[Contribution from the Chemistry Department of the University of Kansas]

# Mechanism of the Acid-catalyzed Hydrolysis of Reissert Compounds

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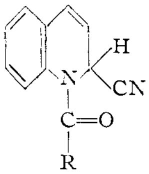
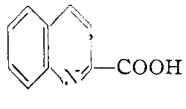
In an acid-catalyzed hydrolysis reaction permitted to go only to 25% of completion, 1-benzoyl-1,2-dihydroquinaldonitrile (V) gave benzaldehyde, quinaldic acid (II), quinaldamide (III) and benzoin quinaldate (IV). No quinaldonitrile (VIII) was isolated. Under identical reaction conditions the hydrolysis of a molar quantity of quinaldonitrile (VIII) equal to that of V consumed proceeded only partially to completion. These facts exclude quinaldonitrile (VIII) from consideration as an intermediate in the acid-catalyzed hydrolysis of V. 1-Benzoyl-1,2-dihydroquinaldamide (XII) was prepared from V by reaction with hydrogen peroxide in the presence of sodium bicarbonate and could be reconverted to V by dehydration with phosphorus pentoxide in the presence of triethylamine. The amide gave no benzaldehyde on treatment with hydrochloric acid and is therefore not an intermediate in the hydrolysis of V. Treatment of 1-benzoyl-1,2-dihydroquinaldonitrile (V) with anhydrous hydrogen chloride in aprotic solvents gave colored precipitates which, in turn, afforded benzaldehyde and quinaldamide (III) on treatment with water, even under alkaline conditions. A new mechanism is proposed for the acid-catalyzed hydrolysis of Reissert compounds.

Aldehydes are formed in excellent yields by the acid-catalyzed hydrolysis of Reissert compounds. The Reissert compounds, in turn, are prepared by reaction of acid chlorides with quinoline, isoquinoline or phenanthridine in the presence of potassium cyanide or hydrogen cyanide in a variety of solvents.[1-9]

A Reissert compound of the quinoline series, a 1-acyl-1,2-dihydroquinaldonitrile (I), gives quinaldic acid (II) and quinaldamide (III) together with the aldehyde in the hydrolysis reaction. Benzoin quinaldate (IV) has also been isolated from the reaction mixture obtained upon hydrolysis of 1-benzoyl-1,2-dihydroquinaldonitrile (V). Analogous by-products are formed from the Reissert compounds derived from the other heterocyclic bases.



I



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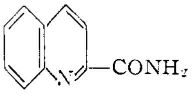
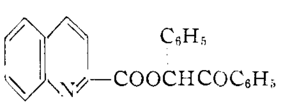
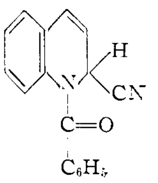


III

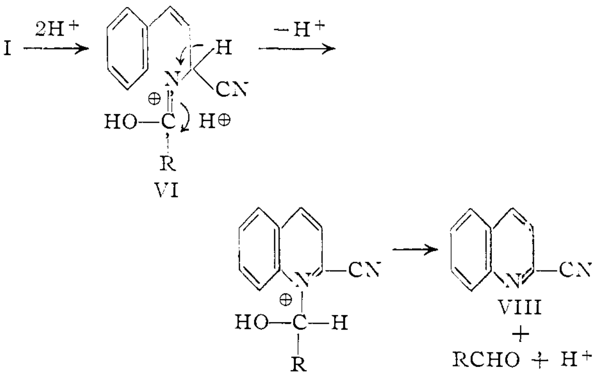


IV



V

McEwen and Hazlett[10] recently proposed a mechanism for the formation of aldehydes from Reissert compounds and provided some evidence in support of that mechanism. They suggested that the first step involves the formation of the conjugate acid VI of the Reissert compound. Then, in a concerted process, a proton is lost from the 2-position of the ring and a second proton is added to the original carbonyl carbon atom to yield VII. Finally, VII collapses to quinaldonitrile (VIII) and the aldehyde. It was assumed that VIII is hydrolyzed to II and III under the conditions of the reaction.

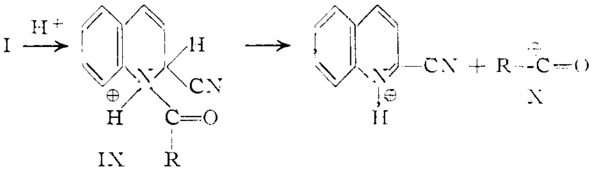


VI

VII

VIII

Colonna[11] has disagreed with this interpretation of the reaction mechanism. He considers the cleavage reaction to be similar in mechanism to some cleavage reactions of O-acyl derivatives of heterocyclic N-oxides. According to his mechanism, the first step involves the formation of the conjugate acid IX of the Reissert compound. A proton is then lost from the 2-position of the ring and the transient acyl anion X is formed. Finally, the acyl anion X combines with a proton from the solution to form the aldehyde.



IX

X

Colonna likened the formation of the acyl anion X to the formation of the carboxylate anion $RCOO^-$, which results from the cleavage of the N-oxide group of heterocyclic N-oxides during reactions such as formation of quinaldonitrile (VIII) from quinoline-1-oxide by reaction with benzoyl chloride and alkali metal cyanide. Apart from

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[1] A. Reissert, *Ber.*, **38**, 1603 (1905); **38**, 3415 (1905).

[2] S. Sugasawa and T. Tsuda, *J. Pharm. Soc. Japan*, **56**, 557 (1936).

[3] H. Rupe, R. Paltzer and K. Engel, *Helv. Chim. Acta*, **20**, 209 (1937).

[4] H. Rupe and W. Frey, *ibid.*, **22**, 673 (1939).

[5] A. Gassmann and H. Rupe, *ibid.*, **22**, 1241 (1939).

[6] R. B. Woodward, This Journal, **62**, 1626 (1940).

[7] J. M. Grosheintz and H. O. L. Fischer, *ibid.*, **63**, 2021 (1941).

[8] G. L. Buchanan, J. W. Cook and J. D. London, *J. Chem. Soc.*, 325 (1944).

