allowed to reflux for 20 min. at 120–130° (oil bath). The mixture was allowed to cool, poured into 400 g. of crushed ice containing 160 ml. of water, and extracted with ether. The ether solution was washed with dilute sodium carbonate solution and then with water, dried, and the ether removed by evaporation. The residue was distilled at 104–107° at 0.25 mm. There was obtained 18.1 g. (94%) of colorless needles, m.p. 47–48°.

Preparation of the 2-quinoxalyl tertiary aminoalkyl ethers. The procedure is illustrated with the synthesis of 2-β-dimethylaminoethoxyquinoxaline. To a solution of 6.5 g. of β-dimethylaminoethanol in 50 ml. of anhydrous benzene was added 0.83 g. of sodium metal and the mixture was allowed to reflux on a steam bath for 1 hr. until all the sodium was dissolved. After cooling in an ice bath, 5.0 g. of 2-chloroquinoxaline was added and the mixture was allowed to reflux for 4 hr. The mixture was diluted with ether and washed with water. After drying and removal of solvents by evaporation, the residue was distilled. There was obtained 6.0 g. (91%) of a light yellow oil, boiling at 112–114° at 0.005 mm.

Acknowledgment. The authors are grateful to the Smith Kline and French Laboratories for a research grant which made this work possible and to Dr. James W. Wilson for his interest in this work.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF NEW MEXICO
ALBUQUERQUE, N. M.

3-Methyl-8-nitroisoquinoline[1]

FRANK D. POPP AND EARL BRILL

Received June 27, 1960

The nitration of isoquinoline has been shown[2] to give 5-nitroisoquinoline as a major product and 8-nitroisoquinoline as a minor product. A methyl group in the 3-position of isoquinoline would not be expected to alter the orientation appreciably and in fact two products, m.p. 109–110° (major product) and m.p. 85–90° (minor product), have been reported from the nitration of 3-methylisoquinoline.[3,4]

Elderfield and co-workers[4] demonstrated that the major product (m.p. 109–110°) of this nitration was indeed 3-methyl-5-nitroisoquinoline by oxidation to the carboxylic acid followed by decarboxylation to 5-nitroisoquinoline. At that time no attempt was made to prove the structure of the minor product from the nitration reaction although it was presumed to be 3-methyl-8-nitroisoquinoline. The earlier workers[3] had considered that the two products might be isomers or that they might be different crystalline modifications of the same substance since amines of identical melting points and mixed melting point were formed on reduction.

Since we required various nitroisoquinolines for several projects in progress in this laboratory, it was decided to investigate the structure of the minor nitration product of 3-methylisoquinoline. In order to determine if the nitration products were isomers or crystalline modifications they were converted to the picrates. 3-Methyl-5-nitroisoquinoline picrate melted sharply at 190–191° without recrystallization while the picrate of the minor product had m.p. 177–186°. Several recrystallizations gave a m.p. 185–187° and a mixed melting point with 3-methyl-5-nitroisoquinoline picrate of 178–188°. These results indicate that while the minor product might contain some 3-methyl-5-nitroisoquinoline it did contain a second substance.

Oxidation of the 3-methylnitroisoquinoline, m.p. 89–91°, with selenium dioxide gave a crude aldehyde which was not purified but rather oxidized in the crude state to a nitroisoquinoline-3-carboxylic acid. The use of hydrogen peroxide, as described for the oxidation of isoquinoline-3-carboxaldehyde,[5] gave somewhat better results than the use of sodium dichromate.[4] When the crude carboxylic acid was heated above its melting point *in vacuo* fine light yellow needles of 8-nitroisoquinoline sublimed indicating that the minor nitration product was, at least in part, 3-methyl-8-nitroisoquinoline.

