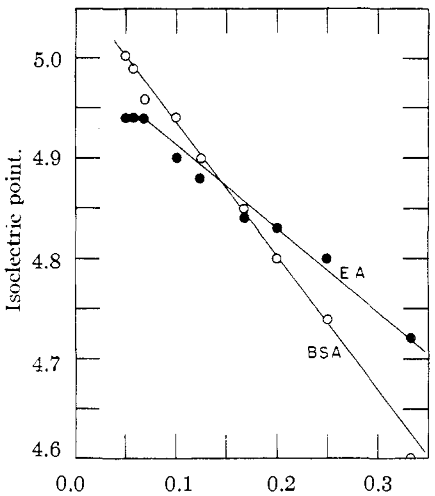

Fig. 4.—The isoelectric point of adsorbed BSA (open circles) and of adsorbed EA (closed circles) as a function of the square root of the ionic strength.

Fig. 2 of some kind of change of the protein surface above an ionic strength of 0.00449. In any event, the plot for EA shown in Fig. 3 is not consistent with the idea that the effective radius of the adsorbed EA is the same as that of the dissolved protein, and it seems probable that the two arrangements of the EA molecules at the glass-water interface both have effective electrophoretic radii which are very much larger than is the thickness of the electrical double layer.

The fact that protein adsorbed on microscopically visible particles behaves electrophoretically as plane plate condensers means a tremendous simplification of the interpretation of electrophoretic measurements on such material. For example, the charge density of such a surface can be calculated from electrophoretic mobilities using the equations for plane surfaces. We are, however, still faced with the problem of the similarity between the mobilities of adsorbed and dissolved protein. It is felt that Abramson, Moyer and Gorin overemphasized the agreement between the electrophoretic mobility of adsorbed and dissolved protein; nevertheless, the fact remains that the mobilities by these two methods do not differ by a large factor; not by the factor to be expected. Thus at an ionic strength of 0.01 and for the same surface charge density the mobility of the adsorbed protein (BSA) should be 2.93 times greater than the mobility of the dissolved molecule.

The only effective explanation for the relatively low observed mobilities of the adsorbed protein is that the charge density per unit area of the adsorbed protein is significantly less than the average surface charge density of the dissolved protein at the same *p*H and ionic strength. It is concluded that when protein molecules are adsorbed on the highly negatively charged glass surface then the protein molecules are oriented and or distorted in such a manner that the ionogenic groups of the protein are preferentially turned inward toward the glass and the charge density per unit area of the protein–water interface suffers a considerable diminution.

The variation of the isoelectric points of the adsorbed protein with ionic strength is not directly related to the problem at hand, but since we now have this information available, we wish to insert it at this point. Shown in Fig. 4 is the variation of the isoelectric points of adsorbed BSA (open circles) and of adsorbed EA (closed circles) as a function of the square root of the ionic strength. As noted by Moyer[20] and confirmed here, the isoelectric point of adsorbed EA is significantly higher than that of the dissolved protein at a given ionic strength. Aoki and Foster[21] report the isoelectric point of dissolved BSA in hydrochloric acid and sodium chloride at an ionic strength of 0.02 of 4.52. The interpolated value of the isoelectric point at this ionic strength of the adsorbed BSA (see Fig. 4) is 4.88; the isoelectric point of adsorbed BSA is also significantly higher than that of the dissolved protein.

(20) L. S. Moyer, *J. Phys. Chem.*, **42**, 71 (1938).

(21) K. Aoki and J. F. Foster, THIS JOURNAL, **79**, 3385 (1957).

IOWA CITY, IOWA

[CONTRIBUTION FROM THE WM. H. NICHOLS CHEMICAL LABORATORY, NEW YORK UNIVERSITY]

The Kinetics of the Sandmeyer and Meerwein Reactions[1]

BY S. CARLTON DICKERMAN, KARL WEISS AND ARTHUR K. INGBERMAN

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The kinetics of the Sandmeyer and Meerwein reactions of 2,4-dichlorobenzenediazonium chloride have been investigated. The rate of the Sandmeyer reaction was found to increase with increasing cupric chloride and acetone concentrations. The generation of cuprous chloride in acetone solutions of cupric chloride was confirmed, and its catalytic activity established by the correlation of the rate of nitrogen evolution with the rate of cuprous chloride formation. A product analysis showed the Sandmeyer product to be accompanied by arene and chloroacetone in equimolar proportion. In the absence of cupric chloride little nitrogen was evolved, and nitrogen-containing products were isolated. In the Meerwein reaction, the rate was found to vary with unsaturate both in the presence and absence of air. The results for both reactions are interpreted in terms of a comprehensive radical mechanism.

The recent confirmation in two laboratories[2,3] of a cryptic report[4] concerning the formation of cuprous chloride from acetone and cupric chloride has led to the realization[3,5] that the Sandmeyer and Meerwein reactions are initiated by essentially

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[1] Presented in part at the 131st Meeting of the American Chemical Society, Miami, Fla., April 8, 1957.

[2] J. K. Kochi, THIS JOURNAL, **77**, 5090, 5274 (1955).

[3] S. C. Dickerman, K. Weiss and A. K. Ingberman, *J. Org. Chem.*, **21**, 380 (1956).

[4] V. Kohlschütter, *Ber.*, **37**, 1153 (1904).

[5] J. K. Kochi, THIS JOURNAL, **79**, 2942 (1957).

the same mechanism. It is of interest to note that experiments designed to detect the radical nature of the Meerwein reaction have demonstrated[6] that aryl radicals are probable intermediates in homogeneous Sandmeyer reactions.

Our interest in this field stems from a report by Meerwein, *et al.*,[7] that the decomposition of diazonium salts in aqueous acetone solutions of cupric chloride was accompanied by the formation of chloroacetone and arene. Of those diazonium salts studied 2,4-dichlorobenzenediazonium chloride (DBC) represented the extreme example and accordingly we have used this diazonium salt for investigations of the Sandmeyer reaction in aqueous acetone and the related Meerwein reaction.

Orienting experiments indicated that the addition of cupric chloride to aqueous acetone solutions of DBC initiated one or more reactions which resulted in loss of nitrogen, since in the absence of cupric chloride only a fraction of the theoretical volume of nitrogen was evolved. Such solvolytic decompositions were accompanied by precipitation of a red solid, 1,5-di-(2,4-dichlorophenyl)-3-acetylformazan.

In an effort to determine which copper species was responsible for the decomposition of the diazonium salt we reinvestigated the products of the cupric chloride–acetone reaction and verified that

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

cuprous chloride and chloroacetone are formed according to equation 1.

