Phytochemistry, Vol 27, No 11, pp 3545–3548, 1988
Printed in Great Britain

0031-9422/88 $3.00+0.00

SESQUITERPENOIDS FROM *COREOCARPUS ARIZONICUS*

SHIVANAND D JOLAD,* BARBARA N. TIMMERMANN, JOSEPH J. HOFFMANN, ROBERT B. BATES,† FERNANDO A. CAMOU† and JACK R COLE*

University of Arizona, Office of Arid Lands Studies, Bioresources Research Facility, 250 E Valencia Road, Tucson, AZ 85706, U.S.A., *University of Arizona, College of Pharmacy, Tucson, AZ 85721, U.S.A., †University of Arizona, Department of Chemistry, Tucson, AZ 85721, U.S.A.

(*Received in revised form* 21 *March* 1988)

Key Word Index—*Coreocarpus arizonicus*. Asteraceae; Heliantheae; Coreopsidinae, biperezone, bi-[12-(2-methylbutyroxy)-perezone], bi-(12-isovaleroxyperezone), bisabolane diols, sesquiterpenoids.

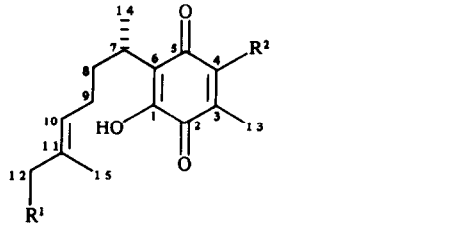
Abstract—Ten sesquiterpenoids were isolated from the methylene chloride extract of *Coreocarpus arizonicus*. Five were new, identified on the basis of spectral data as 1(*R*),4(*R*),7(*S*)- and 1(*S*),4(*S*),7(*S*)-bisabol-2-en-1,4-diols and dimers of perezone (biperezone) and its 12-(2-methylbutyroxyl) and 12-isovaleroxyl derivatives oxidatively coupled through C-4. The known sesquiterpenoids were costunolide, dihydrocostunolide, perezone, α-pipitzol and spathulenol.

INTRODUCTION

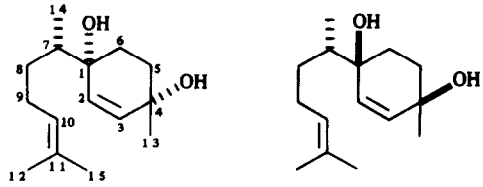
As part of our continuing phytochemical investigation of arid-adapted plants in search of biologically active compounds, we have examined the dichloromethane extract of the aerial parts of *Coreocarpus arizonicus* Gray (Asteraceae, Heliantheae; Coreopsidinae) from Arizona. This species is represented by branching suffrutescent perennials growing in rich soils along streams and on rocky slopes in southern Arizona and northern Mexico.

RESULTS AND DISCUSSION

The dichloromethane extract of the aerial parts of *C. arizonicus* gave a petrol-soluble fraction from which a polar fraction was separated by extracting with aqueous MeOH and submitted to silica gel CC. Preparative TLC of the resulting CC fractions afforded three new sesquiterpenoids (**2**–**4**), five previously reported ones [costunolide (**5**, major constituent), dihydrocostunolide (**6**), perezone (**1**), α-pipitzol (**7**) and spathulenol (**8**)] and two new bisabolane diols (**9** and **10**) The new sesquiterpenoids (**2**–**4**) and diols (**9** and **10**) were identified spectroscopically as 6,6′-bis-[2-(1,5-dimethyl-4-hexenyl)-3-hydroxy-5-methyl-*p*-benzoquinone] (biperezone, **2**), 6′,6-bis-2-[1,5-dimethyl-4-hexenyl-6-(2-methylbutyroxy)]-3-hydroxy-5-methyl-*p*-benzoquinone (**3**), 6,6′-bis-[2-(1,5-dimethyl-4-hexenyl-6-isovaleroxy)-3-hydroxy-5-methyl-*p*-benzoquinone] (**4**) and 1(*R*),4(*R*),7(*S*)- and 1(*S*),4(*S*),7(*S*)-bisabol-2-en-1,4-diols (**9**, **10**). The isomeric biperezone derivatives **3** and **4** were not separated from one another due to their identical R_f values, but their structures were evident from the NMR and mass spectra of the mixture [75% (**3**) and 25% (**4**)]. The 77:23 mixture of bisabolane diols **9** and **10** was not separated for the same reason; their structure determinations were greatly facilitated by ^{1}H NMR spectral comparison with a synthetic 1:1 mixture of their enantiomers [1]. Like earlier work, we have not been able to tell which spectrum corresponds to which structure within the pair.



