Complexation of Anions Including Nucleotide Anions by Open-Chain Host Compounds with Amide, Urea, and Aryl Functions

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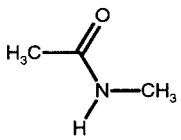
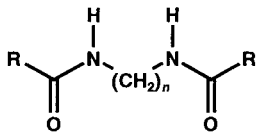
Dedicated to Prof. *Gunther Wulff* on the occasion of his 65th birthday

A systematical evaluation of association constants between halide, phosphate, and carboxylate anions with *N*-methylformamide (**1**) and the related bidentate receptors **2**–**6** (derived from, *e.g.*, phthalic acid or ethylenediamine) in $CDCl_3$ as solvent yielded increments of complexation free-energy $\Delta\Delta G$ for each single H-bond, which varied like, *e.g.*, 5.1 kJ/mol (for Cl^-), 4.0 kJ/mol (for Br^-), 4.0 kJ/mol (for I^-) (with values taken from *Tables 1* and *2*), in line with expected H-bond strength. The observed complexation induced NH-NMR shift (CIS) values also showed a regular change, in the case of **1**, *e.g.*, from 5.0 to 2.8 to 2.1 ppm (*Table 1*), with about half of these values with the bidentate ligands (*Tables 2* and *3*). Tridentate hosts led to a substantial binding increase, if strain-free convergence of all NH donor functions towards the anion was possible. The tris[urea] ligand **10** yielded, even in the polar solvent DMSO, with Cl^- a ΔG of -21.5 kJ/mol and with Br^- of $-10 \cdot 5$ kJ/mol, whereas with I^-, no association was detectable. The results demonstrated that small, inexpensive, and conformationally mobile host compounds can exhibit high affinities as well as descrimination with anions, as much as more preorganized receptors do which require multistep synthesis. The corresponding adamantyl derivative **13** allowed measurements also in $CDCl_3$, with $K = 4.3 \cdot 10^4$ M^{-1} for chloride (*Table 7*). Complexes with nucleotide anions were again particularly strong with the tridentate urea-based ligands, the latter being optimal ligands for chloride complexation. For the association of **10** with AMP^{2-} and GMP^{2-}in (D_6)DMSO, the association constants were $3 \cdot 10^4$ M^{-1} (*Table 8*) and almost the same as with Cl^-. In the case of the urea derivatives **17**, **18**, and **21**, containing only one phenyl or pyrenyl substituent, however, the ΔG values decreased in the order A > C > T > G (*e.g.* -13.6, -11.6, -7.6, -10.5 kJ/mol in the case of **17**, resp.; *Table 8*). In H_2O, the pyrenyl-substituted urea derivatives allow measurements with fluorescence, and, unexpectedly, show only smaller nucleobase discrimination, with constants around $3 \cdot 10^3$ M^{-1}.

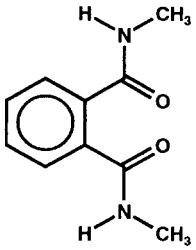
Introduction. – Anion complexation has often been deplored as being a less developed area of supramolecular chemistry: an excellent recent review by *Antonisse* and *Reinhoudt* [1], which allows us to restrict ourselves here to few references, illustrates the current high interest in the field and its rapid expansion. The binding of anions to electroneutral receptors is of special significance, also in view of the absence of competing counterion complexes, which are usually present if one uses cationic host compounds. Recent investigations, particularly by *Reinhoudt et al.* (see [1]), have already shown the potential of amides for complexation of anions. A so-called tuneable amide based on a calixarene has been synthesized by *Cameron* and *Loeb* [2], although the anion-association constants reported were low. Coordination to amide functions is also essential for orthophosphate [3] or sulfate-ion [4] binding in proteins. One aim of the present work was to establish free-energy increments for binding of different anions by a systematic experimental investigation to the ligands **1**–**22** (see *Fig. 1*), and another



1



3 n=2, R=Me
4 n=1, R=Ph
5 n=3, R=Me
6 n=4, R=Me



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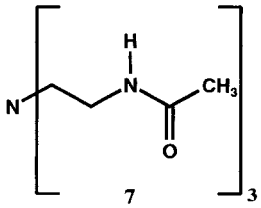

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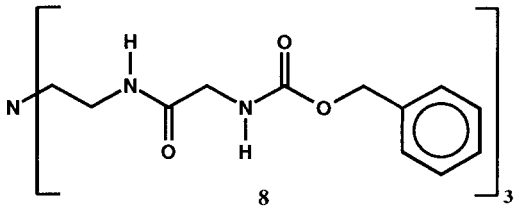

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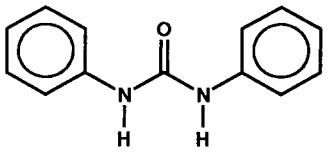

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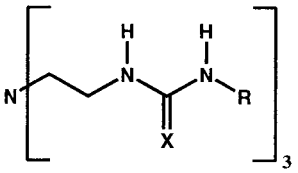
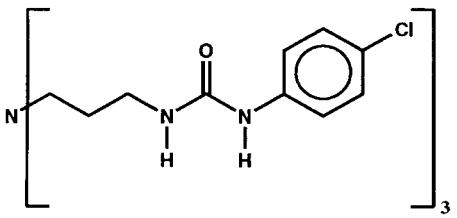


10 R = 4-chlorophenyl, X=O
12 R = 1-naphthyl, X=O
13 R = 1-adamantyl, X=O
14 R = 4-nitrophenyl, X=O
15 R = 4-nitrophenyl, X=S
16 R = 1-Bu, X=O



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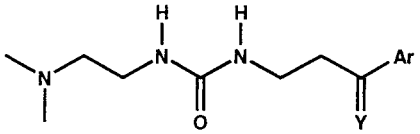
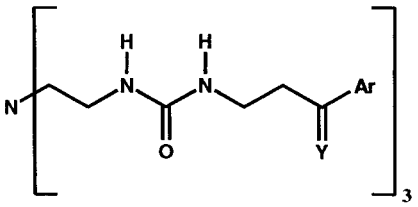




17 Ar = pyren-1-yl, Y = 2H
18 Ar = pyren-1-yl, Y = O
21 Ar = Ph, Y = 2H

19 Ar = pyren-1-yl, Y = O
20 Ar = pyren-1-yl, Y = 2H
22 Ar = Ph, Y = 2H

Fig. 1. *Structures of the ligands*

to explore the use of substituted amide-type derivatives for the biologically particularly interesting complexation of nucleotide anions [5] in water.

Complexation of Simple Anions. – First, we tested the affinity of the amide function for the binding of different anions with the simple ligand *N*-methylacetamide (**1**) which, in contrast to earlier assumptions [6], could well be measured in $CDCl_3$ as solvent and presents a cornerstone for understanding anion-peptide interactions (*Table 1*). ^{1}H-NMR-Shift titrations of **1** with the anions usually showed a nearly perfect nonlinear least-squares fit for a 1:1 stoichiometric model of amide/anion. The observed higher affinity of phosphate *vs.* benzoate likely reflects on the one hand the polydentate advantage of the dihydrogenphosphate anion, and on the other hand the increased charge at the O-atom as confirmed by *ab initio* calculations (preliminary charge calculations with the 6-31G** basis set indicate -0.56 e units at the O-atoms of benzoate, and -1.1 e at the O-atoms of dihydrogenphosphate). The sequence $Cl^- > Br^- > I^-$ reflects the change of the H-bond-acceptor strength of the halides, which is noticeably also found in the case of complexes between hydroxy compounds and the halides [7]; another factor could be the change in anion radii of the halides. The observed **c**omplexation-**i**nduced ^{1}H-NMR **s**hifts (CIS) show typical values for amide protons in $CDCl_3$ involved in H-bonding, again in the $Cl^- > Br^- > I^-$ sequence with decreasing H-bond strength.

