[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ARIZONA, TUCSON, ARIZONA]

Selenium Dioxide Oxidations. II. Base Catalyzed Oxidation of Ketones

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The kinetics of the selenium dioxide oxidation of desoxybenzoin, *p*-nitrobenzylphenyl ketone and *p*-methoxybenzylphenyl ketone in 80 and 99% acetic acid containing sodium acetate were measured. On the basis of the kinetic order and the acidity-rate profiles obtained, a mechanism is proposed which involves the base catalyzed formation of an enolselenite ester which subsequently rearranges and decomposes to give α-diketone, selenium and water.

During a recent study of the oxidation of ketones to α-diketones with selenium dioxide, we found that the reaction was acid and base catalyzed.[1] Although acid catalysis was consistent with the postulated reaction mechanism, the anomalous Hammett correlation obtained in the presence of base left the mechanism of this process obscure. To clarify the details of the base catalyzed reaction, we have carried out a detailed solvent and acidity-rate profile study of this reaction with several selected compounds and now report the results of this investigation.

Experimental

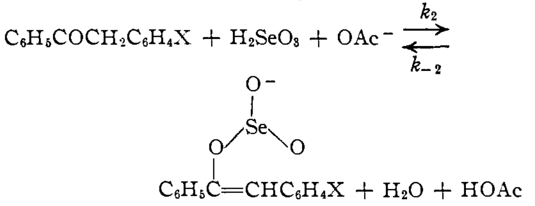
The desoxybenzoins in this study were prepared by the procedures described previously[1] and oxidized using the kinetic method outlined in an earlier study.[2] Reactions in 80% acetic acid were run by dissolving weighed amounts of ketone and sodium acetate in 80 ml. of glacial acetic acid and adding 20 ml. of aqueous selenious acid stock solution from a tip-flask after temperature equilibration. In 99% acetic acid runs were carried out in a similar manner with the exception that 20 ml. of selenious acid dissolved in 95% acetic acid was used.

Rate constants tabulated in Tables I and II represent initial second order rate constants calculated by the method of least squares from data covering 25–50% complete reaction.

Discussion

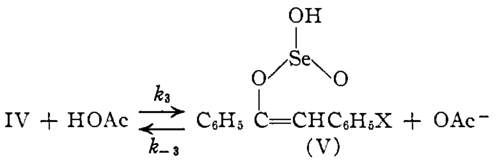
Tables I and II summarize the rate constants obtained in 80 and 99% acetic acid for desoxybenzoin (I), *p*-nitrobenzylphenyl ketone (II) and *p*-methoxybenzylphenyl ketone (III). These data are consistent with the mechanism

$$H_2SeO_3 + OAc^- \underset{k_1}{\overset{k_1}{\rightleftharpoons}} HSeO_3^- + HOAc \qquad (1)$$



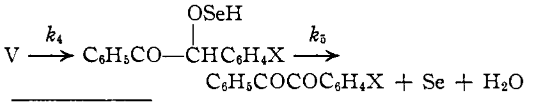
$$C_6H_5COCH_2C_6H_4X + H_2SeO_3 + OAc^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} C_6H_5\overset{\overset{O^-}{|}{O-Se=O}}{C}=CHC_6H_4X + H_2O + HOAc \qquad (2)$$

(IV)



$$IV + HOAc \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} C_6H_5\overset{\overset{OH}{|}{O-Se=O}}{C}=CHC_6H_5X + OAc^- \qquad (3)$$

(V)



$$V \xrightarrow{k_4} C_6H_5CO-\overset{OSeH}{\overset{|}{C}}HC_6H_4X \xrightarrow{k_5} C_6H_5COCOC_6H_4X + Se + H_2O \qquad (4)$$

TABLE I[a]

