Artabotryols A – E, New Lanostane Triterpenes from the Seeds of *Artabotrys odoratissimus*

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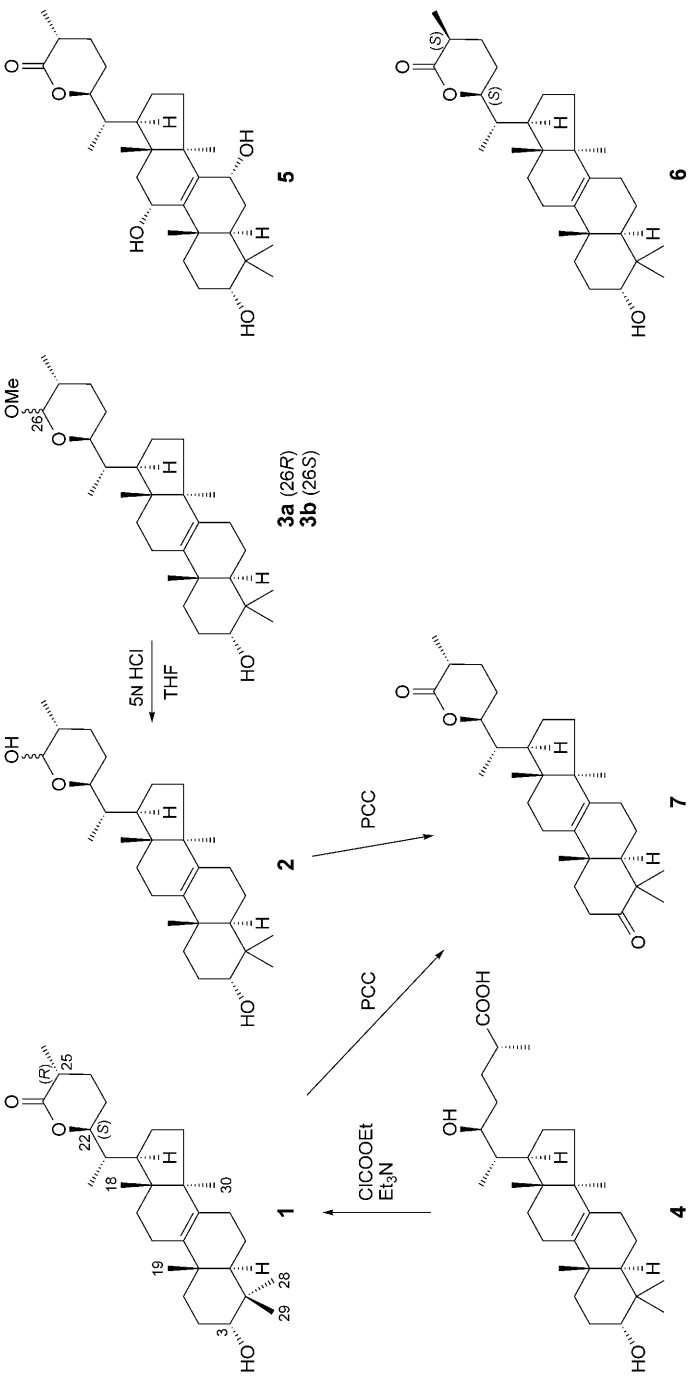
Six new lanostane triterpenes, artabotryols A, B, C1, C2, D, and E (**1**, **2**, **3a**, **3b**, **4**, and **5**, resp.) have been isolated from the seeds of *Artabotrys odoratissimus* (Annonaceae). Their structures have been established as (3α,22*S*,25*R*)-3-hydroxy-22,26-epoxylanost-8-en-26-one (**1**), (3α,22*S*,25*R*)-22,26-epoxylanost-8-ene-3,26-diol (**2**), (3α,22*S*,25*R*,26*R*)-26-methoxy-22,26-epoxylanost-8-en-3-ol (**3a**), (3α,22*S*,25*R*,26*S*)-26-methoxy-22,26-epoxylanost-8-en-3-ol (**3b**), (3α,22*S*,25*R*)-3,22-dihydroxylanost-8-en-26-oic acid (**4**) and (3α,7α,11α,22*S*,25*R*)-3,7,11-trihydroxy-22,26-epoxylanost-8-en-26-one (**5**) by spectroscopic studies and chemical correlations.

