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THE DIASTEREOSPECIFIC APROTIC CONJUGATE ADDITION REACTIONS OF CARBANIONS DERIVED FROM ALLYLIC SULFOXIDES AND ALLYLIC PHOSPHINE OXIDES.

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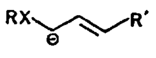
Summary: The title carbanions undergo conjugate addition to cyclic enones in THF to deliver vinylic sulfoxides and vinylic phosphine oxides as single diastereomers.

The carbanions 1 and 3 derived from allylic sulfides[1] and sulfones[2] undergo kinetically-controlled conjugate addition to 2-cyclopenten-1-one in THF at -78° in the presence of HMPA to give diastereomeric mixtures of the allylic sulfides 4 and sulfones 6. Those examples of conjugate addition reactions of allylic sulfoxide carbanions 2 thus far reported indicate that such carbanions display a markedly different regiochemical behaviour in delivering the vinylic sulfoxides 5.[1a,3] As, quite obviously, electronic effects cannot account for the anomalous behaviour of the sulfoxide carbanions, we have studied in some detail the aprotic conjugate addition reactions of these, and related carbanions to transoid enones, and herewith report our results.

Deprotonation (LDA, 1-1.2 equiv) of a mixture of (*E*)-1-(benzenesulfinyl)-2-octene 7 containing 15% of the (*Z*)-isomer 8[4] in THF at -78° gave a bright yellow solution which after 5 min was treated with 4-*tert*-butoxycyclopent-2-en-1-one. Quenching of the reaction mixture after a further 2 min gave the (*E*)-vinylic sulfoxides 9 and 10 (9:10 = 83:17, 80% overall). On the other hand, a mixture of the (*Z*)-sulfoxide 8 containing 17% of the (*E*)-isomer 7[4] gave a mixture of 9 and 10 in which now 10 was predominant (10:9 = 79:21, 79% overall). Remarkably, each of 9 and 10 is formed as a *single diastereomer*,[5] and given the experimental error associated with the measurement of the *E*:*Z* ratios in the starting sulfoxide mixtures,[4] it is clear that 9 arises almost exclusively from the (*E*)-sulfoxide 7, and 10 from the (*Z*)-sulfoxide 8. Also occasionally isolated from reaction mixtures whenever excess LDA was used to deprotonate the sulfoxide mixture rich in the (*E*)-isomer 7, were small amounts of the highly crystalline bis-adduct 12, whose relative configuration was established by an X-ray structural determination.[6] This product must arise by carbonyl addition of the dianion 11, generated from the enolate of 9 produced in the conjugate addition by the excess LDA, to the enone,[7] and hence its relative configuration must reflect that of 9. Thus, as depicted, 9 has a relative configuration of S^* at sulfur. That 10 possesses the *same* configuration at sulfur follows from the structure of the product obtained from another (*Z*)-allylic sulfoxide, and from mechanistic considerations, as is described in the accompanying communication. Thus, 9 and 10 differ in configuration at the allylic carbon atom, which was also verified by the formation of the respective vinylic sulfides 13 and 14 obtained upon deoxygenation (Bu_3PI_2-HMPA-ether, 20°; 70-75%)[8] of each of 9 and 10.[9]



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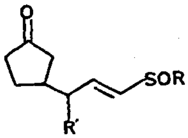
2 X = SO

3 X = SO_2



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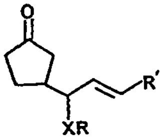
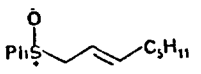


4 X = S

6 X = SO_2



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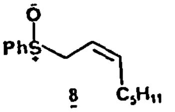

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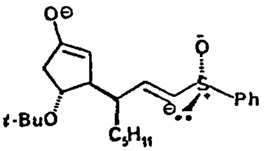

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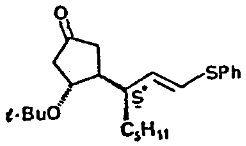

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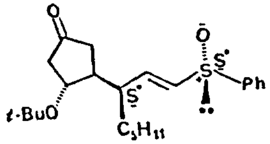

