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^{13}C NMR AND ^{1}H LANTHANIDE INDUCED SHIFTS OF NATURALLY OCCURRING ALKAMIDES WITH CYCLIC AMIDE MOIETIES - AMIDES FROM ACHILLEA FALCATA

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Abstract – The ^{13}C NMR spectra of 12 alkamides, especially of piperidides and piperideides isolated from different *Achillea* species were recorded. Assignments were based on systematic comparisons within the series of spectra and on selective ^{13}C-{^{1}H} decoupling experiments. Due to the dynamic behaviour of α,β-unsaturated 5- and 6-ring amides some carbon atoms of the cyclic amine moiety and the acid rest give rise to rather broad signals. Complementary information on the conformation of the amide bond and the geometry of the acid chain was obtained by means of ^{1}H-lanthanide induced shifts (LIS).
A re-investigation of the roots of *Achillea falcata* afforded in addition to known olefinic C10-carbonic acid amides a further new derivative of that series, 2E,4E,8Z-deca-2,4,8-trienoic acid piperideide, together with three known acetylenic C11-carbonic acid amides, all derived from 2E,4E-undeca-2,4-diene-8,10-diynoic acid.

At present the alkamides comprise a class of about 80 closely related unsaturated fatty acid amides with variable acid and amine parts. Since these compounds have been shown to possess considerable biological activity, interest in this group of naturally occurring amides has been growing continuously. For a recent review on structural relationships, distribution and biological activity of alkamides see Ref.[1].

^{1}H NMR spectra are usually well documented – at least in the most recent literature. However, data on ^{13}C NMR are rather scarce. Yasuda et al.[2-4] have reported and discussed the ^{13}C NMR of several C10-, C12-, and C14-acid isobutyl amides; Banerji et al.[5] have repeated the data for one isobutyl amide which has been treated already in Ref.[3]. All this literature is only concerned with isobutylamides, up to date no ^{13}C NMR spectra for the most interesting saturated and unsaturated 5- and 6-ring amides (pyrrolidides, pyrrolideides, piperidides, and piperideides) are reported. One reason might be the difficulty to obtain a sufficient amount of material of some of these rather rare natural products. For the cyclic amides this lack of material complicates matters considerably because some of the ^{13}C resonances appear as very broad and hardly detectable signals – especially in diluted solutions (3-5 mg / 0.5 ml $CDCl_3$).

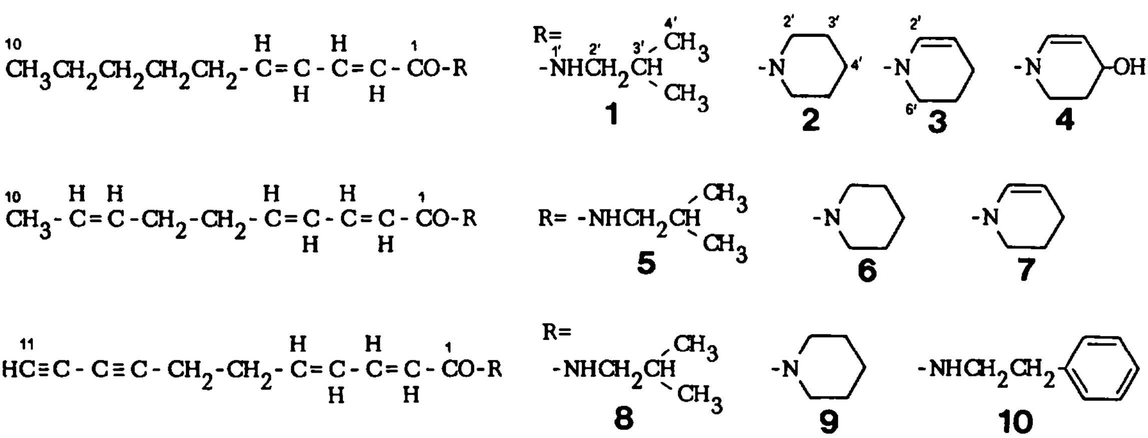
However, a systematic study of a set of suitable compounds (some of them available in "large" amounts up to 20 mg) allowed clear and unambiguous assignments in most cases.

Typical for the spectra are rather broad signals for the carbon atoms of the cyclic amide moiety and — in case of unsaturated cyclic amides — for carbon at position 3 of the acid rest. The reason for this behaviour is the hindered rotation about the amide C–N bond, leading to magnetic non-equivalence of α- and ß-C in the cyclic amides and to two conformers (rotamers) for the α,ß-unsaturated 5- and 6-ring amides. The broad lines are therefore the result of the usual N-quadrupole relaxation and the dynamic behaviour of the alkamides with coalescence temperatures not far above room temperature[6]. The lanthanide induced shift technique (^{1}H-LIS) was used to identify the rotamers and to obtain information on the stereochemistry of the amide bond and — to some extent — of the unsaturated fatty acid chain moiety of several representative alkamides. In one example the LIS method was tested as well for the assignment of the ^{13}C NMR resonances.

