116. *N*-Alkyl-2-pyrrolidones as Derivatives for the Structure Elucidation of Long-chain Primary Alcohols by Mass Spectrometry

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Dedicated to Professor Dr. *Walter Boguth* on the occasion of his 60th birthday

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Summary

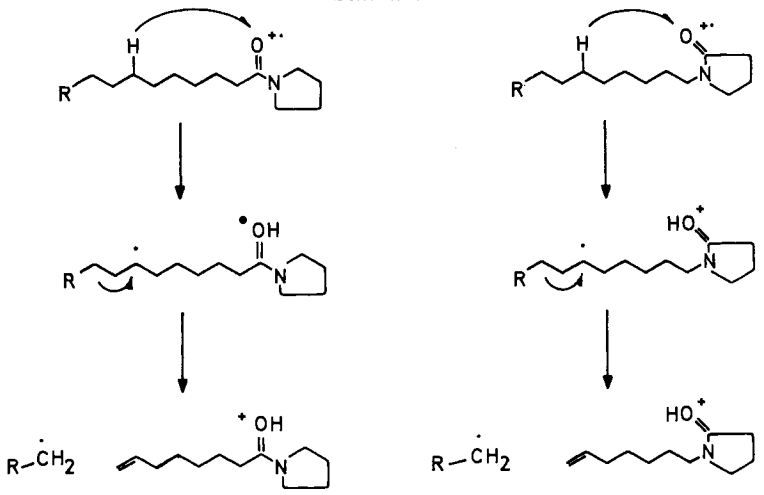
One unsaturated and three branched long-chain primary alcohols have been converted into *N*-alkyl-2-pyrrolidones for investigation by mass spectrometry. The EI. mass spectra of these derivatives have been found to exhibit unambiguously the branching points and, albeit less clearly, the position of a double bond in the chain.

Introduction. – The localization of branchings and double bonds in long-chain aliphatic compounds is still a domain of mass spectrometry [1], despite the remarkable progress made by NMR. spectroscopy in this field, following the introduction of shift reagents [2]. The success of mass spectrometry with such problems depends, however, largely on the functionalization of the chain. While in esters of fatty acids methyl branchings can be readily located [1], this is more difficult in long-chain primary alcohols and their common derivatives like acetates or trimethylsilyl ethers. Some improvements have been achieved for particular branchings by conversion of the alcohols into dimethylsilyl [3] or methyl ethers [4]. The localization of double bonds, however, appears neither possible in esters nor in alcohols without reference spectra [5]; but it is possible in tertiary amides [6].

If long-chain primary alcohols are to be identified, as in the analysis of waxes, they are usually oxidized to the corresponding acids to facilitate the interpretation of the spectra [7]. It appeared interesting to search for a derivative of the alcohol group, which would cause a clearer exhibition of the chain structure in its mass spectrum than the ester. By analogy with the pyrrolidides [6] [8], used successfully as derivatives of fatty acids for this purpose, *N*-alkyl-2-pyrrolidones appeared to be promising substrates. Considering the mechanism of chain fragmentation [8] [9], which is probably initiated by a H-transfer from a random chain position to the functional group, a *N*-alkyl-2-pyrrolidone should indeed behave quite like a pyrrolidide with regard to chain cleavage (*Scheme 1*).

Although there exists no proof for such a mechanism [10], it is in good agreement with all known experimental data of long-chain esters and amides and thus serves well as a working hypothesis. Details of the mechanism, *e.g.* the question of the

Scheme 1

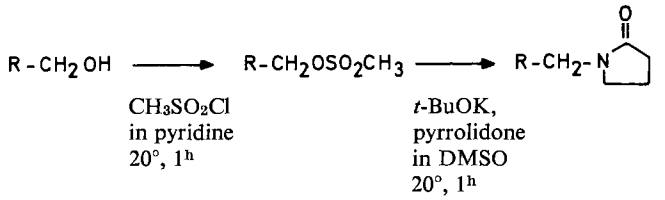


concertedness of the steps, or the possible occurrence of multiple H-rearrangements along the chain [9] [11] are unknown.

The fragmentation of 2-pyrrolidones, N-substituted with short alkyl chains, have been investigated by *Djerassi et al.* [12]. Therefore the fragmentation of the 2-pyrrolidone ring needs not be discussed here.

Preparation of derivatives. – The conversion of an alcohol into a *N*-alkyl-2-pyrrolidone on a microgram scale, although not as simple as the conversion of an acid into a pyrrolidide, is feasible *via* the corresponding mesylate (*Scheme 2*).

Scheme 2



The mesylate is prepared by the procedure of *Tipson* [13]. In the conversion of the mesylate into the *N*-alkyl-2-pyrrolidone, care has to be taken to keep the reagent dry.

