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A New Route to N-Substituted Heterocycles

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Abstract: *N-(Benzotriazol-1-ylmethyl)-indole, -pyrrole, -carbazole, and -benzimidazole, and analogs substituted in the methylene group are converted by lithium aluminum hydride, or by Grignard reagents, or in two cases by organozinc reagents, into the N-substituted heterocycles in good yields.*

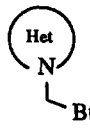
The N-alkylation of indole is usually accomplished utilizing the indole anion. A wide variety of methods have been developed for the generation of indole anions[1-5] including alkali salts and indole Grignard reagents. In some cases, exclusive N-alkylation is observed; in others this is accompanied by C-3(β)-alkylation. It is found that the regioselectivity depends on the metal counter ion, the solvent and the alkylating reagent used.[6-10] The alkylating reagents used include alkyl halides,[3,4,11,12] alkyl esters of toluenesulfonic acid[13,14] and even alcohols[15,16] (which react via the corresponding carbonyl compounds in the presence of aluminum alkoxide and Raney nickel). Some alkylations of indole have been carried out at neutral pH or below, but relatively vigorous conditions are then required[6] and both C- and N-alkylations usually occur giving complex mixtures.

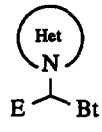
The N-alkylation of pyrrole shows many similarities to that of indole. Direct alkylation of the pyrrole anion gives mainly 1-alkylpyrrole, but 2- and 3-alkylpyrroles may also be formed in varying amounts depending on the solvent, the nature of the cation, and the alkylating agent.[17,18] A strong base[8] is needed and sometimes a phase-transfer reagent.[19] Alkyl halides,[19,20] alkyl sulfates,[17,21] and trialkyl phosphates[22,23] are the commonly used alkylating reagents. The alkylation of carbazole has been less investigated. Direct alkylation with alkyl halides, with a base and a phase-transfer reagent,[4,24,25] or with TlOEt[26] has been reported. The N-alkylation of imidazoles can be effected in the presence of alkaline reagents[27] such as alkali metal hydroxides,[28-30] sodium in ammonia,[31] and sometimes with a phase-tranfer catalyst.[29] Direct alkylations of imidazoles and benzimidazoles[32,33] under neutral conditions are also common.

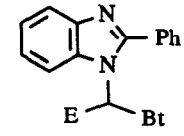
However, in most of the alkylations described above, only primary alkyl groups could be introduced efficiently. Low yields were obtained with sterically hindered alkyl halides in the alkylation of pyrrole[19] and benzimidazole,[33] and no reaction was observed with branched-chain alkyl halides in the case of carbazole.[26]

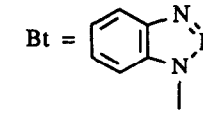
Previous work in our laboratory has demonstrated benzotriazole to be a useful synthetic auxiliary in the elaboration of many classes of compound.[34] In particular, we previously have demonstrated[35] that the reactions of indole, pyrrole, carbazole and benzimidazoles with 1-chloromethylbenzotriazole give the corresponding N-(benzotriazol-1-ylmethyl)-heterocycles **1-4**. We showed that compounds **1-3** were converted via lithiation and subsequent reaction with electrophiles into **5-7**. The lithiation of the

benzimidazole derivative **4** occurred at the 2- position, but the 2-phenylbenzimidazole derivative **8** underwent lithiation at the active methylene groups followed by reaction with electrophiles to give **9**.[35] (For a survey of extensive literature work of the lithiation of CH adjacent to heterocyclic nitrogen see ref.[35])





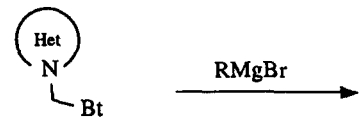




1	Indol-1-yl	**5**	Indol-1-yl	**8**	E = H
2	Pyrrol-1-yl	**6**	Pyrrol-1-yl	**9**	E ≠ H
3	Carbazol-9-yl	**7**	Carbazol-9-yl		
4	Benzimidazol-1-yl				

Displacements of the benzotriazole group in the N-heterocycle derivatives of types **1-7** by hydride with lithium aluminum hydride ($LiAlH_4$) or by carbon anions with Grignard reagents should provide synthetic routes to N-substituted heterocycles. In our earlier work,[35] no such displacements of the benzotriazole moiety in heterocycles **1-7** by nucleophiles were reported. In the present work, we have carried out a variety of such transformations, and have demonstrated that this methodology offers an attractive synthetic route for the introduction of complex N-substituents into heterocycles (see Scheme 1).