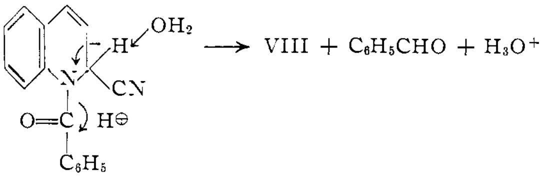
[9] G. Wittig, M. A. Jesaitis and M. Glos, *Ann.*, **577**, 1 (1952).

[10] W. E. McEwen and R. N. Hazlett, This Journal, **71**, 1949 (1949).

[11] M. Colonna, *Gazz. chim. ital.*, **82**, 503 (1952).

other difficulties which this mechanism presents in common with that proposed by McEwen and Hazlett,[10] the suggestion that there is an analogy between formation of an acyl anion X and a carboxylate anion $RCOO^-$ is not convincing when the difference in stabilities, hence ease of formation, of the two anions is considered. It would not seem unreasonable to propose elimination of a carboxylate anion in a base-catalyzed reaction of an O-acyl derivative of a heterocyclic N-oxide, but it would seem unreasonable to propose elimination of a considerably less stable acyl anion in an acid-catalyzed reaction of a Reissert compound.

Swain and Sheppard[12] have prepared benzaldehyde-$\alpha$-*t* (in addition to unlabeled benzaldehyde) by carrying out the hydrolysis of 1-benzoyl-1,2-dihydroquinaldonitrile (V) in mineral acid solution containing tritium oxide. On the basis of a small isotope effect observed in the reaction, Swain and Sheppard concluded that the formation of the new carbon–tritium bond (or new carbon–hydrogen bond) is involved in the rate-determining step of the reaction. Although this observation was consistent with the mechanism of acid-catalyzed hydrolysis proposed by McEwen and Hazlett,[10] Swain and Sheppard nevertheless proposed a modification of the mechanism, symbolized by the activated complex XI, in order to circumvent the energetically unfavorable situation of having the positively charged conjugate acid VI of the Reissert compound react with a proton (hydronium ion) in the rate-determining step of the reaction.

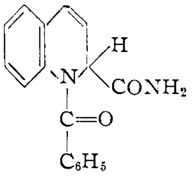


XI

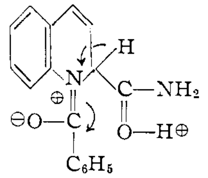
All three mechanisms which have been proposed[10–12] are based on the assumption that quinaldonitrile (VIII) is formed as an intermediate and is subsequently converted to quinaldic acid (II) and quinaldamide (III) on hydrolysis. However, this assumption has never actually been proved. The qualitative observation that some 1-benzoyl-1,2-dihydroquinaldonitrile (V) could be recovered after about a half hour period of reaction with hydrochloric acid, whereas an equimolar quantity of quinaldonitrile (VIII) was completely hydrolyzed under the same conditions was without significance since the reaction with the Reissert compound represents a heterogeneous reaction, while quinaldonitrile (VIII) is soluble in the acidic hydrolysis medium.

Therefore somewhat more precise studies on the relative rates of hydrolysis of 1-benzoyl-1,2-dihydroquinaldonitrile (V) and quinaldonitrile (VIII) were undertaken. After a limited solvolysis reaction. of V in ethanolic hydrogen chloride solution, the only products isolated were benzaldehyde, quinaldic acid (II), quinaldamide (III) and ethyl quinaldate. Similar reactions in a concentrated aqueous hydrochloric acid mixture yielded only benzaldehyde, quinaldic acid (II), quinaldamide (III) and benzoin quinaldate (IV), together with recovered V. In no case was quinaldonitrile (VIII) isolated. When a molar quantity of quinaldonitrile (VIII) equal to that of V consumed, either by itself or in a mixture with V, was treated with hydrochloric acid under the same conditions, however, 11–39% of it was recovered unchanged; the remainder was converted to quinaldic acid (II) and quinaldamide (III). These facts exclude quinaldonitrile (VIII) from further consideration as an intermediate in the hydrolysis of V.

The next mechanism which was taken under consideration involved an initial hydrolysis of V to 1-benzoyl-1,2-dihydroquinaldamide (XII). It was thought that the conjugate acid of this amide might give benzaldehyde and quinaldamide *via* the quasi six-membered ring transition, XIII, or some species closely related to it.



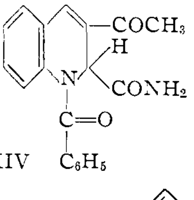
XII



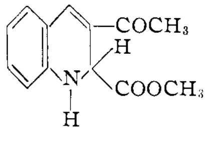
XIII

This possibility was rejected when it was shown that authentic 1-benzoyl-1,2-dihydroquinaldamide (XII) and also 1-benzoyl-3-acetyl-1,2-dihydroquinaldamide (XIV) failed to give benzaldehyde on treatment with concentrated hydrochloric acid. The amide XII was prepared by the action of hydrogen peroxide on V in the presence of sodium bicarbonate. The proof of structure of XII was based on elemental analyses, the infrared absorption spectrum, the reconversion of XII to V by dehydration with phosphorus pentoxide in the presence of triethylamine, the catalytic hydrogenation of XII to 1-benzoyl-1,2,3,4-tetrahydroquinaldamide and the independent synthesis of the latter compound.

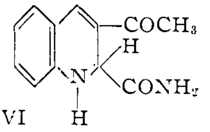
The synthesis of XIV was achieved by ammonolysis of methyl 3-acetyl-1,2-dihydroquinaldate (XV),[13] followed by benzoylation of the amide XVI with benzoyl chloride in hot benzene. Benzoylation of XV with benzoyl chloride in pyridine solution afforded methyl 1-benzoyl-3-acetyl-1,2-dihydroquinaldate as reported by Woodward and Kornfeld,[13] but attempted ammonolysis



XIV



XV



XVI

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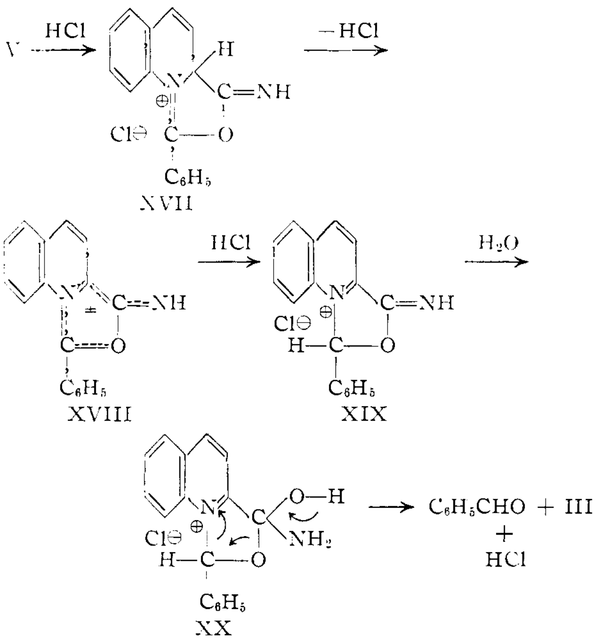
[12] C. G. Swain and W. A. Sheppard, Abstracts of Papers Presented at Cincinnati, Ohio, March 29 to April 7, 1955, p. 40N.

