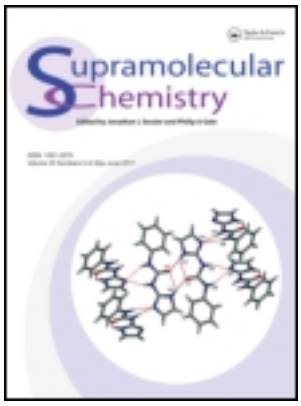


Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gsch20

Anion recognition properties of pyridine-2,6-dicarboxamide and isophthalamide derivatives containing l-tryptophan moieties

Claudia Caltagirone [a], Carla Bazzicalupi [b], Andrea Bencini [b], Francesco Isaia [a], Alessandra Garau [a] & Vito Lippolis [a]

[a] Dipartimento di Chimica Inorganica ed Analitica, Universita' degli Studi di Cagliari, S.S. 554 Bivio per Sestu, Monserrato (CA), Italy

[b] Dipartimento di Chimica 'Ugo Schiff', Universita' degli Studi di Firenze, via della Lastruccia 3, Sesto Fiorentino (FI), 50019, Italy

Available online: 03 Nov 2011

To cite this article: Claudia Caltagirone, Carla Bazzicalupi, Andrea Bencini, Francesco Isaia, Alessandra Garau & Vito Lippolis (2012): Anion recognition properties of pyridine-2,6-dicarboxamide and isophthalamide derivatives containing l-tryptophan moieties, Supramolecular Chemistry, 24:2, 95-100

To link to this article: http://dx.doi.org/10.1080/10610278.2011.628391

Supramolecular Chemistry
Vol. 24, No. 2, February 2012, 95–100

Anion recognition properties of pyridine-2,6-dicarboxamide and isophthalamide derivatives containing L-tryptophan moieties

Claudia Caltagirone[a]*, Carla Bazzicalupi[b], Andrea Bencini[b], Francesco Isaia[a], Alessandra Garau[a] and Vito Lippolis[a]

[a]*Dipartimento di Chimica Inorganica ed Analitica, Universita' degli Studi di Cagliari, S.S. 554 Bivio per Sestu, Monserrato (CA), Italy;*
[b]*Dipartimento di Chimica 'Ugo Schiff', Universita' degli Studi di Firenze, via della Lastruccia 3, Sesto Fiorentino (FI) 50019, Italy*

(*Received 30 June 2011; final version received 23 September 2011*)

L-Tryptophan containing anion receptors **1** and **2** have shown interesting features. Receptor **1** behaves as a hetero-ditopic dicompartimental receptor for fluoride and chloride with a certain selectivity for fluoride as supported by ^{1}H NMR titrations and molecular modeling, while receptor **2** forms only 1:1 complexes. Moreover, receptor **1** reveals a certain affinity towards the L enantiomers of amino acids alanine and serine.

Keywords: anion recognition; ditopic receptors; enantiomeric discrimination

Introduction

Anion recognition and sensing have attracted considerable interest due to their importance from industrial, biological/medicinal and environmental points of view (*1*). In biological systems, highly efficient and selective anion receptors are constructed from a relatively small number of amino acids containing coordinating functional groups able to contribute to anion binding, namely the OH group of serine, threonine and tyrosine, the guanidinium group of arginine and the NH group of tryptophan. In fact, natural anion-binding systems such as the phosphate-binding protein (*2*), the sulphate-binding protein (*3*) and the chloride channel proteins (*4*) of bacteria *Escherichia coli* and *Salmonella typhimurium*, all containing residues of the above-cited amino acids, are extremely efficient receptors for phosphate, sulphate and chloride, respectively.

Chemically, the design and development of new anion receptors have emerged substantially during the last decade and several groups, following the strategy and the building blocks adopted by nature, have started using amino acids for the design and construction of efficient anion receptors, and remarkably efficient systems have been obtained (*5*). An alternative strategy consists of designing artificial receptors featuring hydrogen bond donor groups which are part of amino acid residues such as guanidinium (*6*) (contained in arginine) or indole (*7*) groups (contained in tryptophan).

