

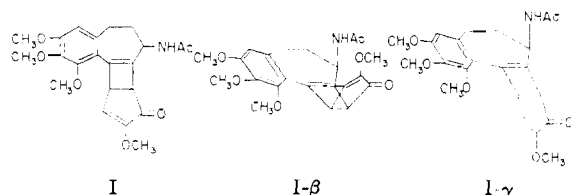
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

The Structures of β - and γ -Lumicolchicine. Ring-D Elaboration ProductsBY PETE D. GARDNER, RICHARD L. BRANDON¹ AND G. RUFUS HAYNES²

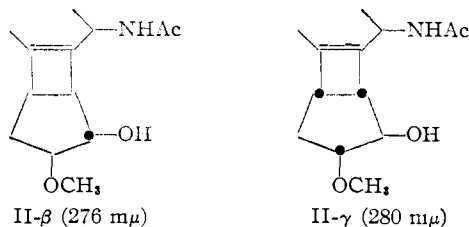
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Evidence is presented which suggests the stereochemical assignment of I- β and I- γ as the structures of β - and γ -lumicolchicine, respectively. This assignment is based on a measure of intramolecular hydrogen bonding in each of the corresponding tetrahydro derivatives by studying relative deviations from the Beer-Lambert law. The conversion of β -lumicolchicine to the γ -isomer in basic medium lends support to the hypothesis of a stereomeric relationship between the two. Spectral evidence is presented for the existence of a cyclobutene ring in these substances, and a reduction experiment, from which an amine was obtained, suggests that the acetamido function was not altered in the isomerization of colchicine to I- β and I- γ . Solvolysis studies with the methanesulfonate derivatives of tetrahydro- β - and γ -lumicolchicine led to a series of ring-D elaboration products (X and XII).

Although originally produced artificially,^{3,4} the lumicolchicines have since been isolated from the plant⁵ and are therefore natural products. A recent paper⁶ which appeared after our structure-study with these substances had begun describes evidence leading to the structural assignment of I to the β - and γ -isomers, the two being related as diastereoisomers. Since both substances are optically active, it is reasonable to assume that the configuration about the point of attachment of the acetamido function is the same in the two isomers and identical with that in colchicine. Only a *cis* fusion of the C-D ring system need be considered and thus, accepting I as the gross structure, I- β and I- γ represent the only reasonable structures for these two substances (disregarding for the moment the specific β - and γ -assignment). Chemical^{4,6,7} and spectral evidence are consistent with formulation I.

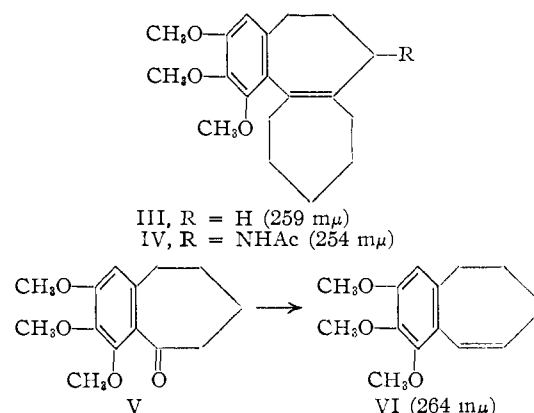


A four-membered ring has been shown to exert an auxochromic effect in ultraviolet spectra of its derivatives, a substantial bathochromic shift being observed in all examples studied.⁸ The ultraviolet spectra of II- β (tetrahydro- β -lumicolchicine),



- (1) American Oil Co. Fellow, 1956-1957.
- (2) General Electric Co. Fellow, 1955-1956.
- (3) F. Šantavý, *Biol. Listy*, **31**, 246 (1950).
- (4) R. Grewe and W. Wulf, *Ber.*, **84**, 621 (1951).
- (5) F. Šantavý, *Collection Czechoslov. Chem. Commun.*, **15**, 552 (1950); *C. A.*, **46**, 126 (1952).
- (6) E. J. Forbes, *J. Chem. Soc.*, 3864 (1955).
- (7) F. Šantavý, *Collection Czechoslov. Chem. Commun.*, **16**, 655 (1951); *C. A.*, **48**, 10715 (1954).
- (8) J. J. Wren, *J. Chem. Soc.*, 2208 (1956). The effect is illustrated, for example, by the comparison of ethyl maleate (λ_{\max} 198 m μ) with ethyl cyclobutene-1,2-dicarboxylate (λ_{\max} 232 m μ).

