piperidines and their relatively inaccessible 2,6-disubstituted derivatives.

Experimental Section

Melting points were determined on a Kofler hot-state apparatus and are uncorrected. The ^{1}H NMR (300-MHz) spectra were recorded on a Varian VXR-300 spectrometer with tetramethylsilane as the internal standard. ^{13}C NMR spectra were taken on Varian VXR-300 (75-MHz) and JEOL JNM FX-100 (25-MHz) instruments. Elemental analyses were carried out in this department. Tetrahydrofuran was distilled under nitrogen from sodium benzophenone immediately before use.

Double Condensation. Typical Procedure. Benzotriazole (40 mmol), the appropriate amine or hydrazine (20 mmol), and distilled water (200 mL) were stirred vigorously for 10 min at 20 °C. Glutaraldehyde (20 mmol, 25% aqueous solution; Aldrich) was slowly added to the reaction mixture, and the stirring was continued for 1-2 h at room temperature. The products were filtered off, washed with water, and dried under vacuum.

For acylhydrazines and alkyl carbazates the procedure is similar, except ethanol was used as the solvent instead of water.

2,6-Bis(benzotriazolyl)-*N*-[(ethoxycarbonyl)amino]piperidine (7e): ^{1}H NMR (DMSO-d_6) δ 8.10-8.70 (m), 7.62-7.98 (m), 7.02 (m), 6.30 (m), 4.28 (d), 3.82 (m), 3.05-3.40 (m), 2.85 (d), 2.25-2.75 (m), 1.22-1.60 (m), 0.80-1.00 (m); ^{13}C NMR δ 155.5, 154.6, 145.6, 145.5, 132.3, 127.2, 126.8, 124.0, 123.8, 119.2, 118.9, 117.9, 117.7, 113.0, 111.3, 72.8, 60.0, 58.7, 29.8, 29.5, 20.7, 14.7, 14.5.

Reduction of Benzotriazole Adducts. Typical Procedure. Adduct **4** or **7** (5 mmol) suspended in THF (30 mL) was stirred at room temperature with sodium borohydride (0.6 g, 15 mmol) overnight. The reaction was quenched with water, and the product was extracted with hexane or diethyl ether. The extract was dried ($MgSO_4$), and the solvent evaporated under reduced pressure to obtain N-substituted piperidines. In some cases, the products were purified by column chromatography (silica gel) or recrystallization from aqueous ethanol.

Reaction with Grignard Reagents. Typical Procedure. To the Grignard reagent prepared from magnesium turnings (11 mmol for **4** and 16.5 mmol for **7**) and alkyl or aryl halide in diether ether (30 mL) was added the benzotriazole adduct (**4** or **7**) (5 mmol) in tetrahydrofuran dropwise under nitrogen. After the addition was complete, the reaction mixture was refluxed for 2 h, then poured in ice-water containing NH_4Cl, and extracted with diethyl ether. The organic layer was washed with NaOH (2 × 30 mL, 1 N) and water (2 × 30 mL) and dried over $MgSO_4$. Evaporation of the solvent gave the crude products, which were purified by crystallization or by column chromatography.

2,6-Dibutyl-*N*-benzylpiperidine (9a): oil (45%); ^{1}H NMR ($CDCl_3$) δ 7.20-7.50 (m, 5 H), 3.70 (s, 2 H, $PhCH_2$), 2.85 (m, 2 H, CH), 1.00-1.80 (m, 18 H), 0.82 (t, 6 H, CH_3); ^{13}C NMR δ 143.5, 128.4, 127.7, 125.8, 63.2, 51.6, 34.6, 29.1, 27.8, 23.8, 22.9, 14.0. MS (m/e) for $C_{20}H_{33}N$, calcd 287.4874, found 287.4892.

2,6-Dimethyl-*N*-benzylpiperidine (9b): oil (48%); ^{1}H NMR ($CDCl_3$) δ 7.15-7.45 (m, 5 H), 3.72 (s, 2 H, $PhCH_2$), 2.90 (m, 2 H, CH), 1.75-1.45 (m, 6 H), 0.98 (d, 6 H, CH_3). MS (m/e) for $C_{14}H_{21}N$, calcd 203.1675, found 203.1651.

2,6-Dimethyl-*N*-(benzoylamino)piperidine (10a): 70%; mp 176-178 °C (lit.[23] mp 179-180 °C); ^{1}H NMR ($CDCl_3$) δ 7.75-7.25 (m, 5 H), 7.00 (s, 1 H, NH), 2.95 (m, 2 H, CH), 195-155 (m, 6 H), 1.00 (d, J = 6.5 Hz, 6 H, CH_3).