Scheme 1



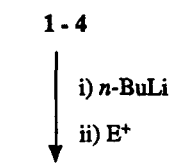
Designation of Het-N

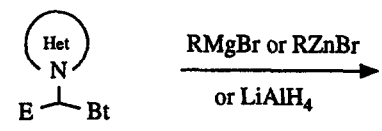
1,5,10,14	Indol-1-yl
2,6,11,15	Pyrrol-1-yl
3,7,12,16	Carbazol-9-yl
4,13	Benzimidazol-1-yl

1 - 4

10 - 13

a	R = Ph
b	R = $PhCH_2$
c	R = *n*-Bu





5 - 7:	E
a	$PhCH_2$
b	*n*-Bu
c	$(CH_2)_5C(OH)$
d	4-$CH_3C_6H_4CH(OH)$

14 - 16:	E	R
a	$PhCH_2$	*n*-Bu
b	$PhCH_2$	Ph
c	$(CH_2)_5C(OH)$	Ph
d	4-$CH_3C_6H_4CH(OH)$	Ph
e	$PhCH_2$	H
f	*n*-Bu	H

Heating N-(benzotriazol-1-ylmethyl)indole (**1**) with an excess of phenylmagnesium bromide in benzene under reflux for 25 h gave N-benzylindole (**10a**) in 74% yield. Butylmagnesium bromide reacted

similarly with **1** to give **10c**, though in a lower yield. N-(Benzotriazol-1-ylmethyl)-derivatives of pyrrole, carbazole, and benzimidazole **2-4** reacted with both aryl- and alkyl- Grignard reagents to give the expected products **11-13** in good yields. The benzotriazole generated was readily removed by alkali during work-up making the isolation and purification of the desired products easier. The substrate, Grignard reagents used, and other preparative data are given in Table 1.

Table 1 N-Substituted Heterocycles **10-16**

Product	Reactant	Reagent	Solvent	Reaction Time (h)	Yield (%)	M.p. (°C)	Lit. m.p. (°C) or b.p (°C/mm) or Calcd. (Found) C	H	N	Purifying solvent[a]
10a	**1**	PhMgBr	benzene	25	74	oil	45 [10]			50 ·1
10c	**1**	*n*-BuMgBr	benzene	25	37	oil	110-113/2 [10]			50 1
10c(14f)	**5b**	$LiAlH_4$	toluene	5 5	92	oil	110-113/2 [10]			20 1
11a	**2**	PhMgBr	THF	72	73	oil	116-119/11 [36]			hexane
11b	**2**	$PhCH_2MgBr$	THF	15	72	oil	100/3 [37]			hexane
11b (15e)	**6a**	$LiAlH_4$	THF	24	96	oil	100/3 [37]			hexane
11c	**2**	*n*-BuMgBr	THF	20	42	oil	80-82/15 [38]			hexane
12a	**3**	PhMgBr	benzene	20	96	118-119	118-119 [24]			-
13a	**4**	PhMgBr	toluene	24	86	113-115	114-115 [30]			4 1
13c	**4**	*n*-BuMgBr	toluene	72	56	oil	133-134/picrate [39]			1 .1
14a	**5a**	*n*-BuMgBr	toluene	12	94	oil	86 59 (87.00)	8.36 (8 11)	5 05 (4.79)	20:1
14d	**5d**	PhZnBr	toluene	20	55	44-45	84.37 (84 14)	6.46 (6 63)	4 28 (4.08)	30 1
15c	**6c**	PhMgBr	THF	16	50	64-65	79.96 (79 96)	8.28 (8.28)	5.49 (5.49)	10.1
15d	**6d**	PhZnBr	benzene	36	60	oil	b			50:1
16b	**7a**	PhMgBr	toluene	24	45	133-135	89 88 (89.86)	6.09 (6 09)	4.03 (3.98)	100.1
16d	**7d**	PhMgBr	benzene	6	50	248-250	85 91 (85.83)	6.14 (6 26)	3 71 (3.61)	50:1

