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CARYOPHYLLENE DERIVATIVES AND A HYDROXYISOCOMENE FROM *PULICARIA DYSENTERICA**

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Key Word Index—*Pulicaria dysenterica*; Compositae; sesquiterpenes; caryophyllene derivatives; sesquiterpene esterified with a sesquiterpenic acid; hydroxyisocomene.

Abstract—The investigation of the aerial parts of *Pulicaria dysenterica* afforded, in addition to known compounds, nine new caryophyllene derivatives with oxygen functions at C-7, C-13 and either C-14 or C-5. One of the keto diols was also present as an ester of a caryophyllenic acid. The roots afforded a new derivative of isocomene together with its precursor. The structures were elucidated by highfield ^{1}H NMR spectroscopy and by some chemical transformations.

INTRODUCTION

Pulicaria dysenterica Gaertn. (Compositae, tribe Inuleae) has been investigated previously. In addition to tridecapentaynene and tridecа-1,11-diene-3,5,7,9-tetrayne only thymol derivatives [1] and flavones [2] were isolated. A re-investigation gave nine new caryophyllene derivatives, a hydroxyisocomene and several known compounds.

RESULTS AND DISCUSSION

The aerial parts of *P. dysenterica* afforded tridecapentaynene, caryophyllene, phytol, geranyl isobutyrate, and the thymol derivatives **15** [3] and **16** [4], while the polar fractions gave in addition to stigmasterol a complex mixture of sesquiterpenes, which were difficult to separate. Finally, nine caryophyllene derivatives were obtained: the 5,6-*trans* compounds **1**–**4**, the 5,6-*cis* derivatives **5**–**7** and the isomer of **2**, the hydroxyketone **12** together with the ester **13**. As both **1** and **2** on acetylation afforded **3**, they were isomeric hydroxyacetates. The nature of the carbon skeleton was deduced from the ^{1}H NMR spectra (Table 1). Spin decoupling allowed the assignment of all signals, though some of the signals of the allylic protons were overlapping multiplets. However, the presence of caryophyllene derivatives clearly followed from the signals of H-1, H-9 and H-10. Irradiation of the H-1 signal collapsed the double doublets of H-9 and H-10 to doublets, while spin decoupling of H-9 showed that the double doublet at δ 2.97 was that of H-8β. The latter was coupled with a doublet at δ 2.54. As the IR spectrum showed the presence of a conjugated keto group, the signals obviously indicated a keto group at C-7, which was further supported by the downfield olefinic double doublet at δ 6.51 in the spectrum of the diacetate **3**. The chemical shift indicated a *trans* 5,6-double bond. As only one methyl signal in addition to those of the acetate methyls was visible in the spectra of **1**–**3**, the two methyl groups were oxygenated. The corresponding signals in the spectra of **1** and **2** together with those already discussed clearly showed that **1** was a 14-acetoxy-13-hydroxy-carophyllen-7-one, while **2** was the corresponding isomeric hydroxy acetate. The stereochemistry at C-11 was supported by the unchanged chemical shift of H-8β in the spectra of **1** and **3**. Consideration of models would require deshielding H-8β, if the oxygen function was at C-12. In the spectra of **5**–**7** the chemical shift of the H-14 signal was changed and the signal of H-5 was shifted drastically upfield. Models showed that this upfield shift could be explained by a change in configuration at C-9 or by a *cis*-5,6-double bond. The latter was more likely as the IR band of the conjugated keto group was not influenced. This would be the case, if a non-planar conformation was present, as expected for a 1-epi compound. The presence of a 5,6-*cis* double bond was established by oxidation of **5**, to form the isomeric aldehydes **9** and **10**. The spectrum of **9** (Table 1) clearly showed that only a *cis*-configuration was in agreement with the observed chemical shifts of H-5 and H-14. Acetylation of **5**, **6** and **7** afforded the diacetate **8**. Consequently, **5**–**7** had the same carbon skeleton. Furthermore, **6** was transformed to the aldehyde **11**. The spectra of **10** and **11** supported the proposed position of oxygen function at C-13, as again models showed that an aldehyde group at C-12 should cause deshielding of H-8β. Though the conformations of the different isomers were slightly different, as deduced from the values of $J_{8,9}$, identical stereochemistry at C-11 in both series was very likely. The ^{1}H NMR spectrum of **4** (Table 1) clearly showed that the acetate group was at C-14, while that of **12** (Table 2) indicated an isomeric situation at C-5 and C-14. Additional downfield signals at δ 5.81 and 5.78 showed the presence of a second exomethylene group, while a broadened three-fold doublet at 4.49 indicated an allylic hydroxyl group. The latter was coupled with one of the vinylic protons, a hydroxy proton (δ 2.48, *d*) and two further signals at δ 2.25 and 2.41. The other signals were similar to those of **5**, indicating the same stereochemistry at C-1, C-9 and C-11. The stereochemistry at C-5 was proposed from the couplings observed and from the chemical shifts of H-14 as well as from the allylic coupling $J_{5,14}$.

