This instability is obviously to be expected of a β-quaternary ammonium substituted ketone. Thus, the initial step in the base-catalyzed decomposition of the tropinone derivative should lead to an α,β-unsaturated ketone intermediate.

Serving to underline the pronounced lability of the tropinone quaternary system in the presence of alkali is ultraviolet spectral evidence, which, incidentally, provides support for the formation of such an intermediate in the process of degradation. V is apparently stable in 95% ethanol solution; such solutions showed no change in absorption spectrum over a period of 48 hours. However, when the ultraviolet absorption was measured immediately after dissolving V at room temperature in 0.01 N (or even 0.001 N) sodium hydroxide in 95% ethanol, a new absorption maximum (228 mμ, log ϵ 4.00) had developed. This peak is in good agreement with that which would be expected for an α,β-unsaturated ketone with a single substituent in the β (or α) position.[5]

Tropane and tropine were prepared by known methods from tropinone. The bases were quaternized in a manner similar to that previously described[2,3] by refluxing in acetonitrile solution with a slight excess of the appropriate 3-bromopropyl quaternary ammonium bromide.[6] Fair yields (50–60%) of the unsymmetric bis-salts were obtained.

Experimental[7]

Preparation of Intermediates.—Tropine was prepared by catalytic hydrogenation[8] of tropinone[9] or by the hydrolysis of atropine.[10] Dehydration of tropine in a sulfuric acid–acetic acid mixture, essentially as described by Ladenburg,[11] afforded a 70% yield of tropidine, b.p. 158–161°, n^{25}D 1.4860, picrate m.p. 289–290° dec. Tropane, b.p. 166–169°, n^{25}D 1.4732, picrate m.p. 284–285°, was prepared by hydrogenation of tropidine in methanol solution with Adams platinum oxide, in a similar manner to that described by Willstätter.[12]

The methods of preparation of the 3-bromopropyl quaternary ammonium bromides have been described earlier.[6]

Reaction of Tropine with 3-Bromopropyltrimethylammonium Bromide. Compound II.—A representative example will illustrate the procedures used for obtaining the salts listed in Table I. A solution of 33.6 g. (0.25 mole) of tropine and 68.0 g. (0.26 mole) of 3-bromopropyltrimethylammonium bromide in 300 ml. of acetonitrile was refluxed for 24 hours. The precipitate was recrystallized from ethanol–ethyl acetate to yield 63.0 g. (63%) of colorless crystals, melting at 247° and above with evolution of gas.

Ultraviolet absorption spectra were determined with a Beckman DU quartz spectrophotometer.

Acknowledgment.—The authors are indebted to the Messrs. Donald L. Miller and Dean F. Cortright of these laboratories for the ionic halogen determinations and for the measurements of ultraviolet spectra.

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[5] R. B. Woodward, THIS JOURNAL, **63**, 1123 (1941).

[6] A. P. Gray, D. C. Schlieper, E. E. Spinner and C. J. Cavallito, *ibid.*, **77**, 3648 (1955).

[7] Microanalyses were performed by the Clark Microanalytical Laboratories, Urbana, Illinois. Melting points were corrected for stem exposure.

[8] L. C. Keagle and W. H. Hartung, THIS JOURNAL, **68**, 1608 (1946).

[9] Winthrop-Stearns, Special Chemicals Division.

[10] S. P. Findlay, THIS JOURNAL, **75**, 3204 (1953).

[11] A. Ladenburg, *Ann.*, **217**, 118 (1883).

[12] R. Willstätter and E. Waser, *Ber.*, **43**, 1182 (1910).

DECATUR, ILLINOIS

[CONTRIBUTION FROM THE MALLINCKRODT CHEMICAL LABORATORIES, HARVARD UNIVERSITY]

The Kinetics of the Meerwein Reaction

BY JAY K. KOCHI

RECEIVED JULY 1, 1955

The Meerwein reaction has been studied kinetically. The similarity between this reaction and the Sandmeyer reaction is postulated to lie in the nature of the catalytic cuprous complex. The yields of the Meerwein reaction are found to be a critical function of the relative cupric, chloride and olefin concentrations.

It has been shown earlier[1] that the Meerwein and Sandmeyer reactions are related, in that both reactions are catalyzed by cuprous chloride. We have undertaken a kinetic study of the Meerwein reaction in order to attempt to elucidate the mechanism of this reaction and to compare it to the Sandmeyer reaction which already has been extensively studied.[2]

We examined the reaction of p-chlorobenzenediazonium chloride with acrylonitrile and with styrene in 65 volume per cent. acetone–water solutions at 24.8°. Cupric nitrate and lithium chloride and chloroacetate buffer were used in most runs. These systems were selected because of the high yields obtainable,[3] the ease of isolation and analysis of the products and the solubility of reactants and products at fairly high olefin and salt concentrations.

Although acetone is not required[4] when the reactions are catalyzed by cuprous chloride, we have found it convenient to investigate the reaction in aqueous acetone solutions because of the high catalytic effect of cuprous chloride in this medium. Moreover, side reactions involving azo compound formation and concomitant consumption of cuprous catalyst are either minimized or completely eliminated under these conditions.

