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DITERPENES DERIVED FROM CLERODANES FROM *PULICARIA ANGUSTIFOLIA*

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Key Word Index—*Pulicaria angustifolia*; Compositae; diterpenes; clerodane derivatives; seco-clerodanes; conyscabric acid derivative.

Abstract—The investigation of *Pulicaria angustifolia* afforded, in addition to known triterpenes and caryophyllene epoxide, four methyl esters of diterpenes, all derived from clerodane. Three of them are derivatives of seco-nidoresedic acid. The structures were elucidated by spectroscopic methods.

So far, from the genus *Pulicaria* (tribe Inuleae, subtribe Inulinae) [1] widespread compounds like flavones [2] and acetylenes [3] have been isolated. From a few species more unusual caryophyllene derivatives are reported [4] and only one species gives sesquiterpene lactones [5], while others [4, 6] contain thymol derivatives and a clerodane was isolated from *P. gnaphaloides* [7]. We have now studied *P. angustifolia* DC, a species from Rajasthan, India. The separation of the extract of the whole air-dried plants afforded in addition to widespread triterpenes (Experimental) four diterpenes, the seco-nidoresedic acid derivatives **1–3** and methyl-5α-hydroxyconyscabroate (**4**).

The molecular formula of the methyl ester of **1** was $C_{21}H_{28}O_4$ while the IR spectrum indicated the presence of an ester and a lactone group (1765 and 1720 cm^{-1}). The ^{1}H NMR spectrum (Table 1) was in part similar to that of methyl seconidoresedoate [8].† However, the signals of the β-substituted furan were replaced by a double triplet at δ4.73 (2H) and a triplet of triplet at δ7.09 (1H), which are typical for the lactone moiety in **1**.

The ^{1}H NMR spectral data of **2a** (Table 1), which had the same molecular formula as **1**, was also similar to that of methyl seco-nidoresedoate. This time the furan signals were replaced by a doublet at δ4.76 (2H) and a triplet of triplets at δ5.84 indicating that the isomeric 15-acid lactone was present, as followed from the chemical shift of the olefinic signal (H-14).

The molecular formula of **3a** ($C_{21}H_{28}O_5$) indicated that this compound differed from **1a** and **2a** by an additional oxygen. The ^{1}H NMR spectrum of **3a** (Table 1) indicated that this oxygen had to be placed at C-14 and C-15. A triplet at δ3.87 was coupled with a double doublet at δ5.60 and with a four-fold doublet at δ2.77. The chemical shifts and the couplings required a 14,15-epoxide. The remaining signals, except those for H-12, were again very similar to those of **1a** and **2a**. However, the methyl signals for H-17 and H-20 were doubled, indicating the presence of two epimeric epoxides. While in deuteriochloroform nearly all signals were identical for both epimers, in deuteriobenzene many signals were doubled. All signals could be assigned by spin decoupling. A similar pair of epimeric lactones with an epoxide group was isolated from *Conyza scabrida* [8].† Accordingly, the

Table 1. ^{1}H NMR spectral data of **1a–3a** (400 MHz, $CDCl_3$, TMS as internal standard)

H	**1a**	**2a**	**3a** (C_6D_6)
1	5.40 *dddd*	5.25 *dddd*	5.31 and 5.18 *dddd*
2	5.93 *ddd*	5.94 *ddd*	5.70 *d* (*br*)
3	7.26 *dd* (*br*)	7.26 *dd* (*br*)	7.36 and 7.34 *dd* (*br*)
6α	2.61 *ddddd*	2.60 *dddd*	2.65 *ddddd**
6β	2.06 *ddd*	2.06 *ddd*	2.09 *ddd**
7α	1.55 *m*	1.55 *m*	1.57 *m**
7β	0.81 *m*	0.81 *m*	0.85 *m**
8	1.36 *ddq*	1.35 *ddq*	1.37 *ddq**
10α	2.25 *dd*	2.27 *dd*	2.23 *dd**
10β	1.78 *dddd*	1.70 *dddd*	1.72 *dddd**
11	1.50 *m*	1.50 *m*	1.50 *m**
12	2.25 *m*	2.25 *m*	1.87 *m** 1.72 *m**
13	—	—	2.91 *m*
14	7.09 *tt*	5.84 *tt*	2.69 and 2.64 *t*
15	4.73 *dt*	—	4.63 and 4.61 *d*
16	—	4.76 *d*	—
17	0.72 *d*	0.75 *d*	0.71 and 0.68 *d*
18	5.02 *dd*	5.07 *dd*	5.04 *s* (*br*)
19′	4.79 *s* (*br*)	4.84 *s* (*br*)	4.84 and 4.82 *s* (*br*)
20	0.67 *s*	0.68 *s*	0.45 and 0.44 *s*
OMe	3.77 *s*	3.77 *s*	3.40 and 3.39 *s*

*In $CDCl_3$.

