the hydrogen electrode in alkaline media may be described similarly once the exchange constant for the hydroxyl ion has been evaluated from the e. m. f. data. This constant has the value $K = 0.348$. Calculated and experimental values, in good agreement, are compared in the upper curve of Fig. 3.

Hydrogen Ion Equilibria.—The following expression (9a) is of considerable interest. It is

$$\frac{(H_2OD^+ + HDOD^+ + D_2OD^+)(H_2O)}{(H_2OH^+ + HDOH^+ + D_2OH^+)(HDO)} = K_{ap.} = K_9 \qquad (9a)$$

$$\frac{(K_3 + K_3K_4R + K_3K_4K_5R^2)}{(1 + K_3R + K_3K_4R^2)} = K_9 \qquad (9b)$$

readily converted to (9b) and $K_{ap.}$ is seen to have the limiting values $K_9 = K_3 = 0.93$ in H_2O and $K_9 = K_5 = 0.138$ in D_2O. This equilibrium has been expressed in the simplified manner of (10).[6,7] In accordance with the considerations above, however, K_{10} must be considered the limiting value in D_2O of an apparent constant and is not to be confused with (11) which is a true equilibrium expression (if the existence of H_3O^+, etc., be granted).

$$\frac{(D^+)(H_2O)}{(H^+)(HDO)} = K_{10} = 0.141 \qquad (10)$$

$$\frac{(D_3O^+)}{(H_3O^+)}\frac{(H_2O)^3}{(HDO)^3} = K_3K_4K_5 = 0.044 \qquad (11)$$

The various equilibria involved in the conductance of strong acids[8] are readily evaluated. In addition to the fundamental equilibria (3, 4, 5) there are the equilibria (12), Table I.

The author is grateful to Prof. V. K. La Mer for helpful criticism.

Summary

Upon the basis of the assumed existence of the ions H_3O^+, H_2DO^+, HD_2O^+ and D_3O^+ it is possible to describe consistently the behavior of conductance and e. m. f. data in H_2O–D_2O mixtures in terms of the various isotopic equilibria.

New York, N. Y. Received June 1, 1937

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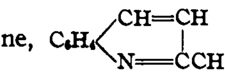
[7] Hamill and La Mer, *J. Chem. Phys.*, 4, 395 (1936).

[8] Baker and La Mer, *ibid.*, 3, 406 (1935).

[Contribution from the Chemical Laboratory of Stanford University]

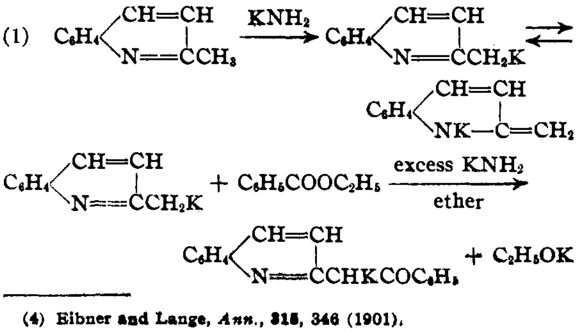
Claisen Type Condensations with Quinaldine and Related Ammono Ketone Ethers

By F. W. Bergstrom and Alan Moffat

Quinaldine,  (a cyclic ammono ketone ether), has long been known to undergo many of the reactions of an aquo ketone, in which one of the two groups attached to carbonyl is methyl. Previous work bearing out this statement has been reviewed briefly in earlier articles,[2] where it was shown that quinaldine and other 2-alkylquinolines react with the alkali amides in liquid ammonia to form salts which can be alkylated. In the present investigation, it will be shown that quinaldine and many related compounds undergo the Claisen condensation with aromatic esters in the presence of potassium amide. Quinaldine and lepidine (an expanded ketone ether of the ammonia system (Ingold) or a vinylog of quinaldine (Fuson)) are known to react with diethyl oxalate in absolute ether in the presence of potassium ethylate[3] to form quinaldine and lepidine oxalic esters. Another possible Claisen condensation of this type occurs when quinaldine reacts with diethyl phthalate, in the presence of sodium metal.[4]

Discussion of the Experimental Results

2-Phenacylquinoline (ω-benzoylquinaldine, α-quinolylacetophenone) is prepared readily and in fairly good yield by the action of potassium quinaldyl on one equivalent of ethyl benzoate in absolute ether, preferably in the presence of an excess of amide. The reaction follows the equations



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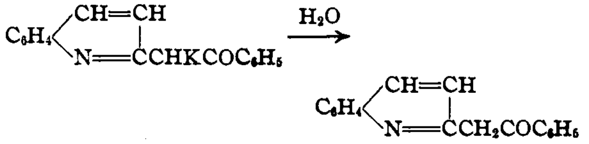
[1] Presented at the Pittsburgh meeting of the American Chemical Society, September, 1936.

