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The Preparation of 5,8-Quinolinediol and 1,4-Acridinediol Derivatives[1)]

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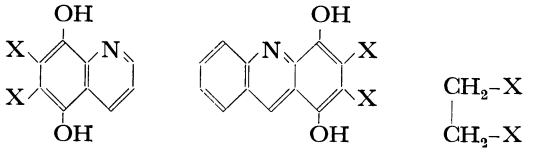
Synopsis. Compounds of 6,7-di X substituted 5,8-quinolinediol (X=$COOC_2H_5$; CN; $COCH_3$) have been prepared from diethyl pyridine-2,3-dicarboxylate and the respective active methylene compounds. Similarly, 2,3-di X substituted 1,4-acridinediol (X=$COOC_2H_5$) has been prepared.

In previous papers, it was reported that ethyl pyrazine-2,3-dicarboxylate and quinoxaline-2,3-dicarboxylate condensed with ethyl succinate to form 5,8-dihydroxyquinoxaline[2)] and 1,4-dihydroxyphenazine derivatives respectively. The condensation of pyridine 2,3-dicarboxylate or quinoline 2,3-dicarboxylate with a compound which has two adjacent active methylenes like ethyl succinate would lead to the formation of the analogous rings. Both 5,8-quinolinediol[3)] and 1,4-acridinediol derivatives contain an oxine-type structure and are expected to form a metal chelate.[4)] Quinolino-5,8-quinone and its dioxime are also interesting in their bacteriostatic properties.[5)]



I: X=$COOC_2H_5$ IV: X=$COOC_2H_5$ V: X=$COOC_2H_5$
II: X=CN VI: X=CN
III: X=$COCH_3$ VII: X=$COCH_3$

Thus, 6,7-di X substituted 5,8-quinolinediols (I: X=$COOC_2H_5$, II: X=CN, III: X=$COCH_3$) have been prepared from diethylpyridine 2,3-dicarboxylate and the respective active methylene compounds (V, VI, VII) by procedure analogous to that previously reported.[2)] Similarly, the condensation of diethyl quinoline-2,3-dicarboxylate with ethyl succinate gave diethyl 1,4-dihydroxyacridine-2,3-dicarboxylate (IV: X=$COOC_2H_5$). However, the analogous compounds of IV, X=CN and X=$COCH_3$, were not obtained under similar conditions. The oxidation of I and IV with silver oxide gave the corresponding quinoline 5,8-quinone and acridino-1,4-quinone respectively.

Experimental

Diethyl 5,8-dihydroxyquinoline-6,7-dicarboxylate (I). Procedure A: A mixture of 2.23 g (0.010 mol) of diethyl pyridine-2,3-dicarboxylate, 1.92 g (0.011 mol) of diethyl succinate, and 0.50 g (0.022 mol) of powdered sodium in 6 ml of xylene was heated at 110 °C under stirring and with moisture excluded. If the reaction did not start within ten minutes after stirring, a few drops of ethanol were added; then the reaction definitely began and the solution turned reddish brown and viscous. After an hour the solution was cooled and most of the unreacted sodium was destroyed by the addition of ethanol; then the mixture was acidified with hydrochloric or acetic acid. The mixture was extracted twice with 10 ml portions of xylene, and the solvent was removed by steam distillation. The residue from steam distillation was filtered and washed with water. Yield, 2.2 g (73.7%). Pale yellow needles (from methanol); mp 112.5—113 °C. It forms reddish precipitates in concentrated aqueous sodium hydroxide and turns yellow with concentrated sulfuric acid. Found: C, 58.58; H, 4.95; N, 4.63%. Calcd for $C_{15}H_{15}O_6N$ (I): C, 59.01; H, 4.95; N, 4.59%. IR: (KBr) ~3420 (OH), 1730 (C=O) cm^{-1}.

Diacetate of I: mp 162.5—163 °C. Colorless pillows (from ethanol); Found: N, 3.62%. Calcd for $C_{19}H_{19}O_8N$: N, 3.60% IR: 1775 (OAc), 1725 (C=O) cm^{-1}. *Dibenzoate of I*: mp 183—183.5 °C. Colorless needles (from ethanol); Found: N, 2.73%; Calcd for $C_{29}H_{23}O_8N$: N, 2.78%.

Oxidation of I. I (0.2 g) in benzene was shaken with silver oxide (prepared from 1 g of silver nitrate) for two hours. The precipitate which was subsequently filtered out was extracted with ethyl acetate. The extract from the ethyl acetate was recrystallized from chloroform and petroleum ether. Yield, 0.04 g. Yellowish crystals, mp 176 °C (decomp.). Found: C, 59.22; H, 4.30; N, 4.59%. Calcd for $C_{15}H_{13}O_6N$ (Quinone of I): C, 59.40; H, 4.32; N, 4.62%. IR: (KBr) 1742, 1690 cm^{-1}.

