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FURTHER AMIDES FROM *ECHINACEA PURPUREA*[*]

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Abstract—The aerial parts of *Echinacea purpurea* afforded, in addition to known compounds, five further highly unsaturated amides and a derivative of linolenic acid. The structures were elucidated by high field ^{1}H NMR spectroscopy. The isolation of a known labdane derivative may be of chemotaxonomic relevance.

From *Echinacea purpurea* Moench. several highly unsaturated amides were isolated [1,2]. We now have reinvestigated the aerial parts In addition to compounds isolated previously [1,2], germacrene D, methyl *p*-hydroxycinnamate, vanillin, the labdane derivative **6** [3] and five new amides (**1**–**5**) were obtained. The separation of these amides caused problems Only by repeated HPLC (reversed phase) were all the amides obtained pure. In addition to the molecular formulae, the ^{1}H NMR spectra allowed a clear assignment of the structures (Table 1). All five compounds differed from those isolated previously by lacking the second double bond which in most cases is conjugated with the amide group Accordingly, in all spectra the lowest signal was a double triplet which had to be assigned to the proton *β* to the amide group. The *trans* configuration followed from the coupling, while **1**–**4** further had an isolated *cis*-double bond. Compound **5** was a conjugated diene diyne, as was deduced from the UV maxima. The configuration could be assigned from the couplings observed while spin decoupling allowed the assignment of all signals in the spectra of **1**–**5**. In the spectra of **1**–**4** the acetylene proton showed, as usual in such diynes, a small triplet coupling which was missing in the spectrum of **5**. The corresponding signal was shifted downfield due to the conjugation with double bonds.

Amide **2** is of biogenetic interest since its isolation supports the proposed biogenesis of these amides from oleic acid [4]. The *cis*-9,10-double bond of oleic acid is still present in **2** whereas three carbons have disappeared from the end of the chain. A similar pathway has been established by feeding experiments [4]. Most likely **1** is formed by chain shortening through *β*-oxidation from the carboxyl end (Scheme 1). The amide groups in **3** and **4**,

Table 1. ^{1}H NMR spectral data of compounds **1**–**5** (400 MHz, $CDCl_3$, TMS as internal standard)

	1	**2**	**3**	**4**	**5**
H_A	5.78 *dt*	5.76 *dt*	5.78 *dt*	5.79 *dt*	5.78 *br d*
H_B	6.80 *dt*	6.82 *dt*	6.80 *dt*	6.86 *dt*	6.81 *dt*
H_C	2.19 *ddt*	2.18 *ddt*	2.19 *ddt*	2.19 *ddt*	2.36 *m*
H_D	1.54 *tt*	1.42 *m* 1.33 *m*	1.55 *m*	1.45 *m* 1.33*m*	
H_E	2.06 *br dt*	2.02 *br dt*	2.06 *br dt*	2.03 *br dt*	5.94 *dt*
H_F	5.44 *m*	5.39 *m*	5.45 *m*	5.38 *m*	6.62 *br dd*
H_G		5.49 *m*		5.50 *m*	6.52 *dd*
H_H	2.99 *br d*	2.99 *br d*	2.99 *br d*	2.99 *br d*	5.35 *br d*
H_I	1.99 *t*	1.98 *t*	1.99 *t*	2.00 *t*	2.09 *s*
H_K	3.15 *t*	3.15 *t*	3.15 *t*	3.33 *br d*	3.15 *t*
H_L	1.80 *tqq*	1.79 *tqq*	1.80 *m*	—	*
H_M	0.91 *d*	0.90 *d*	0.88 *d*	1.24 *s*	0.96 *d*
H_N					
H_O	—	—	0.89 *t*	—	—

*Not assigned

J (Hz) Compounds **1**–**4** A, D = 15; AC = 1.3; BC = CD = DE = EF = GH = 7, H, I = 1, compound **5**: 2, 3 = 15, 2, 4 = 1; 3, 4 = 5, 6 = 7, 6, 7 = 15; 7, 8 = 8, 9 = 11, $NHCH_2CHMe_2$: NH, 1′ = 1′, 2′ = 2′, 3′ = 2′, 4′ = 7, $NHCH_2CH(Me)Et$ NH, 1′ = 1′, 2′ = 2′, 3′ = 2′, 4′ = 3′, 5′ = 7

