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Received September 16, 1993

Lithiation of 2-, 3- and 4-[α -(benzotriazol-1-yl)methyl]pyridines with butyllithium followed by reactions with electrophiles (alkyl halides, aldehydes, ethyl benzoate and diphenyl disulfide) gave the corresponding α -substituted derivatives in good yields. Repetition of the reaction sequence allowed substitution of the second α -proton by an electrophile. 2-[α -(Benzotriazol-1-yl)- α -(phenylthio)pentyl]pyridine thus obtained gave an unusual attack of the Grignard reagents at C-3a of the benzotriazole system on treatment with arylmagnesium bromides.

J. Heterocyclic Chem., **31**, 757 (1994).

Introduction.

The unusual ability of benzotriazole to act both as an α -carbanion stabilizing moiety and as a good leaving group has provided the basis for many useful synthetic transformations. Thus, *N*-(benzotriazol-1-yl)methylpyrrole, -indole, -carbazole, -imidazole and -benzimidazole readily undergo lithiation and reactions with electrophiles [1]; subsequent treatment of the resulting products with Grignard reagents, organic thiolates or other nucleophiles results in the displacement of the benzotriazolyl group to give the corresponding functionalized *N*-substituted heterocycles [2]. (Benzotriazol-1-yl)methylphenols [3], -methoxyarenes [4] or -anilines [5] also undergo lithiations and reaction with electrophiles: subsequent displacements of the benzotriazolyl group by electron-rich aromatics or other nucleophiles produces a variety of industrially useful compounds [6]. Continuing our studies of the utilization of benzotriazole in organic synthesis, we have investigated the synthetic transformations of (benzotriazol-1-ylmethyl)pyridines.

Substitution of an *N*-linked benzotriazolyl moiety by the alkyl or aryl group of a Grignard reagent proceeds smoothly when the electron donor groups are attached to the α -carbon atom [7]. If such activating groups are absent or insufficiently activating, organomagnesium reagents attack the N-2 and/or the N-3 atom causing opening of the heterocyclic ring and further conversions with loss of one or two nitrogen atoms [8-11]. The strong electron acceptor effect imposed by the α -pyridyl substituent in α -(benzotriazol-1-yl)alkylpyridines caused the unexpected results described in this paper.

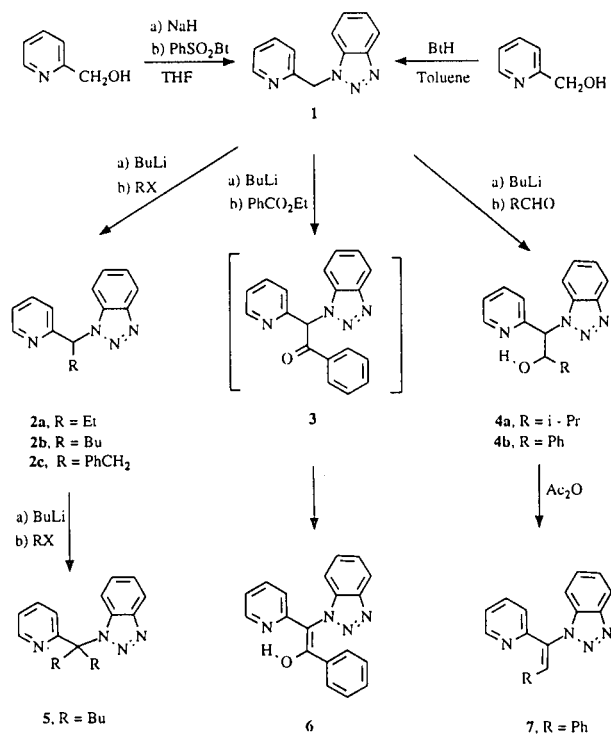
Results and Discussion.

Derivatives of 2-[(Benzotriazol-1-yl)methyl]pyridine.

2-[(Benzotriazol-1-yl)methyl]pyridine (**1**) was prepared by reaction of 2-pyridylcarbinol with 1-(phenylsulfonyl)benzotriazole in the presence of sodium hydride or by direct condensation of 2-pyridylcarbinol with benzotriazole under azeotropic conditions in toluene. Lithiation of

1 with butyllithium at -78° followed by treatment with alkyl halides gave 2-[1-(benzotriazol-1-yl)alkyl]pyridines **2** in good yields (Scheme 1). Small amounts of dialkylated product **5** were also detected in the reaction mixtures. Using two molar equivalents of butyllithium and two molar equivalents of butyl bromide under similar conditions allowed the direct preparation of the dialkylated product **5** in good yield (Table 1). The unusual upfield shifts of the H-3 pyridyl (δ 6.87) and the H-7 benzotriazol-1-yl (δ 6.65) resonances in the ^1H nmr spectrum of dibutyl derivatives **5** (Table 2) can be explained in terms of steric hindrance in the molecule resulting in the location of these protons in the shielding zones of the aromatic rings.