6,7-Dicyanoquinoline-5,8-diol (II). Procedure B: A mixture of 2.23 g of diethyl pyridinedicarboxylate (0.01 mol), 0.80 g of succinonitrile (0.01 mol) and 0.88 g of powdered metal potssium (0.022 mol) in 5 ml of xylene was stirred, with moisture excluded for half an hour at room temperature. By the same treatment of the product as with I, 0.64 g (30%) of pale yellowish crystals (from ethanol) was obtained. mp> 320 °C. Found: C, 62.53; H, 2.50; N, 19.73%: Calcd for $C_{11}H_5O_2N_3$ (II): C, 62.45; H, 2.55; N, 19.87%. IR: (KBr) ~3200 (OH), 2200 cm^{-1} (CN). *Monoacetate*: Colorless plates (from ethanol) mp 232 °C. Found: C, 61.09; H, 2.86; N, 16.48%. Calcd for $C_{13}H_7O_3N_5$ (Monoacetate of II): C, 61.66; H, 2.79; N, 16.60%. IR: (KBr) ~3200 (OH), 2490 (CN), 1788 cm^{-1} (OAc).

6,7-Diacetylquinoline-5,8-diol (III). By Procedure A, III was prepared by the condensation of diethyl 2,3-pyridinedicarboxylate with acetonylacetone. Yield, 36%; mp 243 °C (decomp.). Yellowish crystals (from aqueous ethanol). Found: C, 63.24; H, 4.48; N, 5.71%. Calcd for $C_{13}H_{11}O_4N$ (III): C, 63.67; H, 4.52; N, 5.71%. IR: (KBr) ~3220 (OH), 1682 cm^{-1} (C=O).

Diethyl 1,4-dihydroxyacridine-2,3-dicarboxylate (IV). By Procedure A IV was prepared from diethyl quinoline-2,3-dicarboxylate, ethyl succinate, and sodium metal. Recrystallization from ethanol gave 43% of pale yellowish needles (mp 177 °C). Found: C, 63.91; H, 5.05; N, 4.04%. Calcd for $C_{19}H_{17}O_6N$ (IV): C, 64.22; H, 4.82; N, 3.94%. IR: (KBr) ~3350 (OH), 1690 (C=O), 1660 cm^{-1} (C=O). NMR: (δ in $CDCl_3$) 1.43 (t, 6H, CH_3–), 4.41 (quart, 4H, –CH_2–), 7.5—8.4 (m, 5H, aromatic), 9.24 (s, 2H, -OH). *Diacetate*: mp 149—150 °C (from ethanol) Pale yellowish pillows. Found: C, 62.59; H, 5.05; N, 3.30%: Calcd for $C_{23}H_{21}O_8N$:

C 62.86; H 4.82; N, 3.19%. IR: (KBr) ~1780 (OAc) 1730 cm^{-1} (C=O). NMR: (δ in $CDCl_3$) 1.32 (t, 6H, CH_3–), 2.32 (s, 6H, $COCH_3$), 4.30 (quart, 4H, –CH_2–), 7.3—8.3 (m, 5H, aromatic).

Oxidation of IV. By a procedure analogous to that described before, IV (0.1 g) in an ether solution was oxidized to the corresponding quinone (0.07 g) with silver oxide. The quinone was yellowish needles. Mp 184 °C (from ether). Found: C, 64.23; H, 4.20; N, 3.95%. Calcd for $C_{19}H_{15}O_6N$ (quinone of IV) C, 64.58; H, 4.28; N, 3.96%. IR: (KBr) 1762, 1685 cm^{-1}.

References.

1) Studies of Chelating Reagents Containing *N*-Heterocycles. Part VI; for Part V, see This Bulletin, **41,** 980 (1968).

2) S. Kawai, M. Torigoe, S. Fujiki, S. Odaki, N. Sakakibara, and S. Oguchi, *Nippon Kagaku Zasshi* **80,** 788 (1959); *Chem. Abstr.* **55,** 3597 (1961); S. Oguchi, *Nippon Kagaku Zasshi,* **86,** 435 (1965); *Chem. Abstr.,* **63,** 7011 (1965).

3) R. G. W. Hollingshead, "Oxine and its Derivatives," Vol. I, Butterworths Scientific Publications, London (1956), p. 969.

4) H. Diehl and F. H. Lohman, *Proc. Iowa Acad. Sci.* **61,** (1954) 255; *Chem. Abstr.,* **49,** 2929 (1955).

5) a) R. Long, and K. Schofield, *J. Chem. Soc.* **1953,** 3161. b) T. Urbanski, *Roczniki Chem.* **25,** 297 (1951); *Chem. Abstr.,* **48,** 4546 (1954).