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

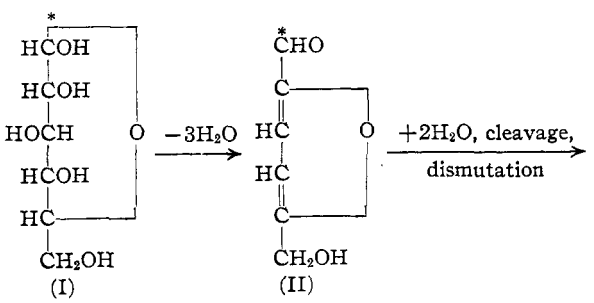
THE LABORATORY OF THE
LINDE AIR PRODUCTS COMPANY
TONAWANDA, NEW YORK RECEIVED JUNE 29, 1949

The Action of Hydrobromic Acid on 1-C^{14}-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[1] 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[2] 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.[3]

The mechanism of the reaction remained obscure until comparatively recent times: 5-Hydroxymethyl-2-furaldehyde was recognized as a probable intermediate by Kiermayer[4] and by van Ekenstein and Blanksma.[5] Following a critical study of the reaction, Pummerer and co-workers[6] 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^{14}-D-glucose[7] 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^{14}-D-glucose, showing radioactivity of 860 ± 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.[8] 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°.[9]

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°.[10] This product when counted in the same manner[7] as the original 1-C^{14}-D-glucose showed radioactivity of 650 ± 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 ± 20 c. p. m./mg.

(8) Ploetz, *Naturwiss.*, **29**, 707 (1941).
(9) Fischer, *Ann.*, **236**, 146 (1886).
(10) Drake and Bronitsky, THIS JOURNAL, **52**, 3715 (1930).

RADIOCHEMISTRY LABORATORY
DEPARTMENT OF CHEMISTRY
WASHINGTON UNIVERSITY
SAINT LOUIS, MISSOURI RECEIVED MAY 9, 1949

An Antistine Intermediate

BY ARTHUR J. TOMISEK[1]

This synthesis of (N-phenyl-N-benzylglycyl)-2′-aminoethylamide, $Ph(PhCH_2)NCH_2CONHCH_2CH_2NH_2$, 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[2] 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

(1) Present address: Institute for Enzyme Research, University of Wisconsin, Madison, Wis.
(2) Willson and Wheeler, "Organic Syntheses," Coll. Vol. I, 102 (1941).

acid.[3,4] The yield of crude, pale blue dihydrochloride was 6.8 g. (33% based on ethyl bromoacetate). For purposes of analysis a sample was purified by chromatography of an absolute alcoholic solution over hydrochloric acid-washed alumina. Pure samples of the monohydrochloride were readily obtained by diluting the first few fractions with dry acetone, then adding dry ether to incipient turbidity. The white leaflets melted at 189° (microblock). *Anal.* Calcd. for $C_{17}H_{21}N_3O\cdot HCl$: C, 63.84; H, 6.93; N, 13.14; Cl, 11.09. Found: C, 63.68; H, 6.85; N, 13.13; Cl, 11.17.

(N-Phenyl-N-benzylglycyl)-2'-benzamidoethylamide.—This was prepared in excellent yield from the preceding compound by the Schotten–Baumann method and recrystallized from pyridine–water and from alcohol; m. p. 165–166° (microblock). *Anal.* Calcd. for $C_{24}H_{25}N_3O_2$: C, 74.40; H, 6.50; N, 10.85. Found: C, 74.36; H, 6.65; N, 10.64.

(3) The color test is negative for the ethyl phenylbenzylglycinate.

(4) Bischoff, *Ber.*, **31**, 2675 (1898), reports the benzaldehyde test as characteristic of N-phenyl-N-benzylglycine.

NUTRITION RESEARCH LABORATORIES
CHICAGO 30, ILL.

