

SESQUITERPENE POLYOL ESTERS FROM *EUONYMUS BUNGEANUS*

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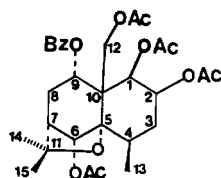
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ABSTRACT.—From the MeOH extract of the seed oil of *Euonymus bungeanus*, four new β -dihydroagarofuran sesquiterpene polyol esters were isolated. Their structures were established on the basis of chemical reactions and spectral analyses.

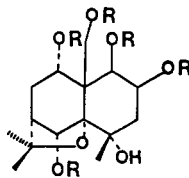
The plants of the Celastraceae are widely distributed in China. The root bark of some species has traditionally been used as natural insecticides (1). Previous studies (2) on *Euonymus bungeanus* Max. have disclosed the presence of three β -dihydroagarofuran sesquiterpene polyol esters, which exhibits antifeedant effects against insects of *Pieris rapae* and *Ostrina furnacolis*. This paper reports the continued study on *E. bungeanus*, from which four new sesquiterpene components have been isolated and elucidated as 1 β ,2 β ,6 α ,12-tetraacetoxy-9 α -benzoyloxy- β -dihydroagarofuran [1], 2 β ,6 α ,12-triacetoxy-1 β ,9 α -di(β -furancarboxyloxy)-4 α -hydroxy- β -dihydroagarofuran [4], 2 β ,6 α ,12-triacetoxy-1 β ,9 α -dibenzoyloxy-4 α -hydroxy- β -dihydroagarofuran [6], and 2 β ,6 α ,12-triacetoxy-1 β -benzoyloxy-9 α - β -furancarboxyloxy-4 α -hydroxy- β -dihydroagarofuran [8].

RESULTS AND DISCUSSION

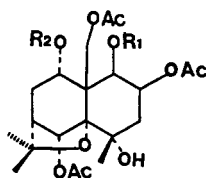
Compound 1 analyzed for $C_{30}H_{38}O_{11}$ by hrms. Its ir spectrum revealed characteristic absorptions of ester groups at 1740 and 1710 cm^{-1} . In good agreement with these data its nmr and mass spectra showed the presence of four acetate esters (1H nmr δ 1.55, 2.09, 2.12, and 2.26, $4 \times s$, $4 \times 3H$; ^{13}C nmr δ 20.3, 21.2, 21.2, and 21.3, $4 \times Me$, δ 169.2, 169.8, 169.9, and 170.5, $4 \times -COO-$; ms m/z 43, Ac) and one benzoate ester (1H nmr δ 7.43–8.06, m, 5H; ^{13}C nmr δ 128.3–133.4, C_6H_5 , δ 165.3, $-COO-$; ms m/z 105, C_6H_5CO) (1). In addition, the ^{13}C -nmr (Table 1) and DEPT spectra indicated that the parent skeleton of 1 consisted of three methyl carbons (δ 17.8, 26.0, and





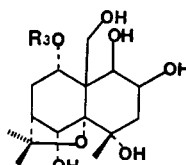
1



2 R=Ac
 3 R=H



4 $R_1=R_2=$ 
 6 $R_1=R_2=Bz$
 8 $R_1=Bz, R_2=$ 




5 $R_3=$ 
 7 $R_3=Bz$

TABLE 1. ^{13}C -nmr Chemical Shifts of **1**, **4**, **6**, and **8** (400 MHz) in CDCl_3 .

Carbon	Compound			
	1	4	6	8
C-1 ^a	69.4	68.6	68.6	68.6
C-2 ^a	69.5	68.6	69.4	68.8
C-3	30.9	42.0	42.1	42.0
C-4	33.2	69.7	69.7	69.8
C-5	89.3	91.2	91.3	91.2
C-6 ^a	71.6	70.7	71.3	71.2
C-7	48.9	49.1	49.2	49.2
C-8	34.9	34.7	34.7	34.7
C-9 ^a	78.1	78.3	78.3	78.2
C-10	53.4	55.2	55.6	55.3
C-11	82.7	84.5	84.6	84.5
C-12	65.5	65.4	65.7	65.7
Me-13 ^b	17.8	25.1	25.1	25.1
Me-14 ^b	26.0	25.4	25.8	25.6
Me-15 ^b	30.3	29.4	29.4	29.4

^{a,b}The data in same column are exchangeable.