Scheme 1



Reaction of lithiated **1** with ethyl benzoate gave the benzoyl derivative **3** which was found to exist in solutions

Table 1
Reaction of Lithiated (Benzotriazol-1-yl)methylpyridines with Electrophiles

Product	Reagent	Yield (%)	Melting Point (°C)	Found (%)			Calcd. (%)		
				C	H	N	C	H	N
2a	EtI	83	63-64	70.32	5.95	23.64	70.56	5.92	23.51
2b	BuI	83	oil	72.26	6.89	21.15	72.15	6.81	21.04
2c	PhCH ₂ Br	65	86-87	76.28	5.39	18.76	75.97	5.37	18.65
4a	<i>i</i> -Pr-CHO	79	135-136	68.22	6.47	20.04	68.06	6.42	19.85
4b	PhCHO	89	136-137	71.91	5.06	17.80	72.13	5.10	17.71
5	BuBr	78	94-95	74.38	8.19	17.45	74.49	8.13	17.38
6	PhCO ₂ Et	77	168-170	72.20	4.50	17.67	72.59	4.48	17.82
7	Ac ₂ O	86	146-148	76.62	4.71	18.88	76.49	4.73	18.78
8a	EtI	85	90-91	70.67	5.96	23.75	70.56	5.92	23.51
8b	BuI	56	oil	71.94	6.86	21.05	72.15	6.81	21.04
8c	<i>i</i> -BuI	82	89-90	72.10	6.88	20.95	72.15	6.81	21.04
8d	PhCH ₂ Br	71	136-138	75.99	5.43	18.61	75.97	5.37	18.65
10	PhCHO	56	102-103	71.95	5.20	17.39	72.13	5.10	17.71
11	PhSSPh	81	152-153	70.65	5.99	14.67	70.56	5.92	14.96
12	PhCO ₂ Et	71	202-203	72.76	4.48	17.91	72.59	4.48	17.82
13a	BuI	84	82-83	71.86	6.84	21.07	72.15	6.81	21.04
13b	PhCH ₂ Br	80	131-132	76.18	5.36	18.73	75.97	5.37	18.65
15a	<i>i</i> -PrCHO	74	207-208	68.08	6.46	19.95	68.06	6.42	19.85
15b	PhCHO	82	204-205	72.21	5.14	17.64	72.13	5.10	17.71
16	PhSSPh	80	125-126	70.56	5.92	14.96	70.50	5.96	14.94

exclusively in the tautomeric form **6**. The ¹³C nmr spectrum showed two quaternary carbon signals at δ 103.3 (C- α) and δ 172.0 (C- β) instead of a C-H carbon and a carbonyl signals expected for **3** (Table 3). The unusually high field doublet (δ 6.13) in the ¹H nmr spectrum of **6** was assigned to the H-7 peak of the benzotriazole system (2D proton-carbon correlation - HETCOR). This upfield shift must be caused by location of the H-7 atom in the shielding zone of the pyridine system and it therefore indicates that the molecules of **6** are nonplanar.

Treatment of lithiated **1** with isobutyraldehyde gave a mixture of two diastereomers of **4a** in approximately equimolar amounts. Recrystallization of **4a** provided 90% pure one diastereomer. The vicinal coupling constant ($J_{\alpha,\beta}$ = 4.3 Hz) in the ¹H nmr spectrum of **4a** indicates an H-C- α -C- β -H dihedral angle of 43° or 122° (Karplus correlation). The first of these possibilities should be excluded due to the strong repulsive interactions between bulky substituents on the C- α and C- β atoms. The second of these angles means a staggered conformation which can be justified only by strong hydrogen bonding between the hydroxy group and one of the substituents on C- α . Because the pyridine nitrogen is much more basic than the benzotriazolyl N-2 atom, the existing situation can be depicted as in Chart 1 giving rise to the assignment of the relative configuration as $\alpha R^*, \beta S^*$. Evaporation of the filtrate from the above recrystallization gave a sample of **4a** enriched in another diastereomer (60%) exhibiting the H- α resonance as a doublet at δ 6.18. The coupling constant of this doublet (7.8 Hz) indicates a dihedral angle of 142°, reflecting much weaker

hydrogen bonding between the OH group and N-2 of the benzotriazolyl substituent in the $\alpha S^*, \beta S^*$ diastereomer.

Reaction of lithiated **1** with benzaldehyde also produced a mixture of two diastereomers, from which a single diastereomer of **4b** was isolated by recrystallization from ethyl acetate. Attempted acylation of **4b** with acetic anhydride caused elimination of the hydroxy group to produce β, β -disubstituted styrene **7** (Scheme 1). The remarkable upfield shift of the H-3 pyridyl and the phenyl *ortho* proton resonances (δ 6.49 and 6.78, respectively) indicates strong diamagnetic shielding effects imposed on these aromatic rings by each other (in analogy to α -substituted *cis*-stilbenes [12]) and therefore the *E* configuration of the molecule of **7**.

Derivatives of 3- and 4-[(Benzotriazol-1-yl)methyl]pyridines.

