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THE STRUCTURE OF NARDOSTACHONE

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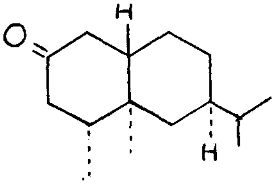
(+)-Nardostachone is a sesquiterpenoid ketone occurring in Indian spikenard oil (*Nardostachys jatamansi* D.C.).[1,2] On the basis of spectral evidence, and conversion to tetrahydronootkatone (1) on hydrogenation, structure and stereochemistry 2 have been advanced for the ketone.[1,2]



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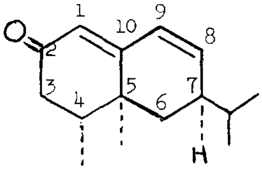

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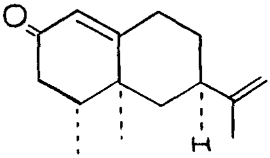

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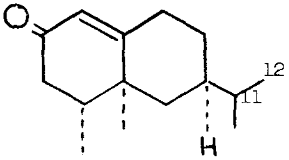

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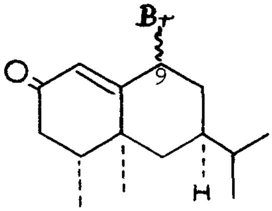
The reported[1,2] ultraviolet principal absorption maximum ($\lambda^{EtOH}_{max.}$ 298 mμ, ε 15,200) of nardostachone, however, is not in agreement with structure 2, for which the calculated value is 280 mμ, on the basis of Woodward's rules.[3] Nor is the reported[1] maximum (317 mμ) for the semicarbazone consistent with this structure for the ketone.

Because of these discrepancies, an unambiguous synthesis of 2 was effected, starting from (+)-nootkatone, of known structure and absolute configuration 3[4]. Selective hydrogenation of (+)-nootkatone, using tristriphenylphosphinechlororhodium as homogeneous catalyst,[5] afforded 11,12-dihydronootkatone (4) ($\lambda^{EtOH}_{max.}$ 238 mμ, no $C=CH_2$ band in infrared spectrum). Reaction of the latter with *N*-bromosuccinimide in carbon tetrachloride yielded the 9-bromoketone 5,[6] which was not purified but dehydrobrominated directly by heating with γ-collidine.[6] One mole of collidine hydrobromide was formed, and a homogeneous (t.l.c. and g.l.c.) product obtained which, on the basis of its analysis and spectral and chemical properties must be formulated as 2. The compound had $\lambda^{EtOH}_{max.}$



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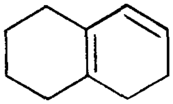

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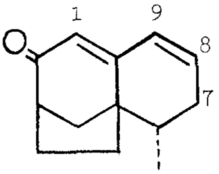

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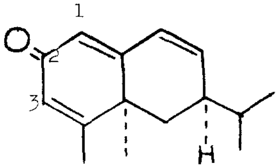

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283 mμ (ε 18,500), $\nu_{max.}^{film}$ 1661 (conjugated C=O), 1623, 1590 (conjugated C=C), 1416 (CH_2CO) and 1389 cm.$^{-1}$ (CMe_2). Its n.m.r. spectrum in the olefinic hydrogen region was very simple: two signals only appeared, at 6.2 (singlet, 2H, C_8-H and C_9-H in 2), and at 5.7 ppm (TMS=0) (singlet, slight evidence of splitting into a doublet, 1H, C_1H). A pair of doublets (6H and 3H) and a singlet (3H) (methyl groups in 2) were observed in the 1.0 ppm region. This spectrum is very different in the low field region from that of nardostachone,[1,2] and it is apparent that the natural ketone cannot be represented by 2. Support for this view is provided by the fact that the semicarbazones of nardostachone and 2, m.pp. 230-232° (decomp.) and 213° (decomp.) respectively, are different, showing a large m.p. depression on admixture.[7]

The simplicity of the low field n.m.r. spectrum of 2 indicates absence of coupling between the C_8 and C_9 hydrogens, which presumably have the same chemical shift. Further, the absence of coupling between these protons and the allylic proton at C_7 is explained by the dihedral angle between them, which is about 90°. Cases for comparison include 6, the spectrum of which shows but a single peak in the vinyl hydrogen region,[8] and 7, which shows a high field singlet (C_1-H) and a low field doublet (C_8-H and C_9-H, coupled to one hydrogen at C_7, J=2 cps).[9]

A re-examination of the published evidence[1,2] suggests that nardostachone may be better formulated as the cross-conjugated trienone 8, $C_{15}H_{20}O$. The analytical figures for the ketone[2,10] (found: C, 82.62; H, 9.75; $C_{15}H_{20}O$ requires: C, 82.28; H, 9.32) and for its semicarbazone (found: C, 70.05; H, 8.91; N, 15.41; $C_{16}H_{23}N_3O$ requires: C, 70.29; H, 8.48; N, 15.37) are in reasonable agreement with this molecular formula for the ketone. Ultraviolet absorption maxima for this structure would be expected in the

220, 250 and 300 (principal) mμ regions.[11] The natural ketone is reported[1,2] to have a subsidiary maximum at 232 mμ. The new structure can be reconciled reasonably with the published n.m.r. spectrum, with the exception of the doublet appearing at 0.90 ppm (3H), assigned to a $>CHCH_3$ group, and the integration of (1H) of the signal at 5.58 ppm, which would have to be 2H, assuming that the hydrogens at C_1 and C_3 in 8 have the same chemical shift.

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5. Cf. M. Brown and L. W. Piskiewicz, J. Org. Chem., 32, 2013 (1967), who reduced eremophilone selectively by this procedure.
6. Cf. C. Meystre and A. Wettstein, Experientia, 2, 408 (1946), for an analogous sequence in the steroid field.
7. Sample of nardostachone semicarbazone kindly supplied by Dr. K. K. Chakravarti, National Chemical Laboratory, Poona, India.
8. R. B. Bates, R. H. Carnighan and C. E. Staples, J. Amer. Chem. Soc., 85, 3030 (1963).
9. J. A. Marshall and S. F. Brady, Tetrahedron Letters, 1387 (1969). Spectrum kindly supplied by Dr. Brady, Northwestern University, Evanston, Illinois.
10. An error appears in the analytical figures quoted[1,2] for the ketone. $C_{15}H_{22}O$ requires: H, 9.32 should be requires: H, 10.16%.
11. For analogues of 8 in the steroid field see C. Djerassi, G. Rosenkranz, J. Romo, St. Kaufmann and J. Pataki, J. Amer. Chem. Soc., 72, 4534 (1950).