Experimental

Materials. Acetone and crystalline p-chlorobenzenediazonium chloride were prepared pure in a manner described previously.[1] Standard aqueous solutions of the diazonium salt (1.42 M) were prepared using deionized water. Aliquots

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[1] J. Kochi, THIS JOURNAL, **77**, 5090 (1955).

[2] (a) W. Cowdrey and D. Davies, *J. Chem. Soc.*, **5**, S49 (1949); (b) E. Pfeil, *Angew. Chem.*, **65**, 155 (1953); *Ann.*, **562**, 163 (1949); **565**, 183 (1949).

[3] W. Brunner and H. Perger, *Monatsh.*, **79**, 187 (1948).

[4] The "cupric chloride" reactions have been reported[5] to go in the absence of acetone. In the majority of these cases, however, we have found[6] that cuprous chloride is formed by the reduction of cupric chloride by the organic solvent used.

[5] (a) J. Rai and K. Mathur, *J. Indian Chem. Soc.*, **24**, 413 (1947); (b) O. Vogl and C. Rondestvedt, THIS JOURNAL, **77**, 3401 (1955); see also ref. 3.

[6] J. Kochi, THIS JOURNAL, **77**, 5274 (1955).

of this solution were sealed in ampules, frozen and maintained at Dry-Ice temperatures for prolonged periods without apparent deterioration. **Cupric nitrate** was recrystallized Mallinckrodt analytical reagent grade material; it was assayed (1.76 *M*) by a standard method.[7a] A qualitative test for nitrite[7b] was negative. An aqueous **lithium chloride** solution (3.52 *M*) was prepared from Mallinckrodt reagent grade materials and the chloride content determined potentiometrically. **The buffer** consisted of an equimolar mixture of 1.0 *M* chloroacetic acid and its sodium salt and was prepared by neutralizing the pure acid half-way with sodium hydroxide. **Acrylonitrile and styrene** were commercial samples (Eastman Kodak Co.) which were washed with aqueous sodium hydroxide, dried and distilled twice under reduced pressure. A small middle cut of each distillation was used.

Kinetic Procedure.—Since the reaction is extremely sensitive to oxygen (*vide infra*) extreme care was required to prepare the reaction in a system from which oxygen had been rigorously eliminated before the components were mixed. The reaction vessel is shown in Fig. 1[8]; its capacity was approximately 100 ml. In other runs a vessel designed to hold components in three separate compartments was used. There was, however, no significant difference in the kinetic behavior whether all the components were initially separated or not. In most runs, the diazonium solution and lithium chloride solutions were pipetted into the center well. Acetone, cupric nitrate and buffer were then placed in the outer well. Variation in the placement of these components (as long as the cupric and chloride ions were separated)[6] did not affect the kinetics. Slightly better kinetic results at greater than 70% reaction were obtained when buffer was present; the initial portion of the reaction (less than 70%) was unaffected by the absence of buffer. All runs were made at least in duplicate and checked periodically for consistency. The yields were also determined in duplicate.

The reaction was degassed by a standard procedure involving repeated (three times) freezings with liquid nitrogen, evacuations at 0.01 μ and thawings of the contents of the reaction vessel. Purified argon was then introduced into the chilled (−70°) vessel at approximately 100 cm. pressure *via* the capillary tip which had been previously flushed of oxygen. The last trace of oxygen was removed from Mathieson grade argon (less than 0.05% oxygen) by passing the gas through a 2.5 × 75 cm. Pyrex tube filled with short (3 cm.) strips of fine copper wire and maintained at about 450° with muffle furnaces. The copper was rejuvenated occasionally by passing hydrogen over it.

The rate of the reaction was followed volumetrically[9] at atmospheric pressure and 24.8 ± 0.02°. The gas was measured in a standard thermostated eudiometer filled with 65 volume per cent. acetone–water. The shaking was achieved with the usual type of rapidly oscillating concentric wheel shaker. The shaking in this apparatus was sufficiently vigorous to maintain a small "head" of foam. The rates of the fastest reactions were unaffected by changing the shaking speed.

The Products of the Reactions.[1]—After the nitrogen evolution was complete the generated cuprous chloride was titrated at a specified time by the method described previously.[6] An aliquot (15 or 5 ml.) of carbon tetrachloride was then added to the reaction mixture in order to extract the Meerwein and Sandmeyer products. The organic layer was washed several times with water, with saturated sodium bisulfite and several more times with water to remove salts, acetone and chloroacetone. It was diluted to volume in a volumetric flask (25 or 5 ml.) and dried with sodium sulfate.