The kinetics of this reaction in aqueous acetone solutions of various compositions have been studied,[8a,b] and data pertinent to this paper are presented in Fig. 1.

The Sandmeyer Reaction in Aqueous Acetone

The rate of decomposition of DBC was measured eudiometrically at 35° and at various acetone and initial cupric chloride concentrations. Figure 2 shows the dependence of rate on initial cupric chloride concentrations, while Fig. 3 gives the results of varying the acetone–water ratio at a constant cupric chloride concentration. All kinetic data were obtained from solutions which were homogeneous throughout the period of observation. The slower reactions were followed for longer periods of time than indicated, but the volume of nitrogen evolved never reached the theoretical value. In agreement with eq. 1, it was found that increasing acetone and/or cupric chloride concentration accelerates the rate of decomposition of the diazonium salt.

The general shape of the curves of Figs. 2 and 3 is characteristic of consecutive reactions, suggesting that cuprous chloride is involved in the rate-determining step.

If it is assumed that nitrogen evolution results from the reaction between diazonium cation and cuprous chloride, the rate law would be given by

$$-\,d\,\ln D/dt = kC \quad (2)$$

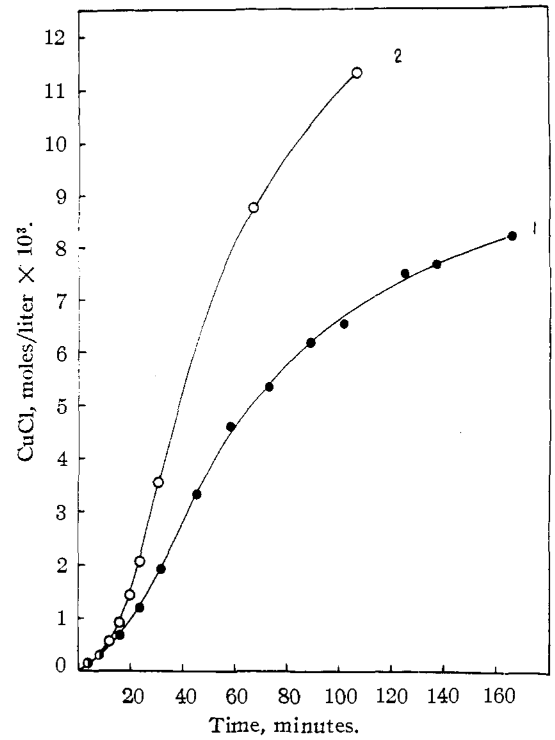

Fig. 1.—Rate of formation of CuCl in aqueous acetone solutions of $CuCl_2$ at 35°: curve 1, 0.0558 *M* $CuCl_2$, 0.0490 *M* NaCl, 64.8% acetone by wt.; curve 2, 0.0418 *M* $CuCl_2$, 0.0490 *M* NaCl, 75.9% acetone by weight.

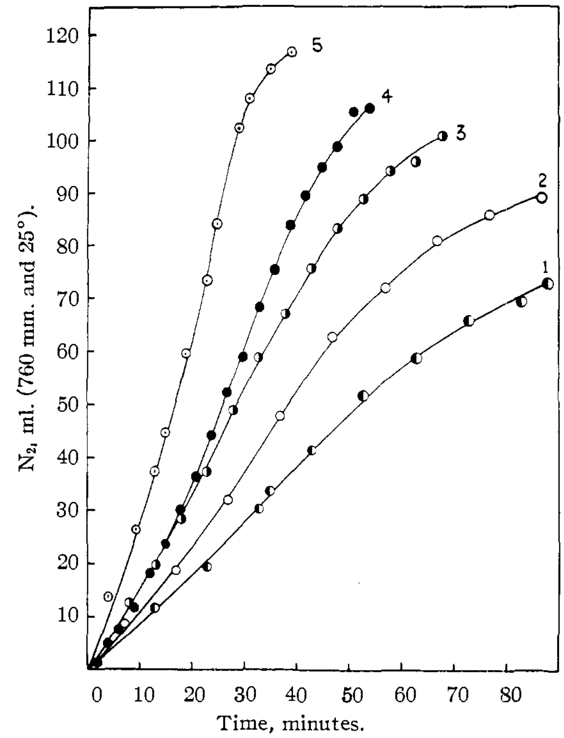

Fig. 2.—Decomposition of DBC in aqueous acetone; variation of rate with $CuCl_2$ concentration in 64.8% by weight acetone solutions initially 0.0490 *M* in DBC: curve 1, 0.0232 *M* $CuCl_2$; curve 2, 0.0335 *M* $CuCl_2$; curve 3, 0.0456 *M* $CuCl_2$; curve 4, 0.0558 *M* $CuCl_2$; curve 5, 0.0837 *M* $CuCl_2$.

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[6] S. C. Dickerman and K. Weiss, *J. Org. Chem.*, **22**, 1070 (1957).

[7] H. Meerwein, E. Büchner and K. van Emster, *J. prakt. Chem.*, **152**, 237 (1939).

[8] (a) S. C. Dickerman and K. Weiss, unpublished results. (b) The kinetics of this reaction also have been investigated by Kochi.[2]

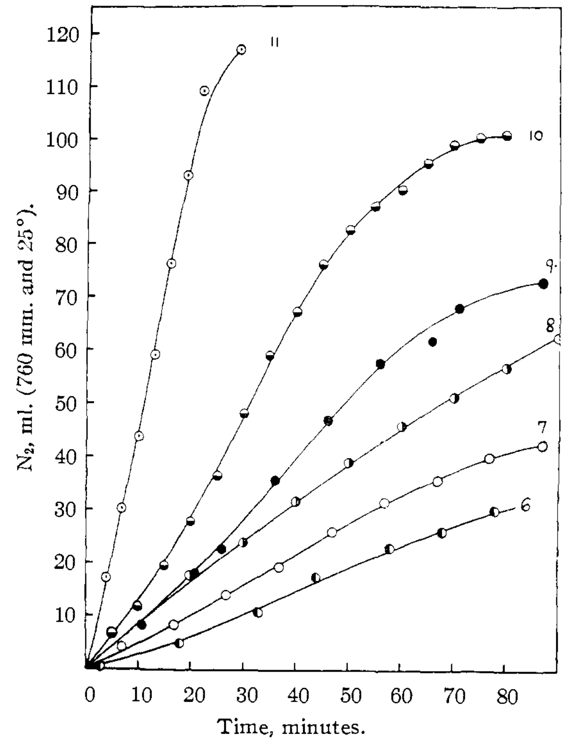

Fig. 3.—Decomposition of DBC in aqueous acetone; variation of rate with acetone concentration in solutions initially 0.0490 M in DBC and 0.0418 M in $CuCl_2$: curve 6, 44.1%; curve 7, 49.1%; curve 8, 54.5%; curve 9, 59.8%; curve 10, 64.8%; curve 11, 75.9% acetone by weight.

where D and C are the instantaneous concentrations of DBC and cuprous chloride, respectively. Tests of equation 2 for two runs in which the nitrogen evolution was approximately quantitative are presented in Fig. 4. The linearity of these plots for 60–70% of reaction bears out the essential correctness of the postulate regarding the rate-determining step and, furthermore, supports the view that cuprous chloride is not consumed in the over-all reaction.[9] The same result, obtained under different experimental conditions, will be presented as part of the kinetics of the Meerwein reaction (*vide infra*).

