Ring and side chain reactivities of 1-([1,3,4]oxadiazol-2-ylmethyl)-1*H*-benzotriazoles

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Submitted in honor of the 70th birthday of Fritz Sauter, Emeritus Professor at the Technical University of Vienna, in friendship, respect, and admiration for his success in forging international contacts between chemists as exemplified by the "Blue Danube Symposia" and the "Ibn Sina" Conferences
(received 03 Nov 00; accepted 30 Oct 01; published on the web 07 Nov 01)

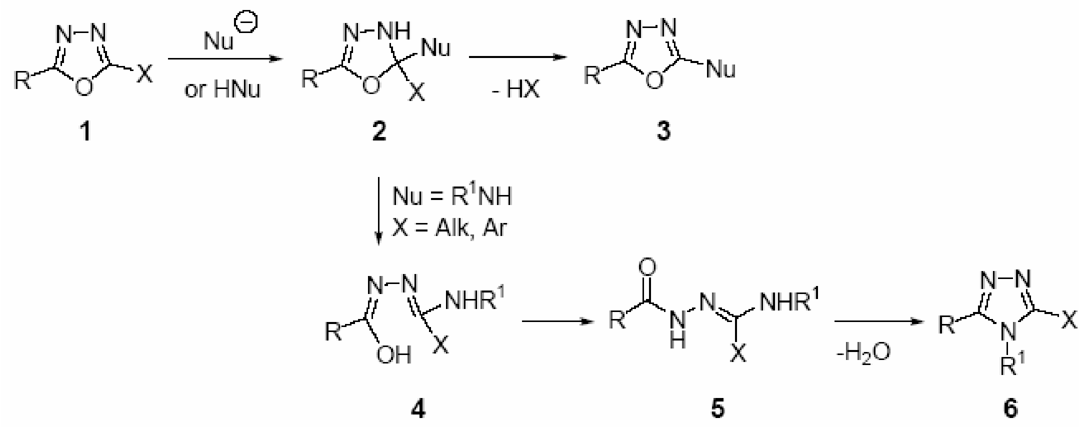
Abstract
1-([1,3,4]Oxadiazol-2-ylmethyl)-1*H*-benzotriazoles **10a-d** and 1-([1,2,4]triazol-3-ylmethyl)-1*H*-benzotriazoles **15a,b** are synthesized and used for side chain elaboration.

Keywords: Heteroaromatics, α-benzotriazolylmethyl, [1,3,4] oxadiazole, [1,2,4] triazole, synthesis, reactivity

Introduction

Nucleophilic attack at ring carbon is a major reaction mode of [1,3,4]oxadiazoles **1**.[1a,b] Such reactions (Scheme 1) lead *via* **2** to nucleophilic displacement products **3** or to the ring cleavage with the formation of intermediates **4** and **5**,[2a,b] which, in the case of *N*-nucleophiles, frequently recyclise into [1,2,4]triazoles **6**.[3a-c] *C*-Alkyl side chain transformations are less common because of the inclination of 2-alkyl derivatives to dimerisation upon lithiation[4] and of the acid and base sensitivity of [1,3,4]oxadiazole rings. However, activated 2(5) methylene groups undergo facile electrophilic substitution.[5]