II- γ (tetrahydro- γ -lumicolchicine), III⁹, IV⁹ and VI are shown with the formulas representing these substances. A comparison of those values for II- β or II- γ with that for IV ($\Delta\lambda$ 22 and 26 m μ) reveals a large bathochromic shift which corresponds with the auxochromic effect cited above and is en-



tirely consistent with the Forbes formulation (I) for the lumicolchicines. Although it does not bear on the present problem, it is of interest to note that 2,3,4-trimethoxybenzosuber-5-one (VI), prepared earlier for another purpose, absorbs at longer wave lengths than does III, the converse of which would be predicted on the basis of the Woodward rules.¹⁰ This is further evidence that additional conformational possibilities in larger ring systems make it hazardous to apply such rules at the present time.

The assignment of structure I- β and I- γ to the β - and γ -isomer, respectively, is based on the effect of concentration on the extinction coefficient in the ultraviolet spectra of the tetrahydro derivatives, II. It has been shown that weak intermolecular hydrogen bonding manifests itself as an abnormal increase of extinction coefficient as the concentration is increased (in a non-polar solvent) even though the chromophore responsible for the maximum under observation does not appear to be directly involved in the bonding.¹¹

Data obtained using both chloroform (relatively non-polar) and 95% ethanol (polar) are summarized in Table I.

- (9) H. Rapoport, A. R. Williams, J. E. Campion and D. E. Pack, *This Journal*, **76**, 3693 (1954).
- (10) R. B. Woodward, *ibid.*, **64**, 72 (1942).
- (11) W. F. Forbes and J. F. Templeton, *Chemistry & Industry*, 77 (1957).

TABLE I

Solvent	Concn., g./l. II- β		Solvent	Concn., g./l. II- γ	
CHCl ₃	0.0080	20,900	CHCl ₃	0.0088	18,400
CHCl ₃	.986	22,700	CHCl ₃	.998	19,900
C ₂ H ₅ OH	.0088	20,800	C ₂ H ₅ OH	.0092	21,100
C ₂ H ₅ OH	.992	22,800	C ₂ H ₅ OH	.998	21,600

From these data it can be seen that $\Delta\epsilon$, the increase in going from dilute to more concentrated solutions, is 1,800 (CHCl₃) for the β -isomer and 2,700 (CHCl₃) for the γ -isomer. The much larger increase in the case of the γ -isomer indicates that it is significantly more intermolecularly hydrogen bonded than is the β -isomer. $\Delta\epsilon$ values for ethanolic solutions are 2,000 for the β -isomer and 1,700 for the γ -isomer, which is as expected since the more polar solvent should preclude significant intermolecular association in any system.

Model constructions of II- β and II- γ reveal that in only one of them (II- β , derived from I- β) is there a possibility for appreciable intramolecular hydrogen bonding. This "cis" arrangement permits ready interaction of the hydroxyl group of ring D with the acetamido group of ring B, whereas in the "trans" structure (II- γ) this is not possible. These data thus suggest that β -lumicolchicine is represented by I- β and the γ -isomer by I- γ .

The stereochemical assignment of ring D functionality is based upon an examination of molecular models and the application of the von Auwers-Skita rule.¹² Structure I- β clearly offers an "open" side to the catalyst surface more readily than it does the other side for reduction of the double bond. Subsequent reduction of the carbonyl group in neutral medium (ethanol), according to the rule, should normally give a *trans* relationship between the methoxyl and hydroxyl functions. This leads to the stereochemical assignment of II- β to the product obtained from β -lumicolchicine and to II- γ as that from the γ -isomer. In a case such as this where it is known that different isomers are obtained in both series when acetic acid is used as a reduction solvent⁴ (predicted by the rule to be *cis* with regard to methoxy-hydroxy), there seems to be little reason to suspect abnormal (non-compliance with the rule) reduction.

When β -lumicolchicine was allowed to reflux in methanolic potassium hydroxide, in an attempt to hydrolyze the amide linkage,¹³ there occurred instead an efficient conversion to the γ -isomer. On the basis of the above assignment of structure, this indicates a flipping of the C-D ring fusion and lends further support to the stereomeric relationship between the two.

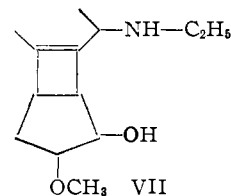
The tetrahydro derivatives (II- β and II- γ) exhibited unexpected basicity, both readily forming salts with hydrogen chloride. Although many "onium" salts are reported for highly oxygenated substances,¹⁴ the fact that this behavior was so

(12) D. von Auwers, *Ann.*, **420**, 91 (1920); A. Skita, *Ber.*, **53**, 1792 (1920).

