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BIOSYNTHETICALLY SIMPLE C_{18}-ALKAMIDES FROM *ACHILLEA* SPECIES

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Key Word Index—*Achillea lycaonica*; *A. chamaemelifolia*; Compositae; Anthemideae; C_{18}-alkamides; piperidides; isobutylamides; biosynthetic pathways.

Abstract—The petrol–diethyl ether extracts of the underground parts of *Achillea lycaonica* and *A. chamaemelifolia* afforded, in addition to known derivatives, 10 new alkamides. Their structures and stereochemistries were elucidated on the basis of spectroscopic evidence. Besides a new C_{15}-piperidide, the derivatives fall into a series of structurally closely related C_{18}-piperidides and -isobutylamides. A comparison of the different patterns of unsaturation allows some general conclusions about the biosynthetic pathways of the acid moieties.

INTRODUCTION

The accumulation of amides with characteristic olefinic and acetylenic patterns represents a typical trend of the genus *Achillea* (Compositae, Anthemideae) [1]. This biogenetic capacity apparently replaces those polyacetylenes which are otherwise characteristic for this tribe [2]. Apart from the more widespread isobutylamides, this genus is particularly characterized by the frequent occurrence of saturated and unsaturated 5- and 6-ring amides (piperidides, pyrrolidides, piperideides, pyrrolideides) [3–6].

Biosynthetically, the amine parts may be regarded as amino acid derivatives, whereas the acid residues are derived from unsaturated fatty acids [1]. As demonstrated in a previous study, at least some acetylenic amides are unambiguously derived from oleic acid [7]. In that case, the main line of the biosynthetic sequence resembles that known from general polyacetylene biosynthesis [8]. However, apart from the amide linkage there are some biosynthetic steps in the acid residue which are obviously confined to the alkamides. Moreover, many of the purely olefinic derivatives are supposed to be derived separately from common biogenetic precursors [1, 9]. Many of the biosynthetic pathways presented in a recent review on alkamides [1] are hypothetically and were mainly based on the results obtained by comparative phytochemical analyses. Especially the structures of some C_{18} and C_{16} amides which were shown to suggest direct connexions with oleic and linoleic acid [1].

Up to the present time, only a few reports on C_{18} amides are available. They are isolated from two *Heliopsis* species (Compositae, Heliantheae) [10, 11], *Achillea lycaonica* Boiss. et Heldr. [3] and *Piper amalago* L. (Piperaceae) [12]. In the case of *Heliopsis*, the highly unsaturated amides may be regarded as biosynthetically advanced, whereas the corresponding derivatives of the two latter genera with only one or two double bonds appear to be more 'primitive'.

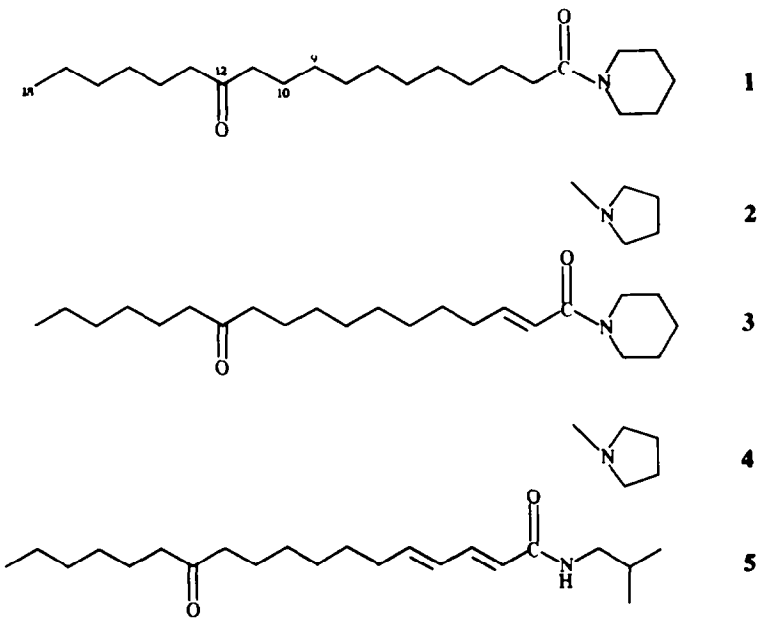
In *A. lycaonica* four C_{18} amides (**1**–**4**) have been detected, they are easily crystallized, even from the crude column fractions [3]. They were suggested to be derived from linoleic acid via epoxidation followed by successive hydrogenation, oxidation and dehydration [1]. All the other amides detected in this species were not identified in that examination because they could not be separated sufficiently on thin-layer chromatography. However, the spectra of preliminary UV and IR analyses suggested a set of closely related derivatives which might be of special significance for biosynthetic considerations. In continuation of these studies, we have now separated the amides of *A. lycaonica* by reversed phase MPLC and HPLC, as well as some amides from *A. chamaemelifolia* Pourr. whose UV and IR spectra suggested closely related derivatives.

