CHAPTER 2
EXPERIMENTAL

2.1 Instrument and Equipment

Melting points were measured on a Fisher-Johns melting point apparatus or Electrothermal digital melting point apparatus model IA9100 and are uncorrected. Thin-layer chromatography (TLC) was carried out on aluminium sheets precoated with silica gel (Merck Kieselgel 60 PF_{254}). Column chromatography was performed on silica gel (Merck Kieselgel 60, 70-230 mesh). The FT-IR spectra were recorded on a Nicolet Fourier-Transform Infrared Spectrophotometer model Impact 410, solid samples were incorporated to potassium bromide to form a pellet. The ^{1}H- and ^{13}C-NMR spectra were performed in deuterated chloroform ($CDCl_3$), dimethylsulfoxide (DMSO-d_6) or deuterium oxide (D_2O) with tetramethylsilane (TMS) as an internal reference on a Bruker model ACF 200 spectrometer which was operated at 200.13 MHz for ^{1}H and 50.32 MHz for ^{13}C nuclei.

2.2 Chemicals

All solvents used in this research were purified prior to use by standard methodology except for those which were reagent grades. The substrates and reagents employed for synthesizing the precursors and phenoxyacetic acids used in this work were purchased from as Fluka Chemical Company and were used without further purification.

2.3 Synthesis of Substituted Phenoxyacetic Acids

General Procedure: [10, 31, 32]

A solution of sodium hydroxide (0.94 g, 23.5 mmol) in water (5 mL) was justified added dropwise to a mixture of selected phenol (10 mmol) and chloroacetic acid (15 mmol) in a round bottom flask. The solution was refluxed approximately 2 hours. After the reaction mixture was cooled down, the solution was acidified with a dilute hydrochloric acid, filtered the precipitate and extracted the filtrate twice with ether (25 mL each). The ethereal extracts were washed with water (10 mL), dried over anhydrous sodium sulfate, evaporated *in vacuo* and recrystallized.

Thirty-eight phenoxyacetic acids and analogues were synthesized. The structures of all studied compounds are shown below.

Compound	R^1	R^2	R^3	R^4	R^5
1	H	H	H	H	H
2	H	**F**	H	H	H
3	H	H	**F**	H	H
4	**Cl**	H	H	H	H
5	H	**Cl**	H	H	H
6	H	H	**Cl**	H	H
7	H	**CH_3**	**Cl**	H	H
8	**Cl**	H	**Cl**	H	H
9	**Cl**	H	**Cl**	**Cl**	H
10	**Cl**	**Cl**	**Cl**	**Cl**	**Cl**
11	H	**Br**	H	H	H
12	H	H	**Br**	H	H

Compound	R^1	R^2	R^3	R^4	R^5
13	**Br**	**CH_3**	**Br**	H	**Br**
14	**CH_3**	H	H	H	H
15	H	**CH_3**	H	H	H
16	H	H	**CH_3**	H	H
17	**CH_3**	**CH_3**	H	H	H
18	**CH_3**	H	**CH_3**	H	H
19	**CH_3**	H	H	H	**CH_3**
20	H	**CH_3**	**CH_3**	H	H
21	H	**CH_3**	H	**CH_3**	H
22	H	**CH_3**	H	H	**NO_2**
23	**$C(CH_3)_3$**	H	**CH_3**	H	H
24	**CH_2CH_3**	H	H	H	H
25	H	H	**CH_2CH_3**	H	H
26	**$CH(CH_3)_2$**	H	H	H	H
27	**$C(CH_3)_3$**	H	H	H	H
28	H	H	**$C(CH_3)_3$**	H	H
29	**CH_2Ph**	H	H	H	H
30	H	H	**Ph**	H	H
31	**$COCH_3$**	H	H	H	H
32	H	H	**OCH_3**	H	H
33	**OCH_3**	H	H	H	**OCH_3**
34	H	**OCH_3**	H	**OCH_3**	H
35	**NO_2**	H	H	H	H
36	H	**NO_2**	H	H	H
37	H	H	**NO_2**	H	H
38	**$NHCOCH_3$**	H	H	H	H

Phenoxyacetic acid **(1)** White needle (30%), m.p. 98-99°C (lit.[33] m.p. 98-99 °C) (ethanol), R_f 0.66 (ethanol). IR (KBr) 3062, 2926, 1674, 1596, 1500, 1442 1233 and 1080 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.39 (2H, s), 4.75 (1H, s, br), 6.83 (1H, d, J = 8.33 Hz), 6.88 (1H, t, J = 7.97 Hz) and 7.24 (1H, t, J = 7.97 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 71.8 (1C, C-2), 120.2 (2C, C-b, C-f), 126.0 (1C, C-d), 135.0 (2C, C-c, C-e), 164.1 (1C, C-a) and 176.6 (1C, C-1).

3-Fluorophenoxyacetic acid **(2)** White plate (40%), m.p. 92-93°C (lit.[34] m.p. 114°C) (hexane-ethyl acetate), R_f 0.18 (dichloromethane/methanol 2:8). IR (KBr) 3076, 2940, 1722, 1615, 1494, 1432, 1243, 1146 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.67 (2H, s), 6.77-6.60 (3H, m), 7.23 (1H, t, J = 8.23 Hz) and 7.65 (1H, s, br); ^{13}C-NMR ($CDCl_3$) δ (ppm): 64.8 (1C, C-2), 102.5 (1C, C-b), 108.8 (1C, C-d), 110.1 (1C, C-f), 130.4 (1C, C-e), 158.7 (1C, C-c), 166.0 (1C, C-a) and 173.7 (1C, C-1).

4-Fluorophenoxyacetic acid **(3)** White plate (20%), m.p. 108-110°C (lit.[34] m.p. 105°C) (ethanol), R_f 0.20 (dichloromethane/methanol 8:2). IR (KBr) 3100-3000, 1634, 1514, 1427, 1233 and 1075 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.41 (2H, s), 6.87 (2H, d, J = 8.84 Hz) and 7.09 (2H, d, J = 8.84 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 66.6 (1C, C-2), 115.5 (2C, C-b, C-f), 115.7 (2C, C-c, C-e), 154.7 (1C, C-d), 158.7 (1C, C-a) and 170.7 (1C, C-1).

2-Chlorophenoxyacetic acid **(4)** White needle (52%), m.p. 142-145°C (lit.[35] m.p. 146-147°C) (hexane-dichloromethane), R_f 0.20 (dichloromethane/methanol 9:1). IR (KBr) 3287-2358, 1713, 1590, 1496, 1418 and 1100 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.73 (2H, s), 6.88 (1H, dd, J = 8.20, 1.40 Hz), 6.98 (1H, dt, J = 7.80, 1.40 Hz), 7.22 (1H, dt, J = 7.60, 1.70 Hz) and 7.40 (1H, dd, J = 7.80, 1.70 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 65.8 (1C, C-2), 114.0 (1C, C-d), 114.1 (1C, C-e), 123.0 (1C, C-c), 123.1 (1C, C-f), 127.6 (1C, C-b), 130.7 (1C, C-a) and 170.8 (1C, C-1).

3-Chlorophenoxyacetic acid **(5)** White needle (60%), m.p. 118-119°C (lit.[36] m.p. 109.5-111°C) (dichloromethane-ethanol), R_f 0.71 (ethanol). IR (KBr) 3220, 2926, 1683, 1611, 1490, 1427, 1238 and 1064 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.18 (2H, s), 6.81 (1H, d, J = 8.01 Hz), 6.86 (1H, s), 6.89 (1H, d, J = 7.88 Hz), 7.23 (1H, t, J = 8.01 Hz) and 11.25 (1H, s, br); ^{13}C-NMR (DMSO-d_6) δ (ppm): 73.5 (1C, C-2), 119.5 (1C, C-f), 120.3 (1C, C-b), 125.4 (1C, C-d), 136.1 (1C, C-e), 139.0 (1C, C-c), 165.7 (1C, C-a) and 176.4 (1C, C-1).

4-Chlorophenoxyacetic acid **(6)** White microcrystalline product (50%), m.p. 157-159°C (lit.[36] m.p. 157-158°C) (hexane-ethyl acetate), R_f 0.33 (dichloromethane/ methanol 9:1). IR (KBr) 3190, 2899, 1690, 1610, 1498, 1420, 1230 and 1090 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.80 (1H, s), 6.71 (2H, d, J = 7.80 Hz) and 7.10 (2H, d, J = 7.80 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 68.4 (1C, C-2), 114.9 (2C, C-b, C-f), 127.0 (1C, C-d), 130.0 (2C, C-c, C-e), 156.0 (1C, C-a) and 170.0 (1C, C-1).

4-Chloro-3-methylphenoxyacetic acid **(7)** White microcrystalline product (47%), m.p. 141-142°C (hexane-dichlromethane), R_f 0.10 (dichloromethane/methanol 9:1). IR (KBr) 3277-2422, 1715, 1618, 1480, 1429, 1239 and 1173 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.27 (3H, s), 4.65 (2H, s), 6.76 (1H, dd, J = 8.80, 3.04 Hz), 6.92 (1H, d, J = 3.04 Hz) and 7.28 (1H, d, J = 8.80 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 19.7 (1C, CH_3), 64.5 (1C, C-2), 113.5 (1C, C-f), 117.2 (1C, C-b), 125.0 (1C, C-d), 129.4 (1C, C-e), 136.4 (1C, C-c), 156.5 (1C, C-a) and 170.0 (1C, C-1).

2,4-Dichlorophenoxyacetic acid **(8)** White needle (57%), m.p. 141-142°C (lit.[33] m.p. 141°C) (ethanol), R_f 0.22 (dichloromethane/methanol 9:1). IR (KBr) 3200-2810, 2715, 1710, 1480, 1235 and 1115 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.78 (2H, s), 5.17 (1H, s, br), 7.03 (1H, d, J = 8.88 Hz), 7.32 (1H, dd, J = 8.88, 2.64 Hz) and 7.55 (1H, d, J = 2.64 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 65.2 (1C, C-2), 114.9 (1C, C-f), 122.2 (1C, C-b), 124.8 (1C, C-d), 127.9 (1C, C-e), 129.3 (1C, C-c), 152.3 (1C, C-a) and 169.5 (1C, C-1).

