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Dedicated to Professor Alexandru T. Balaban on the occasion of his 80th anniversary

SYNTHESIS OF A TRIPHENYLAMINE-BASED MACROCYCLE WITH RHOMBIMINE SHAPE

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A Schiff base macrocycle having rhomboidal shape was synthesized through [2+2] cyclocondensation reaction between 4,4'-diformyl triphenylamine with (R,R)-1,2-diaminocyclohexane. The macrocyle structure was unambiguously proved by electrospray ionization mass spectrometry (ESI-MS), FTIR and ^{1}H-NMR spectroscopy. The change of macrocycle's conformation in solution was observed by ^{1}H-NMR and UV spectroscopy. Reduction of rhombimine led to a rhombamine macrocycle.

INTRODUCTION

The shape-persistent imine macrocycles[1] derived from (R,R)-1,2-diaminocyclohexane and aromatic dialdehydes[2-6] have attracted much attention in the last years due to their exotic shapes and potential applications in supramolecular chemistry and materials science as host-guest complexes, tubular channels, porous organic solids, etc.[1b,7] They are build of a rigid amine and π-conjugated aldehydes and have specific shapes; triangle, rhombus, rectangle, spherand, etc. Thus, depending on dialdehyde geometry, chiral imine macrocycles with different persistent shapes, such as trianglimines,[2a,b,e,3a,b,4a-c,e,f,5a-c,6] rhombimines,[2c,h,4c,f,5b,6] rectanglimines[2f] and spherands[2h] are obtained. Similar geometrical shapes (triangle, parallelogram, rhombus and pentagon) were also evidenced for [4.4] and [7.7] cyclophanes synthesized by etherification or esterification reactions.[8] The purpose of this communication is to present synthesis of an imine macrocycle by [2+2] cyclocondensation of 4,4'-diformyl triphenylamine (**1**) with (R,R)-1,2-diaminocyclohexane (**2**). The change of macrocycle conformation in solution was observed by ^{1}H-NMR and UV spectroscopy. The ability of this macrocycle to complex metal ions was tested for Sn^{2+}.

RESULTS AND DISCUSSION

A Schiff base macrocycle (**3**) was synthesized in one-step by [2+2] cyclocondensation starting from 4,4'-diformyl triphenylamine (**1**) with (R,R)-1,2-diaminocyclohexane (**2**) (Scheme 1). Condensation of **1** with **2**, in dichloromethane at room temperature yielded rhombimine-shaped macrocycle **3** in nearly quantitative yield without the use of dehydrating conditions and without any external template.

The condensation between an amine and an aldehyde to give imine (Schiff base) compounds is a very known and old reaction. The reaction is reversible, highly selective, the intermediate reaction products are dynamically interconvertible and the composition of the library is determined by the thermodynamic stability of the library members. Therefore, under thermodynamically controlled conditions and dynamic combinatorial chemistry, the imine condensation proceeded with

