TABLE III

RATE CONSTANTS[a] AND ENERGIES OF ACTIVATION

Reaction between aniline and									
Nitrosobenzene		*p*-Nitronitrosobenzene		*m*-Nitronitrosobenzene		*o*-Nitronitrosobenzene		*p*-Chloronitrosobenzene	
Temp., °C.	*k*	Temp., °C.	*k*	Temp., °C.	*k*	Temp., °C.	*k*	Temp., °C.	*k*
21.0	0.0742	21.4	0.966	20.0	0.852	19.0	0.448		
				25.2	1.14	25.4	.669		
29.7	.110			30.1	1.73	30.3	.872	31.1	0.192
35.1	.146	34.8	2.32	35.6	2.38	35.0	1.15		
		40.0	3.35						
Energy of activation, cal.									
8.85×10^3		11.8×10^3		11.8×10^3		10.6×10^3			

[a] k, $(\text{min.})^{-1}(\text{mole/l.})^{-1}$.

the *p*-Cl should stabilize form B and thus promote the reaction, although probably to a lesser extent than for a *p*-nitro group.

The plot of log k against $1/T$ is in accord with the Arrhenius equation as shown in Fig. 1; the apparent activation energies of these reactions are given in Table III.

Acknowledgment.—We are grateful to Prof. A. E. Martell of Clark University, for his kindness in reading this manuscript.

KUMAMOTO, JAPAN

[CONTRIBUTION FROM THE HAND CHEMICAL LABORATORY, MISSISSIPPI STATE COLLEGE]

Position Isomerism in the Azoxybenzenes

BY LYELL C. BEHR

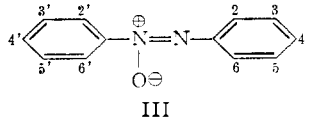
RECEIVED FEBRUARY 16, 1954

Because the azoxy group is unsymmetrical, the rings in azoxybenzene are different and position isomerism can occur in unsymmetrically substituted azoxybenzenes. The assignment of structure to these isomers has in the past been made on the basis of certain substitution reactions, but assumptions have been necessary. The structures of the two *p*-bromoazoxybenzenes and the two *p*-ethoxyazoxybenzenes have now been established by synthesis, the procedure involving the vigorous oxidation of indazole oxides of known structure, followed by decarboxylation of the resultant azoxybenzene-2′-carboxylic acids. In this way the structures previously proposed for the two pairs of isomers have been confirmed.

The proof that the azoxy group is unsymmetrical[1] pointed up the problem of the synthesis of the two possible position isomers (I and II), and the determination of their structure. The preparation of the two isomers had in a number of cases been

I II

accomplished by Angeli and his school[2] chiefly by peroxyacetic acid oxidation of unsymmetrical azo compounds. Assignment of structure to the two isomers has in general been made by comparison of their substitution reactions. Thus the bromination of azoxybenzene yields a single *p*-bromoazoxybenzene, which is probably 4-bromoazoxybenzene[3] since substitution would likely occur there in preference to the 4′-position (see formula III[3]) which is in an electronically deficient ring.[4] Further, of the two *p*-bromoazoxybenzenes, the so-called β-isomer[5] undergoes substitution readily in the *para* position whereas the α-isomer does not undergo substitution readily. The conclusion[4] is that the α-isomer is 4-bromoazoxybenzene and the β-isomer 4′-bromoazoxybenzene. By similar arguments, structures have been assigned to the two *p*-nitroazoxybenzenes[6] and the two *p*-ethoxyazoxybenzenes.[7,8]



III

In order to provide a firmer basis for the assignment of structures to the position isomers and to supply a method for the assignment of structures where the substitution methods are not applicable a synthetic method was sought. This was found in the vigorous oxidation of indazole oxides,[9] followed by decarboxylation of the acids produced, and has been applied to the two *p*-bromoazoxybenzenes and the two *p*-ethoxyazoxybenzenes. It can be seen that barring rearrangements (see below), this scheme provides an unequivocal route to the azoxybenzenes, since the oxygen which appears in the azoxy group comes originally from the nitro group of the aldehyde. As an example of the procedure, there may be cited the synthesis of 4-bromoazoxy-

(1) T. Chu and C. S. Marvel, THIS JOURNAL, **55**, 2841 (1933).

