Syntheses and Transformations of Substituted Benzazolyl- and Tetrazolyl(benzotriazol-1-yl)methanes

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Condensation reactions of *o*-hydroxy- and *o*-mercaptoanilines, and *o*-phenylenediamine with (benzotriazol-1-yl)acetic acid result in (1,3-benzazol-2-yl)(benzotriazol-1-yl)methanes. Cycloaddition of sodium azide to (benzotriazol-1-yl)acetonitrile leads to (1,2,3,4-tetrazol-5-yl)(benzotriazol-1-yl)methane. The diazolo-substituted benzotriazolylmethanes thus obtained were mono- and di-alkylated at the methylene group and the displacement of the benzotriazole group by nucleophiles was investigated.

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Introduction.

Benzotriazole chemistry allows the facile syntheses of many classes of functionalized compounds *via* displacement of the benzotriazole group assisted by electron donation from a substituent at the α-(benzotriazolyl)carbon atom. We have used the general strategy of α-benzotriazolylalkylation to achieve this [1]. Thus, α-lithiation of 1-(methoxymethyl)- [2], 1-(alkylthio)alkyl- or 1-(arylthio)alkyl- [3] benzotriazole followed by reactions with electrophiles affords substitution products. Grignard reagents replace the benzotriazole residues of the compounds thus obtained to give the corresponding methyl ethers or *tert*-alkyl sulfides. Alternatively, π-electron rich aromatic substituents at the α-(benzotriazolyl)carbon atom in similar reactions led to 2- and 3-substituted indoles [4,5], 2-substituted furans [6], or 2-substituted thiazoles [7].

We now report syntheses of novel (benzotriazol-l-yl)methyl-substituted benzazoles and tetrazole and their investigation with respect to α-lithiation, and reactions with Grignard reagents and other nucleophiles. Successful reactions of these types could result in the development of a novel approach to 2-substituted 1,3-benzazoles, and to 5-substituted 1,2,3,4-tetrazoles *etc.* displacements of the benzotriazole group. The importance of 1,3-benzazoles is determined by their various types of biological activity such as antiepileptic, sedative [8], antiinflammatory, antihelmintic, antifungal, *via* [9]. Structural modifications of benzimidazoles can produce marked effects on physiological activity [10]. 1,2,3,4-Tetrazole derivatives have numerous applications as biologically active compounds [11].

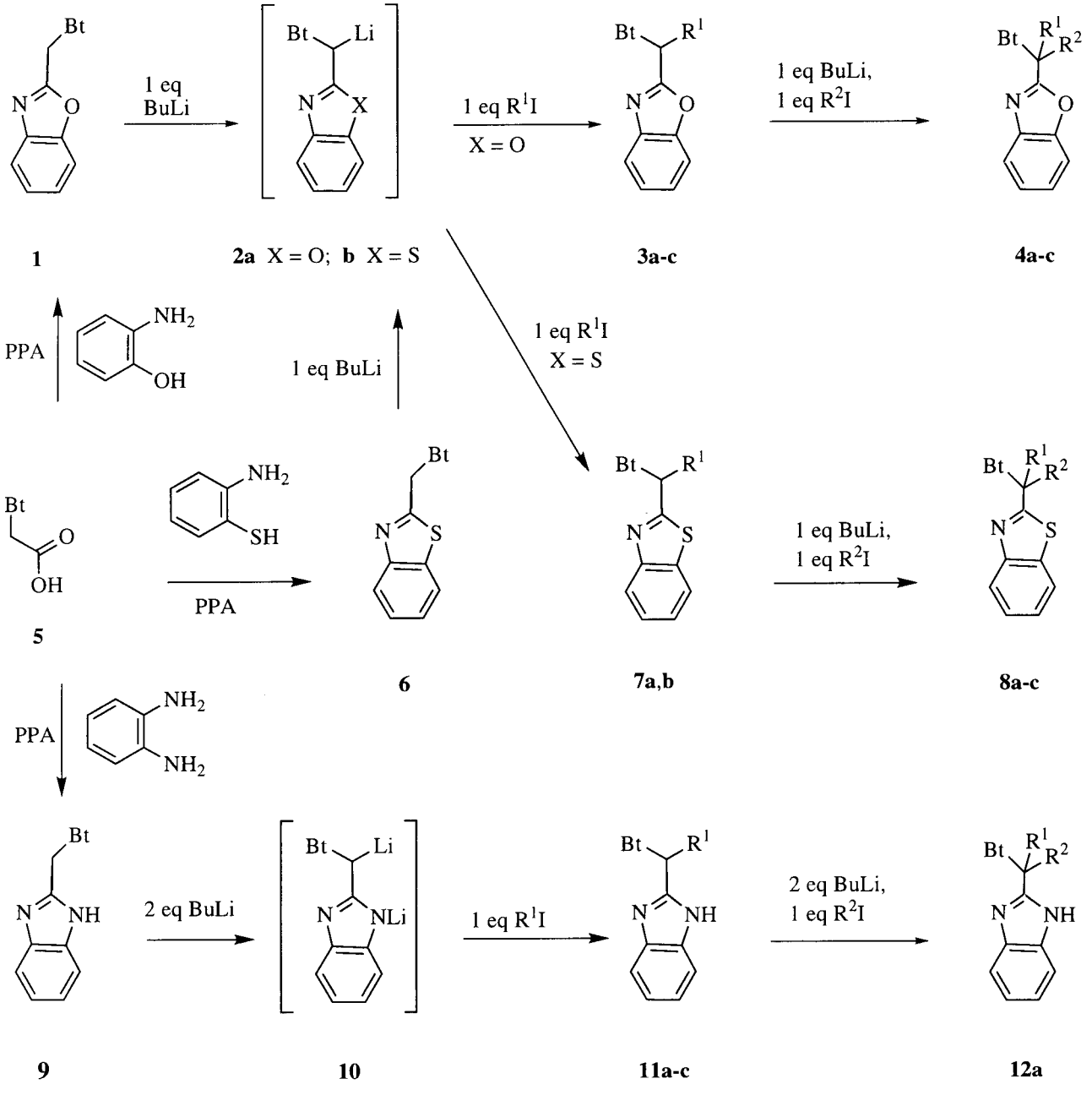
Results and Discussion.

(i) Substituted (1,3-Benzazol-2-yl)(benzotriazol-1-yl)-methanes.

Among numerous synthetic routes to benzazoles, the condensation reactions of ortho-substituted anilines with carboxylic acid derivatives in the presence of polyphosphoric acid are well established [12-14]. We successfully applied this method to achieve the synthesis of all three benzazoles **1**, **6** and **9** in 50%, 40% and 70% yields, respectively (Scheme 1). We used (benzotriazol-1-yl)acetic acid **5** [15,16], which was obtained in 90% yield by refluxing the mixture of benzotriazole and chloroacetic acid in toluene, as the carboxylic acid fragment.