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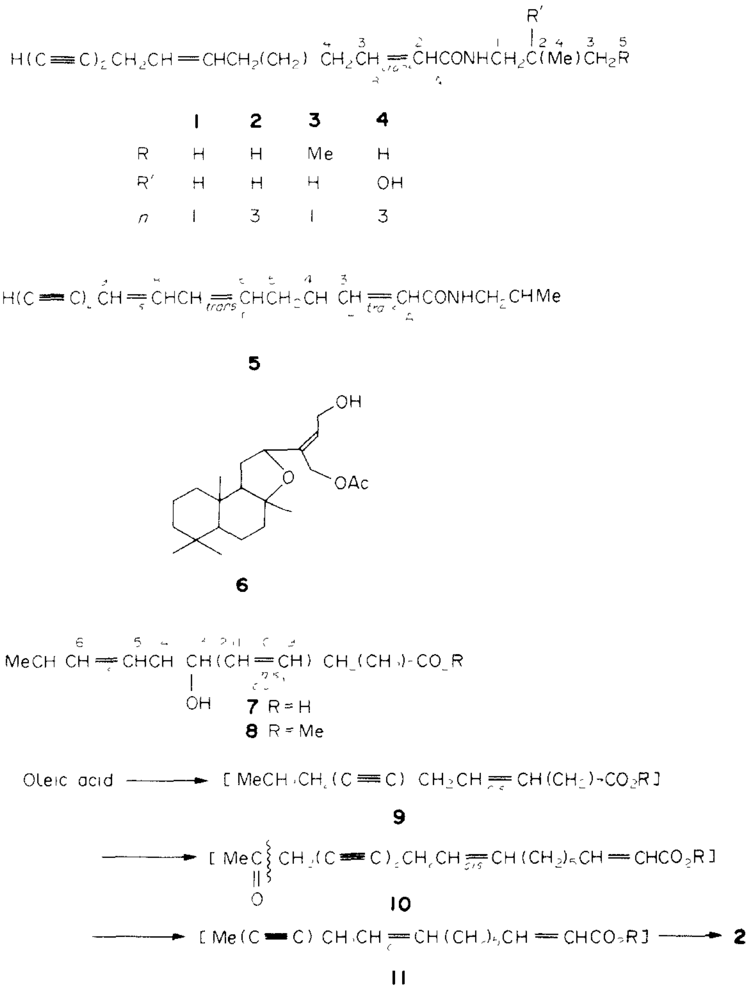
[*] Part 265 in the series "Polyacetylenic Compounds" For Part 264 see El-Masry, S, Ghazy, N M, Zdero, C and Bohlmann, F (1983) *Phytochemistry* **22**, 592

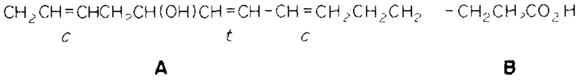


Scheme 1

probably formed from the corresponding decarboxylated amino acids, have not been isolated before Their structures clearly follow from the ^{1}H NMR spectra and the mass spectra (see Experimental)

Furthermore, a hydroxy acid was isolated, the structure of which is probably **7** The mass spectrum of the corresponding methyl ester showed no molecular ion Even by chemical ionization only a $[M - H_2O + 1]^+$ peak was observed The strong fragment $[M - C_5H_9]^+$ indicated that the hydroxyl was at C-13 while the ^{1}H NMR spectrum (see Experimental) clearly showed the presence of the sequence **A** and **B** These sequences, however, did not indicate where the remaining methylene groups were placed The structural assignment is, therefore, based only on the mass spectrum but is also supported by the fact that **7** could be formed by allylic oxidation of linolenic acid

The isolation of **6** is of chemotaxonomic interest This compound was isolated previously from a *Silphium* species, a genus which is also placed in the somewhat diverse subtribe Ecliptinae of the Compositae [5] Highly unsaturated amides are also present in *Spilanthes*, *Heliopsis* and *Acmella* which belong in this same subtribe [5]



$$\underset{}{CH_2}\underset{c}{CH=CH}CH_2CH(OH)\underset{t}{CH=CH}-\underset{c}{CH=CH}CH_2CH_2CH_2 \qquad -CH_2CH_2CO_2H$$

