Linker effects on Amino Acid and Peptide Recognition by Molecular Tweezers

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Abstract: Transition from monotopic symmetrical to ditopic unsymmetrical molecular recognition frequently occurs when a general powerful, but unspecific receptor molecule is transformed into a specific ditopic host. Especially in water, this endeavor is accompanied with great challenges, comprising inter alia host-guest orientation, orthogonal recognition modes and – the nature of the linker unit.

This work represents a case study for a powerful general host for basic amino acids and peptides. The symmetrical molecular tweezer skeleton was systematically desymmetrized and modified with various common linker units, whose profound influence on the molecular recognition profile was studied in detail by NMR spectroscopy, fluorescence titrations, X-ray crystallography and molecular simulations.

A number of diverse effects was discovered and could be attributed to the chemical nature of the different linkers. In general, long alkyl tethers block the tweezers cavity by van-der-Waals contacts to CH groups around its entrance; alkoxyalkyl tethers likewise lower tweezer affinities for basic amino acids by competing self-inclusion. As a general trend, affinities for linkers with ester and carboxylate moieties are substantially higher than those for tethers with ethers and alcohols, most likely, because the electron-rich carbonyl group keeps the cavity open. Additional hydrogen bonds between the linker unit and suitable amino acid or peptide guests greatly support the complexation process; finally high solvent polarity and salt load shift the binding equilibrium from external ion pairing to guest inclusion.

Introduction. Some of the most versatile and powerful classes of artificial receptor molecules which operate in water, contain highly symmetric macrocycles: thus the host compound can completely surround its guest, maximize attractive interactions and efficiently desolvate the contact area. Crown ethers and cryptands, calixarenes and cucurbiturils all benefit from this design, with the disadvantage, that it favors cyclic or symmetric guests. For tight and specific binding to non-symmetric molecules, additional binding sites must be introduced, with a considerable synthetic effort.[1-3] Inter alia, it must be strictly avoided, that the new side arms can be accomodated in the interior of the macrocycle, because this severely impedes guest inclusion.[4]

In recent years, our group has explored new mechanisms of supramolecular interference with protein and peptide activity by means of molecular clips and tweezers.[4-13] These draw the biologically active part of the respective cofactor (NAD^+ or $NADP^+$)[5,6,9] or amino acid (the side chain of Lys and Arg)[5-14] into their cavities, which enables them to reversibly inhibit enzymatic processes as well as protein aggregation events. To develop further their diagnostic as well as therapeutic potential these new drugs must become protein- or peptide-specific, and thus avoid unwanted side effects. Since only one phosphate is used for ammonium- or guanidinium recognition, the other one may be replaced by a second binding site, connected to the parent tweezers by a suitable linker, which corresponds to the distance between both functional groups on the protein surface.[11-12]

This new concept of ditopic peptide and protein recognition critically depends on the choice of the appropriate linker. Important prerequisites are hydrolytic stability under physiological conditions and sufficient conformational flexibility to adjust to dynamic changes and to

maintain complexation entropy terms low. A linker can contribute favorably to the overall protein binding event, if it engages in additional attractive interactions and displaces solvent molecules from the protein surface. On the other hand, a linker can also inhibit peptide or protein recognition, if it is repelled from the protein surface or if it prevents the access of surface–bound amino acid residues to one of the connected binding sites. Earlier observations from substituted neutral tweezer derivatives in organic media quite often demonstrated self-inclusion of extended aliphatic side chains, with the result, that guest affinities remained very modest, if binding was not blocked at all.[4] This unsatisfying behavior poses the open question, if also in buffered aqueous solution, certain linkers block the cavity entrance to our anionic phosphate tweezers, and prevent free access of amino acid and peptide guests. In this manuscript we would like to answer this question and adress some of the above-mentioned issues. By choosing common linker types and by their systematic introduction to the same tweezer functionality, we hope to present an interesting case study, which will reveal typical aspects of the individual linkers' supramolecular properties.[15]

Results and Discussion. Common linkers which are often used in synthetic drug candidates to combine an alcohol with another active part of the molecule, are mainly based on ether and ester functionalities. Ethers are usually preferred over esters because of their greater hydrolytic stabilities. On the other hand, polar chains are considered to avoid unwanted hydrophobic clustering as well as increase water solubility of the resulting drug candidates.[16]

In Figure 1, both lines are headed by our parent diphosphate tweezer **5** and its truncated monophosphate analogue **1**, which represent the reference compounds. The remaining derivatives show our synthetic models for unsymmetric molecular arginine and lysine tweezers which carry the above-mentioned linker units on one side and a phosphate anion on the other side of their central hydroquinone. The top row continues with ether junctions of various size and polarity, whereas the bottom row shows unsymmetrical tweezers with esters and carboxylate moieties. **4** and **7/8** carry anchor points for the covalent attachment of a secondary binding site (Fig. 1).

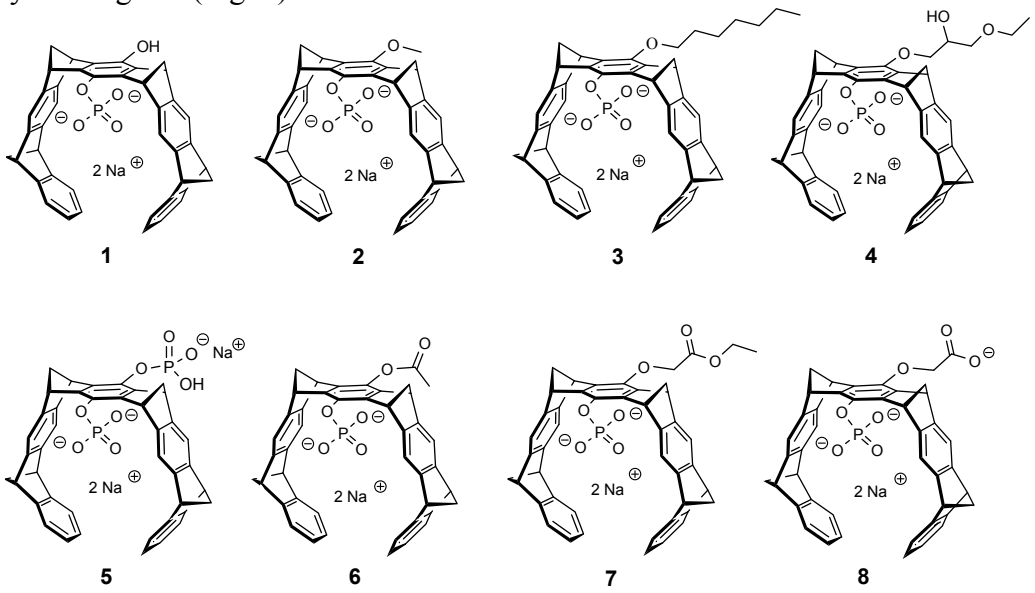
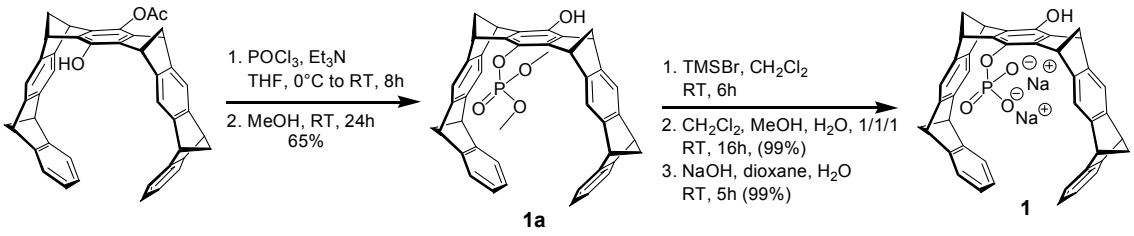
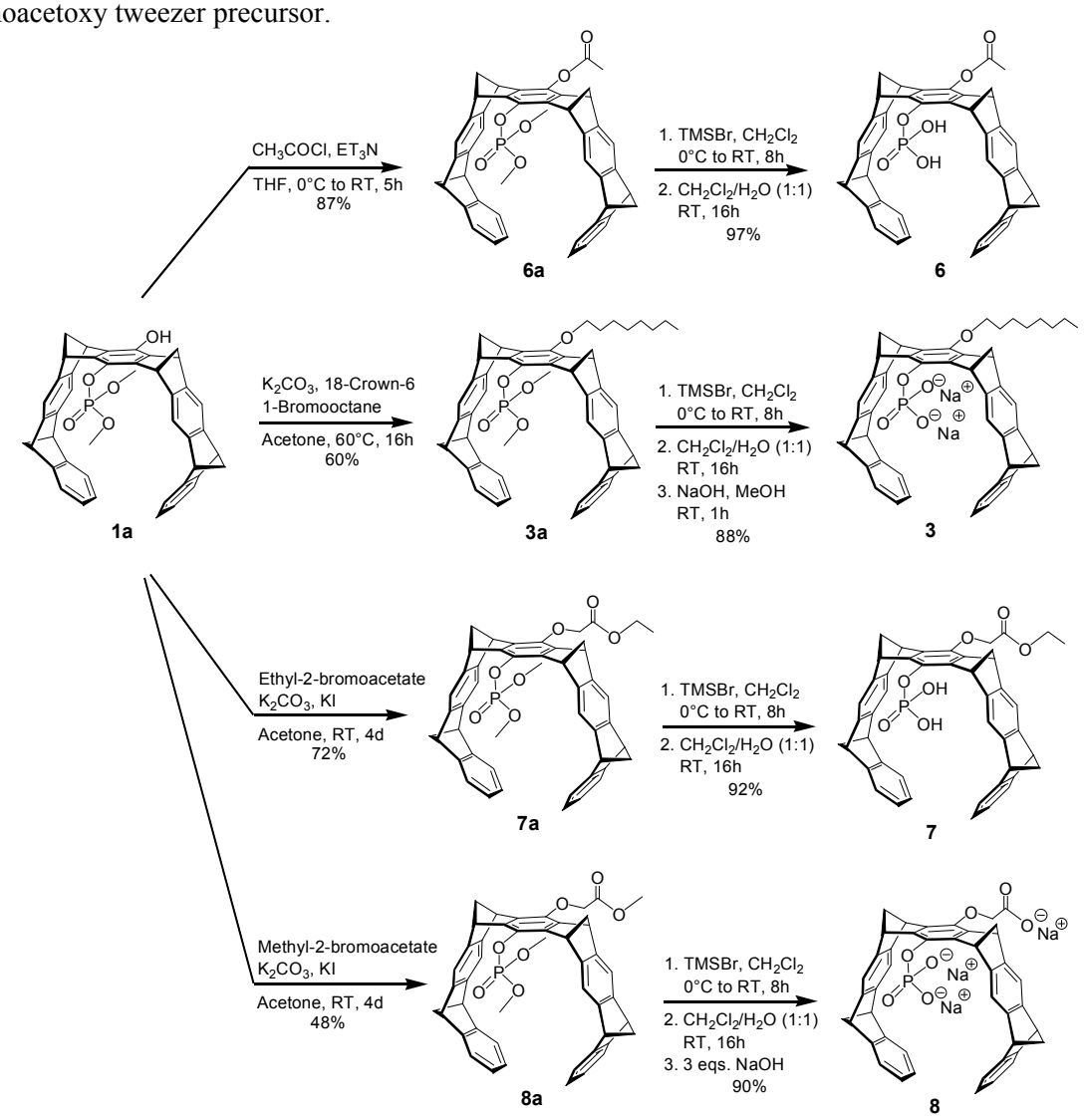


Figure 1. Reference compound **1** and **5** together with models for unsymmetrical Arg- and Lys-tweezers as monophosphate anions with varying ether (top row) and ester links (bottom row).

Synthesis of New Tweezers. Most synthetic routes start from protected monophosphate tweezer **1a** (Scheme 1). This in turn can be prepared from the known monoacetoxy tweezer by phosphorylation with $POCl_3$/triethylamine. As a convenience, esterification of the intermediate phosphoryl chloride with excess methanol also cleaves the acetyl group and directly furnishes **1a**. For complete removal of both methyl esters on phosphorus, trimethylsilylbromide qualified as a powerful reagent, which acts under mild conditions and leaves ester as well as ether links untouched.[17,18]



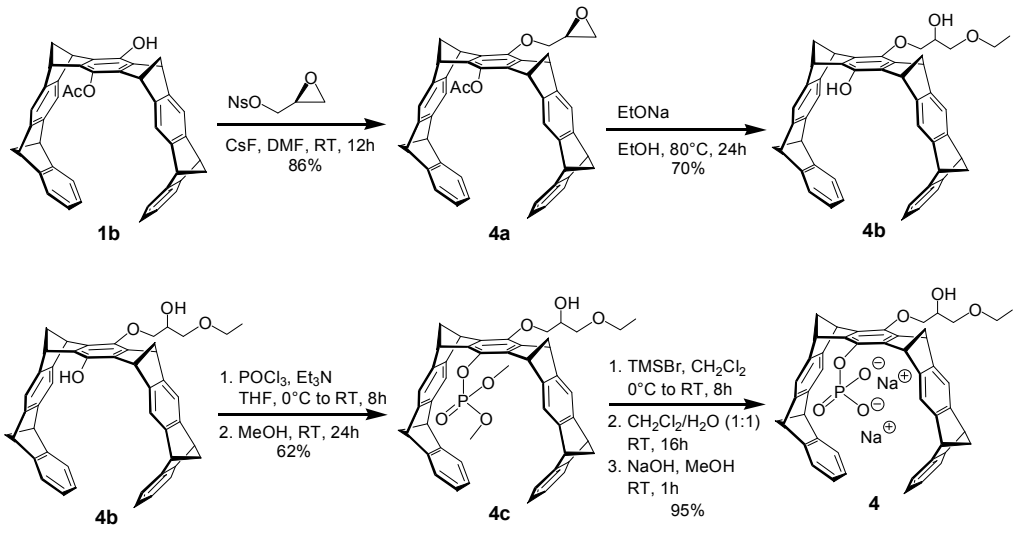
Scheme 1. Synthesis of monophosphate tweezer in its protected (**1a**) and anionic form (**1**) from the monoacetoxy tweezer precursor.



Scheme 2. Introduction of aliphatic ester and ether moieties via acylation and alkylation of **1a** to afford unsymmetrical tweezers **3** and **6-8**.

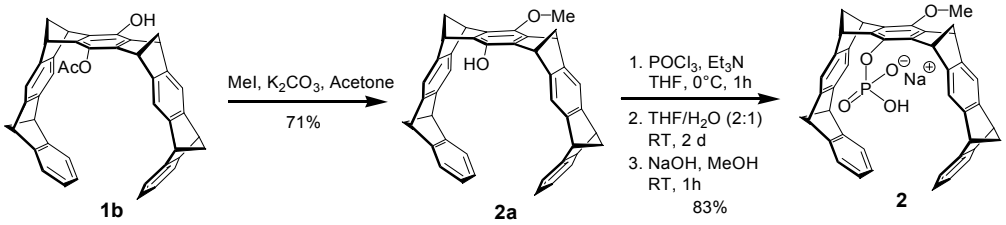
Acetylation of the free hydroxyl group in **1a** followed by complete dealkylation on phosphorus leads to the acetoxy tweezer **6** (Scheme 2). All alkyl ethers were made via nucleophilic displacement strategies on alkyl halides (**3**,**7**) or epoxides (**4**). Herein, the mono(dimethylphosphate) tweezer **1a** was deprotonated to generate the nucleophilic phenoxide anion, which reacted with 1-bromooctane under phase transfer catalysis with the aid of 18-crown-6.[19] Alternatively, Finkelstein conditions were established by addition of KI in acetone, so that ethyl (2-bromoacetate) was also smoothly displaced by the tweezer phenoxide. Treatment with trimethylsilyl bromide selectively cleaved both methyl esters on phosphorus **(7)**; subsequent saponification allowed quantitative removal of a carboxylate methyl ester group leading to **8**.

Finally, the monoacetoxy precursor was treated with glycidyl nosylate and furnished the respective epoxide ether **4a** (Scheme 3). Following a protocol from Furukawa and Otera[20], a 6-fold excess of CsF was employed which served a dual purpose: one equivalent deprotonates the phenol as a non-nucleophilic base and generates the highly nucleophilic cesium phenoxide, another equivalent binds the resulting sulfonic acid. The nitrobenzenesulfonate derivative directs the nucleophilic attack exclusively to the C-1 position, so that no racemization occurs at C-3. During subsequent ring opening with excess sodium ethoxide, the acetoxy group is once more simultaneously cleaved, leading to intermediate **4b** with a phenolic and a secondary aliphatic hydroxyl moiety. This reaction can later be used to introduce the second binding site from alcohols or amines. Phosphorylation with $POCl_3/Et_3N$ takes place exclusively on the phenol (**4c**), and generates, after hydrolysis and neutralisation, the disodium salt of glycerol tweezer phosphate **4**.



Scheme 3. Introduction of epoxide ethers by regioselective attack of the monoacetoxy precursor on glycidyl nosylate, assisted by excess CsF, and further processing into glycerol tweezer phosphate **4**.

Similarly, monomethylation of the monoacetoxy precursor with methyl iodide, followed by phosphorylation with $POCl_3$, hydrolysis and neutralization afforded the short methyl ether derivative **2** (Scheme 4).



Scheme 4. Generation of a methyl ether by attack of the monoacetoxy precursor on methyl iodide, and further processing into methoxy tweezer phosphate **2**.

Characterization of the new unsymmetric tweezers. All new tweezer derivatives as well as their intermediates have been fully characterized by spectroscopic methods. The existence of the phosphate moiety has been unequivocally established by HRMS and ^{31}P NMR spectroscopy. The unsymmetrical tweezers are all soluble in water (1 - 50 μM). Only for NMR measurements at millimolar concentrations, methanol was added to the aqueous buffer (CD_3OD/D_2O phosphate buffer 2:1).

Inspection of NMR spectra of the pure host derivatives in the above-mentioned buffer at pH 7.2 revealed that the short acetyl tether in **6** does not undergo self-inclusion in the tweezer cavity. However, the highly flexible ether moieties in **7** ($\Delta\delta \sim 2.0$ ppm in 2:1 methanol/aqueous buffer) as well as **4** ($\Delta\delta \sim 0.5$ ppm in 2:1 methanol/aqueous buffer) displayed significant upfield-shifts compared with their isolated counterparts, indicating that especially the terminal methyl group pointed inside the open cavity. The size of this effect depends on the polarity of the solvent and increases from methanol to water – obviously a hydrophobic interaction. Interestingly, the O-*n*-octyl derivative does not include its alkyl chain inside the cavity – a counterintuitive observation.

Evidently, besides the hydrophobic effect electrostatic interactions are also important for the threading of the side chains into the tweezers' cavity. The inductive electron-withdrawing effect of the ester or ether oxygen atoms in **4** and **7** causes a more positive electrostatic potential surface on the terminal side chain methyl group than in **3** (Figure 2), so that these groups are preferentially bound inside the tweezers' cavity as opposed to the O-*n*-octyl group in **3**.

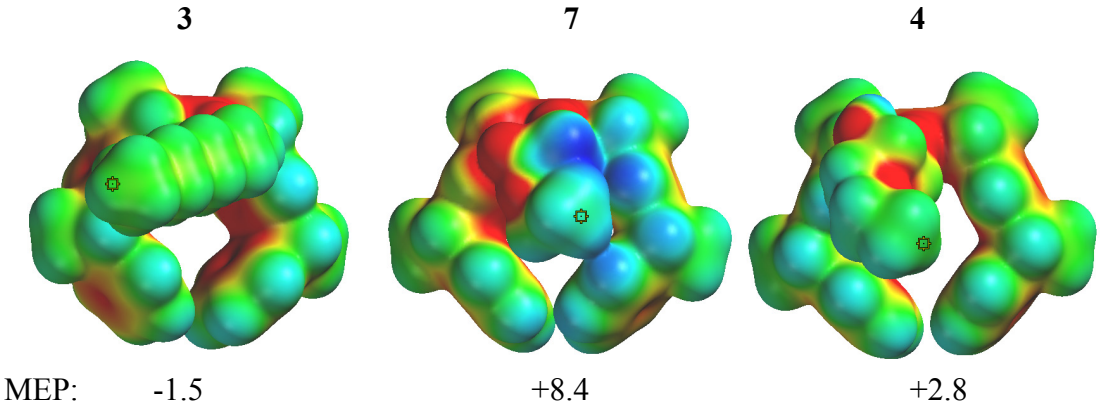


Figure 2. Electrostatic potential surface (EPS) calculated by AM1 for the molecular tweezers substituted in the central benzene bridge by O-*n*-octyl (left, **3**), $OCH_2CO_2CH_2CH_3$ (middle, **7**), and $OCH_2CH(OH)CH_2OCH_2CH_3$ (right, **4**). The color code spans from -25 (red) to +25 kcal/mol (blue). The molecular electrostatic potentials (MEPs in kcal/mol) are calculated at the marked positions at the terminal methyl group of the side chain. (For a better visibility of the side chain alkyl groups tweezers' conformations with extended side chains were used for the EPS calculations.)

The aromatic tweezer signals do not show any concentration-dependent upfield-shifts and thus confirm the absence of entangled dimers; in addition, no experimental evidence was found for intermolecular self-association.[9]

For **3** and its protected dimethyl phosphate precursor **3a**, single crystals could be grown and their solid state structure was determined by means of X-ray diffraction. Free phosphoric acid **3** crystallizes in the tetragonal space group $I4_1/a$; in the asymmetric unit, one tweezers molecule is accompanied by two water and two methanol molecules (Fig. 3). One methanol molecule is located inside the tweezers cavity, with its OH-group oriented towards the phosphate moiety. In accordance with the NMR evidence, no intramolecular alkyl inclusion takes place, but instead the *n*-octyl chains group in a helical arrangement around a 4_1 screw axis, most likely engaged in van-der-Waals and CH-π interactions. Due to the limited crystal quality these are not discussed in detail (see SI). A view of the packing along [001] brings forward some intermolecular inclusion effects (hydrophilic groups and solvents conglomerate around a 4_1 screw axis) which are, however, absent in aqueous solution.

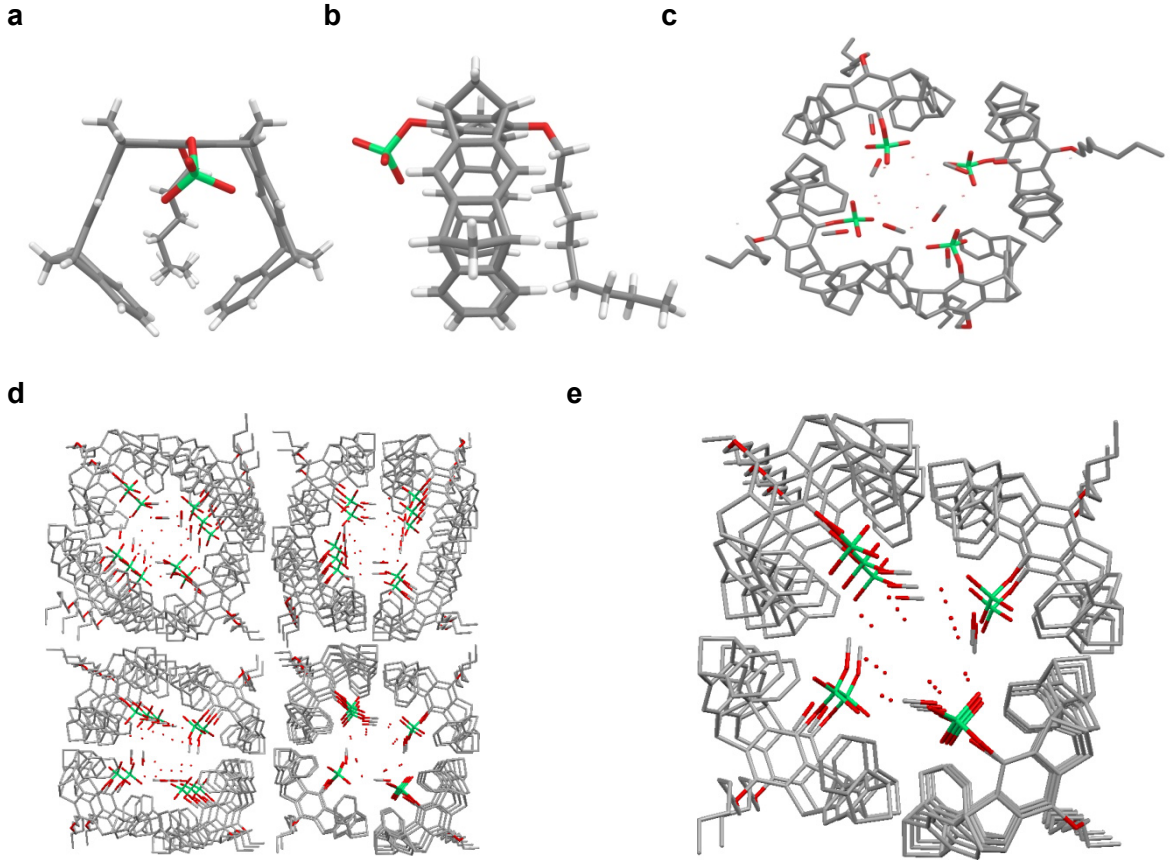


Figure 3. Crystal structure and packing for **3**: **a** front view into the cavity; **b** side view; **c** Arrangement of four tweezer molecules around a 4_1 screw axis each complexing a methanol molecule (view parallel to [001]); **d** and **e** Molecule packing produces a helical tube or channel like structure along a 4_1 screw axis with hydrophobic exterior (octyl chain and tweezer backbone) and hydrophilic interior (phosphate groups, solvent molecules).

The crystal structure for dimethyl phosphate precursor **3a** is shown and discussed in detail in the Supporting Information. Again, the octyl tail is not inserted into the tweezers cavity.

Molecular mechanics calculations followed by extensive Monte-Carlo simulations were carried out for all new tweezer derivatives **2-8**, and the best final structures which were confined to a narrow energy window of 10 kJ/mol were analyzed with respect to their conformational preference (Maestro 9.2, OPLS_2005, water, 5000 steps). The results beautifully confirmed the NMR-spectroscopic evidence (Fig. 4): Open conformations prevail for monoacetoxy tweezer **6**. By contrast, the octyl chain in **3** remains in close van-der-Waals contact with the CH groups flanking the cavity opening, precisely as depicted in the crystal structure. The flexible ester and ether tethers in **7** and **4**, finally both insert their terminal ethyl group into the tweezer cavity, in perfect agreement with the observed upfield-shifts in the ^{1}H NMR spectrum. It may be hence expected, that **6** with its open cavity is superior in binding of amino acid and peptide guests, whereas the octyl group in **3** blocks the cavity entrance and in **4/7**, the cavity is already occupied, leading to lowered guest affinities.

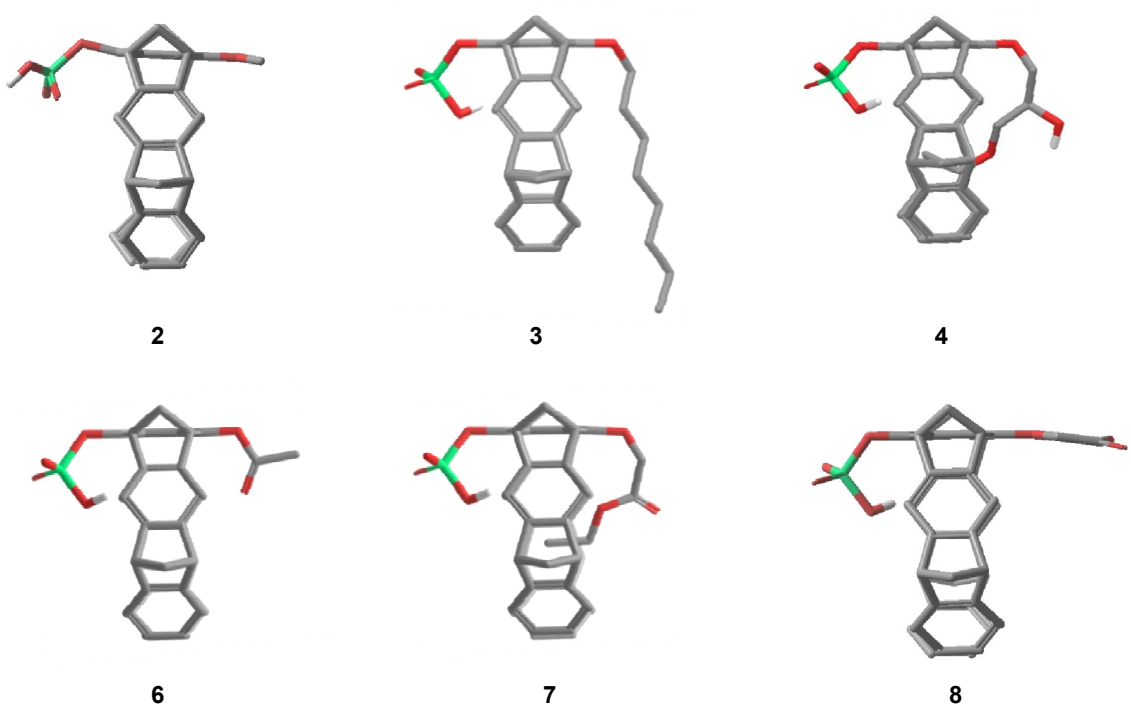


Figure 4. Lowest energy conformations found for tweezers **2-4** and **6-8** in Monte-Carlo simulations in water (Maestro 9.2, OPLS_2005, water, 5000 steps). Stick models, non polar hydrogen atoms omitted for clarity.

Guest Binding – Amino Acids. For a reliable determination of Arg and Lys affinities, fluorescence titrations were carried out with representative *N/C*-protected amino acid derivatives in aqueous buffer with all new unsymmetric tweezer derivatives. At pH 7.6 the phosphate groups of the tweezers **2-8** are partially protonated. Thus, these compounds exist as mixtures of the phosphate ($ROPO_3^{2-}$ $2Na^+$) and hydrogenphosphate salts ($ROP(OH)O_2^-$ Na^+). The high fluorescence emission intensity of the tweezer skeleton is efficiently quenched by guest binding, if the guest is included inside the cavity (vide infra; external binding leads to a significant fluorescence increase). K_d values cover a relatively broad range from the low millimolar to the low μM regime.

Replacement of one phosphate anion in **5** by a hydroxyl moiety in **1** leads to a substantial loss in free binding energy (~ 1.99 kcal/mol for AcLysOMe). This is mainly an entropy effect, because the amino acid guest can enter the tweezer cavity of diphosphate **5** in either orientation, whereas in monophosphate **1** the cationic side chain must be placed on the

phosphate site. The simple ester linkers in **6** and **7** can counterbalance this effect, indicating, that the acetyl as well as the ethoxycarbonylmethyl group must take part in molecular recognition of their amino acid guests in a positively cooperative fashion. As a general trend, affinities for linkers with ester moieties (**6-8**) are substantially higher than those for tethers with ethers and alcohols (**2-4**). Thus, the octyl and the self-included glycerol side chain represent the most critical obstacles for guest inclusion.

Table 1. Affinities of di- and monophosphate reference **1-8** as well as unsymmetrical monophosphate tweezers **2-4** and **6-8** with ether and ether linkages for N/C-protected lysine and arginine derivatives, displayed as K_d values (dissociation constants). Fluorescence titrations were carried out in 10 mM phosphate buffer at pH 7.6. At this pH the phosphate groups of the tweezers are partially protonated.

Tweezer	Amino Acid	K_d [μM]	ΔI_{max} [% change]
1	AcLysOMe ⋅HCl	260 (±06%)	146 [26%]
	AcArgOMe ⋅HCl	110 (±18%)	372 [50%]
2	AcLysOMe ⋅HCl	**40** (±11%)	190 [36%]
	AcArgOMe ⋅HCl	120 (±18%)	120 [23%]
3	AcLysOMe ⋅HCl	>1000	<10 [<2%]
	AcArgOMe ⋅HCl	>1000	<10 [<2%]
4	AcLysOMe ⋅HCl	370 (±23%)	380 [60%]
	AcArgOMe ⋅HCl	620 (±42%)	440 [75%]
5	AcLysOMe ⋅HCl	**9** (±06%)	240 [40%]
	AcArgOMe ⋅HCl	**20** (±05%)	280 [47%]
6	AcLysOMe ⋅HCl	**35** (±10%)	200 [34%]
	AcArgOMe ⋅HCl	**45** (±13%)	190 [31%]
7	AcLysOMe ⋅HCl	**45** (±04%)	280 [46%]
	AcArgOMe ⋅HCl	**90** (±07%)	230 [40%]
8	AcLysOMe ⋅HCl	**70** (±05%)	430 [59%]
	AcArgOMe ⋅HCl	100 (±11%)	350 [56%]

[a] 10 mM Bis-Tris buffer, pH 6.0

In line with observations from other tweezer derivatives, affinities for lysine are usually 2-3 times higher than those for arginine, with one interesting exception: The short acetyl derivative **6** binds arginine equally well as lysine (K_d < 50 μM) and thus becomes the first arginine-and-lysine tweezer. Its K_d value is the lowest ever reported for an arginine derivative in aqueous buffer and holds promise for specific interference with biological processes which critically depend on strategic arginine residues.

NMR experiments offer more structural information than fluorescence titrations, if chemical shift changes of sensor protons occur during the addition of the host to its amino acid guest. (Fig. 5). Representative new tweezer derivatives (**4**, **6, 7**) were therefore first measured alone and then in their complexes with AcLysOMe and AcArgOMe. Stoichiometric ratios varied

from host excess over 1:1 ratio to guest excess. All chemical shift changes in guest protons are listed in Tables 1-2 of the Supporting Information.

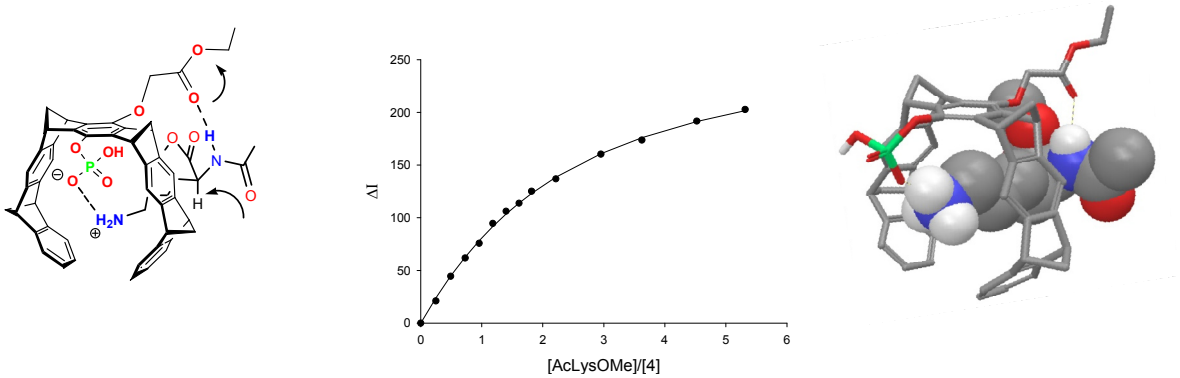


Figure 5. Left: Schematic representation of the preferred complexation mode for Ac-Lys-OMe by tweezer **7** with ethyl hydroxyacetate linker; center: fluorescence titration binding isotherm; right: molecular dynamics simulation after 70 ns (MacroModel 9.2, OPLS_2005, water/GBA, 298 K, no restraints).

In all cases, **lysine** methylene signals are broadened and drastically shift upfield (to smaller δ values) in aqueous buffer, indicating specific inclusion of its ammonium butyl side chain (methanol-aqueous buffer). These chemical shift changes are accompanied by sizeable downfield shifts of the self-included receptor tethers of **4** and **7**. With increasing excess of the lysine guest, the receptor molecule releases its non-polar arm from its own cavity to accommodate the amino acid side chain – a beautiful illustration of two competing inclusion processes. There is a substantial difference in the K_d values between the arginine (or lysine) complexes of the self-included tweezers **4** and **7** (Table 1: 8-fold K_d values ~ +1.2 kcal/mol in ΔG). If the calculated structures shown in Fig 4 represent the tweezers correctly, the ^{1}H NMR shift differences Δδ of the terminal side chain methyl groups should be similar in both compounds **4** and **7**. In order to explain the different Δδ values of ~2 ppm for **4** and ~0.5 ppm for **7**, we have to assume different equilibrium states between tweezers with folded or extended side chain. Most likely **4** prefers the folded structure whereas **7** favors the extended structure. Consequently, the additional attractive host-guest interactions gained from amino acid inclusion in **4** (Fig. 5) must be largely used to compensate the costly extrusion of its side chain out of the tweezers' cavity. By contrast, the full binding energy is gained in complexes with **7**.

Due to their somewhat lower solubilities at millimolar concentrations, **arginine** complexes were intially measured by NMR spectroscopy in methanol/water mixtures. Contrary to the lysine complexes, only very small upfield-shifts of the side chain methylene protons were produced, incompatible with their inclusion inside the tweezers cavity.[21] However, when the solvent composition was gradually shifted towards pure aqueous buffer, the upfield shifts became successively restored. This important observation was independently confirmed by fluorescence titrations with **6** and **7** in methanol/buffer mixtures of increasing polarity (Table 2): in pure methanol almost no interaction could be observed (negligible fluorescence changes); however, successive addition of aqueous buffer (PB) to the methanol solution lead to increasing fluorescence quenching, strictly correlating with increasing guest affinity. The table also reveals a special case: **6** bound AcLysOMe weakly in pure methanol, accompanied by a seizable increase in fluorescence emission intensity. In a (1:9) mixture of MeOH/PB no change in the fluorescence intensity was observed; finally, in pure PB the tweezers' emission was again partially quenched by the addition of the amino acid guest, as already pointed out above (Table 1). We conclude that in methanol lysine derivatives are bound weakly outside

the tweezers cavity (leading to the observed increase in the fluorescence intensity). In this less polar solvent the salt bridge between negatively charged tweezers phosphate groups and positively charged guest ammonium or guanidinium groups is the dominating host-guest binding force which does not require a threading of the amino acid side chain into the tweezers' cavity. In aqueous buffer the salt bridge becomes weaker and the host-guest binding is governed by π-cation, dispersive, and hydrophobic forces, which are evidently optimal in the host-guest complex structures with the side chain threaded into the tweezers' cavity.[22] The assumption, that dispersive and hydrophobic forces dominate the internal binding mode in aqueous solution, is supported by the finding that addition of 150 mM NaCl does not have a profound influence on tweezer affinities, which are lowered only by a factor of ~ 2 (see below PB vs. PBS). The findings, that in pure methanol the tweezers' emission intensity is increased by the addition of a guest and in pure PB decreased, whereas the complexation-induced shifts of the ^{1}H NMR guest signals in methanol are small in contrast to the large shifts found in PB, indicate that the different changes in the emission intensities observed either in methanol or PB also provide information on the host-guest complex structures comparable to the ^{1}H NMR spectra. Evidently, the tweezers' emission is quenched by the threading of the guest side chain into the tweezers'cavity and increased by binding the guest molecule outside the cavity. In the cases where no change in the emission was observed, one can assume that there is an equilibrium between outside and inside bound guest molecule, so that the two effects on the emission just compensate each other. The above described solvent dependence was recently also discovered for symmetrical diphosphate and disulfate tweezers.[21]

Table 2. Dissociation constants K_d [μM] and % fluorescence changes determined for tweezers **6** and **7** interacting with N/C-protected lysine and arginine in solvents of increasing polarity (methanol, methanol/buffer, pure phosphate buffer, 10 mM, pH 7.6) by fluorescence titrations.

Host molecule	Amino acid guest	Solvent	K_d [μM]	ΔI_{max} [relative change]
Acetoxy-Phosphate Tweezers **6**	AcLysOMe	MeOH	641 ± 18 %	-317 (50 %)
		MeOH:PB (1:4)	129 ± 16%	-54 (9%)
		MeOH:PB (1:9)	n.d.	n.d.
		PB	34 ± 10 %	203 (34%)
		PBS	72 ± 13 %	161 (30%)
	AcArgOMe	MeOH	n.d.	No change in FL
		MeOH:PB (1:4)	n.d.	16 (3%)
		MeOH:PB (1:9)	166 ± 41%	37 (6%)
		PB	44 ± 13 %	188 (31%)
		PBS	94± 15 %	223 (42%)
Ethoxycarbonyl-Phosphate Tweezers **7**	AcLysOMe	MeOH	n.d.	No change in FL
		MeOH:PB (2:1)	n.d.	No change in FL
		MeOH:PB (1:9)	n.d.	10 (2%)
		PB	44 ± 4%	277 (46%)
	AcArgOMe	MeOH	n.d.	No change in FL
		MeOH:PB (2:1)	n.d.	No change in FL
		MeOH:PB (1:9)	n.d.	31 (4%)
		PB	92 ± 7%	227 (40%)

PBS: phosphate buffer saline (150 mM NaCl, pH 7.6). Negative ΔI_{max} values indicate an increase in fluorescence emission intensity upon guest addition. Positive ΔI_{max} values stand for a decrease in fluorescence emission intensity (quenching) upon guest addition; n.d.: not determined, due to very small or no changes in fluorescence emission intensity.

The structural information available from ^{1}H NMR and fluorescence experiments was fed into starting geometries for molecular mechanics calculations of all lysine and arginine

complexes with our new unsymmetrical phosphate tweezers. Minimizations were followed by Monte-Carlo and subsequent Molecular Dynamics simulations. In all complexes the amino acid side chain is easily threaded through the tweezer cavity and locks its ammonium or guanidinium cation into a strong ion pair with the phosphate anion, without the need to pay the penalty for phosphate desolvation. Additional attractive interactions occur between oxygen atoms of the tethers and the carboxamide NH protons. These hydrogen bonds are especially effective and short in complexes with tweezers **6** and **7**.

A unique difference in threading between all lysine and all arginine derivatives is suggested from the calculations: the tweezer phosphate prefers a double hydrogen bond interaction with the included guanidinium cation and thus extracts it out of the cavity, whereas the ammonium ion remains singly hydrogen bonded hidden inside (Figure 6). The double NH…O hydrogen bond is indeed the most favorable guanidinium phosphate interaction, which is also formed in complexes between regulatory proteins and DNA.

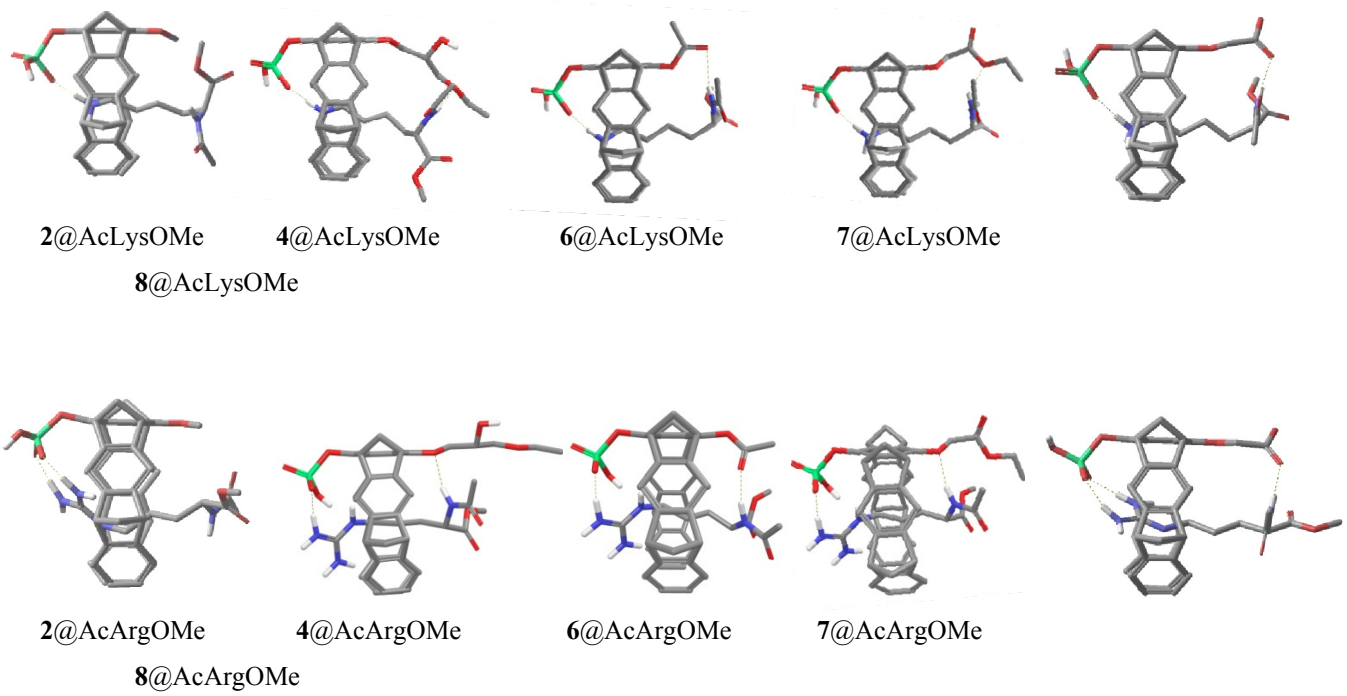


Figure 6. Lowest energy structures found for complexes between unsymmetrical tweezers **2, 4**, **6-8** and AcLysOMe (top row) as well as AcArgOMe (bottom row) by Monte-Carlo simulations in water (MacroModel 9.2, OPLS_2005, water/GBA, 5000 steps).

