

sodium hydroxide, 16 g. of sodium hydrosulfite was added and the mixture warmed to 50° with stirring for fifteen minutes. The resulting dark green solution was diluted with 400 cc. of water and aerated for ten to fifteen minutes until a deep purple precipitate of the 2-amino quinone was formed. This, after washing and drying, was crystallized from alcohol; yield 4 g., 91% of the theoretical. Since the product did not have a definite melting point, it was identified by conversion into the monoacetyl derivative prepared by boiling in acetic acid with the addition of a small amount of acetic anhydride. The product, dark red-violet crystals, recrystallized from nitrobenzene, melted sharply at 324°, as recorded in the literature.

Sodium hydrosulfide was also used as the reducing agent, but the yield was only 63.6% of the theoretical.

**Preparation of the 2-Iodophenanthrenequinone.**—Six grams of the 2-amino compound was dissolved in 75 cc. of sulfuric acid (sp. gr. 1.84) and the solution kept at 0–5° with vigorous stirring. Two grams of sodium nitrite was added slowly and the stirring continued for two hours. The mixture was poured onto cracked ice and carefully diluted to 2 liters with water, and 6 g. of potassium iodide added. The cooled mixture, containing the diazonium salt in fine suspension, was stirred for three hours, then warmed on a water-bath for two hours, and

sufficient sodium bisulfite solution added to remove the free iodine. The reddish-orange material was filtered off, washed with water, dried at 100° and crystallized several times from glacial acetic acid. Orange colored crystals were formed. They melted at 223–224° (corr.); yield 2.7 g., 30%.

*Anal.* Calcd. for  $C_{14}H_7O_2I$ : I, 38.0. Found: (micro) I, 37.84; 37.93.

The compound was stable at ordinary temperatures but decomposed with the liberation of iodine at temperatures well above its melting point. It sublimes, with slight decomposition, under reduced pressure to needle-shaped crystals of above melting point. It is only moderately soluble in benzene, toluene and alcohol. It dissolves in concentrated sulfuric acid, forming a dark green solution which turns to deep red when partly diluted. On continued dilution, the orange colored material is reprecipitated.

### Summary

2-Iodophenanthrenequinone has been prepared from phenanthrene and some of its properties recorded.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OHIO STATE UNIVERSITY]

## A Synthesis of Pseudoephedrine

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The synthesis of pseudoephedrine as described in this paper is based on the same methods as have been described previously for  $\beta$ -ethoxy amines<sup>1</sup> with the subsequent splitting of the ether to yield the amino alcohol.

Among the previously described syntheses of ephedrine and pseudoephedrine<sup>2</sup> the methods of Späth and Göhring, Späth and Koller, and Kanao and Nagai<sup>3</sup> approach to some extent the procedure used in the present synthesis. However, the variation in the order in which certain groups are introduced, with the possibility of inversion due to the existence of a second asymmetric atom in the molecule is important from the standpoint of the mechanism of the reactions. Since this method follows the Boord synthesis of olefins,<sup>4</sup> the known configuration of the final product in this pseudoephedrine synthesis should be

(1) Brode and Wernert, *THIS JOURNAL*, **54**, 4365 (1932); **55**, 1685 (1933).

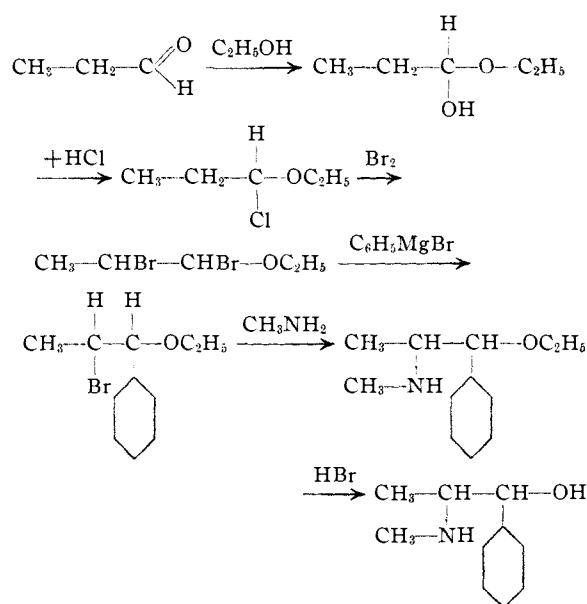
(2) Chen and Schmidt, "Ephedrine and Related Substances," Williams and Wilkins Co., Baltimore, Md., 1930.

(3) (a) Späth and Koller, *Ber.*, **68**, 1268 (1925); (b) Späth and Göhring, *Monatsh.*, **41**, 319 (1920); (c) Nagai and Kanao, *Ann.*, **470**, 159 (1929).