In the work-up procedure reagents and solvent should be separated as completely as possible from the reaction products to avoid complicated purification procedures. Therefore in the first step the excess mesylchloride is converted into a water-soluble compound by reaction with excess of glycerol. The reaction mixture is then distributed between hexane and water. In the second step unused reagents are removed by distributing the acidified reaction mixture between water and hexane. The overall yield of the reaction is high, usually above 90%. As usual after derivatization on a microscale, GC./MS. is the method of choice for examining the products in the final solution.

Retention times of the *N*-alkyl-2-pyrrolidones are considerably longer than those of the corresponding alcohols, but their thermal stability is excellent.

Experimental procedure. – Approximately 1 μmol of the alcohol is added to a solution of 2 μmol of methylsulfonylchloride in 0.5 ml pyridine and left for 1 h at RT. Then a few drops of glycerol are added. After 15 min work up with hexane and water. The hexane solution is dried over Na_2SO_4 and concentrated. This solution is added to 0.5 ml of a reagent solution consisting of 19 mg potassium *t*-butoxide and 25 μl 2-pyrrolidone dissolved in 10 ml DMSO (distilled over CaH_2). After 1 h at RT, work-up with hexane and 1 N HCl. The hexane solution is dried over Na_2SO_4, concentrated, and used for GC./MS. analysis.

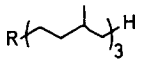
For the preparation of compounds 1 to 5 the following alcohols were used: Octadecanol and oleyl-alcohol, commercially available (*Fluka AG*, Buchs, Switzerland); 3,7,11-trimethyl-dodecanol, synthesized according to *Isler et al.* [14]; 3,7,11,15-tetramethyl-hexadecanol, obtained by hydrogenation of phytol (from *Fluka AG*, Buchs) with Pd/C in ethyl acetate, and 9-(2′,2′,6′-trimethyl-cyclohexyl)-3,7-dimethyl-nonanol, prepared by hydrogenation of retinol (from *Fluka AG*, Buchs).

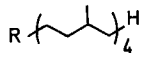
GC./MS. analysis. Varian 1740 gas chromatograph coupled *via* a frit separator with a *Varian* MAT CH7 mass spectrometer. GC.: 3% OV 17 on Gaschrom Q, 150–300° 8°/min. MS.: EI, 70 eV, 250°.

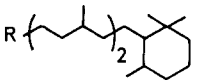
Results and Discussion. – Compounds **1** to **5** have been investigated (*Scheme 3*).

Scheme 3

1 $R-(CH_2)_{17}-CH_3$

2 

3 

4 

5 $R-(CH_2)_8-CH=CH-(CH_2)_7-CH_3$

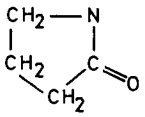
R = 

Figure 1 shows the mass spectrum of *N*-octadecyl-2-pyrrolidone (**1**) to exemplify the regular pattern exhibited by a straight hydrocarbon chain over the whole range, where the proposed mechanism (*Scheme 1*) can operate, that is from *m/e* 112 to $M-CH_3$ at *m/e* 322.

The formation of the most abundant fragments in the spectrum, *m/e* 98 and 99, must be discussed separately. While *m/e* 98 is formed in a simple cleavage of the C–C-bond next to the pyrrolidone ring, the mechanism leading to *m/e* 99 is probably similar to that depicted in *Scheme 1*, with the important difference that the radical stays with the charged fragment and an olefinic particle is lost [12].

The regular pattern starting with *m/e* 112 is reminiscent of the patterns of straight-chain hydrocarbons. From a mechanistic point of view, there are, however, two important differences. Almost all the fragments of the pyrrolidones are primary fragments, generated by the mechanism given in *Scheme 1*, whereas the ions formed in hydrocarbons are in considerable part secondary fragments [15]. This difference is due to the different stability of the primary fragments: protonated amides *versus* carbenium ions.

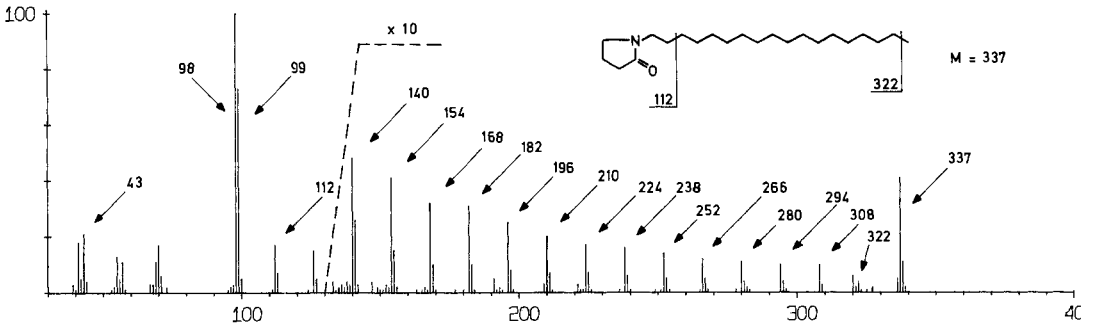


Fig. 1. *Mass spectrum of* N-*octadecyl-2-pyrrolidone* (**1**)