RECEIVED JUNE 13, 1949

NEW COMPOUNDS

Symmetrical Morpholinium and Thiamorpholinium Alkyl Sulfates[1]

The previously reported studies in "Symmetrical Morpholinium Alkyl Sulfates"[2] dealt with the reaction of dimethyl, diethyl, di-*n*-butyl, di-*n*-hexyl and di-*n*-hexadecyl sulfates with N-*n*-dodecyl, N-*n*-tetradecyl, N-*n*-hexadecyl and N-*n*-octadecyl morpholines. The purpose of the present communication is to report the extension of these reactions to include di-*n*-octyl, di-*n*-decyl and di-*n*-dodecyl sulfates and the reaction of di-*n*-hexadecyl sulfate with the corresponding previously described thiamorpholines, oxides and dioxides.[3]

TABLE I

SYMMETRICAL N,N-DIALKYL MORPHOLINIUM ALKYL SULFATES $O(CH_2CH_2)_2N(R)(R')^+SO_4R'^-$

R	R'	Formula	M. p., °C. (uncor.)	N analyses, % Calcd.	Found
n-Dodecyl	*n*-Octyl	$C_{32}H_{67}O_6NS$	112	2.43	2.46
n-Tetradecyl	*n*-Octyl	$C_{34}H_{71}O_6NS$	122	2.31	2.37
n-Hexadecyl	*n*-Octyl	$C_{36}H_{75}O_6NS$	132	2.21	2.27
Methyl	*n*-Decyl	$C_{26}H_{53}O_6NS$	99	2.92	2.99
n-Dodecyl	*n*-Decyl	$C_{36}H_{75}O_6NS$	81	2.21	2.26
n-Tetradecyl	*n*-Decyl	$C_{38}H_{79}O_6NS$	79	2.10	2.11
n-Hexadecyl	*n*-Decyl	$C_{40}H_{83}O_6NS$	82	2.03	2.03
Methyl	*n*-Dodecyl	$C_{30}H_{61}O_6NS$	87	2.60	2.57
n-Dodecyl	*n*-Dodecyl	$C_{40}H_{83}O_6NS$	53	2.03	2.06
n-Tetradecyl	*n*-Dodecyl	$C_{42}H_{87}O_6NS$	63	1.95	1.93
n-Hexadecyl	*n*-Dodecyl[a]	$C_{44}H_{91}O_6NS$	93	1.88	1.85
Methyl	*n*-Hexadecyl[b]	$C_{37}H_{77}O_6NS$	99.5	2.16	2.11

[a] Calculated: C, 70.81; H, 12.29. Found: C, 70.88; H, 12.08. [b] Calculated: C, 68.57; H, 11.97; S, 4.93. Found: C, 68.91; H, 11.63; S, 4.84.

(1) Abstracted in part from the thesis presented by C. T. Camilli to the Graduate School of St. John's University in partial fulfillment of the requirements for the degree of Master of Science, April, 1948.

(2) J. B. Niederl and co-workers, THIS JOURNAL, **70**, 618 (1948).

(3) W. F. Hart and J. B. Niederl, *ibid.*, **66**, 1610 (1944); **68**, 714 (1946).

Dialkyl sulfates were prepared by the method of Barkenbus and Owen.[4]

N-Alkyl thiamorpholines, oxides and dioxides were prepared by the methods previously described.[3]

