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^{1}H NMR studies of homo and mixed ligand complexes of Tl^+ ion with several polyazamacrocycles

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Abstract—Proton NMR was used as a probe to study the interaction of the Tl^+ ion with 9–18-membered macromonocyclic tri-, tetra-, and hexaamines in dimethylformamide (DMF) solution. A study of proton chemical shift of ligands as a function of Tl^+ ion to ligand mole ratio revealed that the complexation reactions occur in a stepwise manner. Formation of a 1:1 complex is followed by the addition of a second complexant molecule to form a homo-sandwich complex for triazamacrocycle ligands and a mixed ligand complex in the case of hexamethylhexacyclen (HMHCY) and 1,4,7-triazacyclononane ([9]aneN_3). The formation constants of resulting 1:1 and 1:2 (homo and mixed ligand sandwich) complexes in DMF solution were evaluated from computer fitting of the chemical shift-mole ratio data. The mixed ligand complexes may be more stable than the parent complex in which both ligands are the same. The influence of cavity size and substitution of methyl groups on nitrogen atoms of the macrocyclic ring the stability of the resulting complexes is discussed. The geometries of the tri- and tetraazamacrocycle ligands and their Tl^+ ion complexes were optimized by an ab initio method, and the calculated binding energies of resulting complexes were compared. Both the experimental and theoretical studies revealed that, in the presence of methyl groups, the stability of triazamacrocycle complexes with Tl^+ ion was decreased.

1. Introduction

Recognition and binding of ionic substrates to organic host molecules (e.g., enzymes, antibodies, or membrane transporters) are of vital importance in biological reactions. Model studies so far have centered mainly on the recognition of cations using synthetic host compounds, such as macrocyclic polyethers[1–6] and polyamines.[7,8] The chemistry of polyazamacrocycles is interesting because of their special ligational properties, which enables them to form stable complexes with both cationic and anionic species.[9–17] Almost all of the transition and heavy metal ions form stable complexes with these ligands.[18–22] It has been shown that nitrogen methylation of polyazamacrocycles produces significant changes in complexation reactions.[23–25] Structural factors have been shown to play significant roles in the determination of the strength of the interactions between the polyaza ligands and the guest species.[26–34] However, there are very few studies on the study of polyazamacrocyclic complexes with transition metal ions,[18–22] and the polyazamacrocycle-Tl^+ complexes, have received much less attention.[35] The bonding interaction between closed-shell, heavy metal ions is gaining increasing attention.[36,37] Even if thallium compounds can be poisonous to human, its compounds are used in different area such as radiopharmaceutical in cardiac imaging. The monovalent thallium ion has been suggested as a probe for potassium ion in biological systems.[38–40] It can substitute for K^+ ion activation of some important enzymes such as ATP ase[41] and pyruvate kinase.[42] Thus, the stability of Tl^+ complexes with macrocyclic ligands is of special interest with this respect.

One of the interesting features of polyazamacrocyclic ligands as nearly two dimensional ligands is their ability to form 1:2 (metal to ligand) sandwich complexes with metal ions that have larger ionic sizes than the ligand cavity. The formation of 1:2 complexes in solution and in the crystalline state, in which both complexant molecules are the same and different has already been reported.[28,43–47] The mixed ligand complexes may be more stable than the parent complexes in which both

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Keywords: Thallium(I); Mixed ligand complexes; NMR study; Azamacrocycles; Ab initio calculations.

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ligands are the same. Hoepping and et al. was synthesized a series of rhenium complexes as model compounds for the corresponding radioactive technetium-99m complexes for preliminary biological investigations.[48] In a mixed-ligand approach the tropanol molecule was linked with the metal core through a *o*-mercaptoester group as monodentate ligand. Bis(thioethyl)sulfide was used as the tridentate dithiol ligand to block the remaining free coordination sites. Parmar and co-workers are reported substantiating such a viewpoint, and demonstrating the formation of ADP-Fe-DHMC (7,8-dihydroxy-4-methylcoumarin) ternary complex with highest stability, while Fe-DHMC had negligible stability concluding that ADP-perferryl ion formation is prevented by DHMC resulting in the production of stable ternary mixed ligand complex (ADP-Fe-DHMC).[49] Ballesteros and co-workers reported a series of complexones with bis- or biazole structure as mixed ligands of paramagnetic contrast agents for magnetic resonance imaging (MRI).[50]

In this paper, we used ^1H NMR as a probe to study the complexation of Tl^+ ion with 9–18-membered macromonocycles (i.e., tri-, tetra-, and hexaamines) in DMF solution. The formation of homo and mixed ligand sandwich complexes of Tl^+ ion with N_3 series such as [9]aneN_3, [12]aneN_3, and Me_3[12]aneN_3, the N_4 and N_6 series containing [12]aneN_4, [14]aneN_4, and [18]aneN_6 (HCY), and Me_6[18]aneN_6 (HMHCY) was observed in DMF solution at 300 K. The effect of changing the macrocycle ring size, flexibility and number of nitrogen donor atoms on the stoichiometry and stability of the resulting complexes was investigated. The computational geometries of the tri- and tetraazamacrocycle ligands and their Tl^+ ion complexes were also optimized by an ab initio method, and the calculated binding energies of the resulting complexes were compared.

2. Result and discussion

2.1. Complexation with a single polyazamacrocycle

It is well known that the stability of the azamacrocycle complexes with metal ions depends on the relative dimensions of both the macrocyclic cavity and ionic radius of the metal ions, as well as on the degree of flexibility of the ligand and the number and substituent groups.[7–9,21,51] These factors determine either the fitting of the cation into the macrocycles cavity, or occupying a central position between two paralled planes defined by the rings nitrogen atoms. The metal ion will coordinate totally or only partially to the cyclic ligands, according to its electronic structure and size, in order to attain an optimum fit, yielding a cage type structure. The kinetics of complexation and dissociation processes and the solution structures of these chalets are also generally affected by the factors described above.[21,35,52–55]