An aliquot (5 or 1 ml.) of the carbon tetrachloride solution was transferred to a test-tube and the solvent and other volatile components including chloroacetone, removed smoothly *in vacuo* in a heated (50°) vacuum desiccator at aspirator pressures. To the residue was added 2 ml. of 0.5 *N* aqueous sodium hydroxide and it was washed down with approximately 2 ml. of 95% ethanol. The sealed tubes were heated on a steam-bath for 24 hours diluted with water and acidified with concentrated nitric acid. The liberated chloride was titrated potentiometrically with silver electrodes on a Beckman Model K automatic titrator. Results were reproducible to within 3%. Control runs with added *p*-dichlorobenzene, chlorobenzene and chloroacetone gave no titrable chloride. The α,*p*-dichlorodihydrocinnamonitrile and α,*p*′-dichlorobibenzyl gave 0.98–1.02 equivalents of analyzable chloride. The combined hydrolyzates were then extracted with ether. The ethereal solutions yielded colorless materials; from acrylonitrile runs, *p*-chlorocinnamic acid, m.p. 249–250°, and from styrene, *p*-chlorostilbene, m.p. 129–130°, were obtained.

The Sandmeyer and reduced product were determined spectroscopically with a Perkin–Elmer infrared spectrometer, model 21. The 1010 and 1390^{-1} cm.$^{-1}$ bands for *p*-dichlorobenzene and the 680, 900 and 1585 cm.$^{-1}$ bands of chlorobenzene were used in the analyses.[10]

In most of the runs, the Meerwein product, Sandmeyer product and small amounts of reduced material (chlorobenzene) accounted for 95 ± 5% of the diazonium salt. Under these conditions, azo compounds were not found in yields greater than a few per cent. as indicated qualitatively by the colorless carbon tetrachloride extracts and quantitatively by the material balance. In large-scale runs we were able to isolate 85–90% of the *p*-dichlorobenzene, m.p. 52–53°. In exceptional cases, *viz.*, when the diazonium decompositions were carried out at very low cupric concentrations in the absence of olefin, small amounts of colored materials were formed.

Attempts were made to catalyze the diazonium salt decompositions in aqueous acetone with pure cuprous chloride obtained by (1) dissolving crystalline cuprous chloride in acetone with lithium chloride and (2) heating a dilute solution of cupric chloride in acetone until reduction was complete. We found that under these conditions the reactions are much too fast to follow by ordinary means. If exceedingly small amounts of cuprous chloride are used, slight losses due to extraneous oxidation (mentioned later) are sufficient to render the kinetic results erratic. Furthermore, runs at relatively high cuprous chloride concentrations (0.004 *M*) resulted in consumption of the cuprous catalyst by a process which may be analogous to that postulated by Cowdrey and Davies.[2a] Lowering the temperature to −40° did not aid sufficiently in slowing down the reaction since the activation energy for this reaction is unusually low.[2a] We found it convenient, thus, to study the reaction by the method outlined above although it introduced another variable, *viz.*, the rate of formation of cuprous chloride.

Reaction in the Absence of Copper.—Several attempts were made to decompose the diazonium salt in acetone or methanol and acrylonitrile or styrene with added lithium chloride and in the absence of copper. In a thoroughly degassed system, *p*-chlorobenzenediazonium chloride undergoes slow decomposition[11] with slight coloration. A theoretical volume of nitrogen is evolved (half-time about 4 hours). Neither α,*p*-dichlorodihydrocinnamonitrile nor α,*p*′-dichlorostilbene nor a compound possessing solvolyzable chlorine (with the exception of chloroacetone) could be detected in the reaction mixture. Vogl and Rondestvedt[5b] recently have reported similar results with other olefins under various conditions.

Attempted Meerwein Reaction with Cyanide.[12]—We attempted to effect the Meerwein reaction with cyanide replacing the chloride. Either crystalline *p*-chlorobenzenediazonium bisulfate or chloride was dissolved in aqueous acetone with added sodium cyanide and cuprous cyanide catalyst. Nitrogen was evolved smoothly and good yields (90% isolable) of *p*-chlorobenzonitrile, m.p. 92–93°, were obtained. In the presence of excess chloride (10–15 equivalents), the predominant product is still the nitrile. When olefin (acrylonitrile or 1,3-butadiene) was added, a large amount of *p*-chlorobenzonitrile was still formed together with unidentified oils. With styrene a small amount (approximately 1%) of crystalline material, m.p. 111–111.5°, was obtained. Slightly better yields were obtained in methanol. The infrared spectrum of this compound showed a very weak nitrile absorption at 2250 cm.$^{-1}$.

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[7] (a) I. Kolthoff and E. Sandell, "Textbook of Quantitative Inorganic Analysis," Third Edition, The Macmillan Co., New York, N. Y., 1952, pp. 600 ff.; (b) F. Feigl, "Spot Tests," Elsevier Publishing Co., Fourth Ed., Houston, Texas, 1954, p. 302.

[8] I am indebted to Dr. J. Kumamoto for suggesting the design of the splash arrester.

[9] E. Lewis and W. Hinds, THIS JOURNAL, **74**, 304 (1952).

[10] W. West, "Physical Methods of Organic Chemistry," A. Weissberger, Editor, Interscience Publishers, Inc., New York, N. Y., 1949, Vol. I, part II, pp. 1241 *ff*.

[11] D. DeTar and M. Turetzky, THIS JOURNAL, **77**, 1745 (1955).

[12] Experiments by Mr. Eric Alving.

Anal. Calcd. for $C_{15}H_{12}ClN$: C, 74.5; H, 5.00. Found[13]: C, 74.6; H, 4.90.

