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STEREOCHEMISTRY OF A [2,3]SIGMATROPIC ALLYL-SULFOXIDE/ALLYL SULFENATE REARRANGEMENT

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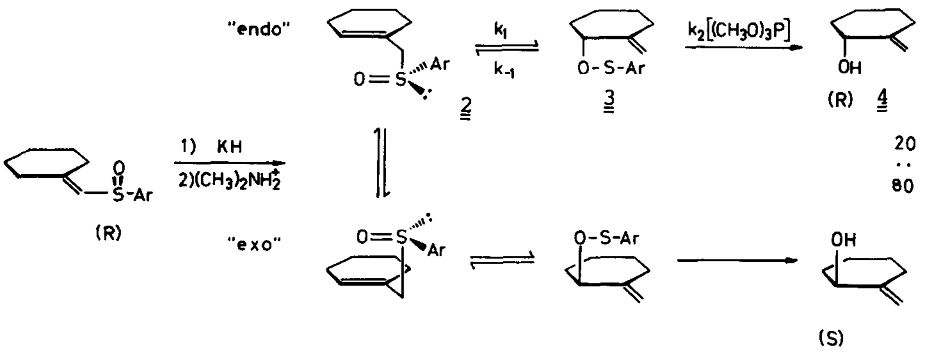
[3,3]Sigmatropic rearrangements follow a well defined stereochemistry$^{1)}$ and lend themselves for asymmetric syntheses$^{2)}$. Much less is known about the stereochemistry of [2,3]sigmatropic rearrangements$^{3)}$, which also show high stereoselectivities$^{4)}$, being even stereospecific in some cases$^{5)}$. We were interested in applying the MISLOW/EVANS sequence$^{6)}$ to the asymmetric synthesis of alcohols by chirality transfer from sulfur to carbon and report here on the stereochemistry of the conversion of 2 via 3 to methylenecyclohexanol (4).



Starting from a single enantiomer of 1 the above sequence led to 4 of 60% ee$^{*)}$ in 75% yield$^{7)}$. Provided that $k_2[(CH_3O)_3P]$ is > k_{-1} $^{8)}$ the stereochemistry of 4 is defined in the thus irreversible step 2 → 3. Starting from two different rotamers of 2 the [2,3]sigmatropic rearrangement can proceed via two diastereomeric transition states$^{3)}$, called "exo" and "endo" $^{10)}$. It is recognized that starting from the (R)-sulfoxide 2 the endo transition state leads to (R)-4, whereas (S)-4

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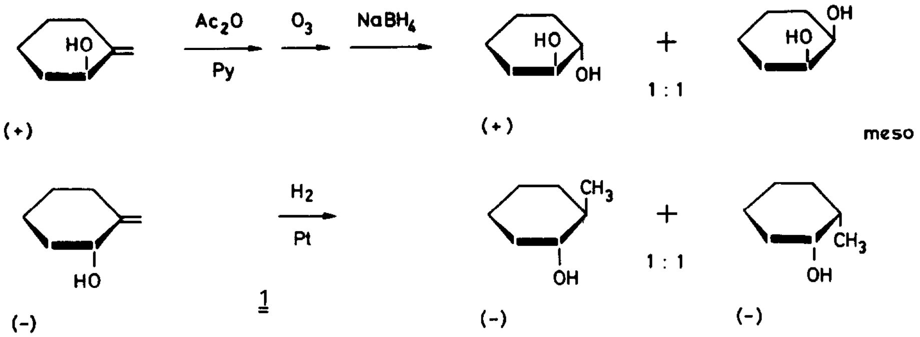
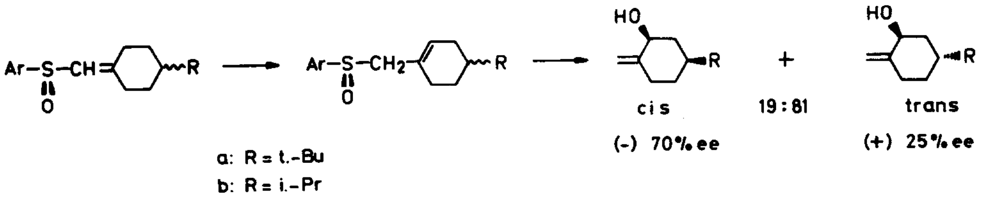
*) ee stands for enantiomeric excess and corresponds to optical purity.

is formed via the exo transition state. In order to assign the predominant path we have established the absolute configuration of 4 by chemical correlation of (+)-4 with (1S,2S)-cyclohexanediol[11] and of (-)-4 with (1R,2RS)-methylcyclohexanol[12].