It is instructive to compare the new unsymmetrical tweezer derivatives **2** and **8** with closely related structures: Thus methoxyphosphate **2** stands between the simple monophosphate **1** and the octyloxy phosphate **3**, and carboxylate/phosphate **8** is a hybrid between diphosphate (**5**) and the tweezer substituted by two OCH_2COO^- Na^+ groups in the central benzene bridge.[21] An extended selection of basic amino acid derivatives with free N-terminus or N- and C-terminus (Table 3) illustrates the hybrid character of **2** and **8**: even the small methoxy group in **2** seems to partially block the cavity entrance, so that even the doubly cationic free *N*-terminus of C-protected and free amino acids cannot be engaged in an additional ion pair (supported by MD simulations). Similarly, janus-shaped **8** combines two drastically different anionic moieties which seem to act independent of each other: the phosphate operates efficiently and draws amino acid guests inside the cavity, but the methylcarboxylate is unable to further increase free binding energies to any basic amino acid derivative. Even the self-included ethyl ester derivative **7** binds lysine and arginine derivatives more efficiently than its

charged counterpart **8**. Measurement at acidic pH (4.0) further lowers amino acid affinities; however, this effect may also be explained by partial phosphate protonation. The total failure of the tweezers-based methylcarboxylate anion to recognize basic amino acids remains hard to explain. It must be connected with the additional methylene group between the oxygen atom and the carboxylate ($O\mathbf{CH_2}COO^-$).

Table 3. Affinities of unsymmetrical monophosphate tweezers **1**, **2** and **8** for N/C-protected, C-protected and free lysine and arginine derivatives, displayed as K_d values (dissociation constants). Fluorescence titrations were carried out in 10 mM phosphate buffer at pH 7.6.

Guest	Tweezers **1** K_d [μM]	Tweezers **2** K_d [μM]	Tweezers **8** K_d [μM]	Tweezers **8**[a] K_d [μM]
AcLysOMe • HCl	260 (±23%)	40 (±11%)	70 (±05%)	193 (±08%)
AcArgOMe • HCl	110 (±18%)	120 (±18%)	100 (±11%)	—
HLysOMe • 2HCl	**15** (±21%)	45 (±12%)	40 (±17%)	90 (±08%)
HArgOMe • 2HCl	**15** (±05%)	440 (±06%)	100 (±14%)	—
HLysOH • HCl	150 (±09%)	800(±14%)	300 (±19%)	520 (±13%)
HArgOH • HCl	130 (±14%)	340(±14%)	330 (±13%)	—

[a] 10 mM citric acid / phosphate buffer, pH 4.0

Guest Binding – Peptides. In order to test, if lysine and arginine inclusion by our new unsymmetrical tweezers also operate efficiently in a peptidic environment, several biologically important short peptidic guests were selected and titrated with the best binders. KAA builds bacterial cell walls,[23] KLVFF is the central hydrophobic cluster (CHC) within the Aβ sequence,[24] which is discussed as potential nucleation site for pathological protein aggregation (Alzheimer's disease); $IAPP_{1-7}$ and $IAPP_{2-14}$ finally represent C-terminal fragments of the islet amyloid polypeptide, whose unwanted aggregation is resonsible for diabetes mellitus type II.[25] All these peptides carry critical lysine or arginine residues, which are most likely involved in biological recognition processes - many of them at the (doubly cationic) *N*-terminus.

Table 4. Affinities of unsymmetrical monophosphate tweezers **1**, **2**, **6**, **7** and **8** for free peptides of biological relevance, displayed as K_d values (dissociation constants). Fluorescence titrations were carried out in 10 mM phosphate buffer at pH 7.6.

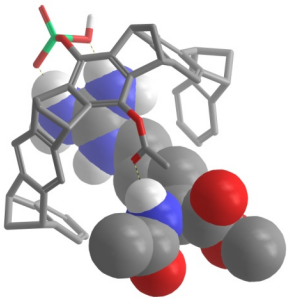
Guest	Tweezers **1** K_d [μM]	Tweezers **2** K_d [μM]	Tweezers **6** K_d [μM]	Tweezers **7** K_d [μM]	Tweezers **8** K_d [μM]
KAA	76 (± 08%)	690 (± 26%)	100 (± 07%)	658 (± 48%)	390 (± 08%)
KLVFF	72 (± 06%)	420 (± 47%)	**44** (± 08%)	114 (± 14%)	-
$IAPP_{1-7}$	48 (± 09%)		**41** (± 12%)	118 (± 06%)	-
$IAPP_{2-14}$	149 (± 24%)		82 (± 17%)	96 (± 36%)	-

Conclusion. In summary, new unsymmetrical monophosphate tweezers have been synthesized, which carry ester and ether linkers on the opposite side. Fluorescence and NMR binding studies with N/C-protected basic amino acids and peptides are supported by molecular simulations and crystal structure analyses. The synopsis of all experimental results draws a picture of the influence of certain linkers on their complexation ability that helps to answer the introductory question: Do certain spacer moieties block the cavity entrance to our anionic phosphate tweezers, and prevent free access of amino acid and peptide guests? And can we identify favorable arrangements, which take part in ditopic molecular recognition of amino acid and peptide guests in a positively cooperative fashion?

This investigation has shown, that long alkyl tethers block the tweezers cavity by van-der-Waals contacts to CH groups around its entrance (**3**); alkoxyalkyl tethers likewise lower tweezer affinities for basic amino acids by competing self-inclusion (**4, 7**). As a general trend, affinities for linkers with ester and carboxylate moieties (**6-8**) are substantially higher than those for tethers with ethers and alcohols (**2-4**). Most likely, the strongly polarized carbonyl group in short esters maximizes electronic repulsion with the electron rich cavity and thus keeps the cavity open. The acetyl tweezer **2** is the first arginine-and-lysine tweezer, which actively supports arginine and lysine complexation in peptides by additional strong hydrogen bonds; it seems well suited for specific interaction with biological processes which rely on critical *N*-terminal lysines.

Outlook. From the above-discussed series of unsymmetrical molecular tweezers, ester links seem to guarantee an open cavity for the efficient inclusion of both lysine and arginine derivatives. However, for their use, hydrolysis at lower or higher pH or by enzymes must be prevented by all means. For this reason, slim ester types with pronounced stability towards pH changes must be found; alternatively, the OH group of the monophosphate tweezer **1** could be replaced by a primary amine via Smiles rearrangement.[26] Its connection to secondary binding sites could then be smoothly effected with carboxylic acid derivatives by conventional peptide coupling. Research in this direction is underway in our laboratory.

Acknowlegments. We thank the University of Duisburg Essen and the Bruno-Werdelmann foundation for continued support of this project.



TOC Figure. Unsymmetrical molecular tweezers with an acetyl linker bind tightly to AcArgOMe by ditopic recognition and simultaneous inclusion within the aromatic cavity (100 ns MD simulation).

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Supporting Information

Linker effects on Amino Acid and Peptide Recognition by Molecular Tweezers

Som Dutt, Constanze Wilch, Thomas Gersthagen, Cristoph Wölper, Andrea Anna Sowislok, Frank-Gerrit Klärner,* Thomas Schrader*

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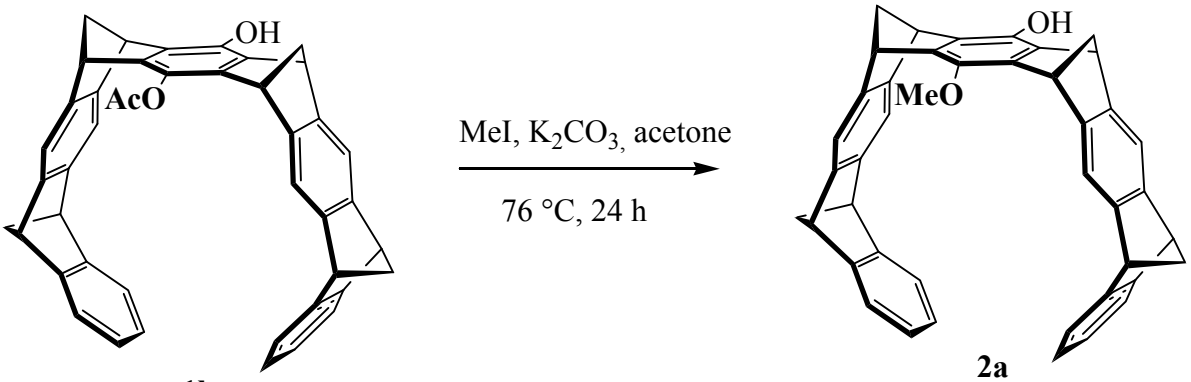


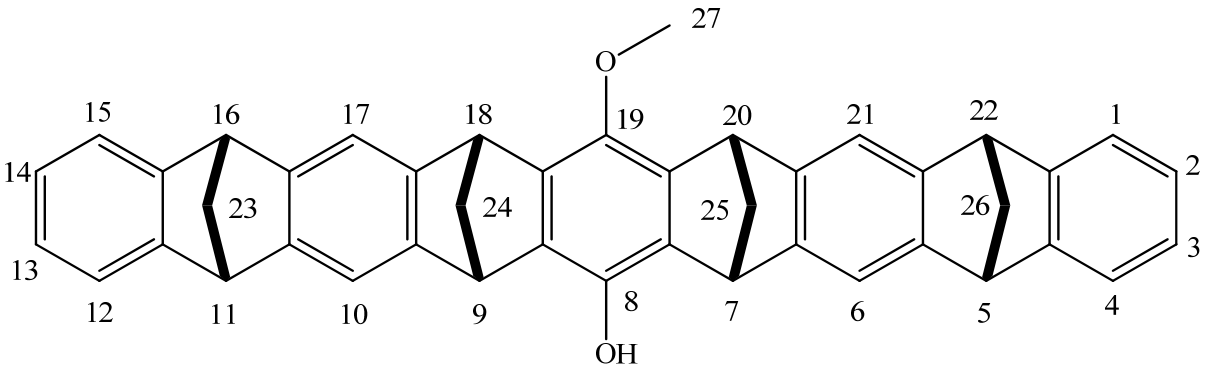
1b
$C_{44}H_{32}O_3$
608.72 g/mol

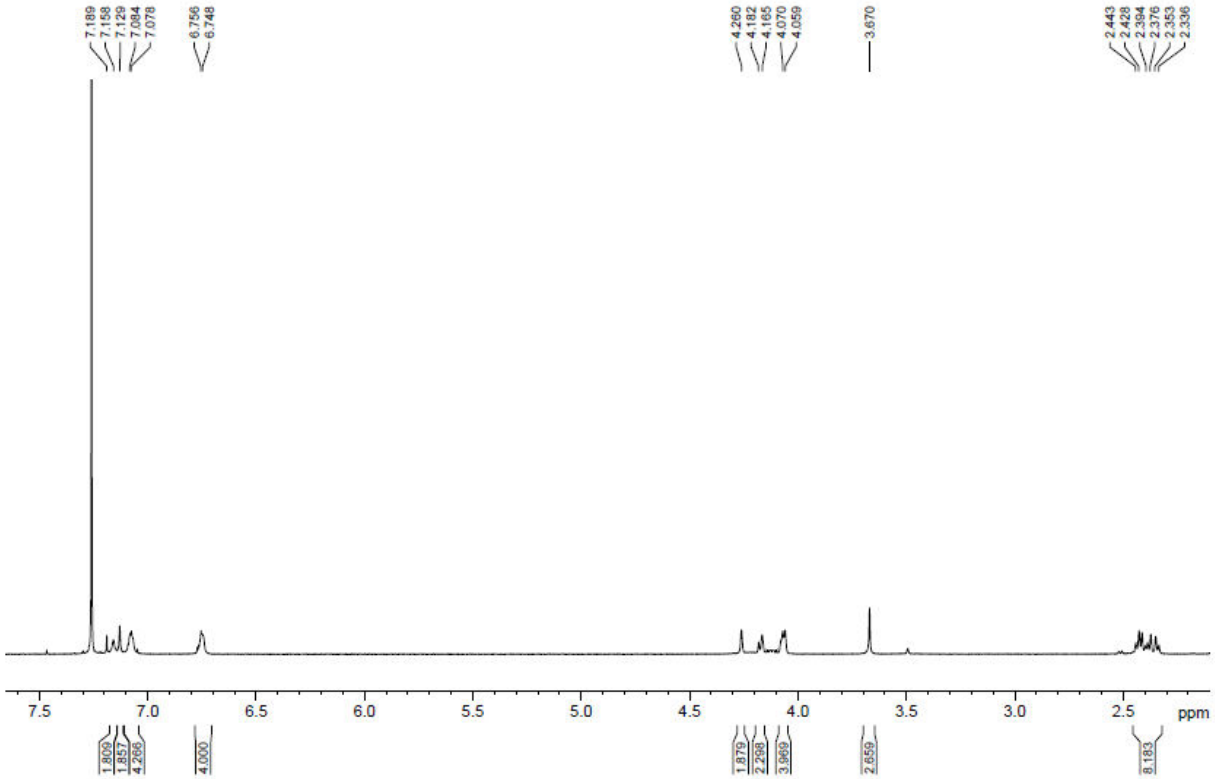
2a
$C_{43}H_{32}O_2$
580.71 g/mol

Procedure: Under argon atmosphere 41.46 mg (0.3 mmol) of potassium carbonate and 0.1 mL of methyl iodide was added to the stirred solution of 88 mg (0.145 mmol) monohydroxy tweezer **1b** in 10 mL of anhydrous acetone. The mixture was stirred for 24 hours under reflux, then cooled to RT and the solvent was removed in vaccuo. The residue was dissolved in 15 mL of 1,4-dioxan and 1 mL of aqueous 1M NaOH was added. The mixture was stirred for 30 minutes at 80°C, then cooled to RT, acidified with 30 mL of aqueous 1M HCl, and extracted three times with 20 mL of dichloromethane. The organic layers were combined, washed with 50 mL of H_2O and saturated aqueous NaCl, dried over $MgSO_4$ and filtrated. The solvent of the filtrate was distilled off in vacuum by the use of a rotary evaporator. The oily product was purified by column chromatography (*n*-hexane/ethyl acetate 3:1) leading to the product as a colorless solid.

Yield: 60.00 mg (0.103 mmol, 71%)

Melting point: 210 °C





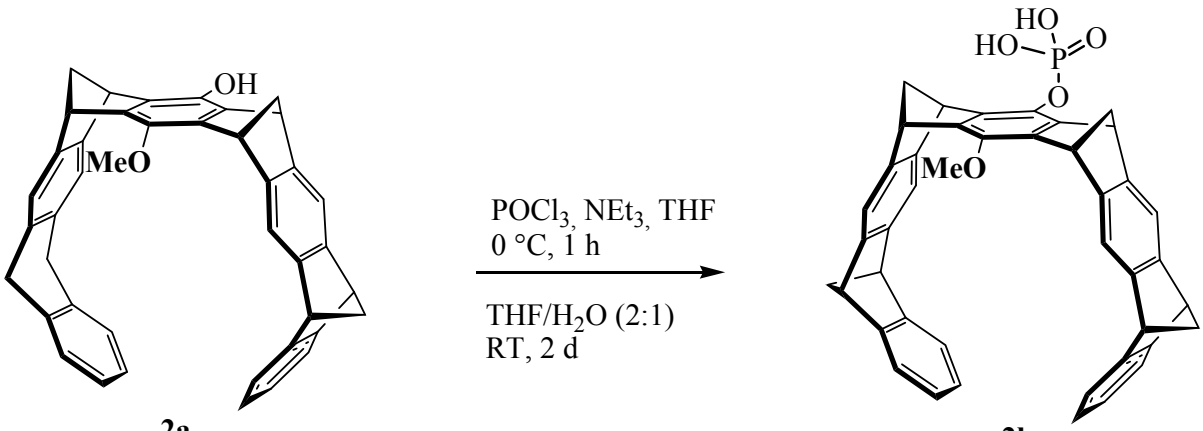
^{1}H-NMR in $CDCl_3$

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 7.15 (s, 2H, H-6, H-10), 7.13 (s, 2H, H-17, H-21), 7.07 (m, 4H, H-1, H-4; H-12, H-15), 6.75 (m, 4H, H-2, H-3, H-13, H-14), 4.26 (s, 2H, H-7, H-9), 4.17 (m, 2H, H-18, H-20), 4.06 (s, 4H, H-5, H-11, H-16, H-22), 3.67 (s, 3H, H-27), 2.41 (d, 2H, $^{2}J_{24a\text{-}H/24i\text{-}H}$ = 7.8 Hz, H-24, H-25) 2.39 (d, 2H, H-24, H-25), 2.36 (d, 2H, $^{2}J_{23a\text{-}H/23i\text{-}H}$ = 7.4 Hz, H-23, H-26), 2.32 (d, 2H, H-23, H-26).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 150.37 (4a-C, 11a-C), 150.29 (15a-C, 22a-C), 147.56 (5a-C, 10a-C), 147.47 (16a-C, 21a-C), 147.21 (6a-C, 9a-C, 17a-C, 20a-C), 143.97

(19-C), 140.81 (18a-C, 19a-C), 139.87 (7a-C, 8a-C), 134.69 (8-C), 124.68 (3-C, 13-C), 124.54 (2-C, 14-C), 121.67 (4-C, 12-C), 121.34 (1-C, 15-C), 116.81 (6-C, 10-C), 116.35 (17-C, 21-C), 69.96 (24-C, 25-C), 69.22 (23-C, 26-C), 61.76 (27-C), 51.40 (5-C, 11-C), 51.35 (16-C, 22-C), 48.38 (18-C, 20-C), 47.45 (7-C, 9-C).

HR-MS: ESI+ (480 eV) m/z (%) = 603.2293obs. 603.2295calc. $[M+Na]^+$



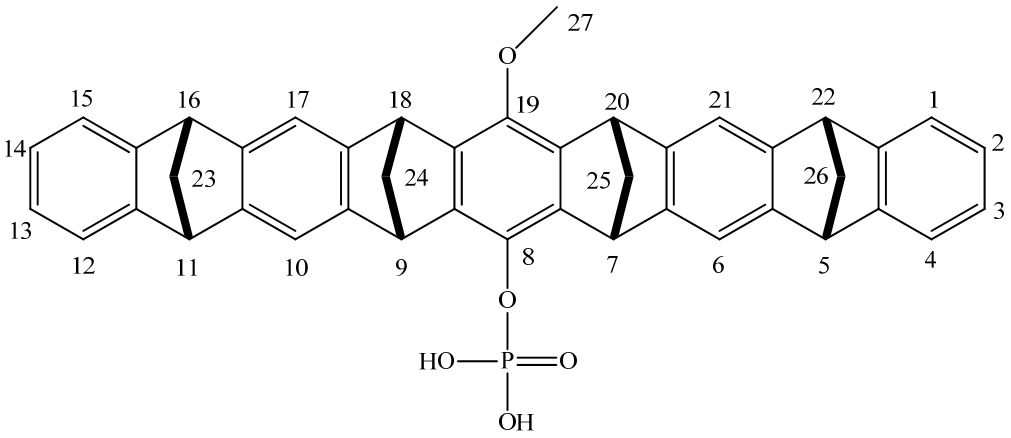
2a
$C_{43}H_{32}O_2$
580.71 g/mol

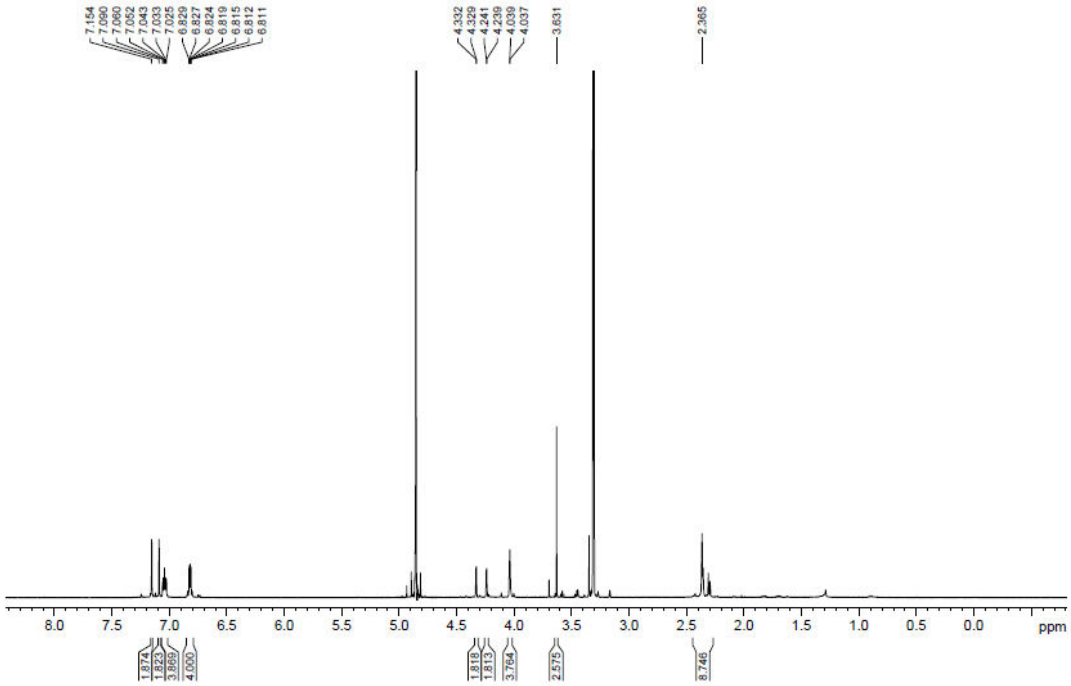
2b
$C_{43}H_{33}O_5P$
660.69 g/mol

Procedure: Under argon atmosphere 95 mg of methoxyhydroxy tweezer **2a** (0.164 mmol) was dissolved in 20 mL THF abs. and added with $POCl_3$ (210 µL, 2.3 mmol) at 0 °C. After ten minutes stirring triethylamine (70 µL, 0.5 mmol) was added, and the mixture was stirred for 1h at 0°C. The excess of inorganic salts is filtered off by a glass filter (D4) and the filtrate was removed from solvent. The residuum in the glass filter was washed a few times with 2.5% HCl-solution and the intermediate was removed from the glass filter with a THF/H_2O-mixture (2:1). The solution was stirred for two days at room temperature. The THF was removed at the rotary evaporator; the solution was washed with 2.5% HCl-solution and sonicated for ten minutes. The last THF solvent was removed and the solution was sonicated for the second time. The solid was filtered off by a glass filter (D4) and washed a few times with 2.5% HCl-solution. The white solid was dried at air and was dissolved with methanol. The solvent was removed and the solid was dried in vacuo.

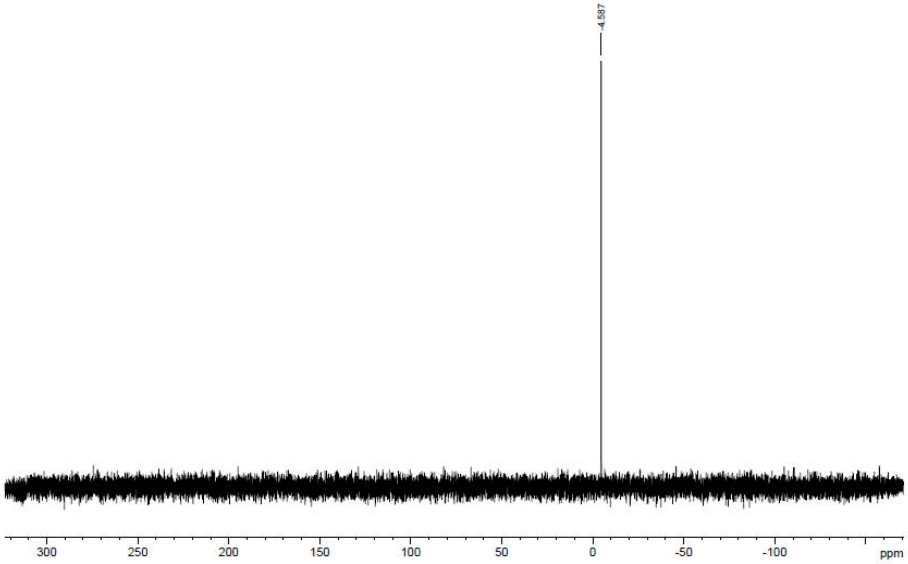
Yield: 90.00 mg (0.136 mmol, 83%)

Melting point: > 210 °C Decomposition





^{1}H-NMR in $CDOD_3$



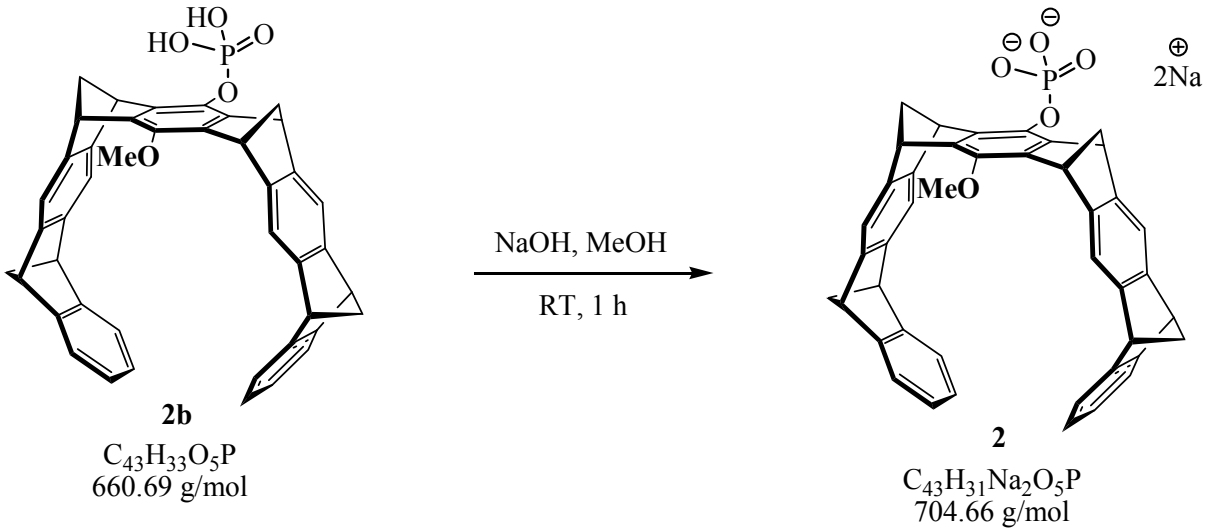
^{31}P-NMR in $CDOD_3$

^{1}H-NMR (500 MHz, $CDOD_3$): δ [ppm] = 7.15 (s, 2H, 6-H, 10-H), 7.09 (s, 2H, 17-H, 21-H), 7.04 (m, 4H, 1-H, 4-H; 12-H, 15-H), 6.82 (m, 4H, 2-H, 3-H, 13-H, 14-H), 4.33 (m, 2H, 7-H, 9-H), 4.24 (m, 2H, 18-H, 20-H), 4.03 (m, 4H, 5-H, 11-H, 16-H, 22-H), 3.63 (s, 3H, 27-H), 2.36 (m, 4H, 24-H; 25-H), 2.30 (m, 4H, 23-H, 26-H).

^{13}C-NMR (125 MHz, $CDOD_3$): δ [ppm] = 150.74 (4a-C, 11a-C), 150.69 (15a-C, 22a-C), 147.92 (5a-C, 10a-C), 147.49 (16a-C, 21a-C), 147.44 (6a-C, 9a-C, 17a-C, 20a-C), 141.43 (8-C), 141.40 (19-C), 140.82 (7a-C, 8a-C, 18a-C, 19a-C), 124.62 (3-C, 13-C), 124.60 (2-C, 14-C), 120.82 (4-C, 12-C), 120.57 (1-C, 15-C), 116.57 (6-C, 10-C), 114.95 (17-C, 21-C), 67.64 (23-C, 26-C), 67.53 (24-C, 25-C), 60.39 (27-C), 50.96 (5-C, 7-C, 9-C, 11-C, 16-C , 18-C, 20-C, 22-C).

^{31}P-NMR (202 MHz, $CDOD_3$): δ [ppm] = -4.59.

HRMS:	ESI+ (480 eV)	m/z (%) = 683.2101 obs.	683.1958 calc.	$[M+Na]^+$
	ESI- (480 eV)	m/z (%) = 659.2103 obs.	659.1982 calc.	$[M-H]^-$



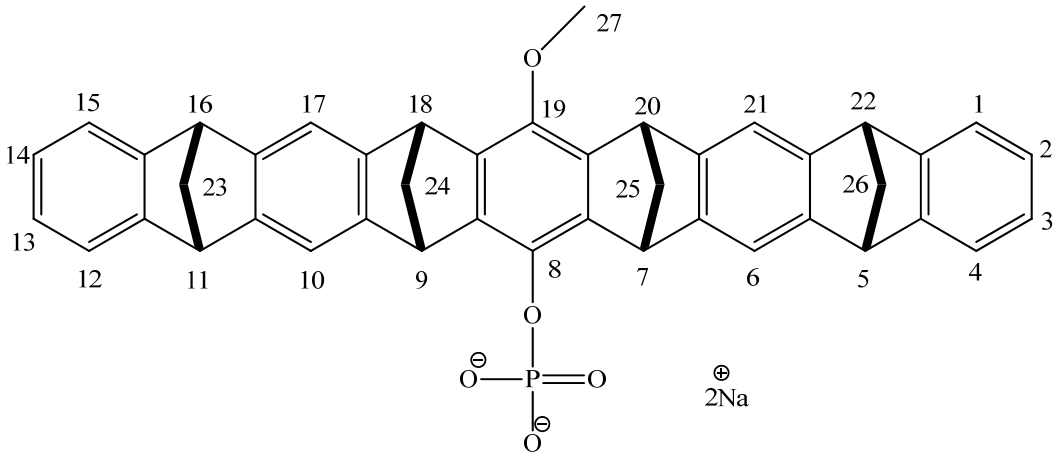
2b
$C_{43}H_{33}O_5P$
660.69 g/mol

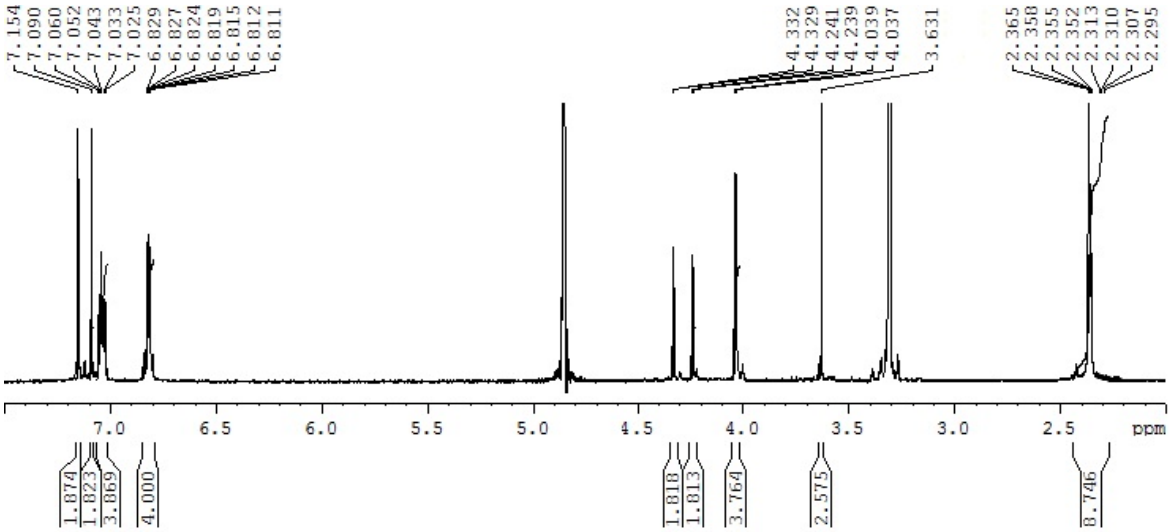
2
$C_{43}H_{31}Na_2O_5P$
704.66 g/mol

Procedure: Under argon atmosphere 86.00 mg of Hydrogenphosphate tweezer **2b** (0.13 mmol) was dissolved in 20 mL Methanol abs. and added with sodium hydroxide-Monohydrate (15.083 mg, 0.26 mmol). The mixture was stirred for one hour at room temperature. The solvent was removed and the solid was dried in vacuo.

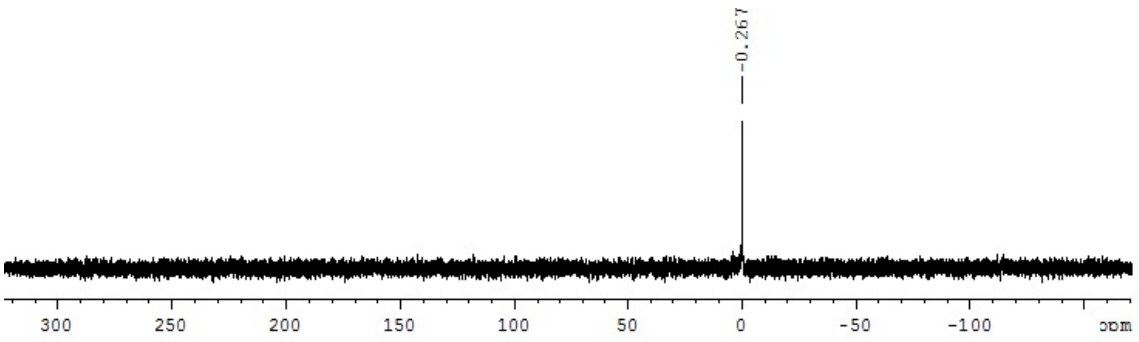
Yield: 94.00 mg (0.13 mmol, 100%)

Melting point:> 210 °C Decomposition





^{1}H-NMR in $CDOD_3$



^{31}P-NMR in $CDOD_3$

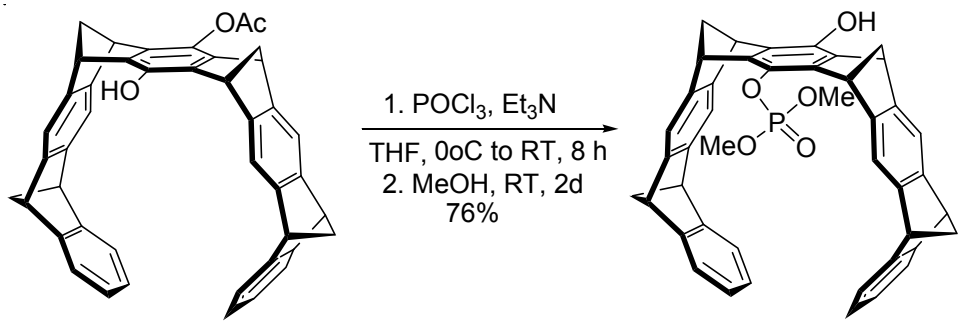
^{1}H-NMR (500 MHz, $CDOD_3$):δ [ppm] = 7.18 (s, 2H, 6-H, 10-H), 7.04 (s, 2H, 17-H, 21-H), 7.02 (m, 4H, 1-H, 4-H, 12-H, 15-H), 6.79 (m, 4H, 2-H, 3-H, 13-H, 14-H), 4.63 (s, 2H, 7-H, 9-H), 4.15 (s, 2H, 18-H, 20-H), 4.01 (s, 4H, 5-H, 11-H, 16-H, 20-H), 3.61 (s. 3H, 27-H), 2.44 (m, 2H, 24-H, 25-H), 2.35 (m, 4H, 23-H, 26-H), 2.24 (m, 2H, 24-H, 25-H).

^{13}C-NMR (125 MHz, $CDOD_3$): δ [ppm] = 152.33 (4a-C, 11a-C), 152.24 (15a-C, 22a-C), 150.14 (5a-C, 10a-C), 149.66 (16a-C, 21a-C), 148.79 (6a-C, 9a-C), 148.71(17a-C, 20a-C), 146.11 (19-C), 143.42 (18a-C, 19a-C), 143.40 (7a-C, 8a-C), 141.21 (8-C), 126.12 (3-C, 13-C), 125.99 (2-C, 14-C), 122.24 (4-C, 12-C), 122.12 (1-C, 15-C), 117.90 (6-C, 10-C), 116.38 (17-C, 21-C), 69.23 (24-C, 25-C), 69.19 (23-C, 26-C), 62.08 (27-C), 52.54 (5-C, 11-C, 16-C, 22-C), 52.52 (18-C, 20-C, 7-C, 9-C).

^{31}P-NMR (202 MHz, $CDOD_3$):δ [ppm] = 0.27.

HRMS:	ESI+ (480 eV)	m/z (%) = 705.1782 obs.	705.1777 calc.	$[M+H]^+$
	ESI- (480 eV)	m/z (%) = 659.1902 obs.	659.1982 calc.	$[M-H]^-$

Synthesis of the octyl phosphate tweezer 3



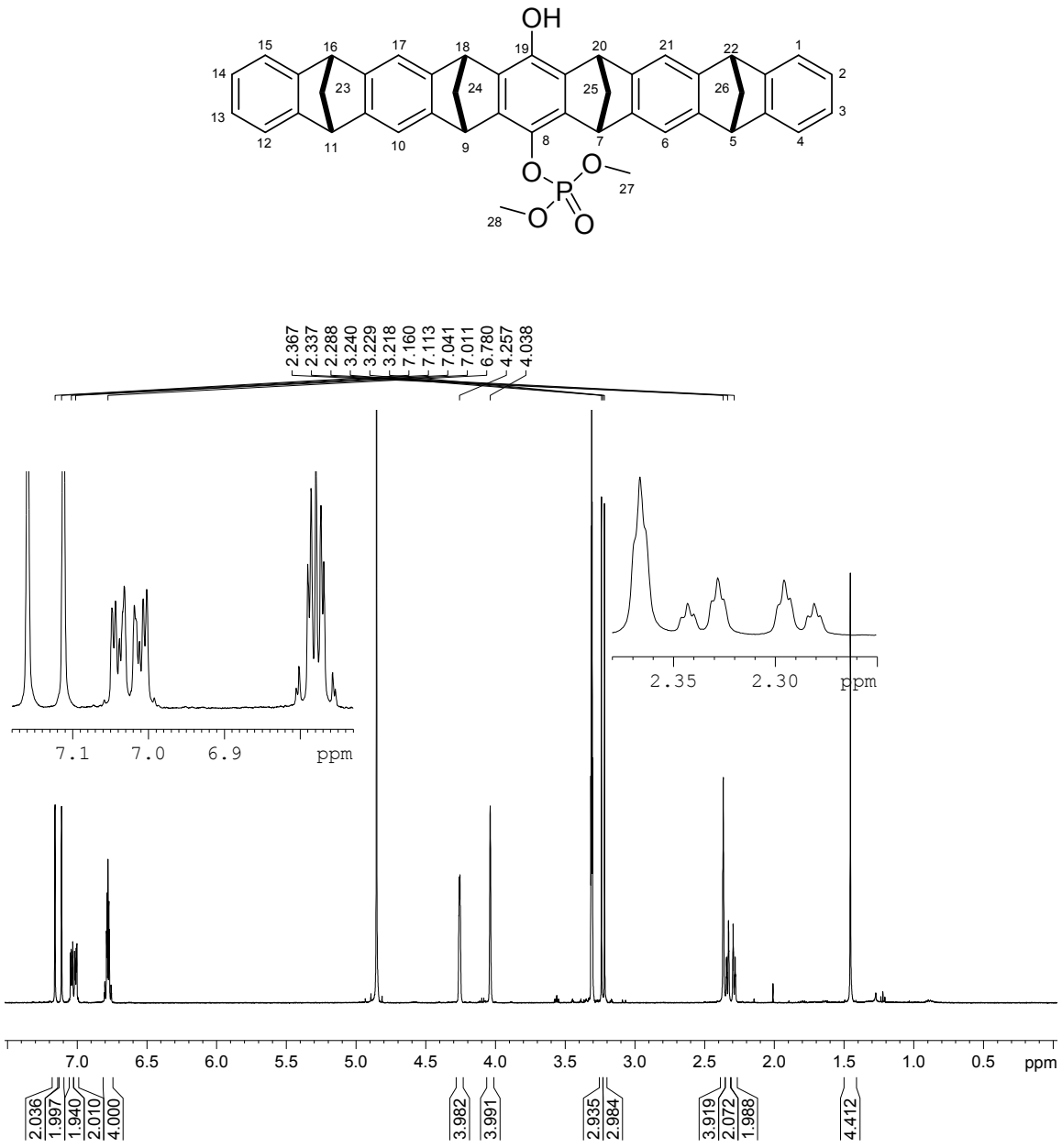
1b
$C_{44}H_{32}O_3$
608,72 g/mol

1a
$C_{44}H_{35}O_5P$
674,72 g/mol

Under argon atmosphere, 300 mg (0.493 mmol) tweezer **1b** was dissolved in 40 ml anhydrous THF and cooled the solution to 0 ^oC. To this cooled solution 90 µl (0.987 mmol) $POCl_3$ and after 10 min. 137 µl (0.987 mmol) Et_3N were added. The reaction mixture is stirred from 0^oC to RT for 8 h and then 8 ml dry methanol were added and stirred again at RT for 2 days. The solvent was removed on rotary evaporator and to the crude 50 ml sat.NH_4Cl solution were added and extracted with CH_2Cl_2 (3×100 ml). The organic layer was washed the with brine solution. Solvent was removed on rotary evaporator and solid purified by column chromatography using EtOAc//cyclohexane (1:3) eluent.

Yield: 250 mg, white solid, 76 %.

Melting Point: > 240 ^oC brown coloration.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P
O
O
O
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2.288
3.240
3.229
3.218
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7.113
7.041
7.011
6.780
4.257
4.038
7.1
7.0
6.9
ppm
2.35
2.30
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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ppm
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1.997
1.940
2.010
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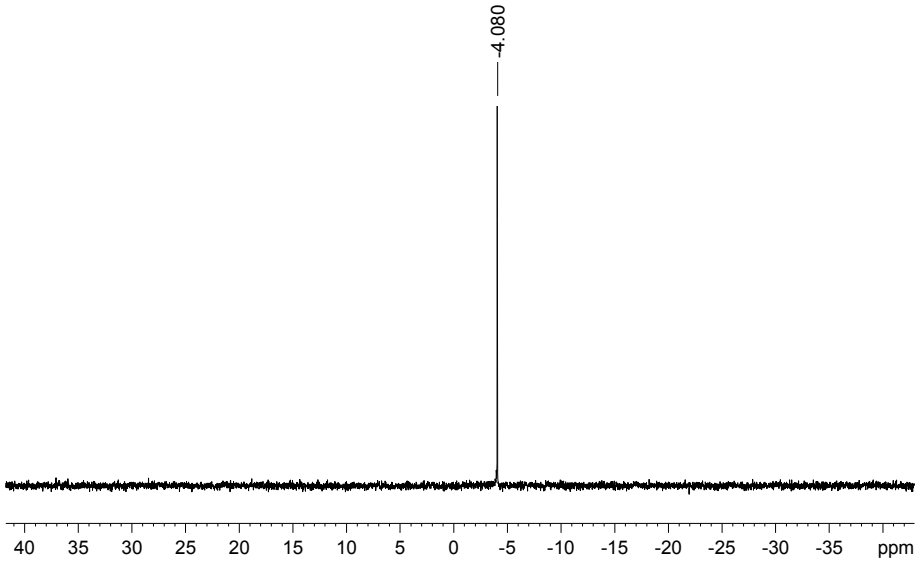
2.072
1.988
4.412

^{1}H-NMR



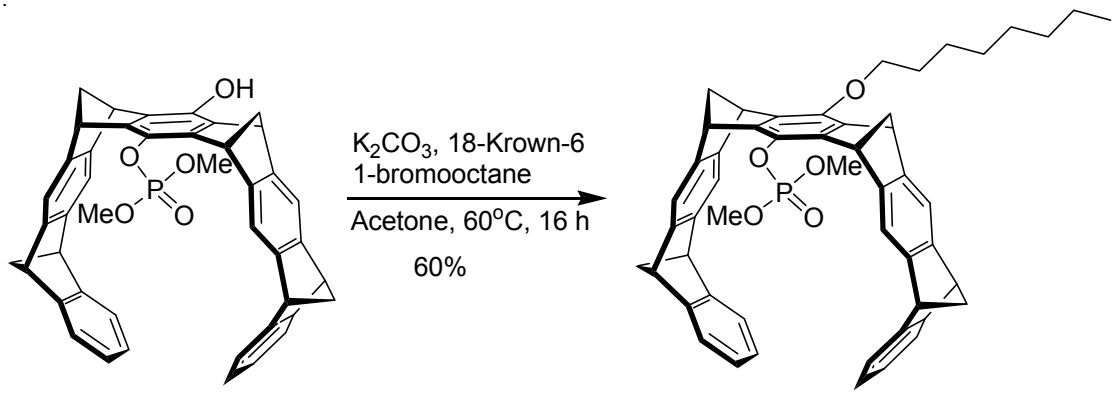
^{31}P-NMR

^{1}H-NMR (500MHz, CD_3OD): δ [ppm] = 2.28 (dt, 2H, H-24a, H-25a), 2.33 (dt, 2H, H-24i, H-25i), 2.36 (s, 4H, H-23, H-26), 3.99 (s, 2H), 3.22 (d, $^{3}J_{\text{H-27/P, H-28/P}}$ = 11.00, 6H, H-27, H-28), 4.03 (s, 4H, H-5, H-11, H-16, H-22), 4.25 (s, 4 H, H-7, H-9, H-18, H-20), 6.78 (m, 4H, H-2, H-3, H-13, H-14), 7.01 (m, 2H, H-1, H-15), 7.04 (m, 2H, H-4, H-12), 7.11 (s, 2H, H-17, H-21), 7.15 (s, 2H, H-6, H-10).

^{13}C-NMR (125.7MHz, CD_3OD): δ [ppm] = 48.6-49.3 (C-7, C-9, C-18, C-20), 52.4(d, C-5, C-11, C-16, C-22), 55.8(d, C-27, C-28), 68.8, 69.2 (C-23, C-24, C-25, C-26), 117.0 (C-17, C-21), 117.8 (C-6, C-10), 121.8 (C-1, C-15), 122.3 (C-4, C-12), 126.0 (d, C-2, C-3, C13, C-14), 138.4, 141.7, 144.0 (C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 148.4, 148.9, 149.2 (C-6a, C-9a, C-17a, C-20a, C-8, C-9), 152.2 (d, C-4a, C-11a, C-15a, C-22a).

