

MECHANISTIC ASPECTS OF THE DIENOL-BENZENE REARRANGEMENT

V. P. Vitullo* and Michael J. Cashen

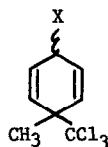
Department of Chemistry, University of Maryland Baltimore County

Baltimore, Maryland 21228

(Received in USA 21 August 1973; received in UK for publication 16 October 1973)

Herein we report our studies on the mechanism of the dienol-benzene rearrangement, an interesting and biologically¹ important transformation.

Reduction of 4-methyl-4-trichloromethylcyclohexadienone according to Plieninger² afforded crystalline alcohol 1a (80%, mp 141-141.5, lit² 142-142.5). 1a rearranged smoothly in aqueous acid with excellent first-order kinetics to o-toluic acid. In all of the solutions for which

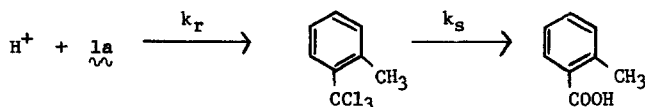


1a; X = OH

1a; X = Cl

1a; X = OCH₃

kinetic data were obtained, the solvolysis of the intermediate o-methylbenzotrichloride is at



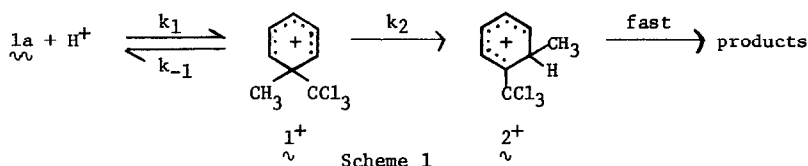
least 1.5×10^2 faster than the observed rate of appearance of o-toluic acid, k_{obs} . We conclude that k_{obs} is k_r with no contribution from k_s .

Rates of rearrangement were obtained over a range of acidities for both sulfuric and perchloric acids. The acidity dependence as measured by the response of k_{obs} to changes in the Hammett acidity function H_0 , is very steep (eq. 1 and 2). These results suggest a transition state with considerable carbonium ion character.³ An approximate bimolecular rate constant of $10^{-8} \text{ M}^{-1} \text{ sec}^{-1}$ can be estimated by extrapolating these data to $H_0 \approx \text{pH} = 0$.

$$\log k_{\text{obs}} = (-7.99 \pm 0.06) - (1.70 \pm 0.02)H_0 \quad \text{HClO}_4 \quad (1)$$

$$\log k_{\text{obs}} = (-8.60 \pm 0.02) - (1.68 \pm 0.01)H_0 \quad \text{H}_2\text{SO}_4 \quad (2)$$

A reasonable mechanism for the dienol-benzene rearrangement (given below) allows the possibility of two different rate-determining steps either of which could have substantial carbonium ion character. It appeared, therefore, of some interest to determine which step is rate-determining.



Generation of 1^+ in a nucleophilic solvent under non-equilibrating conditions and measuring the amount of capture product relative to the amount of rearrangement product gives a direct measure of k_{-1}/k_2 . For this purpose we undertook an investigation of the solvolysis of $1b$ in buffered methanol.

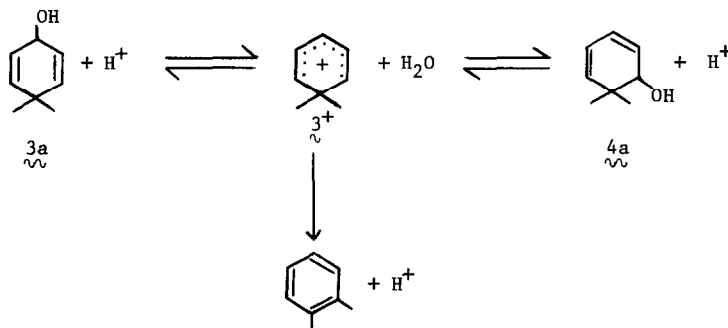
It has been shown recently that methanol is only 2 - 3x more nucleophilic than water towards covalent⁴ and carbonium ion⁵ substrates. Thus, k_{-1}/k_2 is expected to be similar for both solvents. $1b$ was obtained by treatment of $1a$ with SOCl_2 in CHCl_3 (white crystals, 75% after sublimation; 50°/0.05 mm). This material exhibited a wide melting range and consisted of a 61:39 mixture of the two isomeric chlorides (nmr). Solvolysis of freshly prepared $1b$ in methanol buffered with triethylamine at 63° for 24 hours afforded a single product by glpc which was collected and shown by nmr to consist solely of a mixture (56:44) of the isomeric methyl ethers, $1c$. A similar distribution of methyl ethers (71:29) was obtained from the solvolysis of a 25:75 mixture of chlorides and suggested the presence of carbonium ion intermediates in these solvolyses.⁶ Significantly, there was no detectable (< 1%) methyl *o*-toluate in the crude solvolysis product. Thus $k_{-1} \geq 100 k_2$ and the rearrangement of $1^+ \rightarrow 2^+$ is the rate-determining step in the dienol-benzene rearrangement for $1a$.

