CRYSTALLOGRAPHIC DATA

Compound	Space group	a	b	c	No. in cell	No. asymmetric unit	Density	Mol. wt.
Cinobufagin	$P2_12_12_1$	7.61 α	15.79 γ	19.45 β	4	1	1.261	447 ± 10
Acetylcinobufagin	$C222_1$	28.74 γ	8.14 β	44.76 α	16	2	1.229	487 ± 10
Cinobufagone	$P2_12_12_1$	21.79 β	8.62 γ	24.22 α	8	2	1.280	443 ± 10

Acetylcinobufagin: fine orthorhombic needles elongated along (010), (001) dominating. Birefringence low.

Cinobufagone: small orthorhombic needles elongated along (010) and growing least on (001). The crystals appear partly redissolved and show curved surfaces instead of the c face. Birefringence low.

The densities of both compounds were determined by flotation in zinc sulfate solutions, the centrifuge being used to hasten equilibrium. These are correct to ±0.4%. The probable error on the x-ray dimensions is not more than ±0.5%.

graphic arrangement of the molecules as is found, for example, in the study of the sugars. Both the presence of the hydroxyl groups and the orthorhombic symmetry shown by the crystals of these cinobufagin compounds render it impossible to make deductions in regard to the molecular arrangement and molecular dimensions from the combination of the optical with the crystallographic data. One can only state that the data are not incompatible with formulas of the cardiac aglucone type and for comparison reference may be made to the complex crystal structures assumed by strophanthidin and certain of its derivatives.

Summary

The determinations of molecular weights of cinobufagin and two of its derivatives, acetylcinobufagin and cinobufagone, indicate that cinobufagin has the composition $C_{26}H_{34}O_6$. The analytical data previously reported for cinobufagin and certain of its derivatives agree with this new formula.

OXFORD, ENGLAND
BALTIMORE, MARYLAND RECEIVED JULY 27, 1936

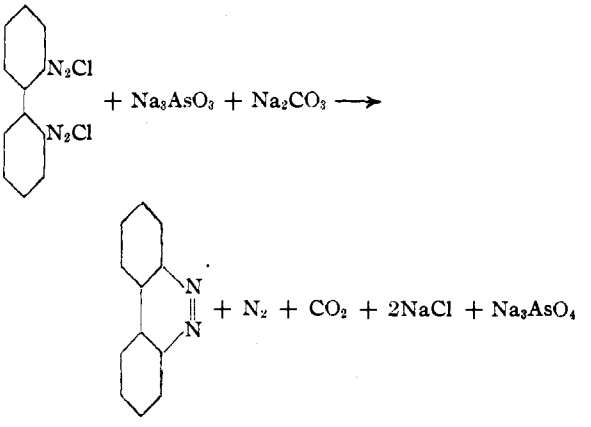
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ALBERTA]

The Formation of Cyclic Azo Compounds from 2,2′-Diaminodiphenyls

BY R. B. SANDIN AND T. L. CAIRNS

The compound 4,4′-diarsonodiphenyl[1,2] has been prepared from benzidine, according to the method of Bart. In an attempt to prepare the isomeric 2,2′-diarsonodiphenyl by an analogous procedure, the authors of this paper have found that when tetrazotized 2,2′-diaminodiphenyl is treated with arsenious oxide in sodium carbonate solution, a considerable part of the tetrazotized compound is converted into *o,o′*-azodiphenyl.[3] The authors believe it to be a general reaction. It is also believed that the arsenite functions as a reducing agent instead of proceeding according to the typical Bart reaction.

The proposed equation for this reaction is



(1) Bauer and Adams, THIS JOURNAL, **46**, 1925 (1924).

(2) Hill, *ibid.*, **46**, 1855 (1924).

(3) This compound is also called phenazone and *o*-diphenyleneazone [Täuber, *Ber.*, **24**, 3081 (1891)]. Bigelow [*Chem. Rev.*, **9**, 117 (1931)] has suggested the name cyclic *o,o*-azoxydiphenyl, in place of diphenazonoxyd. For that reason it might, perhaps, be better to call phenazone or *o*-diphenyleneazone, cyclic *o,o*-azodiphenyl.

