Semicarbazone of 2-Methyl-8-quinolyl Methyl Ketone.—This salt, prepared by treating the ketone with molar amounts of semicarbazide hydrochloride and sodium acetate in a small volume of water, melts at 209° after recrystallization from dilute alcohol.

Anal. Calcd. for $C_{13}H_{14}ON_4$: C, 64.46; H, 5.79; N, 23.13. Found: C, 64.38; H, 5.86; N, 22.92.

Oxidation of 2-Methyl-8-quinolyl Methyl Ketone.[11]—To a mixture of 0.8 g. of ketone and 42 ml. of 7% caustic at 0° was added slowly 1.1 ml. of bromine with stirring for an hour and a half. The excess sodium hypobromite was destroyed by addition of sulfur dioxide, followed by two extractions with chloroform. Evaporation of the solvent left 2-methylquinoline-8-carboxylic acid in poor yield. After recrystallization from water in fine needles, it showed no depression in a mixed melt with an authentic sample melting at 152–153°.

Anal. Calcd. for $C_{11}H_9O_2N$: N, 7.49. Found: N, 7.62.

Oxidation of 8-Ethylquinoline.—To a boiling solution of the base (1 g.) in 40 ml. of 6 *N* sulfuric acid, the theoretical amount of potassium dichromate for ketone formation was added slowly during one hour. The cooled solution was basified with ammonium hydroxide, acidified with acetic acid and extracted with chloroform. The chloroform layer was extracted twice with 10-ml. portions of 10% sodium hydroxide. Evaporation of the solvent layer left an oil which readily formed 0.6 g. of *semicarbazone* (40% yield). Recrystallized from dilute alcohol, it melts at 225°.[15]

Anal. Calcd. for $C_{12}H_{12}ON_4$: C, 63.16; H, 5.26; N, 24.56. Found: C, 63.43; H, 5.24; N, 24.35.

The aqueous layer was acidified to the phenolphthalein end-point with acetic acid and extracted with two 5-ml. portions of chloroform. Evaporation of the solvent left 0.45 g. (40% yield) of quinoline-8-carboxylic acid[9] which, recrystallized from methanol, melts at 184°.

Anal. Calcd. for $C_{10}H_7O_2N$: N, 8.09. Found: N, 8.20.

Summary

1. The isolation of two new $C_{12}H_{13}N$ bases from the Edeleanu kerosene extract of California petroleum is reported.

2. The structure of one of the bases has been established as 2-methyl-8-ethylquinoline through degradation and synthesis.

3. The formation of 8-quinolyl methyl ketones in potassium dichromate oxidation of 2-methyl-8-ethyl- and 8-ethylquinoline is described.

[15] Howitz and Koepke (ref. 8) report a melting point of 223° for the semicarbazone of 8-quinolyl methyl ketone.

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[CONTRIBUTION NO. 208 FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF TEXAS]

A Contribution to Chromic Acid Oxidation of Quinoline Homologs and Oxidation of *Bz*-Ethylquinolines to Quinolyl Methyl Ketones

BY RICHARD A. GLENN AND J. R. BAILEY

Introduction

In the Texas Laboratory, chromic acid in dilute sulfuric acid either as (1) anhydride or (2) dichromate has been employed exclusively as an oxidizing agent for conversion of alkyls at position 8 on the quinoline nucleus to carboxyl. With 2 the reaction proceeds with much greater velocity than with 1. The suggested explanation of this difference is, acid potassium sulfate catalyzes chromic acid oxidation. Comparative data on *step-wise* oxidation of *Bz*-alkylquinolines with anhydride and dichromate are submitted in Tables I and II, respectively.

It has been found that where quinoline-8-carboxylic acids are desired, a decidedly increased yield can be obtained by using a fractional part of the calculated amount of oxidant. The advantage of step-wise oxidation is the maintenance of a favorable equilibrium between the original base and its primary oxidation products in order to circumvent, as far as possible, excessive degradation of the latter. At the end of the reaction, unchanged base is recovered for recycling.

Certain *Bz*-ethylquinolines are converted to quinolyl methyl ketones; others yield mixtures of ketone and carboxylic acid[1] and a few only carboxylic acids. As concerns a restricted number of bases, the results obtained depend on whether the anhydride or dichromate is used. In dichromate oxidation of 2,3-dimethyl-8-ethyl- and 2,4-dimethyl-8-ethylquinoline, only carboxylic acids are obtained; however, in chromic anhydride oxidation, quinolyl methyl ketones are readily formed. From 8-methyl- and 8-*n*-propylquinolines, only carboxylic acids have been obtained.