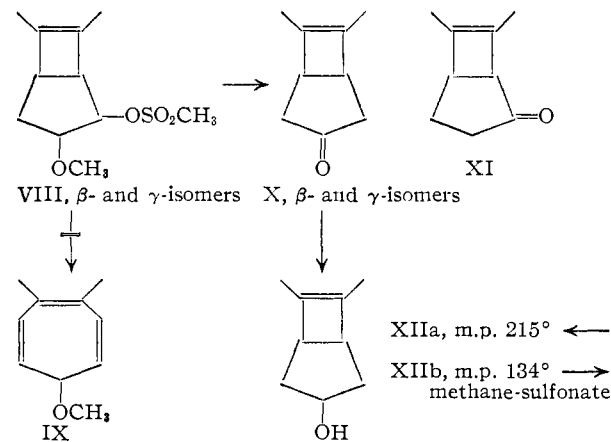
(13) Experiments using basic media followed many unsuccessful attempts at acid hydrolysis. The lability of these substances to acid is adequately summarized by Forbes.

(14) W. Lange, R. G. Polzenlogen and D. G. Koip, *This Journal*, **71**, 1733 (1949); see also W. J. Horton and J. T. Spence, *ibid.*, **77**, 2894 (1955).

pronounced with these two substances, coupled with the finding that they show a zero value in an N-acetyl determination,¹⁵ prompted the search for evidence of an intact acetamido function. Consequently, II- β was submitted to reduction with lithium aluminum hydride from which there was obtained the expected amine (VII). The replacement of an oxygen atom by two hydrogen atoms is characteristic of the behavior of amides under these conditions and gives further evidence for the presence of the acetamido group.



We became interested in the lumicolchicines primarily because of the possibility of reconverting them to tropolonoid substances. Such a transformation would then afford colchicine-like compounds, the structures of which would depend upon the extent of alteration of the lumicolchicines before isomerization. It was anticipated that, discounting the possibility of neighboring group participation, the methanesulfonate VIII (β - or γ -series) should be capable of solvolyzing with accompanying Wagner-type rearrangement to give the cycloheptatriene derivative IX.¹⁶ Accordingly, the required methanesulfonates were prepared and solvolized in an aqueous acetic acid solution containing sodium acetate. The products were not those expected but, instead, two isomeric ketones retaining the four-ring system, X (β - and γ -series). That X was the correct formulation, and not XI, was shown by reduction of the carbonyl group in the β -isomer to the two possible carbinols (XII), conversion of one of these to the methanesulfonate derivative and solvolysis of that derivative. The only substance identified from the final solvolysis of the derivative of the high-melting isomer (isomer b) of XII was the low-melting isomer of XII (isomer a). Two other, unidentified, substances



(15) It was subsequently found that colchicine itself gives a zero value in this determination as usually made.

(16) This was suggested by the preparation of cycloheptatriene by Dryden and Burgert; H. L. Dryden and B. E. Burgert, *This Journal*, **77**, 5633 (1955).

were isolated from the reaction mixture, but spectral data suggested that neither had suffered ring isomerization. Rearrangement to a cycloheptatriene derivative would be expected to occur readily upon application of this sequence of reactions to the methanesulfonate derived from XI. Formulation X is therefore proposed to represent the ketone obtained from each series. It is apparent that the formation of X did indeed involve neighboring group participation sufficient to preclude ring isomerization.¹⁷

Experimental¹⁸

Tetrahydro- β -lumicolchicine Hydrate (II- β).—Five grams of β -lumicolchicine (I- β)¹⁹ was partially dissolved in 40 ml. of ethanol, and the mixture was shaken with 0.1 g. of platinum oxide under one atm. of hydrogen. Most experiments were conducted at room temperature but in one run the temperature was maintained at *ca.* 60° in order to keep the starting material in solution. The results were the same under either condition; an initial mole equivalent of hydrogen was absorbed rapidly (olefinic linkage) followed by the slower uptake of a second mole equivalent. The product (3.8 g., 76%) was a hydrate of the product previously reported, m.p. 88–90° after crystallization from water. A sample further crystallized from ethyl acetate–petroleum ether (60–68°) and dried at room temperature (0.1 mm.) had m.p. 94–96°.

