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SELF-ASSOCIATION AND INTRAMOLECULAR HYDROGEN BONDING OF N-MONOSUBSTITUTED PYRUVAMIDES

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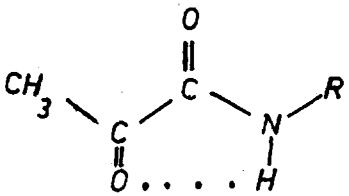
Former investigations of the solvent dependence of the n-π^*-transistions of α-oxo acid amides had suggested that these compounds exist, in nonpolar as well as some weakly basic aprotic solvents (e.g.dioxan), as structures wich can be assumed to be like the following [1]



If such structures exist, the self-association of alkylpyruvamides in inert solutions must be reduced as compared to N-alkylacetamides. Therefore, the present nmr-investigation of the concentration dependence of the NH-proton resonances of N-alkylsubstituted pyruvamides with R = n-C_3H_7- (1), iso-C_3H_7- (2) and tert. C_4H_9- (3) in CCl_4 was undertaken, to provide data on intramolecular H-bonding. A summary of results is presented in Fig. 1. It is indicated that, contrary to N-alkylacetamides [2], at relativly high concentrations δ_{NH} of 1, 2 and 3 will be nearly constant. Assuming that only a monomer-dimer equilibrium exists, we have analysed the concentration dependences of δ_{NH} in 1, 2 and 3 according to a method developed by Jentschura and Lippert [3].

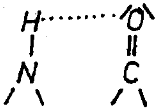
Table 1

Equilibrium constants K_D, NH-resonances of monomers (δ_m) and dimers (δ_d) for the H-bonded dimerisation of N-alkylpyruvamides and N-alkylacetamides in CCl_4 at 30 ± 1 °C

Amides	K_D (mf^{-1})	δ_m (Hz)^a	δ_d (Hz)^a	$\Delta\delta=\delta_d-\delta_m$
1	0,72	673	797	124
2	0,80	647	775	128
3	0,22	656	711	55
N-isoprop.acetamide 4 [2]	10,0	520	825	305
N-tert.butylacetamide 5 [2]	6,0	540	788	248

[a] At 100 MHz (Varian HA 100)

The trend of 1, 2 and 3 toward smaller dimerisation constants in comparison to 4 and 5 suggests a five-membered protonchelate. These -NH...O=C- interaction can be represented by 2 isomer H-bonded structures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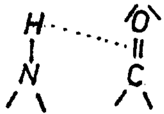
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In the isomers the hydrogen acceptors are either the sp^2-directed lone pairs of electrons of the α-carbonyl group or the π-electrons, respectivly. It was shown that changes in the preferred linear orientation of proton acceptor orbital and proton donor do not weaken the hydrogen bonding energy to a large extent [4]. But with a difference angle $|\Phi| \approx 120^0$ the proton-electron interaction in 6 is too unfavourable to explain the thermodynamic parameters of the intramolecular hydrogen bond ($\Delta H^0 \approx 2$ kcal/mol in 1-3)[5]. An approximation using the angle dependence of strength of intermolecular hydrogen bonds reported by Luck[6] shows for the steric situation in 6 ranges of $\Delta H^0 < 1$ kcal/mol.

The existance of structure 7 is supported directly by the monomer NH-shifts in 1-3. In 4 and 5 the differences $\Delta\delta$ are produced by free nitrogen protons and by H-bonded protons. In contrast, $\Delta\delta$ in 1-3 is the result of a difference between inter- and intramolecular H-bonded protons. The NH-shift δ_m^H of the

