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TRIPLE ION CHELATE STRUCTURE OF AN EQUILIBRIUM MICHAEL ADDUCT

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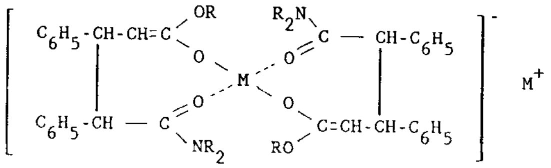
The equilibrium adduct from the Michael reaction between lithium dimethylphenylacetamide enolate and methyl cinnamate has been studied by means of ^{7}Li, ^{13}C and ^{1}H NMR and IR spectroscopy as well as by electrical conductivity measurements in THF and diethyl ether. The ^{7}Li NMR and the electrical conductivity measurements data are consistent with a triple ion structure of $[A^-M^+A^-]^-$ M^+ type, favoured in THF. All other spectral data support an intramolecular chelation in the triplet fragment.

INTRODUCTION

In the course of a recent study on the addition of sodium and lithium *N,N*-dialkylphenylacetamide enolates to cinnamic acid dialkyl amides and esters and to cinnamic aldehyde, we observed a high thermodynamic diastereoselectivity (*erythro* : *threo* = 5 : 95), explained by stabilizing chelation in the reaction adduct.[1,2] Such chelation has been postulated previously to explain the equilibrium stereochemistry in some aldol-type reactions.[3,4] The structures of the corresponding chelates, however, have not been investigated.

We found a strong dependence of the *threo*-chelate stability on the metal counter ion, temperature, concentration and the presence of dechelating agents such as crown ethers or neutral carbonyl compounds. The action of the dechelating agents leads to a strong decrease in diastereoselectivity (*erythro* : *threo* = 40 : 60) accompanied by an increase in the electrical conductivity of the reaction mixture. This reaches a maximum after the addition of 0·5 equiv. of dechelating agent. This fact allowed us to postulate for the equilibrium adduct a triple ion chelate structure, represented below for the case studied in the present work by means of ^{7}Li, ^{13}C and ^{1}H NMR and IR spectroscopy (for **1**) and electroconductivity measurements (for **1** and **2**):



where M = Li (**1**); M = Na (**2**).

EXPERIMENTAL

The ^{7}Li NMR spectra were measured on a Bruker WH-90 spectrometer at 34·98 MHz and the chemical shifts were assigned with respect to 0·5 M solution of $LiClO_4$ in D_2O. The ^{13}C NMR spectra were recorded on a Bruker WH-90 spectrometer at 22·63 MHz relative to TMS as external standard using the off-resonance technique. Only some of the signals were assigned. The ^{1}H NMR spectra of **1** and of the neutral *threo* isomer were recorded on a Bruker WH-250 spectrometer in THF-d_8 with TMS as internal standard. IR spectra were measured on a Beckman IR 20 spectrometer. The

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erythro : *threo* ratios were determined using the resolved $COOCH_3$ proton resonances.

Electrical conductivity of THF solutions was measured at 25 °C in a cell with platinum electrodes (cell constant 0·01098 cm^{-1}) on a Tesla BM 509 semiautomatic capacitance bridge.

The solvents used were freshly dried, distilled and degassed. The syntheses of **1** and **2** were carried out under an argon atmosphere as described[1,2] and the samples for spectral studies were taken with a syringe and kept under argon.

RESULTS AND DISCUSSION

^{7}Li NMR data

The organolithium compounds are known to show a definite tendency to triple ions formation.[5–9] Both lithium atoms in the triple ion pairs can be easily detected by means of ^{7}Li spectroscopy.[6,10]

The ^{7}Li NMR spectra of **1** in THF and diethyl ether at ambient temperature show two signals (Figure 1 a and b) which differ from those of the metallating agent BuLi (1·32 ppm) and the starting enolate (– 0·18 ppm).