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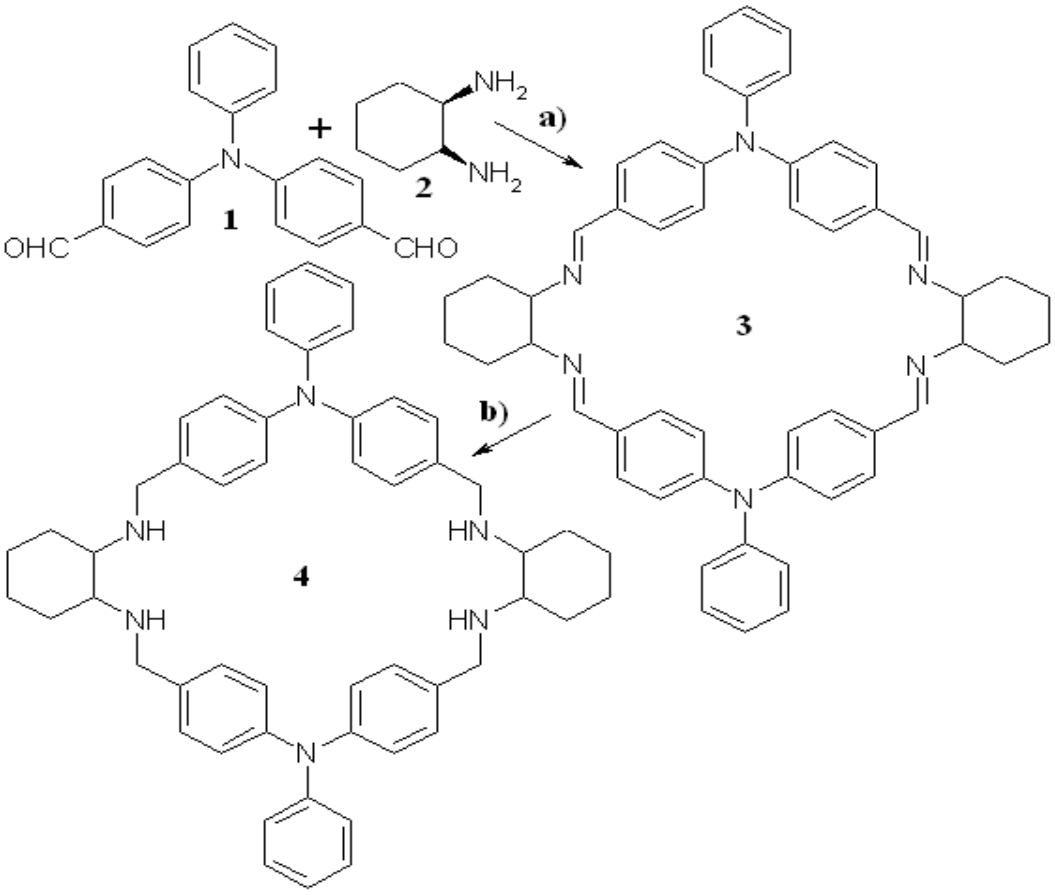
high efficiency generating the most stable product. The reversibility of the imine condensation allows to self-correct the eventually errors in the bond-forming step. Formation of macrocyclics is favourized over linear oligomerization if diamine, dialdehyde or both reactants have a predisposed structure for the formation of cyclic products: a bent structure with restricted conformations.

It is noteworthy that the [2+2] macrocycle is the only cyclic compound observed by ESI-MS spectroscopy in the crude product of condensation reaction. Usually, the size and shape of macrocycle is determined by geometry of the building blocks.[2c,g] (1R,2R)-*trans*-1,2-Diaminocyclohexane (**2**) is a rigid molecule with *ortho* NH_2 functions having bond angles of 60° while dialdehyde (**1**) has the angle between OHC-C_6H_4-N-C_6H_4-CHO bonds close to 120°. Therefore, a free-strain macrocycle of rhomboidal shape (**3**) was obtained as the dominant product by [2+2] cyclocondensation. The cyclic compound was highly soluble in halogenated solvents and less soluble in polar solvents and insoluble in methanol or ethanol. It was purified by dissolving in DMF at high temperature but the solution immediately became as a gel-like by cooling and macrocycle was separated by filtration and drying. The gel structure results due to inclusion of solvent as guest in macrocyle's cavity. Tanaka *et al.*[9] have also recently reported obtaining a gel when the macrocyle synthesized by [3+3] cyclocondensation of trans-1,2-diaminocyclohexane with azobenzene-4,4'-dicarbaldehyde was dissolved in benzene. Macrocycle **3** retained solvent molecules and even after 24 h of vacuum drying at 50 °C the presence of DMF was observed by TGA or ^{1}H-NMR spectroscopy. The differences between calculated and founded values from elemental analysis can be explained by retention of the solvent in macrocyclic cavity. The thermal stability of macrocycle was studied by TGA measurements in nitrogen atmosphere. TG curves evidenced a very good thermal stability up to 340 °C with onset degradation temperature at 348 °C and high melting temperature (325 °C) (Fig. 1). The high thermal stability is due to the imine structure and the absence of end groups.



Scheme 1 – Synthesis of triphenylamine-based rhombimine and rhombamine macrocycles: a) CH_2Cl_2, 25 °C, 24h, b) $NaBH_4$, ethanol/THF, reflux.