[a]Eluent for column chromatography on silica gel, ratio for hexane/EtOAc.

[b]HRMS found M=277.1485. C19H19NO requires M=277.1467.

As we reported previously,[35] the derivatives **1-3** of indole, pyrrole, and carbazole were easily lithiated and the lithium derivatives were quenched with a variety of electrophiles to give **5-7**, respectively. These derivatives obtained in turn reacted easily with various Grignard reagents, or in two cases organozinc reagents, to give compounds **14-16**. It is noteworthy that the derivatives obtained via lithiation from trapping with cyclohexanone and 4-tolualdehyde reacted with phenylmagnesium bromide or phenylzinc bromide to give the desired products in good yields. Thus, the pyrrole derivative **6c** and the carbazole derivative **7d** reacted with phenylmagnesium bromide to give compounds **15c** and **16d**, respectively. Although the indole

derivative **5d** reacted with phenylmagnesium bromide to lead to only decomposition products and the pyrrole derivative **6d** reacted with phenylmagnesium bromide to give elimination product **26** instead of the expected compound **15d** (*vide infra*), these two derivatives **5d** and **6d** did react with phenylzinc bromide to afford the desired compounds **14d** and **15d**, respectively, in good yields. These reactions affording **14d** and **15d** succeeded despite the low solubilities of the salts formed from the alcohols with phenylmagnesium bromide or phenylzinc bromide. Since different aldehydes or ketones could be used as electrophiles, and different Grignard reagents or organozinc reagents could be used, other alcohols of types **(14-16)c-d** should be obtainable by this route in which a hydroxy functionality is introduced. The preparative data are given in Table 1.

The benzotriazole moiety in the derivatives obtained via lithiation is displaced by H on reduction with lithium aluminum hydride ($LiAlH_4$), as demonstrated by heating **5b** with an excess of $LiAlH_4$ in toluene for 5.5 h to give the desired product **14f** (= **10c**) in 92% yield. Similarly, the pyrrole derivative **6a** was reduced by $LiAlH_4$ to give **15e** (= **11b**) in 96% yield.

Table 2 ^{1}H NMR Spectral Data of Compounds **10, 11, 12, 13, 14, 15** and **16** Prepared

