acetate gave colorless plates which sintered at 199° and melted with decomposition at 213° when placed in the bath at 188° and heated at the rate of 2°/min. The ultraviolet spectrum exhibited λ_{max} 279 mμ, ε 20,800. The infrared spectrum was nearly identical with that of X in the β-series. These substances formed carbonyl derivatives.

Anal. Calcd. for $C_{21}H_{25}O_5N$: C, 67.91; H, 6.79; N, 3.77. Found: C, 67.82; H, 6.86; N, 3.44.

One preparation of this compound gave material having m.p. 254–255° and giving a satisfactory analysis. It was shown to be dimorphic with the other form by cross-seeding experiments and mixed melting points.

Sodium Borohydride Reduction of the Ring D Ketone of the β-Series (X).—Reduction of a suspension of 0.50 g. of X (β-series) in isopropyl alcohol using an excess of sodium borohydride during a reaction time of 3 hr. (room temperature) gave a mixture of the isomeric ring D carbinols. The oil, resulting from a normal isolation procedure, was triturated with a small volume of ethyl acetate. Solid thus formed was collected by suction filtration, 0.17 g. (34%), m.p. 205–207°. The addition of cyclohexane to the crystallization liquor induced the separation of a second isomer, 0.25 g. (50%), m.p. 130–132°.

The high-melting isomer was further purified by recrystallization from ethyl acetate–cyclohexane to pure XII (isomer a), m.p. 214–215°. The infrared spectrum revealed no bands assignable to ketonic carbonyl.

Anal. Calcd. for $C_{21}H_{27}O_5N$: C, 67.39; H, 7.29. Found: C, 67.55; H, 7.15.

The acetate, formed in acetic anhydride–pyridine and purified by recrystallization from ethyl acetate–petroleum ether (60–68°), melted at 178–179°.

Anal. Calcd. for $C_{23}H_{29}O_6N$: C, 66.48; H, 7.04. Found: C, 66.39; H, 7.08.

The low-melting carbinol (XII, isomer b) was purified by further crystallization from aqueous ethanol to give colorless needles, m.p. 134.0–134.5°.

Anal. Calcd. for $C_{21}H_{27}O_5N$: C, 67.39; H, 7.29. Found: C, 67.12; H, 7.26.

The acetate, prepared and purified as was isomer a, had m.p. 158–160°.

Anal. Calcd. for $C_{23}H_{29}O_6N$: C, 66.48; H, 7.04. Found: C, 66.40; H, 6.83.

Preparation and Solvolysis of the Methanesulfonate of XIIb.—The methanesulfonate of XIIb was prepared by treating a cold solution of 0.41 g. in 2 ml. of pyridine with a cold solution of 0.20 g. of methanesulfonyl chloride in 1 ml. of pyridine. The mixture was stored at 0° for 15 min. and then allowed to warm to room temperature over 2 hr. Isolation of the product as described for other cases gave only an amorphous material which could not be crystallized and so was directly submitted to solvolysis. A solution of this product in 5 ml. of acetic acid and 10 ml. of water containing 0.5 g. of sodium acetate was heated at 100° for 3.5 hr. The product was isolated as in the other solvolysis reactions as a gum which, upon trituration with ethyl acetate, afforded 0.020 g. of the other isomer of the ring D carbinol XIIa, m.p. and mixed m.p. 213–214°.

Two other substances were isolated in very small amounts from this reaction mixture which have not yet been identified. One of these (0.040 g.) had m.p. 147.5–149.0° and showed λ_{max} 276 mμ, ε 25,400. The other (trace) melted at 97–98° and its spectrum exhibited λ_{max} 275 mμ, ε 23,000. Thus, no product could be isolated, the spectrum of which would suggest that rearrangement had occurred.

2,3,4-Trimethoxybenzosuber-5-ene (VI).—2,3,4-Trimethoxybenzosuber-5-one (V)[21] (2.20 g.) dissolved in 75 ml. of anhydrous ether was added with stirring during 30 min. to a solution of 1.0 g. of lithium aluminum hydride in 75 ml. of ether. Following the destruction of excess hydride with ethyl acetate, the mixture was processed in the usual manner to give the carbinol as a viscous liquid. It was not purified but was dehydrated directly by distilling from 1.0 g. of fused, powdered potassium hydrogen sulfate. Dehydration occurred at about 100° as evidenced by a vigorous evolution of gas (0.25 mm.), and the residue was then distilled at that pressure to give the crude olefin as 1.61 g. of liquid, b.p. 112–118°. A solution of this in petroleum ether (60–68°) deposited solid upon being cooled to −60°. Recrystallization in this manner (−60°) gave 1.01 g. (49%) of VI as colorless solid, m.p. 37–38°. The sample for analysis was prepared by a final distillation, b.p. 112–113° (0.25 mm.), and had m.p. 38.0–38.5°. The ultraviolet spectrum exhibited λ_{max} 264 mμ, ε 15,300.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.58; H, 7.88.

