Pergamon

Tetrahedron Vol. 51, No. 4, pp. 1143-1166, 1995

0040-4020/95 $9.50+0.00

0040-4020(94)01015-3

Constituents of Cimicifugae Rhizoma II. Isolation and Structures of New Cycloartenol Triterpenoids and Related Compounds from *Cimicifuga foetida* L.[1]

Shigetoshi Kadota,[a,*] Jian Xin Li,[a] Ken Tanaka,[b] and Tsuneo Namba[a]

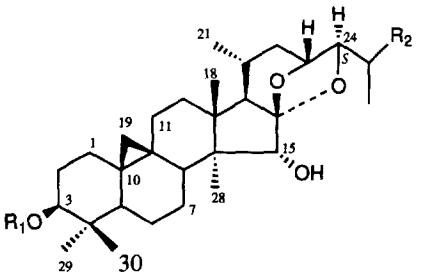
Research Institute for Wakan-Yaku (Traditional Sino-Japanese Medicines),[a] Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-01, Japan; National Research Institute of Police Science,[b] 6 Sanban-cho, Chiyoda-ku, Tokyo 102, Japan

Abstract: Neutral constituents of *Cimicifuga foetida* L. were examined. Eight new triterpenoids and three new trinor-triterpenoids were isolated from the rhizoma of *C. foetida* L. (Ranunculaceae) along with six known compounds and their structures were determined by the use of 2D NMR techniques and chemical methods.

"Shengma", the rhizoma of *Cimicifuga* species belonging to Ranunculaceae, is an important constituent of traditional Chinese medicines for the treatment of an anti-inflammatory, antipyretic and analgesic remedy.[2] Three *Cimicifuga* species (*C. heracleifolia*, *C. dahurica*, and *C. foetida*) are officially listed in the Chinese Pharmacopoeia and used as an anti-inflammatory and antipyretic agent.[2] Moreover, it has been used in combination with other herbs in the ancient Kampo medicine (Shouma-kakon-to and Otsu-ji-to, in Japanese) as anti-inflammatory drugs. Chemical constituents of *Cimicifuga* species have been studies by several groups.[3] In the previous paper,[4] we reported the structures of ten new triterpenoids from *Cimicifuga heracleifolia* Komarov. However, no paper has been published so far on the constituents of *C. foetida* up to now. In the present paper, we wish to describe in detail isolation and the structure elucidation of eleven new compounds named 25-anhydrocimigenol-3-*O*-β-xyloside (**1**), acetylacteol-3-*O*-arabinoside (**2a**), cimicinol (**3**), cimicifol (**4a**), cimicidanol-3-*O*-arabinoside (**5a**), cimicidanol (**6a**), cimicidol-3-*O*-β-xyloside (**7a**), 15α-hydroxycimicidol-3-*O*-β-xyloside (**8**), foetidinol (**9a**), foetidinol-3-*O*-β-xyloside (**10**), and 15α-hydroxyfoetidinol-3-*O*-β-xyloside (**11**) by use of 2D NMR spectral techniques and chemical methods.

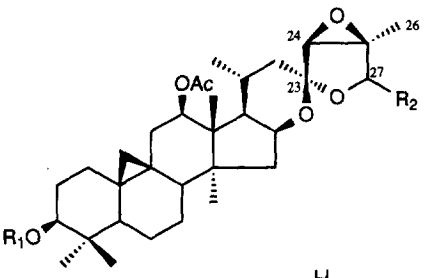
Air-dried rhizoma of *C. foetida*, grown in Sichuan province of China, was pulverized and extracted with hot methanol. The methanol extract was roughly separated into hexane-, EtOAc- and *n*-BuOH-soluble fractions. Of the three fractions, the EtOAc-soluble fraction showed a significant anti-inflammatory activity in rats by carrageen method. So that chemical analysis of EtOAc-soluble fraction was performed to find an active principle. From the EtOAc extract, eight new triterpenoids (**1-8**) and three new trinor-triterpenoids (**9a-11**) were isolated together with six known compounds: 25-acetylcimigenol xyloside (**12**),[5] 27-desoxyacetylacteol (**13**),[6] norvisnagin, angelicain, isoferulic acid, and isoimperatorin (see Experimental). The structures of **1-11** were determined as described below.

25-Anhydrocimigenol-3-*O*-β-xyloside (**1**) was isolated as colorless needles, mp 245-246°C, and showed $[\alpha]_D$ +8.42° (c=0.14, $CHCl_3$). The positive ion FAB-MS and high resolution (HR) FAB-MS showed an ion peak at *m/z* 603 $[M+H]^+$ and *m/z* 603.3938 (Calcd 603.3897), indicating the molecular formula $C_{35}H_{55}O_8$. The IR spectrum of **1** showed absorption bands at 3400 (OH) and 1400 cm^{-1}. The ^1H-NMR spectrum of **1**, analyzed with aid of ^1H-^1H COSY, showed signals due to a cyclopropane methylene (δ_H 0.30 and 0.55, each d, *J*=4.0 Hz), one double bond protons (δ_H 4.88 and 5.33), a five membered sugar protons (δ_H 3.73, 4.02,



1: R_1=β-xylosyl, R_2= $=CH_2$

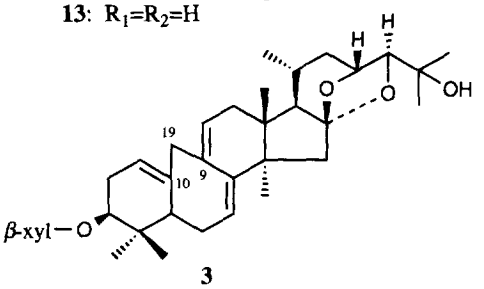
12: R_1=β-xylosyl, R_2= $\langle^{CH_3}_{OAc}$



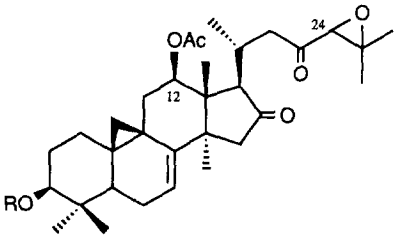
2a: R_1=arabinosyl, R_2= $\langle^{H}_{OH}$

2b: R_1=H, R_2= $\langle^{H}_{OH}$

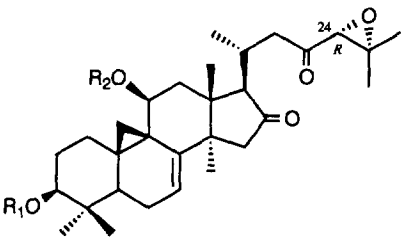
13: R_1=R_2=H



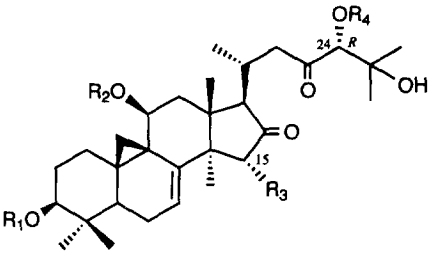
3



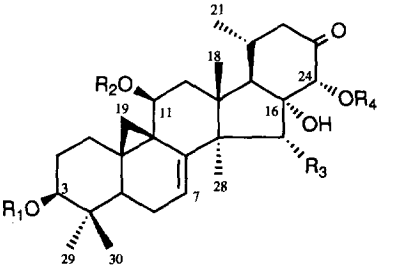
4a: R=β-xylosyl
4b: R=tri-*O*-acetyl-β-xylosyl



5a: R_1=arabinosyl, R_2=H
5b: R_1=tri-*O*-acetyl arabinosyl, R_2=Ac
6a: R_1= R_2=H
6b: R_1= R_2=Ac

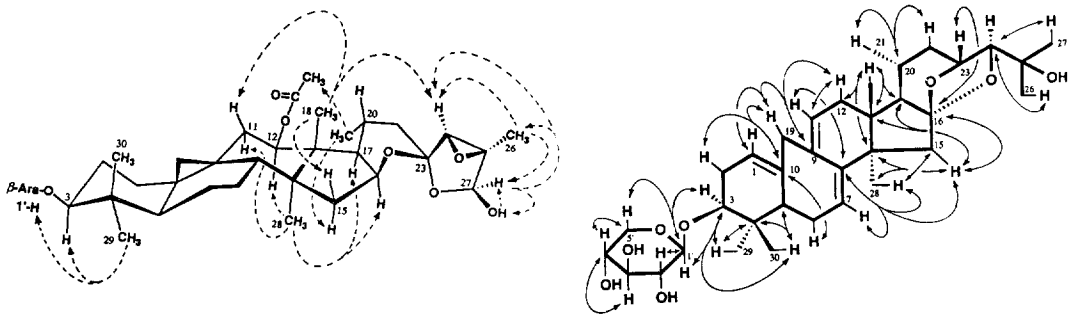


7a: R_1=β-xylosyl, R_2=R_3=R_4=H
7b: R_1=tri-*O*-acetyl-β-xylosyl, R_2=R_4=Ac, R_3=H
8: R_1=β-xylosyl, R_2=R_4=H, R_3=OH



9a: R_1=R_2=R_3=R_4=H
9b: R_1=R_2=R_4=Ac, R_3=H
10: R_1=β-xylosyl, R_2=R_3=R_4=H
11: R_1=β-xylosyl, R_2=R_4=H, R_3=OH

Chart 1.



[A] [B]

Chart 2. [A] NOE's observed in difference NOE experiment of **2a**
[B] Significant long-range correlations observed in ^{1}H-^{13}C long-range COSY experiment of **3**

4.15, 4.22, 4.34, and 4.86), four oxygen substituted methine protons (δ_H 3.57, 4.17, 4.29, and 4.30), a vinyl methyl group (δ_H 1.84), a secondary methyl group (δ_H 0.86), along with four *tert*-methyl groups (δ_H 1.08, 1.16, 1.18, and 1.33)(Table I). The sugar was identified as xylose by acid hydrolysis. Xylose is anticipated to be D-xylose, since it is the only naturally occurring isomer. Based on a comparison of the ^{1}H- and ^{13}C-NMR spectral data with those reported in the literature, we speculated that the structure of **1** should be very similar to that of cimigenol,[7] but the ^{1}H- and ^{13}C-NMR spectra of **1** clearly showed characteristic signals due to a double bond which did not appear in cimigenol (Table II). Hence, **1** was suggested to be dehydroxycimigenol xyloside, a conclusion which was also supported by the ^{1}H-^{13}C and ^{1}H-^{13}C long-range COSY spectra. The relative stereochemistry of **1** was determined on the basis of the coupling constants of each proton and NOE experiments. Thus, the structure of **1** was consequently assigned as 25-anhydrocimigenol-3-*O*-β-xyloside.

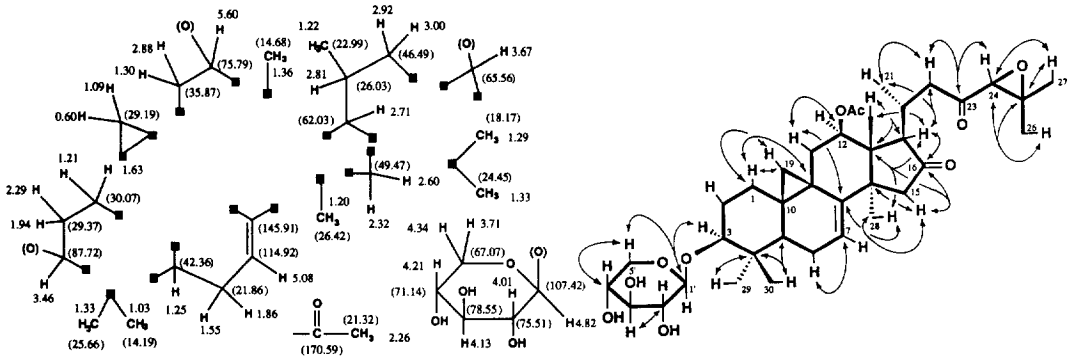
Acetylacteol-3-*O*-arabinoside (**2a**) was obtained as a white powder, and showed $[\alpha]_D$ -66.06° (c=0.30, $CHCl_3$:MeOH=1:1) and IR absorptions at 3420 (OH), 2960, 2920, and 1740 (C=O) cm^{-1}. The positive ion FAB-MS of **2a** exhibited the quasi-molecular ion peak at *m/z* 677 $[M+H]^+$ and its molecular formula was determined to be $C_{37}H_{57}O_{11}$ [$(M+H)^+$ 677.3381, Calcd 677.3401] by HR-FAB-MS. The ^{1}H- and ^{13}C-NMR spectral patterns of **2a** were similar to those of acetylacteol xyloside(=actein)[8] except for the ^{1}H- and ^{13}C-signals due to xylose (Tables I and II). The sugar was identified as arabinose by acid hydrolysis and followed by comparison of TLC analysis with an authentic sample. This suggested that **2a** might be arabinoside of acetylacteol. Enzymatic hydrolysis of **2a** with molsin yielded acetylacteol (**2b**) and its identification was performed by comparisons of the specific rotation, MS, and ^{1}H-NMR spectra data with those described in the literature.[9] These findings revealed that the plane structure of **2a** was determined to be acetylacteol arabinoside. Since the stereochemistry around the spiro carbon (C_{23}), epoxide carbons (C_{24} and C_{25}), and hydroxy bearing carbon (C_{27}) of **2a** was still ambiguous,[8, 10] and C_{27} stereochemistry has not been determined yet. We investigated it in more detail by means of NOE experiments. Irradiation at 18-H_3 and 26-H_3 increased the signal intensity of the 11β-, 15β-, and 24-protons and 24- and 27-protons, respectively, and irradiation at 28-H_3 enhanced the signal intensities of the 11_α-, 12_α-, 16_α-, and 17_α-protons. Some of the significant NOE's

observed are illustrated by arrow (Chart 2 [A]). These data showed that the configurations at C_{23}, C_{24}, C_{25}, and C_{27} of **2a** were assigned as *R*, *S*, *R*, and *S*, respectively. Based on these findings, the structure of **2a** was determined to be 23(*R*), 24(*S*), 25(*R*), 27(*S*)-acetylacteol-3-*O*-arabinoside.

