[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE GEORGIA INSTITUE OF TECHNOLOGY]

The Mechanism of the Reimer–Tiemann Reaction[1]

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Chloroform reacts with aqueous sodium phenoxide only very slowly at 35°, but in the presence of sodium hydroxide it reacts rapidly to give *o*- and *p*-hydroxybenzaldehydes (the Reimer–Tiemann reaction). This observation shows that the Reimer–Tiemann reaction is *not* initiated by the nucleophilic attack of phenoxide ion on chloroform. The reaction instead appears to involve the reaction of chloroform with hydroxide ion to give dichloromethylene which then reacts with phenoxide ion. From the effect of sodium phenoxide concentration on the yields of aldehydes, the relative rate constant for the combination of dichloromethylene with the oxygen atom as well as the *o*- and *p*-carbon atoms of the phenoxide ion may be calculated (relative to the rate constant for combination with water).

Introduction

The reaction of phenols with chloroform and aqueous alkali to give *o*- and *p*-hydroxybenzaldehydes was discovered by Reimer[2] and elucidated in collaboration with Tiemann.[3] The mechanism most commonly written in current references to the reaction involves an SN2 attack of the *o*- or *p*-carbon atom of a phenoxide ion on chloroform followed by tautomerism of the product to a substituted benzal chloride that is then rapidly hydrolyzed. It has also been proposed that the

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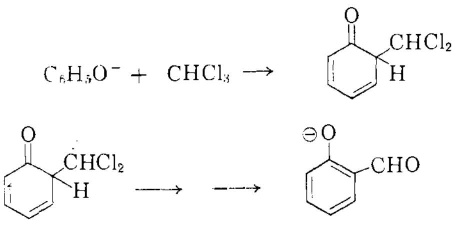
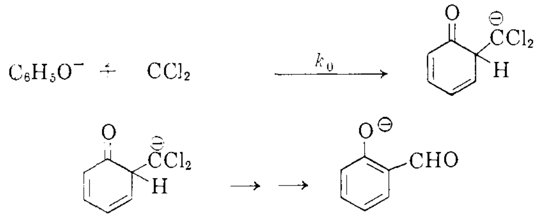


phenoxide ion combines with dichloromethylene generated by the action of alkali on chloroform.[4,5]

II

$$CHCl_3 + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} CCl_3^- + H_2O$$

$$CCl_3^- \xrightarrow{k_2} CCl_2$$



Results and Discussion

Kinetics and Product Distribution.—In order to distinguish between mechanisms I and II we have studied the kinetics of the reaction. The rate of reaction of chloroform was followed by measurements of chloride ion concentrations since every chloroform molecule liberates three chloride ions whether it enters into the Reimer–Tiemann reaction or is simply hydrolyzed to carbon monoxide and formate. It was found that in the absence of added alkali, less than 3% of 0.0267 *M* chloroform had reacted with 0.57 *M* sodium phenoxide in water at 35° during eight hours. Under similar conditions, however, with 0.08 *M* sodium hydroxide the chloroform had a half-life of about eight hours. Since about 45% of the chloroform that reacts under the latter set of conditions enters into the Reimer–Tiemann reaction (as shown by spectrophotometric measurements of the amounts of *o*- and *p*-hydroxybenzaldehyde formed), it is clear that the Reimer–Tiemann reaction does not proceed by mechanism I, which gives no explanation for the powerful catalytic action of hydroxide ion. In Table I are data on the fractions of *o*- and *p*-hydroxybenzaldehydes formed in the presence of various concentrations of sodium phenoxide.

TABLE I

YIELDS OF *o*- AND *p*-HYDROXYBENZALDEHYDES IN AQUEOUS SOLUTION AT 35°[a]

$[C_6H_5ONa]_0$	$[NaOH]_0$	f_o[b]	f_p[c]
1.445	0.247	0.326	0.342
1.090	.200	.273	.295
0.599	.233	.232	.229
.508	.199	.208	.214
.108	.364	.074	.079

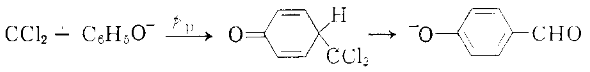
[a] $[CHCl_3]_0 \sim 0.0267$ *M* in all runs. [b] Yield of *o*-hydroxybenzaldehyde based on chloroform reacted. [c] Yield of *p*-hydroxybenzaldehyde.

