COMMUNICATIONS TO THE EDITOR

SILICICOLIN, A NEW COMPOUND ISOLATED FROM *JUNIPERUS SILICICOLA*

Sir:

The finding[1] that an aqueous suspension of the pulverized dried needles of *Juniperus silicicola* (Small) Bailey[2] (Fam. *Pinaceae*) produced damage to Sarcoma 37 in mice, prompted a search for the active agent or agents. After a process involving successive extractions with different organic solvents and chromatography with activated alumina, similar to that described for other junipers,[3] a pure crystalline compound was obtained in 0.11% yield which was highly active against the tumor.

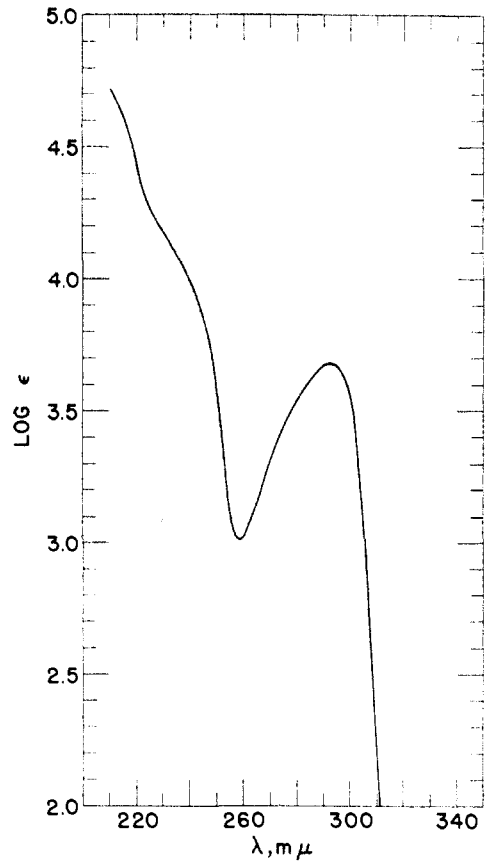

Fig. 1.—Ultraviolet absorption spectrum of silicicolin in 95% ethanol.

The new compound, for which we propose the name silicicolin, crystallizes from absolute ethanol in large, colorless, transparent prisms, m.p. 173.9–175.5° (cor.); $[\alpha]^{19}D$ −119° (*c*, 0.40, chloroform). *Anal.* Calcd. for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57; 3-OCH_3, 23.37; mol. wt., 398.4. Found: C, 66.34; H, 5.52; OCH_3, 23.25; mol. wt. (Rast, camphor), 395. The Gaebel test[4] for the methylenedioxy group was positive.

The insolubility of silicicolin in water and cold 5% sodium hydroxide solution indicates the absence of acidic function such as carboxylic acid and phenolic hydroxyl groups. The slow solubility of the compound in boiling 5% sodium hydroxide solution, with separation of a white gelatinous precipitate on acidification, is strong evidence of a lactone group.

The ultraviolet spectrum (Fig. 1), showing $\lambda_{max.}^{EtOH}$ 293.5 mμ (log ε 3.68) and $\lambda_{min.}^{EtOH}$ 258.5 mμ (log ε 3.01), is similar to that of podophyllotoxin[5] [$\lambda_{max.}^{EtOH}$ 292 mμ (log ε 3.65) and $\lambda_{min.}^{EtOH}$ 260 (log ε 3.07)]. Bands in the infrared (Fig. 2) at 1780 cm.$^{-1}$ (γ-lactone) and 1593 cm.$^{-1}$ (aromatic ring) approximate closely the corresponding ones in podophyllotoxin (1785 cm.$^{-1}$ and 1595 cm.$^{-1}$)[5]. Hydroxyl group absorption around 3450 cm.$^{-1}$ is negligible.

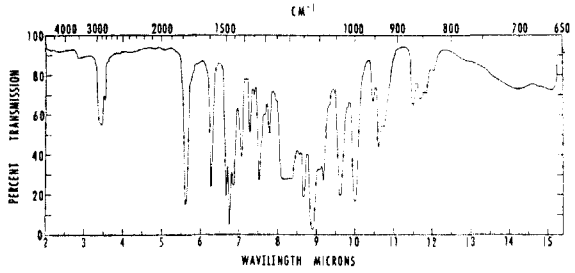

Fig. 2.—Infrared absorption spectrum of silicicolin in chloroform.