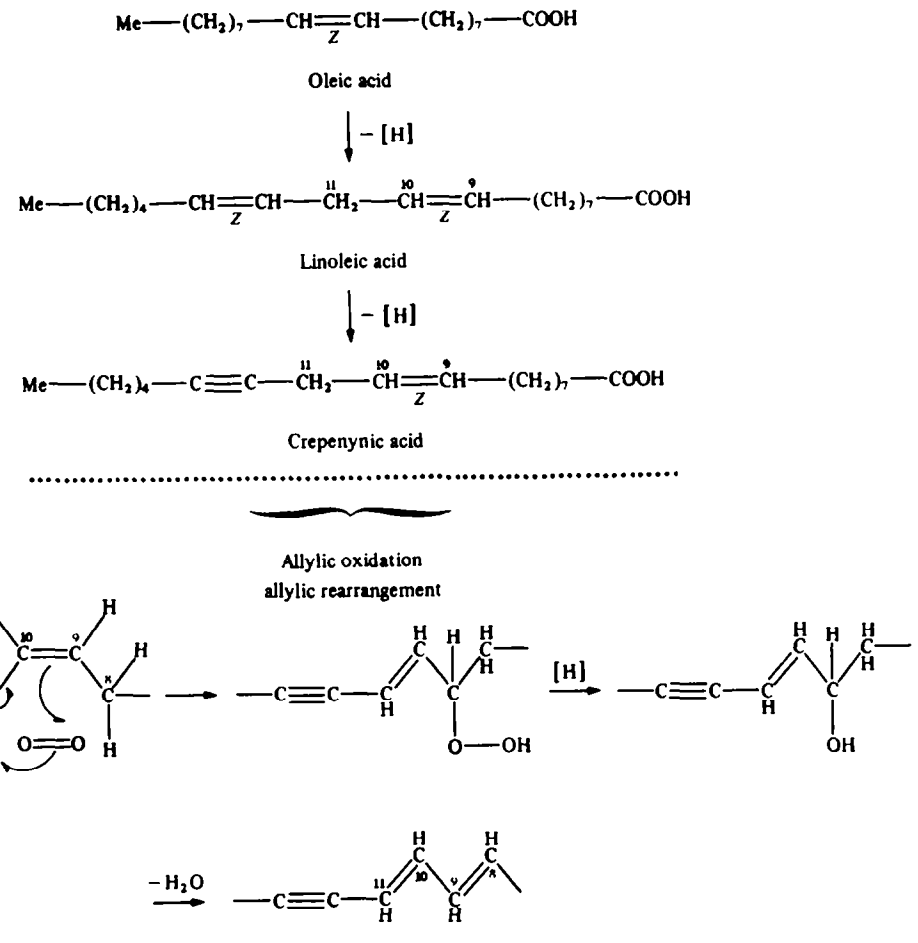
The present paper describes the structure elucidation by spectroscopic methods which has resulted in the identification of 10 previously unknown alkamides. The new structures lead to some general conclusions about the biogenetic connections of the acid moieties.

RESULTS AND DISCUSSION

The petrol–ethyl ether extract of the underground parts of *A. lycaonica*, originating from Turkey, afforded a series of piperidides, whereas that of *A. chamaemelifolia*, endemic in the Pyrenees, is mainly characterized by a preponderance of isobutylamides. However, both species show a common trend in accumulating amides with C_{18} acid moieties. In a previous paper, the major amides of *A. lycaonica* were shown to be piperidides and pyrrolidides based either on a saturated C_{18} keto-acid (lycaonic acid) (**1**, **2**) or the corresponding 2,3-dehydro derivative (**3**, **4**) [3]. Now, from *A. chamaemelifolia* a further new compound (**5**) of the keto series has been isolated in small amounts. In this case the keto-acid is linked with isobutylamine and additionally deviates from the former derivatives by two (2*E*,4*E*) orientated double bonds.

As has already been suggested previously [1], the oxygenation at position C-12 may be explained by epoxidation of linoleic acid (vernolic acid). If this hypo-

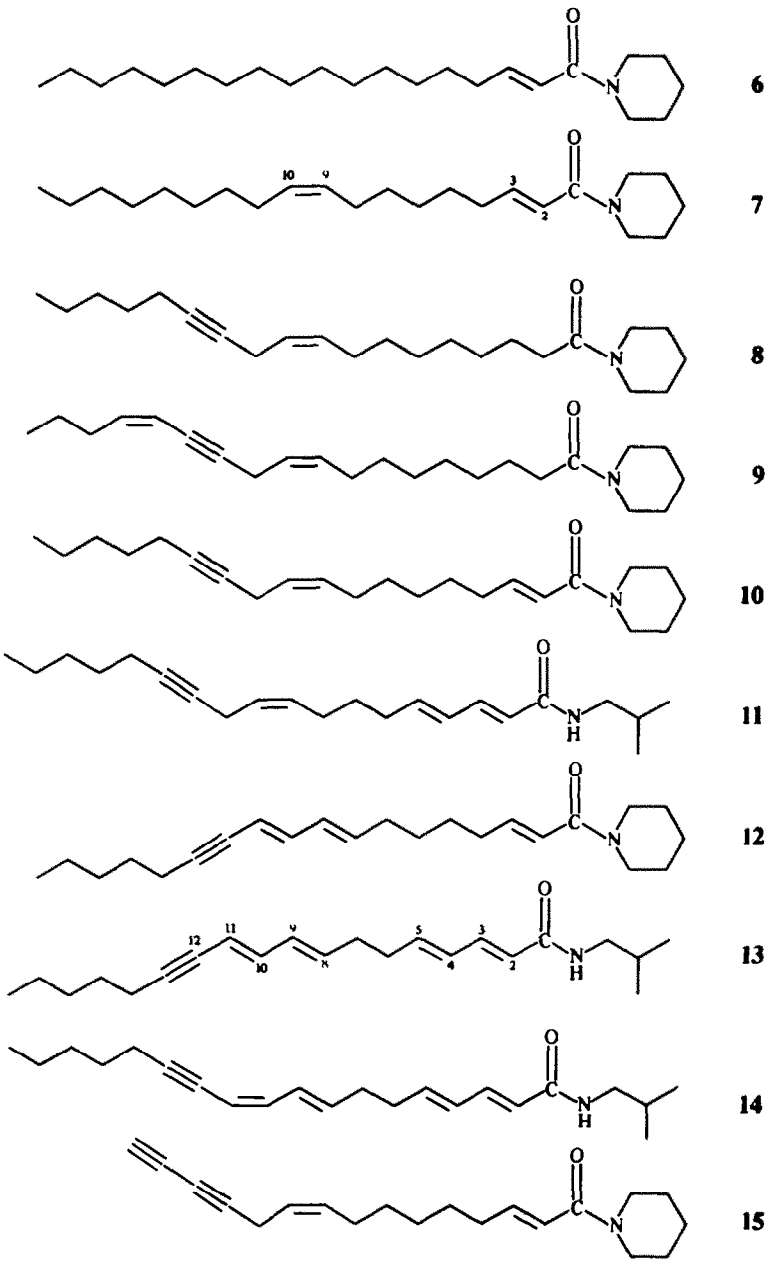

1
2
3
4
5


Oleic acid
– [H]
Linoleic acid
– [H]
Crepenynic acid
Allylic oxidation
allylic rearrangement
[H]
– H2O