The effect of phenoxide ion concentration on the fraction of the chloroform that reacts by the various paths may be analyzed in terms of mechanism II. In addition to the attack of *o*-carbon shown in this mechanism, the following reaction paths would be expected to be available for intermediate dichloromethylene

$$CCl_2 + H_2O \xrightarrow{k_w} H_2\overset{\oplus}{O}\text{–}\overset{\ominus}{C}Cl_2 \longrightarrow \longrightarrow CO \text{ and } HCO_2^-$$

$$CCl_2 + OH^- \xrightarrow{k_h} HO\overset{\ominus}{C}Cl_2 \longrightarrow \longrightarrow CO \text{ and } HCO_2^-$$

$$CCl_2 + C_6H_5O^- \xrightarrow{k_{ox}} C_6H_5O\overset{\ominus}{C}Cl_2 \longrightarrow \longrightarrow CO \text{ and } HCO_2^- \text{ and } (C_6H_5O)_3CH$$



The fraction of chloroform that reacts *via* combination with the *p* position of the phenoxide ring (f_p) may be expressed

$$f_p = \frac{(k_p/k_w)[C_6H_5O^-]}{[(k_p/k_w) + (k_o/k_w) + (k_{ox}/k_w)][C_6H_5O^-] + (k_h/k_w)[OH^-] + [H_2O]} \quad (1)$$

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(1) Part XVIII in the series "Methylene Derivatives as Intermediates in Polar Reactions"; for XVII see ref. 7.

(2) K. Reimer, *Ber.*, **9**, 423 (1876).

(3) K. Reimer and F. Tiemann, *ibid.*, **9**, 824, 1285 (1876).

(4) J. Hine, THIS JOURNAL, **72**, 2438 (1950).

(5) H. Wynberg, *ibid.*, **76**, 4998 (1954).

with an analogous expression being applicable to f_o, the fraction of *o*-substitution. Combination of the expressions for f_o and f_p gives

$$\frac{1}{f_o + f_p} = 1 + \frac{k_{ox}/k_w}{(k_o/k_w) + (k_p/k_w)} + \frac{(k_h/k_w)[OH]^- + [H_2O]}{[(k_o/k_w) + (k_p/k_w)][C_6H_5O^-]} \qquad (2)$$

Thus, a plot of $1/(f_o + f_p)$ *vs.*

$$(k_h/k_w)[OH^-] + [H_2O]/[C_6H_5O^-]$$

should give a straight line. Such a plot[6] is shown in Fig. 1. The points seem to fall reasonably near a straight line whose slope (0.0105) is equal to $1/[(k_o/k_w) + (k_p/k_w)]$. From this slope and the average value of $(k_o/k_w)/(k_p/k_w)$ obtained from the data of Table I, k_o/k_w and k_p/k_w are seen to have the values 46.5 and 48.5. From the intercept at 1.14 a value of 13 may be calculated for k_{ox}/k_w, albeit with considerably less precision, since the intercept is so close to 1.00.

The kinetics of the reaction were also studied in the presence of various concentrations of sodium hydroxide and sodium phenoxide. Rate constants were calculated from the following second-order rate equation[4]

$$k = \frac{2.303}{t[a(3 + f) - b]} \log \frac{b(a - x)}{a[b - (3 + f)x]} \qquad (3)$$

where $a = [CHCl_3]_0$, $b = [OH^-]_0$, $x = \Delta[CHCl_3]_t$ and f = fraction of the chloroform giving formate. The calculated rate constants were found to remain reasonably constant within a given run[9] and are listed, with the average deviations, in Table II.