*Part 371 in the series "Naturally Occurring Terpene Derivatives". For Part 370 see Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 2389.

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

	1	**2**	**3**	**4**(C_6D_6)	**5**	**6**	**7**	**8**	**9**	**9**(C_6D_6)	**10**	**11**
H-1	2.50 *ddd*	2.45 *ddd*	2.45 *ddd*	1.97 *ddd*	2.62 *ddd*	2.55 *ddd*	2.17 *ddd*	2.51 *ddd*	2.50 *m*	2.24 *ddd*	2.74 *ddd*	2.71 *ddd*
H-3α	2.6 *m*	2.57 *m*	2.57 *m*	2.36 *m*	2.38 *m*	2.37 *m*	2.05 *m*	2.40 *m*	2.50 *m*	2.05 *m*	2.38 *m*	2.41 *m*
H-3β				1.77 *m*								
H-4α	2.6 *m*	2.67 *dd*	2.65 *dd*	2.31 *ddd*	2.58 *m*	2.46 *m*	1.72 *m*	2.45 *m*	2.62 *m*	2.66 *ddd*	2.56 *m*	2.41 *m*
H-4β	2.25 *ddd* (*br*)	2.27 *ddd* (*br*)	2.26 *ddd* (*br*)	2.03 *ddd*	2.24 *ddd* (*br*)	2.20 *ddd* (*br*)	2.05 *m*	2.22 *ddd* (*br*)	2.36 *m*	1.98 *m*		2.25 *dd* (*br*)
H-5	6.54 *dd*	6.37 *dd*	6.51 *dd*	5.88 *dd*	5.91 *dd*	5.84 *dd*	5.43 *dd*	5.83 *dd*	6.63 *dd*	5.75 *dd*	5.88 *dd*	5.86 *dd*
H-8α	2.57 *d*	2.53 *d*	2.54 *d*	2.38 *dd*	2.83 *dd*	2.82 *dd*	2.57 *dd*	2.77 *d*	2.88 *d*	2.93 *dd*	2.67 *dd*	2.67 *dd*
H-8β	2.98 *dd*	2.96 *dd*	2.97 *dd*	2.56 *dd*	2.97 *dd*	2.91 *dd*	2.80 *dd*	2.83 *dd*		2.85 *dd*	2.90 *dd*	2.99 *dd*
H-9	1.86 *dd*	1.88 *dd*	1.86 *dd*	1.69 *m*	1.93 *ddd*	2.03 *ddd*	2.05 *m*	2.05 *m*	2.03 *m*	1.84 *ddd*		2.41 *m*
H-10α	2.03 *dd*	2.03 *dd*	2.02 *dd*		1.90 *m*	1.94 *dd*	1.72 *m*	1.88 *d*	2.03 *m*	1.88 *dd*		2.34 *dd*
H-10β	1.57 *dd*	1.58 *dd*	1.58 *dd*	1.49 *dd*	1.80 *m*	1.85 *dd*			1.78 *dd*	1.62 *dd*		1.99 *dd*
H-12	1.06 *s*	1.12 *s*	1.12 *s*	0.88 *s*	1.07 *s*	1.08 *s*	0.97 *s*	1.12 *s*	1.09 *s*	0.82 *s*	1.27 *s*	1.26 *s*
H-13	3.65 *d* (*br*)	4.08 ABq	4.11 *d*	0.83 *s*	3.67 *d*	3.67 *d* (*br*)	4.08 *d*	4.12 *d*	3.62 *s* (*br*)	3.07 *s* (*br*)	9.85 *s*	9.85 *s*
H-13′	3.59 *d* (*br*)		4.07 *d*		3.62 *d*	3.62 *d* (*br*)	3.95 *d*	4.07 *d*				
H-14	4.75 *d*	4.25 *dd*	4.74 *d*	4.91 *d*	4.15 *s* (*br*)	4.73 *ddd*	4.19 *dd* (*br*)	4.73 *ddd*	9.42 *s*	9.11 *s*	4.13 *d*	4.73 *ddd*
H-14′	4.65 *d* (*br*)	4.10 *dd*	4.64 *d* (*br*)	4.87 *d*		4.53 *d*	3.99 *d* (*br*)	4.52 *d*			4.07 *d*	4.49 *d*
H-15	5.02 *s* (*br*)	5.06 *s* (*br*)	5.01 *s* (*br*)	4.89 *s* (*br*)	4.93 *s* (*br*)	4.95 *s* (*br*)	4.89 *s* (*br*)	4.95 *s* (*br*)	5.00 *s* (*br*)	4.90 *s* (*br*)	4.95 *s* (*br*)	4.97 *s* (*br*)
H-15′	4.93 *s* (*br*)	4.99 *s* (*br*)	4.94 *s* (*br*)	4.77 *s* (*br*)	4.87 *s* (*br*)	4.88 *s* (*br*)	4.82 *s* (*br*)	4.89 *s* (*br*)	4.93 *s* (*br*)	4.73 *s* (*br*)	4.93 *s* (*br*)	4.95 *s* (*br*)
OAc	2.00 *s*	2.10 *s*	2.10 *s*	1.67 *s*		2.00 *s*	1.72 *s*	2.09 *s*		—	2.10 *s*	2.01 *s*
			1.99 *s*	—	—	—	—	2.01 *s*	—	—	—	—
OH		2.27 *d* (*br*)					1.72 *m*					

