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Synthesis of *N*-acyl-benzotriazole using Mukaiyama reagent

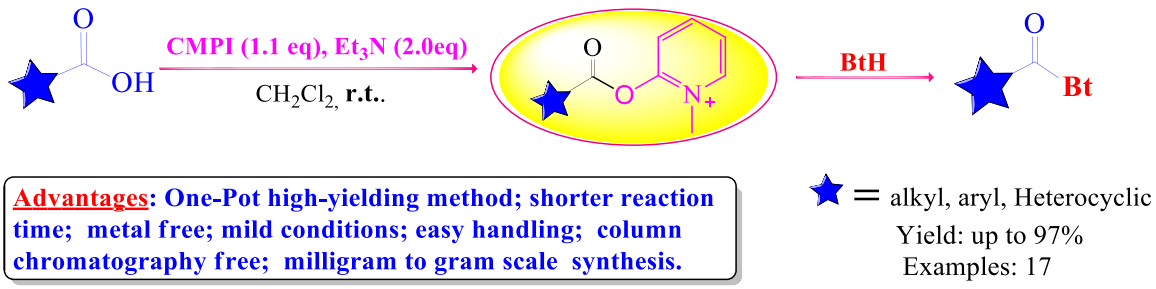
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Abstract

An unprecedented use of Mukaiyama reagent in the conversion of carboxylic acids into corresponding *N*-acyl benzotriazoles has been established with reliable and reproducible outcomes. Advantages associated with the developed method are easy handling, shorter reaction time, wide substrate scope and one-pot high-yielding reaction under mild conditions. Moreover, elimination of the column chromatography and use of green solvent make this procedure immensely useful for facile synthesis of *N*-acyl benzotriazole.



Keywords:*N*-acyl benzotriazole, benzotriazole, Mukaiyama reagent, coupling reaction

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Introduction

Ever since the introduction of the Mukaiyama reagent (2-chloro-1-methylpyridinium iodide, CMPI) in 1975 by Teruaki Mukaiyama for the synthesis of carboxylic esters[1], it has been employed as one of the most suitable and convenient reagents for hydroxyl group activation in carboxylic acids to synthesize various lactones[2], esters[3], ketenes[4-7], amides[8] and lactams[9]. This reagent is equally useful for synthesis of alkyl thiocyanates[10]and carbodimides[11] from corresponding alcohols and thioureas respectively[12].Furthermore, Mukaiyama reagent has been significantly used in peptide synthesis[13] and C-N bond formation in synthesis of 3-alkylquinazolin-4-ones[14] and dihydro quinazoline[15]. Very recently this reagent has been reported for a mild and facile synthesis of acyl sulphonamides from carboxylic acids and sulphonamides[16]. Easy synthesis of this reagent from 2-chloropyridine and methyliodide[17,18] further adds advantage to the use of Mukaiyama reagent in organic synthesis.

Research and efforts of previous decades have established *N*-Acyl benzotriazoles as a pharmacologically important moiety and a facile acylating reagent. This moiety is known to have antibacterial, anti-protozoal, antifungal, anti-cancer, anti-oxidative, anti-helmentic, anti-depressant, anti-corrosive, and anti-tubercular properties.[19-21] In synthetic chemistry, *N*-acyl benzotriazole is significant as the reliable substitute of acid chlorides under neutral and mild reaction conditions. Also, during reaction course, it forms highly stable reaction intermediates with substrate which undergo easy transformation towards desired final product.This moiety has given new dimensions to the benzotriazole methodology in organic synthesis[22-24] and shown its potential for *N*-, *O*-, *S*-, and *C*- acylation to produce esters, peptides, amides, acid azides, diketones, oxazolines and thiazolines.[25-40] Combining with Curtius rearrangement, *N*-acyl benzotriazole has been used for the synthesis of urea, carbamate, thiocarbamates and tetrazole also.[41,42] Benzotriazole ring cleavage strategy has also been successfully used for the facile synthesis of *N*-phenylamides and benzoxazoles.[43-46]