2,6-Diethyl-*N*-(benzoylamino)piperidine (10b): 72%; mp 152-154 °C; ^{1}H NMR ($CDCl_3$) δ 7.76-7.25 (m, 5 H), 7.00 (s, 1 H, NH), 2.90 (m, 2 H, CH), 1.95-1.05 (m, 10 H), 0.90 (t, 6 H, J = 6 Hz, CH_3); ^{13}C NMR δ 166.7 (CO), 135.1, 130.9, 128.7, 126.8, 66.5 (CH), 26.7, 25.9, 23.0, 17.0. Anal. Calcd for $C_{16}H_{24}N_2O$: C, 73.81; H, 9.29; N, 10.75. Found: C, 74.11; H, 9.11; N, 10.48.

2,6-Diphenyl-*N*-(benzoylamino)piperidine (10c): 49%; mp 126-128 °C; ^{1}H NMR ($CDCl_3$) δ 7.75 (m, 2 H), 7.45-7.05 (m, 13 H), 4.57 (m, 2 H, CH), 2.00 (m, 4 H), 1.75 (m, 2 H); ^{13}C NMR δ 165.9 (CO), 141.2, 137.1, 130.9, 128.7, 128.0, 127.2, 126.5, 126.2, 36.8, 25.5, 23.7. Anal. Calcd for $C_{24}H_{24}N_2O$: C, 80.89; H, 6.74; N, 7.87. Found: C, 81.21; H, 6.43; N, 7.52.

2,6-Dibenzyl-*N*-[(*tert*-butoxycarbonyl)amino]piperidine (10d): 52%; mp 115-117 °C; ^{1}H NMR ($CDCl_3$) δ 7.40-7.15 (m, 10 H), 6.00 (s, 1 H, NH), 3.24 (m, 2 H, CH), 2.75 (d, J = 7 Hz, 4 H, CH_2), 2.05 (m, 4 H), 1.75 (m, 2 H), 1.25 [s, 9 H, $C(CH_3)_3$]; ^{13}C NMR 154.6, 137.1, 129.3, 127.5, 126.6, 78.0 (C), 60.2 (CH), 34.2 (CH_2), 28.3, 26.9, 18.5. Anal. Calcd for $C_{24}H_{32}N_2O_2$: C, 75.79; H, 8.42; N, 7.37. Found: C, 75.52; H, 8.71; N, 7.05.

2,6-Diphenyl-*N*-[(*tert*-butoxycarbonyl)amino]piperidine (10e): 75%; mp 168-170 °C; ^{1}H NMR ($CDCl_3$) δ 7.58 (d, J = 8 Hz, 4 H), 7.40-7.20 (m, 6 H), 5.95 (s, 1 H, NH), 4.22 (m, 2 H, CH), 2.00 (m, 4 H, CH_2), 1.78 (m, 2 H), 1.25 (s, 9 H); ^{13}C NMR δ 154.0 (CO), 140.8, 127.4, 127.3, 126.1, 78.3 (C), 62.4 (CH), 28.2, 27.4, 18.8. Anal. Calcd for $C_{22}H_{28}N_2O_2$: C, 75.00; H, 7.95; N, 7.95. Found: C, 74.60; H, 8.23; N, 7.91.

Registry No. 1, 95-14-7; **2**, 111-30-8; **3** (R = $PhCH_2$), 100-46-9; **3** (R = Ph), 62-53-3; **3** (R = *n*-$CH_3C_6H_4$), 108-44-1; **3** (R = *n*-C_4H_9), 109-73-9; **3** (R = *i*-C_3H_7), 75-31-0; **3** (R = 2-Py), 504-29-0; **4a**, 126216-53-3; **4b**, 126216-55-5; **4c**, 126216-57-7; **4d**, 126255-29-6; **4e**, 126216-59-9; **4f**, 126216-61-3; **5a**, 2905-56-8; **5b**, 4096-20-2; **5c**, 71982-24-6; **5d**, 4945-48-6; **5e**, 766-79-0; **5f**, 68654-52-4; **6a**, 100-63-0; **6b**, 57-14-7; **6c**, 613-94-5; **6d**, 1068-57-1; **6e**, 4114-31-2; **6f**, 870-46-2; **7a**, 126216-63-5; **7b**, 126216-65-7; **7c**, 126216-67-9; **7d**, 126216-69-1; **7e**, 126216-71-5; **7f**, 126216-73-7; **7g**, 126216-75-9; **8a**, 126216-44-2; **8b**, 49840-60-0; **8c**, 5454-07-9; **8d**, 31507-04-7; **8e**, 4663-84-7; **8f**, 126216-45-3; **8g**, 126216-46-4; **9a**, 126216-47-5; **9b**, 4209-63-6; **10a**, 100875-43-2; 10b, 126216-48-6; **10c**, 126216-49-7; **10d**, 126216-50-0; **10e**, 126216-51-1; $H_2NNHCOOCH_2Ph$, 5331-43-1.

