absolute ethanol; yield 45 g. (41%); m.p. 187–188°. A sample was recrystallized again from ethanol; m.p. 191–192°.

N-Guanyl-5-oxo-2-pyrrolidinecarboxamide. A mixture of 50 g. (0.53 mole) of guanidine hydrochloride and 28 g. (0.52 mole) of sodium methoxide in 200 cc. of methanol was stirred for 10 minutes. The sodium chloride then was filtered off and the filtrate was mixed with 55 g. (0.27 mole) of diethyl L-glutamate. After about two minutes the product crystallized; yield 33 g. (72%); m.p. 180–182°. A portion of the compound was recrystallized from water; m.p. 187–189°.

Anal. Calc'd for $C_6H_{10}N_4O_2$: C, 42.3; H, 5.9; N, 32.9. Found: C, 42.0; H, 6.2; N, 32.9.

N,N-Dimethyl-5-oxo-2-pyrrolidinecarboxamide. Diethyl L-glutamate (66 g.) (0.32 mole) and an excess of anhydrous dimethylamine (68 g., 100 cc.) (1.5 moles) were mixed in a pressure bottle and allowed to stand at room temperature for 4 weeks. The excess dimethylamine then was evaporated and the residue was distilled; b.p. 210–214°/0.3 mm. Shortly the product began to crystallize. The mixture was quickly poured into a small amount of ethanol, cooled, and the solid was collected; yield 32 g. (63%); m.p. 114–116°. The product then was recrystallized from 350 cc. of ethyl acetate; yield 28.8 g.; m.p. 115–117° (corrected); $[\alpha]_D^{23}$ −33.5° (*c*, 2 in water).

Anal. Calc'd for $C_7H_{12}N_2O_2$: C, 53.8; H, 7.7; N, 17.9. Found: C, 53.6; H, 7.1; N, 18.3.

N,N-Tetramethylene-5-oxo-2-pyrrolidinecarboxamide. Diethyl L-glutamate (88 g.) (0.43 mole) and an excess of pyrrolidine (136 g., 160 cc.) (1.9 moles) were mixed and allowed to stand at room temperature for 4 weeks. The excess pyrrolidine then was distilled under reduced pressure on the steam-bath. The resulting sirup was diluted with two volumes of ethyl acetate and seeded with crystals obtained by distilling the product from a previous small run (b.p. 225°/0.4 mm.). After cooling, the product was collected; yield 47 g. (60%). This was recrystallized from 250 cc. of ethyl acetate; yield 38 g.; m.p. 111–112° (corrected); $[\alpha]_D^{23}$ −40.5° (*c*, 2 in water).

Anal. Calc'd for $C_9H_{14}N_2O_2$: C, 59.3; H, 7.7; N, 15.4. Found: C, 59.5; H, 8.0; N, 15.4.

N,N'-(2-Hydroxytrimethylene)bis-(5-oxo-2-pyrrolidinecarboxamide). 1,3-Diamino-2-hydroxypropane (35 g., 30 cc.) (0.33 mole), an excess of diethyl L-glutamate (198 g.) (0.97 mole), and 150 cc. of absolute ethanol were mixed and allowed to stand at room temperature for 4 days. The mixture then was cooled overnight and the product was collected; yield 78 g. This was dissolved in 350 cc. of warm water, decolorized with Norit, and the filtrate was diluted with one liter of acetone. Upon cooling overnight the product crystallized; yield 52 g. (50%); m.p. 227–229° (corrected).

A sample of this material was dissolved in 50 cc. of water, diluted with 150 cc. of acetone, filtered hot, and cooled overnight; yield 7.7 g. This process was repeated twice; yield 4.7 g., m.p. 235–237° (corrected); $[\alpha]_D^{23}$ −22.1° (*c*, 2 in water).

Anal. Calc'd for $C_{13}H_{20}N_4O_5$: C, 50.0; H, 6.4; N, 17.9. Found: C, 50.2; H, 7.0; N, 18.2.

Attempts to prepare and isolate the monosubstituted derivative of 1,3-diamino-2-hydroxypropane were unsuccessful.

