Additions of 1-(α-Aminoalkyl)benzotriazoles to *N*-Vinylamines and *N*-Vinylamides. A Novel and Versatile Method for the Preparation of Unsymmetrically Substituted 1,3-Diamines

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Received February 24, 1994®

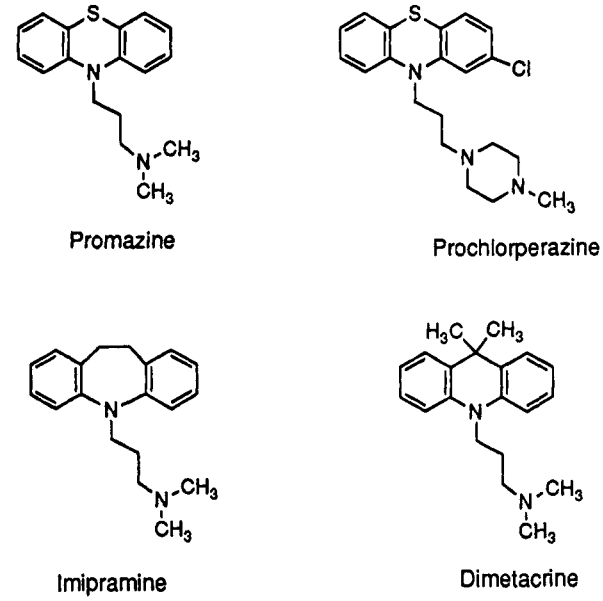
Additions of *N,N*-dialkyl-1*H*-benzotriazole-1-methanamines **1** to 9-vinylcarbazole followed by reduction of the adducts with lithium aluminum hydride gave the corresponding 9-(3-(dialkylamino)-propyl)carbazoles **8** in good yield. Treatment of the adducts with Grignard reagents gave products **9** with an alkyl or aryl group at the C-1 atom of the propylene linkage. Use of α-phenyl-*N,N*-dialkyl-1*H*-benzotriazole-1-methanamine (**14**) in the addition led to the C-3 phenyl substituted products **15–18**. Similar additions to *N*-vinyl-*N*-methylacetamide or 1-vinyl-2-pyrrolidinone followed by reduction of the adducts gave unsymmetrically substituted 1,3-propanediamines. Triamine **36** was obtained by condensation of ethylamine with formaldehyde and benzotriazole, addition of the product to 1-vinylpyrrolidinone, and reduction of the adduct with lithium aluminum hydride. 1,3-Propanediamine used in this process gave hexahydropyrimidine **39** while 1,6-hexanediamine gave hexamine **42**.

Introduction

Linkage of two nitrogen atoms by a three-carbon-atom chain plays an important role in medicinal chemistry. Most therapeutic agents of this type consist of a nitrogen heterocycle fused with two benzene rings, an amine moiety, and a three-methylene bridge between the heterocyclic and amino nitrogen atoms.[1] In Chart 1 four examples are shown: Promazine (tranquilizer), Prochlorperazine (antiemetic, antipsychotic), Imipramine (antidepressant), and Dimetacrine (antidepressant).

Reaction of 1,3-dibromopropane with dialkylamines provides an easy access to symmetrical *N,N,N',N'*-tetraalkyl-1,3-diaminopropanes.[2] N-Alkylations of amines,[3] amides,[4] and especially N–H heterocyclic systems[5–9] with 3-(dialkylamino)propyl chlorides readily provide 1,3-propanediyl linkages between two nitrogens. Modifications of this method involve stepwise procedures: (i) treatment of a heterocyclic amine with 3-chloro-1-bromopropane followed by reaction of the *N*-(3-chloropropyl) intermediate with an amine;[10,11] (ii) a procedure similar to (i) employing 3-bromopropyl tosylate instead of 3-chloro-1-bromopropane;[12] and (iii) alkylation of the heterocyclic amine with 3-bromopropanol, conversion of the *N*-(3-hydroxypropyl) intermediate to an *N*-(3-bromopropyl) derivative by reaction with phosphorus tribromide and finally treatment of the resulting bromide with an amine.[13] An alternative method is based on an treatment of an amine with phosgene followed by a 3-(dialkylamino)propanol. The 3-(dialkylamino)propyl carbamate obtained is decarboxylated at elevated temperature.[14,15] Several further methods are based on N-cyanoethylation with acrylonitrile: the intermediate nitrile is (i) reduced to an amine and alkylated;[16] (ii) hydrolyzed, reduced to an alcohol, esterified with a sulfonyl chloride, and treated with an amine;[17] or (iii) alcoholyzed to produce an ester which is treated with an amine. The resultant amide is

Chart 1



® Abstract published in *Advance ACS Abstracts,* August 1, 1994.

(1) Windholz, M.; Budavari, S.; Blumetti, R. F.; Otterbein, E. S., Eds. *The Merck Index—An Encyclopedia of Chemicals, Drugs and Biologicals*; Merck & Co., Inc.: Rahway, NJ, 1983.
(2) Knapick, E. G.; Ander, P.; Hirsch, J. A. *Synthesis* **1985**, 58.
(3) Vanhoff, P.; Clarebout, P. Ger. Pat. 2 060 721, **1971**; *Chem. Abstr.* **1971**, *75*, 76463x.
(4) Testa, E.; Pifferi, G.; Fontanella, L.; Ares, V. *Liebigs Ann. Chem.* **1966**, *696*, 108.
(5) Hromatka, O.; Sauter, F.; Grass, I. *Monatsh. Chem.* **1957**, *88*, 56.
(6) Schuler, W. A.; Klebe, H. *Liebigs. Ann. Chem.* **1962**, *653*, 172.
(7) Schindler, W.; Hafliger, F. *Helv. Chim. Acta* **1954**, *37*, 472.
(8) Hoerlein, U.; Risse, K. H.; Wirth, W. Ger. Pat. 1 120 451, **1961**; *Chem. Abstr.* **1962**, *57*, 4677b.
(9) Ivanov, P. Yu.; Bokanov, A. I.; Budanova, L. I.; Kuzovkin, V. A.; Shvedov, V. I. *Khim.-Farm. Zh.* **1987**, *21*, 1119; *Chem. Abstr.* **1988**, *108*, 167404v.
(10) Yale, H. L.; Sowinski, F. *J. Am. Chem. Soc.* **1960**, *82*, 2039.
(11) Ratouis, R.; Boissier, J. R. *Bull. Soc. Chim. Fr.* **1966**, 2963.
(12) Hromatka, O.; Stehlik, G.; Sauter, F. *Monatsh. Chem.* **1960**, *91*, 107.
(13) Hromatka, O.; Sauter, F.; Schlager, L. H. *Monatsh. Chem.* **1957**, *88*, 193.
(14) Schmitt, J.; Boitard, J.; Comoy, P.; Hallot, A.; Suquet, M. *Bull. Soc. Chim. Fr.* **1957**, 938.
(15) Hebky, J.; Radek, O.; Kejha, J. *Collect. Czech. Chem. Commun.* **1959**, *24*, 3988.
(16) Yale, H. L.; Sowinski, F.; Bernstein, J. *J. Am. Chem. Soc.* **1957**, *79*, 4375.

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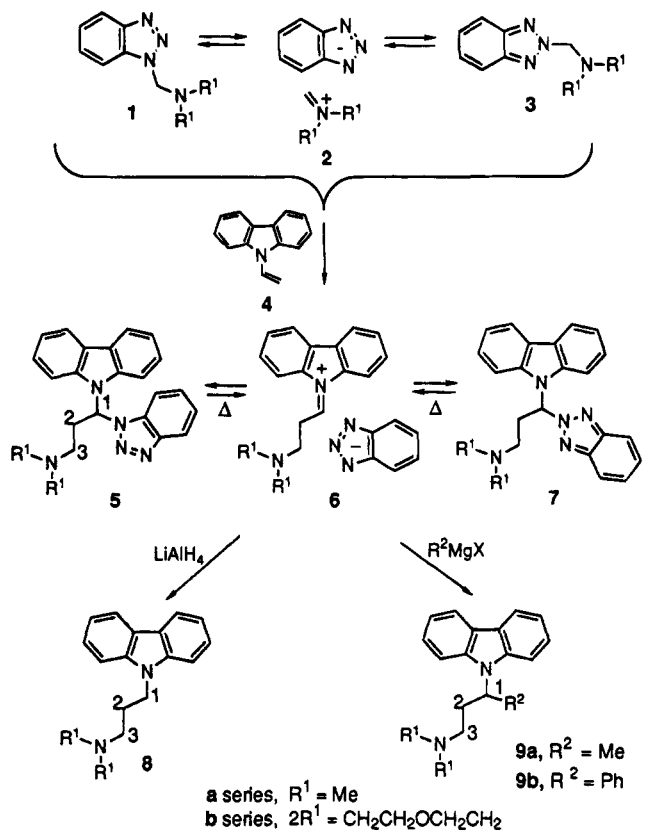
Scheme 1



reduced to a dialkylamino group.[18] None of these literature methods are easily adapted for the preparation of 1,3-diaminopropanes bearing an additional substituent on a terminal carbon atom of the N–C–C–C–N chain. Such compounds have remained relatively unexplored due to their inaccessibility. We have now found that our benzotriazole methodology shows great utility for preparation of compounds of this type.

In solution, *N,N*-disubstituted (aminomethyl)benzotriazoles **1** reversibly dissociate to give low concentrations of the benzotriazolide anion (Bt^-) and immonium cation (**2**) as shown by NMR investigations of the equilibrium between **1** and its benzotriazol-2-yl isomer (**3**) (Scheme 1).[19-22] Cations **2** can be trapped by nucleophiles like organometallic reagents or by sodium borohydride leading to valuable synthetic methods for various types of amines.[23-36] The recently discovered addition of 1-(α-aminoalkyl)benzotriazoles to enol ethers allowed extension of this methodology to the preparation of 1,3-amino ethers.[37] We now discuss the more complex problem of the addition of 1-(α-aminoalkyl)benzotriazoles to C=C bonds activated by an adjacent nitrogen atom which provides a new approach to the synthesis of unsymmetrically substituted 1,3-diamines; our preliminary results have been published.[38]

Results and Discussion

Simple Adducts of 9-Vinylcarbazole. Our results indicate that only a relatively narrow class of unsaturated compounds successfully trap cations **2**. On one hand, the C=C bond must be nucleophilic enough for the reaction to occur; an adjacent electron donor group is required. On the other, too high electron density of this bond results in the formation of a reactive adduct which spontaneously undergoes addition to the activated olefin, this whole process repeats, and finally a polymer is produced. Enol ethers were reported to fit well into this niche, giving adducts in which the N–C–N grouping was replaced by a less reactive N–C–O one,[37] whereas enamines derived from dialkyl and alkyl aryl amines gave polymeric materials.

In the present research, we have found that enamines originating from amines of low basicity can also be used satisfactorily for trapping cations **2**; commercially available 9-vinylcarbazole (**4**) is an excellent example. Addition of immonium cation **2** (derived from **1a** or **1b**[39]) to the β carbon atom of **4** produced a less stable cation (**6**) with a strong tendency to exit from the process by addition of the benzotriazolide anion, to give a mixture of **5** and **7** in a ratio of 5:1 (Scheme 1); recrystallization gave the pure benzotriazol-1-yl isomer (**5**). Column chromatography of the concentrated mother liquor afforded the benzotriazol-2-yl isomer **7**.

At elevated temperatures, adduct **5** can dissociate into the benzotriazolide anion and immonium cation **6**. The dissociation constant is very small; however, complexing the benzotriazolide anion with metal cations can significantly shift the equilibrium toward the ionized form and allow nucleophiles to trap cations **6**. Thus, treatment of **5a** with lithium aluminum hydride in refluxing THF substituted the benzotriazolyl group by a hydrogen atom, giving diamine **8a**. Adduct **5b** was converted in a similar manner to diamine **8b**. Treatment of **5a** with methylmagnesium iodide in refluxing ether/toluene substituted the benzotriazolyl by a methyl group, producing diamine **9a**. Reaction of **5b** with phenylmagnesium bromide in refluxing toluene gave diamine **9b**.

