Tetrahedron Letters, Vol.32, No.35, pp 4481-4482, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

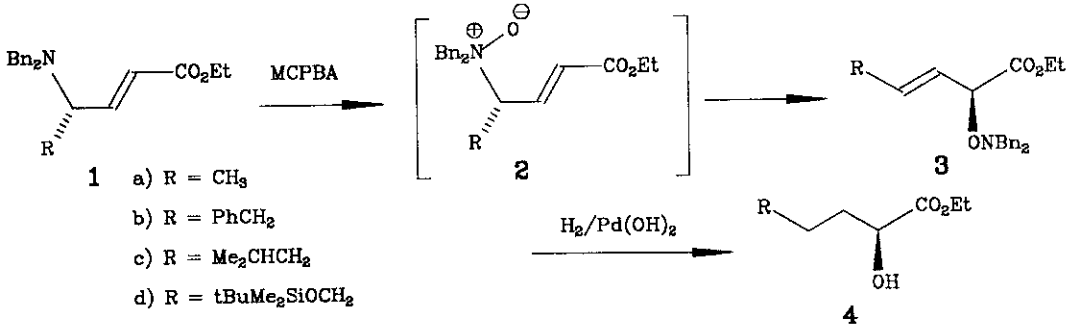
STEREOSELECTIVE [2,3]-SIGMATROPIC REARRANGEMENT OF CHIRAL AMINE OXIDES DERIVED FROM AMINO ACIDS

M.T. Reetz* and E.H. Lauterbach
Fachbereich Chemie der Universitaet, Hans-Meerwein-Strasse, 3550 Marburg, Germany

Key Words: Amino acids, amine oxides, [2,3]-sigmatropic rearrangement, diastereoselectivity

Summary: Chiral γ-N,N-dibenzylamino α,β-unsaturated esters **1** are oxidized by m-chloro perbenzoic acid to form the amine oxides **2** which undergo a [2,3]-sigmatropic rearrangement with complete 1,3-transfer of chirality.

α,β-Unsaturated methyl or ethyl esters **1**, prepared in enantiomerically pure form from the corresponding amino acids, undergo highly stereoselective Michael-type addition reactions with such nucleophiles as cuprates$^{1)}$ or tBuOOK$^{2)}$. In this Letter we report the reaction of the esters **1** with an electrophilic oxidizing agent, m-chloro perbenzoic acid (MCPBA). Upon treating the esters **1** with MCPBA in CH_2Cl_2 at -50°C (2 d), the hydroxylamines **3** were formed as the sole products (70-80% isolated yields).

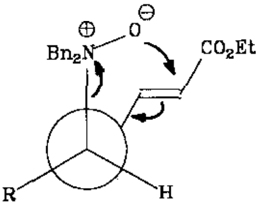


1 **2** **3** **4**

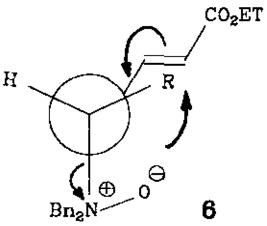
a) R = CH_3
b) R = $PhCH_2$
c) R = Me_2CHCH_2
d) R = $tBuMe_2SiOCH_2$

In order to determine the absolute configuration and enantiomeric purity of the products **3**, they were reduced with $H_2/Pd(OH)_2$ to form the α-hydroxy esters **4** (90%). In the case of **4a** the configuration was found to be S, as shown by a comparison of the observed optical rotation $[\alpha]_D^{22}$ of -5.17 (c = 2.32, $CHCl_3$) with that of the known compound $^{3)}$. Using the Mosher procedure$^{4)}$, the ee-values of the esters **4a-d** were determined to be >95%$^{5)}$.

The results are best interpreted by invoking formation and [2,3]-sigmatropic rearrangement$^{6)}$ of amine oxides **2** to form products **3** with essentially complete [1,3]-transfer of chirality. In a single known example of a related reaction, enantiomerically enriched (S)-N,N-dimethyl-3-(trans)-1-phenyl-1-butenyl)amine oxide was shown to rearrange with 85% stereoselectivity at -20°C (24 days)$^{7)}$. We propose transition state **5** leading to the observed trans-configurated products **4**, as opposed to the sterically less favorable transition state **6**, which would provide the R-configurated cis-analogs of **4**$^{8)}$ (not observed). A radical component is not involved$^{7)}$.



5



6

The present reactions$^{8)}$ extend the utility of N,N-dibenzylamino α,β-unsaturated esters$^{1,2)}$ as chiral building blocks in organic synthesis. Related self-immolative asymmetric synthesis involving ketene additions to the amino function of **1** followed by [3,3]-sigmatropic rearrangement$^{9)}$ is the subject of further work in our laboratory.

Acknowledgement: This work was supported by the Deutsche Forschungsgemeinschaft (Leibniz-Programm) and the Fonds der Chemischen Industrie.

References and Notes:

1) M.T. Reetz, D. Röhrig, <u>Angew. Chem.</u> **101** (1989) 1732; <u>Angew. Chem. Int. Ed. Engl.</u> **28** (1989) 1706.
2) See preceeding Letter in this issue. It makes no difference whether methyl or ethyl esters are used.
3) H.C. Brown, B.T. Cho, W.S. Park, <u>J. Org. Chem.</u> **51** (1986) 3396.
4) *J.A. Dale, D.L. Dull, H.S. Mosher, <u>J. Org. Chem.</u>* **34** *(1969) 2543.*
5) HPLC-analyses of the "Mosher-Ester" of compounds **4** show a trace (2%) of a second diastereomer which may be due to the presence of a small amount of **4** (enant.) or to enantiomeric inpurity of the Mosher-Chloride.
6) Review of [2,3]-sigmatropic rearrangements: R.W. Hoffmann, <u>Angew. Chem.</u> **91** (1979) 625; <u>Angew. Chem. Int. Ed. Engl.</u> **18** (1979) 563.
7) *Y. Yamamoto, I. Oda, Y. Inouye, <u>J. Org. Chem.</u>* **41** *(1976) 303.*
8) To the suspension of m-chloro perbenzoic acid (242 mg, 1.4 mmol) and $\mathrm{NaHCO_3}$ (500 mg) in 15 ml of dry $\mathrm{CH_2Cl_2}$ is slowly added at -50°C an ester **1** (1 mmol) in 4 ml of $\mathrm{CH_2Cl_2}$. After stirring for 2 d at -50°C, NaI (1ml of a sat. acetone soln.) is added, the mixture is allowed to reach room temp. and 5% $\mathrm{NaHSO_3}$-soln. is added to destroy the $\mathrm{I_2}$. The aqueous phase is extracted twice with $\mathrm{CH_2Cl_2}$ and the combined org. phases are dried over $\mathrm{MgSO_4}$. After removal of the solvent, the products **3** are chromatographed over $\mathrm{SiO_2}$ using pet-ether/acetic acid ethyl ester (20:1).
9) R. Oehrlin, R. Jeschke, B. Ernst, D. Bellus, <u>Tetrahedron Lett.</u> **30** (1989) 3517.

(Received in Germany 28 May 1991)