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THE DIASTEREOSPECIFIC APROTIC CONJUGATE ADDITION REACTIONS OF ALLYLIC ANIONS-MECHANISTIC ASPECTS.

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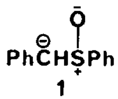
Summary: A ten-membered cyclic "chair-chair" - or "trans-decalyl"-like TS is proposed to account for the diastereospecific aprotic conjugate addition reactions of allylic carbanions bearing polar, charge-stabilizing groups.

The reactions described in the foregoing communication are unique to allylic systems, and are sensitive to other polar groups, either in the carbanions, or in the cyclic enones. Thus, the carbanions 1 and 2 with cyclopentenone in THF at -78° give, after quenching, carbonyl-addition products, such as 3 as mixtures of diastereomers. Deprotonation of each of the



$Ph\overset{\ominus}{C}H\overset{+}{S}(\bar{O})Ph$

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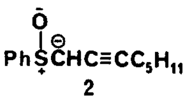

$Ph\overset{+}{S}(\bar{O})\overset{\ominus}{C}HC\equiv CC_5H_{11}$

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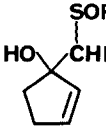

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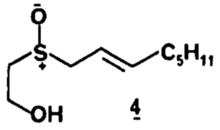

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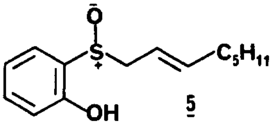

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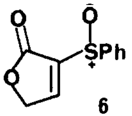
(β-hydroxyethyl)octenyl sulfoxide 4 and (o-hydroxyphenyl)octenyl sulfoxide 5 with firstly LDA (1 equiv) and then with BuLi (1 equiv), and treatment of the respective carbanion solutions with cyclopentenone in THF at -78° gives both carbonyl and conjugate addition products. The latter consist of mixtures of allylic and vinylic sulfoxides, none of which is formed as a single diastereomer. Treatment of the carbanion of (E)-1-(benzenesulfinyl)-2-octene[1] with the α-(benzenesulfinyl)-γ-crotonlactone 6[2] yields not the "normal" vinylic sulfoxide , as exemplified by the reaction of this carbanion with γ-crotonolactone itself,[1] but rather a mixture of products including the highly unstable allylic sulfoxide 7 (60%). This upon chromatography is cleanly transformed into the dienone 8 which in possessing but one chiral centre, gives no information on the diastereochemical purity of 7. We note also that,



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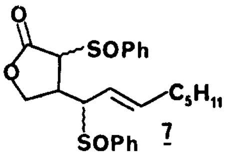

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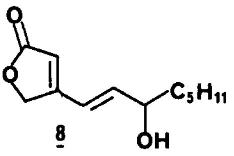

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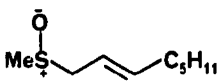

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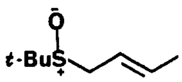

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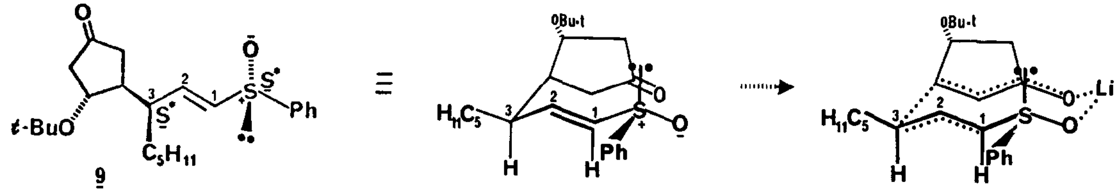
providing no polar groups are present therein (cf 4), the nature of the non-allylic substituents attached to the sulfur is unimportant. Thus, the alkyl allyl sulfoxides 10 and 11 undergo "normal" conjugate addition with cyclic enones to give the corresponding vinylic sulfoxides as single diastereomers[3].