Anal. Calcd. for $C_{22}H_{31}O_7N$: C, 62.65; H, 7.41; N, 3.34; C-methyl, 1.00; N-acetyl, 1.00. Found: C, 62.95; H, 7.48; N, 3.10; C-methyl, 0.96; N-acetyl, 0.00.

The anhydrous crystalline form of this substance (m.p. 118°)⁴ occasionally was obtained, but it invariably became hydrated upon recrystallization from moist solvents.

Treatment of a solution of the hydrate in anhydrous ether with hydrogen chloride caused immediate precipitation of the hydrochloride salt, m.p. 138–139° dec. after recrystallization from methanol–ether or ethanol.

Anal. Calcd. for $C_{22}H_{30}O_6NCl$: C, 60.06; H, 6.87; N, 3.18; Cl, 8.06. Found: C, 59.85; H, 6.81; N, 3.28; Cl, 8.14.

Equilibration of 1.00 g. of II- β between 50 ml. of ether and 50 ml. of 6 *N* hydrochloric acid gave an aqueous solution containing 0.91 g. of solute, obtained by basification of this phase. II- β did not form carbonyl derivatives. The infrared spectrum possessed bands at 3.0 μ (N–H, O–H) and at 6.0–6.1 μ (amide carbonyl). There was also present a strong band at 4.2 μ which cannot be assigned.

Tetrahydro- γ -lumicolchicine also formed a hydrochloride salt readily, but it was very hygroscopic and was not examined further. This and the salt described above gave an immediate precipitate with silver nitrate solution. Ultraviolet spectral data of II- β and II- γ at two concentrations in chloroform and in ethanol are shown in Table I. Chloroform was the least polar solvent in which these substances could be dissolved to give the required concentrations. The cell-spacer combinations used were calibrated with solutions of potassium chromate.²⁰

Isomerization of β -Lumicolchicine to the γ -Isomer.—A solution of β -lumicolchicine (2.0 g.) in 30 ml. of 2 *N* methanolic potassium hydroxide was heated under reflux for 12 hr. Dilution with water, followed by extraction with ether and isolation in the usual manner, gave 1.2 g. (60%) of γ -

(17) Neighboring group participation by the methoxy group has been demonstrated in other systems; S. Winstein, C. R. Lindgren and L. L. Ingraham, *THIS JOURNAL*, **75**, 155 (1953); S. Winstein and L. L. Ingraham, *ibid.*, **74**, 1160 (1952).

(18) Melting points are corrected. Infrared spectra were determined using the potassium bromide wafer method. Ultraviolet spectra were determined in 95% ethanol except where noted. All of the spectra of the lumicolchicine derivatives possessed, in addition to those maxima given in the Experimental section, a strong band in the 220 $m\mu$ region. This was not used for characterization purposes.

(19) Prepared as described by Grewe and Wulf.⁴ It should be mentioned that under the conditions employed (5-l. flasks, Texas sunlight) none of the α -isomer was obtained.

(20) M. G. Mellon, "Analytical Absorption Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 261.

lumicolchicine, after crystallization from ethanol, m.p. and mixed m.p. 264–265°.

Anal. Calcd. for $C_{22}H_{28}O_6N$: C, 66.13; H, 6.13; N, 3.52. Found: C, 66.20; H, 6.19; N, 3.32.

The oxime, prepared in ethanolic pyridine and crystallized from methanol, had m.p. 283–285° dec. (lit.⁶ 284–286°), undepressed on admixture with a sample of the authentic oxime.

Lithium Aluminum Hydride Reduction of Tetrahydro- β -lumicolchicine.—A solution of 1.00 g. of tetrahydro- β -lumicolchicine in 100 ml. of anhydrous ether was added dropwise during 30 min. to a stirred solution of 0.475 g. of lithium aluminum hydride in 50 ml. of ether. After being stirred at room temperature for 17 hr., the mixture was then treated cautiously with excess ethyl acetate and finally with water and dilute hydrochloric acid. Processing in the usual manner afforded the amine VII as a very viscous, colorless oil. Treatment of an ethereal solution of this with hydrogen chloride followed by recrystallization of the resulting solid from ethanol–ether gave 0.8 g. of colorless needles of the amine hydrochloride, m.p. 204–206° dec. This material was water soluble and gave a precipitate with aqueous silver nitrate solution.

Anal. Calcd. for $C_{22}H_{32}O_6NCl$: C, 62.03; H, 7.55; N, 3.29. Found: C, 62.33; H, 7.61; N, 3.30.

