[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Decarboxylation of Nitro Substituted 3-Carboxy-4-quinolinols by Pyrolysis of Their Silver Salts[1]

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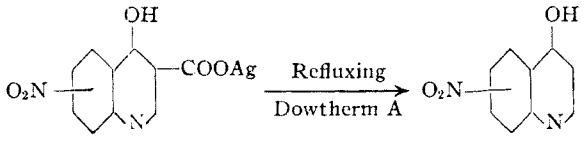
In the preparation of nitro substituted 4-quinolinols by the ethoxymethylenemalonic ester method,[2] it was found that the usual decarboxylation methods were unsatisfactory. When small amounts of the 3-carboxy-4-quinolinols were heated by fusion or in Dowtherm the yield of nitro-4-quinolinols was never greater than 50% and often none of the desired product was obtained. With large quantities of the acids these procedures were even less satisfactory; thus it was desirable to find a more reliable method for decarboxylation.

At the suggestion of Prof. C. D. Hurd we tried the pyrolysis of the silver salts. Koenigs and coworkers[3] used this method on α-hydroxyquinolinic acid and α-hydroxycinchoninic acid to produce α-hydroxypyridine and carbostyril, respectively.

We have prepared the silver salts of 3-carboxy-8-nitro-4-quinolinol, 3-carboxy-6-methoxy-8-nitro-4-quinolinol, and 3-carboxy-6-nitro-4-quinolinol. These salts decomposed violently when dry distillation was attempted. However, pyrolysis of them in refluxing Dowtherm A gave yields of 45–60% of the corresponding 4-quinolinols which were very reproducible even in rather large runs.



Experimental[4]

8-Nitro-4-quinolinol.—To a suspension of 415 g. (1.77 moles) of 3-carboxy-8-nitro-4-quinolinol in 4 l. of boiling water was added 107.6 g. (1.77 moles) of 28% aqueous ammonia solution. To the resulting solution of the ammonium salt was added a saturated aqueous solution containing 303 g. (1.77 moles) of silver nitrate and the mixture was heated on the steam-bath for twelve hours. The precipitated silver salt was collected by filtration and dried in an oven at 170°. The finely powdered silver salt was added in small portions to 3 l. of well-stirred, vigorously refluxing Dowtherm A[5] and vigorous refluxing was continued for two hours after the addition was completed. The cooled suspension was filtered and the filtrate diluted with 4 liters of hexane and again filtered. The combined precipitates were refluxed with 3.5 liters of ethanol for six hours and the suspension was filtered hot. The filtrate was treated with decolorizing carbon, filtered, and the ethanol was removed under reduced pressure to give 160 g. (45%) of a yellow solid, m. p. 198–200°. After crystallization from ethanol the substance melted at 199–200° and showed no depression of melting point when mixed with an authentic sample of 8-nitro-4-quinolinol.[2]

6-Nitro-4-quinolinol and 4-Chloro-6-nitroquinoline.—The finely powdered silver salt prepared from 15 g. (0.064 mole) of 3-carboxy-6-nitro-4-quinolinol by the above described method was added in small portions to 100 ml. of well-stirred, vigorously refluxing Dowtherm A and refluxing was continued for two hours after the addition was completed. The cooled suspension was diluted with 200 ml. of hexane and filtered. The precipitate was extracted with ethanol in a Soxhlet extractor for six hours. Evaporation of the ethanol extract gave 6.1 g. (50%) of a red solid which on crystallization from an ethanol–pyridine mixture gave an orange solid, m. p. 290–295° with decomposition.

Anal. Calcd. for $C_9H_6N_2O_3$: N, 14.73. Found: N, 13.92.

This compound was converted to 4-chloro-6-nitroquinoline in 70% yield by the usual manner, m. p. 141–141.5° after crystallization from ethanol.

Anal. Calcd. for $C_9H_5ClN_2O_2$: N, 13.43. Found: N, 13.05.

6-Methoxy-8-nitro-4-quinolinol.—The finely powdered silver salt prepared by the above described method from 15 g. (0.057 mole) of 3-carboxy-6-methoxy-8-nitroquinoline was decarboxylated in 100 ml. of Dowtherm A and the product isolated as described for 6-nitro-4-quinolinol. The yield of red solid was 7.6 g. (61%), m. p. 221–222° after crystallization from ethanol. When mixed with an authentic sample of 6-methoxy-8-nitro-4-quinolinol[2] there was no depression of melting point.

Summary

1. An improved method of decarboxylation of nitro substituted 3-carboxy-4-quinolinols to nitro-4-quinolinols through the pyrolysis of the silver salts has been described.

2. In each case the yield of nitro-4-quinolinol was considerably better than by previously known methods.

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(1) The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Northwestern University.

(2) B. Riegel, G. R. Lappin, B. H. Adelson, R. I. Jackson, C. J. Albisetti, Jr., R. M. Dodson and R. H. Baker, THIS JOURNAL, **68**, 1264 (1946).

(3) W. Koenigs and R. Geigy, *Ber.*, **17**, 585 (1884); W. Koenigs and G. Koerner, *ibid.*, **16**, 2152 (1883).

(4) Microanalyses by Margaret Ledyard, Winifred Brandt and Rita Pivan.

(5) A commercial mixture of diphenyl ether and biphenyl, b. p. *ca.* 240°.