Table I. TIC Parameters and Ambient Temperature Kinetic Deuterium Isotope Magnitudes in the Cr(VI) Oxidation[a] of Di-*tert*-butylcarbinol

$[H^+]^h$	$-[(\Delta E_a)_D{}^H]^b$	$[A_H/A_D]^b$	R^c	$(k_H/k_D)_{25°}{}^{b,d}$	T (°C) at which $k_H/k_D = 1$
0.1^e	3.0	0.066	0.997, 0.999	10.5	283
3.5^f	1.2	0.69	0.997, 0.998	5.2	1340
5.9^g	3.6	0.0023	0.994, 0.998	1.0	25

[a] See ref 1 for a description of the kinetic conditions and treatment of data. [b] Defined by the relationship $k_H/k_D = A_H/A_D \exp(-(\Delta E_a)_D{}^H/RT)$, where A is the usual Arrhenius frequency factor, and $(\Delta E_a)_D{}^H$ is the activation energy difference between hydrogen and deuterium substrates in the Cr(VI) oxidation. The units of $(\Delta E_a)_D{}^H$ are kcal/mol. [c] R = the correlation coefficient. [d] The value of k_H/k_D at 25°. [e] In 50% aqueous acetic acid, $[Cr(VI)]_0 = 8 \times 10^{-4}$ M, $[NaClO_4] = 0.2$ M. [f] In 50% aqueous acetic acid, $[Cr(VI)]_0 = 8 \times 10^{-4}$ M, $[LiClO_4] = 0.16$ M. [g] In 40% aqueous acetic acid, $[Cr(VI)]_0 = 8 \times 10^{-4}$ M, $[LiClO_4] = 0.16$ M. [h] Concentration of perchloric acid in moles per liter in the reaction medium.

now be contended that a primary kinetic deuterium isotope effect determined at a single temperature is substantially meaningless. Clearly, k_H/k_D of any magnitude expressed at a given temperature cannot be correlated with the extent of bond making or breaking in the transition state as has been conventional practice.[6] The TIC parameters constitute the only valid, mechanistic criterion when kinetic isotope measurements are invoked. Only this practice can provide full insight into both the nature and geometry of H-transfer transition states.

One of the principal bases for the proposal of a rate determining decomposition of chromate ester in ordinary Cr(VI) alcohol oxidations rests upon a kinetic investigation[7] of the sterically hindered 3β,28-diacetoxy-6-hydroxy-8(*H*)-12-oleane (DAHO). In these studies the observation that k_H/k_D approached 1.0 near ambient temperatures was interpreted to signify a change in mechanism from rate determining decomposition to formation of a chromate ester intermediate, brought about by the assumed operation of steric hindrance to the formation of ester. However, the justification for this assumption can now be questioned on the following grounds. (i) Tertiary alcohols, which are sterically more hindered than the secondary alcohol DAHO, are esterified[8] almost instantaneously with chromic acid. (ii) Examined with the aid of molecular models, di-*tert*-butylcarbinol is clearly no less hindered than DAHO in the availability of its -OH for esterification. (iii) The $k_H/k_D \rightarrow 1.0$ for di-*tert*-butylcarbinol cannot be related to the incidence of a mechanistic change of the nature inferred from the analogous results reported for DAHO. A more plausible interpretation is one which correlates the observed isotope effect with the occurrence of quantum mechanical tunneling in the H-transfer step of the chromate ester decomposition. Tending to support this view is a full inventory of both normal and abnormal examples, characterized by means of the TIC parameters, which will be presented in a future article[2] from these laboratories.

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(5) See, for examples, K B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).
(6) See ref 5 as well as a typical contemporary textbook, R. D. Gilliom, "Introduction to Physical-Organic Chemistry," Addison-Wesley, New York, N. Y., 1970; the following is a relevant quotation from Chapter 8 on isotope effects (p 138). "The primary isotope effect is a very useful tool to determine whether a C–H bond is broken in the rate determining step of a reaction. The observance of an isotope effect suggests the symmetry, in terms of the force constants, of the transition state. If no isotope effect is observed, the C–H bond is broken in some step other than the slow one, or else, the transition state is highly asymmetric."
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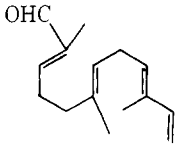
Received August 26, 1974

A Stereoselective Synthesis of α-Sinensal

Sir:

Chinese orange oil (*Citrus sinensis L.*) contains the two sesquiterpene aldehydes α-sinensal (**1**)[1] and β-sinensal (**2**),[2] which make critical contributions to the odor and taste of the fruit. Syntheses of β-sinensal (**2**)[3-6] and two stereo nonselective syntheses of the α-isomer **1**[4,6] were announced years ago, but the work described here represents the first stereorational preparation of the physiologically more important α-sinensal (**1**).