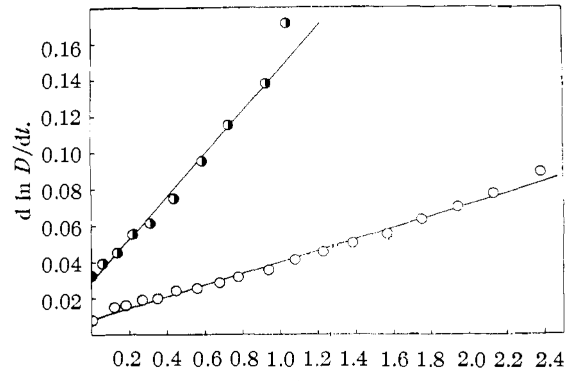

Fig. 4.—Test of equation 2: ○, run 4, Fig. 2; ◑, run 11, Fig. 3.

Product isolation was carried out in a large-scale duplication of run 4, Fig. 2, with these results: chloroacetone, 64%; 1,3-dichlorobenzene, 47%; and 1,2,4-trichlorobenzene, 26% based on DBC. A similar experiment at a higher initial concentration of cuprous chloride gave the values: chloroacetone, 52%; 1,3-dichlorobenzene, 42%; and 1,2,4-trichlorobenzene, 26%. Since chloroacetone is also produced by the cupric chloride–acetone reaction a blank was determined in the absence of DBC and was used to adjust the yields of chloroacetone to represent only that produced from the diazonium salt. These revised values are 49 and 38%, respectively, and are identical within experimental error with the amounts (47 and 42%) of 1,3-dichlorobenzene isolated. This result strongly implies that acetone is the source of hydrogen for arene formation.

The Meerwein Reaction

It has been observed qualitatively that, for a given diazonium salt, the rate of nitrogen evolution in the Meerwein reaction depends upon the nature of the unsaturated compound.[7,10] Furthermore, it has been reported[9] that *p*-chlorobenzenediazonium chloride decomposes more rapidly in the presence of styrene than in the presence of acrylonitrile, at least at low unsaturate concentrations.[5]

To gain further insight into the nature of the interaction between the diazonium salt and the unsaturate we have made a quantitative study of the rate of decomposition of DBC in Meerwein reactions with four unsaturated compounds and one arene. Since good evidence has now been presented for the radical nature of these reactions,[3,5] the kinetic measurements were carried out both in the presence and absence of air. To facilitate comparison, constant initial concentrations of DBC, cupric chloride and unsaturate (or arene) were used in the absence of added chloride ion. The results in the presence of air are shown in Fig. 5. All the curves are sigmoidal in shape and the theoretical volume of nitrogen was evolved only with benzene and in the absence of unsaturated compounds (Sandmeyer reaction). Acrylonitrile, methyl methacrylate, styrene and α-methylstyrene depress both the rate and total nitrogen yield in that order.

Kinetic studies in the absence of air were complicated by the formation of small amounts of cuprous chloride during the standard degassing operations. Also, apparently in contrast to *p*-chlorobenzenediazonium chloride,[9] DBC is so extraordinarily sensitive to catalysis by cuprous ion that it was necessary to reduce the cupric chloride and acetone concentrations in order to bring the decompositions into a measurable range. This prior formation of cuprous ion could not be prevented by separation of cupric and chloride ions in the reaction vessel through the use of cupric nitrate.[11] By careful control of the degassing time it was possible to keep the amount of preformed cuprous chloride constant at 3.2 × 10^{-4} mole/liter

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[9] J. K. Kochi, This Journal, **78**, 1228 (1956).

[10] C. F. Koelsch and V. Boekelheide, *ibid.*, **66**, 412 (1944).

[11] This finding is in disagreement with Kochi[9] who reported that the presence of chloride ion is essential for the reduction of cupric to cuprous ion by acetone.

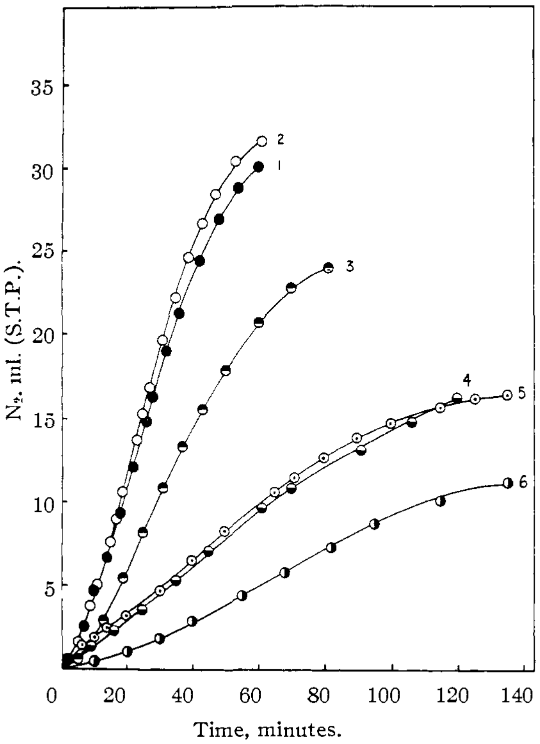

Fig. 5.—Meerwein reactions of DBC in air; variation of rate with unsaturates in 64.8% by weight acetone solutions initially 0.0558 *M* in $CuCl_2$, 0.0490 *M* in DBC and 0.0490 *M* in unsaturate: curve 1, no unsaturate; curve 2, benzene; curve 3, acrylonitrile; curve 4, styrene; curve 5, methyl methacrylate; curve 6, α-methylstyrene.

as determined by titration with standard ceric ammonium sulfate solution. Under these conditions the nitrogen evolution was rapid and complete in every case, so that if the symbols V and V_∞ refer to the volumes of nitrogen collected at time t and at the end of the reaction, respectively, the quantity $(V_\infty - V)$ is directly proportional to the instantaneous DBC concentration. Figure 6 shows the results in the form of plots of log $(V_\infty - V)$ against time. Linearity of the plots over the initial 60–85% of the reaction suggests adherence to a first-order rate law in this region. Since the rate of formation of cuprous chloride in these solutions is extremely slow,[8a] its concentration in the initial portion of the reaction may be assumed to remain essentially constant. This assumption permits the integration of equation 2 to yield

$$\ln D = k(3.2 \times 10^{-4})t + \text{constant} \qquad (3)$$

Deviation from linearity toward the end of the reactions (as reflected by an *increase* in rate) may be ascribed to the slow, continuous formation of cuprous chloride from the reaction medium. That the linear portions are longer for fast reactions than for slow ones tends to support this view.

