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Base promoted isomerization of aziridinyl ethers: a new access to α - and β -aminoacids

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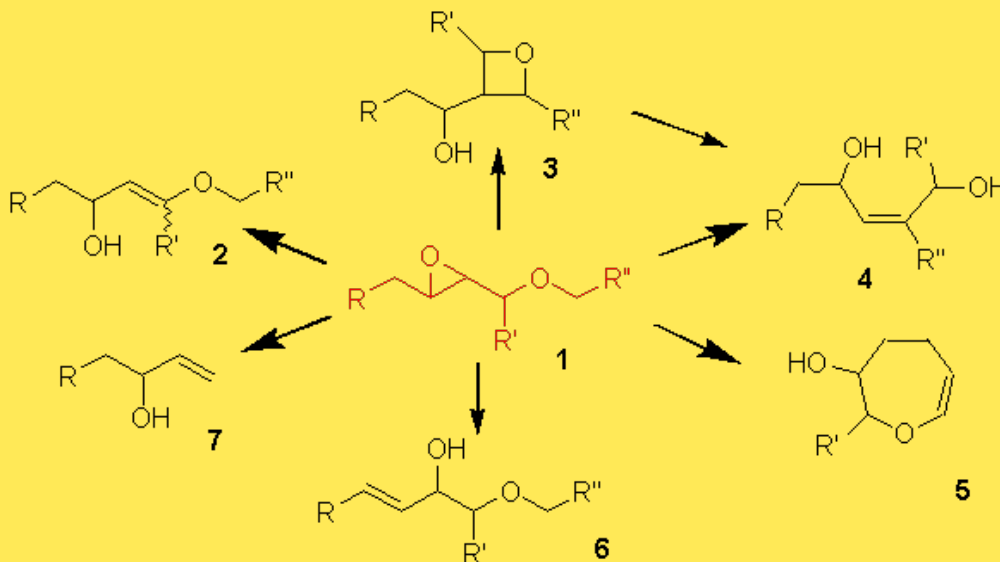
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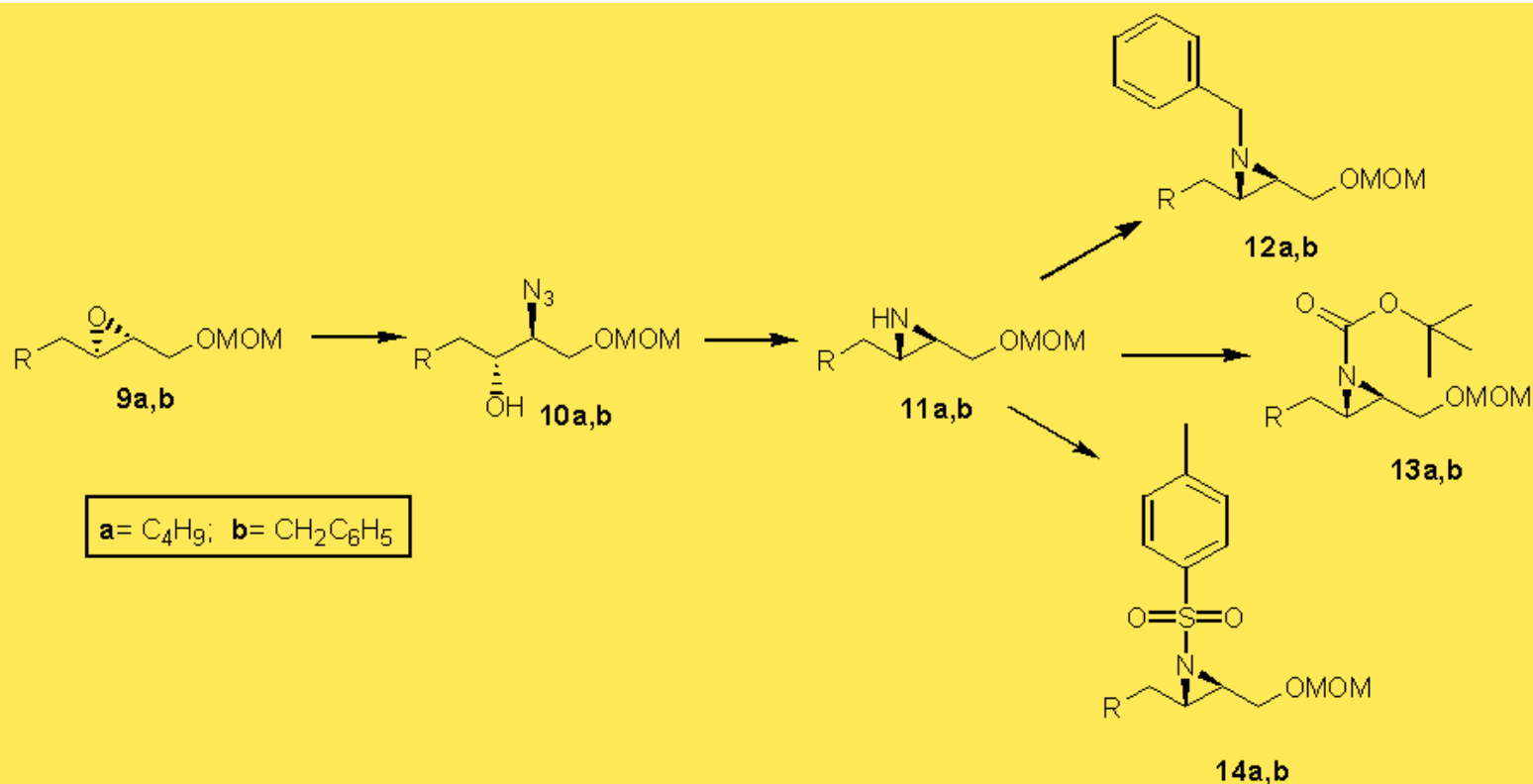