Methanesulfonate Derivative of Tetrahydro- β -lumicolchicine (VIII).—A solution of 1.30 g. of tetrahydro- β -lumicolchicine hydrate in 2 ml. of pyridine was treated with a cold solution of 0.92 g. of methanesulfonyl chloride in 6 ml. of pyridine. The mixture was allowed to warm to room temperature during 2 hr. and was then poured into dilute, cold hydrochloric acid solution. Extraction with chloroform followed by removal of solvent gave the crude amorphous derivative which crystallized upon trituration with ether. Recrystallization from ether gave 0.93 g. (61%) of the derivative in two crops, m.p. 125–126°, 123–125°. The sample for analysis had m.p. 127.5–128.5°. Upon standing for two months at 0° the m.p. was 171.0–172.5°, indicating a second crystal form of this substance. In subsequent preparations the high melting form was invariably obtained directly from the reaction mixture. The ultraviolet absorption spectrum exhibited λ_{max} 277 $m\mu$, ϵ 23,100.

Anal. Calcd. for $C_{22}H_{31}O_8NS$: C, 57.36; H, 6.49; N, 2.89; S, 6.66. Found: C, 57.53; H, 6.53; N, 2.56; S, 6.37.

Methanesulfonate Derivative of Tetrahydro- γ -lumicolchicine (VIII).—The reaction between 2.02 g. of tetrahydro- γ -lumicolchicine and 0.81 g. of methanesulfonyl chloride exactly as described above for the β -isomer gave 2.15 g. (87%) of the crude derivative, m.p. 181–183° dec. Recrystallization from ethanol–water gave colorless plates, m.p. 187° dec. The ultraviolet spectrum exhibited λ_{max} 279 $m\mu$, ϵ 20,900.

Anal. Calcd. for $C_{22}H_{31}O_8NS$: C, 57.36; H, 6.49; N, 2.88; S, 6.66. Found: C, 57.67; H, 6.64; N, 2.50; S, 6.47.

Solvolysis of Tetrahydro- β -lumicolchicine Methanesulfonate (VIII).—A suspension containing 0.29 g. of VIII (β -series), 0.5 g. of sodium acetate, 2 ml. of acetic acid and 6 ml. of water was heated at 90° for 3 hr. Dilution with water and isolation by chloroform extraction afforded a viscous liquid which crystallized upon rubbing with a spatula. Recrystallization from ethyl acetate gave 0.16 g. (75%) of ketone X (β -series), m.p. 183–185° dec. Further purification in the same manner afforded a cotton-like sample having m.p. 214–215° dec. The ultraviolet spectrum exhibited λ_{max} 276 $m\mu$, ϵ 20,000. The infrared spectrum possessed, in addition to bands present in that of the tetrahydro compound, a sharp absorption at 5.75 μ (ketone carbonyl). This substance formed carbonyl derivatives readily but none had crystalline properties favorable for purification by crystallization.

Anal. Calcd. for $C_{21}H_{28}O_5N$: C, 67.91; H, 6.79; N, 3.77. Found: C, 68.30; H, 6.82; N, 3.40.

Solvolysis of Tetrahydro- γ -lumicolchicine Methanesulfonate (VIII).—The solvolysis of 1.00 g. of VIII (γ -series) in a medium consisting of 0.70 g. of sodium acetate, 8 ml. of acetic acid and 4 ml. of water gave, after isolation as described above, 0.55 g. (73%) of ketone X (γ -series), m.p. 201–203° dec. Purification by recrystallization from ethyl

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 m μ , 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 $C_{21}H_{25}O_6N$: 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 $C_{21}H_{27}O_6N$: 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 $C_{21}H_{27}O_6N$: 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. Iso-

lation 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 m μ , ϵ 25,400. The other (trace) melted at 97–98° and its spectrum exhibited λ_{\max} 275 m μ , 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-ene (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 m μ , 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 3 α -CHLOROTROPANE

Sir:

In a previous communication¹ we reported that the reaction between the 3-chlorotropene derived from tropine and potassium cyanide afforded a mixture of 2-allyl-1-methylpyrrolidine-5-nitriles. Subsequently² 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

(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.

chloride, when treated with benzylamine furnished the known 3 α -benzylaminotropene³ (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 debenzoylation of the new specimen gave 3 α -aminotropene 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 $C_{16}H_{26}NO_6S_2$: C, 49.10; H, 6.44; S, 16.38. Found: C, 49.28; H, 6.43; S, 16.27) which reacted with

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