Table 1. *Titration of* N-*Methylacetamide* (**1**) *with Different Anions*

Proton	Anion[a])									
	Dihydrogenphosphate		Benzoate		Chloride		Bromide		Iodide	
	K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])
NH	26	4.49	14	3.99	10	4.99	8	2.84	5	2.11
MeN	35	−0.084	16	−0.1	−[e])	−[e])	5	−0.09	3	−0.10
MeCO	−[e])	(0.07[f]))	14	0.015	−[e])	−[e])	−[e])	(0.08[f]))	8[g])	0.06
$\Delta G_\varnothing$[d])	−8.4		−6.6		−5.7		−4.6		−4.1	

[a]) Measured as Bu_4N^+ salts in $CDCl_3$. [b]) In l/mol; calculated from δ(H) for a 1:1 model; error < 10% from $\Delta\delta$ (NH); < 15% from $\Delta\delta$ (CH). [c]) Complexation-induced NMR shifts (CIS) in ppm relative to $SiMe_4$ in CCl_4 (external); positive sign, deshielding; negative sign, shielding. [d]) Average value from evaluation of several proton shifts, in kJ/mol at 298 K. [e]) Not observable, due to overlapping Bu_4N^+ ion signals. [f]) Calculated with the K value obtained from other proton shifts. [g]) Error > 20%.

The results of the diamide titrations with 1,2-phthalodiamide (**2**) or *N*,*N*′-(ethane-1,2-diyl)bis[acetamide] (**3**) (*Table 2*) clearly establish a chelate effect, with more or less additive ΔG increments. Even the CIS values are smaller by a rather constant factor of nearly 50% in comparison to the monofunctional ligand **1**, in line with the charge distribution over two NH bonds instead of one. The increased affinity of **2** in comparison to **3** is due to the preorganization of the two amide functions (see *Fig. 2* for the structure of benzoate·**2**), although preliminary molecular-mechanics calculations show a rather unfavorable geometry in the ground state of **2**. *Crabtree* and co-workers [8] have obtained K values (l/mol) of $6 \cdot 10^4$ for Cl^-, of $7 \cdot 10^3$ for Br^-, and of $5 \cdot 10^2$ for I^- with isophthalamides, however, in the particularly unpolar solvent CH_2Cl_2. Energetic disadvantages are even more pronounced for the diamides **4**–**6**, which must adopt

Table 2. *Titrations of Hosts* **2** *and* **3** *with Different Anions*

Proton		Anion[a])							
		Benzoate		Chloride		Bromide		Iodide	
		K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])
2	NH	54	2.750	21	2.001	16	1.270	9	0.802
	MeN	17	−0.095	−[e])	−[e])	−[e])	−[e])	−[e])	−[e])
	H−C(3)/H−C(6)	12	−0.175	−[e])	−[e])	−[e])	−[e])	11	0.071
	$\Delta G_{\varnothing}$[d])	−9.9		−7.5		−6.9		−5	
3	NH	328	3.45	108	2.82	18	2.25	39	1.510
	MeCO	−[e])	−[e])	−[e])	(0.13[f]))	−[e])	−[e])	37	0.076
	$\Delta G_{\varnothing}$[d])	−14.4		−11.6		−7.2		−9	

[a])–[f]) See *Table 1*.

partial *gauche* conformations for the anion complexation and, therefore, exhibit decreasing affinities (*Table 3*). In another context, it has been shown that the decrease in affinity of H-bond complexes for open-chain ligands like **3**, **5**, and **6** is, with only *ca.* 1.3 kJ/mol disadvantage per additional single bond, relatively small [9], as long as there is no built-up of steric strain by complexation. Therefore, open-chain combinations of receptor sites offer an attractive alternative to synthetically difficult to obtain and expensive preorganized receptors. Derivatives of tris(aminoethyl)amin (tren) offer a convenient entry to tridentate ligands such as **7**, or to ligands with more binding sites such as **8**. The increase of association constants by introduction of a third function, however, is only moderate (*Table 4*), in agreement with related literature data [10].

Significantly improved affinities can be achieved with urea derivatives [6][11–13] which are easily prepared from isocyanates and the corresponding amines. The ^{1}H-NMR spectra of the *N*,*N*′-disubstituted ureas show only the (*E*,*E*)-isomer (> 99%) around the CO−N pseudo-double bond, which is due to the high strain energy of the

Table 3. *Titrations of Hosts* **4**–**6** *with Different Anions*

Proton		Anion[a])							
		Benzoate		Chloride		Bromide		Iodide	
		K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])
4	NH	53	3.12	< 10	−[f])	< 5	−[f])	< 5	−[f])
	CH_2	52	0.22	−[f])	−[f])	−[f])	−[f])	−[f])	−[f])
	H−C(2)/H−C(5)	56	0.33	−[f])	−[f])	−[f])	−[f])	−[f])	−[f])
	H−C(3)/H−C(6)	48	−0.11	−[f])	−[f])	−[f])	−[f])	−[f])	−[f])
	$\Delta G_{\varnothing}$[d])	−9.8		> −5.7		> −4		> −4	
5	NH	78	3.03	37	3.22	21	2.03	27	1.39
	MeCO	−[e])	−[e])	−[e])	−[e])	−[e])	−[e])	40	0.03
	$\Delta G_{\varnothing}$[d])	−10.8		−8.9		−7.5		−8.2	
6	NH	48	2.65	29	2.38	28	1.77	26	1.12
	MeCO	−[e])	−[e])	15	0.09	18	0.08	21	0.06
	CH_2(2)/CH_2(3)	−[e])	−[e])	−[e])	−[e])	−[e])	−[e])	18	0.09
	$\Delta G_{\varnothing}$[d])	−9.6		−8.3		−8.3		−8.1	

[a])–[f]) See *Table 1*.

Table 4. *Titrations of Triamide* **7** *and Hexamide* **8** *as Hosts*

Proton		Anion[a])							
		Benzoate		Chloride		Bromide		Iodide	
		K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])
7	NH	195	2.90	307	2.45	125	1.81	52	1.17
	CH_2(2)	–[e])	–[e])	–[e])	–[e])	94	– 0.05	–[e])	–[e])
	CH_2(1)	(436)[f])	– 0.03	–[e])	–[e])	46	– 0.05	20	0.02
	MeCO	(390)[f])	– 0.02	–[e])	–[e])	81	0.143	39	0.08
	$\Delta G_{\varnothing}$[d])	– 13.1		– 14.2		– 12.0		– 9.8	
8	NH (imino)	213	1.26	395	0.30	30	0.36	17	0.30
	NH (carbam.)	348	1.89	1504	1.68	175	1.09	31	0.53
	PhCH_2	–[e])	–[e])	1537	0.19	150	0.183	38	0.10
	$COCH_2$	–[e])	–[e])	–[e])	–[e])	–[e])	–[e])	40	0.08
	$\Delta G_{\varnothing}$[d])	– 14		– 18.2		– 12.6		– 8.8	

[a]) – [f]) See *Table 1*.