EXPERIMENTAL[6]

Selenium dioxide oxidation. A solution of 8.66 g. of the minor product from the nitration of 3-methylisoquinoline,[3,4] m.p. 89–91°, in 130 ml. of nitrobenzene was added slowly with agitation to a suspension of 6.5 g. of selenium dioxide in 60 ml. of nitrobenzene. During the addition the mixture was brought to reflux and refluxing was continued for 1.5 hr. After cooling, the solution was washed with 100 ml. of 5% sodium hydroxide solution and 100 ml. of water and then extracted with five 50-ml. portions of 10% hydrochloric acid. The acid extracts were neutralized with 20% sodium hydroxide solution, chilled, and filtered. The filtrate was extracted with chloroform and the filter cake was leached with chloroform. Concentration of the combined chloroform solutions gave 2.6 g. of solid, m.p. 140–160° which gave positive tests with 2,4-dinitrophenylhydrazine and had an infrared spectrum indicating a mixture of aldehyde and unoxidized methyl compound.

Hydrogen peroxide oxidation. An acetone solution of 1 g. of the crude aldehyde prepared above and 3 ml. of hydrogen peroxide (30%) was allowed to stand several hours at room temperature. An additional 5 ml. of hydrogen peroxide was added and the solution allowed to stand overnight. Partial evaporation and filtration gave a solid. A solution of this solid percarboxylic acid was boiled in water for an hour. Upon partial evaporation and cooling about 0.8 g. of crude carboxylic acid, m.p. 230–240° was obtained.

---

(1) This investigation was supported in part by funds from an Institutional Grant of the American Cancer Society to the University of Miami, in part by Research Grant CY 4814 from the National Cancer Institute, U.S. Public Health Service, and in part by a grant from the Research Corporation.

(2) M. J. S. Dewar and P. M. Maitlis, *J. Chem. Soc.*, 2521 (1957).

(3) F. W. Bergstrom and R. E. Patterson, *J. Org. Chem.*, 10, 479 (1945).

(4) R. C. Elderfield, J. M. Lagowski, O. L. McCurdy, and S. L. Wythe, *J. Org. Chem.*, **23**, 435 (1958).

(5) C. E. Teague, Jr., and A. Roe, *J. Am. Chem. Soc.*, **73**, 688 (1951).

(6) All melting points are uncorrected.

Decarboxylation. The crude carboxylic acid was heated above its melting point in a sublimation apparatus at 35 mm. A sublimate of fine yellow needles was obtained. After recrystallization from aqueous ethanol this material was identified by m.p. (87–88°) as 8-nitroisoquinoline. This solid gave a picrate, m.p. 183–184°; reported for 8-nitroisoquinoline, m.p. 87–87.5[2]; reported for 5-nitroisoquinoline, m.p. 110.5–111.5°[2]; picrate, m.p. 220°.[7] The ultraviolet spectrum of this solid had maximum at 234 mμ, 292 mμ, and 330 mμ; reported[2] for 8-nitroisoquinoline 235 mμ, 292 mμ, and 328 mμ.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF MIAMI
CORAL GABLES, FLA.

---

(7) P. Fortner, *Monatsh.*, 14, 146 (1893).

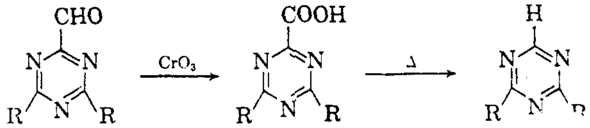
Reactions of *s*-Triazine Aldehydes[1]

EHRENFRIED KOBER[2]

Received June 29, 1960

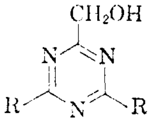
After synthesis and properties of 4,6-dimethoxy-*s*-triazine-2-aldehyde (I) and 4,6-bis(methylthio)-*s*-triazine-2-aldehyde (II) had been reported,[3] the reactivity of these first representatives of a novel class of aldehydes was investigated.