J (Hz): compounds **1**–**3**: 1,9 = 9.5 (compound **2**: 12.5); 1,10α = 10; 1,10β = 9; 3α,3β = 12; 3α,4α = 4; 3α,4β = 10; 3β,4α = 4; 4α,4β = 12; 4α,5 = 5.5 (compound **2**: 4); 4β,5 = 10 (compound **2**: 12); 8α,8β = 15; 8β,9 = 12; 10α,10β = 11.5; 13,13′ = 11; 14,14′ = 12 (compound **2**: 14,OH = 9; 14′,OH = 2.5); (compound **4**: 8α,9 = 2; 8β,9 = 11.5; 8α,8β = 15); compounds **5**–**11**: 1,9 = 1,10α = 1,10β = 9.5; 10α,10β ~ 11; 4α,5 = 11.5; 4β,5 = 5; 4,14 = 5,14 = 1; 8α,8β = 17; 8α,9 = 2; 8β,9 = 10; (compound **8**: 6.5); 13,13′ = 11; 14,14′ = 12 (compound **9**: 4α,5 = 10.5; 4β,5 = 5.5; 8,9 = 8 (in C_6D_6 8α,9 = 4; 8β,9 = 12; 8α,8β = 16); compounds **10** and **11**: 4α,5 = 12; 4β,5 = 5; 8α,9 = 1.5; 8β,9 = 10.5; 8α,8β = 18.

Table 2. ^{1}H NMR spectral data of compounds **12** and **14** (400 MHz, TMS as internal standard)

	12($CDCl_3$)		**14**(C_6D_6)	
H-1	2.55 *ddd*	2.44 *ddd*	H-1′	1.84 *ddd* (*br*)
H-3α	2.15 *m*	1.89 *m*	H-2	2.33 *d* (*br*)
H-3β	2.05 *m*	2.12 *m*	H-3α′	1.35 *m*
H-4	1.84 *m*	1.89 *m*	H-3β′	2.23 *ddd*
H-5	4.49 *ddd*	5.96 *t* (*br*)	H-4α′	2.63 *dddd*
H-8α	2.75 *dd*	2.77 *dd*	H-4β′	2.01 *m*
H-8β	3.03 *dd*	2.50 *dd*	H-5	5.91 *dd* (*br*)
H-9	2.15 *dd*	2.01 *ddd*	H-8α′	2.70 *dd*
H-10α	2.04 *dd*	1.82 *dd*	H-8β′	2.44 *d* (*br*)
H-10β	1.74 *dd*	1.62 *dd*	H-9′	2.82 *dd* (*br*)
H-12	1.11 *s*	0.99 *s*	H-10α′	1.82 *dd*
H-13	3.69 *d* (*br*)	4.02 *d*	H-10β′	1.56 *dd*
H-13′	3.60 *d* (*br*)	3.96 *d*	H-12′	0.90 *s*
H-14	5.81 *d*	5.53 *d*	H-13′	0.86 *s*
H-14′	5.78 *s*	5.49 *s*	H-14′	1.91 *s* (*br*)
H-15	4.85 *s* (*br*)	4.79 *s* (*br*)		
H-15′	4.81 *s* (*br*)	4.76 *s* (*br*)		
OAc	—	1.72 *s*		