Compd	$HetCH_2R$ or HetCH(E)R	E	R	Other groups
10a	5 11(s, 2H)	-	-[a]	6 48-6 52 (m, 1H), 6 9-7 2 (m, 9H), 7 55-7 65 (m, 1H)
10c	4 00 (t, 2H, J=7 2)	0 85 (t, 3H, J=6 4), 1.1-1.4(m, 4H), 1 7-1 9(m, 2H)	-	6 4-6 5 (m, 1H), 7 0-7 4 (m, 4H), 7 5-7 7 (m, 1H)
11a	4 92(s,2H)	-	7 04(d, 2H, J=7 1), 7 15-7 35 (m, 3H)	6 16(t, 2H, J=2 1), 6 61(t, 2H, J=2 1)
11b	4 03(t, 2H, J=7.4)	-	2.99(t, 2H, J=7 4), 7.0-7.3(m, 5H)	6 10(t, 2H, J=2.0), 6 54(t, 2H, J=2 0)
11c	3 86(t, 2H, J=7.0)	-	0.88(t, 3H, J=6.7), 1 20-1.45(m, 4H) 1.65-1.85(m, 2H)	6.11(t, 2H, J=1 6), 6 62(t, 2H, J=1 6)
12a	5.4(s, 2H)	-	-[a]	7 1-7 6(m, 11H), 8 22(d, 2H, J=7 6)
13a	5 26(s, 2H)	-	-[a]	7 1-7 4(m, 8H), 7 8-7 9(m, 2H)
13c	4 05(t, 2H, J=7 1)	-	0 85(t, 3H, J=6 7), 1 2-1.4(m, 4H), 1 7-1 9(m, 2H)	7 2-7 4(m, 3H), 7 7-7 9(m, 2H)
14a	4 4-4 5 (m, 1H)	3 0-3.2 (m, 2H)[b]	0 76(t, 3H, J=7 2), 1 0-1 3 (m, 4H), 1 8-2 0(m, 2H)	6 50 (d, 1H, J=3 2), 6 9-7 0 (m, 2H), 7 0-7 3 (m, 7H), 7 6-7 7 (m, 1H)
14d	5 41(t, 1H, J=5 7)	2.20(s, 3H), 2.50(s, 1H), 5.56(d, 1H, J=6.2)[b]	-[a]	6 45(d, 1H, J=2 6), 6 8-7 2(m, 12H), 7.4-7 6(m, 2H)
15c	4 77(s, 1H)	1.2-1.7(m, 10H), 1.95(s, 1H)	7.25(d, 3H, J=6.6), 7.51(d, 2H, J=6 2)	6 09(s, 2H), 6 96(s, 2H)
15d	5 02(d, 1H, J=7.4)	2.23(s, 3H), 2 45(s, 1H) 5 17(d, 1H, J=7 4)[b]	-[a]	5 97(t, 2H, J=3 5), 6 54(t, 2H, J=3.5) 6 9-7 1(m, 4H), 7 2-7 3(m, 5H)
16b	6.06(t, 1H, J=7.5)	3 76(d, 2H, J=7 6)[b]	-[a]	6 7-6 8(m, 2H), 6.8-6.9(m, 3H), 7.0-7 3(m, 11H), 7 99(d, 2H, J=7.6)
16d	-[a]	2 03(s, 3H), 2.45(s, 1H)[b]	-[a]	5.95(d, 2H, J=2 4), 6.72(d, 2H, J=7.8) 6.94(d, 2H, J=8 1), 7 11(t, 2H, J=6 6) 7 2-7.4(m, 7H), 7 54(d, 2H, J=6 6),. 7 91(d,2H, J=7.0)

[a] Signals are overlapped and are reported in the column for other groups.

[b] Other signals are overlapped and are reported in the column for other groups.

These displacements of the benzotriazole group by Grignard reagents, organozinc reagents, or $LiAlH_4$ were carried out in benzene or toluene solutions. However, all the reactions with the pyrrole derivatives were carried out in refluxing THF, because the use of benzene or toluene as solvent caused decomposition.

The structures of the displacement products have been confirmed by their NMR spectral data and elemental analyses. The data for the known compounds have been compared with that reported in the literature. The NMR spectra of the displacement products clearly showed the disappearance of the characteristic benzotriazolyl signals. The methylene (in compounds **10-13**) or the methine [in compounds **(14-16)a-d**] signals in both ^1H and ^{13}C NMR spectra were shifted upfield as compared to those of their precursors due to the loss of the electron-withdrawing benzotriazole group (see Table 2,3).

Table 3 ^{13}C NMR Spectral Data of Compounds **10, 11, 12, 13, 14, 15** and **16** Prepared

