

N-N distances. However, it is not possible to determine the direction of the covalent bonds, since the differences<sup>6</sup> in the interatomic distances are not significant in most cases. This is so because the *x*-coordinates were not directly determined and also because the standard deviations of the remaining parameters are rather large. An accurate determination of bond distances will have to wait until three-dimensional neutron data can be obtained.

**Acknowledgment.**—Thanks are due to Dr. J. V. R. Kaufman for bringing this problem to my attention and to Mr. I. Kluger for performing all the computer calculations. The author also is grateful to Dr. H. Danner, Brookhaven National Laboratory, for the neutron data and for the information on the work done at Pennsylvania State University.

(8) The Atlantic Refining Company, Philadelphia, Pa.

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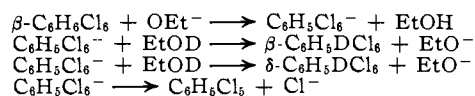
G. L. GLEN<sup>8</sup>

RECEIVED JUNE 1, 1963

### The Mechanism of the Dehydrochlorination of $\beta$ -Benzene Hexachloride<sup>1</sup>

Sir:

Cristol proposed that the marked unreactivity of the  $\beta$ -isomer of benzene hexachloride (relative to that of the other isomers) is due to the absence, in that and only that isomer, of hydrogen and chlorine atoms *trans* to each other and on adjacent carbon atoms.<sup>2</sup> Although this proposal seems generally accepted, there is less agreement concerning the mechanism of the *cis*-dehydrochlorination of  $\beta$ -benzene hexachloride. Cristol and Fix<sup>3</sup> pointed out that in a deuterated solvent the intermediate carbanion suggested for the reaction could either be deuterated with retention of configuration to yield labeled starting material, be deuterated with inversion of configuration to give labeled  $\delta$ -benzene hexachloride, or lose a chloride ion to give a pentachlorocyclohexene. Either the  $\delta$ -isomer or the pentachlorocyclohexene would then be rapidly dehydrochlorinated to a mixture of trichlorobenzenes.



As evidence for the intermediacy of a carbanion, Cristol and Fix reported 0.08% deuterium present in the  $\beta$ -benzene hexachloride isolated after about 50% dehydrohalogenation in 70% EtOD-30% EtOH.

Cram has stated that the most probable path of decomposition of the carbanion is *via* the formation of  $\delta$ -benzene hexachloride, *cis* elimination from the carbanion being improbable, and that deuterated trichlorobenzenes should be produced in a deuterated solvent, since the deuterium atom of any intermediate  $\delta$ -benzene hexachloride could be removed in a *trans* elimination only *via* a conformation with five axial chlorine atoms.<sup>4</sup>

In relation to our interest in the carbanion mechanism for  $\beta$ -elimination reactions,<sup>1</sup> we have examined the trichlorobenzene mixture produced in deuterated methanol.<sup>5</sup> When 2.19 mmoles of  $\beta$ -benzene hexachloride was 70% dehydrohalogenated by 6.9 mmoles of sodium methoxide in 98% MeOD-2% MeOH, the trichlorobenzene mixture (containing 88% of the 1,2,4-isomer) produced had n.m.r. and infrared spectra almost identical with those of the trichlorobenzene mixture produced under very similar conditions in "light" methanol. From blank experiments we conclude that  $3.1 \pm 1.0\%$  1,2,4-trichlorobenzene-3-*d* and much less of any other deuterated trichlorobenzene were present in the products of reaction in MeOD. Determination of the rate constant for the dehydrochlorination of  $\beta$ -benzene hexachloride in methanol and comparison with that for the exchange of 1,2,4-trichlorobenzene-3-*d*<sup>1b</sup> showed that between 1 and 5%<sup>6</sup> of the 1,2,4-trichlorobenzene produced in the reaction in MeOD would have been transformed to 1,2,4-trichlorobenzene-3-*d*.

We therefore conclude that if the alkaline dehydrochlorination of  $\beta$ -benzene hexachloride is initiated to any major extent by carbanion formation, the intermediate carbanions almost always lose chloride ions and are only rarely reprotonated. The possibility that the reaction proceeds only to a minor extent *via* intermediate carbanions but consists largely of a concerted *cis* elimination from a conformation, like the boat form, in which the dihedral angle between the hydrogen and chlorine atoms being removed is quite small<sup>7</sup> has not been ruled out. However, in view of the slow rate of such *cis* eliminations<sup>8</sup> and the added energy that would be required in the present case to reach such a conformation, the dehydrohalogenation of  $\beta$ -benzene hexachloride seems surprisingly fast to be a reaction of this type.

