dered anhydrous potassium pyrosulfate and 14.9 g. (0.062 mole) of p-tolylmercapto diethylacetal and then heated in an oil-bath with efficient stirring. At about 140° (oil-bath temperature) the elimination began and alcohol slowly distilled. This temperature was maintained until ethanol ceased to distil. The reaction mixture was cooled, filtered and then distilled on the spinning band column under vacuum to yield four fractions: (1) *trans*-isomer V (1.5 g.), b.p. 130-131° (7 mm.), n^{25}D 1.5405; (2) an intermediate fraction (1.3 g.), b.p. 131-34° (7 mm.), n^{25}D 1.5455; (3) *cis*-isomer I (7.5 g.), b.p. 135° (7 mm.), n^{25}D 1.5500; (4) residue (0.83 g.), mainly unreacted IV.

An infrared spectrum of fraction 1 showed *trans*-ethylenic in-plane and out-of-plane bending vibration bands at 8.47(m) and 11.05(s) μ.

Anal. Calcd. for $C_{11}H_{14}OS$: C, 68.0; H, 7.27. Found: C, 67.69; H, 7.25.

Fraction 2 exhibited two (C=C) stretching vibrations at 6.14 and 6.25 μ. Fraction 3 had the same infrared spectrum as that obtained from the reaction product of p-toluenethiol and ethoxyacetylene.

Attempted Isomerizations of *cis*- and *trans*-1-Ethoxy-2-p-tolylmercapto)-ethene.—*cis*-1-Ethoxy-2-(p-tolylmercapto)-ethene (1.94 g., 0.01 mole) was dissolved in 200 ml. of a solution of 0.01 mole of sodium ethoxide in absolute ethanol. After 48 hours of refluxing, ethanol was evaporated and distilled water was added. This mixture was neutralized with cold dilute hydrochloric acid, extracted with ether and dried over sodium sulfate. This material distilled at the same temperature as starting material, b.p. 135° (7 mm.), and had the same infrared spectrum. Similar results were obtained with the *trans* isomer, V.

Reaction of *cis*-1-Chloro-2-(p-tolylmercapto)-ethene with Sodium Ethoxide. Preparation of I.—*cis*-1-Chloro-2-(p-tolylmercapto)-ethene (VI) was prepared by treating chloroacetylene with p-toluenethiol; b.p. 89-91° (0.75 mm.) (lit.[7] b.p. 99-102° (2.2 mm.). A soluton of VI (4.33 g., 0.0235 mole) in 30 ml. of absolute ethanol was slowly added to 50 ml. of an ethanolic sodium ethoxide solution [1.08 g. (0.047 g. atom) of sodium] at reflux with good stirring and under a nitrogen atmosphere. After 10 hours 0.66 g. (0.011 mole) of sodium chloride was isolated upon filtering the reaction mixture and washing the salt with hot absolute ethanol. The extract was combined with the filtrate, concentrated, diluted with water, and extracted with ether. The ether layer was neutralized with cold dilute hydrochloric acid, washed with water, dried over sodium sulfate and evaporated. Distillation on the spinning band column gave the same material as that formed from the addition of p-toluenethiol to ethoxyacetylene, b.p. 135° (7 mm.), 43.9% yield.

Elimination Reactions of Bicyclic Quaternary Salts. IV.[1] The Conversion of Scopinone into *m*-Hydroxybenzaldehyde

BY JERROLD MEINWALD AND ORVILLE L. CHAPMAN[2]

The report that scopinium bromide (II) gives rise to *m*-hydroxybenzaldehyde (III) upon treatment with base has led to a study of the corresponding ketone, scopinone (IV); IV, as well as its methobromide VI, was found to suffer a degradative rearrangement, yielding III, with extreme readiness. This observation presents a sharp contrast to the behavior of many closely related tropane derivatives, which are generally more stable to base, and whose quaternary salts undergo normal eliminations unaccompanied by skeletal rearrangement. Some tentative mechanisms for the transformation of IV and VI into III are discussed briefly.