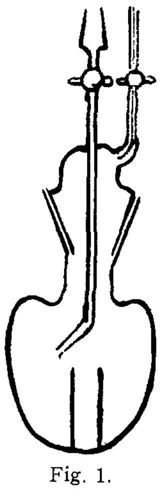

Fig. 1.

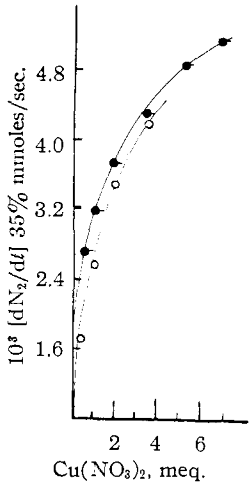

Fig. 2.—Rate of nitrogen evolution at 35% reactions *vs.* $Cu(NO_3)_2$ in aqueous acetone solutions containing 2 meq. of buffer, 7.02 meq. of LiCl and 1.42 meq. of diazonium salt: ○, no olefin; ●, 4.2 meq. of acrylonitrile per 22 ml. of solution.

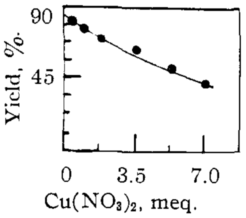

Fig. 3.—Yield of Meerwein product as a function of $Cu(NO_3)_2$ in aqueous acetone solutions containing 7.02 meq. of LiCl, 2 meq. of buffer, 1.42 meq. of diazonium salt and 4.2 meq. of acrylonitrile per 22 ml. of solution.

Results

Sandmeyer Reaction.—Initial studies were made on the nature of the Sandmeyer reaction in acetone with cupric chloride. The rate of nitrogen evolution showed sigmoid curves typical of successive reactions. This is the type of curve we would expect if we assume that there are two slow reactions: (1) the generation of catalyst, cuprous chloride, from cupric chloride[6] and (2) the bimolecular reaction of the catalyst with diazonium ion, *i.e.*

$$2CuCl_2 + CH_3COCH_3 + Cl^- \longrightarrow 2CuCl_2^- + ClCH_2COCH_3 + H^+ \quad (1)$$

$$ArN_2^+ + CuCl_2^- \longrightarrow \text{Sandmeyer product} + CuCl \quad (2)$$

Since the amount of cuprous chloride required to catalyze the diazonium decomposition in 15 minutes is exceedingly small (0.004 meq.) the extent to which reaction 1 proceeds before the diazonium ion is completely consumed is of the order of 2% or less even in the slowest cases represented by low cupric and chloride ion concentrations. For all practical purposes, therefore, the cuprous chloride formation can be approximated as zero order in gross cupric ion, Cu_g^{II}.

$$CuCl_2^- = \int k_1 (Cu_g^{II}) (Cl^-)^n \, dt = k_1 (Cu_g^{II}) (Cl^-)^n t = k_0 t \quad (3)$$

The process then reduces simply to

$$\frac{d\,N_2}{dt} = k_2 (Cu^ICl_2^-) (ArN_2^+) \quad (4)$$

or

$$-\ln ArN_2^+ = \tfrac{1}{2} k_1 k_2 (Cu_g^{II}) (Cl^-)^n t^2 = \tfrac{1}{2} k_0 k_2 t^2 \quad (5)$$

Logarithmic plots of diazonium concentration against t^2 yielded straight lines for 70–90% of the reaction.

In separate experiments the rates of cuprous chloride formation were determined at various cupric concentrations, at constant pH and chloride ion concentrations as those used in the diazonium decompositions. The pseudo zero-order rate constants, k_0, are listed in Table I. The rates were substantially unaffected by the presence of small amounts of either acrylonitrile or styrene.

TABLE I

RATE CONSTANTS FOR CUPROUS CHLORIDE FORMATION[a]

Cu^{II},[b] meq.	Cu^I,[c] meq.	$10^7 k_0$, moles/liter-sec.
0.352	0.00800	3.16
0.830	.0120	4.74
1.76	.0168	6.64
3.52	.0248	9.80
5.28	.0328	12.9
7.04	.0400	15.8

[a] In 22 ml. of 65 volume per cent. acetone–water containing 7.02 meq. of LiCl and 2 meq. of chloroacetate buffer at 24.8°. [b] Initial cupric concentration. [c] Amount formed in nineteen minutes.

In order to strengthen our assumption concerning the rate processes, the reaction was studied at various levels of diazonium and cupric concentrations. The experimental rate constant, k_2, was obtained by dividing the slope (of the nitrogen *versus* time curves) at 35% reaction by the cuprous chloride concentration obtained from the data in Table I and the diazonium concentration at this point. The slope is easily obtained at 35% reaction because the rate of nitrogen evolutions is approximately linear between 20 and 60% reaction. The rate constants obtained in this manner are listed in Table II. The relatively constant value for k_2 obtained in aqueous acetone solutions supports the kinetic scheme given above and is in agreement with previous studies by Cowdrey and Davies[2a] in aqueous solutions at relatively high cuprous concentrations.

