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SHORT COMMUNICATION

STRUCTURE AND ABSOLUTE CONFIGURATION OF NARCHINOL A*

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Abstract—From Chinese spikenard, *Nardostachys chinensis* (Valerianaceae), a new trisnorsesquiterpenic diketo-alcohol, narchinol A has been isolated and its stereostructure deduced as I on the basis of chemical, and physical data.

INTRODUCTION

THE CRUDE drug spikenard prepared from the rhizomes and roots of both *Nardostachys jatamansi* De Candolle, indigenous to India, and *N. chinensis* Batalin, indigenous to China (Valerianaceae), have been used as an Oriental medicine (aromatic stomachic and sedative) and a native perfume. The constituents of *N. jatamansi* have been subjected to numerous investigations. On the other hand, those of *N. chinensis* have been examined only by Rücker *et al.*, who reported the occurrence of several sesquiterpenoids.[1]

As part of our chemical investigation on valerianaceous plants, we have recently carried out analysis of the Chinese spikenard prepared from *N. chinensis* and, as a result, isolated a novel trisnorsesquiterpenoid for which the name narchinol A is proposed. We now wish to describe evidence which indicates the structure I for this norisoprenoid.

RESULTS

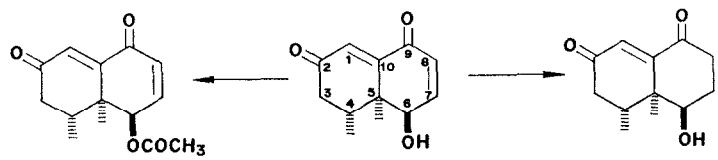
The light petroleum soluble portion of the methanol extract of the crude drug was submitted to chromatography over neutral alumina and separated into light petroleum, light petroleum–benzene, benzene, and ethyl acetate eluted fractions. Careful rechromatography of the ethyl acetate eluted fraction over silica gel gave the new diketo-alcohol, narchinol A, as yellow crystals.

Narchinol A analyzed for $C_{12}H_{14}O_3$ which was confirmed by the occurrence of the molecular ion peak at *m/e* 206 in the mass spectrum. The IR spectrum of narchinol A shows strong bands at 1663 and 1647 cm^{-1} associated with conjugated carbonyl groups and at 3390 cm^{-1} indicating a hydroxyl group. Consistent with this observation, the UV spectrum exhibits maxima at 265 and 400 nm (log ϵ 4·06 and 1·62, respectively), indicating the presence of a notable conjugation. Narchinol A was acetylated to give the monoacetate (II) (IR spectrum: acetoxyl group at 1730 and 1226 cm^{-1}). The NMR spectrum of the mono-acetate

* Part XLV of the series "Sesquiterpenoids". For Part XLIV see H. HIKINO, M. ONO and T. TAKEMOTO, *Yakugaku Zasshi* in press.

[1] K. E. SCHULTE, G. RÜCKER and G. GLAUCH, *Planta Med.* **15**, 274 (1967); G. RÜCKER, *Liebigs Ann. Chem.* **717**, 221 (1968); G. RÜCKER, *Chem. Ber.* **102**, 2691 (1969); G. RÜCKER, *ibid.* **102**, 2697 (1969); G. RÜCKER, *ibid.* **102**, 2707 (1969); G. RÜCKER, *Planta Med.* **19**, 16 (1970); G. RÜCKER, *Liebigs Ann. Chem.* **733**, 152 (1970).

(II) shows the presence of an acetoxyl methyl (δ 2·04 ppm), a methine bearing the acetoxyl (δ 5·27 ppm), an α-hydrogen and a β-hydrogen on a β-substituted, α,β-unsaturated carbonyl (δ 6·38 and 7·19 ppm, respectively), an α-hydrogen on a β,β-disubstituted, α,β-unsaturated carbonyl (δ 6·74 ppm), a secondary methyl (δ 1·00 ppm), a tertiary methyl (δ 1·22 ppm), a methylene (δ 2·38 and 2·40 ppm), and a methine (δ 2·72 ppm), all the hydrogens in the molecule being accommodated. NMDR experiments revealed that the vinyl hydrogen at 6·38 ppm is coupled with the vinyl hydrogen at 7·19 ppm (J = 10 Hz), that the carbinyl hydrogen at 5·27 ppm coupled with the vinyl hydrogens at 7·19 ppm (J = 6 Hz), that the vinyl hydrogen at 6·74 ppm coupled with one of the methylene at 2·40 ppm ($J \simeq 0$ Hz), and that the methine hydrogen at 2·72 ppm coupled with the methylene hydrogens at 2·38 ppm (J = 11 Hz) and 2·40 ppm (J = 6 Hz) and with the methyl hydrogens at 1·00 ppm (J = 6 Hz). Although a long range coupling was observed between the carbinyl hydrogen at 5·27 ppm and the vinyl hydrogen at 6·74 ppm (J = 0·7 Hz), there was an intramolecular nuclear Overhauser effect (NOE) between the secondary methyl hydrogens and the carbinyl hydrogen (10%), demonstrating that those hydrogens are situated in a spatially close relationship. Combined evidence leads to the gross structure of narchinol A as I.



