Mechanism of Hydride-induced Cyclopropane Formation from Allylic Alcohols. Stereochemistry of Ring Closure

By M. J. JORGENSON* and A. F. THACHER

(*Department of Chemistry, University of California, Berkeley, California* 94720)

Summary High sensitivity towards *m*-substituents ($\rho = +3{\cdot}8$) in cinnamyl alcohols and the stereochemistry of ring closure in 2-methyl-3-phenylprop-2-en-1-ol(IV), 2,3-dimethyl-3-phenylprop-2-en-1-ol, and in 4-phenylbut-3-en-2-ol(V), support the intervention of carbanions in the phenylcyclopropane yielding 1,3-elimination of the organoaluminium intermediate (I).

CURRENT interest in 1,3-eliminations[1] prompts us to report our conclusions concerning the mechanism and stereochemical course of the transformation of cinnamyl alcohols to phenylcyclopropanes, effected by lithium aluminium hydride.[2]

Conversion of cinnamyl alcohol into the organoaluminium intermediate (I) occurs more rapidly, by a factor estimated to be about 10^{10}, than cyclopropane formation; rates of production of cyclopropane, therefore, correspond to the rates of transformation of (I) to (II). When cinnamyl alcohol and its *m*-fluoro- and *m*-methoxy-derivatives were reacted with lithium dimethoxyaluminum hydride, the appearance of cyclopropane (II; X = H, F, OMe) followed a unimolecular rate law. Rate constants (Table I) correlate well with σ inductive parameters, affording a ρ value of

Formation of phenylcyclopropanes from m-*substituted cinnamly alcohols*[a]

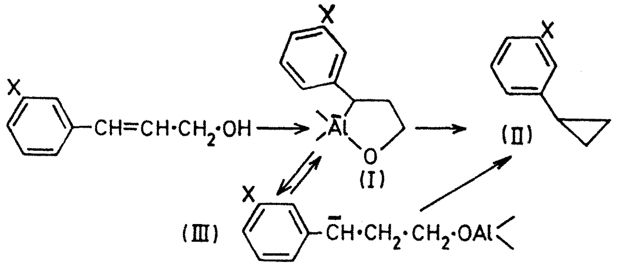
Substituent	10^6k, sec.$^{-1}$	T, °c
H	$0{\cdot}665 \pm 0{\cdot}06$[b]	80·0°[c]
m-OMe	1·47	80·0°
m-F	12·2	80·0°
H	0·306	70·0°[c]

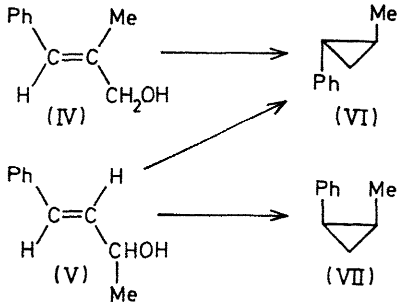
[a] A 100% excess of lithium dimethoxyaluminum hydride in 1,2-dimethoxyethane was employed. The conversion was found to be quantitative, as determined by internal standard. Kinetic studies were carried out in sealed tubes.

[b] Duplicate runs.

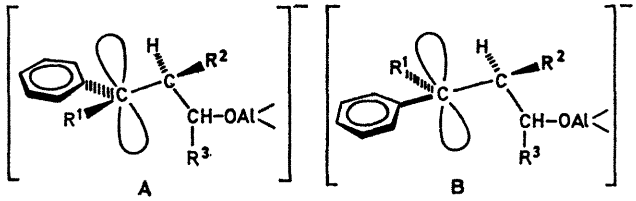
[c] Calculated activation parameters: $\Delta F\ddagger$ 26·1 kcal; $\Delta H\ddagger$ 16·1 kcal; $\Delta S\ddagger$ − 28·6 e.u.

+3·8. The high sensitivity to ring substituents is indicative of a highly developed carbanion character in the transition state and militates against a concerted mechanism [*i.e.* (I) to (II)]. The intermediacy of carbanion (III) is also supported by the strong acceleration caused by the β-phenyl substituent in the formation of 1,1-diphenylcyclopropane from β-phenylcinnamyl alcohol.[3]





The stereochemistry of the cyclopropane products also corroborates a carbanion mechanism. Both *cis*- and *trans*-$\alpha\beta$-dimethylcinnamyl alcohol yielded only *cis*-1,2-dimethyl-1-phenylcyclopropane.[2] More significantly, alcohol (IV) yielded exclusively *trans*-2-methyl-1-phenylcyclopropane (VI), whereas alcohol (V) produced (VI) and (VII) in a 1 : 1 ratio.† These stereochemical results are best interpreted in terms of steric effects present in the transition states of each reaction. In transition states A and B stabilization of the negative charge by the phenyl group is crucial in facilitating ring closure.‡ In transition state B the adjacent methyl group, present both in $\alpha\beta$-dimethylcinnamyl alcohol (R^1 = R^2 = Me; R^3 = H) and in α-methylcinnamyl alcohol (R^1 = R^3 = H; R^2 = Me), will interfere with the conformational freedom of the phenyl group. If the requisite orthogonal alignment of the benzene ring with respect to the carbanion is sterically precluded, resonance stabilization of the negative charge as a benzyl anion will not be feasible. This steric inhibition of resonance induces ring closure for $\alpha\beta$-dimethylcinnamyl alcohol and for α-methylcinnamyl alcohol (IV) to occur exclusively *via* transition state A. In the absence of the eclipsing effects by the vicinal methyl group, no such preference is exhibited. Thus, in the case of alcohol (V) (R^1 = R^2 = H; R^3 = Me); cyclopropane formation occurs indiscriminately from both transition states.§



The observed selectivity is another case of the operation of the "overlap control" factor[5] in carbanion stabilization. The importance of this feature in cyclopropane formation is underlined in the above examples.[6]

This work was supported by grants from the American Academy of Arts and Sciences and from the Petroleum Research Fund of the American Chemical Society.

(*Received, July 4th*, 1969; *Com.* 978.)

---

† Geometrical assignments were made by comparison with published spectral data (J. P. Freeman, *J. Org. Chem.*, 1964, **29**, 1379.); the two isomers exhibit distinct and characteristic differences in their n.m.r. spectra.

‡ The transition states are depicted as resembling carbanions. However, if bond making has proceeded significantly, the eclipsing interactions under consideration will be more severe.

§ Whether ring closure takes place with inversion [1b,c] or retention [1a] of configuration at the carbinol carbon will be established in subsequent studies.

[1] (a) A. Nickon and N. H. Werstiuk, *J. Amer. Chem. Soc.*, 1967, **89**, 3914; (b) F. G. Bordwell, B. B. Jarvis, and P. R. Corfield, *ibid.*, 1968, **90**, 5298; (*c*) J. A. Marshall and J. H. Babler, *Chem. Comm.*, 1968, 993.

[2] M. J. Jorgenson and A. W. Friend, *J. Amer. Chem. Soc.*, 1965, **87**, 1815; M. J. Jorgenson and A. F. Thacher, paper presented at the 153rd National Meeting of the American Chemical Society, Miami Beach, Florida, April, 1967.

[3] M. J. Jorgenson and A. F. Thacher, *Org. Synth.*, 1968, **48**, 75.

[4] H. E. Zimmerman, L. Singer, and B. S. Thyagarajan, *J. Amer. Chem. Soc.*, 1959, **81**, 108.

[5] For another case of stereoselective cyclopropane formation, interpreted in similar terms, see C. L. Bumgardner and H. Iwerks, *J. Amer. Chem. Soc.*, 1966, **88**, 5518.