Scheme 1

thesis is accepted, then firstly the absence of the second double bond at position C-9 may be interpreted as successive hydrogenation and secondly the one or two *E*-orientated double bonds conjugated with the carbonyl of the amide group arise independently from biogenetic steps further along the chain. In the case of acetylenic amides, these steps are expected to be in line with those biosynthetic reactions which are already known from other polyacetylenes [8].

From *A. lycaonica*, two further purely olefinic piperidides have been isolated which may be derived formally from 2,3-dehydrostearic acid (**6**) and 2,3-dehydrooleic acid (**7**). Biosynthetically, they may be interpreted either as most primitive or, with regard to the keto-acids **1**–**4**, as hydrogenation products of formerly more unsaturated derivatives. The frequent occurrence of crepenynic acid derived amides in that species (**8**–**10**) and in *A. chamaemelifolia* (**11**) may be of special biogenetic significance, since this acid is generally accepted as key precursor of polyacetylenes. In fact, the co-occurrence of crepenynic acid piperidide (**8**) and dehydrocrepenynic acid piperidide (**9**) in *A. lycaonica*, as well as the structurally closely related piperidide **12** and the isobutylamides **11**, **13**, and **14** in *A. chamaemelifolia*, points to a biosynthetic sequence which has been established for polyacetylenes [8]. As demonstrated in Scheme 1 for the formation of compounds **12**–**14**, allylic oxydation of the isolated methylene group at position C-11 may be assumed, accompanied by allylic rearrangement. The latter mechanism may be best explained by oxygenation at C-11 and isomerization of the *Z*-orientated double bond at position 9–10 into the *E*-orientated double bond at

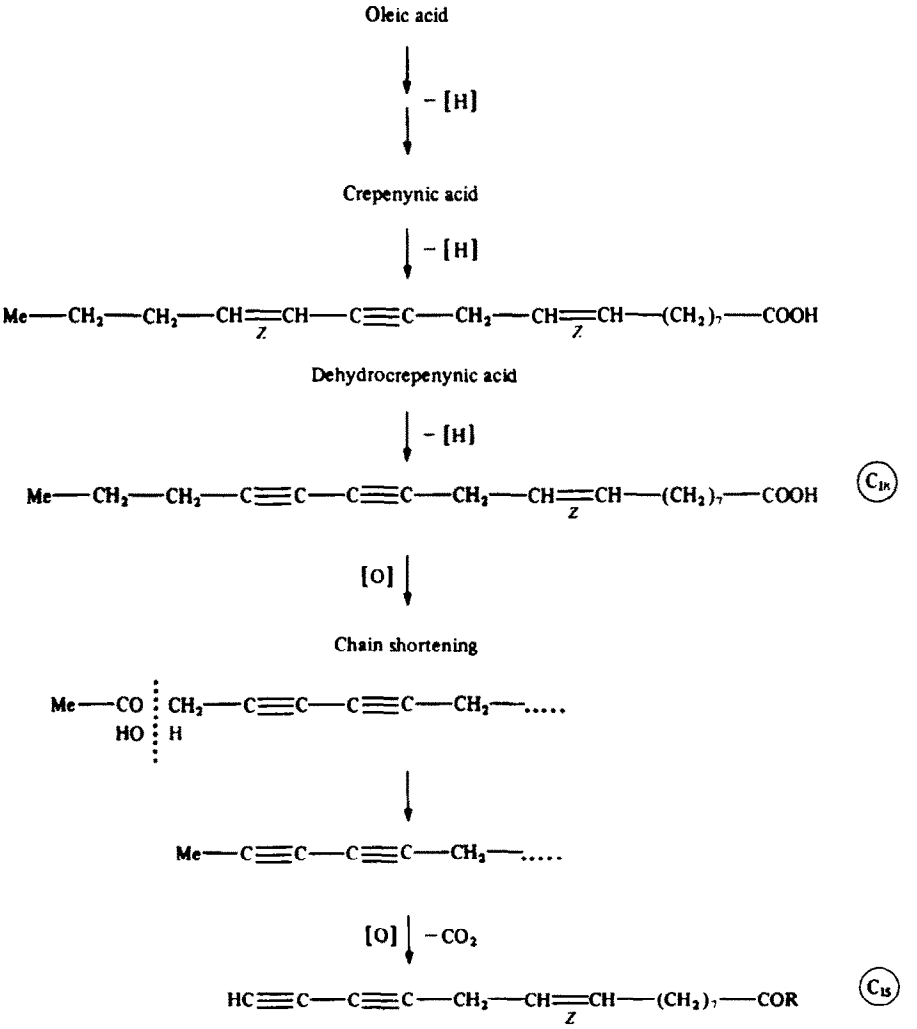


position 10–11. The second *E*-orientated double bond at position 8–9 is most likely formed via a hydroperoxide, followed by successive hydrogenation and dehydration of the corresponding alcohol [8] (Scheme 1). The major amide **14** with a 10*Z*-orientated double bond is an isomerization product of the all-*trans* derivative **13**. Compound **14** has already been isolated from *Heliopsis* species [10, 11].

