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Formylcamphor Condensed with Amines. The Structure in Solution as Obtained by NMR, UV Absorption, and Circular Dichroism Spectroscopy

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The condensation products of diamines and two molecules of formylcamphor have been investigated by means of nuclear magnetic resonance, UV absorption, and circular dichroism spectroscopy. It is shown that the configuration of the ketoenamine depends strongly on the choice of solvent. Thus in chloroform these molecules have dominantly a *syn* structure with intramolecular hydrogen bonding. The condensation product of the stereochemically rigid *trans*-1,2-cyclohexanediamine is used to demonstrate that the exciton theory can be used to rationalize the absorption and circular dichroism spectra of chloroform solutions. Then for derivatives of less rigid diamines the exciton model has been used to study the rotational conformation of the diamine bridge. The spectra obtained from methanol solutions where the *anti* structure of the ketoenamines dominates are discussed and it is tentatively suggested that a "chelating solvation" is the reason for the observed very big Cotton effects.

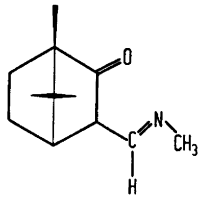
During many years Schiff bases or enamines of β-diketones and diamines and also their transition metal complexes have enjoyed study by a variety of techniques. Dudek and Holm [1] studied by ^{1}H NMR the equilibrium composition for the tautomers of bis(acetylacetone)ethylenediimine, and related compounds and concluded that these compounds were largely in the ketoenamine form. In this tautomer form the "acetylacetoneimine" unit is presumed to be planar as found experimentally in a large number of copper(II) complexes (see Baker, Hall, and Waters [2] and references therein). The "acetylacetoneimine" units have been treated as weakly (*i.e.* electrostatically) interacting chromophores (having $\pi \rightarrow \pi^*$ transitions polarized approximately in the N—O direction) and the average structure in solution has thus been determined for (*R*)-propylene-bis(acetylacetoneimine) using the exciton theory to interpret UV-absorption and circular dichroism spectra.[3] The same method has been used to discuss the structure in solution for VO^{2+}, Ni^{2+}, and Cu^{2+} complexes of this and related ligands.[4] The results were shown to be in accordance with ^{1}H NMR for the ligands and the diamagnetic nickel(II) complexes.[5]

The use of the exciton model for the complexes must necessarily be crude since it considers only the two acetylacetoneimine parts as weakly coupled chromophores and thus ignores the presence of the metal ion. This model has been valuable in explaining electronic spectra of many organic molecules [6] but when used for tris *o*-phenanthroline and tris α,α'-bipyridyl complexes to assign absolute configuration it has been the source of much controversy.[7]

Most of the difficulty in the application of exciton theory to such complexes seems to arise from charge transfer transitions of energies close to the internal ligand $\pi \rightarrow \pi^*$ transitions. The oxovanadium(IV) and copper(II) Schiff base complexes investigated by us earlier have the internal ligand $\pi \rightarrow \pi^*$ transitions well isolated from charge transfer bands and are, therefore, suited for an investigation of the usefulness of exciton theory for metal complexes. The predictions arrived at should preferably be checked by independent means. For

the complex Cu R-pn(acac)$_2$ it was found that in solution the two acetylacetonate parts deviate considerably (some 40°) from being coplanar.[4] However, absorption and circular dichroism spectra of this compound in the crystalline state dispersed in pressed KBr plates indicate [8] a smaller but still significant deviation from planarity. A crystal structure determination for this compound has shown that the two planes form a dihedral angle of 10°.[8]

The absolute configuration of the complex defined as the chirality of a pair of non-crossing, non-parallel lines representing the oxygen-nitrogen directions within the ligand was found [8] by the X-ray structure analysis to be that arrived at by means of the exciton model.[4] Thus we feel it worthwhile to pursue the more delicate problems presented by the stereochemically varied Schiff bases of diamines with formylcamphor. Recently a paper [9] has occurred in the literature dealing with this subject. However, as shown below, experimental insufficiencies render the derived conclusions unreliable when the free ligands are considered.