**Acknowledgment.**—We wish to thank the National Science Foundation for partial support of this investigation.

it seems that intermediate carbanions should be captured more efficiently in this solvent than in ethanol. If  $k_H/k_D$  is 5.0, 9% of the captured intermediates will escape deuteration in 98% MeOD but 68% will in 70% EtOD.

(6) Assuming that  $k_H/k_D$  is between 1 and 5.

(7) Cf. C. H. DePuy, R. D. Thurn, and G. F. Morris, *J. Am. Chem. Soc.*, **84**, 1314 (1962).

(8) Some of the data of Cristol and co-workers<sup>9</sup> provide maximum values for the rates of such processes.

(9) S. J. Cristol and N. L. Hause, *J. Am. Chem. Soc.*, **74**, 2193 (1952); S. J. Cristol and E. F. Hoegger, *ibid.*, **79**, 3438 (1957).

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RECEIVED OCTOBER 28, 1963

### Photochemical and Thermal Rearrangement of $\alpha,\beta$ -Epoxyketones

Sir:

Investigations during the past decade have revealed the carbonyl group as an important and versatile chromophore in photochemical reactions.<sup>1,2</sup> In view of the many acid- and base-catalyzed rearrangements exhibited by  $\alpha,\beta$ -epoxyketones,<sup>3</sup> it is surprising that the photochemical behavior of these substrates has not been widely studied.<sup>4</sup> A recent investigation<sup>5</sup> of the photolysis of some steroidal epoxyketones represents the only published case in which skeletal rearrangement occurs. We take this opportunity to report<sup>6</sup>

(1) P. de Mayo, *Advan. Org. Chem.*, **2**, 367 (1960).

(2) P. de Mayo and S. T. Reid, *Quart. Rev. (London)*, **15**, 393 (1961).

(3) R. Parker and N. Isaacs, *Chem. Rev.*, **59**, 737 (1959).

(4) The first of a few recent endeavors is that by H. E. Zimmerman, Abstracts of the Seventeenth National Organic Chemistry Symposium, June, 1961, Bloomington, Indiana, p. 31.

(5) C. Lehmann, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **45**, 1031 (1962).

(6) Part of this work was presented by W. Reusch and C. K. Johnson,

(1) (a) Part V in the series "The Carbanion Mechanism for  $\beta$ -Elimination Reactions"; (b) for part IV see J. Hine and P. B. Langford, *J. Org. Chem.*, **27**, 4149 (1962).

(2) S. J. Cristol, *J. Am. Chem. Soc.*, **69**, 338 (1947); cf. S. J. Cristol, N. L. Hause, and J. S. Meek, *ibid.*, **73**, 674 (1951).

(3) S. J. Cristol and D. D. Fix, *ibid.*, **75**, 2647 (1953).

(4) D. J. Cram in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 321.

(5) In view of the greater acidity and ion-solvating power of methanol



at 200°, extensive rearrangement, isomerization, and fragmentation occurs. A 2:1 mixture of XII, disemicarbazone, m.p. 222°, and XI, semicarbazone, m.p. 213°, was obtained in 75% yield after heating X for 10 hr. The diastereoisomer IX is slower to react, giving 43% rearrangement to a similar mixture in the same period. An independent preparation of XI and XII by ozonolysis of a mixture of 4-methylisopulegone diastereoisomers<sup>22</sup> completed the proof of structure and enabled us to assign configurations to these isomers. Appropriate experiments have established that this unusual thermal rearrangement<sup>23</sup> is not catalyzed by acids or radical initiators and is insensitive to increases in surface area.

(22) C. Djerassi, J. Osiecki, and E. J. Eisenbraun, *J. Am. Chem. Soc.*, **83**, 4433 (1961). In our hands the methylation of pulegone yielded a mixture of 76% (-)-4-methylisopulegone and 24% of the dextrorotatory diastereomer, identified by semicarbazone derivatives.

(23) Epoxyketones I and III do not exhibit similar thermal reactions, but are transformed instead by a high temperature, free-radical decomposition initiated by oxirane hydrogen abstraction: W. Reusch and C. K. Johnson, *J. Am. Chem. Soc.*, **84**, 1759 (1962).