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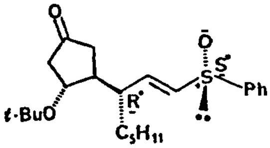

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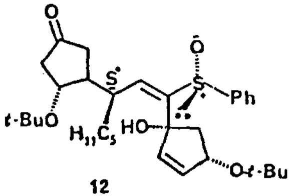

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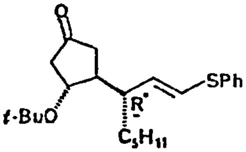

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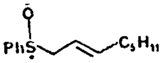
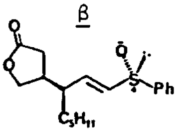
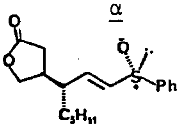
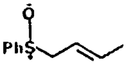
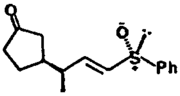
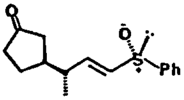
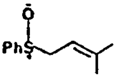
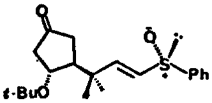
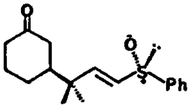
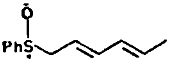
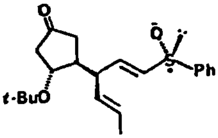
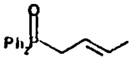
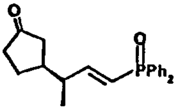
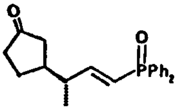
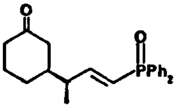
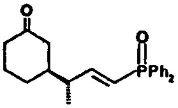
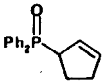
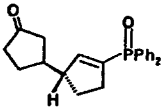
As set out in Table 1, other allylic sulfoxide carbanions and cyclic enones react in similar fashion. The prenyl sulfoxide (entry 3) is noteworthy in giving the corresponding vinylic sulfoxide, which possesses a quarternary allylic centre, as the sole product. The carbanion of the dienylic sulfoxide (entry 5) also reacts exclusively through the γ-carbon atom to give the corresponding (*E*,*E*)-1,4-diene. No other products were isolated from the reaction of this carbanion with the enone. Noteworthy also is the finding that carbanions derived from allylic phosphine oxides and butyllithium in THF at -78° react in the same way to give the corresponding vinylic phosphine oxides (entries 6-8), again as *single diastereomers*. In contrast to allylic sulfoxides, allylic phosphine oxides are not prone to geometric isomerisation, and it was thus possible to measure accurately the *E*:*Z* ratios of the starting phosphine oxides and to correlate these with configurations of the allylic carbon atoms in the products. As may be gauged from the Table, no "crossover" was able to be detected. Increasing the ring size of the enone to six-membered had the effect of depressing formation of the conjugate addition product at the expense of formation of 1,2- (or carbonyl) addition products in the case of an allylic sulfoxide (entry 4), but *not* in the case of an allylic phosphine oxide (entry 7) where only the conjugate addition product was obtained. In all cases, reactions were complete upon addition of the enones to the carbanion solutions, and in certain cases, were able to be conducted in diethyl ether, and proceeded at temperatures as high as 0° without detectable loss of diastereoselection. In no case was HMPA necessary for the conjugate addition, and indeed, its presence has a deleterious effect upon overall yields of the products.[10]

The reactions are thus remarkable in delivering products of such high diastereochemical purity in a situation where the intercession of the conventional six-membered cyclic transition state held to be involved in other reactions of allylic carbanions with carbonyl compounds is clearly impossible. The evolution of a model to account for this diastereoselection is outlined in the accompanying communication.

Acknowledgement. We thank the Australian Research Grants Scheme for support of this work.