[2] Bergstrom, This Journal, 53, 3027, 4065 (1931).

[3] Wislicenus and Kleisinger, *Ber.*, 42, 1141 (1909).

[4] Eibner and Lange, *Ann.*, 315, 346 (1901).



Two and a half or three moles of potassium amide is used for each mole of quinaldine (or ethyl benzoate) because the phenacylquinoline otherwise would form a potassium salt at the expense of potassium quinaldyl.

It was found that this reaction is not general, since aromatic esters appear to be the only ones that may be used with success. Ethyl acetate, and other compounds of this type, which contain enolizable hydrogen, do not give definite products with potassium quinaldyl, nor do acetyl chloride and benzoyl chloride, possibly in part because of the effect of ammonia, which cannot be entirely removed before the reaction is carried out.[5]

The following quinaldyl ketones were prepared in the present work by the method outlined above: 2-phenacylquinoline, *p*-bromophenacylquinoline, *o*-chlorophenacylquinoline, 2-furoylquinaldine, 2-*p*-methoxyphenacylquinoline, 2-*p*-methylphenacylquinoline, 2-phenacyl-4,5-benzoquinoline, 2-*p*-methoxyphenacyl-4,5-benzoquinoline, 2-methyl-3-phenacylquinoxaline, 2,3-diphenacylquinoxaline (?). The following esters failed to react with potassium quinaldyl under the same conditions: ethyl acetate, ethyl *p*-aminobenzoate, ethyl *p*-hydroxybenzoate (the hydrogens of the amino group, and the hydroxylic hydrogen are acidic), ethyl diethylmalonate and ethyl oxalate. Presumably the excess potassium amide saponifies the ester more rapidly than the ester reacts with potassium quinaldyl. Attempts to benzoylate 2-*n*-propylquinoline, 4-methylquinoline and 2,4-dimethylquinoline and α-picoline were unsuccessful, since the potassium salts of these alkylated quinolines have extremely low solubilities in ether.

The aroyl quinaldines are all yellow or orange solids, having weakly basic properties since their hydrochlorides are readily hydrolyzed by water. 2-Phenacylquinoline has not yet been reduced to the corresponding carbinol, nor has it been oxidized directly to quinaldic acid (benzoic acid has been obtained). The ketonic properties of the carbonyl group are not pronounced, since no oxime, phenylhydrazone or anil of definite characteristics is formed by the usual methods. No conclusive evidence has been obtained to decide between the alternate structures 2-phenacylquinoline and 1-benzoyl-2-methylene-1,2-dihydroquinoline but its chemical inertness is more in agreement with the first. Moreover, a substance melting at 116°, as does the present preparation, has been synthesized recently by methods which leave no doubt that it is 2-phenacylquinoline.[6]

Experimental Part

2-Phenacylquinoline.—Into a 500-cc. three-necked Pyrex flask are introduced 150–200 cc. of liquid ammonia,[7] 10 g. (0.26 mole) of clean potassium metal, cut into pieces of about a gram each,[8] and 0.05 g. of ferric oxide. After the conversion of the bulk of the metal to amide, potassium spattered on the walls is washed down by swirling the solution around, or by introduction of a small volume of fresh solvent; 14.3 g. (0.1 mole) of quinaldine is then slowly run into the potassium amide solution through a dropping funnel. After five to ten minutes, 150 cc. of anhydrous ethyl ether is added and the ammonia allowed to evaporate. The flask is attached to a reflux condenser and fitted with a mercury sealed stirrer, the ether being refluxed gently for a few minutes to remove the bulk of remaining ammonia. Fifteen grams (0.10 mole) of ethyl benzoate is introduced, from a dropping funnel, with vigorous stirring, the reaction taking place with evolution of heat and ammonia. After four to six hours of continuous stirring, the contents of the flask are a light yellow-green, and the reaction is complete. Excess amide is destroyed by the addition of 10–20 cc. of alcohol (stirring), and the potassium salt of the product hydrolyzed by adding 100 cc. of water. The yellow precipitate of phenacylquinoline is filtered off, a further small quantity being obtained by evaporating the ethereal layer to dryness. The combined precipitates are crystallized from alcohol, filtering the hot solution to remove iron and iron oxide; yield, 15 g. (60%); m. p. 114–115° (uncorr.) (see Table I). A high melting yellow precipitate is probably the potassium salt of the product. It can be hydrolyzed by washing (or grinding in a mortar) with water.

