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Synthesis, structure and the binding properties of the amide-based anion receptors derived from 1*H*-indole-7-amine

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Abstract

Indole-7-amine was investigated as an alternative to aniline in construction of amide-based anion receptors. Replacement of aniline with indolamine introduces additional binding site—indolyl NH, which can enhance anion binding for more than five times. The molecular modelling of indole-containing receptors revealed the correlation between their conformational preferences and their affinity towards anions.

Keywords: Anion recognition; Indole; Hydrogen bond; Amides

1. Introduction

Coordination chemistry of anions is one of the most active fields of supramolecular chemistry.[1] In this research area, construction of neutral hosts for anions is especially attractive due to the many possible applications of such receptors.[2] Binding by uncharged ligands is generally achieved by the usage of hydrogen bond formed by amide,[3] thioamide,[4,5] urea,[6,7] thiourea[8–11] and hydroxyl[12] groups or a pyrrole moiety.[13,14] A single hydrogen bond is weak and thus multiple such interactions must be applied for efficient complexation of anions. However, the groups mentioned above consist of both hydrogen bond donor and acceptor fragments, and as a result, they often participate in intramolecular hydrogen bonds that must be broken upon complexation, which decrease the affinity of hosts towards anions.[15] The pyrrole subunit is exceptional because it can only act as a hydrogen bond donor, and due to this feature, the construction of pyrrole-based receptors is of great interest.[13,14]

In order to improve anion binding, the acidity of hydrogen bond donor groups can be increased. It has been achieved by the introduction of electron-withdrawing substituents[7,8,16] or by conversion of amide or urea groups into their thio-analogues.[4,5,11] Also fusion of pyrrole with a benzene ring leads to an increased acidity of pyrrolic NH, as expressed by values of pK_a for pyrrole, indole and carbazole in DMSO: 23.0, 20.9 and 19.9, respectively.[17] Moreover, the indole moiety has been a part of binding sites in some natural systems, mainly as the tryptophan residue.[18] These aspects make benzopyrroles an important subject of studies, and there are published examples of successful application of benzopyrroles as building blocks for anion receptors.[19] In this communication, we would like to present our studies of the amides **1**–**3** derived from indole-7-amine (Scheme 1).[20] Independently Gale has published in Chem. Commun.[21] his studies on similar derivatives of 2,3-dimethyl-indole-7-amine. We hope that readers will find our results complementary to those reported by Gale and co-workers.

2. Results and discussion

There are many known ligands the binding sites of which are derived from aniline, usually in the form of amides or ureas.[7,9,14] By replacement of the aniline subunit with indole-7-amine, a new hydrogen bond donor, namely indole NH, can be introduced into such systems, and thus an increased affinity towards anions may be expected. To check

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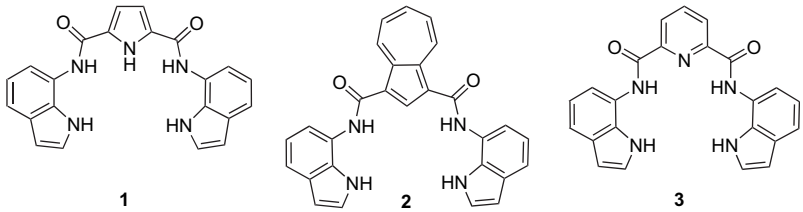
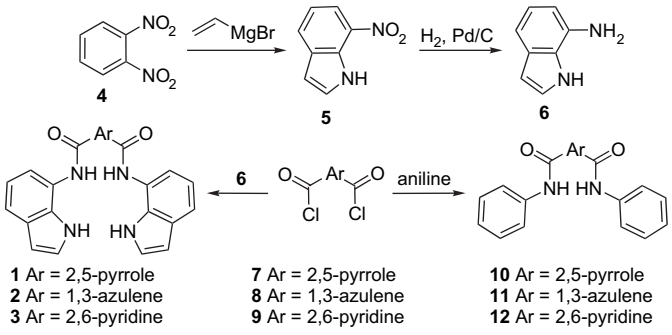


Scheme 1.