Cimicinol (**3**) was obtained as an yellow powder and showed $[\alpha]_D$ +14.02° (c=0.30, $CHCl_3$:MeOH =1:1). The positive ion FAB-MS and HR-FAB-MS showed an ion peak at *m/z* 601 $[M+H]^+$ and *m/z* 601.3760 (Calcd 601.3780), indicating the molecular formula $C_{35}H_{53}O_8$. In the UV spectrum, it showed absorption bands at 207 and 248 nm (log ε: 3.02 and 3.24, respectively). The ^1H- and ^{13}C-NMR spectrum of **3** exhibited signals due to three double bonds (δ_H 5.39, 5.52, and 5.58; δ_C 120.41, 121.75, 124.36, 137.63, 138.87, and 144.43), a five membered sugar (δ_H 3.68, 3.97, 4.10, 4.18, 4.32, and 4.75; δ_C 67.01, 71.11, 75.36, 78.46, and 107.18), three oxygen substituted methines (δ_H 3.65, 3.67, and 4.74; δ_C 71.78, 83.95, and 90.48), two quaternary carbons substituted by oxygen (δ_C 70.99 and 114.43), and one *sec*- and six *tert*-methyl groups along with other signals, which were analyzed by ^1H-^1H and ^1H-^{13}C COSY(Tables I and II). However, characteristic proton and carbon signals due to three membered ring were disappeared. Also, the sugar was identified as xylose by acid hydrolysis. From the above spectral data, this compound might be 9,10-*seco* related derivative of **1**. In the ^1H-^{13}C long-range COSY spectrum of **3**, the carbon signals at δ_C 120.41 (C-1) and 121.75 (C-11) are correlated with proton signals at δ_H 3.21 (19-H) and 2.25 (12-Hβ) and 3.15 (19-H), respectively. Some of the other significant long-range correlations observed are shown by arrows in Chart 2 [B]. Long-range correlations observed in the ^1H-^{13}C long-range COSY confirmed the proposed structure (Chart 2 [B]). The relative stereochemistry of **3** was deduced by consideration of the coupling constants and the NOE difference spectra. The configuration at the C-24 position of **3** could be assigned as 24 α-H by comparing the coupling constant of the C-23 and C-24 proton signals of **3** with those of 24-epimeric triterpenes.[4,11] Accordingly, the structure of this compound was concluded to be as shown by formula **3** and named cimicinol.

Cimicifol (**4a**), white powder, and showed $[\alpha]_D$ -99.33° (c=0.30, $CHCl_3$:MeOH=1:1). The positive ion FAB-MS of **4a** exhibited the quasi-molecular ion peak at *m/z* 659 $[M+H]^+$ and its molecular formula was determined to be $C_{37}H_{55}O_{10}$ [$(M+H)^+$ 659.3896, Calcd 659.3900] by HR-FAB-MS. IR spectrum of **4a** showed absorption bands at 3420 (OH), 2950, 1740 (C=O), 1720 (C=O). The ^1H- and ^{13}C-NMR of **4a**, indicated the presence of two carbonyl (δ_C 205.23 and 216.98), a acetoxyl group (δ_H 2.26; δ_C 21.32 and 170.59), and a double bond (δ_H 5.08; δ_C 114.92 and 145.91), three methines substituted by oxygen (δ_H 3.46, 3.67, and 5.60; δ_C 87.72, 65.56, and 75.79), a five membered sugar (δ_H 3.71, 4.01, 4.13, 4.21, 4.34, and 4.82; δ_C 67.07, 71.14, 75.51, 78.55, and 107.42), a cyclopropyl methylene (δ_H 0.60 and 1.09; δ_C 29.19), six *tert*-methyl groups (δ_H 1.03, 1.20, 1.29, 1.33, 1.33, and 1.36; δ_C 14.19, 26.42, 18.17, 24.45, 25.66, and 14.68), a secondary methyl group (δ_H 1.22; δ_C 22.99), six sp^3 methylenes (δ_H 1.21, 1.63, 1.94, 2.29, 1.55, 1.86, 1.30, 2.88, 2.32, 2.60, 2.29, and 3.00; δ_C 30.07, 29.37, 21.81, 35.87, 49.47, and 46.49), three sp^3 methines (δ_H 1.25, 2.71, and 2.81; δ_C 42.36, 62.03, and 26.03), six sp^3 quaternary carbons (δ_C 21.11, 28.97, 40.36, 46.40, 47.61, and 60.28)(Tables I and II). These data coupled with the detailed analyses of ^1H-^1H and ^1H-^{13}C COSY spectra suggested that **4a** has the partial structure as shown in Chart 3 [A]. Acetylation of **4a** with acetic anhydride-pyridine gave an amorphous tetraacetate (**4b**), whose positive ion FAB-MS exhibited the $[M+Na]^+$ peak at *m/z*: 807 ($C_{43}H_{60}O_{13}Na$: 807.3910, Calcd 807.3922). The sugar was identified as xylose by acid hydrolysis.

Next, we measured the ^1H-^{13}C long-range COSY of **4a** in order to determine the connectivities of these



[A] [B]

Chart 3. [A] Deduced partial structures of **4a**
[B] Significant long-range correlations observed in ^{1}H-^{13}C long-range COSY experiment of **4a**

partial structure. As shown in Chart 3 [B], the carbon signal at δ_C 65.56 (d, C-24) showed long-range correlations with the proton signals at δ_H 1.29 (26-H_3) and 1.33 (27-H_3) and the carbon signal at δ_C 205.23 (s, C-23) with the proton signals at δ_H 3.67 (24-H) and 2.92 (22-H). Next, the carbon signals δ_C 216.98 (s, C-16) and 145.91 (s, C-8) showed long-range correlations with the proton signals at δ_H 2.32 (15-Hα) and 2.71 (17-H), and at δ_H 1.20 (28-H_3), respectively. From these results and other long-range correlations depicted the structural in Chart 3 [B] by arrows, the planner structure of **4a** was determined.

The relative stereochemistry of **4a** was determined on the basis of coupling constants of the protons and the result of NOE experiments. Irradiation at the 18-H_3 and 28-H_3 increased the signal intensities of 2.26 ($COCH_3$) and 2.60 (15-Hβ) and 2.32 (15-Hα), 2.71 (17-Hα), 2.88 (11-Hα), and 5.60 (12-Hα), respectively, and irradiation at the 21-H_3 and 26-H_3 enhanced the signal intensity of the 2.71 (17-Hα) and 3.67 (24-H), respectively. Therefore, the stereostructure of this compound was proved to be **4a** except for the configuration of C_{24}-C_{25} epoxide and named as cimicifol.

Cimicidanol-3-*O*-arabinoside (**5a**) was isolated as colorless plates, mp 214-215°C, and showed $[\alpha]_D$ -42.32° (c=0.20, $CHCl_3$:MeOH=1:1). The negative ion FAB-MS of **5a** exhibited the $[M-H]^-$ peak at *m/z* 615 and the molecular formula was determined to be $C_{35}H_{51}O_9$ [$(M-H)^-$ 615.3528, Calcd 615.3520] by high-resolution FAB-MS. In the IR spectrum, it showed absorptions at 3450 (OH), 2960, 2925, 1720 (C=O). The ^{1}H- and ^{13}C-NMR spectral patterns of **5a** were similar to those of cimicifol (**4a**), except for the ^{1}H- and ^{13}C-signals due to xylose and cyclopropane methylene (Tables III and IV).

In the ^{1}H-NMR spectrum of **5a**, the cyclopropane methylene protons (δ_H 0.91 and 1.87) revealed a marked downfield shift compared with those of **1** (δ_H 0.30 and 0.55) and **4a** (δ_H 0.60 and 1.09), which led us to suppose displacement of 11-H by a hydroxy group.

Acetylation of **5a** gave an amorphous tetraacetate (**5b**), $[\alpha]_D$ -10.67 (c=0.08, $CHCl_3$), whose positive ion FAB-MS exhibited the $[M+H]^+$ peak at *m/z*: 785 ($C_{43}H_{61}O_{13}$: 785.4090, Calcd 785.4112). Also, Acid hydrolysis of **5a** with 0.5N HCl afforded arabinose, which was identified by TLC comparison with an authentic sample. Enzymatic hydrolysis of **5a** with molsin yielded arabinose and compound (**6a**), which will be discussed later.

Table I. ^{1}H-NMR Spectral Data for Triterpenoids from *Cimicifuga foetida*

^{1}H	**1**[a]	**2a**[b]	**3**[a]	**4a**[a]	**12**[a]	**13**[a]
1	1.25 m	1.11 m	5.52 brd (5.0)	1.21 m	1.26 m	1.08 m
	1.61 m	1.48 m	———	1.63 td (12.5, 4.0)	1.59 m	1.47 m
2	1.97 m	1.51 m	2.35 m	1.94 m	1.97 m	1.79 m
	2.37 m	1.81 m	2.77 dt (17.5, 5.0)	2.29 m	2.35 m	1.91 m
3	3.57 dd (11.5, 4.5)	3.06 dd (13.0, 4.5)	3.65 m	3.46 dd (11.5, 4.0)	3.50 dd (11.0, 4.2)	3.46 dd (11.5, 4.2)
5	1.37 dd (12.5, 4.5)	1.23 dd (11.0, 4.5)	2.38 m	1.25 m	1.35 dd (12.0, 4.5)	1.24 m
6	0.74 qd (12.5, 1.5)	0.82 m	2.62 dt (14.5, 5.0)	1.55 m	0.73 brq (12.0)	0.69 qd (12.5, 3.0)
	1.58 td (7.0, 1.5)	1.51 m	2.39 m	1.86 ddd (12.5, 7.5, 5.0)	1.54 m	1.42 m
7	2.09 m	1.28 brt (13.0)	5.58 brd (7.5)	5.08 dd (7.5, 2.0)	1.10 m	0.94 qd (12.5, 3.0)
	1.10 qd (7.0, 1.5)	1.71 dd (13.0, 3.5)	———	———	2.09 m	1.21 m
8	1.68 m	1.58 m	———	———	1.70 dd (12.0, 5.0)	1.61 dd (12.5, 5.0)
11_α	2.14 m	2.48 m	5.39 brd (5.5)	2.88 dd (16.0, 9.0)	2.11 m	2.74 dd (15.5, 9.0)
11_β	1.21 m	0.99 m	———	1.30 m	1.17 m	1.16 dd (15.5, 3.5)
12_α	1.71 m	4.74 dd (9.0, 3.5)	1.95 dd (17.5, 5.5)	5.60 dd (9.0, 1.5)	1.67 m	5.11 dd (9.0, 3.5)
12_β	1.55 m	———	2.25 brd (17.5)	———	1.56 m	———
15_α	———	1.44 m	2.05 d (13.0)	2.32 d (17.5)	4.49 d (9.0, -OH)	1.91 dd (12.5, 7.5)
15_β	4.29 brs	1.79 m	2.32 d (13.0)	2.60 d (17.5)	4.25 d (9.0)	1.76 dd (12.5, 6.0)
16	———	4.26 td (8.0, 7.0)	———	———	———	4.23 td (7.5, 6.0)
17	1.46 d (11.0)	1.69 t (8.0)	1.55 d (10.5)	2.71 d (2.5)	1.45 d (11.5)	1.79 t (7.5)
18-H_3	1.16 s	1.13 s	0.77 s	1.36 s	1.14 s	1.43 s
19	0.30 d (4.0)	0.33 d (4.5)	3.15 d (14.0)	0.60 d (4.0)	0.30 d (4.0)	0.23 d (4.5)
	0.55 d (4.0)	0.60 d (4.5)	3.21 d (14.0)	1.09 d (4.0)	0.55 d (4.0)	0.58 d (4.5)
20	1.66 m	1.59 m	1.60 m	2.81 m	1.64 m	2.23 m
21-H_3	0.86 d (7.0)	0.87 d (6.0)	0.83 d (6.0)	1.22 d (7.0)	0.86 d (6.5)	1.03 d (6.5)
22	1.00 brt (12.5)	0.94 m	0.99 m	2.92 dd (18.0, 4.0)	0.98 brt (13.0)	1.50 m
	2.26 ddd (12.5, 9.5, 7.5)	1.32 m	2.23 m	3.00 dd (18.0, 8.0)	2.26 ddd (13.0, 9.0, 7.0)	1.58 dd (12.5, 3.0)
23	4.30 brd (7.5)	———	4.74 brd (9.5)	———	4.58 brd (9.0)	———
24	4.17 brs	3.53 s	3.67 brs	3.67 s	4.10 s	3.63 s
26	4.88 brs	1.43 s	1.51 s	1.29 s	1.68 s	1.47 s
	5.33 brs	———	———	———	———	———
27	1.84 s	4.99 d (5.5)	1.443 s	1.33 s	1.65 s	3.61 d (10.0)
	———	6.49 d (5.5, -OH)	———	———	———	4.05 d (10.0)
28-H_3	1.18 s	0.84 s	1.29 s	1.20 s	1.18 s	0.86 s
29-H_3	1.33 s	0.96 s	1.437 s	1.33 s	1.32 s	1.28 s
30-H_3	1.08 s	0.77 s	0.94 s	1.03 s	1.06 s	1.01 s
1'	4.86 d (7.5)	4.12 d (7.5)	4.75 d (7.5)	4.82 d (7.5)	4.84 d (7.5)	———
2'	4.02 t (7.5)	2.95 td (8.5, 5.0)	3.97 t (7.5)	4.01 t (7.5)	4.00 t (7.5)	———
2'-*OH*	———	4.90 d (5.0)	———		———	———
3'	4.15 t (8.5)	3.05 m	4.10 t (8.5)	4.13 t (8.5)	4.13 t (8.5)	———
4'	4.22 ddd (11.0, 8.5, 5.0)	3.24 m	4.18 ddd (11.0, 8.5, 5.0)	4.21 ddd (10.0, 8.5, 5.0)	4.19 ddd (11.0, 8.5, 5.0)	———
5'	3.73 t (11.0)	3.00 t (11.0)	3.68 t (11.0)	3.71 dd (11.0, 10.0)	3.71 t (11.0)	———
	4.34 dd (11.0, 5.0)	3.64 dd (11.0, 5.5)	4.32 dd (11.0, 5.0)	4.34 dd (11.0, 5.0)	4.34 dd (11.0, 5.0)	———
$COCH_3$	———	1.96 s	———	2.26 s	1.96 s	2.17 s

^{1}H-^{1}H shift correlation spectra and NOE spectra were measured. δ value in a) pyridine-d_5 or b) DMSO-d_6 and coupling constants in Hz.

