Molecular Tweezers as Synthetic Receptors: Molecular Recognition of Electron-Deficient Aromatic Substrates by Chemically Bonded Stationary Phases

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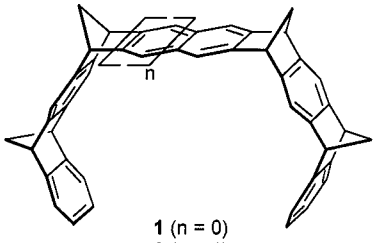
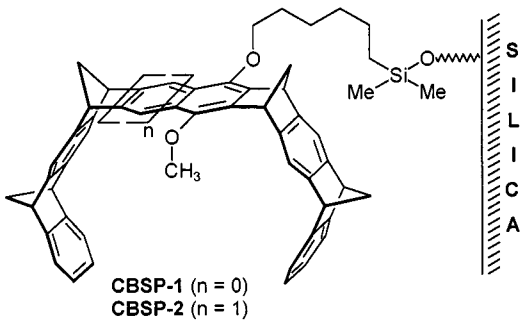
The synthesis and chromatographic properties of novel chemically-bonded stationary phases **CBSP-1** and **CBSP-2**, containing substituted molecular tweezers with benzene and naphthalene spacer-units, are described. These phases selectively retain electron-deficient aromatic and quinoid analytes of appropriate size and topography, such as 1,4-dinitrobenzene, 1,2-, 1,3-, and 1,4-dicyanobenzenes, and 7,7,8,8-tetracyano-*p*-quinodimethane (TCNQ), in HPLC studies. The good qualitative correlation between the capacity factors k' derived from the HPLC retention times and the association constants K_a obtained from binding studies in solution using molecular tweezers **1** and **2** as receptors, indicates that the mechanism of retention involves selective complexation by the molecular tweezers on the silica surface. As expected from the solution experiments, higher capacity factors and selectivities were obtained with **CBSP-2** than with **CBSP-1** because of a better structural fit of the naphthalene-spaced receptor with the aromatic analytes. Capacity factors, k', and enthalpies of retention, ΔH_R, were measured for four different aromatic analytes in 15 solvents. Chromatographic separation factors, α, were determined for seven structurally-related nitroaromatic compounds. The results of these measurements allow for the conclusion that the electrostatic nature and steric complementarity of the receptors and analytes is most important in determining selectivities.

Introduction

The study of molecular recognition phenomena has emerged as a broad and dynamic field of research, largely as a result of the fundamental importance of noncovalent interactions in biological processes.[1] In addition to the relatively strong and, therefore, often dominating hydrogen-bonding,[2] ion-pairing,[3] and hydrophobic forces,[4] arene−arene interactions[5] are of particular importance for the formation of supermolecules. We recently reported that molecular tweezers **1** and **2** can act as synthetic receptors due to their ability to selectively bind electron-deficient aromatic and aliphatic compounds, as well as organic cations in solution.[6]

The demand for rapid, convenient, and accurate quantitative measurements of intermolecular interactions is likely to increase as combinatorial methods of drug design are developed. Chemically-bonded stationary phases (CBSPs) have proven to be very useful for the simultaneous evaluation of noncovalent binding interactions.[7] We report the synthesis and chromatographic properties of the chemically-bonded stationary phases **CBSP-1** and **CBSP-2**, which selectively retain several electron-deficient aromatic analytes due to the highly selective complexation properties of the molecular tweezers' binding sites.





Results and Discussion

The syntheses of **CBSP-1** and **CBSP-2** start with the unsymmetrical functionalization of diacetate-substituted molecular tweezers **3** and **4**, which can be converted into the ω-alkenyl-substituted compounds **7** and **8** in 79% and 60%

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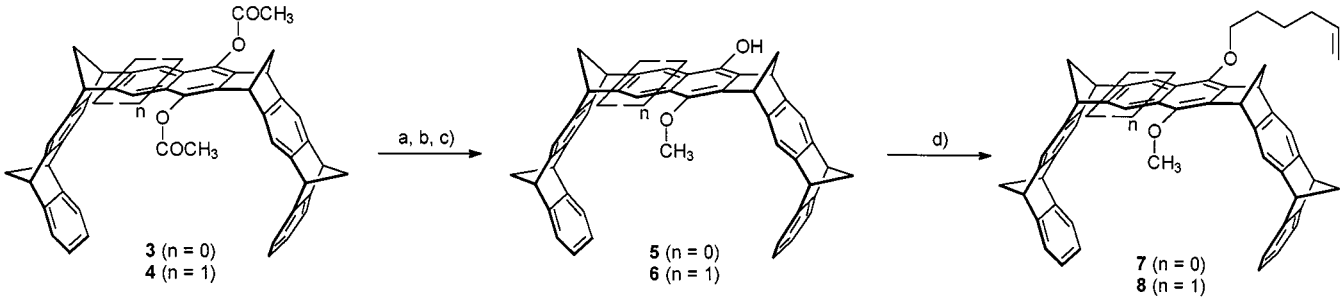
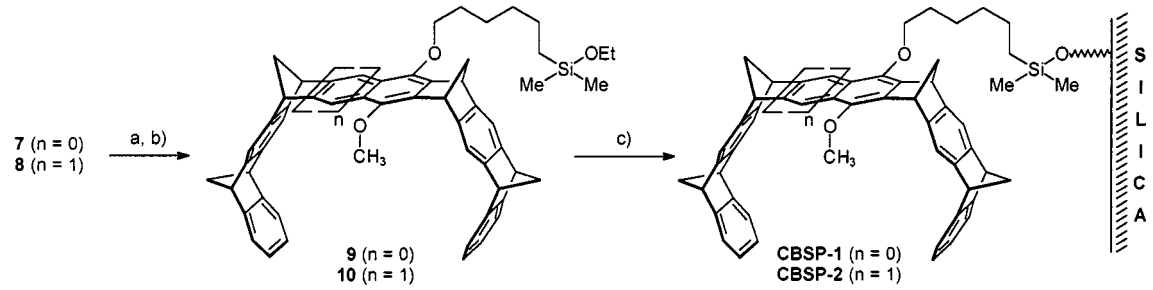


Scheme 1. Synthesis of molecular tweezers **7** and **8**; reaction conditions and yields: (a) aq. NaOH, 1,4-dioxane, 20°C; (b) MeI, K_2CO_3, acetone, 55°C, 20 h; (c) aq. NaOH, 1,4-dioxane, 60°C; (d) 6-bromo-1-hexene, K_2CO_3, acetone, 55°C, 20 h; overall yields for a−d are 79% **(7)** and 60% **(8)**

yield, respectively, by standard procedures (Scheme 1).[6][8] The key step is the hydrolysis of only one of the acetate groups in tweezers **3** and **4** using aqueous NaOH in 1,4-dioxane. The chemically-bonded stationary phases **CBSP-1** and **CBSP-2** were prepared from **7** and **8** as outlined in Scheme 2. Regioselective hydrosilylation of **7** and **8** with dimethylchlorosilane and hexachloroplatinic acid in dichloromethane and subsequent esterification of the chlorosilanes with ethanol produced the ethoxysilanes **9** and **10** in 92% and 87% yields, respectively.[9] The monofunctional ethoxysilanes were covalently attached to 5 μm Spherisorb silica by standard methods,[9] leading to brush phases[10] **CBSP-1** and **CBSP-2**. Loadings were determined by combustion analyses to be 0.07 and 0.03 mmol host/g silica for **CBSP-1** and **CBSP-2**, respectively. The loaded silica was slurry-packed into commercially available stainless-steel HPLC-columns and residual silanol groups were capped with trimethylsilane (TMS) groups to minimize nonspecific retention of the analytes (see Experimental Section for details). To evaluate the nonspecific retention of the silica surface, a reference column was packed with unloaded silica that was capped with TMS groups in the same manner as the chemically-bonded HPLC columns.