In particular, Gale and co-workers have recently reported on pyridine-2,6-dicarboxamide and isophthalamide (*8*) cleft molecules, containing pendant 2,3-dimethylindole groups linked *via* the 7-position (receptors **A** and **B** in scheme 1) (*9*). These new compounds showed a high selectivity for fluoride binding in DMSO/water mixtures, attributed to the possibility of assuming a 'twisted' conformation in the binding process. In this conformation, the receptors are able to efficiently encapsulate the small fluoride anion, while the 'perching' binding mode observed for the bigger chloride anion is not as much efficient in binding.

Starting from Gale's results we decided to synthesise two new receptors containing pyridine-2,6-dicarboxamide and isophthalamide cleft molecules functionalised with L-tryptophan methyl ester (**1** and **2**). This design would allow to take advantage of the presence of an amino acid and to introduce a chiral centre in the receptors. During the preparation of this paper, Gunnlaugsson and co-workers reported on compound **1** and used it as a ligand in Tb(III) and Eu(III) luminescent complexes (*10*) (Scheme 1).

Experimental

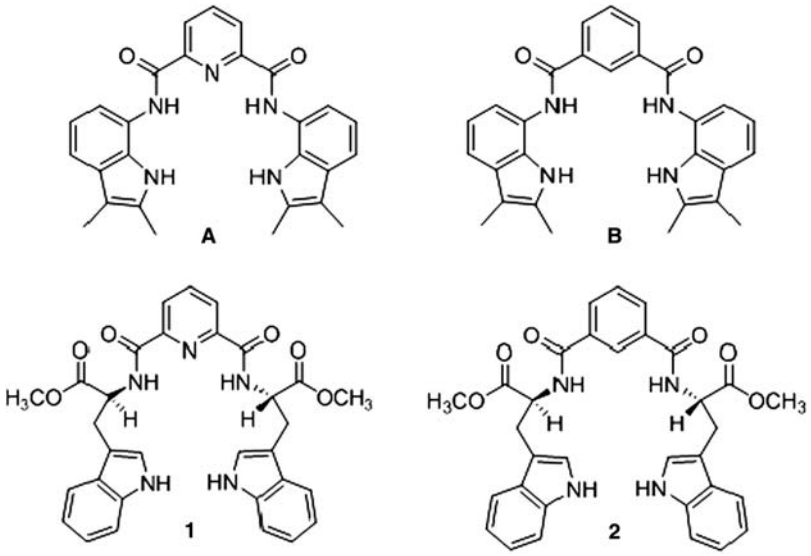
General remarks

All reactions were carried out using oven-dried glassware under a slight positive pressure of nitrogen. ^{1}H NMR (300 MHz) and ^{13}C{^{1}H} NMR (75 MHz) spectra were recorded on a Bruker AV300 spectrometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AV400 spectrometer. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm) and calibrated to the solvent peak set, with coupling constants reported in Hz. The following abbreviations are used for spin multiplicity: s, singlet; d, doublet; t, triplet and m, multiplet. Chemical shifts for ^{13}C{^{1}H} NMR are reported in ppm, relative to the central line of a septet at $d = 39.52$ ppm for deuterodimethylsulphoxide.

*Corresponding author. Email: ccaltagirone@unica.it

ISSN 1061-0278 print/ISSN 1029-0478 online

http://dx.doi.org/10.1080/10610278.2011.628391
http://www.tandfonline.com



Scheme 1. Receptors considered in this paper.

All solvents and starting materials were purchased from chemical sources where available. NMR titrations were carried out by adding aliquots of the putative anionic guest [as their tetrabutylammonium (TBA) salt (0.15 M) in a solution of the receptor (0.01 M) in DMSO-d_6]. In the case of amino acids, the titrations were carried out by the addition of 0.05 M solutions of the substrates in DMSO-d_6 as sodium salts to 0.005 M solutions of **1** in the same solvent.