this assumption we decided to investigate aromatic bisamides **1**–**3** (Scheme 1) derived from indole-7-amine and compare them with their aniline-based analogues **10**–**12**. As building blocks for ligands' construction, we chose pyrrole-, azulene- and pyridine-dicarboxylic acids for the following reasons. Ligand **1** derived from 2,5-pyrroledicarboxylic acid[22] contains five hydrogen bond donors in its structure, and in consequence, strong anion binding could be expected. The 1,3-azulenedicarboxylic acid[23] offers an arrangement of hydrogen bond donors similar to its pyrrole analogue due to the five-membered ring geometry, but ligand **2** can bind only by four such interactions. The derivatives of dipicolinic acid are often used for construction of anion receptors[24] and this building block is well known for its preorganisation in the *syn*–*syn* conformation.

Indole-7-amine (**6**) was easily prepared by the catalytic reduction (H_2, Pd/C 5%) of 7-nitroindole (**5**), which is commercially available, or can be synthesised by the Bartoli method[25] from 1,2-dinitrobenzene (**4**). The desired amides **1**–**3** and **10**–**12** were obtained by reactions of the corresponding acetic dichlorides **7**–**9** with indolyl-7-amine (**6**) or aniline (Scheme 2).



Scheme 2.

To determine the anion binding properties of our ligands we used ^{1}H NMR titration technique with DMSO+0.5% H_2O as a solvent. Although this is a very competitive medium, it will allow further comparison with known ligands. Upon addition of tetrabutylammonium salts, the signals of the amide and pyrrole-type protons were shifted downfield and used to calculate the values of binding constants (Table 1). Interactions of all the ligands with bromide were too weak to determine association constants. Although the K_a values obtained for interaction with the chloride anion are small, they are reliable, and since they were measured in the same conditions, they can be used for comparison. We observed typical selectivity for oxoanions over halogens and all complexes are formed with 1:1 stoichiometry. The replacement of the aniline subunit with indoleamine does not influence remarkably the relative selectivity towards anions.

Table 1
The binding constants (M^{-1}) for the formation of 1:1 complexes of model ligands with various anions in DMSO-d_6+0.5% H_2O at 296 K[a]

		1	**10**[5]	**2**	**11**[23]	**3**	**12**
$PhCO_2^-$	NH pyrrole	327	—[b]				
	NH indole	33		526		28	
	NH amide	83	80	544	105	24	3.4
$H_2PO_4^-$	NH pyrrole	—[b]	—[b]				
	NH indole	35		2400		164	
	NH amide	84	203	2300	496	100	9.5
Cl^-	NH pyrrole	11	5.2				
	NH indole	5.7		36		2.5	—[d]
	NH amide	5.2	3.8	50[c]	9.3	1.7	

[a] Determined by ^{1}H NMR titration. Errors estimated to be <10%. TBA salts were used as a source of anions.
[b] Cannot be determined due to disappearing of the pyrrole NH signal.
[c] Error 15%, too small value of chemical shift.
[d] Interaction to weak to be measured.

Contrary to our predictions, the replacement of aniline moiety with indoleamine **6** in pyrrole-based ligand **1** failed to increase its affinity towards anions (Table 1). Moreover, the values of binding constants differ depending on which type of protons was used for calculations. The highest values were determined for the pyrrole NH, and the lowest values were for the indole NHs. It may seem that the indolyl NH is too far away to participate in the anion binding, similarly as was observed by Gale for a pyrrole-based ligand with pendant arms.[26] However, our structural studies suggest a different explanation.

The azulene-based ligand **2**, which also contains a five-membered aromatic scaffold, turned out to bind anions fairly strongly. Its affinity towards anions is almost five times higher than for the aniline derivative **11** (Table 1). There is a good agreement between the values of binding constants determined for amide and indolyl protons. In contrast to its pyrrole-based analogue **1**, the azulene derivative **2** is able to bind anions by concerted hydrogen bonds formed by both amide groups and indole NH.

