The Reaction of Quinoline 1-Oxide with 1,3-Diketones

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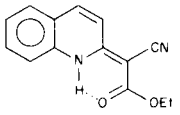
We recently reported (1) that ethyl-α-(2-quinolyl)-cyanoacetate, the product of the reaction of quinoline 1-oxide with ethyl cyanoacetate in the presence of acetic anhydride (2), exists exclusively in the tautomeric intramolecularly hydrogen-bonded form **1**.



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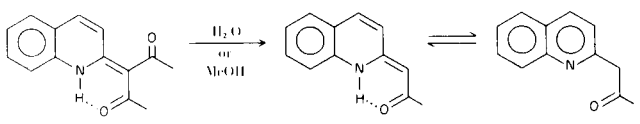
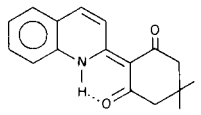
In order to test the generality of this structural preference, several related 2-substituted quinolines were synthesized in which the substituents were derived from 1,3-diketones. 2,4-Pentanedione and 5,5-dimethyl-1,3-cyclohexanedione (dimedone) were selected to complement the known reactivity of 1,3-indanedione (2).

The reaction of 2,4-pentanedione with quinoline 1-oxide in acetic anhydride is quite exothermic (and indeed is best done at 0°), however, the only isolable product proved to be 2-quinolylacetone (**3**) rather than the expected diketone **2**. Even when the system is carefully protected from moisture and when methanol, rather than water is used to remove unreacted acetic anhydride, compound **3** remains the only product. It is reasonable to postulate that **2** is the immediate product of the reaction, but that it is quite susceptible to acid-catalyzed cleavage in the presence of either water or methanol. Based upon its nmr spectrum (*ca.* 20% w/v deuteriochloroform), 2-quinolylacetone is a tautomeric mixture containing 73% quinolylidene ketone (**3a**) and 27% quinaldyl ketone (**3b**) (3). In view of its experimental simplicity and reasonable yields, this reaction appears to have advantages over previously reported methods for preparing 2-quinolylacetone (4).



2 3a 3b



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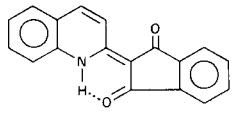

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Dimedone was found to react in the expected manner to give the previously unreported 2-(2-quinolyl)-5,5-dimethyl-1,3-cyclohexanedione, which judging from its spectra exists entirely in the intramolecularly hydrogen-bonded form (**4**).

The nmr spectra of **3** and **4**, along with that of the known (**5**) compound quinophthalone (5), have two particularly distinctive features (see Table I): (a) a far downfield singlet due to the intramolecularly hydrogen-bonded proton, and (b) a doublet (half of an AB pattern) due to 3-H on the quinoline ring whose position is markedly dependent upon the nature of the 2-substituent. These features are most striking in compound **4**, in which the hydrogen-bonded proton is unusually far downfield (δ 18.1) and 3-H appears 1.95 ppm downfield from its position in quinoline (δ 7.26). The latter deshielding effect is undoubtedly due to the close proximity of the free carbonyl group to 3-H (6).

TABLE I

Table of 60 MHz Proton Nmr Data

Compound	δ, ppm ($CDCl_3$, TMS) N . . H . . O	3-H	4-H	J_{34} (Hz)
3a	14.8	6.50	8.03	8.5
4	18.1	9.21	8.12	9.5
5	14.1	8.58	8.02	8.0

EXPERIMENTAL

2-Quinolylacetone (**3**).

Acetylacetone (4.0 g., 40 mmoles) was added dropwise over a period of ½ hour to a stirred, ice-cold solution of 5.8 g. (40 mmoles) of anhydrous quinoline 1-oxide dissolved in 8.2 g. (80 mmoles) of acetic anhydride. The resulting deep red solution

was allowed to warm to room temperature and to stand overnight. After adding 10 ml. of water and warming the mixture at 50° for ½ hour, the volatile liquids were removed on a rotary evaporator by means of the toluene azeotropes. The semi-solid residue was triturated with 5 ml. of cold ether and the remaining solid was recrystallized from cyclohexane to yield 5.1 g. (68%) of yellow needles, m.p. 77-78° (reported (4) m.p. 76-77°).

2-(2-Quinolyl)-5,5-dimethyl-1,3-cyclohexanedione (**4**).

A solution of 5.6 g. (40 mmoles) of dimedone dissolved in 120 ml. of chloroform was added over a period of an hour to a stirred solution of 5.8 g. (40 mmoles) of quinoline 1-oxide in 8.2 g. (80 mmoles) of acetic anhydride. The resulting solution was heated under reflux for 4 hours and then allowed to stand at room temperature overnight. Ten ml. of water was added and the volatiles were removed as described in the previous experiment. The residue was recrystallized from 95% alcohol to afford 5.5 g. (52%) of yellow flakes, m.p. 188-189°; ir (potassium bromide) 1690 (free C=O) and 1635 cm^{-1} (H-bonded C=O); uv max (chloroform) 282 (log ϵ 3.93), 385 (4.28), and 428 nm (4.15).

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.34; H, 6.41; N, 5.24. Found: C, 76.16; H, 6.48; N, 5.30.

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(3) For detailed discussion of the tautomeric composition of this and related compounds see (a) M. Yamazaki, N. Koda, and M. Hamana, *Chem. Pharm. Bull. (Tokyo)*, **18**, 908 (1970); (b) R. Mondelli and L. Merlini, *Tetrahedron*, **22**, 3253 (1966); and (c) G. Klose and E. Uhlemann, *ibid.*, **22**, 1373 (1966).

(4a) J. F. Wolfe and T. P. Murray, *J. Org. Chem.*, **36**, 354 (1971); (b) T. Okamoto and H. Takayama, *Chem. Pharm. Bull. (Tokyo)*, **11**, 514 (1963).

(5) See B. K. Manukian, P. Niklaus, and H. Ehrsam, *Helv. Chim. Acta.*, 52, 1259 (1969), for earlier references to and a discussion of the nmr spectrum of the long known compound quinophthalone (**5**).

(6) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", Pergamon Press, Elmsford, N. Y., 1969, pp. 91-92 and 200-207.