TABLE II

SYMMETRICAL N,N-DIALKYL THIAMORPHOLINIUM ALKYL SULFATES

R	R'	Formula	M. p., °C. (uncor.)	N analyses, % Calcd.	Found
Thiamorpholium $S(CH_2CH_2)_2N(R)(R')^+SO_4R'^-$					
n-Dodecyl	*n*-Hexadecyl	$C_{48}H_{99}O_4NS_2$	160	1.71	1.70
n-Tetradecyl	*n*-Hexadecyl	$C_{50}H_{103}O_4NS_2$	127	1.65	1.59
n-Hexadecyl	*n*-Hexadecyl	$C_{52}H_{107}O_4NS_2$	84	1.60	1.63
n-Octadecyl	*n*-Hexadecyl[a]	$C_{54}H_{111}O_4NS_2$	86	1.55	1.57
Thiamorpholinium-1-oxide $OS(CH_2CH_2)_2N(R)(R')^+SO_4R'^-$					
n-Dodecyl	*n*-Hexadecyl	$C_{48}H_{99}O_5NS_2$	124	1.67	1.71
n-Tetradecyl	*n*-Hexadecyl	$C_{50}H_{103}O_5NS_2$	121	1.62	1.64
n-Hexadecyl	*n*-Hexadecyl	$C_{52}H_{107}O_5NS_2$	126	1.57	1.60
n-Octadecyl	*n*-Hexadecyl[b]	$C_{54}H_{111}O_5NS_2$	92	1.52	1.54
Thiamorpholinium-1-dioxide $O_2S(CH_2CH_2)_2N(R)(R')^+SO_4R'^-$					
n-Dodecyl	*n*-Hexadecyl	$C_{48}H_{99}O_6NS_2$	71	1.64	1.68
n-Tetradecyl	*n*-Hexadecyl	$C_{50}H_{103}O_6NS_2$	78	1.60	1.61
n-Hexadecyl	*n*-Hexadecyl	$C_{52}H_{107}O_6NS_2$	117	1.54	1.55
n-Octadecyl	*n*-Hexadecyl[c]	$C_{54}H_{111}O_6NS_2$	116	1.49	1.48

[a] Calculated: C, 71.85; H, 12.39. Found: C, 71.65; H, 12.33. [b] Calculated: C, 70.60; H, 12.18. Found: C, 70.42; H, 12.07. [c] Calculated: C, 69.39; H, 11.97. Found: C, 69.45; H, 11.74.

N,N-Dialkylmorpholinium alkyl sulfates were obtained by the reaction of equimolecular quantities (approximately 0.003 mole) of the N-alkylmorpholine and the appropriate dialkyl sulfate in a tightly stoppered Pyrex test-tube. The reaction mixture was heated to 115° (external temperature) by means of an oil-bath, held at this temperature for six hours and then allowed to remain at room temperature overnight. The reactions employing di-*n*-dodecyl and di-*n*-hexadecyl sulfates were heated at 150° for five hours. The resultant products were washed with 3 cc. of ether at 33°, cooled and centrifuged. The ether layer containing the more soluble unreacted starting materials was decanted. The washed products were crystallized three times from ethyl acetate and dried on a porous tile. Yields by this method varied from 25 to 47%, in most cases from 40 to 45%.

It was found that carrying out the reaction by refluxing the reactants in toluene for eight hours gave somewhat lower yields.

N,N-Dialkylthiamorpholinium Alkyl Sulfates.—Equimolecular quantities (approximately 0.003 mole) of the N-alkylthiamorpholine, oxide or dioxide and di-*n*-hexadecyl sulfate were added to 5 cc. of toluene which had been dried over sodium. The solution was refluxed for four hours, using an oil-bath, with an external temperature of 160–170°. Lower temperatures were found to give incomplete reaction. The toluene was distilled off *in vacuo* a little alcohol was added and distilled *in vacuo* to remove the last traces of toluene. The residue was taken up in ethyl acetate and crystallized from this solvent. In cases where decolorization was necessary, this was done with Darco in alcohol solution. The compounds were recrystallized three times from ethyl acetate or from ethyl acetate containing a little ethyl alcohol.

CHEMICAL LABORATORIES
LAFAYETTE COLLEGE
EASTON, PENNA.
AND ST. JOHN'S UNIVERSITY
BROOKLYN, N. Y.

WILLIAM F. HART
MARTIN E. MCGREAL
CONCETTO F. CAMILLI

RECEIVED JUNE 14, 1949[5]

(4) Barkenbus and Owen, *ibid.*, **56**, 1204 (1934).

(5) Original manuscript received January 17, 1949.