Introduction. – There are more than 100 species of the genus *Artabotrys* throughout tropical Africa and East Asia [1]. *Artabotrys odoratissimus* R. BR. (Syn: *A. uncinatus* MERR. and *A. hexapetalus* (L. F.) BHANDARI) of the family of Annonaceae is a shrub distributed in tropical and temperate Asia from the southern part of China to India. The roots and fruits of the plant are being used for the treatment of malaria and scrofula in traditional Chinese medicine [2]. Previous phytochemical studies of the plant have yielded aliphatic alcohols and esters [3][4], a long chain alkylated α-methylene-γ-butyrolactone [5], sesquiterpenes [6], alkaloids [7][8], and anthraquinones [9]. A Chinese group recently reported the isolation of more than 30 secondary metabolites, including steroids and alkaloids, as well as two terpenoids, 24-methylenelanosta-7,9(11)-dien-3β-ol and its 3-oxo analog [10]. In the previous article, we reported the isolation of flavonol glycosides from the leaves of the plant [11]. The isolation of decaffeoylacetosides, 6-hydroxyluteolin-7-*O*-rutenoside, and verbascoside were reported from the seeds of this plant [12]. As a continuation of this study, we have now investigated the hexane as well as MeOH extracts of the seeds of the plant. In this article, we report the isolation and structure elucidation of six new lanostane triterpenes, named artabotryols A, B, C1, C2, D, and E (**1**, **2**, **3a**, **3b**, **4**, and **5**, resp.).

Results and Discussion. – The hexane extract of the seeds was chromatographed on silica gel, and elution of the column with solvents of increasing polarity resulted in the isolation of artabotryols A, B, and C1/C2 (**1**, **2** and **3a**/**3b**, resp.; *Scheme*). After extraction with hexane, the residue of seeds was further extracted with MeOH, and the

Scheme 1. *Chemical Structures of Compounds* **1**–**5** *and Their Chemical Correlations*



extract was chromatographed with solvents of increasing polarity to give artabotryols D and E (**4** and **5**, resp.; *Scheme*).

Artabotryol A (**1**) was isolated as colorless needles. The molecular formula of **1** was determined as $C_{30}H_{48}O_3$ on the basis of HR-EI-MS data. The IR spectrum of **1** indicated the presence of OH (3610 cm^{-1}) and ester COO (1715 cm^{-1}) groups. The ^{1}H-NMR spectrum showed the presence of two secondary and five tertiary Me groups. In addition, signals of two CH−O H-atoms were observed at δ 3.42 (br. *s*) and 4.41. The ^{13}C-NMR spectrum showed 30 signals, among which those of an ester COO at δ 174.88, two olefinic C-atoms at δ 133.96 and 134.77, and two CH−O C-atoms at δ 76.00 and 84.11 were characteristic. The EI-MS spectrum of **1** exhibited fragment ions at *m*/*z* 314 and 299, which were assignable to [*M* − side chain − H] and [*M* − side chain − Me − H], respectively. The spectral data described above suggested that compound **1** is a 3-hydroxy-Δ^8-lanostane-triterpene with a lactone group in the side chain. It appeared that C(26) was oxidized to a carboxylic acid to form a lactone, since the signal of one (C(27)) of the Me groups (*doublet*) was considerably shifted downfield (δ 1.30). Such lactone-containing lanostane triterpenes, astrahygrol and 3-epiastrahygrol (**6**), were previously reported from *Astraeus hygrometricus* [13]. Comparison of the ^{13}C-NMR spectroscopic data with those of these samples indicated that compounds **1** and **6** have the same triterpene skeleton, whereas the resonances for the side chain exhibited minor deviations. It was, therefore, suggested that artabotryol A could be a stereoisomer of **6** at C(22) and/or C(25). In an earlier communication, we reported the synthesis of the corresponding four stereoisomeric lactones (starting from 6β-methoxy-3α,5α-cyclocholestane) along with their ^{1}H-NMR spectroscopic data [14]. Comparison of the ^{1}H-NMR data (*e.g.*, Me(27) (δ 1.30) and H−C(25) (δ 2.40)) of **1** with those of the configurationally defined lactones ruled out the possibility of (22*R*,25*S*)- and (22*S*,25*R*)-lactones. Further comparison of the ^{1}H-NMR data, in particular the coupling pattern of H−C(22) (δ 4.41 (*dd*, J = 11.5, 3.1)), led us to conclude that compound **1** is the (22*S*,25*R*)-isomer (δ 4.39 (*dd*, J = 11.7, 3.2, H−C(22))) rather than the (22*R*,25*S*)-isomer (δ 4.37 (*dd*, J = 10.9, 3.6, H−C(22))). HMBC Correlations, shown in *Fig. 1*, verified the lanostane lactone structure. The broad *singlet* of H−C(3) (δ 3.42) indicated an α-orientation of the 3-OH group. Hence, the structure of artabotryol A was established as (3α,22*S*,25*R*)-3-hydroxy-22,26-epoxylanost-8-en-26-

