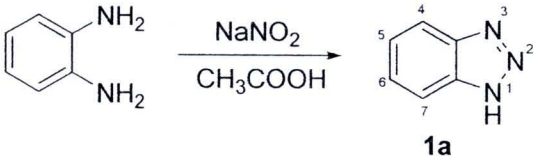
CHAPTER II
RESULTS AND DISCUSSION

N-Acylbenzotriazoles could be synthesized by several methods either directly by reacting benzotriazole itself with acyl chlorides [46,47] or indirectly by using previously activated benzotriazoles to react with acyl chlorides or carboxylic acids.[48-50] Apparently, in the search for a simple, convenient and high yielding method for the synthesis of *N*-acylbenzotriazoles, it became clear that fusing an equimolar mixture of benzotriazole and the respective acid chloride at 80-100 °C seemed to be the method of choice.[32] Unfortunately, benzotriazole could not be purchased from any sources throughout Thailand due to a strict transportation regulation. To overcome this difficulty, we had to prepare benzotriazole by a well established method as indicated in Vogel's Textbook of Practical Organic Chemistry.[51] Thus, treatment of *o*-phenylenediamine with sodium nitrite in glacial acetic acid gave crude benzotriazole as highly colored precipitates which were further treated with activated charcoal and subjected to repeated recrystallization using water as a solvent to finally give pure benzotriazole as white fine needles in 67 % yield as shown in Figure 2.1.



1a

Figure 2.1 Preparation of benzotriazole

The IR spectrum of benzotriazole (**1a**) showed a broad N-H stretching at $\bar{\nu}_{max}$ 3254 cm^{-1}. The aromatic C-H stretching appeared at $\bar{\nu}_{max}$ 3080 and 3030 cm^{-1}. The C-N stretching appeared as a strong band at $\bar{\nu}_{max}$ 1210 cm^{-1}. The C-H out of plane bending of the aromatic ring showed up at $\bar{\nu}_{max}$ 752 and 741 cm^{-1}.The ^1H NMR spectrum showed aromatic proton H_4 and H_7 resonances as a compact doublet at δ 7.94 (J = 6.2 Hz, 2H) ppm and H_5 and H_6 resonances as a doublet at 7.49 (J = 6.2 Hz, 2H) ppm. The ^{13}C NMR spectrum showed only three resonances of aromatic carbon

atoms at δ 138.65, 126.23 and 114.94 ppm. All the physical data are in well agreement with those reported in the literature[51] which confirmed that **1a** is the required target compound.

Having a quantity of **1a** in hand, treatment of **1a** with propionyl chloride without any solvent according to Katrizky's protocol[32] gave *N*-propanoyl benzotriazole (**2a**) in modest yield. Later it was found that large excess of acid chloride had to be employed in order to drive the reaction to completion. With the concept of atom economy in mind, we were finally able to prepare *N*-acylbenzotriazole in excellent yields by using only slight excess of either aliphatic or aromatic acid chloride in a milder condition. This procedure involved heating under reflux a mixture of **1a** and a slight excess of acid chloride in tetrahydrofuran in the presence of anhydrous potassium carbonate. Thus, treatment of **1a** with either propionyl chloride or benzoyl chloride under this condition gave *N*-propionylbenzotriazole (**2a**) or *N*-benzoylbenzotriazole (**2b**) in 94 % or 98 % yields respectively as shown in Figure 2.2.

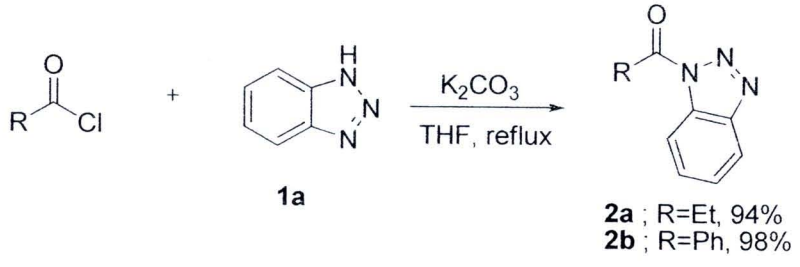


Figure 2.2 Preparation of *N*-acylbenzotriazole

The presence of the ethyl group in *N*-propionylbenzotriazole (**2a**) was indicated by a group of C-H stretching bands at $\bar{\nu}_{max}$ 2985, 2940 and 2882 cm^{-1}. The C=O streching band appeared at $\bar{\nu}_{max}$ 1736 cm^{-1}. The ^1H NMR spectrum showed signals of aromatic protons at δ 8.29 (d, J = 8.3 Hz, 1H), 8.13 (d, J = 8.3 Hz, 1H), 7.65 (t, J = 8.1 Hz, 1H) and 7.50 (t, J = 8.1 Hz, 1H) ppm, signals of methylene protons and methyl protons at δ 3.46 (q, J = 7.4 Hz, 2H) and 1.42 (t, J = 7.4 Hz, 3H) ppm respectively. The ^{13}C NMR spectrum showed the carbonyl carbon resonance at δ 173.28 ppm, signals of methylene carbon and methyl carbon at δ 29.08 and 8.34 ppm respectively.

The IR spectrum of *N*-Benzoylbenzotriazole (**2b**) showed a characteristic C-H bending out of plane of monosubstituted benzene at $\bar{\nu}_{max}$ 696 and 752 cm^{-1}, the C=O stretching band appeared at $\bar{\nu}_{max}$ 1712 cm^{-1}. The ^{1}H NMR spectrum showed signals of aromatic protons at δ 8.40 (d, J = 8.3 Hz, 1H), 8.22 (d, J = 7.3 Hz, 2H), 8.17 (d, J = 8.3 Hz, 1H), 7.70 (m, 2H) and 7.60 (m, 3H) ppm. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 166.74 ppm, ten signals of aromatic carbons at δ 145.77, 133.67, 132.35, 131.72, 131.48, 130.38, 128.43, 126.33, 120.19 and 114.79 ppm.

Preparation of esters from aliphatic alcohols

Having both acylating agents **2a** and **2b** as representatives of activated aliphatic acid and activated aromatic acid respectively, we allowed them to react with variety of aliphatic alcohols in order to test their reactivity and efficiency in ester synthesis. A procedure reported by Katrizky[52] called for the conversion of an alcohol into its sodium salt prior to allowing it to react with *N*-acylbenzotriazoles in a strictly anhydrous condition. Sought for a much simpler and milder procedure, we have found that ester **4c-j** and **5a-j** could be synthesized in good to excellent yields when alcohols **3a-j** were treated with either **2a** or **2b** in refluxing tetrahydrofuran in the presence of two-fold excess anhydrous potassium carbonate (Figure 2.3, Table 2.1**).** Attempts to isolate and purify the esters with simple extraction method also gave satisfactory results. Pure esters could be obtained by repeated extraction of the crude esters with 2 M sodium carbonate. This finding would also be beneficial to organic laboratory teaching since the costly chromatography could be avoided.

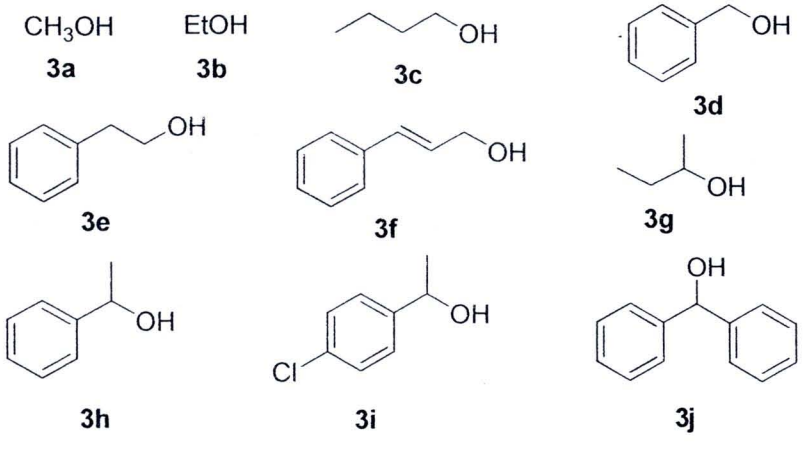
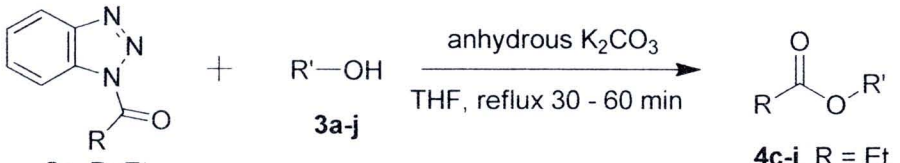


Figure 2.3 Alcohols **3a-j**

Table 2.1 Synthesis of esters from alcohols **3a-j**



2a, R=Et
2b, R=Ph

3a-j

4c-j, R = Et
5a-j, R = Ph

	Compound	Alcohol	Product	Yield (a) (%)
1	**2a**	**3c**; $CH_3(CH_2)CH_2$-OH	**4c**	74(58)
2	**2a**	**3d**; $PhCH_2$-OH	**4d**	95(64)
3	**2a**	**3e**;$PhCH_2CH_2$-OH	**4e**	85(87)
4	**2a**	**3f**; PhCH=$CHCH_2$-OH	**4f**	95(89)
5	**2a**	**3g**; $CH_3CH_2(CH_3)CH$-OH	**4g**	70(57)
6	**2a**	**3h**; Ph $(CH_3)CH$-OH	**4h**	72(68)
7	**2a**	**3i**; *p*-ClPh$(CH_3)CH$-OH	**4i**	85(79)
8	**2a**	**3j**; $(Ph)_2CH$-OH	**4j**	75(70)
9	**2b**	**3a**; CH_3-OH	**5a**	64(84)
10	**2b**	**3b**; CH_3CH_2-OH	**5b**	69(71)
11	**2b**	**3c**; $CH_3(CH_2)_2CH_2$-OH	**5c**	95(68)
12	**2b**	**3d**;$PhCH_2$-OH	**5d**	95(78)
13	**2b**	**3e**;$PhCH_2CH_2$-OH	**5e**	85(69)
14	**2b**	**3f**; PhCH=$CHCH_2$-OH	**5f**	89(92)
15	**2b**	**3g**; $CH_3CH_2(CH_3)CH$-OH	**5g**	80(75)
16	**2b**	**3h**; Ph $(CH_3)CH$-OH	**5h**	61(55)
17	**2b**	**3i**; *p*-ClPh$(CH_3)CH$-OH	**5i**	91(82)
18	**2b**	**3j**; $(Ph)_2CH$-OH	**5j**	73(70)

yield obtained from column chromatography

[a] % yield in parenthesis obtained from extraction method

The structure of esters **4c-j** and **5a-j** are shown in Figure 2.4 and Figure 2.5 respectively. Their physical data are as follows:

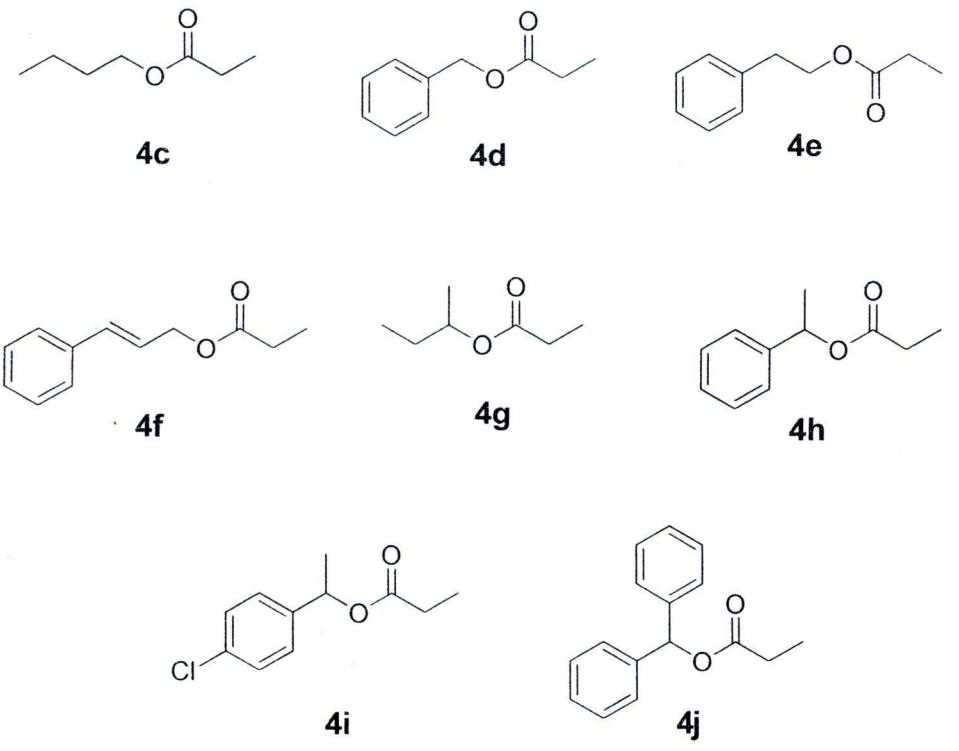


Figure 2.4 Esters **4c-j**

N-Butyl propionate (**4c**): IR spectrum showed strong bands of CH_3 and CH_2 stretching at $\bar{\nu}_{max}$ 2961 and 2875 cm^{-1} while absorption bands at $\bar{\nu}_{max}$ 1740 and 1189 cm^{-1} were corresponded to C=O and C-O stretching respectively. The ^1H NMR spectrum showed a triplet signal of methylene protons connected to oxygen atom at δ 4.04 (J = 6.7 Hz) ppm. The methylene protons connected to carbonyl group showed a quartet signal at δ 2.28 (J = 7.6 Hz) ppm. The ^{13}C NMR spectrum of **4c** showed a signal of carbonyl carbon at δ 174.49 ppm. A signal of methylene carbon connected to oxygen atom was found at δ 64.06 ppm, while methylene carbon connected to carbonyl group showed a signal at δ 27.54 ppm.

Benzyl propionate (**4d**): IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3066 and 3034 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2982, 2944 and 2884 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 1738 and 1175 cm^{-1} were corresponded to C=O stretching and C-O stretching respectively. The ^1H NMR spectrum showed a multiplet signal of aromatic protons at δ 7.37 (m) ppm. Benzylic protons showed a singlet signal at 5.14 ppm. The ^{13}C NMR spectrum of **4d**

showed a signal of carbonyl carbon at δ 174.22 ppm and a signal of benzylic carbon at δ 66.10 ppm.

2-Phenylethyl propionate (**4e**): IR spectrum showing absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3064 and 3029 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2981 and 2943 cm^{-1}. The C=O stretching and C-O stretching showed absorption bands at $\bar{\nu}_{max}$ 1738 and 1184 cm^{-1} respectively. The ^1H NMR spectrum showed signals of methyl protons at δ 1.14 (t, J = 7.6 Hz) ppm. Methylene protons connected to an oxygen atom showed a triplet at δ 4.32 (J = 7.1 Hz) and a quartet at δ 2.32 (J = 7.6 Hz) ppm was assigned to methylene protons connected to a carbonyl group. Benzylic protons showed a triplet at δ 2.95 (J = 7.1 Hz) ppm, while a multiplet at δ 7.30 ppm was the resonance of the aromatic protons. The ^{13}C NMR spectrum of **4e** showed a signal of a carbonyl carbon at δ 174.15 ppm. Benzylic carbon showed a signal at 64.73 ppm.

Cinnamyl propionate (**4f**): IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3083, 3059 and 3028 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2982, 2943 and 2882 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 1738 and 1179 cm^{-1} were the C=O stretching and C-O stretching respectively.The ^1H NMR signals at δ 7.40 (d, J = 7.4 Hz, 2H), 7.32 (t, J = 7.2 Hz, 2H) and 7.26 (t, J = 7.2 Hz, 1H) ppm were corresponded to aromatic protons. Two signals at δ 6.65 (d, J = 15.9 Hz) and 6.30 (m) ppm were assigned to vinyl proton H-3' and H-2' respectively. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 174.21 ppm and signals of vinyl carbon C-3' and C-2'at δ 134.05 and 123.34 ppm respectively.

sec-Butyl propionate (**4g**): IR spectrum showing absorption bands of sp^3 C-H stretching at $\bar{\nu}_{max}$ 2976, 2941 and 2881 cm^{-1} and an absorption band of C=O stretching at $\bar{\nu}_{max}$ 1735 cm^{-1}. The C-O stretching showed an absorption band at $\bar{\nu}_{max}$ 1195 cm^{-1}. The ^1H NMR spectrum showed signals of three methyl protons at δ 1.10 (d, J = 6.3 Hz), 1.02 (t, J = 7.6 Hz) and 0.80 (t, J = 7.4 Hz) ppm. Methylene protons connected to the carbonyl group showed signal at δ 2.20 (q, J = 7.6 Hz) and signal at δ 1.45 (m) ppm was assigned to the methylene protons connected to the methyne proton. A multiplet signal at δ 4.72 ppm was assigned to the methyne proton. The ^{13}C NMR spectrum of **4g** showed a signal of carbonyl carbon at δ 173.94 ppm.

1-Phenylethyl propionate (**4h**): IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3065 and 3034 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2982, 2941 and 2882 cm^{-1}. The C=O stretching and C-O stretching showed absorption bands at $\bar{\nu}_{max}$ 1738 and 1189 cm^{-1} respectively. The ^1H NMR spectrum showed a multiplet signal of aromatic protons at δ 7.24 ppm. Benzylic protons showed a quartet signal at δ 5.81 (J = 6.6 Hz) ppm, while the methyl group connected to the benzylic group showed a doublet signal at δ 1.44 (J = 6.6 Hz) ppm. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 173.59 ppm and a signal of benzylic carbon at δ 72.06 ppm.

1-(4-Chlorophenyl)ethyl propionate (**4i**): IR spectrum of **4i** showed absorption bands of sp^3 C-H stretching at $\bar{\nu}_{max}$ 2983, 2941 and 2882 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 1739 and 1186 cm^{-1} were assigned to C=O stretching and C-O stretching respectively. The ^1H NMR spectrum showed a multiplet signal at δ 7.28 ppm which was assigned to the aromatic protons. Benzylic proton showed a quartet signal at δ 5.84 (J = 6.6 Hz) ppm, while the methyl group connected to the benzylic group showed a doublet signal at δ 1.50 (J = 6.6 Hz)ppm . The ^{13}C NMR spectrum showed a signal of the carbonyl carbon at δ 173.44 ppm.

Benzhydryl propionate (**4j**): IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3088, 3064 and 3032 cm^{-1}, while sp^3 C-H stretching appeared at $\bar{\nu}_{max}$ 2982, 2941 and 2882 cm^{-1}. The C=O stretching and C-O stretching showed absorption bands at $\bar{\nu}_{max}$ 1740 and 1171 cm^{-1} respectively. The ^1H NMR spectrum showed a triplet signal of methyl protons at δ 2.22 (J = 7.6 Hz) ppm. Methylene protons showed a quartet signal at δ 2.48 (J = 7.6 Hz) ppm. A multiplet signal at δ 7.36 ppm was corresponded to aromatic protons, while a singlet signal at δ 6.95 ppm was assigned to benzylic protons. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 173.37 ppm and a signal of benzylic carbon at δ 76.70 ppm.

