J Incl Phenom Macrocycl Chem (2008) 62:203–207
DOI 10.1007/s10847-008-9459-8

ORIGINAL ARTICLE

Complexation of α, ω-dicarboxylates by 3,3′-bis (5-phenyl-1,4-dioxo-2,3,5-triaza)-2,2′-bipyridine

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Received: 14 March 2008 / Accepted: 30 April 2008 / Published online: 27 May 2008

Abstract A new bipyridine derivative has been synthesized and characterized. The UV spectra of the prepared ligand are strongly dependent on the solvent, probably due to the different conformations present in each solvent. The ability of this ligand to act as chemosensor for α,ω-dicarboxylates has been evaluated by UV–vis and fluorescence studies. The stoichiometry of the formed complexes was always 1:2. The rigidity induced by the complexation gives rise to an enhancement of the fluorescence emission when DMSO was used.

Keywords Chemosensor · Solvatochromism · Complexation · Carboxylates · Fluorescence

Introduction

Obtention of novel multicomponent molecular systems is a key step in the development of new supramolecular systems mainly for application in catalysis and chemical sensing [1]. Thus, the design and synthesis of chemosensors for different species have became one of the more active field in supramolecular chemistry [2]. Sensing of anionic guests has lately become an area of focus because anions play a fundamental role in many biological and chemical processes [3]. During the last years we have been working in the design and use of chemosensors based on the binging site-signaling unit approach. Thus, we have prepared ligands derived from bipyridine, as transductor subunits, able to act as fluorescent or colorimetric sensors for cations and anions [4]. The experiments carried out with these and other related ligands have demonstrated that conformational changes induced by modification in the dihedral angle of the bipyridine or biphenyl moiety have strong influence in the fluorescent properties of the sensor [5].

The previously reported ligands were 3,3′-disubstituted bipyridines containing thiourea groups as binding site. They showed interesting properties as receptors and sensors for different dicarboxylates. However, due to the good complexing properties showed by some amidourea derivatives [6] we decided to explore the use of this type of binding groups in a new bipyridine derivate ligand. Thus, we now report the preparation of ligand **1** (Chart 1) and the results and discussion of its complexation study with selected carboxylic acids.

Experimental section

General procedures and materials

All reagents were commercially available, and were used without purification. Triethylamine was freshly distilled from CaH_2. Water sensitive reactions were performed under argon. ^1H and ^{13}C NMR spectra were recorded on either Bruker Avance 300 or 400 MHz spectrometers, with the deuterated solvent as the lock and residual solvent as the internal reference. High-resolution mass spectra (FAB) were recorded in the positive ion mode on a VG-AutoSpecE.

Electronic supplementary material The online version of this article (doi:10.1007/s10847-008-9459-8) contains supplementary material, which is available to authorized users.

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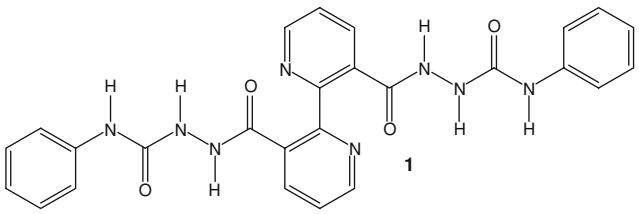

Chart 1 Structure of ligand **1**

Melting points were determined in a microscope equipped with a heating slide from Cambridge Instruments. Infrared spectra were registered in a Bruker Equinox 55 FT-IR, with a screen-width from 4,000 to 400 cm^{-1}. All spectra are an average of 10 scans and 0.5 cm^{-1} was the step wavelength. Spectra were performed as KBr disks. Values of IR data belong to the maximum of absorbance for the more characteristic bands of the compounds. UV spectra were run at room temperature on a Shimadzu UV-2102 PC. Steady-state fluorescence measurements were carried out using a Varian Cary Eclipse Fluorimeter.