Addition of 1-[α-(morpholin-4-yl)benzyl]benzotriazole (14).[24] Column chromatography of the mixture obtained from the addition of **14** to 9-vinylcarbazole (**4**)

(17) Molnar, I.; Wagner-Jauregg, Th. *Helv. Chim. Acta* **1965**, *48*, 1782.
(18) Owen, T. C. *J. Heterocycl. Chem.* **1984**, *21*, 265.
(19) Lindsay Smith, J. R.; Sadd, J. S. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1181.
(20) Katritzky, A. R.; Yannakopoulou, K.; Kuzmierkiewicz, W.; Aurrecoechea, J. M.; Palenik, G. J.; Koziol, A. E.; Szczesniak, M.; Skarjune, R. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2673.
(21) Katritzky, A. R.; Yannakopoulou, K. *Heterocycles* **1989**, *28*, 1121.
(22) Katritzky, A. R.; Rachwal, S.; Wu, J. *Can. J. Chem.* **1990**, *68*, 446.
(23) Katritzky, A. R.; Rachwal, S.; Rachwal, B. *J. Chem. Soc., Perkin Trans. 1* **1987**, 805.
(24) Katritzky, A. R.; Yannakopoulou, K.; Lue, P.; Rasala, D.; Urodgi, L. *J. Chem. Soc., Perkin Trans. 1* **1989**, 225.
(25) Katritzky, A. R.; Akutagawa, K. *Org. Prep. Proced. Int.* **1989**, *21*, 340.
(26) Katritzky, A. R.; Gallos, J. K.; Yannakopoulou, K. *Synthesis* **1989**, 31.
(27) Katritzky, A. R.; Najzarek, Z.; Dega-Szafran, Z. *Synthesis* **1989**, 66.
(28) Katritzky A. R.; Yannakopoulou, K. *Synthesis* 1989, 747.
(29) Katritzky A. R. ; Lang, H.; Lan, X. *Tetrahedron* **1993**, *49*, 2829.
(30) Katritzky, A. R.; Noble, G.; Pilarski, B.; Harris, P. *Chem. Ber.* **1990**, *123*, 1443.
(31) Katritzky, A. R.; Rachwal, S.; Wu, J. *Can. J. Chem.* **1990**, *68*, 456.
(32) Katritzky, A. R.; Latif, M.; Urodgi, L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 667.
(33) Katritzky, A. R.; Borowiecka, J.; Fan, W. Q. *Synthesis* **1990**, 1173.
(34) Katritzky, A. R.; Fan, W. Q. *J. Fluorine Chem.* **1991**, *51*, 33.
(35) Katritzky, A. R.; Zhao, X., Hitchings, G. J. *Synthesis* **1991**, 703.
(36) Katritzky, A. R.; Jurczyk, S.; Rachwal, B.; Rachwal, S.; Shcherbakova, I.; Yannakopoulou, K. *Synthesis* **1992**, 1295.
(37) Katritzky, A. R.; Rachwal, S.; Rachwal, B.; Steel, P. J. *J. Org. Chem.* **1992**, *57*, 4932.
(38) Katritzky, A. R.; Rachwal, B.; Rachwal, S. *J. Org. Chem.* **1993**, *58*, 812.
(39) Burckhalter, J. H.; Stephens, V. C.; Hall, L. A. R. *J. Am. Chem. Soc.* **1952**, *74*, 3868.

Scheme 2

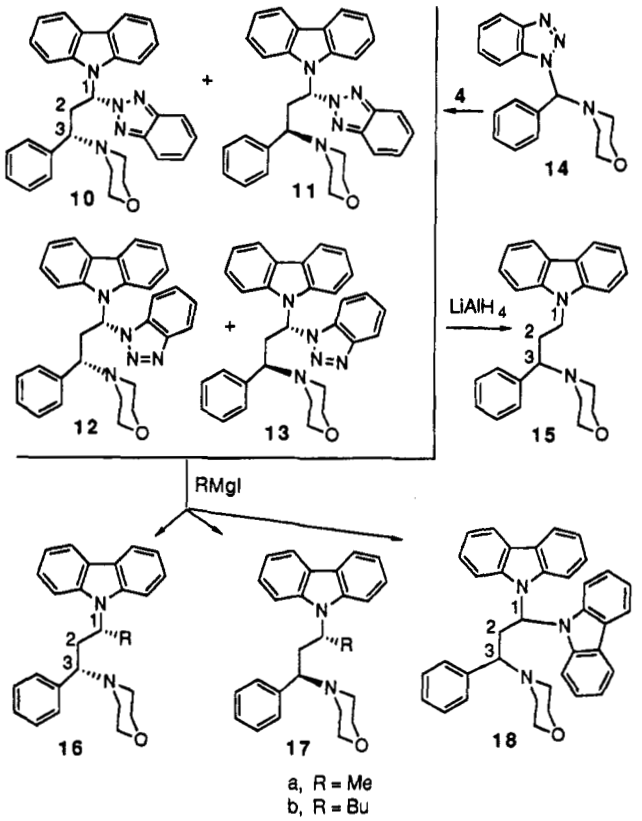
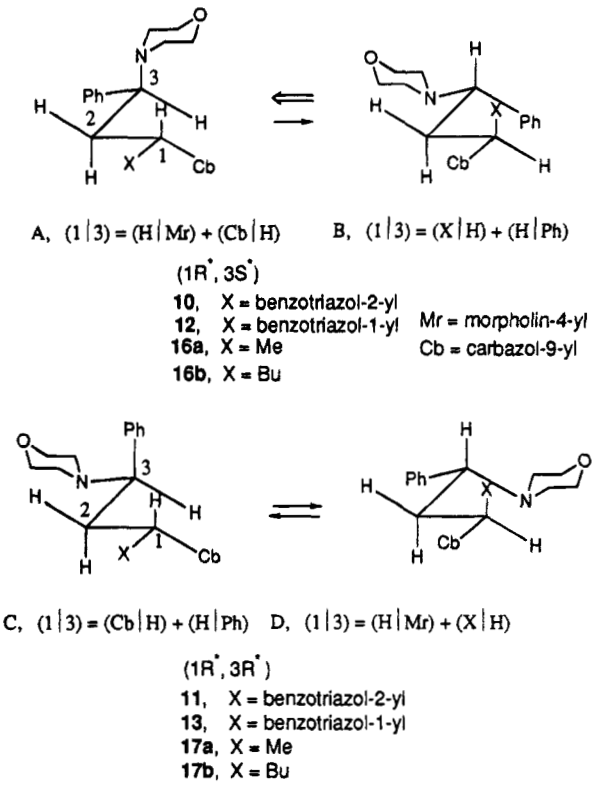


Chart 2



separated four isomeric products, **10**, **11**, **12**, and **13**, with yields of 9, 11, 42, and 26%, respectively (Scheme 2). The products consist of one pair of benzotriazol-1-yl (**12** and **13**) and one of benzotriazol-2-yl (**10** and **11**) diastereomers. The first two compounds obtained from column chromatography, **10** and **12**, exhibit interesting sets of ^{1}H NMR resonances in which the H-2 protons can be observed as two independent ddd patterns at δ 3.48 and 3.82 for **10** and δ 3.45 and 4.10 for **12**. Protons H-1 and H-3 of **10** and **12** are observed as dd patterns with two very different couplings to the particular H-2 protons, e.g. coupling constants of the H-3 proton are 4.7 and 10.8 Hz for **10** and 4.6 and 10.9 Hz for **12**, respectively. The two remaining isomers with lower R_f values, **11** and **13**, exhibit much simpler spectra. The H-1 and H-3 protons are observed as triplets with coupling constants in the range of 6.7−8.1 Hz.

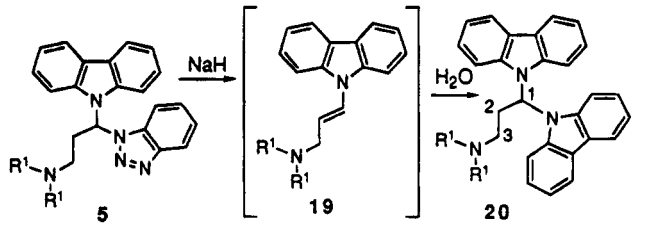
Conformational analysis of the molecular models revealed that if all conformers with energetically unfavorable parallel interactions (1|3) between bulky substituents are excluded,[40-42] only conformations A and B remain for the molecules of the 1*R**,3*S** diastereomers (Chart 2). As shown in numerous studies, (1|3) interactions between a hydrogen and an electron pair of a heteroatom do not contribute significantly to the total molecular energy whereas such interactions between a hydrogen atom and an alkyl or phenyl group cause an energy increase of a few kcal per mole for each interaction.[41-46] In previous studies,[37,47] we found that the (H|Bt) is similar in nature to the (H|Ph) disfavorable "hard" interaction, contributing significantly to the molecular energy.

In the present case, conformation A with the "soft" (H|Mr) and (H|Cb) interactions (Mr = morpholin-4-yl, Cb = carbazol-9-yl) should be of significantly lower energy than conformation B with the strong (H|Ph) and (H|Bt) repulsive interactions. Because the 1*R**,3*S**molecule exists most of the time in conformation A, the H-1 and H-3 interactions with the two H-2 protons are quite different (gauche vs anti), leading to two different coupling constants. By contrast, both conformers of the 1*R**,3*R** isomers, C and D, possess comparable (1|3) interactions and therefore similar molecular energy; hence the 1*R**,3*R** diastereomers are expected to show equal coupling constants of H-1 and H-3 with the two H-2 protons. These considerations lead to the conclusion that the first two compounds obtained from the column chromatography (**10** and **12**) are the 1*R**,3*S** diastereomers and the two following ones (**11** and **13**) are of the 1*R**,3*R** configuration.

Upon reduction with lithium aluminum hydride in refluxing THF, a mixture of isomers **10**−**13** was converted into a single diamine (**15**). Treatment of adducts **10**−**13** with methylmagnesium iodide in refluxing toluene gave three compounds: two are the expected diastereomers obtained by substitution of the benzotriazolyl moiety in **10**−**13** by a methyl group (**16**, **17**), the third compound (**18**) possesses two carbazol-9-yl groups. The 1*R**,3*S** configuration was assigned for isomer **16a** on the basis of the two different coupling constants of its H-3 to the H-2 protons (5.4 and 9.3 Hz), by analogy to the considerations described above for the isomeric pairs among compounds **10**−**13**. The coupling constants be-

(40) Spiessens, L. I.; Becu, C.; Hosten, N.; Anteunis-De Ketelaere, F.; Anteunis, M. J. O.; Tavernier, D. *Bull. Soc. Chim. Belg.* **1982**, *91*, 845.
(41) Kleinpeter, E.; Meusinger, R.; Duschek, Ch.; Borsdorf, R. *Magn. Reson. Chem.* **1987**, *25*, 990.
(42) Wertz, D. H.; Allinger, N. L. *Tetrahedron* **1974**, *30*, 1579.
(43) Booth, H.; Everett, J. R. *J. Chem. Soc., Chem. Commun.* **1976**, 278.
(44) Eliel, E. L.; Manoharan, M. *J. Org. Chem.* **1981**, *46*, 1959.
(45) Schneider, H. J.; Agrawal, P. K. *Tetrahedron*, **1984**, *40*, 1025.
(46) Schneider, H. J.; Hoppen, V. *J. Org. Chem.* **1978**, *43*, 3866.
(47) Katritzky, A. R.; Rachwal, S.; Rachwal, B.; Steel, P. J. *J. Org. Chem.* **1992**, *57*, 4925.