Compd.	$HetCH_2R$ or HeCH(E)R	E	R	Other groups
10a	49 9	-	-[a]	101 6, 109.6, 119 5, 120 9, 121.6, 126 7, 127.4, 128 1, 128.6, 128 7, 136 2, 137.5
10c	46 2	13 9, 22.2, 29 0, 29.8	-	100.7, 109 3, 119.1, 120 8, 121.2, 127.6, 128 5, 135.9
11a	53	-	126.8, 127 4, 128.5, 138 1	108 3, 120 9
11b	51	-	38.2, 126 5, 128 4, 128.6, 138 4	107.9, 120.3
11c	49 5	-	13.8, 22.2, 28.8, 31.2	107 7, 120.3
12a	46.3	-	-[a]	108 8, 119 2, 120 3, 123 0, 125 8, 126 3 127 3, 128 6, 137.1, 140.6
13a	48 6	-	-[a]	109.9, 120.2, 122.1, 122 9, 126 9, 128 1, 128 8, 133.8, 135 3, 143 1, 143 8
13c	44 6	-	13 5, 21 8, 28 5, 29 1	109 4, 119 9, 121 6, 122 4, 133 5, 142 6, 143 6
14a	58 1	42 3[b]	13 8, 22 4, 28 3, 34 1	101 4, 109 5, 119 1, 120 8, 121 1, 124 5, 126 4, 128.3, 128.4, 129 0, 136.2, 138.2
14d	65.3	21.1, 75.2[b]	-[a]	101 8, 109 6, 119 4, 120 7, 121 4, 126 1, 126 2, 126 8, 128.1, 128 2, 128.3, 128 4, 129 0, 129 2, 136.8, 137.8
15c	71 7	21.5, 21.8, 25 4, 35.2, 36 0, 73 9	127 6, 128 2, 129.0, 137.8	107 6, 121.3
15d	69 3	21.3, 75.3[b]	-[a]	108 0, 120.0, 126 1, 128 1 128 3, 128.5, 128 9, 137.4, 137.6, 137 9
16b	59 0	37.2[b]	-[a]	110.1, 118 8, 120.0, 123 1, 125 3, 126.3, 126.8, 127.4, 128.1, 128.6, 138 0, 139.7, 140.1
16d	63.0	20.9, 73.3[b]	-[a]	110.2, 118.8, 119.9, 123.1, 125 2, 125 9, 127.7, 128.2, 128.5, 128.6, 128 7, 137 66 137 7, 140.0

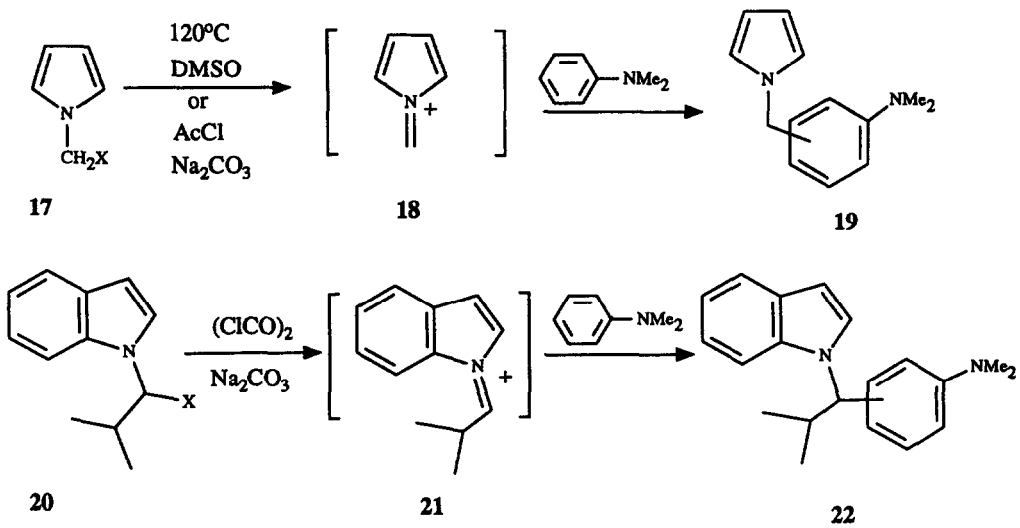
[a]Signals are indistinguishable and are reported in the column for other groups

[b]Other signals are indistinguishable from signals in other groups and are reported in the column for other groups