2,4,5-Trichlorophenoxyacetic acid **(9)** White plate (45%), m.p. 157-159°C (lit.[37] m.p. 157-158°C) (hexane-ethyl acetate), R_f 0.44 (dichloromethane/methanol 9:1). IR (KBr) 3250-2350, 1720, 1598, 1465, 1420, 1240 and 1123 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.78 (2H, s), 6.68 (1H, s) and 7.10 (1H, s); ^{13}C-NMR (DMSO-d_6) δ (ppm): 77.3 (1C,C-2), 114.9 (1C,C-b), 116.8 (1C,C-f), 127.5 (1C,C-d), 131.4 (1C,C-e), 133.5 (1C,C-c), 157.0 (1C,C-a) and 171.0 (1C,C-1).

2,3,4,5,6-Pentachlorophenoxyacetic acid **(10)** White needle (35%), m.p. 195-196°C (lit.[38] m.p. 198-199°C) (dichloromethane-ethanol), R_f 0.15 (dichloromethane/ acetone 7:3). IR (KBr) 3215, 1703, 1611, 1543, 1422, 1194 and 774 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.68 (2H,s) and 6.07 (1H, s, br); ^{13}C-NMR (DMSO-d_6) δ (ppm): 68.6 (1C, C-2), 119.7 (2C, C-b, C-f), 128.2 (1C, C-d), 132.2 (2C, C-c, C-d), 148.1 (1C, C-a) and 170.8 (1C, C-1).

3-Bromophenoxyacetic acid **(11)** White needle (76%), m.p. 111-113°C (lit.[32] m.p. 108.5-108.8°C) (dichloromethane-ethanol), R_f 0.49 (ethyl acetate/ethanol 5:5). IR (KBr) 3226, 2941, 1605, 1485, 1427, 1238 and 1078 cm^{-1}; ^{1}H-NMR (D_2O) δ (ppm): 4.30 (2H, s), 6.74 (1H, td, J = 7.76, 2.03 Hz), 7.01 (1H, dd, J = 7.76, 2.03 Hz), 7.04 (1H, s), 7.08 (1H, t, J = 7.76 Hz) and 11.10 (1H, s, br); ^{13}C-NMR (D_2O) δ (ppm): 65.7 (1C, C-2), 112.4 (1C, C-f), 116.7 (1C, C-b), 121.2 (1C, C-c), 123.2 (1C, C-d), 130.0 (1C, C-e), 157.5 (1C, C-a) and 175.3 (1C, C-1).

4-Bromophenoxyacetic acid **(12)** White plate (31%), m.p. 155-156°C (lit.[37] m.p. 161-162°C) (ethanol), R_f 0.25 (dichloromethane/methanol 8:2). IR (KBr) 3090, 2931, 1668, 1601, 1500, 1446, 1238 and 1064 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.12 (1H, s, br), 4.40 (2H, s), 6.81 (1H, d, J = 8.99 Hz) and 7.39 (1H, d, J = 8.99 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 66.2 (1C, C-2), 114.5 (1C, C-d), 115.6 (2C, C-b, C-f), 129.9 (2C, C-c, C-e), 154.3 (1C, C-a) and 170.1 (1C, C-1).

2,4,6-Tribromo-3-methylphenoxyacetic acid **(13)** White needle (38%), m.p. 230-231°C (dichloromethane-ethanol), R_f 0.78 (dichloromethane). IR (KBr) 3076, 1630, 1446, 1296 and 1030 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.43 (3H, s), 3.86 (1H, s, br), 4.36 (2H, s) and 7.95 (1H, s); ^{13}C-NMR (DMSO-d_6) δ (ppm): 24.0 (1C, CH_3), 68.2 (1C, C-2), 109.8 (1C, C-f), 111.5 (1C, C-b), 116.0 (1C, C-e), 133.5 (1C, C-d), 136.6 (1C, C-c), 152.2 (1C, C-a) and 170.0 (1C, C-1).

2-Methylphenoxyacetic acid **(14)** White plate (51%), m.p. 160-161°C (lit.[32] m.p. 156.8-157.4°C) (hexane-dichloromethane), R_f 0.25 (dichloromethane/methanol 9:1). IR (KBr) 3247-2366, 1705, 1593, 1501, 1419, 1239 and 1130 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.28 (3H, s), 5.29 (2H, s), 6.73 (1H, d, J = 7.30 Hz), 6.92 (1H, t, J = 7.30 Hz), 7.14 (1H, t, J = 7.50 Hz) and 7.16 (1H, d, J = 7.50 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 16.2 (1C, CH_3), 65.1 (1C, C-2), 111.3 (1C, C-f), 121.9 (1C, C-d), 126.7 (1C, C-b), 127.2 (1C, C-e), 131.2 (1C, C-c), 155.6 (1C, C-a) and 173.0 (1C, C-1).

3-Methylphenoxyacetic acid **(15)** Pale brown powder (48%), m.p. 105-106°C (lit.[39] m.p. 104.5-105.5°C) (hexane-dichloromethane), R_f 0.26 (dichloromethane/methanol 9:1). IR (KBr) 3203-2213, 1707, 1610, 1578, 1425, 1270 and 1165 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.32 (3H, s), 4.66 (2H, s), 6.72 (1H, dd, J = 8.20, 0.60 Hz), 6.74 (1H, s), 6.83 (1H, dd, J = 8.20, 0.60 Hz) and 7.18 (1H, t, J = 8.20 Hz); ^{13}C-

NMR (DMSO-d_6) δ (ppm): 21.5 (1C, CH_3), 64.7 (1C, C-2), 111.4 (1C, C-f), 115.5 (1C, C-b), 123.0 (1C, C-d), 129.4 (1C, C-e), 139.9 (1C, C-c), 157.4 (1C, C-a) and 174.2 (1C, C-1).

4-Methylphenoxyacetic acid **(16)** White needle (57%), m.p. 143-144°C (lit.[40] m.p. 140-141°C) (hexane-dichloromethane), R_f 0.27 (dichloromethane/methanol 9:1). IR (KBr) 3267-2320, 1710, 1588, 1506, 1424, 1239 and 1125 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.28 (3H, s), 4.64 (2H, s), 6.81 (2H, d, J = 8.50 Hz) and 7.09 (2H, d, J = 8.50 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 20.5 (1C, CH_3), 65.0 (1C, C-2), 114.5 (2C, C-b, C-f), 130.1 (1C, C-d), 131.5 (2C, C-c, C-e), 155.3 (1C, C-a) and 174.1 (1C, C-1).

2,3-Dimethylphenoxyacetic acid **(17)** White powder (55%), m.p. 187-189°C (lit.[41] m.p. 180-182°C) (hexane-dichloromethane), R_f 0.92 (dichloromethane/methanol 9:1). IR (KBr) 3232-2347, 1707, 1585, 1458, 1423, 1251, and 1128 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.19 (3H, s), 2.26 (3H, s), 4.46 (2H, s), 6.61 (1H, d, J = 8.20 Hz), 6.83 (1H, d, J = 7.60 Hz) and 7.03 (1H, t, J = 7.60 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 11.8 (1C, *o*-CH_3), 20.1 (1C, *m*-CH_3), 65.7 (1C, C-2), 109.2 (1C, C-f), 123.1 (1C, C-d), 125.7 (1C, C-b), 125.7 (1C, C-e), 138.2 (1C, C-c), 154.0 (1C, C-a) and 173.3 (1C, C-1).

2,4-Dimethylphenoxyacetic acid **(18)** White needle (52%), m.p. 136-138°C (lit.[40] m.p. 140-142°C) (hexane-dichloromethane), R_f 0.89 (dichloromethane/methanol 9:1). IR (KBr) 3198-2380, 1707, 1501, 1445, 1429, 1256 and 1141 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.24 (6H, s), 4.64 (2H, s), 6.62 (1H, d, J = 8.10 Hz), 6.93 (1H, dd, J = 8.10, 2.20 Hz) and 6.97 (1H, s); ^{13}C-NMR (DMSO-d_6) δ (ppm): 16.1 (1C, *p*-CH_3), 20.5 (1C, *o*-CH_3), 65.4 (1C, C-2), 111.4 (1C, C-f), 127.0 (1C, C-b), 131.2 (1C, C-e), 132.0 (1C, C-c), 132.0 (1C, C-d), 153.7 (1C, C-a) and 174.0 (1C, C-1).

2,6-Dimethylphenoxyacetic acid **(19)** White microcrystalline product (54%), m.p. 137-139°C (lit.[38] m.p. 137-138.5°C) (hexane-dichloromethane), R_f 0.26 (dichloromethane/methanol 9:1). IR (KBr) 3298-2570, 1717, 1479, 1423, 1268, 1195 and 1100 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.29 (6H, s), 4.46 (2H, s) and 7.05-6.91 (3H, m); ^{13}C-NMR (DMSO-d_6) δ (ppm): 16.2 (2C, CH_3), 68.4 (1C, C-2), 124.8 (1C, C-d), 129.1 (2C, C-b, C-f), 130.6 (2C, C-c, C-e), 154.6 (1C, C-a) and 173.3 (1C, C-1).

3,4-Dimethylphenoxyacetic acid **(20)** White needle (61%), m.p. 161-163°C (lit.[42] m.p. 162.5°C) (hexane-dichloromethane), R_f 0.91 (dichloromethane/methanol 9:1). IR (KBr) 3143-2375, 1702, 1624, 1501, 1429, 1245 and 1145 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.18 (3H, s), 2.22 (3H, s), 4.63 (2H, s), 6.64 (1H, dd, J = 8.20, 2.80 Hz), 6.73 (1H, d, J = 2.80 Hz) and 7.04 (1H, d, J = 8.20 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.8 (1C, *p*-CH_3), 20.0 (1C, *m*-CH_3), 65.0 (1C, C-2), 111.4 (1C, C-f), 116.3 (1C, C-b), 130.3 (1C, C-e), 130.5 (1C, C-d), 138.2 (1C, C-c), 155.4 (1C, C-a) and 172.9 (1C, C-1).

