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PYRONES AND OTHER CONSTITUENTS FROM *PODOLEPIS* SPECIES

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Key Word Index—*Podolepis canescens*; *P. capillaris*; *P. lessonii*; *P. longipedata*; *P. rugata*; Compositae; pyrones; lignans; coumarins; sesquiterpenes; bisabolol derivatives.

Abstract—Investigation of five Australian *Podolepis* species afforded in addition to two previously described pyrones seven new ones. Furthermore, two new lignans, one unusual oxidation product of hydroxyobliquin as well as three sesquiterpenes derived from bisabolol were isolated. The structures were determined by spectroscopic methods.

INTRODUCTION

From the Australian genus *Podolepis* so far only one species has been investigated chemically, affording tetra-substituted γ-pyrones [1]. We now present results on five further species.

RESULTS AND DISCUSSION

The aerial parts of *Podolepis canescens* Cunn. ex DC and of *P. lessonii* (Cass.) Benth. both gave the known lignans **3a** [2], **3b** [3], **3d** [4] and **3e** [5] while those of *P. longipedata* A. Cunn. ex DC afforded in addition to the pyrones **1a** [1] and **1b** [1] large amounts of **1i**. Furthermore, **3a–c** [6] were isolated. The roots of *P. rugata* Labill. var. *rugata* gave in addition to podopyrone (**1a**) six new pyrones **1c–h**, sesamin (**2a**) [7] and two closely related derivatives **2b** and **c**, further lignans **3d–f** [8], the obliquins **4a** [9] and **4b** [5] and **4c**, an oxidation product of the former, as well as the sesquiterpenes **5a–c**. The aerial parts gave the same compounds, except for **1c**, and instead of **3d–f** the lignans **3a** and **3b**. No characteristic compounds could be obtained from *P. capillaris*.

The ^{1}H NMR spectra of **1e** and **f**, respectively, (Table 1) differed from that of podopyrone (**1a**) only in the signals for an ethyl group which replaced one of the methyl singlets. The relative position of the substituents followed from the NOE effect between H-7 and H-1′ and the length of the side chain from the mass spectra. The ^{13}C NMR data (Table 2) are also in accordance with the structure.

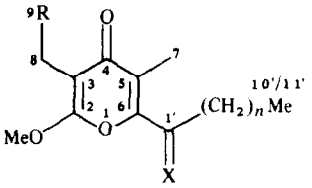
The ^{1}H NMR spectra of **1c/d** and **1g/h** (Table 1) differed also in the signals for a methyl and ethyl group, respectively. From the ^{13}C NMR spectra (Table 2) of **1g/h** the presence of an unsaturated keto group (δ195.9 *s*) could be deduced which could only be placed at C-1′. This explained also the downfield shift of the H-7 methyl singlet in the ^{1}H NMR spectra compared with podopyrone. In the case of **1h** the arrangement of the substituents was confirmed by means of selective INEPT experiments through long range coupling. In this way the protons of the methoxy group were connected with C-2, H-7 with C-4, C-5 and C-6 and H-8 with C-2, C-3 and C-4. Again, the length of the side chain followed from the mass spectrum. The ^{1}H NMR spectrum of **1i** (Table 1) was again very similar to that of podopyrone. An additional low field singlet at δ2.12 *s* and the absence of the terminal methyl triplet of the side chain required a methyl ketone which was further supported by the ^{13}C NMR spectrum (Table 2). A similar compound with an ethyl group at C-3 has previously been isolated from *P. hieracioides* [1].

The structure of the sesamin derivatives **2b** and **2c** followed from the ^{1}H NMR spectra (see Experimental). The additional methoxy group in **2b** led to nonequivalence of all protons which could be assigned by spin decoupling. The relative position of the methoxy group and the stereochemistry were established by NOE experiments. Thus, the methoxy group gave an effect with H-7 and not with H-5. Further effects were observed between H-8 and H-9$_1$, between H-7, H-5 and H-9$_2$, between H-8′ and H-9′$_1$ as well as between H-7′, H-2′, H-6′ and H-9′$_2$. The symmetrical arrangement of the substituents in **2c** led to an identical coupling pattern as in the spectrum of sesamin. The relative position of the methoxy group was further established by *ortho*-coupling of two aromatic protons and was very likely from biogenetical considerations.