The foregoing results clearly demonstrate that the geometry of the allylic anion, and the chelating ability of the sulfoxide group are crucial in determining both the regiochemical and diastereochemical behaviour of the carbanions in the conjugate addition reactions. A model of the TS which accounts for this is derived in Scheme 1, in which the product 9[1] is redrawn such that the side chain lies over the plane of the ring. Extrapolation back along the reaction coordinate then gives a ten-membered cyclic TS, which may best be described as "trans-fused chair-chair"- or "trans-decalyl"-like, as discussed below. Note that the S^*-configuration at sulfur is essential for accommodation of the oxygen atom within the cycle, and for the assumption of the pseudo-equatorial disposition by the phenyl substituent. Thus, for a carbanion from a (Z)-allylic sulfoxide, the TS will differ only in the stereochemistry of the substituent at C-3.



Scheme I

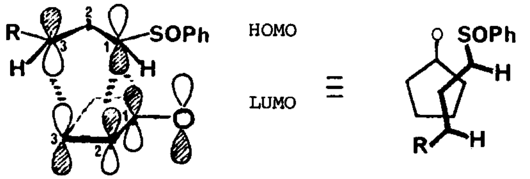
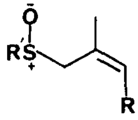


Fig. I: Orbital Interactions between enone LUMO and allyl anion HOMO

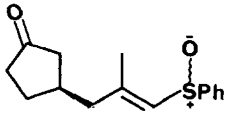
Although the model as drawn implies that chelation between the sulfoxide oxygen atom, the lithium cation, and the carbonyl oxygen atom plays the pivotal role in determining the regiochemical outcome of the reaction, it is likely that frontier orbital control is important in this conjugate addition process. Thus, interaction between the AOs at C-1 and C-2, and C-3 in the LUMO of the enone and the AOs at C-1 and C-3 in the HOMO of the anion is allowed (fig. 1). The interaction between C-1 and C-2 of the enone, and C-1 of the anion will confer the "decalyl-like" character to the TS.[4] Note that the carbanion thereby achieves an "endo" orientation with respect to the enone.

If the model is a reasonable representation of the TS, then the placement of a substituent at C-2 of the allylic system should destabilize the "chair-chair" or "trans-decalyl"-like TS with respect to others. As gauged by reactions of the 2-methallyl system 12, this is indeed found to be the case. The products 13 and 14 (13:14=9:2, 75% overall) from 12 and cyclopentenone in THF at -15° were shown to be geometric isomers by ^{1}H NMR NOE difference experiments involving preirradiation of the vinylic protons, which induced enhancement (5%) of the methyl signal in the spectrum of 14, but not in that of 13. However, as clearly indicated by 400 MHz ^{1}H NMR spectra, 13 consists of a 1:1 mixture of diastereomers, and 14 of a 9:1 mixture of diastereomers, which must thus be epimeric at sulfur. The epimers of 13 may arise either through the normal "chair-chair"-like TS 15, which is now destabilized by 1,3-diaxial interactions, and which gives the S_S^* epimer, or through the "cis-fused boat-boat"-like TS 16,[5] which gives the R_S^* epimer. A "cis-fused chair-chair"-like, and a "trans-fused boat-chair"-like TS can be drawn to account for the epimers of the minor (Z)-isomer 14. By contrast, the angelyl tert-butyl sulfoxide carbanion 17 reacts at -78° with cyclopentenone to give the crystalline (E)-vinylic sulfoxide 18 (75%) as a single diastereomer, and a small amount (6%) of a second vinylic sulfoxide of as yet undetermined stereochemistry. The structure of 18 has been fully confirmed by an X-ray crystallographic study.[6] Presumably, in the reaction of 17, the "cis-fused boat-boat"-like TS 20 now experiences a destabilising, eclipsing interaction between the pseudoaxial methyl group at C-3 of the allylic system and C-4 of the cyclopentenone ring, and the reaction now proceeds predominantly via the "trans-fused chair-chair"-like TS 19.



12: R = H, R' = Ph

17: R = Me, R' = *t*-Bu



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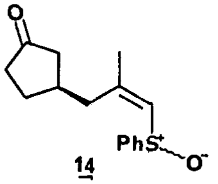

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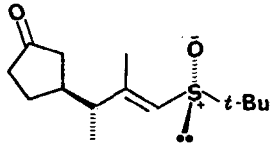

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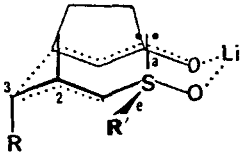
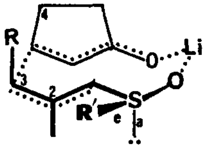