Diazolomethanes **1** and **6** readily reacted with one equivalent of *n*-butyllithium in tetrahydrofuran solution at -100° to form anions **2a,b**; subsequent addition of one equivalent of alkyl iodide then gave the monoalkyl-substituted derivatives **3a-c** and **7a,b** in 72-92% yields. If the reaction was carried out at -78°, the mixtures of mono- and di-alkylated compounds **3,4a-c** were isolated in ~3:1 ratio. Benzimidazole derivative **9** was treated with two equivalents of *n*-butyllithium to give dianion **10** which, on addition of one equivalent of alkyl iodide, was alkylated exclusively at the carbon atom to form **11a-c** in 57-68% yields. Symmetrical or unsymmetrical di-substituted derivatives **4a-c**, **8a-c** and **12a** were obtained if the corresponding mono-substituted compounds were treated *in situ* with one (or with two, for **11a**) equivalents of *n*-butyllithium followed by addition of one equivalent of alkyl iodide. The structures of mono- and di-alkylated diazolomethanes **3**, **4**, **7**, **8**, **11** and **12** were confirmed by nmr spectral data and elemental analyses (see Experimental). We failed to get the products of electrophilic substitution of the anions **2a,b** or **10** with benzophenone, carbon disulfide, 2-bromoacetophenone or benzaldehyde: the starting materials or products of decomposition were isolated. All attempts to displace the benzotriazole group in **3**, **4**, **7**, **8**, **11** or **12** in reactions with sodium phenolate or with thiophenol in the presence of zinc bromide, or with Grignard reagents according to previously described procedures [17,18], also failed and the starting materials or products of decomposition were isolated. The recently reported successful displacement of the benzotriazolyl

Scheme 1



Bt = 1*H*-Benzotriazol-1-yl; PPA = polyphosphoric acid

3a R^1 = Me, **b** R^1 = *n*-C_5H_{11}, **c** R^1 = *n*-C_8H_{17};

4a $R^1 = R^2$ = Me, **b** $R^1 = R^2$ = *n*-C_5H_{11}, **c** $R^1 = R^2$ = *n*-C_8H_{17};

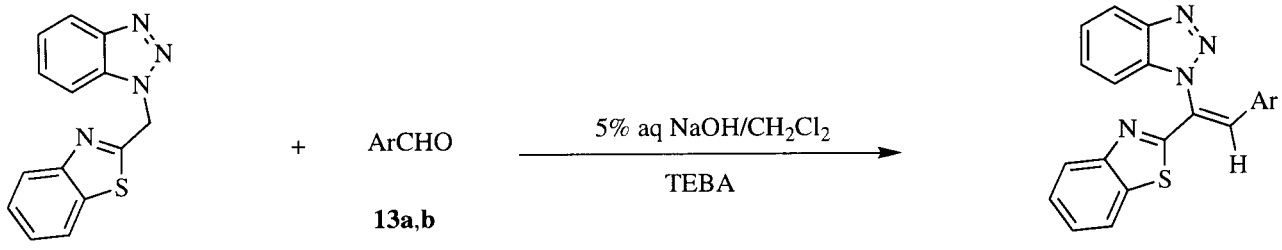
7a R^1 = *n*-C_4H_9, **b** R^1 = *n*-C_8H_{17};

8a $R^1 = R^2$ = Me, **b** $R^1 = R^2$ = *n*-C_4H_9, **c** R^1 = Me, R^2 = *n*-C_8H_{17};

11a R^1 = Me, **b** R^1 = *n*-C_4H_9, **c** R^1 = *n*-C_8H_{17};