(4) Boord *et al.*, *THIS JOURNAL*, **52**, 651, 3396 (1930); **53**, 1505, 2427 (1931); **54**, 751 (1932); **55**, 3293 (1933).

of some assistance in the explanation of certain reactions and the formation of certain products in the olefin synthesis.

The reactions involved in this synthesis of *dl*-pseudoephedrine may be indicated as



The steps leading to  $\alpha$ - $\beta$ -dibromopropyl ethyl ether, affording a yield of 66% based on the aldehyde, have already been described by Boord.

### Experimental

**2-Bromo-1-phenyl-1-ethoxypropane.**—A mixture of 815 g. of the dibromo ether and an equal volume of ether was added in drops, over nine hours, to a 10% excess of a cold ethereal solution of phenylmagnesium bromide and was then stirred continuously for twelve hours. The resulting mixture was poured upon cracked ice, neutralized with dilute sulfuric acid, washed with water and dilute sodium carbonate and dried. After removal of the ether, distillation with steam gave 666 g. (83%) of a clear, colorless oil. Redistillation *in vacuo* gave 445 g. of the  $\beta$ -bromo ether, b. p. 114° (9 mm.). The corresponding product obtained by Schmidt, Bartholomé and Lübke,<sup>5</sup> by a wholly different method, boiled at 119–120° (13 mm.).

**Ethyl Ether of di-Pseudoephedrine.**—Ninety grams (0.37 mole) of 2-bromo-1-phenyl-1-ethoxypropane was dissolved in 450 cc. of anhydrous methanol and placed in a 1-liter steel bomb together with a sealed glass tube containing 22.8 g. (0.73 mole) of methylamine. After breaking the tube and heating for fifty hours at 125–130° the bomb was cooled and opened. The excess methylamine and methyl alcohol were removed by distillation. The solution was made slightly acid, the non-basic constituents were extracted with ether and the remaining solution neutralized with sodium hydroxide and washed with water. The ether extract of the resulting oil yielded, on distillation, 10.5 g. of the ethoxyamine (15%), b. p. 116–122° (18 mm.). When the bomb was heated at a higher temperature (150–155°) a small quantity (2–3 g.) of a solid basic compound (m. p. 134.5–135°) was formed, which was characterized as a tertiary amine ( $\text{CH}_3\text{—N—}(\text{CH—CH—OC}_2\text{H}_5)_2$ ), similar in nature to the

$$\begin{array}{c} \text{CH}_3 \quad \text{C}_6\text{H}_5 \\ | \quad | \\ \text{CH—CH—OC}_2\text{H}_5 \end{array}$$

secondary amines obtained by the analogous reaction of

ammonia with  $\beta$ -bromo ethers which has been previously described.<sup>1</sup>

**Hydrolysis of the Ethyl Ether of Pseudoephedrine to Pseudoephedrine.**—The hydrolysis of the ethyl ether was accomplished by heating in a sealed tube with fuming (sp. gr. 1.68 at 0°) hydrobromic acid or by refluxing with 48% hydrobromic acid. Ten and one-half grams of the amino ether, placed in a combustion tube with 36 cc. of fuming hydrobromic acid, was heated for one and one-half hours in a combustion furnace at 100°. The tube showed no evidence of internal pressure when cooled and opened. The contents of the tube was placed in a vacuum desiccator over sulfuric acid and lime at 30 mm. for nine days. The brown viscous sirup was dissolved in 200 cc. of water, placed in a reflux apparatus, and heated gently in an atmosphere of carbon dioxide for an hour. The solution was cooled and extracted with ether to remove the non-basic constituents. The solution was then made alkaline with potassium hydroxide and the liberated amine extracted with ether. Evaporation of the ether solution gave a white crystalline product which was recrystallized from ethyl alcohol, m. p. 117.8–118.2° (corr.) (litt. 118°). The identity of this compound with pseudoephedrine was further confirmed by numerous chemical tests and the melting point of the hydrochloride (litt. 163–164°), observed 161–164° (corr.).

### Summary

The  $\alpha$ , $\beta$ -dibromo ether synthesis has been employed successfully in the preparation of racemic pseudoephedrine. The known configuration of the ephedrine formed by this method may offer some assistance in the determination of the configuration of the intermediate asymmetric  $\alpha$ , $\beta$ -dibromo ethers. The development of the synthesis of substituted  $\alpha$ , $\beta$ -dibromo ethers<sup>4</sup> provides a method for the synthesis of an extended series of substituted ephedrine derivatives.

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(5) Schmidt, Bartholomé and Lübke, *Ber.*, **55**, 2099 (1922).