CHAPTER II

EXPERIMENTAL

2.1 Instruments and Equipment

Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was performed on aluminium sheets pre-coated with silica gel (Merck's, Kieselgel 60 PF_{254}) and column chromatography was performed on silica gel; Merck's silica gel 60 G Art 7734 (70-230 mesh) were used as adsorbents.

The IR spectra were recorded on Nicolet model Impact 410 FT/IR spectrophotometer. Solid samples were incorporated into a pellet of potassium bromide. Liquid samples were dropped on sodium chloride plates. The ^{1}H- and ^{13}C-NMR spectra were performed in deuterated chloroform ($CDCl_3$) or deuterated dimethylsulfoxide (DMSO-d_6) with tetramethylsilane (TMS) as an internal reference on the Varian nuclear magnetic resonance spectrometer, model Mercury plus 400 NMR spectrometer which operated at 399.84 MHz for ^{1}H and 100.54 MHz for ^{13}C nuclei. The chemical shifts (δ) are assigned by comparison with residue solvent protons.

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 reagents used for synthesis were purchased from Fluka chemical company or otherwise stated and were used without further purification.

2.3 Preparation of Substrates

2.3.1 Halogenated Reagents

Ethyl trichloroacetate, ethyl tribromoacetate and *i*-propyl trichloroacetate[50,51]

1 mL of concentrated sulfuric acid was cautiously added to the mixture of trichloroacetic acid or tribromoacetic acid 40 mmol and ethanol or *i*-propanol 20 mmol. The mixture in the rounded bottom flask fitted by a condenser was refluxed for 3-6 hours and then poured into 100 mL of water in a separatory funnel. The upper layer of crude ester was removed and washed with 50 mL of water, saturated aqueous $NaHCO_3$ and water, respectively, and dried over Na_2SO_4.

ethyl trichloroacetate; colorless oil (75%). IR (neat): 2981, 1762, 1465, 1367, 1240 and 1014 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.38 (3H, t, J = 7.20 Hz, CH_2CH_3) and 4.39 (2H, q, J = 7.20 Hz, CH_2CH_3).

ethyl tribromoacetate: colorless oil (72%). IR (neat): 2981, 1750, 1469, 1361, 1233 and 1021 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.44 (3H, t, J = 7.20 Hz, CH_2CH_3) and 4.46 (2H, q, J = 7.20 Hz, CH_2CH_3).

***i*-propyl trichloroacetate**: colorless oil (69%). IR (neat): 2984, 2937, 1766, 1466, 1376, 1256 and 1100 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.41 (6H, d, J = 6.28 Hz, $CH(CH_3)_2$) and 5.18 (1H, sep, J = 6.28 Hz, $CH(CH_3)_2$).

Trichloroacetanilide[52]

Into a three-necked flask, fitted with a hot plate stirrer, a reflux condenser, a thermometer, and a dropping funnel, was placed a solution of hexachloroacetone 0.1 mol in 40 mL of hexane. To the stirred solution was added, dropwise, aniline 0.1 mol over a period of 35- 40 minutes. During this time, the temperature was rised to about 55 °C. After the addition was completed, stirring was continued at 65-70 °C for another 45 minutes. The hot solution was poured into a beaker and then cooled to 0-5 °C. The solid was collected upon filtration and air-dried. Recrystallization from 90% ethanol to obtain white crystal (73%), m.p. 93-94 °C (EtOH) (lit.[52] 92.5-93 °C), R_f 0.62 (CH_2Cl_2). IR (KBr): 3307, 3054, 1699, 1598, 1524, 1443, 1315 and 1245 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.24 (1H, t, J = 8.40 Hz, Ar-*H*), 7.41 (2H, t, J = 8.40 Hz, Ar-*H*), 7.57 (2H, d, J = 8.40 Hz, Ar-*H*) and 8.31 (1H, br s, N*H*).

***N,N*-Diethyltrichloroacetamide and *N,N*-diethyltribromoacetamide**[7,50]

In a round bottom flask, the neck of which was ground to fit the bottom of a reflux condenser, was placed one mole of trichloroacetic acid or tribromoacetic acid, 2-2.5 moles of oxalyl chloride and 1-2 drops of dimethylformamide. The reaction was proceeded spontaneously for 15-20 minutes or sometimes even longer. After this period of time the mixture was refluxed for about 2 hours. The reaction mixture was then evaporated *in vacuo* till the excess of oxalyl chloride was collected. The mixture was added dropwise to well stirred, aqueous diethylamine solution and stirred for 1 hour at RT. When the reaction was completed, the organic layer was extracted with 10% HCl, saturated aqueous $NaHCO_3$ and H_2O, respectively, dried over Na_2SO_4 and evaporated *in vacuo*.