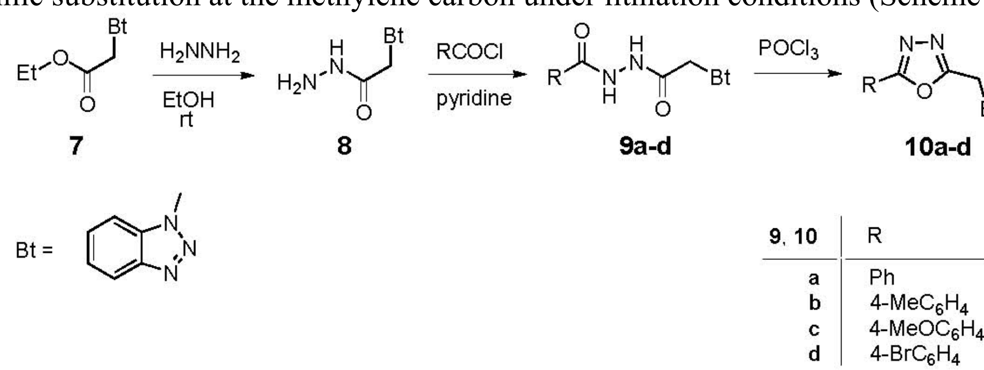
We recently synthesized α-benzotriazolylmethyl heteroaromatics containing advantageously activated methylene groups in thiophene,[6a-c] benzothiophene,[7] indole and pyrrole,[8a,b] benz(thia)oxazole,[9] and indolizine and imidazo[1,2-*a*]pyridine[10] ring systems. The present study of 1-([1,3,4]oxadiazol-2-ylmethyl)-1*H*-benzotriazoles **10** offers an efficient method of methylene group activation for acid and base sensitive [1,3,4]oxadiazoles. The reactivity of such novel intermediates was investigated in two key types of transformations: (i) electrophilic substitution at the 2-methylene carbon and (ii) nucleophilic substitution at the ring 2-carbon (*cf.* **10**).



Scheme 1

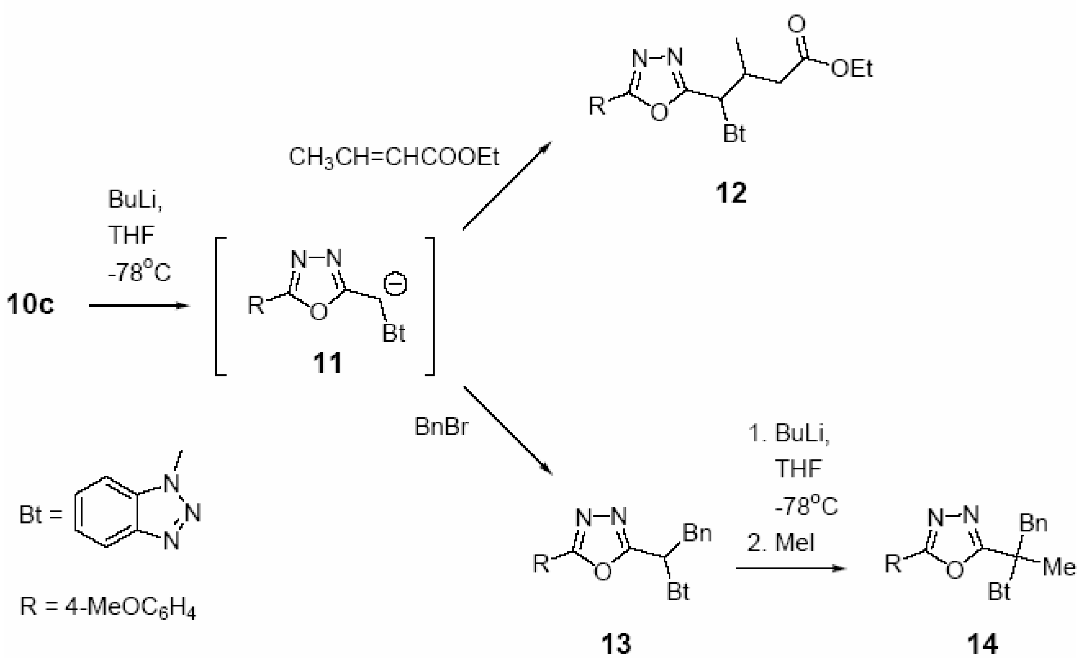
Results and Discussion

1-([1,3,4]Oxadiazol-2-ylmethyl)-1*H*-benzotriazoles **10a-d** are readily available from the known ester **7**[11] *via* the hydrazide **8** and unsymmetrical diacylhydrazines **9**. Compound **10c** underwent electrophilic substitution at the methylene carbon under lithiation conditions (Scheme 3).