Scheme 3



a, R^1 = Me
b, $2R^1$ = $CH_2CH_2OCH_2CH_2$

tween the H-3 and H-2 protons for the second diastereomer (**17a**) are much closer (6.5 and 8.7 Hz) but are not equal as in the idealistic case discussed for **10**–**13**. This can be explained by the stronger repulsive (H|Me) interaction in conformation D than the corresponding (H|Ph) interaction in conformation C. As a result of this difference form C is slightly favored.

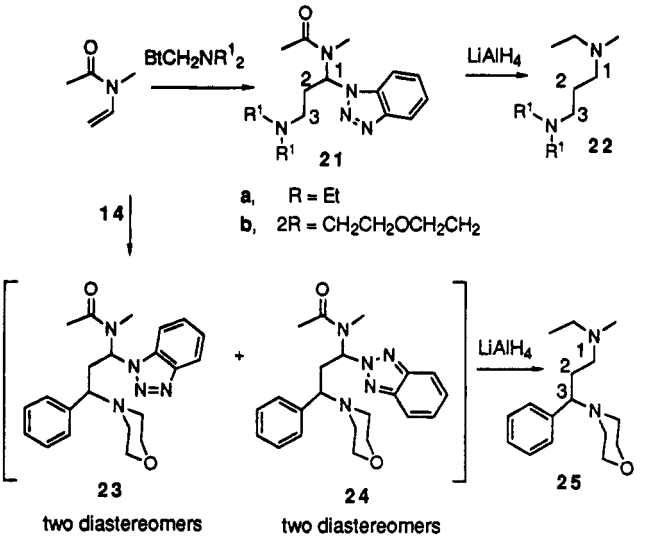
Because this evidence for stereochemical assignments for compounds **16a** and **17a** is not as strong as those for **10**–**13**, further support from the NMR spectra was obtained. Comparison of the ^{1}H NMR spectra of **16a** and **17a** clearly showed that the biggest difference between them is the H-2 resonances which are exhibited as relatively close ddd patterns in the spectrum of **16a** (δ 2.52 and 2.64) and widely spread ddd patterns in the spectrum of **17a** (δ 2.29 and 3.02). Examination of the molecular models revealed that in conformation C one of the H-2 atoms is located in the deshielding zone of the phenyl group shifting it downfield, whereas in conformation D, the other one H-2 atom is located in a shielding zone of the carbazolyl system shifting its resonance upfield. In conformes A and B, the shielding and deshielding effects of the aromatic group are balanced. Further support for the structural assignments is provided by the morpholine proton resonances: the morpholine H-3 protons are observed as two multiplets at δ 2.04 and 2.41 in the spectrum of **16a** and as an only one (four proton) multiplet at δ 2.15 in the spectrum of **17a**, by analogy to the diastereomeric pairs among **10**–**13**.

Reaction with butylmagnesium iodide gave a pair of diastereomers **16b** and **17b** which were separated by repeated column chromatography. Analogously to the above case, the 1*R**,3*S** configuration was assigned to the less polar isomer exhibiting differences between the morpholinyl H-3 resonances (**16b**). The carbon-chain H-1, H-2, and H-3 resonances of diastereomer **17b** overlap those of the butyl group and could not be used for diagnosis.

The third compound from the above reactions is structure **18**, formed by elimination of benzotriazole from the adduct **10**–**13** followed by addition of carbazole to the enamine system obtained. The Grignard reagents evidently act as strong bases in this elimination. No such bis-carbazolyl products were formed in the Grignard reactions of simpler adducts **5**; however, compounds **5** are also susceptible to basic elimination. When treated with sodium hydride, they gave bis-carbazolyl derivatives **20** (Scheme 3). The reaction is believed to proceed via an enamine form (**19**) which during workup undergoes partial hydrolysis to carbazole and 3-aminopropionaldehyde. The released carbazole adds to the remaining molecules of enamines **19**, producing the relatively inert adducts (**20**).

In the Grignard reactions of **10**–**13**, elimination of benzotriazole or substitution of the benzotriazolyl moiety

Scheme 4



by an alkyl group were two competing reactions. It is well known that two organomagnesium halide molecules are needed in the transition state for the Grignard addition to a carbonyl group and this probably also applies to the iminium cation **6**. When there is insufficient space around the carbonyl group, other reactions of the Grignard reagent may prevail.[48,49] We observed such a phenomenon in the reactions of more sterically hindered molecules of types **10**–**13**. Because the additional substituent (phenyl) is located on a relatively remote β carbon atom, this observation suggests that it is a complex of the organomagnesium molecule with the morpholine group of the iminium cation derived from **10**–**13** which participates in the Grignard reaction.

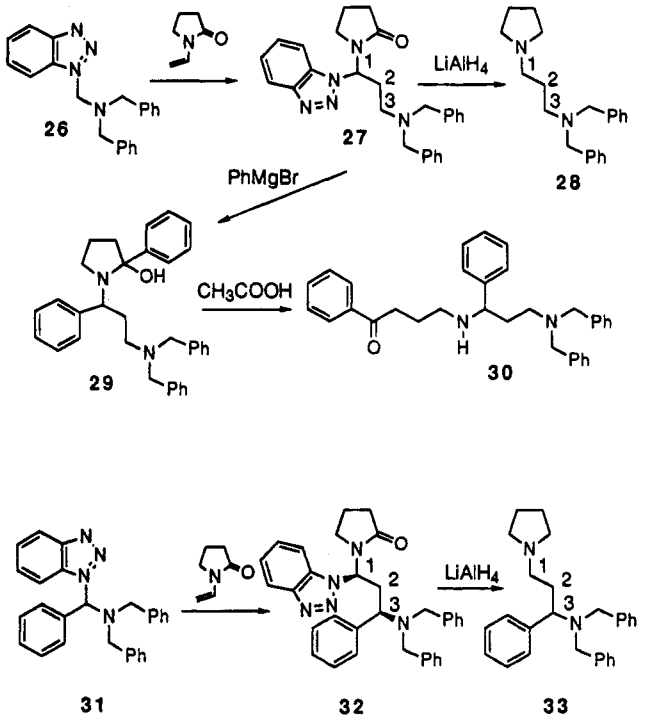
***N*-Vinylamides.** *N*-Vinylamides form a second class of *N*-vinyl derivatives of moderate electron density which are suitable for the addition of 1-(α-aminoalkyl)benzotriazoles. Thus, reaction of *N*,*N*-diethyl-1*H*-benzotriazole-1-methanamine[24] (**1a**) with *N*-methyl-*N*-vinylacetamide gave adduct **21a** in good yield (Scheme 4). In a similar way, the morpholin-4-yl derivative **21b** was obtained from **1b**. Both adducts (**21a** and **21b**) were reduced with lithium aluminum hydride to the corresponding 1,3-diamines **22**. Addition of the benzyl derivative **14** to *N*-methyl-*N*-vinylacetamide produced a difficult-to-separate mixture of four isomers (**23** and **24**) which was smoothly converted by reduction to diamine **25**. This is potentially a very effective and versatile method for the synthesis of unsymmetrically substituted aliphatic 1,3-diamines which are difficult to access by existing literature methods.

Addition of *N*,*N*-dibenzyl-1*H*-benzotriazole-1-methanamine[24] (**26**) to *N*-vinyl-2-pyrrolidinone gave adduct **27** which was then reduced to diamine **28** (Scheme 5). In the Grignard reaction, the attack of phenylmagnesium bromide on the carbonyl group of **27** released the benzotriazolyl substituent from its deactivating influence, allowing substitution of the benzotriazolyl by a phenyl group in the following step under mild conditions. During workup, unstable product **29** was converted to amino ketone **30** which was then characterized as its dipicrate.

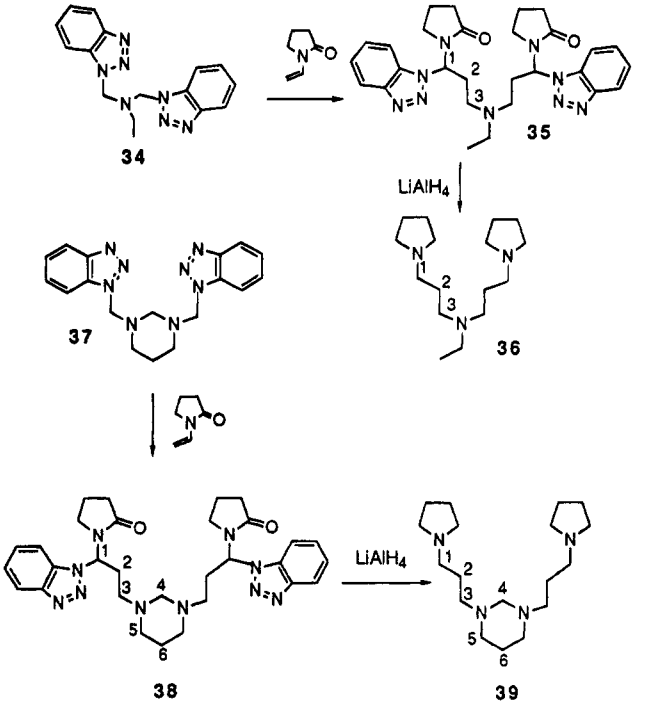
Contrary to the behavior of *N*-vinylacetamide discussed above, addition of a derivative of **26**, α-substituted with a phenyl group (**31**), to *N*-vinyl-2-pyrrolidinone gave

(48) Miller, J.; Gregoriou, G.; Mosher, H. S. *J. Am. Chem. Soc.* **1961**, *83*, 3966.
(49) Dunn, G. E.; Warkentin, J. *Can. J. Chem.* **1956**, *34*, 75.

Scheme 5



Scheme 6



predominantly a single diastereomer which was easily separated by column chromatography and further purified by recrystallization. The H-3 resonance in the ^1H NMR spectrum of adduct **32** is a triplet (δ 3.75), indicating the $1R^*,3R^*$ configuration, in accordance with the previous discussion on carbazolyl derivatives (Scheme 2). Reduction of adduct **32** with lithium aluminum hydride gave diamine **33**.

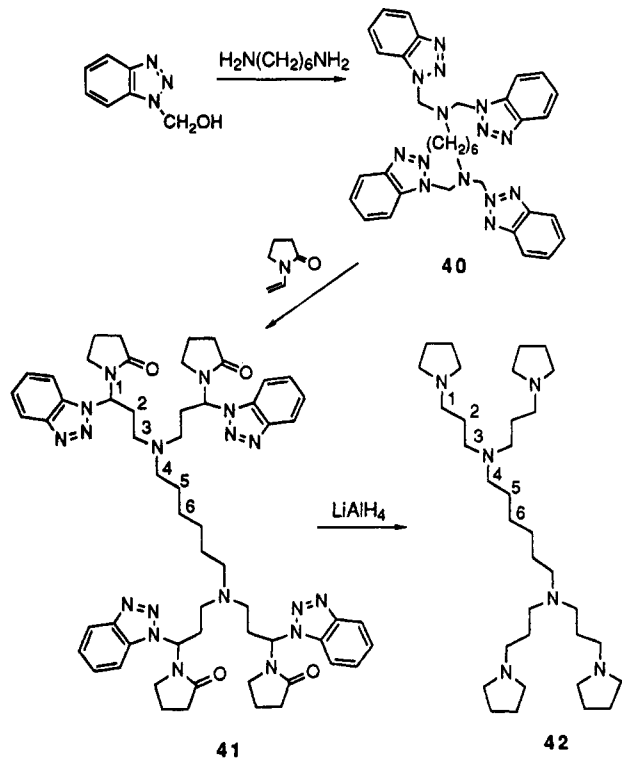
Additions of *N,N*-Bis(benzotriazol-1-ylmethyl)-amines. Condensation of primary aliphatic amines with 1-(hydroxymethyl)benzotriazole gives the corresponding *N,N*-bis(benzotriazol-1-ylmethyl) derivatives.[50] In these compounds, both benzotriazol-1-ylmethyl groups can undergo ionization and consequently easily add two molecules of *N*-vinylamide to produce the corresponding triamines. Thus, reaction of *N,N*-bis(benzotriazol-1-ylmethyl)ethanamine (**34**) with *N*-vinylpyrrolidinone gave adduct **35** (Scheme 6). Because the two chiral carbon atoms are distant, the two diastereomers of **35** formed cannot be distinguished by NMR. Adduct **35** was smoothly reduced to triamine **36**.