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The Acid Catalyzed Cleavage of a Substituted Cyclopentane-1,3-diol. I. 1,3-Diphenyl-1,3-dihydroxy-2,2-dimethylhydrindene

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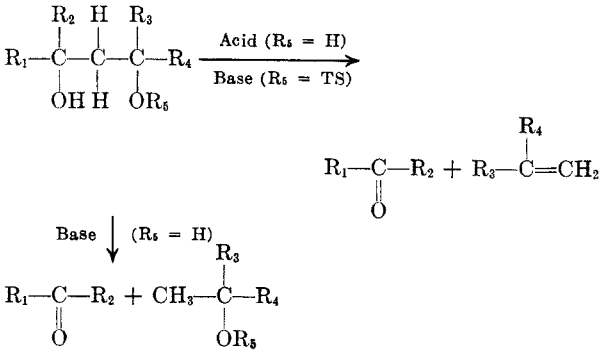
The cleavage reactions of 1,3-diols have been studied in some detail.[1–5] The products obtained from the acid catalyzed cleavage[1,2] are the corresponding carbonyl compound and olefin while the products from the base cleavage depend on whether the free diol or monotosylate is employed. The free diol with base yields a carbonyl compound[6] and, unlike the other cleavage reactions, a derived alcohol,[4] while the monotosylate[3] gives a carbonyl compound and olefin much like the acid catalyzed cleavage.



These studies, however, have not included the cleavage of a cyclopentane-1,3-diol. We have prepared 1,3-diphenyl-1,3-dihydroxy-2,2-dimethylhydrindene (I) and studied its behavior under acidic conditions which previously led to cleavage in simpler aliphatic cases. This paper reports the acid catalyzed cleavage of I and a structural proof of its cleavage product.

A mixture of I, readily prepared by the method of Geissman and Tulagin,[7] and fused potassium bisulfate was heated for 8 hours at 150–160° to yield a non-crystalline material characterized by a strong band in the infrared at 5.98μ. This band suggested the presence of a conjugated carbonyl group. Ozonization of the oil and subsequent workup led

(1) J. English Jr. and F. V. Brutcher Jr., *J. Am. Chem. Soc.*, **74**, 4279 (1952).

(2) H. E. Zimmerman and J. English Jr., *J. Am. Chem. Soc.*, **76**, 2285, 2291, 2294 (1954).

(3) R. B. Clayton and H. B. Henbest, *Chemistry & Industry*, 1315 (1953).

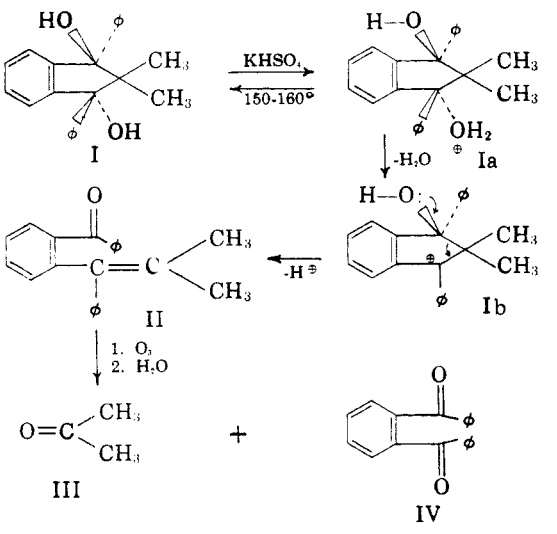
(4) S. Searles and E. K. Ives, *Abstracts of 127th Meeting Amer. Chem. Soc.*, Cincinnati, Ohio, P. 24N, 1955.

(5) For a recent review see H. H. Wasserman in M. S. Newman, *Steric Effects in Organic Chemistry*, J. Wiley & Sons, Inc., N. Y., 1956, p. 375–378.