It is known that *N*-heterocyclic 2-aldehydes, containing the partial structure —N═C—CHO, are remarkably resistant to oxidation.[4] Therefore, it is not surprising that the formation of the triazine carboxylic acids III and IV from aldehydes I and II by autoxidation could not be realized.[3] Conversion to the desired carboxylic acids could also not be achieved by oxidizing agents such as hydrogen peroxide, nitric acid, potassium permanganate, or silver oxide which either did not affect the aldehyde group at all or attacked simultaneously the methoxy or methylthio substituents. The carboxylic acids III and IV were formed, however, when the oxidation was carried out with chromic acid. 4,6-Dimethoxy-*s*-triazine-2-carboxylic acid (III) could not be separated from its reaction mixture by means of solvents. Isolation by vacuum sublimation could not be accomplished, since compound III decarboxylated to give 2,4-dimethoxy-*s*-triazine (V). In contrast to III, the corresponding 4,6-bis(methylthio)-*s*-triazine-2-carboxylic acid (IV) is soluble in ether and was, therefore, easily isolated. When subjected to thermal decarboxylation, IV yielded 2,4-bis(methylthio)-*s*-triazine (VI).

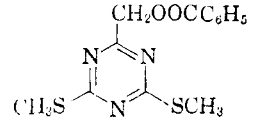


I. R = OCH_3
II. R = SCH_3
III. R = OCH_3
IV. R = SCH_3
V. R = OCH_3
VI. R = SCH_3

The hydrogenation of compounds I and II with sodium borohydride gave, as expected, 2-hydroxymethyl-4,6-dimethoxy-*s*-triazine (VII) and 2-hydroxymethyl-4,6-bis(methylthio)-*s*-triazine (VIII). Compound VII proved to be identical with an authentic sample,[5] whereas VIII was identified by its reaction with benzoyl chloride which afforded 2-benzoxymethyl-4,6-bis(methylthio)-*s*-triazine (IX).



VII. R = OCH_3
VIII. R = SCH_3



IX

The acyloin condensation of compounds I and II resulted in yellow precipitates which were insoluble or only slightly soluble in the usual organic solvents, but could be recrystallized from pyridine. Analyses of the yellow, crystalline products thus obtained, corresponded perfectly with those of the expected acyloins; however, in view of their low solubility and their color it is assumed that these products are endiols, represented by structural formulas X and XI. Corresponding structures have also been postulated for the compounds obtained from the acyloin condensation of quinoline-2-aldehydes[6,7] and of pyridine-2-aldehyde.[8,9]

As additional products of the condensation, the corresponding glycols (XII and XIII) were isolated. Their formation can be explained by the assumption that a Cannizzaro reaction, catalyzed by potassium cyanide, took place as a side reaction In the case of aldehyde II, the occurrence of a simultaneous Cannizzaro reaction was confirmed by the isolation of a third reaction product, namely ethyl 4,6-bis(methylthio)-*s*-triazine-2-carboxylate (XIV). Apparently, the aldehyde II reacts in ethanolic solution in form of its ethyl hemi-acetal[3] to give the ethyl ester (XIV) instead of the free acid.

In this connection it should be noted that the Cannizzaro reaction of aldehydes I and II, carried out in the presence of potassium hydroxide, did not result in the expected compounds III and VII, or IV and VIII, respectively. As experienced in some

---

[1] This article is based on work performed under Project 116-B of The Ohio State University Research Foundation sponsored by Olin Mathieson Chemical Corp., New York, N. Y.

[2] Olin Mathieson Chemical Corp., New Haven, Conn.

[3] E. Kober and Ch. Grundmann, *J. Am. Chem. Soc.*, 80, 5547 (1958).

[4] Houben-Weyl, *Methoden der Organischen Chemie*, Vol. VII, I, p. 498, Georg Thieme Verlag, Stuttgart, 1954.

[5] Ch. Grundmann and E. Kober, *J. Am. Chem. Soc.*, 79, 944 (1957).

[6] C. A. Buehler and J. O. Harris, *J. Am. Chem. Soc.*, 72, 5015 (1950).

[7] C. A. Buehler and S. P. Edwards, *J. Am. Chem. Soc.*, 74, 977 (1952).

[8] F. Cramer and W. Krum, *Ber.*, 86, 1586 (1953).

[9] W. Mathes, W. Sauermilch, and Th. Klein, *Ber.*, 84, 452 (1951).