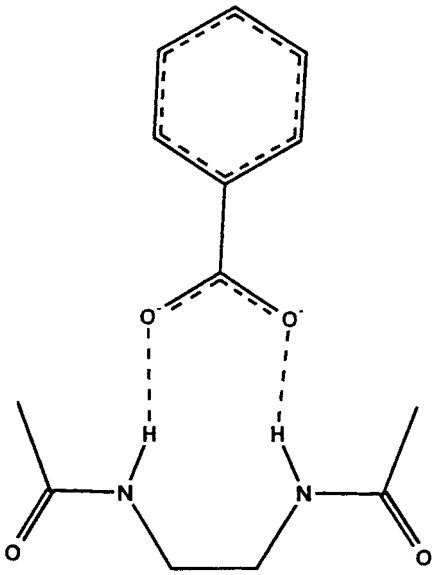


Fig. 2. *Structure of the benzoate* · **3** *complex* (from CHARMm energy minimization)

(*Z*,*Z*)- and (*E*,*Z*)-conformers; thus they provide two NH protons pointing towards the anion. As a result, even the simple *N*,*N*′-diphenylurea (**9**) allows measurement of anion complexation in the highly competitive solvent DMSO with chloride and bromide (*Table 5*). If one makes such urea derivatives tridentate (see ligands **10** and **11**), affinities with a ΔG of up to – 21.3 kJ/mol are observed (*Table 6*), which, to the best of our knowledge, are the highest observed with electroneutral ligands in such a polar solvent (see *Fig. 3* for the structure of chloride · **10**). At the same time, these easily accessible ligands discriminate the different halides quite well. Besides this, *Alcazar* and co-workers [13] described ureas bound to chromane skeletons which associate the

Table 5. *Titrations of* N,N′*-Diphenylurea* (**9**) *as Host*

Proton	Anion[a])							
	Chloride		Bromide		Iodide		Iodide[f])	
	K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])
NH	40	1.52	4	1.51	< 1	–[e])	1070	1.21
H_o	28	0.029	–[e])	–[e])	–[e])	–[e])	1380	0.322
H_m	47	– 0.029	–[e])	–[e])	–[e])	–[e])	–[g])	–[g])
H_p	50	– 0.044	–[e])	–[e])	–[e])	–[e])	1290	– 0.192
$\Delta G_\varnothing$[d])	– 9.2		– 3.4		> 0		– 20.4	

[a])–[g]) See *Table 1*, except that (D_6)DMSO was used as solvent. [h]) In $CDCl_3$.

Table 6. *Titrations of Tren-Based Urea Derivatives* **10** *and* **11**

Proton		Anion[a])					
		Chloride		Bromide		Iodide	
		K[b])	CIS[c])	K[b])	CIS[c])	K[b])	CIS[c])
10	NHAr	1300	0.63	48	0.30	*ca.* 0	–[e])
	$NHCH_2$	1800	0.41	47	0.45	*ca.* 0	–[e])
	H_o	1050	0.05	85	– 0.01	*ca.* 0	–[e])
	H_m	1300	– 0.03	43	0.07	*ca.* 0	–[e])
	H_p	–	–	85	– 0.07	*ca.* 0	–[e])
	$\Delta G_\varnothing$[d])	– 21.3		– 10.2		> 0	
11	NHAr	88	0.60	9	0.51	*ca.* 1	–[e])
	$NHCH_2$	77	0.41	11	0.26	–[e])	–[e])
	H_o	40	0.08	9	0.06	–[e])	–[e])
	H_m	–[e])	–[e])	–[e])	–[e])	–[e])	–[e])
	H_p	–[e])	–[e])	–[e])	–[e])	–[e])	–[e])
	$\Delta G_\varnothing$[d])	– 10.5		– 5.6		*ca.* 0	

[a])–[f]) See *Table 1*, except that (D_6)DMSO was used as solvent.

di- or trianion sulfate or phosphate, respectively, in MeOH with association constants of up to $6 \cdot 10^4$ l/mol. A report of *Reinhoudt* and co-workers [14] citing comparable constants suffers from unsuitable measurement conditions (the anion concentration was at least $5 \cdot 10^{-4}$ mol/l, being more than 30-fold too high following general considerations (see [15a]; in addition, Bu_4NF was used, which is not stable without crystal water according to [15b]).

The ligand **10**, derived from tris(2-aminoethyl)amine, and the ligand **11**, derived from tris(3-aminopropyl)amine, differ substantially in affinity towards anions, in spite of their quite similar structure. Computer-aided molecular modelling shows that ligand **10** can form a complex with chloride without substantial strain. Preliminary force-field calculations in the gas phase indicate that a closed conformation of **10** is favored by *ca.* 90 kJ/mol in comparison to an open conformation, similar to that shown in *Fig. 8*, whereas for **11**, the open form seems to be favored by *ca.* 5 kJ/mol. These predictions are confirmed by the observation of vicinal coupling constants ^3J, which remain constant during the ^{1}H-NMR titration of **10** with chloride, but change from 7.5 to 6.8 Hz

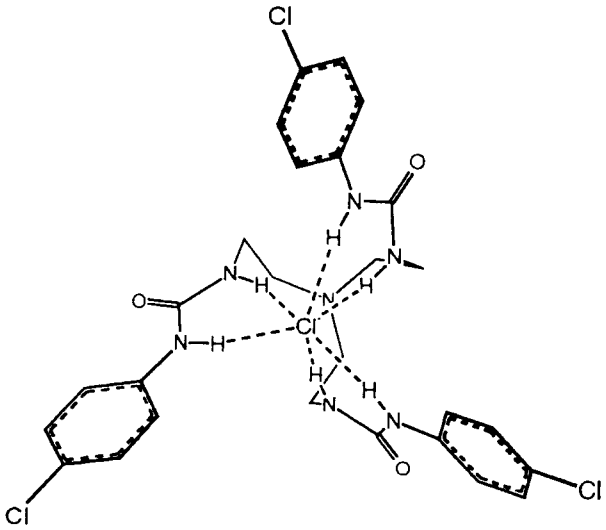


Fig. 3. *Structure of the chloride·***10** *complex* (from CHARMm energy minimization)

in the case of **11**. The closed conformation of **10** is also in agreement with the starting NH shift which is 0.2 ppm higher for **10** than for **11**, indicating a stabilization due to *intra*molecular H-bonding.

To study the influence of different substituents on the 'isocyanate side', we synthesized compounds **12**–**16**. The results of the chloride titrations (*Table 7*) show that the nature of the 'isocyanate' substituent has little influence on the association constants. The recently reported K value of $5 \cdot 10^4$ l/mol in DMSO for the **16**·chloride complex [16] could not be reproduced in our hands. Deviations due to different water content can be excluded, as addition of even 5 vol-% of water reduced the constant only from 360 l/mol to 110 l/mol. The adamantyl derivative **13** was also titrated with chloride in the solvent $CDCl_3$: the ΔG value of $-$ 26.9 kJ/mol is at the measuring limit of NMR titrations and showed the expected increase.

Complexation of Nucleotide Anions. – Ligands containing aromatic units besides amide-type functions for anion complexation can be expected to provide additional

Table 7. *Chloride*[a]) *Titrations of Urea Derivatives* **12**–**22**

Ligand	NH (A)		NH (B)		$\Delta G_{\varnothing}$[d])
	K[b])	CIS[c])	K[b])	CIS[c])	
12	1191	0.805	971	0.460	– 17.6
13	811	0.756	868	0.512	– 16.9
13 ($CDCl_3$)	43123	0.825	43890	0.709	– 26.9
14	1859	0.567	1931	0.427	– 19.0
15	1979	0.371	1596	0.642	– 18.9
16	363	0.646	363	0.571	– 14.8
22	819	0.693	805	0.584	– 16.9

[a])–[d]) See *Table 1*, except that (D_6)DMSO was used instead of $CDCl_3$.