(6) This cleavage of the free diol with base to carbonyl compound was first reported in 1951 (F. V. Brutcher Jr., *Ph.D. Thesis*, Yale University, P. 67, 68) and later studied in some detail by S. Searles and E. K. Ives.[4]

(7) T. A. Geissman and V. Tulagin, *J. Am. Chem. Soc.*, **63**, 3354 (1941).

to two products, a distillate and a stillpot residue. The distillate on treatment with 2,4-dinitrophenylhydrazine yielded an acetone-2,4-dinitrophenylhydrazone m.p. 121–123°, identical with an authentic sample,[8] m.p. 123–124°, m.m.p. 121–123°. From the stillpot residue was isolated *o*-dibenzoyl benzene, m.p. 143.5–145°, identical with an authentic sample,[9] m.p. 146–146.5,° m.m.p. 144–145.5° prepared from diethyl phthalate and phenylmagnesium bromide. This evidence is consistent with structure II for the oil which is the cleavage product to be expected on mechanistic grounds.



A detailed mechanism requires knowledge of the stereochemistry of I. To this end, Dr. Lester Kuhn[10] of the Ballistics Research Proving Ground, Aberdeen, Maryland has kindly measured the infrared hydroxyl absorption and reports that I has a single hydroxyl band at 2.78μ where the free hydroxyl band is expected. This means that there is no internal hydrogen bond, but it does not rule out a *cis* structure. However, based on the mode of formation of I,[11] a *trans* structure is more likely.

The mechanism shown is not concerted in view of the possible resonance stabilization of the carbonium ion in Ib. However, because of the conditions, potassium bisulfate and melted diol in the absence of a solvent, carbonium character may well be diminished and a concerted process might be involved as has been shown in other cases by Zimmerman and English.[2]

It is interesting to note that no evidence for Wagner-Meerwein rearrangement was obtained. The strain due to the eclipsed groups on the highly substituted cyclopentane ring is presumably relieved more readily by ring cleavage.

EXPERIMENTAL[12]

1,3-Diphenyl-1,3-dihydroxy-2,2-dimethylhydrindene (I). This compound was readily prepared by the method of Geissman and Tulagin.[7] For the preparation of the intermediate, 1,3-diketo-2,2-dimethylhydrindene, see Wislicenus and Kötzle.[13]

Cleavage of 1,3-diphenyl-1,3-dihydroxy-2,2-dimethylhydrindene (I). A mixture of 3.4 g. (0.010 mole) of 1,3-diphenyl-1,3-dihydroxy-2,2-dimethylhydrindene and 12.0 g. (0.088 mole) of fused potassium bisulfate was heated in an oil-bath at 150–160° for eight hours. After cooling, the mixture was extracted with ether; the ether extracts were dried with magnesium sulfate and the ether was removed at reduced pressure. A transparent, light brown, viscous oil (II) weighing 3.0 g. remained which could not be crystallized. An infrared absorption spectra of the oil (II) in chloroform was characterized by an absorption band at 5.98 μ[14] which indicated the presence of a conjugated carbonyl group.

Ozonization of the cleavage product (II) *from 1,3-diphenyl-1,3-dihydroxy-2,2-dimethylhydrindene.* The oil (II) obtained from the cleavage of the 1,3-glycol was dissolved in 40 ml. of chloroform and treated with ozone at −5 to −10° until ozone was no longer absorbed. The chloroform was removed at reduced pressure and room temperature and a yellow, wax-like residue remained which was decomposed by refluxing for 30 minutes with water and zinc dust, in the presence of traces of silver nitrate and hydroquinone. The mixture then was distilled and upon treating the aqueous distillate with 2,4-dinitrophenylhydrazine, a yellow-orange precipitate formed. The precipitate was recrystallized from aqueous ethanol to give 0.33 g. (14% yield) of acetone 2,4-dinitrophenylhydrazone, m.p. 121–123°. A mixture melting point with an authentic sample[8] which had a m.p. 123–124° caused no depression, m.m.p. 121–123°. The stillpot residue from the distillation was extracted with several portions of ether and the ether solution was dried over magnesium sulfate. When most of the ether was removed at reduced pressure a fine white precipitate of *o*-dibenzoylbenzene was formed which weighed 0.75 g. (26% yield), m.p. 143.5–145°, lit.[9], m.p. 146–147°. An authentic sample of *o*-dibenzoylbenzene m.p. 146–146.5°, synthesized by an alternate route, gave no depression in melting point, m.m.p. 144–145.5°. The infrared absorption spectra for the two compounds were also identical, each having a carbonyl absorption band at 6.05μ.