Table II. ^{13}C-NMR Spectral Data for Triterpenoids from *Cimicifuga foetida*

^{13}C	**1**[a, c]	**2a**[b, c]	**3**[a, d]	**4a**[a, c]	**12**[a, e]	**13**[a, c]
1	32.40 (t)	31.15 (t)	120.41 (d)	30.07 (t)	32.43 (t)	32.19 (t)
2	30.07 (t)	28.97 (t)	32.34 (t)	29.37 (t)	30.10 (t)	31.04 (t)
3	88.51 (d)	86.89 (d)	83.95 (d)	87.72 (d)	88.51 (d)	77.70 (d)
4	41.30 (s)	40.11 (s)	38.96 (s)	40.36 (s)	41.32 (s)	40.94 (s)
5	47.58 (d)	46.30 (d)	51.44 (d)	42.36 (d)	47.55 (d)	46.92 (d)
6	21.02 (t)	19.92 (t)	38.08 (t)	21.81 (t)	21.05 (t)	20.66 (t)
7	26.10 (t)	36.65 (t)	124.36 (d)	114.92 (d)	26.33 (t)	25.82 (t)
8	48.59 (d)	45.27 (d)	144.43 (s)	145.91 (s)	48.62 (d)	45.91 (d)
9	19.96 (s)	19.40 (s)	137.63 (s)	21.11 (s)	19.99 (s)	20.02 (s)
10	26.64 (s)	25.96 (s)	138.87 (s)	28.97 (s)	26.67 (s)	27.00 (s)
11	26.39 (t)	35.83 (t)	121.75 (d)	35.87 (t)	26.39 (t)	36.84 (t)
12	33.98 (t)	76.02 (d)	37.99 (t)	75.79 (d)	34.01 (t)	77.18 (d)
13	41.63 (s)	47.76 (s)	44.70 (s)	47.61 (s)	41.79 (s)	48.80 (s)
14	47.16 (s)	47.18 (s)	47.83 (s)	46.40 (s)	47.16 (s)	47.83 (s)
15	80.31 (d)	42.93 (t)	43.72 (t)	49.47 (t)	80.10 (d)	44.21 (t)
16	112.22 (s)	72.04 (d)	114.43 (s)	216.98 (s)	112.37 (s)	74.48 (d)
17	59.82 (d)	55.43 (d)	59.91 (d)	62.03 (d)	59.36 (d)	56.24 (d)
18	19.44 (q)	13.00 (q)	17.29 (q)	14.68 (q)	19.47 (q)	13.51 (q)
19	30.89 (t)	29.15 (t)	43.72 (t)	29.19 (t)	30.92 (t)	29.85 (t)
20	23.84 (d)	24.99 (d)	23.87 (d)	26.03 (d)	23.90 (d)	23.27 (d)
21	19.44 (q)	20.52 (q)	20.02 (q)	22.99 (q)	19.45 (q)	21.32 (q)
22	37.99 (t)	25.11 (t)	25.15 (t)	46.49 (t)	37.90 (t)	37.57 (t)
23	78.49 (d)	104.68 (s)	71.78 (d)	205.23 (s)	71.62 (d)	105.87 (s)
24	86.59 (d)	61.94 (d)	90.48 (d)	65.56 (d)	86.68 (d)	62.46 (d)
25	145.82 (s)	64.49 (s)	70.99 (s)	60.28 (s)	83.10 (s)	62.25 (s)
26	113.01 (t)	12.42 (q)	27.88 (q)	18.17 (q)	23.36 (q)	14.26 (q)
27	18.17 (q)	96.57 (d)	24.63 (q)	24.45 (q)	21.48 (q)	68.11 (t)
28	11.79 (q)	19.16 (q)	24.75 (q)	26.42 (q)	11.73 (q)	19.71 (q)
29	25.66 (q)	24.99 (q)	24.85 (q)	25.66 (q)	25.70 (q)	26.15 (q)
30	15.37 (q)	14.76 (q)	15.28 (q)	14.19 (q)	15.43 (q)	14.71 (q)
1'	107.48 (d)	105.95 (d)	107.18 (d)	107.42 (d)	107.48 (d)	-------
2'	74.91 (d)	73.77 (d)	75.36 (d)	75.51 (d)	75.48 (d)	-------
3'	78.49 (d)	76.69 (d)	78.46 (d)	78.55 (d)	78.52 (d)	-------
4'	71.14 (d)	69.59 (d)	71.11 (d)	71.14 (d)	71.14 (d)	-------
5'	67.01 (t)	65.58 (d)	67.01 (t)	67.07 (t)	67.04 (t)	-------
C=O	-------	169.89 (s)	-------	170.59 (s)	170.11 (s)	170.59 (s)
COCH3	-------	21.38 (q)	-------	21.32 (q)	22.26 (q)	21.63 (q)

δ value in a) pyridine-d_5 or b) DMSO. The multiplicities of carbon signals were determined by the distortionless enhancement by polarization transfer (DEPT) method and are indicated as s, d, t and q. c) ^{1}H-^{13}C and ^{1}H-^{13}C long-range COSY spectra were measured. d) ^{1}H-^{13}C COSY, ^{1}H-^{13}C long-range COSY and HMBC spectra were measured. e) ^{1}H-^{13}C COSY spectrum was measured.

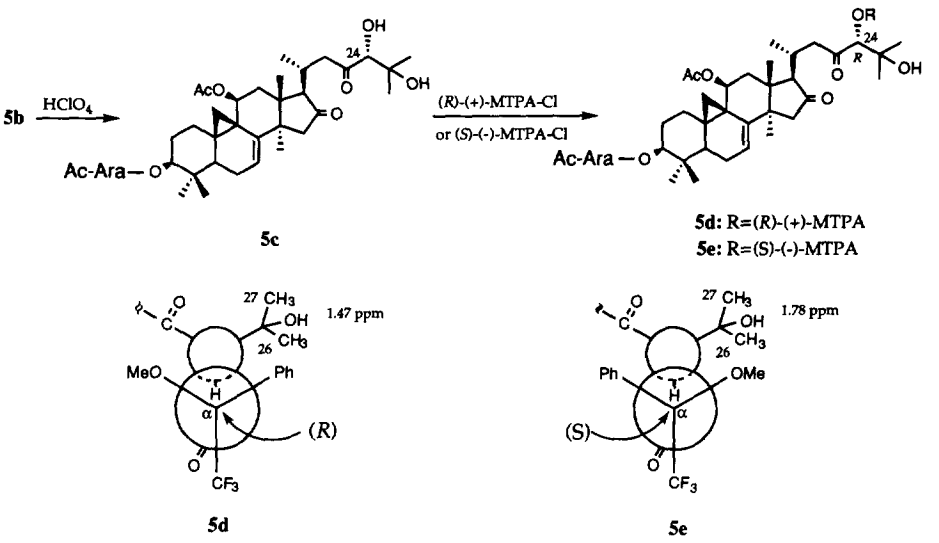


Chart 4

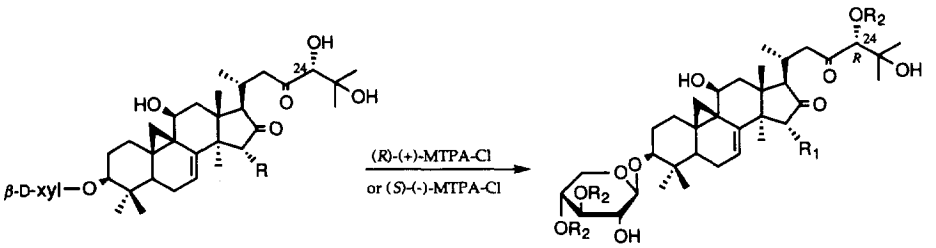
Then, we measured the long-range COSY of **5a** in order to clarify the structure. The carbon signal at δ_C 43.58 (C-5) is correlated with the proton signals at the 1.07 (30-H_3), 1.62 (1-H), 1.68 (6-H), 0.91 (19-H), and 1.87 (19-H) in terms of long-range correlation, while the hydroxy-bearing methine carbon signal at δ_C 62.70 (C-11) with the proton at δ_H 1.87 (19-H). Thus, the structure of this compound was assigned to **5a.**

In order to confirm the stereostructure of **5a**, NOE spectra were measured.[12] Irradiation at 29-H_3 (δ_H 1.00) enhanced the signal intensity of the 3.48 (3-H) and 4.74 (1'-H). Similarly, the C-11 hydroxy-bearing methine signal (δ_H 4.46) showed NOE enhancement on irradiation of the 28-methyl protons (δ_H 1.17), indicating that the 11-hydroxy group is in β-configuration. These findings coupled with the coupling constants of each proton indicated the stereostructure of this compound to be **5a** except for the configuration of C_{24}-C_{25} epoxide.

Treatment of **5b** with 3M $HClO_4$ in THF gave a diol (**5c**), $[\alpha]_D$ -34.12 (c=0.50, $CHCl_3$), whose positive ion FAB-MS exhibited the $[M+Na]^+$ peak at *m/z*: 825 ($C_{43}H_{62}O_{14}Na$: 825.4036, Calcd 825.4038).. Esterification of **5c** with *R*-(+)-MTPA-Cl or *S*-(-)-MTPA-Cl[13] afforded a MTPA ester (**5d** or **5e**)(Chart 4). Comparison of the ^{1}H-NMR data of **5d** with that of **5e** indicated that the signal due to 26- and 27-H_3 of **5d** shifted upfield by 0.31 ppm as shown in Chart 4. Thus, the configuration of C-24 is concluded to be *R*.

From the above spectral data, the structure was determined to be as represented by the formula **5a** and named cimicidanol-3-*O*-arabinoside.

Cimicidanol (**6a**), colorless needles, mp 197-198°C, and showed $[\alpha]_D$ -50.58° (c=0.16, $CHCl_3$:MeOH =1:1). In the EI-MS, it showed a molecular ion peak at *m/z* 484 along with fragment ion peak at *m/z* 468 (M^+-H_2O), 269, and 251, and its molecular formula was determined to be $C_{30}H_{44}O_5$ by high-resolution EI-MS. The IR spectrum of **6a** showed absorption bands at 3450 (OH), 1720 (C=O), 1700, 1440, and 1380 cm^{-1}. Acetylation of **6a** gave a diacetate (**6b**). The ^{1}H- and ^{13}C-NMR spectra of **6a** were identical with the compound obtained from enzymatic hydrolysis of **5a** with molsin as described above (Tables III and IV).



7a: R=H
8: R=OH

7c: R_1=H, R_2=*R*-(+)-MTPA
7d: R_1=H, R_2=*S*-(-)-MTPA
8a: R_1=OH, R_2=*R*-(+)-MTPA
8b: R_1=OH, R_2=*S*-(-)-MTPA

Chart 5

From these comparisons of the ^{1}H- and ^{13}C-NMR data and specific rotation, it was concluded the structure of this compound is represented by the formula **6a** and named cimicidanol.

Cimicidol-3-*O*-β-xyloside (**7a**) is obtained as an amorphous powder, $[\alpha]_D$ -30.73°(c=0.60, $CHCl_3$:MeOH=1:1). The positive ion FAB-MS of **7a** exhibited the quasi-molecular ion peak at *m/z* 635 $[M+H]^+$ and its molecular formula was determined to be $C_{35}H_{55}O_{10}$ [$(M+H)^+$ 635.3826, Calcd 635.3795] by HR-FAB-MS. Its IR spectrum showed 3400, 2950, 2900, 1720, 1040 cm^{-1}. The ^{1}H- and ^{13}C-NMR were closely similar to that of cimicidanol-3-*O*-arabinoside (**5a**) except for the signals due to a five membered sugar and a remarkably down-field shift of a hydroxy-bearing methine (δ_H 4.49; δ_C 84.01) assignable to C-24 position (Tables III and IV).

Acetylation of **7a** gave a pentaacetate (**7b**), whose positive ion FAB-MS exhibited the $[M+H-H_2O]^+$ peak at *m/z*: 827 ($C_{45}H_{63}O_{14}$: 827.4236, Calcd 827.4217) and IR spectrum showed the absorptions at 3450 (OH), 1740 (C=O) and 1720 (C=O) cm^{-1}. Therefore, **7a** has a *tert*-hydroxy, a *O*-glycosyl group and two secondary hydroxyl groups except for the hydroxyl group of sugar.

Acid hydrolysis of **7a** with 0.5N HCl afforded xylose, which was identified by TLC comparison with an authentic sample.

These findings indicated the structure of this compound to be **7a** except for the configuration of C-24. The Mosher's method[13] applied to MTPA esters (**7c** or **7d**) of **7a** led to the conclusion of the (*R*)-configuration of 24-hydroxyl group, since the chemical shift due to 26- and 27-H_3 signal of **7c** was shifted to the upfield by 0.30 ppm compared with that of **7d**. (Chart 5).

Based on these spectral data, cimicidol-3-*O*-β-xyloside was determined to be **7a**.

15α-Hydroxycimicidol-3-*O*-β-xyloside (**8**) was obtained as a white amorphous powder, $[\alpha]_D$ -45.70° (c=0.38, $CHCl_3$:MeOH=1:1). It showed IR absorptions at 3400, 2950, 2900, 1720, 1040 cm^{-1}. The positive ion FAB-MS of **8** exhibited the quasi-molecular ion peak at *m/z* 651 $[M+H]^+$ and its molecular formula was determined to be $C_{35}H_{55}O_{11}$ [$(M+H)^+$ 651.3756, Calcd 651.3744] by HR-FAB-MS. The ^{1}H- and ^{13}C-NMR spectra were closely similar to that of **7a** except for a remarkable down-field shift of a signal (δ_H 4.56; δ_C 80.64) due to C-15 position (Tables III and IV). From these comparisons of ^{1}H- and ^{13}C-NMR data, it was concluded that **8** possesses a hydroxyl group at C-15 position. The C-15 hydroxy-bearing methine signal (δ_H 4.56) showed NOE enhancement on irradiation of the 18-methyl protons (δ_H 1.40), indicating that the 15-hydroxyl group is in α-configuration. In the same method as above, the MTPA esters (**8a** or **8b**) of **8** led to the

conclusion that the configuration of 24-hydroxy group was *R*, since the signal due to 26- and 27-H_3 of **8a** was conclusion was shifted to the upfield by 0.33 ppm compared with that of **8b** (Chart 5).

Therefore, the structure of 15α-hydroxycimicidol-3-*O*-β-xyloside was proved to be **8**.

Foetidinol (**9a**), colorless needles (hexane-EtOAc), mp 255-256°C, $[\alpha]_D$ -93.5° (c=0.12, $CHCl_3$:MeOH =1:1), showed IR absorptions at 3450 (OH), 1718 (C=O), and 1620 cm^{-1}. It showed the molecular ion peak at *m/z* 444 in the EI-MS and its molecular formula was determined to be $C_{27}H_{40}O_5$ (M^+ 444.2909, calcd. 444.2873) by high-resolution MS. The ^1H-NMR spectrum of **9a** was analyzed by the application of ^1H-^1H COSY, and indicated the presence of four *tert*-methyl groups (δ_H 1.21, 1.29, 1.30, and 1.62), a *sec*-methyl group (δ_H 0.93), a cyclopropyl proton (δ_H 1.08 and 2.04), three hydroxy-bearing methine (δ_H 3.63, 4.50, and 4.62), and a double bond (δ_H 5.25)(Table III). On the other hand, the ^{13}C-NMR and DEPT spectra of **9a** exhibited signals due to a ketone (δ_C 211.27), two carbons of a pair of double bond (δ_C 113.95 and 149.28), three hydroxy-bearing methine carbons (δ_C 63.61, 78.03, and 82.01), four *tert*-methyl groups (δ_C 13.92, 21.23, 26.39, and 28.15), a *sec*-methyl group (δ_C 20.72), seven methylene carbons (δ_C 18.80, 22.36, 27.70, 31.07, 44.85, 48.62, and 48.95), three methine carbons (δ_C 25.85, 43.88, and 63.61), and six quaternary sp^3 carbons (δ_C 27.49, 29.52, 40.54, 46.34, 50.86, and 82.37)(Table IV).

These data coupled with the detailed analyses of the ^1H-^1H and ^1H-^{13}C COSY spectra showed fewer methine and methyl groups than usual cycloartenol as discussed above, but the chemical shift for five methyl groups at C_{18}, C_{21}, C_{28}, C_{29}, and C_{30} of **9a** were similar to those of **6a**. Hence, it was assumed that basic structure of **9a** was similar to that of **6a**, but total number of carbons was less than that of common cycloartenol. Also, the cyclopropane methylene protons (δ_H 1.08 and 2.04) of **9a** revealed a marked down-field shift, which led us to suppose the basic structure of **9a** was similar to that of **6a**.