3,5-Dimethylphenoxyacetic acid **(21)** White microcrystalline product (56%), m.p. 77-79°C (lit.[43] m.p. 110-111°C) (hexane-dichloromethane), R_f 0.31 (dichloromethane/methanol 9:1). IR (KBr) 3120-2347, 1713, 1624, 1596, 1441, 1245 and 1178 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.28 (6H, s), 4.63 (2H, s), 6.54 (2H, s) and 6.65 (1H, s); ^{13}C-NMR (DMSO-d_6) δ (ppm): 21.4 (2C, CH_3), 64.7 (1C, C-2), 112.3 (2C, C-b, C-f), 123.6 (1C, C-d), 139.5 (2C, C-d, C-e), 157.4 (1C, C-a) and 174.1 (1C, C-1).

5-Methyl-2-nitrophenoxyacetic acid **(22)** Yellowish needle (70%), m.p. 157-158°C (lit.[44] m.p. 157-158°C) (hexane-dichloromethane), R_f 0.34 (dichloromethane/methanol 8:2). IR (KBr) 3071, 2921, 1751, 1611, 1519, 1413, 1243 and 1190 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.43 (3H, s), 3.80 (1H, s, br), 4.79 (2H, s), 6.82 (1H, s), 6.95 (1H, dd, J = 8.38 Hz) and 7.90 (1H, d, J = 8.38 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 21.7 (1C, CH_3), 65.8 (1C, C-2), 115.2 (1C, C-b), 121.8 (1C, C-d), 125.6 (1C, C-e), 126.6 (1C, C-f), 145.7 (1C, C-c), 151.3 (1C, C-a) and 169.4 (1C, C-1).

2-tert-Butyl-4-methylphenoxyacetic acid **(23)** White powder (15%), m.p. > 300°C (dichloromethane-methanol), R_f 0.13 (dichloromethane/methanol 8:2). IR (KBr) 3020, 2951, 1751, 1640, 1500, 1432, 1180 and 1098 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.33 (9H, s), 2.20 (3H, s), 3.37 (1H, s, br), 4.61 (2H, s), 6.71 (1H, d, J = 8.16 Hz), 6.93 (1H, dd, J = 8.16, 1.95 Hz) and 7.00 (1H, d, J = 1.95 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 20.4 (1C, CH_3), 29.7 (3C, CH_3), 34.3 (1C, CH), 64.8 (1C, C-2), 112.1 (1C, C-f), 127.0 (1C, C-c), 127.1 (1C, C-e), 129.0 (1C, C-d), 137.0 (1C, C-b), 155.9 (1C, C-a) and 170.2 (1C, C-1).

2-Ethylphenoxyacetic acid **(24)** White microcrystalline product (42%), m.p. 140-141°C (lit.[45] m.p. 140-142°C) (hexane-dichloromethane), R_f 0.76 (dichloromethane/methanol 9:1). IR (KBr) 3277-2479, 1710, 1495, 1424, 1234 and

1124 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.21 (3H, t, J = 7.50 Hz), 2.70 (2H, q, J = 7.50 Hz), 4.96 (2H, s), 6.73 (1H, d, J = 8.30 Hz), 6.95 (1H, dt, J = 7.60, 0.90 Hz) and 7.20-7.11 (2H, m); ^{13}C-NMR (DMSO-d_6) δ (ppm): 14.1 (1C, $CH_2\underline{C}H_3$), 23.2 (1C, $\underline{C}H_2CH_3$), 65.0 (1C, C-2), 111.2 (1C, C-f), 122.0 (1C, C-d), 126.8 (1C, C-c), 129.5 (1C, C-e), 133.2 (1C, C-b), 155.3 (1C, C-a), 174.3 (1C, C-1).

4-Ethylphenoxyacetic acid **(25)** White needle (75%), m.p. 72-73°C (lit.[46] m.p. 92-94°C) (hexane-dichloromethane), R_f 0.33 (dichloromethane/methanol 8:2). IR (KBr) 3033, 2960, 1708, 1611, 1514, 1437, 1238 and 1088 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.19 (3H, t, J = 7.59 Hz), 2.59 (2H, q, J = 7.59 Hz), 4.65 (2H, s), 6.83 (2H, d, J = 8.55 Hz), 7.12 (2H, d, J = 8.55 Hz) and 8.51 (1H, s, br); ^{13}C-NMR ($CDCl_3$) δ (ppm): 17.0 (1C, CH_3), 28.0 (1C, CH_2), 65.0 (1C, C-2), 116.1 (2C, C-b, C-f), 130.6 (2C, C-c, C-e), 138.0 (1C, C-d), 155.3 (1C, C-a), 174.6 (1C, C-1).

2-iso-Propylphenoxyacetic acid **(26)** White microcrystalline product (48%), m.p. 133-134°C (lit.[47] m.p. 132-133°C) (hexane-dichloromethane), R_f 0.75 (dichloromethane/methanol 9:1). IR (KBr) 3277-2479, 1711, 1495, 1424, 1235 and 1114 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.23 (6H, d, J = 7.20 Hz), 3.38 (1H, hept, J = 7.00 Hz), 4.68 (2H, s), 6.73 (1H, dd, J = 7.80, 1.00 Hz), 6.99 (1H, dt, J = 7.40, 1.00 Hz), 7.14 (1H, dt, J = 7.80, 1.00 Hz) and 7.25 (1H, dd, J = 7.40, 1.00 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 22.7 (2C, CH_3), 26.6 (1C, $CH(CH_3)_2$), 65.1 (1C, C-2), 111.4 (1C, C-f), 122.1 (1C, C-d), 126.6 (1C, C-c), 126.6 (1C, C-e), 137.6 (1C, C-b), 154.7 (1C, C-a) and 174.2 (1C, C-1).

2-tert-Butylphenoxyacetic acid **(27)** White plate (54%), m.p. 145-146°C (lit.[48] m.p. 148°C) (hexane-dichloromethane), R_f 0.77 (dichloromethane/methanol 8:2). IR (KBr) 3267-2735, 1741, 1603, 1450, 1401, 1203 and 1095 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.42 (9H, s), 4.71 (2H, s), 6.75 (1H, dd, J = 7.88, 1.22 Hz), 6.95 (1H, dt, J = 7.60, 1.22), 7.17 (1H, dt, J = 7.88, 1.82 Hz) and 7.33 (1H, dd, J = 7.60, 1.82 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 29.8 (3C, CH_3), 34.9 (1C, CH), 64.7 (1C, C-2), 111.9 (1C, C-f), 121.6 (1C, C-d), 127.1 (1C, C-c), 127.1 (1C, C-e), 138.7 (1C, C-b), 156.3 (1C, C-a) and 174.7 (1C, C-1).

4-tert-Butylphenoxyacetic acid **(28)** White plate (45%), m.p. 84-86°C (lit.[42] m.p. 86-88°C) (dichloromethane-methanol), R_f 0.18 (dichloromethane/ethanol 8:2). IR (KBr) 3280-2699, 1710, 1610, 1521, 1450, 1244 and 1105 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.28 (9H, s), 4.64 (2H, s), 6.32 (1H, s, br), 6.75 (1H, d, J = 8.74 Hz), 6.85

(1H, d, J = 8.82 Hz), 7.25 (1H, d, J = 8.74 Hz), 7.30 (1H, d, J = 8.82 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 31.3 (3C, CH_3), 33.7 (1C, CH), 64.5 (1C, C-2), 113.8 (1C, C-b, C-f), 126.0 (2C, C-c, C-e), 143.1 (1C, C-d), 155.5 (1C, C-a), 170.4 (1C, C-1).

2-Benzylphenoxyacetic acid **(29)** White needle (27%), m.p. 130-131°C (lit.[49] m.p. 130°C) (hexane-dichloromethane), R_f 0.70 (ethanol). IR (KBr) 3028, 2951, 1751, 1596, 1504, 1427, 1228 and 1122 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.04 (2H, s), 4.62 (2H, s), 5.28 (1H, s, br), 6.76 (1H, d, J = 8.18 Hz), 6.96 (1H, t, J = 7.38 Hz), 7.30-7.13 (7H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm): 36.7 (1C, CH_2), 65.6 (1C, C-2), 113.3 (1C, C-f), 119.8 (1C, C-d), 125.0 (1C, C-e), 125.7 (1C, C-d'), 126.0 (1C, C-c), 127.9 (2C, C-b', C-f'), 128.4 (2C, C-c', C-e'), 129.1 (1C, C-b), 144.2 (1C, C-a'), 154.7 (1C, C-a) and 173.6 (1C, C-1).

4-Phenylphenoxyacetic acid **(30)** White plate (66%), m.p. 159-161°C (dichloromethane-methanol), R_f 0.20 (dichloromethane/methanol 8.5:1.5). IR (KBr) 3023, 2897, 1712, 1659, 1606, 1485, 1432, 1243 and 1069 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.56 (2H, s), 6.95 (2H, d, J = 8.36 Hz), 7.29 (1H, t, J = 7.15 Hz), 7.41 (2H, t, J = 7.21 Hz), 7.65 (2H, d, J = 8.36 Hz) and 7.59 (2H, d, J = 7.21 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 65.4 (1C, C-2), 114.9 (2C, C-b, C-f), 115.9 (1C, C-d'), 125.9 (2C, C-b', C-f'), 126.1 (1C, C-d), 127.6 (2C, C-c, C-e), 128.8 (2C, C-c', C-e'), 139.8 (1C, C-a'), 157.7 (1C, C-a) and 170.3 (1C, C-1).

