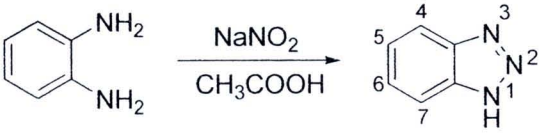
CHAPTER III
EXPERIMENTAL

Melting points were determined on a Sanyo-Gallenkamp melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded as KBr disks for solids and thin films on sodium chloride plates for liquids on Perkin-Elmer Spectum One FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were obtained using a VARIAN MERCURY plus 400 MHz FT-NMR spectrometer (tetramethylsilane (TMS) was used as internal standard). Chemical shifts (δ) were expressed in parts per million (ppm), positive shifts being downfield from TMS. ^{1}H NMR data were listed in order of the number of proton, multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) and doublet of doublet (dd)], coupling constant in Hertz (Hz) and assignment of nuclei concerned.

Thin layer chromatography (TLC) was carried out on MERCK silica gel 60 F_{254} TLC aluminum sheets. Column chromatography was done with silica gel 0.063-0.200 mm. All solvents were routinely distilled prior to use.

1. Preparation of Benzotriazole (1a)



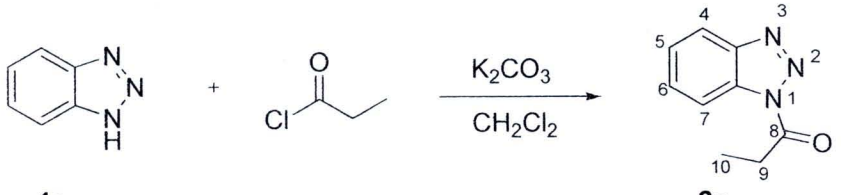
1a

To a stirred cooled solution (15°C) of *o*-phenylenediamine (10.8 g, 100 mmol) in glacial acetic acid (11.5 ml) was added a solution of sodium nitrite (7.5 g, 110.0 mmol) in water (15.0 ml). Mild exothermic reaction commensed within a few minutes and rapidly subsided while the deep red color faded into pale brown. Stirring was continued for 15 minutes until the temperature dropped to 35-40 °C and the mixture was then chilled in an ice-water bath for 30 minutes. The pale brown precipitates were collected by vacuum filtration and washed with ice-cold water. Highly colored crude product was purified by repeated recrystallization from water using activated charcoal

as a decolorizing agent. Benzotriazole (**1a**) was obtained as fine white needles (8.0 g, 70.0 mmol, 67%).

1*H*-benzo[*d*][1,2,3]triazole (1a). mp. 95-97 °C (lit.mp 96-97 °C)[51] R_f = 0.30 (30 % ethyl acetate:hexane). IR (KBr) : $\bar{\nu}_{max}$ 3254, 3080, 2959, 2794, 2711, 1623, 1595, 1511, 1458, 1420, 1384, 1210, 1006, 752, 741 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 7.94 (d, J = 6.2 Hz, $1H_4$), 7.93 (d, J = 6.2 Hz, $1H_7$), 7.46 (m, $1H_5$), 7.46 (m, $1H_6$). ^{13}C NMR ($CDCl_3$) : δ 138.65 ($C_{3'}$), 138.65 ($C_{7'}$), 126.23 (C_5), 126.23 (C_6), 114.94 (C_4), 114.94 (C_7).

2. Preparation of *N*-propionyl benzotriazole (2a)

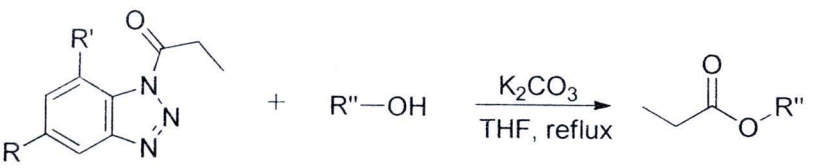


1a **2a**

To a stirred mixture of benzotriazole (**1a**) (1.2 g, 10.0 mmol) and anhydrous potassium carbonate (2.8 g, 20.0 mmol) in dichloromethane (30.0 ml) was slowly added propionyl chloride (1.1 ml, 12 mmol). The mixture was refluxed for 30 minutes and filtered under reduced pressure through a celite pad. The filtrate was evaporated using a rota-vaporator to dryness and the residue was purified by recrystallization from hexane to afford *N*-propionyl benzotriazole (**2a**) as a white crystalline solid (1.7 g, 9.4 mmol, 94%).

1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)propan-1-one (2a). mp. 79-80 °C (lit.mp 80-82 °C)[32] R_f = 0.65 (30 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3457, 3050, 2985, 2940, 2882, 1736, 1454, 1413, 1379, 1287, 1174, 1073, 1007, 951, 773, 759 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.29 (d, J = 8.3 Hz, $1H_7$), 8.13 (d, J = 8.3 Hz, $1H_4$), 7.65 (t, J = 8.1 Hz, $1H_6$), 7.50 (t, J = 8.1 Hz, $1H_5$), 3.46 (q, J = 7.4 Hz, $2H_9$), 1.42 (t, J = 7.4 Hz, $3H_{10}$). ^{13}C NMR ($CDCl_3$) : δ 173.28 (C_8), 146.13 ($C_{3'}$), 131.12 ($C_{7'}$), 130.31 (C_6), 126.03 (C_5), 120.09 (C_4) 114.38 (C_7), 29.08 (C_9), 8.34 (C_{10}).

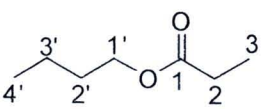
3. General method for the preparation of esters using *N*-propionyl-benzotriazoles



2a, R = H, R' = H
12a, R = Br, R' = Br
12b, R = Cl, R' = Cl
22b, R = COOEt, R' = H

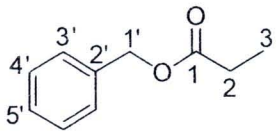
A mixture of *N*-propionyl benzotriazole (0.2 g, 1.1 mmol), alcohol (1.0 mmol) and anhydrous potassium carbonate (0.3 g, 1.2 mmol) in tetrahydrofuran (5.0 ml) was refluxed for 30-60 minuts. The mixture was cooled to room temperature and the solvent was evaporated under reduced pressure to dryness. Purification of the crude ester by column chromatography (ethyl acetate:hexane) gave the pure ester in 70-95 %yield. In addition, purification by aqueous basic extraction could be done as follows: the residue was dissolved in a mixture of dichloromethane (2.0-3.0 ml) and methanol (2.0 ml) and stirred for 5 minutes. The resulting mixture was added 2M sodium carbonate (2.0 ml) and stirring was continued for 30 minutes then extracted with dichloromethane (2x5.0 ml). Combined organic layers were dried and concentrated under reduced pressure to give the pure ester in 57-89 % yield.

Butyl propionate (4c). R_f = 0.72 (25 % ethyl acetate:hexane).



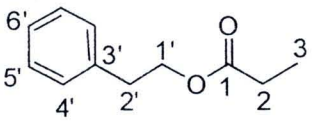
IR (neat) : $\bar{\nu}_{max}$ 3456, 2961, 2875, 1740, 1464, 1382, 1349, 1275, 1189, 1083, 1026, 951, 844, 808, 738 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 4.04 (t, J = 6.7 Hz, $2H_{1'}$), 2.28 (q, J = 7.6 Hz, $2H_2$), 1.58 (quint, J = 7.1 Hz, $2H_{2'}$), 1.35 (m, $2H_{3'}$), 1.10 (t, J = 7.6 Hz, $3H_3$), 0.90 (t, J = 7.4 Hz, $3H_{4'}$). ^{13}C NMR ($CDCl_3$) : δ 174.49 (C_1), 64.09 ($C_{1'}$), 30.65 ($C_{2'}$), 27.54 (C_2), 19.07 ($C_{3'}$), 13.61 ($C_{4'}$), 9.07 (C_3).

Benzyl propionate (**4d**). R_f = 0.65 (25 % ethyl acetate:hexane).



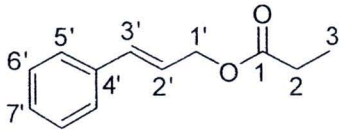
IR (neat) : 3538, 3461, 3066, 3034, 2982, 2944, 2884, 1738, 1497, 1455, 1380, 1347, 1273, 1175, 1082, 1016, 750, 698 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 7.37 (m, $5H_{Ar}$), 5.14 (s, $2H_{1'}$), 2.40 (q, J = 7.6 Hz, $2H_2$), 1.18 (t, J = 7.6 Hz, $3H_3$. ^{13}C NMR ($CDCl_3$) : δ 174.22 (C_1), 136.16 ($C_{2'}$), 128.53 ($C_{4'}$), 128.15 ($C_{3'}$), 66.10 ($C_{1'}$), 27.58 (C_2), 9.10 (C_3).

Phenethyl propionate (**4e**). R_f = 0.78 (25 % ethyl acetate:hexane).



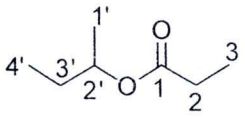
IR (neat) : $\bar{\nu}_{max}$ 3458, 3064, 3029, 2981, 2943, 1738, 1497, 1455, 1384, 1349, 1274, 1184,1083, 1016, 749, 700 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 7.30 (m, $5H_{Ar}$), 4.32 (t, J = 7.1 Hz, $2H_{1'}$), 2.95 (t, J = 7.1 Hz, $2H_{2'}$), 2.32 (q, J = 7.6 Hz, $2H_2$), 1.14 (t, J = 7.6 Hz, $3H_3$). ^{13}C NMR ($CDCl_3$) : δ 174.15 (C_1), 137.92 ($C_{3'}$), 128.90 ($C_{4'}$), 128.46 ($C_{5'}$), 126.51 ($C_{6'}$), 64.73 ($C_{1'}$), 35.17 ($C_{2'}$), 27.51 (C_2), 9.08 (C_3).