In initial HPLC experiments, retention times, t_r, and capacity factors, $k' = (t_r - t_0)/t_0$ (t_0 = column deadtime), of several aromatic and quinoid compounds were measured with chloroform as the mobile phase. The electron-rich, bulky analyte 1,3,5-tri-*tert*-butylbenzene **TTBB** (which should not be significantly retained by any of the prepared columns) was used to determine t_0.[11] Chloroform was chosen as the mobile phase to allow a qualitative comparison of the capacity factors with the association constants measured for **1** and **2** in $CDCl_3$ (Table 1). From this comparison it is clear that the electron-deficient substrates which are complexed most strongly in solution are retained more ($k' > 0.1$) by **CBSP-1** and **CBSP-2**. The observation that the capacity factors k' determined for aromatic and quinoid analytes are always larger with **CBSP-2** is in good agreement with our previous finding that the naphthalene tweezer **2** forms more stable complexes with aromatic and quinoid guests in $CDCl_3$ than does benzene tweezer **1**.[6b] The superior complexation by **2** is due to its better structural fit with this class of guest molecules. From previous solution binding studies with several substituted molecular tweezers, it was known that substituents attached to the central benzene- or naphthalene-unit of **1** and **2** substantially affect their binding of aromatic and aliphatic substrates[12] so that the unsubstituted receptors **1** and **2** are not ideal model compounds for a quantitative correlation with the substituted CBSPs. Nevertheless, the qualitative correlation between K_a and k' clearly indicates that the mechanism of retention on both CBSPs involves the complexation of the analytes by the molecular tweezers bonded to the stationary phase. It should be noted that none of the analytes listed in Table 1 are significantly retained on the unloaded reference column, and that no electron-rich aromatic analytes, such as toluene, anisol, aniline or phenol, are retained by the CBSPs in chloroform (Figure 1).

The contributions of enthalpy, ΔH, and entropy, ΔS, to the complex stability gives an important insight into the nature of the binding event.[13] The enthalpy of retention, ΔH_R, can be determined from the temperature-dependence



Scheme 2. Synthesis of the CBSPs; reaction conditions and yields: (a) $HSiMe_2Cl$, H_2PtCl_6 (cat.), CH_2Cl_2, 42°C, 3 h; (b) EtOH, NEt_3, 20°C, 2 h; yields for a−b: 92% **(9)** and 87% **(10)**; (c) silica, 130°C, 48 h

Table 1. Capacity factors k' for **CBSP-1** and **CBSP-2** and association constants K_a of molecular tweezers **1** and **2** with different electron-deficient analytes in chloroform

analyte	k' (**CBSP-1**)[a]	K_a (**1**)[b]	k' (**CBSP-2**)[a]	K_a (**2**)[b]
1,3,5-trinitrobenzene	< 0.1	–	< 0.1	–
nitrobenzene	< 0.1	–	< 0.1	< 1
dimethylterephtalate	< 0.1	–	< 0.1	< 1
1,4-diacetylbenzene	< 0.1	–	0.14	10
p-benzoquinone	0.10	< 1	0.22	15
1,2-dicyanobenzene **1,2-DCB**	0.10	< 1	0.4	40
1,3-dicyanobenzene **1,3-DCB**	0.10	< 1	0.6	85
1,4-dicyanobenzene **1,4-DCB**	0.25	10	1.4	110
1,2-dinitrobenzene **1,2-DNB**	< 0.1	–	< 0.1	< 1
1,3-dinitrobenzene **1,3-DNB**	< 0.1	–	<0.1	< 1
1,4-dinitrobenzene **1,4-DNB**	0.25	17	2.3	45
4-nitrocyanobenzene	0.23		1.3	
TCNQ[c]	2.3	1100	> 60[d]	> 10^5

[a] Capacity factor $k' = (t_r - t_0)/t_0$ at 298 K. – [b] K_a at 294 K in M^{-1}, determined by ^{1}H-NMR titration in $CDCl_3$, see ref.[6b] – [c] **TCNQ** = 7,7,8,8-tetracyano-*p*-quinodimethane. – [d] Analyte was not eluted after 2.5 h.

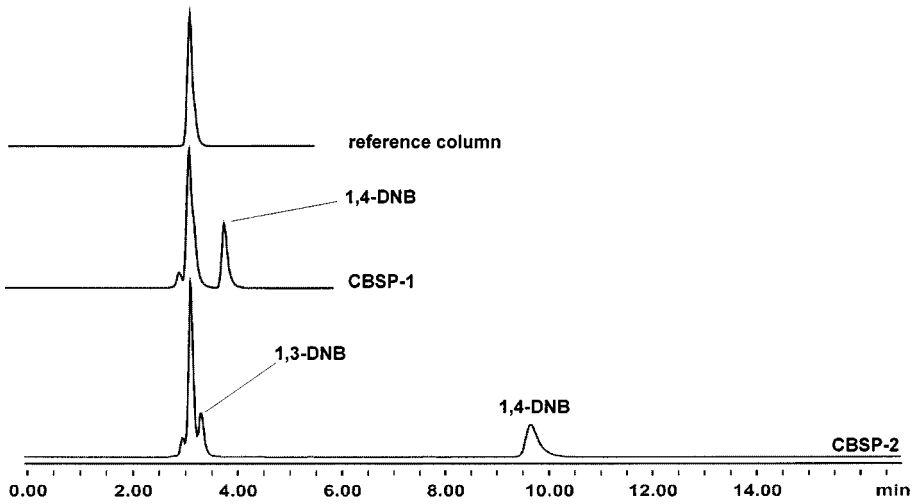


Figure 1. HPLC retention chromatograms (1 mL min^{-1} chloroform, 298 K) of the three dinitrobenzenes **DNB**s on the unloaded reference column (top), **CBSP-1** (center), and **CBSP-2** (bottom); **1,4-DNB** is selectively retained on both CBSPs while all other substrates are eluted at t_0 on the reference column

of k' by using the equation $R \cdot \ln k' = -\Delta H_R/T + \Delta S_R + R \cdot \ln \Phi$, where Φ is the phase ratio, usually defined as the volume of the stationary phase divided by the volume of the mobile phase in a chromatographic system.[14] The linear plot of $R \cdot \ln k'$ vs. $1/T$ affords $-\Delta H_R$ as the slope and the term $\Delta S_R + R \cdot \ln \Phi$ as the *y*-intercept. Because the measurement of the phase ratio Φ is difficult, the entropy of retention, ΔS_R, cannot be directly derived from the temperature-dependence of k'. Furthermore, because of the modest solubility of hydrocarbon tweezers **1** and **2**, binding studies in solution are restricted to a very small number of solvents whereas the solubility of the receptors is no longer a limiting factor in the HPLC experiments with chemically-bonded stationary phases **CBSP-1** and **CBSP-2**. Therefore, valuable information about solvent-effects on the intermolecular complexation[13a] can be achieved by measuring capacity factors k' and enthalpies of retention ΔH_R in a variety of solvents.[7][15] The comparison between Figures 1 and 2 illustrates the solvent-dependence and selectivity of the HPLC method.

We have measured the temperature-dependence of k' and, hence, ΔH_R for the electron-deficient aromatic analytes 1,4-dinitrobenzene **1,4-DNB**, 1,4-, 1,3-, and 1,2-dicyanobenzene **1,4-DCB**, **1,3-DCB**, and **1,2-DCB**, respectively, in 15 different solvents.

Due to the stronger binding of the naphthalene-spaced receptors, the k' as well as the ΔH_R values are larger in the experiments with **CBSP-2** than in those with **CBSP-1** (Tables 2 and 3). The results in Table 2 show that the values for k' and $|\Delta H_R|$ are large in protic solvents (e.g., MeOH, EtOH, and *i*PrOH) and nonpolar solvents (e.g., MTBE, CCl_4, and cyclohexane), but significantly smaller in polar aprotic solvents (e.g., CH_3CN, DMF, and 1,4-dioxane). This indicates that solvophobic effects might be the driving force for binding in protic solvents. Although the solvent dependencies of the k' and ΔH_R values are found to be

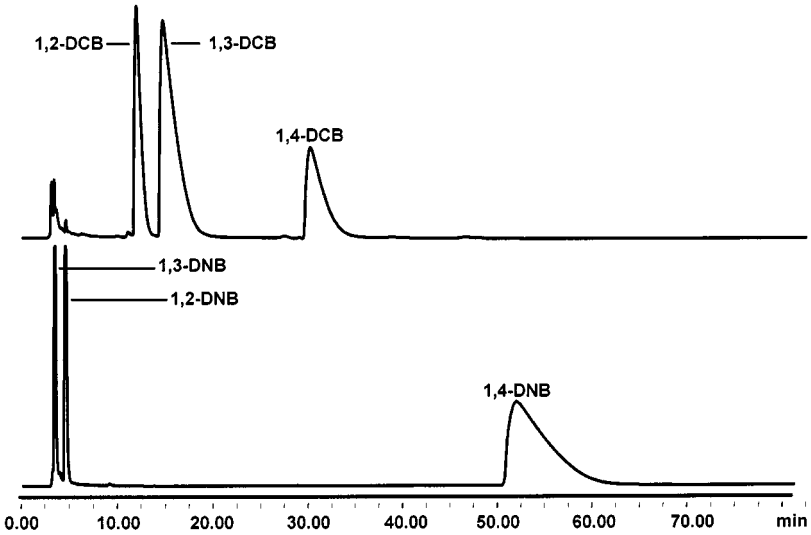


Figure 2. HPLC chromatograms (1 mL min^{-1} MTBE, 298 K) of the three isomeric dicyanobenzenes **DCBs** and dinitrobenzenes **DNBs**, respectively, with **CBSP-2**; in agreement with the results obtained in the study of **1,2-** and **1,3-DNB** with **2** in solution (Table 1), **1,2-** and **1,3-DNB** are not significantly retained