(2) See A. Angeli, *Ahrens Sammlung*, **19**, 447 (1913), and D. Bigiavi, *Gazz. chim. ital.*, **64**, 900 (1934), and leading references therein.

(3) The numeration in this paper is that used in *Chemical Abstracts*.

(4) A. Angeli and B. Valori, *Atti accad. naz. Lincei, Rend., Classe ci. fis. mat. e nat.*, [5], **21**, I, 155 (1912).

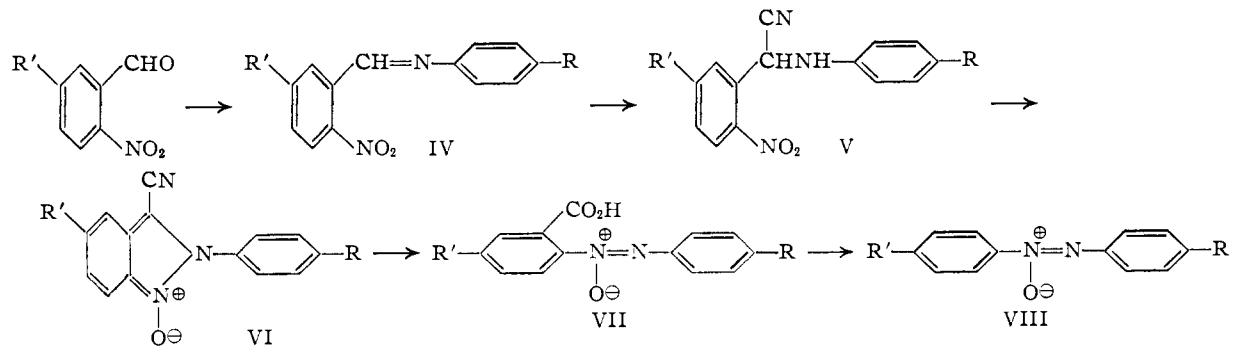
(5) The prefix "β" has been used generally in the literature to denote the isomer more readily substituted.

(6) A. Angeli and L. Alessandri, *Atti accad. naz. Lincei, Rend., Classe sci. fis. mat. e nat.*, [5], **20**, II, 170 (1911).

(7) A. Angeli and B. Valori, *ibid.*, [5] **21**, I, 729 (1912).

(8) A. Angeli, *ibid.*, [5] **23**, I, 557 (1914).

(9) A. Reissert and F. Lemmer, *Ber.*, **59B**, 351 (1926). See also G. Heller and G. Spielmeyer, *ibid.*, **58B**, 834 (1925) and K. Akashi, *C. A.*, **43**, 7934 (1949); *Bull. Inst. Phys. Chem. Research (Tokyo)*, **20**, 798 (1941).



benzene (VIII, R = Br, R′ = H). *o*-Nitrobenzaldehyde was heated with *p*-bromoaniline to give the anil (IV, R = Br, R′ = H) which upon treatment with aqueous sodium bisulfite gave the *p*-bromoanilino compound (V),[10] which upon heating with alcohol and a trace of calcium carbonate yielded the indazole oxide (VI, R = Br, R′ = H). Vigorous oxidation with aqueous alkaline permanganate or chromic anhydride in acetic acid gave 4-bromoindazole-2′-carboxylic acid (VII, R = Br, R′ = H) which was decarboxylated to 4-bromoazoxybenzene by heating it at 160–170° in a benzene solution with copper powder and a trace of copper acetate. The product melted at 73–73.5° and no depression in melting point was observed when it was mixed with the product obtained by the bromination of azoxybenzene. By use of the same series of reactions, but using as starting materials 5-bromo-2-nitrobenzaldehyde and aniline, the position isomer, 4′-bromoazoxybenzene (VIII, R = H, R′ = Br) has been synthesized. It melted at 92–93° and no depression in melting point was observed when it was mixed with a sample of the product (m.p. 93.5–94.5°) obtained by the peracetic acid oxidation of *p*-bromoazobenzene. The conclusion, therefore, is that the structures assigned by Angeli to the two *p*-bromoazoxybenzenes[4] are correct. The "*α*"-isomer is thus 4-bromoazoxybenzene and the "*β*"-isomer, 4′-bromoazoxybenzene.