Cinnamyl propionate (**4f**). R_f = 0.68 (25 % ethyl acetate:hexane).



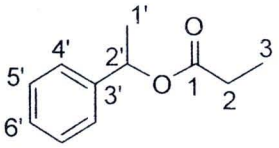
IR (neat) : $\bar{\nu}_{max}$ 3455, 3083, 3059, 3028, 2982, 2943, 2882, 1738, 1495, 1462, 1380, 1347, 1271, 1179, 1081, 1013, 967, 746, 693 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 7.40 (d, J = 7.4 Hz, $2H_{5'}$), 7.32 (t, J = 7.2 Hz, $2H_{6'}$), 7.26 (t, J = 7.2 Hz, $1H_{7'}$), 6.65 (d, J = 15.9 Hz, $1H_{3'}$), 6.30 (m, $1H_{2'}$), 4.74 (d, J = 6.4 Hz, $2H_{1'}$), 2.38 (q, J = 7.6 Hz, $2H_2$), 1.17 (t, J = 7.6 Hz, $3H_3$). ^{13}C NMR ($CDCl_3$) : δ 174.21 (C_1), 136.24 ($C_{4'}$), 134.05 ($C_{3'}$), 128.57 ($C_{6'}$), 128.01 ($C_{5'}$), 126.58 ($C_{7'}$), 123.34 ($C_{2'}$), 64.90 ($C_{1'}$), 27.59 (C_2), 9.11 (C_3).

***sec*-Butyl propionate (4g).** R_f = 0.75 (25 % ethyl acetate:hexane).



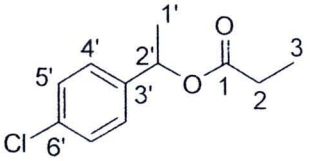
IR (neat) : $\bar{\nu}_{max}$ 3451, 2976, 2941, 2881, 1735, 1464, 1378, 1338, 1274, 1195, 1116, 1096, 910, 734 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 4.72 (m, $1H_{2'}$), 2.20 (q, J = 7.6 Hz, $2H_2$), 1.45 (m, $2H_{3'}$), 1.10 (d, J = 6.3 Hz, $3H_{1'}$), 1.02 (t, J = 7.6 Hz, $3H_3$), 0.80 (t, J = 7.4 Hz, $3H_{4'}$). ^{13}C NMR ($CDCl_3$) : δ 173.94 (C_1), 71.74 ($C_{2'}$), 28.68 ($C_{3'}$), 27.75 (C_2), 19.27 ($C_{1'}$), 9.46 ($C_{4'}$), 9.02 (C_3).

1-phenylethyl propionate (4h). R_f = 0.58 (30 % ethyl acetate:hexane).



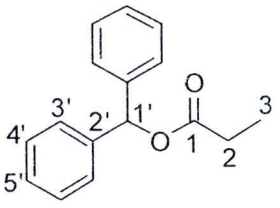
IR (neat) : $\bar{\nu}_{max}$ 458, 3065, 3034, 2982, 2941, 2882, 1738, 1495, 1454, 1368, 1273, 1189,1082, 1064, 761, 699 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 7.24 (m, $5H_{Ar}$), 5.81 (q, J = 6.6 Hz, $1H_{2'}$), 2.25 (q, J = 7.6 Hz, $2H_2$), 1.44 (d, J = 6.6 Hz, $3H_{1'}$), 1.05 (t, J = 7.6 Hz, $3H_3$). ^{13}C NMR ($CDCl_3$) : δ 173.59 (C_1), 141.89 ($C_{3'}$), 128.47 ($C_{5'}$), 127.78 ($C_{6'}$), 126.03 ($C_{4'}$), 72.06 ($C_{2'}$), 27.86 (C_2), 22.27 ($C_{1'}$), 9.08 (C_3).

1-(4-chlorophenyl)ethyl propionate (4i). R_f = 0.75 (30 % ethyl acetate:hexane).



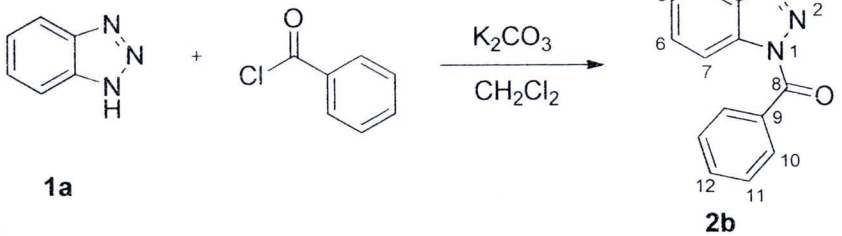
IR (neat) : $\bar{\nu}_{max}$ 3454, 2983,2941, 2882, 1739, 1494, 1462, 1365, 1273, 1189,1082, 1064,1015, 827 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 7.28 (m, $4H_{Ar}$), 5.84 (q, J = 6.6 Hz, $1H_{2'}$), 2.32 (m, $2H_2$), 1.50 (d, J = 6.6 Hz, $3H_{1'}$), 1.12 (t, J = 7.6 Hz, $3H_3$). ^{13}C NMR ($CDCl_3$): δ 173.44 (C_1), 140.41 ($C_{3'}$), 133.48 ($C_{6'}$), 128.61 ($C_{5'}$), 127.44 ($C_{4'}$), 71.31 ($C_{2'}$), 27.76 (C_2), 22.14 ($C_{1'}$), 9.01 (C_3).

Benzhydryl propionate (4j). R_f = 0.48 (25 % ethyl acetate:hexane).



IR (KBr) : $\bar{\nu}_{max}$ 3457, 3088, 3064, 3032, 2982, 2941, 2882, 1740, 1495, 1454, 1363, 1269,1171, 1081, 1010, 758, 744, 699 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 7.36 (m, $10H_{Ar}$), 6.95 (s, $1H_{1'}$), 2.48 (q, J = 7.6 Hz, $2H_2$), 2.22 (t, J = 7.6 Hz, $3H_3$). ^{13}C NMR ($CDCl_3$) : δ 173.37 (C_1), 140.44 ($C_{2'}$), 128.53 ($C_{4'}$), 127.89 ($C_{3'}$), 127.12 ($C_{5'}$), 76.70 ($C_{1'}$), 27.91 (C_2), 9.14 (C_3).

4. Preparation of *N*-benzoyl benzotriazole (2b)



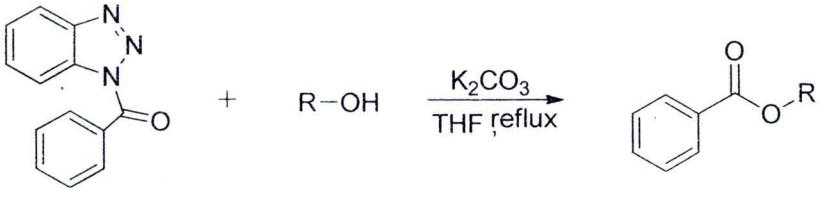
1a **2b**

To a stirred mixture of benzotriazole (**1a**) (1.2 g, 10.0 mmol) and anhydrous potassium carbonate (2.8 g, 20.0 mmol) in dichloromethane (30.0 ml) was slowly added benzoyl chloride (1.7 ml, 12 mmol). The mixture was refluxed for 30 minutes and filtered under reduced pressure through a celite pad. The filtrate was evaporated using a rota-vaporator to dryness and the residue was purified by recrystallization from hexane to afford *N*-benzoyl benzotriazole (**2b**) as a white crystalline solid (2.3 g, 10.0 mmol, 98%).

(1*H*-benzo[*d*][1,2,3]triazol-1-yl)(phenyl)methanone (2b). mp. 113-115 °C (lit.mp 112-113 °C)[32] R_f = 0.70 (30 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3379, 3102, 3068, 1712, 1600, 1451, 1379, 1365, 1247, 1051, 941, 886 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.40 (d, J = 8.3 Hz, $1H_7$), 8.22 (d, J = 7.3 Hz, $2H_{10}$), 8.17 (d, J = 8.3 Hz, $1H_4$), 7.70 (m, $1H_5$), 7.70 (m, $1H_6$), 7.60 (m, $2H_{11}$), 7.60 (m, $1H_{12}$). ^{13}C NMR ($CDCl_3$) : δ 166.74

(C_8), 145.77 ($C_{3'}$), 133.67 (C_{12}), 132.35 ($C_{7'}$), 131.72 (C_{10}), 131.48 (C_9), 130.38 (C_6), 128.43 (C_{11}), 126.33 (C_5), 120.19 (C_4) 114.79 (C_7).

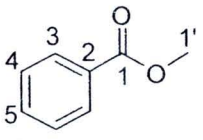
5. General method for the preparation of esters using *N*-benzoyl-benzotriazoles



2b

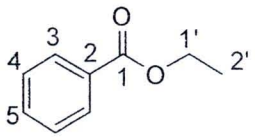
A mixture of *N*-benzoyl benzotriazoles (1.1 mmol), alcohol (1.0 mmol) and anhydrous potassium carbonate (1.2 mmol) in tetrahydrofuran (5.0 ml) was refluxed for 30-60 minutes. The mixture was cooled to room temperature and the solvent was evaporated under vacuum to dryness. Purification of the crude ester by column chromatography (ethyl acetate:hexane) gave the pure ester in 64-96 %yield. In addition, purification by aqueous basic extraction could be done as follows: the residue was added dichloromethane (2.0-3.0 ml) and 2M sodium carbonate (2.0 ml) and stirring was continued for 30 minutes. After twice similar treatments, the mixture was extracted with dichloromethane (2x5 ml). Combine organic layers were dried and concentrated under reduced pressure to give the pure ester in 55-93 %yield.