In order to study the stoichiometry and stability of Tl^+ complexes with different aza-containing macrocycles used, the variations in chemical shifts of CH_2-groups (–CH_3 groups for HMHCY) of the ligands as a function of [Tl^+]/[macrocycle] mole ratio were measured. Upon complexation with the thallium ion, all methylene proton resonances of ligands display downfield shifts (cation-induced shift), indicating that nitrogen atoms intract with the cation. In the case of HMHCY, Tl^+ causes upfield shifts for methyl protons. These shifts result from the electrostatic effect of the cation on the ligand nuclei, which is proportional to charge density of metal ion and depends on the geometry of the complex, as the electric field effect caused by the metal ion on the polarization of each C–H bond depends on the component of the electric field of the cation at the C–H hydrogen atom along the direction of the C–H bond.[25,33] In all cases, except with [12]aneN_4, only one population average resonance was observed, indicating that the exchange rate of the ligand between the bulk solution and the complexed sites is fast on the NMR time scale (see Fig. 2). However, in the case of [12]aneN_4, any mixture of ligand and Tl^+ with [Tl^+]/[macrocycle] mole ratios between 0 and 1 resulted in three NMR resonance signals, revealing a slow exchange of the ligand between

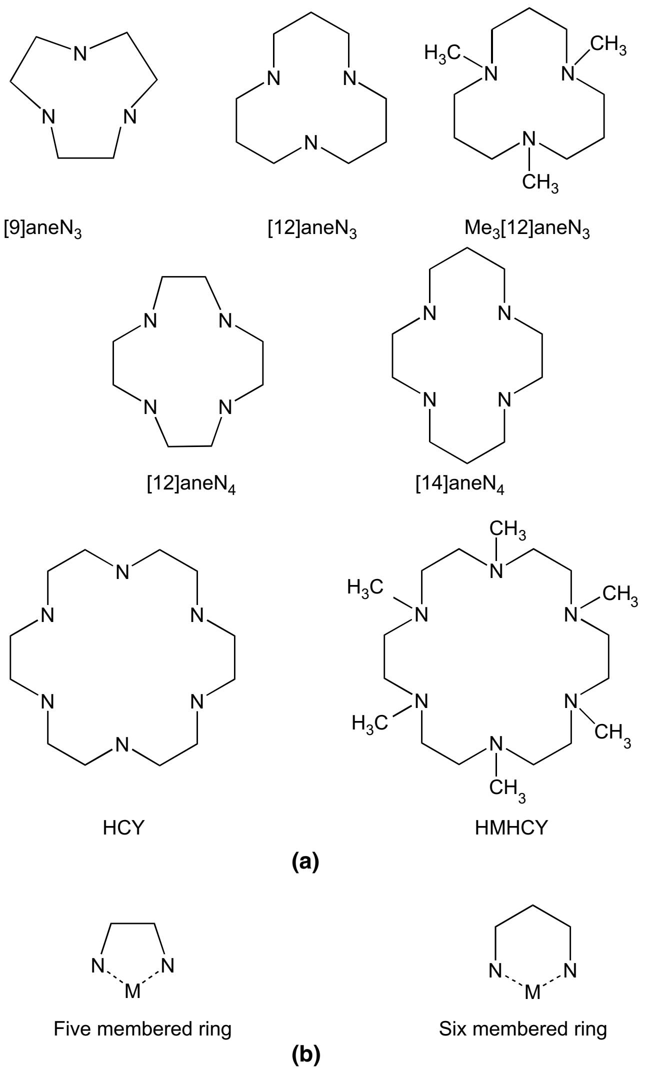

Figure 1. (a) Structures of the polyazamacrocyclic ligands, (b) five and six-membered chelate rings.

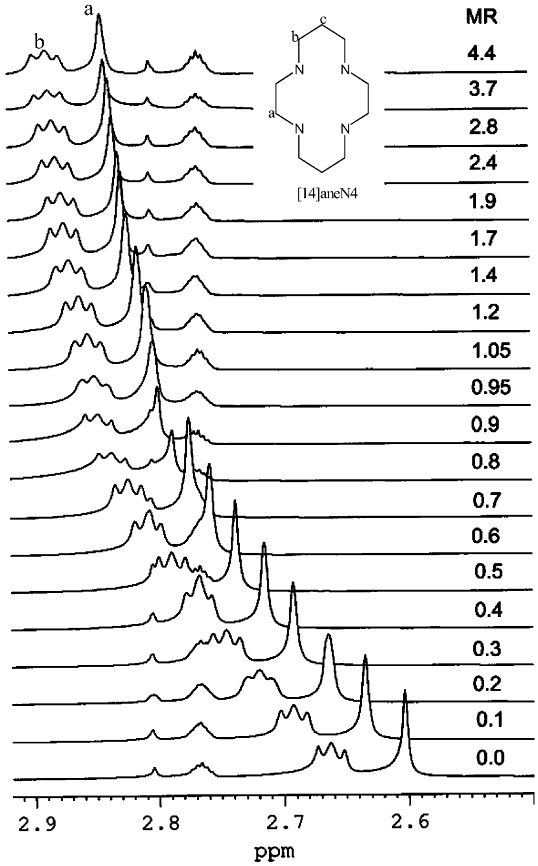

Figure 2. Proton NMR spectra of [14]aneN$_4$ at various Tl$^+$/ligand mole ratio in DMF at 300 K (H$_C$, multiple signal was not show).

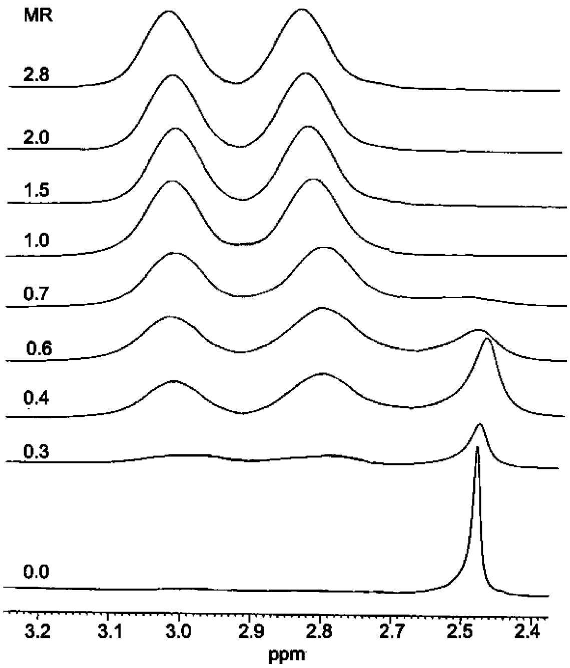

Figure 3. Proton NMR spectra of [12]aneN$_4$ at various Tl$^+$/ligand mole ratio in DMF at 300 K; chemical shifts of free ligand, $\delta = 2.48$ and complex, $\delta = 2.81$ and $\delta = 3.02$ ppm.

the free and complexed sites (see Fig. 3 and details in the text). Typical NMR spectra of [14]aneN$_4$ upon titration with Tl$^+$ ion are shown in Figure 2 and all the resulting chemical shift versus [Tl$^+$]/[macrocycle] mole ratio plots are given in Figure 4.