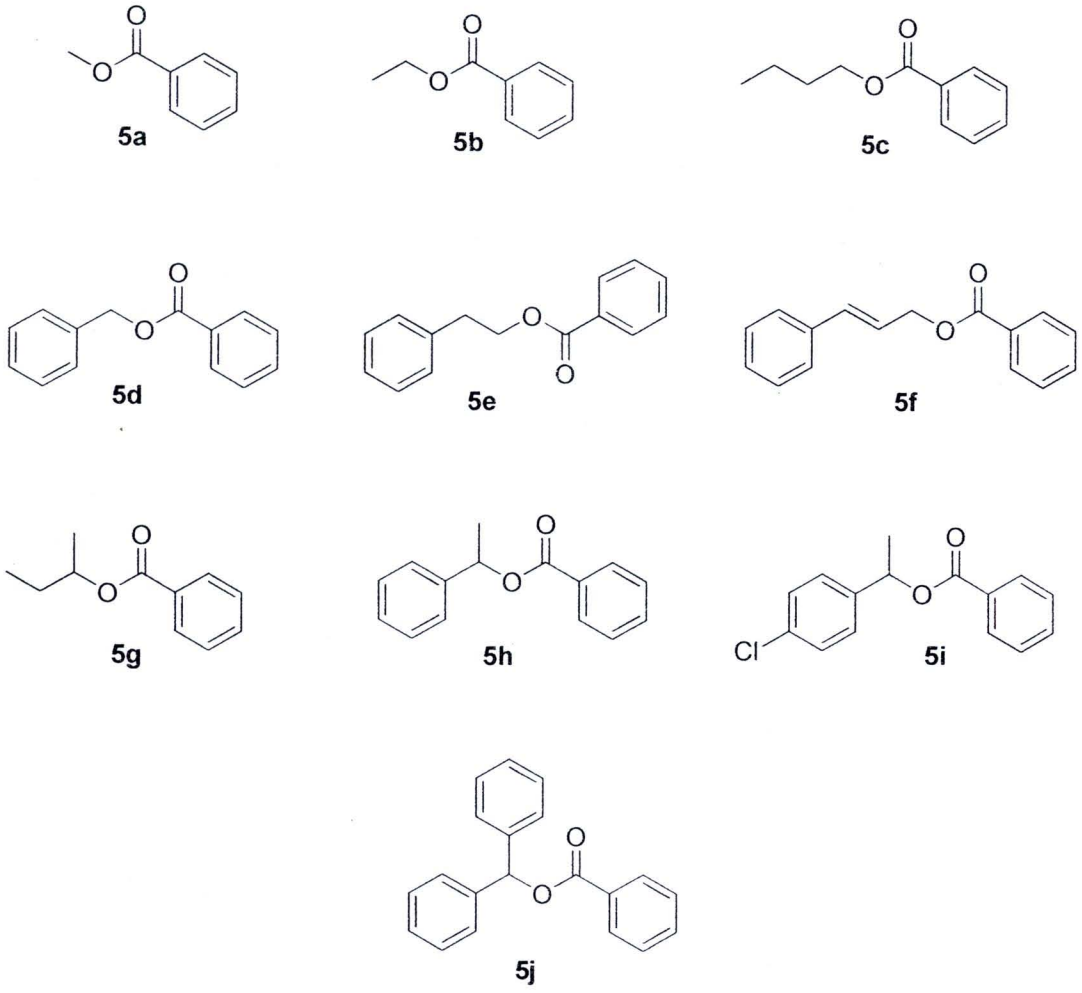


Figure 2.5 Ester **5a-j**

Methyl benzoate (**5a**): The IR spectrum showed an absorption band of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3064 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2999 and 2952 cm^{-1}. The C=O stretching and C-O stretching showed absorption bands at $\bar{\nu}_{max}$ 1732 and 1278 cm^{-1} respectively. The ^1H NMR spectrum showed a singlet signal of methoxy protons at δ 3.88 ppm. The aromatic protons showed signals at δ 8.03 (d, J = 7.7 Hz, 2H), 7.52 (t, J = 7.5 Hz, 1H), and 7.40 (t, J = 7.6 Hz, 2H) ppm. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 167.05 ppm and a signal of methoxy carbon at δ 52.00 ppm.

Ethyl benzoate (**5b**): IR spectrum showed an absorption band of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3063 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2988, 2938 and 2906 cm^{-1}. The C=O stretching and C-O stretching showed

absorption bands at $\bar{\nu}_{max}$ 1716 and 1274 cm^{-1} respectively. The ^1H NMR spectrum showed signals of aromatic protons at δ 8.05 (d, J = 7.2 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H) and 7.43 (t, J = 7.7 Hz, 2H) ppm. Methylene protons showed a quartet signal at δ 4.37 (J = 7.1 Hz) ppm and methyl protons at δ 1.38 (t, J = 7.1 Hz) ppm. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 166.56 ppm. The signal at δ 60.88 ppm was assigned to methylene carbon, while methyl carbon showed a signal at δ 14.29 ppm.

Butyl benzoate (**5c**): IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3064 and 3034 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2960, 2934 and 2874 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 1720 and 1275 cm^{-1} were corresponed to C=O stretching and C-O stretching respectively. The ^1H NMR spectrum showed a triplet signal at δ 4.32 (J = 6.6 Hz, 2H) was assigned to the methylene protons connected to an oxygen atom. Methyl protons at side chain showed a triplet signal at δ 0.97 (J = 7.4 Hz) ppm. The aromatic protons showed signals at δ 8.05 (d, J = 7.2 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H) and 7.43 (t, J = 7.7 Hz, 2H) ppm. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 166.60 ppm.

Benzyl benzoate (**5d**): IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3090, 3065 and 3033 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2953 and 2891 cm^{-1}. The C=O stretching and C-O stretching showed absorption bands at $\bar{\nu}_{max}$ 1717 and 1269 cm^{-1} respectively. The ^1H NMR spectrum showed signals of aromatic protons at δ 8.11 (d, J = 7.9 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H) and 7.44 (m, 7H) ppm. A singlet signal at δ 5.40 ppm was assigned to the benzylic protons. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 166.42 ppm. A signal at δ 66.70 ppm was assigned to the benzylic carbon.

2-Phenylethyl benzoate (**5e**): IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3063 and 3029 cm^{-1}, while sp^3 C-H stretching showed an absorption band at $\bar{\nu}_{max}$ 2956 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 1719 and 1274 cm^{-1} were corresponded to C=O stretching and C-O stretching respectively. The ^1H NMR spectrum showed a triplet signal at δ 4.58 (J = 7.0 Hz) ppm was assigned to the methylene protons connected to an oxygen atom. Benzylic protons showed a triplet signal at δ 3.12 (J = 7.0 Hz) ppm. Aromatic protons showed signals at δ 8.07 (d, J = 7.4 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H) and 7.34 (m, 5H) ppm.

The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 166.51 ppm. A signal at δ 72.06 ppm was assigned to the benzylic carbon and a signal at δ 65.49 ppm as a methylene carbon connected to an oxygen atom.

Cinnamyl benzoate (**5f**): IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3060 and 3028 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2944 and 2879 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 1716 and 1268 cm^{-1} were corresponded to C=O stretching and C-O stretching respectively. The ^1H NMR spectrum showed signals of vinyl protons at δ 6.78 (d, J = 15.9 Hz) and 6.44 (m) ppm. A doublet signal at δ 5.02 (J = 6.4 Hz) ppm was assigned to the methylene protons connected to an oxygen atom. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 166.37 ppm. Signals at δ 134.29 and 123.32 ppm were assigned to the vinyl carbon C-3' and C-2' respectively. Methylene carbon showed a signal at δ 65.55 ppm.

sec-Butyl benzoate (**5g**): IR spectrum showing an absorption band of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3064 cm^{-1}, while sp^3 C-H stretching bands were found at $\bar{\nu}_{max}$ 2974, 2937 and 2879 cm^{-1}. The C=O stretching and C-O stretching showed absorption bands at $\bar{\nu}_{max}$ 1716 and 1276 cm^{-1} respectively. The ^1H NMR spectrum showed a multiplet signal of methyne protons at δ 5.10 ppm. The methyl protons connected to the methyne proton showed a doublet signal at δ 1.33 (J = 6.3 Hz) ppm, while a triplet signal at 0.97 (J = 7.5 Hz) ppm was assigned to methyl protons at the side chain. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 167.17 ppm. The methyne carbon showed a signal at δ 72.78 ppm. Methyl carbon at the side chain and the methyl carbon connected to the methyne carbon appeared at δ 9.69 and 19.51 ppm respectively.

1-Phenylethyl benzoate (**5h**): IR spectrum showed an absorption band of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3038 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2920 and 2862 cm^{-1}. The C=O stretching and C-O stretching showed absorption bands at $\bar{\nu}_{max}$ 1727 and 1270 cm^{-1} respectively. The ^1H NMR spectrum showed a quartet signal of benzylic protons at δ 6.18 ppm. The methyl protons connected to the benzylic proton showed a doublet signal at δ 1.72 (J = 6.6 Hz) ppm, while signals at δ 8.14 (d, J = 7.5 Hz, 2H), 7.58 (t, J = 7.3 Hz, 1H) and 7.45 (m, 7H) ppm were assigned to aromatic protons. The ^{13}C NMR spectrum showed a signal of

carbonyl carbon at δ 165.81 ppm. The benzylic carbon showed a signal at δ 72.94 ppm. Methyl carbon showed a signal at δ 22.44 ppm.

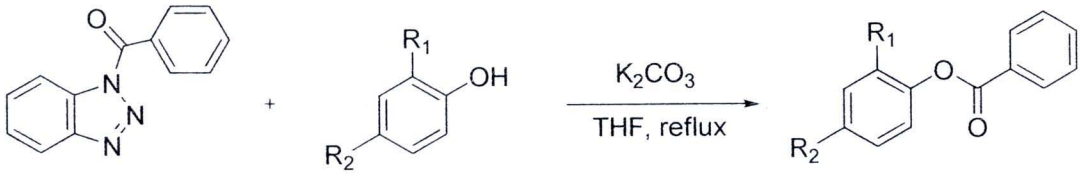
1-(4-Chlorophenyl)ethyl benzoate (**5i**): IR spectrum showed an absorption band of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3063 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2982 and 2933 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 1719 and 1270 cm^{-1} were corresponded to C=O stretching and C-O stretching respectively. The ^1H NMR spectrum showed a quartet signal of the benzylic proton at δ 6.18 ppm. Methyl protons showed a doublet signal at δ 1.66 (J = 6.6 Hz) ppm. Aromatic protons showed signals at δ 8.07 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.2 Hz, 1H) and 7.40 (m, 6H) ppm. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 165.69 ppm. A signal at δ 72.19 ppm was assigned to the benzylic carbon and a signal at δ 22.30 ppm as a methyl carbon.

Benzhydryl benzoate (**5j**): The IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3058 and 3030 cm^{-1}, while sp^3 C-H stretching showed an absorption band at $\bar{\nu}_{max}$ 2948 cm^{-1}. The C=O stretching and C-O stretching showed absorption bands at $\bar{\nu}_{max}$ 1712 and 1266 cm^{-1} respectively. The ^1H NMR spectrum showed a singlet signal of the benzylic proton at δ 7.16 ppm. Multiplet signals at δ 8.18, 7.58, 7.48, 7.38 and 7.32 ppm were assigned to fifteen protons of aromatic rings. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 165.55 ppm. The benzylic carbon showed a signal at δ 77.43 ppm.

Preparation of esters from aromatic alcohols

In order to widen the scope of applications for ester synthesis, we treated phenol **6a-c** with **2a** in a similar fashion as were previously done. However, the acylation of phenols with aliphatic acid presented difficulties, and mixtures were obtained. Contrastingly, ester **7a-c** were obtained in excellent yields when **6a-c** were allowed to react with **2b** (Figure 2.6, Table 2.2).