30.3), three methylene carbons (δ 30.9, 34.9, and 65.5), six methine carbons (δ 33.2, 48.7, 69.4, 69.5, 71.6, and 78.1), and three quaternary carbons (δ 53.4, 82.7, and 89.3). This parent was identified as the β -dihydroagarofuran that had five substituents at four methine carbons (δ 69.4, 69.5, 71.6, and 78.1) and one methylene carbon (δ 65.5) (3). Moreover, the ^1H -nmr spectrum (Table 2) of **1** was very similar, in terms of coupling patterns and coupling constants, to those of derivatives of the 1,2,6,9,12-hexasubstituted β -dihydroagarofuran (**4**). Therefore, the parent of **1** was identified as a 1,2,6,9,12-hexasubstituted- β -dihydroagarofuran, and thus had the five esters mentioned above located at C-1, C-2, C-6, C-9, and C-12.

TABLE 2. ^1H -nmr Spectral Data of **1**, **2**, and **4-8** (400 MHz) in CDCl_3 .

Proton	Compound						
	1	2	4	5^a	6	7^a	8
H-1	5.71 d 3.4	5.50 d 3.5	5.67 d 3.2	4.10 d 3.3	5.82 d 3.4	4.19 d 3.2	5.77 d 3.2
H-2	5.58 dd 3.3, 3.4	5.41 dd 3.5, 3.6	5.60 m	3.84 m	5.67 m	3.85 m	5.65 m
H-6	5.98 s	6.04 s	6.15 s	4.89 s	6.20 s	4.94 s	6.18 s
H-9	5.42 d 7.2	5.10 d 6.9	5.33 d 7.2	5.34 d 7.0	5.47 d 7.2	5.42 d 7.1	5.38 d 7.5
2H-12	4.36 5.06 ABq 13	4.32 4.90 ABq 13	4.54 5.02 ABq 13	3.94 4.00 ABq 12	4.62 5.11 ABq 13	3.98 4.01 ABq 13	4.58 5.12 ABq 13
Me-13 ^b	1.19 d 7.5	1.47 s	1.50 s	1.40 s	1.53 s	1.39 s	1.52 s
Me-14 ^b	1.43 s	1.52 s	1.52 s	1.45 s	1.56 s	1.46 s	1.53 s
Me-15 ^b	1.46 s	1.54 s	1.57 s	1.66 s	1.59 s	1.67 s	1.58 s

^aThese data were determined in DMSO.

^bThe data in same column are exchangeable.

In this class of compounds, H-1 and H-6 generally have the axial configuration (5). The coupling constant ($J = 3.4$ Hz) between Hax-1 and H-2 suggested the presence of an equatorial H-2. One doublet at δ 5.42 ($J = 7.2$ Hz) of H-9 suggested the presence of an equatorial H-9 (4). Inspection of molecular model showed that the double-faced angle between Heq-8 and Heq-9 was near 90° .

In this class of compounds, if an acetate ester and an aromatic acid ester are situated at C-1 and C-9 (or C-9 and C-1), respectively, the acetate methyl has its $^1\text{H-nmr}$ signal at higher field than normal (1.9–2.7 ppm) (1,5). Compound **1** had a high-field $^1\text{H-nmr}$ signal of an acetate methyl at δ 1.55, indicating that the benzoate ester was situated at C-1 or C-9. A careful comparison of the $^1\text{H-nmr}$ chemical shifts with a derivative (2) of alcohol **3** (2,6) indicated that the signal for H-1 of **1** was shifted 0.21 ppm downfield from the corresponding signal of **2**, while the signal for H-9 of **1** was shifted 0.32 ppm downfield from the corresponding signal of **2**. This fact suggested that the benzoate ester was located at C-9. As a result, compound **1** was elucidated as $1\beta, 2\beta, 6\alpha, 12$ -tetraacetoxy-9 α -benzoyloxy- β -dihydroagarofuran.