Alkylations of the lithiated 3-(benzotriazol-1-ylmethyl)pyridine (**9**) [13] with equimolar amounts of three alkyl

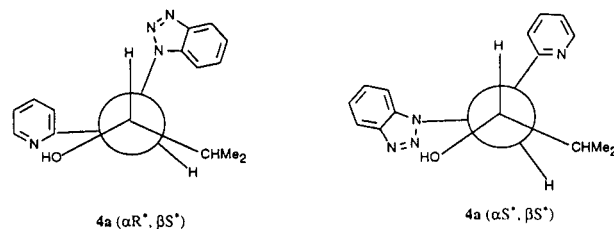


Chart 1

Table 2
 ^1H NMR Spectral Data [a] for the New Pyridine Benzotriazol-1-yl Derivatives

No	Pyridyl				Benzotriazol-1-yl				Other		
	H-2	H-3	H-4	H-5	H-6	H-4	H-5	H-6		H-7	Ha
1a	-	7.04 (d, 7.9)	7.59 (dt, 7.8, 1.8)	7.20 (dd, 6.0, 7.6)	8.58 (ddd, 0.9, 1.7, 4.9)	8.06 (dt, 8.2, 1.0)	7.34 (ddd, 1.2, 6.9, 8.2)	7.42 (ddd, 1.0, 6.9, 8.0)	7.52 (dt, 8.3, 1.0)	5.97 (s)	-
2a	-	7.20 (m)	7.60 (m)	7.20 (m)	8.60 (m)	8.06 (dt, 8.1, 1.0)	7.33 (ddd, 1.2, 6.9, 8.1)	7.41 (ddd, 1.1, 6.9, 8.1)	7.59 (m)	5.93 (dd, 6.3, 9.3)	0.98 (t, 7.4, 3H), 2.68 (m, 1H), 2.77 (m, 1H)
2b	-	7.21 (dt, 8.0, 1.1)	7.57 (dt, 7.7, 1.8)	7.17 (ddd, 1.0, 4.9, 7.5)	8.59 (ddd, 1.0, 1.8, 4.9)	8.05 (dt, 8.2, 1.0)	7.32 (ddd, 1.1, 6.9, 8.1)	7.40 (ddd, 1.1, 7.0, 8.1)	7.62 (dt, 8.3, 1.0)	6.03 (dd, 6.0, 9.6)	0.85 (t, 7.2, 3H), 1.35 (m, 4H), 2.62 (m, 1H), 2.78 (m, 1H)
2c	-	7.19 (d, 7.8)	7.51 (dt, 7.6, 1.7)	7.14 (dd, 5.4, 8.3)	8.58 (d, 4.8)	7.97 (d, 8.4)	7.23 (t, 7.6)	7.30 (t, 7.0)	7.51 (d, 8.4)	6.26 (dd, 6.1, 9.5)	3.96 (dd, 6.1, 14.1, 1H), 4.05 (dd, 9.6, 14.0, 1H), 7.09 (m, 5H)
4a	-	7.07 (d, 7.8)	7.61 (m)	7.26 (m)	8.63 (dd, 0.9, 4.9)	8.06 (m)	7.35 (m)	7.35 (m)	7.58 (m)	6.25 (d, 4.3)	1.05 (d, 6.7, 3H), 1.06 (d, 6.6, 3H), 1.50 (m, 1H), 4.37 (d, 6.1, 1H, OH), 6.53 (m, 1H)
4b [b]	-	7.73 (m)	7.73 (m)	7.27 (m)	8.59 (ddd, 1.0, 1.7, 4.9)	7.81 (dt, 8.3, 1.0)	7.21 (ddd, 1.1, 7.0, 8.1)	7.34 (ddd, 1.0, 6.9, 8.1)	7.77 (m)	6.26 (d, 9.5)	6.00 (dd, 4.4, 9.5, 1H), 6.08 (dd, 4.5, OH), 7.04 (m, 3H), 7.27 (m, 2H)
5	-	6.87 (dt, 8.0, 1.0)	7.55 (dt, 7.5, 1.8)	7.22 (m)	8.68 (ddd, 0.9, 1.9, 4.9)	8.06 (dt, 8.3, 1.0)	7.26 (m)	7.14 (ddd, 1.1, 6.9, 8.1)	6.65 (dt, 8.4, 1.0)	-	0.80 (t, 7.1, 6H), 1.20 (m, 5H), 3.50 (m, 3H)
6	-	6.11 (d, 8.8)	7.50 (ddd, 1.7, 7.4, 8.7)	7.04 (m)	8.25 (d, 4.9)	8.03 (m)	7.30 (m)	7.30 (m)	7.22 (m)	-	7.05 (m, 3H), 7.20 (m, 2H)