[13] R. B. Woodward and E. C. Kornfeld, THIS JOURNAL, **70**, 2508 (1948).

of this compound resulted in the cleavage of the benzoyl group.

The new data clearly require a modification of the previously proposed[10] mechanism for the acid-catalyzed formation of aldehydes from Reissert compounds. We now propose the following mechanism. (1) Reaction of V with hydrochloric acid first gives the cyclic intermediate XVII. (2) Rearrangement of XVII affords XIX possibly *via* the meso-ionic intermediate XVIII.[14] It is noteworthy that the reaction mixture always turns a bright yellow after a short period of time. (3) Addition of water to XIX affords XX. (4) Finally, collapse of XX gives benzaldehyde plus quinaldamide (III). Since quinaldamide (III) has actually been isolated from the hydrolysis mixture of V there is nothing speculative in regarding it as a primary product of reaction.



XVII

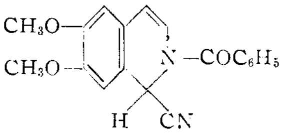
XVIII

XIX

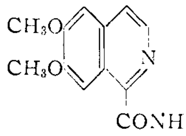
XX

Further work was carried out in an attempt to isolate the proposed intermediates or to obtain some evidence for their existence. It was thought that a modification of the reaction conditions might permit isolation of the meso-ionic compound, XVIII, or one of its conjugate acids, XVII or XIX. Attention was turned primarily to the use of hydrogen chloride in an inert, anhydrous solvent, instead of the use of hydrochloric acid in aqueous or alcoholic solution.

A search of the literature revealed that anhydrous solvents had been used previously as media for the action of anhydrous hydrogen chloride on Reissert compounds. Kaufmann and Dandliker,[15] in an attempt to prepare quinaldonitrile (VIII) from V, observed that action of anhydrous hydrogen chloride on V in anhydrous benzene, chloroform or ether solution yielded an unstable yellow precipitate which had an odor of benzaldehyde. Similarly, McEwen, Kindall, Hazlett and Glazier[16] found that a solution of V in anhydrous ether gave, upon treatment with anhydrous hydrogen chloride, a yellow solid which yielded quinaldamide (III) in 45% yield upon hydrolysis. Haworth and Perkin[17] made an observation which is even more significant. These workers reported that passage of anhydrous hydrogen chloride into a cold chloroform solution of 2-benzoyl-6,7-dimethoxy-1,2-dihydroisoquinaldonitrile (XXI) yielded an orange solid which, after being washed with ether, gave benzaldehyde and 6,7-dimethoxyisoquinaldamide (XXII) upon steam distillation. As any initially formed benzaldehyde would have been removed by the ether wash, its origin, by necessity, was from the action of water upon the orange solid.



XXI



XXII

Similar results have now been observed in reactions of anhydrous hydrogen chloride with V in various inert solvents. In anhydrous chloroform as a solvent, an odorless, yellow precipitate formed. The solid was very reactive toward moist air; it darkened rapidly and the odor of benzaldehyde developed. Even more spectacularly, breathing upon an odorless sample of the yellow solid caused the odor of benzaldehyde to develop. Hydrolysis of the solid yielded, in addition to benzaldehyde, quinaldamide (III), quinaldic acid (II) and a very small amount of a compound $C_{20}H_{14}N_2O$. Analytical data for the yellow solid indicated that it was a mixture of two or more products.

In anhydrous benzene, action of hydrogen chloride on V gave an unstable red-violet precipitate which smelled of benzaldehyde. Hydrolysis of the solid under slightly acidic conditions gave benzaldehyde and quinaldamide (III). Similarly, alkaline hydrolysis of some of the solid, previously washed free of benzaldehyde with benzene, gave essentially the same yield of benzaldehyde, in addition to quinaldamide (III). That the red-violet solid gave benzaldehyde under alkaline conditions is particularly significant since it indicates that only water is necessary for completion of the reaction once the necessary intermediate has been formed. Again, analytical data indicated that the colored solid was a mixture of products.

Reissert[1] reported that hydrolysis of 1-benzoyl-1,2-dihydroquinaldonitrile (V) in concentrated hydrochloric acid containing an excess of benzaldehyde gave a fair yield of benzoin quinaldate (IV). Other Reissert compounds were found to behave similarly.[10] As it was thought that this might be a convenient synthetic route to such esters, and as a continuation of the study of the action of anhydrous hydrogen chloride on Reissert compounds in anhydrous solvents, benzaldehyde was next used as the solvent for the reaction. There was

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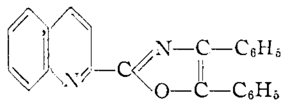
(14) Although it is not symbolized in structure XVIII the π-electrons of the 5-membered ring would also enter into resonance interaction with the π-electrons of the aromatic rings.

(15) A. Kaufmann and P. Dandliker, *Ber.*, **46**, 2924 (1914).

(16) W. E. McEwen, J. V. Kindall, R. N. Hazlett and R. H. Glazier, This Journal, **73**, 4591 (1951).

(17) R. D. Haworth and W. H. Perkin, *J. Chem. Soc.*, **127**, 1434 (1925).