(24) Holder of a National Science Foundation Cooperative Graduate Fellowship, 1962-1963.

(25) National Science Foundation Undergraduate Research Participant.

(26) This investigation was supported in part by a research grant, AM 04936-03, from the National Institutes of Health.

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RECEIVED SEPTEMBER 9, 1963

### The Absolute Configuration of Streptidine in Streptomycin

Sir:

The gross structural features of the potent antibiotic substance streptomycin were derived<sup>1</sup> many years ago. The component fragments are N-methyl-L-glucosamine, the elusive L-streptose (which has been assigned the structure 5-deoxy-3-C-formyl-L-lyxose),<sup>2</sup> and streptidine. The configuration of the glycosidic linkage between N-methyl-L-glucosamine and streptose has been shown to be  $\alpha$ ,<sup>3</sup> that between streptose and streptidine has been shown to be  $\beta$ .<sup>3</sup> Streptidine was shown to be a *meso* form of 1,3-diguanido-2,4,5,6-tetrahydroxycyclohexane<sup>4</sup> and, furthermore, by synthesis<sup>5</sup> and degradation<sup>6</sup> to possess the all *trans* configuration. The streptobiosamine moiety of streptomycin has been shown to be attached to position 4' of streptidine in either the R or S<sup>9</sup> absolute configuration by the degradation of streptomycin of optically active ( $[\alpha]_D - 4^\circ$  (*c* 1.1, 50% acetic acid)) N,N'-dibenzoyl-4-deoxystreptamine (I).<sup>10</sup> Although streptidine is a *meso* form, the asymmetric attachment of streptobiosamine to it causes each of the ring carbons of streptidine in streptomycin to be asym-

(1) R. U. Lemieux and M. L. Wolfrom, *Advan. Carbohydrate Chem.*, **3**, 337 (1948), and references cited therein.

(2) F. A. Kuehl, Jr., R. L. Clark, M. N. Bishop, E. H. Flynn, and K. Folkers, *J. Am. Chem. Soc.*, **71**, 1445 (1949).

(3) M. L. Wolfrom, M. J. Cron, C. W. DeWalt, and R. M. Husband, *ibid.*, **76**, 3675 (1954).

(4) H. E. Carter, R. K. Clark, Jr., S. R. Dickman, Y. H. Loo, P. S. Skell, and W. A. Strong, *Science*, **103**, 540 (1946).

(5) M. L. Wolfrom, S. M. Olin, and W. J. Polglase, *J. Am. Chem. Soc.*, **72**, 1724 (1950).

(6) O. Wintersteiner and A. Klingsberg, *ibid.*, **73**, 2917 (1951).

(7) The numbering system used here is that suggested by Rinehart, *et al.*<sup>8</sup> for the 2-deoxystreptamine moiety of the neomycin antibiotic group. For streptomycin, this attaches the streptobiosamine fragment at C-4 of streptidine.

(8) K. L. Rinehart, Jr., M. Hichens, A. D. Argoudelis, W. S. Chilton, H. E. Carter, M. P. Georgiadis, C. P. Schaffner, and R. T. Schillings, *J. Am. Chem. Soc.*, **84**, 3218 (1962).

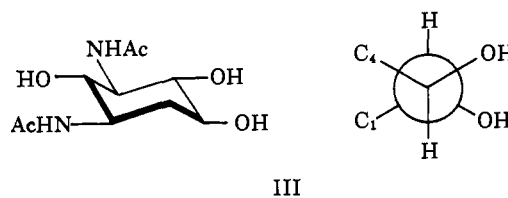
(9) R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).

(10) F. A. Kuehl, Jr., R. L. Peck, C. E. Hoffhine, Jr., and K. Folkers, *J. Am. Chem. Soc.*, **70**, 2325 (1948). The hydroxyl group of streptidine that is replaced by hydrogen in this degradation sequence is that to which streptobiosamine is glycosidically attached in streptomycin.

