The Chemistry of *N*-Substituted Benzotriazoles. Part 14.[1] Novel Routes to Secondary and Tertiary Amines and to *N,N*-Disubstituted Hydroxylamines

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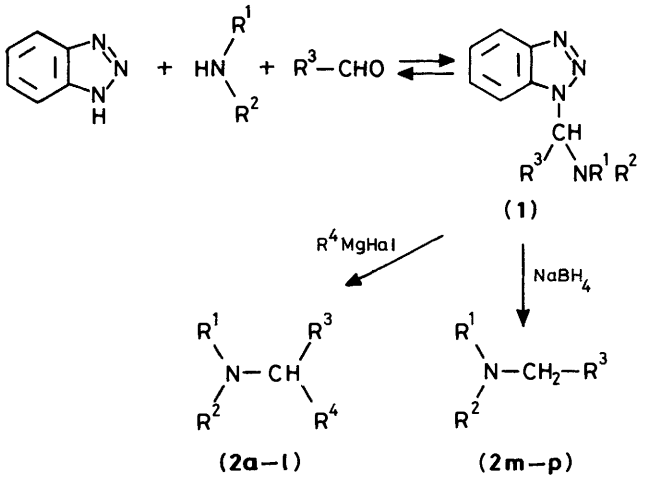
Tertiary amines of types $R^4R^3CHNR^1R^2$ (**2**), $(R^2CH_2)_2NR^1$ (**10**) and (**11**), or $(R^2CH_2)_3N$ (**12**), secondary amines of type $(R^2CH_2)_2NH$ (**8**), and *N,N*-disubstituted hydroxylamines of type $(R^2CH_2)_2NOH$ (**9**), are prepared in high yield by the action of Grignard reagents or sodium borohydride on easily available *N,N*-dialkyl-*N*-[benzotriazolylalkyl-(or arylalkyl-)]amines (**1**) or tris(benzotriazolylmethyl)amine (**7**), on bis(benzotriazolylmethyl)amines (**3**), (**5**), and (**6**), and on *N,N*-bis(benzotriazolylmethyl)hydroxylamine (**4**), respectively.

In Part 3 of this series,[2] we described the condensation of benzotriazole and an aldehyde with aromatic or heteroaromatic primary amines. Part 4[3] was concerned with the utilization of these adducts to produce the mono-*N*-alkylation products of such aromatic and heteroaromatic amines (see also ref. 4). The present paper deals with the extension of this work to the similar conversion of secondary amines into tertiary amines of type (**2**) *via* the intermediate adducts (**1**) (Scheme 1) and also presents

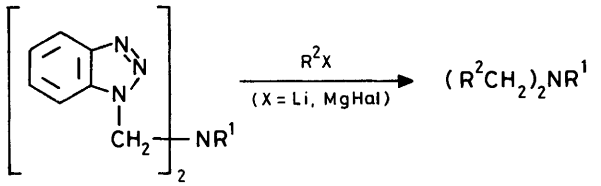


Scheme 1.

efficient routes to symmetrical secondary (**8**) and tertiary amines (**10**)—(**12**) and to hydroxylamines (**9**) *via* the adducts (**3**), (**5**)—(**7**) and (**4**), respectively.

Secondary and tertiary amines can be prepared by many varied methods,[5] most of which have disadvantages or limitations. Thus, the alkylation of ammonia or a primary amine generally leads to a mixture of primary, secondary, and tertiary amines and/or quaternary ammonium salts; the separation of a pure product is tedious and usually affords low yields.[5a] Satisfactory preparation of secondary amines by such alkylation usually requires temporary protection of one nitrogen position, *e.g.*, by $ArSO_2$,[5c] F_3CSO_2,[6] $(EtO)_2PO$,[7] or CN[8] groups. Alkylation of secondary amines is a useful tool for synthesis of tertiary amines; however, in unhindered cases there is a danger of over-reaction to quaternary salts, and sterically hindered tertiary amines are not easily prepared in this way as reactions are slow and yields low to moderate.[9,10]

Reductive alkylation,[10–13] although versatile and high



(**3**) R^1 = H
(**4**) R^1 = OH
(**5**) R^1 = Me
(**6**) R^1 = n-C_8H_{17}
(**7**) R^1 =

(**8**) R^1 = H
(**9**) R^1 = OH
(**10**) R^1 = Me
(**11**) R^1 = n-C_8H_{17}
(**12**) R^1 = R^2CH_2

Scheme. 2

yielding, often requires tedious procedures.[12,13] Dealkylation of tertiary amines (with BrCN or with acid chlorides)[14,15] readily gives secondary amines, but availability of more complex starting materials is required. Reductions of iminium salts (largely confined to formaldehyde derivatives) or tertiary amides[5a] require availability of the appropriate precursor and do not allow for versatility in the structural features of the products.[5a] Reduction of mono- or di-substituted amides,[16] imines,[17] or iminium salts[18] also requires starting materials which are often as difficult to obtain as the desired amine. Reductive dealkylations of quaternary ammonium salts,[5a] give good yields of tertiary amines but the starting material is itself usually made from a tertiary amine. Deamination of dimethylhydrazinium salts[19] affords dimethylalkyl- or dimethyl-arylamines in high yields, but involves the carcinogenic *N,N*-dimethylhydrazine.

Reaction of imines[5b] or iminium salts[20–22] with organometallic reagents provides a useful route to structurally diverse secondary and tertiary amines, however, the required intermediates are often unstable and very hygroscopic.[23] The conversion of primary amines with formaldehyde–ethylene glycol into perhydrodioxazepines and subsequent treatment with Grignards[15] leads to tertiary amines in a more direct way, but is limited to compounds containing two identical primary alkyl groups. Methods involving metal catalysts are available,[12] especially in the patent literature,[24] but almost invariably require heating under pressure. In reactions which are related to those described in the present paper, tertiary amines have been

prepared by the reaction of organometallic derivatives with various compounds of type R_2NCH_2X *e.g.*, alkoxymethylamines,[25] α-dialkylamino nitriles,[26] chloromethylamines,[27] or phenylthiomethylamines;[28] however, all these starting materials are less readily available than those we shall describe.

Methods for synthesis of *N,N*-disubstituted hydroxylamines have been reviewed.[29] Symmetrical *N,N*-dialkylhydroxylamines $(R^2CH_2)_2NOH$ have been prepared by; (*i*) direct alkylation of hydroxylamine with alkyl halides[30–33] (yields mixed di- and mono-alkylhydroxylamines[29b]); (*ii*) reaction of organometallics with NOCl or NO_2 (low yield[34,35]) or with alkyl nitrates and nitrites (higher yield,[36] but inaccessible and unstable starting materials); (*iii*) oxidation of secondary amines with peroxides[37] (erratic, low yield[29b]); (*iv*) thermal decomposition (Cope reaction) of tertiary amine *N*-oxides[38] (often leads to mixtures); (*v*) reduction of nitrones with $LiAlH_4$[39] or H_2–Pt[40] (requires preparation of starting nitrones).

