[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Studies on the Mechanism of Oxidation of Ketones by Selenium Dioxide (Part I)[1]

BY E. J. COREY* AND J. P. SCHAEFER

RECEIVED MAY 25, 1959

The oxidation of desoxybenzoin by selenious acid in 70% acetic acid is catalyzed both by acids and by the base acetate ion. The rate expression for the acid-catalyzed reaction is $-d[SeO_2]/dt = k[SeO_2][C_6H_5COCH_2C_6H_5][H^+]$ and that for the acetate-catalyzed process seems best represented as $-d[SeO_2]/dt = k[SeO_2][C_6H_5COCH_2C_6H_5][AcO^-]$. For the acid-catalyzed reaction the effect of a *p*-substituent on either ring of the ketone on rate is virtually identical with that for acid-catalyzed enolization, indicating that the two reactions are of similar type. The presence of two *o*-substituents on the ring adjacent to the carbonyl group does not depress the rate of either the acid or acetate-catalyzed oxidation, which eliminates the possibility that carbonyl addition is involved. Replacement of the α-hydrogens of desoxybenzoin by deuterium results in a several-fold decrease in rate for both the acid-catalyzed and acetate-catalyzed processes. On the basis of these and other data it is proposed that the rate-determining step in the oxidation of desoxybenzoin is the formation of an enol selenite ester directly from the ketone by a process mechanistically related to enolization in which the electrophile–nucleophile pairs are $H_3SeO_3^+$ and H_2O (acid-catalyzed process) and H_2SeO_3 and acetate ion (based-catalyzed process). The enol selenite ester is considered to rearrange to an α-substituted selenium(II) ester which decomposes rapidly to diketone and selenium. In certain instances reversion of the enol selenite ester to starting materials is considerable. In the case of the acetate ion-catalyzed oxidation of phenyl *p*-nitrobenzyl ketone, formation of the enol selenite ester is fast and rapidly reversible and the rate-determining step is formation of the α-substituted selenium(II) ester.

Considerable progress has been made in the application of selenium dioxide as a selective reagent in organic synthesis and degradation since the pioneering researches of Riley.[2–4] In contrast, however, very little is known about the way in which this remarkable oxidizing agent functions, a fact which is even more striking in view of the advances made recently in the field of oxidation mechanisms.[5]

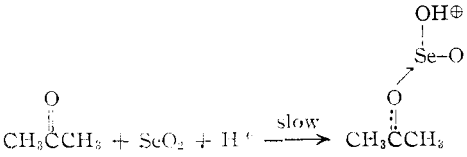
This paper describes attempts to achieve a more fundamental understanding of the reactions of selenium dioxide and is concerned specifically with the oxidation of ketones by selenium dioxide, now a standard synthetic operation which can lead to 1,2-diketones, hydroxyketones, α,β-unsaturated ketones and, in certain instances, to rearrangement[6] or ring formation,[7] depending on the structure of the ketone and the reaction conditions. It should be noted here that in aqueous media selenium dioxide is present mainly as selenious acid and that description of the reagent as selenium dioxide in aqueous systems is a matter of common usage and not an indication of the reactive species.[8]

Mel'nikov and Rokitskaya[9–15] have made numerous but rather rough kinetic measurements of the rate of oxidation of various aldehydes and ketones by selenium dioxide and have reported that in all cases the reaction is second order: first order in selenium dioxide and first order in the organic compound. A parallelism was noted between the rate of oxidation and the rate of enolization of these compounds. The Russian workers also prepared dialkyl selenites from selenium dioxide and primary alcohols and observed that aldehydes are formed by thermal decomposition. On this evidence it was postulated that the reaction path consists of enolization followed by complex formation with selenium dioxide and subsequent decomposition of the complex to give the dicarbonyl compound, selenium and water. It was also proposed that the relative degree of enolization of a ketone could be ascertained from rates of oxidation by selenium dioxide (see, *e.g.*, ref. 15). These conclusions are generally incorrect and will be discussed in more detail in a later section.

In 1948, Duke[16] published an account of the kinetics of oxidation of acetone by selenious acid. It was found that the reaction was catalyzed by acid and that the rate of disappearance of selenious acid is governed by the rate law

$$-d(H_2SeO_3)/dt = k(\text{acetone})(H_2SeO_3)(H^+)$$

As a result of this, an intermediate of structure I was postulated and its formation was regarded as rate determining. It was proposed that the intermediate I undergoes rapid decomposition to give pyruvaldehyde, selenium and water. For the



I

---

* Department of Chemistry, Harvard University, Cambridge 38, Mass.

(1) Taken in part from the Ph.D. thesis of John P. Schaefer submitted to the University of Illinois in August, 1958. Presented at the 16th National Organic Chemistry Symposium, Seattle, Wash., June, 1959.

(2) H. L. Riley, J. F. Morley and N. A. Friend, *J. Chem. Soc.*, 1875 (1932).

(3) N. Rabjohn, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, Chap. 8.

(4) G. R. Watkins and C. W. Clark, *Chem. Revs.*, **36**, 235 (1945).

(5) For a recent review, see W. A. Waters, *Quart. Revs.*, **12**, 277 (1958).

(6) L. Ruzicka, R. Roegg, E. Volli, O. Jeger, *Helv. Chim. Acta*, **30**, 140 (1947).

(7) E. J. Corey and H. J. Burke, THIS JOURNAL, **78**, 174 (1956).

(8) In the solid state selenium dioxide is polymeric; see J. D. McCullough, *ibid.*, **59**, 789 (1937).

(9) N. N. Mel'nikov and M. S. Rokitskaya, *J. Gen. Chem. U.S.S.R.*, **7**, 1532 (1937); *C. A.*, **31**, 8502 (1937).

(10) N. N. Mel'nikov and M. S. Rokitskaya, *ibid.*, **7**, 2738 (1937); *C. A.*, **32**, 2903 (1938).

(11) N. N. Mel'nikov and M. S. Rokitskaya, *ibid.*, **8**, 1369 (1938); *C. A.*, **33**, 4194 (1939).

(12) N. N. Mel'nikov and M. S. Rokitskaya, *ibid.*, **9**, 1158, 1808 (1939); *C. A.*, **34**, 1233, 3676 (1940).

(13) N. N. Mel'nikov and M. S. Rokitskaya, *ibid.*, **10**, 1439 (1940); *C. A.*, **35**, 2400 (1941).

(14) N. N. Mel'nikov and M. S. Rokitskaya, *ibid.*, **10**, 1713 (1940); *C. A.*, **35**, 3226 (1941).

(15) N. N. Mel'nikov and M. S. Rokitskaya, *ibid.*, **15**, 657 (1945); *C. A.*, **40**, 5702 (1946).

(16) F. R. Duke, THIS JOURNAL, **70**, 419 (1948).

reasons indicated below this proposal also must be disregarded.

Results

In the present investigation attention was centered about the oxidation by selenious acid of desoxybenzoin and various substituted derivatives to the corresponding benzils, since the reaction

$$\mathrm{ArCOCH_2Ar' + SeO_2 \longrightarrow ArCOCOAr' + Se + H_2O}$$

is sufficiently dominant to permit meaningful kinetic analysis and since the correlation of rates for this series using the Hammett equation can provide valuable mechanistic information. Acetic acid–water (7:3) was chosen as the reaction medium because this mixture permitted a wide range of concentrations with both organic and inorganic reagents. Under the kinetic conditions only one equivalent of selenious acid was consumed per equivalent of ketone and the yields of diketone were well over 90%. The velocity of reaction was determined by titration of unreacted selenious acid.

The oxidation of desoxybenzoin in 70% acetic acid at 89.2° was found to be second order over-all: first order in ketone and first order in the selenium-(IV) reagent. A summary of the rate constants obtained at various concentrations appears in Table I. These constants were calculated from the best straight line through the points as determined visually or, in the cases with appreciable scatter, by the method of least squares. Some typical rate curves appear in Fig. 1. The symbol $[\mathrm{SeO_2}]$ denotes the total concentration of selenium (IV) species.

TABLE I

RATE CONSTANTS AT 89.2° AT VARIOUS CONCENTRATIONS

Run	$[\mathrm{SeO_2}]$, M	$[\mathrm{C_{14}H_{12}O}]$, M	$k_2 \times 10^4$, M^{-1} sec.$^{-1}$
1	0.366	0.366	2.80
2	.360	.271	2.56
3	.338	.691	2.50
4	.594	.344	2.54
5	.364	.364	2.59
		Av.	2.60

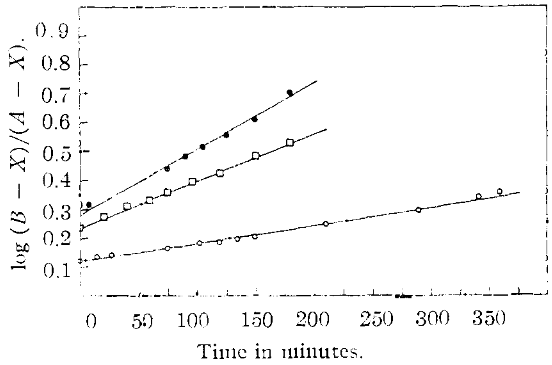


Fig. 1.—Oxidation of desoxybenzoin; t = 89.2°; run 2, ○; run 3, ●; run 4, □.

To evaluate the sensitivity of the reaction rate to solvent composition a kinetic run was made in 90% acetic acid. The observed rate constant of 2.92×10^{-4} M^{-1}sec.$^{-1}$ indicated that the reaction was not much influenced by solvent composition in this range.

Preliminary studies of acid ionization in 70% acetic acid at 90° by conductometric titration with sodium acetate indicated that selenious acid was only slightly ionized, but that the first ionization of sulfuric acid was essentially complete. The ratio of ionization constants for selenious acid and acetic acid was estimated to be in the range of 10–50. Consequently, the effect of added strong acid was studied using both sulfuric acid and oxalic acid. In each case the rate of oxidation was found to increase linearly with acid concentration as indicated by the data in Tables II and III and the graphs in Figs. 2 and 3, but was *still dependent on the concentration of ketone and of selenious acid.* In each run excellent second-order kinetics were observed even beyond 75% reaction. The apparent lack of second-power dependence of the rate on selenious acid concentration out to *ca.* 70% reaction in the experiments without added strong acid implies that the medium (70% acetic acid) is somewhat more important acid catalyst than is the relatively dilute, albeit somewhat stronger acid, selenious acid. Doubtless a dependence higher than first power would be detected by very accurate kinetic measurements.