7	-	6.49 (d, 8.0)	7.51 (td, 7.8, 2.5)	7.21 (ddd, 1.0, 4.7, 7.5)	8.68 (ddd, 0.9, 1.7, 4.6)	8.16 (m)	7.35 (m)	7.35 (m)	7.15 (m)	-	6.78 (d, 7.4, 2H), 7.08 (m, 3H) 8.32 (s, 1H)
8a	8.74 (d, 2.2)	-	7.71 (dt, 8.0, 1.8)	7.26 (dd, 4.8, 8.0)	8.55 (dd, 1.6, 4.8)	8.08 (dt, 8.2, 1.0)	7.35 (m)	7.43 (m)	7.43 (m)	5.72 (dd, 6.5, 9.2)	0.99 (t, 7.3, 3H), 2.53 (m, 1H) 2.82 (m, 1H)
8b	8.74 (d, 2.4)	-	7.74 (dt, 7.9, 2.1)	7.26 (ddd, 1.1, 4.8, 8.0)	8.55 (dd, 1.6, 4.8)	8.07 (dt, 8.2, 1.1)	7.34 (ddd, 1.4, 6.6, 8.1)	7.42 (ddd, 1.1, 6.5, 8.3)	7.47 (dt, 8.3, 1.1)	5.85 (dd, 6.4, 9.1)	0.86 (t, 7.3, 3 H), 1.27 (m, 2 H), 1.38 (m, 2H), 2.50 (m, 1H), 2.79 (m, 1H)
8c [c]	8.75 (m)	-	7.99 (dt, 8.1, 2.1)	7.29 (m)	8.54 (d, 4.8)	8.06 (d, 8.4)	7.35 (ddd, 1.2, 6.8, 8.2)	7.47 (t, 7.4)	7.53 (m)	5.36 (d, 10.7)	0.88 (t, 7.4), 0.95 (d, 6.8), 1.00-1.50 (m, 2H), 3.02 (m, 1H)
8d	8.60 (d, 2.2)	-	7.76 (dt, 8.1, 2.2)	7.26 (dd, 4.8, 9.0)	8.54 (dd, 1.2, 4.6)	8.03 (m)	7.33 (m)	7.33 (m)	7.33 (m)	5.96 (dd, 6.9, 8.6)	3.75 (dd, 6.8, 13.9), 4.12 (dd, 8.6, 13.9)
10	8.25 (d, 2.2)	-	7.53 (dt, 8.1, 1.6)	7.14 (dd, 4.8, 8.0)	8.42 (dd, 1.6, 4.8)	8.07 (m)	7.40 (m)	7.40 (m)	7.40 (m)	5.85 (d, 8.3)	7.06 (m, 2H), 7.15 (m, 3H) 3.93 (d, 3.6, 1H, OH) 5.94 (dd, 3.7, 8.3, 1H), 7.24 (m, 5H)
11	8.60 (m)	-	7.50 (dt, 8.1, 2.1)	7.27 (m)	8.60 (m)	8.09 (d, 7.7)	7.30 (td, 8.1, 1.4)	7.36 (td, 8.3, 1.1)	7.13 (d, 8.5)	-	0.83 (t, 6.9, 3H), 1.20 (m, 1H), 1.30 (m, 2H), 1.60 (m, 1H), 2.72 (m, 2H), 6.66 (d, 7.1, 2H), 7.08 (t, 7.6, 2H), 7.26 (m, 1H)
12	8.69 (d, 2.4)	-	7.71 (dt, 8.0, 2.0)	7.33 (m)	8.63 (dd, 1.5, 4.8)	8.07 (m)	7.36 (m)	7.36 (m)	7.36 (m)	7.81 (s)	7.45 (t, 7.4, 2H), 7.59 (tt, 1.2, 7.4) 7.98 (m, 2 H)
13a	8.57 (d, 5.9)	7.22 (d, 6.1)	-	7.22 (d, 6.1)	8.57 (d, 5.9)	8.09 (m)	7.40 (m)	7.40 (m)	7.40 (m)	5.77 (dd, 5.9, 9.5)	0.87 (t, 7.1, 3H), 1.35 (m, 4H) 2.44 (m, 1H), 2.78 (m, 1H)
13b	8.53 (d, 6.1)	7.19 (d, 6.1)	-	7.19 (d, 6.1)	8.53 (d, 6.1)	8.03 (m)	7.30 (m)	7.30 (m)	7.30 (m)	5.98 (dd, 6.8, 8.8)	3.73 (dd, 6.8, 13.9, 1H), 4.08 (dd, 8.9, 13.9, 1H), 7.05 (m, 2H), 7.13 (m, 3H)