Table 2.2 Synthesis of esters **7a-c** from phenol **6a-c**

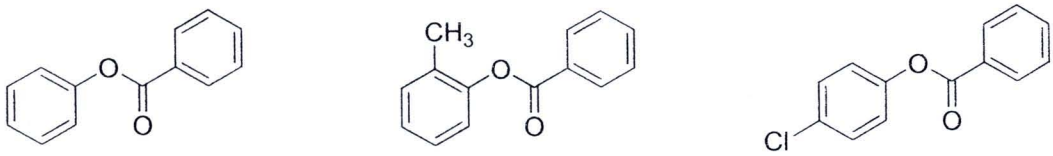


2b **6a**, R_1=H, R_2=H; **6b**, R_1=CH_3, R_2=H; **6c**, R_1=H, R_2=Cl **7a-c**

	Compound	Phenol		Product	Yield (a)
		R_1	R_2		(%)
1	**2b**	**6a** ; H	H	**7a**	85(88)
2	**2b**	**6b** ; CH_3-	H	**7b**	96(93)
3	**2b**	**6c** ; H	Cl	**7c**	90(83)

[a] % yield in parenthesis obtained from extraction method

The structures of esters **7a-c** are shown in Figure 2.6. Their physical and spectroscopic data are as follows:



7a **7b** **7c**

Figure 2.6 Ester **7a-c**

Phenyl benzoate (**7a**): The IR spectrum showed aromatic C-H stretching band at $\bar{\nu}_{max}$ 3058 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 1731 and 1262 cm^{-1} were corresponded to C=O stretching and C-O stretching respectively. The ^{1}H NMR spectrum showed aromatic protons resonance at δ 8.24 (d, J = 8.0 Hz, 2H), 7.64 (t, J = 6.9 Hz, 1H), 7.52 (t, J = 7.4 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.28 (t, J = 8.1 Hz, 1H) and 7.22 (d, J = 8.5 Hz, 2H) ppm. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 165.17 ppm. The eight signals at δ 150.96, 133.55, 130.15, 129.59, 129.47, 128.55, 125.86 and 121.70 ppm were assigned to twelve carbons of aromatic rings.

o-Tolyl benzoate (**7b**): The IR spectrum showed aromatic C-H stretching at $\bar{\nu}_{max}$ 3064 and 3033 cm^{-1}, while sp^3 C-H stretching showed absorption bands at $\bar{\nu}_{max}$ 2981 and 2932 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 1717 and 1270 cm^{-1} were corresponded to C=O stretching and C-O stretching respectively. The ^1H NMR spectrum showed a singlet signal of methyl protons at δ 2.38 ppm. Signals at δ 8.20 (d, J = 7.6 Hz, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 7.24 (m, 2H) and 7.10 (d, J = 8.4 Hz, 2H) ppm were assigned to aromatic protons. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 165.36 ppm. A signal at δ 20.88 ppm was assigned to the methyl carbon. The nine signals at δ 148.71, 135.48, 133.46, 130.12, 129.97, 129.69, 128.51, 121.34 and 121.34 ppm were assigned to twelve carbons of aromatic rings.

4-Chlorophenyl benzoate (**7c**): The IR spectrum showed aromatic C-H stretching at $\bar{\nu}_{max}$ 3063 cm^{-1}. The C=O stretching and C-O stretching showed absorption bands at $\bar{\nu}_{max}$ 1734 and 1219 cm^{-1}, respectively. The ^1H NMR signals at δ 8.19 (d, J = 7.5 Hz, 2H), 7.65 (t, J = 7.3 Hz, 1H), 7.52 (t, J = 7.8 Hz, 2H), 7.40 (d, J = 8.7 Hz, 2H) and 7.17 (d, J = 8.7 Hz, 2H) ppm were assigned to nine protons of aromatic rings. The ^{13}C NMR spectrum showed a signal of carbonyl carbon at δ 164.92 ppm. The eight signals at δ 149.41, 133.76, 131.26, 130.17, 129.52, 129.18, 128.61, 123.08 ppm were assigned to twelve carbons of aromatic rings.

With our main objective accomplished, we attempted to improve the efficiency of this method furthermore by lessening the reaction time. Since benzotriazole moiety took part in the reaction pathway as a leaving group, electron-withdrawing groups attached to the benzene ring of benzotriazole should stabilize the benzotriazolide anion and thus facilitate the decomposition of the tetrahedral intermediate (Figure 2.7). As a result, the overall reaction should speed up to some extent.

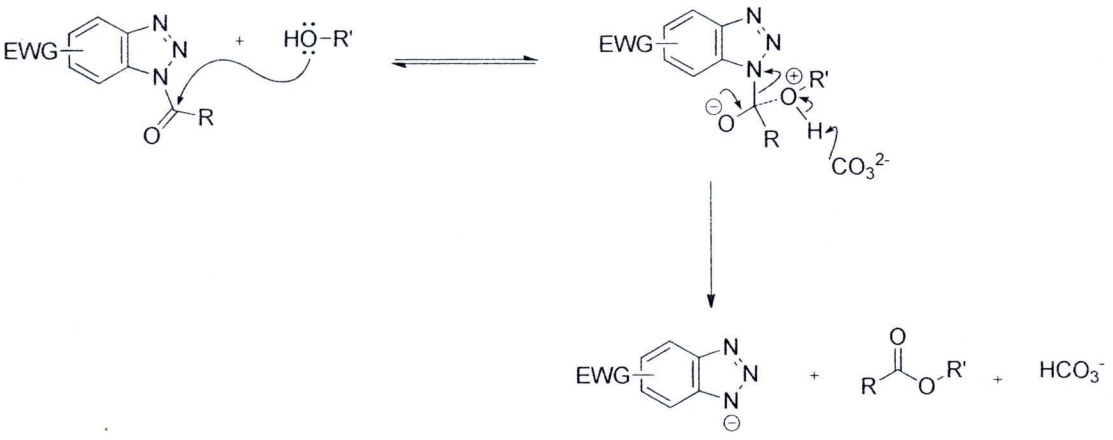


Figure 2.7 Ester synthesis using *N*-acylbenzotriazole with an electron-withdrawing group

Attempted nitration of benzotriazole with a mixture of conc. nitric acid and conc. sulfuric acid[53] did not give the desired 4-nitrobenzotriazole. Several nitrating conditions, i.e. conc. HNO_3 in glacial acetic acid[54] , conc. HNO_3 and $(NH_4)_6Mo_7O_{24}$ in $CHCl_3$[55], 100 % HNO_3 in CH_2Cl_2[56] were also applied but did not resolve the matter. Attempts to nitrate **2a** under acid conditions were also unsuccessful. Conducting the reactions at high temperature led to decomposition.

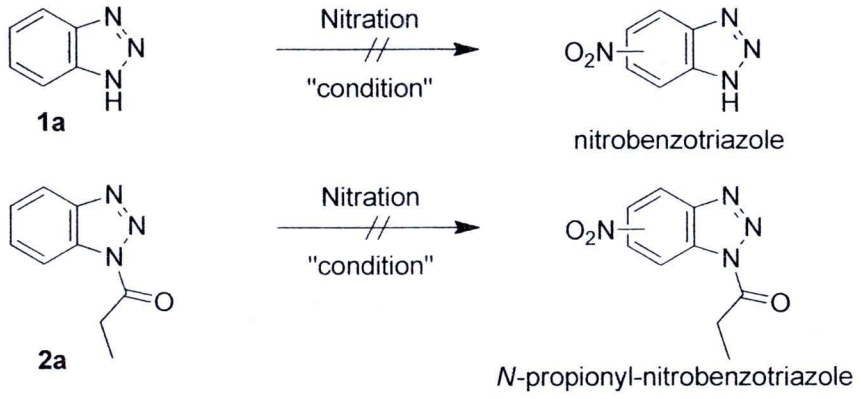


Figure 2.8 Attempted nitration of **1a** and **2a**

This finding realized us to turn to another approach that the required substituents had to be attached to the benzene ring beforehand and building up the triazole ring in the later stage as illustrated in general retrosynthetic Figure 2.9 below.

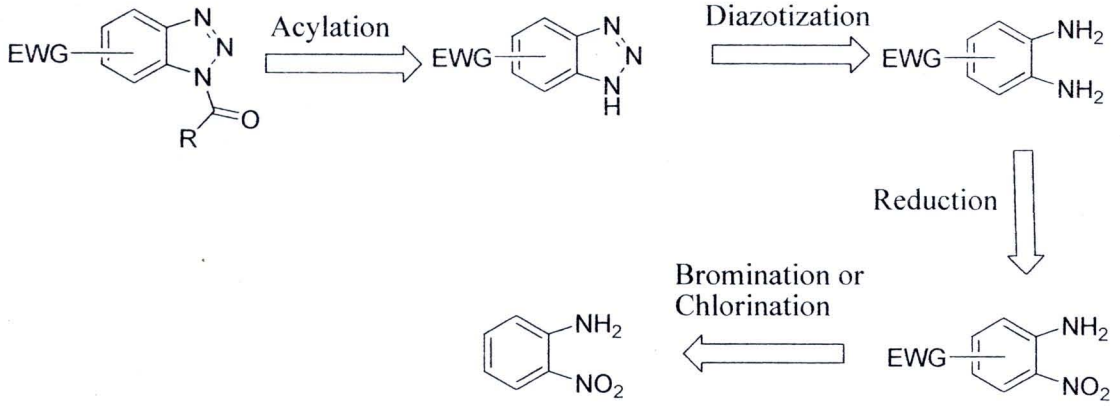


Figure 2.9 General retrosynthesis of *N*-acylbenzotriazole with Electron-withdrawing groups attached

Preparation of propionyldibromobenzotriazole (12a)

Acetylation of *o*-nitroaniline with acetic anhydride in pyridine gave *N*-acetyl-*o*-nitroaniline which was futher treated with a mixture of $KBrO_3$-HBr in glacial acetic acid[57] to give the monobrominated product **8** in low yield along with the deacetylated dibromonitroaniline **9a** as a major product. At this stage, we turned to the synthesis of **9a** using a simple bromination procedure by treating *o*-nitroaniline with bromine in methanol which gave **9a** in 92 % yield (Figure 2.10).