Apparent initial second-order rate constants calculated from equation 3 (Table I) show that in the absence of air α-methylstyrene, acrylonitrile and methyl methacrylate *increase* the rate of decomposition of DBC, and styrene and benzene *depress* it. It is significant to note, however, that in no case is the rate of the reaction greatly affected by the presence of the unsaturates or benzene. The rate is changed at the most by a factor of approximately two, in strong contrast with the situation in the presence of air. In the case of acrylonitrile the rate increases, but not in direct proportion, with increasing acrylonitrile concentration (run 7, Table I).[9]

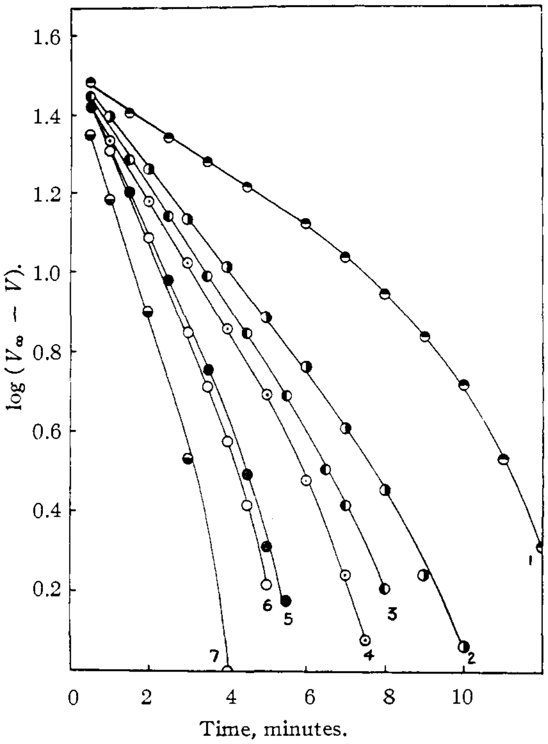

Fig. 6.—Meerwein reactions of DBC in the absence of air; variation of rate with unsaturates in 54.5% by weight acetone solutions initially 3.2×10^{-4} *M* in CuCl, 0.0279 *M* in $CuCl_2$, 0.0490 *M* in DBC and 0.0490 *M* in unsaturate: curve 1, styrene; curve 2, benzene; curve 3, no unsaturate; curve 4, α-methylstyrene; curve 5, acrylonitrile; curve 6, methyl methacrylate; curve 7, acrylonitrile (0.1480 *M*).

TABLE I

APPARENT INITIAL RATE CONSTANTS FOR THE MEERWEIN REACTION IN THE ABSENCE OF AIR[a]

Run	Unsaturated or aromatic compound	k, l./mole sec.
1	Styrene[b]	7.7
2	Benzene[b]	16.1
3	None	17.8
4	α-Methylstyrene[b]	19.1
5	Acrylonitrile[b]	26.5
6	Methyl methacrylate[b]	27.6
7	Acrylonitrile[c]	37.6

[a] At 35° in 54.5% by weight aqueous acetone containing 3.2×10^{-4} mole/liter cuprous chloride initially, 0.0279 mole/liter cupric chloride and 0.0490 mole/liter DBC. [b] 0.0490 mole/liter. [c] 0.1480 mole/liter.

To establish whether radical-induced decomposition of DBC occurs, the Sandmeyer reaction in the absence of air was studied at several initial DBC concentrations.[12] The rate constants were

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(12) In the thermal decomposition of benzoyl peroxide in various solvents it has been shown that induced decomposition results in an increase of the apparent first-order rate constant with increasing initial peroxide concentration. See P. D. Bartlett and R. Altschul,

Table II

Apparent Initial Rate Constants for the Sandmeyer Reaction in the Absence of Air[a]

DBC, mole/liter	k, l./mole. sec.
0.0245	26.5
.0490	17.8
.0980	10.4

[a] At 35° in 54.5% by weight aqueous acetone containing 3.2×10^{-4} mole/liter cuprous chloride initially and 0.0279 mole/liter cupric chloride.

found to vary approximately in inverse proportion to the initial concentration (Table II). This result rules out induced decomposition. Since an increase in DBC concentration amounts to an increase of the chloride ion concentration, the formation of a catalytically inactive complex between cuprous and chloride ions could be responsible for the decreased rates.[13]

Discussion

Recently, we presented an oxidation–reduction radical mechanism, eq. 4 through 9 for the Sandmeyer (in acetone) and Meerwein reactions.[3]

$$ArN_2^+ + CuCl_2^- \longrightarrow Ar\cdot + N_2 + CuCl_2 \quad (4)^{14}$$

$$Ar\cdot + CuCl_2 \longrightarrow ArCl + CuCl \quad (5)$$

$$Ar\cdot + CH_3COCH_3 \longrightarrow ArH + CH_3COCH_2\cdot \quad (6)$$

$$CH_3COCH_2\cdot + CuCl_2 \longrightarrow CH_3COCH_2Cl + CuCl \quad (7)$$

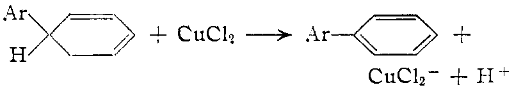
$$Ar\cdot + {>}C{=}C{<} \longrightarrow Ar\underset{|}{\overset{|}{C}}{-}\underset{|}{\overset{|}{C}}\cdot \quad (8)$$

$$Ar\underset{|}{\overset{|}{C}}{-}\underset{|}{\overset{|}{C}}\cdot + CuCl_2 \longrightarrow Ar\underset{|}{\overset{|}{C}}{-}\underset{|}{\overset{|}{C}}{-}Cl + CuCl \quad (9)$$

In the presence of unsaturate, reactions 5, 6 and 7 are suppressed but apparently still occur sufficiently to account for the observed by-products in Meerwein reactions.[7] Although this simple mechanism has found some support, interpretations of the kinetics of Meerwein reactions with DBC, Figs. 5 and 6, may require a more complicated scheme.