TABLE II

RATE CONSTANT FOR DIAZONIUM DECOMPOSITION BY CUPROUS CHLORIDE[a]

ArN_2^+, meq.	$Cu(NO_3)_2$, meq.	k_2, liters/mole-sec.
0.710	1.76	10.1
1.42	1.76	10.9
2.84	1.76	10.4
1.42	0.352	9.80
1.42	0.830	11.4
1.42	3.52	11.0
1.42	5.28	10.7

[a] In 22 ml. of 65 volume per cent. acetone–water and 7.02 meq. of lithium chloride and 2 meq. of chloroacetate buffer.

The half-times of the reactions varied from three minutes for the fastest to 20 minutes for the slow-

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[13] Microanalysis by Swarzkopf Laboratories, New York, N. Y.

est reactions. When the decompositions were much slower relatively large amounts of colored and hydrolysis products of the diazonium salt were formed. We were thus restricted to a rather narrow range of rates in order to avoid extraneous side reactions.

The cuprous chloride formed was titrated at a given time after each run was complete. Its titer was the same in those runs in which decomposing diazonium salt was present as those runs in which there were no diazonium ions. This indicated that *cuprous chloride was not consumed* in the diazonium salt decomposition and it was, therefore, acting as a true catalyst under these conditions. Subsequent experiments showed that the catalytic activity of cuprous chloride was also applicable to those reactions in which olefin was present (*i.e.*, the Meerwein reaction).

Meerwein Reaction.—Olefin has an interesting effect on the decomposition of diazonium salts in aqueous solutions containing cupric chloride. The rates of diazonium decomposition and product formation were studied under varying conditions of gross cupric chloride and olefin concentrations. In Fig. 2 is shown the rate of nitrogen evolution as a function of the gross cupric concentration with and without added olefin.

Under the same conditions, the yield of Meerwein product *decreases* with increasing cupric nitrate in solutions of constant olefin and chloride concentrations. Figure 3 shows this effect.

The rate shows an interesting variation with olefin concentration when the cupric nitrate and chloride are kept constant. At high cupric concentrations (0.079 *M*) the rate is relatively insensitive to olefin concentration whereas at low cupric levels (0.016 *M*) and the same chloride concentrations, the rate is rather highly dependent on olefin concentration (Fig. 4).

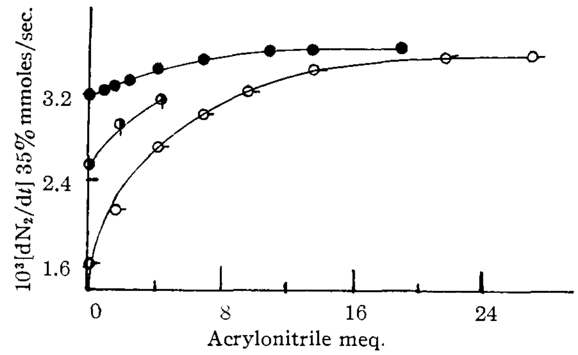

Fig. 4.—Rate of nitrogen evolution at 35% reaction as a function of acrylonitrile concentration in aqueous acetone solutions containing 7.02 meq. of LiCl, and 2 meq. of buffer: O-, 0.352 meq. of $Cu(NO_3)_2$; ◐, 0.830 meq. of $Cu(NO_3)_2$; ●, 1.76 meq. of $Cu(NO_3)_2$ per 22 ml. of solution.

The formation of Meerwein product is shown as a function of the olefin concentration in Fig. 5. The chloride and cupric ions have been kept constant in each series.

The variations in rate with chloride ion at constant cupric and olefin concentrations follow approximately the same order as that for copper variation (Table III).

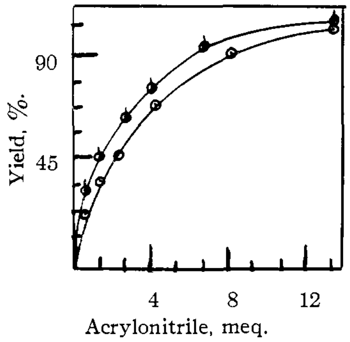

Fig. 5.—Yield of Meerwein product *vs.* olefin concentration in 22 ml. of aqueous acetone solutions containing 7.02 meq. of LiCl, 2 meq. of buffer and 1.42 meq. of diazonium salt: ⊙, 1.76 meq. of $Cu(NO_3)_2$; ◐, 0.352 meq. of $Cu(NO_3)_2$.

Similar effects were observed with styrene, except in most cases the yield of Meerwein product was greater and the rates faster than with acrylonitrile.

TABLE III

VARIATION IN RATE AND YIELD WITH CHLORIDE ION CONCENTRATION[a]

$Cu(NO_3)_2$, meq.	Cu^I,[b] meq.	LiCl, meq.	Yield,[c] %	k_2',[d] liters/mole-sec.
0.352	0.010	10.53	49	10.3
.352	.0064	7.02	73	10.7
.352	.0036	3.51	74	18.3
.830	.015	10.53	56	10.6
.830	.012	7.02	66	11.4
.830	.0072	3.51	68	15.5
1.76	.016	10.53	60	10.5
1.76	.016	7.02	67	10.9
1.76	.012	3.51	71	11.7

[a] In 22 ml. of 65 volume per cent. acetone–water containing 2 meq. of buffer, 4.2 meq. of acrylonitrile and 1.42 meq. of diazonium salt at 24.8°. [b] Cuprous chloride formed in 19 minutes in the presence of diazonium salt. [c] Meerwein product. [d] $k_2' = k_{11} + k_{12}$; $k_2 = k_{11}$ (subscripts refer to equations in text).