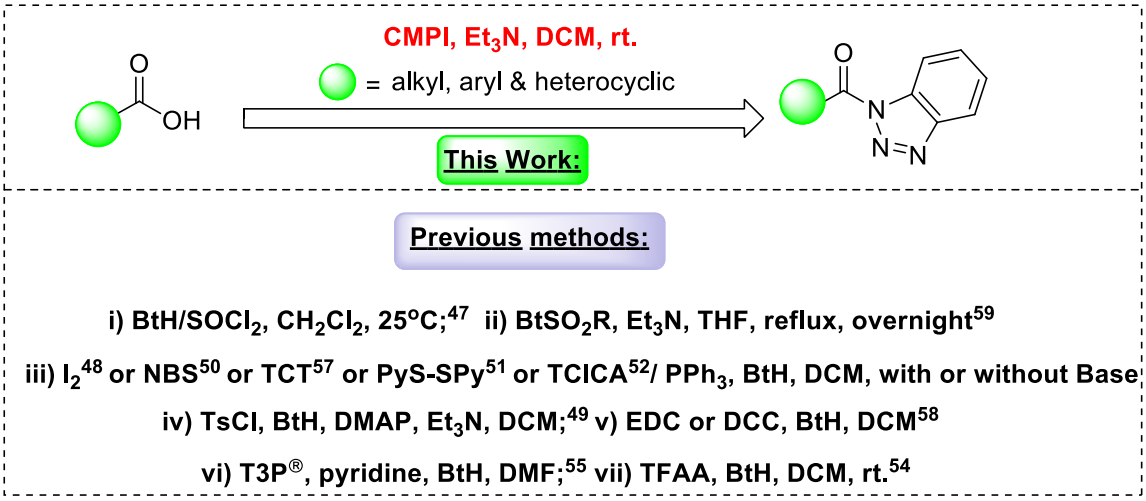


Figure 1. Common approaches for the synthesis of *N*-Acyl benzo- triazoles from carboxylic acids.

Even after so many advantages and versatility associated with *N*-acyl benzotriazole ring cleavage methodology, it falls one step back when it comes to the synthesis of *N*-acyl benzotriazoles as the starting material. All the synthetic routes reported till date for the acylation of benzotriazole at *N*-1 (Figure 1)[47-59] bear multiple downsides, such as, use of toxic reagents, application of an external base, tedious purification by column chromatography and low yield. To overcome these disadvantages, we started our search for a new reagent which can provide a mild, easy and high yielding approach for the synthesis of *N*-acyl benzotriazole

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contrary to previously reported reagents. Keeping in mind these requirements, we scrutinized Mukaiyama reagent as a better alternative and wished to report herein.

Results and Discussion

Considering the activation of carboxylic acid as the most crucial step in the synthesis of *N*-acyl benzotriazole, we intended to utilize Mukaiyama reagent as activating reagent. A comparative schematic diagram of carboxylic acid activation by previously reported reagents and our visionary approach for the same has been depicted in the Figure 2.

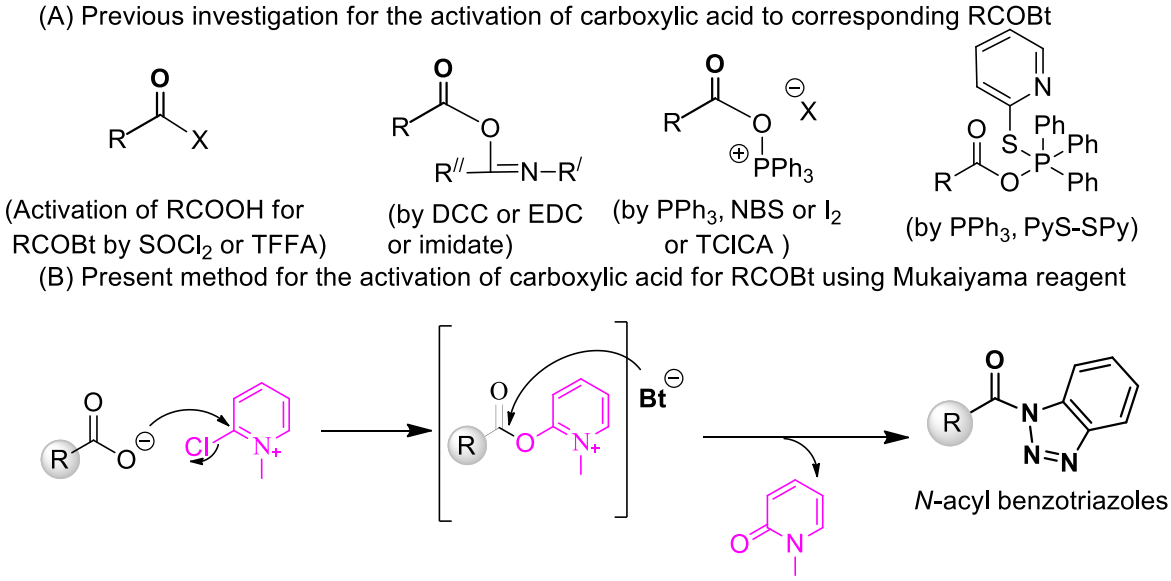
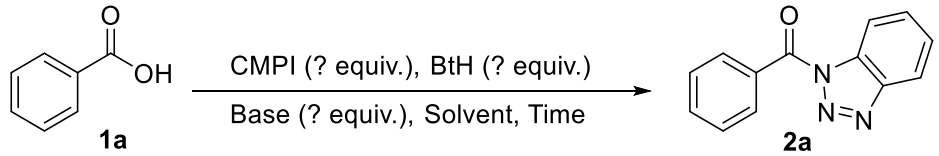


Figure 2. Schematic presentation of the previous activation methods for carboxylic acid and the present investigation to obtain *N*-acyl benzotriazoles.

