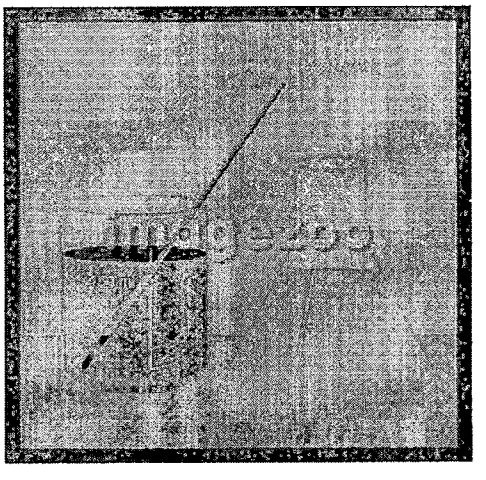
CHAPTER-4



Experimental

4 EXPERIMENTAL

All the reagents and solvents required for syntheses were purified by general laboratory techniques before use. Melting points were determined using silicon oil bath type melting points apparatus (Veego) and are uncorrected. The completion of the reaction was monitored by thin layer chromatography (TLC) on silica gel pre-coated plates (60 F_{254}, Merck), visualizing in ultraviolet light and iodine vapors. The yields reported here are un-optimized. Ultraviolet spectra were recorded on Shimadzu UV 1700. FT-IR spectra were recorded using potassium bromide disc on a Shimadzu FT-IR (Model 8300). PMR spectra were recorded using Bruker 300/400 MHz spectrometer in suitable deuterated solvents and expressed as δ, ppm. The assignment of exchangeable protons was confirmed by D_2O exchange studies wherever required. Mass spectra were recorded using Shimadzu ESI-MS. Microwave reactions were carried out in CEM-Discovery, USA microwave reactor. Sodium hydride was washed with dry benzene or petroleum ether to remove the mineral oil before using it in the reaction. Optical rotations were determined on Autopol IV polarimeter. Elemental analyses were obtained on Perkin-Elmer instrument.

The inhibitory activities of the synthesized compounds were experimentally determined using an ELISA kit (Innozyme™ TACE activity kit) procured from Calbiochem, USA. The micro-balance used for weighing in biological screening was manufactured by Mettler-Toledo (Model No. MX5). Enzyme inhibition studies were carried out on a spectrofluorometric ELISA reader, Perkin-Elmer (Victor-3V).

The experimental work has been divided into two parts:

1. Synthetic Work
2. Biological Work

4.1 Synthetic Work

4.1.1 4-Methoxybenzyl alcohol (3)

Anisaldehyde (1) (5.0 g, 36 mmole) was dissolved in methanol (50 mL) and cooled to 0 ° C. Sodium borohydride (0.68 g, 18 mmole) was added portion-wise at such a rate that the temperature of the reaction mixture did not rise above 10 °C. The reaction mixture was stirred at RT (about 40 °C) for 30 mins. Methanol was removed from the reaction mixture and the remaining mass was poured into ice-water (250 mL). The aqueous solution was extracted with chloroform (4 x 20 mL); the combined organic layer

was dried over anhydrous sodium sulphate and recovered to get the title compound as oil. (4.5 g, 89.3 %).

Anal.:

TLC :R_f 0.24 (30 % EtOAc in n-hexane).

4.1.2 2-Hydroxymethylpyridine (4)

The title compound was prepared from pyridine-2-carboxaldehyde (2) (5.0 g, 46.7 mmole) and sodium borohydride (0.88 g, 23 mmole) following the method described for the synthesis of compound (3). The title compound was obtained as oil. (4.8 g, 94.3 %).

Anal.:

TLC :R_f 0.20 (20 % EtOAc in n-hexane).

4.1.3 4-Phenylbenzyl alcohol (6)

Biphenyl-4-carboxylic acid (5) (2.0 g, 10 mmole) was dissolved in dry THF (30 mL) and cooled to -5° C. Lithium aluminium hydride (0.77 g, 20 mmole) was added portion-wise at such a rate that the temperature of the reaction mixture did not rise above 0 °C. The temperature of the reaction mixture was allowed to come to RT (about 30 °C) and the reaction mixture stirred for 1 hour followed by refluxing for another 2 hours. The reaction mixture was again cooled to -5 °C. Ethyl acetate was added to it drop-wise cautiously. After excess of the metal hydride was destroyed, the reaction mixture was poured into ice-water (10 mL). Immediately, a white viscous slurry was obtained. It was filtered through filter aid (hyflosupercel). The residue was washed with hot methanol (5 x 50 mL). The filtrate was diluted with water (100 mL) and extracted with ethyl acetate (10 x 20 mL); the combined organic layer was dried over anhydrous sodium sulphate and the solvent removed to get the desired product as white solid. (1.5 g, 81.5 %), m.p. 97-98 °C (Lit.[142] 96-100 °C).

Anal.:

TLC :R_f 0.37 (30 % EtOAc in n-hexane).

4.1.4 2-Isobutylquinoline-4-carboxylic acid (11)

Isatin (7) (2.0 g, 13 mmole) was suspended in ethanol (9 mL). Potassium hydroxide (3.64 g, 65 mmole) was added to the above suspension and stirred for 5 mins. Isobutyl methyl ketone (8) (3.25 mL, 26 mmole) was added to the above mixture and the reaction mixture placed in microwave reactor with the given conditions (Power, 300W;

Temp., 100 °C; Run Time, 1.00 min.; Hold Time, 5.00 min.; Stirrer Speed, High). After the reaction was over, the reaction mixture was removed from the reactor and ethanol was completely removed from the reaction mixture under vacuum. The semi-solid mass thus obtained was dissolved in ice-water (20 mL). The aqueous layer was acidified with conc. HCl upto pH 4. The precipitated material was filtered and dried in oven. The crude product thus obtained was purified by crystallization from methanol to afford a off white solid. (1.25g, 42.0 %), m.p. 188-89 °C. (Lit.[144] 187-189 °C).

Anal.:

TLC :R_f 0.60 (50 % EtOAc in n-hexane).

4.1.5 2-Ethylquinoline-4-carboxylic acid (12)

The title compound was prepared from isatin (7) (10.0 g, 68 mmole), 2-butanone (9) (12.2 mL, 136 mmole) and potassium hydroxide (19.04 g, 340 mmole) following the method described for the synthesis of compound (11). The crude solid so obtained was crystallized from methanol to afford the title product as off white solid. (8.5 g, 62.2 %). m.p. 225-27 °C (dec).

Anal.:

TLC	:R_f 0.51 (50 % EtOAc in n-hexane)
IR (KBr, cm^{-1})	:3412, 1660, 1610, 1315, 1238, 854, 769.
PMR (DMSO-d_6)	:7.93-7.95 (m, 1H), 7.76-7.78 (m, 1H), 7.64-7.68 (m, 1H), 7.51-7.55 (m, 2H), 3.01-3.04 (q, 2H, J = 7.72 Hz), 1.37-1.41 (t, 3H, J = 7.62 Hz).

4.1.6 2-Phenylquinoline-4-carboxylic acid (13)

The title compound was prepared from isatin (7) (10.0 g, 68 mmole), acetophenone (10) (15.9 mL, 136 mmole) and potassium hydroxide (19.04 g, 340 mmole) following the method described for the synthesis of compound (11). The crude solid thus obtained was crystallized from methanol to afford the title compound as a white solid. (10.9 g, 64.4 %). m.p. 209-10 °C (Lit.[144] 210-12 °C).

Anal.:

TLC :R_f 0.18 (30 % EtOAc in n-hexane).

4.1.7 Methyl 2-isobutylquinoline-4-carboxylate (14)

2-Isobutylquinoline-4-carboxylic acid (11) (1.25 g, 5.4 mmole) was dissolved in methanol (10 mL) and cooled to 0-5° C. Thionyl chloride (0.60 mL, 8.2 mmole) was

added drop-wise to the above solution under stirring. After the addition was over, the reaction mixture was refluxed for 2 hours. Excess methanol and thionyl chloride were removed from the reaction mixture, which was poured into saturated solution of sodium bicarbonate (50 mL). The aqueous layer was extracted with chloroform (3 x 20 mL); the combined organic layer was dried over anhydrous sodium sulphate and recovered to get the title compound as off white solid. (0.62 g, 47.2 %). m.p 46-48 °C.

Anal.:

TLC :R_f 0.82 (30 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2956, 1724, 1591, 1508, 1433, 1246, 1147, 1022, 800.

4.1.8 Methyl 2-ethylquinoline-4-carboxylate (15)

The title compound was prepared from 2-ethylquinoline-4-carboxylic acid (12) (7.2 g, 36 mmole) and thionyl chloride (3.4 mL, 33 mmole) following the method described for the synthesis of compound (14). The title compound was obtained as an oil. (5.1 g, 65.9 %).

Anal.:

TLC :R_f 0.52 (30 % EtOAc in n-hexane).

4.1.9 Methyl 2-phenylquinoline-4-carboxylate (16)

The title compound was prepared from 2-phenylquinoline-4-carboxylic acid (13) (10.9 g, 43 mmole) and thionyl chloride (6.5 mL, 86 mmole) following the method described for the synthesis of compound (14). The title compound was obtained as white solid. (9.6 g, 84.9 %). m.p. 68-70 °C.

Anal.:

TLC :R_f 0.79 (30 % EtOAc in n-hexane).

PMR ($CDCl_3$) :8.73-8.75 (m, 1H), 8.40 (s, 1H), 8.18-8.23 (m, 3H), 7.74-7.78 (m, 1H), 7.59-7.64 (m, 1H), 7.50-7.56 (m, 2H), 7.46-7.49 (m, 1H), 4.06 (s, 3H).

4.1.10 4-Hydroxymethyl-2-isobutylquinoline (17)

Methyl 2-isobutylquinoline-4-carboxylate (14) (0.52 g, 2.1 mmole) was dissolved in methanol (15 mL) and cooled to 0-5 °C. Sodium borohydride (0.81 g, 21 mmole) was added in fractions to the above solution under stirring in such a manner that the temperature of the reaction mixture did not rise above 10 °C. The reaction mixture was stirred overnight at RT (about 35 °C). Methanol was recovered from the reaction mixture

and cold water (10 mL) was added to it. The solid so precipitated out was filtered and dried to get the desired compound as white solid. (0.45 g, 99.7 %). m.p. 85-88 °C.

Anal.:

TLC	:R_f 0.27 (30 % EtOAc in n-hexane).
PMR ($CDCl_3$)	:8.06-8.09 (m, 1H), 7.89-7.91 (m, 1H), 7.64-7.66 (m, 1H), 7.47-7.51 (m, 1H), 7.41 (s, 1H), 5.20 (s, 2H), 2.80-2.82 (d, 2H), 2.16-2.23 (m, 1H), 0.94-0.96 (d, 6H).

4.1.11 2-Ethyl-4-hydroxymethylquinoline (18)

The title compound was prepared from methyl 2-ethylquinoline-4-carboxylate **(15)** (7.0 g, 32.5 mmole) and sodium borohydride (8.7 g, 228 mmole) following the same method as described for the synthesis of compound **(17)**. The title compound was obtained as white solid. (5.7 g, 93.8 %). m.p. 113-14 °C.

Anal.:

TLC	:R_f 0.15 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3124, 2968, 1604, 1566, 1446, 1134, 1089, 883, 754.
PMR ($CDCl_3$)	:8.06-8.08 (m, 1H), 7.89-7.91 (m, 1H), 7.66-7.70 (m, 1H), 7.52-7.58 (m, 1H), 7.46 (s, 1H), 5.21 (s, 2H), 2.96- 3.02 (q, 2H, J = 7.64 Hz), 1.37-1.41 (t, 3H, J = 7.66 Hz).

4.1.12 4-Hydroxymethyl-2-phenylquinoline (19)

The title compound was prepared from methyl 2-phenylquinoline-4-carboxylate **(16)** (9.6 g, 37 mmole) and sodium borohydride (9.8 g, 250 mmole) following the same method as described for the synthesis of compound **(17)**. The title compound was obtained as white solid. (8.1 g, 93.2 %). m.p. 102-04 °C.

Anal.:

TLC	:R_f 0.65 (30 % EtOAc in n-hexane).
PMR ($CDCl_3$)	:8.17-8.21 (m, 3H), 8.10 (s, 1H), 7.95-7.97 (m, 1H), 7.69-7.74 (m, 1H), 7.50-7.56 (m, 3H), 7.43-7.48 (m, 1H), 5.21 (s, 2H), 4.90 (bs, 1H).

4.1.13 4-Methoxybenzyl chloride (21)

4-Methoxybenzyl alcohol **(3)** (4.0 g, 28.5 mmole) was dissolved in dry chloroform (20 mL) and cooled to 5 °C. Thionyl chloride (3.1 mL, 42.8 mmole) was added to this solution at such a rate that the temperature of the reaction mixture did not

rise above 10 °C. After the addition was over, the reaction mixture was allowed to come to RT (30 °C) and stirred further for about 30 minutes. The Reaction mixture was basified to pH 8 by slow and careful addition of saturated sodium bicarbonate solution, extracted with chloroform (3 x 30 mL); the combined organic layer was washed with water (3 x 20 mL), dried over anhydrous sodium sulphate and the solvent removed to get the title product as an oil. (3.8 g, 85.2 %).

Anal.:

TLC :R_f 0.60 (30 % EtOAc in n-hexane).

4.1.14 2-Chloromethylpyridine (22)

The title compound was prepared from 2-hydroxymethylpyridine (4) (4.8 g, 44 mmole) and thionyl chloride (6.4 mL, 88 mmole) following the same method as described for the synthesis of compound (21). The title compound was obtained as oil. (5.1 g, 90.9 %).

Anal.:

TLC :R_f 0.77 (30 % EtOAc in n-hexane).

4.1.15 4-Chloromethylbiphenyl (23)

The title compound was prepared from 4-phenylbenzyl alcohol (6) (2.5 g, 13 mmole) and thionyl chloride (2.0 mL, 27 mmole) following the same method as described for the synthesis of compound (21). The title compound was obtained as off white soild. (2.0 g, 77.9 %). m. p. 73-76 °C. (Lit.[145] 71-73 °C).

Anal.:

TLC :R_f 0.83 (30 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3057, 3032, 1487, 1404, 823, 761, 727, 690.

4.1.16 4-Chloromethyl-2-isobutylquinoline (24)

The title compound was prepared from 4-hydroxymethyl-2-isobutylquinoline (17) (0.45 g, 2.1 mmole) and thionyl chloride (0.23 mL, 3.1 mmole) following the method described for the synthesis of compound (21). The title compound was obtained as oil. (0.35 g, 71.4 %).

Anal.:

TLC :R_f 0.83 (30 % EtOAc in n-hexane).

4.1.17 4-Chloromethyl-2-ethylquinoline (25)

The title compound was prepared from 2-ethyl-4-hydroxymethylquinoline (**18**) (5.7 g, 30.4 mmole) and thionyl chloride (4.4 mL, 61 mmole) following the method described for the synthesis of compound (**21**). The title compound was obtained as oil. (6.0 g, 96.04%).

Anal.:

TLC :R_f 0.53 (30 % EtOAc in n-hexane)

4.1.18 4-Chloromethyl-2-phenylquinoline (26)

The title compound was prepared from 4-hydroxymethyl-2-phenylquinoline (**19**) (4.5 g, 19.1 mmole) and thionyl chloride (2.5 mL, 38.3mmole) following the method described for the synthesis of compound (**21**). The title compound was obtained as white solid (4.5 g, 92.9 %). m.p. 82-85 °C.

Anal.:

TLC :R_f 0.84 (30 % EtOAc in n-hexane).

4.1.19 1-Chloromethylnapthalene (27)

The title compound was prepared from 1-naphthalenemethanol (**19**) (3.0 g, 19 mmole) and thionyl chloride (2.8 mL, 38 mmole) following the same method as described for the synthesis of compound (**21**). The title compound was obtained as brownish oil. (3.3 g, 98.4 %).

Anal.:

TLC :R_f 0.62 (10 % EtOAc in n-hexane).

4.1.20 1-(4-Nitrophenoxymethyl)-4-methoxybenzene (29)

4-Nitrophenol (**28**) (5.26 g, 38 mmole) was dissolved in dry DMF (10.5 mL). Anhydrous potassium carbonate (8.71 g, 63 mmole) was added to the above solution under stirring followed by 4-methoxybenzyl chloride (5.0 g, 31.5 mmole). The reaction mixture was heated to 80 °C for 4 hours and poured into ice-water (250 mL) under stirring. The solid so separated was filtered and washed with cold methanol (30 mL) to afford pure title compound as white solid. (7.1 g, 87.0 %). m.p. 102-04 °C.

Anal.:

TLC :R_f 0.53 (30 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2926, 1591, 1516, 1454, 1336, 1249, 1176, 1028.

4.1.21 2-(4-Nitrophenoxymethyl)pyridine (30)

The title compound was prepared from 4-nitrophenol (**28**) (6.7 g, 48 mmole), anhydrous potassium carbonate (11.0 g, 80 mmole) and 2-chloromethylpyridine (**22**) (5.1 g, 40 mmole) following the method described for the synthesis of compound (**29**). The title compound was obtained as brownish solid. (5.0 g, 54.3 %). m.p. 138-40 °C.

Anal.:

TLC	:R_f 0.43 (30% EtOAc in n-hexane).
PMR ($CDCl_3$)	:8.62-8.63 (m, 1H), 8.19-8.23 (d, 2H), 7.72-7.77 (m, 1H), 7.47-7.49 (m, 1H), 7.26-7.29 (m, 1H), 7.04-7.08 (d, 2H), 5.30 (s, 2H).

4.1.22 4-(4-Nitrophenoxymethyl)biphenyl (31)

The title compound was prepared from 4-nitrophenol (**28**) (1.0 g, 7 mmole), anhydrous potassium carbonate (1.7 g, 12 mmole) and 4-chloromethylbiphenyl (**23**) (1.2 g, 6 mmole) following the same method as described for the synthesis of compound (**29**). The title compound was obtained as brownish solid. (0.9 g, 50.3 %). m.p. 158-60 °C.

Anal.:

TLC	:R_f 0.74(30 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3072, 1587, 1512, 1491, 1384, 1338, 1251, 1170, 1109, 955.

4.1.23 2-Isobutyl-4-(4-nitrophenoxymethyl)quinoline (32)

The title compound was prepared from 4-nitrophenol (**28**) (4.6 g, 33 mmole), anhydrous potassium carbonate (7.5 g, 54 mmole) and 4-chloromethyl-2-isobutylquinoline (**24**) (6.5 g, 27 mmole) following the same method as described for the synthesis of compound (**29**). The impure compound was obtained as brownish solid which was crystallized from methanol to afford the pure title product as white solid. (5.6 g, 61.7 %). m.p. 95-97 °C.

Anal.:

TLC	:R_f 0.67 (30 % EtOAc in n-hexane).
PMR ($CDCl_3$)	:8.23-8.25 (d, 2H), 8.12-8.14 (m, 1H), 7.90-7.92 (m, 1H), 7.72-7.76 (m, 1H), 7.54-7.58 (m, 1H), 7.38 (s, 1H), 7.10-7.12 (d, 2H), 5.62 (s, 2H), 2.84-2.86 (d, 2H), 2.22-2.28 (m, 1H), 0.95-0.97 (d, 6H).

4.1.24 2-Ethyl-4-(4-nitrophenoxymethyl)quinoline (33)

The title compound was prepared from 4-nitrophenol (**28**) (4.9 g, 35 mmole), anhydrous potassium carbonate (8.0 g, 58 mmole) and 4-chloromethyl-2-ethylquinoline (**25**) (6.0 g, 29 mmole) following the method described for the synthesis of compound (**29**). The impure compound was obtained as brownish solid which was crystallized from methanol to afford the pure title product as white solid. (5.0 g, 55.9 %). m.p. 145-148 °C.

Anal.:

TLC	:R_f 0.56 (30 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:1604, 1502, 1446, 1338, 1267, 1172, 1109, 846, 754.
PMR (DMSO-d_6)	:8.23-8.25 (d, 2H, J = 8.84 Hz), 7.98-8.07 (m, 2H), 7.70-7.75 (m, 1H), 7.55-7.59 (m, 1H), 7.50 (s, 1H), 7.21-7.23 (d, 2H, J = 8.88 Hz), 5.67 (s, 2H), 2.98-3.03 (q, 2H, J = 7.51 Hz), 1.37-1.41 (t, 3H, J = 7.50 Hz).

4.1.25 2-Phenyl-4-(4-nitrophenoxymethyl)quinoline (34)

The title compound was prepared from 4-nitrophenol (**28**) (3.3 g, 23.7 mmole), anhydrous potassium carbonate (5.4 g, 39.4 mmole) and 4-chloromethyl-2-phenylquinoline (**26**) (5.0 g, 19.7 mmole) following the method described for the synthesis of compound (**29**). The impure compound was obtained as brownish solid which was crystallized from methanol to afford the pure title product as white solid. (5.0 g, 71.3 %). m.p. 155-57 °C.

Anal.:

TLC	:R_f 0.83 (50 % EtOAc in n-hexane).
PMR ($CDCl_3$)	:8.25-8.28 (m, 3H), 8.14-8.16 (m, 2H), 8.00 (s, 1H), 7.95-7.97 (m, 1H), 7.77-7.81 (m, 1H), 7.59-7.61 (m, 1H), 7.48-7.56 (m, 3H), 7.14-7.16 (d, 2H), 5.69 (s, 2H).

4.1.26 1-(4-Nitrophenoxymethyl)naphthalene (35)

The title compound was prepared from 4-nitrophenol (**28**) (3.1 g, 22.6 mmole), potassium carbonate (5.2 g, 37.6 mmole) and 1-chloromethylnapthalene (**27**) (3.3 g, 18.8 mmole) following the same method as described for the synthesis of compound (**29**). The brownish impure compound was crystallized from methanol to afford the pure title product as off white solid. (4.5 g, 99.1 %). m.p. 142-45 °C.

Anal.:

TLC	:R_f 0.68 (30 % EtOAc in n-hexane) .
PMR (DMSO-d_6)	:8.22-8.24 (d, 2H), 8.01-8.03 (m, 1H), 7.89-7.94 (m, 2H), 7.59-7.63 (m, 1H), 7.48-7.58 (m, 3H), 7.15-7.18 (d, 2H), 5.62 (s, 2H).

4.1.27 4-(4-Methoxybenzyloxy)aniline (36)

To a refluxing solution of 1-(4-nitrophenoxymethyl)-4-methoxybenzene (**29**) (4.5 g, 17.1 mmole) in methanol (700 mL), iron powder (0.9 g, 17.1 mmole) and saturated solution of sodium chloride (1 g, 17.1 mmole) were added every 30 minutes in fractions. The reaction was over after 11 hours. The reaction mixture was filtered through filter aid (hyflosupercel) to remove iron powder. The filtrate so obtained was evaporated under vacuum and saturated sodium bicarbonate solution was added (until the pH was about 8) to the reaction mass. The slurry was extracted with chloroform (4 x 50 mL); the combined organic layer was dried over anhydrous sodium sulphate and the solvent removed to get the desired compound as brown solid. (4.1 g, 100 %). m.p. 97-99 °C.

Anal.:

TLC	:R_f 0.37 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3419, 3346, 3010, 1610, 1510, 1249, 1178, 1028.

4.1.28 4-(2-Pyridinylmethoxy)aniline (37)

The title compound was prepared from 2-(4-nitrophenoxymethyl)pyridine (**30**) (2.1 g, 9.1 mmole), iron powder (1.0 g, 18.2 mmole) and saturated solution of sodium chloride (1 g, 18.2 mmole) following the method described for the synthesis of compound (**36**) to obtain the desired product as semi-solid. (1.4 g, 76.9 %).

Anal.:

TLC	:R_f 0.27 (50 % EtOAc in n-hexane).

4.1.29 4-(4-Aminophenoxymethyl)biphenyl (38)

The title compound was prepared from 4-(4-nitrophenoxymethyl)biphenyl (**31**) (0.8 g, 2.6 mmole), iron powder (0.3 g, 5.2 mmole) and saturated solution of sodium chloride (0.3 g, 5.2 mmole) following the method described for the synthesis of compound (**36**) to obtain the desired product as brown solid. (0.7 g, 96.1 %). m.p. 132-35 °C.

Anal.:

TLC :R_f 0.53 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3460, 3385, 1240, 1182, 1020, 848.

4.1.30 4-(2-Isobutyl-4-quinolinylmethoxy)aniline (39)

The title compound was prepared from 2-isobutyl-4-(4-nitrophenoxymethyl)quinoline (**32**) (2.5 g, 7.4 mmole), iron powder (0.9 g, 14.8 mmole) and saturated solution of sodium chloride (1 g, 14.8 mmole) following the method described for the synthesis of compound (**36**) to obtain the desired product as brown solid. (2.0 g, 80.3 %). m.p. 78-80 °C.

Anal.:

TLC :R_f 0.28 (30 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3390, 3323, 2955, 1608, 1512, 1232, 1182, 1018, 813, 748.

4.1.31 4-(2-Ethyl-4-quinolinylmethoxy)aniline (40)

The title compound was prepared from 2-ethyl-4-(4-nitrophenoxymethyl)quinoline (**33**) (5.0 g, 16 mmole), iron powder (1.7 g, 32 mmole) and saturated solution of sodium chloride (1.8 g, 32 mmole) following the method described for the synthesis of compound (**36**) to obtain the desired product as semi-solid. (3.7 g, 83.2 %).

Anal.:

TLC :R_f 0.30 (30 % EtOAc in n-hexane)

4.1.32 4-(2-Phenyl-4-quinolinylmethoxy)aniline (41)

The title compound was prepared from 2-phenyl-4-(4-nitrophenoxymethyl)quinoline (**34**) (5.0 g, 14 mmole), iron powder (1.6 g, 28 mmole) and saturated solution of sodium chloride (1.6 g, 28 mmole) following the same method as described for the synthesis of compound (**36**) to obtain the desired product as brown solid. (3.3 g, 72.3 %). m.p. 128-31 °C.

Anal.:

TLC :R_f 0.50 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3423, 3331, 1604, 1514, 1238, 1078, 815, 769.

4.1.33 1-(4-Aminophenoxymethyl)naphthalene (42)

The title compound was prepared from 1-(4-nitrophenoxymethyl)naphthalene (**35**) (2.0 g, 7.1 mmole), iron powder (0.8 g, 14.1 mmole) and saturated solution of sodium chloride (0.8 g, 14.1 mmole) following the same method as described for the synthesis of compound (**36**) to obtain the desired product as brown solid. (1.7 g, 97.3 %). m.p. 78-81 °C.

Anal.:

TLC :R_f 0.23 (30 % EtOAc in n-hexane).

4.1.34 2-Amino-5-benzyl-1,3,4-thiadiazole (47)

Phenylacetic acid (**43**) (1.0 g, 7.3 mmole), phosphorous oxychloride (0.9 mL, 9.6 mmole) and thiosemicarbazide (**46**) (0.9 g, 9.6 mmole) were taken together in a round bottom flask and the reaction mixture was heated on a water bath for 6 hours. Water (40 mL) was added to the reaction mixture and it was further heated on a water bath for 1 hour. The insoluble material was filtered out and the filtrate was cooled in ice-bath. Sodium hydroxide solution (50 % w/v) was added drop-wise to the cooled filtrate to bring its pH to 9. The solid so precipitated out was filtered and dried to get the title product as white solid. (1.2 g, 86.0 %). m.p. 200-03 °C.

Anal.:

TLC :R_f 0.26 (EtOAc).

IR (KBr, cm^{-1}) :3101, 3084, 1610, 1518, 1494, 1145, 700.

4.1.35 2-Amino-5-(4-methoxyphenyl)-1,3,4-thiadiazole (48)

The title compound was prepared from 4-methoxybenzoic acid (**44**) (1.0 g, 6.5 mmole), phosphorous oxychloride (0.8 mL, 8.5 mmole) and thiosemicarbazide (**46**) (0.8 g, 8.5 mmole) following the same method as described for the synthesis of compound (**47**) to obtain the desired product as off white solid. (1.1 g, 81.7 %). m.p. 190-191 °C. (Lit.[147] 192-194 °C).

Anal.:

TLC :R_f 0.54 (EtOAc).

IR (KBr, cm^{-1}) :3406, 3379, 3097, 1643, 1606, 1512, 1464, 1303, 1246, 1172.

4.1.36 2-Amino-5-(4-methoxybenzyl)-1,3,4-thiadiazole (49)

The title compound was prepared from 4-methoxyphenylacetic acid (**45**) (2.0 g, 12 mmole), phosphorous oxychloride (1.5 mL, 15.7 mmole) and thiosemicarbazide (**46**)

(1.4 g, 15.7 mmole) following the method described for the synthesis of compound (**47**) to obtain the desired product as white solid. (2.2 g, 82.9 %). m.p. 235-36 °C.