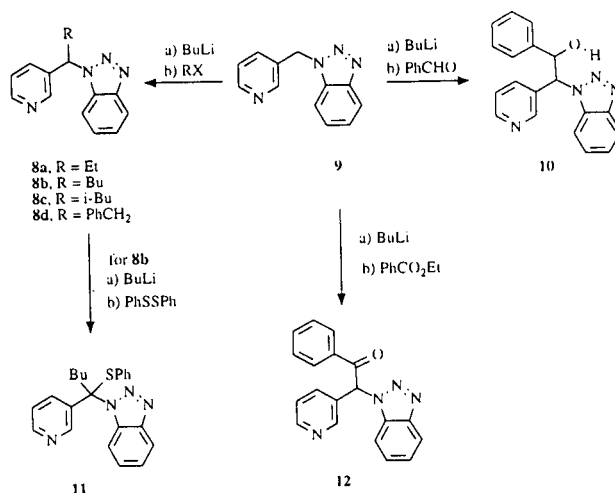
Table 2 (Continuation)

15a	8.56 (d, 6.0)	7.49 (d, 6.1)	-	7.49 (d, 6.1)	8.56 (d, 6.0)	7.99 (d, 8.3)	7.35 (ddd, 0.9, 7.0, 8.1)	7.47 (ddd, 1.0, 6.9, 8.3)	7.79 (d, 8.0)	5.91 (d, 8.1)	1.00 (d, 6.4, 1H), 1.50 (m, 1H), 4.65 (m, 1H), 5.03 (d, 6.2, 1H, OH), 4.14 (d, 3.9), 5.93 (m, 1H), 7.50 (m, 5H)
15b	8.38 (d, 6.2)	6.93 (d, 6.1)	-	6.93 (d, 6.1)	8.38 (d, 6.2)	8.06 (d, 8.2)	7.80 (m)	7.80 (m)	7.80 (m)	5.80 (d, 8.1)	0.86 (t, 7.2, 3H), 1.02 (m, 1H), 1.32 (sextet, 7.4, 2H), 1.81 (m, 1H), 2.84 (m, 2H), 6.65 (d, 7.8, 2H), 7.05 (t, 7.8, 2H), 7.24 (m, 1H)
16	-	6.90 (d, 8.0)	7.59 (dt, 8.0, 1.8)	7.30 (m)	8.57 (m)	8.05 (d, 8.0)	7.33 (m)	7.26 (m)	7.10 (d, 7.8)	-	

[a] Chemical shifts are given in ppm vs. TMS; coupling constants (in parentheses) are in Hz. [b] Spectrum taken in DMSO-d₆. [c] Data for the predominant diastereomer.

iodides and of benzyl bromide produced the corresponding products **8** in good yields (Scheme 2). Introduction of one more asymmetric carbon atom to the molecule resulted in formation of a mixture of two diastereomers of **8c** in an approximate ratio of 5:4. The mixture was not separated and only the predominant diastereomer was characterized by nmr. Further treatment of **8b** with butyllithium, followed by a reaction with diphenyl disulfide produced the sulfide **11**.

Scheme 2



Reaction of lithiated **9** with benzaldehyde gave carbinol **10** in 56% yield. Similar to **4b**, only one of the diastereomers of **10** was separated and characterized. Contrary to **4b**, the large coupling constant between the H_α and H_β in **10** indicated a dihedral angle of almost 180° (Karplus correlation) and because of a lack of hydrogen bonding, the stereochemical assignment could not be deduced by analysis of the ¹H nmr spectrum. Interestingly, reaction of lithiated **9** with ethyl benzoate gave derivative **12** which existed exclusively in the keto form as demonstrated by ¹H and ¹³C nmr spectroscopy (δ (C-α) 65.2, δ (C=O) 191.3). This difference from **6** can be attributed to the lack of hydrogen bonding in **12**.

Similar to the 3-pyridyl derivative, 4-(benzotriazol-1-ylmethyl)pyridine (**14**) underwent lithiation and reaction with butyl iodide and with benzyl bromide yielding compounds **13a** and **13b**, respectively (Scheme 3). Reaction of **14** with aldehydes gave compounds **15**, and again only one predominant diastereomer was separated.

Scheme 3

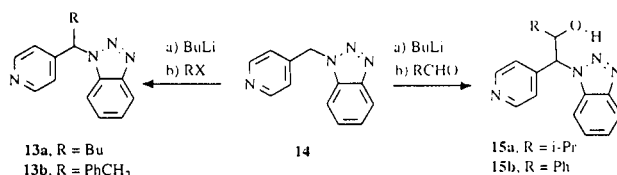


Table 3
 ^{13}C nmr Spectral Data [a] of the New Pyridine Benzotriazol-1-yl Derivatives