VARIATION OF RATE CONSTANT FOR OXIDATION WITH INITIAL SODIUM ACETATE CONCENTRATIONS

Compound	[Ketone]	[H_2SeO_3]	[NaOAc]	$k \times 10^4$ (l. mole^{-1} sec.$^{-1}$)
I	0.0954	0.0670	0	6.67
I	.0953	.0647	0.0257	8.43
I	.0954	.0639	.0580	11.3
I	.0956	.0639	.0923	12.2
I	.0953	.0654	.2064	14.4
I	.0939	.0636	.3739	12.4
I	.0929	.0631	.5820	9.82
I	.0902	.0608	.9178	5.70
II	.0944	.0733	0	3.91
II	.0945	.0716	0.0572	4.21
II	.0937	.0720	.2064	3.35
II	.0926	.0708	.4045	2.77
II	.0910	.0707	.6920	2.13
III	.0943	.0696	0	7.00
III	.0926	.0654	0.2939	25.3
III	.0651	.0686	0.7002	36.7

[a] All data refer to oxidation in 80% acetic acid at 90°. Concentrations units are moles/liter.

TABLE II[a]

VARIATION OF RATE CONSTANT FOR OXIDATION WITH INITIAL SODIUM ACETATE CONCENTRATIONS

Compound	[Ketone]	[H_2SeO_3]	[NaOAc]	$k \times 10^4$ (l. mole^{-1} sec.$^{-1}$)
I	0.0955	0.0567	0	10.5
I	.0954	.0580	0.0777	20.4
I	.0947	.0586	.1605	33.9
I	.0945	.0564	.2390	43.4
I	.0929	.0560	.4600	76.0
I	.0914	.0556	.7730	102
II	.0944	.0638	0	27.6
II	.0945	.0599	0.0965	191
II	.0938	.0627	.2330	145
II	.0929	.0614	.3560	112
II	.0908	.0603	.6950	56.6
III	.0944	.0632	0	10.8
III	.0940	.0612	0.2931	48.5
III	.0910	.0609	0.7005	98.8

[a] All data refer to oxidation in 99% acetic acid at 90°. Concentrations units are moles/liter.

Examination of this reaction path reveals that acetate plays several conflicting roles. Acidity measurements indicate that acetate is a sufficiently strong base to neutralize selenious acid partially.[3,4] Since the biselenite formed by this reaction is ineffective as an oxidant,[2] the effect of equilibrium 1 will be to make acetate behave as an oxidation inhibitor. On the other hand, an important factor

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[1] E. J. Corey and J. P. Schaefer, *J. Am. Chem. Soc.*, **82**, 918 (1960).

[2] J. P. Schaefer, *ibid.*, **84**, 713 (1962).

[3] H. Hagisawa, *Bull. Inst. Phys. Chem. Res. Tokyo*, **18**, 648 (1939); *C. A.*, **34**, 4965 (1940).

[4] J. F. J. Dippy, *Chem. Revs.*, **25**, 151 (1939).

influencing the overall rate of reaction will be the formation of enol ester IV.[5] Since this step 2 is base catalyzed, the addition of a strong base such as acetate should have a large rate enhancing effect.

A third factor of importance in certain cases (*vide infra*) is the effect of acetate on equilibrium 3. Since the formation of V is a necessary precedent for product production, acetate will inhibit product formation by reconverting V to IV and thereby diminishing the fraction which rearranges to VI. The over-all effect of acetate for any particular compound will reflect varying contributions of each of these three factors to the total rate of oxidation.

These factors can be evaluated more significantly in terms of a steady state treatment of the above reaction mechanism. This leads to equation 5 if it is assumed that k_4 is rate determining.[6] A plot of v as a function of $[\mathrm{OAc}^-]_{\mathrm{eq}}$ indicates that v will increase, go through a maximum and then decrease as $[\mathrm{OAc}]_{\mathrm{eq}}$ increases.

$$v = a[\mathrm{C_6H_5COCH_2C_6H_4X}][\mathrm{H_2SeO_3}]_t \left\{ \frac{1}{\frac{b}{[\mathrm{OAc}^-]_{\mathrm{eq}}} + c + d\,[\mathrm{OAc}^-]_{\mathrm{eq}}} \right\} \quad (5)$$