The alkamide samples have been obtained from different plant sources. However, in continuation of current studies on secondary constituents of the genus *Achillea* (*Asteraceae-Anthemideae*) we report in this paper additional material for the completion of the analysis of unsaturated alkamides from the roots of *Achillea falcata* L. The most interesting result with this respect was the isolation of three C11-acetylenic carbonic acid amides (so far unknown for *A. falcata*) and one new C10-olefinic piperideide; for previously isolated alkamides from *A. falcata* see Ref.[7]. Supplementary ^{1}H NMR data on the complete set of alkamides from *A. falcata* are included in the present report.

^{13}C NMR Spectra

Table 1 records the chemical shifts of 12 alkamides from different natural sources (see Exp.). The multiplicities of the signals — determined by J-modulation — were in accordance with the proposed assignments. In many cases the assignments follow directly from the comparison of closely related structures, in several cases selective ^{13}C-{^{1}H} decoupling experiments were used; the latter is especially useful for C-3, since the corresponding olefinic proton resonance of 3-H is well separated from all other olefinic signals. In one case (compound 17) ^{13}C-lanthanide induced shifts were used to confirm the assignments; however,

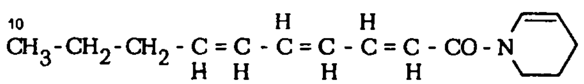


this method is of limited use for the stretched chain structures of alkamides, since induced shifts less than 0.2-0.3 ppm are not reliable on the ^{13}C NMR scale and therefore all carbons more distant than ca. 5 bonds from the coordinating amide-carbonyl group show no significant lanthanide induced shifts (compare Tab. 1, footnote [e]). For all compounds the assignment was additionally checked using a computer program with a data base containing carbon-centered substructural environments[8].

Amine Moieties

Up to date only ^{13}C NMR spectra of isobutyl amides have been reported in literature[2-5]. We will therefore focus our attention to the cyclic amides: piperidides (2, 12, 14 - 16), piperideides (3, 7, 11), pyrrolidides (13), and pyrrolideides (17). A special feature of the cyclic amides is caused by the partial double bond character of the C–N bond.

In the piperidides two distinct (although very broad) signals appear for the two different α-carbons (C-2′ and C-6′, syn or anti to the carbonyl oxygen at 47 and 44 ppm, respectively). The two β-C signals (C-3′ and C-5′) are found at 26-27 ppm (always very broad; two distinct signals for amides 12, 14, and 16, only one very broad signal for 2 and 15 (see Tab. 1). The C-4′ signals of the piperidides were found to be intense and sharp in all cases (24.7 ppm); the carbon atom in para position to the nitrogen atom is unaffected by the dynamic behaviour of the amide bond. Compound 16 was especially advantageous for the identification of the piperidide resonances because no other $-CH_2-$ triplets were present in the molecule.



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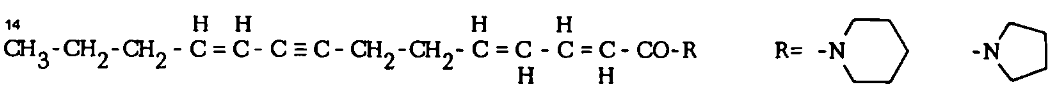

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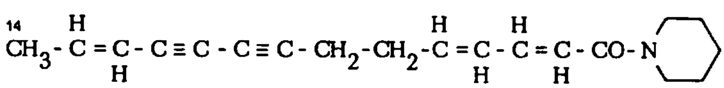

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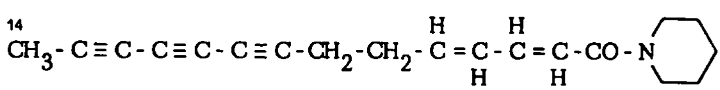

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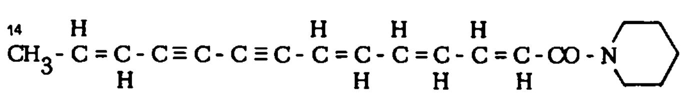

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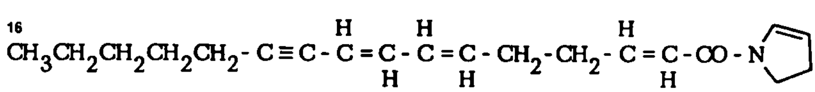

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In piperideides 3, 7, and 11 matters are more complicated. The two possible conformations (populated differently, see Ref.[9] and discussion of the lanthanide induced shifts) should produce two different sets of data for C-2′ - C-6′ (compare Fig. 3). Indeed, the olefinic signals C-2′ and C-3′ appear either very broad with a clearly unsymmetric curvature (a shoulder for the less favoured rotamer; see Fig.1, 3) or at distinctly different chemical shifts for the s-E and s-Z amide (Fig.1, compound 7). C-6′ shows distinctly separated signals in all cases, the shift difference for s-E and s-Z beeing 2.5 ppm. The signals for C-4′ and C-5′ are very close, giving a relatively intense and broad signal at 22 ppm.