Introduction.—Recent studies have shown that the base-catalyzed elimination reactions of tropinone methiodide (Ia)[3] and of a variety of closely related, substituted quaternary salts (Ib-f)[1,4,5] proceed to give the expected derivatives of cycloheptanone, without rearrangement of the parent carbon skeleton. In view of these results, the report by Polonovski and Polonovski that scopinium bromide (II) is degraded by base to *m*-hydroxybenzaldehyde (III)[6] as shown in equation 1 is of particular interest. The work described in this paper was undertaken with the aim of casting additional light on this anomalous transformation.

$$\text{(1)}$$

$$\text{II} \qquad \text{III}$$
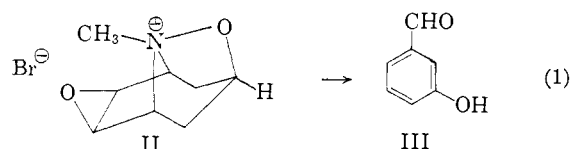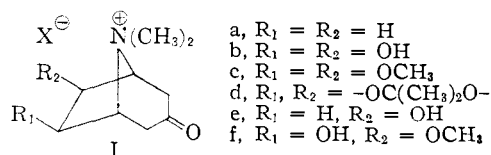
Discussion.—The preparation of scopinium bromide (II) was the first objective of the present study. Although the conversion of scopolamine to II by the action of hydrogen peroxide has been described in a fairly detailed manner,[6] several attempts to reproduce the procedure gave scopolamine-N-oxide hydrobromide as the only characterizable product.[7] A variety of other attempts

$$\begin{array}{ll} \text{a, } R_1 = R_2 = H \\ \text{b, } R_1 = R_2 = OH \\ \text{c, } R_1 = R_2 = OCH_3 \\ \text{d, } R_1, R_2 = -OC(CH_3)_2O- \\ \text{e, } R_1 = H, R_2 = OH \\ \text{f, } R_1 = OH, R_2 = OCH_3 \end{array}$$

(1) For the previous paper in this series see J. Meinwald and O. L. Chapman, THIS JOURNAL, **80**, 633 (1958). A preliminary Communication describing some of the present results has appeared in *Tetrahedron*, **3**, 311 (1958). For an excellent review of the elimination reactions of bicyclic compounds, see A. Heusner, *Angew. Chem.*, **70**, 639 (1958).

(2) Procter and Gamble Fellow, 1956-1957.

(3) J. Meinwald, S. L. Emerman, N. C. Yang and G. Büchi, THIS JOURNAL, **77**, 4401 (1955).

(4) J. Meinwald and O. L. Chapman, *ibid.*, **78**, 4816 (1956).

(5) E. E. van Tamelen, P. Barth and F. Lornitzo, *ibid.*, **78**, 5442 (1956).

(6) M. Polonovski and M. Polonovski, *Compt. rend.*, **180**, 1775 (1925); **185**, 277 (1927); **186**, 147 (1928); *Bull. soc. chim. France*, **43**, 79 (1928); **42**, 1468 (1927); **39**, 1162 (1926). See also R. H. F. Manske and H. C. Holmes, "The Alkaloids," Vol. I, Academic Press, Inc., New York, N. Y., 1950, pp. 302-307.

(7) Professor G. Fodor has kindly informed us that the published procedure for obtaining scopinium bromide was unsuccessful in his Laboratory as well.

to generate the scopinium ion by rational variations of this route were pursued, but without success.