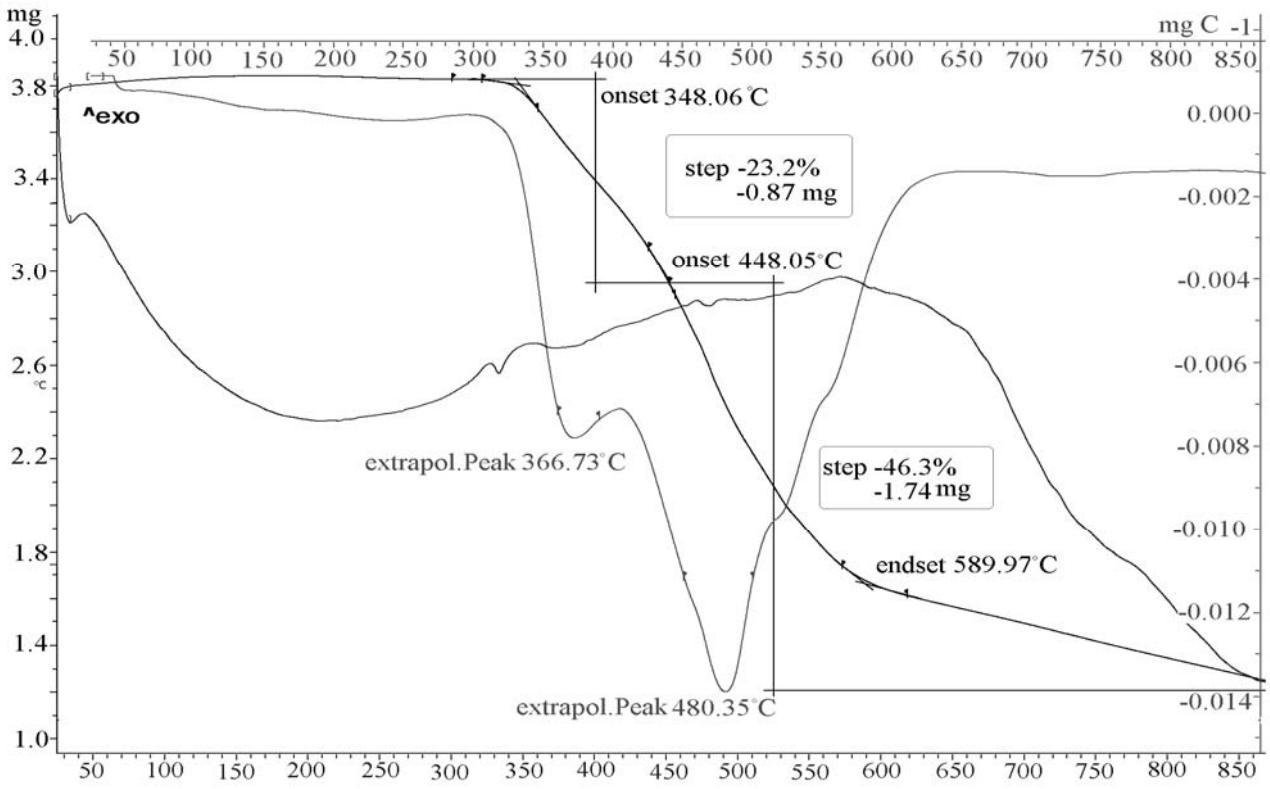


Fig. 1 – TG, DTG and DTA curves for **3**.

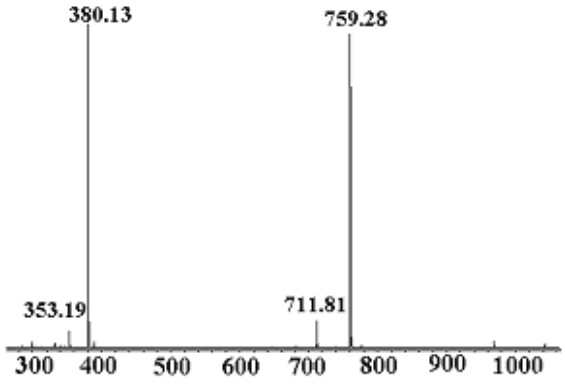


Fig. 2 – ESI-MS for **3**.

The structure of the compound was assigned on the basis of ESI-MS, FTIR, ^{1}H-NMR and UV spectroscopy. X-ray data showed the compound is crystalline one but single crystals suitable for exact structure determination could not be obtained.

