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10α-METHYL-EUDESMAN-8αH,12-OLIDES AND OTHER CONSTITUENTS FROM *WEDELIA PINETORUM*

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Key Word Index—*Wedelia pinetorum*; Compositae; Heliantheae; eudesmanolides; sesquiterpene lactones; *ent*-kauranes; 8,12,13-trihydroxyoctadeca-10(*E*),15(*Z*)-dienoic acid; 9,12,13-trihydroxydeca-10(*E*)-enoic acid.

Abstract—The aerial parts of *Wedelia pinetorum* furnished small amounts of three new 10α-methyl-eudesman-8αH,12-olides. Other constituents were angelylgrandifloric acid, its 9β-hydroxy derivative and its 16,17-epoxide, 2,6-dimethoxybenzoquinone, 9,12,13-trihydroxyoctadeca-10(*E*),15(2*Z*)-dienoic acid and 9,12,13-trihydroxyoctadec-10(*E*)-enoic acid.

Since our last summary on constituents of *Wedelia* species [1], sesquiterpenes and *seco*-kauranoids have been reported from *Wedelia regis* [2] and the structures of several lactones from *W.* grandiflora, earlier assumed to be pseudoguaianolides, have been corrected to eudesmanolides with '5,10-anti' stereochemistry [3]. We now report the occurrence of three new such eudesmanolides **1a** and **2a, c** in *W. pinetorum* (Standl. et Steyerm) Becker (syn. *Zexmenia pinetorum* Standl. et Steyerm. [4]). Other compounds found were angelylgrandifloric acid (**3a**), its 9-hydroxy derivative characterized as the methyl ester **3b** [5], the 16,17-epoxide **4a** previously characterized only as its methyl ester **4b** [6], 2,6-dimethoxybenzoquinone and two trihydroxy-C_{18}-acids **5a** and **5c** recently isolated by us from *Rudbeckia fulgida* [7]. It is interesting that two antifungal acids apparently identical with **5a, c** have recently been isolated from a rice cultivar suffering from rice blast disease [8].

Lactones **1a** and **2a, b** were a mixture from which small amounts of pure **2a** were isolated by radial chromatography. Acetylation of the mixture and separation by radial chromatography gave **1b** and **2b**; angelate **2c** or its acetate could not be isolated in pure form although the presence of **2c** was inferred from the ^{1}H NMR spectrum of the mixture. Comparison of the ^{1}H NMR spectra of **1a**, **1b** and **2b** (Table 1) with the spectra of lactones from *Wedelia hispida* [1] showed that these compounds differed from the earlier ones only in the absence of the oxygen function on C-3. The usual decoupling experiments which will not be detailed established the sequences H-1 through H-3 and H-6 through H-9; distribution of the acetate and tiglate (or angelate) moieties over C-6 and C-15 as shown in the formulae was assumed by analogy with the compounds from *W. hispida*.

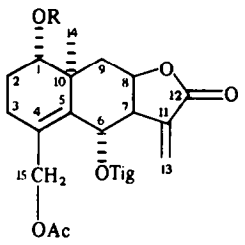
The stereochemistry at C-11 of **2a** was deduced on the following grounds: (a) the value of $J_{7,11}$ (11 Hz) and the solvent induced chemical shift of the H-13 doublet ($\Delta\delta_{H\text{-}13} = 0.16$) which indicated that the C-11 methyl group was pseudoequatorial; (b) the observed NOE between H-11 and H-9β (9%) and between H-13 and H-7 (~6%). The stereochemistry assigned to C-1 is based on the coupling constants which duplicate those found in the compounds from *Wedelia hispida** and on the observed NOE between H-1 and H-9 (9%). *cis*-Lactone ring closure to C-8 can be deduced from $J_{7,8}$; a small NOE (2%) between H-8 and H-14 supported the conclusion (model) that H-8 and H-14 are *cis*. Lastly coupling constants and the observed NOE between H-6 and H-15a (15%) agree with the stereochemistry shown for C-6.

