Additions of 1-(Aminomethyl)benzotriazoles to Enamines, Enamides, and Vinyl Ethers: Novel Routes to 1,3-Diamines and Tetrahydroquinolines

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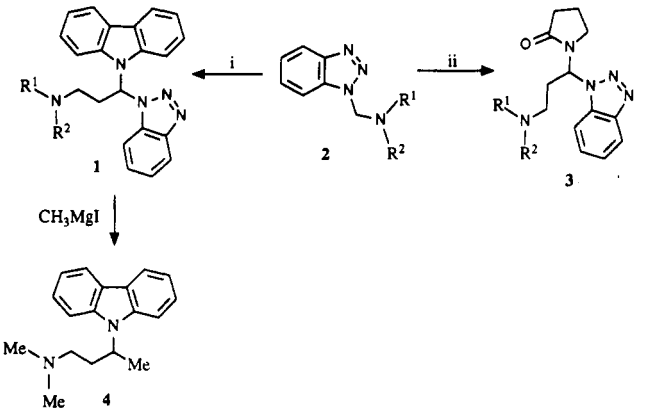
Received November 2, 1992

Summary: New methods for the synthesis of 1,3-diamines and of 4-substituted tetrahydroquinolines are described in which the key step is the addition of the condensation products derived from amines, aldehydes, and benzotriazole to enamines, enamides, and vinyl ethers.

1-(α-Alkoxyalkyl)- and 1-(α-aminoalkyl)benzotriazoles in solution undergo partial ionization giving benzotriazolyl anion and the corresponding oxocarbenium or iminium cation. Trapping these oxocarbenium or iminium cations with organometallic reagents has given many new synthetic methods, e.g., for ethers[1-3] and various amino compounds.[4] Recently, we have reported that oxocarbenium and iminium cations produced in this way can also be trapped by enol ethers giving the corresponding *N*-(1,3-dialkoxyalkyl)-[5] and *N*-(1-alkoxy-3-aminoalkyl)benzotriazoles,[6] useful intermediates for the preparation of 1,3-diethers and 3-amino ethers, respectively. We now report that enamines and enamides, as exemplified by 9-vinylcarbazole and 1-vinyl-2-pyrrolidinone, can also trap these oxocarbenium and iminium cations to give adducts of considerable synthetic potential.

When *N*-[(dimethylamino)methyl]benzotriazole (**2a**) was heated with an equimolecular quantity of 9-vinylcarbazole under nitrogen at 130 °C without any solvent or catalyst for 24 h, it gave *N*,*N*-dimethyl-3-(carbazol-9-yl)-3-(benzotriazol-*N*-yl)propanamine (**1a**) in 75% yield. Similar treatment with 1-vinyl-2-pyrrolidone gave *N*,*N*-dimethyl-3-(benzotriazol-*N*-yl)-3-(2-oxopyrrolid-1-yl)propanamine (**3a**) in 64% yield (Scheme I). The reactions are general for *N*-[(dialkylamino)methyl]benzotriazoles: other examples are shown in Table I. Acidic catalysts (H_2SO_4, *p*-$MeC_6H_4SO_3H$) decreased the required reaction temperature and time but gave less pure products. The crude products, represented in Scheme I as the benzotriazol-1-yl isomers, also contained small amounts of the corresponding benzotriazol-2-yl isomers. Recrystallization (solids) or column chromatography (oils) yielded pure regioisomers **1** and **3**, but as with other benzotriazole intermediates this is not required for their further transformations.[4] The synthetic potential of compounds of type **1** and **3** is illustrated by the ready substitution of the benzotriazolyl group in **1a** on treatment with methyl Grignard reagent to give **4** in 76% yield. We have already reported the substitution of the benzotriazolyl moiety by organometallic reagents and thiols in the simple adducts of benzotriazole with 9-vinylcarbazole and 1-vinyl-2-pyrrolidone.[7]

Scheme I[a]



[a] Key: (i) 9-vinylcarbazole; (ii) 1-vinyl-2-pyrrolidinone.

Table I. Adducts 1 and 3

compd	R^1	R^2	mp (°C)	isolated yield (%)
1a	CH_3	CH_3	124–5	75
1b	$CH_2CH_2OCH_2CH_2$		145–50	43
3a	CH_3	CH_3	75–7	64
3b	C_2H_5	C_2H_5	oil	85
3c	$CH_2CH_2CH_2CH_2$		oil	89

Table II. Tetrahydroquinolines 11, 13, 14, and 15

compd	R	mp (°C)	isolated yield (%)
11	CH_3	208–10	53
13a	CH_3	77–8	90
13b	$PhCH_2$	oil	92
13c	H	oil	65
14		125–6	32
15		oil	79

Using aniline derivatives (**6**) in reactions of this type gave 4-substituted tetrahydropyridines **11** and **13** (Scheme II). When an equimolar mixture of 1-[(*N*-methylanilino)-methyl]benzotriazole (**6a**) and 9-vinylcarbazole was heated at 75 °C for 150 min with 1 mol % of *p*-toluenesulfonic acid, 1-methyl-4-(carbazol-9-yl)-1,2,3,4-tetrahydroquinoline (**11**) was produced in 53% yield. Preheating of a mixture of **6a** and 1-vinyl-2-pyrrolidinone to 120 °C and addition of the catalyst (as above) caused an exothermic reaction to give the 4-pyrrolidone analog (**13a**) in 90% yield (Table II).

