Tetrahedron Letters No.22, pp. 1381-1385, 1964. Pergamon Press Ltd.
Printed in Great Britain.

Steroid Alkaloids of Pachysandra terminalis (Buxaceae)

William F. Knaack, Jr. and T. A. Geissman

Department of Chemistry, University of California,

Los Angeles, U.S.A.

Contribution No. 1643
(Received 27 February 1964; in revised form 7 April 1964)

Pachysandra terminalis Sieb. and Zucc. is a member of the hitherto little-investigated family Buxaceae. The recent isolation from Buxus sempervirens L.[1] of cyclobuxine was of special interest, and it is of considerable significance that P. terminalis has now been found to contain 3β,20α-diaminopregn-5-ene and -pregnane derivatives. The occurrence of cyclobuxine and 3,20-diaminopregnane derivatives in two genera of this plant family is a reflection of a metabolic pathway in higher plants like that of the well-established biogenetic route from lanostane derivatives to steroids. In addition, the Pachysandra alkaloids are the first pregnane-derived alkaloids to be found outside of the Apocynaceae.

Thin-layer chromatograms of the total alkaloid mixture from P. terminalis* disclose about eleven Dragendorff-staining components. A comparison of the thin-layer chromatogram of the Pachysandra alkaloids with that of the total alkaloid mixture of Buxus sempervirens L. showed a similarity between these two members of the same plant

---

*The authors are grateful to Drs. G. E. Ullyot and R. F. Raffauf of Smith, Kline and French Laboratories for bringing P. terminalis to their attention and for making it available for chemical study.

family, but it was not possible at that stage to establish the identities of any of the components of these mixtures.

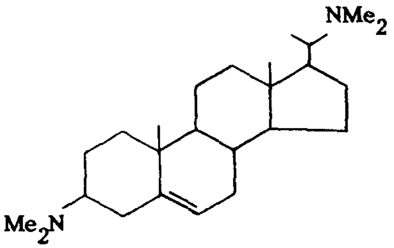
Isolation of the Pachysandra alkaloids and fractionation by systematic solvent extraction (petroleum ether, ether, acetone, methanol) permitted a partial separation of the mixture into several groups of bases, the application to which of a variety of techniques at length provided the following crystalline bases: (a) a mixture, not yet separated, of two closely similar alkaloids, A and B; (b) an alkaloid E and its dihydro derivative, alkaloid D; and an alkaloid C which remains to be studied.

Alkaloids D and E are the products of N-methylation of that part of the crude alkaloid mixture soluble in petroleum ether and ether, and thus do not represent alkaloids present in the plant. They do, however, provide information about the basic structure of the (presumably) primary and secondary amines from which they are derived. Alkaloid E has been identified as 3β,20α-bisdimethylaminopregn-5-ene by its properties (m.p. 135-8°; $[\alpha]_D^{27}$ -37±4°)[2,3] and its n.m.r. spectrum (Fig. 1). The n.m.r. spectrum shows a total of 44±1 protons (corresponding to $C_{25}H_{44}N_2$), with six-proton signals at 7.69 and 7.81 τ for each of the two $-NMe_2$ groupings (singlets), the methyl groups at C_{10} and C_{18} (singlets) and that at C_{20} (doublet). The signal for the vinyl proton at C_6 is seen as a one-proton triplet. Final confirmation of the identity of alkaloid E was made by direct comparison with an authentic specimen* of the base kurchessine;[2,3] the compounds had identical melting points and showed no depression on mixing; they were indistinguishable on thin-layer chromatograms.

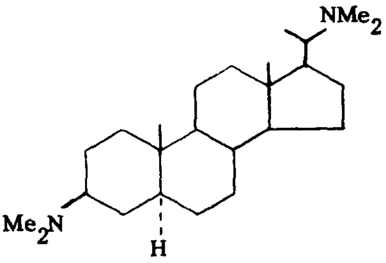
---

*Kindly provided by Professor F. Šorm. The specimen had m.p. 139-40°; mixed with alkaloid E the m.p. was 139-40°.

Alkaloid D, separated from E by chromatography of the N-methylated alkaloid mixture, was also obtained from E by catalytic hydrogenation. Its n. m. r. spectrum showed the expected features for the structure assigned to it: the complete lack of signals downfield from those for the N-methyl groups showed the absence of vinyl protons, and the shift upfield of the three-proton singlet for the C_{10}-methyl group from 9.01 τ to 9.22 τ. The signal for the corresponding methyl group in conessine shifts from 9.07[4] to 9.26 τ [5] on hydrogenation. Alkaloid D was obtained in sufficient amount for analysis, and gave C, 80.27; H, 12.04; N, 7.61; calc. for $C_{25}H_{46}N_2$, C, 80.15; H, 12.38; H, 7.48. It had m.p. 109-10°, $[\alpha]_D^{27}$ + 13° (C=3.72, $CHCl_3$)[6].