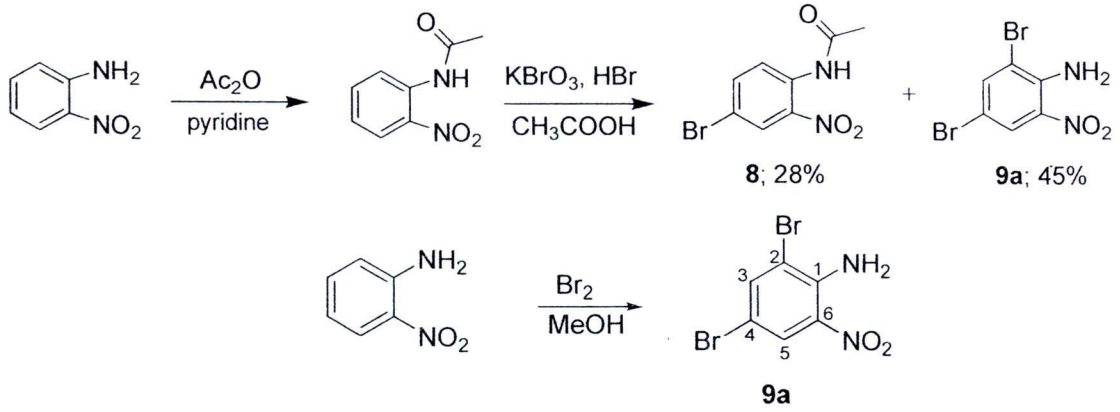


Figure 2.10 Preparation of dibromonitroaniline (**9a**)

Dibromonitroaniline (**9a**): The IR spectrum showed a characteristic N-H stretching for the NH_2 group at $\bar{\nu}_{max}$ 3465 and 3353 cm^{-1} and N-H bending at 1265 cm^{-1}. The ^1H NMR spectrum showed two singlets at δ 8.10 and 7.80 ppm corresponded to H-3 and H-5, respectively. Amino protons resonance appeared as a broad singlet at δ 6.60 (2H) ppm. The ^{13}C NMR showed resonances of the aromatic carbon connected to the bromo groups at δ 112.73 and 106.87 ppm respectively.

Dibromonitroaniline (**9a**) was subjected to reduction with H_2/Pd on C in ethanol to give the unstable phenylenediamine **10a** which was treated with sodium nitrite in glacial acetic acid without purification to afford dibromobenzotriazole **11a** in 68 % yield (Figure 2.11).

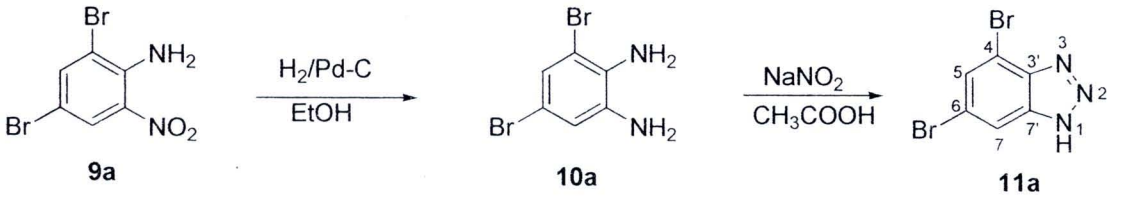


Figure 2.11 Preparation of dibromobenzotriazole (**11a**)

Dibromobenzotriazole (**11a**): The IR spectrum showed an absorption band of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3086 cm^{-1}. The absorption bands at $\bar{\nu}_{max}$ 3435 cm^{-1} were corresponded to N-H streching. The ^1H NMR spectrum showed singlet signals at δ 8.10 (1H) and 7.80 (1H) ppm which were assigned to H-7 and H-5 respectively. The ^{13}C NMR spectrum showed signals of aromatic carbon at δ 140.35, 138.93, 130.38, 119.49, 116.45 and 110.47 ppm.

Acylation of **11a** with a mixture of propionyl chloride and anhydrous potassium carbonate in tetrahydrofuran gave propionylbromobenzotriazole (**12a**) in 94 % yield (Figure 2.12).

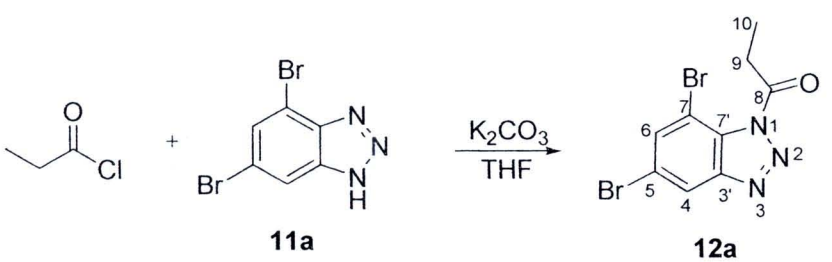
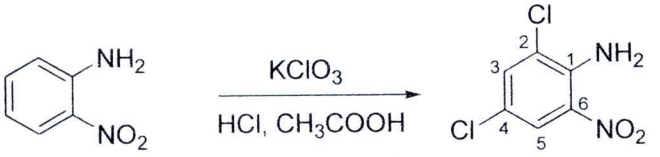


Figure 2.12 Preparation of propionylbromobenzotriazole (**12a**)

Propionylbromobenzotriazole (**12a**): The IR spectrum showed an absorption band of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3075 cm^{-1}. The absorption bands at $\bar{\nu}_{max}$ 2983 and 2941 cm^{-1} were corresponded to sp^3 C-H stretching. Absorption bands at $\bar{\nu}_{max}$ 1740 cm^{-1} was corresponded to C=O stretching. The ^{1}H NMR spectrum showed singlet signals at δ 8.46 (1H) and 7.82 (1H) ppm which were assigned to H-4 and H-6 respectively. Signals at δ 3.45 (q, J = 7.4 Hz) and δ 1.41 (t, J = 7.4 Hz) ppm were corresponded to H-9 and H-10 respectively. The ^{13}C NMR spectrum showed signal of a carbonyl carbon at δ 172.98 ppm. The signals at δ 29.19 and 8.19 ppm were assigned to C-9 and C-10 respectively.

Preparation of propionyldichlorobenzotriazole (12b)

Following the previous synthetic protocol, *o*-nitroaniline was treated with a mixture of $KClO_3$-HCl in glacial acetic acid to give dichloronitroaniline **9b** in 85 % yield (Figure 2.13).



9b

Figure 2.13 Preparation of dichloronitroaniline (**9b**)

Dichloronitroaniline (**9b**): The IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3086 and 3060 cm^{-1}. N-H Streching of the amino group appeared at $\bar{\nu}_{max}$ 3473 and 3360 cm^{-1}. The ^{1}H NMR spectrum showed two the singlet signals at δ 8.10 and 7.54 ppm which were assigned to H-5 and H-3 respectively. Amino protons showed a board singlet signal at δ 6.55 (2H) ppm. The ^{13}C NMR spectrum showed signals of the aromatic carbon C-2 and C-4 connected to the chloro groups at δ 122.69 and 120.36 ppm respectively.

In a similar manner as the preparation of **12a, 9b** was transformed into **11b** in 75 % yield which was finally converted to **12b** in 96 % yield (Figure 2.14).

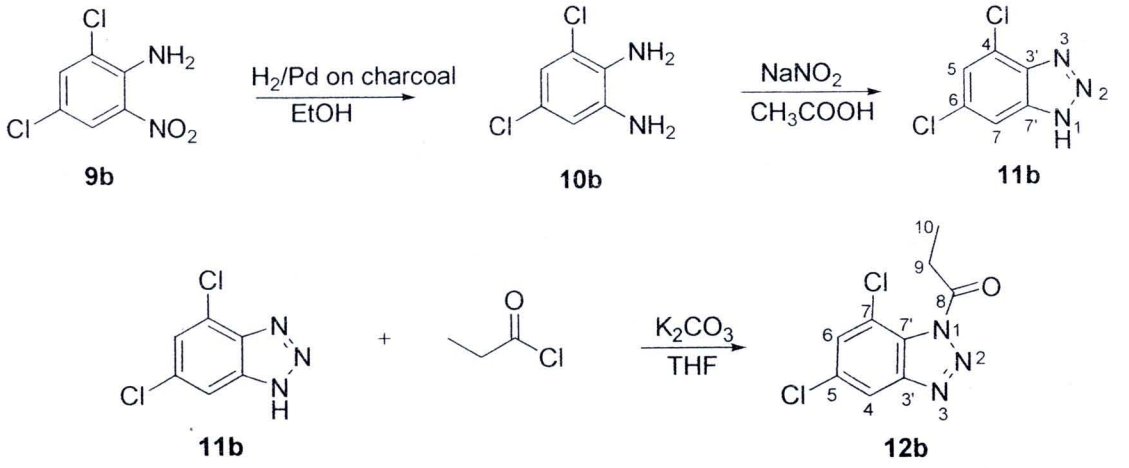


Figure 2.14 Preparation of dichlorobenzotriazole (**11b**) and propionyl dichlorobenzotriazole (**12b**)

Dichlorobenzotriazole (**11b**): The IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3080 and 3020 cm^{-1}. The absorption bands at $\bar{\nu}_{max}$ 3436 cm^{-1} was corresponded to N-H streching. The ^1H NMR spectrum showed singlet signals at δ 7.82 (1H) and 7.50 (1H) ppm which were assigned to H-7 and H-5 respectively. The ^{13}C NMR spectrum showed signals of aromatic carbon at δ 140.05, 139.13, 133.44, 126.66 123.48 and 113.44 ppm.

Propionyldichlorobenzotriazole (**12b**): The IR spectrum showed absorption bands of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3106 and 3084 cm^{-1}. The absorption bands at $\bar{\nu}_{max}$ 2985 and 2944 cm^{-1} were corresponded to sp^3 C-H stretching. Absorption bands at $\bar{\nu}_{max}$ 1740 cm^{-1} was corresponded to C=O stretching. The ^1H NMR spectrum showed singlet signals at δ 8.23 (1H) and 7.50 (1H) ppm which were assigned to H-4 and H-6 respectively. Signals at δ 3.45 (q, J = 7.4 Hz) ppm and δ 1.42 (t, J = 7.4 Hz) ppm were corresponded to H-9 and H-10 respectively. The ^{13}C NMR spectrum showed signal of a carbonyl carbon at δ 172.93 ppm. The signals at δ 29.21 and 8.21 ppm were assigned to C-9 and C-10 respectively.