With II unavailable, it seemed desirable to study the degradation of scopinone (IV), on the grounds that the first step in Polonovski's reaction might have been the transformation of II to IV, as shown in equation 2. Although IV was unknown at the time this work was begun, another
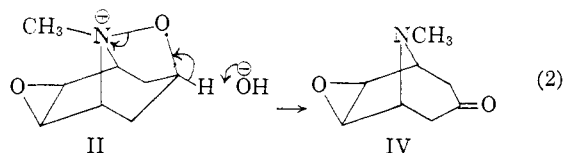
indication that it might be involved in further transformations to III was the report that chromic acid oxidation of pseudo-scopine (the cis-alcohol corresponding to IV) yields m-hydroxybenzaldehyde rather than the expected ketone.[6]

To permit a rapid test of these speculations, scopine methobromide[8] (V) was oxidized with sodium dichromate to give scopinone methobromide (VI), which was degraded without preliminary isolation by treatment with base. Ether extraction of the acidified reaction mixture gave m-hydroxybenzaldehyde, identified by comparison with an authentic sample. This qualitative result, summarized in equation 3, served to confirm the essential authenticity of the rearrangements reported by the Polonovskis.
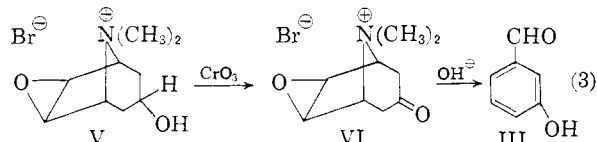
An attempt was next made to find a method to prepare and characterize scopinone (IV) itself. The most attractive route involved the oxidation of the corresponding alcohol, scopine, which had recently become readily available.[9] A technique for the successful oxidation of scopine to scopinone using Sarett's pyridine–chromic oxide complex was developed by Heusner while the above work was in progress.[10] Following Heusner's procedure, it became possible to prepare scopinone in quantities sufficient for the present degradative study.

Scopinone was found to be remarkably unstable. It dissolved in distilled water to give a solution which, after standing for four hours at room temperature, had developed a 16% yield of m-hydroxybenzaldehyde, as indicated by ultraviolet absorption data. Heating scopinone with aqueous sodium bicarbonate gave the same aldehyde in 41% yield. Moreover, the same transformation could be brought about in 94% yield in aqueous hydrobromic acid. It is perhaps significant that the reaction was slowest in the acidic medium, although the best yields were obtained under these conditions.

tions. One possible explanation of this might be that the acid serves to suppress undesirable side-reactions, rather than acting as a catalyst for the aromatizing rearrangement.[11]

There are, then, two striking aspects of the behavior of scopinone. First of all, there is the extreme ease with which the nitrogen bridge is eliminated. Secondly, there is the unprecedented skeletal rearrangement whereby the seven-membered ring contracts to a benzenoid ring. The propensity to lose the nitrogen bridge is enhanced in the methobromide derived from IV, which gave m-hydroxybenzaldehyde in 80% yield when treated with one equivalent of sodium bicarbonate at steam-bath temperatures. In the absence of any external base, a 52% yield of m-hydroxybenzaldehyde was formed. It is possible, in this case, that the transformation was catalyzed by the dimethylamine formed at first by a slow, uncatalyzed elimination.

Given the fact of ready skeletal rearrangement of scopinone or its quaternary salts, it is interesting to consider what paths may be responsible for the transformation. These paths should not be readily applicable to Ia-f, all of which fail to rearrange.

The first nitrogen-free product to be expected from IV or VI would be tropone epoxide (VII), which would result from two β-eliminations, as shown in equation 4. Acid- or base-catalyzed opening of the epoxide ring in VII might then give γ-tropolone (VIII). If VIII suffered a reverse
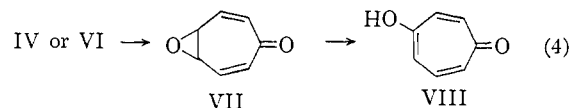
aldol condensation followed by cyclization in an alternate direction (equation 5), a route to III would be provided. When this possibility was subjected to a simple test, however, it was found to
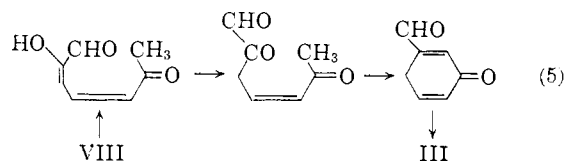
be untenable. Thus γ-tropolone (VIII), prepared by an independent route,[1,4] remained unchanged even after prolonged heating with aqueous base[12]; it therefore could not possibly be the precursor of the m-hydroxybenzaldehyde (III) formed under much milder basic conditions.