Anal.:

TLC	:R_f 0.50 (EtOAc).
IR (KBr, cm^{-1})	:3254, 3103, 1616, 1518, 1496, 1261, 1178, 1030, 846.
PMR (DMSO-d_6)	:7.17-7.19 (d, 2H), 6.83-6.85 (d, 2H), 6.01 (bs, 2H), 4.12 (s, 2H), 3.79 (s, 3H).

4.1.37 4,5-Diphenyl-2-thiazolylamine (53)

A mixture of desoxybenzoin (**50**) (1.0 g, 5.1 mmole), iodine (1.3 g, 5.1 mmole) and thiourea (**52**) (0.8 g, 10 mmole) were heated in oil bath at 100 °C overnight. The reaction mixture was washed with ether (2 x 25 mL) to remove the color impurities. The residue was dissolved in hot water (30 mL), basified with liquor ammonia to pH 9 and kept in refrigerator for 2 hours. The precipitated out solid was filtered, washed with ether (2 x 10 mL) and dried to afford the desired compound as off white solid. (1.0 g, 77.8 %). m.p. 184-85 °C. (Lit.[148] 184-85 °C).

Anal.:

TLC	:R_f 0.59 (50 % EtOAc in n-hexane).

4.1.38 4-(*p*-Tolyl)-2-thiazolylamine (54)

The title compound was prepared from 4-methylacetophenone (**51**) (1.0 mL, 7.5 mmole), iodine (1.9 g, 7.5 mmole) and thiourea (**46**) (1.1 g, 15 mmole) following the same method as described for the synthesis of compound (**53**) to obtain the desired product as white solid. (1.2 g, 84.2 %). m.p. 128-30 °C. (Lit.[148] 124-25 °C).

Anal.:

TLC	:R_f 0.32 (30 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3237, 3119, 1637, 1539, 1489, 1332, 1035, 823, 731.

4.1.39 1-(4-Aminothiophenoxymethyl)-4-methoxybenzene (56)

4-Aminothiophenol (**55**) (1.1 g, 8.7 mmole) was dissolved in dry DMF (3 mL). Potassium carbonate (1.2 g, 17 mmole) was added to the above solution under stirring followed by 4-methoxybenzyl chloride (**21**) (1.5 g, 9.6 mmole). The reaction mixture was stirred at RT (around 35 °C) for 1 hour, poured into ice-water (100 mL) under stirring and extracted with chloroform (3 x 50 mL). The combined organic layer was dried over anhydrous sodium sulphate and the solvent removed under vacuum to get a sticky compound. The crude compound thus obtained was purified by column chromatography

over neutral alumina using 10 - 25 % ethyl acetate in n-hexane as eluant to afford the desired product as off white solid. (1.1 g, 48.9 %). m.p. 78-80 °C.

Anal.:

TLC	:R_f 0.42 (50 % EtOAc in n-hexane).
PMR ($CDCl_3$)	:7.09-7.25 (m, 4H), 6.76-6.79 (m, 2H), 6.51-6.57 (m, 2H), 4.23 (s, 2H), 3.77 (s, 3H), 3.68 (bs, 2H).

4.1.40 2-Chloroethyl isocyanate (61)

Sodium azide (2.64 g, 40 mmole) was dissolved in distilled water (9 mL) and the solution cooled to -5° C. 3-Chloropropionyl chloride (**57**) (3.50 mL, 36 mmole) was added drop-wise to the above solution at such a rate that the temperature of the reaction mixture did not rise above 0 °C. The reaction mixture was stirred at -5 °C for 1 hour and extracted with benzene (3 x 20 mL). The organic layer was dried over anhydrous sodium sulphate to afford the corresponding acyl azide (**59**) in benzene. The acyl azide (**59**) was refluxed for 3 hours under anhydrous conditions to afford the title compound (**61**) in benzene as slightly yellow colored liquid.

4.1.41 3-Chloropropionyl isocyanate (62)

The title compound was prepared from sodium azide (10.0 g, 153 mmole), 4-chlorobutyryl chloride (**58**) (14.5 mL, 138 mmole) following the same method as described for the synthesis of compound (**61**) to obtain the desired product in benzene as transparent liquid.

4.1.42 1-(2-Chloroethyl)-3-[4-(4-methoxybenzyloxy)phenyl]urea (69)

4-(4-Methoxybenzyloxy)aniline (**36**) (1.5 g, 6.6 mmole) was dissolved in dry benzene (7 mL). 2-Chloroethyl isocyanate (**61**) (5.6 mL, 7.0 mmole) was added to the above solution under stirring. The reaction mixture was stirred for 30 minutes. The precipitated material was filtered and dried to get the desired compound as white solid. (1.5 g, 67.6 %). m.p. 135-38 °C.

Anal.:

TLC	:R_f 0.32 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3292, 2958, 1653, 1599, 1508, 1242, 1178, 1006, 827.

4.1.43 1-(2-Chloroethyl)-3-[4-(2-pyridinylmethoxy)phenyl]urea (70)

The title compound was prepared from 4-(pyridinylmethoxy)aniline (**37**) (1.4 g, 7 mmole) and 2-chloroethyl isocyanate (**61**) (5.5 mL, 7 mmole) following the method

described for the synthesis of compound (**69**) to obtain the desired product as white solid. (1.8 g, 84.1 %). m.p. 145-46 °C.

Anal.:

TLC	:R_f 0.25 (50 % EtOAc in n-hexane).
UV (MeOH)	:245.0 nm (log ε 4.32).
PMR ($CDCl_3$)	:8.57-8.59 (m, 1H), 8.09-8.11 (m, 1H), 7.72-7.76 (m, 1H), 7.51-7.53 (m, 1H), 7.24-7.32 (m, 3H), 6.86-6.90 (m, 2H), 6.19-6.21 (t, 1H), 5.15 (s, 2H), 3.62-3.65 (m, 2H), 3.51-3.56 (m, 2H).

4.1.44 1-[4-(4-Biphenylmethoxy)phenyl]-3-(2-chloroethyl)urea (71)

The title compound was prepared from 4-(4-aminophenoxymethyl)biphenyl (**38**) (1.8 g, 6.5 mmole) and 2-chloroethyl isocyanate (**61**) (5.1 mL, 6.5 mmole) following the same method as described for the synthesis of compound (**69**) to obtain the desired product as white solid. (1.6 g, 64.8 %). m.p. 190-92 °C.

Anal.:

TLC	:R_f 0.41 (50 % EtOAc in n-hexane)
IR (KBr, cm^{-1})	:3309, 3034, 1639, 1573, 1512, 1236, 1174, 1041, 825, 754.

4.1.45 1-(2-Chloroethyl)-3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]urea (72)

The title compound was prepared from 4-(2-isobutyl-4-quinolinyl-methoxy)aniline (**39**) (2.0 g, 6.5 mmole) and 2-chloroethyl isocyanate (**61**) (5.1 mL, 6.5 mmole) following the method described for the synthesis of compound (**69**) to obtain the desired product as white solid. (2.4 g, 89.7 %). m.p. 130-31 °C.

Anal.:

TLC	:R_f 0.86 (80 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3325, 2956, 1641, 1602, 1510, 1236, 1172, 1018, 827, 763.
PMR ($CDCl_3$)	:8.11-8.13 (m, 1H), 7.91-7.93 (m, 1H), 7.69-7.73 (m, 1H), 7.51-7.55 (m, 1H), 7.41 (s, 1H), 7.22-7.26 (m, 2H), 6.97-7.0 (m, 2H), 6.77 (bs, 1H), 5.47 (s, 2H), 5.38-5.41 (t, 1H), 3.62-3.65 (m, 2H), 3.55-3.59 (m, 2H), 2.84-2.86 (d, 2H), 2.17-2.21 (m, 1H), 0.94-0.96 (d, 6H).

4.1.46 1-(2-Chloroethyl)-3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]urea (73)

The title compound was prepared from 4-(2-ethyl-4-quinolinylmethoxy)aniline (**40**) (1.0 g, 3.6 mmole) and 2-chloroethyl isocyanate (**61**) (2.8 mL, 3.6 mmole) adopting

the same method as described for the synthesis of compound (**69**) to obtain the desired product as white solid. (0.9 g, 65.2 %). m.p. 148 °C (dec.).

Anal.:

TLC	:R_f 0.32 (50 % EtOAc in n-hexane)
IR (KBr, cm^{-1})	:3329, 2964, 1633, 1610, 1508, 1251, 1170, 1020, 833, 759.
PMR (DMSO-d_6)	:8.20-8.22 (m, 1H), 8.08-8.10 (m, 1H), 7.98-8.00 (m, 1H), 7.70-7.74 (m, 1H), 7.52-7.59 (m, 2H), 7.32-7.36 (d, 2H), 6.94-6.98 (d, 2H), 6.24-6.27 (t, 1H), 5.49 (s, 2H), 3.62-3.65 (m, 2H), 3.52-3.56 (m, 2H), 2.99-3.05 (q, 2H, J = 7.61 Hz), 1.37-1.41 (t, 3H, J = 7.62 Hz).

4.1.47 1-(2-Chloroethyl)-3-[4-(2-phenyl-4-quinolinylmethoxy)phenyl]urea (74)

The title compound was prepared from 4-(2-phenyl-4-quinolinyl-methoxy)aniline (**41**) (1.3 g, 4 mmole) and 2-chloroethyl isocyanate (**61**) (3.1 mL, 4 mmole) following the method described for the synthesis of compound (**69**) to obtain the desired product as white solid. (1.3 g, 78.2 %). m.p. 168-70 °C.

Anal.:

TLC	:R_f 0.35 (50 % EtOAc in n-hexane).
UV (MeOH)	:253.0 nm (log ε 4.74).
PMR ($CDCl_3$)	:8.24-8.26 (m, 1H), 8.15-8.17 (m, 2H), 8.07 (s, 1H), 8.01-8.03 (m, 1H), 7.75-7.80 (m, 3H), 7.58-7.60 (m, 1H), 7.46-7.56 (m, 3H), 7.35-7.37 (m, 2H), 6.24-6.26 (t, 1H), 5.45 (s, 2H), 3.63-3.65 (m, 2H), 3.52-3.56 (m, 2H).

4.1.48 1-(2-Chloroethyl)-3-[4-(1-naphthylmethoxy)phenyl]urea (75)

The title compound was prepared from 1-(4-aminophenoxymethyl)-naphthalene (**42**) (1.0 g, 4 mmole) and 2-chloroethyl isocyanate (**61**) (3.1 mL, 4 mmole) adopting the same method as described for the synthesis of compound (**69**) to obtain the desired product as white solid. (0.9 g, 65.6 %). m.p. 150-51 °C.

Anal.:

TLC	:R_f 0.41 (50 % EtOAc in n-hexane).
PMR (DMSO-d_6)	:8.04-8.06 (m, 2H), 7.84-7.90 (m, 2H), 7.51-7.57 (m, 3H), 7.46-7.50 (m, 1H), 7.31-7.35 (m, 2H), 6.93-6.99 (m, 2H), 6.15-6.18 (t, 1H) 5.44 (s, 2H), 3.64-3.66 (m, 2H), 3.53-3.57 (m, 2H).

4.1.49 1-(5-Benzyl-1,3,4-thiadiazol-2-yl)-3-(2-chloroethyl)urea (76)

The title compound was prepared from 2-amino-5-benzyl-1,3,4-thiadiazole (47) (0.5 g, 2.6 mmole) and 2-chloroethyl isocyanate (61) (2.2 mL, 2.9 mmole) following the same method as described for the synthesis of compound (69) to obtain the desired product as white solid. (0.7 g, 90.8 %). m.p. 140-42 °C.

Anal.:

TLC :R_f 0.48 (EtOAc).

IR (KBr, cm^{-1}) :3383, 2980, 1697, 1587, 1448, 1323, 1244, 1057, 752, 700.

4.1.50 1-(2-Chloroethyl)-3-[5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl]urea (77)

The title compound was prepared from 2-amino-5-(4-methoxyphenyl)-1,3,4-thiadiazole (48) (1.5 g, 7.2 mmole) and 2-chloroethyl isocyanate (61) (6.2 mL, 7.9 mmole) following the method described for the synthesis of compound (69) to obtain the desired product as white solid. (1.7 g, 75.6 %). m.p. 151-53 °C.

Anal.:

TLC :R_f 0.28 (EtOAc).

IR(KBr, cm^{-1}) :3379, 1703, 1606, 1450, 1251, 1174.

4.1.51 1-(2-Chloroethyl)-3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]urea (78)

The title compound was prepared from 2-amino-5-(4-methoxybenzyl)-1,3,4-thiadiazole (49) (0.9 g, 4.3 mmole) and 2-chloroethyl isocyanate (61) (4.0 mL, 5 mmole) following the method described for the synthesis of compound (69) to obtain the desired product as off white solid. (1.4 g, 100 %). m.p. 140-42 °C.

Anal.:

TLC :R_f 0.25 (EtOAc).

IR (KBr, cm^{-1}) :3450, 1639, 1606, 1512, 1246, 1176, 1035.

4.1.52 1-(2-Chloroethyl)-3-(4,5-diphenyl-2-thiazolyl)urea (79)

The title compound was prepared from 4,5-diphenyl-2-thiazolylamine (53) (1.1 g, 4.6 mmole) and 2-chloroethyl isocyanate (61) (4.3 mL, 5.5 mmole) following the method described for the synthesis of compound (69). After the reaction was over solvent was removed from the reaction mixture under vacuum to obtain the desired product as oil. (1.6 g, 100 %).

Anal.:

TLC :R_f (30 % EtOAc in n-hexane).

4.1.53 1-(2-Chloroethyl)-3-(4-*p*-tolyl-2-thiazolyl)urea (80)

The title compound was prepared from 4-(*p*-tolyl)-2-thiazolylamine (**54**) (4.0 g, 21 mmole) and 2-chloroethyl isocyanate (**61**) (18 mL, 23 mmole) following the same method as described for the synthesis of compound (**69**) to obtain the desired product as off white solid. (4.6 g, 74.1 %). m.p. 174-75 °C.

Anal.:

TLC :R_f 0.31 (30 % EtOAc in n-hexane).

PMR (DMSO-d_6) :10.41 (bs, 1H), 7.63-7.60 (m, 2H), 7.17-7.19 (m, 2H), 7.15 (s, 1H), 6.98 (bs, 1H), 3.61-3.65 (m, 2H), 3.47-3.49 (m, 2H), 2.36 (s, 3H).

4.1.54 1-(2-Chloroethyl)-3-[4-(4-methoxythiobenzyloxy)phenyl]urea (81)

The title compound was prepared from 1-(4-aminothiophenoxymethyl)-1-methoxybenzene (**56**) (1.1 g, 4.5 mmole) and 2-chloroethyl isocyanate (**61**) (3.5 mL, 4.5 mmole) following the same method as described for the synthesis of compound (**69**) to obtain the desired product as off white solid. (1.2 g, 76.0 %). m.p. 158-59 °C.

Anal.:

TLC :R_f 0.43 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3304, 1637, 1604, 1514, 1253, 1033, 819, 744.

4.1.55 1-(2-Chloroethyl)-3-phenylurea (82)

The title compound was prepared from aniline (**63**) (0.71 mL, 8 mmole) and 2-chloroethyl isocyanate (**61**) (6.1 mL, 8 mmole) following the method described for the synthesis of compound (**69**) to obtain the desired product as off white solid. (0.8 g, 52.9 %). m.p.125-26 °C.

Anal.:

TLC :R_f 0.80 (50 % EtOAc in n-hexane).

UV(MeOH) :239.5 (log ε 4.33)

IR (KBr, cm^{-1}) :3323, 1639, 1596, 1500, 1444, 1244.

PMR ($CDCl_3$) :7.30-7.33 (m, 4H), 7.10-7.14 (m, 1H), 6.55 (bs, 1H), 5.30 (bs, 1H), 3.65-3.68 (m, 2H), 3.62-3.65 (m, 2H), 3.58-3.62 (m, 2H).

4.1.56 1-(2-Chloroethyl)-3-(4-methoxyphenyl)urea (83)

The title compound was prepared from 4-methoxyaniline (**64**) (5 g, 40 mmole) and 2-chloroethyl isocyanate (**61**) (31.8 mL, 40 mmole) following the method described for the synthesis of compound (**69**) to obtain the desired product as off white solid. (8.5 g, 98.1 %). m.p. 157-60 °C.

Anal.:

TLC	:R_f 0.59 (70 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3301, 1629, 1596, 1508, 1454, 1305, 1238, 1037.
PMR (DMSO-d_6)	:8.00 (bs, 1H), 7.26-7.30 (d, 2H), 6.78-6.81 (d, 2H), 6.16 (bs, 1H), 3.76 (s, 3H), 3.62-3.65 (m, 2H), 3.52-3.56 (m, 2H).

4.1.57 1-(2-Chloroethyl)-3-(3,4-dimethoxyphenyl)urea (84)

The title compound was prepared from 3,4-dimethoxyaniline (**65**) (5 g, 33 mmole) and 2-chloroethyl isocyanate (**61**) (25.5 mL, 33 mmole) following the method described for the synthesis of compound (**69**) to obtain the desired product as off white solid. (7 g, 82.0 %). m.p. 108-10 °C.

Anal.:

TLC	:R_f 0.35 (70 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3299, 1627, 1596, 1514, 1409, 1267, 1172, 1032.
PMR ($CDCl_3$)	:6.99-7.00 (d, 1H, J = 2.0 Hz), 6.79-6.81 (d, 1H, J = 8.48 Hz), 6.71-6.74 (dd, 1H, J = 2.04 Hz & 8.44 Hz), 5.45 (bs, 1H), 3.86 (s, 6H), 3.63-3.65 (m, 2H), 3.55-3.59 (m, 2H).

4.1.58 1-(2-Chloroethyl)-3-(3,4,5-trimethoxyphenyl)urea (85)

The title compound was prepared from 3,4,5-trimethoxyaniline (**66**) (2.8 g, 15.6 mmole) and 2-chloroethyl isocyanate (**61**) (12.2 mL, 15.6 mmole) following the method described for the synthesis of compound (**69**) to obtain the desired product as off white solid. (4.1 g, 91.0 %). m.p. 155-56 °C.

Anal.:

TLC	:R_f 0.77 (EtOAc).
IR (KBr, cm^{-1})	:3367, 3307, 2974, 1647, 1596, 1508, 1413, 1299, 1232, 1172, 1130.
PMR (DMSO-d_6)	:8.65 (bs, 1H), 6.8 (s, 2H), 6.38-6.40 (t, 1H), 3.73 (s, 6H), 3.68-3.72 (m, 2H), 3.64 (s, 3H), 3.43-3.49 (m, 2H).

4.1.59 1-(4-Benzyloxyphenyl)-3-(2-chloroethyl)urea (86)

4-Benzyloxyaniline hydrochloride (**67**) (3.6 g, 15 mmole) was supended in DCM (10 mL) and cooled to 0-5 °C. Triethylamine (3.3 mL, 23 mmole) was added to the above suspension drop-wise and the reaction mixture was stirred for 30 minutes at RT. 2-Chloroethyl isocyanate (**61**) (12.2 mL) was added to the above reaction mixture and it was stirred for 1 hour. Solvent was removed under vacuum and dil. HCl (10 %, 100 mL) was added to the slurry so obtained. The solid obtained was filtered and dried to afford the desired product as white solid. (2.4 g, 52.5 %). m.p. 168-70 °C.

Anal.:

TLC	:R_f 0.50 (50 % EtOAc in n-hexane).
UV (MeOH)	:244.0 nm (log ε 4.28).
IR (KBr, cm^{-1})	:3310, 1639, 1600, 1508, 1382, 1236, 1006.
PMR (DMSO-d_6)	:8.46 (bs, 1H), 7.40-7.44 (m, 2H), 7.36-7.38 (m, 2H), 7.31-7.33 (m, 1H), 7.27-7.29 (m, 2H), 6.88-6.90 (m, 2H), 6.29-6.33 (t, 1H), 5.03 (s, 2H), 3.62-3.65 (m, 2H), 3.35-3.41 (m, 2H).

4.1.60 1-(2-Chloroethyl)-3-(4-hydroxyphenyl)urea (87)

4-Aminophenol (**68**) (1g, 8 mmole) was suspended in a mixture of THF (10 mL) and benzene (10 mL). Drop-wise 2-chloroethyl isocyanate (**61**) (16.1 mL, 8 mmole) was added to the above suspension and the reaction mixture was heated to reflux for 3 hours. The solvent was removed from the reaction mixture in vacuum and the remaining mass was suspended in ice-water (5 mL). Concentrated hydrochloric acid was added drop-wise to the above suspension to adjust the pH to 2 and the solid so obtained was filtered quickly and dried to afford the title product as off-white solid. (1.9 g, 87.6 %). m.p. 135-37 °C.

Anal.:

TLC	:R_f 0.68 (EtOAc).
IR (KBr, cm^{-1})	:3307, 3031, 1635, 1585, 1508, 1465, 1238, 835.

4.1.61 1-(2-Chloroethyl)-3-[4-(4-nitrobenzyloxy)phenyl]urea (88)

1-(2-Chloroethyl)-3-(4-hydroxyphenyl)urea (**87**) (0.5 g, 2.1 mmole) was dissolved in dry DMF (2 mL). 4-Nitrobenzyl bromide (**165**) (0.45 g, 2.1 mmole) and potassium carbonate (0.63 g, 4.6 mmole) was added to the above solution under stirring. The

reaction mixture was stirred for 30 minutes at 20 °C. To the reaction mixture aqueous sodium hydroxide solution (10 %, 30 mL) was added under stirring. The precipitate so obtained was filtered and dried. The crude product was crystallized from methanol to afford the pure desired product. (0.5 g, 62.2 %), m.p. 191-93 °C.

Anal.:

TLC	:R_f 0.31 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3301, 1629, 1595, 1527, 1515, 1452, 1344, 1244, 1174, 1109, 1047, 835, 736.
PMR ($CDCl_3$)	:8.20-8.23 (d, 2H), 8.15 (bs, 1H), 7.61-7.64 (d, 2H), 7.30-7.32 (d, 2H), 6.85-6.87 (d, 2H), 6.22-6.24 (t, 1H), 5.14 (s, 2H), 3.62-3.65 (m, 2H), 3.51-3.55 (m, 2H).

4.1.62 1-[4-(4-Methoxybenzyloxy)phenyl]imidazolidin-2-one (89)

1-(2-Chloroethyl)-3-[4-(4-methoxybenzyloxy)phenyl]urea (**69**) (0.8 g, 2.3 mmole) was dissolved in dry THF (10 mL) and cooled to 0-5 °C. Sodium hydride (0.2 g, 4.6 mmole) was added to the above solution in fractions at such a rate that the temperature of the reaction mixture did not rise above 10 °C. After the addition was over the reaction mixture was stirred at RT (about 30 °C) for 1 hour. The reaction mixture was poured into ice-water (150 mL) and the solid so appeared was filtered and dried to get the title compound as white solid. (0.5 g, 72.9 %). m.p. 192-93 °C.

Anal.:

TLC	:R_f 0.64 (70 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3265, 2912, 1681, 1516, 1246, 1020, 827.
PMR (DMSO-d_6)	:7.91 (bs, 1H), 7.40-7.46 (m, 2H), 7.33-7.38 (m, 2H), 7.21-7.23 (m, 1H), 6.85-6.93 (m, 3H), 4.96 (s, 2H), 3.74-3.84 (m, 5H), 3.30-3.35 (m, 2H).

4.1.63 1-[4-(2-Pyridinylmethoxy)phenyl]imidazolidin-2-one (90)

The title compound was prepared from 1-(2-chloroethyl)-3-[4-(2-pyridinyl-methoxy)phenyl]urea (**70**) (1.7 g, 5.6 mmole) and sodium hydride (0.3 g, 8.3 mmole) following the method described for the synthesis of compound (**89**) to obtain the desired product as off white solid. (1.2 g, 81.1 %). m.p. 184-85 °C.

Anal.:

TLC	:R_f 0.13 (50 % EtOAc in n-hexane).
UV (MeOH)	:248.5 nm (log ε 4.38).

PMR ($CDCl_3$) :8.58-8.60 (m, 1H), 7.68-7.72 (m, 1H), 7.50-7.52 (m, 1H), 7.40-7.44 (m, 2H), 7.20-7.23 (m, 1H), 6.95-6.99 (m, 2H), 5.19 (s, 2H), 4.95 (bs, 1H), 3.87-3.91 (m, 2H), 3.53-3.57 (m, 2H).

4.1.64 1-[4-(4-Biphenylmethoxy)phenyl]imidazolidin-2-one (91)

The title compound was prepared from 1-[4-(4-biphenylmethoxy)phenyl]-3-(2-chloroethyl)urea (71) (1.5 g, 3.9 mmole) and sodium hydride (0.4 g, 7.8 mmole) following the method described for the synthesis of compound (89) to obtain the desired product as off white solid. (1.3 g, 98.0 %). m.p. 262-63 °C.

Anal.:

TLC :R_f 0.17 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3257, 2924, 1681, 1516, 1246, 1153, 1016, 825.

4.1.65 1-[4-(2-Isobutyl-4-quinolinylmethoxy)phenyl]imidazolidin-2-one (92)

The title compound was prepared from 1-(2-chloroethyl)-3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]urea (72) (2.4 g, 5.8 mmole) and sodium hydride (0.6 g, 11.6 mmole) following the method described for the synthesis of compound (89). The crude product thus obtained was purified by column chromatography over neutral alumina using 10 - 70 % ethyl acetate in n-hexane as eluant to obtain the desired product as off white solid. (0.5 g, 23 %). m.p. 154-55 °C.

Anal.:

TLC :R_f 0.39 (70 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3242, 2955, 1685, 1606, 1516, 1292, 1240, 1024, 827.

PMR (DMSO-d_6) :8.00-8.04 (m, 2H), 7.80 (s, 1H), 7.69-7.73 (m, 1H), 7.54-7.57 (m, 1H), 6.44 (bs, 1H), 5.51 (s, 2H), 3.85-3.89 (m, 2H), 3.48-3.50 (m, 2H), 2.82-2.84 (d, 2H), 2.14-2.21 (m, 1H), 0.95-0.97 (d, 6H).

4.1.66 1-[4-(2-Ethyl-4-quinolinylmethoxy)phenyl]imidazolidin-2-one (93)

The title compound was prepared from 1-(2-chloroethyl)-3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]urea (73) (0.8 g, 2.1 mmole) and sodium hydride (0.2 g, 4.2 mmole) following the same method as described for the synthesis of compound (89) to obtain the desired product as off white solid. (0.6 g, 82.3 %). m.p. 159-61 °C.

Anal.:

TLC	:R_f 0.17 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3209, 2964, 1701, 1512, 1487, 1267, 1188, 1022, 825.

4.1.67 1-[4-(2-Phenyl-4-quinolinylmethoxy)phenyl]imidazolidin-2-one (94)

The title compound was prepared from 1-(2-chloroethyl)-3-[4-(2-phenyl4-quinolinylmethoxy)phenyl]urea (**74**) (1.3 g, 3 mmole) and sodium hydride (0.3 g, 6 mmole) following the method described for the synthesis of compound (**89**) to obtain the desired product as off white solid. (1.0 g, 84.3 %). m.p. 195-97 °C.

Anal.:

TLC	:R_f 0.48 (EtOAc).
UV (MeOH)	:254.0 nm (log ε 4.66).
PMR ($CDCl_3$)	:8.22-8.24 (m, 1H), 8.15-8.17 (m, 2H), 8.04 (s, 1H), 7.97-7.99 (m, 1H), 7.74-7.78 (m, 1H), 7.44-7.60 (m, 6H), 7.03-7.07 (m, 2H), 5.57 (s, 2H), 4.72 (bs, 1H), 3.89-3.93 (m, 2H), 3.54-3.58 (m, 2H).

4.1.68 1-[4-(1-Naphthylmethoxy)phenyl]imidazolidin-2-one (95)

The title compound was prepared from 1-(2-chloroethyl)-3-[4-(1-naphthylmethoxy)phenyl]urea (**75**) (0.9 g, 2.5 mmole) and sodium hydride (0.2 g, 3.8 mmole) following the same method as described for the synthesis of compound (**89**) to obtain the desired product as off white solid. (0.8 g, 98.1 %). m.p. 190-91 °C.