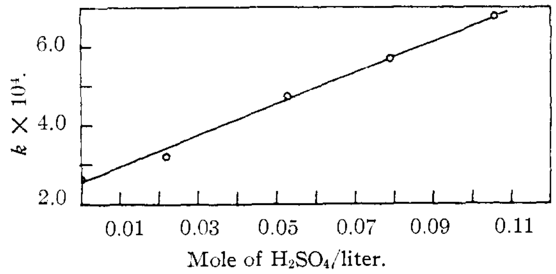


Fig. 2.—Rates of oxidation of desoxybenzoin at various sulfuric acid concentrations: correlation of constants.

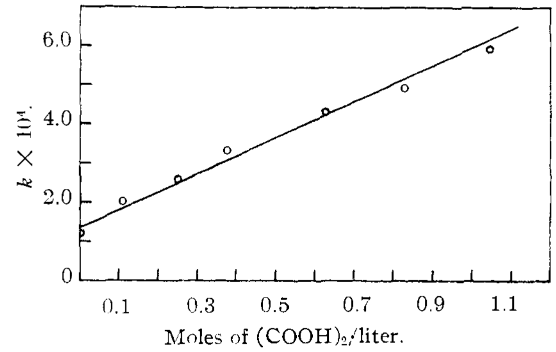


Fig. 3.—Rates of oxidation of desoxybenzoin at various oxalic acid concentrations: correlation.

TABLE II

SULFURIC ACID CATALYSIS AT 89.2°

Run	$[\mathrm{SeO_2}]$, M	$[\mathrm{C_{14}H_{12}O}]$, M	$[\mathrm{H_2SO_4}]$, M	$k \times 10^4$, M^{-1} sec.$^{-1}$
5	0.364	0.364	0.0000	2.59
6	.348	.348	.0221	3.41
7	.387	.386	.0529	4.76
8	.389	.389	.0795	5.68
9	.390	.390	.1060	6.75

TABLE III

OXALIC ACID CATALYSIS AT 80.1°

Run	$[SeO_2]$, M	$[C_{14}H_{12}O]$, M	$[C_2H_2O_4]$, M	$k \times 10^4$, M^{-1} sec.$^{-1}$
10	0.357	0.356	0.000	1.25
11	.361	.360	.111	2.26
12	.358	.358	.249	2.62
13	.351	.352	.375	3.36
14	.358	.358	.625	4.35
15	.351	.350	.828	4.96
16	.350	.350	1.045	5.91

As a result of these experiments the rate expression for the disappearance of selenium(IV) can be written as

$$-\,d[SeO_2]/dt = k[SeO_2][C_6H_5COCH_2C_6H_5][H^+]$$

a result which is in agreement with the observations of Duke[16] for the oxidation of acetone by selenious acid in aqueous solution.

The influence of ionic strength was measured by adding varying amounts of sodium benzene sulfonate to the reaction mixture. The results of these investigations, which appear in Table IV and Fig. 4, indicate that the salt effect obtained is of the order of magnitude expected for a reaction between a neutral and a charged species.[17] Also, since an increase in the ionic strength of the reaction medium will increase the degree of dissociation of acetic and selenious acids, thereby increasing the hydronium ion concentration in solution, a small acceleration of the reaction rate due to this effect is expected.

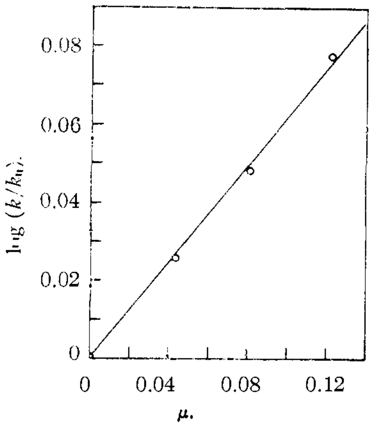


Fig. 4.—Correlation of salt effect.

TABLE IV

SALT EFFECT OF SODIUM BENZENESULFONATE AT 89.2°

Run	$[SeO_2]$, M	$[C_{14}H_{12}O]$, M	$[C_6H_5SO_3Na]$, M	$k \times 10^4$, M^{-1} sec.$^{-1}$
5	0.364	0.364	0.000	2.59
17	.382	.382	.432	2.75
18	.389	.389	.810	2.88
19	.389	.389	1.220	3.08

The dependence of reaction rate upon electron supply was determined by the study of the kinetics of oxidation of various *p*-substituted desoxybenzoins using the Hammett equation[18] to calculate reaction constants for substituents in the *p*-position of the benzoyl and benzyl moieties. As indicated in Table V and Figs. 5–7 electron-supplying substituents in the benzoyl group increase the rate of reaction (ρ_{ArCO} −0.56) whereas the opposite is true for substituents in the benzyl part ($\rho_{ArCH_2} \cong +0.25$) (excluding phenyl *p*-nitrobenzyl ketone which is discussed below). The value of ρ_{ArCH_2} is only an approximate one since, as is mentioned in a later section, this Hammett correlation breaks down with increasing σ-values. It is especially noteworthy that the ρ-value obtained for *p*-substitution in the benzoyl residue is the same as that measured for the acid-catalyzed enolization of substituted acetophenones under similar conditions (ρ_{AcO} = −0.56),[19] suggesting that the transition states for the two reactions possess similar electron distribution on carbon.

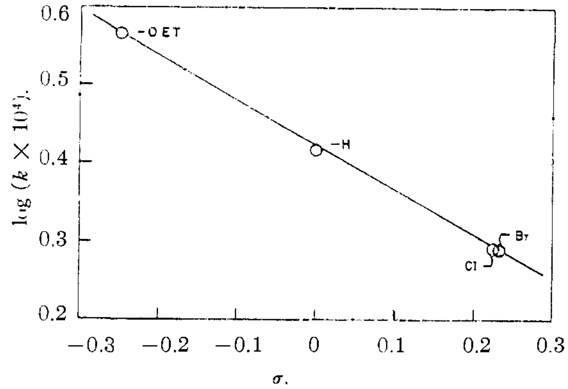


Fig. 5.—Hammett correlation for rates of oxidation of p-$XC_6H_4COCH_2C_6H_5$; t = 89.2°.

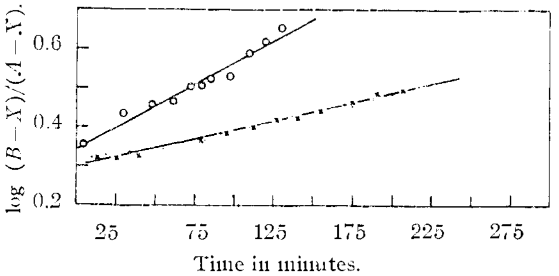


Fig. 6.—Rates of oxidation of p-$XC_6H_4COCH_2C_6H_5$: run 22, ○, X = EtO–; run 24, ×, X = Cl–; run 25, ●, X = Br–.

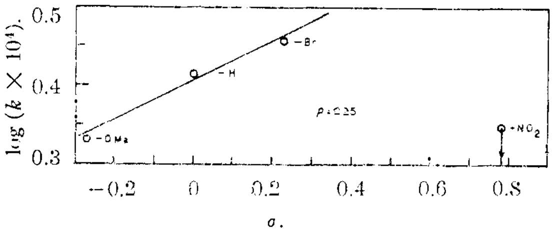


Fig. 7.—Hammett correlation for rates of oxidation of p-$XC_6H_4CH_2COC_6H_5$; t = 89.2°.

Measurements of the velocity of enolization of substituted desoxybenzoins possessing substituents *para* to the methylene group indicate that electron-

---

(17) A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, Chap. 3.

(18) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII.

(19) D. P. Evans, V. G. Morgan and H. B. Watson, *J. Chem. Soc.*, 1167 (1935).

TABLE V

SUBSTITUENT EFFECTS ON THE RATE OF OXIDATION

Run	Compound	[Ketone], M	[SeO$_2$], M	t, °C.	$k \times 10^4$, M^{-1} sec.$^{-1}$	E_a
10	$C_6H_5COCH_2C_6H_5$	0.357	0.356	80.1	1.25	
5	$C_6H_5COCH_2C_6H_5$	.364	.364	89.2	2.59	20.4
20	p-$C_2H_5OC_6H_4COCH_2C_6H_5$	.174	.389	80.1	1.78	
21	p-$C_2H_5OC_6H_4COCH_2C_6H_5$	.189	.395	80.1	1.69	21.1
22	p-$C_2H_5OC_6H_4COCH_2C_6H_5$	.186	.396	89.2	3.70	
23	p-$ClC_6H_4COCH_2C_6H_5$	.192	.383	80.1	0.97	20.1
24	p-$ClC_6H_4COCH_2C_6H_5$	.192	.392	89.2	1.91	..
25	p-$BrC_6H_4COCH_2C_6H_5$	.183	.370	89.2	1.97	..
26	p-$CH_3OC_6H_4CH_2COC_6H_5$	.167	.369	89.2	2.08	..
27	p-$BrC_6H_4CH_2COC_6H_5$	.045	.190	89.2	2.86	..
28	p-$NO_2C_6H_4CH_2COC_6H_5$	.093	.200	89.2	1.28	..
29	p,p'-$NO_2C_6H_4CH_2COC_6H_4OC_2H_5$	.083	.083	89.2	2.28	..
30	2,4,6-$(CH_3)_3C_6H_2COCH_2C_6H_5$	.360	.360	89.2	4.10	..
31	2,4,6-$(CH_3)_3C_6H_2H_2CH_2COC_6H_5$	.0800	.0304	89.2	0.37	..

withdrawing substituents in the benzyl part facilitate enolization ($\rho_{ArCH_2} \cong +0.5$) as was found to be the case in selenium dioxide oxidation (Table VI).