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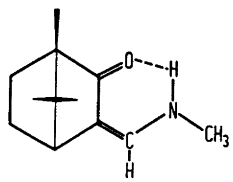

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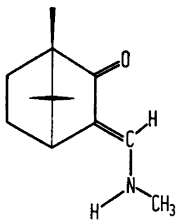

III

The complexity of the stereo-chemistry for condensation products between formylcamphor and primary amines is demonstrated by the various possibilities of ma(fmcH) (for abbreviations see the experimental section) shown by structure I – III. When the condensation products of diamines are considered, *e.g.* en(fmcH)$_2$, evidently the number of possibilities increases. In this paper these structural possibilities have been considered and NMR spectroscopy has been used to obtain information on the tautomer distribution. This distribution has been found to vary with the solvent, with temperature and for chloroform solutions also with time. The spectra reported by Ugo *et al.*[9] are in some cases recorded during the transformation of one tautomer to the other before equilibrium between the tautomers was established.

It seems natural first to answer the question why are the condensation products of formylcamphor much more complicated than the formally analogous enamines of acetylacetone? The working hypothesis for us has been that the presence of two conjugated double bonds on the camphor skeleton (II and III) is not completely energetically favourable relative to the Schiff base form (I). A small population of the latter tautomer (I) in dynamic equilibrium with the enamines serves as a "catalyst" in the *syn-anti* rearrangement. A similar situation has been examined for bis(*anti*-camphorquinonedioximato)nickel(II) which rearranges to the complexes of the *amphi* ligands.[10] For the enamine system the relative concentrations of the tautomers in the equilibrium may be determined by the competition between *inter* and *intra*-molecular hydrogen bonding. The rate of conversion of *anti* ketoamine to the *cis* form can be accelerated by acid in qualitatively the same way as for the oximes.[10]

EXPERIMENTAL

Formylcamphor was prepared by formylation of natural $(+)_D$-camphor.[11]

(*R*)-1,2-Propanediamine and (*R,R*)-1,2-cyclohexanediamine were obtained from the racemic diamines by resolution with natural tartaric acid.[12,13] 1,3-Butanediamine was prepared from acetonitrile [14] and resolved with tartaric acid.[15] 2,3-Butanediamine was prepared from dimethylglyoxime and the two isomers separated through the different solubilities of the hydrochlorides in methanol.[16] The racemic diamine was resolved with tartaric acid.[9]

Schiff bases were prepared according to Pfeiffer *et al.*[17] and recrystallized from methanol. The identity of the compounds was established through chemical analyses and NMR spectra.

Ultraviolet spectra were measured with a Cary 14 spectrophotometer and the circular dichroism spectra with a Roussel-Jouan dichrograph II. ^{13}C NMR spectra were recorded at

22.63 MHz with a Bruker WH 90 and ^{1}H NMR spectra at 90 MHz with a Bruker HX-90E.

Abbreviations. Amines: ma = methylamine, en = 1,2-ethanediamine, R-pn = (*R*)-(−)$_D$-1,2-propanediamine, R-2,3-bn = (*R,R*)-(−)$_D$-2,3-butanediamine, R-1,3-bn = (*R*)-(−)$_D$-1,3-butanediamine, R-chxn = *trans*-(*R,R*)-1,2-cyclohexanediamine, tn = 1,3-propanediamine. Dioxo-compounds: acacH = acetylacetone, fmcH = formylcamphor obtained from natural (+)$_D$-camphor. ma(fmcH) *etc.* symbolizes the condensation product of an amine and a dioxocompound.

RESULTS AND DISCUSSION

During the process of the spectral investigation of the formyl derivatives very strong solvent dependence and spectral changes with time in some solvents were observed. In attempting to correlate UV absorption and circular dichroism measurements with ^{1}H NMR results it became clear that the relatively simple behaviour observed for acetylacetone derivatives was not found for the analogous formylcamphor products. In the following we shall try to use NMR data to establish which isomers, tautomers, or rotamers are present in chloroform and methanol solutions and this knowledge is then correlated with UV absorption and circular dichroism spectra.