To examine the validity of the projected utility of Mukaiyama reagent in the synthesis of *N*-acyl benzotriazoles, a pilot reaction was carried out with benzoic acid (1.0 equiv.) and Mukaiyama reagent (1.0 equiv.) in dry DCM. After 5 minutes stirring at room temperature, *1H*-benzotriazole (1.0 equiv.) was added to this reaction mixture and the resulting mass was stirred at room temperature. After 3 hours of stirring, the reaction did not move at all and showed only starting material spot on TLC and no desired product. We further added 1.0 eq of Et_3N and allowed the stirring for another 3 hours which resulted into formation of *N*-benzoyl benzotriazole **2a** in 57% yield. This experimental trial proved the necessity of an external base for the reaction.To achieve the most suitable condition for the proposed reaction, different combinations of solvent, temperature, time, amount of reagent and base were tried which have been summarized in table 1. Considering the quantity of reagents, the best yield was afforded with 1.1 equiv. of CMPI, 1.1 equiv. of BtH and 2.0 equiv. of Et_3N (entry 7, table 1). While the optimization of solvent conditions with the favorable reagent equivalents, dichloromethane, chloroform, toluene, tetrahydrofuran, and 2-Methyl tetrahydrofuran were found to show best results with comparable product yields (entries 7-13 table 1).

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Table 1. Reaction optimization study



entry[a]	CMPI (equiv.)	BtH (equiv.)	Base (equiv.)	Time hour	Solvent [b]	Yield (%) [c]
1	1.0	1.0	Et_3N (1.0)	3.0	DCM	57
2	1.0	1.0	Et_3N (1.5)	3.0	DCM	77
3	1.0	1.0	Et_3N (2.0)	3.0	DCM	87
4	1.0	1.0	Et_3N (2.5)	3.0	DCM	86
5	1.5	1.5	Et_3N (2.0)	3.0	DCM	91
6	1.2	1.2	Et_3N (2.0)	3.0	DCM	91
7	1.1	1.1	Et_3N (2.0)	3.0	DCM	91
8	1.1	1.1	Et_3N (2.0)	3.0	Toluene	87
9	1.1	1.1	Et_3N (2.0)	3.0	$CHCl_3$	91
10	1.1	1.1	Et_3N (2.0)	3.0	DMF	67
11	1.1	1.1	Et_3N (2.0)	3.0	THF	90
12	1.1	1.1	Et_3N (2.0)	3.0	Water	0
13	1.1	1.1	Et_3N (2.0)	3.0	2-meTHF	87
14	1.1	1.1	Et_3N (2.0)	1.0	DCM	90
15	1.1	1.1	Et_3N (2.0)	0.75	DCM	90
16	1.1	1.1	Et_3N (2.0)	0.5	DCM	91
17	1.1	1.1	Pyridine (2.0)	0.5	DCM	80
18	1.1	1.1	DIPEA (2.0)	0.5	DCM	87
19	1.1	1.1	K_2CO_3 (2.0)	3.0	DCM	89
20	1.1	1.1	KOH (2.0)	3.0	DCM	76

[a] Molar ratio: carboxylic acid (1.0 mmol), [b]dry solvents, [c]Yields reported after recrystallization.

Among the most preferable solvents for the reaction, i.e. dichloromethane, chloroform, toluene, tetrahydrofuran and 2-Methyl tetrahydrofuran, we intended to choose dichloromethane for its low boiling point and 2-Methyl tetrahydrofuran (biomass-derived) for its green aspects and high solubility for a large variety of carboxylic acids. After optimizing the equivalents of reagents and suitable solvent, the reaction was further optimized for the most preferable base and time. Et_3N was found to be the most apt base due to its low boiling point and homogeneity which reduces the reaction time and remaining base can be easily removed from reaction mixture after completion of reaction (entries 16-20, table 1). 30 minutes time was found to be appropriate for completion of reaction for good yield (entry 16, table 1).