Anal.:

TLC	:R_f 0.64 (70 % EtOAc in n-hexane).
PMR ($CDCl_3$)	:8.04-8.07 (m, 1H), 7.87-7.91 (m, 2H), 7.59-7.61 (m, 1H), 7.52-7.55 (m, 2H), 7.44-7.49 (m, 3H), 6.99-7.02 (m, 2H), 6.29 (bs, 1H), 5.46 (s, 2H), 3.85-3.89 (m, 2H), 3.49-3.53 (m, 2H).

4.1.69 1-(5-Benzyl-1,3,4-thiadiazol-2-yl)imidazolidin-2-one (96)

The title compound was prepared from 1-(5-benzyl-1,3,4-thiadiazol-2-yl)-3-(2-chloroethyl)urea (**76**) (0.6 g, 2 mmole) and sodium hydride (0.2 g, 4 mmole) following the method as described for the synthesis of compound (**89**) to obtain the desired product as off white solid. (0.2 g, 95.3 %). m.p. 136-38 °C.

Anal.:

TLC : R_f 0.24 (EtOAc).

IR (KBr, cm^{-1}) :3250, 2924, 1678, 1514, 1479, 1263, 1128, 1049, 752, 705.

4.1.70 1-[5-(4-Methoxyphenyl)-1,3,4-thiadiazol-2-yl]imidazolidin-2-one (97)

The title compound was prepared from 1-(2-chloroethyl)-3-[5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl]urea (77) (1.2 g, 3.8 mmole) and sodium hydride (0.3 g, 5.8 mmole) following the method described for the synthesis of compound (89) to obtain the desired product as off white solid. (1 g, 95.3 %). m.p. 215-17 °C.

Anal.:

TLC :R_f 0.20 (EtOAc).

IR (KBr, cm^{-1}) :3097, 2924, 1680, 1510, 1462, 1255, 1174, 1030, 827, 715.

4.1.71 1-[5-(4-Methoxybenzyl)-1,3,4-thiadiazol-2-yl]imidazolidin-2-one (98)

The title compound was prepared from 1-(2-chloroethyl)-3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]urea (78) (1.4 g, 4.3 mmole) and sodium hydride (0.3 g, 8.5 mmole) following the method described for the synthesis of compound (89) to obtain the desired product as off white solid. (1 g, 81.3 %). m.p. 225-27 °C.

Anal.:

TLC :R_f 0.15 (EtOAc).

IR (KBr, cm^{-1}) :3209, 2924, 1697, 1514, 1247, 1182, 1031, 715.

4.1.72 1-(4,5-Diphenyl-2-thiazolyl)imidazolidin-2-one (99)

The title compound was prepared from 1-(2-chloroethyl)-3-(4,5-diphenyl-2-thiazolyl)urea (79) (1.6 g, 4.6 mmole) and sodium hydride (0.3 g, 7 mmole) following the same method as described for the synthesis of compound (89) to obtain the desired product as off white solid. (1.1 g, 74.5 %). m.p. 204-06 °C.

Anal.

TLC :R_f 0.36 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3223, 1691, 1516, 1271, 1072, 752, 696.

4.1.73 1-(4-*p*-Tolyl-2-thiazolyl)imidazolidin-2-one (100)

The title compound was prepared from 1-(2-chloroethyl)-3-(4-*p*-tolyl-2-thiazolyl)urea (80) (4.6 g, 15.5 mmole) and sodium hydride (1.5 g, 31.1 mmole) following the method described for the synthesis of compound (89) to obtain the desired product as off white solid. (3.5 g, 87.2 %). m.p. 228-30 °C.

Anal.:

TLC	:R_f 0.11 (30 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3236, 1685, 1516, 1477, 1267, 821, 734.

4.1.74 1-[4-(4-Methoxythiobenzyloxy)phenyl]imidazolidin-2-one (101)

The title compound was prepared from 1-(2-chloroethyl)-3-[4-(4-methoxythiobenzyloxy)phenyl]urea (**81**) (1.1 g, 3.1 mmole) and sodium hydride (0.3 g, 6.2 mmole) following the method described for the synthesis of compound (**89**) to obtain the desired product as off white solid. (1.0 g, 100 %). m.p. 190-93 °C.

Anal.:

TLC	:R_f 0.14 (50% EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3265, 2924, 1685, 1608, 1500, 1483, 1251, 1151, 1031, 835, 812.

4.1.75 1-Phenylimidazolidin-2-one (102)

The title compound was prepared from 1-(2-chloroethyl)-3-phenylurea (**82**) (2.4 g, 12 mmole) and sodium hydride (0.9 g, 18 mmole) following the method (only change being DMF was used as solvent instead of THF) described for the synthesis of compound (**89**) to obtain the desired product as white solid. (1.8 g, 92.6 %). m.p. 156-58 °C.

Anal.:

TLC	:R_f 0.25 (50 % EtOAc in n-hexane).
UV (MeOH)	:245.0 nm (log ε 3.99).
IR (KBr, cm^{-1})	:3259, 2916, 1683, 1598, 1481, 1323, 1151.
PMR ($CDCl_3$)	:7.53-7.55 (m, 2H), 7.32-7.36 (m, 2H), 7.04-7.07 (m, 1H), 4.95 (bs, 1H), 3.94-3.97 (m, 2H), 3.56-3.60 (m, 2H).

4.1.76 1-(4-Methoxyphenyl)imidazolidin-2-one (103)

The title compound was prepared from 1-(2-chloroethyl)-3-(4-methoxyphenyl)urea (**83**) (6 g, 26.3 mmole) and sodium hydride (1.6 g, 39.5 mmole) following the method described for the synthesis of compound (**102**) to obtain the desired product as white solid. (4.7 g, 93.2 %). m.p. 212-14 °C.

Anal.:

TLC	:R_f 0.34 (EtOAc).
IR (KBr, cm^{-1})	:3257, 2923, 1681, 1515, 1483, 1328, 1249, 1182, 1151, 1035, 831.

PMR (DMSO-d_6) :7.41-7.44 (d, 2H), 6.85-6.87 (d, 2H), 6.05 (bs, 1H), 3.85-3.89 (m, 2H), 3.78 (s, 3H), 3.50-3.54 (m, 2H).

4.1.77 1-(3,4-Dimethoxyphenyl)imidazolidin-2-one (104)

The title compound was prepared from 1-(2-chloroethyl)-3-(3,4-dimethoxyphenyl)urea (**84**) (7 g, 27 mmole) and sodium hydride (1.6 g, 41 mmole) following the method described for the synthesis of compound (**102**) to obtain the desired product as white solid. (4.5 g, 75.0 %). m.p. 168 °C.

Anal.:

TLC :R_f 0.43 (EtOAc).

IR (KBr, cm^{-1}) :3361, 2920, 1697, 1458, 1425, 1249, 1195, 1134, 1020.

PMR ($CDCl_3$) :7.51-7.50 (d, 1H, J = 2.52 Hz), 6.81-6.84 (d, 1H, J = 8.68 Hz), 6.70-6.73 (dd, 1H, J = 2.56 Hz & 8.68 Hz), 5.15 (bs, 1H), 3.89-3.93 (m, 5H), 3.86 (s, 3H), 3.54-3.58 (m, 2H).

4.1.78 1-(3,4,5-Trimethoxyphenyl)imidazolidin-2-one (105)

The title compound was prepared from 1-(2-chloroethyl)-3-(3,4,5-trimethoxyphenyl)urea (**85**) (4 g, 13.8 mmole) and sodium hydride (1 g, 21 mmole) following the same method as described for the synthesis of compound (**102**) to obtain the desired product as white solid. (3 g, 86.2 %). m.p. 190-92 °C.

Anal.:

TLC :R_f 0.34 (EtOAc).

UV (MeOH) :253.0 nm (log ε 4.10).

IR (KBr, cm^{-1}) :3371, 2895, 1697, 1465, 1271, 1126, 1076, 1001, 831.

PMR (DMSO-d_6) :6.92 (bs, 1H), 6.88 (s, 2H), 3.82-3.86 (m, 2H), 3.74 (s, 6H), 3.60 (s, 3H), 3.35-3.39 (m, 2H).

4.1.79 1-(4-Benzyloxyphenyl)imidazolidin-2-one (106)

The title compound was prepared from 1-(4-benzyloxyphenyl)-3-(2-chloroethyl)urea (**86**) (2 g, 6.5 mmole) and sodium hydride (0.4 g, 9.8 mmole) following the method described for the synthesis of compound (**102**) to obtain the desired product as white solid. (1.7 g, 99.3 %). m.p. 216-19 °C.

Anal.:

TLC :R_f 0.24 (50 % EtOAc in n-hexane).

UV (MeOH) :248.0 nm (log ε 4.32).

IR (KBr, cm^{-1}) :3259, 1681, 1514, 1245, 1150, 1004, 827.

PMR ($CDCl_3$) :7.40-7.48 (m, 4H), 7.35-7.39 (m, 2H), 7.29-7.33 (m, 1H), 6.91-6.94 (m, 2H), 6.29 (bs, 1H), 5.04 (s, 2H), 3.83-3.89 (m, 2H), 3.47-3.53 (m, 2H).

4.1.80 1-[4-(4-Nitrobenzyloxy)phenyl]imidazolidin-2-one (107)

The title compound was prepared from 1-(2-chloroethyl)-3-[4-(4-nitrobenzyloxy)phenyl]urea (88) (2.2 g, 6 mmole) and sodium hydride (0.4 g, 12 mmole) following the method described for the synthesis of compound (89) to obtain the desired product as white solid. (1.7 g, 85.2 %). m.p. 200-01 °C.

Anal.:

TLC :R_f 0.37 (EtOAc).

IR (KBr, cm^{-1}) :3273, 2929, 1693, 1583, 1514, 1433, 1350, 1257, 1232, 1186, 1051, 827.

4.1.81 Ethyl 2-{3-[4-(4-methoxybenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (109)

1-[4-(4-Methoxybenzyloxy)phenyl]imidazolidin-2-one (89) (0.8 g, 2.5 mmole) was dissolved in dry THF (10 mL) and cooled to 0 – 5 °C. Sodium hydride (0.34 g, 7.5 mmole) was added at this temperature to the reaction mixture. The reaction mixture was refluxed for 2 hours. Ethyl 2-bromopropionate (108) (0.66 mL, 5.0 mmole) was added to the reaction mixture drop-wise and it was further refluxed for 2 hours. The reaction mixture was allowed to cool to RT and poured into ice-water (100 mL). The aqueous solution was extracted with chloroform (4 x 25 mL); the combined organic layer was dried over anhydrous sodium sulphate and the solvent removed to get crude oily product. The crude product thus obtained was purified by column chromatography over silica gel using 10 - 20 % ethyl acetate in n-hexane as eluant to afford the desired compound as semi-solid. (0.3 g, 64.2 %).

Anal.:

TLC :R_f 0.55 (50 % EtOAc in n-hexane).

4.1.82 Ethyl 2-{2-oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propionate (110)

The title compound was prepared from 1-[4-(2-pyridinylmethoxy)phenyl]imidazolidin-2-one (90) (1.5 g, 5.6 mmole), sodium hydride (0.4

g, 11 mmole) and ethyl 2-bromopropionate (108) (1.4 mL, 11 mmole) following the method described for the synthesis of compound (109). The crude product thus obtained was crystallized from a mixture of ethyl acetate in n-hexane to obtain the desired product as white solid. (1 g, 48.9 %). m.p. 80-83 °C.

Anal.:

TLC	:R_f 0.28 (50 % EtOAc in n-hexane).
PMR ($CDCl_3$)	:8.56-8.60 (m, 1H), 7.68-7.72 (m, 1H), 7.50-7.52 (m, 1H), 7.42-7.46 (m, 2H), 7.20-7.22 (m, 1H), 6.94-6.98 (m, 2H), 5.19 (s, 2H), 4.69-4.75 (q, 1H, J = 7.51 Hz), 4.16-4.21 (m, 2H), 3.76-3.86 (m, 2H), 3.61-3.68 (m, 1H), 3.48-3.54 (m, 2H), 1.45-1.47 (d, 3H, J = 7.48 Hz), 1.25-1.29 (t, 3H).

4.1.83 Ethyl 2-{3-[4-(4-biphenylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (111)

The title compound was prepared from 1-[4-(4-biphenylmethoxy)phenyl]imidazolidin-2-one (91) (0.7 g, 2.2 mmole), sodium hydride (0.2 g, 4.4 mmole) and ethyl 2-bromopropionate (108) (0.6 mL, 4.4 mmole) following the method described for the synthesis of compound (109). The crude product thus obtained was purified by column chromatography over silica gel using 30 % ethyl acetate in n-hexane as eluant to obtain the desired product as white solid. (0.3 g, 35.8 %). m.p. 163-64 °C.

Anal.:

TLC	:R_f 0.63 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:2982, 1739, 1689, 1514, 1278, 1242, 1182, 1014, 825, 744.

4.1.84 Ethyl 2-{3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (112)

The title compound was prepared from 1-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]imidazolidin-2-one (92) (0.5 g, 1.3 mmole), sodium hydride (0.3 g, 6.5 mmole) and ethyl 2-bromopropionate (108) (0.5 mL, 4 mmole) following the method described for the synthesis of compound (109). The crude product thus obtained was purified by column chromatography over neutral alumina using 20 – 30 % ethyl acetate in n-hexane as eluant to obtain the desired product as white solid (0.3 g, 48.5 %). m.p. 122-23 °C.

Anal.:

TLC	:R_f 0.39 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:2953, 1739, 1689, 1518, 1278, 1245, 1182, 1076, 831, 769.

4.1.85 Ethyl 2-{3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl} propionate (113)

The title compound was prepared from 1-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]imidazolidin-2-one (93) (0.7 g, 2 mmole), sodium hydride (0.2 g, 4 mmole) and ethyl 2-bromopropionate (108) (0.5 mL, 4 mmole) following the same method as described for the synthesis of compound (109) to obtain the desired product as oil. (0.5 g, 56 %).

Anal.:

TLC	:R_f 0.53 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:2926, 1739, 1701, 1518, 1437, 1280, 1242, 1180, 1020, 835, 763.

4.1.86 Ethyl 2-{2-oxo-3-[4-(2-phenyl-4-quinolinmethoxy)phenyl]-1-imidazolidinyl}propionate (114)

The title compound was prepared from 1-[4-(2-phenyl-4-quinolinylmethoxy)-phenyl]imidazolidin-2-one (94) (0.2 g, 0.5 mmole), sodium hydride (0.05 g, 1 mmole) and ethyl 2-bromopropionate (108) (0.1 mL, 1 mmole) following the method described for the synthesis of compound (109). The only difference was that the reaction was carried out at RT instead of refluxing conditions. The crude product thus obtained was purified by column chromatography over neutral aluminium oxide using 30 % ethyl acetate in n-hexane as eluant to obtain the desired product as oil. (0.2 g, 61 %).

Anal.:

TLC	:R_f 0.32 (30 % EtOAc in n-hexane).

4.1.87 Ethyl 2-{3-[4-(1-naphthylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (115)

The title compound was prepared from 1-[4-(1-naphthylmethoxy)phenyl]imidazolidin-2-one (95) (0.8 g, 2.5 mmole), sodium hydride (0.3 g, 7.5 mmole) and ethyl 2-bromopropionate (108) (0.7 mL, 5 mmole) following the

method described for the synthesis of compound (114) to obtain the desired product as oil. (0.5 g, 48 %).

Anal.:

TLC :R_f 0.31 (30 % EtOAc in n-hexane).

4.1.88 Ethyl 2-[3-(5-benzyl-1,3,4-thiadiazol-2-yl)-2-oxo-1-imidazolidinyl]propionate (116)

The title compound was prepared from 1-(5-benzyl-1,3,4-thiadiazol-2-yl)imidazolidin-2-one (96) (0.2 g, 0.6 mmole), sodium hydride (0.06 g, 1.3 mmole) and ethyl 2-bromopropionate (108) (0.2 mL, 1.3 mmole) following the same method as described for the synthesis of compound (109) to obtain the desired product as oil. (0.2 g, 69.6 %).

Anal.:

TLC :R_f 0.49 (EtOAc).

4.1.89 Ethyl 2-{3-[5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionate (117)

The title compound was prepared from 1-[5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl]imidazolidin-2-one (97) (0.9 g, 3.3 mmole), sodium hydride (0.3 g, 6.5 mmole) and ethyl 2-bromopropionate (108) (0.8 mL, 6.5 mmole) following the method described for the synthesis of compound (109) to obtain the desired product as white solid. (0.7 g, 56.4 %). m.p. 145-47 °C.

Anal.:

TLC :R_f 0.35 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2924, 1741, 1712, 1602, 1519, 1433, 1276, 1255, 1180, 1074, 1030, 842, 742.

PMR ($CDCl_3$) :7.83-8.87 (d, 2H), 6.695-6.98 (d, 2H), 4.72-4.77 (q, 1H, J = 7.49 Hz), 4.22-4.32 (m, 1H), 4.20-4.17 (m, 3H), 3.85-3.80 (m, 4H), 3.66-3.72 (m, 1H), 1.53-1.51 (d, 2H, J = 7.52 Hz), 1.27-1.30 (t, 3H).

4.1.90 Ethyl 2-{3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionate (118)

The title compound was prepared from 1-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]imidazolidin-2-one (98) (0.3 g, 1 mmole), sodium hydride (0.08 g, 2 mmole) and

ethyl 2-bromopropionate (108) (0.3 mL, 2 mmole) following the method described for the synthesis of compound (109) to obtain the desired product as oil. (0.3 g, 77 %).

Anal.:

TLC :R_f 0.55 (EtOAc).

4.1.91 Ethyl 2-[3-(4,5-diphenyl-2-thiazolyl)-2-oxo-1-imidazolidinyl]propionate (119)

The title compound was prepared from 1-(4,5-diphenyl-2-thiazolyl)imidazolidin-2-one (99) (1 g, 3.1 mmole), sodium hydride (0.3 g, 6.2 mmole) and ethyl 2-bromopropionate (108) (0.8 mL, 6.2 mmole) following the method described for the synthesis of compound (114). The crude product thus obtained was purified by column chromatography over silica gel using 10 – 30 % ethyl acetate in n-hexane as eluant to obtain the desired product as off white solid. (0.7 g, 50 %).

Anal.:

TLC :R_f 0.40 (30 % EtOAc in n-hexane).

PMR (DMSO-d_6) :7.40-7.43 (m, 2H), 7.31-7.38 (m, 3H), 7.24-7.30 (m, 5H), 4.53-4.58 (q, 1H), 4.14-4.19 (m, 3H), 4.03-4.12 (m, 1H), 3.33-3.70 (m, 2H), 1.41-1.43 (d, 3H), 1.18-1.21 (t, 3H).

4.1.92 Ethyl 2-[2-oxo-3-(4-*p*-tolyl-2-thiazolyl)-1-imidazolidinyl]propionate (120)

The title compound was prepared from 1-(4-*p*-tolyl-2-thiazolyl)-imidazolidin-2-one (100) (2 g, 7.7 mmole), sodium hydride (0.9 g, 23 mmole) and ethyl 2-bromopropionate (108) (2 mL, 15.4 mmole) following the method described for the synthesis of compound (114). The crude product thus obtained was purified by column chromatography over silica gel using 10 – 30 % ethyl acetate in n-hexane as eluant to obtain the desired product as off white solid. (0.8 g, 28.9%). m.p. 110-13 °C.

Anal.:

TLC :R_f 0.55 (30 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2989, 1735, 1716, 1514, 1421, 1267, 1197, 1022, 825, 742.

4.1.93 Ethyl 2-{3-[4-(4-methoxythiobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl} propionate (121)

The title compound was prepared from 1-[4-(4-methoxythiobenzyloxy)phenyl]imidazolidin-2-one (101) (1 g, 3.2 mmole), sodium hydride (0.3 g, 6.3 mmole) and ethyl 2-bromopropionate (108) (0.8 mL, 6.3 mmole) following the

same method as described for the synthesis of compound (**114**) to obtain the desired product as white solid. (0.8 g, 60.4 %). m.p. 92-95 °C.

Anal.:

TLC	:R_f 0.49 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:2924, 1732, 1701, 1514, 1273, 1199, 1031, 842, 754.

4.1.94 Ethyl 2-(2-oxo-3-phenyl-1-imidazolidinyl)propionate (122)

The title compound was prepared from 1-phenylimidazolidin-2-one (**102**) (1.5g, 9.2 mmole), sodium hydride (0.6 g, 13.8 mmole) and ethyl 2-bromopropionate (**108**) (1.8 mL, 13.8 mmole) following the method (only change being DMF was used as solvent instead of THF) described for the synthesis of compound (**114**). The crude product so obtained was purified by column chromatography over silica gel using 20 % ethyl acetate in n-hexane as eluant to afford the title product as white solid. (0.8 g, 31.1 %). m.p. 85-87 °C.

Anal.:

TLC	:R_f 0. 83 (50 % EtOAc in n-hexane).
UV (MeOH)	:246.8 nm (log ε 4.12).
IR (KBr, cm^{-1})	:2950, 1747, 1699, 1600, 1508, 1415, 756.
PMR ($CDCl_3$)	:7.54-7.56 (m, 2H), 7.30-7.34 (m, 2H), 7.03-7.05 (m, 1H), 4.71-4.77 (q, 1H, J = 7.49 Hz), 4.16-4.22 (m, 2H), 3.80-3.92 (m, 2H), 3.64-3.70 (m, 1H), 3.50-3.56 (m, 1H), 1.46-1.48 (d, 3H, J = 7.48 Hz), 1.26-1.29 (t, 3H).

4.1.95 Ethyl 2-[3-(4-methoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (123)

The title compound was prepared from 1-(4-methoxyphenyl)imidazolidin-2-one (**103**) (4.5g, 23.4 mmole), sodium hydride (1.9 g, 46.8 mmole) and ethyl 2-bromopropionate (**108**) (6.1 mL, 46.8 mmole) following the method described for the synthesis of compound (**114**) to afford the title product as semi-solid. (3.0 g, 44.7 %).

Anal.:

TLC	:R_f 0. 54 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:2981, 1737, 1699, 1514, 1431, 1247, 1190, 1047, 829, 752.
PMR ($CDCl_3$)	:7.36-7.38 (d, 2H), 6.79-6.82 (d, 2H), 4.64-4.66 (q, 1H, J = 7.49 Hz), 4.09-4.15 (m, 2H), 3.70-3.80 (m, 5H), 3.55-3.61 (m, 1H), 3.43-3.47 (m, 1H), 1.38-1.40 (d, 3H, J = 7.52 Hz), 1.19-1.22 (t, 3H).

4.1.96 Ethyl 2-[3-(3,4-dimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (124)

The title compound was prepared from 1-(3,4-dimethoxyphenyl)imidazolidin-2-one (104) (2.2 g, 10 mmole), sodium hydride (0.6 g, 15 mmole) and ethyl 2-bromopropionate (108) (2.6 mL, 20 mmole) following the method described for the synthesis of compound (109) to afford the title product as semi-solid. (2.1 g, 65.8 %).

Anal.:

TLC	:R_f 0. 54 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:2920, 1731, 1681, 1519, 1417, 1250, 1139, 1076, 858, 763.
PMR ($CDCl_3$)	:7.65-7.66 (d, 1H, J = 2.52 Hz), 6.80-6.82 (d, 1H, J = 8.68 Hz), 6.63-6.66 (dd, 1Hz, J = 2.56 Hz & 8.72 Hz), 4.70-4.75 (q, 1H, J = 7.49 Hz), 4.17-4.22 (m, 2H), 3.87-3.91 (m, 4H), 3.85 (s, 3H), 3.79-3.82 (m, 1H), 3.65-3.69 (m, 1H), 3.53-3.65 (m, 1H), 1.46-1.48 (d, 3H, J = 7.48 Hz), 1.26-1.30 (t, 3H).

4.1.97 Ethyl 2-[3-(3,4,5-trimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (125)

The title compound was prepared from 1-(3,4,5-trimethoxyphenyl)imidazolidin-2-one (105) (4.7 g, 18.7 mmole), sodium hydride (1.5 g, 37.3 mmole) and ethyl 2-bromopropionate (108) (4.9 mL, 37.3 mmole) following the method described for the synthesis of compound (114). The crude product thus obtained was washed with n-hexane (5 x 20 mL) to afford the title product as white solid. (3.2 g, 48.2 %). m.p. 71-73 °C.

Anal.:

TLC	:R_f 0. 59 (70 % EtOAc in n-hexane).
UV (MeOH)	:255.5 nm (log ε 4.20).
IR (KBr, cm^{-1})	:2925, 1739, 1697, 1512, 1425, 1271, 1178, 1072, 858, 763.
PMR ($CDCl_3$)	:6.85 (s, 2H), 4.69-4.75 (q, 1H, J = 7.49 Hz), 4.16-4.22 (q, 2H, J = 7.14 Hz), 3.88-3.92 (m, 8H), 3.86 (s, 3H), 3.79-3.84 (m, 1H), 3.58-3.74 (m, 1H), 1.47-1.48 (d, 3H, J = 7.48 Hz), 1.26-1.30 (t, 3H, J = 7.16 Hz).

4.1.98 Ethyl 2-[3-(4-benzyloxyphenyl)-2-oxo-1-imidazolidinyl]propionate (126)

The title compound was prepared from 1-(4-benzyloxyphenyl)imidazolidin-2-one (106) (1.5 g, 5.6 mmole), sodium hydride (0.5 g, 11.0 mmole) and ethyl 2-

bromopropionate (108) (1.4 mL, 11.0 mmole) following the method described for the synthesis of compound (122). The crude product thus obtained was purified by column chromatography over silica gel using 20 % ethyl acetate in n-hexane as eluant to afford the title product as white solid. (1.1 g, 53.3 %). m.p. 102-04 °C.

Anal.:

TLC	:R_f 0.82 (50 % EtOAc in n-hexane).
UV (MeOH)	:250.0 nm (log ε 4.32).
IR (KBr, cm^{-1})	:2985, 1732, 1685, 1519, 1438, 1280, 1242, 1008, 831, 738.
PMR ($CDCl_3$)	:7.45-7.48 (m, 4H), 7.41-7.42 (m, 2H), 7.33-7.35 (m, 1H), 6.95-6.99 (m, 2H), 5.06 (s, 2H), 4.71-4.77 (q, 1H, J = 7.50 Hz), 4.18-4.24 (m, 2H), 3.82-3.88 (m, 2H), 3.66-3.70 (m, 1H), 3.51-3.56 (m, 1H), 1.47-1.49 (d, 3H , J = 7.60 Hz), 1.28-1.31 (t, 3H).

4.1.99 Ethyl 2-{3-[4-(4-nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (127)

The title compound was prepared from 1-[4-(4-nitrobenzyloxy)phenyl]imidazolidin-2-one (107) (1.5 g, 4.8 mmole), sodium hydride (0.4 g, 9.6 mmole) and ethyl 2-bromopropionate (108) (1.2 mL, 9.6 mmole) following the method described for the synthesis of compound (122) to afford the title product as off white solid. (1.6 g, 80.7 %). m.p. 126-28 °C.

Anal.:

TLC	:R_f 0.47 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:2923, 1732, 1693, 1514, 1487, 1352, 1272, 1197, 1047, 835, 738.

4.1.100 2-{3-[4-(4-Methoxybenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionic acid (128)

Ethyl 2-{3-[4-(4-methoxybenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (109) (0.3 g, 0.7 mmole) was dissolved in methanol (5 mL). Sodium hydroxide (0.2 g, 3.7 mmole) was dissolved in distilled water (5 mL) and the solution was added to the above reaction mixture drop-wise with stirring at RT for 2 hours. Methanol was recovered from the reaction mixture and ice-water (20 mL) was added to it. The reaction mixture was acidified with conc. HCl (5 mL). The solid so appeared was filtered and dried. The crude

product so obtained was crystallized from methanol to afford the title compound. (0.2 g, 77.2 %). m.p. 159-60 °C.

Anal.:

TLC :R_f 0.14 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2900, 1749, 1658, 1490, 1444, 1282, 1244, 1180, 1008, 873, 752.

PMR (DMSO-d_6) :7.42-7.45 (m, 2H), 7.32-7.35 (m, 2H), 6.88-6.94 (m, 4H), 4.95 (s, 2H), 4.60-4.63 (q, 1H, J = 7.52 Hz), 3.80-3.86 (m, 5H), 3.65-3.69 (m, 1H), 3.51-3.55 (m, 1H), 1.45-1.47 (d, 3H, J = 7.48 Hz).

Calculated for $C_{20}H_{22}N_2O_5$: C, 64.85, H, 5.99, N, 7.56; Found C, 65.10, H, 6.29, N, 7.12 %.