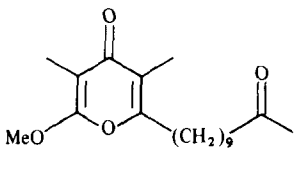
Apart from differences in chemical shifts, the ^{1}H NMR spectrum of **4c** (see Experimental) was identical to that of methoxy obliquine. As the mass spectrum required one more oxygen the proposed structure was likely. An isomer with a methoxy group at C-4a could be excluded due to the missing NOE of H-4 with the methoxy group. The ^{13}C NMR spectrum (see Experimental) supported the structure. We have named compound **4c** podorugatin.

The ^{1}H NMR spectra of **5a** and **b** (see Experimental) were very similar to those of known aldehydes (**5**) [10, 11]. The absence of the aldehyde signals and additional methyl singlets at δ3.73 and 3.83 respectively, indicated carbomethoxy groups.

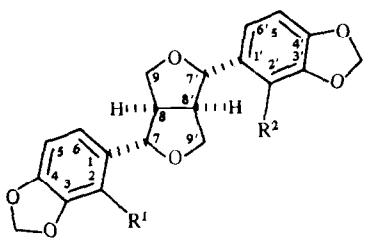
The upfield shift of the olefinic proton signal in the spectrum of **5c** and the broad singlet at δ4.70 (2H) required an acyloxy methylene group. The nature of the ester group followed from the typical signals for an α-furan carboxylate (see Experimental). As the remaining signals were similar to those of α-bisabolol the structure was established.



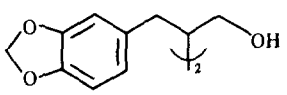
	1a	1b	1c	1d	1e	1f	1g	1h
R	H	H	H	H	Me	Me	Me	Me
X	H_2	H_2	O	O	H_2	H_2	O	O
n	9	10	8	9	8	9	8	9



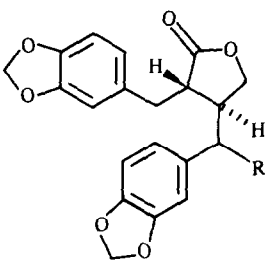
1i



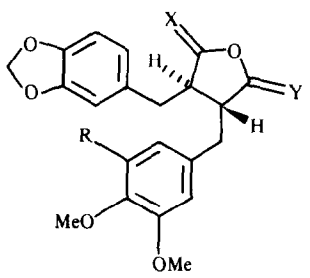
	2a	2b	2c
R^1	H	H	OMe
R^2	H	OMe	OMe



3a



	3b	3c
R	H	OH



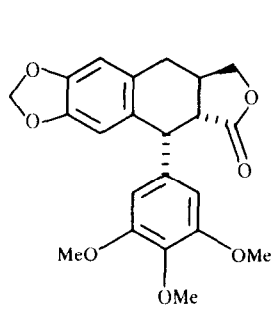
	3d	3e
R	H	OMe
X	O	H_2
Y	H_2	O

The chemistry of the five investigated *Podolepis* species is not uniform. Obviously the pyrones are characteristic as well as the lignans. Obliquins and pyrone derivatives are common in *Helichrysum* but the relevance of bisabolene derivatives is not yet clear. The placement of *Podolepis* next to the Australian *Helichrysum* species [12] is supported by their chemistry. Further studies may show whether the Australian *Athrixia* species are chemically related as they are proposed to be close to *Podolepis* [12].