Effect of Oxygen.—The decomposition of diazonium salts in aqueous acetone solution either in the presence or absence of olefin by cupric chloride is strongly inhibited by oxygen. Previous investigators have noted an "incubation period" in the reaction which varied from a few seconds to several minutes. We have found that the induction period is roughly proportional to the amount of oxygen present in the system. Figure 6 shows the rate of nitrogen evolution in systems containing various amounts of oxygen (curves 2 and 3, Fig. 6). Those runs in which relatively large amounts of oxygen were present showed a large induction period and in general the products from these reactions were more highly colored yellow than those runs which contained no oxygen.

We have found that the induction is due to the consumption of cuprous catalyst. If an inhibited reaction is quickly quenched with acidic ferric ammonium sulfate solution the amount of cuprous chloride present is found to be nil. Figure 7 shows the rate of cuprous chloride formation from the reduction of cupric chloride in the presence and absence of diazonium salt and olefin.

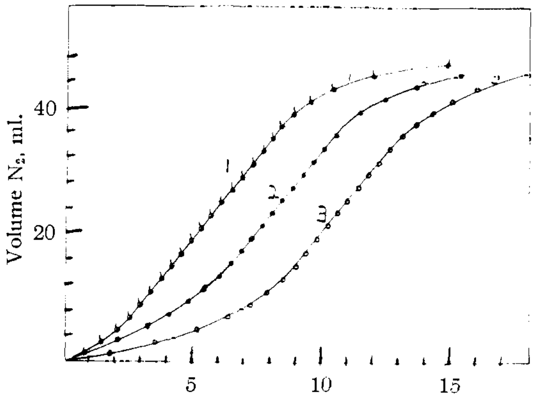

Fig. 6.—Inhibition of diazonium decomposition by oxygen: ◑ (curve 1) uninhibited.

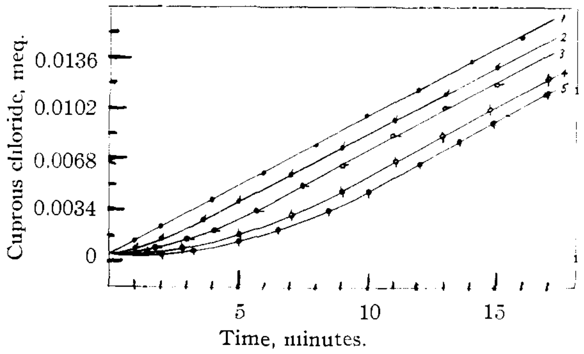

Fig. 7.—Inhibition of cuprous chloride formation in the presence of decomposing diazonium salt and traces of oxygen. All solutions (22 ml.) contain 7.02 meq. of LiCl, 2 meq. of buffer and 1.76 meq. of $Cu(NO_3)_2$: ● (curve 1), no diazonium salt; ● (curve 2), 0.28 meq. of diazonium salt; ○ (curve 3), 0.56 meq. of diazonium salt; ϕ (curve 4), 0.84 meq. of diazonium salt and 4.2 meq. of acrylonitrile; ◑ (curve 5), 0.84 meq. of diazonium salt.

Discussion

Aqueous acetone solutions of cuprous and cupric ions in the presence of chloride ions show complex behavior even in dilute solution because of the numerous complexes which are formed.[6] The addition of olefin to the system magnifies the complexity since now complexes[14] between olefin and cuprous ions must be considered. In a system of this nature we can, at present, only attempt to give a qualitative interpretation of the results.

Our results are consistent with the processes

$$2CuCl_2 + Cl^- + CH_3COCH_3 \longrightarrow 2CuCl_2^- + ClCH_2COCH_3 + H^+ \tag{1}$$

$$CuCl_2^- + 2Cl^- \rightleftharpoons CuCl_4^{-3} \tag{6}$$

$$CuCl_2 \rightleftharpoons CuCl^+ + Cl^- \tag{7}$$

$$CuCl_2^- + CuCl^+ \rightleftharpoons Cu_2Cl_3 \tag{8}$$

$$Cu_2Cl_3 + \Pi \rightleftharpoons (CuCl_2 \cdot \Pi)^- + CuCl^+ \tag{9}$$

$$CuCl_4^{-3} + \Pi \rightleftharpoons (CuCl_2 \cdot \Pi)^- + 2Cl^- \tag{10}$$

$$ArN_2^+ + CuCl_2^- \longrightarrow \text{Sandmeyer product} \tag{11}$$

$$ArN_2^+ + (CuCl_2 \cdot \Pi)^- \longrightarrow \text{Meerwein product} \tag{12}$$

(Π indicates olefin)

Indications from the data in Fig. 4, curve 1, and Fig. 5 are that rate constants k_{11} and k_{12} are approximately equal (*i.e.*, increasing olefin concentrations at high cupric to chloride ratios do not affect the rate but change the relative amounts of Meerwein and Sandmeyer products). Complexes higher than the dichlorocuprous anion are not effective catalysts[15] because at low chloride concentrations the effective rate constant, k_2, is larger than that calculated at higher chloride concentrations (see runs 3, 6 and 9, Table III). A further indication of the presence of an inactive complex, *e.g.*, $CuCl_4^{-3}$, is found in the profound effect olefin (equation 10)[16] has on the rate of nitrogen evolution at low cupric concentrations, a situation in which cupric ions are not significantly competing for the chloride (equation 7).