Synthesis of **1**

2,2′-Binicotinic acid (1 g, 4 mmol) was added to thionyl chloride (40 mL) and the solution stirred at 80 °C during 2 h. $SOCl_2$ was evaporated under reduced pressure; the resulting product was then extracted by dry benzene (2 × 30 ml) and the solvent evaporated. A solution of the resulting product in dichloromethane (35 mL) was added drop by drop to a solution of 4-phenylsemicarbazide (1.22 g, 8 mmol) and tri-ethylamine (1.14 mL) in dichloromethane (20 mL). The mixture was left under stirring over night at room temperature. **1** was collected by filtration (yields 0.83 g, 84%). M.p. = 221–223 °C, ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.01 (2H, s, NH), 8.53 (4H, d, J = 7.55 Hz, NH + Ar–H), 8.00 (2H, d, J = 7.75 Hz, Ar–H), 7.48 (2H, t, J = 4.80 Hz, Ar–H), 7.40 (2H, s, NH), 7.34 (4H, d, J = 8.25 Hz, Ar–H), 7.19 (4H, t, J = 7.93 Hz, Ar–H), 6.89 (2H, t, J = 7.80 Hz, Ar–H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 167.67, 155.84, 155.62, 150.12, 139.88, 137.20, 130.72, 129.15, 123.38, 122.50, 118.98. IR (KBr): ν_{max} 3330, 3071, 2938, 1694, 1597, 1546, 1498, 1446, 1340, 1300, 1248, 1035, 742, 691, 635 cm^{-1}. HR-MS (FAB^+): (M + 1) found 511.1833. $C_{26}H_{23}N_8O_4$ calculated 511.1842.

Binding studies

Binding constants of ligands **1** towards tetramethylammonium dicarboxylates were evaluated by UV–vis titrations in DMSO. Typically, 3 × 10^{-4} M solutions of the receptors in DMSO (3 mL) were titrated by adding 2 μL aliquots of the envisaged carboxylates (as their TMA salts) in DMSO and registering the UV–vis spectrum after each addition. Log β was calculated by fitting all spectrophotometric titration curves with the SPECFIT program [7].

Results and discussions

Synthesis

The new bipyridine based-ligand **1** is presented in Chart 1.

It was easily prepared in 84% yield by reaction between 2,2′-binicotinic acid dichloride and phenylsemicarbazyne [8]. The reactivity of 2,2′-binicotinic acid strongly contrasts with that observed in 4,4′-dinitro-2,2′-diphenic acid. In fact, all the attempts of obtaining the double functionalization of the acid groups in the later fail and usually cyclic products were obtained [9].

Spectroscopic studies

Initially, absorption and emission spectra of ligand **1** were registered in both acetonitrile and DMSO solutions (10^{-4} M). The obtained results showed that the spectrum of absorption strongly depended on the solvent as can be observed in Fig. 1. Thus, the maximum of absorption appears at 236 nm in acetonitrile and at 258 nm in DMSO; in both solvents a shoulder, corresponding to the phenylamido chromophore, was observed around 280 nm. The changes in the UV spectra seem to be associated with a solvatochromic behaviour of ligand **1**. To understand this behaviour a set of additional solvents (MeOH, EtOH, THF, ethyl acetate and chloroform) showing different polarity-polarizability, hydrogen bond donor (HBD) and hydrogen bond aceptor (HBA) characteristics were used [10]. The maximum of the absorption in these solvents (see supplementary material) shows that solvents with strong HBA