The chemistry of *W. pinetorum* is not significantly different from that of other *Wedelia* species which have been studied. Lactones of type **1** or **2** have now been found in six of them as well as in some apparently closely related genera of subtribe Ecliptinae. Further phytochemical studies may possibly shed light on generic limits in the *Zexmenia–Wedelia–Aspilia* complex which are in need of revision.

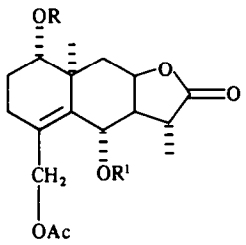
EXPERIMENTAL

Aerial parts (10.2 kg) of *Wedelia pinetorum* (Standl. et Steyerm) Becker, collected by Mr. Gustavo Cruz in the vicinity of Tegucigalpa, Honduras, in late summer 1975 were extracted with $CHCl_3$ and worked up in the usual manner [9]. The crude gum (16.8 g) was adsorbed on 26 g of silicic acid (Mallinckrodt 100 mesh) and chromatographed over 200 g of the same adsorbent packed in C_6H_6, 200 ml fractions being collected as follows: fr. 1 and 2 (C_6H_6) fr. 3 and 4 (C_6H_6–EtOAc, 4:1), fr. 5 and 6 (C_6H_6–EtOAc, 3:2), fr. 7 and 8 (C_6H_6–EtOAc, 2:3), fr. 9 and 10 (C_6H_6–EtOAc, 1:4), fr. 11 and 12 (EtOAc), fr. 13 and 14 (EtOAc–MeOH, 49:1), fr. 15 and 16 (EtOAc–MeOH, 19:1), fr. 17 and 18 (EtOAc–MeOH, 9:1), fr. 19–24 (MeOH).

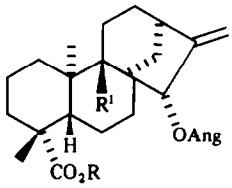
*The values of $J_{1,2a}$ and $J_{1,2b}$ for **2a** depend on the solvent; in $CDCl_3$ they differ somewhat from those for **2b** (see Table 1) which together with values reported earlier [1] suggests that the conformation of ring A is slightly affected by small changes in substitution.



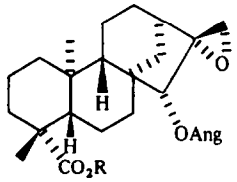
1a R = H
2b R = Ac



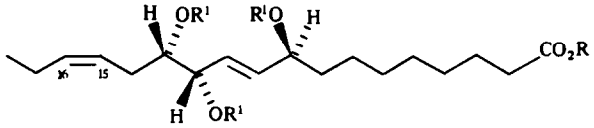
2a R = H, R^1 = Tig
2b R = Ac, R^1 = Tig
2c R = H, R^1 = Ang



3a R, R^1 = H
3b R = Me, R^1 = OH



4a R = H
4b R = Me



5a R, R^1 = H
5b R = Me, R^1 = Ac
5c R, R^1 = H, 15,16-dihydro
5d R = Me, R^1 = Ac, 15,16-dihydro

Table 1. ^{1}H NMR spectra of **1a, b** and **2a** ($CDCl_3$, 270 MHz, *J* in Hz in parentheses)