Methyl benzoate (5a). R_f = 0.60 (25 % ethyl acetate:hexane).



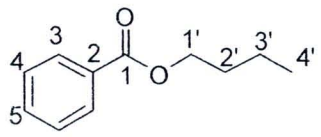
IR (neat) : $\bar{\nu}_{max}$ 3432, 3064, 2999, 2952, 2844, 1723, 1601, 1452, 1435, 1315, 1278, 1177,1111, 1071, 1027, 966, 711 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.03 (d, J = 7.7 Hz, $2H_3$), 7.52 (t, J = 7.5 Hz, $1H_5$), 7.40 (t, J = 7.6 Hz, $2H_4$), 3.88 (s, $3H_{1'}$). ^{13}C NMR ($CDCl_3$) : δ 167.05 (C_1), 132.85 (C_5), 130.12 (C_3), 128.30 (C_4), 52.00 ($C_{1'}$).

Ethyl benzoate (5b). R_f = 0.65 (25 % ethyl acetate:hexane).



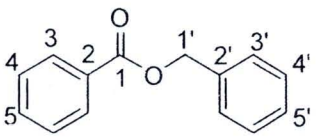
IR (neat) : $\bar{\nu}_{max}$ 3422, 3063, 3034, 2988, 2938, 2906, 1716, 1602, 1451, 1367, 1314, 1274, 1175,1108, 1071, 1028, 711 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.05 (d, J = 7.2 Hz, $2H_3$), 7.53 (t, J = 7.4 Hz, $1H_5$), 7.43 (t, J = 7.7 Hz, $2H_4$), 4.37 (q, J = 7.1 Hz, $2H_{1'}$), 1.38 (t, J = 7.1 Hz, $3H_{2'}$). ^{13}C NMR ($CDCl_3$) : δ 166.56 (C_1), 132.74 (C_5), 130.49 (C_2), 129.49 (C_3), 128.26 (C_4), 60.88 ($C_{1'}$), 14.29 ($C_{2'}$).

Buthyl benzoate (5c). R_f = 0.60 (25 % ethyl acetate:hexane).



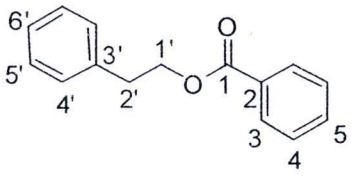
IR (neat) : $\bar{\nu}_{max}$ 3423, 3064, 2960, 2934, 2874, 1720, 1602, 1452, 1385, 1314, 1275, 1176, 1111, 1070, 1027, 711 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.05 (d, J = 7.2 Hz, $2H_3$), 7.53 (t, J = 7.4 Hz, $1H_5$), 7.43 (t, J = 7.7 Hz, $2H_4$), 4.32 (t, J = 6.6 Hz, $2H_{1'}$), 1.74 (quint, J = 7.8 Hz, $2H_{2'}$), 1.47 (m, $2H_{3'}$), 0.97 (t, J = 7.4 Hz, $3H_{4'}$). ^{13}C NMR ($CDCl_3$) : δ 166.60 (C_1), 132.72 (C_5), 130.53 (C_2), 129.49 (C_3), 128.26 (C_4), 64.76 ($C_{1'}$), 30.77 ($C_{2'}$), 19.25 ($C_{3'}$), 13.72 ($C_{4'}$).

Benzyl benzoate (5d). R_f = 0.60 (30 % ethyl acetate:hexane).



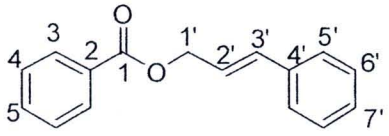
IR (neat) : $\bar{\nu}_{max}$ 3421, 3090, 3065, 3033, 2953, 2891, 1717, 1601, 1497, 1451, 1376, 1314, 1269, 1175,1110, 1026, 711 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.11 (d, J = 7.9 Hz, $2H_3$), 7.58 (t, J = 7.4 Hz, $1H_5$), 7.44 (m, $7H_{Ar}$), 5.40 (s, $2H_{1'}$). ^{13}C NMR ($CDCl_3$) : δ 166.42 (C_1), 136.12 ($C_{2'}$), 133.04 (C_5), 130.19 (C_2), 129.73 (C_3), 128.62 ($C_{4'}$), 128.40 ($C_{5'}$), 128.26 (C_4), 128.19 ($C_{3'}$), 66.70 ($C_{1'}$).

Phenethyl benzoate (5e). R_f = 0.74 (30 % ethyl acetate:hexane).



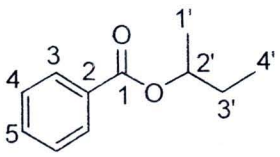
IR (neat) : $\bar{\nu}_{max}$ 3422, 3063, 3029, 2956, 1719, 1602, 1497, 1452, 1274, 1176, 1115, 1070, 1026, 749, 711 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.07 (d, J = 7.4 Hz, $2H_3$), 7.58 (t, J = 7.4 Hz, $1H_5$), 7.46 (t, J = 7.8 Hz, $2H_4$), 7.34 (m, $5H_{Ar}$), 4.58 (t, J = 7.0 Hz, $2H_{1'}$), 3.12 (t, J = 7.0 Hz, $2H_{2'}$). ^{13}C NMR ($CDCl_3$) : δ 166.51 (C_1), 137.94 ($C_{3'}$), 132.92 (C_5), 130.35 (C_2), 129.59 (C_3), 128.99 ($C_{5'}$), 128.57 (C_4), 128.37 ($C_{4'}$), 126.62 ($C_{6'}$), 65.49 ($C_{1'}$), 35.28 ($C_{2'}$).

Cinnamyl benzoate (5f). R_f = 0.64 (30 % ethyl acetate:hexane).



IR (neat) : $\bar{\nu}_{max}$ 3422, 3060, 3028, 2944, 2879, 1716, 1601, 1495, 1450, 1376, 1314, 1295, 1268, 1176, 1117, 1070, 965, 746, 711, 692 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.13 (d, J = 7.1 Hz, $2H_3$), 7.58 (t, J = 7.2 Hz, $1H_5$), 7.46 (m, $3H_{Ar}$), 7.36 (t, J = 7.2 Hz, $2H_4$), 7.29 (d, J = 7.4 Hz, $2H_{5'}$), 6.78 (d, J = 15.9 Hz, $1H_{3'}$), 6.44 (m, $1H_{2'}$), 5.02 (d, J = 6.4 Hz, $2H_{1'}$). ^{13}C NMR ($CDCl_3$) : δ 166.37 (C_1), 136.28 ($C_{4'}$), 134.29 ($C_{3'}$), 133.02 (C_5), 130.28 (C_2), 129.70 (C_3), 128.66 ($C_{6'}$), 128.42 ($C_{5'}$), 128.13 (C_4), 126.70 ($C_{7'}$), 123.32 ($C_{2'}$), 65.55 ($C_{1'}$).

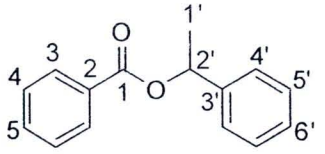
***sec*-Buthyl benzoate (5g)**. R_f = 0.60 (25 % ethyl acetate:hexane).



IR (neat) : $\bar{\nu}_{max}$ 3064, 2974, 2937, 2879, 1716, 1602, 1451, 1379, 1355,1314, 1276, 1175, 1108, 1070, 1026, 711 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.05 (d, J = 7.2 Hz, $2H_3$), 7.55 (t, J = 7.3 Hz, $1H_5$), 7.42 (t, J = 7.7 Hz, $2H_4$), 5.10 (m, $1H_{2'}$), 1.70 (m, $2H_{3'}$), 1.33 (d, J = 6.3 Hz, $3H_{1'}$), 0.97 (t, J = 7.5 Hz, $3H_{4'}$). ^{13}C NMR ($CDCl_3$) : δ

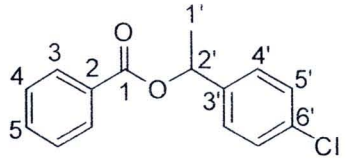
166.17 (C_1), 132.63 (C_5), 130.92 (C_2), 129.46 (C_3), 128.23 (C_4), 72.78 ($C_{2'}$), 28.93 ($C_{3'}$), 19.51 ($C_{1'}$), 9.69 ($C_{4'}$).

1-phenylethyl benzoate (**5h**). R_f = 0.68 (30 % ethyl acetate:hexane).



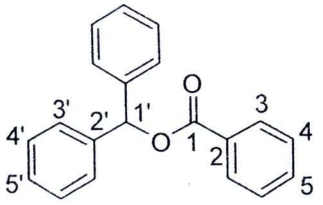
IR (neat) : $\bar{\nu}_{max}$ 3433, 3038, 2920, 2862, 1727, 1598, 1583, 1508, 1452, 1270, 1198, 1165, 1083, 1065, 1023, 875, 803, 707 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.14 (d, J = 7.5 Hz, $2H_3$), 7.58 (t, J = 7.3 Hz, $1H_5$), 7.45 (m, $7H_{Ar}$), 6.18 (q, J = 6.7 Hz, $1H_{2'}$), 1.72 (d, J = 6.6 Hz, $3H_{1'}$). ^{13}C NMR ($CDCl_3$) : δ 165.81 (C_1), 141.83 ($C_{3'}$), 132.93 (C_5), 130.58 (C_2), 129.67 (C_3), 128.58 ($C_{5'}$), 128.36 (C_4), 127.91 ($C_{6'}$), 126.07 ($C_{4'}$), 72.94 ($C_{2'}$), 22.44 ($C_{1'}$).