Garbisch [18] has investigated the enolization of formyl derivatives of cyclic ketones including formylcamphor. In tetrachloromethane formylcamphor was found to exist mainly in the s-*cis* or *syn*-hydroxymethylene form stabilized by intramolecular hydrogen bonds together with 5 – 30 % of the s-*trans* or *anti* form and 5 – 10 % of the two ketoaldehyde forms. The 90 MHz proton NMR data for ma(fmcH) in $CDCl_3$ is listed in Table 1. The spectrum recorded soon after preparing the solution is different from spectra obtained later. After 10 h no change in the spectrum is observed. The assignments indicated in Table 1 are similar to those of Garbisch when appropriate. The spectrum obtained at first in $CDCl_3$ shows that an *anti* conformation of the enamine is dominant and, therefore, this isomer probably is the species which builds up the crystalline material used. This is also the configuration which is likely to be most abundant in strongly hydrogen bonding solvents as was also shown by Garbisch introducing DMSO into CCl_4 solutions of formylcamphor.[17] In $CDCl_3$ after 24 h the ratio of *syn*/*anti* is approximately 6:1 as obtained from integration of the vinyl proton signals. The spectrum of ma(fmcH) in CD_3OD shows that the same ratio in methanol solution is 1:3. In benzene and acetone solutions the *anti* form III is dominant. There is not enough of the Schiff base forms (I) to allow their detection.

The coupling constant between the vinyl proton and the NH proton is the same for the forms II and III, *i.e.* 12 – 13 Hz (Table 1). This magnitude is characteristic for a *trans* coupling of *vic.* protons and thus we conclude that the carbon-nitrogen bond CH – $NHCH_3$ has some double bond character and that the two hydrogen atoms are *trans* also in III.

Table 1. Proton magnetic resonance data (90 MHz) for some of the protons of ma(fmcH) in deuterated chloroform, methanol, benzene, and acetone. For the signals from chloroform solution it is indicated how these vary the first hours after dissolution and for all solvents the equilibrium ratio between the isomers II and III are given. δ is measured from TMS as an internal standard.

Protons of structure		$CDCl_3$ δ	Variation with time	(J Hz)	CD_3OD δ	(J Hz)	C_6D_6 δ	(J Hz)	CD_3COCD_3 δ	(J Hz)
N – H···O = C	II	7.39	increases				7.55			
N – H	III	4.25	decreases				3.71		5.54	
= CHN	III	7.00	decreases	(12.6)	7.09		7.00	(12.6)	6.88	(12.7)
= CHN	II	6.29	increases	(12.6)	6.51		5.85	(12)	6.41	(12)
CH_3N	III	2.94	decreases	(5.0)	2.96		2.11		2.93	(4.8)
CH_3N	II	2.91	increases	(5.0)	2.93		2.34	(3.5)		
CH	III	2.48	decreases	(3.6)	2.63	(3.6)			2.65	(4)
CH	II	2.30	increases	(3.7)	2.33	(3.6)				
The ratio of II:III after 24 h		6:1			1:3		changing from 1:10 to 10:1 during 24 h		~1:20	

Table 2. Wave-length of absorption maxima and the associated molar absorptivity to the left and corresponding circular dichroism data to the right.

Compound	Absorption spectra Solvent	λ nm	$\varepsilon_{mol} \times 10^{-4}$	λ nm	$\varepsilon_{mol} \times 10^{-4}$	Circular dichroism spectra λ nm	$\Delta\varepsilon_{mol}$	λ nm	$\Delta\varepsilon_{mol}$
ma(fmcH)	CH_3OH	314	2.2			295	10.6		
ma(fmcH)	$CHCl_3$, aged	313	1.3[a]			298	7.6	338	−3.5
tn(fmcH)$_2$	CH_3OH	322	4.3			295	19.0		
tn(fmcH)$_2$	$CHCl_3$, aged	310	2.8[a]			298	17.3	330	−3.7
R-chxn(fmcH)$_2$	CH_3OH	300	4.1	326	1.9	298	−51.6	333	60.8
R-chxn(fmcH)$_2$	$CHCl_3$, aged	293	2.9	312	2.2	300	44.7	340	−46.5
R-pn(fmcH)$_2$	CH_3OH	298	3.6	326	2.4	295	−24.3	333	35.7
R-pn(fmcH)$_2$	$CHCl_3$, aged	298	2.3	311	2.5	296	23.1	333	−30.0
en(fmCH)$_2$	CH_3OH	298	3.3	326	2.9	297	−4.7	335	24.0
en(fmcH)$_2$	$CHCl_3$, aged	292[b]	2.5	311	2.8	308	19.6	344	−2.1
	$CHCl_3$, aged, at −60 °C					297	−9.9	324	23.8
						332	20.7	337	22.0

[a] shoulder on low energy side. [b] shoulder.