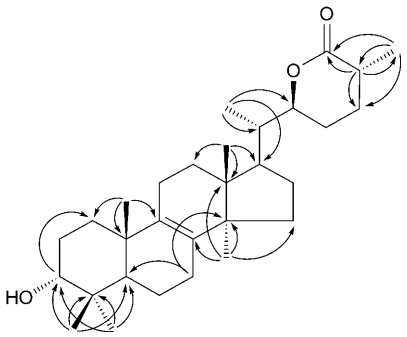


Fig. 1. *HMBC Correlations* (H → C) *for compound* **1**

one. Compound **1** corresponds to a C(25)-epimer of the known 3-epiastrahydrol (**6**). The ^{13}C-NMR signal assignments for **1**, which were achieved by 2D-NMR (HMBC and HMQC), are listed in the *Table*. It was found that the reported assignments of C(7), C(12), and C(16) for 3-epiagasterol (**6**) needed to be revised [13][15].

Table. *^{13}C-NMR Data* (125 MHz, $CDCl_3$) *of Compounds* **1**–**5**[a])

Position	**1**	**2** (major/minor)	**3a**	**3b**	**4**[b])	**5**[b])	**7**
1	30.05	30.07	30.10	30.10	29.95	29.13	35.99
2	25.74	25.77	25.75	25.75	25.52	25.39	34.58
3	76.00	76.01	76.06	76.06	75.81	75.49	217.79
4	37.60	37.59	37.60	37.60	37.43	37.10	47.35
5	44.20	44.22	44.25	44.25	44.11	38.26	51.16
6	18.17	18.19	18.19	18.19	18.05	28.49[c])	19.47
7	26.04	26.07	26.08	26.08	25.95	66.41	26.30[d])
8	133.96	134.06	133.96	133.96	133.92	141.48	133.24
9	134.77	134.73	134.85	134.85	134.67	141.33	135.21
10	36.92	36.92	36.93	36.93	36.80	38.26	36.92
11	20.94	20.98	20.97	20.97	20.83	64.54	21.07
12	30.87	30.83/30.97	30.88	30.89	30.94	44.68	30.83
13	44.48	44.35/44.30	44.30	44.25	44.30	48.48	44.48
14	49.89	49.90	50.00	50.00	49.80	50.13	49.96
15	30.81	31.42/31.04	30.88	30.89	30.67	30.62	30.92
16	27.62	26.07/26.16	28.44	28.46	27.46	26.97[e])	26.33[d])
17	46.01	46.49/46.62	46.45	46.32	46.61	46.72	46.04
18	15.63	15.61	15.36	15.36	15.55	17.01	15.76
19	18.98	18.97	18.98	18.98	18.85	18.74	18.71
20	41.38	40.91/40.63	41.47	41.72	41.01	41.11	41.39
21	12.84	13.43/13.15	13.00	12.93	11.46	12.59	12.80
22	84.11	78.56/69.78	69.64	70.09	73.35	83.98	84.00
23	27.19	27.70/27.61	29.07	24.48	32.87	27.00[e])	27.11
24	28.69	28.66/29.03	26.77	23.10	30.44	28.52[c])	28.69
25	36.39	37.77/34.87	34.85	31.41	39.23	36.31	36.40
26	174.88	101.81/95.28	102.23	103.23	179.35	175.17	174.86
27	17.49	16.74/17.08	16.82	16.41	16.95	17.33	17.49
28	28.02	28.03	28.03	28.03	27.87	27.81	27.60
29	22.20	22.20	22.20	22.20	22.08	22.06	21.28
30	24.37	24.51	24.34	24.34	24.08	26.51	24.46
MeO			55.02	54.67			

[a]) The assignments for **1**, **2**, **3a**, and **5** are based on 2D-NMR studies, including an HMBC spectrum, while signals for **3b**, **4**, and **7** were assigned by analogy. [b]) Recorded in $CDCl_3/CD_3OD$ 10 : 1. [c])–[e]) Assignments may be interchanged.

