secondary alcohol group resulted in a very low yield of the desired α-D-linked disaccharide. Condensation of 3,4,6-tri-*O*-acetyl-2-*O*-nitro-β-D-glucopyranosyl chloride with 1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose[9] under the conditions employed in the synthesis of β-isomaltose octaacetate[4] gave only 1.5% yield of crystalline 2-*O*-(α-D-glucopyranosyl)-β-D-glucopyranose (β-kojibiose) octaacetate with no 2-*O*-(β-D-glucopyranosyl)-D-glucopyranose (β-sophorose) octaacetate being detected. This low yield is undoubtedly due to steric reaction hindrance at the secondary hydroxyl position of the substituted hexose. The isolation of this small yield of product illustrates the power of the separation methods employed. Other methods for the chemical synthesis of kojibiose, isolated in low yield (3.2–2.8%) as the octaacetate, have been reported.[10,11] The relationship between crystalline α-kojibiose and its β-acetate is well established.[12]

Experimental

Materials.—The "active" silver carbonate was prepared by the method developed in this laboratory by Klemm and described by Wolfrom and co-workers.[4]

The silver perchlorate catalyst was prepared according to the general method described by Bredereck and co-workers.[13] A suspension of 5.5 g. (0.02 mole) of silver carbonate in 50 ml. of water stirred in the dark at 100° and 3.90 g. (0.0388 mole) of 60% perchloric acid was added dropwise. The mixture was then heated for 8 hr. at 95–103° and filtered hot through a sintered-glass filter funnel. The solution was evaporated to dryness in a porcelain dish on a steam bath, with occasional filtration, and the crystalline solid dried in a vacuum oven for 3.5 days at 100–110°; yield 6.5 g. The silver perchlorate was stored in the dark over solid potassium hydroxide. For best results, the silver perchlorate catalyst must be completely water-soluble. CAUTION! While this laboratory has never experienced any difficulties with silver perchlorate, it has been reported to detonate occasionally. Bredereck and co-workers observe no precautions regarding its use.

Isopropyl Tetra-*O*-acetyl-α-D-glucopyranoside.—An amount of 3.0 g. of 3,4,6-tri-*O*-acetyl-2-*O*-nitro-β-D-glucopyranosyl chloride[4] was treated as described by Wolfrom and co-workers[4] for the synthesis of methyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside except that about double the amount of "active" silver carbonate was used and stirring was maintained at room temperature for 77 hr. The nitrate group was removed by hydrogenation and the product was acetylated as described[4] previously. The resultant sirupy acetate was dissolved in 25 ml. of benzene. This solution was chromatographed, in equal amounts, on two 210 × 53 mm. (diam.) columns of Magnesol–Celite[14] (5:1 by wt.). Development with 500 ml. of benzene–2-methyl-2-propanol (100:1 by vol.), extrusion, and streaking with alkaline permanganate solution resulted in the appearance of two zones 50–90 and 130–180 mm. from the column top. The combined and sectioned zones were twice extracted with acetone, the combined extracts filtered, the solvent removed under reduced pressure, and the resulting sirups dissolved in ethanol. The ethanol solutions were decolorized with carbon, filtered, the solvent removed under reduced pressure, and the resulting sirups dissolved in hot absolute ethanol. The slower moving zone furnished crystalline isopropyl tetra-*O*-acetyl-β-D-glucopyranoside; yield 160 mg. (4.65%), m.p. 137–138°, $[\alpha]^{24}D$ −23° (*c* 2.0, chloroform) [reported[15]: m.p. 136–137°, $[\alpha]^{20}D$ −24.4° (*c* 2.0, chloroform)], X-ray powder diffraction pattern[16]: 11.19 s (3), 9.31 s (2), 7.63 vw, 6.11 w, 5.64 vw, 4.96 vs (1), 4.53 m, 4.13 m, 3.80 m, 3.49 vw, 3.14 w, 2.95 w, 2.77 w, 2.10 vw.