A closely related route, involving possible ring opening and closing of the tropone epoxide (VII) itself, cannot be rigorously tested until a synthesis of VII can be achieved. However, it would be

(8) R. B. Moffett and E. R. Garrett, THIS JOURNAL, **77**, 1245 (1955).

(9) J. Meinwald and O. L. Chapman, *ibid.*, **79**, 665 (1957).

(10) A. Heusner and K. Zeile, *Tetrahedron*, **3**, 312 (1958). The authors are most grateful to Dr. A. Heusner, Boehringer Sohn, for making these results available prior to publication, as well as for generous gifts of scopinone methobromide and scopinone hydrobromide.

(11) The facility of the scopinone → m-hydroxybenzaldehyde rearrangement may provide an explanation of the failure of the Robinson–Schöpf biogenetic technique to yield scopinone (J. C. Sheehan and B. M. Bloom, THIS JOURNAL, **74**, 2825 (1952)). It would be interesting to know whether m-hydroxybenzaldehyde is formed under these conditions.
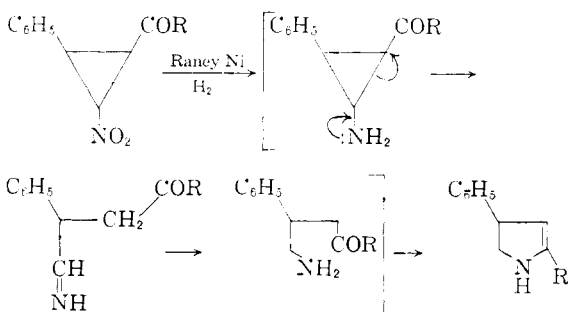
(12) A preliminary indication of the stability of γ-tropolone to base had already been provided by the work of T. Nozoe, T. Mukai, Y. Ikegama and T. Toda, *Chemistry & Industry*, 66 (1955).

surprising if VII were not rapidly converted into γ-tropolone under hydrolytic conditions.[13]

Finally, there are mechanisms which might proceed without the intermediacy of open-chain compounds. One of these is shown in outline in equation 6. It would involve formation of a cyclo-

$$\text{VI} \longrightarrow \longrightarrow \text{III} \qquad (6)$$
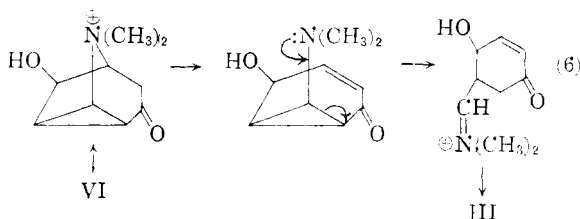
propane ring by intramolecular nucleophilic opening of the epoxide ring, followed by straightforward steps resulting in the further relief of strain (opening of the cyclopropane ring) and ultimate aromatization.[14] This scheme seems to be the most at-

tractive of the possibilities so far considered. The rearrangement of scopinone itself can be rationalized along similar lines.

In the light of the limited evidence available, reaction sequence 6 seems to offer the best rationalization of the unique tendency of the tropane epoxides to undergo rearrangements, since these alone would be in a position to give cyclopropanes readily.

Acknowledgment.—The authors are indebted to the Research Corporation for their continued interest in and support of this work.