	R^1	R^2	
1	—H	—H	
2	—H		(= sym dimer)
3	—O(CO)CHMeCH$_2$Me		
4	—O(CO)CH$_2$CHMe$_2$		



1(*S*),4(*S*),7(*S*) 1(*R*),4(*R*),7(*S*)

9, **10**

The IR (neat) spectrum of **2**, $[\alpha]_D^{25}$ −6° ($CHCl_3$; *c* 1.8), $C_{30}H_{38}O_6$ by HR mass spectrometry, displayed absorption bands at 3390 (OH), 1655, 1630 (conjugated ketone), 1390–1375 doublet [–C(Me)$_2$–] and 820 (>C=CH–) cm^{-1}. The ^{1}H NMR spectrum (Table 1) was similar to that of perezone (**1**) but lacked the absorption at C-4,

Table 1 ^{1}H NMR (250 MHz) chemical shifts (δ, $CDCl_3$) and coupling constants (J, in parentheses) for **1–4**

H	1	2	3*	4†
4	6.48 *q* (1.8)			
7	3.05 ~*sextet* (7.0)	3.05 ~*sextet* (7.1)		3.05 ~*sextet* (6.8)
10	5.07 ~*t* (6.7)	5.08 ~*t* (6.7)		5.43 *br t* (7.0)
12	1.64 *br s*	1.65 *br s*		4.43 ~*s*
13	2.06 *d* (1.8)	1.88 *s*		1.88 *s*
14	1.19 *d* (7.0)	1.20 *d* (7.0), 1.22 *d* (7.0)		1.21 *d* (6.9), 1.23 *d* (7.0)
15	1.53 *br s*	1.54 *br s*		1.59 *br s*
OH	6.99 *s*	7.07 *s*		7.09 *s*

*2′ 2.38 *sextet* (6.0), 3′ ~1.47 *d quintet* (14.0, 7.0), 4′ 0.90 *t* (7.4), 5′ 1.14 *d* (6.9).
†2′ 2.21 *d* (6.3), 3′ ~1.67 *d quintet* (14.0, 7.0), 4′ 0.95 *d* (6.5).

Table 2 ^{13}C NMR (22.63 MHz) chemical shifts (δ, $CDCl_3$) for **1–4**

C	1	2	3†		4‡
1	150.9	150.9	-	151.0	--
2	187.3*	184.8, 184.9*	--	184.8, 184.9*	—
3	140.5	138.3		138.3	
4	135.8	140.3	-	140.2	
5	184.3*	183.2*	--	183.2*	--
6	124.5	124.8		124.5	-
7	29.3	29.5, 29.6	—	29.5	
8	34.1	34.1, 34.2	--	33.5, 33.6	--
9	26.7	26.6	--	26.7	-
10	124.4	124.2	129.1	--	129.3
11	131.4	131.5	130.3		130.2
12	25.7	25.7	- -	69.8	
13	14.7	12.9, 13.0	-	12.9, 13.0	
14	18.2	18.1, 18.2	-	18.1	
15	17.6	17.6	-	13.8	

*May be reversed within columns
†1′ 176.6, 2′ 41.1, 3′ 26.3, 4′ 11.6, 5′ 16.6.
‡1′ 173.1, 2′ 43.4, 3′ 25.7, 4′ 22.4.

suggesting the possibility that it was an oxidative dimer through C-4. The ^{13}C NMR spectrum (Table 2) supported this view in that the off-resonance doublet for C-4 in **1** was replaced by an off-resonance singlet. A doubling of five of the peaks in the ^{1}H spectrum and one peak in the ^{13}C spectrum for some of the nuclei near the centre of this dimer molecule was consistent with the presence of equal amounts of both rotamers about the central bond, with a high energy barrier between them.