Reaction Mechanism. Burger, *et al*[40-44] have investigated the formation of the 5-azoniafulvene ion **18** and benzo-annellated analogue **21** from N-Mannich bases of pyrrole and indole and found that treatment of **17** with N,N-dimethylaniline gave the *ortho*- and *para*-substituted products **19.** Similarly,

treatment of **20** with N,N-dimethylaniline gave products **22**. The investigations suggested that 5-azoniafulvene ion **18** or its benzo-annellated analogue **21** were the intermediates which combined structural and functional features. Attack of nucleophiles occurred at the exo-cyclic carbon atoms, under both orbital and charge control, and restored the pyrrole or indole π-system. They have also investigated the cycloadditions of these ions **18** and **21** with nitrones or azomethine imines.[41] Although they obtained the preparation of N-(benzotriazol-1-ylmethyl)pyrrole (**2**)[43] (which was reported by us previously[35]), they did not use this compound in their synthetic experiments.

Scheme 2



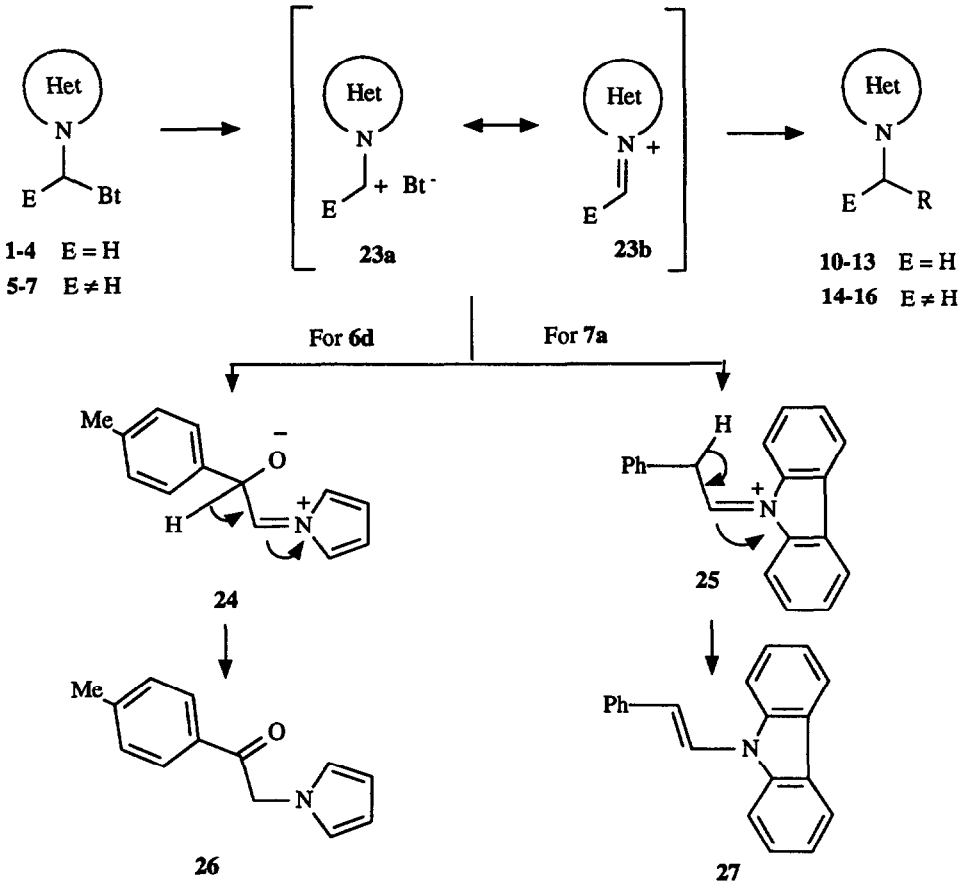
17 **18** **19**

20 **21** **22**

X=NR_2, OR, SR

Under the relatively vigorous conditions we utilized, ionization of compounds **1-7** causes dissociation of the benzotriazolyl ion to give the 5-azoniafulvene ion **18** and its analogues (cf.**23**), which further react with Grignard or hydride to yield the products **10-16**. Although in Burger's case, proton elimination from the intermediates **21** is slow in comparison to the substitution reaction, we did observe two examples of such eliminations. Thus, reaction of the pyrrole derivative **6d** with phenylmagnesium bromide gave compound **26** in 42% yield; initial proton elimination was followed after quenching with water by tautomerization of the enol to the ketone. Reaction of the carbazole derivative **7a** with phenylmagnesium bromide affords a mixture of the desired product **16b** and the proton elimination product **27** in yields of 45% and 48%, respectively. Compound **27** has been proved to be the more stable *trans* isomer, according to the NMR spectra, with a large coupling constant for one of the olefinic proton (J = 14.8) and by comparison with the literature data.[45]

Scheme 3



Conclusion. The presently reported method allows the introduction of branched as well as normal alkyl groups at the heterocyclic nitrogen atom of pyrrole, indole, carbazole and imidazole. The heterocyclic NH hydrogen atom can be replaced by a (E)(R)CH group where E comes from the electrophile in the lithiation step (E = H, in cases with the parent derivatives) and R from the Grignard reagent or organozinc reagents. Another advantage over classical methods is that our reaction affords regiospecifically N-alkylated heterocycles. Our method is also versatile in the sense that different groups including (α-hydroxyalkyl)s are easily introduced via lithiation. Various Grignard reagents, organzinc reagents as well as $LiAlH_4$ can be employed. In conclusion, we have developed a new and efficient method for the preparation of N-substituted heterocycles.