Table 2. Solvent-dependence of the capacity factors k' and enthalpies of retention ΔH_R determined for 1,4-dinitrobenzene (**1,4-DNB**), 1,4-, 1,3-, and 1,2-dicyanobenzene (**1,4-DCB**, **1,3-DCB**, and **1,2-DCB**) with **CBSP-2**

Mobile phase	k'[a] **1,4-DNB**	ΔH_R[b] **1,4-DNB**	k'[a] **1,4-DCB**	ΔH_R[b] **1,4-DCB**	k'[a] **1,3-DCB**	ΔH_R[b] **1,3-DCB**	k'[a] **1,2-DCB**	ΔH_R[b] **1,2-DCB**
MeOH	44	−6.0	22	−5.9	10.1	−6.1	6.1	−5.9
EtOH	66[c]	−7.5	33[c]	−7.4	17.5[c]	−7.8	9.0[c]	−7.2
*i*PrOH	102[c]	−9.0	53[c]	−9.0	33[c]	−9.6	15.1[c]	−8.8
CH_3CN	0.65		0.31		< 0.1		0	
DMF	0		0		0		0	
$(CH_2Cl)_2$	1.0	−3.4	0.64	−3.5	0.26	−3.6	0.15	−3.2
CH_2Cl_2	1.6	−3.6	0.89	−3.5	0.36	−3.6	0.21	−3.2
$(CHCl_2)_2$	2.7	−3.6	1.7	−3.5	0.65	−3.3	0.40	−2.8
$CHCl_3$	2.1	−2.7	1.3	−2.6	0.57	−2.4	0.36	−2.0
AcOEt	3.1	−2.1	1.7	−2.0	0.74	−2.1	0.50	−1.8
THF	0.71	−1.6	0.41	−1.5	0.17	−1.5	0.13	−1.4
1,4-dioxane	0.21		0.16		< 0.1		< 0.1	
MTBE	16.7	−3.4	8.9	−3.0	4.0	−3.0	2.9	−2.9
CCl_4	50	−7.3	23.5	−6.9	20.0	−7.0	8.9	−6.8
Cyclohexane	245[c]	−8.5	150[c]	−8.8	102[c]	−8.3	81[c]	−8.7

[a] Capacity factor at 298 K, multiple runs were within 10%. − [b] In $kcalmol^{-1}$, temperature ranges were from −10°C to 70°C with a minimum range of 55°C, standard errors for the linear regression were < 0.1 $kcalmol^{-1}$, multiple runs were within 5%. − [c] k' values are extrapolated to 298 K from higher temperature measures using the regression function (ln k' vs. $1/T$).

Table 3. Solvent-dependence of the capacity factors k' and enthalpies of retention ΔH_R determined for 1,4-dinitrobenzene (**1,4-DNB**), 1,4-, and 1,3-dicyanobenzene (**1,4-DCB**, and **1,3-DCB**) with **CBSP-1**

Mobile phase	k'[a] **1,4-DNB**	ΔH_R[b] **1,4-DNB**	k'[a] **1,4-DCB**	ΔH_R[b] **1,4-DCB**	k'[a] **1,3-DCB**	ΔH_R[b] **1,3-DCB**
MeOH	0.24	−3.0	0.13	−4.4	0	
EtOH	0.30	−2.5	0.20	−3.0	0.1	−2.9
*i*PrOH	3.7	−5.2	2.5	−5.6	1.2	−5.8
CH_2Cl_2	0		0		0	
$CHCl_3$	0.27	−0.6	0.22	−0.8	< 0.1	−0.8
MTBE	5.2	−1.9	3.7	−1.9	1.3	−1.4
CCl_4	3.4	−3.6	5.2	−4.6	2.9	−5.1

[a] Capacity factor at 298 K, multiple runs were within 10% − [b] In kcal mol^{-1}, standard errors for the linear regression were < 0.1 kcal mol^{-1}, multiple runs were within 5%.

large (Table 2), it is somewhat surprising that the separation factors, $\alpha = k'_1/k'_2$, and hence, the selectivities between different analytes are almost solvent-independent (Table 4), indicating that in each complex the solvent has a similar effect

on the binding between the analyte and the receptor. This is most likely due to the structural similarity of the analytes studied here.[16] The finding that the ΔH_R values for the four different analytes (Table 2) are very similar in each solvent, while $\Delta\Delta G_R = -RT \ln \alpha$ (Table 4) is different, implies that the entropy term ΔS_R is responsible for the observed selectivities (ΔS_R: **1,4-DNB** > **1,4-DCB** > **1,3-DCB** > **1,2-DCB**). This finding is in good agreement with the thermodynamic data from solution binding studies with the hydrocarbon receptor **2**. In this case, a similar trend in ΔS values was observed (**1,4-DNB**: +2.8, **1,4-DCB**: +0.6, **1,3-DCB**: −3.1, and **1,2-DCB**: −4.4 cal·mol^{-1}·K^{-1} in $CDCl_3$).[6b] The trend of increasing k' and $|\Delta H_R|$ values affected by the change of the mobile phase from methanol to 2-propanol was unexpected.

Table 4. Averaged separation factors α and differences in Gibbs enthalpy of retention $\Delta\Delta G_R$ for the three dicyanobenzenes **DCB**s with respect to **1,4-DNB** for **CBSP-2** in all solvents where significant retention was observed for the listed analytes (Table 2). Cyclohexane and CCl_4 are excluded, because nonspecific retention of the **DCB**s is observed ($0 < k' < 1$) in these nonpolar solvents

Analyte	$\alpha = k'_{\mathbf{1,4\text{-}DNB}}/k'$	$\Delta\Delta G_R$ [a]
1,4-DNB	1	0
1,4-DCB	1.8 ± 0.2	0.36 ± 0.06
1,3-DCB	3.8 ± 0.6	0.8 ± 0.1
1,2-DCB	6.6 ± 0.7	1.1 ± 0.06

[a] In kcal mol^{-1}, 298 K.

To understand the relationship between the solvent and retention behavior, linear solvation energy relationships (LSER) based on the Kamlet-Taft multiparameter scale[17] were calculated on four different substrates (**1,4-DNB**, **1,4-DCB**, **1,3-DCB**, and **1,2-DCB)** on **CBSP-2**. For phase-transfer processes, LSER correlate solute properties with three terms: a cavity term, a dipolar term, and a hydrogen-bonding term.[18] For a system with a fixed solute and a fixed stationary phase, the chromatographic equation becomes:[17b,19]

$$\log k' = \log k'_0 + s\pi + d\delta + a\alpha + b\beta + e\varepsilon + mV/100$$

where k' is the capacity factor, π is a measure of dipolarity/polarizability, δ is a polarizability correction parameter, π is a scale of (hydrogen-bond donor) acidities, β is a scale of (hydrogen bond acceptor) basicities, ε, a coordinate covalency factor used to correlate the basicity properties of a lone pair of electrons, and V is the van der Waals molar volume. The solute coefficients *s, d, a, b, e, m*, are calculated from linear regression of the capacity factor, k', vs. the solvent values of the solvatochromic parameters π, δ, α, β, ε,[20] and V, which is either known or calculated by the method of Abraham and McGowan.[21] Normally, the cavity term is expressed as the square of the Hildebrand solubility value of the solvent;[17b] however, the V of the solvent was used instead because the size of the solvent influences the degree of solvation of the tweezer cavity. The capacity factors and the solvents except chloroform, DMF and 1,4-dioxane given in Table 2 were used in the linear regression. The results of the linear regression are given in Table 5.