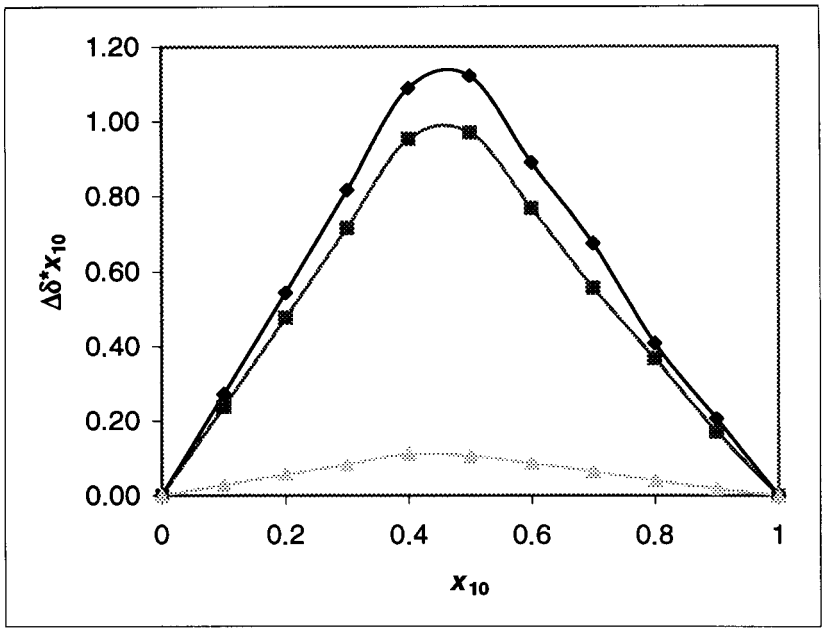
stacking interactions. Similarly to the halides, the tridentate **10** carrying aryl substituents showed in (D_6)DMSO with nucleotide anions promising K values of *ca.* $3 \cdot 10^4$ M^{-1} (*Table 8*), with negligible difference between nucleotides since stacking in solvents like (D_6)DMSO can contribute little. With the analogous ligand **11**, different protons in the titration yielded association isotherms which could not be evaluated, estimated K's derived from the NH shifts of **11** ranging from $1 \cdot 10^2 - 1 \cdot 10^3$ M^{-1}, these characteristics being likely due to the formation of several complexes. In contrast to **11**, ligand **10** titrated with AMD^{2-} showed a maximum near $x = 0.5$ for all three protons in a *Job*'s plot (*Fig. 4,a*; modification of methods developed by *Ostromisslensky* [17] and *Denison* [18]); also a modified 'one-species test', as proposed for spectrophotometric measurements [19], plotted with a common origin for all lines, clearly demonstrated for **10** a predominant 1:1 complex with the nucleotide anions, with higher complexes contributing only to a minor extent (*Fig. 4,b*).

The introduction of pyrene units into urea-derived host compounds **17**–**20** with the simultaneous implementation of hydrophilic amino groups was initiated in the hope of allowing larger stacking effects, measuring also in D_2O with better discrimination between the nucleobases, and of allowing of the highly sensitive fluorescence method for detection. Ligands like **19** or **20** which were only sparingly soluble in D_2O due to the aromatic units and the absence of an; additional hydrophilic amino group (like in **17** and **18**), showed in (D_6)DMSO much weaker complexes with the nucleotides than, *e.g.*, **10**. By comparison with NH shifts of other ligands, we could estimate the K values to be below 10 l/mol.

Table 8. *Titrations with Nucleotide Anions*

Ligand	Solvent	AMP[a])		CMP[a])		GMP[a])		TMP[a])	
		K[b])	ΔG[d])	K[b])	ΔG[d])	K[b])	ΔG[d])	K[b])	ΔG[d])
NMR[a])									
20	(D_6)DMSO	< 10[e])	> −5.8[e])	< 10[e])	> −5.8[e])	< 10[e])	> −5.8[e])	< 10[e])	> −5.8[e])
19	(D_6)DMSO	< 10[e])	> −5.8[e])	< 10[e])	> −5.8[e])	< 10[e])	> −5.8[e])	< 10[e])	> −5.8[e])
21	(D_6)DMSO	180	−13.0	80	−11.0	18	−7.2	50	−9.8
17	(D_6)DMSO	220	−13.6	100	−11.6	20	−7.6	64	−10.5
18	(D_6)DMSO	78	−11	–	–	–	–	–	–
10	(D_6)DMSO	30000	−26.0[d])	42000	–	29000	−25.9	36000	–
12	(D_6)DMSO	25000[f])	−25.5	–	–	22000[f])	−25.2	–	–
22	(D_6)DMSO	[g])	[g])	[g])	[g])	[g])	[g])	[g])	[g])
Fluorescence[h])									
20	H_2O	< 10[i])	> −5.8	< 10[i])	> −5.8	< 10[i])	> −5.8	< 10[i])	> −5.8
19	H_2O	< 10[i])	> −5.8	< 10[i])	> −5.8	< 10[i])	> −5.8	< 10[i])	> −5.8
17	H_2O	2680	−19.9	2857	−20.0	3300	−20.4	4120	−21.0
18	H_2O	2310	−19.5	2540	−19.8	2960	−20.1	3750	−20.7
Pyrene	H_2O	1205	−17.8	396	−15.1	1250	−17.9	572	−16.0
Pyrene[j])	H_2O	52	−9.9	13	−6.4	45	−9.6	14	−6.6

[a])[b])[d])[e]) See *Table 1.* [f]) Error > 20% due to high association constant. [g]) No consistent association constants; values varied more than one order of magnitude for different protons, K ranged from 10^3–10^4 l/mol. [h]) At pH 6.2 ± 0.07; no added buffer, no additional salts, no organic solvents; nucleotides as disodium salts; λ_{Ex} 320 nm, λ_{Em} = 373, 384, 393 nm; slit width 10 nm; measurements in triplicate, association constants differed by less than 10%. [i]) Calculated from estimated fluorescence changes taken from other measurements. [j]) From [20], in H_2O with 5 vol-% MeOH; pH 7; 1 mM sodium cacodylate.



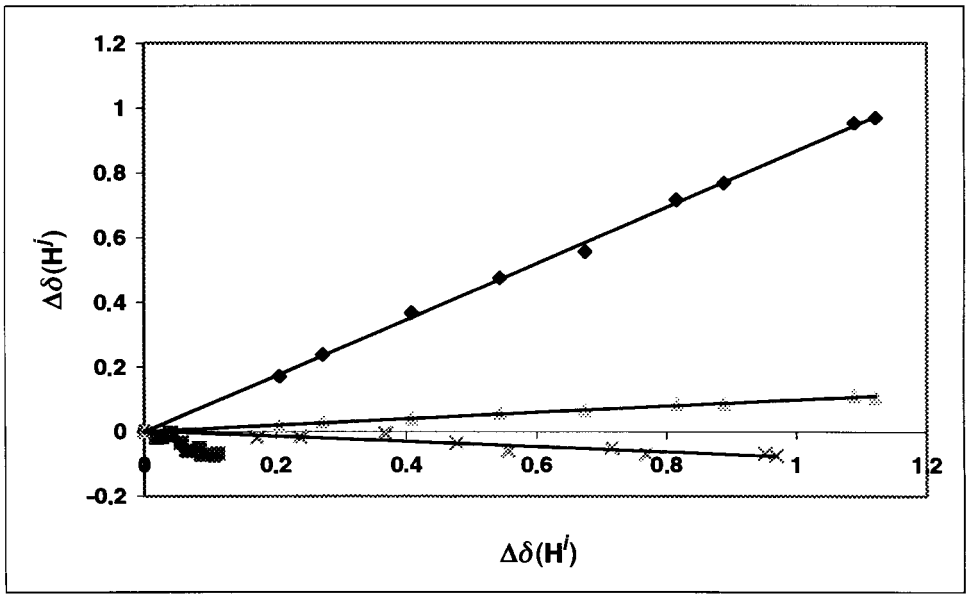


Fig. 4. a) Job's *plot* (◆: NH^a, ■: NH^b, ▲: CH(arom.)), *and* b) *one-species test for the* **10**·AMP^{2-} *complex* (◆: NH^a *vs.* NH^b, ▲: NH^a *vs.* CH(arom.), × : NH^b *vs.* CH(arom.), ■: CH(arom.) *vs.* CH′(arom.))