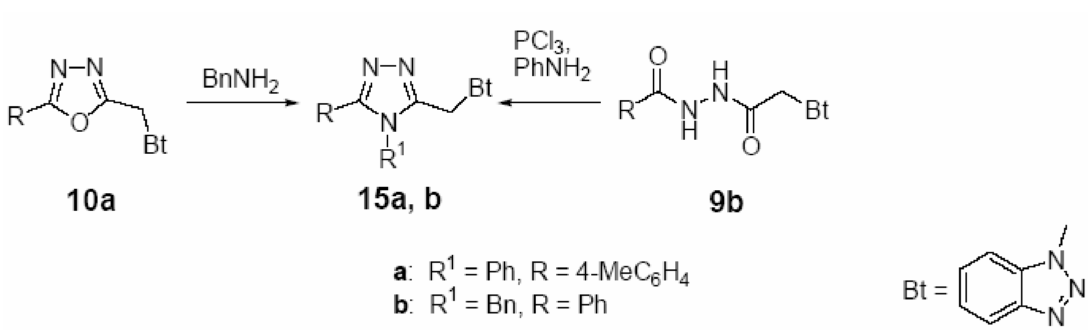
Scheme 2

Michael-type reaction of anion **11** with ethyl crotonate yielded the corresponding ester **12** (82%, E = $CH(CH_3)CH_2COOEt$) (Scheme 3). Alkylation of **11** with benzyl bromide afforded the derivative **13** in 85% yield, which was further successfully transformed under the similar reaction conditions into the disubstituted compound **14** (65%). Surprisingly, attempted reactions of anions derived from **10a,c** with oxiranes and trimethylsilyl chloride did not lead to the expected substitution products and the starting materials **10a,c** were recovered in 70-80% yields. Such stability of the oxadiazole moiety under lithiation conditions prompted us to investigate methods for elimination of the benzotriazolyl group. Surprisingly, weaker bases and higher temperatures (*t*-BuOK, BuOH, reflux for **13** and **14**; *t*-BuOK, BuOH, reflux or $ZnBr_2$, THF, reflux for **13**) did not yield the expected 3-alkenyloxadiazoles but led to oxadiazole ring cleavage.



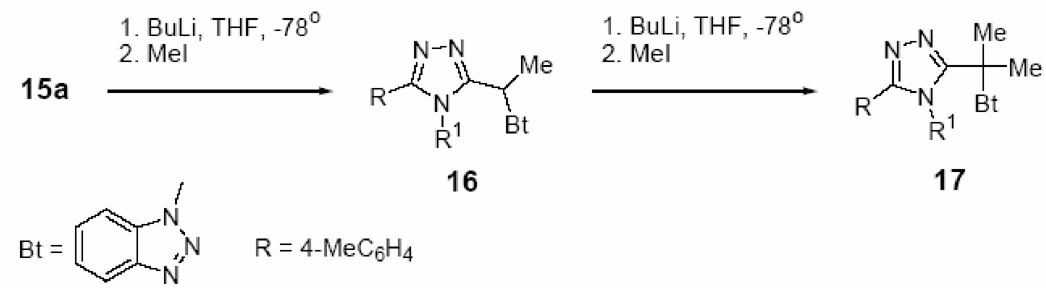
Scheme 3

We further studied nucleophilic substitution at the ring 2-carbon of **10a** (Scheme 4). The reaction with benzylamine in *n*-butanol gave 1-[(4-benzyl-5-phenyl-4*H*-[1,2,4]triazol-3-yl)methyl]-1*H*-benzotriazole (**15b**) in 41% yield. Analogous treatment with substituted anilines did not afford the expected 4-aryl[1,2,4]triazoles. Alternatively, dihydrazide **9b** was converted into [1,2,4]-triazole **15a** in 86% yield.