By the use of the same series of reactions, the two *p*-ethoxyazoxybenzenes have been synthesized, and the structure assignments given by Angeli[7,8] found also to be correct. Thus 4-ethoxyazoxybenzene (VIII, R = OC_2H_5, R′ = H), the "*α*"-isomer, melted at 73–74° (Angeli gives 72°), and 4′-ethoxyazoxybenzene (VIII, R = H, R′ = OC_2H_5), the "*β*"-isomer melted, at 76–76.5° (Angeli gives 76°). A mixture of equal amounts of the isomers melted at 47–64°.

Objections to the validity of these conclusions might be made on two bases. First, stereoisomers, as with azobenzenes, are known in symmetrical azoxy compounds. However, in every case one of the stereoisomers (almost certainly *trans*) is much more stable and the labile compound readily isomerizes to it, especially in the presence of light.[11] It, therefore, seems unlikely that there could be any confusion of stereoisomers with position isomers.

(10) Usually, this type of compound and its homologs underwent spontaneous dehydration during recrystallization.

(11) See the following and references cited therein: G. M. Badger, R. G. Buttery and G. E. Lewis, *J. Chem. Soc.*, 2143 (1953); K. E. Calderbank and R. J. W. Le Fèvre, *ibid.*, 1949 (1948); K.-A. Gehrckens and E. Müller, *Ann.*, **500**, 296 (1933).

Second, it has been reported that 4′-nitroazoxybenzene is converted to 4-nitroazoxybenzene by heating with chromic anhydride in acetic acid.[7] It is believed that this observation does not obviate the conclusions reached above for several reasons. Attempts to demonstrate similar isomerization with the *p*-bromoazoxybenzenes have failed.[4] Further, the synthesis of both position isomers by essentially similar methods appears to preclude rearrangement. Finally, oxidation of the indazole oxides with alkaline permanganate yields the same azoxybenzenecarboxylic acids, although in lower yield.

Acknowledgment.—The author wishes to thank the National Science Foundation for a grant in support of this work. A portion of it was done during the summer of 1953 at the University of Illinois, and thanks are extended to the Department of Chemistry and Chemical Engineering of that institution for the use of its facilities.

Experimental[12,13]

2-*p*-Bromophenyl-3-cyanoindazole-1-oxide (VI, R = Br, R′ = H).—A mixture of 15.1 g. (0.1 mole) of *o*-nitrobenzaldehyde and 17.2 g. (0.1 mole) of *p*-bromoaniline was heated carefully until ebullition occurred and held at this temperature (about 120°) for five minutes. The anil after cooling was ground well and added to 50 ml. of 40% aqueous sodium bisulfite and the mixture shaken vigorously at intervals. After 24 hours, the viscous solution was diluted with 150 ml. of water and filtered. To the filtrate, containing the bisulfite addition product of the anil, there was added a solution of 5.5 g. of sodium cyanide in 10 ml. of water; the mixture was allowed to stand at room temperature for three days. The insoluble material was removed by filtration, washed well with water, dried and recrystallized from 95% ethanol, about 600 ml. of which was required. The product, which was the indazole oxide, crystallized as yellow cottony needles, m.p. 210–211°. A second recrystallization from 95% ethanol raised the m.p. to 213–214°. The yield was 10 g. (30% over-all).

Anal. Calcd. for $C_{14}H_8N_3OBr$: C, 53.52; H, 2.56; N, 13.37; Br, 25.44. Found: C, 53.69; H, 2.33; N, 13.01; Br, 25.22.

4-Bromoazoxybenzene-2′-carboxylic Acid (VII, R = Br, R′ = H).—To a solution of 2.0 g. of 2-*p*-bromophenyl-3-cyanoindazole-1-oxide in 35 ml. of acetic acid, there was added 0.5 g. of chromic anhydride. The mixture was warmed on the hot-plate until reaction commenced, as indicated by the appearance of a greenish color. A second 0.5-g. portion of the anhydride was added after the mixture had stood an hour at room temperature and, after 12 hours additional, the mixture was poured into 150 ml. of water. The acid precipitated as a gum at first, but later solidified. It was removed by filtration, washed with water and taken up in ether. The solution was washed with water twice and and the acid extracted with two 25-ml. portions of 10%

(12) Melting points are corrected for exposed mercury column.