***N,N*-diethyltrichloroacetamide** Yellow oil (76%). IR (neat): 2980, 1672, 1423, 1248 and 1014 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.22 (3H, t, J = 6.87 Hz, CH_2CH_3) , 1.30 (3H, t, J = 6.78 Hz, CH_2CH_3) , 3.46 (2H, q, J = 6.87 Hz, CH_2CH_3) and 3.76 (2H, q, J = 6.78 Hz, CH_2CH_3).

***N,N*-diethyltribromoacetamide** Yellow oil (65%). IR (neat): 2972, 2933, 1645, 1427, 1376, 1262, 1209 and 1018 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.28 (3H, t, J = 6.44 Hz, CH_2CH_3), 1.36 (3H, t, J = 6.34 Hz, CH_2CH_3), 3.31 (2H, q, J = 6.44 Hz, CH_2CH_3) and 3.58 (2H, q, J = 6.34 Hz, CH_2CH_3).

2.3.2 Starting Materials

Vanillylamine[53]

A mixture of vanillin 0.1 mol and ammonium formate 0.32 mol was heated at 180 °C for 3 hours and, after cooling, evaporated until the odor of ammonia disappeared. To the residue was added concentrated HCl. The mixture was refluxed for 1 hour and then evaporated until the odor of HCl disappeared. The HCl salt was crystallized by adding EtOH. Two recrystallizations from 95% EtOH yielded pure vanillylamine hydrochloride. To a vigorously stirred solution of vanillylamine hydrochloride in water was added 2M NaOH solution. The resulting white solid of free vanillylamine was collected by suction filtration, washed with water, dried over in a desiccator to obtain white solid (40%), m.p. 135-137 °C (EtOH) (lit.[54] 131-133 °C), R_f 0.11 (MeOH). IR (KBr): 3168, 3107, 3024, 1612, 1525, 1321, 1265 and 1012

cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 3.59 (2H, s, ArC*H*$_2$NH$_2$), 3.75 (3H, s, OC*H*$_3$), 6.68 (2H, s, Ar*H*) and 6.91 (1H, s, Ar*H*).

2.4 General Procedure for the Synthesis Amides and Esters

Step 1: Triphenylphosphine 2 eq (6 mmol, 1.57 g) in CH_2Cl_2 3 mL was added to a mixture of carboxylic acid 1 eq (3 mmol) and selected halogenated reagent 2 eq (6 mmol) in CH_2Cl_2 3 mL at room temperature. The mixture was stirred for approximately 1 hour.

Step 2: A mixture of amine 1 eq (3 mmol) and selected base 3 eq (9 mmol) was added to the above mixture. The reaction continued stirring for another 20 minutes or followed by TLC at selected temperature. When the reaction was completed, the organic layer was extracted with 10% HCl and saturated aqueous $NaHCO_3$, respectively, dried over Na_2SO_4 and evaporated *in vacuo*. The mixture was separated with silica gel column chromatography eluting with 4:1 hexane/ethyl acetate. Purification by recrystallization with a mixture of CH_2Cl_2 and hexane or another appropriate solvent was conducted to achieve the desired amide or ester products.

2.5 Study on the Optimum Conditions

2.5.1 Effect of Halogenated Reagent

The synthesis of *N*-cyclohexylbenzamide was carried out using the reaction conditions described in the general procedure (base: triethylamine), by using twelve different halogenated reagents in the same manner: trichloroacetonitrile (Cl_3CCN), trichloroacetamide (Cl_3CCONH_2), ethyl trichloroacetate (Cl_3CCO_2Et), ethyl tribromoacetate (Br_3CCO_2Et), iodoic acid (ICH_2CO_2H), trichloroacetic acid (Cl_3CCO_2H), tribromoacetic acid (Br_3CCO_2H), trichloroacetic anhydride ($(Cl_3CCO)_2O$), *i*-propyl trichloroacetate ($Cl_3CCO_2CH(CH_3)_2$), trichloroacetanilide ($Cl_3CCONHC_6H_5$), *N,N*-diethyltrichloroacetamide ($Cl_3CCONEt_2$) and *N,N*-diethyl-tribromoacetamide ($Br_3CCONEt_2$).