Table 5. Relationship between log k' of the analytes and the π, α, ε, and V of the eluent for **CBSP-2** using LSER

Entry	Analyte	Multiparameter Relationship	r
1	1,4-DNB	$\log k' = 1.48 - 3.16\pi + 2.39\alpha - 2.32\varepsilon + 1.63V/100$	0.9975
2	1,4-DCB	$\log k' = 1.21 - 3.26\pi + 2.41\alpha - 2.67\varepsilon + 1.85V/100$	0.9978
3	1,3-DCB	$\log k' = 1.17 - 3.81\pi + 2.65\alpha - 3.38\varepsilon + 1.93V/100$	0.9972
4	1,2-DCB	$\log k' = 1.87 - 3.46\pi + 2.42\alpha - 2.52\varepsilon + 1.87V/100$	0.9987

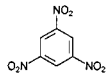
Only four factors are important in determining retention, and they are listed in order of decreasing importance: π, dipolarity/polarizability, α, (hydrogen-bond donor) acidities, ε, correlation of the basicity properties of a lone pair of electrons, and V, van der Waals molar volume. It is not surprising that the π parameter has the largest influence on retention and that the sign of the π coefficient is negative. Electrostatic, polarization, and dispersion forces are likely to be the important driving forces of host−guest complexation, and the strength of these forces will be diminished by solvents with high π values.[5a,22] The positive sign of the α coefficient indicates that as the hydrogen-bond capabilities of the solvent increase, the retention time will also increase. Thus, the lack of solvation of the non-hydrogen-bonding analytes in hydrogen-bonding solvents drives the analyte into the tweezer cavity. Solvation of the analyte by the solvent principally determines the relative retention in solvophobic chromatography.[23] The positive sign of the ε coefficient indicates that for solvents containing ether or nitrile functional groups, the basicity of the lone pair interacting with the solute decreases retention time. It is well-known that such solvents act as increvalent donors [lone-pair (n)-donor] to bind electron-deficient π systems.[22] The least significant factor influencing retention is V. Linear regression results indicate that increasing solvent size increases retention time. Larger solvents are unable to solvate the cavity. Although the increase in k' from methanol to 2-propanol was unexpected, the result can clearly be explained by applying LSER in chromatography. Even though 2-propanol has a lower α value than methanol, the higher π and smaller V values of methanol cause the retention times to increase in 2-propanol over methanol.

Due to the lower stability of the complexes formed between the benzene-spaced tweezer and the aromatic analytes, HPLC experiments with **CBSP-1** were limited to the three analytes, **1,4-DNB**, **1,4-DCB**, and **1,3-DCB**, in seven solvents (Table 3). Here, the effect of solvent-size on the binding properties of the analytes is even more obvious. From both intermolecular and intramolecular (i.e., folding) complexation studies with molecular tweezer **1**,[6] it was known that solvents with small partial molar volumes (e.g., CD_2Cl_2) are able to solvate the cavity of **1** and, therefore, serve as strong competitors for inter- and intramolecular

complexation.[24] These findings are in good agreement with the observation that no analyte is retained by **CBSP-1** with CH_2Cl_2 as a mobile phase.

Molecular tweezers **1** and **2** are receptors that selectively bind electron-deficient aromatic and aliphatic substrates. Due to their relatively small size and their ribbon-type concave preorganization, they are highly selective toward substrates with complementary steric surfaces. This combination of electronic and geometrical effects allows **CBSP-1** and **CBSP-2** to separate mixtures of analytes, even when they possess very similar structures. Table 6 shows the capacity factors k' (20°C) and the selectivities α for different nitroaromatic analytes with 2-propanol as the mobile phase. It should be noted that none of the listed nitroaromatic analytes is retained on the unloaded reference column under the same conditions. The observed selectivities (Table 6), related to 1,3,5-trinitrobenzene (**1,3,5-TNB**), can be expressed as the differerences in the Gibbs enthalpies of retention $\Delta\Delta G_R = \Delta G_R$ (analyte) $- \Delta G_R$ (**1,3,5-TNB**) $= - RT \cdot \ln \alpha$ (Figure 3).

Table 6. Capacity factors k' and separation factors α of different nitroaromatic analytes eluted on **CBSP-1** and **CBSP-2** in 2-propanol

analyte	CBSP-1		CBSP-2	
	k' (20°C)	α between adjacent peaks	k' (20°C)	α between adjacent peaks
	< 0.1		< 0.1	
	0.10	> 1.5	0.25	> 2.5
	0.19	1.9	0.54	2.2
	0.40	2.1	0.79	1.5
	0.41	1.0	3.03	3.8
	0.89	2.2	3.7	1.2
	4.3	4.8	133[a]	36

[a] k' value is extrapolated to 20°C from higher temperature measures using the regression function (ln k' vs. $1/T$).

The observed trend in the binding affinities between **CBSP-1** and **CBSP-2** and the analytes agrees well with the findings for the complexation between the molecular tweezers **1** and **2** and the corresponding substrates in solution

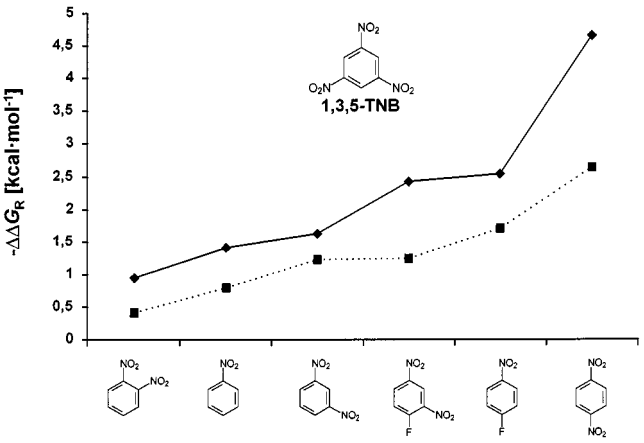


Figure 3. Differences in Gibbs enthalpy of retention $\Delta\Delta G_R = RT \cdot \ln \alpha$ with respect to **1,3,5-TNB** for the nitroaromatic analytes in 2-propanol (see Table 6)

and can be rationalized by two factors − the electrostatic model of the arene−arene interactions[5][25] and the structural shape and size of the tweezer cavities. According to semiempirical (AM1) calculations of the electrostatic potential surfaces (EPSs), molecular tweezers **1** and **2** show surprisingly negative potentials on their concave sides.[25] The more electron-deficient the analyte is, the stronger the receptor−substrate interaction is and hence the larger its k' value (compare nitrobenzene < 4-fluoronitrobenzene < 1,4-dinitrobenzene). On the other hand, the more branched substrates deviate from the ideal shape[6] in which the substituents can avoid pointing into the tweezer cavity, and their k' values are consequently smaller (compare 1,3,5-trinitrobenzene < 1,2- < 1,3- < 1,4-dinitrobenzene).

The studies described here serve to further emphasize the advantages of using chemically-bonded stationary phases to evaluate supramolecular properties of potential synthetic receptors.[7][26] All of the experiments described here using several different solvents and analytes used less than 1 g of **7** and **8**, with no recycling of the receptor being required. The columns appear to be indefinitely stable. Furthermore, ΔH_R and $\Delta\Delta G_R$ values can be determined simultaneously for several analytes, and the ΔH_R values come from van't Hoff plots that span a broader temperature range than is typically accessible in solution (>70°C), thus providing higher accuracy

Experimental Section

IR: Bio-Rad FTS 135. − UV: J+M Tidas FG Cosytec RS 422. − ^{1}H NMR, ^{13}C NMR, DEPT, H,H-COSY, C,H-COSY, NOESY, HMQC, HMBC: Bruker AMX 300; solvents with residual H were used as internal standard. Positions of the protons of the methano bridges are indicated by the letters i (*innen*, towards the center of the molecule) and a (*außen*, away from the center of the molecule). − MS: Fison Instruments VG ProSpec 3000 (70 eV). − All melting points are uncorrected. − Column chromatography: Silica gel 0.063−0.2 mm. − All solvents were distilled prior to use. Solvents were degassed by a minimum of 3 cycles of ultrasonification (20 min) and subsequent saturation with argon using a glass frit

(20 min) − The HPLC experiments were performed with a JASCO PU-980 pump and a JASCO UV-975 UV/VIS-detector.