Table 1. Reactions of Allylic Carbanions with α-Enones

Entry	Carbanion from	Enone^{a}	Products	Ratio	Yield(%)^{b}
				β:α	
1.	 E:Z = 85:15	B	β  β α  α	83:17	83
2.	 E:Z = 80:20	C	 β  α	80:20	64 74 (-10°)
3.		A		-	80
4.	"	D		-	50
5.		A		-	63
6.	 E:Z = 0:100	C	 β  α	0:100	80
7.	" E:Z = 95:5	D	 β  α	95:5	60
8.		C		-	63

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[a] A = 4-tert-butoxy-2-cyclopenten-1-one; B = γ-crotonolactone : C = 2-cyclopenten-1-one; D = 2-cyclohexen-1-one. [b] From reactions at -78° except where indicated.

References and Notes

(1) (a) Binns, M.R.; Haynes, R.K.; Houston, T.L.; Jackson, W.R. *Tetrahedron Lett.* 1980, 21 573. (b) Binns, M.R.; Haynes, R.K. *J. Org. Chem.*, 1981, 46, 3790.

(2) (a) Krauss, G.A.; Frazier, K. *Synth. Commun.* 1978, 8, 483; (b) Hirama, M. *Tetrahedron Lett.* 1981, 22, 1905.

(3) (a) Vasileva, L.L.; Melnikova, V.I.; Gainullina, E.T.; Pivnitskii, K.K. *Zh. Org. Khim.* 1980, 16, 261 (b) Binns, M.R.; Haynes, R.K.; Houston, T.L.; Jackson, W.R. *Aust. J. Chem.* 1981, 34, 2465 (c) Nokami, J.; Toshio, O.; Iwao, A.; Wakabayashi, S. *Bull. Chem. Soc. Jap.* 1982, 55, 3043.

(4) The isomer ratios in the starting allylic sulfoxide mixtures were established by ^{1}H NMR analysis at 100 MHz. Attempts to analyse the mixtures by HPLC were unsuccessful, presumably because incipient resolution of each mixture into geometric isomers on the column competed with equilibration of each isomer via the sulfoxide-sulfenate rearrangement. While each of the (E)- and (Z)-isomers was able to be prepared essentially free of the other isomer, manipulation of each compound led to formation of appreciable amounts of its geometric isomer. The (Z)-isomer in particular is prone to isomerisation, and its preparation, and subsequent manipulation were carried out, where possible, below 5°.

(5) Products were purified by flash chromatography in order to remove the small amounts ($\cong$5%) of unreacted starting materials prior to HPLC and 400 MHz ^{1}H NMR analyses.

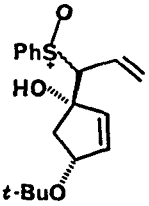
(6) Binns, M.R., Haynes, R.K., and White, A.H., in preparation. Details of the determination, including a structural commentary, atom coordinates, geometry, thermal and hydrogen atom parameters are available on request.

(7) The yield of 12 may be increased to 75% by adding firstly 1 equiv. BuLi to the enolate of 9 produced in the conjugate addition at -78° and then 1 equiv. of 4-*tert*-butoxycyclopentenone, a result which is of no small synthetic consequence. Further examples of the reactions of these novel dianions will be described shortly.

(8) The deoxygenating ability of Bu_3PI_2 has been described elsewhere: Haynes, R.K.; Holden, M. *Aust. J. Chem.* 1982, 35, 517. In combination with HMPA (1-2 equiv.) the reagent serves as a considerably milder and more efficient deoxygenating agent of sulfoxides than most of the vast number of other reagents prescribed for this purpose.

(9) In order to assure ourselves that ^{1}H NMR spectroscopic and HPLC analyses were sufficient to establish diastereochemical purities, we reoxidized the sulfide 13 (*m*-CPBA, CH_2Cl_2, -78°) to a sulfoxide mixture containing equal amounts of 9 and the "unnatural" epimer, whose presence in the mixture was clearly evident through use of the foregoing methods.

(10) There is no doubt that kinetic control operates in the formation of these products. The reactions are extremely rapid, even at -100°, and we have been unable to intercept any possible intermediates. The lithium alkoxide of the sulfoxide i (obtained from the corresponding sulfide) which can in principle rearrange by a [3,3]-sigmatropic shift to a vinyl sulfoxide, is stable under the reaction conditions.



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