1-(4-chlorophenyl)ethyl benzoate (**5i**). R_f = 0.66 (30 % ethyl acetate:hexane).



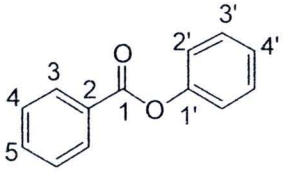
IR (neat) : $\bar{\nu}_{max}$ 3421, 3063, 2982, 2933, 1719, 1601, 1493, 1450, 1315, 1270,1175, 1109, 1094, 1069, 826, 711 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.07 (d, J = 7.2 Hz, $2H_3$), 7.56 (t, J = 7.2 Hz, $1H_5$), 7.40 (m, $6H_{Ar}$), 6.10 (q, J = 6.6 Hz, $1H_{2'}$), 1.66 (d, J = 6.6 Hz, $3H_{1'}$). ^{13}C NMR ($CDCl_3$) : δ 165.69 (C_1), 140.31 ($C_{3'}$), 133.65 ($C_{6'}$), 133.03 (C_5), 130.30 (C_2), 129.61 (C_3), 128.75 ($C_{5'}$), 128.36 (C_4), 127.47 ($C_{4'}$), 72.19 ($C_{2'}$), 22.30 ($C_{1'}$).

Benzhydryl benzoate (**5j**). mp. 86-88 °C. R_f = 0.55 (30 % ethyl acetate:hexane).



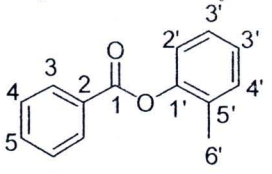
IR (KBr) : $\bar{\nu}_{max}$ 3412, 3058, 3030, 2948, 1712, 1600, 1585, 1495, 1453, 1266, 1100, 1097, 970, 759, 749, 702 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 7.58, 7.48, 7.38, 7.32 (m, $15H_{Ar}$), 7.16 (s, $1H_{1'}$). ^{13}C NMR ($CDCl_3$) : δ 165.55 (C_1), 140.29 ($C_{2'}$), 133.13 (C_5), 130.24 (C_2), 129.79 (C_3), 128.56 ($C_{4'}$), 128.44 ($C_{3'}$), 127.95 (C_4), 127.14 ($C_{5'}$), 77.43 ($C_{1'}$).

Phenyl benzoate (**7a**). mp. 67-69 °C. R_f = 0.60 (30 % ethyl acetate:hexane).



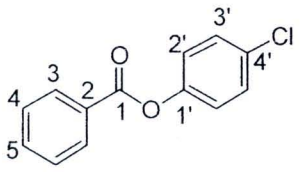
IR (KBr) : $\bar{\nu}_{max}$ 3438, 3058, 2339, 1731, 1596, 1487, 1450, 1262, 1199, 1062, 751, 704, 692 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.24 (d, J = 8.0 Hz, $2H_3$), 7.64 (t, J = 6.9 Hz, $1H_5$), 7.52 (t, J = 7.4 Hz, $2H_4$), 7.42 (t, J = 7.6 Hz, $2H_{3'}$), 7.28 (t, J = 8.1 Hz, $1H_{4'}$), 7.22 (d, J = 8.5 Hz, $2H_{2'}$). ^{13}C NMR ($CDCl_3$) : δ 165.17 (C_1), 150.96 ($C_{1'}$), 133.55 (C_5), 130.15 (C_2), 129.59 ($C_{3'}$), 129.47 (C_3), 128.55 (C_4), 125.86 ($C_{4'}$), 121.70 ($C_{2'}$).

***o*-Tolyl benzoate** (**7b**). mp. 68-70 °C. R_f = 0.72 (30 % ethyl acetate:hexane).



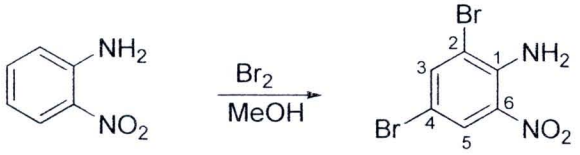
IR (KBr) : $\bar{\nu}_{max}$ 3420, 3064, 3033, 2981, 2932, 1717, 1601, 1494, 1451, 1270, 1110, 1068,1026, 761, 712, 699 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.20 (d, J = 7.6 Hz, $2H_3$), 7.64 (t, J = 7.5 Hz, $1H_5$), 7.51 (t, J = 7.7 Hz, $2H_4$), 7.24 (m, $1H_{2'}$,$1H_{4'}$), 7.10 (d, J = 8.4 Hz, $2H_{3'}$), 2.38 (s, $3H_{6'}$). ^{13}C NMR ($CDCl_3$) : δ 165.36 (C_1), 148.71 ($C_{1'}$), 135.48 ($C_{5'}$), 133.46 (C_5), 130.12 ($C_{3'}$), 129.97 (C_3), 129.69 (C_2), 128.51 (C_4), 121.34 ($C_{4'}$), 121.34 ($C_{2'}$), 20.88 ($C_{6'}$).

4-chlorophenyl benzoate (**7c**). mp. 85-87 °C. R_f = 0.75 (30 % ethyl acetate:hexane).



IR (KBr) : $\bar{\nu}_{max}$ 3063, 1734, 1490, 1450, 1285, 1219, 1061, 876, 807, 705, 685 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 8.19 (d, J = 7.5 Hz, $2H_3$), 7.65 (t, J = 7.3 Hz, $1H_5$), 7.52 (t, J = 7.8 Hz, $2H_4$), 7.40 (d, J = 8.7 Hz, $2H_{3'}$), 7.17 (d, J = 8.7 Hz, $2H_{2'}$). ^{13}C NMR ($CDCl_3$) : δ 164.92 (C_1), 149.41 ($C_{1'}$), 133.76 (C_5), 131.26 ($C_{4'}$), 130.17 ($C_{3'}$), 129.52 (C_3), 129.18 (C_2), 128.61 (C_4), 123.08 ($C_{2'}$).

6. Preparation of 2,4-dibromo-6-nitroaniline (9a)

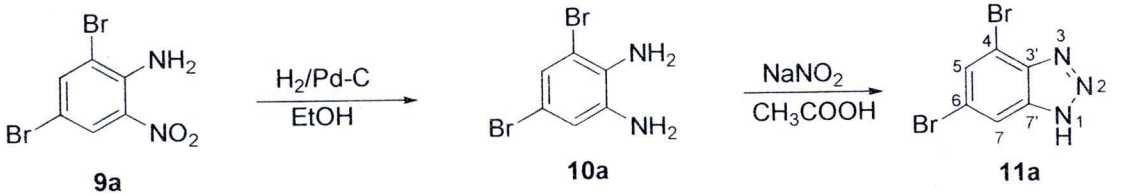


9a

To a solution of *o*-nitroaniline (1.1 g, 8.0 mmol) in methanol (12.0 ml) was slowly added bromine (1.1 ml, 19.0 mmol). The mixture was stirred for 30 minutes at room temperature. The reaction mixture was poured into the ice cold water. The yellow solid precipitates were collected by vacuum filtration and washed with cold water. The residue was purified by recrystallization from 10% dichloromethane: hexane to afford 2,4-dibromo-6-nitroaniline (**9a**) as an orange crystalline solid (2.1 g, 7 mmol, 92%).

2,4-dibromo-6-nitroaniline (**9a**). mp. 114-116 °C (lit.mp 129-133 °C)[57] R_f = 0.52 (25 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3564, 3465, 3353, 3085, 1767, 1625, 1579, 1542, 1495, 1445, 1386, 1345, 1317, 1255, 1118, 1097, 888, 874, 833, 761, 724, 691, 594, 543 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 8.25 (s, $1H_3$), 7.80 (s, $1H_5$), 6.60 (brs, NH_2). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 141.27 (C_1), 140.80 (C_5), 132.90 (C_2), 128.19 (C_3), 112.73 (C_6), 106.87 (C_4).

7. Preparation of 4,6-dibromo-1*H*-benzo[*d*][1,2,3]triazole (11a)

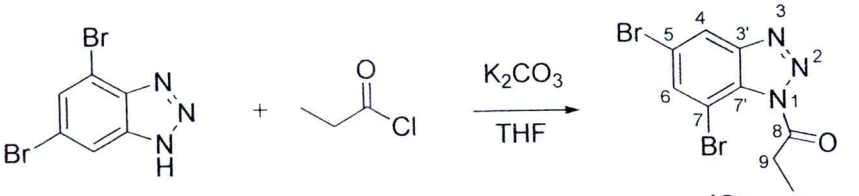


9a **10a** **11a**

To a solution of 2,4-dibromo-6-nitroaniline (**9**, 1.1 g, 4.0 mmol) in ethanol (15.0 mL) was added a catalytic amount of palladium on activated charcoal (60.0 mg). The solution was stirred under hydrogen gas atmosphere at the balloon pressure at room temperature for 24 h. The mixture was filtered and evaporated to dryness under reduced pressure and the residue was dissolved in glacial acetic acid (5.0 ml) and cooled to 15 °C. To this stirred solution was added a solution of sodium nitrite (0.3 g, 4.0 mmol) in water (5.0 ml). Stirring was continued for 15 minutes and then the mixture was chilled in an ice-water bath for 30 minutes. The brown precipitates were collected by vacuum filtration and washed with cold water. Highly colored crude product was purified by repeated recrystallization from ethyl acetate using activated charcoal as a decolorizing agent. 4,6-Dibromo-1*H*-benzo[*d*][1,2,3]triazole (**11a**) was obtained as fine white needles (0.7 g, 2.0 mmol, 68%).

