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UNUSUAL PHENYLPROPANOID GLYCOSIDES FROM *PARANEPHELIUS UNIFLORUS*

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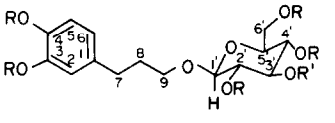
Key Word Index—*Paranephelius uniflorus*; Compositae; Liabae; glycosides; phenylpropane derivatives.

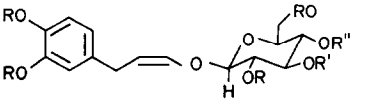
Abstract—Investigation of the aerial parts of *Paranephelius uniflorus* afforded a complex mixture of glycosides. High field ^{1}H NMR spectroscopy of the acetylated compounds led to the structures of six glucopyranosides which differed in the nature of the ester group and in that of the phenylpropane derivative. Three of them were enolglucopyranosides of dihydroconiferyl aldehyde.

The small genus *Paranephelius* (Compositae, tribe Liabae) is confined to Peru, Bolivia and northern Argentina. So far nothing is known of the chemistry. We have now investigated one species, *P. uniflorus* Poepp. et End. The aerial parts afforded lupeyl acetate and its Δ^{12} isomer. The polar fractions contained a complex mixture of glycosides which could not be separated. The ^{1}H NMR spectrum of the crude product showed that, in addition to a sugar moiety, an aromatic moiety and unsaturated esters were present. Mild acetylation gave a mixture of tetra-acetates which could be separated into two groups of glycosides. The somewhat less polar fraction on acetylation in the presence of 4-pyrrolidinopyridine [1] afforded a mixture of pentaacetates which could be separated by HPLC (reversed phase). The ^{1}H NMR spectra (Table 1) indicated that the three compounds only differed in the nature of the ester group. The characteristic ^{1}H NMR signals clearly indicated the presence of an angelate, a tiglate and a 4-methylsenecioate. The mass spectra showed very weak peaks of molecular ions for $C_{30}H_{38}O_{14}$ and $C_{31}H_{40}O_{14}$ as well as strong peaks for $C_{17}H_{23}O_9$ and $C_{18}H_{25}O_9$, respectively. These peaks agreed with the ions which should be observed if glucoside triacetates with an additional unsaturated C-5 or C-6 ester were present. Accordingly, the molecular formula of the aglycone should be $C_{13}H_{16}O_5$. As followed from the ^{1}H NMR spectra, this aglycone was a 1,3,4-substituted aromatic, two of the substituents being acetates as could be deduced from the typical chemical shifts of phenol acetates. Careful spin decoupling allowed the assignment of all signals. Those of the sugar moiety clearly showed that a β-glucopyranoside was present while the remaining low field signals indicated 9-*O*-β-glucosides of diacetyldihydroconiferyl alcohol. Irradiation of a multiplet at δ 1.90 collapsed a pair of double triplets at 3.90 and 3.48 to doublets and altered a second pair of double triplets around 2.67. This obviously required the sequence $PhCH_2CH_2CH_2OR$. The asymmetric C-1′ center of the glucoside resulted in a non-equivalence of the protons H-7–H-9. The positions of the unsaturated ester groups most likely was the same as in the corresponding esters **8–10** (see below). The structure of the natural glycosides, therefore, should be **1–3**.

The more polar fraction of tetra-acetates contained a mixture of three glucosides which differed again in the nature of the ester groups. The ^{1}H NMR spectra (Table 1) showed that an angelate, a tiglate and a senecioate were present. Spin decoupling further indicated that the C-4′ hydroxyl was not acetylated obviously due to steric hindrance. Accordingly, the C_5 esters most likely were at C-3′ though a rigorous proof of this assumption was not possible. Acetylation in the presence of 4-pyrrolidinopyridine gave penta-acetates. The observed shift differences of the protons of the sugar moiety supported the proposed position of the unsaturated acid. The remaining ^{1}H NMR signals indicated that the aglycone part was the *cis*-enol of dihydroconiferyl aldehyde. Accordingly, a lowfield doublet at δ 6.28 was narrowly split by an allylic coupling with a pair of broadened double doublets at 3.42 and 3.32 which showed vicinal couplings with a three-fold doublet at 4.78. The olefinic protons showed a vicinal coupling of only 6.5 Hz which at first caused some confusion concerning their assignments. The presence of an enol ether linkage, however, could be established by the result of the hydrogenation of this double bond and that