A Novel Method for the Synthesis of Symmetrical Vicinal Tertiary and Secondary Diamines[1]

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A variety of symmetrical vicinal tertiary and secondary diamines are readily prepared in good to excellent yields by either Grignard reaction or reduction of the glyoxal bisproducts with benzotriazole and secondary or primary amines.

Vicinal diamino compounds are of importance in medicinal chemistry,[2] in metal chelation,[3] and in polyaza macrocyclic and cryptate chemistry.[4] They are also useful synthetic intermediates, particularly in the formation of heterocyclic rings.[5]

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(1) The Chemistry of Benzotriazole. See: (a) Katritzky, A. R.; Fan, W. Q. *J. Org. Chem.*, previous paper in this issue. (b) Katritzky, A. R.; Urogdi, L.; Mayence, A. *J. Chem. Soc., Chem. Commun.* **1989**, 337.

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Table I. Preparation and ^{1}H NMR Spectral Data of 1,2-Bis(benzotriazolyl)-1,2-(dialkylamino)ethanes 4

					calcd			found			
no.	R	R′	yield (%)	mp (°C)	C	H	N	C	H	N	^{1}H NMR (δ, $CDCl_3$ + DMSO-d_6)
4a	$-CH_2(CH_2)_3CH_2-$		92	153–155	66.98	6.98	26.05	66.69	6.97	25.94	2.30–3.00 (m, 12 H), 3.60 (m, 8 H), 7.25–7.85 (m, 10 H)
4b	$-CH_2CH_2OCH_2CH_2-$		94	157–160	60.83	5.99	25.81	61.01	6.11	26.05	2.50–3.00 (m, 8 H), 3.45–3.80 (m, 8 H), 7.20–8.20 (m, 10 H)
4c	n-C_4H_9	n-C_4H_9	85	oil[a]							
4d	$PhCH_2$	$PhCH_2$	88	140–142	77.06	5.81	17.13	76.84	5.98	16.90	3.00–3.40 (m, 8 H, CH_2), 6.80–8.30 (m, 30 H)
4e	C_6H_5	H	90	159–161	69.96	4.93	25.11	69.67	5.12	24.70	2.50 (br, 2 H, NH), 6.70–7.95 (m, 18 H), 8.25 (m, 2 H)
4f	p-$CH_3C_6H_4$	H	84	164–166	70.89	5.49	23.63	70.52	5.77	23.26	2.40 (s, 6 H, CH_3), 3.40 (br, NH), 6.60–8.20 (m, 18 H)
4g	m-$CH_3C_6H_4$	H	82	155–156	70.89	5.49	23.63	71.06	5.58	23.81	2.25 (s, 6 H), 3.40 (NH), 6.60–8.00 (m, 16 H), 8.20 (s, 2 H)

[a] Very sticky oil and used without purification for the further reaction.

Previously available methods for preparing vicinal diamines are of relatively limited applicability, and most have additonal disadvantages. The reduction of diazides, obtained by reaction of dihalides[7] or of olefines[6] (in the presence of Mn(III)) with azide anion, has generally been used to prepare primary vicinal diamines:[8] the drawbacks to this route lie in the possible explosive nature of diazides and the requirement of careful selection of reductants.[9] The preparation of vicinal diamines by the ring opening of an aziridine by an amine[10] requires starting materials that are often as difficult to obtain as the desired diamine. Recently, Jones[9] reported a four-step preparation of 3-substituted 1,2-diaminopropanes in which the amino groups are obtained as bis(carbamates) or bis(sulfonamides) by the nucleophilic ring opening of the corresponding N,N′-bisprotected 2-(aminomethyl)aziridines derived from 2-hydroxy-1,3-diaminopropane. Olefins react with the cyclopentadienylnitrosylcobalt dimer and nitrous oxide in a somewhat tedious procedure to give adducts that can be reduced to vicinal diamines with lithium aluminum hydride.[11]

