

duced. The ether layer was separated, dried over potassium hydroxide and slowly run into a small warmed flask through a dropping funnel, in such a manner as to get rid of the ether by distillation without having too large a container for the amine. The residual products were generally distilled at atmospheric pressures.

We have obtained 2-diethylaminoquinoline by the action of lithium diethylamide on 2-chloroquinoline, in agreement with the results of Gilman and co-workers.<sup>30</sup> Triphenylmethyl lithium, prepared by treating an ethereal solution of lithium diethylamide with triphenylmethane, did not react with phenyl bromide in two days in ether at room temperatures, nor was any phenylacetonitrile similarly formed from the lithium salt of acetonitrile and bromobenzene.

**N-Phenylpiperidine.**—Piperidine (45 g., dried over sodium ribbon and distilled) and bromobenzene (18.1 g.) were placed in a 500-cc. 3-necked flask with ground joints. A reflux condenser and a mercury-sealed stirrer were attached to the flask; the third opening, used for the introduction of lithium, was closed with a glass stopper.

Lithium (0.923 g. in several small slices) was introduced and the mixture refluxed gently for three hours; 0.055 g. of the metal was recovered unchanged at the end. The flask was then heated in an oil-bath and most of the piperidine boiled off and condensed; a solid, probably

$\text{LiBr} \cdot x\text{C}_6\text{H}_5\text{NH}$ , remained. Water was added, after cooling, and the resulting aqueous solution and oil extracted several times with benzene. The latter was distilled to obtain N-phenylpiperidine, b. p. 245–255°, in a yield of 6.4 g., or 70%, based on equation (1).

**N,N-Diethylaniline.**—In a similar fashion, N,N-diethylaniline (b. p. 207–212°) was obtained in 33% yield from bromobenzene, diethylamine and lithium. The reaction was much more rapid than in the preceding case, but was greatly hindered at the end by the formation of a coating of  $\text{LiBr} \cdot x(\text{C}_2\text{H}_5)_2\text{NH}$  over the lithium.

### Summary

Lithium diethylamide, lithium N-piperidyl- and lithium di-n-butylamide react with phenyl chloride or phenyl bromide in ether at ordinary temperatures to form diethylaniline, N-phenylpiperidine and di-n-butylaniline, respectively. Metallic lithium reacts with phenyl bromide in piperidine or in diethylamine to give N-phenylpiperidine or N,N-diethylaniline, respectively.

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## A Comparison between Certain Reactions of the Aloins and those of Glucose

BY JOHN H. GARDNER<sup>1</sup>

Some years ago, it was shown that, under a variety of conditions, the aloins yield formaldehyde and furfural, although in extremely small amounts.<sup>2</sup> The formation of formaldehyde from glucose and other sugars during the distillation of neutral, acid and alkaline solutions was reported earlier by Klein,<sup>3</sup> and Rosenthaler<sup>4</sup> obtained it as a product of the oxidation of glucose and other sugars and of barbaloin with potassium permanganate in the presence of sulfuric acid. An indication of the possible formation of furfural from a mixture of sucrose and invert sugar was obtained by Englis and Hale.<sup>5</sup> It has now been found that glucose, like the aloins, yields a very small quantity of formaldehyde on treatment with sodium perborate, with a considerable increase when the reaction is followed by acidification to 12% hydrochloric acid before distillation. The acidified solution also yields furfural. With borax alone, glucose gives only a trace of formaldehyde and no furfural. When the borax hydrolyzate is adjusted to 12% hydrochloric acid before distillation, both furfural and formaldehyde are found in the distillate. The aloins gave formaldehyde from the acidified hydrolyzate only, and no furfural after borax hydrolysis with or without acidification. Glucose also yields both

formaldehyde and furfural on distillation with 12% hydrochloric acid.

The glucose was Mallinckrodt c. p. anhydrous. The hydrolyses were carried out with the same concentrations and conditions that were previously used for the decompositions of the aloins.<sup>2</sup> Formaldehyde was detected as formaldimethone which was dried, weighed and then recrystallized from alcohol. The purified samples all melted between 188 and 191°, and showed no depression in melting point when mixed with an authentic sample of formaldimethone, m. p. 189–191°. Furfural was detected by the addition of a freshly prepared, filtered solution of 1 g. of 2,4-dinitrophenylhydrazine in 10 cc. of concd. hydrochloric acid and 60 cc. of water. The precipitate was filtered out, dried, and weighed. For proof of identity, the product was converted into furfural acetyl 2,4-dinitrophenylhydrazone,<sup>6</sup> since Bredereck has shown that furfural 2,4-dinitrophenylhydrazone is commonly formed as a mixture of two stereoisomers with no definite melting point. We have found indications that the same thing is true of the *p*-nitrophenylhydrazone. The products obtained from the glucose hydrolyzates melted between 166 and 172°, showing no depression when mixed with an authentic sample of furfural acetyl 2,4-dinitrophenylhydrazone, m. p. 171–171.5°. The results of the individual experiments, together with the earlier results of Gardner and Campbell on aloin, are collected in Table I.

(1) Present address, J. T. Baker Chemical Co., Phillipsburg, N. J.  
(2) J. H. Gardner and J. A. Campbell, *THIS JOURNAL*, **64**, 1378 (1942).