In view of the continuous interest in the physiological

Table 1. Preparation of aminoalkylbenzotriazoles (**1**)

Triazole	R^1	R^2	R^3	Method of preparation	Yield (%)	M.p. (°C) or b.p. (°C/mmHg)	Purification[a]
(**1a**)	CH_2Ph	CH_2Ph	H	A	95	120—122[b]	95% EtOH
(**1b**)	n-C_8H_{17}	n-C_8H_{17}	H	A	100	Oil	*c*
(**1c**)	Ph	Me	H	A	64	72—75[d]	Et_2O–hexane
(**1d**)	Et	Et	H	A	96	120—124/0.65	Distillation[e]
(**1e**)	$-(CH_2)_4-$		Pr^i	B	76[f]	49—51	Light petroleum/Et_2O
(**1f**)	CH_2Ph	CH_2Ph	Pr^i	B	78[f]	83—85	Et_2O
(**1g**)	$-(CH_2)_5-$		Ph	B	59[f]	Oil	
(**1h**)	$-(CH_2)_2O(CH_2)_2-$		Pr	B	79[f]	Oil	
(**1i**)	$-(CH_2)_2O(CH_2)_2-$		Ph	B	87	104—105	Et_2O

[a] Recrystallized from the solvent given. [b] Lit.,[43] m.p. 121—123 °C. [c] Decomp. on distillation at 150 °C/0.25 mmHg. [d] Lit.,[43] m.p. 76—78 °C. [e] See ref. 42. [f] The yield was estimated as being at least equal to that of the subsequent Grignard reaction.

Table 2. Preparation of tertiary amines $R^1R^2NCHR^3R^4$ (**2**)

Amine	Reagent	Adduct	R^1	R^2	R^3	R^4	Method	Yield (%)	B.p. (°C/mmHg) or m.p. (°C)	Lit. m.p. (°C) or b.p. (°C/mmHg)	Lit. ref.
(**2a**)[a]	PhMgBr	(**1a**)	CH_2Ph	CH_2Ph	H	Ph	A	83[b]	91—93	91—94	*c*
(**2b**)	$PhCH_2MgCl$	(**1a**)	CH_2Ph	CH_2Ph	H	CH_2Ph	A	88[d]	180—185/0.5	206—211/3	46
(**2c**)	MeMgI	(**1a**)	CH_2Ph	CH_2Ph	H	Me	A	80[e]	132—136/0.5	101—106/0.35	10
(**2d**)	PhMgBr	(**1b**)	n-C_8H_{17}	n-C_8H_{17}	H	Ph	A	58[f,n]	110—112/0.4		
(**2e**)	BuMgBr	(**1c**)	Me	Ph	H	Bu	A	73.5[d]	97—98/0.8	107—108/4—5	28
(**2f**)	$PhCH_2MgCl$	(**1d**)	Et	Et	H	CH_2Ph	A	91[g]	*m*	223/760	25[a]
(**2g**)	$PhCH_2MgCl$	(**1e**)	$-(CH_2)_4-$		Pr^i	CH_2Ph	B	76[d,h,l]	105—112/0.3	88/0.2	41[b]
(**2h**)	PhMgBr	(**1e**)	$-(CH_2)_4-$		Pr^i	Ph	B	64[h,i]	86—91/0.25	91—98/0.4	41[c]
(**2i**)	MeMgI	(**1f**)	CH_2Ph	CH_2Ph	Pr^i	Me	B	78[d,h,j]	125—150/0.2		
(**2j**)	Pr^iMgBr	(**1g**)	$-(CH_2)_5-$		Ph	Pr^i	B	59[e,h]	107—112/0.8		
(**2k**)	PrMgBr	(**1h**)	$-(CH_2)_2O(CH_2)_2-$		Pr	Pr	B	79[d,h]	71—74/0.6		
(**2l**)	BuMgBr	(**1i**)	$-(CH_2)_2O(CH_2)_2-$		Ph	Bu	B	82[h,k]	120—121/0.6		
(**2m**)	$NaBH_4$	(**1c**)	Me	Ph	H	H	C	82[k]	192—193/760	193—194/760	*c*
(**2n**)	$NaBH_4$	(**1a**)	CH_2Ph	CH_2Ph	H	H	C	75[k]	134—135/0.7	114—115/2	49
(**2o**)	$NaBH_4$	(**1f**)	CH_2Ph	CH_2Ph	Pr^i	H	C	83[k]	132/0.3		
(**2p**)	$NaBH_4$	(**1i**)	$-(CH_2)_2O(CH_2)_2-$		Ph	H	C	91[k]	250—254/760	253/760	48

[a] Purified by recrystallization from 95% EtOH. [b] The yield refers to recrystallized product. [c] Identified by comparing m.p. and n.m.r. spectra with those of a commercial sample. [d] The crude yield is reported since ^1H and ^{13}C n.m.r. spectra were perfectly clean. [e] Clean after distillation. [f] A small amount (0.7 g) of the crude product was purified by column (3 cm × 15 cm) chromatography on silica gel [eluant: hexane, hexane–$CHCl_3$ (7:3 and then 3:7, v/v), $CHCl_3$]; 0.435 g of oil collected, 58%. [g] G.c. yield. [h] Yield calculated from benzotriazole (two steps). [i] A part of the product (0.51 g) was purified on a silica gel column (2 cm × 17 cm) packed in $CHCl_3$ [eluant: $CHCl_3$, $CHCl_3$–EtOAc (6:2 and then 2:6, v/v), EtOAc]; 0.38 g of oil collected, 64% overall). [j] During work-up, unchanged dibenzylamine was removed by treating the ether extracts with concentrated HCl and filtering off the salt. The organic layer was then washed with 2M NaOH to remove benzotriazole. [k] One step yield. [l] The product was separated from by-product bibenzyl by washing the ether layer with 50% aqueous HCl, basifying with solid NaOH and extracting with Et_2O. [m] The amine was directly converted into its picrate (see Table 3). [n] (Found: M^+, 331.3253. $C_{23}H_{41}N$ requires *M*, 331.3238).

Table 3. Characterization of tertiary amines (**2**)[a] as picrates[b]

Amine	Picrate M.p. (°C)	Picrate Lit. m.p. (°C)	Found (%) C	Found (%) H	Found (%) N	Formula	Requires (%) C	Requires (%) H	Requires (%) N
(**2b**)	118—120		62.9	4.85	10.35	$C_{28}H_{26}N_3O_7$	63.39	4.94	10.56
(**2c**)	116—118	110—111[c]							
(**2e**)	94—96		52.55	5.4	13.65	$C_{18}H_{22}N_4O_7$	53.20	5.46	13.79
(**2f**)	90—92	94[d]							
(**2g**)	136—139		56.5	6.0	12.4	$C_{21}H_{26}N_4O_7$	56.50	5.87	12.55
(**2h**)	129—132		55.6	5.5	12.85	$C_{20}H_{24}N_4O_7$	55.55	5.59	12.96
(**2i**)	124—127		60.2	5.85	11.1	$C_{25}H_{28}N_4O_7$	60.48	5.68	11.28
(**2j**)	157—159		56.1	5.9	12.25	$C_{21}H_{26}N_4O_7$	56.50	5.87	12.55
(**2k**)	115—116.5		49.0	6.55	13.0	$C_{17}H_{26}N_4O_8$	49.27	6.32	13.52
(**2l**)	160—162		54.2	5.95	11.95	$C_{21}H_{26}N_4O_8$	54.54	5.67	12.11
(**2n**)	105—108	101—103[e]							
(**2o**)	132—135		59.55	5.05	11.65	$C_{24}H_{26}N_4O_7$	59.74	5.43	11.61
(**2p**)	186—189	188—190[f]							