^{31}P-NMR (202MHz, CD_3OD): δ [ppm] = -4.08

HR-MS (ESI pos., MeOH): m/z $[M+Na]^+$: cal. 697.2114, obs. 697.2133.



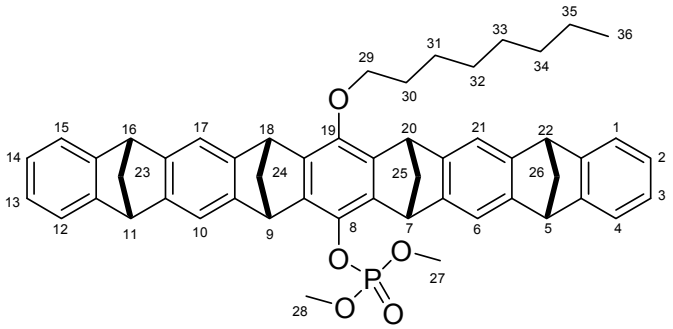
1a
$C_{44}H_{35}O_5P$
674,72 g/mol

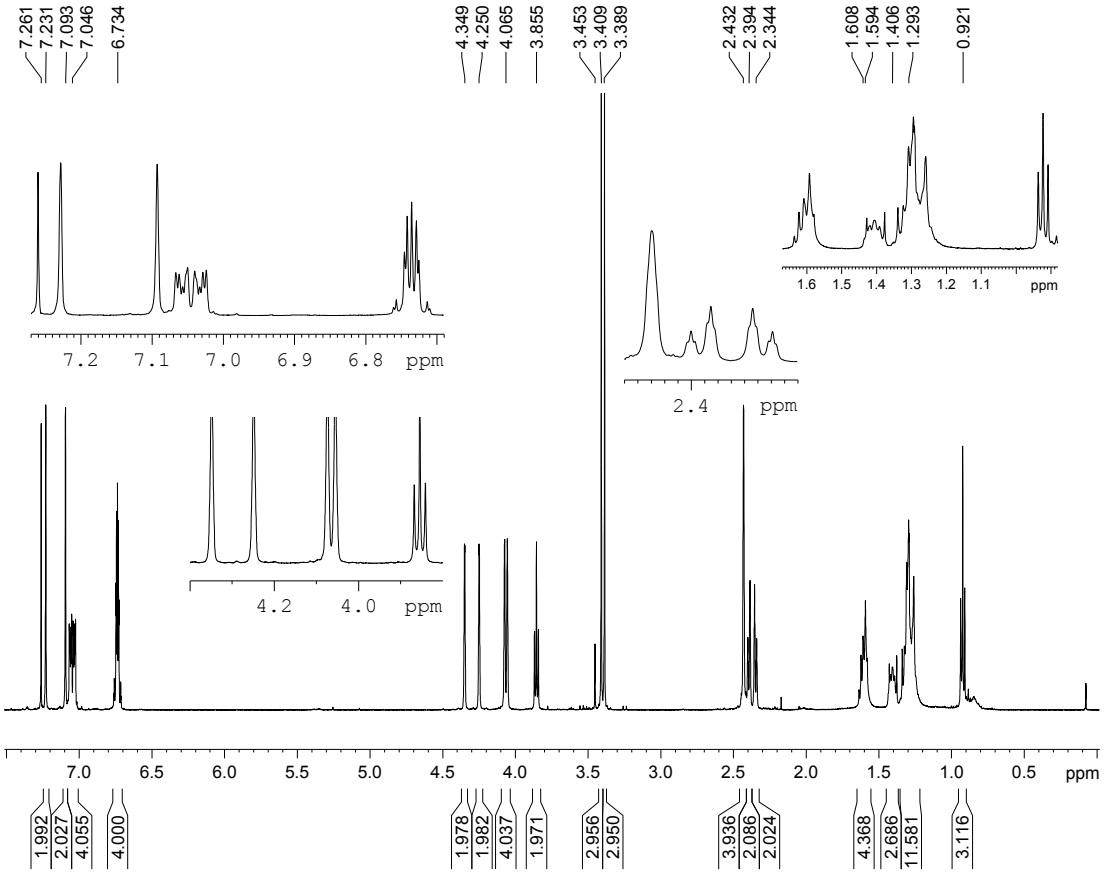
3a
$C_{52}H_{51}O_5P$
786,93 g/mol

In a suspension of 22 mg (0.0326 mmol) tweezer **1a** and 5.0 mg (0.0326 mmol) K_2CO_3 in abs acetone, 9 µl (0.0489 mmol) 1-bromooctane were added. A catalytic amount of 18-Krown-6 was also added and the reaction mixture was stirred at 60 °C for 24 h. The mixture was then cooled to RT and transferred into a separating funnel. After adding sat $NaHCO_3$, the mixture was extracted three times with dichloromethane. The combined organic layer was washed once with sat NH_4Cl and once with brine solution. Organic phase was dried over Na_2SO_4 and the solvent was removed by reduced pressure. Product was purified by column chromatography using 1:3 (EtOAc/ Cyclohexane) as eluent. Compound **3a** also crystallized in methanol.

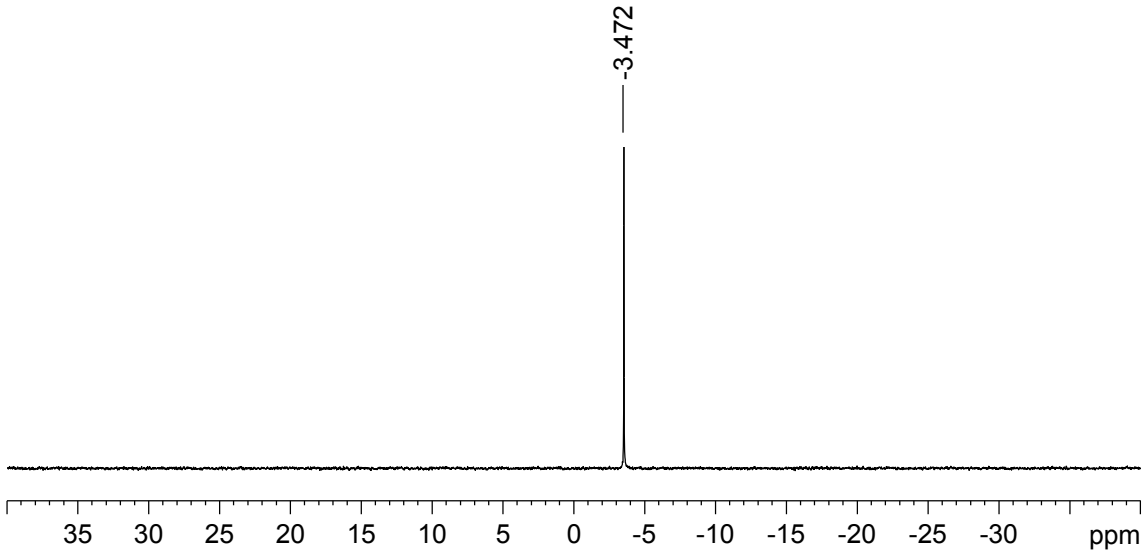
Yield: 15 mg, 60%

Melting Point: 188 °C





^{1}H-NMR



^{31}P-NMR

^{1}H-NMR (500MHz, $CDCl_3$): δ [ppm] = 0.92 (t, 3H, H-36), 1.29 (m, 8H, H-32, H-33, H-34, H-35), 1.40 (m, 2H, H-31), 1.59 (m, 2H, H-30), 2.35 (d, 2H, H-24a, H-25a), 2.39 (d, 2H, H-24i, H-25i), 2.43 (s, 4H, H-23, H-26), 3.39 (d, $^{3}J_{\text{H-27/P, H-28/P}}$ = 11.00, 6H, H-27, H-28), 3.85 (t,

2H, H-29), 4.06 (d, 4H, H-5, H-11, H-16, H-22), 4.25 (s, 2 H, H-18, H-20), 4.35 (s, 2H, H-7, H-9), 6.73 (m, 4H, H-2, H-3, H-13, H-14), 7.05 (dm, 4H, H-1, H-15, H-4, H-12), 7.09 (s, 2H, H-17, H-21), 7.23 (s, 2H, H-6, H-10).

^{13}C-NMR (125.7MHz, $CDCl_3$): δ [ppm] = 14.3 (C-36), 22.9 (C-35), 26.2 (C-34), 29.5 (C-32, C-33), 30.4 (C-31), 31.9 (C-30), 48.6, 51.4 (d, C-7, C-9, C-18, C-20, C-5, C-11, C-16, C-22), 68.8, 69.7 (C-23, C-26, C-24, C-25), 74.1 (C-29), 116.1, 117.2 (C-17, C-21, C-6, C-10), 121.2, 121.6 (C-1, C-15, C-4, C-12), 124.7 (d, C-2, C-3, C13, C-14), 134.9, 140.8, 141.2, 145.8 (C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 147.1, 147.7 (C-6a, C-9a, C-17a, C-20a, C-8, C-9), 150.6 (d, C-4a, C-11a, C-15a, C-22a).

^{31}P-NMR (202MHz, $CDCl_3$): δ [ppm] = -3.47

HR-MS (ESI pos., MeOH): m/z $[M+Na]^+$: cal. 809.3366, obs. 809.3442.

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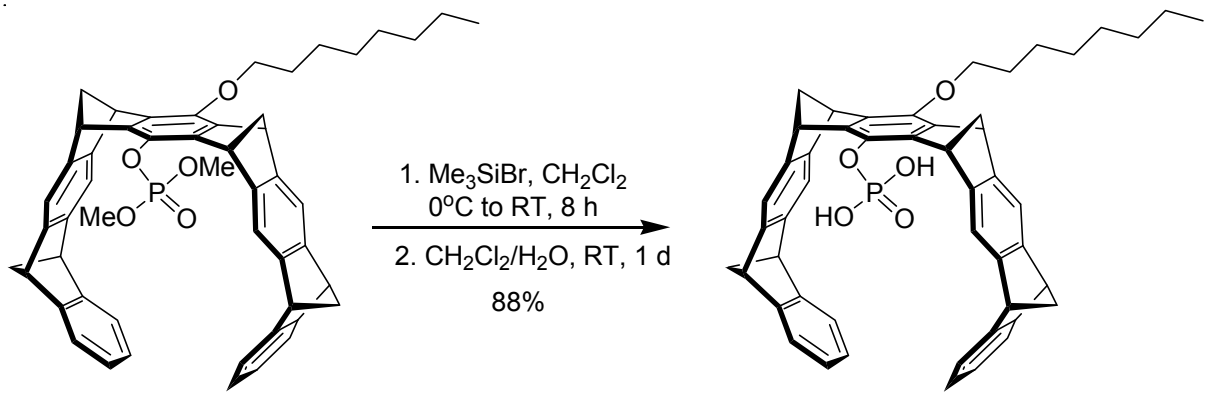


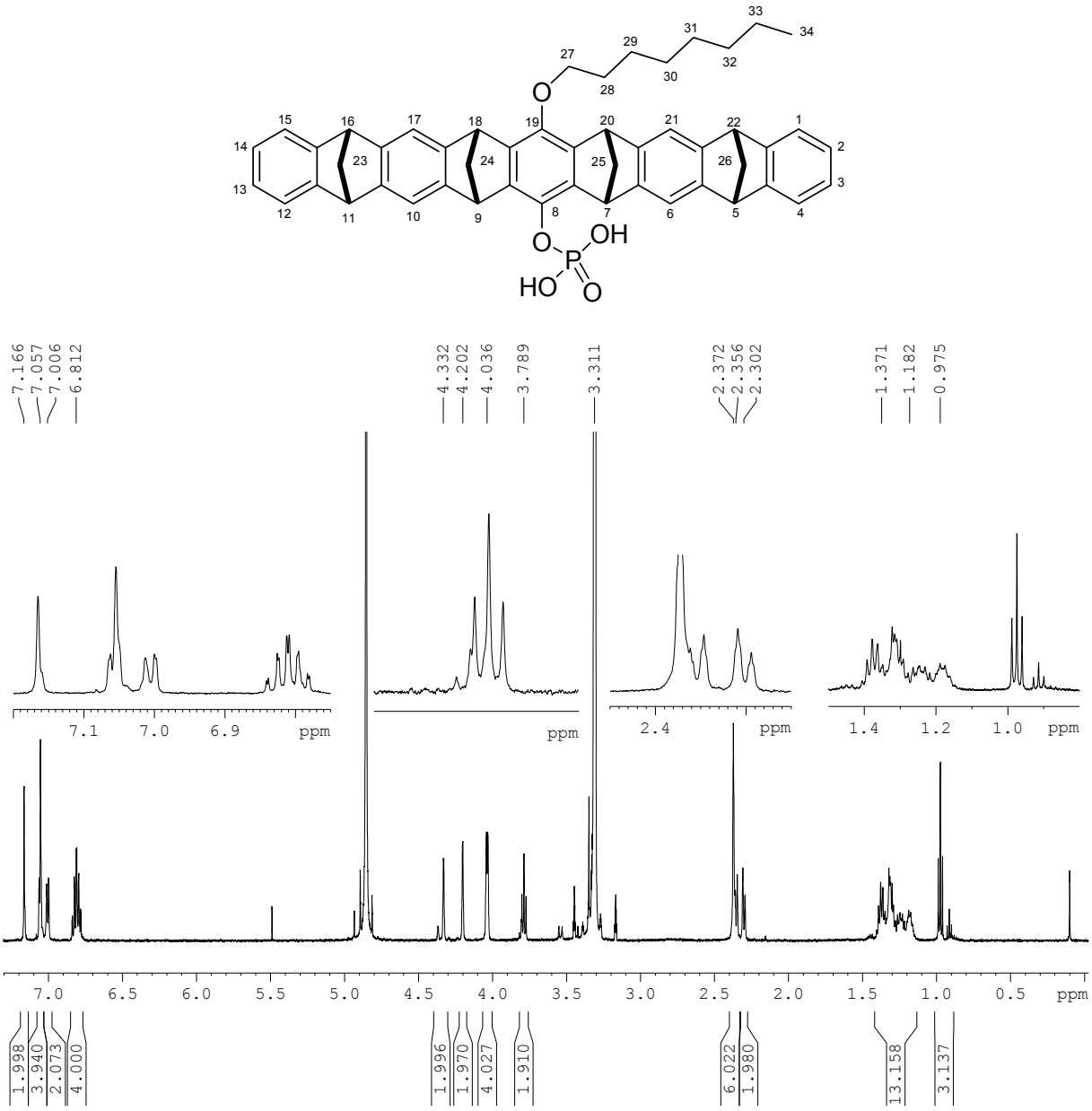
3a
$C_{52}H_{51}O_5P$
786,93 g/mol

3b
$C_{50}H_{47}O_5P$
758,88 g/mol

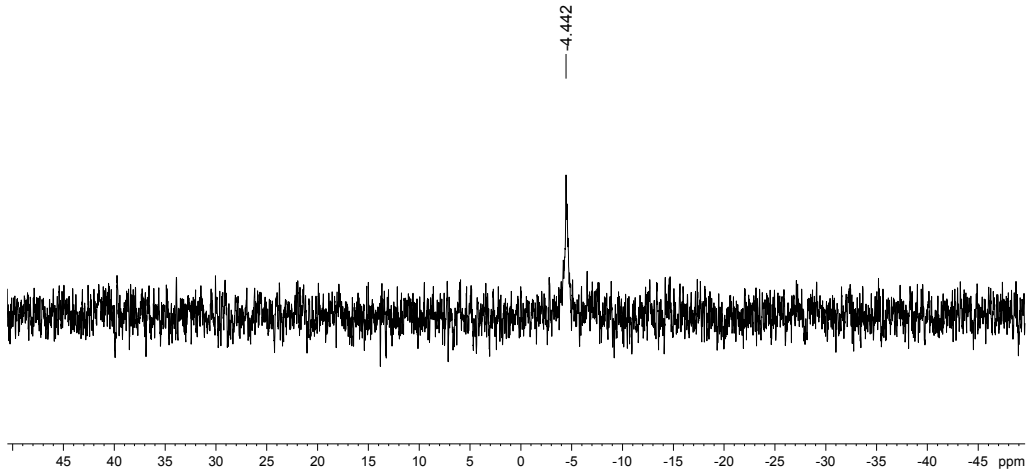
To a 0 °C cooled solution of 13 mg (0.0165mmol) of **3a** in anhydrous CH_2Cl_2, 22 µl (0.165mmol) trimethylsilyl bromides (TMSBr) were added dropwise and then stirred at RT for 8 hour. The excess of TMSBr and solvent were removed by condensation and remaining residue was dried on oil pump for 2-5 h. The solid residue was then dissolved in CH_2Cl_2/H_2O (1:1) and stirred at RT for 24 h. Two phases were separated, and after drying organic phase on *rota vap,* 12 mg of white solid were collected. The crude was washed with n-hexane or acetonitrile to remove the trace amount of grease from the product.

Yield: 11 mg, 88 %.

Melting Point: > 185 ^{o}C brown coloration.



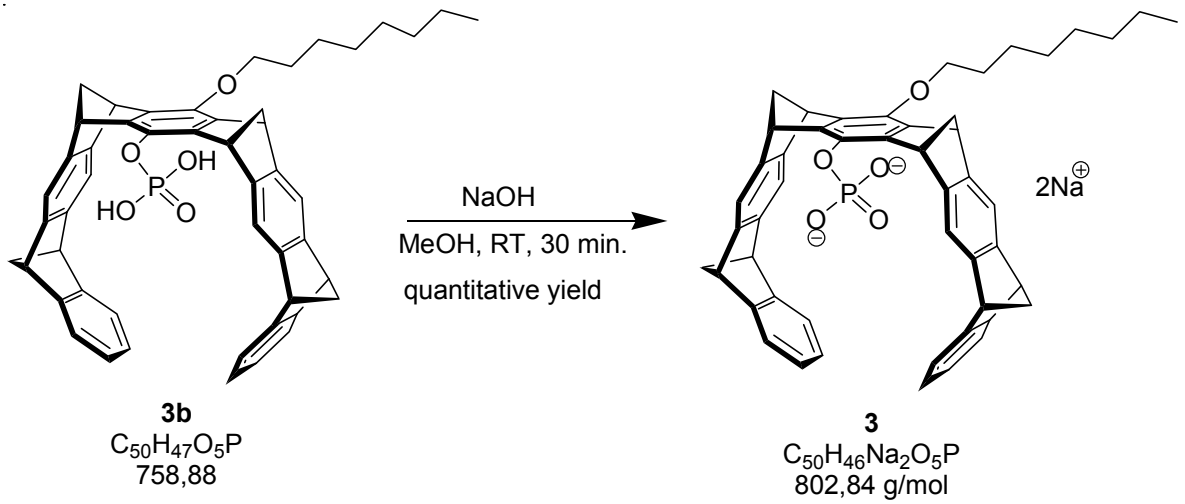
^{1}H-NMR



^{31}P-NMR

^{1}H-NMR (500MHz, CD_3OD): δ [ppm] = 0.97 (t, 3H, H-34), 1.18-1.37 (m, 12H, H-28, H-29, H-30, H-31, H-32, H-33), 2.30 (d), 2.35 (d), 2.37(s) (8H, H-24, H-25, H-23, H-26), 3.79 (t, 2H, H-27), 4.04 (ds, 4H, H-5, H-11, H-16, H-22), 4.20 (s, 2 H, H-18, H-20), 4.33 (s, 2H, H-7, H-9), 6.81 (m, 4H, H-2, H-3, H-13, H-14), 7.00 (d, 2H, H-1, H-15), 7.06 (m, 4H, H-4, H-12, H-17, H-21), 7.17 (s, 2H, H-6, H-10).

^{31}P-NMR (202MHz, CD_3OD): δ [ppm] = -4.44.

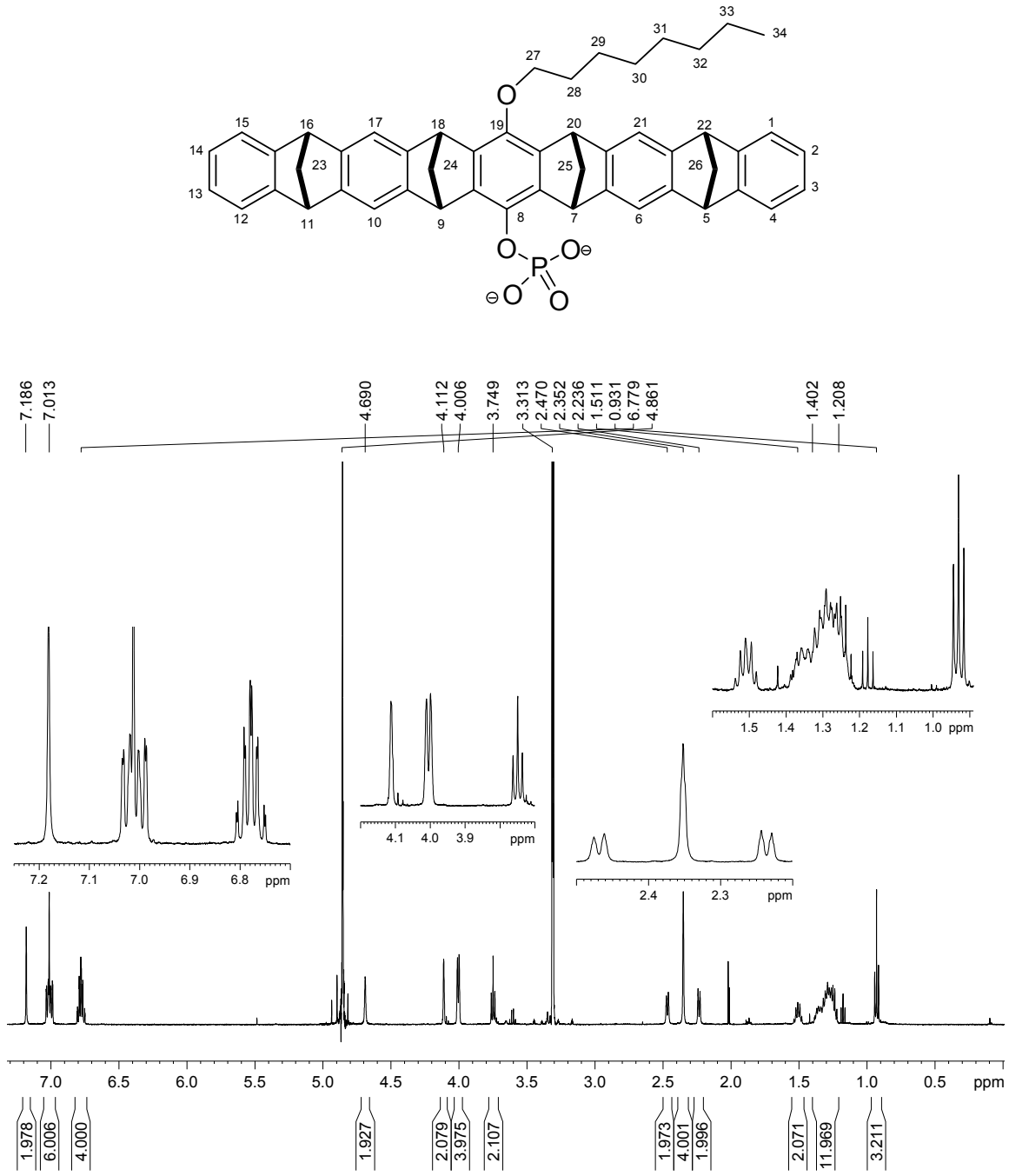


3b
$C_{50}H_{47}O_5P$
758,88

3
$C_{50}H_{46}Na_2O_5P$
802,84 g/mol

In a solution of 9.0 mg (0.0118 mmol) tweezer **3b,** 0.316 mg (0.948 mmol) sodium hydroxide was added and stirred the solution for 30 min. at RT. The solvent was removed on a *rota vap* and white solid product was obtained in quantitative yield.

Melting Point: > 220 °C, decomposition.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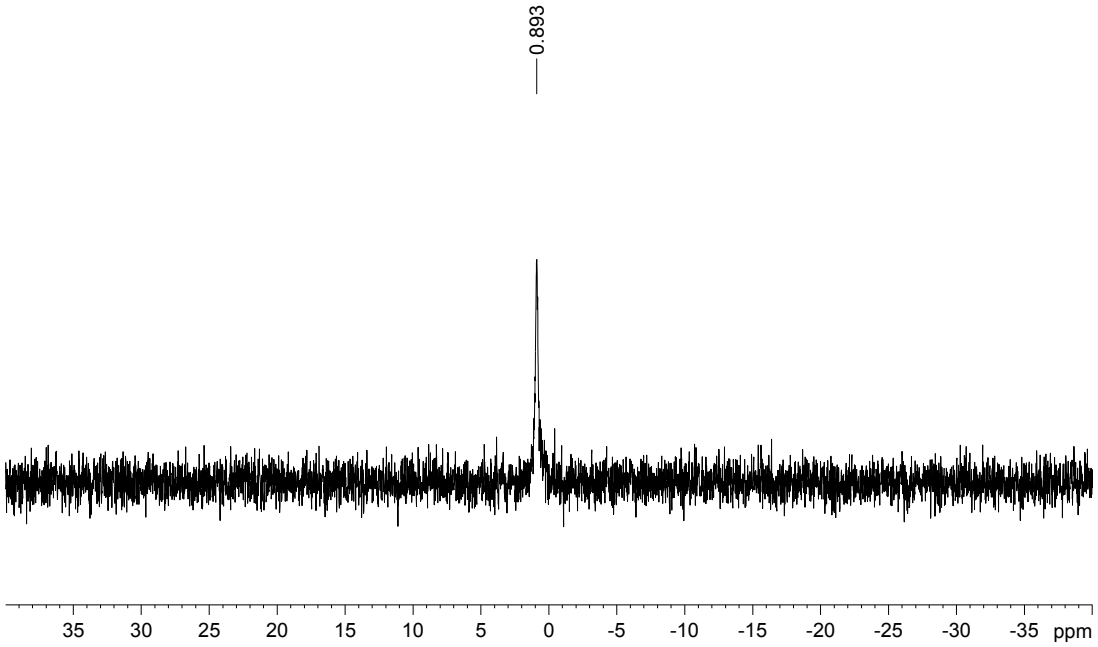
^{1}H-NMR



^{31}P-NMR

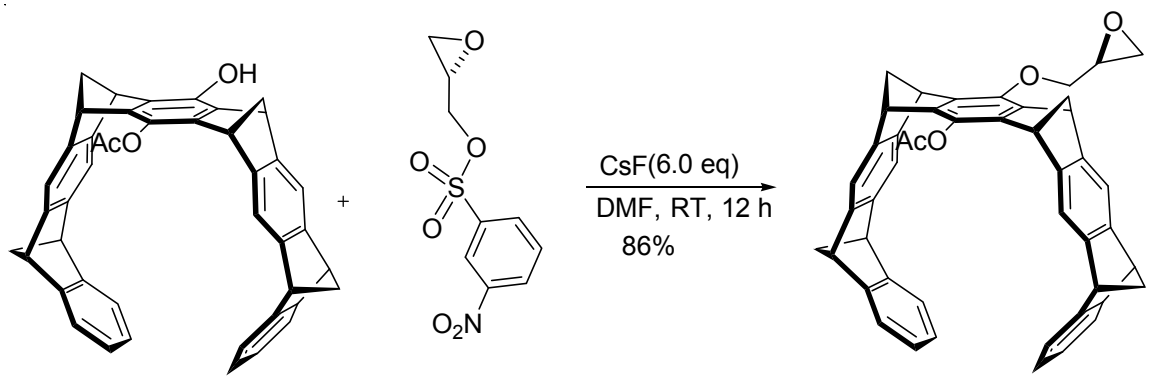
^{1}H-NMR (500MHz, CD_3OD): δ [ppm] = 0.93 (t, 3H, H-34), 1.23-1.38 (m, 10H, H-29, H-30, H-31, H-32, H-33), 1.51 (m, 2H, H-28), 2.24 (d, 2H, H-24a, H-25a), 2.35 (s, 4H, H-23, H-26), 2.47 (d, 2H, H-24i, H-25i), 3.75 (t, 2H, H-27), 4.00 (ds, 4H, H-5, H-11, H-16, H-22), 4.11 (s, 2 H, H-18, H-20), 4.69 (s, 2H, H-7, H-9), 6.78 (m, 4H, H-2, H-3, H-13, H-14), 7.01 (m, 6H, H-1, H-15, H-4, H-12, H-17, H-21), 7.18 (s, 2H, H-6, H-10).

^{13}C-NMR (125.7MHz, CD_3OD): δ [ppm] = 14.6 (C-34), 23.8 (C-33), 27.1 (C-32), 30.5 (d, C-31, C-30), 31.2 (C-29), 32.9 (C-28), 49.3-49.6 (C-7, C-9, C-18, C-20), 52.4 (C-5, C-11, C-16, C-22), 69.1 (d, C-23, C-26, C-24, C-25), 74.9 (C-27), 116.3, 117.6 (C-17, C-21, C-6, C-10), 122.0 (d, C-1, C-15, C-4, C-12), 125.9 (d, C-2, C-3, C13, C-14), 141.3, 143.2, 144.6 (C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 148.5(d), 149.6, 150.1 (C-6a, C-9a, C-17a, C-20a, C-8, C-9), 152.1 (d, C-4a, C-11a, C-15a, C-22a).

^{31}P-NMR (202MHz, CD_3OD): δ [ppm] = 0.893

HR-MS (ESI pos., MeOH): m/z $[M+H]^+$: cal. 803.2873, obs. 803.2904.

Synthesis of the glycerol phosphate tweezer 4



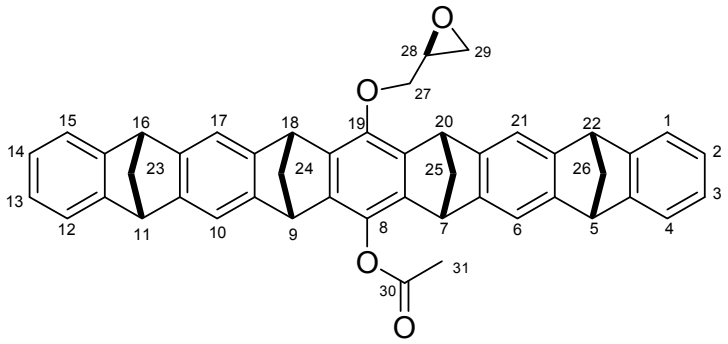
1b
$C_{44}H_{32}O_3$
608,72 g/mol

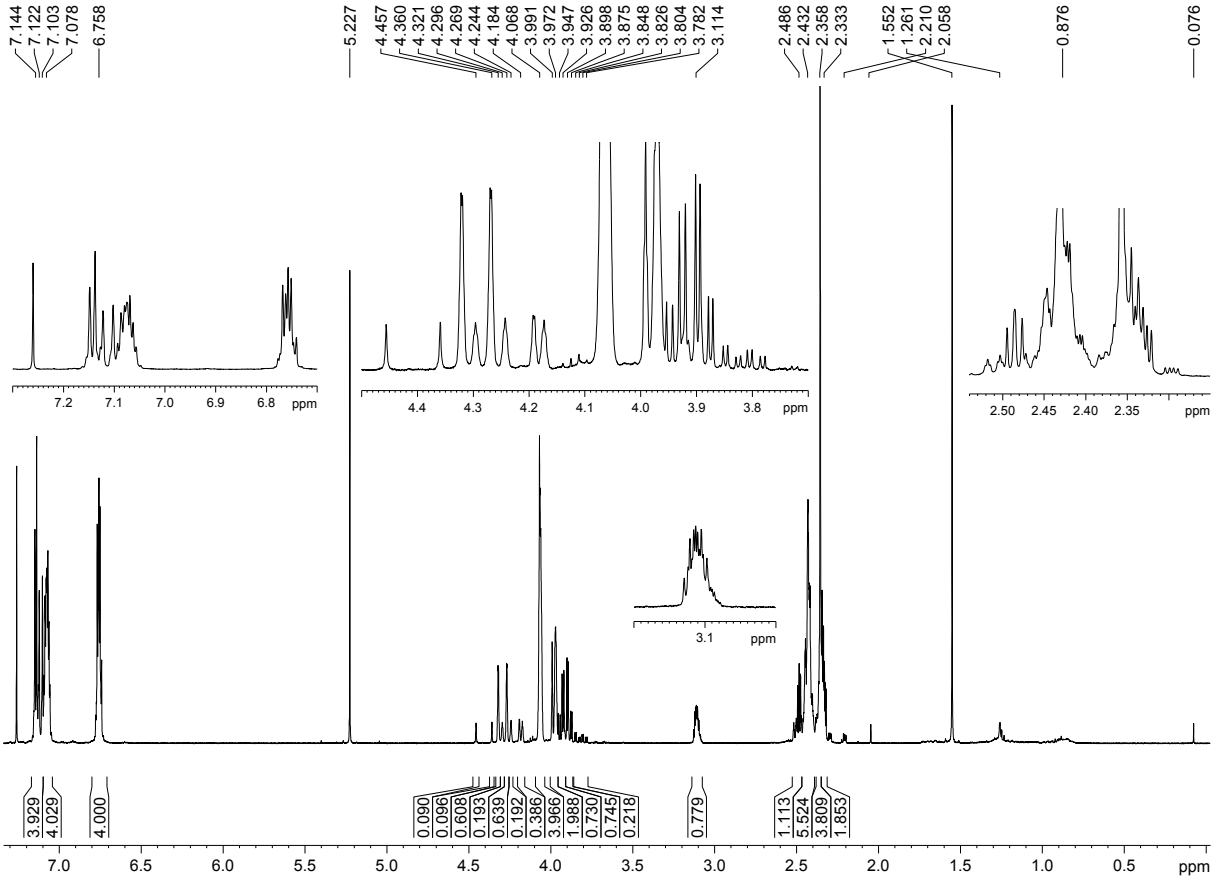
4a
$C_{47}H_{36}O_4$
664,79 g/mol

Under argon atmosphere, to a solution of 165 mg (0.271 mmol) tweezer **1b** in 5 ml anhydrous DMF, 124 mg (0.814 mmol) CsF were added. The reaction mixture was stirred at RT for 1 h and 84 mg (0.325 mmol) glycidyl nosylate were added and stirred the mixture at 40 °C for 24 h. After cooling to RT, water was added and extracted three times with EtOAc. Organic phase was dried over $MgSO_4$ and solvent was removed by reduced pressure. The residue was purified by column chromatography over silica gel (1:5, EtOAc/cyclohexane).

Yield: 155 mg, 86%.

Melting Point: > 230 °C, brown coloration.

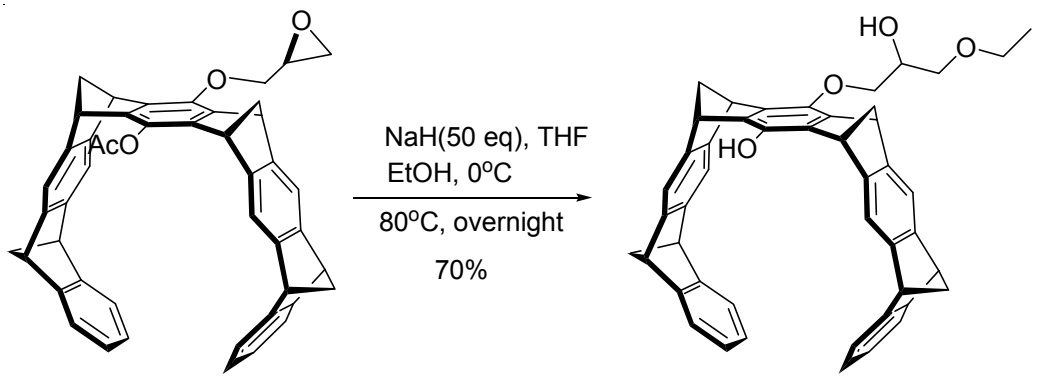




^{1}H-NMR (500MHz, $CDCl_3$): δ [ppm] = 2.33-2.48 (m, 13H, H-29a, H-29i, H-31, 24a, H-25a, H-24i, H-25i, H-23, H-26), 3.11 (m, 1H, H-28), 3.88, 3.94 (m, 2H, H-27a, H-27i), 3.98 (ds, H-7, H-9), 4.07 (s, 4H, H-5, H-11, H-16, H-22), 4.26, 4.31 (dd, 2 H, H-18, H-20), 6.76 (m, 4H, H-2, H-3, H-13, H-14), 7.08 (m, 4H, H-1, H-15, H-4, H-12), 7.10-7.15 (m, 4H, H-17, H-21, H-6, H-10).

^{13}C-NMR (125.7MHz, $CDCl_3$): δ [ppm] = 21.0 (C-31), 44.9 (C-29), 48.7 (m, C-7, C-9, C-18, C-20), 50.4 (C-28), 51.4(C-5, C-11, C-16, C-22), 69.1, 70.1 (C-23, C-26, C-24, C-25), 74.4 (C-27), 116.1, 116.8 (m, C-17, C-21, C-6, C-10), 121.6 (m, C-1, C-15, C-4, C-12), 124.8 (m, C-2, C-3, C13, C-14), 135.7, 141.0 (C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 145.7, 146.4, 146.7, 147.0 (C-6a, C-9a, C-17a, C-20a, C-8, C-9), 150.4 (C-4a, C-11a, C-15a, C-22a), 169.2 (C-30).

HR-MS (ESI pos., MeOH): m/z $[M+Na]^+$: cal. 687.2506, obs. 687.2607.



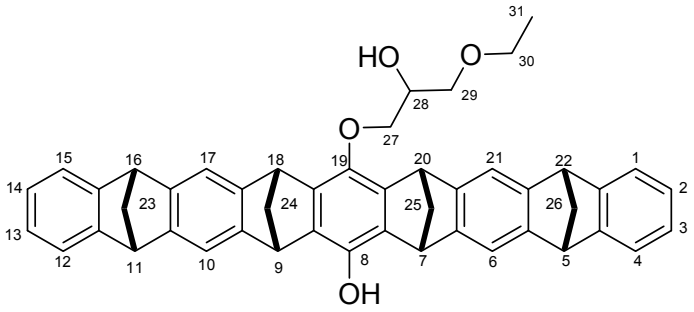
4a
$C_{47}H_{36}O_4$
664,79 g/mol

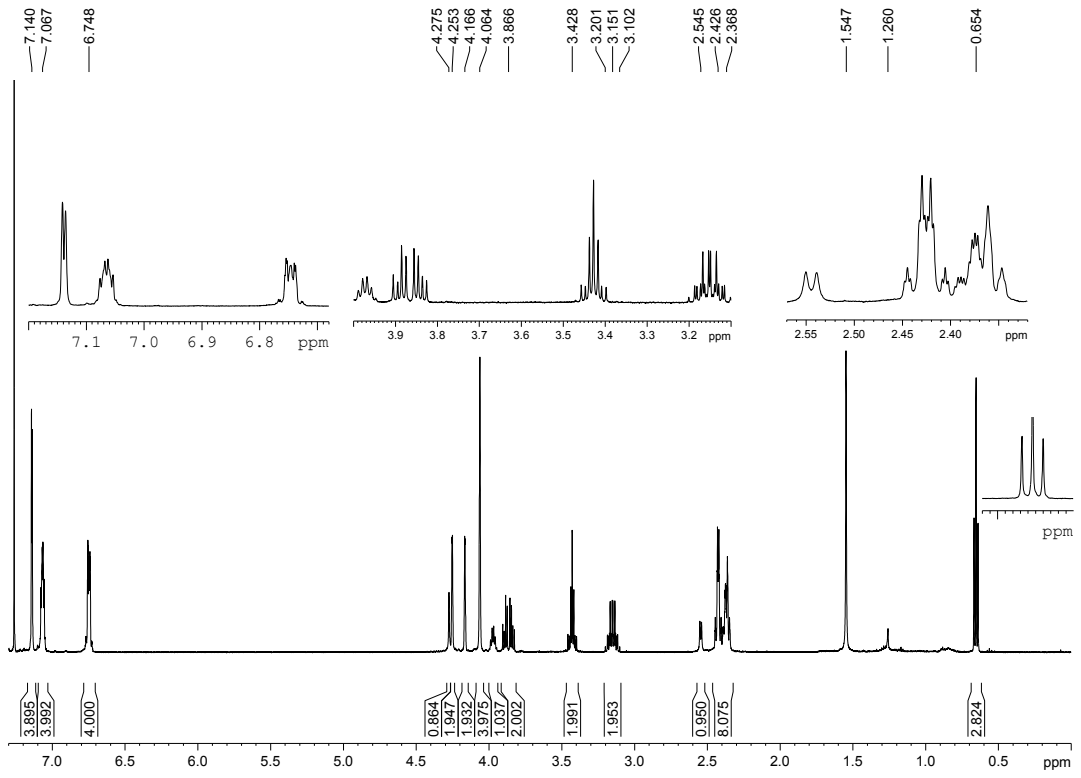
4b
C47H40O4
668,82 g/mol

120 mg (3.0 mmol) NaH (60%) were suspended in 2 ml anhydrous THF and cooled to 0°C. To this suspension, 1.0 ml dry ethanol was added dropwise and stirred for 10 min. This solution was transferred with the syringe to a solution of 40 mg (0.06 mmol) **4a** in 7 ml dry ethanol and stirred the reaction mixture at 80 °C for 12 h. After cooling the mixture to RT, 5% aq. HCl were added and extracted with EtOAc for three times. The organic phase was washed with sat. NH_4Cl and brine and the solvent were evaporated. The product was purified by column chromatography over silica gel (1:3, EtOAc/cyclohexane).

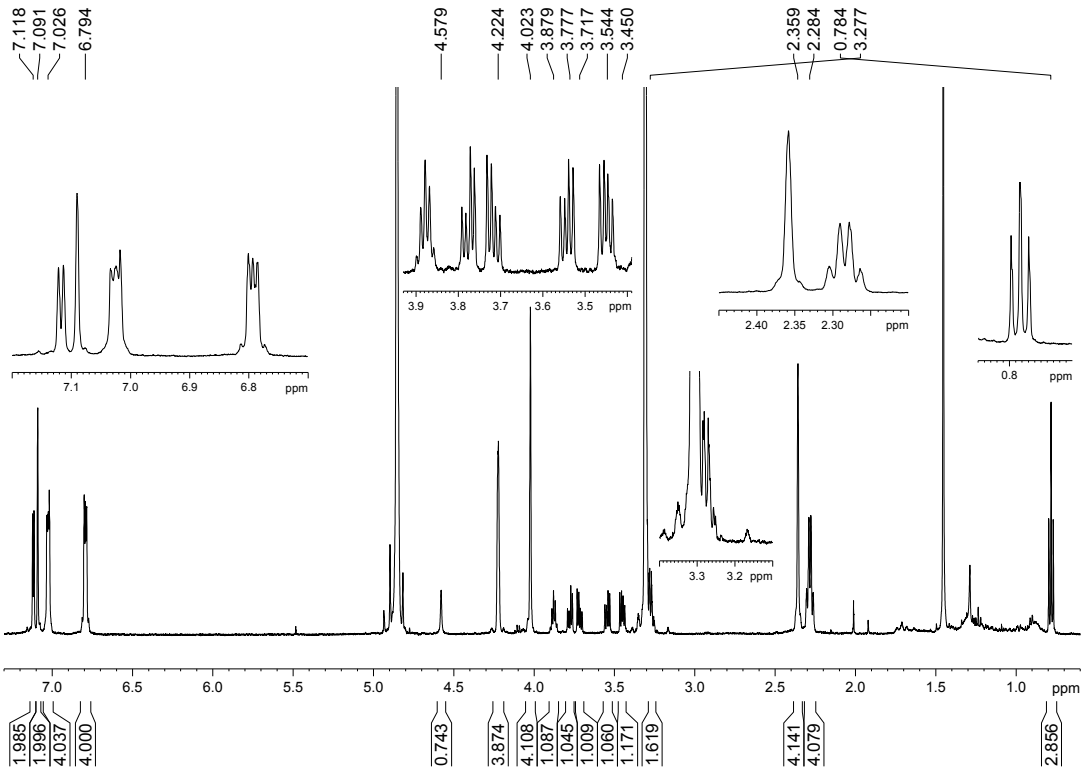
Yield: 25 mg, 62%.

Melting Point: >160 °C, brown coloration





^{1}H-NMR in $CDCl_3$



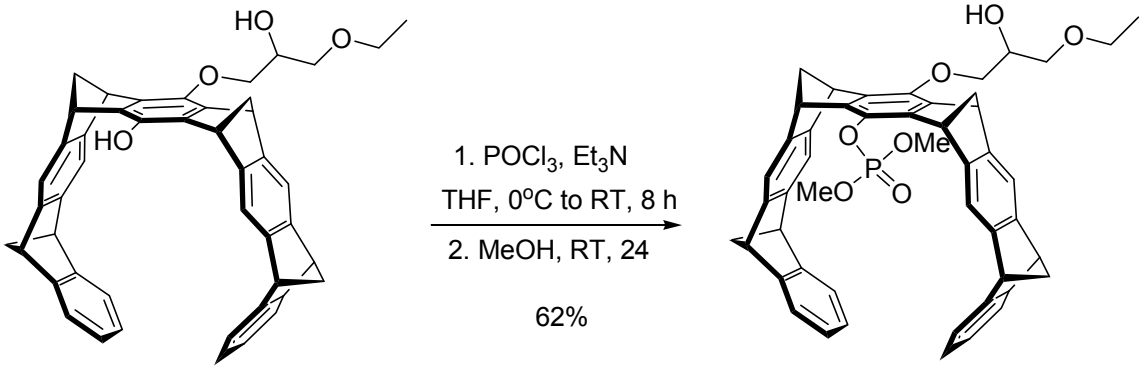
^{1}H-NMR in CD_3OD

^{1}H-NMR (500MHz, $CDCl_3$): δ [ppm] = 0.65 (t, 3H, H-31), 2.37, 2.43 (m, 8H, 24, H-25, H-23, H-26), 2.54 (d, 1H, OH), 3.15 (m, 2H, H-30), 3.43 (m, 2H, H-29a, H-29i), 3.84, 3.89 (m, 2H, H-27a, H-27i), 3.97 (m, 1H, H-28), 4.06 (s, 4H, H-5, H-11, H-16, H-22), 4.17 (s, 2 H, H-7, H-9), 4.25 (s, 2H, H-18, H-20), 4.27 (s, 1H, OH), 6.75 (m, 4H, H-2, H-3, H-13, H-14), 7.07 (m, 4H, H-1, H-15, H-4, H-12), 7.14 (d, 4H, H-17, H-21, H-6, H-10).