H	1a	1b	2a*	2a (C_6D_6)	2b
1	3.80 *dd* (10.5, 7)	4.88 *dd* (11.5, 4)	3.56 *dd* (9, 7)	3.11 *dd* (12, 4)	4.71 *dd* (11, 4)
2a			1.77 *m*	1.23–1.42 *m*	
2b			1.39 *m*		
3a			2–2.4 *c*	1.72–1.84 *m*	
3b					
6	5.82 *d* (2)	5.93 *d* (1.5)	6.02 *d* (1.5)	6.02 *d*	6.10 *d*
7	3.46 *dq* (7)	3.42 *br dt* (7, 2.5, 1.5)	2.48 *br dd* (10.5, 7)	2.04 *br dd*	2.48 *br dd* (12, 7)
8	4.87 *ddd*	4.82 *ddd* (7, 5, 4)	4.89 *ddd* (9, 7, 5)	4.42 *ddd*	4.85 *td* (9, 7)
9	2.60 *dd* (15, 4)	2.10	2.38 *dd* (15, 5)	2.07 *dd*	2.21 *dd* (15, 9)
9	‡	‡	1.56 *dd* (15, 9)	1.31 *dd*	1.38 *dd*
11	—	—	2.35 *dq* (10.5, 7)	2.19 *dq*	2.36 *dq* (12.5, 7)
13	6.35 *d* (2.5)	6.36 *d*	1.39 *d* (7)†	1.23 *d*†	1.38 *d*†
	5.88 *d* (2)	5.88 *d*			
14†	1.10	1.26	1.21 *br*	1.13	1.29 *br*
15a	4.51 *d* (13)	4.55 *d* (12)	4.97 *d* (13)	4.35 *d*	5.01 *d*
15b	4.63 *d* (13)	4.61 *d* (12)	4.46 *d* (13)	4.35 *d*	4.40 *d*
3′	6.84 *qq* (7, 1.5)	6.88 *qq*	6.85 *qq*	6.86 *qq* (7, 1)	6.83 *qq* (7, 1.5)
4′†	1.80 (7)	1.84 *br d*	1.81 *br d*	1.39 *dq* (7, 1)	1.81 *br d*
5′†	1.81 *br*	1.86 *br*	1.82 *br*	1.74 *q* (1)	1.82 *br*
Ac†	2.03	2.03	2.04	1.67	2.03
		2.09			2.09

* Signals of **2c** in 5 : 1 : 1 mixture of **1a**, **2a** and **2c** superimposed on those of **2a** except for H-2 at 6.04 *d*, H-13 at 1.37 *d*, H-14 at 1.20, H-15*b* and 4.48 *d* and H-3′ at 6.12 *qq*.

†Intensity three protons.

‡Obscured.

Fr. 4 and 5 on standing overnight with cyclohexane–Et_2O gave 54 mg of a mixture of **3a** and **4a** which was rechromatographed over 20 g of silica gel using $CHCl_3$ containing increasing amounts of Me_2CO. This furnished 10 mg of **3a** identical with authentic material and 9 mg of **4**, mp 235° (dec); IR ν_{max}^{KBr} cm^{-1}: 1725, 1695, 1690, 1165, 1055; ^1H NMR (270 MHz, $CDCl_3$): δ6.04 (*br q*, J = 7 Hz, H-3'), 4.80 (*br*, H-15), 3.12 (*d*) and 2.76 (*d*, J = 6 Hz, H-17a, b), 2.18 (*br d*, H-14a), 1.98 (*c*) and 1.94 (*c*, H-4' and H-5'), 1.26 (H-18) and 1.01 (H-20); MS *m/z* (rel. int.): 416 $[M]^+$ (2.3), 333 (1.1), 316 (9.7), 301 (10.4), 283 (7.4), 83 (100). [Calc. for $C_{25}H_{36}O_5$: M_r, 416.2563. Found: M_r (MS), 416.2563]. An authentic sample was synthesized by oxidation of 5 mg of **3a** with 10 mg of *m*-chloroperbenzoic acid.

Fr. 3 and 4, after filtration from the mixture of **3a** and **4**, wt 1.17 g, were chromatographed over 50 g of silica gel packed in $CHCl_3$, 20 ml fractions being collected in the following order: fr. 1–5 ($CHCl_3$), 6–10 ($CHCl_3$–Me_2CO, 99:1), fr. 11–15 ($CHCl_3$–Me_2CO, 49:1), 16–20 ($CHCl_3$–Me_2CO, 24:1), 21–25 ($CHCl_3$–Me_2CO, 47:3), 26–30 ($CHCl_3$–Me_2CO, 9:1) and 31–35 ($CHCl_3$–Me_2CO, 5:1). Fr. 19–28 (518 mg) contained a mixture of acids. Methylation followed by prep. TLC afforded a mixture of fatty acid methyl esters, 10 mg of **4b** [6] and **3b** [5, 10].