Scheme 4

Generation of the benzotriazole stabilized anion from **15a** under lithiation conditions and its trapping with methyl iodide yielded derivative **16** (67%), which was further converted under similar conditions into **17** in 91% yield (Scheme 5). Both steps demonstrated the high stability of [1,2,4]-triazole ring in lithiation reactions, similar to [1,3,4]oxazole systems **10** and **12**. However, attempted reactions of compounds **15-17** with methyl and phenyl magnesium halides did not lead neither to the cleavage of the triazole ring nor to the displacement of the benzotriazole moiety.



Scheme 5

In conclusion, syntheses of 1-([1,3,4]oxadiazol-2-ylmethyl)-1*H*-benzotriazoles **10a-d** and 1-([1,2,4]triazol-3-ylmethyl)-1*H*-benzotriazoles **15a,b** are described and their side chain transformations were investigated.

Experimental Section

General Procedures. Melting points were determined on a MEL-TEMP capillary melting point apparatus equipped with a Fluka 51 digital thermometer. NMR spectra were taken in DMSO-d_6 with tetramethylsilane as the internal standard for ^{1}H (300 MHz) or a solvent as the internal standard for ^{13}C (75 MHz). THF was distilled from sodium/benzophenone under nitrogen immediately prior to use. All reactions with air-sensitive compounds were carried out under argon atmosphere. Column chromatography was conducted on silica gel 230-400 mesh. Hexanes were used as the mixture of hexane isomers and methylcyclopentane from Fisher (A.C.S. reagent grade) in the preparation of eluents for column chromatography.
2-(1*H*-benzotriazol-1-yl)acetohydrazide (**8**) was synthesized according to the known procedure. [12]

General procedure for the preparation of 9a-d
A mixture of 2-(benzotriazol-1-yl)acetohydrazide (**8**) (0.96 g, 5 mmol) and the corresponding acyl chloride (5 mmol) in pyridine (10 mL) was stirred at room temperature for 6 h. The reaction mixture was poured into ice-cold dilute hydrochloric acid. The solid product was filtered off and washed with diethyl ether to give analytically pure compounds **9a-d**.
2-(1*H*-Benzotriazol-1-yl)-*N*'-benzoylacetohydrazide (9a). Colorless plates, 0.75 g, 52%, mp 233 - 235 °C; ^{1}H NMR: δ 10.67 (br s, 1H), 10.58 (br s, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.95-7.85 (m, 3H), 7.61-7.40 (m, 5H), 5.64 (s, 2H); ^{13}C NMR: δ 165.5, 165.2, 145.1, 133.7, 132.2, 132.0, 128.5, 127.5, 124.0, 119.0, 111.0, 48.7. Anal. Calcd for $C_{15}H_{13}N_5O_2$: C, 61.01; H, 4.44; N, 23.72. Found: C, 61.02; H, 4.32; N, 24.02.
2-(1*H*-Benzotriazol-1-yl)-*N*'-(4-methylbenzoyl)acetohydrazide (9b). Colorless microcrystals, 1.43 g, 93%, mp 254 - 256 °C; ^{1}H NMR: δ 10.68 (br s, 1H), 10.54 (br s, 1H), 8.08 (d, *J* = 7.7 Hz, 1H), 7.96-7.80 (m, 3H), 7.60 (t, *J* = 6.2 Hz, 1H), 7.47-7.41 (m, 1H), 7.30 (d, *J* = 7.0 Hz, 2H), 5.66 (s, 2H), 2.36 (s, 3H).; ^{13}C NMR: δ 165.6, 165.4, 145.2, 142.1, 133.8, 129.1, 127.7, 126.8,

124.1, 119.2, 118.0, 111.0, 48.8, 21.1. Anal. Calcd for $C_{16}H_{15}N_5O_2$: C, 62.13; H, 4.89; N, 22.64. Found: C, 62.03; H, 4.84; N, 22.77.

