2,08, s, 17-OCOCH$_3$; 3,51 + 3,68 sowie 3,68 + 4,03, je 2d, $J_{5',5'} = J_{19,19} = 9$, CH$_2$(5') + CH$_2$(19); 5,40, d, $J_{6,7} = 10$ (zusätzliche Feinstruktur durch $J_{7,8} = 3$), CH(7); 5,72, d, $J_{6,7} = 10$ (zusätzliche Feinstruktur durch $J_{6,8} = 1$) CH(6). – MS.: $M^+ = 358$.

$$C_{22}H_{30}O_4 \ (358,46) \qquad \text{Ber. C 73,71} \quad \text{H 8,44\%} \qquad \text{Gef. C 73,68} \quad \text{H 8,39\%}$$

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195. A Thermodynamic and Kinetic Study on the Stability of the Conformational States of N-Acetyl-proline-methylamide by IR. Spectroscopy and Chemical Relaxation

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Summary. N-Acetyl-proline-methylamide (APMA) was synthesized by the mixed anhydride method and investigated by IR. spectroscopy and chemical relaxation measurements. The temperature-induced variation of the IR. absorption bands of the internally hydrogen bonded (b) and of the extended, unbonded (e) species at 3330 and 3450 cm^{-1} respectively, were used to evaluate the molar absorptivities, a(b) = 280 and a(e) = 50 l/mol · cm, the equilibrium constant $K = 0.70$, and the molar enthalpy of reaction $\Delta H = -2280 \pm 60$ cal/mol. The entropy was estimated to be in the range -8 to -9 e.u. The reaction rates of this conformational transition were measured by the chemical dipole field effect. The relaxation time of the rate process is $\tau = 2.7 \cdot 10^{-9}$ s, the rate constant for the formation of the hydrogen bond k(b) is $2.2 \cdot 10^8$ s^{-1}, and that for the unfolding accompanied by the breakage of the amide hydrogen bond k(e) is $1.5 \cdot 10^8$ s^{-1}.

The interest in small molecules containing peptide bonds, *e.g.* N-acetyl amino acid alkylamides, has increased during the last few years because of their importance for the understanding of the forces and interactions responsible for the intrinsic structures and stabilities of polypeptides and enzymes. Moreover, since the introduc-

tion of chemical relaxation techniques, considerable effort has been made to under-
stand the dynamics of conformational transitions of biopolymers, but almost nothing
is known about the dynamic properties of relevant monomeric units such as those
mentioned above. N-Acetyl-prolinemethylamide (APMA) prepared by the mixed
anhydride procedure using ethyl chloroformate – a route different from that reported
elsewhere [1] – was chosen for study, with the object of determining the thermo-
dynamic and kinetic features of the conformational change of the molecule by IR.
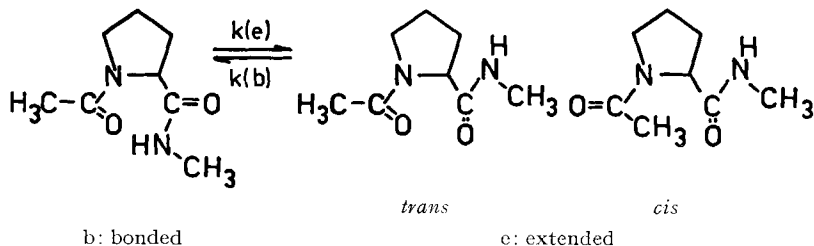
b: bonded   e: extended

spectroscopy and chemical relaxation measurements. As depicted above, APMA can
exist in an intramolecularly hydrogen bonded (b) and in two extended, unfolded (e)
configurations [2–5].

The IR. spectra in the range of interest, viz. 3700 to 2700 cm^{-1}, were taken from
dilute tetrachloromethane solutions in which intermolecular hydrogen bonding is
suppressed. The dominant band at 3330 cm^{-1} has previously been assigned to the
hydrogen bonded proton, and that at 3450 cm^{-1} to the non-associated amide proton [2].
The latter band has a distinct high frequency shoulder at 3460 cm^{-1}, recognized in
later work [3] and indicating that the extended form occurs, perhaps, in two different
conformational states. The variations of the absorbances of these bands with tem-
perature are rather small. A rise in temperature increases A(e) and decreases A(b),
the respective absorbances of the extended and bonded structures. Thus, the bonded
configuration will be unfolded to give the extended forms as the temperature increases.
If c(x) is the equilibrium concentration, where x is b or e, a(x) is the molar absorptivity
of the respective absorption bands, and the initial concentration is $C = c$(e) $+ c$(b),
then consideration of the incremental change of the absorbance with either equilibrium
concentration, δA(x) $= a$(x) $\cdot \delta c$(x), gives:

$$\delta \ln A(\text{b})/\delta \ln A(\text{e}) = K = c(\text{e})/c(\text{b}) \tag{1}$$

and, together with the differentiated law of mass action, $\delta \ln K = \delta c(\text{x}) \cdot C/c(\text{x}) \cdot [C - c(\text{x})]$, and *van't Hoff*'s equation, we have:

$$\Delta H = (RT^2/\delta T) \cdot (1 + K) \cdot \delta \ln A(\text{e}) . \tag{2}$$