Acetylation of **9a** gave an amorphous triacetate (**9b**), whose positive ion FAB-MS exhibited the $[M+Na]^+$ peak at *m/z*: 571 ($C_{33}H_{47}O_8$: 571.3273, Calcd 571.3271), and its showed IR absorption at 3540 (OH) and 1725 (C=O) cm^{-1}, and three acetyl methyl signals at δ_H 2.03, 2.07, and 2.24 in ^1H-NMR spectrum. The positive ion FAB-MS exhibited a quasi-molecular ion peak at *m/z* 571 $[M+H]^+$. Therefore, all these spectral informations of **9a** and **9b** suggested that **9a** must contain a *tert*-hydroxyl and three secondary hydroxyl groups.

Next, we measured the HMBC spectrum of **9a** in order to determine the structure. As shown in Fig. 1, the carbon signals at δ_C 29.52 (s. C-10) showed long-range correlations with the proton signals at δ_H 1.85 (6-H), and the carbon signals at δ_C 43.88 (d, C-5) with the proton signals at δ_H 1.08 (19-H), 1.30 (29-H_3), and 5.25 (7-H), and the carbon signals at δ_C 149.28 (s, C-8) with the proton signals at δ_H 1.08 (19-H) and 2.27 (15-Hα). Therefore, the quaternary carbon C-10 should be connected with the carbons C-5 (δ_C 43.88), C-9 (δ_C 7.49), and C-19 (δ_C 18.80), and the quaternary carbon C-8 with the carbon C-14 (δ_C 50.86). Next, the carbon signal at δ_C 27.49 (s, C-9) showed long-range correlation with the proton signal at δ_H 5.25 (7-H) and 2.09 (12-Hβ), so that it is reasonable to connect the carbons C-9 and C-11. On the other hand, the carbon signal at δ_C 46.34 (s, C-13) showed long-range correlations with the proton signals at δ_H 1.62 (28-H_3), 2.27 (15-H), and 2.26 (17-H), while the carbon signals at δ_C 50.86 (s, C-14) showed long-range correlations with the proton signals at δ_H 1.29 (18-H_3), 2.09 (12-H), 5.25 (7-H), 2.27 (15-H), and 2.26 (17-H). Thus, the quaternary carbon C-13 must be connected with the carbons C-14 and C-17. Further, the carbon signal at δ_C 82.37 (C-16) showed long-range correlations with the proton signals at δ_H 2.26 (17-H), 2.27 (15-H), and 4.50 (24-H), while the carbon signal at δ_C 211.27 (C-23) with the proton signals at δ_H 2.42 (22-H) and 4.50 (24-H). Therefore,

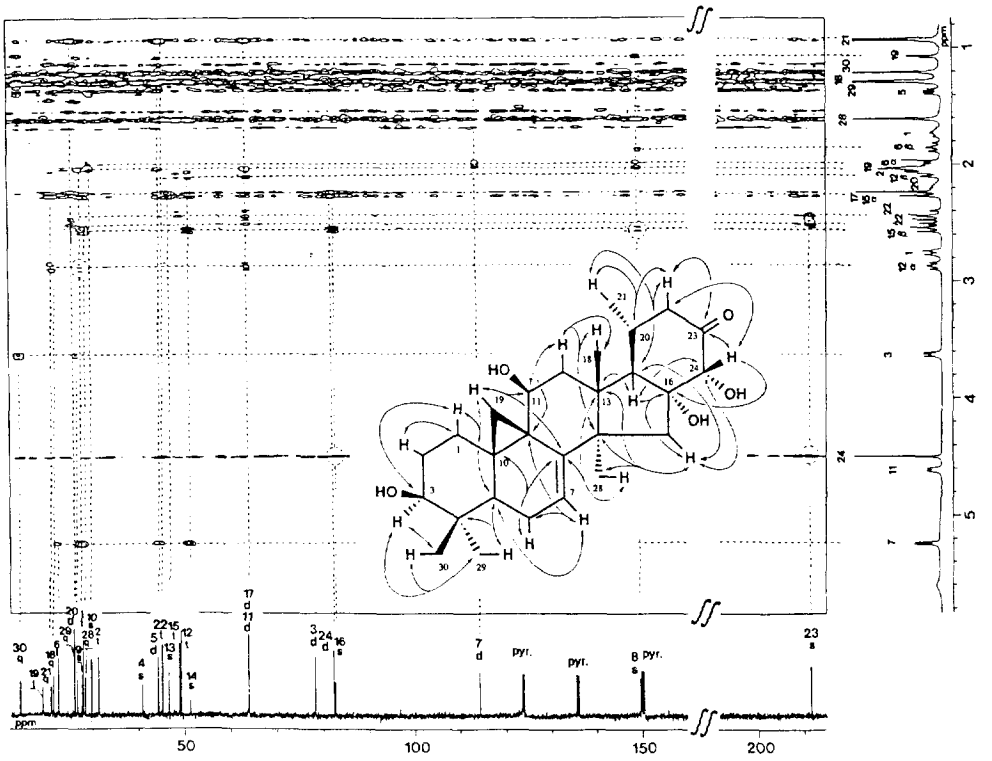


Fig. 1. HMBC spectrum of Foetidinol (**9a**) in Pyridine-d_5

the quaternary carbon C-16 should be connected with the carbons C-15 (δ_C 48.62), C-17 (δ_C 63.61), and C-24 (δ_C 82.01), and the quaternary carbon C-23 (δ_C 211.27) with the carbons C-22 (δ_C 44.85) and C-24 (δ_C 82.01). Thus, the structure of foetidinol was assigned to the formula in Fig. 1, in which other significant long-range correlations observed are also shown by arrows.

The relative stereochemistry of **9a** was determined on the basis of the coupling constants of each proton (Table III) and NOE experiment. As shown in Fig. 2, irradiation at 21-H_3 and 30-H_3 increased the signal intensities of the 12β-, 17-, and 22-protons and of the 6β- and 2-protons, respectively, and irradiation at 18-H_3 and 29-H_3 enhanced the signal intensities of the 12β-, 20-, 15β-, and 24-protons and of the 6α- and 3-protons, respectively. Also, irradiation at 28-H_3 and 24-H gave NOE enhancement of the 17-, 15α-, 12α-, 11-, and 7-protons and the 18-, 20-, and 15β-protons, respectively. These findings with other pertinent NOE enable us to determine the stereostructure of foetidinol to be **9a** as depicted in Fig. 2.

Next, we examined the CD spectrum of foetidinol (**9a**). It showed a negative Cotton effect due to the optically active ketone chromophore in the CD spectra in MeOH (CD maximum: $[\theta]_{213}$ -47870 and $[\theta]_{284}$ -17700)(Fig. 3) and it was also supported by ORD spectrum. Octant projection of the structure **9a** reasonably supports these assignments, which are parallel with the absolute configuration of 3-keto-24-*epi*-7,8-didehydrocimigenol.[4]

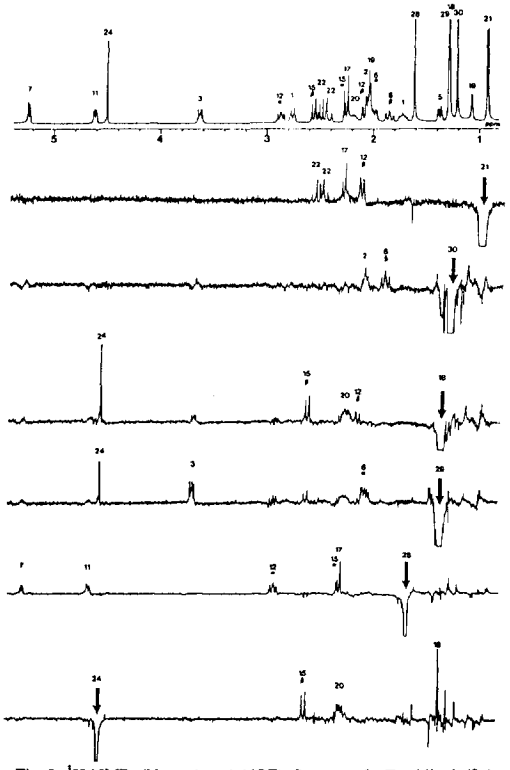
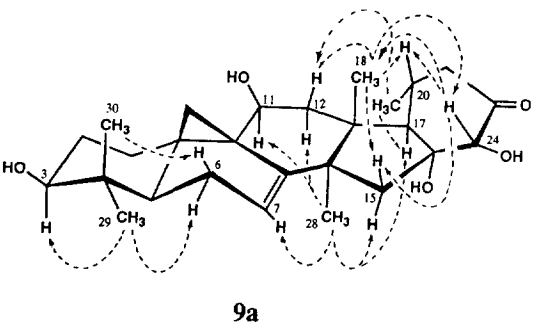


Fig. 2. ^{1}H-NMR (Normal and NOE) Spectra of Foetidinol (**9a**)
a) Normal ^{1}H-NMR spectrum.
b~g) NOE difference spectra on irradiation at δ 0.93, 1.21, 1.29, 1.30, 1.62, and 4.50, respectively.



9a

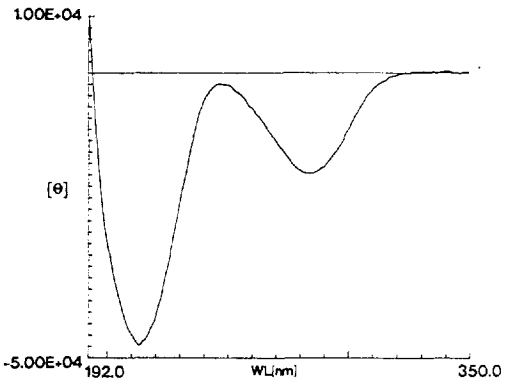


Fig. 3. CD Curve of Foetidinol (9a) in MeOH

Foetidinol-3-*O*-β-xyloside (**10**) was obtained as a slightly yellow amorphous solid and showed $[\alpha]_D$ -43.46° (c=0.27, $CHCl_3$:MeOH=1:1). The positive ion FAB-MS and HR-FAB-MS showed an ion peak at *m/z* 577 $[M+H]^+$ and *m/z* 577.3372 (Calcd 577.3377), indicating the molecular formula $C_{32}H_{49}O_9$. The IR spectrum revealed absorptions at 3400, 2900, 2850, 1720, 1040 cm^{-1}. The ^{1}H- and ^{13}C-NMR spectra were closely similar to that of **9a** except for the appearance of a new signals due to a five membered sugar (Tables III and IV). Its sugar was determined to xylose by the detailed analyses of ^{1}H- and ^{13}C-NMR.

Therefore, structure of foetidinol-3-*O*-β-xyloside was determined to be **10**.

15α-Hydroxyfoetidinol-3-*O*-β-xyloside (**11**) was also obtained as a white amorphous powder and showed $[\alpha]_D$ -73.64° (c=0.36, $CHCl_3$:MeOH=1:1). The positive ion FAB-MS of **11** exhibited the quasi-molecular ion peak at *m/z* 593 $[M+H]^+$ and its molecular formula was determined to be $C_{32}H_{49}O_{10}$ [$(M+H)^+$ 593.3324, Calcd 593.3326] by HR-FAB-MS. The ^{1}H- and ^{13}C-NMR spectra were almost identical with those of **10** except for the signal of hydroxy-bearing methine assignable to C-15 position (Tables III and IV). The C-15 hydroxy-bearing methine signal (δ_H 4.76) showed NOE enhancement on irradiation of the 18-methyl protons (δ_H 1.30), indicating that the 15-hydroxyl group is in α-configuration.

On the basis of these findings, the structure 15α-hydroxyfoetidinol-3-*O*-β-xyloside was determined to be **11**.

Table III. ^{1}H-NMR Spectral Data for Triterpenoids from *Cimicifuga foetida*

^{1}H	5a	6a	7a	8	9a	10	11
1	1.62 td (13.5, 5.5)	1.68 td (12.5, 5.5)	1.68 m	1.68 m	1.73 td (12.5, 6.5)	1.73 m	1.73 td (12.5, 6.0)
	2.66 dt (13.5, 3.5)	2.76 dt (12.5, 3.5)	2.76 m	2.81 m	2.76 dt (12.5, 3.5)	2.75 dt (12.0, 3.5)	2.77 dt (12.5, 3.5)
2	1.96 dt (13.5, 3.5)	2.23 m	2.08 qd (12.5, 4.0)	2.05 m	2.06 m	2.10 m	2.13 m
	2.27 m	———	2.41 m	2.39 m	———	2.41 m	2.42 m
3	3.48 dd (11.5, 3.0)	3.60 dd (10.0, 5.5)	3.59 dd (11.5, 3.0)	3.58 dd (11.5, 3.5)	3.63 dd (10.0, 5.5)	3.59 dd (11.5, 3.5)	3.61 dd (11.0, 4.0)
5	1.30 m	1.33 dd (12.5, 6.5)	1.34 dd (12.5, 5.5)	1.34 m	1.38 dd (12.5, 5.5)	1.35 dd (12.0, 5.5)	1.44 dd (12.0, 5.5)
6	1.68 brt (12.5)	1.77 ddd (17.5, 12.5, 2.0)	1.73 m	1.73 m	1.85 ddd (16.0, 12.5, 2.0)	1.77 ddd (16.0, 12.5, 2.0)	1.81 ddd (16.0, 12.0, 2.0)
	1.92 m	2.00 m	1.93 m	2.03 m	2.01 ddd (16.0, 7.5, 5.5)	1.95 ddd (16.0, 7.5, 5.5)	2.10 m
7	5.12 dd (7.5, 2.0)	5.17 dd (7.5, 2.0)	5.13 dd (7.5, 2.0)	6.18 dd (7.5, 2.0)	5.25 dd (7.5, 2.0)	5.22 dd (7.5, 2.0)	6.23 dd (7.5, 2.0)
11_α	4.46 dd (9.5, 3.5)	4.54 dd (9.5, 3.5)	4.53 dd (9.0, 3.5)	4.60 dd (9.0, 3.5)	4.62 ddd (9.0, 5.5, 3.5)	4.59 dd (9.0, 3.5)	4.61 dd (9.0, 3.5)
11_β	———	———	———	———	6.01 d (5.5, -OH)	———	———
12_α	2.76 dd (14.5, 9.5)	2.82 dd (14.0, 9.5)	2.77 dd (13.5, 9.0)	2.80 dd (13.5, 9.0)	2.87 dd (13.5, 9.0)	2.85 dd (13.5, 9.0)	2.81 dd (13.5, 9.0)
12_β	2.12 dd (14.5, 3.5)	2.19 dd (14.5, 3.5)	2.20 dd (13.5, 3.5)	2.23 dd (13.5, 3.5)	2.09 dd (13.5, 3.5)	2.07 dd (13.5, 3.5)	2.06 dd (13.5, 3.5)
15_α	2.25 d (18.0)	2.30 d (18.0)	2.26 d (18.0)	———	2.27 d (13.5)	2.26 d (13.5)	———
15_β	2.44 d (18.0)	2.50 d (18.0)	2.47 d (18.0)	4.56 s	2.56 d (13.5)	2.55 d (13.5)	4.76 s
17	2.33 d (9.0)	2.38 d (9.0)	2.42 d (9.0)	2.25 d (7.5)	2.26 d (10.0)	2.25 d (10.0)	2.45 d (10.0)
18-H_3	1.17 s	1.23 s	1.22 s	1.40 s	1.29 s	1.26 s	1.30 s
19	0.91 d (4.0)	0.98 d (4.0)	0.95 d (4.0)	1.02 d (4.5)	1.08 d (4.0)	1.02 d (4.0)	1.06 d (4.0)
	1.87 d (4.0)	1.96 d (4.0)	1.95 d (4.0)	1.96 d (4.5)	2.04 d (4.0)	2.00 d (4.0)	2.02 d (4.0)
20	2.51 m	2.59 m	2.74 m	2.79 m	2.19 m	2.19 m	2.15 m
21-H_3	1.00 d (6.0)	1.04 d (6.5)	1.13 d (6.5)	1.13 d (6.5)	0.93 d (5.5)	0.92 d (6.0)	0.92 d (5.5)
22	2.59 dd (16.5, 9.5)	2.63 dd (15.5, 8.0)	3.43 dd (18.0, 9.0)	3.43 dd (18.0, 9.0)	2.42 dd (18.5, 4.0)	2.42 dd (18.5, 4.0)	2.41 dd (18.5, 4.0)
	3.55 dd (16.5, 7.0)	3.61 dd (15.5, 9.5)	3.85 dd (18.0, 3.0)	3.86 dd (18.0, 3.0)	2.52 dd (18.5, 12.0)	2.52 dd (18.5, 12.0)	2.49 dd (18.5, 11.5)
24	3.66 d (0.5)	3.72 s	4.49 s	4.46 s	4.50 s	4.50 s	4.53 s
26-H_3	1.37 s	1.37 s	1.66 s	1.63 s	———	———	———
27-H_3	1.31 s	1.35 s	1.54 s	1.50 s	———	———	———
28-H_3	1.17 s	1.21 s	1.16 s	1.28 s	1.62 s	1.60 s	1.51 s
29-H_3	1.33 s	1.28 s	1.41 s	1.38 s	1.30 (s)	1.41 s	1.41 s
30-H_3	1.07 s	1.18 s	1.15 s	1.15 s	1.21 (s)	1.16 s	1.16 s
1'	4.74 d (7.5)	———	4.87 d (7.5)	4.85 d (7.5)	———	4.88 d (7.5)	4.88 d (7.5)
2'	3.87 t (7.5)	———	4.03 t (7.5)	4.00 t (7.5)	———	4.03 t (7.5)	4.01 t (7.5)
3'	4.00 t (8.5)	———	4.15 t (8.5)	4.13 t (8.5)	———	4.15 t (8.5)	4.14 t (8.5)
4'	4.06 m	———	4.21 ddd (10.0, 8.5, 5.0)	4.16 ddd (10.0, 8.5, 5.0)	———	4.20 ddd (11.0, 8.5, 5.0)	4.20 ddd (11.0, 8.5, 5.0)
5'	3.61 t (11.0)	———	3.73 dd (11.0, 10.0)	3.71 dd (11.0, 10.0)	———	3.73 t (11.0)	3.72 t (11.0)
	4.23 dd (11.0, 4.5)	———	4.34 dd (11.0, 5.0)	4.31 dd (11.0, 5.0)	———	4.34 dd (11.0, 5.0)	4.33 dd (11.0, 5.0)
$COCH_3$	———	———	———	———	———	———	———