2-(1*H*-Benzotriazol-1-yl)-*N*'-(4-methoxybenzoyl)acetohydrazide (9c). Colorless plates, 1.45 g, 95%, mp 244-245 °C; ^{1}H NMR: δ 10.52 (br s, 2H), 8.06 (d, *J* = 7.3 Hz, 1H), 7.85 (d, *J* = 8.8 Hz, 3H), 7.58 (dd, *J* = 6.1, 4.9 Hz, 1H), 7.42 (dd, *J* = 6.1, 4.9 Hz, 1H), 7.02 (d, *J* = 7.0 Hz, 2H), 5.62 (s, 2H), 3.81(s, 3H); ^{13}C NMR: δ 165.3, 165.0, 162.1, 145.1, 133.7, 129.4, 127.4, 124.3, 124.0, 119.1, 113.7, 111.0, 55.4, 48.7. Anal. Calcd for $C_{16}H_{15}N_5O_3$: C, 59.07; H, 4.65; N, 21.53. Found: C, 58.69; H, 4.53; N, 21.47.

2-(1*H*-Benzotriazol-1-yl)-*N*'-(4-bromobenzoyl)acetohydrazide (9d). Brown plates, 1.22 g, 68%, mp 264 - 266 °C; ^{1}H NMR: δ 10.82 - 10.66 (m, 2H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.89-7.70 (m, 5H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.42 (t, *J* = 7.3 Hz, 1H), 5.65 (s, 2H); ^{13}C NMR: δ 165.2, 164.6, 145.1, 133.6, 131.6, 131.2, 129.5, 127.4, 125.7, 124.0, 119.1, 110.9, 48.6. HRMS (M+1 FAB) Calcd for $C_{15}H_{12}BrN_5O_2$: 374.0252 (M+1). Found: 374.0253.

General procedure for the preparation of 10a-d

2-(1*H*-Benzotriazol-1-yl)-*N*′-acylacetohydrazides (**9a-d**) (5 mmol) were refluxed with phosphorus oxychloride (6 mL) for 6 h on water-bath. The reaction mixtures were allowed to cool, and poured into ice-cold water. The solid products were filtered off, and recrystallized from ethanol to give **10a-d**.

1-[(5-Phenyl[1,3,4]oxadiazol-2-yl)methyl]-1*H*-benzotriazole (10a). Gray plates, 0.75 g, 51%, mp 133-135 °C; ^{1}H NMR: δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 7.1 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.57-7.40 (m, 5H), 6.17 (s, 2H); ^{13}C NMR: δ 166.2, 160.0, 146.3, 132.7, 132.3, 129.1, 128.4, 127.1, 124.6, 122.9, 120.4, 109.3, 42.6. Anal. Calcd for $C_{15}H_{11}N_5O$: N, 25.26. Found: N, 25.21.

1-{[5-(4-Methylphenyl)[1,3,4]oxadiazol-2-yl]methyl}-1*H*-benzotriazole (10b). Plates, 0.98 g, 72%, mp 167-169 °C; ^{1}H NMR: δ 8.08 (d, *J* = 8.3 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.56 (t, *J* = 7.1 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 2H), 6.21 (s, 2H), 2.40 (s, 3H); ^{13}C NMR: δ 165.8, 159.6, 145.7, 142.6, 132.4, 129.4, 128.8, 128.0, 126.6, 124.2, 119.7, 109.2, 42.1, 21.3. Anal. Calcd for $C_{16}H_{13}N_5O$: N, 24.04. Found: N, 23.88.

1-{[5-(4-Methoxyphenyl)[1,3,4]oxadiazol-2-yl]methyl}-1*H*-benzotriazole(10c). Yellow plates, 1.11 g, 75%, mp 152-153 °C; ^{1}H NMR: δ 8.10 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 4.8 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.54 (t, *J* = 6.0, 1H), 7.42 (t, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 4.8 Hz, 2H), 6.15 (s, 2H), 3.85 (s, 3H).; ^{13}C NMR: δ 166.2, 162.7, 159.4, 146.2, 132.7, 128.9, 128.4, 124.5, 120.3, 115.3, 114.5, 109.4, 55.4, 42.6. Anal. Calcd for $C_{16}H_{13}N_5O_2$: C, 62.53; H, 4.26; N, 22.79. Found: C, 62.15; H, 4.21; N, 22.59.