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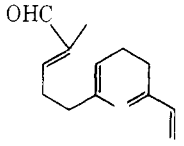

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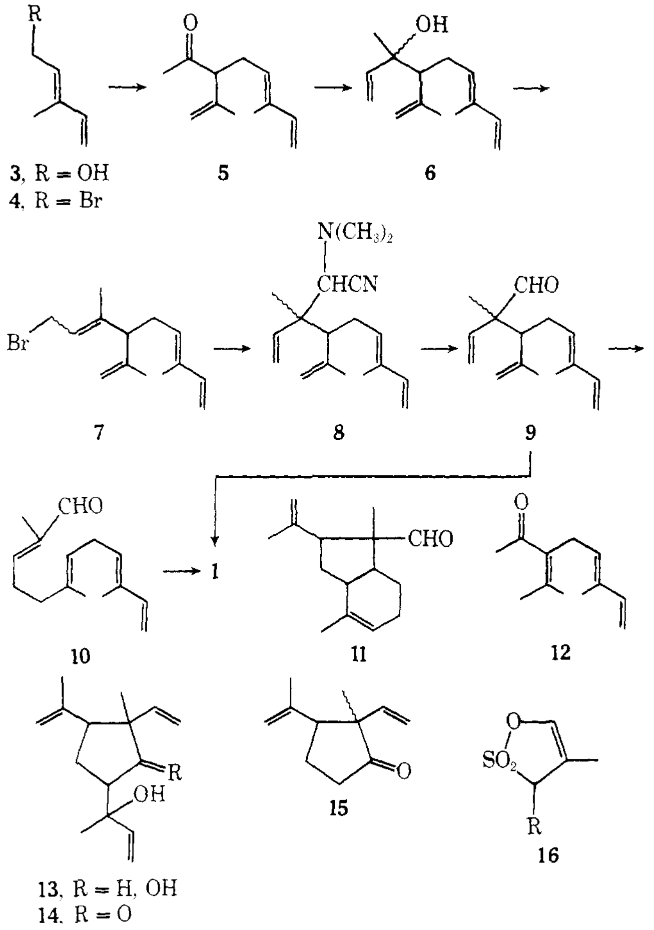
Condensation of (*E*)-3-methyl-2,4-pentadien-1-ol (**3**)[7] from semihydrogenation of the corresponding acetylene, in ether solution containing 0.05 mol equiv of pyridine with 0.4 mol equiv of phosphorus tribromide at 5°, produced the bromide **4**, bp 45° (10 mm) in 84% yield. Transformation to the ketone **5** was initiated by adding mesityloxide to a suspension of sodium amide (0.84 mol equiv) in refluxing ammonia and continued after 10 min by adding the bromide **4** (0.84 mol equiv) within 15 min at the same temperature. The ammonia was then replaced by gradual addition of ether and when the temperature of the mixture reached −10° aqueous ammonium chloride was added. The β,γ-unsaturated ketone **5**, bp 60° (0.1 mm), ir ($CHCl_3$) 1710 cm^{-1}, was isolated in 88% yield.[8] The absence of dialkylated ketones and the nearly exclusive formation of the β,γ-unsaturated isomer is remarkable[9] because an equilibrium mixture of the two ketones, **5** and **12**, contained 74% of the conjugated isomer. Steric crowding seemingly opposes proton removal necessary for both isomerization and dialkylation. Carbinol **6**, bp 67° (0.1 mm), was obtained in 84% yield from the ketone **5** and vinylmagnesium bromide in tetrahydrofuran. Phosphorus tribromide served to convert **6** to the stereochemically undefined primary bromide **7** which was alkylated directly with *N*-cyanomethyldimethylamine[10] in tetrahydrofuran (16 hr, 20°). Addition of an equimolar quantity of potassium *tert*-butoxide at −30° caused nearly instantaneous transformation to the diastereomeric nitriles **8** undoubtedly by [2,3] sigmatropic rearrangement of the intermediate ammonium ylide.[11-13] Aqueous oxalic acid[12] failed to give the aldehyde **9**, and it and the nitrile **8** were transformed to a crystalline mixture of diastereomeric diols **13**, mp 70-72°. Their structures were confirmed by Jones oxidation to **14** ir ($CHCl_3$) 3500 and 1720 cm^{-1}, followed by retroaldol cleavage to the two cy-