The identification of the pyrrolidide resonances of compound 13 was particularly convenient by comparison with 12 (identical acid component). In contrast to the six-ring amides the four resonances of the pyrrolidide moiety of 13 are all represented by clear and sharp signals at 46.5 and 45.9 ppm (C-2′ syn and C-5′ anti to the carbonyl oxygen), and 26.2 and 24.4 ppm (C-3′ syn and C-4′ anti).

Table 1. ^{13}C NMR data of alkamides 2, 3, 5, 7, and 10-17 ($CDCl_3$, δ /ppm)

No.	2	3	5	7	10	11	12	13	14	15	16	17
1	166.0	164.7	166.5	165.0	166.0	165.0	165.7	165.1	165.5	165.5	165.0	165.5
2	118.7	118.0	122.2	118.6	123.2	119.3	119.7	120.9	120.0	120.3	123.0	121.8[a]
3	142.8	143.9[a]	141.1	144.1[a]	138.9	143.9 143.6[a]	142.2	141.7	141.9	141.7	143.5	145 146[a]
4	128.9	128.9	128.6	129.6[b]	129.9	130.2	130.0	129.9	130.3	130.5	133.9	31.5[b]
5	142.4	143.6	142.1	143.1	140.4	135.3[b]	139.7	140.2	138.7	138.2	141.2	32.1[b]
6	32.9	33.0	32.8	33.2	31.3	128.3	32.3	32.3	31.6	31.4	137.0	134.3[c]
7	28.5	28.5	26.2	26.6	18.9	136.9[b]	19.4	19.3	19.4	19.3	112.9	131.0[c]
8	31.4	31.4	129.3	129.5[b]	75.0[b]	30.1	78.3	78.3	66.0[b]	75.2[b]	72.6[b]	140.3
9	22.5	22.5	124.7	125.1	68.4[b]	22.7	92.9	92.9	72.5[b]	61.1[b]	79.0[b]	110.7
10	13.9	13.9	12.8	15.6	65.7[b]	13.7	109.4	109.3	74.4[b]	65.0[b]	80.3[b]	80.0
11	–	–	–	–	65.0	–	142.8	142.8	82.0[b]	66.6[b]	83.1[b]	65.0
12	–	–	–	–	–	–	32.1	32.1	109.9	59.7[b]	110.1	19.7
13	–	–	–	–	–	–	22.2	22.1	143.2	?[f]	143.8	28.6
14	–	–	–	–	–	–	13.7	13.7	18.8	4.4	18.9	31.2[b]
15	–	–	–	–	–	–	–	–	–	–	–	22.2
16	–	–	–	–	–	–	–	–	–	–	–	13.8
2′	47.0[a]	125.5 125.1	47.0	125.9	40.7	125.4 124.8	47.0[a]	46.5	47.0[a]	47.0[a]	47.0[a]	130.5 129.5[a]
3′	26.2[a]	108.6 108.2	28.7	109.5 108.6	35.8	109.2 108.4	27 25.5[a]	26.2	27 26[a]	26.5[a]	27.0[a]	111.5 110.8[a]
4′	24.7	22.0	20.1	22.3[a]	138.9	22.0[c]	24.7	24.4	24.7	24.7	24.7	26.5[a]
5′	26.2[a]	22.0	–	22.3[a]	128.7[c]	21.8[c]	26.5[a]	45.9	26.0[a]	26.5[a]	26.0[a]	45.4[a]
6′	43.5[a]	43.9 40.8	–	43.5 41.0	128.8[c]	43.5 40.8	43.5[a]	–	44.0[a]	43.5[a]	44.0[a]	–
7′	–	–	–	–	126.6	–	–	–	–	–	–	–

[a] Small and broad; [b,c] interchangeable; [d] obscured by C-9; [e] LIS values: 3.1 (C-2), 12.0 (C-3), 0.50 (C-4), 3.3 (C-5), 0.3 (C-6), 11.0 (C-2′), 2.2 (C-3′), 3.3 (C-4′), 5.2 (C-5′), all others < 0.2 ppm; [f] obscured by $CDCl_3$.

(compare Tab.1 and Fig.2, 13). The assignments are supported by the ^{13}C-lanthanide induced shifts: large LIS value for C-2′, compared to C-5′; and a larger value for C-4′, compared to C-3′ (see Tab.1, footnote[e]). The interpretation of the C-α pair (C-2′ and C-5′) is plausible and straightforward, the larger value for C-3′ (anti to C=O) is a consequence of the angular dependence of lanthanide induced shifts; the somewhat more distant C-3′ is – due to the smaller deviation from the C=O axis – in a favourable position with respect to the paramagnetic field strengh. The same effect is found for all ß-protons of cyclic alkamides (compare Tab.2, exp. and calc. ^{1}H-LIS).