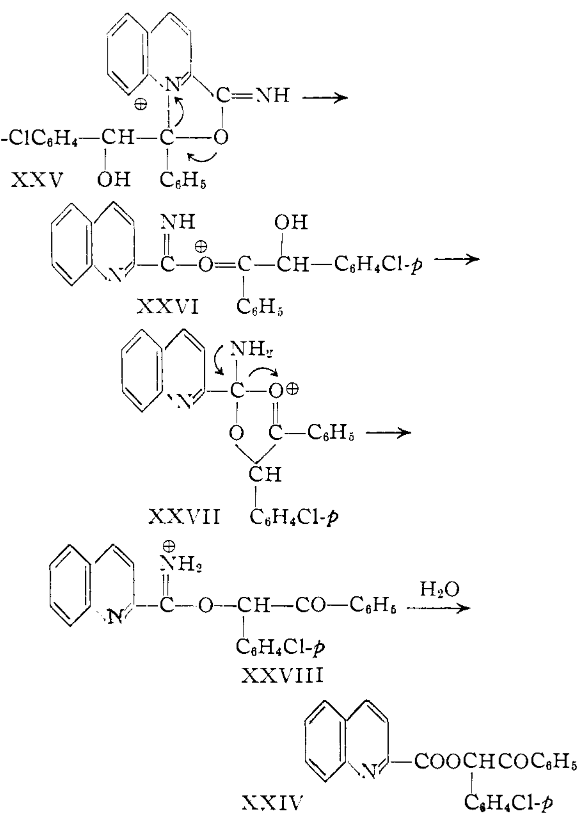
obtained a mixture of benzoin quinaldate (IV) and 2-(2-quinolyl)-4,5-diphenyloxazole (XXIII). The properties of XXIII were found to be very similar to those of the isoquinoline analog.[16] Upon prolonged acid-catalyzed hydrolysis, XXIII gave benzoin and quinaldic acid (II).



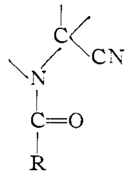
XXIII

It is necessary, of course, that the new mechanism for the acid-catalyzed hydrolysis of Reissert compounds be capable of explaining the data uncovered earlier by McEwen and Hazlett.[10] In brief, these workers found that reaction of 1-benzoyl-1,2-dihydroquinaldonitrile (V) with hydrochloric acid in the presence of an excess of *p*-chlorobenzaldehyde gave a significant yield of *p*′-chlorobenzoin quinaldate (XXIV). Also, the isomeric ester, *p*-chlorobenzoin quinaldate, was obtained by reaction of 1-(*p*-chlorobenzoyl)-1,2-dihydroquinaldonitrile with hydrochloric acid in the presence of an excess of benzaldehyde. Furthermore, evidence was presented to show that the two esters arose from some intermediate condensation product by way of an intramolecular rearrangement.

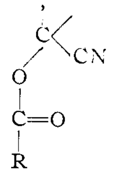
The new mechanism as applied to the case of V and *p*-chlorobenzaldehyde can accommodate these facts as follows. The conjugate acid of *p*-chlorobenzaldehyde can add to XVIII (or XVII) to produce XXV. In turn, XXV can rearrange intramolecularly to XXVIII *via* XXVI and XXVII, respectively. Hydrolysis of XXVIII finally gives *p*′-chlorobenzoin quinaldate (XXIV). An analogous adaptation, together with the other data presented by McEwen, Kindall, Hazlett and Glazier,[16] readily accommodates the formation of 2-(1-isoquinolyl)-4,5-diphenyl-oxazole from 2-benzoyl-1,2-dihydroisoquinaldonitrile and benzaldehyde and of XXIII from V and benzaldehyde in the presence of hydrochloric acid.



The infrared spectra of a number of Reissert compounds have been measured, both in solution (chloroform, carbon tetrachloride, benzene, pyridine, triethylamine and acetone) and in the form of nujol or perfluorocarbon mulls, and the most striking feature about these spectra is the complete lack of absorption in the range 2200–2400 cm.$^{-1}$, the frequency range in which absorption due to a cyano group is observed. It has been found that the intensity of absorption due to the presence of a cyano group is dependent on the structure of the rest of the molecule.[18] In a simple nitrile, the band is usually intense, but its intensity decreases as the molecular weight of the compound increases. Furthermore, the intensity decreases when the cyano group is conjugated with other unsaturated groups or when oxygen-containing functional groups are also present in the molecule. In ketone cyanohydrins, for example, the nitrile band is very weak, but when the cyanohydrin is acylated, the nitrile absorption peak disappears. Since Reissert compounds are nitrogen analogs of acyl derivatives of ketone cyanohydrins, as shown in the partial structures XXIX and XXX, it might have been anticipated that nitrile absorption peaks also would be absent in the infrared spectra of Reissert compounds.

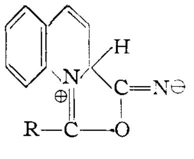


XXIX



XXX

There is some possibility that Reissert compounds may receive a relatively large contribution from resonance structures such as XXXI. Examination of a Fisher–Hirschfelder model of a Reissert compound reveals that the carbonyl oxygen atom may practically touch the carbon atom of the cyano group. The existence of such an interaction might be the basis for the lack of a cyano group absorption peak in the infrared spectra of Reissert compounds.



XXXI

**Acknowledgment.**—The authors wish to thank the Eastman Kodak Company for financial aid in the form of a fellowship and also the University of Kansas for a research grant from the General Research Fund.

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(18) R. E. Kitson and H. E. Griffith, *Anal. Chem.*, **24**, 334 (1952).

## Experimental[19]

**1-Benzoyl-1,2-dihydroquinaldonitrile (V).**—This compound was prepared by the method of Rupe, Paltzer and Engel,[3] colorless crystals from ethanol, m.p. 153–154.5°; reported m.p. 153–154°[3] and 154–155°.[1]

**Acid-catalyzed Solvolysis of 1-Benzoyl-1,2-dihydroquinaldonitrile (V). A. In Ethanol.**—A suspension of finely divided 1-benzoyl-1,2-dihydroquinaldonitrile (V) was prepared by dissolving 10.00 g. of V in 500 cc. of hot 95% ethanol and allowing the solution to cool to room temperature with vigorous stirring. To this suspension was added 1000 cc. of a saturated ethanolic solution of hydrogen chloride (*ca.* 10 *N*); the slightly exothermic reaction was allowed to proceed for 3.5 minutes with continued stirring. The reaction mixture was then poured into a large flask externally cooled by an ice-bath and containing 850 g. of crushed sodium bicarbonate and 1 kg. of crushed ice. When the evolution of carbon dioxide had ceased, as much of the solvent as possible was distilled *in vacuo*, the temperature being kept below 40°. Treatment of the distillate, consisting of a solution of benzaldehyde in ethanol, with 7.5 g. of 2,4-dinitrophenylhydrazine dissolved in 100 cc. of 60% sulfuric acid gave 10.26 g. (93.4%) of benzaldehyde 2,4-dinitrophenylhydrazone.

