[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Syntheses in the Quinoline Series. I. 2-Hydroxy- and 2-Chloroquinolinearsonic Acids

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This investigation deals with the preparation of several quinoline amines and quinoline arsonic acids, most of the amines being produced by the catalytic reduction of certain nitroquinolines and most of the arsonic acids by diazotization of these amines and subsequent treatment with sodium arsenite. 2-Hydroxyquinolinearsonic and 2-chloroquinolinearsonic acids are given extensive consideration.

The 2-hydroxy-4-methyl-7-aminoquinoline used in this investigation was prepared according to the procedure of Besthorn and Byvanck[2] by condensing *m*-phenylenediamine with ethyl acetoacetate. The proof of structure of this product follows from its conversion to 2-chloro-4-methyl-7-methoxyquinoline, which was originally obtained by another method.[3] This structure was further confirmed in our experimental work by its conversion to 2-hydroxy-4-methyl-7-chloroquinoline.[4]

2-Chloroquinolines have been prepared by the replacement of hydroxyl through the use of phosphorus pentachloride and phosphorus oxychloride. Hydrochloric acid was found to hydrolyze 2-chloroquinoline-8-arsonic acid to give 2-hydroxyquinoline-8-arsonic acid.

2-(β-Ethoxyethoxy)-quinoline derivatives were made from 2-chloroquinolines by the use of ethylcellosolve to which had been added metallic sodium.

Experimental

2-Chloro-4-methyl-7-methoxyquinoline was prepared by treating 2-chloro-4-methyl-7-hydroxyquinoline, obtained from 2-hydroxy-4-methyl-7-aminoquinoline according to the method of Besthorn and Byvanck,[2] in 10% by weight sodium hydroxide solution with dimethyl sulfate as well as by refluxing 2-hydroxy-4-methyl-7-methoxyquinoline with phosphorus oxychloride.[3]

Nitroquinolines.—**5-Nitroquinoline** was obtained in a 32% yield by nitrating quinoline sulfate and in a much poorer yield by subjecting *m*-nitroaniline to the conditions of the Skraup reaction. A slight modification of the method of Meigen[5] proved satisfactory for the nitration of quinoline sulfate and for the separation of the isomers formed during the nitration. **6-Nitroquinoline** in a 45% yield and **7-nitroquinoline** in a 5% yield were produced by the method of Knueppel,[6] the procedure of Kochanska and Bobranski[7] being used for the isolation of the 7-nitroquinoline rather than that given by Knueppel.

2-Hydroxyquinolines.—Ten grams of 5-nitroquinoline, dissolved in 50 ml. of water by the addition of sulfuric acid, was poured into 2 liters of water at 60°. Sodium hydroxide solution was added until the *p*H was just sufficient to keep the nitroquinoline in solution. Upon introducing, with stirring, a 5.25% by weight solution of sodium hypochlorite, a solid began to appear. After standing overnight, filtering off the solid, digesting it with 10% by weight sodium hydroxide solution and making acid with sulfuric acid, an 85% yield of **2-hydroxy-5-nitroquinoline** precipitated.[8] When 6-nitroquinolinoline was treated in a similar manner and the resulting product recrystallized from glacial acetic acid, a 46% yield of **2-hydroxy-6-nitroquinoline** was obtained. An 85% yield of **2-hydroxy-7-nitroquinoline** likewise resulted from 7-nitroquinoline.

2-Hydroxyaminoquinolines.—**2-Hydroxy-4-methyl-7-aminoquinoline** in 45 to 60% yields was obtained by heating 30 g. of dry crystalline *m*-phenylenediamine and 37.8 ml. of ethyl acetoacetate in an autoclave at 130° for nineteen hours. Almost quantitative yields of **2-hydroxy-5-aminoquinoline** and **2-hydroxy-7-aminoquinoline** were obtained by the catalytic reduction of 2-hydroxy-5-nitroquinoline in 95% ethanol and 2-hydroxy-7-nitroquinoline in acetone, respectively, using Raney nickel catalyst.