4,6-dibromo-1*H*-benzo[*d*][1,2,3]triazole (11a). mp. 268–270 °C R_f = 0.43 (30 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3435, 3086, 3013, 2935, 2857, 2759, 1618, 1578, 1502, 1416, 1390, 1262, 1241, 1188, 1063, 1027, 963, 853, 729, 607, 587 cm^{-1}. ^1H NMR (400 MHz;$DMSO_{d-6}$) : δ 8.10 (s, $1H_7$), 7.80 (s, $1H_5$). ^{13}C NMR (100 MHz; $DMSO_{d-6}$) : δ 140.35 ($C_{7'}$), 138.93 ($C_{3'}$), 130.38 (C_5), 119.49 (C_7), 116.45 (C_6), 110.47 (C_4).

8. Preparation of 1-(5,7-dibromo-1*H*-benzo[*d*][1,2,3]triazol-1-yl)propan-1-one (12a)

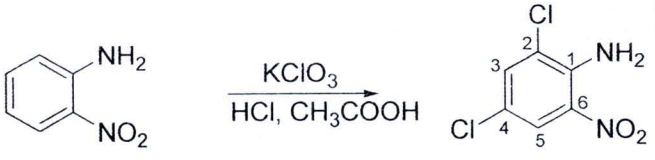


11a **12a**

To a stirred mixture of 4,6-dibromo-1*H*-benzo[*d*][1,2,3]triazole (**11a**, 0.5 g, 2.0 mmol) and anhydrous potassium carbonate (0.4 g, 3.0 mmol) in tetrahydrofuran (5.0 ml) was slowly added propionyl chloride (1.7 ml, 2.0 mmol). The mixture was refluxed for 30 minutes and filtered under reduced pressure through a celite pad. The filtrate was evaporated using a rota-vaporator to dryness and the residue was purified by recrystallization from hexane to afford 1-(5,7-dibromo-1*H*-benzo[*d*][1,2,3]triazol-1-yl)propan-1-one (**12a**) as a white crystalline solid (0.6 g, 2.0 mmol, 96%).

1-(5,7-dibromo-1*H*-benzo[*d*][1,2,3]triazol-1-yl)propan-1-one (12a). mp.136-138 °C R_f = 0.52 (25 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3458, 3100, 3075, 2983, 2941, 1740, 1597, 1575, 1449, 1413, 1301, 1167, 1098, 1058, 1005, 958, 862 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 8.46 (s, $1H_4$), 7.82 (s, $1H_6$), 3.45 (q, J = 7.4 Hz, $2H_9$), 1.41 (t, J = 7.4 Hz, $3H_{10}$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 172.97 (C_8), 144.29 ($C_{3'}$), 132.71 ($C_{7'}$), 132.29 (C_6), 125.11 (C_5), 116.53 (C_4), 114.25 (C_7), 29.19 (C_9), 8.19 (C_{10}).

9. Preparation of 2,4-dichloro-6-nitroaniline (9b)



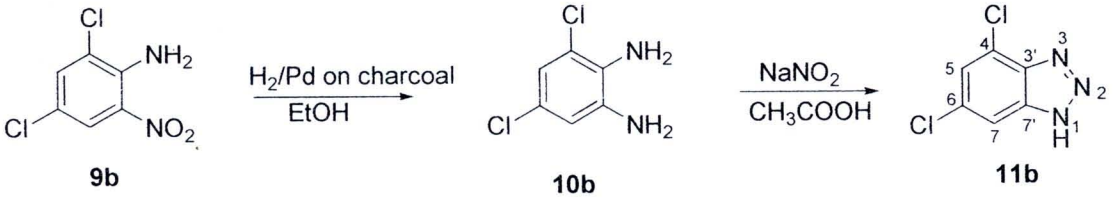
9b

To a solution of *o*-nitroaniline (1.2 g, 9.0 mmol) in glacial acetic acid (10.0 ml) was added potassium chlorate (0.7 g, 6.0 mmol) at room temperature. The solution was slowly added conc. hydrochloric (2.5 ml, 29.0 mmol) and was stirred at room temperature for 30 minutes. The reaction mixture was poured into ice cold water and the yellow solid precipitates were collected by vacuum filtration and washed with cold water. The residue was purified by recrystallization from 10% dichloromethane: hexane to afford 2,4-dichloro-6-nitroaniline (**9b**) as a yellow crystalline solid (1.53 g, 7.4 mmol, 85 %).

2,4-dichloro-6-nitroaniline (9b). mp. 105 - 106 °C (lit.mp 101-103 °C)[58] R_f = 0.78 (30 % ethyl acetate:hexane). IR (KBr): $\bar{\nu}_{max}$ 3473, 3060, 3086, 2703, 2340, 1766, 1633, 1549, 1503, 1452, 1394, 1352, 1320, 1255, 1227, 1141, 1084, 899, 875, 849,

757, 728, 553 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 8.10 (d, J = 2.4 Hz, $1H_5$), 7.54 (d, J = 2.4 Hz, $1H_3$), 6.55 (brs, NH_2). ^{13}C NMR (100 MHz; $CDCl_3$) : δ 140.20 (C_1), 135.13 (C_5), 132.68 (C_2), 124.53 (C_3), 122.69 (C_6), 120.36 (C_4).

10. Preparation of 4,6-dichloro-1*H*-benzo[*d*][1,2,3]triazole (11b)

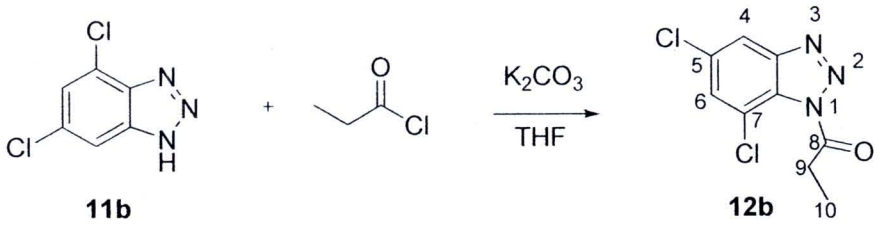


9b **10b** **11b**

To a solution of 2,4-dichloro-6-nitroaniline (**9b**, 1.2 g, 6.0 mmol) in ethanol (15.0 mL) was added a catalytic amount of palladium on activated charcoal (60.0 mg) under hydrogen gas atmosphere at the balloon pressure at room temperature for 24 h. The mixture was filtered and evaporated to dryness under reduced pressure and the residue was dissolved in glacial acetic acid (5.0 ml) and cooled to 15 °C. To this stirred solution was added a solution of sodium nitrite (0.5 g, 7.0 mmol) in water (10.0 ml). Stirring was continued for 15 minutes and then the mixture was chilled in an ice-water bath for 30 minutes. The brown precipitates were collected by vacuum filtration and washed with cold water. Highly colored crude product was purified by repeated recrystallization from ethyl acetate using activated charcoal as a decolorizing agent. 4,6-Dichloro-1*H*-benzo[*d*][1,2,3]triazole (**11b**) was obtained as fine white needles (0.8 g, 4 mmol, 75%).

4,6-dichloro-1*H*-benzo[*d*][1,2,3]triazole (11b) mp. 220 - 221 °C R_f = 0.31 (50 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3436, 3080, 3020, 2950, 2862, 2762, 2719, 2675, 2593, 2510, 2412, 1613, 1585, 1503, 1420, 1395, 1281, 1239, 1187, 1071, 1033, 984, 865, 850, 773, 624, 592 cm^{-1}. ^1H NMR (400 MHz;$DMSO_{d\text{-}6}$) : δ 7.82 (s, $1H_7$), 7.50 (s, $1H_5$). ^{13}C NMR (100 MHz;$DMSO_{d\text{-}6}$) : δ 140.05 ($C_{7'}$), 139.13 ($C_{3'}$), 133.44 (C_5), 126.66 (C_7), 123.48 (C_6), 113.44 (C_4).

11. Preparation of 1-(5,7-dichloro-1*H*-benzo[*d*][1,2,3]triazol-1-yl)propan-1-one (12b)

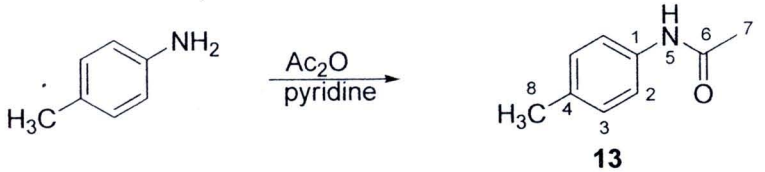


11b **12b**

To a stirred mixture of 4,6-dichloro-1*H*-benzo[*d*][1,2,3]triazole (**11b**, 1.2 g, 6.0 mmol) and anhydrous potassium carbonate (0.5 g, 8.0 mmol) in tetrahydrofuran (15.0 ml) was slowly added propionyl chloride (1.2 ml, 8.0 mmol). The mixture was refluxed for 30 minutes and filtered under reduced pressure through a celite pad. The filtrate was evaporated using a rota-vaporator to dryness and the residue was purified by recrystallization from 30% ethyl acetate/hexane to afford 1-(5,7-dichloro-1*H*-benzo[*d*][1,2,3]triazol-1-yl)propan-1-one (**12b**) as a white crystalline solid (1.5 g, 6.0 mmol, 96%).