Synthesis of compound 1

To a solution of L-tryptophan methyl ester hydrochloride (0.99 g, 3.92 mmol) in acetonitrile (50 ml), in the presence of triethylamine (5 ml) and a catalytic amount of dimethylaminopyridine (DMAP), a solution of pyridine-2,6-dicarbonyl dichloride (0.4 g, 1.96 mmol) in acetonitrile (50 ml) was added dropwise under nitrogen atmosphere. The resulting yellow solution was refluxed for 24 h. The solvent was then removed under reduced pressure and the residue was taken up in dichloromethane and washed with water. The organic fractions were dried over Na_2SO_4 and the solvent removed under reduced pressure to give a pale yellow solid (0.843 g, 1.48 mmol). Yield: 76%. M.p. 141–144°C; ^{1}H NMR (300 MHz, DMSO-d_6, 298 K): δ_H 3.10–3.30 (m, 4H, CH_2), 3.66 (s, 6H, CH_3), 4.75–4.84 (m, 2H), 6.96 (t, $J = 7.32$ Hz, 2H), 7.05 (t, $J = 7.32$ Hz, 2H), 7.22 (s, 2H), 7.32 (d, $J = 8.04$ Hz, 2H), 7.61 (d, $J = 8.04$ Hz, 2H), 8.10–8.15 (m, 3H), 9.46–9.50 (m, 2H, amide NH), 10.79 (s, 2H, indole NH). ^{13}C NMR (75 MHz, DMSO-d_6, 298 K): δ_C 26.85 (CH_2), 52.06 (CH_3), 53.79 (CH), 109.80 (C), 111.46 (CH), 118.11 (CH), 118.43 (CH), 121.00 (CH), 123.69 (CH), 124.88 (CH), 127.05 (C), 136.13 (C), 139.54 (CH), 148.26 (C), 163.26 (C), 172.01 (C). LRMS (ESI^-, m/z): 567.5 $[M - H]^-$. Elemental analysis: found % (calculated % for $C_{31}H_{29}N_5O_6$): C 65.86 (65.60), H 5.38 (5.15), N 12.18 (12.34).

Synthesis of compound 2

To a solution of L-tryptophan methyl ester hydrochloride (1.003 g, 3.94 mmol) in acetonitrile (40 ml), in the presence of triethylamine (5 ml) and a catalytic amount of DMAP, a solution of isophthaloyl chloride (0.4 g, 1.96 mmol) in acetonitrile (25 ml) was added dropwise under nitrogen atmosphere. The resulting yellow solution was refluxed for 24 h. The solvent was then removed under reduced pressure and the residue was taken up in dichloromethane and washed with water. The organic fractions were dried over Na_2SO_4 and the solvent removed under reduced pressure to give a bright yellow solid (1.019 g, 1.80 mmol). Yield: 92%. M.p. 153–156°C; ^{1}H NMR (300 MHz, DMSO-d_6, 298 K): δ_H 3.20–3.40 (m,

Table 1. The stability constants (K_a, M^{-1})[a] of compounds **1** and **2** with a variety of anionic guests (added as TBA salts) at 298 K in DMSO-d_6/0.5% water as determined by following the NH resonance of the tryptophan.

Anion	Compound **1**	Compound **2**
Fluoride	$K_1 = 675$, $K_2 = 373$	Deprotonation
Chloride	$K_1 = 65$, $K_2 \leq 10$	< 10
Acetate	22	< 10
Benzoate	< 10	< 10
Dihydrogen phosphate	28	20

[a] Errors on association constants are $< 15\%$.

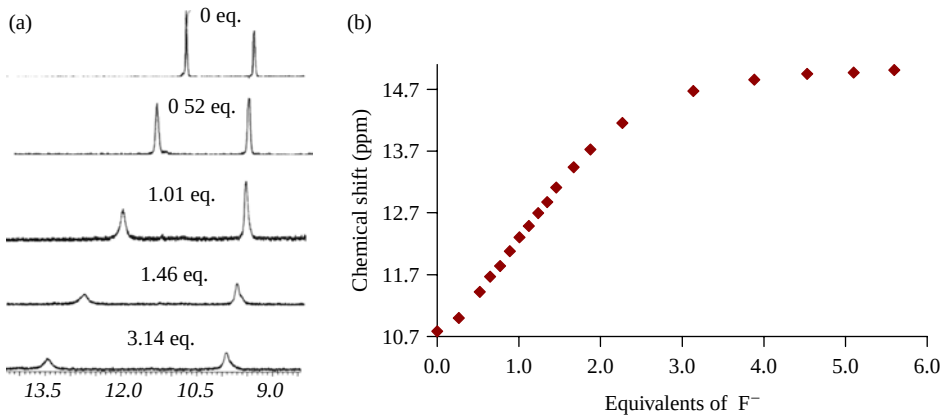


Figure 1. Stack plot (**a**) relative to the NH peaks and ^{1}H NMR titration curve (**b**) for the titration of **1** with fluoride in DMSO-d_6.