Figures 2 and *3* show the patterns obtained from methyl-branched chains. The positions of all methyl groups are obvious from the interruptions in the 14 amu-intervals of the peaks. The intensities of the peaks within the groups between the branching points differ considerably, but show a fairly regular pattern, with the third peak, counting from low mass, always being the smallest. Considering the proposed mechanism (*Scheme 1*) these differences in intensity are not surprising. The details of the mechanism of the formation of the corresponding ions are different, in that primary, secondary or tertiary radicals, and terminal or disubstituted double bonds are formed

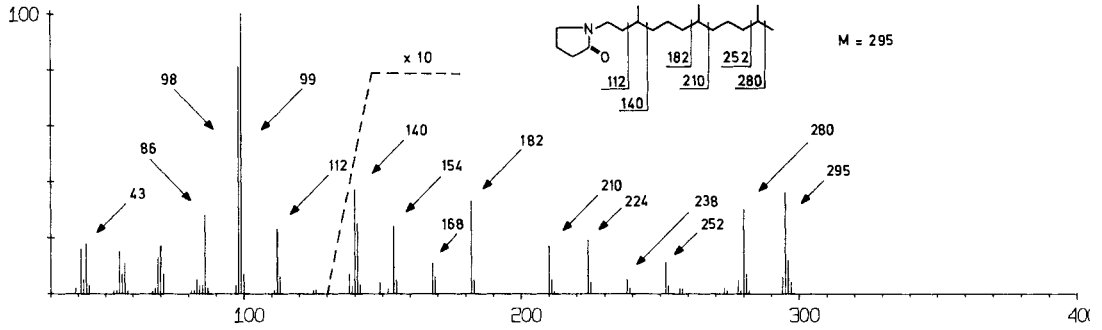


Fig. 2. *Mass spectrum of* N-(*3,7,11-trimethyl-dodecyl*)-*2-pyrrolidone* (**2**)

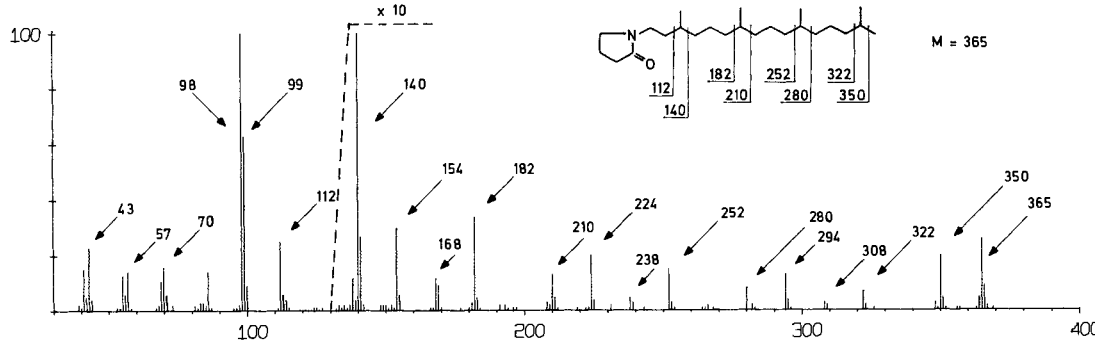


Fig. 3. *Mass spectrum of* N-(*3,7,11,15-tetramethyl-hexadecyl*)-*2-pyrrolidone* (**3**)

in the process. At the 'forbidden positions', 126, 196 and 266 in *Figure 3* peaks of very low intensities can nevertheless be observed. These fragments are probably the result of cleavage reactions in molecular ions or primary fragments, which have undergone skeletal rearrangements in low yield despite the strong competing process depicted in *Scheme 1*.

In *Figure 4* an example of a chain is shown, which is methyl-branched and terminated by an alicyclic ring. Besides the branching points, the spectrum reveals clearly the length of the chain by the abrupt decrease in peak intensities at the onset of the cyclic part.