1-{5-(4-Bromophenyl)[1,3,4]oxadiazol-2-yl]methyl}-1*H*-benzotriazole (10d). Pale yellow plates, 23%, mp 167-168 °C; ^{1}H NMR: δ 8.10 (d, *J* = 8.3 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.62(d, *J* = 8.5 Hz, 2H), 7.56 (t, *J* = 8.1 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 6.16 (s, 2H); ^{13}C NMR: δ 165.6, 160.2, 146.2, 139.3, 132.5, 131.9, 131.1, 128.5, 127.2, 124.7, 120.4, 109.3, 42.5. Anal. Calcd for $C_{15}H_{10}N_5O$: N, 19.66. Found: N, 19.89.

1-{1-[5-(4-Methoxyphenyl)[1,3,4]oxadiazol-2-yl]-2-phenylethyl}-1*H*-benzotriazole (13). To a solution of **10c** (0.34 g, 1.1 mmol) in THF (40 mL), a solution of *n*-BuLi (1.5 mmol, 1.8 mL, 1.5 M solution in hexanes) was added at −78 °C. The resulting mixture was stirred at this temperature for 30 min. Then a solution of benzyl bromide (1.1 mmol) in THF (10 mL) was added, and the reaction mixture was stirred at −78 °C for 12 h. Saturated NH_4Cl solution (100 mL) was added, and the mixture was extracted with ethyl acetate (100 mL). The organic phase was separated, washed with saturated NH_4Cl solution (3 x 50 mL), and dried ($MgSO_4$). Evaporation of the solvent followed by column chromatography, using hexanes/ethyl acetate (4:1) as an eluent, gave the desired product. Yellow oil (85%); ^{1}H NMR: δ 8.04 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 8.8 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 1H), 7.45 (t, *J* = 9.2 Hz, 1H), 7.36 (t, *J* = 6.0 Hz, 1H), 7.20-7.09 (m, 5H), 6.94 (d, *J* = 9.1 Hz, 2H), 6.51 (dd, *J* = 8.7, 7.0 Hz, 1H), 4.13-3.97 (m, 2H), 3.84 (s, 3H); ^{13}C NMR: δ 165.8, 162.6, 161.9, 146.2, 134.8, 132.3, 129.0, 128.9, 128.8, 128.0, 127.5, 124.3, 120.2, 115.4, 114.4, 109.7, 56.6, 55.4, 37.8. HRMS (M+1 FAB) Calcd for $C_{23}H_{19}N_5O_2$: 398.1617 (M+1) Found: 398.1619.

Ethyl 4-(1*H*-benzotriazol-1-yl)-4-[5-(4-methoxyphenyl)-[1,3,4]-oxadiazol-2-yl]-3-methylbutanoate (12). To a solution of **10c** (0.95 g, 3.1 mmol) in THF (50 mL), a solution of LDA (3.5 mmol, 2.1 mL, 1.5 M solution in hexanes) was added at −78 °C. The solution was stirred at this temperature for 30 min. Then a solution of ethyl (*E*)-2-butenoate (3.1 mmol, 0.38 mL) in THF (10 mL) was added. The reaction mixture was stirred at −78 °C for 16 h. Saturated NH_4Cl solution (100 mL) was added, and the mixture was extracted with ethyl acetate (100 mL). The organic phase was separated, washed with saturated NH_4Cl solution (3 x 50 mL), and dried ($MgSO_4$). Evaporation of the solvent followed by column chromatography, using hexanes/ethyl acetate (4:1) as an eluent, gave the desired product. Yellow oil, 70%; ^{1}H NMR: δ 8.08 (dd, J = 5.2, 7.3Hz, 1H), 7.92 (m, 2H), 7.79 (dd, J = 8.5, 15.6 Hz, 1H), 7.56-7.49 (m, 1H), 7.40 (t, J = 7.1 Hz, 1H), 6.95 (dd, J =3.9, 10.8 Hz, 2H), 6.46 (dd, J = 10.0, 1.0 Hz, 1H), 4.14 (q, J = 7.3 Hz, 2H), 4.01 (q, J = 7.3 Hz, 1H), 3.85 [3.82] (s, 3H), 3.72-3.57 (m, 1H), 2.72-2.56 (m, 1H), 2.38-2.11 (m, 1H), 1.38-1.23 (m, 3H), 0.94.2 (d, J = 6.7 Hz, 2H); ^{13}C NMR: δ 171.2, 165.8, 162.7, 161.4, 146.2, 132.5, 129.0, 128.2, 124.5, 120.3, 115.5, 114.4, 110.2, 60.7, 60.4, 58.8, 58.4, 55.4, 37.8, 36.8, 32.7, 21.0, 17.0, 16.4, 14.1. Anal. Calcd for $C_{22}H_{23}N_5O_4$: C, 62.70; H, 5.50;. Found: C, 62.46; H, 5.86.