^{1}H-NMR (500MHz, CD_3OD): δ [ppm] = 0.78 (t, 3H, H-31), 2.28 (m, 4H, H-24, H-25), 2.36 (s, 4H, H-23, H-26), 3.28 (m, 2H, H-30), 3.45, 3.54 (m, 2H, H-29a, H-29i), 3.72, 3.78 (m, 2H, H-27a, H-27i), 3.88 (m, 1H, H-28), 4.02 (s, 4H, H-5, H-11, H-16, H-22), 4.22 (s, 4H, H-7, H-9, H-18, H-20), 4.57 (s, 1H, OH), 6.79 (m, 4H, H-2, H-3, H-13, H-14), 7.03 (m, 4H, H-1, H-15, H-4, H-12), 7.09 (s, 2H, H-6, H-10), 7.12 (d, 2H, H-17, H-21).

^{13}C-NMR (125.7MHz, CD_3OD): δ [ppm] = 15.3 (C-31), 28.1, 49.4, 52.6, 67.9, 69.1, 69.3, 70.9, 72.5, 76.2, 117.1 (t), 122.3 (d), 126.1(d), 137.3, 141.5, 142.5, 143.6, 148.9, 149.2, 149.5, 152.2 (d).

HR-MS (ESI pos., MeOH): m/z $[M+Na]^+$: cal. 691.2819, obs. 691.2930.



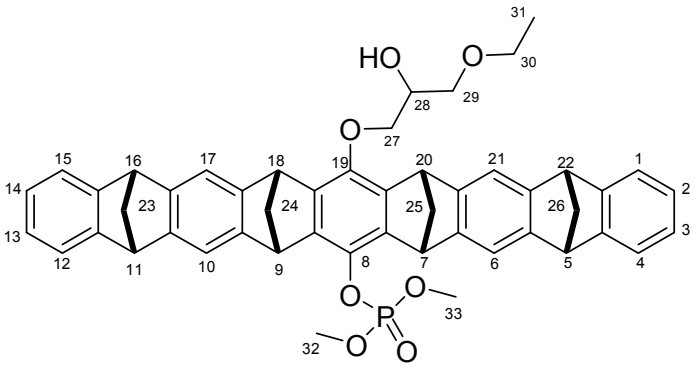
4b
$C_{47}H_{40}O_4$
668,82 g/mol

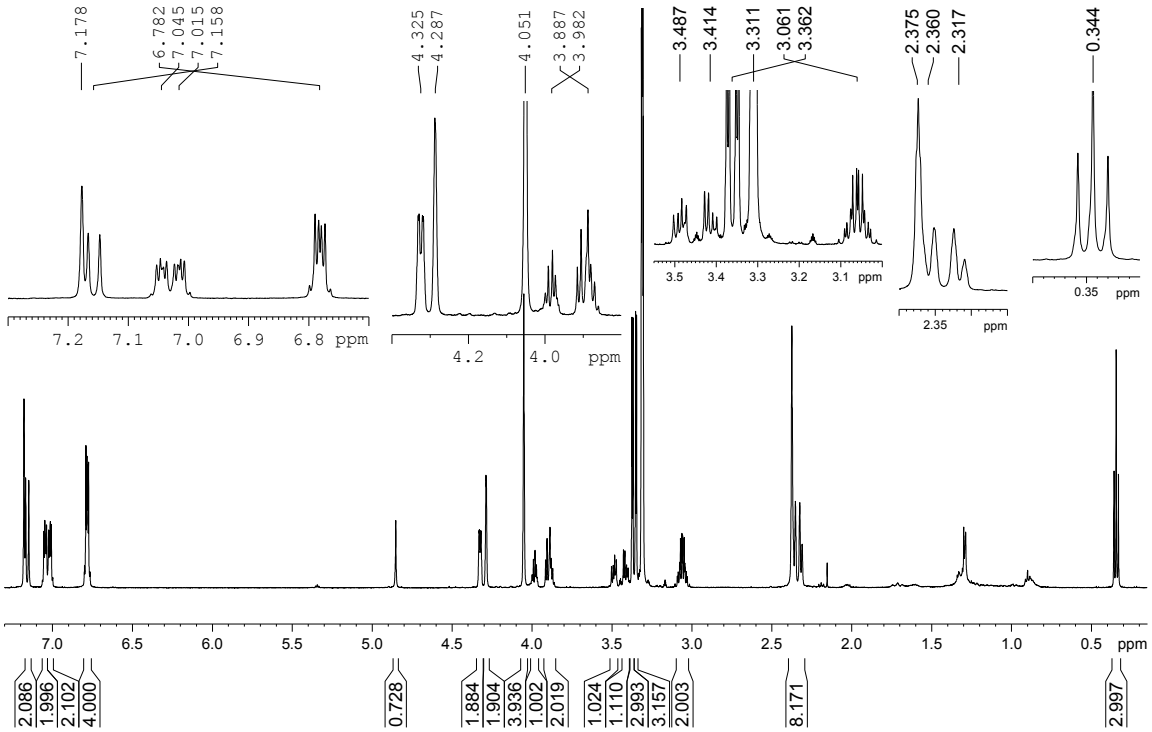
4c
$C_{49}H_{45}O_7P$
776,85 g/mol

A solution of 21 mg (0.0313 mmol) **4b** in 5 ml anhydrous THF was cooled to 0 °C. To the stirred solution under inert atmosphere, 26 µl (0.1878 mmol) Et_3N were added. After 10 min 57 µl (0.627 mmol) $POCl_3$ were added and the reaction mixture stirred from 0 °C to RT for 8 h. Thereafter, 4 ml dry methanol was added and stirred again for 24 h at RT. Solvent was removed on rotary evaporator and after adding 30 ml Dist. H_2O, the crude is extracted with CH_2Cl_2 (3×20 ml). Organic layer is dried on rotary evaporator and residue is purified by column chromatography on silica gel (1:3, EtOAc/cyclohexane).

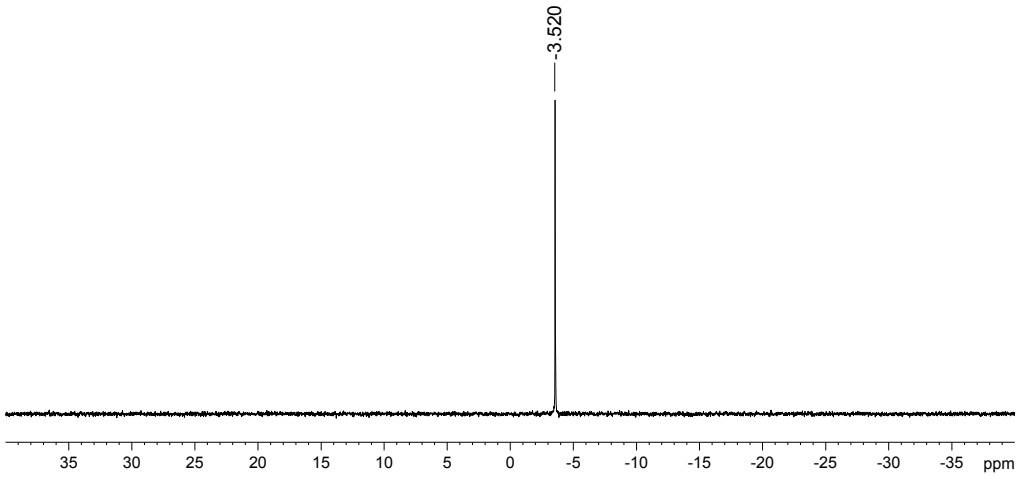
Yield: 15 mg, 62%, white solid.

Melting Point: 195 ^{o}C.





^{1}H-NMR in CD_3OD



^{31}P-NMR in $CDCl_3$

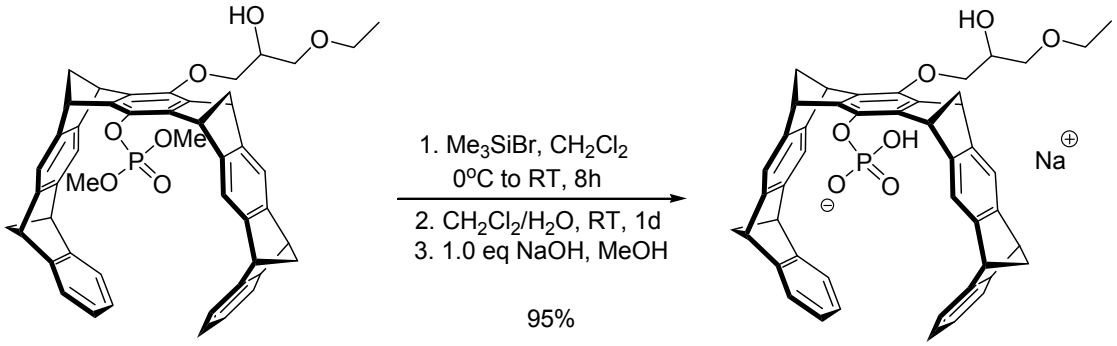
^{1}H-NMR (500MHz, CD_3OD): δ [ppm] = 0.34 (t, 3H, H-31), 2.32, 2.36 (d, 4H, H-24, H-25), 2.37 (s, 4H, H-23, H-26), 3.06 (m, 2H, H-30), 3.36 (dd, 6H, $^{3}J_{\text{H-32/P, H-33/P}}$ = 11.3 Hz, H-32, H-33), 3.41, 3.49 (m, 2H, H-29a, H-29i), 3.89 (m, 2H, H-27a, H-27i), 3.98 (m, 1H, H-28), 4.05 (s, 4H, H-5, H-11, H-16, H-22), 4.29(s), 4.32(d) (4H, H-7, H-9, H-18, H-20), 6.78 (m, 4H, H-2, H-3, H-13, H-14), 7.01, 7.04 (m, 4H, H-1, H-15, H-4, H-12), 7.16 (d, 2H, H-17, H-21), 7.18 (s, 2H, H-6, H-10).

^{1}H-NMR (500MHz, $CDCl_{3)}$: δ [ppm] = 0.30 (t, 3H, H-31), 2.38 (m, 4H, H-24, H-25), 2.43 (s, 4H, H-23, H-26), 3.02 (m, 2H, H-30), 3.40 (m, 2H, H-29), 3.42 (d, 6H, $^{3}J_{\text{H-32/P, H-33/P}}$ = 11.3 Hz, H-32, H-33), 3.98 (m, 3H, H-27, H-28), 4.07 (s, 4H, H-5, H-11, H-16, H-22), 4.27 (s, 2H, H-18, H-20), 4.36 (s, 2H, H-7, H-9), 6.73 (m, 4H, H-2, H-3, H-13, H-14), 7.04 (dd, 4H, H-1, H-15, H-4, H-12), 7.13 (d, 2H, H-17, H-21), 7.23 (s, 2H, H-6, H-10).

^{13}C-NMR (125.7MHz, $CDCl_3$): δ [ppm] = 14.1 (C-31), 48.5-48.8 (m, C-7, C-9, C-18, C-20), 50.4 (C-28), 51.3 (C-5, C-11, C-16, C-22), 54.9 (d, C-32, C-33), 66.6 (C-30), 68.8, 69.4 (d, C-23, C-26, C-24, C-25), 69.7 (C-28), 70.3 (C-29), 74.0 (C-27), 116.2, 117.2 (C-17, C-21, C-6, C-10), 121.1, 121.7 (C-1, C-15, C-4, C-12), 124.7 (d, C-2, C-3, C13, C-14), 134.9, 140.5, 141.1, 145.7(s) (d, C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 146.8, 147.1, 147.7 (d, C-6a, C-9a, C-17a, C-20a, C-8, C-9), 150.6, 150.8 (C-4a, C-11a, C-15a, C-22a).

^{31}P-NMR (202MHz, $CDCl_3$): δ [ppm] = -3.52 ppm.

HR-MS (ESI pos., MeOH): m/z $[M+Na]^+$: cal. 799.2795, obs. 799.2860.

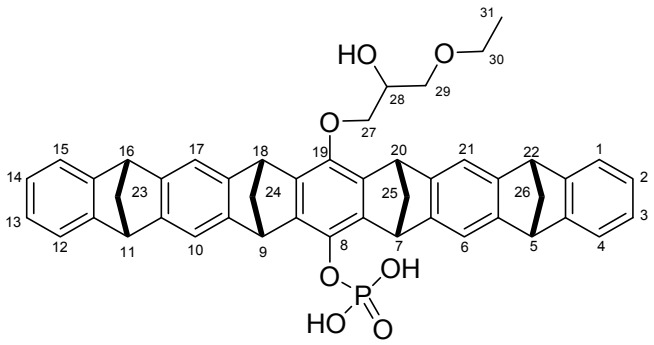


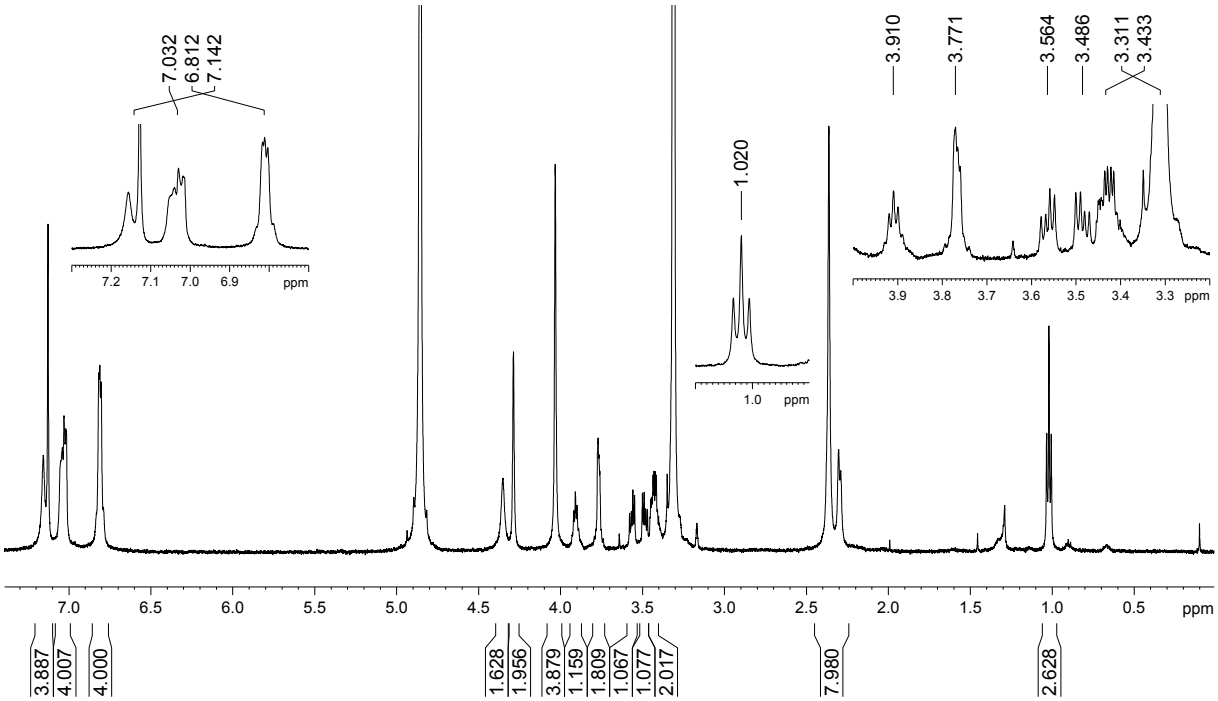
4c
$C_{49}H_{45}O_7P$
776,85 g/mol

4
$C_{47}H_{40}NaO_7P$
770,78 g/mol

To a 0°C cooled solution of 13 mg (0.0167 mmol) **4c** in anhydrous CH_2Cl_2, 22 µl (0.167 mmol) TMSBr were added dropwise and solution was stirred at RT for 8 hour. The excess of TMSBr and solvent were removed by condensation and remaining residue dried on oil pump for 4 h. The solid residue was dissolved in 10 ml CH_2Cl_2/H_2O (1:1) and stirred at RT for 24 h. Two phases were separated, and from organic phase collected 12 mg (95%) of white solid. For the neutralization of phosphate, to a solution of 5.0 mg (0.0067 mmol) of phosphoric acid tweezers in 5 ml methanol 0.27 mg (0.0067 mmol) NaOH were added and stirred at RT for 30 min., dried the solvent and collected white solid in quantitative yield.

Melting Point: > 215 °C, brown coloration.





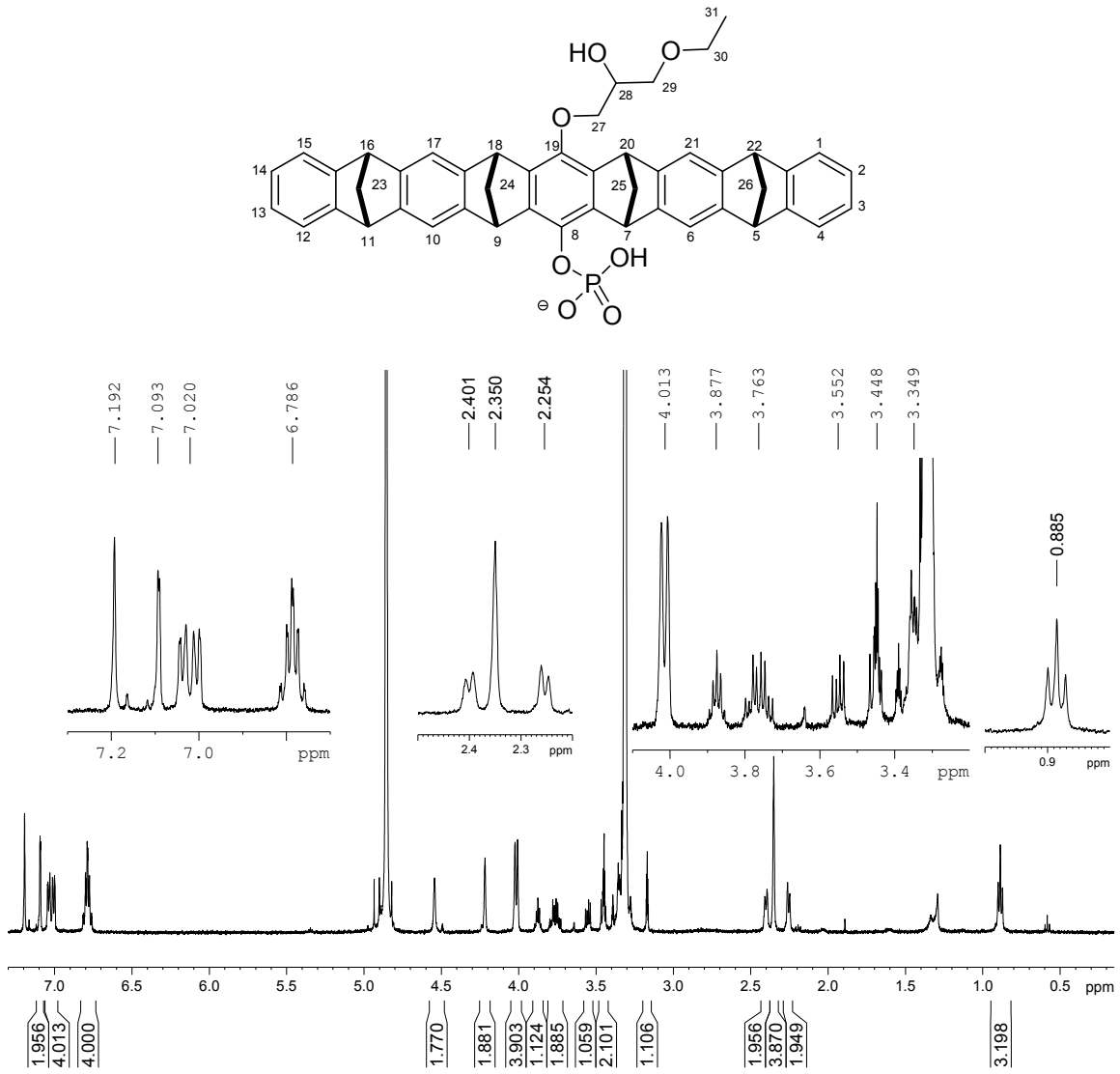
^{1}H-NMR in CD_3OD

^{1}H-NMR (500MHz, CD_3OD): δ [ppm] = 1.02 (t, 3H, H-31), 2.29-2.36 (m, 8H, H-24, H-25, H-23, H-26), 3.43 (m, 2H, H-30), 3.48, 3.56 (m, 2H, H-29a, H-29i), 3.77 (m, 2H, H-27), 3.91 (m, 1H, H-28), 4.03 (s, 4H, H-5, H-11, H-16, H-22), 4.29, 4.35 (s, 4H, H-7, H-9, H-18, H-20), 6.81 (m, 4H, H-2, H-3, H-13, H-14), 7.03 (m, 4H, H-1, H-15, H-4, H-12), 7.14 (d, 4H, H-17, H-21, H-6, H-10).

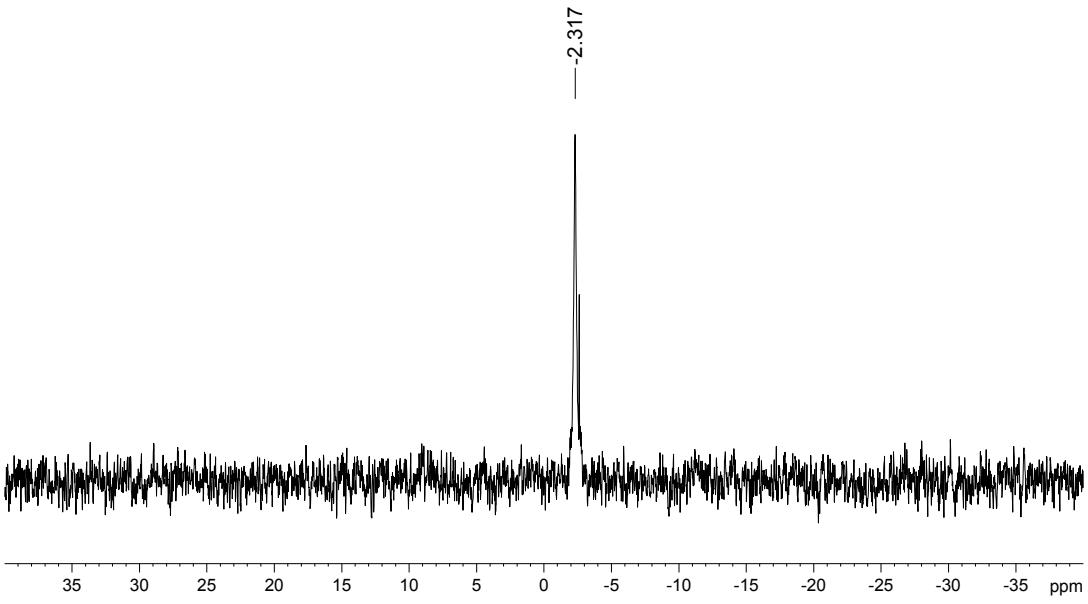
^{13}C-NMR (125.7MHz, CD_3OD): δ [ppm] = 15.5 (C-31), 49.0 (m, C-7, C-9, C-18, C-20), 52.4 (C-5, C-11, C-16, C-22), 67.9 (C-30), 69.0 (d, C-23, C-26, C-24, C-25), 70.7 (C-28), 72.4 (C-29), 75.9 (C-27), 116.6(d), 118.2 (C-17, C-21, C-6, C-10), 122.0, 122.2 (C-1, C-15, C-4, C-12), 125.9 (d, C-2, C-3, C13, C-14), 142.4, 142.9, 146.3 (C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 148.8, 149.1 (m, C-6a, C-9a, C-17a, C-20a, C-8, C-9), 152.1 (C-4a, C-11a, C-15a, C-22a).

^{31}P-NMR (202MHz, $CDCl_3$): δ [ppm] = -4.16 ppm.

HR-MS (ESI pos., neg., MeOH): m/z $[M+Na]^+$: cal. 771.2482, obs. 771.2538, m/z $[M-H]^-$: cal. 747.2517, obs. 747.2591.



^{1}H-NMR in CD_3OD

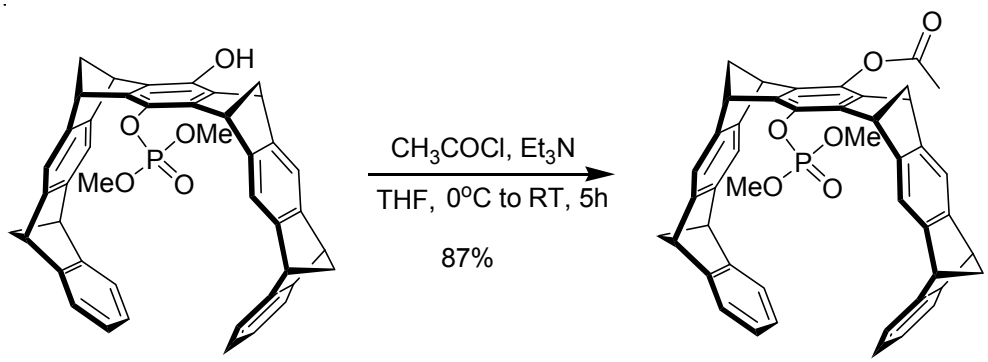


^{31}P-NMR in CD_3OD

^{1}H-NMR (500MHz, CD_3OD): δ [ppm] = 0.88 (t, 3H, H-31), 2.25 (d, 2H, H-24a, H-25a), 2.35 (s, 4H, H-23, H-26), 2.40 (d, 2H, H-24i, H-25i), 3.35 (m, 2H, H-30), 3.45, 3.55 (m, 2H, H-29a, H-29i), 3.76 (m, 2H, H-27), 3.88 (m, 1H, H-28), 4.01 (d, 4H, H-5, H-11, H-16, H-22), 4.22 (s, 4H, H-18, H-20), 4.54 (s, 2H, H-7, H-9), 6.78 (m, 4H, H-2, H-3, H-13, H-14), 7.02 (m, 4H, H-1, H-15, H-4, H-12), 7.09 (s, 2H, H-17, H-21), 7.19 (d, 2H, H-6, H-10).

^{31}P-NMR (CD_3OD): δ [ppm] = -2.32 ppm.

Synthesis of the acetoxy phosphate tweezer 6



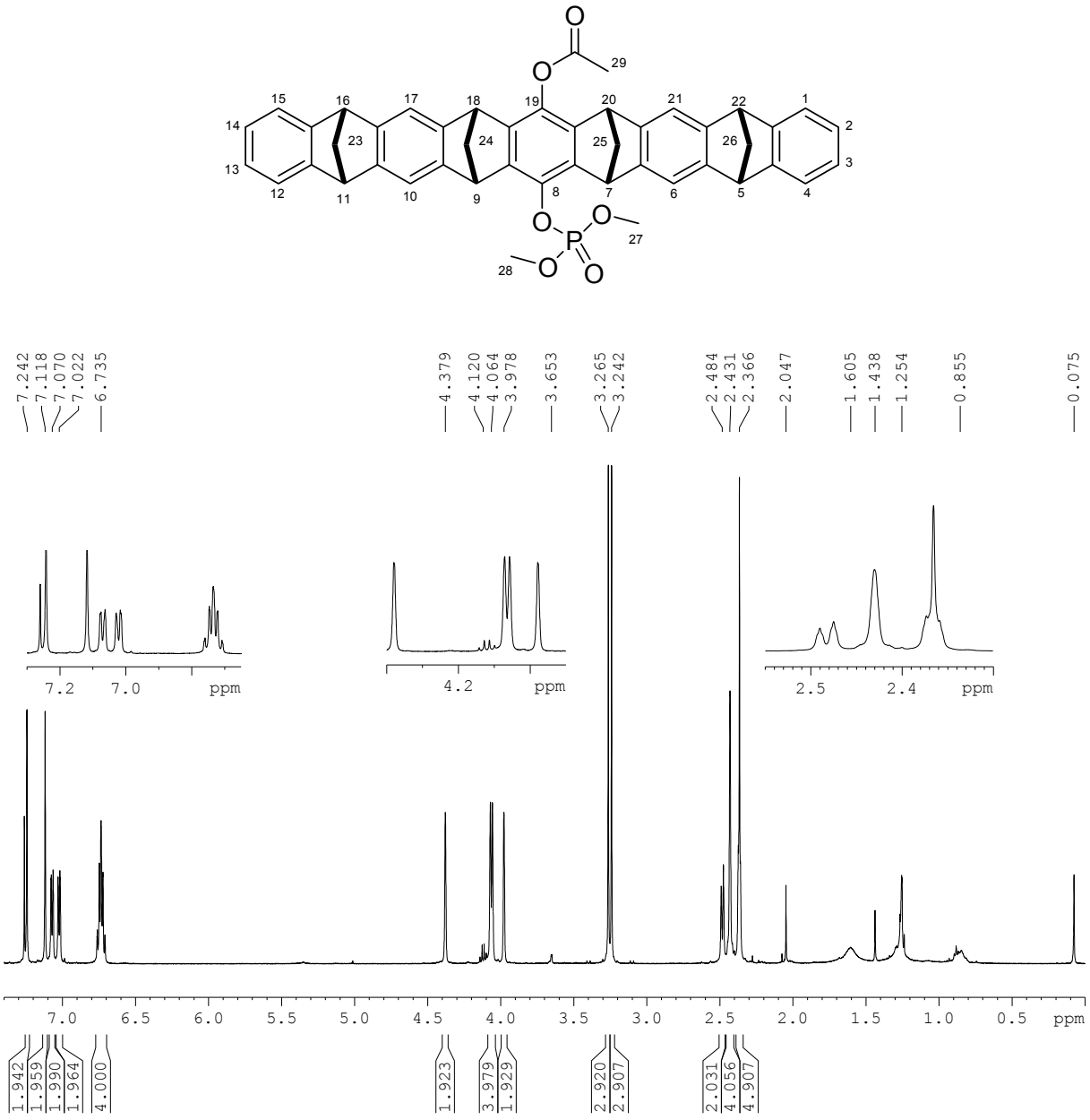
1a
$C_{44}H_{35}O_5P$
674,72 g/mol

6a
$C_{46}H_{37}O_6P$
716,76 g/mol

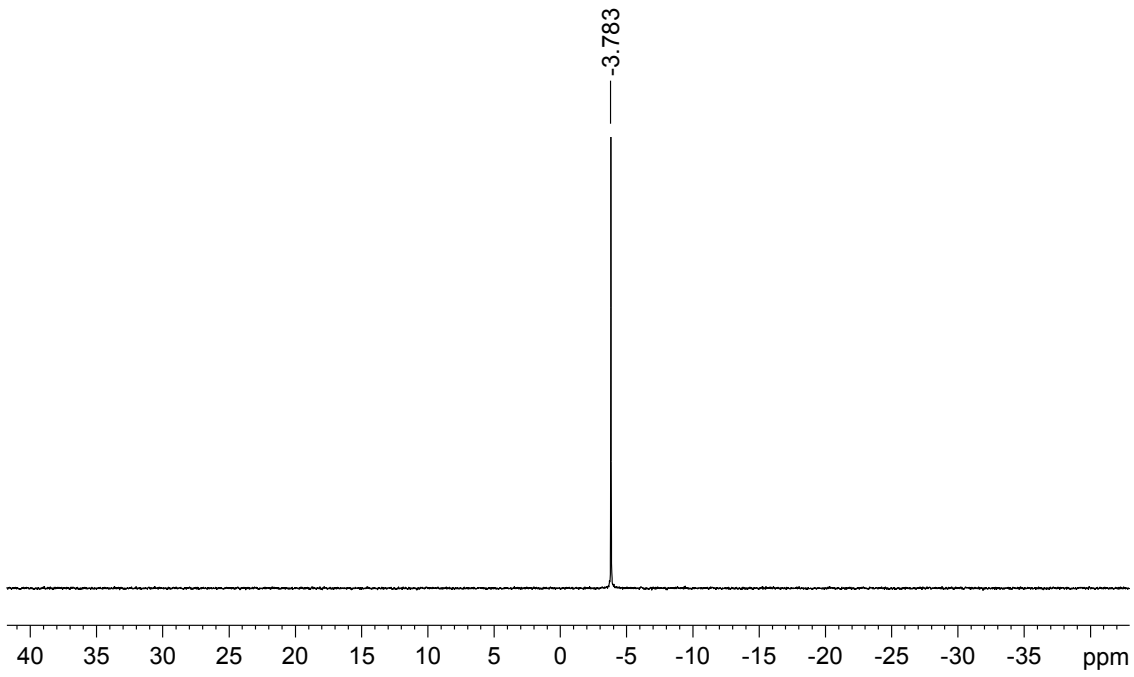
Under argon atmosphere, 30 mg (0.044 mmol) tweezer **1a** were dissolved in 5 ml anhydrous THF and cooled to 0 °C. Then 9 µl (0.066 mmol) Et_3N were added by micro syringe. After 5 min. were added 5 µl (0.066 mmol) of acetyl chloride with subsequent formation of white precipitate of $Et_3N{\cdot}HCl$. The reaction stirred for 5 hour from 0 °C to rt and then added sat. $NaHCO_3$ solution and extracted three times with CH_2Cl_2. The combined organic phase is then washed with dist. water and dried over $MgSO_4$. Solvent removed on a *rota vap* and thus collected 27 mg pure white solid.

Yield: 27 mg, 87%

Melting Point: > 200 °C brown coloration.


7.242
7.118
7.070
7.022
6.735
4.379
4.120
4.064
3.978
3.653
3.265
3.242
2.484
2.431
2.366
2.047
1.605
1.438
1.254
0.855
0.075
7.2
7.0
ppm
4.2
ppm
2.5
2.4
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.942
1.959
1.990
1.964
4.000
1.923
3.979
1.929
2.920
2.907
2.031
4.056
4.907

^{1}H-NMR



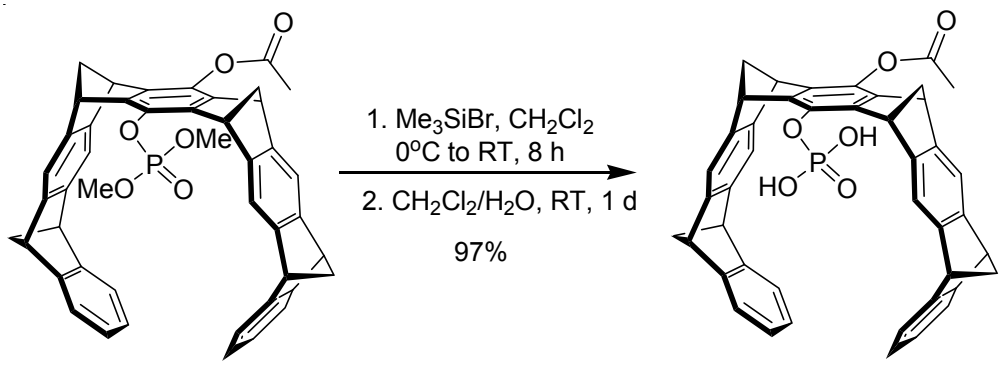
^{31}P-NMR

^{1}H-NMR (500MHz, $CDCl_3$): δ [ppm] = 2.36 (m, 5H, H-24a, H-25a, H-29), 2.43 (s, 4H, H-23, H-26), 2.48 (d, 4H, H-23, H-26), 3.25 (d, $^{3}J_{\text{H-27/P, H-28/P}}$ =1.00, 6H, H-27, H-28), 3.97 (s, 2H, H-7, H-9), 3.06 (d, 4H, H-5, H-11, H-16, H-22), 4.38 (s, 2H, H-18, H-20), 6.73 (m, 4H, H-2, H-3, H-13, H-14), 7.02 (d, 2H, H-4, H-12), 7.07 (d, 2H, H-1, H-15), 7.12 (s, 2H, H-6, H-10), 7.24 (s, 2H, H-17, H-21).

^{13}C-NMR (125.7MHz, $CDCl_3$): δ [ppm] = 20.9 (C-29), 48.7 (C-7, C-9, C-18, C-20), 51.3(d, C-5, C-11, C-16, C-22), 54.9(d, C-27, C-28), 68.5, 69.7 (C-23, C-24, C-25, C-26), 116.6 (C-17, C-21), 117.2 (C-6, C-10), 121.0 (C-1, C-15), 121.8 (C-4, C-12), 124.8 (d, C-2, C-3, C13, C-14), 136.7, 141.4, 142.3 (C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 146.4, 146.8, 147.8 (C-6a, C-9a, C-17a, C-20a, C-8, C-9), 150.6 (d, C-4a, C-11a, C-15a, C-22a), 169.0 (-CH_3CO).

^{31}P-NMR (202MHz, CD_3OD): δ [ppm] = -3.78

HR-MS (ESI pos., MeOH): m/z $[M+Na]^+$: cal. 739.2220, obs. 739.2281.



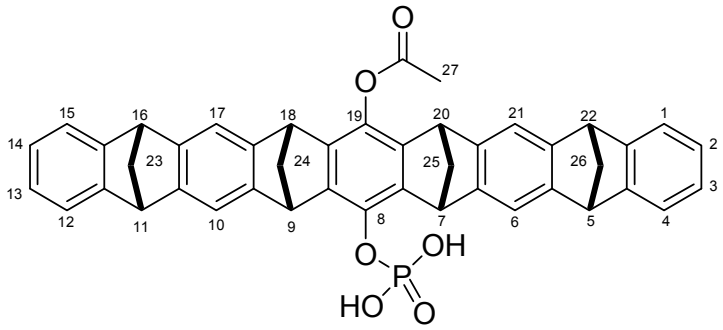
6a
$C_{46}H_{37}O_6P$
716,76 g/mol

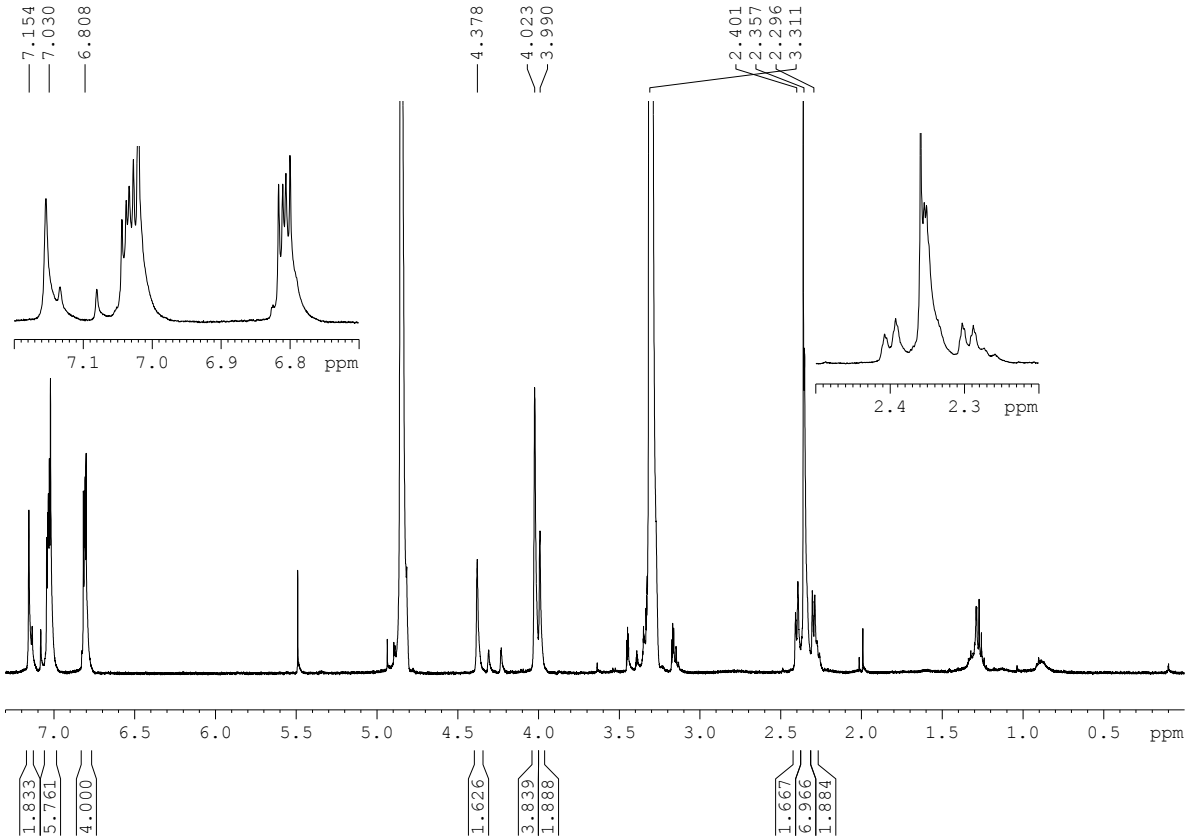
6
$C_{44}H_{33}O_6P$
688,7 g/mol

To a 0 ^oC cooled solution of 24 mg (0.0336 mmol) tweezer **2a** in anhydrous CH_2Cl_2, 44 µl (0.336 mmol) trimethylsilyl bromides (TMSBr) were added dropwise and then stirred at RT for 8 hour. The excess of TMSBr and solvent were removed by condensation and remaining residue was dried on oil pump for 2-5 h. The solid residue was then dissolved in CH_2Cl_2/H_2O (1:1) and stirred at RT for 24 h. Two phases were separated, and after drying organic phase on *rota vap,* 22 mg of white solid were collected. The crude was washed with n-hexane or acetonitrile to remove the trace amount of grease from the product.

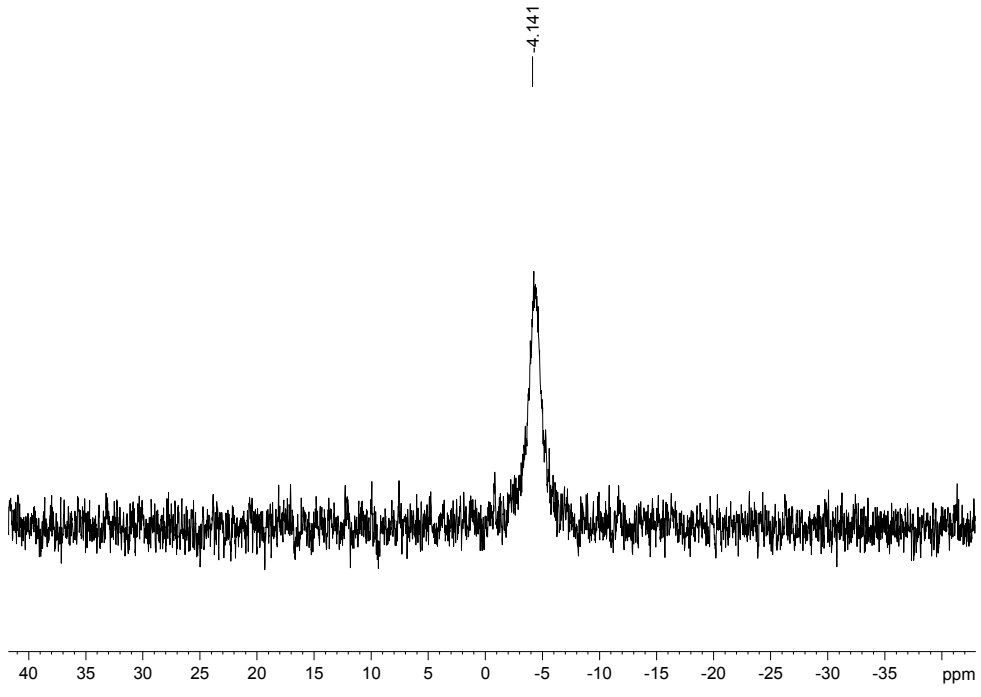
Yield: 22 mg, 97 %.

Melting Point: > 221 ^oC brown coloration.





^{1}H-NMR



^{31}P-NMR

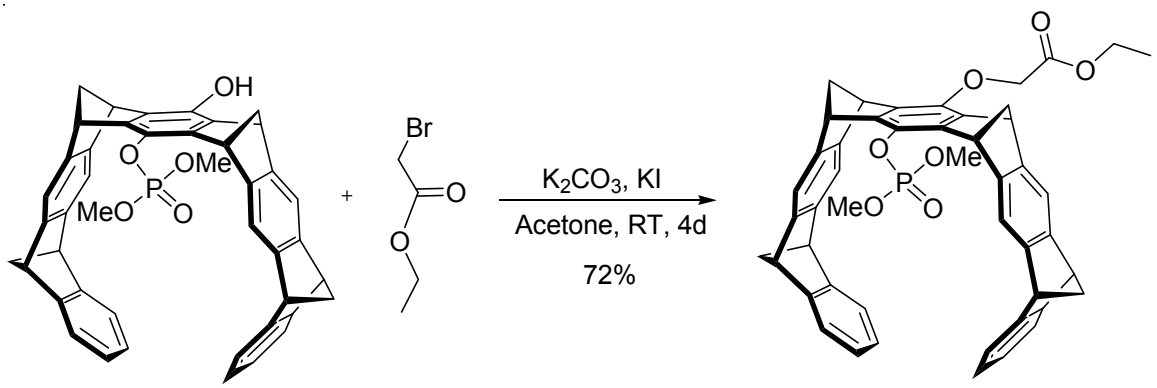
^{1}H-NMR (500 MHz, CD3OD): δ [ppm] = 2.29 (d, 2H, H-24a, H-25a), 2.35 (m, 7H, H-23, H-26, H-27), 2.40 (d, 2H, H-24i, H-25i), 3.99 (2H, H-7, H-9), 4.02 (s, 4H, H-5, H-11, H-16, H-22), 4.38 (s, 2H, H-18, H-20), 6.81 (m, 4H, 4H, H-2, H-3, H-13, H-14), 7.03 (m, 6H, H-6, H-10, H-4, H-12, H-1, H-15), 7.15 (s, 2H, H-17, H-21).