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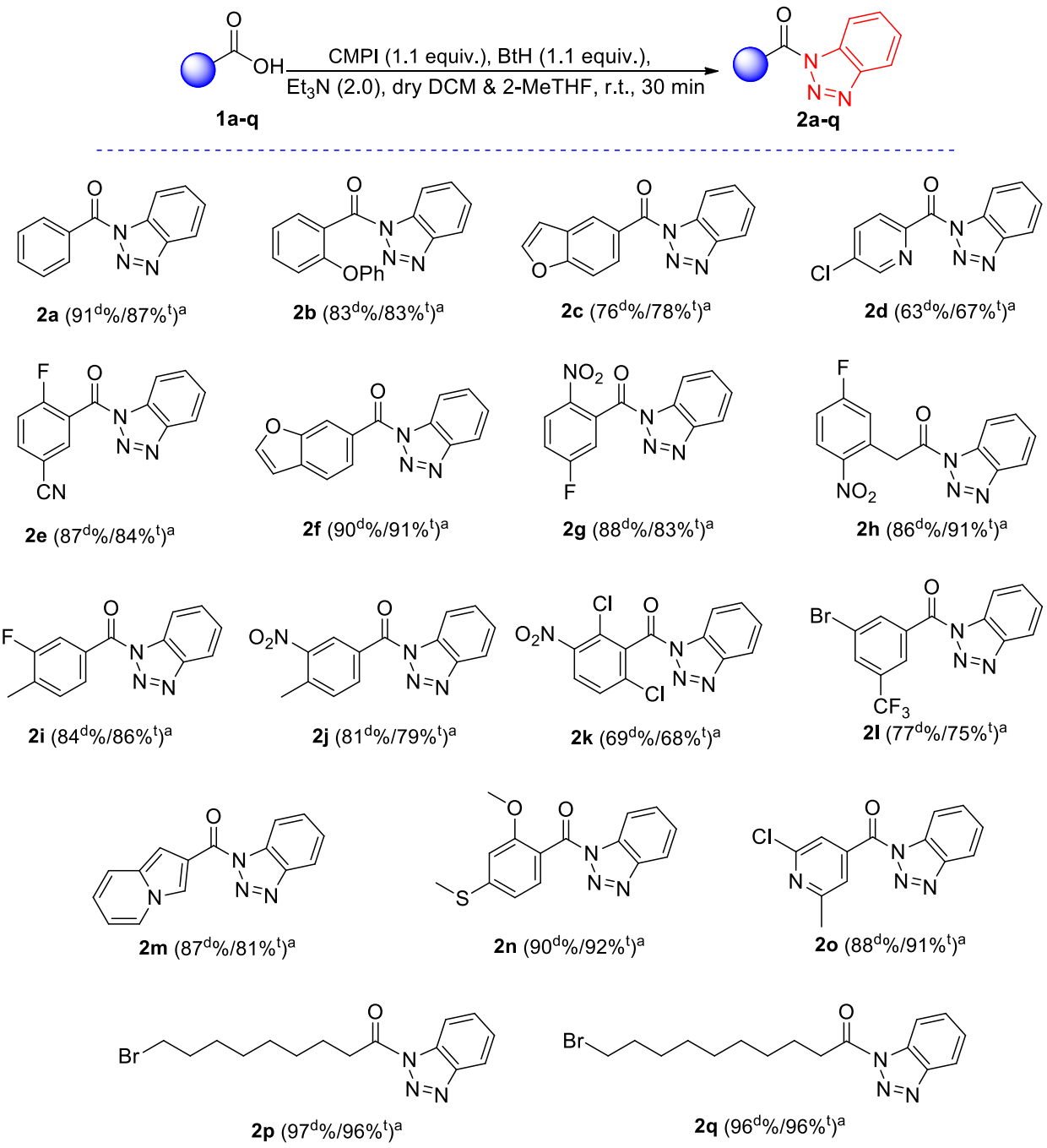


Figure 3. Molar ratios : carboxylicacids (**1a-q**) (1.0 equiv.), benzotriazole (1.1 equiv.), CMPI (1.1 equiv.) and Et_3N (2.0 eq),[a]Yields after recrystallization, [d]dry DCM, [t]dry 2-meTHF.

Further we evaluated the compatibility of our optimized reaction conditions with a variety of carboxylic acid substrate including aliphatic, aromatic and heterocyclic carboxylic acids. Results did not exhibit any interrelation of the product yield with the variation of substitution at aromatic ring or the length of the aliphatic chain of carboxylic acids. To our delight, all the final products (**2a-q**) did not require lengthy purification processes and could be easily recrystallized by methanol with good yields.

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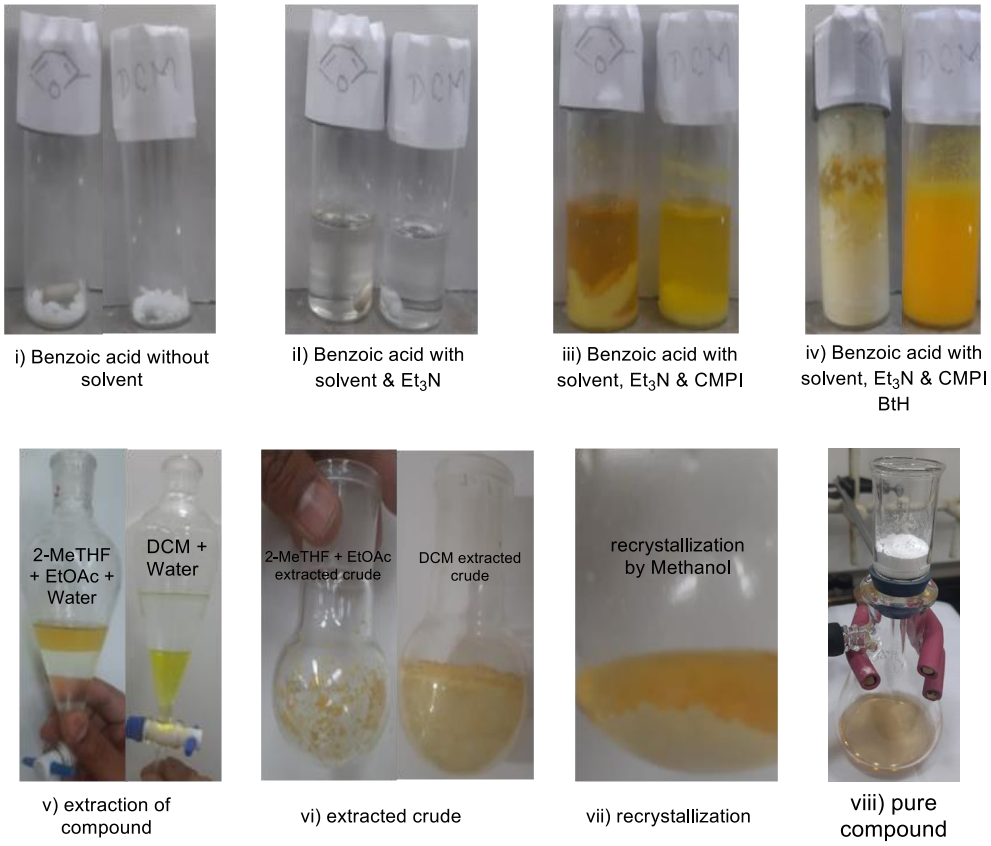