4H, CH_2), 3.63 (s, 6H, CH_3), 4.67–4.76 (m, 2H), 6.98 (t, $J = 6.96$ Hz, 2H), 7.06 (t, $J = 7.29$ Hz, 2H), 7.20 (s, 2H), 7.32 (d, $J = 7.68$ Hz, 2H), 7.56 (d, $J = 7.68$ Hz, 3H), 7.96 (d, $J = 7.68$ Hz, 2H), 8.31 (s, 1H), 8.95–8.99 (m, 2H, amide NH), 10.83 (s, 2H, indole NH). ^{13}C NMR (75 MHz, DMSO-d_6, 298 K): δ_C 26.61 (CH_2), 51.91 (CH_3), 53.91 (CH), 109.90 (C), 111.46 (CH), 117.98 (CH), 118.43 (CH), 120.98 (CH), 123.62 (CH), 126.84 (CH), 127.03 (C), 128.26 (CH), 130.20 (CH), 133.90 (C), 136.10 (C), 165.98 (C), 172.44 (C). LRMS (ESI^-, m/z): 565.3 $[M - H]^-$. Elemental analysis: found % (calculated % for $C_{32}H_{30}N_4O_6$): C 67.58 (67.83), H 5.60 (5.34), N 10.00 (9.89).

Results and discussion

Compounds **1** and **2** were easily synthesised from commercially available L-tryptophan methyl ester hydrochloride and pyridine-2,6-dicarbonyl dichloride (for compound **1**) or isophthaloyl chloride (for compound **2**) in acetonitrile in the presence of triethylamine and DMAP in catalytic amount, and were isolated in good yields (76% and 92% for **1** and **2**, respectively).

Anion-binding studies were carried out by means of ^{1}H NMR titrations in DMSO-d_6/0.5% water. The EQNMR program (*11*) was used to calculate stability constants of the anion–receptor adducts from the NMR titration curves obtained following the shift of the NH resonance of the tryptophan (see Supplementary Information available online). As shown in Table 1 and Figure 1 (in the case of fluoride) fluoride and chloride form with receptor **1** both 1:1 and 2:1 anion to receptor complexes and the receptor shows a certain degree of selectivity for fluoride ($K_1 = 675\,M^{-1}$ and $K_2 = 373\,M^{-1}$) over chloride ($K_1 = 65\,M^{-1}$ and $K_2 < 10\,M^{-1}$). In the case of compound **2**, only the formation of the 1:1 complex is observed with chloride, having a formation constant lower than that observed for the corresponding species with **1** ($K_1 < 10\,M^{-1}$), while deprotonation occurs in the case of fluoride. With the other anions considered, the observed stability constants are lower than $30\,M^{-1}$ with both receptors.

We hypothesised that receptor **1** behaves as a dicompartmental receptor with two binding pockets available for spherical halides, one involving the amidic NH groups and the other involving the NH of the tryptophan residues, as shown in Figure 2. In fact, in the ^{1}H NMR titrations we observed a shift for both the amidic NHs and the indole NHs (see Supplementary Information available online).

Despite numerous attempts, we were not able to grow crystals of anion adducts with **1** and **2** suitable for X-ray diffraction analysis. For this reason, to support our experimental data and our coordination hypothesis, molecular modelling investigation on the adducts formed by fluoride and chloride with receptors **1** and **2** in 1:1 or 2:1 ratio were carried out. Conformational searches by means of simulated annealing ($T = 600$ K, equilibration time = 5 ps, run time = 10 ps and cooling time = 15 ps,

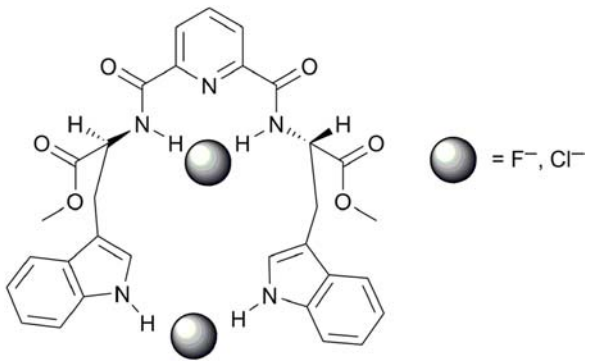


Figure 2. Hypothesis of coordination for the formation of 2:1 anion to receptor complexes of receptor **1** with fluoride and chloride.