The available evidence is consistent with the assumption that silicicolin is a lignan, perhaps the previously unknown desoxypodophyllotoxin.[6]

Structural and biological studies are in progress.

(1) D. B. Fitzgerald, M. Belkin, M. D. Felix and M. K. Carroll, to be published in *J. Nat. Cancer Inst.*

(2) Provided through the courtesy of Mr. R. A. Bonninghausen, Florida Board of Forestry, Tallahassee, Fla.

(3) J. L. Hartwell, J. M. Johnson, D. B. Fitzgerald and M. Belkin, This Journal, in press.

(4) G. O. Gaebel, *Arch. pharm.*, **248**, 225 (1910).

(5) A. W. Schrecker and J. L. Hartwell, This Journal, in press (1952). Podophyllotoxin itself was first suspected because of its isolation from other species of juniper.[3]

(6) Compounds of the same empirical formula, possibly structurally similar, have been isolated from plants of the family *Umbelliferae*, by K. Noguchi and M. Kawanami, *J. Pharm. Soc. Japan*, **60**, 629 (1940), and by L. Marion, *Can. J. Research*, **20B**, 157 (1942).

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11α-HYDROXYSTEROIDS. SYNTHESIS OF Δ^4-PREGNEN-11α,17α,21-TRIOL-3,20-DIONE 11,21-DIACETATE (11-EPI-COMPOUND F DIACETATE)

Sir:

We wish to report a general method for the reduction of the 11-carbonyl group in steroids to the

11α-hydroxy group.[1] This method, coupled with our observation that the 11α-hydroxyl group is not oxidized readily by N-bromoacetamide, has made possible the preparation of Δ^4-pregnen-11α,17α,-21-triol-3,20-dione 11,21-diacetate (11-epi-Compound F Diacetate).

Etiocholan-3α-ol-11,17-dione[2] was reduced with sodium in refluxing *n*-propyl alcohol in excellent yield to etiocholan-3α,11α,17β-triol (I), m.p. 245–247°, $[\alpha]^{25}D$ +13° (0.5% in ethanol). *Anal.* Calcd. for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. Found: C, 73.82; H, 10.72. The configuration of the 11-hydroxyl group was inferred from the acetylation of I, which gave a triacetate, m.p. 161–162°, $[\alpha]^{25}D$ −2° (0.9% in ethanol). *Anal.* Calcd. for $C_{25}H_{38}O_6$: C, 69.09; H, 8.81. Found: C, 69.31; H, 8.94. Oxidation of I with excess N-bromoacetamide (NBA) in aqueous methanol–acetone solution at room temperature gave, in good yield, etiocholan-11α-ol-3,17-dione (II), m.p. 143–144°, $[\alpha]^{25}D$ +72° (1% in acetone). *Anal.* Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.87; H, 9.24. The structure of II was established by independent synthesis from I. Oxidation of I with chromic anhydride in aqueous acetic acid at room temperature afforded etiocholan-3,11,17-trione (III),[3] m.p. 135–136°, $[\alpha]^{23}D$ +151° (1% in acetone). Upon refluxing III with ethylene glycol and *p*-toluenesulfonic acid in benzene solution, there was obtained etiocholan-3,11,17-trione 3,17-bisdioxolane (IV), m.p. 122–123°, $[\alpha]^{26}D$ +30° (1% in chloroform). *Anal.* Calcd. for $C_{23}H_{34}O_5$: C, 70.73; H, 8.77. Found: C, 70.75; H, 9.07. Reduction of IV with sodium in refluxing *n*-propyl alcohol, followed by hydrolysis of the product with methanol–hydrochloric acid, yielded II, identical in all respects with the sample from NBA oxidation of I.