In contrast to these results, the ligands **17** and **18** with only one pyrene unit showed fairly good complexation in D_2O with K values around $3 \cdot 10^3$ (*Table 8*), slightly increasing in the order $A < C < G < T$ (see *Fig. 5* for the structure of $AMP^{2-} \cdot$ **17**). Larger differences, remarkably however, in the reverse order $A > C > T > G$ were observed with ligands **17** and **21** in (D_6)DMSO as solvent. While these differences hold promise for applications, the elucidation of their origin requires further studies. In view of the rather uniform affinities observed with the pyrene-substituted ligands **17** and **18** in D_2O, association with unsubstituted pyrene as ligand[1]) was also investigated, yielding free association energies ΔG which are 2–5 kJ/mol smaller than those obtained with **17** and **18**. The relatively small contribution of the urea anion-binding centers in **17** and **18** to the association can be a consequence of the geometric disposition preventing simultaneous full contact at the stacking and anion-binding sites, in analogy to the situation found with cyclophane complexes [21]. The distinct upfield CIS of – 0.07 ppm for pyrene signals, as seen in the complex of **17** with AMP^{2-}, indicate that face-to-face stacking interactions play a major role here.

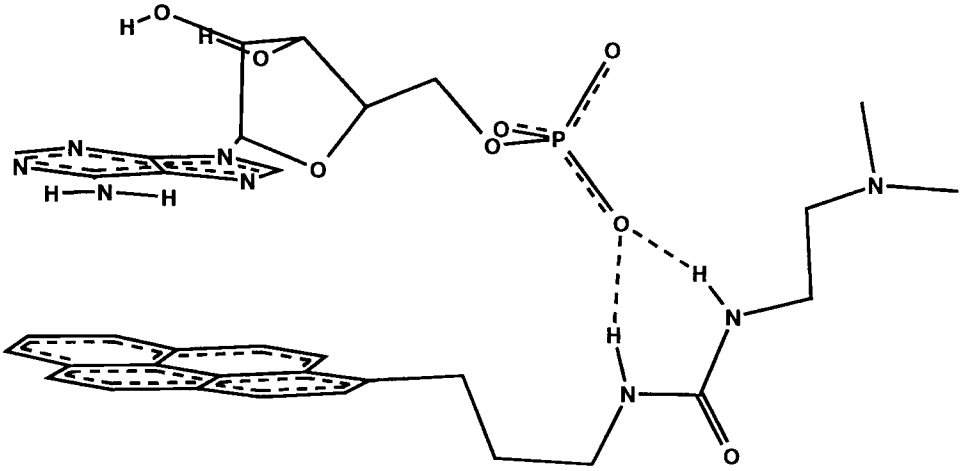


Fig. 5. *Structure of the* $AMP^{2-} \cdot$ **17** *complex* (from CHARMm energy minimization)

Experimental Part

General. Unless stated otherwise, all reagents were obtained from commercial sources and used without further purification. Tris(3-aminopropyl)amine was a kind gift from Dr. *R. Hettich* [22]. Solvents for reactions were purified and dried as described in [23], except DMF, which was bought from *Fluka* (> 99.5%, over 3-Å molecular sieves). All synthetic operations were carried out in a fume hood under a protective layer of dry N_2. Care should be taken in the case of the isocyanates as they are extremely toxic. Column chromatography (CC): silica gel. ^{1}H-NMR Measurements: 99.8% deuterated solvents, dried with small amounts of 3-Å molecular sieves that had been pre-dried by prolonged heating to 480 K at $8 \cdot 10^{-3}$ mbar; to $CDCl_3$, a tiny amount of anh. K_2CO_3 was added to remove traces of HCl; *Bruker-400* or *-500-MHz* spectrometers, FID editing with either the WINNMR or XWINNMR program provided by *Bruker Instruments*. Fluorescence measurements: *Hitachi-F-2000* spectrometer. Combustion analyses: *Carlo-Erba-Analyzer*, model *1106*.

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[1]) ΔG Values for association of pyrene and nucleotide anions in water with only 5% of MeOH added are lower by 8–10 kJ/mol [20].

Optimized concentrations and steps for NMR titrations were calculated by known equations [24]. An EXCEL spreadsheet comprising them can be found on our website. Evaluations of isotherms were done with Sigmaplot Version 4.0. Molecular modelling was done with the CHARMm force field (Version 6.02) and with the MM+force field in the 'bond dipole' option (Hyperchem 5.02 modified version of MM2 from 1992).

Phthalodiamide (= Benzene-1,2-dicarboxamide; **2**) was synthesized according to [25]. N,N′*-(Ethane-1,2-diyl)*-N,N′*-(Propane-1,3-diyl), and* N,N′*(Butane-1,4-diyl)bis[acetamide]* (**3**, **5**, and, resp. **6**) were synthesized from the corresponding diamines and acetic acid anhydride (50% excess) according to [26][27][29], resp.

N,N′,N″*-(Nitrilotriethone-2,1-diyl)tris[acetamide]* (**7**) was obtained according to [28].

N,N′*-Methylenebis[benzamide]* (**4**) was synthesized according to [29], with trioxane instead of formaldehyde. M.p. 219° ([29]: 218°).^{1}H-NMR ((D$_6$)DMSO): 4.891 (*t*, 2 H); 9.078 (*t*, 4 H); 7.915 (*dd*, 4 H); 7.486–7.449 (*m*, 4 H); 7.534 (*t*, 2 H). ^{13}C-NMR ((D$_6$)DMSO): 45.19; 166.49; 133.96; 128.21; 127.39; 131.36.

N,N′,N″*-[Nitrilotris[ethane-2,1-diylimino(2-oxoethane-2,1-diyl)]tris[carbamic Acid] Tribenzyl Ester* (**8**). To a soln. of *N*-[(benzyloxy)carbonyl]glycine (6.28 g, 30 mmol) in DMF (100 ml), Bu$_3$N (5.56 g, 30 mmol; stored over solid KOH) was added. After 15 min, the soln. was cooled to 10° and 3.26 g of carbonochloridic acid ethyl ester in DMF (10 ml) was carefully added at 10°. After 30 min stirring at 10°, a soln. of tren (= tris(2-aminoethyl)amine; 1.46 g) in DMF (10 ml) was added at once. After stirring overnight at r.t., the cloudy soln. was filtered through a layer of *Celite* and was washed with an additional portion of DMF (20 ml). The combined solns. were evaporated at r.t. The residue was taken up with CHCl$_3$, washed with H$_2$O, dried (MgSO$_4$), and purified by CC (CHCl$_3$/MeOH/NH$_3$ 100 : 10 : 1): 3.74 g (90%) of **8**. Colorless viscous oil which was used without further purification. ^{1}H-NMR (CDCl$_3$): 2.438 (br., 6 H); 3.178 (br. 6 H); 3.798 (*d*, 6 H); 5.04187 (*s*); 7.244–7.313 (*m*, 15 H); 6.237 (*d*, 3 H). ^{13}C-NMR (CDCl$_3$): 37.720; 44.456; 157.023; 54.494; 170.165; 67.004; 136.255; 127.926–128.452.

