

The mixture in the receiver was distilled at atmospheric pressure in an atmosphere of carbon dioxide. Two layers formed in the distillate—a lower cacodyl chloride layer and an upper aqueous layer. The lower cacodyl chloride layer was separated, washed with 100 ml. of water and dried over 20 g. of calcium chloride. There was obtained 150 g. of product (28% of theoretical based on potassium acetate), which had a boiling point of 106–109° at atmospheric pressure.

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The Skraup Reaction with Acrolein and its Derivatives. I. The Preparation of 6-Methoxy-8-nitroquinoline

BY HARRY L. YALE

The role of acrolein as an intermediate in the Skraup reaction has been accepted generally. The poor yield of quinoline from the product of the reaction between aniline and acrolein has been considered, however, as indirect evidence for another mechanism.¹ The Doebner–Miller modification of the Skraup reaction, which employs β -substituted acrolein derivatives, has been used with success in the preparation of 2-substituted quinolines and this has given additional weight to the probability that acrolein does exist, at least momentarily, during the Skraup reaction. Recently, Manske² has employed α -methylacrolein and its dimethyl acetal and Utermohlen³ has used α -methylacrolein, α -ethylacrolein, their diacetates and dipropionates, to prepare a number of 3-substituted quinoline compounds. Quinoline compounds with alkyl substituents in the 4-position have been prepared by the reaction of alkyl vinyl ketones with aniline. In 1907, Blaise and Maire⁴ reported that the condensation product of ethyl vinyl ketone and aniline gave 4-ethylquinoline on heating with aniline hydrochloride. Later, Prill and Walter⁵ found that 4-substituted quinolines could be prepared in good yield by the reaction between methyl vinyl ketone, its homologs and derivatives, and an aromatic amine in the presence of sulfuric acid and an oxidizing agent such as nitrobenzene or arsenic acid. Recently Campbell and his associates⁶ have further developed this modification of the Skraup reaction to prepare a number of lepidines.

Our interest in preparing 6-methoxy-8-nitroquinoline caused us to investigate the same reaction, employing acrolein in place of methyl vinyl ketone under somewhat milder conditions.

(1) Bergstrom, *Chem. Rev.*, **35**, 77 (1944); Manske, *ibid.*, **30**, 113 (1942).

(2) Manske, Marion and Leger, *Can. J. Research*, **B20**, 133 (1942).

(3) Utermohlen, *J. Org. Chem.*, **8**, 544 (1943).

(4) Blaise and Maire, *Compt. rend.*, **144**, 93 (1907); *Bull. soc. chim.*, [4] **3**, 667 (1908).

(5) Prill and Walter, U. S. Patent 1,806,563 and 1,806,564; *C. A.*, **25**, 3668 (1931).

(6) Campbell, *et al.*, *THIS JOURNAL*, **67**, 86 (1945); **68**, 1837 (1946); abstracts of the American Chemical Society, Chicago meeting, Sept. 9–13, 1946.

We wish to report at this time that the desired quinoline derivative was obtained in 42.3% yield. Since aniline and acrolein under these conditions gave no more than traces of quinoline, it appears likely that some activation of the *ortho* hydrogen is necessary for ring closure.

Work is now in progress in these laboratories on the further development of this reaction.

Experimental

All melting points are uncorrected.

Preparation of 6-Methoxy-8-nitroquinoline.—An intimate mixture of 168 g. (1.0 mole) of 3-nitro-4-aminoanisole, 132 g. of arsenic pentoxide, 152 ml. of concentrated sulfuric acid and 72 ml. of water was heated to 80°. To this was added dropwise 70 ml. of acrolein during two hours, maintaining the temperature at 75–80°. After the addition of the acrolein, the mixture was heated to 120° during one hour, cooled, diluted to five liters with water and filtered. The filtrate was neutralized with ammonia and the precipitated 6-methoxy-8-nitroquinoline was collected on a filter and air dried. After purification it melted at 157° and a mixed melting point with an authentic sample of 6-methoxy-8-nitroquinoline, prepared by the Skraup reaction, was 157°. The yield was 86.5 g. or 42.3% of the theoretical amount.

Reaction between Aniline and Acrolein.—The reaction was carried out as above except that 93 g. (1.0 mole) of aniline was substituted for the 3-nitro-4-aminoanisole. Subsequent to heating the reaction mixture to 120°, it was diluted with water and made alkaline with 40% sodium hydroxide solution. A large amount of semi-solid black material separated. The mixture was steam distilled to isolate any quinoline as well as the unreacted aniline. The steam distillate was extracted with ether, the ether extracts were dried and the ether removed by distillation. The entire residual oil distilled at 79–82° (20 mm.), weighed 12.0 g. and was identified as aniline by conversion to the *p*-toluenesulfonanilide, m. p. 109–110°. The reported melting point of this compound is 112°.

THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH
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NEW COMPOUNDS

Methylammonium Sulfamate

Ten grams of sulfamic acid was dissolved in water and neutralized with aqueous methylamine. The water was removed under reduced pressure on a steam-bath and the warm liquid residue (quantitative yield) was crystallized from methyl alcohol and dried *in vacuo* at 75°. The dense white needles melted at 91–93° and were found to be deliquescent.

Anal. Calcd. for $\text{CH}_5\text{O}_3\text{SN}_2$: N, 21.87. Found: N, 21.9.

Solubility in 100 g. of boiling solvent: methyl alcohol, over 124 g.; 2-B anhydrous ethyl alcohol, 2.3 g. From ethyl alcohol it separates in thin clear plates, m. p. 91–93°.

GEORGE A. BREON AND COMPANY
KANSAS CITY, MISSOURI

LOUIS H. GOODSON

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Some Esters of 2-Furoic Acid

The new compounds listed in Table I were prepared through the acid chloride.