(13) Microanalyses by the Micro-Tech Laboratories, Skokie, Illinois, and by J. Nemeth, E. Fett and L. Chang of the University of Illinois.

aqueous sodium hydroxide. Pouring the alkaline solution into an excess of 10% phosphoric acid precipitated the azoxy acid as a sticky substance which later solidified. After having been air-dried, it was recrystallized from benzene–hexane as small, slightly orange crystals, m.p. 143–143.5°, yield 0.5 g.

Anal. Calcd. for $C_{13}H_9N_2O_3Br$: C, 48.62; H, 2.82; N, 8.73; Br, 24.89. Found: C, 48.76; H, 2.77; N, 8.62; Br, 25.09.

The oxidation was also successful with boiling aqueous alkaline permanganate, but the yield was lower.

4-Bromoazoxybenzene by Decarboxylation.—A mixture of 0.2 g. of 4-bromoazoxybenzene-2′-carboxylic acid, 10 ml. of benzene, 2.0 g. of copper powder and 0.1 g. of copper acetate was heated in a sealed tube at 160–170° for four hours. After the tube had cooled, the contents were filtered and the insoluble matter washed with benzene. The combined benzene solutions were washed as follows: once with water, twice with 5% hydrochloric acid, once with water, twice with 10% aqueous sodium hydroxide and twice with water. After drying with calcium chloride and filtration, the benzene was allowed to evaporate spontaneously. The residue was recrystallized from methanol to give 0.11 g. of yellow blunt needles, m.p .73–73.5°.

4-Bromoazoxybenzene by Bromination.—A solution of recrystallized azoxybenzene in 30 ml. of acetic acid was treated with 3 ml. of bromine and heated on the steam-bath for four hours. The reaction mixture was poured into 300 ml. of water, and sufficient sodium bisulfite added to remove the bromine color. The bromo compound was removed by filtration, washed with water, dried and recrystallized from methanol. The yield was 3.9 g. (50%), m.p. 73–74°. A mixture of equal parts of this product and that from the decarboxylation melted at 73–74°.

5-Bromo-2-nitrobenzaldehyde.—*m*-Bromobenzaldehyde[14] was nitrated in the manner described in the literature[15] for *m*-chlorobenzaldehyde to give a 75% yield of slightly-colored needles which melted at 61–62° after recrystallization from methanol–water. A second recrystallization, from benzene–cyclohexane, raised the m.p. to 68–69° (literature[16] gives 74°).

5-Bromo-3-cyano-2-phenylindazole-1-oxide (VI, R = H, R′ = Br).—Using 5-bromo-2-nitrobenzaldehyde and aniline as starting materials, this indazole oxide was prepared in essentially the same manner as 2-*p*-bromophenyl-3-cyanoindazole-1-oxide. The over-all yield of yellow cottony needles, m.p. 227–228° after recrystallization from benzene, was 15%.

Anal. Calcd. for $C_{14}H_8N_3OBr$: C, 53.52; H, 2.56; N, 13.37. Found: C, 53.78; H, 2.78; N, 13.22.

4′-Bromoazoxybenzene-2′-carboxylic Acid (VII, R = H, R′ = Br).—To a solution of 0.6 g. of 5-bromo-3-cyano-2-phenylindazole-1-oxide in 35 ml. of warm acetic acid, there was added 0.9 g. of chromic anhydride. The mixture was shaken vigorously for ten minutes, then allowed to stand for four hours at room temperature, and poured into 500 ml. of water. The acid thus precipitated was purified in the manner described above for its isomer. There was obtained, after recrystallization from benzene–cyclohexane, 0.30 g. (49%) of glistening orange platelets, m.p. 172–173°.

Anal. Calcd. for $C_{13}H_9N_2O_3Br$: N, 8.73; Br, 24.89. Found: N, 8.69; Br, 24.55.

Oxidation with hot alkaline permanganate gave the same acid but in lower yield.