Ketone formation from *Bz*-ethylquinolines is analogous to the oxidation of ethylbenzene to acetophenone.[2] Oxidation of *n*-propylbenzene to

[1] Glenn and Bailey, THIS JOURNAL, **63**, 639 (1941).

[2] Friedel and Balsohn, *Bull. soc. chim.*, [2] **32**, 616 (1800).

phenyl ethyl ketone is not reported in the literature.

TABLE I

DATA ON CHROMIC ANHYDRIDE OXIDATION OF 8-ALKYLQUINOLINES

Base, 1 g.	Time, hrs.	Recovered base, g.	Yield of acid Wt.	Yield of acid %	Yield of ketone, %
2,3,8-Me$_3$-Q	3.0	0.80	0.20	85[a]	..
2,3-Me$_2$-8-Et-Q	1.0	.65	.10	56[b]	12
2,4-Me$_2$-8-Et-Q	1.0	.60	..	..	36
2,3-Me$_2$-8-n-Pr-Q	0.8	.70	.25	83[c]	..
2,3,4,8-Me$_4$-Q	2.5	.80	.20	86[d]	..

[a] King and Bailey, THIS JOURNAL, **52**, 1239 (1930), reported a yield of 16% in 30 hr. using chromic anhydride. [b] Key and Bailey, *ibid.*, **60**, 763 (1938), reported a yield of 19% in 60 hr. using chromic anhydride. [c] Axe and Bailey, *ibid.*, **60**, 3030 (1938), reported a yield of 27% in 1 hr. using potassium dichromate. [d] Axe and Bailey, *ibid.*, reported a yield of 14% in 4 hr. using potassium dichromate. [e] W. Nelson Axe, *ibid.*, **61**, 1017 (1939), reported a 18% yield of acid in less than an hour using potassium dichromate.

TABLE II

DATA ON DICHROMATE OXIDATION OF *Bz*-ETHYLQUINOLINES

Base	Me ketone, %	Acid, %	Rec. base, %
8-Et-Q[a]	40	40	..
2-Me-8-Et-Q[a]	75	..	..
2-Me-6-Et-Q[b]	75	..	..
3-Me-8-Et-Q	80	..	..
2,3-Me$_2$-8-Et-Q	..	50	50
2,4-Me$_2$-8-Et-Q	..	30	60
2,4-Me$_2$-6-Et-Q	30	..	60
2,3,4-Me$_3$-8-Et-Q[c]	50	25	..
3-Me-2,8-Et$_2$-Q	55	10	..
3-Me-2,6-Et$_2$-Q	85	..	..

[a] Glenn and Bailey, THIS JOURNAL, **63**, 639 (1941). [b] Mills, Harris and Lambourne, *J. Chem. Soc.*, **119**, 1300 (1921). [c] Glenn and Bailey, THIS JOURNAL, **61**, 2612 (1939).

TABLE III

DATA ON SEMICARBAZONES OF QUINOLYL METHYL KETONES

Ketone	M. p., °C.	Crystalline appearance	Nitrogen analyses, % Calcd.	Nitrogen analyses, % Found
2-Me-6-quinolyl	262[a]	Yellow needles	23.13	23.32
3-Me-8-quinolyl	226–227	Tan needles	23.13	22.93
2,3-Me$_2$-8-quinolyl	239	Yellow needles	20.44[c]	20.58
2,4-Me$_2$-6-quinolyl	251	Tan needles	19.15[d]	19.18
2,4-Me$_2$-8-quinolyl	262	Yellow needles	19.15[d]	19.24
2,3,4-Me$_3$-8-quinolyl	258–259	Tan needles	18.30[d]	18.40
2-Et-3-Me-8-quinolyl	243	White needles	20.74	20.52
2-Et-3-Me-6-quinolyl	251	White needles	20.74	20.71
2-Et-3-Me-Q-8-COOH	223[b]	White needles	6.51	6.55

[a] There was no depression in a mixed melt with a synthetic sample; Behrend and Thomas, *Ber.*, **25**, 2548 (1892). [b] Niementowski and Orzechowski, *ibid.*, **28**, 2813 (1895), reported 221°; v. Miller, *ibid.*, **23**, 2268 (1890), reported 215–216°. [c] Calculated for 1H$_2$O of crystallization. [d] Calculated for 2H$_2$O of crystallization.

