Reactions of Quinaldil and its Related Compounds with Alkali. I. Quinaldil and Phenyl-2-quinolyl Diketone

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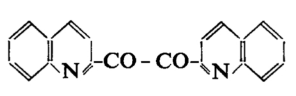
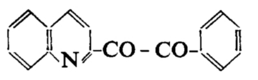
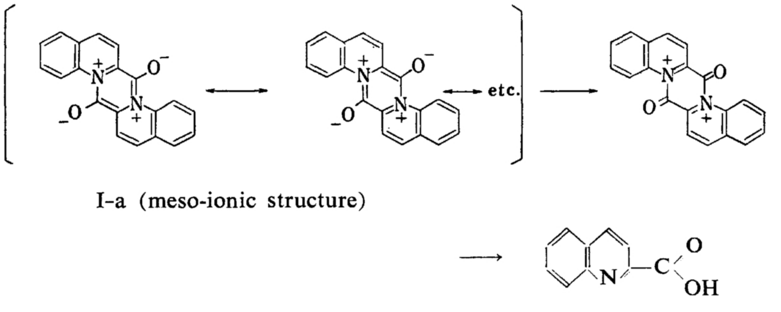
Previous investigations[1,2] have shown that under the action of aqueous alkali, the pyridil containing 2- or 4-pyridyl group was subjected to the fission of the C-C bond of dicarbonyl and simultaneously the decomposition of these groups, accompanied with the evolution of ammonia. In the present paper, the reaction of quinaldil (I) or phenyl-2-quinolyl diketone (II) with alkali was investigated, and compared with that of pyridil.


I

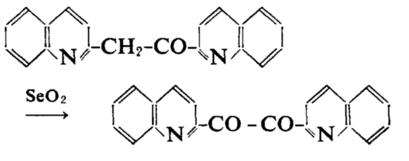

II

Hammick and Brown[3] have reported that I reacts with aqueous alkali to yield 60% of quinaldic acid. From this fact and some other properties of I, i. e., its high melting point, its low solubility and its lack of properties associated with the carbonyl group, these investigators have proposed a meso-ionic structure named "Quinocoll" for I, instead of the usual benzil structure and suggested that the structure I-a, similar to that of a quinol ion, should readily undergo autoxidation to yield a quinone, which is the cation of an acylquinolinium hydroxide and hence would be expected to hydrolyse readily to quinaldic acid:


I-a (meso-ionic structure)

Buehler and Harris[4], however, have obtained different results that I forms various carbonyl derivatives, and its infrared absorption spectrum has the characteristic CO band, and so they doubted the validity of the structure I-a, but did not refer to the reaction with alkali.

Now, in order to confirm the structure of I, it was independently prepared from desoxyquinaldoin as follows:



and compared with Hammick's "Quinocoll" and usual "Quinaldil". Then, all these products were proved to be identical with each other in melting point, mixed melting point and infrared absorption spectrum respectively. This means the validity of benzil structure of I and thus Hammick's explanation about the reaction of I with alkali seems to be inadequate. II was also prepared from phenacyl quinaldine by the same way as above.

These diketones were reacted with alkali under several conditions shown in Tables I and II. In these reactions, the evolution of ammonia observed in pyridil did not occur at all. I was certainly found to afford quinaldic acid as Hammick had reported, while in II benzoic acid was alternatively obtained in about 90% yield. These results seem to be quite

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[1] D. Oda, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **82**, 478 (1961).

[2] D. Oda, ibid., **82**, 480 (1961).

[3] D. Ll. Hammick and B. R. Brown, *J. Chem. Soc.*, **1950**, 628.

[4] C. A. Buehler and J. O. Harris, *J. Am. Chem. Soc.*, **72**, 5015 (1950).

