Pergamon

Tetrahedron Letters 39 (1998) 6835–6836

TETRAHEDRON LETTERS

The Synthesis of 3,5-Di- and 3,5,5-Trisubstituted-1,3-oxazolidines from Primary Amines and Carbonyl Compounds

Alan R. Katritzky,* Daming Feng, and Ming Qi

Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, FL 32611-7200

Received 26 May 1998; accepted 10 July 1998

Abstract: A variety of 3,5-substituted 1,3-oxazolidines are synthesized from primary amines by a novel, two step sequence. © 1998 Elsevier Science Ltd. All rights reserved.

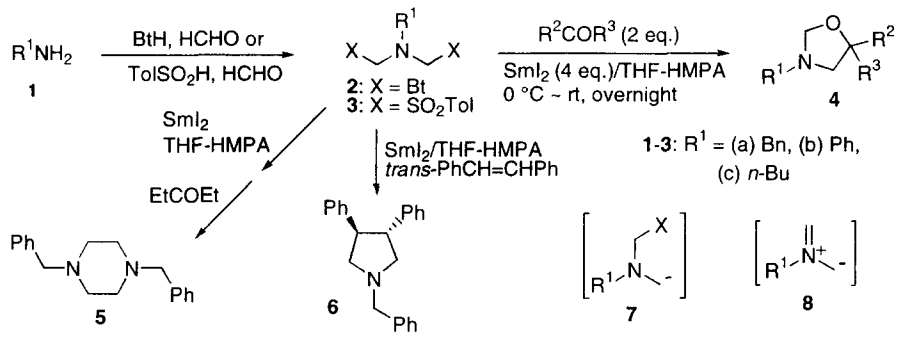
1,3-Oxazolidines are useful synthetic intermediates as equivalents of iminium ions,[1a,b] or of imines,[2] and as chiral auxiliaries.[3a,b] They are usually prepared from β-hydroxy amines by a [4+1] ring synthesis,[4a,b] although a few examples were reported from the [3+2] cycloaddition of azomethine ylides and carbonyl compounds (mostly benzaldehyde),[5a-e] and in other ways.[5f] The present work describes a related [3+2] ring synthesis of 1,3-oxazolidines from readily available starting materials.

N,N-Bis(benzotriazolylmethyl)alkyl amines (**2**)[6a] and *N,N*-Bis(sulphonylmethyl)alkyl amines (**3**)[6b] are easily prepared from primary amines (**1**) following literature procedures. *N,N*-Bis(benzotriazolylmethyl)phenyl amine (**2a**) reacted with 3-pentanone in the presence of samarium diiodide in THF-HMPA to give oxazolidine **4a** as the major product (30% by GC/MS) (Scheme). Under the same conditions, the use of *N,N*-bis(tosylmethyl)benzylamine **3a** as the starting material resulted in 90% isolated yield of oxazolidine **4a**. Similarly, reactions of **3a,c** with the appropriate carbonyl compounds gave oxazolidines **4b-e,g-i** in 39-81% isolated yields.[7] Compound **4f** was obtained from **2b** since **3b** could not be prepared.[6b]

When amine **3a** was first treated with samarium diiodide in THF-HMPA (10:1) for 5 min (during which time the purple color dissipated) and then quenched with 3-pentanone, only piperazine **5** was isolated in 65% yield. This result demonstrated that the formation and the further reaction of the reactive intermediate (whether it be a non-stabilized α-aminocarbanion or azomethine ylide) is very fast, and the preparation of 1,3-oxazolidines needs to be carried out in one step. When amine **3a** was reacted with SmI_2/THF-HMPA in the presence of *trans*-stilbene, pyrrolidine **6** was isolated in 81%. This result may suggest an azomethine ylide intermediate (**8**)[8], but it is still insufficient to exclude a non-stabilized α-aminocarbanion (**7**) intermediate. In order to understand the real reactive intermediate involved in this reaction, more experimental work is underway and will be reported in due course.

