ing cobaloximes and has implications for the discussion of vitamin B_{12} catalyzed reactions in living organisms.[11]

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properties of the basis gel: chemical structure and surface of the basis gel, and the nature, chain length, and density of the hydrophobic ligands. In this study, we have determined the mobility of *n*-alkyl ligands on silica gel using ^{13}C CP/MAS NMR spectroscopy and have correlated this with the unusual retention behavior of paracelsin peptides on these RP carriers. The natural mixture of sequence-analogous eicosapeptides (Scheme 1) which was used is of great interest because of its antibiotic and membrane active properties, such as hemolysis of erythrocytes and voltage dependent ionic conductivity in liquid bilayer membranes.[1-3]

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
Ac-	Aib-	Ala-	Aib-	Ala-	Aib-	**Ala**-	Gln-	Aib-	**Val**-	Aib-	Gly-	Aib-	Aib-	Pro-	Val-	Aib-	Aib-	Gln-	Gln-	Pheol **A**
Ac-	Aib-	Ala-	Aib-	Ala-	Aib-	**Ala**-	Gln-	Aib-	**Leu**-	Aib-	Gly-	Aib-	Aib-	Pro-	Val-	Aib-	Aib-	Gln-	Gln-	Pheol **B**
Ac-	Aib-	Ala-	Aib-	Ala-	Aib-	**Aib**-	Gln-	Aib-	**Val**-	Aib-	Gly-	Aib-	Aib-	Pro-	Val-	Aib-	Aib-	Gln-	Gln-	Pheol **C**
Ac-	Aib-	Ala-	Aib-	Ala-	Aib-	**Aib**-	Gln-	Aib-	**Leu**	Aib-	Gly-	Aib-	Aib-	Pro-	Val-	Aib-	Aib-	Gln-	Gln-	Pheol **D**

Scheme 1. Structure of the paracelsin peptides **A**–**D**. Ac = Acetyl; Aib = α-aminobutyric acid (2-methylalanine), Pheol = phenylalaninol; all chiral components have the L configuration.

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[8] The structures of the cobaloximes **23** (X = CO_2Et, CN) were confirmed by elemental analyses and IR and NMR spectroscopy. The ^1H NMR data (300 MHz, $CDCl_3$) are particularly characteristic: **23** (X = CO_2Et): δ = 0.55–1.17 (m, 8H, cyclohexyl + CH_2), 1.22 (t, 3H, J = 7.5 Hz, CH_3, ethylester), 1.50–1.64 (m, 5H, cyclohexyl + CH_2), 2.09–2.13 (m, 1H, Co–CH), 2.18 (s, 6H, CH_3, Hdmg), 2.21 (s, 6H, CH_3, Hdmg), 3.89–3.91 (m, 2H, CH_2, ethyl ester), 7.27–7.30 (m, 2H, pyridine), 7.68–7.73 (m, 1H, pyridine), 8.49–8.51 (m, 2H, pyridine), 17.89 (s, 2H, OH).—**23** (X = CN): δ = 0.48–2.20 (m, 14H), 2.23 (s, 6H, CH_3), 2.26 (s, 6H, CH_3), 7.28–7.34 (m, 2H, pyridine), 7.71–7.77 (m, 1H, pyridine), 8.45–8.49 (m, 2H, pyridine), 18.05 (s, 2H, OH).

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Correlation of the Dynamic Behavior of *n*-Alkyl Ligands of the Stationary Phase with the Retention Times of Paracelsin Peptides in Reversed Phase HPLC

By *Bettina Pfleiderer, Klaus Albert, Klaus D. Lork, Klaus K. Unger, Hans Brückner,* and *Ernst Bayer**

In reversed phase high performance liquid chromatography (RP-HPLC), the retention of substances and the selectivity of the separation are influenced by the following

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RP materials with *n*-alkyl chain lengths $1 < n < 20$ were prepared by reacting LiChrospher (Si 100, 10 μm) with the appropriate *n*-alkyldimethylchlorosilane.[4] The ligand density was 3.5 ± 0.2 mol m^{-2}.