Compound **4** analyzed for $\text{C}_{31}\text{H}_{36}\text{O}_{14}$ by hrms. Its nmr, mass, and ir spectra indicated that **4** contained three acetate esters and two β -furancarboxylate esters (2). The $^1\text{H-nmr}$ (Table 2) and $^{13}\text{C-nmr}$ (Table 1) spectra of **4** were very similar to those of the derivative of alcohol **3** (2). In fact, a complete hydrolysis of **4** with NaOMe/MeOH gave the major product which had the same R_f value on tlc as alcohol **3**. Thus the parent of **4** was identified as $1\beta, 2\beta, 4\alpha, 6\alpha, 9\alpha, 12$ -hexahydroxy- β -dihydroagarofuran (2,6). One free hydroxyl must be present in **4** due to the presence of five esters, and this was confirmed by an ir absorption at 3550 cm^{-1} . This free hydroxyl group was located at C-4 because the 4-OH in all other compounds of this class is not esterified (5). Therefore, **4** had the five esters mentioned above located at C-1, C-2, C-6, C-9, and C-12 of 4 α -hydroxy- β -dihydroagarofuran.

Compound **4** gave three normal $^1\text{H-nmr}$ signals at δ 2.06, 2.12, and 2.28 for three acetate methyls, which suggested that the esters located at C-1 and C-9 were both acetate esters or both β -furancarboxylate esters (1). A partial hydrolysis of **4** with aqueous Na_2CO_3 (7) gave a major product **5**, whose $^1\text{H-nmr}$ spectrum exhibited the presence of only one β -furancarboxylate ester and retained the signal of H-9 at δ 5.33. This fact suggested that one β -furancarboxylate ester was located at C-9, and the second thus must be located at C-1. As a result, compound **4** was elucidated as $2\beta, 6\alpha, 12$ -triacetoxy- $1\beta, 9\alpha$ -di(β -furancarboxyloxy)-4 α -hydroxy- β -dihydroagarofuran.

Compound **6** analyzed for $\text{C}_{35}\text{H}_{40}\text{O}_{12}$ by hrms. Its nmr, mass, and ir spectra indicated that **6** contained three acetate esters and two benzoate esters (1). As with compound **4**, the similarity of $^1\text{H-nmr}$ (Table 2) and $^{13}\text{C-nmr}$ (Table 1) spectra for **6** to those of the derivatives of alcohol **3** and the same R_f value on tlc for the complete hydrolysis product of **6** as alcohol **3** indicated that **6** also was a derivative of alcohol **3** and thus had the five esters mentioned above located at C-1, C-2, C-6, C-9, and C-12 of 4 α -hydroxy- β -dihydroagarofuran.

Compound **6** also gave three normal $^1\text{H-nmr}$ signals at δ 2.02, 2.14, and 2.32 for three acetate methyls. Thus the esters at C-1 and C-9 were both acetate esters or both benzoate esters. A partial hydrolysis of **6** with aqueous Na_2CO_3 gave a major product **7**, whose $^1\text{H-nmr}$ spectrum exhibited only the presence of one benzoate ester, and retained the signal of H-9 at δ 5.47, which suggested that one benzoate ester was situated at C-9 and the second at C-1. As a result, compound **6** was elucidated as $2\beta, 6\alpha, 12$ -triacetoxy- $1\beta, 9\alpha$ -dibenzoyloxy-4 α -hydroxy- β -dihydroagarofuran.

Compound **8** analyzed for $\text{C}_{33}\text{H}_{38}\text{O}_{13}$ by hrms. Its nmr and mass spectra indicated that **8** contained three acetate esters, one benzoate ester, and one β -furancarboxylate ester. The similarity of $^1\text{H-nmr}$ (Table 2) and $^{13}\text{C-nmr}$ (Table 1) spectra to those of **4**

