Tetrahedron Letters, Vol. 33, No. 33, pp. 4763-4766, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Synthesis of Vicinal Diamines by SmI_2-Promoted Reduction of N-(N',N'-Dialkylaminoalkyl)benzotriazoles

José M. Aurrecoechea* and Alvaro Fernández-Acebes

Departamento de Química Orgánica. Facultad de Ciencias. Universidad del País Vasco. Apartado 644. 48080 Bilbao. Spain.

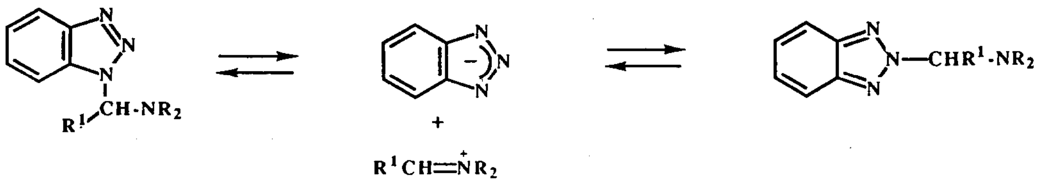
Abstract: N-(N',N'-Dialkylaminoalkyl)benzotriazoles, derived from aldehydes and secondary amines, react with one equivalent of samarium iodide (SmI_2), under mild conditions, to afford tertiary vicinal diamines, as a result of C-C coupling between two dialkylaminoalkyl moieties.

Vicinal diamines have drawn considerable attention in recent years, mainly due to their applications as ligands in enantioselective processes. These have included the dihydroxylation[1-4] and epoxidation[5] of olefins, as well as Diels-Alder[6] and aldol[6,7] reactions.

While a number of methods have been developed[8-17] to synthesize this important class of compounds[18], many suffer from limitations[19]. Particularly scarce in the literature are methods that directly afford tertiary diamines[20].

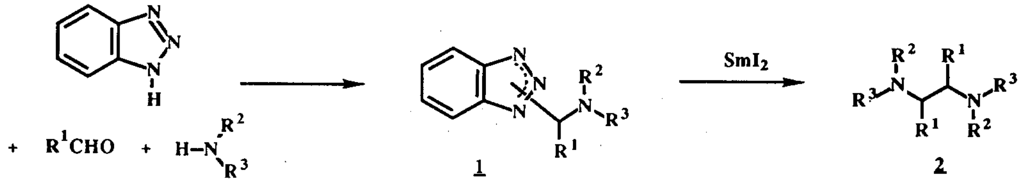
The C-C coupling of two alkylamino fragments represents a simple, convenient strategy to form vicinal diamines. Thus, imine derivatives were reported to yield vicinal diamines[21,22] when treated with the one electron reducing agent SmI_2[23]. However, the method is not suitable for the direct preparation of tertiary diamines and requires relatively high temperatures (refluxing THF) and excess SmI_2, these latter observations probably being a reflection of the relatively poor electron-accepting ability of the imine functional group. Iminium cations would be expected to undergo the reaction much more easily and allow the preparation of tertiary diamines.

N-(N',N'-Dialkylaminoalkyl)benzotriazoles have been shown to exist in solution in equilibrium with iminium ions[24] (Scheme 1) and this characteristic has led to the development of a number of useful synthetic applications[24] based on their reactions with nucleophiles with the expulsion of the benzotriazole moiety.



Scheme 1

As part of a broader program aimed at the generation and synthetic use of α-aminoalkyl radicals derived from simple carbonyl derivatives, we considered the benzotriazole derivatives **1** as a possible source of those radicals. In this Letter we report the application of these ideas to a new synthesis of tertiary vicinal diamines **2** based on the SmI_2-promoted reductive coupling of iminium ions generated from N-(N',N'-dialkylaminoalkyl)benzotriazoles **1** (Scheme 2, Table 1).