Synthesis of 7. − 8-Acetoxy-19-hydroxy-(5α,7α,9α,11α,16α,18α,20α,22α)-5,7,9,11,16,18,20,22-octahydro-5,22:7,20:9,18:11,16-tetramethanononacene: Aqueous NaOH (1 M, 3.0 mL) was slowly added to a vigorously stirred solution of diacetate **3** (210 mg, 0.32 mmol) in dioxane (20 mL) and left at room temperature for 30 min. The yellow reaction mixture was poured into a 1:1 mixture of saturated aqueous NH_4Cl/5 M aqueous HCl (50 mL) and extracted three times with dichloromethane. The combined organic layers were washed with water then brine and dried with anhydrous $NaSO_4$. After evaporation of the solvent in vacuo, the product was obtained as a colorless solid (189 mg, 96%). − m.p. 285−287°C. − MS (70 eV); *m*/*z* (%): 608 (82) [M^+], 566 (100) [$M^+ - COCH_3$]. − HR-MS (70 eV); $C_{46}H_{34}O_4$: calcd. 608.2351; found 608.2350. − IR (KBr): $\tilde{\nu}$ = 3420 cm^{-1} (OH), 3009 (CH), 2970 (CH), 2936 (CH), 2863 (CH), 1762 (C=O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, $COCH_3$), 2.35 [d, 2 H, ^2J(24i-H, 24a-H) = 7.5 Hz, 24i-H, 25i-H], 2.40 (s, 4 H, 23-H, 26-H), 2.44 (d, 2 H, 24a-H, 25a-H), 3.96 (s, 2 H, 7-H, 9-H), 4.08 (s, 4 H, 5-H, 11-H, 16-H, 22-H), 4.20 (s, 2 H, 18-H, 20-H), 4.49 (s, 1 H, O−H), 6.74 (m, 4 H, 2-H, 3-H, 13-H, 14-H), 7.07 (m, 4 H, 1-H, 4-H, 12-H, 15-H), 7.11 (s, 2 H, 6-H, 10-H), 7.14 (s, 2 H, 17-H, 21-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.81 (q, CH_3), 47.29 (d, C-18, C-20), 48.66 (d, C-7, C-9), 51.20 (d, C-5, C-11, C-16, C-22), 68.87 (t, C-24, C-25), 70.14 (t, C-23, C-26), 116.25 (d), 116.52 (d), 121.40 (d), 121.48 (d), 124.59 (d), 124.62 (d), 133.63 (s), 135.30 (s), 140.79 (s), 141.95 (s), 146.43 (s), 146.63 (s), 147.49 (s), 147.53 (s), 150.24 (s), 150.26 (s), 169.44 (s, C=O).

8-Hydroxy-19-methoxy-(5α,7α,9α,11α,16α,18α,20α,22α)-5,7,9,11,16,18,20,22-octahydro-5,22:7,20:9,18:11,16-tetramethanononacene (5): To a solution of the 8-acetoxy-19-hydroxyoctahydrotetramethanononacene (130 mg, 0.21 mmol) in anhydrous acetone (10 mL), methyl iodide (0.1 mL), and potassium carbonate (55 mg, 0.4 mmol) were added, and the stirred reaction mixture was heated at reflux for 20 h under argon. After cooling to room temperature, the solvent was evaporated in vacuo. The remaining solid was dissolved in 1,4-dioxane (15 mL), aqueous NaOH (1 M, 1.0 mL) was added, and the reaction mixture was heated at 60°C for 30 min. After cooling to room temperature, the yellow solution was poured into aqueous HCl (1 M, 30 mL) and extracted three times with dichloromethane. The combined organic layers were washed with water then brine and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo. The crude product was purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) to yield **5** as a colorless solid (113 mg, 91%). − m.p. > 300°C. − MS (70 eV); *m*/*z* (%): 580 (100) [M^+], 565 (28) [$M^+ - CH_3$]. − HR-MS (70 eV); $C_{43}H_{32}O_2$: calcd. 580.2402; found 580.2404. − IR (KBr): $\tilde{\nu}$ = 3450 cm^{-1} (OH), 3015 (CH), 2964 (CH), 2948 (CH). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.32 [d, 2 H, ^2J(23i-H, 23a-H) = 7.4 Hz, 23-H, 26-H], 2.36 (d, 2 H, 23-H, 26-H), 2.39 [d, 2 H, ^2J(24i-H, 24a-H) = 7.8 Hz, 24-H, 25-H], 2.41 (d, 2 H, 24-H, 25-H), 3.65 (s, 3 H, 27-H), 4.04/4.05 (s, 4 H, 5-H, 11-H, 16-H, 22-H), 4.15 (s, 2 H, 18-H, 20-H), 4.2 (br, 1 H, O−H), 4.24 (s, 2 H, 7-H, 9-H), 6.73 (m, 4 H, 2-H, 3-H, 13-H, 14-H), 7.05 (m, 4 H, 1-H, 4-H, 12-H, 15-H), 7.11 (s, 2 H, 17-H, 21-H), 7.14 (s, 2 H, 6-H, 10-H). − ^{13}C NMR (126 MHz, $CDCl_3$): δ = 47.23 (d, C-18, C-20), 48.35 (d, C-7, C-10), 51.29 (d, C-5, C-11, C-16, C-22), 61.83 (q, C-27), 69.15 (t, C-23, C-26), 69.98 (t, C-24, C-25), 116.03/116.33 (d, C-6, C-10, C-17, C-21), 121.41/121.50 (d, C-1, C-4, C-12, C-15), 124.55/124.65 (d, C-2, C-3, C-13, C-14), 134.91 (s, C-8), 139.75 (s, C-7a, C-8a), 140.22 (s, C-18a, C-19a), 143.86 (s, C-19), 146.97/147.13/147.37/147.49 (s, C-5a, C-6a, C-9a, C-10a, C-16a, C-17a, C-20a, C-21a), 150.36 (s, C-4a, C-11a, C-15a, C-22a).

8-(1-Hexenyloxy)-19-methoxy-(5α,7α,9α,11α,16α,18α,20α,22α)-5,7,9,11,16,18,20,22-octahydro-5,22:7,20:9,18:11,16-tetramethanononacen (7): To a solution of **5** (0.4 g, 0.66 mmol) and 6-bromo-1-hexene (0.1 g, 1.0 mmol) in acetone (25 mL), anhydrous potassium carbonate (0.15 g, 1.1 mmol), and a small amount of sodium iodide were added. The reaction mixture was heated at 50°C for 24 h. After cooling, the reaction mixture was transferred into a separatory funnel using dichloromethane (50 mL), and washed successively with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and water. The organic layer was dried with anhydrous Na_2SO_4, and the solvent was removed in vacuo. The crude product was purified by column chromatography (*n*-hexane/ethyl acetate, 10:1) to yield **7** as a colorless solid (390 mg, 90%). − m.p. 235°C. − MS (70 eV); *m*/*z* (%): 662 (100) [M^+], 579 (18) [$M^+ - C_6H_{12}$], 565 (7) [$M^+ - CH_3 - C_6H_{12}$]. − IR (KBr): $\tilde{\nu}$ = 3045 cm^{-1} (CH), 3015 (CH), 2964 (CH), 2948 (CH), 1635 (C=C). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.4−1.6 (m, 4 H, 28-H, 29-H), 1.99 [m, 2 H, ^3J(30-H, 31-H) = 7.1 Hz, 30-H], 2.33 (m, 4 H, 23-H, 26-H), 2.41 (m, 4 H, 24-H, 25-H), 3.66 (s, 3 H, 33-H), 3.74 [t, 2 H, ^3J(27-H, 28-H) = 7.4 Hz, 27-H], 4.10 (s, 4 H, 5-H, 11-H, 16-H, 22-H), 4.21/4.24 (s, 4 H, 7-H, 9-H, 18-H, 20-H), 4.96 [dm, 1 H, ^2J(32*Z*-H, 32*E*-H) = 1 Hz, ^3J(32*E*-H, 31-H) = 12 Hz, 32*E*-H], 4.97 [dm, 1 H, ^3J(32*Z*-H, 31-H) = 16 Hz, 32*Z*-H], 5.77 (m, 1 H, 31-H), 6.73 (m, 4 H, 2-H, 3-H, 13-H, 14-H), 7.05 (m, 4 H, 1-H, 4-H, 12-H, 15-H), 7.09/7.12 (s, 4 H, 6-H, 10-H, 17-H, 21-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.34 (t, C-28), 29.64 (t, C-29), 33.52 (t, C-30), 48.28/48.31 (d, C-7, C-9, C-18, C-20), 51.30 (d, C-5, C-11, C-16, C-22), 61.55 (q, C-33), 69.21 (t, C-23, C-26), 69.75 (t, C-24, C-25), 73.89 (t, C-27), 114.54 (t, C-32), 116.05/116.14 (d, C-1, C-4, C-12, C-15), 121.37/121.51 (d, C-6, C-10, C-17, C-21), 124.60 (d, C-2, C-3, C-13, C-14), 138.75 (d, C-31), 139.47 (s, C-7a, C-8a, C-18a, C-19a), 140.23 (s, C-6a, C-9a, C-17a, C-20a), 144.29 (s, C-8), 145.39 (s, C-19), 147.28 (s, C-5a, C-10a, C-16a, C-21a), 150.60 (s, C-4a, C-11a, C-15a, C-22a). − $C_{49}H_{42}O_2$ (662.87): calcd. C 88.79, H 6.39; found C 88.48, H 6.51.