and **6** suggested that **8** contained the same parent skeleton as **4** and **6**. Thus **8** also had the five esters mentioned above located at C-1, C-2, C-6, C-9, and C-12 of 4 α -hydroxy- β -dihydroagarofuran. Furthermore, three normal ^1H -nmr signals at δ 2.06, 2.14, and 2.35 for three acetate methyls suggested that two acetate esters or two aromatic acid esters (benzoate and β -furancarboxylate esters) were located at C-1 and C-9, respectively. A partial hydrolysis of **8** with aqueous Na_2CO_3 gave a major product that had the same R_f value as **5** on tlc and thus was identified as **5**. Therefore, the β -furancarboxylate ester was determined to be at C-9, and the benzoate ester thus was at C-1. As a result, compound **8** was elucidated as 2 β ,6 α ,12-triacetoxy-1 β -benzoyloxy-9 α - β -furancarboxyloxy-4 α -hydroxy- β -dihydroagarofuran.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Kofler apparatus. ^1H -nmr and ^{13}C -nmr spectra were recorded on a Bruker AM-400 nmr spectrometer with TMS as internal standard, CDCl_3 and DMSO as solvent. Uv spectra in EtOH were obtained on a UV-210A spectrophotometer. Eims were obtained on VG ZAB-HS mass spectrometer operating at 70 eV ionizing energy. Ir spectra were determined on a Perkin-Elmer 577 instrument. Cc was carried out on Si gel (200–300 mesh) column with petroleum ether/EtOAc as eluent. Hplc was carried out on a Merck RP-8 column with MeOH/ H_2O as eluent. Preparative tlc was carried out on Merck Si gel 60 F254 plates with petroleum ether/ Me_2CO and cyclohexane/ Me_2CO as eluent. Detection of components was with a uv lamp. Voucher specimens have been deposited at the Botanical Garden of Kunming Institute of Botany (Academy of Science of China).

EXTRACTION AND ISOLATION.—Dried and pulverized seed (3 kg) of *E. bungeanus* (collected in Yunnan Province, China, and authenticated by the faculty of Department of Systematic Botany, Kunming Institute of Botany, the Academy of Science of China) was extracted with petroleum ether (5 liters) at room temperature for 6 days. Removal of solvent under reduced pressure left reddish-brown oil (533 g). After extraction of the oil with MeOH- H_2O (90:10) (3×500 ml) and concentration of MeOH/ H_2O solution under reduced pressure, a crude extract (110 g) was obtained as reddish-brown semisolid. A portion (20 g) of the crude extract was chromatographed on a Si gel column (200–300 mesh, 400 g) with petroleum ether-EtOAc (80:20, 70:30 \rightarrow 20:80) as eluent to give 86 fractions, which were combined on detection of tlc to give 11 pools. Four minor pools were subjected to reversed-phase hplc on a Merck RP-8 short column with MeOH- H_2O (80:20) as eluent to give compounds **1** (41 mg), **4** (68 mg), **6** (55 mg), and **8** (22 mg), respectively.

COMPOUND 1.—Compound **1** was obtained as amorphous white powder: $[\alpha]^{14}_D +44.49$ ($c = 0.517$, CHCl_3); uv λ max nm (log ϵ) 281 (1.125), 273 (1.320), 232 (2.369), 201 (2.504); ir ν max cm^{-1} (KBr) 2970, 2940, 1740, 1710, 1600, 1450, 1385, 1360; eims m/z $[\text{M}]^+$ 574, $[\text{M} - 42]^+$ 532, $[\text{M} - 59]^+$ 515, $[\text{M} - 60]^+$ 472, $[\text{M} - 15]^+$ 457, $[\text{M} - 120]^+$ 352, 202, 105 (100), 77, 43; hrms m/z 574.2429 (calcd for $\text{C}_{30}\text{H}_{38}\text{O}_{11}$, 547.2403); ^{13}C nmr see Table 1; ^1H nmr see Table 2.

COMPOUND 2.—The solution of alcohol **3** (40 mg), 3 ml Ac_2O , and a little $\text{C}_5\text{H}_5\text{N}$ was set aside at room temperature for 6 days. After Ac_2O was blown off with N_2 gas, the reaction mixture was subjected to preparative chromatography on a Si gel plate with petroleum ether- Me_2CO (60:40) as eluent to give the major product **2** (25 mg, 38%) as an amorphous powder; ^1H nmr see Table 2.