The first steps in the reaction sequence leading to tetrahydroquinolines **11** and **13** involve ionization of **6** into **9** and addition of iminium ion **9** to 9-vinylcarbazole or 1-vinyl-2-pyrrolidinone to form new iminium cations **8** and **10**. These can then re-add the benzotriazole cation to give adducts **5** and **7** which are of type **2** (or **4**). However, adducts **5** and **7** are in reversible equilibrium with **8** and **10**, and now an irreversible intramolecular electrophilic attack of the iminium cation on an electron rich ortho carbon atom of the aniline ring leads to the tetrahydro-

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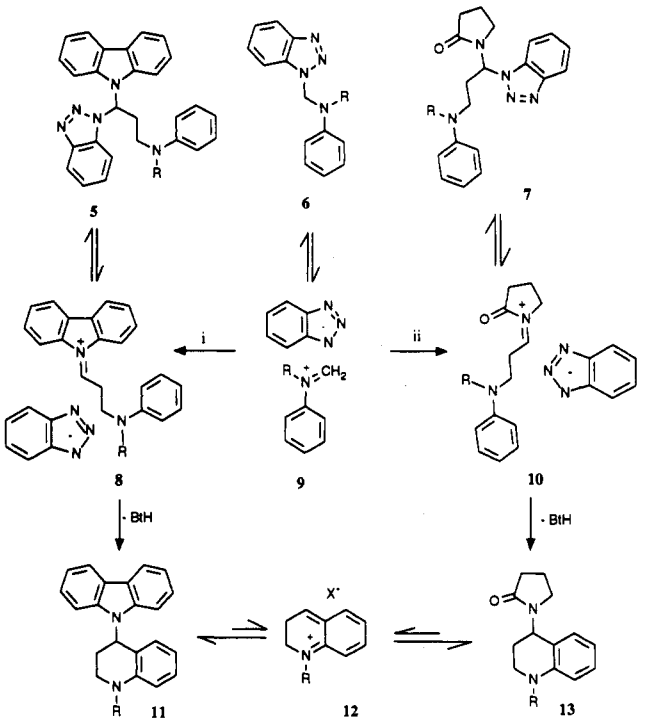
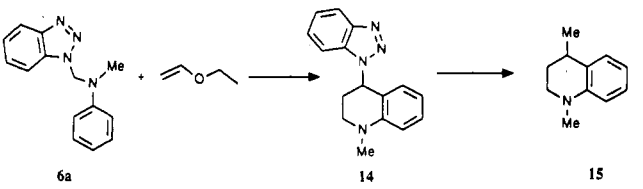
Scheme II[a]



[a] Key: (i) 9-vinylcarbazole; (ii) 1-vinyl-2-pyrrolidinone; BtH–benzotriazole.

quinolines **11** and **13**. Again, these reactions are general and further examples are given in Table II. Previously reported reactions of *N*-(methoxymethyl)-*N*-methylaniline with alkenes, enol ethers, and enamines giving the corresponding 4-substituted 1-methyl-1,2,3,4-tetrahydroquinolines[8] are of a similar type but they are synthetically less useful due to the low stability of the starting material and its preparation by an electrochemical method[8,9] which is not available in many organic chemical laboratories.

Scheme III



The corresponding reaction of **6a** with ethyl vinyl ether produced 1-methyl-4-(benzotriazol-*N*-yl)-1,2,3,4-tetrahydroquinoline (**14**) (Scheme III) demonstrating that, under acidic conditions, the protonated ethoxy substituent is a better leaving group than the benzotriazolyl moiety. Location of the carbazole, pyrrolidinone, and benzotriazolyl groups in **11**, **13**, and **14** in an active aminobenzyl position makes possible its substitution with other nucleophiles via intermediate of type **12** opening a new gate to various 4-substituted tetrahydroquinolines. As an illustration of this synthetic potential, we converted **14** smoothly into 1,4-dimethyl-1,2,3,4-tetrahydroquinoline (**15**)[10] in 79% yield by reaction with methylmagnesium iodide.

Supplementary Material Available: General procedures for compounds **1**, **3**, **11**, and **13**, procedures for **4**, **14**, and **15**, and full ^1H and ^{13}C NMR spectral assignments based on 2D ^1H–^1H (COSY) and ^1H–^{13}C (HETCOR) correlations (5 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.

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