TABLE II

KINETICS OF THE REACTION OF CHLOROFORM WITH AQUEOUS ALKALI AND SODIUM PHENOXIDE AT 35.0°

$[C_6H_5ONa]_0$	$[CHCl_3]_0$	$[NaOH]_0$	f^a	$k \times 10^{4b}$
1.127	0.0127	0.133	0.32	2.93 ± 0.19[c]
1.101	.0241	.160	.45	2.91 ± .09
1.072	.0196	.066	.39	3.37 ± .07
0.742	.0267	.165	.60	3.18 ± .09
.582	.0187	.082	.53	3.50 ± .14
.383	.0253	.196	.50	3.28 ± .09
.202	.0250	.181	.70	2.95 ± .06
.000	.0293	.166	.27	2.87 ± .05
.000	~.03	~.04	.15	2.41 ± .03[d]

[a] $f = 3(\Delta[OH^-]-[Cl^-])/[Cl^-]$. Because of the experimental difficulties[9] this number could not be determined with much precision, but fortunately k is relatively insensitive to changes in f. [b] In liters·moles^{-1}·sec.$^{-1}$. [c] Reaction followed by measurements of salicylaldehyde concentration. [d] Data from ref. 11.

From the values obtained it appears that sodium hydroxide has a considerable positive salt effect[10] and sodium phenoxide has a smaller one. Previous work has shown that at concentrations of 0.2 *M* neither sodium fluoride, nitrate nor perchlorate has a significant salt effect, but that 1.7 *M* sodium perchlorate decreases the rate by about 17%.[11]

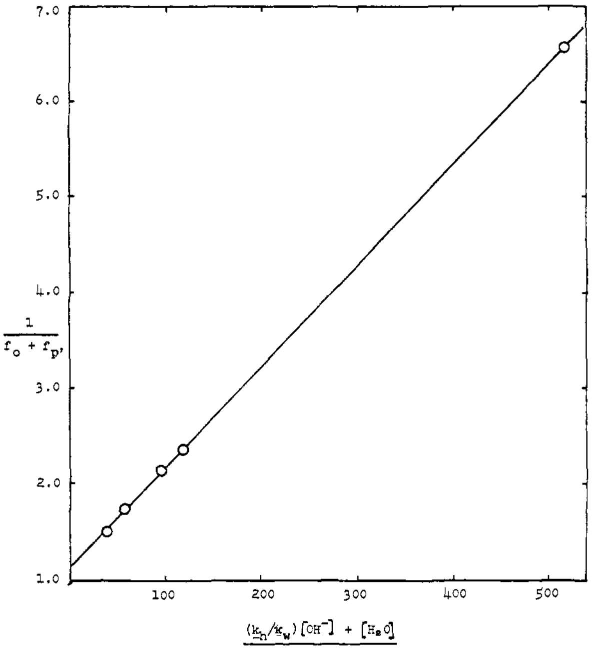
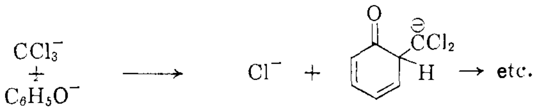


Fig. 1.—Plot of data on hydroxybenzaldehyde yields, using eq. 2.

Nucleophilic Attack on the Trichloromethyl Anion.—These kinetic results, with the data on product distributions, seem to us to rule out an alternate mechanism III in which the aldehydes are formed by an initial attack of phenoxide ions on trichloromethyl anions followed by steps like those of mechanism II. In this mechanism the



III

Reimer–Tiemann reaction is shown as a process that goes on *in addition* to the hydrolysis reaction that takes place in the absence of phenoxide ions. Thus the second-order rate constants calculated from eq. 3 and listed in Table II would have to be considered to have the significance

$$k = k_{hyd} + k_{RT}[C_6H_5O^-]$$

The values of k_{hyd} and k_{RT} may be calculated from the runs listed in Table II and the effect of sodium phenoxide concentration on yields of aldehydes as shown in Table I. The resultant hydrolysis rate constants (k_{hyd}) fall more sharply than would appear to be reasonable for a salt effect, but more critical is the fact that the proposed Reimer–Tiemann rate constant, k_{RT}, is approximately halved by an increase in ionic strength from 0.38 to *ca.* 1.2 *M*. Such a rate constant, governing a reaction between two like-charged ions, should *increase* with increasing ionic strength,[12] even at salt

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(6) It has been pointed out elsewhere[7] that the recent data of Horiuti and Katayama[8] on the effect of base concentration on rates of chloride exchange of chloroform show that the k_h/k_w value estimated previously is considerably too high and the correct value is around 27.