Additional amino functionality can be introduced by starting from diamines. Thus, condensation of 1,3-propanediamine with formaldehyde and benzotriazole gave cyclic product **37**. Reaction of **37** with 1-vinyl-2-pyrrolidinone produced diadduct **38**. Just as for compound **35**, NMR spectra did not distinguish between the diastereomers of product **38**. Reduction of **38** with lithium aluminum hydride gave tetramine **39**.

Aliphatic diamines bearing a longer linkage between the amino groups have no tendency to undergo cyclocondensation with formaldehyde, opening new possibilities to the design of complex molecules. Thus, tetrabenzotriazolyl derivative **40** (Scheme 7) was obtained from the reaction of 1-(hydroxymethyl)benzotriazole with 1,6-hexanediamine. Addition to **40** of 4 molar equiv of 1-vinyl-2-pyrrolidinone produced tetraadduct **41**.

One problem concerning adduct **41**, and also to some degree compounds **35** and **38**, requires mention. Structure **41** represents an idealized symmetrical molecule. In reality, individual additions to *N*-vinyl groups give also minor amounts of the corresponding benzotriazol-2-yl isomers. When, there is only one benzotriazolyl group in the molecule, the benzotriazol-2-yl isomer (usually below 10%) can be neglected. However, in the case of adduct **41**, the probability that at least one of the benzotriazolyl groups will be bound by the N-2 atom should be multiplied by four. The obtained product contains also bis(benzotriazol-2-yl) derivatives (two possible isomers), tris(benzotriazol-2-yl) derivatives (two isomers), and even the tetrakis(benzotriazol-2-yl) derivative; all of which exist in various possible diastereomeric

Scheme 7



(50) Katritzky, A. R.; Rachwal, S.; Rachwal, B. *J. Chem. Soc., Perkin Trans. 1* **1987**, 799.

forms. Such complications make the product mixture a difficult-to-handle glassy material which cannot even be characterized by NMR. Column chromatography allowed separation of a fraction containing about 50% of the (4 Bt-1) isomer and 50% of the (3 Bt-1 + 1 Bt-2) isomer. Nevertheless, lithium aluminum hydride caused reduction of this isomeric mixture to a single product, hexamine **42**.

Conclusion

A three-carbon-atom linkage between two nitrogen atoms is easily attained by addition of an *N*-(benzotriazol-1-ylmethyl)amine to an *N*-vinyl heterocyclic system or an *N*-vinylamide. Reduction with lithium aluminum hydride or reaction with a Grignard reagent allows substitution of the benzotriazolyl moiety in the adduct by a hydrogen atom or an alkyl (or aryl) group, respectively. α-Substituted 1*H*-benzotriazole-1-methanamines used in the addition allow the introduction of an additional substituent to a terminal carbon atom of the linkage.

Experimental Section

General. Melting points were determined on a capillary melting point apparatus and are uncorrected. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as an internal standard. Solvents for the Grignard reactions (ether, THF, toluene, benzene, dioxane) were dried by reflux with sodium benzophenone under nitrogen and distilled immediately before use. Column chromatography was conducted with silica gel grade 60–200 mesh. Abbreviations used for assignment of the NMR spectra: Bt = benzotriazol-1-yl or benzotriazol-2-yl, Mr = morpholin-4-yl, Cb = carbazol-9-yl, Pl = 2-oxopyrrolidin-1-yl, Pn = pyrrolidin-2-yl.

9-[1-(Benzotriazol-1-yl)-3-(dimethylamino)propyl]carbazole (5a). p-Toluenesulfonic acid monohydrate (0.04 g, 0.2 mmol) was added to a mixture of **1a** (1.76 g, 10 mmol) and **4** (1.93 g, 10 mmol) preheated to 110 °C (oil bath). Heating at 110 °C was continued for an additional 10 min and the mixture was allowed to cool to room temperature. Trituration of the obtained glassy material with ether produced crystals. Final recrystallization of the product from ethanol gave analytically pure **5a** (2.40 g, 65%) as colorless prisms: mp 124–125 °C; ^{1}H NMR δ 2.15 (s, 6 H), 2.15 (m, 1 H), 2.30 (dt, *J* = 12.9 and 4.9 Hz, 1 H), 3.31 (m, 1 H), 3.44 (m, 1 H), 7.09 (m, 1 H), 7.22 (m, 4 H), 7.42 (t, *J* = 7.4 Hz, 2 H), 7.62 (dd, *J* = 4.7 and 9.2 Hz, 1 H), 7.70 (d, *J* = 8.3 Hz, 2 H), 8.0 (m, 1 H), 8.04 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR δ 29.1, 45.4 (2 C), 54.4, 65.7, 109.8, 110.1 (2 C), 119.9, 120.2 (2 C), 120.4 (2 C), 123.7 (2 C), 124.3, 126.2 (2 C), 127.8, 133.1, 139.0 (2 C), 146.2. Anal. Calcd for $C_{23}H_{23}N_5$: C, 74.77; H, 6.27; N, 18.96. Found: C, 74.62; H, 6.36; N, 19.02.

Evaporation of the mother liquor and column chromatography (chloroform) of the residue afforded isomer **7a** (0.37 g, 10%) which was recrystallized from ethanol to give prisms: mp 132–133 °C; ^{1}H NMR δ 2.13 (s, 6 H), 2.22 (m, 2 H), 3.21 (m, 1 H), 3.32 (m, 1 H), 7.24 (t, *J* = 7.3 Hz, 2 H), 7.33 (m, 2 H), 7.45 (t, *J* = 7.4 Hz, 2 H), 7.77 (dd, *J* = 6.1 and 8.3 Hz, 1 H), 7.84 (m, 2 H), 7.94 (d, *J* = 8.3 Hz, 2 H), 8.03 (m, 2 H); ^{13}C NMR δ 29.9, 45.3 (2 C), 54.7, 72.4, 110.9 (2 C), 118.5 (2 C), 120.2 (4 C), 123.8 (2 C), 126.0 (2 C), 126.7 (2 C), 139.5 (2 C), 144.1 (2 C). Anal. Calcd for $C_{23}H_{23}N_9$: C, 74.77; H, 6.27; N, 18.96. Found: C, 74.71; H, 6.30; N, 18.95.

The second fraction from column chromatography gave an additional portion of **5a** (0.65 g, 18%).

9-[1-(Benzotriazol-1-yl)-3-(morpholin-4-yl)propyl]carbazole (5b). Addition of **2b** (2.18 g, 10 mmol) to **4** carried out according to the above procedure gave pure **5b** (1.77 g, 43%) as colorless needles: mp 145–150 °C; ^{1}H NMR δ 2.14 (m, 3 H), 2.42 (m, 3 H), 3.42 (m, 2 H), 3.69 (m, 4 H), 7.06–7.28 (m, 5 H), 7.41 (t, *J* = 7.7 Hz, 2 H), 7.62 (dd, *J* = 5.9 and 8.2 Hz, 1 H), 7.69 (d, *J* = 7.9 Hz, 2 H), 7.99 (m, 1 H), 8.05 (d, *J* = 7.7 Hz, 2 H); ^{13}C NMR δ 27.6, 53.4 (2 C), 53.5, 65.8, 67.0 (2 C), 109.7, 110.0 (2 C), 120.0, 120.3 (2 C), 120.5 (2 C), 123.7 (2 C), 124.3, 126.2 (2 C), 127.9, 133.1, 139.0 (2 C), 146.3. Anal. Calcd for $C_{25}H_{25}N_5O$: C, 72.96; H, 6.12; N, 17.02. Found: C, 72.96; H, 6.17; N, 16.86.

Evaporation of the mother liquor and column chromatography (chloroform) of the residue afforded as the first fraction isomer **7b** (0.45 g, 11%) which was recrystallized from ethanol to give colorless needles: mp 65–67 °C; ^{1}H NMR δ 2.09 (m, 3 H), 2.36 (m, 3 H), 3.27 (m, 2 H), 3.62 (t, *J* = 4.4 Hz, 4 H), 7.23 (t, *J* = 7.5 Hz, 2 H), 7.32 (m, 2 H), 7.45 (t, *J* = 7.8 Hz, 2 H), 7.79 (dd, *J* = 6.8 and 8.6 Hz, 1 H), 7.84 (m, 2 H), 7.93 (d, *J* = 7.8 Hz, 2 H), 8.02 (d, *J* = 7.5 Hz, 2 H); ^{13}C NMR δ 28.4, 53.3 (2 C), 53.7, 66.9 (2 C), 72.3, 110.9 (2 C), 118.4 (2 C), 120.2 (4 C), 123.7 (2 C), 126.0 (2 C), 126.8 (2 C), 139.4 (2 C), 144.1 (2 C). Anal. Calcd for $C_{25}H_{25}N_5O$: C, 72.96; H, 6.12; N, 17.02. Found: C, 72.84; H, 6.14; N, 17.06.

The second fraction from the column chromatography gave an additional portion of **5b** (1.26 g, 30%).

9-[3-(Dimethylamino)propyl]carbazole (8a). To a solution of **5a** (2.22 g, 6 mmol) in THF (20 mL) was added $LiAlH_4$ (0.30 g, 8 mmol), and the mixture stirred at reflux for 2 h. After cooling to room temperature, the mixture was poured into ice–water (100 g) and extracted with diethyl ether (3 × 50 mL). The combined extracts were washed with water (100 mL), dried over Na_2CO_3, and evaporated to give analytically pure amine **8a** (0.90 g, 59%) as an oil: ^{1}H NMR δ 1.95 (quintet, *J* = 6.8 Hz, 2 H), 2.17 (s, 6 H), 2.21 (t, *J* = 6.9 Hz, 2 H), 4.31 (t, *J* = 6.8 Hz, 2 H), 7.19 (m, 2 H), 7.41 (m, 4 H), 8.06 (d, *J* = 7.7 Hz, 2 H); ^{13}C NMR δ 26.9, 40.5, 45.3 (2 C), 56.5, 108.7 (2 C), 118.7 (2 C), 120.2 (2 C), 122.7 (2 C), 125.5 (2 C), 140.4 (2 C). Picrate: mp 175 °C. Anal. Calcd for $C_{23}H_{23}N_5O_7$: C, 57.38; H, 4.82; N, 14.55. Found: C, 57.39; H, 4.76; N, 14.71.

9-[3-(Morpholin-4-yl)propyl]carbazole (8b). By the procedure described for **8a**, starting from **5b** (1.65 g, 4 mmol), amine **8b** (0.62 g, 53%) was obtained as a sticky oil: ^{1}H NMR δ 1.92 (quintet, *J* = 6.6 Hz, 2 H), 2.18 (t, *J* = 6.6 Hz, 2 H), 2.27 (m, 4 H), 3.66 (t, *J* = 4.7 Hz, 4 H), 4.29 (t, *J* = 6.6 Hz, 2 H), 7.19 (m, 2 H), 7.40 (m, 4 H), 8.05 (d, *J* = 7.7 Hz, 2 H); ^{13}C NMR δ 25.3, 40.2, 53.4 (2 C), 55.2, 66.9 (2 C), 108.7 (2 C), 118.7 (2 C), 120.2 (2 C), 122.7 (2 C), 125.4 (2 C), 140.4 (2 C). Anal. Calcd for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.51. Found: C, 77.34; H, 7.45; N, 9.22. Picrate: mp 207–208 °C.

