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Substituent Effects in Double-Helical Hydrogen-Bonded AAA-DDD Complexes

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Abstract: Two series of DDD and AAA hydrogen-bond arrays were synthesized that form triply-hydrogen-bonded double-helical complexes when combined in $CDCl_3$ solution. Derivatization of the DDD arrays with electron-withdrawing groups increases the complex association constants by up to a factor of 30 in those arrays examined. Derivatization of the AAA arrays with electron donating substituents reveals a similar magnitude effect on the complex stabilities. The effect of substitution on both types of arrays are modeled quite satisfactorily ($R^2 > 0.96$ in all cases) as free energy relationships with respect to the sums of their Hammett substituent constants. In all, the complex stabilities can be manipulated over more than three orders of magnitude ($>20\,kJ\,mol^{-1}$) using this type of modification.

Keywords: helical structures · hydrogen bonds · linear free energy relationships · self-assembly · supramolecular chemistry

Introduction

Hydrogen bonds have been used to construct supramolecular assemblies and materials that respond to environmental changes such as temperature, pH, and solvent.[1] A milestone in this area was the development by Meijer and co-workers of supramolecular polymers based on self-complementary 2-ureido-4[1H]-pyrimidinone units.[2] Since the introduction of these materials, reversible hydrogen-bonded polymers have been extensively investigated.[3] One of the key factors this work has highlighted is the requirement of a high stability constant ($\geq 10^5\,M^{-1}$) for the hydrogen-bonded motif in the formation of main-chain supramolecular polymers.[4] The binding strengths of multiple-point hydrogen-bond arrays used in these applications are highly dependent on the numbers and arrangement of hydrogen-bonding donors (D) and acceptors (A).[5] As the number of hydrogen bonds increases, cooperativity generally results in an increasing association constant.[6] Complementary systems including four or more hydrogen bonds often exhibit strong binding properties, however their design can be complicated by a number of factors such as difficult or expensive syntheses,[7] intramolecularly hydrogen-bonded conformers,[8] tautomerism[9] or undesirable self-association.[10] Triple hydrogen-bond systems potentially offer three complementary binding arrays (ADA-DAD, AAD-DDA and AAA-DDD) but only AAA-DDD complexes have been shown to provide the stability required for main-chain supramolecular polymer applications.

There are very few examples of AAA-DDD complexes. Zimmerman and co-workers described the first neutral AAA-DDD complex ($K_a > 10^5\,M^{-1}$), but it is unstable due to a hydride shift from one component to the other.[11] Leigh and co-workers demonstrated that modification of the AAA component in this system could be used to improve the stability of the complex and observed extremely high association constants.[12] Cationic DDD subunits can also form even more stable complexes with AAA components, although currently reported systems are likely sensitive to the character of the counter anion, proton transfer and solvent dependent pK_a changes.[13]

As an alternative, we have recently described an AAA-DDD hydrogen-bond system that is based on a different design in which oligoheterocyclic strands wrap around one another to form a double-helical complex.[14–16] In the absence of the AAA partner, the DDD components we initially synthesized displayed very poor solubility in non-polar solvents due to intermolecular hydrogen-bonding. The solubility can be greatly improved by using sterics to restrict access to the sulfone functional group. The resulting methylated analogue (Scheme 1, **6a**) was markedly more soluble but exhibited an association constant (K_a) of only $3700\,M^{-1}$ (RT in $CDCl_3$). However, using the same synthetic approach the skatole (3-methylindole) subunits of this design are easily derivatized at their respective 5-positions with electron-withdrawing groups to improve the hydrogen-bond-donating character of the corresponding NH protons. We were interested in synthesizing several DDD and AAA analogues of this reported system to determine the effect of electron-withdrawing and -donating substituents on the stabilities of their resultant complexes. These observations were anticipated to provide a gauge of what upper limit the stability of