The electrospray ionization (ESI) mass spectrum of the solution in methanol/chloroform of **3** (Fig. 2) showed signals at the expected mass-to-charge ratio for ions $[3+H]^+$ at m/z 759.28 and $[3+2H]^{2+}$ at m/z 380.13, which are consistent with the structure proposed in Scheme 1. The absence of higher protonated ions might be explained by stronger charge repulsions.

The FTIR spectrum doesn't show any absorption for aldehyde C=O (1680 cm^{-1}) and amine N-H (3390 and 3315 cm^{-1}) stretches (Fig. 3). The absorption bands characteristic to C=N (1634 cm^{-1}) and C=C (1597 and 1507 cm^{-1}) are observed. The absorption bands localized between 607 and 837 cm^{-1} (ν C-H aromatic from benzene rings), 1286 cm^{-1} (the stretching vibration of tertiary amine) and 2 856-2 930 (C-H aliphatic from cyclohexane) are also evidenced.

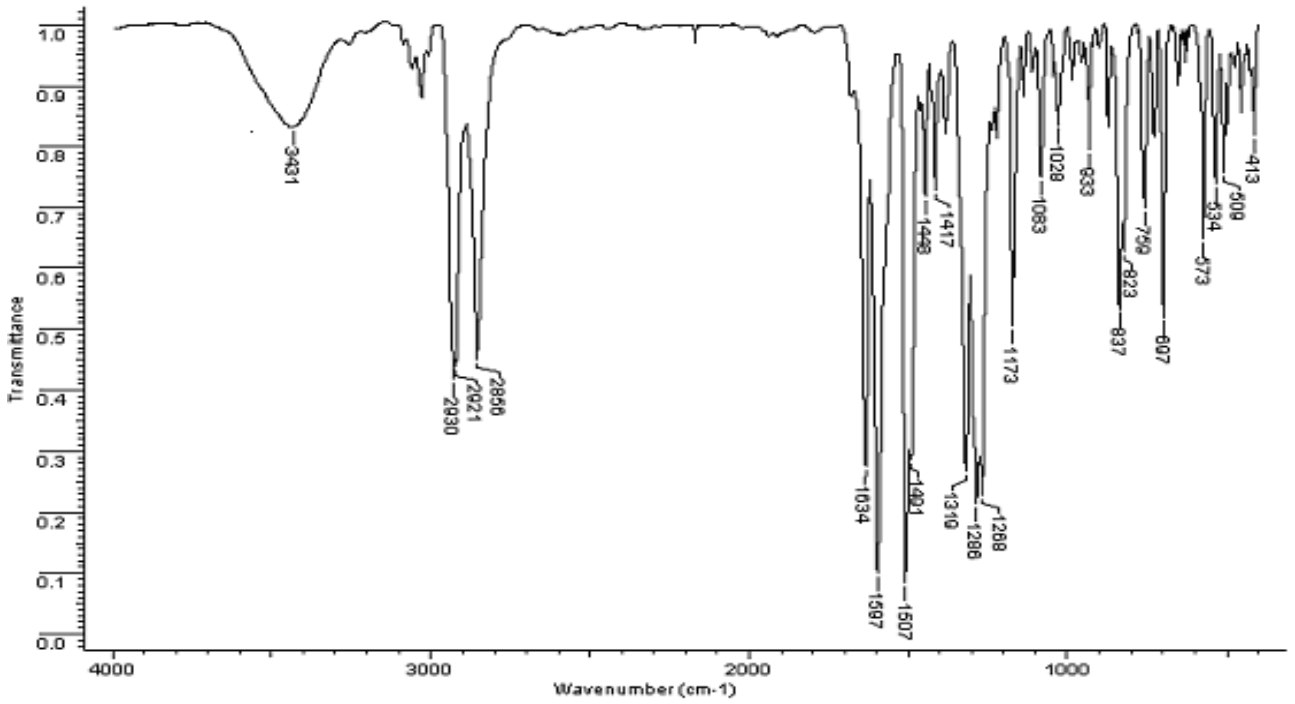


Fig. 3 – FTIR spectrum (KBr pellet) of **3**.