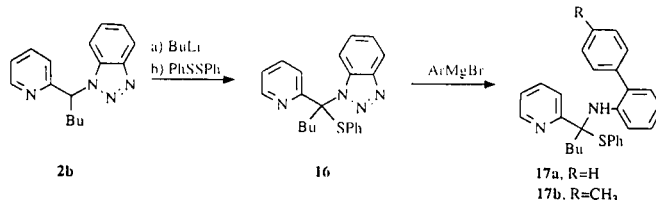
No	Pyridyl					Benzotriazol-1-yl							Other
	C-2	C-3	C-4	C-5	C-6	C4	C-5	C-6	C-7	C4 α	C-7 α	C- α	
1	154.8	121.8	137.1	123.1	149.5	119.9	124.0	127.5	109.9	146.1	133.0	53.8	-
2a	158.2	121.5	137.1	123.8	149.1	119.8	123.8	127.1	110.4	146.1	132.9	67.1	11.0, 26.8
2b	158.5	121.5	137.2	123.0	149.2	119.8	123.9	127.2	110.5	146.2	133.0	65.6	13.8, 22.2, 28.5, 33.2
2c	157.5	123.2	137.1	121.8	149.2	119.7	123.8	127.2	110.2	146.0	133.0	66.6	39.5, 126.7, 128.4 (2 C), 129.0 (2 C), 137.0
4a	157.3	124.6	137.8	123.5	149.3	120.3	123.7	128.1	111.6	146.4	133.9	66.6	18.3, 20.1, 31.0, 78.3, 126.6 (2 C), 127.5, 127.7 (2 C), 141.4
4b [b]	156.4	123.8	136.8	123.2	148.8	118.8	123.5	126.9	110.8	144.9	132.7	69.1	73.4, 126.6 (2 C), 127.5, 127.7 (2 C), 141.4
5	161.3	121.5	136.5	122.4	148.3	119.7	123.3	126.2	111.4	146.5	131.9	71.8	13.7, 22.5, 25.0, 35.4
6	155.8	117.4	130.0	118.5	140.9	119.8	124.0	128.0	109.8	145.7	134.8	103.9	127.0 (2 C), 127.9 (2 C), 129.6, 135.9, 172.6
7	153.2	120.0	137.0	123.3	149.7	119.8	124.3	128.2	110.1	145.9	133.2	120.0	128.5 (2 C), 129.1 (2 C), 129.2, 131.2
8a	148.8	135.2	134.8	124.3	150.2	120.6	124.5	127.9	109.7	146.6	133.1	63.3	11.6, 28.6
8b	148.4	135.1	134.5	123.9	149.8	120.1	124.1	127.5	109.4	146.1	132.7	61.2	13.9, 22.2, 28.5, 34.6
8c [c]	149.6	135.0	135.7	124.3	150.2	120.5	124.4	127.9	109.5	146.1	133.6	66.5	10.9, 16.8, 26.3, 39.1
8d	148.4	136.2	134.5	123.7	149.8	119.9	124.0	127.4	109.0	145.8	132.7	62.6	41.4, 127.0, 128.5 (2 C), 128.9 (2 C), 134.3
10	149.7	133.8	136.2	123.5	149.3	119.0	124.1	127.3	111.3	144.8	132.5	65.8	74.7, 127.7 (2 C), 127.8, 128.1 (2 C), 141.3
11	149.7	135.6	134.2	123.3	147.9	129.1	124.1	126.9	113.8	146.9	131.9	78.0	14.0, 22.3, 26.3, 40.3, 127.9, 128.9 (2 C), 130.3, 136.5
12	150.5	134.1	134.5	123.8	149.8	120.2	124.2	128.0	110.4	146.4	132.7	65.2	128.8 (2 C), 129.0 (2 C), 129.3, 136.5, 191.3
13a	150.4	121.6	148.1	121.6	150.4	120.2	124.2	127.5	109.3	146.2	132.8	62.5	13.8, 22.2, 28.5, 34.2
13b	150.3	121.7	147.4	121.7	150.3	120.1	124.1	127.5	109.2	145.9	132.9	63.9	41.0, 127.1, 128.6 (2 C), 129.0 (2 C), 136.1
15a	149.7	122.2	145.3	122.2	149.7	119.2	123.7	127.1	109.7	145.1	133.2	65.0	15.3, 19.7, 29.5, 77.4
15b	149.4	122.5	144.6	122.5	149.4	119.3	123.8	127.2	109.7	145.2	133.4	68.6	75.0, 126.6 (2 C), 127.8, 127.9 (2 C)
16	158.6	121.2	137.2	123.4	148.6	119.9	124.0	126.7	113.4	146.7	132.2	81.2	14.0, 22.5, 26.1, 39.1, 128.6 (2 C), 129.5, 129.8, 136.4 (2 C)

[a] Chemical shifts are in ppm from the TMS ($\delta = 0$) reference. [b] Spectrum taken in DMSO- d_6 . [c] Data for the predominant diastereomer in the mixture.

Grignard Reactions.

Reaction of lithiated **2b** with diphenyl disulfide gave sulfide **16** in good yield (Scheme 4). Unexpectedly, we have found that treatment of **16** with phenylmagnesium and *p*-tolylmagnesium bromides, instead of giving substitution of the benzotriazolyl moiety [14], led to a new class of compounds. Detailed analysis of the nmr spectra of these products, **17a** and **17b**, including selective decoupling and 2D proton-carbon correlation (HETCOR) techniques, allowed assignments of the resonances to the 2-pyridyl, phenylthio and the aryl groups derived from the Grignard reagents. Some additional aromatic resonances were observed at an unusually high field in the ^1H nmr spectra of **17a** (doublet of doublets at δ 6.15 and triplet of doublets at δ 6.56) and **17b** (doublet of doublets at δ 6.18 and triplet of doublets at δ 6.54). These and their corresponding ^{13}C nmr resonances at δ 112.8 and 115.7, for **17a**, δ 112.9 and δ 115.6, for **17b**, indicated the presence of an *ortho* substituted aniline ring [15,16]. The remaining resonances of such aniline systems, partially overlapped with other aromatic resonances, were also located.

Scheme 4



The simplest pathway leading to compounds **17** is nucleophilic attack of the Grignard reagent on the benzotriazolyl C-3 α atom followed by elimination of a molecule of nitrogen. Such behavior appears to be unprecedented for benzotriazol-1-yl derivatives. Probably, coordination of the Grignard magnesium atom with the pyridinyl nitrogen (with help from the sulfur atom) of **16** activates the system for this new type of reaction. Attempted reaction of compound **11**, the 3-pyridyl analog of **16**, with phenylmagnesium bromide produced a complex mixture which could not be separated by column chromatography; no product of structure similar to **17a** was detected in the mixture by nmr spectroscopy.