TABLE VI

FIRST-ORDER CONSTANTS FOR DEPENDENCE OF RATE OF ENOLIZATION ON KETONE CONCENTRATION (0.5 M H_2SO_4–70% HOAc)

Run	Compound	[Ketone], M	[Br$_2$], M	$k \times 10^4$, sec.$^{-1}$
32	$C_6H_5COCH_2C_6H_5$	0.1000	0.00415	1.11
33	$C_6H_5COCH_2C_6H_4NO_2$-p	0.0405	0.00423	1.55

The rate of oxidation of phenyl p-nitrobenzyl ketone is anomalous in that there is a large discrepancy between the observed rate constant (1.28×10^{-4} M^{-1}sec.$^{-1}$) and that predicted from the Hammett correlation (4×10^{-4} M^{-1}sec.$^{-1}$). The unusually low rate constant is not due to the formation of by-products since almost the theoretical yield of p-nitrobenzil can be obtained. Rate-retarding complex formation between the nitro group and the electrophilic reagent also seems to be unlikely since the addition of nitrobenzene or dioxane to the oxidation mixture causes an increase in rate. For reasons outlined in the Discussion the rates of oxidation of phenyl p-nitrobenzyl ketone in acetic acid–water–dioxane mixtures were measured. For mixtures of volume ratio 7:2:1, 7:1:2 and 7:0.35:2.65 (progressively replacing water by dioxane) the measured rate constants at 89.2° were 3.35, 5.80 and 7.58 M^{-1}sec.$^{-1}$ $\times 10^4$, respectively. In contrast, the rate constant for oxidation of desoxybenzoin was *decreased* by replacement of water by dioxane; in acetic acid–water–dioxane 7:2:1 the observed rate constant at 89.2° was $2.45 \times 10^{-4} M^{-1}$sec.$^{-1}$. However, the rate constant for oxidation of phenyl p-nitrobenzyl ketone *increased linearly* with the concentration of added strong acid, as was observed with desoxybenzoin; for example the observed second-order rate constants in 70% acetic acid containing 0.25 and 0.50 M p-toluenesulfonic acid monohydrate were 3.40×10^{-4} and 5.15×10^{-4} M^{-1}sec.$^{-1}$, respectively.

The hydrogen–deuterium kinetic isotope effect for the oxidation of desoxybenzoin by selenious acid was measured using α,α-dideuteriodesoxybenzoin as the labeled substrate and a value (k_H/k_D) of 6.0 was obtained at 89.2°. The isotope effect for the reaction under catalysis by oxalic acid was found to be virtually the same (5.8). In neither case did deuterium exchange with solvent occur at a rapid rate relative to oxidation since rate constants were steady until the latter stages of the reaction when some upward drift was detected (Fig. 8).

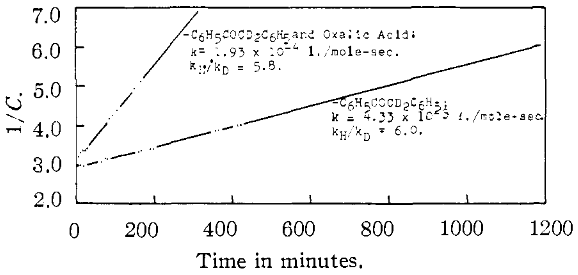


Fig. 8.—Isotope effect studies; t = 89.2°.

The sensitivity of reaction rate to steric effects was ascertained from the kinetics of oxidation of 2,4,6-trimethylphenyl benzyl ketone and 2,4,6-trimethylbenzyl phenyl ketone, obtained as second order rate constants (89.2°) equal to 4.1×10^{-4} M^{-1}sec.$^{-1}$ and *ca.* 0.4×10^{-4} M^{-1}sec.$^{-1}$ as compared to $2.59 \times 10^{-4} M^{-1}$sec.$^{-1}$ for desoxybenzoin. It should also be noted that the ratio of oxidation rate constants for trimethylphenyl benzyl ketone and desoxybenzoin (1.58) is close to the ratio of enolization rate constants for acetomesitylene and acetophenone (1.47) under comparable conditions,[19a] which again illustrates the parallelism between these two reactions.

The possibility that benzoin might be an intermediate in the oxidation of desoxybenzoin to benzil was ruled out by the fact that the observed rate constant at 89.2° (0.11×10^{-4} M^{-1}sec.$^{-1}$) is only about one-twentieth as large as is that of desoxybenzoin under comparable conditions.

Lastly it was ascertained that the reaction rate was insensitive to free radical initiators and inhibitors; neither oxygen, nor potassium persulfate

[19a] L. Zucker and L. P. Hammett, THIS JOURNAL, **61**, 2779 (1939).

influenced the rate appreciably and with *p*-quinone only a slight deceleration was noted, possibly due to complex formation with the reagent.

Catalysis by Sodium Acetate.—To gain further information concerning catalysis in the selenium dioxide oxidation of ketones, the effect of added acetate ion upon the rate of reaction was measured. (In this connection it had been reported that sodium acetate markedly slows down the rate of oxidation of 1,4-diketones.[22]) At equivalent concentrations of desoxybenzoin and selenious acid it was found that by the addition of up to one molar equivalent of sodium acetate the *initial* second-order rate constant was increased up to a factor of three, the maximum acceleration occurring at one equivalent. At greater than one molar equivalent of sodium acetate the initial rate constant decreased with increasing acetate ion concentration (Fig. 9).

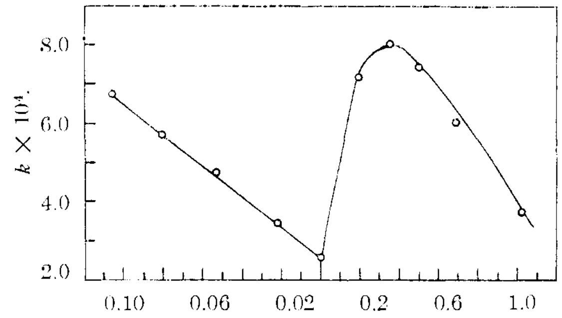


Fig. 9.—Rate of oxidation of desoxybenzoin as a function of "acidity."

The kinetics of each reaction were not cleanly second order, but showed a complex dependence upon the concentration of sodium acetate. At low acetate concentrations the rate constant gradually increased, went through a maximum in the range where the concentrations of acetate and total selenium(IV) species were the same, and then decreased. At higher concentrations of sodium acetate the rate of oxidation gradually decreased as the reaction proceeded. The only product of oxidation which could be detected was benzil, which was obtained in quantitative yield. The kinetic data are summarized in Table VII and Figs. 9 and 10.

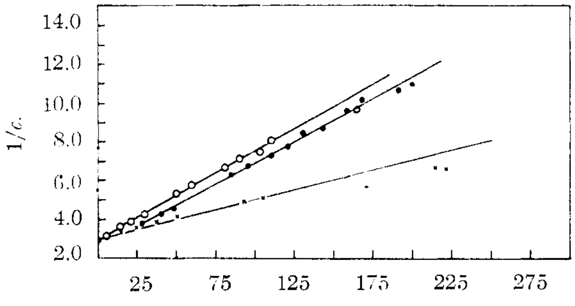


Fig. 10.—Oxidation of desoxybenzoin in the presence of sodium acetate: run 39, O; run 38, ●; run 42, ×.

To evaluate the effect of sodium acetate upon the substituted desoxybenzoins, kinetic runs were made in the region of concentrations where the maximum acceleration for desoxybenzoin occurred. Surprisingly, electron-withdrawing groups attached to the phenyl ring increased the rate of oxidation while those on the benzyl group decreased the reaction rate, a result which was a complete inversion of those previously obtained under acid-catalyzed conditions. These results, along with the Hammett correlations, appear in Table VIII and Figs. 11 and 12.

Table VII

The Effect of Sodium Acetate upon Rate t = 89.2°

Run	$[SeO_2]$, M	$[C_{14}H_{20}O]$, M	[NaOAc], M	$k \times 10^4$, M^{-1} sec.$^{-1}$ (init.)
5	0.364	0.364	0.000	2.59
38	.345	.347	.188	7.19
39	.355	.352	.349	8.03
40	.345	.345	.502	7.38
41	.351	.351	.685	6.06
42	.345	.342	1.020	3.85

Table VIII

Substituent Effects in the Acetate-catalyzed Oxidation of Substituted Desoxybenzoins at 89.2°

Run	Ketone	[Ketone], M	$[SeO_2]$, M	[NaOAc], M	$k \times 10^4$, M^{-1} sec.$^{-1}$
39	$C_6H_5COCH_2C_6H_5$	0.355	0.352	0.349	8.03
43	p-$C_2H_5OC_6H_4COCH_2C_6H_5$	.183	.363	.366	5.19
44	p-$ClC_6H_4COCH_2C_6H_5$	.178	.355	.363	11.90
45	p-$CH_3OC_6H_4CH_2COC_6H_4$	.235	.358	.356	9.55
46	p-$BrC_6H_4CH_2COC_6H_4$	.043	.164	.164	6.61
47	p-$NO_2C_6H_4CH_2COC_6H_4$	.078	.377	.377	1.60

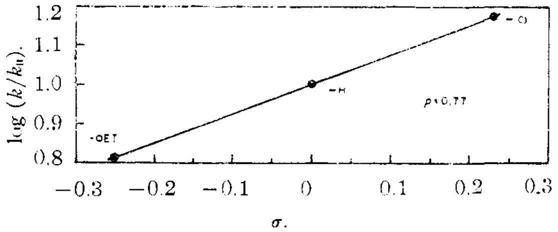


Fig. 11.—Hammett correlation for rates of oxidation of p-$XC_6H_4COCH_2C_6H_5$ in the presence of sodium acetate.

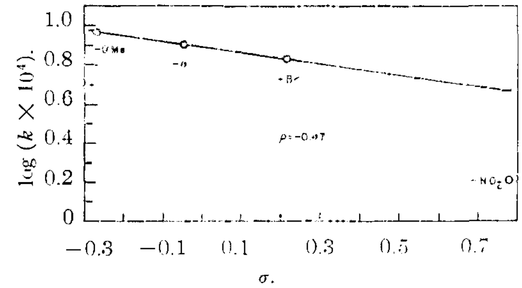


Fig. 12.—Hammett correlation for rates of oxidation of p-$XC_6H_4CH_2COC_6H_5$ in the presence of sodium acetate.