^{13}C NMR is consistent with the above results. However, this method is a less accurate measure of the isomer distribution and will, therefore, not be discussed here.

For the *trans*-(−)$_D$-(*R*,*R*)-1,2-cyclohexanediamine derivative, R-chxn(fmcH)$_2$, the same kind of *syn-anti* isomerization is noticed in the ^1H NMR spectra of $CDCl_3$ solutions. Intergration of the vinyl proton signals gives a ratio of *syn*/*anti* of *ca.* 10:1 in aged $CDCl_3$ solution. For other formylcamphor derivatives used in this work a similar analysis has been carried out to ensure that in aged chloroform solutions the major constituents are the *syn* isomers.

The optical properties vary with the choice of solvent in accordance with the isomer distribution. Absorption and circular dichroism data for methanol and aged chloroform solutions are shown in Table 2. The monomeric ma(fmcH) in methanol has a much more intense absorption than it has in chloroform after 4 h whereas there is little change in the band position. This is in perfect agreement with the usual behaviour for $\pi \rightarrow \pi^*$ transitions in systems having conjugated double bonds either s-*trans* or s-*cis*. Two small Cotton effects are found under this absorption band, for methanol and chloroform solutions. The larger CD maximum is found at 298 − 295 nm for the two solvents, *i.e.* significantly displaced from the absorption maximum at 314 − 313 nm. This leads us to attribute the Cotton effect not to the $\pi \rightarrow \pi^*$ transition but to the magnetically allowed $n \rightarrow \pi^*$ transition. This may be supported by the fact that the sign of the Cotton effect is the same as for camphor.

The dimeric molecules formed by condensation of diamines and formylcamphor will then have two reasons to exhibit Cotton effects, *i.e.* the inherent Cotton effect from the presumed $n \rightarrow \pi^*$ transition and the Cotton effects produced by the coupling of the two $\pi \rightarrow \pi^*$ transitions. Only when very intense Cotton effects are observed can they be assigned as arising from exciton coupling. This can be illustrated by tn(fmcH)$_2$ and R-chxn(fmcH)$_2$. The former molecule has CD bands in $CHCl_3$ having $\Delta\varepsilon$ approximately twice that of ma(fmcH) while the latter has two large Cotton effects of opposite sign (Fig. 1) associated with the exciton split transitions. The insignificant electronic coupling during excitation between two formylcamphor groups attached to a bridge of three carbons is further demonstrated by the fact that R-(1,3)-bn(fmcH)$_2$ exhibits exactly the same UV absorption and circular dichroism as tn(fmcH)$_2$.

The analyses of the exciton transitions for R-chxn(fmcH)$_2$ follows closely the treatment outlined earlier.[3] It is gratifying to notice that in solutions where the *syn* forms are the

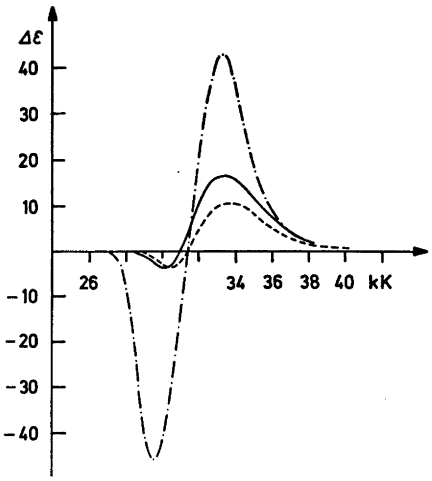

Fig. 1. Circular dichroism spectra of aged (24 h) chloroform solutions of ma(fmcH) - - - -, tn(fmcH)$_2$ ———, and R-chxn(fmcH)$_2$ —.—.—.

dominant the geometry of the set of lines defined by the N—O directions within the π system is the same as for R-chxn(acacH)$_2$. The exciton splitting for R-chxn(fmcH)$_2$ is *ca.* 2.0 kK and therefore, the two split components show considerable circular dichroism in spite of partial cancellation.