A radical mechanism for the Meerwein reaction was first suggested by Koelsch and Boekelheide[10] to explain arylation on the β-carbon atom of substituted olefins.[15] The evidence which directed our thoughts along radical lines was the high yield of arene from DBC and the formation of an equivalent amount of chloroacetone. However, the most convincing demonstration for the presence of aryl radicals in such systems is the arylation of arenes and, particularly, the characteristic radical orientation observed in the p-nitrophenylation of nitrobenzene under Meerwein conditions.[3,6] Iodine also has been used to trap aryl radicals in these systems.[5] The radical mechanism did not find general acceptance because of the unexplained absence of olefin polymerization. In order to get around this discrepancy, it was suggested that the reaction is not radical in the generally accepted sense of the term.[16] The suggestion that cupric chloride destroys aralkyl radicals, eq. 9, and also acetonyl radicals, eq. 7, provides an answer to the difficulty. These reactions furnish the most obvious explanation for the formation of the products and, at the same time, for the maintenance of the cuprous concentration as demanded by the kinetics. Similar suggestions have been made by Waters,[17] and Koelsch and Boekelheide.[10] The efficiency with which cupric and ferric chlorides terminate aralkyl chain reactions has been demonstrated recently.[5,18] It is pertinent to observe that at low concentrations such oxidation–reduction systems in conjunction with p-nitrobenzenediazonium chloride do, in fact, initiate the polymerization of acrylonitrile.[19]

In the Meerwein arylation of arenes the cuprous salt may be regenerated as shown in eq. 10 although loss of a hydrogen atom would achieve the same result.



(10)

The kinetics of the Sandmeyer reaction with DBC are in agreement with previous studies[9,20] which showed the reaction to be first order in both diazonium salt and cuprous halide. In formulating eq. 4 we have accepted the suggestion of Cowdrey and Davies that the probable cuprous species is the dichlorocuprate I ion. The definite radical character of the Sandmeyer reaction in acetone confirms Waters' view that the mechanism is essentially an oxidation–reduction reaction,[21] and suggests that homogeneous Sandmeyer reactions in general may proceed *via* a stepwise mechanism. The stability of the arylazo radical will determine whether a two or three-step process is operative. From this point of view the synthetic usefulness of the classical Sandmeyer reaction may be a reflection of the inertness of water to attack by aryl radicals[22] leading to preferential reaction with cupric halide. The observation that some racemization occurred in a Sandmeyer reaction with an optically active biphenyldiazonium salt[23] also supports the radical mechanism.

The kinetics of the Meerwein reactions may be qualitatively interpreted in at least two ways: firstly, as a property of the chain reaction or secondly, in terms of complexes. The first possibility leads to the postulate that the different rates of decomposition of DBC with various olefins reflect the stability of the particular aralkyl radical

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This Journal, **67**, 816 (1945); K. Nozaki and P. D. Bartlett, *ibid.*, **68**, 1686 (1946); **69**, 2299 (1947); W. E. Cass, *ibid.*, **68**, 1976 (1946).

(13) W. A. Cowdrey and D. S. Davies, *J. Chem. Soc.*, S 48 (1949), have proposed that the chlorocuprous species $CuCl_4^{-3}$ does not catalyze the decomposition of diazonium salts.

(14) Arylazo radicals are possible intermediates in the electron-transfer reaction.

(15) See also E. Müller, *Angew. Chem.*, **61**, 179 (1949).

(16) The term "radicaloid" to describe the Meerwein reaction was proposed by O. Vogl and C. S. Rondestvedt, Jr., This Journal, **77**, 3067 (1955).

(17) W. A. Waters, "Chemistry of Free Radicals," 2nd ed., Oxford Univ. Press, London, 1948, pp. 162–165.

(18) R. Haines and W. Waters, *J. Chem. Soc.*, 4256 (1955); C. Bamford, A. Jenkins and R. Johnston, *Nature*, **177**, 992 (1956); E. Collinson and F. Dainton, *ibid.*, **177**, 1224 (1956); J. K. Kochi, This Journal, **78**, 4815 (1956).

(19) W. Cooper, *Chemistry & Industry*, 407 (1953).

(20) For a recent review of the Sandmeyer reaction see W. A. Cowdrey and D. S. Davies, *Quart. Revs.* (*London*), **6**, 358 (1952).

(21) W. A. Waters, *J. Chem. Soc.*, 266 (1942).

(22) J. Baxendale and J. Magee, *Trans. Faraday Soc.*, **51**, 204 (1955).

(23) D. F. DeTar and J. C. Howard, This Journal, **77**, 4393 (1955).

insofar as this radical is involved in the regeneration of cuprous chloride, equation 9. If some allowance is made for a steric factor which decreases resonance stabilization of the radical, the order of reactivity of the olefins is not unreasonable.[24]

A second interpretation of the kinetics is based on the participation of unsaturate in the rate-determining step. This requires the presence of either a reactive unsaturate–cuprous halide complex or a reactive unsaturate–diazonium cation complex.[26] Under these circumstances the nitrogen would be liberated by reaction of the unsaturate–diazonium complex or unsaturate–cuprous complex with either cuprous halide or diazonium cation, respectively, as well as according to eq. 4. Both of these reactions lead to the same rate expression which cannot at present be integrated owing to the presence of terms involving the unsaturate concentration. This expression does predict, in agreement with the experimental findings, that the effect of the unsaturate on the rate would not be particularly large.[27]

A reactive unsaturate–cuprous halide complex has been proposed previously by Kochi[9] on the basis of a kinetic study of the Meerwein reaction of *p*-chlorobenzenediazonium chloride with acrylonitrile. As expected, DBC reacts more rapidly than *p*-chlorobenzenediazonium chloride with cuprous chloride. The specific rate constants for these two diazonium salts in the Sandmeyer reaction are 18 liters/mole. sec. and 11 liters/mole. sec. in 54.5 weight % and 59.8 weight % acetone, respectively.

The possible participation of complexes in the Meerwein reaction does not affect its radical character. It does suggest that aryl radicals may be generated within a solvent cage in the close vicinity of the unsaturate molecules, and subsequently react very rapidly with the unsaturate, cupric chloride or acetone to produce Meerwein product, aryl halide or arene, respectively. This interpretation offers an attractive explanation for the observed high yields of Meerwein product in solutions where the analytical concentration of the unsaturate is relatively low.[28,30]

The inhibitory effect of unsaturates in the presence of air may be explained in terms of destruction of cuprous catalyst, probably through the intervention of intermediate peroxy radicals. Such radicals have been postulated for the inhibition by oxygen of typical radical reactions such as polymerization.[31] Furthermore, polymeric peroxides have been isolated from the reaction of oxygen with methyl methacrylate, styrene and α-phenylstyrene,[32] and Kochi[5] has obtained *p*-nitrodesoxybenzoin from the reaction of *p*-nitrobenzenediazonium chloride and styrene under Meerwein conditions in the presence of oxygen.