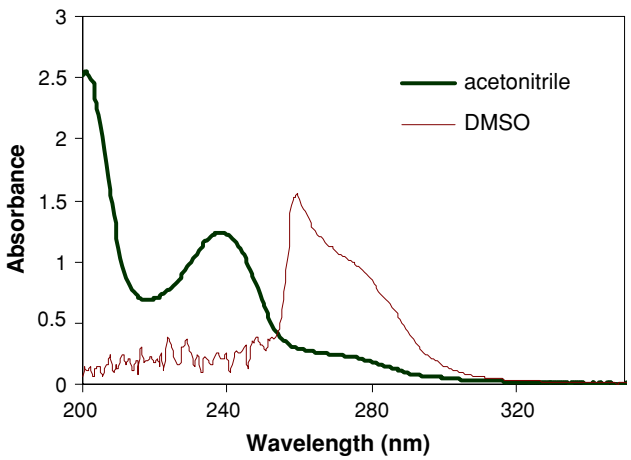

Fig. 1 UV spectra of ligand **1** (10^{-4} M) in acetonitrile and DMSO

properties and no HBD properties (DMSO, THF and ethyl acetate) induce a bathochromic shift whereas solvents with strong HBD properties (MeOH and EtOH) gives rise to a clear hypsochormic shift. The behaviour of ligand **1** in acetonitrile was similar to this showed in HBD solvents what could be related to similar values of their solvent polarity parameters *F*, (0.308 for methanol and 0.305 for acetonitrile) [11]. Finally, chloroform exhibits an intermediate behaviour not according with its HBD capabilities described in the literature [12].

Theoretical modellization of ligand **1** by using PcModel 8.0 showed that compound **1** can be present in two different conformations with a similar energy (118.3 Kcal/mol for **1a** and 119.5 Kcal/mol for **1b**) (Fig. 2). In conformation **1a**, intramolecular hydrogen bonds are formed between both substituent branches. This forces the carbonyl groups attached to the bipyridine system to lay out the aromatic main plane with the corresponding loose of conjugation. This conformation seems to be the prefered one in acetonitrile and also in HBD solvents. The stabilization in HBD solvents could be due to their interaction with the pyridin nitrogen atoms that are good receptors for hydrogen bonds. By contrast, in conformation **1b**, conjugation in the bipyridine moiety is higher as no intramolecular hydrogen bounds are formed. This conformation seems to be stabilized in solvents with HBA properties that are able to form hydrogen bonds with the NH groups of the amidourea moieties. However, even so, the observed maxima are lower than in other bipyridine derivatives [13]. This could be related to the presence of the carbonyl groups at the 3,3′-possitions that precludes the coplanarity of the aromatic rings. The two proposed conformations for ligand **1** could be responsible of its absorption spectra being dependent on the solvents used.

The fluorescence spectrum of ligand **1** in acetonitrile shows a band at 305 nm ($\lambda_{exc} = 240$ nm); the same ligand in DMSO solutions shows an emission band at 345 nm ($\lambda_{exc} = 305$ nm) but the intensity in this second solvent was much lower than in acetonitrile. The two different conformations described before could also explain the higher fluorescence emission that ligand **1** shows in acetonitrile. The rigidity induced by the hydrogen bonds present in acetonitrile increases the quantum yield in this solvent whereas in DMSO, the fluorescence of ligand **1** is very low.

Complexation studies with mono and α,ω-dicarboxylates

To study the ability of the new ligand to complex carboxylates, a series of α,ω-dicarboxylates (oxalate, malonate and succinate), all as their tetrabutylammonium (TBA) salts were studied in order to evaluate the effect of the length of the carboxylic chain in the complexation constants. We also decided to test acetate as the simplest model. The carboxylates were prepared from the corresponding carboxylic acids and TBA hydroxide in DMSO. Acetate of TBA was commercially available. All the complexation studies were carried out by, UV, fluorescence and ^{1}H NMR.

UV–vis and fluorescence studies

The anion binding ability of receptor **1** was evaluated by UV–vis titration of the receptor with the appropriate anion in DMSO solution. UV–vis studies reveal that **1** is able to complex mono and dicarboxylates, however all the studied anions induced the same changes in the UV spectra: apparition of a new band at 326 nm that increase with the anion concentration (Fig. 3). This band was stronger in the presence of any of the studied dicarboxylates than with acetate. Complexation constants and stoichiometries of the different complexes were also evaluated by using UV–vis spectroscopy (Job Plot method for stoichiometry. See supplementary material). The obtained results are summarized in Table 1.

All the complexes formed by the studied dicarboxylates showed a 1:2 stoichiometry even though a 1:1 stoichiometry had been observed with related phenyl-thiourea ligands [4]. Similar complexation constants are observed when compared with related naphtyl-thiourea derivatives where 1:2 stoichiometries apply [4]. The same 1:2 stoichiometry was determined for acetate. However, a too high value was evaluated for the complexation constant (log $\beta > 12.5$), suggesting a deprotonation rather than a real complexation process.