In four comparative experiments (*cf.* above) phenacylquinoline was prepared with a total of one, two, two and a half and three moles of potassium amide per mole of quinaldine (ethyl benzoate, in equimolar quantity). The yields of phenacylquinoline were, respectively, (less than 30%), 35, 60 and 65%.

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(5) B. Bergmann and W. Rosenthal, *J. prakt. Chem.*, [2] 135, 278 (1932), prepared 2-phenacylpyridine by treating lithium-2-picolyl with benzoyl chloride in absolute ether, in the absence of ammonia.

(6) C. H. Boehringer Sohn A. G., German Patent 594,849, Mar. 22, 1934; *C. A.*, 28, 4541 (1934).

(7) Liquid ammonia is conveniently distilled into small cylinders containing about 15–25 pounds (6.8–11.3 kg.). The valve, of a commercial type for use with ammonia cylinders, is attached on the inside to a 1.26 cm. steel pipe, which goes almost to the bottom of the vessel. Thus, with the cylinder in an upright position, and with the valve partially opened, liquid ammonia is forced into the reaction flask through a rubber tube attached to an adapter screwing into the valve opening.

(8) It is most convenient to use potassium balls or sticks from which the oxide has been cut or scraped. Badly oxidized metal may be melted, with stirring, under dioxane, the molten metal coalescing and forming a homogeneous globule, which may be cut as desired after cooling.

TABLE I

HOMOLOGS OF PHENACYLQUINOLINE AND RELATED COMPOUNDS

The first six experiments duplicated the preparation of phenacylquinoline, with 0.10 mole of quinaldine, 2.5 moles of KNH_2 and 0.10 mole of ester, $RC_6H_4COOC_2H_5$ (or $COOCH_3$. In 4, ethyl furoate).

No.	Product[a]	Time of reaction,[b] hours	Yield G.	Yield %	M. p. (purest specimens) uncorr.,[a] °C.
1	2-Phenacylquinoline	4–6		60–65	116.4–117.1
2	2-*p*-Bromophenacylquinoline	4	14	43	165.7–167.2
3	2-*o*-Chlorophenacylquinoline	18	9.8	35	115.9–117.0
4	2-Furoylquinaldine	20	6.6	28	102.9–103.4
5	2-*p*-Methoxyphenacylquinoline[e,g]	4–6	20	72	154.5–155
6	2-*p*-Methylphenacylquinoline	4–6	15.7	60	170–1
7	2-Phenacyl-5,6-benzoquinoline[c,d] (—*β*-naphthoquinoline)	4	2.31	37.6	207.8–208.8
8	2-*p*-Methoxyphenacyl[c,e] 5,6-benzoquinoline	6.5	3.44	42	158–158.5
9	2-Methyl-3-phenacylquinoxaline[c,f]	16	1.05	32	125.6–126.5
10	2,3-Diphenacylquinoxaline[c,f,i]	By prod. of above	Very small		204.5–205.2

TABLE II

No.	Found,[h] % C	Found,[h] % H	Found,[h] % N	Formula	Calculated, % C	Calculated, % H	Calculated, % N	Cryst. from
1	82.58	5.31	5.80	$C_{17}H_{13}ON$	82.6	5.3	5.6	EtOH
2	62.50	3.90	Br, 25.13	$C_{17}H_{12}ONBr$	62.5	3.71	Br, 24.5	EtOH
3	72.61	4.52	4.85	$C_{17}H_{12}ONCl$	72.46	4.26	4.97	C_6H_6
4[i]	76.08	4.75	5.70	$C_{15}H_{11}O_2N$	75.91	4.68	5.91	Ligroin 60–70° b. p.
5	77.85	5.45	5.05	$C_{18}H_{15}O_2N$	78.0	5.4	5.1	Hexone[j]
6	82.39	5.82	5.52	$C_{18}H_{15}ON$	82.8	5.7	5.4	Hexone
7	84.87	5.31	4.89	$C_{21}H_{15}ON$	84.82	5.09	4.72	Pyridine (or hexone)
	84.51	5.23	4.84					
8	80.34	5.31	4.47	$C_{22}H_{17}O_2N$	80.7	5.2	4.3	Hexone
9[i]	77.41	5.45	10.53	$C_{17}H_{14}ON_2$	77.80	5.38	10.69	Ligroin, 60–70° b. p.
	77.94	5.30	10.60					
10	79.79	4.93	7.59	$C_{24}H_{18}O_2N_2$	78.7	4.9	7.6	Dil. pyridine