(7) J. Hine, *J. Research Inst. Catalysis, Hokkaido Univ.*, **6**, 202 (1959).

(8) J. Horiuti and M. Katayama, *ibid.*, **6**, 57 (1958).

(9) The uncertainty in the rate constants, however, is probably considerably larger than the average deviations, largely because hydroxide ion concentrations had to be determined essentially as fairly small differences between large concentrations of total base (hydroxide plus phenoxide) determined by titration and large amounts of phenol known to have been used.

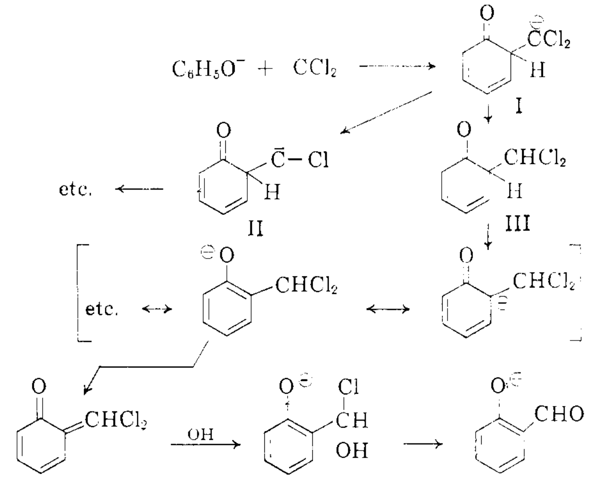
(10) *Cf.* E. Abel, *Z. Elektrochem.*, **29**, 391 (1923).

(11) J. Hine and A. M. Dowell, Jr., THIS JOURNAL, **76**, 2688 (1954).

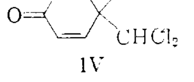
(12) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 84.

concentrations well above those at which the Debye–Hückel equation is applicable.[13] For this reason and reasons like those given previously with reference to a hydrolysis mechanism involving attack of water on the trichloromethyl anion,[4,11] we have ruled out mechanism III.

Mechanistic Details.—While we believe that it is thus reasonably well established that it is a nucleophilic attack of the *o*-carbon atom of a phenoxide ion on dichloromethylene that leads to the salicylaldehyde produced in the Reimer–Tiemann reaction, there are certain details of the reaction that we have not settled. Some of the possibilities are outlined in the reaction scheme



Thus, for example, the further replacement of chlorine could be shown as proceeding by a continuation of the methylene mechanism, with intermediate I being formed either from the carbanion II or directly, by a concerted process.[14] However, since the ability of halogens to stabilize a dihalomethylene seems to depend on the ability of the halogen atom's unshared electrons to interact with the vacant orbital of the divalent carbon,[15] it would seem that a R–C–Cl type intermediate like II, having one substituent with *no* unshared electrons, would not be stable enough to figure importantly in the reaction mechanism. In any case, it seems clear that II is not the principal intermediate at this stage of the reaction, since a dichloro intermediate like III seems assured by analogy with the isolation, from the Reimer–Tiemann reaction of *p*-cresol, of compound IV.[16]



IV

It is not clear, however, whether III is formed by a concerted path or *via* the intermediate carbanion I.[14]

By various combinations of reaction at oxygen and carbon, phenoxide ions, dichloromethylene and water could yield tris-hydroxyphenylmethanes,[3] bis-hydroxyphenylcarbinols, diphenylacetals of hydroxybenzaldehydes, triphenyl orthoformate[17] and numerous other products. Since all of these compounds except the orthoester should be alkali-soluble, we extracted one of the basic reaction solutions with petroleum ether and obtained about a 1% yield of triphenylorthoformate in an experiment in which about 65% (based on chloroform reacted) of *o*- and *p*-hydroxybenzaldehyde was produced. The extent of formation of products other than these three cannot be very large. In fact, since k_o/k_w and k_p/k_w were determined by use of measurements on the amounts of *o*- and *p*-hydroxybenzaldehydes formed, the resultant values refer only to those attacks of the *o*- and *p*-carbon atoms of the phenoxide ion that lead to the corresponding aldehyde. Similarly, it may be shown that k_{ox}/k_w is a measure of that part of the reaction whose extent is proportional to the first power of the phenoxide ion concentration but which does not yield *o*- or *p*-hydroxybenzaldehyde. By most plausible mechanisms, the formation of acetals and bis- and tris-hydroxyphenylmethane derivatives from intermediate III and its *p*-analog would occur to an extent proportional to the greater-than-first power of the phenoxide concentration. The occurrence of any major amount of such reactions would lead to a plot of eq. 2 that is concave upward; yet the actual plot in Fig. 1 is, if anything, concave downward. Hence, under our conditions, none of the side reaction paths is followed to a major extent. This may not be the case under synthetically useful conditions where concentrations of reactants are higher and the further reaction of primary products is much more likely.