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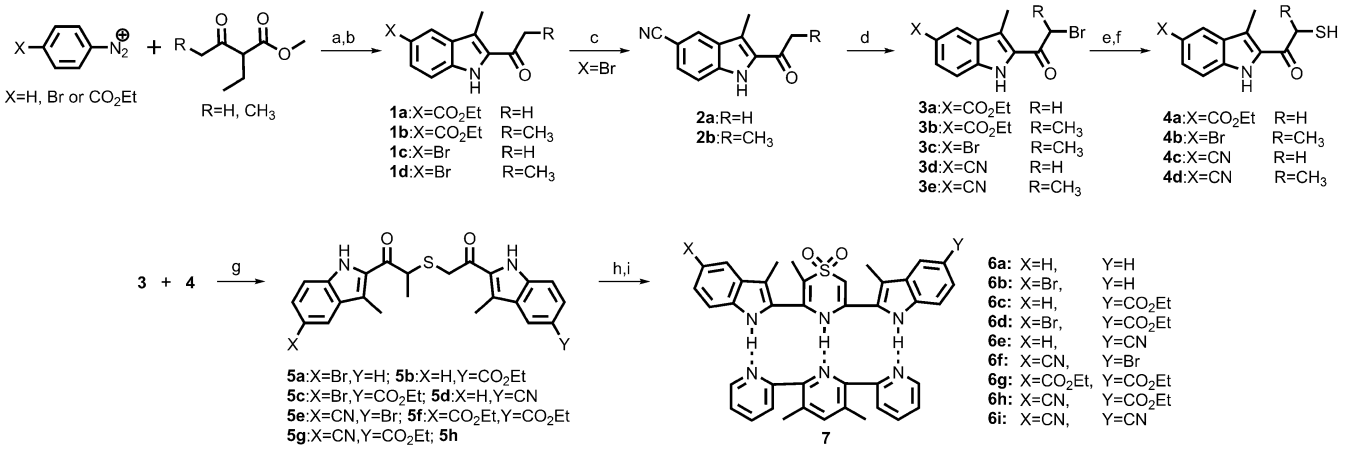


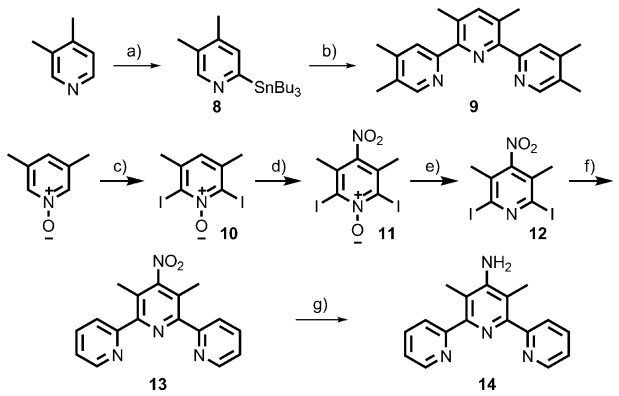
Scheme 1. Synthesis of DDD hydrogen bond arrays. Reagents and conditions: a) NaOH, EtOH/H_2O, NaOAc, 0 °C to RT, 8 h; b) formic acid, reflux, 16 h; c) $Zn(CN)_2$, DMF, $[Pd(PPh_3)_4]$, reflux, 2 days; d) $PhNMe_3Br_3$, THF, reflux, 1.5 h; e) KSAc, DMF, 12 h; f) $NaHCO_3$, cysteamine hydrochloride, CH_3CN, 12 h; g) Et_3N, CH_3CN, 12 h; h) *meta*-chloroperbenzoic acid (*m*CPBA), DMF, −25 °C to RT., 12 h; i) NH_4OAc, glacial acetic acid, microwave, 180 °C, 3 h.

these complexes could be manipulated to within the confines of this particular design.

Results and Discussion

Synthesis: The synthesis of the DDD hydrogen bonding arrays (Scheme 1) was initiated using a Japp–Klingeman/Fischer indole approach[17] employing the diazonium salts of anilines containing the desired substituents and either methyl 2-ethylacetoacetate or the one carbon homologue methyl 2-ethyl-3-oxopentanoate to yield 5-substituted acetyl- or propionylskatoles **1a–d**. The 5-cyanoskatoles **2** were obtained by Pd-catalyzed cyanation of the bromides **1c** and **1d**. Acylskatole derivatives **1** and **2** were then α-brominated and the resulting bromides **3** converted to their corresponding mercaptans **4**. Thioethers **5** were generated by substitution of **3** by **4**, oxidized to the resultant sulfones and cyclized with ammonium acetate to give **6a–i** as final DDD products substituted with electron-withdrawing groups on one or both of the skatole rings. Unfortunately, the dinitrile **6i** was completely insoluble in chloroform and could not, therefore, be evaluated alongside the other DDD molecules in the present study. It should also be noted that all of our attempts to cyclize sulfones that would result in 2,6-dimethylthiazinedioxide products (i.e., elaboration of the thioethers generated from substitution of **3b, 3c, 3e** by **4b** and **4d**) were unsuccessful despite the investigation of a wide variety of reagents and conditions that typically yield the desired transformation.