^{13}C-NMR (125.7 MHz, CD_3OD): δ [ppm] = 20.6 (C-27), 49.4 (C-7, C-9, C-18, C-20), 52.5(C-5, C-11, C-16, C-22), 69.2, 69.4 (C-23, C-24, C-25, C-26), 117.2 (C-6, C-10), 118.3 (C-17, C-21), 122.3 (d, C-4, C-12, C-1, C-15), 126.1 (d, C-2, C-3, C13, C-14), 137.7, 138.9, 143.4 (C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 148.2, 148.7, 149.2 (C-6a, C-9a, C-17a, C-20a, C-8, C-9), 150.2 (d, C-4a, C-11a, C-15a, C-22a), 170.9 (-CH_3CO).

^{31}P-NMR (202MHz, CD_3OD): δ [ppm] = -4.14

HR-MS (ESI pos., neg., MeOH): m/z $[M+Na]^+$: cal. 711.1907, obs. 711.2030, m/z $[M-H]^-$: cal. 687.1942, obs. 687.2061.

Synthesis of the ethoxycarboxymethyl phosphate tweezer 7



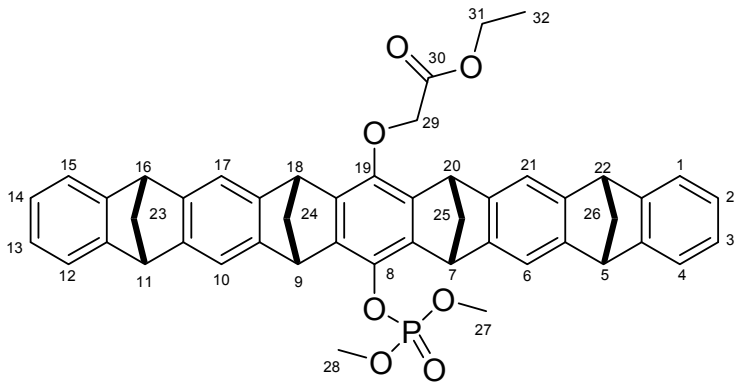
1a
$C_{44}H_{35}O_5P$
674,72 g/mol

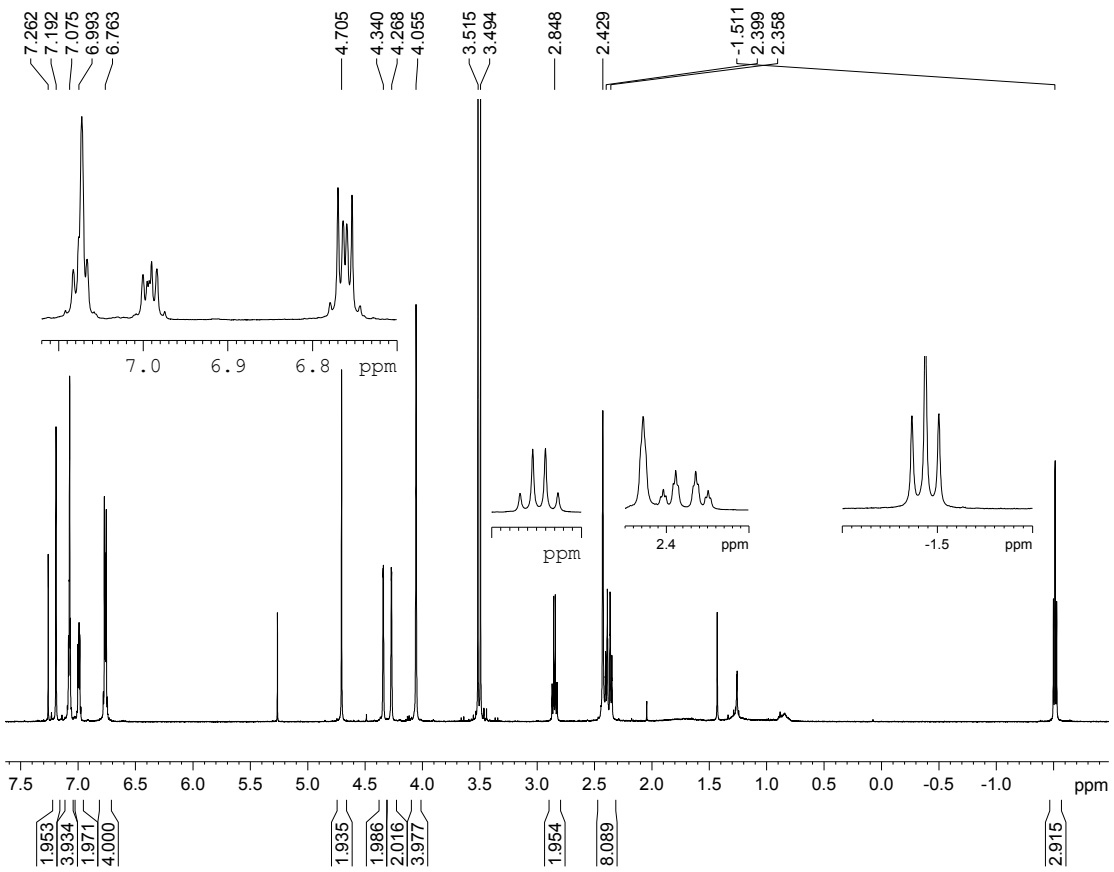
7a
$C_{48}H_{41}O_7P$
760,81 g/mol

Under argon atmosphere, in a solution of 30 mg (0.044 mmol) tweezer **1a** in 5 ml absolute acetone 9.0 mg (0.066 mmol) K_2CO_3, 7.0 µl (0.066 mmol) ethylbromoacetate and a few granules of KI were added and then the reaction mixture is stirred at RT for 4 days. The reaction mixture was diluted with CH_2Cl_2 and washed with sat NH_4Cl and finally with dist water. Organic phase was dried over Na_2SO_4. Solvent removed on a rotary evaporator and crude was purified by column chromatography using EtOAc/cyclohexane (1:3) eluent.

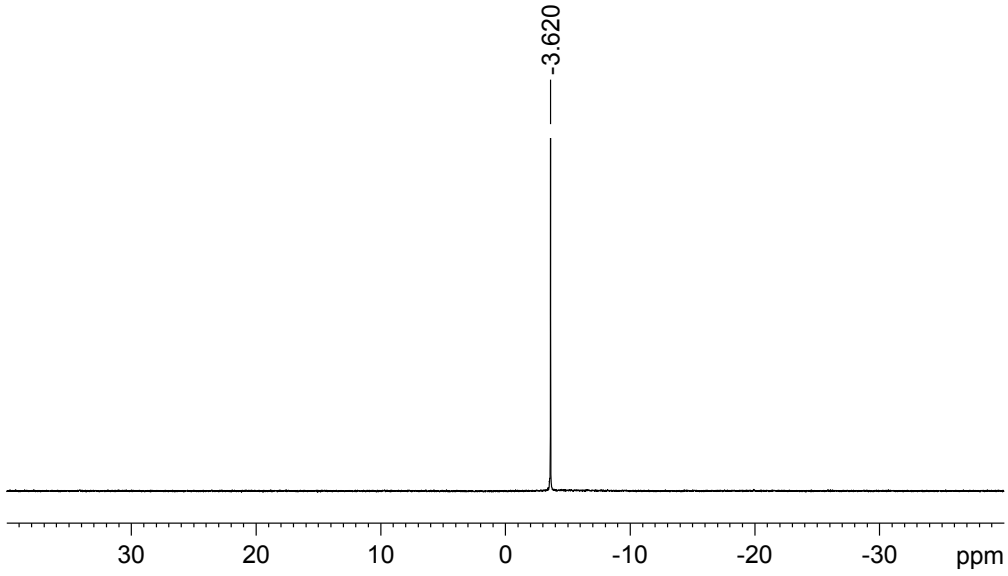
Yield: 24 mg, 72%

Melting Point: > 170 ^{o}C brown coloration.





^{1}H-NMR



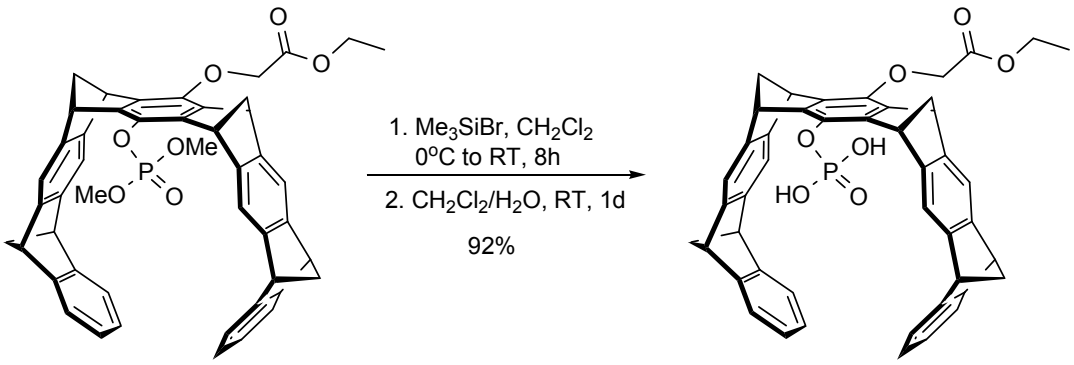
^{31}P-NMR

^{1}H-NMR (500MHz, $CDCl_3$): δ [ppm] = -1.51 (t, 3H, H-32), 2.37 (tm, 4H, 24a, H-25a, H-24i, H-25i), 2.43 (s, 4H, H-23, H-26), 2.85 (m, 2H, H-31), 3.50 (d, $^{3}J_{H\text{-}27/P,\ H\text{-}28/P}$ = 11.00, 6H, H-27, H-28), 4.05 (s, 4H, H-5, H-11, H-16, H-22), 4.27 (s, 2 H, H-18, H-20), 4.34 (s, 2H, H-7, H-9), 4.70 (s, 2H, H-29), 6.76 (m, 4H, H-2, H-3, H-13, H-14), 6.99 (m, 2H, H-1, H-15), 7.07 (m, 4H, H-4, H-12, H-17, H-21), 7.19 (s, 2H, H-6, H-10).

^{13}C-NMR (125.7MHz, $CDCl_3$): δ [ppm] = 10.9 (C-32), 48.1, 48.8 (C-7, C-9, C-18, C-20), 51.2(C-5, C-11, C-16, C-22), 54.9 (d, C-27, C-28), 61.1 (C-31), 68.5 (C-23, C-26, C-24, C-25), 69.1 (C-29), 116.3, 117.0 (C-17, C-21, C-6, C-10), 120.9, 121.5 (C-1, C-15, C-4, C-12), 124.8 (d, C-2, C-3, C13, C-14), 134.7(d), 139.8, 141.1(d), 145.0 (C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 146.9, 147.2, 147.5, 147.7 (C-6a, C-9a, C-17a, C-20a, C-8, C-9), 150.8, 151.0 (C-4a, C-11a, C-15a, C-22a), 169.1 (C-30).

^{31}P-NMR (202MHz, $CDCl_3$): δ [ppm] = -3.62

HR-MS (ESI pos., MeOH): m/z $[M+Na]^+$: cal. 783.2482, obs. 783.2550.



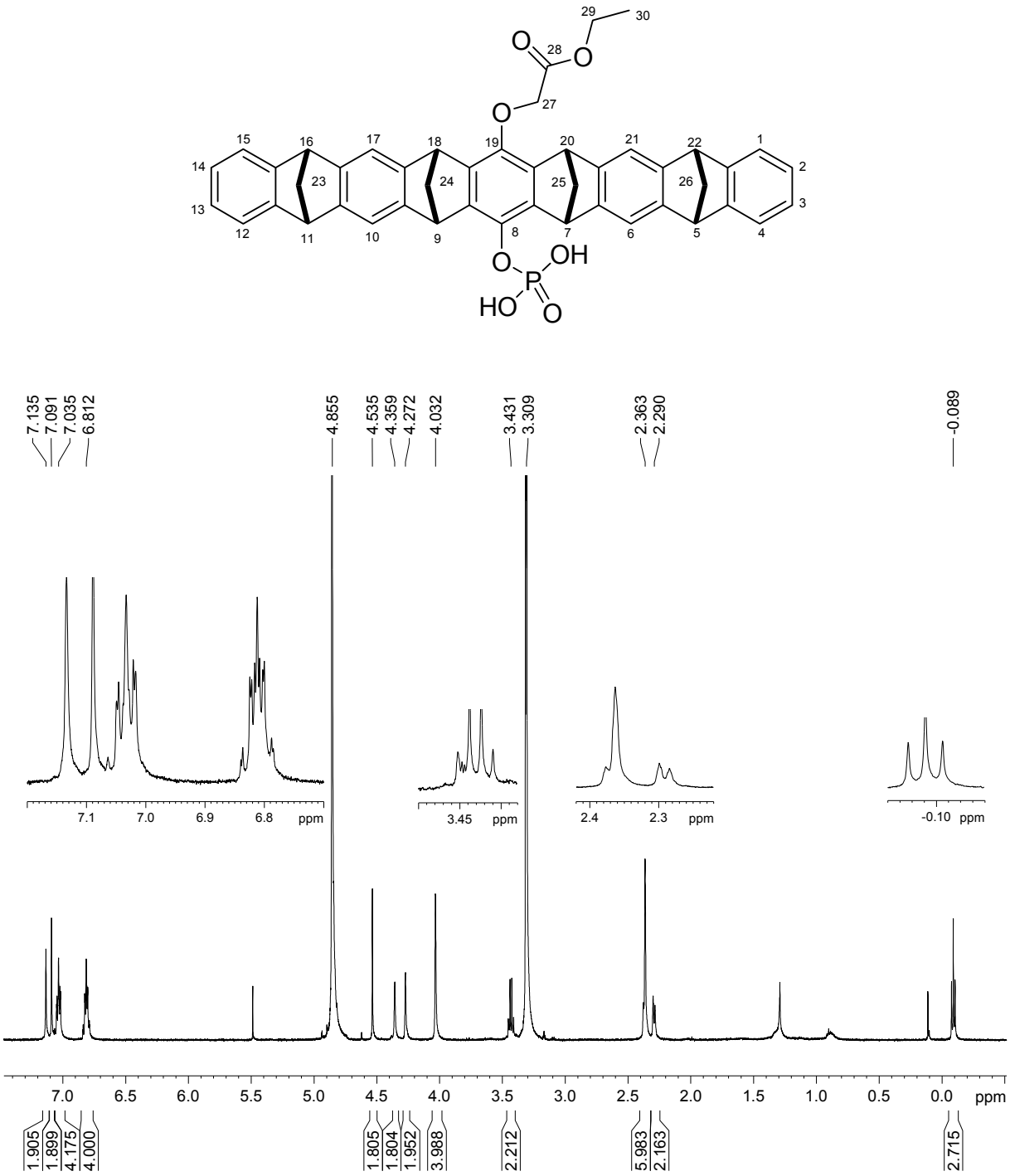
7a
$C_{48}H_{41}O_7P$
760,81 g/mol

7b
$C_{46}H_{37}O_7P$
732,76 g/mol

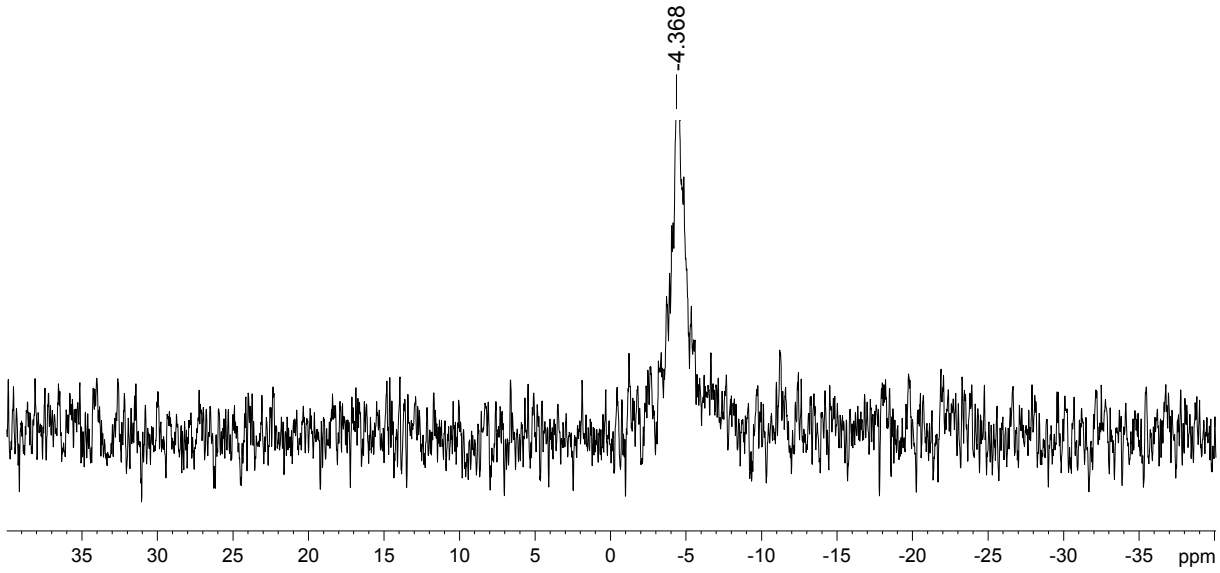
28 mg (0.0368 mmol) **7a** were treated with 48 µl (0.368 mmol) TMSBr using the general procedure.

Yield: 24 mg, 92%.

Melting Point: > 282 °C brown coloration.


7.135
7.091
7.035
6.812
4.855
4.535
4.359
4.272
4.032
3.431
3.309
2.363
2.290
-0.089
7.1
7.0
6.9
6.8
ppm
3.45
ppm
2.4
2.3
ppm
-0.10
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.905
1.899
4.175
4.000
1.805
1.804
1.952
3.988
2.212
5.983
2.163
2.715

^{1}H-NMR



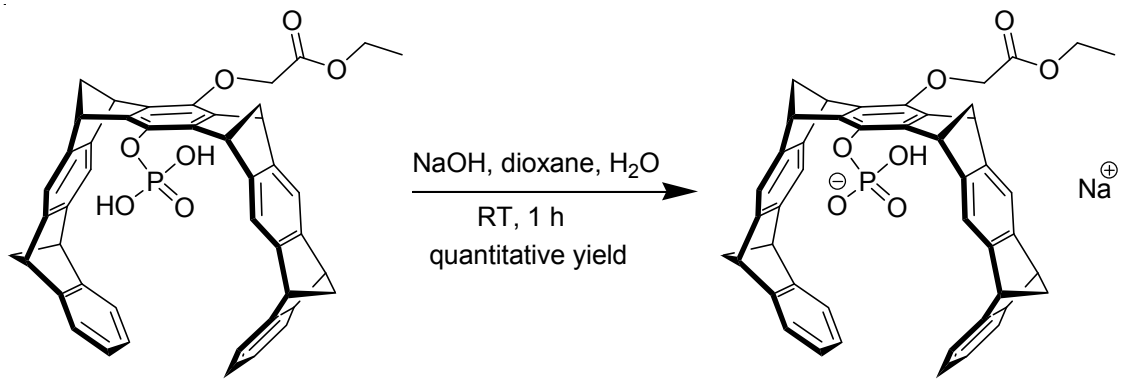
^{31}P-NMR

^{1}H-NMR (500MHz, CD_3OD): δ [ppm] = -0.089 (t, 3H, H-30), 2.29 (d, 2H, 24a, H-25a), 2.36 (m, 6H, H-23, H-26, H-24i, H-25i), 3.43 (m, 2H, H-29), 4.03 (s, 4H, H-5, H-11, H-16, H-22), 4.27 (s, 2 H, H-18, H-20), 4.36 (s, 2H, H-7, H-9), 4.53 (2H, H-27), 6.81 (m, 4H, H-2, H-3, H-13, H-14), 7.03 (m, 4H, H-1, H-15, H-4, H-12), 7.09 (s, 2H, H-17, H-21), 7.13 (s, 2H, H-6, H-10).

^{13}C-NMR (125.7MHz, CD_3OD): δ [ppm] = 13.4 (C-30), 49.4 (m, C-7, C-9, C-18, C-20), 52.5 (C-5, C-11, C-16, C-22), 62.4 (C-29), 69.1 (C-23, C-26, C-24, C-25), 70.8 (C-27), 117.1, 118.1 (C-17, C-21, C-6, C-10), 122.3 (d, C-1, C-15, C-4, C-12), 126.1 (d, C-2, C-3, C13, C-14), 141.8, 143.1 (C-5a, C-16a, C-21a, C-10a,C-7a, C-8a, C-18a, C-19a), 148.7, 148.9, 149.1(d) (C-6a, C-9a, C-17a, C-20a, C-8, C-9), 152.3 (C-4a, C-11a, C-15a, C-22a), 171.1 (C-28).

^{31}P-NMR (202MHz, CD_3OD): δ [ppm] = -4.37

HR-MS (ESI pos., neg., MeOH): m/z $[M+Na]^+$: cal. 755.2169, obs. 755.2237. m/z $[M-H]^-$: cal. 731.2204, obs. 731.2301.



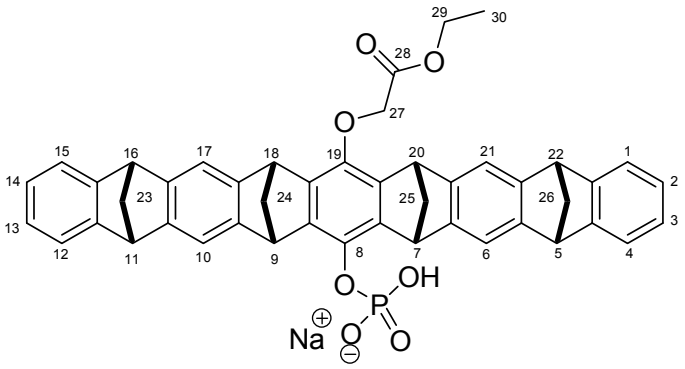
7b
C46H37O7P
732,76 g/mol

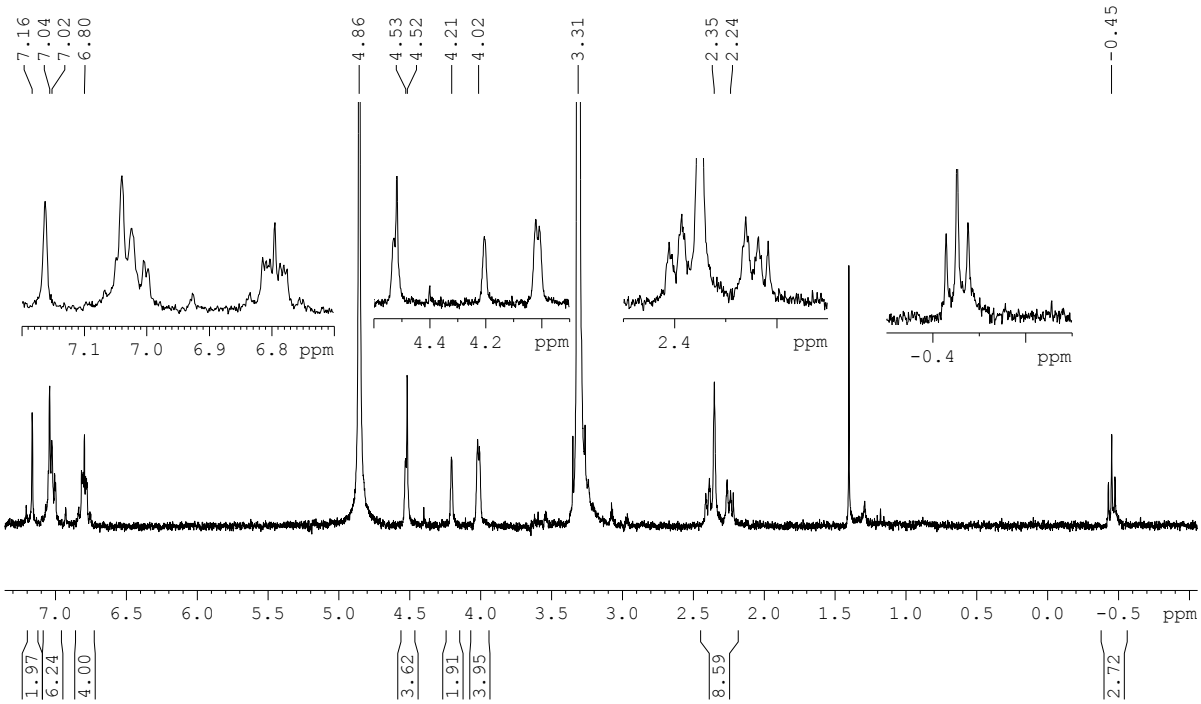
7
C46H36O7PNa
754,74 g/mol

To a solution of 16 mg (0.022 mmol) ethoxycarboxy hydrogen phosphate tweezer **7b** in 10 ml dioxane, 0.813 mg (0.022 mmol) NaOH in 1.0 ml water was added and stirred for 1 h at RT. Solvent removed in *vacuo* and solid was supended in 5 ml water and dried on lyophilization apparatus.

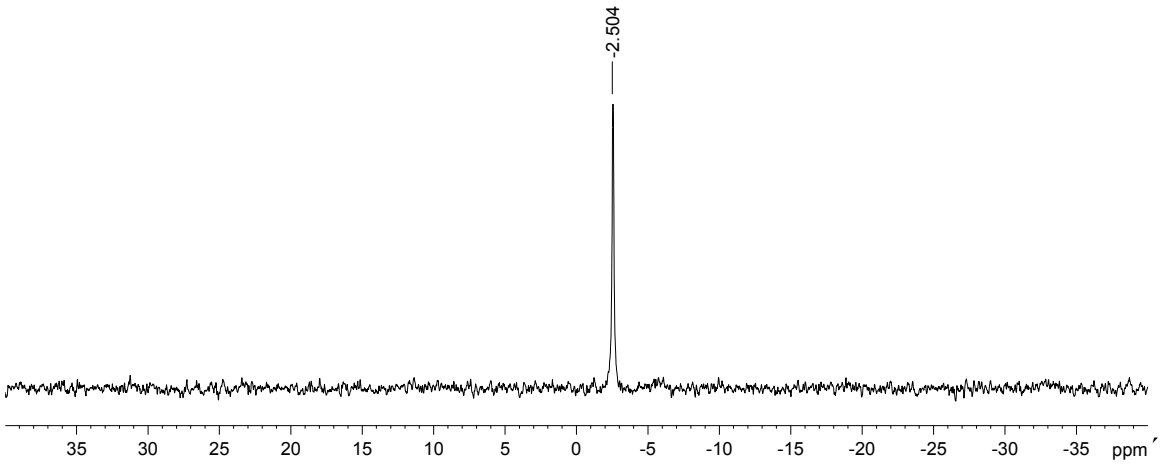
Yield: quantitative.

Melting Point: > 225 ^{o}C brown coloration.

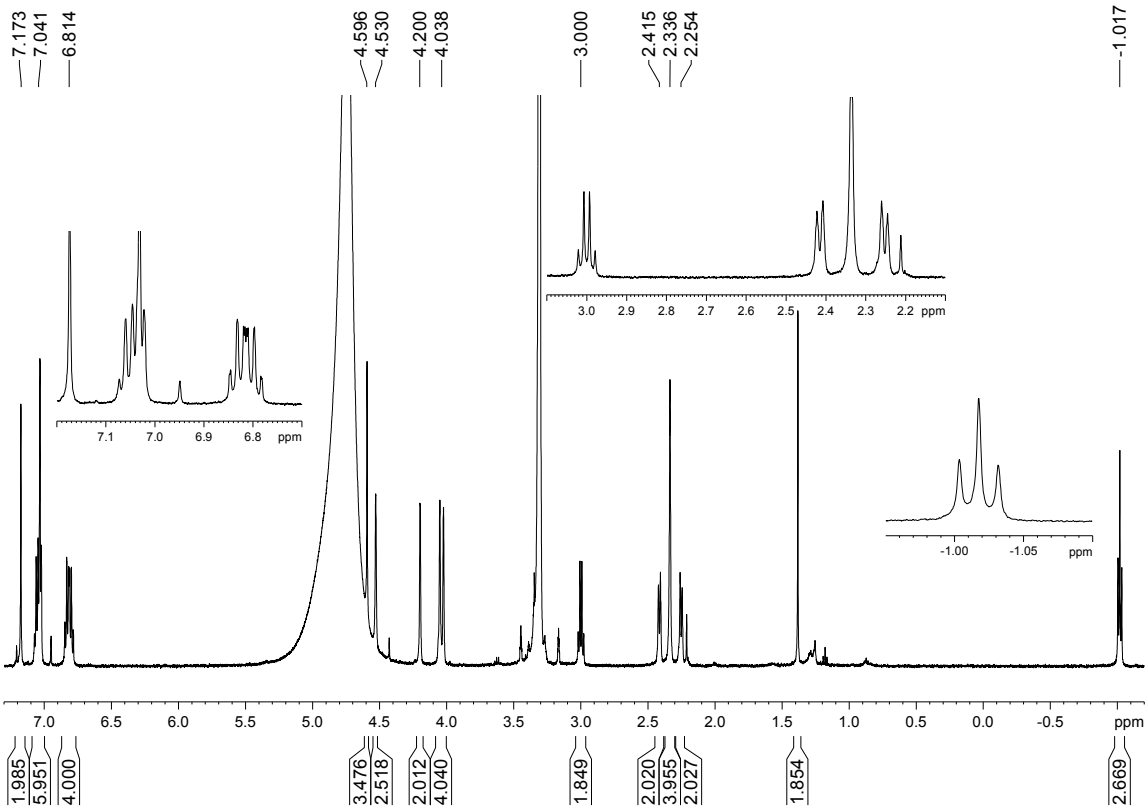




^{1}H-NMR in CD_3OD



^{31}P-NMR in CD_3OD



^{1}H-NMR in CD_3OD/D_2O buffer 10 mM, pH 7.2 (2:1)

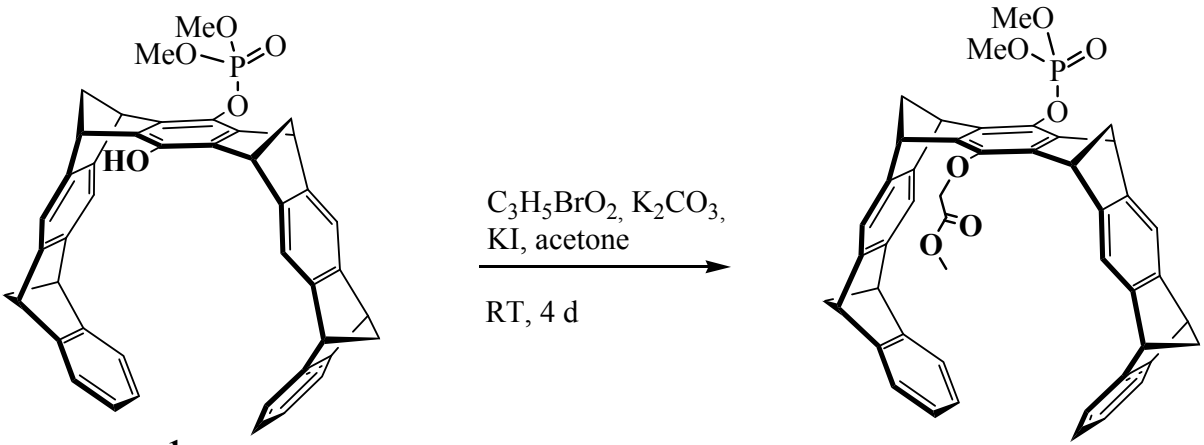
^{1}H-NMR (300 MHz, CD_3OD): δ [ppm] = -0.45 (2H, H-30), 2.24 (d, 2H, 24a, H-25a), 2.35 (s, 4H, H-23, H-26), 2.39 (d, 2H, H-24i, H-25i), 3.30 (m, 2H, H-29), 4.02 (ds, 4H, H-5, H-11, H-16, H-22), 4.21 (s, 2H, H-18, H-20), 4.52 (s, 2H, H-27), 4.53 (s, 2H, H-7, H-9), 6.80 (m, 4H, H-2, H-3, H-13, H-14), 7.02, 7.04 (m, 6H, H-1, H-15, H-4, H-12, H-17, H-21), 7.16 (s, 2H, H-6, H-10).

^{1}H-NMR {500MHz, CD_3OD/D_2O buffer (2:1)}: δ [ppm] = -1.01 (3H, H-30), 2.25 (d, 2H, 24a, H-25a), 2.34 (s, 4H, H-23, H-26), 2.41 (d, 2H, H-24i, H-25i), 3.00 (m, 2H, H-29), 4.04 (d, 4H, H-5, H-11, H-16, H-22), 4.20 (s, 2H, H-18, H-20), 4.53 (s, 2H, H-7, H-9), 4.59 (s, 2H, H-27), 6.81 (m, 4H, H-2, H-3, H-13, H-14), 7.04 (m, 6H, H-1, H-15, H-4, H-12, H-17, H-21), 7.17 (s, 2H, H-6, H-10).

^{31}P-NMR (202MHz, CD_3OD): δ [ppm] = -2.50

HR-MS (ESI pos., neg., MeOH): m/z $[M+H]^+$: cal. 755.2169, obs. 755.2289, m/z $[M+Na]^+$: cal. 777.1989, obs. 777.2096, m/z $[M-Na]^-$: cal. 731.2204, obs. 731.2329.

Synthesis of carboxymethyl phosphate tweezer 8



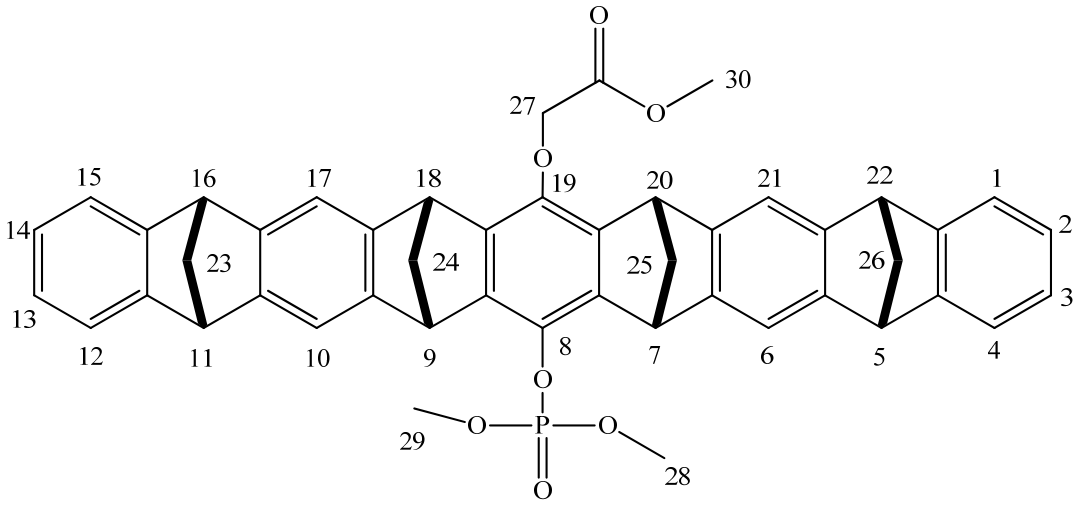
1a
$C_{44}H_{35}O_5P$
674.72 g/mol

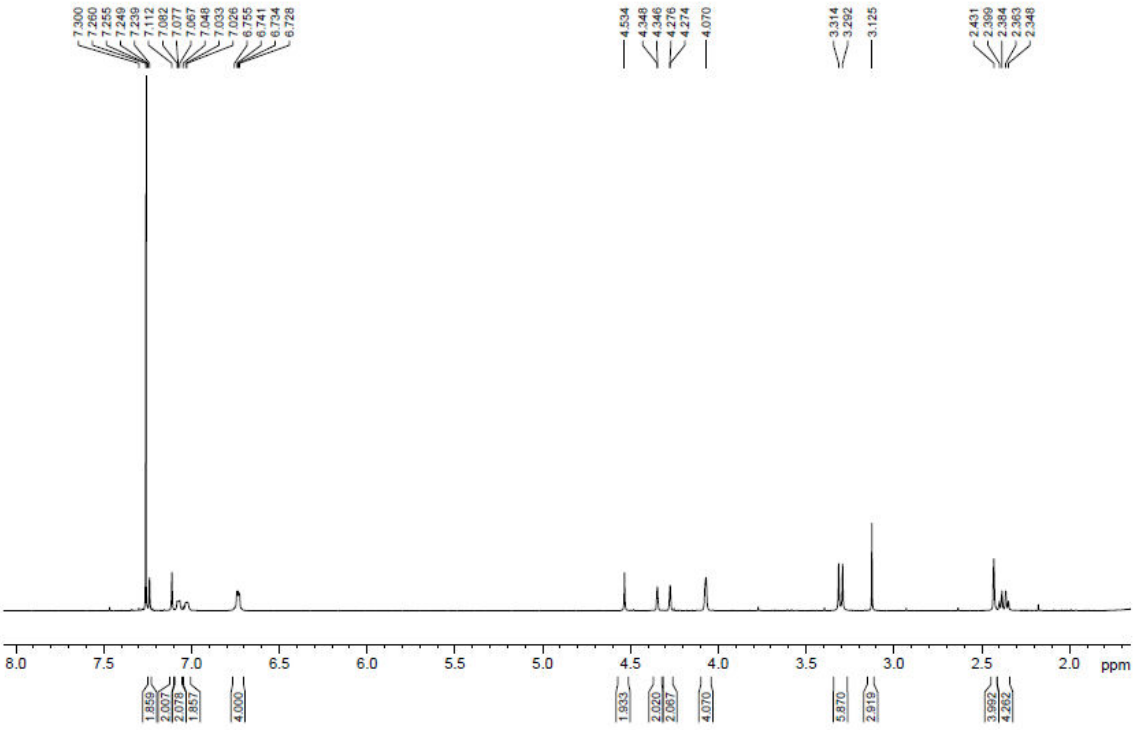
8a
$C_{47}H_{39}O_7P$
746.78 g/mol

Procedure: Under argon atmosphere 33 mg of monophosphate tweezers **1a** (0.048mmol) were dissolved in 20 mL dry acetone and methyl bromoacetate (8.11 mg, 0.053mmol, 0.005 mL), potassium carbonate (7.46 mg, 0.054 mmol) and a few granules of potassium iodide were added to this solution and stirred the mixture for 4 days at room temperature. To the mixture was added dichloromethane and washed with sat NH_4Cl solution, sat $NaHCO_3$ solution and dist water. The organic phase is dried over Na_2SO_4, filtrated and dried on the rotary evaporator. The organic oil was purified by SC (CH/EA 3:1) and white solid product was obtained.

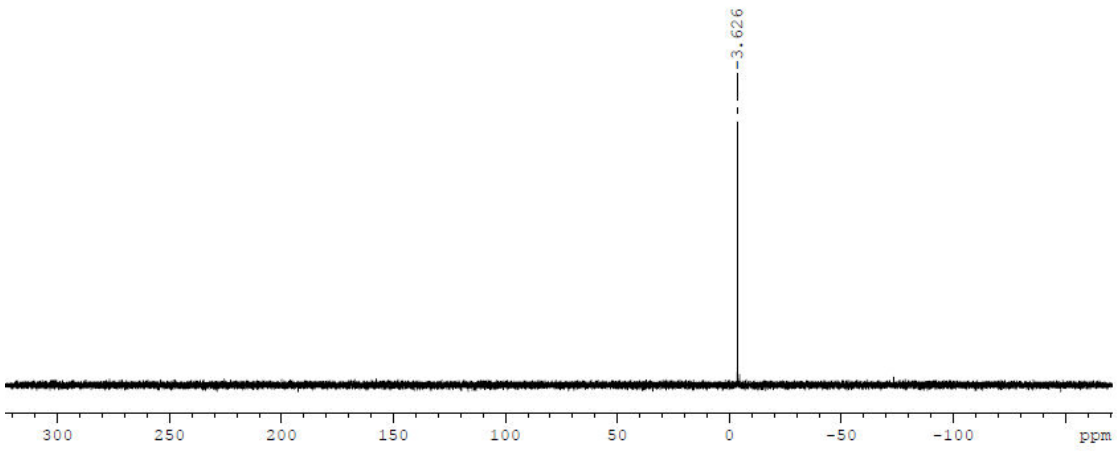
Yield: 17.00 mg (0.023 mmol, 48%)

Melting point: > 240 °C Decomposition





^{1}H-NMR in $CDCl_3$



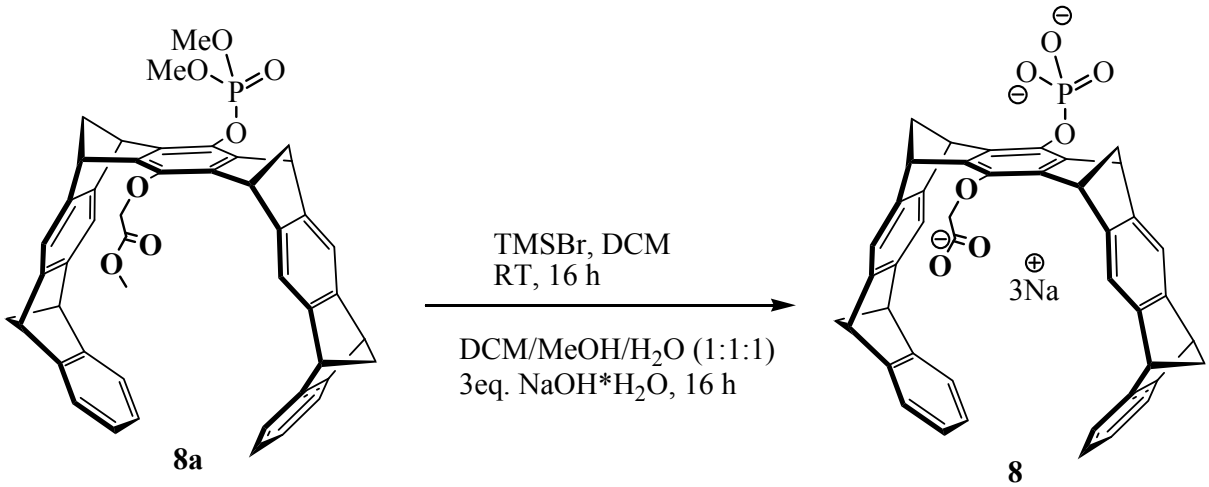
^{31}P-NMR in $CDCl_3$

^{1}H-NMR (500 MHz, $CDCl_3$):δ [ppm] = 7.24 (s, 2H, 6-H, 10-H), 7.14 (s, 2H, 17-H, 21-H), 7.08 (m, 2H, 4-H, 12-H), 7.03 (m, 2H, 1-H, 15-H), 6.74 (m, 4H, 2-H, 3-H, 13-H, 14-H), 4.53 (s, 2H, 7-H, 9-H), 4.34 (s, 2H, 27-H), 4.27 (s, 2H, 18-H, 20-H), 4.08 (s, 4H, 5-H, 11-H, 16-H, 22-H), 3.30 (d, 6H, $^{3}J_{28\text{-H/P, }29\text{H-P}}$ = 11.1 Hz, 28-H, 29-H), 3.12 (s, 3H, 30-H), 2.43 (m, 4H, 24-H, 25-H), 2.37 (m, 4H, 23-H, 26-H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 169.87 (27a-C), 150.60 (4a-C, 11a-C), 150.68 (15a-C, 22a-C), 147.78/147.76 (6a-C, 9a-C), 147.02 (5a-C, 10a-C), 146.77 (17a-C, 20a-C), 145.16 (16a-C, 21a-C), 141.32/141.30 (8-C), 140.71 (19-C), 135.23/135.17 (7a-C, 8a-C, 18a-C, 19a-C), 124.79 (3-C, 13-C), 124.69 (2-C, 14-C), 121.63 (4-C, 12-C), 121.12 (1-C, 15-C), 117.29 (6-C, 10-C), 116.28 (17-C, 21-C), 70.21 (27-C), 69.34 (23-C, 26-C), 68.64 (24-C, 25-C), 54.98 (29-C), 54.93 (28-C), 51.91 (18-C, 20-C), 51.32/51.30 (7-C, 9-C), 48.70 (5-C, 11-C), 48.46 (16-C, 22-C), 27.06 (30-C).

^{31}P-NMR (202 MHz, $CDCl_3$): δ [ppm] = -3.63.