Artabotryol B (**2**), a white amorphous solid, exhibited the molecular formula $C_{30}H_{50}O_3$, as determined by HR-EI-MS data. The compound displayed a pair of peaks for several H- and C-atom signals in *ca.* 2.5 : 1 ratio in the NMR spectra. In the ^{13}C-NMR spectrum, acetal C-atom signals (δ 101.81/95.28) were observed with disappearance of the lactone COO signal found in **1**. The ^{1}H-NMR spectrum showed signals of acetal CH H-atoms at δ 4.24 (*dd*, $J = 7.8, 5.9, 0.7$ H) and 5.03 (br. *s*, 0.3 H) and CH–O H-atoms at δ 3.45 (*d*, $J = 11.5$, 0.7 H) and 3.98 (*d*, $J = 10.5$, 0.3 H), in addition to

the resonance of H_β–C(3) at δ 3.42 (br. *s*). These data suggested that compound **2** has a lactol structure, a reduced form of the lactone in **1**. The NMR data for the steroidal core were essentially identical to those of **1**. Compound **2** could be converted to (22*S*,25*R*)-3-oxo-lactone **7** (*vide infra*). Thus, the structure of artabotryol B was determined as (3α,22*S*,25*R*)-22,26-epoxylanost-8-ene-3,26-diol (*Scheme*). There was no indication that the (26*R*)- and (26*S*)-epimers of **2** were separable on TLC. The major, more stable epimer was established to have a (26*R*)-configuration, since a clear NOE correlation was observed between H–C(26) (δ 4.24) and H–C(22) (δ 3.45). The most stable conformation for the major epimer, which was deduced from MM2 calculation, is depicted in *Fig. 2*.

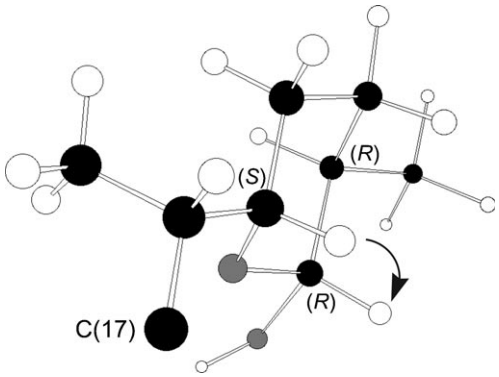


Fig. 2. *Most stable conformation for the major (26*S*)-epimer of compound* **2**. Key NOE correlation is indicated by an arrow. For clarity, the steroidal core is not shown.

Artabotryols C1/C2 (**3a**/**3b**) were obtained as a 2:1 mixture. They have the molecular formula $C_{31}H_{52}O_3$, containing an additional CH_2 unit compared to **2**. The ^{1}H- and ^{13}C-NMR spectra of the mixture were similar to those of **2**, except for the presence of MeO signals at δ(H) 3.38 (major epimer **3a**)/3.39 (minor epimer **3b**), which are associated with δ(C) 55.02/54.67 (*Table*). Several other signals were also observed as a pair in a 2:1 ratio (*e.g.*, H–C(22) at δ 3.77 and H–C(26) at δ 4.46 for the major epimer **3a**; the corresponding signals at δ 3.82 and δ 4.37 for the minor epimer **3b**). These spectroscopic data indicated that compounds **3a**/**3b** correspond to the methyl acetal derivatives of **2**. The configurations at C(22) and C(25) of **3a**/**3b** were unambiguously established by the following chemical transformation. Demethylation of **3a**/**3b** under acidic conditions yielded artabotryol B (**2**). Compound **2** derived from **3a**/**3b** was oxidized with pyridinium chlorochromate (PCC) to give the 3-oxo-lactone **7**. This lactone was identical to compound **7** obtained by PCC oxidation of **1**. These chemical correlations evidenced that artabotryols A, B and C1/C2 have a common (22*S*,25*R*)-configuration. We subsequently noticed that compounds **3a**/**3b** were detected as two spots on TLC (multiple development with hexane/AcOEt 10:1) and succeeded in the separation of the less polar **3a** and the more polar **3b** (both were obtained as white crystals) by medium-pressure liquid chromatography (MPLC) with a silica-gel column. The major epimer **3a**, named artabotryol C1, showed an NOE correlation between H–C(22) at δ 3.77 and H–C(26) at δ 4.46. Hence, artabotryol C1 was determined to be

(3α,22*S*,25*R*,26*R*)-26-methoxy-22,26-epoxylanost-8-en-3-ol. The minor epimer **3b**, designated as artabotryol C2, was, therefore, (3α,22*S*,25*R*,26*S*)-26-methoxy-22,26-epoxylanost-8-en-3-ol.

