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New α-Cyclocostunolide and Isocostic Acid Derivatives from *Pluchea dioscoridis*[1)]

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The aerial parts of *Pluchea dioscoridis* yielded two new isocostic acid derivatives (Ia and Ie), in addition to the eudesmanolide IIa.

Keywords——*Pluchea dioscoridis*; Compositae; sesquiterpene; eudesmanolide; isocostic acid derivatives

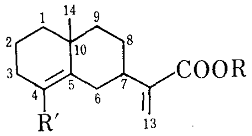
The biological activities of natural products isolated from some plants belonging to Compositae are well known.[2)] The genus *Pluchea* (Compositae, tribe Inuleae) is placed in the subtribe Inulinae.[2)] About nine of the forty species of this genus have been studied chemically. Typical thiophenacetylenes,[3)] eudesmane derivatives such as the plucheines,[4-10)] and a few eudesmanolides have been reported [10-13)] and may be of chemotaxonomic importance. We reinvestigated the aerial parts of *P. dioscoridis* (L.) DC. [=*Conyza dioscoridis* (L.) desf.], which grows wild in Egypt, to see whether there is a seasonal variation in the chemical constituents. Our results are discussed in this paper.

This work afforded three new compounds, *i.e.*, 15-hydroxyisocostic acid (Ia), the corresponding aldehyde (Ie) and the eudesmanolide (IIa). Other known products were also isolated, including the thiopheneacetylenes (IIIa, b).[3,13)] eudesmanolides (IV, V)[13)] and 9β-hydroxycostunolide (VI).[13)]

15-Hydroxyisocostic acid Ia and the corresponding Ie are rather polar, and hence their separation was difficult. However, it was achieved after diazomethane treatment. Thus, Ia was transformed to the methyl ester Ic as well as to the 15-*O*-methyl ether Id. Compound Ic gave no molecular ion, but the observed fragment *m/z* 246, corresponding to $C_{16}H_{22}O_2$, was clearly formed by loss of water from the parent ion. The presence of a hydroxyl group was indicated by the infrared (IR) spectrum ($3615\,cm^{-1}$) and also by the oxidation of Ia with manganese dioxide to give an aldehydic product (Ib). The latter compound was identical with that obtained by esterification of the corresponding naturally occurring acid Ie. The proton nuclear magnetic resonance (^{1}H-NMR) (400 MHz) spectrum of Ic was in part similar to that of the known 15-desoxy derivative,[14)] but the signal of the olefinic methyl group was replaced by a pair of doublets at $\delta=4.09$ and 3.02. These signals were replaced by a singlet at $\delta=10.17$, after oxidation of Ic (see Experimental). Thus, the structures of Ib and Ic were settled and the natural products were identified as Ia and Ie.

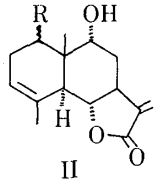
The structure of IIa was deduced from the ^{1}H-NMR spectrum, which displayed signals at δ 3.08 br d (H-5), 4.05 t (H-6) and 3.28 ddddd (H-7). The signal of H-1 appeared at 3.89 br d ($J=4$ Hz), which differed from that of IIb[13)] in the changed couplings of H-1, indicating the presence of the epimer. Further evidence for structure IIa was obtained from the mass and IR spectra (see Experimental).

The seasonal difference in the constituents of *P. dioscoridis* is worthy of comment. The sample collected in August from the same locality did not contain any isocostic acid



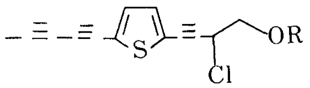
I

a : R=H , R'=CH_2OH
b : R=Me, R'=CHO
c : R=Me, R'=CH_2OH
d : R=Me, R'=CH_2OMe
e : R=H , R'=CHO



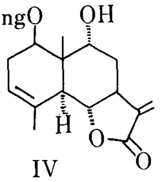
II

a : R=αOH
b : R=βOH

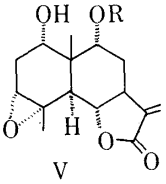


III

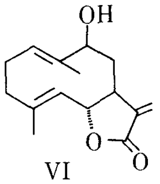
a : R=iso-Val
b : R=H



IV



V



VI

a: R=iso-Val
b: R=Ang Ang=angelate

derivatives, while the sesquiterpene lactones and other constituents were nearly the same.[13] Only II was not present, though 1α-acyloxy derivatives with a 3,4-epoxide group (Va, b) were isolated.