2-Acetylphenoxyacetic acid **(31)** White plate (37%), m.p. 85-86°C (hexane-dichloromethane), R_f 0.29 (dichloromethane/methanol 8:2). IR (KBr) 3020, 2912, 1712, 1645, 1490, 1430, 1243 and 1059 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.66 (3H, s), 4.75 (2H, s), 4.80 (1H, s), 6.94 (1H, dd, J = 8.11, 0.80 Hz), 7.12 (1H, dt, J = 7.70, 0.80 Hz), 7.52 (1H, dt, J = 8.11, 1.80 Hz) and 7.78 (1H, dd, J = 7.70, 1.80 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 30.0 (1C, CH_3), 66.9 (1C, C-2), 114.7 (1C, C-f), 122.5 (1C, C-d), 127.5 (1C, C-b), 131.2 (1C, C-c), 134.7 (1C, C-e), 156.8 (1C, C-a), 170.3 (1C, C-1) and 200.5 (1C, $\underline{C}OCH_3$).

4-Methoxyphenoxyacetic acid **(32)** White plate (71%), m.p. 110-111°C (lit.[32] m.p. 110.5-111.0°C) (hexane-dichloromethane), R_f 0.45 (dichloromethane/methanol 8:2). IR (KBr) 3047, 2960, 2834, 1736, 1509, 1422, 1296 and 1088 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.76 (3H, s), 4.61 (2H, s), 5.07 (1H, s, br) and 6.84 (4H, d, J = 1.77 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 55.7 (1C, OCH_3), 65.8 (1C, C-2), 114.8 (2C, C-b, C-f), 115.9 (2C, C-c, C-e), 151.6 (1C, C-a), 154.8 (1C, C-d) and 173.6 (1C, C-1).

2,6-Dimethoxyphenoxyacetic acid **(33)** White plate (57%), m.p. 81-82°C (lit.[50] m.p. 79-80°C) (hexane-dichloromethane), R_f 0.41 (dichloromethane/methanol 9:1). IR (KBr) 3050, 2950, 1736, 1485, 1424, 1265 and 1198 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.29 (6H, s), 4.46 (2H, s) and 7.02-6.95 (3H, m); ^{13}C-NMR (DMSO-d_6) δ (ppm): 16.2 (1C, OCH_3), 68.3 (1C, C-2), 124.9 (1C, C-d), 129.1 (2C, C-c, C-e), 130.5 (2C, C-b, C-f), 154.5 (1C, C-a) and 172.5 (1C, C-1).

3,5-Dimethoxyphenoxyacetic acid **(34)** White plate (71%), m.p. 140-142°C (lit.[42] m.p. 142-144°C) (hexane-dichloromethane), R_f 0.36 (dichloromethane/methanol 8:2). IR (KBr) 3100, 2955, 2869, 1751, 1596, 1475, 1427, 1252 and 1165 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.75 (6H, s), 4.62 (2H, s), 6.08 (2H, d, J = 2.04 Hz), 6.12 (1H, d, J = 2.04 Hz) and 6.38 (1H, s, br); ^{13}C-NMR ($CDCl_3$) δ (ppm): 55.4 (2C, OCH_3), 64.7 (1C, C-2), 93.5 (2C, C-b, C-f), 94.2 (1C, C-d), 159.2 (1C, C-a), 161.6 (2C, C-c, C-e) and 173.5 (1C, C-1).

2-Nitrophenoxyacetic acid **(35)** Pale yellow plate (89%), m.p.156-157°C (lit.[32,51] m.p. 158.2-158.5°C) (hexane-dichloromethane), R_f 0.18 (dichloromethane/ethanol 8:2). IR (KBr) 3052, 2911, 1737, 1606, 1529, 1427, 1248 and 1098 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.89 (1H, s), 7.11 (1H, dt, J = 7.75, 1.05 Hz), 7.23 (1H, dd, J = 8.25, 1.05 Hz), 7.59 (1H, dt, J = 8.25, 1.71 Hz) and 7.84 (1H, dd, J = 7.75, 1.71 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 65.3 (1C, C-2), 115.0 (1C, C-f), 121.0 (1C, C-d), 124.9 (1C, C-c), 134.0 (1C, C-e), 139.7 (1C, C-b), 150.4 (1C, C-a) and 169.3 (1C, C-1).

3-Nitrophenoxyacetic acid **(36)** Pale yellow powder (23%), m.p. 137-138°C (lit.[32,51] m.p. 156.4-156.7°C) (dichloromethane-methanol), R_f 0.18 (dichloromethane/ethanol 8:2). IR (KBr) 3100, 2921, 1751, 1620, 1514, 1432, 1243 and 1107 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 3.53 (1H, s, br), 4.85 (2H, s), 7.40 (1H, dd, J = 8.06, 2.50 Hz), 7.57 (1H, t, J = 8.06 Hz), 7.68 (1H, t, J = 2.23 Hz) and 7.82 (1H, dd, J = 8.06, 2.23 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 64.9 (1C, C-2), 108.9 (1C, C-b), 115.9 (1C, C-d), 121.9 (1C, C-f), 130.7 (1C, C-e), 148.6 (1C, C-c), 158.3 (1C, C-a) and 169.7 (1C, C-1).

4-Nitrophenoxyacetic acid **(37)** Pale yellow plate (64%), m.p. 187-188°C (lit.[32,51] m.p. 187.2-187.5°C) (hexane-ethyl acetate), R_f 0.20 (dichloromethane/methanol 8:2). IR (KBr) 3086, 2907, 1708, 1596, 1509, 1427, 1252 and 1112 cm^{-1};

^{1}H-NMR (DMSO-d_6) δ (ppm): 4.87 (2H, s), 7.12 (2H, d, J = 9.30 Hz) and 8.19 (2H, d, J = 9.30 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 64.9 (1C, C-2), 115.1 (2C, C-b, C-f), 125.7 (2C, C-c, C-e), 141.1 (1C, C-d), 163.0 (1C, C-a) and 169.4 (1C, C-1).

(p-Acetamidophenoxy)acetic acid **(38)** *p*-Hydroxyacetanilide was used as the substrate to obtain the product as pale purple powder (74%), m.p. 165-166°C (lit.[52] m.p. 175-177°C) (hexane-dichloromethane), R_f 0.19 (dichloromethane/methanol 8:2). IR (KBr) 3226, 3129, 2917, 2917, 1727, 1635, 1519, 1432, 1228 and 1088 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.99 (3H, s), 3.37 (1H, s, br), 4.60 (2H, s), 6.83 (2H, d, J = 9.05 Hz), 7.45 (2H, d, J = 9.05 Hz) and 9.79 (1H, s); ^{13}C-NMR ($CDCl_3$) δ (ppm): 23.8 (1C, NHCO<u>C</u>H$_3$), 64.6 (1C, C-2), 114.4 (2C, C-b, C-f), 120.4 (2C, C-c, C-e), 132.9 (1C, C-d), 153.4 (1C, C-a), 167.8 (1C, NH<u>C</u>OCH$_3$) and 170.3 (1C, C-1).

2.4 Synthesis of 2,4-Dichlorophenoxyalkanoic Acids

General Procedure:[10, 31]

A solution of sodium hydroxide (0.94 g, 23.5 mmol) in water (5 mL) was added dropwise to a mixture of 2,4-dichlorophenol (10 mmol) and selected chlorocarboxylic acid (15 mmol) in a round bottom flask. The solution was refluxed approximately 2 hours. After the reaction mixture was cooled down, the solution was acidified with a dilute hydrochloric acid, filtered the precipitate and extracted the filtrate twice with ether (25 mL each). The ethereal extracts were washed with water (10 mL), dried over anhydrous sodium sulfate, evaporated *in vacuo* and recrystallized.

Compound	R^1
39	CH_2CH_2COOH
40	$CH(CH_3)COOH$
41	CHClCOOH

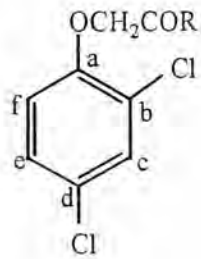
2,4-Dichlorophenoxypropanoic acid **(39)** White needles (46%), m.p. 87-89°C (lit.[53] m.p. 117-118°C) (dichloromethane-ethanol), R_f 0.58 (dichloromethane/ethanol 9:1). IR (KBr) 2379-2485, 1700, 1595, 1480, 1410, 1240 and 1093 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.90 (2H, d, J = 5.90 Hz), 4.27 (2H, t, J = 5.90 Hz), 6.87 (1H, d, J = 9.00 Hz), 7.17 (1H, d, J = 9.00 Hz) and 7.34 (1H, s); ^{13}C-NMR (DMSO-d_6) δ (ppm): 34.1 (1C, OCH$_2$<u>C</u>H$_2$), 64.7 (1C, O<u>C</u>H$_2$CH$_2$), 114.7 (1C, C-e), 124.1 (1C, C-f),

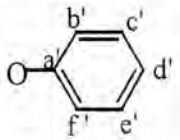
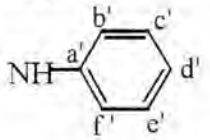
126.4 (1C, C-c), 127.1 (1C, C-d), 130.1 (1C, C-b), 152.9 (1C, C-a) and 176.2 (1C, COOH).

2-(2,4-Dichlorophenoxy)-propanoic acid **(40)** White needle (50%), m.p. 115-117°C (lit.[33] m.p. 117-118°C) (dichloromethane-ethanol), R_f 0.33 (dichloromethane/ethanol 9:1). IR (KBr) 2350-2710, 1720, 1590, 1475, 1250 and 1125 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.70 (3H, d, J = 6.80 Hz), 4.75 (1H, q, J = 6.80 Hz), 6.81 (1H, d, J = 8.73 Hz), 7.15 (1H, dd, J = 8.73, 2.60 Hz) and 7.38 (1H, d, J = 2.60 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.3 (1C, OCH<u>C</u>H$_3$), 73.9 (1C, O<u>C</u>H), 116.4 (1C, C-e), 124.9 (1C, C-f), 127.7 (1C, C-c), 130.4 (1C, C-b), 130.4 (1C, C-d), 151.8 (1C, C-a) and 176.2 (1C, COOH).