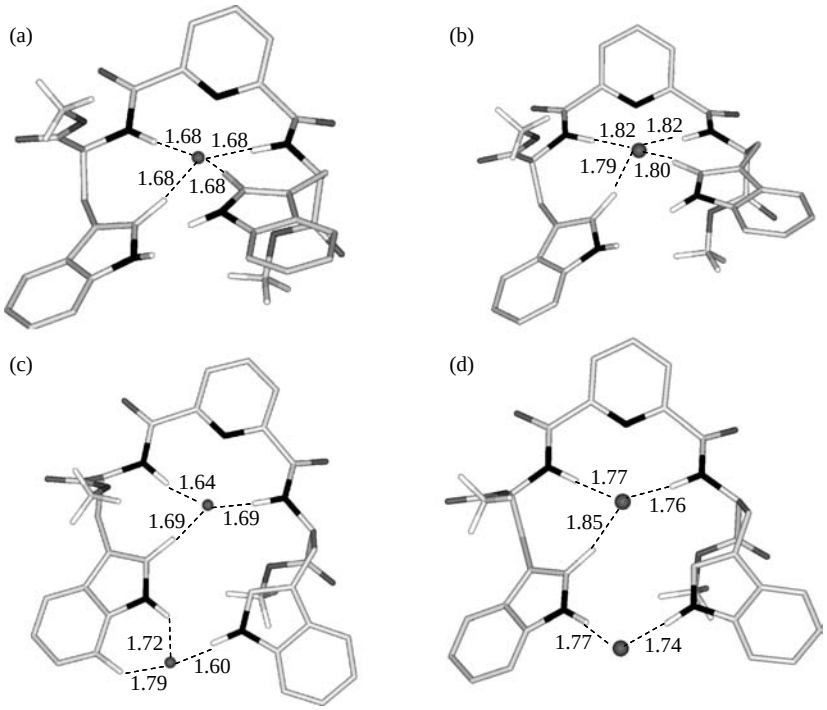


Figure 3. Calculated structures of the 1:1 and 2:1 complexes of receptor **1** with fluoride and chloride and calculated distances (Å): (a) $[\mathbf{1}\cdot F]^-$, (b) $[\mathbf{1}\cdot Cl]^-$, (c) $[\mathbf{1}\cdot 2F]^{2-}$ and (d) $[\mathbf{1}\cdot 2Cl]^{2-}$.

time step = 1.0 fs, 80 saved conformations) were preliminarily carried out on the ligands alone by means of an empirical force field method (AMBER3) implemented in the HyperChem software (*12*), evaluating the atomic partial charges at the PM3 semi-empirical level of theory (*13*). Starting conformations for the adducts formed by each ligand and fluoride or chloride were then obtained by adding the anions to the lowest energy conformers derived from the conformational search performed on the ligands alone and then by minimising up to an energy gradient lower than 0.001 kcal mol^{-1} $Å^{-1}$.

Results from these preliminary calculations, carried out in the gas phase, evidenced the amidic and heteroaromatic nitrogens, in the case of **1**, and only the amidic nitrogens, in the case of **2**, as preferential binding sites for both anions. Therefore, conformational searches, in the same conditions used to understand the binding mode of **1** and **2**, were carried out on the adducts $[\mathbf{1}\cdot F]^-$, $[\mathbf{1}\cdot 2F]^{2-}$, $[\mathbf{1}\cdot Cl]^-$, $[\mathbf{1}\cdot 2Cl]^{2-}$, $[\mathbf{2}\cdot F]^-$ and $[\mathbf{2}\cdot Cl]^-$ constraining the anion to be 2.8 Å apart from amidic nitrogens, and the second anion, in the case of **1**, to be 2.8 Å apart from heteroaromatic nitrogens (additional force constant 7 kcal mol^{-1} $Å^{-2}$). The lowest energy conformers so obtained were then minimised at the PM3 semi-empirical level of theory.

As shown in Figure 3, our calculations indicate that the first fluoride or chloride anion binds to **1** at the dicarboxamide moiety, involving both the amidic groups in hydrogen bonding. The overall coordination environment is completed by $CH\cdots A^-$ interactions involving the tryptophan aromatic moiety. Despite the similarity between the conformations adopted by fluoride and chloride adducts with **1**, a significant higher stability was calculated in the case of the fluoride adduct (Table 2).