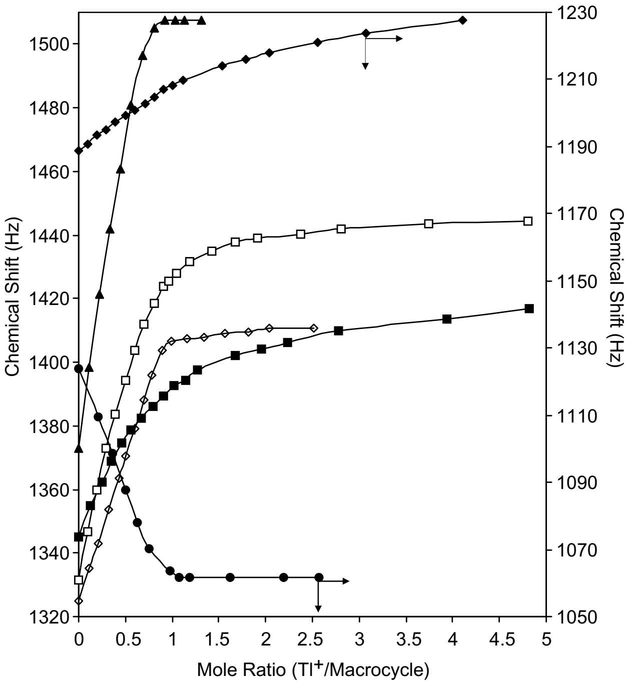

Figure 4. Proton chemical shift as a function of Tl$^+$/ligand mole ratio in DMF at 300 K: (▲) [9]aneN$_3$, (■) Me$_3$[12]aneN$_3$, (□) [14]aneN$_4$ and (◇) HCY left scale; (●) HMHCY, and (◆) [12]aneN$_3$ right scale.

In the cases of N$_3$ series, the addition of thallium ion to the ligand, produced a gradual nonlinear increase in paramagnetic shift of ligand protons until a mole ratio of about 1 is reached; further increase of the thallium concentration does not change the resonance frequency considerably. Qualitatively, the observed chemical shift-mole ratio behavior for small cavity N$_3$ azacrown ethers is indicative of the formation of relatively stable complexes of both 1:1 and 1:2 (metal to ligand) stoichiometries. It should be noted that, in all three N$_3$ systems, the convenient fit of the chemical shift-mole ratio data to equations dealing with the stepwise formation of 1:1 and 1:2 complexes further supports the existence of such two-step complexation reaction. A sample computer fit of the chemical shift-mole ratio data of this model is shown in Figure 5. Yang and Zompa have also reported the formation of 1:1 and 1:2 complexes between cyclic triamines and Ni^{2+}, Cu^{2+}, and Zn^{2+} ions that formed a 1:1 and 1:2 complexes in aqueous solution.[28]

Since the stoichiometry of complexes of the thallium ion with azacrowns depends on the number of nitrogen atoms in the ligand ring, and consequently the stability is related to the chelate ring size effect, the increase in the number of nitrogen atoms of the crown cavity was expected to change the stoichiometry and stability of the resulting Tl$^+$ complexes. In fact, the N$_4$ and N$_6$ series of polyazazamacrocycles used formed only 1:1 complexes with thallium ion in DMF solution (Fig. 4). A comparison between the formation constants of 1:1

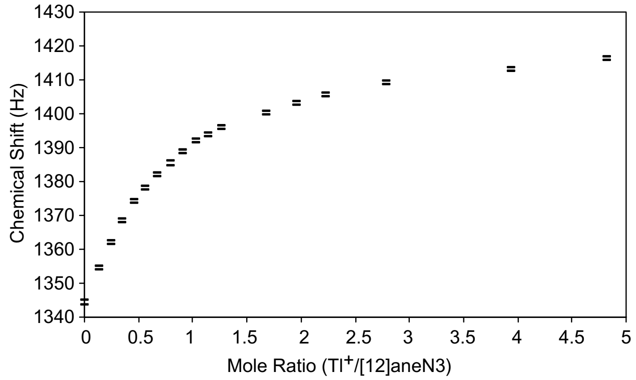

Figure 5. Computer fit of –CH_2– protons [12]aneN_3 chemical shift as a function of Tl^+/ligand mole ratio in DMF at 300 K: (=) experimental and calculated points are the same within the resolution of the plot.

complexes of N_3, N_4, and N_6 series with Tl^+ ion showed that the 18-membered ligands interact with the thallium cation more strongly in comparison with smaller azacrowns (Table 1). This indicates that N_6 series provide a favorable conformation for the inclusion of Tl^+ ion inside the cavity and binding of the nitrogen atoms of the ligand with it. The observed trend in the 1:1 complexes of N_3, N_4, and N_6 series with Tl^+ ion is consistent with the complexation constants reported in the literature for analogous complexes with a relatively large metal ion such as Pb(II).[26,27] The stability sequence of 1:1 complexes for tri-, tetra-, and hexaaza-macrocycles, in DMF solution is HMHCY > HCY > [12]aneN_4 > [14]aneN_4 $\geqslant$ [9]aneN_3 > [12]aneN_3 > Me_3[12]aneN_3.