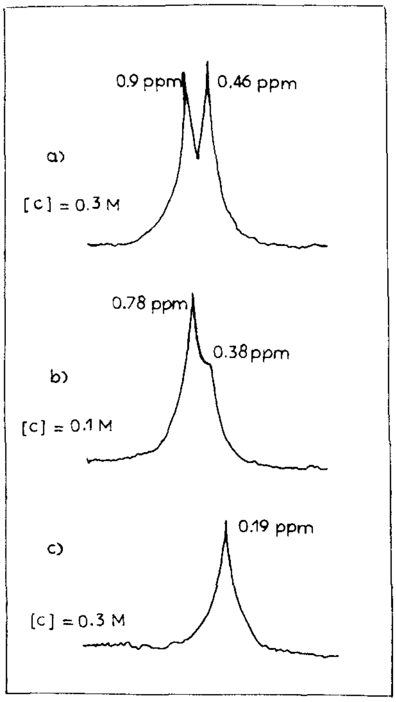

Figure 1. ^{7}Li NMR spectra (34·98 MHz, 0·5 M solution of $LiClO_4$ in D_2O as external standard) of **1**: (a) in THF; (b) in diethyl ether; (c) in THF in the presence of 0·5 M bicyclohexyl-18-crown-6

The up-field signal (0·56 ppm in THF and 0·48 ppm in diethyl ether) does not significantly depend on the solvent. This allows us to assign it to the included in the triple ion lithium by analogy with the data reported for the ^{7}Li resonance in cryptand [2.1.1] complex.[6,11,12]

We assume the following equilibrium to exist in the solution of **1**:

$$[A^-M^+]_2 \cdot x\ \text{Solv.} \rightleftharpoons [A^-Li^+A^-]^-, Li^+ \cdot x\ \text{Solv.}$$

The ratio of both ^{7}Li resonances in THF is approximately 1 : 1 and does not depend on the concentration (c = 1·0–0·1 mol/l). This excludes a possible coincidental ratio of aggregates.[13] Hence, the downfield signal can be assigned to the 'external', uncomplexed lithium ion from the triple ion pair. From the absence of a third peak we conclude that the above equilibrium is shifted completely to the right.

In a medium with lower polarity (diethyl ether), the upfield peak appears as a well depicted shoulder whereas the area of the downfield peak strongly increases. Probably the weaker solvation of the 'external' lithium destabilizes the triple ion and the equilibrium shifts to the left. The signal at 0·78 ppm (Figure 1 b), in our opinion is due to the overlapping of the resonances of the lithium ion in the dimer and the 'external' one in the triple ion pair. Both lithium atoms are peripherally, non-symmetrically solvated in tight ion pairs (see the results of the electrical conductivity measurements).

The observed ^{7}Li signals do not represent an ion-pair equilibrium because, according to literature data, the exchange of ion pairs usually is very fast relative to the NMR time scale at ambient temperature.[10]

In the presence of 0·5 equiv. of bicyclohexyl-18-crown-6 a single peak at 0·19 ppm appears (Figure 1 c), which is accompanied by a change of the stereochemistry as was mentioned before. A logical explanation is that the signal observed is an average one for ^{7}Li in the dechelating metal form, and that in the bicyclohexyl-18-crown-6 complex, a result of a fast exchange at ambient temperature.

The results obtained support the postulated triple ion chelate structure. The tendency for its formation is stronger in THF than in diethyl ether.