Interestingly, the same trend is observed also for the 2:1 anion to receptor complexes, where the second binding site is localised at the NHs of the tryptophan residues. Thus, receptor **1** represents a rare example of an open-chain hetero-ditopic dicompartimental anion receptor (*14*).

Molecular modelling results for the 1:1 adducts formed with **2** are shown in Figure 4 and Table 2. The binding site for both adducts is localised nearby the isophthalamide cleft, with formation of $NH\cdots A^-$ and $CH\cdots A^-$ interactions involving the carboxamide and the phenyl ring, respectively. Interestingly, deprotonation of an amidic group

Table 2. ΔE (kcal/mol) for the reported reactions, obtained at the semi-empirical level of calculation: $\Delta E = E([\mathbf{1}\cdot A]^-) - E(\mathbf{1}) - E(A^-)$ or $\Delta E = E([\mathbf{1}\cdot 2A]^{2-}) - E(\mathbf{1}) - 2\,E(A^-)$.

Reaction/anion	Fluoride	Chloride
$\mathbf{1} + A^- \leftrightharpoons [\mathbf{1}\cdot A]^-$	−90.37	−56.41
$\mathbf{1} + 2\,A^- \leftrightharpoons [\mathbf{1}\cdot 2\,A]^{2-}$	−104.21	−59.50
$[\mathbf{1}\cdot A]^- + A^- \leftrightharpoons [\mathbf{1}\cdot 2\,A]^{2-}$	−13.84	−3.09
$\mathbf{2} + A^- \leftrightharpoons [\mathbf{2}\cdot A]^-$	–	−56.41
$\mathbf{2} + A^- \leftrightharpoons [(\mathbf{2}\text{-H})\,(HA)]^-$	−67.78	–

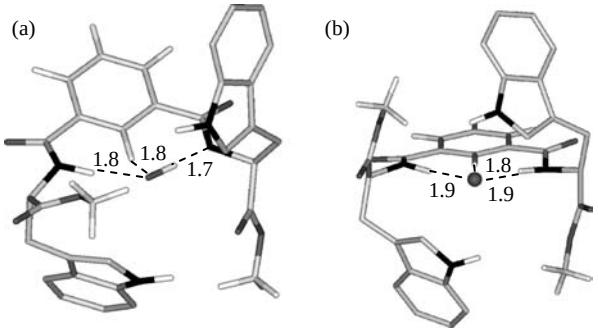


Figure 4. Calculated structures of the 1:1 complexes of receptor **2** with fluoride and chloride and calculated distances (Å): (a) $[(\mathbf{2}\text{-H})\ (HF)]^-$ and (b) $[\mathbf{2}\cdot Cl]^-$.

occurs in the case of the fluoride 1:1 complex modelling, in agreement with ^{1}H NMR data, while in the case of the chloride complex the ligand maintains its neutral form. Moreover, a higher stability has been found for the fluoride adduct formed upon deprotonation of **2** with respect to the chloride adduct. The performed calculations appear to suggest that the CH···A$^-$ interaction involving the phenyl ring of the isophthalamide group in **2** modifies the reciprocal disposition of the two tryptophan units in a way the coordination of a second anion to the tryptophan NHs is hampered; this would, therefore, favour the formation of only 1:1 complexes with halides. On the other hand, in the case of **1** this interaction is impossible and the two tryptophan units can adopt a more planar disposition which allows the coordination of a second halide.

The ^{1}H NMR titrations results reported above outline that **1** is more promising as anion receptor than **2**, both in terms of selectivity and pre-organisation to anion binding. Therefore, as a first attempt of analysis of the recognition properties of this type of receptors for chiral anions, we tested the binding ability of **1** towards the enantiomers of the amino acids serine (Ser) and alanine (Ala) in their anionic form as sodium salts (*15*).[1] To this purpose, we analysed complexation of the D/L-Ser and D/L-Ala couples of the two amino acids with **1** by means of ^{1}H NMR titrations carried out in DMSO-d_6 in the presence of increasing amounts of the substrates.

The addition of increasing amounts of the amino acids as sodium salts to solutions of receptor **1** gives rise to a progressive downfield shifts of the ^{1}H NMR signals of the amide moiety at 9.48 ppm and, at a minor extent, of the indole NH group at 10.79 ppm, allowing the determination of the stability constant of the 1:1 complexes, which are shown in Table 3 together with the complexation-induced chemical shift (CIS) of the signals measured in the presence of a large excess of the substrates (20 eq.).