The distillation residue was made acidic by addition of concentrated hydrochloric acid and extracted with ether. Distillation of the ether left a trace of red-brown oil. The aqueous layer was neutralized with solid sodium bicarbonate, made distinctly alkaline by addition of 25 cc. of 10% sodium hydroxide solution and extracted with ether. After distillation of the ether, the liquid residue was steam distilled. No quinaldonitrile (VIII) came over in the steam distillate. Crystallization from ether solution of the residual oil (nonvolatile in steam) in a Dry Ice–acetone bath gave 1.18 g. (15.2%) of ethyl quinaldate, m.p. 30–33°; reported for ethyl quinaldate, m.p. 36°.[20] In another identical run, there was also obtained a 15% yield of quinaldamide (III) from this oil. From the aqueous solution there was obtained 2.58 g. (38%) of quinaldic acid *via* the copper salt.[1]

**B. In Water.**—A suspension of 10.00 g. (0.0385 mole) of V in 45 cc. of concentrated hydrochloric acid was stirred vigorously for 15 minutes. The heterogeneous reaction mixture, bright yellow in color, was poured into a large flask containing 35 g. of crushed sodium bicarbonate and 150 g. of crushed ice. After the evolution of carbon dioxide had subsided, the mixture was filtered and the solid residue washed with 20 cc. of 10% hydrochloric acid and 50 cc. of cold ether. There remained 7.46 g. (0.0287 mole) of recovered Reissert compound, V, m.p. 153–154.5° after one recrystallization from ethanol.

The aqueous filtrate, combined with the wash solutions, was extracted with ether. From the ether solution there was obtained a 76% yield of benzaldehyde as the 2,4-dinitrophenylhydrazone derivative (yield based on 0.0098 mole of V, the amount of V not recovered).

Upon making the aqueous solution basic and working up the reaction mixture as described above, there was obtained quinaldamide (III), benzoin quinaldate (IV) and quinaldic acid (II). Again, no quinaldonitrile (VIII) was obtained.

When 1.00 g. (0.0065 mole) of quinaldonitrile (VIII) was treated with acid under the same conditions, and the reacaction mixture worked up in the same way, 0.39 g. (39%) of quinaldonitrile (VIII) was recovered from the steam distillate. There was also obtained a 41% crude yield of quinaldamide (III) and a 22% crude yield of quinaldic acid (II). In another run carried out under as nearly as possible the same conditions, 14% of quinaldonitrile (VIII) was recovered, and there was isolated a 44% crude yield of quinaldamide (III) and a 49% crude yield of quinaldic acid (II).

When 1.00 g. of quinaldonitrile (VIII) was mixed with 2.0 g. of V and treated under the same conditions, 0.11 g. of quinaldonitrile (VIII) was recovered from the steam distillate.

**Quinaldonitrile (VIII).**—This compound was prepared from quinoline-1-oxide, benzoyl chloride and potassium cyanide by the method of Henze.[21] The material was purified by steam distillation followed by recrystallization from ligroin; m.p. 93°, reported m.p. 93°.[21]

**1-Benzoyl-1,2-dihydroquinaldamide (XII).**—To a solution of 5.0 g. of 1-benzoyl-1,2-dihydroquinaldonitrile (V) in 500 cc. of acetone was added 2 g. of powdered sodium bicarbonate. The mixture was placed in a bath of cold water and stirred for 10 minutes; 75 cc. of 30% hydrogen peroxide was added dropwise with continued stirring over a period of about an hour. Then 3 cc. of 5% sodium bicarbonate was added and the stirring continued for another hour. The solution was then concentrated to 75 cc. by distillation under reduced pressure; 200 cc. of water was added to the resulting solution and the mixture was cooled in an ice-bath. A gummy solid which formed was filtered, washed with water, dried and recrystallized from absolute ethanol to yield 2.53 g. of 1-benzoyl-1,2-dihydroquinaldamide (XII), m.p. 169.5–171°. An additional 0.92 g. of product was recovered from the filtrate to give a total yield of 65%. Recrystallization from 95% ethanol four times gave heavy white crystalline clusters, m.p. 172.8–173.2°.

*Anal.* Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.07; N, 10.07. Found: C, 73.10; H, 4.80; N, 9.78.

**Dehydration of 1-Benzoyl-1,2-dihydroquinaldamide (XII).**—To a solution of 0.35 g. of triethylamine in 25 cc. of benzene, both dried over phosphorus pentoxide, was added 0.50 g. of 1-benzoyl-1,2-dihydroquinaldamide (XII). To this solution was added 0.2–0.3 g. of phosphorus pentoxide and the mixture was heated under reflux for 30 minutes; then approximately the same quantity of phosphorus pentoxide was added as at first and heating was continued for an additional 30 minutes. The mixture was allowed to stand at room temperature overnight, and then the benzene was decanted from an insoluble sludge. The benzene was removed by distillation and the residue heated on the steam-bath under reduced pressure. Recrystallization of the residue from 5 cc. of ethanol produced 0.14 g. (30%) of 1-benzoyl-1,2-dihydroquinaldonitrile (V), pale yellow crystals, m.p. 149–152°. Recrystallization from ethanol gave colorless needles, m.p. 153–154.5°, also in admixture with authentic V.

**Hydrogenation of 1-Benzoyl-1,2-dihydroquinaldamide (XII).**—A suspension of 1.00 g. of 1-benzoyl-1,2-dihydroquinaldamide (XII) and 0.1 g. of platinum oxide catalyst in 50 cc. of absolute ethanol was allowed to absorb one molar equivalent of hydrogen at atmospheric pressure and room temperature. The absorption was extremely rapid; the hydrogenation was complete in 20 minutes. The mixture was heated to boiling and the platinum removed by filtration; the green-yellow filtrate was decolorized with charcoal, filtered and concentrated to 15 cc. Chilling the filtrate overnight gave 0.34 g. of colorless solid, m.p. 188–189°. A second crop of crystals, m.p. 190–192°, was obtained after concentration of the mother liquor. The crude yield of 1-benzoyl-1,2,3,4-tetrahydroquinaldamide was 51%. Four crystallizations from ethanol gave material of m.p. 193.8–194.4°.