4.1.101 2-{2-Oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propionic acid (129)

The title compound was prepared from ethyl 2-{2-oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propionate (110) (0.3 g, 0.8 mmole) and sodium hydroxide (0.07 g, 1.6 mmole) following the method described for the synthesis of compound (128). The crude solid thus obtained was purified by column chromatography over neutral aluminium oxide using ethyl acetate as eluant to afford the title product as white solid. (0.2 g, 73.3 %). m.p. 179-80 °C.

Anal.:

TLC :R_f 0.35 (70 % EtOAc in n-hexane).

UV (MeOH) :253.5 nm (log ε 3.91).

IR (KBr, cm^{-1}) :3444, 2980, 1752, 1652, 1506, 1436, 1250, 1134, 1027, 813, 744.

PMR (DMSO-d_6) :8.57-8.58 (m, 1H), 7.71-7.75 (m, 1H), 7.51-7.52 (m, 1H), 7.42-7.46 (m, 2H), 7.23-7.26 (m, 1H), 6.93-6.96 (m, 2H), 5.17 (s, 2H), 4.60-4.65 (q, 1H, J = 7.39 Hz), 3.77-3.85 (m, 2H), 3.65-3.68 (m, 1H), 3.50-3.54 (m, 1H), 1.45-1.47 (d, 3H, J = 7.48 Hz).

Calculated for $C_{18}H_{19}N_3O_4$: C, 63.33, H, 5.61, N, 12.31; Found C, 63.84, H, 5.98, N, 12.01 %.

4.1.102 2-{3-[4-(4-Biphenylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionic acid (130)

The title compound was prepared from ethyl 2-{3-[4-(4-biphenylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (**111**) (0.4 g, 0.9 mmole) and sodium hydroxide (0.07 g, 1.8 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.3 g, 80.12 %). m.p. 249-51 °C.

Anal.:

TLC	:R_f 0.24 (EtOAc).
UV (MeOH)	:254.0 nm (log ε 4.46).
IR (KBr, cm^{-1})	:3446, 2982, 1734, 1652, 1512, 1456, 1241, 1014, 826, 746.
PMR (DMSO-d_6)	:7.56-7.61 (m, 4H), 7.42-7.50 (m, 6H), 7.32-7.36 (m, 1H), 6.93-6.96 (m, 2H), 5.07 (s, 2H), 4.56-4.60 (q, 1H, J = 7.44 Hz), 3.76-3.83 (m, 2H), 3.65-3.67 (m, 1H), 3.49-3.50 (m, 1H), 1.43-1.45 (d, 3H, J = 7.44 Hz).

4.1.103 2-{3-[4-(2-Isobutyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionic acid (131)

The title compound was prepared from ethyl 2-{3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (**112**) (0.3 g, 0.6 mmole) and lithium hydroxide (0.1 g, 3.2 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.2 g, 69.9 %). m.p. 192-95 °C.

Anal.:

TLC	:R_f 0.55 (70 % EtOAc in n-hexane).
UV (MeOH)	:232.0 nm (log ε 4.84).
IR (KBr, cm^{-1})	:3483, 2981, 1748, 1652, 1512, 1487, 1248, 1075, 827, 750.
PMR (DMSO-d_6)	:8.02-8.04 (m, 1H), 7.78-7.82 (m, 1H), 7.62-7.66 (m, 1H), 7.57 (s, 1H), 7.43-7.52 (m, 3H), 7.01-7.04 (m, 2H), 5.56 (s, 2H), 4.64-4.70 (q, 1H, J = 7.50 Hz), 3.82-3.90 (m, 2H), 3.68-3.72 (m, 1H), 3.52-3.56 (m, 1H), 2.90-2.99 (m, 2H), 2.24-2.28 (m, 1H), 1.47-1.49 (d, 3H, J = 7.52 Hz), 0.98 -1.00 (d, 6H).

MS (m/z) :470.0 $(M+Na)^+$, 447.9 $(M+H)^+$.

4.1.104 2-{3-[4-(2-Ethyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionic acid (132)

The title compound was prepared from ethyl 2-{3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (**113**) (0.2 g, 0.4 mmole) and sodium hydroxide (0.1 g, 2.2 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.15 g, 89.5 %). m.p. 214-15 °C.

Anal.:

TLC :R_f 0.50 (70 % EtOAc in n-hexane).

UV (MeOH) :238.0 nm (log ε 4.54).

IR (KBr, cm^{-1}) :3446, 1730, 1637, 1514, 1485, 1442, 1242, 831, 746.

PMR (DMSO-d_6) :8.25-8.27 (m, 1H), 7.99-8.03 (m, 2H), 7.84-7.88 (m, 1H), 7.67 (s, 1H), 7.51-7.55 (m, 2H), 7.08-7.11 (m, 2H), 5.74 (s, 2H), 4.58-4.62 (q, 1H, *J* = 7.58 Hz), 3.81-3.91 (m, 2H), 3.65-3.71 (m, 1H), 3.51-3.58 (m, 1H), 3.42-3.46 (q, 2H, J = 7.61 Hz), 1.52-1.55 (t, 3H, *J* = 7.60 Hz), 1.46-1.48 (d, 3H, J = 7.52 Hz).

4.1.105 2-{3-[4-(2-Phenyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionic acid (133)

The title compound was prepared from ethyl 2-{3-[4-(2-phenyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (**114**) (0.15 g, 0.3 mmole) and sodium hydroxide (0.02 g, 0.6 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.1 g, 71.3 %). m.p. 120-22 °C.

Anal.:

TLC :R_f 0.22 (EtOAc).

UV (MeOH) :254.0 nm (log ε 4.56).

IR (KBr, cm^{-1}) :3442, 2980, 1751, 1652, 1512, 1419, 1237, 1181, 1076, 836, 756.

PMR ($CDCl_3$) :8.36-8.38 (m, 2H), 8.15-8.17 (m, 2H), 8.05 (s, 1H), 7.97-7.99 (m, 1H), 7.76-7.80 (m, 2H), 7.46-7.55 (m, 4H), 7.02-7.06 (m, 2H), 5.57 (s, 2H), 4.66-4.71 (q, 1H), 3.81-3.86 (m, 2H), 3.60-3.66 (m, 1H), 3.50-3.55 (m, 1H), 1.49-1.51 (d, 3H).

MS (m/z) :490.1 $(M+Na)^+$, 468.1 $(M+H)^+$, 422.1 $(M-COOH)^+$.

4.1.106 2-{3-[4-(1-Naphthylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionic acid (134)

The title compound was prepared from ethyl 2-{3-[4-(1-naphthylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (**115**) (0.3 g, 0.7 mmole) and lithium hydroxide (0.15 g, 3.5 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.15 g, 54.9 %). m.p. 187-90 °C.

Anal.:

TLC :R_f 0.41 (70 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2926, 1728, 1635, 1510, 1446, 1276, 1170, 835, 756.

PMR ($CDCl_3$) :7.84-7.87 (m, 1H), 7.84-7.91 (m, 2H), 7.59-7.60 (m, 1H), 7.54-7.57 (m, 2H), 7.45-7.53 (m, 3H), 7.00-7.03 (m, 2H), 5.47 (s, 2H), 4.62-4.66 (q, 1H, J = 7.52 Hz), 3.78-3.88 (m, 2H), 3.65-3.71 (m, 1H), 3.50-3.56 (m, 1H), 1.47-1.48 (d, 2H, J = 7.48 Hz).

MS (m/z) :412.8 $(M+Na)^+$, 390.9 $(M+H)^+$.

4.1.107 2-[3-(5-Benzyl-1,3,4-thiadiazol-2-yl)-2-oxo-1-imidazolidinyl]propionic acid (135)

The title compound was prepared from ethyl 2-[3-(5-benzyl-1,3,4-thiadiazol-2-yl)-2-oxo-1-imidazolidinyl]propionate (**116**) (0.6 g, 1.7 mmole) and sodium hydroxide (0.35 g, 8.6 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.3 g, 53.1 %). m.p. 171-73 °C.

Anal.:

TLC :R_f 0.20 (2 % MeOH in EtOAc).

PMR ($CDCl_3$) :7.24-7.32 (m, 5H), 4.67-4.70 (q, 1H), 4.31 (s, 2H), 4.19-4.23 (m, 1H), 4.09-4.16 (m, 1H), 3.72-3.78 (m, 1H), 3.60-3.64 (m, 1H), 1.49-1.51 (d, 3H).

4.1.108 2-{3-[5-(4-Methoxyphenyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionic acid (136)

The title compound was prepared from ethyl 2-{3-[5-(4-methoxy-phenyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionate (**117**) (0.5 g, 1.3 mmole) and sodium hydroxide (0.1 g, 2.6 mmole) following the method described for the synthesis of

compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.3 g, 69.5 %). m.p. 195-97 °C.

Anal.:

TLC	:R_f 0.19 (10 % MeOH in EtOAc).
IR (KBr, cm^{-1})	:3446, 2987, 1746, 1687, 1606, 1508, 1425, 1276, 1174, 1028, 831, 746.
PMR (DMSO-d_6)	:8.07-8.09 (d, 2H, J = 7.92 Hz), 7.53-7.56 (d, 2H, J = 7.89 Hz), 4.44-4.52 (q, 1H, J = 7.43 Hz), 4.05-4.17 (m, 2H), 3.80 (s, 3H), 3.63-3.68 (m, 2H), 1.40-1.43 (d, 3H, J = 7.44 Hz).
MS (m/z)	:349.0 $(M+H)^+$, 302.9 $(M-COOH)^+$.

4.1.109 2-{3-[5-(4-Methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionic acid (137)

The title compound was prepared from ethyl 2-{3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionate (**118**) (0.1 g, 0.26 mmole) and sodium hydroxide (0.02 g, 0.52 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.07 g, 79.7 %). m.p. 108-10 °C.

Anal.:

TLC	:R_f 0.29 (10 % MeOH in EtOAc).
PMR (DMSO-d_6)	:7.20-7.22 (d, 2H), 6.87-6.89 (d, 2H), 4.39-4.44 (q, 1H, J = 7.4 Hz), 4.17 (s, 2H), 4.08-4.13 (m, 1H), 4.01-4.07 (m, 1H), 3.71 (s, 3H), 3.60-3.68 (m, 2H), 1.36-1.37 (d, 3H, J = 7.5 Hz).

4.1.110 2-[3-(4,5-Diphenyl-2-thiazolyl)-2-oxo-1-imidazolidinyl]propionic acid (138)

The title compound was prepared from ethyl 2-[3-(4,5-diphenyl-2-thiazolyl)-2-oxo-1-imidazolidinyl]propionate (**119**) (0.2 g, 0.4 mmole) and sodium hydroxide (0.04 g, 0.1 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.15 g, 95.4 %). m.p. 180-83 °C.

Anal.:

TLC	:R_f 0.28 (80 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2933, 1745, 1718, 1581, 1462, 1431, 1282, 1157, 1030, 756, 694.

PMR (DMSO-d_6) :7.48-7.50 (m, 2H), 7.26-7.30 (m, 8H), 4.62-4.66 (q, 1H, *J* = 7.37 Hz), 4.26-4.31 (m, 1H), 4.17-4.20 (m, 1H), 3.76-3.81 (m, 1H), 3.67-3.70 (m, 1H), 1.52-1.54 (d, 3H, *J* = 7.40 Hz).

Calculated for $C_{21}H_{19}N_3O_3S$: C, 64.10, H, 4.87, N, 10.68; Found C, 63.84, H, 4.53, N, 10.09 %.

4.1.111 2-[2-Oxo-3-(4-*p*-tolyl-2-thiazolyl)-1-imidazolidinyl]propionic acid (139)

The title compound was prepared from ethyl 2-[2-oxo-3-(4-*p*-tolyl-2-thiazolyl)-1-imidazolidinyl]propionate (**120**) (0.2 g, 0.6 mmole) and lithium hydroxide (0.12 g, 2.8 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.09 g, 48.5 %). m.p. 222-24 °C.

Anal.:

TLC : R_f 0. 16 (60 % EtOAc in n-hexane).

UV (MeOH) :267.5 nm (log ε 4.13)
239.0 nm (log ε 4.26).

PMR (DMSO-d_6) :7.76-7.79 (d, 2H, J = 7.98 Hz), 7.47 (s, 1H), 7.19-7.22 (d, 2H, J = 7.95 Hz), 4.42-4.47 (q, 1H, *J* = 7.38 Hz), 4.05-4.18 (m, 2H), 3.60-3.67 (m, 2H), 2.31 (s, 3H), 1.38-1.41 (d, 3H, *J* = 7.38 Hz).

4.1.112 2-{3-[4-(4-Methoxythiobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionic acid (140)

The title compound was prepared from ethyl 2-{3-[4-(4-methoxythiobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (**121**) (0.3 g, 0.7 mmole) and sodium hydroxide (0.15 g, 3.6 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.12 g, 44.4 %). m.p. 156-58 °C.

Anal.:

TLC :R_f 0.61 (EtOAc).

UV (MeOH) :273.5 nm (log ε 3.98).

PMR ($CDCl_3$) :7.42-7.44 (d, 2H, *J* = 8.28 Hz), 7.26-7.28 (d, 2H, *J* = 8.36 Hz), 7.12-7.14 (d, 2H, *J* = 8.36 Hz), 6.78-6.80 (d, 2H, *J* = 8.32 Hz), 4.68-4.72 (q, 1H, J = 6.84 Hz), 3.99 (s, 2H), 3.80-3.84 (m, 2H), 3.77 (s, 3H), 3.62-3.66 (m, 1H), 3.51-3.55 (m, 1H), 1.50-1.52 (d, 3H, J = 6.72 Hz).

MS (m/z) :409.3 $(M+Na)^+$, 387.1 $(M+H)^+$, 341.1 $(M-COOH)^+$.

4.1.113 2-(2-Oxo-3-phenyl-1-imidazolidinyl)propionic acid (141)

The title compound was prepared from ethyl 2-(2-oxo-3-phenyl-1-imidazolidinyl)propionate (**122**) (0.1 g, 0.4 mmole) and lithium hydroxide (0.08 g, 1.9 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.07 g, 78.7 %). m.p.202-03 °C.

Anal.:

TLC :R_f 0.60 (70 % EtOAc in n-hexane).

UV (MeOH) :249.0 nm (log ε 4.46).

IR (KBr, cm^{-1}) :2953, 1753, 1658, 1598, 1485, 1444, 1286, 1188, 754.

PMR ($CDCl_3$) :7.52-7.56 (m, 2H), 7.31-7.35 (m, 2H), 7.04-7.07 (m, 1H), 4.69-4.74 (q, 1H, *J* = 7.49 Hz), 3.85-3.92 (m, 2H), 3.62-3.70 (m, 1H), 3.53-3.59 (m, 1H), 1.51-1.54 (d, 3H, *J* = 7.60 Hz).

$[\alpha]^{25}_D$:+0.06° (5 % MeOH)

4.1.114 2-[3-(4-Methoxyphenyl)-2-oxo-1-imidazolidinyl)propionic acid (142)

The title compound was prepared from ethyl 2-[3-(4-methoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**123**) (0.1 g, 0.4 mmole) and lithium hydroxide (0.07 g, 1.8 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.05 g, 55.1 %). m.p.145-47 °C.

Anal.:

TLC :R_f 0.69 (EtOAc.)

IR (KBr, cm^{-1}) :2925, 1741, 1654, 1515, 1488, 1444, 1282, 1251, 1178, 1033, 821, 750.

PMR ($CDCl_3$) :12.8 (bs, 1H), 7.48-7.50 (d, 2H), 6.92-6.95 (d, 2H), 4.34-4.38 (q, 1H, J = 7.48 Hz), 3.78-3.81 (m, 1H), 3.71-3.76 (m, 1H), 3.70 (s, 3H), 3.43-3.49 (m, 2H), 1.34-1.36 (d, 3H, J = 7.40 Hz).

Calculated for $C_{13}H_{16}N_2O_4$: C, 59.08, H, 6.10, N, 10.60; Found C, 58.84, H, 5.72, N, 10.49 %.

4.1.115 2-[3-(3,4-Dimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionic acid (143)

The title compound was prepared from ethyl 2-[3-(3,4-dimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**124**) (0.15 g, 0.5 mmole) and lithium hydroxide (0.1 g, 2.3 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.1 g, 73.9 %). m.p.204-06 °C.

Anal.:

TLC :R_f 0.17 (EtOAc).

UV (MeOH) :257.5 nm (log ε 4.21).
220.0 nm (log ε 4.32).

IR (KBr, cm^{-1}) :2922, 1745, 1652, 1517, 1488, 1448, 1284, 1193, 1024, 842, 750.

PMR ($CDCl_3$) :7.63-7.64 (d, 1H, J = 2.52 Hz), 6.81-6.83 (d, 1H, J = 8.72 Hz), 6.66-6.69 (dd, 1H, J = 2.56 Hz & 8.68 Hz), 4.63-4.69 (q, 1H, J = 7.50 Hz), 3.87 (s, 3H), 3.81-3.86 (m, 4H), 3.77-3.79 (m, 1H), 3.50-3.56 (m, 2H), 1.46-1.48 (d, 3H, J = 7.52 Hz).

4.1.116 2-[3-(3,4,5-Trimethoxyphenyl)-2-oxo-1-imidazolidin-1-yl]propionic acid (144)

The title compound was prepared from ethyl 2-[3-(3,4,5-trimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**125**) (0.2g, 0.6 mmole) and lithium hydroxide (0.1 g, 2.8 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.2 g, 94.7 %). m.p.157-60 °C.

Anal.:

TLC :R_f 0.53 (EtOAc).

UV (MeOH) :261.0 nm (log ε 4.23).
222.5 nm (log ε 4.54).

IR (KBr, cm^{-1}) :2999, 1753, 1654, 1510, 1427, 1276, 1236, 1124, 999, 802, 756.

PMR ($CDCl_3$) :6.80 (s, 2H), 4.68-4.74 (q, 1H, J = 7.49 Hz), 3.88-3.92 (m, 8H), 3.86 (s, 3H), 3.81-3.83 (m, 1H), 3.67-3.76 (m, 1H), 1.50 -1.52 (d, 3H, J = 7.52 Hz).

$[\alpha]^{25}_D$:+0.08° (3 % MeOH)

Calculated for $C_{15}H_{20}N_2O_6$: C, 55.55, H, 6.22, N, 8.64, Found C, 55.17, H, 5.97, N, 8.12 %.

4.1.117 2-[3-(4-Benzyloxyphenyl)-2-oxo-1-imidazolidinyl]propionic acid (145)

The title compound was prepared from ethyl 2-[3-(4-benzyloxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**126**) (0.1g, 0.3 mmole) and lithium hydroxide (0.06 g, 1.4 mmole) following the method described for the synthesis of compound (**128**). The crude solid thus obtained was crystallized from methanol to afford the pure title compound. (0.09 g, 97.8 %). m.p.214-17 °C.

Anal.:

TLC :R_f 0.24 (70 % EtOAc in n-hexane).

UV (MeOH) :251.0 nm (log ε 4.47).

IR (KBr, cm^{-1}) :2916, 1751, 1666, 1492, 1450, 1282, 1255, 1184, 1053, 819, 734.

PMR ($CDCl_3$) :7.43-7.58 (m, 4H), 7.36-7.41 (m, 2H), 7.31-7.33 (m, 1H), 7.03-7.06 (m, 2H), 5.04 (s, 2H), 4.62-4.68 (q, 1H, J = 7.48 Hz), 3.90-3.98 (m, 2H), 3.62-3.66 (m, 1H), 3.54-3.58 (m, 1H), 1.51-1.53 (d, 3H, J = 7.48 Hz).

4.1.118 2-{3-[4-(4-Nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionic acid (146)

The title compound was prepared from ethyl 2-{3-[4-(4-nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidin-1-yl}propionate (**127**) (0.1 g, 0.2 mmole) and lithium hydroxide (0.05 g, 1.2 mmole) following the method described for the synthesis of compound (**128**). The crude solid was crystallized from methanol to afford the pure title compound. (0.05 g, 54.0 %). m.p.167-69 °C.

Anal.:

TLC	:R_f 0.67 (EtOAc).
UV (MeOH)	:253.0 nm (log ε 4.35)
IR (KBr, cm^{-1})	:2923, 1724, 1695, 1515, 1483, 1433, 1352, 1251, 1110, 839, 734.
PMR ($CDCl_3$)	:8.22-8.24 (d, 2H), 7.61-7.66 (d, 2H), 7.46-7.48 (d, 2H), 6.92-6.94 (d, 2H), 5.16 (s, 2H), 4.64-4.69 (q, 1H, J = 7.49 Hz), 3.80-3.88 (m, 2H), 3.73-3.78 (m, 1H), 3.49-3.55 (m, 1H), 1.46-1.48 (d, 3H, J = 7.52 Hz).

4.1.119 *N*-Hydroxy-2-{3-[4-(4-methoxybenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionamide (147)

Hydroxylamine hydrochloride (5.2 g, 75 mmole) was suspended in dry methanol (10 mL). Potassium hydroxide (4.3 g, 77 mmole) was dissolved in methanol (10 mL) and added to the above suspension. The reaction mixture was stirred at RT (around 35 °C) for 30 minutes. Ethyl 2-{3-[4-(4-methoxybenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (109) (0.3 g, 0.7 mmole) was added to the above reaction mixture and it was stirred at RT for 3 hours. Ice-water (15 mL) was added to the reaction mixture. The reaction mixture was cooled below 0 °C and conc. HCl was added drop-wise until the pH was around 6 and it was further stirred for 30 minutes. The aqueous layer was extracted with chloroform (3 x 20 mL); the combined organic layer was dried over anhydrous sodium sulphate and the solvent removed to afford an oily product. The oil thus obtained was triturated with ether to obtain the desired product. (0.1 g, 40.0 %). m.p.147-48 °C.

Anal.:

TLC	:R_f 0.68 (70 % EtOAc in n-hexane).
UV (MeOH)	:250.0 nm (log ε 4.30).
IR (KBr, cm^{-1})	:3448, 2985, 1695, 1506, 1456, 1245, 1175, 1007, 826.
PMR (DMSO-d_6)	:7.41-7.45 (m, 2H), 7.33-7.35 (m, 2H), 6.89-6.94 (m, 4H), 4.96 (s, 2H), 4.63-4.66 (q, 1H, J = 7.48 Hz), 3.79-3.82 (m, 5H), 3.65-3.69 (m, 1H), 3.48-3.52 (m, 1H), 1.46-1.48 (d, 3H, J = 7.56 Hz).
MS (m/z)	:403.1 $(M+NH_4)^+$, 371.1 $(M-14)^+$, 325.1 $(M-CONHOH)^+$.

4.1.120 *N*-Hydroxy-2-{2-oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}-propionamide (148)

The title compound was prepared from ethyl 2-{2-oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propionate (110) (0.3 g, 0.9 mmole), hydroxylamine hydrochloride (6.1 g, 90 mmole) and potassium hydroxide (5.5 g, 99 mmole) following the same method as described for the synthesis of compound (147). The crude solid so obtained was triturated with ether to afford the pure title compound. (0.1 g, 37.4 %). m.p.170-71 °C.

Anal.:

TLC	:R_f 0.12 (70 % EtOAc in n-hexane).
UV (MeOH)	:251.5 nm (log ε 4.32).
IR (KBr, cm^{-1})	:3448, 1684, 1615, 1517, 1436, 1248, 1056, 827, 749.
PMR ($CDCl_3$)	:8.58-8.59 (m, 1H), 7.71-7.75 (m, 1H), 7.51-7.53 (m, 1H), 7.41-7.44 (m, 2H), 7.23-7.26 (m, 1H), 6.94-6.96 (m, 2H), 5.17 (s, 2H), 4.61-4.65 (q, 1H), 3.77-3.90 (m, 2H), 3.64-3.68 (m, 1H), 3.51-3.55 (m, 1H), 1.45-1.47 (d, 3H).
MS(m/z)	:374.1 $(M+NH_4)^+$, 341.9 $(M-14)^+$, 296.4 $(M-CONHOH)^+$.

4.1.121 2-{3-[4-(4-Biphenylmethoxy)phenyl]-2-oxo-1-imidazolidin}-N-hydoxypropion-amide (149)

The title compound was prepared from ethyl 2-{3-[4-(4-biphenylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (111) (0.2 g, 0.5 mmole), hydroxylamine hydrochloride (3.5 g, 52 mmole) and potassium hydroxide (3.2 g, 57 mmole) following the same method described (only change being refluxing the reaction mixture for 6 hours) as for the synthesis of compound (147). The crude solid thus obtained was triturated with ether to afford the pure title compound. (0.1 g, 55.0 %). m.p. 242-43 °C.

Anal.:

TLC	:R_f 0.25 (EtOAc).
UV (MeOH)	:254.0 nm (log ε 4.68).
IR (KBr, cm^{-1})	:3493, 1684, 1506, 1484, 1277, 1242, 1014, 826.

PMR (DMSO-d_6) :7.59-7.62 (m, 4H), 7.49-7.51 (m, 2H), 7.42-7.47 (m, 4H), 7.33-7.36 (m,1H), 6.95-6.97 (d, 2H), 5.09 (s, 2H), 4.62-4.66 (q, 1H, J = 7.48 Hz), 3.79-3.86 (m, 2H), 3.66-3.68 (m, 1H), 3.52-3.56 (m, 1H), 1.46-1.48 (d, 3H, J = 7.48 Hz).

Calculated for $C_{25}H_{25}N_3O_4$: C, 69.59, H, 5.84, N, 9.74; Found C, 69.07, H, 6.03, N, 9.59 %.

4.1.122 *N*-Hydroxy-2-{3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl} propionamide (150)

The title compound was prepared from ethyl 2-{3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate **(112)** (0.8 g, 1.7 mmole), hydroxylamine hydrochloride (11.7 g, 168 mmole) and potassium hydroxide (10.4 g, 185 mmole) following the method described for the synthesis of compound **(147)**. The crude solid thus obtained was triturated with ether to afford the pure title compound. (0.25 g, 32.2 %). m.p. 190-92 °C.

Anal.:

TLC :R_f 0.24 (EtOAc).

UV (MeOH) :231.5 nm (log ε 4.41).

IR (KBr, cm^{-1}) :3440, 2985, 1684, 1623, 1506, 1456, 1241, 1076, 827.

PMR ($CDCl_3$) :8.17-8.19 (m, 1H), 7.92-7.94 (m, 1H), 7.70-7.73 (m, 1H), 7.52-7.55 (m, 1H), 7.39-7.45 (m, 3H), 6.98-7.02 (m, 2H), 5.49 (s, 2H), 4.71-4.68 (q, 1H, J = 7.28 Hz), 3.88-3.92 (m, 1H), 3.80-3.84 (m, 1H, 3.67-3.70 (m, 1H), 3.52-3.57 (m, 1H), 2.86-2.87 (d, 2H, J = 6.48 Hz), 2.16-2.21 (m, 1H), 1.50-1.52 (d, 3H, J = 7.32 Hz), 0.95-0.96 (d, 6H).

4.1.123 2-{3-[4-(2-Ethyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}-*N*-hydroxypropionamide (151)

The title compound was prepared from ethyl 2-{3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate **(113)** (0.4 g, 0.9 mmole), hydroxylamine hydrochloride (6.2 g, 89 mmole) and potassium hydroxide (5.5 g, 98 mmole) following the method described for the synthesis of compound **(147)**. The crude solid thus obtained was triturated with ether to afford the pure title compound. (0.1 g, 25.6 %). m.p. 130 °C.

Anal.:

TLC	:R_f 0.25 (EtOAc).
UV (MeOH)	:232.0 nm (log ε 4.50).
IR (KBr, cm^{-1})	:3444, 2972, 1684, 1506, 1387, 1254, 1018, 825.
PMR (DMSO-d_6)	:8.04-8.06 (m, 1H), 7.94-7.96 (m, 1H), 7.68-7.72 (m, 1H), 7.48-7.54 (m, 4H), 7.00-7.21 (m, 2H), 5.47 (s, 2H), 4.53-4.57 (q, 1H), 3.81-3.77 (m, 2H), 3.65-3.68 (m, 2H), 2.96-3.01 (q, 2H), 1.36-1.40 (m, 6H).

Calculated for $C_{24}H_{26}N_4O_4$: C, 66.34, H, 6.03, N, 12.89; Found C, 65.98, H, 6.28, N, 12.69 %.

4.1.124 *N*-Hydroxy-2-{3-[4-(1-naphthylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionamide (152)

The title compound was prepared from ethyl 2-{3-[4-(1-naphthylmethoxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (**115**) (1.0 g, 2.4 mmole), hydroxylamine hydrochloride (16.1 g, 240 mmole) and potassium hydroxide (14.8 g, 264 mmole) following the method (only change being refluxing the reaction mixture for 12 hours) described for the synthesis of compound (**147**). The crude solid thus obtained was triturated with ether to afford the pure title compound. (0.3 g, 30.9 %). m.p. 172-73 °C.