Secondary vicinal diamines have usually been prepared by an active metal-induced reductive dimerization of substituted Schiff bases;[12] Na, Li, K, Mg, Al(Hg), and Ba have been used for this purpose. Zinc dust was claimed to induce the reductive coupling of Schiff bases to 1,2-bis(anilino)ethane in good yield;[13] however, it was later reported that the expected 1,2-diamines were usually accompanied by byproducts of incomplete reduction.[14] Irradiation also converts imines to the vicinal diamines,[15] although often accompanied by byproducts. Major disadvantages of the reductive dimerization of Schiff bases are as follows: (1) It can only be used for secondary aromatic amines and not for tertiary or aliphatic amines. (2) Competition between mono- and bimolecular reduction means that the monoamine is usually produced as a byproduct.[14] (3) Difficulties arise due to the radical-anion intermediates.[16] Alternatively, vicinal diamines can also be prepared by reductive amination of α-amino ketones,[17] reduction of α-amino amides,[18] and reduction of α-amino nitriles.[3] None of these methods are general because of the limited accessibility of suitable starting materials. N,N'-Dialkyl- or N,N,N',N'-tetraalkyloxamides have been reduced to N,N'-dialkyl- or N,N,N',N'-tetraalkylethylenediamines by lithium aluminum hydride.[19] 1,2-Diimines or 1,2-dioximes, obtained from 1,2-diketones, have been reduced catalytically to vicinal diamines,[20,21] but yields are low due to the formation of byproduct pyrazines.[21]

In addition to the reduction of tetraalkyloxamides, tertiary vicinal diamines were previously synthesized by the coupling reaction of certain aromatic aldehydes and secondary amines by using [tris(dialkylamino)methyl]vanadium(IV) compounds in low to moderate yields (14–54%)[22] and by the addition of aromatic amines to olefinic double bonds in the presence of thallium(III) acetate.[23] Both methods, however, require severe conditions and a special reagent. In some cases, tertiary vicinal diamines were prepared by the bisalkylation of ethylenediamine derivatives in low yields.[21,24] α-Cyano-substituted tertiary amines underwent decyanative coupling by treatment with sodium in toluene to give tertiary vicinal diamines, but the monomolecular decyanidative reduction was usually the major pathway.[25]

In view of the continuous interest in the properties and applications of vicinal diamines, new general methods for their preparation are of considerable significance. As a

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Table II. Preparation of Symmetrical Vinical Diamines 5-9

no.	reagent	yield (%)	meso/*dl*[a]	mp (°C)[b]	lit. mp (bp), °C/pressure, mmHg	calcd C	calcd H	calcd N	found C	found H	found N	ref
5a	$NaBH_4$	79		oil	76/0.4							33
5b	$NaBH_4$	76		68-69	70							33
5c	$NaBH_4$	70		oil	156-158/11							19
5d	$NaBH_4$	87		90-91	93-94							19
5e	$NaBH_4$	90		64-65	68							23
5f	$NaBH_4$	93		92-93	96-97							34
5g	$NaBH_4$	90		56-57	58.5							35
6a	PhMgBr	78	4/1	174-177	177-179[c]							22
6b	$PhCH_2MgCl$	77	*f*	125-126		82.98	9.57	7.45	83.12	9.41	7.30	
6c	CH_3MgBr	70	2/3	oil	126-128/4							36
6d	n-C_4H_9MgCl	62	4/1	oil								
7a	PhMgBr	75	3/1[e]	223-236		75.00	7.95	7.95	74.86	8.10	8.07	
7b	$PhCH_2MgCl$	69	*g*	157-159		75.79	8.42	7.37	75.78	8.23	7.90	
7c	CH_3MgBr	74	*f*	150-151	152							20
7d	n-C_4H_9MgCl	68	3/1[e]	oil								
8a	PhMgBr	81	*g*	176-178		88.11	6.99	4.90	87.86	7.20	5.15	
8c	CH_3MgBr	83	6/1[e]	151-155		85.71	8.04	6.25	85.57	8.29	5.98	
8d	n-C_4H_9MgCl	68	*g*	143-145		85.71	9.01	5.26	85.82	9.25	5.03	
9a	PhMgBr	62	1/5	156-159	152.5-153.5[d]							16
9b	$PhCH_2MgCl$	69	*g*	103-105		85.71	7.14	7.14	85.61	7.14	7.03	
9c	CH_3MgBr	51	*g*	171-173	174							13

[a] Ratios for the isolated products, determined by ^1H NMR integrals. [b] Melting point range in the cases of mixtures containing *dl* and meso forms. [c] Mp of the meso form. [d] Mp of *dl* form. [e] Assignment could be reversed. [f] One form was obtained and assigned as meso form. [g] One form was obtained without assignment.