The complementary terpyridyl-based AAA hydrogen-bond arrays studied were elaborated from lutidine-*N*-oxide in three to five linear steps depending on the absence or nature of substitution at the 4′-position (Scheme 2). The nitro- and amino substituents of **13** and **14** were installed first through nitration of common intermediate **10** and later reduction of the nitroterpyridine **13** obtained from Stille



Scheme 2. Synthesis of AAA hydrogen-bond arrays. Reagents and conditions: a) i) *n*BuLi, 2-dimethylaminoethanol, hexane, 0 °C, 1 h, ii) Bu_3SnCl, THF, −78 °C to RT, 1 h, 40 %; b) 2,6-diiodo-3,5-lutidine, $[Pd(PPh_3)_4]$, toluene, reflux, 5 days, 41 %; c) i) *n*BuLi, hexane, THF, −78 °C, 1 h, ii) I_2, THF, −78 °C to RT, 14 h, 45 %; d) conc. HNO_3, conc. HSO_4, 70 °C, 12 h, 72 %; e) PCl_3, $CHCl_3$, reflux, 12 h, 90 %; f) 2-tributyltinpyridine, $[Pd(PPh_3)_4]$, toluene, reflux, 16 h, 86 %; g) 10 % Pd/C, hydrazine hydrate, EtOH, reflux, 1.5 h, 91 %.

coupling of the deoxygenated nitro derivative **12**. The terlutidine **9** was similarly provided by Stille coupling of 2-tributyltin-4,5-lutidine to 2,6-diiodo-3,5-lutidine that is easily derived by deoxygenation of **10**.

Complexation of 6 with 7: The interaction between each of the eight DDD arrays that were soluble in $CDCl_3$ (**6a–h**) and the AAA array **7** was observed using ^1H NMR spectroscopy. A $CDCl_3$ solution of each of **6a–h** was titrated with **7** and the resulting change in chemical shift of the three N-H protons was used to determine the binding constant ($K_{X,Y}$) by non-linear curve fitting of the data to a simple 1:1 binding model (Table 1).[18] In all cases, the three N-H protons of **6** undergo large downfield shifts upon addition of excess **7** ($4.02 \geq \Delta\delta_{max} \geq 2.36$ ppm) indicating a strong hydrogen bond

Table 1. Changes in the chemical shifts of N-H protons ($\Delta\delta_{max}$), Hammett substituent constants (σ_p), association constants ($K_{X,Y}$), and free energies of complexation (ΔG), between each of **6a–h** and **7** determined by ^{1}H NMR in $CDCl_3$ at 298 K (experimental errors in brackets).

	6a	**6b**	**6c**	**6d**	**6e**	**6f**	**6g**	**6h**
X, Y	H, H	Br, H	H, CO_2Et	Br, CO_2Et	H, CN	Br, CN	CO_2Et, CO_2Et	CN, CO_2Et
$\Delta\delta_{max}$ [ppm]	3.00[a]	2.60[a]	3.09[a]	2.86[a]	2.72[a]	2.80[a]	2.78[a]	3.90
	2.79[b]	3.88[b]	2.71[b]	2.46[b]	2.36[b]	2.36[b]	3.94[b]	3.19
	3.51[c]	3.22[c]	3.56[c]	3.21[c]	3.02[c]	3.93[c]	4.02[c]	3.29[c]
$\Sigma\sigma_p$	0.00	0.26	0.44	0.70	0.71	0.97	0.88	1.15
$K_{X,Y}$ [M^{-1}][d]	3.7×10^3	7×10^3	1.1×10^4	2.6×10^4	2.9×10^4	4.9×10^4	5.4×10^4	1.1×10^5
	(±180)	(±280)	(±340)	($\pm1.1\times10^3$)	($\pm1.6\times10^3$)	($\pm1.3\times10^3$)	($\pm1.7\times10^3$)	($\pm5.0\times10^3$)
ΔG [kJ mol^{-1}]	−20.4	−21.9	−23.1	−25.2	−25.5	−26.8	−27.0	−28.8
$\Delta\Delta G$ [kJ mol^{-1}]	0	1.5	2.7	4.8	5.1	6.4	6.6	8.4

[a] Change in the chemical shift of thiazine dioxide N-H proton. [b] Change in the chemical shift of X-substituted indole N-H proton. [c] Change in the chemical shift of Y-substituted indole N-H proton. [d] Values are averages and errors reported beneath are twice the standard deviations calculated from triplicate measurements.

interaction with all three sites. A molecular model of the complex (geometry optimized at the Hartree–Fock 6-31G* level of theory) between **6a** and **7** illustrates the presumed arrangement of the two arrays in the complex (Figure 1).

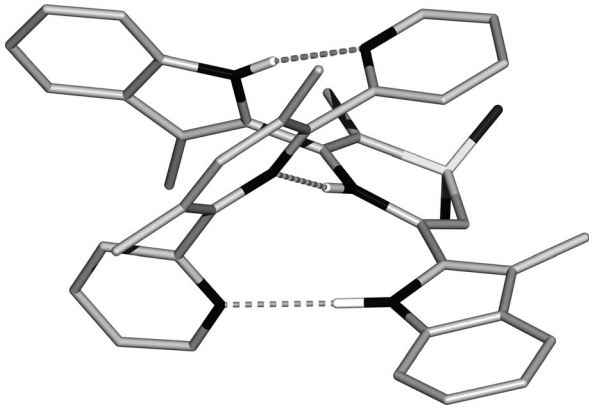


Figure 1. Optimized (HF 6-31G*) structure of the complex formed between **6a** and **7**.

