Tetrahedron Letters Vol. 21, pp 2647 - 2648 0040-4039/80/0701-2647$02.00/0

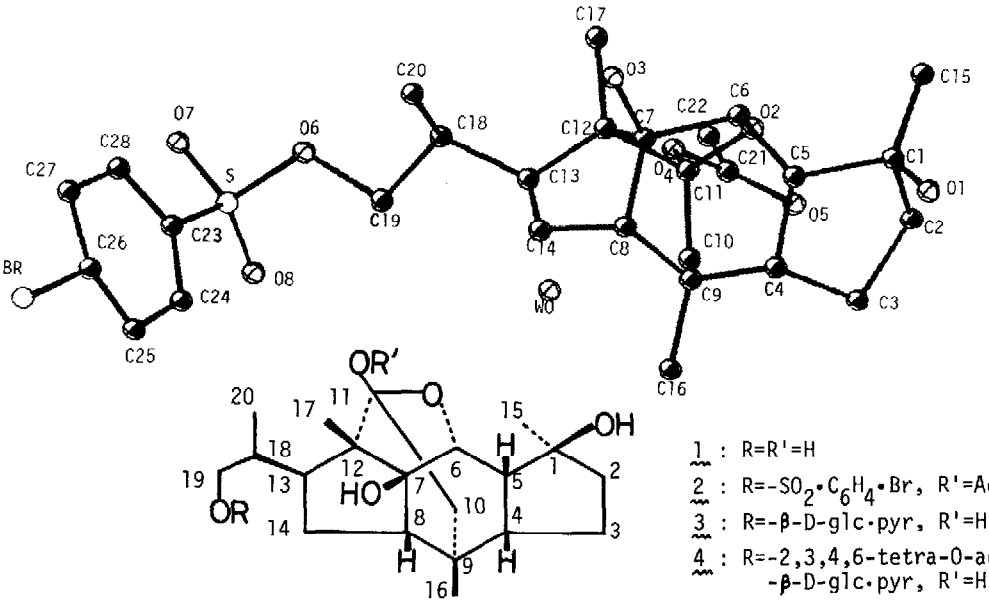
CINNCASSIOL D_1 AND ITS GLUCOSIDE, NOVEL PENTACYCLIC DITERPENES FROM CINNAMOMI CORTEX

T.Nohara*, Y.Kashiwada and T.Tomimatsu
Faculty of Pharmaceutical Sciences, Tokushima University
Shomachi 1-78, Tokushima 770, Japan
M.Kido
Laboratory of Natural Products Chemistry, Otsuka Pharmaceutical Co., Ltd.
Kawauchi-cho, Tokushima 770, Japan
N.Tokubuchi and I.Nishioka
Faculty of Pharmaceutical Sciences, Kyushu University
Higashi-ku, Fukuoka 812, Japan

Summary : A new pentacyclic diterpene with a new skeleton and its glucoside were obtained from the fraction exhibiting anti-complement activity of the water extractive of Cinnamomi Cortex. Their structures were elucidated as 1 and 3 by chemical, spectral and X-ray crystallographic studies.

Two new pentacyclic diterpenes, named cinncassiol D_1 (1) and cinncassiol D_1 glucoside (3), were isolated from the fraction exhibiting anti-complement activity[1] of the water extractive of Cinnamomi Cortex ("Tōkō Keihi"; the dried bark of Cinnamomum cassia Blume).

