925, 2854, 1714, 1612, 1581, 1556, 1500, 1440, 1315, 1236, 1190, 1143, 1070, 993, 866, 804, 731 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.23 (s, 3H), 2.38 (s, 3H), 2.40 (s, 3H), 4.07 (s, 2H), 4.60 (s, 2H), 5.16 (s, 2H), 6.56 (d, *J* = 8.5 Hz, 1H), 7.10-7.15 (m, 4H), 7.20-7.25 (m, 3H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.50 (s, 1H), 7.90 (d, *J* = 7.9 Hz, 2H)

^{13}C NMR ($DMSO$-d_6) : δ 10.1, 16.2, 20.0, 31.1, 64.7, 67.0, 12.0, 124.4, 125.4, 125.6, 126.0, 126.1, 127.0, 128.4, 128.5, 129.7, 132.7, 136.8, 140.1, 147.4, 155.8, 156.9, 158.8, 170.1

ESI/MS (m/z) : 485.1 $(M+H)^+$

4.1.36.3 (*E*)-2-(4-(1-((2-(*9H*-Carbazol-9-yl)ethoxy)imino)-2-phenyl ethyl)-2-methylphenoxy)acetic acid (61c)



61c (0.34 gm, 90%) was prepared from **60c** (0.4 gm, 0.77 mmol) following the general procedure described above as a white solid. m.p. 148-150 ^{o}C; Purity by HPLC: 97.3%.

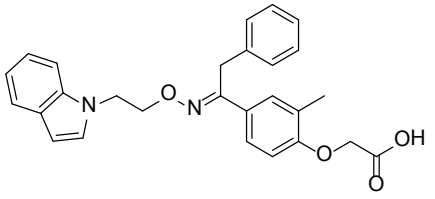
IR (KBr) : 3057, 2927, 2873, 1737, 1600, 1502, 1460, 1350, 1240, 1141, 1070, 958, 804, 759 cm^{-1}

^{1}H NMR (CDCl$_3$) : δ 2.24 (s, 3H), 3.84 (s, 2H), 4.59-4.63 (m, 6H), 6.61 (d, *J* = 8.5 Hz, 1H), 6.99-7.00 (m, 2H), 7.10-7.11 (m, 3H), 7.19-7.23 (m, 2H), 7.29-7.40 (m, 6H), 8.07 (d, *J* = 7.7 Hz, 2H)

^{13}C NMR (DMSO-d_6) : δ 16.1, 31.2, 42.1, 64.8, 71.6, 109.5, 110.8, 118.8, 120.2, 122.2, 125.4, 125.6, 125.9, 125.9, 126.9, 128.3, 128.3, 128.5, 136.5, 140.2, 156.1, 156.9, 170.2

ESI/MS (m/z) : 493.1 $(M+H)^{+}$

4.1.36.4 (*E*)-2-(4-(1-((2-(*1H*-Indol-1-yl)ethoxy)imino)-2-phenyl ethyl)-2-methylphenoxy)acetic acid (61d)



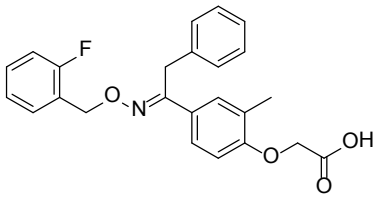
61d (0.28 gm, 75%) was prepared from **60d** (0.4 gm, 0.85 mmol) following the general procedure described above as a pale yellow solid. m.p. 128-130 ^{o}C; Purity by HPLC: 92.7%.

IR (KBr) : 3348, 3028, 2929, 2873, 1602, 1502, 1463, 1406, 1332, 1315, 1228, 1137, 1056, 958, 885, 806, 740 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.11 (s, 3H), 3.94 (s, 2H), 4.20 (s, 2H), 4.44-4.51 (m, 4H), 6.40 (d, *J* = 2.4 Hz, 1H), 6.61 (d, *J* = 8.5 Hz, 1H), 7.00-7.11 (m, 7H), 7.33-7.39 (m, 3H), 7.45-7.54 (m, 2H)

ESI/MS (m/z) : 442.9 $(M+H)^+$

4.1.36.5 (*E*)-2-(4-(1-(((2-Fluorobenzyl)oxy)imino)-2-phenylethyl)-2-methylphenoxy)acetic acid (61e)



61e (0.33 gm, 36%) was prepared from **60e** (1.0 gm, 2.30 mmol) following the general procedure described above as an off white solid. m.p. 72-74 ^oC; Purity by HPLC: 95.6%.