The Effect of Ion-pair Formation on Orientation.—While we have observed that dichloromethylene attacks the *p*-position of the phenoxide ion slightly faster than it attacks the *o*-position, it has long been known that under synthetically useful conditions the yield of *o*-hydroxybenzaldehyde is considerably higher than that of the *para* compounds. From the data of Brady and Jakobovits[18] it seems likely that in the concentrated solutions there are large amounts of phenoxide–metal ion pairs that give considerably more *o*-substitution than do dissociated phenoxide ions. The reliability of isolation experiments as a measure of the relative rates of attack on the *o*- and *p*-positions, however, is diminished by the possibility that the lowered yield of *p*-hydroxybenzaldehyde in the more concentrated solutions is due to its subsequent destruction or loss in handling. To test this possibility we have spectrophotometrically determined the ratio of *ortho* to *para* product formed in the presence of 11.7 *M* sodium hydroxide under conditions where such a small fraction of the phenoxide present was transformed to aldehyde that the subsequent reaction of aldehyde seems improbable. The ratio of *ortho* to *para* product was found to be 2.21, showing that the tendency toward *o*-substitution is indeed increased under conditions where ion-pair formation is encouraged. One factor that would certainly be expected to be present and that would tend to favor *o*-substitution is an electrostatic

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[13] *Cf.* A. v. Kiss and P. Vass, *Z. anorg. allgem. Chem.*, **209**, 236 (1932); **217**, 305 (1934); *Z. physik. Chem.*, **160**, 290 (1932); A. N. Kappanna, *J. Indian Chem. Soc.*, **6**, 419 (1929); **8**, 541 (1931).

[14] *Cf.* J. Hine and K. Tanabe, THIS JOURNAL, **80**, 3002 (1958).

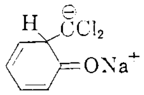
[15] J. Hine and S. J. Ehrenson, *ibid.*, **80**, 824 (1958).

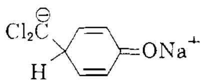
[16] K. Auwers and F. Winternitz, *Ber.*, **35**, 465 (1902).

[17] F. Tiemann, *ibid.*, **15**, 2686 (1882).

[18] O. L. Brady and J. Jakobovits, *J. Chem. Soc.*, 767 (1950).

effect. When a dichloromethylene molecule attacks the *o*-position of a sodium phenoxide ion-pair to yield the probable initial product V, there is less separation of the unlike charges than when the analogous *para* product VI is formed. If the other factors that influence the orientation are the same in the ion-pair as in the free phenolate anion (where the electrostatic effect cannot operate) this should result in an increase in the fraction of *o*-substitution in concentrated sodium hydroxide solutions.


V


VI

Experimental

Purification of Material.—All solutions were made with water that had been boiled and cooled under nitrogen. Phenol was purified by distilling under nitrogen and taking the fraction boiling at 179–180° (737 mm.). This remained colorless when stored for two months under nitrogen in the dark. Chloroform was purified by Fieser's method[19] and stored in sealed ampoules under nitrogen.