Acknowledgment.—The authors are indebted to Research Corporation for the financial support of this work. We also wish to thank Mr. Heron E. Peña for his assistance in obtaining infrared data, and members of the Biochemical Institute, the University of Texas, for several of the microanalyses. We are grateful to Dr. W. F. Hamner, Monsanto Chemical Co., for his assistance in the interpretation of some of the infrared data.

(21) P. D. Gardner, W. J. Horton, G. Thompson and R. R. Twelves, THIS JOURNAL, **74**, 5527 (1952).

AUSTIN, TEXAS

COMMUNICATIONS TO THE EDITOR

THE ACTION OF NUCLEOPHILIC AGENTS ON 3α-CHLOROTROPANE

Sir:

In a previous communication[1] we reported that the reaction between the 3-chlorotropane derived from tropine and potassium cyanide afforded a mixture of 2-allyl-1-methylpyrrolidine-5-nitriles. Subsequently[2] it was shown that this halide was the β-chloride since the toluenesulfonate ester of pseudotropine gave the identical mixture.

The isomeric α-chloride (b.p. 83–85° (5.0 mm.); *Anal.* Calcd. for $C_8H_{14}ClN$: N, 8.77. Found: N, 8.66), derived from pseudotropine and thionyl chloride, when treated with benzylamine furnished the known 3α-benzylaminotropane[3] (identical infrared spectra), which afforded a dihydrochloride (m.p. 272° dec.; *Anal.* Calcd. for $C_{15}H_{24}Cl_2N_2$: N, 9.24. Found: N, 9.16) identical with that prepared from the previous sample. Catalytic debenzylation of the new specimen gave 3α-aminotropane isolated as the phenylthioureide, m.p. 157–158°, undepressed when mixed with the previously described material.[3] Tropine furnished a mesylate ester isolated as the toluenesulfonic acid salt (m.p. 158–158.5°; *Anal.* Calcd. for $C_{16}H_{25}NO_6S_2$: C, 49.10; H, 6.44; S, 16.38. Found: C, 49.28; H, 6.43; S, 16.27) which reacted with

(1) S. Archer, T. R. Lewis and B. Zenitz, THIS JOURNAL, **79**, 3603 (1957).

(2) S. Archer, T. R. Lewis and B. Zenitz, *ibid.*, in press.

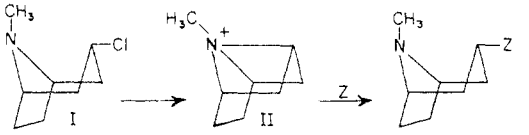
(3) S. Archer, T. R. Lewis and M. J. Unser, *ibid.*, **79**, 4194 (1957).

benzylamine to give 3α-benzylaminotropane isolated as the dihydrochloride, m.p. 272° dec., undepressed when mixed with the above samples. This result confirms the belief that chloride belonged in the alpha series.

The previous assignment[3] of configuration to the isomeric 3-aminotropanes was based on analogy. Direct and independent chemical evidence was obtained by transforming authentic methyl tropane-3β-carboxylate[4] (our oxalate melted 149–151°, undepressed with an authentic sample[4]) to be the corresponding carboxamide (m.p. 151–152°; *Anal.* Calcd. for $C_9H_{16}N_2O$: N, 16.66. Found: N, 16.34). The latter was converted to 3β-aminotropane (phenylthioureide, m.p. 174.5–175°, undepressed when admixed with an authentic sample[3]) by the Hofmann rearrangement, a reaction known to proceed with retention of configuration.[5]

Sodium azide and 3α-chlorotropane gave a liquid azide (b.p. 58–60° (0.2 mm.) *Anal.* Calcd. for $C_8H_{14}N_4$: N_{AP}, 8.47. Found: N_{AP}, 8.53.[6] Hydrochloride, m.p. 167–169°, *Anal.* Calcd. for $C_8H_{13}ClN$: C, 47.42; H, 7.41; N, 27.66; Cl, 17.50. Found: C, 46.55; H, 7.66; N, 27.54; Cl, 17.35) which on catalytic hydrogenation afforded 3α-aminotropane isolated as the phenylthioureide, m.p. 156–158° (no depression when mixed with other samples).