1-(5,7-dichloro-1*H*-benzo[*d*][1,2,3]triazol-1-yl)propan-1-one (12b) mp. 125-126 °C R_f = 0.64 (50 % ethyl acetate:hexane) IR (KBr): $\bar{\nu}_{max}$ 3464, 3106, 3084, 2985, 2944, 1740, 1599, 1583, 1457, 1415, 1379, 1303, 1181, 1099, 1064, 1008, 968, 956, 862, 773, 725 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 8.23 (s, $1H_4$), 7.50 (s, $1H_6$), 3.45 (q, J = 7.4 Hz, $2H_{10}$), 1.42 (t, J = 7.4 Hz, $3H_9$). ^{13}C NMR (100 MHz; $CDCl_3$) : δ 172.93 (C_8), 142.60 ($C_{3'}$), 137.16 (C_7), 132.70 ($C_{7'}$), 126.89 (C_6), 126.37 (C_5), 113.06 (C_4), 29.21 (C_9), 8.21 (C_{10}).

12. Preparation of *N*-*p*-tolylacetamide (13)



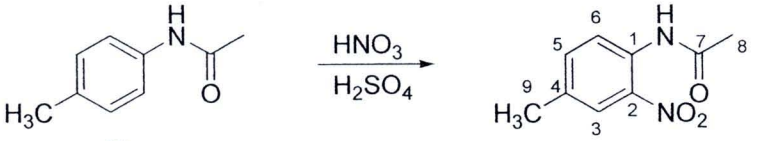
13

To a solution of *p*-toluidine (4.9 g, 46.0 mmol) in pyridine (30.0 mL) was added acetic anhydride (5.0 mL, 50.0 mmol), the reaction mixture was refluxed for 30 minutes. The resulting mixture was cooled to room temperature, and then poured into ice water (150.0 mL). The white solid precipitates were collected by vacuum filtration and washed with cold water. The residue was purified by recrystallization from 20 %

dichloromethane:hexane to afford *N*-*p*-tolylacetamide (**13**) as a white crystalline solid (5.4 g, 26.0 mmol, 96%).

***N*-*p*-tolylacetamide (13)**. R_f = 0.32 (50 % ethyl acetate:hexane) mp. 124-126 °C (lit.mp 150 °C)[59] IR (KBr) : $\bar{\nu}_{max}$ 3290, 3187, 3122, 3066, 2965, 2943, 2865, 2798, 1900, 1654, 1515, 1402, 1364, 1321, 1264, 1040, 1013, 819, 751, 605, 504 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 9.10 (brs, $1H_6$), 7.52 (d, J = 8.4 Hz, $2H_4$), 7.08 (d, J = 8.4 Hz, $2H_3$), 3.00 (s, $3H_1$), 2.25 (s, $3H_8$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 167.89 (C_7), 137.10 (C_2), 132.30 (C_5), 128.97 (C_3), 119.14 (C_4), 23.30 (C_8), 19.90 (C_1).

13. Preparation of *N*-(4-methyl-2-nitrophenyl)acetamide (14)

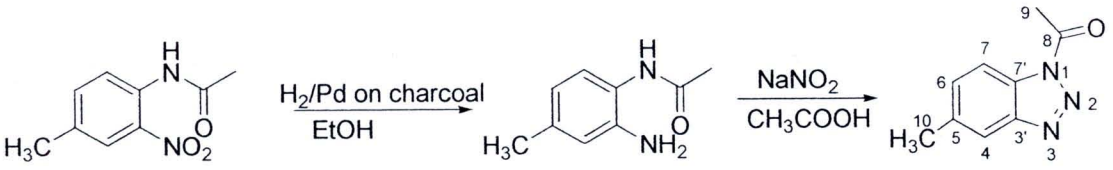


13 **14**

A solution of *N*-*p*-tolylacetamide (**1d**, 2.3 g, 15.0 mmol) in a mixture of nitric acid, sulfuric acid and acetic acid (2:2:3, 7.0 mL) at 0 °C was stirred and warmed up to 15 °C for 15 minutes. The reaction mixture was poured into ice cold 100.0 mL. of water The yellow solid precipitates were collected by vacuum filtration and washed with ice cold water. The residue was purified by repeated recrystallization from water. *N*-(4-methyl-2-nitrophenyl)acetamide (**2d**) was obtained as fine yellow needle crystals (2.5 g, 13 mmol, 84%).

***N*-(4-methyl-2-nitrophenyl)acetamide (2d)**. mp. 89-91 °C R_f = 0.72 (50 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3382, 3359, 2925, 1719, 1709, 1577, 1525, 1444, 1371, 1342, 1276, 1229, 1149, 1082, 1045, 1002, 913, 826, 794, 758, 588, 529 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 10.20 (brs, $1H_8$), 8.62 (d, J = 8.6 Hz, $1H_6$), 8.00 (s, $1H_3$), 7.44 (d, J = 8.6 Hz, $1H_7$), 2.38 (s, $3H_1$), 2.25 (s, $3H_{10}$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 168.87 (C_9), 136.79 (C_7), 136.23 (C_4), 133.46 (C_2), 132.41 (C_5), 125.44 (C_3), 122.14 (C_6), 25.51 (C_{10}), 20.50 (C_1).

14. Preparation of 1-(5-methyl-1*H*-benzo[*d*][1,2,3]triazol-1-yl)ethanone (16)

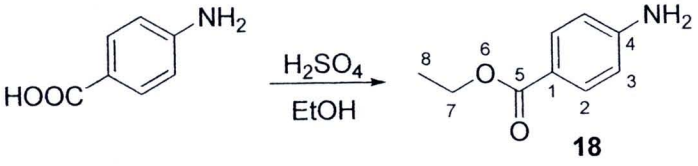


14 **15** **16**

To a solution of *N*-(4-methyl-2-nitrophenyl)acetamide (**14**, 2.3 g, 12.0 mmol) in ethanol (15.0 mL) was added a catalytic amount of palladium on activated charcoal (100.0 mg). The solution was stirred under hydrogen gas atmosphere at the balloon pressure at room temperature for 24 h. The mixture was filtered and evaporated to dryness under reduced pressure and the residue was dissolved in glacial acetic acid (5.0 ml) and cooled to 15 °C. To this stirred solution was added a solution of sodium nitrite (1.0 g, 14.8 mmol) in water (10.0 ml). Stirring was continued for 15 minutes and then the mixture was chilled in an ice-water bath for 30 minutes. The brown precipitates were collected by vacuum filtration and washed with cold water. Highly colored crude product was purified by repeated recrystallization from ethyl acetate using activated charcoal as a decolorizing agent. 1-(5-Methyl-1*H*-benzo[*d*][1,2,3]triazol-1-yl)ethanone (**16**) was obtained as fine white needles (1.6 g, 9.0 mmol, 75%).

1-(5-methyl-1*H*-benzo[*d*][1,2,3]triazol-1-yl)ethanone (16) mp. 115 - 117 °C R_f = 0.70 (30% ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3450, 3071, 2921, 1736, 1592, 1493, 1425, 1382, 1353, 1332, 1316, 1281, 1238, 1210, 1135, 1082, 1035, 950, 935, 841, 817, 639, 598, 563 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 8.13 (d, J = 8.4 Hz, $1H_7$), 7.86 (s, $1H_4$), 7.46 (d, J = 8.4 Hz, $1H_6$), 2.97 (s, $3H_{10}$), 2.53 (s, $3H_8$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 169.43 (C_9), 146.80 ($C_{3'}$), 136.34 (C_5), 132.15 (C_7), 129.29 ($C_{7'}$), 119.22 (C_6), 113.73 (C_4), 23.06 (C_8), 21.40 (C_{10}).

15. Preparation of ethyl 4-aminobenzoate (18)

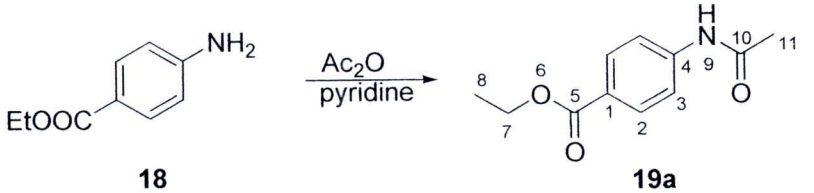


18

To a solution of *p*-aminobenzoic acid (4.9 g, 36.0 mmol) in absolute ethanol (30.0 ml) at room temperature was added dropwise conc. sulfuric (2.5 mL). The solution was refluxed for 30 minutes and was cooled to room temperature. The solution was basified with 2 M sodium hydrogencarbonate and extracted with dichloromethane (15.0 mL x3). The organic layer was dried over anhydrous sodium sulphate. After evaporation of solvent, the crude product was purified by recrystallization from 20% dichloromethane:hexane to afford ethyl-4-aminobenzoate (**18**) as a white crystalline solid (5.8 g, 35.0 mmol, 98%).

Ethyl-4-aminobenzoate (18). mp. 88-89 °C (lit.mp.90-93 °C)[60] R_f = 0.62 (30 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3423, 3343, 3223, 2983, 2899, 1685, 1635, 1597, 1514, 1474, 1441, 1367, 1311, 1281, 1172, 1125, 1110, 1025, 846, 773, 701, 615, 504 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 7.85 (d, J = 8.6 Hz, $2H_2$), 6.63 (d, J = 8.6 Hz, $2H_3$), 4.31 (q, J = 7.1 Hz, $2H_7$), 4.05 (brs, NH_2), 1.35 (t, J = 7.1 Hz, $3H_8$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 166.67 (C_5), 150.70 (C_4), 131.52 (C_2), 120.11 (C_1), 113.75 (C_3), 60.28 (C_7), 14.40 (C_8).