TABLE I. REACTION OF QUINALDIL (I) WITH ALKALI

Sample	Conditions			Products		
Quinaldil g.	Temp. °C	Time hr.	Atmosphere	Quinaldic acid, g.	III g.	Hydroquinaldoin, g.
3.1	20	2	N_2	1.3	1.1	0.18
3.1	50	1	N_2	1.3	1.3	0.20
3.1	80	1	—	1.5	1.1	0.20

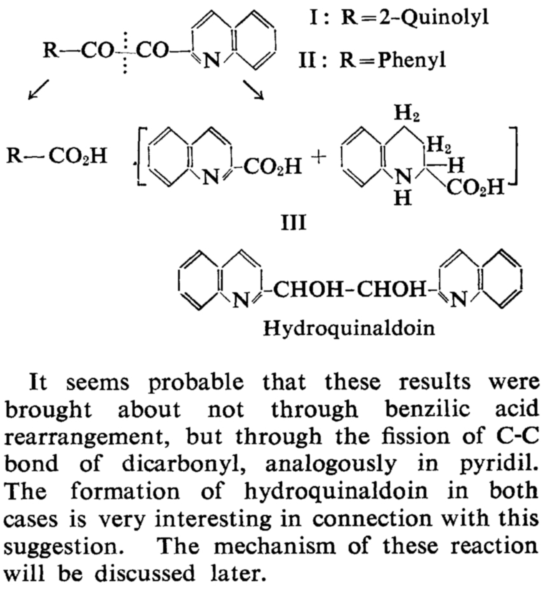
TABLE II. REACTION OF PHENYL-2-QUINOLYL DIKETONE (II) WITH ALKALI

Sample	Conditions			Products		
Diketone g.	Temp. °C	Time hr.	Atmosphere	Benzoic acid, g.	III g.	Hydroquinaldoin, g.
3.2	20	5	N_2	1.2	1.1	0.05
3.2	50	2	N_2	1.3	1.4	0.08
3.2	50	2	—	1.3	1.3	0.07
3.2	80	1	—	1.3	1.1	0.05

parallel to the facts that picolic acid was obtained from 2, 2′-pyridil and that benzoic acid was obtained from phenyl-2-pyridyl diketone, each as main product. So these carboxylic acids should be derived from the half parts of the diketones respectively, and also indicated not to be yielded through oxydative cleavage of these diketones as Hammick described, because in either nitrogen atmosphere or not, the results obtained were shown to be scarcely affected.

In addition to these carboxylic acids, a red-orange compound III and small amount of hydroquinaldoin were obtained from I or II equally. III is an acidic compound, soluble in both acid and alkali and easily reduces Tollens' reagent at room temperature. Its melting point was not clear, i. e. 130∼135°C, even after repeated crystallizations from benzene or water. A mixture of III and quinaldic acid melted at 120∼150°C, so it might be suggested that III consists of quinaldic acid and other compounds; the latter may be of reducing property with color. On the other hand, the elementary analysis and molecular weight determination revealed that the formula of III closely resembled to $C_{10}H_9O_2N$, for example that of dihydroquinaldic acid, though III was much more stable than other dihydro compounds. Direct benzoylation or acetylation of III yielded only dark red resinous paste, from which not any compound could be isolated. However, preliminary esterification of III and then benzoylation of the resulting viscous oil yield methyl 1-benzoyl-1, 2, 3, 4-tetrahydroquinaldate and methyl quinaldate, so it was suggested that III contained 1, 2, 3, 4-tetrahydroquinaldic acid (IV) and quinaldic acid. In fact, it was found that when the aqueous solutions of equi-molecular amounts of IV and quinaldic acid were mixed, a red color immediately appeared and a red-orange compound was precipitated. It was identical with III, in melting point and other properties. These results indicate that III consists of IV and quinaldic acid; III might be an addition compound of these components.* Hammick and Brown have experimented in a small scale (0.5 g. of I was treated) and isolated quinaldic acid as hydrochloride, which must also contain that of the component of III; for, according to their analytical procedure, only quinaldic acid hydrochloride was precipitated and IV remained in the acid solution.

Then, the reactions of these diketones are summarized as follows:



It seems probable that these results were brought about not through benzilic acid rearrangement, but through the fission of C-C bond of dicarbonyl, analogously in pyridil. The formation of hydroquinaldoin in both cases is very interesting in connection with this suggestion. The mechanism of these reaction will be discussed later.

Experimental

Quinaldil (I) from Desoxyquinaldoin.—Desoxyquinaldoin was prepared, according to the method

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* *N*-Phenyl glycine, the structure of which is analogous to IV, was also found to give a yellow compound on mixing with quinaldic acid.

of Weiss and Hauser[5], by the condensation of quinaldine and ethyl quinaldate with potassium amide in liquid ammonia. Recrystallization from dioxane gave yellow crystals, m. p. 218.5~220°C, yield 31.5% (lit.[4] 221°C).