Chloro-(2,4-dichlorophenoxy)-acetic acid **(41)** White powder (30%), m.p. 97-98°C (dichloromethane-ethanol), R_f 0.18 (dichloromethane/methanol 9:1). IR (KBr) 3468, 3110, 2960, 1732, 1587, 1485, 1228 and 1073 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 6.78 (1H, s), 7.26 (1H, d, J = 8.89 Hz), 7.41 (1H, dd, J = 8.89, 2.44 Hz) and 7.65 (1H, d, J = 2.44 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 95.5 (1C, C-2), 118.5 (1C, C-f), 124.1 (1C, C-b), 127.6 (1C, C-d), 128.3 (1C, C-e), 129.9 (1C, C-c), 149.6 (1C, C-a) and 165.0 (1C, C-1). The FT-IR, ^{1}H-NMR and ^{13}C-NMR of **41** are shown in Figures A.1, A.2 and A.3 (see Appendices A), respectively.

2.5 Synthesis of 2,4-Dichlorophenoxyacetic Acids Derivatives and Analogues



Compound	R
42	OCH_3
43	OCH_2CH_3
44	
45	NH_2
46	
47	

2.5.1 Synthesis of 2,4-Dichlorophenoxyacetate Esters

Methyl 2,4-dichlorophenoxyacetate **(42)**[54] A solution of 2,4-dichlorophenoxy-acetic acid (4.42 g, 0.02 mol) and 0.50 mL of conc. sulfuric acid in anhydrous methanol (12.5 g, 0.39 mol) was refluxed for 20 hours. After cooling, the solution was neutralized with sodium carbonate. The reaction mixture was then extracted three times with 10 mL of ether. The combined extracts were washed twice with 10 mL of water, dried over anhydrous sodium sulfate, evaporated *in vacuo*, and the residue fractionally distilled to give a colorless oil (84%), (lit.[55] b.p. 119°C/ 1 mm.), R_f 0.64 (dichloromethane). IR (neat) 3100, 2950, 2853, 1768, 1582, 1485, 1180 and 1101 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.77 (3H, s), 4.66 (2H, s), 7.74 (1H, d, J = 8.85 Hz), 7.13 (1H, dd, J = 8.85, 2.60 Hz) and 7.35 (1H, d, J = 2.60 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 52.4 (1C, OCH_3), 66.3 (1C, C-2), 114.8 (1C, C-f), 124.2 (1C, C-b), 127.1 (1C, C-d), 127.6 (1C, C-e), 130.3 (1C, C-c), 152.4 (1C, C-a) and 168.6 (1C, C-1).

Ethyl 2,4-dichlorophenoxyacetate **(43)**[4,54,56] 0.03 Mol of 2,4-dichlorophenoxy acetic acid was dissolved in 20 mL of anhydrous ethanol. Conc. sulfuric acid 0.9 mL was added and the mixture was refluxed for 5 hours. Ethanol (about 14 mL) was partially distilled off *in vacuo* and the residue was poured into 25 mL of ice water. The mixture was extracted three times with 10 mL of ether. The combined extracts were washed twice with 10 mL of water, dried over anhydrous sodium sulfate, evaporated *in vacuo*, and residue was fractionally distilled to give a colorless oil (97 %), R_f 0.71 (dichloromethane). IR (neat) 3072, 2978, 1762, 1584, 1489, 1296 and 1193 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.19 (3H, t, J = 7.10 Hz), 4.16 (2H, q, J = 7.10 Hz), 4.96 (2H, s), 7.08 (1H, d, J = 8.90 Hz), 7.31 (1H, dd, J = 8.90, 2.68 Hz) and 7.52 (1H, d, J = 2.68 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 8.9 (1C, $CH_2\underline{C}H_3$), 56.3 (1C, $\underline{C}H_2CH_3$), 61.1 (1C, C-2), 109.5 (1C, C-f), 118.9 (1C, C-b), 121.7 (1C, C-d), 122.3 (1C, C-e), 125.0 (1C, C-c), 147.2 (1C, C-a) and 162.9 (1C, C-1).

Phenyl 2,4-dichlorophenoxyacetate **(44)**[54] The same procedure for preparation of ethyl 2,4-dichlorophenoxyacetate **(43)** was employed but a solution of phenol in toluene was used instead of anhydrous ethanol. After the reaction mixture was evaporated *in vacuo*, the residue was purified by column chromatography on silica gel eluting with dichloromethane to give a white powder (63%), m.p. 93-95°C (lit.[57] m.p. 100-101°C) (hexane-dichloromethane), R_f 0.70 (dichloromethane). IR (KBr) 3056,

2985, 1754, 1481, 1265 and 1212 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 5.24 (2H, s), 7.18 (2H, d, J = 8.33 Hz), 7.19 (1H, d, J = 8.84 Hz), 7.27 (1H, t, J = 7.35 Hz), 7.30 (2H, t, J = 8.33 Hz), 7.40 (1H, dd, J = 8.84, 2.50 Hz) and 7.62 (1H, d, J = 2.50 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 65.4 (1C, C-2), 115.3 (1C, C-f), 121.6 (2C, C-b', C-f'), 122.4 (1C, C-b), 125.3 (1C, C-d), 126.2 (1C, C-d'), 128.0 (1C, C-e), 129.5 (1C, C-c), 129.6 (2C, C-c', C-e'), 152.1 (1C, C-a'), 155.9 (1C, C-a) and 167.1 (1C, C-1).

2.5.2 Synthesis of 2,4-dichlorophenoxyacetamides

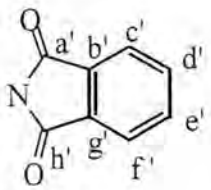
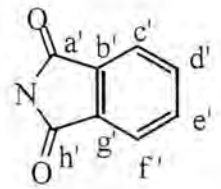
2,4-Dichlorophenoxyacetamide **(45)**[18] 2,4-Dichlorophenoxyacetic acid (5 mmol) and thionyl chloride (5 mL) were put into a round bottom flask and stirred under heating at a temperature from 60°C to 70°C for 2 hours. The excess thionyl chloride was removed. The concentration solution, as 2,4-dichlorophenoxyacetyl chloride, was then gradually added upon cooling to a solution containing 12.5 mL of acetone dissolved in 1 mL of aqueous ammonia of 25%. After stirring the mixture at room temperature for 2 hours, 37.50 mL of water was added to the reaction solution. The mixture was extracted twice with 12.50 mL of ethyl acetate. The extract was washed with water and then dried over anhydrous sodium sulfate, evaporated *in vacuo* and recrystallized with hexane-dichloromethane to obtain pale brown needle (21%), m.p. 133-135°C (lit.[58] m.p. 130°C) (hexane-dichloromethane), R_f 0.40 (dichloromethane/methanol 8:2). IR (KBr) 3475, 3072, 2976, 1733, 1586, 1476, 1234 and 1157 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.71 (2H, s), 5.28 (2H, s, br), 6.80 (1H, d, J = 8.80 Hz), 7.17 (1H, dd, J = 8.80, 2.45 Hz) and 7.39 (1H, d, J = 2.45 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 65.9 (1C, C-2), 114.9 (1C, C-f), 124.3 (1C, C-b), 127.6 (1C, C-d), 127.7 (1C, C-e), 130.5 (1C, C-c), 152.0 (1C, C-a) and 161.1 (1C, C-1).

N-Phenyl-2,4-dichlorophenoxyacetamide **(46)**[18,59] The same procedure for preparation of 2,4-dichlorophenoxyacetyl chloride was employed. At 0°C to 5°C, 5 mmol of selected amine in 5 mL of tetrahydrofuran was added to the solution of 2,4-dichlorophenoxyacetyl chloride in 5 mL of tetrahydrofuran. After the mixture has been stirred for 2 hours, the solvent was removed, and the residue was dissolved in dichloromethane and extracted with 10% hydrochloric acid and 5% sodium hydroxide solution. The organic phase was then washed with water, dried over anhydrous sodium sulfate, evaporated *in vacuo* and recrystallized with hexane-dichloromethane. Pale brown needle (97%), m.p. 104-105°C, R_f 0.45 (dichloromethane). IR (KBr)

3290, 3100, 2920, 1660, 1580, 1460, 1235 and 1100 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.61 (2H, s), 6.88 (1H, d, *J* = 8.81 Hz), 7.15 (1H, t, *J* = 7.44 Hz), 7.24 (1H, dd, *J* = 8.81, 2.44 Hz), 7.36 (1H, d, *J* = 7.44 Hz), 7.44 (1H, d, *J* = 2.44 Hz) and 7.58 (1H, d, *J* = 7.56 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 68.4 (1C, C-2), 114.9 (1C, C-f), 119.9 (2C, C-b', C-f'),123.8 (1C, C-b), 125.0 (1C, C-d'), 127.8 (1C, C-d), 128.2 (1C, C-e), 129.2 (2C, C-c', C-e'), 130.3 (1C, C-c), 136.8 (1C, C-a'), 151.4 (1C, C-a) and 165.0 (1C, C-1).

N-Cyclohexyl-2,4-dichlorophenoxyacetamide **(47)** The same procedure for the preparation of *N*-Phenyl-2,4-dichlorophenoxyacetamide **(46)** was employed, but cyclohexylamine was used instead of aniline to obtain white cream needle (39%), m.p. 152-153°C (hexane-dichloromethane), R_f 0.30 (dichloromethane). IR (KBr) 3284, 3091, 2936, 1664, 1558, 1480, 1248 and 1117 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.47-1.12 (4H, m), 1.73-1.55 (4H, m), 2.01-1.87 (2H, m), 3.86 (1H, m), 4.45 (2H, s), 6.67 (1H, d, *J* = 5.39 Hz), 6.80 (1H, d, *J* = 8.84 Hz), 7.19 (1H, dd, *J* = 8.84, 2.44 Hz) and 7.38 (1H, d, *J* = 2.44 Hz); ^{13}C-NMR ($CDCl_3$) δ (ppm): 24.5 (2C, C-c', C-e'), 25.4 (1C, C-d'), 32.8 (2C, C-b', C-f'), 47.7 (1C, C-a'), 68.3 (1C, C-2), 114.7 (1C, C-f), 123.7 (1C, C-b), 127.4 (1C, C-d), 128.0 (1C, C-e), 130.2 (1C, C-c), 151.7 (1C, C-a) and 166.0 (1C, C-1).