Experimental Section

General: Melting points were determined with a Kofler hot stage apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian VXR 300 MHz spectrometer in $CDCl_3$ using TMS as

an internal reference for ^1H spectra and $CDCl_3$ for ^{13}C NMR spectra (abbreviations used: s singlet; d doublet; t triplet; q quartet; m multiplet; and dd doublet of doublets). Elemental analyses were performed on a Carlo Erba-1106 instrument under the supervision of Dr. D. Powell. High resolution mass measurement was recorded on an AEI MS-30 mass spectrometer. Tetrahydrofuran, diethyl ether, benzene, and toluene were predried and freshly distilled from sodium and benzophenone. Column chromatography was carried out on MCB silica gel (230-400 mesh) unless stated otherwise.

The benzotriazole adducts **1-4, 5a,d, 6a,c,d,** and **7a,d** were prepared according to the previously described methods.[35]

N-[1-(Benzotriazol-1-yl)pentyl]indole (5b): This novel compound was prepared according to the literature procedure[35] by quenching with *n*-butyl iodide and purified by column chromatography on silica gel with hexane:EtOAc (5:1) as an oily product. Yield: 64%. (Found: C, 74.91; H, 6.70; N, 18.27. $C_{19}H_{20}N_4$ requires C, 74.97; H, 6.62; N, 18.41.). ^1H NMR 0.83 (t, 3 H, J = 7.0), 1.2-1.5 (m, 4 H), 2.7-3.0 (m, 2 H), 6.59 (d, 1 H, J = 3.2), 7.0-7.3 (m, 6 H), 7.47-7.59 (m, 2 H), 7.65-7.85(m, 1 H), 7.96-8.00 (m, 1 H). ^{13}C NMR 13.6, 21.9, 27.5, 33.0, 69.1, 104.0, 109.4, 118.3, 120.0, 120.5, 121.2, 122.6, 124.1, 126.6, 127.7, 128.7, 131.7, 135.8, 146.2.

Reaction of Benzotriazole Adducts with Grignard Reagents: General Procedure

To a solution of the benzotriazole adduct **1-7** (5 mmol) in the appropriate solvent (30 ml) under nitrogen was added the appropriate Grignard reagent solution in Et_2O (15 ml; 1 mmol/ml; freshly prepared from magnesium and the appropriate bromide). Et_2O was distilled off until the vapor temperature reached the boiling point of benzene or toluene and refluxing was continued for the appropriate time (Table 1). The reaction was monitored by TLC until the starting material had been consumed. The reaction mixture was cooled, poured onto ice-water (30 ml). The Grignard reagent was decomposed by 2 N HCl and the solution then rendered basic (pH 9) with 10% NaOH solution. The organic layer was separated and the aqueous layer extracted with Et_2O (3 X 60 ml). The combined extracts were washed with H_2O (50 ml), and dried ($MgSO_4$). Evaporation of the solvent gave the crude product which was purified by column chromatography using the eluent given in Table 1. Preparative details and the NMR spectral data of the products are given in Tables 1-3.

