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The Melting Point Alternation in the Short-Chain *n*-Alkanes: Single-Crystal X-Ray Analyses of Propane at 30 K and of *n*-Butane to *n*-Nonane at 90 K**

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*Dedicated to Professor Reiner Sustmann
on the occasion of his 60th birthday*

It was probably A. Baeyer who first stated in 1877 that the melting points of the fatty acids do not show a monotonic increase with increasing chain length as do their boiling points. Instead the melting points of the members with even numbers of C atoms are relatively higher than those of the members with odd numbers.[1] The longer the chain length, the smaller are the relative differences. This is true for the *n*-alkanes as well as for most[2] of the α-substituted and α,ω-disubstituted *n*-alkane derivatives; a fact that is mentioned in almost all standard text books of organic chemistry. Mostly, "packing effects" are given as an explanation for such an alternation in melting points. This is justified insofar as physical properties, such as sublimation enthalpy and solubility, that are related to the solid state display a similar alternation whereas the properties of the liquid phase have a monotonic dependency on increasing chain length.[3]

For the *n*-alkanes with $n = 6-24$ (n = number of C atoms) the even numbered members crystallize at low temperatures in a triclinic space group, while for $n = 26$ monoclinic packing is observed. It is possible to define an orthorhombic sub-cell for the latter,[3a] which is also found as the real cell for polyethylene[4] and mixed paraffins.[5] When $n = 7$ the odd-numbered *n*-alkanes also crystallize in a triclinic, ordered modification with an orthorhombic sub-cell. Glassy crystalline "rotator phases" with hexagonal symmetry are found below the melting points for the odd-numbered *n*-alkanes with $n \geq 9$, and the difference between the phase transition and melting point increases with an increase in the chain length. From $n = 22$ hexagonal modifications are also observed for the even-numbered *n*-alkanes.

Although the phenomenon of the even/odd alternation has been known for a very long time, there does not exist a plausible explanation pattern, not even for the short chain ($n < 10$) *n*-alkanes with a triclinic crystal system. Kitaigorodski[6a] analyzed the arrangements of sections through the long axes of the aliphatic chains, and distinguished between triclinic, monoclinic, and hexagonal subcells. At longer chain lengths these represent the real cells. Further considerations referred to parallel arrangements of cylinderlike units, in

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which the main molecular axis inclines with the cylinder axis. These cylindrical units form layers and the difference in the arrangements of the layers result in a plausible explanation for the polymorphism of the long-chain systems. The reason why the short-chain, triclinic *n*-alkanes display the melting point alternation is still unclear. An explanation seems to be only possible if precise crystal structure investigations are carried out at the same temperature. The subtle differences that are possibly present in the packing patterns may then be identified. With such structural investigations the densities in the solid state could be correlated with the melting points, because the density depends on the number of the van der Waals contacts and the lattice energies. These are again correlated with the sublimation enthalpies, which have an effect on the melting point temperature. For short chain *n*-alkanes, unfortunately, there are neither experimental densities of sufficient precision available, nor can they be obtained by existing X-ray results.

The crystal structures of an ordered and a disordered phase of ethane at −188 and −183 °C, respectively, are known with sufficient precision.[7] *n*-Butane has a melting point of −138.6 °C and exists in three modifications, a disordered high temperature phase and two coexisting low temperature phases below −165.2 °C, as shown by neutron powder diffraction experiments at −268, −208, −183, and −153 °C.[8] To the best of our knowledge solid-state diffraction experiments of propane have not been reported. The X-ray measurement temperature is not given for *n*-pentane.[9] *n*-Hexane was investigated at −115 °C,[10] *n*-heptane at −173 °C,[11] and *n*-octane at approximately −60 °C.[9, 12] The structure determinations for $n = 5$, 6, 8 were undertaken with Weissenberg techniques and for $n = 7$ with a two circle diffractometer. Single-crystal investigations of the ordered phase of *n*-nonane do not exist, obviously because of the experimental difficulties described below. From the existing investigations it is also unknown if there are differences not only in the packing patterns but also in the molecular structures in respect of their torsion angles along the C−C axes.