9-[3-(Dimethylamino)-1-methylpropyl]carbazole (9a). An ethereal solution of CH_3MgI (15 mmol) was added to a solution of **5a** (1.85 g, 5 mmol) in toluene (20 mL). The obtained mixture was heated at reflux for 8 h, cooled to room temperature, and poured into ice–water. The mixture was extracted with ether (3 × 30 mL). The combined extracts were washed with water, dried over Na_2CO_3, and evaporated. The residue was subjected to column chromatography (ethyl acetate) to give pure **9a** (0.96 g, 76%) as an oil: ^{1}H NMR δ 1.69 (d, *J* = 7.1 Hz, 3 H), 2.00 (m, 2 H), 2.08 (s, 6 H), 2.12 (m, 1 H), 2.40 (m, 1 H), 4.90 (m, 1 H), 7.18 (ddd, *J* = 1.0, 6.9 and 8.0 Hz, 2 H), 7.39 (ddd, *J* = 1.2, 7.1 and 8.3 Hz, 2 H), 7.50 (d, *J* = 8.3 Hz, 2 H), 8.07 (dd, *J* = 0.8 and 7.7 Hz, 2 H); ^{13}C NMR δ 19.2, 32.8, 45.4 (2 C), 48.8, 56.5, 110.0 (2 C), 118.5 (2 C), 120.2 (2 C), 123.2 (2 C), 125.3 (2 C), 140.0 (2 C). Picrate: mp 170–172 °C. Anal. Calcd for $C_{24}H_{25}N_5O_7$: C, 58.18; H, 5.09; N, 14.13. Found: C, 58.17; H, 5.02; N, 14.19.

9-[3-(Morpholin-4-yl)-1-phenylpropyl]carbazole (9b). An ethereal solution of phenylmagnesium bromide (10 mL, 20 mmol) was added dropwise to a boiling solution of **5b** (2.07 g, 5 mmol) in toluene (20 mL) with simultaneous distillation of the ether. After the addition, the obtained solution was heated at reflux for 2 h, then cooled, poured into ice–water (100 g), and extracted with ether (3 × 50 mL). The combined extracts were washed with 10% NaOH followed by water, dried over Na_2CO_3, and evaporated. Column chromatography (toluene) of the residue afforded amine **9b** (1.35 g, 73%) as white needles: mp 93–94 °C; ^{1}H NMR δ 2.05 (m, 4 H), 2.33 (m, 2 H), 2.70 (m, 2 H), 3.62 (m, 4 H), 6.19 (dd, *J* = 6.1 and 9.0 Hz, 1 H), 7.17–7.38 (m, 11 H), 8.09 (d, *J* = 7.7 Hz, 2 H); ^{13}C NMR δ 27.7, 53.4 (2 C), 54.4, 54.9, 66.9 (2 C), 110.5 (2 C), 115.0, 119.0 (2 C), 120.2 (2 C), 123.2 (2 C), 125.4 (2 C), 125.9, 126.6,

127.3, 128.6, 138.9, 140.2 (2 C). Anal. Calcd for $C_{25}H_{26}N_2O$: C, 81.05; H, 7.07; N, 7.56. Found: C, 81.00; H, 7.10; N, 7.35.

(1*R,3*S**)- and (1*R**,3*R**)-9-[1-(Benzotriazol-2-yl)-3-(morpholin-4-yl)-3-phenylpropyl]carbazole (10 and 11) and (1*R**,3*S**) - and (1*R**,3*R**)-9-[1-(Benzotriazol-2-yl)-3-(morpholin-4-yl)- 3-phenylpropyl]carbazole (12 and 13).** *p*-Toluenesulfonic acid monohydrate (0.02 g, 0.1 mmol) was added to a mixture of **14**[24] (2.96 g, 10 mmol) and **4** (1.93 g, 10 mmol) preheated to 130 °C (oil bath). Heating at 130 °C was continued for an additional 10 min. After cooling to room temperature, the reaction mixture was dissolved in chloroform and subjected to column chromatography (chloroform). The first fraction gave the benzotriazol-2-yl isomer **10** (0.44 g, 9%) as a glassy material which crystallized from ether as colorless grains: mp 193–194 °C; ^{1}H NMR δ 2.06 (m, 2 H), 2.47 (m, 2 H), 3.23 (dd, J = 4.7 and 10.8 Hz, 1 H), 3.48 (ddd, J = 4.7, 9.3 and 15.4 Hz, 1 H), 3.66 (m, 4 H), 3.82 (ddd, J = 5.1, 10.9 and 15.6 Hz, 1 H), 7.02 (m, 2 H), 7.26 (m, 5 H), 7.36 (m, 2 H), 7.40 (m, 2 H), 7.85 (m, 5 H), 8.03 (d, J = 7.8 Hz, 2 H); ^{13}C NMR δ 33.2, 49.6 (2 C), 65.3, 67.4 (2 C), 72.5, 111.1 (2 C), 118.6 (2 C), 120.36 (2 C), 120.43 (2 C), 123.9 (2 C), 126.2 (2 C), 127.0 (2 C), 128.0, 128.3 (2 C), 128.8 (2 C), 135.9, 139.5 (2 C), 144.3 (2 C). Anal. Calcd for $C_{31}H_{29}N_5O$: C, 76.36; H, 5.93; N, 14.36. Found: C, 76.27; H, 5.98; N, 14.18.

The second fraction gave isomer **12** (2.04 g, 42%), colorless grains: mp 205 °C; ^{1}H NMR δ 2.16 (m, 2 H), 2.52 (m, 2 H), 3.32 (dd, J = 4.7 and 10.8 Hz, 1 H), 3.43 (ddd, J = 4.8, 9.5 and 14.4 Hz, 1 H), 3.73 (m, 4 H), 4.10 (ddd, J = 4.6, 10.9 and 14.6 Hz, 1 H), 6.99 (m, 3 H), 7.08 - 7.28 (m, 7 H), 7.37 (m, 2 H), 7.62 (m, 3 H), 7.99 (d, J = 8.1 Hz, 1 H), 8.02 (d, J = 8.3 Hz, 2 H); ^{13}C NMR δ 32.6, 49.4 (2 C), 64.8, 65.9, 67.2 (2 C), 109.5, 110.0 (2 C), 120.0, 120.3 (2 C), 120.5 (2 C), 123.7 (2 C), 124.3, 126.2 (2 C), 127.9 (2 C), 128.1 (2 C), 128.7 (2 C), 133.0, 135.8, 138.9 (2 C), 146.2. Anal. Calcd for $C_{31}H_{29}N_5O$: C, 76.36; H, 5.93; N, 14.36. Found: C, 76.31; H, 6.00; N, 13.98.

The third fraction gave isomer **11** (0.52 g, 11%) as colorless grain: mp 197–198 °C; ^{1}H NMR δ 2.31 (m, 4 H), 3.34 (dd, J = 7.1 and 8.1 Hz, 1 H), 3.57–3.76 (m, 6 H), 7.00 (m, 2 H), 7.27 (m, 5 H), 7.33 (m, 2 H), 7.45 (m, 2 H), 7.65 (t, J = 7.0 Hz, 1 H), 7.82 (m, 4 H), 8.05 (d, J = 7.8 Hz, 2 H); ^{13}C NMR δ 34.1, 50.0 (2 C), 66.1, 67.2 (2 C), 72.4, 111.0 (2 C), 118.5 (2 C), 120.2 (2 C), 120.3 (2 C), 123.9 (2 C), 126.1 (2 C), 126.7 (2 C), 128.0, 128.3 (2 C), 128.8 (2 C), 136.6, 139.4 (2 C), 144.2 (2 C). Anal. Calcd for $C_{31}H_{29}N_5O$: C, 76.36; H, 5.93; N, 14.36. Found: C, 76.36; H, 6.14; N, 14.14.

The fourth fraction appeared to be isomer **13** (1.27 g, 26%), colorless needles: mp 113–115 °C; ^{1}H NMR δ 2.12 (m, 2 H), 2.30 (m, 2 H), 3.52 (m, 4 H), 3.63 (m, 2 H), 3.92 (dt, J = 14.1 and 6.4 Hz, 1 H), 7.04 (m, 2 H), 7.10–7.30 (m, 8 H), 7.38 (dd, J = 7.3 and 8.1 Hz, 2 H), 7.50 (t, J = 6.7 Hz, 1 H), 7.55 (d, J = 8.3 Hz, 2 H), 7.96 (m, 1 H), 8.02 (d, J = 7.6 Hz, 2 H); ^{13}C NMR δ 33.1, 49.7 (2 C), 65.8, 65.9, 67.1 (2 C), 109.5, 110.0 (2 C), 120.0, 120.4 (2 C), 120.5 (2 C), 123.8 (2 C), 124.2, 126.3 (2 C), 127.8, 128.0, 128.3 (2 C), 129.0 (2 C), 133.0, 135.7, 138.9 (2 C), 146.2. Anal. Calcd for $C_{31}H_{29}N_5O$: C, 76.36; H, 5.93; N, 14.36. Found: C, 75.99; H, 5.94; N, 13.98.

9-[3-(Morpholin-4-yl)-3-phenylpropyl]carbazole (15). $LiAlH_4$ (0.228 g, 6 mmol) and $AlCl_3$ (0.266 g, 2 mmol) were added to a solution of product mixture **10–13** (0.97 g, 2 mmol) in THF (5 mL). The reaction mixture was stirred at reflux for 5 h. Progress of the reaction was monitored by TLC. The mixture was then poured into ice–water, extracted with chloroform (50 mL), washed with water, and dried over Na_2SO_4. Evaporation of the solvent gave 0.65 g of a crude glassy product (yield 58%) which was purified by column chromatography (chloroform) to give **15** (0.26 g, 35%): sticky oil; ^{1}H NMR δ 2.16 (m, 1 H), 2.28 (m, 2 H), 2.36 (m, 3 H), 3.34 (t, J = 7.3 Hz, 1 H), 3.64 (m, 4 H), 4.21 (t, J = 7.3 Hz, 2 H), 7.10–7.43 (m, 11 H), 8.05 (d, J = 7.8 Hz, 2 H); ^{13}C NMR δ 30.7, 40.2, 50.2 (2 C), 67.1, 67.3 (2 C), 108.8 (2 C), 118.9 (2 C), 120.4 (2 C), 123.0 (2 C), 125.7 (2 C), 127.8, 128.4 (2 C), 128.7 (2 C), 138.1, 140.4 (2 C). Anal. Calcd for $C_{25}H_{26}N_2O$: C, 81.05; H, 7.07; N, 7.56. Found: C, 80.84; H, 7.17; N, 7.24.

(1*R,3*S**)-9-[1-Methyl-3-(morpholin-4-yl)-3-phenylpropyl]carbazole (16a), (1*R**,3*R**)- 9-[1-Methyl-3-(morpholin-4-yl)-3-phenylpropyl]carbazole (17a), and [1-(Carbazol-9-yl)- 3-(morpholin- 4-yl)-3-phenyl]carbazole (18).** Starting from a mixture of **10–13** (4.87 g, 10 mmol) and methylmagnesium iodide (20 mmol), and following the procedure for the preparation of **5b**, a crude mixture of compounds **16a**, **17a**, and **18** was obtained. The mixture was subjected to column chromatography (chloroform). As the first fraction, compound **18** (0.80 g, 30%) was obtained, prisms (from ether): mp 206 °C; ^{1}H NMR δ 2.18 (m, 2 H), 2.42 (m, 2 H), 3.20–3.50 (m, 3 H), 3.69 (m, 4 H), 6.97 (m, 2 H), 7.16–7.28 (m, 7 H), 7.32 (td, J = 8.4 and 1.3 Hz, 2 H), 7.38 (td, J = 8.5 and 1.3 Hz, 2 H), 7.57 (dd, J = 4.5 and 8.6 Hz, 1 H), 7.60 (d, J = 8.3 Hz, 2 H), 7.65 (d, J = 8.3 Hz, 2 H), 8.07 (m, 4 H); ^{13}C NMR δ 34.9, 49.2 (2 C), 64.8, 65.7, 67.2 (2 C), 110.4 (2 C), 111.0 (2 C), 119.8 (2 C), 120.0 (2 C), 120.4 (4 C), 123.8 (2 C), 124.0 (2 C), 126.0 (2 C), 126.4 (2 C), 127.9, 128.2 (2 C), 128.7 (2 C), 135.9, 139.4 (2 C), 140.5 (2 C). Anal. Calcd for $C_{37}H_{33}N_3O$: C, 82.96; H, 6.21; N, 7.84. Found: C, 82.85; H, 6.49; N, 7.45.