Stabilized α-aminocarbanions are important and well investigated reactive synthetic intermediates.[9a,b] Non-stabilized α-aminocarbanions have thus found less use largely due to the lack of appropriate methods for their generation.[10a,b] Recently we described novel methodologies which provide easy access from *N*-(α-aminoalkyl)benzotriazoles or *N*-(sulphonylmethyl)amines to a variety of substituted α-aminocarbanions and reported their capture by various electrophiles.[11a,b] We have now shown that this technique can be applied to allow a two step preparation of 1,3-oxazolidines from primary amines.

0040-4039/98/$ - see front matter © 1998 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)01487-7



4	a	b	c	d	e	f	g	h	i
R^1	Bn	Bn	Bn	Bn	Bn	Ph	*n*-Bu	*n*-Bu	*n*-Bu
R^2	Et	$-(CH_2)_5-$	*i*-Pr	Pr	*t*-Bu	Et	Et	*t*-Bu	Me
R^3	Et		H	Me	H	Et	Et	H	Pr
yield (%)	90	43	39	81	68	38	54	73	64

REFERENCES AND NOTES

1. (a) Senkus, M. *J. Am. Chem. Soc.* **1945**, *67*, 1515-1519; (b) Heaney, H.; Papageorgiou, G.; Wilkins, R. F. *Tetrahedron* **1997**, *53*, 14381-14396; and references cited therein.
2. Wu, M.-J.; Pridgen, L. N. *J. Org. Chem.* **1991**, *56*, 1340-1344.
3. (a) Agami, C.; Couty, F. *Tetrahedron Lett.* **1987**, *28*, 5659-5660; (b) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835-875; and references cited therein.
4. (a) Bergmann, E. D. *Chem. Rev.* **1953**, *53*, 309-340; (b) Hénin, F.; Létinois, S.; Muzart, J. *Tetrahedron Lett.* **1997**, *38*, 7187-7190.
5. (a) Padwa, A.; Chen, Y.-Y.; Chiacchio, U.; Dent, W. *Tetrahedron* **1985**, *41*, 3529-3535; (b) Padwa, A.; Dent, W.; Nimmesgern, H.; Venkatramanan, M. K.; Wong, G. S. K. *Chem. Ber.* **1986**, *119*, 813-828; (c) Padwa, A.; Dent, W. *J. Org. Chem.* **1987**, *52*, 235-244; (d) Wittland, C.; Arend, M.; Risch, N. *Synthesis* **1996**, 367-371; (e) Pearson, W. H.; Mi, Y. *Tetrahedron Lett.* **1997**, *38*, 5441-5444; (f) Yli-Kauhaluoma, J. T.; Harwig, C. W.; Wentworth, P. Jr.; Janda, K. D. *Tetrahedron Lett.* **1998**, *39*, 2269-2272.
6. (a) Katritzky, A. R.; Rachwal, S.; Rachwal, B. *J. Chem. Soc., Perkin Trans. I* **1987**, 799-804; (b) Bäder, E.; Hermann, H. D. *Chem. Ber.* **1955**, *88*, 41.
7. Compounds **4a-i** were all isolated as oils which gave satisfactory C-13 and proton NMR spectra. **4f** and **4h** were further characterization by HRMS, all other gave satisfactory CHN elemental analysis (± 0.4%).
8. Chastanet, J.; Roussi, G. *J. Org. Chem.* **1988**, *53*, 3808-3812.
9. (a) Beak, P.; Zajdel, W. J.; Reitz, D. B. *Chem. Rev.* **1984**, *84*, 471-523; (b) Beak, P.; Basu, A.; Gallagher, D. J.; Park, Y. S.; Thayumanavan, S. *Acc. Chem. Res.* **1996**, *29*, 552-560.
10. (a) Kessar, S. V.; Singh, P. *Chem. Rev.* **1997**, *97*, 721-737; (b) Katritzky, A. R.; Qi, M. *Tetrahedron* **1998**, *54*, 2647-2668.
11. (a) Katritzky, A. R.; Qi, M.; Feng, D.; Nichols, D. A. *J. Org. Chem.* **1997**, *62*, 4121-4124; (b) Katritzky, A. R.; Feng, D.; Qi, M. *J. Org. Chem.* **1997**, *62*, 6222-6225.