We investigated the crystal structures of the series of *n*-alkanes from propane to nonane by X-ray diffraction. The gaseous compounds were first condensed in high vacuum, and thereby purified, and then transferred into an attached Lindemann capillary at −196 °C. The sealed capillaries were transferred to the diffractometer with a detachable cooling device,[13] where the low temperature device of our own design with an open cold gas stream provided the permanent cooling process. Single crystals suitable for X-ray diffraction were grown with the help of the in situ method by using a computer controlled device that applied a focused CO_2-laser beam along the capillary.[14]

Propane has a melting point of −190 °C, but crystallizes at even lower temperatures and therefore it was necessary to apply liquid helium as the coolant. Helium was also used as the surrounding gas steam to avoid icing at the capillary, and the measurement was performed at −243 °C.

n-Nonane shows a solid-state phase transition at −48.4 °C, about 3 °C below the melting point, from the "rotator phase" into the desired, ordered low temperature phase. Single crystals, grown in the rotator phase, shattered to polycrystalline material on further cooling. For a direct crystallization into the ordered phase and thus circumventing the high temperature phase, an approximately 40:60 mixture of *n*-pentane and *n*-nonane was used and crystallized at −100 °C. Such a strategy has also been applied for circumventing plastic phases.[15] Similar experiments to crystallize *n*-decane, however, were not successful thus far. The disorder in the high temperature phase of *n*-butane could not be resolved during the structure refinement and led to high anisotropic displacement parameters, high residual electron densities, too short C−C bond distances, and a relatively high *R* value.[16] All experiments to obtain a usable single crystal in the ordered low temperature phase by annealing for several days at 183 °C were unsuccessful. All the other crystal structure investigations were relatively simple and follow the reported procedure.[14]

A summary of the results is given in Table 1, and details of the crystal structure investigations are listed in reference [16]. The molecular structures of the *n*-alkanes have, within the precision of the experiments, a planar arrangement of the carbon skeleton. The mean $C(H_3)-C(H_2)$ and $C(H_2)-C(H_2)$ distances of the investigated *n*-alkanes (except disordered *n*-butane) are both 1.521(1) Å. The mean angles for $C(H_3)$-$C(H_2)$-C and $C(H_2)$-$C(H_2)$-$C(H_2)$ are 112.8(1) and 113.5(1), respectively. These values represent the X-ray standard values of undistorted *n*-alkanes.

Figure 1 shows the melting points of the *n*-alkanes together with the densities obtained from X-ray data at −183 °C, the value for propane was extrapolated from −243 °C to −183 °C. It is clear that the experimental X-ray densities follow the trend of melting points if the density calculated from the cell dimensions of the ordered phase of deuterated *n*-butane at −183 °C is taken. As expected, the density of the disordered phase of *n*-butane is lower.[16]

Table 1. Crystallographic data of the investigated compounds.

No. of C atoms	Space group	*a* [Å]	*b* [Å]	*c* [Å]	α [°]	β [°]	γ [°]	*V* [Å^3]	Z	*T* [°C]	ρ [g cm^{-3}]
2[a]	$P2_1/n$	4.226(3)	5.623(4)	5.845(4)	90	90.41(6)	90	139	2	−188	0.719
3	$P2_1/n$	4.1480(14)	12.612(5)	6.977(3)	90	91.28(3)	90	364.9(2)	4	−243	0.743[b]
4	$P2_1/c$	5.7027(15)	5.5247(15)	8.389(2)	90	115.22(2)	90	239.11(10)	2	−183	0.816
5	*Pbcn*	4.1357(8)	9.025(3)	14.815(5)	90	90	90	553.0(2)	4	−183	0.867
6	$P\bar{1}$	4.1309(7)	4.6963(10)	8.5392(17)	83.398(17)	87.265(15)	75.172(15)	159.05(5)	1	−183	0.900
7	$P\bar{1}$	4.116(2)	4.686(3)	20.348(13)	78.11(5)	81.79(5)	74.25(4)	368.0(4)	2	−183	0.904
8	$P\bar{1}$	4.1230(9)	4.6860(13)	10.974(3)	85.063(22)	83.72(3)	75.10(2)	203.30(9)	1	−183	0.933
9	$P\bar{1}$	4.1180(12)	4.6739(17)	24.693(9)	86.27(3)	87.80(3)	74.52(3)	457.0(3)	1	−183	0.932