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In the last few years we have extensively studied the base-promoted isomerization of oxiranyl ethers showing that they can be stereoselectively converted in a number of synthetically useful products by treatment with mixed metal reagents (superbases) [1,2]. Depending on the substrate and the base used oxiranyl ethers **1** can be transformed into hydroxy enethers **2** [3,4] ($R' = H$), di- and tri-substituted oxetanes **3** via a 4-*endo* process [5-7] ($R' = H$ or alkyl), 1,4-diols **4** using an excess of base [8], tetrahydrooxepines **5** ($R'' = CH=CH_2$) [9] and terminal allylic alcohols **7** ($R'' = SPh$) when radical anions are used. The use of superbasic mixtures is essential in order to have processes with a highly regio- and stereoselective behaviour and high yields of converted products.



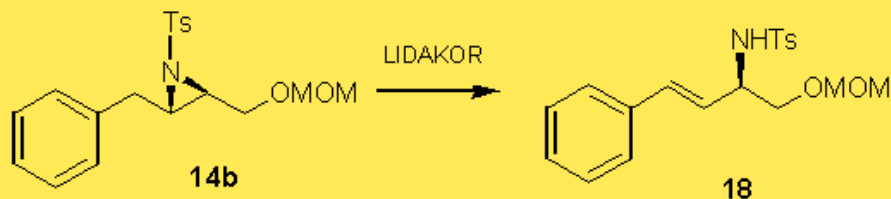
In order to further extend the scope of our studies, we have recently undertaken an investigation of the reactivity of aziridinyl ethers with superbasic reagents, aiming at the synthesis of hydroxy amines and α - or β -aminoacids. Enantiomerically enriched aziridinyl ethers **11** can be prepared in a number of ways [10] among which we have selected the sequences starting from epoxy ethers **9**, through ring opening with sodium azide and ring closure to aziridine with triphenyl phosphine [11]. The aziridinyl ethers **11** have then been protected with some different groups on nitrogen, namely as benzyl- (**12**), *tert*-butoxycarbonyl- (BOC, **13**) and *para*-toluenesulfonyl- (Ts, **14**) aziridines.



Compounds **12a**, **13a** and **14a** have been submitted to treatment with the superbasic mixture lithium diisopropylamide/ potassium *tert*-butoxide (LIDAKOR) in order to first test the influence of the group on nitrogen on the isomerization process. We have found that only the tosyl aziridine **14a** can be isomerized to the corresponding amino vinyl ether **15**, while the benzyl derivative **12a** doesn't react and the BOC-aziridine **13a** is simply deprotected to the starting aziridine **11a** under the same reaction conditions. The conversion aziridine-amino vinyl ether is highly regio- and stereoselective and compound **15** is a very useful building block for further transformations. As an example **15** has been cleanly deprotected to the amino aldehyde **16** and the latter oxidized [12] to the β -amino acid **17**.



The formation of vinyl ether **15** is obviously due to selective deprotonation of the methylene group adjacent to the OMOM group and the aziridinyl ring. When we have applied the same reaction conditions to the aziridine **14b**, having an additional acidic position (the benzylic methylene group), we have found a different reaction pathway, leading this time to the cinnamyl amino alcohol **18** in a very selective manner. Compound **18** is the precursor of the β,γ -unsaturated α -amino acid, phenyl glycine and the extension of this methodology to other similar substrates could lead to a new approach to a large variety of unsaturated α -amino acids.



Both the reaction sequences illustrated above disclose new methods for the synthesis of unnatural α - and β -amino acids.

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References

- [1] A. Mordini in *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995 Vol. 11, p 93.
- [2] A. Mordini in *Advances in Carbanion Chemistry*; Snieckus, V., Ed.; JAI Press: Greenwich, CT, 1992; Vol. 1, p 1.
- [3] A. Mordini, S. Pecchi, G. Capozzi, A. Capperucci, A. Degl'Innocenti, G. Reginato, A. Ricci, *J. Org. Chem.* **1994**, *59*, 4784.
- [4] A. Mordini, M. Valacchi, S. Pecchi, A. Degl'Innocenti, G. Reginato *Tetrahedron Lett.* **1996**, *37*, 5209.
- [5] A. Mordini, S. Bindi, S. Pecchi, A. Degl'Innocenti, G. Reginato, A. Serci *J. Org. Chem.* **1996**, *61*, 4374.
- [6] A. Mordini, S. Bindi, S. Pecchi, A. Capperucci, A. Degl'Innocenti, G. Reginato *J. Org. Chem.* **1996**, *61*, 4466.
- [7] A. Mordini, M. Valacchi, C. Nardi, S. Bindi, G. Poli, G. Reginato *J. Org. Chem.* **1997**, *62*, 8557.
- [8] A. Thurner, F. Faigl, A. Mordini, A. Bigi, G. Reginato, L. Toke *Tetrahedron* **1998**, *54*, 11597.
- [9] A. Mordini, S. Bindi, D. Nistri, G. Reginato, M. Valacchi *J. Org. Chem.* **2000**, *65*, 0000.
- [10] H. M. I. Osborn, J. Sweeney *Tetrahedron: Asymmetry* **1997**, *8*, 1693; R. S. Atkinson *Tetrahedron* **1999**, *55*, 1519.
- [11] D. Tanner, P. Somfai *Tetrahedron Lett.* **1987**, *28*, 1211-1214.
- [12] M. Zhao, J. Li, Z. Song, R. Desmond, D. M. Tschaen, E. J. J. Grabowski, P. J. Reider *Tetrahedron Lett.* **1998**, *39*, 5323.

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