The aralkyl radicals react with oxygen to form peroxy radicals which then oxidize cuprous chloride,[5] leading to a much slower, solvolytic decomposition of the diazonium salt and accompanying coupling reactions. Azo dye formation was evidenced by more highly colored reaction mixtures in the presence of air than in its absence.

The order of retardation (α-methylstyrene > styrene ≃ methyl methacrylate > acrylonitrile > benzene) probably reflects the reactivity of the corresponding aralkyl radical with oxygen since the subsequent reaction of the intermediate peroxy radical can be assumed to be very rapid. That benzene does not inhibit the decomposition may be ascribed to the reluctance of aromatic compounds to form peroxides. The strong inhibition by α-methylstyrene correlates with the ease of oxidation of olefins bearing allylic hydrogen.[33] Since all the unsaturates examined inhibit the decomposition of DBC, it is evident that aralkyl radicals react more readily than aryl radicals with oxygen. The variation in rates in the decomposition of diazonium salts with various unsaturates in the presence of air thus probably reflects different oxygen affinities of the aralkyl radicals.[33a]

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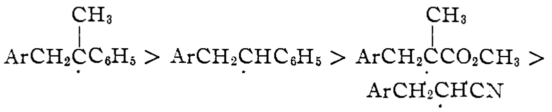
[24] The stabilities of the aralkyl radicals would be expected[25] to decrease in the order



$$\mathrm{ArCH_2\dot{C}(CH_3)C_6H_5 > ArCH_2\dot{C}HC_6H_5 > ArCH_2\dot{C}(CH_3)CO_2CH_3 > ArCH_2\dot{C}HCN}$$

where Ar represents the 2,4-dichlorophenyl group. Both α-methylstyrene and methyl methacrylate are displaced somewhat from this "normal" sequence, perhaps due to the steric effect of the α-methyl group.

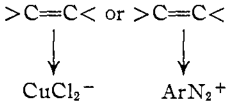
[25] K. Nozaki, *Disc. Faraday Soc.*, **2**, 341 (1947).

[26] (a) There is much evidence that cuprous salts form complexes with unsaturated compounds. See J. Chatt, "Cationic Polymerization and Related Complexes," Proc. Conf. Univ. Coll. North Staffordshire (England), 40, 52 (1952); A. L. Ward and E. E. Makin, Jr., THIS JOURNAL, **69**, 657 (1947); L. F. Hatch and G. B. Roberts, *ibid.*, **68**, 1196 (1946); R. M. Keefer, L. J. Andrews and R. E. Kepner, *ibid.*, **71**, 3906 (1949); L. J. Andrews and R. M. Keefer, *ibid.*, **71**, 2379, 2381 (1949); W. A. Schulze and G. H. Short, U. S. Patent 2,401,114 (1946); *C. A.*, **40**, P5443[6] (1946). (b) Complexes between diazonium salts and unsaturates have been described by R. Wizinger and B. Cyriax, *Helv. Chim. Acta*, **28**, 1018 (1945).

[27] The observed rate constant, k is given by

$$k = \frac{k_4 + k_c K_c(>\mathrm{C}{=}\mathrm{C}<)}{1 + K_c(>\mathrm{C}{=}\mathrm{C}<)} \qquad (10)$$

where k_4 is the specific rate constant for eq. 4 and K_c and k_c represent the equilibrium and specific rate constants for the formation and subsequent reaction of complexes of the type



$$\underset{\mathrm{CuCl_2^-}}{\overset{}{>\mathrm{C}{=}\mathrm{C}<}} \downarrow \quad \text{or} \quad \underset{\mathrm{ArN_2^+}}{>\mathrm{C}{=}\mathrm{C}<} \downarrow$$

Depending on the relative magnitudes of k_c and K_c, eq. 10 can accommodate observed rate constants which are either larger or smaller than k_4.

[28] The relatively low activation energy for radical addition to a double bond (about 4 kcal. in the case of addition polymerization[29]) would explain the preference for this reaction over abstraction reactions.

[29] C. E. H. Bawn, "The Chemistry of High Polymers," Interscience Publishers, Inc., New York, N. Y., 1948, p. 74.

[30] Some support for the solvent cage theory is to be found in the work of Vogl and Rondestvedt[16] who investigated the phenylation of coumarin with a variety of radical sources in the absence of metal halides. The yields of phenylcoumarin were much lower than in the Meerwein reaction, perhaps owing to the random generation of phenyl radicals and their rapid reaction with the more abundant solvent molecules. See, however, Kochi, ref. 5, footnote 27.

[31] P. D. Bartlett, *Angew. Chem.*, **67**, 45 (1955); P. Flory, "Principles of Polymer Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, p. 168.

[32] C. E. Barnes, R. M. Elofson and G. D. Jones, THIS JOURNAL, **72**, 210 (1950); F. A. Bovey and I. M. Kolthoff, *ibid.*, **69**, 2143 (1947); H. Staudinger, *Ber.*, **58**, 1075 (1925).

[33] E. H. Farmer, *Trans. Faraday Soc.*, **38**, 340 (1942); E. H. Farmer, H. P. Koch and D. A. Sutton, *J. Chem. Soc.*, 541 (1943).

[33a] See, however, Kochi, ref. 5, p. 2946.

Experimental[34]

2,4-Dichlorobenzenediazonium Chloride (DBC).—2,4-Dichloroaniline hydrochloride (30.0 g.), prepared by the hydrolysis of 2,4-dichloroacetanilide with dilute hydrochloric acid, was suspended in 300 ml. of anhydrous ethyl ether and was diazotized at 0° by the addition within 10 minutes of 18.0 g. of isoamyl nitrite. After 2.5 hours the mixture was cooled in a Dry Ice–acetone-bath, was centrifuged and the solid was washed with fresh ether to yield 29.6 g. of diazonium salt, m.p. 165–170° dec.

Anal. Calcd. for $C_6H_3Cl_3N_2$: Cl^-, 16.9. Found: Cl^-, 16.4.

Samples of DBC used for the study of the Sandmeyer reaction were stored under ethyl ether at Dry Ice temperature and were purified prior to use by reprecipitation from methanol with ether. This procedure was repeated until the kinetics before and after a reprecipitation were identical.[35]

DBC coupled with 2-naphthol to a quantitative yield of 1-(2,4-dichlorophenylazo)-2-naphthol, m.p. 190°, reported[36] 190°. Spectrophotometric analysis at 483 mμ for this derivative gave values of from 97–99% purity for various samples.