EXPERIMENTAL

The ^1H and ^{13}C nmr spectra were recorded on a Varian XL300 spectrometer (300 and 75 MHz, respectively) in deuteriochloroform or DMSO- d_6 referenced to TMS. Elemental analyses were performed on a Carlo Erba 1106 elemental analyser. Melting points ($^{\circ}\text{C}$) were determined on a Fisher-Johns hot stage apparatus and are uncorrected.

2-(Benzotriazol-1-ylmethyl)pyridine (**1**).

Method A.

To a suspension of sodium hydroxide (2.64 g, 110 mmoles) in anhydrous THF (300 ml) was added a solution of 2-pyridylcarbinol (10.9 g, 100 mmoles) in dry THF (100 ml) at room temperature. The reaction mixture was stirred for 4 hours and a solution of 1-(phenylsulfonyl)benzotriazole (26.9 g) in dry THF (200 ml) was added slowly. The resultant mixture was refluxed overnight. Most of the solvent was evaporated to yield an oily product which was extracted with methylene chloride (3 x 100 ml). The combined extracts were successively washed with 5% sodium hydroxide (1 x 100 ml) followed by water (2 x 100 ml) and then dried over magnesium sulfate. Evaporation of the solvent gave a dark brown crude product which was purified by column chromatography (silica gel, ethyl acetate/hexane, 1:1) yielding **1** (14.5 g, 69%) as a yellow solid.

Method B.

A mixture of benzotriazole (5.5 g, 46 mmoles), 2-pyridylcarbinol (4.4 g, 40 mmoles) and 37% hydrochloric acid (10 ml) in toluene (100 ml) was heated under a Dean Stark trap for 24 hours. The reaction mixture was successively washed with 5% sodium hydroxide (1 x 30 ml) and water (1 x 50 ml), and dried over magnesium sulfate. Evaporation of the solvent and column chromatography of the residue (silica gel, ethyl acetate/hexane, 1:1) afforded **1** (1.5 g, 17.9%).

General Procedure for Lithiation and Reaction with Electrophiles.

To a solution of 2-(benzotriazol-1-ylmethyl)pyridine (**2**) (2.10 g, 10 mmoles) in anhydrous THF (30 ml) at -78° under nitrogen was added 2.5 *M* butyllithium in hexane (4 ml, 10 mmoles). The reaction mixture was stirred at -78° for 2 hours and then an appropriate electrophile (10 mmoles) in THF (20 ml) was added to the obtained deep purple solution. The reaction mixture was stirred for one additional hour at -78° and then allowed to warm to room temperature overnight. Most of the solvent was evaporated to give an oily residue which was mixed with 50 ml of water and extracted 3 times with 50 ml of dichloromethane. The combined organic layers were washed with water (2 x 50 ml) and then dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a yellow oil. Column chromatography (silica gel, ethyl acetate/hexane) yielded the pure product.

E-1-(Benzotriazol-1-yl)-1-(pyrid-2-yl)-2-phenylethene (**7**).

A solution of 1.0 g of 2-[1-(benzotriazol-1-yl)-2-hydroxy-2-phenylethyl]pyridine (**4b**) in 20 ml of acetic anhydride was refluxed for 12 hours. Analysis (tlc) indicated that complete dehydration had occurred. Acetic anhydride was neutralized with 5% sodium hydroxide and the resulting solution was extracted twice with 30 ml of methylene chloride. The combined extracts were washed with water and dried over magnesium sulfate. Evaporation of the solvent gave a white solid which was recrystallized from ethyl ace-

tate and hexane to afford pure **7** (0.81 g, 86%).

Reaction of **16** with Phenylmagnesium Bromide.

The Grignard reagent was prepared from magnesium turnings (6.08 g, 250 mmoles) and bromobenzene (21.1 ml, 200 mmoles) in dry diethyl ether (100 ml). A small amount of iodine was used to initiate the reaction. After reflux for 4 hours, the solution was decanted from the excess magnesium to give 100 ml of the Grignard reagent (2 mmoles/ml) which was stored under nitrogen.