^{1}H-^{1}H shift correlation spectra and NOE spectra were measured. δ value in pyridine-d_5 and coupling constants in Hz.

Table IV. ^{13}C-NMR Spectral Data for Triterpenoids from *Cimicifuga foetida*

^{13}C	**5a**[a]	**6a**[a]	**7a**[a]	**8**[a]	**9a**[c]	**10**[b]	**11**[b]
1	27.24 (t)	27.64 (t)	27.40 (t)	27.73 (t)	27.70 (t)	28.09 (t)	27.46 (t)
2	29.49 (t)	30.92 (t)	29.79 (t)	29.70 (t)	31.07 (t)	32.10 (t)	29.85 (t)
3	88.08 (d)	77.91 (d)	88.32 (d)	88.29 (d)	78.03 (d)	88.45 (d)	88.48 (d)
4	40.45 (s)	40.48 (s)	40.69 (s)	40.60 (s)	40.54 (s)	40.69 (s)	40.69 (s)
5	43.58 (d)	43.52 (d)	43.79 (d)	43.79 (d)	43.88 (d)	44.09 (d)	44.00 (d)
6	21.84 (t)	22.26 (t)	21.99 (t)	21.84 (t)	22.36 (t)	22.05 (t)	22.05 (t)
7	115.16 (d)	115.56 (d)	115.28 (d)	115.71 (d)	113.95 (d)	113.70 (d)	114.16 (d)
8	147.01 (s)	147.13 (s)	147.28 (s)	146.40 (s)	149.28 (s)	149.31 (s)	148.16 (s)
9	27.00 (s)	27.51 (s)	27.49 (s)	28.06 (s)	27.49 (s)	27.43 (s)	27.67 (s)
10	29.10 (s)	29.64 (s)	29.31 (s)	29.10 (s)	29.52 (s)	29.13 (s)	29.07 (s)
11	62.70 (d)	63.04 (d)	62.19 (d)	62.94 (t)	63.61 (d)	63.58 (d)	63.31 (d)
12	47.01 (t)	47.25 (t)	47.19 (t)	49.40 (d)	48.95 (t)	48.89 (t)	49.56 (t)
13	44.15 (s)	44.37 (s)	44.43 (s)	40.87 (s)	46.34 (s)	46.31 (s)	42.54 (s)
14	45.88 (s)	46.10 (s)	46.07 (s)	49.56 (s)	50.86 (s)	50.83 (s)	52.65 (s)
15	49.50 (t)	49.74 (t)	49.17 (d)	80.64 (d)	48.62 (t)	48.55 (t)	77.03 (d)
16	218.23 (s)	218.44 (s)	218.35 (s)	220.54 (d)	82.37 (s)	82.34 (s)	79.22 (s)
17	60.85 (d)	61.06 (d)	61.37 (d)	58.88 (d)	63.61 (d)	63.58 (d)	61.61 (d)
18	19.90 (q)	20.08 (q)	20.14 (q)	20.93 (q)	21.23 (q)	21.17 (q)	21.54 (q)
19	18.38 (t)	18.65 (t)	18.53 (t)	18.35 (t)	18.80 (t)	18.68 (t)	18.56 (t)
20	27.33 (d)	27.58 (d)	27.70 (d)	27.61 (d)	25.85 (d)	25.85 (d)	25.63 (d)
21	20.17 (q)	20.32 (t)	20.41 (q)	20.93 (q)	20.72 (q)	20.66 (q)	20.66 (q)
22	47.10 (t)	47.31 (t)	47.58 (t)	47.10 (t)	44.85 (t)	44.82 (t)	45.22 (t)
23	205.32 (s)	205.54 (s)	213.70 (s)	213.49 (s)	211.27 (s)	211.24 (s)	210.91 (s)
24	65.49 (d)	65.71 (d)	84.01 (d)	83.89 (d)	82.01 (d)	81.98 (d)	82.25 (d)
25	60.48 (s)	60.61 (s)	72.45 (s)	72.39 (s)	-------	-------	-------
26	24.48 (q)	24.57 (q)	28.00 (t)	27.91 (q)	-------	-------	-------
27	18.20 (q)	18.31 (q)	25.73 (q)	25.45 (d)	------	-------	-------
28	27.58 (q)	27.73 (q)	27.70 (q)	19.44 (q)	28.15 (q)	28.09 (q)	19.99 (q)
29	25.73 (q)	26.30 (q)	25.88 (q)	25.85 (q)	26.39 (q)	25.93 (q)	25.97 (q)
30	14.31 (q)	13.79 (q)	14.49 (q)	14.43 (q)	13.92 (q)	14.55 (q)	14.55 (q)
1'	107.02 (d)	-------	107.45 (d)	107.33 (d)	-------	107.45 (d)	107.45 (d)
2'	75.03 (d)	-------	75.48 (d)	75.36 (d)	-------	75.51 (d)	75.48 (d)
3'	78.06 (d)	-------	78.55 (d)	78.40 (d)	-------	78.55 (d)	78.52 (d)
4'	70.78 (d)	-------	71.17 (d)	71.05 (d)	-------	71.17 (d)	71.17 (d)
5'	66.68 (t)	-------	67.07 (t)	66.92 (d)	-------	67.07 (t)	67.04 (t)
C=O	-------	-------	-------	-------	-------	-------	-------
$CO\underline{C}H_3$	-------	-------	-------	-------	-------	-------	-------

δ value in pyridine-d_5. The multiplicities of carbon signals were determined by the distortionless enhancement by polarization transfer (DEPT) method and are indicated as s, d, t and q. a) ^1H-^{13}C and ^1H-^{13}C long-range COSY spectra were measured. b) ^1H-^{13}C COSY and HMBC spectra were measured. c) ^1H-^{13}C COSY, ^1H-^{13}C long-range COSY and HMBC spectra were measured.

In addition, a comparative study of the ^{1}H- and ^{13}C-NMR data of the cycloartenol and related compounds in the literature as well as the compounds reported by us is shown in the Table V. From the example **i), ii), iii),** and **iv),** we can see that the hydroxyl or acetoxyl group substitution at C_{12} or C_7 do not change the chemical shift of the cyclopropane methylene proton and carbon at C_{19}. But presence of double bond at C_7 position as compound (**v**), considerably shifted the chemical shift of one of the protons to the down-field but slightly deshielded the chemical shift of C_{19} carbon compared with compound (**i**). It was found that the presence of one more hydroxyl or acetoxyl group substituted at C_{11} position of compound (**v**) very remarkably shifted the chemical shifts of C_{19}-H to the down-field, while the chemical shift of carbon to the upper-field as in compounds **vi** and **vii**. Two more examples (**viii** and **ix**) from literature are also mentioned in the Table V. This comparative study clearly suggests that the hydroxyl or acetoxyl group substituted at C_{12} position do not have shielding or deshielding effects on C_{19} position but in contrast the presence of hydroxyl or acetoxyl group, at C_{11} very strongly shielded the carbon while protons of cyclopropyl methylene are deshielded.

To the best of our knowledge, our present result provided the first example of trinor-triterpenoids having a novel carbon skeleton. These compounds are of interest from a biogenetic viewpoints. The biogenetic pathways of these compounds are still unclear, but treatment of **4b**, **6a**, and **6b** with 3M $HClO_4$ in THF afforded pentacyclic foetidinol-type compounds **14, 9a**, and **15,** respectively (Chart 6), however, the stereochemistry of epoxide of **4b** has not been confirmed. In contrast, compound **8** did not follow the same reaction as **4b**, **6a**, and **6b** did under similar condition. The possible mechanism for this reaction is illustrated in Chart 7. These experimental facts strongly suggest that these **9a**, **14**, and **15** are considered most likely to be produced by above cleavage of C_{24}-C_{25} and followed condensation with retention of C-24 configuration in the organism.

The biological activities of these triterpenoids are now under investigation in our laboratory.

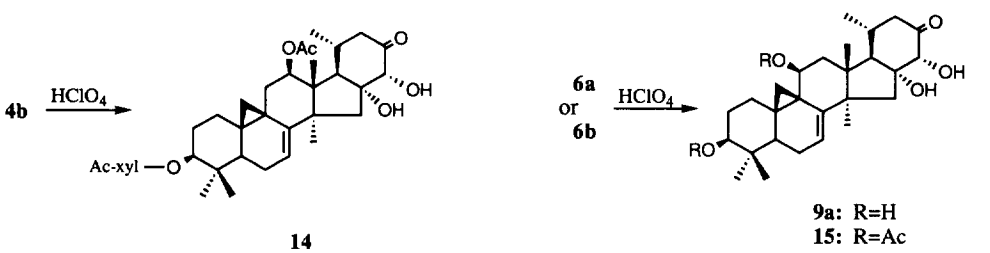


Chart 6

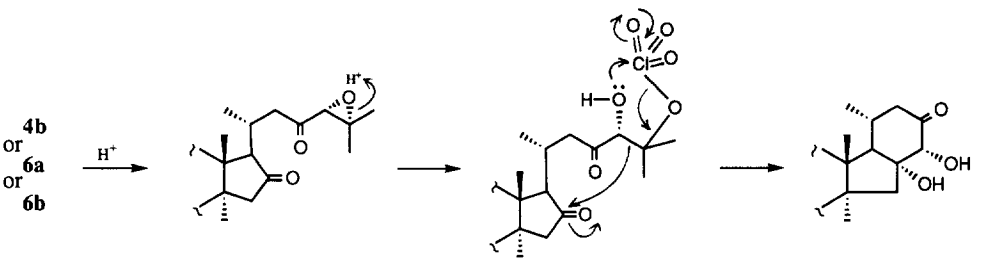
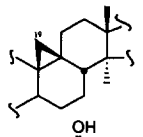
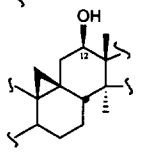
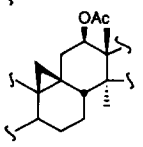
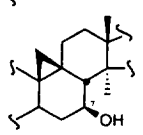
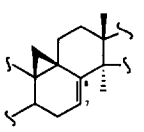
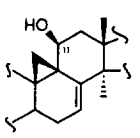
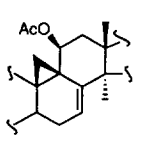
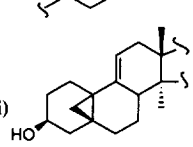
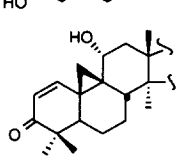


Chart 7

Table V. ^{1}H- and ^{13}C-NMR Data of Cyclopropyl Methylene for Cycloartenol and Related Compounds

		Chemical shift (ppm)		Solvent	Names and literatures
		19-H_2	C-19		
i)		**0.37, 0.55, d, *J*=4.0Hz**	**30.92**	pyridine-d_5	25-*O*-acetylcimigenol[4]
ii)		**0.35, 0.59, d, *J*=3.9Hz**	**30.7**	pyridine-d_5	cimiside A[14]
iii)		**0.23, 0.58, d, *J*=4.5Hz**	**29.85**	pyridine-d_5	27-deoxyacetylacteol (**13**)
iv)		**0.37, 0.70, d, *J*=4.0Hz**	**30.40**	pyridine-d_5	7β-hydroxycimigenol[3b]
v)		**0.55, 1.06, d, *J*=4.0Hz**	**28.35**	pyridine-d_5	24-*epi*-7,8-dehydrocimigenol[4]
vi)		**0.98, 1.96, d, *J*=4.0Hz**	**18.80**	pyridine-d_5	cimicidanol (**6a**)
vii)		**0.95, 1.56, d, *J*=4.5Hz**	**20.11**	pyridine-d_5	cimicidanol diacetate (**6b**)
viii)		**0.63, 0.67, d, *J*=4.0Hz**	**25.07**	$CDCl_3$	cyclonervilasterol[15]
ix)		**1.25, s, 2H**	**29.7**	$CDCl_3$	11α-hydroxybuxatenone[16]

EXPERIMENTAL

General Experimental Procedures. Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ or MeOH solutions on a JASCO DIP-360 digital polarimeter at 25°C. CD spectra were recorded with a JASCO J-720 automatic recording spectropolarimeter in MeOH. IR spectra were recorded on a Hitachi 260-01 spectrometer in KBr discs. UV spectrum was taken on a Shimadzu UV-2200 UV-VIS spectrophotometer. EI-MS (ionization voltage, 70 eV; accelerating voltage, 3kV) and FAB-MS were measured with a JEOL JMS DX-300 or JMS-SX 102 spectrometer using a direct inlet system and glycerol, glycerol-thioglycerol (1:1), or nitrobenzyl alcohol were used as a matrix in positive or negative ion FAB-MS measurements. ^1H- and ^{13}-NMR spectra were taken on a JEOL JNM-GX 400 spectrometer with tetramethylsilane as an internal standard and chemical shifts were recorded in δ values. Multiplicities of ^{13}C-NMR signals were determined by means of the distortionless enhancement by polarization transfer (DEPT) method and are indicated as s (singlet), d (doublet), t (triplet), and q (quartet). 2D NMR spectra (^1H-^1H COSY, ^1H-^{13}C COSY, and ^1H-^{13}C long-range COSY) were measured by the use of JEOL standard pulse sequences and collected data were treated by JEOL standard software. Difference NOE spectra were obtained by the use of JEOL standard pulse sequences with 5s irradiation. Column chromatography was performed with Wakogel C-200 (Wako Pure Chemical Co., Japan) or Cosmosil 140 C_{18} (Nakarai tesque, Inc., Japan). TLC and preparative TLC were carried out on precoated Kieselgel F_{254} plates (0.25 or 0.5 mm) or Merck RP-18 F_{254} reversed-phase plates (0.25 mm) with hexane-EtOAc (7:3) and hexane-EtOAc-MeOH (1:1:0.1) as a developing solvent, and spots were detected under a UV lamp, or by spraying with $Ce(SO_4)_2$-10% H_2SO_4 (1:99).