	1	2	3	4	5	6	7
R	H	H	H	Ac	Ac	Ac	Ac
R′	Ang	Tigl	MeSen*	Ang	Tigl	MeSen	MeBu



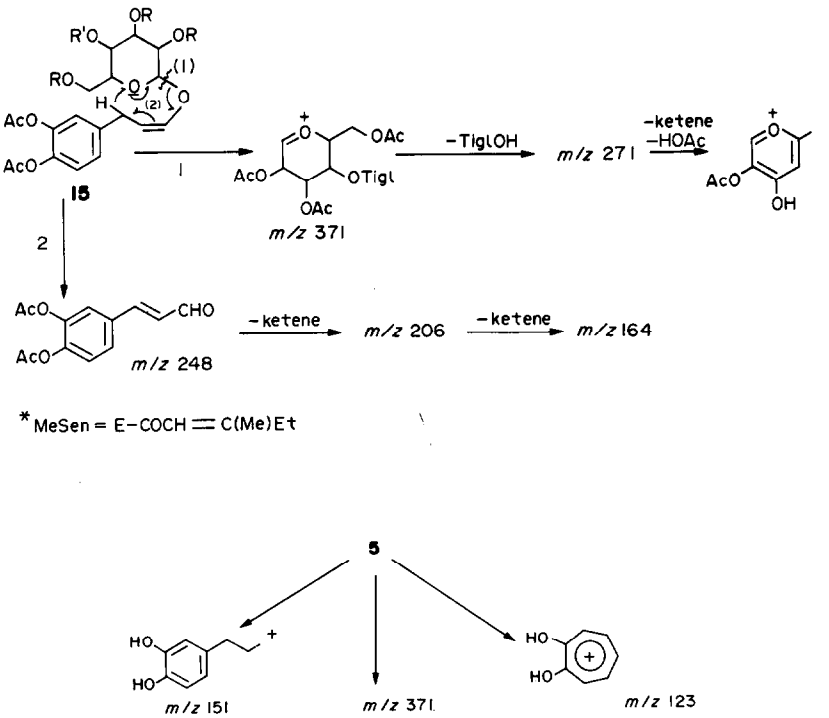
	8	9	10	11	12	13	14	15	16
R	H	H	H	Ac	Ac	Ac	Ac	Ac	Ac
R′	Ang	Tigl	Sen	Ang	Tigl	Sen	Ang	Tigl	Sen
R″	H	H	H	H	H	H	Ac	Ac	Ac

Table 1. ^{1}H NMR spectral data of compounds **4–7** and **11–16** (400 MHz, $CDCl_3$, TMS as internal standard)