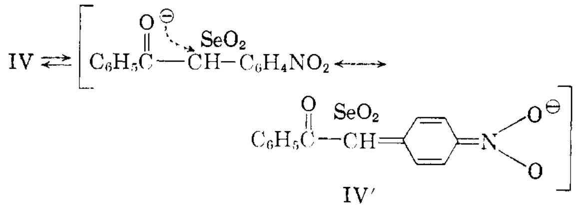
When k_2 is rate determining, eq. 5 simplifies to (6) since d will approach zero. Now a plot of v as a function of

$$v = a[\mathrm{C_6H_5COCH_2C_6H_4X}][\mathrm{H_2SeO_3}]_t \left\{ \frac{(\mathrm{OAc}^-)_{\mathrm{eq}}}{b + c\,[\mathrm{OAc}^-]} \right\} \quad (6)$$

$[\mathrm{OAc}^-]_{\mathrm{eq}}$ would increase and approach a maximum value asymtotically as the concentration of acetate increases. Which of these situations obtains will be determined by the structure of the ketone. This is best understood by an individual discussion of each of the ketones used in the present study.

A. *p*-Nitrobenzylphenyl Ketone.—Since II is the most acidic ketone studied,[7] we would expect k_2 to be relatively large and the formation of IV ($\mathrm{X = NO_2}$) to be fast. This is substantiated by the results in 99% acetic acid where addition of a small amount of acetate causes a large rate increase. The question which we must now answer is why does increasing the concentration of base even further bring about a decrease in rate? The answer most probably lies in the stability of IV.

Dissociation of IV into an intimate ion-molecule pair (IV′) should be favored by the stability of the two species produced, in particular, that of the resonance stabilized enolate anion. The stability of IV′ will make the formation of V more difficult and, furthermore, favor the return of V to IV as the acetate concentration increases. The addition of water to the solvent will favor the return of IV to starting material (eq. 2) and further slow down the oxidation. These conclusions are supported by a comparison of data in 80 and 99% acetic acid and equation 5 will be the kinetic law obeyed by II.



IV′

B. *p*-Methoxybenzylphenyl Ketone.—In the case of III we would expect k_2 to be relatively small in comparison to II.[8] However, the ester (IV, $\mathrm{X = OCH_3}$) once formed should be far less stable than the nitro ester (IV, $\mathrm{X = NO_2}$) and favor protonation and rapid decomposition to product. Tables I and II bear this out since in 99% acetic acid there is no rate decrease in the concentration range studied and in 80% acetic acid, the decrease is small. The reaction kinetics should obey 6 to a good first approximation, but unfortunately solubility considerations did not allow a wide enough range of concentrations to verify this point.

C. Desoxybenzoin.—The factors mentioned for the above two compounds are intermediate in this case and are again substantiated by the data.

To summarize, for electron donating substituents in the benzyl moiety, reaction 2 is rate determining. This is indicated by the deuterium isotope effect,[1] the rate law, and supported by the order of substituent effects in essentially non-aqueous solvent ($\mathrm{NO_2 > H > OCH_3}$). As the amount of water in the solvent increases, the apparent rate determining step gradually changes to one later in the sequence. Additional base will cause an analogous effect.

These findings have interesting synthetic implications since they indicate that sodium acetate in acetic acid along with selenious acid is a very effective oxidizing system for ketones. Since selenium dioxide oxidations parallel the direction of enolization of ketones[9] and since acid and base catalyzed enolization take different directions,[10] this discovery promises a substantial extention of the selenium dioxide reaction. We are currently investigating these possibilities.

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[5] Support for this statement stems from the substantial C–D isotope effect observed in the base catalyzed oxidation of desoxybenzoin.[1]

[6] In eq. 5 a, b, c and d are constants and selenious acid is expressed in terms of total concentration of selenium whereas acetate is in terms of equilibrium concentration.

[7] The deep blue anion is readily formed by dissolving II in ethanol and adding a drop of aqueous potassium carbonate.

[8] The relative rates[1] of enolization of I and II in acetic acid catalyzed by sodium acetate differ by at least 10^3.

[9] Ref. 1 reviews the pertinent papers which document this fact.

[10] E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Company, New York, N. Y., 1959, p. 372.