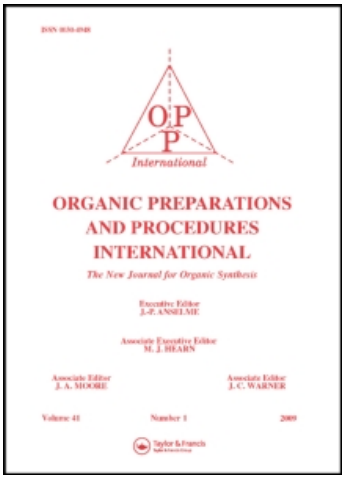

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A SIMPLE PREPARATION OF 6-CHLORO-5, 8-QUINOLINEDIONE

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OPPI BRIEFS

A SIMPLE PREPARATION OF 6-CHLORO-5,8-QUINOLINEDIONE

Submitted by Arthur Haber*†
(02/05/86)

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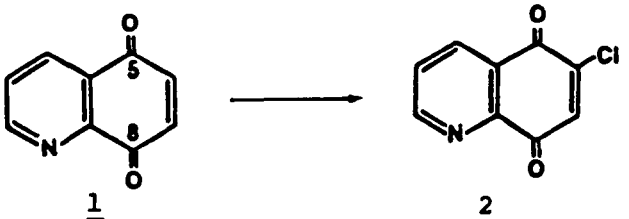
The reported method for the synthesis of the title compound (1) via a Skraup reaction on 4-chloro-2-nitroaniline[1] appeared unnecessarily long and tedious.[2] We have developed a simple and highly regioselective preparation of 6-chloro-5,8-quinolinedione (1) from 5,8-quinolinedione (2) by utilizing an observation made by Pratt and Drake.[2] Addition of dry hydrogen chloride to a benzene solution of 5,8-quinolinedione afforded an intermediate chlorohydroquinone, which was isolated rapidly and oxidized by ferric chloride to 1; the by-product 7-chloro-5,8-quinolinedione (7% of the total product) was removed by precipitation. The isomeric chloroquinolinediones can be easily separated from each other and from the parent 5,8-quinolinedione by TLC on silica gel.



1 2

EXPERIMENTAL SECTION

7-Chloro-5,8-quinolinedione and 2 were prepared from 8-hydroxyquinoline in yields of 25% and 27%, respectively, as described.[2] Thin layer chromatographic analysis was performed with 20 x 20 cm x 250 micron Analtech silica gel GF Uniplates.

6-Chloro-5,8-quinolinedione (1).- A stirred mixture of 10.2 g (64.1 mmol) of 2 and 600 mL of azeotropically dried benzene was treated with a moderate

stream of hydrogen chloride for 3 hrs. The resulting precipitate was collected and transferred to a separatory funnel containing 250 mL of chloroform, 71 g of ferric chloride hexahydrate, 125 mL of water, and 25 mL of conc. hydrochloric acid. After shaking for 1 min, the layers were separated. The aqueous phase was extracted again with chloroform, and the combined organic phase was dried (anhydrous magnesium sulfate), filtered, and concentrated. Precipitation of 1 by the addition of excess hexane afforded 7.0 g (56%) of yellow solid, mp. 176° (dec.), lit.[2] 187° (dec.). IR (KBr): 1680, 1665, 1597 cm^{-1}. PMR (300 MHz, rel to TMS): δ 9.09 (H-2, dd, 4.7 Hz, 1.7 Hz), 8.52 (H-4, dd, 7.9 Hz, 1.7 Hz), 7.74 (H-3, dd, 7.9 Hz, 4.7 Hz), 7.40 (H-7, s). MS [70 eV, m/e (rel intensity)]: 195 (22), 193 (M^+, 51), 167 (14), 165 (44), 139 (10), 137 (33), 130 (59), 102 (100), 77 (66), 76 (51), 75 (52), 53 (43), 52 (18), 51 (38), 50 (66).

Anal. Calcd for $C_9H_4ClNO_2$: C, 55.84; H, 2.08; N, 7.24; Cl, 18.31

Found: C, 55.84; H, 2.10; N, 7.16; Cl, 18.53

After evaporation of the filtrate from above, the mother liquor weighed 1.60 g and consisted of 61% of 1 and 39% of 7-chloro-5,8-quinolinedione as determined by ^1H NMR (using peak at δ 7.40 for 1 and 7.32 for the other isomer). The R_f values on silica gel developed with dichloromethane-ethyl acetate (6:4) were: 1, 0.66; 2, 0.56; and 7-chloro-5,8-quinolinedione, 0.73.

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2. Y. T. Pratt and N. L. Drake, ibid., 82, 1155 (1960) and references cited therein.