Although the CIS values cannot be directly related to the strength and mode of the interaction of the substrates with the receptor, the data in Table 3 clearly outline that, for all four anions, the ^{1}H NMR signal of the NH amide hydrogens is more influenced by substrate binding than the indole NH one. This may suggest that the charged carboxylate group of amino acids preferentially interacts *via* hydrogen bonding with the pyridine-2,6-dicarboxamide binding units rather than with the tryptophan moieties, in contrast to what is observed for acetate in which the larger CIS was observed for the indole NHs (see Supplementary Information available online). However, the NH indole groups appear to be also involved in the process of amino acids binding. We can speculate that the NH_2 function of the alanine or the OH group in the case of serine could interact *via* hydrogen bonding with the indole moieties. However, this proposed bifunctional binding mode, involving both the carboxylate and amine (or hydroxyl group in the case of serine) of amino acids in complex stabilisation, could explain the observed higher stability constant of the adducts of the amino acids than those with simple carboxylate anions.

Table 3. Stability constants (K_a, M^{-1}) for the amino acid adducts with **1** and CIS of the amide and indole NH ^{1}H NMR signals.

Eq.	K^a	$CIS_{NH\ amide}{}^b$	$CIS_{NH\ indole}{}^b$
(L-Ser)$^-$ + **1** [**1**·L-Ser]$^-$	450	0.13	0.05
(D-Ser)$^-$ + **1** [**1**·D-Ser]$^-$	320	0.09	0.04
(L-Ala)$^-$ + **1** [**1**·L-Ala]$^-$	380	0.12	0.05
(D-Ala)$^-$ + **1** [**1**·D-Ala]$^-$	230	0.10	0.04

[a] Errors on association constants are ±5%.
[b] Errors on CIS values are ±0.01 ppm.

Nevertheless, receptor **1** does not show a marked discriminating ability for the different enantiomers of the two tested amino acids, although a somewhat binding preference for the L forms of both serine and alanine can be inferred from the data reported in Table 3. It is interesting to note that in our case, albeit the enantioselectivity is not high, the L enantiomer is favoured over the D, in contrast to what is observed in the literature for anion receptors containing the L-tryptophan moiety. In fact, He and co-workers have recently reported on a two-armed chiral calix[4]arene functionalised at the lower ring with L-tryptophan and studied its selectivity towards N-Boc-alanine and phenylalanine in DMSO (*16*). A good selectivity for D-Ala over L-Ala was observed although the calculated association constant (53.56 M^{-1} for D-Ala; the association constants for L-Ala could not be calculated precisely because the signal change was too small to provide reliable data with tolerable error) is much lower than that observed in our case.

The same authors also reported a naphthalene-containing receptor functionalised with L-tryptophan that showed a good enantioselectivity towards D-dibenzoyl tartrate anion ($2.61 \times 10^5\ M^{-1}$) over L-dibenzoyl tartrate (stability constant too low to be determined) in DMSO (*17*).

Conclusions

Very few examples of L-tryptophan containing anion receptors are known in the literature. We have reported the synthesis and the anion-binding studies of compounds **1** and **2** containing pyridine-2,6-dicarboxamide and isophthalamide, respectively, functionalised with L-tryptophan. These new receptors have revealed preliminary interesting anion-binding features. In particular, compound **1** can be defined as a hetero-ditopic dicompartimental receptor for halides (namely fluoride and chloride). Both ^{1}H NMR studies and modelling calculations have shown that 1:2 receptor to anion adducts are formed in which the two halides are bound *via* hydrogen bonds in the pyridine-2,6-dicarboxamide cleft and between the tryptophan NHs. In contrast, receptor **2** forms only 1:1 complexes. Moreover, the affinity of receptor **1** towards amino acids, namely D/L-alanine and D/L-serine, was tested revealing a certain affinity towards the L enantiomers. The difference observed in the association constants of the enantiomers is quite promising and we are currently developing similar receptor systems by modulating the distance between the two binding sites (the dicarboxamide and the tryptophan units) in order to increase the enantioselectivity in the amino acids recognition process and improving enantiomeric discrimination.

Note

1. DMSO is highly solvating for hard metal ions. In particular, the solvation free energy for Na^+ in DMSO is 13.4 kJ/mol lower than that in water (*15*). This should make the formation of ionic couples in DMSO less favoured.