[a] Data for the ordered phase from reference [7]. [b] Density extrapolated to −183 °C

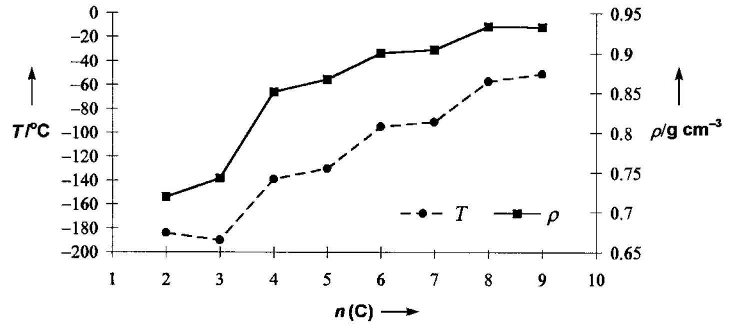

Figure 1. Trends in the melting points [T/°C] and densities [ρ/g cm^{-3}] of the *n*-alkanes with increasing number of C atoms [n(C)].

The *n*-alkanes from *n*-hexane crystallize in the space group $P\bar{1}$ and show some regularities. The centrosymmetric, even-numbered members of the *n*-alkanes have one molecule in the unit cell whereas the C_2 symmetric, odd-numbered members have two molecules in the unit cell (Table 1). The lengths of the *a* and *b* axes remain similar with increasing chain length. In fact they are slightly shorter for the odd-numbered members relative to the even ones, which contradict the trend that the odd-numbered members have a lower density than the even ones. However, this effect is a consequence of the pronounced differences in the *c* axes, which compensate for the minor differences in the other axes. The crystal packing of *n*-hexane and *n*-heptane is shown along the *a* axes in Figures 2a and 2b. It is clear that the CH_2 groups fit into the hollows of the neighboring chains, which causes a shift along the *c* axis. In a projection along the main axis of the molecules (not shown here) it is clear that the interchain arrangement is similar along the axis for even- and odd-numbered *n*-alkanes.