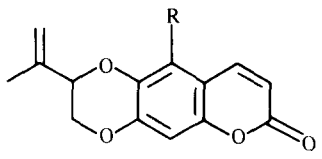
EXPERIMENTAL

Air-dried plant material (vouchers deposited in US National Herbarium, Washington) was extracted with MeOH–Et_2O–petrol (1:1:1) and the exts obtained sepd by CC and further by TLC and HPLC (always RP 8, *ca* 100 bar), MeOH–H_2O mixts in different ratios: HP1: (9:1); HP2: (17:3); HP3: (4:1); HP4: (7:3); HP5: (13:7). The conditions of the final purification of new compounds are given in parenthesis (see below).

An extract of *P. canescens* (200 g, voucher RMK 9563) gave 30 mg **3a**, 440 mg **3b**, 330 mg **3d** and 60 mg **3e**. *Podolepis lessonii* (100 g, voucher RMK 9539) gave 72 mg **3a**, 140 mg **3b**, 450 mg **3d** and 110 mg **3e**. *Podolepis longipedata* (480 g, voucher 86/0192) afforded 300 mg **1a**, 50 mg **1b**, 800 mg **1i** (HP4, R_t 19 min), 10 mg **3a**, 33 mg **3b** and 50 mg **3c**. From *P. rugata* (voucher RMK 9602), both, aerial parts and the roots were investigated. The amounts from the roots are given in parenthesis. 900 g aerial parts (65 g roots) gave 60 mg (15 mg) **1a**, 2 mg (13 mg) **1d** (HP2, R_t 12.2 min), 7 mg (2 mg) **1e** (HP1, R_t 13.4 min), 15 mg (3 mg) **1f** (HP1, R_t 15.6 min), 12 mg (5 mg) **1g** (HP3, R_t 18.6 min), 22 mg (19 mg) **1h** (HP3, R_t 25 min), 9 mg (15 mg) **2a**, 13 mg (12 mg) **2b** (HP3, R_t 8.2 min), 10 mg (8 mg) **2c** (HP3, R_t 9.8 min), 300 mg **3a**, 7 mg **3b**, 150 mg (7 mg) **4a**, 23 mg (4 mg) **4b**, 4 mg (4 mg) **4c** (HP5, R_t 8.1), 2 mg (2 mg) **5a** (TLC, CH_2Cl_2–Et_2O, 97:3, R_f 0.4), 2 mg (21 mg) **5c** (TLC as **5a**, R_f 0.6) and 2 mg (12 mg) **5b** (HP5, R_t 16.3 min). Additionally the roots gave 4 mg **1c** (HP2, R_t 10.2 min), 3 mg **3d**, 3 mg **3e** as well as 3 mg **3f**. Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic materials.

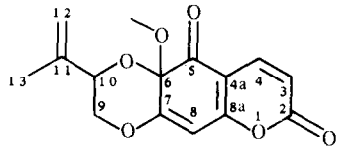


3f

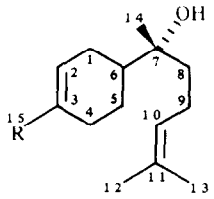


4a **4b**

R OH OMe

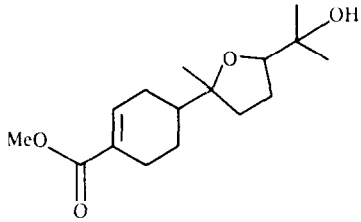


4c

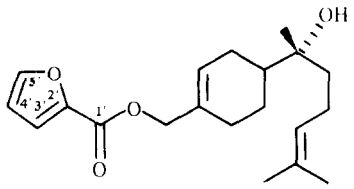


5 **5a**

R CHO COOMe



5b



5c

Table 1. ^{1}H NMR spectral data of compounds **1c–i** (400 MHz, $CDCl_3$, δ-values)