N-(4-Methylbenzoylmethyl)pyrrole (26): This compound was obtained as a solid from the reaction of **6d** with phenylmagnesium bromide in THF under reflux for 20 h according to the general procedure (yield: 42%), and purified by column chromatography (hexane/ethyl acetate: 30:1). mp 144-146 °C, (Lit.[35] mp 144-146 °C). ^1H NMR: 2.42 (s, 3 H), 5.28 (s, 2 H), 6.20 (d, 2 H, J = 1.8), 6.64 (d, 2 H, J = 1.8), 7.29 (d, 2 H, J = 7.9), 7.85 (d, 2 H, J = 8.3); ^{13}C NMR: 21.3, 54.8, 108.3, 121.5, 127.6, 129.2, 131.8, 144.4, 192.7.

N-(2-phenylethylenyl)carbazole (27); This compound was obtained as a by-product from the reaction of **7a** with phenylmagnesium bromide in toluene under reflux for 24 h according to the general procedure (yield: 42%; the purification is same as for compound **16b** see Table 1). mp 90-92 °C (Lit.[45] mp 90-92 °C. ^1H NMR: 7.02 (d, 1 H, J = 14.4), 7.2-7.7 (m, 12 H), 8.0 (d, 2 H, J = 7.1); ^{13}C NMR: 110.5, 119.7, 120.3, 120.7, 123.3, 124.1, 125.8, 126.2, 127.2, 128.8, 136.3, 139.5.

Reaction of Benzotriazole Adducts with $LiAlH_4$: General Procedure

To a solution of the benzotriazole adduct **5b** or **6e** (5 mmol) in the appropriate solvent (30 ml) under nitrogen was added $LiAlH_4$ (0.5 g, 13 mmol). The solution was heated under reflux for the appropriate time given in Table 1. The reaction was monitored by TLC until the starting material had been consumed. The reaction mixture was cooled, poured into ice-water (30 ml), and the solution was made slightly acidic with 2 N HCl. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 X 60 ml). The combined extracts were washed with H_2O (50 ml), and dried ($MgSO_4$). Evaporation of the solvent gave the crude product which was purified by column chromatography using the eluent given in Table 1. Preparative details and the NMR spectral data of the products are given in Tables 1-3.

Reaction of Benzotriazole Adducts with Organozinc Reagents: General Procedure

To a solution of the $ZnBr_2$ (4.5 g, 20 mmol) (Aldrich, dried 30 min at 20 °C/2 mm Hg) in Et_2O (30 ml) under nitrogen was added the phenylmagnesium bromide solution in Et_2O (20 ml, 1 mmol/ml; freshly prepared from magnesium and bromobenzene). The solution was kept at room temperature for 1 h. The benzotriazole adduct **5d**, or **6d** (5 mmol) was added followed by the appropriate solvent (80 ml). The Et_2O was distilled off until the vapor temperature reached the boiling point of benzene or toluene and refluxing was continued for the appropriate time (Table 1). The reaction was monitored by TLC until the starting material had been consumed. The reaction mixture was cooled, poured onto ice-water (30 ml), the organozinc reagent decomposed by 2 N HCl and the solution rendered basic (pH 9) with 10% NaOH solution. The organic layer was separated and the aqueous layer extracted with Et_2O (3 X 60 ml). The combined extracts were washed with H_2O (50 ml), and dried ($MgSO_4$). Evaporation of the solvent gave the crude product which was purified by column chromatography using the eluent given in Table 1. Preparative details and the NMR spectral data of the products are given in Tables 1-3.

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