We could find no obvious correlations to draw between either the electronic character of the substituents X and Y (expressed as Hammett σ_p values)[19] or the stabilities of the resulting complexes ($K_{X,Y}$) with the δ_{free}, δ_{max} and $\Delta\delta_{max}$ values obtained from the titration curves. The effects are therefore the result of a more complex relationship with the chemical shifts of the NMR resonances than the simple linear variance that one might expect.[20] The results imply that the effect of X and Y on **6a–h** is not only electronic and perturbing the N-H hydrogen-bond acidities but also conformational. We interpret the apparently random variation of the δ_{free}, δ_{max} and $\Delta\delta_{max}$ values in the series of eight donor molecules to indicate that, in their free states, they have very different average conformations with respect to their interplanar dihedral angles.

However, there is a clear linear free-energy relationship between the magnitude of the complex stability and the electronic character of the substituents on the indole rings. It is apparent that, as one might expect, the installation of electron-withdrawing substituents at the 5-positions of either skatole ring system in **6** results in a predictable increase in the stability of the complex with **7**. A plot of the sum of the Hammett substituent constants for X and Y ($\Sigma\sigma_p$) against $\log(K_{X,Y}/K_{H,H})$ displays a linear correlation with $\rho=1.3$ and $R^2=0.99$ (Figure 2). The positive value of ρ indicates that electron-withdrawing groups stabilize the developing partial negative charge on the nitrogen atom of the skatole rings that forms as a result of the hydrogen-bonding interaction. Though electron-donating groups have not been specifically explored in this context it is reasonable to assume that the linear relationship observed here extends to these cases as well.

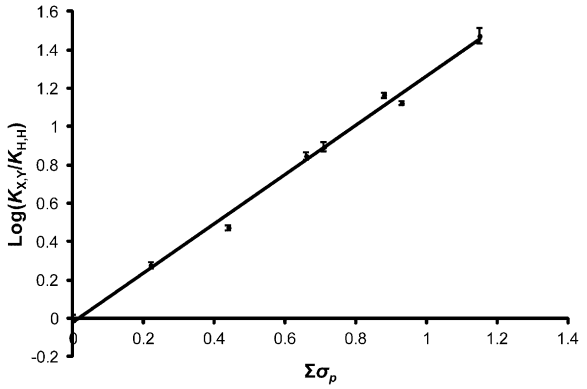


Figure 2. Plot of $\log(K_{X,Y}/K_{H,H})$ versus $\Sigma\sigma_p$ for the interaction of **6a–h** with **7**.

Complexation of 6a, 6c, 6g and **6h with 7, 9, 13 and 14**: Complex formation between four representative DDD molecules (**6a, 6c, 6g** and **6h**) and the four AAA molecules **7**, **9**, **13** and **14** were examined in chloroform to provide a measure of the influence that electron-donating/withdrawing groups attached to the acceptor components have on the complex stabilities. In these cases, except those involving complexation with **13**, the association constants were determined using isothermal titration calorimetry (ITC) to establish not only the free energies but also the enthalpies and entropies of complexation. In the case of **13**, none of the ITC experiments performed with **6a, 6c, 6g** and **6h** gave

satisfactory results due to a combination of weak binding and solubility constraints. Consequently, these association constants were instead determined using ^{1}H NMR spectroscopy in the manner described above. All of the titration data (ITC and ^{1}H NMR) were fit successfully to 1:1 binding models. Examination of the results of these ITC and ^{1}H NMR experiments reveals several trends.

As might be expected, a plot of the sum of the Hammett substituent constants for X and Y ($\Sigma\sigma_p$) against $\log(K_{X,Y}/K_{H,H})$ displays a linear correlation for each of **7**, **9**, **13** and **14** yielding $\rho = 1.3$ for all four and $R^2 \geq 0.97$ (Figure 3a). Thus, regardless of the AAA component examined, the complex stability varies in the same way with the character of X and Y in **6**. A similar plot of the sum of the Hammett substituent constants ($\Sigma\sigma_{m/p}$) of **9**, **13** and **14** (using **7** as the unsubstituted AAA reference) against $\log(K_{m/p}/K_{H/H})$ with each of **6a, 6c, 6g** and **6h** also yielded a linear relationship with a similar correlation (Figure 3b). In all four of these cases, $\rho = -1.4$ and $R^2 \geq 0.97$ indicating the magnitude of the influence of substitution on the AAA components towards complex stability is nearly identical to that observed upon substitution of the DDD partner **7**. This observation is somewhat surprising considering the closer proximity of the substituents to the interacting atoms in the AAA versus DDD arrays (i.e., three/four bonds distant (**9**, **13** and **14**) vs. six (**6a, 6c, 6g** and **6h**)).[21] The negative value of ρ indicates that electron-donating groups stabilize the developing partial positive charge on the nitrogen atom of the pyridyl rings in **7**, **9**, **13** and **14** as a result of the hydrogen-bonding interaction with **6**.