Alkaloid E



Alkaloid D

Alkaloids A and B were convertible into alkaloids D and E by N-methylation (identity shown by TLC in three solvent systems), and could be converted into a mixture of two (by TLC) acetates. These are so nearly identical in properties that separation has not yet been accomplished. The n. m. r. spectrum of the acetylated material (Fig. 2) is revealing. This spectrum is exactly what would be expected for the 3-dimethylamino-20-methyl-20-acetaminopregnene/pregnane pair: the split signals for the N-methyl and acetyl-methyl groups are characteristic of the $-N(CH_3)COCH_3$ grouping. The six-proton singlet at 7.70 τ represents the 3-dimethylamino grouping. The presence of a signal of less than one proton intensity in the vinyl region indicates that the mixture contains both the pregnene and the pregnane.

Alkaloid C appears to contain oxygen; it has not yet been studied in detail.

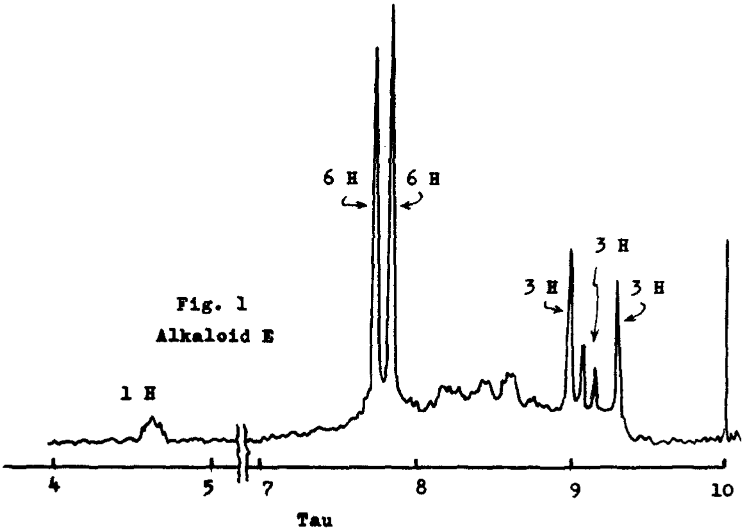


Fig. 1
Alkaloid E

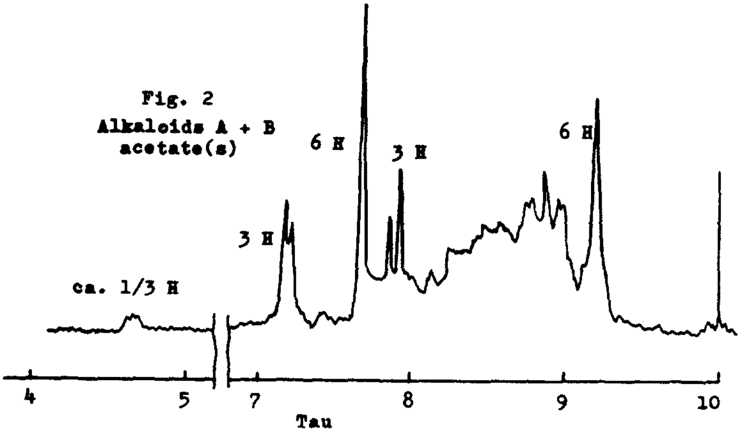


Fig. 2
Alkaloids A + B acetate(s)

References

1. K. S. Brown and S. M. Kupchan, J. Am. Chem. Soc., 84, 4592 (1962).

2. L. Lábler and F. Šorm, Coll. Czech. Chem. Comm., 28, 2345 (1963). Reported for kurchessine, m.p. 140-141°, $[\alpha]_D^{20}$ - 40° (see also ref. 3).

3. V. Cerny, L. Lábler and F. Šorm, ibid., 24, 378 (1959).

4. N.M.R. Spectra catalog, Varian Assoc., Palo Alto, Calif., Spectrum No. 359.

5. M. M. Janot, X. Monseur, C. Conreur and R. Goutarel, Bull. Soc. chim. France, 1962, 285.

6. M. M. Janot, F. Lainé, Q. Khuong-Huu and R. Goutarel, Bull. Soc. chim. France, 1962, 111. Reported for 3β,20α-bisdimethylamino-5α-pregnane, m.p. 112°, $[\alpha]_D^{20}$ +22°.