Cinncassiol D_1 (1), a white powder, $[\alpha]_D$ +12.7° (MeOH), $C_{20}H_{32}O_5$ (FD-MS (m/z) : 352 (M^+), 335 (M^+-OH); EI-MS (m/z) : 352.220 (M^+)), showed in the IR spectrum the absorption due to hydroxyl (3440 cm^{-1}). NMR spectra (in Py-d_5) are as follows; ^{13}C δ : 10.6, 13.5, 24.4, 28.1 (4 x CH_3-), 25.2, 25.5, 37.3, 40.4 (4 x -CH_2-), 36.9, 40.4, 48.6, 51.0, 54.1 (5 x >CH-), 41.0, 57.1 (2 x >C<), 67.3 (-CH_2-O-), 77.2 (>CH-O-), 82.0, 88.6 (2 x >C-O-) and 107.5 (>C<), ^1H δ : 0.90, 1.69, 1.69 (3H each, all s, 3 x tert.CH_3), 1.37 (3H, d, J=7 Hz, sec.CH_3), 3.80 (2H, d, J=8 Hz, -CH_2-O-), 4.44 (1H, br. s, >CH-CH-O-). Based on the above spectral data, 1 was supposed to be a new diterpene. 1 was treated with p-bromobenzenesulfonyl chloride and Py and the product was acetylated (Ac_2O-Py, overnight at r.t.) to give the monoacetyl monobrosylate (2), colorless plates, mp 104-105°, $[\alpha]_D$ 0° (MeOH), ^1H-NMR (in $CDCl_3$) δ : 2.03 (3H, s, -OAc), 7.69, 7.81 (2H each, double d of J=10 Hz, 4 x arom. proton). A single crystal of 2 suitable for a X-ray diffraction study was obtained by recrystallization from dil.MeOH and its data are as follows; $C_{28}H_{37}SO_8Br \cdot H_2O$; monoclinic, space group $P2_1$ (Z=2); lattice constants a=10.222(6), b=10.271(7), c=15.155(6) Å, β=96.91(4)°, V=1579.6 $Å^3$; $D_{(calcd.)}$=1.33, $D_{(obsd.)}$=1.37 g/cm^3. The intensity data of 2192 ($2\theta \leq 45°$) were measured with a Syntex R_3 full automated four-circle diffractometer using ω-2θ scan technique and graphite-monochromated Mo (Kα) radiation (λ=0.71069 Å). The structure was solved by heavy atom method. Block diagonal least squares refinements with isotropic nonhydrogen atoms have currently converged to a standard residual of 0.105 for the 1284 obseved reflections ($I \geq 2.0\sigma(I)$). A computer-generated perspective drawing thus obtained is shown in Fig. 1. Therefore, the molecular structure of cinncassiol D_1 is represented by the formula 1 or its enantiomer.



1 : R=R'=H
2 : R=-SO_2·C_6H_4·Br, R'=Ac
3 : R=-β-D-glc·pyr, R'=H
4 : R=-2,3,4,6-tetra-O-acetyl -β-D-glc·pyr, R'=H

Cinncassiol D_1 glucoside (3), a white powder, $[\alpha]_D$ -4.1° (MeOH), $C_{26}H_{42}O_{10}$ (FD-MS (m/z) : 553 ($M + K^+$), 537 ($M + Na^+$)), on enzymatic hydrolysis with crude hesperidinase liberated cinncassiol D_1 (1) and D-glucose. While 3 was acetylated (Ac_2O-Py, for 20 min. at r.t.)[2] to yield the tetraacetate (4), a white powder, $[\alpha]_D$ -18.6° (MeOH), $C_{34}H_{50}O_{14}$, ^{1}H-NMR (in $CDCl_3$) δ : 2.00, 2.03, 2.05 and 2.09 (4 x OAc), 4.49 (1H, d, J=7 Hz, anomeric proton of glucoside), EI-MS (m/z) : 331.102 ($C_{14}H_{19}O_9^+$; terminal peracetylated hexosyl cation). The above spectral data for 4 indicate that D-glucosyl moiety is linked to the C-19 hydroxy group[3] of 1 and is β-configuration. The structure of 3 was threfore elucidated as cinncassiol D_1 19-O-β-D-glucopyranoside.

They are woth of note as novel type diterpenes (1 and 3) with a new skeleton which are assumed to be the key substances possessing anti-complement activity.

Acknowledgement : The authors thank Mr.s I.Yabuuchi and I.Fujiwara (Research Institutes of Otsuka group Co., Ltd.) for the use of automatic diffractometer and for measurement of NMR (^{1}H and ^{13}C) spectra, respectively. They are also grateful to Dr. Y.Egawa (Tanabe Pharm. Co., Ltd.) for supply of crude hesperidinase and to Mrs. M.Kobayashi (Kyushu University) for measurement of mass (FD and EI) spectra.

References and Notes

1) A.Koda, E.Katsuta, S.Watanabe and M.Mizuno, Nippon Yakurigaku Zasshi, 66, 366 (1970).
2) On acetylation in the same way, 1 gave 19-O-monoacetyl cinncassiol D_1.
3) It was also supported from the evidence of ^{13}C-NMR spectrum of 4. Comparison of the ^{13}C-NMR spectra of 4 with that of 1 indicated that C-19 signal is shifted downfield by 7.8 ppm and C-18 signal is shifted upfield by 3.1 ppm due to glycosylation shifts (R.Kasai, M.Suzuo, J.Asakawa and O.Tanaka, Tetrahedron Lett., 1977, 175; K.Tori, S.Seo, Y.Yoshimura, H.Arita and Y.Tomita, Tetrahedron Lett., 1977, 179).

(Received in Japan 1 April 1980