12a $R^1 = R^2$ = *n*-C_4H_9

Scheme 2

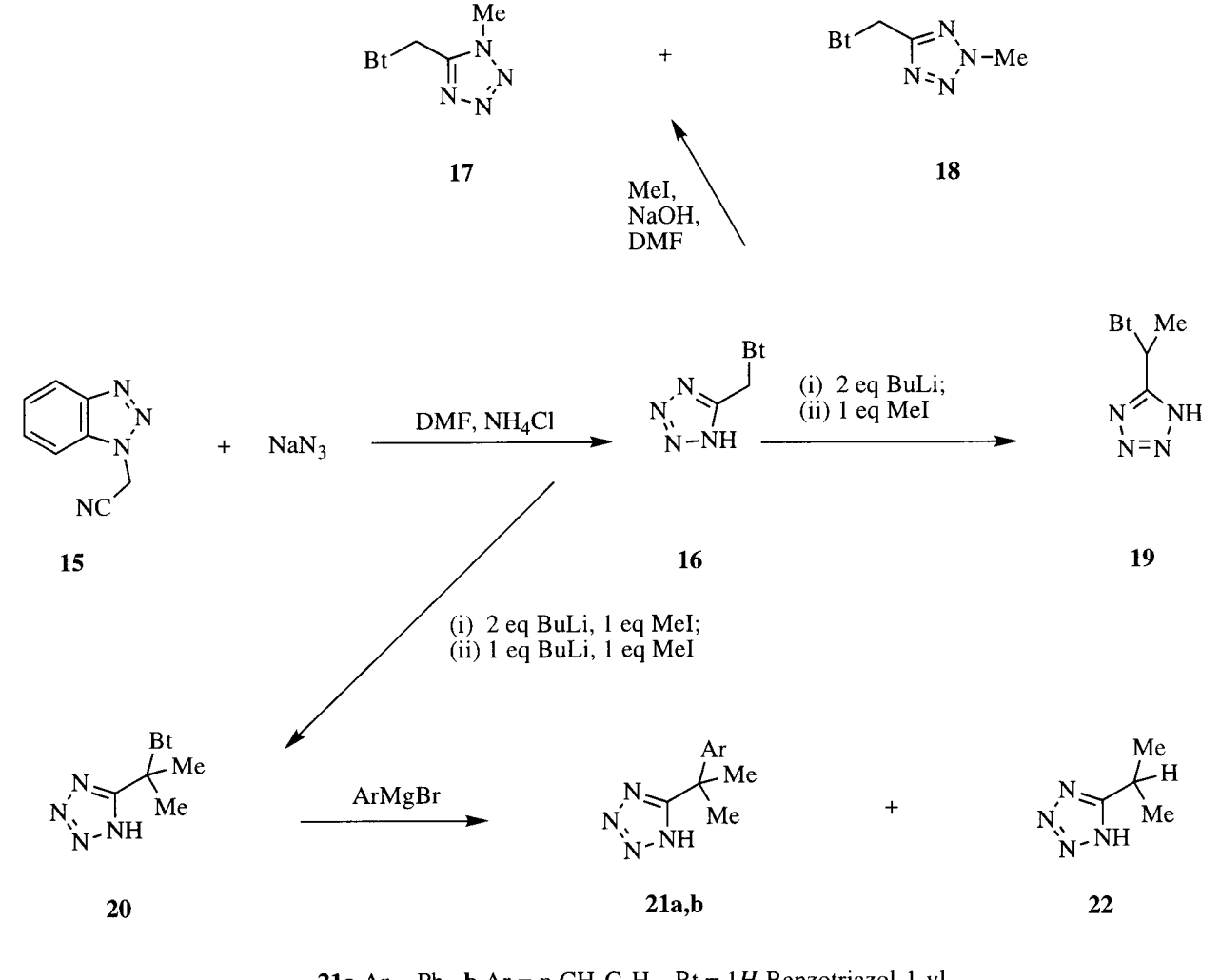


6 **14a,b**

13,14a Ar = Ph; **b** Ar = *p*-$NO_2C_6H_4$

group in the Grignard reaction for the series of substituted (1,3-thiazol-2-yl)(benzotriazol-1-yl)methanes [7] leads to the conclusion that the benzannelation of the thiazole-, oxazole-, or imidazole ring has a stronger electron-withdrawing effect than could be expected. This effect evidently decreases nucleophilicity of the anions **2b** and **10** that allows them to react only with strong electrophiles such as alkyl iodides. An additional consideration is that according to the suggested mechanism of the benzotriazole displacement in the Grignard reaction [19], the process is governed by a thermodynamically controlled equilibrium with formation of the benzotriazolyl anion and the corresponding carbocation. The latter readily reacts with the Grignard reagent to yield a product of the benzotriazole displacement. The formation of a carbocation from diazolomethanes **3**, **4**, **7**, **8**, **11** and **12** is proba-

Scheme 3



21a Ar = Ph, **b** Ar = *p*-$CH_3C_6H_4$; Bt = 1*H*-Benzotriazol-1-yl

bly rendered less thermodynamically favorable because of the effect of benzannelation.

We explored the reactivity of the methylene group in the benzothiazolyl derivative **6** in the aldol-type condensation with aromatic aldehydes **13a,b** (Scheme 2). The reaction was carried out under conditions of phase-transfer catalysis [20] and resulted in the styryl derivatives **14a,b** isolated as the single isomers in 70% and 58% yields, respectively.

(ii) Substituted (1,2,3,4-Tetrazol-5-yl)(benzotriazol-1-yl)methanes.

The general approach to the synthesis of 5-substituted 1,2,3,4-tetrazoles includes 1,3-cycloaddition of azides to alkyl-, hetaryl- or aryl-nitriles [21]. We employed this method for synthesis of (benzotriazol-l-yl)(1,2,3,4-tetrazol-5-yl)methane **16** from 1-(cyanomethyl)benzotriazole **15** in 94% yield (Scheme 3).

Alkylation of **16** with methyl iodide gave the mixture 1- and 2- methyl-substituted isomers **17** and **18** in 33% and 59% yields, respectively. The signal of the *N*-methyl group in the ^{1}H nmr spectra for compounds **17** and **18** appeared at δ 4.10 and 4.29, respectively, that allowed the isomers to be distinguished and is in agreement with the literature data [11]. Attempted benzotriazole displacement in **16-18** with sodium phenolate or with Grignard reagents failed and the starting materials were recovered, even after prolonged refluxing of the reaction mixtures. Lithiation of **16** with two equivalents of *n*-butyllithium followed by addition of one equivalent of methyl iodide resulted in the *C*-methylated derivative **19** in 92% yield. The one-pot stepwise reaction of **16** with two equivalents of *n*-butyllithium and one equivalent of methyl iodide followed by addition of one equivalent of *n*-butyllithium and one equivalent of methyl iodide resulted in the *C,C*-dimethylated derivative **20** in 72% yield. These reactions are similar to the mono- and di-alkylation procedures of the benzimidazole derivative **9** (Scheme 1).

Whereas the *C*-methylated derivative **19** also did not give the products of the benzotriazole displacement with the Grignard reagents, the *C,C*-dimethylated compound **20** reacted with aryl magnesium bromides in refluxing toluene to give the expected products **21a,b** in 37% and 40% yields respectively. The reduced derivative **22** appeared to be formed in ~15% yield in both reactions as judged from the nmr spectra of the crude reaction mixtures. However, attempted benzotriazole displacement in **20** with methyl magnesium iodide in toluene, or with phenyl magnesium bromide in dioxane, or with sodium thiophenolate in butanol failed even after prolonged refluxing: the starting materials were recovered or the complex mixtures of decomposition were formed. The failures with the benzotriazole displacement in compounds **16-19** reveal a surprisingly weak electron-donor effect of the 1,2,3,4-tetrazole ring. This effect, however, can be enhanced to some extent by introduction of the two alkyl groups at the methylene carbon atom as in **20**.

Discussion and Conclusions.

Recently we reported the synthesis of (benzotriazol-l-yl)methyl-substituted 1,2,3-triazoles and 1,2,3-triazolines by 1,3-cycloaddition of alkenes to 1-(azidomethyl)benzotriazole [22]. In order to work out a new approach to 1-substituted 1,2,3-triazolines and 1,2,3-triazoles, we unsuccessfully attempted to replace the benzotriazole group in such (benzotriazol-l-yl)azolo-substituted methanes *via* reactions with nucleophiles, or with Grignard reagents. The limit to the scope for benzotriazole group displacements is probably determined by the electron-donor effect of the azole moiety at the α-carbon atom in the (benzotriazol-1-yl)methyl azoles. We anticipated that 1,3-benzazol-2-yl and 1,2,3,4-tetrazol-5-yl substituents should possess larger electron-donor effects compared to that of 1,2,3-triazol-1-yl- and 1,2,3-triazolin-1-yl-groups. Thus, substituted (1,3-benzazol-2-yl)- and (1,2,3,4-tetrazol-5-yl)(benzotriazol-1-yl)methanes were investigated in terms of the electron-donor effect of the azole ring under conditions of the benzotriazole group displacement. However, the electron-donor effect of the benzazolyl substituents is evidently not strong enough to allow the benzotriazolyl substitution; it is more pronounced for the tetrazolyl derivatives, and can be strengthened by the introduction of two alkyl groups at the methylene group of (tetrazolyl)(benzotriazolyl)-methane.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. The ^{1}H and ^{13}C nmr spectra were recorded on a Gemini 300 spectrometer (300 and 75 MHz respectively) using deuteriochloform as solvent (unless otherwise stated) and tetramethylsilane as an internal reference. Commercially available reagent grade solvents were dried over sodium-benzophenone. Flash chromatography was run over EM Science silica gel (230-400 mesh).

1-(Carboxymethyl)benzotriazole (**5**).