Since changes in the mobility of *n*-alkyl groups are revealed by the relaxation behavior of the carbon atoms, they can be characterized through determination of the spin-lattice relaxation times T_1[5] or the relaxation times in the rotating coordinate system $T_{1\rho H}$.[6] We chose the $T_{1\rho H}$ values of the protons as a measure of the mobility of the alkyl chains, since $T_{1\rho H}$ gives information about rates of motion in the kHz range,[6] and because relatively small changes in the mobility result in large changes in the $T_{1\rho H}$ times. In contrast, the T_1 times, which are sensitive in the MHz range, exhibit only small differences.[7] In the range of slow molecular motions, the $T_{1\rho H}$ values are averaged completely by ^{13}C-^1H dipolar interactions.[8] However, the high mobility of the alkyl chains, which exhibit liquid-like behavior, and the additional rapid rotation of the probe at the magic angle (MAS, $\nu_{rot} = 4000$–5000 Hz) lead to a drastic reduction in the dipolar interactions, so that averaging by spin diffusion does not occur in these systems. This phenomenon has been observed by *Alemany* et al. for highly mobile molecules.[9, 10]

Solid-state NMR spectroscopy on C_8 and C_{18} phases has shown that the total mobility of the C_{18} chain is smaller than that of the C_8 chain.[11] For a more thorough investigation, materials with $n = 4$, 5, 6, 8, 10, 12, 14, and 18 were selected for $T_{1\rho H}$ measurements using ^{13}C CP/MAS NMR spectroscopy. Figure 1 shows the dependence of the relaxation times $T_{1\rho H}$ of the terminal methyl groups of the stationary phase upon the alkyl chain length n. Analogous behavior was observed for the $(n-1)$ and $(n-2)$ methylene groups of the respective *n*-alkyl ligands. Surprisingly, a maximum in the $T_{1\rho H}$ value of ca. 80 ms occurs for a chain length of $n = 6$–8. The $T_{1\rho H}$ values of the alkyl chain carbon atoms of the C_4 and C_8 phases are given for comparison in Table 1. In the case of the C_8 phase (and also the C_5 and C_6 phases), they increase in the direction of the terminal methyl group, whereas in the C_4 phase they are practically identical for all positions.

The temperature dependence of the relaxation times revealed that an increase in the $T_{1\rho H}$ values corresponds to a higher mobility of the *n*-alkyl chain. Thus, the relatively small $T_{1\rho H}$ values of the C_4 phase indicate a low motional

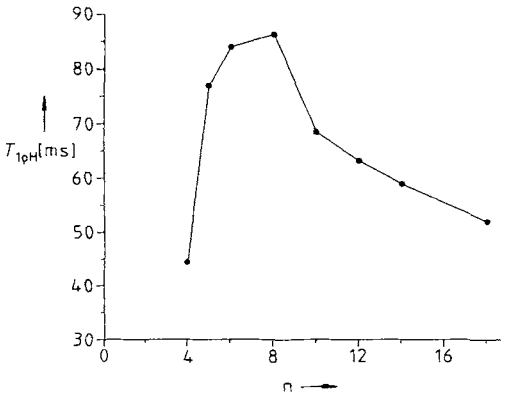

Fig. 1. Dependence of the $T_{1\rho H}$ values of the terminal methyl groups on the chain length n of the *n*-alkyl ligands.

Table 1. $T_{1\rho H}$ values [ms] of the alkyl chain carbon atoms of the C_4 and C_8 phases.

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8
C_4 phase	37.0	41.0	42.5	44.4				
C_8 phase	56.2	62.5	61.8	71.8	71.8	64.7	78.0	86.3

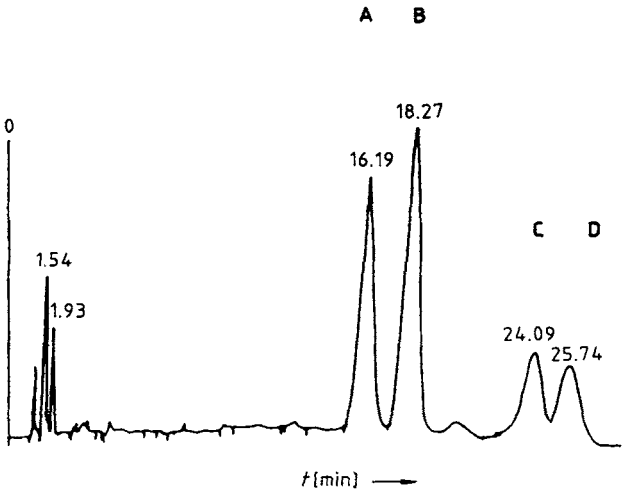

Fig. 2. HPLC chromatogram of the natural mixture of paracelsin peptides **A**, **B**, **C**, and **D**; t = retention time. Chromatographic conditions: column: 250 mm × 4.6 mm; stationary phase: LiChrospher RP-8, Si 100 (Merck), 5 μm; eluent: acetonitrile/methanol/water (39/39/22); UV detection at $\lambda = 206$ nm; $T = 303$ K; flow rate: 1 mL min^{-1}; quantity injected: ca. 20 μg peptide mixture in 20 μL methanol.