2-Chloroaminoquinolines.—The catalytic reduction of an acetone solution of 2-chloro-5-nitroquinoline at 50° gave an almost quantitative yield of **2-chloro-5-aminoquinoline.** The amine was isolated by partial distillation of the acetone and the addition of water to the concentrated solution resulting. Recrystallization from dilute ethanol-water solution gave long, slender, light green colored needles belonging to the orthorhombic system; soluble in acetone, ethanol, benzene, diethyl ether and acids; m. p. 110–111° (corr.).

Anal. Calcd. for $C_9H_7ClN_2$: N, 15.67; Cl, 19.88. Found: N, 15.60; Cl, 19.72.

Dry 2-chloro-6-nitroquinoline was dissolved in a small quantity of cold hydrochloric acid (sp. gr. 1.19) and the amount of dry powdered stannous chloride calculated for complete reduction added slowly with stirring. The tin double salt, that formed upon standing, was filtered off on a dry filter, dried and dissolved in a small amount of water. After making acid, bringing to the boiling temperature and saturating with hydrogen sulfide, the tin sulfide was removed by filtration. The filtrate was neutralized with ammonium hydroxide, concentrated by evapora-

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(1) Parke, Davis and Company Fellow.

(2) Besthorn and Byvanck, *Ber.*, **31**, 798 (1898).

(3) Späth and Brunner, *ibid.*, **57B**, 1243 (1924).

(4) Soc. Anon. pour l'ind. Chim. à Bâle, German Patent 556,324 (1930); *C. A.*, **26**, 5573 (1932).

(5) Meigen, *J. prakt. Chem.*, [2] **77**, 472 (1908).

(6) Knueppel, *Ber.*, **29**, 703 (1896).

(7) Kochanska and Bobranski, *ibid.*, **69B**, 1809 (1936).

(8) See Claus and Setzer, *J. prakt. Chem.*, [2] **53**, 390 (1896); Einhorn and Lauch, *Ber.*, **19**, 53 (1886); *Ann.*, **243**, 342 (1888).

	Name	Crystalline form	% yield	M. p., °C. (corr.)	Formula	As analyses, %[10] Calcd.	Found
1	2 - Hydroxy - 4 - methylquinoline-7-arsonic acid	Orthorhombic plates	31	...	$C_{10}H_{10}AsNO_4 \cdot H_2O$	24.88	24.83
2	1 Anhydrous	....	..	...	$C_{10}H_{10}AsNO_4$	26.48	26.44
3	Sodium salt of 1	Tetragonal granules	88	...	$C_{10}H_9AsNNaO_4 \cdot 2H_2O$	21.97	22.07
4	3 Anhydrous	....	..	...	$C_{10}H_9AsNNaO_4$	24.56	24.47
5	2 - Hydroxyquinoline - 5 - arsonic acid	Tetragonal plates	23	...	$C_9H_8AsNO_4 \cdot H_2O$	26.11	26.00
6	5 Anhydrous	....	..	...	$C_9H_8AsNO_4$	27.85	27.70
7	2 - Hydroxyquinoline - 7 - arsonic acid	Orthorhombic needles	13	...	$C_9H_8AsNO_4$	27.85	28.00
8	2 - Hydroxyquinoline - 8 - arsonic acid	Orthorhombic needles	Quant.	...	$C_9H_8AsNO_4$	27.85	28.00
9	2 - Chloro - 4 - methylquinoline-7-arsonic acid	Orthorhombic needles	7	192	$C_{10}H_9AsClNO_3$	24.86	24.90
10	2 - Chloroquinoline - 5 - arsonic acid	Orthorhombic needles	24	...	$C_9H_7AsClNO_3$	26.07	26.10
11	2 - Chloroquinoline - 6 - arsonic acid	Orthorhombic needles	18	...	$C_9H_7AsClNO_3$	26.07	26.00
12	2 - Chloroquinoline - 8 - arsonic acid	Orthorhombic needles	11	273–276	$C_9H_7AsClNO_3$	26.07	26.12
13	2-(β-Ethoxyethoxy)-4-methylquinoline-7-arsonic acid	Monoclinic needles	59	183	$C_{14}H_{18}AsNO_5$	21.11	21.20
14	2 - (β - Ethoxyethoxy) - quinoline-5-arsonic acid	Flat prisms	90	172	$C_{13}H_{16}AsNO_5$	21.96	22.00