[a] Amines (**2a**) and (**2m**) were identified by comparing their m.p. and b.p., respectively, as well as their ^1H and ^{13}C n.m.r. spectra with those of commercial samples. In spite of several attempts the picrate of (**2d**) did not crystallize. [b] All picrates were prepared in 95% EtOH and recrystallized from the same solvent. [c] Ref. 10. [d] Ref. 48*b*. [e] Ref. 49. [f] Ref. 48.

properties of amines,[5,41] new general methods for their preparation are of considerable significance. Within the context of investigating the chemistry and properties of benzotriazole and its derivatives, we now report a facile, two-step sequence leading to products (**2**) and (**8**)—(**12**) in good yields (Schemes 1 and 2, Tables 2 and 4).

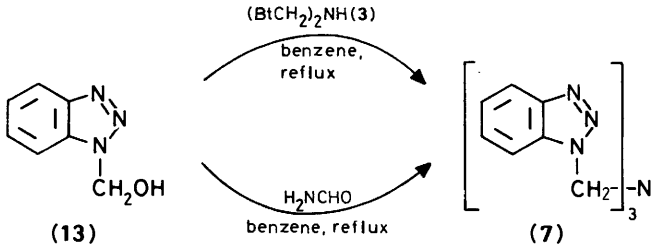
Preparation of Adducts (**1**).—Adducts (**1**) derived from formaldehyde (R^3 = H) have previously been prepared.[42,43] The Mannich reaction between a secondary amine, benzotriazole and formaldehyde is straightforward and stable adducts (**1a**—**d**) have been prepared in excellent yields. Compounds of the type (**1e**—**h**; $R^3 \neq$ H) derived from other aldehydes have not been reported before, except for the adduct of dimethylamine–benzaldehyde, whose sole identification was a ^1H n.m.r. spectrum taken at −30 °C.[44] Adducts (**1e**—**i**) were first prepared by mixing the three components (Scheme 1) in dry tetrahydrofuran (THF) in the presence of a drying agent;[44] however with this method it is difficult to decide at which point the reversible reaction leading to (**1**) (Scheme 1) is complete. Grignard reactions using the THF solutions obtained do provide the expected products (**2**) but the yields are low and by-products, resulting from reaction of the Grignard reagent with the starting aldehyde, were detected by g.l.c.–m.s. Much better for the preparation of (**1e**—**i**) is the azeotropic distillation of the water produced from a benzene solution containing all three constituents in equivalent amounts (see Experimental section).

The products (**1e**—**i**) were oils or low melting solids (see Table 1). Several difficulties were initially encountered on attempting their isolation: they are unstable, and do not withstand heating, thus making conventional methods of purification unusable. Furthermore, they hydrolyse easily with weak acids (silica gel), and some decompose on distillation. However, if the solvent benzene is removed under reduced pressure, a solid is usually obtained by triturating the resulting oil with diethyl ether (Et_2O) in a solid CO_2–acetone bath. Some of these solids melt at room temperature. Compounds (**1e**) and (**1f**) were obtained crystalline in this way, (**1g**) and (**1h**) remained as oils, whereas (**1i**) solidified more readily (Table 1). Compounds (**1f**) and (**1i**) gave satisfactory elemental analysis; the others were characterized by their n.m.r. spectra.

Adducts (**1**) derived from formaldehyde (R^3 = H) have previously been shown [42,43] to exist in solution as mixtures of the benzotriazol-1-yl and benzotriazol-2-yl isomers. Due to considerably lower energy barriers for the equilibration between the benzotriazol-1-yl and benzotriazol-2-yl isomers for (**1e**—**h**) relative to those observed for adducts (**1a**—**d**),[45] both the ^1H and ^{13}C n.m.r. spectra of (**1e**—**h**) showed broad signals at room temperature, evidently owing to coalescence phenomena. The factors governing the free energy of activation for this isomerization process and the stability of these adducts are discussed in detail in a separate report.[45]

Preparation of Adducts (**3**)—(**7**).—Preparations of compounds (**3**)—(**6**) have been published.[2] However, considerable improvement was achieved in preparation of derivatives (**4**) and (**6**): the yield of (**4**) was increased to 87% (lit.,[2] 44%) using hydroxylamine hydrochloride without neutralisation; preparation of (**6**) was improved by running the reaction in a water suspension at room temperature (see Experimental section).

Compound (**7**) was prepared by two alternative methods (Scheme 3). Reaction of 1-hydroxymethylbenzotriazole (**13**)



(Bt = benzotriazol-1-yl)

Scheme 3.

with bis(benzotriazolylmethyl)amine (**3**) gave a good yield of the tris-adduct (**7**). Alternatively, reaction of (**13**) with formamide in benzene with removal of the water also yielded compound (**7**), directly. Furthermore, formation of (**7**) was also observed when compound (**3**) was either heated at 200 °C, or brominated and subsequently treated with aqueous base.

Table 4. Preparation of secondary amines (**8**), hydroxylamines (**9**), and tertiary amines (**10**)—(**12**)