The introduction of two additional binding sites has a positive effect on anion binding also in the case of the dipicolinic acid derivative **3** (Table 1). The indole-containing ligand **3** is a better receptor than its aniline analogue **12**. Moreover, the binding constants calculated for indolyl NHs are higher than determined on the basis of amide groups.

The results for amides **2** and **3** confirmed that the replacement of the aniline subunit with the indole-7-amine (**6**) can lead to over five times stronger interaction with anions. However, the interesting question is why no such improvement is observed for the pyrrole-containing ligand **1**. Molecular modelling gave us some insight into this problem.

We performed a conformational search for ligands **1**–**3** using semi-empirical AM1 method. The resulting conformations could be sorted according to two attributes: the *syn* or *anti* orientation of the amide groups, and the presence or absence of the intramolecular hydrogen bond between indolyl NH and carbonyl group. As could be predicted, the structures with this intramolecular interaction have the lowest energy. For further studies, we chose conformations with the inner hydrogen bond, and investigated the influence of orientation of carbonyl groups on energy using DFT B3LYP method at the 6-31G level.

The pyrrole derivative **1** prefers the conformation in which carbonyl groups are in the *anti*–*anti* orientation (Table 2), the same preference was observed for simple pyrrole-based bisamide.[5] The intramolecular hydrogen bonds between indolyl and pyrrolic NHs and carbonyl groups assure that aromatic rings are coplanar and as a result the ligand **1** is completely flat (Fig. 1a). To bind anions with convergent hydrogen bonds that originate from amide groups and pyrrole NHs, the ligand **1** must adopt the *syn*–*syn* conformation. In the *syn*–*syn* conformation, carbonyl groups of **1** are tilted, thus two conformers are possible: one with amides on the same side of pyrrole plane (denoted as ++), and the other in which amides point to opposite directions (denoted as +−). Both *syn*–*syn* conformers have energy higher by more than 40 kJ/mol than *anti*–*anti* one (Table 2). This strong preference for the *anti*–*anti* conformation was also observed in solution, since the NOESY experiment in DMSO shows the NOE effect between amide NH and pyrrole CH.

On the contrary to pyrrole derivative **1**, the azulene-based ligand **2** is already preorganised in the favourable *syn*–*syn* conformation (Table 2). The carbonyl groups are deviated from the plane of azulene ring, thus two structures are possible: one in which the amide groups occupy the same side of azulene (noted as *syn*–*syn*++, Fig. 1c) and the other in which the carbonyl groups point in opposite directions (noted as *syn*–*syn*+−, Fig. 1b). Both conformers have similar energy.

Table 2
The relative energies (kJ/mol) for the conformers of ligands **1**–**3**[a]

	1	**2**	**3**
$E_{anti-anti}$	0	27.4 (+−)[b]	112.0
		29.4 (++)	
$E_{syn-anti}$	17.2	10.7 (+−)	36.8
		11.5 (++)	
$E_{syn-syn}$	47.0 (+−)	0 (+−)	0
	44.0 (++)	1.1 (++)	

[a] Calculations in the gas phase using DFT B3LYP/6-31G method and basis sets. In the considered conformers, the indole NH was involved in hydrogen bond with the carbonyl group, the *syn*, *anti* attributes concern orientation of the carbonyl groups.

[b] (+−) denotes energy for the *anti*–*anti*+− conformation, (++) marks energy for the *anti*–*anti*++ conformation, similarly for other conformers.