The oxidation of *p*-nitrobenzyl phenyl ketone was again found to be anomalously slow, and the deviation (Fig. 14) was far more pronounced in the presence of sodium acetate. Addition of nitrobenzene to the reaction mixture increased the initial rate of reaction markedly, but this acceleration soon disappeared. The effect of nitrobenzene upon the rate of oxidation of desoxybenzoin was to diminish the rate constant slightly. The results of these experiments are shown in Table IX.

TABLE IX

Run	Ketone	[Ketone], *M*	[SeO$_2$], *M*	[NaOAc], *M*	[C$_6$H$_5$NO$_2$], ml./25 ml. of 70% acetic acid	$k \times 10^4$, M^{-1} sec.$^{-1}$
47	p-NO$_2$C$_6$H$_4$CH$_2$COC$_6$H$_5$	0.078	0.377	0.377	0	1.60
48	p-NO$_2$C$_6$H$_4$CH$_2$COC$_6$H$_5$	.164	.318	.318	2.5	4.16
39	C$_6$H$_5$COCH$_2$C$_6$H$_5$	.355	.352	.349	0	8.03
49	C$_6$H$_5$COCH$_2$C$_6$H$_5$	.316	.316	.316	2.5	6.90

Steric effects in the base-catalyzed reaction were evaluated by a study of 2,4,6-trimethylphenyl benzyl ketone (II), 2,4,6-trimethylbenzyl phenyl ketone (III) and 2,4,6-triisopropylphenyl benzyl ketone (IV). From the rates of oxidation of II and IV it may be concluded that increasing the bulk of the *o*-substituents proximate to the carbonyl group does not decrease the rate of oxidation. The extremely slow rate found for III indicates that the rate of reaction is relatively sensitive to *o*-substitution in the ring attached to the methylene group, the effect being to slow down the oxidation rate drastically (Table X).

TABLE X

STERIC EFFECTS ON THE SODIUM ACETATE-CATALYZED OXIDATION OF DESOXYBENZOINS AT 89.2°

Run	Ketone	[Ketone], *M*	[SeO$_2$], *M*	[NaOAc], *M*	$k \times 10^4$, M^{-1} sec.$^{-1}$
39	C$_6$H$_5$COCH$_2$C$_6$H$_5$	0.355	0.352	0.349	8.03
50	II	.204	.380	.380	8.25
51	III	.0304	.0954	.954	0.36
52	IV	.021	.094	.094	15.00

Measurement of the rate of acetate-ion-catalyzed oxidation of α,α-dideuteriodesoxybenzoin revealed an isotope effect k_H/k_D of *ca.* 7.6 at the start of the reaction (at 89.2°) and a subsequent steady decrease in isotope effect as the reaction proceeded (Fig. 13).

The effect of *p*-substituents in the benzoyl moiety on the rate of acetate ion-catalyzed oxidation ($\rho_{ArCO} = +0.77$) is quite similar to that in the acetate ion-catalyzed enolization of acetophenones[20] ($\rho = +0.5$), and for this reason it seemed of interest to compare the substituent effects for acetate ion-catalyzed oxidation and enolization of desoxybenzoin with substituents in the benzyl part. The measurements on the rate of acetate ion-catalyzed enolization given in Table XI show a striking lack of correspondence with the data for oxidation; *p*-nitro substitution decreases the rate of oxidation but enhances greatly the rate of enolization.

TABLE XI

ENOLIZATION RATES AT 38.8° IN 90% ACETIC ACID; 0.5 *N* NaOAc

Run	Ketone	[Ketone]	[Br$_2$]	$k_1 \times 10^1$, l./sec.
53	C$_6$H$_5$CH$_2$COC$_6$H$_5$	0.05045	0.00262	4.52
54	p-NO$_2$C$_6$H$_4$CH$_2$COC$_6$H$_5$	0.05000	0.00262	Immeasurably fast

Discussion

A. Acid-catalyzed Oxidation.—The permissible mechanistic interpretations of the reaction of desoxybenzoin with selenious acid in aqueous acetic acid are sharply limited by the observed rate equation: velocity $= k[\text{SeO}_2][\text{C}_6\text{H}_5\text{COCH}_2\text{C}_6\text{H}_5][\text{H}^+]$; kinetic isotope effect: $k_H/k_D = 6(89.2°)$; and substituent effects including: $\rho_{ArCO} = -0.56$, $\rho_{ArCH_2} \cong +0.25$. For example the intermediacy of the enol of desoxybenzoin can be excluded. If the reaction were to involve rate-determining enolization followed by a fast reaction of the enol with selenium dioxide (a mechanism analogous to halogenation of ketones),[21] the rate of reaction would not depend on the selenium dioxide concentration, contrary to observations. If the reaction were to involve rapid, reversible enolization followed by slow reaction of the enol with the conjugate acid of selenious acid, the ratio k_H/k_D should have been equal to unity instead of 6. Thus, the enol is clearly *not* an important intermediate in the oxidation of desoxybenzoin by selenious acid as has been supposed previously,[8-15,22] although the substituent effects are very similar for enolization and oxidation.

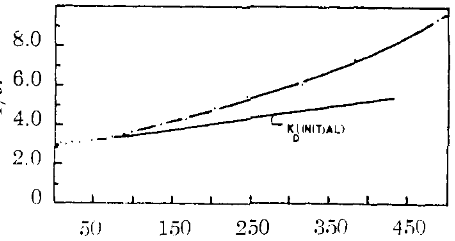


Fig. 13.—Isotope effect in the presence of sodium acetate; $t = 89.2°$; k_D (initial) $= 1.06 \times 10^{-4}$ l./mole-sec.; $k_H/k_D = 7.59$.

Another type of process which must be considered since it is commonly encountered in reactions of ketones, is nucleophilic addition to the carbonyl group. This possibility is decisively excluded by the failure of the *ortho* group in 2,4,6-trimethylphenyl benzyl ketone to depress the rate of oxidation as would be expected from the large *ortho* effects operative in the acid-catalyzed esterification of substituted benzoic acids.[23]

The reasonable alternatives which remain can be summarized as: (1) electrophilic attack on the carbonyl oxygen with simultaneous or subsequent nucleophilic attack on the α-hydrogens, (2) electrophilic attack on the α-hydrogen with subsequent or simultaneous nucleophilic attack on the α-carbon atom and (3) a cyclic process involving simultaneous attack on an α-hydrogen and (a) the carbonyl oxygen or (b) the α-carbon. The possibilities 2 and 3b can be discounted since these cannot be reconciled with the observed ρ-values nor with the fact that the presence of a carbonyl group enhances enormously the ease of oxidation of a methylene group to a carbonyl function.

In contrast, possibility 1 is consistent with all our data when considered in terms of HSeO$_2^+$ or H$_2$SeO$_3^+$ as electrophile and an available base,

---

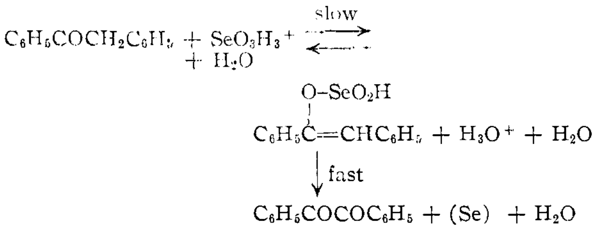
(20) V. G. Morgen and H. B. Watson, *J. Chem. Soc.*, 1173 (1935).

(21) See ref. 18, Chapter VIII

(22) See also J. C. Banerji, D. H. R. Barton and R. C. Cookson, *J. Chem. Soc.*, 5041 (1957), concerning the selenium dioxide oxidation of 1,4-diketones.

(23) C. N. Hinshelwood and A. R. Legard, *ibid.*, 592 (1935), found that the rate of acid-catalyzed esterification of 2,4,6-trimethylbenzoic acid by benzyl alcohol is 600 times slower than that of benzoic acid.

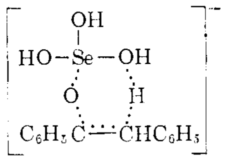
probably water, as nucleophile; the reaction may be concerted



$$C_6H_5COCH_2C_6H_5 + SeO_3H_3^+ + H_2O \overset{slow}{\rightleftarrows} \overset{O-SeO_2H}{C_6H_5C{=}CHC_6H_5} + H_3O^+ + H_2O \xrightarrow{fast} C_6H_5COCOC_6H_5 + (Se) + H_2O$$

or may involve reaction of a preformed ketone–selenium(IV) proton complex with water, or both. This process is very suggestive of acid-catalyzed enolization[24] (the only difference being in the electrophilic reagent) and on the basis of this formulation it is not unexpected that the ρ-values should be very similar for both reactions, as is observed. It is also pertinent that with an unsymmetrical ketone which forms one enol faster than the alternative enol the kinetically preferred direction of enolization parallels the direction of oxidation by selenious acid. Thus, for example cholestanone forms the Δ^2-enol much faster than the Δ^3-enol (as indicated by the occurrence of acid-catalyzed halogenation at C_2) and similarly forms the 2,3-diketone with selenium dioxide.[25,26]

The cyclic version of mechanism 1, which corresponds to possibility 3a and which involves a transition state of the type

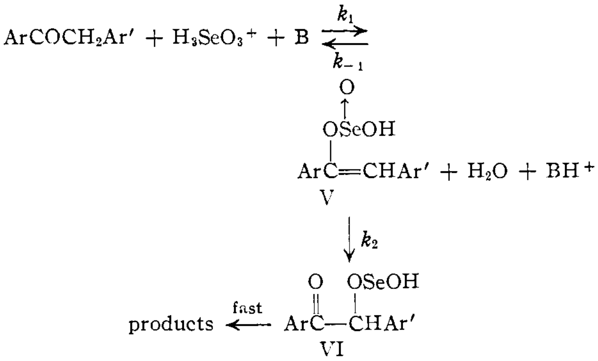


cannot be excluded rigorously by our data. However, acceptance of such a possibility creates the problem of explaining (among other things) the occurrence of acid catalysis since it is not clear why a similar process involving unprotonated selenium dioxide or selenious acid should not be comparably facile; protonation of the oxidizing agent cannot enhance both its electrophilic and nucleophilic capacities but, if anything, should favor one at the expense of the other.