Sodium and *n*-propyl alcohol reduction of pregnan-3α,17α-diol-11,20-dione 20-dioxolane[4] yielded the corresponding 11α-hydroxy compound (V), m.p. 213.2–214.0°, $[\alpha]D$ −13° (1% in acetone). *Anal.* Calcd. for $C_{23}H_{38}O_5$: C, 70.01; H, 9.71. Found: C, 69.70; H, 9.74. Hydrolysis of V with aqueous methanol–hydrochloric acid gave pregnan-3α,11α,17α-triol-20-one (VI) as the monohydrate, $[\alpha]D$ +25° (0.5% in acetone). *Anal.* Calcd. for $C_{21}H_{34}O_4 \cdot H_2O$: C, 68.44; H, 9.85. Found: C, 68.14; H, 10.07. Bromination of VI in chloroform at C-21 followed by acetoxylation according to the method of Gallagher[5] yielded an oil which was not further purified, but was oxidized at C-3 with NBA and then acetylated at C-11 to give pregnan-11α,-17α,21-triol-3,20-dione 11,21-diacetate (VII), m.p. 232–233° dec., $[\alpha]^{25}D$ +44° (1% in dioxane). *Anal.* Calcd. for $C_{25}H_{36}O_7$: C, 66.94; H, 8.09. Found: C, 66.59; H, 8.29. Bromination at C-4 followed by semicarbazone formation, elimination of HBr and acid hydrolysis of the semicarbazone[6] gave Δ^4-pregnen-11α,17α,21-triol-3,20-dione 11,21-diacetate (11-epi-compound F diacetate), m.p. 223.0–225.8, $[\alpha]D$ +116° (1% in dioxane), ϵ_{240}^{alc} 16,800. *Anal.* Calcd. for $C_{25}H_{34}O_7$: C, 67.24; H, 7.68. Found: C, 67.12; H, 7.85.

(1) F. Sondheimer, R. Yashin, G. Rosenkranz and C. Djerassi (THIS JOURNAL, **74**, 2696 (1952)) noted that the carbonyl group and the double bond conjugated with it in Δ^8-22-isoallospirosten-3β-ol-11-one propionate are both reduced to yield the saturated 11α-ol with the aid of lithium, liquid ammonia and alcohol.

(2) L. H. Sarett, *ibid.*, **70**, 1454 (1948).

(3) S. Lieberman and K. Dobriner, *J. Biol. Chem.*, **166**, 773 (1946).

(4) The preparation of the various pregnane dioxolanes will be the subject of another paper.

(5) T. H. Kritchevsky, D. L. Garmaise and T. F. Gallagher, THIS JOURNAL, **74**, 483 (1952).

(6) V. R. Mattox and E. C. Kendall, *J. Biol. Chem.*, **188**, 287 (1951); B. Koechlin, T. Kritchevsky and T. F. Gallagher, *ibid.*, **184**, 393 (1950); E. B. Hershberg, *J. Org. Chem.*, **13**, 542 (1948).

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RECEIVED JUNE 9, 1952

THE ION-EXCHANGE SEPARATION OF ISOMERIC DINITROTETRAMMINECOBALT(III) IONS[1]

Sir:

Recently it has been shown that the octahedral complex ions $Cr(H_2O)_6^{+++}$, $Cr(SCN)(H_2O)_5^{++}$, and $Cr(SCN)_2(H_2O)_4^{+}$ are readily separated by an ion-exchange technique.[2] The possibility of using this same technique to separate the isomeric *cis* and *trans* complexes having the general formula $MA_4B_2^{+n}$ was suggested at that time. The isomeric dinitrotetramminecobalt(III) ions have been prepared,[3] and their elution characteristics have been studied. An elution curve of a mixture of the two complex ions is shown in Fig. 1. Since the absorption spectra of these complex ions are different,[4] it is convenient to make use of the spectra in following the elution and identifying the eluted species. The more easily eluted ion is the *trans* complex.