Contrary to the sharp pyrrolidide resonances, the pyrrolideide resonances of compound 17 are all broad and rather weak. C-2′ and C-3′ give rise to four extremely broad signals in the olefinic region (corresponding to the s-E and s-Z rotamers, see Fig.2, 17). For C-5′ only one fairly broad signal was found at 45.4 ppm. The signal for C-4′ was again broad and very weak (one signal at 26.5 ppm). However, the available amount of pure compound 17 was small (ca. 3 mg) and the signal-to-noise ratio was therefore rather unfavourable. A larger quantity of one of these rare and rather unstable pyrrolideide amides may facilitate a detailled analysis of the ^{13}C resonances.

A c i d   M o i e t i e s

Most of the compounds included in Table 1 are characterized by a 2E,4E-diene arrangement, followed by two methylene groups at positions 6 and 7. For these compounds the assignment of C-2 (at ca. 120 ppm) and C-4 (at ca. 130 ppm) is straightforward, C-3 and C-5 lie close together in the range of 138-144 ppm. C-5 is sensitive to the high field shifts caused by 8,9-triple bonds (acting through

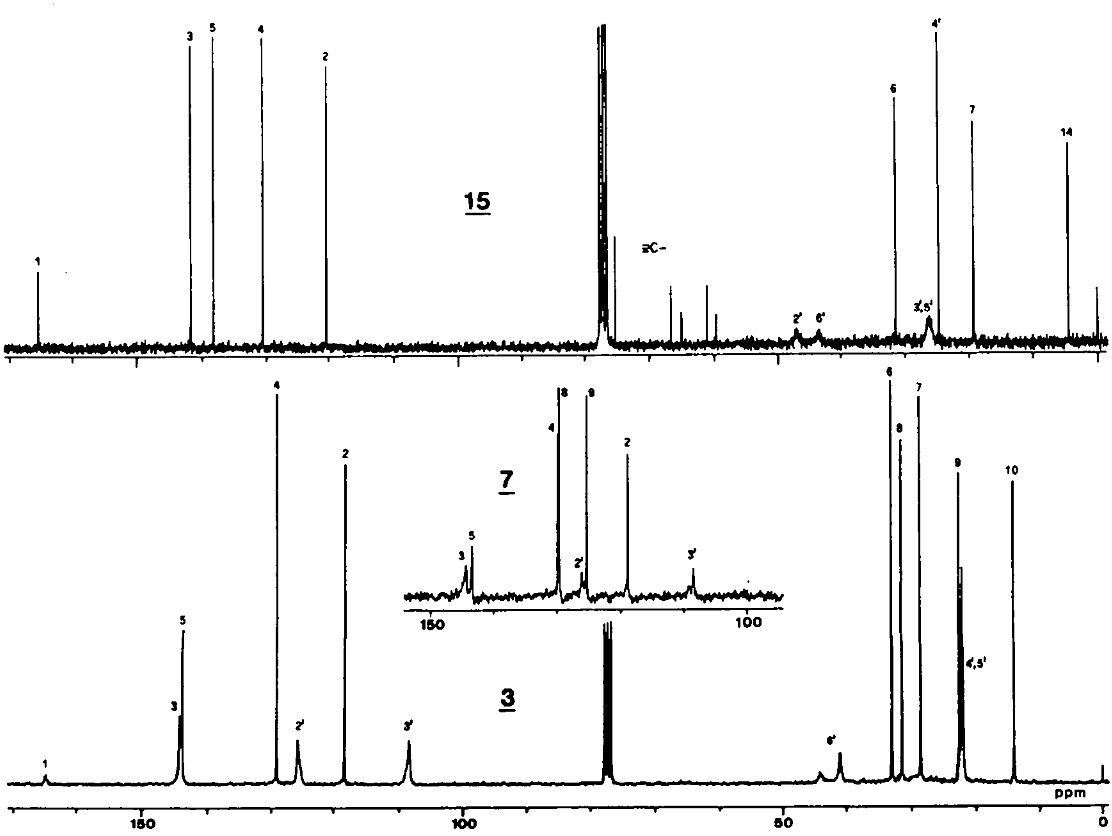

Fig. 1. ^{13}C NMR of piperidide 15 and piperideide 3 (+olefinic region of piperideide 7)

the 6,7-dimethylene groups): 138-140 ppm for compounds 12, 14, and 15, compared to 142-144 ppm for 2, 3, and 7. Most C-5 resonances were assigned unambiguously by selective $^{13}C-\{^1H\}$ decoupling.

The C-3 resonances for all α,β-unsaturated cyclic alkamides (piperideides 3, 7, 11, and pyrrolideide 17) are rather broad. In case of 11 and 17 carbon-3 for the two possible rotamers give rise to two close, but still clearly separated signals. Obviously (i) the conformational equilibrium of the two rotamers is slow enough on the NMR time scale and (ii) the shift differences for the rotamers are large enough for a clear separation of the signals (see Fig. 1, 3 and 7; and Fig.2, compound 17). Even C-5, which is quite distant from the amide bond, shows a significant broadening in the ^{13}C NMR spectra of all unsaturated amides. It is remarkable that C-2 shows only little broadening and C-4 reaches the usual height for olefinic carbons in the broad band decoupled spectra. The average ratio of signal heights for comparable compounds 3, 7, and 11 is: 0.17 (± 0.01) / 1.00 / 0.36 (±0.04) / 0.80 (±0.07) for carbons no. 2 / 3 / 4 / 5 (compare Fig.1, compound 3).