Artabotryol D (**4**) was isolated as colorless needles. The molecular formula was determined as $C_{30}H_{50}O_4$ on the basis of HR-FAB-MS (negative-ion mode) data. A broad absorption around 3400 cm^{-1} in the IR spectrum indicated the presence of a COOH functionality. The ^{1}H-NMR spectrum of **4** showed an CH−O signal at δ 3.63 (*dd*, *J* = 8.0, 3.5) in addition to that of H_β−C(3) (δ 3.41, br. *s*). These spectral data suggested that compound **4** could be a hydroxy acid corresponding to a hydrolysis product of **1**. Treatment of compound **4** with ClCOOEt and Et_3N gave artabotryol A (**1**). Hence, artabotryol D was determined as (3α,22*S*,25*R*)-3,22-dihydroxylanost-8-en-26-oic acid.

Artabotryol E (**5**) was isolated as white needles, hardly soluble in $CHCl_3$. The molecular formula of **5**, $C_{30}H_{48}O_5$, deduced from HR-FAB-MS data for $[M+Na]^+$ ion, indicated two O-units more than that of **1**. The molecular formula and ^{1}H-NMR resonances of two CH−O H-atoms at δ 4.16 (br. *d*, *J* = 1.5, linked to a C-atom with a signal at δ 64.54) and 4.36 (*dd*, *J* = 13.5, 3.7, linked to a C-atom with a signal at δ 66.41) together with those of H_β−C(3) (δ 3.45 (br. *s*)) and H−C(22) (δ 4.42 (*dd*, *J* = 12.0, 3.0)) suggested that compound **5** could be a dihydroxy derivative of **1**.

The (22*S*,25*R*)-configuration of **1** was assigned from the coupling constants of H−C(22) (*vide infra*) as well as a close similarity of the side-chain ^{13}C resonances of **5** to those of **1** (*Table*). The downfield shifts of the two CH−O H-atom signals suggested their allylic nature. In accord with this expectation, the two olefinic C-atom signals (δ 141.48 and 141.33) in **5** shifted downfield by *ca.* 7 ppm compared to those of **1**. These data suggested a 7,11-dihydroxy-9-ene partial structure. This structure was verified by HMBC correlations from Me(30) (δ 1.28, this resonance being shifted downfield considerably due to the effect of the axially oriented 7α-OH group, *vide infra*) to C(8) (141.48), from Me(19) (0.97) to C(9) (141.33), and from Me(18) (0.60) to C(12) (44.68). The orientation of the 7-OH group was determined to be α (axial) from the coupling constant of H−C(7) (br. *d*, *J* = 1.5), while to the 11-OH group was assigned α (equatorial) from the coupling constant of H−C(11) (*dd*, *J* = 13.5, 3.7). An NOE correlation between Me(19) and H−C(11) provided further evidence for an α-orientation of the 11-OH group. The (22*S*,25*R*)-configuration of **5** was established by a close similarity of the ^{1}H- and ^{13}C-NMR data for the side chain of **1** and **5**. Hence, the structure of artabotryol E (**5**) was determined as (3α,7α,11α,22*S*,25*R*)-3,7,11-trihydroxy-22,26-epoxylanost-8-en-26-one. Complete assignments of the ^{13}C-NMR signals, based on 2D-NMR (HMQC and HMBC), are listed in the *Table*.

In conclusion, we have isolated six new lanostane triterpenes, named artabotryols A, B, C1, C2, D, and E, and established their structures, including the absolute configuration.

Experimental Part

1. *General.* Column chromatography (CC): silica gel 60*N* (SiO_2; 60–210 mesh; *Kanto Chemical*, Japan). TLC: silica gel *F254* pre-coated glass plates (0.25 mm, *Merck*). MPLC: *Yamazen Pump-540* apparatus using *Yamazen Ultra pack-A* silica-gel glass column (30 cm × 1.1 cm i.d.). M.p.: *Yazawa BY-1* micro-melting-point apparatus; uncorrected. Optical rotation: *Jasco DIP-360 polarimeter*. IR Spectra:

Perkin-Elmer FT-IR Paragon 500 spectrophotometer. ^{1}H-, ^{13}C-, and 2D-NMR Spectra: *Bruker DRX500* spectrometer; at 500 (^{1}H) and 125 MHz (^{13}C); in $CDCl_3$ or $CDCl_3$/CD_3OD 10:1; δ(H) in ppm, rel. to Me_4Si, *J* in Hz; δ(C) in ppm referenced to the solvent $CDCl_3$ (δ 77.00). EI-MS (70 eV), and FAB- and HR-FAB-MS: *Jeol JMS-700* mass spectrometer.