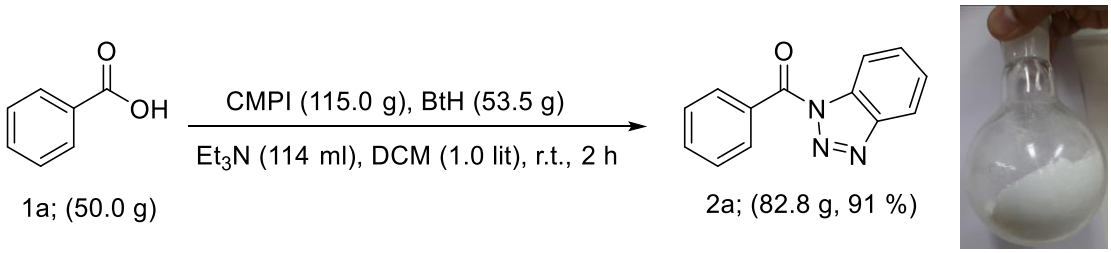
Figure 4. Physical changes during the course of reaction.

To verify the utility and simplicity of this method, we directed to illustrate the physical changes during the course of reaction. A small-scale reaction was set into a vial with white solid benzoic acid as starting material (Figure 4, image (i)). Then we added the solvent (DCM or 2-meTHF) and Et_3N to the vial and stirred for a minute to get a colorless solution (Figure 4, image (ii)). Addition of CMPI made the solution yellow colored within 5 minutes of addition as depicted in Figure 4 image (iii). When benzotriazole was added to this yellow solution, the reaction mass became turbid immediately which proved the formation of our desired product *N*-benzoyl benzotriazole (Figure 4, image (iv)). For work-up, a mixture of ethyl acetate/water was added in 2-meTHF containing reaction vial and the ethyl acetate layer was extracted and concentrated. On the other hand, DCM containing reaction vial was added only water and the DCM layer was extracted and concentrated (Figure 4, image (v) & (vi)). In the last the crude mass was recrystallized to afford final product (Figure 4, image (vii) & (viii)).

Application of the reaction in synthesis of *N*-Acyl benzotriazole in gram scale

We carried out a reaction with 50 gram benzoic acid as starting material for establishing the synthetic utility of the present method in large scale production of *N*-acyl benzotriazole. The reaction was found efficient to afford 91% yield of the final product **2a** in large scale also. Therefore, the efficacy of the protocol was shown in both milligram and gram scales (Scheme 1).

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Scheme 1. Gram scale Synthesis of *N*-acyl benzotriazole **2a** with present method.

Conclusions

Conclusively, we have developed an effective, facile, and dependable protocol to synthesize *N*-acylbenzotriazoles using Mukaiyama reagent. Use of 2-meTHF as solvent, no requirement of column purification and metal-free conditions make this approach green, cost effective, and low toxic. The method was found dependable for a broad spectrum of carboxylic acid substrates including aliphatic, aromatic and heterocyclic carboxylic acids with various substitutions and performs under very mild conditions to achieve good yields of *N*-acyl benzotriazoles in milligram to gram scale. The wide substrate scope, relevance and green approach of the reaction make this protocol a better alternative for the synthesis of a variety of *N*-acyl benzotriazoles which can be further explored in the lab synthesis, as well as, industrial production. Moreover, mild reaction conditions, no requirement of column chromatography and use of green solvent make this protocol convenient for beginners and students.

Experimental Section

General. All the starting materials and reagents were purchased from commercial source Sigma Aldrich, and Alfa Aesar. These materials were used without further purification or drying. Thin-layer chromatography (TLC) was performed on, pre-coated aluminium plates, and displayed with Ultraviolet lamp (λ_{max} = 254 nm).^{1}H, and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively by Bruker Avance NEO-400. Chemical shifts given in ppm downfield from residual solvent signal at 7.26 ppm for ^{1}H NMR and 77.16 ppm for ^{13}C NMR; *J* values in Hz. Infrared spectra recorded as Nujol mulls in KBr pellets.