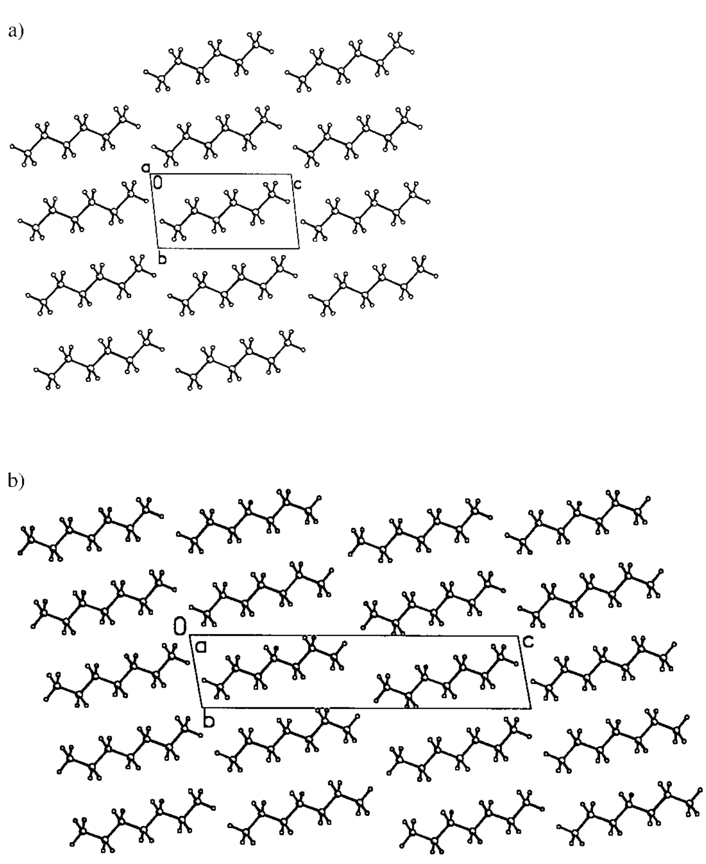

Figure 2. Packing of *n*-hexane (a) and of *n*-heptane (b) viewed along the *a* axis.

The *c* axes, which are responsible for the differences in the cell volumes and the densities (Table 1), are directed along the main axis of the molecules (Figure 2a and 2b). Therefore the differences in the packing (even/odd) are sought in this direction. Consequently, the way in which the molecules are packed laterally does not play any role in the differences in the packing density of the even- and odd-numbered triclinic *n*-alkanes. The length of the main molecular axis increases by a constant value of 1.268 Å with each additional CH_2 group. Therefore the intermolecular distances between the end groups, namely, the CH_3 groups, are responsible for the alternation in the densities. But the decisive question is, why are the end groups of the even- and odd-numbered *n*-alkanes are not able to approach to the same distances?

A simplified, geometrical description in a planar view reveals the background (Figure 3): The shape of an even-numbered *n*-alkane (C_i symmetry) can be described in the plane of the carbon skeleton as a parallelogram, that of an odd-numbered *n*-alkane (C_2 symmetry) as a trapezoid (Figure 3a). If a dense packing of parallelograms is required, a pattern may result as shown in Figure 3b. However, an analogous packing is also possible for the trapezoids (Figure 3c). If the main axis of the molecules is increased by an

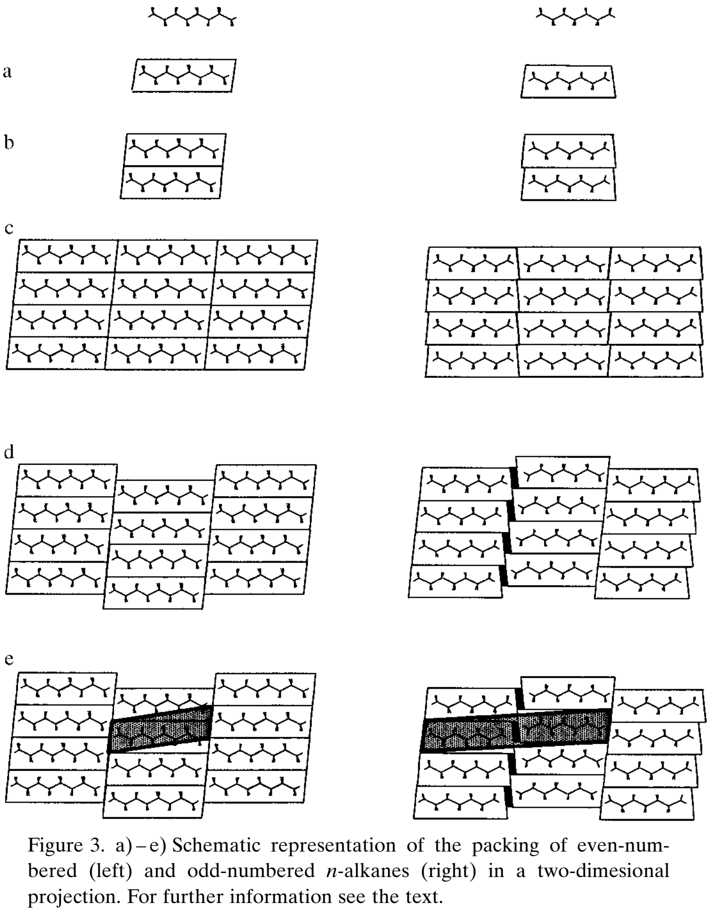

Figure 3. a)–e) Schematic representation of the packing of even-numbered (left) and odd-numbered *n*-alkanes (right) in a two-dimesional projection. For further information see the text.