Extraction and Separation of Constituents of the Rhizome of *Cimicifuga foetida* L

The dried ground rhizome of *C. foetida* L. (4 kg), collected at Sichuan province of China in July, 1993, was successively extracted three times with MeOH for 3h under reflux. The MeOH extract was evaporated to dryness and the residue (600 g) was suspended in water (1000 ml) and fractionated by successive extraction with hexane (1000 ml x 3), EtOAc (1000 ml x 3), and *n*-BuOH (1000 ml x 3) to give a hexane-soluble fraction (130 g), an EtOAc-soluble fraction (236 g) and a *n*-BuOH-soluble fraction (50 g).

The EtOAc-soluble fraction (200 g) was subjected to column chromatography on silica gel (1.8 kg). Elution with $CHCl_3$ and $CHCl_3$-MeOH (19:1, 4:1, 7:3, and 6:4) gave the 7 fractions, I (1.5 g), II (1.0 g), III (12.0 g), IV (36.0 g), V (43.0 g), VI (19.0 g), and VII (15.0 g).

Fraction I was rechromatographed on a silica gel column with hexane-EtOAc (4:1 and 3:2), giving two fractions. The product of the first fraction (50 mg) was further isolated by preparative TLC with benzene to give norvisnagin (6 mg) and isoimpertorin (25 mg).

Fraction II (1.0 g) was subjected to silica gel column chromatography with hexane-EtOAc (4:1 and 3:2) to give isoferulic acid(50 mg) and 27-deoxyacetylacteol (**13**)(15 mg).

Fraction III (12.0 g) was chromatographed on a charcoal column with EtOAc and then re-chromatographed on a silica gel column with hexane-EtOAc (7:3, 3:2, and 1:1) to give isoferulic acid (3.0 g) and cimicidanol (**6a**)(100 mg).

Fraction IV (36.0 g) was chromatographed on a silica gel column with hexane-EtOAc-MeOH (1:1:0.01 and 1:1:0.05) to give five fractions, fr.IV-1 (8.0 g), fr. IV-2 (2.5 g), fr. IV-3 (1.5 g), fr. IV-4 (4.0 g), and fr. IV-5 (15.0 g). Fr. IV-1 was further purified by silica gel column chromatography with benzene-EtOAc (7:3) to

give angelicain (0.5 g). Fr. IV-2 was re-chromatographed on a silica gel column chromatography with hexane-EtOAc-MeOH (1:1:0.01) to give foetidinol (**9a**)(25 mg) and 25-anhydrocimigenol-3-*O*-β-xyloside (**1**) (30 mg).Fr. IV-3 was purified by silica gel column chromatography to give 25-acetylcimigenol xyloside (**12**)(30 mg). Fr. IV-4 was subjected to silica gel column chromatography with hexane-EtOAc-MeOH (1:1:0.05) to give cimicinol (**3**)(20 mg), cimicifol (**4a**)(25 mg), and acetylacteol arabinoside (**2a**)(3.0 g).

Fraction V was crystallized from $CHCl_3$-MeOH (7:3) to give an additional crop of cimicidanol-3-*O*-arabinoside (**5a**) (2.0 g).

Fraction VI was subjected to Cosmosil 140 C_{18} (85.0 g) column chromatography with MeOH-H_2O (1:1 and 7:3), giving two fractions. The first eluate fraction (3.0 g) gave cimicidol-3-*O*-β-xyloside (**7a**) (1.5 g). The second fraction was further purified by Cosmosil 140 C_{18} (50.0 g) column chromatography with MeOH-H_2O (1:1 and 7:3), giving foetidinol-3-*O*-β-xyloside (**10**)(3 mg) and 15α-hydroxyfoetidinol-3-*O*-β-xyloside (**11**)(5 mg).

Fraction VII (10.0 g) was passed through a charcoal column with MeOH to give MeOH eluate (8.0 g). A part of MeOH eluate fraction (2.0 g) was subjected to Cosmosil 140 C_{18} column chromatography with MeOH-H_2O (1:1 and 7:3), giving 15α-hydroxycimicidol-3-*O*-β-xyloside (**8**)(20 mg).

Identification of Known Compounds

Norvisnagin,[17] isoimperatorin,[18] and angelicain[19] were confirmed by comparisons ^{1}H-and ^{13}C-NMR and specific rotation with data in the literature, respectively. Isoferulic acid was identified by comparison with an authentic sample.

25-Acetylcimigenol xyloside (**12**): A colorless needles (*n*-hexane-EtOAc), mp 245-246°C, $[\alpha]_D$ +0.82° (c=0.14, $CHCl_3$:MeOH=1:1). IR ν max cm^{-1}: 3400 (OH) and 1400. Positive ion FAB-MS *m/z*: 665 $[M+H]^+$. ^{1}H- and ^{13}C-NMR: Tables I and II.

27-Deoxyacetylacteol (**13**): A colorless needles (*n*-hexane-EtOAc), mp 290-295°C, $[\alpha]_D$ -80.4° (c=0.16, $CHCl_3$). IR ν max cm^{-1}: 3500 (OH), 1740 (C=O), 1240, and 1030. EI-MS *m/z*: 528 (M^+), 510 (M^+-H_2O), 500, 336, and 238. ^{1}H- and ^{13}C-NMR: Tables I and II.

25-Anhydrocimigenol-3-*O*-β-xyloside (1): A colorless needles (*n*-hexane-EtOAc), mp 245-246 °C, $[\alpha]_D$ +8.42° (c=0.14, $CHCl_3$:MeOH=1:1). IR ν max cm^{-1} 3400 (OH) and 1400. Positive ion FAB-MS *m/z*: 603 $(M+H)^+$. HR-FAB-MS *m/z*: 603.3938, [$(M+H)^+$, Calcd for $C_{35}H_{55}O_8$, 603.3897]. ^{1}H- and ^{13}C-NMR: Tables I and II.

Acetylacteol-3-*O*-arabinoside (2a): White powder, $[\alpha]_D$ -66.06° (c=0.30, $CHCl_3$:MeOH =1:1). IR ν max cm^{-1}: 3420 (OH), 2960, 2920, and 1740 (C=O). Positive ion FAB-MS *m/z*: 677 $[M+H]^+$. HR-FAB-MS *m/z*: 677.3381, [$(M+H)^+$, Calcd for $C_{37}H_{57}O_{11}$, 677.3401]. ^{1}H- and ^{13}C-NMR: Tables I and II.

Cimicinol (3): Yellow powder, $[\alpha]_D$ +14.02° (c=0.30, $CHCl_3$:MeOH=1:1). IR ν max cm^{-1}: 3420 (OH), 2960, 2920, 1620, 1380, and 1040. UV λ_{max} MeOH (log ε): 207 (3.02) and 248 (3.24). Positive ion FAB-MS *m/z*: 601 $[M+H]^+$. HR-FAB-MS *m/z*: 601.3760, [$(M+H)^+$, Calcd for $C_{35}H_{53}O_8$, 601.3780]. ^{1}H- and ^{13}C-NMR: Tables I and II.

Cimicifol (4a): White powder, $[\alpha]_D$ -99.33° (c=0.30, $CHCl_3$:MeOH=1:1). IR ν max cm^{-1}: 3420 (OH), 2950, 1740 (C=O) and 1720 (C=O). Positive ion FAB-MS *m/z*: 659 $[M+H]^+$. HR-FAB-MS *m/z*: 659.3896, [$(M+H)^+$, Calcd for $C_{37}H_{55}O_{10}$, 659.3900]. ^{1}H- and ^{13}C-NMR: Tables I and II.

Cimicidanol-3-*O*-arabinoside (5a): A colorless plates ($CHCl_3$-MeOH); mp 214-215 °C; $[\alpha]_D$ -42.32° (c=0.20, $CHCl_3$:MeOH=1:1). IR ν max cm^{-1}: 3450 (OH), 2960, 2925, 2850, 1720 (C=O), 1380, and 1040. Negative ion FAB-MS *m/z* 615 $[M-H]^-$. HR-FAB-MS *m/z*: 615.3528, $[(M-H)^-$, Calcd for $C_{35}H_{51}O_9$, 615.3520]. ^1H- and ^{13}C-NMR: Tables III and IV.

Cimicidanol (6a): A colorless needles (*n*-hexane-EtOAc), mp 197-198 °C, $[\alpha]_D$ -50.58° (c=0.16, $CHCl_3$:MeOH=1:1). IR ν max cm^{-1}: 3450 (OH), 1720 (C=O), 1700 (C=O), 1440, and 1380. EI-MS *m/z*: 484 (M^+), 468 ($M-H_2O$), 269, 251, and 95. HR-EI-MS *m/z*: 484.3230, (M^+, Calcd for $C_{30}H_{44}O_5$, 484.3199). ^1H- and ^{13}C-NMR: Tables III and IV.

Cimicidol-3-*O*-β-xyloside (7a): White powder, $[\alpha]_D$ -30.73° (c=0.60, $CHCl_3$:MeOH =1:1). IR ν max cm^{-1}: 3400 (OH), 2950, 2900, 1720 (C=O), and 1040. Positive ion FAB-MS *m/z*: 635 $[M+H]^+$. HR-FAB-MS m/z: 635.3826 $[(M+H)^+$, Calcd for $C_{35}H_{55}O_{10}$, 635.3795]. ^1H- and ^{13}C-NMR: Tables III and IV.

15α-Hydroxycimicidol-3-*O*-β-xyloside (8): White powder, $[\alpha]_D$ -45.70° (c=0.38, $CHCl_3$:MeOH=1:1). IR ν max cm^{-1}: 3400 (OH), 2950, 2900, 1720 (C=O), and 1040. Positive ion FAB-MS *m/z*: 651 $[M+H]^+$. HR-FAB-MS *m/z*: 651.3756 $[(M+H)^+$, Calcd for $C_{35}H_{55}O_{11}$, 651.3744. ^1H- and ^{13}C-NMR: Tables III and IV.

Foetidinol (9a): A colorless needles (*n*-hexane-EtOAc), mp 255-256 °C; $[\alpha]_D$ -93.50° (c=0.12, $CHCl_3$:MeOH=1:1). IR ν max cm^{-1}: 3450 (OH), 1718 (C=O), and 1620. EI-MS *m/z*: 444 (M^+) and 438 ($M-H_2O$). HR-EI-MS *m/z*: 444.2909, (M^+, Calcd for $C_{27}H_{40}O_5$, 444.2873). Elemental analysis, Calcd for: C, 72.94, H, 9.07, Found: C, 73.18, H, 8.79. CD (c=0.61 mM, MeOH): $[\theta]_{213}$ -47870, $[\theta]_{247}$ -1981, $[\theta]_{284}$ -17700. ORD (c=2.55 mM, MeOH) [M](nm): -1.19 $x10^4$ (230), +0.93 $x10^4$ (264), -1.14 $x10^4$ (303).^1H- and ^{13}C-NMR: Tables III and IV.

Foetidinol-3-*O*-β-xyloside (10): Slightly yellow amorphous, $[\alpha]_D$ -43.46° (c=0.27, $CHCl_3$:MeOH =1:1). IR ν max cm^{-1}: 3400 (OH), 2900, 2850, 1720 (C=O), and 1040. Positive ion FAB-MS *m/z*: 577 $[M+H]^+$. HR-FAB-MS 577.3372*m/z*: $[(M+H)^+$, Calcd for $C_{32}H_{49}O_9$, 577.3377]. ^1H- and ^{13}C-NMR: Tables III and IV.

15α-Hydroxyfoetidinol-3-*O*-β-xyloside (11): White powder, $[\alpha]_D$ -73.64° (c=0.36, $CHCl_3$:MeOH=1:1). IR ν max cm^{-1}: 3400 (OH), 2900, 2850, 1720 (C=O), and 1040. Positive ion FAB-MS *m/z*: 593 $[M+H]^+$. HR-FAB-MS *m/z*: 593.3324, $[(M+H)^+$, Calcd for $C_{32}H_{49}O_{10}$, 593.3326]. ^1H- and ^{13}C-NMR: Tables III and IV.

Acid Hydrolysis of Compounds 1-8

Compounds **1-8** (each 5 mg) were each hydrolyzed in 0.5 N HCl for 3 h at 100 °C. After neutralization with NH_4OH, followed by extraction with EtOAc (20 ml x 3), the aqueous layer was lyophilized *in vacuo* to give a residue. The residue was applied to a TLC plate and developed with EtOAc-MeOH-H_2O-AcOH (13:6:3:3). The Rf values of the products were in agreement with that (Rf=0.59) of xylose and (Rf=0.42) of arabinose.