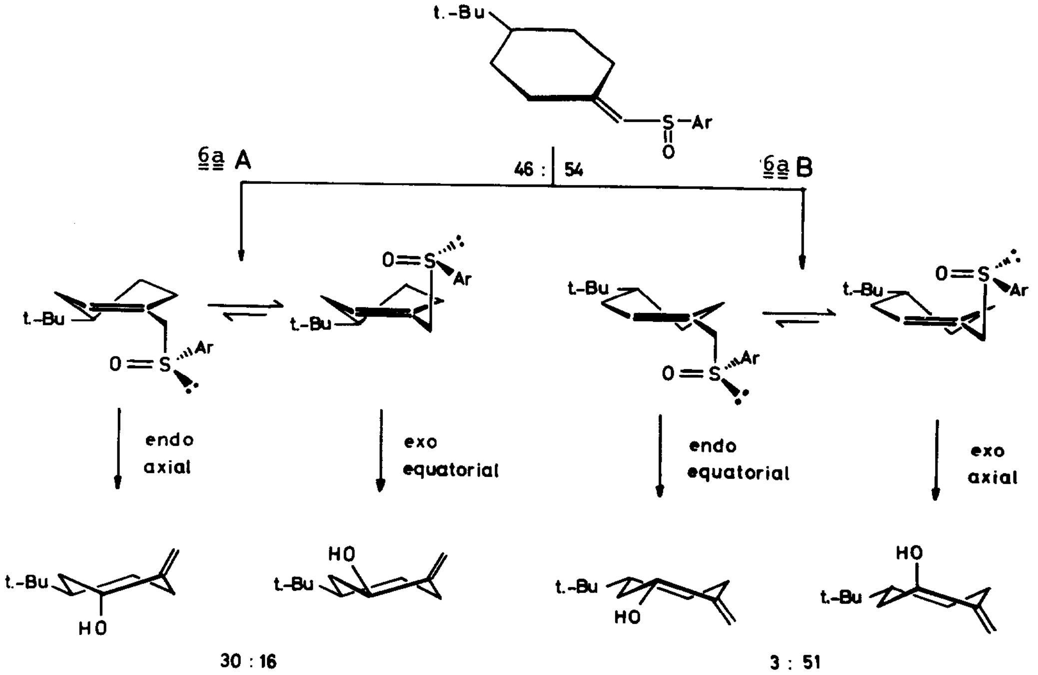
The obtention of dextrarotatory 4 from the (R)-sulfoxide 1 demonstrates the predominance of the exo transition state. This contrasts to the corresponding rearrangement of straight chain allyl sulfoxides via the endo transition state[7].

More insight into the stereochemistry of the 2 → 3 rearrangement can be gained by dissecting the pathways leading to an equatorial and axial sulfenate. This has been accomplished with the tert.-butyl group as conformation anchor. A presumably 1:1 mixture of the diastereomers 5 was obtained from 4-tert.-butyl-cyclohexanone as described before[7] and rearranged to the cis/trans-mixture of the 3-tert.-butyl-6-methylene-cyclohexanols 7a and 8a in 71% overall yield. The isomers were separated by vpc. Structural assignments rest on the following data: trans: ^{1}H-NMR CH-O m, half width 6 Hz, ^{13}C-NMR C-3 40.4 ppm; =CH$_2$ 109.1; cis: ^{1}H-NMR CH-O m, half width 19 Hz; ^{13}C-NMR C-3 47.0 ppm; =CH$_2$ 103.0.



5 6 7

The optical purities were determined from the Eu/TFC-shifted[13] spectra. Since 7b and 8b are compounds of known absolute configuration[14] the reaction sequence was repeated with an isopropyl-substituent. Yields, product ratios and signs of rotation [15] of 7b and 8b were the same as in the tert.-butyl-series. We therefore assume that in both cases the reaction follows the same stereochemistry and that the absolute configuration of the pairs 7a, 7b and 8a, 8b are each the same. This then allows the following partial rate constants to be derived[16]:



The [2,3]sigmatropic rearrangement of 6 is apparently subject to two controlling factors: 1. a 6.2 fold preference for an axial versus an equatorial formation of the carbon-oxygen-bond. 2. a 3.1 fold preference for an exo versus and endo transition state. These effects enforce each other in the B-diastereomer and counteract in the A-isomer.

Applying the above partial rate constants to the rearrangement of 2 in which the A and B-isomers are conformers and not diastereomers, it may be surmised that the following reaction paths are used: exo axial: endo axial: exo equatorial: endo equatorial = 72:16:8:4. Thus the reaction via conformer B is 3 times favoured over a reaction via A.

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8) We assume that this condition is fulfilled, since on applying the technique of intramolecular thiophilic cleavage9) to the conversion 3 → 4 , 4 was obtained with the same 60% ee as in lit7).

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15) 7b: 76 ± 10% ee from EuTFC shifted ^{1}H-NMR spectra; 94 ± 8% ee from rotation; 8b: 25 ± 10% ee from EuTFC shifted ^{1}H-NMR spectra; 21 ± 0.5% ee from rotation.

16) It is not known whether the 46:54 partitioning between the diastereomers 6aA and 6aB is significantly different from 50:50. In the 6b series the value is 47:53. This might imply a slight stereoselectivity in the deprotonation of 5