[a] Melting points of recrystallized specimens. The yields reported melted from 1–4° lower, as a rule. [b] The reactions were allowed to proceed until most or all of the dark red potassium quinaldyl had disappeared. The times given do not necessarily indicate the speed with which the reaction occurs, since solubility relationships enter. [c] Expts. 7–10 were carried out in 200-cc. Erlenmeyer flasks, without mechanical stirring. (Otherwise as described under the preparation of phenacylquinoline.) The precipitate on the walls of the flasks was loosened from time to time with a stirring rod. [d] 4.00 g. of 5,6-benzoquinaldine, the potassium amide from 2.04 g. potassium and 3.15 g. of ethyl benzoate. [e] 3.6 g. of 5,6-benzoquinaldine, the KNH_2 from 2.46 g. of potassium and 4.55 g. of ethyl *p*-methoxybenzoate. [f] Two g. of 2,3-dimethylquinoxaline, the sodium amide from 1.5 g. of sodium and 4.5 g. of ethyl benzoate. The reaction product was hydrolyzed with water, the ether evaporated and the aqueous solution filtered. The yellow-brown ppt. was extd. with boiling alcohol, leaving an insoluble orange ppt., which was dissolved through the filter with a small amt. of boiling pyridine and crystallized from dil. pyridine (diphenacylquinoxaline). Crystals separating from alcohol are monophenacylquinoxaline. [g] Tribromoquinaldine, *p*-methoxybenzoyl bromide (isolated as *p*-methoxybenzanilide, and *p*-methoxybenzoic acid (by hydrolysis of *p*-methoxybenzoyl bromide not converted to anilide) were isolated in a bromination experiment with 6 equivs. of bromine: yields, 30, 22 and 17%, respectively. [h] Analyses by Fred Hall, Oxford, unless otherwise mentioned. [i] Microanalyses by P. Weiler, Oxford. [j] Methyl isobutyl ketone.

Phenacylquinoline was formed in poor yield by adding ethyl benzoate to a liquid ammonia solution of potassium quinaldyl or by adding ethyl benzoate to an ethereal solution of lithium quinaldyl.[9] The reaction between quinaldine, ethyl benzoate and sodium amide in ether will be described later.

Reduction and Oxidation.—Reduction of phenacylquinoline was unsuccessful with the following reagents: zinc amalgam in 35% hydrochloric acid 80–90° (Clemmensen reduction), 2% sodium amalgam in alcohol (80°); excess sodium in liquid ammonia at −33° or +20° (phenacylquinoline is only slightly soluble in liquid ammonia). Oxidation with permanganate under a variety of conditions gives tarry products. Benzoic acid was obtained in 50% yield (together with tar) when phenacylquinoline in 18 *N* sulfuric acid was shaken with three equivalents of potassium dichromate for several hours at room temperature. No quinaldic acid was isolated.

Bromination.—3.22 g. (13.0 millimoles) of phenacylquinoline is dissolved in 25 cc. of glacial acetic acid, and to this solution is added 3 g. of sodium acetate and then, slowly, 4.2 g. (4 equivalents) of bromine in 10 cc. of glacial acetic acid. The containing flask was tightly stoppered and shaken for eight hours. To the solution and solid, 50 cc. of water was added, the resulting copious precipitate being filtered and washed with water; m. p. 128–129°,

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(9) Ziegler, *Ber.*, **63B**, 1847 (1930); Ziegler and Zeiser, *Ann.*, **485**, 174 (1931).

after cryst. from glacial acetic acid and methanol; mixed m. p. with tribromoquinaldine, prepared from quinaldine, 127.5–128.5°, showing their identity; yield, 2.9 g. crude product, m. p. 120–124°, or 88% of that calcd. (on the basis of the bromine used) from the equation

$$C_9H_6NCH_2COC_6H_5 + 3Br_2 = C_6H_5COBr + C_9H_6NCBr_3 + 2HBr$$

In a repetition, six equivalents of bromine were used, but the rate of addition was too rapid and some tar formed, which was removed readily with a stirring rod. The acetic acid solution was filtered and the precipitate washed with water to remove sodium bromide, leaving tribromoquinaldine.

