covered material amounted to 1.04 g. (91% yield of bibenzyl). Recrystallization from ethanol gave a product, m.p. 52.5° (reported[10] 52°). A mixed melting point with an authentic sample of bibenzyl showed no depression. The infrared spectra were identical.

Alkaline Degradation of Dihydrostreptomycin

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Wolfrom and Polglase[1] have reported the preparation of a compound, designated decaacetyldideguanyldihydrostreptomycin, from dihydrostreptomycin, by alkaline degradation followed by acetylation. The intermediate compound, herein designated dideguanyldihydrostreptomycin was not isolated.[1] This latter compound was required for studies on the mechanism of action of streptomycin,[2] and the present note is concerned with its preparation and characterization.

Experimental

Dideguanyldihydrostreptomycin Bicarbonate.—Dihydrostreptomycin sesquisulfate (5.0 g.) was dissolved in 20 ml. of water and 250 ml. of a saturated solution of barium hydroxide was added. The barium sulfate precipitate was filtered off and the filtrate was refluxed for 28 hr. (until evolution of ammonia had ceased). The straw-colored reaction mixture was cooled and the excess of barium hydroxide was neutralized with carbon dioxide gas. The solution was filtered and concentrated to a sirup. The sirup was dissolved in warm methanol and filtered. Crystalline material (2.48 g., 68%) was obtained following cooling overnight. A portion of the product was recrystallized from hot methanol and dried at room temperature for analysis. M.p., 156°; $[\alpha]^{24}\text{D}$ −121° (*c* 1, water).

Anal. Calcd. for $(C_{19}H_{37}O_{12}N_3)_2 \cdot H_2CO_3$: C, 44.2; H, 7.2; N, 7.9. Found: C, 44.4; H, 7.4; N, 7.9.

Acetylation with acetic anhydride and pyridine gave the decaacetate (m.p. 259–260°) described previously.[1]

Dideguanyldihydrostreptomycin.—This was obtained from the bicarbonate derivative described above following heating for 2 hr. at 110° *in vacuo*.

Anal. Calcd. for $C_{19}H_{37}O_{12}N_3$: C, 45.6; H, 7.5; N, 8.3; N—CH_3, 5.8; C—CH_3, 5.4. Found: C, 45.3; H, 7.7; N, 8.1; N—CH_3, 5.0; C—CH_3, 5.6.

Dideguanyldihydrostreptomycin Trihydrochloride.—Dideguanyldihydrostreptomycin bicarbonate (2.0 g.) was suspended in 25 ml. of cold methanol and concd. hydrochloric acid was added dropwise until the mixture was acidic to Congo Red paper. The solution was filtered and seven volumes of acetone were added. The amorphous precipitate was collected by centrifuging, washed with acetone, and dried; yield 2.1 g. (91%).

Anal. Calcd. for $C_{19}H_{37}O_{12}N_3 \cdot 3HCl$: N, 6.9. Found: N, 6.9.

In a potentiometric titration of dideguanyldihydrostreptomycin trihydrochloride, 3 equivalents of sodium hydroxide were consumed. The two primary amino groups are weakly basic (*pK* about 6.3). The secondary amino group had a *pK* of 7.9, corresponding to the *pK* of this group in streptomycin.[3]

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[1] M. L. Wolfrom and W. J. Polglase, *J. Am. Chem. Soc.*, **70**, 2835 (1949).

[2] W. J. Polglase, to be published.

[3] J. Fried and O. Wintersteiner, *J. Am. Chem. Soc.*, **69**, 79 (1947).

The Nitration of 2′,5′-Dialkoxyacetophenones[1]

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The compositions of the products obtained from nitration of 2′, 5′-diethoxy- and 2′, 5′-di-*n*-butoxyacetophenone have been determined and compared with those previously reported for 2′,5′-dimethoxyacetophenone.[2]

For nitrations carried out at −20° in concentrated nitric acid, all three 2′,5′-dialkoxyacetophenones yielded mixtures of the 4′- and 6′-nitro derivatives, with the latter accounting for approximately three fourths of the product (see Table I). A small increase in the proportion of 4′-substitution with increasing alkoxy group size was observed. The results are consistent with a direct attack on the ring by the electrophilic reagent[3] and with preferential stabilization of the transition state involved in 6′-substitution through conjugation of the 2′-alkoxy group with the carbonyl side chain.[2]

TABLE I

NITRATION[a] OF 2′,5′-DIALKOXYACETOPHENONES IN CONCENTRATED NITRIC ACID

Run	Alkoxy Groups	%, 4′Nitro[b]	%, 6′-Nitro[b]
A[c]	Dimethoxy	21	79
B[c,d]	Dimethoxy	23	77
1	Diethoxy	28 (26)	72 (74)
2[e]	Diethoxy	27	73
3	Di-*n*-butoxy	26	74
4	Di-*n*-butoxy	31 (31)	69 (69)

[a] At −20°; addition and aging periods 4 and 2.5 hr., respectively, unless otherwise noted. [b] Data in parentheses based on infrared analyses; all others based on alumina chromatography. [c] Ref. 2. [d] Addition and aging periods 90 and 15 min., respectively. [e] Addition and aging periods 1 and 2.5 hr., respectively.

Product compositions for nitrations carried out at −20° in a mixture of nitric and sulfuric acids

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[2] C. A. Howe, C. R. Hamel, E. D. Stedman, and F. Hyman, *J. Org. Chem.*, **25**, 1245 (1960).

[3] An increase in the proportion of 6′ substitution with increasing alkoxy group size would have provided evidence for attack *via* the carbonyl side chain [see K. L. Nelson, *J. Org. Chem.*, **21**, 153 (1956)].