Tris[ureas] **10**–**16**: *General Procedure.* The tris[ureas] were obtained from the corresponding amine and the iso(thio)cyanate as described for **10**. To a soln. of tren (1.46 g; 10 mmol) in CH$_2$Cl$_2$ (100 ml), a soln. of 4-chlorophenyl isocyanate (4.61 g, 30 mmol) in CH$_2$Cl$_2$ (100 ml) was added slowly and dropwise. After some seconds (R = 4-Cl-C$_6$H$_4$) to some hours (R = Bu), the corresponding urea precipitated. The mixture was stirred overnight. Then the mother liquor was removed and the residue crystallized from the appropriate solvents.

N′,N‴,N⁗,N⁗′*-Tris(4-chlorophenyl)*-N,N″,N‴′*-(nitrilotriethane-2,1-diyl)tris[urea]* (**10**): 4.5 g (90%). M.p. 240° (AcOH/MeOH). ^{1}H-NMR ((D$_6$)DMSO): 2.583 (*t*, 6 H); 3.175 (*m*, 6 H); 6.187 (*t*, 3 H); 8.632 (*s*, 3 H); 7.386 (*d*, 6 H); 7.217 (*dd*, H). ^{13}C-NMR ((D$_6$)DMSO): 37.011; 53.284; 154.582; 138.898; 127.800; 118.659; 123.933. Anal. calc. for C$_{27}$H$_{30}$N$_7$O$_3$ (500.580): C 53.43, H 4.98, N 16.15; found: C 53.36, H 5.09, N 15.94.

N′,N‴,N⁗,N⁗′*-Tris(4-chlorophenyl)*-N,N″,N‴′*-(nitrilotripropane-3,1-diyl)tris[urea]* (**11**): 4.5 g (90%). M.p. 220° (AcOH/i-PrOH). ^{1}H-NMR ((D$_6$)DMSO): 2.402 (*t*, 6 H); 1.573 (*t*, 6 H); 3.108 (*t*, 6 H); 6.185 (*t*, 3 H); 8.463 (*s*, 3 H); 7.373 (*dd*, 6 H); 7.211 (*dd*, 6 H). ^{13}C-NMR ((D$_6$)DMSO): 37.340; 27.177; 50.938; 154.962; 39.332; 128.158; 119.144; 124.339. Anal. calc. for C$_{30}$H$_{36}$N$_7$O$_3$ (542.66): C 55.52, H 5.59, N 15.11; found: C 55.15, H 5.71, N 15.08.

N′,N‴,N⁗,N⁗′*-Tri(naphthalen-1-yl)*-N,N″,N‴′*-(nitrilotriethane-2,1-diyl)tris[urea]* (**12**): 5.88 g (90%). M.p. 242° (AcOH/i-PrOH). ^{1}H-NMR ((D$_6$)DMSO): 6.699 (*t*, 3 H); 8.611 (*s*, 3 H); 2.698 (*t*, 6 H); 3.309 (*dt*, 6 H); 8.056 (*d*, 3 H); 7.929 (*d*, 3 H); 7.838 (*d*, 3 H); 7.313–7.519 (*m*, 9 H). ^{13}C-NMR ((D$_6$)DMSO): 37.911; 54.385; 155.994; 117.224; 135.055; 133.723; 121.514–128.240. Anal. calc. for C$_{39}$H$_{39}$N$_7$O$_3$ (653.783): C 71.65, H 7.48, N 12.17; found: C 72.93, H 7.36, N 12.47.

N′,N‴,N⁗,N⁗′*-Tri(adamantan-1-yl)*-N,N″,N‴′*-(nitrilotriethane-2,1-diyl)tris[urea]* (**13**): 3.63 g (60%). M.p. 183° (CHCl$_3$/cyclohexane), after CC (CHCl$_3$/MeOH 95 : 5). ^{1}H-NMR (CDCl$_3$): 2.448 (*t*, 6 H); 3.099 (*m*, 6 H); 5.085 (*s*, 3 H); 5.903 (br., 3 H); 1.979 (br., 18 H); 2.046 (br., 9 H); 1.665 (br., 18 H). ^{13}C-NMR (CDCl$_3$): 56.290; 50.684; 158.576; 38.594; 42.692; 36.557; 29.667. Anal. calc. for C$_{33}$H$_{63}$N$_7$O$_3$ (605.907): C 69.09, H 9.37, N 14.46; found: C 68.80, H 9.37, N 14.24.

N′,N‴,N⁗,N⁗′*-Tris(4-nitrophenyl)*-N,N″,N‴′*-(nitrilotriethane-2,1-diyl)tris[urea]* (**14**): 5.74 g (90%). M.p. >183° (dec.; acetone/MeCN). ^{1}H-NMR ((D$_6$)DMSO): 2.646 (*t*, 6 H); 3.236 (*m*, 6 H); 6.426 (*t*, 3 H); 7.589 (*dd*, 6 H); 8.088 (*dd*, 6 H); 9.333 (*s*, 3 H). ^{13}C-NMR ((D$_6$)DMSO): 37.561; 53.467; 116.727; 124.973; 140.279; 147.087; 154.427. Anal. calc. for C$_{27}$H$_{30}$N$_{10}$O$_9$ (638.589): C 50.78, H 4.74, N 21.93; found: C 50.80, H 4.57, N 21.70.

N′,N‴,N⁗,N⁗′*-Tris(4-nitrophenyl)*-N,N″,N‴′*-(nitrilotriethane-2,1-diyl)tris[thiourea]* (**15**): 6.18 g (90%). M.p. >185° (dec.; acetone/MeCN). ^{1}H-NMR ((D$_6$)DMSO): 2.815 (*t*, 6 H); 3.2756 (*m*, 6 H); 7.775 (*dd*, 6 H); 8.130 (*dd*, 6 H); 10.1581 (*s*, 3 H). ^{13}C-NMR ((D$_6$)DMSO): 41.802; 51.522; 120.282; 124.450; 141.681; 146.160; 179.844. Anal. calc. for C$_{27}$H$_{30}$N$_{10}$O$_6$S$_3$ (686.789): C 47.22, H 4.40, N 20.39; found: C 47.80, H 4.57, N 20.50.

N′,N‴,N⁗,N⁗′*-Tributyl*-N,N″,N‴′*-(nitrilotriethane-2,1-diyl)tris[urea]* (**16**): 3.99 g (90%). M.p. 162° (nitromethane). ^{1}H-NMR ((D$_6$)DMSO): 0.851 (*t*, 9 H); 1.251 (*m*, 6 H); 1.323 (*m*, 6 H); 1.255 (*t*, 6 H); 2.411 (*t*, 3 H);

2.966 (*m*, 6 H); 2.991 (*m*, 6 H). ^{13}C-NMR ((D$_6$)DMSO): 13.652; 19.523; 32.124; 37.737; 38.933; 54.409; 158.211. Anal. calc. for $C_{21}H_{45}N_7O_3$ (443.627): C 56.86, H 10.22, N 22.10; found: C 56.76, H 10.57, N 22.40.

γ-Oxopyrene-1-butanoic Acid. According to [30], with necessary modifications: At 0°, $AlCl_3$ (46.2 g, 228 mmol) was slowly added to a well-stirred soln. of succinic anhydride (17.5 g, 227 mmol) and pyrene (46.2 g, 228 mmol) in dry nitromethane (300 ml). The soln. turned red, and a precipitate was formed slowly. One hour after all $AlCl_3$ had been added, the mixture was allowed to reach r.t. until HCl evolution ceased. The resulting red soln. was quenched with ice/HCl (1 l). The slurry was extracted with CH_2Cl_2 (4 × 200 ml) and the extract dried ($MgSO_4$) and evaporated. The resulting acid was transformed to the sodium salt by means of a 10% ethanolic NaOH soln. The precipitating salt was crystallized from H_2O (3 ×) and then hydrolyzed in the warmth with HCl soln. and the acid recrystallized from AcOH: 18 g (26%). M.p. 184° ([30]: 172°; [31]: 184°). ^{1}H-NMR ((D$_6$)DMSO): 2.758 (*t*, 2 H); 3.472 (*t*, 2 H); 8.090–8.761 (*m*, 9 H); 12.23 (*s*, 1 H); ^{13}C-NMR ((D$_6$)DMSO): 28.462; 36.809; 123.373–132.923; 173.844; 203.046.