Scheme 2

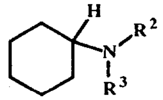
The procedure has been successfully applied (Table 1)[25] to the coupling of benzotriazole adducts derived from formaldehyde, aliphatic, and aromatic aldehydes, the yields being uniformly high. The reaction takes place at low temperatures, with the exception of those adducts derived from formaldehyde, which require ambient temperature conditions. Since compounds **1** are easily prepared[24], at room temperature, from benzotriazole, an aldehyde or ketone and a secondary amine, the whole procedure benefits from the use of readily available starting materials and very mild reaction conditions.

Table 1. Preparation of Vicinal Diamines from N-(N',N'-Dialkylaminoalkyl)benzotriazoles **1**

Substrate	R^1	R^2	R^3	T (°C)	Yield of 2[a] (%)
1a	^{n}Pr	$(CH_2)_4$		-70	85
1b	Ph	$(CH_2)_4$		-70	75
1c	H	$(CH_2)_4$		20	82
1d	^{i}Pr	$(CH_2)_4$		0	87
1e	^{i}Pr	$(CH_2)_2$-O-$(CH_2)_2$		-30	61
1f	2-(3-phenyl-2-propenoxy)phenyl	$(CH_2)_2$-O-$(CH_2)_2$		20	70
1g	H	CH_2Ph	CH_2Ph	30	55
1h	Ph	CH_2Ph	CH_2Ph	-20	80

[a] Mixtures of diastereoisomers, where appropriate

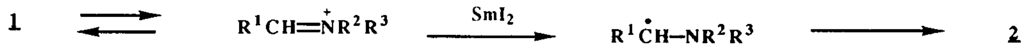
Adducts derived from cyclohexanone and primary or secondary amines failed to give any diamine product; instead, only the monoamines 3 were obtained[26]. Therefore, the method appears to be limited to substrates derived from aldehydes.



3

In a typical experiment, a solution of SmI_2 (5 mmol) in THF (15 ml) is added dropwise to a stirred solution of **1b**[27] (5 mmol) in THF (20 ml) at -78°C. Under these conditions the blue color, characteristic of SmI_2-THF solutions, disappears almost instantly. After one equivalent of the reagent has been added, the blue color persists. The reaction mixture is then quenched with saturated K_2CO_3. Extractive work-up and purification by column chromatography affords the diamine **2b** as a 3/2 mixture of diastereoisomers in 75% yield.

As a mechanistic rationale to explain the observed results, it is suggested that the iminium cations **4**, present in solution as the result of the dissociation[24] of the adducts **1**, are reduced by SmI_2 to generate the α-aminoalkyl radicals[28] **5**. The coupling of two such radicals affords the 1,2-diamines (Scheme 3).



$$\underset{}{1} \rightleftharpoons \underset{4}{R^1CH{=}\overset{+}{N}R^2R^3} \xrightarrow{SmI_2} \underset{5}{R^1\overset{\bullet}{C}H{-}NR^2R^3} \longrightarrow 2$$

4 5

Scheme 3

As these results suggest, the combination of easily available N-(N',N'-dialkylaminoalkyl)benzotriazoles and SmI_2 represents a convenient entry into reactive intermediates whose behaviour parallels that expected for the synthetically useful α-aminoalkyl radicals[28-31]. The application of this methodology to the synthesis of carbocycles and heterocycles will be the subject of a forthcoming paper.

Acknowledgments. Financial support by the Dirección General de Investigación Científica y Técnica (DGICYT PB89-0412) and by the Universidad del País Vasco (UPV 170.310-E166/90) is gratefully acknowledged. We also thank the Departamento de Educación, Universidades e Investigación (Gobierno Vasco) for a Fellowship (to A.F.A.).

References and Notes.