increment of 1.268 Å, as it is in the case when going from *n*-heptane to *n*-octane, it is expected that the area (in the three-dimensional case the volume) increases by similar proportions (Figure 3c). Such a packing would lead to a monotonic increase in the density, because a parallelogram and a trapezoid have the same area with the same length of the center line and height.

However, the methyl groups situated opposite to each other try to adopt a staggered conformation as may be seen from Figure 2a and 2b. Thus the columns of the parallelograms have to be shifted with respect to each other so as to achieve the staggered arrangement of methyl groups (Figure 3d, left). Such an arrangement is indeed found for the triclinic even-numbered *n*-alkanes. A similar shift is possible in the trapezoid pattern only on one side, on the other side the shift results in very long distances and the methyl groups are not really situated opposite to each other (Figure 3d, right). However, this arrangement has larger gaps (marked in black), compared to the right and center layer. The triclinic unit cells in a two-dimensional projection are shown in Figure 3e.

Thus, the even-numbered *n*-alkanes have optimal intermolecular contacts at both ends, whereas the odd ones possess these at one end, and at the other end the distances are longer. This leads to a less dense packing for the odd *n*-alkanes and as a consequence, as shown above, to relatively lower melting points.

In this description we disregarded the third dimension and indeed, the parallelograms and trapezoids are shifted in height with respect to each other. But this shift is about the same in both even and in odd *n*-alkanes, which allows the simplification to a two-dimensional presentation.

In Table 2 the distances between the methyl C atoms of adjacent columns are listed. For the even-numbered *n*-alkanes they are equal because of the crystallographic centrosymmetry. For the odd *n*-alkanes two different distances are found, one of them corresponds to those of the even-numbered members, and on the other side, where the gaps exist, the distances are longer. Thus the melting point alternation of the *n*-alkanes can be explained from *n*-hexane and higher on the basis of a simple and geometrical model, by the interaction of methyl groups. The same or similar model does not apply to the shorter *n*-alkanes and also not to the α-substituted and α,ω-disubstituted *n*-alkane derivatives, some of which do not display the same alternating pattern.[2] For this it is necessary to have further structural investigations and packing calculations,[17] which are currently in progress.

Table 2. Intermolecular distances of the terminal C atoms between the layers.

No. of C atoms	Distance 1 [Å]	Distance 2 [Å]
6	3.623	3.623
7	3.605	3.734
8	3.617	3.617
9	3.606	3.737

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[1] A. Baeyer wrote in *Ber. Chem. Ges.* **1877**, *10,* 1286: "From this compilation it can be seen that without any exception a member with an odd number of carbon atoms has a lower melting point than that with an additional carbon atom, while in both series the melting points increase with the exception of the first members. If there is a genernal law in this pattern it would be the easiest to study the melting points of the anilides and normal fatty acids and it would be desirable that colleagues who have the necessary material available would expand our knowledge in this direction. A law which would say that in homologous series a odd number of carbon atoms has a relatively lower melting point than those with an even number would have a considerable interest in molecular physics and ask for investigations if the crystal form, solubility etc. are correlated with the nature of the number, which is expressed by the quantity of carbon atoms."

[2] Exceptions are the 1-chloro-, 1-bromo-, and 1-sulfanylalkanes, which display an inverted alternancy, as well as *n*-alkane derivatives which have large terminal substituents such as $(C_6H_5)(CH_3)(HCl^-)N^+$, $(H_{27}C_{13})_2(OH)C$, or $(C_{10}H_7)(H)(HBr)N^+$.