J (Hz): compounds **12** and **14**: 1,9 = 1,10α = 1,10β = 9.5; 4,5 = 7.5; 4′,5 = 4.5; (**12**: 5,OH = 7); 5,14 = 1.5; 8α,9 = 6; 8β,9 = 8α,8β = 12; 10α,10β = 11.5; 13,13′ = 10.5; compound **14**: 1′,2′ ~ 1; 1′,9′ = 10; 1′,10α′ = 1′,10β′ = 9; 2′,3α′ ~ 1,3′,3′ = 14; 2′,3β′ = 4; 3α′,4α′ = 4; 3β′,4α′ = 4α′,4β′ = 4α,5 = 12; 4β′,5 = 3; 8α′8β′ = 14; 8α′9′ = 11.5; 8β′,9′ ~ 1.

13 could only be separated from **7** after acetylation. The molecular formula of the acetate **14** ($C_{32}H_{44}O_6$) indicated that a sesquiterpene was present, which in addition to the acetate group must bear a sesquiterpenic acid as a further ester residue. The ^{1}H NMR data (Table 2) clearly showed that the diol part was identical with **12**. From the signals of the crude mixture of **7** and **13** it could be deduced that a free 13-hydroxy group was present. Therefore, the sesquiterpenic acid part was at C-5. The nature of the latter could be established by careful spin decoupling in deuteriobenzene. Irradiation of the H-8′ signals led to the identification of H-9′, which was further coupled with a threefold doublet at δ 1.84. Irradiation of the latter signal collapsed the double doublet at δ 1.82 and 1.56 to doublets and sharpened the broadened doublet at 2.33. The latter was further coupled with signals at δ 2.23 and 1.35. As irradiation of these signals changed the signals at δ 2.01 and 2.63, which were coupled with the broadened olefinic doublet at 5.91 the whole sequence H-1′–H-5′ and that of H-1′ (H-10′), H-9′ and H-8′ was confirmed. The stereochemistry at C-2′ followed from the small couplings of H-2′ and from the observed deshielding of H-9′ caused by the β-orientated carboxyl group. The *E*-configuration of the 5′,6′-double bond was deduced from the chemical shift of H-5′. The couplings observed for $J_{4,5}$ supported the proposed stereochemistry at C-5, which most probably was the same in **12** and **14**. The mass spectrum of **14** also supported the proposed structure. Due to the allylic nature of the ester group at C-5 a major fragmentation ion was observed at *m/z* 275 ($C_{17}H_{23}O_3$) which after loss of AcOH led to *m/z* 215. The acid part was recognized by the ions *m/z* 250 ($C_{15}H_{22}O_3$), 233 ($C_{15}H_{21}O_2$) and 232 ($C_{15}H_{20}O_2$). Furthermore, the usual fragments found in the other caryophyllene derivatives were observed. In the spectra of **1**–**8**, splitting of the 7,8-bond followed by a retro 2 + 2-addition led to the characteristic fragment *m/z* 147, which was further transformed by loss of CO to *m/z* 119 (scheme). The latter after loss of C_2H_2 led to the base fragment *m/z* 93 ($C_7H_9^+$).

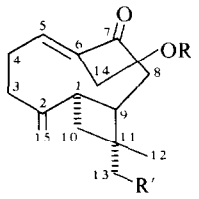
13 we have named pulidysenterin. It is an additional example of a sesquiterpene alcohol esterifying with a sesquiterpenic acid. A compound of this type has so far been isolated only from a *Hypochoeris* species [5].