Besides the C_{18} alkamides, *A. lycaonica* additionally accumulates a C_{15} piperidide (**15**). The acid moiety of this amide is already known from *Echinacea purpurea* (L.) Moench [13] where, however, it was shown to be linked with isobutylamines. Considering the biosynthetic pathway for several acetylenic amides established by feeding experiments with ^{14}C-labelled precursors [7], this type of C_{15}-derivatives may be directly derived from C_{18}-compounds with the same pattern of unsaturation. In that case, an oxidative chain shortening may occur at the methyl end of the diyne-enoic residue to split off an acetyl unit, followed by a subsequent loss of one carbon by decarboxylation (Scheme 2). This transformation of Me–C≡C– into H–C≡C– obviously represents a significant sequence in the biosynthesis of alkamides which is also supported by the frequent co-occurrence of both derivatives [1, 14, 15].

In the following section the structure elucidation of the new alkamides is outlined. Apart from the detailed discussion of the ^1H NMR data (Table 1) special attention is also paid to a systematic comparison of UV and IR data. It has been pointed out in a previous paper [16] that the characteristic absorption bands in the IR spectra show regularities which allow a rapid determination of the amine parts as well as of the configurations of the double bonds in the acid moieties (Table 2).

5: The structure of keto-amide **5** follows from combined UV, IR, ^1H NMR, and MS data. The (2*E*, 4*E*)-dienamide moiety is indicated by the typical sharp UV maximum at 252 nm, by the characteristic olefinic out of plane vibrations at 994 cm^{-1} (Table 2), and by the ^1H NMR pattern of the olefinic resonances (*dd* for 3-H at 7.20 ppm, 4-H and 5-H rather close at 6.14 and 6.05, and *d* for 2-H at 5.76; Table 1). The nature of the amide follows immediately from the ^1H NMR signals for NH (5.46 ppm), NH–C<u>H</u>$_2$–CH< (*t*, at 3.18), CH (*m* at 1.80), and 2 × Me (*d* at 0.93 ppm). In the IR spectrum the >N–H stretching at 3451 cm^{-1} (indicative for secondary amides),



Scheme 2.

Table 1. ^{1}H NMR data* of compounds 1–13 and 15 (250 MHz, δ/ppm, $CDCl_3$/TMS)

H	5	6	7	8	9	10	11	12	13	15
2	5.76 *d*	6.25 *d*	6.25 *d*	2.32 *t*	2.31 *t*	6.25 *d*	5.75 *d*	6.24 *d*	5.75 *d*	6.25 *d*
3	7.20 *dd*	6.84 *dt*	6.84 *dt*	1.50 *m*	1.50 *m*	6.83 *dt*	7.19 *dd*	6.80 *dt*	7.17 *dd*	6.83 *dt*
4	6.14 *dd*	2.19‡	2.20‡	1.33 *m*	1.34 *m*	2.20‡	6.14 *dd*	2.21‡	6.13 *dd*	2.20‡
5	6.05 *dt*	1.46 *m*	1.48 *m*	1.33 *m*	1.34 *m*	1.47 *m*	6.04 *dt*	1.45 *m*	6.03 *dt*	1.48 *m*
6	2.14 *q*	1.30 *m*	1.32 *m*	1.33 *m*	1.34 *m*	1.35 *m*	2.14 *m*	1.45 *m*	2.23 *m*	1.36 *m*
7	1.42 *m*	1.30 *m*	1.35 *m*	1.33 *m*	1.34 *m*	1.35 *m*	1.47 *m*	2.10 *m*	2.23 *m*	1.36 *m*
8	1.30 *m*	1.30 *m*	2.01 *m*	2.03‡	2.05‡	2.05‡	2.05‡	5.72 *dt*	5.68 *dt*	2.04‡
9	1.30 *m*	1.30 *m*	5.35 *m*	5.42 *m*	5.48 *m*	5.43 *t*	5.44 *m*	6.05 *dd*	6.08 *dd*	5.40 *m*
10	1.55 *m*	1.30 *m*	5.35 *m*	5.42 *m*	5.48 *m*	5.43 *t*	5.44 *m*	6.47 *dd*	6.47 *dd*	5.50 *m*
11	2.38 *t*	1.30 *m*	2.01 *m*	2.91 *m*	3.09 *m*	2.90 *m*	2.89 *m*	5.49 *d*	5.49 *d*	3.00 *d*
12	—	1.30 *m*	1.32 *m*	—	—	—	—	—	—	—
13	2.38 *t*	1.30 *m*	1.32 *m*	—	—	—	—	—	—	—
14	1.55 *m*	1.30 *m*	1.32 *m*	2.15 *tt*	5.48 *m*	2.15 *tt*	2.14 *m*	2.32 *dt*	2.30 *dt*	—
15	1.30 *m*	1.30 *m*	1.32 *m*	1.50 *m*	5.83 *dt*	1.52 *m*	1.50 *m*	1.52 *m*	1.53 *m*	1.98 *s*
16	1.30 *m*	1.30 *m*	1.32 *m*	1.33 *m*	2.27 *q*	1.35 *m*	1.30 *m*	1.35 *m*	1.33 *m*	—
17	1.30 *m*	1.30 *m*	1.32 *m*	1.33 *m*	1.34 *m*	1.35 *m*	1.30 *m*	1.35 *m*	1.33 *m*	—
18	0.88 *t*	0.89 *t*	0.90 *t*	0.90 *t*	0.93 *t*	0.90 *t*	0.87 *t*	0.90 *t*	0.89 *t*	—
1′	5.46 *t*†	—	—	—	—	—	5.45 *t*†	—	5.45 *t*†	—
2′	3.18 *t*	3.61 *m*†	3.61 *m*†	3.57 *t*†	3.56 *t*†	3.62 *m*†	3.16 *t*	3.60 *m*†	3.16 *t*	3.61 *m*†
3′	1.80 *m*	1.60 *m*	1.60 *m*	1.60 *m*	1.60 *m*	1.60 *m*	1.80 *m*	1.60 *m*	1.80 *m*	1.60 *m*
4′	0.93 *d*	1.65 *m*	1.65 *m*	1.60 *m*	1.60 *m*	1.65 *m*	0.92 *d*	1.65 *m*	1.92 *d*	1.65 *m*
5′	—	1.60 *m*	1.60 *m*	1.60 *m*	1.60 *m*	1.60 *m*	—	1.60 *m*	—	1.60 *m*
6′	—	3.50 *m*†	3.50 *m*†	3.41 *t*†	3.40 *t*†	3.50 *m*†	—	3.50 *m*†	—	3.50 *m*†