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[16] Crystal structure analyses: $Mo_{K\alpha}$-radiation, graphite monochromator, four circle diffractometer Nicolet R3, structure solution by direct methods (Siemens SHELXTL-Plus, Version 5.03). All non-hydrogen atoms were refined anisotropically on F^2. The hydrogen atom positions were taken from a difference Fourier map and refined without constraints and isotropically. Except for propane, which was measured at −243 °C, all other measurements were performed at −183 °C. Mean C−C distances [Å] and C-C-C angles [°] for the measured *n*-alkanes except *n*-butane: $C(H_3){-}C(H_2)$ 1.521(1), $C(H_2){-}C(H_2)$ 1.521(1), $C(H_3)$-$C(H_2)$-C 112.8(1), $C(H_2)$-$C(H_2)$-$C(H_2)$ 113.5)1); for the disordered *n*-butane: $C(H_3){-}C(H_2)$ 1.517(4), $C(H_2){-}C(H_2)$ 1.470(7), $C(H_3)$-$C(H_2)$-$C(H_2)$ 113.6(4). a) Propane: growing temperature −243 °C, space group $P2_1/n$ (no. 14), $2\Theta_{max} = 60°$, reflections measured: 1420, independent: 971, of which 794 had $I > 2\sigma(I)$, 60 parameters, $R1 = 0.0468$, $wR2 = 0.1206$, residual electron density +0.34/−0.14 e Å^{-3}. (CCDC-103186). b) *n*-Butane: growing temperature −158 °C, space group $P2_1/c$ (no. 14), $2\Theta_{max} = 60°$, reflections measured: 2358, independent: 693, of which 556 had $I > 2\sigma(I)$, 19 parameters, $R1 = 0.1922$, $wR2 = 0.5413$, residual electron density +1.03/−0.26 e Å^{-3} (CCDC-103187). c) *n*-Pentane: growing temperature −158 °C, space group *Pbcn* (no. 60), $2\Theta_{max} = 60°$, reflections measured: 1774, independent: 804, of which 644 had $I > 2\sigma(I)$, 48 parameters, $R1 = 0.0402$, $wR2 = 0.1238$, residual electron density +0.38/−0.10 e Å^{-3} (CCDC-103188). d) *n*-hexane: growing temperature −113 °C, space group $P\bar{1}$ (no. 2), $2\Theta_{max} = 60°$, reflections

measured: 1400, independent: 920, of which 789 had $I > 2\sigma(I)$, 56 parameters, $R1 = 0.0342$, $wR2 = 0.1076$, residual electron density $+0.33/-0.15\,e\,Å^{-3}$ (CCDC-103189). e) *n*-Heptane: growing temperature $-110\,°C$, space group $P\bar{1}$ (no. 2), $2\Theta_{max} = 60°$, reflections measured: 1750, independent: 1674, of which 1388 had $I > 2\sigma(I)$, 128 parameters, $R1 = 0.0499$, $wR2 = 0.3756$, residual electron density $+0.39/-0.19\,e\,Å^{-3}$ (CCDC-103190). f) *n*-Octane: growing temperature $-78\,°C$, space group $P\bar{1}$ (no. 2), $2\Theta_{max} = 60°$, reflections measured: 1356, independent: 1187, of which 991 had $I > 2\sigma(I)$ 73 parameters, $R1 = 0.0386$, $wR2 = 0.1285$, residual electron density $+0.48/-0.15\,e\,Å^{-3}$ (CCDC-103191). g) *n*-Nonane: growing temperature $-98\,°C$, space group $P\bar{1}$ (no. 2), $2\Theta_{max} = 55°$, reflections measured: 3288, independent: 2089, of which 1396 had $I > 2\sigma(I)$, 162 parameters, $R1 = 0.0468$, $wR2 = 0.1549$, residual electron density $+0.31/-0.15\,e\,Å^{-3}$ (CCDC-103192). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publicationnos CCDC-103186–CCDC-103192. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CD2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.uk).