Pyrene-1-butanoic Acid. According to [30], but with necessary modifications: A soln. of γ-oxopyrene-1-butanoic acid (12.09 g, 0.04 mol) in triethylene glycol (150 ml) and hydrazine hydrate (100 ml) was slowly heated to 100° and kept at 100° for 1 h. Then, the soln. was cooled to r.t., and KOH (20 g) was added. The mixture was heated 3 h to 140° (oil bath) until gas evolution ceased. Then, the H_2O/hydrazine mixture was distilled until the boiling temp. reached 150°. Then, the mixture was cooled to r.t. and carefully acidified. The precipitate was recrystallized from AcOH/AcOEt: 10 g (87%). M.p. 189–190° ([30]: 166°; [32]: 190°). ^{1}H-NMR ((D$_6$)DMSO): 2.009 (*m*, 2 H); 2.384 (*t*, 2 H); 3.3201 (*t*, 2 H); 7.890–8.376 (*m*, 9 H); 11.93 (*s*, 1 H). ^{13}C-NMR ((D$_6$)DMSO): 26.795; 31.980; 123.379–136.290; 174.355.

Acyl Azides for Curtius *Rearrangement: General Procedure*[2]. A soln. of Et_3N (1.44 g, 14 mmol) in acetone (10 ml) was added dropwise to a soln. of the corresponding carboxylic acid (12 mmol) in acetone (20 ml) at 0°. After 10 min at 0°, a soln. of carbonochloridic acid ethyl ester (1.67 g, 15.4 mmol) was added at once. Then, the mixture was stirred at 0° for another 30 min. Then, a soln. of NaN_3 (1.18 g, 18 mmol) in H_2O (5 ml) was added at once. In case of pyrene-containing azides, the product precipitated within 15 min and was dried over P_4O_{10} overnight at 9 mbar at r.t., the dried azides having a sufficient purity for synthesis. In case of benzenebutanoic acid [34] the mixture was extracted after 15 min with Et_2O (3 × 30 ml), dried ($MgSO_4$) and evaporated at r.t. The residue was mixed with toluene (20 ml) and heated to reflux until N_2 evolution ceased (*caution:* foaming may occur). The isocyanate was distilled (156°/10–12 mbar) and could be stored for prolonged time under N_2.

Aryl-Containing Ureas. The acyl azides were suspended in toluene and heated to reflux until N_2 evolution ceased. The ureas were obtained by addition of stoichiometric amounts of the corresponding amines to this isocyanate soln. at r.t.

N-*[2-(Dimethylamino)ethyl]*-N′-*[3-(pyren-3-yl)propyl]urea* (**17**): 3.59 g (80%). M.p. >185° (dec.; toluene). ^{1}H-NMR ((D$_6$)DMSO): 1.881 (*m*, 2 H); 2.171 (*s*, 6 H); 2.302 (*t*, 2 H); 3.125 (*m*, 4 H); 3.323 (*m*, 2 H); 5.764 (*t*, 3 H); 6.183 (*t*, 3 H); 7.953–8.359 (*m*, 27 H). ^{13}C-NMR ((D$_6$)DMSO): 29.922; 32.151; 37.147; 39.039; 44.905; 58.823; 123.183–127.235; 157.972. Anal. calc. for $C_{27}H_{30}N_{10}O_6S_3$ (373.491): C 77.18, H 7.29, N 11.25; found: C 77.28, H 7.47, N 11.40.

N-*[2-(Dimethylamino)ethyl]*-N′-*[3-oxo-3-(pyren-3-yl)propyl]urea* (**18**): 3.71 g (80%). M.p. 160° (toluene). ^{1}H-NMR ((D$_6$)DMSO): 2.072 (*s*, 2 H); 2.201 (*t*, 2 H); 3.074 (*m*, 2 H); 3.396 (*t*, 2 H); 3.503 (*m*, 3 H); 5.911 (*t*, 3 H); 6.234 (*t*, 3 H); 8.099–8.829 (*m*, 27 H). ^{13}C-NMR ((D$_6$)DMSO): 35.378; 37.254; 42.788; 45.046; 58.949; 123.415–133.109; 158.029; 203.610. Anal. calc. for $C_{24}H_{25}N_3O_2$: C 74.39, H 6.50, N 10.84; found: C 74.60, H 6.57, N 10.70.

N′,N‴,N⁗,N⁗′-*Tris[3-oxo-3-(pyren-1-yl)propyl]*-N,N″,N⁗″-*(nitrilotriethan-2,1-diyl)tris[urea]* (**19**): 2.92 g (70%). M.p. 179° (dec.; DMF/toluene). ^{1}H-NMR ((D$_6$)DMSO): 2.449 (*m*, 6 H); 3.091 (*m*, 6 H); 3.391 (*m*, 6 H); 3.536 (*m*, 6 H); 6.147 (*t*, 3 H); 6.293 (*t*, 3 H); 7.974–8.778 (*m*, 27 H). ^{13}C-NMR ((D$_6$)DMSO): 30.683; 35.353; 35.690; 38.943; 42.667; 54.309; 123.265–132.973; 158.234; 162.235; 203.453. Anal. calc. for $C_{66}H_{57}N_7O_6$ (1044.202): C 75.91, H 5.50, N 9.39; found: C 75.80, H 5.57, N 9.45.

N′,N‴,N⁗,N⁗′-*Tris[3-(pyren-1-yl)propyl]*-N,N″,N⁗″-*(nitrilotriethan-2,1-diyl)tris[urea]* (**20**): 2.8 g (70%). M.p. 138° (methylcellosolve). ^{1}H-NMR ((D$_6$)DMSO): 1.779 (*m*, 6 H); 2.471 (*m*, 6 H); 3.072 (*m*, 6 H); 3.169 (*t*, 6 H); 5.909 (*t*, 3 H); 6.094 (*t*, 3 H); 7.746–8.172 (*m*, 27 H). ^{13}C-NMR ((D$_6$)DMSO): 30.060; 32.288; 37.921; 40.413; 54.568; 123.260–136.449; 158.430. Anal. calc. for $C_{66}H_{63}N_7O_3$ (1002.252): C 79.09, H 6.34, N 9.78; found: C 79.08, H 6.57, N 9.70.

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[2]) Analogously to a procedure described in [33a]. The mixed-anhydride reaction gave purer compounds than the diphenylphosphoryl-azide method for the preparation of the pyren-1-yl isocyanate described in [33b].

N-*[2-(Dimethylamino)ethyl]*-N′-*(3-phenylpropyl)urea* (**21**): 2.10 g (70%). M.p. 106° (acetone). ^{1}H-NMR ((D$_6$)DMSO): 1.797 (*m*, 2 H); 1.993 (*t*, 2 H); 2.272 (*s*, 6 H); 2.504 (*t*, 2 H); 2.589 (*t*, 2 H); 2.841 (*t*, 2 H); 7.136–7.257 (*m*, 5 H); *ca*. 7.8 (br., 1 H); *ca*. 10.7 (br., 1 H). ^{13}C-NMR (CD$_3$OD): 32.955; 34.116; 36.783; 40.925; 43.914; 60.030; 72.596; 126.924; 129.436; 143.074; 161.527. Anal. calc. for $C_{14}H_{23}N_3O$ (249.352): C 67.43, H 9.30, N 16.85; found: C 67.63, H 9.57, N 16.70.