The absorption and circular dichroism of R-chxn(fmcH)$_2$ in methanol (Fig. 3 of Ref. 3) is very different from the spectra in aged chloroform. The general characteristics for exciton coupled transitions are present and realizing that only *ca.* 2/3 of the sample is in the *anti* configuration the rotatory strengths are very high indeed. The energy separation of the two transitions is found to be ~2.6 kK and for exciton coupling it is calculated as

$$\Delta E = 2\frac{D_{\text{monomer}}}{r^3_{\text{AB}}}(\cos\theta - 3\cos\phi_{\text{A}}\cos\phi_{\text{B}})$$

with symbols explained in Ref. 3. Considering the length of a O=C—C=C—N chromophore in the *trans* configuration we must conclude that in order for ΔE to be larger than for the *cis* isomer the value in the parenthesis must be larger. Therefore, we tentatively suggest that the solvation in methanol is of a special nature, *e.g.* such that one solvent molecule coordinates to both nitrogen atoms forcing ϕ_{A} and ϕ_{B} to be close to 90°.

In order to verify that the *syn-anti* equilibrium is established in methanol the following experiments were performed. Aged solutions of R-chxn(fmcH)$_2$ in $CHCl_3$ were evaporated, and when the residue was redissolved in $CHCl_3$ it showed immediately the CD spectrum characteristic for aged $CHCl_3$ solutions. However, when dissolved in methanol it took several hours before the CD-spectrum had reached the normal shape for CH_3OH solutions.

When $CHCl_3$ is used without purification or when HCl is added to the solvent the change with time in the spectra is accelerated, probably because the *anti/syn* interconversion is sensitive to acid catalysis. The effect is only of a catalytic nature since the same final results are obtained for pure and acidified solvents.

Condensation products of 1,2-ethanediamine and 1,2-propanediamine with formylcamphor have low barriers for rotation around the C—C bond of the diamine. If equal amounts of the two *gauche* isomers exist in equilibrium with the *trans* isomer for en(fmcH)$_2$ then the circular dichroism is expected to be similar to that of ma(fmcH) but twice as intense. The extremum values from Table 2 show that in $CHCl_3$ this is not too far from being the case at room temperature.

However, at lower temperatures aged chloroform solutions of en(fmcH)$_2$ exhibit circular dichroism curves which gradually approach the characteristic shape for exciton bands of dimers. At −60 °C the circular dichroism spectrum is still rather far from the supposed final band shape (Table 2). The dichroism variation with temperature is explained as a displacement of the equilibrium between the three rotamers towards the most stable rotamer. This should be the one having the opposite absolute configuration of R-chxn(fmcH)$_2$ as judged from the CD spectrum. R-chxn(fmcH)$_2$ does not exhibit a similar variation of CD with temperature consistent with the non-existance of rotamers.

As expected there is some stabilisation of one *gauche* rotamer over the other for R-pn(fmcH)$_2$ in $CHCl_3$. However, the methyl group of the diamine interacts much less with the camphor group than with the methyl group of acetylacetone in R-pn(acacH)$_2$, and, therefore, the circular dichroism is small compared to that of R-pn(acacH)$_2$ and also smaller than that of R-chxn(fmcH)$_2$. For an aged chloroform solu-

tion of R-pn(fmcH)$_2$ a small (5 – 10 %) increase of the circular dichroism on cooling to – 60 °C was observed. This effect is smaller for R-2,3-bn(fmcH)$_2$ where the intensity enhancement is very close to that caused by contraction of the solution. These findings could be explained in several ways, *e.g.* as due to the *syn*, *anti* equilibrium. The ^{1}H-NMR is not sensitive enough to exclude such an explanation but one would then be left with the problem of why R-chxn(fmcH)$_2$ has no temperature dependent Cotton effects in aged chloroform. Therefore, it is assumed that the variable temperature circular dichroism reflects the rotamer equilibrium and it follows as expected that the derivatives of 1,2-ethanediamine, 1,2-propanediamine, and 2,3-butanediamine have increasing barriers towards rotation.

The above illustrates that the stereochemistry of the condensation products between diamines and formylcamphor can be understood. These molecules are unfortunately not well suited for a quantitative investigation of the exciton coupling mechanism and as here demonstrated mistakes were introduced if one relied on the exciton theory alone.

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