H	1c	1d	1e	1f	1g	1h	1i
7	2.31 *s*	2.31 *s*	1.95 *s*	1.94 *s*	2.30 *s*	2.29 *s*	1.92 *s*
8	1.91 *s*	1.91 *s*	2.41 *q*	2.40 *q*	2.44 *q*	2.43 *q*	1.83 *s*
9	—	—	1.04 *t*	1.03 *t*	1.05 *t*	1.04 *t*	—
1′	—	—	2.58 *t*	2.57 *t*	—	—	2.56 *t*
2′	2.85 *t*	2.84 *t*	1.65 *tt*	1.64 *tt*	2.85 *t*	2.84 *t*	1.62 *tt*
3′	1.69 *tt*	1.69 *tt*			1.69 *tt*	1.69 *tt*	1.2 – 1.4 *m*
4′							
7′	1.2 – 1.4 *m*		1.2 – 1.4 *m*		1.2 – 1.4 *m*		
8′		1.2 – 1.4 *m*		1.2 – 1.4 *m*		1.2 – 1.4 *m*	1.54 *tt*
9′							2.40
10′	0.88 *t*		0.88 *t*		0.88 *t*		—
11′	—	0.88 *t*	—	0.88 *t*	—	0.87 *t*	2.12 *s*
OMe	4.07 *s*	4.07 *s*	3.96 *s*	3.95 *s*	4.07 *s*	4.06 *s*	3.98 *s*

J [Hz]: All coupling constants *ca* 7 Hz.

1′-*Oxo*-nor-*podopyrone* (**1c**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715 (C=O), 1640, 1620 (γ-pyrone); MS *m/z* (rel. int.): 308.199 $[M]^+$ (26) (calc. for $C_{18}H_{28}O_4$: 308.199), 293 $[M-Me]^+$ (32), 209 $[M-C_7H_{15}]^+$ (100), 181 (63), 149 (87), 57 (96).

1′-*Oxopodopyrone* (**1d**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715 (C=O), 1640, 1615 (γ-pyrone); MS *m/z* (rel. int.): 322.214 $[M]^+$ (19) (calc. for $C_{19}H_{30}O_4$: 322.214), 307 (8), 293 (11), 263 (15), 209 (34), 181 (38), 149 (70), 57 (100).

8-*Methyl*-nor-*podopyrone* (**1e**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660, 1580 (γ-pyrone); MS *m/z* (rel. int.): 308.235 $[M]^+$ (48) (calc. for $C_{19}H_{32}O_3$: 308.235), 293 (100), 195 (20), 182 (18), 113 (30).

8-*Methylpodopyrone* (**1f**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1670,

Table 2. ^{13}C NMR spectral data of **1e**, **g–i** (67.9 MHz, $CDCl_3$)

C	1e	1g	1h	1i	Multiplicity
2	162.2	161.3	161.3	162.1	*s*
3	105.4	107.7	107.7	99.3	*s*
4	180.5	179.8	179.8	181.0	*s*
5	118.6	126.7	126.6	118.2	*s*
6	158.5	148.6	148.6	158.4	*s*
7	9.9	10.0	10.0	9.9	*q*
8	15.2 *t*	15.5 *t*	15.5 *t*	6.8 *q*	—
9	12.9	12.5	12.5	—	*q*
1′	27.0 *t*	195.9 *s*	195.9 *s*	27.0 *t*	—
2′	30.7	40.0	40.0	30.6	*t*
3′	29.6	23.3	23.3	29.2	*t*
4′	29.6	29.2	29.2	29.3	*t*
5′	29.7	29.4	29.4	29.3	*t*
6′	29.7	29.3	29.5	29.1	*t*
7′	19.6	29.3	29.5	29.0	*t*
8′	29.4	31.8	29.3	23.8	*t*
9′	31.9	22.6	31.8	43.7	*t*
10′	22.7 *t*	14.1 *q*	22.6 *t*	209.3 *s*	—
11′	14.1	—	14.1	29.8	*q*
OMe	55.3	55.7	55.7	55.2	*q*

1590 (γ-pyrone); MS *m/z* (rel. int.): 322.251 $[M]^+$ (24) (calc. for $C_{20}H_{34}O_3$: 322.251), 307 (100), 209 (10), 195 (14), 182 (14), 113 (18).