Experimental

General Oxidation Procedure.—The base (1 g.) and an amount of oxidant sufficient to assure molar equivalents of oxygen and base are employed. To a boiling solution of the base and 0.2 g. of potassium bisulfate[3] in 50 ml. of 6 *N* sulfuric acid, is added intermittently twenty 0.5-ml. portions of 6 *N* sulfuric acid containing chromic anhydride or potassium dichromate, time being allowed for appearance of a green coloration after each addition.

To the cooled reaction mixture ammonium hydroxide is added with stirring to incipient precipitation of chromic hydroxide. The solution is acidified with a slight excess of acetic acid and extracted with chloroform. Next, the solvent layer is extracted with dilute caustic. Here, unchanged base and any ketone formed remain in the chloroform. From the aqueous layer after acidification with a slight excess of acetic acid, chloroform extraction withdraws any quinoline carboxylic acid formed in the oxidation and it remains as a residue on evaporation of the solvent.

After evaporation of the chloroform used in the initial extraction, the residue suspended in aqueous solution of semicarbazide hydrochloride and sodium acetate is agitated for thirty minutes. From this mixture, unchanged base is extracted with petroleum ether and converted to the picrate. The water insoluble material remaining behind and consisting of the semicarbazone of any ketone formed in the oxidation is filtered off.

The subjoined preparations were used in oxidation experiments:

3 - Methyl - 8 - ethylquinoline.[4]—2,3 - Dimethyl - 8-ethylquinoline (10 g.) was refluxed overnight with the calculated amount of selenium dioxide dissolved in 75 ml. of alcohol.[5] The residue from removal of the solvent was dissolved in 40 ml. of benzene and agitated with 100 ml. of saturated sodium bisulfite solution for thirty minutes. The addition product was removed by filtration and decomposed with dilute alkali. The aldehyde was extracted with ether and, after evaporation of the solvent, the residue was oxidized in acetone with 15 ml. of 30% hydrogen peroxide. Through the employment of the general procedure for isolation of quinoline carboxylic acids, 7 g. or a 60% yield of crude 3-methyl-8-ethylquinoline-2-carboxylic acid was obtained. It crystallized from alcohol in needles melting at 84° as reported by Key and Bailey.[4] 3-Methyl-8-ethylquinoline was obtained in practically quantitative yield from the acid on decarboxylation by simple fusion.

Anal. of acid. Calcd. for $C_{13}H_{13}O_2N$: N, 6.57. Found: N, 6.59.

Anal. of base picrate. Calcd. for $C_{18}H_{16}O_7N_4$: N, 14.00. Found: N, 14.04.

Credit is due W. Nelson Axe and J. R. Bailey for the synthesis described below of 2,4-dimethyl-6-ethylquinoline, 3-methyl-2,8-diethylquinoline and 3-methyl-2,6-diethylquinoline.

2,4-Dimethyl-6-ethylquinoline.—This base was prepared by a slight modification of the procedure of Koenigs and

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(3) The acid sulfate is omitted when dichromate is used.

(4) *Cf.* Key and Bailey, THIS JOURNAL, **60**, 763 (1938).

(5) *Cf.* Burger and Modlin, *ibid.*, **62**, 1081 (1940).

Mengel[6] for the production of 2,4-methylated quinolines: *p*-aminoethylbenzene (8 g.) and 6.6 g. of acetylacetone were refluxed for thirty minutes and then, for removal of water formed in the reaction, refluxing was continued for fifteen minutes with the condenser steam-heated. After addition of 115 cc. of concentrated sulfuric acid and heating on a steam cone for twenty minutes, the mixture was poured onto ice. The base was liberated with caustic and extracted with ether. Next, diazotization in dilute hydrochloric acid for removal of *p*-aminoethylbenzene was carried out in the usual way. After removal of non-basic admixtures by ether extraction, the solution was made alkaline with caustic and the liberated base was extracted with ether. The yield of crude 2,4-dimethyl-6-ethylquinoline was 4 g. (33%). The picrate prepared in alcohol solution crystallizes from alcohol in fine needles melting at 190–191°.

Anal. Calcd. for $C_{19}H_{18}O_7N_4$: C, 55.07; H, 4.35; N, 13.53. Found: C, 54.99; H, 4.66; N, 13.56.

The following constants were determined on the base prepared from the picrate: b. p. 299–300° (742 mm.), $n^{25}\mathrm{D}$ 1.5860.