General procedure for synthesis of *N*-acyl benzotriazoles

Triethyl amine (2.0 equiv.) was added into a solution of Acid **1a** (1.0 g, 1.0 equiv., 8.19 mmol) in dry DCM (50 mL) in a round bottom flask. CMPI (1.1 equiv.) was added at same temperature and stirred for 5 minutes. Then, 1*H*-Benzotriazole (1.1 equiv.) was added and, the resulting mixture was stirred for 30 minutes at room temperature. After completion of reaction (monitored by TLC), water (20 volume) was added, then stirred and organic layer was separated, concentrated under reduced pressure. Then, methanol (5 volume) was added in to resulting crude stirred this mixture for 10 minutes, filtered solid product and wash with fresh methanol (1 volume) through sintered glass funnel to obtained white solid product **2a** (91%) in pure form.

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Physical data of developed *N*-acyl benzotriazoles:

(1*H*-1,2,3-Benzotriazole-1-yl)-phenyl-methanone (2a).[54] White crystalline Solid, yield 1.66g (91%)[d]/ 1.58g (87%)[t]; R_f = 0.6 (5% ethyl acetate/n-hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41 (d, *J* = 8.0 Hz, 1H), 8.23-8.17 (m, 3H), 7.74-7.68 (m, 2H), 7.61-7.54 (m, 3H).

(1H-benzo[d][1,2,3]triazol-1-yl)(2-phenoxyphenyl)methanone (2b). White crystalline Solid, yield 1.22g (83%)[d]/ 1.21g (83%)[t]; m.p. 81-82 °C; R_f = 0.6 (5% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1716, 1587, 1477, 1449, 1369, 1290, 1230, 1052, 861, 747 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.73-7.71 (dd, *J* = 6.4 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.31-7.22 (m, 3H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.6, 156.5, 155.7, 146.1, 133.4, 131.4, 130.6, 130.3, 129.9, 126.3, 124.5, 124.4, 122.6. 120.2, 120.1, 117.5 and 114.5 ppm. HRMS: Calc. for $C_{19}H_{13}N_3O_2$ (M+H) $^+$: 316.1081; found: 316.1076.

(1H-benzo[d][1,2,3]triazol-1-yl)(benzofuran-5-yl)methanone (2c). White crystalline Solid, yield 1.23g (76%)[d]/ 1.26g (78%)[t]; m.p. 155-156 °C; R_f = 0.5 (5% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1708, 1536, 1488, 1449, 1362, 1319, 1270, 1226, 1120, 1045, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59(s, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.19 (t, *J* = 9.2 Hz, 2H), 7.76-7.66 (m, 3H), 7.56 (t, *J* = 7.6 Hz, 1H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.6, 157.8, 146.8, 145.8, 132.6, 130.3, 128.3, 127.5, 126.6, 126.4, 126.3, 120.2, 114.9, 111.7 and 107.4 ppm; HRMS: Calc. for $C_{15}H_{10}N_3O_2$ (M+H) $^+$: 264.0768; found: 264.0760.

(1H-benzo[d][1,2,3]triazol-1-yl)(5-chloropyridin-2-yl)methanone (2d). White crystalline Solid, yield 1.03g (63%)[d]/ 1.10g (67%)[t]; m.p. 114-115 °C; R_f = 0.6 (10% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1721, 1590, 1483, 1448, 1366, 1324, 1288, 1217, 1099, 1046, 941, 861, 747 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.80 (s, 1H), 8.37 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.96-7.93 (m, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1, 148.9, 147.7, 145.7, 136.4, 135.8, 131.9, 130.6, 127.2, 126.6, 120.3 and 114.4 ppm. HRMS: Calc. for $C_{12}H_8ClN_4O$ (M+H) $^+$: 259.0381; found: 259.0375.

3-(1H-benzo[d][1,2,3]triazole-1-carbonyl)-4-fluorobenzonitrile (2e). White crystalline Solid, yield 1.40g (87%)[d]/ 1.35g (84%)[t]; m.p. 187-188 °C; R_f = 0.5 (10% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 2236, 1699, 1607, 1492, 1452, 1417, 1380, 1325, 1289, 1248, 1174, 1035, 967, 917, 769, 755 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.38 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 4.4 Hz, 1H), 7.95 (bs, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.6, 162.0, 161.0, 146.3, 138.1, 138.0, 135.6, 135.5, 131.2, 127.2, 123.3, 123.1, 120.7, 118.4, 118.1, 116.9, 114.4, 109.4 and 109.3 ppm. HRMS: Calc. for $C_{14}H_8FN_4O$ (M+H) $^+$: 267.0677; found: 267.0652.

