

THE RELATIVE RATES OF CHROMATE OXIDATION
OF STEREOISOMERIC cis-CARANOLS

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Publications⁽¹⁻⁶⁾ from several schools giving the correct stereochemistry of the caranes, caranones and caranols have prompted us to investigate the relative rates of chromic acid oxidation of the caranols as an additional means of distinguishing between these alcohols and particularly between epimeric pairs. Increase in rate of oxidation is obtained with increase in steric crowding of the OH group.⁽⁷⁾

Although the precise configurations and even approximate conformations of the caranols (I - VI) are now known with certainty,^(4,5,6) the conformational mobility of these fused cyclopropyl-cyclohexane molecules is evidently greater than that of simpler cyclohexane derivatives. The most probable conformations are however the half-chair forms (Ia - VIa), analogous to the cyclohexenes.

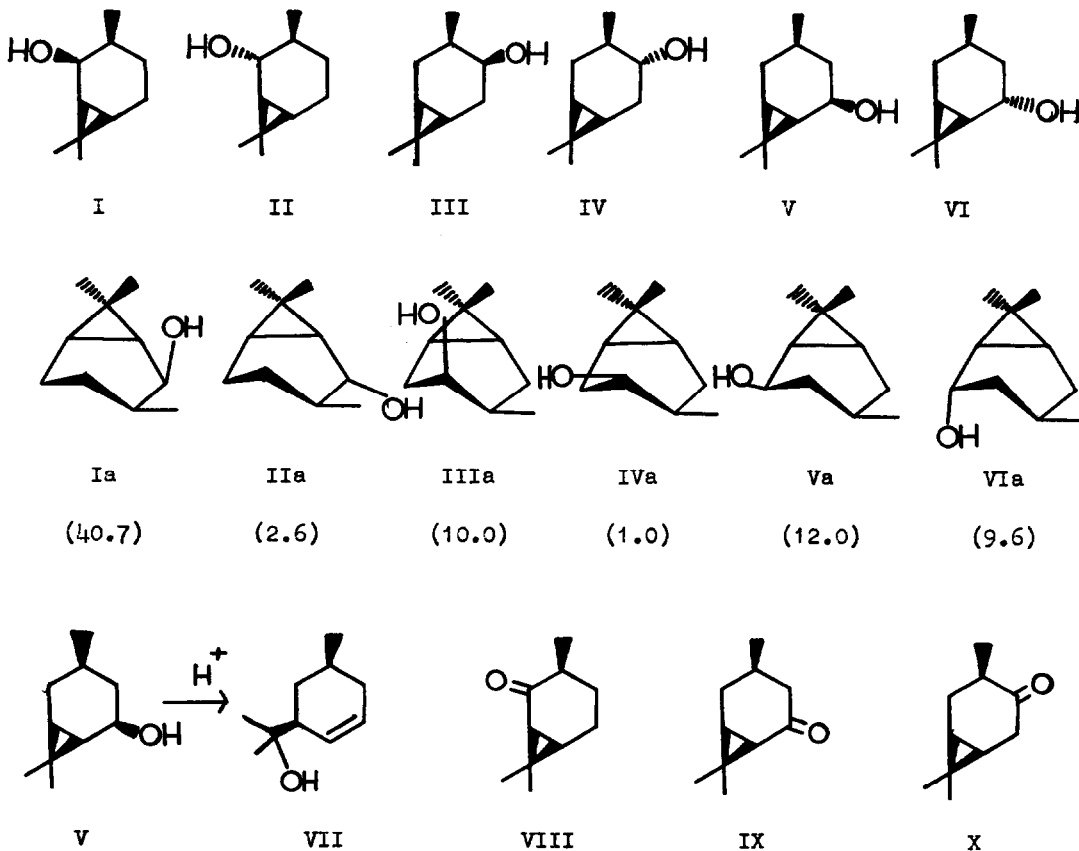
Unlike the cyclohexanols,⁽⁸⁾ the conformational energies relevant to the caranols are quantitatively unknown and comparisons of the relative stabilities of different isomers can, at present, be obtained only qualitatively from a study of molecular models.