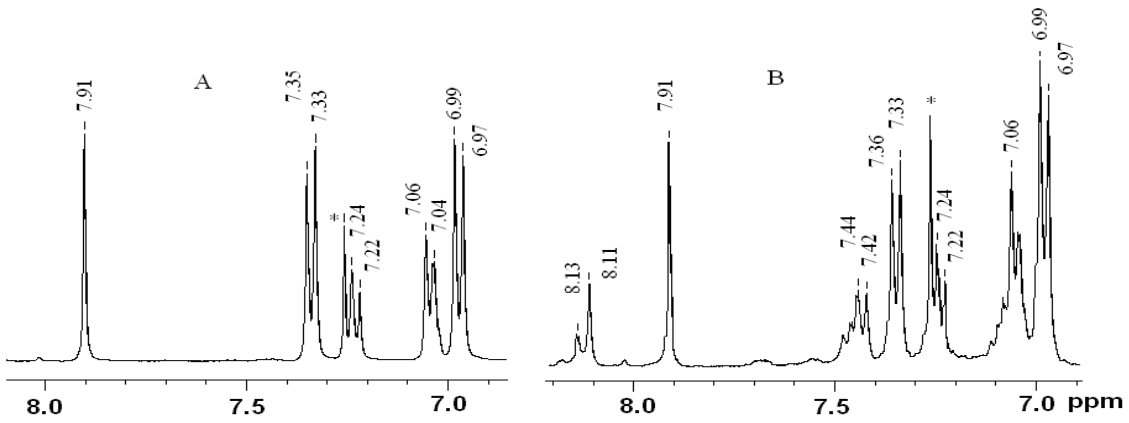


Fig. 4 – ^{1}H-NMR ($CDCl_3$) spectra (aromatic region) of **3** recrystallyzed from DMF (A) and after 3 days (B).

The ^{1}H-NMR spectrum of **3** is consistent with the proposed structure, showing only a singlet signal at 7.91 ppm for the four imine protons (Fig. 4A) suggesting a highly symmetric macrocycle. Some signals positioned at 7.26, 2.96 and 2.88 ppm came from $CHCl_3$ and DMF included in the macrocycle. When $CDCl_3$ solution of **3** was left several days at room temperature its proton NMR spectrum showed significant modifications, mostly observed in the aromatic region (Fig. 4B). Thus, new signals appeared for imine (8.11-8.13 ppm), aromatic (7.42-7.44 ppm) and -CH-N= diamine (3.35 ppm) protons, suggesting presence of non-equivalent triphenylamine groups. The intensities of the new signals integrals are correlated between them. It was observed that the modifications are enhanced by increasing the temperature and solvent polarity.

The changes observed in the NMR spectra could be explained based on the structure of imine compounds. The imine linkage in Schiff base compounds could adopt *E* or *Z* configuration, therefore **3** should exist as all-*E*, all-*Z* or *E*-*Z* isomers. However, it is recognized that *E* isomer is the only product obtained due to its higher thermodinamical stability.

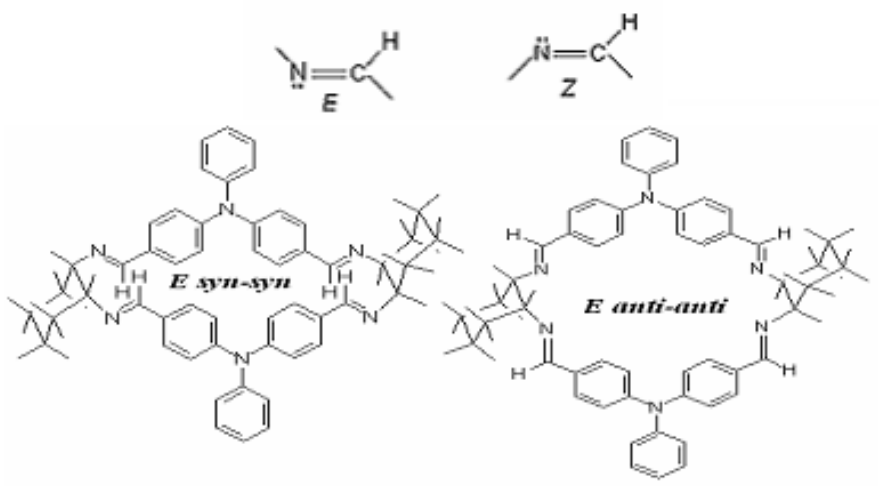


Fig. 5 – *E/Z* configuration and *syn/anti* conformation isomers.