4′-Bromoazoxybenzene by Decarboxylation.—The decarboxylation of 4′-bromoazoxybenzene-2′-carboxylic acid was effected in the same way as for its isomer. Using the crude acid, there was obtained a 50% yield of deep yellow plates, m.p. 92–93°.

***p*-Bromoazobenzene.**—Solutions of 6.48 g. of *p*-bromoaniline in 25 ml. of acetic acid and 4.28 g. of nitrosobenzene[17] in 45 ml. of acetic acid were mixed and allowed to stand at room temperature for 15 hours. The crystals which appeared were removed by filtration through sintered-glass, washed with a small amount of acetic acid and with water. The yield of copper-orange flakes, melting[18] at 90–91°, was 6.40 g. (68%). No attempt was made to recover additional product which crystallized from the filtrate.

4′-Bromoazoxybenzene by Oxidation.—A mixture of 2.5 g. of *p*-bromoazobenzene and 25 ml. of 40% peracetic acid was heated on the steam-bath for two hours. After cooling, the mixture was poured into 200 ml. of water, and allowed to stand for one hour. Filtration gave 2.5 g. of oxidized product melting at 65–72°. Fractional recrystallization from petroleum ether afforded 0.4 g. of 4′-bromoazoxybenzene, m.p. 93.5–94.5°. A mixture of equal amounts of this product and that obtained by decarboxylation melted at 92.5–93.5°.

No attempt was made to isolate the more soluble 4-bromoazoxybenzene.

3-Cyano-2-*p*-ethoxyphenylindazole-1-oxide (VI, R = OC_2H_5, R′ = H).—Using 15.1 g. of *o*-nitrobenzaldehyde and 13.7 g. of *p*-phenetidine and essentially the same procedure as for 2-*p*-bromophenyl-3-cyanoindazole-1-oxide, there was obtained 6.0 g. (22%) of yellow cottony needles which, upon recrystallization from a benzene–methanol mixture, melted at 216–218° with some browning.

Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.64; H, 4.51; N, 14.93.

4-Ethoxyazoxybenzene-2′-carboxylic acid (VII, R = OC_2H_5, R′ = H).—The oxidation of the above indazole oxide was accomplished in the manner previously described. The yield of crude acid, m.p. 118–119.5°, was 76%; it recrystallized from benzene–cyclohexane as short yellow prisms (80% recovery), m.p. 118.5–119.5°.

Anal. Calcd. for $C_{15}H_{14}N_2O_4$: C, 62.92; H, 4.93; N, 9.79. Found: C, 62.73; H, 4.79; N, 9.95.

4-Ethoxyazoxybenzene.—The decarboxylation of 4-ethoxyazoxybenzene-2′-carboxylic acid was accomplished as described for the other azoxy acids. A yield of 30% of the desired compound was obtained, m.p. 73–74° after recrystallization from a 10% cyclohexane–90% hexane mixture.

5-Hydroxy-2-nitrobenzaldehyde.[19]—To a mechanically stirred mixture of 100 ml. of concentrated nitric acid and 350 ml. of water, there was added 45 g. of *m*-hydroxybenzaldehyde at a rate such that the temperature was maintained at 40–45°. Heat was necessary during the later stages. The hydroxyaldehyde dissolved as it was added, but the mixture of nitrated compounds began to precipitate after about 0.5 hour. The whole addition required 1.25 hours, and the temperature was maintained and stirring continued for two hours additional. The mixture was then cooled to 2° by surrounding it with an ice-bath and adding small pieces of ice. It was filtered with a sintered-glass funnel, sucked as dry as possible and washed with several small portions of ice-water. The mixture of nitrohydroxybenzaldehydes, which weighed 39.5 g. after air-drying, was heated under reflux with 185 ml. of benzene for 30 minutes, and then cooled with stirring at 45°. The crude 5-hydroxy-2-nitrobenzaldehyde was separated by rapid filtration; no effort was made to isolate the isomers in the filtrate. After it had been air-dried, the desired aldehyde weighed 14.5 g. Recrystallization from 200 ml. of water containing a little decolorizing charcoal gave 12.0 g. of buff needles, m.p. 169–170° (literature[19] gives 167°). The hydroxynitrobenzaldehydes are potent sternutators.