*Anal.* Calcd. for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 10.00. Found: C, 73.01; H, 5.96; N, 9.99.

**1-Benzoyl-1,2,3,4-tetrahydroquinaldamide.**—An ice-cold solution of 3.0 g. of 1,2,3,4-tetrahydroquinaldic acid hydrochloride[22] in 30 cc. of absolute methanol was saturated with dry hydrogen chloride and allowed to stand at room temperature for 48 hours. The solvent was removed under reduced pressure and the residue, a yellow solid, was mixed with 25 g. of crushed ice and 25 cc. of water. The solution was made basic by addition of 5 g. of sodium bicarbonate and 10 cc. of 10% sodium hydroxide solution. The yellow oil which formed was extracted with ether, dried over Drierite and the ether distilled. The residue, crude methyl 1,2,3,4-tetrahydroquinaldate, was dissolved in 50 cc. of absolute methanol. The solution was cooled in an ice-bath and saturated with anhydrous ammonia. After having been allowed to stand at room temperature for 48 hours, the solvent was distilled *in vacuo*. The residue was mixed with water and 1.66 g. of crude 1,2,3,4-tetrahydroquinaldamide, m.p. 105–110° after one crystallization from ethanol, was collected by filtration.

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[19] All m.p.'s are corrected. Analyses were performed by Clark Microanalytical Laboratory, Urbana, Illinois; Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.; and Weiler and Strauss, Oxford England.

[20] D. L. Hammick and W. P. Dickinson, *J. Chem. Soc.*, **132**, 214 (1929).

[21] M. Henze, *Ber.*, **69**, 1566 (1936).

[22] H. Wieland, O. Hettche and T. Hoshino, *ibid.*, **61**, 2371 (1928).

A solution of 0.67 g. of the crude 1,2,3,4-tetrahydroquinaldamide, m.p. 105–110°, in 25 cc. of anhydrous pyridine was mixed with 0.67 cc. of benzoyl chloride. After having been allowed to stand at room temperature for 10 days, the solvent was distilled *in vacuo*. The residue was neutralized with 5% sodium bicarbonate solution, and a solid was collected by filtration. Crystallization from ethanol gave 0.20 g. of 1-benzoyl-1,2,3,4-tetrahydroquinaldonitrile,[23,24] m.p. 147–148° after two additional crystallizations from ethanol.

The neutralized aqueous filtrate upon longer standing deposited 0.10 g. of 1-benzoyl-1,2,3,4-tetrahydroquinaldamide, m.p. 193.8–194.4° after several crystallizations from ethanol. The infrared spectrum of this sample in chloroform solution was identical with that of the sample obtained by hydrogenation of XII. A mixture of the two samples showed no depression of m.p.

**Treatment of 1-Benzoyl-1,2-dihydroquinaldamide (XII) with Mineral Acid.**—No benzaldehyde 2,4-dinitrophenylhydrazone was formed upon heating a mixture of 0.25 g. of XII, 0.20 g. of 2,4-dinitrophenylhydrazine and 25 cc. of concentrated hydrochloric acid on the steam-bath for 15 minutes; 1-benzoyl-1,2-dihydroquinaldonitrile (V) gives an immediate precipitate of the hydrazone under the same conditions.

**3-Acetyl-1,2-dihydroquinaldamide (XVI).**—Dry ammonia was passed through a cold solution of 2.00 g. of methyl 3-acetyl-1,2-dihydroquinaldate (XV)[13] in 100 cc. of absolute methanol for 1.5 hours. After allowing the solution to stand overnight, the methanol was removed by distillation and the bright orange residue was taken up in hot 95% ethanol. Cooling to −10° gave 0.95 g. of the amide as fine yellow-orange plates, m.p. 174–178°. A second crop of crystals was obtained from the mother liquor; the total yield of XVI was 63.5%. Four recrystallizations from ethanol gave yellow plates, m.p. 181.5–182.5°.

*Anal.* Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.60; N, 12.96. Found: C, 66.42; H, 5.98; N, 12.53.

**1-Benzoyl 3-acetyl-1,2-dihydroquinaldamide (XIV).**—To a solution of 0.60 g. of 3-acetyl-1,2-dihydroquinaldamide (XVI) in 50 cc. of dry benzene was added 0.65 cc. of benzoyl chloride and 0.80 cc. of triethylamine. The mixture was heated under reflux for an hour, an additional 25 cc. of benzene added and then heating was continued for another hour. The mixture was concentrated to dryness and the residue washed with water. The dark colored residue was taken up in 20 cc. of hot ethanol, decolorized and filtered. Concentration of the solution to about 5 cc. gave 0.14 g. (15.5%) of pale yellow-green pellets, m.p. 190–194°. After four recrystallizations the colorless crystals started to melt at 197°, resolidified and then melted at 230–231°.

*Anal.* Calcd. for $C_{19}H_{16}N_2O_3$: C, 71.23; H, 5.04; N, 8.75. Found: C, 71.42; H, 5.24; N, 8.97.

**Ammonolysis of Methyl 1-Benzoyl-3-acetyl-1,2-dihydroquinaldate.**—Dry gaseous ammonia was bubbled into a cold solution of 1.00 g. of methyl 1-benzoyl-3-acetyl-1,2-dihydroquinaldate[13] in 50 cc. of absolute methanol for about 45 minutes. After allowing to stand overnight, the solution was transferred to a sealed glass bomb and heated on a steam-bath for 20 minutes. Working up the reaction mixture gave, after crystallization of the resulting solid from methanol, bright yellow plates, m.p. 178–180°, also in admixture with an authentic sample of 3-acetyl-1,2-dihydroquinaldamide (XVI).

**Treatment of 1-Benzoyl-3-acetyl-1,2-dihydroquinaldamide (XIV) with Mineral Acid.**—No benzaldehyde 2,4-dinitrophenylhydrazone was obtained upon heating XIV in a concentrated hydrochloric acid solution of 2,4-dinitrophenylhydrazine.