A mixture of benzotriazole (2.62 g, 22 mmoles) and monochloroacetic acid (1.89 g, 20 mmoles) in dry toluene (20 ml) was refluxed for 18 hours. The mixture was cooled and washed with a concentrated solution of sodium bicarbonate (3 x 20 ml). The aqueous layer was separated, extracted with methylene chloride (2 x 20 ml) and acidified with concentrated hydrochloric acid to *p*H 4. The precipitate obtained was filtered off, washed with methanol (3 x 5 ml), dried and recrystallized from methanol to give **5** (90%), mp 216° (lit. mp 214-216° [15]); ^{1}H nmr (DMSO-d_6): δ 8.09 (dd, 1H, J_1 = 8.4 Hz, J_2 = 0.9 Hz), 7.87 (dd, 1H, J = 8.4 Hz, J_2 = 0.9 Hz), 7.57 (t, 1H, J = 7.6 Hz), 7.43 (t, 1H, J = 7.6 Hz), 5.69 (s, 2H); ^{13}C nmr: δ 168.8, 145.2, 133.6, 127.5, 124.0, 119.1, 110.8, 48.8. The signal corresponding to CO_2H is not observed in the ^{1}H nmr spectrum.

General Procedure for Synthesis of Dibenzazoles **1**, **6** and **9**.

A mixture of 1-carboxymethylbenzotriazole **5** (9.8 mmoles), the appropriate *o*-substituted aniline (9.8 mmoles) and polyphosphoric acid (10 g) was vigorously stirred at 170° for 4 hours. The hot mixture was poured onto ice (50 g) under vigorous stirring and the resulting suspension was extracted with chloroform (3 x 20 ml). The combined organic layers were dried over anhydrous sodium sulfate, filtered and the solvent evaporated *in vacuo*. The residue was purified by flash chromatography (hexane-diethyl ether, 5:1) and recrystallized to give **1** (50%), **6** (40%) and **9** (70%). In the case of **9**, after hydrolysis of the reaction mixture, the resulting solution was basified with sodium bicarbonate to *p*H 7 and then extacted with chloroform.

2-(Benzotriazol-l-ylmethyl)benzoxazole (**1**).

This compound was obtained as light yellow needles (ethyl alcohol), mp 118°; ^{1}H nmr: δ 8.08 (d, 1H, J = 8.3 Hz), 7.74-7.71 (m, 1H), 7.65 (d, 1H, J = 8.3 Hz), 7.52-7.32 (m, 5H), 6.12 (s, 2H); ^{13}C nmr: δ 158.8, 151.0, 146.1, 140.6, 132.9, 128.0, 125.9, 124.8, 124.2, 120.5, 120.2, 110.9, 109.4, 45.4

Anal. Calcd. for $C_{14}H_{10}N_4O$: C, 67.19; H, 4.03; N, 22.39. Found: C, 67.19; H, 3.99; N, 22.31.

2-(Benzotriazol-l-ylmethyl)benzothiazole (**6**).

This compound was obtained as light yellow needles (ethyl alcohol), mp 120°; ^{1}H nmr: δ 8.12-8.04 (m, 2H), 7.82-7.78 (m, 1H), 7.63-7.58 (m, 1H), 7.53-7.36 (m, 4H), 6.27 (s, 2H); ^{13}C nmr: δ 163.8, 152.4, 146.0, 135.3, 132.6, 127.7, 126.2, 125.6, 124.1, 123.2, 121.6, 119.9, 109.4, 49.8.

Anal. Calcd. for $C_{14}H_{10}N_4S$: C, 63.14; H, 3.78; N, 21.04. Found: C, 63.02; H, 3.76; N, 21.18.

2-(Benzotriazol-l-ylmethyl)benzimidazole (**9**).

This compound was obtained as light yellow needles (ethyl alcohol), mp 195°; ^{1}H nmr (DMSO-d_6): δ 12.77 (br s, 1H), 8.10 (d, 1H, J = 8.3 Hz), 7.88 (d, 1H, J = 8.3 Hz), 7.58-7.53 (m, 3H), 7.43 (t, J = 7.1 Hz), 7.21-7.18 (m, 2H), 6.29 (s, 2H); ^{13}C nmr (DMSO-d_6): δ 148.4, 145.3, 138.6 (br), 133.1, 127.5, 124.1, 122.1, 119.1, 114.5 (br), 110.8, 45.7.

Anal. Calcd. for $C_{14}H_{11}N_5$: C, 67.46; H, 4.45; N, 28.09. Found: C, 67.09; H, 4.76; N, 28.18.

General Procedure for the Synthesis of **3a-c, 7a,b and 11a- c.**

n-Butyllithium (5.5 ml, 11 mmoles, 2*M* solution in hexane) was added to a solution of **1** (10 mmoles), **6** (10 mmoles) or **9** (5 mmoles) in tetrahydrofuran (150 ml) under nitrogen at -100°, and the solution was stirred at this temperature for 2 hours. The appropriate alkyl iodide (11 mmoles) in tetrahydrofuran (10 ml) was added, and the mixture was stirred at -100° for 2 hours and then at room temperature overnight. The mixture was quenched with water (100 ml) and extracted with diethyl ether (3 x 100 ml). The combined organic layers were washed with water (2 x 50 ml) and dried over magnesium sulfate. The solvent was removed *in vacuo* to give the crude product which was purified by flash chromatography (hexane-diethyl ether, 1:1).

1-(Benzotriazol-1-yl)-1-(benzoxazol-2-yl)ethane (**3a**).

This compound was obtained as a light yellow oil in 92% yield; ^{1}H nmr: δ 7.96 (d, 1H, J = 8.2 Hz), 7.66-7.63 (m, 1H), 7.46 (d, 1H, J = 8.2 Hz), 7.34-7.19 (m, 5H), 6.37 (q, 1H, J = 7.2 Hz), 2.20 (d, 3H, J = 7.1 Hz); ^{13}C nmr: δ 162.2, 150.8, 146.3, 140.4, 132.1, 127.7, 125.8, 124.7, 124.1, 120.4, 120.1, 110.8, 109.7, 53.1, 17.7.

Anal. Calcd. for $C_{15}H_{12}N_4O$: C, 68.14; H, 4.58; N, 21.20. Found: C, 68.35; H, 4.40; N, 21.60.

1-(Benzotriazol-1-yl)-1-(benzoxazol-2-yl)hexane (**3b**).

This compound was obtained as a light yellow oil in 80% yield; ^{1}H nmr: δ 8.09 (d, 1H, J = 8.3 Hz), 7.77-7.74 (m, 1H), 7.66 (d, 1H, J = 8.3 Hz), 7.47-7.29 (m, 5H), 6.33 (t, 1H, J = 7.9 Hz), 2.83-2.75 (m, 2H), 1.45-1.22 (m, 6H), 0.83 (t, 3H, J = 7.1 Hz); ^{13}C nmr: δ 161.8, 150.7, 146.3, 140.4, 132.2, 127.6, 125.7, 124.6, 124.0, 120.4, 120.1, 110.9, 109.9, 57.8, 31.5, 30.8, 25.4, 22.1, 13.7.