J (Hz): 1, 2 = 11; 1, 3 = 4, 1, 10α = 13, 1, 10β = 2; 2, 3 = 2.5, 2, 10 = 1.5, 6α, 6β = 13.5; 6α, 7α = 6α, 7β = 6α, 8α = 2; 6β, 19 = 2; 7α, 7β = 14; 7α, 8 = 10; 7β, 8 = 3, 8, 17 = 7; 10α, 10β = 13; compound **1a**. 12, 14 = 14, 15 ~ 1.5; compound **2a**: 12, 14 = 14, 16 = 1.5, compound **3a**: 13, 14 = 2, 14, 15 = 2.5

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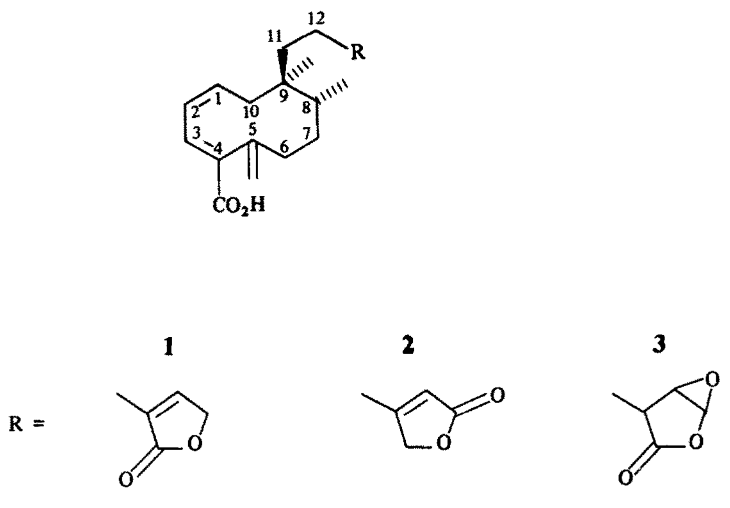
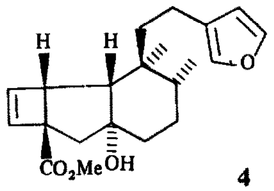
†N.B. Stereochemistry wrong at C-9 in refs [9] and [10].



1a – 3a are the corresponding methyl esters



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signals of H-13 to H-15 were nearly the same.

All the spectral data of the last diterpene (**4**) were identical to those of a methyl ester of an acid which was also obtained from the *Conyza* species [11].

EXPERIMENTAL

Air-dried whole plants (500 g) (collected from Ramgarh, Rajasthan, India, voucher deposited at RUBL Herbarium, Jaipur) were extracted with Et_2O–petrol (1:2) and the resulting extract was worked up in the usual way [12]. CC fractions were as follows: 1 (petrol), 2 (Et_2O–petrol, 1:4), 3 (Et_2O–petrol, 1:1) and 4 (Et_2O). TLC (Et_2O–petrol, 1.10) of fraction 1 gave 5 mg taraxasteryl acetate and 5 mg lupeyl acetate. TLC of fraction 2 (Et_2O–petrol, 1:10; several developments) gave 2 mg caryophyllene epoxide, 5 mg benzoic acid, 7 mg lupeol, 10 mg taraxasteryl acetate and 3 mg **4** (^{1}H NMR, IR and MS identical to those of authentic material [8]). TLC of fraction 3 (C_6H_6–CH_2Cl_2–Et_2O, 4 5:4.5:1) gave 20 mg stigmasterol, 15 mg sitosterol and 1 5 mg **3** (R_f 0.45). TLC of fraction 4 (C_6H_6–CH_2Cl_2–Et_2O, 1:1:1) afforded after addition of CH_2N_2 2 mg **1** (R_f 0.5) and 2.3 mg **2** (R_f 0.4). Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material. Compounds **1a**–**3a** and **4** showed no impurities in the ^{1}H NMR spectra and were homogeneous by TLC in different solvent mixtures

Compound **1a**. Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1765 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 344.199 $[M]^+$ (6) (calc. for $C_{21}H_{28}O_4$: 344.199), 314 $[M-CH_2O]^+$ (26), 312 $[M-MeOH]^+$ (32), 297 $[312-Me]^+$ (10), 91 (80), 55 (100).