**Action of Hydrogen Chloride on 1-Benzoyl-1,2-dihydroquinaldonitrile (V) in Chloroform Solution.**—About 150 cc. of C.P. chloroform, previously washed with concentrated sulfuric acid and then dried over anhydrous calcium chloride, was distilled into a flask containing 10.00 g. of 1-benzoyl-1,2-dihydroquinaldonitrile (V). After the Reissert compound had dissolved, the solution, maintained under an atmosphere of nitrogen (dried and free of oxygen), was placed in an ice-bath, and anhydrous hydrogen chloride was passed into the solution. The solution turned yellow almost immediately, and a yellow solid precipitated after about 10 minutes. Under a positive pressure of nitrogen, the mass was broken up with a stirring rod, and addition of hydrogen chloride was continued for another 15 minutes. The yellow solid was filtered in a nitrogen atmosphere, washed well with anhydrous ether and dried in a vacuum desiccator over anhydrous calcium chloride.[25]

The yellow solid was very reactive toward air and moisture. In contact with air it rapidly turned dark. The dry solid was odorless but, by breathing across a sample, the odor of benzaldehyde developed. The solid was subjected to the following hydrolysis experiments.

(a) A mixture of 4.0 g. of the yellow solid and 100 cc. of distilled water was allowed to stand with occasional shaking for 15 minutes. The reaction mixture, consisting of a dark tar and a turbid aqueous solution, was extracted with ether; the tar was practically insoluble in ether. The ether solution was washed with 6 *N* hydrochloric acid, dried over Drierite and the ether distilled. The residue was mixed with a solution of 2,4-dinitrophenylhydrazine in ethanolic sulfuric acid, and 0.58 g. of benzaldehyde 2,4-dinitrophenylhydrazone was obtained.

The tar was removed from the aqueous layer, and the solution was made basic by addition of 10% sodium hydroxide solution. The acid washes from the ether solution were also made basic and added to the aqueous mixture. A gummy solid which precipitated was collected by filtration and weighed 0.65 g. The solid was digested with 20 cc. of hot ethanol. An insoluble residue, 0.14 g., was crystallized three times from ethanol–acetone, giving colorless crystals, m.p. 222.5–223°.

*Anal.* Calcd. for $C_{20}H_{14}N_2O$: C, 80.51; H, 4.73; N, 9.39. Found: C, 80.23; H, 4.67; N, 9.30.

This material has not been identified positively, but its analysis and m.p. correspond to those of desoxyquinaldoin.[26]

Dilution of the ethanolic extract with water caused 0.50 g. of quinaldamide (III) to precipitate. After crystallization from ligroin, the m.p. was 132–133°, also in admixture with an authentic sample.

From the aqueous filtrate there was obtained 0.07 g. of quinaldic acid (II), isolated *via* the copper salt.

The tar which had been removed from the original aqueous solution was heated with 20 cc. of ethanol, leaving an additional 0.10 g. of the compound of m.p. 222.5–223°. No other pure material could be obtained from the ethanol wash solution.

(b) A mixture of 1.2 g. of the yellow solid and 15 cc. of concentrated hydrochloric acid was shaken for 5–10 minutes. The resulting red-brown solution was mixed with 15 cc. of water and products isolated as described under (a). There was obtained 0.51 g. of benzaldehyde 2,4-dinitrophenylhydrazone, 0.35 g. of quinaldamide (III) and 0.33 g. of quinaldic acid (II). No appreciable amount of tar was formed in this hydrolysis experiment.

(c) A suspension of 2.8 g. of the yellow solid in 10 cc. of water was subjected to steam distillation. The distillate was run directly into a sulfuric acid solution of 2,4-dinitrophenylhydrazine, and 0.32 g. of benzaldehyde 2,4-dinitrophenylhydrazone was obtained.

From the distillation residue there was isolated 0.50 g. of quinaldamide (III) and 0.80 g. of tar.

**Action of Hydrogen Chloride on 1-Benzoyl-1,2-dihydroquinaldonitrile (V) in Benzene Solution.**—To a saturated solution of anhydrous hydrogen chloride in anhydrous benzene was added 10.00 g. of 1-benzoyl-1,2-dihydroquinaldonitrile (V). Hydrogen chloride was passed through the resulting solution for 15 minutes, and a yellow-orange solid precipitated. The reaction mixture was allowed to stand overnight in a nitrogen atmosphere, whereupon the solid material gradually became colored red-violet. The material was filtered in a dry-box in an atmosphere of nitrogen, then dried in a vacuum desiccator.[27]

The solid smelled of hydrogen chloride. In contact with moist air, the odor of benzaldehyde also developed. The

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[23] This compound will be described more fully in a future paper.

[24] Dehydration of amides to nitriles by solutions of acid chlorides in pyridine has been obesrved before; *cf.* Q. E. Thompson, *ibid.*, **73**, 5841 (1951).

[25] The yellow solid was undoubtedly a mixture of two or more substances. *Anal.* Found: C, 57.63, 57.38; H, 4.58, 4.83; N, 10.04, 9.88; Cl, 15.00, 15.24.

[26] C. A. Buehler and J. O. Harris, THIS JOURNAL, **72**, 5015 (1950).

[27] The red-violet solid was undoubtedly a mixture of products. *Anal.* Found: C, 62.11; H, 4.77; N, 8.94; Cl, 13.35.

solid was subjected to the following hydrolysis experiments.

(a) A mixture of 1.00 g. of the solid and 50 cc. of distilled water was shaken for 5 minutes. The resulting mixture, consisting of a black tar and red solution, was extracted thoroughly with ether. The ether solution was washed with 6 *N* hydrochloric acid, dried over Drierite and the ether distilled. The residual yellow oil gave 0.33 g. of benzaldehyde 2,4-dinitrophenylhydrazone when treated in the usual way.

The aqueous layer was combined with the acid wash and made basic with sodium bicarbonate. Quinaldamide (III), 0.43 g., was collected by filtration and an additional 0.03 g. was obtained by ether extraction of the alkaline filtrate. No copper quinaldate was isolated after acidification of the alkaline solution with acetic acid and treatment with copper sulfate.