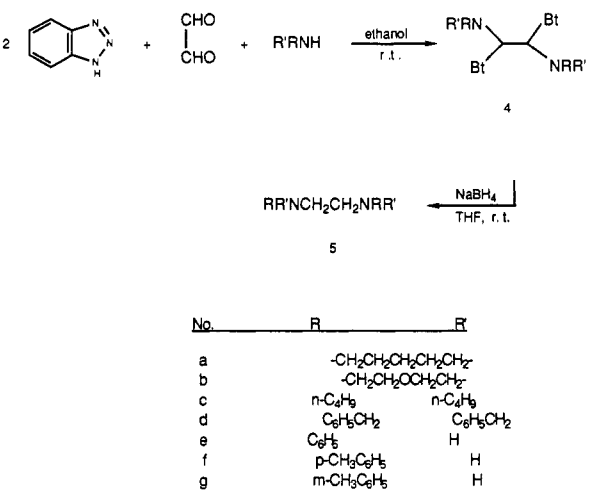
continuation of our recent investigation of the chemistry of benzotriazole and its derivatives, this paper describes a simple, two-step sequence leading to tertiary and secondary vicinal diamines in good yields from easily available benzotriazole, glyoxal, and secondary or primary amines.

We have already demonstrated the versatile synthetic utility of benzotriazole in the alkylation of amines,[26] hydrazines,[27] and amides[28] and in the preparation of amino esters[29] and aromatic ketones.[30] In the preceding paper of this series,[1a] we described the novel synthesis of a variety of 1-substituted and 1,2,6-trisubstituted piperidines by double condensation of benzotriazole and glutaraldehyde with primary amines and subsequent reduction by sodium borohydride or reaction with Grignard reagents. We now report that the products of reactions of glyoxal with two molecules of benzotriazole and an amine are good precursors for the preparation of vicinal amines.

Results and Discussion

Double condensations between benzotriazole and glyoxal and either an aromatic amine or an aliphatic secondary amine proceeded smoothly in ethanol at room temperature. The resulting stable adducts **4** were obtained in excellent yields (Scheme I, Table I). These double condensations could be carried out on a large scale in a very simple procedure (see Experimental Section). However, aliphatic primary amines failed to give the expected simple double-condensation products of type **4** under the same conditions, forming instead oligomers or polymers. Reactions of benzotriazole and an aldehyde with aliphatic primary amines usually do not stop at the monocondensation stage.[31]

Scheme I



No.	R	R'
a	$-CH_2CH_2CH_2CH_2CH_2-$	
b	$-CH_2CH_2OCH_2CH_2-$	
c	n-C_4H_9	n-C_4H_9
d	$C_6H_5CH_2$	$C_6H_5CH_2$
e	C_6H_5	H
f	p-$CH_3C_6H_5$	H
g	m-$CH_3C_6H_5$	H

Benzotriazole products of the type **4** derived from glyoxal have not been reported before. Their structures were identified by their ^1H NMR spectra (Table I) and confirmed by elemental analyses. As previously described, *N*-(aminoalkyl)benzotriazoles generally exist as mixtures of the benzotriazol-1-yl and benzotriazol-2-yl isomers.[32] There are six possible forms of bis(benzotriazole) adducts of the type **4** if the diastereoisomers (meso and *dl* forms) are also considered. Therefore, their NMR spectra, particularly ^{13}C NMR spectra, are rather complex.

Bis(benzotriazole) products **4** derived from glyoxal and amines were readily reduced by sodium borohydride to the expected *N,N'*-dialkyl- or *N,N,N',N'*-tetraalkylethylene-

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Table III. ^1H and ^{13}C NMR Spectral Data of 1,2-(Dialkylamino)ethane 5

	^1H NMR (δ, $CDCl_3$, TMS)		^{13}C NMR (δ)	
no.	2 CH_2 (s, 4 H)	NRR′	CH_2	NRR′
5a	2.55	1.60–1.25 (m, 12 H), 2.50–2.20 (m, 8 H)	45.0	50.0, 26.4, 24.7
5b	2.60	2.50–2.40 (m, 8 H), 3.50–3.35 (m, 8 H)	46.5	66.5, 49.0
5c	2.50	0.95 (t, 12 H), 1.65–1.20 (m, 16 H), 2.30 (m, 8 H)	44.8	47.6, 26.5, 22.8, 13.5
5d	2.62	3.52 (s, 8 H, CH2), 7.23 (s, 20 H)	51.0	139.6, 128.7, 128.1, 126.7, 58.6 (CH2)
5e	3.36	3.80 (s, 2 H, NH), 6.62 (m, 4 H), 6.75 (t, 2 H), 7.20 (m, 4 H)	43.2	148.0, 129.3, 117.7, 112.9
5f	3.26	2.22 (s, 6 H), 3.45 (br, NH), 6.52 (d, 4 H), 6.98 (d, 4 H)	43.6	145.7, 129.7, 126.8, 113.1, 20.3 (CH_3)
5g	3.20	2.23 (s, 6 H), 3.50 (br, NH), 6.37 (m, 4 H), 6.52 (d, 2 H) 7.02 (m, 2 H)	42.9	147.9, 138.7, 128.9, 118.4, 113.6, 109.9 21.4 (CH_3)