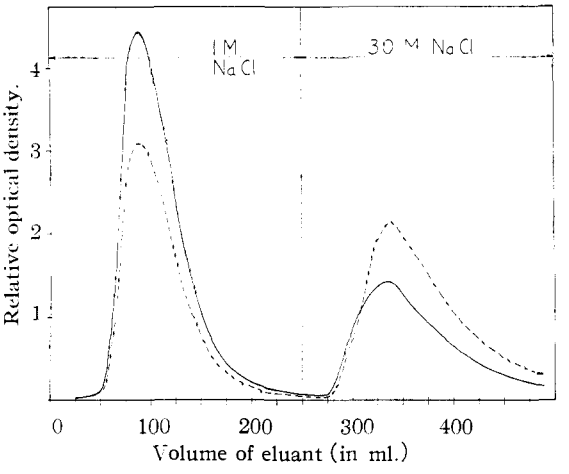

Fig. 1.—Relative optical density of eluant *versus* volume of eluant (in ml.). —350 mμ, - - - - - 325 mμ. For *trans* complex $\epsilon_{350} > \epsilon_{325}$. For *cis* complex $\epsilon_{325} > \epsilon_{350}$. Notice that the relative optical densities in the first part of the second peak indicate that the *trans* complex had not been completely eluted when the eluting agent was changed. Individual portions of eluant were 12.5 ml.

(1) This work has been supported in part by a grant from the U. S. Atomic Energy Commission.

(2) E. L. King and E. B. Dismukes, THIS JOURNAL, **74**, 1674 (1952).

(3) *cis:* H. Biltz and W. Biltz, "Laboratory Methods of Inorganic Chemistry," John Wiley and Sons, New York, N. Y., 1928, p. 179. *trans:* S. M. Jorgensen, *Z. anorg. Chem.*, **17**, 469 (1898).

(4) F. Basolo, THIS JOURNAL, **72**, 4393 (1950).

In an octahedral complex of the composition $Ma_4B_2^{+n}$, the *trans* isomer has no net dipole moment while the *cis* isomer does. It seems reasonable for the polar ion to be more strongly held in the resin phase than the non-polar ion of the same composition and charge. Since the nitro group is one of the most polar groups, the system studied here may prove to be the one in which the separation of isomers by this method is most easily accomplished.

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RECEIVED JULY 21, 1952

THE ISOMERIZATION OF CYCLOPROPANE—A QUASI-UNIMOLECULAR REACTION

Sir:

In 1942 Pease[1] concluded that with the possible exception of the thermal isomerization of cyclopropane investigated by Chambers and Kistiakowsky,[2] there was no case of quasi-unimolecular reaction known, which provided unequivocal confirmation of the theory of unimolecular reactions proposed by Lindemann, Hinshelwood, Rice, Ramsperger, Kassel[3] and others. Later Corner and Pease[4] reinvestigated the isomerization of cyclopropane to propylene and concluded that as the addition of unreactive gases had little effect, the fall-off of the apparent first-order rate constant was more reasonably explained by a complex reaction mechanism than by an energy transfer process.

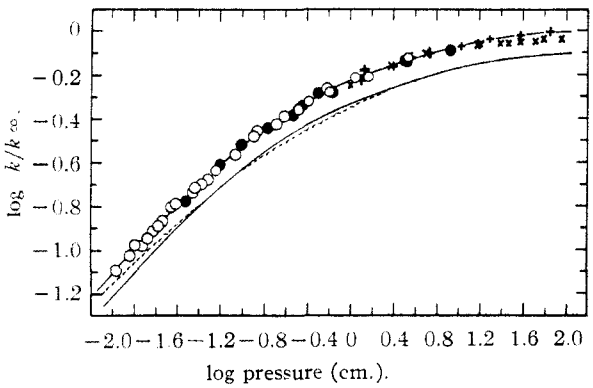

Fig. 1.