Anal.[15] Calc'd for $C_{20}H_{14}O_2$: C, 83.90; H, 4.93. Found: C, 83.63; H, 4.67.

Alternate synthesis of o-dibenzoylbenzene. To a solution of 111 g. (0.500 mole) of diethyl phthalate in dry benzene was added an ether solution of one mole of phenylmagnesium

(8) R. L. Shriner and R. C. Fuson, *The Systematic Identification of Organic Compounds*, 3rd edition, J. Wiley and Sons, New York, N. Y. 1948, p. 171.

(9) A. Luttringhaus and K. Scholtis, *Ann.*, **557**, 70 (1945) report m.p. 146–147°.

(10) (a) L. P. Kuhn, private communication; (b) L. P. Kuhn, *J. Am. Chem. Soc.*, **74**, 2492 (1952); (c) L. P. Kuhn, *J. Am. Chem. Soc.*, **76**, 4323 (1954).

(11) (a) D. Y. Curtin, E. E. Harris, and E. K. Meislich, *J. Am. Chem. Soc.*, **74**, 2901 (1952); (b) D. J. Cram and F. A. A. Elhafez, *J. Am. Chem. Soc.*, **74**, 5828 (1952); (c) D. J. Cram and F. D. Greene, *J. Am. Chem. Soc.*, **75**, 6005 (1953).

(12) All melting points are uncorrected.

(13) W. Wislicenus and A. Kötzle, *Ann.*, **252**, 82 (1889); see also C. F. Koelsch and D. J. Byers, *J. Am. Chem. Soc.*, **62**, 560 (1940).

(14) All the infrared absorption spectra were determined in chloroform solution using fixed cells in a Perkin-Elmer Model 21 spectrophotometer.

(15) Analysis performed by Galbraith Laboratories, Knoxville, Tenn.

bromide. After working up the reaction mixture in the usual way, the infrared spectrum indicated the presence of unreacted ester by an absorption peak at 5.82 μ. The unreacted ester was saponified by refluxing with methanolic potassium hydroxide. Water then was added to the reaction mixture and the *o*-dibenzoylbenzene was extracted with benzene and ether. The benzene-ether solution was dried over magnesium sulfate and then removed at reduced pressure to give an orange-green oil. Upon addition of a small amount of ether, *o*-dibenzoylbenzene precipitated as a fine white powder. The product after recrystallization from absolute ethanol weighed 11.5 g. (8% yield) m.p. 146–146.5°, lit.[9] m.p. 146–147°.

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Mescaline Analogs. VI. Mescaline Homologs[1]

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To examine the effect of structural variations on the unique physiological action of mescaline, 3,4,5-trimethoxy-β-phenethylamine, a number of closely related phenethylamines have been synthesized, and their effect on certain enzyme systems vital to brain function has been examined.[4]

All of the compounds previously reported[5] were β-phenethylamines with nuclear substituents which varied in type, number and position. A series of compounds related to mescaline now has been synthesized in which a 3,4,5-trimethoxybenzene nucleus is attached to aminoalkyl groups both longer and shorter than the aminoethyl side-chain of mescaline. These include 3,4,5-trimethoxybenzylamine and γ-(3,4,5-trimethoxyphenyl)propylamine. A sidechain isomer of mescaline, N-methyl-3,4,5-trimethoxybenzylamine, was also prepared. γ-(3,4-Dimethoxyphenyl)propylamine is a mescaline analog lacking one of the nuclear methoxyl groups and having an extra methylene group in the aminoalkyl side-chain. The physiological properties of these compounds are being examined to determine the influence of the nature of the aminoalkyl sidechain on the unique hallucinating properties of mescaline; the results of these studies will be reported elsewhere.

