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COMPLETE ASYMMETRIC INDUCTIONS IN DIELS-ALDER REACTIONS OF CHIRAL SULFINES

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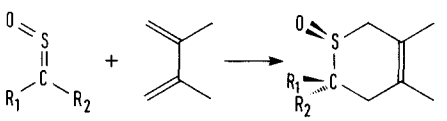
Abstract. Complete asymmetric induction was observed during the cycloaddition reaction of 2,3-dimethyl-1,3-butadiene with chiral, camphor or sulfoximino substituted, sulfines.

Sulfines (thione *S*-oxides) are sulfur-centered heterocumulenes that can undergo a variety of cycloaddition reactions[1], *e.g.* with 1,3-dienes[2]. The Diels-Alder reaction of appropriately substituted sulfines with 2,3-dimethyl-1,3-butadiene leads to dihydropyran *S*-oxides. The dienophilicity of sulfines strongly depends on the nature of the substituent(s) at the sulfine carbon atom. Electron withdrawing groups, *e.g.* Cl, enhance the reactivity, whereas sterically filled substituents have a strong retarding effect.[1,2] When a [4+2]-cycloaddition reaction is performed with geometrically isomeric sulfines the stereochemical relationship in the sulfine is predominantly retained in the cycloadduct.[2] As a consequence of this stereospecific course of the cycloaddition reaction the two newly formed chiral centres in the adduct are stereochemically coupled(Scheme 1).



(scheme 1)

This communication deals with the asymmetric induction during cycloaddition reactions of 2,3-dimethyl-1,3-butadiene with sulfines bearing a chiral substituent. Tremendous efforts have been devoted to accomplish enantioselective versions of Diels-Alder reactions using chiral olefinic dienophiles[3], chiral dienes[4] and chiral Lewis acid catalysts[5]. Sofar, asymmetric induction during cycloaddition reactions with hetero double bonds in chiral dienophiles has not been investigated.

For the selection of appropriate chiral sulfines it is desirable that chirality can be introduced in a relatively simple manner and that the sulfines

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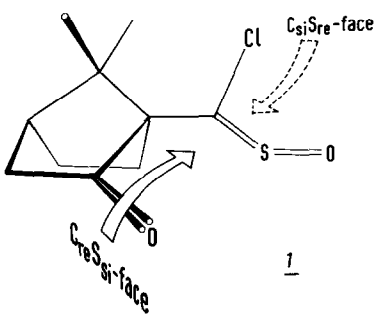
be sufficiently reactive in Diels-Alder reactions. Thioamide *S*-oxides derived from α-amino acids would be suitable candidates as far as chirality is concerned, however, these types of sulfines do not react with dienes. Sulfoxides are considered as excellent chiral inducing substituents[6], however, the preparation of sulfoxide sulfines using the alkylidenation of sulfur dioxide with α-silyl carbanions is met with difficulties.[7] Chlorosulfines usually are sufficiently reactive towards dienes. Accordingly, 10-chloro-10-sulfinylcamphor 1 (Figure 1), in fact the first stable sulfine ever reported in the literature[8] seems an attractive chiral substrate. At room temperature the Diels-Alder reaction of 1 with 2,3-dimethyl-1,3-butadiene proceeds very slowly, about 10% of adduct was obtained after 10 days. However, at 70° the cycloaddition was complete in one week (yield on purified product: 80%). According to the ^{1}H-NMR spectrum, the sharp m.p. (118-119°) and an extensive HPLC- and TLC-analysis only a single diastereomer was obtained.[9,10] No trace of another cycloadduct could be detected. Therefore, we conclude that the cycloaddition with the optically active sulfine 1 proceeds with complete asymmetric induction.

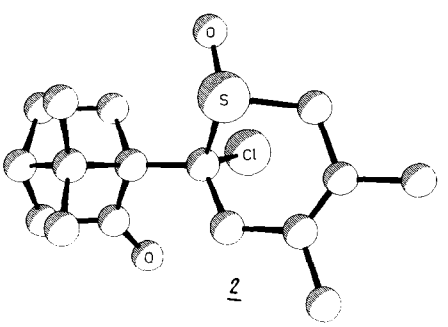
In order to establish the steric course of the cycloaddition an X-ray analysis of the adduct was performed.[11] It was found that the configuration both at sulfur and the halogen bearing carbon atom is R (Figure 2). In addition, the geometry of the starting sulfine was established to be *Z* by means of an X-ray analysis.[11] As can be seen in Figure 2 the chlorine and sulfoxide oxygen in the adduct are in *cis*-position with respect to each other, meaning that the stereochemistry present in the sulfine is retained in the product. From the structure of the adduct shown in Figure 2 it can be reconstructed that the diene has approached the plane of the sulfine moiety from the $C_{si}S_{re}$-face.