Our data are not sufficient to allow a peremptory choice between the electrophiles $SeO_3H_3^+$ and SeO_2H^+; however, the available evidence points to the former possibility. The relative insensitivity of the rate constant for the oxidation of desoxybenzoin to water concentration and, even more important, the behavior of phenyl p-nitrobenzyl ketone (discussed below) are more readily interpreted on the assumption that $SeO_3H_3^+$ is involved as electrophile. This cation can serve as an effective electrophile even if the displacement of water from $SeO_3H_2^+$ is not concerted because of the availability of low energy 4d-orbitals of selenium for bonding.[27] Although SeO_2H^+ is certainly a much more powerful electrophile and although the existence of this ion has been demonstrated by isolation of the salt $SeO_2H^+ClO_4^-$,[28] it would seem that this species is probably not present in sufficiently high concentration in the aqueous media employed in our studies to be an important factor.

The conversion of enol selenite V to diketone can be formulated reasonably in terms of a selenium(II) ester intermediate VI which would yield diketone by 1,2-elimination of $[H_2SeO]$ in some way leading ultimately to $(Se)_n$ and water. The isomerization of the enol selenite to the selenium(II) ester is considered as an internal rearrangement which as indicated below seems to be subject to acid catalysis. The low reactivity of benzoin as compared to desoxybenzoin indicates that the selenium(II) ester decomposes oxidatively to benzil rather than indirectly by hydrolysis to benzoin followed by a second stage of oxidation.

It is desirable to consider here the anomalously slow rate of oxidation of phenyl p-nitrobenzyl ketone by selenious acid, the observed rate constant (1.28×10^{-4} M sec.$^{-1}$, Table V) being much less than that predicted from the Hammett equation ($>4 \times 10^{-4}$ M sec.$^{-1}$), and even smaller than that of desoxybenzoin itself (2.59×10^{-4} M sec.$^{-1}$). As indicated by the data in Table VI the rate of acid-catalyzed *enolization* of phenyl p-nitrobenzyl ketone is not at all unusual and agrees with the expected ρ-values for enolization of *ca.* +0.5. This dichotomy of effects due to substitution of p-nitro in the benzyl part, increasing the rate of enolization but decreasing the rate of selenium dioxide oxidation, can be explained, accepting the mechanism proposed above for the oxidation reaction, by supposing that the enol selenite reverts to starting materials to a considerable extent in the case of phenyl p-nitrobenzyl ketone. The appropriate analysis can be made based on the system *with $H_3SeO_3^+$ definitely specified as the*



$$ArCOCH_2Ar' + H_3SeO_3^+ + B \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \underset{V}{ArC(OSeOH){=}CHAr'} + H_2O + BH^+ \xrightarrow{k_2} \underset{VI}{ArC(=O)-CH(OSeOH)Ar'} \xrightarrow{fast} products$$

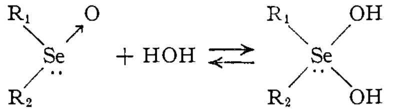
---

[24] For recent studies see (a) C. G. Swain, E. C. Stivers, J. F. Reuwer and L. J. Schaad, THIS JOURNAL, **80**, 5885 (1958), and (b) C. G. Swain, A. J. DeMilo and J. P. Cordner, *ibid.*, **80**, 5983 (1958).

[25] L. F. Fieser, M. Fieser, "Natural Products Related to Phenanthrene," 3rd ed., Reinhold Publ. Corp., New York 18, N. Y., pp. 262–267.

[26] See E. J. Corey and R. A. Sneen, THIS JOURNAL, **77**, 2505 (1955).

[27] There are numerous indications that the 4d-orbitals of selenium are of sufficiently low energy to induce electrophilic behavior. These include (1) non resolvability of selenoxides, probably a consequence of the process



and (2) stability of diphenyldichloroselenium and similar compounds; see T. W. Campbell, H. G. Walker and G. M. Coppinger, *Chem. Revs.*, **50**, 280 (1952).

[28] E. J. Arlman, *Rec. trav. chim.*, **58**, 871 (1939).

electrophile. Assuming that the selenium(II) ester VI is converted rapidly to products, the expression for the reaction velocity is

$$v_{\text{obs}} = \frac{k_2k_1[\mathrm{H_3SeO_3^+}][\mathrm{ArCOCH_2Ar'}][\mathrm{B}]}{k_2 + k_{-1}[\mathrm{H_2O}][\mathrm{BH^+}]} \quad (1)$$

The symbol B denotes the available bases water or acetate ion and, although there should be a different term for each with a different k_1 and k_{-1}, this complication can be ignored in the present treatment. The reaction velocity predicted from the Hammett correlation (v_{H}) is for $k_2 > k_{-1} > k$

$$v_{\text{H}} = k_1[\mathrm{H_3SeO_3^+}][\mathrm{ArCOCH_2Ar'}][\mathrm{B}]$$

$$\frac{v_{\text{obs}}}{v_{\text{H}}} = \frac{k_2}{k_2 + k_{-1}\,[\mathrm{H_2O}][\mathrm{BH^+}]} \cong 0.25 \quad (2)$$

$$k_2 \cong {}^1/_3k_{-1}[\mathrm{H_2O}][\mathrm{BH^+}] \quad (3)$$

and consequently in 70% aqueous acetic acid the enol selenite V returns to the starting materials at a rate which is faster than that for rearrangement to the selenium(II) ester VI. Equation 2 predicts that decreasing the quantity [H_2O] at constant [B] should cause v_{obs} to increase and to approach a limit, v_{H}. This is indeed observed experimentally as indicated by the rate data for phenyl *p*-nitrobenzyl ketone in acetic acid–water–dioxane mixtures. It is important to note that there is no such effect in the case of desoxybenzoin, but instead only a small decrease in rate constant when solvent water is replaced by dioxane. We conclude, therefore, that $H_3SeO_3^+$ (and not $HSeO_2^+$) is the important electrophile for the formation of enol selenite and that reversion of enol selenite to starting materials occurs to a large extent in the oxidation of phenyl *p*-nitrobenzyl ketone in 70% aqueous acetic acid.

Equation 1 does not predict a linear increase of v_{obs} for phenyl *p*-nitrobenzyl ketone with increasing concentration of strong acid. The fact that such a relationship is observed experimentally necessitates modification of the above scheme and of equation 1. Specifically, the data on acid catalysis suggest that the rearrangement of enol selenite to selenium(II) ester (V → VI) is acid catalyzed at rate = k_2[V][HA]. Equation 1 then becomes

$$v_{\text{obs}} = \frac{k_2k_1[\mathrm{H_3SeO_3^+}][\mathrm{ArCOCH_2Ar'}][\mathrm{B}]}{k_2 + k'_{-1}[\mathrm{H_2O}]} \quad (2)$$

which is in harmony with all of our observations. Although the occurrence of acid catalysis in the conversion of V to VI is unexpected, it is certainly plausible, and we adopt this view subject to the results of further experimentation.

It is instructive to consider the energetics of the acid-catalyzed oxidation of desoxybenzoin and phenyl *p*-nitrobenzyl ketone by selenious acid. A graphical representation is shown in Fig. 14. For the oxidation of phenyl *p*-nitrobenzyl ketone the energies of the transition states V‡ and VI‡ are similar, where as for desoxybenzoin the energy of VI‡ is much less than that of V‡. Since $\Delta E^{\ddagger}_{\mathrm{V}^{\ddagger}}(\mathrm{Ar'} = C_6H_5)$ is only *ca.* 0.1 kcal./mole more than $\Delta E^{\ddagger}_{\mathrm{V}^{\ddagger}}(\mathrm{Ar'} = C_6H_4NO_2)$, it follows that $\rho_{(\mathrm{V} \rightarrow \mathrm{VI})}$ is opposite in sign to $\rho_{(\mathrm{ketone} \rightarrow \mathrm{V})}$ and is much larger. The large negative value of ρ for the rearrangement of V to VI must be associated with unusually large electron demand by the selenium containing group during attachment to the α-carbon atom (*i.e.*, compared to attack by a proton acid). This feature of the oxidation reaction is elegantly and simply accounted for by the postulate that the rearrangement product would then be the conjugate acid of the selenium(II) ester which can be represented as

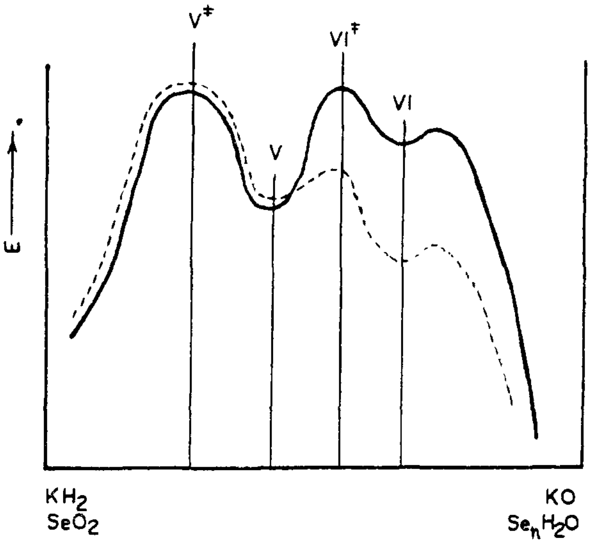
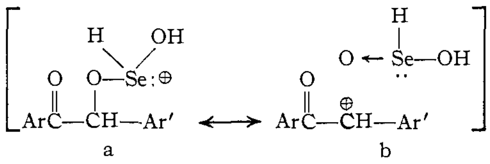


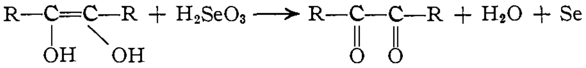
Fig. 14.—Reaction coördinate *vs.* energy for selenium dioxide oxidation of desoxybenzoin (dashed curve) and phenyl *p*-nitrobenzyl ketone (solid curve).