There now appear to be two well-established cases of the falling-off of unimolecular rate constants in the decomposition of nitrogen pentoxide[5] and nitrous oxide.[6] We have reinvestigated the isomerization of cyclopropane at 492° in a 2-l. Pyrex reaction vessel extending the measurements below the 10 mm. pressure limit of previous workers down to 0.1 mm. The reaction was followed by the analysis of the cyclopropane–propylene mixture for olefin content on a Blacet–Leighton[7] apparatus using a mercuric acetate bead.[8] There is good evidence that no side-reactions occurred for in an aged reaction vessel no condensation took place and no products non-condensable in liquid nitrogen were formed. Our results are shown together with those of other workers in Fig. 1. The theoretical curve, following Chambers and Kistiakowsky,[2] is calculated from Kassel's[3] equation using a collision diameter of 3.9 Å., 13 oscillators and a value of k_∞, the rate at infinite pressure, given by

$$\log k_\infty = 15.17 - \frac{65{,}000}{2.3RT}$$

Furthermore we have investigated the effect of added hydrogen on the rate constant at low cyclopropane pressures. The hydrogen causes a marked increase in the rate constant and is about one-fifth as efficient as cyclopropane or propylene in restoring the rate constant. The comparatively low efficiency of hydrogen is evidently the reason why Corner and Pease could find no effect which in their case would have been 4%, for this is the order of their experimental error. Accordingly it seems that this reaction is a clear cut case of the falling-off of the rate of a unimolecular gas reaction with pressure.

We are now investigating the effect of the addition of a number of non-reacting gases to the system and hope to publish the results in detail when a full survey has been completed.

(1) R. N. Pease, "Equilibrium and Kinetics of Gas Reactions," Princeton, N. J., 1942, p. 147.
(2) T. S. Chambers and G. B. Kistiakowsky, THIS JOURNAL, **56**, 399 (1934).
(3) L. S. Kassel, "Kinetics of Homogeneous Gas Reactions," Chemical Catalog Co., New York, N. Y., 1932, p. 93.
(4) E. S. Corner and R. N. Pease, THIS JOURNAL, **67**, 2067 (1945).
(5) H. S. Johnston and R. L. Perrine, *ibid.*, **73**, 4782 (1951).
(6) H. S. Johnston, *J. Chem. Phys.*, **19**, 663 (1951).
(7) F. E. Blacet and P. A. Leighton, *Ind. Eng. Chem., Anal. Ed.*, **3**, 266 (1931).
(8) R. Pyke, A. Cahn and D. J. LeRoy, *Anal. Chem.*, **19**, 65 (1947).

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EFFECT OF PURINES ON A SUCCINYLSULFATHIAZOLE (SST)-INDUCED DEFICIENCY IN MICE

Sir:

The addition of succinylsulfathiazole (SST) to a purified diet having a low fat content was reported to cause a retardation of growth in weanling mice.[1] This effect on growth was prevented if such materials as fat, a defatted cottonseed meal, or rolled oats were added to the basal diet. Whereas whole liver was found to be without effect it has since been found that a water extracted liver residue is also effective. It was tentatively concluded in this earlier report that fat *per se* is an essential nutrient for animal growth. It was further suggested that in the absence of adequate quantities of dietary fat a factor, or factors, synthesized by SST-susceptible intestinal microorganisms is essential for fat synthesis by the animal. This factor, or factors, was postulated to be present in those fat-free natural materials that are capable of preventing the SST-induced growth retardation.

(1) D. K. Bosshardt, W. J. Paul, R. H. Barnes and J. W. Huff, *Proc. Soc. Exptl. Biol. Med.*, **75**, 722 (1950).

Studies were initiated in these laboratories to isolate the active ingredient from cottonseed. During the course of this investigation a compound was obtained in crystalline form which was found to be partially effective in preventing the SST-induced growth retardation in mice. This compound was identified as the purine, guanine.

TABLE I

EFFECT OF PURINES AND PURINE RIBOSIDES ON A SST-INDUCED GROWTH RETARDATION IN MICE[a]

Diet	Av. 12-day wt. gain, g.
Control	9.1
2% SST	4.6
2% SST + 5% Cottonseed meal[b]	8.6
2% SST + 15% Cottonseed meal	10.8
2% SST + 0.02% Adenine	8.3
2% SST + 0.08% Adenine	8.8
2% SST + 0.02% Guanine	7.8
2% SST + 0.08% Guanine	7.4
2% SST + 0.02% Xanthine	8.1
2% SST + 0.08% Xanthine	8.9
2% SST + 0.02% Hypoxanthine	9.5
2% SST + 0.08% Hypoxanthine	8.2
2% SST + Adenosine equiv. to 0.02% adenine	7.8
2% SST + Adenosine equiv. to 0.08% adenine	9.0
2% SST + Guanosine equiv. to 0.2% guanine	7.6
2% SST + Guanosine equiv. to 0.08% guanine	8.1
2% SST + Inosine equiv. to 0.02% hypoxanthine	8.2
2% SST + 1% Yeast Ribonucleic acid (GBI)	9.0

[a] Eight male mice per group. [b] Proflo, Traders Oil Mill Co., Fort Worth, Texas.

