Dr. V. B. Fish and Mr. C. T. Kleppinger for the analyses.

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1,8-Naphthalide

BY REYNOLD C. FUSON AND GEORGE MUNN

1,8-Naphthalide, previously prepared by an indirect method,[1] has been made in 90% yield by a crossed Cannizzaro reaction between 1,8-naphthaldehydic acid and formaldehyde. The 1,8-naphthaldehydic acid was prepared from acenaphthenequinone by the use of 30% aqueous potassium hydroxide, the method being an adaptation of that employed by Graebe and Gfeller.[2]

Reduction of 1,8-naphthalide with Raney nickel-aluminum alloy and sodium hydroxide[3] produced a tetrahydro-8-methyl-1-naphthoic acid, a compound which was formed also by the catalytic reduction of naphthalic anhydride.

A Clemmensen reduction of 1,8-naphthaldehydic acid afforded a low yield of 8-methyl-1-naphthoic acid. This acid was found to melt at 153° instead of 130-131° as has been reported by Errera and Ajon.[1] These authors prepared the acid from naphthalonic acid by reduction with phosphorus and hydriodic acid followed by decarboxylation. If the treatment was not very vigorous, naphthalide was the principal product. It seems probable, then, that the lactone was present as a contaminant in the methylnaphthoic acid reported to melt "not very sharply" at 130-131°.

Experimental

1,8-Naphthaldehydic Acid.—Twenty grams of acenaphthenequinone[4] and 140 ml. of 30% potassium hydroxide solution were heated with constant stirring at 150° for ten minutes. The reaction mixture was then diluted with water and filtered with suction. The filtrate was acidified with hydrochloric acid, and the white precipitate which formed was separated by filtration and dissolved as completely as possible in sodium bicarbonate solution. The solution was treated with charcoal, and acidified to reprecipitate the product. The resulting 1,8-naphthaldehydic acid was recrystallized from toluene to give a yield of 14 to 16 g. (68 to 73%); m. p. 167°. This is the same melting point that has been reported by Graebe and Gfeller.[2]

1,8-Naphthalide.—Ten grams of 1,8-naphthaldehydic acid was dissolved in 300 ml. of 30% potassium hydroxide solution, and 10 ml. of formalin was added. The reaction mixture was heated to 50-60° and stirred at that temperature for three and one-half hours, an additional 5 ml. of formalin being added at the end of the first hour. The reaction mixture was acidified, and the white solid which formed was collected on a filter and washed with sodium bicarbonate solution. When recrystallized from high-boiling petroleum ether, this solid yielded 8.4 g. of 1,8-naphthalide melting at 156-157°. The yield was 90% of the theoretical. This compound has been reported to melt at 159-160°.[1]

Tetrahydro-8-methyl-1-naphthoic Acid.—Ten grams of 1,8-naphthalide was dissolved in 150 ml. of 10% sodium hydroxide, and the solution was heated to 90°. Fifteen grams of Raney nickel-aluminum alloy was added in small portions with stirring and the reaction was allowed to continue at the same temperature for an additional hour. The original volume was maintained by the addition of water and a few drops of octyl alcohol were added to prevent foaming. The reaction mixture was then filtered and the filtrate was poured into an excess of hydrochloric acid. When the reaction mixture had cooled, it was extracted with ether and the ether layer was washed with sodium bicarbonate solution. Acidification of the sodium bicarbonate solution produced a white precipitate. When recrystallized from high-boiling petroleum ether, the precipitate yielded 2.2 g. of tetrahydro-8-methyl-1-naphthoic acid which melted at 150°. This same compound was formed when naphthalic anhydride was reduced catalytically in the presence of a copper chromite catalyst with 3000 lb. pressure of hydrogen at 260°.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.85; H, 7.43.

8-Methyl-1-naphthoic Acid.—A mixture of 33 g. of amalgamated mossy zinc, 54 ml. of glacial acetic acid, 54 ml. of concentrated hydrochloric acid and 6 g. of 1,8-naphthaldehydic acid dissolved in 50 ml. of toluene was heated under reflux for thirty hours. Three 15-ml. portions of concentrated hydrochloric acid were added during this time at six- to eight-hour intervals. The toluene layer was washed with several portions of water and extracted with sodium bicarbonate solution. The sodium bicarbonate solution was acidified, allowed to stand overnight, and filtered with suction. When recrystallized from high-boiling petroleum ether, the residue yielded 0.5 g. of 8-methyl-1-naphthoic acid melting at 153°. This acid has been reported to melt "not very sharply" at 130-131°.[1]

Anal. Calcd. for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found: C, 77.39; H, 5.63.

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[1] Errera and Ajon, *Gazz. chim. ital.*, **41**, II, 92 (1914).

[2] Graebe and Gfeller, *Ann.*, **276**, 1 (1893).

[3] Papa, Schwenk and Whitman, *J. Org. Chem.*, **7**, 587 (1942).

[4] Graebe and Gfeller, *Ber.*, **25**, 653 (1892); Maxwell and Allen, *Org. Syntheses*, **24**, 1 (1944).

Metalation of Thiophene by *n*-Butyllithium

BY HENRY GILMAN AND DAVID A. SHIRLEY[1]

Metalation of thiophene and certain of its derivatives has been effected by the use of ethylmagnesium bromide,[2] diethylmercury and sodium,[3] sodium metal,[4] mixtures of sodium and alkyl halides[5] and sodium and 2,2′-difurylmercury.[6] In all cases the metallic atom is substituted in the reactive 2-position of thiophene.

As a part of a general investigation of the metalation of heterocyclic types by organolithium compounds, thiophene has been treated with *n*-butyllithium in ether solution forming 2-thienyllithium in 87% yield, as shown by conversion of the 2-thienyllithium to 2-thiophenecarboxylic acid by treatment with solid carbon dioxide.

Addition of 2-thienyllithium to the 1,2-position of quinoline followed by hydrolysis and oxidation of the resulting 1,2-dihydro compound

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[2] Challenger and Gibson, *J. Chem. Soc.*, 305 (1940).

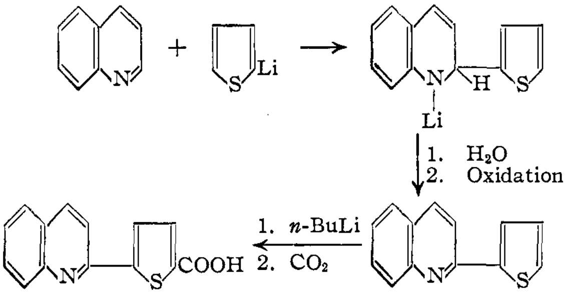
[3] Schorigin, *Ber.*, **43**, 1938 (1910).

[4] Schick and Hartough, THIS JOURNAL, **70**, 286 (1948).

[5] Schick and Hartough, *ibid.*, **70**, 1645 (1948).

[6] Gilman and Breuer, *ibid.*, **56**, 1123 (1934).

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.

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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.

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

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

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

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