2.5.2 Effect of Base

According to the general procedure (halogenated reagent: trichloroacetamide), a base was altered from triethylamine to DMAP, pyridine, *4*-picoline, imidazole, quinaldine, *3*-cyanopyridine, pyridine-*N*-oxide and quinoline.

2.5.3 Effect of Solvent System

Solvents for the synthesis of *N*-cyclohexylbenzamide according to the general procedure (halogenated reagent: trichloroacetamide, base: *4*-picoline) were varied from CH_2Cl_2 to chloroform, acetonitrile, tetrahydrofuran and ethyl acetate.

2.5.4 Effect of Temperature and Reaction Time

The general synthesis procedure of *N*-cyclohexylbenzamide using trichloroacetamide, *4*-picoline and dichloromethane as halogenated reagent, base and solvent, respectively was carried out at different reaction time and temperature: (30, 50 and 60 minutes) and (0-5, 28-30 and 38-40 °C).

2.5.5 Variation of Carboxylic Acid

The general procedure using trichloroacetamide, *4*-picoline and dichloromethane as halogenated reagent, base and solvent, respectively at reflux temperature for 1 hour was conducted. With different carboxylic acids: cyclopropane carboxylic acid, methacrylic acid, butyric acid, *6*-bromocaproic acid, nonanoic acid, lauric acid, palmitic acid, *4*-nitrobenzoic acid and *4*-methoxybenzoic acid were employed instead of benzoic acid.

2.5.6 Variation of Amine

The reaction was carried out using reaction conditions described in 2.5.5, but different amines: benzylamine, *2,6*-dimethylaniline, *4*-phenoxyaniline, ethanolamine, octadecylamine and α-naphthylamine were employed instead of cyclohexylamine.

2.6 Synthesis of Target Molecules

2.6.1 Amide Compounds

***N*-cyclohexylbenzamide** white needle (99%), m.p. 147-148 °C (CH_2Cl_2-hexane) (lit.[55] 147 °C), R_f 0.56 (50% EtOAc/hexane). IR (KBr): 3242, 2924, 2852, 1629, 1562, 1493, 1444 and 1332 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.12-2.03 (10H,

m, alkyl group), 3.88-4.02 (1H, m, NHC*H*), 6.03 (1H, br s, N*H*) and 7.24-7.75 (5H, m, Ar*H*).

***N*-benzylcyclopropanecarboxamide** white needle (97%), m.p. 132-135 °C (CH_2Cl_2-hexane), R_f 0.51 (50% EtOAc/hexane). IR (KBr): 3288, 3069, 2999, 1634, 1544, 1459, 1396, 1353 and 1241 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.76 (2H, q, *J* = 2.93 Hz, alkyl group), 1.09 (2H, q, *J* = 2.93 Hz, alkyl group), 1.36 (1H, m, C*H*C=O), 4.56 (2H, d, *J* = 5.86 Hz, CH_2-Ar), 5.91 (1H, br s, N*H*) and 7.29-7.37 (5H, m, Ar-*H*); ^{13}C-NMR ($CDCl_3$) δ (ppm): 7.29, 14.77, 43.84, 127.49, 127.86, 128.72, 138.50 and 173.61.

***N*-benzylmethacrylamide** white needle (15%), m.p. 82-85 °C (CH_2Cl_2-hexane) (lit[56] 82-83 °C), R_f 0.62 (50% EtOAc/hexane). IR (KBr): 3377, 2929, 1696, 1607, 1540, 1451, 1373 and 1241 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.99 (3H, s, C=CCH_3), 4.51 (2H, d, *J* = 5.86 Hz, CH_2-Ar), 5.36, 5.72 (2H, s, *H*C=C*H*), 6.08 (1H,br s, N*H*) and 7.29-7.35 (5H, m, Ar-*H*).

***N*-benzylbutanamide** white semi solid (94%), R_f 0.42 (50% EtOAc/hexane). IR (neat): 3293, 3073, 2955, 2818, 1634, 1547, 1455, 1383 and 1214 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.96 (3H, t, *J* = 7.38 Hz, CH_2CH_3), 1.68 (2H, sextet, *J* = 7.38 Hz, C$H_2$$CH_2$CO), 2.20 (2H, t, *J* = 7.38 Hz, CH_2CO), 4.42 (2H, d, *J* = 5.72 Hz, CH_2Ar), 6.58 (1H, br s, N*H*) and 7.26-7.35 (5H, m, Ar*H*).

