

Jacobs⁴ have presented supporting evidence in favor of the atisine structure.

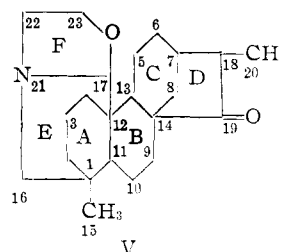
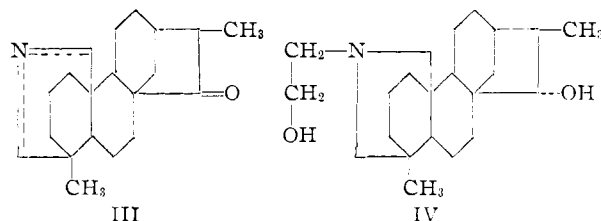
In connection with a study of the alkaloids of the bark of the Mexican tree *Garrya laurifolia* ("cuauchichic"), we have isolated in crystalline form a new alkaloid isomeric with garryine, veatchine and atisine which we have named cuauchichicine. We should like to record the pertinent experiments which demonstrate that this alkaloid is an additional member of this biogenetically important class of diterpenoid alkaloids and that it possesses a modified phyllocladene skeleton typical of veatchine (I) and garryine (II).

Cuauchichicine was obtained by counter-current distribution of the crude alkaloid fraction at pH 7.4 followed by crystallization from methanol: m.p. 143–145°, $[\alpha]_D -76^\circ$ (CHCl_3), $\lambda_{\text{max}}^{\text{CHCl}_3} 5.78 \mu$ but no free OH or NH bands, no high selective absorption in the ultraviolet; (*Anal.* Calcd. for $\text{C}_{22}\text{H}_{33}\text{NO}_2$: C, 76.92; H, 9.68; N, 4.08. Found: C, 76.75; H, 9.79; N, 4.26); hydrochloride, m.p. 259–262° (*Anal.* Calcd. for $\text{C}_{22}\text{H}_{34}\text{ClNO}_2$: C, 69.53; H, 9.02; Cl, 9.33; N, 3.69. Found: C, 69.44; H, 9.32; Cl, 9.47; N, 3.89). A Kuhn-Roth determination carried out parallel with veatchine (I)⁵ (found, 2.87; calcd. for 1 C- CH_3 , 4.37) and cuauchichicine (found, 5.04) shows that the latter contains two C-methyl groups. In contrast to veatchine, garryine and atisine, cuauchichicine does not possess an exocyclic methylene group as demonstrated by ozonization experiments. The infrared carbonyl band at 5.78μ can be attributed to a five-membered ring ketone, which could be characterized as the *oxime*, m.p. 192–194° (*Anal.* Calcd. for $\text{C}_{22}\text{H}_{34}\text{N}_2\text{O}_2$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.27; H, 9.89; N, 7.60). Pyrolysis of the alkaloid with selenium at 290° afforded *pyrolysis base A* (III) (m.p. 133–136°, identical infrared spectrum with authentic material⁶), already isolated^{2b} by Wiesner, *et al.*, from similar treatment of veatchine (I), thus accounting for five of the six rings of cuauchichicine. Sodium borohydride or lithium aluminum hydride reduction of the alkaloid (V) yielded a tetrahydro (dihydroxy) derivative, m.p. 175–177°, $[\alpha]_D -86.7^\circ$ (CHCl_3) (*Anal.* Calcd. for $\text{C}_{22}\text{H}_{37}\text{NO}_2$: C, 76.03; H, 10.73; N, 4.03. Found: C, 76.11; H, 10.71; N, 4.43; 2 active H; pK 6.84 (cellosolve–20% water)), which proved to be identical (mixture melting point, rotation and infrared comparison) with *tetrahydroveatchine* (IV) (observed values in our laboratory for authentic material⁶: m.p. 175–178°, $[\alpha]_D -85.2^\circ$), obtained earlier^{2b} by partial syn-

(4) S. W. Pelletier and W. A. Jacobs, *THIS JOURNAL*, **76**, 4496 (1954).