The roots contained tridecapentaynene, caryophyllene, caryophyllene-5,6-epoxide, α-humulene, **15**, **16** as well as the precursor (**17**) of the polycyclopentanoid hydrocarbons [5], and **18**, whose structure followed from the ^{1}H NMR data and those of the corresponding acetate **19** (Table 3). **18** could not be obtained completely free from **17**. However, treatment with acetic anhydride led to the acetate **19**, while **17** was transformed to silphiperfol-6-ene [6]. In the ^{1}H NMR spectrum of **19** (Table 3) all the signals could be assigned by spin decoupling. Starting with the double doublet at δ 5.21 which was obviously the signal of the hydrogen at the carbon bearing the acetoxy group, the neighbouring protons could be assigned (1.60 *dddd* and 1.71 *dddd*). The corresponding protons were further coupled with signals at δ 1.47 and 2.08, leading to the sequence ■–CH(OAc)CH_2CH_2–■. As the olefinic proton showed only allylic coupling with the methyl group, a second sequence was ■–CH=C(Me)–■. Though the third sequence could be assigned only indirectly, comparison with the spectra of **20** and **21**, obtained from a tricyclic hydrocarbon from *Silphium* species [7], and with that of isocomene [8], clearly showed that the proposed structure agreed with all ^{1}H NMR data. The chemical shifts of H-15 showed characteristic differences in the spectra of **20** and **21** due to the deshielding effect of the neighbouring oxygen function. As in the spectrum of **18** and **19** the chemical shift of H-15 was influenced by a deshielding effect, and hence the 1β-orientation of the oxygen function was established. The couplings of H-1 further supported this assignment. Inspection of a model showed that all couplings observed were in good agreement with the angles between the vicinal protons. Also the ^{13}C NMR data (Table 3) supported the structure of **19**. The natural alcohol therefore was 1β-hydroxy isocomene. Though the absolute configuration of these compounds was not known, the probable biogenetic pathway from caryophyllene [6] supported the one proposed.

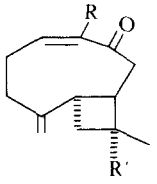
This investigation showed that more species of the genus *Pulicaria* need to be investigated to get some idea of the chemotaxonomic relationships of this genus to other genera of the subtribe Inulinea. Xanthanolides and some other sesquiterpene lactones which show relationships to those of *Inula* have been isolated from *P. crispa* [10].

EXPERIMENTAL

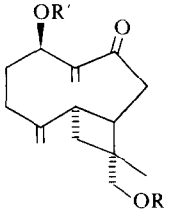
The fresh plant material (voucher 80/1466), grown from seeds supplied by the Botanic Garden Liège, was extracted with Et_2O–petrol (1:2) and the resulting extracts were first sepd by CC (SiO_2) and further by repeated TLC (SiO_2). The aerial parts (900 g) afforded 5 mg tridecapentaynene, 20 mg caryophyllene, 100 mg stigmasterol, 15 mg phytol, 30 mg geranyl isobutyrate, 20 mg **1** (Et_2O–petrol, 2:1), 80 mg **2** (Et_2O–petrol, 2:1), 20 mg **3** (Et_2O–petrol, 1:1), 300 mg **4** (Et_2O–petrol, 1:1), 5 mg **5** (Et_2O–petrol, 3:1), 20 mg **6** (Et_2O–petrol, 2:1), 10 mg **7** (Et_2O–petrol, 2:1), 3 mg **12** (Et_2O–petrol, 3:1), 3 mg **13** [isolated



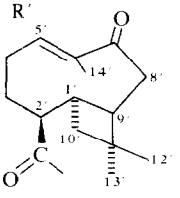
	1	2	3	4
R	Ac	H	Ac	Ac
R′	OH	OAc	OAc	H



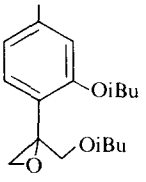
	5	6	7	8	9	10	11
R	CH_2OH	CH_2OAc	CH_2OH	CH_2OAc	CHO	CH_2OH	CH_2OAc
R′	CH_2OH	CH_2OH	CH_2OAc	CH_2OAc	CH_2OH	CHO	CHO



12 R = R′ = H **13** R = H, R′ = α-OH; **14** R = Ac, R′ = α-OH



1–8 —AcOH → *m/z* 147 (**A**) —CO→ *m/z* 119 (**B**) —C_2H_2→ *m/z* 93



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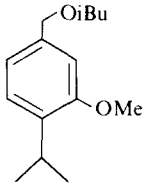

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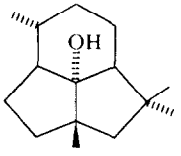

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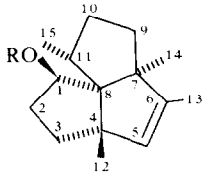
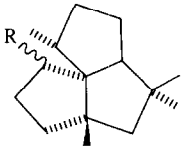