15: R = H, R' = Ph

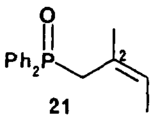
19: R = Me, R' = *t*-Bu



16: R = H, R' = Ph

20: R = Me, R' = *t*-Bu

In the case of the allylic phosphine oxides, similar transition states can be drawn to account for the products obtained from the reactions of the corresponding carbanions with cyclic enones. Thus, a "chair-chair"- or "trans-decalyl"-like TS in which the phenyl groups attached to phosphorus are pseudoaxial and pseudoequatorial will lead to the products obtained from the (E)- and (Z)-allylic phosphine oxides described in the preceding communication. There are, nevertheless, indications that such a TS is more tolerant of steric crowding than is the case with the corresponding sulfoxides. For example, the carbanions of the angelyl- and tiglyl phosphine oxides 21 and 23 give as predominant products with cyclopentenone, the vinylic phosphine oxides 22 (93%) and 24 (86%)[7]. By contrast, the carbanion of the tiglyl sulfoxide 25 delivers four diastereomeric vinylic sulfoxides which differ in geometry of the double bond, and of the configuration at the allylic carbon atom, in a ratio of 43:43:10:4[8]. Presumably, the "cis-fused boat-boat"-like TS corresponding to 16, and related transition states, are destabilized with respect to the normal "trans-fused chair-chair"-like TS by virtue of repulsive interactions between the π-system of the pseudoaxial phenyl group attached to phosphorus and the pseudoaxial lone pair of electrons on the oxygen atom of the carbonyl group.



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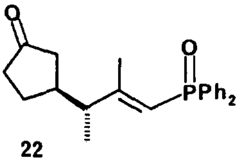

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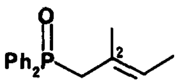

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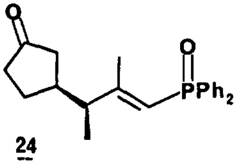

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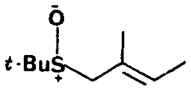

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In summary, we may note that the allyl system reacts selectively at one face of the enone in a manner which is conditioned by the configuration of the sulfoxide or phosphine oxide and the geometry and substitution pattern of the double bond. The challenge is, therefore, to prepare configurationally stable, enantiomerically pure allylic sulfoxides and phosphine oxides, and thus to extend these novel reactions to the preparation of enantiomerically pure conjugate addition products.

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References and Notes

(1) Binns, M.R.; Haynes, R.K.; Katsifis, A.; Schober, P.A.; Vonwiller, S.C., preceding communication.

(2) Iwai, K.; Kosugi, H.; Uda, H.; Kawai, M. Bull. Chem. Soc. Jap. 1977, 50, 242.

(3) This contrasts with other diastereoselective or enantioselective processes involving sulfoxides, where the presence of, for example, aryl substitutents appear essential for attainment of the stereoselective process: Posner, G.H.; Mallamo, J.P.; Hulce, M.; Frye, L.L. J. Am. Chem. Soc. 1982, 104, 4180; Posner, G.H.; Hulce, M. Tetrahedron Lett. 1984, 25, 379.

(4) Lithium cation complexation of the carbonyl oxygen will increase the AO coefficient at C-1 relative to that at C-2 : Sauvetre, R.; Roux-Schmitt, M.-C.; Seyden-Penne, J. Tetrahedron 1978, 2135. In figure 1, association of Li^+ with the $2p_z$ orbital on the sulfoxide oxygen and the enone HOMO is assumed, but is omitted for clarity.

(5) Note that TS 16 corresponds to an "exo" orientation of the allylic carbanion with respect to the enone.

(6) Hambley, T.W.; Haynes, R.K.; Vonwiller, S.C., unpublished work. Details of the determination, including a structural commentary, atom coordinates, geometry, thermal and hydrogen atom parameters are available on request.

(7) The structures of 22 and 24 follow from highfield ^1H NMR NOE experiments which indicate their (E)-geometry, and from an X-ray crystal structure determination of the conjugate addition product obtained from an (E)-crotyldiphenylphosphine oxide derivative, as will be reported separately.

(8) Oxidation of this mixture (m-CPBA, CH_2Cl_2, 0°) gave a sulfone mixture which consisted of the same number of diastereomers, in the same ratio.

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