The deleterious effect of high cupric concentrations shown in Fig. 3 is presumably operative through a process such as in equation 9, which shows the decrease in the cuprous–olefin complex concentration relative to the cuprous chloride complex.[17] Since the cuprous chloride complex, $CuCl_2^-$, is governed by equations 6 and 8, we must assume that the equilibrium constant for equation 9 is larger than that for equation 8.[18] Evidence has been given previously for the existence of cuprous–cupric complexes.[6,19]

Effect of Oxygen.—The oxygen inhibition of the catalytic decomposition of diazonium salts by cuprous halide can be rationalized on a basis similar to the Sandmeyer and Meerwein reactions. Here we postulate

$$CuCl_2^- + O_2 \rightleftharpoons (CuCl_2 \cdot O_2)^- \tag{13}$$

$$ArN_2^+ + (CuCl_2 \cdot O_2)^- \longrightarrow \text{Reduction products} + CuCl_2 \tag{14}$$

Equilibrium constant for equation 13 must be larger than that for either equation 6 or 10 and likewise the rate constant for process 14 must be smaller than that for either 11 or 12 or the autoxidation of cuprous halide.[20]

The Mechanism of the Reaction.—At present we are unable to give a detailed mechanism for the process whereby the olefin or chloride is transferred to the aromatic nucleus (equations 11 and 12).

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(14) (a) R. Keefer, L. Andrews and R. Kepner, THIS JOURNAL, **71**, 3906 (1949), and earlier papers; (b) M. Lur'e, *et al.*, *Sintet Kauchuk*, **3**, 13 (1934); *C. A.*, **32**, 6098, 6099 (1938); (c) E. Gilliland, *et al.*, THIS JOURNAL, **61**, 1960 (1939).

(15) There appears to be some disagreement regarding the particular chlorocuprous complex responsible for the Sandmeyer reaction (ref. 2). Whether it is CuCl or $CuCl_2^-$ does not materially affect the substance of our point.

(16) The $(CuCl_2 \cdot \Pi)^-$ catalytic species was chosen only in analogy to $CuCl_2^-$, postulated by Cowdrey and Davies to be effective in the aqueous Sandmeyer reaction. Keefer, *et al.* (ref. 14a), have successfully rationalized the solubility of cuprous chloride in aqueous olefin solutions on the basis of $(Cu \cdot \Pi)^+$ and $CuCl \cdot \Pi$ complexes as the predominant species. Although we cannot disregard the former complex, it appears likely that either $CuCl \cdot \Pi$ or $(CuCl_2 \cdot \Pi)^-$ is the catalyst for the Meerwein reaction in aqueous acetone.

(17) An alternative explanation for the cupric effect on the yield involves an inactive cupric–olefin complex which competes with tbe cuprous–olefin system for the olefin. We have examined the visible spectra of aqueous acetone solutions containing cupric chloride in the presence of gross amounts of acrylonitrile and have been unable to detect significant differences from those solutions containing no olefin.[6]

(18) Our experiments, however, do not rule out the possibility of the binuclear cuprous–cupric chloride complex as also being a catalyst in the Sandmeyer reaction.

(19) H. McConnell and N. Davidson, THIS JOURNAL, **72**, 3168 (1950); H. Diehl, *et al.*, *Proc. Iowa Acad. Sci.*, **55**, 241 (1948).

(20) Nord recently has given evidence for a cuprous–oxygen complex in aqueous solutions (H. Nord, *Acta Chem. Scand.*, **9**, 430, 438 (1955)).

The reaction can be pictured as (1) a bimolecular reaction between diazonium ion and cuprous complex to give products directly or (2) the formation of an intermediate diazonium–cuprous complex which then slowly decomposes to products or reactive fragments leading to products. These two processes are kinetically indistinguishable.[21,22] In either case there arises a question concerning the electronic requirements of this transfer. There are several schools of thought on this point[5,23] none of which have been satisfactorily demonstrated. We have designed experiments to distinguish among these possibilities.

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(21) See, however, G. Ropp and V. Raaen, THIS JOURNAL, **76**, 4484 (1954).

(22) Although we have not conclusively eliminated the possibility of a radical chain process for either the Sandmeyer reaction, Meerwein reaction or the inhibition of both by oxygen, we believe that these reactions have a common mechanistic path through the cuprous catalyst. The absence of vinyl polymers and recent experiments by O. Vogl and C. Rondestvedt, THIS JOURNAL, **77**, 3067 (1955), indicate that free radicals in the usual sense are not responsible for the Meerwein reaction.