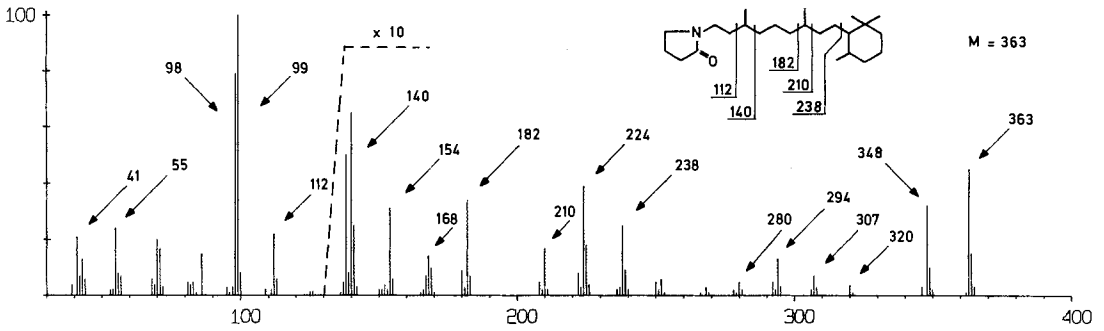


Fig. 4. *Mass spectrum of* N-[*9-(2',2',6'-trimethyl-cyclohexyl)-3,7-dimethyl-nonyl*]-*2-pyrrolidone* (**4**)

Figure 5 shows the mass spectrum of *N*-oleyl-pyrrolidone, as an example of an unsaturated chain. If the behaviour of the chain were completely described by the mechanism depicted in *Scheme 1*, then two series of peaks should be present, one in the high mass range owing to loss of C_nH_{2n+1} – radicals, extending from $M-CH_3$ down to $M-C_7H_{15}$, the last requiring rupture of the C–C bond allylic to the double bond (*m/e* 236). The other series of peaks should be due to loss of portions of the chain including the double bond. Extending from the allylic position (*m/e* 182) downward a series of peaks at $M-(C_nH_{2n-1})$ should appear. In the region of the double bond, between *m/e* 194 and *m/e* 224, no peaks should be present. A comparison of these predictions with the results depicted in *Figure 5* shows only partial agreement. The two series of peaks are indeed present; however, they do not terminate at the

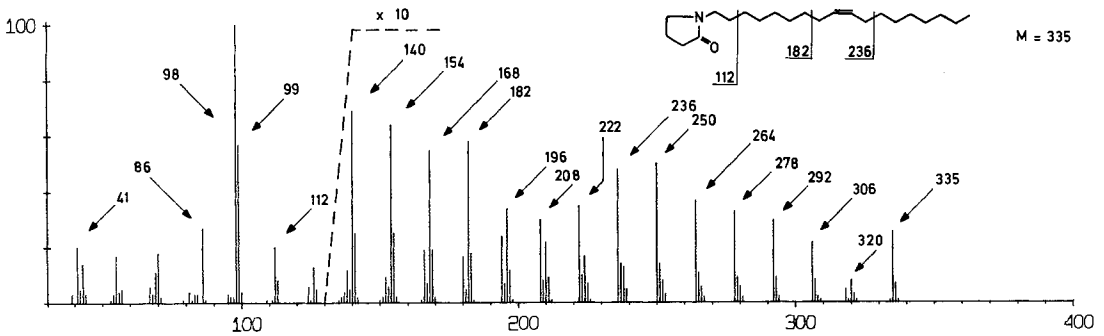


Fig. 5. *Mass spectrum of* N-(*9-octadecenyl*)-*2-pyrrolidone* (**5**)

double bond, but rather extend several CH_2-units beyond it, although with progressively lower intensities. This result is in remarkable contrast to the picture obtained with pyrrolidides, where both series finish indeed largely at the corresponding allylic bonds [6]. The extension of the series beyond the double bond must probably be explained by shifts in the position of the double bond prior to the mechanism shown in *Scheme 1* or, if in this mechanism the H-shift is not immediately followed by the rupture of the C–C-bond, by shifts of the double bond *via* the intermediate, where the charge and the radical are separated.

Nevertheless, the change in peak intensities in the region of the original double bond position allows apparently to localize this position: The intensities of the two series cross exactly at this point (*Figure 5*). Obviously more than one positional isomer has to be studied to establish the reliability of such structural assignments.

No ready explanation is available for the difference in the behaviour of the pyrrolidides and the *N*-alkyl-2-pyrrolidones. Besides *N*-oleyl-2-pyrrolidone (**5**), *N*-acetyl-*N*-oleyl-amine and *N*-acetyl-*N*-methyl-*N*-oleyl-amine have been examined. Both behave very similarly to the *N*-alkyl-2-pyrrolidone. No other lactams have been investigated.

Conclusions. – The results so far obtained show that a *N*-alkyl-2-pyrrolidone is a promising derivative to clarify the structural details of a long-chain primary alcohol (or halogenide), which are not apparent from the mass spectrum of the original compound or the common derivatives like methyl- or silyl-ethers. Due to the rather low intensity of the relevant peaks, care has to be taken to obtain clean spectra.

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