All of the compounds reported here were obtained by reduction of the corresponding amides with lithium aluminum hydride. 3,4,5-Trimethoxybenzylamine has been prepared previously[6] by reduction of 3,4,5-trimethoxybenzaldoxime with sodium amalgam. Reduction of the more readily available 3,4,5-trimethoxybenzamide with lithium aluminum hydride was convenient and proceeded in high yield. N-Methyl-3,4,5-trimethoxybenzylamine has been obtained by catalytic hydrogenation of the Schiff base obtained from 3,4,5-trimethoxybenzaldehyde and methylamine.[7] Lithium aluminum hydride reduction of N-methyl-3,4,5-trimethoxybenzamide resulted in an excellent yield of the corresponding amine. γ-(3,4,5-Trimethoxyphenyl)propylamine does not appear to have been synthesized previously; it was formed by lithium aluminum hydride reduction of β-(3,4,5-trimethoxyphenyl)propionamide, which was obtained from 3,4,5-trimethoxybenzaldehyde by the method of Slotta and Heller.[8] Similarly, γ-(3,4-dimethoxyphenyl)propylamine, also a new compound, was obtained from β-(3,4-dimethoxyphenyl)propionamide.

EXPERIMENTAL[9]

3,4,5-Trimethoxybenzylamine. To a solution of 2 g. of lithium aluminum hydride in 50 ml. of absolute ether was added 4.3 g. of 3,4,5-trimethoxybenzamide, m.p. 178–179°, obtained in quantitative yield from redistilled 3,4,5-trimethoxybenzoyl chloride and aqueous ammonia, by the Soxhlet extraction technique. Because of the low solubility of the amide in ether, transfer by extraction required over 100 hours. Using the procedure of Ramirez and Burger,[10] the reaction mixture was treated cautiously with water and then with 10% sulfuric acid to obtain two clear layers. The aqueous layer was neutralized to about *p*H 6 with solid lithium carbonate while stirring and heating on the steam-bath. The precipitated alumina was removed by filtration and the clear filtrate was treated at about 70° with a hot alcoholic solution of 8 g. of picric acid; on cooling, the picrate of 3,4,5-trimethoxybenzylamine crystallized; yield, 7.6 g. (89%); m.p. 195–196° after recrystallization from ethanol.

Anal. Calc'd for $C_{16}H_{18}N_4O_{10}$: C, 45.1; H, 4.2. Found: C, 45.2; H, 4.1.

The *hydrochloride* of 3,4,5-trimethoxybenzylamine was obtained by treatment of a solution of 7.5 g. of the picrate in 125 ml. of boiling water with 20 ml. of hydrochloric acid, removal of picric acid by filtration, and extraction with nitrobenzene, and evaporation of the resulting aqueous solution under reduced pressure; yield, 3.6 g. (91%); m.p. 205–206° (dec.), after recrystallization from methanol-ethyl acetate. The only salt of this amine recorded in the literature[6] is the *chloroplatinate*, m.p. 197°.

Anal. Calc'd for $C_{10}H_{16}ClNO_3$: Cl, 15.2; N, 6.0. Found: Cl, 15.0; N, 5.9.

N-Methyl-3,4,5-trimethoxybenzylamine. A hot solution of 8.1 g. of N-methyl-3,4,5-trimethoxybenzamide,[11] m.p. 136–137°, in 150 ml. of boiling reagent benzene was added to a stirred and refluxing solution of 7 g. of lithium aluminum

(1) This research was supported by Battelle Memorial Institute funds and in part by Public Health Service Grant No. M-600(R).

(2) Battelle Memorial Institute.

(3) Fels Research Institute.

(4) Clark, Fox, Benington, and Morin, *Federation Proc.*, **13**, 27 (1954).

(5) Benington, Morin, and Clark, *J. Org. Chem.*, **19**, 11 (1954); **20**, 102 (1955); **20**, 1292 (1955).

(6) Heffter and Capellmann, *Ber.*, **38**, 3634 (1905).

(7) Sonn, Müller, Bülow, and Meyer, *Ber.*, **58**, 1103 (1925).

(8) Slotta and Heller, *Ber.*, **63**, 3029 (1930).

(9) Melting points are uncorrected.

(10) Ramirez and Burger, *J. Am. Chem. Soc.*, **72**, 2781 (1950).

(11) Sonn and Meyer, *Ber.*, **58**, 1096 (1925).