Inspection of molecular models reveals that conceivable rotamers about the C_1-C_{10} bond in 1 with minimized steric and electrostatic interactions are those having the chlorine atom and the CSO moiety in the bisecting plane of the C_7-*gem.* dimethyl group with the Cl either *syn* or *anti* to C_7. The donor-acceptor complex of sulfine and diene preceding the cycloaddition reaction will probably arise from an approach of the diene to the sulfine conformer which has the least hindered $C_{si}S_{re}$-face. As illustrated in Figure 1 this clearly is a diene reaction



1

(fig. 1)

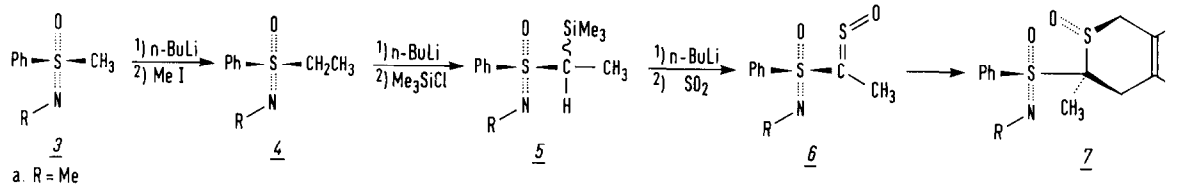


2

(fig. 2)

of the rotamer with the Cl positioned *syn* to C_7 from the side opposite to the carbonyl function at C_2. Remarkably, this process is favoured over attack at the $C_{re}S_{si}$-face of the sulfine conformer with the Cl *anti* to C_7, even to such an extend that complete asymmetric induction is achieved.

For a second type of chiral sulfines the sulfoximino group was chosen as the chiral substituent. Sulfoximines have been used as chiral inductors in several reactions, *e.g.*, synthesis of optically active oxiranes[12] and cyclopropanes[12], resolution of ketones[13], preparation of optically active alcohols[14] and stereoselective alkylations[15]. Usually, a derivative of readily available optically active (+)-(*S*)-*S*-methyl-*S*-phenylsulfoximine[12b] is utilized as starting material. *N*-methylation[16] or *N*-tosylation[17] provided compounds 3 (a,b) which on C-methylation (-78°, THF) gave the suitable precursors 4 (a,b) for the synthesis of sulfines by the modified Peterson reaction (Scheme 2). Reaction of 4 (a,b)



3 4 5 6 7

(scheme 2)

in THF with one equiv. of butyllithium, followed by one equiv. of trimethylsilyl chloride at -78° gave silyl compounds 5 (a,b), which, without isolation, were treated with one equiv. of butyllithium at -78°. Addition of the thus-formed α-silyl carbanions to an excess of sulfur dioxide in THF at -78° gave sulfines 6 (a,b) in solution. These were converted into the dihydrothiapyran derivatives 7 by treatment with an excess of 2,3-dimethyl-1,3-butadiene (16 h at 20°). After work-up and chromatography on silica gel (ether/ethyl acetate) 7a was obtained as an oil and 7b as a crystalline product (m.p. 61.5-63°)[10,18] (yields based on 4 (a,b) 40% and 66%, respectively). According to the ^{1}H-NMR spectrum, and an extensive HPLC- and TLC-analysis in both cases only one diastereomer was obtained. Following the same procedure the racemic substrate 4a was also converted into the cycloadduct 7a, which now, consists of a 1:1 mixture of enantiomers as was established by means of ^{1}H-NMR using optishift reagents. No trace of diastereomeric products could be detected. Similarly, the cycloadduct 7b obtained from racemic substrate 4b was shown to consist of a 1:1 mixture of enantiomers. From these experiments it is concluded that the sulfoximino sulfines also show complete asymmetric induction during the cycloaddition reaction with dimethylbutadiene.

Studies of molecular models reveal that the asymmetric induction with the sulfines 6 is probably caused by a steric shielding of one diastereotopic face of the sulfine moiety by the N-R substituent. Experiments to elucidate the stereochemical course of this and related cycloaddition reactions with chiral sulfines are in progress.