In Table 1 are given the overall and stepwise formation constants obtained from computer fitting of the chemical shift-mole ratio data for N_3, N_4, and N_6 series of polyazamacrocycles with Tl^+ in DMF solution at 300 K. From the data given in Table 1 it is obvious that, in the case of the N_6 ligands studied, the stability of the resulting Tl^+ complex with HMHCY complex is higher than that with HCY. This is most probably due to the inductive electron pumping of the –CH_3 groups of the HMHCY, which can increase the basicity of the donating nitrogen atoms of its macrocyclic ring over that of HCY. However, in contrast to the N_6 series, the presence of –CH_3 groups in a smaller size azacrown such as [12]aneN_3 caused a significant decrease in the stability of both 1:1 and 1:2 resulting complexes with a large metal ion such as Tl^+. In fact, the metal ions that are too large for the cavity of a macrocycle are simply coordinated out of the plane of the donor atoms in different conformers. In these out of plane positions the size of the macrocyclic cavity is unimportant, and stability is controlled by the same geometrical factors that control stability in open chain ligands, namely, the size of the chelate ring.[26] Molecular mechanics calculation shows that as the metal ion gets larger, the chelate ring flattens, and the hydrogens rotate into eclipsed positions, with a rise in strain energy. Thus, very small metal ions (Ni^{2+}, Cu^{2+}, and Zn^{2+}) may coordinate best in the six-membered (M–N–C–C–C–N–) chelate rings, while complexes of large metal ions such as Pb^{2+} are destabilized by six-membered chelate rings. Increase of chelate ring size from five to six-membered rings (Fig. 1b) in a complex (e.g., [9]aneN_3 to [12]aneN_3) will decrease the stability of complexes of larger relative to smaller metal ions.[27,30] This rule holds for both macrocyclic and non-macrocyclic ligands. Five-membered (M–N–C–C–N–) chelate rings have minimum strain energy with large metal ions of high coordination number and thus small N–M–N angle. We found that in N_3 series with six-membered chelate rings (i.e., [12]aneN_3 and Me_3[12]aneN_3), addition of –CH_3 groups to the nitrogen atoms increases the strain energy when is complexed with a large metal ion such as Tl^+. Thus, the Tl^+–Me_3[12]aneN_3 system showed a strong decreases in complex stability, as it compared with Tl^+–[12]aneN_3 complex.

In Figure 6 are plotted the $\log\beta$ values for Tl^+ complexes with N_3, N_4, and N_6 series ligands against complex symbols given in Table 1. It is seen that Tl^+ has a $\log\beta$ with [9]aneN_3 some two orders of magnitude larger than that with Me_3[12]aneN_3. Hancock and co-workers used molecular mechanics calculations to examine stereochemical relationships associated with chelate ring size and concluded that saturated five-membered chelate rings favor binding to large metal ions and that similar six-membered rings favor small metal ion.[29,30]

In the case of [12]aneN_4, a peak broadening was observed when the Tl^+ ion concentration was increased, and two broad peaks having relative equal areas were observed for the complex ($\delta = 3.02$ and $\delta = 2.81$ ppm, Fig. 3). The area of the two peaks of equal intensity are directly proportional to the population of the complexed [12]aneN_4. The broad peak of the ligand disappeared while the mole ratio of Tl^+/[12]aneN_4 was increased to about 1. The results revealed both the formation of a stable 1:1 complex and very slow exchange of the ligand between the free and complexed sites on the NMR time scale. At mole ratio >1, the population of the two resonances of complex was kept constant

Table 1. Equilibrium constant for various complexes of Tl^+ in dimethyl formamide

Symbol	System	$\log k_1$	$\log k_2$	$\log\beta$
C_6N_3	Tl^+–([9]aneN_3)$_2$	3.33 ± 0.56	2.87 ± 0.21	6.20 ± 0.59
C_9N_3	Tl^+–([12]aneN_3)$_2$	2.58 ± 0.06	2.54 ± 0.12	5.12 ± 0.13
$C_{12}N_3$	Tl^+–(Me_3[12]aneN_3)$_2$	2.33 ± 0.04	2.24 ± 0.24	4.57 ± 0.24
$C_{10}N_4$	Tl^+–[12]aneN_4	4.42 ± 0.30	—	4.42 ± 0.30
$C_{12}N_6$	Tl^+–[14]aneN_4	3.77 ± 0.21	—	3.77 ± 0.21
$C_{12}N_6$	Tl^+–HCY	4.89 ± 0.50	—	4.89 ± 0.50
$C_{18}N_6$	Tl^+–HMHCY	5.82 ± 0.72	—	5.82 ± 0.72
$C_{24}N_9$	Tl^+–([9]aneN_3)(HMHCY)	6.51 ± 0.40	1.68 ± 0.35	8.19 ± 0.75

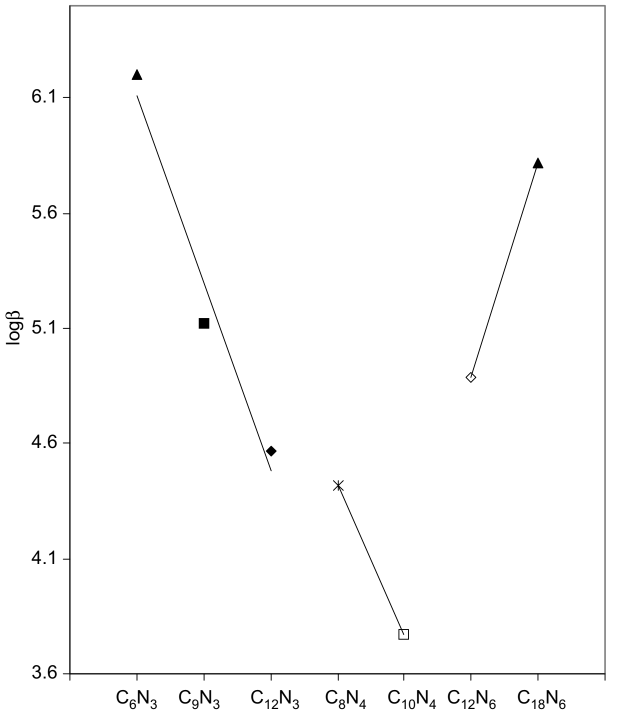

Figure 6. Plotes of the log β values for Tl^+ complexes with N_3, N_4, and N_6 series ligands against complex symbols given in Table 1.

and the chemical shifts did not show any variation. This is indicative of two possible types of methylene protons, distinctively assignable to the axial and equatorial forms in the complex (the conformation change of the complexes is slow). The peak broadening and very slow exchange rate existed in this complex system prevented quantitative fits of the data.