The 5-Ethoxy-2-nitrobenzaldehyde.—To a mechanically stirred solution of 1.9 g. of metallic sodium in 150 ml. of absolute ethanol there was added 13.7 g. of 5-hydroxy-2-nitrobenzaldehyde. Some of the orange sodium salt precipitated. The mixture was heated to reflux and 25.0 g. of ethyl iodide added over a period of 40 minutes. Stirring and heating were continued for five hours, when about half of the alcohol was removed by distillation. The contents of the flask were added with stirring to 400 ml. of cold water. The aldehyde crystallized well on standing. Recrystallized from heptane it formed buff plates, m.p. 58.5–59.5° (literature[20] gives 62°). The yield was 7.5 g. (47%).

3-Cyano-5-ethoxy-2-phenylindazole-1-oxide (VI, R = H, R′ = OC_2H_5).—Prepared as described for its close relatives, using 5-nitro-2-ethoxybenzaldehyde and aniline as starting

(14) F. T. Tyson, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 132.

(15) E. J. Alford and K. Schofield, *J. Chem. Soc.*, 2105 (1952).

(16) A. Einhorn and A. Gernsheim, *Ann.*, **284**, 144 (1894).

(17) G. H. Coleman, C. M. McCloskey and F. A. Stuart, *Org. Syntheses*, **25**, 80 (1945).

(18) E. Bamberger, *Ber.*, **29**, 102 (1896), gives 89°.

(19) The procedure described here is a composite of those in the following references: R. Pschorr and C. Seydel, *Ber.*, **34**, 4000 (1901); R. Pschorr, *Ann.*, **391**, 28 (1912); P. Friedländer and O. Schenk, *Ber.*, **47**, 3040 (1914).

(20) G. Maffei, *Gazz. chim. ital.*, **59**, 3 (1929).

materials, the indazole oxide was obtained in 15% yield as yellow, cottony needles, m.p. 202–203° from ethanol.

Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05. Found: C, 69.11; H, 4.66; N, 15.11.

4'-Ethoxyazoxybenzene-2'-carboxylic Acid (VII, R = H, R' = OC_2H_5).—The oxidation of the above indazole oxide by the usual method afforded a 20% yield of small yellow spears of the acid, m.p. 134–135°, after recrystallization from heptane.

Anal. Calcd. for $C_{15}H_{14}N_2O_4$: C, 62.92; H, 4.93; N, 9.79. Found: C, 62.60; H, 5.21; N, 9.80.

4'-Ethoxyazoxybenzene.—Decarboxylation of the acid was accomplished by the usual procedure. A 50% yield of yellow flakes, m.p. 76–76.5° after two recrystallizations from hexane, was obtained. A 50–50 mixture of this compound with 4-ethoxyazoxybenzene melted at 47–64°.

STATE COLLEGE, MISSISSIPPI

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Configuration of the Glycosidic Unions in Streptomycin[1]

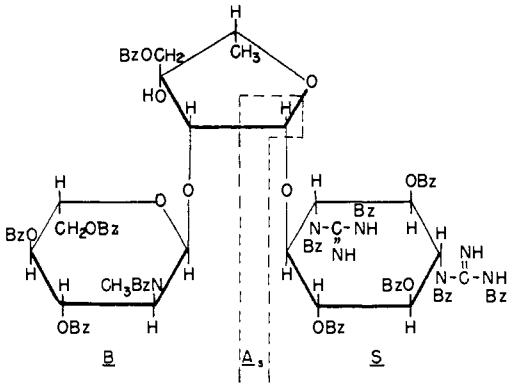
BY M. L. WOLFROM, M. J. CRON,[2] C. W. DEWALT[2] AND R. M. HUSBAND[2]

RECEIVED JUNE 6, 1954

Measurements of the optical rotation of an amorphous but chromatographically homogeneous preparation of dodecabenzoyl- (and acetyl)-dihydrostreptomycin and of that of a crystalline methyl pentabenzoyldihydrostreptobiosaminide, together with other rotatory data, allow calculations to be made which demonstrate that the streptose-streptidine linkage in streptomycin is in all probability β-L and that the hexosamine–streptose linkage is in all probability α-L. It is pointed out that the hydroxyls in streptidine on C-4 and C-6, one of which is involved in the streptose linkage, are not sterically equivalent; this configurational point in the streptomycin molecule remains to be elucidated.