The faster moving zone furnished 1.67 g. of a sirup which produced crystalline isopropyl tetra-*O*-acetyl-α-D-glucopyranoside following nucleation[17]; yield 1.21 g. (35.1%), m.p. 85–88°, $[\alpha]^{24}D$ +143° (*c* 2.0, chloroform) [reported[7]: m.p. 85.5–86.5°, $[\alpha]^{20}D$ +143° (*c* 2.0, chloroform)], X-ray powder diffraction pattern[16]: 10.65 vw, 8.59 s (2), 7.69 s (3), 6.33 w, 5.72 vs (1), 4.98 m, 4.33 w, 3.99 w, 3.77 w, 3.53 m, 3.03 vw, 2.87 vw.

The condensation reaction was repeated with 0.5 g. (2 mmoles) of iodine in the original mixture. Processing in the manner described above yielded 157 mg. (5.90%), m.p. 135–137°, of crystalline isopropyl tetra-*O*-acetyl-β-D-glucopyranoside and 1.17 g. (34.1%), m.p. 84–87°, of crystalline isopropyl tetra-*O*-acetyl-α-D-glucopyranoside.

The condensation was carried out in 100 ml. of dry ether using 2.10 g. (35 mmoles) of isopropyl alcohol and processed as described above to yield 109 mg. (3.18%), m.p. 136–137.5°, of the isopropyl tetra-*O*-acetyl-β-D-glucopyranoside and 525 mg. (15.3%), m.p. 84–87°, of the isopropyl tetra-*O*-acetyl-α-D-glucopyranoside.

β-Kojibiose Octaacetate.—An amount of 2.6 g. (7.5 mmoles) of 1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose[9] was treated as described[4] for the synthesis of β-isomaltose octaacetate except that the reaction mixture was stirred at room temperature for 7.5 days and treatment with carbon was omitted. The reaction solution was then processed, hydrogenated, acetylated,[4] and chromatographed as described above (1500 ml. of developer). Extrusion and streaking with alkaline permanganate solution resulted in the appearance of one zone 65–90 mm. from the column top. The zone was sectioned, combined, and processed as previously described to yield 25 mg. (1.5%) of β-kojibiose octaacetate, m.p. 123–125°, no depression upon admixture with known β-kojibiose octaacetate, X-ray powder diffraction pattern identical to that of known β-kojibiose octaacetate. Processing the column effluent yielded 1.86 g. of β-D-glucopyranose pentaacetate, m.p. 127–129°.

(9) E. Hardegger and J. de Pascual, *Helv. Chim. Acta*, **31**, 281 (1948); R. U. Lemieux and G. Huber, *Can. J. Chem.*, **31**, 1040 (1953).
(10) S. Haq and W. J. Whelan, *Nature*, **178**, 1222 (1956).
(11) K. Matsuda, *ibid*, **180**, 985 (1957); *Nippon Nogeikagaku Kaishi*, **33**, 714 (1959).
(12) F. Yamauchi and K. Aso, *Nature*, **189**, 753 (1961).
(13) H. Bredereck, A. Wagner, G. Faber, H. Ott, and J. Rauther, *Ber.*, **92**, 1135 (1959).
(14) W. H. McNeely, W. W. Binkley, and M. L. Wolfrom, *J. Am. Chem. Soc.*, **67**, 527 (1945).
(15) B. Lindberg, *Acta Chem. Scand.*, **3**, 151 (1949).
(16) Interplanar spacing, Å., CuK_α radiation. Relative intensities, estimated visually: s, strong; m, medium; w, weak; v, very. Strongest lines numbered, 1 strongest.
(17) Kindly furnished by Dr. B. Lindberg.

Sulfamylguanidines

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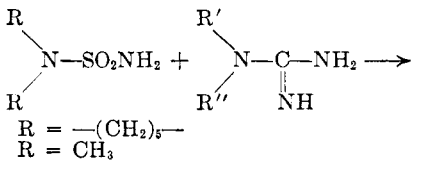
Reactions of sulfamide or mono-substituted sulfamides (*i.e.*, sulfamylamines) with primary or secondary amines to displace ammonia are well known.[1–3]