	4	**5**	**6**	**7**	**11***	**12***	**13***	**14**	**15**	**16**
H-2	—	7.00 *d*	—	7.00 *d*	—	6.99 *br s*	—	—	6.99 *br s*	—
H-5	—	7.09 *d*	—	7.09 *d*	—	7.06 *br s*	—	—	7.06 *br s*	—
H-6	—	7.04 *dd*	—	7.04 *dd*	—		—	—		—
H-7	—	2.69 *ddd*	—	2.69 *ddd*	—	3.42 *br dd*	—	—	3.43 *br dd*	—
H-7′	—	2.63 *ddd*	—	2.63 *ddd*	—	3.32 *br dd*	—	—	3.33 *br dd*	—
H-8	—	1.90 *m*	—	1.90 *m*	—	4.78 *ddd*	—	—	4.79 *ddd*	—
H-9	—	3.90 *dt*	—	3.91 *dt*	—	6.28 *dt*	—	—	6.27 *dt*	—
H-9′	—	3.48 *ddd*	—	3.47 *ddd*	—		—	—		—
H-1′	4.56 *d*	4.56 *d*	4.54 *d*	4.53 *d*	4.73 *d*	4.73 *d*	4.72 *d*	—	4.78 *d*	—
H-2′	5.09 *dd*	5.08 *dd*	5.06 *dd*	5.06 *dd*	5.18 *dd*	5.18 *dd*	5.18 *dd*	—	5.18 *t*	—
H-3′	5.33 *t*	5.29 *t*	5.28 *t*	5.27 *t*	5.05 *dd*	5.05 *dd*	5.05 *dd*	—	5.31 *t*	—
H-4′	5.16 *t*	5.14 *t*	5.13 *t*	5.13 *dd*	3.68 *ddd*	3.68 *ddd*	3.68 *ddd*	—	5.18 *t*	—
H-5′	3.73 *ddd*	3.73 *ddd*	3.73 *ddd*	3.71 *ddd*	3.62 *ddd*	3.62 *ddd*	3.61 *ddd*	—	3.80 *ddd*	—
H-6_1′	4.29 *dd*	4.29 *dd*	4.26 *dd*	4.28 *dd*	4.22 *dd*	4.22 *dd*	4.23 *dd*	—	4.28 *dd*	—
H-6_2′	4.16 *dd*	4.16 *dd*	4.14 *dd*	4.13 *dd*	4.16 *dd*	4.16 *dd*	4.14 *dd*	—	4.15 *dd*	—
OCOR	6.07 *qq*	6.84 *br q*	5.60 *tq*	2.34 *tq*	6.05 *qq*	6.92 *br q*	5.60 *qq*	6.09 *qq*	6.84 *br q*	5.60 *qq*
	1.96 *dq*	1.80 *br s*	2.16 *br q*	1.61 *ddq*	1.92 *dq*	1.74 *br d*	2.16 *d*	1.94 *dq*	1.75 *br d*	2.13 *d*
	1.84 *dq*		1.08 *t*	1.41 *ddq*	1.80 *dq*	1.75 *br s*	1.91 *d*	1.82 *dq*	1.76 *br s*	1.88 *d*
			2.13 *d*	0.86 *t*						
				1.07 *d*						
OAc	2.31 *s*	2.31 *s*	2.31 *s*	2.31 *s*	2.27 *s*	2.27 *s*	2.28 *s*	2.26 *s*	2.26 *s*	2.26 *s*
	2.30 *s*	2.30 *s*	2.30 *s*	2.30 *s*	2.26 *s*	2.26 *s*	2.26 *s*	2.25 *s*	2.25 *s*	2.25 *s*
	2.10 *s*	2.09 *s*	2.08 *s*	2.09 *s*	2.10 *s*	2.10 *s*	2.10 *s*	2.08 *s*	2.08 *s*	2.08 *s*
	2.05 *s*	2.03 *s*	2.03 *s*	2.04 *s*	1.96 *s*	1.96 *s*	1.98 *s*	2.00 *s*	1.97 *s*	1.99 *s*
	2.02 *s*	2.00 *s*	2.00 *s*	2.02 *s*				1.97 *s*	1.94 *s*	1.96 *s*

*OH 3.37 *d* (J = 4 Hz).

J (Hz): 2, 6 = 2; 5, 6 = 8.5; 1′, 2′ = 8; 2′, 3′ = 3′, 4′ = 4′, 5′ = 9.5; 5′, 6_1′ = 4.5; 5′, 6_2′ = 2.5; 6_1′, 6_2′ = 13; compounds **4–7**: 7, 7′ ~ 14; 7, 8 ~ 7; 8, 9 = 8, 9′ = 5; 8′, 9 = 5; 8′, 9′ = 8; 9, 9′ = 10; compounds **11–16**: 7, 7′ = 15; 7, 8 = 8.5; 7′, 8 = 7.5; 7, 9 = 7, 9′ = 1; 8, 9 = 6.5; OAng: 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1; OTigl: 3′, 4′ = 7; OSen: 2′, 4′ = 2′, 5′ = 1; OMeSen: 2′, 4′ = 2′, 5′ = 5′, 6′ = 7.