HRMS: ESI+ (480 eV) m/z (%) = 769.2321 obs. 769.2326 calc. $[M+Na]^+$



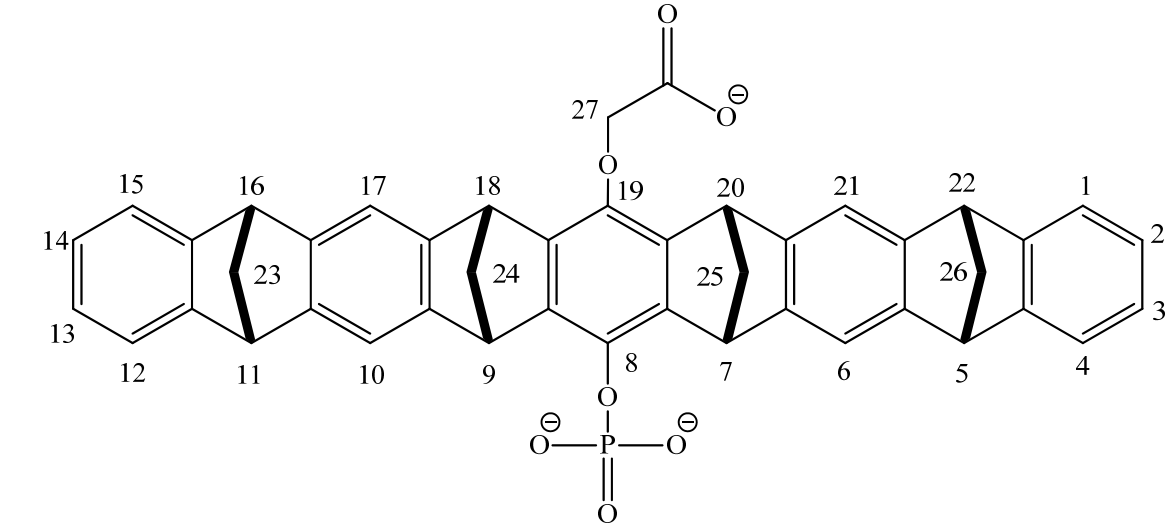
8a
$C_{47}H_{39}O_7P$
746.78 g/mol

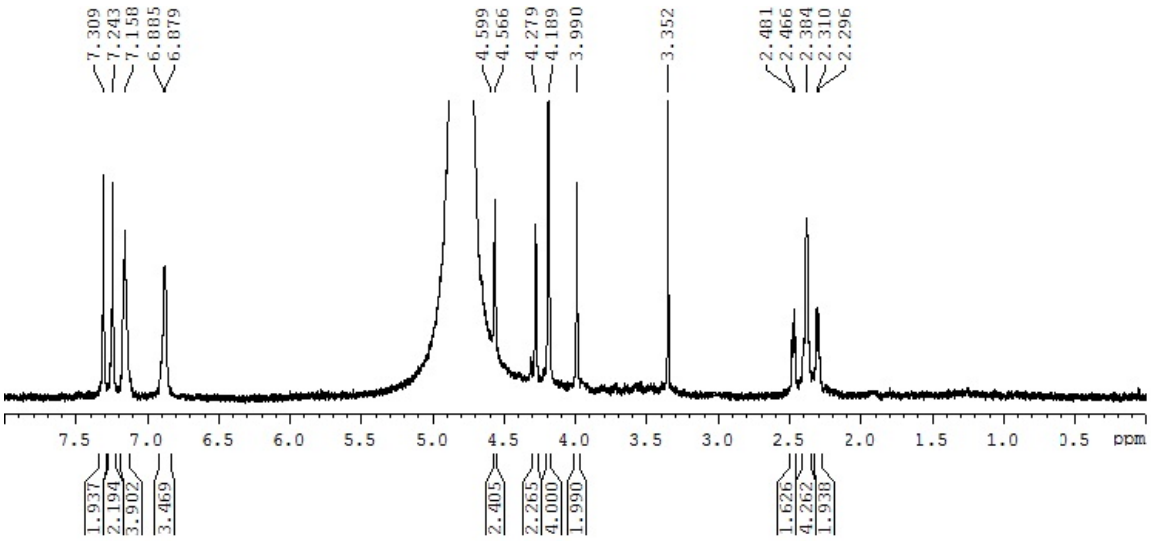
8
$C_{44}H_{30}Na_3O_7P$
770.65 g/mol

Procedure: Under argon atmosphere 16 mg of phosphatemethoxycarbonyl tweezer **8a** (0.023 mmol) was dissolved in 10 mL dichloromethane abs. and added with trimethylsilylbromide (23.4 µL, 0.18 mmol). After stirring for six hours at RT the solvent was condensed and the residuum was dissolved in a mixture of 15 mL DCM/MeOH/H_2O (1:1:1) and added with NaOH*monohydrate (4.00 mg, 0.069 mmol). After stirring for 16 hours the aqueous phase is dried on rotary evaporator and solid residue suspended in acetonitrile and filtered. Solvent removed in *vacuo* and collected white solid.

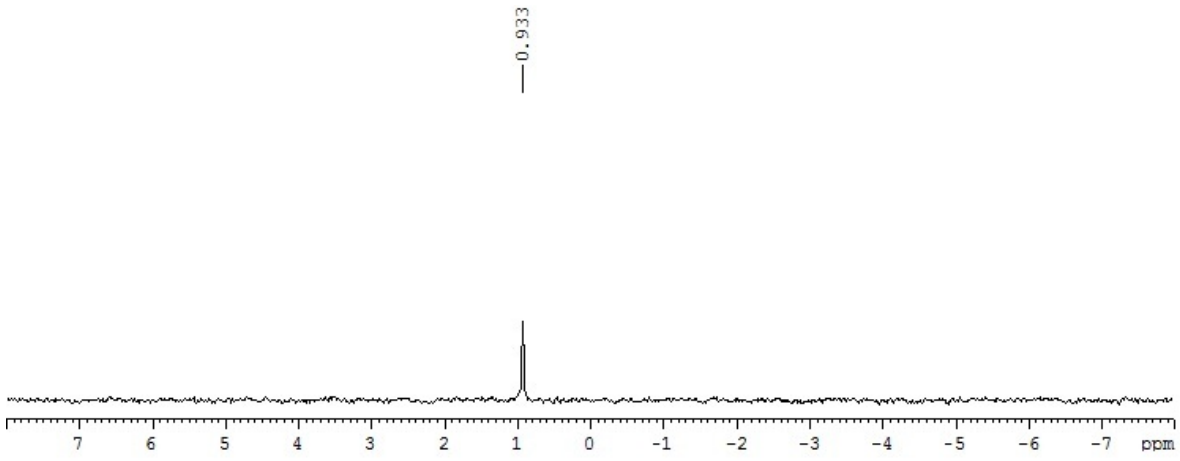
Yield: 18.00 mg (0.023 mmol, 100%)

Melting point: > 200 °C Decomposition





^{1}H-NMR in D_2O



^{31}P-NMR in D_2O

^{1}H-NMR (500 MHz, D_2O):δ [ppm] = 7.31 (s, 2H, 6-H, 10-H), 7.24 (s, 2H, 17-H, 21-H), 7.16 (m, 4H, 1-H, 4-H, 12-H, 15-H), 6.88 (m, 4H, 2-H, 3-H, 13-H, 14-H), 4.57 (s, 2H, 7-H, 9-H), 4.28 (s, 2H, 18-H, 20-H), 4.19 (s, 4H, 5-H, 11-H, 16-H, 22-H), 3.99 (s, 2H, 27-H), 2.47 (m, 2H, 24-H, 25-H), 2.38 (m, 4H, 23-H, 26-H), 2.30 (m, 2H, 24-H, 25-H).

^{13}C-NMR (125 MHz, D_2O): δ [ppm] = 168.22 (27a-C), 151.11 (4a-C, 11a-C, 15a-C, 22a-C), 148.15 (6a-C, 9a-C, 17a-C, 20a-C), 144.43 (5a-C, 10a-C, 16a-C, 21a-C), 142.57 (8-C), 140.28 (7a-C, 8a-C, 18a-C, 19a-C), 127.80 (19-C), 125.14 (2-C, 3-C, 13-C, 14-C), 121.33 (1-C, 4-C, 12-C, 15-C), 118.34 (6-C, 10-C), 116.64 (17-C, 21-C), 115.96 (27-C), 68.18 (23-C, 24-C, 25-C, 26-C), 50.77 (7-C, 9-C, 18-C, 20-C), 48.23 (5-C, 11-C, 16-C, 22-C).

^{31}P-NMR (202 MHz, D_2O): δ [ppm] = 0.93.

HRMS:	ESI+ (480 eV)	m/z (%) = 771.1499 obs.	771.1495 calc.	$[M+H]^+$
		m/z (%) = 793.1317 obs.	793.1314 calc.	$[M+Na]^+$
	ESI- (480 eV)	m/z (%) = 351.0816 obs.	351.0909 calc.	$[M-2Na+H]^-$

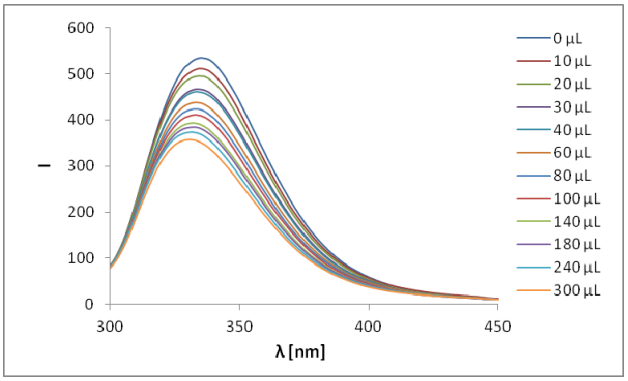
Fluorescence titrations

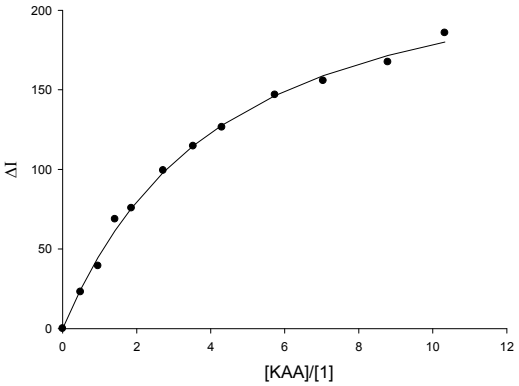
Fluorescence titrations of the monophosphate tweezer 1

Fluorescence titration of monophosphate tweezer **1** with KAA in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **1**	Guest KAA
Amount [mg]:	0.113	0.164
Volume [mL]:	7.505	0.758
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.18E-05	0.00E+00	0.00	533.747	0.000	0.000
10	710	2.18E-05	1.06E-05	0.48	510.772	22.975	24.441
20	720	2.18E-05	2.08E-05	0.96	494.361	39.386	44.636
30	730	2.18E-05	3.08E-05	1.41	465.000	68.747	61.478
40	740	2.18E-05	4.06E-05	1.86	458.085	75.662	75.660
60	760	2.18E-05	5.92E-05	2.72	434.420	99.327	98.063
80	780	2.18E-05	7.70E-05	3.53	419.149	114.598	114.825
100	800	2.18E-05	9.38E-05	4.30	407.294	126.453	127.757
140	840	2.18E-05	1.25E-04	5.74	386.912	146.835	146.292
180	880	2.18E-05	1.53E-04	7.04	378.048	155.699	158.861
240	940	2.18E-05	1.92E-04	8.79	366.358	167.389	171.542
300	1000	2.18E-05	2.25E-04	10.33	348.009	185.738	180.033





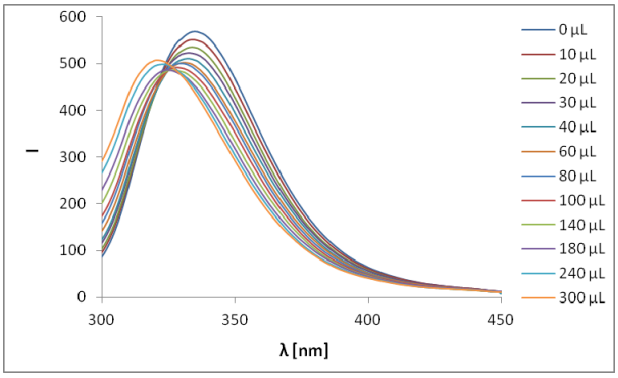
K_a [M^{-1}] = 13200 ± 8 %

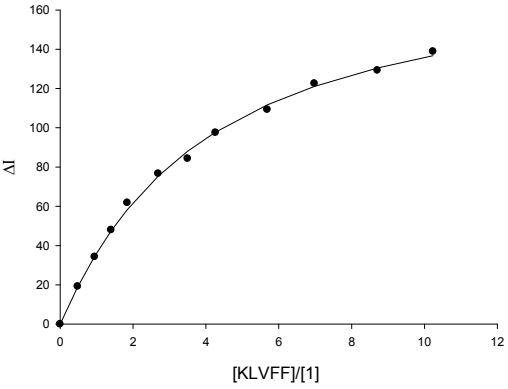
K_d [µM] = 76 ± 8 %

Fluorescence Titration of monophosphate tweezer **1** with KLVFF in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **1**	Guest KLVFF
Amount [mg]:	0.152	0.307
Volume [mL]:	10.010	0.627
Concentration [mol/L]:	$2.20 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.20E-05	0.00E+00	0.00	567.618	0.000	0.000
10	710	2.20E-05	1.06E-05	0.48	548.432	19.186	18.928
20	720	2.20E-05	2.08E-05	0.95	533.361	34.257	34.508
30	730	2.20E-05	3.08E-05	1.40	519.690	47.928	47.450
40	740	2.20E-05	4.05E-05	1.84	505.796	61.822	58.308
60	760	2.20E-05	5.92E-05	2.69	490.949	76.669	75.373
80	780	2.20E-05	7.69E-05	3.50	483.296	84.322	88.064
100	800	2.20E-05	9.38E-05	4.26	470.104	97.514	97.807
140	840	2.20E-05	1.25E-04	5.69	458.373	109.245	111.692
180	880	2.20E-05	1.53E-04	6.98	445.093	122.525	121.053
240	940	2.20E-05	1.91E-04	8.71	438.377	129.241	130.451
300	1000	2.20E-05	2.25E-04	10.23	428.782	138.836	136.717





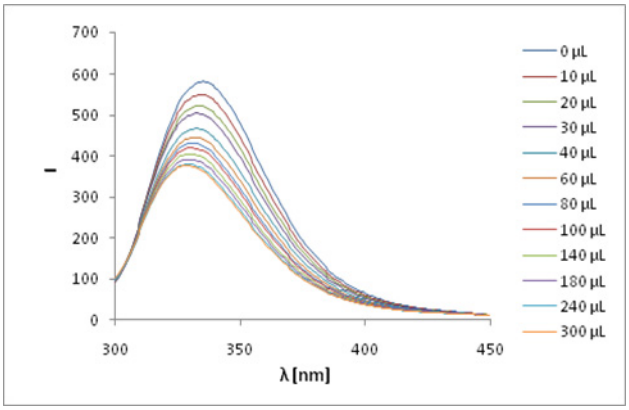
K_a [M^{-1}] = 13800 ± 6 %

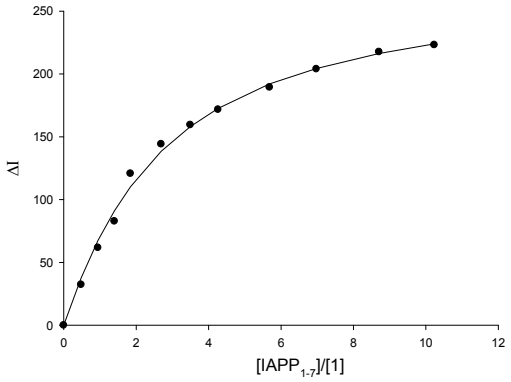
K_d [µM] = 72 ± 6 %

Fluorescence Titration of monophosphate tweezer **1** with $IAPP_{1-7}$ in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **1**	Guest $IAPP_{1-7}$
Amount [mg]:	0.152	0.344
Volume [mL]:	10.010	0.622
Concentration [mol/L]:	$2.20 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2,20E-05	0,00E+00	0,00	581,506	0,000	0,000
10	710	2,20E-05	1,06E-05	0,48	549,257	32,249	37,711
20	720	2,20E-05	2,08E-05	0,95	519,846	61,660	67,470
30	730	2,20E-05	3,08E-05	1,40	498,749	82,757	91,138
40	740	2,20E-05	4,05E-05	1,84	460,802	120,704	110,176
60	760	2,20E-05	5,92E-05	2,69	437,440	144,066	138,488
80	780	2,20E-05	7,69E-05	3,50	422,047	159,459	158,231
100	800	2,20E-05	9,38E-05	4,26	409,937	171,569	172,628
140	840	2,20E-05	1,25E-04	5,69	392,213	189,293	192,034
180	880	2,20E-05	1,53E-04	6,98	377,623	203,883	204,409
240	940	2,20E-05	1,92E-04	8,71	364,023	217,483	216,290
300	1000	2,20E-05	2,25E-04	10,23	358,503	223,003	223,923





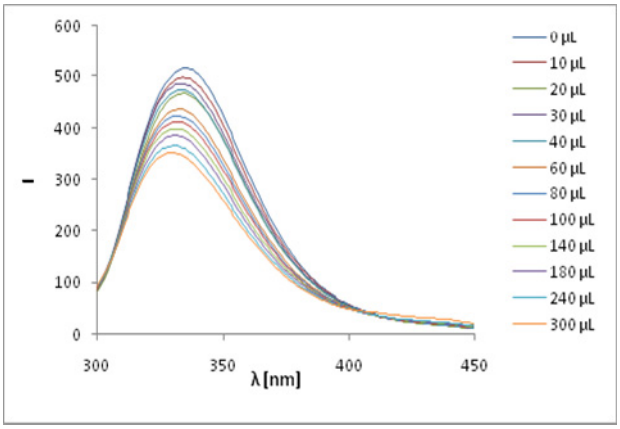
K_a [M^{-1}] = 21000 ± 9 %

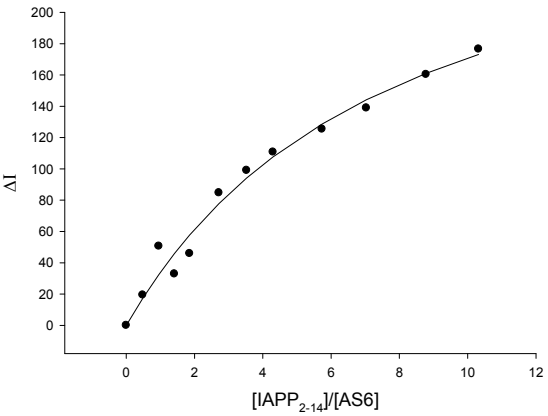
K_d [µM] = 489 µM ± 9 %

Fluorescence Titration of monophosphate tweezer **1** with $IAPP_{2-14}$ in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **1**	Guest $IAPP_{2-14}$
Amount [mg]:	0.113	0.454
Volume [mL]:	7.505	0.444
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.18E-05	0.00E+00	0.00	515.924	0.000	0.000
10	710	2.18E-05	1.06E-05	0.48	496.481	19.443	17.303
20	720	2.18E-05	2.08E-05	0.96	465.297	50.627	32.471
30	730	2.18E-05	3.08E-05	1.41	483.039	32.885	45.854
40	740	2.18E-05	4.05E-05	1.86	470.036	45.888	57.733
60	760	2.18E-05	5.92E-05	2.72	431.208	84.716	77.847
80	780	2.18E-05	7.69E-05	3.53	416.878	99.046	94.190
100	800	2.18E-05	9.37E-05	4.30	405.158	110.766	107.701
140	840	2.18E-05	1.25E-04	5.73	390.477	125.447	128.682
180	880	2.18E-05	1.53E-04	7.04	376.963	138.961	144.177
240	940	2.18E-05	1.91E-04	8.78	355.600	160.324	161.022
300	1000	2.18E-05	2.25E-04	10.32	339.330	176.594	173.068





K_a [M^{-1}] = 6730 ± 24 %

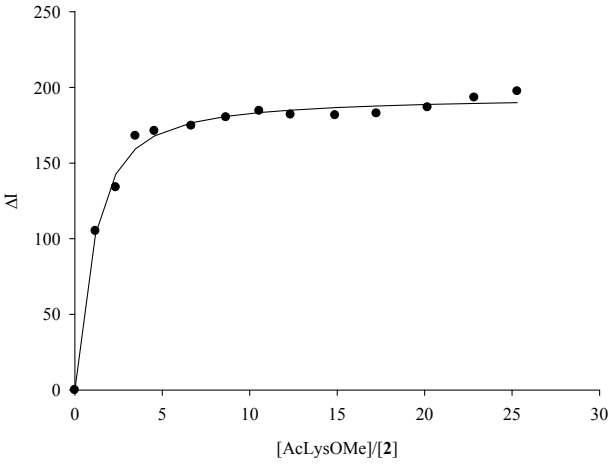
K_d [µM] = 148 µM ± 24 %

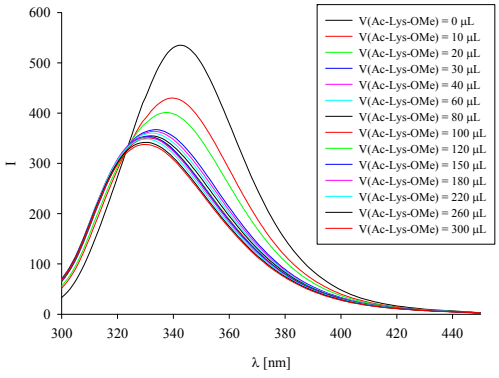
Fluorescence titrations of the methoxy phosphate tweezer 2

Fluorescence titration of tweezer **2** with AcLysOMe in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **2**	Guest AcLysOMe · HCl
amount [mg]:	0.304	1.058
volume [mL]:	6.00	0.800
concentration [mol/L]:	$7.19 \cdot 10^{-05}$	$5.54 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{343})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	7.19E-05	0.0000	0.0000	535.0180	0.0000	0.0000
10	710	7.19E-05	8.54E-05	1.1878	429.9110	105.1070	103.0820
20	720	7.19E-05	1.68E-04	2.3426	401.0750	133.9430	142.7324
30	730	7.19E-05	2.49E-04	3.4658	367.0290	167.9890	159.3577
40	740	7.19E-05	3.28E-04	4.5586	363.8030	171.2150	167.9647
60	760	7.19E-05	4.79E-04	6.6580	360.3270	174.6910	176.5670
80	780	7.19E-05	6.22E-04	8.6497	354.7720	180.2460	180.8154
100	800	7.19E-05	7.58E-04	10.5418	350.5240	184.4940	183.3362
120	820	7.19E-05	8.87E-04	12.3416	352.9850	182.0330	185.0024
150	850	7.19E-05	1.07E-03	14.8826	353.4310	181.5870	186.6560
180	880	7.19E-05	1.24E-03	17.2502	352.2680	182.7500	187.7508
220	920	7.19E-05	1.45E-03	20.1669	348.2370	186.7810	188.7405
260	960	7.19E-05	1.64E-03	22.8406	341.7500	193.2680	189.4225
300	1000	7.19E-05	1.82E-03	25.3003	337.6090	197.4090	189.9209





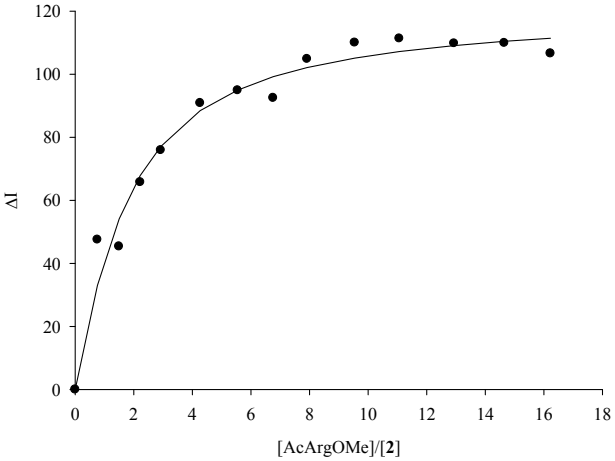
$K_a[M^{-1}] = 23849 \pm 11\%$ $\Delta I_{max} = 194$

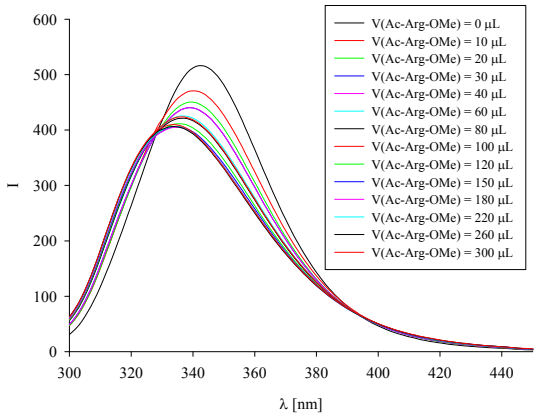
$K_d[M] = 42 \pm 11\%$

Fluorescence titration of tweezer **2** with AcArgOMe in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **2**	Guest AcArgOMe · HCl
amount [mg]:	0.126	1.032
volume [mL]:	2.00	0.8
concentration [mol/L]:	$8.94 \cdot 10^{-05}$	$4.84 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{342})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	8.94E-05	0.00E+00	0.00	516.286	0.000	0.0000
10	710	8.94E-05	6.81E-05	0.726	468.764	47.522	33.0515
20	720	8.94E-05	1.34E-04	1.503	470.929	45.357	54.1819
30	730	8.94E-05	1.99E-04	2.223	450.532	65.754	67.8681
40	740	8.94E-05	2.61E-04	2.924	440.380	75.906	77.1075
60	760	8.94E-05	3.82E-04	4.270	425.428	90.858	88.4485
80	780	8.94E-05	4.96E-04	5.548	421.397	94.889	94.9986
100	800	8.94E-05	6.05E-04	6.762	423.814	92.472	99.2158
120	820	8.94E-05	7.08E-04	7.916	411.456	104.830	102.1439
150	850	8.94E-05	8.53E-04	9.546	406.260	110.026	105.1615
180	880	8.94E-05	9.89E-04	11.065	404.940	111.346	107.2208
220	920	8.94E-05	1.16E-03	12.936	406.508	109.778	109.1242
260	960	8.94E-05	1.31E-03	14.651	406.355	109.931	110.4586
300	1000	8.94E-05	1.45E-03	16.228	409.676	106.610	111.4455





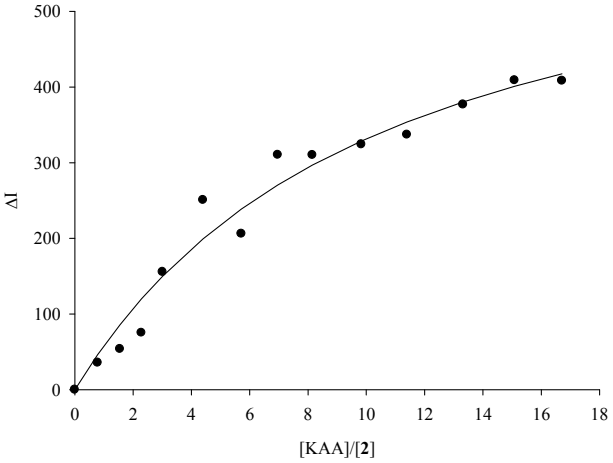
$K_a[M^{-1}] = 8614 \pm 18\%$ $\Delta I_{max} = 121$

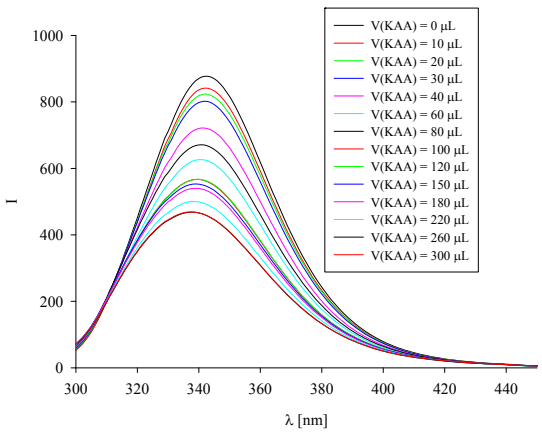
$K_d[M] = 116 \pm 18\%$

Fluorescence titration of tweezer **2** with the peptide KAA in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **2**	Guest KAA
amount [mg]:	0.304	0.924
volume [mL]:	6.00	0.80
concentration [mol/L]:	$7.19 \cdot 10^{-05}$	$4.00 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{342})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	7.19E-05	0.00E+00	0.000	877.179	0.000	0.0000
10	710	7.19E-05	5.64E-05	0.785	841.550	35.629	46.2060
20	720	7.19E-05	1.22E-04	1.547	823.453	53.726	85.7995
30	730	7.19E-05	1.65E-04	2.289	802.055	75.124	120.0446
40	740	7.19E-05	2.17E-04	3.011	721.636	155.543	149.9164
60	760	7.19E-05	3.16E-04	4.398	626.528	250.651	199.4193
80	780	7.19E-05	4.11E-04	5.714	671.073	206.106	238.6818
100	800	7.19E-05	5.01E-04	6.964	566.759	310.420	270.5253
120	820	7.19E-05	5.86E-04	8.152	567.082	310.097	296.8390
150	850	7.19E-05	7.07E-04	9.831	552.956	324.223	328.6923
180	880	7.19E-05	8.19E-04	11.395	540.116	337.063	353.9081
220	920	7.19E-05	9.58E-04	13.322	500.249	376.930	380.3271
260	960	7.19E-05	1.08E-03	15.088	468.292	408.887	400.9680
300	1000	7.19E-05	1.20E-03	16.712	468.827	408.352	417.5307





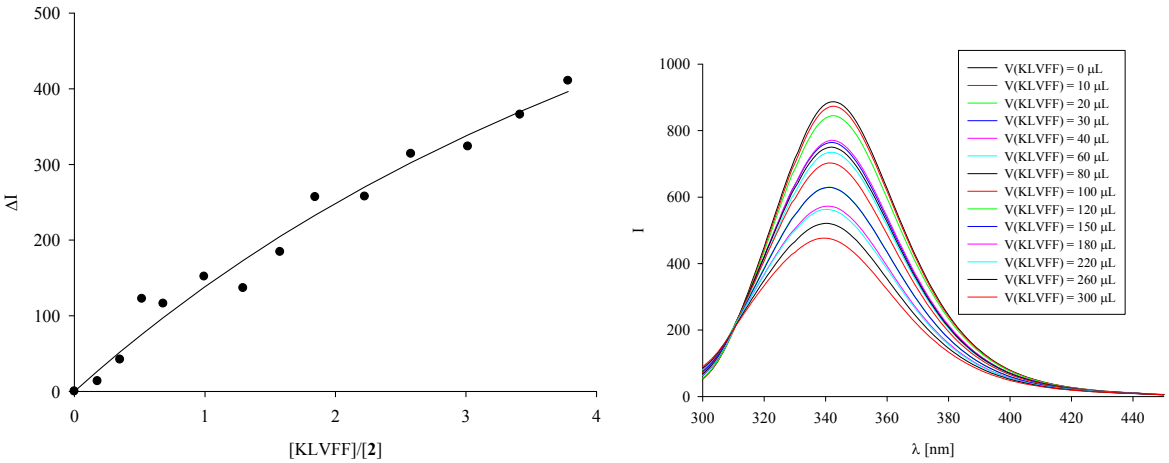
$K_a[M^{-1}] = 1447 \pm 26\%$ $\Delta I_{max} = 667$

$K_d[M] = 691 \pm 26\%$

Fluorescence titration of tweezer **2** with the peptide KLVFF in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **2**	Guest KLVFF
amount [mg]:	0.196	0.229
volume [mL]:	4.00	0.40
concentration [mol/L]:	$6.95 \cdot 10^{-05}$	$8.77 \cdot 10^{-04}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{342})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	6.95E-05	0.00E+00	0.000	886.740	0.000	0.000
10	710	6.95E-05	1.24E-05	0.177	873.200	13.540	27.0234
20	720	6.95E-05	2.44E-05	0.350	844.815	41.925	52.2146
30	730	6.95E-05	3.60E-05	0.518	764.512	122.228	75.7449
40	740	6.95E-05	4.74E-05	0.682	770.833	115.907	97.7660
60	760	6.95E-05	6.92E-05	0.996	735.125	151.615	137.8042
80	780	6.95E-05	8.99E-05	1.293	750.248	136.492	173.2385
100	800	6.95E-05	1.10E-04	1.576	702.537	184.203	204.7954
120	820	6.95E-05	1.28E-04	1.846	629.999	256.741	233.0607
150	850	6.95E-05	1.55E-04	2.226	629.272	257.468	270.3053
180	880	6.95E-05	1.79E-04	2.579	572.838	313.902	302.4622
220	920	6.95E-05	2.10E-04	3.016	563.058	323.682	339.0447
260	960	6.95E-05	2.38E-04	3.416	521.057	365.682	369.9413
300	1000	6.95E-05	2.63E-04	3.783	476.342	410.398	396.3654



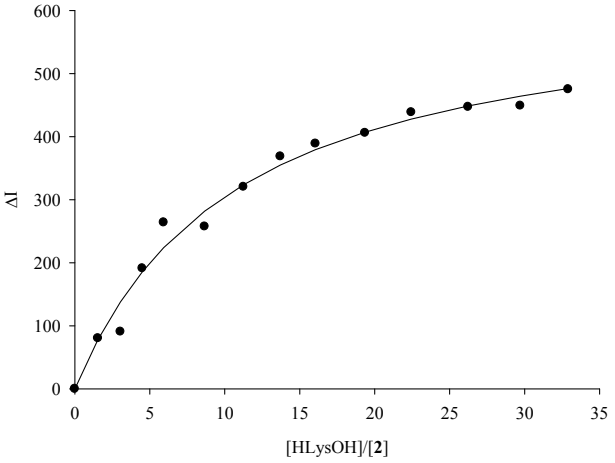
$K_a[M^{-1}] = 2366 \pm 47\%$

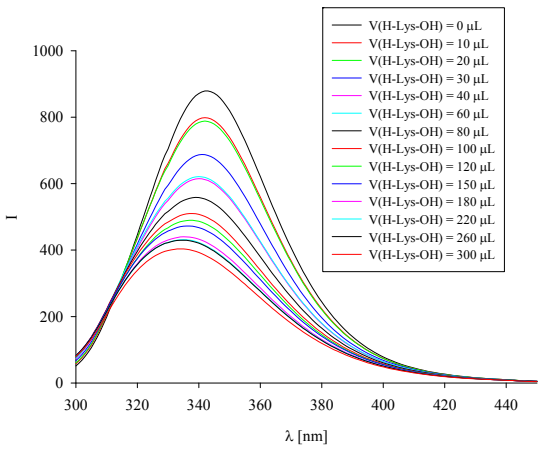
$K_d[M] = 423 \pm 47\%$

Fluorescence titration of tweezer **2** with HLysOH in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor	Guest
λ_{em}= 342nm	**2**	HLysOH
amount [mg]:	0.343	1.301
volume [mL]:	6.00	0.80
concentration [mol/L]:	$8.11 \cdot 10^{-05}$	$8.90 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{342})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	8.11E-05	0.00E+00	0.000	878.844	0.000	0.0000
10	710	8.11E-05	1.25E-04	1.545	798.668	80.176	77.9281
20	720	8.11E-05	2.47E-04	3.048	788.161	90.683	137.9991
30	730	8.11E-05	3.66E-04	4.509	687.736	191.108	185.5052
40	740	8.11E-05	4.81E-04	5.931	614.851	263.993	223.9036
60	760	8.11E-05	7.03E-04	8.662	621.353	257.491	281.9770
80	780	8.11E-05	9.13E-04	11.253	558.492	320.350	323.6725
100	800	8.11E-05	1.11E-03	13.715	510.254	368.590	354.9888
120	820	8.11E-05	1.30E-03	16.057	489.979	388.865	379.3397
150	850	8.11E-05	1.57E-03	19.362	472.754	406.090	407.1324
180	880	8.11E-05	1.82E-03	22.443	440.157	438.687	427.9325
220	920	8.11E-05	2.13E-03	26.237	431.650	447.194	448.6795
260	960	8.11E-05	2.41E-03	29.716	429.857	448.987	464.1970
300	1000	8.11E-05	2.67E-03	32.916	403.812	475.032	476.2367





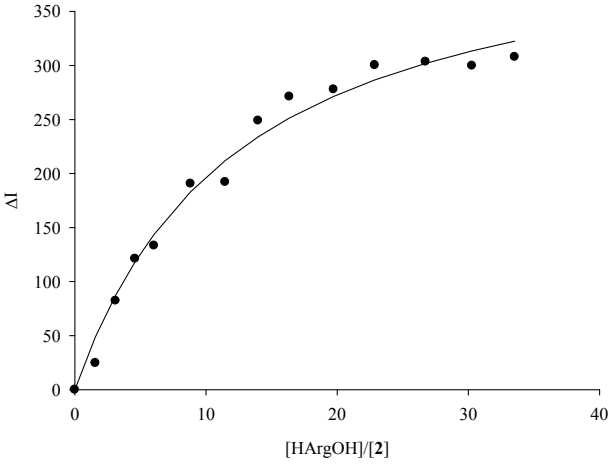
$K_a[M^{-1}] = 1240 \pm 14\%$ $\Delta I_{max} = 624$

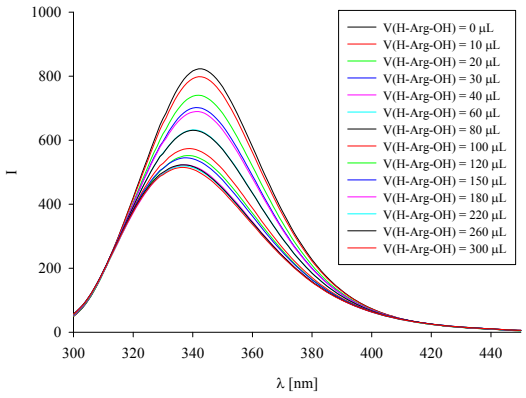
$K_d[M] = 806 \pm 14\%$

Fluorescence titration of tweezer **2** with HArgOH in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor	Guest
λ_{em}= 342nm	**2**	HArgOH
amount [mg]:	0.304	1.355
volume [mL]:	6.00	0.80
concentration [mol/L]:	$7.19 \cdot 10^{-05}$	$8.04 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{342})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	7.19E-05	0.00E+00	0.00	822.979	0.000	0.0000
10	710	7.19E-05	1.13E-05	1.575	798.339	24.640	48.7154
20	720	7.19E-05	2.23E-04	3.106	740.753	82.226	87.1753
30	730	7.19E-05	3.30E-04	4.595	701.848	121.131	118.2081
40	740	7.19E-05	4.35E-04	6.043	689.627	133.352	143.7201
60	760	7.19E-05	6.35E-04	8.826	632.373	190.606	183.0831
80	780	7.19E-05	8.24E-04	11.467	630.868	192.111	211.9595
100	800	7.19E-05	1.00E-03	13.975	573.986	248.993	234.0041
120	820	7.19E-05	1.18E-03	16.361	551.887	271.092	251.3649
150	850	7.19E-05	1.42E-03	19.729	545.191	277.788	271.4210
180	880	7.19E-05	1.64E-03	22.868	522.721	300.258	286.6038
220	920	7.19E-05	1.92E-03	26.735	519.543	303.436	301.8985
260	960	7.19E-05	2.18E-03	30.279	523.274	299.705	313.4379
300	1000	7.19E-05	2.41E-03	33.540	515.069	307.910	322.4510





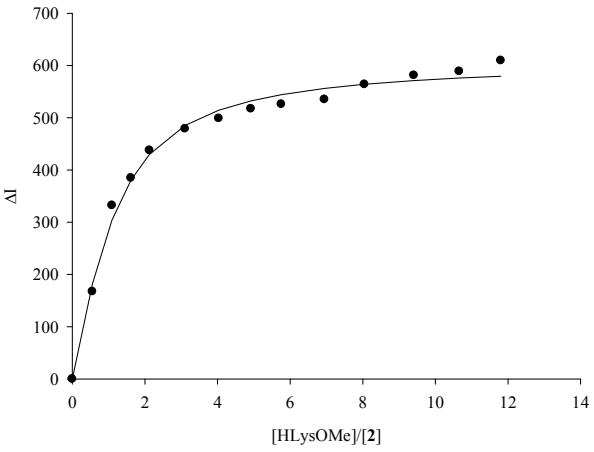
$K_a[M^{-1}] = 1192 \pm 14\%$ $\Delta I_{max} = 437$

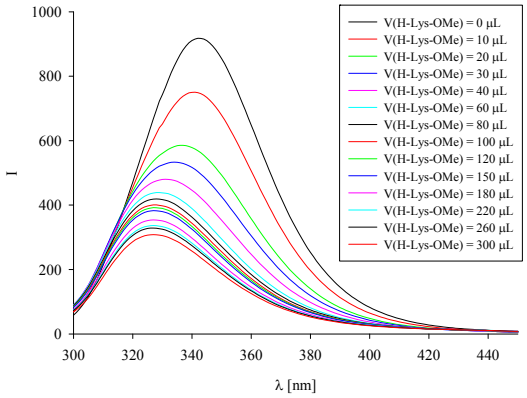
$K_d[M] = 839 \pm 14\%$

Fluorescence titration of tweezer **2** with HLysOMe·HCl in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **2**	Guest HLysOMe · HCl
amount [mg]:	0.100	0.739
volume [mL]:	2.00	0.8
concentration [mol/L]:	$7.10 \cdot 10^{-05}$	$2.79 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{342})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	7.10E-05	0.0000	0.0000	917.8870	0.0000	0.0000
10	710	7.10E-05	3.93E-05	0.5543	750.5460	167.3410	182.3800
20	720	7.10E-05	7.76E-05	1.0932	585.6300	332.2570	304.0934
30	730	7.10E-05	1.15E-04	1.6173	533.3120	384.5750	380.8484
40	740	7.10E-05	1.51E-04	2.1272	480.2350	437.6520	429.7989
60	760	7.10E-05	2.21E-04	3.1069	439.0810	478.8060	485.2437
80	780	7.10E-05	2.86E-04	4.0363	419.0990	498.7880	514.5903
100	800	7.10E-05	3.49E-04	4.9192	400.6720	517.2150	532.4130
120	820	7.10E-05	4.09E-04	5.7591	392.1080	525.7790	544.2993
150	850	7.10E-05	4.93E-04	6.9448	382.8170	535.0700	556.1399
180	880	7.10E-05	5.71E-04	8.0496	354.0370	563.8500	563.9874
220	920	7.10E-05	6.68E-04	9.4107	336.7020	581.1850	571.0773
260	960	7.10E-05	7.56E-04	10.6583	328.9630	588.9240	575.9563
300	1000	7.10E-05	8.38E-04	11.8061	308.4040	609.4830	579.5169





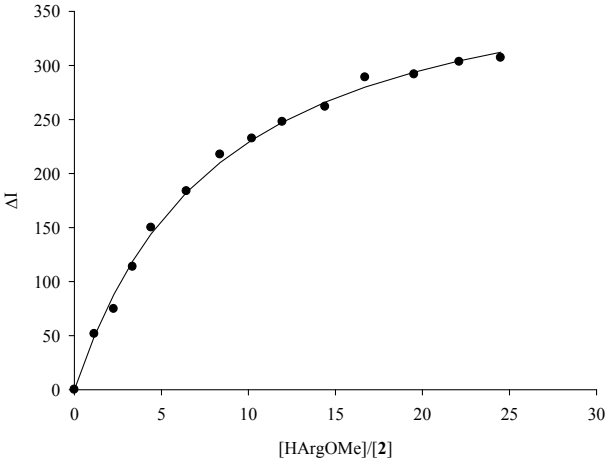
$K_a[M^{-1}] = 23376 \pm 12\%$ $\Delta I_{max} = 612$

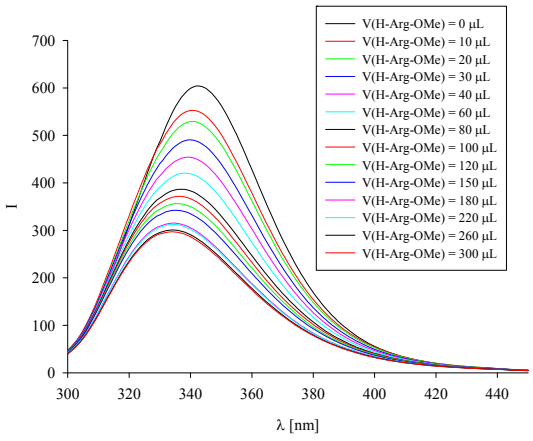
$K_d[M] = 43 \pm 12\%$

Fluorescence titration of tweezer **2** with HArgOMe·HCl in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **2**	Guest HArgOMe · HCl
amount [mg]:	0.164	0.993
volume [mL]:	4.00	0.8
concentration [mol/L]:	$5.82 \cdot 10^{-05}$	$4.75 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{342})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	5.82E-05	0.00E+00	0.00	604.088	0.000	0.0000
10	710	5.82E-05	6.69E-05	1.150	552.620	51.468	49.5756
20	720	5.82E-05	1.32E-04	2.269	529.439	74.649	88.2920
30	730	5.82E-05	1.95E-04	3.356	490.462	113.626	119.1955
40	740	5.82E-05	2.57E-04	4.414	454.165	149.923	144.3430
60	760	5.82E-05	3.75E-04	6.448	420.535	183.553	182.6317
80	780	5.82E-05	4.87E-04	8.377	386.551	217.537	210.2868
100	800	5.82E-05	5.94E-04	10.209	371.742	232.346	231.1337
120	820	5.82E-05	6.95E-04	11.952	356.240	247.848	247.3818
150	850	5.82E-05	8.39E-04	14.413	342.380	261.708	265.9602
180	880	5.82E-05	9.72E-04	16.706	315.217	288.871	279.8838
220	920	5.82E-05	1.14E-03	19.531	312.433	291.655	293.7848
260	960	5.82E-05	1.29E-03	22.119	300.718	303.370	304.1883
300	1000	5.82E-05	1.43E-03	24.502	297.042	297.046	312.2630





