

BUXUS ALKALOIDS. PART III.* THE STRUCTURE OF "ALKALOID-L"
AND ITS CORRELATION WITH CYCLOMICROPHYLLINE-A.

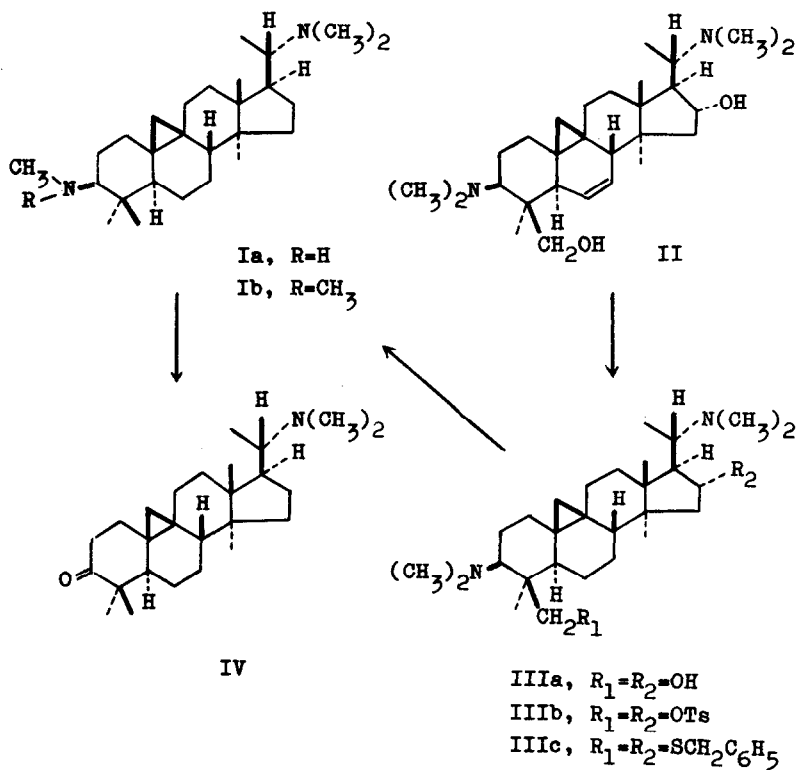
T. Nakano and M. Hasegawa

Faculty of Pharmaceutical Sciences, Kyoto University,
Kyoto, Japan

(Received 12 October 1964)

Investigation of the alkaloidal constituents of Buxus microphylla Sieb. et Zucc. var. suffruticosa Makino forma major Makino¹ has led us to the isolation of a new alkaloid, $C_{27}H_{48}N_2$, m.p. 200-202°, $[\alpha]_D^{25} +76^\circ$ (c, 1.09 in $CHCl_3$). This alkaloid, unlike the other known groups of alkaloids,² contains no oxygen function, but its close similarity to the latter alkaloids was indicated by the n.m.r. signals³ in pyridine at 7.50 (3H, N-CH₃), 7.80 (6H, N-(CH₃)₂), 8.87 (3H, quaternary CH₃), 8.98 (3H, quaternary CH₃), 9.03 (3H, quaternary CH₃), 9.10 (3H, quaternary CH₃), 9.16 (3H, doublet, J 6 cps; tertiary CH₃), and 9.51 and 9.72 τ (2H, doublets, J 4 cps; cyclopropyl methylene). From biogenetic considerations as well as the finding of four instead of three quaternary methyl groups in the above n.m.r. spectrum, assumed that this alkaloid has structure (Ia).

For part II, see T. Nakano and S. Terao, Tetrahedron Letters, No. 18, 1045 (1964).



On methylation with formic acid-formalin, this alkaloid afforded the *N,N'*-dimethyl derivative (Ib), C₂₈H₅₀N₂, m.p. 206-207°, [α]_D +31° (c, 0.54 in CHCl₃), with the n.m.r. peaks at 7.70 (6H, N-(CH₃)₂) and 7.80 τ (6H, N-(CH₃)₂). This *N,N'*-dimethyl compound could be derived from cyclomicrophylline-A² as follows. Catalytic hydrogenation of cyclomicrophylline-A (II) yielded the dihydro derivative²

(IIIa), which, on heating with tosyl chloride in pyridine, was led to the ditosylate (IIIb). Treatment of the ditosylate (IIIb) with sodium benzylmercaptide⁴ in dimethylformamide at 100° for 4 hours gave the bis-benzyl thioether (IIIc). This benzyl thioether, after purification by chromatography on alumina and subsequent desulphurisation with Raney nickel, furnished the hydroxyl-free compound (Ib). The identity of both samples was established by m.p., mixed m.p., rotation, and infrared and n.m.r. spectra.

Evidence for the assignment of the methylamino group to the 3-position was provided by subsequent experiments. Ruschig degradation⁵ of this alkaloid led through the chloramine to the amino ketone (IV), m.p. 194°, $[\alpha]_D +14^\circ$ (c, 0.82 in CHCl_3), $\lambda_{\text{max}}^{\text{KBr}}$ 5.84 μ (C=O). In the n.m.r. spectrum of this amino ketone, a signal corresponding to six protons appeared at 7.78 τ . Since it was shifted downfield upon addition of trifluoroacetic acid, this signal is apparently due to a dimethylamino grouping. The negative Cotton effect curve⁶ of the amino ketone (IV), as well as the absence of the n.m.r. signal of a methyl ketone group, confirmed that this amino ketone has not the 20-keto but the 4,4'-dimethyl-3-keto system.

After our present work had been completed, the structure of "Alkaloid-L",⁷ one of the alkaloids of Buxus sempervirens L. appeared in the preliminary form. Our alkaloid seems to correspond to this "Alkaloid-L", and the conclusion obtained by us is completely consistent with that arrived at by Arigoni et al.⁸ through a different sequence of reactions.

All compounds reported in this paper gave satisfactory elementary analyses.

Acknowledgments. This work was supported by the National Heart Institute (grant No. GM 09362-03) of the National Institutes of Health, U.S. Public Health Service.

References

1. This plant is a variety of B. microphylla Sieb. et Zucc. var. suffruticosa Makino which we previously investigated.
2. T. Nakano and S. Terao, Tetrahedron Letters, No. 18, 1035, 1045 (1964).
3. The spectra were measured on a Varian A-60 spectrometer in deuterated chloroform unless otherwise stated; chemical shifts are reported in τ values using tetramethylsilane as internal standard. We are indebted to Dr. T. Shingu for these determinations.
4. C. A. Henrick and P. R. Jefferies, Tetrahedron Letters, No. 24, 1507 (1964); A. S. Hussey, H. P. Liao, and R. H. Baker, J. Amer. Chem. Soc., 75, 4727 (1953).
5. L. Labler and F. Sorm, Coll. Czech. Chem. Comm., 24, 2975 (1960).
6. G. Djerassi, Optical Rotatory Dispersion, p. 90. McGraw-Hill, New York (1960).
7. E. Schlittler, K. Heusler, and W. Friedrich, Helv. Chim. Acta, 32, 2209 (1949); K. Heusler and E. Schlittler, ibid., 32, 2226 (1949); W. Friedrich and E. Schlittler, ibid., 33, 873 (1950); E. Schlittler and W. Friedrich, ibid., 33, 878 (1950).
8. J. P. Calame and D. Arigoni, Chimia, 18, 185 (1964).