Finally, as it is obvious from Table 1 and Figure 6, among different azacrowns tested, there are strong interactions between Tl^+ ion and [9]aneN_3 and HMHCY in DMF solution. The overall stability constants of the resulting Tl^+ complexes with these two ligands are several orders of magnitude larger than those with other macrocyclic azacrown ethers studied.

2.2. Mixed ligand sandwich complex

The 1:1 complexes, ML_1, in which the chelating ligand L_1 is not able to fully enclose the central metal ion can have some sites available for the coordination of a second ligand L_2, thus allowing for the formation of mixed ligand complexes ML_1L_2. Complexes of this kind are quite common when the individual ligands L_1 and L_2 contain from one to three available donor atoms. The formation of sandwich complexes in solution[56–58] and in the crystalline state, in which both complexant molecules are the same, has already been extensively reported.[59,60]

We report here the behavior of the 1:1 Tl^+ complex with the HMHCY in the presence of [9]aneN_3 as a coligand, which leads the formation of a mixed ligand sandwich complex in DMF solution. The formation of the mixed ligand sandwich complex Tl^+ (HMHCY)([9]aneN_3) was studied in three separate experiments. In the first and second experiments, either [9]aneN_3, or HMHCY (as coligand) was added to a solution with an Tl^+/ligand mole ratio of 1.0. In the third experiment Tl^+ ion was added to a solution containing equimolar both complexant of [9]aneN_3 and HMHCY. For the comparison of chemical shift variations as function of mole ratio, $\Delta\delta$ (Hz) was calculated as follows:

$$\Delta\delta\ (\mathrm{Hz}) = \delta_{\mathrm{complex}} - \delta_{\mathrm{ligand}} \qquad (1)$$

where δ_{ligand} and $\delta_{\mathrm{complex}}$ represent the proton chemical shifts of the initial (in the absence of Tl^+) and complexed ligand, respectively. The results are shown in Figure 7. The formation of a mixed complex of Tl^+ ion with HMHCY and [9]aneN_3 was studied first by the addition of [9]aneN_3 to a DMF solution with a Tl^+/HMHCY mole ratio of 1.0 (Fig. 7a). The first point to note is that, the chemical shift observed for the $–CH_2–$ protons of coligand in mole ratio of 0.5 (see the right scale of chemical shift in Fig. 7a) agrees well with that observed for the titration of [9]aneN_3 alone with Tl^+ at a [Tl^+]/[ligand] mole ratio of 0.5 (Fig. 4). From Figure 7a it is obvious that, during titration with [9]aneN_3, the chemical shifts of $–CH_2–$ and $–CH_3$ protons of HMHCY show a negligible shift upon addition of the coligand ([9]aneN_3) up to a mole ratio of about 1 ($\Delta\delta \sim 0$). While, the NMR signal corresponding to the $–CH_2–$ protons of coligand ([9]aneN_3) shifted upfield very significantly and tended to level off at mole ratios >2.0 (at a chemical shift corresponding to the free [9]aneN_3 at 1372 Hz), indicating the formation of a mixed sandwich complex of Tl^+(HMHCY)([9]anaN_3) (Fig. 7a).

In the second experiment, a 1:1 Tl^+:[9]aneN_3 solution in DMF was prepared and titrated with HMHCY (Fig. 7b). As obvious, in this case, the $–CH_2–$ and $–CH_3$ proton chemical shifts of HMHCY will remain almost constant until a mole ratio of 1 is reached, and then tend to shift to the values belong to the chemical shift of its free state in DMF (see Fig. 4), indicating the formation of a mixed Tl^+(HMHCY)([9]anaN_3) complex. On the other hand, addition of HMHCY resulted in first significant upfield shift of $–CH_2–$ protons of [9]aneN_3 from 1:1 complex toward first the values between to its 1:2 complex with Tl^+ (1460 Hz), and then to the value belong to free ligand (1372 Hz). It should be noted this later shift to the free [9]aneN_3 state is due to the high stability of the Tl^+–HMHCY complexes especially in the presence of such excess amount of HMHCY.

Reproducibility of the data for the formation of mixed ligand sandwich complex was studied by the addition of a Tl^+ ion to a 1:1 mixture of HMHCY and [9]aneN_3 solution (third experiment). The resulting chemical shift-mole ratio plots are shown in Figure 7c. From Table 1 it is obvious that both HMHCY and [9]aneN_3 form relatively stable 1:1 complexes with Tl^+ ion. Thus, when Tl^+ ion is added to a 1:1 mixture of the two complexants, the chemical shift difference ($\Delta\delta$) of $–CH_2–$ and $–CH_3$ groups of HMHCY vary nonlinearly with the metal to ligand mole ratio up to a mole ratio of about