***N*-benzyl-*6*-bromohexanamide** yellow liquid (67%), R_f 0.47 (50% EtOAc/hexane). IR (neat): 3293, 2934, 2858, 1639, 1547, 1455, 1373 and 1235 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.50 (2H, quin, *J* = 7.80 Hz, $BrCH_2CH_2CH_2$-), 1.71 (2H, quin, *J* = 7.80 Hz, $BrCH_2CH_2$ CH_2CH_2-), 1.89 (2H, quin, *J* = 7.80 Hz, $BrCH_2CH_2$ CH_2-), 2.25 (2H, t, *J* = 7.02 Hz, $BrCH_2(CH_2)_3CH_2$C=O), 3.42 (2H, t, *J* = 7.02 Hz, $BrCH_2CH_2CH_2$-), 4.44 (2H, d, *J* = 6.24 Hz, CH_2-Ar), 6.00 (1H, br s, N*H*) and 7.29-7.38 (5H, m, Ar*H*).

***N*-benzylnonanamide** white needle (89%), m.p. 69-70 °C (CH_2Cl_2-hexane), R_f 0.64 (50% EtOAc/hexane). IR (KBr): 3295, 3081, 2921, 2848, 1637, 1548, 1454, 1330 and 1232 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.91 (3H, t, *J* = 7.36 Hz, CH_2CH_3), 1.29-1.33 (10H, m, $(CH_2)_5$), 1.69 (2H, sextet, *J* = 7.76 Hz, C$H_2$$CH_2$CO), 2.25 (2H, t, *J* = 7.76 Hz, CH_2CO), 4.48 (2H, d, *J* = 5.45 Hz, CH_2Ar), 5.78 (1H, br s, N*H*) and 7.29-7.39 (5H, m, Ar*H*).

***N*-benzyldodecanamide** white needle (83%), m.p. 74-76 °C (CH_2Cl_2-hexane), R_f 0.60 (50% EtOAc/hexane). IR (KBr): 3295, 3069, 2915, 2851, 1630, 1552, 1431, 1330 and 1201 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.91 (3H, t, *J* = 6.90 Hz, CH_2CH_3), 1.28 (16H, m, $(CH_2)_8$), 1.69 (2H, sextet, *J* = 7.58 Hz, CH_2CH_2CO), 2.25 (2H, t, *J* = 7.58 Hz, CH_2CO), 4.48 (2H, d, *J* = 5.42 Hz, CH_2Ar), 5.73 (1H, br s, N*H*) and 7.29-7.37 (5H, m, Ar*H*).

***N*-benzylhexadecanamide** white needle (44%), m.p. 112-116 °C (CH_2Cl_2-hexane), R_f 0.60 (50% EtOAc/hexane). IR (KBr): 3293, 2914, 2843, 1634, 1552, 1434, 1332, 1189 and 1112 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.92 (3H, t, *J* = 7.02 Hz, CH_2CH_3), 1.29 (24H, m, $(CH_2)_{12}$), 1.68 (2H, sextet, *J* = 7.80 Hz, CH_2CH_2CO), 2.24 (2H, t, *J* = 7.80 Hz, CH_2CO), 4.48 (2H, d, *J* = 5.48 Hz, CH_2Ar), 5.70 (1H, br s, N*H*) and 7.30-7.39 (5H, m, Ar*H*).

***4*-nitro-*N*-cyclohexylbenzamide** white needle (93%), m.p. 207-209 °C (CH_2Cl_2-hexane), R_f 0.62 (50% EtOAc/hexane). IR (KBr): 3308, 2924, 2859, 1629, 1593, 1536, 1449, 1342 and 1326 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.25-2.09 (10H, m, alkyl group), 3.97-4.06 (1H, m, NHC*H*), 6.07 (1H, br s, N*H*), 7.34 (2H, d, *J* = 8.78 Hz, Ar*H*) and 8.30 (2H, d, *J* = 8.78 Hz, Ar*H*).

***4*-methoxy-*N*-cyclohexylbenzamide** white needle (91%), m.p. 153-157 °C (CH_2Cl_2-hexane), R_f 0.66 (50% EtOAc/hexane). IR (KBr): 3298, 2934, 2852, 1624, 1541, 1445, 1332 and 1255 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.64-2.07 (10H, m, alkyl group), 3.87 (3H, s, OCH_3), 3.95-4.00 (1H, m, NHC*H*), 5.91 (1H, br s, N*H*), 6.94 (2H, d, *J* = 8.78 Hz, Ar*H*) and 7.74 (2H, d, *J* = 8.78 Hz, Ar*H*).