1. Wu, Y. D.; Wang, Y.; Houk, K. N. *J. Org. Chem.*. **1992**, *57*, 1362.
2. Corey, E. J.; Da Silva Jardine, P.; Virgil, S.; Yuen, P. W.; Connell, R. D. *J. Am. Chem. Soc.* **1989**, *111*, 9243.
3. Oishi, T.; Hirama, M. *J. Org. Chem.* **1989**, *54*, 5834.
4. Tokles, M.; Snyder, J. K. *Tetrahedron Lett.* **1986**, *27*, 3951.
5. Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801.
6. Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493.
7. Corey, E. J.; Kim, S. S. *J. Am. Chem. Soc.* **1990**, *112*, 4976.
8. Reetz, M. T.; Jaeger, R.; Drewlies, R.; Hübel, M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 103, and references cited therein.

9. Zhang, W.; Jacobsen, E. N. *Tetrahedron Lett.* **1991**, *32*, 1711.
10. Barluenga, J.; Aznar, F.; de Mattos, M. C. S.; Kover, W. B.; García-Granda, S.; Pérez-Carreño, E. *J. Org. Chem.* **1991**, *56*, 2930.
11. Katritzky, A. R.; W.Q., F.; Fu, C. *J. Org. Chem.* **1990**, *55*, 3209.
12. Takaki, K.; Tsubari, Y.; Tanaka, S.; Beppu, F.; Fujiwara, Y. *Chem. Lett.* **1990**, 203.
13. Tanaka, H.; Dhimane, H.; Fujita, H.; Ikemoto, Y.; Torii, S. *Tetrahedron Lett.* **1988**, *29*, 3811.
14. Moriarty, R. M.; Khosrowshahi, J. S. *Tetrahedron Lett.* **1986**, *27*, 2809.
15. Fristad, W. E.; Brandvold, T. A.; Peterson, J. R.; Thompson, S. R. *J. Org. Chem.* **1985**, *50*, 3647.
16. Fraenkel, G.; Pramanik, P. *J. Org. Chem.* **1984**, *49*, 1314.
17. Bäckwall, J. E. *Tetrahedron Lett.* **1978**, 163.
18. See Ref. 8 for papers related to their biological and medicinal relevance.
19. Commonly encountered problems include: low yields, lengthy reaction sequences, lack of generality, and the use of high temperatures.
20. For exceptions see Ref.'s 9, 11, and 16
21. Imamoto, T.; Nishimura, S. *Chem. Lett.* **1990**, 1141.
22. Enholm, E. J.; Forbes, D. C.; Holub, D. P. *Synth. Commun.* **1990**, *20*, 981.
23. Molander, G. A. *Chem. Rev.* **1992**, *92*, 29.
24. Katritzky, A. R.; Rachwal, S.; Hitchings, G. J. *Tetrahedron* **1991**, *47*, 2683.
25. Known diamine products were characterized by comparison of their physical and spectroscopic data with those reported in the literature. New compounds were characterized by their spectroscopic (^{1}H-, ^{13}C-NMR, IR), as well as combustion (C, H, N) analyses or HR-MS.
26. For a similar observation with ketimine derivatives see Ref. 21
27. Prepared by stirring overnight at 25°C an equimolar mixture of benzaldehyde, pirrolidine, and benzotriazole, in the presence of 4 Å molecular sieve.
28. The generation of carbon radicals from iminium salts and SmI_2 has been reported: Martin, S. F.; Yang, C. P.; Laswell, W. L.; Rüeger, H. *Tetrahedron Lett.* **1988**, *29*, 6685.
29. Choi, J. K.; Ha, D. C.; Hart, D. J.; Lee, C. S.; Ramesh, S.; Wu, S. *J. Org. Chem.* **1989**, *54*, 279.
30. Padwa, D., W.; Nimmesgern, H.; Venkatramanan, M. K.; Wong, G. S. K. *Chem. Ber.* **1986**, *119*, 813.
31. Padwa, A.; Nimmesgern, H.; Wong, G. S. K. *J. Org. Chem.* **1985**, *50*, 5620.

(Received in UK 29 May 1992)