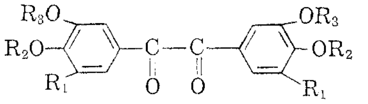
reports the preparation of the bisbenzyl ethers of several reduction products of I by the reduction of II.

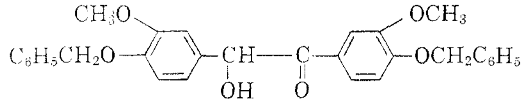
Reduction of II under conditions previously employed for the reduction of I[6] gave three monomolecular reduction products of II, but there appeared to be very little correlation between reductions of II and those of I, syringil (III),[7] and 3,3′-4,4′-tetrahydroxybenzil (IV).[1]

EXPERIMENTAL[8]

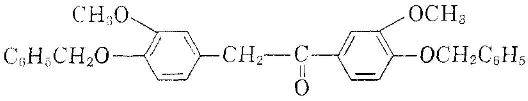
4,4′-Dibenzyloxy-3,3′-dimethoxybenzoin (V). A solution of 10 g. of II[2] in 150 ml. of glacial acetic acid was heated to boiling, removed from the source of heat, and treated with an excess (10 g.) of reduced iron powder. The mixture was shaken for approximately 15 min. during which time the color of the solution changed from yellow to brown. The mixture was filtered, and the brown filtrate was diluted with ten volumes of water. The resulting white precipitate was filtered, washed with water, and allowed to air dry to yield 7.2 g. of yellowish horny solid. This product was recrystallized from methanol and from ethanol to yield colorless crystals of V melting at 110–111° and not depressing a mixed melting point with authentic V prepared by condensing *O*-benzylvanillin with potassium cyanide.[2] The ultraviolet absorption spectrum showed the following maxima: λ_{max} 232 mμ, ε 25680; λ_{max} 280 mμ, ε 14250; λ_{max} 310 mμ, ε 10103.



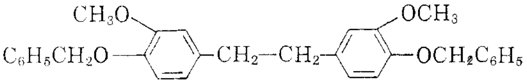
I. $R_1 = R_2 = H; R_3 = CH_3$
II. $R_1 = H; R_2 = C_6H_5CH_2; R_3 = CH_3$
III. $R_1 = OCH_3; R_2 = H; R_3 = CH_3$
IV. $R_1 = R_2 = R_3 = H$



V



VI



VII

Anal. Calcd. for $C_{30}H_{28}O_6$: C, 74.36; H, 5.83. Found: C, 74.33; H, 5.92.

V was also prepared by reduction of II with tin granules in boiling glacial acetic acid in the presence of a few crystals of mercuric chloride.

4,4′-Dibenzyloxy-3,3′-dimethoxydeoxybenzoin (VI). A warm (65°) solution of 10 g. of II in 150 ml. of glacial acetic acid was treated with 10 g. of zinc dust, and the mixture was shaken. After a few minutes, decolorization was complete. The mixture was heated on the steam bath for 30 min. and filtered hot. The filtrate was cooled and diluted with ten volumes of water. The precipitate was filtered, washed with water, and air dried to yield 7.6 g. of colorless crystals melting at 142–143°. Recrystallization from methanol and then from ethanol yielded crystals of pure VI melting at 144–145° and having the following maxima in its ultraviolet absorption spectrum: λ_{max} 230 mμ, ε 26350; λ_{max} 27 mμ, ε 14920; λ_{max} 305 mμ, ε 10320. The ultraviolet spectrum was almost identical with that for V, thus establishing the similarity of the structure between the benzylated guaiacyl units in the compounds.

Anal. Calcd. for $C_3OH_{28}O_5$: C, 76.90; H, 6.02. Found: C, 76.91; H, 6.41.

4,4′-Dibenzyloxy-3,3′-dimethoxybibenzyl (VII). A mixture of 4 g. of II and 400 ml. of 95% ethanol was heated to boiling and removed from the source of heat. The hot mixture was treated with 20 g. of granulated zinc and then with concentrated hydrochloric acid in small portions. Each addition of acid caused the mixture to boil, and boiling was allowed to subside before the next addition. After approximately 75 ml. of acid had been added, the yellow color of the solution disappeared. The colorless mixture was filtered, and the zinc was washed with a little hot ethanol. The crystalline precipitate which separated on cooling was filtered and recrystallized from acetic acid to yield colorless crystals (3.0 g.) of VII melting at 129–130° and having the following maxima in its ultraviolet absorption spectrum: λ_{max} 230 mμ, ε 18900; λ_{max} 280 mμ, ε 6910. VII has a strong white fluorescence under ultraviolet light.

Anal. Calcd. for $C_{30}H_{30}O_4$: C, 79.27; H, 6.65. Found: C, 79.26; H, 7.12.