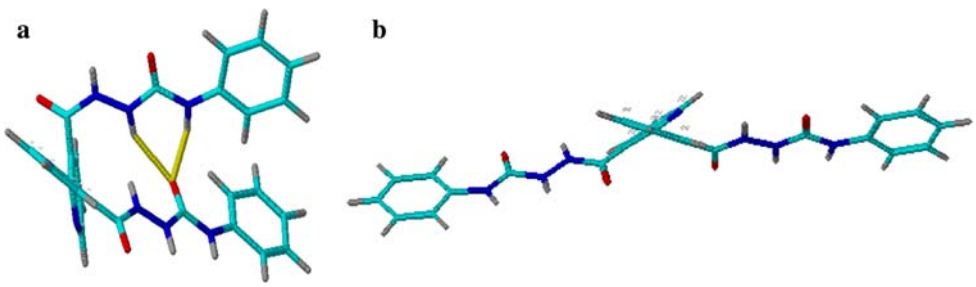

Fig. 2 PcModel modellization for the two possible conformations showed by ligand **1**

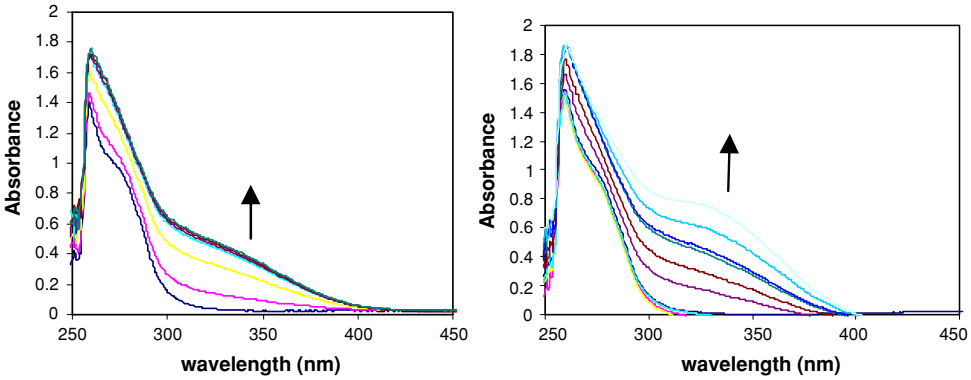

Fig. 3 UV titration of ligand **1** plus (left) TBA acetate and (right) TBA succinate, both in DMSO (3.10^{-4} M) (for the other studied anions see supplementary material)

Table 1 Stoichiometry and logβ in DMSO for **1** versus the studied anions, by UV–vis at 25 °C

Anion	Oxalate	Malonate	Succinate
logβ	7.7 ± 0.3	8.9 ± 0.2	7.9 ± 0.2
Stoichiometry	1:2	1:2	1:2

All anions were used as their TBA salts

Calculated by SpecFit software

Fluorescence studies carried out in acetonitrile showed that the presence of the studied dicarboxylates induced a small quenching of the fluorescence (see Fig. 4 for oxalate). By contrast, a clear enhancement of the fluorescence was observed in DMSO. This behavior agrees with the idea of two different conformations being responsible for the fluorescence emission. Thus, the hydrogen bonds present in acetonitrile in ligand **1** are necessarily broken after complexation inducing a conformational change toward conformation **1b** less fluorescent than **1a**. By contrast, in DMSO the anion binding induces a higher rigidity because rotation around the bipyridine bond is now restricted by steric reasons. This rigidity gives rise to an enhancement in the emission.

^{1}H NMR studies

Due to solubility reasons all the ^{1}H NMR experiments were carried out in DMSO-d_6. The obtained results confirm the deprotonation induced by acetate. In fact, after addition of two equiv. of TBA acetate those signals corresponding to NH protons disappear. At the same time a new set the signals is observed in the spectrum that seems to be related to hydrolysis products. By contrast, on addition of α,ω-dicarboxylates a shift in H_e and H_f (for example $\Delta\delta$ were 0.22 and 0.27 ppm for oxalate) was observed. This agrees with the formation of a Y-type complex. In addition, clear changes were observed in the signals corresponding to the phenyl ring. Thus, for example $\Delta\delta$ for H_g, H_h and H_i were respectively 0.03, 0.08 and 0.07 ppm for oxalate. Very similar values arise for maleate and succinate. By contrast, those signals assigned to the bipyridine moiety suffered smaller modification. All this data suggest the complex structure shown in Chart 2.