^{13}C NMR data

The ^{13}C NMR data cannot be used for complete confirmation of the postulated triple ion, but they indicate the participation of the carbonyl functional groups in the chelation process. Thus, the ^{13}C NMR spectrum of **1** contains signals that exceed the number of expected carbon atoms; this may be due to restricted rotation around some bonds or to a change in the aggregation state.[14–16] The signals for the carbonyl carbon atoms in the neutral *threo* isomer appears as a single peak at 172·17 ppm, whereas in the lithium salt **1** two new signals at 175·12 ppm and 165·17 ppm are observed. We consider the up-field shift to be caused by the shielding of the ester CO atom because of enolization. This is supported by the fact that the metal counter ion is at C_4 position (heavy water hydrolysis). Downfield shift of the CO group is usually connected with a strong coordination of this group. We assign the signal at 175·12 ppm to the coordinated amide group, which is known to possess a good complexing power.[17] In the presence of bicyclohexyl-18-crown-6 when the *erythro*:*threo* ratio changes from 5:95 to 37:63 a signal for uncoordinated amide group appears. The observed shifts of +2·9 ppm and −6·52 ppm allow a significant intramolecular coordination to be assumed.

^{1}H NMR data

The $N(CH_3)_2$ group in the neutral *threo* product gives two signals at 3·44 and 3·34 ppm. No change in the position of these peaks is observed in the metal form **1**. This rejects the participation of the nitrogen atom in the coordination.

The doublet for $-C_3H{=}$ at 4·1 ppm in the spectrum of **1** is consistent with the enolization of the ester group. The J(C-3, C-4) vicinal coupling constant is about 11 Hz. This value and the requirement that the two carbonyl centres be in closer proximity during chelation suggest a *Z*-configuration for the adduct enolate.

IR data

In the spectrum of **1** in THF shown in Figure 2, the band of ν $COOCH_3$ at 1735 cm^{-1} disappears and a new strong band at 1620 cm^{-1} is observed due to an enolate double bond.[16,18] The $CON(CH_3)_2$ absorption band shifts from 1750 cm^{-1} in the neutral product to 1740 cm^{-1} in **1** which is an indication of chelation.

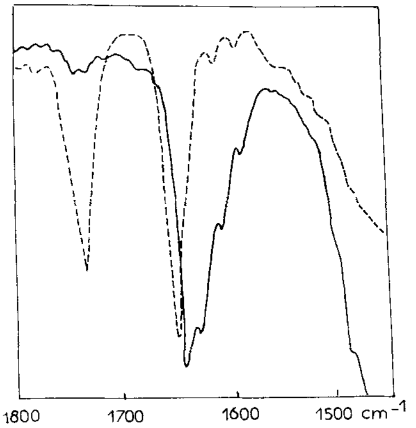

Figure 2. Infrared spectra in the 1500–1600 cm^{-1} region: (----) of the neutral *threo* isomer; (———) of the lithium salt **1**

Electrical conductivity data

The results from the electrical conductivity measurements are given in Table 1. In the concentration range of 5×10^{-2}–1×10^{-3} M the value of equivalent conductivity Λ remains almost independent for both **1** and **2**. According to de Groof *et al.*[19] this finding indicates the formation of only one type of triple ion. We assume the predominance of the negative triple ion $[A^-M^+A^-]^-$ because it is more stable[20] and tends to form 'ate' complexes within lithium and sodium counter ions.[21]

According to Hirohara and Ise,[20]

$$\Lambda = [K_T^{1/2}/(1 + K_T^{1/2})]\,\lambda_0, \tag{1}$$

where λ_0 denotes the sum of limiting conductances of the ions in the triple ion pair, it is possible to establish the equilibrium constant K_T:

$$[A^-M^+]_2 \underset{}{\overset{K_T}{\rightleftharpoons}} [A^-M^+A^-]^- + M^+ \tag{2}$$

Actually the system consists of the following equilibria:

$$[A^-M^+]_2 \overset{k'}{\rightleftharpoons} [A^-M^+A^-]^-,$$

$$M^+ \overset{K_T^\prime}{\rightleftharpoons} [A^-M^+A^-]^- + M^+ \tag{3}$$

where $K_T = k' \cdot K_T^\prime$ and

$$[A^-M^+A^-]^- \overset{k_T}{\rightleftharpoons} A^- + A^-M^+ \tag{4}$$

$$A^-M^+ \overset{K_D}{\rightleftharpoons} A^- \qquad M^+ \tag{5}$$

where $K_T = K_D/k_T$.