(3) G. Klein, *Biochem. Z.*, **160**, 132 (1926).

(4) L. Rosenthaler, *Arch. Pharm.*, **261**, 587 (1913).

(5) D. T. Englis and C. Hale, *THIS JOURNAL*, **47**, 446 (1925).

(6) H. Bredereck, *Ber.*, **65**, 1833 (1932).

TABLE I

Reagents	Glucose, g.	Formal-dimethone, mg.	Furfural 2,4-dinitrophenylhydrazone, mg.	Aloin, g.	Formal-dimethone, mg.	Furfural
NaBO <sub>3</sub>	10	10	None	80	Found	None
NaBO <sub>3</sub> + HCl to 12%	10	65	365	80	60	2 cc.
Borax	20	1	None	60	0	0
Borax + HCl to 12%	60	35	215	60	15	0 to trace
12% HCl	50	Some	105	3 <sup>a</sup>		0.0134 g. phloroglucide

<sup>a</sup> L. Joseph, unpublished results. Compare Goldner, *J. Am. Pharm. Assoc.*, **21**, 658 (1932).

### Discussion

The majority of investigators who have suggested possible structures for barbaloin and isobarbaloin have postulated that the substances are either D-arabinosides or D-arabinose ethers of aloe-emodin or its anthranol,<sup>7,8,9</sup> despite the fact that no published analyses agree with such a formula. The main support for these postulations has been Léger's<sup>7</sup> demonstration of the formation of D-arabinose and aloe-emodin by slow acid hydrolysis of barbaloin and the discovery by Hauser that aloe-emodin anthrone is produced when borax is used. Earlier papers from this Laboratory have indicated that the aloins are not glycosides,<sup>10</sup> and Rosenthaler<sup>9</sup> has presented convincing arguments against the D-arabinose formula based upon the absence of aldehyde reactions.

Recently, Owen and Simonsen<sup>11</sup> have presented evidence that the molecular formula for barbaloin is C<sub>21</sub>H<sub>24</sub>O<sub>11</sub>, in agreement with analyses carried out in this Laboratory by Joseph and with many published analyses. This is consistent with a carbon skeleton having a β-methylanthracene ring structure with a six carbon side chain.

(7) E. Léger, *Ann. chim.*, [9] **6**, 339 (1916).

(8) F. Hauser, *Pharm. Acta Helv.*, **6**, 79 (1931).

(9) L. Rosenthaler, *ibid.*, **7**, 19 (1932).

(10) J. H. Gardner and T. F. McDonnell, *THIS JOURNAL*, **59**, 857 (1937), and earlier papers.

(11) L. N. Owen and J. L. Simonsen, *THIS JOURNAL*, **64**, 2516 (1942).

The formation of furfural and formaldehyde is not specific for glucose as preliminary experiments have shown that D-fructose behaves similarly and presumably other hexoses and pentoses yield the same products. We may then conclude that the formation of furfural under the conditions described in this paper is characteristic of a five or six carbon sugar or sugar-like molecule, and the formation of formaldehyde presumably of a polyhydroxy alcohol. By analogy, we may now assign to the aloins either a five or a six carbon side chain, but can not determine which is correct until further evidence is available. Obviously, a five carbon side chain leaves one carbon atom to be accounted for in an additional group. This problem will be considered further in a subsequent paper.

### Summary

It has been shown that D-glucose yields furfural and formaldehyde under the same conditions as do the aloins. This makes possible the consideration of a six carbon chain as a part of the aloin molecule instead of the five carbon atom chain hitherto being considered as necessary to explain the results obtained with these compounds.

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## Quinazolines. II. Properties of 4-Substituted Quinazolines<sup>1</sup>

BY ARTHUR J. TOMISEK AND BERT E. CHRISTENSEN

In the attempted synthesis of 4-acetylquinazoline, 4-chloroquinazoline was used as a synthetic intermediate. During the course of this work certain interesting properties of the latter compound were observed which have not been previously recorded. In particular, it was noted that the pH had a marked influence on the stability of this compound. For this reason the work was extended to include a study of acid activation of 4-substituted quinazolines in general.

The reactivity of 4-chloroquinazoline has been demonstrated by the ability of 4-chloroquinazoline

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to give active halide condensations with Grignard reagents<sup>2</sup> and of 2,4-dichloroquinazoline to react with atmospheric moisture.<sup>3</sup> These observations were augmented by the discovery in this Laboratory that pure 4-chloroquinazoline reacts spontaneously with absolute methanol at room temperature, evolving considerable heat,<sup>4,5</sup> and yield-

(2) Hentrich, Hardtman and Knoche, U. S. Patent 1,780,879 (Nov. 1930).

(3) Abt, *J. prakt. Chem.*, [2] **39**, 150 (1889).

(4) This phenomenon was first observed by Bruce Graham, of this Laboratory.

(5) Lange and Sheibley<sup>6</sup> did find that 4-alkoxy quinazolines could be prepared by using potassium cyanide, sodium carbonate or sodium acetate in place of sodium alkoxide, and on these grounds postulated an alkoxy-chloro equilibrium, which proceeded to completion only