Asymmetric Induction in the Cope Rearrangement

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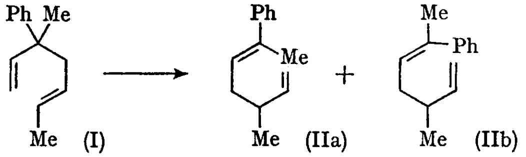
IMPLICIT in the tightly ordered transition state for the Cope rearrangement of 1,5-dienes, characterized by large negative entropies of activation,[1] is the expectation that a high degree of stereospecificity should attend the formation of new double bonds and asymmetric centres. A convincing demonstration of geometrical stereospecificity has been reported[2] and used to prove the preference for a four-centre cyclohexane chair-like conformation in the transition state. We now report the first study of *optical* stereospecificity, which augments previous results and provides a quantitative assessment of conformational preferences.

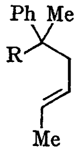
trans-3-Methyl-3-phenylhepta-1,5-diene (I), prepared from aldehyde (III) by condensation with methylenetriphenylphosphorane, rearranged quantitatively at 250° to an 87 : 13 mixture of *cis*- and *trans*-3-methyl-6-phenylhepta-1,5-diene (IIa) and (IIb). The structures of (IIa) and (IIb) are in accord with their infrared, n.m.r., and ultraviolet spectra; the latter establish[3] the double-bond geometry; (IIa): λ_{max} 249 nm, log ϵ 4·09; (IIb): λ_{max} 235 nm, log ϵ 3·78. Separate experiments showed that (IIa) and (IIb) are not interconverted at 250°.

Optically active (I) was prepared by resolution of acid (IV) with dehydroabietylamine, conversion of (IV), $[\alpha]_D^{22}$ + 40·3°, into (+)-(III) by lithium aluminium hydride reduction followed by oxidation with Sarett reagent, and use of (+)-(III) in the Wittig synthesis. The absolute configuration of (+)-(IV) was established by ozonolysis to

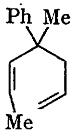
(+)-2-methyl-2-phenylsuccinic acid, which was then independently related to (*R*)-(−)-2-methyl-2-phenylbutyric acid. Since the absolute configuration and maximum rotation of the latter acid are known,[4] this sequence of correlations showed that (I), $[\alpha]_{\mathrm{D}}^{22}$ + 13·7°, has the (*R*)-configuration and an optical purity of 95%.

Cope rearrangement of (*R*)-(+)-(I) gave (IIa) and (IIb), which proved to be optically active. Ozonolysis of (IIa), $[\alpha]_{\mathrm{D}}^{22}$ + 8·27°, afforded (*S*)-(−)-methylsuccinic acid, $[\alpha]_{\mathrm{D}}^{22}$ − 14·1°, while ozonolysis of (IIb), $[\alpha]_{\mathrm{D}}^{22}$ + 14·9°, led to (*R*)-(+)-methylsuccinic acid, $[\alpha]_{\mathrm{D}}^{22}$ + 13·8°, showing that (+)-(IIa) and (+)-(IIb) have opposite configurations at the new asymmetric centre as well as at the double bond. Based on the maximum rotation of methylsuccinic acid, (IIa) and (IIb) are formed in optical purities of 91 and 89%, which corresponds to an optical yield of 94—96% in the Cope rearrangement.





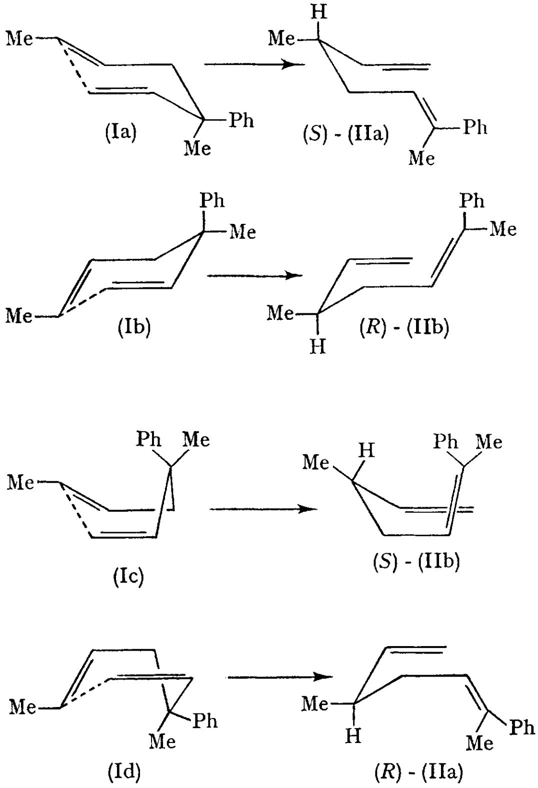
(III) R=CHO
(IV) R=CO_2H



(V)

The nearly quantitative transfer of asymmetry to the newly developing asymmetric centre of (IIa) and (IIb) may be taken as strong additional evidence for a concerted cyclic rearrangement. In addition, the results may be used to deduce the preferred reaction geometry. The four possible transition-state conformations resembling puckered cyclohexane rings are shown in the Scheme; each leads to a unique product. The virtually exclusive formation of (*S*)-(+)-(IIa) and (*R*)-(+)-(IIb) confirms the preference for chair conformations (Ia) and (Ib) and places an upper limit of 2—3% on the contribution of boat conformations (Ic) and (Id). Finally, the 87 : 13 preference for (IIa), corresponding to a free-energy difference of about 2 kcal./mole between transition states (Ia) (phenyl equatorial) and (Ib) (phenyl axial), lends confidence to the prediction of favoured transition-state conformations in four-centre thermal rearrangements on the basis of cyclohexane conformational analysis.

Similar results have been obtained in the Cope rearrangement of optically active (V), and will be reported in detail later.



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(*Received, May 18th,* 1967; *Com.* 485.)

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[1] For a recent Review, see: S. J. Rhoads, in "Molecular Rearrangements", Part 1, ed. P. de Mayo, Interscience, New York, 1963, p. 655.

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[4] D. J. Cram, *J. Amer. Chem. Soc.*, 1952, **74**, 2149; S. Mitsui, S. Imaizumi, Y. Senda, and K. Konno, *Chem. and Ind.*, 1964, 233.