Acetylation of Cimicifol (4a)

A mixture of **4a** (10 mg), acetic anhydride (0.5 ml) and pyridine (1.0 ml) was left to stand at room temperature for 12 h. After decomposition of the excess reagent with water, the reaction mixture was extracted with EtOAc. The EtOAc layer was washed with brine, dried, and concentrated *in vacuo*. The residue was separated by preparative TLC with EtOAc-hexane (6:4) to yield a tetraacetate (**4b**) (9 mg). Tetraacetate (**4b**):

$[\alpha]_D$ -26.09° (c=0.60, $CHCl_3$). Positive ion FAB-MS *m/z*: 807 $[M+Na]^+$. HR-FAB-MS *m/z*: 807.3910, $[(M+Na)^+$, Calcd for $C_{43}H_{60}O_{13}Na$, 807.3922]. ^{1}H-NMR (pyridine-d_5) δ_H: 0.59 (1H, d, *J*=4.0Hz, 19-H), 0.92 (3H, s, 30-H_3), 1.03 (3H, s, 29-H_3), 1.06 (1H, d, *J*=4.0Hz, 19-H), 1.15 (1H, m, 5-H), 1.18 (1H, m, 1-H), 1.20 (3H, s, 28-H_3), 1.22 (3H, d, *J*=7.0Hz, 21-H_3), 1.29 (1H, dd, *J*=16.0, 4.0Hz, 11-H), 1.30 (3H, s, 27-H_3), 1.34 (3H, s, 26-H_3), 1.36 (3H, s, 16-H_3), 1.55 (1H, m, 6-H), 1.57 (1H, m, 1-H), 1.81 (1H, m, 2-H), 1.86 (1H, m, 6-H), 1.97 (-$COCH_3$), 2.05 (-$COCH_3$), 2.13 (1H, m, 2-H), 2.15 (-$COCH_3$), 2.26 (-$COCH_3$), 2.35 (1H, *J*=17.5Hz, 15-H), 2.63 (1H, *J*=17.5Hz, 15-H), 2.72 (1H, d, *J*=2.5Hz, 17-H), 2.81 (1H, m, 20-H), 2.88 (1H, dd, *J*=16.0, 9.0Hz, 11-H), 2.92 (1H, dd, *J*=18.0, 4.0Hz, 22-H), 3.00 (1H, dd *J*=18.0, 8.0Hz, 22-H), 3.46 (1H, dd, *J*=11.5, 4.0Hz, 3-H), 3.62 (1H, t, *J*=11.0Hz, 5'-H), 3.67 (1H, s, 24-H), 4.28 (1H, dd, *J*=11.0, 5.0Hz, 5'-H), 4.85 (1H, d, *J*=7.5Hz, 1'-H), 5.08 (1H, dd, *J*=7.5, 2.0Hz, 7-H), 5.30 (1H, m 4'-H), 5.43 (1H, dd, *J*=7.5Hz, 2'-H), 5.60 (1H, dd, *J*=7.5, 2.0Hz, 12-H), 5.69 (1H, t, *J*=8.5, 3'-H).

Acetylation of Cimicidanol-3-*O*-arabinoside (5a)

Acetylation of cimicidanol-3-*O*-arabinoside (**5a**) (100 mg) in the same way as above and purification of the product by preparative TLC and give tetraacetate (**5b**) (102 mg). Tetraacetate (**5b**): $[\alpha]_D$ -10.67° (c=0.08, $CHCl_3$). Positive ion FAB-MS *m/z*: 785 $[M+H]^+$. HR-FAB-MS *m/z*: 785.4090, $[(M+H)^+$, Calcd for $C_{43}H_{61}O_{13}$, 785.4112]. ^{1}H-NMR (pyridine-d_5) δ_H: 0.95 (1H, d, *J*=4.5Hz, 19-H), 0.96 (3H, s, 30-H_3), 1.00 (3H, d, *J*=6.0Hz, 21-H_3), 1.06 (3H, s, 29-H_3), 1.17 (6H, s, 18, 28-H_3), 1.19 (1H, m, 5-H), 1.35 (H, s, 27-H_3), 1.37 (3H, s, 26-H_3), 1.48 (2H, m, 1-H_2), 1.56 (1H, d, *J*=4.5Hz, 19-H), 1.62 (1H, brt, *J*=14.5Hz, 6-H), 1.83 (1H, dd, *J*=14.5, 3.5Hz, 12-H), 1.85 (1H, m, 2-H), 1.89 (1H, m, 6-H), 1.98 (-$COCH_3$), 2.04 (-$COCH_3$), 2.06 (-$COCH_3$), 2.09 (1H, m, 2-H), 2.15 (-$COCH_3$), 2.30 (1H, *J*=18.0Hz, 15-H), 2.37 (1H, d, *J*=9.0Hz, 17-H), 2.48 (1H, *J*=18.0Hz, 15-H), 2.59 (1H, m, 20-H), 2.61 (1H, dd *J*=20.0, 8.0Hz, 22-H), 2.96 (1H, dd, *J*=14.5 9.5Hz, 12-H), 3.29 (1H, dd, *J*=11.5, 4.0Hz, 3-H), 3.60 (1H, dd, *J*=20.0, 7.0Hz, 22-H), 3.68 (1H, t, *J*=11.0Hz, 5'-H), 3.73 (1H, s, 24-H), 4.35 (1H, dd, *J*=11.0, 5.0Hz, 5'-H), 4.86 (1H, d, *J*=7.5Hz, 1'-H), 5.14 (1H, dd, *J*=7.5, 2.0Hz, 7-H), 5.30 (1H, ddd, *J*=11.0, 8.5, 5.0Hz, 4'-H), 5.41 (1H, t, *J*=7.5Hz, 2'-H), 5.49 (1H, dd, *J*=9.5, 3.5Hz, 11-H), 5.68 (1H, t, *J*=8.5, 3'-H).

Acetylation of Cimicidanol (6a)

Acetylation of cimicidanol (**6a**) (15 mg) in the same way as above and purification of the product by preparative TLC and gave 3,11-*O*-diacetylcimicidanol (**6b**)(12 mg). 3,11-*O*-Diacetylcimicidanol (**6b**): $[\alpha]_D$ -11.67° (c=0.09, $CHCl_3$). Positive ion FAB-MS *m/z*: 569 $[M+H]^+$. HR-FAB-MS *m/z*: 569.3434, $[(M+H)^+$, Calcd for $C_{34}H_{49}O_7$, 569.3478]. ^{1}H-NMR (pyridine-d_5) δ_H: 0.90 (3H, s, 30-H_3), 0.94 (3H, s, 29-H_3), 0.95 (3H, d, *J*=7.5Hz, 21-H_3), 1.02 (1H, d, *J*=4.0Hz, 19-H), 1.11 (3H, s, 18-H_3), 1.14 (3H, s, 28-H_3), 1.29 (H, s, 27-H_3), 1.30 (1H, m, 5-H), 1.35 (1H, m, 1-H), 1.44 (3H, s, 26-H_3), 1.52 (1H, d, *J*=4.0Hz, 19-H), 1.60 (1H, dd, *J*=14.0, 3.5Hz, 12-H), 1.65 (1H, m, 2-H), 1.67 (1H, m, 1-H), 1.71 (1H, m, 6-H), 1.79 (1H, m, 2-H), 1.97 (1H, qd, *J*=17.5, 5.5Hz, 6-H), 2.04 (-$COCH_3$), 2.07 (-$COCH_3$), 2.17 (1H, d, *J*=9.0Hz, 17-H), 2.18 (1H, *J*=19.0Hz, 15-H), 2.35 (1H, *J*=19.0Hz, 15-H), 2.38 (1H, m, 20-H), 2.45 (1H, dd *J*=17.5, 9.0Hz, 22-H), 2.77 (1H, dd, *J*=14.0 9.5Hz, 12-H), 3.35 (1H, dd, *J*=15.5, 3.0Hz, 22-H), 3.47 (1H, s, 24-H), 4.59 (1H, dd, *J*=11.0, 3.5Hz, 3-H), 5.16 (1H, dd, *J*=8.0, 2.5Hz, 7-H), 5.22 (1H, dd, *J*=9.5, 3.5Hz, 11-H).

Acetylation of Cimicidol-3-*O*-β-xyloside (7a)

Acetylation of cimicidol-3-*O*-β-D-xyloside (**7a**) in the same way as above and purification by preparative TLC and gave pentaacetate (**7b**)(8.0 mg). Pentaacetate (**7b**): $[\alpha]_D$ -14.29° (c=0.13, $CHCl_3$). IR ν max cm^{-1}:

3450 (OH), 1740 (C=O) 1720 (C=O), 1380 and 1235. Positive ion FAB-MS *m/z*: 827 $[M+H-H_2O]^+$. HR-FAB-MS *m/z*: 827.4236, $[(M+H-H_2O)^+$, Calcd for $C_{45}H_{63}O_{14}$, 827.4217]. ^{1}H-NMR (pyridine-d_5) δ_H: 0.95 (1H, d, *J*=4.5Hz, 19-H), 0.97 (3H, s, 30-H_3), 1.07 (3H, s, 29-H_3), 1.08 (3H, d, *J*=6.5Hz, 21-H_3), 1.15 (3H, s, 28-H_3), 1.18 (3H, s, 18-H_3), 1.19 (1H, dd, *J*=12.5, 5.5Hz, 5-H), 1.47 (2H, m, 1-H_2), 1.55 (1H, d, *J*=4.5Hz, 19-H), 1.63 (1H, m, 6-H), 1.73 (H, s, 27-H_3), 1.74 (3H, s, 26-H_3), 1.81 (1H, dd, *J*=14.5, 3.5Hz, 12-H), 1.84 (1H, m, 2-H), 1.87 (1H, m, 6-H), 1.98 (-$COCH_3$), 2.04 (-$COCH_3$), 2.10 (1H, m, 2-H), 2.14 (-$COCH_3$), 2.15 (-$COCH_3$), 2.16 (-$COCH_3$), 2.29 (1H, *J*=18.0Hz, 15-H), 2.46 (1H, d, *J*=8.0Hz, 17-H), 2.48 (1H, *J*=18.0Hz, 15-H), 2.63 (1H, m, 20-H), 2.94 (1H, dd, *J*=14.5, 9.5Hz, 12-H), 3.00 (1H, dd *J*=19.0, 9.5Hz, 22-H), 3.29 (1H, dd, *J*=11.5, 4.0Hz, 3-H), 3.68 (1H, dd, *J*=11.5, 9.5Hz, 5'-H), 3.76 (1H, dd, *J*=19.0, 2.0Hz, 22-H), 4.35 (1H, dd, *J*=11.5, 5.5Hz, 5'-H), 4.87 (1H, d, *J*=7.5Hz, 1'-H), 5.14 (1H, dd, *J*=7.5, 2.5Hz, 7-H), 5.31 (1H, td, *J*=9.5, 5.5Hz, 4'-H), 5.42 (1H, dd, *J*=9.5, 7.5Hz, 2'-H), 5.48 (1H, dd, *J*=9.5, 3.5Hz, 11-H), 5.69 (1H, t, *J*=9.5, 3'-H).

Acetylation of Foetidinol (9a)

Acetylation of foetidinol (**9a**)(2.0 mg) in the same way as above and purification by preparative TLC and gave triacetate (**9b**)(1.3 mg). Triacetate (**9b**): $[\alpha]_D$ -15.46° (c=0.10, $CHCl_3$). IR *v* max cm^{-1}: 3540 (OH), 1725 (C=O), and 1060. Positive ion FAB-MS *m/z*: 571 $[M+H]^+$. HR-FAB-MS *m/z*: 571.3273, $[(M+H)^+$, Calcd for $C_{33}H_{47}O_8$, 571.3271]. ^{1}H-NMR ($CDCl_3$) δ_H: 0.90 (3H, s, 30-H_3), 0.94 (3H, s, 18-H_3), 0.98 (1H, d, *J*=5.0Hz, 19-H), 1.01 (3H, d, *J*=5.5Hz, 21-H_3), 1.13 (3H, s, 28-H_3), 1.25 (3H, s, 29-H_3), 1.26 (1H, m, 1-H), 1.30 (1H, m, 5-H), 1.45 (1H, dd, *J*=13.5, 3.0Hz, 12-H), 1.50 (1H, d, *J*=5.0Hz, 19-H), 1.65 (1H, m, 2-H), 1.68 (1H, m, 6-H), 1.78 (1H, m, 2-H), 1.95 (1H, ddd, *J*=16.5, 7.5, 5.0Hz, 6-H), 2.01 (1H, m, 1-H), 2.02 (2H, m, 22-H), 2.03 (-$COCH_3$), 2.07 (-$COCH_3$), 2.24 (-$COCH_3$), 2.78 (1H, dd, *J*=13.5, 9.5Hz, 12-H), 2.29 (1H, m, 20-H), 2.31 (1H, *J*=13.5Hz, 15-H), 2.35 (1H, d, *J*=11.5Hz, 17-H), 2.41 (1H, *J*=13.5Hz, 15-H), 4.58 (1H, dd, *J*=10.0, 5.5Hz, 3-H), 5.08 (1H, dd, *J*=7.5, 2.0Hz, 7-H), 5.21 (1H, dd, *J*=9.5, 3.0Hz, 11-H), 5.29 (1H, s, 24-H)

Acid Hydrolysis of Tetraacetate (5b)

3M $HClO_4$ (0.3 ml) was added to a solution of tetraacetate (**5b**)(100 mg) in THF (3 ml) and the mixture was stirring for 20 min under ice-cooling. Then, stirring was continued for 2.5 h at room temperature. After cooling, the mixture was neutralized with 30% NH_3 aq and the reaction mixture was concentrated *in vacuo*. The product was extracted with EtOAc and the EtOAc extract was washed with brine, dried, and concentration. The residue was separated by preparative TLC with hexane-EtOAc (6:4) to give diol (**5c**) (21 mg). Diol (**5c**): $[\alpha]_D$ -34.12° (c=0.50, $CHCl_3$). Positive ion FAB-MS *m/z*: 825 $[M+Na]^+$. HR-FAB-MS *m/z*: 825.4036, $[(M+Na)^+$, Calcd for $C_{43}H_{62}O_{14}Na$, 825.4038]. ^{1}H-NMR (pyridine-d_5)δ_H: 0.96 (3H, s, 30-H_3), 1.06 (3H, s, 29-H_3), 1.10 (3H, d, *J*=6.5Hz, 21-H_3), 1.12 (3H, s, 28-H_3), 1.16 (3H, s, 18-H_3), 1.54 (3H, s, 27-H_3), 1.66 (3H, s, 26-H_3), 3.42 (1H, dd, *J*=18.0, 9.0Hz, 22-H), 3.79 (1H, dd, *J*=18.0, 3.0Hz, 22-H), 4.48 (1H, s, 24-H).

Preparation of *R*-(+) MTPA ester of Diols (5c, 7a, and 8)

R(+) MTPA-Cl (100 mg) was added to a solution of diols (**5c, 7a,** and **8**) (each 12 mg) in CCl_4 (0.5 ml) and pyridine (0.5 ml) and the mixture was stirring for 12 h at room temperature. The reaction mixture was purified by preparative TLC with EtOAc-hexane (1:1) to give an *R*-(+)-MTPA esters **5d, 7c,** and **8a**, respectively. (each ca 14 mg).

R-(+)-MTPA ester (**5d**): Positive ion FAB-MS *m/z*: 1041 $[M+Na]^+$. HR-FAB-MS *m/z*: 1041.4469, $[(M+Na)^+$, Calcd for $C_{53}H_{69}O_{16}F_3Na$, 1041.4435]. ^{1}H-NMR (pyridine-d_5) δ_H: 1.47 (6H, s, 26, 27-H_3), 5.56 (1H, s, 24-H).