Scheme I



clopentaneous **15**, ir ($CHCl_3$) 1740 cm^{-1}. Hydrolysis of the nitrile **8** with 2 *N* ethanolic sodium hydroxide[11] (90 min, reflux) did afford aldehyde **9** but the propensity of α-disubstituted aldehydes to undergo the Cannizzaro reaction in alkali led us to search for a superior method. The aminonitrile **8** was hydrolyzed within 5 min when ethanol solutions were refluxed with slightly less than equimolar amounts of $FeSO_4 \cdot 7H_2O$ or preferably with the more soluble $CuSO_4 \cdot 5H_2O$. Filtration followed by distillation gave a 6:4 mixture of diastereomeric aldehydes **9** (nmr δ 9.35 (s) and 9.4 (s)), bp 65° (0.1 mm), in over 80% yield. Cupric and ferrous ions presumably remove cyanide from the aminonitrile–iminium cyanide equilibrium by precipitating insoluble $[Cu(CN)_4]^{3-}$ or $[Fe(CN)_6]^{4-}$ salts.

Cope rearrangement of **9** in refluxing xylene (40 min) produced a 4:6 mixture of the *E*-isomer **1** (nmr δ 9.3 (s)) and the *Z*-isomer **10** (nmr δ 10.1 (s)) (Scheme I).[14] Quantitative isomerization of the latter to the more stable *E*-isomer **1** was achieved by heating the mixture over anhydrous sodium carbonate (xylene–methanol 1:1, 18 hr, reflux) or more interestingly by storing xylene solutions containing 1% gaseous SO_2 at 20° for 20 hr. This seemingly novel isomerization may proceed *via* the intermediate **16**. Gas chromatography revealed crude synthetic α-sinensal (**1**) to contain 10% of the bicyclic aldehydes **11** resulting from intramolecular Diels–Alder reaction of **9** and approximately 5% of what may be the Δ^6-cis isomer formed in the Cope rearrangement.[15] Infrared, mass, ultraviolet, and proton spectra of distilled material, bp 82° (0.1 mm), were identical with those of natural α-sinensal (**1**) and a mixture of the synthetic 2,4-dinitrophenylhydrazone mp 98–100° and the "natural" derivative mp 100–102° melted at 98–101°. Preparative runs gave α-sinensal (**1**) in 44% yield from alcohol **6.**

Acknowledgments. We are indebted to Firmenich S. A. Geneva for generous financial support, to Drs. A. Brossi and L. Foley, Hoffmann-LaRoche Inc., Nutley, N.J., for supplies of the starting material, and to Mrs. R. Lüthy for technical assistance.

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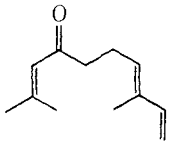

i

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Received August 8, 1974

Acid Homoketonization with Inversion of Configuration. A Dramatic Effect of Water in Control of Stereochemistry[1]

Sir:

Homoketonizations in deuterated media provide generally useful ways for site-selective and stereoselective placement of deuterium at β,[2-7] γ,[8-10] and δ[11,12] positions with respect to carbonyl groups. The stereochemistry of these ring openings can differ markedly in alkaline and acid media.

In alkaline solutions, studies on a variety of substrates have revealed that homoketonizations can proceed with high inversion,[2,3,6] with high retention,[4,5,8-12] or with low stereospecificity[4,5,7,11] depending on the structure of the substrate and on the reaction medium. Mechanistic interpretations have been proposed but have been of limited predictive value for new structural types, especially in constrained polycycles. Although high stereospecificity in alkaline homoketonizations can sometimes be diminished by solvent changes, no case has yet been found where it can be completely reversed by change in the alkaline solvent system.[13]