NEW 4-QUINALDINOL DERIVATIVES

XVII.* 2-METHYL-3-(3-CHLORO-2-BUTEN-1-YL)-4-HYDROXYQUINOLINE-6-CARBOXYLIC ACID AND SOME OF ITS TRANSFORMATIONS

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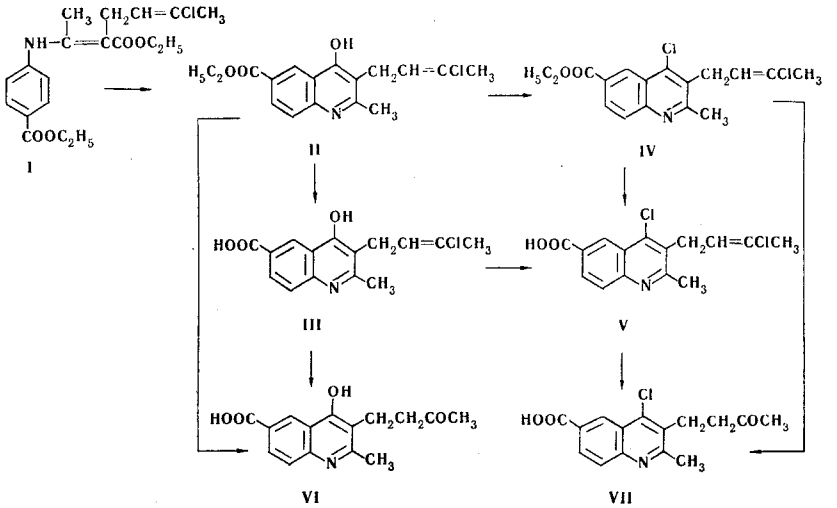
1-(2-Methyl-4-hydroxy-6-carboxy-3-quinolinyl)-3-butanone and 1-(2-methyl-4-chloro-6-carboxy-3-quinolinyl)-3-butanone were obtained by the acid hydrolysis of 2-methyl-3-(3-chloro-2-buten-1-yl)-4-hydroxy(chloro)quinoline-6-carboxylic acids and their esters.

In our previous papers, we described the synthesis and a number of transformations of 2-methyl-4-hydroxy-3-(p-alkoxybenzyl)quinoline-6-carboxylic acids and their esters [1, 2] and of a number of substituted 2-methyl-3-(3-chloro-2-buten-1-yl)-4-hydroxyquinolines and investigated several of their reactions [3-5].

In a continuation of this research, we accomplished the synthesis of 2-methyl-3-(3-chloro-2-buten-1-yl)-4-hydroxyquinoline-6-carboxylic acid (III) and investigated the reaction of III and its ester (II) with phosphorus oxychloride and concentrated sulfuric acid. In analogy with the research in [6], we were able to obtain 2-methyl-3-(3-chloro-2-buten-1-yl)-4-chloroquinoline-6-carboxylic acid (V) from III.

Compound III was obtained by the saponification of II, which was synthesized by thermal cyclization of ethyl 2-(3-chloro-2-buten-1-yl)-3-(p-carbethoxyanilino)crotonate (I), which in turn was obtained by the reaction of ethyl aminobenzoate with ethyl 2-(3-chloro-2-buten-1-yl)acetoacetate.



*See [6] for communication XVI.

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Compounds II and III are converted to 1-(2-methyl-4-hydroxy-6-carboxy-3-quinolinyl)-3-butanone (VI) by sulfuric acid hydrolysis, while II reacts with phosphorus oxychloride to give its 4-chloro analog (IV), which is converted to the corresponding 4-chloroquinoline-6-carboxylic acid (V) by saponification. The same compound – 1-(2-methyl-4-chloro-6-carboxy-3-quinolinyl)-3-butanone (VII) – was obtained from IV and V.

EXPERIMENTAL

2-Methyl-(3-chloro-2-buten-1-yl)-4-hydroxy-6-carbethoxyquinoline (II). Compound I, obtained by the method in [1], was subjected to cyclization by heating in mineral oil [1] at 245° to give 26.52 g (83%) of white crystals with mp 270° (alcohol). Found: Cl 10.87; N 4.52%. $C_{17}H_{18}ClNO_3$. Calculated: Cl 11.09; N 4.38%.

2-Methyl-3-(3-chloro-2-buten-1-yl)-4-hydroxyquinoline-6-carboxylic Acid (III). A) A 3.2-g (0.01 mole) sample of II was dissolved in 100 ml of alcohol containing 2 g of sodium hydroxide, and the solution was heated for 0.5 h. The alcohol was removed by distillation, and 10 ml of water was added to the residue. The mixture was filtered and neutralized to pH 6-6.5, and the precipitated crystals were removed by filtration and recrystallized from glacial acetic acid to give a quantitative yield of white crystals with mp 314-316°.