8-*Methyl*-1′-*oxo*-nor-*podopyrone* (**1g**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (C=O), 1640, 1595 (γ-pyrone); MS *m/z* (rel. int.): 322.215 $[M]^+$ (86) (calc. for $C_{19}H_{30}O_4$: 322.215), 307 (100), 223 $[M-C_7H_{15}]^+$ (12), 209 $[M-C_8H_{17}]^+$ (10).

8-*Methyl*-1′-*oxopodopyrone* (**1h**). Colourless crystals, mp 63.5°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (C=O), 1650, 1610 (γ-pyrone); MS *m/z* (rel. int.): 336.230 $[M]^+$ (84) (calc. for $C_{20}H_{32}O_4$: 336.230), 231 (100), 223 (20), 209 (16), 195 (18).

10′-*Oxopodopyrone* (**1i**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (C=O), 1660, 1605 (γ-pyrone); MS *m/z* (rel. int.): 322.215 $[M]^+$ (66) (calc. for $C_{19}H_{30}O_4$: 322.215), 307 (27), 279 $[M-MeCO]^+$ (31), 265 (84), 181 (94), 168 (100), 59 (94).

3-*Methoxysesamin* (**2b**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1655, 1630, 1525, 1510; MS *m/z* (rel. int.): 384.121 $[M]^+$ (100) (calc. for $C_{21}H_{20}O_7$: 384.121), 353 (3), 256 (2), 232 (3), 191 (17); ^1H NMR ($CDCl_3$): δ6.86 (*d*, H-2′), 6.77 (*d*, H-5′), 6.81 (*dd*, H-6′), 6.50 (*d*, H-5), 6.84 (*dd*, H-6), 5.02 (*d*, H-7), 3.01 (*dddd*, H-8), 4.31 (*dd*, H-9_1), 3.99 (*dd*, H-9_2), 4.65 (*d*, H-7′), 2.94 (*dddd*, H-8′), 4.19 (*dd*, H-$9'_1$), 3.90 (*dd*, H-$9'_2$), 4.01 (*s*, OMe), 5.92 (ABq, $-OCH_2O-$), 5.95 (*s*, $-OCH_2O-$) (*J* [Hz]: 2′, 6′ = 2; 5′, 6′ = 5, 6 = 8; 7′, 8′ = 6; 7, 8 = 4.5; 8′, 8 = 9; 8, 9_1 = 7.5; 8, 9_2 = 4.5; 8′, $9'_1$ = 7; 8′, $9'_2$ = 4; 9_1, 9_2 = 9; $9'_1$,$9'_2$ = 9.5).

3,3′-*Dimethoxysesamin* (**2c**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1650, 1630, 1490; MS *m/z* (rel. int.): 414.131 $[M]^+$ (60) (calc. for $C_{22}H_{22}O_8$: 414.131), 383 (18), 249 (10), 233 (18), 191 (95), 179 (100), 165 (78); ^1H NMR ($CDCl_3$): δ6.85 (*d*, H-5 and H-5′), 6.50 (*d*, H-6 and H-6′), 4.99 (*d*, H-7 and H-7′), 2.93 (*ddd*, H-8 and H-8′), 4.25 (*dd*, H-9_1 and H-9_1′), 4.03 (*dd*, H-9_2 and H-9_2′), 5.92 (ABq, $-OCH_2O-$), 4.01 (*s*, OMe) (*J* [Hz]: 5, 6 = 8; 7, 8 = 4; 8, 9_1 = 7; 8, 9_2 = 4; 9_1, 9_2 = 9; OCH_2O: 1.5); $[\alpha]_D^{24°}$ −23° ($CHCl_3$; *c* 1).