Kinetic Runs.—In a typical run about 10 g. of phenol was melted, poured into a stoppered weighing bottle, cooled and weighed. The phenol was then transferred quantitatively to a 100-ml. volumetric flask with the minimum quantity of water. Nitrogen was blown into the flask and an excess of 18 *M* carbonate-free sodium hydroxide was added. The solution was diluted to 100 ml. at 35°. Two 5-ml. aliquots were withdrawn with nitrogen-filled pipets and titrated with standard perchloric acid to the first green color of brom thymol blue indicator. After subtracting the known phenoxide ion concentration, this gave the initial hydroxide ion concentration. Chloroform (0.25 ml.) was added with a calibrated syringe and the flask was shaken violently to effect solution. Since most reactions required 2 or 3 days there was a negligible error in the starting time. Periodically 5-ml. aliquots were withdrawn and titrated, first with perchloric acid and then with silver nitrate to a dichlorofluorescein end-point. In most runs the concentration of chloride ion formed was used as a measure of the extent of reaction of the chloroform in the calculation of rate constants by use of eq. 3. The value of f used in a given run was an average of the values determined from the hydroxide and chloride titrations for each of the individual points. The chloride concentration at "infinite" time was used as a check on the amount of chloroform delivered by the syringe. In one run, however, the extent of reaction of the chloroform was determined by spectrophotometric measurements of the salicylaldehyde concentration at various times and by the determination of f_o at the end of the reaction.

Measurement of f_o and f_p.—Solutions containing known amounts of phenoxide, hydroxide and chloroform were made up as described for the kinetic runs. After standing for one week in a thermostated bath at 35°, aliquots were withdrawn and diluted to a convenient range to measure the optical densities at 330 and 378 mμ on a Beckman model DU spectrophotometer. Separate experiments showed that 1 *M* sodium phenoxide had a small absorption at 330 mμ and virtually no absorption at 378 mμ. *p*-Hydroxybenzaldehyde in base had an intense band at 330 mμ (ϵ 26,400) and no absorption at 378 mμ. Salicylaldehyde had a band at 378 mμ (ϵ 5500) and a weaker absorption at 330 mμ (ϵ 1420). Thus salicylaldehyde could be determined directly from the optical density at 378 mμ while *p*-hydroxybenzaldehyde could be determined from the optical density at 330 mμ after this was corrected for the absorption of the salicylaldehyde.

In all our reactions the solutions quickly became cloudy and a solid substance settled out. In order to isolate a reasonable amount of this solid, a solution of 1.374 *M* sodium phenoxide plus 0.658 *M* sodium hydroxide in a 500-ml. volumetric flask was saturated with 1.5 ml. of chloroform and allowed to react at 35.0°. This was repeated two more times (a total of 0.0556 mole of chloroform) and the solution was then allowed to stand for one week. The solid was extracted with petroleum ether, dried over calcium chloride, and finally concentrated in a stream of nitrogen. A light yellow powder (0.13 g.) remained. This was dissolved in one ml. of hot 95% ethanol and allowed to stand four days at 0° to give 22 mg. of long white needles, m.p. 73–74° (literature value for phenyl orthoformate, 76–77°,[20] 75°[21]). After concentrating the filtrate plus washings, the solution was treated with water to the cloud point at 70°. A copious precipitate of needles settled out overnight, but on standing for a week in the refrigerator, had redissolved. Apparently the orthoformate decomposed under these conditions. The weight of the original crude precipitate shows that, at most, 0.80% of the chloroform yielded phenyl orthoformate.

Concentration of Water in the Presence of Phenoxide.—Sodium phenoxide (17.392 g.) was diluted to 100 ml. with distilled water at 20°. The resulting solution weighed 105.797 g., showing there were 88.405 g. of water present. The assumption that the concentration of water in sodium phenoxide solutions is a linear function of the sodium phenoxide concentration may be expressed

$$[H_2O] = 55.41\,(1 - x[NaOC_6H_5])$$

From the data above, x is found to be 0.0764. This relation was used to calculate the water concentrations required in the plot of eq. 2 shown in Fig. 1.

Acknowledgment.—The authors would like to express their indebtedness to the Office of Naval Research and the Alfred P. Sloan Foundation for support of this investigation.

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[19] L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., Inc., New York, N. Y., 1941, part II, chap. III.

[20] K. Auwers, *Ber.*, **18**, 2657 (1885).

[21] H. Baines and J. E. Driver, *J. Chem. Soc.*, **125**, 907 (1924).