The purines adenine, guanine, xanthine and hypoxanthine as well as the ribosides adenosine, guanosine and inosine were tested with growing mice using the SST containing low fat basal diet. The results obtained are shown in Table I. All of the purines and purine ribosides that were studied as well as yeast ribonucleic acid were found to be able partially to replace cottonseed in preventing the SST-induced growth retardation.

On the basis of the data presented here purines may function to modify the action of succinylsulfathiazole thus permitting the intestinal microorganisms to synthesize an as yet unknown factor which possibly plays some role in fat metabolism. On the other hand purines or nucleic acids may represent essential accessory food factors required for fat metabolism in the mouse.

In other studies, to be reported later, it has been found that other stress agents such as thyroid active materials or atabrine administered orally, or injected thyroxine cause a retardation of growth in mice fed a low fat diet. In these cases it is also possible to prevent this growth retardation by the feeding of cottonseed meal, fat, or a water extracted liver residue. It is possible that the beneficial effects of extracted liver residue in overcoming the toxicity of thyroxine or atabrine in the rat that were reported by Ershoff[2-4] may be due to the nucleic acids or their degradation products present in the extracted liver residue.

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RECEIVED JULY 28, 1952

(2) B. H. Ershoff, *Arch. Bio.*, **15**, 365 (1947).
(3) B. H. Ershoff and H. B. McWilliams, *Science*, **108**, 632 (1948).
(4) B. H. Ershoff, *J. Nut.*, **35**, 269 (1948).

HYPOTENSIVE ALKALOIDS OF VERATRUM FIMBRIATUM GRAY

Sir:

Two new hypotensively active ester alkaloids, germanitrine and germinitrine, have been isolated from *Veratrum fimbriatum* Gray.

The extraction procedure employed was essentially the same as the one reported in our previous investigation of *Veratrum viride* Ait.[1] The crude amorphous fraction thus obtained was subjected to an eight plate countercurrent distribution using benzene–2*M* acetate buffer *p*H 5.5 as the solvent system with the lower phase moving. This yielded two main fractions, A (tubes 0–1) and B (tubes 2–5).

Fraction A was distributed on a 24-plate countercurrent machine with 0.5 *M* sodium acetate buffer *p*H 5.0—benzene–cyclohexane 40:60. Careful fractional crystallization of the material recovered from tubes 4–14 from acetone–water gave germanitrine, and germinitrine.

Germanitrine crystallized as heavy needles; m.p. 228–229°; $[\alpha]^{24}D$ −61 ± 2° (*C* 1.0 in pyr.); 0.0 ± 2° (*C* 1.15 in $CHCl_3$). Analytical data indicate the empirical formula $C_{39}H_{59}O_{11}N$; calcd. C, 65.25; H, 8.28; N, 1.95; eq. wt., 717.87; found: C, 65.30; H, 8.26; N, 1.99; eq. wt., 721; picrate, m.p. 240–241° (dec.), $C_{39}H_{59}O_{11}N\cdot HOC_6H_6(NO_2)_3$: C, 57.07; H, 6.60; found: C, 56.68; H, 6.52. Volatile acid determination, found: 2.66 equivalents of acid. Alkaline hydrolysis of germanitrine yielded germine, acetic acid, methylethylacetic acid and tiglic acid.[2]

On methanolysis germanitrine was converted to a di-ester, germanidine, by the loss of the labile acetyl group; m.p. 221–222°; $[\alpha]^{24}D$ −4.1 ± 2° (*C* 1.0 in pyr.); + 18.1 ± 2° (*C* 0.49 in $CHCl_3$). Analytical data indicate the empirical formula $C_{37}H_{57}O_{10}N$: (calcd. C, 65.75; H, 8.50; eq. wt., 675.84; found: C, 65.66; H, 8.61; eq. wt., 672). Volatile acid determination, found: 1.97 equivalents of acid.