To 20 ml of the above Grignard reagent was added slowly a solution of 1.87 g (5 mmoles) of compound **16** in 30 ml of dry diethyl ether. The color of the mixture became dark brown and the temperature rose to cause refluxing of the diethyl ether. After refluxing ceased, 50 ml of dry toluene was added and the ether was distilled off. The reaction mixture was heated at $95-100^{\circ}$ overnight. The resulting mixture was poured into ice-water (50 g) and extracted with toluene (2 x 50 ml). The combined extracts were washed with water (2 x 50 ml) and dried over magnesium sulfate. The volatiles were evaporated under vacuum and the crude product was purified by column chromatography (silica gel, methylene chloride/hexanes, 2:1) to afford 2-phenyl-*N*-[1-(phenylthio)-1-(pyridin-2-yl)pentyl]aniline (**17a**) (1.1 g, 52%). Recrystallizations from ethanol gave an analytical sample, mp $103-104^{\circ}$; ^1H nmr (deuteriochloroform): 300 MHz, δ 0.47 (m, 1H, Bu), 0.63 (t, J = 7.1 Hz, 3H, Bu), 0.90 (m, 1H, Bu), 1.07 (m, 2H, Bu), 2.38 (m, 1H, Bu), 2.76 (td, J = 13.4 and 4.5 Hz, 1H, Bu), 6.15 (d, J = 7.4 Hz, 1H, Anl), 6.56 (td, J = 7.4 and 0.7 Hz, 1H, Anl), 6.93 (td, J = 6.8 and 1.7 Hz, 1H, Anl), 6.98 (d, J = 8.8 Hz, 1H, Pyr), 7.04 (m, 1H, Pyr), 7.09 (m, 1H, PhS), 7.22 (m, PhS (2H) and Ph (3H)), 7.34 (m, PhS (2H) and Ph (2H)), 7.45 (dt, J = 8.0 and 1.8 Hz, 1H, Pyr), 7.54 (dd, J = 1.6 and 7.6 Hz, 1H, Anl), 7.99 (s, 1H, N-H), 8.50 (dt, J = 4.9 and 0.9 Hz, 1H, Pyr); ^{13}C nmr: 75 MHz δ 13.9 (Bu), 22.7 (Bu), 25.0 (Bu), 35.2 (Bu), 64.4 (N-C-S), 112.8 (Anl), 115.7 (Anl), 115.7 (Anl), 121.2 (Pyr), 121.5 (Pyr), 125.5 (PhS), 126.7 (3 C, Ph), 127.8 (2 C, PhS), 128.5 (4 C, Ph and PhS), 130.2 (Anl), 136.5 (Pyr), 137.1 (PhS), 137.7 (Anl), 145.7 (Ph), 146.3 (Anl), 146.9 (Pyr), 163.3 (Pyr). *Anal. Calcd. for* C₂₆H₂₈N₂S: C, 79.20; H, 6.65; N, 6.60. Found: C, 79.22; H, 6.76; N, 6.42.

Reaction of **16** with *p*-Tolylmagnesium Bromide.

The Grignard reagent was prepared from magnesium turnings (2.40 g, 100 g-atoms) and benzyl bromide (13.70 g, 80 mmoles) in diethyl ether. To 20 ml of the above Grignard reagent (about 20 mmoles) was added dropwise compound **16** (1.5 g, 4 mmoles) in 30 ml of dry diethyl ether. After the addition was complete, 30 ml of dry toluene was added. Diethyl ether was evaporated and the resulting mixture was heated at 70° overnight. After cooling to room temperature, the reaction mixture was poured into ice-water (50 g) and extracted with toluene (3 x 20 ml). The combined extracts were washed with 20% ammonium chloride solution (30 ml), 5% sodium hydroxide solution (30 ml) and then dried over magnesium sulfate. Evaporation of the solvent gave the crude product which was purified by column chromatography (methylene chloride/hexanes) to afford 2-(4-methylphenyl)-*N*-[1-(phenylthio)-1-(pyridin-2-yl)pentyl]aniline (**17b**), (0.82 g, 47%), mp $105-106^{\circ}$; ^1H nmr (deuteriochloroform): 300 MHz δ 0.42 (m, 1H, Bu), 0.56 (t, J = 7.3 Hz, 3H, Bu), 0.83 (m, 1H, Bu), 1.00 (m, 2H, Bu), 2.19 (s, 3H, Tol), 2.30 (m, 1H, Bu), 2.69 (td, J = 13.4 and 4.4 Hz, 1H, Bu), 6.18 (dd, J = 1.0 and 8.3 Hz, 1H, Anl), 6.54 (td, J = 7.4 and 1.2 Hz, 1H, Anl), 6.93 (td, J = 1.7 and 8.6 Hz, 1H, Anl), 6.96-7.10 (m, PhS (3H), Tol (2H) and Pyr (2H)), 7.21 (m, PhS (2H) and Tol (2H)), 7.31 (m, 2H, PhS), 7.41 (td, J = 7.6 and 1.8 Hz, 1H,

Pyr), 7.54 (dd, $J = 1.7$ and 7.6 Hz, 1H, Anl), 7.97 (s, 1H, N-H), 8.48 (dd, $J = 0.8$ and 4.1 Hz, 1H, Pyr); ^{13}C nmr: 75 MHz δ 13.9 (Bu), 20.9 (Tol), 22.8 (Bu), 25.0 (Bu), 35.2 (Bu), 64.2 (N-C-S), 112.9 (Anl), 115.6 (Anl), 115.6 (Anl), 121.1 (Pyr), 121.5 (Pyr), 125.5 (PhS), 126.5 (2 C, Tol), 127.4 (2 C, PhS), 128.5 (2 C, PhS), 129.6 (2 C, Tol), 130.2 (Anl), 136.2 (Tol), 136.5 (Pyr), 137.2 (PhS), 137.7 (Anl), 142.7 (Tol), 146.4 (Anl), 146.9 (Pyr), 163.6 (Pyr).

Anal. Calcd. for $\text{C}_{29}\text{H}_{30}\text{N}_2\text{S}$: C, 79.41; H, 6.89; N, 6.39. Found: C, 79.54; H, 6.90; N, 6.33.

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