B) This compound was also obtained by heating II with 2 N hydrochloric acid. Found: Cl 12.38%. $C_{15}H_{14}ClNO_3$. Calculated: Cl 12.52%.

2-Methyl-3-(3-chloro-2-buten-1-yl)-4-chloro-6-carbethoxyquinoline (IV). Phosphorus oxychloride (10 ml) was added to 3.2 g (0.01 mole) of II, and the mixture was heated on a water bath for ~3 h. The excess phosphorus oxychloride was then removed by distillation under reduced pressure, ~20 g of ice was added to the residue, and the mixture was allowed to stand overnight. It was then neutralized with sodium hydroxide, and the precipitate was removed by filtration and washed with water. The reaction product was recrystallized from 50% alcohol to give 2.57 g (76.1%) of violet crystals with mp 102-103°. Found: Cl 20.75%. $C_{17}H_{17}Cl_2NO_2$. Calculated: Cl 20.64%.

2-Methyl-3-(3-chloro-2-buten-1-yl)-4-chloroquinoline-6-carboxylic Acid (V). A 10.15-g (0.03 mole) sample of IV was dissolved in 50 ml of alcohol, 2.5 g of sodium hydroxide dissolved in a small amount of alcohol was added to the solution, and the mixture was refluxed on a water bath for ~2 h. The alcohol was removed by distillation, and 50 ml of water was added to the cooled residue. The mixture was filtered, and the solution was neutralized to pH 6-6.5 with 2N hydrochloric acid. The resulting precipitate was removed by filtration and recrystallized from glacial acetic acid to give a quantitative yield of white crystals with mp 162°. Found: Cl 22.41%. $C_{15}H_{13}Cl_2NO_2$. Calculated: Cl 22.6%.

1-(2-Methyl-4-hydroxy-6-carboxy-3-quinolinyl)-3-butanone (VI). A 3.1-g (0.01 mole) sample of III was dissolved in 10 ml of sulfuric acid, and the solution was heated on a water bath at 50° until hydrogen chloride evolution ceased. The mixture was cooled and poured into 50 g of ice, and the resulting solution was neutralized with ammonium hydroxide. The precipitate was removed by filtration and recrystallized from alcohol to give 2.3 g (76.6%) of white crystals with mp 272-273°. The semicarbazone was obtained as crystals with mp 294-294°. Found: N 17.14%. $C_{16}H_{18}N_4O_4$. Calculated: N 16.97%. Compound VI was also obtained by sulfuric acid hydrolysis of II. The product did not depress the melting point of the ketone obtained from III.

1-(2-Methyl-4-chloro-6-carboxy-3-quinolinyl)-3-butanone (VII). A 3.1-g (0.01 mole) sample of V was dissolved in 10 ml of concentrated sulfuric acid, and the solution was heated at 40° until hydrogen chloride evolution ceased. The reaction mixture was then worked up as in the preparation of VI to give 2.03 g (72.3%) of white crystals with mp 114°. The semicarbazone was obtained as white crystals with mp 141°. Found: N 13.59; Cl 10.42%. $C_{16}H_{17}ClN_4O_3$. Calculated: N 13.76; Cl 10.19%. Compound VII was also obtained by sulfuric acid hydrolysis of IV. The product did not depress the melting point of the ketone obtained from V.

LITERATURE CITED

1. L. V. Gyul'budagyan and V. G. Durgaryan, Khim. Geterotsikl. Soedin., No. 1, 273 (1967).
2. L. V. Gyul'budagyan, É. S. Avanesyan, and V. A. Grigoryan, Uch. Zap. Erevansk. Gos. Univ., 107, No. 1, 80 (1968).

3. L. V. Gyul'budagyan, Nauchn. Trudy Erevansk. Gos. Univ., 53, No. 3, 57 (1956).
4. L. V. Gyul'budagyan and Kh. V. Abovyan, Nauchn. Trudy Erevansk. Gos. Univ., 60, No. 4, 59 (1957).
5. L. V. Gyul'budagyan and M. A. Kaldrikyan, Nauchn. Trudy Erevansk. Gos. Univ., 60, No. 4, 67 (1957).
6. L. V. Gyul'budagyan and G. A. Gevorkyan, Uch. Zap. Erevansk. Gos. Univ., No. 2, 70 (1969).