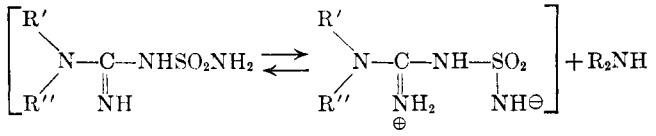
$$RNHSO_2NH_2 + R'NH_2 \longrightarrow RNHSO_2NHR' + NH_3$$

However, when we attempted to treat substituted guanidines with N,N-disubstituted sulfamylamines, such as N-sulfamylpiperidine, 3-methyl-N-sulfamylpiperidine, or N-sufamyldimethylamine in dimethyl sulfoxide, no ammonia could be detected. Instead, further examination showed the products to be sulfamylguanidines (I). This unexpected reaction provides a facile method for preparing the heretofore unknown sulfamylguanidines and appears to be of general application when guanidine, mono-substituted or N,N-disubstituted guanidines are reacted with N,N-

(1) E. Müller, "Methoden der Organischen Chemie," Vol. 11, Part 2, Georg Thieme Verlag, Stuttgart, 1958, p. 720.
(2) A. Paquin, *Angew Chem.*, **A60**, 316 (1948).
(3) K. Hamaan, German Patent 869,065 (1953).



R = —(CH₂)₅—
R = CH₃

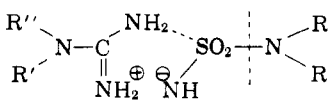


I

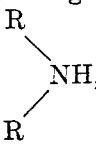
Ia. R′ = H, R″ = H
b. R′ = CH₃, R″ = H
c. R′ = C₆H₅CH₂, R″ = H
d. R′ = CH₃(CH₂)₄, R″ = H
e. R′ = CH₃, R″ = CH₃

disubstituted sulfamylamines. Failures occurred only with two β-phenethylguanidines for reasons which are discussed below.

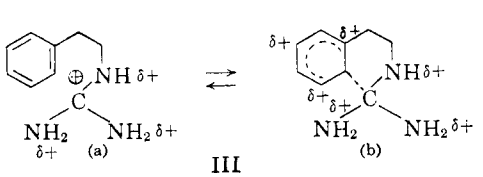
In considering the reaction mechanism we would propose an initial proton transfer from the slightly acidic sulfamylamine to the very basic guanidine. In its anionic form, the sufamylamine, unable to lose ammonia, forms a cyclic ion pair (II) with the guanidinium cation.



II

Facilitated by this five-membered ring intermediate, bond formation between the guanidine nitrogen and the sulfamylamine sulfur atom displacing  yields I.

Unsuccessful attempts to treat either β-phenethylguanidine or β-(3,4-dimethoxyphenethyl)guanidine with N-sulfamylpiperidine (paper chromatography in acidic systems of reaction mixtures heated at 100° for twenty-four hours indicating only starting materials to be present) may be explained by the possible failure of these compounds to form the cyclic intermediate II. Instead, following proton transfer these cationic guanidines are probably intramolecularly associated in an intermediate such as III with the equilibrium greatly favoring form b. This intermediate may be compared with one proposed for the cyclization of N-(β-phenethyl)amides to dihydroisoquinolines in the Bishler–Napieralski reaction[4] except that III would be expected to be much more stable due to interaction of the guanidinium function and the aromatic ring. Delocalization of the positive change through guanidinium and aromatic interactions could render III stable enough to resist reaction with sulfamylamine and to discourage intramolecular cyclization to a 3,4-dihydroisoquinoline. Attempts to cyclize β-phenethylguanidinium sulfate *via* the intermediate III (with loss of ammonia) to 1-amino-3,4-dihydroisoquinoline were unsuccessful at temperatures of up to 100° for twenty-four hours. Resistance to these conditions again suggests an unusual stability for III.



