The Structure of Nepetidin
a New Triterpenoid from
Nepeta hindostana

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Nepetidin, a new triterpene isolated from
Nepeta hindostana has been assigned the struc-
ture lup-20(29)-ene-1β,3β,11α-triol.

Recently we reported [1] the isolation of a tri-
terpene diol, nepeticin, from Nepeta hindostana
and the structure lup-20(29)-ene-3β,11α-diol (1) was
suggested for it. In the present paper we wish to
report the isolation of another closely related tri-
terpene alcohol, nepetidin (2) from the same plant.

Nepetidin was isolated in a small quantity from
the hexane extract of Nepeta hindostana. It crystal-
lized from ethyl acetate in the form of short colour-
less rods m.p. 290° [α]D + 16. The field ionization
mass spectrum (M+ at 458) suggested the molecular
formula C30H50O3 which was further confirmed
through elemental analysis. The UV spectrum in
methanol shows only end absorption at 208 nm.
The IR spectrum (CHCl3) shows absence of ab-
sorption in carbonyl region but a band due to OH
group was present at 3400 cm⁻¹. The PMR spectrum of nepetidin in CDCl3 at 400 MHz
shows methyl singlets at δ 0.70 (1 × CH₃), 0.72
(1 × CH₃), 0.90 (3 × CH₃) and 0.95 (1 × CH₃). There
is a broad singlet at δ 1.68 due to the vinylic methyl
group. Two olefinic protons of the isopropenyl
group appeared at δ 4.58 and 4.71 (each d, J = 1 Hz).
Two carboxylic methine proton signals of nepetidin,
similar in shape, are visible as four line pattern each
centred at δ 3.20 and 3.50. Both of these carboxylic
methine protons showed one axial-axial and one
axial-equitorial coupling (Jaa = 11.3, Jae = 5.5 Hz).
This suggest that both hydroxyl groups are equi-
torial. The signal centred at δ 3.20 possessed an
identical chemical shift and coupling constants of proton geminal to βOH group attached to C-3 in
triterpene. The third carboxylic proton appeared as
sexett at δ 3.89 (two Jaa = 9.5 Hz, one
Jae = 6.34 Hz) showing that hydroxyl group is at
equitorial position with two axial and one equitorial
protons at neighbouring carbon atoms. The shape
of signal, chemical shift and coupling constants
resembled closely to H-11β signal in nepeticin [1].

The spectroscopic data suggest that nepetidin
belongs to the lup-20(29)-ene series of triterpenoids,
which finds supports from biogenetic point of view,
since from the same plant nepeticin* (lup-20(29)-ene
3β, 11α-diol) has been isolated.

The electron impact mass spectrum of nepetidin
showed the highest peak at m/e 440.3554 correspond-
ting to (M+-H₂O). Other peaks were seen m/e 425 and
m/e 389 due to (M+-H₂O-CH₃) and (M+-3H₂O-CH₃)
respectively. The mass spectrum of nepetidin ex-
hibits a peak at m/e 325.289518 corresponding to
C₂₅H₄₇, according to high resolution mass measure-
ment, presumably resulting from characteristic
fragmentation involving the loss of ring A together
with the two hydroxyl groups from the ion (M+-H₂O).
It is assumed here that a elimination of molecule of
water from the two hydroxyl group present at C-1
and C-11 is followed by further fragmentation as
shown in chart-I. Other peaks were present at
m/e 255, 229, 217, 203, 189 and 175. The last two
peaks shows the absence of any substitution in
either ring D or E.

From the mass spectrum it was concluded that
the two hydroxyl groups are present in ring A. The
vincinal position of these hydroxyl groups is ruled
out on the basis of negative result of attempted

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Chart I.

* The skeleton of nepeticin was also confirmed through the Jones oxidation followed by Huang-Minion
reduction whereby lup-20(29)-ene m.p. 163 °C (M*-410) lit. [2] m.p. 163 °C was obtained.
oxidation with sodium metaperiodate and also the observed splitting pattern in the NMR spectrum. Any hydroxyl group could not be situated at C-23 or C-24 position since the presence of hydroxyl group at either of these positions would have exhibition an ABq (or a singlet) for two hydroxy methylene protons [3]. The only position left for hydroxyl group is C-1.

In the presence of acetone and catalytic amount of sulphuric acid nepetidin forms an acetonide m.p. 230 °C. The field ionization mass spectrum of nepetidin acetonide shows the molecular ion peak at m/e 498, while E.I. mass spectrum showed the highest peak at m/e 440 (M$^+$-(CH$_3$)$_2$C=O). The acetonide is apparently formed involving OH groups at C-1 and C-11. Dreiding model shows that the 1β-OH and 11α-OH are close together and can easily react with acetone to form an acetonide.

With acetic anhydride and pyridine at room temperature nepetidin forms a monoacetate m.p. 128 °C. The IR spectrum of nepetidin monoacetate shows strong peak at 1720 cm$^{-1}$ for C=O group, apart from peak at 3500 cm$^{-1}$ for OH groups which resisted acetylation under these condition. The mass spectrum of nepetidin monoacetate shows the highest peak at m/e 482 corresponding to (M$^+$-H$_2$O). Other important peaks were at m/e 422 (M$^+$-H$_2$O-CH$_3$-COOH), 407 (M$^+$-H$_2$O-CH$_3$-COOH-CH$_3$). The presence of peak at m/e 389 shows the loss of two water molecules along with acetic acid and methyl group. When acetylation was carried out with heating a mixture of mono and diacetates was obtained. The diacetate was purified through preparative chromatography whereby it was obtained in an amorphous but pure state. The NMR spectrum of diacetate in CDC$_3$ and 400 MHz shows the methyl singlets at δ 0.72 (1 × CH$_3$), 0.76 (1 × CH$_3$), 0.79 (1 × CH$_3$), 0.92 (1 × CH$_3$), 0.93 (1 × CH$_3$), 0.98 (1 × CH$_3$), and a broad singlet at δ 1.60. The two OAc groups were confirmed through the singlets at δ 1.89 and 1.99 in NMR spectrum. The proton geminal to unreacted hydroxyl group in diacetate gave multiplet centred at δ 3.62 which is close to the chemical shift of δ 3.5 assigned for C-1 proton in nepetidin. The carboxylic protons on C-3 and C-11 are shifted to δ 4.5 and 4.95 respectively in the diacetyl derivative, the multiplicity and the coupling constant remaining the same as in nepetidin. It is therefore concluded that the acetylation occurs only at C-3 and C-11 hydroxyl group.

The formation of diacetate was further confirmed through F.I. mass spectrum, M$^+$ at 542 while E.I. mass spectrum shows very weak molecular ion peak at m/e 542 and a strong peak at m/e 524 (M$^+$-H$_2$O).

On Jones oxidation nepetidin forms monoketone as major product along with two minor products. The monoketone was separated and purified through preparative chromatography, m.p. 104 °C. It shows strong peak at 1700 cm$^{-1}$ in IR spectrum for carbonyl group. The mass spectrum exhibits highest peak at 438 (M$^+$-H$_2$O).

In view of the chemical and spectral data discussed above the structure lup-(29)-ene-1β,3β,11α-triol (II) is suggested for nepetidin. The structure is further supported by the $^{13}$C NMR spectrum (Table I).

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