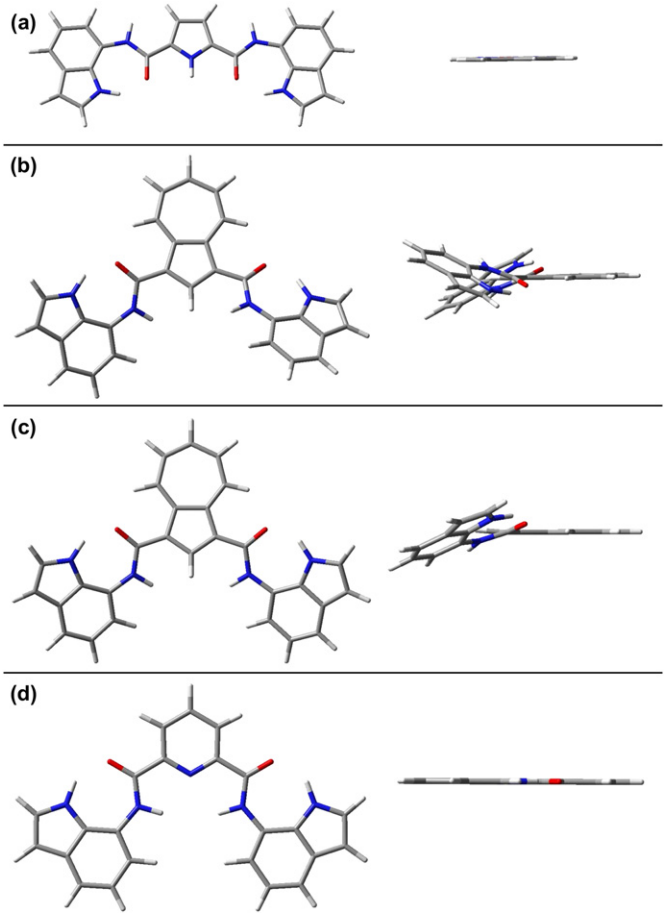


Figure 1. The conformers of ligands **1**–**3** having the lowest energy as calculated with DFT B3LYP/6-31G method. (a) **1**; (b) **2**; (c) **2**; (d) **3**.

Again, the ligand structure is induced by the preferences of the building block used for its construction, since such a preference for the *syn*–*syn* conformation was found for simple azulene-based bisamide.[23]

The dipicolinic acid derivatives are known for their preference for advantageous *syn*–*syn* conformation, thus it is not surprising that the carbonyl groups adopt the *syn*–*syn* orientation in the ligand **3** (Fig. 1d; Table 2). The structure is flat due to the presence of intramolecular hydrogen bonds.

In all ligands studied (**1**–**3**), the introduced additional binding site—indole NH is involved in hydrogen bonding with the carbonyl groups. We decided to determine the strength of this bond using DFT B3LYP method. We optimised the structures of conformations in which the carbonyl groups adopted the *syn*–*syn* orientation, but one of the indole subunits was twisted and its NH was directed into the binding cleft and thus one hydrogen bond was broken. Then we compared the energies of such conformers with the undisturbed ones. The breaking of the hydrogen bond and changing position of indole subunit require 31 kJ/mol in the case of pyrrole-based ligand **1**, and this value is higher than the corresponding values for azulene and pyridine derivatives **2** and **3**: 29 and 27 kJ/mol, respectively. It should be noted that if the energy differences of about 3 kJ contributed to the ΔG^{o} of complexation, the values of binding constants would be three times higher.

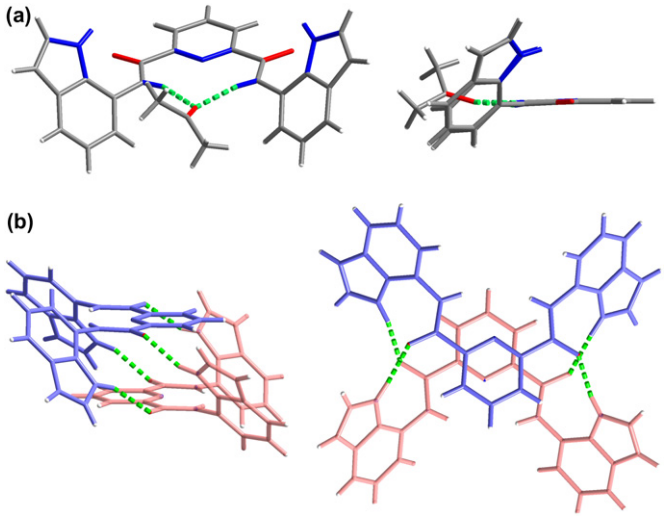


Figure 2. Crystal structure of acetone solvate of ligand **3**. (a) Different views of the independent part; (b) different views of ligand dimer (the acetone has been removed for clarity).