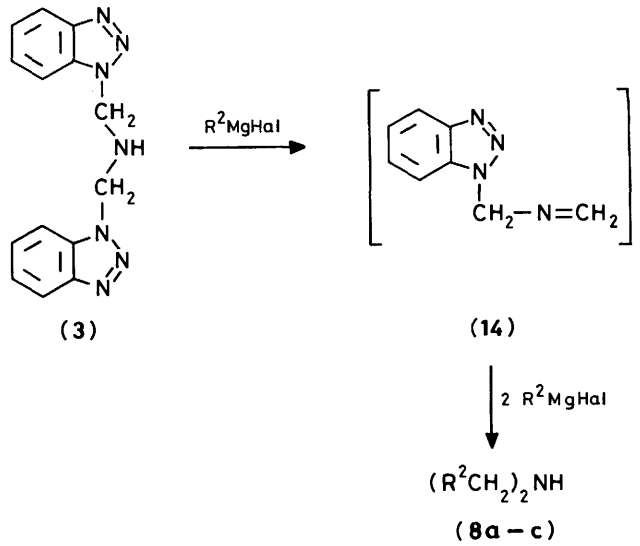
Compound	Starting adduct	Reagent R^2X	Purification[a]	Yield[b] (%)	M.p. or b.p. (°C)	Identifying lit. data	Lit ref.
(**8a**)	(**3**)	PhMgBr	A	75	Oil	^{13}C n.m.r.	50*a*
(**8b**)	(**3**)	$PhCH_2MgCl$	A	95	Oil	^{13}C n.m.r.	50*b*
(**8c**)	(**3**)	BuMgBr	A	65	272—274 (HCl)	m.p. (HCl): 275 °C	51
(**9a**)	(**4**)	PhMgBr	B/85% EtOH	94	121—123	m.p. 123 °C	32
(**9b**)	(**4**)	BuMgBr	B/85% MeOH	89	56—57	m.p. 57—58 °C	52
(**9c**)	(**4**)	$n\text{-}C_8H_{17}MgBr$	B/hexane	92	76—78[c]		
(**9d**)	(**4**)	$C_6H_{11}MgCl$	B/85% EtOH	86	69—72		
(**9e**)	(**4**)	PhC≡CLi	A; B/EtOAc + l.pet.	87	94—95[c]		
(**10a**)	(**5**)	Pr^iMgBr	A	66	Oil[d]	b.p. 143 °C	53
(**10b**)	(**5**)	PhMgBr	A	90	Oil	^{13}C n.m.r.	50*c*
(**11a**)	(**6**)	Pr^iMgBr	A	88	Oil[e]		
(**11b**)	(**6**)	$n\text{-}C_8H_{17}MgBr$	A	95	Oil[e]		
(**12a**)	(**7**)	PhMgBr	C[f]	74	88—90	^{13}C n.m.r.	50*d*
						m.p. 91 °C	54
(**12b**)	(**7**)	$p\text{-}MeC_6H_4MgBr$	C[g]	51	56.5—57	m.p. 55 °C	55
(**12c**)	(**7**)	1-naphthylMgBr	B/EtOH	55	176.5—178	m.p. 178 °C	56
(**12d**)	(**7**)	PrMgBr	D	75	105 (Picrate)	m.p. 106.9 °C (Picrate)	57
(**12e**)	(**7**)	BuMgBr	E	40[h]	b.p. 232—240 °C	b.p. 235—240 °C	58
						I.r.	50*e*
(**12f**)	(**7**)	$C_6H_{11}MgCl$	B/EtOH	66	94—94.5	m.p. 91—94 °C	59

[a] A: column chromatography on silica gel, eluted with ether–hexane. B: recrystallization from the given solvent. C: column chromatography on silica gel, eluted first with hexane, then with benzene. D: column chromatography on silica gel, eluted with chloroform. E: distillation. [b] Isolated yield, not optimized. [c] Characterized by C, H, N, analysis (±0.3%) and n.m.r. spectra (see Experimental section). [d] Characterized also by n.m.r. spectra (see Experimental section). [e] Characterized by their M^+ ions in the m.s. and n.m.r. spectra (see Experimental section). [f] From hexane fraction biphenyl (m.p. 69—70.5 °C) was isolated. [g] From the hexane fraction *p,p'*-dimethylbiphenyl (m.p. 115—118 °C) was isolated. [h] The lower yield is due to the small scale (0.3 g) distillation.

Adducts (**3**)—(**6**) are stable solids that can be stored at room temperature for a long time without decomposition.

Preparation of Tertiary Amines (**2**).—THF solutions of the isolated adducts (**1a**—**d**) react with Grignard reagents to afford amines (**2a**—**f**) (Table 2, method A). Advantageously, adducts (**1e**—**i**) are not isolated and the benzene solutions from the azeotropic distillation are added directly to the Grignard reagents, yielding tertiary amines (**2g**—**l**) (Table 2, method B) in very good overall yields, in an essentially one-pot reaction. In a similar fashion, sodium borohydride reduction of the isolated adducts (**1b**), (**1c**), (**1f**), and (**1i**) proceeded very smoothly to afford the amines (**2m**—**p**) (Table 2, method C).

Preparation of Symmetrical Secondary and Tertiary Amines and Hydroxylamines (**8**—**12**).—When bis(benzotriazol-1-ylmethyl)amine (**3**) is treated with Grignard reagents at room temperature, the two benzotriazole moieties can readily be replaced by two alkyl groups leading to the corresponding symmetrical secondary amines (**8a**—**c**) (Scheme 4). The reaction proceeds probably *via* an initial deprotonation and elimination of one benzotriazole to form intermediate (**14**) which can react further with the Grignard reagent to afford the final product. The results are listed in Table 4.

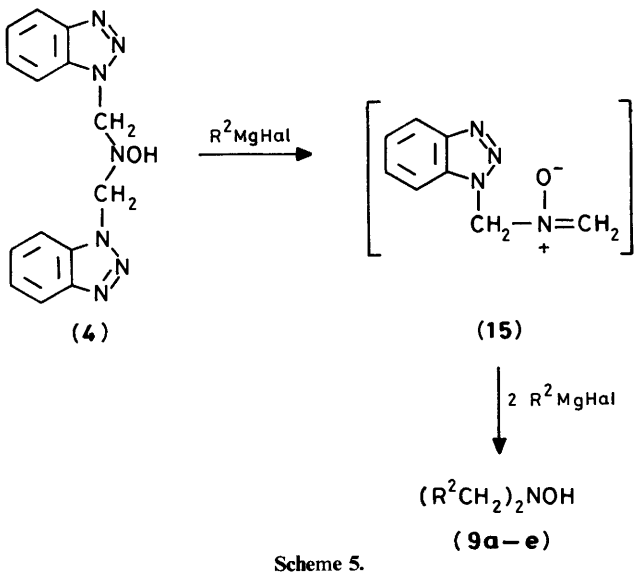


Scheme 4.

In a similar fashion, *N,N*-bis(benzotriazol-1-ylmethyl)-hydroxylamine (**4**) reacts with various Grignard reagents or with lithium phenylacetylene in THF–Et_2O to give the corresponding *N,N*-disubstituted hydroxylamines (**9a**—**e**) in high yields. In a typical case, the yield of *N,N*-dibenzylhydroxylamine was 60% by the previously reported procedure,[33] while it is 93% by the present method. In this case, the reaction presumably proceeds *via* the intermediate nitrone (**15**) (Scheme 5). The results are summarized in Table 4.

Reactions of compounds (**5**)—(**7**) with Grignard reagents also proceed smoothly yielding tertiary amines of the type $(R^2CH_2)_2NR^1$ (**10a**—**b**), (**11a**—**b**), and $(R^2CH_2)_3N$ (**12a**—**f**), respectively. Although the substitution of the benzotriazole moieties by the alkyl groups presumably occur stepwise, no products of partial reaction were detected in these transformations.

Tertiary amines (**2**) were characterized as their salts with 2,4,6-trinitrophenol (Table 3) and by their ^1H and ^{13}C n.m.r. spectra (Tables 5 and 6). Many of these amines are either novel or found only in the patent literature where they have received interest due to their considerable physiological activity (central nervous system stimulants, antihypertensives, spasmolytics, *etc.*).[24,41] Compounds (**8**)—(**12**) were identified by their ^1H, ^{13}C n.m.r. spectra (Tables 7 and 8), elemental analysis data or mass



Scheme 5.

spectra, as well as by comparison of the appropriate physical properties with literature data.