The selectivity of the reactions (nitrile > Meerwein > Sandmeyer) under various conditions involving halide, cyanide and olefin, present alone or acting in combination, leads us to believe that the group (halide, cyanide or alkyl) which replaces the diazonium group is attached to the cuprous catalyst as a complex. The rate of formation of each product will then depend on the equilibrium constant controlling the concentration of each catalytic cuprous complex species and the rate at which these complexes react with diazonium ion. The factors which influence this latter rate must be scrutinized in greater detail.

(23) H. Meerwein, E. Buchner and K. VanEmster, *J. prakt. Chem.*, **152**, 237 (1939); C. Koelsch and V. Boekelheide, THIS JOURNAL, **66**, 412 (1944); E. Muller, *Angew. Chem.*, **61**, 179 (1949); W. Brunner and J. Kustascher, *Monatsh.*, **82**, 100 (1951); J. Rai and K. Mathur, *J. Indian Chem. Soc.*, **24**, 413 (1947), earlier and later papers.

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[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

A Study of an Oxidative-amination Method for the Synthesis of Aminoquinones[1]

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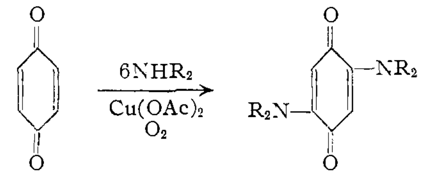
The oxidative-amination of 1,4-benzoquinones, and the amine displacements of alkoxyls from 2,5-dialkoxyquinones, to give 2,5-bis-(dialkylamino)-benzoquinones, are shown to be limited to active amines. The failure of diisopropylamine to react in these ways is attributed to its relatively weak basicity with respect to the Lewis acid quinone. The oxidative-amination method has been shown to be applicable to 1,4-naphthoquinone also.

Amines of many types, including even tertiary amines,[3] react with quinones,[4–10] but the usual method for the synthesis of aminoquinones (using the quinone itself as oxidant) is often very unsatisfactory. Since a series of aminoquinones was desired for testing as possible antimalarials or tumor-necrotizing agents,[1a] it was of interest to study the applicability of the elegant method developed by Baltzly and Lorz[9] for the preparation of 2,5-bis-(dimethylamino)-benzoquinone (II, $R = CH_3$).

This oxidative-amination reaction or a suitable modification of it was successfully applied to the direct synthesis from benzoquinone of seven 2,5-bis-(dialkylamino)-1,4-benzoquinones which are listed and described in Table I. The secondary amines used in this study were chosen so as to investigate any limitations of the reaction occasioned by steric relations within the amine component. Such a limitation was found when diisopropylamine, in contrast with di-*n*-propyl-, methylisopropyl- and benzylmethylamines, did not yield an aminobenzoquinone. The method has not been successful with primary amines.[9] In the naphthoquinone series, 1,2-naphthoquinone did not give a piperidyl derivative under conditions which converted 1,4-naphthoquinone into 2-(1-piperidyl)-1,4-naphthoquinone. It thus appears that this oxidative amination method is limited to 1,4-quinones and to relatively unbranched secondary amines.



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The limitation of the reaction with respect to the branching of the chains of the secondary amines can be explained by a mechanism which postulates that quinone functions as a Lewis acid and undergoes nucleophilic attack by the amine as the first step in the reaction sequence leading to the aminoquinones; and, therefore, if the amine is of insufficient base strength with respect to quinone as a Lewis acid (because of steric hindrances such as B

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(1) (a) This investigation was supported in part by a grant from the National Institutes of Health under recommendation by the National Cancer Institute. It was initiated under an earlier N.I.H. antimalarial grant for the purpose of ascertaining whether dialkylaminoquinones would possess greater activity than the dialkylaminodibenzoylethylenes and related compounds [R. E. Lutz, T. A. Martin, *et al.*, *J. Org. Chem.*, **14**, 982 (1949)]. (b) Abstracted in part from the dissertation of A. H. Crosby submitted to the Graduate Faculty of the University of Virginia in partial fulfillment of the requirement for the degree of Doctor of Philosophy.

(2) National Cancer Institute Pre-doctoral Fellow, 1949–1950. Northwestern State College, Natchitoches, La.

(3) O. Diels and R. Kassebart, *Ann.*, **530**, 51 (1937).

(4) H. Suida and W. Suida, *ibid.*, **416**, 113 (1918).

(5) M. Martynoff and G. Tsatsas, *Bull. soc. chim. France*, **52**, (1947M).

(6) S. Kanao and S. Inagawa, *J. Pharm. Soc. Japan*, **58**, 347 (1938); *C. A.*, **32**, 5805 (1938).

(7) C. J. Cavallito, A. E. Soria and J. O. Hoppe, THIS JOURNAL, **72**, 2661 (1950).

(8) J. V. Schurman and E. I. Becker, *J. Org. Chem.*, **18**, 211 (1953).

(9) R. Baltzly and E. Lorz, THIS JOURNAL, **70**, 861 (1948).

(10) R. A. Henry and W. M. Dehn, *ibid.*, **74**, 278 (1952).