2. *Plant.* The seeds of *Artabotrys odoratissimus* were collected from the campus of Banaras Hindu University, Varanasi in September, 2006. A specimen sample of the plant material has been deposited with the Department of Medicinal Chemistry, IMS, Banaras Hindu University, Varanasi, India.

3. *Extraction and Isolation of Artabotryols* **1**–**5**. Well-ground seeds of *A. odoratissimus* (800 g) were defatted with hexane (3 l × 3) at r.t. by stirring magnetically, and hexane-soluble part was discarded. The seeds obtained by filtration were extracted in *Soxhlet* extractor for 24 h with hexane (5 l). The hexane extract was concentrated to 0.5 l and left overnight at r.t., and the supernatant layer was filtered off to give a solid residue (6.29 g). This was subjected to CC (hexane/AcOEt of increasing polarity, total volume 6 l). Fraction eluted with hexane/AcOEt 8:1 afforded a 2:1 mixture **3a**/**3b** (1.03 g). Fraction eluted with hexane/AcOEt 4:1 → 3:1 yielded **1** (571 mg). Continued elution with hexane/AcOEt 3:1 yielded a white amorphous power, which was further subjected to CC (hexane/AcOEt 3:1) to give **2** (1.73 g). The mixture **3a**/**3b** (20 mg) were separated by MPLC (solvent, hexane/AcOEt 2.5:1, flow rate 1.5 ml/min) to give the faster eluting epimer **3a** (12 mg) and the more polar epimer **3b** (6 mg). The residual mass of seeds (500 g) after extraction with hexane was extracted with MeOH (2 l) in a *Soxhlet* extractor for 24 h. The extract was concentrated to a viscous residue (11.3 g), which was subjected to CC ($CHCl_3$/AcOEt of increasing polarity, total volume 10 l; and AcOEt/MeOH of increasing polarity, total volume 5 l). The fraction eluted with AcOEt yielded **4** (230 mg). The fraction eluted with AcOEt/MeOH 15:1 furnished **5** (114 mg).

4. *Artabotryol A* (= *(3α,22*S*,25*R*)-3-Hydroxy-22,26-epoxylanost-8-en-26-one*; **1**). Colorless needles. M.p. 230–233° ($CHCl_3$). $[\alpha]_D^{25} = +38.7$ ($c = 0.60$, $CHCl_3$). IR ($CHCl_3$): 3610, 3010, 2950, 2870, 1715. ^{1}H-NMR ($CDCl_3$): 0.70 (*s*, Me(18)); 0.87 (*s*, Me(29)); 0.92 (*s*, Me(30)); 0.96 (*d*, *J* = 6.7, Me(21)); 0.97 (*s*, Me(28)); 0.99 (*s*, Me(19)); 1.30 (*d*, *J* = 7.1, Me(27)); 2.40 (*dqd*, *J* = 12.0, 7.1, 6.3, Me(25)); 3.42 (br. *s*, H–C(3)); 4.41 (*dd*, *J* = 11.5, 3.1, H–C(22)). ^{13}C-NMR: *Table.* EI-MS: 456 (M^+, 100), 441 (90), 423 (80), 314 (13), 299 (41), 281 (56), 44 (100). HR-EI-MS: 456.3574 (M^+, $C_{30}H_{48}O_3^+$; calc. 456.3603).

5. *Artabotryol B* (= *(3α,22*S*,25*R*)-22,26-Epoxylanost-8-ene-3,26-diol*; **2**). Amorphous powder. $[\alpha]_D^{25} = +17.6$ ($c = 0.47$, $CHCl_3$). IR ($CHCl_3$): 3610, 3000, 2950, 2870. ^{1}H-NMR ($CDCl_3$): 0.69 (*s*, Me(18)); 0.87 (*s*, Me(29)); 0.92 (*s*, Me(30)); 0.94 (*d*, *J* = 6.4, Me(27)); 0.95 (*d*, *J* = 6.7, Me(21)); 0.97 (*s*, Me(28)); 0.99 (*s*, Me(19)); 2.29 (br. *s*, OH, minor epimer); 2.77 (*d*, *J* = 5.9, OH, major epimer); 3.42 (br. *s*, H–C(3)); 3.45 (*d*, *J* = 11.5, H–C(22), major epimer); 3.98 (*d*, *J* = 10.5, H–C(22), minor epimer); 4.24 (*dd*, *J* = 7.8, 5.9, H–C(26), major epimer); 5.03 (br. *s*, H–C(26), minor epimer). ^{13}C-NMR: *Table.* EI-MS: 458 (M^+, 67), 443 (84), 425 (100), 314 (34), 311 (49), 299 (51), 281 (41). HR-EI-MS: 458.3769 (M^+, $C_{30}H_{50}O_3^+$; calc. 458.3760).