Our next endeavor in improving the efficiency of the acylating agent was to synthesize *N*-acylbenzotriazole with a carboxyl group attached to the benzene ring. We reasoned that the carboxyl group should serve not only as an electron withdrawing group but also rendered easier separation with a mild basic extraction via its water soluble carboxylate anion as outlined in Figure 2.15.

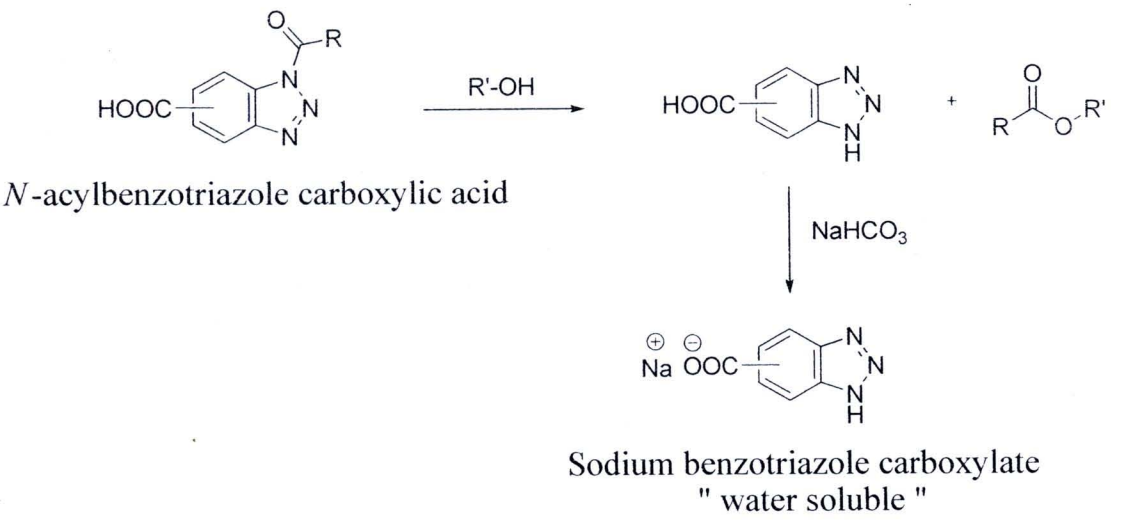


Figure 2.15 *N*-Acylbenzotriazole carboxylic acid as an acylating agent

The first retrosynthetic for *N*-acylbenzotriazole-5-carboxylic acid (**17**) as showed in Figure 2.16.

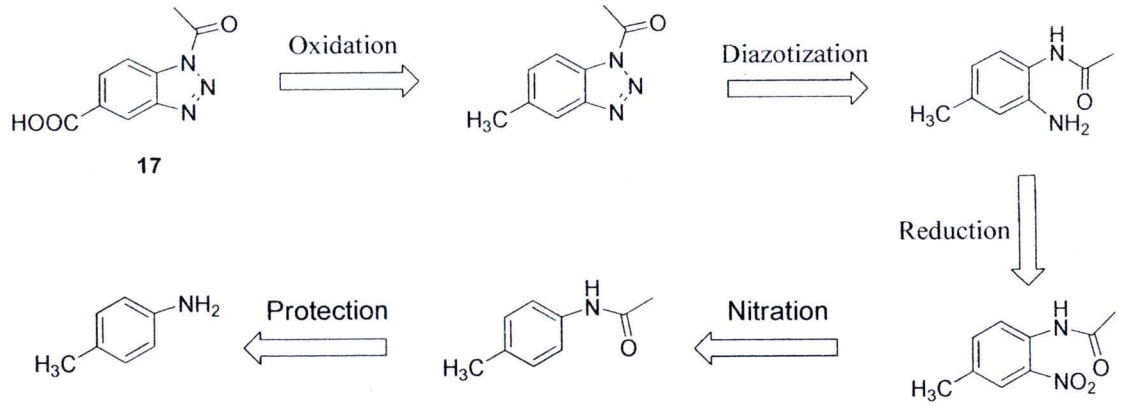


Figure 2.16 Retrosynthesis of *N*-acylcarboxylbenzotriazole-5-carboxylic acid (**17**)

The synthesis started with acetylation of *p*-toluidine with acetic anhydride in pyridine to give *N*-*p*-tolylacetamide (**13**) in 96 % yield (Figure 2.17).

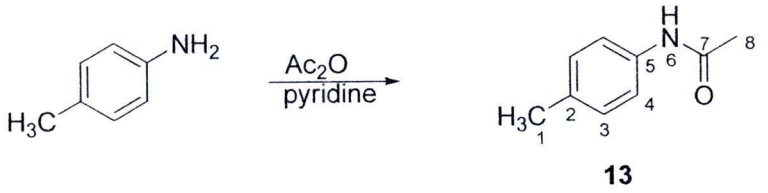
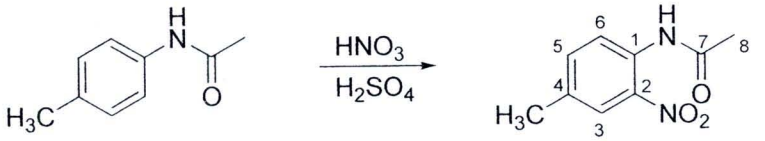


Figure 2.17 Synthesis of *N*-*p*-tolylacetamide (**13**)

N-*p*-Tolylacetamide (**13**): The IR spectrum showed an N-H stretching band at $\bar{\nu}_{max}$ 3290 cm^{-1}. The C=O stretching appeared at $\bar{\nu}_{max}$ 1654 cm^{-1}. The ^1H NMR spectrum showed a singlet resonance of the CH_3 attached to benzene ring at δ 3.00 ppm (3H) while the acetyl CH_3 resonance showed up as a singlet at δ 2.25 ppm (3H). Aromatic protons appeared as a doublet pair at δ 7.25 and 7.08 (J=8.4 Hz, 4H) ppm. The ^{13}C NMR spectrum showed signals at δ 167.89 and 23.30 ppm which were assigned to C-7 and C-8 respectively.

Treatment of **13** with a mixture of conc. nitric acid and conc. sulfuric acid gave *N*-(4-methyl-2-nitrophenyl)acetamide (**14**) in 90 % yield (Figure 2.18).

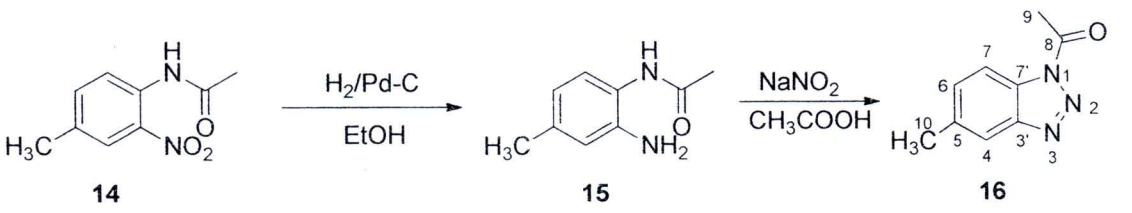


13 **14**

Figure 2.18 Synthesis of *N*-(4-methyl-2-nitrophenyl)acetamide (**14**)

N-(4-Methyl-2-nitrophenyl)acetamide (**14**): The IR spectrum showed hypsochromic shift of both the N-H and C=O stretching at $\bar{\nu}_{max}$ 3382, 3359 and 1719, 1709 cm^{-1} respectively. The NO_2 stretching appeared at $\bar{\nu}_{max}$ 1525 and 1342 cm^{-1}. The ^1H NMR signals at δ 8.62 (d, J = 8.6 Hz, $1H_6$), 8.00 (s, $1H_3$) and 7.44 (d, J = 8.6 Hz, $1H_5$) ppm were assigned to H-6, H-3 and H-5 respectively. The ^{13}C NMR spectrum showed a lowfield shift signal of carbon connected to the nitro group at 136.23 ppm.

The nitro compound **14** was hydrogenated in the presence of a catalytic amount of palladium on activated charcoal to give amide **15** which was treated with sodium nitrite in glacial acetic acid to afford *N*-acetylbenzotriazole (**16**) in 75 % yield (Figure 2.19).

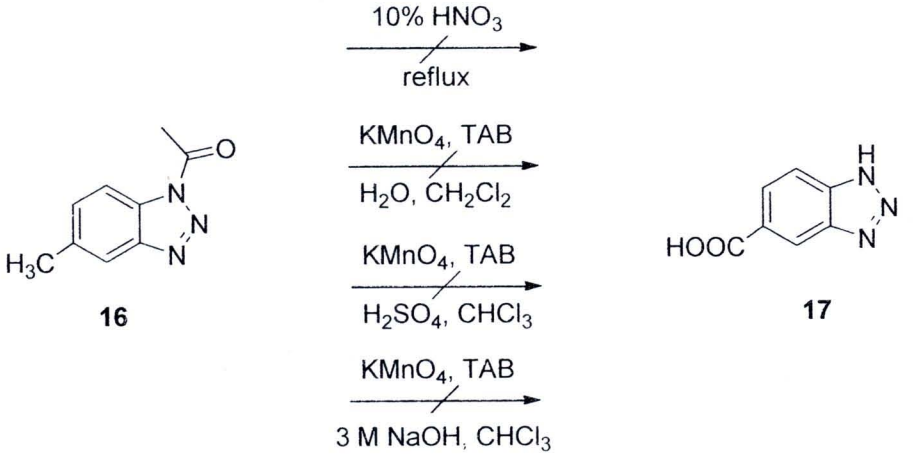


14 **15** **16**

Figure 2.19 Synthesis of *N*-acetylbenzotriazole (**16**)

N-Acetylbenzotriazole (**16**): The IR spectrum showed an absorption band of sp^2 C-H stretching at $\bar{\nu}_{max}$ 3071 cm^{-1}. Absorption bands at $\bar{\nu}_{max}$ 2921 and 1736 cm^{-1} were corresponded to sp^3 C-H stretching and C=O stretching respectively. The ^1H NMR spectrum showed signals at δ 8.13 (d, J = 8.4 Hz, $1H_7$), 7.86 (s, $1H_4$) and (d, J = 8.4 Hz, $1H_6$) ppm which were assigned to H-7, H-4 and H-6 respectively. The ^{13}C NMR spectrum showed signals of aromatic carbon at δ 146.80, 136.34, 132.15, 129.29, 119.22 and 113.73 ppm which assigned to C-3', C-5, C-7, C-7', C-6 and C-4 respectively.