Podorugatin (**4c**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1695; MS *m/z* (rel. int.): 290.079 $[M]^+$ (9) (calc. for $C_{15}H_{14}O_6$: 290.079), 259 $[M-OMe]^+$ (11), 206 $[M-C_5H_8O]^+$ (15), 163 (100); ^1H NMR ($CDCl_3$): δ6.39 (*d*, H-3), 7.89 (*d*, H-4), 5.97 (*s*, H-8), 4.71 and 4.25 (*dd*, H-9), 4.57 (*br dd*, H-10), 5.25 and 5.12 (*br s*, H-12), 1.85 (*br s*, H-13), 3.38 (*s*, OMe) (*J* [Hz]: 3, 4 = 10, 9, 9′ = 11, 9, 10 = 3.5; 9′, 10 = 11.5); ^{13}C NMR ($CDCl_3$, C-2–C-4, C-4a, C-5–C-8, C-8a, C-9 C-13): 162.8 *s*, 116.0 *d*, 138.8 *d*, 112.2 *s*, 180.8 *s*, 90.2 *s*, 160.7 *s*, 105.4 *d*, 158.9 *s*, 63.3 *t*, 77.3 *d*, 138.7 *s*, 116.4 *t*, 18.6 *q*; OMe: 51.9 *s*.

Methyl-7α-*hydroxybisabola*-2,10-*dien*-15-*oate* (**5a**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1720 (ester); MS *m/z* (rel. int.): 266.189 $[M]^+$ (1) (calc. for $C_{16}H_{26}O_3$: 266.189), 248 $[M-H_2O]^+$ (9), 143 (35), 69 (100); ^1H NMR ($CDCl_3$): δ6.98 (*m*, H-2), 5.13 (*br t*, H-10), 1.69 (*br s*, H-12), 1.62 (*br s*, H-13), 1.14 (*s*, H-14), 3.73 (*s*, OMe) (*J* [Hz]: 9, 10 = 7).

Methyl-7,10-*epoxy*-11-*hydroxybisabol*-2-*en*-15-*oate* (**5b**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1730, 1630 (C=C–COOR); MS *m/z* (rel. int.): 267 $[M-Me]^+$ (2), 223.133 $[M-C_3H_7O]^+$ (10), (calc. for $C_{13}H_{19}O_3$: 223.133), 205 $[223-H_2O]^+$ (18), 143 (100), 59 (54); ^1H NMR ($CDCl_3$): δ2.29 (*br d*, H-1), 1.97 (*m*, H-1′), 6.98 (*br ddd*, H-2), 2.51 (*br d*, H-4), 2.18 (*m*, H-4′), 1.99 (*br d*, H-5), 1.24 (*dddd*, H-5′), 1.65 (*m*, H-6), 1.85 and 1.65 (*m*, H-8, H-9), 3.68 (*dd*, H-10), 1.21 (*s*, H-12), 1.14 (*s*, H-13), 1.11 (*s*, H-14), 3.83 (*s*, OMe) (*J* [Hz]: 1, 1′ = 19; 1, 2 = 5; 1, 2′ = 2, 4 = 2.5; 4, 4′ = 18; 4, 5′ = 5; 4′, 5 = 5, 5′ = 5′, 6 = 12.5; 9, 10 = 5.5; 9′, 10 = 10); $[\alpha]_D^{24°}$ −29° ($CHCl_3$; *c* 1).

15-(α-*furoyloxy*)-*Bisabolol* (**5c**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1725, 1630 (ester); MS *m/z* (rel. int.): 332.199 $[M]^+$ (1) (calc. for $C_{20}H_{28}O_4$: 332.199), 314 $[M-H_2O]^+$ (3), 202 $[314-RCOOH]^+$ (18), 95 $[RCO]^+$ (50), 69 (100); ^1H NMR ($CDCl_3$): δ7.19 (*dd*, H-3′), 6.51 (*dd*, H-4′), 7.58 (*dd*, H-5′), 5.82 (*m*, H-4), 5.13 (*br t*, H-10), 1.69 (*br s*, H-12), 1.63 (*br s*, H-13), 1.13 (*s*, H-14), 4.70 (*br s*, H-15) (*J* [Hz]: 3′, 4′ = 3.5; 3′, 5′ = 1; 4′, 5′ = 2; 9, 10 = 7).

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