1-{1-[5-(4-Methoxyphenyl)[1,3,4-oxadiazol-2-yl]-1-methyl-2-phenylethyl}-1*H*-benzotriazole (14). A solution of *n*-BuLi (0.6 mmol, 0.9 mL, 1.5 M solution in hexanes) was added to a solution of **13** (0.21 g, 0.5 mmol) in THF (40 mL) at −78 °C. The solution was stirred at this temperature for 30 min. Then a solution of methyl iodide (0.5 mmol) in THF (5 mL) was added, the reaction mixture was stirred at −78 °C for 12 h. Saturated NH_4Cl solution (50 mL) was added, and the reaction mixture was extracted with ethyl acetate (100 mL). The organic phase was separated, washed with saturated NH_4Cl solution (3 x 50 mL), and dried ($MgSO_4$). Evaporation of the solvent followed by column chromatography, using hexanes/ethyl acetate (4:1) as an eluent, gave the product. Yellow oil, 65%; ^{1}H NMR: δ 8.12-8.08 (m, 1H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.38-7.32 (m, 2H), 7.30-7.26 (m, 1H), 7.25-7.10 (m, 3H), 6.93 (d, *J* = 8.1 Hz, 2 H), 6.75-6.71 (m, 2H), 4.25 (d, *J* = 14.0, 1H), 4.04 (d, *J* = 14.0 Hz, 1H) 3.84 (s, 3H), 2.30 (s, 3H); ^{13}C NMR: δ 165.9, 165.5, 162.7, 146.8, 133.4, 132.3, 130.2, 128.9, 128.4, 127.9, 127.6, 124.1, 120.4, 115.4, 114.5, 110.6, 62.8, 55.4, 43.6, 23.8. Anal. Calcd for $C_{24}H_{21}N_5O_2$: N, 17.02. Found: N, 17.11.

1-{[5-(4-Methylphenyl)-4-phenyl-4*H*[1,2,4]triazol-3-yl]methyl}-1*H*-benzotriazole (15a). Phosphorus trichloride (4.80 g, 5 mmol) was added slowly to a solution of aniline (2.79 g, 30 mmol) in *o*-dichlorobenzene (30 mL). The reaction was immediate and could be completed by gentle warming on steam bath for a few minutes. After the addition of **9b** (1.55 g, 5 mmol), the mixture was stirred under reflux for 6 h in oil bath. Efficient stirring is desirable. After cooling, the byproduct was collected by filtration, and hexanes (100 mL) was added to the filtrate. The desired product was collected and recrystallized from ethyl acetate to give the pure sample. Plate-shaped crystals, 86%, mp 154-155 °C; ^{1}H NMR: δ 7.99 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.47-7.33 (m, 5H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 7.5 Hz, 2H), 5.97 (s, 2H), 2.3 (s, 3H).; ^{13}C NMR: δ 155.4, 149.3, 146.0, 140.2, 133.4, 132.7, 130.3, 130.1, 129.2, 128.1, 127.9, 127.0, 124.2, 123.2, 119.8, 110.3, 43.1, 21.3. Anal. Calcd for $C_{22}H_{18}N_6$: N, 22.93. Found: N, 23.13.