With **16** in hand, the stage was set for oxidation of the methyl group into a carboxyl group. Unfortunately, this transformation could not be realized even various oxidizing agents were tried. Phase-transfer oxidation with $KMnO_4$ under various conditions were also failed to give the desired product (Figure 2.20).



16 **17**

Figure 2.20 Attempted oxidation of *N*-acetylbenzotriazole (**16**)

The synthetic plan was adjusted by using *p*-aminobenzoic acid as a starting material and the retrosynthetic method was shown in Figure 2.21.

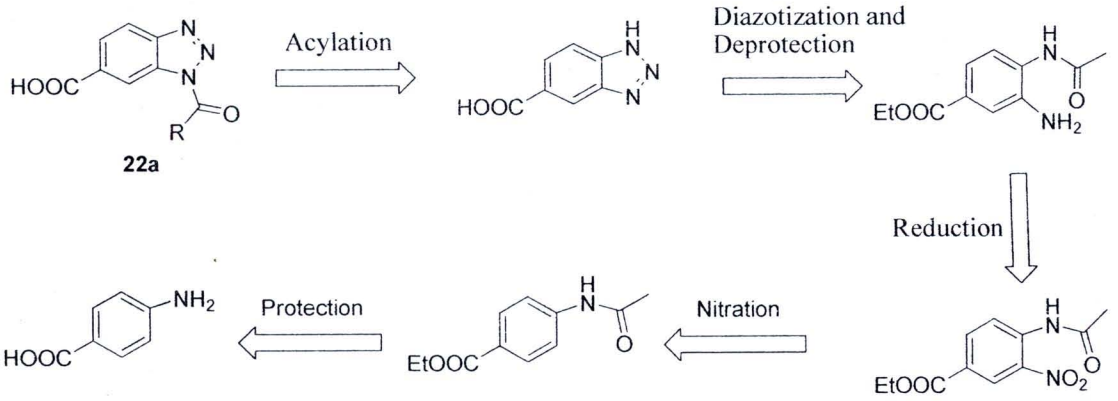


Figure 2. 21 Retrosynthesis of *N*-acylbenzotriazole-6-carboxylic acid **(22a)**

Esterification of *p*-aminobenzoic acid with ethanol in the presence of conc. sulfuric acid afforded ethyl-4-aminobenzoate (**18**) in 98 % yield. The aminoester **18** was acetylated with acetic anhydride in pyridine to give ethyl-4-acetamidobenzoate (**19a**) in 96 % yield which was treated with a mixture of conc. nitric acid and conc. sulfuric acid to give ethyl-4-acetamido-3-nitrobenzoate (**20a**) in 84 % yield. Reduction of **20a** under hydrogen gas and palladium on activated charcoal at room temperature gave aminoester **21a** in 90 % yield which was subsequently treated with sodium nitrite in glacial acetic acid to afford *N*-acetylbenzotriazole carboxylate ester (**22a**) in 81 % yield (Figure 2.22).

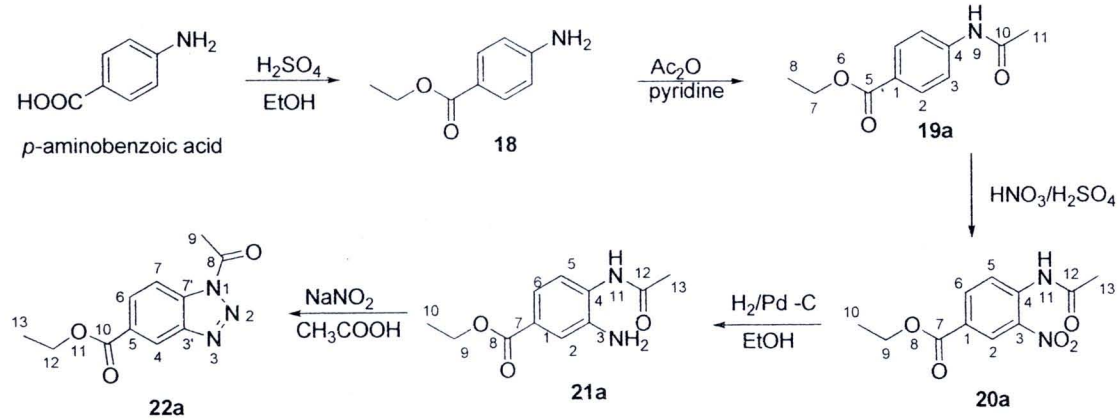


Figure 2.22 Synthesis of *N*-acetylbenzotriazole carboxylate ester (**22a**)

Ethyl-4-acetamidobenzoate (**19a**): The IR spectrum showed absorption bands at $\bar{\nu}_{max}$ 1706 and 1682 cm^{-1} which were assigned to C=O stretching of ester and amide group respectively. The ^{1}H NMR spectrum showed the disappearance of the amino protons at δ 4.05 (2H) ppm and instead a singlet signal appeared at δ 2.20 (3H) ppm which was assigned to the methyl group of C-11. The ^{13}C NMR spectrum showed signals at δ 168.82 and 14.31 ppm which were assigned to C-10 and C-11 respectively.

Ethyl-4-acetamido-3-nitrobenzoate (**20a**): The IR spectrum showed absorption bands at $\bar{\nu}_{max}$ 1717 cm^{-1} which was assigned to C=O stretching of ester. The NO_2 stretching appeared at $\bar{\nu}_{max}$ 1512 and 1340 cm^{-1}. The ^{1}H NMR showed the disappearance of aromatic proton at C-3 from and the signals at δ 8.90 (d, J = 8.9 Hz, 1H), 8.87 (s, 1H) and 8.26 (d, J = 8.9 Hz, 1H) ppm which assigned to H-6, H-2 and H-5, respectively. The ^{13}C NMR spectrum showed a lowfield shift signal of carbon connected to the nitro group from δ 118.79 to 138.14 ppm.

Ethyl-4-acetamido-3-aminobenzoate (**21a**): The IR absorption bands at $\bar{\nu}_{max}$ 3422, 3356 and 3278 cm^{-1} were corresponded to the N-H streching. The ^{1}H NMR spectrum showed a singlet signal of the amino group at δ 3.85 ppm. The ^{13}C NMR spectrum showed signals of aromatic carbon connected to the amino group at δ 139.57 ppm.

Ethyl-1-acetylbenzotriazole-5-carboxylate (**22a**): The IR spectrum showed absorption bands at $\bar{\nu}_{max}$ 1746 and 1708 cm^{-1} which were corresponded to C=O streching of the ester and amide groups respectively. The ^{1}H NMR spectrum showed the absence of the amino proton resonance at δ 3.85 ppm, the signals at δ 8.80 (s, 1H), 8.30 (d, J = 8.6 Hz, 1H) and 8.30 (d, J = 8.6 Hz, 1H) ppm were assigned to H-4, H-6 and H-7 respectively. The ^{13}C NMR showed lowfield shift signals of aromatic carbon C-3' and C-7' at δ 146.19 and 133.32 ppm respectively.

In order to perform exact reactivity comparison of **22a** with **2a, 12a** and **12b** the acetyl group had to be replaced with the propionyl group together with the ethoxyl group also had to be removed as well. Double hydrolysis were accomplished in one-pot style when **22a** was treated with 2M sodium hydroxide in tetrahydrofuran at reflux. The desired benzotriazole-5-carboxylic acid (**23**) was obtained in 80 % yield,

but much to our surprise, this compound was unable to be acylated with propionyl chloride under our usual condition (Figure 2.23).

Figure 2.23 Attempted synthesis of propionylbenzotriazole-5-carboxylic acid (**24**)

Benzotriazole-5-carboxylic acid (**23**): mp 310-311 °C (decompose). The IR spectrum showed a broad of O-H stretching from $\bar{\nu}_{max}$ 3205 cm^{-1}. The ^1H NMR spectrum showed signals at δ 8.50 (s, $1H_4$), 7.98 (d, J = 8.4 Hz, $1H_6$) and 7.92 (d, J = 8.4 Hz, $1H_7$) ppm which were assigned to H-4, H-6 and H-7 respectively.

Due to the lack of target compound **24**, we decided to carry on synthesizing the *N*-propionyl analogue of **22a** and intended to use it in reactivity test whatsover. Synthesis of the *N*-propionyl analogue **22b** started with **18** and followed exactly the same path as that of **22a** excepted for the use of propionyl chloride instead of acetic anhydride in the first step of synthesis (Figure 2.24).

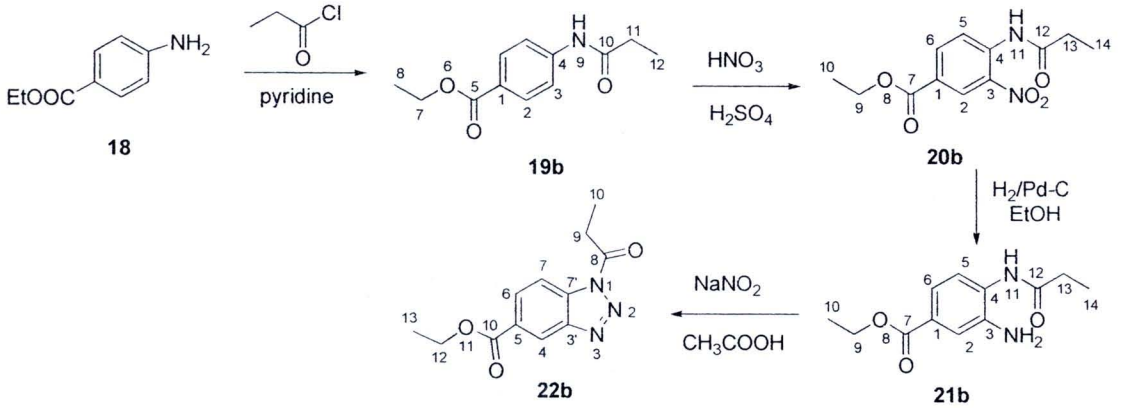


Figure 2.24. Synthesis of the *N*-propionyl analogue (**22b**)

Thus treatment of **18** with propionyl chloride in pyridine gave **19b** in 84% yield. Nitration of **19b** using a mixture of conc. nitric acid and conc. sulfuric acid afforded **20b** in 86% yield which upon reduction with hydrogen gas and palladium on

activated charcoal gave **21b** in 93%. Diazotization of **21b** gave the desired ester **22b** in 80% yield.