The second fraction gave isomer **16a** (0.96 g, 25%) which when recrystallized from ethanol gave thin needles: mp 106–108 °C; ^{1}H NMR δ 1.69 (d, J = 6.8 Hz, 3 H), 2.04 (m, 2 H), 2.41 (m, 2 H), 2.52 (ddd, J = 6.1, 9.0 and 14.6 Hz, 1 H), 2.64 (ddd, J = 5.3, 9.5 and 14.6 Hz, 1 H), 3.15 (dd, J = 5.4 and 9.3 Hz, 1 H), 3.68 (m, 4 H), 5.11 (m, 1 H), 6.97 (m, 2 H), 7.22 (m, 5 H), 7.37 (m, 2 H), 7.45 (m, 2 H), 8.08 (d, J = 7.8 Hz, 2 H); ^{13}C NMR δ 19.3, 36.7, 47.9, 49.7 (2 C), 66.4, 67.3 (2 C), 110.4 (2 C), 118.6 (2 C), 120.2 (2 C), 123.4 (2 C), 125.2 (2 C), 127.4, 127.9 (2 C), 128.6 (2 C), 137.3, 139.8 (2 C). Anal. Calcd for $C_{26}H_{28}N_2O$: C, 81.21; H, 7.34; N, 7.29. Found: C, 81.23; H, 7.40; N, 7.13.

The third fraction gave compound **17a** (0.84 g, 22%), prisms (from ether): mp 105–106 °C; ^{1}H NMR δ 1.55 (d, J = 7.0 Hz, 3 H), 2.15 (m, 4 H), 2.29 (ddd, J = 5.6, 8.8 and 13.9 Hz, 1 H), 3.02 (ddd, J = 6.2, 9.1 and 13.9 Hz, 1 H), 3.12 (dd, J = 6.4 and 8.6 Hz, 1 H), 3.45 (m, 4 H), 4.67 (m, 1 H), 6.96 (m, 2 H) 7.10–7.25 (m 7 H), 7.32 (m, 2 H), 8.05 (d, J = 7.6 Hz, 2 H); ^{13}C NMR δ 19.4, 36.8, 48.3, 50.3 (2 C), 67.0 (2 C), 67.4, 109.0, 111.3, 118.6 (2 C), 120.2 (2 C), 124.0 (2 C), 125.2 (2 C), 127.5, 128.1 (2 C), 129.0 (2 C), 138.0, 139.0, 141.0. Anal. Calcd for $C_{26}H_{28}N_2O$: C, 81.21; H,7.34; N,7.29. Found: C, 81.53; H,7.43; N, 7.23.

(1*R,3*S**)-9-[1-Butyl-3-(morpholin-4-yl)-3-phenylpropyl]-carbazole (16b) and (1*R**,3*R**)-9-[1-Butyl-3-(morpholin-4-yl)-3-phenylpropyl]carbazole (17b).** Starting from a mixture of **10–13** (4.87 g, 10 mmol) and butylmagnesium iodide (20 mmol), and following the procedure for preparation of **5b**, a crude mixture of compounds **16b**, **17b**, and **18** was obtained. Column chromatography (chloroform) of the mixture gave **18** (0.92 g, 34%) as the first fraction. An oil obtained as the second fraction appeared to be **16b** (0.92 g, 22%): ^{1}H NMR δ 0.74 (t, J = 7.4 Hz, 3 H), 1.00 (m, 1 H), 1.20 (m, 3 H), 1.92 (m, 1 H), 2.03 (m, 2 H), 2.32 (m, 1 H), 2.40 (m, 2 H), 2.49 (ddd, J = 5.3, 9.3 and 14.5 Hz, 1 H), 2.63 (ddd, J = 4.7, 9.8 and 14.4 Hz, 1 H), 3.10 (dd, J = 5.3 and 10.0 Hz, 1 H), 3.66 (m, 4 H), 4.98 (m, 1 H), 6.90 (m, 2 H), 7.17 (m, 5 H), 7.30 (m, 1 H), 7.41 (m, 1 H), 7.47 (d, J = 8.6 Hz, 2 H), 8.07 (m, 2 H); ^{13}C NMR δ 13.8, 22.4, 28.9, 33.3, 35.2, 49.6 (2 C), 52.7, 66.0, 67.3 (2 C), 109.6, 111.4, 118.6 (2 C), 119.9, 120.4, 122.4, 124.1, 125.1, 125.3, 127.3, 127.9 (2 C), 128.6 (2 C), 137.2, 138.5, 142.0. Anal. Calcd for $C_{29}H_{34}N_2O$: C, 81.65; H, 8.03; N, 6.57. Found: C, 81.69; H, 8.02; N, 6.25.

The third fraction gave isomer **17b**, oil (1.05 g, 25%): ^{1}H NMR δ 0.68 (t, J = 7.2 Hz, 3 H), 0.85 (m, 1 H), 1.14 (m, 3 H), 1.86 (m, 1 H), 2.16 (m, 5 H), 2.35 (m, 1 H), 3.06 (m, 2 H), 3.47 (m, 4 H), 4.45 (m, 1 H), 6.79 (d, J = 8.1 Hz, 1 H), 6.98 (m, 2 H), 7.14–7.31 (m, 6 H), 7.42 (m, 1 H), 7.62 (d, J = 8.3 Hz, 1 H), 8.07 (d, J = 7.6 Hz, 1 H), 8.14 (d, J = 7.8 Hz, 1 H); ^{13}C NMR δ 13.8, 22.3, 28.6, 33.6, 35.5, 50.4 (2 C), 53.2, 67.0 (2 C), 67.5, 109.3, 111.4, 118.5, 118.6, 119.8, 120.5, 122.3, 124.0, 125.17, 125.25, 127.6 , 128.1 (2 C), 129.1 (2 C), 138.1, 138.5, 141.5. Anal. Calcd for $C_{29}H_{34}N_2O$: C, 81.65; H, 8.03; N, 6.57. Found: C, 81.73; H, 8.00; N, 6.29.

9-[1-(Carbazol-9-yl)-3-(dimethylamino)propyl]carbazole (20a). A mixture of **5a** (1.11 g, 3 mmol) and NaH (0.12 g, 5 mmol) was heated under nitrogen in an oil bath at 180–200 °C for 5 h. After cooling, the reaction mixture was transfered to a beaker with ice–water, neutralized with CH_3COOH, and extracted with chloroform (3 × 50 mL). The combined extracts were dried over Na_2CO_3 and evaporated to

give an oily product which was subjected to column chromatography (chloroform) to give pure **20a** (0.28 g, 46%) as a solid which was recrystallized from toluene: white prisms, mp 209–210 °C; ^{1}H NMR δ 2.15 (s, 6 H), 2.21 (t, J = 6.1 Hz, 2 H), 3.19 (q, J = 6.3 Hz, 2 H), 7.21 (t, J = 7.3 Hz, 4 H), 7.37 (dd, J = 7.2 and 8.4 Hz, 4 H), 7.56 (t, J = 6.8 Hz, 1 H), 7.70 (d, J = 8.3 Hz, 4 H), 8.06 (d, J = 7.8 Hz, 4 H); ^{13}C NMR δ 31.8, 45.3 (2 C), 55.0, 65.8, 110.9 (4 C), 119.7 (4 C), 120.3 (4 C), 123.8 (4 C), 126.1 (4 C), 140.1 (4 C). Anal. Calcd for $C_{29}H_{27}N_3$: C; 83.42, H; 6.52; N, 10.06. Found: C, 83.34; H, 6.50; N, 9.92.

9-[1-(Carbazol-9-yl)-3-(morpholin-4-yl)propyl]carbazole (20b). Compound **20b** (0.25 g, 33%) was obtained from a reaction of **5b** (1.25 g, 3 mmol) with NaH (0.12 g, 5 mmol) following the procedure above: white grains (MeOH), mp 104–105 °C; ^{1}H NMR δ 2.18 (m, 2 H), 2.25 (m, 4 H), 3.18 (q, J = 6.6 Hz, 2 H), 3.68 (t, J = 4.6 Hz, 4 H), 7.20 (m, 4 H), 7.36 (m, 4 H), 7.54 (t, J = 6.8 Hz, 1 H), 7.70 (d, J = 8.4 Hz, 4 H), 8.04 (d, J = 7.8 Hz, 4 H); ^{13}C NMR δ 30.1, 53.2 (2 C), 53.8, 65.7, 66.9 (2 C), 110.8 (4 C), 119.8 (4 C), 120.4 (4 C), 123.8 (4 C), 126.1 (4 C), 140.0 (4 C). Anal. Calcd for $C_{31}H_{29}N_3O$: C, 81.02; H, 6.36; N, 9.14. Found: C, 80.98; H, 6.40; N, 9.26.

***N*-[1-(Benzotriazol-1-yl)-3-(diethylamino)propyl]-*N*-methylacetamide (21a).** *p*-Toluenesulfonic acid (200 mg) was added to a mixture of *N*-vinylacetamide (5.00 g, 50 mmol) and *N*,*N*-diethyl-1*H*-benzotriazole-1-methanamine[24] (10.2 g, 50 mmol). The mixture was heated and stirred under nitrogen at 120 °C (oil bath) until homogenous, and then was kept at 110 °C for an additional 6 h to give **21a** of purity 91%, according to NMR. Column chromatography (ethyl acetate) of the crude product gave analytically pure **21a:** an oil; ^{1}H NMR δ 0.90 (t, J = 7.1 Hz, 6 H), 2.10 (s, 3 H), 2.46 (m, 6 H), 2.89 (m, 2 H), 2.97 (s, 3 H), 7.37 (m, 1 H), 7.48 (m, 1 H), 7.57 (dd, J = 5.0 and 8.1 Hz, 1 H), 7.84 (d, J = 8.3 Hz, 1 H), 8.02 (d, J = 8.3 Hz, 1 H); ^{13}C NMR δ 11.4 (2 C), 21.8, 28.2, 29.7, 46.6 (2 C), 48.0, 62.4, 110.6, 119.1, 124.0, 127.3, 132.8, 145.3, 171.0. Anal. Calcd for $C_{16}H_{25}N_5O$: C, 63.34; H, 8.31; N, 23.08. Found: C, 63.33; H, 8.38; N, 22.85.