Conclusions

This account, together with parts 3 and 4 of this series, demonstrates the synthetic utility of the adducts of benzotriazole with amines and aldehydes, the ease by which the benzotriazol-1-yl moiety is displaced, and the ease with which benzotriazole is removed from the reaction mixture with a simple basic work-up (recoverable on acidification). The present methods possess many advantages including simplicity of procedure, easily available starting materials, and yields usually better than those previously reported. Thus, the methods described here can advantageously be utilized in the preparation of secondary and tertiary amines and of *N*,*N*-disubstituted hydroxylamines.

Experimental

M.p.s were determined on a hot stage microscope and are uncorrected. ^1H and ^{13}C n.m.r. spectra were recorded on a

Table 5. ^1H N.m.r. chemical shifts of tertiary amines (**2**) (δ_H p.p.m., in $CDCl_3$)

Amine	R^1	R^2	R^3	R^4	CH
(**2a**)	7.39—7.14 (m, 15 H), 3.51 (s, 6 H, CH_2)	*a*	*b*	*c*	3.51[d]
(**2b**)	7.28—7.02 (m, 15 H), 3.60 (s, 4 H, CH_2)	*a*	*b*	2.87—2.63 (2 m, 4 H)	*e*
(**2c**)	7.38—7.17 (m, 10 H), 3.54 (s, 4 H)	*a*	*b*	1.07—1.00 (t,[f] 3 H)	2.53—2.43 (q,[f] 2 H)
(**2d**)	2.42—2.34 (t,[f] 4 H), 1.48—1.42 (m, 4 H) 1.25 (ap. s, 24 H), 0.90—0.84 (t,[g] 6 H)	*a*	*b*	7.33—7.17 (m, 5 H)	3.52 (s, 2 H)
(**2e**)	7.21—7.13 (2 d,[f] 1 H), 6.67—6.63 (d,[h] 2 H)	2.84 (s, 3 H)	*b*	1.53 (q,[f] 2 H), 1.29 (m, 4 H), 0.89 (t,[g] 3 H)	3.26—3.19 (t,[f] 2 H)
(**2f**)	2.60—2.50 (q,[f] 4 H), 1.06—0.99 (t,[f] 6 H)	*a*	*b*	7.30—7.12 (m, 5 H), 2.69—2.65 (m, 4 H)	*e*
(**2g**)	2.56—2.49 (m, 4 H), 1.72—1.66 (m, 4 H)	*a*	2.35—1.55 (9 peaks, 1 H) 0.97—0.92 (2 d,[f] 6 H)	7.21 (m, 5 H), 2.78—2.72 (t,[g] 2 H)	*o*
(**2h**)	2.45—2.41 (m, 2 H), 1.70—1.68 (m, 2 H)	*a*	2.28—2.12 (10 peaks,[i] 1 H) 0.86—0.74 (2 d,[f] 6 H)	7.27—7.23 (m, 5 H)	3.03—3.01 (d,[i] 1 H)
(**2i**)	7.40—7.25 (m, 10 H), 3.80—3.73 (d, 2 H) 3.34—3.27 (d,[j] 2 H)	*a*	1.75—1.63 (10 peaks, 1 H) 1.03—0.96 (2 d,[h] 6 H)	0.81—0.77 (d,[k] 3 H)	2.30—2.16 (2 q[k])
(**2j**)	2.33—2.19 (m, 4 H), 1.57—1.47 (m, 4 H) 1.33—1.02 (ap. q.,[n] 2 H)	*a*	7.27—7.08 (m, 5 H)	2.19 (1 H),[p] 1.02—0.99 (d, 3 H) 0.71—0.68 (d,[k] 3 H)	2.98—2.93 (d,[l] 1 H)
(**2k**)	3.69—3.65 (t,[i] 4 H, CH_2O) 2.52—2.48 (t,[i] 4 H, CH_2N)	*a*	1.50—1.16 (m,[f] 8 H) 0.93—0.86 (t,[i] 6 H)		2.33—2.27 (t,[k] 1 H)
(**2l**)	3.67—3.61 (m, 4 H, CH_2O) 2.41—2.34 (m, 4 H, CH_2N)	*a*	7.28—7.18 (m, 5 H)	1.88—1.83 (m, 1 H)[q] 1.72—1.64 (m, 1 H)[r] 1.26—1.19 (m, 2 H) 1.11—1.03 (m, 2 H) 0.84—0.76 (t, 3 H)	3.21—3.14 (2 d[l])
(**2m**)	7.23—7.15 (2 d,[m] 2 H_m) 6.72—6.65 ($H_{o,p}$, 3 H)	2.82 (s, 6 H)	*b*	*s*	
(**2n**)	7.35—7.15 (m, 10 H), 3.51 (s, 4 H)	*a*	*b*	*s*	2.16 (s, CH_3)
(**2o**)	7.38—7.18 (m, 10 H), 3.50 (s, 4 H)	*a*	1.91—1.75 (m, 1 H) 0.87—0.84 (d,[f] 6 H)	*s*	2.16—2.13 (d,[f] 2 H)
(**2p**)	3.65—3.60 (t,[n] 4 H, CH_2O) 2.38—2.33 (t,[n] 4 H, CH_2N)	*a*	7.30—7.15 (m, 5 H)	*s*	3.39 (s, 2 H)

[a] $R^1 = R^2$. [b] R^3 = H. [c] Overlaps with aromatic peaks of R^1. [d] Overlaps with aliphatic peaks of R^1. [e] Overlaps with aliphatic peaks of R^2. [f] *J* 7 Hz. [g] *J* 6 Hz. [h] *J* 8 Hz. [i] *J* 4 Hz, [j] *J* 14 Hz. [k] *J* 6.5 Hz. [l] *J* 9 Hz. [m] J_m 0.8 Hz, J_p 0.6 Hz. [n] *J* 5 Hz. [o] Hidden under signals at 2.4—2.8 p.p.m. [p] Hidden under signals at 2.33—2.19 p.p.m. [q] C*H*HCHPh. [r] CH*H*CHPh. [s] R^4 = H.

Table 6. ^{13}C N.m.r. chemical shifts (δ_C p.p.m., in $CDCl_3$) of tertiary amines (**2**)