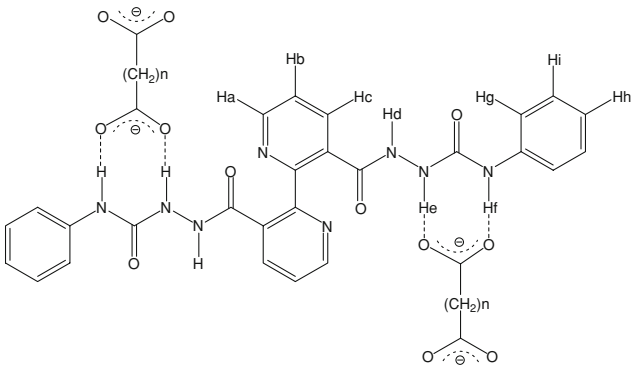

Chart 2 Structural proposal for the 1:2 complexes formed by ligand **1**

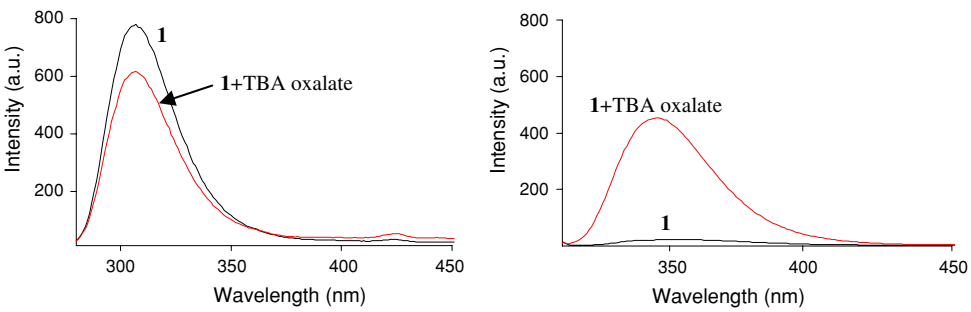

Fig. 4 Fluorescence emission of ligand **1** and **1** + TBA oxalate (both 10^{-5} M, 3.0 equiv. of oxalate): (left) in acetonitrile (λ_{exc} = 240 nm) and (right) in DMSO (λ_{exc} = 305 nm)

Conclusions

The maximum of absorption showed by ligand **1** is strongly dependent on the solvent. Thus, in acetonitrile and HBD a clear hypsochromic effect is observed in relation with the behavior in DMSO, THF and ethyl acetate. Two different conformations seem to be responsible for the different absorptions depending where intramolecular hydrogen bonds are stabilized by the solvent or not. In addition, **1** is able of complexing different α,ω-dicarboxylates giving rise to modifications in the fluorescence emission. The maxima and intensity of this emision after complexation are also strongly dependent on the solvent (a light quenching in acetonitrile and a clear enhancement in DMSO). Finally, acetate is basic enough to induce deprotonation in the ligand. This agrees with the disappearance of the NH signals in the ^{1}H NMR spectra.

Acknowledgements The present research has been financed by A.E.C.I. (ref. 803/2006). We acknowledge the Universitat de Valencia (S.C.I.E.) for most of the equipment employed. We thank the Spanish Ministerio de Ciencia y Tecnología for financial support (Project CTQ2006-15456-02) and the Generalitat Valenciana for the projects ACOMP07-080 and GV/2007/061.