Scheme 1.

of the tiglate which led to the formation of **7**. Thus, the second group of natural compounds had structures **8–10**.

The mass spectra of the penta-acetate, **15**, showed some interesting aspects. No molecular ion was observed and the first strong fragment was due to the sugar (*m/z* 371, see Scheme 1). This fragment was further degraded by loss of tiglic acid, ketene and acetic acid, leading to a strong fragment *m/z* 169. The aglycone moiety gave a weak fragment *m/z* 250 ($C_{13}H_{44}O_5$) and a stronger one at *m/z* 248 which most likely was formed in a direct way from the molecular ion (see Scheme 1). Double elimination of ketene gave *m/z* 206 and 164. In the mass spectrum of **5** only the dihydroxyphenyl propyl and the corresponding dihydroxytropylium ions (*m/z* 151 and 123) were visible. So far our knowledge of the chemistry of the tribe Liabae is not very extensive [2–5]. However, no compounds have been isolated which are typical for the tribe Senecioneae, where the species of the tribe Liabae were placed previously. Many more species have to be investigated to get a clear picture concerning the chemotaxonomy of this tribe.

EXPERIMENTAL

The air-dried plant material (130 g), collected in January 1982 in Peru (voucher RMK 9053), deposited in the U.S. National Herbarium, Washington, was extracted with Et_2O–petrol (1:2) and the resulting extract was treated with MeOH to remove satd long chain hydrocarbons. The soln was evaporated and the residue separated by CC (Si gel). With Et_2O–petrol (1:10) 30 mg lupeyl acetate and 20 mg of its Δ^{12} isomer were obtained and with Et_2O–MeOH (10:1) 300 mg of a crude mixture of **1–3** and **8–10**; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.83 (*br s*, H-2), 6.50 (*d*, H-5), 6.70 (*br d*, H-6), 6.11 [*br d* (**8–10**), H-9], 5.0–2.5 (*m*, H-1′–H-6′, H-8, H-9), 6.85 (*br q*), 1.75 (*br s*), 1.73 (*br d*) (OTigl). Acetylation (Ac_2O, 1 hr, 70°) afforded a mixture of tetra-acetates which were separated by TLC (Si gel, Et_2O) affording a mixture of two groups of tetra-acetates. The less polar fraction (20 mg) on acetylation ($CHCl_3$, 0.1 ml Ac_2O, 20 mg 4-pyrrolidinopyridine) afforded a mixture of **4–6**, which could not be separated by TLC. HPLC (reversed phase, MeOH–H_2O, 3:1) afforded 3 mg **4**, 2 mg **5** and 2 mg **6**. The more polar mixture of tetra-acetates on TLC (Et_2O–petrol, 3:1, several times) afforded 40 mg **12**, while **11** and **13** (each 2 mg) could not be obtained pure. Acetylation of the mixture of **11–13** in the presence of 4-pyrrolidinopyridine afforded 2 mg **14**, 12 mg **15** and 2 mg **16**, which could be separated by HPLC (see above). Much material was lost during the extensive separations.

3,4-*O*-*Diacetyl*-7,8-*dihydroconiferyl*-(2′,4′,6′-O-*triacetyl*-3′-O-*angeloyl*-1′*β*-*glucopyranoside*) (**4**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (PhOAc), 1750 (OAc), 1725, 1650 (C=CCO$_2$R); MS *m/z* (rel. int.): 622.226 [M]$^+$ (0.5) ($C_{30}H_{38}O_{14}$), 580 [M − ketene]$^+$ (5), 538.205 [580 − ketene]$^+$ (33) ($C_{26}H_{34}O_{12}$), 371.134 [M − (AcO)$_2$C$_6$H$_3$(CH$_2$)$_3$OH]$^+$ (25) ($C_{17}H_{23}O_9$), 329 [372 − ketene]$^+$ (1), 271 [371 − AngOH]$^+$ (2), 211 [271 − HOAc]$^+$ (2), 169.050 [211 − ketene]$^+$ (50) ($C_8H_9O_4$), 151 [(HO)$_2$C$_6$H$_3$(CH$_2$)$_3$]$^+$ (14), 123 [dihydroxytropylium ion]$^+$ (14), 109 [169 − HOAc]$^+$ (20), 83 [C$_4$H$_7$CO]$^+$ (100), 55 [83 − CO]$^+$ (23).