Experimental

Oxidation and Degradation of Scopine Methobromide.— A solution of chromic acid (133.5 g.) and concentrated sulfuric acid (130 ml.) in water (200 ml.) was prepared and diluted to 500 ml.[15] This solution (3 ml.) was added dropwise to a stirred solution of scopine methobromide (1 g.) in water (ca. 3 ml.). The solution was then stirred for a short time at room temperature. The aqueous reaction mixture was treated with a suspension of barium hydroxide (35.5 g.) in water (250 ml.) and heated at 95–100° for one hour. Extraction of the basic reaction mixture followed by drying and evaporation gave no residue. Acidification of the reaction mixture (pH 1) followed by extraction with ether, drying over anhydrous magnesium sulfate and evaporation of the

solvent gave a mobile red oil. This oil was taken up in ether, washed three times with 5% aqueous sodium bicarbonate, twice with 0.1 N hydrochloric acid and finally with water. Drying over anhydrous magnesium sulfate and evaporation of the ether in vacuo gave a white, crystalline solid (m.p. 105–107°) which had an infrared absorption spectrum identical to that of authentic m-hydroxybenzaldehyde.

Scopinone.[10]—Scopine was oxidized with Sarett reagent according to the procedure developed by Heusner. The crude product showed two bands in the carbonyl region (5.85 and 5.93 μ). After sublimation (60° (0.1 mm.)), the scopinone showed carbonyl absorption at 5.85 μ and epoxide absorption at 11.70 μ. In methanolic solution, the product gave a nicely crystalline picrate, m.p. 174–176° (reported for scopinone picrate, m.p. 177°).[10]

Rearrangement of Scopinone.—A. Scopinone (25.7 mg.) was dissolved in 50 ml. of distilled water at room temperature. Immediately after preparation, this solution did not absorb in the ultraviolet. After four hours at room temperature, the solution had ultraviolet absorption maxima in distilled water and 0.1 N sodium hydroxide identical to those of authentic m-hydroxybenzaldehyde.[16] Analysis of the solution (based on the intensity of the 253 mμ maximum in distilled water) showed a 16% yield of m-hydroxygenzaldehyde.

B. A solution of scopinone (12.8 mg.) and sodium bicarbonate (0.1 g.) in 25 ml. of distilled water was heated on the steam-bath for one hour. This solution showed the ultraviolet maxima characteristic of m-hydroxybenzaldehyde. Analysis as above indicated a 38% yield of m-hydroxybenzaldehyde. Heating the solution for an additional 5 hours raised the yield to 41%. Sodium hydroxide (0.05 g.) was added, and the solution was heated for an hour. The yield of III did not change.

C. Scopinone hydrobromide (58.5 mg., 0.25 mmole) was dissolved in 50 ml. of distilled water, treated with one ml. of 48% aqueous hydrobromic acid, and heated at 95 ± 5°. One-ml. aliquot portions were withdrawn periodically, diluted with distilled water and analyzed by measuring the intensity of absorption at 253 mμ. The ultraviolet spectrum reported[16] for m-hydroxybenzaldehyde is λλmax 315 mμ (log E 3.42) and 253 mμ (4.00).

Time, hr.	E at 253 mμ	m-Hydroxybenzaldehyde, %
0	0	0
3[a]	1390	14
10.5[b]	6100	61
25[c]	9400	94

[a] Spectrum: 315 mμ (370) and 253 (1390). [b] Spectrum: 315 mμ (1650) and 253 (6100). [c] Spectrum: 315 mμ (3300) and 253 (9400).

After heating for 25 hours, the solution was cooled to room temperature, and the colorless solution was evaporated to dryness in a stream of dry air. The residue was triturated several times with ether. The ethereal solution, after drying over anhydrous magnesium sulfate and evaporation of the ether, gave a light tan powder (20 mg.), m.p. 98–100° with an infrared spectrum in chloroform identical in every respect to that of authentic m-hydroxybenzaldehyde.