COMPOUND 4.—Compound **4** was obtained as amorphous white powder: $[\alpha]^{14}_D +40.85$ ($c = 0.538$, CHCl_3); uv λ max nm (log ϵ) 240 (1.805), 201 (2.207); ir ν max cm^{-1} (KBr) 3550, 2970, 2940, 1570, 1450, 1385, 1365; eims m/z $[\text{M} - 15]^+$ 617, $[\text{M} - 60]^+$ 572, $[\text{M} - 120]^+$ 512, $[\text{M} - 112]^+$ 460, $[\text{M} - 112]^+$ 400, 192, 95 (100), 43; hrms m/z 617.1888 (calcd for $\text{C}_{30}\text{H}_{33}\text{O}_{14}$, 617.1860); ^{13}C nmr see Table 1; ^1H nmr see Table 2.

COMPOUND 5.—The solution of compound **4** (60 mg) and 3 ml MeOH was mixed with 1 ml $\text{Na}_2\text{CO}_3/\text{H}_2\text{O}$ solution (0.1 M), and then set aside at 25 $^\circ$ for 2 days. After the solvent was evaporated under reduced pressure, the reaction mixture was subjected to preparative chromatography on a Si gel plate with Me_2CO -cyclohexane (1:1) as eluent to afford the major product **5** (18 mg, 46%) as an amorphous powder. The ^1H -nmr data are summarized in Table 2.

COMPOUND 6.—Compound **6** was obtained as an amorphous white powder: uv λ max nm (log ϵ) 281 (1.519), 272 (1.492), 232 (2.379), 201 (2.537); ir ν max cm^{-1} (KBr) 3550, 2970, 2940, 1745, 1720, 1600, 1450, 1380, 1365; eims m/z $[\text{M} - 60]^+$ 592, $[\text{M} - 2 \times 60]^+$ 532, $[\text{M} - 15 - 122]^+$ 515,

[532 - 122]⁺ 410, 202, 105 (100), 77, 43; hrms *m/z* 592.2321 (calcd for C₃₃H₃₆O₁₀, 592.2298); ¹³C nmr see Table 1; ¹H nmr see Table 2.

COMPOUND 7.—Compound 6 (55 mg) was subjected to partial hydrolysis by the same method as mentioned in 5 to give the major product 7 (23 mg, 65%) as colorless crystals from MeOH: mp 273—275° (dec); ¹H nmr see Table 2.

COMPOUND 8.—Compound 8 was obtained as an amorphous white powder: eims *m/z* [M - 15]⁺ 627, [M - 60]⁺ 582, [M - 120]⁺ 522, [627 - 122]⁺ 505, 202, 192, 105 (100), 95, 77, 43; hrms *m/z* 627.2091 (calcd for C₃₂H₃₅O₁₃, 627.2067); ¹³C nmr data see Table 1; ¹H nmr see Table 2.

LITERATURE CITED

1. N. Wakabayashi, W.J. Wu, R.M. Waters, R.E. Redfern, G.D. Mills Jr., A.B. DeMilo, W.R. Lusby, and D. Andrzejewski, *J. Nat. Prod.*, **51**, 537 (1988).
2. Y.Q. Tu, D.G. Wu, J. Zhou, Y.Z. Chen, and X.F. Pan, *J. Nat. Prod.*, **53**, 603 (1990).
3. H.J. den Hertog Jr., C. Kruk, D.D. Nanavati, and S. Dev, *Tetrahedron Lett.*, 2219, (1974).
4. G. Baudouin, F. Tillequin, M. Koch, M.E. Tran Huu Dau, J. Guilhem, and H. Jacquemin, *Heterocycles*, **22**, 2221 (1984).
5. R. Brüning and H. Wagner, *Physicochemistry*, **17**, 1821 (1978).
6. S.M. Kupchan, R.M. Smith, and R.F. Bryan, *J. Am. Chem. Soc.*, **92**, 6667 (1970).
7. R.L. Baxter, L. Crombie, D.J. Simmonds, and D.A. Whiting, *J. Chem. Soc., Perkin Trans. 1*, 2972 (1979).

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