Anal. Calcd. for $C_{19}H_{20}N_4O$: C, 71.23; H, 6.29; N, 17.49. Found: C, 71.53; H, 6.43; N, 17.10.

1-(Benzotriazol-1-yl)-1-(benzoxazol-2-yl)nonane (**3c**).

This compound was obtained as a light yellow oil in 85% yield; ^{1}H nmr: δ 8.09 (d, 1H, J = 8.2 Hz), 7.77-7.74 (m, 1H), 7.66 (d, 1H, J = 8.2 Hz), 7.47-7.29 (m, 5H), 6.32 (t, 1H, J = 7.9 Hz), 2.83-2.75 (m, 2H), 1.45-1.18 (m, 12H), 0.85 (t, 3H, J = 6.7 Hz); ^{13}C nmr: δ 161.8, 150.7, 146.3, 140.4, 132.2, 127.6, 125.7, 124.6, 124.0, 120.4, 120.2, 110.9, 109.9, 57.8, 31.6, 31.5, 29.0, 28.9, 28.7, 25.7, 22.4, 13.9.

Anal. Calcd. for $C_{22}H_{26}N_4O$: C, 72.90; H, 7.23; N, 15.46. Found: C, 72.70; H, 7.42; N, 15.38.

1-(Benzotriazol-1-yl)-1-(benzothiazol-2-yl)pentane (**7a**).

This compound was obtained as colorless crystals in 43% yield, mp 89° (from hexane); ^{1}H nmr: δ 8.11-8.04 (m, 2H), 7.79 (d, 1H, J = 8.0 Hz), 7.63 (d, 1H, J = 8.3 Hz), 7.52-7.34 (m, 4H), 6.35 (dd, 1H, J_1 = 9 4 Hz, J_2 = 6.2 Hz), 2.88-2.79 (m, 2H), 1.45-1.29 (m, 4H), 0.88 (t, 3H, J = 7.0 Hz); ^{13}C nmr: δ 168.6, 152.5, 146.3, 135.3, 132.6, 127.6, 126.2, 125.6, 124.2, 123.4, 121.7, 120.1, 109.9, 62.2, 33.6, 28.2, 22.0, 13.7.

Anal. Calcd. for $C_{18}H_{18}N_4S$: C, 67.05; H, 5.63; N, 17.38. Found: C, 67.09; H, 5.64; N, 17.39.

1-(Benzotriazol-1-yl)-1-(benzothiazol-2-yl)nonane (**7b**).

This compound was obtained as a light yellow oil in 72% yield; ^{1}H nmr: δ 8.09 (d, 1H, J = 8.2 Hz), 8.05 (d, 1H, J = 8.2 Hz), 7.81 (d, 1H, J = 8.1 Hz), 7.63 (d, 1H, J = 8.2 Hz), 7.52-7.34 (m, 4H), 6.35 (dd, 1H, J_1 = 9.5 Hz, J_2 = 6.1 Hz), 2.94-2.72 (m, 2H), 1.45-1.17 (m, 12H), 0.85 (t, 3H, J = 6.7 Hz); ^{13}C nmr: δ 168.1, 152.1, 145.8, 134.8, 132.2, 127.1, 125.7, 125.1, 123.6, 122.9, 121.2, 119.6, 109.6, 61.6, 33.4, 31.2, 28.6, 28.5, 28.4, 25.6, 22.0, 13.6.

Anal. Calcd. for $C_{22}H_{26}N_4S$: C, 69.81; H, 6.92; N, 14.80. Found: C, 69.93; H, 7.06; N, 14.85.

1-(Benzotriazol-1-yl)-1-(benzimidazol-2-yl)ethane (**11a**).

This compound was obtained as colorless crystals in 68% yield, mp 80° (from hexane); ^{1}H nmr: δ 12.68-12.21 (br s, 1H), 7.48 (d, 2H, J = 8.3 Hz), 7.34 (d, 2H, J = 8.4 Hz), 7.19-7.10 (m, 3H), 7.02-6.94 (m, 1H), 6.44 (q, 1H, J = 7.0 Hz), 2.17 (d, 3H, J = 7.1 Hz); ^{13}C nmr: δ 151.2, 145.6, 132.0, 127.8, 124.5, 122.6, 118.9, 110.2, 54.6, 18.9. Two of the aromatic carbon atoms are not observed in the ^{13}C nmr spectrum.

Anal. Calcd. for $C_{15}H_{13}N_5$: C, 68.43; H, 4.98; N, 26.60. Found: C, 68.49; H, 5.35; N, 26.50.

1-(Benzotriazol-1-yl)-1-(benzimidazol-2-yl)pentane (**11b**).

This compound was obtained as light yellow needles in 57% yield, 152°; ^{1}H nmr: δ 12.24-11.95 (br s, 1H), 7.84-7.72 (m, 1H), 7.69 (d, 1H, J = 8.2 Hz), 7.60 (d, 1H, J = 8.5 Hz), 7.36 (t, 1H, J = 7.7 Hz), 6.40 (dd, 1H, J_1 = 8.2 Hz, J_2 = 7.4 Hz), 2.79-2.73 (m, 2H), 1.36-1.17 (m, 4H), 0.80 (t, 3H, J = 6.8 Hz); ^{13}C nmr: δ 150.8, 145.6, 132.5, 127.9, 124.6, 122.0 (br), 119.1, 111.3 (br), 110.3, 59.0, 33.1, 28.1, 22.0, 13.7. One of the aromatic carbon atoms is not observed in the ^{13}C nmr spectrum.

Anal. Calcd. for $C_{18}H_{19}N_5$: C, 70.80; H, 6.27; N, 22.93. Found: C, 70.80; H, 6.37; N, 22.70.

1-(Benzotriazol-1-yl)-1-(benzimidazol-2-yl)nonane (**11c**).

This compound was obtained as an oil in 62% yield; ^{1}H nmr: δ 12.88-12.83 (broad s, 1H), 7.81-7.18 (m, 1H), 7.70-7.64 (m, 2H), 7.52-7.42 (m, 1H), 7.35-7.30 (m, 1H), 7.24-7.17 (m, 3H), 6.50 (t, 1H, J = 7.8 Hz), 2.78-2.88 (m, 2H), 1.26-1.11 (m, 12H), 0.80 (t, 3H, J = 6.9 Hz); ^{13}C nmr: δ 150.9, 145.5, 142.4, 134.5, 132.5, 127.7, 124.4, 123.3, 122.2, 119.2, 118.9, 111.5, 110.3, 58.9, 32.9, 31.5, 29.0, 28.9, 28.7, 25.8, 22.4, 13.8.

Anal. Calcd. for $C_{22}H_{27}N_5$: C, 73.10; H, 7.53; N, 19.37. Found: C, 73.22; H, 7.45; N, 19.16.