***N*-[1-(Benzotriazol-1-yl)-3-(morpholin-4-yl)propyl]-*N*-methylacetamide (21b).** Following a procedure similar to the above and starting from **1b** (4.36 g, 20 mmol) and *N*-vinylacetamide (2.00 g, 20 mmol), **21b** was obtained of purity 95% (according to NMR). Column chromatography as above gave pure **21b** as an oil: ^{1}H NMR δ 2.11 (s, 3 H), 2.29 (m, 2 H), 2.44 (m, 4 H), 2.96 (m, 2 H), 2.97 (s, 3 H), 3.64 (m, 4 H), 7.38 (m, 1 H), 7.50 (dd, J = 7.5 and 8.1 Hz, 1 H), 7.59 (dd, J = 6.6 and 8.1 Hz, 1 H), 7.81 (d, J = 8.3 Hz, 1 H), 8.03 (d, J = 8.3 Hz, 1 H). ^{13}C NMR δ 21.7, 27.3, 29.6, 53.1 (2 C), 53.7, 62.2, 66.4 (2 C), 110.3, 119.0, 124.0, 127.3, 132.6, 145.0, 171.0. Anal. Calcd for $C_{16}H_{23}N_5O_2$: C, 60.55; H, 7.30; N, 22.07. Found: C, 60.55; H, 7.57; N, 21.68.

***N*-Methyl-*N*,*N*′,*N*′-triethyl-1,3-propanediamine (22a).** To a stirred solution of **21a** (4.1 g, 13 mmol) in dry THF was added $LiAlH_4$ (0.80 g, 20 mmol) portionwise. The reaction mixture was refluxed then for 1 h. After cooling, the mixture was poured onto ice-cold 20% KOH and extracted with Et_2O (3 × 50 mL). The combined extracts were dried over NaOH and evaporated under reduced pressure to give pure **22a** (1.46 g, 65%): oil; ^{1}H NMR δ 1.03 (t, J = 7.1 Hz, 6 H), 1.06 (t, J = 7.1 Hz, 3 H), 1.66 (m, 2 H), 2.23 (s, 3 H), 2.36 (t, J = 7.8 Hz, 2 H), 2.43 (q, J = 7.0 Hz, 2 H), 2.47 (t, J = 7.4 Hz, 2 H), 2.55 (q, J = 7.1 Hz, 4 H). ^{13}C NMR δ 11.3 (2 C), 12.0, 24.4, 41.4, 46.6 (2 C), 50.8, 51.1, 55.3. Picrate: yellow needles, mp 164–166 °C. Anal. Calcd for $C_{22}H_{30}N_8O_{14}$: C, 41.91; H, 4.80; N, 17.77. Found: C, 41.62; H, 4.69; N, 17.49.

4-[3-(*N*-Ethyl-*N*-methylamino)propyl]morpholine (22b). $LiAlH_4$ (0.76 g, 20 mmol) was added portionwise to a solution of **21b** (3.65 g, 10 mmol) in dry THF (50 mL), and the solution was stirred under nitrogen. After the addition was accomplished, the reaction mixture was stirred at reflux for 2 h (monitored by TLC), cooled, poured onto ice-cold 20% KOH, and extracted with Et_2O (3 × 50 mL). The combined extracts were dried over NaOH and evaporated under reduced pressure to give pure **22b** (1.66 g, 89%): oil; ^{1}H NMR δ 1.05 (t, J = 7.2 Hz, 3 H), 1.67 (m, 2 H), 2.21 (s, 3 H), 2.33 - 2.46 (m, 10 H), 3.72 (t, J = 4.7 Hz, 4 H); ^{13}C NMR δ 12.1, 24.3, 41.5, 51.2, 53.6 (2 C), 55.1, 57.0, 66.8 (2 C). Dipicrate: mp 139–142 °C. Anal. Calcd for $C_{22}H_{28}N_8O_{15}$: C, 41.00; H, 4.38; N, 17.39. Found: C, 40.99; H, 4.40; N, 17.24.

***N*-[1-(Benzotriazol-1-yl)-3-(morpholin-4-yl)-3-phenylpropyl]-*N*-methylacetamide (23) and Its Bt-2 Isomer (24).** A mixture of **14** (2.95 g, 10 mmol) and *N*-methyl-*N*-vinylacetamide (1.0 g, 10 mmol) was heated at 110 °C (oil bath) under nitrogen for 10 min before *p*-toluenesulfonic acid (20 mg) was added and heating at 110 °C was continued for a further 30 min. After cooling, the crude glassy product was dissolved in $CHCl_3$ and washed with 10% Na_2CO_3 followed by water. Separation of the organic layer, drying over $MgSO_4$, and evaporation of the solvent gave a pure mixture of four isomers, two diastereomers of **23** and two of **24**. HRMS calcd for $C_{22}H_{27}N_5O_2$ (M^+): 394.2243, found 394.2206.

4-[3-(*N*-Ethyl-*N*-methylamino)-1-phenylpropyl]morpholine (25). $LiAlH_4$ (0.38 g, 10 mmol) was added portionwise to a solution of **23** and **24** (3.93 g, 10 mmol) in dry THF (50 mL), the solution was stirred under nitrogen at 25 °C, and the obtained mixture was heated at reflux for 1 h. After cooling and workup (procedure as for **22**), pure oily product (2.05 g, 78%) was obtained: ^{1}H NMR δ 0.97 (t, J = 7.3 Hz, 3 H), 1.85 (m, 1 H), 2.10 (m, 1 H), 2.16 (s, 3 H), 2.25 (m, 1 H), 2.30 (m, 1 H), 2.34 (m, 2 H), 2.40 (m, 4 H), 3.29 (dd, J = 4.6 and 9.1 Hz, 1 H), 3.65 (m, 4 H), 7.28 (m, 5 H); ^{13}C NMR δ 12.1, 29.9, 41.6, 50.9 (2 C), 51.4, 54.1, 67.2 (2 C), 68.6, 127.2, 128.1 (2 C), 128.5 (2 C), 139.9. Dipicrate (from MeOH): yellow needles, mp 174–176 °C. Anal. Calcd for $C_{28}H_{32}N_8O_{15}$: C, 46.67; H, 4.48; N, 15.55. Found: C, 46.63; H, 4.45; N, 15.38.

1-[1-(Benzotriazol-1-yl)-3-(dibenzylamino)propyl]-2-pyrrolidinone (27). To a mixture of **26**[24] (9.84 g, 30 mmol) and *N*-vinyl-2-pyrrolidinone (3.33 g, 30 mmol) preheated to 140 °C (oil bath) was added *p*-toluenesulfonic acid (60 mg, 0.3 mmol), and heating at 140 °C was continued for an additional 20 min. After cooling, the crude glassy product was triturated with Et_2O to give crystalline **27** (6.35 g, 48%). An analytical sample was prepared by recrystallization from EtOH: needles, mp 150 °C; ^{1}H NMR δ 1.70 (quintet, J = 7.6 Hz, 2 H), 2.19 (m, 2 H), 2.52 (m, 2 H), 2.56 (m, 1 H), 2.86 (m, 1 H), 2.98 (m, 1 H), 3.30 (m, 1 H), 3.42 (d, J = 13.3 Hz, 2 H), 3.65 (d, J = 13.2 Hz, 2 H), 7.00 (t, J = 7.1 Hz, 1 H), 7.16 (m, 6 H), 7.30 (d, J = 7.8 Hz, 4 H), 7.35 (m, 1 H), 7.48 (m, 1 H), 7.83 (dd, J = 0.8 and 8.4 Hz, 1 H), 7.99 (dd, J = 0.8 and 8.3 Hz, 1 H); ^{13}C NMR δ 17.6, 28.2, 30.7, 41.9, 48.6, 58.7 (2 C), 60.8, 110.7, 119.4, 124.2, 126.8 (2 C), 127.6, 128.1 (4 C), 128.8 (4 C), 132.7, 138.9 (2 C), 145.6, 175.1. Anal. Calcd for $C_{27}H_{29}N_5O$: C, 73.78; H, 6.65; N, 15.93. Found: C, 73.83; H, 6.68, N; 16.01.

1-[3-(Dibenzylamino)propyl]pyrrolidine (28). To a solution of **27** (2.30 g, 5 mmol) in dry THF stirred under nitrogen was added $LiAlH_4$ (0.76 g, 20 mmol) portionwise. The reaction mixture was then refluxed for 3 h (monitored by TLC), cooled, and worked up as described for **22**. Evaporation of the solvent gave pure **28** (1.32 g, 84%): oil; ^{1}H NMR δ 1.72 (m, 6 H), 2.44 (m, 8 H), 3.55 (s, 4 H), 7.10–7.40 (m, 10 H); ^{13}C NMR δ 23.4 (2 C), 26.6, 51.7, 54.2 (2 C), 54.5, 58.2 (2 C), 126.7, 128.1 (4 C), 128.7 (4 C), 139.9 (2 C). Dipicrate (from MeOH), mp 193–195 °C. Anal. Calcd for $C_{33}H_{34}N_8O_{14}$: C, 51.70; H, 4.47; N, 14.62. Found: C, 51.40; H, 4.33; N, 14.67.

4-[*N*-(3-(Dibenzylamino)-1-phenylpropyl)amino]-1-phenyl-1-butanone (30). To a THF solution of **27** (4.40 g, 10 mmol) kept under nitrogen and in an ice–water bath was added PhMgBr (50 mmol in Et_2O) portionwise within 30 min. The reaction mixture was then stirred at room temperature for 1 h, poured into ice–water, acidified with acetic acid (pH 6), and extracted as fast as possible with ether (3 × 50 mL). The combined extracts were washed with ice-cold 10% NaOH, followed by water, dried over Na_2CO_3, and evaporated to give **30** as yellowish oil which became dark green when exposed to air. Crude **30** (by NMR, contaminated with biphenyl) was subjected to column chromatography (toluene/Et_3N 9:1) to give pure **30** (3.65 g, 76%): ^{1}H NMR δ 1.72–1.90 (m, 3 H), 2.15 (m, 1 H), 2.30–2.48 (m, 4 H), 2.91 (m, 2 H), 3.40–3.63 (m, 6 H), 7.16–7.44 (m, 18 H), 7.90 (d, J = 7.0 Hz, 2 H); ^{13}C NMR δ 24.8, 35.5, 36.4, 47.0, 50.7, 58.4 (2 C), 61.9, 126.7, 126.8 (2 C), 127.0 (2 C), 127.96 (2 C), 128.15 (4 C), 128.18 (2 C), 128.4 (2 C), 128.7, 128.9 (4 C), 132.8 (2 C), 139.5, 144.7, 200.0 (C=O). Dipicrate, orange grains, mp 102–105 °C. Anal. Calcd for

$C_{45}H_{42}N_8O_{15}$: C, 57.81; H, 4.53; N, 11.99. Found: C, 57.46; H, 4.29; N, 12.33.

1-[α-(Dibenzylamino)benzyl]benzotriazole (31). Benzaldehyde (10.6 g, 100 mmol) followed by dibenzylamine (19.7 g, 100 mmol) was added slowly to a suspension of benzotriazole (11.91 g, 100 mmol) in a mixture of MeOH and Et_2O (50 mL + 50 mL) . The mixture became homogenous but very soon crystals started to precipitate. After storing at 0 °C for 6 h, the precipitate was separated and dried in a vacuum oven to give **31** (35.6 g, 89%), by NMR a mixture of Bt-1 and Bt-2 isomers in a molar ratio of 3:1: prisms, mp 153 °C; ^{1}H NMR (predominant isomer) δ 3.49 (d, J = 14.2 Hz, 2 H), 4.25 (d, J = 14.2 Hz, 2 H), 7.27−7.38 (m, 17 H), 8.17 (d, J = 7.8 Hz, 1 H). Anal. Calcd for $C_{27}H_{24}N_4$: C, 80.17; H, 5.98; N, 13.85. Found: C, 79.95, H, 6.02; N, 13.57.