The isolation of these further sesquiterpenes clearly supports the replacement of Pluchea in the Inulinae since this type of sesquiterpene is widespread among other genera of this subtribe.[2]

Experimental

Isolation of Compounds I—VI——The air-dried plant material (73 g), collected in April 1984 from Mansoura, Egypt, was extracted with ether : pet. ether : methanol = 1 : 1 : 1. The extract of the aerial parts was first treated with methanol to remove long-chain hydrocarbons and then partially separated by column chromatography (CC) (SiO_2) with pet. ether and increasing amounts of ether, and finally ether : methanol = 10 : 1. The fraction obtained with 10% ether was further separated by thin-layer chromatography (TLC) (5% ether) and afforded IIIa (5 mg). The fraction eluted with 25% ether gave IIIb (5 mg) and that with 50% ether yielded IV (3 mg). Half of the ether fraction was treated with diazomethane. TLC (SiO_2, PF 254, ether : pet. ether = 4 : 1) gave Id (5 mg) (*Rf* 0.96); Ib (3 mg) (*Rf* 0.9); Ic (10 mg) (*Rf* 0.84); haagenolide VI (3 mg) (*Rf* 0.72); 3α,4α-epoxy-1α-hydroxy-9α-isovaleryloxy-α-cyclocostunolide (Va)[13] (3 mg) (*Rf* 0.42); the corresponding angelate (Vb)[13] (5 mg) (*Rf* 0.36) and IIa (3 mg) (*Rf* 0.21). The fraction eluted with ether : methanol = 9 : 1 gave IV (5 mg).

The known compounds were identified by comparing their spectral data with those of authentic materials.

15-Hydroxyisocostic Acid——This compound was isolated as its methyl ester Ic, colorless oil. IR cm^{-1}: 3615 (OH), 1720, 1630 ($C=CCO_2R$). MS *m/z* (rel. int.): 246.163 $[M-H_2O]^+$ (100) (Calcd for $C_{16}H_{22}O_2$: 246.163), 231 $[246-Me]^+$ (57), 214 $[246-MeOH]^+$ (28), 186 $[214-CO]^+$ (47), 171 $[186-Me]^+$ (46). ^{1}H-NMR (always $CDCl_3$, 400 MHz) δ: 2.17, 2.10 m (H-3), 1.78 ddt (H-6, J = 14, 14, 1.5 Hz), 2.71 dd (H-6', J = 14, 3 Hz), 2.39 dddd (H-7, J = 13, 13, 3, 3 Hz), 6.18, 5.57 s (H-13), 1.06 s (H-14), 4.09, 4.02 d (H-15, J = 11.5 Hz), 3.75 s (OMe). Product Ic (10 mg) was stirred in ether (2 ml) with manganese dioxide (100 mg) for 1 h. TLC (ether : pet. ether = 4 : 1) gave Ib (5 mg), identical with the methyl ester of Ie.

15-*O*-Methyl Ether Id——Colorless oil, IR cm^{-1}: 1730, 1630 ($C=CCO_2R$). MS *m/z* (rel. int.): 278 $[M]^+$ (1.3), 246 $[M-MeOH]^+$ (12), 231 $[246-Me]^+$ (7), 205 $[246-OMe]^+$ (10), 55 (100). ^{1}H-NMR ($CDCl_3$) δ: 2.10 m (H-3), 1.72 ddt (H-6), 2.72 dd (H-6'), 6.18, 5.57 s (H-13), 1.10 s (H-14), 3.98, 3.76 d (H-15), 3.77, 3.27 s (OMe).

Methyl 15-Oxo-eudesmane-4,11 (13)-dien-12-oate Ib——Colorless oil. IR cm^{-1}: 2730, 1720 (CHO), 1720, 1630 ($C=CCO_2R$). MS *m/z* (rel. int.): 262.157 $[M]^+$ (61) (Calcd for $C_{16}H_{22}O_3$: 262.157), 244 $[M-H_2O]^+$ (14), 230 $[M-MeOH]^+$ (83), 202 $[230-CO]^+$ (83), 187 $[202-Me]^+$ (46), 91 (100). ^{1}H-NMR ($CDCl_3$) δ: 2.17, 2.07 m (H-3), 2.60 m (H-7), 6.24, 5.63 s (H-13), 1.21 s (H-14), 10.17 s (H-15), 3.77 s (OMe).

1α,9α-Dihydroxy-α-cyclocostunolide IIa——Colorless oil. IR cm^{-1}: 3420 (OH), 1780 (γ-lactone). MS *m/z* (rel. int.): 246.125 $[M-H_2O]^+$ (100) (Calcd for $C_{15}H_{18}O_3$, 246.126), 228 $[246-H_2O]^+$ (10), 213 $[228-Me]^+$ (12). ^{1}H-NMR

($CDCl_3$) δ: 3.89 br d (H-1, $J=4$ Hz), 5.32 br s (H-3), 3.08 br d (H-5, $J=11$ Hz), 4.05 t (H-6, $J=11$ Hz), 3.28 ddddd (H-7, $J=11$, 11, 3.5, 3, 3 Hz), 3.97 t (H-9, $J=2.5$ Hz), 6.07 d (H-13, $J=3.5$ Hz), 5.32 d (H-13′, $J=3$ Hz), 0.82 s (H-14), 1.92 br s (H-15). $[\alpha]_D^{25}$ +135 in $CHCl_3$ $c=0.1$.

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