Scopinone Quaternary Salts.—Scopinone (39.4 mg.) was treated with excess methyl bromide at 6°. The solution was left standing for one hour at 6°. The excess methyl bromide was then blown off in a stream of dry nitrogen. This gave some white crystals embedded in a viscous, colorless oil. The crude product smelled distinctly of dimethylamine. A solution of the product (oil and crystals together) in 59 ml. of distilled water showed immediately after preparation an ultraviolet absorption identical to that of authentic m-hydroxybenzaldehyde. Analysis as above indicated a 14% yield. The solution was treated with 0.1 g. of sodium bicarbonate and heated on the steam-bath. The results are

Time of heating, min.	m-Hydrobenzaldehyde, %
15	44
90	48
240	51

Scopinone methiodide prepared in a similar manner gave similar results. The crude product, however, was a powdery, tan solid (m.p. 188–191° dec.) which darkened on

(13) No evidence for the build-up of an intermediate such as VII could be obtained by following the course of the degradation spectrophotometrically.

(14) The authors would like to thank Professor Ernest Wenkert for stimulating discussions of this problem. The authors are particularly grateful to a Referee for calling their attention to some work of L. I. Smith and E. R. Rogier, THIS JOURNAL, 73, 3837 (1951), which may provide an analogy for the type of cleavage postulated in equation 6.

(15) A. Bowers, T. G. Halsall, E. R. H. Jones and A. J. Lemin, J. Chem. Soc., 2555 (1953).

(16) R. A. Morton and A. L. Stubbs, ibid., 1347 (1940).

standing at room temperature and smelled strongly of dimethylamine.

Degradation of Scopinone Methobromide with Sodium Bicarbonate.—Scopinone methobromide[10] (62 mg., 0.25 mmole) and sodium bicarbonate (21 mg., 0.25 mmole) dissolved in 50 ml. of distilled water were heated on the steambath. Periodically 1-ml. samples were withdrawn, diluted 1:100 with distilled water (concentration = $5 \times 10^{-5} M$) and the ultraviolet spectrum taken. The yield of m-hydroxybenzaldehyde was estimated on the basis of the intensity of the 253 mμ absorption maximum. Heating was stopped after 9 hours, and the solution was concentrated to a volume of approximately 10 ml. by evaporation in a stream of dry air at room temperature. This solution was acidified (pH 3, hydrion paper) with 7 drops of 1 N sulfuric acid. The acidic solution was extracted four times with ether, and the ethereal extract was dried over anhydrous magnesium sulfate. Evaporation of the ether *in vacuo* gave a white solid (25 mg., 82%), m.p. 100–102° (authentic m-hydroxybenzaldehyde recrystallized from water, m.p. 102–103°). A mixture melting point with authentic m-hydroxybenzaldehyde was undepressed (100–102°). The infrared spectra of the product and authentic m-hydroxybenzaldehyde in chloroform solution were identical. The product was recovered from the chloroform solution and converted to the 2,4-dinitrophenylhydrazone, m.p. 261–262° (m-hydroxybenzaldehyde, 2,4-DNP, m.p. 259°), mixture m.p. 257–260°.

Degradation of Scopinone Methobromide without Base.—Scopinone methobromide (62 mg., 0.25 mmole) was dissolved in distilled water and heated on the steam-bath. Periodically 1-ml. samples were withdrawn and analyzed as above. Heating was stopped after 14 hours, and the solution was evaporated to dryness at room temperature in a stream of dry air. m-Hydroxybenzaldehyde (15 mg., 49%) was isolated from the residual product.

Stability of γ-Tropolone in Base.—An aqueous solution of γ-tropolone was prepared as described previously[1,4] by dissolving teloidinone methobromide (66.5 mg.) and barium hydroxide (5.0 g.) in 50 ml. of distilled water. The solution was heated on the steam-bath until the yield of γ-tropolone was constant. The solution was then heated for 12 additional hours with no significant change in the intensity or location of the γ-tropolone absorption maxima.

ITHACA, N. Y.

