Experimental

Materials.[3]—Aluminum chloride, anhydrous, Eastman Kodak Co. practical; ethyl chloride, U. S. P.; styrene, Eastman, stabilized with *t*-butyl catechol, found free from polymer; 2,5-dichlorostyrene, freshly distilled at 7 mm.; vinyl *n*-butyl ether, freshly distilled; vinylidene chloride, freshly distilled; stannic chloride, General Chemical Co.

Polymerizations.—About 2–5 g. of monomer mixture was prepared by weighing components into a stoppered test-tube, and the tube transferred to an ice-bath. An equal volume (±1 ml.) of ethyl chloride was added. A catalyst solution was prepared by dissolving 20–100 mg. of aluminum chloride in 10 ml. of cold ethyl chloride; it was pale yellow in color. Small increments of this solution, 0.1–0.5 ml. at a time, were added to the monomer solution with shaking and stirring until slight coloration and an increase in viscosity were observed. There were no special precautions to exclude moisture. A threshold amount of 1–2 ml. solution was required for reaction, which then took place rapidly to the extent of 5–10% conversion in one to five minutes upon adding a single increment, but would proceed no farther in several hours without adding more catalyst. Mixtures containing much vinylidene chloride reacted much more slowly. The product was diluted with 1 ml. of methanol and 5–10 ml. of chloroform, and precipitated as a powder by stirring into 150–200 ml. methanol. After two reprecipitations, it was filtered in a Selas sintered-glass crucible, dried for two days at 70°, and weighed.

Chlorine Determinations.—A 0.1–0.3-g. sample was fused for three hours with two to four times its weight of sodium in a sealed Pyrex tube at 470°. After destroying sodium with methanol, contents were boiled thirty minutes with 50–100 ml. water, neutralized with nitric acid, and filtered. High chlorines were determined gravimetrically, low chlorines by the Volhard titration.

Errors were estimated by repeating the Mayo and Lewis calculation, assuming conversion 2% higher and chlorine 0.5% lower for no. 4, and chlorine 0.1% lower for no. 1.

TABLE I

COPOLYMERIZATION OF STYRENE (M_1) AND 2,5-DICHLOROSTYRENE (M_2) IN ETHYL CHLORIDE AT 0°

Experiment	Styrene, g.	2,5-Dichlorostyrene, g.	Conversion, %	Cl in polymer %
Sn[a]	6.2567	0.6699	60–70	0.558
1[b]	2.6055	0.6665	4.64	0.739
2[b]	1.9415	1.9675	13.29	3.05
3[b]	0.6672	2.4975	27.19	17.9
4[b]	0.2691	2.5385	48.30	34.0

[a] Catalyst, two drops $SnCl_4$ in 10 ml. of ethyl chloride. [b] Catalyst, $AlCl_3$.

The principal conclusion is obviously identical with that expressed by Alfrey and Wechsler: the form of the copolymerization equation is satisfied, and the relative magnitudes of r_1 and r_2 are in inverse order to those reported for the free-radical catalyzed reaction. It is not certain whether r_1 and r_2 will be invariant for the same monomers with all catalysts of the Friedel–Crafts type; the experiment Sn, Table I, suggests that at least they may not differ widely for $AlCl_3$ and $SnCl_4$.

Results satisfy the mechanism of Alfrey and Wechsler.[1] They can also satisfy a mechanism of the type proposed by Fontana and Kidder,[4] involving rearrangement of a complex. We may write, for example

$$M_1^*C + M_2 \overset{K_{12}}{\rightleftarrows} M_1^*CM_2$$

$$M_1^*CM_2 \xrightarrow{k_{12}} M_2C$$

where K_{12} is the equilibrium constant for formation of a complex containing a polymer molecule having end-group M_1, a molecule of M_2, and a molecule of catalyst, and k_{12} is the rate constant for rearrangement of this complex to one containing only a polymer molecule with end-group M_2 and a molecule of catalyst. By using fundamental rate equations of this type in the derivation of the original copolymerization equation,[2] with low catalyst concentration and short-time steady state, one arrives at the same equation, but with $r_1 = k_{11}K_{11}/k_{12}K_{12}$, $r_2 = k_{22}K_{22}/k_{21}K_{21}$. In this case, it is unlikely that the various K's and their ratios would remain equal for all catalysts, and r_1 and r_2 should depend upon the specific catalyst used.

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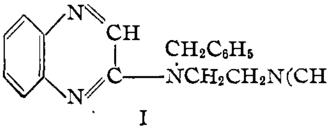
[3] Thanks are due to Professor C. S. Marvel, University of Illinois, for the 2,5-dichlorostyrene used; to Dow Chemical Co., and Professor F. T. Wall, University of Illinois, for the vinylidene chloride; and to General Aniline and Film Corp. for the vinyl *n*-butyl ether.