General Procedure for the Synthesis of **4a-c**, **8a-c** and **12a.**

n-Butyllithium (5.5 ml, 11 mmoles, 2*M* solution in hexane) was added to a solution of **1** (10 mmoles), **6** (10 mmoles) or **9** (5 mmoles) in tetrahydrofuran (150 ml) under nitrogen at -100°, and the solution was stirred at this temperature for 2 hours. The appropriate alkyl iodide (11 mmoles for **1** and **6**, or 5.5 mmoles for **9**) in tetrahydrofuran (10 ml) was added, and the mixture was stirred at -100° for 2 hours and then at room temperature overnight. The mixture was cooled to -100°, butyllithium (5.5 ml, 11 mmoles, 2*M* solution in hexane) was added, and the mixture was stirred at this temperature for 2 hours. The appropriate alkyl iodide (11 mmoles for **1** and **6**, or 5.5 mmoles for **9**) was added, and the mixture was stirred at -100° for 2 hours and then at room temperature overnight. The mixture was quenched with water (100 ml) and extracted with diethyl ether (3 x 100 ml). The combined organic layers were washed with water (2 x 50 ml) and dried over magnesium sulfate. The solvent was removed *in vacuo* to give the crude product which was purified by flash chromatography (hexane-diethyl ether, 1:1).

2-(Benzotriazol-1-yl)-2-(benzoxazol-2-yl)propane (**4a**).

This compound was obtained as light yellow needles in 32% yield, mp 126°; ^{1}H nmr: δ 8.09-8.06 (m, 1H), 7.83-7.80 (m, 1H), 7.42-7.25 (m, 5H), 7.17-7.14 (m, 1H), 2.41 (s, 6H); ^{13}C nmr: δ 165.5, 151.0, 146.9, 140.0, 132.0, 127.4, 125.9, 124.8, 123.8, 120.6, 120.2, 111.0, 110.6, 61.1, 26.8.

Anal. Calcd. for $C_{16}H_{14}N_4O$: C, 69.05; H, 5.07; N, 20.13. Found: C, 69.25; H, 5.12; N, 20.38.

6-(Benzotriazol-1-yl)-6-(benzoxazol-2-yl)undecane (**4b**).

This compound was obtained as light yellow plates in 40% yield, mp 158°; ^{1}H nmr: δ 8.07 (d, 1H, J = 8.1 Hz), 7.86-7.82 (m, 1H), 7.41-7.22 (m, 5H), 6.98 (d, 1H, J = 8.2 Hz), 2.93-2.82 (m, 4H), 1.63-1.20 (m, 10H), 1.20-0.90 (m, 2H), 0.79 (t, 6H, J = 6.9 Hz); ^{13}C nmr: δ 165.1, 150.8, 146.7, 140.2, 132.1, 127.4, 125.9, 124.8, 123.8, 120.6, 120.2, 111.1, 110.5, 67.5, 34.9, 31.5, 22.7, 22.3, 13.8.

Anal. Calcd. for $C_{24}H_{30}N_4O$: C, 73.81; H, 7.74; N, 14.35. Found: C, 74.10; H, 7.86; N, 14.12.

9-(Benzotriazol-1-yl)-9-(benzoxazol-2-yl)heptadecane (**4c**).

This compound was obtained as a light yellow oil in 38% yield; ^{1}H nmr: δ 8.07 (d, 1H, J = 8.1 Hz), 7.86-7.83 (m, 1H), 7.42-7.19 (m, 5H), 7.00 (d, 1H, J = 8.2 Hz), 2.93-2.82 (m, 4H), 1.33-1.18 (m, 22H), 1.09-0.94 (m, 2H), 0.83 (t, 6H, J = 6.8 Hz); ^{13}C nmr: δ 165.1, 150.8, 146.7, 140.2, 132.3, 127.3, 125.8, 124.8, 123.8, 120.6, 120.2, 111.1, 110.5, 67.5, 34.9, 31.7, 29.3, 29.1, 29.0, 22.9, 22.6, 14.0.

Anal. Calcd. for $C_{30}H_{42}N_4O$: C, 75.91; H, 8.92; N, 11.80. Found: C, 75.51; H, 8.72; N, 11.63.

2-(Benzotriazol-1-yl)-2-(benzothiazol-2-yl)propane (**8a**).

This compound was obtained as light yellow plates in 35% yield, mp 127° (from methyl alcohol); ^{1}H nmr: δ 8.10-8.05 (m, 2H), 7.72 (d, 1H, J = 7.5 Hz), 7.50-7.44 (m, 1H), 7.37-7.31 (m, 1H), 7.28-7.14 (m, 3H), 2.39 (s, 6H); ^{13}C nmr: δ 173.4, 152.1, 146.8, 135.4, 132.0, 127.0, 126.1, 125.6, 123.6, 123.4, 121.6, 120.0, 111.3, 65.0, 28.6.

Anal. Calcd. for $C_{16}H_{14}N_4S$: C, 65.28; H, 4.79; N, 19.03. Found: C, 65.51; H, 4.80; N, 18.94.

5-(Benzotriazol-1-yl)-5-(benzothiazol-2-yl)nonane (**8b**).

This compound was obtained as light yellow plates in 35% yield, mp 112° (from hexane); ^{1}H nmr: δ 8.14 (d, 1H, J = 8.2 Hz), 8.08-8.05 (m, 1H), 7.76 (d, 1H, J = 8.0 Hz), 7.54-7.51 (m, 1H), 7.49-7.36 (m, 1H), 7.29-7.15 (m, 2H), 7.04 (d, 1H, J = 8.3 Hz), 3.08-2.96 (m, 2H), 2.86-2.75 (m, 2H), 1.37-1.20 (m, 6H), 1.03-0.92 (m, 2H), 0.82 (t, 6H, J = 7.1 Hz); ^{13}C nmr: δ 173.5, 151.9, 140.3, 135.5, 132.2, 127.0, 126.1, 125.7, 123.7, 123.7, 121.8, 120.1, 111.3, 71.0, 36.1, 25.0, 22.3, 13.7.

Anal. Calcd. for $C_{22}H_{26}N_4S$: C, 69.81; H, 6.92; N, 14.80. Found: C, 70.16; H, 7.13; N, 14.79.

2-(Benzotriazol-1-yl)-2-(benzothiazol-2-yl)nonane (**8c**).

This compound was obtained as a light yellow oil in 40% yield; ^{1}H nmr: δ 8.11-8.04 (m, 2H), 7.70 (d, 1H, J = 7.4 Hz), 7.47-7.42 (m, 1H), 7.34-7.29 (m, 1H), 7.24-7.16 (m, 3H), 3.07-2.97 (m, 1H), 2.82-2.72 (m, 1H), 2.78 (s, 3H), 1.50-0.92 (m, 12H), 0.82 (t, 3H, J = 6.8 Hz); ^{13}C nmr: δ 173.3, 151.8, 146.5, 135.0, 131.9, 126.7, 125.8, 125.3, 123.4, 123.2, 121.4, 119.7, 111.1, 67.7, 39.4, 31.3, 29.0, 28.7, 28.6, 25.7, 22.9, 22.1, 13.6.