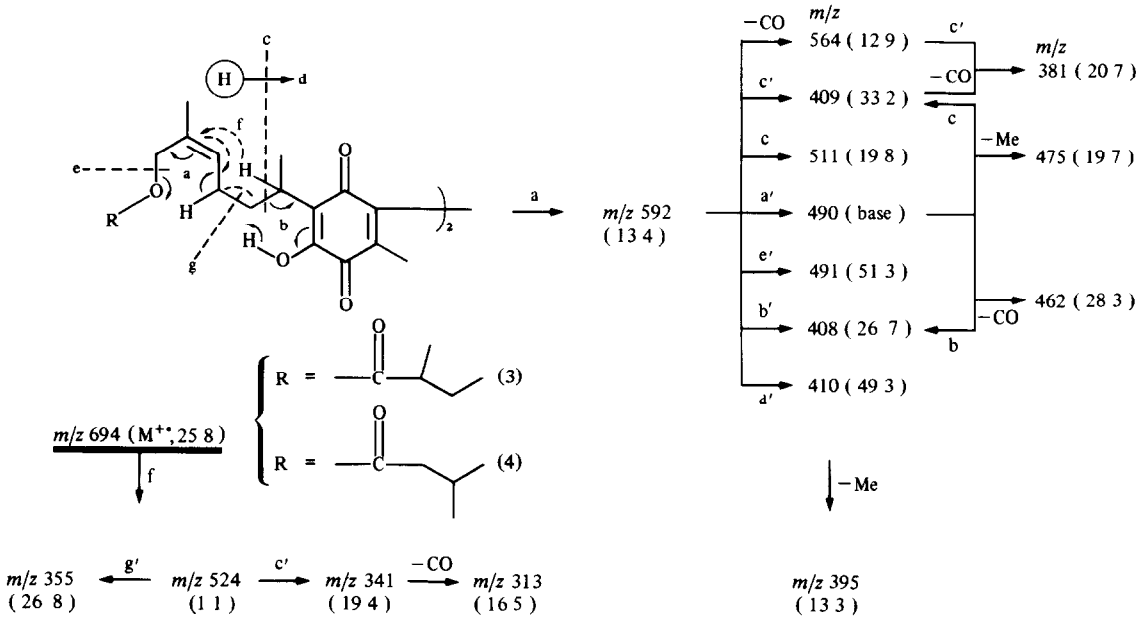
The mass spectrum gave strong confirmation for structure **2**. In the lower mass region of the EI mass spectrum, perezone fragments (*m/z* 205, 191, 177, 167, 166, 149, 109, 69, 55) were seen, but in the upper mass region the two most abundant peaks, at *m/z* 412 and 330, were associated with the loss of 82 and 2 × 82 mass units from the $[M]^+$ (*m/z* 494) from the dimer **2** *via* six-membered cyclic transition states. Additional peaks at *m/z* 383 and 301, corresponding to the successive loss of side chains at C-6 and C-6′ from the $[M]^+$ and *m/z* 412, respectively, and peaks associated with the loss of carbon monoxide from the $[M]^+$ (*m/z* 466), 412 (*m/z* 384), 383 (*m/z* 355), and 301 (*m/z* 273) further supported this view. A group of unexpected peaks at *m/z* 495–498 (above the $[M]^+$) appears to be due to the addition of 1 to 4 extra hydrogens to the four carbonyl functions of the diquinone $[M]^+$ during heating of the sample for volatilization in the ion source (e.g. the *m/z* 498 peak is probably the $[M]^+$ of the bis-hydroquinone from the reduction of **2**). Fragments of appreciable intensity, at *m/z* 415 and 413, derived from the hydroquinone species (*m/z* 498 and 496, respectively) *via* β-cleavage were also present. The absolute configuration depicted for **2** is based on it having a negative optical rotation, like perezone (**1**), and its co-occurrence with perezone (**1**) in this plant.

