

Complexation of Dibenzylammonium Salt by *N,N*-Dimethyl-1,7-diaza-4,10-dioxacyclododecane. A Reinvestigation

JOSTEIN KRANE* and ODDVAR AUNE

Kjemisk institutt, NLHT, Universitetet i Trondheim, N-7000 Trondheim, Norway

The previously reported structure for *N,N*-dimethyl-1,7-diaza-4,10-dioxacyclododecane complexed with dibenzylammonium ion is not compatible with results obtained from both ^1H and ^{13}C DNMR studies.

In ^{13}C NMR one conformational process is visible in the complexed ligand with a barrier of 7.7 kcal/mol (ΔG^\ddagger).** The ^1H spectra show two barriers to conformational exchange of ~ 11 and 7.8 kcal/mol. The decomplexation barrier, as determined by ^{13}C DNMR, is ~ 8.5 kcal/mol.

These results are consistent with a [3333] conformation for the ring, and the conformational mobility may be rationalized on the basis of multi-step processes.

A large ^{13}C chemical shift variation with temperature is observed for the benzylic carbons in the complexed dibenzylammonium ion.

Stoddart and his coworkers¹ recently communicated their interpretation of ^1H DNMR spectra of complexes of primary alkylammonium salts and secondary dialkylammonium salts with *N,N*-dimethyl-1,7-diaza-4,10-dioxacyclododecane (*I*) as a host molecule. They claim that the temperature dependent ^1H NMR spectra of the 1:1 complexes formed between *I* and $\text{R}_2\text{NH}_2^+\text{X}^-$ salts are consistent with complexes having C_{2v} symmetry as depicted in Fig. 1A. The conclusion is mainly based upon the observation that the signal for the NCH_2 protons in the ring separates into two groups of signals of equal intensity at low temperatures. The claim is, of course, correct provided that all dynamic processes in the host molecule have become slow on the NMR time scale.

The conformation of *I* proposed by these authors, has two serious trans-annular hydrogen-hydrogen interactions as shown in Fig. 1B, where Dale's wedge representation has been used.² In Dale's nomenclature this is a [2424] form.

In our work on 1,4,7,10-tetraoxacyclododecane (12-crown-4) (2) complexes³ we have found that the [3333] form is the preferred conformation when 2 acts as host in solution.

By analogy, we were surprised that the high-energy conformation [2424] would be the preferred conformation of *I*, even in a complex with secondary ammonium salts.

If the [2424] conformation is the correct one for

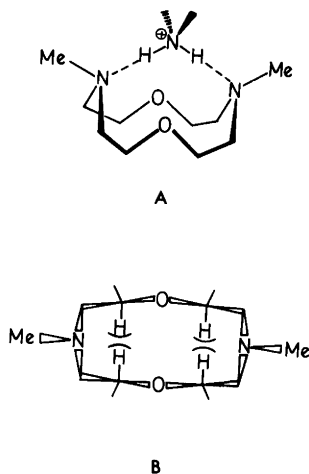


Fig. 1. A, The previous proposed structure¹ for complexes between dialkylammonium ions and *I*. B, Dale's wedge representation of the [2424] conformation.

* To whom correspondence should be addressed.