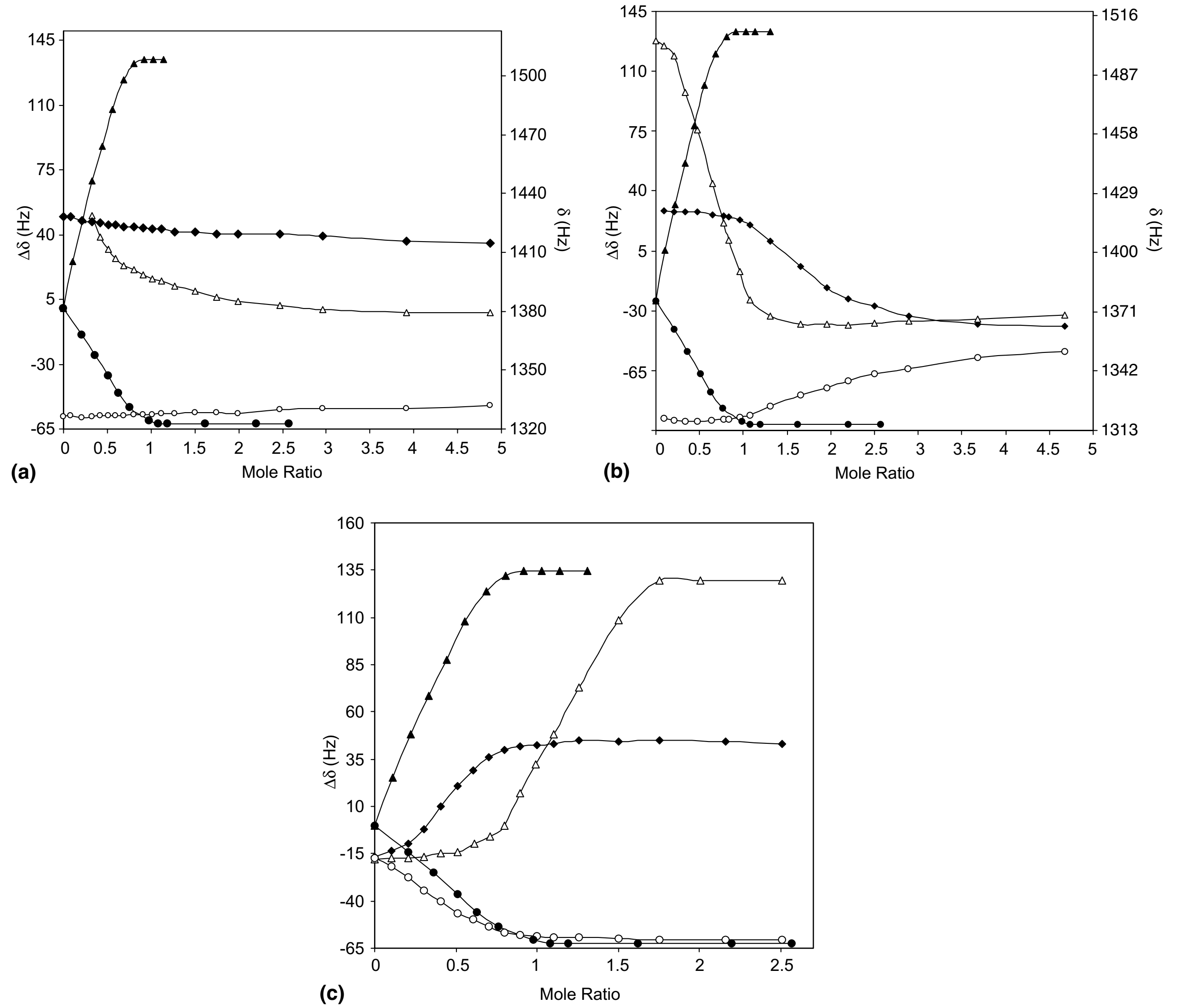

Figure 7. Proton chemical shift difference, Δ*δ* (Hz), as a function of mole ratio in DMF at 300 K: (a) the addition of [9]aneN_3 to a DMF solution with a Tl^+/HMHCY mole ratio of 1.0; (b) the addition of HMHCY to a DMF solution with a Tl^+/[9]aneN_3 mole ratio of 1.0; (c) addition of Tl^+ ion to a 1:1 mixture of HMHCY and [9]aneN_3 solution. Methylene protons chemical shift of [9]aneN_3, (▲) absence and (△) in the presence of HMHCY; methyl protons chemical shift of HMHCY, (●) absence and (○) in the presence of [9]aneN_3, methylene protons chemical shift of HMHCY, (◆) in the presence of [9]aneN_3.

0.5 and then begin to level off at higher mole ratio. (Fig. 7c). On the other hand, the Δ*δ* of [9]aneN_3 will remain constant upon addition of Tl^+ ion up to a metal to ligand mole ratio of 0.5 and then significantly shifted downfield to the 1:2 chemical shift in Tl^+ ([9]aneN_3)$_2$ system at a mole ratio about 1. These results indicated that the formation of 1:1:1 Tl^+(HMHCY)([9]aneN_3) mixed complex could be completed at mole ratio of 1. Further addition of Tl^+ ion tends to take a [9]aneN_3 ligand away from the mixed complex and form a 1:1 complex with it. Of course, the extent of the mixed complex formation during titration with Tl^+ is determined by the relative thermodynamic stability of the existing homo and mixed complexes.

The formation constant of mixed ligand complex Tl^+(HMHCY)([9]aneN_3) in solution was evaluated from the observed chemical shift variation of the probe ligand (methyl and methylene protons of HMHCY or [9]aneN_3) as a function of Tl^+/ligand mole ratio (Fig. 7c). When the solution containing two ligands, HMHCY (L_1) and [9]aneN_3 (L_2), we have the two stepwise equilibria

$$M + L_1 \leftrightarrow ML_1 \tag{2}$$

$$ML_1 + L_2 \leftrightarrow ML_1L_2 \tag{3}$$

A polynomial equation in the free metal concentration [M] was derived from the mass balance and equilibrium constant expression:

$$CM = [M] + [ML_1] + [ML_1L_2] \tag{4}$$

$$\mathrm{CL}_1 = [\mathrm{L}_1] + [\mathrm{ML}_1] + [\mathrm{ML}_1\mathrm{L}_2] \tag{5}$$

$$\mathrm{CL}_2 = [\mathrm{L}_2] + [\mathrm{ML}_1\mathrm{L}_2] \tag{6}$$

$$\begin{aligned}&[\mathrm{M}]^4(k_1^2k_2) + [\mathrm{M}]^3(k_1k_2 - 2k_1^2k_2\mathrm{CM} + 2k_1^2k_2\mathrm{CL}_1)\\ &\quad + [\mathrm{M}]^2(k_1 + 2k_1k_2\mathrm{CM} + k_1k_2\mathrm{CL}_1 + k_1^2k_2\mathrm{CM}^2\\ &\quad - 2k_1^2k^2\mathrm{CMCL}_1 + k_1^2k_2\mathrm{CL}_1^2 + k_1k_2\mathrm{CL}_2)\\ &\quad + [\mathrm{M}](1 - k_1\mathrm{CM} + k_1\mathrm{CL}_1 + k_1k_2\mathrm{CM}^2 - k_1k_2\mathrm{CL}_1\mathrm{CM}\\ &\quad - k_1k_2\mathrm{CMCL}_2 + k_1k_2\mathrm{CL}_1\mathrm{CL}_2) - \mathrm{CM} = 0\end{aligned} \tag{7}$$