Ethyl 4-propionamidobenzoate (**19b**): The IR spectrum showed the C=O stretching of ester and amide group at $\bar{\nu}_{max}$ 1717 and 1672 cm^{-1} respectively. The ^1H NMR spectrum showed the disappearance of the amino protons at δ 4.05 (2H) ppm, signals of methylene proton at δ 2.43 (q, J = 7.5 Hz, 2H) and 4.34 (q, J = 8.0 Hz, 2H), methyl proton at δ 1.29 (t, J = 7.5 Hz, 3H) and 1.39 (t, J = 8.0 Hz, 3H) ppm were assigned to protons at C-11 and C-12 respectively. The ^{13}C NMR spectrum showed a signal at δ 172.68 ppm which were assigned to C-10, while signals at δ 14.35 and 9.55 ppm were corresponded to C-11 and C-12 respectively.

Ethyl 3-nitro-4-propionamidobenzoate (**20b**): The IR spectrum showed NO_2 stretching appeared at $\bar{\nu}_{max}$ 1530 and 1366 cm^{-1}. The ^1H NMR showed the disappearance signal of an aromatic proton at C-3 and the signals at δ 8.94 (d, J = 8.9 Hz, 1H), 8.88 (d, J = 2.0 Hz, 1H) and 8.27 (dd, J = 8.9, 2.0 Hz, 1H) ppm which were assigned to H-6, H-2 and H-5 respectively. The ^{13}C NMR spectrum showed a lowfield shift signal of carbon connected to the nitro group from δ 118.79 to 138.35 ppm.

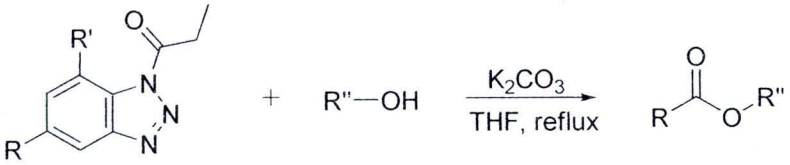
Ethyl 3-amino-4-propionamidobenzoate (**21b**): The IR spectrum showed absorption bands at $\bar{\nu}_{max}$ 3415, 3357 and 3281 cm^{-1} which were corresponded to N-H streching. The ^1H NMR spectrum showed a singlet signal of amino group at δ 3.85 ppm. The ^{13}C NMR spectrum showed signals of aromatic carbon connected to the amino group at δ 139.11 ppm.

Ethyl-1-propionyl-1*H*-benzo[*d*][1,2,3]triazole-5-carboxylate (**22b**): The IR absorption bands at $\bar{\nu}_{max}$ 1745 and 1708 cm^{-1} were corresponded to C=O streching of the ester and amide group respectively. The ^1H NMR spectrum showed the disappearence of the amino protons at δ 3.85 ppm. The signals at δ 8.81 (s, 1H), 8.38 (d, J = 8.6 Hz, 1H) and 8.38 (d, J = 8.6 Hz, 1H) ppm were assigned to H-4, H-6 and H-7 respectively. The ^{13}C NMR spectrum showed lowfield shift signals of aromatic carbon C-3' and C-7' at δ 146.10 and 133.48 ppm respectively.

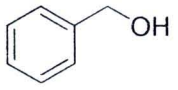
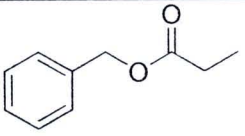
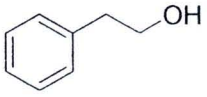
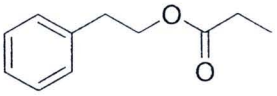
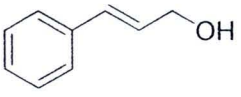
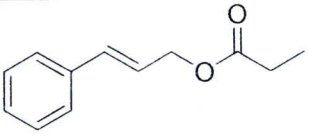
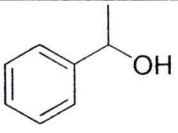
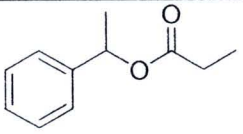
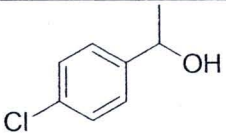
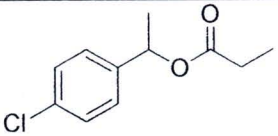
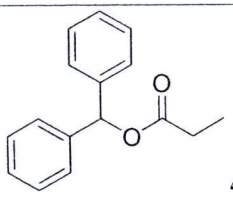
With all the requisite reagents **2a**, **12a**, **12b** and **22b** in hands, the acylation reactivity tests were performed under exactly the same condition for variety of alcohols. The times required for completion were monitored by TLC. Products were isolated and purified using standard method. Using **2a** as a reference compound, it

was found that all reagents gave esters in compairably high yields. The reaction time of **12a** and **12b** were unexpectedly longer than that of **2a** (60 min vs. 45 min) while **22b** underwent faster reaction than the reference compound **2a** (20 min vs. 45 min) (Table 2.3).

Table 2.3 Esterification of 1° and 2° alcohols with **2a**, **12a**, **12b** and **22b**



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

Reagent	Alcohol	Ester	Time (min.)	Yield
2a			30	95
12a			60	90
12b			60	90
22b	**3d**	**4d**	15	92
2a			45	85
12a			60	87
12b			60	86
22b	**3e**	**4e**	15	87
2a			45	95
12a			60	91
12b			60	93
22b	**3f**	**4f**	15	91
2a			45	72
12a			60	75
12b			60	76
22b	**3h**	**4h**	20	73
2a			45	85
12a			60	84
12b			60	85
22b	**3i**	**4i**	20	85
2a			45	75
12a			60	77
12b			60	77
22b	**3j**	**4j**	20	75

Visibly from Table 2.3, although **12a** and **12b** each contains two halogen atoms on the benzene ring, their reactivity as acylating agent for alcohol are perplexingly lessen while **22b** with only one carboethoxy group attached exhibits reactivity enhancement as expected. This finding led to a closer look at the reaction mechanism which suggests that the formation of the tetrahedral intermediate **25** showed be the rate determining step (Figure 2.25).

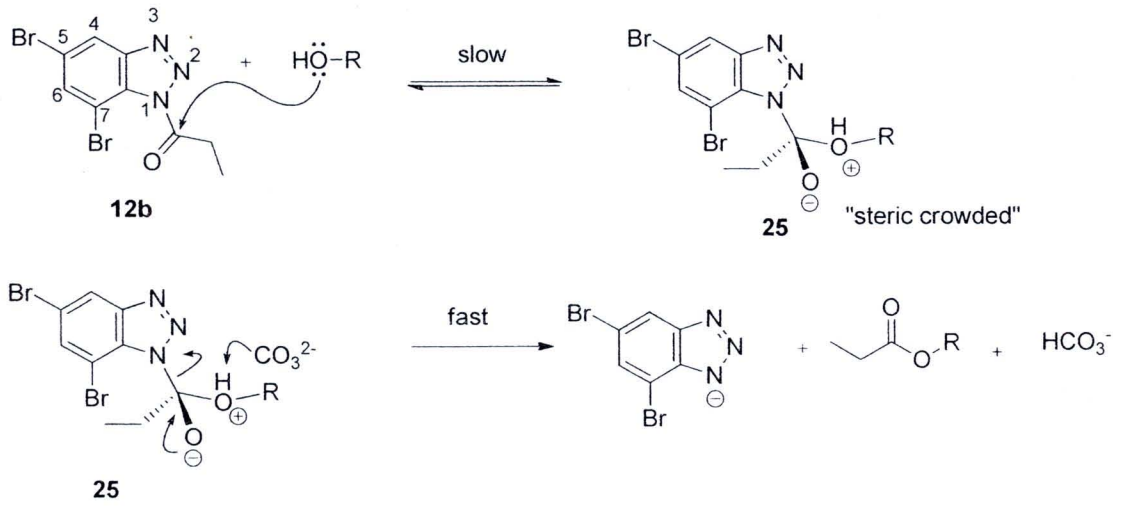


Figure 2.25 Mechanism of acylation of alcohol with **12b**

For the attack of a nucleophilic oxygen atom of an alcohol toward the carbonyl carbon atom of the acyl group of **12b** would be more difficult due to the steric hindrance from the halogen atom at position 7. Futhermore, **25** should become very crowded at the reaction site which would slow down the overall reaction as well. Contrasingly, when **22b** is subjected to nucleophlie attack in the same manner as **12b** no such hindrance should be encountered in **26**. Moreover, the carboxy group enhances the electrophilicity of the acyl group further and leads to a faster overall reaction (Figure 2.26).

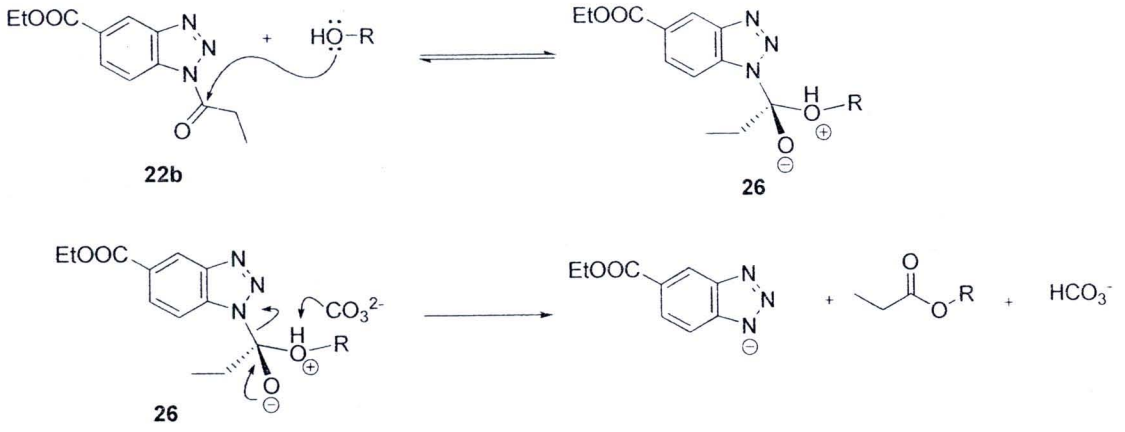


Figure 2.26 Mechanism of acylation of alcohol with **22b**