We obtained diffraction-grade single crystal of **3** by slow evaporation of its acetone solution. However, the structural analysis revealed that receptor **3** binds one solvent molecule (Fig. 2), so we cannot compare this structure directly with the calculated one. In the solid state, the indole moieties are tilted and as a result the ligand is not flat. An acetone molecule occupies the centre of the binding cleft and is bound by two hydrogen bonds formed by amide groups (N–O distances are 2.94 and 3.02 Å). The indole NHs are engaged in hydrogen bonds with carbonyl groups (N–O distances are 2.84 and 2.88 Å), however, contrary to the modelled structure, the hydrogen bonds involve carbonyl groups belonging to the neighbouring molecule, and the ligands actually form a dimer (Fig. 2, bottom). The distance between ligands' pyridine rings is 3.2 Å, the rings are parallel to each other and shifted in such a manner that the pyridine nitrogen is almost at the middle of the neighbouring aromatic ring, thus it seems likely that not only hydrogen bonds stabilise the dimer structure but also π-stacking. This structure resembles the one published by Gale for the DMSO solvate of analogue **3**.[21] In both structures amide groups form hydrogen bonds with solvent oxygen, also indole moieties are tilted from the plane of pyridine ring.

We also simulated the structures of the complexes of our ligands with a chloride anion. However, interpretation of calculations for anion complexes must always be taken very carefully. Interactions of anions with solvent molecules are crucial for the complexation process that takes place in solution and are more critical than for the coordination chemistry of cations.[27] Therefore, consideration of energies obtained for the gas phase is irrelevant to the complexation in solution. However, time-consuming computations for anionic species with either continuum solvation model or explicit solvent approach also lack accuracy.[28] Thus, computation of the anion complexes should be rather limited to the structural investigations like geometric fit, strain present, etc. We decided to base such analysis only on gas phase modelling, since for non-macrocyclic ligands, without anion encapsulation, shape disturbance invoked by solvation sphere should be negligible.

We calculated the structure of the chloride anion complex with pyrrole-containing ligand **1**. The anion is bound by five hydrogen bonds that involve all NH protons. The complex is flat and symmetrical (Fig. 3a). The hydrogen bond lengths (distance between N and Cl) are about 3.2 Å for both pyrrolyl/indolyl NHs and 3.5 Å for amide groups, thus dismissing the hypothesis that the indolyl binding sites are too far to interact with anions (Table 3). However, this is not the structure with lowest energy, we found another, the energy of which was lower by 0.6 kJ/mol. This complex is also planar, but the chloride anion is bound by two amide groups, NHs from pyrrole ring and only one of the indole moieties (Fig. 3b). In this

Table 3
The calculated distances between hydrogen bond donors and chloride anion for ligands **1**–**3** complexes[a]

	1[b]	**2**	**3**
d Amide NH–Cl	3.55	3.61	3.50
d Indole NH–Cl	3.25	3.20	3.16
d X–Cl[c]	3.17	3.36	3.47

[a] Calculations in gas phase using DFT B3LYB/6-31G method.
[b] Distances for the complex with five hydrogen bonds with anions (Fig. 3a).
[c] The X stands for the central atom in aromatic ring between carbonyl groups: X=N in **1**, **3** and X=2-C in **2**.