Experimental

Cyclic *o,o′*-Azodiphenyl.—In a mixture of 250 cc. of 2 *N* hydrochloric acid and 150 cc. of water, 18.4 g. of 2,2′-diaminodiphenyl was dissolved. The solution was cooled to 0°, and to it was added gradually 100 cc. of 2 *N* sodium nitrite and an excess of nitrite was maintained for thirty minutes. The clear solution of the tetrazotized compound

was made neutral to Congo red by the addition of 50 cc. of 2 *N* sodium carbonate which had been diluted to 100 cc. A solution of sodium arsenite was prepared by dissolving 30 g. of arsenious oxide in 300 cc. of 2 *N* sodium carbonate, and to it was added 2 g. of copper sulfate to serve as a catalyst. After this had been cooled to 0°, the tetrazotized diaminodiphenyl solution was siphoned into the arsenite solution during fifteen to twenty minutes. During this procedure there was much gas evolved and there was considerable foaming, which was very difficult to get rid of. An olive-green precipitate was produced, which was filtered by suction and washed with water. The precipitate was extracted with hot 10% hydrochloric acid and the extract was neutralized with ammonia or sodium hydroxide. This gave a precipitate of crude cyclic *o,o'*-azodiphenyl. The yield was 7.5 g. or 45% of the theoretical amount. The crude material melted at 153–154°. It was crystallized from alcohol and gave yellow crystals melting at 155°. A mixed melting point carried out with a sample of the cyclic azo compound prepared according to Täuber,[3] showed no depression of the melting point. It also gave a picrate melting at 191°.

Cyclic Azo Compound from 2,2'-Diamino-4,4'-dimethyldiphenyl.[4]—This compound was prepared in a manner similar to the above, from 2,2'-diamino-4,4'-dimethyldiphenyl. It consisted of yellow needles, soluble in dilute hydrochloric acid, and melted at 184–185°. A mixed melting point carried out with this sample and the compound produced by the sodium amalgam and methanol reduction of 2,2'-dinitro-4,4'-dimethyldiphenyl showed no depression of the melting point.

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Summary

Tetrazotized diaminodiphenyls, when treated with arsenious oxide in sodium carbonate solution, are in part converted into cyclic azo compounds.

(4) Ullmann and Dieterle, *Ber.*, **37**, 24 (1904).

EDMONTON, ALBERTA, CANADA RECEIVED JUNE 2, 1936

[CONTRIBUTION FROM THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, COLUMBIA UNIVERSITY]

Carboxymethoxylamine

BY E. BOREK[1] AND H. T. CLARKE

In the course of experiments on the synthesis of canaline and analogous compounds, the need arose for a convenient process for preparing carboxymethoxylamine (hydroxylamineacetic acid). In view of the recent report by Anchel and Schoenheimer[2] of the use of this substance as a reagent for the isolation of ketones from natural sources, an early description of our method of preparation seems advisable.

Carboxymethoxylamine was first prepared by Werner[3,4] by the hydrolysis of ethylbenzhydroximinoacetic acid; it has also very recently been prepared by Kitagawa and Takani[5] by condensation of benzhydroxamic acid and ethyl bromoacetate, with subsequent hydrolysis by hydrochloric acid.

The method here described consists in condensing the sodium derivative of acetoxime with ethyl chloroacetate, followed by successive alkaline and acid hydrolysis of the condensation product. The intermediate acetone carboxymethoxime may also be prepared, though in somewhat smaller yields, by condensing acetoxime with sodium chloroacetate in alkaline solution by a modification of the method of Hantzsch and Wild.[6]

The carboxymethoxylamine is isolated in the form of its hydrochloride, which melts at 151°. This product in our hands has invariably proved to consist of the hemihydrochloride; that prepared by Werner was reported to melt at 147–148°[3] and at 156°[4,5] and to give analytical figures agreeing satisfactorily with the normal hydrochloride. We are unable to account for this discrepancy.

Experimental

A solution of 24.4 g. of acetoxime in 250 cc. of absolute alcohol was added to a solution of 7.7 g. of sodium in 150 cc. of absolute alcohol. The alcohol was removed by distillation under diminished pressure and the white crystalline residue was dried *in vacuo* over phosphorus pentoxide. To the dry salt 100 cc. of ethyl chloroacetate was added and the mixture refluxed for thirty minutes. When cool, the salt was filtered off and well washed with absolute alcohol. The alcohol and the unreacted ethyl chloroacetate were removed under diminished pressure, the fraction distilling up to 52° under 28 mm. being discarded.

The sirupy residue, which consisted mainly of acetone carbethoxymethoxime, together with the corresponding

(1) This report is from a dissertation submitted by Ernest Borek in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

(2) Anchel and Schoenheimer, *J. Biol. Chem.*, **114**, 539 (1936).

(3) Werner, *Ber.*, **26**, 1567 (1893).

(4) Werner and Sonnenfeld, *ibid.*, **27**, 3350 (1894).

(5) Kitagawa and Takani, *J. Biochem. (Tokio)*, **23**, 181 (1936).

(6) Hantzsch and Wild, *Ann.*, **289**, 285 (1896).