This signal broadening must be an effect caused by different conformers, because in the case of saturated cyclic amides the signals for C-2 – C-5 are all equal in height (see Fig.1, 15). In principle four geometries are possible for 2Z,4Z-dienoic acid amides: (a) and (b) with the C=N partial double bond in all s-trans conformation with the other double bonds; and (c), (d) with C=O in zig-zag arrangement with the C=C double bonds of the acid moiety (Fig.3). Since the broadening effect is much stronger for C-3 and C-5 (than for C-2 and C-4) one should expect conformers where these atoms are close to the conformationally changing unsaturated amine moiety; rotamers (c) and (d) fulfill these requirements. On the other hand, sterical reasons are clearly in favour of rotamers (a) and (b). NOE and lanthanide induced shift experiments indicated clearly that only conformations (a) and (b) are appreciably populated in the cyclic amides.

NOE experiments for compound 3 showed a strong effect between 2′-H and 2-H and no effect between 2′-H and 3′-H. However, due to signal overlap the ^1H resonances were not well suited for a detailled NOE analysis. So the results were additionally confirmed by lanthanide induced shifts (LIS) data. The conformational analysis of compounds 2, 3, 13, and 17 showed unambiguously that only rotamers (a) and (b) were of importance in the conformational equilibria of cyclic amides: the LIS values for 3-H were in all cases larger than for 2-H and the LIS values for 5-H were negative (upfield) for the 2E,4E-dienoic acid amides 2, 3, and 13 (compare Tab.2). Especially the negative LIS values provide clear evidence for rotamers (a) and (b), because only in these rotamers the angular dependence of the dipolar paramagnetic field of the lanthanide ion is able to dominate the induced shift (for details see below).

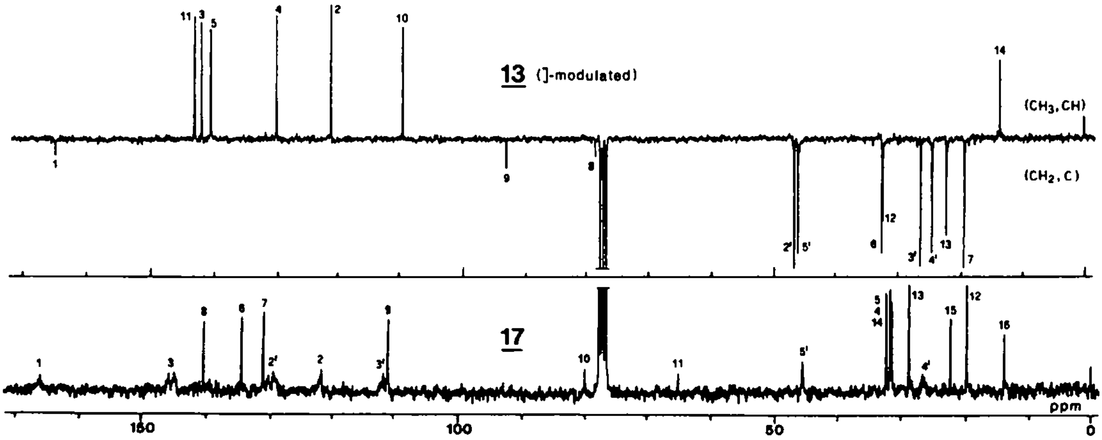

Fig. 2. ^{13}C NMR of pyrrolidide 13 and pyrrolideide 17

The assignment of the other olefinic doublets and aliphatic triplets followed general rules of ^{13}C NMR spectroscopy. The upfield shift of carbon resonances next to triple bonds is useful for the identification of resonances in the acetylenic fatty acid residues of these compounds: for instance the olefinic CH in 12-14, and 17, with typical doublets at ca. 110 ppm (compound 12, C-10; 13, C-10; 14, C-12; 17, C-9); and the aliphatic CH_2 for 10, 12, 14, 15, and 17, with triplets at ca. 19 ppm, compared to the usual 33 ppm (compound 10, C-7; 12, C-7; 14, C-7; 15, C-7; 17, C-12). (For the assignments of olefinic carbon resonances for 17 with only one double bond in conjugation to C=O compare also Ref.[4]).

In case of Z-configurated double bonds the adjacent $-CH_2-$ groups appear at higher field[3] [e.g. C-7 at 26.2 (5) or 26.6 (7)], compared to the usual value of 33 ppm in E-configurated moieties. However, if an acetylenic group is directly attached to the cis-double bond, the corresponding $-CH_2-$ carbon (C-12 in 12 and 13) remains at ca. 33 ppm.