where CM, CL_1, CL_2 are the analytical concentration of the Tl^+ ion, HMHCY, and [9]aneN_3 ligands, respectively. The observed chemical shift, δ_{obsd}, of the probe ligand is given by the expression:

$$\delta_{\mathrm{obs}} = p_{\mathrm{L}_1} \cdot \delta_{\mathrm{L}_1} + p_{\mathrm{ML}_1} \cdot \delta_{\mathrm{ML}_1} + p_{\mathrm{ML}_1\mathrm{L}_2} \cdot \delta_{\mathrm{ML}_1\mathrm{L}_2} \tag{8}$$

where p_{L_1}, p_{ML_1}, and $p_{\mathrm{ML}_1\mathrm{L}_2}$ are populations, and δ_{L_1}, δ_{ML_1}, and $\delta_{\mathrm{ML}_1\mathrm{L}_2}$ are chemical shifts of ligand, complex, and mixed complex, respectively. Thus, the mole ratio data for Tl^+(HMHCY)([9]aneN_3) mixed complex in Figure 7c were used to calculate the formation constants of the resulting mixed ligand complex. The data were analyzed with the use of the nonlinear least-squares curve-fitting program KINFIT,[61] and the result is included in Table 1.

The data given in Table 1 clearly indicate that the formation constant for Tl^+(HMHCY)([9]aneN_3) mixed complex is much larger than the corresponding values for Tl^+–HMHCY and Tl^+([9]aneN_3)$_2$. Since the ionic size of Tl^+ (3.0 Å) is somewhat larger than the cavity size of HMHCY (smaller than 2.86 Å),[9] it can only partially penetrate inside the ligand cavity and will mostly remain above the plane of the ligand. So that it can be coordinated by a second smaller ligand ([9]aneN_3). A similar situation has already been reported by Ellaboudy et al. for the Cs^+–HMHCY complex in crystalline state.[62] Thus, it is possible that, in 1:1 complex formation of Tl^+ ion with HMHCY, the most stable configuration for the HMHCY molecule has a rigid bowl-shaped structure in which more than half of the Tl^+ ion is surrounded by the HMHCY molecule and a [9]aneN_3 molecule can easily cover the open side of the bowl to form a three-dimensional cavity, which can bind more or less strongly to all nine donating nitrogen atoms available.

2.3. Ab initio calculations

In order to investigate the dependence of the stoichiometry, stability and structure of Tl^+–azamacrocycle complexes to relative dimensions the metal ion and macrocyclic cavity, some theoretical calculations were carried out on the tri- and tetraazamacrocycle ligands and their Tl^+ ion complexes. All ab initio (RHF) calculations were carried out using the program package GAUSSIAN-98[63] with input files (*z* matrices) being generated using the program package HYPERCHEM.[64] All structures were fully optimized without symmetry constraints. The geometries of the tri- and tetraazamacrocycle ligands were optimized at the RHF/6-31G* level of theory, then at the RHF/lanl2DZ. The Tl^+ ion complexes were optimized using RHF/lanl2DZ level.

Samples of the resulting optimized structures are shown in Figure 8 and some geometrical parameters of the optimized structures of ligands and their Tl^+ complexes are also listed in Table 2. From the data given in Table 2, the energies of tri- and tetraazamacrocycle complex formation reactions with Tl^+ ion in gas phase (ΔE_{g}) were calculated. In Table 2 are also included shown the Tl–N bond lengths and overall stability constants for each system. It is well known that, in the process of complexation of metal ions with aza-substituted crown ethers, the distance of the central metal ion to the nitrogen atoms of the ring plays an important role in controlling the stability of the resulting complex. Using the molecular mechanics calculations, Zhang and Busch[31] have reported the optimum Ni^{2+}–N distances of 2.37 and 2.12 Å at minimum energies for Ni^{2+} complexes with 1,5,9-tris(pyridylmethyl)-1,5,9-triazacyclododecane and 1,4,7-tris(pyridylmethyl)-1,4,7-triaza-cyclononane, respectively. The results obtained in this work, for the complexation of Tl^+ with some aneN_3 and aneN_4 macrocycles, the optimum Tl^+–N distance at the minimum energy was found to be 2.5–3.0 Å (see Table 2). As is obvious from Table 2, the addition of methyl groups to nitrogen atoms of the macrocyclic ring results in an increase in the optimum Tl^+–N distance, most probably due to an enhanced steric effect on the metal–ligand systems.

The ab initio optimized structures of 1:1 and 1:2 (sandwich) complexes of Tl^+ ion with [9]aneN_3, Me_3[12]aneN_3, and [12]aneN_4 are illustrated in Figure 8. As obvious, in the resulting complexes the Tl^+ ion may possess tetrahedral (N_3 series and [14]aneN_4) and square planar (Fig. 8c) structure. It is interesting to note that, in the case of Tl^+–[12]aneN_4 complex, a quite symmetrical square planar structure is formed with the four Tl^+–N equal optimum distances of 2.7 Å (Fig. 8c and Table 2). It is noteworthy that a comparison between the ΔE_{g} values reported in Table 2 with the corresponding overall stability constants obtained in DMF solution ($\log\beta$, Table 1), there is a satisfactory correlation between ΔE_{g} and $\log\beta$ values.

3. Experimental

Reagent grade [9]aneN_3 (1,4,7-triazacyclononane), [12]aneN_3 (1,5,9-triazacyclododecane), Me_3[12]aneN_3 (trimethyl-1,5,9-triazacyclododecane), [12]aneN_3 (1,4,7,10-tetraazacyclododecane), and [14]aneN_3 (1,4,8,11-tetraazacyclotetradecane) from Aldrich. Hexacyclen (1,4,7,10,13,16-hexaazacyclooctadecane, HCY), and hexamethylhexacyclen (1,4,7,10,13,16-hexamethyl-1,4,7,10,13,16-hexaazaoctadecane, HMHCY), from Fluka, were of the highest purity available and used as received. Analytical grade TlNO_3 (Merck) was used without any further purification. Deuterated dimethylformamide (DMF) ($\mathrm{C}_3\mathrm{D}_7\mathrm{NO}$, Aldrich gold label) was used throughout.