*Coupling constants (Hz): **5**: 2,3 = 4,5 = 15; 3,4 = 11; 5,6 = 6, 7 = 10, 11 = 13, 14 = 17, 18 = 1′,2′ = 2′,3′ = 3′,4′ = 7. **6**: 2,3 = 15; 3,4 = 4,5 = 17,18 = 7. **7**: 2,3 = 15; 3,4 = 4,5 = 17,18 = 7. **8**: 2,3 = 14,15 = 17,18 = 7; 11,14 = 2. **9**: 2,3 = 15,16 = 7; 14,15 = 11. **10**: 2,3 = 15; 3,4 = 4,5 = 7,8 = 8,9 = 14,15 = 17,18 = 7; 11,14 = 2. **11**: 2,3 = 4,5 = 15; 3,4 = 11; 5,6 = 17,18 = 1′,2′ = 2′,3′ = 3′,4′ = 7. **12**: 2,3 = 8,9 = 10,11 = 15; 9,10 = 11; 3,4 = 4,5 = 7,8 = 14,15 = 17,18 = 7; 11,14 = 2. **13**: 2,3 = 4,5 = 8,9 = 10,11 = 15; 3,4 = 9,10 = 11; 5,6 = 17,18 = 1′,2′ = 2′,3′ = 3′,4′ = 7; 11,14 = 2. **15**: 2,3 = 15; 3,4 = 4,5 = 7,8 = 8,9 = 10,11 = 7.

†Broad.

‡*dt* (broad pseudo q).

together with the strong bands at 2951 and 1498 cm^{-1} are typical for *all* isobutylamides in the alkamide series. The >N–C=O/C=C IR region (bands at 1673, 1636, and 1613 cm^{-1}) is also characteristic for this type of dienamides (identical pattern in this region for **5**, **11**, **13**, and **14**; Table 2). An additional keto function is indicated by the C=O frequency in the IR (1710 cm^{-1}, compare ketopiperidide **3**) and by the magnetically equivalent α-CH_2 next to C=O in the ^{1}H NMR (*t* of 4H at 2.38 ppm). The chain length is derived from the M_r (high resolution MS) and the position of the keto function follows from the fragmentation in the EIMS: the fragment m/z = 279 (rel. int. = 35%) is a product of McLafferty rearrangement caused by the loss of C_5H_{10}, which is expected for a carbonyl group at position C-12.

6: In compound **6** the (2*E*)-enamide structure is reflected in the UV spectrum (maximum at 219 nm with a shoulder at 243 nm; very similar spectra for **7** and **10**), in the IR spectrum (969 cm^{-1} in the region of =C–H out of plane, and 1654, 1615 cm^{-1} in the >N–C=O/C=C stretching region; compounds **7**, **10**, and **12** show a comparable pattern), and in the ^{1}H NMR with the characteristic olefinic protons (*dt* for 3-H at 6.84 ppm, *d* for 2-H at 6.25 ppm). The piperidide moiety is indicated by the strong band at 1428 cm^{-1} (found in *all* piperidides in the alkamide series) and by the typical resonances in the ^{1}H NMR (*m*'s at 3.60, 3.50, 1.65, and 1.60 ppm, see Table 1). The length of the aliphatic chain follows from the molecular weight (FDMS).

7: Compared with the ^{1}H NMR spectrum of **6** the additional olefinic protons of compound **7** show up as a very narrow *m* of 2H at 5.35 ppm (comparable pattern of the 9- and 10-H for compounds **7**–**11** and **15**; the *Z*-configuration, determined by oleic acid as precursor, is clear in **15** and was checked additionally for **8**, see below). The 9–10 position for the double bond was confirmed by lanthanide induced shifts (LIS) and agrees also with biosynthetic considerations. The Eu(fod)$_3$ shifts for protons 8-H to 11-H for compounds **7**, **10**, and **15** are almost identical (8-H: -15 ± 1 Hz; 9-H: -12 ± 2 Hz; 10-H: -5 ± 1 Hz; 11-H: -9 ± 1 Hz). Due to the terminal CH≡C–C≡C–CH_2–CH=CH– unit the position of the 9–10 double bond is clear for **15** and follows unambiguously for related compounds as well. In compound **8** the corresponding LIS values are somewhat different because **8** lacks the C-2–C-3 double bond; however, the LIS values are still comparable, indicating that the zig-zag arrangement for the methylene elements is similar to the geometry of the 2,3-unsaturated chain. The chain length was proved by FD- and EIMS. UV and IR of compound **7** are very similar to **6**.

8: For compound **8** the ^{1}H NMR spectrum in the olefinic region shows only the close and unresolved resonances of 9- and 10-H. However, the spectrum in C_6D_6 as solvent showed two well separated signals at 5.62 and 5.43 ppm with a vicinal coupling constant of 10 Hz, proving clearly the *Z*-configuration of the C-9–C-10 double bond. The resonance of the proton at C-11

Table 2. IR absorptions in the region 4000–400 cm^{-1} (CCl_4)

Alkamides	N–H	H–C≡	C–H stretching		C=O	O ‖ N–C–(C=C)$_n$				N–H, Piperidide C–H bend		
3			2922	2849	1709	1653			1614	1428		
5	3451	2951	2924	2852	1710	1673		1636	1613	1498		1462
6			2922	2849		1654			1615	1428		
7			2920	2849		1653			1615	1429		
8			2924	2850			1642			1429		
9			2924	2849			1641			1429		
10			2924	2849		1653			1614	1428		
11	3449	2954	2924	2865		1673		1635	1613	1499		1463
12			2926	2850		1654			1614	1428		
13	3449	2953	2922	2851		1672		1635	1613	1499		1463
14	3450	2954	2927	2867		1671		1635	1613	1500		1464
15*		3304	2926	2849		1653			1613	1429		

*C≡C stretching frequencies at 2290 and 2222 cm^{-1}.

