EXCISANIN A AND B, NEW DITERPENOIDS FROM RABDOSIA EXCISA

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Chemical investigation of the bitter principles from Rabdosia Excisa
has led to the isolation and characterization of two new diterpenoids
having an ωnt-kaurene skeleton, excisinan A and B, and their
structures were established by spectroscopic and chemical data.

We wish to report the isolation and structural elucidation of excisinan
A (1) and B (2), new ωnt-kaurenoinds from the leaves of Rabdosia Excisa (Maxim.)
Hara (collected at Anshan district of China in July of 1979) together with
kamebakaurin (3), kamebactetal B' (4), and kamebanin (5). Excisinan A and B show
a prominent cytotoxic effect against Ehrlich carcinoma cells in vitro and have a
significant anti-neoplastic effect on some of transplantable animal tumors, such
as ECA, S180, P388, etc., and appear to be the first 12-oxygenated ωnt-kaurenoinds
from Rabdosia plants.

Excisinan A [1] ; C_{20}H_{30}O_5 (M+ 350) ; mp. 262-264 °C ; [α]_D^20 -27.7 (c=1.01,
C_5H_5N) ; λ max (EtOH) 234 nm (ε 5660) ; ν max (KBr) 1713 and 1645 cm⁻¹ ; H nmr
(C_5D_5N) δ 5.38 and 6.31 (each 1H, s) ; 13C nmr (CDCl₃ + CH₂OH) δ 118.5 (t) and
147.0 (s) (exomethylene), and δ 210.6 (s, ketone) gave a dihydro compound [9 ;
C_{20}H_{32}O_5 ; mp. >308 °C] by catalytic hydrogenation in PtO₂, which showed a negative
cd effect [Δε_{307} -0.37] in methanol. These spectroscopic data suggest that
Excisinan A (1) has four secondary hydroxyl groups: \( \text{IR } 3430-3380 \text{ cm}^{-1} \); 
\(^1H\text{ nmr } \delta 3.48 (1H, dd, 6 and 10 Hz), 4.41 (1H, t, 4 Hz), 4.87 (1H, dd, 8 and 11 Hz), and 5.99 (1H, s); \(^13C\text{ nmr } \delta 81.8, 75.3, 73.8, and 72.0 \text{ (each doublet).} \)

This was confirmed by conversion of (1) to a tetraacetate \([6; \text{ mp. } 206-208 ^\circC]\) by acetylation (acetic anhydride-pyridine). On the other hand, (1) gave the 7,14-monoacetone \([7; \text{ C}_{24}H_{34}O_5 \text{; mp. } 244-246 ^\circC]\) on treatment with acetone and anhydrous copper (II) sulfate. Oxidation of (1) with Beckmann mixture afforded a trione \([8; \text{ C}_{20}H_{26}O_5 \text{; mp. } 247-250 ^\circC]; \text{ }^1H\text{ nmr (CDCl}_3\text{) } \delta 4.87 (s, 14a-H); 4.46 (dd, 7 and 10 Hz, 7b-H)\]. These results revealed that two hydroxyl groups are placed at 14b (\( \delta 5.99, 14a-H \)) and 7a (\( \delta 4.87, 7b-H \)) in (1). In fact, NOE (10%) on 14a-H was observed upon irradiation at the signal (\( \delta 1.91, s \)) of the 10-CH\(_3\).

EI-MS peaks of excisinan A (1) at m/z 192 (C\(_{11}H_{12}O_3\)) and 174 (C\(_{11}H_{10}O_2\)), which were formed by cleavage of the B-ring, showed the existence of one hydroxyl group in the A-ring and two hydroxyl groups in the C-ring. The location of the hydroxyl group other than C-14b in the C-ring was elucidated to be at C-12a by the abnormally low chemical shifts of 10-CH\(_3\) and 14a-H, and further the following decoupling experiments. On irradiation at \( \delta 4.41 \) (12b-H), the doublet at \( \delta 3.67 \) (d, 4 Hz, 13a-H) changed into a singlet and the signal pattern at \( \delta 2.07-2.27 \) (m, 11b-H) was deformed. On irradiation at \( \delta 3.67 \), the triplet at \( \delta 4.41 \) collapsed to a doublet (4 Hz). On the other hand, on irradiation at \( \delta 2.17 \), the triplet at \( \delta 4.41 \) collapsed to a doublet (4 Hz) and the doublet at \( \delta 3.98 \) (d, 16 Hz, 11a-H) changed into a singlet. These results suggested that the dihedral angles of 12b-H and 11a-H, and 11a-H and 9b-H are \( \alphaa \), 90\(^\circ\), respectively. Thus, the C-ring of (1) seems to be a deformed chair form. The location of the hydroxyl group in the A-ring to be at 1a position of (1) was shown by the coupling pattern of the signal at \( \delta 3.48 \) (18-H) and the unusually low chemical shift of 11a-H.

Consequently, the structure of excisinan A is represented as (1).

Excisinan B \([2; \text{ C}_{22}H_{32}O_6 \text{ (M}^+\text{ 392)}]; \text{ mp. } 240-243 ^\circC; [\alpha]_D^{28} -13.9 (c=1.00, \text{ C}_{10}H_{20}N\text{ )}; \lambda_{max} (\text{EtOH}) 230 \text{ nm (e 7900)}; \nu_{max} (\text{KBr}) 3400, 1740, 1726, 1713, \text{ and } 1646 \text{ cm}^{-1}\text{]}\) is 12-acetylexcisinan A. The \(^1H\text{ nmr spectrum (C}_{12}D_{2}N\text{) is very similar to that of (1) except for the presence of signal due to an acetyl group (\( \delta 2.07 \)) and down-field shift of 12b-H signal, from \( \delta 4.41 \) in (1) to \( \delta 5.26 \) in (2).}
Excisianin A, $^1$H nmr data in C$_5$D$_5$N solution; $\delta$ values, multiplicity and $J$ values (in Hz) in parentheses

(3) $\delta$ 3.67 (s)
(4) $\delta$ 1.91 (s)
(5) $\delta$ 5.99 (s)

Excisianin B, $^1$H nmr data in CDCl$_3$+CD$_3$OH solution

(6) $R_1=R_2=R_3=R_4=Ac$
(7) $R_1=R_3=H$, $R_2=Ac$, $R_4=CH_3(11) R_1=O$, $R_2=OAc$
(8) $R_1=R_2=O$
(9) $R_1=H$, $R_3=Ac$, $R_2=\text{Other}$
The $^{13}$C nmr of (2), comparing with that of (1), differs only in number of methyl and carbonyl carbons due to acetyl group. Acetylation (acetic anhydride-pyridine) of (2) gave a tetraacetate [mp. 206-208 °C], which was identical with (6) derived from (1). On the other hand, saponification of (2) with 1 N NaOH afforded (1). Excisanin B (2) gave rise to an acetone [10 ; mp. 272-274 °C] and the 1-oxo compound [11 ; mp. 230-233 °C] on treatment with acetone-anhydrous copper (II) sulfate and Beckmann mixture, respectively. In addition, an NOE (18 %) was observed for the singlet at δ 5.62 (14α-H) on irradiation at δ 1.54 (10-CH₃) in (2).

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REFERENCES AND FOOTNOTES


5. The results will be published elsewhere.

6. All crystalline compounds have been characterized by concordant elemental and spectral (ir, uv, nmr, and mass spectra) analyses.


9. The assignments are based on a combination of PND, off-resonance decoupling and comparison with data of kamebain.

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