Anal.:

TLC	:R_f 0.73 (EtOAc).
UV (MeOH)	:222.5 nm (log ε 5.11).
IR (KBr, cm^{-1})	:3446, 1684, 1506, 1277, 1232, 996.
PMR (DMSO-d_6)	:8.03-8.05 (m, 1H), 7.83-7.89 (m, 2H), 7.43-7.58 (m, 6H), 6.98-7.01 (m, 2H), 5.44 (s, 2H), 4.57-4.61 (q, 1H), 3.80-3.83 (m, 2H), 3.64-3.68 (m, 2H), 1.44-1.45 (d, 3H).
MS (m/z)	:428.6 $(M+Na)^+$, 404.8 $(M-H)^+$, 391.0 $(M-14)^+$, 344.8 $(M-CONHOH)^+$.

4.1.125 *N*-Hydroxy-2-{2-oxo-3-[5-benzyl-1,3,4-thiadiazol-2-yl]-1-imidazolidinyl}propionamide (153)

The title compound was prepared from ethyl 2-[3-(5-benzyl-1,3,4-thiadiazol-2-yl)-2-oxo-1-imidazolidinyl]propionate (**116**) (0.5 g, 1.4 mmole), hydroxylamine hydrochloride (9.6 g, 140 mmole) and potassium hydroxide (8.5 g, 152 mmole) following the same method (only change being refluxing the reaction mixture for 10 hours) as

described for the synthesis of compound (147). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 25 g, 62.6 %). m.p. 149-50 °C.

Anal.:

TLC	:R_f 0.45 (10 % MeOH in EtOAc).
UV (MeOH)	:259.5 nm (log ε 3.86).
IR (KBr, cm^{-1})	:3244, 1660, 1518, 1433, 1280, 750, 705.
PMR (DMSO-d_6)	:10.65 (bs, 1H), 9.06 (bs, 1H), 7.24-7.76 (m, 5H), 4.30-4.36 (m, 3H), 3.96-4.07 (m, 2H), 3.59-3.67 (m, 2H), 1.22-1.25 (d, 3H).

Calculated for $C_{15}H_{17}N_5O_3S$: C, 51.86, H, 4.93, N, 20.16; Found C, 51.21, H, 5.14, N, 19.92 %.

4.1.126 *N*-Hydroxy-2-{3-[5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionamide (154)

The title compound was prepared from ethyl 2-{3-[5-(4-methoxyphenyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionate (117) (0.5 g, 1.3 mmole), hydroxylamine hydrochloride (9.0 g, 130 mmole) and potassium hydroxide (7.8 g, 143 mmole) following the same method (only change being refluxing the reaction mixture for 6 hours) as described for the synthesis of compound (147). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 25 g, 58.1 %). m.p. 190-92 °C.

Anal.:

TLC	:R_f 0.17 (10 % MeOH in EtOAc).
UV (MeOH)	:311.5 nm (log ε 4.12). 215.5 nm (log ε 4.34).
IR (KBr, cm^{-1})	:3446, 3142, 3001, 1687, 1602, 1518, 1487, 1438, 1401, 1280, 1255, 1180.
PMR (DMSO-d_6)	:7.79-7.82 (d, 2H, J = 8.79 Hz), 7.03-7.06 (d, 2H, J = 8.82 Hz), 4.45-4.50 (q, 1H, J = 7.30 Hz), 4.07-4.18 (m, 2H), 3.80 (s, 3H), 3.59-3.64 (m, 2H), 1.32-1.34 (d, 3H, J = 7.26 Hz).
$[\alpha]^{25}_D$	:-0.07° (3 % MeOH).

4.1.127 *N*-Hydroxy-2-{3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionamide (155)

The title compound was prepared from ethyl 2-{3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1-imidazolidinyl}propionate (**118**) (0.4 g, 1 mmole), hydroxylamine hydrochloride (7.0 g, 100 mmole) and potassium hydroxide (6.1 g, 110 mmole) following the same method (only change being refluxing the reaction mixture for 7 hours) as described for the synthesis of compound (**147**). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 25 g, 66.3 %). m.p. 148-50 °C.

Anal.:

TLC	:R_f 0.19 (10 % MeOH in EtOAc).
IR (KBr, cm^{-1})	:3421, 2931, 1652, 1514, 1431, 1274, 1247, 1176, 1030, 744.
PMR (DMSO-d_6)	:7.37-7.44 (d, 2H), 6.73-6.88 (d, 2H), 4.61-4.67 (q, 1H), 4.40 (s, 2H), 4.27-4.32 (m, 1H), 4.22-4.26 (m, 1H), 3.71 (s, 3H), 3.53-3.63 (m, 2H), 1.65-1.67 (d, 3H).

4.1.128 2-[3-(4,5-Diphenyl-2-thiazolyl)-2-oxo-1-imidazolidinyl]-*N*-hydroxypropionamide (156)

The title compound was prepared from ethyl 2-[3-(4,5-diphenyl-2-thiazolyl)-2-oxo-1-imidazolidinyl]propionate (**119**) (0.4 g, 1.1 mmole), hydroxylamine hydrochloride (7.4 g, 110 mmole) and potassium hydroxide (6.6 g, 152 mmole) following the same method (only change being refluxing the reaction mixture for 10 hours) as described for the synthesis of compound (**147**). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 23 g, 51.2 %). m.p. 155-56 °C.

Anal.:

TLC	:R_f 0.21 (80 % EtOAc in n-hexane).
UV (MeOH)	:236.5 nm (log ε 4.03).
IR (KBr, cm^{-1})	:3423, 1697, 1514, 1435, 1273, 1126, 756, 696.
PMR ($CDCl_3$)	:7.49-7.51 (m, 2H), 7.20-7.25 (m, 8H), 5.25-5.29 (q, 1H, J = 7.27 Hz), 4.34-4.37 (m, 1H), 4.01-4.04 (m, 1H), 3.32-3.35 (m, 2H), 2.04-2.10 (m, 2H), 1.25-1.27 (d, 3H, J = 7.30 Hz).
MS (m/z)	:409.4 $(M+H)^+$, 394.0 $(M-14)^+$, 348.0 $(M-CONHOH)^+$.

4.1.129 *N*-Hydroxy-2-[2-oxo-3-(4-*p*-tolyl-2-thiazolyl)-1-imidazolidinyl]propionamide (157)

The title compound was prepared from ethyl 2-[2-oxo-3-(4-*p*-tolyl-2-thiazolyl)-1-imidazolidinyl]propionate (**120**) (0.3 g, 0.8 mmole), hydroxylamine hydrochloride (5.8 g, 83 mmole) and potassium hydroxide (5.1 g, 92 mmole) following the same method (only change being refluxing the reaction mixture for 15 hours) as described for the synthesis of compound (**147**). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 15 g, 52.2 %). m.p. 220-21 °C.

Anal.:

TLC	:R_f 0.24 (60 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3215, 1683, 1516, 1278, 1041, 825, 740.
PMR (DMSO-d_6)	:7.77-7.79 (d, 2H), 7.48 (s, 1H), 7.20-7.22 (d, 2H), 4.53-4.58 (q, 1H), 4.32-4.37 (m, 1H), 4.12-4.20 (m, 1H), 3.65-3.70 (m, 2H), 2.30 (s, 3H), 1.39-1.41 (d, 3H).
Mass (m/z)	:347.1 $(M+H)^+$, 331.9 $(M-14)^+$, 286.0 $(M-CONHOH)^+$.
$[\alpha]^{25}_D$	:-0.10° (5 % MeOH)

4.1.130 *N*-Hydroxy-2-{3-[4-(4-methoxythiobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionamide (158)

The title compound was prepared from ethyl 2-{3-[4-(4-methoxythiobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (**121**) (0.4 g, 0.9 mmole), hydroxylamine hydrochloride (6.7 g, 96 mmole) and potassium hydroxide (5.9 g, 106 mmole) following the same method as described for the synthesis of compound (**147**). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 23 g, 63.7 %). m.p. 112-14 °C.

Anal.:

TLC	:R_f 0.40 (EtOAc).
UV (MeOH)	:273.5 nm (log ε 3.93).
PMR (DMSO-d_6)	:7.52-7.55 (d, 2H, J = 8.76 Hz), 7.33-7.35 (d, 2H, J = 8.80 Hz), 7.21-7.23 (d, 2H, J = 8.52 Hz), 6.85-6.87 (d, 2H, J = 8.56 Hz), 4.65-4.69 (q, 1H, J = 7.40 Hz), 4.06 (s, 2H), 3.94-3.96 (m, 1H), 3.83-3.86 (m, 4H), 3.75-3.78 (m, 1H), 3.61-3.64 (m, 1H), 1.49-1.51 (d, 3H, J =7.36 Hz).

Calculated for $C_{20}H_{23}N_3O_4S$: C, 59.83, H, 5.77, N, 10.47; Found C, 59.48, H, 6.01, N, 10.29 %.

4.1.131 *N*-Hydroxy-2-(2-oxo-3-phenyl-1-imidazolidinyl)propionamide (159)

The title compound was prepared from ethyl 2-(2-oxo-3-phenyl-1-imidazolidinyl)propionate (**122**) (0.05 g, 0.2 mmole), hydroxylamine hydrochloride (1.5 g, 21 mmole) and potassium hydroxide (1.7 g, 30.5 mmole) following the method described for the synthesis of compound (**147**). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 03 g, 67.0 %). m.p. 123-24 °C.

Anal.:

TLC :R_f 0.42 (EtOAc).

UV (MeOH) :247.0 nm (log ε 4.14).

IR (KBr, cm^{-1}) :3232, 2902, 1654, 1600, 1483, 1269, 1024, 758.

PMR (DMSO-d_6) :10.70 (bs, 1H), 8.92 (bs, 1H), 7.60-7.62 (m, 2H), 7.35-7.39 (m, 2H), 7.03-7.07 (m, 1H), 4.37-4.42 (q, 1H, J = 7.18 Hz), 3.80-3.89 (m, 2H), 3.63-3.69 (m, 1H), 3.55-3.61 (m, 1H), 1.34-1.35 (d, 3H, J = 7.20 Hz).

Calculated for $C_{12}H_{15}N_3O_3$: C, 57.82, H, 6.07, N, 16.86; Found C, 57.24, H, 6.33, N, 16.47 %.

4.1.132 *N*-Hydroxy-2-[3-(4-methoxyphenyl)-2-oxo-1-imidazolidinyl]propionamide (160)

The title compound was prepared from ethyl 2-[3-(4-methoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**123**) (0.2 g, 0.7 mmole), hydroxylamine hydrochloride (4.8 g, 70 mmole) and potassium hydroxide (4.2 g, 75 mmole) following the method described for the synthesis of compound (**147**). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 11 g, 56.3 %). m.p. 126-27 °C.

Anal.:

TLC : R_f 0.34 (EtOAc).

IR (KBr, cm^{-1}) :3228, 2908, 1654, 1514, 1483, 1269, 1242, 1022, 829.

PMR (DMSO-d_6) :10.40 (bs, 1H), 8.70 (bs, 1H), 7.41-7.43 (d, 2H, J = 8.84 Hz), 6.85-6.87 (d, 2H, J = 8.76 Hz), 4.50-4.54 (q, 1H), 3.81-3.87 (m, 2H), 3.78 (s, 3H), 3.70-3.75 (m, 2H), 1.40-1.42 (d, 3H).

4.1.133 *N*-Hydroxy-2-[3-(3,4-dimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionamide (161)

The title compound was prepared from ethyl 2-[3-(3,4-dimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**124**) (0.3 g, 0.9 mmole), hydroxylamine hydrochloride (6.5

g, 93 mmole) and potassium hydroxide (5.7 g, 100 mmole) following the same method as described for the synthesis of compound (**147**). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 12 g, 41.7 %). m.p. 126-27 °C. Anal.:

TLC	:R_f 0.40 (EtOAc).
UV (MeOH)	:257.0 nm (log ε 4.27).
	219.5 nm (log ε 4.44).
IR (KBr, cm^{-1})	:3234, 2933, 1666, 1512, 1434, 1274, 1250, 1029, 846.
PMR ($CDCl_3$)	:10.10 (bs, 1H), 8.62 (bs, 1H), 7.26-7.47 (m, 1H), 6.66-6.80 (m, 2H), 4.50-4.54 (q, 1H), 3.53-3.87 (m, 10H), 1.40-1.42 (d, 3H).

4.1.134 *N*-Hydroxy-2-[3-(3,4,5-trimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionamide (162)

The title compound was prepared from ethyl 2-[3-(3,4,5-trimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**125**) (0.1 g, 0.3 mmole), hydroxylamine hydrochloride (2.2 g, 31 mmole) and potassium hydroxide (2.5 g, 45 mmole) following the method described for the synthesis of compound (**147**). The oily product thus obtained was triturated with ether to afford the pure title compound. (0. 03 g, 36.9 %). m.p. 161-62 °C. Anal.:

TLC	:R_f 0.56 (9 % MeOH in $CHCl_3$).
IR (KBr, cm^{-1})	:3259, 1660, 1589, 1514, 1433, 1276, 1128, 1004.
PMR (DMSO-d_6)	:10.60 (bs, 1H), 8.68 (bs, 1H), 6.85 (s, 2H), 4.50-4.55 (q, 1H), 3.69-3.89 (m, 11H), 3.45-3.58 (m, 2H), 1.41-1.42 (d, 3H).

Calculated for $C_{15}H_{21}N_3O_6$: C, 53.09, H, 6.24, N, 12.38; Found C, 52.80, H, 6.72, N, 12.03 %.

4.1.135 2-[3-(3-Benzyloxyphenyl)-2-oxo-1-imidazolidinyl]-*N*-hydroxypropionamide (163)

The title compound was prepared from ethyl 2-[3-(4-benzyloxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**126**) (0.12 g, 0.3 mmole), hydroxylamine hydrochloride (2.7 g, 38 mmole) and potassium hydroxide (3.1 g, 160 mmole) following the same method as described for the synthesis of compound (**147**). The crude solid was triturated with ether

and crystallized from methanol to afford the pure title compound. (0. 09 g, 77.8 %). m.p. 208-11 °C.

Anal.:

TLC	:R_f 0.30 (EtOAc).
UV (MeOH)	:251.0 nm (log ε 4.29).
IR (KBr, cm^{-1})	:3197, 2995, 1664, 1517, 1485, 1260, 1039, 735.
PMR ($CDCl_3$)	:10.70 (bs, 1H), 8.90 (bs, 1H), 7.48-7.52 (m, 4H), 7.42-7.46 (m, 2H), 7.35-7.39 (m, 1H), 7.02-7.04 (m, 2H), 4.35-4.40 (q, 1H, *J* = 7.08 Hz), 3.78-3.87 (m, 2H), 3.62-3.68 (m, 1H), 3.51-3.58 (m, 1H), 1.32-1.34 (d, 3H, *J* = 7.16 Hz).
$[\alpha]^{25}_D$	:+0.03° (5 % MeOH)

4.1.136 *N*-Hydroxy-2-{3-[3-(4-nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionamide (164)

The title compound was prepared from ethyl 2-{3-[4-(4-nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (127) (0.2 g, 0.5 mmole), hydroxylamine hydrochloride (3.4 g, 5 mmole) and potassium hydroxide (3 g, 5.3 mmole) following the same method as described for the synthesis of compound (147). The oily product thus obtained was triturated with ether to obtain the solid product which was crystallized from aqueous methanol to afford the pure title compound. (0. 05 g, 22.5 %). m.p. 128-29 °C.

Anal.:

TLC	:R_f 0.42 (70 % EtOAc in n-hexane).
UV (MeOH)	:253.0 nm (log ε 4.43).
IR (KBr, cm^{-1})	:3232, 2923, 1670, 1515, 1483, 1436, 1346, 1249, 1058, 827.
PMR ($CDCl_3$)	:10.60 (bs, 1H), 8.80 (bs, 1H), 8.23-8.25 (d, 2H), 7.68-7.70 (d, 2H), 7.44-7.46 (d, 2H), 6.97-7.00 (d, 2H), 5.23 (s, 2H), 4.26-4.30 (q, 1H, *J* = 7.16 Hz), 3.70-3.77 (m, 2H), 3.54-3.60 (m, 2H), 1.25-1.27 (d, 3H, *J* = 7.20 Hz).

4.1.137 2-{2-Oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propanol (166)

Ethyl 2-{2-oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propionate (110) (1.0 g, 2.7 mmole) was dissolved in methanol (10 mL) and cooled to 0-5 °C.

Sodium borohydride (0.5 g, 13 mmole) was added to the above solution under stirring in fractions so that the temperature of the reaction mixture did not rise. The reaction mixture was stirred overnight at RT. The reaction mixture was poured into ice-water (50 mL) under stirring to get the solid product which was filtered and dried. (0.5 g, 56.6 %), m.p. 162-165 °C.

Anal.:

TLC	:R_f 0.41 (EtOAc).
IR (KBr, cm^{-1})	:3358, 2924, 1664, 1516, 1487, 1280, 1247, 1147, 1051, 825.

4.1.138 2-[3-(4-Methoxyphenyl)-2-oxo-1-imidazolidinyl)propanol (167)

The title compound was prepared from ethyl 2-[3-(4-methoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**123**) (2.0 g, 7.1 mmole) and sodium borohydride (1.9 g, 5 mmole) following the method described for the synthesis of compound (**166**) to afford the title product as white solid. (1.5 g, 84.5 %). m.p. 134-37 °C.

Anal.:

TLC	:R_f 0.33 (EtOAc)
IR (KBr, cm^{-1})	:3371, 1664, 1517, 1488, 1284, 1251, 1033, 827.
PMR ($CDCl_3$)	:7.38-7.42 (d, 2H), 6.86-6.89 (d, 2H), 4.00-4.05 (m, 1H), 3.79-3.81 (m, 5H), 3.74-3.78 (m, 1H), 3.70-3.72 (m, 1H), 3.50-3.64 (m, 2H), 1.18-1.20 (d, 3H).

4.1.139 2-[2-Oxo-3-(3,4,5-trimethoxyphenyl)-1-imidazolidinyl]propanol (168)

The title compound was prepared from ethyl 2-[3-(3,4,5-trimethoxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**125**) (1.7 g, 4.8 mmole) and sodium borohydride (1.8 g, 48 mmole) following the method described for the synthesis of compound (**166**) to afford the title product as white solid. (1.35 g, 90.72 %). m.p. 145-48 °C.

Anal.:

TLC	:R_f 0.18 (EtOAc).
IR (KBr, cm^{-1})	:3450, 2972, 1687, 1589, 1510, 1429, 1282, 1238, 1128, 1028.
PMR ($CDCl_3$)	:6.81 (s, 2H), 4.20-4.25 (m, 1H), 3.86 (s, 6H), 3.79-3.81 (m, 5H), 3.71-3.75 (m, 1H), 3.61-3.66 (m, 1H), 3.46-3.54 (m, 2H), 1.19-1.20 (d, 3H).

4.1.140 2-[3-(4-Benzyloxyphenyl)-2-oxo-1-imidazolidinyl]propanol (169)

The title compound was prepared from ethyl 2-[3-(4-benzyloxyphenyl)-2-oxo-1-imidazolidinyl]propionate (**126**) (1 g, 2.7 mmole) and sodium borohydride (2 g, 54 mmole) following the method described for the synthesis of compound (**166**) to afford the title product as white solid. (0.75 g, 85.2 %). m.p. 162-63 °C.

Anal.:

TLC	:R_f 0.18 (50 % EtOAc in n-hexane).
UV (MeOH)	:250.0 nm (log ε 4.31).
IR (KBr, cm^{-1})	:3373, 1662, 1514, 1488, 1446, 1282, 1245, 1053, 1002, 825, 738.
PMR ($CDCl_3$)	:7.43-7.46 (m, 4H), 7.36-7.40 (m, 2H), 7.30-7.33 (m, 1H), 6.95-6.98 (m, 2H), 5.06 (s, 2H), 4.74 (bs, 1H), 3.86-3.91 (m, 1H), 3.70-3.74 (m, 2H), 3.39-3.42 (m, 4H), 1.03-1.05 (d, 3H).

4.1.141 2-{3-[4-(4-Nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propanol (170)

The title compound was prepared from ethyl 2-{3-[4-(4-nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propionate (**127**) (2.4 g, 5.8 mmole) and sodium borohydride (1 g, 29 mmole) following the method described for the synthesis of compound (**166**) to afford the title product as white solid. (1.5 g, 69.7 %). m.p. 128-30 °C.

Anal.:

TLC	:R_f 0.33 (EtOAc).
IR (KBr, cm^{-1})	:3411, 2923, 1685, 1515, 1433, 1350, 1247, 1026.
PMR (DMSO-d_6)	:8.22-8.24 (d, 2H, *J* = 8.60 Hz), 7.62-7.64 (d, 2H, *J* = 8.48 Hz), 7.45-7.47 (d, 2H, J = 9.00 Hz), 6.92-6.94 (d, 2H, J = 9.00 Hz), 5.17 (s, 2H), 4.26 (bs, 1H), 4.05-4.10 (m, 1H), 3.73-3.82 (m, 2H), 3.44-3.62 (m, 4H), 1.15-1.17 (d, 3H).

4.1.142 1-Iodo-2-{2-oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propane (171)

2-{2-Oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propanol (**166**) (0.4 g, 1.2 mmole) was dissolved in DCM (10 mL). Imidazole (0.1 g, 1.5 mmole), iodine (0.4 g, 1.5 mmole) and triphenyl phosphine (0.4 g, 1.5 mmole) were added to the above solution successively. The reaction mixture was stirred at RT for 1 hour and diluted

further with DCM (50 mL). The precipitated solid was filtered out and the organic layer was washed with water (2 x 20 mL), saturated aqueous sodium metabisulphite solution (2 x 30 mL) and water (3 x 20 mL), successively. The organic layer was dried over sodium sulphate and evaporated to afford oily product. (0.5 g, 95.35 %).

Anal.:

TLC :R_f 0.42 (50 % EtOAc in n-hexane).

4.1.143 1-Iodo-2-[2-oxo-3-(4-methoxyphenyl)-1-imidazolidinyl]propane (172)

The title compound was prepared from 2-[3-(4-methoxyphenyl)-2-oxo-1-imidazolidinyl]propanol (**167**) (1.2 g, 4.8 mmole), imidazole (0.4 g, 5.8 mmole), iodine (1.5 g, 5.8 mmole) and triphenyl phosphine (1.5 g, 5.8 mmole) following the method described for the synthesis of compound (171). The crude product obtained so was purified by column chromatography using 0 - 20 % ethyl acetate in n-hexane as eluant to afford the title product as white solid. (1.2 g, 72.3 %). m.p. 90-92 °C.

Anal.:

TLC :R_f 0.60 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :1681, 1517, 1433, 1267, 1244, 1157, 1029, 817, 748.

PMR ($CDCl_3$) :7.42-7.45 (d, 2H), 6.87-6.89 (d, 2H), 4.17-4.22 (m, 1H), 3.81-3.87 (m, 5H), 3.57-3.68 (m, 2H), 3.51-3.55 (m, 1H), 3.45-3.49 (m, 1H), 1.31-1.32 (d, 3H).

4.1.144 1-Iodo-2-[2-oxo-3-(3,4,5-trimethoxyphenyl)-1-imidazolidinyl]propane (173)

The title compound was prepared from 2-[2-oxo-3-(3,4,5-trimethoxyphenyl)-1-imidazolidinyl]propanol (**168**) (1.3 g, 4.4 mmole), imidazole (0.4 g, 5.2 mmole), iodine (1.3 g, 5.2 mmole) and triphenyl phosphine (1.3 g, 5.2 mmole) following the method described for the synthesis of compound (**172**) to afford the title product as white solid. (1.4 g, 75.8 %). m.p. 92-94 °C.

Anal.:

TLC :R_f 0.76 (EtOAc).

IR (KBr, cm^{-1}) :1701, 1589, 1485, 1413, 1238, 1122, 1002, 833, 752.

PMR ($CDCl_3$) :6.85 (s, 2H), 4.19-4.21 (m, 1H), 3.86-3.89 (m, 7H), 3.81-3.84 (m, 3H), 3.46-3.56 (m, 2H), 3.35-3.39 (m, 1H), 3.25-3.30 (m, 1H), 1.34-1.36 (d, 3H).

4.1.145 1-Iodo-2-[2-oxo-3-(4-benzyloxyphenyl)-1-imidazolidinyl)propane (174)

The title compound was prepared from 2-[3-(4-benzyloxyphenyl)-2-oxo-1-imidazolidinyl]propanol (169) (0.6 g, 1.8 mmole), imidazole (0.15 g, 2.2 mmole), iodine (0.6 g, 2.2 mmole) and triphenyl phosphine (0.6 g, 2.2 mmole) following the method described for the synthesis of compound (172) to afford the title product as white solid. (0.5 g, 63.7 %). m.p. 98-100 °C.

Anal.:

TLC	:R_f 0.76 (50 % EtOAc in n-hexane).
UV (MeOH)	:251.5 (log ε 4.32).
IR (KBr, cm^{-1})	:2889, 1689, 1517, 1485, 1433, 1251, 1190, 1145, 1045, 827, 732.
PMR ($CDCl_3$)	:7.31-7.45 (m, 7H), 6.93-6.97 (m, 2H), 5.04 (s, 2H), 4.16-4.21 (m, 1H), 3.75-3.83 (m, 2H), 3.48-3.56 (m, 2H), 3.38-3.46 (m, 1H), 3.32-3.36 (m, 1H), 1.32-1.36 (d, 3H).

4.1.146 1-Iodo-2-(3-[4-(4-nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl)propane (175)

The title compound was prepared from 2-{3-[4-(4-nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propanol (170) (0.5 g, 1.3 mmole), imidazole (0.05 g, 1.6 mmole), iodine (0.4 g, 1.6 mmole) and triphenyl phosphine (0.4 g, 1.6 mmole) following the same method as described for the synthesis of compound (172) to afford the title product as white solid. (0.3 g, 51.1 %). m.p. 129-30 °C.

Anal.:

TLC	:R_f 0.46 (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:687, 1512, 1488, 1433, 1346, 1271, 1238, 1186, 1147, 1028, 842, 746.

4.1.147 2-{2-Oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propyl thio-acetate (176)

1-Iodo-2-{2-oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propane (171) (0.5 g, 1.2 mmole) was dissolved in chloroform (15 mL). Thiolacetic acid (0.46 mL, 6 mmole) was added to the aqueous solution of sodium bicarbonate (1.0 g, 12 mmole in 10 mL of water) drop-wise. This aqueous solution was added to the above chloroform solution with stirring. Tetrabutyl ammonium bromide (0.37 g, 1.2 mmole) was added to the reaction mixture. The reaction mixture was vigorously stirred for 26 hours at room

temperature (around 35-40 °C). The organic layer was separated and the aqueous layer was extracted with chloroform (2 x 10 mL). The combined organic layer was washed with water (5 x 10 mL), dried over anhydrous sodium sulphate and evaporated to get the desired black sticky solid. (0.3 g, 64.9 %).

Anal.:

TLC :R_f 0.41 (50 % EtOAc in n-hexane).

4.1.148 2-[3-(4-methoxyphenyl)-2-oxo-1-imidazolidinyl]propyl thioacetate (177)

The title compound was prepared from 1-iodo-2-[2-oxo-3-(4-methoxyphenyl)-1-imidazolidinyl]propane (**172**) (0.75 g, 2.1 mmole), thiolacetic acid (0.47 mL, 6.2 mmole), sodium bicarbonate (0.87 g, 10 mmole in 10 mL of water) and tetrabutyl ammonium bromide (0.64 g, 2.1 mmole) following the method described for the synthesis of compound (**176**). The black sticky solid thus obtained was crystallized from ether to afford the pure title compound as brownish solid. (0.6 g, 92.7 %). m.p. 83-86 °C.

Anal.:

TLC :R_f 0.57 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2932, 1685, 1517, 1483, 1431, 1267, 1253, 1029, 825, 750.

PMR ($CDCl_3$) :7.41-7.45 (d, 2H), 6.85-6.89 (d, 2H), 4.16-4.22 (m, 1H), 3.74-3.83 (m, 5H), 3.35-3.45 (m, 2H), 3.09-3.15 (m, 2H), 2.33 (s, 3H), 3.73-3.82 (m, 2H), 1.31-1.32 (d, 3H).