(b) About 1.5 g. of the solid was washed thoroughly with anhydrous benzene to remove any adhering benzaldehyde. The insoluble residue weighed 1.32 g. after having been dried in a vacuum desiccator. This was added to 50 cc. of 5% sodium carbonate solution and shaken for 8 minutes. There was an immediate reaction to give a yellow solid and a black tar The mixture was worked up as described under (a), and there was obtained 0.32 g. of benzaldehyde 2,4-dinitrophenylhydrazone and 0.31 g. of quinaldamide (III). A few mg. of unidentified material of m.p. 220–221° was also isolated.

**Action of Hydrogen Chloride on 1-Benzoyl-1,2-dihydroquinaldonitrile (V) in Benzaldehyde Solution.**—Anhydrous hydrogen chloride was bubbled into a suspension of 10.00 g. of V in 50 cc. of freshly distilled benzaldehyde for 15 minutes and then the reaction mixture was allowed to stand overnight. The mixture was filtered to remove ammonium chloride which had precipitated, and 12 cc. of concentrated hydrochloric acid was added to the filtrate. More ammonium chloride precipitated and was removed by filtration. Addition of 100 cc. of ether and 20 cc. of ethanol to the filtrate caused 2.48 g. of an orange solid A to precipitate. The mother liquor was extracted with dilute hydrochloric acid. Upon making the acid extract basic by addition of sodium bicarbonate, 0.32 g. of an unidentified yellow solid precipitated, m.p. 100–110° dec. Extraction of the alkaline filtrate with ether afforded a trace of organic material. After acidification of the alkaline filtrate with acetic acid, 1.75 g. of quinaldic acid was obtained *via* the copper salt.

The benzaldehyde–ether layer was washed with sodium bicarbonate solution, the ether distilled and the benzaldehyde steam distilled. Upon trituration of the gummy, yellow residue with a small amount of ethanol, 3.44 g. of colorless solid, m.p. 100–146°, was obtained. This consisted of a mixture of benzoin quinaldate (IV) and 2-(2-quinolyl)-4,5-diphenyloxazole (XXIII). By fractional crystallization from ethanol there was obtained 0.44 g. of pure benzoin quinaldate (IV), m.p. 163–164°, also in admixture with an authentic sample of IV, as the least soluble fraction. From the mother liquors there was obtained 0.28 g. of pure 2-(2-quinolyl)-4,5-diphenyloxazole (XXIII), m.p. 140.5–141.5° after recrystallization from ligroin.

*Anal.* Calcd. for $C_{24}H_{16}N_2O$: C, 82.74; H, 4.63; N, 8.04. Found: C, 82.87; H, 5.08; N, 8.29.

To 2.00 g. of the orange solid A was added 50 cc. of distilled water and the mixture was stirred for 30 minutes. A precipitate which formed weighed 0.23 g. and consisted of a mixture of IV and XXIII. The aqueous filtrate was extracted with ether. Evaporation of the ether gave no benzaldehyde and only a trace of organic material. The aqueous residue was made basic by addition of sodium bicarbonate and extracted with ether. Again, distillation of the ether left only a trace of organic material. The aqueous solution was acidified with acetic acid, and 0.42 g. of quinaldic acid (II) was isolated *via* the copper salt.

**Acid-catalyzed Hydrolysis of 2-(2-Quinolyl)-4,5-diphenyloxazole (XXIII).**—A mixture of 0.25 g. of XXIII and 10 cc. of 25% sulfuric acid was heated under reflux for 6 days. Some solid which had steam distilled into the condenser was washed down with water. The mixture was extracted with ether, and the ether solution was washed with sodium bicarbonate solution. No organic material was obtained upon acidification of the sodium bicarbonate solution. The ether solution was dried over anhydrous sodium sulfate and the ether distilled. There remained 0.07 g. (89% net yield) of benzoin, m.p. 132–133° after two crystallizations from ethanol, also in admixture with authentic benzoin.

The original acid layer was made basic by addition of sodium hydroxide solution. Ether extraction gave 0.12 g. of recovered XXIII.

After acidification of the basic solution with acetic acid, a few mg. of quinaldic acid was isolated *via* the copper salt.

LAWRENCE, KANSAS

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUQUESNE UNIVERSITY]

# The Basicity of Hydrazones[1]

BY HUGH F. HARNSBERGER, EDWARD L. COCHRAN AND H. HARRY SZMANT[2]

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Acidity constants for a number of substituted acetophenone and benzophenone hydrazones were determined spectrophotometrically. The resultant *pK* values can be correlated with the Hammett $\sigma$-values when the hypothetical formaldehyde hydrazone is considered to be the parent structure and when the sum of the $\sigma$-constants of all substituents is employed.

## Introduction

The relative basicity of hydrazones is probably of some significance in the acid-catalyzed conversion of hydrazones to azines[3] since the reaction proceeds with increasing difficulty as one compares dialkyl, alkaryl and diaryl ketone hydrazones. Also, in the case of the Wolff–Kishner reaction it was shown[4] that the base-dependent reaction involves the formation of the hydrazone anion, and while it is experimentally difficult to determine the relative acidity of various hydrazones it is to be expected that the relative acidities are inversely related to the basicities studied here.

## Experimental

Since hydrazones tend to hydrolyze rather readily under acidic conditions all of the work reported here was performed using an essentially anhydrous methanol medium. Known volumes of standard solutions of trichloroacetic acid and of the hydrazone were mixed and the resulting hydrogen ion concentration was immediately measured by the spectrophotometric method of Brode.[5] This method requires the measurement of the extinction coefficient of a suitable indicator at its wave length of maximum absorption in a series of buffer solutions covering the useful *p*H range of the indicator. The *p*H of any solution can then be determined by reference to the plot of the extinction coefficient *vs.* *p*H.

Trichloroacetate buffers were prepared by adding known volumes of standard trichloroacetic acid solutions to stand-

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(1) From the M.S. thesis of E. L. C., Duquesne University, 1951.

(2) To whom requests for reprints should be sent.

(3) H. H. Szmant and C. McGinnis, THIS JOURNAL, **72**, 2890 (1950).

(4) H. H. Szmant, H. F. Harnsberger, T. J. Butler and W. P. Barie, *ibid.*, **74**, 2724 (1952).

(5) W. R. Brode, *ibid.*, **46**, 581 (1924).