(II) (I) (III)

When narchinol A was subjected to catalytic hydrogenation over Adams' catalyst in methanol, hydrogen was consumed very rapidly. The reaction was stopped immediately after the consumption of 1 mole of hydrogen, when the original yellow solution turned nearly colorless. The dihydro-derivative (III) obtained, retained the 1(10)-ene-2,9-dione system as was shown by UV maxima at 251, 318, and 400 nm (log ε 4·04, 2·15, and 1·56, respectively), IR bands at 1658 and 1622 cm^{-1}, and an NMR signal at 6·41 ppm, but the saturation of the C-7:C-8 ethylenic linkage was revealed by the disappearance of the C-7 and C-8 vinyl hydrogen signals present in the spectrum of narchinol A and instead by the formation of 4H signals in the region 2–3 ppm. It may be noted that a long range coupling between the C-1 and C-6 hydrogens was observed also in this case. The CD curve of the enedione (III) ($[\theta]_{330}$ −1980, $[\theta]_{268}$ −14 200, $[\theta]_{232}$ +34 700) is comparable with that of cholest-4-ene-3,6-dione ($[\theta]_{360}$ −3570, $[\theta]_{325}$ −2970, $[\theta]_{266}$ −5710, $[\theta]_{226}$ +25 000), though the maxima of both the curves showed slight displacements. This observation not only confirms the gross structure but also indicates the α-configuration of the C-5 methyl group. The coupling constants between the C-3 hydrogens and the C-4 hydrogen (J = 11 and 6 Hz) in the spectrum of the acetate (II) show the quasi-equatorial situation (consequently α-orientation) of the C-4 methyl group. The quasi-axial nature (consequently β-orientation) of the C-6 hydroxyl group was deduced by the facts that in the NMR spectrum of the acetate (II); (1) the coupling constant between the C-6 carbinyl hydrogen and the C-7 vinyl hydrogen is 6 Hz, showing the dihedral angle is fairly small, (2) an NOE was observed between the C-6 and C-7 hydrogens (5%), indicating the spatially close relationship of both the hydrogens, (3) as has been mentioned before, an NOE was found between the C-4 (equatorially oriented) methyl and the C-6 hydrogen, and (4) in the NMR spectrum of

the dihydro-derivative (III), the coupling constants between the C-6 carbinyl hydrogen and the C-7 methylene hydrogens are fairly small (J = both 2·5 Hz). Accumulated data have established that narchinol A has the stereostructure I. From the biogenetic point of view, it is thought that narchinol A is derived from a sesquiterpenic intermediate of the eremophilane type by loss of a C_3 unit (the C-7 isopropyl residue).

EXPERIMENTAL

M.ps are uncorrected. NMR spectra were recorded at 100 MHz unless otherwise stated. Chemical shifts are expressed in ppm from Me_4Si as internal standard, and coupling constants (J) in Hz. Abbreviations: s = singlet, d = doublet, and dd = doublet of doublets.

Isolation of narchinol A. The crude drug Chinese spikenard (2 kg), the dried rhizomes and roots of *Nardostachy chinensis* De Candolle, was extracted 4 times with refluxing MeOH (14 l. each) for 5 hr (each extraction). The combined MeOH soln was concentrated to give an extract, which on extraction with light petroleum (1·2 l.) and evaporation yielded a residue (126 g). Chromatography of the residue (126 g) over neutral alumina afforded light petroleum, light petroleum–benzene (10:1), benzene, and EtOAc eluted fractions. The EtOAc eluted fraction was subjected to rechromatography over silica gel. Elution with benzene–EtOAc (1:1) furnished a crystalline mass (0·34 g) which on crystallization from EtOAc gave *narchinol A* as yellow plates (328 mg), m.p. 146–148°. CD (c = 0·213, MeOH): $[\theta]_{460}$ 0, $[\theta]_{436}$ −610, $[\theta]_{426}$ −510, $[\theta]_{416}$ −800, $[\theta]_{402}$ −260, $[\theta]_{396}$ −350, $[\theta]_{390}$ 0, $[\theta]_{355}$ +800, $[\theta]_{320}$ 0, CD (c = 0·0125, MeOH): $[\theta]_{270}$ −22 900, $[\theta]_{254}$ 0, $[\theta]_{236}$ +21 800, $[\theta]_{222}$ 0. MS *m/e*: 206 (M^+ peak), 189, 188, 177, 162, 145, 135, 121, 107, 91, 79, 55 (base peak), 39; UV λ_{max}^{EtOH} nm (log ϵ): 265 (4·06), 400 (1·62); IR ν_{max}^{KBr} cm^{-1}: 3390 (OH), 1663, 1647, 1605 (enones); NMR (C_5H_5N, 60 MHz): 3H d at 1·00 (J = 6, $C_{(14)}\underline{H}_3$), 3H s at 1·05 ($C_{(15)}\underline{H}_3$), 1Hd* at 2·41 (J = 10, $C_{(3)}\underline{H}$), 1H d* at 2·44 (J = 7·5, $C_{(3')}\underline{H}$), 1H m at ~3·25 ($C_{(4)}\underline{H}$), 1H d at 4·23 (J = 6, $C_{(6)}\underline{H}$), 1H d at 6·33 (J = 10, $C_{(8)}\underline{H}$), 1H s at 6·90 ($C_{(1)}\underline{H}$). (Found: C, 69·52; H, 6·91. $C_{12}H_{14}O_3$ required: C, 69·88; H, 6·84%).