A further complicating factor in the acid chromate oxidations of the α -cyclopropyl carbinols (I), (II), (V) and (VI) is the possibility of a competing acid-catalysed allylic-type rearrangement to tertiary alcohols, which has been demonstrated in the conversion of (V) to (VII).⁽⁹⁾ This reaction competed seriously with the oxidation in 75% aqueous acetic acid⁽¹⁰⁾ but under our modified conditions (1.7×10^{-2} molar in CrO_3 , 0.2 molar in alcohol, pH = 2.24

in buffered 75% v/v aqueous acetic acid at 25°) the rate of the rearrangement reaction became negligible relative to the oxidation rate. The pseudo-first order rate constants $k^1 = \frac{k_{\text{experimental}}}{[\text{ROH}]}$ were obtained by plotting $\log [\text{HCrO}_4^-]$ against time assuming the previously demonstrated rate equation. ⁽¹¹⁾

$$-\frac{d[\text{HCrO}_4^-]}{dt} = k[\text{ROH}][\text{H}^+][\text{HCrO}_4^-]$$

A linear relationship was obtained in all cases. The chromate concentration was followed spectrophotometrically by automatic measurement of the optical density of the reaction solution at 3480 Å. The oxidation rates relative to (-)-cis-caran-trans-4-ol, taken as unity, are shown under the formulae (Ia - VIa).



Detailed interpretation of the relative rates must await further investigations, now in progress, but it is clear that the results so far obtained bear out the recently published stereostructures of the alcohols. Two reinforcing or opposing factors are important in considering the results:

- (1) The cis or trans configuration of the OH group relative to the cyclopropyl and methyl groups.
- (2) The axial* or equatorial* disposition of the OH group.

Greater steric overcrowding is associated with cis rather than trans configurations and axial (or pseudo-axial) rather than equatorial (or pseudo-equatorial) dispositions. Thus the following four possible dispositions of the OH group of increasing steric strain exist:

- | | |
|--------------------------------|-------------------------|
| (1) <u>trans</u> , equatorial* | smallest crowding |
| (2) <u>trans</u> , axial* | } intermediate crowding |
| (3) <u>cis</u> , equatorial* | |
| (4) <u>cis</u> , axial* | greatest crowding |

It is impossible to decide, a priori, whether the system (2) or (3) involves the greater steric overcrowding.

In the first pair of epimers (I and II), the more crowded cis, pseudo-axial isomer (I) reacts approximately sixteen times as fast as its epimer (II) which has a trans, pseudo-equatorial OH group. The alcohol (III) with cis axial OH likewise shows an enhanced rate over its epimer (IV), with trans equatorial OH, of the same order of magnitude (x 10). Inspection of models of the final pair (V and VI) shows that it is difficult to predict even qualitatively the relative rates of oxidation. Thus in compound (V) although the OH group is cis it occupies the pseudo-equatorial position whilst in its epimer (VI) the OH group, although pseudo-axial, is trans to the other substituents. It would seem from the similarity of rates of oxidation of (V) and (VI) that the crowding effects on the OH group of (a) a pseudo-equatorial-cis- combination and (b) a pseudo-axial-trans combination are nicely balanced.

(* or pseudo-axial or equatorial)

Finally a comparison of the three groups of epimers reveals that (III and IV) have lower rates than would at first be expected. A reasonable explanation of this is that in the pairs (I and II) and (V and VI) the oxidation rates are enhanced because of the incipient conjugated cyclopropyl ketone chromophore which can influence the stability of the transition state^(c.f.12) in the rate-determining breakdown of the chromate ester.⁽¹³⁾ This conjugation, for which there is spectroscopic evidence⁽⁴⁾ in the ketones (VIII) and (IX) is, of course, absent in (X).

REFERENCES

1. K. Gollnick, Tetrahedron Letters, No. 3, 327 (1966).
2. K. Gollnick, S. Schroeter, G. Ohloff, G. Schade and G.O. Schenck, Annalen, 687; 14 (1965).
3. W. Cocker, P.V.R. Shannon and P.A. Staniland, Tetrahedron Letters, No. 13, 1409 (1966).
4. W. Cocker, P.V.R. Shannon and P.A. Staniland, J. Chem. Soc., (C), 485 (1967).
5. S.P. Acharya and H.C. Brown, J. Am. Chem. Soc., 89, 1925 (1967).
6. H.C. Brown and A. Suzuki, J. Am. Chem. Soc., 89, 1933 (1967).
7. H.O. House, "Modern Synthetic Reactions", p.83, W.A. Benjamin Inc. New York, Amsterdam, 1965.
8. E.L. Eliel, Angew. Chem. internat. edit., 4, 761 (1965).
9. W. Cocker, P.V.R. Shannon and P.A. Staniland, J. Chem. Soc., (C), 915 (1967).
10. J.C. Richer and C. Gilardeau, Can. J. Chem., 43, 538 (1965).
11. F.H. Westheimer and A. Novick, J. Chem. Phys., 11, 506 (1943).
12. H. Kwart and P.S. Francis, J. Am. Chem. Soc., 81, 2116 (1959).
13. F.H. Westheimer and N. Nicolaides, J. Am. Chem. Soc., 71, 25 (1949).