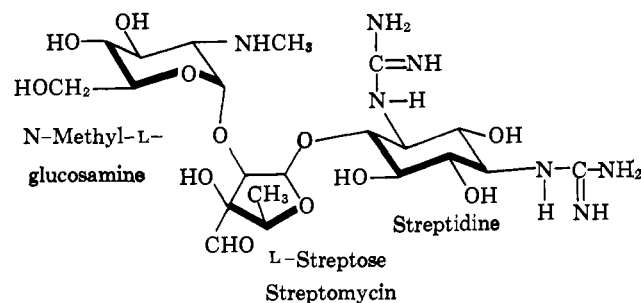
metric. We wish to report the determination of the absolute configuration of N,N'-diacetyl-4-deoxystreptamine, derived from N,N'-dibenzoyl-4-deoxystreptamine and, hence, the complete configurational assignment of streptomycin and other members of the streptomycin antibiotic group.

Acid hydrolysis of N,N'-dibenzoyl-4-deoxystreptamine (I), m.p. 284-286° dec. (lit.<sup>10</sup> m.p. 287-289°), furnished 4-deoxystreptamine, which on acetylation gave pentaacetyl-4-deoxystreptamine (II), m.p. 319-320° (*Anal. Calcd.* for C<sub>16</sub>H<sub>24</sub>O<sub>8</sub>N<sub>2</sub>: C, 51.60; H, 6.50; N, 7.52. Found: C, 51.39; H, 6.47; N, 7.48). The polyacetate II, on treatment with methanolic ammonia, gave N,N'-diacetyl-4-deoxystreptamine (III), m.p. 291-292°,  $[\alpha]_D^{29} + 5^\circ$  (*c* 0.97, water) (*Anal. Calcd.* for C<sub>10</sub>H<sub>18</sub>O<sub>5</sub>N<sub>2</sub>: C, 48.77; H, 7.36; N, 11.37. Found: C, 48.50; H, 7.29; N, 11.15).

The absolute configuration of III was determined by the application of Reeves' cuprammonium method.<sup>11</sup> Compound III showed  $[\alpha]_D^{29} + 5^\circ$  (*c* 0.97, water) and  $[\alpha]_D^{29} - 970^\circ$  (*c* 0.88, Cupra B); this gives the result  $\Delta[M]_{\text{Cupra B}} - 2400^\circ$ .<sup>12</sup> The strong negative increment is similar to that obtained for the 2,3-glycol complex of D-glucosides ( $\Delta[M]_{\text{Cupra B}} \sim -2075^\circ$ ) but opposed to that obtained for the 3,4-glycol complex of D-glucosides ( $\Delta[M]_{\text{Cupra B}} \sim +2150^\circ$ ).<sup>11</sup> Interferences from a potential *trans* 1,3-glycol complex are not observed,<sup>11</sup> and interference from acetamido groups does not occur.<sup>13</sup> Thus, the dihedral angle of the 5,6-glycol grouping (formed from the planes of HO-C<sub>5</sub>-C<sub>6</sub> and C<sub>5</sub>-C<sub>6</sub>-OH) of N,N'-diacetyl-4-deoxystreptamine (III) is *clockwise*<sup>11</sup> 60° and III has the absolute configuration shown rather than its mirror image.<sup>14</sup>



Using this configurational assignment, the structure of streptomycin in complete stereochemical detail may be written as indicated.<sup>15</sup> This stereochem-



ical result also establishes the complete structure

(11) R. E. Reeves, *Advan. Carbohydrate Chem.*, **6**, 107 (1951), and references cited therein.

(12)  $\Delta[M]_{\text{Cupra B}} = ([\alpha]_{\text{Cupra B}} - [\alpha]_{\text{water}}) \times (\text{mol. wt.}/100)$ .

(13) M. Hichens and K. L. Rinehart, Jr., *J. Am. Chem. Soc.*, **85**, 1547 (1963).

(14) Using the R, S<sup>9</sup> convention, the absolute configuration of III may be written 1(R),3(R)-diacetamido-2(S),5(S),6(S)-trihydroxycyclohexane.

(15) The asymmetry of the streptidine ring in streptomycin is thus 1(R),2(R),3(S),4(R),5(R),6(S). This assignment is in agreement with the suggestion of Tatsuoka,<sup>16</sup> which was based on the fact that N,N'-diacetyl-2,5,6-tri-O-methylstreptamine, derived from dihydrostreptomycin, has the same sign (positive) of rotation as N,N'-diacetyl-5,6-di-O-methyl-2-deoxystreptamine, derived from pseudoneamine. We thank Dr. K. L. Rinehart, Jr., for bringing this suggestion to our attention.

(16) S. Tatsuoka and S. Horii, *Proc. Japan Acad.*, **39**, 314 (1963).