Consequently, the spectra were recorded at 20, 30 and 40°, so that the desired
quantities could be calculated using the two equations above. Knowing the equilibrium
constant, the absorptivities a(x) $= A$(x)/c(x) could then be calculated. All data of
interest appear in the Table. The data refer to 30°. The signs in the table apply to
the temperature increment $\delta T = +10°$. In the case of $\delta T = -10°$, we obtained, within
experimental accuracy, the same figures but with opposite sign. Because of the low

Table. *Experimental data and calculated parameters of the temperature induced changes of the two IR. absorption bands due to the extended* (e) *and hydrogen bonded* (b) *conformations of N-acetyl-proline-methylamide for two different concentrations*

C $(10^{-3}$ mol/l)	2.78		3.93	
K	0.46		0.70	
$\nu(x)$ (cm^{-1})	(e) 3450	(b) 3330	(e) 3450	(b) 3330
$c(x)$ $(10^{-3}$ mol/l)	0.86	1.92	1.62	2.31
$A(x)$	0.054	0.52	0.075	0.68
$\delta A(x) \cdot 10^3$	+4.5	−20	+5.5	−35
$\delta \ln A(x)$	+0.083	−0.038	+0.073	−0.052
$a(x)$ (l/mol · cm)	62	270	46	294
ΔH (cal/mol)	+2224	−2263	+2293	−2334

magnitude of the absorbance of the 3450 cm^{-1}-band, the error of the values referring to this band is about 10% whereas the error of the values pertinent to the other band is about 6%. The estimated error of the calculated constants is therefore about 15%. Note that the determination of the absorptivities suffers most from the difficulty of correcting properly for the overlap of the two absorption bands. Since no significant variation of the CH-stretching bands with temperature was observed, no correction for the volume expansion was necessary.

The large difference between the two absorptivities leading to a disproportionate appearance of the two absorption bands in question may become quite misleading in the interpretation of the IR. spectrum [2], but it is well known that an IR. absorption arising from a hydrogen bonded proton is much stronger than that of the unbonded proton. The equilibrium constant agrees well with an estimate of conformer percentage in tetrachloromethane by NMR. measurements [4] and in tetrachloroethylene at elevated temperature by IR. spectroscopy [5]. It indicates that the hydrogen bonded state is only slightly favoured over the extended configuration.

It is generally accepted that the formation of a CO···HN-hydrogen bond liberates some 3 to 4 kcal/mol. The calculated molar enthalpy of 2.28 ± 0.06 kcal/mol remains below the expected value. This can be explained by enthalpic contributions caused by the internal motion of the polar groups which oppose the hydrogen bonding. Thus, the measured enthalpy should be regarded as the sum of a negative term due to hydrogen bond formation and a positive term arising from the conformational transition to the hydrogen bonded state. Evidently, this reasoning does not eliminate the possibility that the hydrogen bond is weaker than it would otherwise be because of an unfavourable steric situation. The molar entropy, which can be estimated from the calculated data, is about −8 to −9 e.u., and supports the view that the formation of the hydrogen bond is accompanied by a considerable loss of rotational degree of freedom of the molecule. These questions, arising from a consideration of the thermodynamic data, could be answered in part by the kinetics, since rate constants can yield information with regard to the potential barrier hindering conformational transitions.

The relaxation kinetic measurements were carried out by means of the chemical dipole field effect. In principle, the electrical susceptibility of chemical systems in solution depends on the equilibrium, because the reactants and the products have different dipole moments. In analogy to the molar heat of reaction, a molar moment

of reaction can be defined which contains the difference of the squared dipole moments of the reactants and the products as the most interesting contribution [6]. In our case, there is a change of the molecular moment between the hydrogen bonded and the extended conformers by virtue of the internal motion of the polar groups brought about by a strong electric field. Thus, the resulting dielectric loss increment is measured at various frequencies and concentrations; the apparatus, the technique of measurement and instructive examples of intermolecular hydrogen bonding are discussed elsewhere [7] [8]. The measurements were carried out in benzene because the solubility in tetrachloromethane was too low to yield accurately measurable effects; nevertheless, the effect was not very large, e.g. for a 0.0336M solution the maximal loss increment was $1.16 \cdot 10^{-6}$. The relaxation frequency $f(R) = 58$ MHz corresponds to a relaxation time $\tau = 2.7 \cdot 10^{-9}$ s. The reciprocal relaxation time of an intramolecular rate process of this kind is given by:

$$1/\tau = k(b) \cdot (1 + K) \tag{3}$$

where $k(b)$ is the rate constant of the formation of the hydrogen bonded state. Thus, by calculation $k(b) = 2.2 \cdot 10^8$ s^{-1} and $k(e) = 1.5 \cdot 10^8$ s^{-1}, this order of magnitude being typical for rate constants of rotational isomerism [6]. Of course, these figures are only correct for this system to the extent that a two-state model is applicable. Even for the case of a three-state model, namely that in which the unfolded state exists in two conformers, as postulated earlier [4] and as indicated by the high frequency shoulder of the 3450 cm^{-1}-band, no considerable alteration of the values of the rate constants would be expected. From the kinetic data, therefore, no particular conclusion can be drawn with regard to the conformational transitions. Altogether, the kinetic properties indicate a high degree of flexibility of APMA which would not be the case if one rate constant was much smaller than the other.

Finally, from the amplitudes, the difference of the squared dipole moments of the two species can be derived: $\Delta\mu^2 = \mu(e)^2 - \mu(b)^2 = 5.1 \pm 0.2$ Debye^2. *Nakagawa* [9] has reported a dipole moment of 3.3 Debye for APMA; however, it is not clear whether this value refers to either one of the conformational states. Provided the assumption that this value refers to one of the conformational states is correct, the other conformer would have a dipole moment of about 2.2 Debye no matter to which species either value is assigned, – and no definite assignment is possible. A consideration of the structures suggests that the bonded state should have the smaller dipole moment.

In conclusion, the physical properties of this compound show that a high dynamic flexibility is combined with a low thermodynamic stability of the conformers, two properties generally characteristic of primary biological reactions. For a particular biopolymer, each monomeric unit will contribute to the overall thermodynamic stability in an additive manner while its dynamic properties are essentially preserved. As we have shown earlier by a chemical relaxation study of the purine-pyrimidine-base pairing [7], this reasoning is as pertinent to the building blocks of the polynucleotides as to polypeptides and enzymes (setting aside particular stabilizing and bonding forces like salt bridges, hydrogen bonds, *van der Waals* and other interactions).

Experimental. – N-Acetyl-proline was prepared as described [10]. Three grams of this compound were dissolved in 200 ml anhydrous tetrahydrofurane (THF) and 2.6 ml triethylamine were added, then, at – 10°, slowly 1.8 ml ethyl chloroformate. After stirring for 0.5 h, the solution

was filtered and brought to dryness at $<10°$. The residue was treated with methylamine in about 30 ml THF left overnight, and all volatile material removed. The product was chromatographed on 150 g silica (0.08 mm) with acetone, recrystallized from ethyl acetate, m.p. 96–98°, and sublimed under high vacuum, m.p. 101° uncorr., lit.: 104–105° [1]. The elemental analysis was satisfactory and the NMR. spectrum agreed with the data in the literature [4].

The IR. spectra were measured with a *Perkin-Elmer* Grating instrument (slit 3 cm^{-1}, scan rate 400 cm^{-1} · min^{-1}). The tetrachloromethane solutions were thermostatted in infrasil quartz cuvettes (*Hellma*) by means of brass cuvette-holders of our design which were connected to a circulating water bath. The temperature, monitored with a thermistor inside the cuvettes, was measured by a *Knauer* Temperatur-Messgerät, and the readings compared with a calibrated thermometer. The spectrophotometer was connected to a precision recorder (*Houston* Instr.) so that accurate voltage readings could be made, especially those of temperature dependence which was measured on a fivefold expanded scale. Tetrachloromethane of spectrophotometric quality (*Fluka* AG) was treated with dried potassium carbonate AR. and cycled over phosphorus pentoxide as described earlier [8]. The solutions were made by weight directly in the cuvettes.

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196. Synthesis and Structure of Tris(2'-[2-phenyl-1,3-dioxolano])-chromium(III)

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Summary. Tris(2'-[2-phenyl-1,3-dioxolano])chromium(III) **3** has been synthesised and has been shown to have the *cis* (or *fac*) configuration **3a** by X-ray analysis: the Cr–C bond length is 2.037 (10) Å.

We have reported on the structures of the octahedral σ-bonded mono- and bis-(organo)chromium(III) compounds **1** and **2a,b,c** [1–4]: now we wish to report on the structure of the σ-bonded tris(organo)chromium(III) compound **3**.

The compound **3**, which possesses masked aldehydo-groups in the aryl rings bonded to chromium, was synthesised by the usual *Grignard* route [5]. It is formulated as the unsolvated tris(aryl)Cr(III) compound $C_{27}H_{27}O_6Cr$, M.W. = 499.5 on the basis of its analysis, its magnetic moment (3,74 BM) [1]), its reaction with HgCl$_2$ to give three

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