In addition, all-*E* isomer can exist in many conformations, according to the orientation of the lone electrons pair located at imine nitrogens as *syn* or *anti* rotamers (Fig. 5). The lowest energy was observed for the structures where the lone electrons pair is oriented outside (*exo*) of the macrocycle, as *syn* conformer when imine and =N-CH- (from cyclohexane) hydrogens are in *syn* position.[2a] There being a singlet signal for the all imine protons, the spectrum in Fig. 4A must belong to one of the isomers *syn-syn* or *anti-anti*. Being placed at the lowest field by comparing with other imine signals, this signal (7.91 ppm) may be assigned to the isomer *syn-syn*, where the imine protons are placed inside of the macrocycle, therefore feeling an aromatic ring current shielding which is stronger than in other isomers. It is interesting the observation that the spectrum in Fig. 4A changes when the corresponding isomer is maintained in solution, so that the signal at 7.91 ppm decreases while new imine proton signals appear between 8.1 and 8.25 ppm (Fig. 4B). The changes observed in solution can be assigned to an interconversion process that takes place *via* the concerted rotation of triphenylamine group around flexible cyclohexane-N bonds (Fig. 6). In the solid state the open conformation of **3** is stabilized by solvent molecules included in the cavity.

UV absorption spectrum of **3** showed also important changes in the shape and positions of the absorption maxima of $CHCl_3$ solution (Fig. 7). Thus, **3** (having ^{1}H-NMR spectrum presented in Fig. 4A) presented three absorption maxima (in $CHCl_3$ solution), the first two being characteristic of the π-π* transitions in triphenylamine group (240-250 and 336 nm). The third absorption can be attributed to n-π* transition in imine linkages conjugated with triphenylamine moiety (356 nm). After few minutes the solution showed a new broad absorption band at 422 nm and its intensity gradually increased in time (correlated with the disappearance of the 356 nm band) and after 24 h attained the saturate level. We assume that, in $CHCl_3$ solution, the all-*syn* macrocycle **3** spontaneously isomerizes to thermodynamically more stable rotamer, having better n-π* electronic conjugation between imine and triphenylamine bridge.

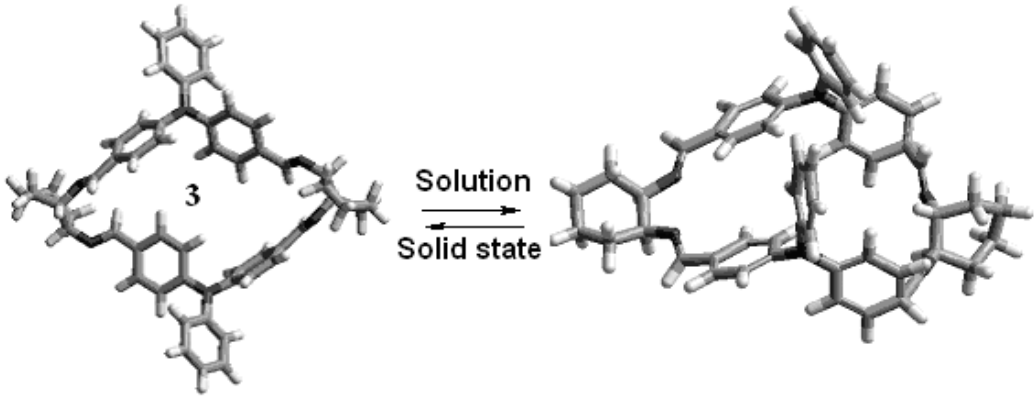


Fig. 6 – Rotamer isomerization in solution.