Anal. Calcd. for $C_{23}H_{28}N_4S$: C, 70.37; H, 7.19; N, 14.27. Found: C, 70.70; H, 7.33; N, 14.28.

5-(Benzotriazol-1-yl)-5-(benzimidazol-2-yl)nonane (**12a**).

This compound was obtained as light yellow plates in 40% yield, mp 109°; ^{1}H nmr: δ 12.74 (s, 1H), 7.90 (d, 1H, J = 8.0 Hz), 7.50 (d, 1H, J = 7.1 Hz), 7.28-7.18 (m, 2H), 6.94 (t, 1H, J = 7.5 Hz), 6.80-6.67 (m, 3H), 2.89-2.78 (m, 4H), 1.35-1.18 (m, 6H), 0.85-0.74 (m, 8H); ^{13}C nmr: δ 154.6, 145.2, 142.5, 134.9, 131.8, 127.1, 124.3, 123.3, 122.0, 120.0, 117.6, 111.5, 111.1, 68.5, 35.4, 25.1, 22.6, 13.9.

Anal. Calcd. for $C_{22}H_{27}N_5$: C, 73.10; H, 7.53; N, 19.37. Found: C, 73.02; H, 7.55; N, 19.70.

General Procedure for the Synthesis of **14a,b**.

A mixture of dibenzazole **6** (10 mmoles), the appropriate aldehyde **13** (10 mmoles), 50% aqueous solution of sodium hydroxide (3 ml), methylene chloride (50 ml) and a catalytic amount of triethylbenzylammonium chloride was stirred at room tempera-

ture for 14 hours. The mixture was extracted with methylene chloride (3 x 20 ml), the combined organic layers were washed with a 10% aqueous solution of acetic acid (3 x 100 ml), water (2 x 50) and dried over magnesium sulfate. The solvent was removed *in vacuo* to give crude compounds **14a** (70%) and **14b** (58%). The analytically pure samples were obtained as precipitates on treatment of the crude compounds **14a,b** with ether (3 x 5 ml).

1-(Benzothiazol-2-yl)-1-(benzotriazol-1-yl)-2-phenylethene (**14a**).

This compound was obtained as yellow crystals, mp 154°; ^{1}H nmr: δ 8.28 (s, 1H), 8.21-8.18 (m, 1H), 8.04 (d, 1H, J = 8.2 Hz), 7.76 (d, 1H, J = 8.0 Hz), 7.52-7.38 (m, 4H), 7.25-7.09 (m, 4H), 6.80 (d, 2H, J = 7.4 Hz); ^{13}C nmr: δ 164.9, 153.7, 145.7, 135.2, 133.1, 132.9, 131.8, 130.1, 129.5, 128.7, 128.5, 127.0, 126.6, 125.6, 124.5, 123.3, 121.5, 120.1, 110.0.

Anal. Calcd. for $C_{21}H_{14}N_4S$: C, 71.17; H, 3.98; N, 15.81. Found: C, 71.20; H, 3.73; N, 15.76.

1-(Benzothiazol-2-yl)-1-(benzotriazol-1-yl)-2-(4-nitrophenyl)-ethene (**14b**).

This compound was obtained as yellow crystals, mp 210°; ^{1}H nmr: δ 8.30 (s, 1H), 8.24-8.21 (m, 1H), 8.07 (d, 1H, J = 8.2 Hz), 7.97 (d, 2H, J = 8.8 Hz), 7.82 (d, 1H, J = 8.0 Hz), 7.55 (t, 1H, J = 7.4 Hz), 7.48-7.40 (m, 3H), 7.27-7.21 (m, 1H), 6.98 (d, 2H, J = 8.8 Hz); ^{13}C nmr: δ 163.7, 153.7, 147.8, 145.9, 138.3, 135.6, 132.9, 130.4, 130.1, 129.8, 129.1, 127.1, 126.3, 125.0, 123.9, 123.8, 121.8, 120.6, 109.8.

Anal. Calcd. for $C_{21}H_{13}N_5O_2S$: C, 63.15; H, 3.28; N, 17.53. Found: C, 63.00; H, 3.12; N, 17.42.

5-(Benzotriazol-1-ylmethyl)-1*H*-tetrazole (**16**).

A mixture of 1-(cyanomethyl)benzotriazole **15** [23] (0.58 g, 10 mmoles), sodium azide (0.78 g, 12 mmoles), ammonium chloride (0.65 g, 12 mmoles) and dimethylformamide (20 ml) was heated under stirring at 120° for 24 hours. The solvent was removed *in vacuo,* the residue treated with cold water (20 ml) and the mixture was acidified with concentrated hydrochloric acid to *p*H 2. The solid formed was filtered off, washed with water and diethyl ether, and dried to give **16** (94%), mp 207-209° dec (needles from ethyl acetate); ^{1}H nmr (DMSO-d_6): δ 8.15 (d, 1H, J = 8.4 Hz), 7.92 (d, 1H, J = 8.4 Hz), 7.64 (t, 1H, J = 7.6 Hz), 7.48 (t, 1H, J = 7.6 Hz), 6.51 (s, 2H); ^{13}C nmr (DMSO-d_6): δ 153.7, 145.3, 133.0, 127.8, 124.3, 119.3, 110.6, 41.2.

Anal. Calcd. for $C_8H_7N_7$: C, 47.76; H, 3.51; N, 48.73. Found: C, 47.52; H, 3.47; N, 49.02.

5-(Benzotriazol-1-ylmethyl)-1-methyl-1*H*-tetrazole (**17**) and 5-(benzotriazol-1-ylmethyl)-2-methyl-2*H*-tetrazole (**18**).

A mixture of **16** (5.03 g, 25 mmoles), sodium hydroxide (1.10 g, 27.5 mmoles) and dimethylformamide (50 ml) was stirred at room temperature for 2 hours, and then methyl iodide (3.90 g, 27.5 mmoles) was added. The mixture was stirred at room temperature for 12 hours, the solvent removed *in vacuo,* and the residue treated with cold water (50 ml). The solid formed was filtered off and dried to give a mixture of **17** and **18** which was separated by flash chromatography (ethyl acetate-hexane, 1:1) to give **17** (33%) and **18** (59%).

Compound **17** was obtained as colorless crystals, mp 155-156°; ^{1}H nmr: δ 8.07 (d, 1H, J = 8.4 Hz), 7.69 (d, 1H, J = 8.4 Hz), 7.54 (t, 1H, J = 7.4 Hz), 7.42 (t, 1H, J = 7.4 Hz), 6.21 (s, 2H), 4.10 (s, 3H); ^{13}C nmr: δ 149.3, 146.2, 132.5, 128.7, 124.8, 120.2, 109.4, 40.3, 34.3.