(5) We are indebted to Prof. K. Wiesner, University of New Brunswick, for this sample.

thesis from pyrolysis base A (III). The pK value (10.98)⁶ of cuauchichicine is comparable to that of veatchine (I) (pK 11.5)^{2a} rather than that of garryine (II) (pK 8.7) thus indicating that the oxazolidine ring is fused to C-17 rather than C-16. The above described data are only compatible with expression V⁷ for cuauchichicine.



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(6) This value is obtained (cellosolve–20% water) if the alkaloid is titrated immediately with 0.1 N HCl. If the solution is allowed to stand under nitrogen for 12 hours prior to titration, two breaks in the titration curve are observed corresponding to pK 11.15 and 8.80.

(7) In view of the structural similarity with the diterpenes, we are employing a numbering system based on that of abietane (*cf.* W. Klyne, *J. Chem. Soc.*, 3072 (1953)).

(8)(a) Eli Lilly Predoctorate Research Fellow 1953–1954; (b) Post-doctorate Research Fellow at Wayne University, 1953–1954.

SYNTHESIS OF PICROPODOPHYLLIN¹

Sir:

We wish to report the successful conversion of synthetic DL- β -apopicropodophyllin² to picropodophyllin,³ and thereby the completion of a total synthesis of picropodophyllin. Saponification of DL- β -apopicropodophyllin furnished DL- α -apopodophyllinic acid⁴ melting at 170–171°. *Anal.* Calcd. for $\text{C}_{22}\text{H}_{22}\text{O}_8$: C, 63.7; H, 5.3. Found: C, 63.5; H, 5.3. The infrared and ultraviolet absorption curves of the DL-acid were the same, respectively, as those determined for authentic α -apopodophyllinic acid. Treatment of the racemic acid with

(1) This work has been supported by grants-in-aid from the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council.

(2) W. J. Gensler, C. M. Samour and Shi Yi Wang, *THIS JOURNAL*, **76**, 315 (1954).

(3) *Cf.*, W. Borsche and J. Niemann, *Ann.*, **494**, 59 (1932); *Ber.*, **65**, 1633, 1790 (1932); E. Späth, F. Wessely and E. Nadler, *ibid.*, **65**, 1773 (1932); **66**, 125 (1933).

(4) Saponification of optically active β -apopicropodophyllin has been shown by Robertson and Waters⁵ and again by Schrecker and Hartwell⁶ to give optically active α -apopodophyllinic acid.

(5) A. Robertson and R. B. Waters, *J. Chem. Soc.*, **83** (1933).

(6) A. W. Schrecker and J. L. Hartwell, *THIS JOURNAL*, **74**, 5676 (1952).

one-half mole of quinone afforded the optically active quinine salt of α -apopodophyllic acid with a melting point of 213–214° and a rotation $[\alpha]^{25D} - 232^\circ$. *Anal.* Calcd. for $C_{42}H_{46}N_2O_{10}$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.1; H, 6.2; N, 3.9. A mixture of this salt with the quinine salt of authentic α -apopodophyllic acid (m.p. 214–215°; $[\alpha]^{27D} - 235^\circ$) melted at 213–214°. The synthetic α -apopodophyllic acid $[\alpha]^{26D} - 158^\circ$) regenerated from the salt melted at 168–169° and did not depress the melting point of an authentic sample $[\alpha]^{24.5D} - 158^\circ$). Determination and comparison of the infrared and ultraviolet absorption curves confirmed the identity of the synthetic and authentic acids. Lactonization of α -apopodophyllic acid to α -apopodophyllin (with its double bond in the 1,2-position⁶) was effected by heating as described in the literature⁵ or preferably by boiling the acid with 10% sulfuric acid. The α -apopodophyllin melted alone or admixed with authentic α -apopodophyllin (m.p. 235–237°) at 233–235°. The action of dry hydrogen chloride in glacial acetic acid followed by hot aqueous acetone containing calcium carbonate transformed α -apopodophyllin to picropodophyllin, m.p. 216–217°. *Anal.* Calcd. for $C_{22}H_{22}O_3$: C, 63.75; H, 5.35. Found: C, 63.5; H, 5.4. The melting point of a mixture of this material with authentic picropodophyllin (m.p. 214–215°) was 214–215°. To clinch the identity, the acetate of the picropodophyllin from α -apopodophyllin was prepared⁷ and compared with an authentic sample. The melting points and the rotations of the two acetates were, respectively, 209–211° and 210–211°, and $[\alpha]^{26D} + 26.5$ and $[\alpha]^{28D} + 28.8^\circ$; the melting point of a mixture of the two acetates was not depressed.