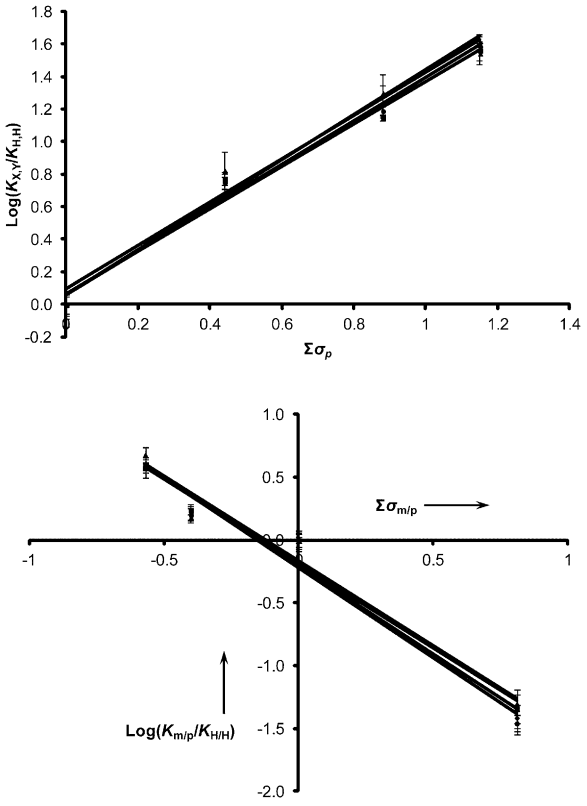


Figure 3. a) Plot of $\log(K_{X,Y}/K_{H,H})$ versus $\Sigma\sigma_p$ for the interaction of each of **7** (●), **9** (■), **13** (▲), and **14** (◆) with **6a**, **c**, **g** and **h**. b) Plot of $\log(K_{m/p}/K_{H/H})$ versus $\Sigma\sigma_{m/p}$ for the interaction of each of **6a** (◆), **6c** (■), **6g** (▲), and **6h** (●) with **7**, **9**, **13** and **14**. Lines depict linear least squares fits for each data set.

The ITC experiments also allowed an examination of the relationship between the free energies of complexation between **6** and **7**, **9**, and **14** and the enthalpic and entropic contributions to binding (Table 2). In all the cases tested, the driving force for complexation is enthalpic, as should be expected from complementary hydrogen-bond association between two molecules in a non-polar solvent such as chloroform. The data demonstrate the difficulty of rationalizing incremental free energy relationships using enthalpic and entropic data in this system. A plot of ΔH versus $T\Delta S$ (see the Supporting Information) does not display a linear correlation that would indicate a straightforward entropy–enthalpy compensation effect. The linearity of the free energy data when examined with respect to the sums of the Hammett substitutent parameters in the present cases must therefore result from a more complex compensation between entropic and enthalpic contributions to binding.

Table 2. Association constants (K_a), free energies (ΔG), enthalpies (ΔH), and entropies ($T\Delta S$) of complexation, between each of **6a, 6c, 6g** and **6h**, and **7, 9, 13** and **14** in $CHCl_3$ at 298 K (experimental errors in brackets) determined by ITC (or ^{1}H NMR titration where indicated).

	K_a [M^{-1}][a]	ΔG [kJ mol^{-1}]	ΔH [kJ mol^{-1}]	$T\Delta S$ [kJ mol^{-1}]
6a·7	3100 (±380)	−19.9 (±0.3)	−35.1 (±0.6)	−15.2 (±0.7)
6a·9	5200 (±760)	−21.2 (±0.4)	−31.4 (±1.8)	−10.2 (±1.8)
6a·13	120 (±32)[b]	−11.9 (±0.7)	–	–
6a·14	$1.18\ (\pm 0.22)\times 10^4$	−23.2 (±0.5)	−32.1 (±2.4)	−8.9 (±2.5)
6c·7	$1.76\ (\pm 0.26)\times 10^4$	−24.2 (±0.4)	−40.4 (±3.0)	−16.2 (±3.0)
6c·9	$3.04\ (\pm 0.24)\times 10^4$	−25.6 (±0.2)	−36.2 (±2.6)	−10.6 (±2.6)
6c·13	800 (±240)[b]	−16.6 (±0.7)	–	–
6c·14	$6.6\ (\pm 0.54)\times 10^4$	−27.5 (±0.2)	−41.3 (±2.8)	−13.8 (±2.8)
6g·7	$4.8\ (\pm 0.30)\times 10^4$	−26.7 (±0.2)	- 33.8 (±1.6)	−7.1 (±1.6)
6g·9	$7.3\ (\pm 0.32)\times 10^4$	−27.7 (±0.1)	−29.5 (±1.8)	−1.8 (±1.8)
6g·13	2400 (±720)[b]	−19.3 (±0.7)	–	–
6g·14	$2.3\ (\pm 0.30)\times 10^5$	−30.6 (±0.3)	−42.7 (±3.2)	−12.1 (±3.2)
6h·7	$1.2\ (\pm 0.22)\times 10^5$	−29.0 (±0.4)	−45.2 (±2.8)	−16.2 (±2.8)
6h·9	$1.9\ (\pm 0.26)\times 10^5$	−30.1 (±0.3)	−42.4 (±2.6)	−12.3 (±2.6)
6h·13	4200 (±620)[b]	−20.7 (±0.4)	–	–
6h·14	$4.8\ (\pm 0.23)\times 10^5$	−32.4 (±0.2)	−47.7 (±2.2)	−15.3 (±2.2)