IR (KBr) : 3030, 2906, 2785, 1749, 1706, 1604, 1585, 1492, 1431, 1367, 1286, 1139, 1058, 756, 630 cm^{-1}

^{1}H NMR ($CDCl_3$) : δ 2.22 (s, 3H), 4.12 (s, 2H), 4.60 (s, 2H), 5.31 (s, 2H), 6.59 (d, *J* = 8.5 Hz, 1H), 7.01-7.37 (complex, 10H), 7.49 (s, 1H)

^{13}C NMR (DMSO-d_6) : δ 16.2, 24.9, 65.1, 69.3, 111.0, 115.2, 115.4, 124.4, 124.6, 124.8, 125.4, 126, 126.2, 126.8, 128.4, 128.5, 130.1, 130.2, 131.0, 136.7, 156.2, 157.1, 159.3, 161.7, 170.3

ESI/MS (m/z) : 430.0 $(M+Na)^+$

4.2 Biology

4.2.1 in vitro PPAR transactivation assay

Principle: HepG2 cells are transfected with human full length PPARa, PPARb (or d) and PPARg 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 Mg2+ 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 b- 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 PPARa or PPARg or PPARd and cotransfected with PPRE3-TK-luc. Cells were incubated at 37 °C, 5% CO2 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% CO2 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 b-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]. b-Galactosidase activity was determined in ELISA reader at 415 nm. The ratio of luciferase versus bgalactosidase was calculated and fold induction was calculated with respect to DMSO. Fold inductions of the standard compounds were also calculated with respect to DMSO. EC50 values for the test compounds were calculated by nonlinear regression analysis using graph pad prism software. Each concentration point represents values in duplicates.

4.2.2 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.

4.2.2.1 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).

4.2.2.2 Hypolipidemic activity in HF-HC-Sucrose fed Female Hamster

Female hamster of 8-12 weeks age (80-150 gm body weight) were taken for study. Six animals whose average body weight was not significantly different from the rest of the animals were selected for normal NIN diet. Other animals were put on HF-HC-Sucrose (High fat, high cholesterol and Sucrose) diet for 14 days. On day 14 all the HF-HC-Sucrose diet fed animals were selected which had gained their body weight significantly more than the normal diet group animals. The selected animals were divided into different groups in such a way that the average bodyweight of the animals in each group was not significantly

different from the other groups. All the animals were orally dosed once daily either with vehicle (0.5% polyethylene glycol in water) or test compounds (10 mpk, dissolved in 0.5% polyethylene glycol in water) for 14 days. Fasted blood samples were collected from each animal on day 7 and 14, after 1 hour of dose administration and separated serum samples were subjected for the estimation of high density lipoprotein (HDL) and low density lipoprotein (LDL).

4.2.2.3 LPS induced endotoxemia

Male Swiss albino mice (SAM) of 6-8 week age or female BALB/c mice (6–8 weeks old) were randomly placed in groups (n=8) and kept on overnight fasting. The animals were administered per os with test compound or vehicle (10% polyethylene glycol in 0.5% carboxy methyl cellulose sodium) 1 h prior to the intravenous injection of LPS (100µg/kg of Escherichia coli LPS (Sigma, USA) while control mice were injected with PBS (10 ml/kg). Animals were bled by retroorbital puncture at 1 and 4h after the LPS administration. Serum was separated for estimation of TNF alpha (1 h sample) and IL-6 (4 h sample).

4.2.2.4 Pharmacokinetics experiment

Pharmacokinetic behavior of the test compounds was studied via per-oral route of administration in S.D. 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 (Cmax), time point of maximum plasma concentration (tmax), area under the plasma concentration-time curve from 0 hour to infinity (AUC0-µ) and half-life of drug elimination during the terminal phase (t1/2) 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.