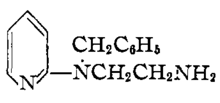
[4] C. M. Fontana and G. A. Kidder, THIS JOURNAL, **70**, 3745 (1948).

Some Heterocyclic Derivatives of Ethylenediamine

BY JOHN H. GARDNER[1] AND JOSEPH R. STEVENS

In an attempt to obtain compounds exhibiting antihistamine activity, two new heterocyclic derivatives of ethylenediamine have been prepared, 2-N-benzyl-N-(2-dimethylaminoethyl)-aminoquinoxaline (I) and N-benzyl-N-2-pyridylethylenediamine (II). For the preparation of I, dimethylaminoethyl chloride was condensed with N-benzylbenzamide to give N-benzoyl-N-benzyl-N′,N′-dimethylethylenediamine, which was hydrolyzed to N-benzyl-N′,N′-dimethylethylenediamine. This was condensed with 2-chloroquinoxaline to form I. In an effort to develop a more satisfactory synthesis, 2-N-benzylaminoquinoxaline was prepared by condensing benzyl chloride and 2-aminoquinoxaline in the presence of sodium hydride. Further condensation with dimethylaminoethyl chloride failed, 2-N-benzylaminoquinoxaline being recovered unchanged.


I


II

II was prepared by condensing β-bromoethylphthalimide with 2-N-benzylaminopyridine and

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decomposing the resulting product with hydrazine hydrate in alcohol.

Experimental

N-Benzyl-N',N'-dimethylethylenediamine.—A suspension of 12 g. of lithium amide in a solution of 42.2 g. of N-benzylbenzamide in 300 ml. of benzene was refluxed with stirring for two hours. Then, 32.3 g. of dimethylaminoethyl chloride hydrochloride was added and the mixture was refluxed overnight. A mixture of 50 ml. of 20% hydrochloric acid and 50 ml. of water was added and the layers were separated. The benzene layer was washed with 50 ml. of 20% hydrochloric acid followed by 150 ml. of water. The aqueous layer and washings were combined and washed twice with benzene.

The benzene solution was dried over potassium carbonate and evaporated to dryness. The residue yielded 8 g. of N-benzylbenzamide after crystallization from alcohol.

The aqueous solution was clarified with Nuchar W and made alkaline to phenolphthalein with 50% sodium hydroxide. It was extracted three times with benzene. The extract was dried over potassium carbonate and the benzene distilled in a water aspirator vacuum. The residue was dissolved in 200 ml. of 20% hydrochloric acid and the solution was refluxed twenty-three hours. After cooling, the benzoic acid was filtered out. The filtrate was made alkaline to phenolphthalein with 50% sodium hydroxide. The oil which formed was separated and the water layer was extracted with ether. The combined organic material was dried over potassium carbonate. After removal of the ether, the residue was distilled in vacuum. The yield was 14 g. of a nearly colorless oil, b. p. 115–117° under 4 mm., $n^{27}\mathrm{D}$ 1.5052.

For proof of identity, the hydrochloride was prepared and analyzed. A solution of 1 g. of the oil in 2 ml. of 20% hydrochloric acid was evaporated to dryness. The residue was crystallized twice from isopropyl alcohol. The yield was 1.2 g., m. p. 205–207° after drying for two hours at 100° under 2 mm. pressure.

Anal. Calcd. for $C_{11}H_{20}N_2Cl_2$: N, 11.15; Cl, 28.23. Found: N, 11.25, 11.20; Cl, 28.25, 28.10.

2-Chloroquinoxaline.—The best procedure found is a selection of reactions described by Gowenlock, Newbold and Spring,[2] with one modification. 2-Hydroxyquinoxaline-3-carboxylic acid was prepared by condensing *o*-phenylenediamine and ethyl ketomalonate and saponifying the resulting ester as described by Gowenlock, *et al.* For decarboxylation, a mixture of 12.5 g. of the acid with 100 ml. of nitrobenzene was refluxed ten minutes. After cooling to room temperature, the product was filtered out, washed well with petroleum ether and dried in a vacuum desiccator. The yield was 10.1 g., m. p. 262–264°.

2-Chloroquinoxaline was prepared from 2-hydroxyquinoxaline and phosphorus oxychloride by the procedure of Gowenlock, *et al.*

2-N-Benzyl-N-(2-dimethylaminoethyl)-aminoquinoxaline Hydrochloride.—A mixture of 1.7 g. of 2-chloroquinoxaline and 4 g. of N-benzyl-N',N'-dimethylethylenediamine was heated to 145–150° for two hours. After cooling, the mixture was dissolved in dilute hydrochloric acid and the solution was clarified with Nuchar W. It was made alkaline with 50% sodium hydroxide, cooled and extracted three times with ether. The ether extract was dried over potassium carbonate and partially decolorized with Nuchar GFO. Excess absolute alcoholic hydrogen chloride was added and the precipitate was filtered out. It was crystallized from a large volume of isopropyl alcohol, giving 3 g. of white crystals, m. p. 200–203°; mixed with N-benzyl-N',N'-dimethylethylenediamine hydrochloride, m. p. 203–205.5°.

