sodium sulfate, dried over sodium sulfate, and the solvent distilled. The residue was chromatographed on silica gel. Elution with ethyl acetate and subsequent crystallization from aqueous methanol yielded the lactam V as plates, 7.14 g. (50%), m.p. 238–239°; $[\alpha]^{27}D$ +14° (*c* 1, methanol); λ_{max}^{MeOH} 220 mμ, ε 16,500.

Anal. Calcd. for $C_{22}H_{33}NO_3$: C, 73.50; H, 9.25; N, 3.90. Found: C, 73.17; H, 9.04; N, 4.02.

3-Aza-17β-hydroxy-A-homo-4a-androsten-4-one (VI).—Compound V (1.08 g., 0.003 mole) in 50 ml. of methanol was treated with 3.0 ml. of 4 *N* lithium hydroxide and the solution allowed to stand 4 hr. at room temperature. Neutralization with acetic acid, dilution with 50 ml. of water, and concentration under vacuum to approximately 50 ml. gave the desired lactam VI as needles, 0.91 g. (100%), m.p. 278–281°. Crystallization from ethanol raised the m.p. to 288–291°; $[\alpha]^{24}D$ +23° (*c* 0.5, chloroform); λ_{max}^{MeOH} 221 mμ, ε 17,700.

Anal. Calcd. for $C_{19}H_{29}NO_2$: C, 75.20; H, 9.63; N, 4.62. Found: C, 74.95; H, 9.65; N, 4.73.

17β-Acetoxy-3-aza-17-methyl-A-homo-4a-androsten-4-one (VII).—Oxime IV (3.59 g., 0.01 mole) in 80 ml. of purified dioxane was stirred with 1.44 ml. (0.02 mole) of thionyl chloride for 1 hr. at room temperature. The work-up was essentially as described for compound V. Chromatography of the crude product on silica gel and elution with 50% ethyl acetate in benzene yielded lactam VII, 2.13 g. (59%), m.p. 250–252°. Crystallization from 50% ethanol gave needles, m.p. 253–254°; $[\alpha]^{25}D$ +2° (*c* 1, methanol); λ_{max}^{MeOH} 220 mμ, ε 17,200.

Anal. Calcd. for $C_{22}H_{33}NO_3$: C, 73.50; H, 9.25; N, 3.90. Found: C, 73.66; H, 9.26; N, 3.93.

3-Aza-17β-hydroxy-17-methyl-A-homo-4a-androsten-4-one (VIII).—Acetate VII (3.59 g., 0.01 mole) in 225 ml. of methanol containing 22.4 g. (0.40 mole) of potassium hydroxide was allowed to stand 48 hr. at room temperature. The solution was neutralized with acetic acid, diluted with 400 ml. of water, and concentrated under vacuum to approximately 400 ml. to give the hydroxylactam VIII, 3.08 g. (97%), m.p. 287–290°. Crystallization from 50% methanol yielded needles, m.p. 291–293°; $[\alpha]^{25}D$ −3° (*c* 1, methanol); λ_{max}^{MeOH} 221 mμ, ε 17,100.

Anal. Calcd. for $C_{20}H_{31}NO_2$: C, 75.67; H, 9.84; N, 4.41. Found: C, 75.76; H, 9.88; N, 4.52.

The Epoxidation of Certain α,β-Unsaturated Ketones with Sodium Hypochlorite

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The epoxidation of α,β-unsaturated carbonyl compounds[1] and of 1,4-naphthoquinones[2] may be effected by means of hydrogen peroxide in alkaline medium. In most such cases the reactions are run under homogeneous conditions, whereby an organic solvent such as methanol, ethanol, or dioxane is employed if the unsaturated compound is not soluble in water. The anion of *t*-butyl hydroperoxide has also been found to convert α,β-unsaturated ketones to the corresponding epoxides.[3] The hypochlorite ion has also been used as an epoxidizing agent, wherein it presumably behaves analogously to the hydroperoxide and alkylhydroperoxide ions. Thus, 1,4-naphthoquinone has been converted to 2,3-epoxy-2,3-dihydro-1,4-naphthoquinone by reaction with aqueous calcium hypochlorite under heterogeneous conditions.[4] The epoxides of some α,β-unsaturated aldehydes were isolated, in low yield, from the products of the reactions of the carbonyl compounds with sodium hypochlorite.[5] *trans*-Dibenzoylethylene oxide has been prepared by the hypochlorite oxidation of the unsaturated diketone in dioxane,[6] although no report of the yield was included.