3,4-O-*Diacetyl*-7,8-*dihydroconiferyl*-(2′,4′,6′-O-*triacetyl*-3′-O-*tigloyl*-1′*β*-*glucopyranoside*) (**5**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (PhOAc), 1750 (OAc), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 622.226 [M]$^+$ (0.2) ($C_{30}H_{38}O_{14}$), 580 (3), 538 (23), 371 (25), 271 (1), 211 (1), 169 (35), 151 (80), 123 (11), 109 (15), 83 (100), 55 (25).

3,4-O-*Diacetyl*-7,8-*dihydroconiferyl*-[2′,4′,6′-O-*triacetyl*-3′-O-(4′-*methylsenecioyl*)-1′*β*-*glucopyranoside*] (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (PhOAc), 1750 (OAc), 1725 (C=CCOOR); MS

m/z (rel. int.): 636.242 $[M]^+$ (0.1) ($C_{31}H_{40}O_{14}$), 594 [M − ketene]$^+$ (2), 252 [594 − ketene]$^+$ (18), 385 [M − $(AcO)_2C_6H_3(CH_2)_3OH]^+$ (20), 271 [385 − $RCO_2H]^+$ (1.5), 211 [271 − HOAc]$^+$ (1), 169 [211 − ketene]$^+$ (43), 151 (10), 123 [151 − CO]$^+$ (10), 109 (19), 97 $[C_5H_9CO]^+$ (100), 69 [97 − CO]$^+$ (4).

3,4-O-*Diacetyl*-7,8-*dihydroconiferyl aldehyde enol*-(2′,6′-O-*diacetyl*-3′-O-*tigloyl*-1′*β*-*glucopyranoside*) (**12**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1770 (PhOAc), 1750 (OAc), 1725, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 578.200 $[M]^+$ (0.05) ($C_{28}H_{34}O_{13}$), 536 [M − ketene]$^+$ (0.1), 329 $[M-(AcO)_2C_6H_3CH_2CH{=}CHOH]^+$ (19), 250 $[(AcO)_2C_6H_3CH_2CH{=}CHOH]^+$ (0.2), 229 [329 − TiglOH]$^+$ (14), 169 [229 − HOAc]$^+$ (24), 166 [250 − 2 × ketene]$^+$ (3), 83 $[C_4H_7CO]^+$ (100).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+6 \quad +7 \quad +8 \quad +15} \ (CHCl_3; c\ 0.86).$$

10 mg **12** containing small amounts of **11** and **13** were acetylated in the presence of 4-pyrrolidino pyridine (see above). The mixture of **14**–**16** obtained was separated by HPLC (reversed phase, MeOH–H_2O, 3:1). **14**: colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (PhOAc), 1750 (OAc), 1725 (C=CCO_2R); ^{1}H NMR see Table 1. **15**: colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (PhOAc), 1750 (OAc), 1725 (C=CCO_2R); MS *m/z* (rel. int.): 371 $[C_{17}H_{23}O_9]^+$ (41), 271 [371 − TiglOH]$^+$ (2), 250 $[C_{13}H_{14}O_5]^+$ (1), 248 $[C_{13}H_{12}O_5]^+$ (3), 229 [271 − ketene]$^+$ (1), 206 [248 − ketene]$^+$ (15), 169 [229 − HOAc]$^+$ (88), 164 [206 − ketene]$^+$ (38), 109 [169 − HOAc]$^+$ (54), 83 $[C_4H_7CO]^+$ (100), 55 [83 − CO]$^+$ (27). **16**: colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (PhOAc), 1750 (OAc), 1720 (C=CCO_2R); ^{1}H NMR see Table 1.

Hydrogenation of 3 mg **15** in Et_2O in the presence of Pd–$BaSO_4$ afforded **7**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (PhOAc), 1750 (OAc, CO_2R); ^{1}H NMR see Table 1.

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