N′,N‴,N⁗-*Tris(3-phenylpropyl)*-N,N″,N‴-*(nitrilotriethan-2,1-diyl)tris[urea]* (**22**): 1.76 g (70%). M.p. 136° (acetone). ^{1}H-NMR ((D$_6$)DMSO): 1.637 (*m*, 6 H); 2.436 (*m*, 6 H); 2.531 (*t*, 6 H); 2.976 (*m*, 6 H); 3.021 (*m*, 3 H); 5.831 (*t*, 3 H); 5.971 (*t*, 3 H); 7.128–7.256 (*m*, 15 H). ^{13}C-NMR ((D$_6$)DMSO): 31.810; 32.481; 37.764; 38.882; 54.415; 125.610; 128.197; 141.759; 158.211. Anal. calc. for $C_{66}H_{63}N_7O_3$ (629.835): C 68.65, H 8.16, N 15.57; found: C 68.70, H 8.17, N 15.70.

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REFERENCES

[1] M. M. G. Antonisse, D. N. Reinhoudt, *Chem. Commun*. **1998**, 443.
[2] R. C. Cameron, S. J. Loeb, *Chem. Commun*. **1997**, 573.
[3] H. Luecke, F. A. Quiocho, *Nature (London)* **1990**, *347*, 402, J. J. He, F. A. Quiocho, *Science (Washington, D.C.)* **1991**, *251*, 1497.
[4] F. A. Quiocho, J. W. Pflugrath, *Nature (London)* **1985**, *314*, 257; *J. Mol. Biol.* **1988**, *200*, 163.
[5] P. Schwinte, R. Darcy, F. O'Keeffe, *J. Chem. Soc., Perkin Trans. 2* **1998**, 805; Y. Shi Youheng, H.-J. Schneider, *J. Chem. Soc.*, *Perkin Trans. 2* **1999**, in press; D. A. Nation, Q. Lu, A. E. Martell, *Inorg. Chim. Acta* **1997**, *263*, 209; J. A. Aguilar, E. Garcia-Espana, J. A. Guerrero, S. V. Luis, *Inorg. Chim. Acta* **1996**, *246*, 287; K. G. Ragunathan, H.-J. Schneider, *J. Chem. Soc., Perkin Trans. 2* **1996**, 2597; V. Kral, A. Andrievsky, J. L. Sessler, *Chem. Commun*. **1995**, 2349; S. M. Lacy, D. M. Rudkevich, W. Verboom, D. N. Reinhoudt, *Tetrahedron Lett*. **1994**, *35*, 5953; A. V. Eliseev, H.-J. Schneider, *J. Am. Chem. Soc*. **1994**, *116*, 6081; J. Rebek, Jr., *Acc. Chem. Res*. **1990**, *23*, 399; A. D. Hamilton, in '*Bioorg. Chem. Frontiers*', Ed. H. Dugas, Springer, Berlin-Heidelberg, 1991, Vol. 2, p. 115.
[6] D. N. Reinhoudt, J. Scheerder, J. F. J. Engbersen, *Rec. Trav. Chim. Pays-Bas* **1996**, *115*, 307.
[7] J. M. Coterón, F. Hacket, H.-J. Schneider, *J. Org. Chem*. **1996**, *61*, 1429.
[8] K. Vavallieratos, S. R. de Gala, D. J. Austin, R. H. Crabtree, *J. Am. Chem. Soc*. **1997**, *119*, 2325.
[9] F. Eblinger, H.-J. Schneider, *Angew. Chem.* **1998**, *110*, 821; *Angew. Chem., Int. Ed.* **1998**, *37*, 826.
[10] D. N. Reinhoudt, S. Valiyaveettil, J. F. J. Engbersen, W. Verboom, *Angew. Chem*. **1993**, *105*, 942; D. N. Reinhoudt, J. Scheerder, M. Fochi, J. F. J. Engbersen, *J. Org. Chem*. **1994**, *59*, 7815.
[11] R. Jairam, P. G. Potvin, *J. Org. Chem*. **1992**, *57*, 4136.
[12] D. Hamilton, *J. Am. Chem. Soc*. **1993**, *115*, 369, and lit. cit. therein.
[13] V. Alcazar, *Chem. Lett*. **1995**, 759.
[14] H. Baerrigter, L. Grave, J. W. M. Nissink, L. A. J. Chrisstoffels, J. H. van der Maas, W. Verboom, F. de Jong, D. N. Reinhoudt, *J. Org. Chem.* **1998**, *63*, 4174.
[15] a) G. Carta, G. Crisponi, V. Nurchi, *Tetrahedron* **1981**, *37*, 2115; D. A. Deranleau, *J. Am. Chem. Soc*. **1969**, *91*, 4044; b) J. L. Fry, R. K. Sharma, *J. Org. Chem*. **1983**, *48*, 2112.
[16] Kyu-Sung Jeon, Kyu-Myoung Hahn, Young Lag Cho, *Tetrahedron Lett*. **1998**, *39*, 3779.
[17] I. Osromisslensky, *Chem. Ber.* **1911**, *44*, 268.
[18] R. B. Denison, *Trans Farad. Soc*. **1921**, *8*, 20.
[19] F. R. Hartley, C. A. Burgess, R. M. Alcock, 'Solution Equilibria', Ellis Horwood Ltd., Chichester 1980, p. 36 ff.
[20] P. Lianos, S. Georghiou, *Photochem. Photobiol*. **1979**, *29*, 13.
[21] H.-J. Schneider, I. Theis, *Angew. Chem*. **1989**, *101*, 757; *Angew. Chem. Int. Ed.* **1989**, *28*, 753.
[22] R. Hettich, Dissertation, University of the Saarland, 1997.
[23] D. D. Perrin, W. L. F. Armarego, D. R. Perrin, 'Purification of Laboratory Chemicals', Elsevier Science, 1980, and lit. cit. therein.
[24] J. Granot, *J. Magn. Res.* **1983**, *55*, 216.
[25] L. J. Spiessens, M. Anteunis, *Bull Soc. Chim. Belg*. **1983**, *92*, 1; S. Wolfe, K. S. Hasan, *Can. J. Chem*. **1970**, *48*, 3577.

[26] B. Strache, *Chem. Ber*. **1923**, *21*, 2359.
[27] M. Haga, W. Wesser, *Chem. Ber*. **1938**, *36*, 338.
[28] J. S. Bradshaw, K. E. Krakowiak, R. M. Izatt, *J. Org. Chem.* **1990**, *55*, 3364.
[29] A. W. Hofmann, *Chem. Ber.* **1923**, *21*, 2332.
[30] O. Perin-Roussel, N. P. Buu-Hoi, Do-Phuoc-Hien, *Bull. Soc. Chim. Fr.* **1971**, *6*, 2160.
[31] E. Buchta, P. Vincke, *Chem. Ber*. **1965**, *98*, 208.
[32] E. Fieser, A. Fieser, G. Hershberg, *J. Am. Chem. Soc.* **1936**, *58*, 1463.
[33] a) J. Weinstock, *J. Am. Chem. Soc*. **1961**, *26*, 3511; b) G. Read, N. R. Richardson, *J. Chem. Soc., Perkin Trans. 1* **1996**, 167.
[34] P. F. Dicks, S. A. Glover, A. Goosen, C. W. McCleland, *Tetrahedron* **1987**, 923.
[35] M. Sirish, H.-J. Schneider, *Chem. Commun.* **2000**, 23.

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