(isolated CH_2 between a double and a triple bond) is characteristic (2.91 ppm, narrow *dt* due to long range coupling through C≡C; very similar in **10** and **11**). The 2′ and 6′ protons of the piperidide moiety are different from the usual ones (with one or more double bonds in conjugation to the amide carbonyl): the relatively narrow, clear triplets at 3.57 and 3.41 ppm are typical for piperidide alkamides with saturated C-2, C-3 positions (compare Table 1). The triple bond is indicated by the long range couplings through C≡C: 11-H (see above) and 14-H (clear *tt* at 2.15 ppm). In the IR spectrum compound **8** is characterized by only one band in the >N–C=O/C=C region (1642 cm^{-1}). In the UV the maximum at a rather short wave length (216 nm) indicates the lack of double bonds in conjugation to the amide C=O. The mass spectrum again confirmed the molecular formula and the chain length.

9: Compound **9** differs from **8** by an additional *Z*-configurated double bond in conjugation to the triple bond. One of these olefinic protons is obscured by 9-H/10-H, but the second one (15-H) is a clear *dt* at 5.83 ppm with coupling constants of 7 and 11 Hz, proving *Z*-configuration. The resonance of 11-H is shifted downfield by the additional double bond (3.09 ppm, compared to 2.91 for **8**). In the UV spectrum the maximum at 226 nm with shoulders at 217 and 235 nm is typical for an en-yne chromophor. The IR spectra of **8** and **9** are very similar. The mass spectrum is in agreement with the proposed molecular formula.

10: For compound **10** the ^{1}H NMR and the IR arguments for a C=C–CO– piperidine arrangement (compare compds **6** and **7**) and a 9*Z*-en-12-yne unit (compare **8**) may be applied for the structure elucidation (see Tables 1 and 2).

11: Compound **11** is characterized by the (2*E*,4*E*)–C=C–C=C–CO-isobutylamide partial structure and the (9*Z*)-en-12-yne unit. The former is reflected in the sharp UV maximum at 251 nm (see **5**), the IR resonances at 1673, 1635, 1613 (>N–C=O/C=C) and 994 cm^{-1} (*trans* –CH=CH–CH=CH–) (compare **5**, **13**, and **14**), and the ^{1}H NMR resonances in the olefinic region (see **5**). Most typical for the latter structural element is the methylene group at C-11 showing resonance at 2.89 ppm (compare compound **8**).

12: In compound **12** the –C=C–CO– partial structure is characterized by the IR bands at 1654 and 1614 cm^{-1} (>N–C=O/C=C stretching; compare **3**, **6**, **7**, **10**, and **15**) and the olefinic ^{1}H NMR resonances for 2-H and 3-H (see Table 1). The (8*E*,10*E*)-dien-12-yne element shows up in the UV (maximum at 265 nm; similar in **13** and **14**), in the IR (=CH out of plane at 980 cm^{-1}; found as well in **13** and **14**), and in the olefinic region of the ^{1}H NMR spectrum (Table 1). The vicinal olefinic coupling constants for all six well separated =CH– protons are 15 Hz, indicating an all *trans* configuration.

13: Compared with **12**, the acid moiety in compound **13** is further dehydrogenated to (2*E*,4*E*,8*E*,10*E*)-tetraen-12-yne. All important coupling constants may be derived from the ^{1}H NMR spectrum, proving an all *trans* configuration (compare Table 1). In the IR the >N–C=O/C=C region and the isobutylamide bands are found as usual (compare **5**). In the UV (see Experimental) both chromophors are superimposed to a rather complex pattern with prominent bands at 268 nm (dienyne, compare **12**) and a significant shoulder at 252 nm (dienone, compare **5** and **11**).

14: For compound **14** (see refs [11, 12] the ^{13}C NMR spectrum is listed in the Experimental section.

15: Compound **15** is a piperidide with a (2*E*)-double bond (IR and ^{1}H NMR; compare compound **6**). The terminal acetylenic H shows up in the ^{1}H NMR spectrum (*s* at 1.98 ppm) and in the IR (H–C≡C at 3304 and 615 cm^{-1}). The C-11 methylene resonance is a clear *d* at 3.00 ppm, the relatively narrow multiplets for 9-H and 10-H at 5.50 and 5.40 ppm prove a *Z*-configurated 9,10-double bond. The MS confirms the molecular formula and proves a chain length of C_{15} for the acid moiety.

EXPERIMENTAL

Plant material was grown from achenes received from wild collection (*Achillea lycaonica*; Turkey, Antalya, near Emali, A-1542) and from Botanical Garden (*A. chamaemelifolia*; France, Nice, A-1675). Both species were cultivated under field conditions in the Botanical Garden of the University of Vienna. Voucher specimens are deposited at the herbarium of the Institute of Botany, University of Vienna (WU).