***N*-benzylbenzamide** white needle (93%), m.p. 103-105 °C (CH_2Cl_2-hexane) (lit.[55] 105-106 °C), R_f 0.58 (50% EtOAc/hexane). IR (KBr): 3292, 3062, 1641, 1548, 1450, 1419, 1317 and 1256 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.66 (2H, d, *J* = 6.50 Hz, CH_2-Ar), 6.39 (1H, br s, N*H*), 7.26-7.51 (8H, m, Ar-*H*) and 7.79 (2H, d, *J* = 7.62 Hz, Ar-*H*).

***N*-(*2,6*-dimethylphenyl)benzamide** white needle (97%), m.p. 155-157 °C (CH_2Cl_2-hexane) (lit.[57] 159-161 °C), R_f 0.60 (50% EtOAc/hexane). IR (KBr): 3280, 5050, 2953, 2914, 1642, 1579, 1520, 1474, 1302 and 1213 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.33 (6H, s, $ArCH_3$), 7.17 (3H, s, Ar*H*), 7.44 (1H, br s, N*H*), 7.54 (2H, t, *J* = 7.14 Hz, Ar*H*), 7.61 (1H, t, *J* = 7.29 Hz, Ar*H*) and 7.96 (2H, d, *J* = 7.14 Hz, Ar*H*).

***N*-(*4*-phenoxyphenyl)benzamide** white needle (84%), m.p. 157-160 °C (CH_2Cl_2-hexane), R_f 0.62 (50% EtOAc/hexane). IR (KBr): 3316, 1645, 1593, 1516, 1491, 1409, 1317 and 1224 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.07-7.15 (6H, m, Ar*H*), 7.37 (2H, t, *J* = 7.04 Hz, Ar*H*), 7.54 (2H, t, *J* = 7.04 Hz, Ar*H*), 7.64 (2H, d, *J* = 8.79 Hz, Ar*H*), 7.83 (1H, br s, N*H*) and 7.91 (2H, d, *J* = 7.04 Hz, Ar*H*); ^{13}C-NMR ($CDCl_3$) δ (ppm): 118.53, 119.66, 122.19, 123.19, 127.11, 128.81, 129.81, 131.90, 133.44, 134.86, 153.75, 157.67 and 165.98.

***N*-(*2*-hydroxyethyl)benzamide** colorless liquid (11%), R_f 0.13 (50% EtOAc/hexane). IR (neat): 3120-3452, 3015, 2929, 1637, 1540, 1493, 1439, 1306, 1217 and 1073 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.66 (2H, t, *J* = 4.51 Hz, C*H*$_2$OH), 3.86 (2H, t, *J* = 4.51 Hz, C*H*$_2$NH), 6.86 (1H, br s, N*H*), 7.42-7.53 (3H, m, Ar*H*) and 7.82 (2H, d, *J* =7.48 Hz, Ar*H*).

***2*-benzamidoethyl benzoate** colorless liquid (51%), R_f 0.40 (50% EtOAc/hexane). IR (neat): 3334, 3017, 1706, 1644, 1537, 1490, 1450, 1388 and 1270 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.87 (2H, t, *J* = 5.44 Hz, C*H*$_2$O), 4.56 (2H, t, *J* = 5.44 Hz, C*H*$_2$NH), 7.00 (1H, br s, N*H*), 7.42-7.61 (6H, m, Ar*H*), 7.80 (2H, d, *J* =7.14 Hz, Ar*H*) and 8.07 (2H, d, *J* =9.17 Hz, Ar*H*).

***N*-octadecylbenzamide** white needle (63%), m.p. 88-89 °C (CH_2Cl_2-hexane), R_f 0.67 (50% EtOAc/hexane). IR (KBr): 3334, 2919, 2843, 1634, 1532, 1465 and 1296 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.92 (3H, t, *J* = 7.02 Hz, CH_2CH_3), 1.29 (30H, m, $(CH_2)_{15}$), 1.64 (2H, quin, *J* = 7.02 Hz, C*H*$_2$CH$_2$NHCO), 3.49 (2H, q, *J* = 7.02 Hz, C*H*$_2$NHCO), 6.11 (1H, br s, N*H*), 7.45-7.55 (3H, m, Ar*H*) and 7.79 (2H, d, *J* = 7.02 Hz, Ar*H*).