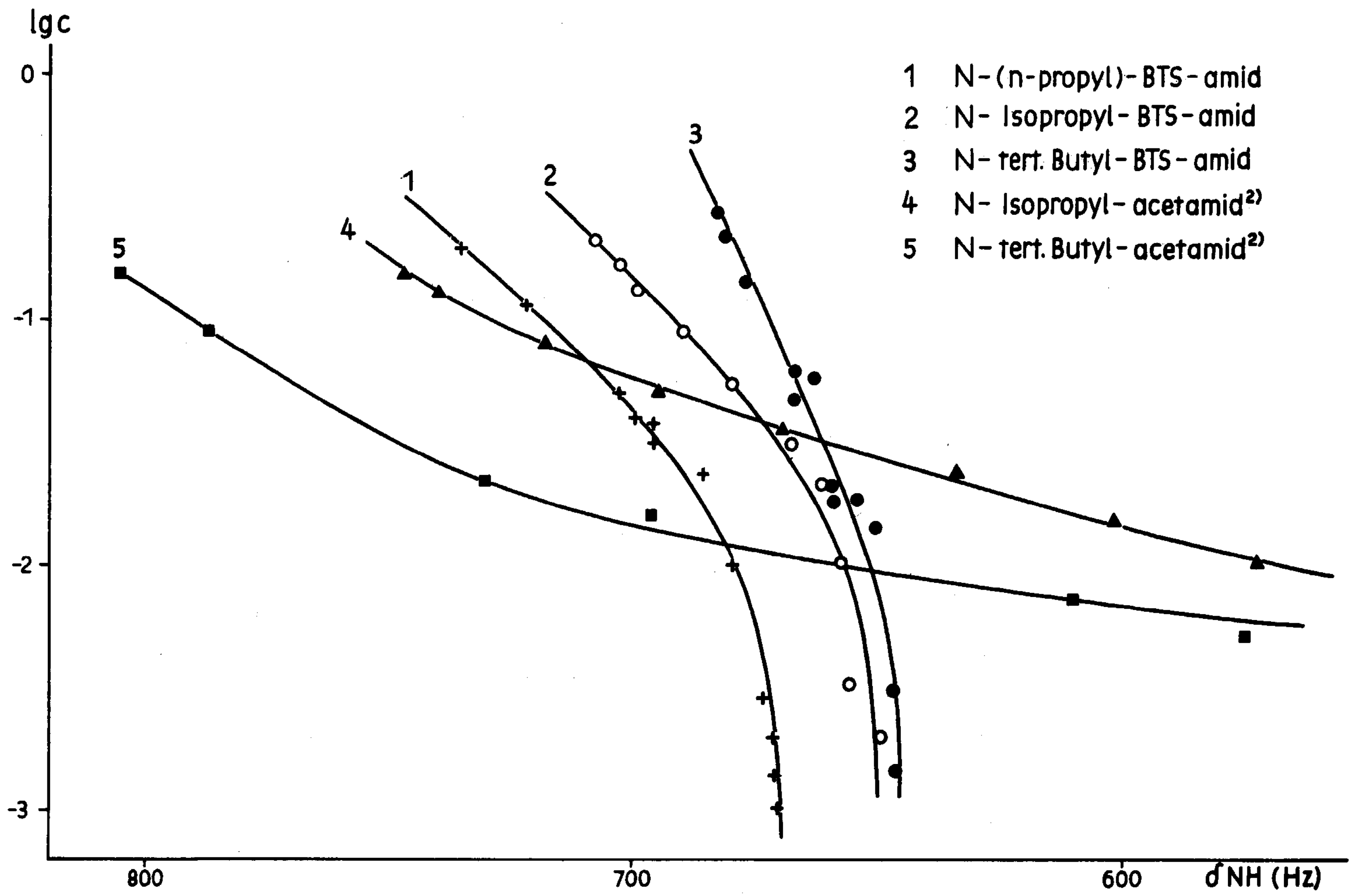

Fig. 1 Variation of the observed chemical shifts δ_{NH}(Hz from internal TMS at 100 MHz) with the logarithm of the concentration c in CCl_4 at 30± 1°C

hypothetical monomer 3 with a free NH-proton is estimated to be δ^H_m 3 = δ_m 5, considering the stronger electron accepting properties of the acetyl group in comparison to the methyl group. Thus, the chemical shift δ_{ch} for the hydrogen bonded interaction in 5 is calculated to be 195 Hz, after making corrections for anisotropic effects of the amide group [7] and assuming $\Delta\delta = \delta_{aniso.} + \delta_{ch}$. Since the strength of hydrogen bonding did not differ greatly in the inter- and intramolecular case [5], the hypothetical NH-resonance of the intramolecular bondes monomer 3 is roughly 700 Hz <u>without</u> anisotropic shifts. The observed value δ_m = 647 Hz is possible only as a result of an anisotropic upfield shift, typical of hydrogen bonding with π-acceptors. [8]

Further support for structure 7 in monomer 1-3 was obtained by the influence of alkyl groups on K_D and δ_m. Although the behaviour within the dimerisation is identical in 1 and 2 (K_D 1 $\approx K_D$ 2), the nitrogen proton of intramolecular H-bonded 3 is more strongly shielded than in 2. We propose a steric compression of the NH-proton toward the π-electrons of the α-carbonyl group. This compression increases further in 4, corresponding to a particularly strong intramolecular hydrogen bond [9]. But the increase in the upfield shift by the nearer anisotropic center will be opposed in this case by the lowfield shift due to stronger H-bonding.

The results support an intramolecular hydrogen bonding of structure 7 in N-alkylpyruvamides and probably in other α-oxo acid amides too.

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