(1H-benzo[d][1,2,3]triazol-1-yl)(benzofuran-6-yl)methanone (2f). White crystalline Solid, yield 1.45g (90%)[d]/ 1.47g (91%)[t]; m.p. 145-146 °C; R_f = 0.5 (5% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1704, 1482, 1453, 1432, 1363, 1292, 1272, 1210, 1146, 1045, 1026, 900, 827, 779, 769, 747, 728 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.49 (s, 1H), 8.41 (d, *J* = 8.0 Hz, 1H), 8.20-8.18 (m, 2H), 7.86 (d, *J* = 2.0 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 154.1, 148.9, 145.8, 132.7, 132.6, 130.4, 127.2, 126.4, 126.3, 121.1, 120.2, 115.9, 114.9 and 107.0 ppm. HRMS: Calc. for $C_{15}H_{10}N_3O_2$ (M+H) $^+$: 264.0768; found: 264.0761.

(1H-benzo[d][1,2,3]triazol-1-yl)(5-fluoro-2-nitrophenyl)methanone (2g). White crystalline Solid, yield 1.36g (88%)[d]/ 1.28g (83%)[t]; m.p. 159-160 °C; R_f = 0.4 (10% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1713, 1587, 1527, 1485, 1381, 1345, 1292, 1271, 1231, 1048, 974, 851, 817, 773, 756, 742 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44-8.39 (m, 2H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.79-7.75 (m, 1H), 7.61-7.57 (m, 1H), 7.48-7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.8, 164.2, 163.7, 146.4, 132.6, 132.5, 131.2, 127.7, 127.6, 127.1, 120.6, 118.9, 118.7, 117.4, 117.1 and 114.3 ppm. HRMS: Calc. for $C_{13}H_8FN_4O_3$ (M+H) $^+$: 287.0575; found: 287.0564.

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1-(1H-benzo[d][1,2,3]triazol-1-yl)-2-(5-fluoro-2-nitrophenyl)ethanone (2h). White crystalline Solid, yield 1.29g (86%)[d]/ 1.37g (91%)[t]; m.p. 128-129 °C; R_f = 0.5 (10% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1731, 1589, 1517, 1482, 1449, 1382, 1341, 1251, 1167, 1073, 1060, 878, 847, 768, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.35-8.32 (m, 1H), 8.22-8.16 (m, 2H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.29-7.21 (m, 2H), 5.18 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 166.4, 156.7, 146.4, 132.3, 132.2, 131.2, 130.9, 128.7, 128.6, 126.6, 121.1, 120.8, 120.5, 116.4, 116.2, 114.4 and 41.7 ppm. HRMS: Calc. for $C_{14}H_{10}FN_4O_3$ (M+H) $^+$: 301.0731; found: 301.0729.

(1H-benzo[d][1,2,3]triazol-1-yl)(3-fluoro-4-methylphenyl)methanone (2i).

White crystalline Solid, yield 1.39g (84%)[d]/ 1.42g (86%)[t]; m.p. 110-111 °C; R_f = 0.5 (5% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1707, 1484, 1452, 1414, 1367, 1255, 1231, 1150, 1121, 1051, 981, 917, 823, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.38 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.99 (m, 2H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 162.0, 159.6, 145.8, 132.4, 132.0, 131.8, 131.6, 131.5, 130.7, 130.5, 127.7, 127.6, 126.5, 120.3, 118.6, 118.3, 114.9, 15.1 and 15.0 ppm. HRMS: Calc. for $C_{14}H_{11}FN_3O$ (M+H) $^+$: 256.0881; found: 256.0877.

(1H-benzo[d][1,2,3]triazol-1-yl)(4-methyl-3-nitrophenyl)methanone (2j).

White crystalline Solid, yield 1.26g (81%)[d]/ 1.23g (79%)[t]; m.p. 167-168 °C; R_f = 0.5 (10% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1709, 1615, 1526, 1485, 1381, 1320, 1231, 1052, 976, 916, 852, 765, 749, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.87 (s, 1H), 8.41-8.37 (m, 2H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.60-7.56 (m, 2H), 2.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.3, 149.1, 145.8, 139.4, 135.5, 133.1, 132.1, 130.9, 130.5, 128.2, 126.8, 120.5, 114.8 and 20.9 ppm. HRMS: Calc. for $C_{14}H_{11}N_4O_3$ (M+H) $^+$: 283.0826; found: 283.0819.

(1H-benzo[d][1,2,3]triazol-1-yl)(2,6-dichloro-3-nitrophenyl)methanone (2k).

White crystalline Solid, yield 0.98g (69%)[d]/ 0.97g (68%)[t]; m.p. 164-165 °C; R_f = 0.5 (10% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1719, 1583, 1563, 1530, 1485, 1452, 1380, 1347, 1160, 1139, 961, 861, 842, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.44 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 7.6 Hz, 1H), 8.08 (d, *J* = 7.2 Hz, 1H), 7.80 (t, *J* = 7.6 Hz, 1H), 7.65-7.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.5, 146.6, 136.9, 136.2, 131.4, 131.0, 130.6, 129.0, 127.9, 127.4, 126.6, 120.8 and 114.3 ppm. HRMS: Calc. for $C_{13}H_7Cl_2N_4O_3$ (M+H) $^+$: 336.9890; found: 336.9871.