Synthesis of 8. − 8-Acetoxy-21-hydroxy-(5α,7α,10α,12α,17α,19α,22α,24α)-5,7,10,12,17,19,22,24-octahydro-5,24:7,22:10,19:12,17-tetramethanodecacene: Degassed aqueous NaOH (1.0 M, 1.0 mL) was slowly added to a vigorously stirred solution of diacetate **4** (260 mg, 0.37 mmol) in degassed dioxane (10 mL) and left at room temperature for 20 h. The yellow reaction mixture was poured into a degassed 1:1 mixture of saturated aqueous NH_4Cl and 5 M aqueous HCl (50 mL) and extracted three times with dichloromethane. The combined organic layers were washed with water then brine and dried with anhydrous Na_2SO_4. After evaporation of the solvent in vacuo, the product was obtained as a colorless solid (212 mg, 87%). − m.p. > 300°C. − MS (70 eV); *m*/*z* (%): 658 (25) [M^+], 616 (100) [$M^+ - COCH_3$]. − IR (KBr): $\tilde{\nu}$ = 3390 cm^{-1} (OH), 2987 (CH), 2945 (CH), 1758 (C=O). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, $COCH_3$), 2.44 (m, 6 H, 25i-H, 25a-H, 26a-H, 27a-H, 28i-H, 28a-H), 2.49 [dm, 1 H, ^2J(27i-H, 27a-H) = 8 Hz, 27i-H], 2.51 [dm, 1 H, ^2J(26i-H, 26i-H) = 8 Hz, 26i-H], 4.05 (s, 2 H, 12-H, 17-H), 4.06 (s, 2 H, 5-H, 24-H), 4.13 (s, 1 H, 10-H), 4.15 (s, 1 H, 19-H), 4.18 (s, 1 H, 7-H), 4.34 (s, 1 H, 22-H), 6.76 (m, 4 H, 2-H, 3-H, 14-H, 15-H), 7.04 (m, 4 H, 1-H, 4-H, 13-H, 16-H), 7.06 (s, 1 H, 23-H), 7.07 (s, 1 H, 6-H), 7.09 (s, 2 H, 11-H, 18-H), 7.26 (s, 1 H, 9-H), 7.62 (s, 1 H, 20-H). − ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.84 (q, C−H_3), 46.36 (d, C-22), 48.09 (d, C-7), 50.59 (d, C-19), 50.66 (d, C-10), 51.02 (d, C-5, C-12, C-17, C-24), 64.04 (t, C-26), 64.86 (t, C-27), 67.61 (t, C-25, C-28), 112.77 (d, C-9), 113.39 (d, C-20), 116.06 (d, C-23), 116.23 (d, C-18), 116.27 (d, C-

11), 116.83 (d, C-6), 121.54 (d, C-4), 121.57 (d, C-1), 121.61 (d, C-13, C-16), 122.74 (s, C-8a), 124.06 (d, C-3), 124.10 (d, C-2), 124.18 (d, C-14, C-15), 124.21 (s, C-20a), 128.54 (s, C-7a), 133.65 (s, C-8), 137.52 (s, C-21a), 141.93 (s, C-21), 145.71 (s, C-23a), 146.07 (s, C-5a), 146.66 (s, C-17a), 146.81 (s, C-11a), 147.32 (s, C-22a), 147.67 (s, C-6a), 147.74 (s, C-18a), 147.80 (s, C-10a), 147.95 (s, C-4a, C-24a), 148.32 (s, C-12a, C-16a), 150.48 (s, C-19a), 150.58 (s, C-9a), 169.66 (s, C=O).

8-Acetoxy-21-methoxy-(5α,7α,10α,12α,17α,19α,22α,24α)-5,7,10,12,17,19,22,24-octahydro-5,24:7,22:10,19:12,17-tetramethanodecacene: To a degassed solution of 8-acetoxy-21-hydroxyoctahydrotetramethanodecacene (198 mg, 0.3 mmol) in anhydrous acetone (10 mL), methyl iodide (0.425 g, 3.0 mmol), and potassium carbonate (138 mg, 1.0 mmol) were added, and the reaction mixture was heated at reflux for 20 h under argon. After cooling to room temperature, aqueous HCl (10%, 10 mL) was added, and the aqueous solution was extracted three times with dichloromethane. The combined organic layers were washed with water then brine and dried with anhydrous Na_2SO_4. The colorless oil obtained after evaporation of the solvent in vacuo was dissolved in toluene and purified by column chromatography (cyclohexane/ethyl acetate, 5:1). The title compound was obtained as a colorless solid (188 mg, 92%). − m.p. > 300°C. − MS (70 eV); *m/z* (%): 673 (30) [M^+], 630 (100) [$M^+ - COCH_3$]. − IR (KBr): $\tilde{\nu}$ = 2978 cm^{-1} (CH), 2945 (CH), 1760 (C=O). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.44 (s, 3 H, -$COCH_3$), 2.44 (m, 6 H, 25i-H, 25a-H, 26a-H, 27a-H, 28i-H, 28a-H), 2.49 [dm, 1 H, ^2J(27i-H, 27a-H) = 8 Hz, 27i-H], 2.51 [dm, 1 H, ^2J(26i-H, 26a-H) = 8 Hz, 26i-H], 3.87 (s, 3 H, -OCH_3), 4.05 (s, 2 H, 12-H, 17-H), 4.07 (s, 2 H, 5-H, 24-H), 4.10 (s, 1 H, 10-H), 4.15 (s, 1 H, 19-H), 4.17 (s, 1 H, 7-H), 4.54 (s, 1 H, 22-H), 6.76 (m, 4 H, 2-H, 3-H, 14-H, 15-H), 7.03 (m, 4 H, 1-H, 4-H, 13-H, 16-H), 7.06 (s, 1 H, 23-H), 7.08 (s, 1 H, 6-H), 7.09 (s, 2 H, 11-H, 18-H), 7.26 (s, 1 H, 9-H), 7.65 (s, 1 H, 20-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.29 (q, -COCH_3), 48.24 (d, C-22), 48.36 (d, C-7), 51.06 (d, C-19), 51.10 (d, C-10), 51.48 (d, C-5, C-12, C-17, C-24), 62.10 (q, -OCH_3), 64.21 (t, C-26), 65.33 (t, C-27), 68.05 (t, C-25, C-28), 113.16 (d, C-9), 114.72 (d, C-20), 116.50 (d, C-23), 116.61 (d, C-18), 116.76 (d, C-11), 117.24 (d, C-6), 121.96 (d, C-4), 122.02 (d, C-1), 122.12 (d, C-13, C-16), 124.51 (s, C-8a), 124.58 (d, C-2, C-3), 125.22 (d, C-14, C-15), 126.40 (s, C-20a), 134.93 (s, C-7a), 135.21 (s, C-8), 135.67 (s, C-21a), 138.32 (s, C-21), 146.75 (s, C-23a C-17a), 147.19 (s, C-5a, C-11a), 147.33 (s, C-22a), 147.53 (s, C-6a), 148.09 (s, C-18a), 148.12 (s, C-10a), 148.48 (s, C-4a, C-24a), 148.69 (s, C-12a, C-16a), 150.10 (s, C-19a), 151.10 (s, C-9a), 169.83 (s, C=O).