18 R = H
19 R = Ac



20 R = α-OH
21 R = β-OH

as its acetate **14** by heating the mixture of **7** and **13** for 1 hr in 0.5 ml Ac_2O at 70° and separation by repeated TLC (Et_2O–petrol, 1:1)], 30 mg **15** and 20 mg **16**. The roots (450 g) gave 10 mg tridecapentaynene, 50 mg caryophyllene, 5 mg α-humulene, 5 mg caryophyllene-5,6-epoxide, 80 mg **15**, 50 mg **16**, 30 mg **17** and 40 mg **18** (Et_2O–petrol, 1:3, still containing *ca* 25% **17**). Heating of 20 mg **18** (containing *ca* 5 mg **17**) for 1 hr at 70° in 0.5 ml Ac_2O afforded 15 mg **19** (Et_2O–petrol, 1:20). Known compounds were identified by comparing the IR and ^1H NMR spectra with those of authentic material.

14-*Acetoxy*-13-*hydroxycaryophyllen*-7-*one* (**1**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3640 (OH), 1750, 1245 (OAc), 1695 (C=CCO), 3075, 905 (C=CH_2); MS *m/z* (rel. int.): 292 $[M]^+$ (0.1), 261.149 $[M - CH_2OH]^+$ (3) ($C_{16}H_{21}O_3$), 232 $[M - AcOH]^+$ (2), 217 $[232 - Me]^+$ (1), 214 $[232 - H_2O]^+$ (1), 201 $[232 - CH_2OH]^+$ (2), 147 $[A]^+$ (30), 119 $[147 - CO]^+$

Table 3. ^{1}H NMR spectral data of compounds **18** and **19** (400 MHz, $CDCl_3$, TMS as internal standard)

	18	**19**		**19** (^{13}C NMR)		
H-1α	4.25 *dd* (*br*)	5.21 *dd*	C-1	80.0 *d*	C-10	35.5 *t*
H-2α	1.76 *m*	1.71 *dddd*	C-2	34.5 *t**	C-11	45.1 *d*
H-2β		1.60 *dddd*	C-3	34.4 *t**	C-12	29.6 *q*
H-3α	2.06 *m*	2.08 *ddd*	C-4	46.5 *s*	C-13	14.0 *q*†
H-3β	1.57 *m*	1.47 *ddd*	C-5	137.5 *d*	C-14	25.9 *q*
H-5	4.84 *q*	4.84 *q*	C-6	139.1 *s*	C-15	15.3 *q*†
H-9α	1.5 *m*	1.36 *ddd*	C-7	66.4 *s*	OAc	170.5 *s*
H-9β	1.84 *m*	1.84 *m*	C-8	76.1 *s*		21.8 *q*
H-10		1.79 *m*	C-9	37.2 *t*		
		1.89 *m*				
H-11	1.8 *m*	1.82 *m*				
H-12	0.96 *s*	0.97 *s*				
H-13	1.70 *d*	1.68 *d*				
H-14	0.98 *s*	0.99 *s*				
H-15	1.34 *d*	1.12 *d*				
OAc	—	2.05 *s*				

*,†, may be interchangeable.

J (Hz): 1,2α = **4**; 1,2β = 2.5; 2α,2β = 13; 2α,3α = 6; 2α,3β = 13; 2β,3α = 2.5; 2β,3β = 6; 3α,3β = 13; 5,13 = 1; 9α,9β = 13; 9α,10α = 3.5; 9α,10β = 2.5; 11,13 = 6.

(21), 93 $[C_7H_9]^+$ (50), 43 $[MeCO]^+$ (100). 10 mg **1** in 0.5 ml Ac_2O were heated for 30 min at 70°. TLC (Et_2O–petrol, 1:1) afforded 10 mg **3**, identical with the natural compound.

13-*Acetoxy*-14-*hydroxycaryophyllen*-7-*one* (**2**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610, 3520 (OH), 1740, 1250 (OAc), 1670 (C=CCO), 3070, 900 (C=CH_2); MS *m/z* (rel. int.): 292.167 $[M]^+$ (1) ($C_{17}H_{24}O_4$), 261 $[M - CH_2OH]^+$ (4), 232 $[M - AcOH]^+$ (10), 147 (30), 119 (31), 93 (80), 43 $[MeCO]^+$ (100); acetylation (see above) afforded **3**, identical with the natural compound.