6. *Artabotryol C1* (= *(3α,22*S*,25*R*,26*R*)-26-Methoxy-22,26-epoxylanost-8-en-3-ol*; **3a**). Colorless needles. M.p. 187–189° (MeOH). $[\alpha]_D^{25} = 47.7$ ($c = 1.7$, $CHCl_3$). IR ($CHCl_3$): 3615, 3000, 2950, 2870. ^{1}H-NMR ($CDCl_3$): 0.70 (*s*, Me(18)); 0.86 (*d*, *J* = 6.8, Me(27)); 0.87 (*s*, Me(29)); 0.90 (*s*, Me(30)); 0.93 (*d*, *J* = 6.8, Me(21)); 0.97 (*s*, Me(28)); 0.99 (*s*, Me(19)); 3.38 (*s*, MeO); 3.42 (br. *s*, H–C(3)); 3.77 (br. *d*, *J* = 11.2, H–C(22)); 4.46 (*d*, *J* = 3.3, H–C(26)). ^{13}C-NMR: *Table.* EI-MS: 472 (M^+, 39), 457 (38), 439 (18), 425 (59), 407 (30), 314 (14), 299 (15), 281 (12), 129 (100). HR-EI-MS: 472.3913 (M^+, $C_{31}H_{52}O_3^+$; calc. 472.3916).

7. *Artabotryol C2* (= *(3α,22*S*,25*R*,26*S*)-26-Methoxy-22,26-epoxylanost-8-en-3-ol*; **3b**). Colorless needles. M.p. 208–210° (MeOH). IR ($CHCl_3$): 3615, 3000, 2950, 2870. ^{1}H-NMR ($CDCl_3$): 0.70 (*s*, Me(18)); 0.87 (*s*, Me(29)); 0.90 (*s*, Me(30)); 0.97 (*d*, *J* = 6.7, Me(21)); 0.97 (*s*, Me(28)); 0.99 (*s*, Me(19)); 1.03 (*d*, *J* = 7.2, Me(27)); 3.38 (*s*, MeO); 3.42 (br. *s*, H–C(3)); 3.82 (*dd*, *J* = 10.6, 1.8, H–C(22)); 4.37 (br. *s*, H–C(26)). ^{13}C-NMR: *Table.* EI-MS: 472 (M^+, 39), 457 (38), 439 (18), 425 (59), 407 (30), 314 (14), 299 (15), 281 (12), 129 (100). HR-EI-MS: 472.3912 (M^+, $C_{31}H_{52}O_3^+$; calc. 472.3916).

8. *Artabotryol D* (= *(3α,22*S*,25*R*)-3,22-Dihydroxylanost-8-en-26-oic acid*; **4**). Colorless needles. M.p. 223–237° (AcOEt). $[\alpha]_D^{25} = +19.3$ ($c = 0.6$, $CHCl_3$/CH_3OH, 10:1). IR (KBr): 3600–3100, 2945, 2870, 1710. ^{1}H-NMR ($CDCl_3$/CD_3OD, 10:1): 0.70 (*s*, Me(18)); 0.87 (*d*, *J* = 6.8, Me(21)); 0.87 (*s*, Me(29)); 0.91 (*s*, Me(30)); 0.97 (*s*, Me(28)); 1.00 (*s*, Me(19)); 1.18 (*d*, *J* = 7.0, Me(27)); 2.44 (*sext.*, *J* = 7.0,

H–C(25)); 3.41 (br. *s*, H–C(3)); 3.63 (*dd*, *J* = 8.0, 3.5, H–C(22)). ^{13}C-NMR: *Table*. EI-MS: 456 ([*M* – H_2O]$^+$, 37), 441 (38), 423 (100), 314 (7), 299 (23), 281 (28). HR-FAB-MS (neg.): 473.3586 ([*M* – H]$^-$, $C_{30}H_{49}O_4^-$; calc. 473.3631).