2.5.3 Synthesis of Aminophenoxyacetic Acids and Their Analogues

Compound	R^1	R^2
48	**NH_2**	H
49	H	**NH_2**
50		H
51	H	

General Procedure : (for the preparation of aminophenoxyacetic acid)[59]

Nitrophenoxyacetic acid (16.3 mmol) was added into a mixture of iron powder (48.3 mmol), methanol 27 mL and glacial acetic acid 13.5 mL. The mixture was heated 80°C and kept at that temperature for 2 hours. Upon completion of the reaction, the mixture was poured into water, the solid was precipitated to give the product as powder which could be used without further purification.

2-Aminophenoxyacetic acid **(48)** Pale yellow powder (98%), m.p. 219-220°C (lit[60] m.p. 153-154°C), R_f 0.78 (dichloromethane/methanol 7:3). IR (KBr) 3342, 2936, 1543, 1451, 1354, 1219 and 1015 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.62 (2H, s), 6.05-7.35 (4H, m) and 7.67 (2H, s, br); ^{13}C-NMR (DMSO-d_6) δ (ppm): 65.3 (1C, C-2), 114.3 (1C, C-f), 120.1 (1C, C-d), 121.0 (1C, C-c), 123.1 (1C, C-e), 124.5 (1C, C-b), 150.9 (1C, C-a) and 170.3 (1C, C-1).

4-*Aminophenoxyacetic acid* **(49)** Dark brown powder (98%), m.p. 217-218°C (dec.) (lit.[60] m.p. 220°C), R_f 0.77 (dichloromethane/methanol 7:3). IR (KBr) 3468, 2931, 1601, 1514, 1423, 1238 and 1185 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.68 (2H, s), 6.05-6.35 (4H, m) and 7.70 (2H, s, br); ^{13}C-NMR (DMSO-d_6) δ (ppm): 65.5 (1C, C-2), 114.8 (2C, C-b, C-f), 115.9 (2C, C-c, C-e), 138.7 (1C, C-d), 151.6 (1C, C-a), 170.3 (1C, C-1).

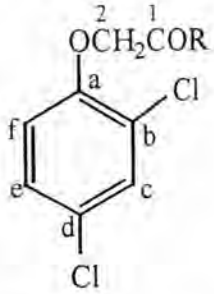
General Procedure : (for the preparation of phthalimide)[61]

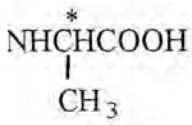
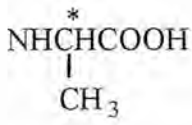
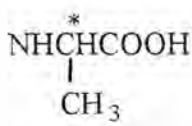
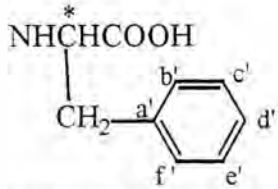
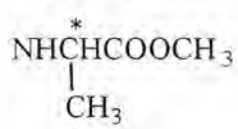
The mixture of aminophenoxyacetic acid (10 mmol) and phthalic anhydride (10 mmol) in acetic acid (8.50 mL) was stirred and heated under reflux for 5 hours. The solvent was evaporated *in vacuo* and the residual material was recrystallized from methanol-water.

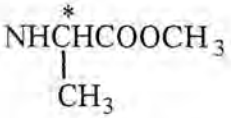
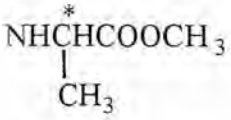
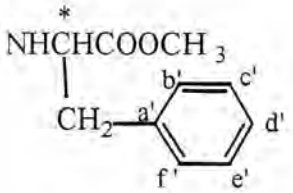
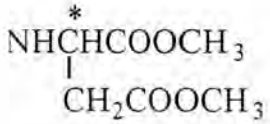
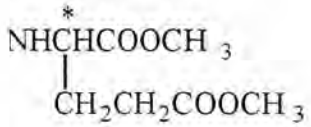
2-(*N-Phthalimido*)-*phenoxyacetic acid* **(50)** Brown-orange powder (63%), m.p. 238-240°C (dec) (methanol), R_f 0.13 (dichloromethane/methanol 7:3). IR (KBr) 3444, 3070, 1716, 1616, 1520, 1419, 1295 and 1153 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.74 (2H, s, br), 6.13-6.82 (3H, m), 7.30-7.89 (5H, m); ^{13}C-NMR (DMSO-d_6) δ (ppm): 64.6 (1C, C-2), 114.4 (1C, C-f), 119.3 (1C, C-d), 121.2 (1C, C-c), 123.2 (1C, C-b), 124.8 (1C, C-e), 127.9 (2C, C-c', C-f'), 131.4 (2C, C-d', C-e'), 134.0 (2C, C-b', C-g'), 157.1 (1C, C-a), 167.0 (2C, C-a', C-h') and 170.0 (1C, C-1). The FT-IR and ^{13}C-NMR of **(50)** are shown in Figures A.4 and A.5 (see Appendices A), respectively.

4-(*N-Phthalimido*)-*phenoxyacetic acid* **(51)** Pale brown powder (50%), m.p. 205-206°C (methanol), R_f 0.61 (dichloromethane/methanol 7:3). IR (KBr) 3440, 3147, 3095, 1751, 1716, 1608, 1512, 1410, 1254 and 1176 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 4.75 (2H, s, br), 7.04-7.93 (8H, m); ^{13}C-NMR (DMSO-d_6) δ (ppm): 64.5 (1C, C-2), 114.6 (2C, C-b, C-f), 123.3 (2C, C-c, C-e), 124.8 (1C, C-d), 128.7 (2C, C-c', C-f'), 131.5 (2C, C-d', C-e'), 134.6 (2C, C-b', C-g'), 157.3 (1C, C-a), 167 (2C, C-a', C-h') and 170.1 (1C, C-1). The FT-IR and ^{13}C-NMR of **(51)** are shown in Figures A.6 and A.7 (see Appendices A), respectively.

2.6 Synthesis of 2,4-Dichlorophenoxyacetyl Derivatives



Compound	Configuration	R
52	DL	
53	L	
54	D	
55	L	
56	-	$NHCH_2COOCH_3$
57	DL	

Compound	Configuration	R
58	L	
59	D	
60	L	
61	L	
62	L	

2.6.1 Synthesis of 2,4-Dichlorophenoxyacetyl Derivatives of Amino Acids

General Procedure:

2,4-Dichlorophenoxyacetyl chloride[18] 2,4-Dichlorophenoxyacetic acid (10 mmol), thionyl chloride (10 mL) and *N,N*-dimethylformamide (2 drops) were put into a round-bottomed flask and stirred under heating at a temperature from 60°C to 70°C for 2 hours. The reaction solution followed by concentration to remove excess thionyl chloride to obtain in a 76% yield (lit.[54] b.p. 167-174°C/ 59-61 mm.).

Amide[20, 54] Amino acid (10 mmol) was dissolved in dilute sodium hydroxide (0.2 g of sodium hydroxide in 15 mL of water), chilling the solutions of the sodium

salts to about 5°C in an ice-bath, and adding with rapid stirring a solution of the 2,4-dichlorophenoxyacetyl chloride (10 mmol) in benzene and a solution of 0.6 g of sodium hydroxide in 3 mL of water were added dropwise, keeping this temperature over 5 to 10 minutes. After the addition of the acid chloride was completed, the ice-bath was removed, and stirring was continued for 2 to 3 hours. The reaction mixture was extracted with ether, and the aqueous phase was separated and acidified with 50% hydrochloric acid solution, filtered the precipitate, washed with water, and recrystallized from 50% ethanol.

N-(2,4-Dichlorophenoxyacetyl)-DL-alanine **(52)** White needle (69%), m.p. 213-214°C (lit.[20] m.p. 212.8-213.8°C) (ethanol-water), R_f 0.69 (ethanol). IR (KBr) 3410, 3028, 2955, 1737, 1683, 1529, 1485, 1238 and 1074 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.30 (3H, d, J = 7.27 Hz), 4.26 (1H, p, J = 7.27 Hz), 4.67 (2H, s), 7.05 (1H, d, J = 8.94 Hz), 7.34 (1H, dd, J = 8.94, 2.64 Hz), 7.59 (1H, d, J = 2.64 Hz) and 8.31(1H, d, J = 7.40 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 17.2 (1C, CH_3), 47.4 (1C, CH), 67.4 (1C, C-2), 115.4 (1C, C-f), 122.4 (1C, C-b), 125.0 (1C, C-d), 127.9 (1C, C-e), 129.3 (1C, C-c), 152.4 (1C, C-a), 166.7 (1C, C-1) and 173.7 (1C, COOH).

N-(2,4-Dichlorophenoxyacetyl)-L-alanine **(53)** White needle (33%), m.p. 204-205°C (lit.[20] m.p. 197.2-199.2°C) (ethanol-water), R_f 0.69 (ethanol). IR (KBr) 3362, 2926, 1727, 1640, 1543, 1485, 1214 and 1151 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.30 (3H, d, J = 7.28 Hz), 4.27 (1H, p, J = 7.28 Hz), 4.66 (2H, s), 7.04 (1H, d, J = 8.89 Hz), 7.33 (1H, dd, J = 8.89, 2.59 Hz), 7.58 (1H, d, J = 2.59 Hz) and 8.30 (1H, d, J = 7.40 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 17.2 (1C, CH_3), 47.3 (1C, CH), 67.4 (1C, C-2), 115.4 (1C, C-f), 122.4 (1C, C-b), 125.0 (1C, C-d), 127.9 (1C, C-e), 129.3 (1C, C-c), 152.4 (1C, C-a), 166.7 (1C, C-1) and 173.7 (1C, COOH).