1-[(4-Benzyl-5-phenyl-4*H*-[1,2,4]triazol-3-yl)methyl]-1*H*-benzotriazole (15b). A mixture of **10a** (0.28 g, 1 mmol) and benzylamine (0.33 mL, 3 mmol) was refluxed in *n*-butanol for 24 h. The solvent was evaporated and the residue was subjected to column chromatography using hexanes/ethyl acetate as an eluent. Pale yellow plates, 41%, mp 122-123 °C; ^{1}H NMR: δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.80-7.65 (m, 6H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.33-7.25 (m, 4H), 7.19 (t, *J* = 6.2 Hz, 1H), 5.64 (s, 2H), 3.70 (s, 2H).; ^{13}C NMR: δ 165.4, 165.2, 145.1, 144.3, 141.9, 133.7, 129.3, 129.0, 128.0, 127.8, 127.4, 126.9, 126.0, 123.9, 119.0, 110.9, 48.6, 45.6. Anal. Calcd for $C_{22}H_{18}N_6$: N, 22.93. Found: N, 23.16.

1-{1-[5-(4-Methylphenyl)-4-phenyl-4*H*-[1,2,4]triazol-3-yl]ethyl}-1*H*-benzotriazole (16). *n*-BuLi (1.63 mL, 1.6 M solution in hexanes, 2.6 mmol) was added to a solution of **15a** (0.73 g, 2 mmol) in dry THF at −78 °C under nitrogen. Methyl iodide (0.34 g, 2.4 mmol) was added dropwise and the mixture was stirred for 12 h while the temperature was allowed to rise up to room temperature. The reaction mixture was quenched with water (50 mL), extracted with methylene chloride (2 x 30 mL), and the organic fractions were dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was washed with diethyl ether to give the pure product. Plates, 67%, mp 203-205 °C; ^{1}H NMR: δ 7.99 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H) 7.47-7.33 (m, 5H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.88 (m, 1H), 7.29 (d, *J* = 7.5 Hz, 2H), 5.97 (s, 2H), 2.27 (s, 3H); ^{13}C NMR: δ 155.4, 152.2, 146.3, 140.1, 133.3, 131.4, 130.1, 129.9, 129.1, 128.0, 127.6, 126.7, 124.0, 123.2, 119.8, 110.5, 51.3, 21.2, 18.3. Anal. Calcd for $C_{23}H_{20}N_6$: N, 22.09. Found: N, 22.33.

1-{1-Methyl-1-[5-(4-methylphenyl)-4-phenyl-4*H*-[1,2,4]triazole-3-yl]ethyl}1*H*-benzotriazole (17). *n*-BuLi (1.63 mL, 1.6 M solution in hexanes, 2.6 mmol) was added to a solution of **16** (0.76 g, 2 mmol) in dry THF at −78 °C under nitrogen. Methyl iodide (0.34 g, 2.4 mmol) was added dropwise and the mixture was stirred for 12 h while the temperature was allowed to rise up to room temperature. The reaction mixture was quenched with water (50 mL), extracted with methylene chloride (2 x 30 mL), and the organic fractions were dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, and the residue was washed with diethyl ether to give the pure product. Microcrystals, 92%, mp 162 - 164 °C; ^{1}H NMR: δ 8.04 (d, *J* = 8.0 Hz, 1H), 7.38-7.26 (m, 4H), 7.15-7.04 (m, 4H), 6.97 (d, *J* = 7.7 Hz, 2H), 6.16 (d, *J* = 7.5 Hz, 2H), 2.27 (s, 6H), 2.24 (s, 3H); ^{13}C NMR: δ 156.6, 155.5, 146.8, 140.0, 133.7, 132.1, 129.9, 129.3, 129.0, 128.2, 127.7, 127.0, 124.0, 123.4, 120.0, 111.0, 60.3, 27.7, 21.2. Anal. Calcd for $C_{24}H_{22}N_6$: N, 21.30. Found: N, 21.10.

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