VII was also prepared in almost quantitative yield by reduction of II with amalgamated zinc and hydrochloric acid in ethanolic solution.

Unsuccessful reductions of II. Attempted reductions of II with granulated tin and hydrochloric acid, Raney nickel in alkaline solution, sodium hydrosulfite in alkaline solution, magnesium amalgam in acetic acid solution, and aluminum amalgam in acetic acid solution under conditions reported previously[6,7,9] resulted in either the recovery of starting material or in the production of unidentified mixtures.

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(4) I. A. Pearl and D. L. Beyer, *J. Am. Chem. Soc.*, **76**, 6106 (1954).

(5) I. A. Pearl and D. L. Beyer, *Tappi*, **39**, 171 (1956).

(6) I. A. Pearl, *J. Am. Chem. Soc.*, **74**, 4593 (1952).

(7) I. A. Pearl, *J. Org. Chem.*, **22**, 1229 (1957).

(8) All melting points are uncorrected. Ultraviolet spectral data are for solutions in 95% ethanol (concentration, 0.02 g. per liter). Analyses and spectra were determined by the Analytical Department of The Institute of Paper Chemistry.

(9) I. A. Pearl and W. M. Dehn, *J. Am. Chem. Soc.*, **60**, 57 (1938).

Amide Derivatives of D-Glucosamine

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In connection with a problem requiring the availability of sulfur-containing amide derivatives of D-glucosamine we have been interested in the development of a simple, acceptable-yield procedure for the *N*-acylation of *O*-acetylated D-glucosamine with a variety of acyl functions. Bergmann and Zervas[2] as well as Link and co-workers[3]

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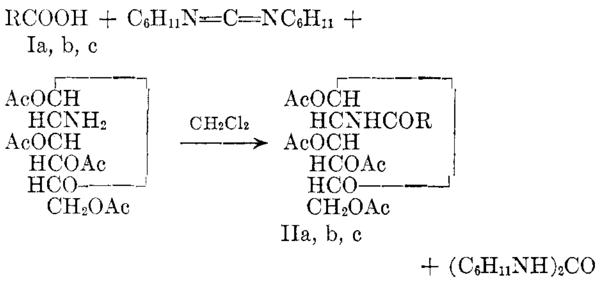
(1) The authors are indebted to the U. S. Army Medical Research and Development Command (Contract DA-49-193-MD-2070) for its generous support of this investigation.

(2) M. Bergmann and L. Zervas, *Ber.*, **65**, 1201 (1932).

have prepared several amino acid amide derivatives of D-glucosamine, the so-called "glucopeptides," by interaction of carbobenzoxy derivatives of amino acid chlorides with 1,3,4,5-tetra-*O*-acetyl-β-D-glucosamine. While the final step in these reactions took place in acceptable yield the need for preparing the intermediate acid chloride appeared to us a disadvantage, and we accordingly elected to attempt an adaptation of the "carbodiimide" synthesis of Sheehan[4] and du Vigneaud,[5] wherein a carboxylic acid interacts with an amine in the presence of *N,N'*-dicylohexylcarbodiimide to produce a carboxamide and *N,N'*-dicyclohexylurea. Our preliminary efforts to employ this reaction to the synthesis of acyl derivatives of D-glucosamine are summarized in Chart I, where the preparations of a "glucopeptide" as well as two other amide derivatives of 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine are summarized. Yields ranged from about 55 to 80% and the brief required reaction time of fifteen minutes permitted the frequently analytically pure product to be obtained in less than an hour. In contrast, the acid chloride procedure[2,3] requires more than a day to complete and extensive purification by acid and alkali washes are necessary during product isolation.

Chart I



Ia, IIa. R = CH_3COSCH_2—
Ib, IIb. R = $PhCH_2SCH_2$—
Ic, IIc. R = $PhCH_2SCH_2CH(NHCOOCH_2Ph)$—

Structure proof of our *N*-(*S*-acetylmercaptoacetyl)-1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine (IIa) and *N*-(*S*-benzylmercaptoacetyl)-1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine (IIb) products was undertaken by reductive desulfurization with Raney nickel, wherein each product yielded authentic *N*-acetyl-1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine.