***N*-(*1*-naphthyl)benzamide** white needle (62%), m.p. 164-166 °C (CH_2Cl_2-hexane) (lit.[58] 159-161 °C), R_f 0.56 (50% EtOAc/hexane). IR (KBr): 3237, 3047, 1649, 1593, 1526, 1501, 1429, 1393, 1342 and 1285 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.58-7.67 (5H, m, Ar*H*), 7.80 (1H, d, *J* = 7.80 Hz, Ar*H*), 7.96-7.97 (3H, m, Ar*H*), 8.04 (2H, d, *J* = 7.02 Hz, Ar*H*), 8.11 (1H, d, *J* = 7.02 Hz, Ar*H*) and 8.24 (1H, br s, N*H*).

***N,N*-diethylbenzamide (T1)** yellow liquid (99%), R_f 0.51 (50% EtOAc/hexane). IR (neat): 2970, 1629, 1524, 1450, 1372, 1291 and 1096 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.10 (3H, br s, CH_2CH_3), 1.25 (3H, br s, CH_2CH_3), 3.26 (2H, br s, C*H*$_2$CH$_3$), 3.55 (2H, br s, C*H*$_2$CH$_3$) and 7.38 (5H, br s, Ar*H*).

***N,N*-diethyl-*3*-methylbenzamide or *N,N*-diethyl-*m*-toluamide or DEET (T2)** yellow liquid (99%), R_f 0.75 (50% EtOAc/hexane). IR (neat): 2970, 1619, 1564, 1460, 1367, 1219 and 1091 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.10 (3H, br s, CH_2CH_3), 1.28 (3H, br s, CH_2CH_3), 2.40 (3H, s, Ar-CH_3), 3.25 (2H, br s, CH_2CH_3), 3.58 (2H, br s, CH_2CH_3) and 7.15-7.28 (4H, m, Ar*H*).

***2*-methylbenzanilide or mebenil (T3)** white needle (91%), m.p. 124-126 °C (CH_2Cl_2-hexane) (lit.[59] 126 °C), R_f 0.73 (50% EtOAc/hexane). IR (KBr): 3227, 3119, 1645, 1594, 1439, 1326 and 1265 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.55 (3H, s, CH_3), 7.18-7.67 (9H, m, Ar-*H*).

***2*-iodobenzamide or benodanil (T4)** white needle (88%), m.p. 147-148 °C (CH_2Cl_2-hexane) (lit.[59] 143-144 °C), R_f 0.71 (50% EtOAc/hexane). IR (KBr): 3307, 3032, 1660, 1598, 1524, 1439 and 1322 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.20 (2H, q, *J* = 7.62 Hz, Ar-*H*), 7.40-7.59 (4H, m, Ar-*H*), 7.68 (2H, d, *J* = 7.62 Hz, Ar-*H*), 7.97 (1H, d, *J* = 7.62 Hz, Ar-*H*).

***2*-chloro-*N,N*-diethylcinnamamide (T5)** yellow liquid (79%), R_f 0.42 (50% EtOAc/hexane). IR (neat): 2947, 1643, 1601, 1564, 1465, 1367 and 1046 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.26 (6H, br s, CH_2CH_3), 3.55 (4H, q, *J* = 7.04 Hz, CH_2CH_3), 6.84 (1H, d, *J* = 15.24 Hz, C*H*=CHC=O), 7.30 (2H, d, *J* = 4.69 Hz, Ar-*H*), 7.43 (1H, d, *J* = 4.69 Hz, Ar-*H*), 7.61 (1H, d, *J* = 4.69 Hz, Ar-*H*) and 8.04 (1H, d, *J* = 15.24 Hz, C=C*H*C=O).

***N*-(*3,4*-methylenedioxycinnamoyl)phenethylamide (T6-1)** white needle (79%), m.p. 120-123 °C (CH_2Cl_2-hexane) (lit.[60] 117 °C), R_f 0.42 (50% EtOAc/ hexane). IR (KBr): 3073, 2904, 1645, 1547, 1495, 1439, 1321 and 1250 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.92 (2H, t, *J* = 7.04 Hz, CH_2-Ar), 3.69 (2H, q, *J* = 7.04, CH_2CH_2-Ar), 5.60 (1H, br s, N*H*), 6.02 (2H, s, OCH_2O), 6.17 (1H, d, *J* = 15.24 Hz, C*H*=CHC=O), 6.82 (1H, d, *J* = 7.62 Hz, Ar-*H*), 7.00 (2H, d, *J* = 7.62 Hz, Ar-*H*), 7.27 (3H, q, *J* = 7.04 Hz, Ar-*H*), 7.37 (2H, t, *J* = 7.04 Hz, Ar-*H*) and 7.57 (1H, d, *J* = 15.24 Hz, C=C*H*C=O).