Amine	R^1	R^2	R^3	R^4	CH
(**2a**)	139.6, 128.7, 128.2 126.8, 57.8	*a*	*e*	*a*	57.8
(**2b**)	139.6,[c] 128.8, 128.6 126.7, 58.1	*b*	*e*	140.5,[c] 125.8 33.4	55.1
(**2c**)	140.0, 128.7, 128.1 126.7, 57.0	*b*	*e*	11.8	47.0
(**2d**)	53.8, 31.8, 29.5 29.3, 27.4, 27.0, 22.6,[d] 14.0[d]	*b*	*e*	140.2, 128.7 127.9, 126.5	58.7
(**2e**)	149.3, 128.9, 115.7 112.0	38.0	*e*	29.3, 26.3, 22.5 14.0	52.6
(**2f**)	32.89, 11.35	*b*	*e*	140.4, 128.4 128.1, 126.5, 46.5	54.5
(**2g**)	51.9, 24.0	*b*	31.4, 20.7 18.4	143.1, 129.5 128.5, 125.8 35.4	70.5
(**2h**)	52.0, 23.2	*b*	30.5, 20.6 16.3	139.7, 129.4 127.2, 126.5	75.6
(**2i**)	140.7, 128.8, 128.0 126.5, 59.0	*b*	31.7, 21.1 20.6	9.6	53.7
(**2j**)	50.8, 26.0, 24.9	*b*	138.2, 129.2 128.1, 127.4	28.0, 20.7 19.6	77.0
(**2k**)	67.6, 48.8	*b*	32.7, 20.2 14.26	32.1, 20.2 14.3	63.6
(**2l**)	67.1, 51.0	*b*	140.7, 128.4 127.9, 126.8	32.1, 28.2 22.6, 13.8	70.5
(**2m**)	150.4, 128.8, 116.5 112.5	40.5			40.3
(**2n**)	138.8, 128.9, 128.1 126.9, 61.6	*b*	*e*	*f*	42.0
(**2o**)	139.9, 128.8, 128.0 126.7, 62.2	*b*	26.1, 20.8	*f*	58.8
(**2p**)	66.4, 53.1	*b*	137.3, 128.7 127.8, 126.7	*f*	62.9

[a] The molecule is symmetrical, therefore $R^1 = R^2 = CHR^3R^4$. [b] $R^1 = R^2$. [c] Assignments can be interchanged. [d] The two methyl groups adjacent to an asymmetric carbon are not equivalent. [e] $R^3 = H$. [f] $R^4 = H$.

JEOL JNM FX-100 (99.5 MHz or 25 MHz), or a Varian XL 200 (200 MHz or 50 MHz) instrument as solutions in deuteriochloroform ($CDCl_3$), using TMS (δ 0.0 p.p.m.), for ^1H, and the solvent signal at δ 77.00 p.p.m., for ^{13}C spectra, as reference. Mass spectra were recorded on an AEI MS 30 mass spectrometer. Exact mass measurements were performed on a KRATOS MS-80-RFA double focusing spectrometer using the peak matching technique at nominal resolution of 5 000 (10% valley definition). Perfluorokerosene ions were used as mass standards. Combustion analyses were carried out using a Carlo Erba 1106 elemental analyser or by the Atlantic Microlab. G.l.c. was carried out on a Hewlett Packard 5890A instrument using a 5 m HP-1 column (conditions: initial temperature = 70 °C; initial time = 0 min; rate = 15 °/min; final temperature = 250 °C). Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled under nitrogen from sodium–benzophenone immediately before use. Thiophene-free reagent grade benzene (obtained from Fisher Scientific) was used without further drying (0.02 p.p.m. H_2O). Silica gel (230—240 mesh) was obtained from Merck.

The following compounds were prepared by the literature methods: *N,N*-dibenzylbenzotriazol-1-ylmethylamine (**1a**);[43] *N*-methyl-*N*-phenylbenzotriazol-1-ylmethylamine (**1c**);[43] *N,N*-diethylbenzotriazol-1-ylmethylamine (**1d**)[42] (see Table 1), bis-(benzotriazol-1-ylmethyl)amine (**3**),[2] and methylbis(benzotriazol-1-ylmethyl)amine (**5**).[2]

N,N-*Dioctylbenzotriazol-1-ylmethylamine* (**1b**).—*Method A*: cf. *the standard literature procedure*.[43] Benzotriazole (0.1 mol, 11.9 g) was dissolved, with stirring, in methanol (45 ml) and then *N,N*-dioctylamine (0.11 mol, 26.56 g) followed by 37% aqueous formaldehyde (0.12 mol, 9.7 ml) was added. A two-layer system resulted which contained starting materials after 7 h of stirring [t.l.c. on silica gel; eluted with EtOAc–$CHCl_3$, 1:1 (v/v)]. The mixture was made homogeneous with Et_2O and heated under reflux overnight. It was then poured onto ice (100 g), extracted with Et_2O (5 × 40 ml), the extracts dried ($MgSO_4$), the solvent evaporated, and the residue dried *in vacuo* (10 mmHg, 24 h; 1.5 mmHg, heat, 1 h) to give an almost colourless oil in quantitative yield (38 g). The analytical sample was obtained by drying a small amount of the oil at 10 mmHg, over P_2O_5 at 78 °C for 5 days (Found: C, 74.05; H, 10.85; N, 14.95. $C_{23}H_{40}N_4$ requires C, 74.14; H, 10.82; N, 15.04%).

N,N-*Dialkyl-benzotriazol-1-yl-alkyl* (*or arylalkyl*)*amines:* (**1e—i**).—*Method B*. Benzotriazole (66 mmol) and a secondary amine (66 mmol) were mixed in dry benzene (50 ml). The aldehyde (66 mmol) was then added and the mixture was heated under reflux with a Dean–Stark trap, until the calculated amount of water (~1.2 ml) had been collected. Subsequent treatment depended on the compound.

N-(1-Benzotriazol-1-yl-2-methylpropyl)pyrrolidine (**1e**). This compound was obtained by evaporating the solvent at room temperature (0.2 mmHg) and triturating the resulting oil with light petroleum–Et_2O in a solid CO_2–acetone bath. A beige solid was obtained which was washed several times with cold, dry Et_2O and dried at 0.2 mmHg for 2 days.

N-(1-Benzotriazol-1-yl-2-methylpropyl)dibenzylamine (**1f**).

Table 7. ^{1}H N.m.r. chemical shifts[a] (δ_H p.p.m.) of secondary amines (**8**), hydroxylamines (**9**), and tertiary amines (**10**)—(**12**) [$(R^2CH_2)_2NR^1$].