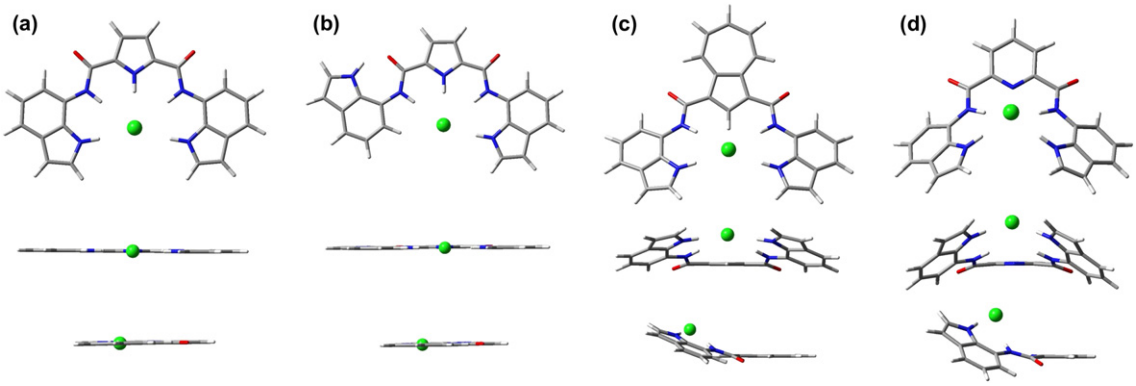


Figure 3. Calculated structures of chloride anion complexes with ligands **1**–**3** by DFT B3LYP/6-31G method. (a) and (b) **1**·Cl⁻; (c) **2**·Cl⁻; (d) **3**·Cl⁻.

structure, one of the indole subunits does not rotate to interact with anions but is still engaged in hydrogen bond with the carbonyl group. Both structures of $\mathbf{1}\cdot Cl^-$ are energetically almost equivalent, and as we stated above, they do not necessarily reflect the complex behaviour in solution. However, this surprising result is in good agreement with titration experiments. The values of the association constants determined on the basis of indolyl NH are the lowest. Probably, the indole group switches between two hydrogen bonds: with the anion or with the carbonyl group, since both interactions are similarly attractive.

A different binding mode was obtained for the chloride complex with the azulene-based ligand **2** (Fig. 3c). The anion is located above the azulene ring, the side chains—indole moieties are tilted, and the chloride anion is anchored by two pairs of hydrogen bonds: involving indole moieties (N–Cl distance 3.2 Å), and amide groups (N–Cl distance 3.6 Å). The results are summarised in Table 3.

Calculations reveal that pyridine containing ligand **3** also forms a non-planar complex with the chloride anion (Fig. 3d). The side chains are twisted even more than in the case of amide **2**, so the anion is farther from the pyridine plane, probably in order to minimise the repulsion with the electron pair of pyridine nitrogen. This modelled structure is in good agreement with the crystal structure of the chloride complex published by Gale for the dipicolinic bisamide of 2,3-dimethyl-indole-7-amine.[21] The main difference is that the indole pendant arms are tilted with different angles in the solid state, and as a result the ligand structure is unsymmetrical, also the hydrogen bonds are slightly shorter, and the chloride anion is closer to the pyridine scaffold.

There is a correlation between length of hydrogen bonds in the all three calculated chloride complexes with ligands **1**–**3**. The bond formed by indole NH is longest for the pyrrole-based ligand **1**, whereas the distance between chloride and the aromatic ring is shortest. In the case of pyridine-based ligand **3**, the distance between chloride and aromatic ring is longest and hydrogen bond involving indole is shortest (Table 3). It is understandable, since in the complex of ligand **1** chloride anion is attracted by pyrrole NH in **1**, whereas it is pushed out by the free electron pair of ligand **3**.

For azulene and pyridine ligands **2** and **3** we also optimised the complex structures in which one of the hydrogen bond between indole NH and carbonyl group was preserved. On the contrary to the pyrrole-based ligand **1**, such complexes have higher energies: about 6 kJ/mol for azulene-containing **2** and 8 kJ/mol for the derivative of pyridine **3**.

On the basis of this conformational analysis, it is apparent that the pyrrole derivative **1** has a structure that is poorly suitable for anion recognition. It is the only ligand studied that upon anion complexation must accomplish rotation of its carbonyl groups. The intramolecular hydrogen bonds between indolyl NHs and carbonyl groups are the strongest in **1**, and these bonds must be broken in order to coordinate anions. Moreover, computation showed that binding of the chloride anion by five and by only four hydrogen bonds is energetically similar for the ligand **1**, at least in the gas phase.

3. Conclusions

To summarise, indole-7-amine (**6**) is an interesting alternative to aniline for the construction of anion receptors. Introduction of indole NH as an additional binding site can improve anion binding more than five times as was demonstrated by azulene- and pyridine-based bisamides **2** and **3**. However, the advantageous presence of the additional hydrogen bond donor can be diminished by strong intramolecular hydrogen bonds and unfavourable ligand preorganisation as exemplified by receptor **1**. Molecular modelling seems to be able to predict the case, which would take place and save the synthetic effort.