***N*-(*3,4*-methylenedioxycinnamoyl)piperidide (T7)** white needle (99%), m.p. 80-82 °C (CH_2Cl_2-hexane) (lit.[60] 83 °C), R_f 0.40 (50% EtOAc/hexane). IR (neat): 3001, 2934, 2858, 1645, 1593, 1495, 1439, 1352 and 1245 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 1.63 (6H, br s, alkyl group), 3.68 (4H, br s, alkyl group), 6.02 (2H, s, OCH_2O), 6.76 (1H, d, *J* = 15.60 Hz, C*H*=CHC=O), 6.82 (1H, d, *J* = 7.62 Hz, Ar-*H*),

7.02 (1H, d, J = 7.62 Hz, Ar-*H*), 7.07 (1H, s, Ar-*H*) and 7.59 (1H, d, J = 15.60 Hz, C=C*H*C=O).

***3',4'*-dichlorocyclopropanecarboxanilide or cypromid (T8)** white needle (80%), m.p. 130-132 °C (CH_2Cl_2-hexane) (lit.[61] 130-131 °C), R_f 0.56 (50% EtOAc/hexane). IR (KBr): 3283, 3098, 1665, 1588, 1470, 1398 and 1265 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.88 (2H, q, J = 4.00 Hz, alkyl group), 1.09 (2H, q, J = 4.00 Hz, alkyl group), 1.50 (1H, m, C*H*C=O), 7.34 (2H, s, Ar-*H*), 7.57 (1H, br s, N*H*) and 7.77 (1H, s, Ar-*H*).

***N*-vanillylpelargonamide or capsaicine synthetic (T9)** white needle (28%), m.p. 62-65 °C (CH_2Cl_2-hexane), R_f 0.62 (50% EtOAc/hexane). IR (KBr): 3158-3009, 3311, 2919, 1651, 1377, 1278 and 1156 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.88 (3H, t, J = 4.69 Hz, C*H*$_3$), 1.29 (10H, br s, alkyl group), 1.74 (2H, m, C*H*$_2$CH$_2$C=O), 2.21 (2H, t, J = 7.62 Hz, CH$_2$C*H*$_2$C=O), 3.81 (3H, s, OC*H*$_3$), 4.41 (2H, d, J = 5.86 Hz, C*H*$_2$Ar), 5.70 (1H, br s, N*H*), 6.84 (1H, d, J = 7.62 Hz, Ar-*H*), 6.89 (1H, s, Ar-*H*) and 6.96 (1H, d, J = 8.21 Hz, Ar-*H*).

***N*-palmitoylethanolamine or PEA (T10)** white needle (31%), m.p. 96-98 °C (EtOH) (lit.[62] 98-99 °C), R_f 0.11 (50% EtOAc/hexane). IR (KBr): 3631-3365, 3291, 2909, 1644 and 1372 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.86 (3H, t, J = 7.03 Hz, C*H*$_3$), 1.24 (24H, s, alkyl group), 1.46 (2H, m, C*H*$_2$CH$_2$C=O), 2.04 (2H, t, J = 7.62 Hz, CH$_2$C*H*$_2$C=O), 2.55 (1H, s, O*H*), 3.09 (2H, q, J = 5.85 Hz, C*H*$_2$OH), 4.67 (2H, t, J = 5.27 Hz, C*H*$_2$NH) and 7.78 (1H, br s, N*H*).

***N,N'-bis*(*3*-chlorophenyl)butanediamide (T11)** white needle (25%), m.p. 238-240 °C (EtOH) (lit.[47] 233-235 °C), R_f 0.44 (50% EtOAc/hexane). IR (KBr): 3288, 1668, 1589, 1410 and 1321 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.68 (4H, s, C*H*$_2$C=O), 7.09 (2H, d, J = 8.40 Hz, Ar-*H*), 7.33 (2H, t, J = 8.40 Hz, Ar-*H*), 7.43 (2H, d, J = 8.40 Hz, Ar-*H*), 7.83 (2H, s, Ar-*H*) and 10.23 (2H, s, N*H*).

