

tion (2), or by loss of a chloride ion by reaction (3) to give chloroacetylene.

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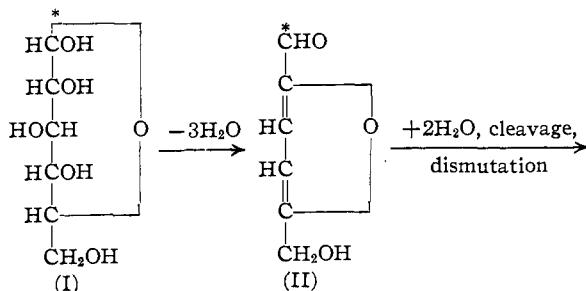
RECEIVED JUNE 29, 1949

### The Action of Hydrobromic Acid on 1-C<sup>14</sup>-D-Glucose

BY JOHN C. SOWDEN

The dehydration and cleavage of D-glucose by vigorous treatment with mineral acids was first studied by Grote and Tollens<sup>1</sup> who recognized the principal products of the reaction as levulinic acid and formic acid, which are formed along with varying amounts of highly colored polymeric "humins." Earlier, Mulder<sup>2</sup> had obtained formic acid from the action of sulfuric acid on sucrose and undoubtedly the other product he obtained, "glucinic acid," was in reality levulinic acid, later purified, characterized and renamed by Grote and Tollens.<sup>3</sup>

The mechanism of the reaction remained obscure until comparatively recent times: 5-Hydroxymethyl-2-furaldehyde was recognized as a probable intermediate by Kiermayer<sup>4</sup> and by van Ekenstein and Blanksma.<sup>5</sup> Following a critical study of the reaction, Pummerer and co-workers<sup>6</sup> concluded that 5-hydroxymethyl-2-furaldehyde (II) is first formed from the hexose (I) with the loss of three molecules of water and that this intermediate then undergoes hydration, cleavage and dismutation to produce levulinic and formic acids (III)



According to this proposed mechanism, the aldehyde carbon of the hexose eventually becomes the carbon of the resultant formic acid. This latter assumption has now been substantiated by an examination of the products from 1-C<sup>14</sup>-D-glucose<sup>7</sup> and hydrobromic acid: The levulinic acid produced was devoid of radioactivity whereas the formic acid showed quantitatively the radioactivity previously possessed by the aldehyde carbon of the glucose.

- (1) Grote and Tollens, *Ann.*, **206**, 226 (1880).
- (2) Mulder, *J. prakt. Chem.*, **21**, 229 (1840).
- (3) Grote and Tollens, *Ber.*, **7**, 1375 (1874).
- (4) Kiermayer, *Chem. Z.*, **19**, 1004 (1895).
- (5) van Ekenstein and Blanksma, *Ber.*, **43**, 2355 (1910).
- (6) Pummerer and Gump, *ibid.*, **56**, 999 (1923); Pummerer, Guyot and Birkofer, *ibid.*, **68**, 480 (1935).
- (7) Sowden, *Science*, **109**, 229 (1949).

### Experimental

One gram of 1-C<sup>14</sup>-D-glucose, showing radioactivity of 860  $\pm$  20 c.p.m./mg., was heated with 10.0 cc. of 10% hydrobromic acid in a sealed tube at 130° for twenty-four hours.<sup>8</sup> The resulting slight precipitate of "humins" was filtered off and washed. Sufficient sodium hydroxide solution was then added to the filtrate to exactly neutralize the hydrobromic acid. The resulting solution was distilled to dryness, using an oil-bath, and water was added and the distillation repeated twice.

The residue was extracted with anhydrous ether and the extract concentrated. The residual liquid, on treatment with phenylhydrazine, yielded 0.55 g. (48%) of non-radioactive levulinic acid phenylhydrazone, m. p. after recrystallization 109–110°.<sup>9</sup>

The distillate from the reaction mixture was titrated with 0.1 N sodium hydroxide solution to neutralize the distilled formic acid, requiring 44.7 cc. (80%) to the methyl red end-point. The resulting sodium formate was converted to *p*-phenylphenacyl formate, m. p. after recrystallization 74–75°.<sup>10</sup> This product when counted in the same manner<sup>7</sup> as the original 1-C<sup>14</sup>-D-glucose showed radioactivity of 650  $\pm$  20 c.p.m./mg. On the assumption that the formic acid was produced from the aldehyde carbon of the D-glucose the predicted radioactivity was 645  $\pm$  20 c. p. m./mg.

(8) Floetz, *Naturwiss.*, **29**, 707 (1941).

(9) Fischer, *Ann.*, **236**, 146 (1886).

(10) Drake and Bronitsky, *THIS JOURNAL*, **52**, 3715 (1930).

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RECEIVED MAY 9, 1949

### An Antistine Intermediate

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This synthesis of (N-phenyl-N-benzylglycyl)-2'-aminoethylamide, Ph(PhCH<sub>2</sub>)NCH<sub>2</sub>-CONHCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, represents an abandoned project in which it was desired to test a synthetic route leading to compounds of antistine-like structure.

**Ethyl N-Benzyl-N-phenylglycinate.**—Twenty-one and two-tenths grams (0.116 mole) of benzylaniline<sup>2</sup> and 6.42 ml. (0.058 mole) of ethyl bromoacetate in a stoppered flask were heated in a 45° oven for twenty hours. The pasty product was churned for two hours with 585 ml. of 0.3 N hydrochloric acid (0.174 mole) in order to extract unreacted benzylaniline. The viscous, semi-crystalline phase was crude ethyl N-benzyl-N-phenylglycinate hydrochloride. This was an unstable product, and was therefore dried in a desiccator and used directly in the next step.

**(N-Phenyl-N-benzylglycyl)-2'-aminoethylamide.**—The crude ethyl N-phenyl-N-benzylglycinate and 35 ml. of ethylenediamine (95–100%) were refluxed for five hours, cooled and poured into water. The oily phase was extracted with methylene chloride, washed with water and dried over sodium sulfate. Solvent was removed on a steam-bath and the residue was crystallized and recrystallized from anhydrous butanol-ethanol-hydrogen chloride. The white powder separated very slowly. It was characterized by the benzaldehyde odor and the intense red color which result from its contact with strong nitric

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(2) Willson and Wheeler, "Organic Syntheses," Coll. Vol. I, 102 (1941).