1-[1-(Benzotriazol-1-yl)-3-(dibenzylamino)-3-phenylpropyl]-2-pyrrolidinone (32). A mixture of **31** (4.04 g, 10 mmol) and *N*-vinyl-2-pyrrolidinone (1.2g , 10 mmol) was preheated to 120 °C for 10 min. *p*-Toluenesulfonic acid (20 mg, 0.1 mmol) was added and heating was continued for 30 min to give a crude mixture of **32**, its diastereomer (minor quantities), and the corresponding Bt-2 isomers (by NMR). An analytical sample was prepared by column chromatography with (i) chloroform and (ii) ethyl acetate as the eluents to give pure **32** (2.45 g, 46%): white needles (after trituration with ether), mp 153 °C; ^{1}H NMR δ 1.74 (m, 2 H), 2.21 (m, 2 H), 2.87 (m, 1 H), 3.03 (d, J = 13.3 Hz, 2 H), 3.04 (m, 1 H), 3.35 (m, 2 H), 3.74 (dd, J = 7.1 and 7.7 Hz, 1 H), 3.90 (d, J = 13.4 Hz, 2 H), 7.09 (m, 6 H), 7.20−7.51 (m, 12 H), 7.76 (d, J = 8.3 Hz, 1 H), 7.99 (d, J = 8.3 Hz, 1 H); ^{13}C NMR δ 17.6, 30.6, 33.6, 41.9, 53.9 (2 C), 57.9, 61.0, 110.8, 119.6, 124.2, 126.9 (2 C), 127.7, 127.8, 128.2 (4 C), 128.3 (2 C), 128.9 (4 C), 129.2 (2 C), 132.8, 136.0, 139.3 (2 C), 145.9, 175.0. Anal. Calcd for $C_{33}H_{33}N_5O$: C, 76.87; H, 6.45; N, 13.58. Found: C, 76.78; H, 6.49; N, 13.64.

1-[3-(Dibenzylamino)-3-phenylpropyl]pyrrolidine (33). Reduction of **32** (5.15 g, 10 mmol) with $LiAlH_4$ (1.90 g, 50 mmol) in a procedure analogous to **28**, and column chromatography (ethyl acetate/MeOH 4:1) of the crude product, gave pure **33** as an oil (2.75 g, 72%): ^{1}H NMR δ 1.72 (m, 4 H), 2.05 (m, 1 H), 2.27 (m, 2 H), 2.45 (m, 4 H), 2.62 (m, 1 H), 3.15 (d, J = 13.9 Hz, 2 H), 3.74 (m, 1 H), 3.81 (d, J = 13.9 Hz, 2 H), 7.19 −7.39 (m, 15 H); ^{13}C NMR δ 23.3 (2 C), 30.6, 53.5 (2 C), 54.07, 54.13 (2 C), 60.3, 126.6 (2 C), 127.0, 127.9 (2 C), 128.1 (4 C), 128.6 (4 C), 128.9 (2 C), 138.5, 140.2 (2 C). Anal. Calcd for $C_{27}H_{32}N_2$: C, 84.33; H, 8.39; N, 7.28. Found: C, 84.62; H, 8.56; N, 7.22. Dipicrate (from MeOH): yellow needles, mp 170−171 °C.

***N,N*-Bis-[3-(benzotriazol-1-yl)-3-(2-oxopyrrolidin-2-1-yl)propyl]ethylamine (35).** A mixture of **34** (3.07 g, 10 mmol) and *N*-vinyl-2-pyrrolidone (2.42 g, 22 mmol) was stirred at 120 °C (oil bath) until melted. *p*-Toluenesulfonic acid (20 mg, 0.1 mmol) was added and heating (under nitrogen) was continued for 5 h. After cooling, the crude product was subjected to column chromatography (ethyl acetate) to give the bis-adduct (glassy material) as a mixture of Bt-1 and Bt-2 isomers (3.50 g, 66%). One small fraction appeared to be pure Bt-1 isomer **35**: ^{1}H NMR δ 0.83 (t, J = 6.9 Hz, 3 H), 1.86 (m, 2 H), 2.00 (m, 2 H), 2.17−2.50 (m, 12 H), 2.78 (m, 2 H), 3.13 (m, 2 H), 3.52 (m, 2 H), 6.93 (dd, J = 5.4 and 8.1 Hz, 2 H), 7.35 (m, 2 H), 7.47 (m, 2 H), 7.86 (d, J = 8.3 Hz, 2 H), 8.02 (d, J = 8.3 Hz, 2 H); ^{13}C NMR δ 11.6, 17.8 (2 C), 28.9 (2 C), 30.9 (2 C), 42.3 (2 C), 47.7, 49.3 (2 C), 61.3 (2 C), 110.6 (2 C), 119.4 (2 C), 124.4 (2 C), 127.8 (2 C), 132.9 (2 C), 145.6 (2 C), 175.3 (2 C). HRMS calcd for $C_{28}H_{35}N_9O_2$ (M^+): 530.299, found 530.300.

***N,N*-Bis[3-(pyrrolidin-2-yl)propyl]ethylamine (36).** Following the procedure given for reduction of **28** and starting from **35** (5.29 g , 10 mmol) and $LiAlH_4$ (1.52g, 40 mmol), pure **36** was obtained as an oil (2.30 g, 85%) : ^{1}H NMR δ 1.00 (t, J = 7.1 Hz, 3 H), 1.65 (m, 4 H), 1.77 (m, 8 H), 2.48 (m, 18 H); ^{13}C NMR δ 11.0, 22.8 (4 C), 26.0 (2 C), 46.8, 51.0 (2 C), 53.6 (4 C), 54.2 (2 C). Tripicrate (from THF/H_2O 4:1), mp 111−112 °C. Anal. Calcd for $C_{34}H_{42}N_{12}O_{21}$: C, 42.77; H, 4.43; N, 17.60. Found: C, 42.77; H, 4.33; N, 17.66.

1,3-Bis[(benzotriazolyl)methyl]hexahydropyrimidine (37). A mixture of benzotriazole (11.93 g, 100 mmol), 37% formaldehyde (10 mL,) and 1,3-propanediamine (4.0 mL, 50 mmol) in ethanol was stirred at room temperature until a white precipitate was formed and then left overnight at 20 °C. The solid was separated by filtration, washed with ether, and dried to give fine needles, mp 128−133 °C (14.5 g, 83%) as a mixture of Bt-1 and Bt-2 isomers of **37**: ^{1}H NMR δ 1.72 (m, 2 H), 2.74 (t, J = 5.4 Hz, 4 H), 3.67 (s, 2 H), 5.51 (s, 4 H), 7.36 (m, 2 H), 7.48 (m, 2 H), 7.58 (d, J = 8.3 Hz, 2 H), 8.04 (d, J = 8.3 Hz, 2 H); ^{13}C NMR δ 22.3, 49.2 (2 C), 66.7 (2 C), 70.2, 109.9 (2 C), 119.8 (2 C), 124.1 (2 C), 127.7 (2 C), 133.4 (2 C), 145.9 (2 C). Anal. Calcd for $C_{18}H_{20}N_8$: C, 62.05; H, 5.79; N, 32.16. Found: C, 61.95; H, 5.72; N, 32.38.

1,3-Bis[3-(benzotriazol-1-yl)-3-(2-oxopyrrolidin-1-yl)-propyl]hexahydropyrimidine (38). A mixture of **37** (6.96 g, 20 mmol) and *N*-vinyl-2-pyrrolidinone (4.84 g, 44 mmol) was heated at 130 °C (oil bath) under nitrogen for 5 min. *p*-Toluenesulfonic acid (0.40 g, 0.2 mmol) was added and the reaction mixture was heated for an additional 1 h. Column chromatography (ethyl acetate) gave an analytical sample of a mixture of isomeric products as glassy material containing about 75% of the Bt-1 isomer **38**: ^{13}C NMR δ 17.6 (2 C), 21.9, 28.5 (2 C), 30.7 (2 C), 42.3 (2 C), 49.6 (2 C), 52.2 (2 C), 61.3 (2 C), 75.1, 110.4 (2 C), 119.3 (2 C), 124.2 (2 C), 127.6 (2 C), 132.8 (2 C), 145.4 (2 C), 175.2 (2 C). HRMS calcd for $C_{30}H_{38}N_{10}O_2$ (M^+): 570.318, found 570.313.

1,3-Bis[3-(pyrrolidin-1-yl)propyl]hexahydropyrimidine (39). Starting from **38** (5.30 g, 10 mmol) and $LiAlH_4$ (1.52 g, 40 mmol) and following the procedure for **28**, pure **39** (2.25 g, %) was obtained as an yellowish oil: ^{1}H NMR δ 1.60−1.85 (m, 14 H), 2.30−2.60 (m, 20 H), 3.10 (m, 2 H); ^{13}C NMR δ 23.2 (4 C), 23.6, 26.6 (2 C), 52.3 (2 C), 53.5 (2 C), 54.1 (4 C), 54.6 (2 C), 76.5. Tetrapicrate, mp 123−125 °C. Anal. Calcd for $C_{42}H_{48}N_{16}O_{28}$: C, 41.12; H, 3.69; N, 18.06. Found: C, 41.18; H, 3.95; N, 18.30.

***N,N,N'N'*-Tetrakis[(benzotriazol-1-yl)methyl]hexanediamine (40).** 1,6-Hexanediamine (2.91 g, 25 mmol) was added to a stirred suspension of 1-(hydroxymethyl)benzotriazole (15.0 g, 100 mmol) in 95% ethanol. The reaction mixture quickly became transparent and a new precipitate started to form. After cooling at 0 °C for a few hours, the white precipitate was separated, washed with ether, and dried to give **40** (14.1 g, 88%) as white powder, highly insoluble in most organic solvents, a complex mixture of Bt-1 and Bt-2 isomers. Recrystallization from 95% ethanol gave small analytical sample, containing 76% of the tetra Bt-1 isomer (**40**): mp 145−148 °C: ^{1}H NMR δ 0.67 (m, 4 H), 1.09 (m, 4 H), 2.55 (m, 4 H), 5.81 (s, 8 H), 7.38 (t, J = 7.6 Hz, 4 H), 7.53 (t, J = 7.9 Hz, 4 H), 7.90 (d, J = 8.3 Hz, 4 H), 8.03 (d, J = 8.3 Hz, 4 H); ^{13}C NMR δ 25.2 (2 C), 26.1 (2 C), 49.0 (2 C), 64.8 (4 C), 110.6 (4 C), 118.8 (4 C), 123.6 (4 C), 127.0 (4 C), 132.7 (4 C), 145.0 (4 C). Anal. Calcd for $C_{34}H_{36}N_{14}$: C, 63.73; H, 5.66; N, 30.60. Found: C, 63.65; H, 5.77; N, 30.83.

***N,N,N'N'*-Tetrakis[3-(pyrrolidin-1-yl)propyl]hexanediamine (42).** A mixture of **40** (6.40 g, 10 mmol) and *N*-vinyl-2-pyrrolidinone (4.89 g, 44 mmol) was heated under nitrogen at 130 °C (oil bath) for 5 min. *p*-Toluenesulfonic acid (0.10 g, 0.5 mmol) was added and the heating was continued for 1 h to give crude product **41**. The crude product mixture (11.0 g, 10 mmol) was reduced with $LiAlH_4$ (3.85 g, 100 mmol) in dry dioxane, following a procedure given for **28** to give crude **42** as an oil (4.30 g, 77%). An analytical sample was purified by column chromatography (hexane/Et_3N 9:1): ^{1}H NMR δ 1.27 (m, 4 H), 1.43 (m, 4 H), 1.66 (m, 8 H), 1.77 (m, 16 H), 2.35−2.70 (m, 36 H); ^{13}C NMR δ 23.3 (8 C), 26.6 (4 C), 27.0 (2 C), 27.6 (2 C), 52.2 (4 C), 54.2 (8 C), 54.7 (4 C), 57.6 (2 C). Hexapicrate (EtOH), mp 82−85 °C. Anal. Calcd for $C_{70}H_{86}N_{24}O_{42}$: C, 43.44; H, 4.48; N, 17.37. Found: C, 43.44; H, 4.18; N, 17.31.

Supplementary Material Available: Full ^{1}H and ^{13}C NMR spectral data with resoance assignments for the prepared compounds (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.