tion and cooled. **2-Chloro-6-aminoquinoline** precipitated as long, slender, light yellow colored needles belonging to the orthorhombic system; soluble in ethanol, acetone, hot water, warm petroleum ether, diethyl ether and benzene; m. p. 149° (corr.); yield, 67% of the theoretical.

Anal. Calcd. for $C_9H_7ClN_2$: N, 15.67; Cl, 19.88. Found: N, 15.70; Cl, 19.75.

Catalytic reduction of 2-chloro-8-nitroquinoline[9] in absolute ethanol under the same conditions used for reducing 2-chloro-5-nitroquinoline gave **2-chloro-8-aminoquinoline.** After concentrating the alcoholic solution of the amine by distillation and adding water to the resulting concentrated solution, an oil separated; this crystallized upon standing. Recrystallization from dilute ethanol–water solution gave light green colored (almost white) needle-like leaflets, soluble in ethanol, acetone, warm benzene and acids, m. p. 84° (corr.), yield, 98% of the theoretical.

Anal. Calcd. for $C_9H_7ClN_2$: N, 15.67; Cl, 19.88. Found: N, 15.70; Cl, 19.75.

2-Hydroxyquinolinearsonic Acids.—Crushed ice was added to a solution of 0.16 mole of the hydroxyquinoline amine in 2 moles of hydrochloric acid. When a temperature below 5° had been attained, the amine was diazotized with sodium nitrite solution. After making just basic to litmus paper by the careful addition, in the presence of ice with stirring, of 5 *N* sodium hydroxide solution, the diazotized solution was poured slowly with good mechanical mixing into a water solution of 26 g. of sodium metaarsenite to which previously had been added 5–6 ml. of a saturated water solution of copper sulfate. After being stirred for one hour and having stood overnight, the resulting mixture was brought slowly to the boiling temperature and boiled for five minutes. This hot mixture was filtered and the filtrate carefully neutralized with hydrochloric acid. Upon charcoaling this neutral solution, evaporating until a volume of 350 ml. remained, and making acid to Congo red paper with hydrochloric acid, the crude hydroxyquinolinearsonic acid precipitated. When this acid was dissolved in a small quantity of hot dilute sodium hydroxide solution, 3% hydrogen peroxide solution added, the solution boiled for five minutes and made acid to Congo red paper with hydrochloric acid, the pure acid precipitated.

Hydrolysis resulted when 2-chloroquinoline-8-arsonic acid was heated in an autoclave with 12 parts by weight of hydrochloric acid (sp. gr. 1.19) at 125° for one and one-half hours, and 2-hydroxyquinoline-8-arsonic acid was obtained.

When a solution of 2-hydroxy-4-methylquinoline-7-arsonic acid in one equivalent of hot sodium hydroxide solution was added dropwise to cold 95% ethanol in a container fitted with a mechanical stirrer, the monosodium salt of 2-hydroxy-4-methylquinoline-7-arsonic acid precipitated.

2-Chloroquinolinearsonic Acids.—The 2-chloroquinolinearsonic acids were prepared from the corresponding 2-chloroaminoquinolines by a slight modification of the method used for synthesizing the 2-hydroxyquinolinearsonic acids. Instead of neutralizing the diazotized solution of the amine before it was added to the arsenite solution, enough alkali was added to the arsenite solution to neutralize exactly the acid in which the amine was dissolved, and the diazotized amine was added directly.

2 - (β-Ethoxyethoxy) - 4 - methylquinoline - 7 - arsonic Acid.—Five-tenths gram of dry 2-chloro-4-methylquinoline-7-arsonic acid was refluxed with a solution of 0.60 g. of clean dry sodium in 50 ml. of ethylcellosolve for two and one-half hours. After cooling and filtering, the filtrate was made neutral to litmus paper by the careful addition of hydrochloric acid (sp. gr. 1.19). The sodium chloride

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[9] Fischer and Guthmann, *J. prakt. Chem.*, [2] **93**, 378 (1916).