8-(1-Hexenyloxy)-21-methoxy-(5α,7α,10α,12α,17α,19α,22α,24α)-5,7,10,12,17,19,22,24-octahydro-5,24:7,22:10,19:12,17-tetramethanodecacene (8): Degassed aqueous NaOH (1 M, 1.0 mL) was added dropwise to a vigorously stirred solution of 8-acetoxy-21-methoxyoctahydrotetramethanodecacene (135 mg, 0.20 mmol) in degassed dioxane (10 mL) and was heated at reflux for 6 h. After cooling to room temperature, the reaction mixture was poured into a degassed 1:1 mixture of saturated aqueous NH_4Cl and 4 M aqueous HCl (20 mL) and extracted three times with dichloromethane. The combined organic layer was washed with water then brine and dried with anhydrous Na_2SO_4. After evaporation of the solvent in vacuo, the crude product 6 was obtained as a colorless oil and used without further purification due to its instability in the presence of oxygen. The crude 6 was dissolved in anhydrous acetone (15 mL) containing potassium carbonate (83 mg, 0.6 mmol) and 6-bromo-1-hexene (326 mg, 2.0 mmol). A small amount of sodium iodide was added, and the stirred reaction mixture was heated at reflux for 20 h. After cooling, the reaction mixture was transferred to a separatory funnel using dichloromethane (50 mL), washed successively with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and water. The organic layer was dried with anhydrous $NaSO_4$, and the solvent was removed in vacuo. The crude product was purified by column chromatography (cyclohexane/ethyl acetate, 5:1) to yield **8** as a colorless solid (107 mg, 75%). − m.p. > 300°C. − MS (70 eV); *m/z* (%): 712 (100) [M^+], 629 (25) [$M^+ - C_6H_{12}$]. − IR (KBr): $\tilde{\nu}$ = 3052 cm^{-1} (CH), 2985 (CH), 2962 (CH), 2934 (CH), 1625 (C=C). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.63 (m, 2 H, 31-H), 1.79 (m, 2 H, 30-H), 2.14 (m, 2 H, 32-H), 2.42 (m, 7 H, 25i-H, 25a-H, 26a-H, 27i-H, 27a-H, 28i-H, 28a-H), 2.51 [dm, 1 H, ^2J(26i-H, 26a-H) = 8 Hz, 26i-H], 3.77 (s, 3 H, -OCH_3), 3.76 [dm, 1 H, ^2J(29-H, 29′-H) = 7 Hz, 29-H], 3.90 (dm, 1 H, 29′-H), 4.04 (s, 4 H, 5-H, 12-H, 17-H, 24-H), 4.15 (s, 2 H, 10-H, 19-H), 4.41 (s, 1 H, 7-H), 4.47 (s, 1 H, 22-H), 5.04 [dm, 1 H, ^3J(34*Z*-H, 33-H) = 10 Hz, 34*Z*-H], 5.09 [dm, 1 H, ^3J(34*E*-H, 33-H) = 16 Hz, 34*E*-H], 5.90 (dm, 1 H, 33-H), 6.74 (m, 4 H, 2-H, 3-H, 14-H, 15-H), 7.02 (m, 4 H, 1-H, 4-H, 13-H, 16-H), 7.05 (s, 1 H, 23-H), 7.07 (s, 1 H, 6-H), 7.10 (s, 2 H, 11-H, 18-H), 7.57 (s, 1 H, 9-H), 7.59 (s, 1 H, 20-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.51 (t, C-31), 29.88 (t, C-30), 33.64 (t, C-32), 47.58 (d, C-22), 47.67 (d, C-7), 50.67 (d, C-19), 50.68 (d, C-10), 51.05 (d, C-5, C-12, C-17, C-24), 61.71 (q, -OCH_3), 73.99 (t, C-29), 63.63 (t, C-26), 65.01 (t, C-27), 67.57 (t, C-25), 67.67 (t, C-28), 113.82 (d, C-9), 113.95 (t, C-34), 114.69 (d, C-20), 116.15 (d, C-23), 116.17 (d, C-11 C-18), 116.24 (d, C-6), 121.50 (d, C-4), 121.54 (d, C-1), 121.64 (d, C-13, C-16), 124.06 (d, C-2, C-3), 124.13 (d, C-14, C-15), 125.85 (s, C-20a), 126.25 (s, C-8a), 135.44 (s, C-21a), 135.72 (s, C-7a), 138.85 (d, C-33), 144.47 (s, C-8), 145.21 (s, C-21), 146.62 (s, C-5a, C-23a), 147.02 (s, C-11a, C-17a), 147.05 (s, C-22a), 147.32 (s, C-6a), 147.34 (s, C-18a), 147.52 (s, C-10a), 147.80 (s, C-4a, C-24a), 147.85 (s, C-12a, C-16a), 150.55 (s, C-19a), 150.71 (s, C-9a).

Synthesis of the Ethoxysilanes 9 and 10. − 8-[6-(Ethoxydimethylsilyl)hexyloxy]-19-methoxy-(5α,7α,9α,11α,16α,18α,20α,22α)-5,7,9,11,16,18,20,22-octahydro-5,22:7,20:9,18:11,16-tetramethanononacene (9): A solution of $H_2PtCl_6 \cdot x\ H_2O$ (10 mg) in 2-propanol (0.2 mL) was added to a solution of **7** (340 mg, 0.51 mmol) in anhydrous dichloromethane (5 mL) and dimethylchlorosilane (6 mL). The reaction mixture started to boil (after ca. 2 min), and was heated at reflux for another 3 h. After most of the solvent was removed by distillation (under N_2), additional dichloromethane (5 mL) was added and again distilled off. Ethanol (10 mL) and triethlyamine (10 mL) were added to the crude chlorosilane-product, and the brown reaction mixture was stirred at room temperature for 2 h. The solvents were then removed in vacuo. Column chromatography (*n*-hexane/ethyl acetate, 5:1) of the crude product yielded **9** (366 mg, 92%) as a colorless oil. − HR-MS (70 eV): $C_{53}H_{54}O_3Si$: calcd. 766.3842; found 766.3844. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.20 (s, 6 H, $SiCH_3$), 0.71 (m, 2 H, 32-H), 1.26 [t, 3 H, ^3J(33-H, 34-H) = 7.0 Hz, 34-H], 1.4−1.5 (m, 6 H, 29-H, 30-H, 31-H), 1.64 (m, 2 H, 28-H), 2.33 [dm, 2 H, ^2J(24i-H, 24a-H) = 6.0 Hz, 24i-H, 25i-H], 2.37 (dm, 2 H, 24a-H, 25a-H), 2.44 (m, 4 H, 23-H, 26-H), 3.70 (s, 3 H, OCH_3), 3.75 (q, 2 H, 33-H), 4.09 (s, 4 H, 5-H, 11-H, 16-H, 22-H), 4.25/4.28 (s each, 4 H, 7-H, 9-H, 18-H, 20-H), 6.77 (m, 4 H, 2-H, 3-H, 13-H, 14-H), 7.09 (m, 4 H, 1-H, 4-H, 12-H, 15-H), 7.13/7.17 (s each, 4 H, 6-H, 10-H, 17-H, 21-H). − ^{13}C NMR (126 MHz, $CDCl_3$): δ = −2.01 (d), −1.11 (t), 16.46 (q), 18.62(t), 23.30 (t), 25.85 (t), 30.21 (t), 33.29 (t), 48.30 (d), 51.32 (d), 61.49 (q), 69.23 (t), 69.76 (t), 74.22 (t), 116.03 (d), 116.12 (d), 121.36 (d), 121.51 (d), 124.59 (d), 124.62 (d), 139.43 (s), 140.27 (s), 144.40 (s), 145.40 (s), 147.35 (s), 147.40 (s), 150.41 (s), 150.42 (s).

8-[6-(Ethoxydimethylsilyl)hexyloxy]-21-methoxy-(5α,7α,10α,12α,17α,19α,22α,24α)-5,7,10,12,17,19,22,24-octahydro-5,24:7,

22:10,19:12,17-tetramethanodecacene (10): The naphthalene-spaced ethoxysilane **10** was prepared in the same manner as **9**. Ethoxysilane **10** was obtained as a colorless oil (yield: 200 mg, 87%) starting from **8** (200 mg, 0.29 mmol) and was linked to the silica without further characterization.

Preparation of CBSP-1 and CBSP-2: 5-μm Waters Spherisorb® silica (5.0 g) was mixed with a solution of **9** (360 mg, 0.47 mmol) and with a solution of **10** (200 mg, 0.25 mmol), in dichloromethane (each in 15 mL). The solvent was carefully removed in vacuo. The silica was then heated at 130°C for 48 h at 0.1 mbar in a rocking kugelrohr apparatus. After cooling to room temperature, the modified silica was washed thoroughly with dichloromethane and dried in vacuo for several hours. The loadings of the CBSPs were determined by combustion analyses to be 0.07 mmol host/g silica (**CBSP-1**) and 0.03 mmol host/g silica (**CBSP-2**), respectively. The CBSPs were slurry-packed (methanol) into stainless steel HPLC columns (250 × 4.6 mm) with a pressure of about 55 bar. A solution of hexamethyldisilazane (10 mL) in dichloromethane (50 mL) was passed through the columns at a constant flow-rate (0.5 mL/min) to cap the residual silanol functionalities with TMS groups.