Three grams of desoxyquinaldoin was dissolved in 50 cc. of hot dioxane and oxidized with 1.4 g. of selenium oxide under reflux and stirring for 4 hr. The liquid was filtered hot from precipitated selenium, and the latter washed with hot dioxane. After removal of the solvent from the combined filtrate in vacuo, ca. 20 cc. of saturated sodium bicarbonate solution was added to the resulting viscous oil. Acid contaminates were dissolved foaming and insoluble oil was solidified. The dark brown solid was collected, washed with water and recrystallized from pyridine to yield 2.2 g. (71%) of yellow-brown crystals, m.p. 265~272°C. Successive crystallizations from dioxane gave pale yellow needles, m. p. 271~272°C.

Found: C, 76.87; H, 3.92; N, 8.86. Calcd. for $C_{20}H_2O_2N_2$: C, 76.92; H, 3.84; N, 8.97%.

The product showed no melting point depression when mixed with that obtained by the decarboxylation of picolic acid in quinoline-2-aldehyde (Hammick's method) or by the oxidation of quinaldoin (Buehler's and usual method). The identity of these products was further confirmed by the comparison of their infrared absorption spectra which could be overlapped in every detail.

Phenyl-2-quinolyl Diketone (II).—Similarly as in the case of I, 19.1 g. of phenacylquinaldine prepared by the method of Weiss and Hauser[5] was oxidized with selenium oxide. After removal of the solvent and treatment of the residue with sodium bicarbonate solution, extraction of the resulting dark brown solid with hot ligroin yielded 9.9 g. (49%) of yellow crystals. Recrystallization from ligroin gave pale yellow crystals, m. p. 109~110°C.

Found: C, 77.84; H, 4.25; N, 5.35. Calcd. for $C_{17}H_{11}O_2N$: C, 78.14; H, 4.24; N, 5.36%.

Reaction of Quinaldil (I) with Alkali.—A typical procedure is as follows: to a suspension of 3.1 g. of I in 10 cc. of ethanol, a 30% aqueous solution of 3.1 g. of potassium hydroxide was added. The mixture was heated at 50°C under nitrogen atmosphere. The initially appearing red-brown color was gradually turned to light orange, while I disappeared and new precipitates began to deposit. After the reaction was continued for 2 hr., the precipitates were filtered, washed with water and dried, amounting 0.2 g. Recrystallization from pyridine gave colorless crystals, m. p. 215~217°C (decomp.). The melting point showed no depression when mixed with an authentic sample of hydroquinaldoin[4].

Found: C, 75.47; H, 5.03; N, 8.89. Calcd. for $C_{20}H_{16}O_2N_2$: C, 75.93; H, 5.10; N, 8.86%.

The filtrated was extracte with ether or chloroform. Evaporation of the solvent from the extract yielded but a little amount of residue, from which not any compound could be isolated. Acidification of the mother liquor to pH 3 with concentrated hydrochloric acid gave precipitates, which were washed with water, and dried, m. p. 110~114°C. The precipitates were boiled with ether and the solution was filtered while hot. Cooling the filtrate yielded 0.2 g. of pale orange crystals, m. p. 130~150°C. Recrystallization from benzene gave colorless crystals, m.p. 154~155°C, which were proved identical with quinaldic acid. The orange substance (1.3 g.) insoluble in ether was recrystallized from benzene and water to give beautiful red-orange crystals III, which melted at 130~135°C. Repeated crystallization could not improve the melting point. A mixture of this compound and quinaldic acid melted at 120~150°C. Analytical results were shown below together with reference data:

	C, %	H, %	N, %	Mol.	wt.
Found:	68.69	5.12	7.81	180.2	(Rast)
	68.68	5.24	7.88	182.6	(titration)
Calcd. for					
$C_{10}H_7O_2N$: (quinaldic acid)	69.36	4.07	8.09	173.17	
$C_{10}H_9O_2N$:	68.56	5.17	7.99	175.19	

To the weak acid filtrate from these compounds a saturated aqueous solution of cupper sulfate was added. Green-blue cupper salt was precipitated, washed with water and treated with hydrogen sulfide. The filtrated from the precipitated cupper sulfide was evaporated to dryness in vacuo to give a pale orange residue (1.2 g.), which melted at 120~150°C and consisted mostly of quinaldic acid.