The Absolute Configuration of the C8-Atom in the Pyrrolizidine Moieties of the Senecio Alkaloids

BY ROGER ADAMS AND D. FLEŠ[1,2]

(−)-Methyl 2-acetyl-1-pyrrolidineacetate, a degradation product of monocrotaline, was condensed with methylmagnesium iodide to yield (−)-1-(2-hydroxy-2-methylpropyl)-2-(1-hydroxy-1-methylethyl)-pyrrolidine. The same carbinol was prepared from (S)(−)-proline by converting it first to the methyl ester, condensing this ester with methyl bromoacetate, and finally treating the methyl (−)-2-carbomethoxy-1-pyrrolidineacetate with methylmagnesium iodide. The configuration of the C8-atom in the pyrrolizidine moiety of monocrotaline was thus related to (S)(−)-proline.

In a recent paper[3] a proof of the absolute configuration of the C_1 atom of retronecanone was established as S[4]. This was effected by correlating the configuration of (−)-3-methyl-5-aminovaleric acid, which had previously been converted into retronecanone,[5] with that of (S)(−)-methylsuccinic acid. The results were in agreement with the findings deduced by Warren and Klemperer[6] on the basis of the degradation of (−)-heliotridane to (S)(+)-3-methylheptane.
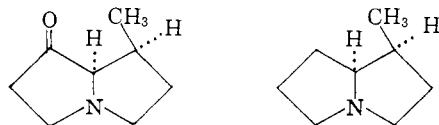
(−)-retronecanone[7]   (−)-heliotridane

The absolute configuration of the C8-atom in desoxyretronecine (V) has now been undertaken.

(1) "Pliva" Pharmaceutical and Chemical Works, Zagreb, Yugoslavia.

(2) The authors are grateful for a grant from the Alfred P. Sloan Foundation which made this investigation possible.

(3) R. Adams and D. Fleš, THIS JOURNAL, **81**, 4946 (1959).

(4) The symbolism presented by R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia*, **12**, 81 (1956).

(5) R. Adams and N. J. Leonard, THIS JOURNAL, **66**, 257 (1944).

(6) F. L. Warren and M. E. von Klemperer, *J. Chem. Soc.*, 4574 (1958).

(7) The structural formulas of the pyrrolizidine bases are drawn in such a way that the $\diagdown$C$\diagup$ bond is in the plane of the paper, while the
$\quad\quad\quad\quad|$
$\quad\quad\quad\quad$N$\diagdown$
two rings are inclined on the carbon–nitrogen axis toward each other above the plane of the paper.

From a consideration of the scale molecular models of anhydroplatynecine[8] (I), Leonard and Felley[9] concluded that the methyl group in heliotridane must be *trans* to the hydrogen attached to the C8-atom. Dry, Koekemoer and Warren[10] performed experiments that led them to the same conclusion. Adams and Van Duuren[11] converted platynecine (II) into a tricyclic product, platynecine sulfite (III), by treatment with thionyl chloride. Hydrolysis of compound III with cold dilute alkali regenerated platynecine. They deduced also a *trans* relationship of the C_1-methyl group and the C8-hydrogen atom in heliotridane.

I   II   III
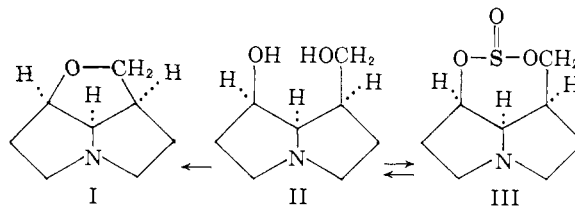
Since the absolute configuration of the C_1-atom of the pyrrolizidine moiety of the necine alkaloids has been experimentally proved,[3,6] the absolute configuration of the C8-atom can be deduced on the basis of the relationships established

(8) A. Orekhov, R. A. Konovalova and W. Tiedebel, *Ber.*, **68**, 1886 (1935); R. A. Konovalova and A. Orekhov, *ibid.*, **69**, 1908 (1936).

(9) N. J. Leonard and D. L. Felley, THIS JOURNAL, **72**, 2537 (1950).

(10) L. J. Dry, M. J. Koekemoer and F. L. Warren, *J. Chem. Soc.*, 59 (1955).

(11) R. Adams and B. L. Van Duuren, THIS JOURNAL, **76**, 6379 (1954).