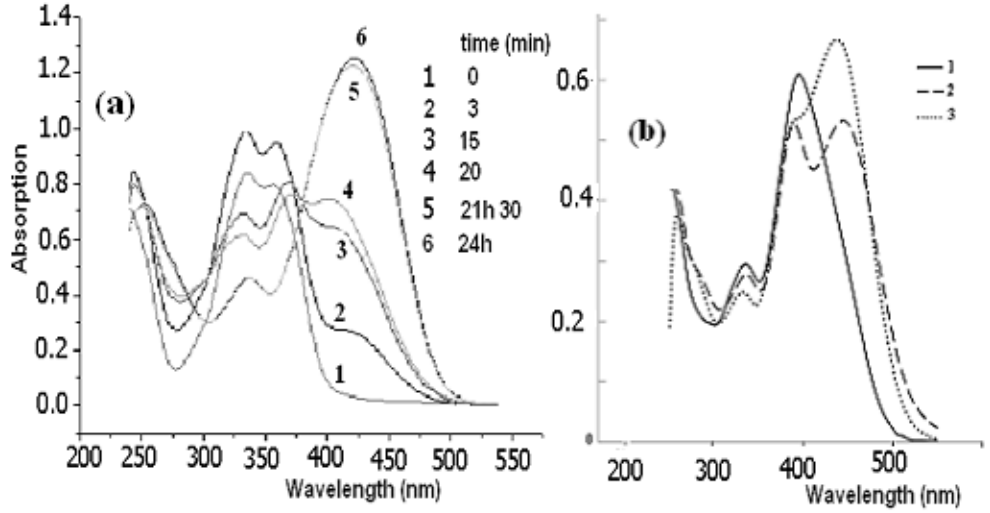


Fig. 7 – (a) In time evolution of UV spectra ($CHCl_3$) of **3** and (b) UV-vis spectra change of **3** during the addition of $SnCl_2$: (1) 0, (2) **3**/$SnCl_2$=1/1 molar ratio and (3) **3**/ $SnCl_2$=1/2 molar ratio. (solvent: dichloromethane/acetonitrile =1/1) [**3**]=1.10^{-5} M.

The bathocromic shifting of absorption could be explained considering the sterical structure of the Schiff base compounds. It is recognized that the imine group itself is nonplanar with adjacent groups of aldehyde and amine. The amine substituent at –N=C is out of the imine group plane with 40-55^o while the aromatic ring linked at –CH= is out of plane with 10^o, but in opposite sense.[10] This arrangement allows lone electron pair of nitrogen to be in conjugation with amine substituent (cyclohexyl) rather the π-conjugated imine functionality in symmetrical isomer. By rotation of triphenylamine groups around cyclohexane-N simple linkages, the conjugation of lone electron pair of imine nitrogen with triphenylamine group is possible with effect on electronic absorption maximum (bathocromic shifting). Moreover, this rotation allows apparition of a transanular electronic interaction between the cofacial benzene rings of triphenylamine. The conjugation length increased also *via* the through space interactions, similar with [2,2]paracyclophane.

The addition of transitional metal salt ($SnCl_2.2H_2O$ as acetonitrile solution) to **3** showed also changes in the electronic spectrum, the peak at 420 nm is bathochromically shifted at 444 nm and its intensity increased with the quantity of the salt. The cations were complexed by azomethine bonds leading to more extended planar structures and higher absorption wavelengths.

Based on NMR and UV data we assume that **3** obtained by crystallization from DMF has an *E* configuration and all imine linkages as syn conformation (according to the orientation of the lone electrons pair located at imine nitrogens) but in $CHCl_3$ solution it spontaneously isomerized to a rotamer or rotamer mixture, more thermodinamically stable, having lower sterical hindrances and more extended conjugation between triphenylamine group and imine linkage. Interconversions between conformers take place *via* the concerted rotation of triphenylamine group around flexible cyclohexane-N bonds. ESI-MS spectrum of **3** after keeping in $CHCl_3$ solution for some days is unchanged, therefore the modifications observed from ^{1}H-NMR and UV spectra couldn't be associated with hydrolysis of imine linkage or formation of larger macrocycles ([3+3] or [4+4] type) by dynamic chemistry.

Reduction of **3** with $NaBH_4$ in methanol/THF mixture gave rhombamine **4** in almost quantitative yield. The NMR spectrum showed the disappearance of the imine proton signals (7.9-8.2 ppm) and the appearance of new signals at 3.5-3.9 ppm (-CH_2-) and 2.3 ppm (-NH-). Rhombamine **4** shows absorptions only at 250 and 310 nm, the absorption associated to imine group being absent. More, the UV and NMR spectra were unchanged in time.