Lanthanide Induced Shifts

Table 2 lists the ^1H-LIS values for piperidide 2, piperideide 3, pyrrolidide 13, and pyrrolideide 17.

In case of the unsaturated amides 3 and 17 two sets of LIS values can be determined according to the two different rotamers. The identification of the rotamers is straightforward. The more intense ^1H signals can be attributed to the s-E conformer: large LIS values for C-6′ (compound 3) and C-5′ (17), and small values for C-2′. For both types of unsaturated amides (5- and 6-ring) the population ratios are 58 : 42 % ($\pm$ 3%) in favour of the s-E rotamer. This agrees with the conclusions drawn previously for piperideides, using acetic acid piperideide as a model compound for lanthanide induced shift measurements[9].

For the acid moieties of 3 and 17 the LIS values of the two rotamers are practically identical; however, the shifted signals are rather broad and may hide some fine structure for a small separation of signals for the two rotamers; especially for 2-H and 3-H the lanthanide shifted resonance signals are extremely broad, even at very low reagent concentrations ($L_0:S_0 < 0.1$).

The most striking feature of the 2E,4E-dienoic acid amides 2, 3, and 17 is the negative LIS value for all protons in the fatty acid chain (except for positions 2, 3, and 4). This is only possible for the geometries of rotamers (a) and (b) with the coordinating C=O group "rectangular" to the aliphatic chain (see Fig.3). For (c) and (d) no negative LIS values are possible for reasonable lanthanide ion

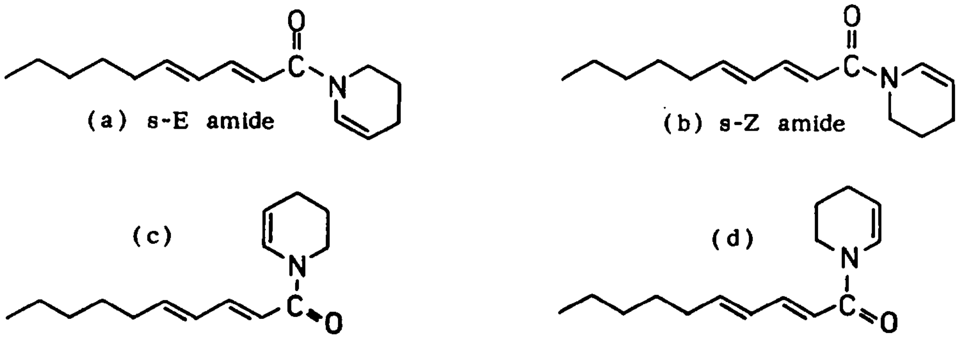

Fig. 3. Possible conformers for piperideide 3

positions within the substrate-reagent complex. This was checked quantitatively by LIS calculations using the McConnell-Robertson equation. Table 2 includes the results for compounds 2 and 3 (3 in s-E conformation). The good agreement between the calculated and the experimental values proves that other conformations than (a) and (b) (see Fig.3) are not important in the equilibrium.

The calculations [10,11] were carried out assuming an average position for the magnetically equivalent protons of methylene and methyl groups (one LIS value corresponding to one particular average position) and adopting an idealized zig-zag chain for the acid rest (as shown in Fig.3). A more sophisticated treatment of the geometrical parameters may increase the quality of the LIS simulation and, most interesting, may provide further details of the conformations of the different fatty acid residues in the molecules. Some preliminary conclusions may be drawn directly from the data presented in Table 2. For compound 13 the LIS values for the olefinic protons at C-10 and C-11 are still negative (-0.33 and -0.20 ppm), the value for 12-H is 0.00 ppm, 13-H and 14-H show positive values, indicating that a bend of the chain, away from the coordinating C=O, must have taken place (at least for the average of possible conformations). In compound 17 (only one double bond in conjugation with C=O) this bending occurs already between the bonds C3-C4 or C4-C5 (gauche and anti conformations). However, a careful conformational analysis needs a rather extensive computational study of possible conformations contributing to the averaged LIS values, to account for all substrate-reagent complexes which are present in the equilibrium in solution.

Table 2. LIS data[a] for piperidide 2, piperideide 3, pyrrolidide 13, and pyrrolideide 17

No.	2	3 s-Z	3 s-E	13	17 s-Z	17 s-E	2 calc.[f]	3 (s-E) calc.[g]
2	7.00	7.00		7.00	7.00		7.34	7.43
3	10.07	10.08		11.26	9.41		10.26	10.46
4	2.05	2.16		2.70	1.63		2.16	2.20
5	−2.26	−1.62		−1.60	0.47		−3.05	−2.22
6	−0.40	−0.09		−0.16	0.59		−0.30	−0.14
7	b	−0.55		−0.45	0.39		h	i
8	b	c		–	0.23		h	i
9	b	c		–	0.23		h	i
10	−0.45	−0.38		−0.33	–		−0.38	−0.33
11	–	–		−0.20	–		–	–
12	–	–		d	e		–	–
2'	12.91	15.62	6.02	16.91	13.74	5.00	11.98	6.09
3'	3.21	1.60	2.97	3.68	1.82	2.18	3.05	2.46
4'	2.73	2.09	1.97	3.93	2.12	1.45	2.49	2.12
5'	3.65	2.95	2.23	6.92	5.48	10.33	3.17	2.36
6'	5.56	5.41	12.45	–	–	–	6.58	11.73