References

(1) Sessler, J.L.; Gale, P.A.; Cho, W.S. *Anion Receptor Chemistry*, The Royal Society of Chemistry: Cambridge, **2006**; Gale, P.A.; Gunnlaugsson, T., Ed. Supramolecular chemistry of anionic species themed issue, *Chem. Soc. Rev.* **2010**, *39*, 3581–4008; Caltagirone, C.; Gale, P.A. *Chem. Soc. Rev.* **2009**, *38*, 520–563; Gale, P.A.; Garcìa-Garrido, S.E.; Garric, J. *Chem. Soc. Rev.* **2008**, *37*, 151–190.
(2) Leucke, H.; Quiocho, F.A. *Nature* **1990**, *347*, 402–406.
(3) He, J.J.; Quiocho, F.A. *Science* **1991**, *251*, 1479–1481.
(4) Dutzler, R.; Campbell, E.B.; Cadene, M.; Chait, B.T.; MacKinnon, R.; Quiocho, F.A. *Nature* **2002**, *415*, 287–294.
(5) Kubik, S. *Chem. Soc. Rev.* **2009**, *38*, 585–605, and references therein.
(6) Rether, C.; Schmuck, C. *Eur. J. Org. Chem.* **2011**, *17*, 1459–1466; Jadhav, V.D.; Schmidtchen, F.P. *J. Org. Chem.* **2008**, *73*, 1077–1087; Blondeau, P.; Segura, M.; Pérez-Fernández, R.; De Mendoza, J. *Chem. Soc. Rev.* **2007**, *36*, 198–210.
(7) For reviews on indole containing receptors see, Gale, P.A. *Chem. Commun.* **2008**, 4525–4540; Bao, X.; Zhou, Y.; Song, B. *Minirev. Org. Chem.* **2011**, *8*, 17.
(8) Kavallieratos, K.; de Gala, S.R.; Austin, D.J.; Crabtree, R.H. *J. Am. Chem. Soc.* **1997**, *119*, 2325–2326.
(9) Bates, G.W.; Gale, P.A.; Light, M.E. *Chem. Commun.* **2007**, *43*, 2121–2123.
(10) Lincheneau, C.; Leonard, J.P.; McCabe, T.; Gunnlaugsson, T. *Chem. Commun.* **2011**, *47*, 7119–7121.
(11) Hynes, M.J. *J. Chem. Soc. Dalton Trans.* **1993**, 311–312.
(12) *HyperChem release 7.51 for Windows MM System*; Hypercube, Inc. Gainesville, FL, 2002.
(13) Stewart, J.J.P. *J. Comput. Chem.* **1989**, *10*, 209–220; Stewart, J.J.P. *J. Comput. Chem.* **1989**, *10*, 221.
(14) Hossain, Md.A.; Llinares, J.M.; Mason, S.; Morehouse, P.; Powell, D.; Bowman-James, K. *Angew. Chem. Int. Ed.* **2002**, *41*, 2335–2338; Mason, S.; Clifford, T.; Seib, L.; Kuczera, K.; Bowman-James, K. *J. Am. Chem. Soc.* **1998**, *120*, 8899–8900; Kang, S.O.; Powell, D.; Bowman-James, K. *J. Am. Chem. Soc.* **2005**, *127*, 13478–13479; Kang, S.O.; Day, V.W.; Bowman-James, K. *Org. Lett.* **2008**, *10*, 2677–2680; Hirata, O.; Takeuchi, M.; Shinkai, S. *Chem. Commun.* **2005**, 3805–3807; Shionoya, M.; Furuta, H.; Lynch, V.; Hamiman, A.; Sessler, J.L. *J. Am. Chem. Soc.* **1992**, *114*, 5714–5722.
(15) Cox, B.G.; Schneider, H. *Coordination and Transport Properties of Macrocyclic Compounds in Solution*; Elsevier, Amsterdam, 1992.
(16) Qing, G.-Y.; He, Y.-B.; Wang, F.; Qin, H.-J.; Hu, C.-G.; Yang, Y. *Eur. J. Org. Chem.* **2007**, 1768–1778.
(17) Xu, K.-X.; He, Y.-B.; Qin, H.-J.; Qing, G.-Y.; Liu, S.-Y. *Tetrahedron: Asymmetry* **2005**, *16*, 3042–3048.