N-(2,4-Dichlorophenoxyacetyl)-D-alanine **(54)** White powder (40%), m.p. 208-209°C (lit.[21] m.p. 203.7-204.7°C) (ethanol-water), R_f 0.69 (ethanol). IR (KBr) 3366, 2980, 1732, 1635, 1485, 1234 and 1098 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.30 (3H, d, J = 7.30 Hz), 4.26 (1H, p, J = 7.30 Hz), 4.81 (2H, s), 7.04 (1H, d, J = 8.89 Hz), 7.33 (1H, dd, J = 8.89, 2.52 Hz), 7.56 (1H, d, J = 2.52 Hz) and 8.30 (1H, d, J = 7.34 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 17.2 (1C, CH_3), 47.4 (1C, CH), 67.4 (1C, C-2), 115.4 (1C, C-f), 122.4 (1C, C-b), 125.0 (1C, C-d), 127.9 (1C, C-e), 129.3 (1C, C-c), 152.3 (1C, C-a), 166.7 (1C, C-1) and 173.7 (1C, COOH).

N-(2,4-Dichlorophenoxyacetyl)-L-phenylalanine **(55)** White powder (91%), m.p. 176-177°C (lit.[20] m.p. 178.2-179.2°C) (ethanol-water), R_f 0.49 (dichloromethane/methanol 8:2). IR (KBr) 3410, 3086, 2926, 1741, 1688, 1630, 1553, 1485, 1253 and 1180 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.97 (1H, dd, J = 13.90, 8.91 Hz), 3.11 (1H, dd, J = 13.90, 4.92 Hz), 4.52 (1H, q, J = 3.98 Hz), 4.61 (2H, s), 6.85 (1H, d, J = 8.95 Hz), 7.28-7.17 (5H, m), 7.25 (1H, dd, J = 8.95, 2.66 Hz), 7.57 (1H, d, J = 2.66 Hz) and 8.20 (1H, d, J = 8.03 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 36.5 (1C, CH_2), 53.0 (1C, CH), 67.3 (1C, C-2), 115.2 (1C, C-f), 122.4(1C, C-b), 125.0 (1C, C-d'), 126.5 (1C, C-d), 127.9 (1C, C-e), 128.2 (2C, C-b', C-f'), 129.1 (2C, C-c', C-e'), 129.3 (1C, C-c), 137.2 (1C, C-a'), 152.2 (1C, C-a), 166.8 (1C, C-1), 172.4 (1C, COOH).

2.6.2 Synthesis of 2,4-Dichlorophenoxyacetyl Derivatives of Methyl Ester of Amino Acid Hydrochlorides

General Procedure:[20]

Amino Acid Hydrochloride[62,63] Thionyl chloride (1 mL) was carefully added to methanol (20 mL) in a 50-mL round-bottomed flask fitted with a reflux condenser and cooled in an ice-salt bath for 10 minutes. After that, amino acid (5 mmol) was added, removed the ice-salt bath and heated the mixture at reflux for 2 hours. The mixture was concentrated on the rotary evaporator to about 2 to 5 mL. The product was precipitated by slow addition of diethyl ether or cooled the flask in an ice bath until the oil crystallizes. The crystals were filtered and washed with diethyl ether.

Amide At 0-5°C, triethylamine (0.7 mL) was added to a solution of amino acid methyl ester hydrochloride (5 mmol) in tetrahydrofuran (4 mL). Then, 2,4-dichlrophenoxyacetyl chloride was added to the mixture. After stirred for 2 hours, the solvent was removed and the residue was dissolved in dichloromethane and extracted with 10% hydrochloric acid and saturated sodium hydrogen carbonate solution. The organic phase was then washed with water, dried over anhydrous sodium sulfate, evaporated *in vacuo* and recrystallized with hexane-dichloromethane or purified by column chromatography on silica gel eluting with dichloromethane.

N-(2,4-Dichlorophenoxyacetyl)-glycine methyl ester **(56)**[64] Pale yellow powder (43%), m.p. 116-117°C (column chromatography), R_f 0.13 (dichloro-

methane). IR (KBr) 3405, 3057, 2931, 1741, 1688, 1533, 1485, 1253 and 1074 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 3.77 (3H, s), 4.14 (2H, d, J = 5.41 Hz), 4.54 (1H, s), 6.83 (1H, d, J = 8.81 Hz), 7.21 (1H, dd, J = 8.81, 2.55 Hz), 7.28 (1H, br), 7.40 (1H, d, J = 2.55 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 40.8 (1C, CH_2), 52.5 (1C, OCH_3), 68.1 (1C, C-2), 114.6 (1C, C-f), 123.9 (1C, C-b), 127.5 (1C, C-d), 128.0 (1C, C-e), 130.3 (1C, C-c), 151.5 (1C, C-a), 167.5 (1C, C-1), 169.7 (1C, $\underline{C}OOCH_3$).

N-(2,4-Dichlorophenoxyacetyl)-DL-alanine methyl ester **(57)**[64] Pale brown oil (30%), (column chromatography), R_f 0.53 (dichloromethane). IR (neat) 3415, 2960, 1756, 1693, 1485, 1214 and 1166 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.46 (3H, d, J = 7.24 Hz), 3.76 (3H, s), 4.51 (2H, s), 4.67 (1H, p, J = 7.24 Hz), 6.82 (1H, d, J = 8.78 Hz), 7.19 (1H, d, J = 8.78, 2.55 Hz), 7.38 (1H, d, J = 2.55 Hz) and 8.03 (1H, d, br, J = 7.22 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 20.0 (1C, CH_3), 45.8 (1C, OCH_3), 52.6 (1C, CH), 66.2 (1C, C-2), 115.0 (1C, C-f), 124.3 (1C, C-b), 127.6 (1C, C-d), 127.9 (1C, C-e), 130.5 (1C, C-c), 151.6 (1C, C-a), 161.7 (1C, C-1), 171.7 (1C, $\underline{C}OOCH_3$).

N-(2,4-Dichlorophenoxyacetyl)-L-alanine methyl ester **(58)**[64] Colorless oil (54 %), (column chromatography), R_f 0.53 (dichloromethane). IR (neat) 3417, 2962, 1754, 1693, 1485, 1214 and 1167 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.48 (3H, d, J = 7.24 Hz), 3.78 (3H, s), 4.21 (2H, s), 4.67 (1H, p, J = 7.24 Hz), 6.75 (1H, d, J = 8.82 Hz), 7.14 (1H, d, J = 8.82, 2.53 Hz), 7.37 (1H, d, J = 2.53 Hz) and 7.79 (1H, d, br, J = 7.26 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 28.9 (1C, CH_3), 44.3 (1C, OCH_3), 52.4 (1C, CH), 64.7 (1C, C-2), 114.6 (1C, C-f), 124.2 (1C, C-b), 127.1 (1C, C-d), 127.6 (1C, C-e), 130.4 (1C, C-c), 152.3.6 (1C, C-a), 168.1 (1C, C-1), 168.6 (1C, $\underline{C}OOCH_3$).

N-(2,4-Dichlorophenoxyacetyl)-D-alanine methyl ester **(59)**[64] Pale brown oil (49%), (column chromatography), R_f 0.53 (dichloromethane). IR (neat) 3416, 2965, 1758, 1694, 1483, 1215 and 1163 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.45 (3H, d, J = 7.24 Hz), 3.73 (3H, s), 4.48 (2H, s), 4.63 (1H, p, J = 7.24 Hz), 6.80 (1H, d, J = 8.78 Hz), 7.18 (1H, d, J = 8.78, 2.55 Hz), 7.37 (1H, d, J = 2.55 Hz) and 7.33 (1H, d, br, J = 7.22 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.3 (1C, CH_3), 47.8 (1C, OCH_3), 52.6 (1C, CH), 68.2 (1C, C-2), 114.7 (1C, C-f), 123.9 (1C, C-b), 127.4 (1C, C-d), 127.9 (1C, C-e), 130.2 (1C, C-c), 151.6 (1C, C-a), 166.7 (1C, C-1), 172.7 (1C, $\underline{C}OOCH_3$).

N-(2,4-Dichlorophenoxyacetyl)-L-phenylalanine methyl ester **(60)**[64] (lit.[65] m.p.162-164°C of *L-phenylalanine methyl ester hydrochloride*) White powder (79 %), m.p. 112-114°C (column chromatography), R_f 0.73 (dichloromethane/acetone

9.5:0.5). IR (KBr) 3415, 3090, 2925, 1761, 1685, 1632, 1556, 1483, 1250 and 1183 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 3.14 (2H, dd, J = 5.98, 2.06 Hz), 3.73 (3H, s), 4.47 (2H, d, J = 2.68 Hz), 4.93 (1H, q, J = 7.14 Hz), 6.74 (1H, d, J = 8.79 Hz), 7.16 (1H, dd, J = 8.79, 2.45 Hz), 7.26-7.07 (5H, m), 7.37 (1H, d, J = 2.45 Hz) and 7.98 (1H, d, J = 7.40 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 37.9 (1C, CH_2), 52.5 (1C, OCH_3), 52.8 (1C, CH), 68.1 (1C, C-2), 114.5 (1C, C-f), 123.9 (1C, C-b), 127.3 (1C, C-d'), 127.4 (1C, C-d), 127.9 (1C, C-e), 128.7 (2C, C-b', C-f'), 129.1 (2C, C-c', C-e'), 130.2 (1C, C-c), 135.4 (1C, C-a'), 151.5 (1C, C-a), 167.0 (1C, C-1), 172.4 (1C, $\underline{C}OOCH_3$).