A **B**

EXPERIMENTAL

The fresh aerial parts (2 5 kg) were extracted first with Et_2O-petrol (1 2) and then with MeOH The combined extracts were separated by CC (Si gel) and further by TLC (Si gel) and HPLC (reversed phase) In addition to compounds isolated previously 300 mg germacrene D, 15 mg methyl *p*-hydroxycinnamate, 6 mg vanillin, 5 mg **6** and a complex mixture of the amides **1**–**5** and **7** were obtained Separation of **1**–**5** was achieved by HPLC (MeOH-H_2O 7 3) Finally, 50 mg **1**, 20 mg **2**, 3 mg **3**, 25 mg **4**, 8 mg **5** and 20 mg **7** were obtained Known compounds were identified by comparing the ^{1}H NMR spectra with those of authentic material

*Trideca-*2t 7c-*dien-*10,12-*diynoic acid isobutylamide* (**1**) Colourless crystals from petrol, mp 40 , IR $\nu_{max}^{CCl_4}$ cm^{-1} 3450 (NH), 3318, 2235 (C≡CH), 1680, 1640, 1510, 980 (C=CCONHR), MS *m/z* (rel int) 257 178 $[M]^+$ (10) ($C_{17}H_{23}NO$), 185 $[M - NHR]^+$ (22), 57 $[C_4H_9]^+$ (100)

Pentadeca-2t,9c-*dien*-12,14-*diynoic acid isobutylamide* (**2**) Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1} 3450 (NH), 3320, 2240 ($\mathrm{C{\equiv}CH}$), 1685, 1650, 1515, 980 ($\mathrm{CH{=}CHCONHR}$), MS (CI, isobutane) *m/z* (rel int) 286 $[\mathrm{M}+1]^+$ (100) $[\mathrm{C_{19}H_{27}NO}+1]^+$

Trideca-2t,7c-*dien*-10,12-*diynoic acid* (2-*methylbutyl*)*amide* (**3**) Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1} 3450 (NH), 3300 ($\mathrm{C{\equiv}CH}$), 1680 ($\mathrm{C{=}CCONHR}$), MS (CI, isobutane) *m/z* (rel int) 272 $[\mathrm{M}+1]^+$ (100) $[\mathrm{C_{18}H_{25}NO}+1]^+$

Pentadeca-2t,9c-*dien*-12,14-*diynoic acid* (2-*hydroxyisobutyl*)-*amide* (**4**) Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1} 3445 (NH), 3320, 2230 ($\mathrm{C{\equiv}CH}$), 1680, 1640, 1515, 980 ($\mathrm{CH{=}CHCONHR}$); MS (CI, isobutane) *m/z* (rel int) 302 $[\mathrm{M}+1]^+$ (100) $[\mathrm{C_{19}H_{27}NO_2}+1]^+$

Trideca-2t,6t,8c-*trien*-10,12-*diynoic acid isobutylamide* (**5**) Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1} 3450 (NH), 3320 ($\mathrm{C{\equiv}CH}$), 1680 ($\mathrm{C{=}CCONHR}$), MS (CI, isobutane) *m/z* (rel int) 256 $[\mathrm{M}+1]^+$ (100) $[\mathrm{C_{17}H_{21}NO_2}+1]^+$

13-*Hydroxyoctadeca*-9c,11t,15c-*trienoic acid* (**7**) Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1} 3600–2600, 1715 ($\mathrm{CO_2H}$), UV $\lambda_{\max}^{\mathrm{Et_2O}}$ nm 235 ^{1}H NMR ($\mathrm{CDCl_3}$) 2 34 (H-2, *t*, *J* = 7 Hz), 2 17 (H-8, *br dt*, *J* = 7, 7 Hz), 4 92 (H-9, *dt*, *J* = 11, 7 Hz), 5 97 (H-10, *br dd*, *J* = 11, 11 Hz), 6 52 (H-11, *br dd*, *J* = 11, 15 Hz), 5 68 (H-12, *dd*, *J* = 15, 6 Hz), 4 22 (H-13, *dt*, *J* = 6, 6 Hz), 2 07 (H-14, *dd*, *J* = 7, 6 Hz), 4 85 (H-15, H-16, *m*), 2 07 (H-17, *dq*, *J* = 7, 7 Hz), 0 96 (H-18, *t*, *J* = 7 Hz) Addition of $\mathrm{CH_2N_2}$ in $\mathrm{Et_2O}$ afforded **8**, colourless gum, MS *m/z* (rel int) 277 $[\mathrm{M}-\mathrm{OMe}]^+$ (0 3), 239 $[\mathrm{M}-\mathrm{C_5H_9}]^+$ (19), 207 $[239-\mathrm{MeOH}]^+$ (33), 67 (100), CI (isobutane) 291 $[\mathrm{M}-\mathrm{H_2O}+1]^+$ (100)

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