Table IV. ^1H NMR Spectral Data of Symmetrical Vicinal Diamines 6–9 (δ, $CDCl_3$, TMS)

no.	CH (2 H)	RR′N	R^2
6a	4.09 (s), 4.06 (s)	1.60–1.10 (m, 12 H), 2.60–2.10 (m, 8 H)	7.40–7.00 (m, 10 H)
6b	3.00 (t)	1.40–1.20 (m, 12 H), 2.40 (m, 8 H)	2.80 (d, 4 H, CH_2), 7.28–7.05 (m, 10 H)
6c	*a*	1.65–1.35 (m, 12 H), 2.63–2.25 (m, 10 H)	0.95 (d) and 0.91 (d)
6d	*a*	1.65–1.14 (m, 24 H),[b] 2.63–2.38 (m, 10 H)	0.95 (m, 6 H, CH_3)
7a	4.21 (s), 4.10 (s)	2.70–2.23 (m, 8 H), 3.73 and 3.40–3.20 (m, 8 H)	7.40–7.00 (m, 10 H)
7b	3.75 (m)	2.50 (m, 8 H), 3.60–3.32 (m, 8 H)	2.90 (m, 4 H, CH_2), 7.30–7.05 (m, 10 H)
7c	2.55 (m)	2.46–2.33 (m, 8 H), 3.73–3.58 (m, 8 H)	1.03 (d, 6 H, CH_3)
7d	*a*	2.35 (m, 12 H),[b] 3.64 (m, 10 H)	1.60–1.20 (m, 12 H), 0.91 (t, 6 H, CH_3)
8a	4.54 (s)	3.00, 4.02 (AB system, J = 13 Hz, 8 H, CH_2), 7.65–7.43 (m, 8 H), 7.32–6.78 (m, 22 H)[b]	
8c	2.92 (m), 2.73 (m)	3.25, 3.57 (AB, J = 14 Hz, 8 H), 7.36–7.15 (m, 20 H)	0.95 (d) and 1.10 (d)
8d	2.73 (t)	3.48, 3.56 (AB, J = 15 Hz, 8 H), 7.34–7.13 (m, 20 H)	1.60 (m, 4 H), 1.44 (m, 4 H), 1.30–1.13 (m, 4 H), 0.87 (t, J = 7 Hz, 6 H, CH_3)
9a	5.05 (s), 4.60 (s)	7.04 (m, 4 H), 6.72–6.55 (m, 6 H), 3.86 (br, 2 H, NH)	7.45–7.10 (m, 10 H)
9b	3.78 (t, J = 7 Hz)	7.02 (m, 4 H), 6.71 (t, J = 7 Hz, 2 H), 6.57 (d, J = 7 Hz, 4 H), 3.60 (br, 2 H, NH)	7.24–7.12 (m, 10 H), 2.88 (d, J = 7 Hz, 4 H)
9c	2.40 (m)	7.10–7.00 (m, 4 H), 7.80–7.60 (m, 6 H), 4.25 (br, NH)	1.10 (d, 6 H, CH_3)

[a] Overlapped with RR′ group. [b] Overlapped R^2 signals.

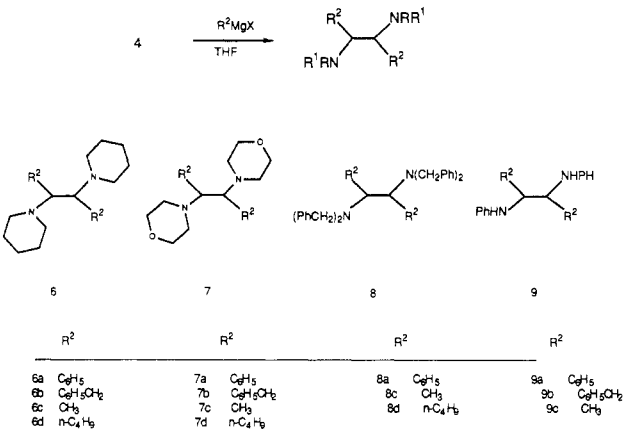
diamine in excellent yields. As described in our previous papers, the reduction proceeded very smoothly in tetrahydrofuran at room temperature within a few hours. The benzotriazole produced during the reaction dissolved in basic aqueous solution and was easily separated by extraction with alkali, making the whole procedure very simple. The results are listed in Table II. The *N,N′*-dialkyl- and *N,N,N′,N′*-tetraalkylethylenediamine thus afforded were characterized by their ^1H and ^{13}C NMR (Table III) and by comparison with the literature data (Table II).