2.6.2 Ester Compounds

benzyl benzoate (T13) colorless liquid (85%), R_f 0.53 (20% EtOAc/hexane). IR (neat): 3063, 3030, 2952, 1719, 1598, 1493, 1450 and 1372 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 5.40 (2H, s, OC*H*$_2$Ar), 7.35-7.48 (7H, m, Ar-*H*), 7.62 (1H, t, J = 7.62 Hz, Ar-*H*) and 8.12 (2H, d, J = 7.62 Hz, Ar-*H*).

phenethyl cinnamate (T14) colorless liquid (98%), R_f 0.62 (50% EtOAc/hexane). IR (neat): 3057, 3018, 2954, 1716, 1634, 1501, 1450 and 1311 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.07 (2H, t, *J* = 7.04 Hz, CH_2CH_2Ar), 4.46 (2H, t, *J* = 7.04 Hz, CH_2CH_2Ar), 6.47 (1H, d, *J* = 15.83 Hz, *H*C=CHC=O), 7.29-7.57 (8H, m, Ar-*H*), 7.57 (2H, m, Ar-*H*) and 7.72 (1H, d, *J* = 15.83 Hz, C=C*H*C=O).

cinnamoyl cinnamate (T15) colorless liquid (84%), R_f 0.57 (50% EtOAc/hexane). IR (neat): 3063, 1710, 1629, 1495, 1450, 1301 and 1260cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 6.42 (1H,d, *J* = 15.83 Hz, *H*C=CH-O), 6.53 (1H, d, *J* = 16.02 Hz, *H*C=CHC=O), 6.75 (1H, d, *J* = 15.83 Hz, HC=C*H*-O), 7.29-7.47 (8H, m, Ar-*H*), 7.59 (2H, m, Ar-*H*) and 7.78 (1H, d, *J* = 16.02 Hz, C=C*H*C=O).

cholesteryl butyrate (T16) white solid (78%), m.p. 99-101 °C (CH_2Cl_2-hexane) (lit.[63] 110-111 °C), R_f 0.62 (10% EtOAc/hexane). IR (KBr): 2939, 1734, 1475, 1373, 1301 and 1189 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.71 (3H, s, CH_3), 0.89 (6H, d, *J* = 6.44 Hz, $(CH_3)_2CH$), 0.95-2.06 (37H, m, alkyl group), 2.29 (2H, t, *J* = 7.03 Hz), 2.34 (2H, d, *J* = 7.62 Hz), 4.65 (1H, m, *H*CCO_2) and 5.41 (1H, d, *J* = 4.10 Hz, *H*C=C); ^{13}C-NMR ($CDCl_3$) δ (ppm): 11.9, 13.7, 18.6, 18.7, 19.4, 21.1, 22.6, 22.9, 23.9, 24.3, 27.8, 28.1, 28.3, 31.8, 31.9, 35.8, 36.2, 36.6, 37.0, 38.2, 39.5, 39.7, 42.3, 50.0, 56.1, 56.7, 73.7, 122.6, 139.7 and 173.2.

cholesteryl nonanoate (T17) white solid (79%), m.p. 82-83 °C (CH_2Cl_2-hexane), R_f 0.82 (10% EtOAc/hexane). IR (KBr): 2930, 2858, 1737, 1460, 1372, 1168 and 999 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 0.71 (3H, s, CH_3), 0.90 (6H, d, *J* = 7.99 Hz, $(CH_3)_2CH$), 0.93-2.06 (47H, m, alkyl group), 2.29 (2H, t, *J* = 7.03 Hz), 2.33 (2H, d, *J* = 7.62 Hz), 4.65 (1H, m, *H*CCO_2) and 5.40 (1H, d, *J* = 4.25 Hz, *H*C=C); ^{13}C-NMR ($CDCl_3$) δ (ppm): 11.9, 14.2, 18.7, 19.4, 21.1, 22.6, 22.7, 22.9, 23.9, 24.3, 25.1, 27.8, 28.1, 28.3, 29.2, 29.3, 31.8, 31.9, 34.7, 35.8, 36.2, 36.6, 37.0, 38.2, 39.5, 39.7, 42.3, 50.0, 56.1, 56.7, 73.7, 122.6, 139.7 and 173.3.