[a] Values are averages and errors reported in brackets are twice the standard deviations calculated from triplicate measurements. [b] Determined by ^{1}H NMR titration in $CDCl_3$ at 298 K.

Conclusion

We have synthesized two series of DDD and AAA hydrogen-bond arrays that form triply-hydrogen-bonded double-helical complexes when combined in $CDCl_3$ solution. The addition of electron-withdrawing groups to the 5-positions of the skatole rings in the DDD arrays increase the complex association constants by up to a factor of 30 in the cases studied. These increases, expressed in terms of their free

energy, are a linear function of the sum of the Hammett constants of the substituents on both skatole rings. Similarly, introduction of electron-donating or -withdrawing groups into the AAA arrays produces a nearly identical but opposite linear response with respect to complex stability. Overall, the various combinations of these modifications demonstrate a control over complex affinities of more than three orders of magnitude from 10^2 to $>10^5\,\text{M}^{-1}$ (or $>20\,\text{kJ mol}^{-1}$) within the same underlying recognition motif. The predictable nature of these effects could be used to easily tailor a particular stability complex for applications in which complementary hydrogen-bond association is desirable as a design feature (e.g., supramolecular polymerization).

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[1] a) Y. He, B. Zhu, Y, Inoue, *Prog. Polym. Sci.* **2004**, *29*, 1021–1051; b) J.-M. Lehn, *Prog. Polym. Sci.* **2005**, *30*, 814–831; c) H. C. Lin, C. M. Tsai, G. H. Huang, Y. T. Tao, *Macromolecules* **2006**, *39*, 557–568; d) J.-M. Lehn, *Chem. Soc. Rev.* **2007**, *36*, 151–160; e) S. W. Kuo, *J. Polym. Res.* **2008**, *15*, 459–486; f) G. Qing, X. Wang, L. Jiang, H. Fuchs, T. Sun, *Soft Matter* **2009**, *5*, 2759–2765; g) K. P. Nair, V. Breedveld, M. Weck, *Soft Matter* **2011**, *7*, 553–559; h) K. P. Nair, V. Breedveld, M. Weck, *Macromolecules* **2011**, *44*, 3346–3357.

[2] a) R. P. Sijbesma, F. H. Beijer, L. Brunsveld, B. J. B. Folmer, J. H. K. K. Hirschberg, R. F. M. Lage, J. K. L. Lowe, E. W. Meijer, *Science* **1997**, *278*, 1601–1604; b) A. T. ten Cate, H. Kooijman, A. L. Spek, R. P. Sijbesma, E. W. Meijer, *J. Am. Chem. Soc.* **2004**, *126*, 3801–3808; c) S. P. Dudek, M. Pouderoijen, R. Abbel, A. P. H. J. Schenning, E. W. Meijer, *J. Am. Chem. Soc.* **2005**, *127*, 11763–11768; d) O. A. Scherman, G. B. W. L. Ligthart, R. P. Sijbesma, E. W. Meijer, *Angew. Chem.* **2006**, *118*, 2126–2130; *Angew. Chem. Int. Ed.* **2006**, *45*, 2072–2076; e) T. F. A. de Greef, G. Ercolani, G. B. W. L. Ligthart, E. W. Meijer, R. P. Sijbesma, *J. Am. Chem. Soc.* **2008**, *130*, 13755–13764; f) E. J. Foster, E. B. Berda, E. W. Meijer, *J. Am. Chem. Soc.* **2009**, *131*, 6964–6966.

