

## References and Notes

- (1) Y. T. Lee, P. R. LeBreton, J. D. McDonald, and D. R. Herschbach, *J. Chem. Phys.*, **51**, 455 (1969).
- (2) D. Beck, F. Engelke, and H. J. Loesch, *Ber. Bunsenges. Phys. Chem.*, **72**, 1105 (1968).
- (3) J. M. Parson, K. Shobatake, Y. T. Lee, and S. A. Rice, *Discuss. Faraday Soc.*, **55**, 344 (1973).
- (4) J. T. Cheung, J. D. McDonald, and D. R. Herschbach, *J. Amer. Chem. Soc.*, **95**, 7889 (1973).
- (5) J. M. Farrar, Ph.D. dissertation, University of Chicago, Chicago, Illinois, 1974.
- (6) R. A. Marcus, *J. Chem. Phys.*, **20**, 359 (1952).
- (7) Y. T. Lee, J. D. McDonald, P. R. LeBreton, and D. R. Herschbach, *Rev. Sci. Instrum.*, **40**, 1402 (1969).
- (8) V. I. Vedenev, L. V. Gurvich, V. N. Kondrat'yev, V. A. Medvedev, and Ye L. Frankevich, "Bond Energies, Ionization Potentials and Electron Affinities," St. Martins Press, New York, N.Y., 1962.
- (9) D. L. Bunker and N. Davidson, *J. Amer. Chem. Soc.*, **80**, 5090 (1958).
- (10) G. Porter, *Discuss. Faraday Soc.*, **33**, 198 (1962).
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### An Unusual Inverse Primary Deuterium Isotope Effect. Factors Operating in the Tunneling Mechanism of Chromium(VI) Oxidation of Alcohols

Sir:

In an earlier article<sup>1</sup> it has been shown through application of the temperature dependent isotope effect criterion (TIC) that typical alcohol oxidations with Cr(VI) proceed through the decomposition of an initially formed chromate ester in a pericyclic transition state of H transfer (Figure 1a). Moreover, abnormal cases involving steric hindrance or highly electron withdrawing substituent effects<sup>2</sup> take place via a quantum mechanical tunneling process, (Figure 1b).

Lee and Stewart<sup>3</sup> report that the value of  $k_H/k_D$  declines with increasing acidity of the medium. These authors have advanced the interpretation that a change in mechanism is induced by  $[H^+]$ , so that at  $k_H/k_D = 1$  the rate determining step is the formation of chromate ester rather than its decomposition in which H transfer is occurring. However, in view of the demonstration<sup>1</sup> that  $k_H/k_D$  in the abnormal cases is determined by both TIC parameters,  $[(\Delta E_a)_D^H$  and  $A_H/A_D]$ , an alternative interpretation involving hydrogen tunneling may be considered. This explanation can be reasoned from the fact that the associated water structure involved in the asymmetric H-transfer mechanism depicted in Figure 1b is strongly influenced by the presence of acidic components of the medium and from the fact that this type of transition state structure may be implicated in quantum mechanical tunneling attending the "proton jump" transport<sup>4</sup> mechanism.

This possibility has now been investigated in the case of the sterically hindered alcohol di-*tert*-butylcarbinol which exhibits direct evidence of undergoing, at least in part, the tunneling mechanism formulated in Figure 1b. The results, indeed show that the TIC parameters for its Cr(VI) oxidation are sensitively dependent on  $[H^+]$ . Table I summarizes the data derived from nearly 100 kinetic runs correlated in Arrhenius relationships encompassing temperature ranges of  $>20$  to  $>50^\circ$ . Product identification was carried out for each reaction acidity, using gas chromatographic analysis. In each case, only the "normal" (di-*tert*-butyl ketone) product was detected along with unreacted and unrear-

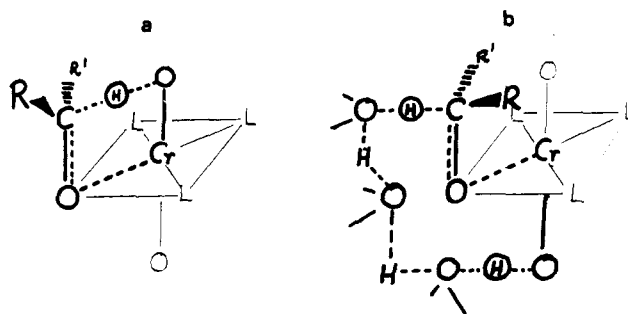


Figure 1. Critical bonds are represented by heavy lines; L = ligand structures; R, R' = alkyl or aryl.

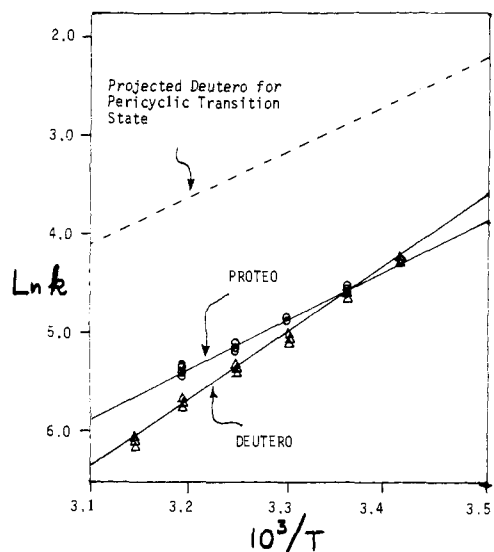


Figure 2. Inverse isotope effect on the rates of Cr(VI) oxidation of di-*tert*-butylcarbinol in 5.9 *M* perchloric-acetic acid medium as a function of absolute temperature.