** 1 kcal = 4.184 kJ.

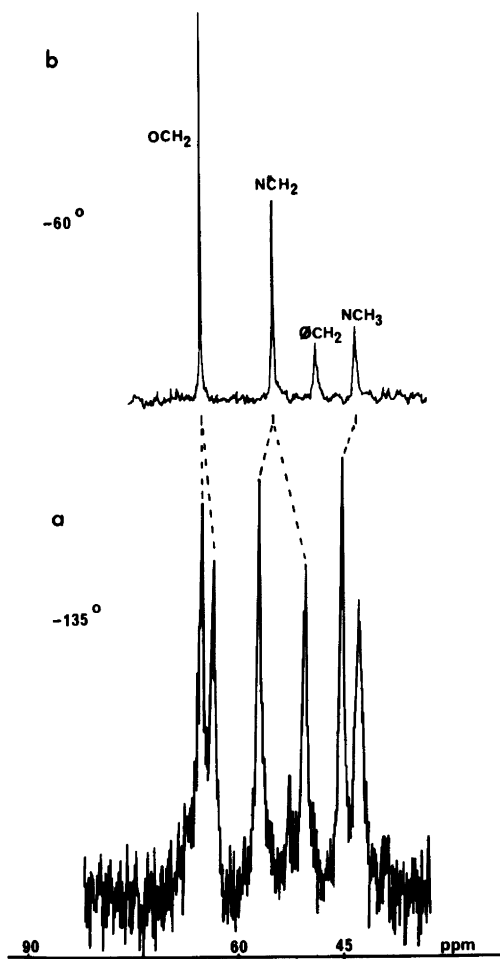


Fig. 2. The ^{13}C spectrum of the 1-dibenzylammonium complex (the phenyl carbons are not shown) at -135°C (a) and the ^{13}C spectrum at -60°C (b). The chemical shifts are relative to TMS.

1 as a host, the dynamic ^{13}C NMR spectrum should be temperature independent.

When a solution in CHCl_2F and CHClF_2 (in the ratio of 1:1) containing a 1:1 complex of dibenzylammonium thiocyanate with 1⁴ is cooled, a low temperature ^{13}C NMR spectrum as shown in Fig. 2 is obtained at 25 MHz. At higher temperatures the carbons α to oxygen and nitrogen coalesce pairwise to two single lines. The calculated activation free energy,⁵ ΔG_c^\ddagger , for the ^{13}C visible process is 7.7 kcal/mol at -98°C for the coalescence of the α -nitrogen carbons.

The ^{13}C chemical shift of the benzylic carbons in the dibenzylammonium ion show a strong temperature dependence in a very peculiar way. Above -50°C the chemical shift is ~ 51 ppm. Between -50 and -100°C the resonance moves to high field and stops at 43.4 ppm. Below -100°C there is almost no change in resonance frequency.

It is interesting to note that the dramatic shift change occurs over a temperature range where the decomplexation rate becomes slow (see below). It would be presumptuous at this stage to claim that we understand the temperature dependent shift behaviour of the benzylic carbons. One explanation, however, can be ruled out; it is not due to a proton transfer from the secondary ammonium salt (guest) to the tertiary amine (host) giving secondary dibenzyl amine, because the effect of deprotonation is a downfield shift for the benzylic carbons.

A ^1H NMR investigation of the same solution reveals two dynamic processes, one with an activation free energy barrier of about 11 kcal/mol, identical with the one observed by Stoddart *et al.*,¹ the other with a barrier of 7.8 kcal/mol, (ΔG_c^\ddagger), identical with the ^{13}C visible process.

The results clearly demonstrate that the previously reported suggestion¹ concerning the preferred conformation of 1 in secondary ammonium salt

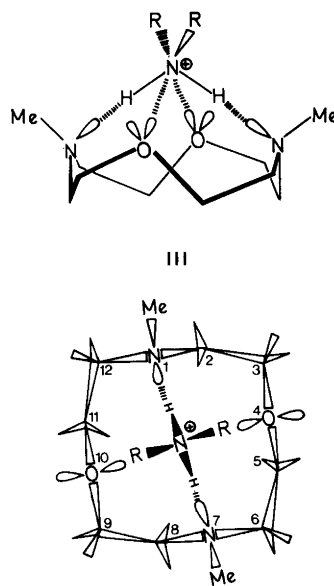


Fig. 3. The [3333] conformation of 1 complexed with dialkylammonium ion.

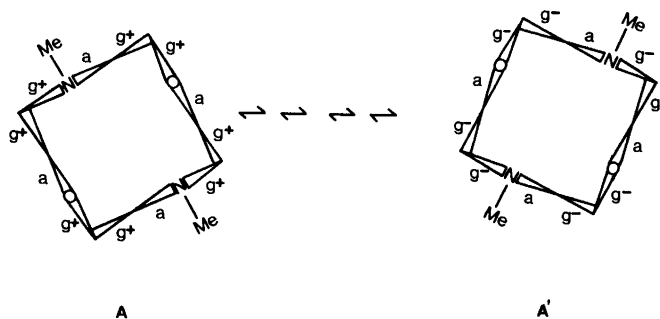


Fig. 4. Interconversion scheme leading to ^{13}C exchange in the [3333] conformation of **1**. Four low-energy corner-moving steps over CC *syn*-eclipsing barriers are involved.

complexes is wrong and based upon insufficient DNMR evidences. On the other hand, the DNMR results demonstrated here are consistent with a [3333] conformation of **1** as shown in Fig. 3. At slow exchange, the non-corner carbons C-2, C-5, C-8 and C-11 should show upfield shifts due to $\text{CH}_2\cdots\text{CH}_2$ γ -effects.