[10] See Cislak and Hamilton, THIS JOURNAL, **52**, 638 (1930).

formed was filtered off and the filtrate diluted with 50 ml. of water. When this was evaporated on a hot-plate until 25 ml. remained and made acid to Congo red paper with hydrochloric acid, 2-(β-ethoxyethoxy)-4-methylquinoline-7-arsonic acid precipitated.

2-(β-Ethoxyethoxy)-quinoline-5-arsonic acid was obtained from 2-chloroquinoline-5-arsonic acid by the same method used in preparing 2-(β-ethoxyethoxy)-4-methylquinoline-7-arsonic acid.

Summary

1. It was proved that 2-hydroxy-4-methyl-7-aminoquinoline rather than 2-hydroxy-4-methyl-5-aminoquinoline resulted when equimolecular quantities of *m*-phenylenediamine and ethyl acetoacetate condensed in an autoclave at 130°.

2. A number of quinoline amines were produced by the reduction of nitroquinolines.

3. Several 2-hydroxyquinoline and 2-chloroquinolinearsonic acids were obtained from the corresponding quinoline amines by diazotization and coupling with sodium arsenite. The monosodium salt of 2-hydroxy-4-methylquinoline-7-arsonic acid was made.

4. The hydrolysis of 2-chloroquinoline-8-arsonic acid resulted in the formation of 2-hydroxyquinoline-8-arsonic acid.

5. 2-Chloro-4-methylquinoline-7-arsonic acid and 2-chloroquinoline-5-arsonic acid reacted with the monosodium salt of ethylcellosolve to give 2-(β-ethoxyethoxy)-4-methylquinoline-7-arsonic acid and 2-(β-ethoxyethoxy)-quinoline-5-arsonic acid, respectively.

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The Viscosity Function

BY E. P. IRANY

Viscosity is well defined as a physical quantity and accurately measurable. Yet, so far, its relations to temperature, pressure, dilution, chemical constitution, and so forth, are somewhat obscure.

Numerous empirical rules have been proposed but none of them can claim general validity or real physical significance. It may even be questioned whether the task of formulating the exact viscosity laws is not far beyond our present knowledge of the liquid state as such.

It is the main purpose of this paper to offer evidence that such laws exist and can be expressed. Of course, without reliable mathematical assumptions, explicit formulas cannot be derived; the method adopted is one of graphical analysis. It will be shown that, if applied to the large number of measurements and data already available in the literature, this method reveals in them fundamental but so far undiscovered regularities.

Viscosity may be considered a form of friction if the latter is explained in terms of internal forces. Few molecules—probably none—are in so perfect equilibrium that no attractions would be active between them. These forces are chemical by nature though not in intensity, and it is obvious that they are the cause of the mutual interference with motions and mobility of the molecules which is observable as viscosity. The effect may vary between actual chemical union, association, and mere transitory attraction.

For considerations of viscosity the usual distinction between associated and non-associated liquids is only secondary. It is conceivable that a substance may be so perfectly associated that in its larger complexes all residual forces are well compensated; reversely, in a non-associated liquid the identity of the molecules as the structural units may be preserved, but not their independent mobility. Hence, the fundamental distinction should rather be drawn between "ideal" and "non-ideal" conditions, depending not only on existence and magnitude of the intermolecular forces but, primarily, on their constancy. What the mobile entities are—molecules or molecular complexes of some kind—is immaterial as long as problems of internal constitution are not dealt with; for the time being, these must be left outside the scope of this investigation.

The supposed general law of viscosity can only appear in substances of constant structure and force disposition. The question now arises as to where to find and how to recognize "ideal" liquids which may serve as objects of study. Experimental proof of "ideality" such as, *e. g.*, derived from other physical properties, is of doubtful value because it seems that viscosity is still very sensi-