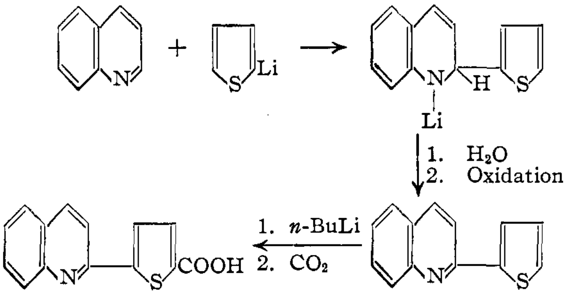
gave 2-(2′-thienyl)-quinoline (I) in 38% yield. Metalation of this quinoline derivative with *n*-butyllithium gave subsequent to carbonation a monocarboxylic acid considered to be 2-(5′-carboxy-2′-thienyl)-quinoline (II) formed by metalation of the thiophene ring at the remaining reactive α-position, namely, the 5-position.



II I

Experimental

Metalation of Thiophene.—An ethereal solution of *n*-butyllithium was prepared by the gradual addition of 27.4 g. (0.20 mole) of *n*-butyl bromide to a stirred suspension of 4.0 g. of lithium (cut into small cubes, 3 to 5 mm. on a side) in 200 ml. of dry ether. Titration[7] of the resulting filtered solution showed the presence of 0.070 mole of *n*-butyllithium, and the solution was added to a solution of 8.4 g. (0.10 mole) of thiophene in 100 ml. of ether. After stirring for fifteen minutes, the mixture was poured on to a slurry of ether and crushed solid carbon dioxide. After evaporation of the carbon dioxide and slow addition of 100 ml. of water, the aqueous layer was separated and acidified with concentrated hydrochloric acid. The precipitated solid was removed by filtration and the filtrate evaporated to a small volume to obtain additional solid. Recrystallization of the resulting dry solid from petroleum ether (b.p. 80–110°) gave 7.8 g. (87% based on *n*-butyllithium) of 2-thiophenecarboxylic acid, m.p. 128°.

2-(2′-Thienyl)-quinoline (I).—Twenty-one grams (0.25 mole) of thiophene was metalated with 0.22 mole of *n*-butyllithium (prepared as above from 54.8 g. (0.40 mole) of *n*-butyl bromide and 7.0 g. of lithium). A solution of 28.1 g. (0.22 mole) of quinoline in 100 ml. of ether was added to the 2-thienyllithium solution, and the mixture stirred at room temperature for two hours. Excess water was added for hydrolysis and a few ml. of nitrobenzene for oxidation of the intermediate 1,2-dihydro-2-(2′-thienyl)-quinoline. After stirring a few minutes longer, the ethereal layer was separated and dried over anhydrous sodium sulfate. The ether was removed by distillation and the residue heated under a water pump vacuum for removal of excess nitrobenzene and quinoline. The residue solidified upon cooling and was recrystallized once from petroleum ether (b.p. 80–110°) and once from dilute ethanol to give 17.5 g. (38%) of yellow needles of 2-(2′-thienyl)-quinoline, m.p. 130°.

A picrate derivative prepared in the usual manner melted at 193.5–194°.

Steinkopf and co-workers[8] report 132–133° as the melting point of 2-(2′-thienyl)-quinoline and 194–195° for the picrate derivative.

2-(5′-Carboxy-2′-thienyl)-quinoline (II).—To a solution of 5.3 g. (0.025 mole) of 2-(2′-thienyl)-quinoline in 200 ml. of ether was added 40 ml. of an ethereal solution containing 0.025 mole of *n*-butyllithium. Stirring was continued for fifteen minutes after completion of the addition, and this was followed by carbonation with solid carbon dioxide and hydrolysis in the usual manner. The mixture was filtered to remove some precipitated solid. The aqueous layer was separated from the filtrate. This aqueous solution was combined with a solution obtained by the extraction of the solid precipitate with concentrated ammonium hydroxide, and the mixture was acidified with hydrochloric acid to precipitate a yellow solid. The solid was recrystallized twice from ethanol to give 1.9 g. (30%) of small yellow prisms which melted at 205–206°. A small amount was recrystallized again from ethanol and this material melted at 206–207°.

Anal. Calcd. for $C_{14}H_9O_2NS$: N, 5.49; neut. equiv., 255. Found: N, 5.48; neut. equiv., 257.

Assignment of the position of metalation of 2-(2′-thienyl)-quinoline as the 5-position is tentative and is based on the known high reactivity of the remaining α-position in the thiophene nucleus.

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA
RECEIVED NOVEMBER 15, 1948

---

[7] Gilman and Haubein, THIS JOURNAL, **66**, 1515 (1944).

[8] Steinkopf, Barlag and Petersdorff, *Ann.*, **540**, 13 (1939).

The Interaction of 4,6-Dichloroquinazoline with Ethylenediamine

BY GORDON M. GOODALE AND ROBERT L. MCKEE

Albert and Gledhill[1] have shown that 9-chloroacridine reacts with excess ethylenediamine to form only the 2:1 condensation product, N,N′-bis-(9-acridyl)-ethylenediamine, and in this Laboratory,[2] 7-chloro-9-phenoxy-2-methoxyacridine formed only the 2:1 product with this amine. We have now investigated the reaction between 4,6-dichloroacridine and ethylenediamine and find by contrast that only traces of N,N′-bis-(6-chloro-4-quinazolyl)-ethylenediamine are formed, the major product being the 1:1 condensation product, 6-chloro-4-(β-aminoethylamino)-quinazoline.

Procedure.—6-Chloro-4-quinazolone (10.8 g., 0.060 mole) was refluxed with 12.7 g. (0.061 mole) of phosphorus pentachloride and 72 ml. of phosphorus oxychloride for five hours. After removal of the latter under diminished pressure (water pump), 25 ml. of dry toluene was added and 15 ml. removed by distillation. To the residue, 18 g. (0.30 mole) of ethylenediamine was added and the mixture refluxed for two hours. Dilute hydrochloric acid was added and the toluene layer was separated and discarded. Addition of dilute sodium hydroxide resulted in the separation of 9.5 g. of a white solid, m. p. 107–111°. This was separated into two fractions by extraction with benzene. The major portion, soluble in benzene, was recrystallized from a benzene-petroleum ether mixture to give 6.5 g. (49% based on quinazolone) of 6-chloro-4-(β-aminoethylamino)-quinazoline, m. p. 140–143°.

Anal. Calcd. for $C_{10}H_{11}N_4Cl$: C, 53.90; H, 4.95; N, 25.16. Found: C, 53.89; H, 5.21; N, 24.95.

The benzene-insoluble product (about 1 g.) was dissolved in dilute hydrochloric acid, treated with norite, precipitated with sodium hydroxide, filtered and washed thoroughly with water and hot ethanol. The quantity of material present did not permit a complete analysis. We believe it to be N,N′-bis-(6-chloro-4-quinazolyl)-ethylenediamine, m. p. 321° (dec.).

Anal. Calcd. for $C_{18}H_{14}N_6Cl_2$: N, 21.82. Found: N, 21.89.

THE VENABLE CHEMICAL LABORATORY
UNIVERSITY OF NORTH CAROLINA
CHAPEL HILL, N. C.
RECEIVED JANUARY 26, 1949

---

[1] Albert and Gledhill, *J. Soc. Chem. Ind.*, **64**, 169 (1945).

[2] McKee and Bost, THIS JOURNAL, **69**, 468 (1947).