If canonical form b contributes to the structure of such a cation, strongly electron-withdrawing groups in the *p*-position of the Ar′ group, such as nitro, would destabilize this structure and inhibit its formation. (The degree of inhibition, of course, will depend on the location of VI‡ along the reaction coördinate.) It should be noted that in form b the selenium atom possesses the electronic configuration of the stable plus four oxidation state and, hence, a large contribution from b is not unreasonable. The same argument can be made with regard to the formation of the unprotonated selenium(II) ester. However, the degree of inhibition by electron-withdrawing groups should be much smaller in this instance.

In the case of desoxybenzoin, the enol selenite rearranges sufficiently rapidly to the selenium(II) ester so that return to the starting materials is quite minor. The strongest evidence on this point derives from the kinetic study of the oxidation of α,α-dideuteriodesoxybenzoin in which only a small increase in rate constant was noted during the course of reaction. The extent of reversion of enol selenite to starting materials in the cases intermediate between desoxybenzoin and phenyl *p*-nitrobenzyl ketone is unknown. However, it seems probable that there is a continuous increase in reversion with substituents of increasing σ-constant in the benzyl part. This question merits careful investigation and further quantitative studies are planned. In addition the importance of the reversion of enol selenite in the oxidation of simple aliphatic and alicyclic ketones must be evaluated.

Although in the case of desoxybenzoin the enol selenite intermediate is formed directly and not *via* desoxybenzoin enol, it is probable that there are instances in which the enol is an intermediate. For example, when a substantial amount of enol structure is in mobile equilibrium with a ketone it is likely that direct combination of the enol with the selenium(IV) reagent will produce the enol selenite rapidly. For the case of enols which do not possess strongly electron-withdrawing substituents this should result in facile oxidation to diketone. In agreement, it is known that 1,2-enediols are rapidly oxidized to 1,2-diketones by selenium dioxide.[29] Certain enols possessing electron-withdrawing, substituents, *e.g.*, enolized 1,3-diketones, can be expected to be relatively less sensitive to oxidation by selenium dioxide despite the rapid formation of enol and enol selenite derivatives. The same effect observed with phenyl p-nitrobenzyl ketone can operate in these systems to make the k_2 step rate determining.

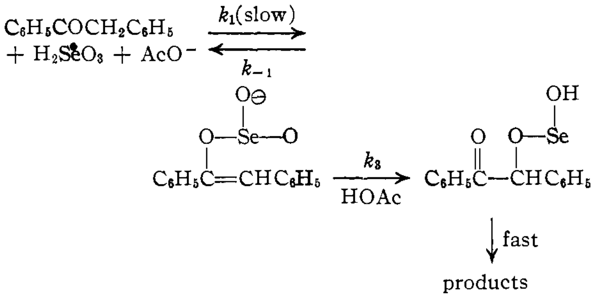


$$R{-}C(OH){=}C(OH){-}R + H_2SeO_3 \longrightarrow R{-}C(=O){-}C(=O){-}R + H_2O + Se$$

B. Acetate Ion-catalyzed Oxidation.—The data obtained on catalysis of the selenium dioxide oxidation of desoxybenzoin by sodium acetate can be interpreted on the basis of the mechanism proposed above with only those changes in the reactive species which are appropriate for a medium of attenuated acidity and enhanced nucleophilic potency. For desoxybenzoin the observed rate dependence, which can be expressed by the rate equation

$$-\,d[SeO_2]/dt = k[SeO_2][C_6H_5COCH_2C_6H_5][AcO^-]$$

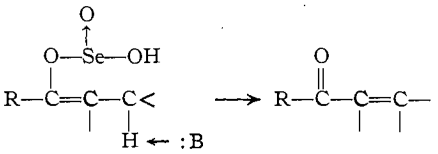
the occurrence of a substantial hydrogen isotope effect ($k_H/k_D = 7.6$), together with the established mechanism for the analogous acetate ion-catalyzed enolization of ketones argue for the process



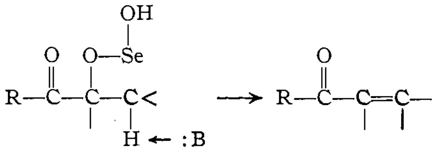
$$C_6H_5COCH_2C_6H_5 + H_2SeO_3 + AcO^- \underset{k_{-1}}{\overset{k_1(\text{slow})}{\rightleftharpoons}} C_6H_5C(OSeO_2^{\ominus}){=}CHC_6H_5 \xrightarrow[HOAc]{k_3} C_6H_5C(=O){-}CH(OSeOH)C_6H_5 \xrightarrow{\text{fast}} \text{products}$$

Further support for this formulation is provided by the similarity of the ρ-value for substitution in the benzoyl moiety (+0.77) with that obtained for the acetate-ion catalyzed enolization of acetophenones (+0.5). In addition the observed o-substituent effects are wholly consistent with this scheme. In sharp contrast, however, are the observed effects of p-substitution in the benzyl moiety; p-nitro substitution decreases the rate of selenium dioxide oxidation but enormously accelerates the rate of enolization of desoxybenzoin. Again, phenyl p-nitrobenzyl ketone by any criterion is clearly quite a different case from desoxybenzoin, *e.g.*, it is again found to be anomalous in the Hammett correlation. Under the conditions used for the acetate-ion catalyzed oxidation of phenyl p-nitrobenzyl ketone the rate of acetate-catalyzed enolization is at least 10^3 times as fast as oxidation. It is necessary to conclude, therefore, that in this case k_1 and k_{-1} are both much greater than k_2 and that the formation of α-substituted selenium(II) ester is rate determining. There are three factors which probably determine this outcome: (1) the accelerating effect of p-nitro on acetate-catalyzed enolization–ketonization, (2) the strong retardation of the rearrangement of enol selenite to selenium(II) ester by p-nitro and (3) the retardation of the rearrangement of enol selenite to selenium(II) ester due to the decreased acidity of the medium. On the basis of the last effect it would be anticipated that reversion of enol selenite would generally be of more importance in the acetate-catalyzed oxidation than in the acid-catalyzed process. Our data on desoxybenzoins tend to substantiate this point and indicate that in the case of desoxybenzoin itself substantial return of enol selenite to starting materials occurs. This would explain the marked drift in the rate constant for the oxidation of α,α-dideuteriodesoxybenzoin to higher values as the reaction proceeds. It also suffices to explain the negative value of $\rho_{Ar'CH_2}$ for the acetate-catalyzed process which contrasts with the positive value of $\rho_{Ar'CH_2}$ in acetate-catalyzed enolization.

Some Observations on Related Reactions.—The conversion of ketones to α,β-unsaturated derivatives by oxidation with selenium dioxide is often competitive with diketone formation and may even be the exclusive reaction. If, as seems likely, this reaction also proceeds *via* an intermediate enol selenite ester, a number of reaction paths require consideration: (1) decomposition of an enolate–$HSeO_2^+$ ion pair by transfer of a hydride ion from C_β of the enolate to $HSeO_2^+$; (2) concerted 1,4-elimination from the enol ester



(3) concerted 1,2-elimination from the selenium(II) ester



At present no decision between the alternatives can be made and, indeed, it is quite possible that more than one is operative and even that acid catalysis is involved. The dehydrogenation of 1,4-diketones which has been regarded as a special case involving a direct removal of two hydrogens by selenium dioxide when those hydrogens are

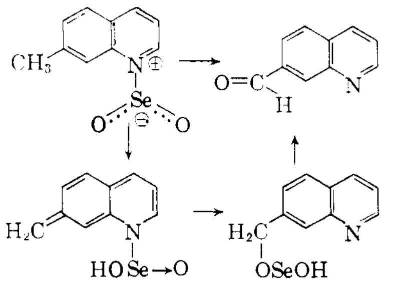
---

[29] J. R. Holker, *J. Chem. Soc.*, 579 (1955).

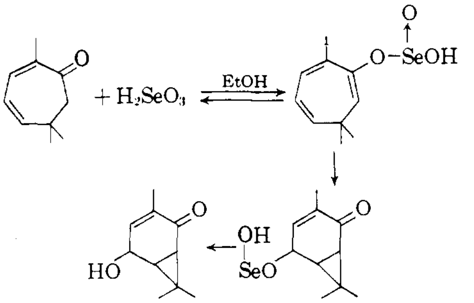
cis[22] is almost certainly not mechanistically unique and can be formulated reasonably in terms of the possibilities 1, 2 or 3 or a combination of these.

The factors which influence the relative amounts of diketone and α,β-unsaturated ketone in structures which permit either are of considerable practical interest and doubtless should be explored experimentally. One factor which deserves mention in this connection is a frequently encountered steric effect: shielding of the α-methylene group by nearby bulky substituents often favors the formation of α,β-unsaturated ketone. Thus, for example, 12-ketosteroids generally afford $\Delta^{9,11}$-12-ketones upon oxidation with selenium dioxide rather than 11,12-diketones.[30] Such an effect is explained reasonably on the basis of the mechanistic details presented above by application of standard stereochemical analysis.

In addition to formation of diketones and unsaturated ketones by the oxidation action of selenium dioxide, there are a number of other more complex changes which have been observed and which merit consideration in the light of our results. For example, the oxidation of methylated quinolines and pyridines, a valuable synthetic method for the preparation of aldehydes, can be interpreted reasonably by analogy with ketone oxidation, as illustrated by the conversion of 7-methylquinoline to the corresponding aldehyde (91% yield).

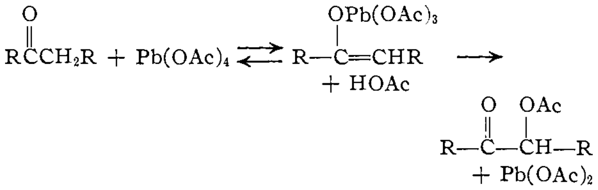


A second reaction of selenium dioxide, the rather unusual oxidation of eucarvone, can also be explained simply and in a manner consonant with the known proclivities of the eucarvone system.[31]



Although one has little direct information on the detailed mechanism of such complex changes involving selenium dioxide, it is now possible, nonetheless, to consider and analyze these processes in more fundamental terms than heretofore possible. This insight ought to be of value in synthetic and structural investigations.