Acetylation of narchinol A. Narchinol A (30 mg) was dissolved in Ac_2O (0·5 ml) and pyridine (1·0 ml) and the mixture set aside at room temp. for 17 hr. Upon isolation in the usual way, the product was crystallized from EtOAc to give *narchinol A acetate* as yellow needles (26 mg), m.p. 96·5–98°. IR ν_{max}^{KBr} cm^{-1}: 1730, 1226 (acetoxyl), 1667, 1610 (enones); NMR ($CDCl_3$): 3H d at 1·00 (J = 6, $C_{(14)}\underline{H}_3$), 3H s at 1·22 ($C_{(15)}\underline{H}_3$), 3H s at 2·04 ($C\underline{H}_3$—COO—), 1H d* at 2·38 (J = 11, $C_{(3)}\underline{H}$), 1H d* at 2·40 (J = 6, $C_{(3')}\underline{H}$), 1H dd at 5·27 (J = 1, 6, $C_{(6)}\underline{H}$), 1H d at 6·38 (J = 10, $C_{(8)}\underline{H}$), 1H d at 6·74 (J = 1, $C_{(1)}\underline{H}$), 1H dd at 7·19 (J = 6, 10, $C_{(7)}\underline{H}$).

Catalytic hydrogenation of narchinol A. Narchinol A (57 mg) in MeOH (5 ml) was hydrogenated over PtO_2 (9 mg). After the uptake of 1 mole of H_2, the mixture was worked up in the customary manner, and the product (50 mg) chromatographed on silica gel (20 g). Benzene–EtOAc (10:1) eluate (38 mg) was crystallized from EtOAc to yield *dihydronarchinol A* as pale yellow prisms (18 mg), m.p. 97–99°. CD (c = 0·226, MeOH): $[\theta]_{447}$ 0, $[\theta]_{410}$ +240, $[\theta]_{388}$ 0, $[\theta]_{330}$ −1980, $[\theta]_{300}$ −990, $[\theta]_{268}$ −14 200, $[\theta]_{254}$ 0, $[\theta]_{232}$ +34 700, $[\theta]_{208}$ 0, MS *m/e*: 208 (M^+, base peak), 165, 151, 123, 109, 85, 53, 41; UV λ_{max}^{MeOH} nm (log ϵ): 251 (4·04), 318 (2·15), 400 (1·56); IR ν_{max}^{KBr} cm^{-1}: 3420 (OH), 1665, 1622 (enedione); NMR ($CDCl_3$): 3H d at 1·02 (J = 7, $C_{(14)}\underline{H}_3$), 3H s at 1·05 ($C_{(15)}\underline{H}_3$), 1H d* at 2·32 (J = 11, $C_{(3)}\underline{H}$), 1H d* at 2·34 (J = 7, $C_{(3')}\underline{H}$), 1H broad dd at 4·03 (J = 2·5, 2·5, $C_{(6)}\underline{H}$), 1H d at 6·41 (J = 0·8, $C_{(1)}\underline{H}$).

Cholest-4-ene-3,6-dione. CD (c = 0·0920, MeOH): $[\theta]_{440}$ 0, $[\theta]_{360}$ −3570, $[\theta]_{325}$ −2970, $[\theta]_{290}$ −710, $[\theta]_{266}$ −5710, $[\theta]_{226}$ +25 000, $[\theta]_{208}$ 0.

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* Part of the A or B part of the ABX spectrum.

Key Word Index—Nardostachys chinensis; Valerianaceae; sesquiterpene; narchinol A.