$K_a[M^{-1}] = 2290 \pm 6\%$ $\Delta I_{max} = 411$

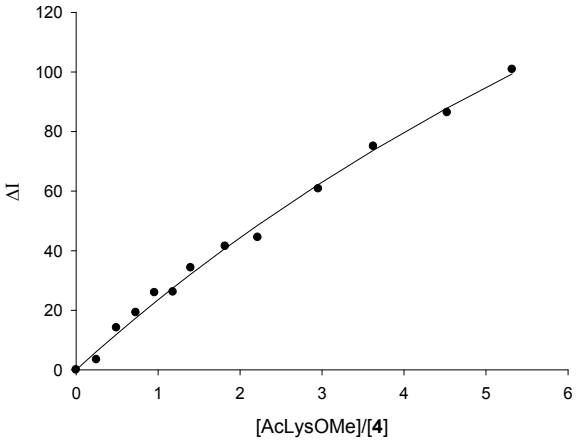
$K_d[M] = 437 \pm 6\%$

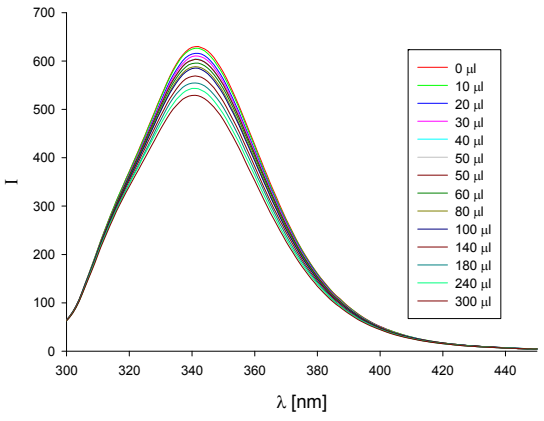
Fluorescence titration of the glycerol phosphate tweezer 4

Fluorescence titration of the tweezer **4** with Ac-Lys-OMe · HCl in phosphate buffer (10mM, pH 7.6)

λ_{exc} = 285 nm	Receptor **4**	Guest Ac-Lys-OMe · HCl
Amount [mg]:	0.092	0.80
Volume [mL]:	4.628	0.733
Concentration [mol/L]:	$2.579 \cdot 10^{-05}$	$4.572 \cdot 10^{-04}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{341})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.579E-05	0.000E+00	0.00	629.793	0.000	0.000
10	710	2.579E-05	6.440E-06	0.25	626.381	3.412	6.137
20	720	2.579E-05	1.270E-05	0.49	615.687	14.106	11.926
30	730	2.579E-05	1.879E-05	0.73	610.584	19.209	17.396
40	740	2.579E-05	2.472E-05	0.96	603.899	25.894	22.571
50	750	2.579E-05	3.048E-05	1.18	603.652	26.141	27.475
60	760	2.579E-05	3.610E-05	1.40	595.550	34.243	32.128
80	780	2.579E-05	4.690E-05	1.82	588.319	41.474	40.753
100	800	2.579E-05	5.715E-05	2.22	585.336	44.457	48.574
140	840	2.579E-05	7.620E-05	2.95	569.057	60.736	62.215
180	880	2.579E-05	9.352E-05	3.63	554.742	75.051	73.705
240	940	2.579E-05	1.167E-04	4.53	543.420	86.373	87.897
300	1000	2.579E-05	1.372E-04	5.32	528.916	100.877	99.365





K_a [M^{-1}] = 2760 ± 23 %

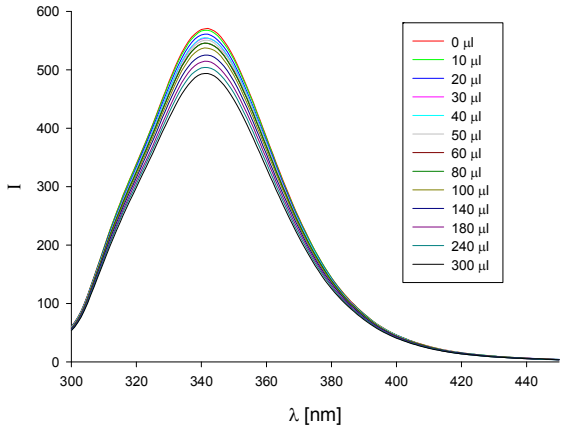
K_d [µM] = 362 ± 23 %

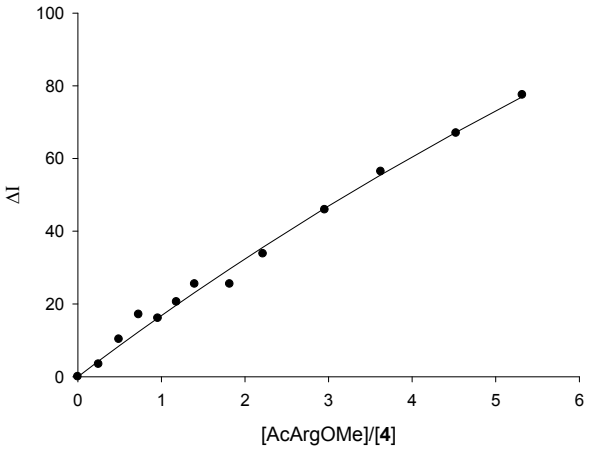
ΔI_{max} = 375 (59 %)

Fluorescence titration of the tweezer **4** with AcArgOMe · HCl in phosphate buffer (10mM, pH 7.6)

λ_{exc} = 285 nm	Receptor **4**	Guest AcArgOMe · HCl
Amount [mg]:	0.092	0.70
Volume [mL]:	4.628	0.574
Concentration [mol/L]:	$2.579 \cdot 10^{-05}$	$4.573 \cdot 10^{-04}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{341})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.579E-05	0.000E+00	0.00	571.170	0.000	0.000
10	710	2.579E-05	6.440E-06	0.25	567.731	3.439	4.317
20	720	2.579E-05	1.270E-05	0.49	560.881	10.289	8.436
30	730	2.579E-05	1.879E-05	0.73	554.084	17.086	12.370
40	740	2.579E-05	2.472E-05	0.96	555.087	16.083	16.132
50	750	2.579E-05	3.048E-05	1.18	550.623	20.547	19.732
60	760	2.579E-05	3.610E-05	1.40	545.689	25.481	23.181
80	780	2.579E-05	4.690E-05	1.82	545.687	25.483	29.661
100	800	2.579E-05	5.716E-05	2.22	537.385	33.785	35.638
140	840	2.579E-05	7.621E-05	2.95	525.274	45.896	46.299
180	880	2.579E-05	9.353E-05	3.63	514.754	56.416	55.525
240	940	2.579E-05	1.167E-04	4.53	504.183	66.987	67.248
300	1000	2.579E-05	1.372E-04	5.32	493.678	77.492	76.999





K_a [M^-] = 1620 ± 42 %

K_d [µM] = 617 ± 42 %

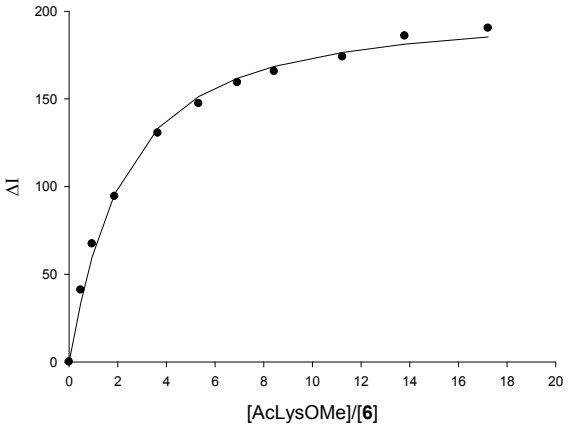
ΔI_{max} = 437

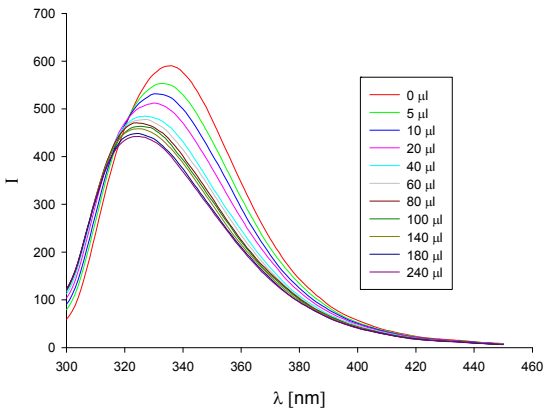
Fluorescence titration of the acetoxy phosphate tweezer 6

Fluorescence titration of the tweezer **6** with AcLysOMe in phosphate buffer (10mM, pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **6**	Guest AcLysOMe · HCl
Amount [mg]:	0.133	0.351
Volume [mL]:	8.858	1.0
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$1.47 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. ($I_{336\ nm}$)**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.180E-05	0.000E+00	0.00	590.348	0.000	0.000
5	705	2.180E-05	1.043E-05	0.48	549.331	41.017	33.753
10	710	2.180E-05	2.071E-05	0.95	523.016	67.332	59.898
20	720	2.180E-05	4.085E-05	1.87	495.942	94.406	95.925
40	740	2.180E-05	7.948E-05	3.65	459.793	130.555	133.326
60	760	2.180E-05	1.161E-04	5.32	442.974	147.374	151.413
80	780	2.180E-05	1.508E-04	6.92	431.023	159.325	161.809
100	800	2.180E-05	1.838E-04	8.43	424.652	165.696	168.502
140	840	2.180E-05	2.451E-04	11.24	416.324	174.024	176.568
180	880	2.180E-05	3.008E-04	13.80	404.437	185.911	181.239
240	940	2.180E-05	3.754E-04	17.22	399.988	190.360	185.434





K_a [M^{-1}] = 29200 ± 10 %

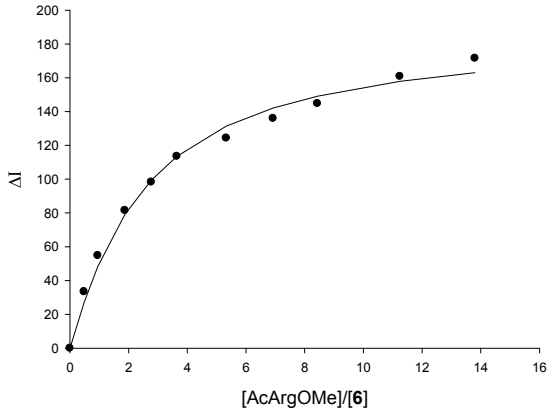
K_d [µM] = 34 ± 10 %

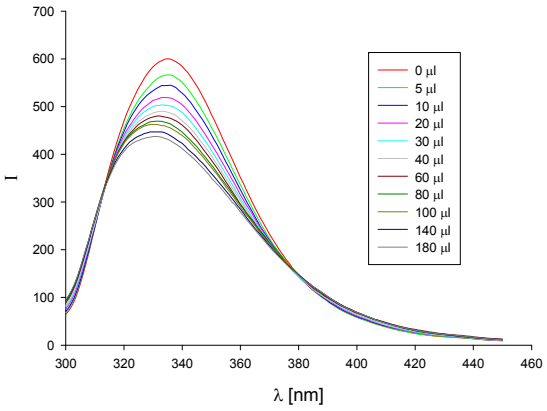
ΔI_{max} = 203 (34%)

Fluorescence titration of the tweezer **6** with AcArgOMe in phosphate buffer (10mM, pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **6**	Guest AcArgOMe · HCl
Amount [mg]:	0.133	0.375
Volume [mL]:	8.858	0.956
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$1.471 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. ($I_{336\ nm}$)**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.180E-05	0.000E+00	0.00	599.607	0.000	0.000
5	705	2.180E-05	1.043E-05	0.48	566.185	33.422	26.951
10	710	2.180E-05	2.072E-05	0.95	544.781	54.826	48.343
20	720	2.180E-05	4.086E-05	1.87	518.092	81.515	79.093
30	730	2.180E-05	6.044E-05	2.77	501.274	98.333	99.400
40	740	2.180E-05	7.950E-05	3.65	486.036	113.571	113.471
60	760	2.180E-05	1.161E-04	5.33	475.263	124.344	131.341
80	780	2.180E-05	1.509E-04	6.92	463.666	135.941	142.051
100	800	2.180E-05	1.838E-04	8.43	454.836	144.771	149.129
140	840	2.180E-05	2.451E-04	11.24	438.828	160.779	157.856
180	880	2.180E-05	3.008E-04	13.80	428.066	171.541	163.010





K_a [M^{-1}] = 22840 ± 13 %

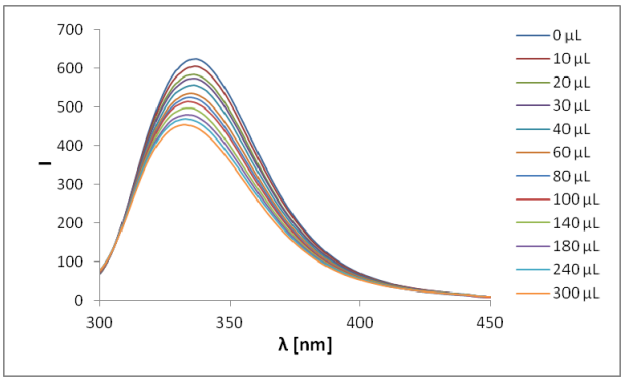
K_d [µM] = 44 ± 13 %

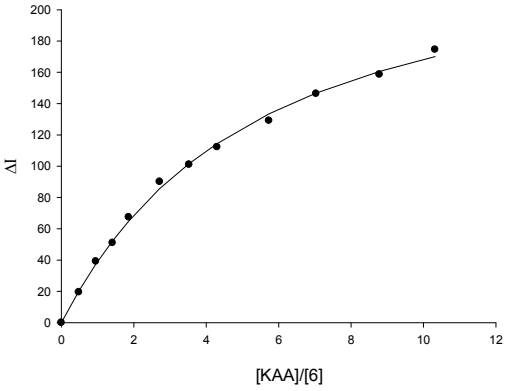
ΔI_{max} = 188 (31%)

Fluorescence titration of the tweezer **6** with KAA in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **6**	Guest KAA
Amount [mg]:	0.143	0.232
Volume [mL]:	9.523	1.073
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.18E-05	0.00E+00	0.00	624.893	0.000	0.000
10	710	2.18E-05	1.06E-05	0.48	605.406	19.487	20.312
20	720	2.18E-05	2.08E-05	0.96	585.662	39.231	37.536
30	730	2.18E-05	3.08E-05	1.41	573.879	51.014	52.264
40	740	2.18E-05	4.05E-05	1.86	557.438	67.455	64.962
60	760	2.18E-05	5.92E-05	2.72	534.839	90.054	85.650
80	780	2.18E-05	7.69E-05	3.53	523.887	101.006	101.704
100	800	2.18E-05	9.37E-05	4.30	512.650	112.243	114.471
140	840	2.18E-05	1.25E-04	5.73	495.772	129.121	133.409
180	880	2.18E-05	1.53E-04	7.04	478.560	146.333	146.721
240	940	2.18E-05	1.91E-04	8.78	466.308	158.585	160.571
300	1000	2.18E-05	2.25E-04	10.32	450.371	174.522	170.093





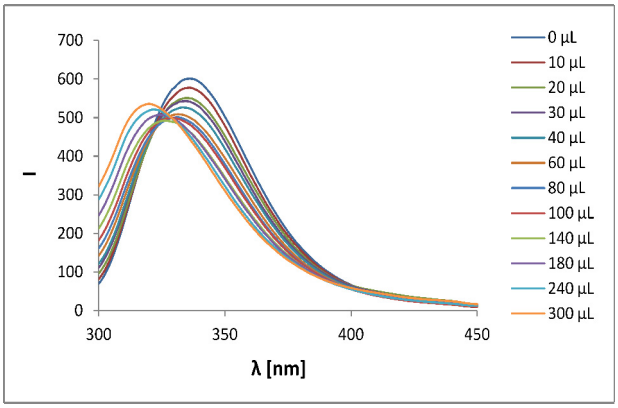
K_a [M^{-1}] = 10000 ± 7 %

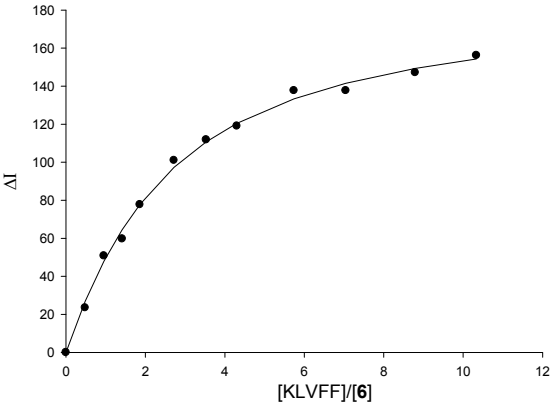
K_d [µM] = 100 ± 7 %

Fluorescence titration of the tweezer **6** with KLVFF in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **6**	Guest KLVFF
Amount [mg]:	0.143	0.328
Volume [mL]:	9.523	0.669
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.51 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.18E-05	0.00E+00	0.00	601.226	0.000	0.000
10	710	2.18E-05	1.06E-05	0.49	577.714	23.512	26.907
20	720	2.18E-05	2.09E-05	0.96	550.459	50.767	47.965
30	730	2.18E-05	3.09E-05	1.42	541.506	59.720	64.568
40	740	2.18E-05	4.06E-05	1.86	523.536	77.690	77.811
60	760	2.18E-05	5.93E-05	2.72	500.276	100.950	97.294
80	780	2.18E-05	7.70E-05	3.53	489.437	111.789	110.716
100	800	2.18E-05	9.39E-05	4.31	482.214	119.012	120.413
140	840	2.18E-05	1.25E-04	5.74	463.563	137.663	133.358
180	880	2.18E-05	1.54E-04	7.05	463.559	137.667	141.538
240	940	2.18E-05	1.92E-04	8.80	454.119	147.107	149.336
300	1000	2.18E-05	2.25E-04	10.33	445.093	156.133	154.318





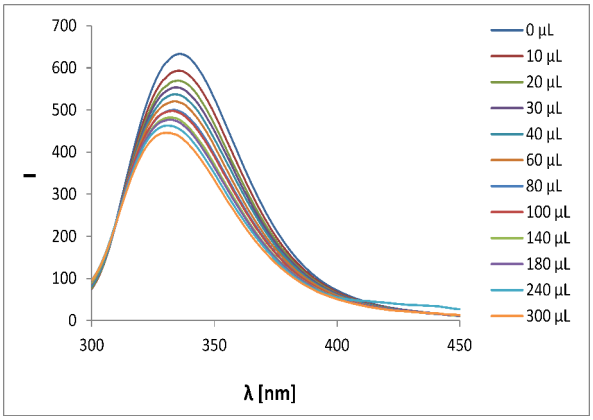
K_a [M^{-1}] = 22500 ± 8 %

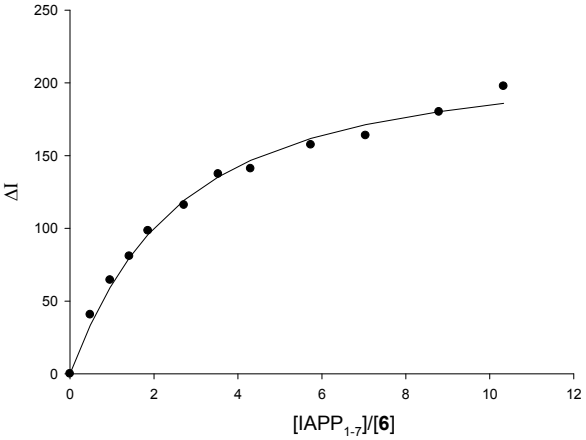
K_d [µM] = 44 ± 8 %

Fluorescence titration of the tweezer **6** with $IAPP_{1-7}$ in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **6**	Guest $IAPP_{1-7}$
Amount [mg]:	0.099	0.310
Volume [mL]:	6.593	0.560
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.51 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.18E-05	0.00E+00	0.00	633.538	0.000	0.000
10	710	2.18E-05	1.06E-05	0.49	592.929	40.609	33.451
20	720	2.18E-05	2.09E-05	0.96	569.126	64.412	59.450
30	730	2.18E-05	3.09E-05	1.42	552.716	80.822	79.789
40	740	2.18E-05	4.06E-05	1.86	535.244	98.294	95.887
60	760	2.18E-05	5.93E-05	2.72	517.558	115.980	119.329
80	780	2.18E-05	7.70E-05	3.53	496.209	137.329	135.292
100	800	2.18E-05	9.38E-05	4.30	492.579	140.959	146.722
140	840	2.18E-05	1.25E-04	5.74	476.164	157.374	161.842
180	880	2.18E-05	1.54E-04	7.04	469.739	163.799	171.312
240	940	2.18E-05	1.92E-04	8.79	453.468	180.070	180.279
300	1000	2.18E-05	2.25E-04	10.33	435.893	197.645	185.978





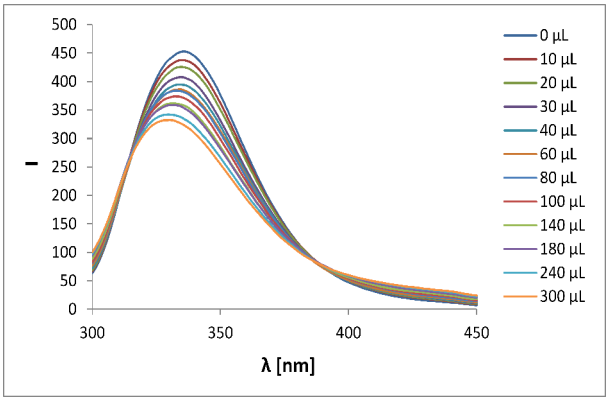
$K_a\ [M^{-1}] = 24100 \pm 12\ \%$

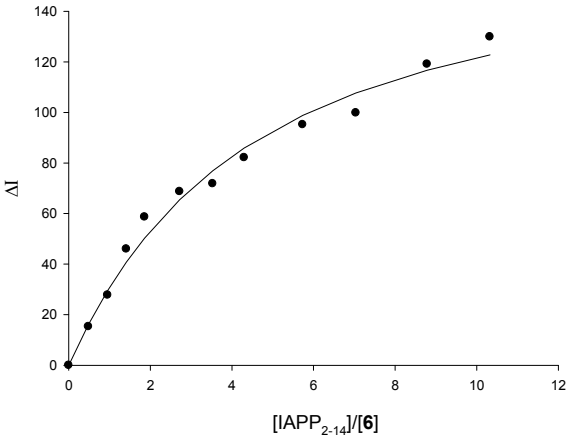
$K_d\ [\mu M] = 41 \pm 12\ \%$

Fluorescence titration of the tweezer **6** with $IAPP_{2-14}$ in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **6**	Guest $IAPP_{2-14}$
Amount [mg]:	0.199	0.758
Volume [mL]:	13.252	0.741
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.18E-05	0.00E+00	0.00	452.757	0.000	0.000
10	710	2.18E-05	1.06E-05	0.48	437.479	15.278	16.095
20	720	2.18E-05	2.08E-05	0.96	425.005	27.752	29.491
30	730	2.18E-05	3.08E-05	1.41	406.789	45.968	40.742
40	740	2.18E-05	4.05E-05	1.86	394.084	58.673	50.280
60	760	2.18E-05	5.92E-05	2.72	384.079	68.678	65.480
80	780	2.18E-05	7.69E-05	3.53	380.939	71.818	76.970
100	800	2.18E-05	9.38E-05	4.30	370.615	82.142	85.912
140	840	2.18E-05	1.25E-04	5.73	357.585	95.172	98.849
180	880	2.18E-05	1.53E-04	7.04	352.933	99.824	107.709
240	940	2.18E-05	1.92E-04	8.79	333.641	119.116	116.724
300	1000	2.18E-05	2.25E-04	10.32	322.837	129.920	122.802





K_a [M^{-1}] = 12200 ± 17 %

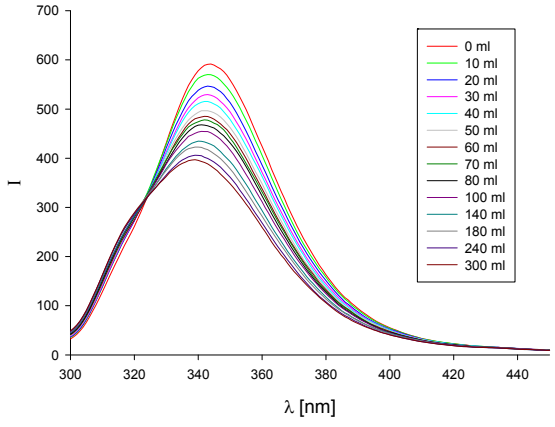
K_d [µM] = 82 ± 17 %

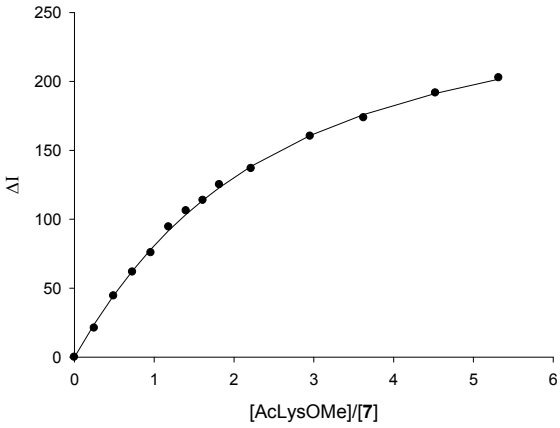
Fluorescence titrations of the ethoxycarboxymethyl phosphate tweezer 7

Fluorescence titration of the tweezer **7** with AcLysOMe · HCl in phosphate buffer (10mM, pH 7.6)

λ_{exc} = 285 nm	Receptor **7**	Guest AcLysOMe · HCl
Amount [mg]:	0.170	0.190
Volume [mL]:	8.996	1.742
Concentration [mol/L]:	$2.579 \cdot 10^{-05}$	$4.57 \cdot 10^{-04}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{343})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.579E-05	0.000E+00	0.00	591.106	0.000	0.000
10	710	2.579E-05	6.437E-06	0.25	570.014	21.092	24.011
20	720	2.579E-05	1.269E-05	0.49	546.695	44.411	44.747
30	730	2.579E-05	1.878E-05	0.73	529.350	61.756	62.678
40	740	2.579E-05	2.470E-05	0.96	515.369	75.737	78.225
50	750	2.579E-05	3.047E-05	1.18	496.607	94.499	91.753
60	760	2.579E-05	3.608E-05	1.40	484.978	106.128	103.574
70	770	2.579E-05	4.155E-05	1.61	477.336	113.770	113.953
80	780	2.579E-05	4.687E-05	1.82	466.028	125.078	123.109
100	800	2.579E-05	5.713E-05	2.22	454.219	136.887	138.455
140	840	2.579E-05	7.617E-05	2.95	430.803	160.303	160.746
180	880	2.579E-05	9.348E-05	3.62	417.400	173.706	175.973
240	940	2.579E-05	1.167E-04	4.52	399.394	191.712	191.344
300	1000	2.579E-05	1.371E-04	5.32	388.433	202.673	201.601





K_a [M^{-1}] = 22600 ± 4 %

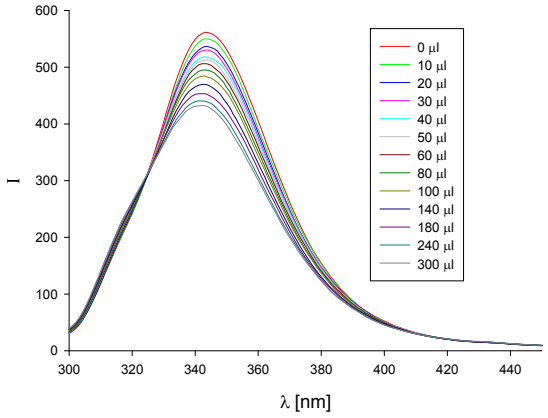
K_d [µM] = 44 ± 4 %

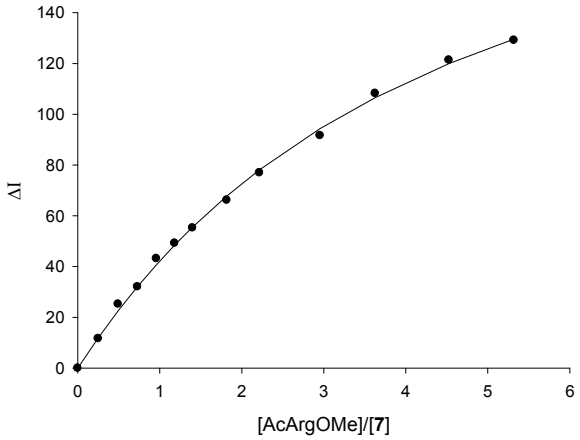
ΔI_{max} = 277 (47%)

Fluorescence titration of the tweezer **7** with AcArgOMe · HCl in phosphate buffer (10mM, pH 7.6)

λ_{exc} = 284 nm	Receptor **7**	Guest AcArgOMe · HCl
Amount [mg]:	0.170	0.145
Volume [mL]:	8.996	1.189
Concentration [mol/L]:	$2.579 \cdot 10^{-05}$	$4.57 \cdot 10^{-04}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{343})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.579E-05	0.000E+00	0.00	561.433	0.000	0.000
10	710	2.579E-05	6.440E-06	0.25	549.806	11.627	11.898
20	720	2.579E-05	1.270E-05	0.49	536.256	25.177	22.538
30	730	2.579E-05	1.879E-05	0.73	529.390	32.043	32.087
40	740	2.579E-05	2.472E-05	0.96	518.275	43.158	40.689
50	750	2.579E-05	3.048E-05	1.18	512.216	49.217	48.466
60	760	2.579E-05	3.610E-05	1.40	506.225	55.208	55.521
80	780	2.579E-05	4.690E-05	1.82	495.273	66.160	67.806
100	800	2.579E-05	5.716E-05	2.22	484.497	76.936	78.114
140	840	2.579E-05	7.621E-05	2.96	469.835	91.598	94.370
180	880	2.579E-05	9.353E-05	3.63	453.226	108.207	106.548
240	940	2.579E-05	1.167E-04	4.53	440.114	121.319	119.927
300	1000	2.579E-05	1.372E-04	5.32	432.272	129.161	129.569





K_a [M^{-1}] = 10880 ± 7 %

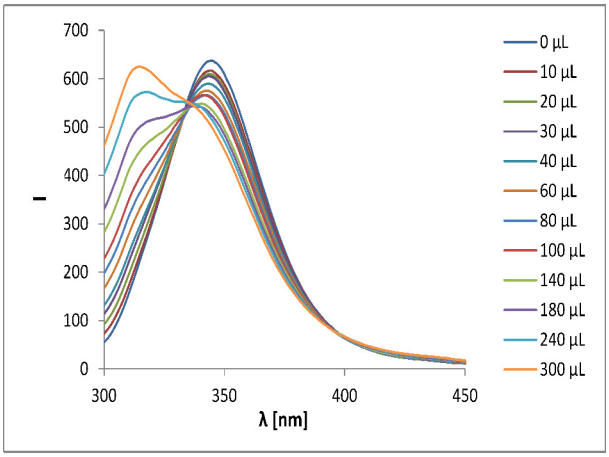
K_d [µM] = 92 ± 7 %

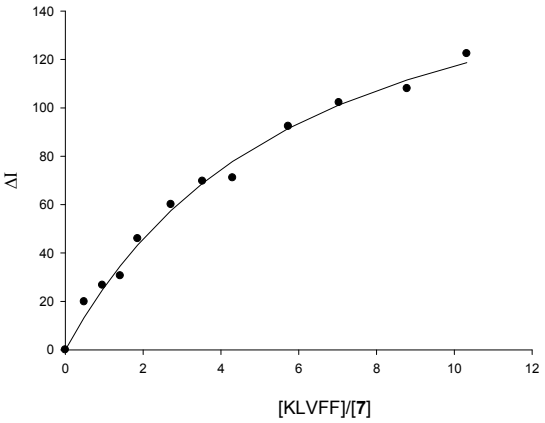
ΔI_{max} = 227 (40 %)

Fluorescence titration of the tweezer **7** with KLVFF in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 343 nm	Receptor **7**	Guest KLVFF
Amount [mg]:	0.153	0.330
Volume [mL]:	9.578	0.674
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.18E-05	0.00E+00	0.00	635.542	0.000	0.000
10	710	2.18E-05	1.06E-05	0.48	615.693	19.849	13.354
20	720	2.18E-05	2.08E-05	0.96	608.846	26.696	24.810
30	730	2.18E-05	3.08E-05	1.41	604.937	30.605	34.713
40	740	2.18E-05	4.05E-05	1.86	589.550	45.992	43.339
60	760	2.18E-05	5.92E-05	2.72	575.477	60.065	57.583
80	780	2.18E-05	7.69E-05	3.53	565.820	69.722	68.815
100	800	2.18E-05	9.37E-05	4.30	564.477	71.065	77.868
140	840	2.18E-05	1.25E-04	5.73	543.174	92.368	91.507
180	880	2.18E-05	1.53E-04	7.04	533.346	102.196	101.257
240	940	2.18E-05	1.91E-04	8.78	527.565	107.977	111.549
300	1000	2.18E-05	2.25E-04	10.32	513.093	122.449	118.717





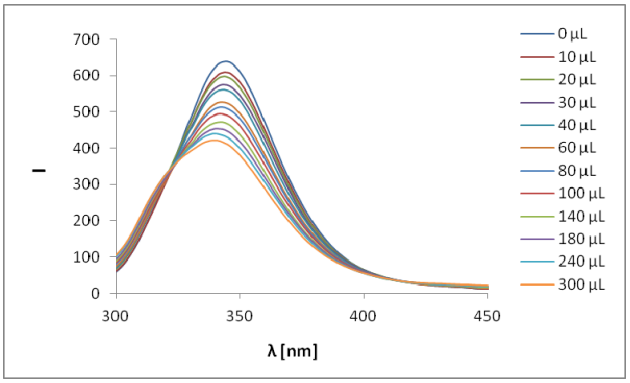
K_a [M^{-1}] = 8790 ± 14 %

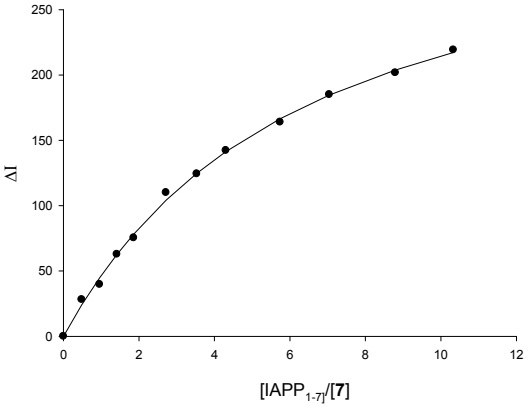
K_d [µM] = 114 ± 14 %

Fluorescence titration of the tweezer **7** with $IAPP_{1-7}$ in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 343 nm	Receptor **7**	Guest $IAPP_{1-7}$
Amount [mg]:	0.153	0.393
Volume [mL]:	9.578	0.710
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.51 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.18E-05	0.00E+00	0.00	636.672	0.000	0.000
10	710	2.18E-05	1.06E-05	0.49	608.513	28.159	24.008
20	720	2.18E-05	2.09E-05	0.96	596.917	39.755	44.672
30	730	2.18E-05	3.09E-05	1.42	573.907	62.765	62.593
40	740	2.18E-05	4.06E-05	1.86	561.312	75.360	78.247
60	760	2.18E-05	5.93E-05	2.72	526.643	110.029	104.200
80	780	2.18E-05	7.70E-05	3.53	512.296	124.376	124.760
100	800	2.18E-05	9.38E-05	4.30	494.406	142.266	141.397
140	840	2.18E-05	1.25E-04	5.74	472.700	163.972	166.580
180	880	2.18E-05	1.54E-04	7.04	451.611	185.061	184.670
240	940	2.18E-05	1.92E-04	8.79	434.884	201.788	203.851
300	1000	2.18E-05	2.25E-04	10.33	417.406	219.266	217.262





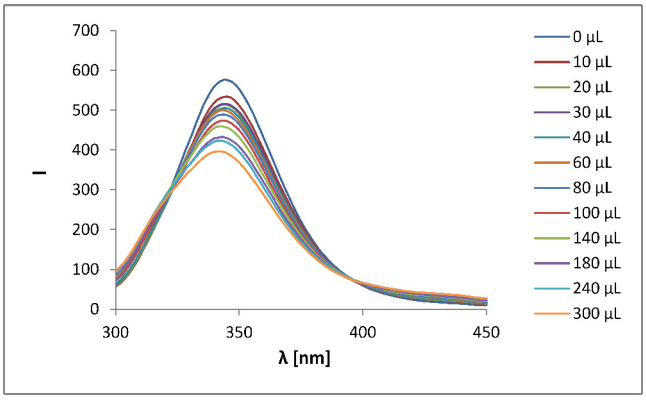
K_a [M^{-1}] = 8440 ± 6 %

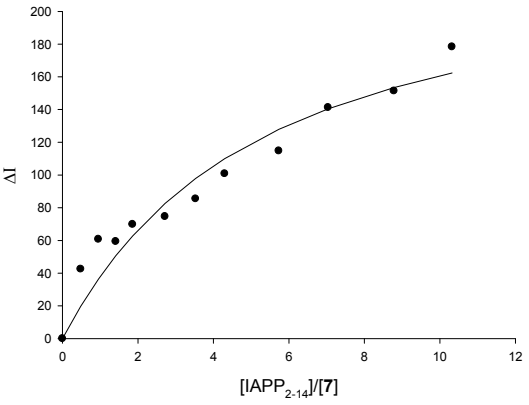
K_d [µM] = 118 ± 6 %

Fluorescence titration of the tweezer **7** with $IAPP_{2-14}$ in phosphate buffer (10mM. pH 7.6)

λ_{exc} = 285 nm λ_{em} = 343 nm	Receptor **7**	Guest $IAPP_{2-14}$
Amount [mg]:	0.134	0.713
Volume [mL]:	3.388	0.697
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{334\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2,18E-05	0,00E+00	0,00	574,307	0,000	0,000
10	710	2,18E-05	1,06E-05	0,48	531,805	42,502	19,721
20	720	2,18E-05	2,08E-05	0,96	513,578	60,729	36,388
30	730	2,18E-05	3,08E-05	1,41	514,928	59,379	50,594
40	740	2,18E-05	4,06E-05	1,86	504,512	69,795	62,805
60	760	2,18E-05	5,92E-05	2,72	499,696	74,611	82,622
80	780	2,18E-05	7,69E-05	3,53	488,894	85,413	97,929
100	800	2,18E-05	9,38E-05	4,30	473,532	100,775	110,054
140	840	2,18E-05	1,25E-04	5,73	459,571	114,736	127,959
180	880	2,18E-05	1,53E-04	7,04	433,034	141,273	140,486
240	940	2,18E-05	1,92E-04	8,79	422,963	151,344	153,465
300	1000	2,18E-05	2,25E-04	10,32	395,952	178,355	162,356





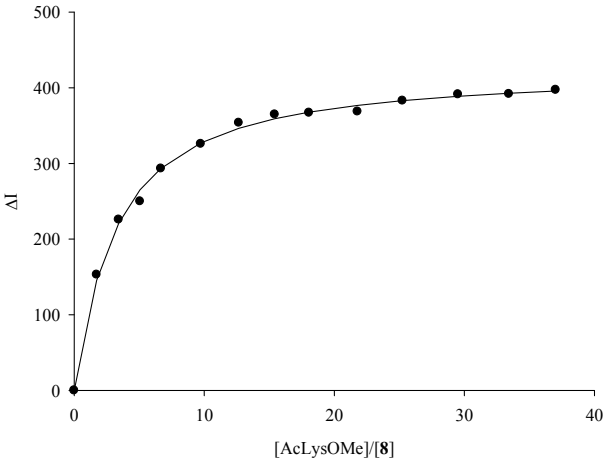
K_a [M^{-1}] = 10400 ± 36 %

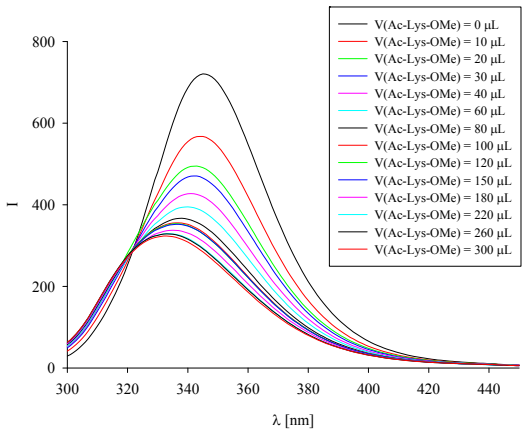
K_d [µM] = 96 ± 36 %

Fluorescence titration of tweezer **8** with AcLysOMe·HCl in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **8**	Guest AcLysOMe · HCl
amount [mg]:	0.158	0.604
volume [mL]:	8.00	0.800
concentration [mol/L]:	$2.56 \cdot 10^{-05}$	$3.16 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{346})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.56E-05	0.0000	0.0000	720.5250	0.0000	0.0000
10	710	2.56E-05	4.45E-05	1.7382	567.6470	152.8780	145.3887
20	720	2.56E-05	8.79E-05	3.4282	494.7360	225.7890	220.9989
30	730	2.56E-05	1.30E-04	5.0718	470.6730	249.8520	265.0654
40	740	2.56E-05	1.71E-04	6.6711	427.4030	293.1220	293.3753
60	760	2.56E-05	2.50E-04	9.7433	394.7620	325.7630	327.2009
80	780	2.56E-05	3.24E-04	12.6579	366.7880	353.7370	346.5476
100	800	2.56E-05	3.95E-04	15.4268	355.8130	364.7120	359.0210
120	820	2.56E-05	4.63E-04	18.0607	353.5080	367.0170	367.7163
150	850	2.56E-05	5.58E-04	21.7790	351.9120	368.6130	376.7256
180	880	2.56E-05	6.47E-04	25.2439	337.6830	382.8420	382.9100
220	920	2.56E-05	7.56E-04	29.5122	329.3100	391.2150	388.6581
260	960	2.56E-05	8.57E-04	33.4248	328.6850	391.8400	392.7087
300	1000	2.56E-05	9.49E-04	37.0244	323.3380	397.1870	395.7163





K_a [M^{-1}] = 14522 ± 5%

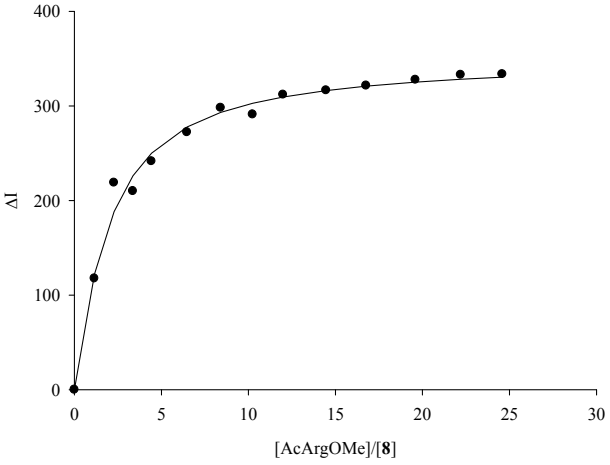
ΔI_{max} = 425

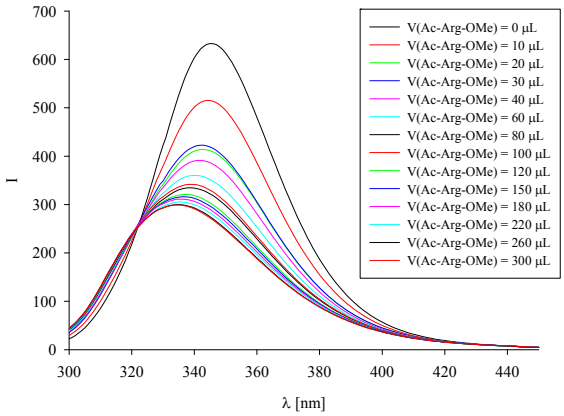
K_d[M] = 69 ± 5%

Fluorescence titration of tweezer **8** with AcArgOMe·HCl in phosphate buffer 10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **8**	Guest AcArgOMe · HCl
amount [mg]:	0.405	1.149
volume [mL]:	8.00	0.8
Concentration [mol/L]:	$6.57 \cdot 10^{-05}$	$5.38 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{345})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	6.57E-05	0.00E+00	0.00	623.715	0.000	0.0000
10	710	6.57E-05	7.58E-05	1.154	515.158	117.557	122.4085
20	720	6.57E-05	1.50E-04	2.277	413.875	218.840	188.3095
30	730	6.57E-05	2.21E-04	3.369	422.767	209.948	226.2282
40	740	6.57E-05	2.91E-04	4.431	391.272	241.443	250.0536
60	760	6.57E-05	4.25E-04	6.471	360.428	272.287	277.7317
80	780	6.57E-05	5.52E-04	8.407	334.752	297.963	293.0995
100	800	6.57E-05	6.73E-04	10.246	341.764	290.951	302.8101
120	820	6.57E-05	7.88E-04	11.995	320.794	311.921	309.4835
150	850	6.57E-05	9.50E-04	14.465	316.156	316.559	316.3126
180	880	6.57E-05	1.10E-03	16.766	311.292	321.423	320.9494
220	920	6.57E-05	1.29E-03	19.601	305.134	327.581	325.2213
260	960	6.57E-05	1.46E-03	22.199	299.782	332.933	328.2095
300	1000	6.57E-05	1.62E-03	24.591	299.101	333.614	330.4166