R-(+)-MTPA ester (**7c**): Positive ion FAB-MS *m/z*: 1305 $[M+Na]^+$. HR-FAB-MS *m/z*: 1305.4838, $[(M+Na)^+$, Calcd for $C_{65}H_{75}O_{16}F_9Na$, 1305.4809]. ^{1}H-NMR (pyridine-d_5) δ_H: 1.47 (6H, s, 26, 27-H_3), 5.53 (1H, s, 24-H), 5.79 (1H, ddd, *J*=10.0, 8.5, 5.0Hz, 4'-H), 6.10 (1H, t, *J*=8.5Hz, 3'-H).

R-(+)-MTPA ester (**8a**): Positive ion FAB-MS *m/z*: 1321 $[M+Na]^+$. ^{1}H-NMR (pyridine-d_5) δ_H: 1.45 (6H, s, 26, 27-H_3), 5.45 (1H, s, 24-H), 5.81 (1H, m, 4'-H), 6.12 (1H, t, *J*=8.5Hz, 3'-H).

Preparation of *S*-(-) MTPA Ester of Diols (5c, 7a, and 8)

S(-) MTPA-Cl (100 mg) was added to a solution of diols (**5c, 7a,** and **8**) (12 mg) in CCl_4 (0.5 ml) and pyridine (0.5 ml) and the mixture was stirring for 12 h at room temperature. The reaction mixture was purified by preparative TLC with EtOAc-hexane (1:1) to give *S*-(-)-MTPA esters **5e, 7d,** or **8b**, respectively. (each ca 6.0 mg).

S-(-)-MTPA ester **5e**: Positive ion FAB-MS *m/z*: 1041 $[M+Na]^+$. ^{1}H-NMR (pyridine-d_5) δ_H: 1.78 (6H, s, 26, 27-H_3), 5.38 (1H, s, 24-H).

S-(-)-MTPA ester **7d**: Positive ion FAB-MS *m/z*: 1305 $[M+Na]^+$. ^{1}H-NMR (pyridine-d_5) δ_H: 1.77 (6H, s, 26, 27-H_3), 5.39 (1H, s, 24-H), 5.62 (1H, m, 4'-H), 6.41 (1H, t, *J*=8.5Hz, 3'-H).

S-(-)-MTPA ester **8b**: Positive ion FAB-MS *m/z*: 1321 $[M+Na]^+$. HR-FAB-MS *m/z*: 1321.4816, $[(M+Na)^+$, Calcd for $C_{65}H_{75}O_{17}F_9Na$, 1321.4759].^{1}H-NMR (pyridine-d_5) δ_H: 1.78 (6H, s, 26, 27-H_3), 5.31 (1H, s, 24-H), 5.54 (1H, m, 4'-H), 6.36 (1H, t, *J*=8.5Hz, 3'-H).

Enzymatic Hydrolysis of Acetylacteol-3-*O*-arabinoside (2a)

A solution of acetylacteol-3-*O*-arabinoside (**2a**) (20 mg) in a mixture of EtOH (5 ml) and 0.2M K_2HPO_4-0.1M citric acid buffer (pH 4.0) (10 ml) was treated with molsin (*Aspergillus saitoi*) (40 mg) in H_2O (10 ml), and the mixture was kept for 10 days with gentle stirring at 37°C. The cultivated mixture was extracted with EtOAc and the EtOAc extract was washed with brine, dried, and concentration. The residue was separated by preparative TLC with EtOAc-hexane (1:1) to give 23(*R*), 24(*S*), 25(*R*), 27 (*S*)-acetylacteol (**2b**) (11 mg). A colorless needles (*n*-hexane-EtOAc), $[\alpha]_D$ -69.20°(c=0.20, EtOH) [Lit.,[9] $[\alpha]_D$ -72.1° (c=0.35, EtOH)]. EI-MS *m/z*: 544 (M^+). ^{1}H-NMR ($CDCl_3$) δ_H: 0.37 (1H, d, *J*=4.0Hz, 19-H), 0.68 (1H, d, *J*=4.0Hz, 19-H), 1.54(1H, dd, *J*=12.0, 6.0Hz, 15-H), 1.62 (3H, s, 26-H_3), 1.91(1H, dd, *J*=12.0, 7.5Hz, 15-H), 2.03 (-$COCH_3$), 3.29(1H, dd, *J*=11.0, 4.5Hz, 3-H), 3.84 (1H, s, 24-H), 4.43 (1H, td, *J*=7.5, 6.0Hz, 16-H), 4.86 (1H, dd, *J*=9.0, 3.5Hz, 12-H), 5.07 (1H, s, 27-H).

Enzymatic Hydrolysis of Cimicidanol-3-*O*-arabinoside (5a)

Enzymatic hydrolysis of cimicidanol-3-*O*-arabinoside (**5a**) (20 mg) in the same way as above and purification of the product by preparative TLC to give cimidanol (**6a**) (10 mg).

Conversion of compounds 4b, 6a, and 6b into pentacyclic products 14, 9a, and 15, respectively

Compounds **4b, 6a, and 6b** (each 10 mg) was dissolved in THF (2 ml) and 3M $HClO_4$ (0.2 ml) was added. The mixture was stirring for 20 min under ice-cooling and then stirring was continued for 1.5 h at room temperature. After cooling, the reaction mixture was neutralized with 30% NH_3 aq and the mixture was concentrated *in vacuo*. The product was extracted with EtOAc and the EtOAc extract was washed with brine,

dried, and concentration. The residue was separated by preparative TLC with hexane-EtOAc (6:4) to give pentacyclic products **14**, foetidinol (**9a**), and **15**, respectively, (each ca 3 mg). Identity of product of **6a** was confirmed by MS, ^{1}H-NMR, ^{1}H-^{1}H COSY, and NOE comparisons with an authentic sample (**9a**).

Product (14): $[\alpha]_D$ -15.35° (c=0.07, $CHCl_3$). Positive ion FAB-MS *m/z*: 685 $[M+H-CH_3COOH]^+$. HR-FAB-MS *m/z*: 685.3572, $[(M+H-CH_3COOH)^+$, Calcd for $C_{38}H_{53}O_{11}$, 685.3588]. ^{1}H-NMR (pyridine-d_5) δ_H: 0.91 (3H, s, 30-H_3), 1.01 (3H, s, 30-H_3), 1.01 (3H, d, *J*=7.0Hz, 21-H_3), 1.09 (1H, dd, *J*=11.0, 4.0Hz, 5-H), 1.16 (1H, m, 1-H), 1.29 (1H, m, 11-H), 1.35 (3H, s, 18-H_3), 1.54 (1H, m, 1-H), 1.61 (3H, s, 28-H_3), 1.63 (1H, m, 6-H), 1.78 (1H, m, 2-H), 1.83 (1H, m, 6-H), 1.96 (-$COCH_3$), 2.02 (1H, m, 2-H), 2.05 (-$COCH_3$), 2.13 (-$COCH_3$), 2.16 (-$COCH_3$), 2.20 (1H, d, *J*=13.5Hz, 15-H), 2.24 (1H, d, *J*=10.0Hz, 17-H), 2.27 (1H, m, 20-H), 2.55 (1H, dd, *J*=18.5, 4.0Hz, 22-H), 2.55 (1H, dd, *J*=18.5, 12.0Hz, 22-H), 2.55 (1H, d, *J*=13.5Hz, 15-H), 3.06 (1H, dd, *J*=16.0, 9.0Hz, 11-H), 3.28 (1H, dd, *J*=11.0, 4.0Hz, 3-H), 3.61 (1H, t, *J*=11.0Hz, 5'-H), 4.25 (1H, dd, *J*=11.0, 5.0Hz, 5'-H), 4.52 (1H, s, 24-H), 4.83 (1H, d *J*=7.5Hz, 1'-H), 5.12 (1H, dd, *J*=7.5, 2.0Hz, 7-H), 5.28 (1H, m, 4'-H), 5.40 (1H, t, *J*=7.5Hz, 2'-H), 5.45 (1H, dd, *J*=9.0, 3.0Hz, 12-H), 5.66 (1H, t, *J*=8.5Hz, 3'-H).

Product (15): $[\alpha]_D$ -8.93° (c=0.06, $CHCl_3$). Positive ion FAB-MS *m/z*: 529 $[M+H]^+$. HR-FAB-MS *m/z*: 529.3163, $[(M+H)^+$, Calcd for $C_{31}H_{45}O_7$, 529.3165]. ^{1}H-NMR (pyridine-d_5) δ_H: 0.89 (3H, d, *J*=6.5Hz, 21-H_3), 0.95 (3H, s, 30-H_3), 1.03 (3H, s, 30-H_3), 1.06 (1H, d, *J*=4.0Hz, 19-H), 1.24 (3H, s, 18-H_3), 1.30 (1H, m, 5-H), 1.48 (1H, m, 1-H), 1.52 (3H, s, 28-H_3), 1.65 (1H, d, *J*=4.0Hz, 19-H), 1.69 (1H, m, 6-H), 1.74 (1H, dd, *J*=14.0, 3.0Hz, 12-H), 1.81 (1H, m, 2-H), 1.83 (1H, m, 1-H), 1.90 (1H, m, 6-H), 2.06 (-$COCH_3$), 2.09 (-$COCH_3$), 2.23 (1H, m, 20-H), 2.24 (1H, d, *J*=13.5Hz, 15-H), 2.26 (1H, d, *J*=10.0Hz, 17-H), 2.42 (1H, dd, *J*=18.5, 4.0Hz, 22-H), 2.48 (1H, dd, *J*=18.5, 12.0Hz, 22-H), 2.52 (1H, d, *J*=13.5Hz, 15-H), 2.71 (1H, m, 2-H), 3.04 (1H, dd, *J*=14.0, 9.5Hz, 12-H), 4.56 (1H, s, 24-H), 4.76 (1H, dd, *J*=11.5, 4.0Hz, 3-H), 5.18 (1H, dd, *J*=7.5, 2.0Hz, 7-H), 5.55 (1H, dd, *J*=9.5, 3.0Hz, 11-H).

Acknowledgement

The authors are indebted to Mr. Akihiko Kusai of the Scientific Instrument Division, JEOL Ltd., for measuring of high-resolution FAB-MS of **5a**, to Prof. T. Tomimori of Hokuriku University and Mr. Takasi Takakuwa of JASCO Co., for measuring the CD and ORD spectra. One of the authors, J.X. Li is grateful to the Rotary club for the Yoneyama Scholarship.

References and Note

1. A part of this work was reported in our preliminary communication: Li, J. X.; Kadota, S.; Pu, X. F.; Namba, T. *Tetrahedron Lett.* **1994**, 35, 4575-4576; A part of this work was presented at the 41st Annual Meeting of the Japanese Society of Pharmacognosy, Abstracts of Papers, Sapporo, 1994, p. 195.
2. "The Pharmacopoeia of Chinese People's Republic" vol. I, The People's Health Publishing House & The Chemical Industry Publishing House, Beijing, 1990, p. 59.

3. a) Sakurai, N.; Koeda, M.; Inoue, T.; Nagai,M. *Chem. Pharm. Bull.* **1994**, 42, 48-51. b) Kusano, G.; Idoji, M.; Sogoh, Y.; Shibano, M.; Kusano, A.; Iwashita, T. *Chem. Pharm. Bull.* **1994**, 42, 1106-1110. c) Linde, H. *Arch. Pharmaz.* **1968**, 301, 120-138.
4. Li, J. X.; Kadota, S.; Hattori, M.; Yoshimachi, S.; Shiro, M.; Oogami, N.; Mizuno, H.; Namba, T. *Chem. Pharm. Bull.* **1993**, 41, 832-841.
5. Takemoto, T.; Kusano, G.; Kawahara, M. *Yakugaku Zasshi* **1970**, 90, 64-67.
6. Linde, H. *Arch. Pharmaz.* **1968**, 301, 335-341.
7. Takemoto, T.; Kusano, G. *Yakugaku Zasshi* **1967**, 87, 1569-1572.
8. Piancatelli, G.; Corsano,; S. Scettri, A. *Gazz. Chem. Ital.* **1971**, 101, 797-802.
9. Linde, H. *Arch. Pharmaz.* **1967**, 300, 982-992.
10. Berger, S; Junior, P; Kopanski, L. *Planta Medica* **1988**, 54, 579-580.
11. Kusano, G.; Takemoto, T. *Yakugaku Zhasshi*, **1975**, 95, 1133-1137.
12. The proton signal of 18-H_3 overlapped with 28-H_3 on measuring ^{1}H-NMR spectrum in pyridine-d_5 (Table III), but they were clearly separated in DMSO-d_6 so that the NOE experiments of **5a** were measured in DMSO-d_6. Cimicidanol-3-*O*-arabinoside (**5a**) ^{1}H-NMR (DMSO-d_6) δ_H: 0.69 (1H, d, *J*=4.0Hz, 19-H), 0.84 (3H, s, 30-H_3), 0.89 (3H, d, *J*=6.5Hz, 21-H_3), 0.99 (3H, s, 18-H_3), 1.00 (3H, s, 29-H_3), 1.03 (3H, s, 28-H_3), 1.09 (1H, dd, *J*=12.5, 4.0Hz, 5-H), 1.15 (H, s, 27-H_3), 1.37 (3H, s, 26-H_3), 1.45 (1H, d, *J*=4.0Hz, 19-H), 1.72 (1H, dd, *J*=14.5, 3.0Hz, 12-H), 2.10 (1H, d, *J*=18.0Hz, 15-H), 2.21 (1H, m, 20-H), 2.24 (1H, d, *J*=18.0Hz, 15-H), 2.26 (1H, d, *J*=9.0Hz, 17-H), 2.44 (1H, dd, *J*=18.0, 8.5Hz, 22-H), 2.58 (1H, dd, *J*=14.5, 9.0Hz, 12-H), 3.13 (1H, dd, *J*=12.5, 4.0Hz, 3-H), 3.28 (1H, m, 22-H), 4.03 (1H, m, 11-H), 4.14 (1H, d, *J*=7.5Hz, 1'-H), 4.61 (1H, d, *J*=6.5Hz, 11-OH), 5.52 (1H, dd, *J*=7.0, 2.0Hz, 7-H).
13. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, 95, 512-519.
14. Li, C. J.; Chen, D. H; Xiao, P. G. *Acta Pharmaceutica Sinica* **1993**, 28, 777-781.
15. Kikuchi, T.; Kadota, S.; Matsuda, S.; Suehara, H. *Chem. Pharm. Bull.* **1986**, 34, 3183-3201.
16. Atta-Ur-Rahman.; Nasir, H.; Iqbal, Z. *Phytochemistry* **1994**, 35, 993-1000.
17. Ito, M.; Kondo, Y.; Takemoto, T. *Chem. Pharm. Bull.* **1976**, 24, 580-583.
18. Lee, K.-H.; Soine, T. O. *J. Pharm. Sci.* **1969**, 58, 681-683.
19. Baba, K.; Hamasaki, F.; Tabata, Y.; Kozawa, M.; Honda, G.; Tabata, M. *Shoyakugaku Zhasshi* **1985**, 39, 282-290.

(*Received in Japan* 13 *October* 1994; *accepted* 11 *November* 1994)