4.1.149 2-[2-Oxo-(3,4,5-trimethoxyphenyl)-1-imidazolidinyl]propyl thioacetate (178)

The title compound was prepared from 1-iodo-2-[2-oxo-3-(3,4,5-trimethoxyphenyl)-1-imidazolidinyl]propane (**173**) (0.35 g, 0.8 mmole), thiolacetic acid (0.2 mL, 2.5 mmole), sodium bicarbonate (0.35 g, 4.2 mmole) and tetrabutyl ammonium bromide (0.25 g, 0.8 mmole) following the method described for the synthesis of compound (**177**) to afford the title product as brownwish solid. (0.2 g, 68 %). m.p. 89-90 °C.

Anal.:

TLC :R_f 0.75 (EtOAc).

IR (KBr, cm^{-1}) :2916, 1685, 1589, 1492, 1425, 1278, 1232, 1128, 1006.

PMR ($CDCl_3$) :6.84 (s, 2H), 4.17-4.22 (m, 1H), 3.86 (s, 6H), 3.77-3.81 (m, 5H), 3.42-3.47 (m, 2H), 3.07-3.12 (m, 2H), 2.33 (s, 3H), 1.27-1.28 (d, 3H).

4.1.150 2-[3-(4-Benzyloxyphenyl)-2-oxo-1-imidazolidinyl]propyl thioacetate (179)

The title compound was prepared from 1-iodo-2-[2-oxo-3-(4-benzyloxyphenyl)-1-imidazolidinyl]propane (**174**) (0.05 g, 0.11 mmole), thiolacetic acid (0.02 mL, 0.34 mmole), sodium bicarbonate (0.05 g, 0.6 mmole) and tetrabutyl ammonium bromide (0.03 g, 0.11 mmole) following the method described for the synthesis of compound (**177**) to afford the title product as brownwish solid. (0.02 g, 47.3 %). m.p. 105-08 °C.

Anal.:

TLC :R_f 0.42 (50 % EtOAc in n-hexane).

UV(MeOH) :250.0 nm (log ε 4.31).

IR (KBr, cm^{-1}) :2958, 1685, 1515, 1479, 1434, 1276, 1251, 1105, 833, 732.

PMR ($CDCl_3$) :7.42-7.44 (m, 4H), 7.37-7.41 (m, 2H), 7.32-7.35 (m, 1H), 6.93-6.96 (m, 2H), 5.04 (s, 2H), 4.14-4.23 (m, 1H), 3.71-3.77 (m, 2H), 3.40-3.49 (m, 2H), 3.05-3.14 (m, 2H), 2.32 (s, 3H), 1.25-1.27 (d, 3H).

4.1.151 2-{3-[4-(4-Nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propyl thioacetate (180)

The title compound was prepared from 1-iodo-2-{3-[4-(4-nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propane (**175**) (0.3 g, 0.62 mmole), thiolacetic acid (0.14 mL, 1.9 mmole), sodium bicarbonate (0.3 g, 3.1 mmole) and tetrabutyl ammonium bromide (0.2 g, 0.62 mmole) following the method described for the synthesis of compound (**177**) to afford the title product as pale yellow solid. (0.15 g, 56.4 %). m.p. 106-09 °C.

Anal.:

TLC :R_f 0.44 (50 % EtOAc in n-hexane)

IR (KBr, cm^{-1}) :2881, 1687, 1515, 1485, 1431, 1350, 1249, 1109, 827, 734.

PMR (DMSO-d_6) :8.22-8.24 (d, 2H), 7.61-7.64 (d, 2H), 7.44-7.46 (d, 2H), 6.92-6.94 (d, 2H), 5.17 (s, 2H), 4.13-4.18 (m, 1H), 3.75-3.77 (m, 2H), 3.42-3.46 (m, 2H), 3.24-3.28 (m, 2H), 3.08-3.10 (m, 2H), 2.32 (s, 3H), 1.26-1.28 (d, 3H).

4.1.152 1-(2-Mercapto-1-methylethyl)-3-[4-(2-pyridinylmethoxy)phenyl]imidazolidin-2-one (181)

2-{2-Oxo-3-[4-(2-pyridinylmethoxy)phenyl]-1-imidazolidinyl}propyl thioacetate (**176**) (0.2 g, 0.5 mmole) was suspended in methanol (5 mL). Nitrogen atmosphere was created inside the reaction vessel. Aqueous solution of sodium hydroxide (0.21 g, 5 mmole in 5 mL of water) was added to the above reaction mixture. The reaction mixture was stirred for 7 hours at RT. After the reaction was over, as checked by TLC, the precipitated solid was filtered out, dried and washed with diisopropyl ether to afford the pure title product. (0.1 g, 58.3 %). m.p. 123-124 °C.

Anal.:

TLC	:R_f 0.61 (EtOAc).
PMR (DMSO-d_6)	:8.57-8.58 (m, 1H), 7.66-7.71 (m, 1H), 7.46-7.51 (m, 1H), 7.37-7.39 (m, 2H), 7.19-7.22 (m, 1H), 6.88-6.91 (m, 2H), 5.15 (s, 2H), 4.29-4.35 (m, 1H), 3.65-3.69 (m, 2H), 3.35-3.40 (m, 2H), 2.85-2.95 (m, 2H), 1.24-1.25 (d, 3H).
$[\alpha]^{25}_D$	:+0.52° (2 % MeOH).

4.1.153 1-(2-Mercapto-1-methylethyl)-3-(4-methoxyphenyl)imidazolidin-2-one (182)

The title compound was prepared from 2-[3-(4-methoxyphenyl)-2-oxo-1-imidazolidinyl]-propyl thioacetate (**177**) (0.18 g, 0.57 mmole) and sodium hydroxide (0.23 g, 5.7 mmole) following the method described for the synthesis of compound (**181**). After the reaction was over, solvent was recovered from the reaction mixture under vacuum and ice-water (20 mL) was added to it. The pH of the reaction mixture was adjusted to 2 by adding dilute hydrochloric acid. The solid so obtained was filtered, dried and subjected to column chromatography over silica gel using 0 - 100 % ethyl acetate in n-hexane as eluant. The solid product thus obtained was triturated with solvent ether to afford pure title product. (0.1 g, 66 %). m.p. 136-38 °C.

Anal.:

TLC	:R_f 0.44 (70 % EtOAc in n-hexane).
UV (MeOH)	:255.5 nm (log ε 4.14).
IR (KBr, cm^{-1})	:2966, 1676, 1516, 1421, 1247, 1180, 1030, 827.
PMR ($CDCl_3$)	:7.37-7.45 (d, 2H), 6.80-6.88 (d, 2H), 4.28-4.33 (m, 1H), 3.71-3.81 (m, 5H), 3.38-3.44 (m, 2H), 2.85-2.97 (m, 2H), 1.24-1.26 (d, 3H).

4.1.154 1-(2-Mercapto-1-methylethyl)-3-(3,4,5-trimethoxyphenyl)imidazolidin-2-one (183)

The title compound was prepared from 2-[2-oxo-(3,4,5-trimethoxyphenyl)-1-imidazolidinyl]propyl thioacetate (**178**) (0.15 g, 0.4 mmole) and sodium hydroxide (0.33 g, 8.2 mmole) following the same method as described for the synthesis of compound (**182**). The crude product thus obtained was crystallized from methanol to afford the title product as white solid. (0.1 g, 74.8 %). m.p. 163-66 °C.

Anal.:

TLC	:R_f 0.30 (80 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:2929, 1687, 1593, 1512, 1413, 1263, 1236, 1128, 1006, 837.
PMR ($CDCl_3$)	:6.84 (s, 2H), 4.29-4.38 (m, 1H), 3.80-3.86 (m, 4H), 3.75-3.79 (m, 7H), 3.64-3.72 (m, 2H), 2.90-2.95 (m, 2H), 1.24-1.27 (d, 3H).

4.1.155 1-(2-Mercapto-1-methylethyl)-3-(4-benzyloxyphenyl)imidazolidin-2-one (184)

The title compound was prepared from 2-[3-(4-benzyloxyphenyl)-2-oxo-1-imidazolidinyl]propyl thioacetate (**179**) (0.5 g, 1.3 mmole) and sodium hydroxide (0.26 g, 6.5 mmole) following the same method as described for the synthesis of compound (**182**). The crude product thus obtained was crystallized from methanol to afford the title product as brownwish solid. (0.1 g, 23 %). m.p. 122-23 °C.

Anal.:

TLC	:R_f 0.43 (50 % EtOAc in n-hexane).
UV(MeOH)	:251.0 nm (log ε 4.53).
IR (KBr, cm^{-1})	:1676, 1517, 1421, 1272, 1245, 1047, 1026, 827, 732.
PMR ($CDCl_3$)	:7.41-7.44 (m, 4H), 7.30-7.38 (m, 3H), 6.92-6.94 (m, 2H), 5.03 (s, 2H), 4.25-4.31 (m, 1H), 3.72-3.80 (m, 2H), 3.37-3.43 (m, 2H), 2.84-2.95 (m, 2H), 1.21-1.23 (d, 3H).

Calculated for $C_{19}H_{22}N_2O_2S$: C, 66.64, H, 6.47, N, 8.18; Found C, 66.04, H, 6.98, N, 8.29 %.

4.1.156 1-(2-Mercapto-1-methylethyl)-3-[4-(4-nitrobenzyloxy)phenyl]imidazolidin-2-one (185)

The title compound was prepared from 2-{3-[4-(4-nitrobenzyloxy)phenyl]-2-oxo-1-imidazolidinyl}propyl thioacetate (**180**) (0.3 g, 0.65 mmole) and sodium hydroxide

(0.26 g, 6.5 mmole) following the method described for the synthesis of compound (**182**). The crude product thus obtained was crystallized from methanol to afford the title product as brownwish solid. (0.05 g, 20 %). m.p. 169-70 °C.

Anal.:

TLC	:R_f 0.43 (70 % EtOAc in n-hexane).
UV(MeOH)	:253.5 nm (log ε 4.30).
IR (KBr, cm^{-1})	:2923, 1685, 1515, 1483, 1431, 1348, 1269, 1249, 829, 732.
PMR ($CDCl_3$)	:8.20-8.24 (d, 2H), 7.61-7.65 (d, 2H), 7.41-7.46 (d, 2H), 6.87-6.94 (d, 2H), 5.17 (s, 2H), 4.13-4.18 (m, 1H), 3.75-3.79 (m, 2H), 3.24-3.28 (m, 2H), 2.86-2.90 (m, 2H), 1.24-1.25 (d, 3H).

Calculated for $C_{19}H_{21}N_3O_4S$: C, 58.90, H, 5.46, N, 10.84; Found C, 59.24, H, 5.89, N, 10.29 %.

4.1.157 1-(3-Chloropropyl)-3-[4-(4-methoxybenzyloxy)phenyl]urea (186)

The title compound was prepared from 4-(4-methoxybenzyloxy)aniline (**36**) (1.5 g, 6.6 mmole) and 3-chloropropyl isocyanate (**62**) (13.3 mL, 6.6 mmole) following the method described for the synthesis of compound (**69**) to afford the title product as brownwish solid. (1.5 g, 65.2 %). m.p. 134-36 °C.

Anal.:

TLC	:R_f 0.69 (70 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3317, 1635, 1518, 1242, 1178, 1031, 825.

4.1.158 1-(3-Chloropropyl)-3-[4-(2-pyridinylmethoxy)phenyl]urea (187)

The title compound was prepared from 4-(2-pyridinylmethoxy)aniline (**37**) (1.8 g, 9 mmole) and 3-chloropropyl isocyanate (**62**) (18.3 mL, 9 mmole) following the method described for the synthesis of compound (**69**) to afford the title product as brownwish solid. (2.2 g, 76.5 %). m.p. 133-34 °C.

Anal.:

TLC	:R_f 0.64 (EtOAc).
UV (MeOH)	:243.0 nm (log ε 4.39).
IR (KBr, cm^{-1})	:3312, 2980, 1648, 1596, 1282, 1252, 1048, 827.
PMR ($CDCl_3$)	:8.49-8.59 (m, 1H), 7.69-7.74 (m, 1H), 7.49-7.51 (m, 1H), 7.22-7.25 (m, 1H), 7.15-7.19 (d, 2H), 6.92-6.95 (d, 2H),

6.51 (bs, 1H), 5.17 (s, 2H), 5.01-5.03 (t, 1H), 3.55-3.58 (m, 2H), 3.34-3.39 (m, 2H), 1.94-2.00 (m, 2H).

4.1.159 1-[4-(4-Biphenylmethoxy)phenyl]-3-(3-chloropropyl)urea (188)

The title compound was prepared from 4-(4-aminophenoxymethyl)biphenyl (**38**) (0.75 g, 2.7 mmole) and 3-chloropropyl isocyanate (**62**) (6.1 mL, 3 mmole) following the same method as described for the synthesis of compound (**69**) to afford the title product as brownwish solid. (0.85 g, 79.8 %). m.p. 145-48 °C.

Anal.:

TLC :R_f 0.61 (50 % EtOAc in n-hexane).]

4.1.160 1-(3-Chloropropyl)-3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]urea (189)

The title compound was prepared from 4-(2-isobutyl-4-quinolinylmethoxy)aniline (**39**) (1.5 g, 5 mmole) and 3-chloropropyl isocyanate (**62**) (11.9 mL, 6 mmole) following the method described for the synthesis of compound (**69**) to afford the title product as brownwish solid. (1.6 g, 89.7 %). m.p. 115-16 °C.

Anal.:

TLC :R_f 0.48 (50 % EtOAc in n-hexane).

UV (MeOH) :231.5 nm (log ε 4.91).

IR (KBr, cm^{-1}) :3358, 3292, 2955, 1637, 1600, 1510, 1236, 1170, 1070, 842, 761.

PMR (DMSO-d_6) :8.14-8.15 (m, 1H), 8.00-8.03 (m, 2H), 7.68-7.72 (m, 1H), 7.52 (s, 1H), 7.45 (bs, 1H), 7.32-7.34 (d, 2H, J = 8.96 Hz), 6.93-6.95 (d, 2H, J = 8.80 Hz), 6.09-6.12 (t, 1H), 5.48 (s, 2H), 3.61-3.65 (m, 2H), 3.29-3.33 (m, 2H), 2.81-2.83 (d, 2H), 2.19-2.23 (m, 1H), 1.92-1.99 (m, 2H), 0.95-0.96 (d, 6H).

4.1.161 1-(3-Chloropropyl)-3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]urea (190)

The title compound was prepared from 4-(2-ethyl-4-quinolinylmethoxy)aniline (**40**) (1.7 g, 6.1 mmole) and 3-chloropropyl isocyanate (**62**) (14.9 mL, 7.3 mmole) following the method described for the synthesis of compound (**69**) to afford the title product as brownwish solid. (1.7 g, 70.1 %). m.p. 130-32 °C.

Anal.:

TLC :R_f 0. 34 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3313, 1635, 1606, 1508, 1244, 1172, 1020, 756.

4.1.162 1-(3-Chloropropyl)-3-[4-(2-phenyl-4-quinolinylmethoxy)phenyl]urea (191)

The title compound was prepared from 4-(2-phenyl-4-quinolinylmethoxy)aniline **(41)** (1 g, 3.1 mmole) and 3-chloropropyl isocyanate **(62)** (7.5 mL, 3.8 mmole) following the method described for the synthesis of compound **(69)** to afford the title product as brownwish solid. (1.2 g, 86.9 %). m.p. 170-72 °C.

Anal.:

TLC :R_f 0.22 (50 % EtOAc in n-hexane).

UV (MeOH) :252.0 nm (log ε 4.78).

IR (KBr, cm^{-1}) :3316, 2985, 1640, 1592, 1281, 1252, 1052, 835.

PMR ($CDCl_3$) :8.16-8.19 (m, 2H), 7.98-8.06 (m, 3H), 7.73-7.77 (m, 1H), 7.44-7.60 (m, 4H), 7.32-7.36 (d, 2H), 6.96-6.99 (d, 2H), 5.98-6.01 (t, 1H), 5.55 (s, 2H), 3.61-3.64 (m, 2H), 3.32-3.37 (m, 2H), 1.94-2.01 (m, 2H).

4.1.163 1-(3-Chloropropyl)-3-[4-(1-naphthylmethoxy)phenyl]urea (192)

The title compound was prepared from 1-(4-aminophenoxymethyl)naphthalene **(42)** (2.5 g, 10 mmole) and 3-chloropropyl isocyanate **(62)** (20.3 mL, 10 mmole) following the method described for the synthesis of compound **(69)** to afford the title product as brownwish solid. (2.7 g, 73.3 %). m.p. 143-45 °C.

Anal.:

TLC :R_f 0.14 (30 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3309, 1639, 1510, 1249, 1224, 1024, 794.

4.1.164 1-(5-Benzyl-1,3,4-thiadiazol-2-yl)-3-(3-chloropropyl)urea (193)

The title compound was prepared from 5-benzyl-1,3,4-thiadiazol-2-ylamine **(47)** (1.2 g, 6.3 mmole) and 3-chloropropyl isocyanate **(62)** (7.8 mL, 6.5 mmole) following the method described for the synthesis of compound **(69)** to afford the title product as brownwish solid. (1.5 g, 76.7 %). m.p. 142-45 °C.

Anal.:

TLC :R_f 0.63 (EtOAc).

4.1.165 1-(3-Chloropropyl)-3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]urea (194)

The title compound was prepared from 5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-ylamine **(49)** (1.4 g, 6.3 mmole) and 3-chloropropyl isocyanate **(62)** (6.2 mL, 7 mmole)

following the method described for the synthesis of compound (**69**) to afford the title product as brownwish solid. (1.5 g, 69.9 %). m.p. 154-55 °C.

Anal.:

TLC :R_f 0.51 (EtOAc).

IR (KBr, cm^{-1}) :3215, 1685, 1514, 1423, 1253, 1174, 1031, 680.

4.1.166 1-(3-Chloropropyl)-3-(4,5-diphenyl-2-thiazolyl)urea (195)

The title compound was prepared from 4,5-diphenyl-2-thiazolylamine (**53**) (2 g, 8.3 mmole) and 3-chloropropyl isocyanate (**62**) (18.6 mL, 9.2 mmole) following the method described for the synthesis of compound (**69**) to afford the title product as brownish solid. (2.2 g, 73.7 %). m.p. 150-51 °C.

Anal.:

TLC :R_f 0.59 (50 % EtOAc in n-hexane).

PMR (DMSO-d_6) :7.26-7.37 (m, 10H), 6.72 (bs, 1H), 3.80-3.84 (m, 2H), 3.26-3.33 (m, 2H), 1.90-2.01 (m, 2H).

4.1.167 1-(3-Chloropropyl)-3-(4-*p*-tolyl-2-thiazolyl)urea (196)

The title compound was prepared from 4-*p*-tolyl-2-thiazolylamine (**54**) (0.5 g, 2.6 mmole) and 3-chloropropyl isocyanate (**62**) (5.3 mL, 2.6 mmole) following the same method as described for the synthesis of compound (**69**). The solvent was removed under vacuum from the reaction mixture to afford the desired product as oil. (0.6 g, 73.7 %).

Anal.:

TLC :R_f 0.21 (30 % EtOAc in n-hexane).

4.1.168 1-(3-Chloropropyl)-3-phenylurea (197)

The title compound was prepared from aniline (**63**) (1 mL, 11 mmole) and 3-chloropropyl isocyanate (**62**) (21.6 mL, 11 mmole) following the method described for the synthesis of compound (**69**) to afford the title product as brownwish solid. (1.2 g, 58.8 %). m.p. 127-28 °C.

Anal.:

TLC :R_f 0.62 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3323, 3029, 1635, 1593, 1500, 1311, 727.

PMR (DMSO-d_6) :8.04 (bs, 1H), 7.37-7.39 (m, 2H), 7.19-7.24 (m, 3H), 6.05 (bs, 1H), 3.61-3.65 (m, 2H), 3.33-3.38 (m, 2H), 1.95-2.01 (m, 2H).

4.1.169 1-(3-Chloropropyl)-3-(4-methoxyphenyl)urea (198)

The title compound was prepared from 4-methoxyaniline (**64**) (5 g, 41 mmole) and 3-chloropropyl isocyanate (**62**) (79.8 mL, 41 mmole) following the method described for the synthesis of compound (**69**) to afford the title product as brownwish solid. (8.4 g, 96.2 %). m.p. 125-26 °C.

Anal.:

TLC :R_f 0.47 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3309, 2929, 1627, 1596, 1452, 1298, 1238, 1039, 831.

PMR (DMSO-d_6) :7.68 (bs, 1H), 7.24-7.28 (d, 2H), 6.77-6.81 (d, 2H), 5.82 (bs, 1H), 3.76 (s, 3H), 3.60-3.63 (m, 2H), 3.32-3.37 (m, 2H), 1.94-2.01 (m, 2H).

4.1.170 1-(3-Chloropropyl)-3-(3,4-dimethoxyphenyl)urea (199)

The title compound was prepared from 3,4-dimethoxyaniline (**65**) (1.1 g, 7.2 mmole) and 3-chloropropyl isocyanate (**62**) (9.7 mL, 8.6 mmole) following the method described for the synthesis of compound (**69**) to afford the title product as brownwish solid. (1.9 g, 97.2 %). m.p. 96-99 °C.

Anal.:

TLC :R_f 0.23 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3309, 2960, 1627, 1604, 1516, 1367, 1240, 1168, 1136, 1024, 858, 790.

4.1.171 1-(4-Benzyloxyphenyl)-3-(3-chloropropyl)urea (200)

The title compound was prepared from 4-benzyloxyaniline hydrochloride (**67**) (4.0 g, 17 mmole), triethylamine (4.7 mL, 34 mmole) and 3-chloropropyl isocyanate (**62**) (34.4 mL, 17 mmole) following the method described for the synthesis of compound (**86**) to afford the title product as brownwish solid. (5.1 g, 94.2 %). m.p. 155-56 °C.

Anal.:

TLC :R_f 0.59 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3310, 2982, 1638, 1598, 1288, 1248, 1036, 831.

PMR (DMSO-d_6) :7.92 (bs, 1H), 7.26-7.53 (m, 7H), 6.84-6.86 (m, 2H), 5.00 (bs, 1H), 3.60-3.63 (m, 2H), 3.32-3.35 (m, 2H), 1.93-2.01 (m, 2H).

4.1.172 1-[4-(4-Methoxybenzyloxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (201)

The title compound was prepared from 1-(3-chloropropyl)-3-[4-(4-methoxybenzyloxy)phenyl]urea (**186**) (1.4 g, 4 mmole) and sodium hydride (0.14 g, 6 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (1 g, 80.1 %). m.p. 218-20 °C.

Anal.:

TLC :R_f 0.45 (70 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3217, 2955, 1647, 1585, 1510, 1244, 1174, 1030, 827, 810.

PMR (DMSO-d_6) :7.33-7.35 (d, 2H), 7.14-7.16 (d, 2H), 6.88-6.90 (m, 4H), 6.27 (bs, 1H), 4.96 (s, 2H), 3.79 (s, 3H), 3.58-3.61 (m, 2H), 3.30-3.330 (m, 2H), 2.00-2.02 (m, 2H).

4.1.173 1-[4-(2-Pyridinylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (202)

The title compound was prepared from 1-(3-chloropropyl)-3-[4-(2-pyridinylmethoxy)phenyl]urea (**187**) (2 g, 6.3 mmole) and sodium hydride (0.6 g, 12.5 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (1 g, 56.1 %). m.p. 211-12 °C.

Anal.:

TLC :R_f 0.57 (EtOAc).

UV (MeOH) :231.0 nm (log ε 4.32).

IR (KBr, cm^{-1}) :3223, 2987, 1670, 1494, 1444, 1249, 1179, 1039, 837.

PMR (DMSO-d_6) :8.58-8.59 (m, 1H), 7.68-7.73 (m, 1H), 7.50-7.52 (m, 1H), 7.18-7.23 (m, 3H), 6.94-6.97 (m, 2H), 5.19 (s, 2H), 4.87 (bs, 1H), 3.62-3.65 (m, 2H), 3.40-3.43 (m, 2H), 2.04-2.17 (m, 2H).

4.1.174 1-[4-(4-Biphenylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (203)

The title compound was prepared from 1-[4-(4-biphenylmethoxy)phenyl]-3-(3-chloropropyl)urea (**188**) (0.8 g, 2 mmole) and sodium hydride (0.2 g, 4.1 mmole)

following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (0.6 g, 83.8 %). m.p. 248-50 °C.

Anal.:

TLC	:R_f 0.17 (EtOAc).
IR (KBr, cm^{-1})	:3221, 1645, 1510, 1242, 1224, 1033, 829, 758, 698.

4.1.175 1-[4-(2-Isobutyl-4-quinolinylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (204)

The title compound was prepared from 1-(3-chloropropyl)-3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]urea (**189**) (1.5 g, 3.5 mmole) and sodium hydride (0.3 g, 7 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (0.8 g, 58.8 %). m.p. 139-40 °C.

Anal.:

TLC	:R_f 0.25 (EtOAc).
UV (MeOH)	:231.5 nm (log ε 4.66).
IR (KBr, cm^{-1})	:3225, 2978, 1671, 1498, 1438, 1241, 1182, 1045, 835.
PMR (DMSO-d_6)	:8.07-8.09 (m, 1H), 7.95-7.98 (m, 1H), 7.69-7.73 (m, 1H), 7.52-7.56 (m, 2H), 7.48 (s, 1H), 7.23-7.25 (m, 1H), 7.00-7.06 (m, 2H), 5.56 (s, 2H), 3.83-3.87 (m, 2H), 3.63-3.66 (m, 1H), 3.40-3.41 (m, 1H), 2.84-2.85 (d, 2H), 2.15-2.23 (m, 2H), 2.06-2.09 (m, 1H), 0.95-0.97 (d, 6H).

4.1.176 1-[4-(2-Ethyl-4-quinolinylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (205)

The title compound was prepared from 1-(3-chloropropyl)-3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]urea (**190**) (1.6 g, 4 mmole) and sodium hydride (0.4 g, 8 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (1.25 g, 86.6 %). m.p. 189-90 °C.

Anal.:

TLC	:R_f 0.1 (EtOAc).
IR (KBr, cm^{-1})	:3213, 1658, 1606, 1508, 1244, 1224, 1174, 885, 835, 759.

4.1.177 1-[4-(2-Phenyl-4-quinolinylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (206)

The title compound was prepared from 1-(3-chloropropyl)-3-[4-(2-phenyl-4-quinolinylmethoxy)phenyl]urea (**191**) (1.1 g, 2.4 mmole) and sodium hydride (0.2 g, 4.8

mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (1 g, 100 %). m.p. 200-01 °C.

Anal.:

TLC	:R_f 0.33 (10 % MeOH in $CHCl_3$).
UV (MeOH)	:255.5 nm (log ε 4.61).
IR (KBr, cm^{-1})	:3223, 2987, 1670, 1494, 1444, 1249, 1179, 1039, 837.
PMR (DMSO-d_6)	:8.17-8.19 (m, 3H), 8.08-8.06 (m, 1H), 8.02-8.04 (m, 1H), 7.75-7.78 (m, 1H), 7.45-7.61 (m, 4H), 7.24-7.26 (d, 2H), 7.05-7.07 (d, 2H), 5.78 (bs, 1H), 5.59 (s, 2H), 3.63-3.66 (m, 2H), 3.37-3.41 (m, 2H), 2.04-2.09 (m, 2H).

4.1.178 1-[4-(1-Naphthylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (207)

The title compound was prepared from 1-(3-chloropropyl)-3-[4-(1-naphthylmethoxy)phenyl]urea (**192**) (2 g, 5.4 mmole) and sodium hydride (0.4 g, 8.1 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (1.5 g, 83.7 %). m.p. 214-17 °C.

Anal.:

TLC	:R_f 0.54 (70 % EtOAc in n-hexane).
PMR (DMSO-d_6)	:8.02-8.04 (m, 1H), 7.85-7.91 (m, 2H), 7.69-7.71 (m, 1H), 7.54-7.59 (m, 2H), 7.50-7.52 (m, 1H), 7.20-7.24 (m, 2H), 6.98-7.02 (m, 2H), 5.92 (bs, 1H), 5.47 (s, 2H), 3.61-3.65 (m, 2H), 3.36-3.40 (m, 2H), 2.03-2.09 (m, 2H).

4.1.179 1-(5-Benzyl-1,3,4-thiadiazol-2-yl)tetrahydropyrimidin-2(1*H*)-one (208)

The title compound was prepared from 1-(5-benzyl-1,3,4-thiadiazol-2-yl)-3-(3-chloropropyl)urea (**193**) (1.9 g, 6.1 mmole) and sodium hydride (0.6 g, 12 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (1.5 g, 89.8 %). m.p. 212-15 °C.