16. Preparation of ethyl 4-acetamidobenzoate (19a)

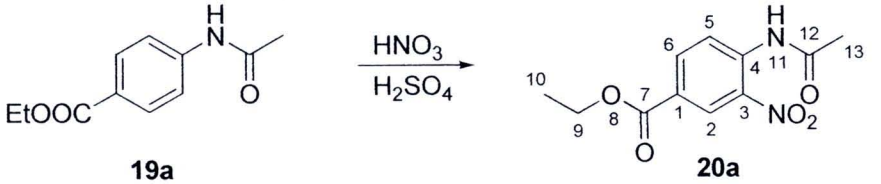


18 **19a**

To a solution of ethyl-4-aminobenzoate (**18**, 4.5 g, 27.0 mmol) in pyridine (30.0 mL) was added acetic anhydride (3.0 mL, 30.0 mmol). The reaction mixture was refluxed for 30 minutes and cooled to room temperature, and then poured into the ice water. The white solid precipitates were collected by vacuum filtration and washed with cold water. The residue was purified by recrystallization from 20% dichloromethane:hexane to afford ethyl-4-acetamidobenzoate (**19a**) as a white crystalline solid (5.4 g, 26.0 mmol, 96%).

Ethyl-4-acetamidobenzoate (19a). mp. 99-100 °C R_f = 0.50 (30 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3334, 3200, 3110, 2996, 2984, 2908, 2318, 1706, 1682, 1607, 1595, 1525, 1402, 1371, 1320, 1304, 1278, 1254, 1232, 1172, 1133, 1111, 1019, 867, 776, 713, 694, 600, 574, 519, 505 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 7.98 (d, J = 8.7 Hz, $2H_2$), 7.60 (d, J = 7.4 Hz, $2H_3$), 4.35 (q, J = 7.1 Hz, $2H_7$), 2.20 (s, $3H_{11}$), 1.37 (t, J = 7.1 Hz, $3H_8$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 168.82 (C_{10}), 166.24 (C_5), 142.17 (C_4), 130.71 (C_2), 125.81 (C_1), 118.79 (C_3), 60.89 (C_7), 24.67 (C_8), 14.31 (C_{11}).

17. Preparation of ethyl-4-acetamido-3-nitrobenzoate (20a)

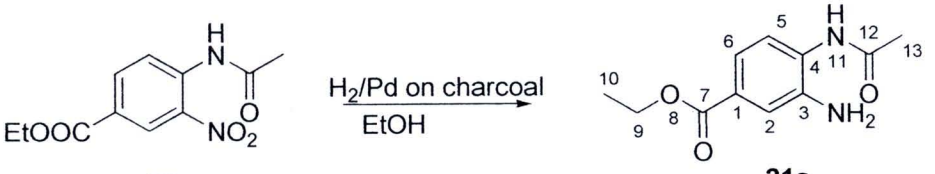


19a **20a**

A solution of ethyl-4-acetamidobenzoate (**19a**, 1.0 mg, 5.0 mmol) in a mixture of nitric acid and sulfuric acid (1:2, 3.0 mL) at 0 °C was stirred and allowed to warm up to room temperature in 15 minutes. The reaction mixture was poured into ice cold water and the yellow solid precipitates were collected by vacuum filtration and washed with ice cold water. Highly colored crude product was purified by repeated recrystallization from water. Ethyl 4-acetamido-3-nitrobenzoate (**20a**) was obtained as fine yellow needle crystals (1.1 g, 4.0 mmol, 84%).

Ethyl-4-acetamido-3-nitrobenzoate (20a) mp. 95-96 °C R_f = 0.72 (50 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3358, 2991, 1717, 1620, 1581, 1512, 1460, 1365, 1340, 1297, 1261, 1224, 1160, 1139, 1115, 1024, 925, 855, 756, 718, 672, 596, 527 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 10.50 (s, $1H_{11}$), 8.90 (d, J = 8.9 Hz, $1H_6$), 8.87 (s, $1H_2$), 8.26 (d, J = 8.9 Hz, $1H_5$), 4.40 (q, J = 7.1 Hz, $2H_9$), 2.31 (s, $3H_{13}$), 1.41 (t, J = 7.1 Hz, $3H_{10}$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 169.07 (C_{12}), 164.14 (C_7), 138.14 (C_3), 136.45 (C_2), 135.54 (C_4), 127.40 (C_6), 125.32 (C_1), 121.59 (C_5), 61.70 (C_9), 25.74 (C_{13}), 14.27 (C_{10}).

18. Preparation of ethyl-4-acetamido-3-aminobenzoate (21a)

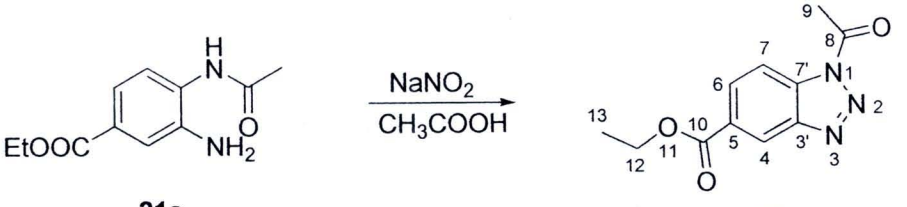


20a **21a**

To a solution of ethyl-4-acetamido-3-nitrobenzoate (**20a**, 1.8 g, 7.0 mmol) in ethanol (15.0 mL) was added a catalytic amount of palladium on activated charcoal (80.0 mg). The solution was stirred under hydrogen gas atmosphere at the balloon pressure at room temperature for 24 h. The mixture was filtered and evaporated under reduced pressure and the residue was purified by recrystallization from hexane to afford ethyl-4-acetamido-3-aminobenzoate (**21a**) as a white crystalline solid (1.43 g, 6.0 mmol, 90%).

Ethyl-4-acetamido-3-aminobenzoate (**21a**). mp. 142-143 °C R_f = 0.18 (50 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3422, 3356, 3278, 2982, 2905, 1709, 1656, 1643, 1607, 1594, 1523, 1477, 1435, 1374, 1309, 1265, 1250, 1220, 1157, 1126, 1080, 1019, 951, 908, 763, 729 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 7.48 (s, $1H_6$), 7.48 (s, $1H_2$), 7.48 (s, $1H_{11}$), 7.40 (d, J = 8.5 Hz, $1H_5$), 4.35 (q, J = 7.1 Hz, $2H_9$), 3.85 (s, NH_2), 2.20 (s, $3H_{13}$), 1.37 (t, J = 7.1 Hz, $3H_{10}$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 169.12 (C_{12}), 166.34 (C_7), 139.57 (C_3), 129.02 (C_4), 128.41 (C_1), 124.14 (C_5), 121.04 (C_6), 119.32 (C_2), 60.97 (C_9), 23.87 (C_{13}), 14.31 (C_{10}).

19. Preparation of ethyl 1-acetyl-1H-benzo[*d*][1,2,3]triazole-5-carboxylate (22a)



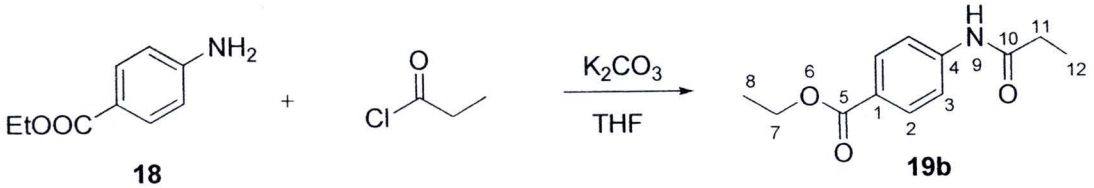
21a **22a**

To a stirred cooled solution (15°C) of ethyl-4-acetamido-3-aminobenzoate (**21a**, 1.1 g, 5.0 mmol) in glacial acetic acid (5.0 ml) was added a solution of sodium nitrite (0.4 g, 6.0 mmol) in water (5.0 ml). Stirring was continued for 15 minutes until the temperature reached 35-40 °C and then chilled in an ice-water bath for 30

minutes. The pale brown precipitates were collected by vacuum filtration and washed with ice-cold water. Highly colored crude product was purified by repeated recrystallization from water using activated charcoal as a decolorizing agent. Ethyl-1-acetyl-1*H*-benzo[*d*][1,2,3]triazole-5-carboxylate (**22a**) was obtained as fine white needles (0.9 g, 4.0 mmol, 81%).

Ethyl-1-acetyl-1*H*-benzo[*d*][1,2,3]triazole-5-carboxylate (22a). mp. 105-107 °C R_f = 0.68 (50 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3473, 3399, 3131, 3064, 2976, 2930, 1746, 1708, 1614, 1593, 1477, 1429, 1379, 1291, 1209, 1181, 1129, 1088, 1066, 1018, 951, 937, 873, 845, 795, 772, 758, 719, 632, 560, 522 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 8.80 (s, $1H_4$), 8.30 (d, J = 8.6 Hz, $1H_6$), 8.30 (d, J = 8.6 Hz, $1H_7$), 4.46 (q, J = 7.1 Hz, $2H_{12}$), 3.02 (s, $3H_9$), 1.45 (t, J = 7.1 Hz, $3H_{13}$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 169.39 (C_8), 165.40 (C_{10}), 146.19 ($C_{3'}$), 133.32 ($C_{7'}$), 131.24 (C_6), 128.90 (C_5), 122.49 (C_7), 114.20 (C_4), 61.66 (C_{12}), 23.24 (C_9), 14.34 (C_{13}).