It was found that the dependence of Λ on the concentration c follows Wooster's equation:[22]

$$\left(\frac{f\Lambda}{m}\right)^2 \frac{c}{(1 - \Lambda/\Lambda_0)} = \Lambda_0^2 K_D + \frac{(2\Lambda_0\lambda_0 - \Lambda_0^2)}{k_T}(1 - \Lambda/\Lambda_0)cK_D \tag{6}$$

where f is the activity coefficient, m is the mobility coefficient and Λ_0 denotes the limiting conductance of the ion pair, $1 - \Lambda/\Lambda_0$ being neglected because of the low value of Λ/Λ_0.

Table 1. Molar conductivity of THF solutions of lithium **1** and sodium **2** salts at 25 °C

1		**2**	
c (M)	(cm^2 $\Omega^{-1}\cdot$M^{-1})	c (M)	(cm^2 $\Omega^{-1}\cdot$M^{-1})
0·1000	0·0164	0·0750	0·0160
0·5250	0·0170	0·0380	0·0180
0·0280	0·0154	0·0220	0·0195
0·0155	0·0150	0·0115	0·0211
0·0086	0·0149	0·0052	0·0244
0·0050	0·0200	0·0025	0·0288
		0·0013	0·0352

Table 2. Dissociation constants of ion pairs (K_{D}) and triple ions k_{T} of **1** and **2** in THF

M^+	K_{D} (10^{11} M)	a[a] (Å)	k_{T} (10^3 M)	K_{T}[b] 10^8	K_{T}[c] 10^8	Λ_0 ($cm^2\ \Omega^{-1}\ mol^{-1}$)	λ_0
Li	6·8	2·85	1·3	5·2	5·9	75·2	61·5
Na	21·9	3·00	4·5	4·9	9·2	83·8	69·5

[a] Average interionic distance for ion pair A^-M^+ according to Fuoss[24]
[b] According to Wooster[22]
[c] According to de Groof *et al.*[19]

The results obtained from equations (1) and (6) are given in Table 2.

The values of Λ_0 and λ_0 are determined from the well known linear correlation $\log \Lambda_0\eta = f(M)$ where M is the molar mass.[23]

The very close values for K_{T} obtained in two different ways show that the λ_0 values have been correctly calculated.

From the data given in Table 2, the following conclusions can be drawn. The K_{D} of **2** is one order of magnitude higher than that of **1** which can be explained by the greater ionic radius of sodium and by its diminished solvation ability in comparison with lithium counter ion. The K_{D} values are very low for both **1** and **2** in comparison with the data theoretically calculated according to Fuoss and Aceascina[24] and those available for some other salts with large anions (e.g. tetraphenylborates).[25] This result and the average interionic distance a for ion pair A^-M^+ are consistent with a strong intramolecular chelation where the metal counter ion penetrates into the anionic sphere.

From the low value of K_{T} as well as from the ^{7}Li NMR data we conclude that the triple ion pair $[A^-M^+A^-]^-$, M^+ is predominant in THF solution, which means that $k' > 1$. Although we can only approximate k', using the equation[24]

$$K_{\mathrm{T}}' = (3000/4\pi a^3 N)\exp(-e^2/aDkT)$$

it is possible to evaluate K_{T}' [equation (3)] and, hence, the average interionic distance **a**′ for the triple ion pair. From $K_{\mathrm{T}} = k'K_{\mathrm{T}}'$ it follows that $K_{\mathrm{T}}' < K_{\mathrm{T}}$. Thus, a' is about 3–3·5 Å, which is smaller than the sum of the ionic radii. Actually from the consideration of molecular models an access to, and therefore coordination of, the 'external' cation to the triple ion polar groups seem quite possible.

This study confirms the postulated triple ion chelate structure which stabilizes the *threo* adduct in the investigated Michael addition.

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