Anal.:

TLC	:R_f 0.33 (EtOAc).
IR (KBr, cm^{-1})	:3207, 2924, 1676, 1494, 1278, 1172, 1008, 748, 700.
PMR ($CDCl_3$)	:7.28-7.30 (m, 4H), 7.22-7.25 (m, 1H), 5.48 (bs, 1H), 4.29 (s, 2H), 4.18-4.21 (m, 2H), 3.39-3.42 (m, 2H), 2.08-2.14 (m, 2H).

4.1.180 1-[5-(4-Methoxybenzyl)-1,3,4-thiadiazol-2-yl]tetrahydropyrimidin-2(1*H*)-one (209)

The title compound was prepared from 1-(3-chloropropyl)-3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]urea (**194**) (1.3 g, 3.8 mmole) and sodium hydride (0.4 g, 7.6 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (0.8 g, 69.2 %). m.p. 189-91 °C.

Anal.:

TLC :R_f 0.24 (EtOAc).

4.1.181 1-(4,5-Diphenyl-2-thiazolyl)tetrahydropyrimidin-2(1*H*)-one (210)

The title compound was prepared from 1-(3-chloropropyl)-3-(4,5-diphenyl-2-thiazolyl)urea (**195**) (2 g, 5.6 mmole) and sodium hydride (0.5 g, 11 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (1.5 g, 82.9 %). m.p. 209-12 °C.

Anal.:

TLC :R_f 0.33 (EtOAc).

IR (KBr, cm^{-1}) :3230, 2924, 1676, 1487, 1437, 1313, 1269, 1176, 756, 694.

4.1.182 1-(4-*p*-Tolyl-2-thiazolyl)tetrahydropyrimidin-2(1*H*)-one (211)

The title compound was prepared from 1-(3-chloropropyl)-3-(4-*p*-tolyl-2-thiazolyl)urea (**196**) (1.7 g, 5.5 mmole) and sodium hydride (0.5 g, 11 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (1.5 g, 100 %). m.p. 209-10 °C.

Anal.:

TLC :R_f 0.14 (30 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3227, 2924, 1681, 1477, 1309, 1271, 1176, 742.

4.1.183 1-Phenyltetrahydropyrimidin-2(1*H*)-one (212)

The title compound was prepared from 1-(3-chloropropyl)-3-phenylurea (**197**) (0.5 g, 2.4 mmole) and sodium hydride (0.14 g, 3.5 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (0.35 g, 82.9 %). m.p. 202-04 °C.

Anal.:

TLC :R_f 0.35 (EtOAc).

IR (KBr, cm^{-1}) :3220, 2923, 1651, 1506, 1444, 1311, 1222, 1176, 765.

PMR ($CDCl_3$) :7.28-7.36 (m, 4H), 7.14-7.19 (m, 1H), 5.19 (bs, 1H), 3.67-3.70 (m, 2H), 3.40-3.43 (m, 2H), 2.05-2.11 (m, 2H).

4.1.184 1-(4-Methoxyphenyl)tetrahydropyrimidin-2(1*H*)-one (213)

The title compound was prepared from 1-(3-chloropropyl)-3-(4-methoxyphenyl)urea (**198**) (5 g, 21 mmole) and sodium hydride (1.24 g, 31 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (4.2 g, 97.1 %). m.p. 204-06 °C.

Anal.:

TLC :R_f 0.45 (EtOAc).

IR (KBr, cm^{-1}) :3213, 2927, 1664, 1488, 1446, 1299, 1249, 1170, 1029, 833.

PMR ($CDCl_3$) :7.18-7.21 (d, 2H), 6.86-6.89 (d, 2H), 5.12 (bs, 1H), 3.79 (s, 3H), 3.61-3.64 (m, 2H), 3.39-3.42 (m, 2H), 2.04-2.10 (m, 2H).

4.1.185 1-(3,4-Dimethoxyphenyl)tetrahydropyrimidin-2(1*H*)-one (214)

The title compound was prepared from 1-(3-chloropropyl)-3-(3,4-dimethoxyphenyl)urea (**199**) (1.6 g, 5.8 mmole) and sodium hydride (0.5 g, 11.7 mmole) following the method described for the synthesis of compound (**89**) to afford the title product as white solid. (1.3 g, 94.8 %). m.p. 157-60 °C.

Anal.:

TLC :R_f 0.12 (EtOAc).

IR (KBr, cm^{-1}) :3209, 2958, 1664, 1593, 1510, 1446, 1244, 1226, 1172, 1024, 844, 763.

4.1.186 1-(4-Benzyloxyphenyl)tetrahydropyrimidin-2(1*H*)-one (215)

The title compound was prepared from 1-(3-chloropropyl)-3-(4-benzyloxyphenyl)urea (202) (3.5 g, 11 mmole) and sodium hydride (0.8 g, 16.5 mmole) following the same method as described for the synthesis of compound (**89**) to afford the title product as white solid. (2.9 g, 93.5 %). m.p. 230-31 °C.

Anal.:

TLC :R_f 0.53 (70 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :3222, 2979, 1666, 1490, 1448, 1248, 1178, 1036, 833.

PMR (DMSO-d_6) :7.35-7.42 (m, 4H), 7.28-7.32 (m, 1H), 7.16-7.19 (d, 2H, *J* = 8.84 Hz), 6.89-6.93 (d, 2H, *J* = 8.88 Hz), 6.01 (bs, 1H), 5.04 (s, 2H), 3.60-3.63 (m, 2H), 3.34-3.37 (m, 2H), 2.01-2.07 (m, 2H).

4.1.187 Ethyl 2-{3-[4-(4-methoxybenzyloxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (216)

The title compound was prepared from 1-[4-(4-methoxybenzyloxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (**201**) (0.8 g, 2.6 mmole), sodium hydride (0.25 g, 5.1 mmole) and ethyl 2-bromopropionate (**108**) (0.7 mL, 5.1 mmole) following the method described for the synthesis of compound (**109**) to afford the title product as oil. (0.5 g, 46.7 %).

Anal.:

TLC :R_f 0.21 (30 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2955, 1737, 1645, 1514, 1249, 1180, 1026, 829, 756.

4.1.188 Ethyl 2-{3-[4-(2-pyridinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (217)

The title compound was prepared from 1-[4-(2-pyridinylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (**202**) (0.9 g, 3.2 mmole), sodium hydride (0.3 g, 6.5 mmole) and ethyl 2-bromopropionate (**108**) (0.8 mL, 6.5 mmole) following the method described for the synthesis of compound (**109**) to afford the title product as oil. (1.0 g, 82.2 %).

Anal.:

TLC :R_f 0.17 (50 % EtOAc in n-hexane).

4.1.189 Ethyl 2-{3-[4-(4-biphenylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (218)

The title compound was prepared from 1-[4-(4-biphenylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (**203**) (0.75 g, 2.1 mmole), sodium hydride (0.17 g, 4.2 mmole) and ethyl 2-bromopropionate (**108**) (0.54 mL, 4.2 mmole) following the same method described for the synthesis of compound (**109**) to afford the title product as white solid. (0.8 g, 83.2 %). m.p. 119-20 °C.

Anal.:

TLC :R_f 0.39 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2966, 1735, 1645, 1508, 1240, 1188, 1016, 840, 765.

4.1.190 Ethyl 2-{3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (219)

The title compound was prepared from 1-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (204) (0.6 g, 1.5 mmole), sodium hydride (0.13 g, 3 mmole) and ethyl 2-bromopropionate (108) (0.4 mL, 3 mmole) following the method described for the synthesis of compound (109) to afford the title product as pale yellow solid. (0.6 g, 79.7 %). m.p. 78-80 °C.

Anal.:

TLC :R_f 0.38 (50 % EtOAc in n-hexane).

4.1.191 Ethyl 2-{3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (220)

The title compound was prepared from 1-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (205) (1.1 g, 3 mmole), sodium hydride (0.3 g, 6.1 mmole) and ethyl 2-bromopropionate (108) (0.8 mL, 6.1 mmole) following the method described for the synthesis of compound (109) to afford the title product as oil. (0.9 g, 65.1 %).

Anal.:

TLC :R_f 0.29 (50 % EtOAc in n-hexane).

4.1.192 Ethyl 2-{3-[4-(2-phenyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (221)

The title compound was prepared from 1-[4-(2-phenyl-4-quinolinylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (206) (0.85 g, 2.1 mmole), sodium hydride (0.2 g, 4.2 mmole) and ethyl 2-bromopropionate (108) (0.55 mL, 4.2 mmole) following the same method as described for the synthesis of compound (109). The crude product thus obtained was purified by column chromatography using 30 % ethyl acetate in n-hexane as eluant to afford the title product as oil. (0.4 g, 46.6 %).

Anal.:

TLC :R_f 0.42 (EtOAc).

4.1.193 Ethyl 2-{3-[4-(1-naphthylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (222)

The title compound was prepared from 1-[4-(1-naphthylmethoxy)phenyl]tetrahydropyrimidin-2(1*H*)-one (207) (1 g, 3 mmole), sodium hydride (0.3 g, 6 mmole) and ethyl 2-bromopropionate (108) (0.8 mL, 6 mmole) following the same method described for the synthesis of compound (109). The crude product thus obtained was purified by column chromatography using 30 % ethyl acetate in n-hexane as eluant to afford the title product as oil. (0.8 g, 61.7 %).

Anal.:

TLC :R_f 0.55 (50 % EtOAc in n-hexane).

PMR ($CDCl_3$) :7.94-7.97 (m, 1H), 7.80-7.83 (m, 1H), 7.63-7.71(m, 1H), 7.45-7.52 (m, 2H), 7.25-7.31 (m, 1H), 7.13-7.18 (m, 2H), 6.95-6.98 (m, 1H), 6.75-6.78 (m, 2H), 5.39 (s, 2H), 4.45-4.49 (q, 1H), 4.07-4.15 (m, 2H), 3.57-3.60 (m, 2H), 3.30-3.34 (m, 2H), 2.05-2.13 (m, 2H), 1.36-1.38 (d, 3H), 1.19-1.22 (t, 3H).

4.1.194 Ethyl 2-[3-(5-benzyl-1,3,4-thiadiazol-2-yl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl] propionate (223)

The title compound was prepared from 1-(5-benzyl-1,3,4-thiadiazol-2-yl)tetrahydropyrimidin-2(1*H*)-one (208) (0.7 g, 2.1 mmole), sodium hydride (0.24 g, 5.1 mmole) and ethyl 2-bromopropionate (108) (0.7 mL, 5.1 mmole) following the method described for the synthesis of compound (109) to afford the title product as oil. (0.6 g, 76.4 %).

Anal.:

TLC :R_f 0.52 (EtOAc).

4.1.195 Ethyl 2-{3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (224)

The title compound was prepared from 1-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]tetrahydropyrimidin-2(1*H*)-one (209) (0.65 g, 2.1 mmole), sodium hydride (0.17 g, 4.3 mmole) and ethyl 2-bromopropionate (108) (0.55 mL, 4.3 mmole) following the method described for the synthesis of compound (109) to afford the title product as oil. (0.6 g, 70.7 %).

Anal.:

TLC :R_f 0.53 (EtOAc).

4.1.196 Ethyl 2-[3-(4,5-diphenyl-2-thiazolyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl] propionate (225)

The title compound was prepared from 1-(4,5-diphenyl-2-thiazolyl)tetrahydropyrimidin-2(1*H*)-one (210) (1.2 g, 3.7 mmole), sodium hydride (0.36 g, 7.4 mmole) and ethyl 2-bromopropionate (108) (0.96 mL, 7.4 mmole) following the method described for the synthesis of compound (109). The crude product thus obtained was purified by column chromatography over silica gel using 20 - 30 % ethyl acetate in n-hexane as eluant to afford the title product as white solid. (1 g, 63.9 %). m.p. 111-113 °C.

Anal.:

TLC :R_f 0.28 (50 % EtOAc in n-hexane).

PMR ($CDCl_3$) :7.51-7.53 (m, 2H), 7.32-7.35 (m, 2H), 7.26-7.30 (m, 6H), 7.23-7.25 (m, 2H), 5.23-5.28 (q, 1H, J = 7.50 Hz), 4.39-4.45 (m, 1H), 4.19-4.24 (m, 3H), 4.09-4.18 (m, 2H), 2.12-2.23 (m, 2H), 1.48-1.50 (d, 3H, J = 7.60 Hz), 1.26-1.30 (t, 3H).

4.1.197 Ethyl 2-[3-(4-*p*-tolyl-2-thiazolyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (226)

The title compound was prepared from 1-(4-*p*-tolyl-2-thiazolyl)tetrahydropyrimidin-2(1*H*)-one (211) (1.5 g, 5.5 mmole), sodium hydride (1.1 g, 27.4 mmole) and ethyl 2-bromopropionate (108) (1.4 mL, 11 mmole) following the same method as described for the synthesis of compound (109) to afford the title product as oil. (1.5 g, 73.1 %).

Anal.:

TLC :R_f 0.57 (30 % EtOAc in n-hexane).

4.1.198 Ethyl 2-[3-phenyl-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (227)

The title compound was prepared from 1-phenyltetrahydropyrimidin-2(1*H*)-one (212) (0.8 g, 4.5 mmole), sodium hydride (0.36 g, 9.1 mmole) and ethyl 2-bromopropionate (108) (1.2 mL, 9.1 mmole) following the method described for the synthesis of compound (109) to afford the title product as white solid. (0.7 g, 58 %). m.p. 164-65 °C.

Anal.:

TLC :R_f 0.43 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2950, 1737, 1647, 1508, 1434, 1238, 1174, 1072, 763.

PMR ($CDCl_3$) :7.27-7.36 (m, 4H), 7.13-7.19 (m, 1H), 5.14-5.18 (q, 1H, *J* = 7.44 Hz), 4.16-4.19 (m, 2H), 3.68-3.73 (m, 2H), 3.39-3.44 (m, 2H), 2.06-2.13 (m, 2H), 1.44-1.46 (d, 3H, *J* = 7.40 Hz), 1.26-1.29 (t, 3H).

4.1.199 Ethyl 2-[3-(4-methoxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (228)

The title compound was prepared from 1-(4-methoxyphenyl) tetrahydropyrimidin-2(1*H*)-one (213) (3 g, 14 mmole), sodium hydride (1.2 g, 29 mmole) and ethyl 2-bromopropionate (108) (3.8 mL, 29 mmole) following the method described for the synthesis of compound (109) to afford the title product as oil. (3.2 g, 75.9 %).

Anal.:

TLC :R_f 0.34 (50 % EtOAc in n-hexane).

IR (KBr, cm^{-1}) :2955, 1733, 1629, 1512, 1248, 1178, 1035, 839, 746.

PMR ($CDCl_3$) :7.17-7.19 (d, 2H, *J* = 8.96 Hz), 6.84-6.87 (d, 2H, *J* = 9.00 Hz), 5.15-5.21 (q, 1H, *J* = 7.44 Hz), 4.13-4.21 (m, 2H), 3.78 (s, 3H), 3.63-3.66 (m, 2H), 3.37-3.41 (m, 2H), 2.08-2.18 (m, 2H), 1.43-1.44 (d, 3H, *J* = 7.40 Hz), 1.25-1.29 (t, 3H).

4.1.200 Ethyl 2-[3-(3,4-dimethoxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (229)

The title compound was prepared from 1-(3,4-dimethoxyphenyl)tetrahydropyrimidin-2(1*H*)-one (217) (1.2 g, 5.1 mmole), sodium hydride (0.4 g, 10 mmole) and ethyl 2-bromopropionate (108) (1.3 mL, 10 mmole) following the method described for the synthesis of compound (109) to afford the title product as oil. (1.5 g, 87.5 %).

Anal.:

TLC :R_f 0.26 (50 % EtOAc in n-hexane).

4.1.201 Ethyl 2-[3-(4-benzyloxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (230)

The title compound was prepared from 1-(4-benzyloxyphenyl)tetrahydropyrimidin-2(1*H*)-one (215) (1 g, 3.5 mmole), sodium hydride

(0.34 g, 7.1 mmole) and ethyl 2-bromopropionate (**108**) (1 mL, 7.1 mmole) following the method described for the synthesis of compound (**109**). The crude product thus obtained was purified by column chromatography over silica gel using 10 - 25 % ethyl acetate in n-hexane as eluant to afford the title product as sticky mass. (0.7 g, 52.3 %).

Anal.:

TLC :R_f 0.66 (50 % EtOAc in n-hexane).

4.1.202 2-{3-[4-(4-Methoxybenzyloxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionic acid (231)

The title compound was prepared from ethyl 2-{3-[4-(4-methoxybenzyloxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**216**) (0.35 g, 0.8 mmole) and lithium hydroxide (0.18 g, 4.2 mmole) following the same method as described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.25 g, 81.4 %). m.p. 184-86 °C.

Anal.:

TLC	:R_f 0.61 (70 % EtOAc in n-hexane).
UV (MeOH)	:231.0 nm (log ε 3.95).
IR (KBr, cm^{-1})	:3446, 2954, 1737, 1685, 1517, 1450, 1251, 1174, 1029, 833, 744.
PMR (DMSO-d_6)	:7.33-7.35 (d, 2H), 7.14-7.16 (d, 2H), 6.88-6.91 (m, 4H), 4.96-5.01 (m, 3H), 3.80 (s, 3H), 3.60-3.65 (m, 2H), 3.40-3.43 (m, 2H), 2.09-2.17 (m, 2H), 1.40-1.42 (d, 3H).
MS (m/z)	:407.0 $(M+Na)^+$, 384.8 $(M+H)^+$.

4.1.203 2-{3-[4-(2-Pyridinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionic acid (232)

The title compound was prepared from ethyl 2-{3-[4-(2-pyridinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**217**) (0.4 g, 1 mmole) and sodium hydroxide (0.1 g, 2.2 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was purified by column chromatography over neutral alumina using ethyl acetate as eluant to afford the title product as white solid. (0.3 g, 84.5 %). m.p. 183-85 °C.

Anal.:

TLC	:R_f 0.27 (80 % EtOAc in n-hexane).
UV (MeOH)	:239.0 nm (log ε 4.09).

IR (KBr, cm^{-1}) :3446, 2984, 1730, 1652, 1502, 1436, 1249, 1178, 1021, 826, 758.

PMR (DMSO-d_6) :8.57-8.58 (m, 1H), 7.69-7.72 (m, 1H), 7.50-7.52 (m, 1H), 7.24-7.27 (m, 1H), 7.16-7.18 (d, 2H, J = 8.88 Hz), 6.91-6.94 (d, 2H, J = 8.96 Hz), 5.17 (s, 2H), 5.03-5.08 (q, 1H, J = 7.41 Hz), 3.62-3.65 (m, 2H), 3.40-3.45 (m, 2H), 2.00-2.08 (m, 2H), 1.42-1.43 (d, 3H, J = 7.40 Hz).

MS (m/z) :394.0 $(M+K)^+$, 378.0 $(M+Na)^+$, 355.8 $(M+H)^+$, 309.7 $(M\text{-}COOH)^+$.

4.1.204 2-{3-[4-(4-Biphenylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionic acid (233)

The title compound was prepared from ethyl 2-{3-[4-(4-biphenylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**218**) (0.18 g, 0.4 mmole) and lithium hydroxide (0.08 g, 2 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.12 g, 69.8 %). m.p. 204-05 °C.

Anal.:

TLC :R_f 0.26 (EtOAc).

UV (MeOH) : 251.0 nm (log ε 4.35).

IR (KBr, cm^{-1}) :2981, 1743, 1641, 1446, 1242, 1180, 1026, 765.

PMR (DMSO-d_6) :7.58-7.61 (m, 4H), 7.49-7.51 (m, 2H), 7.42-7.46 (m, 2H), 7.33-7.38 (m, 1H), 7.18-7.20 (m, 2H), 6.96-6.94 (m, 2H), 5.06-5.10 (m, 3H), 3.63-3.66 (m, 2H), 3.38-3.44 (m, 2H), 2.10-2.19 (m, 2H), 1.44-1.46 (d, 3H).

4.1.205 2-{3-[4-(2-Isobutyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionic acid (234)

The title compound was prepared from ethyl 2-{3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**219**) (0.4 g, 0.8 mmole) and sodium hydroxide (0.06 g, 2 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.2 g, 54.2 %). m.p. 129-31 °C.

Anal.:

TLC :R_f 0.22 (EtOAc).

IR (KBr, cm^{-1}) :3445, 2980, 1734, 1652, 1436, 1242, 1178, 1026, 830.

PMR ($CDCl_3$) :8.11-8.13 (m, 1H), 7.91-7.93 (m, 1H), 7.68-7.72 (m, 1H), 7.55-7.52 (m, 1H), 7.41 (s, 1H), 7.20-7.22 (d, 2H, *J* = 8.84 Hz), 7.01-7.03 (d, 2H, *J* = 8.84 Hz), 5.50 (s, 2H), 4.71-4.74 (q, 1H, *J* = 7.24 Hz), 3.64-3.67 (m, 2H), 3.41-3.44 (m, 2H), 2.84-2.86 (d, 2H), 2.14-2.22 (m, 3H), 1.51-1.53 (d, 3H, *J* = 7.28 Hz), 0.95-0.97 (d, 6H).

4.1.206 2-{3-[4-(2-Ethyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl} propionic acid (235)

The title compound was prepared from ethyl 2-{3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (220) (0.5 g, 1.1 mmole) and sodium hydroxide (0.22 g, 5.4 mmole) following the method described for the synthesis of compound (128). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.35 g, 73.65 %). m.p. 182-83 °C.

Anal.:

TLC :R_f 0.12 (EtOAc).

IR (KBr, cm^{-1}) :3448, 1723, 1652, 1506, 1436, 1248, 1182, 1036, 835.

PMR (DMSO-d_6) :8.03-8.05 (m, 1H), 7.67-7.71 (m, 2H), 7.54-7.56 (m, 1H), 7.45-7.49 (m, 2H), 7.23-7.26 (m, 1H), 6.90-7.03 (m, 2H), 5.34 (s, 2H), 4.75-4.79 (q, 1H), 3.48-3.51 (m, 2H), 3.37-3.42 (q, 2H), 3.26-3.23 (m, 2H), 1.93-2.03 (m, 2H), 1.52-1.54 (t, 3*H*),1.32-1.36 (t, 3H), .

4.1.207 2-{3-[4-(2-Phenyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl} propionic acid (236)

The title compound was prepared from ethyl 2-{3-[4-(2-phenyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (221) (0.15 g, 0.3 mmole) and sodium hydroxide (0.02 g, 0.6 mmole) following the method described for the synthesis of compound (128). The solid product so obtained was crystallized from methanol to afford the title product as white solid. (0.12 g, 86.0 %). m.p. 124-27 °C.

Anal.:

TLC :R_f 0.22 (10 % MeOH in $CHCl_3$).

UV (MeOH) :255.5 nm (log ε 4.28).

IR (KBr, cm^{-1}) :3412, 2937, 1734, 1639, 1602, 1508, 1444, 1298, 1182, 1028, 771.

PMR (DMSO-d_6) :8.17-8.23 (m, 2H), 8.10 (s, 1H), 8.04-8.06 (m, 1H), 7.80-7.86 (m, 2H), 7.61-7.65 (m, 1H), 7.46-7.56 (m, 3H), 7.22-7.24 (d, 2H, J = 8.88 Hz), 7.04-7.06 (d, 2H, J = 8.92 Hz), 5.60 (s, 2H), 5.02-5.08 (q, 1H, J = 7.29 Hz), 3.64-3.67 (m, 2H), 3.42-3.46 (m, 2H), 2.06-2.12 (m, 2H), 1.42-1.44 (d, 3H, J = 7.40 Hz).

Calculated for $C_{29}H_{27}N_3O_4$: C, 72.33, H, 5.65, N, 8.73; Found C, 72.46, H, 5.87, N, 9.02 %.

4.1.208 2-{3-[4-(1-Naphthylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionic acid (237)

The title compound was prepared from ethyl 2-{3-[4-(1-naphthylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**222**) (0.3 g, 0.7 mmole) and lithium hydroxide (0.15 g, 3.5 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.15 g, 54.9 %). m.p. 207-09 °C.

Anal.:

TLC :R_f 0.73 (EtOAc).

UV (MeOH) :222.5 nm (log ε 4.75).

IR (KBr, cm^{-1}) :2985, 1737, 1643, 1502, 1444, 1296, 1180, 1024, 835, 777.

PMR (DMSO-d_6) :δ 8.02-8.05 (m, 1H), 7.85-7.91 (m, 2H), 7.55-7.61 (m, 2H), 7.45-7.52 (m, 2H), 7.20-7.22 (d, 2H, J = 8.92 Hz), 6.99-7.01 (d, 2H, J = 8.88 Hz), 5.47 (s, 2H), 5.04-5.08 (q, 1H, J = 7.44 Hz), 3.62-3.65 (m, 2H), 3.40-3.45 (m, 2H), 2.11-2.18 (m, 2H), 1.43-1.44 (d, 3H, J = 7.40 Hz).

MS (m/z) :343.0 $(M+K)^+$, 427.0 $(M+Na)^+$, 404.9 $(M+H)^+$.

4.1.209 2-[3-(5-Benzyl-1,3,4-thiadiazol-2-yl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionic acid (238)

The title compound was prepared from ethyl 2-[3-(5-benzyl-1,3,4-thiadiazol-2-yl)-2(1*H*)-oxo-tetrahydro-1-pyrimidinyl]propionate (**223**) (0.3 g, 0.8 mmole) and sodium hydroxide (0.08 g, 2 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.25g, 90.3 %). m.p. 147-48 °C.

Anal.:

TLC	:R_f 0.42 (10 % MeOH in EtOAc).
UV (MeOH)	:264.5 (log ε 4.89).
IR (KBr, cm^{-1})	:3423, 2935, 1734, 1654, 1496, 1278, 1201, 1030, 744, 702.
PMR ($CDCl_3$)	:7.20-7.33 (m, 5H), 5.06-5.11 (q, 1H, J = 7.44 Hz), 4.28 (s, 2H), 4.01-4.08 (m, 2H), 3.33-3.43 (m, 2H), 2.07-2.19 (m, 2H), 1.46-1.48 (d, 3H, J = 7.40 Hz).
MS (m/z)	:347.0 $(M+H)^+$, 301.1 $(M-COOH)^+$.

4.1.210 2-{3-[5-(4-Methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2(1*H*)-oxotetrahydro-1-pyrimidin}propionic acid (239)

The title compound was prepared from ethyl 2-{3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2(1*H*)-oxotetrahydropyrimidin-1-yl}propionate (**224**) (0.4 g, 0.9 mmole) and sodium hydroxide (0.08 g, 2 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.25g, 73.9 %). m.p. 112-15 °C.

Anal.:

TLC	:R_f 0.17 (10 % MeOH in EtOAc).
IR (KBr, cm^{-1})	:3367, 2931, 1730, 1649, 1512, 1247, 1178, 1030, 742.
PMR (DMSO-d_6)	:12.78 (bs, 1H), 7.19-7.21 (d, 2H, J = 8.40 Hz), 6.86-6.88 (d, 2H, J = 8.40 Hz), 4.68-4.74 (q, 1H), 4.18 (s, 2H), 4.10-4.13 (m, 1H), 3.95-3.99 (m, 1H), 3.81 (s, 3H), 3.15-3.18 (m, 2H), 2.00-2.04 (m, 2H), 1.32-1.34 (d, 3H).

Calculated for $C_{17}H_{20}N_4O_4S$: C, 54.24, H, 5.36, N, 14.88; Found C, 54.01, H, 5.68, N, 14.56 %.

4.1.211 2-[3-(4,5-Diphenyl-2-thiazolyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionic acid (240)

The title compound was prepared from ethyl 2-[3-(4,5-diphenyl-2-thiazolyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**225**) (0.3 g, 0.7 mmole) and sodium hydroxide (0.06 g, 1.4 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.2 g, 72.3 %). m.p. 188-90 °C.

Anal.:

TLC	:R_f 0.55 (80 % EtOAc in n-hexane).

UV (MeOH) :237.0 nm (log ε 4.18).

IR (KBr, cm^{-1}) :2960, 1751, 1718, 1616, 1479, 1213, 1105, 759.

PMR ($CDCl_3$) :7.51-7.53 (m, 2H), 7.35-7.32 (m, 2H), 7.23-7.29 (m, 6H), 5.22-5.17 (q, 1H, J = 7.37 Hz), 4.42-4.45 (m, 1H), 4.11-4.13 (m, 1H), 3.41-3.44 (m, 2H), 2.15-2.20 (m, 2H), 1.52-1.54 (d, 3H, J = 7.36 Hz).