References

1. Keefe, M.H., Benkstein, K.D., Hupp, J.T.: Luminescent sensor molecules based on coordinated metals: a review of recent developments. Coord. Chem. Rev. **205**, 201–228 (2000)
2. (a) Martínez-Máñez, R., Sancenón, F.: Fluorogenic and chromogenic chemosensors and reagents for anions. Chem. Rev. **103**, 4419–4476 (2003); (b) Gale, P.A.: Structural and molecular recognition studies with acyclic anion receptors. Acc. Chem. Res. **39**, 465–475 (2006)
3. Amendola, V., Esteban-Gómez, D., Fabbrizzi, L., Lucchelli, M.: What anions do to N–H-containing receptors. Acc. Chem. Res. **39**, 343–353 (2006)
4. Costero, A.M., Gil, S., Parra, M., Huguet, N., Allouni, Z., Lakhmiri, R., Atlamsani, A.: New 3,3′-disubstitued 2,2′-bipyridines as carboxylate receptors. Conformational regulation of the bipyridine moiety. Eur. J. Org. Chem. **2008**, 1079–1088 (2008)
5. (a) Benniston, A.C., Harriman, A., Patel, P.V., Sams, C.A.: A strategy for controlling the central torsion angle in biphenyl-based molecular-scale bridges. Eur. J. Org. Chem. **2005**, 4680–4686 (2005); (b) Costero, A.M., Sanchis, J., Peransí, S., Gil, S., Sanz, V., Williams, J.A.G.: Conformationally regulated fluorescent sensors. Study of the selectivity in Zn^{2+} versus Cd^{2+} sensing. Tetrahedron **60**, 6327–6334 (2004)
6. (a) Evans, L.S., Gale, P.A., Light, M.E., Quesada, R.: Pyrrolylamidourea based anion receptors. New J. Chem. **30**, 1019–1025 (2006); (b) Brooks, S.J., García-Garrido, S.E., Light, M.E., Cole, P.A., Gale, P.A.: Conformational control of selectivity and stability in hybrid amide/urea macrocycles. Chem. Eur. J. **13**, 3320–3329 (2007)
7. SPECFIT/32^{TM} GLOBAL ANALYSIS SYSTEM v.3.0, Spectrum Associates (Marlborough, MA, USA).www.bio-logic.info/rapid-kinetics/specfit.html
8. Costero, A.M., Peransí, S., Gil, S.: A selective colorimetric chemodosimeter for the naked eye detection of benzoate anion. Tetrahedron Lett. **47**, 6561–6564 (2006)
9. (a) Hall, D.M., Insole, J.M.: Steric effects of methoxy-groups in 2,2′-bridged biphenyls. Part I. J. Chem. Soc. Pekin Trans 2. 1164–1168 (1972); (b) Insole, J.M.: Steric effects of methoxy-groups in 2,2′-bridged biphenyls. Part II. J. Chem. Soc. Pekin Trans 2. 1168 (1972)
10. (a) Linert, W., Fukuda, Y., Camard, A.: Chromotropism of coordination compounds and its applications in solution. Coord. Chem. Rev. **218**, 113–152 (2001); (b) Linert, W., Camard, A., Armand, M., Michot, C.: Anions of low Lewis basicity for ionic solid state electrolytes.: Coord. Chem. Rev. **218**, 137–141 (2002)
11. Moog, R.S., Burozski, N.A., Deai, M.M., Good, C.D., Silvers, C.D., Thompson, P.A., Simon, J.J.: Solution photophysics of 1- and 3-aminofuorenone: The role of inter- and intramolecular hydrogen bonding in radiationless deactivation. J. Chem. Phys. **95**, 8466–8473 (1991)
12. Kamlet, M.J., Taft, R.W.: Linerar solvation energy relationships. Part 1. solvent polarity-polarizability effects on infrared spectra. J. Chem. Soc. Perkin Trans 2. 337–341 (1979)
13. (a) Palmans, A.R.A., Vekemans, J.A.J.M., Meijer, E.W.: Intramolecular hydrogen-bonding in acetylated 2,2′-bipyridine-3,3′-diamines. Rec. Trav. Chim. **114**, 277–284 (1995); (b) Schilf, W.: The spectroscopic study of hydrogen bonding in some 3,3′-derivatives of 2,2′-bipyridyl. Spectrochimica Acta, PTA Mol. Bio., **60A**, 2695–2701 (2004)