Reaction of Phenyl-2-quinolyl Diketone (II) with Alkali.—The procedure is substantially the same as used with I: in the reaction mixture there was also an insoluble substance, which melted at 215~217°C and was found identical with hydroquinaldoin by the mixed melting point determination.

Found: N, 8.92. Calcd. for $C_{20}H_{16}O_2N_2$: N, 8.86%.

The precipitates obtained by acidification (pH 3) of the filtrate were boiled with petroleum ether and the solution was filtered while hot. Cooling the filtrate gave colorless crystals, m. p. 120~121°C, which were proved to be identical with benzoic acid. The insoluble fraction in petroleum ether was recrystallized from water to give red-orange crystals, which melted at 130~135°C and were found identical with III obtained in the case of I. From the weak acid filtrate, a small amount of quinaldic acid was detected via the cupper salt.

Formation of Methyl 1-Benzoyl-1, 2, 3, 4-tetrahydroquinaldate and Methyl Quinaldate from (III).—A solution of 1.5 g. of III in 20 cc. of absolute methanol was saturated with dry hydrogen chloride. After standing at room temperature for 24 hr. the mixture was concentrated in vacuo and the residue was poured into about 10 cc. of ice water. The solution was made alkaline with sodium bicarbonate, the separating oil was taken up in ether and dried over anhydrous sodium sulfate. The ether was distilled off and 1.1 g. of viscous brown oil was obtained which did not solidify even after standing in the refrigerator for 2 days. The oil was dissolved in 10 cc. of pyridine, then 1 g. of freshly distilled benzoyl chloride was added and the mixture allowed to stand at room temperature for 4 days under

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[5] M. J. Weiss and C. R. Hauser, *J. Am. Chem. Soc.*, 71, 2023 (1949).

seal. After removal of the solvent in vacuo, the residue was poured into excess of sodium bicarbonate solution and the mixture was extracted with ether, washed with dilute hydrochloric acid, and sodium bicarbonate solution, and dried over anhydrous sodium sulfate. On evaporation of ether, there remained 0.4 g. of semi-solid substance. The product was boiled with petroleum ether and the solution filtered while hot. Cooling the filtrate gave colorless crystals which melted at 78~80°C. Recrystallization from petroleum ether improved the melting point to 81~82°C, which showed no depression, when mixed with an authentic sample of methyl quinaldate.

Found: N, 7.59. Calcd. for $C_{11}H_9O_2N$: N, 7.49%.

The semi-solid insoluble in petroleum ether was pressed on a clay plate and recrystallized from a ligroin-benzene mixture (1 : 1) to give long crystals, which melted at 109.5~110.5°C when alone and admixed with an authentic sample of methyl 1-benzoyl-1, 2, 3, 4-tetrahydroquinaldate[6].

Found: C, 73.00; H, 5.63; N, 4.74. Calc. for $C_{18}H_{17}O_3N$: C, 73.54; H, 5.80; N, 4.75%.

Formation of III from Quinaldic Acid and 1, 2, 3, 4-Tetrahydroquinaldic Acid.—A solution of 2.1 g. (0.01 mol.) of pure 1, 2, 3, 4-tetrahydroquinaldic acid hyrochloride[6] in 10 cc. of water was brought to pH 3 with sodium bicarbonate, and 1.7 g. (0.01 mol.) of quinaldic acid was dissolved in 10 cc. of hot water. When both solutions were combined, red color immediately appeared, and then a red-orange compound was precipitated, washed with a little water and dried, m. p. 125~133°C. Recrystallization from water gave beautiful red-orange crystals, m. p. 130~135°C. The melting point showed no change when admixed with the reaction product of the diketone with alkali.

Summary

In the reaction of quinaldil or phenyl-2-quinolyl diketone with alkali, the fission of C-C bond of dicarbonyl occurred and from the half part of diketone common to each, a red-orange compound and a small amount of hydroquinaldoin were obtained and the other half gave the corresponding acid. The colored compound was found to be consisting of quinaldic acid and 1, 2, 3, 4-tetrahydroquinaldic acid. These results refuse to accept Hammick's explanation about the reaction of quinaldil with alkali, in which there is a mistake fundamentally.

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[9] H. Wieland, et al., *Ber.*, **61**, 2371 (1928).