Compound **2a**. Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1790 (γ-lactone), 1725 (C=CCO$_2$R); MS *m/z* (rel. int.): 344.199 $[M]^+$ (6) (calc. for $C_{21}H_{28}O_4$: 344.199), 313 $[M-OMe]^+$ (6), 312 $[M-MeOH]^+$ (9), 91 (65), 55 (100).

Compound **3a**. Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1810 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 360.194 $[M]^+$ (3) (calc. for $C_{21}H_{28}O_5$: 360.194), 345 $[M-Me]^+$ (1), 329 $[M-CHO]^+$ (5), 328 $[M-MeOH]^+$ (2), 299 $[328-CHO]^+$ (6), 91 (72), 55 (100).

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ACUTIFLORIC ACID: A DITERPENE DIMER FROM THE STEM BARK OF *XYLOPIA ACUTIFLORA**

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Key Word Index—*Xylopia acutiflora*; Annonaceae; diterpene dimer; acutifloric acid; kaurane and labdane precursors

Abstract—In addition to four kaurane and kaurene diterpenes, the stem bark of *Xylopia acutiflora* yielded a dimeric diterpene derived via Diels–Alder condensation of kaurene and labdane monomers. The structure of the dimer, which has been given the trivial name acutifloric acid, was assigned on the basis of detailed spectroscopic analysis.

INTRODUCTION

Xylopia acutiflora (Dunal) A. Rich. is a shrub or small tree found in the lowland forests of west Africa [2]. In a previous paper [3] we reported the isolation of four diterpenes from a sample of stem bark collected in the Korup National Park, Cameroun; namely (−)-kauran-16-ol, 7β-acetoxy-(−)-kaur-16-en-19-oic acid, 15-oxo-(−)-kaur-16-en-19-oic acid and 16α-hydroxy-(−)-kauran-19-oic acid. During the extraction of the above, a fifth compound was obtained. In this paper we report on the identification of this compound as a novel diterpene dimer to which we have assigned the trivial name acutifloric acid.

RESULTS AND DISCUSSION

Acutifloric acid separated from the concentrated petrol extract in a yield of 1.1% and was recrystallized from petrol as fine needles, mp 222–227°, $[\alpha]_D$ −127° (*c* 1.0; $CHCl_3$). Accurate mass measurement indicated the empirical formula $C_{40}H_{60}O_3$ (Found: $[M]^+$ at *m/z* 588.4517; required: 588.4542) and the IR spectrum (KCl disc) showed bands for an exocyclic double bond (3080, 1640 cm^{-1}), a carbonyl (1730 cm^{-1}) and a carboxylic acid (1700 cm^{-1}). The presence of the carbonyl was confirmed by reduction to the corresponding alcohol with lithium aluminium hydride (gum: Found: $[M]^+$ at *m/z* 590.4698; $C_{40}H_{62}O_3$ requires: 590.4699; IR ν_{max} cm^{-1}: 3400, 3070, 1700) and that of the carboxylic acid by formation of the methyl ester using ethereal diazomethane (mp 137–140°, Found: $[M]^+$ at *m/z* 602.4732; $C_{41}H_{62}O_3$ requires: 602.4699).

The ^1H NMR spectrum (360 MHz, $CDCl_3$) showed the presence of five methyl groups as singlets at δ0.68, 0.80, 0.87, 1.02 and 1.26, confirmed the exocyclic double bond by two singlets (1H each) resonating at 4.50 and 4.82, and revealed an olefinic proton as a singlet at 5.26. The ^{13}C NMR spectrum (90.56 MHz, $CDCl_3$) showed six downfield resonances: at δ106.1 (*t*) and 148.5 (*s*) for the exocyclic double bond, at 117.5 (*d*) and 138.0 (*s*) for a trisubstituted double bond, and at 183.8 and 227.1 (both *s*) for carboxylic acid and carbonyl, respectively. The above data showed acutifloric acid to have four centres of unsaturation, thus requiring a seven-ring structure for the dimer.

The ^1H NMR resonances for methyl groups at δ0.68, 0.80 and 0.87 and those for the exocyclic double bond were in close accord with published data for diterpenes with a labda-8-en skeleton [4, 5], the highly shielded 0.68 resonance being attributable to an α (axial) C-10 methyl. The presence of this system was also indicated by the electron impact mass spectrum, which gave a base peak at *m/z* 204 $[C_{15}H_{24}]^+$, which can be assigned to the bicyclic

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*Part 13 in the Series "Chemical Studies in the Annonaceae". For Part 12 see ref. [1].