EXPERIMENTAL

N-(S-Acetylmercaptoacetyl)-1,3,4,6-tetra-O-acetyl-β-D-glucosamine (IIa). *S*-Acetylmercaptoacetic acid (Ia; 6.6 g.; 0.05 mole) and 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine[6] (17.3 g.; 0.05 mole) dissolved in methylene chloride (100 ml.) were treated slowly with a solution of *N,N'*-dicyclohexylcarbodiimide (11.5 g.; 0.055 mole) in methylene chloride (100 ml.). The reaction mixture immediately became warm and *N,N'*-dicyclohexylurea separated from the solution. The latter was filtered and the filtrate was evaporated to dryness, whereupon the residue was dissolved in the minimum amount of hot ethyl acetate and the resulting solution was treated with an equal volume of anhydrous ether, then with sufficient ligroin to engender turbidity. On standing overnight, crude IIa separated, 12.6 g. (55%), m.p. 159–170°. The crude product was recrystallized first from a mixture of ethyl acetate, ether, and ligroin and then from water, to yield the pure materal, m.p. 183–185°, $[\alpha]_D^{23}$ + 25.2° (*c*, 3.37; chloroform).

Anal. Calcd. for $C_{18}H_{25}O_{11}NS$: C, 46.64; H, 5.44; N, 3.02; S, 6.92. Found: C, 46.74, 46.79; H, 5.58, 5.60; N, 3.34; S, 7.20.

N-(S-Benzylmercaptoacetyl)-1,3,4,6-tetra-O-acetyl-β-D-glucosamine (IIb). *S*-Benzylmercaptoacetic acid[7] (Ib; 9.9 g.; 0.055 mole) and 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine (18.8 g.; 0.054 mole) in methylene chloride (100 ml.) was treated as above with a solution of *N,N'*-dicyclohexylcarbodiimide (11.5 g.; 0.055 mole) in methylene chloride (100 ml.). The mixture was allowed to stand for 6 hr., when the dicyclohexylurea was filtered and the filtrate was evaporated to dryness. The residue was dissolved in hot ethyl acetate (100 ml.) and the solution was treated with anhydrous ether (100 ml.), whereupon the crude IIb product, m.p. 178–180°, 21.5 g. (77%), was precipitated by addition of ligroin. The crude product was recrystallized twice from methanol to yield a sample having m.p. 180–182° and $[\alpha]_D^{23}$ −16.1° (*c*, 3.60; chloroform).

Anal. Calcd. for $C_{23}H_{29}O_{10}NS$: C, 54.00; H, 5.71; N, 2.74; S, 6.27. Found: C, 53.66, 53.72; H, 5.68, 5.86; N, 2.99; S, 6.80.

N-(S-Benzyl-N-carbobenzoxycysteinyl)-1,3,4,6-tetra-O-acetyl-β-D-glucosamine (IIc). *S*-Benzyl-N-carbobenzoxycysteine (Ic; 4.8 g.; 0.014 mole) and 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine (4.8 g.; 0.014 mole) in methylene chloride (50 ml.) were treated with a solution of *N,N'*-dicyclohexylcarbodiimide (3.0 g.; 0.0146 mole) in the same solvent (50 ml.). After 15 min. the substituted urea precipitate was filtered and the filtrate was stripped of solvent. The residue was dissolved in a minimum of hot ethyl acetate and the IIc product crystallized by the addition of ether, yield 7.4 g. (79%), m.p. 187–189°, $[\alpha]_D^{23}$ + 6.7° (*c*, 4.48; chloroform).

Anal. Calcd. for $C_{32}H_{38}O_{12}N_2S$: C, 56.96; H, 5.68; N, 4.15; S, 4.75. Found: C, 56.98, 57.14; H, 5.74, 5.86; N, 4.24; S, 4.75.

Reductive desulfuration of IIa *and* IIb. The above IIa product (1 g.) and Raney nickel[8] (8 g.) in absolute ethanol (25 ml) were heated under reflux for a period of 5 hr., whereupon the nickel was filtered (Celite) and the filtrate was evaporated to dryness. There resulted 0.6 g. (71%) of crude product which, on recrystallization from 2-propanol, afforded pure *N*-acetyl-1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine have m.p. 182–184° dec. This material showed no mixed melting point depression with an authentic sample of the product, and displayed an infrared spectrum identical in all respects with that of the authentic sample. Precisely similar results were obtained when the above IIb product was subjected to the same desulfuration procedure.

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[3] D. G. Doherty, E. A. Popenoe, and K. P. Link, *J. Am. Chem. Soc.*, **75**, 3466 (1953).

[4] J. C. Sheehan and G. P. Hess, *J. Am. Chem. Soc.*, **77**, 1067 (1955).

[5] R. Roeske, F. H. C. Stewart, R. J. Stedman, and V. du Vigneaud, *J. Am. Chem. Soc.*, **78**, 5883 (1956).

[6] Prepared by the method of M. Bergmann and L. Zervas, *Ber.*, **64**, 975 (1931).

[7] G. G. Stoner and G. Dougherty, *J. Am. Chem. Soc.*, **63**, 1481 (1941).

[8] R. Mozingo, *Org. Syntheses*, 21, 15 (1941).