The structures of **3** and **4** were apparent from comparison of the ^{1}H (Table 1) and ^{13}C (Table 2) NMR

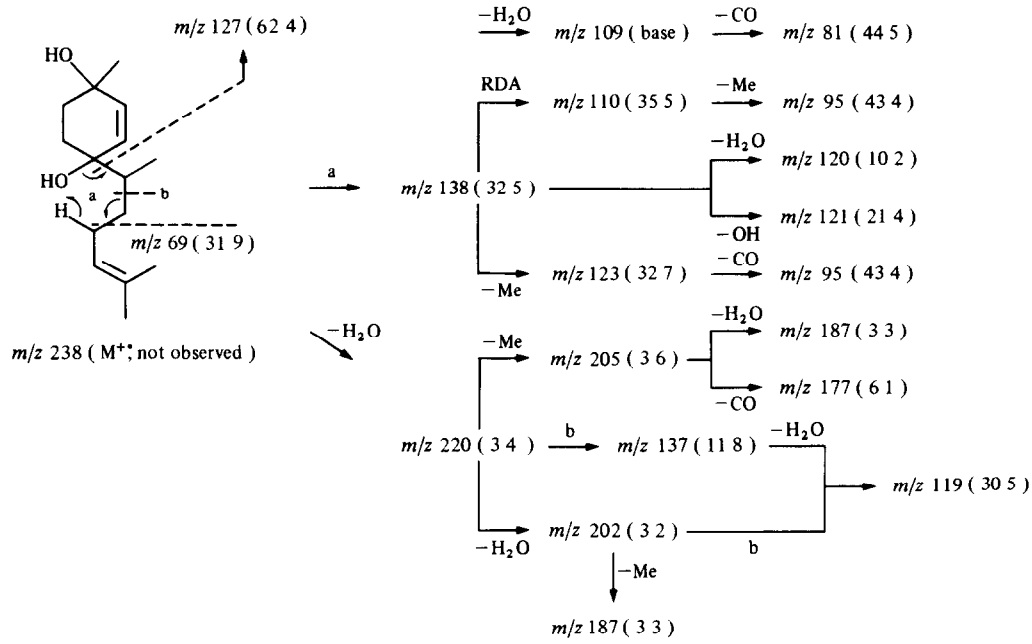
spectra of their 3:1 mixture with those of **2** and 2-methylbutyrate and isovalerate esters of other primary alcohols [2]. The configuration of the double bond follows from the ^{13}C NMR data of monoterpenes (compound number 23 in ref [3]). Again, most of the same doublings of peaks were observed as for **2**. The configurations within the 2-methylbutyrate groups were not determined.

The presence of two saturated 5-carbon acyl groups in **3** and **4** produced peaks in the EI mass spectrum at *m/z* 592 and 490 (base), corresponding to the loss of one (102 mass units) and two (2 × 102 mass units) mol of 5-carbon acid from the $[M]^+$ (*m/z* 694). Further breakdown of these two ions furnished fragments of appreciable intensity as shown in Scheme 1. The mixture of **3** and **4**, like **2**, showed peaks [*m/z* 695 (12.1%) and *m/z* 696 (3.3%)] above the $[M]^+$ [*m/z* 694 (25.8%)] The IR (CCl_4) spectrum of the mixture of **3** and **4** showed bands similar to those of biperezone (**2**), the most striking difference being the appearance of a strong band at 1735 cm^{-1} in **3**–**4** indicating the presence of an ester carbonyl function

The IR (neat) spectrum of mixture of **9** and **10** showed bands for the presence of OH (3380, 1120 cm^{-1}), >C =CH– (3020, 1668, 825 cm^{-1}) and Me (1375 cm^{-1}) groups The EI mass spectrum of **9** and **10** showed no $[M]^+$ (*m/z* 238) but exhibited minor but diagnostic peaks



Scheme 1 The diagnostic fragments in the EIMS of the mixture of **3** and **4** (relative intensities in parentheses).