While alkaline hydrogen peroxide is an excellent reagent for the epoxidation of most α,β-unsaturated carbonyl compounds, there are certain advantages to be realized in the use of sodium hypochlorite or calcium hypochlorite solutions for the same purpose. It was ascertained in this work that an ordinary commercial hypochlorite bleach solution is quite satisfactory and, consequently, provides a much less expensive and less hazardous reagent than concentrated hydrogen peroxide. In the course of an investigation, now in progress, dealing with the reactions of unsaturated carbonyl compounds with hypochlorites and related substances, it was found that the epoxidation is particularly effective when conducted in pyridine solution. The basicity of the solvent precludes the necessity of using another base, such as sodium hydroxide, in conjunction with a water-miscible organic solvent, such as dioxane.[6] Both benzalacetophenone and *trans*-dibenzoylethylene have been epoxidized with the sodium hypochlorite–pyridine reagent. The reactions are rapid and the yields almost quantitative.

The heterogeneous reaction of 1,4-naphthoquinone with aqueous calcium hypochlorite[4] results in a high yield of the corresponding epoxide. However, the reaction requires about twenty-four hours at room temperature for completion. In an effort to reduce the reaction time epoxidation under homogeneous conditions was indicated. The reaction of 1,4-naphthoquinone with aqueous sodium hypochlorite in dioxane led to the formation of the epoxide in 71% yield, after a reaction time of only a few minutes. When pyridine was used in place of dioxane the oxidation apparently proceeded beyond the epoxide stage, since no epoxide could be isolated. Instead, a brown solid, of as yet undetermined structure, was produced. In dioxane, to which dilute sodium hydroxide had been added, the reaction of 1,4-naphthoquinone with aqueous sodium hypochlorite resulted in the formation of about a 50% yield of the epoxide and other colored products. 2-Methyl-1,4-naphthoquinone behaves similarly to 1,4-naphthoquinone. In dioxane, the epoxide is produced in good yield, whereas in the more basic solvents (pyridine, or dioxane plus sodium hydroxide) red-brown solid products are formed.

It is of interest to note that in at least three instances claims to have epoxidized 1,4-naphthoquinone or 2-methyl-1,4-naphthoquinone with hypochlorous acid, according to Zincke's procedure, have been made.[7] As was pointed out previously, the reagent actually employed by Zincke was calcium hypochlorite. In order to verify these assertions, the reactions of 1,4-naphthoquinone and of 2-methyl-1,4-naphthoquinone with hypochlorous acid were investigated. In the case

(1) E. Weitz and A. Scheffer, *Ber.* **54**, 2327 (1921).

(2) (a) E. Weitz, H. Schobbert, and H. Seibert, *ibid.*, **68B**, 1163 (1935); (b) L. F. Fieser, W. P. Campbell, E. M. Fry, and M. D. Gates, *J. Am. Chem. Soc.*, **61**, 3216 (1939).

(3) N. C. Yang and R. A. Finnegan, *ibid.*, **80**, 5845 (1958).

(4) (a) Th. Zincke, *Chem. Ber.*, **25**, 3599 (1892); (b) J. Madinaveitia, *Rev. acad. cienc. Madrid*, **31**, 617 (1934).

(5) C. Schaer, *Helv. Chim. Acta*, **41**, 560 (1958); C. Schaer, *ibid.*, **41**, 614 (1958).

(6) R. C. Fuson and R. Johnson, *J. Am. Chem. Soc.*, **68**, 1668 (1946).

(7) (a) A. Madinaveitia and J. Saenz de Buruaga, *Anales soc. espan. fis. quim.*, **27**, 647 (1929); (b) J. Madinaveitia, *ibid.*, **31**, 750 (1933); and (c) L. F. Fieser, *J. Am. Chem. Soc.*, **70**, 3170 (1948).

of 1,4-naphthoquinone some epoxide was, indeed, produced, but in very low yield and only after reaction times of the order of several days at room temperature. Most of the starting material was recovered unchanged. No detectable amount of epoxide was formed in the reaction of the 2-methyl-1,4-naphthoquinone with hypochlorous acid. It appears that the formation of epoxide from naphthoquinone in contact with aqueous hypochlorous acid was due to the reaction with the hypochlorite ion, which is present in very low concentration.

Experimental[8]

Epoxidation of Benzalacetophenone.—To a solution of 1.0 g. (0.048 mole) of benzalacetophenone in 7.5 ml. of pyridine was added 11 ml. of fresh 5.25% sodium hypochlorite solution (Clorox). The yellow color of the solution faded almost immediately and heat was evolved.[9] When the mixture became colorless, or nearly so, 25 ml. of water was added, causing the precipitation of the white crystals of the epoxide. The product was filtered, washed thoroughly with water and then recrystallized from ethanol. There was obtained 1.0 g. (94%) of the epoxide, m.p. 89–90°. The identity of the compound was verified by a mixed melting point determination with an authentic sample of 1,3-diphenyl-2,3-epoxy-1-propanone, prepared by the method of Weitz and Scheffer.[1] The infrared spectra of the prepared compound and the authentic sample were identical.

trans-Dibenzoylethylene oxide was prepared in the manner described above from *trans*-dibenzoylethylene. A 93% yield of the epoxide, m.p. 131.5–132.0°, was obtained. The identity was verified by a mixed melting point determination and comparison of infrared spectra with an authentic sample.