The filtrate from these crystals was heated to boiling and diluted with diisopropyl ether almost to turbidity. On cooling, a tarry mass separated. This product was crystallized repeatedly from isopropyl alcohol, using Nuchar W the first time. The final yield was 0.5 g. of very light tan crystals, m. p. 217–218° after drying at 100° under 2 mm.

Anal. Calcd. for $C_{19}H_{23}N_4Cl$: N, 16.34; Cl, 10.34. Found: N, 16.18; Cl, 10.55.

2-Benzylaminoquinoxaline Hydrochloride.—To a suspension of 21.75 g. of 2-aminoquinoxaline in 225 ml. of benzene there was added 5.4 g. of sodium hydride. The mixture was refluxed with stirring for seven hours. Then 22.8 ml. of benzyl chloride in 40 ml. of benzene was added slowly and the mixture was refluxed with stirring twenty-two hours. It was then poured into dilute hydrochloric acid. The solid which precipitated was filtered out and recrystallized from methanol using Nuchar W. The yield was 4 g., m. p. 255–256°.

Anal. Calcd. for $C_{15}H_{14}N_3Cl$: C, 66.30; H, 5.19; N, 15.46; Cl, 13.05. Found: C, 66.35; H, 5.23; N, 15.50; Cl, 13.00.

For the preparation of the base, a solution of the hydrochloride in methanol was treated with an excess of 50% sodium hydroxide. The base crystallized on cooling and was recrystallized from methanol, m. p. 62–64°.

Attempts to condense 2-benzylaminoquinoxaline with 2-dimethylaminoethyl chloride using various condensing agents failed; in each case the only identifiable product after working up was 2-benzylaminoquinoxaline hydrochloride.

N-Benzyl-N-2-pyridylaminoethylphthalimide.—A Grignard reagent was prepared from 5.5 g. of magnesium and 22 g. of ethyl bromide in 100 ml. of dry ether. A solution of 17.4 g. of 2-benzylaminopyridine was added during a half-hour. The mixture was refluxed an hour, with stirring. Then 25.4 g. of β-bromoethylphthalimide in 50 ml. of benzene was added. There was a moderately exothermic reaction and a copious yellow precipitate formed. The mixture was refluxed with stirring five and a half hours. After standing overnight, a solution of 50 g. of ammonium chloride in 200 ml. of water was added. A small slimy precipitate was filtered out. The layers were separated and the organic layer was washed twice with water. After drying over magnesium sulfate, it was evaporated to a viscous oil. This was crystallized twice from absolute alcohol giving 3.1 g. of nearly white crystals, m. p. 121–122°.

The same product was obtained using lithium amide as the condensing agent.

Anal. Calcd. for $C_{22}H_{19}O_2N_3$: C, 73.93; H, 5.36; N, 11.76. Found: C, 73.90; H, 5.31; N, 11.69, 11.68.

N-Benzyl-N-2-pyridylethylenediamine Sulfate.—A solution of 3 g. of N-benzyl-N-2-pyridylaminoethylphthalimide and 0.5 g. of hydrazine hydrate in 20 ml. of absolute alcohol was refluxed two hours. The alcohol was removed in vacuum. The residue was partitioned between ether and approximately 30% sodium hydroxide by stirring until two clear layers formed. The layers were separated and the aqueous layer was washed with ether. The ether solution was dried over two portions of potassium hydroxide. An excess of hydrogen chloride in dry ether was added and the hydrochloride was filtered out. This was extremely hygroscopic, becoming pasty after about two minutes of exposure to the air.

The hydrochloride was dissolved in 20 ml. of absolute alcohol and shaken for forty-five minutes with 3 g. of silver sulfate. The mixture was filtered. The filtrate gave a negative test for chloride ion. Dry ether was added to complete precipitation. The mixture was allowed to stand overnight in the refrigerator to complete coagulation of the precipitate. The crystals were filtered out and recrystallized from alcohol containing a little water, using Nuchar C. The yield was 0.8 g., m. p. 156–158° after drying in vacuum at 100° for three hours.

Anal. Calcd. for $C_{14}H_{19}O_4N_3S$: N, 12.91; S, 9.83. Found: N, 13.22; S, 9.81.

Acknowledgment.—We are indebted to Miss Mary L. Evanick for technical assistance and to

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[2] A. H. Gowenlock, G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 622 (1945).

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).