[17] The calculated lattice energies, expressed in $kcal\,mol^{-1}$ per molecule, show a similar alternation as the melting points: propane: -7.504, *n*-butane: -8.814, *n*-pentane: -11.922, *n*-hexane: -14.783, *n*-heptane: -16.690, *n*-octane: -19.657, *n*-nonane: -21.260. The Cerius^2 program (Version 3.5) was used for these calculations. The experimental coordinates serve as the starting points and the electrostatic potentials were assigned from the AM1-Hamiltonian in MOPAC6. The "Crystal Packer" module with a built in Dreiding II force field was used to minimize crystal structures and the lattice energies were obtained from the final minimized crystal structure.

Coordination-Ionspray-MS (CIS-MS), a Universal Detection and Characterization Method for Direct Coupling with Separation Techniques**

Ernst Bayer,* Petra Gfrörer, and Claus Rentel

Spray techniques such as atmospheric pressure chemical ionisation (APCI)[1] or electrospray ionization (ESI)[2–5] have become important techniques in mass spectrometry. In particular their simple coupling with separation techniques such as HPLC,[6] capillary electrophoresis (CE),[7] and capillary electrochromatography (CEC)[8] is the method of choice for characterization, analysis, and structural elucidation. A characteristic common to these techniques is the formation of droplets from which ions are subsequently liberated. In the case of APCI the ionization occurs by charge transfer from a reagent gas plasma formed by corona discharge at the tip of a metal needle. With ESI, the sample solution is nebulized by application of a strong electric field. Spray formation is usually assisted pneumatically by means of a coaxial gas stream. Ionization is achieved by either protonation of basic groups or deprotonation of acidic groups of the analyte molecules depending upon the polarity of the field employed. While electrospray mass spectrometry has found widespread application, for example in the analysis of peptides and proteins, with their readily protonated amino groups, and of the easily deprotonated oligonucleotides, it fails for a large number of nonpolar substances and is of limited utility for substances with only weakly basic or acidic groups. Numerous classes of natural compounds such as terpenes, sugars, alcohols, aromatic compounds, and vitamins in addition to a large number of synthetic organic compounds such as produced in combinatorial chemistry are either inaccessible to analysis by spray techniques or can be detected only with poor sensitivity.

We have developed a new method of chemical ionization in which positively or negatively charged complexes are formed by the addition of a suitable central atom to the analytes, and these complexes can be detected by mass spectrometry. Since both polar and nonpolar organic compounds can form coordination compounds with an appropriate central atom, this form of ionization is highly versatile. The wealth of experience available in the area of coordination chemistry can be drawn upon in this technique and thus new classes of compounds can be analyzed with the spray technique. We therefore refer to this new technique as coordination-ionspray mass spectrometry (CIS-MS). Neither an electric field nor the formation of a reagent gas plasma by corona discharge is necessary for ionization. Efficient nebulization in the ion source is however mandatory. Since pneumatic nebulization in the absence of an electric field is often insufficient to obtain a suitable spray, a supporting voltage was applied in some cases to stabilize the nebulization process.

In the case of poorly ionized compounds, such as fully protected peptides, the formation of clusters leads to complex spectra that are difficult to interpret and to a reduction in sensitivity. In , The ESI mass spectrum of the fully protected 28-mer peptide of the potassium channel of the transmembrane sequence of *Drosophila melanogaster*[9, 10] is shown in Figure 1 a. With the exception of the terminal amino group all the basic groups are protected and are thus not available for protonation, and only the clusters with sodium and potassium ions are observed within the mass range of the quadrupole mass spectrometer. The ion yield is only poor and the interpretation of the spectra is problematic.

It is known that lithium salts form complexes with peptides and that these prevent the association of peptide chains. Seebach et al.[11] have employed lithium salts to increase the solubility and to improve the yield in the solid-phase synthesis of peptides that have a high propensity for aggregation by the formation of β structures. The addition of lithium iodide to the transmembrane peptide leads to specific stable metal complexes that can be detected in high ion yield and which allow simple determination of the molecular mass (Figure 1 b).

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