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REFERENCES

1. B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas* 101, 1 (1982).
2. a) B. Zwanenburg, L. Thijs, J.B. Broens and J. Strating, *Recl. Trav. Chim. Pays-Bas* 91, 443 (1972); b) J.W.H. Handels, *Thesis*, University of Nijmegen, 1979.
3. a) E.J. Corey and H.E. Ensley, *J. Am. Chem. Soc.* 97, 6908 (1975); b) R.K. Boeckman Jr., P.C. Naegely and S.D. Arthur, *J. Org. Chem.* 45, 752 (1980); c) G. Helmchen and R. Schmierer, *Angew. Chem.* 93, 208 (1981); *Angew. Chem. Int. Ed. Engl.* 20, 205 (1981); d) W. Oppolzer, M. Kurth, D. Reichlin and F. Moffatt, *Tetrahedron Lett.*, 2545 (1981); e) W. Oppolzer, M. Kurth, D. Reichlin, C. Chapuis, M. Mohnhaupt and F. Moffatt, *Helv. Chim. Acta* 64, 2802 (1981); f) W. Oppolzer, C. Chapuis, G. Mao Dao, D. Reichlin and T. Godel *Tetrahedron Lett.*, 4781 (1982).
4. a) B.M. Trost, S.A. Godleski and J.P. Genêt, *J. Am. Chem. Soc.* 100, 3930 (1978); b) B.M. Trost, D. O'Krongly and J.L. Belletire, *J. Am. Chem. Soc.* 102, 7595 (1980); c) S. David, J. Eustache and A. Lubineau, *J. Chem. Soc. Perkin I*, 1795 (1979); d) T. Mukaiyama and N. Iwasawa, *Chem. Lett.*, 29 (1981).
5. S. Hashimoto, N. Komeshima and K. Koga, *J. Chem. Soc. Chem. Commun.*, 437 (1979).
6. M. Mikolajczyk and J. Drabowicz, *Topics in Stereochemistry*, Chapter 5, N.L. Allinger, E.L. Eliel and S.H. Wilen, eds., John Wiley & Sons, 1982.
7. a) F.A. Carey and O. Hernandez, *J. Org. Chem.* 38, 2670 (1975); b) A.G. Brook and D.G. Anderson, *Can. J. Chem.* 46, 2115 (1968).
8. E. Wedekind and D. Schenk, *Ber. Dtsch. Chem. Ges.* 44, 198 (1911); J. Strating, *Recl. Trav. Chim. Pays-Bas* 83, 94 (1964).
9. IR (KBr): 1069 cm^{-1} (S=O), 1730 cm^{-1} (C=O); ^{1}H-NMR ($CDCl_3$): δ 1.20 (s, 3H, CH_3), δ 1.44 (s, 3H, CH_3), δ 1.68 (br.s, 3H, CH_3), δ 1.73 (br.s, 3H, CH_3), δ 1.10-3.80 (m, 11H, remaining alif. protons).
10. All new compounds gave correct elemental analyses.
11. H.J. Bruins Slot, R.C. Haltiwanger and J.H. Noordik, to be published.
12. a) C.R. Johnson and C.W. Schroeck, *J. Am. Chem. Soc.* 93, 5303 (1971); b) C.R. Johnson and C.W. Schroeck, *J. Am. Chem. Soc.* 95, 7418 (1973).
13. a) C.R. Johnson and N.A. Meanwell, *J. Am. Chem. Soc.* 103, 7667 (1981); b) C.R. Johnson and J.R. Zeller, *J. Am. Chem. Soc.* 104, 4021 (1982).
14. C.R. Johnson and C.J. Stark Jr., *J. Org. Chem.* 47, 1193, 1196 (1982).
15. R. Annunziata and M. Cinquini, *Synth.* 1982, 767.
16. C.R. Johnson, C.W. Schroeck and J.R. Shanklin, *J. Am. Chem. Soc.* 95, 7424 (1973).
17. C.R. Johnson, R.A. Kirchhoff, R.J. Reischer and G.F. Katekar, *J. Am. Chem. Soc.* 95, 4287 (1973).
18. 7a: IR (NaCl): 1050 cm^{-1} (S=O); ^{1}H-NMR ($CDCl_3$): δ 1.27 (s, 3H, CH_3), δ 1.80 (br.s, 6H, CH_3), δ 2.73 (s, 3H, N-CH_3), δ 2.53 and 3.05 (ABq, 2H, J = 20 Hz, CH_2), δ 3.27 and 3.63 (ABq, 2H, J = 21 Hz, CH_2), δ 7.50-7.70 (m, 3H, arom), δ 7.85-8.10 (m, 2H, arom).
7b: IR (Kbr): 1044 cm^{-1} (S=O); ^{1}H-NMR ($CDCl_3$): δ 1.26 (s, 3H, CH_3), δ 1.77 (br.s, 6H, CH_3), δ 2.37 (s, 3H, *p*-CH_3), δ 2.50 and 2.87 (ABq, 2H, J = 19.5 Hz, CH_2), δ 3.40 (br.s, 2H, CH_2), δ 7.00-8.10 (m, 9H, arom).

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