During the Meerwein phase of this work it was found that stable aqueous solutions of DBC could be prepared as follows: solid dry diazonium salt was dissolved in cold, demineralized water; the solution was treated with Norite and sealed in ampoules which were kept frozen in a Dry Ice cabinet. The DBC concentration of these solutions was determined by potentiometric titration of chloride ion. Such solutions were stable for a minimum of several months.

1,5-Di-(2,4-dichlorophenyl)-3-acetylformazan.—A mixture of 210 ml. of acetone and 90 ml. of water was placed in the same apparatus used for kinetic runs and was thermostated at 35°. To this mixture was added 3.00 g. of DBC of kinetic purity. As the diazonium salt dissolved, the solution assumed a red color and after about 15 minutes a red solid began to precipitate. The reaction was continued for a total of 60 minutes during which 15 ml. of nitrogen was evolved. The formazan (1.03 g.) was recrystallized from pyridine as red needles of m.p. 179–180°.

Anal. Calcd. for $C_{15}H_{10}N_4Cl_2O$: C, 44.5; H, 2.49; N, 13.9; mol. wt., 404. Found: C, 45.1; H, 2.50; N, 14.0; mol. wt., 395.

The mother liquors yielded small amounts of two colorless substances differentiated by their solubilities in ligroin. The ligroin-soluble material consisted of colorless, chunky crystals, m.p. 84–85°.

Anal. Calcd. for $C_{12}H_{10}N_2Cl_2O$: C, 53.6; H, 3.75; N, 10.4; Cl, 26.4; mol. wt., 269. Found: C, 53.6; H, 3.82; N, 10.6; Cl, 25.8; mol. wt., 273.

The fine, colorless needles, m.p. 168–172°, which were less soluble in ligroin were not further investigated.

Acetone–Cupric Chloride Reaction.—A 0.055 *M* solution of cupric chloride in 64.8 wt. % acetone was prepared from 1270 ml. of C.P. acetone, 364 ml. of water and 184 ml. of 0.533 *M* aqueous cupric chloride. After remaining at ambient temperatures for 24 hours, solid sodium chloride was added to separate phases. The aqueous layer was extracted with peroxide-free ether and the combined organic liquids were dried and fractionally distilled to yield 1.12 g. (25%) of chloroacetone, b.p. 119–121°, semicarbazone m.p. 147–148°, reported[37] 147–148°.

Anal. Calcd. for $C_4H_8N_3ClO$: Cl, 23.7. Found: Cl, 23.4.

Another solution of identical concentrations was used for determining total copper. After 7 hours at 35°, the volatile products were removed under reduced pressure and the residue was dissolved in dilute hydrochloric acid. Aliquots of this solution were titrated for Cu(II) iodimetrically and for Cu(I) with permanganate. Of 5.36 millimoles of Cu(II) introduced, 4.99 millimoles were detected as Cu(II) and 0.39 millimole as Cu(I).

Kinetics of the Acetone–Cupric Chloride Reaction.[8a]—The apparatus consisted of a three-necked flask fitted with an automatic pipet and connected to a reservoir of purified nitrogen. Desired mixtures of water, C.P. acetone, and standard solutions of cupric chloride and sodium chloride were thermostated at 35.00 ± 0.01° and 10-ml. aliquots were delivered into excess ferric reagent and titrated with standard ceric ammonium sulfate.[38]

Products of the Sandmeyer Reaction in Aqueous Acetone.—DBC (24.5 g.) was decomposed in 2469 ml. of 64.8 wt. % aqueous acetone 0.056 *M* in cupric chloride. This corresponds to kinetic run 4, Fig. 2. After standing overnight the reaction mixture was saturated with solid sodium chloride. The organic layer which separated was exhaustively extracted with ether and the combined extracts were dried with sodium sulfate and then with Drierite. Ether and acetone were removed by distillation through a packed column and the residue was separated into three major fractions by column distillation.

Fraction I, chloroacetone, was collected from 120–122°, weighed 6.90 g. (64%) and gave a semicarbazone of m.p. 144.5–146° and a 2,4-DNPH of m.p. 126–127° (reported 147–148°[37] and 125–125.5°[39]). Admixture with authentic samples of both of these derivatives failed to depress the melting points.

Fraction II, 1,3-dichlorobenzene, distilled from 170–172°, amounted to 8.10 g. (47%); II yielded a sulfonyl chloride of m.p. 52–53° and a sulfonamide of m.p. 179–180° (reported[40] 52–53° and 179–180°).

Fraction III, 1,2,4-trichlorobenzene, was collected at 115–125° at 65–68 mm. and weighed 5.50 g. (26%); III gave a mononitro derivative of m.p. 55–56° and a dinitro derivative of m.p. 102.5–103.5° (reported[40] 56° and 102.5–103.5°).

A second decomposition was carried out in the following manner: 1820 ml. of 64.8 wt. % aqueous acetone 0.056 *M* in cupric chloride was placed in a flask fitted with Dry Ice condenser and purified nitrogen was bubbled through the mixture for 75 minutes. Addition of 18.0 g. of solid DBC resulted in evolution of the theoretical volume of nitrogen in 1–1.5 minutes. The reaction mixture was worked up in the manner just described and yielded 4.13 g. (52%) of chloroacetone, 5.33 g. (42%) of 1,3-dichlorobenzene and 4.08 g. (26%) of 1,2,4-trichlorobenzene.

Kinetics of the Sandmeyer Reaction.—The apparatus consisted of a three-necked flask fitted with a gas-tight stirrer and a condenser which was connected to a nitrometer filled with mercury. The flask was immersed in a thermostated bath which maintained a temperature 35 ± 0.1°. The required amounts of C.P. acetone and distilled water were placed in the flask and after temperature equilibrium had been reached 1.000 g. of purified DBC was added. Solution of the diazonium salt was followed by addition of standard aqueous cupric chloride prepared from reagent grade $CuCl_2 \cdot 2H_2O$. The total volume of solution for each run was 100 ml. The volume contraction, which occurs when acetone and water are mixed, was taken into account in calculating concentrations. Ordinary distilled water and C.P. acetone were used after it had been ascertained that their rigorous purification did not alter the kinetics.

Kinetics of the Meerwein Reaction.—The unsaturated compounds and benzene were used in the form of standard, freshly prepared, approximately 2.5 *M* solutions in acetone. Acrylonitrile (Matheson–Coleman and Bell), styrene (Eastman Kodak Co.), α-methylstyrene (Hercules Powder Co.), and methyl methacrylate (Rohm and Haas Co.) were purified by treatment with dilute sodium hydroxide solution and then by several distillations under reduced pressure. Samples were stored under nitrogen at Dry Ice temperature. Benzene (J. T. Baker Analyzed Reagent) was fractionally distilled twice at atmospheric pressure.