To the filtrate 1.5 equivalents of aniline was added, and the solution shaken for about an hour at room temperature. The white precipitate, filtered and crystallized from methanol, was identified by m. p. and mixed m. p. as benzanilide (162.0–162.8°), yield 75%, which could only have been formed from benzoyl bromide. A little tribromoquinaldine was obtained by diluting the filtrate with water: total yield, 51%.

Phenacylquinoline dissolves readily in hot concd. hydrochloric acid, the hydrochloride separating in long almost colorless needles on cooling. This may be obtained, without solvent of crystallization, by passing hydrochloric acid gas through an ethereal solution of the ketone. The hydrochloride cannot be crystallized from water because it is hydrolyzed so readily. Phenacylquinoline is readily soluble in cold concd. sulfuric acid, and may be recovered unchanged by diluting the solution and neutralizing with ammonia. Picrate, precipitated in and crystallized from alcohol, yellow, m. p. 171.5–172.5° (uncorr.).

Summary

1. In agreement with the view that it is a cyclic ketone ether of the ammonia system, 2-methylquinoline (quinaldine) has been found to undergo a Claisen type condensation with many esters of aromatic acids in the presence of 2–3 equivalents of potassium amide. The following compounds have been prepared: 2-phenacylquinoline (benzoylquinaldine, α-quinolylacetophenone), *p*-bromophenacylquinoline, *o*-chlorophenacylquinoline, 2-furoylquinaldine, 2-*p*-methoxyphenacylquinoline, 2-*p*-methylphenacylquinoline, 2-phenacyl-4,5-benzoquinoline, 2-*p*-methoxyphenacyl-4,5-benzoquinoline, 2,3-diphenacylquinoxaline (?), 2-methyl-3-phenacylquinoxaline.

STANFORD, UNIV., CALIF. RECEIVED MAY 17, 1937

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

Stereochemistry of Deuterium Compounds of the Type $RR'CX_HX_D$; Ethyl-d_4-ethylcarbinol

BY FRANK C. MCGREW[1] AND ROGER ADAMS

Research intended to investigate the asymmetry of a carbon atom of the type RR'CHD has been carried out by attempting to resolve cinnamic acid dideuteride,[2] succinic-α,α'-d_2 acid,[3] and by the preparation from optically active compounds of camphane-d,[4] camphane-2,3-d_2[5] and benzalacetone dideuteride.[6] In none of these experiments was the slightest indication of optical activity obtained.

The study of compounds of the type $RR'CX_HX_D$, where X_H and X_D indicate groups identical but for one or more hydrogen atoms of one replaced by deuterium atoms in the other, represents an extension of the original problem which would answer equally well the question of the asymmetry conferred by hydrogen and deuterium symmetrically placed. It is possible, though incapable of theoretical demonstration, that such compounds in general would be much more likely to exhibit a measurable optical rotation than the type RR'CHD.

In the first example of the type $RR'CX_HX_D$, Clemo and McQuillen[7] found phenyl-d_5-phenylaminomethane after resolution to have a specific rotation [α] −5.7°, calculated from an observed rotation well beyond experimental error. An analogous compound, phenyl-d_5-phenylacetic acid, however, was found to be optically inactive when prepared from *l*-α-bromophenylacetic acid. Unsuccessful attempts to resolve the product with alkaloidal salts indicated that the inactivity was inherent and not due to racemization during formation.[8] Likewise, the activity found for cumene-d[9] was so slight that it is not beyond controversy.

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(1) This is a portion of a thesis submitted in fulfilment of partial requirements for the degree of Doctor of Philosophy in Chemistry. Chemical Foundation Fellow in Organic Chemistry.

(2) Erlenmeyer and Gärtner, *Helv. Chim. Acta*, **19**, 145, 331 (1936).

(3) Leffler and Adams, THIS JOURNAL, **58**, 1551 (1936).

(4) Biilmann, Jensen and Bak, *Ber.*, **69**, 1947 (1936).

(5) Leffler and Adams, THIS JOURNAL, **58**, 1555 (1936).

(6) Coppock and Partridge, *Nature*, **137**, 907 (1936).

(7) Clemo and McQuillen, *J. Chem. Soc.*, 808 (1936).

(8) Erlenmeyer and Schenkel, *Helv. Chim. Acta*, **19**, 1169 (1936).

(9) Burwell, Hummel and Wallis, *J. Org. Chem.*, **1**, 332 (1936).