Thus the over-all result of the reaction of 3α-chlorotropane with nucleophilic agents is retention of configuration. Undoubtedly this apparent retention is the result of two inversions, one of which involves participation of the nitrogen. Accordingly it is suggested that the reaction of the chloride I with a nucleophile Z proceeds *via* the ion II



This scheme is supported further by the facts that (1) conversion of tropine or pseudotropine to the corresponding chlorides proceeds with inversion and (2) the benzyl bromide quaternary salt of I (m.p. 213°; *Anal.* Calcd. for $C_{15}H_{21}BrClN$: C, 54.47; H, 6.40; Br, 24.17. Found: C, 54.46; H, 6.12; Br, 24.28) does not appear to react with potassium cyanide under conditions sufficient to permit the chloride I, to produce a crystalline nitrile (m.p. 64–66°; *Anal.* Calcd. for $C_9H_{14}N_2$: N_{AP}, 9.33. Found: N_{AP}, 9.28[6]). In both instances the nitrogen is positively charged, a circumstance which precludes participation with C-3 of the tropane nucleus.

The crystalline nitrile furnished a benzoyl ketone[7] (b.p. 130–134° (0.2 mm.), n^{25} 1.5540. *Anal.* Calcd. for $C_{15}H_{23}NO$: N, 6.11. Found: N, 6.05) on treatment with phenylmagnesium bromide. Methanolysis of the nitrile gave a methyl ester, whose oxalate melted at 149–151° and thus must be the β-ester.[4] Since it is not known whether inversion occurred at the alcoholysis stage[4] definite assignment of configuration to the nitrile awaits the preparation of authentic isomers, a project which is engaging our attention at the present time.

(4) C. Zirkle, *et al.*, "Abstracts XVI International Congress for Pure and Applied Chemistry," Paris, July, 1957, Vol. II, p. 153. We are deeply grateful to Dr. Zirkle for supplying us with directions for preparing the isomeric methyl tropane-3-carboxylates, for giving us samples of derivatives of each of the isomers and for informing us that the predominant hydrolysis product of methyl tropane 3α-carboxylate in either water or hydrochloric acid is tropane 3β-carboxylic acid; all by private communication.

(5) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 501.

(6) Perchloric acid titration for basic nitrogen.

(7) This compound is claimed but not described in a patent recently issued to Zirkle, U. S. Patent 2,800,480 (July 23, 1957). Treatment of the benzoyl ketone with phenyllithium gave the corresponding carbinol, m.p. 184–185°, which was reported by Zirkle (U. S. Patent 2,800,478, July 23, 1957) to melt at 185–186°.

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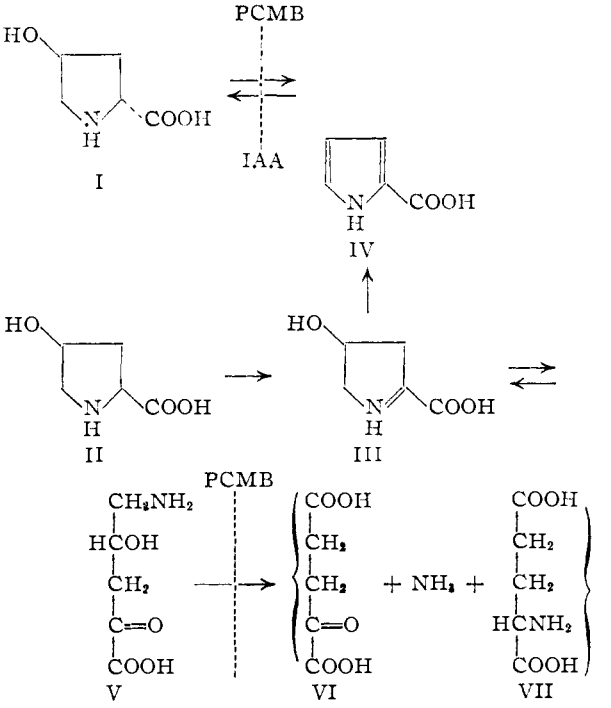
ENZYMATIC CONVERSION OF D-ALLOHYDROXYPROLINE TO L-GLUTAMATE

Sir:

As reported earlier,[1,2] extracts of hydroxyproline-adapted soil bacteria catalyze the conversion of hydroxyproline to glutamic acid. An inducible epimerase,[2] catalyzing rapid interconversion of the two hydroxyproline epimers, permits equally efficient formation of L-glutamate (VII) from either L-hydroxyproline (I) or D-allohydroxyproline (II). The simplest reaction sequence would indicate conversion of L-hydroxyproline to L-glutamate with retention of configuration at the α-carbon. Recent evidence, however, indicates D-allohydroxyproline as the more direct glutamate precursor, according to the tentative reaction sequence



Supernatants of bacterial sonicates centrifuged at 25,000 × *g* catalyze the over-all reaction: L

(1) E. Adams, *Federation Proc.*, **15**, 209 (1956).

(2) E. Adams, *ibid.*, **16**, 142 (1957).