20. Preparation of ethyl 4-propionamidobenzoate (19b)



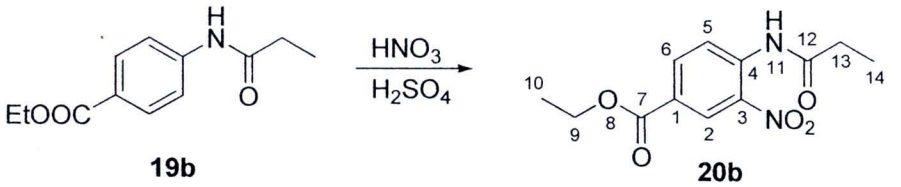
18 **19b**

To a stirred mixture of ethyl 4-aminobenzoate (**18**, 4.8 g, 29.0 mmol) and anhydrous potassium carbonate (4.3 g, 31.0 mmol) in tetrahydrofuran (30.0 ml) was slowly added propionyl chloride (3.5 ml, 30.0 mmol) and the reaction mixture was refluxed for 30 minutes. After cooling to room temperature, the mixture was filtered under reduced pressure through a celite pad. The filtrate was evaporated using a rota-vaporator to dryness and the residue was purified by recrystallization from 10% ethyl acetate:hexane to afford ethyl 4-propionamidobenzoate (**19b**) as a white crystalline solid (5.4 g, 24.0 mmol, 84%).

Ethyl 4-propionamidobenzoate (19b). mp. 100-102 °C R_f = 0.55 (30 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3311, 3202, 3126, 3065, 2989, 2971, 2940, 2905, 1717, 1690, 1672, 1599, 1539, 1409, 1375, 1361, 1304, 1270, 1251, 1171, 1123, 1107, 1022, 852, 766, 735, 693, 502 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 7.98 (d, J = 8.7

Hz, $2H_2$), 7.64 (d, J = 8.6 Hz, $2H_3$), 4.36 (q, J = 7.1 Hz, $2H_7$), 2.43 (q, J = 7.5, $2H_{11}$), 1.39 (t, J = 7.5 Hz, $3H_8$), 1.29 (t, J = 7.5 Hz, $3H_{12}$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 172.68 (C_{10}), 166.33 (C_5), 142.38 (C_4), 130.73 (C_2), 125.70 (C_1), 118.86 (C_3), 60.92 (C_7), 30.78 (C_8), 14.35 (C_{11}), 9.55 (C_{12}).

21. Preparation of ethyl 3-nitro-4-propionamidobenzoate (20b)

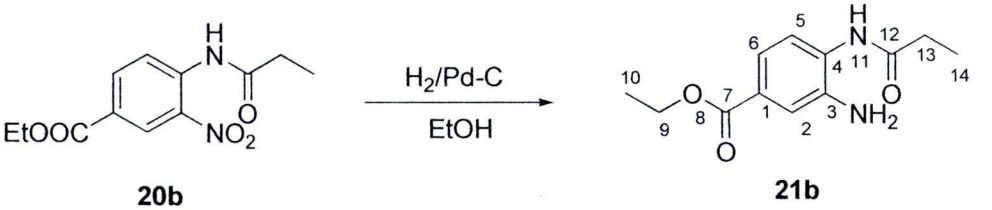


19b **20b**

A solution of ethyl-4-acetamidobenzoate (**19b**, 1.1 g, 5.0 mmol) in a mixture of nitric acid and sulfuric acid (1:2, 3.0 mL) at 0 °C was stirred and allowed to warm to room temperature in 15 minutes. The reaction mixture was poured into ice cold water and the yellow solid precipitates were collected by vacuum filtration and washed with ice-cold water. Highly colored crude product was purified by repeated recrystallization from water. Ethyl 4-acetamido-3-nitrobenzoate (**20b**) was obtained as fine yellow needle crystals (1.1 g, 5.0 mmol, 86%).

Ethyl 3-nitro-4-propionamidobenzoate (20b). mp. 95-96 °C R_f = 0.72 (30 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3368, 2983, 2939, 1707, 1622, 1581, 1516, 1462, 1366, 1341, 1283, 1220, 1172, 1149, 1123, 1018, 925, 860, 757, 702, 660, 526, 498 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 10.52 (s, $1H_{11}$), 8.94 (d, J = 8.9 Hz, $1H_6$), 8.88 (d, J = 2.0, $1H_2$), 8.27 (dd, J = 8.9, 2.0 Hz, $1H_5$), 4.42 (q, J = 7.1 Hz, $2H_9$), 2.57 (q, J = 7.5, $2H_{13}$), 1.42 (t, J = 7.1 Hz, $3H_{10}$), 1.30 (t, J = 7.5 Hz, $3H_{14}$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 172.93 (C_{12}), 164.22 (C_7), 138.35 (C_3), 136.49 (C_2), 135.53 (C_4), 127.47 (C_6), 125.19 (C_1), 121.64 (C_5), 61.73 (C_9), 31.86 (C_{13}), 14.31 (C_{10}), 9.21 (C_{14}).

22. Preparation of ethyl 3-amino-4-propionamidobenzoate (21b)

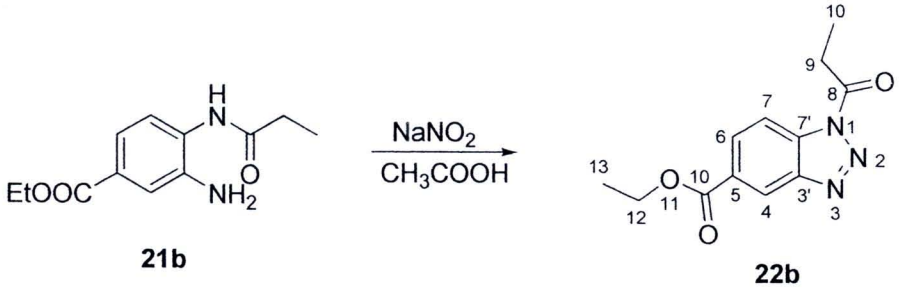


20b **21b**

To a solution of ethyl-4-acetamido-3-nitrobenzoate (**20b**, 2.2 g, 8.0 mmol) in ethanol (15.0 mL) was added a catalytic amount of palladium on activated charcoal (100.0 mg). The solution was stirred with hydrogen gas at room temperature for 24 h. The mixture was filtered and evaporated under reduced pressure and the residue was purified by recrystallization from 20% tetrahydrofuran:H_2O to afford ethyl 3-amino-4-propionamidobenzoate (**21b**) as a white crystalline solid (1.8 g, 8.0 mmol, 93%).

Ethyl 3-amino-4-propionamidobenzoate (21b). mp. 140-141 °C R_f = 0.12 (50 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3415, 3357, 3281, 2974, 2936, 1712, 1651, 1608, 1592, 1525, 1439, 1365, 1303, 1266, 1224, 1127, 1084, 1069, 1028, 954, 930, 907, 763 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 7.53 (s, $1H_6$), 7.53 (s, $1H_2$), 7.53 (s, $1H_{11}$), 7.42 (d, J = 8.5 Hz, $1H_5$), 4.35 (q, J = 7.1 Hz, $2H_9$), 3.85 (s, NH_2), 2.22 (q, J = 7.5, $3H_{13}$), 1.40 (t, J = 7.1 Hz, $3H_{10}$), 1.25 (t, J = 7.5, $3H_{14}$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 172.45 (C_{12}), 166.29 (C_7), 139.10 (C_3), 129.52 (C_4), 128.26 (C_1), 123.66 (C_5), 121.54 (C_6), 119.79 (C_2), 60.95 (C_9), 30.30 (C_{13}), 14.33 (C_{10}), 9.75 (C_{14}).

23. Preparation of ethyl 1-propionyl-1*H*-benzo[*d*][1,2,3]triazole-5-carboxylate (22b)



21b **22b**

To a stirred cooled solution (15°C) of ethyl 3-amino-4-propionamidobenzoate (**21b**, 1.5 g, 6.0 mmol) in glacial acetic acid (8.0 ml) was added a solution of sodium nitrite (0.5 g, 8.0 mmol) in water (5.0 ml). Stirring was continued for 15 minutes until the temperature reached 35-40 °C and the mixture was then chilled in an ice-water bath for 30 minutes. The pale brown precipitates were collected by vacuum filtration and washed with ice-cold water. Highly colored crude product was purified by repeated recrystallization from 10 % ethyl acetate:hexane. Ethyl-1-propionyl-1*H*-benzo[*d*][1,2,3]triazole-5-carboxylate (**22b**) was obtained as fine white needles (1.3 g, 5.0 mmol, 80%).

Ethyl 1-propionyl-1*H*-benzo[*d*][1,2,3]triazole-5-carboxylate (22b). mp. 122-123 °C R_f = 0.60 (30 % ethyl acetate:hexane) IR (KBr) : $\bar{\nu}_{max}$ 3474, 3395, 3130, 3066, 2983, 2943, 2879, 1745, 1708, 1614, 1591, 1474, 1382, 1375, 1289, 1187, 1123, 1086, 1061, 1022, 999, 953, 934, 847, 795, 772, 758, 735, 685, 596, 527 cm^{-1}. ^1H NMR (400 MHz;$CDCl_3$) : δ 8.81 (s, $1H_4$), 8.38 (d, J = 8.6 Hz, $1H_6$), 8.38 (d, J = 8.6 Hz, $1H_7$), 4.42 (q, J = 7.1 Hz, $2H_{12}$), 3.43 (q, J = 7.5, $2H_9$), 1.43 (t, J = 7.1 Hz, $3H_{13}$), 1.43 (t, J = 7.5 Hz, $3H_{10}$). ^{13}C NMR (100 MHz;$CDCl_3$) : δ 173.16 (C_8), 165.51 (C_{11}), 146.09 ($C_{3'}$), 133.48 ($C_{7'}$), 131.23 (C_6), 128.84 (C_5), 122.52 (C_7), 114.23 (C_4), 61.66 (C_{12}), 29.20 (C_9), 14.33 (C_{13}), 8.28 (C_{10}).