4. Experimental

4.1. General remarks

The details concerning structural analysis and determination of binding constants are provided in the Supplementary data. Crystallographic data (excluding structure factors) for the structures discussed in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 654083. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk) .

The aniline-containing ligands **10**–**12** were prepared by reaction of the appropriate acetic dichlorides **7**–**9** with aniline.[5,23] The 7-nitroindole (**5**) is commercially available or can be synthesised from 1,2-dinitrobenzene (**4**) according to the procedure given in the Supplementary data.

4.2. 1H-Indole-7-amine (6)

7-Nitroindole **5** (1.1 g, 6.8 mmol) was dissolved in methanol (50 ml) and 5% palladium on charcoal was added (0.2 g). The mixture was vigorously stirred under hydrogen atmosphere. The reaction was monitored by TLC, and after completion (about 2 h), the catalyst was filtered off on Celite. The solvent was evaporated, and the solid residue was recrystallised from hot $CHCl_3$ to which a small amount of pentane was added after cooling down. This yields 0.71 g (80%) of the desired amine **6** as colourless crystals, mp 94–95 °C.

^{1}H NMR (200 MHz, DMSO) δ=10.64 (br s, 1H, N*H*-indole), 7.25 (t, 1H, J_1=2.8 Hz), 6.76 (m, 2H), 6.35 (d, 1H, J_1=1.4 Hz), 6.31 (t, 1H, J_1=2.6 Hz, J_2=2.4 Hz), 5.01 (br s, 2H, NH_2); ^{13}C NMR (50 MHz, DMSO) δ=134.2, 128.7, 126.1, 124.2, 120.4, 109.1, 105.1, 102.0; HR EI calcd for $C_8H_8N_2$ M^+: 132.06875, found: 132.06863.

4.3. 1H-Pyrrole-2,5-dicarboxylic acid bis-[(1H-indol-7-yl)-amide] (1)

Into the suspension of amine **6** (1.9 g, 14.4 mmol) in dry CH_2Cl_2 (40 ml), *N*,*N*-dimethylaniline was added (1.8 ml, 14.4 mmol), then the solution of acetic dichloride **7**[5] (0.92 g,

4.8 mmol) in CH_2Cl_2 (8 ml) was added dropwise over 20 min. The stirring was continued for 2 h, then the precipitated amine hydrochloride was filtered off, and the solvent was removed in vacuo. The residue was dissolved in ethyl acetate (100 ml) and washed with water (2×25 ml), 1 M HCl (2×25 ml) and brine (25 ml). The organic layer was dried over $MgSO_4$, the solvent was removed, and the crude product crystallised from ethanol/pentane and then recrystallised from hot 1,2-dichloroethane, to which a small amount of pentane was added after cooling down. Yield 1.6 g (85%) of the amide **1** as slightly yellow crystals, mp 232 °C.

^{1}H NMR (500 MHz, DMSO) δ=12.28 (br s, 1H, N*H*-pyrrole), 10.85 (s, 2H, N*H*-indole), 10.02 (s, 2H, N*H*), 7.42 (d, 2H, J_1=7.7 Hz, 4-C*H*), 7.37–7.34 (m, 4H, 2-C*H*+6-C*H*), 7.14 (d, 2H, J_1=1.2 Hz, C*H*-pyrrole), 7.02 (dd, 2H, J_1=J_2=7.7 Hz, 5-C*H*), 6.48 (m, 2H, 3-C*H*); ^{13}C NMR (125 MHz, $CDCl_3$) δ=158.8, 130.0, 129.8, 129.7, 125.7, 123.1, 119.29, 117.7, 115.9, 113.5, 102.0; HR ESI calcd for $C_{22}H_{17}N_5O_2Na$ $[M+Na]^+$: 406.1280, found: 406.1287. Anal. Calcd for $C_{22}H_{17}N_5O_2$: C 68.92, H 4.47, N 18.27, found: C 69.06, H 4.58, N 18.19.