(7) E. Späth, F. Wessely and L. Kornfeld, *Ber.*, **65**, 1536 (1932); W. Borsche and J. Niemann, *Ann.*, **494**, 126 (1932).

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ON THE NON-EXISTENCE OF DISCRETE O_3^- IONS IN K_2O_3

Sir:

The existence of definite oxides of the alkali metals (except lithium) having the formula M_2O_3 , and variously called trioxides or sesquioxides, has been generally accepted since the early investigations of Joannis¹ and Rengade.² These compounds are obtained in the rapid oxidation of the alkali metals dissolved in liquid ammonia or as intermediates in the thermal dissociation of the superoxides MO_2 . They can be identified by the sharp color change and their chemical analysis corresponds closely to the stoichiometric formula M_2O_3 . In some cases their density and melting point have been determined. Furthermore, de Forcrand³ has measured the dissociation pressure and the heat of formation of the potassium compound K_2O_3 .

However, no actual determination of their

- (1) M. A. Joannis, *Compt. rend.*, **116**, 1370 (1893).
(2) E. Rengade, *ibid.*, **140**, 1536 (1905); **144**, 920 (1907).
(3) R. de Forcrand, *ibid.*, **158**, 991 (1914).

structure has been reported so far. Originally they were assumed to contain the O_3^- ion for which the electronic structure may be written⁴



but, of late years, the tendency has been to consider them as lattice compounds of the peroxides and superoxides with general formula $M_2O_2 \cdot 2MO_2$. Recently, in connection with a spectroscopic investigation of the HO_2 radical now under way in this laboratory, we have examined the infrared spectrum of the presumed K_2O_3 made by heating KO_2 in an open crucible until the characteristic brick-red solid was obtained. Because of the extreme hygroscopic nature of these compounds great care was necessary in preparing the samples for spectroscopic studies. A mull in Nujol was found to be the most appropriate technique. Repeated recordings of the spectrum of this material over the whole rock-salt region failed to produce any absorption band attributable to O_3^- ions. Similarly, no specific band was observed in the case of the superoxide KO_2 , either mull in Nujol or as a "dust" film on a rock-salt plate, at least as long as the powder was protected from the atmosphere. Short exposure to damp air immediately brought out nearly a dozen bands belonging to the carbonate, hydroperoxide and, possibly, other ions. In particular the characteristic frequency of the peroxide group at 880 cm^{-1} was prominent under such conditions.

These observations are consistent with the fact that both the peroxide and the superoxide ions, O_2^{2-} and O_2^- , are homopolar, hence their vibrations are infrared inactive. Therefore, we consider the absence of characteristic infrared bands as sufficient evidence to rule out any O_3^- ions in the alkaline sesquioxides. These must be molecular compounds of normal peroxides and superoxides as commonly presumed. This question could best be confirmed by X-ray diffraction or by a study of phase equilibria in the systems: alkali metals–oxygen.

We are grateful to the Callery Chemical Co., Callery, Penn., for a generous sample of potassium superoxide. This work was done while one of us (K.B.H.) held a research fellowship from the Consolidated Mining and Smelting, Trail, B.C.

(4) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939.

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PARAMAGNETIC RESONANCE IN LIQUID SULFUR* Sir:

We have examined liquid sulfur in the range from 190° to 375° by means of paramagnetic resonance absorption spectroscopy and have found that in this temperature range the intensity of the paramagnetism of the melt increases with temperature. These results support the hypothesis, used in

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