Finally, it is possible that the type of mechanism proposed above also operates in other oxidizing systems. For example, the α-acetoxylation of ketones by lead tetraacetate[32] may involve formation of an enol–lead triacetate derivative directly from the ketone followed by subsequent internal rearrangement–elimination.



$$R\overset{O}{\overset{\|}{C}}CH_2R + Pb(OAc)_4 \rightleftarrows R-\overset{OPb(OAc)_3}{\overset{|}{C}}=CHR + HOAc \longrightarrow R-\overset{O}{\overset{\|}{C}}-\overset{OAc}{\overset{|}{C}H}-R + Pb(OAc)_2$$

Acknowledgment.—It is a pleasure to thank the Union Carbide Co. for a fellowship.

Experimental[33]

Kinetic Measurements.—An oil-bath which was stirred by a Bodine motor and insulated with vermiculite was regulated to ±0.005° by means of a thermostat. Temperatures were measured with Moeller thermometers which had been calibrated against Bureau of Standards thermometers. In all kinetics runs, unless otherwise stated, 70% acetic acid, prepared by diluting 7 volumes of du Pont glacial acetic acid with 3 volumes of demineralized water, was used as a solvent.

In the kinetic runs a weighed amount of selenium dioxide, purified by successive sublimations, was placed in a 50-ml. two-necked flask which could be fitted with a rubber stopple and a standard taper glass plug. To this was added 25 ml. of 70% acetic acid and the solution was heated to the desired temperature. The reaction was started by adding a weighed amount of ketone and swirling the stoppered flask in the oil-bath. Less than 15 seconds was required to dissolve the ketone. In the case of difficultly-soluble ketones this procedure was reversed; that is, the ketone was dissolved first and the selenium dioxide added to the solution.

Aliquots were withdrawn at measured time intervals by puncturing the rubber stopple with a hypodermic syringe. These were quenched by injecting the solution into 20 ml. of 10% potassium iodide and 80 ml. of 12% hydrochloric acid. A measured excess of 0.5000 *N* sodium thiosulfate solution was added, the solution filtered into a 500-ml. filter flask through a cotton plug, which was then washed thoroughly with water. The selenious acid solution was titrated to a starch end-point with 0.5000 *N* iodine solution.

It was found that at lower concentrations of hydrochloric acid reproducible results could not be obtained since the equilibrium shown below is not shifted completely to the right.[34] Furthermore, if the solution is not filtered free of

$$H_3SeO_3 + 4I^- + 4H^+ \rightleftarrows Sw + 2I_2 + 3H_2O$$

selenium, the end-point is difficult to see and the accuracy of the method is greatly reduced.[35] Using the above analytical procedure known amounts of selenium dioxide could be determined to within 1% of the total present.

Desoxybenzoin.—Desoxybenzoin was prepared by the method of Billard and Dehn.[36] Powdered tin (100 g., 0.835 mole), mercuric chloride (15.0 g., 0.075 mole) and 100 ml. of water were swirled until the tin was coated with mercury. The tin was then washed several times with water and drained. To this was added benzoin (100.0 g., 0.472 mole),

---

[30] E. Schwenk and E. Stahl, *Arch. Biochem.*, **14**, 125 (1947); B. G. McKenzie, V. R. Mattox, L. L. Engel and E. C. Kendall, *J. Biol. Chem.*, **173**, 271 (1948); L. F. Fieser, S. Rajagopolan, E. Wilson and M. Tishler, THIS JOURNAL, **73**, 4133 (1951).

[31] E. J. Corey, H. J. Burke and W. A. Remers, *ibid.*, **78**, 180 (1956).

[32] (a) See R. Criegee in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 8; (b) an example with steroids: F. Sondheimer, St. Kaufmann, J. Romo, H. Martinez and G. Rosenkranz, THIS JOURNAL, **75**, 4712 (1953).

[33] Deuterium and elemental analyses by Mr. J. Nemeth and associates, Microanalytical Laboratory, University of Illinois.

[34] H. F. Schott, E. H. Swift and D. M. Yost, THIS JOURNAL, **50**, 721 (1928).

[35] F. A. Gooch and W. G. Reynolds, *Z. anorg. Chem.*, **10**, 248 (1895).

[36] D. A. Ballard and W. M. Dehn, THIS JOURNAL, **54**, 3969 (1932).

ethanol (250 ml.) and concentrated hydrochloric acid (200 ml.). The solution was refluxed for 16 hours, after which the flask was filled to the neck with water and cooled until the oil solidified. The solution was filtered, the precipitate dissolved in hot methanol (4 g. per gram of solid) and the solution filtered free from tin. Upon cooling, 81.5 g. or 88% of the theoretical amount of desoxybenzoin crystallized, m.p. 56–58°. Recrystallization from methanol or hexane raised the melting point to 58–58.5°.

***p*-Nitrophenyl Phenyl Ketone.**—To 60.0 g. (0.333 mole) of *p*-nitrophenylacetic acid was added 50.0 g. (0.364 mole) of phosphorus trichloride and the mixture was refluxed for one hour, after which 400 ml. of dry benzene was added and the solution decanted from the residue of phosphorus acid onto 55.0 g. (0.467 mole) of anhydrous aluminum chloride. The mixture was refluxed and stirred for one hour, cooled, and poured onto 500 g. of crushed ice and 200 ml. of concentrated hydrochloric acid. The precipitate was removed by filtration and the filtrate was extracted once with 200 ml. of 1:1 ether–benzene and combined with the precipitate, which readily dissolved. The organic solution was washed with water, dried over anhydrous calcium chloride, and concentrated to give 70.0 g. (87.5%) of ketone, m.p. 140–144°. Recrystallization from acetone–water raised the melting point to 143.5–144°.[37] The workup used will be referred to as the "usual workup."

***p*-Ethoxyphenyl Benzyl Ketone.**—To 68.0 g. (0.500 mole) of phenylacetic acid was added 35.0 g. (0.254 mole) of phosphorus trichloride and the mixture was heated at reflux for one hour, cooled, and decanted into a dropping funnel which contained 50 ml. of benzene.[38] This was added slowly to 100 ml. (0.920 mole) of phenetole, 150 ml. of anhydrous benzene and 150 g. (0.795 mole) of stannic chloride at 0–10° with stirring, after which the solution was stirred at room temperature for three hours and then worked up in the usual manner. Recrystallization from ethanol resulted in 73 g. (60%) of purified ketone, m.p. 104°.[39]

***p*-Bromophenyl Benzyl Ketone.**—A solution of 77.5 g. (0.500 mole) of phenylacetyl chloride in 50 ml. of dry bromobenzene was added to a stirred mixture of 100 ml. of bromobenzene and 70.0 g. (0.530 mole) of anhydrous aluminum chloride over a period of one-half hour. The mixture was heated on a steam-bath for two hours and then worked up in the usual manner to yield 91 g. (66%) of the desired ketone upon distillation of the residue; b.p. 160–170° (5 mm.). Recrystallization from ethanol gave the colorless, crystalline ketone, m.p. 114–115°.[40]

***p*-Chlorophenyl benzyl ketone** was prepared by the procedure used for *p*-bromophenyl benzyl ketone except that distillation was unnecessary. From 77.5 g. (0.500 mole) of phenylacetyl chloride, 58.0 g. (50%) of purified *p*-chlorophenyl benzyl ketone was obtained, m.p. 104–105°.[41]

***p*-Bromobenzyl Phenyl Ketone.**—To 54.0 g. (0.250 mole) of *p*-bromophenylacetic acid[42] dissolved in 100 ml. of benzene was added 30.0 g. (0.220 mole) of phosphorus trichloride and the solution was refluxed for one hour, cooled, and added slowly to an ice-cold solution of 50.0 g. (0.380 mole) of anhydrous aluminum chloride in 250 ml. of benzene. The mixture was refluxed for one hour and then worked up in the usual manner to give 40% of the theoretical amount of ketone, m.p. 149°.

Anal. Calcd. for $C_{14}H_{21}OBr$: C, 61.09; H, 4.02. Found: C, 61.47; H, 4.27.

***p*-Ethoxyphenyl *p*-nitrobenzyl ketone** was prepared from *p*-nitrophenylacetyl chloride and phenetole by the procedure described for *p*-ethoxyphenyl benzyl ketone. From 25.0 g. (0.138 mole) of *p*-nitrophenylacetic acid there was obtained 26.0 g. (66%) of pure ketone, m.p. 116.5–117°.

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.45; H, 5.27; N, 4.92. Found: C, 67.45; H, 5.57; N, 4.74.

***p*-Methoxyphenylacetamide.**—To a mixture of concentrated ammonium hydroxide (100 ml.) and crushed ice (100 g.) there was added cautiously *p*-methoxyphenylacetyl chloride[43] (37.0 g., 0.200 mole). The solution was filtered and the precipitate washed thoroughly with water and dried. A yield of 34.0 g. (100%) of the amide resulted and was used without further purification.

***p*-Methoxybenzyl Phenyl Ketone.**—To a solution of phenylmagnesium bromide (0.500 mole) in ether was added 20.4 g. (0.125 mole) of *p*-methoxyphenylacetamide in small portions during a one-half hour period, after which the solution was refluxed for 44 hours. The suspension formed was poured onto 300 g. of crushed ice and 40 ml. of sulfuric acid, and after one hour the ether was removed and the aqueous layer extracted thoroughly with ether. The ether extracts were combined, washed with 100 ml. of 10% sulfuric acid and 100 ml. of saturated salt solution, dried over anhydrous sodium sulfate, and filtered. To this was added 100 ml. of 1:1 hexane–heptane and the ether was distilled off to give light yellow crystals which were recrystallized from ethanol to give 15.0 g. (53%) of colorless solid, m.p. 96.5–98°.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.70; H, 6.18. Found: C, 79.87; H, 6.34.

α,α-Dideuteriodesoxybenzoin.—To 10 g. (0.051 mole) of desoxybenzoin dissolved in 250 ml. of anhydrous ether was added 61.0 g. (1.00 mole) of deuterioacetic acid and one drop of bromine. The solution was refluxed for 48 hours, after which the ether and the deuterioacetic acid were removed by vacuum distillation. This was repeated twice more, after which the ketone was recrystallized once from anhydrous hexane.