III

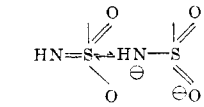
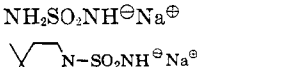
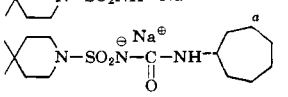
In our hands, no reaction was seen between N,N-disubstituted sulfamylamines (*e.g.*, N-sulfamylpiperidine or N-sulfamyldimethylamine) and amines less basic than guanidine (*e.g.*, cyclohexylamine, morpholine) in dimethyl sulfoxide. No ammonia evolution could be detected in any of these reactions, and approximately 50% of starting sulfamylamines were readily recovered after two hours at 100° in dimethyl sulfoxide. Further, contrary to the claims of Vandi, *et al.*,[5] a search of the literature failed to reveal any examples of deammonation of N,N-disubstituted sulfamylamines by primary or secondary amines to give tri- or tetra-substituted sulfamylamines. Apparently, both the high basicity of guanidines *and* the ability to form a cyclic intermediate (II) encourage the ordinarily unreactive N,N-disubstituted sulfamylamines to react.

Evidence indicates that sulfamylguanidines (I) are best represented by the zwitterionic formula arising from proton transfer from the weakly acidic sulfamyl group to the strongly basic guanidine function. The following data support the zwitterionic structure for I.

(a) The sulfamylguanidines are surprisingly inert toward a variety of amines under various conditions even at temperatures up to 150°. A neutral, non-zwitterionic structure would be expected to lose ammonia under these conditions to form an N¹-guanyl-N²-substituted sulfamide. Unchanged I could be recovered from these reactions indicating a somewhat unexpected heat stability for I. An increased stability of zwitterionic I over the neutral I comes from the guanidinium resonance energy and from the proximity of the opposite charges arranged in a five-membered ring.

TABLE I

INFRARED ABSORPTIONS OF SULFAMYLAMINES AND THEIR SALTS

Compound	O=S=O	
Sulfamylguanidines (I)	*ca.* 7.9, ca. 8.5 μ (Table II)	8.9μ
$RNHSO_2NH_2$	7.5,8.6	None
$NH_2SO_2NH^{\ominus}Na^{\oplus}$	7.4,8.2,8.6	9.0
	8.1,8.7	9.1
	8.1,8.6	9.1
$(CH_3)_2N$-C(=$NH^{\oplus}$,$Cl^{\ominus}$)-$NHSO_2NH_2$ (IV)	7.4,8.5	None

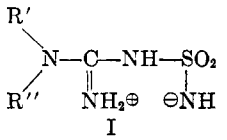
[a] See ref. 7.

(4) W. Whaley and T. Govindachari, *Org. Reactions*, **6**, 80, (1957).

(5) A. Vandi, T. Moeller, and L. F. Audrieth, *J. Org. Chem.*, **26**, 3478 (1961).

TABLE II

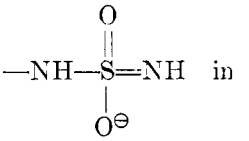
SULFAMYLGUANIDINES



I

R′	R″	M.p., °C	Yield, %	Recryst. solvent	Infrared μ	Calcd. C	Calcd. N	Found N	Found C	Found H	Found N
(a) H	H	167–169	46	Ethanol	7.94,8.36,8.87	8.69	4.38	40.55	8.83	4.18	40.21
(b) CH_3	H	154–155	43	Ethanol	7.85,8.35,9.08	15.78	5.30	36.82	15.84	4.92	36.95
(c) $C_6H_5CH_2$	H	156.5–157.5	50	Acetone	7.95,8.56,8.90	42.09	5.30	24.54	42.19	5.18	24.72
(d) $CH_3(CH_2)_4$	H	83–84	16	Methylene chloride	8.04,8.55,9.01	34.60	7.74	26.90	34.64	7.89	27.22
(e) CH_3	CH_3	132–133.5	52	Ethanol–ether	7.88,8.60,8.95	21.68	6.06	33.71	21.62	5.98	34.10
IV [(Ie) HCl][a]		116–118	93	Ethanol–ether	7.38,8.46,none	17.78	5.47	27.64	17.90	5.12	27.85

[a] Prepared in water solution by addition of an equimolar amount of hydrochloric acid to (Ie) followed by evaporation to dryness under vacuum.