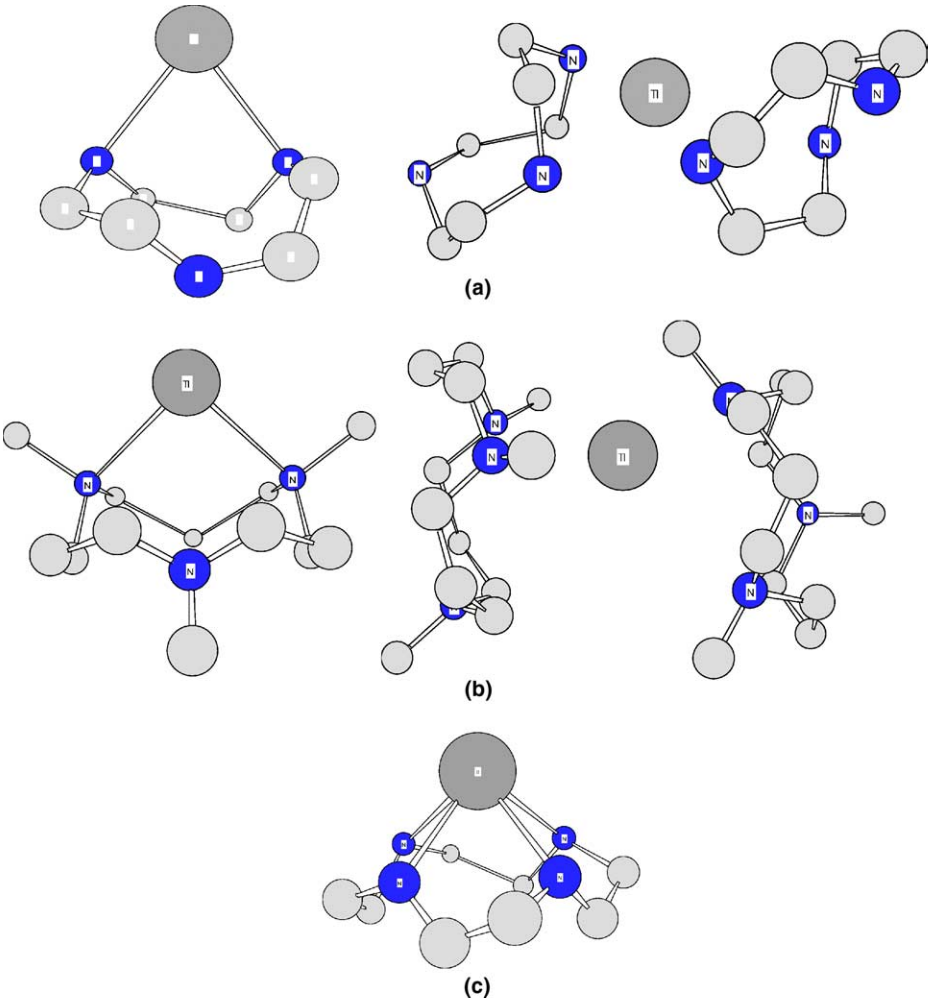

Figure 8. The ab initio optimized structures of 1:1 and 1:2 complexes of Tl^+ ion: (a) Tl^+–[9]aneN_3, (b) Tl^+–Me_3[12]aneN_3, (c) Tl^+–[12]aneN_4.

Table 2. Optimum geometry parameters for azamacrocycles and their complexes with Tl^+ ion obtained by HF/lanl2DZ calculation

System	E (Hartree)	ΔE_g (kcal/mol)	(M–N) band (Å)						
			N_1	N_2	N_3	N_4	N'_1	N'_2	N'_3
Tl^+	−49.9584102								
[9]aneN_3	−399.1029514								
Tl^+–[9]aneN_3	−449.1400813	−49.40	2.6	2.6	4.4				
Tl^+–([9]aneN_3)$_2$	−848.2735538	−19.15	3.0	3.2	5.1		3.0	3.2	5.1
[12]aneN_3	−516.1883567								
Tl^+–[12]aneN_3	−566.2309981	−52.85	2.6	2.8	2.8				
Tl^+–([12]aneN_3)$_2$	−1082.4360124	−10.45	2.8	4.0	4.0		2.7	3.0	3.3
Me_3[12]aneN_3	−633.2176064								
Tl^+–Me_3[12]aneN_3	−683.2471074	−44.57	2.6	2.6	3.7				
Tl^+–(Me_3[12]aneN_3)$_2$	−1316.4693378	−2.86	3.1	3.0	4.3		3.1	3.0	4.3
[12]aneN_4	−532.1590086								
Tl^+–[12]aneN_4	−582.2375808	−75.40	2.7	2.7	2.7	2.7			
[14]aneN_4	−610.1991519								
Tl^+–[14]aneN_4	−660.2503512	−58.25	2.5	2.7	2.8	4.5			

Proton NMR spectra were recorded on a Bruker DRX 500 spectrometer, operating at a field of 117.4 kG. Temperature of the probe was adjusted with a temperature control unit at a 27 °C. To reach the equilibrium temperature, each sample tube was left in the probe for at least 10 min before measurements. At all temperatures used, the accuracy of temperature measurement was ±0.1 °C. In all experiments, TMS was used as an internal standard. Sealed samples were used throughout. The concentration of ligands in all experiments was 0.01 M.

Formation constants of 1:1 and 1:2 (metal to ligand) homo ligand sandwich complexes were calculated by fitting the observed chemical shifts of $-CH_2-$ or $-CH_3$ protons of ligands at various Tl^+/ligand mole ratios to a previously derived equation,[65] which expresses the observed chemical shifts as a function of the free and complexed ligand. The formation constants were evaluated by using a nonlinear least-squares curve-fitting program KINFIT.[61] Figure 1 represents the chemical structures of the polyazamacrocyclic ligands used in this study.

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