4.4. Azulene-1,3-dicarboxylic acid bis-[(1H-indol-7-yl)-amide] (2)

A procedure analogous to that for the amide **1** was performed using the diacid dichloride **8**[23] (0.45 g, 1.8 mmol), but the reaction was left overnight. Then the solid was filtered off and thoroughly washed with 2 M HCl and with $CHCl_3$. The crude product was purified by flushing over silica gel with THF as an eluent. Yield 0.4 g (50%) of the amide **2** as violet-red crystals, mp 276–279 °C.

^{1}H NMR (200 MHz, DMSO) δ=10.91 (s, 2H, N*H*-indole), 10.14 (s, 2H, N*H*), 9.76 (d, 2H, J_1=9.8 Hz, 4-C*H*-azulene), 9.27 (s, 1H, 2-C*H*-azulene), 8.14 (t, 1H, J_1=9.8 Hz, 6-C*H*-azulene), 7.83 (dd, 2H, J_1=J_1=9.8 Hz, 5,7-C*H*-azulene), 7.54 (d, 2H, J_1=7.8 Hz, 6-C*H*), 7.43–7.37 (m, 4H, 3-C*H*+4-C*H*), 7.05 (dd, 2H, J_1=J_1=7.8 Hz, 5-C*H*), 6.49 (m, 2H, 2-C*H*); HR ESI calcd for $C_{28}H_{20}N_4O_2Na$ $[M+Na]^+$: 467.1484, found: 467.1482. Anal. Calcd for $C_{28}H_{20}N_4O_2$: C 75.66, H 4.54, N 12.60, found: C 75.32, H 4.64, N 12.48.

4.5. Pyridine-2,6-dicarboxylic acid bis-[(1H-indol-7-yl)-amide] (3)

The indoleamine **6** (0.6 g, 4.5 mmol) and triethylamine (1.15 ml, 8.3 mmol) were suspended in dry CH_2Cl_2 (40 ml), the mixture was cooled to 0 °C, and then the solution of diacetic dichloride **9** (0.5 g, 2.1 mmol) in CH_2Cl_2 (2 ml) was dropwise added. Stirring was continued for 4 h, then the solid was filtered and washed thoroughly with 1 M HCl. The organic filtrate was washed with 1 M HCl (2×25 ml) and water (25 ml), dried over $MgSO_4$ and combined with the filtered off solid. The combined portions of amide **3** were flushed over silica gel using hexane/ethyl acetate (1:1) as an eluent, and recrystallised from ethyl acetate with a small amount of THF yielding 0.68 g (87%) of slightly yellow crystals of the amide **3**, mp 295–297 °C (with dec).

^{1}H NMR (500 MHz, DMSO) δ=11.19 (s, 2H, N*H*), 11.01 (s, 2H, N*H*-indole), 8.44 (d, 2H, J_1=7.7 Hz, 3,5-C*H*-pyridine), 8.32 (m, 1H, 4-C*H*-pyridine), 7.49 (d, 2H, J_1=7.7 Hz, 4-C*H*), 7.38 (dd, 2H, J_1=J_1=5.5 Hz, 2-C*H*), 7.26 (d, 2H, J_1=7.4 Hz, 6-C*H*), 7.05 (dd, 2H, J_1=J_1=7.6 Hz, 5-C*H*), 6.50 (m, 2H, 3-C*H*); ^{13}C NMR (125 MHz, $CDCl_3$) δ=162.4, 149.4, 140.2, 131.5, 129.7, 125.9, 125.5, 122.4, 119.1, 118.7, 118.2, 101.9; HR ESI calcd for $C_{23}H_{17}N_5O_2Na$ $[M+Na]^+$: 418.1280, found: 418.1271. Anal. Calcd for $C_{23}H_{17}N_5O_2$: C 69.86, H 4.33, N 17.71, found: C 69.81, H 4.53, N 17.52.

Supplementary data

Details concerning binding studies and structural analysis as well the synthetic procedure for compound **5** are available. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.11.012.

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