9. *Artabotryol E* (= *(3α,7α,11α,22*S*,25*R*)-3,7,11-Trihydroxy-22,26-epoxylanost-8-en-26-one*; **5**). Colorless needles. M.p. 128–129° (MeOH). $[\alpha]_D^{25} = +25.0$ (*c* = 0.10, $CHCl_3$/MeOH, 1:1). IR (KBr): 3560–3450, 2945, 2870, 1720. ^{1}H-NMR ($CDCl_3$/CD_3OD, 10:1): 0.60 (*s*, Me(18)); 0.88 (*s*, Me(29)); 0.95 (*d*, *J* = 6.8, Me(21)); 0.97 (*s*, Me(19)); 1.00 (*s*, Me(28)); 1.28 (*s*, Me(30)); 1.30 (*d*, *J* = 7.1, Me(27)); 2.41 (*dqd*, *J* = 12.4, 7.1, 6.4, Me(25)); 3.45 (br. *s*, H–C(3)); 4.16 (br. *d*, *J* = 1.5, H–C(7)); 4.36 (*dd*, *J* = 13.5, 3.7, H–C(11)); 4.42 (*dd*, *J* = 12.0, 3.0, H–C(22)). ^{13}C-NMR: *Table*. HR-FAB-MS: 511.3399 ([*M* + Na]$^+$, $C_{30}H_{48}NaO_5^+$; calc. 511.3399).

10. *Conversion of* **3** *to* **7** via **2**. A soln. of **3** (8.6 mg) in dry THF (0.4 ml) and 5N HCl (60 µl) was heated at 40° overnight. After addition of ice chips, it was partitioned between Et_2O and sat. aq. $NaHCO_3$ soln. The separated org. layer was washed with brine, dried (Na_2SO_4), and concentrated to give a crude 3-ketone. This was separated by CC (hexane/AcOEt 3:1) to afford **2** (6.0 mg, 72%) as amorphous powder, which was identified with artabotryol B (co-TLC, EI-MS, and ^{1}H- and ^{13}C-NMR).

To a soln. of **2** (5.0 mg) derived from **3** in dry CH_2Cl_2 (0.3 ml) were added 4-Å molecular sieves (powder, 30 mg) and pyridinium chlorochromate PCC (4 mg), and the mixture was stirred at r.t. for 30 min. The mixture was diluted with hexane/AcOEt 10:1 and applied to a silica-gel column. Elution with hexane/AcOEt 4:1 gave **7** (3.8 mg, 77%): Colorless crystals. M.p. 175–178° ($CHCl_3$). $[\alpha]_D^{25} = 68.9$ (*c* = 0.38, $CHCl_3$). IR ($CHCl_3$): 3010, 2955, 2870, 1710, 1470, 1390, 1120, 1080. ^{1}H-NMR ($CDCl_3$): 0.72 (*s*, Me(18)); 0.92 (*s*, Me(30)); 0.97 (*d*, *J* = 6.5, Me(21)); 1.07; 1.10; 1.11 (*s* each, Me(19), Me(28), Me(29)); 1.30 (*d*, *J* = 7.0, Me(27)); 4.41 (*dd*, *J* = 11.5, 3.0, H–C(22)). ^{13}C-NMR: *Table*. EI-MS: 454 (*M*$^+$, 26), 439 (79), 421 (6), 312 (13), 297 (27), 44 (100). HR-EI-MS: 454.3429 (*M*$^+$, $C_{30}H_{46}O_3^+$; calc. 454.3447).

11. *Conversion of* **1** *to* **7**. Artabotryol A (**1**) (4.2 mg) was treated with PCC as described above to yield **7** (2.8 mg, 67%) as a white solid, which was identical to the sample derived from **3** (co-TLC, EI-MS, and ^{1}H-NMR).

12. *Conversion of* **4** *to* **1**. To a stirred soln. of artabotryol D (**4**; 5.0 mg) in CH_2Cl_2 (250 µl) containing Et_3N (3 µl) was added ClCOOEt (0.75 µl). The mixture was stirred at r.t. for 5 min, and then diluted with Et_2O and sat. aq. NH_4Cl. The org. layer was washed with brine, dried (Na_2SO_4), and concentrated. The residue was separated by CC ($CHCl_3$/MeOH 40:1) to give **1** (4.0 mg, 83%), which was identical to compound **1** (co-TLC, EI-MS, and ^{1}H-NMR).

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