The anomeric structure of the streptidine–streptose linkage in streptomycin was calculated to be of the α-L-type[1a] on the assumption, at that time reasonable, that a symmetrical point of attachment (C-5, see IV) of the aglycon streptidine, a *meso*-form, was such as to maintain its optical inactivity. It has since been determined[3] that the streptidine aglycon is unsymmetrically attached (C-4 or C-6). It therefore follows that the streptidine moiety is optically active by substitution. This requires a revision in the above calculation.

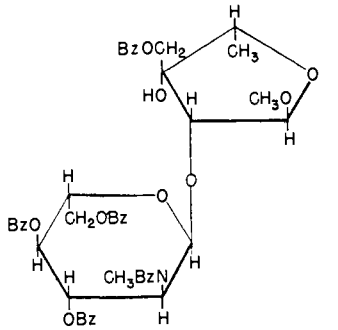
Folkers and co-workers[4] have recorded the rotation for an amorphous dodecabenzoyldihydrostreptomycin (I).



I, Dodecabenzoyldihydrostreptomycin

This preparation was repeated in our laboratories, under milder acylating conditions, with the result that a product with a somewhat higher rotation was obtained. The corresponding acetyl derivative was also prepared. The molecular rotation, [M] = (1833) (+69°) = +126,500,[5] of the benzoate should be the sum of the component parts *S*, A_s and *B*, wherein *S* can be considered to approximate closely the molecular rotation [(991) (+58°) = +57,500] of heptabenzoylstreptidine,[4] A_s is the rotatory contribution of the streptose glycosidic carbon in the streptidine–streptose linkage, and *B* that of the remainder of the benzoylated dihydrostreptomycin, whence (A_s + *B*) = +69,000.

Methanolysis of dihydrostreptomycin with subsequent benzoylation yielded a crystalline methyl pentabenzoyldihydro-L-streptobioseaminide (II) wherein [*M'*] = (874) (−10°) = −8,700. In this glycoside the aglycon, CH_3OH, is optically inactive and should the glycosidic carbon have the same configuration as in streptomycin, then its molecular rotation, A'_s + *B*, should closely approximate that of A_s + *B* = +69,000. Since this is not the case, these glycosides are anomeric with II being the α-L-form on the Hudson classification[6] (it is known that streptose is an L-sugar[7]). In this approximation the size of the aglycon CH_3OH is hardly com-



II, Methyl pentabenzoyldihydro-α-L-streptobioseaminide

(1) Preliminary communications: (a) R. U. Lemieux, C. W. DeWalt and M. L. Wolfrom, THIS JOURNAL, **69**, 1838 (1947); (b) M. L. Wolfrom, M. J. Cron and R. M. Husband, Abstracts Papers Am. Chem. Soc., **118**, 7R (1950); (c) M. L. Wolfrom, paper presented at the Symposium on Antibiotics and Vitamins, Cleveland, Ohio, Meeting, Am. Assoc. for the Advancement of Science, Dec. 29, 1950.

(2) Bristol Laboratories Research Associate (R. M. H.) and Research Fellow of The Ohio State University Research Foundation (Project 224).

(3) F. A. Kuehl, Jr., R. L. Peck, C. E. Hoffhine, Jr., Elizabeth W. Peel and K. Folkers, *ibid.*, **69**, 1234 (1947); F. A. Kuehl, Jr., R. L. Peck, C. E. Hoffhine, Jr., and K. Folkers, *ibid.*, **70**, 2325 (1948).

(4) R. L. Peck, F. A. Kuehl, Jr., C. E. Hoffhine, Jr., Elizabeth W. Peel and K. Folkers, *ibid.*, **70**, 2321 (1948).

(5) All rotations are recorded in chloroform solution at 25 ± 5° with $c < 5$ and λ = 5892.5 Å.

(6) C. S. Hudson, THIS JOURNAL, **31**, 66 (1909).

(7) J. Fried, Doris E. Walz and O. Wintersteiner, *ibid.*, **68**, 2746 (1946).