Epoxidation of 1,4-Naphthoquinone.—Ten milliliters of 5.25% sodium hypochlorite was added to a solution of 1.0 g. of 1,4-naphthoquinone in 20 ml. of dioxane. Heat was evolved and the mixture was cooled by an external water bath. After 2 min., the mixture was pale yellow and remained the same color for an additional minute. Thirty-five milliliters of water was added and the light yellow precipitate was recovered by filtration. After washing thoroughly with water, the crude product was recrystallized from ethanol. A yield of 0.8 g. (71.5%) was realized. The melting point of the product and that of a mixture of the product with 2,3-epoxy-2,3-dihydro-1,4-naphthoquinone was 134–136°.

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(8) All melting points are uncorrected.

(9) It would be advisable to provide external cooling if the reaction is run on a larger scale.

The Stereochemical Configuration of 5-Hydroxylysine and Synthesis of (+)-1,5-Diamino-2-hydroxypentane (Hydroxycadaverine)[1]

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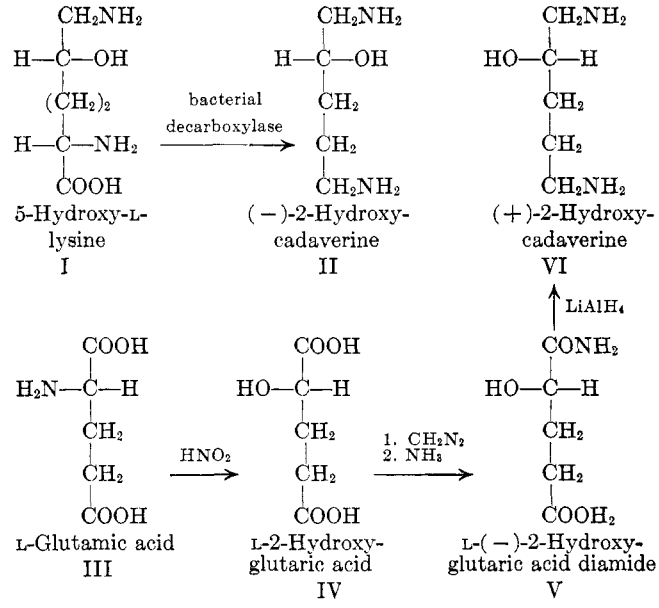
5-Hydroxylysine remains as the last of the protein-bound amino acids for which the stereochemical configuration has not been definitely established by chemical means.



Witkop has applied Hudson's lactone rule to *N*-acylated derivatives of hydroxyamino acids. From the results obtained with natural 5-hydroxylysine[2] he concluded that this amino acid should have the *erythro* configuration.

We have recently studied the decarboxylation of 5-hydroxylysine by bacterial L-lysine decarboxylase.[3] The natural isomer I gave the levorotatory dihydrochloride of 1,5-diamino-2-hydroxypentane [(−)-2-hydroxycadaverine] II, ($[\alpha]_{589}^{25}$ −14.8°]) from which a levorotatory dibenzoate was prepared.

This communication describes the synthesis of the dextro isomer of 2-hydroxycadaverine VI by a route which establishes its absolute configuration and consequently that of the second asymmetric center in 5-hydroxy-L-lysine. The steric correlation is shown in the Fischer projection formulas of the compounds involved. Deamination of L-glutamic acid III is known to proceed with retention of configuration[4] to yield L-2-hydroxyglutaric acid IV. This hydroxy acid was converted to the levorotatory diamine V which on reduction with lithium aluminum hydride in boiling diglyme[5] gave the dextrorotatory diamine dihydrochloride VI ($[\alpha]_{589}^{28}$ +11.1°).

On benzoylation in sodium hydroxide a dextrorotatory dibenzoate ($[\alpha]_{589}^{21}$ +23.6°) was obtained which was identical in melting point and infrared spectrum with the levo-compound, ($[\alpha]_{589}^{25}$ −21.6°), obtained after benzoylation of the amine II formed in decarboxylation of natural 5-hydroxy-L-lysine. These results confirm the *erythro* configuration deduced by Witkop[2] from rotational measurements.

Experimental

L-2-Hydroxyglutaric Acid.—L-Glutamic acid (Merck Co.) was deaminated with nitrous acid[6] and the hydroxyglutaric acid isolated as a crude barium salt.

(1) Supported by a grant from Riksföreningen mot Reumatism.

(2) B. Witkop, *Experientia*, **XII**, 372 (1956).

(3) S. Lindstedt and G. Lindstedt, *Arkiv Kemi*, **19**, 447 (1962).

(4) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, New York, N. Y., 1953.

(5) Diglyme = dimethyl ether of diethylene glycol.

(6) E. Fischer and A Moreschi, *Ber. Deut. Chem. Ges.*, **45**, 2447 (1912).