Nitrogen (Linde High Purity Grade) was freed of the last traces of oxygen by passage over copper at 400°.[41]

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[34] All melting and boiling points are uncorrected. The microanalyses were carried out by the Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.

[35] The dry diazonium salt should be handled with caution and must not be dried on or removed from a porous surface.

(36) K. J. P. Orton, *J. Chem. Soc.*, **83**, 812 (1903).

(37) W. A. Waters, *ibid.*, 2007 (1937).

(38) L. F. Hatch and R. R. Estes, *Ind. Eng. Chem., Anal. Ed.*, **18**, 136 (1946).

(39) C. Bülow and F. Seidel, *Ann.*, **439**, 48 (1924).

(40) E. H. Huntress and F. H. Carten, THIS JOURNAL, **62**, 511 (1940).

(41) R. Ward, R. K. Osterheld and R. D. Rosenstein in "Inorganic Syntheses," Vol. 3, McGraw-Hill Book Co., Inc., New York, N. Y., 1950, p. 14.

The decompositions were carried out in a specially constructed, 200-ml. round-bottom flask in which the reactants could be kept separated. The flask was connected to a jacketed gas buret, the mercury in which was covered with a layer of aqueous acetone of the same composition as the reaction mixture.[42] Mixing the components to start the reaction and agitation during the course of the reaction was achieved by a shaker (200 oscillations per minute) which was totally immersed in a constant temperature bath maintained at $35.00 \pm 0.01°$. Water from this bath was circulated through the jacket of the gas buret. The reaction vessel was charged by placing the required volumes of water, acetone and standard unsaturate, cupric chloride and DBC solutions into three separate compartments.

For runs in the absence of air the separated components were repeatedly degassed at $-196°$ and 10^{-6} mm. pressure by standard procedures. The vessel was finally filled with purified nitrogen, allowed to come to temperature equilibrium in the constant temperature bath, and the reaction was started. Volume readings at constant pressure were taken at regular time intervals. For runs in the presence of air the degassing operation was omitted and the charged reaction flask was immediately placed in the water-bath.

The pre-formed cuprous chloride was determined in separate experiments by treating the unmixed reactants with excess ferric ammonium sulfate solution immediately after the degassing operation and titrating with standard ceric ammonium sulfate solution.

Acknowledgment.—The authors wish to thank Mr. Martin Gottesman for his assistance with some of the experimental work.

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[42] No vapor pressure correction is necessary for gases measured under these conditions. See R. Livingston in "The Technique of Organic Chemistry," Vol. 8, "Investigations of Rates and Mechanisms of Reactions," Interscience Publishers, Inc., New York, N. Y., 1953, p. 53.

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY]

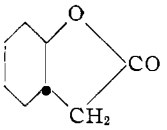
The Friedel–Crafts Condensation of *trans*-2-Hydroxycyclohexaneacetic Acid Lactone with Aromatic Hydrocarbons. II. *p*-Xylene, Tetralin and α-Methylnaphthalene

BY DONALD D. PHILLIPS AND D. N. CHATTERJEE[1]

RECEIVED DECEMBER 16, 1957

The lactone I in the title afforded a complex mixture of isomeric acids when treated with *p*-xylene in the presence of aluminum chloride. The products included the three position isomers of *p*-xylylcyclohexaneacetic acid (II, III and IV, R = *p*-xylyl) as well as the *cis* isomer of IV. Tetralin also yielded II, III and IV (R = β-$C_{10}H_{11}$) although no *cis* isomers were obtained. The reaction between lactone I and 1-methylnaphthalene afforded cyclohexaneacetic acids but of undetermined orientation. Two of these acids have been converted to ketones (XIII and XIV), one of which (XIV) suggests that, at least to some extent, abnormal orientation occurred. The use of some of these arylcyclohexaneacetic acids in the synthesis of several polynuclear aromatic hydrocarbons is discussed.

In a recent communication[2] we reported the abnormal Friedel–Crafts condensation of lactone I with benzene and naphthalene, a reaction that afforded minor amounts of the expected *o*-arylcyclohexaneacetic acids (II, R = C_6H_5 and β-$C_{10}H_7$) and major amounts of the *meta* (III, R = C_6H_5 and β-$C_{10}H_7$) and *para* (IV, R = C_6H_5 and β-$C_{10}H_7$) isomers. The formation of these products was rationalized[2] on the basis of equilibration among three of the possible carbonium ion intermediates (*cf.* V) before attack on the aromatic hydrocarbon took place.



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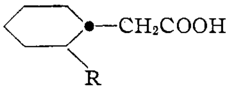

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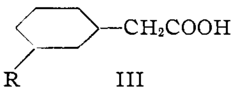

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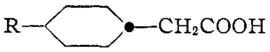

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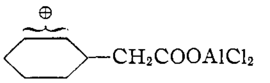
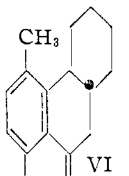


V

To gain further insight into the scope and mechanism of this reaction we have examined the behavior of three more aromatic hydrocarbons and, although the results were similar to those with benzene and naphthalene, some important qualitative differences were observed. For example, the reaction between the lactone I and *p*-xylene afforded a complex mixture of acids from which it was possible to separate about 10% of pure crystalline *trans-p*-acid IV (R = *p*-xylyl) by direct crystallization. The *o*-isomer (*ca.* 10%) was removed from the mother liquor as the ketone VI by hydrogen fluoride cyclization. Its constitution was established by reduction, dehydration and dehydrogenation to 1,4-dimethylphenanthrene (VII).



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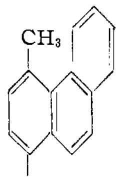
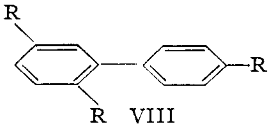


VII

When the residual acidic oil from the cyclization experiment was distilled and allowed to stand in hexane there was deposited a second crystalline acid (*ca.* 9% yield), m.p. 124–125°, which afforded the same hydrocarbon (VIII, R = CH_3) on decarboxylative dehydrogenation as did the *trans-p*-acid (IV, R = *p*-xylyl). This observation sug-



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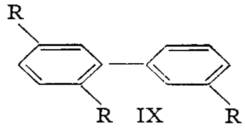

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[2] D. D. Phillips and D. N. Chatterjee, THIS JOURNAL, **80**, 1360 (1958).