ranged di-*tert*-butylcarbinol. Figure 2 is presented to illustrate the conclusion that, at a specific  $[H^+]$ , the TIC parameters have magnitudes which produce  $k_H/k_D = 1.0$  at *ca.*  $25^\circ$ . At other  $[H^+]$  the isotope effect disappears only at much greater temperatures in correspondence to variations of the TIC parameters with acidity. Furthermore, significant inverse isotope effects (for example,  $k_H/k_D = 0.8$ , Figure 2) are realized at near-ambient temperatures ( $35^\circ$ ) with no visible signs of mechanistic change in the pattern of Cr(VI) oxidation, *i.e.*, no curvature or discontinuities in the Arrhenius relationships.<sup>5</sup>

The data in Table I also reveal that the TIC parameters do not vary in a linear manner with acidity, although the isotope effect at  $25^\circ$  is shown to decrease with increasing acidity. This observation is consistent with the results of Lee and Stewart for substituted 2-propanols.<sup>3</sup> An increase from 0.1 to 3.5 *M* in  $[H^+]$  produces a *ca.* 100-fold increase in  $A_H/A_D$  and a reduction of 1.8 kcal in  $(\Delta E_a)_D^H$ ; a further increase from 3.5 to 5.9 *M* in  $[H^+]$  is attended by a steep decline (by a factor of 350) in  $A_H/A_D$  and an increase of 2.4 kcal in  $(\Delta E_a)_D^H$ . Such excursions (in opposite phase) of the magnitudes of  $(\Delta E_a)_D^H$  can be interpreted to reflect the partitioning between tunneling and pericyclic transition states of oxidation, as  $[H^+]$  influences the associated water structure and its ability to participate in the essential H-transfer mechanism of Figure 1b.

Traditionally, kinetic isotope effects are extrapolated to<sup>5</sup> or reported at ambient temperatures; such (single) values are applied as criteria for the identification of rate determining steps in H-transfer mechanisms. In general, it may

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

[H <sup>+</sup> ] <sup>b</sup>	-(ΔE <sub>a</sub> ) <sub>D<sup>H</sup></sub> <sup>b</sup>	[A <sub>H</sub> /A <sub>D</sub> ] <sup>b</sup>	R <sup>c</sup>	(k <sub>H</sub> /k <sub>D</sub> ) <sub>25</sub> <sup>b,d</sup>	T (°C) at which k <sub>H</sub> /k <sub>D</sub> = 1
0.1 <sup>e</sup>	3.0	0.066	0.997, 0.999	10.5	283
3.5 <sup>f</sup>	1.2	0.69	0.997, 0.998	5.2	1340
5.9 <sup>g</sup>	3.6	0.0023	0.994, 0.998	1.0	25

<sup>a</sup> See ref 1 for a description of the kinetic conditions and treatment of data. <sup>b</sup> 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. <sup>c</sup>  $R$  = the correlation coefficient. <sup>d</sup> The value of  $k_H/k_D$  at 25°. <sup>e</sup> In 50% aqueous acetic acid,  $[Cr(VI)]_0 = 8 \times 10^{-4} M$ ,  $[NaClO_4] = 0.2 M$ . <sup>f</sup> In 50% aqueous acetic acid,  $[Cr(VI)]_0 = 8 \times 10^{-4} M$ ,  $[LiClO_4] = 0.16 M$ . <sup>g</sup> In 40% aqueous acetic acid,  $[Cr(VI)]_0 = 8 \times 10^{-4} M$ ,  $[LiClO_4] = 0.16 M$ . <sup>h</sup> 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.<sup>6</sup> 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<sup>7</sup> 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<sup>8</sup> 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<sup>2</sup> from these laboratories.

## References and Notes

- (1) H. Kwart and J. H. Nickle, *J. Amer. Chem. Soc.*, **95**, 3394 (1973).
- (2) The subject of a forthcoming article from these laboratories.
- (3) D. G. Lee and R. Stewart, *J. Org. Chem.*, **32**, 2868 (1967).
- (4) Sometimes referred to as the Grothuis mechanism, this process of proton transport has been discussed in its various aspects by (a) J. D. Bernal and R. N. Fowler, *J. Chem. Phys.*, **1**, 515 (1939); (b) A. Gierer and K. Wirtz, *J. Phys. Chem.*, **56**, 914 (1952); (c) S. Glasstone, K. J. Laidler, and H. Eyring, "The Theory of Rate Processes," McGraw-Hill, New York, N. Y., 1941, Chapter X.
- (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 observation 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."

- (7) J. Roček, F. H. Westheimer, A. Eschenmoser, L. Moldovanyi, and J. Schreiber, *Helv. Chim. Acta*, **45**, 2554 (1962).
- (8) These are the preliminary results of stopped flow kinetic studies in these laboratories.

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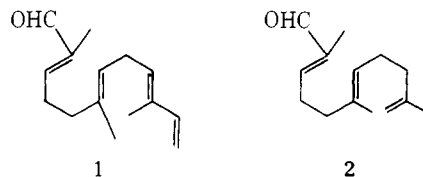
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## A Stereoselective Synthesis of α-Sinensal

Sir:

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



Condensation of (*E*)-3-methyl-2,4-pentadien-1-ol (3)<sup>7</sup> 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<sub>3</sub>) 1710 cm<sup>-1</sup>, was isolated in 88% yield.<sup>8</sup> The absence of dialkylated ketones and the nearly exclusive formation of the β,γ-unsaturated isomer is remarkable<sup>9</sup> 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*-cyanomethyl dimethylamine<sup>10</sup> 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.<sup>11-13</sup> Aqueous oxalic acid<sup>12</sup> 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<sub>3</sub>) 3500 and 1720 cm<sup>-1</sup>, followed by retroaldol cleavage to the two cy-