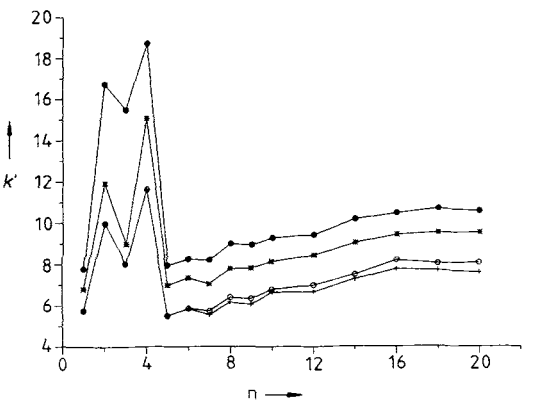

Fig. 3. Dependence of the capacity factors k' of the paracelsin peptides **A** (+), **B** (○), **C** (*), and **D** (●) on the alkyl chain length n; k' is defined as $(t - t_0)/t_0$, where t_0 = retention time of water. Chromatographic conditions as in Fig. 2, but with LiChrospher, Si 100 (Merck), 5 μm, chemically modified with *n*-alkyldimethylchlorosilanes, n = 2–20, as stationary phase.

freedom for all the carbon atoms of this phase, and the maximum of the methyl $T_{1\rho H}$ value at n = 6–8 means that the mobility of the terminal methyl group is highest for chains of these lengths. The mobility becomes increasingly restricted for chains with n > 10 and approaches that found for n = 4. A similar behavior, albeit without a pronounced maximum, has been found in relaxation time measurements on RP phases in suspension.[12] The strength of the dependence of the mobility upon the chain length is influenced by the solvating ability of the suspending liquid.[13, 14]

The mobility of the *n*-alkyl ligands reflects their conformational behavior. Suitable sensors for the determination of conformation are, for example, peptides and proteins, for which the conformation influences the interaction with the stationary phase. A connection between the retention of peptides in RP-HPLC and their conformational behavior has been found by *Houghten* and *Ostrech*.[15] The HPLC elution profile of the paracelsin peptides **A**–**D** (see Scheme 1) on a C_8 phase showed that a complete separation of the compounds is possible, in spite of the extremely small structural differences (only one CH_2 group more from **A** to **B** and from **C** to **D**).

This finding led to a systematic investigation of the dependence of the retention of paracelsin peptides on the alkyl chain length n. In this manner, an unusual behavior was detected (Fig. 3). Maxima in the retention, and therefore also in the capacity factors k', occur for n = 2 and 4. Beyond n = 5, the retention times increase only slightly and are comparable with that retained for a C_1 phase. The same behavior, although less pronounced, was observed also when binary eluents (methanol/water 85/15 *v/v*) were used. It was also found that the retention times of the peptides decrease on going from n to (n + 1) when n is an even number.

Comparing the dependence of the methyl $T_{1\rho H}$ values of the stationary phase and of the capacity factors k' of the paracelsin peptides upon the chain length n shows that a maximum in the retention corresponds to a minimum in the mobility of the *n*-alkyl chain. This can be explained by the assumption that the low mobility of the alkyl chains of the C_4 phase reflects a conformation (preferably a *trans-gauche* conformation) which facilitates a maximum steric interaction with the paracelsin peptides.

A comparison of the parcelsin components **B** and **C** is illustrative for the separation behavior. The replacement of Ala by Aib in position 6 and of Leu by Val in position 9 (cf. Scheme 1) leads to isobaric peptides of nominal atomic mass 1921. Nevertheless, the k' values of **C** are considerably larger than those of **B**. This can be explained by the fact that the (formal) removal of a CH_2 group from position 9 of **B** (replacement of Leu by Val) and its introduction in position 6 (replacement of Ala by Aib) leads to a more lipophilic peptide which interacts more strongly with the RP phase. The interaction with the stationary phase is favored by the remarkably stable helical conformation of the paracelsin peptides, which has been detected by circular dichroic measurements and by temperature dependent ^{13}C NMR spectroscopy.[1] A predominantly α-helical structure is assumed, in analogy with the crystal structure of the paracelsin analogue alamethicin.[16] In contrast, protected homopeptides of Aib have 3_{10} helical structures.[17–19]

From the α-helical projection[20] of the paracelsin peptides, it can be seen that the amino acids in positions 6 and 9 lie on the same side of the helix. If a horizontal interaction of the peptide helix with the stationary phase is assumed, the alkyl side chains of these amino acids point directly towards the relatively rigid alkyl chains of the C_4 phase; this leads to optimum interaction and thus to maximum k' values for the paracelsin peptides on the C_4 phase.