4.1.212 2-[3-(4-*p*-Tolyl-2-thiazolyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionic acid (241)

The title compound was prepared from ethyl 2-[3-(4-*p*-tolyl-2-thiazolyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**226**) (0.5 g, 1.3 mmole) and lithium hydroxide (0.3 g, 6.7 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.25g, 55.7 %). m.p. 230-32 °C.

Anal.:

TLC :R_f 0.13 (60 % EtOAc in n-hexane).

UV (MeOH) :268.0 nm (log ε 3.93).
237.5 nm (log ε 4.06).

IR (KBr, cm^{-1}) :3438, 2924, 1735, 1649, 1618, 1213, 1199, 821, 736.

PMR (DMSO-d_6) :7.76-7.79 (d, 2H, J = 8.05 Hz), 7.36 (s, 1H), 7.17-7.20 (d, 2H, J = 8.00 Hz), 4.61-4.64 (q, 1H, J = 7.35 Hz), 4.14-4.19 (m, 1H), 4.03-4.09 (m, 1H), 3.41-3.47 (m, 1H), 3.18-3.24 (m, 1H), 2.30 (s, 3H), 1.97-2.09 (m, 2H), 1.21-1.23 (d, 3H, J = 7.33 Hz).

4.1.213 2-[3-Phenyl-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionic acid (242)

The title compound was prepared from ethyl 2-[3-phenyl-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**227**) (0.2 g, 0.7 mmole) and lithium hydroxide (0.15 g, 3.5 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.12 g, 69.1 %). m.p. 179-80 °C.

Anal.:

TLC :R_f 0.36 (EtOAc).

UV (MeOH) :244.0 nm (log ε 3.76).

IR (KBr, cm^{-1}) :2920, 1743, 1643, 1593, 1448, 1303, 1180, 1064, 759.

PMR (DMSO-d_6) :7.34-7.37 (m, 2H), 7.26-7.28 (m, 2H), 7.19-7.22 (m, 1H), 4.80-4.85 (q, 1H, *J* = 7.33 Hz), 3.67-3.70 (m, 2H), 3.40-3.46 (m, 2H), 2.11-2.19 (m, 2H), 1.49-1.51 (d, 3H, *J* = 7.32 Hz).

$[\alpha]^{25}_D$:+0.18° (5 % MeOH)

4.1.214 2-[3-(4-Methoxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionic acid (243)

The title compound was prepared from ethyl 2-[3-(4-methoxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**228**) (0.2 g, 0.6 mmole) and lithium hydroxide (0.14 g, 3.3 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.15 g, 89.9 %). m.p. 233-35 °C.

Anal.:

TLC :R_f 0.38 (EtOAc).

UV (MeOH) :236.5 nm (log ε 4.01).

IR (KBr, cm^{-1}) :2950, 1737, 1620, 1596, 1448, 1299, 1172, 1033, 831, 744.

PMR (DMSO-d_6) :12.00 (bs, 1H), 7.14-7.18 (d, 2H), 6.81-6.85 (d, 2H), 5.00-5.05 (q, 1H, *J* = 7.40 Hz), 3.77 (s, 3H), 3.62-3.65 (m, 2H), 3.35-3.44 (m, 2H), 2.05-2.21 (m, 2H), 1.41-1.43 (d, 3H, *J* = 7.40 Hz).

Calculated for $C_{14}H_{18}N_2O_4$: C, 60.42, H, 6.52, N, 10.06; Found C, 60.01, H, 6.98, N, 9.87 %.

4.1.215 2-[3-(3,4-Dimethoxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionic acid (244)

The title compound was prepared from ethyl 2-[3-(3,4-dimethoxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**229**) (0.5 g, 1.5 mmole) and lithium hydroxide (0.3 g, 7.4 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.2 g, 43.9 %). m.p. 125-26 °C.

Anal.:

TLC :R_f 0.14 (EtOAc).

UV (MeOH) :237.0 nm (log ε 3.83).

IR (KBr, cm^{-1}) :3443, 2982, 1730, 1650, 1512, 1448, 1244, 1172, 1028, 856, 763.

PMR (DMSO-d_6) :6.84-6.87(m, 2H), 6.70-6.74 (m, 1H), 4.74-4.82 (q, 1H, *J* = 7.30 Hz), 3.71 (s, 6H), 3.54-3.57 (m, 2H), 3.28-3.31 (m, 2H), 1.94-2.07 (m, 2H), 1.27-1.30 (d, 3H, *J* = 7.34 Hz).

4.1.216 2-[3-(4-Benzyloxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionic acid (245)

The title compound was prepared from ethyl 2-[3-(4-benzyloxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**230**) (0.2 g, 0.5 mmole) and lithium hydroxide (0.1 g, 2.6 mmole) following the method described for the synthesis of compound (**128**). The solid product thus obtained was crystallized from methanol to afford the title product as white solid. (0.09 g, 56.5 %). m.p. 207-09 °C.

Anal.:

TLC :R_f 0.64 (70 % EtOAc in n-hexane).

UV (MeOH) :232.0 nm (3.85).

IR (KBr, cm^{-1}) :2981, 1743, 1643, 1566, 1446, 1298, 1174, 1026, 831, 754.

PMR (DMSO-d_6) :7.38-7.43 (m, 4H), 7.30-7.33 (m, 1H), 7.15-7.18 (d, 2H, *J* = 8.96 Hz), 6.90-6.92 (d, 2H, *J* = 8.92 Hz), 5.03-5.05 (m, 3H), 3.62-3.65 (m, 2H), 3.37-3.42 (m, 2H), 2.09-2.15 (m, 2H), 1.41-1.43 (d, 3H).

4.1.217 *N*-Hydroxy-2-{3-[4-(4-methoxybenzyloxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionamide (246)

The title compound was prepared from ethyl 2-{3-[4-(4-methoxybenzyloxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**216**) (0.3 g, 0.7 mmole), hydroxylamine hydrochloride (5 g, 72 mmole) and potassium hydroxide (4.4 g, 80 mmole) following the same method as described for the synthesis of compound (**147**). The solid product thus obtained was triturated with ether to afford the title product as white solid. (0.17 g, 60.9 %). m.p.169-70 °C.

Anal.:

TLC :R_f 0.68 (70 % EtOAc in n-hexane).

UV (MeOH) :230.0 nm (log ε 4.22).

IR (KBr, cm^{-1}) :3446, 1652, 1616, 1456, 1263, 1177, 1028, 827, 749.

PMR (DMSO-d_6) :7.33-7.35 (d, 2H), 7.15-7.17 (d, 2H), 6.89-6.91 (m, 4H), 5.01-5.05 (q, 1H, J = 7.40 Hz), 4.96 (s, 2H), 3.81 (s, 3H), 3.62-3.65 (m, 2H), 3.47-3.40 (m, 2H), 2.10-2.16 (m, 2H), 1.42-1.44 (d, 3H, J = 7.36 Hz).

MS (m/z) :407.0 $(M-14+Na)^+$, 398.9 $(M-H)^+$, 384.9 $(M-14)^+$, 338.8 $(M-CONHOH)^+$.

4.1.218 *N*-Hydroxy-2-{3-[4-(2-pyridinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionamide (247)

The title compound was prepared from ethyl 2-{3-[4-(2-pyridinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (217) (0.5 g, 1.3 mmole), hydroxylamine hydrochloride (9.9 g, 130 mmole) and potassium hydroxide (8.7 g, 150 mmole) following the method described for the synthesis of compound (147). The oily product thus obtained was triturated with ether to afford the title product as white solid. (0.3 g, 62.4 %). m.p. 175-178 °C.

Anal.:

TLC :R_f 0.28 (80 % EtOAc in n-hexane).

UV (MeOH) :238.0 nm (log ε 4.07).

IR (KBr, cm^{-1}) :3446, 1652, 1250, 1177, 1052, 827, 744.

PMR (DMSO-d_6) :8.56-8.57 (m, 1H), 7.72-7.76 (m, 1H), 7.49-7.51 (m, 1H), 7.25-7.28 (m, 1H), 7.15-7.17 (d, 2H, J = 8.36 Hz), 6.92-6.94 (d, 2H, J = 8.36 Hz), 5.14 (s, 2H), 4.96-4.99 (q, 1H, J = 7.44 Hz), 3.61-3.70 (m, 2H), 3.37-3.48 (m, 2H), 2.05-2.15 (m, 2H), 1.41-1.43 (d, 3H, J = 7.40 Hz).

MS (m/z) :393.0 $(M+Na)^+$, 378.7 $(M-14+Na)^+$, 369.7 $(M-H)^+$, 355.8 $(M-14)^+$, 310.1 $(M-CONHOH)^+$.

4.1.219 2-{3-[4-(4-Biphenylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}-*N*-hydroxypropionamide (248)

The title compound was prepared from ethyl 2-{3-[4-(4-biphenylylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (218) (0.35 g, 0.8 mmole), hydroxylamine hydrochloride (5.3 g, 76 mmole) and potassium hydroxide (4.7 g, 84 mmole) following the method described for the synthesis of compound (147). The oily product thus obtained was triturated with ether to afford the title product as white solid. (0.1 g, 29.7 %). m.p. 233-35 °C.

Anal.:

TLC	:R_f 0.16 (EtOAc).
UV (MeOH)	:250.0 nm (log ε 4.38).
IR (KBr, cm^{-1})	:1643, 1581, 1242, 1172, 1029, 839, 732.
PMR (DMSO-d_6)	:10.09 (bs, 1H), 8.61 (bs, 1H), 7.63-7.58 (m, 4H), 7.49-7.51 (m, 2H), 7.42-7.46 (m, 2H), 7.33-7.37 (m, 1H), 7.17-7.20 (d, 2H), 6.92-6.97 (d, 2H), 5.10 (s, 2H), 4.99-4.95 (q, 1H, J = 7.20 Hz), 3.60-3.63 (m, 2H), 3.39-3.45 (m, 2H), 2.06-2.16 (m, 2H), 1.38-1.37 (d, 3H, J = 7.24 Hz).
MS (m/z)	:484.2 $(M+K)^+$, 473.2 $(M+Na)^+$, 431.1 $(M-14)^+$, 413.1 $(M-NHOH)^+$, 385.1 $(M-CONHOH)^+$.

4.1.220 *N*-Hydroxy-2-{3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionamide (249)

The title compound was prepared from ethyl 2-{3-[4-(2-isobutyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**219**) (0.5 g, 1.8 mmole), hydroxylamine hydrochloride (12.8 g, 184 mmole) and potassium hydroxide (11.3 g, 202 mmole) following the method described for the synthesis of compound (**147**). The oily product thus obtained was triturated with ether to afford the title product as white solid. (0.15 g, 17.5 %). m.p. 116-18 °C.

Anal.:

TLC	:R_f 0. (50 % EtOAc in n-hexane).
IR (KBr, cm^{-1})	:3448, 1652, 1506, 1456, 1246, 1180, 830.
PMR (DMSO-d_6)	:8.11-8.13 (m, 1H), 7.89-7.91 (m, 1H), 7.68-7.72 (m, 1H), 7.49-7.53 (m, 1H), 7.40 (s, 1H), 7.18-7.20 (d, 2H), 6.97-6.99 (d, 2H), 5.45 (s, 2H), 4.69-4.73 (q, 1H), 3.60-3.63 (m, 2H), 3.36-3.40 (m, 2H), 2.83-2.85 (d, 2H), 2.09-2.231 (m, 3H), 1.46-1.47 (d, 3H), 0.94-0.96 (d, 6H).

Calculated for $C_{27}H_{32}N_4O_4$: C, 68.05, H, 6.77, N, 11.76; Found C, 67.85, H, 7.01, N, 11.42 %.

4.1.221 *N*-Hydroxy-2-{3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionamide (250)

The title compound was prepared from ethyl 2-{3-[4-(2-ethyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**220**) (0.7 g,

1.5 mmole), hydroxylamine hydrochloride (10.5 g, 150 mmole) and potassium hydroxide (9.3 g, 170 mmole) following the method described for the synthesis of compound (147). The oily product thus obtained was triturated with ether to afford the title product as white solid. (0.46 g, 46.1 %). m.p. 179-80 °C.

Anal.:

TLC	:R_f 0.17 (EtOAc).
UV (MeOH)	:232.0 nm (log ε 4.39).
PMR (DMSO-d_6)	:10.47 (bs, 1H), 8.78 (bs, 1H), 8.24-8.26 (m, 1H), 8.03-8.07 (m, 2H), 7.88-7.91 (m, 1H), 7.42 (s, 1H), 7.26-7.28 (d, 2H), 7.06-7.08 (d, 2H), 5.75 (s, 2H), 5.06-5.11 (q, 1H, *J* = 7.40 Hz), 3.66-3.69 (m, 2H), 3.49-3.55 (m, 2H), 3.37-3.40 (m, 2H), 2.11-2.21 (m, 2H), 1.55-1.58 (t, 3H), 1.43-1.45 (d, 3H, *J* = 7.40 Hz).
MS (m/z)	:449.4 $(M+H)^+$, 434.1 $(M-14)^+$, 388.1 $(M-CONHOH)^+$.

4.1.222 *N*-Hydroxy-2-{3-[4-(2-phenyl-4-quinolinylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionamide (251)

The title compound was prepared from ethyl 2-{3-[4-(2-phenylquinolin-4-ylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (221) (0.25 g, 0.5 mmole), hydroxylamine hydrochloride (3.4 g, 4.9 mmole) and potassium hydroxide (3 g, 5.4 mmole) following the same method described for the synthesis of compound (147). The crude solid thus obtained was triturated with ether to afford the title product as white solid. (0.05 g, 20.5 %). m.p. 132-34 °C.

Anal.:

TLC	:R_f 0.17 (10 % MeOH in $CHCl_3$).
UV (MeOH)	:255.5 nm (log ε 4.52).
IR (KBr, cm^{-1})	:3414, 3203, 2937, 1680, 1602, 1508, 1444, 1238, 1182, 1028, 771.
PMR (DMSO-d_6)	:8.17-8.19 (m, 2H), 8.08 (s, 1H), 8.03-8.05 (m, 2H), 7.75-7.79 (m, 1H), 7.58-7.62 (m, 1H), 7.52-7.55 (m, 2H), 7.45-7.49 (m, 1H), 7.22-7.25 (d, 2H, *J* = 8.88 Hz), 7.04-7.07 (d, 2H, J = 8.96 Hz), 5.60 (s, 2H), 5.03-5.06 (q, 1H), 3.62-3.68 (m, 2H), 3.39-3.46 (m, 2H), 2.07-2.16 (m, 2H), 1.37-1.39 (d, 3H).

4.1.223 *N*-Hydroxy-2-{3-[4-(1-naphthylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl} propionamide (252)

The title compound was prepared from ethyl 2-{3-[4-(1-naphthylmethoxy)phenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**222**) (0.5 g, 1.1 mmole), hydroxylamine hydrochloride (8 g, 115 mmole) and potassium hydroxide (7.1 g, 127 mmole) following the method described for the synthesis of compound (**147**). The crude solid thus obtained was triturated with ether to afford the title product as white solid. (0.15 g, 32.5 %). m.p. 202-03 °C.

Anal.:

TLC	:R_f 0.72 (EtOAc).
UV (MeOH)	:222.5 nm (log ε 4.87).
IR (KBr, cm^{-1})	:3440, 2991, 1652, 1508, 1436, 1296, 1221, 1169, 835, 750.
PMR ($CDCl_3$)	:8.02-8.04 (m, 1H), 7.85-7.91 (m, 2H), 7.58-7.60 (m, 2H), 7.52-7.55 (m, 2H), 7.50-7.46 (m, 1H), 7.20-7.22 (d, 2H, *J* = 8.84 Hz), 7.00-7.02 (d, 2H, *J* = 8.88 Hz), 5.47 (s, 2H), 5.07-5.13 (q, 1H, *J* = 7.39 Hz), 3.65-3.72 (m, 2H), 3.36-3.45 (m, 2H), 2.17-2.21 (m, 1H), 2.07-2.12 (m, 1H), 1.44-1.45 (d, 3H, *J* = 7.44 Hz).
$[\alpha]^{25}_D$	:+0.14° (2 % MeOH).
MS (m/z)	:442.9 $(M+Na)^+$, 427.0 $(M-14+Na)^+$, 418.9 $(M-H)^+$, 404.9 $(M-14)^+$, 358.8 $(M-CONHOH)^+$.

4.1.224 *N*-Hydroxy-2-{3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionamide (253)

The title compound was prepared from ethyl 2-{3-[5-(4-methoxybenzyl)-1,3,4-thiadiazol-2-yl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionate (**224**) (0.8 g, 2 mmole), hydroxylamine hydrochloride (13.8 g, 200 mmole) and potassium hydroxide (12.2 g, 220 mmole) following the method described for the synthesis of compound (**147**). The crude solid thus obtained was triturated with ether to afford the title product as white solid. (0.20 g, 25.6 %). m.p. 120-21 °C.

Anal.:

TLC	:R_f 0.14 (10 % MeOH in EtOAc).
UV (MeOH)	:257.5 nm (log ε 3.90). 224.5 nm (log ε 3.84).
IR (KBr, cm^{-1})	:3254, 2937, 1651, 1610, 1514, 1247, 1178, 1030, 742.

PMR (DMSO-d_6) :7.18-7.21 (d, 2H, J = 8.36 Hz), 6.81-6.84 (d, 2H, J = 8.40 Hz), 4.97-5.02 (q, 1H, J = 7.28 Hz), 4.20 (s, 2H), 4.01-4.06 (m, 2H), 3.7 (s, 3H), 3.39-3.45 (m, 2H), 2.10-2.20 (m, 2H), 1.43-1.45 (d, 3H, J = 7.36 Hz).

MS (m/z) :392.2 $(M+H)^+$, 377.0 $(M-14)^+$, 331.0 $(M-CONHOH)^+$.

4.1.225 2-[3-(4,5-Diphenyl-2-thiazolyl)-2(1*H*)–oxotetrahydro-1-pyrimidinyl]-*N*-hydroxy- propionamide (254)

The title compound was prepared from ethyl 2-[3-(4,5-diphenyl-2-thiazolyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**225**) (0.4 g, 0.9 mmole), hydroxylamine hydrochloride (6.5 g, 94 mmole) and potassium hydroxide (5.8 g, 104 mmole) following the method described for the synthesis of compound (**147**). The crude solid thus obtained was triturated with ether to afford the title product as white solid. (0.21 g, 56.9 %). m.p. 184-85 °C.

Anal.:

TLC :R_f 0.55 (80 % EtOAc in n-hexane).

UV (MeOH) :237.0 nm (log ε 4.23).

IR (KBr, cm^{-1}) :3414, 2935, 1647, 1481, 1301, 1207, 1192, 756, 696.

PMR ($CDCl_3$) :7.49-7.51 (m, 2H), 7.20-7.25 (m, 8H), 5.36-5.40 (q, 1H), 4.34-4.37 (m, 1H), 4.03-40.6 (m, 1H), 3.34-3.39 (m, 2H), 1.95-2.05 (m, 2H), 1.37-1.40 (d, 3H).

MS (m/z) :423.1 $(M+H)^+$, 408.0 $(M-14)^+$, 362.1 $(M-CONHOH)^+$.

4.1.226 *N*-Hydroxy-2-[3-(4-*p*-tolyl-2-thiazolyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl] propionamide (255)

The title compound was prepared from ethyl 2-[3-(4-*p*-tolyl-2-thiazolyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**226**) (0.8 g, 2.1 mmole), hydroxylamine hydrochloride (14.9 g, 214 mmole) and potassium hydroxide (13.2 g, 235 mmole) following the method described for the synthesis of compound (**147**). The crude solid thus obtained was triturated with ether to afford the title product as white solid. (0.4 g, 53.0 %). m.p. 155-56 °C.

Anal.:

TLC :R_f 0.21 (60 % EtOAc in n-hexane).

UV (MeOH) :267.5 nm (log ε 3.98).
236.5 nm (log ε 4.10).

IR (KBr, cm^{-1}) :3091, 1631, 1487, 1473, 1298, 1193, 1001, 827, 738.

PMR (DMSO-d_6) :7.77-7.80 (d, 2H, J = 8.03 Hz), 7.42 (s, 1H), 7.18-7.21 (d, 2H, J = 7.99 Hz), 4.77-4.84 (q, 1H, J = 7.25 Hz), 4.00-4.09 (m, 2H), 3.34-3.37 (m, 2H), 2.30 (s, 3H), 2.01-2.08 (m, 2H), 1.34-1.36 (d, 3H, J = 7.31 Hz).

Calculated for $C_{17}H_{20}N_4O_3S$: C, 56.65, H, 5.59, N, 15.54; Found C, 56.34, H, 5.24, N, 15.01 %.

4.1.227 *N*-Hydroxy-2-{3-phenyl-2(1*H*)-oxotetrahydro-1-pyrimidinyl}propionamide (256)

The title compound was prepared from ethyl 2-[3-phenyl-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (227) (0.4 g, 1.4 mmole), hydroxylamine hydrochloride (10 g, 140 mmole) and potassium hydroxide (8.9 g, 160 mmole) following the method described for the synthesis of compound (147). The oily compound thus obtained was triturated with ether to afford the title product as white solid. (0.09 g, 24.4 %). m.p. 128-30 °C.

Anal.:

TLC :R_f 0.29 (EtOAc).

UV (MeOH) :245.5 nm (log ε 3.78).

IR (KBr, cm^{-1}) :3213, 2925, 1670, 1496, 1446, 1211, 1097, 1037.

PMR ($CDCl_3$) :7.33-7.37 (m, 2H), 7.26-7.28 (m, 2H), 7.19-7.22 (m, 1H), 4.80-4.86 (q, 1H, J = 7.22 Hz), 3.67-3.72 (m, 2H), 3.40-3.44 (m, 2H), 2.13-2.19 (m, 2H), 1.49-1.51 (d, 3H, J = 7.36 Hz).

4.1.228 *N*-Hydroxy-2-[3-(4-methoxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionamide (257)

The title compound was prepared from ethyl 2-[3-(4-methoxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (228) (0.3 g, 0.9 mmole), hydroxylamine hydrochloride (6.8 g, 98 mmole) and potassium hydroxide (6 g, 108 mmole) following the method described for the synthesis of compound (147). The oily compound thus obtained was triturated with ether to afford the title product as white solid. (0.15 g, 52.2 %). m.p. 216-18 °C.

Anal.:

TLC :R_f 0.28 (EtOAc).

UV (MeOH) : 238.5 nm (log ε 3.81).

IR (KBr, cm^{-1}) :3119, 1687, 1504, 1251, 1172, 1033, 831.

PMR (DMSO-d_6) :δ 9.80 (bs, 1H), 8.55 (bs, 1H), 7.15-7.20 (d, 2H), 6.84-6.87 (d, 2H), 4.95-4.98 (q, 1H, J = 6.88 Hz), 3.79 (s, 3H), 3.59-3.62 (m, 2H), 3.39-3.44 (m, 2H), 2.02-2.12 (m, 2H), 1.37-1.39 (d, 3H, J = 6.92 Hz).

$[\alpha]^{25}_D$:+0.17° (5 % MeOH).

4.1.229 *N*-Hydroxy-2-{3-[3,4-dimethoxyphenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl} propionamide (258)

The title compound was prepared from ethyl 2-[3-(3,4-dimethoxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**229**) (1 g, 2.9 mmole), hydroxylamine hydrochloride (20.1 g, 290 mmole) and potassium hydroxide (18.3 g, 330 mmole) following the method described for the synthesis of compound (**147**). The oily compound thus obtained was triturated with ether to afford the title product as white solid. (0.45 g, 48 %). m.p. 110-12 °C.

Anal.:

TLC :R_f 0.2 (EtOAc).

PMR (DMSO-d_6) :6.83-6.86 (m, 2H), 6.70-6.74 (m, 1H), 4.79-4.84 (q, 1H, J = 7.30 Hz), 3.70 (s, 6H), 3.52-3.55 (m, 2H), 3.20-3.25 (m, 2H0, 1.89-1.99 (m, 2H), 1.20-1.22 (d, 3H, J = 7.16 Hz).

$[\alpha]^{25}_D$:+0.23° (1 % MeOH).

4.1.230 *N*-Hydroxy-2-{3-[4-benzyloxyphenyl]-2(1*H*)-oxotetrahydro-1-pyrimidinyl} propionamide (259)

The title compound was prepared from ethyl 2-[3-(4-benzyloxyphenyl)-2(1*H*)-oxotetrahydro-1-pyrimidinyl]propionate (**230**) (0.3 g, 0.8 mmole), hydroxylamine hydrochloride (5.4 g, 80 mmole) and potassium hydroxide (4.8 g, 86 mmole) following the same method as described for the synthesis of compound (**147**). The oily compound thus obtained was triturated with ether to afford the title product as white solid. (0.2 g, 67.7 %). m.p. 175-77 °C.

Anal.:

TLC :R_f 0.34 (70 % EtOAc in n-hexane).

UV (MeOH) :231.5 nm (3.78).

IR (KBr, cm^{-1}) :3059, 1693, 1566, 1508, 1444, 1242, 1174, 1026, 831, 752.

PMR (DMSO-d_6) :7.31-7.42 (m, 5H), 7.15-7.18 (m, 2H), 6.90-6.92 (m, 2H), 5.03 (s, 2H), 4.38-4.42 (m, 1H), 3.59-3.62 (m, 2H), 3.39-3.41 (m, 2H), 2.07-2.17 (m, 2H), 1.40-1.43 (m, 3H).

Calculated for $C_{20}H_{23}N_3O_4$: C, 65.03, H, 6.27, N, 11.37; Found C, 65.54, H, 6.68, N, 11.12 %.

4.2 Biological Work

The biological work carried out has been divided into two parts as given below:

1. Preparation of Cell Lysate containing TACE, and
2. TACE Inhibition Studies

4.1.1 Preparation of Cell Lysate containing TACE

The cell lysate of Human monocytic leukemia cells (THP-1) were prepared as reported in literature[154]. THP-1 cells were grown in humidified air containing CO_2 (5 %) in COD at 37 °C in RPMI-1640 medium supplemented with *L*-glutamine (2 mM), sodium bicarbonate (1.5 g/L), glucose (4.5 g/L), HEPES (10 mM), sodium pyruvate (1.0 mM) and heat-inactivated fetal calf serum (FCS) (10 %). The cells were allowed to grow for 48 hours and then the whole medium was centrifuged at 1800 rpm for 2 minutes. The supernatant (100 μL) was collected and mixed well with PBS (10 mL). This suspension was again centrifuged at 1800 rpm for 2 minutes. The pellets were collected and lysate buffer (500 μL) (prepared by mixing TRIS (250 mM) and TRITON 600 (0.1 %) to phosphate buffer of pH 7.4) was added to it. The suspension was then sonicated for 30 seconds (9 seconds on and 5 seconds off cycle). This suspension was then centrifuged at 18,000 rpm at 4 °C for 5 minutes. The supernatant (1.90 mL) was collected and stored at -70 °C until used.

4.1.2 TACE Inhibition Studies

Accurately weighed fixed quantities (10 mg) of the compounds were dissolved in DMSO (10 mL) as a solvent. Dilutions were performed with DMSO to obtain concentrations of 50, 2.5 and 0.1 μM/L.

The desired number of strips containing wells from the Innozyme™ TACE activity kit was removed and the remaining strips were resealed in the foil pouch for further use. The wells were washed properly twice with wash buffer provided along with

the kit and then the residual liquid was wiped off with paper towel. The pure enzyme (Control) provided along with the kit was diluted (1:50) with sample buffer provided in the kit as per the protocol. Cell lysate was also diluted (1:50) with sample buffer. Cell lysate (100 μL) was added to all the wells and covered with a plate sealer which was provided along with the kit. It was then incubated at 25 °C for 1 hour. The wells were again washed with wash buffer for five times to remove any deposited material on the wells. In the next step, the test compounds as inhibitors (100 μL) were added to the designated wells. In one of the wells TAPI-1 (100 μL) was used as the positive control at 25 μM/L concentration. In another well (Blank) no inhibitor was added. All wells were incubated for 2 hours at 25 °C. Diluted substrate (20 μL) [diluted (1:10,000) with assay buffer provided along with the kit] was then added to each well and the wells were incubated at 37 °C for 4 hours. They were allowed to come to RT and the fluorescence was recorded in spectrofluorometric ELISA reader. Calculations were performed to obtain the percentage inhibitory activity of the inhibitors by the given formula:

% Inhibition = [1 - (Fluorescence intensity of test/Fluorescence intensity of blank)] x 100

[The blank well contains solvent (DMSO) and the substrate]