Fr. 7 and 8 of the original chromatogram and purification by TLC gave 8 mg of 2,6-dimethoxybenzoquinone. Fr. 9 and 10 (2.70 g) were rechromatographed over 130 g of silica gel using $CHCl_3$ containing amounts of MeOH in 50 ml fractions. Fr. 12 and 13 (0.80 g) was a mixture of three lactones. Repeated radial chromatography of 0.15 g of the mixture (hexane and hexane–Et_2O) eventually gave 5 mg of pure **2a** as a gum, and mixtures containing various proportions of **1a**, **2a** and **2c**. Acetylation of 30 mg of the lactone mixture and further purification by radial chromatography gave 5 mg of **1b** and 15 mg of **2b**, both gums.

1,15-*Diacetoxy*-6α-*tiglyloxy*-10α-*methyl*-7αH,8αH-*eudesma*-4,11-*diene*-8,12-*olide* (**1b**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770, 1730 (br) and 1650; MS (CI) *m/z* (rel. int.): 447 $[M+1]^+$ (3.6), 387 (19.8), 347 (24.8), 289 (42.8), 287 (29.4), 229 (23.5) and 101 (100). The ^1H NMR spectrum is listed in Table 1.

15-*Acetoxy*-1-*hydroxy*-6α-*tiglyloxy*-10α-*methyl*-7αH,8αH,11β*H*-*eudesm*-4-*en*-8,12-*olide* (**2a**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1770, 1740 (br), 1710 and 1650; the ^1H NMR spectrum is listed in Table 1.

1,15-*Diacetoxy*-6α-*tiglyloxy*-10α-*methyl*-7αH,8αH,11β*H*-*eudesm*-4-*en*-8,12-*olide* (**2b**). IR ν_{max}^{film} cm^{-1}: 1780, 1735 (br), 1715 and 1650. The low resolution MS (EI) did not exhibit the molecular ion; significant peaks were at *m/z* (rel. int.): 328 (20), 306 (24), 246, 228 (39.3) and 213 (4.4); MS (CI) *m/z* (%) 449 (4.6), 389 (37.2), 289 (45.2), 269 (9.5), 239 (73.7), 231 (42.8) and 101 (100). The ^1H NMR spectrum is listed in Table 1, the ^{13}C NMR spectrum in Table 2.

Fr. 14 and 15 of the original chromatogram (1.60 g) were rechromatographed over 65 g of silica gel packed in $CHCl_3$. Elution with $CHCl_3$ containing increasing amounts of MeOH gave 230 mg of solid material which on recrystallization from Me_2CO–cyclohexane gave 30 mg of a 1:1 mixture of **5a** and **5c**. Methylation with CH_2N_2 and acetylation (Ac_2O–pyridine) followed by prep. TLC (7% $AgNO_3$, C_6H_6–EtOAc, 9:1, two developments) gave 14 mg of **5b** and 16 mg of **5d** whose ^1H NMR spectra were superimposable on those of authentic material [7].

Table 2. ^{13}C NMR spectrum of **2b** (67.89 MHz, $CDCl_3$)

C	δ
1	77.42 *d**
2	22.65 *t*
3	28.30 *t*
4	138.56 *s*
5	132.46 *s*
6	68.45 *d*
7	48.08 *d*
8	72.89 *d**
9	38.54 *d*
10	38.31 *s*
11	35.76 *d*
12	177.73 *s*
13	13.85 *q*
14	20.16 *s*
15	63.78 *t*
1'	166.46 *s*
2'	128.40 *s*
3'	138.28 *d*
4'	14.48 *q*
5'	12.10 *q*
Ac	170.43 *s*, 170.43 *s*
	21.11 *q*, 20.77 *q*

* Assignments by selective decoupling. The great difference in chemical shift in C-1 of **2** and C-1 of compound **6b** of ref. [1] at 73.45 is notable and difficult to explain.

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