[a]In ppm, extrapolated to the 1:1 complex; [b,c]not resolved, values ca. -0.6 ± 0.2 (2) and -0.35±0.1 (3); [d]values for 12-H: ±0.0, 13-H: 0.12, 14-H: 0.23; [e]values for 12-H: 0.05, 13-H – 16-H: <0.02; [f]agreement factor R= 8.8 % for d= 2.7 Å, ρ = 20°, φ = 120° (definition of the parameters see Ref.[10,11]); [g]R= 6.4 %, d= 2.6 Å, ρ= 30°, φ= 100°; [h,i]values not used in the calculation.

Amides from Achillea falcata

In a previous paper[7] the isolation and identification of six olefinic C10-carbonic acid amides (1-6) from the roots of *Achillea falcata* L. originating from Turkey were reported. Continuing this analysis, we have now isolated four further alkamides (7-10) from the same provenance (A-1541). The unpolar fractions afforded the previously unreported piperideide 7. Its structure was derived from the ^{1}H and ^{13}C NMR spectra. The chemical shifts and the coupling constants for the olefinic protons and the ^{13}C shifts were typical for 2E,4E and one additional Z orientated double bond. The multiplet of 4 H at δ= 2.20 ppm was characteristic for a =CH-CH_2-CH_2-CH= arrangement and the doublet of 3 H at 1.62 ppm for a terminal =CH-CH_3. The amine moiety showed the typical resonance pattern for piperideides[9,12], which is characterized by the occurrence of two rotamers (about the -OC═N< bond) with a population ratio of ca. 65 : 35 % in favour of the s-E rotamer (compare Fig.3). The two rotamers lead to two different resonance signals for 2′-H, 3′-H, and 6′-H; the 4′ and 5′ protons, and the protons of the acid moiety close to the amide linkage show only slight broadening. The structure of compound 7 was supported by ^{13}C NMR, MS (characteristic fragments, high resolution, see Exp.), UV, and IR.

From the more polar fractions compounds 8-10 have been isolated, which have proved to be acetylenic amides uniformly containing 2E,4E-undeca-2,4-diene-8,10-diynoic acid moieties. Whereas the isobutylamide 8 has already been reported for

Table 3. ^{1}H NMR data of alkamides 1, 2, 5, and 7-10 ($CDCl_3$, δ /ppm)

No.	1	2	5	7	8	9	10
2-H	5.77 (d)	6.26 (d)	5.77 (d)	6.28 (d)	5.81 (d)	6.33 (d)	5.75 (d)
3-H	7.20 (dd)	7.25 (dd)	7.23 (dd)	7.28 (dd)	7.20 (dd)	7.24 (dd)	7.19 (dd)
4-H	6.15 (dd)	6.18 (dd)	6.15 (dd)	6.24 (dd)	6.20 (dd)	6.25 (dd)	6.18 (dd)
5-H	6.07 (dt)	6.07 (dt)	6.09 (dt)	6.11 (dt)	6.07 (dt)	6.04 (dt)	6.07 (dt)
6-H	2.15 (dt)	2.15 (dt)	2.18 (m)	2.20 (m)	2.40 (m)	2.41 (m)	2.38 (m)
7-H	1.42 (m)	1.41 (m)					
8-H	1.30 (m)	1.30 (m)	5.36 (dt)	5.38 (dt)	–	–	–
9-H			5.50 (dq)	5.50 (dq)	–	–	–
10-H	0.89 (t)	0.89 (t)	1.61 (d)	1.62 (d)	–	–	–
11-H	–	–	–	–	2.00 (s)	2.00 (s)	2.00 (s)
1′-H	5.65 (br.t)	–	5.52 (br.t)	–	5.51 (br.t)	–	5.48 (br.t)
2′-H	3.18 (t)	3.55 (br.m)	3.17 (t)	6.74, 7.27 (d)	3.17 (t)	3.52, 3.64 (m)	3.61 (q)
3′-H	1.81 (tqq)	1.60 (m)	1.80 (tqq)	4.98, 5.12 (dt)	1.81 (tqq)	1.60 (m)	2.86 (t)
4′-H	0.93 (d)	1.65 (m)	0.94 (d)	2.10 (m)	0.95 (d)	1.66 (m)	–
5′-H	–	–	–	1.88 (m)	–	–	7.2-7.35 (m)
6′-H	–	–	–	3.75, 3.69 (m)	–	–	
7′-H	–	–	–	–	–	–	