Fresh air dried underground parts were cut into small pieces and extracted with Et_2O–petrol (60–80°) (1:2) for several days at room temp. The resulting extracts were separated first by CC (Si

									olefinic C–H out of plane					H–C≡
1363	1347	1273	1247	1213	1135		1121	1018			968		850	
1366	1339		1264			1157			994					
1363	1347	1272	1247	1213	1136		1118	1019			969		850	
1363	1347	1272	1246	1212	1136		1119	1019			968		850	
1364	1347	1277	1248	1215	1134		1124	1022			952		851	
1374	1347	1278	1248	1214	1134		1123	1021			952		851	
1362	1346	1275	1247	1212	1135		1122	1020			969		849	
1366	1335		1257			1161			994					
1363	1347	1275	1249	1213	1135		1120	1020		980			850	
1365	1336		1250			1162			993	981				
1366	1326		1260			1165			994	980		940		
1363	1347	1276	1248	1213	1136		1123	1016			970		850	615

gel) and the polar fractions (Et_2O–petrol 1:1 and Et_2O) further by (i) repeated TLC (Si gel; isolation of **5**, **11**, and **14**), (ii) MPLC (35 × 200 mm SiO_2 or reversed phase with homemade RP-8 material: Merck LiChroprep Si 60, 25–40 μm, modified with octylmethyldichlorosilane; isolation of **6**–**13**), and (iii) HPLC (4 × 250 mm Hypersil ODS 5μ; isolation of **10** and **15**).

From the more polar column fractions (Et_2O) of *A. chamaemelifolia* (78 g underground parts) 5 mg **5**, 15 mg **10**, 12 mg **11**, 30 mg **12**, 12 mg **13**, and 55 mg **14** were isolated.

From 238 g underground parts of *A. lycaonica ca.* 300 mg of a crude amide mixture was obtained from the combined column fractions. The total of the keto derivatives **1**–**4** amounted to *ca* 150 mg (erroneously stated 80 mg in ref. [3]). 18 mg of a less polar TLC fraction of the crude amide (developed with Et_2O–petrol 7:3) yielded 3 mg **6**, 2 mg **7**, 7 mg **8**, and 5 mg **9**. From other TLC fractions 4 mg of **10** and 5 mg of **15** were obtained by HPLC.

(2E)-12-*Oxo-octadec*-2-*enoic acid piperidide* (**3**). See ref. [3]; UV $\lambda_{max}^{Et_2O}$ nm: 243 sh, 216.

(2E,4E)-12-*Oxo-octadeca*-2,4-*dienoic acid isobutylamide* (**5**). Colourless crystals, mp 102–104°; UV $\lambda_{max}^{Et_2O}$ nm: 252; MS *m/z* (rel. int.): 349.298 (11) $[M]^+$ (calc. for $C_{22}H_{39}NO_2$: 349.2981), 279 (35) $[M-C_5H_{10}]^+$ (McLafferty rearrangement), 209 (28), 167 (32), 149 (28), 125 (44), 113 (60), 111 (48), 107 (51), 99 (34), 97 (88).

(2E)-*Octadec*-2-*enoic acid piperidide* (**6**). Colourless oil; UV $\lambda_{max}^{Et_2O}$ nm: 243 sh, 219; MS *m/z* (rel. int.): 349.335 (3) $[M]^+$ (calc. for $C_{23}H_{43}NO$: 349.3345), 178 (18), 138 (100) $[CH{=}CHCONC_5H_{10}]^+$, 112 (35) $[CO{-}NC_5H_{10}]^+$, 84 (41) $[NC_5H_{10}]^+$; FDMS *m/z* (rel. int.): 350 (47) $[M+1]^+$, 349 (100) $[M]^+$.

(2E,9Z)-*Octadeca*-2,9-*dienoic acid piperidide* (**7**). Colourless oil; UV $\lambda_{max}^{Et_2O}$ nm: 242 sh, 218; MS *m/z* (rel. int.): 347.319 (3) $[M]^+$ (calc. for $C_{23}H_{41}NO$: 347.3188), 138 (60) $[CH{=}CHCONC_5H_{10}]^+$, 127 (100) $[CH_2{=}C(OH){-}NC_5H_{10}]^+$, 112 (29) $[CO{-}NC_5H_{10}]^+$, 84 (41) $[NC_5H_{10}]^+$; FDMS *m/z* (rel. int.): 348 (63) $[M+1]^+$, 347 (100) $[M]^+$; ^1H LIS [250 MHz, $CDCl_3$ $Eu(fod)_3$, extrapolated to the 1:1 complex, in Hz]: −14 (8-H), −12 (9-H), −6 (10-H), −10 (11-H).

(9Z)-*Octadec*-9-*en*-12-*ynoic acid piperidide* (**8**). Colourless oil; UV $\lambda_{max}^{Et_2O}$ nm: 235 v.w.sh, 226 v.w.sh, 216; MS *m/z* (rel. int.): 345.303 (6) $[M]^+$ (calc. for $C_{23}H_{39}NO$: 345.3032), 127 (100) $[CH_2{=}C(OH){-}NC_5H_{10}]^+$ (McLafferty), 112 (25) $[CO{-}NC_5H_{10}]^+$, 84 (34) $[NC_5H_{10}]^+$; FDMS *m/z* (rel. int.): 346 (69) $[M+1]^+$, 345 (100) $[M]^+$; ^1H NMR (250 MHz, in C_6D_6) δ/ppm: 5.62 (*dt*, 1H, J = 10 and 7 Hz, 10-H), 5.43 (*dt*, 1H, J = 10 and 7 Hz, 9-H), 3.51 (*br. t*, 2H, $N{-}CH_2$), 2.97 (*br. d*, 2H, 11-H), 2.83 (*br. t*, 2H, $N{-}CH_2$), 2.11 (*tt*, 2H, 14-H), 2.06 (*t*, 2H, 2-H), 1.93 (*br. pseudo q*, 2H, 8-H), 1.74 (*m*, 2H) and 1.05–1.45 (*m*, 20 H) (H nos 3–7, 15–17, and 3'–5'), 0.84 (*t*, 3H, Me); ^1H LIS [250 MHz, $CDCl_3$, $Eu(fod)_3$, extrapolated to the 1:1 complex, in Hz]: −16 (8-H), −16 (9-H), −14(10-H), −12(11-H).