EXPERIMENTAL PART

Instrumentations

The FT-IR spectra were recorded in KBr pellets on a Bruker Vertex 70 spectrometer, while UV-Vis absorption spectra were obtained on a Specord 200 Analytik Jena spectrophotometer using 10 mm quartz cells. ^{1}H-NMR spectra were recorded at room temperature on a Bruker Avance DRX-400 spectrometer (400 MHz) as solutions in $CDCl_3$ and chemical shifts are reported in ppm and referenced to TMS as internal standard. ESI-MS analysis was performed using an AG-QTOF instrument and chloroform/methanol as solvent. Thermal gravimetric analysis (TGA) was performed by means of a Mettler Toledo TGA-SDTA 851e device, in N_2 atmosphere, with a flow of 20 ml/min, and a heating speed of 10 K/min (25-850 ^{0}C range).

Materials

Triphenylamine (Aldrich, 97%) and (1R,2R)-*trans*-1,2-diaminocyclohexane (**2**) (Aldrich, 98%) were used as received. Solvents were purchased from Aldrich source and were dried using the usual procedures. All manipulations of air/moisture-sensitive materials were handled under nitrogen atmosphere. 4,4'-Diformyl triphenylamine (**1**) was synthesized by reported methods.[11,12]

Rhombimine synthesis

*(2R,3R,17R,18R)-1,4,10,16,19,25-hexaaza-10,25-diphenyl-(2,3:17,18)-dibutano-(6:9,11:14,21:24,26:29)-tetraetheno-(2H,3H,17H,18H)-tetrahydro-(30)-annulene (**3**):*

A solution of dialdehyde **1** (0.4457 g, 1.48 mmol) in CH_2Cl_2 (5 mL) was added to a solution of (*1R,2R*)-*trans*-1,2-diaminocyclohexane **2** (0.1691 g, 1.48 mmol) in 5 mL dried CH_2Cl_2 (20 mL) at room temperature and nitrogen atmosphere and stirred for 24 hours. The solvent was evaporated and the crude product was completely dissolved in N,N-dimethylformamide at reflux and by cooling a gel-like system was obtained that was filtered to give colorless fine powder of **3** in 85.7 % yield (0.48 g). Mp=325 ^oC (with decomposition).

^{1}H-NMR ($CDCl_3$), ppm: δ=7.91 (s, 4H, CH=N), 7.34 (d, J=8.8 Hz, 8H, nitrogen *meta* aromatic protons in =CH-C_6H_4-N-), 7.24 (t, J=8.0 Hz, 4H, *meta* protons in –N-C_6H_5), 7.03-7.06 (m, 6H, *ortho* and *para* protons in –N-C_6H_5), 6.97 (d, J=8.8 Hz, nitrogen *ortho* aromatic protons in =CH-C_6H_4-N), 3.22-3.24 (m, 4H, -CH-N=), 2.05 (d, J=11.6 Hz, 4H of C_6H_{10} ring), 1.88 (d, J=7.6 Hz, 8H of C_6H_{10} ring) and 1.48 (q, J=10.4 Hz, 4H of C_6H_{10} ring).

ESI-MS (m/z): 759.28: Calcd for $C_{52}H_{50}N_6$ =758. CHN (Found: C, 81.10; H, 6.78; N, 11.41. $C_{52}H_{50}N_6$ requires: C, 82.32; H, 6.60; N, 11.08.)

Rhombamine derivative (**4**) was obtained by reduction of the corresponding rhombimine (**3**) with $NaBH_4$ in THF/methanol mixture and product was separated by precipitation in water. ^{1}H-NMR ($CDCl_3$): 7.3-6.9 ppm (26H, aromatic protons), 4.0-3.5 ppm (8H,-CH_2-), 2.4-1.0 ppm (12H, -NH- and cyclohexane).

CONCLUSIONS

In this study, an imine macrocycle having rhomb shape was synthesized by [2+2] cyclocondensation of (R,R)-1,2-diaminocyclohexane with 4,4' bis formyltriphenylamine. It was characterized by a combination of ESI-MS, ^{1}H-NMR, FTIR, UV and thermal methods. Imine linkages in macrocycle are in *E* configuration and all-*syn* conformation, macrocycle in this conformation having low energy and highly symmetrical structure. In solution, by rotation of a triphenylamine group around cyclohexane-nitrogen bonds, macrocycle may interconvert to a more stable conformer with enhanced n-π* conjugation between triphenylamine and imine linkages. In solution, the rotation is monitored by changes in the NMR and UV spectra.

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