3-Methyl-2,8-diethylquinoline.—This product was synthesized in poor yield from propionaldehyde and *o*-aminoethylbenzene through the Doebner–Miller synthesis as modified by Harz.[7] After the usual process of isolation of quinolines through picrates, the picrate of the new base was recrystallized from alcohol in needles melting at 194–195°. The free base, prepared from picrate recrystallized to constant melting point, has the following constants: m. p. 18.5–19.5°, b. p. 298° (754 mm.), $n^{25}\mathrm{D}$ 1.5778, d^{20}_4 1.0014.

Anal. Calcd. for $C_{20}H_{20}O_7N_4$: C, 56.07; H, 4.71. Found: C, 56.38; H, 4.70.

3-Methyl-2,6-diethylquinoline.—This product was synthesized from propionaldehyde and *p*-aminoethylbenzene through the Doebner–Miller synthesis as modified by Mills, Harris and Lambourne.[8] It was isolated and purified through the picrate. The yield of the new base was 8 g. from 25 g. of *p*-aminoethylbenzene or 19.5%. The picrate was recrystallized from alcohol in needles melting at 152–153°. The base has the following constants: b. p. 313.5° (748 mm.), $n^{25}\mathrm{D}$ 1.5834, d^{20}_4 1.0049.

Anal. Calcd. for $C_{20}H_{20}O_7N_4$: C, 56.07; H, 4.71. Found: C, 56.26; H, 4.83.

Summary

Experimental proof is presented of (1) an increased yield of carboxylic acids by employing step-wise chromic acid oxidation of 8-alkylquinolines and (2) an increase in the velocity of reaction, where chromic acid anhydride is employed, by the addition of potassium acid sulfate.

The direct conversion of *Bz*-ethylquinolines to corresponding *Bz*-quinolyl methyl ketones through oxidation with chromic acid anhydride or dichromate is reported.

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(6) Koenigs and Mengel, *Ber.*, **37**, 1325, 1333 (1904).

(7) Kurt Harz, *ibid.*, **18**, 33, 84 (1885).

(8) Mills, Harris and Lambourne, *J. Chem. Soc.*, **119**, 1300 (1921).

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Grignard Reductions. IX.[1,2,3] Further Studies on the Reduction of Acid Halides

BY FRANK C. WHITMORE,[1] J. S. WHITAKER, W. A. MOSHER, O. N. BREIVIK, W. R. WHEELER, C. S. MINER, JR., L. H. SUTHERLAND, R. B. WAGNER, T. W. CLAPPER, C. E. LEWIS, A. R. LUX AND A. H. POPKIN

The discovery by F. L. Greenwood and H. M. Crooks of the quantitative reduction of trimethylacetyl chloride by *t*-butylmagnesium chloride to the corresponding primary alcohol[2] represents a new general reaction.[3]

Mechanism of the Reaction

The following steps are apparently involved in the action with a Grignard reagent R′MgX

$$\begin{tikzcd} & \mathrm{RCOR'} \arrow[dr] & \\ \mathrm{RCOCl} \arrow[ur] \arrow[r] & \mathrm{RCHO} \arrow[r] \arrow[d] & \mathrm{RCHOHR'} \\ & \mathrm{RCH_2OH} & \end{tikzcd}$$

The change RCOCl′ to RCOR′ has been observed in the preparation of pinacolone from acetyl chloride and *t*-butylmagnesium chloride[4] and on addition of primary Grignard reagents to primary acid chlorides[3a] and of tertiary Grignard reagents to primary, secondary, and tertiary acid chlorides.[2b,3a]

The reduction RCOR′ to RCHOHR′ is possible by means of Grignard reagents. Thus, methyl isopropyl ketone was reduced to the second-

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(1) The material here presented was originally submitted in about a dozen papers which gave full experimental details; received October 7, 1939.

(2) (a) Whitmore, *Rec. trav. chim.*, **57**, 563 (1938); (b) Greenwood, Whitmore and Crooks, THIS JOURNAL, **60**, 2028 (1938).

(3) Whitmore and co-workers, *ibid.*, **60** (1938); (a) Heyd, 2030; (b) Popkin, Whitaker, Matill and Zech, 2458; (c) 2462; (d) Meyer, Pedlow and Popkin, 2788; (e) Whitaker, Matill and Popkin, 2790; (f) Wheeler, 2899.

(4) Whitmore and Badertscher, *ibid.*, **55**, 1559 (1933).