Anal. Calcd. for $C_{14}H_{10}OD_2$: D, 16.66 atom per cent. Found: D, 16.40 atom per cent. (1.98 deuterium atoms per molecule).

Mesityl Benzyl Ketone.—A sample of this ketone[44] was purified by distillation (b.p. 4 mm. 81°) and was crystallized from absolute methanol at −70°, m.p. 31–32.5°.

2,4,6-Triisopropylphenyl Benzyl Ketone.—A sample of this ketone[45] was purified by vacuum distillation, b.p. (4 mm.) 91°, n^{25}_{D} 1.5440.

2,4,6-Trimethylbenzyl Phenyl Ketone.—Phenylmagnesium bromide prepared from 15.7 g. (0.1 mole) of bromobenzene was added slowly to a solution of 39.4 g. (0.2 mole) of mesitylacetyl chloride and 100 ml. of anhydrous ether at −50° and then was allowed to warm up to room temperature. The solution was worked up in the usual manner to give a 75% yield of the desired ketone, m.p. 162–163°.

Selenium Dioxide Oxidation of the Ketones.—The following procedure was used in all preparative oxidations of the ketones. One equivalent of ketone and 1.1 equivalents of selenium dioxide were dissolved in 70% acetic acid and the solution was heated at 89.2° for 12 hours. The solution was then poured into water and extracted with ether, the ether washed with saturated potassium carbonate solution,

Ketone	Yield benzil, %	M.p., °C.
$C_6H_5COCH_2C_6H_5$[46]	100	95
p-$ClC_6H_4COCH_2C_6H_5$[46]	96	73
p-$BrC_6H_4COCH_2C_6H_5$[46]	95	86–87
p-$C_2H_5OC_6H_4COCH_2C_6H_5$	100	66–67
p-$NO_2C_6H_4CH_2COC_6H_5$[47]	100	142
p-$NO_2C_6H_4CH_2COC_6H_4OC_2H_5$[a]	100	155–156
p-$BrC_6H_4CH_2COC_6H_5$[46]	97	86–87
p-$CH_3OC_6H_4CH_2COC_6H_5$[48]	100	63
2,4,6-$(CH_3)_3C_6H_2COCH_2C_6H_5$[46]	95	137

[a] *Anal.* Calcd. for $C_{16}H_{15}NO_4$: C, 64.20; H, 4.35; N, 4.68. Found: C, 64.10; H, 4.36; N, 4.53.

---

(37) P. Petrenko-Kritschenko, *Ber.*, **25**, 2234 (1892).

(38) C. F. H. Allen and W. E. Barker, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 156.

(39) C. Torres and Y. Gonzales, *Bull. soc. chim.*, [4] **37**, 1595 (1925).

(40) E. P. Kohler and W. D. Peterson, THIS JOURNAL, **55**, 1073 (1933).

(41) S. S. Jenkins, *ibid.*, **56**, 682 (1934).

(42) G. S. Misra and J. S. Shukla, *J. Indian Chem. Soc.*, **28**, 480 (1951).

(43) R. C. Elderfield and V. B. Meyer, THIS JOURNAL, **76**, 1883 (1954).

(44) A. Klages and G. Lickroth, *Ber.*, **32**, 1564 (1899).

(45) R. C. Fuson and R. E. Foster, THIS JOURNAL, **65**, 913 (1943).

(46) H. H. Hatt, A. Pilgrim and W. J. Hurran, *J. Chem. Soc.*, 93 (1936).

(47) F. D. Chattaway and E. A. Coulson, *ibid.*, 1080 (1928).

(48) A. McKenzie, E. M. Luis, M. Tiffeneau and P. Weill, *Bull. soc. chim.*, **45**, 414 (1929).

water, and dried. Removal of the ether by distillation yielded the crude benzil, and an infrared spectrum was obtained. In no case were any organic impurities detectable. The benzils could be recrystallized from ethanol. The table summarizes the results obtained.

In runs with sodium acetate one equivalent of sodium acetate was added. The results were the same, and no by-product could be detected.

Conductometric Titrations.—A 0.1 *M* solution of the acid to be titrated in a titration cell was maintained at 90 ± 1° using an oil-bath with acetic acid–water (7:3) as solvent. To this solution was added measured amounts of 1.06 *M* sodium acetate in the same solvent and the conductivity was measured at increments of *ca.* 0.25 ml. using a conductivity bridge. The conductivities measured initially for solvent alone and the selenious acid, oxalic acid, trifluoroacetic acid and sulfuric acid solutions in mhos $\times 10^3$ were 0.9, 1.5, 3.3, 6.3 and 40, respectively. After the addition of *ca.* two equivalents of the acetate solution the conductivity observed in each case was about 20 mhos $\times 10^3$, and in each case a simple smooth curve connecting the initial and final values was obtained.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INSTITUTE OF POLYMER RESEARCH, POLYTECHNIC INSTITUTE OF BROOKLYN]

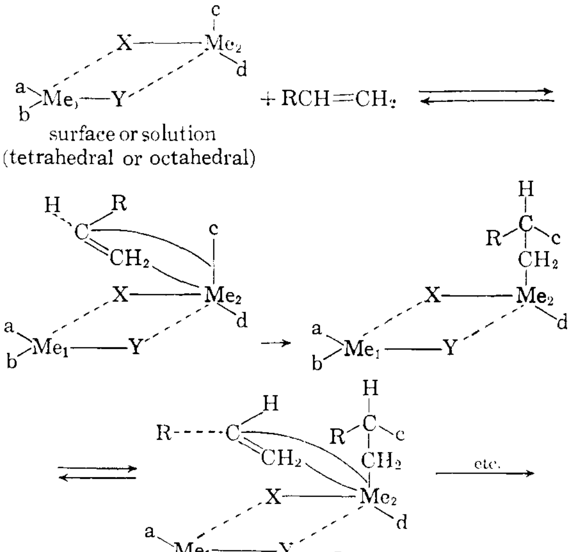
Copolymerization of Styrene and *p*-Alkylstyrenes with an Aluminum Alkyl–Titanium Trichloride Catalyst[1]

BY C. G. OVERBERGER AND F. ANG[2]

RECEIVED APRIL 7, 1959

The copolymerization of styrene and *p*-methylstyrene with the "Ziegler–Natta" catalyst system resulted in an amorphous product. From a study of their molecular weight and copolymer composition distribution, evidence was obtained to demonstrate that the products were copolymers. Additional evidence for a copolymer was obtained by comparing the properties of these products with those of a known mixture of the two homopolymers. Determination of the relative reactivity of styrene and *p*-methylstyrene show them to have about equal reactivity in this catalyst system ($r_1 = 1 \pm 0.12$, $r_2 = 1 \pm 0.12$). Analysis of the copolymer composition distribution indicated the presence of more than one type of copolymer suggesting a polyactivity of the catalyst system. The results are best explained by the assumption that at least two different types of copolymers are being formed. The copolymerization of styrene and *p*-*t*-butylstyrene failed to give appreciable copolymer; instead, from the observed crystallinity of the polystyrene and composition distribution, it was apparent that the product largely contained a mixture of the two homopolymers. The same results were obtained from the copolymerization of styrene and *p*-*n*-butylstyrene. It is tentatively concluded that the reactivity of the monomer is influenced strongly by its tendency to be coördinated on the catalyst sites and that the steric and polar factors responsible for this equilibrium will be different from these same factors which are responsible for the reactivity of monomers in solution in free radical and ionic-catalyzed polymerization.

There is considerable agreement on the over-all mechanism of the aluminum alkyl–titanium halide catalyst type.[3–10] A reduced valence state compound of titanium, vanadium or zirconium either formed *in situ* by reduction or added directly, forms an interstitial type of complex with a Lewis acid. In a heterogeneous catalyst, this interstitial binding occurs occasionally on the transition metal surface and these represent catalyst sites. In homogeneous solution a certain fraction of the reduced metal compound forms a soluble interstitial complex. On these catalyst sites or complexes are adsorbed or coördinated a π-electron system followed by a transfer of a pair of electrons from a metal–alkyl bond. There is a possibility that the pair of electrons originates from the olefin and is transferred to the metal; there is no evidence on this question. A typical representation is indicated. There is an equal possibility that the alkyl group with its electrons is derived from the transition metal. In some cases, it may function as a very labile Lewis acid in the formation of an interstitial compound with a reduced form of a transition metal (Ti, V, Zr). It is also possible that this active site or interstitial compound may have considerable ionic character.[10d]



I

Me_1, Me_2 = Ti, Al a,b,y alkyl, X = halogen
c,d alkyl, X = halogen

---

[1] This is the 13th in a series of papers concerned with ionic polymerization; for the previous paper on this series, see C. G. Overberger, E. Pearce and N. Mayes, *J. Polymer Sci.*, **34**, 109 (1959).

[2] This paper comprises a portion of a dissertation submitted by F. Ang in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the graduate school of the Polytechnic Institute of Brooklyn.

(3) F. J. Welch, B. R. Thompson, F. E. Bailey and S. Gates, Abstracts of Papers, 130th Meeting of the American Chemical Society, Atlantic City, N. J., September, 1956, p. 135.

(4) C. D. Nenitzescu, C. Huch and A. Huch, *Angew. Chem.*, **68**, 438 (1956).

(5) G. Natta, *Sci. American*, September, 98 (1957).

(6) G. Natta, P. Pong, E. Mantica, F. Danusso, G. Mazzanti and M. Peraldo, *Chem. e ind.*, **39**, 19 (1957).

(7) F. Eirich and H. Mark, *J. Colloid Sci.*, **11**, 748 (1956).

(8) D. B. Ludlum, A. W. Anderson and C. E. Ashby, THIS JOURNAL, **80**, 1380 (1958).

(9) H. Uelzmann, *J. Polymer Sci.*, **32**, 457 (1958).

(10) (a) G. Natta, *Angew. Chem.*, **69**, 686 (1957); (b) W. Carrick, THIS JOURNAL, **80**, 6455 (1958); (c) D. Breslow and N. Newburg, *ibid.*, **81**, 81 (1959); (d) H. Uelzmann, *J. Polymer Sci.*, **32**, 457 (1958).