The ^1H NMR visible decomplexation barrier determined by Stoddart *et al.*¹ using a 2:1 ratio between **1** and dibenzylammonium salt is, of course, also visible in ^{13}C NMR. By using the latter probe we have determined a barrier of about 8.5 kcal/mol (ΔG_c^\ddagger) for the decomplexation process.

The thermodynamic and kinetic data obtained in these experiments are interpreted by us in a completely different way compared to the suggestions of Stoddard *et al.*¹ First of all, the term ring inversion as used by these authors, has in our opinion no meaning in large-membered rings without a further definition.⁶

The mechanism for the low energy process, visible both in the ^1H and the ^{13}C spectra, probably consists of a sequence of four steps, each described as a localized movement of the corner position. ($ag^\pm g^\pm \leftrightarrow g^\mp g^\mp a$).⁷ (Fig. 4) At each barrier top the CC bond becomes *syn* eclipsed, whereby one oxygen and one nitrogen atom come close, and therefore the barrier is rather low. It is worth noticing that the oxygens and nitrogens in **A** and its enantiomer **A'** are on the same side of the ring plane. During the four steps the ammonium salt (guest) does not need to become detached from the host, which also is evident from the decomplexation barrier of 8.5 kcal/mol compared to the low energy conformational barrier of 7.8 kcal/mol. This mechanism makes all carbons equivalent (or isochronous), but

geminal hydrogens are not. It might seem surprising that there are fast conformational processes taking place in the macrocycle after the decomplexation process has become slow, but this is a rather common feature in complexes of primary and secondary ammonium salts with crown type ligands.⁸

The mechanism for the decomplexation process is more difficult to evaluate from the DNMR data. The barrier observed may reflect the energy associated with a step-wise breaking and forming of hydrogen bonds and charge-dipole interactions. Support for this is borne out in observations that ΔG_c^\ddagger for decomplexation is sensitive to solvent polarity⁹ and the nature of the counter ion.¹ The kinetic picture for decomplexation might, therefore, be much more varied than what is proposed in schemes like "single face" exchange mechanism,^{1,10} exchange between "back" and "face" sides of the complex¹¹ or that decomplexation barrier reflects some rate-determining conformational step in the host.¹²

The high-energy ^1H DNMR process observed by Stoddart *et al.* of **1** in the secondary ammonium salt complexes makes geminal hydrogens equal. There is a large difference in the barrier height for the process responsible for geminal hydrogen exchange in **1** dependent on whether **1** is complexed or not.¹³ Any mechanism proposed must reflect this fact. The interpretation advocated by Stoddart *et al.* for this process seems ill-described at best. In large-membered rings where multiconformational processes (whose barriers can be different) are operational, the term ring inversion has no meaning without a further definition, except in the trivial case where the transition state is planar.⁶ Such a

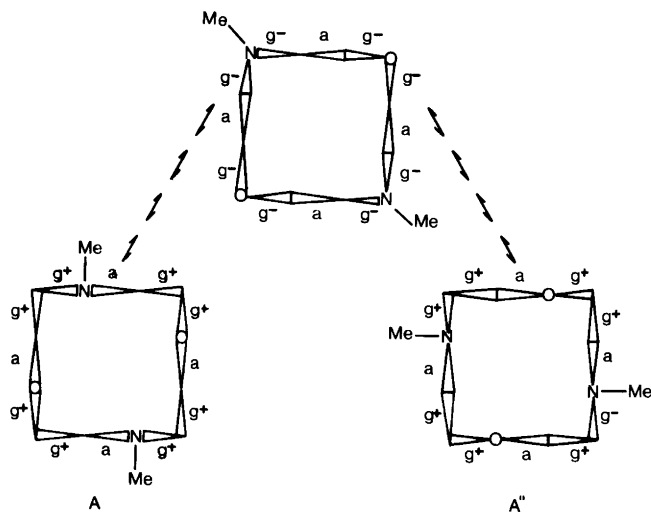


Fig. 5. Interconversion scheme leading to exchange of geminal protons. The hetero atoms pass the corners through *syn*-eclipsing barriers.⁷