(1H-benzo[d][1,2,3]triazol-1-yl)(3-bromo-5-(trifluoromethyl)phenyl)methanone (2l).

White crystalline Solid, yield 1.06g (77%)[d]/ 1.03g (75%)[t]; m.p. 101-102 °C; R_f = 0.5 (10% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1707, 1605, 1484, 1451, 1382, 1314, 1289, 1219, 1185, 1125, 884, 752, 686 cm^{-1}; R_f = 0.6 (10% ethyl acetate/n-hexane); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.51 (d, *J* = 1.6 Hz, 1H), 8.43-8.37 (m, 2H), 8.21 (m, 1H), 8.19 (m, 1H), 7.78-7.74 (m, 1H), 7.67-7.58 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.0, 145.9, 137.8, 134.1, 133.3-133.1 (m, 1C), 133.0, 132.6, 132.3, 132.1, 131.4, 127.3-127.2 (1C), 127.0, 124.0, 123.3, 121.3, 120.6 and 114.8 ppm. HRMS: Calc. for $C_{14}H_8BrF_3N_3O$ (M+H) $^+$: 369.9797; found: 369.9782.

(1H-benzo[d][1,2,3]triazol-1-yl)(indolizin-2-yl)methanone (2m).

White crystalline Solid, yield 1.41g (87%)[d]/ 1.31g (81%)[t]; m.p. 167-168 °C; R_f = 0.5 (10% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1682, 1484, 1447, 1395, 1340, 1288, 1180, 1063, 853, 810, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.56 (s, 1H), 8.65 (d, *J* = 8.0 Hz, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 6.8 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 9.2 Hz, 1H), 7.34 (s, 1H), 6.75-6.71 (m, 1H), 6.60 (t, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.4, 145.7, 132.7, 132.5, 130.2, 126.1, 125.7, 120.6, 120.1, 119.6, 119.2, 118.9, 115.1 and 113.3 ppm. HRMS: Calc. for $C_{15}H_{11}N_4O$ (M+H) $^+$: 263.0927; found: 263.0998.

(1H-benzo[d][1,2,3]triazol-1-yl)(2-methoxy-4-(methylthio)phenyl)methanone (2n).

White crystalline Solid, yield 1.35g (90%)[d]/ 1.38g (92%)[t]; m.p. 97-98 °C; R_f = 0.5 (5% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1708, 1591, 1556, 1482, 1445, 1399, 1363, 1249, 1149, 1020, 934, 893, 747 cm^{-1}; R_f = 0.6 (10% ethyl acetate/n-hexane); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.37 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 8.0

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Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.90 (s, 1H), 3.78 (s, 3H), 2.56 (s, 3H), ; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.3, 158.4, 146.8, 146.1, 131.6, 131.3, 130.2, 126.1, 120.1, 118.8, 117.0, 114.5, 108.9, 55.9 and 15.1 ppm. HRMS: Calc. for $C_{15}H_{13}N_3O_2S$ $(M+Na)^+$: 322.0621; found: 300.0585.

(1H-benzo[d][1,2,3]triazol-1-yl)(2-chloro-6-methylpyridin-4-yl)methanone (2o).

White crystalline Solid, yield 1.40g (88%)[d]/ 1.45g (91%)[t]; m.p. 163-164 °C; R_f = 0.5 (10% ethyl acetate/*n*-hexane); IR (KBr):ν_{max} 1707, 1597, 1542, 1485, 1451, 1377, 1290, 1274, 1164, 1039, 997, 962, 865, 748 cm^{-1}; R_f = 0.6 (10% ethyl acetate/n-hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39 (d, *J* = 8.4 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 7.86 (s, 1H), 7.78-7.74 (m, 2H), 7.61 (t, *J* = 7.6 Hz, 1H), 2.69 (s, 3H), ; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.3, 160.5, 151.3, 145.9, 141.7, 131.8, 131.2, 127.1, 122.6, 122.3, 120.6, 114.7 and 24.5 ppm. HRMS: Calc. for $C_{13}H_{10}ClN_4O$ $(M+H)^+$: 273.0538; found: 273.0529.

1-(1H-benzo[d][1,2,3]triazol-1-yl)-9-bromononan-1-one (2p).[54]

White crystalline Solid, yield 1.39g (97%)[d]/ 1.37g (96%)[t]; R_f = 0.6 (3% ethyl acetate/n-hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 3.46-3.41 (m, 4H), 1.96-1.84 (m, 4H), 1.59-1.36 (m, 8H).

1-(1H-benzo[d][1,2,3]triazol-1-yl)-10-bromodecan-1-one (2q).[54]

White crystalline Solid, yield 1.35g (96%)[d]/ 1.34g (96%)[t]; R_f = 0.6 (3% ethyl acetate/n-hexane); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 7.6 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 3.44-3.38 (m, 4H), 1.94-1.81 (m, 4H), 1.56-1.37 (m, 10H).

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Supplementary Material

Characterization data (for all the developed acyl benzotriazoles) including copies of ^{1}H and ^{13}C NMR spectra associated with this paper can be found in the online version.

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