We next extended our investigation to the acid catalyzed rearrangement of 4,4-dimethylcyclohexadienol ($3a$).

Reduction of 4,4-dimethylcyclohexadienone with excess lithium aluminum hydride in ether at room temperature afforded $3a$ in high yield; δ 5.63 (vinyl, 4H), δ 4.32 (CHOH , 1H), δ 2.63 (OH , 1H), δ 1.08 (CH_3 , 3H), δ 1.02 (CH_3 , 3H). When $3a$ is dissolved in dilute aqueous acid solution and monitored spectrophotometrically, there is observed the formation of a new species which has

$\lambda_{\max} = 259 \text{ nm}$ and $\epsilon_{\max} = 1600 \text{ cm}^{-1}\text{M}^{-1}$. The intermediate species eventually disappears one-twentieth as fast as it is formed. Monitoring the reaction by nmr spectroscopy in 80% CD_3COCD_3 - 20% D_2O containing 0.01 M DCl indicated that this new species is very similar to $\underline{3a}$. The broad singlet for the vinyl hydrogens in $\underline{3a}$ was replaced by a complex multiplet centered at δ 5.69. The methyl resonances were significantly broadened and shifted upfield slightly, δ 0.99 and δ 0.94. Eventually, the spectrum decayed to that of o-xylene; δ 7.03 (aromatic, 4H) and δ 2.17 (CH_3 , 6H). These results indicated that $\underline{3a}$ in acid solution underwent isomerization to 6,6-dimethylcyclohexa-2,4-dien-1-ol ($\underline{4a}$) in an equilibrium reaction followed by a slower reaction leading to o-xylene. From the spectral parameters published⁷ for 5,5-dimethyl-1,3-cyclohexadiene ($\lambda_{\max} = 257 \text{ nm}$, $\epsilon_{\max} = 4300$) we estimate the equilibrium constant, $[\underline{4a}]/[\underline{3a}]$ to be 0.6 independent of pH.

It is clear that Scheme I must be expanded somewhat to include the formation of the new intermediate.



In dilute aqueous HCl solutions both the isomerization (k_i) and rearrangement (k_r) steps were found to be acid catalyzed processes; $k_i/a_{\text{H}^+} = 26.9 \pm 1.9 \text{ M}^{-1}\text{sec}^{-1}$, $k_r/a_{\text{H}^+} = 1.35 \pm 0.10 \text{ M}^{-1}\text{sec}^{-1}$, ($\mu = 0.1$, NaCl). Both steps exhibit a large, near maximum, inverse solvent isotope effect; $(k_{\text{D}_2\text{O}}/k_{\text{H}_2\text{O}})_i = 2.8 \pm 0.2$, $(k_{\text{D}_2\text{O}}/k_{\text{H}_2\text{O}})_r = 3.2 \pm 0.2$.

Recently Ritchie⁸ has shown that the reaction of a highly stabilized carbonium ion with water is a general base catalyzed process. In this connection, it is significant that the conversion $\underline{3a} \rightarrow \underline{4a}$ which probably proceeds via intermediate $\underline{3}^+$ is not detectably catalyzed by HCOOH , CH_3COOH or H_2PO_4^- . It is clear that carbonium ion stability plays a dominant role in determining the form of catalysis observed in these kinds of reactions. This result is highly reminiscent of Fife's results⁹ in acetal hydrolysis.

Finally, we wish to emphasize the substantially faster rates of rearrangement of $\underline{3a}$ compared to $\underline{1a}$ (factor of about 10^8). This is, at least partially, a consequence of the difference in

stability of 1^+ and 3^+ .

Further amplification will be given in our full paper.

We thank the National Science Foundation for generous support of this work (Grant No. GP-29738X). We are also grateful to Professors D. L. Whalen and M. W. Logue for many informative and enlightening discussions.

References

1. H. Plieninger, *Angew. Chem.*, (Intern. Ed. Engl.), 1, 367 (1962).
2. H. Plieninger and G. Keil, *Ber.*, 91, 1891 (1958).
3. C. H. Rochester, "Acidity Functions", Academic Press, New York, New York, 1970, pp. 109-127.
4. P. E. Peterson and F. J. Waller, *J. Amer. Chem. Soc.*, 94, 991 (1972); T. W. Bentley, F. L. Schadt and P. V. R. Schleyer, *J. Amer. Chem. Soc.*, 94, 992 (1972).
5. C. D. Ritchie, *Accts. Chem. Res.*, 5, 348 (1972).
6. A reviewer has suggested that if one assumes that the major chloride isomer and major methyl ether isomer have the same configuration, our product distributions show that these solvolyses proceed with predominant inversion of configuration. We agree with this suggestion, although definitive evidence regarding the relative configurations of the isomers of 1^b and 1^c is lacking.
7. C. W. Spangler and P. L. Boles, *J. Org. Chem.*, 37, 1020 (1972).
8. C. D. Ritchie, *J. Amer. Chem. Soc.*, 94, 3275 (1972).
9. T. H. Fife, *Accts. Chem. Res.*, 5, 264 (1972).