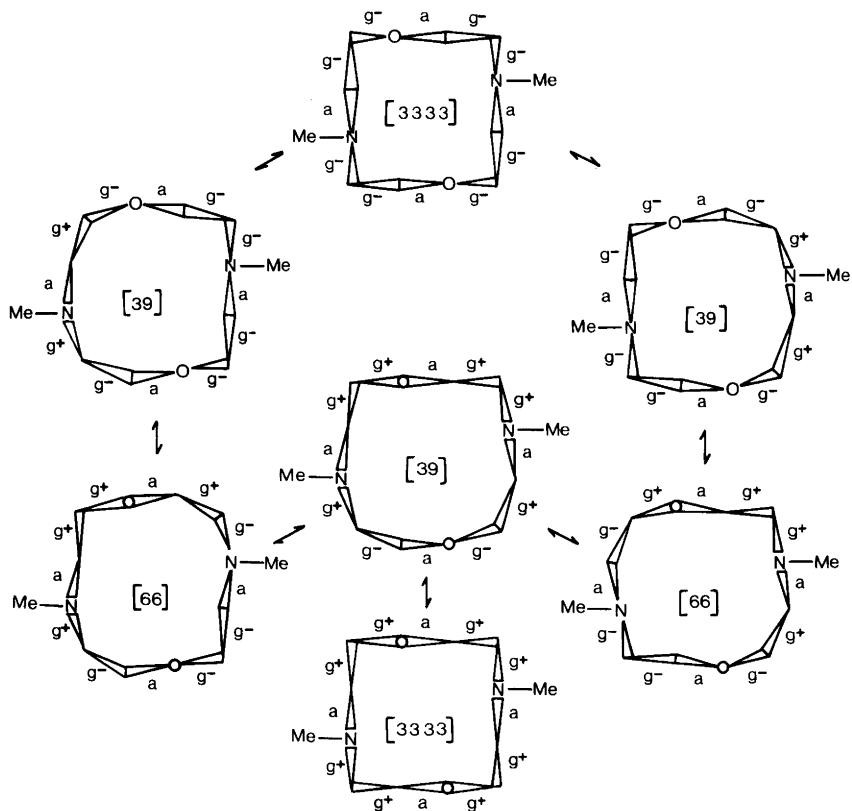
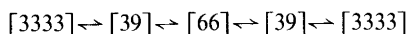


Fig. 6. Interconversion scheme leading to exchange of geminal protons. The interconversions are obtained through CH_2O and CH_2N rotational steps.¹⁴

transition state is of course energetically unrealistic in large-membered rings, making all torsional angles *syn*-eclipsed at the same time.

We tentatively propose two mechanisms for the high-energy process as shown in Figs. 5 and 6. Both have been proposed previously^{7,14} to account for the high-energy process in 2 acting as a host. Both mechanisms explain the increased barrier upon complexation of 1 with ammonium salts. As shown in Fig. 5, to get from A to A" in the complex, hydrogen bonds have to be broken.

The same is true for the mechanism described in Fig. 6 involving the sequence



At present we favour the latter exchange mechanism because it makes 1 consistent with 2 as far as the high energy process is concerned. Decisive conclusion may be reached by performing force-field calculations with proper parameters.

But these results do not warrant the general conclusion that the high-energy barriers observed^{1,10} are a composite of the decomplexation barrier and the energy associated with some so-called inversion processes.¹⁵

In conclusion, DNMR studies should be carried out over as large a temperature range as possible, and preferably with more than one nuclear probe.

The results from studies of complexes between primary ammonium salts and 1, the 1·2HClO₄ complex, and the free ring itself show interesting DNMR features and will be communicated at a later time.

EXPERIMENTAL

1 was synthesized by known procedures.⁴ The dibenzylammonium complex was obtained by dissolving equal molar amounts of 1 and dibenzylammonium thiocyanate in methanol. The solvent was slowly removed and a crystalline complex precipitated out of the solution.

The ¹H and ¹³C NMR spectra was obtained on a JEOL FX-100 instrument in the Fourier transform mode, equipped with a 5 mm dual ¹H/¹³C probe. Tetramethylsilane was used as an internal reference. All temperatures were measured with a copper-constantan thermocouple situated in the probe a few centimeters below the sample.

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