In comparison with the methods described earlier, such as the reduction of *N,N′*-dialkyloxamide or tetraalkyloxamide,[19] our method offers the considerable advantages of a simple procedure, high overall yields, and inexpensive, safe chemicals.

When bis(benzotriazole) products **4a**, **4b**, and **4d** were treated with 2 equiv of a Grignard reagent in tetrahydrofuran, both benzotriazole moieties were readily replaced by alkyl groups, leading to the corresponding symmetrical tertiary vicinal diamines **6–8** in good to excellent yields (Scheme II). Similarly, the bis(benzotriazole) product **4e** reacted with 4 equiv of Grignard reagents to give symmetrical secondary vicinal diamines **9**. In this case, however, the yields were not as high as those for tertiary amines, and the workup process was a little more difficult, presumably due to the presence of an extra 2 equiv of Grignard reagent.

The results shown in Table II demonstrate that a wide range of Grignard reagents can be employed, that the replacement of benzotriazole ring by an alkyl group in all cases proceeded smoothly to give the expected products, and that our present method is particularly suitable for the preparation of symmetrical tertiary vicinal diamines. Thus, this two-step reaction sequence, treatment of glyoxal with two molecules of benzotriazole and subsequent Grignard reaction, provides a novel, simple, and efficient synthetic route to relatively inaccessible vicinal diamines.

Scheme II



All the products obtained, including the novel derivatives, were characterized by analytical means and by their ^1H and ^{13}C NMR spectra. As expected, two possible diastereoisomers, meso and *dl* forms, were formed in most cases when adducts **4** reacted with Grignard reagents. This is clearly indicated in their ^{13}C NMR spectra, in which each carbon has two signals representing the two isomers (Table V), and the ^1H NMR spectra of some products show two CH signals characteristic of the two meso and *dl* forms, respectively (Table IV). However, for some products, especially the sterically hindered vicinal diamines (e.g., 1,2-disubstituted *N,N,N′,N′*-tetrabenzylethylenediamine **8**), only one form was isolated after recrystallization from ethanol. The assignment of the diastereosiomers was achieved by using a chiral shift reagent in the NMR spectra and by comparison of their ^1H NMR spectra with those reported in the literature. For instance, the CH singlet of *meso*-**9a** was reported at δ 5.03 and that of *dl*-**9a** at δ 4.60;[16] therefore, the meso/*dl* ratio is easily determined by their relative integral values. No attempt was made

Table V. ^{13}C NMR Spectral Data of Symmetrical Vicinal Diamines 6–9 (δ, $CDCl_3$)

no.	CH	RR'N	R^2
meso-**6a**	69.6	50.5, 26.3, 24.5	137.2, 129.1, 126.9, 126.1
dl-**6a**	69.0	50.1, 26.9, 25.0	137.0, 129.1, 127.3, 126.3
meso-**6b**	69.7	50.9, 26.4, 24.9	143.9, 129.2, 127.9, 124.9, 33.9 (CH_2)
meso-**6c**	60.9	49.8, 26.7, 25.0	12.9 (CH_3)
dl-**6c**	62.6	49.8, 26.7, 25.1	9.10 (CH_3)
meso-**6d**	66.5	50.4, 26.9, 24.8	31.4, 27.4, 22.9, 13.7 (CH_3)
dl-**6d**	63.5	49.9, 26.5, 24.8	30.0, 27.3, 22.5, 13.7 (CH_3)
dl-**7a**[a]	69.3	67.7 (OCH_2), 49.7 (NCH_2)	136.2, 129.0, 127.4, 126.8
meso-**7a**[a]	68.3	67.1 (OCH_2), 49.3 (NCH_2)	135.9, 129.1, 127.6, 126.9
7b	68.9	66.9, 49.8	142.6, 129.0, 128.1, 125.3, 33.8 (CH_2)
dl-**7c**	62.0	67.4, 49.0	9.42 (CH_3)
meso-**7d**[a]	63.8	67.6, 49.6	30.2, 27.4, 22.8, 14.0
dl-**7d**[a]	63.7	66.0, 49.9	31.2, 27.0, 23.0, 14.0
8a	62.7	140.4, 128.8, 127.3, 126.7, 53.7 (CH_2)	135.1, 130.1, 128.1, 126.6
meso-**8c**[a]	55.4	140.4, 128.9, 127.9, 126.5, 53.4 (CH_2)	10.9 (CH_3)
dl-**8c**[a]	55.6	140.3, 128.7, 128.1, 126.6 53.6 (CH_2)	9.95 (CH_3)
8d	58.2	140.6, 128.7, 127.9, 126.5 54.5 (CH_3)	30.2, 26.2, 23.0, 14.2 (CH_3)
dl-**9a**	64.0	147.1, 128.9, 127.0, 113.5	137.9, 129.1, 126.9, 126.1
meso-**9a**	63.1	147.0, 128.5, 126.9, 113.4	137.5, 129.1, 127.4, 126.2
9b	55.1	147.1, 128.9, 128.0, 113.5	137.9, 128.7, 125.9, 117.5, 35.1
9c	52.5	146.9, 128.5, 127.6, 113.3	13.2