[3] Reviews and books: a) A. Ciferri, *Supramolecular Polymers*, Marcel Dekker, New York, **2000**; b) L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma, *Chem. Rev.* **2001**, *101*, 4071–4098; c) C. Schmuck, W. Wienand, *Angew. Chem.* **2001**, *113*, 4493–4499; *Angew. Chem. Int. Ed.* **2001**, *40*, 4363–4369; d) A. Ciferri, *Macromol. Rapid Commun.* **2002**, *23*, 511–529; e) J.-M. Lehn, *Polym. Int.* **2002**, *51*, 825–839; f) A. Tessa ten Cate, R. P. Sijbesma, *Macromol. Rapid Commun.* **2002**, *23*, 1094–1112; g) W. H. Binder, R. Zirbs, *Adv. Polym. Sci.* **2007**, *207*, 1–78; h) A. J. Wilson, *Soft Matter* **2007**, *3*, 409–425; i) L. S. Shimizu, *Polym. Int.* **2007**, *56*, 444–452; j) M. Weck, *Polym. Int.* **2007**, *56*, 453–460; k) V. Rotello, S. Thayumanavan, *Molecular Recognition and Polymers*, Wiley, Hoboken, New Jersey, **2008**; l) R. Hoogenboom, D. Fournier, U. S. Schubert, *Chem. Commun.* **2008**, 155–162; m) T. F. A. de Greef, M. M. J. Smulders, M. Wolffs, A. P. H. J. Schenning, R. P. Sijbesma, E. W. Meijer, *Chem. Rev.* **2009**, *109*, 5687–5754; n) J. D. Fox, S. J. Rowan, *Macromolecules* **2009**, *42*, 6823–6835; o) A. Ciferri, *Chem. Eur. J.* **2009**, *15*, 6920–6925; p) T. F. A. de Greef, E. W. Meijer, *Aust. J. Chem.* **2010**, *63*, 596–598.

[4] R. B. Martin, *Chem. Rev.* **1996**, *96*, 3043–3064.

[5] a) W. L. Jorgensen, J. Pranata, *J. Am. Chem. Soc.* **1990**, *112*, 2008–2010; b) J. Pranata, S. G. Wierschke, W. L. Jorgensen, *J. Am. Chem. Soc.* **1991**, *113*, 2810–2819; c) J. Sartorius, H.-J. Schneider, *Chem. Eur. J.* **1996**, *2*, 1446–1452.

[6] a) L. J. Prins, D. N. Reinhoudt, P. Timmerman, *Angew. Chem.* **2001**, *113*, 2446–2492; *Angew. Chem. Int. Ed.* **2001**, *40*, 2382–2426; b) G. Cooke, V. M. Rotello, *Chem. Soc. Rev.* **2002**, *31*, 275–286; c) C. A. Hunter, H. L. Anderson, *Angew. Chem.* **2009**, *121*, 7624–7636; *Angew. Chem. Int. Ed.* **2009**, *48*, 7488–7499; d) M. C. Misuraca, T. Grecu, Z. Freixa, V. Garavini, C. A. Hunter, P. W. N. M. van Leeuwen, M. D. Segarra-Maset, S. M. Turega, *J. Org. Chem.* **2011**, *76*, 2723–2732.

[7] a) U. Lüning, C. Kuhl, A. Uphoff, *Eur. J. Org. Chem.* **2002**, 4063–4070; b) X. Z. Wang, X. Q. Li, X. B. Shao, X. Zhao, P. Deng, X. K. Jiang, Z. T. Li, Y. Q. Chen, *Chem. Eur. J.* **2003**, *9*, 2904–2913; c) T. Park, M. F. Mayer, S. Nakashima, S. C. Zimmerman, *Synlett* **2005**, 1435–1436; d) G. B. W. L. Ligthart, H. Ohkawa, R. P. Sijbesma, E. W. Meijer, *J. Org. Chem.* **2006**, *71*, 375–378; e) C. A. Anderson, P. G. Taylor, M. A. Zeller, S. C. Zimmerman, *J. Org. Chem.* **2010**, *75*, 4848–4851.

[8] a) M. F. Mayer, S. Nakashima, S. C. Zimmerman, *Org. Lett.* **2005**, *7*, 3005–3008; b) J. Taubitz, U. Luning, *Aust. J. Chem.* **2009**, *62*, 1550–1555.

[9] a) F. H. Beijer, R. P. Sijbesman, H. Kooijman, A. L. Spek, E. W. Meijer, *J. Am. Chem. Soc.* **1998**, *120*, 6761–6769; b) V. G. H. Lafitte, A. E. Aliev, H. C. Hailes, K. Bala, P. Golding, *J. Org. Chem.* **2005**, *70*, 2701–2707; c) P. K. Baruah, R. Gonnade, U. D. Phalgune, G. J. Sanjayan, *J. Org. Chem.* **2005**, *70*, 6461–6467; d) T. Park, E. M. Todd, S. Nakashima, S. C. Zimmerman, *J. Am. Chem. Soc.* **2005**, *127*, 18133–18142.

[10] P. Corbin, S. C. Zimmerman, *J. Am. Chem. Soc.* **1998**, *120*, 9710–9711.