Determination of Capacity Factors, k', and Enthalpies of Retention, ΔH_R: The retention time of the analyte 1,3,5-tri-*tert*-butylbenzene (**TTBB**) was taken as the column deadtime, t_0, required for the calculation of capacity factors: $k' = (t_r - t_0)/t_0$.[11] All experiments were run at a constant flow-rate of 1.0 mL min^{-1}. To calculate ΔH_R values, k' were measured at various temperatures in the range of −10°C to 70°C with a minimum range of 55°C. To keep the column and the mobile phase at the same temperature the column itself and extra-tubing of 1.0 m (ID 0.25 mm) were placed into a thermostatic bath (water/2-propanol) and the temperature was directly measured at the column with a calibrated Burster S-1220 thermometer. Temperatures were constant (±0.03°C) during all the experiments. The plots of ($R \cdot \ln k'$ vs. $1/T$), each with a minimum of 5 data points, were linear in all studied cases ($R^2 > 0.994$).

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[1] [1a] J.-M. Lehn, *Supramolecular Chemistry, Concepts and Perspectives*, VCH, Weinheim **1995**. – [1b] F. Vögtle, *Supramolekulare Chemie*, Teubner, Stuttgart, **1989**. – [1c] F. Diederich, *Supramolecular Chemistry*, (Eds.: V. Balzani, L. De Cola), Kluwer, Dordrecht, **1992**.

[2] [2a] G. A. Jeffrey, W. Saenger, *Hydrogen Bonding in Biological Structures*, Springer, Berlin, **1994**. – [2b] J. R. Fredericks, A. D. Hamilton, in *Comprehensive Supramolecular Chemistry, Vol. 9* (Eds.: J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle), Pergamon, Oxford, **1996**.

[3] T. H. Webb, C. S. Wilcox, *Chem. Soc. Rev.* **1993**, *22*, 282−292.

[4] [4a] C. Tanford, *The Hydrophobic Effect*, 2nd Ed., Wiley, New York, **1980**. – [4b] J. T. Kellis, K. Nyberg, D. Sali, A. R. Fersht, *Nature* **1988**, *333*, 784−786.

[5] [5a] C. A. Hunter, J. K. M. Sanders, *J. Am. Chem. Soc.* **1990**, *112*, 5525−5534. – [5b] C. A. Hunter, *Chem. Soc. Rev.* **1994**, 101−109.

[6] [6a] F.-G. Klärner, J. Benkhoff, R. Boese, U. Burkert, M. Kamieth, U. Naatz, *Angew. Chem.* **1996**, *108*, 1195−1198; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1130−1133. – [6b] F.-G. Klärner, U. Burkert, M. Kamieth, R. Boese, J. Benet-Buchholz, *Chem. Eur. J.* **1999**, *5*, 1700−1707.

[7] [7a] S. C. Zimmerman, K. W. Saionz, Z. Zeng, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 1190−1193. – [7b] S. C. Zimmerman, K. W. Saionz, *J. Am. Chem. Soc.* **1995**, *117*, 1175−1176. – [7c] S. C. Zimmerman, W.-S. Kwan, *Angew. Chem.* **1995**, *107*, 2589−2592; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2404−2406. Review on chiral recognition by the use of CBSPs: W. H. Pirkle, T.C. Pochapsky, *Chem. Rev.* **1989**, *89*, 347−362.

[8] [8a] J. Benkhoff, R. Boese, F.-G. Klärner, *Liebigs Ann./Recueil* **1997**, 501−516. – [8b] J. Benkhoff, R. Boese, F.-G. Klärner, A. E. Wigger, *Tetrahedron Lett.* **1994**, *35*, 73−76.

[9] W. H. Pirkle, T. C. Pochapsky, G. S. Mahler, D. E. Corey, D. S. Reno, D. M. Alessi, *J. Org. Chem.* **1986**, *51*, 4991−5000.

[10] [10a] C. M. Lochmüller, M. T. Kersey, *Anal. Chem.* **1988**, *60*, 1910−1914. – [10b] C. M. Lochmüller, M. L. Hunnicutt, *J. Phys. Chem.* **1986**, *90*, 4318−4322.

[11] W. H. Pirkle, J. T. Welch, *J. Liq. Chromatogr.* **1991**, *14*, 1−8.

[12] F.-G. Klärner, U. Burkert, M. Kamieth, A. E. Wigger, unpublished results.

[13] [13a] F. Diederich, D. B. Smithrud, E. M. Sanford, T. B. Wyman, S. B. Ferguson, D. R. Carcanague, I. Chao, K. N. Houk, *Acta Chem. Scand.* **1992**, *46*, 205−215. – [13b] J. C. Adrian Jr., C. S. Wilcox, *J. Am. Chem. Soc.* **1992**, *114*, 1398−1403. – [13c] D. A. Stauffer, R. E. Barrans, D. A. Dougherty, *J. Org. Chem.* **1990**, *55*, 2762−2767.

[14] L. R. Snyder in *Chromatography: Fundamentals and Applications of Chromatography and Related Differential Migration Methods, Journal of Chromatography Library*, 5th edition, Elsevier, New York, **1992**, vol. 51A, Chapter 1. It has been argued that the phase ratio Φ should only depend on the amount of stationary phase that can actually interact with the mobile phase, not the total amount of bulk phase, see: C. Horvath, H.-J. Lin, *J. Chromatogr.* **1978**, 149, 43−70.

[15] For potential difficulties in the interpretation of enthalpies of retention see: W. H. Pirkle, R. S. Readnour, *Anal. Chem.* **1991**, *63*, 16−20.

[16] This is not valid for the selectivities in the very nonpolar solvents CCl_4 and cyclohexane. Here the cyano-substituted analytes show nonspecific retention ($0 < k' < 1$ at 298 K) on the reference column.

[17] [17a] P. C. Sadek, P. W. Carr, R. M. Doherty, M. J. Kamlet, R. W. Taft, M. H. Abraham, *Anal. Chem.* **1985**, *57*, 2971−2978. – [17b] P. W. Carr, R. M. Doherty, M. J. Kamlet, R. W. Taft, W. Melander, C. Horvath, *Anal. Chem.* **1986**, *58*, 2674−2680. – [17c] J. H. Park, P. W. Carr, M. H. Abraham, R. W. Taft, R. M. Doherty, M. J. Kamlet, *Chromatographia,* **1988**, *25*, 373−381.

[18] R. W. Taft, J.-L. M. Abboud, M. J. Kamlet, M. H. Abraham, *J. Solution Chem.* **1985**, *14*, 153−175.

[19] W. J. Cheong, P. W. Carr, *Anal. Chem.* **1989**, *61*, 1524−1529.

[20] [20a] M. J. Kamlet, J.-l. M. Abboud, M. H. Abraham, R. W. Taft, *J. Org. Chem.* **1983**, *48*, 2877−2887. – [20b] Y. Marcus, *J. Solution Chem*. **1991**, *20*, 929−942. – [20c] D. C. Leggert, *J. Solution Chem*. **1993**, *22*, 289−296.

[21] [21a] M. J. Kamlet, R. M. Doherty, M. H. Abraham, Y. Marcus, R. W. Taft, *J. Phys. Chem*. **1988**, *92*, 5244−5255. – [21b] M. H. Abraham, J. C. McGowen, *Chromatographia*, **1987**, *23*, 243−246.

[22] R. Foster, *Organic Charge-Transfer Complexes*, (Ed.: A. T. Blomquist), Academic Press, London, **1969**. R. S. Mulliken, *J. Phys. Chem.* **1952**, Ithaca 56, 801.

[23] C. Horváth, W. Melander, I. Molnár, *J. Chromatogr.* **1976**, *125*, 129−156.

[24] [24a] K. T. Chapman, W. C. Still, *J. Am. Chem. Soc.* **1989**, *111*, 3075−3077. – [24b] B. J. Whitlock, H. W. Whitlock, *J. Am. Chem. Soc.* **1994**, *116*, 2301−2311. For the effect of solvent size on noncovalent inter- and intramolecular complexes see also ref.[6]

[25] M. Kamieth, F.-G. Klärner, F. Diederich, *Angew. Chem.* **1998**, *110*, 3497−3500; *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 3303−3306.

[26] This method is similar to affinity chromatography, but does not require elutions with varying concentrations of competing receptor or ligand, thus allowing the simultaneous determination of binding parameters for multiple analytes with a single injection.

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