Compound	R^2	R^1	R^2	CH_2	R^1
(8a)[b]	Ph	H	7.45—7.15 (m, 10 H)	3.68 (s, 4 H)	*d*
(8b)	$PhCH_2$	H	7.3—7.1 (m, 10 H) 2.9—2.7[c] (m, 4 H)	2.9—2.7 (m, 4 H)[c]	3.7 (br, 1 H)
(8c)	Bu	H	1.64—1.1 (m, 12 H) 0.89 (t, 6 H)[e]	2.39 (t, 4 H)[c,e]	*d*
(9a)	Ph	OH	7.4—7.2 (m, 10 H)	3.8 (s, 4 H)	7.82 (s, 1 H)
(9b)	Bu	OH	1.58 (m, 4 H), 1.52 (m, 8 H) 0.92 (t, 6 H)[e]	2.62 (t, 4 H)[e]	*d*
(9c)	$n\text{-}C_8H_{17}$	OH	1.60—1.18 (b 28 H), 0.9 (t, 6 H)[e]	2.62 (t, 4 H)[e]	*d*
(9d)	C_6H_{11}	OH	1.89—0.78 (m, 22 H)	2.48 (d, 4 H)[e]	*d*
(9e)	$PhC{\equiv}C$	OH	7.49—7.44 (m, 4 H) 7.32—7.28 (m, 6 H)	3.99 (s, 4 H)	6.6 (br, 1 H)
(10a)	Pr^i	Me	1.61 (m, 2 H), 0.78 (d, 6 H)[e]	1.90 (m, 4 H)	2.01 (s, 3 H)
(10b)	Ph	Me	7.4—7.1 (m, 10 H)	3.43 (s, 4 H)	2.09 (s, 3 H)
(11a)	Pr^i	$n\text{-}C_8H_{17}$	1.65 (m, 2 H) 0.85 (d, 12 H)[c,e]	2.04 (d, 4 H)[e]	2.29 (t, 2 H)[e] 1.28 (br, 12 H) 0.85 (br d, 3 H)
(11b)	$n\text{-}C_8H_{17}$	$n\text{-}C_8H_{17}$	1.47—1.14 (m, 37 H) 0.88 (m, 12 H)	2.39 (m, 6 H)	*c*
(12a)	Ph	$R^1 = R^2CH_2$	7.45—7.35 (m, 6 H) 7.35—7.15 (m, 9 H)	3.54 (s, 6 H)	$R^1 = R^2CH_2$
(12b)	$p\text{-}MeC_6H_4$	$R^1 = R^2CH_2$	7.27 (d, 6 H), 7.09 (d, 6 H) 2.29 (s, 9 H)	3.48 (s, 6 H)	$R^1 = R^2CH_2$
(12c)	1-naphthyl	$R^1 = R^2CH_2$	7.75—7.68 (m, 6 H) 7.44—7.26 (m, 12 H) 6.72 (t, 3 H)[f]	3.92 (s, 6 H)	$R^1 = R^2CH_2$
(12d)	Pr	$R^1 = R^2CH_2$	1.51—1.30 m, 12 H) 0.97 (t, 9 H)	2.45 (t, 6 H)[e]	$R^1 = R^2CH_2$
(12e)	Bu	$R^1 = R^2CH_2$	1.52—1.42 (m, 6 H) 1.33—1.24 (m, 12 H) 0.88 (t, 9 H)[e]	2.46 (t, 6 H)[e]	$R^1 = R^2CH_2$
(12f)	C_6H_{11}	$R^1 = R^2CH_2$	1.80—1.64 (m, 15 H) 1.4—1.15 (m, 12 H) 0.91—0.68 (m, 6 H)	2.02 (d, 6 H)[e]	$R^1 = R^2CH_2$

[a] Recorded in deuteriated chloroform unless otherwise stated. [b] In deuteriated dimethyl sulphoxide. [c] Overlapping signals. [d] The hetero proton was not observed. [e] *J* 7 Hz. [f] *J* 8 Hz.

The compound was obtained as a white solid after complete evaporation of benzene at room temperature (0.2 mmHg) and trituration with dry Et_2O. The solid was filtered and dried (0.2 mmHg, P_2O_5, 72 h).

N-(α-Benzotriazol-1-ylbenzyl)piperidine (**1g**). Compound (**1g**) failed to solidify under a variety of conditions. It was freed completely of the solvent and the dark oily residue characterized by its ^{1}H and ^{13}C n.m.r. spectra.

N-(1-Benzotriazol-1-ylbutyl)morpholine (**1h**). This compound was a pale yellow viscous oil, obtained after complete removal of the solvent under reduced pressure. It was characterized by its n.m.r. spectra.

N-(α-Benzotriazol-1-ylbenzyl)morpholine (**1i**). On cooling of the hot benzene solution a solid separated which was thinned with dry Et_2O in a cold bath and filtered. A white solid was obtained (Found: C, 69.0; H, 6.2; N, 19.0. $C_{13}H_{18}N_4O$ requires C, 69.37; H, 6.16; N, 19.03%).

N,N-*Bis*(*benzotriazol*-1-*ylmethyl*)*hydroxylamine* (**4**).—To a solution of 1-hydroxymethylbenzotriazole (**13**) (2.98 g, 20 mmol) in methanol (25 ml), hydroxylamine hydrochloride (0.69 g, 10 mmol) was added. The mixture was stirred at 25 °C for 5 h, and kept overnight at −5 °C. The precipitate formed was filtered off, washed with cold water (25 ml), and dried *in vacuo* over P_2O_5 to give hydroxylamine (**4**) (2.57 g, 87%). The analytical sample was obtained by recrystallization from ethanol, m.p. 173—175 °C (lit.,[2] 173—174 °C).

N,N-*Bis*(*benzotriazol*-1-*ylmethyl*)*octylamine* (**6**).—Benzotriazole (11.9 g, 0.1 mol) and octylamine (8.3 ml, 0.05 mol) were stirred in distilled water (100 ml) for a few minutes, until the organic materials formed a lower liquid phase. Formaldehyde (37% aqueous solution; 7.5 ml, 0.1 mol) was added to the vigorously stirred mixture. After 2 h the thick suspension was filtered, and the product was washed with water to give compound (**6**) (17.74 g, 91%). The analytical sample was obtained by recrystallization from ethanol, m.p. 88—89 °C (lit.,[2] 88—89 °C).

Tris(*benzotriazol*-1-*ylmethyl*)*amine* (**7**).—*Method A*. Bis(benzotriazol-1-ylmethyl)amine (**3**) (1.4 g, 5 mmol), 1-hydroxymethylbenzotriazole (**13**) (0.75 g, 5 mmol), and paraformaldehyde (0.5 g) were heated under reflux in benzene (20 ml) with a Dean–Stark adapter for 5 h. After cooling of the solution to room temperature, the white solid that separated from the solution was filtered off, and washed with benzene to give the amine (**7**) (1.7 g, 83%).

Method B. 1-Hydroxymethylbenzotriazole (**13**) (3.0 g, 20 mmol), formamide (1 ml, 25 mmol), and acetic acid (1 ml) were heated under reflux in benzene (30 ml) with a Dean–Stark adapter for 12 h. The solvent was evaporated, and ether (20 ml) and water (20 ml) were added to the residue to give white crystals. The mixture was kept in a refrigerator overnight after which the product was filtered off, and washed with water and ether to give *compound* (**7**) (1.45 g, 52%). An analytical sample

Table 8. ^{13}C N.m.r. chemical shifts[a] (δ_C p.p.m.) of secondary amines (**8**), hydroxylamines (**9**), and tertiary amines (**10**)—(**12**) [$(R^2CH_2)_2NR^1$]