[11] T. J. Murray, S. C. Zimmerman, *J. Am. Chem. Soc.* **1992**, *114*, 4010–4011.

[12] S. Djurdjevic, D. A. Leigh, H. McNab, S. Parsons, G. Teobaldi, F. Zerbetto, *J. Am. Chem. Soc.* **2007**, *129*, 476–477.

[13] a) D. A. Bell, E. V. Anslyn, *Tetrahedron* **1995**, *51*, 7161–7172; b) B. A. Blight, A. Camara-Campos, S. Djurdjevic, M. Kaller, D. A. Leigh, F. M. McMillan, H. McNab, A. M. Z. Slawin, *J. Am. Chem. Soc.* **2009**, *131*, 14116–14122.

[14] For examples of homodimeric double helices: a) J. Sánchez-Quesada, C. Seel, P. Prados, J. de Mendoza, *J. Am. Chem. Soc.* **1996**, *118*, 277–278; b) J. Keegan, P. E. Kruger, M. Nieuwenhuyzen, J. O'Brien, N. Martin, *Chem. Commun.* **2001**, 2192–2193; c) S. J. Coles, J. G. Frey, P. A. Gale, M. B. Hursthouse, M. E. Light, K. Navakhun, G. L. Thomas, *Chem. Commun.* **2003**, 568–569; d) H. Ito, Y. Furusho, T. Hasegawa, E. Yashima, *J. Am. Chem. Soc.* **2008**, *130*, 14008–14015; e) H. Goto, Y. Furusho, K. Miwa, E. Yashima, *J. Am. Chem. Soc.* **2009**, *131*, 4710–4719; f) H. Yamada, K. Maeda, E. Yashima, *Chem. Eur. J.* **2009**, *15*, 6794–6798; g) Y. Furusho, E. Yashima, *J. Polym. Sci. Part A* **2009**, *47*, 5195–5207; h) D. Hu, Z. Yang, G. Zhang, M. Liu, J. Xiang, T. Liang, J. Ma, G. Yang, *CrystEngComm* **2011**, *13*, 6021–6023; i) Y. Furusho, E. Yashima, *Macromol. Rapid Commun.* **2011**, *32*, 136–146; j) Y. Haketa, H. Maeda, *Chem. Eur. J.* **2011**, *17*, 1485–1492; k) N. Saito, R. Terakawa, M. Shigeno, R, Amemiya, M. Yamaguchi, *J. Org. Chem.* **2011**, *76*, 4841–4858.

[15] For examples of heterodimeric double helices: a) H. Goto, Y. Furusho, E. Yashima, *J. Am. Chem. Soc.* **2007**, *129*, 9168–9174; b) F. Reviriego, A. Sanz, P. Navarro, J. Latorre, E. Garcia-Espana, M. Lui-Gonzalez, *Org. Biomol. Chem.* **2009**, *7*, 3212–3214; c) Q. Gan, F. Lie, B. Kauffmann, J. Xiang, I. Huc, H. Jiang, *Chem. Commun.* **2010**, *46*, 297–299; d) Z.-Q. Wu, Y. Furusho, H. Yamada, E. Yashima, *Chem. Commun.* **2010**, *46*, 8962–8964.

[16] a) J. Li, J. A. Wisner, M. C. Jennings, *Org. Lett.* **2007**, *9*, 3267–3269; b) H.-B. Wang, B. P. Mudraboyina, J. Li, J. A. Wisner, *Chem. Commun.* **2010**, *46*, 7343–7345.

[17] a) B. Rajur, A. Y. Merwade, L. D. Basanagoudar, *Synth. Commun.* **1992**, *22*, 421–428; b) M. C. Hillier, J.-F. Marcoux, D. Zhao, E. J. J.

Grabowski, A. E. McKeown and R. D. Tillyer, *J. Org. Chem.* **2005**, *70*, 8385–8394.

[18] A. P. Bisson, F. J. Carver, D. S. Eggleston, R. C. Haltiwanger, C. A. Hunter, D. L. Livingstone, J. F. McCabe, C. Rotger, A. E. Rowan, *J. Am. Chem. Soc.* **2000**, *122*, 8856–8868.

[19] O. Exner in *Correlation Analysis in Chemistry*; (Eds.: N. B. Chapman, J. Shorter), Plenum, London, **1978**.

[20] a) L. K. Dyall, *Aust. J. Chem.* **1964**, *17*, 419–472; b) Y. Asabe, Y. Tsuzuki, *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3482–3483; c) E. Bobko, C. S. Toberico, *J. Org. Chem.* **1983**, *48*, 1368–1369; d) F. L. Setliff, N. G. Soman, A. D. Toland, *J. Chem. Educ.* **1995**, *72*, 362–363.

[21] J. P. Lorand, *J. Phys. Org. Chem.* **2011**, *24*, 267–273.

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