Anal. Calcd. for $C_9H_9N_7$: C, 50.23; H, 4.22; N, 45.56. Found: C, 50.25; H, 4.04; N, 45.87.

Compound **18** was obtained as colorless crystals, mp 141-142°; ^{1}H nmr: δ 8.04 (d, 1H, J = 8.3 Hz), 7.68 (d, 1H, J = 8.3 Hz), 7.49 (t, 1H, J = 7.1 Hz), 7.37 (t, 1H, J = 7.3 Hz), 6.11 (s, 2H), 4.29 (s, 3H); ^{13}C nmr: δ 160.7, 145.9, 132.7, 127.6, 124.0, 119.8, 109.6, 42.7, 39.5.

Anal. Calcd. for $C_9H_9N_7$: C, 50.23; H, 4.22; N, 45.56. Found: C, 50.55; H, 3.90; N, 45.88.

1-(Benzotriazol-1-yl)-1-(1*H*-tetrazol-5-yl)ethane (**19**).

n-Butyllithium (11 ml, 22 mmoles, 2*M* solution in hexane) was added to a solution of **16** (2.01 g, 10 mmoles) in tetrahydrofuran (100 ml) under nitrogen at -78°, and the solution was stirred at this temperature for 1 hour, then at -30° for 1 hour and cooled again to -78°. Methyl iodide (1.56 g, 11 mmoles) in tetrahydrofuran (5 ml) was added, and the mixture was stirred at -78° for 2 hours and then at room temperature overnight. The mixture was quenched with water (50 ml), acidified with concentrated hydrochloric acid to *p*H 2 and extracted with ethyl acetate (3 x 50 ml). The combined organic layers were washed with water (2 x 50 ml) and dried over magnesium sulfate. The solvent was removed *in vacuo* to give **19** (92%) as yellow crystals after recrystallization from ethyl acetate, mp 166-167°; ^{1}H nmr (DMSO-d_6): δ 8.13 (d, 1H, J = 8.5 Hz), 7.86 (d, 1H, J = 8.2 Hz), 7.61 (t, 1H, J = 7.5 Hz), 7.47 (t, 1H, J = 7.5 Hz), 6.94 (q, 1H, J = 7.1 Hz), 2.20 (d, 3H, J = 7.1 Hz); ^{13}C nmr (DMSO-d_6): δ 157.1, 145.4, 132.2, 127.7, 124.3, 119.4, 110.6, 49.1, 18.5.

Anal. Calcd. for $C_9H_9N_7$: C, 50.23; H, 4.22; N, 45.56. Found: C, 50.09; H, 3.94; N, 45.42.

2-(Benzotriazole-1-yl)-2-(1*H*-tetrazol-5-yl)propane (**20**).

n-Butyllithium (8.4 ml, 21 mmoles, 2*M* solution in hexane) was added to a solution of **16** (2.01 g, 10 mmoles) in tetrahydrofuran (100 ml) under nitrogen at -78°, and the solution was stirred at this temperature for 1 hour, then at -30° for 1 hour and cooled again to -78°. Methyl iodide (1.56 g, 11 mmoles) in tetrahydrofuran (5 ml) was added and the mixture was stirred at -78° for 2 hours, at room temperature for 1 hour, and then cooled to -78°. Butyllithium (4.0 ml, 10 mmoles, 2*M* solution in hexane) was added, and the solution was stirred at -78° for 1 hour, then at -30° for 1 hour and cooled again to -78°. Methyl iodide (1.56 g, 11 mmoles) in tetrahydrofuran (5 ml) was added and the mixture was stirred at -78° for 2 hours and at room temperature overnight. The mixture was quenched with water (50 ml), acidified with concentrated hydrochloric acid to *p*H 2 and extracted with ethyl acetate (3 x 50 ml). The combined organic layers were washed with water (2 x 50 ml) and dried over magnesium sulfate. The solvent was removed in *in vacuo* to give **20** (72%) as colorless microcrystals after recrystallization from ethyl acetate-hexane, 1:1,mp 170-171° dec; ^{1}H nmr (DMSO-d_6): δ 8.12 (d, 1H, J = 8.3 Hz), 7.50-7.39 (m, 2H), 7.20 (d, 1H, J = 7.6 Hz), 2.31 (s, 6H); ^{13}C nmr (DMSO-d_6): δ 160.6, 146.2, 131.4, 127.5, 124.0, 119.7, 111.2, 58.7, 27.1.

Anal. Calcd. for $C_{10}H_{11}N_7$: C, 52.39; H, 4.84; N, 42.77. Found: C, 52.64; H, 4.92; N, 42.63.

General Procedure for the Synthesis of **21a,b**.

A solution of the appropriate arylmagnesium bromide in diethyl ether (25 ml, 25 mmoles, 1*M* solution) was added to a solution of **20** (1.15 g, 5 mmoles) in tetrahydrofuran (30 ml) at room temperature. The mixture was refluxed for 24 hours, cooled and 5% aqueous solution of hydrochloric acid was added to *p*H 5. The mixture was extracted with ethyl acetate (3 x 50 ml), the combined organic layers were dried over magnesium sulfate and the solvent was removed *in vacuo* to give **21a** (37%) or **21b** (40%). The crude product was recrystallized from methylene chloride-petroleum ether, 1:1.

2-Phenyl-2-(1*H*-tetrazol-5-yl)propane (**21a**).

This compound was obtained as colorless microcrystals, mp 148-150°; ^{1}H nmr (DMSO-d_6): δ 7.36-7.17 (m, 5H), 1.78 (s, 6H); ^{13}C nmr (DMSO-d_6): δ 161.0, 145.8, 128.5, 126.7, 125.5, 37.8, 28.3.

Anal. Calcd. for $C_{10}H_{12}N_4$: C, 63.81; H, 6.43; N, 29.76. Found: C, 63.45; H, 6.51; N, 30.10.

2-(4-Methylphenyl)-2-(1*H*-tetrazol-5-yl)propane (**21b**).

This compound was obtained as colorless microcrystals, mp 181-183°; ^{1}H nmr (DMSO-d_6): δ 7.10 (d, 2H, J = 8.3 Hz), 7.06 (d, 2H, J = 8.5 Hz), 2.26 (s, 3H), 1.75 (s, 6H); ^{13}C nmr (DMSO-d_6): δ 162.7, 142.9, 135.8, 129.0, 125.3, 37.4, 28.3, 20.4.

Anal. Calcd. for $C_{11}H_{14}N_4$: C, 65.32; H, 6.98; N, 27.70. Found: C, 64.98; H, 7.03; N, 28.03.

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