Scheme 2 Diagnostic fragments in the EIMS of the mixture of **9** and **10** (relative intensities in parentheses)

Table 3

Compound	CC Fr	No of PLC	Solvent/no of developments
1	2	—	Crystallized out
2	3	2	A/1, B/1
3+4	38–39	1	C/2
5	13–23	—	Crystallized out
6	24–29	1	C/1
7	5–6	2	D/multiple
8	3	2	A/1, B/1
9+10	45	2	E/1, F/1, E/1

A petrol–Et_2O (4 1), B petrol–Et_2O (5 1), C petrol–Et_2O (2 1) D petrol–Et_2O (7 1), E. petrol–Et_2O (1 3), F petrol–Et_2O (1 2)

at *m/z* 220 $[M-H_2O]^+$, 205 [*m/z* 220–Me]$^+$, 202 $[M-2H_2O]^+$, 187 [*m/z* 202–Me]$^+$ and very characteristic peaks of appreciable intensity in the lower-mass range as depicted in Scheme 2. The ^1H NMR spectrum showed these substances to have the same constitutions as a 1.1 mix of diols prepared synthetically [1] The absolute configurations of the natural products **9** and **10**, which we assign to have the 7(*S*) configuration on the basis of a common precursor in *C. arizonicus* with (−)-perezone (**1**), are apparently opposite to those of the synthetic substances In the **9, 10** pair, the 14-Me group in the minor component **10** absorbs *up*field (i e it spends more time above the ring double bond) in the ^1H NMR and *down*field (probably indicating that it spends more time *anti* to the 1−OH) in the ^{13}C NMR, but it is not clear which rotamers about the 1,7 bond are favoured and we do not think it safe to assign which structure goes with **9** and which with **10**

There may be chemosystematic significance in the occurrence of sesquiterpene quinones in the subtribe Coreopsidinae since quinones have been reported in species of the related genera *Bidens* and *Coreopsis* [4–6].

EXPERIMENTAL

Plant material was collected in the Coyote Mountains, Pima County, Arizona, in June 1987 A voucher specimen (SPM 4262) has been deposited in the Herbarium at the University of Arizona, Tucson All plant material was air-dried, ground to 3 mm particle size and stored at 5° prior to extn.

Extraction and isolation The solvent-free CH_2Cl_2 extract (21 g) of the aerial parts (1,240 g, cold percolation) was triturated with petrol (600 ml), stirred (2 hr), left at 5° overnight and filtered The petrol-sol filtrate was extracted with 20% aq MeOH (200 ml × 5) and the combined aq. MeOH exts after evapn of solvent gave a residue (9 7 g) which was combined with subsequent batches to give a total of 42 g Silica gel CC (1500 g packed in petrol) eluting with petrol containing increasing concns of Et_2O, Et_2O (100%) and CH_2Cl_2–MeOH (1 1), gave 47 fractions [1800 (1), 250 (2–33), 500 (34–44) and 2000 (45–47) ml], combined on the basis of TLC composition and submitted to prep TLC The isolation of **1–10**, performed qualitatively, is summarized in Table 3

1(*R*),4(*R*),7(*S*)- and 1(*S*),4(*S*),7(*S*)- Bisabol-2-en-1,4-diols (**9** and **10**) The IR (text), $[\alpha]_D^{25}$ +12 5° ($CHCl_3$, *c* 1 6), ^1H NMR [(250 MHz, $CDCl_3$-TMS, δ) **9**, 0 95 *d* (6 8 Hz, H-14), 1 23 *s* (H-13), 1 60 *s* (H-12), 1 68 *s* (H-15), 5 07 *t* (7 2 Hz, H-10), 5 47 *d* and 5 70 *d* (10 2 Hz, H-2 and H-3), **10**, same except 0 86 *d* (6 8 Hz, H-14), 5 10 *t* (7 2 Hz, H-10), 5 49 *d* and 5 69 *d* (10 1 Hz, H-2 and H-3)], ^{13}C NMR [(22 6 MHz, $CDCl_3$-TMS, δ, C 1–15) **9**, 72 0, 132 2, 137 3, 69 4, 34 3, 28 7, 42 1, 32 0, 26 3, 124 4, 131 6, 17 6, 26 7, 13 0, 25 7, **10**, 72 0, 132 0, 136 9, 69 4, 34 5, 28 6, 42 1, 30 2, 26 3, 124 5, 131 5, 17 6, 26 7, 14 4, 25 7] and mass (Scheme 2) spectra were in accord with the structures shown

Acknowledgements—We thank Dr Steven P McLaughlin for plant collection and identification and Mr Peter Baker for MS data This investigation was supported in part by the National Science Foundation (Grant No 8304771) and the Arizona Disease Control Research Commission (Grant No 8277-000000-1-1-7C-7493) whom we gratefully acknowledge

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