Germinitrine crystallized as irregular prisms; m.p. 175–176°; $[\alpha]^{24}D$ −36.0 ± 2° (*C* 1.12 in pyr.); +7.8 ± 2° (*C* 1.35 in $CHCl_3$). Analytical data indicate the empirical formula $C_{39}H_{57}O_{11}N$; calcd. C, 65.43; H, 8.03; N, 1.96; eq. wt., 715.85; found: C, 65.35; H, 8.27; N, 1.61; eq. wt., 722; picrate, m.p. 238° (dec.), $C_{39}H_{57}O_{11}N\cdot HOC_6H_2(NO_2)_3$: C, 57.19; H, 6.40; found: C, 57.17; H, 6.66. Volatile acid determination, found: 2.32 equivalents of acid. Alkaline hydrolysis of germinitrine yielded germine, acetic acid, tiglic acid and angelic acid.[2]

Fraction B was distributed on a 24-plate counter-

(1) M. W. Klohs, R. Arons, M. D. Draper, F. Keller, S. Koster, W. Malesh and F. J. Petracek, THIS JOURNAL, **74**, in press (1952).
(2) The acids were identified by conversion to their *p*-phenylphenacyl esters and characterized after chromatographic separation.

current machine using 2 *M* acetate buffer *p*H 5.5 and benzene. The known triester, neogermitrine,[3] was obtained by crystallizing the material recovered from tubes 6–10 from acetone–water.

The hypotensive activity[4,5] of germanitrine, germanidine, and germanitrine was found to be 0.12 μg. [0.11–0.14], 0.77 μg. [0.46–2.3], and 0.41 μg. [0.36–0.49], respectively.

(3) J. Fried, P. Numerof and N. H. Coy, THIS JOURNAL, **74**, 3041 (1952).

(4) Edward D. Swiss and George L. Maison, Federation Proceedings, Vol. II, No. 1, March, 1952.

(5) Expressed as micrograms per kilogram of anesthetized dog per minute required for a ten-minute intravenous infusion to lower the mean arterial blood pressure 30% when administered according to the method of G. L. Maison and J. W. Stutzman. The bracketed numbers express the 95% confidence limits.

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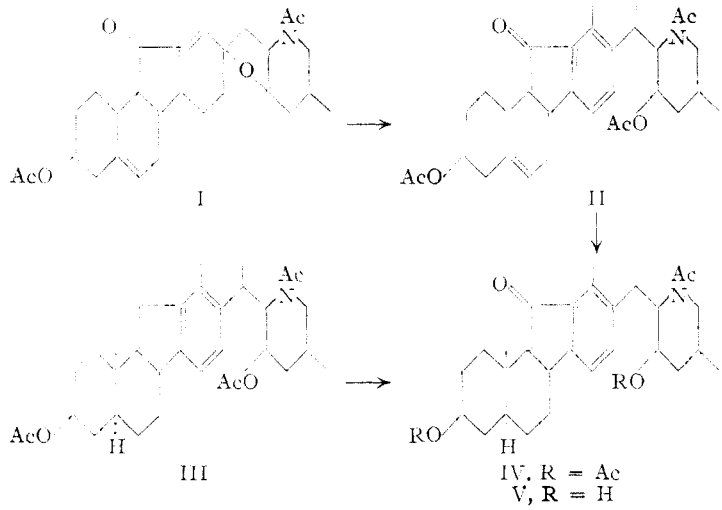
RECEIVED JULY 28, 1952

THE STRUCTURAL CORRELATION OF JERVINE AND VERATRAMINE

Sir:

As reported in preliminary communications from this Laboratory,[1] O,N-diacetyljervine (I) on acetolysis with acetic anhydride–acetic acid containing a catalytic amount of sulfuric acid gave rise to a triacetate, $C_{33}H_{43}O_6N$, (m.p. 239–240°, $[\alpha]^{24}D$ −29°[2]), which on the basis of its ultraviolet and infrared characteristics (λ_{max}^{alc} 251 mμ, log ε 4.08; 300 mμ, log ε 3.30; IR: intense bands at 5.75, 5.88 and 6.09 μ, indicative, respectively, of O-acetyl, ketonic carbonyl and N-acetyl) and other evidence was assigned the indanone structure II. On the other hand, there has been obtained by chromic acid oxidation of triacetyldihydroveratramine ($C_{33}H_{47}O_6N$, now assigned structure III[3]) a compound $C_{33}H_{45}O_6N$ (m.p. 241–245°, $[\alpha]^{21}D$ +59°) which likewise exhibited the above spectral properties, and the new keto group of which, like that of II, was unreactive to ketone reagents.[3] We have now reduced II catalytically with palladium–calcium carbonate in ethanol to its 5,6-dihydro derivative IV,[4] and found the latter identical in all respects, inclusive of the infrared characteristics over the whole measurable range, with the oxidation product from triacetyldihydroveratramine (m.p. 242–245°, $[\alpha]^{23}D$ +57.5°; *Anal.* Calcd. for $C_{33}H_{45}O_6N$: C, 71.83; H, 8.22. Found: C, 71.94; H, 8.26). The respective N-acetates (V), prepared by hydrolysis with methanolic potassium hydroxide, were likewise identical (m.p. 264–266.5°, $[\alpha]^{23.5}D$ +71.7°, +68.8°; *Anal.* Calcd. for $C_{29}H_{41}O_4N$: C, 74.46; H, 8.84. Found: C, 74.57; H, 8.64). The vicinal effect of the indanone grouping on the contribution to molecular rotation of C_5 is evident in the abnormally high $\Delta[M]_D$ for the saturation of the double bond (+484° for II → IV, +495° for O-desacetylated II → V) as compared with the values +399° for triacetylveratramine → triacetyldihydroveratramine, +404° for N-acetylveratramine → N-acetyldihydroveratramine, and +243° for normal Δ^5-stenyl acetates.[5]

The significance of this result lies in the fact that it renders extremely remote the possibility of a rearrangement of the carbon skeleton in the formation of the acetolysis product II from diacetyljervine, since (1) the presence in veratramine of a preformed benzenoid ring has been assured not only by ultraviolet spectrophotometry[6] but also by chemical means,[3] (2) the conversion of triacetyldihydroveratramine to IV obviously cannot involve a change in the skeleton, and (3) it is reasonable on biogenetic grounds to accord also to jervine the abnormal ring structure which has now been shown to pre-exist in veratramine.



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(1) J. Fried, O. Wintersteiner, A. Klingsberg, M. Moore and B. M. Iselin, THIS JOURNAL, **73**, 2970 (1951); O. Wintersteiner and M. Moore, Abstracts, XIIth Internat. Congress of Chemistry, New York, Sept. 10–13, 1951, p. 292.

(2) All melting points corrected; all rotations in chloroform.

(3) Ch. Tamm and O. Wintersteiner, THIS JOURNAL, **74**, 3842 (1952).

(4) The catalytic hydrogenation of II presented unexpected difficulties in that it did not proceed smoothly under any of the conditions tried, and invariably gave rise to mixtures. Thus, with PtO_2 in acetic acid the indanone carbonyl was partly reduced, and the product obtained by reoxidation with chromic acid, (m.p. 214–217°, $[\alpha]D$ +57.5°) was obviously not pure IV. On the other hand, hydrogen uptake in the reaction catalyzed with palladium was very sluggish, and the crude product was contaminated with less dextrorotatory impurities (apparently for the most part unchanged starting material), which could not always be completely removed by recrystallization or eliminated by rehydrogenation, so that the yield of pure dihydro product was always low.

(5) D. H. R. Barton, *J. Chem. Soc.*, 512 (1946).

(6) W. A. Jacobs and L. C. Craig, *J. Biol. Chem.*, **160**, 555 (1945).

(7) This paper is part of the dissertation to be presented by Norman Hosansky in partial fulfillment of the requirements for the Ph.D. degree in the Graduate School of Rutgers University.