N-(2,4-Dichlorophenoxyacetyl)-L-aspartic acid dimethyl ester **(61)** White needle (50%), m.p. 67-70°C (column chromatography), R_f 0.30 (dichloromethane). IR (KBr) 3405, 3052, 2955, 1745, 1658, 1523, 1484, 1286 and 1174 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.86 (1H, dd, J = 17.21, 4.59 Hz), 3.09 (1H, dd, J = 17.21, 4.42 Hz), 3.67 (3H, s), 3.76 (3H, s), 4.53 (2H, s), 4.93 (1H, q, J = 4.49 Hz), 6.81 (1H, d, J = 8.79 Hz), 7.20 (1H, dd, J = 8.79, 2.45 Hz), 7.40 (1H, d, J = 2.45 Hz) and 7.74 (1H, d, J = 8.02 Hz); ^{13}C-NMR (DMSO-d_6) δ (ppm): 36.1 (1C, $\underline{C}H_2COOCH_3$), 48.1 (1C, CH), 52.1 (1C, $CH_2COO\underline{C}H_3$), 53.0 (1C, $CHCOO\underline{C}H_3$), 68.1 (1C, C-2), 114.6 (1C, C-f), 124.1 (1C, C-b), 127.5 (1C, C-d), 127.9 (1C, C-e), 130.3 (1C, C-c), 151.6 (1C, C-a), 167.1 (1C, C-1), 170.5 (1C, $CH_2\underline{C}OOCH_3$), 171.0 (1C, $CHCOOCH_3$).

N-(2,4-Dichlorophenoxyacetyl)-L-glutamic acid dimethyl ester **(62)** Colorless oil (51%) (column chromatography), R_f 0.28 (dichloromethane). IR (neat) 3405, 2951, 1746, 1679, 1480, 1283 and 1113 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.28 (2H, t, J = 7.70 Hz), 2.37 (2H, q, J = 8.52 Hz), 3.64 (3H, s), 3.76 (3H, s), 4.51 (2H, s), 4.71 (1H, q, J = 6.77 Hz), 6.82 (1H, t, J = 8.74 Hz), 7.20 (1H, dd, J = 8.74, 2.52 Hz), 7.40 (1H, d, J = 2.52 Hz) and 7.38 (1H, br); ^{13}C-NMR (DMSO-d_6) δ (ppm): 27.4 (1C, $CH\underline{C}H_2CH_2$), 29.8 (1C, $\underline{C}H_2COOCH_3$), 51.2 (1C, $CH_2COO\underline{C}H_3$), 51.9 (1C, $CHCOO\underline{C}H_3$), 52.7 (1C, CH), 68.2 (1C, C-2), 114.7 (1C, C-f), 124.0 (1C, C-b), 127.6 (1C, C-d), 128.0 (1C, C-e), 130.3 (1C, C-c), 151.6 (1C, C-a), 167.2 (1C, C-1), 171.6 (1C, $CH_2\underline{C}OOCH_3$) and 172.9 (1C, $CH\underline{C}OOCH_3$).

2.7 Synthesis of Phenoxyacetate Salts

2.7.1 Synthesis of Sodium Salts[18]

12.7 Mmol of selected phenoxyacetic acid, 12.5 mmol of sodium hydroxide and 100 mL of toluene were put into a round bottom flask and stirred under reflux for 5 hours. The reaction solution was cooled, and then 100 mL of acetone was added thereto. The precipitate was collected by filtration, and the obtained crude crystals were washed with acetone and dried to obtain the desired compound.

2.7.2 Synthesis of Calcium Salts[18]

12.7 Mmol of interested phenoxyacetic acid and 50 mL of a 1.0% sodium hydroxide aqueous solution were put into a round bottom flask and stirred at room temperature for one hour. Then, 20 mL of a 4.0% calcium chloride aqueous solution was dropwise added thereto at room temperature. Stirring was continued at room temperature for one hour. Then, the formed precipitate was collected by filtration, washed with water and hexane and then dried to obtain the desired compound.

Compound	R^1	R^2	R^3
63	$CH_2COO^-Na^+$	H	Cl
64	$CH_2COO^-Na^+$	Cl	Cl
65	$CH_2COO^-Na^+$	H	OMe
66	$CH_2CONHC^*HCOO^-Na^+$ (CH$_3$)	Cl	Cl
67	$CH_2COO^-.\frac{1}{2}Ca^{2+}$	H	Cl
68	$CH_2COO^-.\frac{1}{2}Ca^{2+}$	Cl	Cl
69	$CH_2COO^-.\frac{1}{2}Ca^{2+}$	H	OMe

Sodium 4-chlorophenoxyacetate **(63)** White crystals of irregular sharpe (98%), m.p. at least 300°C, IR (KBr) 3095, 2916, 1616, 1504, 1350, 1286 and 1185 cm^{-1}.

Sodium 2,4-dichlorophenoxyacetate **(64)**[4] White powder (68%), m.p. at least 300°C, IR (KBr) 3081, 2946, 1712, 1620, 1485, 1330, 1292 and 1069 cm^{-1}.

Sodium 4-methoxyphenoxyacetate **(65)** White crystals of irregular sharpe (96%), m.p. at least 300°C, IR (KBr) 3071, 2955, 2844, 1606, 1509, 1432, 1345, 1238 and 1122 cm^{-1}.

Sodium salt of N-(2,4-dichlorophenoxyacetyl)-L-alanine **(66)** White powder (96%), m.p. at least 300°C, IR (KBr) 3414, 3168, 1674, 1601, 1538, 1485, 1282 and 1107 cm^{-1}.

Calcium 4-chlorophenoxyacetate **(67)** White powder (65%), m.p. at least 300 °C, IR (KBr) 3100, 2979, 1635, 1577, 1500, 1354, 1253 and 1108 cm^{-1}.

Calcium 2,4-dichlorophenoxyacetate **(68)** White powder (88%), m.p. at least 300°C, IR (KBr) 3102, 2980, 1596, 1490, 1335, 1253 and 1103 cm^{-1}.

Calcium 4-methoxyphenoxyacetate **(69)** White powder (70%), m.p. at least 300°C, IR (KBr) 3071, 2965, 2844, 1630, 1577, 1519, 1359, 1238 and 1104 cm^{-1}.

2.8 General Procedure for Bioassay Testing

On account of the goal of this research, two bioassays comprising weed growth inhibition of *Mimosa pigra* Linn. and root growth promotion of *Coleus atropurpurreus* Benth. were selected to carry out.

2.8.1 Weed Growth Inhibition Test[66]

Tested compound was dissolved in an appropriate solvent at concentration of 1000, 100, 10 and 1 ppm, three replications for each concentration. Then, pipette 3 mL of tested solution was added into a glass tube which diameter 30 mm and length 120 mm containing 1.5 g cellulose powder. The controlled tubes were prepared by the same solvent using the same method. All test tubes were covered with aluminium foil, dried up and heated at 50°C in vacuum oven for 12 hours. After that, the cellulose powder was well-mixed and followed by addition of 4.5 mL of distilled water to each tube and adjusted the cellulose surface smoothly. Three seedling of Giant mimosa with radical root length 1-2 mm were transplanted in each tube. Finally, the tubes were sealed with transparent vinyl film and kept in the growth chamber at 30°C for 24

hours daylight. After 7 days, the plants were washed and measured the length of root and shoot of both treated and controlled plants.*

$$\% \text{ Growth Inhibition} = \{(1-T/C)\} \times 100\%$$

where 'T' is root (or shoot) length of treated planting

'C' is root (or shoot) length of controlled planting

Growth inhibition of 100% represents total inhibition growing.

The results of weed growth inhibition of phenoxyacetic acids and their analogues *M. pigra* Linn. are displayed in Table A (see Appendices B)

2.8.2 Root Growth Promotion Test[67]

There are several methods for root growth promotion test. A method of choice in this research is followed by stem-cutting method. The cutting are soaked, dusted, or dipped an aqueous solution containing tested chemicals. The effect on root initiation and growth is determined. In this study, dip method was employed and the general procedure is described as follows:

a) Preparation of Plant Material

Selected plant material is *Coleus atropurpurreus* Benth. Stock plants were maintained under outdoor conditions so that succulent new shoot were available for cutting material throughout the testing period.

Bundles of cutting for treatment were prepared by removing the cutting from the plants with a sharp knife, making one cut on a slant and cutting 8 cm long. Then, the lower leaves were removed while let 3 to 4 of the uppermost leaves were remain attached. (Do not allow cutting to dry out or the leaves to wilt at any time during these preparation.)

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* All assay was performed at Weed Science Sub. Division, Botany and Weed Science Division, Department of Agriculture, Ministry of Agriculture and Cooperatives.

b) Bioassay Procedure

Aqueous solution of tested compound was prepared by dissolving a tested compound in 95% ethanol and diluting to concentration of 1×10^{-6} ppm. For the primary screening of the appropriate concentration, the preparation of 2,4-D concentration was varied in a range of 1×10^{-10}-10 ppm. A controlled solution was prepared using only solvent and distilled water. At least 15 plants were used in each tested concentration for one selected compound.

The base of one bundle cutting was dipped to a depth of 1 cm in one dilution of a tested compound for 4 minutes, allowed to dry in air for 4 minutes. The treated plants were individually dipped in the rooting medium, which contained distilled water in a glass bottle, 4 cm in diameter. Suitable supporters were used to hold cuttings upright in solutions and then the plants were kept maintained under outdoor conditions. After 10 days, the treated plants were removed from the medium, allowed to dry with carefully loosen the rooting. The root of both treated and controlled plants were uprooted, weighed and compared.

All experiments were done with 15 replicates. The results were calculated using means of this 15 replicates and compared by standard deviation values (for measures of variability).

$$\% \text{ Growth Promotion} = \{(T/C) \times 100\} - 100\%$$

where 'T' is root dry weight of treated plant

'C' is root dry weight of controlled plant

Growth Promotion of 0% represents promotion growing

The results of root growth promotion of phenoxyacetic acids and their analogues against *C. atropurpurreus* Benth. are displayed in Table C (see Appendices B).