Compound	R^2	R^1	R^2	CH_2	R^1
(**8a**)[b]	Ph	H	140.7, 128.0, 127.9, 126.4	52.2	
(**8b**)	$PhCH_2$	H	139.5, 128.6, 128.5, 126.2, 35.7	50.6	
(**8c**)	Bu	H	30.5, 27.3, 23.2, 14.6	54.8	
(**9a**)[b]	Ph	OH	138.5, 128.9, 127.9, 126.6	63.7	
(**9b**)	Bu	OH	28.9, 26.2, 22.0, 13.3	60.0	
(**9c**)	n-C_8H_{17}	OH	32.0, 29.7, 29.6, 29.3 27.5, 27.3, 22.7, 14.1	60.9	
(**9d**)	C_6H_{11}	OH	34.9, 34.1, 26.0, 25.4	67.1	
(**9e**)	$PhC{\equiv}C-$	OH	131.8, 128.4, 128.2, 122.7, 85.6, 83.5	48.9	
(**10a**)	Pr^i	Me	25.6, 20.0	66.5	42.3
(**10b**)	Ph	Me	138.8, 128.5, 127.8, 126.5	61.4	41.7
(**11a**)	Pr^i	n-C_8H_{17}	27.5, 21.7	64.9	56.1, 32.7, 30.4, 30.2, 28.3, 28.1, 23.4, 14.8
(**11b**)	n-C_8H_{17}	n-C_8H_{17}	32.9, 30.7, 30.4, 28.6, 28.5 28.3, 23.7, 14.9	55.2	*c*
(**12a**)	Ph	$R^1 = R^2CH_2$	139.7, 128.8, 128.2, 126.9	58.0	$R^1 = R^2CH_2$
(**12b**)	*p*-MeC_6H_4	$R^1 = R^2CH_2$	136.6, 136.2, 128.8, 128.6, 21.1	57.4	$R^1 = R^2CH_2$
(**12c**)	1-naphthyl	$R^1 = R^2CH_2$	134.7, 133.8, 132.5, 128.6, 128.2, 127.9 125.9, 125.5, 125.1, 124.9	58.2	$R^1 = R^2CH_2$
(**12d**)	Pr^n	$R^1 = R^2CH_2$	29.2, 20.7, 14.0	53.9	$R^1 = R^2CH_2$
(**12e**)	Bu	$R^1 = R^2CH_2$	29.8, 26.3, 22.5, 14.0	54.0	$R^1 = R^2CH_2$
(**12f**)	C_6H_{11}	$R^1 = R^2CH_2$	36.3, 31.9, 27.1, 26.3	63.3	$R^1 = R^2CH_2$

[a] Recorded in deuteriated chloroform, unless otherwise specified. [b] In deuteriated dimethyl sulphoxide. [c] Overlapping signals.

was prepared by recrystallization from ethanol, m.p. 180—182 °C (Found: C, 61.7; H, 4.15; N, 34.1. $C_{14}H_{11}N_7$ requires C, 61.45; H, 4.42; N, 34.13%); δ_H(60 MHz; $CDCl_3$) 8.4—7.2 (12 H, m), and 6.2—6.06 (6 H, m); δ_C(100 MHz; $CDCl_3$) 144.97, 132.25, 126.79, 123.47, 118.70, and 110.07 (benzotriazole ring), and 63.18 (CH_2).

Preparation of Tertiary Amines (**2a**—**f**).—*Method A.* The Grignard reagent was prepared from magnesium turnings (11.5 mmol) and the alkyl or aryl halide (11.4 mmol) in dry diethyl ether (10 ml). To this solution, compound (**1a**—**d**) (5 mmol) in dry THF (20 ml) was added dropwise. Immediate frothing and evolution of heat was observed, and reflux was sustained by slow addition. The mixture was heated under reflux for an additional hour and then poured onto crushed ice (100 g) and stirred with saturated aqueous ammonium chloride (20—50 ml) and/or 1M HCl (10 ml) until all solids dissolved. The mixture was extracted with ether (3 × 40 ml), and the extract washed with 2M NaOH (until t.l.c. showed no presence of benzotriazole), dried ($MgSO_4$), and evaporated under reduced pressure to afford the crude product which was purified as shown in Table 2 (see footnotes for the individual compounds).

Preparation of Tertiary Amines (**2g**—**l**).—*Method B.* The Grignard reagents [from Mg (0.05 mol) and halide (0.04 mol) in dry diethyl ether (30 ml)] were prepared as in Method A. To these, adducts (**1e**—**i**) (33 mmol) as solutions in benzene, prepared as described in method B, were added slowly. The reaction mixture was heated under reflux for 2—4 h and worked up as in the preceding method. For amine (**2j**) half amounts of all materials were used. For (**2l**) the adduct (**1i**) was isolated, then dissolved (5 mmol) in benzene (30 ml) and added to the Grignard reagent made from the same amounts as described in method A. All amines were purified as shown in Table 2 (footnotes) and characterized as their picrates (see Table 3).

Preparation of Tertiary Amines (**2m**—**p**).—*Method C.* The adducts (**1c**) (10 mmol), (**1b**) (3 mmol), (**1f**) (1 mmol), and (**1i**) (3 mmol) in THF (20, 20, 10, and 15 ml, respectively) were each stirred at room temperature with 1 mol equiv. of $NaBH_4$ overnight. The reaction was quenched with a small amount of ice (5—15 g), the product extracted with Et_2O, and the extract dried ($MgSO_4$) and evaporated under reduced pressure to give the amines as oils (see Table 2).

General Procedure for Reaction of Compounds (**3**)—(**6**) *with Grignard Reagents: Preparation of Derivatives* (**8**)—(**12**).—Grignard reagents [R^2MgX (25 mmol) in dry ether (20 ml)] were prepared by standard methods. A suspension (**3**) or solution (**4**)—(**6**) of the appropriate bis(benzotriazol-1-ylmethyl) derivative [(**3**),(**4**): 5 mmol/20 ml dry THF; (**5**),(**6**): 12 mmol/45 ml dry THF] was added, and the mixture was heated to reflux for 1 h. It was poured onto ice containing NH_4Cl, extracted with ether, and the extract washed with 2M NaOH (2 × 20 ml) to remove the side-product benzotriazole, and then with water. It was then dried ($MgSO_4$), and evaporated under reduced pressure, and the product was purified by the given method (see Table 4).

Preparation of the Hydroxylamine (**9e**).—To a solution of phenylacetylene (10 mmol) in dry THF (30 ml), butyl-lithium (2.5M solution in hexane; 11 mmol, 4.4 ml) was added dropwise under an argon atmosphere at −78 °C, and the mixture was stirred at room temperature for 2 h. Compound (**4**) (3 mmol) dissolved in dry THF (20 ml) was added over 15 min, and the mixture was stirred at room temperature for an additional

hour. After addition of a few drops of water, the solvent was evaporated. The residue was extracted with ether and water, and the ethereal layer washed with 2M NaOH (2 × 25 ml), and then with water. It was then dried ($MgSO_4$) and evaporated under reduced pressure and the product was purified by the given method (see Table 4) to give (**9e**) (0.68 g, 87%), m.p. 94—95 °C.

General Procedure for Reaction of Compound (**7**) *with Grignard Reagents: Preparation of Amines* (**12a**—**f**).—Grignard reagents [R^2MgX (15 mmol) in dry ether (30 ml) for (**12c**), and THF for the others] were prepared by standard methods. A suspension of compound (**7**) (3 mmol) in ether or THF (20 ml) was added, and the mixture was stirred at room temperature for 1 h, and then heated under reflux for 5 h. It was then poured onto ice containing NH_4Cl, and extracted with ether. The ethereal solution was extracted with 25% NaOH (3 × 50 ml), dried ($MgSO_4$), and evaporated. The product was purified by the given method (see Table 4).

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