(b) Although the sulfamylguanidines exhibit the usual[6] strong sulfonamide S=O stretching absorptions in the infrared (approximately 7.8 and 8.6 μ), they in addition show a strong band near 9.0 μ (Table II) which may be due to the S—O⁻ stretching of the resonating anion:  in zwitterionic I. Spectra of authentic sodium salts of sulfamylamines exhibit this same strong peak near 9.0 μ while no absorption is seen near 9.0 μ in a hydrochloride salt of the sulfamylguanidine Ie (IV) (Table I).

Experimental[8]

A general method was employed in the preparation of all compounds of type I. This method is illustrated below for **Ie**.

N^1,N^1-Dimethyl-N^3-sulfamylguanidine (Ie).—Dimethylguanidine (free base) was prepared from 68 g. (0.50 mole) of the sulfate salt in 600 ml. of ethanol under a nitrogen atmosphere by treatment with 500 ml. of 1 *M* ethanolic sodium ethoxide, filtration of the precipitated sodium sulfate, and evaporation of the clear filtrate under vacuum. The residual cream colored solid was used immediately in the next step.

To a solution of 82 g. (0.50 mole) of N-sulfamylpiperidine[2] in in 100 ml. of dimethyl sulfoxide was slowly added a solution of the above free base in 150 ml. of dimethyl sulfoxide. Heating on the steam bath for 2 hr. followed by distillation of solvent under vacuum yielded a viscous orange oil. Trituration with ethanol readily yielded a pale yellow solid, 43.7 g. (52%), m.p. 126–129°. Recrystallization from ethanol–ether raised the m.p. to 132–133.5°.

Substitution of N-sulfamyldimethylamine for N-sulfamylpiperidine in the above reaction gave detectable evolution of a basic gas (dimethylamine) and 53% of identical product Ie, m.p. 131–132°, mixture m.p. 128–131°.

Table II summarizes pertinent physical data for compounds of type I.

Acknowledgment.—The author wishes to thank Mr. Nelson Treadway, Jr., for his technical assistance.

(6) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 350.

(7) Kindly provided by Dr. J. M. McManus of these laboratories.

(8) Melting points were taken in open capillaries and are corrected. Infrared spectra were measured in potassium bromide pellets.

The Formation and Reactions of Some Phenylphosphonous Diamides and Diphenylphosphinous Amides

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The literature contains many references to the preparation of diphenylphosphinous amides,[1-3] but few references to phenylphosphonous diamides.[4]

In this investigation we prepared additional N-substituted phenylphosphonous diamides by the reaction of phenylphosphonous dichloride with *tert*-butylamine and 3-azabicyclo[3.2.2]nonane according to the general method of Michaelis.[5] These phenylphosphonous diamides behave as typical diphenylphosphinous amides. They add sulfur to give phenylphosphonothioic diamides, oxygen to produce phenylphosphonic diamides, and form adducts with some metal salts. They also form quaternary salts with aralkyl and alkyl halides in which the entering group is attached to phosphorus, not nitrogen.[4,5] P-Alkylation was also observed in our studies of the monoaminophosphonium halides.[6]

Finally, as a corollary to our previous studies of phosphorous–nitrogen compounds,[1,2] it was found that (3-azabicyclo[3.2.2]non-3-yl)diphenylphosphine reacts with methyl iodide to give (3-azabicyclo[3.2.2]non-3-yl) methyldiphenylphosphonium iodide and with carbon disulfide to give a crystalline adduct. On the basis of analogy with the work of Margulis and Templeton[7] the carbon disulfide adduct is tentatively assigned the following structure.

(1) H. H. Sisler and N. L. Smith, *J. Org. Chem.*, **26**, 611 (1961).

(2) N. L. Smith and H. H. Sisler, *ibid.*, **26**, 5145 (1961).

(3) J. R. Van Wazer, "Phosphorus and Its Compounds," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1958.

(4) A. W. Frank, *Chem. Rev.*, **61**, 389 (1961).

(5) A. Michaelis, *Chem. Ber.*, **31**, 1037 (1898).

(6) H. H. Sisler and N. L. Smith, *J. Org. Chem.*, **26**, 4733 (1961).

(7) T. N. Margulis and P. W. Templeton, *J. Am. Chem. Soc.*, **83**, 995 (1961).