13,14-*Diacetoxycaryophyllen*-7-*one* (**3**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750, 1245 (OAc), 1697 (C=CCO), 3080, 900 (C=CH_2); MS *m/z* (rel. int.): 334.178 $[M]^+$ (0.2) ($C_{19}H_{26}O_5$), 274 $[M - AcOH]^+$ (2), 261 $[M - CH_2OAc]^+$ (8), 232 $[274 - ketene]^+$ (10), 214 $[274 - AcOH]^+$ (19), 201 $[232 - CH_2OH]^+$ (17), 147 $[A]^+$ (90), 119 $[147 - CO]^+$ (75), 93 $[C_7H_9]^+$ (82), 43 $[MeCO]^+$ (100); CI (isobutane): 335 $[M + 1]$ (100), 275 $[M + 1 - AcOH]^+$ (15), 215 $[275 - AcOH]^+$ (15), 187 $[215 - CO]^+$ (4);

$$[\alpha]_{24}^{\lambda} = \frac{589}{-135.8} \quad \frac{578}{-141.9} \quad \frac{546\,nm}{-163.0} \quad (c = 1.22, CHCl_3).$$

14-*Acetoxycaryophyllen*-7-*one* (**4**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1235 (OAc), 1685 (C=CCO), 3070, 900 (C=CH_2); MS *m/z* (rel. int.): 276.172 $[M]^+$ (0.5) ($C_{17}H_{24}O_3$), 261 $[M - Me]^+$ (0.3), 234 $[M - ketene]^+$ (3), 216 $[M - AcOH]^+$ (11), 188 $[216 - CO]^+$ (9), 147 $[A]^+$ (68), 199 $[147 - CO]^+$ (41), 93 $[C_7H_9]^+$ (100);

$$[\alpha]_{24}^{\lambda} = \frac{589}{-167.5} \quad \frac{578}{174.9} \quad \frac{546}{-200.6} \quad \frac{436\,nm}{-282.7}$$

($c = 1.58$, $CHCl_3$).

13,14-*Dihydroxy*-5,6-cis-*caryophyllen*-7-*one* (**5**). Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620 (OH), 1680 (C=CCO); MS *m/z* (rel. int.): 250.157 $[M]^+$ (0.2) ($C_{15}H_{22}O_3$), 232 $[M - H_2O]^+$ (2), 219 $[M - CH_2OH]^+$ (5), 204 $[219 - Me]^+$ (3), 201 $[219 - H_2O]^+$ (3), 147 (55), 119 (54), 93 $[C_7H_9]^+$ (100).

5 mg **5** in 2 ml $CHCl_3$ were stirred for 2 hr with 50 mg pyridine dichromate. TLC (Et_2O–petrol, 3:1) afforded 1 mg **9**, 1 mg **10** and 2 mg **5**.

9: Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2750, 1700 (CHO), 1680 (C=CC=O); MS *m/z* (rel. int.): 248.141 $[M]^+$ (1) ($C_{15}H_{20}O_3$), 230 $[M - H_2O]^+$ (2), 205 $[230 - Me]^+$ (4), 217 $[M - CH_2OH]^+$ (4), 93 $[C_7H_9]^+$ (100).

5 mg **5** were heated in 0.5 ml Ac_2O for 30 min at 70°. TLC (Et_2O petrol, 1:1) afforded 5 mg **8**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745, 1240 (OAc), 1685 (C=CCO), 3080, 900 (C=CH_2); MS *m/z* (rel. int.): 334.178 $[M]^+$ (0.4) ($C_{19}H_{26}O_5$), 274 $[M - AcOH]^+$ (1), 261 $[M - CH_2OAc]^+$ (2), 232 $[272 - ketene]^+$ (2), 214 $[274 - AcOH]^+$ (7), 201 $[232 - CH_2OH]^+$ (5), 147 $[A]^+$ (50), 119 $[147 - CO]^+$ (58), 93 $[C_7H_9]^+$ (100);

$$[\alpha]_{24}^{\lambda} = \frac{589}{-65.2} \quad \frac{578}{-68.3} \quad \frac{546}{-77.1} \quad \frac{436\,nm}{-112.1}$$

($c = 0.82$, $CHCl_3$).

14-*Acetoxy*-13-*hydroxy*-5,6-cis-*caryophyllen*-7-*one* (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1740, 1230 (OAc), 1680 (C=CCO), 3070, 900 (C=CH_2); MS *m/z* (rel. int.): 292.167 $[M]^+$ (0.2), 261 $[M - CH_2OH]^+$ (3), 232 $[M - AcOH]^+$ (4), 147 (61), 119 (48), 93 $[C_7H_9]^+$ (100), 43 $[MeCO]^+$ (90).