Coupling constants (Hz): 2,3 = 4,5 = 15; 3,4 = 10; 5,6 = 6.5; 1: 1′,2′ = 2′,3′ = 3′,4′ = 9,10 = 6.5; 2: 9,10 = 6.5; W(1/2) 2′ = 36 Hz; 5: 8,9 = 10; 7,8 = 9,10 = 1′,2′ = 2′,3′ = 3′,4′ = 6.5; 7: 8,9 = 10; 7,8 = 9,10 = 6.5; 1′,2′ = 10; 2′,3′ = 4; 8: 1′,2′ = 2′,3′ = 3′,4′ = 6.5; W(1/2)6+7 = 7 Hz; 9: W(1/2)6+7 = 8 Hz; 10: W(1/2)6+7 = 7 Hz; 1′,2′ = 2′,3′ = 7.

the genera Achillea, Anacyclus, Otanthus, Chamaemelum, and Agyranthemum, the piperidide 9 and the phenethylamide 10 are obviously of more limited distribution (compare Ref.[1]). Compound 9 has been established in Achillea millefolium L.[9,13] and Otanthus maritimus (L.) Hoffm.&.Link.[13], compound 10 was reported only for Anacyclus pyrethrum (L.) Link.[14]. Since the documentation of the NMR spectra in literature is not always complete, we have recorded all supplementary ^{1}H NMR data of alkamides from A. falcata in Table 3 (compounds 1, 2, 5, and 7-10; for 3, 4, and 6 see Ref.[7]).

Experimental

IR: Perkin-Elmer 398. — UV: Perkin-Elmer Lambda 5. — MS: Varian MAT CH-7 and 311A (high resolution). — NMR: Bruker WM-250 spectrometer equipped with an 80 K ASPECT-2000 computer running the DISNMRP-program; the deuterium of the solvent provided the field-frequency lock. Typical NMR parameters were: ^{1}H: NS= 32-120, SI= 16K, SW= 2500 Hz, PW= 2 µs (~25°); $CDCl_3$, concentration 1-6 mg/ml. ^{13}C: J-modulated spectra were recorded using the pulse sequence D1(S1,BB) - D_2(S_2,D0) - 90°(^{13}C) - D_3-180°(^{13}C,BB) - D_3 - acquisition: SF = 62.9 MHz, SI = 32K, SW = 16kHz, AQ = 1.0 s, PW = 17 µs (90°), DP = 6H/12H (2W/0.5W), D_3 = 7.1 ms (=1/J for J = 141 Hz), NS = 5000-20000, recycle delay = 3.5 s, temp. 303 K, concentration 5-30 mg/ ml in $CDCl_3$. For the determination of the LIS values increasing amounts of $Eu(fod)_3$ (Merck) were added to a solution of 1-5 mg of substrate in 0.5 ml $CDCl_3$. Spectra were recorded at 5-6 different reagent concentrations up to a concentration ratio $R_0:S_0 = 0.7:1$. The LIS for the 1:1 complex were obtained by extrapolation. The experimetal data were simulated using a modified PDIGM program [10].

Compounds 1 - 10 were obtained from Achillea falcata, for compounds 11 - 17 compare the corresponding references: 11 (Ref.9); 12,14-16 (15); 13 (16); 17 (7).

Fresh air-dried roots of Achillea falcata L., Turkey, [(A-1541), voucher specimen deposited at the Herbarium of the Institute of Botany, University of Vienna (WU)] were cut into small pieces and extracted for two days with petrol / ether (2:1) at room temperature. The concentrated extract was roughly fractionated on a SiO_2 gel column with petrol/ether (ether increasing from 0 to 100%) followed by ether/methanol (MeOH increasing from 0 to 10%). The polar fractions (ether and ether/methanol) were separated further by TLC [1 mm SiO_2 gel GF 254 (Merck)] using ether/petrol (4:1). 40 g roots afforded in addition to compounds 1-6 (compare Ref.7) 3 mg 7, 2.5 mg 8, 15 mg 9, and 7 mg 10.

2E,4E,8Z-Deca-2,4,8-trienoic acid piperideide (7): Colourless oil. IR (CCl_4, cm^{-1}): 3010m, 2924s, 2854m, 2842m, 1657s, 1642s, 1625s, 1602s, 1462w, 1444m, 1433w, 1412s, 1405s, 1378s, 1353s, 1340m, 1319m, 1304w, 1287m, 1249s, 1231s, 1171m, 1147w, 1133m, 1072s, 1015s, 997s, 945w, 929w, 862w, 710m, 606w. UV (Et_2O): 260 nm, 305 nm (sh). MS [70eV, 80°C, z/e (rel.int.)]: 231 (6%, M^+; $C_{15}H_{21}NO$ affords 231.16232; high resolution 231.1623), 149 (24, $M^+ - C_5H_8N$), 121 (27, $M^+ - COC_5H_8N$), 55 (100, $C_4H_7^+$). For ^{1}H and ^{13}C NMR see Tables 3 and 1.

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