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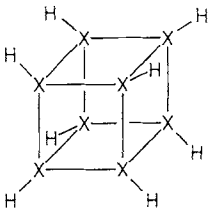
Much Less Strained Cubane Analogues with Si, Ge, Sn, and Pb Skeletons**

By *Shigeru Nagase**

Polyhedral carbon compounds such as tetrahedrane (C_4H_4), prismane (C_6H_6), and cubane (C_8H_8) have long formed interesting synthetic targets in organic chemistry;[1] among these, cubane is especially intriguing because of its high O_h symmetry and high strain.[2] There is currently considerable interest in replacing the carbons in these compounds by heavier homologues such as silicon in the expectation of unprecedented physical and chemical properties.[3]

As we have demonstrated in a recent theoretical study on persilatetrahedrane,[4] polyhedral silicon compounds consisting of only fused three-membered rings possess high strain and are subject to "bond stretch" isomerism.[5,6] In contrast, we have shown that they become significantly less strained than the corresponding carbon compounds as the number of fused four-membered rings increases.[7] Thus, persilacubane **1**, having six fused four-membered Si rings, is much less strained than cubane.[7,8] Indeed, the first polyhedral silicon compound, a persilacubane derivative (**1** with tBuMe$_2$Si instead of H) was recently synthesized and its novel properties were investigated.[9]



1, X = Si
2, X = Ge
3, X = Sn
4, X = Pb

We report now ab initio calculations of the structures and strain of still heavier cubane homologues, pergermacubane **2**, perstannacubane **3**, and perplumbacubane **4**. Geometries were fully optimized at the Hartree-Fock (HF) level with the GAUSSIAN 82 program[10] by using the ab initio effective core potentials[11] and the double-zeta (DZ) basis sets[12] augmented by a set of six d-type polarization functions[13] on each heavy atom.

Table 1. Optimized bond lengths and ionization potentials (I_p) of cubane and its homologues **1**–**4** of O_h symmetry [a].

	C_8H_8 [b]	**1**	**2**	**3**	**4**
d_{X-X} [Å]	1.559	2.382	2.527	2.887	2.949
d_{X-H} [Å]	1.081	1.477	1.542	1.714	1.744
I_p [eV] [c]	10.4	8.3	7.7	7.1	6.6

[a] The total energies are −34.78608 (**1**), −33.85480 (**2**), −30.72293 (**3**), and −31.25989 (**4**) a.u. [b] HF/6-31G* values taken from [7]. For the electron diffraction values of d_{C-C} (1.575 Å) and d_{C-H} (1.100), see A. Almenningen, T. Jonvik, H. D. Martin, T. Urbanek, *J. Mol. Struct. 128* (1985) 239. [c] Based on Koopmans' theorem.

Table 1 shows the optimized structures of **1**–**4** together with the ionization potentials. The Si–Si, Ge–Ge, Sn–Sn, and Pb–Pb bond distances in the cubic skeletons are only ca. 0.02–0.04 Å longer at the HF/DZ+d level than those in the four-membered rings of cyclotetrasilane (2.363 Å), cyclotetragermane (2.508), cyclotetrastannane (2.867), and cyclotetraplumbane (2.908). The bond distances in the strain-free molecules X_2H_6 were calculated to be 2.344 (Si), 2.480 (Ge), 2.839 (Sn). and 2.868 (Pb) Å.

The Si–Si bond distances of 2.382 Å in **1** compare favorably with the values of 2.38–2.45 Å in the X-ray structure of the derivative Si_8R_8 synthesized recently:[9] the somewhat longer bond distances and slightly distorted cubic structure (∢SiSiSi = 87–92°) in this derivative are most likely ascribable to the presence of the bulky tBuMe$_2$Si groups.

$$X_8H_8 + 12\,H_3X{-}XH_3 \longrightarrow 8\,HX(XH_3)_3 \qquad \text{(a)}$$

1–**4**

X = Si, Ge, Sn, Pb

Table 2 summarizes the strain energies calculated from the so-called homodesmotic reactions (a).[14,15] It should be noted that the strain energy of 99.1 kcal mol^{-1} calculated for **1** agrees reasonably well with our previous HF/6-31G* value of 93.5 kcal mol^{-1}.[7]

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