5 mg **6** were acetylated as above. TLC (Et_2O petrol, 1:1) afforded 5 mg **8**. 5 mg **6** in 2 ml $CHCl_3$ were stirred for 2 hr with 50 mg pyridine chlorochromate. TLC (Et_2O–petrol, 1:1) afforded 2 mg unchanged **6** and 2 mg **11**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745, 1235 (OAc), 2710, 1720 (CHO), 1685 (C=CCO), 3070, 900 (C=CH_2); MS *m/z* (rel. int.): 290 $[M]^+$ (0.5), 230 $[M - AcOH]^+$ (3), 202 $[M - CO]^+$ (8), 201 $[M - CHO]^+$ (8), 93 $[C_7H_9]^+$ (48), 43 $[MeCO]^+$ (100).

13-*Acetoxy*-14-*hydroxy*-5,6-cis-*caryophyllen*-7-*one* (**7**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1745, 1240 (OAc), 1680 (C=CCO), 3080, 905 (C=CH_2); MS *m/z* (rel. int.): 292.167 $[M]^+$ (0.5) ($C_{17}H_{24}O_4$), 274 $[M - H_2O]^+$ (0.5), 232 $[M - AcOH]^+$ (5), 219 $[M - CH_2OAc]^+$ (10), 201 $[219 - H_2O]^+$

(6), 147 $[A]^+$ (41), 119 $[147 - CO]^+$ (53), 93 $[C_7H_9]^+$ (100). Acetylation afforded **8** (see above).

5,13-*Dihydroxy*-5,6-*dihydro*-6,14-*dehydrocaryophyllen*-7-*one* (**12**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1700 (C=CCO); MS *m/z* (rel. int.): 250.157 $[M]^+$ (2) ($C_{15}H_{22}O_3$), 221 $[M - CHO]^+$ (8), 219 $[M - CH_2OH]^+$ (8), 201 $[219 - H_2O]^+$ (12), 173 $[201 - CO]^+$ (15), 147 $[A]^+$ (55), 119 $[147 - CO]^+$ (72), 93 $[C_7H_9]^+$ (78), 91 $[C_7H_7]^+$ (100);

$$[\alpha]_{24}^{\lambda} = \frac{589}{-49.4} \quad \frac{578}{-51.3} \quad \frac{546}{-61.3} \quad \frac{436\,nm}{-120.6}$$

($c = 0.16$, $CHCl_3$).

Pulidysenterin-13-O-*acetate* (**14**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1240 (OAc), 1687, 1625 (C=CCO), 2070, 900 ($C=CH_2$); MS *m/z* (rel. int.): 524.314 $[M]^+$ (8) ($C_{32}H_{44}O_6$), 464 $[M - AcOH]^+$ (0.5), 275 $[M - RCO]^+$ (13), 274 $[M - RCO_2H]^+$ (3), 250 $[RCO_2H]^+$ (27), 233 $[RCO]^+$ (13), 232 $[250 - H_2O]^+$ (16), 215 $[275 - AcOH]^+$ (44), 201 $[274 - CH_2OAc]^+$ (3), 147 $[A]^+$ (54), 119 $[147 - CO]^+$ (40), 95 $[C_7H_{11}]^+$ (100), 93 $[C_7H_9]^+$ (58);

$$[\alpha]_{24}^{\lambda} = \frac{589}{-86} \quad \frac{578}{-90} \quad \frac{546}{-105} \quad \frac{436\,nm}{-188}$$ ($c = 0.2$, $CHCl_3$).

1-*Acetoxyisocomene* (**19**). Colourless oil, $bp_{0.1\,torr}$ 110° (bath temp.), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1250 (OAc), 850 (>C=CH); MS *m/z* (rel. int.): 262.193 $[M^+]$ (6) ($C_{17}H_{26}O_2$), 247 $[M - Me]^+$ (38), 202 $[M - AcOH]^+$ (32), 187 $[247 - AcOH]^+$ (100), 174 $[202 - C_2H_4]^+$ (20), 163 $[M - AcOCHCH{=}CH_2]^+$ (40), 145 $[187 - C_3H_6]^+$ (37);

$$[\alpha]_{24}^{\lambda} = \frac{589}{+76.5} \quad \frac{578}{+79.9} \quad \frac{546}{+90.5} \quad \frac{436}{+152.3} \quad \frac{365\,nm}{+234.6}$$

($c = 1.5$, $CHCl_3$).

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