[a] Assignment could be reversed.

to separate diastereoisomers because of extensive previous studies in this field.[12,16,22,37]

A chiral reagent has previously been used to determine the configuration of tertiary vicinal diamines.[22] We employed tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]europium(III) to measure the ratios of the obtained meso and *dl* isomers. It was found that the efficiency of this chiral shift reagent largely depends on the structure of the diamine. In the case of the piperidino and morpholino derivatives, a significant shift was observed; for example, a 1 ppm downfield shift was observed for 1,2-diphenyl-1,2-bis(4-morpholino)ethane (**7a**). The CH_2N or CH_2O signals of the *dl* form in diamines **6** and **7** split into two broad peaks after the addition of chiral shift reagent, by which the *dl* form could be assigned. However, for some tertiary vicinal diamines, particularly for those with bulky alkylamino groups such as dibenzylamino, no significant shift could be observed. For example, the AB pattern of the benzyl methylene group of diamines **8** remains unchanged in the presence of the chiral shift reagent.

In summary, a general approach has been developed to accomplish double condensation of benzotriazole and glyoxal with amines and subsequent replacement of the benzotriazole moieties by hydrogen, aryl, or alkyl groups. In this way, various symmetrical vicinal tertiary and secondary amines were prepared in good yields. The particularly mild reaction conditions, simple procedure, easily available starting materials, and good yields offer considerable advantages over those previously applied for these purposes.

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Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus without correction. the ^1H (300-MHz) and ^{13}C (75-MHz) NMR spectra were obtained on a Varian VXR-300 (FT mode) spectrometer. Tetramethylsilane was used as the internal standard in ^1H NMR spectra. Elemental analyses were carried out in this department. Tetrahydrofuran was distilled under nitrogen from sodium benzophenone immediately before use.

Preparation of Bis(benzotriazolyl) Products 4. Typical Procedure. Benzotriazole (7.14 g, 60 mmol) and the appropriate amine (60 mmol) were stirred in ethanol (100 mL) at 20 °C for 5 min. Glyoxal (30 mmol, 40% aqueous solution) was added to the reaction mixture, and the stirring was continued overnight at 20 °C. The resulting solid was collected by filtration and washed with ethanol (Table I).

Reduction of Bis(benzotriazolyl) Products by $NaBH_4$. Typical Procedure. To product **4** (5 mmol) suspended in THF (30 mL) was added sodium borohydride (0.6 g, 15 mmol) in one portion. The reaction mixture was stirred overnight at 20 °C. After most of the solvent was removed under reduced pressure, the reaction was quenched with water. The solid was filtered and washed with water. Recrystallization from ethanol gave the pure products. For oily products, however, the product was extracted with diethyl ether. The extract was dried over $MgSO_4$ and evaporated. The purification was conducted by column chromatography (silica gel, chloroform).

Reaction with Grignard Reagents. Typical Procedure. To a solution of benzotriazole products **4** (5 mmol) in dry THF (30 mL) under an N_2 atmosphore was added Grignard reagent (Aldrich; in diethyl ether solution, 11 mmol for **4a**, **4b**, and **4d**, and 22 mmol for **4e**). After the addition, the mixture was refluxed for 1 h, then poured into water containing NH_4Cl, and extracted with diethyl ether. The organic layer was washed with NaOH (30 mL, 1 N) and water (2 × 30 mL) and dried over $MgSO_4$. Evaporation of the solvent gave the crude products, which were purified by crystallization from ethanol.