(9Z,14Z)-*Octadeca*-9,14-*dien*-12-*ynoic acid piperidide* (**9**). Colourless oil; UV $\lambda_{max}^{Et_2O}$ nm: 235 sh, 226, 217 sh; MS *m/z* (rel. int.): 343.288 (5) $[M]^+$ (calc. for $C_{23}H_{37}NO$: 343.2875), 138 (77) $[CH{=}CHCONC_5H_{10}]^+$, 127 (100) $[CH_2{=}C(OH){-}NC_5H_{10}]^+$, 112 (22) $[CO{-}NC_5H_{10}]^+$, 84 (29) $[NC_5H_{10}]^+$. FDMS *m/z* (rel. int.): 344 (63) $[M+1]^+$, 343 (100) $[M]^+$.

(2E,9Z)-*Octadeca*-2,9-*dien*-12-*ynoic acid piperidide* (**10**). Colourless oil; UV $\lambda_{max}^{Et_2O}$ nm: 238 sh, 219; MS *m/z* (rel. int.): 343.287 (2.5) $[M]^+$ (calc. for $C_{23}H_{37}NO$: 343.2875), 138 (100) $[CH{=}CHCONC_5H_{10}]^+$, 127 (80) $[CH_2{=}C(OH){-}NC_5H_{10}]^+$, 112 (27) $[CO{-}NC_5H_{10}]^+$, 84 (36) $[NC_5H_{10}]^+$; FDMS *m/z* (rel. int.): 344 (92) $[M+1]^+$, 343 (100) $[M]^+$. ^1H LIS [250 MHz, $CDCl_3$, $Eu(fod)_3$, extrapolated to the 1:1 complex, in Hz]: −16 (8-H), −10 (9-H), −4 (10-H), −8 (11-H).

(2E,4E,9Z)-*Octadeca*-2,4,9-*trien*-12-*ynoic acid isobutylamide* (**11**). Colourless oil; UV $\lambda_{max}^{Et_2O}$ nm: 251; MS *m/z* (rel. int.): 329.272 (4) $[M]^+$ (calc. for $C_{22}H_{35}NO$: 329.2719), 261 (12), 233 (9), 148 (18), 91 (65), 67 (100) $[C_5H_7]^+$; FDMS *m/z* (rel. int.): 330 (58) $[M+1]^+$, 329 (100) $[M]^+$.

(2E,8E,10E)-*Octadeca*-2,8,10-*trien*-12-*ynoic acid piperidide* (**12**). Colourless oil; UV $\lambda_{max}^{Et_2O}$ nm: 276 (smaller max.), 265 (main max.), 256 v.w.sh; MS *m/z* (rel. int.): 341.272 (6) $[M]^+$ (calc. for $C_{23}H_{35}NO$: 341.2719), 186 (18), 127 (100) $[CH_2{=}C(OH){-}NC_5H_{10}]^+$, 112 (23) $[CO{-}NC_5H_{10}]^+$, 84 (27) $[NC_5H_{10}]^+$; FDMS *m/z* (rel. int.): 342 (42) $[M+1]^+$, 341 (100) $[M]^+$.

(2E,4E,8E,10E)-*Octadeca*-2,4,8,10-*tetraen*-12-*ynoic acid isobutylamide* (**13**). Colourless crystals, mp 123–125°C, UV $\lambda_{max}^{Et_2O}$ nm: 278 (smaller max.), 268 (main max.), 252 (st. sh); MS *m/z* (rel. int.): 327.256 (3) $[M]^+$ (calc. for $C_{22}H_{33}NO$: 327.2562), 259 (5), 231 (10), 146 (25), 91 (54), 67 (100) $[C_5H_7]^+$; FDMS *m/z* (rel. int.): 328 (43) $[M+1]^+$, 327 (100) $[M]^+$.

(2E,4E,8E,10Z)-*Octadeca*-2,4,8,10-*tetraen*-12-*ynoic acid isobutylamide* (**14**). See refs. [10, 11]; UV $\lambda_{max}^{Et_2O}$ nm: 283 v.w.sh, 263 (main max.), 254 (max.); ^{13}C NMR ($CDCl_3$, TMS) δ/ppm: 166.3 (*s*, CO), 141.5 (*d*, C-5), 140.9 (*d*, C-3), 138.6, 135.9, 128.9, 128.6 (all *d*, C-10, C-9, C-8, C-4), 122.4 (*d*, C-2), 108.3 (*d*, C-11), 96.6 (*s*, ≡C–), 47.0 (*t*, C-1'), 32.5 (*t*, C-6), 32.1, 31.1, 28.6 (all *t*, C-7, C-15, C-16), 28.7 (*d*, C-2'), 22.2 (*t*, C-17), 20.1 (*q*, C-3'), 19.7 (*t*, C-14), 14.0 (*q*, C-18), compare ref. [17].

(2E,9Z)-*Pentadeca-2,9-dien-12,14-diynoic acid piperidide* (**15**). Colourless crystals, mp 110–112°; UV $\lambda_{max}^{Et_2O}$ nm: 250 w. sh, 238 sh, 218; MS *m/z* (rel. int.): 297.209 (6) $[M]^+$ (calc. for $C_{20}H_{27}NO$: 297.2093), 214 (15), 166 (13) $[CH_2CH_2CH=CH-CO-NC_5H_{10}]^+$, 138 (47) $[CH=CH-CO-NC_5H_{10}]^+$, 129 (14), 128 (11), 115 (13), 112 (29) $[CO-NC_5H_{10}]^+$, 91 (19), 84 (100) $[NC_5H_{10}]^+$; ^1H LIS [250 MHz, $CDCl_3$, Eu(fod)$_3$, extrapolated to the 1:1 complex, in Hz]: −16 (8-H), −10 (9-H), −6 (10-H), −8 (11-H).

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