K_a [M^{-1}] = 10089 ± 11%

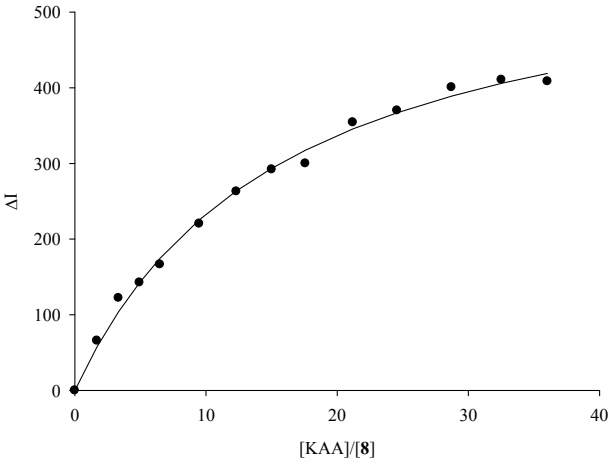
ΔI_{max} = 351

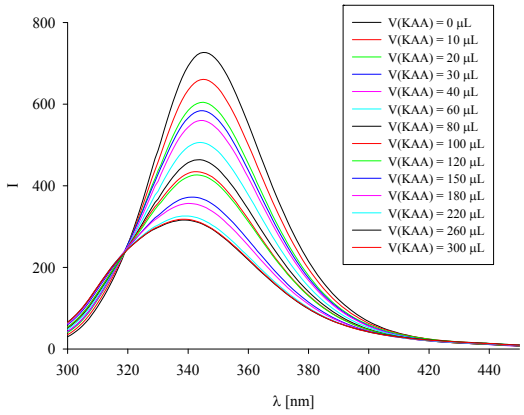
K_d[M] = 99 ± 11%

Fluorescence titration of tweezer **8** with the peptide KAA in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **8**	Guest KAA
amount [mg]:	0.158	0.710
volume [mL]:	8.00	0.80
concentration [mol/L]:	$2.56 \cdot 10^{-05}$	$2.46 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{346})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.56E-05	0.0000	0.0000	726.6050	0.0000	0.0000
10	710	2.56E-05	4.34E-05	1.6915	660.8890	65.7160	57.3689
20	720	2.56E-05	8.55E-05	3.3361	604.4970	122.1080	103.8966
30	730	2.56E-05	1.26E-04	4.9356	583.9810	142.6240	142.3120
40	740	2.56E-05	1.66E-04	6.4918	560.1390	166.4660	174.5208
60	760	2.56E-05	2.43E-04	9.4815	506.2180	220.3870	225.4086
80	780	2.56E-05	3.16E-04	12.3178	463.5680	263.0370	263.7224
100	800	2.56E-05	3.85E-04	15.0123	434.5910	292.0140	293.5671
120	820	2.56E-05	4.50E-04	17.5754	426.5880	300.0170	317.4499
150	850	2.56E-05	5.43E-04	21.1939	372.2460	354.3590	345.4727
180	880	2.56E-05	6.30E-04	24.5657	356.6560	369.9490	367.0045
220	920	2.56E-05	7.36E-04	28.7193	325.9380	400.6670	388.9806
260	960	2.56E-05	8.34E-04	32.5267	315.9770	410.6280	405.7554
300	1000	2.56E-05	9.23E-04	36.0296	318.0840	408.5210	418.9761





K_a [M^{-1}] = 2600 ± 8%

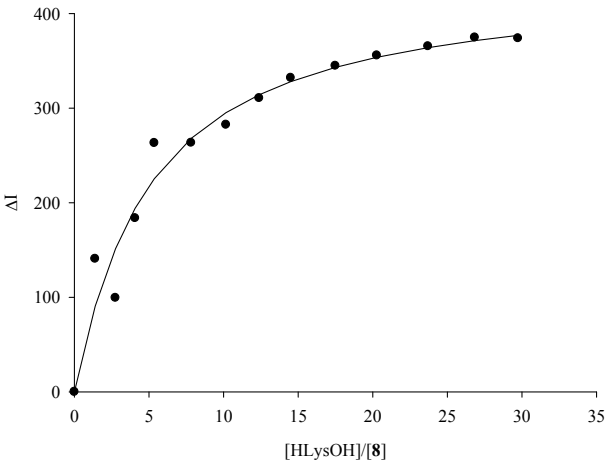
ΔI_{max} = 597

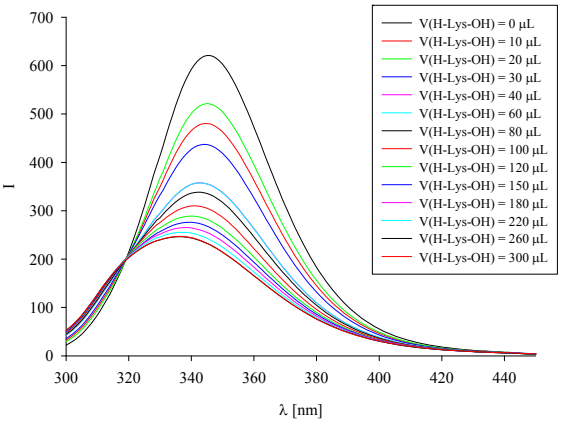
K_d[M] = 384 ± 8%

Fluorescence titration of tweezer **8** with HLysOH in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor	Guest
λ_{em}= 342nm	**8**	HLysOH
amount [mg]:	0.405	0.952
volume [mL]:	8.00	0.80
concentration [mol/L]:	$6.57 \cdot 10^{-05}$	$6.51 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{345})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	6.57E-05	0.00E+00	0.000	620.844	0.000	0.0000
10	710	6.57E-05	9.17E-05	1.397	480.285	140.559	90.6720
20	720	6.57E-05	1.81E-04	2.754	521.405	99.439	151.3640
30	730	6.57E-05	2.68E-04	4.075	437.187	183.657	194.0376
40	740	6.57E-05	3.52E-04	5.359	357.719	263.125	225.3693
60	760	6.57E-05	5.14E-04	7.828	357.514	263.330	267.9143
80	780	6.57E-05	6.68E-04	10.169	338.439	282.405	295.2500
100	800	6.57E-05	8.14E-04	12.394	310.275	310.569	314.2096
120	820	6.57E-05	9.53E-04	14.510	288.897	331.947	328.1010
150	850	6.57E-05	1.15E-03	17.497	276.157	344.687	343.1146
180	880	6.57E-05	1.33E-03	20.281	265.144	355.700	353.8040
220	920	6.57E-05	1.56E-03	23.710	255.391	365.453	364.0299
260	960	6.57E-05	1.76E-03	26.853	246.204	374.640	371.4088
300	1000	6.57E-05	1.95E-03	29.746	247.003	373.841	376.9824





K_a [M^{-1}] = 3362 ± 19%

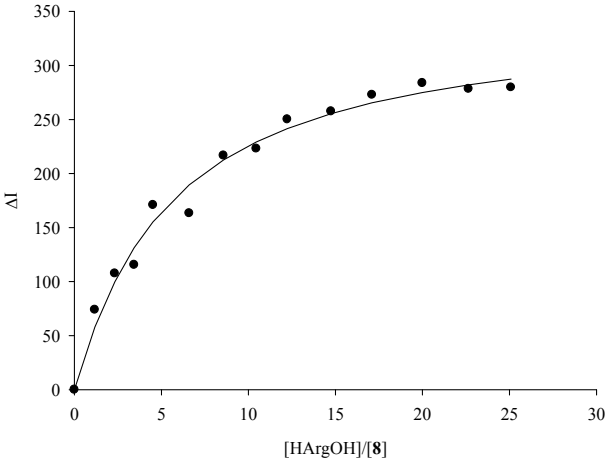
ΔI_{max} = 436

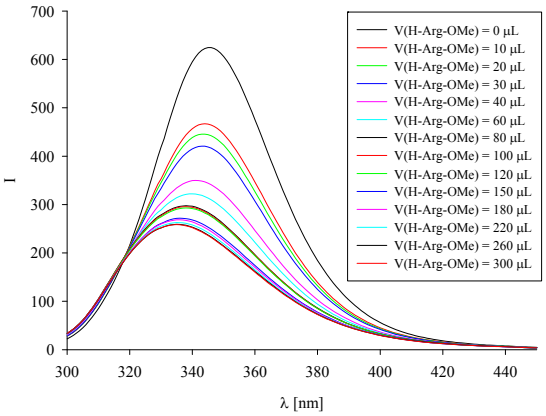
K_d[M] = 297 ± 19%

Fluorescence titration of tweezer **8** with HArgOH in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor	Guest
λ_{em}= 342nm	**8**	HArgOH
amount [mg]:	0.405	0.926
volume [mL]:	8.00	0.80
concentration [mol/L]:	$6.57 \cdot 10^{-05}$	$5.49 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{345})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	6.57E-05	0.00E+00	0.00	621.754	0.000	0.0000
10	710	6.57E-05	7.74E-05	1.178	547.777	73.977	58.0435
20	720	6.57E-05	1.53E-04	2.323	514.180	107.574	99.9385
30	730	6.57E-05	2.26E-04	3.437	506.336	115.418	131.2058
40	740	6.57E-05	2.97E-04	4.520	450.877	170.877	155.2541
60	760	6.57E-05	4.34E-04	6.602	458.538	163.216	189.5573
80	780	6.57E-05	5.63E-04	8.577	405.151	216.603	212.6863
100	800	6.57E-05	6.87E-04	10.453	398.784	222.970	229.2615
120	820	6.57E-05	8.04E-04	12.238	371.640	250.114	241.6933
150	850	6.57E-05	9.69E-04	14.758	364.221	257.533	255.4098
180	880	6.57E-05	1.12E-03	17.106	349.001	272.753	265.3563
220	920	6.57E-05	1.31E-03	19.998	338.100	283.654	275.0139
260	960	6.57E-05	1.49E-03	22.649	343.570	278.184	282.0700
300	1000	6.57E-05	1.65E-03	25.088	342.167	279.587	387.4485





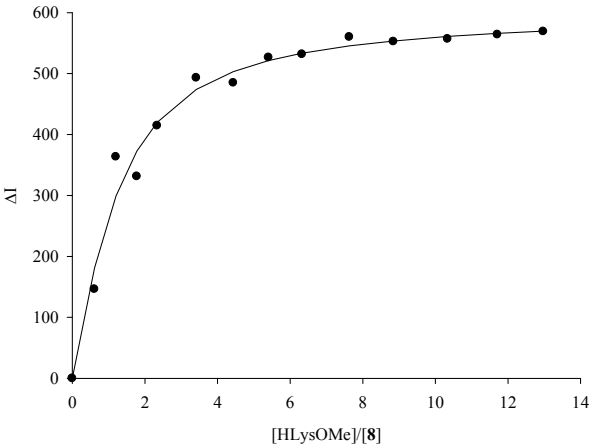
K_a [M^{-1}] = 3025± 13% ΔI_{max} = 347

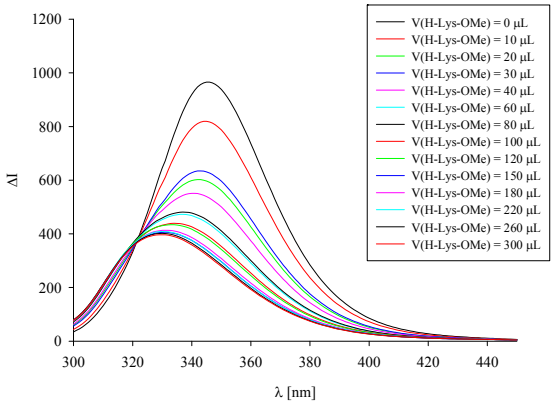
K_d[M] = 331 ± 13%

Fluorescence titration of tweezer **8** with HLysOMe·HCl in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **8**	Guest HLysOMe · HCl
amount [mg]:	0.087	0.646
volume [mL]:	2.00	0.8
concentration [mol/L]:	$5.64 \cdot 10^{-05}$	$2.44 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{345})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	5.64E-05	0.0000	0.0000	965.8020	0.0000	0.0000
10	710	5.64E-05	3.44E-05	0.6091	819.4860	146.3160	181.3552
20	720	5.64E-05	6.78E-05	1.2012	602.4450	363.3570	299.0930
30	730	5.64E-05	1.00E-04	1.7772	634.6210	331.1810	372.7134
40	740	5.64E-05	1.32E-04	2.3375	551.3080	414.4940	419.9035
60	760	5.64E-05	1.93E-04	3.4140	472.7830	493.0190	474.0983
80	780	5.64E-05	2.50E-04	4.4353	481.0750	484.7270	503.2990
100	800	5.64E-05	3.05E-04	5.4056	439.3820	526.4200	521.2605
120	820	5.64E-05	3.57E-04	6.3285	434.1740	531.6280	533.3473
150	850	5.64E-05	4.31E-04	7.6314	405.8300	559.9720	545.4801
180	880	5.64E-05	4.99E-04	8.8455	413.3190	552.4830	553.5747
220	920	5.64E-05	5.84E-04	10.3411	408.8370	556.9650	560.9260
260	960	5.64E-05	6.61E-04	11.7121	401.8520	563.9500	566.0063
300	1000	5.64E-05	7.32E-04	12.9734	396.8240	568.9780	569.7252





K_a [M^{-1}] = 24637 ± 17%

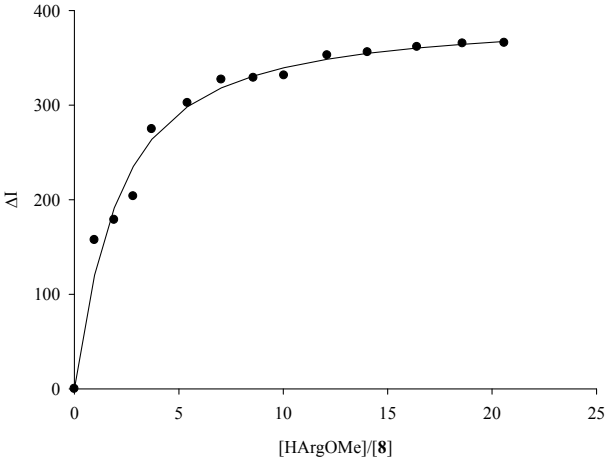
ΔI_{max} = 604

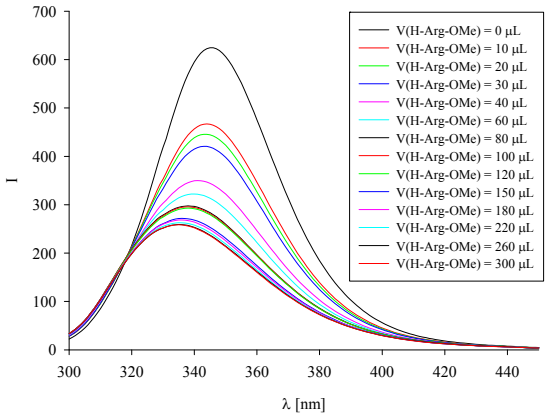
K_d[M] = 41 ± 17%

Fluorescence titration of tweezer **8** with HArgOMe·HCl in phosphate buffer (10mM, pH 7.2)

λ_{exc}= 285 nm	Receptor **8**	Guest HArgOMe · HCl
amount [mg]:	0.405	0.942
volume [mL]:	8.00	0.8
concentration [mol/L]:	$6.57 \cdot 10^{-05}$	$4.51 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{345})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	6.57E-05	0.00E+00	0.00	624.389	0.000	0.0000
10	710	6.57E-05	6.35E-05	0.967	467.043	157.346	120.1632
20	720	6.57E-05	1.25E-04	1.906	445.721	178.668	191.3206
30	730	6.57E-05	1.85E-04	2.820	420.821	203.568	235.1536
40	740	6.57E-05	2.44E-04	3.709	349.782	274.607	263.8995
60	760	6.57E-05	3.56E-04	5.418	322.109	302.280	298.4684
80	780	6.57E-05	4.62E-04	7.038	297.364	327.025	318.1812
100	800	6.57E-05	5.64E-04	8.578	295.565	328.824	330.8132
120	820	6.57E-05	6.60E-04	10.043	293.012	331.377	339.5677
150	850	6.57E-05	7.96E-04	12.110	271.677	352.712	348.5838
180	880	6.57E-05	9.22E-04	14.037	268.475	355.914	354.7366
220	920	6.57E-05	1.08E-03	16.706	262.802	361.587	360.4261
260	960	6.57E-05	1.22E-03	18.586	259.094	365.295	364.4172
300	1000	6.57E-05	1.35E-03	20.587	258.523	365.866	367.3706





K_a [M^{-1}] = 10011 ± 14%

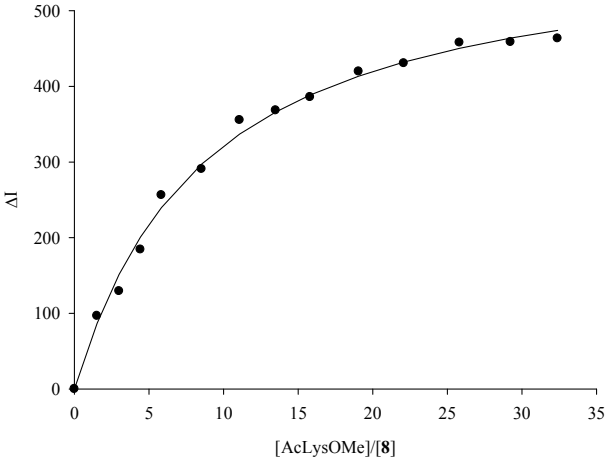
ΔI_{max} = 396

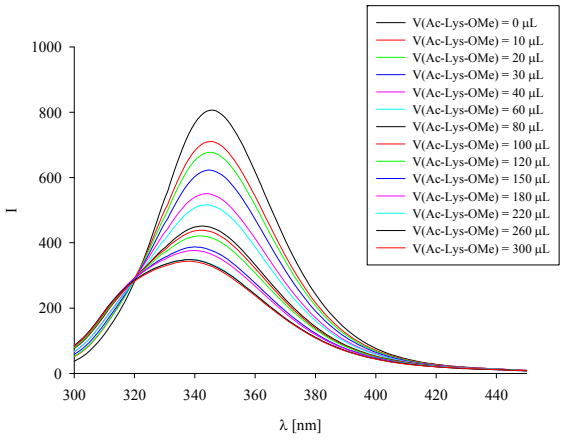
K_d[M] = 100 ± 14%

Fluorescence titration of tweezer **8** with AcLysOMe·HCl in citric acid phosphate buffer (10mM, pH 4.0)

λ_{exc}= 285 nm	Receptor **8**	Guest AcLysOMe · HCl
amount [mg]:	0.111	0.495
volume [mL]:	6.00	0.8
concentration [mol/L]:	$2.40 \cdot 10^{-05}$	$2.59 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{345})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.40E-05	0.0000	0.0000	806.9290	0.0000	0.0000
10	710	2.40E-05	3.65E-05	1.5208	710.2970	96.6320	86.8500
20	720	2.40E-05	7.20E-05	2.9994	677.5980	129.3310	151.3731
30	730	2.40E-05	1.07E-04	4.4374	622.6480	184.2810	200.8564
40	740	2.40E-05	1.40E-04	5.8366	550.7520	256.1770	239.8450
60	760	2.40E-05	2.05E-04	8.5245	516.2150	290.7140	297.0981
80	780	2.40E-05	2.66E-04	11.0745	451.4790	355.4500	336.9441
100	800	2.40E-05	3.24E-04	13.4971	438.6240	368.3050	366.1890
120	820	2.40E-05	3.79E-04	15.8015	421.1090	385.8200	388.5311
150	850	2.40E-05	4.57E-04	19.0547	387.2480	419.6810	413.6127
180	880	2.40E-05	5.30E-04	22.0861	376.3970	430.5320	432.0968
220	920	2.40E-05	6.20E-04	25.8205	348.9920	457.9370	450.2933
260	960	2.40E-05	7.02E-04	29.2437	348.3100	458.6190	463.7486
300	1000	2.40E-05	7.78E-04	32.3930	343.4990	463.4300	474.0985





K_a [M^{-1}] = 5182 ± 8%

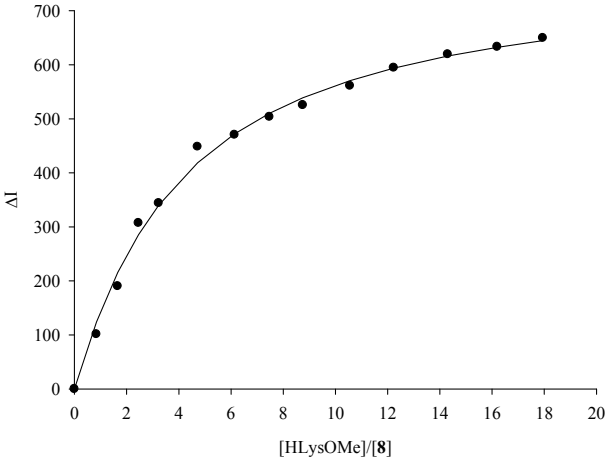
ΔI_{max} = 595

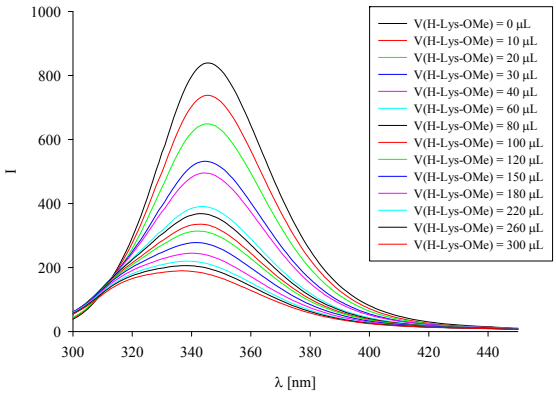
K_d[M] = 193 ± 8%

Fluorescence titration of tweezer **8** with HLysOMe·HCl in citric acid phosphate buffer (10mM, pH 4.0)

λ_{exc}= 285 nm	Receptor **8**	Guest HLysOMe · HCl
amount [mg]:	0.111	0.380
volume [mL]:	6.00	0.8
concentration [mol/L]:	$2.40 \cdot 10^{-05}$	$1.44 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{345})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.40E-05	0.0000	0.0000	839.2670	0.0000	0.0000
10	710	2.40E-05	2.02E-05	0.8424	738.0800	101.1870	123.9390
20	720	2.40E-05	3.99E-05	1.6615	649.0980	190.1690	215.9263
30	730	2.40E-05	5.90E-05	2.4581	532.1560	307.1110	285.8386
40	740	2.40E-05	7.76E-05	3.2332	495.4290	343.8380	340.2512
60	760	2.40E-05	1.13E-04	4.7221	391.0670	448.2000	418.6570
80	780	2.40E-05	1.47E-04	6.1347	368.8610	470.4060	471.9158
100	800	2.40E-05	1.79E-04	7.4767	335.8440	503.4230	510.2106
120	820	2.40E-05	2.10E-04	8.7532	314.0930	525.1740	538.9740
150	850	2.40E-05	2.53E-04	10.5554	278.1860	561.0810	570.7264
180	880	2.40E-05	2.94E-04	12.2346	244.7870	594.4800	593.7482
220	920	2.40E-05	3.43E-04	14.3033	220.0190	619.2480	616.0885
260	960	2.40E-05	3.89E-04	16.1995	206.1370	633.1300	632.3974
300	1000	2.40E-05	4.31E-04	17.9441	189.8170	649.4500	644.8188





K_a [M^{-1}] = 11482 ± 8%

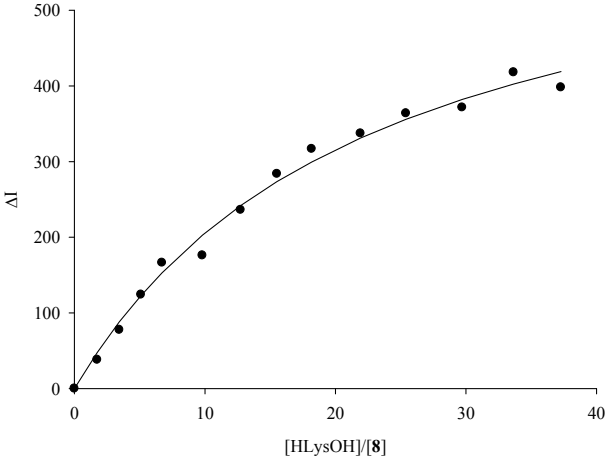
ΔI_{max} = 781

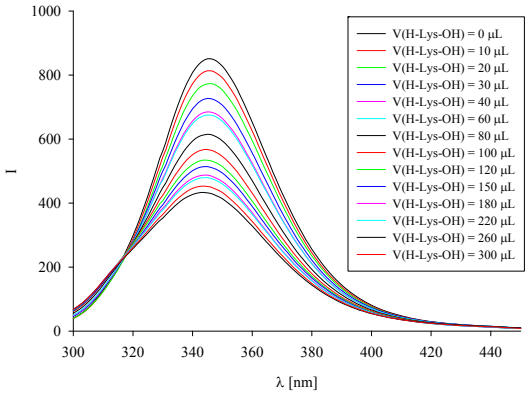
K_d[M] = 87 ± 8%

Fluorescence titration of tweezer **8** with HLysOH in citric acid phosphate buffer (10mM, pH 4.0)

λ_{exc}= 285 nm	Receptor **8**	Guest HLysOH
amount [mg]:	0.111	0.436
volume [mL]:	6.00	0.8
concentration [mol/L]:	$2.40 \cdot 10^{-05}$	$2.98 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{345})**	**ΔI_{obs}**	**ΔI_{calc}**
0	700	2.40E-05	0.0000	0.0000	851.2250	0.0000	0.0000
10	710	2.40E-05	4.20E-05	1.7502	813.2530	37.9720	47.7204
20	720	2.40E-05	8.29E-05	3.4518	773.7240	77.5010	88.2108
30	730	2.40E-05	1.26E-04	5.1067	727.0960	124.1290	122.9680
40	740	2.40E-05	1.61E-04	6.7169	685.0990	166.1260	153.1093
60	760	2.40E-05	2.36E-04	9.8103	675.3750	175.8500	202.7473
80	780	2.40E-05	3.06E-04	12.7450	615.1200	236.1050	241.8889
100	800	2.40E-05	3.73E-04	15.5329	567.5450	283.6800	273.5186
120	820	2.40E-05	4.37E-04	18.1849	534.4250	316.8000	299.5951
150	850	2.40E-05	5.26E-04	21.9288	513.9870	337.2380	331.1085
180	880	2.40E-05	6.10E-04	25.4175	487.5300	363.6950	356.0286
220	920	2.40E-05	7.13E-04	29.7152	479.6840	371.5410	382.1269
260	960	2.40E-05	8.08E-04	33.6547	433.2550	417.9700	402.5180
300	1000	2.40E-05	8.95E-04	37.2790	453.2060	398.0190	418.8858





K_a [M^{-1}] = 1908 ± 13%

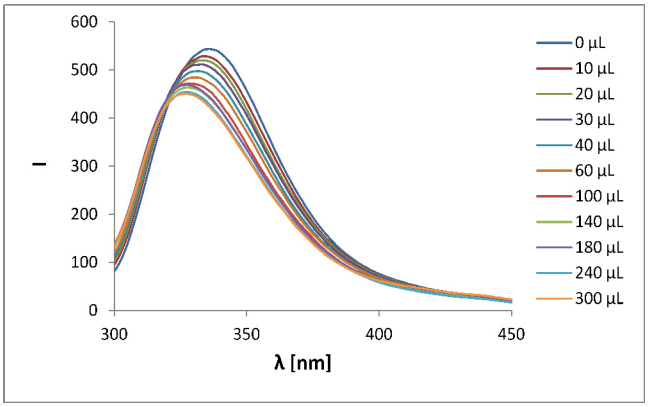
ΔI_{max} = 668

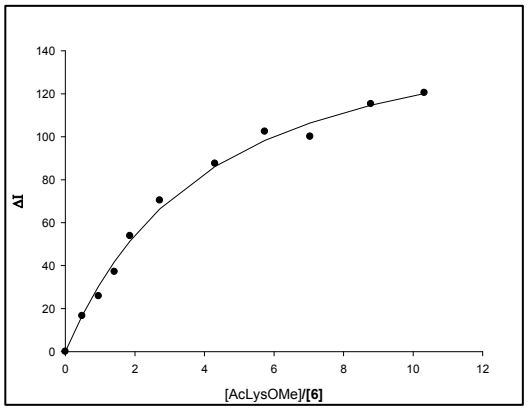
K_d[M] = 524 ± 13%

Fluorescence titration of tweezer **6** with AcLysOMe in phosphate buffer saline (10mM + 150 mM NaCl, pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **6**	Guest AcLysOMe
Amount [mg]:	0.174	0.156
Volume [mL]:	11.587	0.871
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{336\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2.18E-05	0.00E+00	0.00	543.571	0.000	0.000
10	710	2.18E-05	1.06E-05	0.48	526.960	16.611	16.723
20	720	2.18E-05	2.08E-05	0.96	517.754	25.817	30.469
30	730	2.18E-05	3.08E-05	1.41	506.406	37.165	41.873
40	740	2.18E-05	4.06E-05	1.86	489.790	53.781	51.429
60	760	2.18E-05	5.92E-05	2.72	473.229	70.342	66.428
100	800	2.18E-05	9.38E-05	4.30	456.067	87.504	86.106
140	840	2.18E-05	1.25E-04	5.74	441.154	102.417	98.261
180	880	2.18E-05	1.53E-04	7.04	443.515	100.056	106.446
240	940	2.18E-05	1.92E-04	8.79	428.315	115.256	114.656
300	1000	2.18E-05	2.25E-04	10.32	423.093	120.478	120.125





K_a [M^{-1}] = 13900 ± 13 %

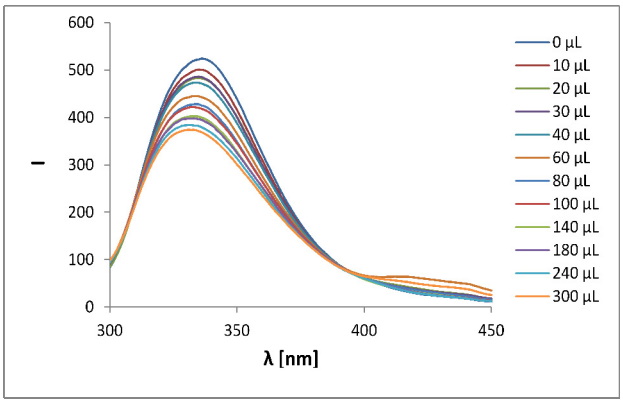
K_d[M] = 72 ± 13 %

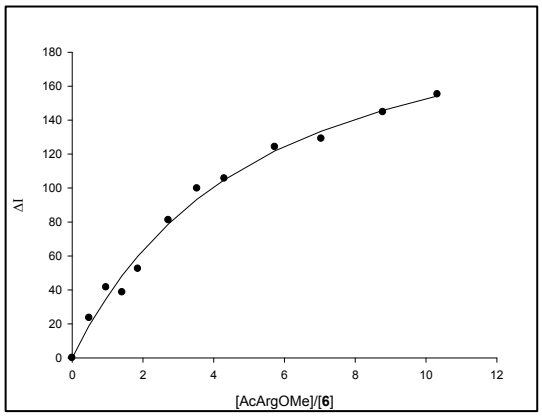
ΔI_{max} = 161 (30%)

Fluorescence titration of tweezer **6** with AcArgOMe in phosphate buffer saline (10mM + 150 mM NaCl, pH 7.6)

λ_{exc} = 285 nm λ_{em} = 336 nm	Receptor **6**	Guest AcArgOMe
Amount [mg]:	0.117	0.213
Volume [mL]:	7.792	1.065
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$7.50 \cdot 10^{-04}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. ($I_{336\ nm}$)	ΔI_{obs}	ΔI_{calc}
0	700	2,18E-05	0,00E+00	0,00	524,186	0,000	0,000
10	710	2,18E-05	1,06E-05	0,48	500,662	23,524	18,951
20	720	2,18E-05	2,08E-05	0,96	482,598	41,588	34,779
30	730	2,18E-05	3,08E-05	1,41	485,487	38,699	48,363
40	740	2,18E-05	4,05E-05	1,86	471,656	52,530	59,987
60	760	2,18E-05	5,92E-05	2,72	443,007	81,179	78,878
80	780	2,18E-05	7,69E-05	3,53	424,356	99,830	93,401
100	800	2,18E-05	9,37E-05	4,30	418,470	105,716	104,875
140	840	2,18E-05	1,25E-04	5,73	399,969	124,217	121,832
180	880	2,18E-05	1,53E-04	7,04	395,088	129,098	133,495
240	940	2,18E-05	1,91E-04	8,78	379,425	144,761	145,726
300	1000	2,18E-05	2,25E-04	10,32	368,945	155,241	154,216





K_a [M^{-1}] = 10600 ± 15 %

K_d[M] = 94 ± 15 %

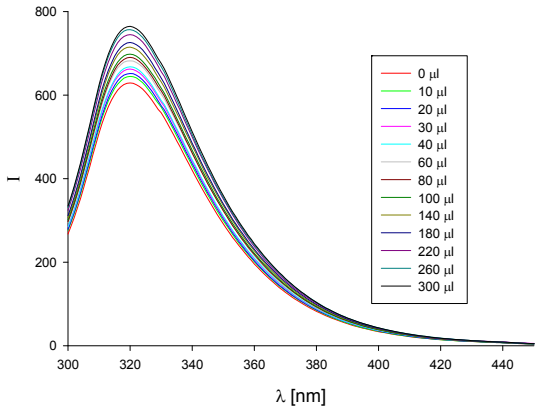
ΔI_{max} = 223 (42%)

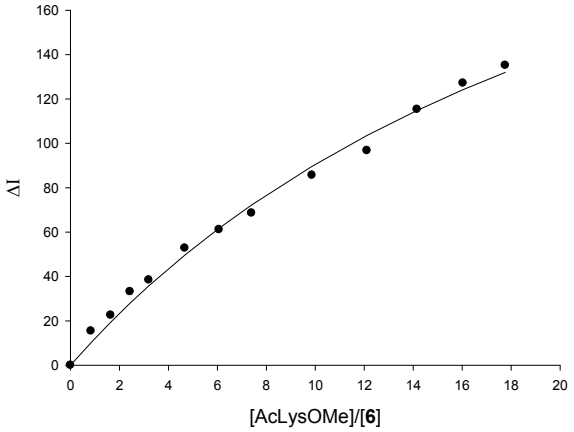
Fluorescence titrations of the tweezers 6 and 7 with lysine and arginine derivatives in varied polarity solvent mixture

Fluorescence titration of the tweezer **6** with AcLysOMe · HCl in methanol

λ_{exc} = 285 nm	Receptor **6**	Guest AcLysOMe · HCl
Amount [mg]:	0.109	0.410
Volume [mL]:	6.000	1.100
Concentration [mol/L]:	$2.638 \cdot 10^{-05}$	$1.561 \cdot 10^{-03}$

Guest V (µL)	Receptor V (µL)	[Receptor] [mol/L]	[Guest] [mol/L]	[Guest]/ [Receptor]	F.I. (I_{320})	$-\Delta I_{obs}$	$-\Delta I_{calc}$
0	700	2.638E-05	0.000E+00	0.00	629.245	0.000	0.000
10	710	2.638E-05	2.199E-05	0.83	644.655	15.410	10.132
20	720	2.638E-05	4.337E-05	1.64	651.782	22.537	19.400
30	730	2.638E-05	6.417E-05	2.43	662.402	33.157	27.910
40	740	2.638E-05	8.440E-05	3.20	667.686	38.441	35.749
60	760	2.638E-05	1.233E-04	4.67	682.056	52.811	49.707
80	780	2.638E-05	1.602E-04	6.07	690.364	61.119	61.756
100	800	2.638E-05	1.952E-04	7.40	697.834	68.589	72.261
140	840	2.638E-05	2.602E-04	9.87	714.910	85.665	89.680
180	880	2.638E-05	3.194E-04	12.11	726.007	96.762	103.531
220	920	2.638E-05	3.734E-04	14.16	744.570	115.325	114.802
260	960	2.638E-05	4.229E-04	16.03	756.452	127.207	124.150
300	1000	2.638E-05	4.684E-04	17.76	764.414	135.169	132.028





K_a [M^{-1}] = 1560 ± 18 %

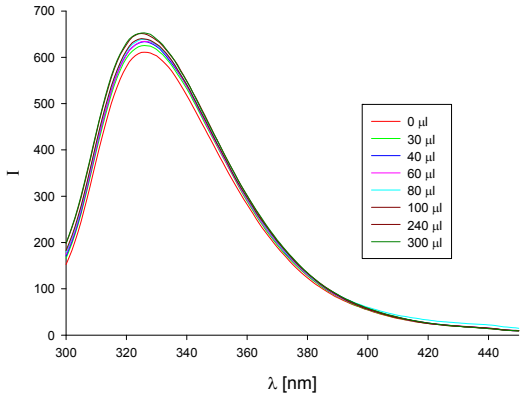
K_d [µM] = 641 ± 18 %

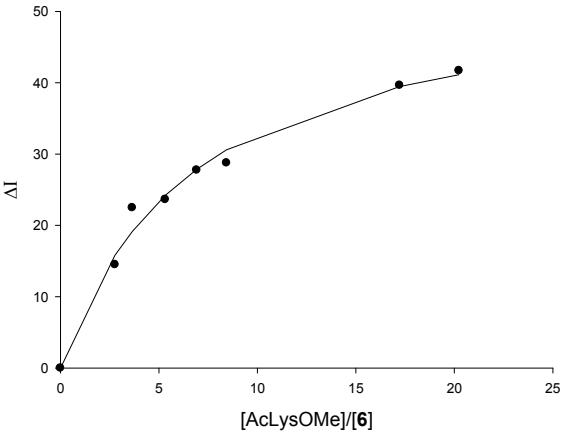
ΔI_{max} = -317 (50 %)

Fluorescence titration of the tweezer **6** with AcLysOMe in 1:4 mixture of methanol/phosphate buffer (10mM, pH 7.6)

λ_{exc} = 285 nm	Receptor **6**	Guest AcLysOMe · HCl
Amount [mg]:	0.139	0.359
Volume [mL]:	9.258	1.023
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$1.47 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{326})**	**$-\Delta I_{obs}$**	**$-\Delta I_{calc}$**
0	700	2.18E-05	0.00E+00	0.000	611.129	0.00	0.00
30	730	2.18E-05	6.04E-05	2.771	625.627	14.50	15.81
40	740	2.18E-05	7.95E-05	3.645	633.618	22.49	19.15
60	760	2.18E-05	1.16E-04	5.324	634.772	23.64	24.21
80	780	2.18E-05	1.51E-04	6.917	638.886	27.76	27.86
100	800	2.18E-05	1.84E-04	8.430	639.889	28.76	30.60
240	940	2.18E-05	3.75E-04	17.218	650.792	39.66	39.48
300	1000	2.18E-05	4.41E-04	20.231	652.833	41.70	41.15





K_a [M^{-1}] = 7730 ± 16 %

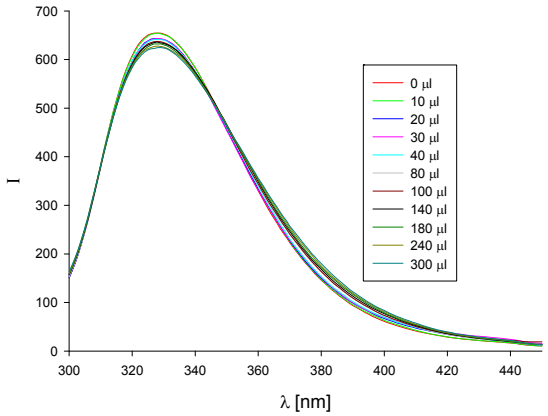
K_d [µM] = 129 ± 16 %

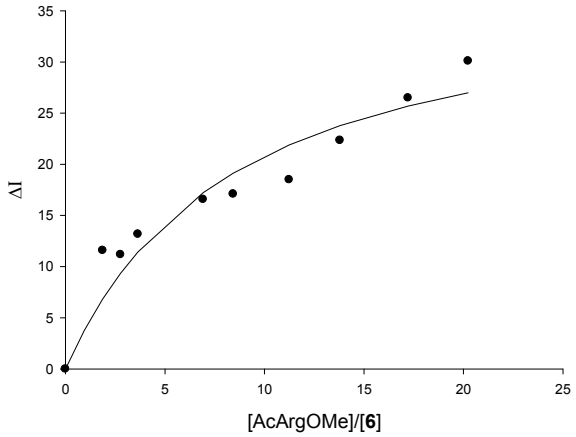
ΔI_{max} = 54 (9 %)

Fluorescence titration of the tweezer **6** with AcArgOMe in 1:9 mixture of methanol/phosphate buffer (10mM, pH 7.6)

λ_{exc} = 285 nm	Receptor **6**	Guest AcArgOMe · HCl
Amount [mg]:	0.111	0.356
Volume [mL]:	7.393	0.908
Concentration [mol/L]:	$2.18 \cdot 10^{-05}$	$1.47 \cdot 10^{-03}$

Guest V (µL)	**Receptor V (µL)**	**[Receptor] [mol/L]**	**[Guest] [mol/L]**	**[Guest]/ [Receptor]**	**F.I. (I_{328})**	**$-\Delta I_{obs}$**	**$-\Delta I_{calc}$**
0	700	2.180E-05	0.000E+00	0.00	654.326	0.000	0.000
10	710	2.180E-05	2.071E-05	0.95	654.430	-0.104	3.769
20	720	2.180E-05	4.084E-05	1.87	642.741	11.585	6.825
30	730	2.180E-05	6.041E-05	2.77	643.148	11.178	9.343
40	740	2.180E-05	7.946E-05	3.64	641.157	13.169	11.448
80	780	2.180E-05	1.508E-04	6.92	637.754	16.572	17.225
100	800	2.180E-05	1.838E-04	8.43	637.231	17.095	19.136
140	840	2.180E-05	2.450E-04	11.24	635.840	18.486	21.890
180	880	2.180E-05	3.007E-04	13.79	631.989	22.337	23.773
240	940	2.180E-05	3.753E-04	17.22	627.840	26.486	25.693
300	1000	2.180E-05	4.410E-04	20.23	624.229	30.097	26.991





K_a [M^{-1}] = 6030 ± 41 %

K_d [µM] = 166 ± 41 %

ΔI_{max} = 37 (6 %)

NMR experiments

Table 1. **Upfield chemical shift changes ($\Delta\delta_{obs}$ in ppm) of the side-chain protons in AcLysOMe at different host/guest ratios of tweezers** 3-7 **in methanol/buffer (2:1). Due to the high methanol content the guest is only partially inserted into the tweezers cavity.**

Tweezers	(host/guest)	$\Delta\delta_{obs}$ 6-H	5-H	4-H	3-H	2-H
3	2:1	a	0.11	a	0.17	0.05
	1:2	0.20	0.00	0.00	0.06	0.02
4	3:1	a	a	a	a	0.06
	1:2	>0.40	0.08	0.24	0.13	0.03
	1:4	0.26	0.02	0.10	0.08	0.02
6	2:1	a	a	a	a	0.09
	1:1	a	0.28	0.66	0.33	0.07
	1:2	a	0.16	0.46	0.22	0.05
	1:4	0.45	0.08	0.28	0.14	0.03
7	2:1	a	0.13	0.40	0.21	0.06
	1:2	>0.50	0.09	0.29	0.15	0.04
	1:4	0.30				

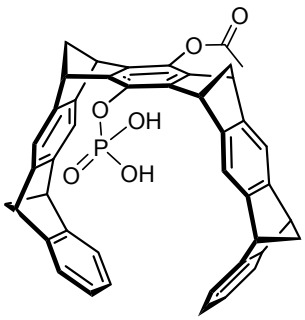
a: signal could not be detected or identified.

Table 2. ^{1}H NMR chemical shift changes ($\Delta\delta_{obs}$) of arginine side chains protons for the 1:1 complex of **6@AcArgOMe** at 0.4 mM. An solvent mixtures, the methanol signal was used as a reference.

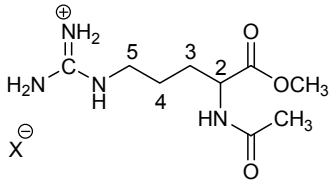
proton	CD_3OD	CD_3OD:PB (2:1)	CD_3OD:PB (1:4)	CD_3OD:PB (1:9)
5-H [ppm]	0.0	0.09	0.27	0.60
4-H [ppm]	0.0	0.06	0.18	0.38

PB: phosphate buffer 10 mM, pH 7.2

NMR spectra of the complex 6@AcArgOMe in solvent mixtures of increasing water content



6



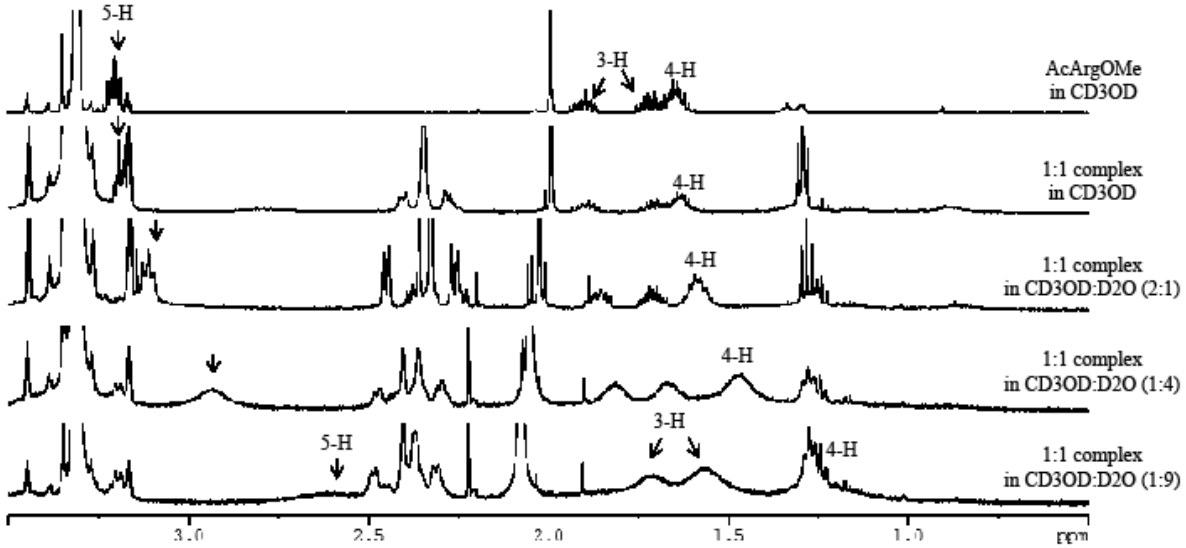
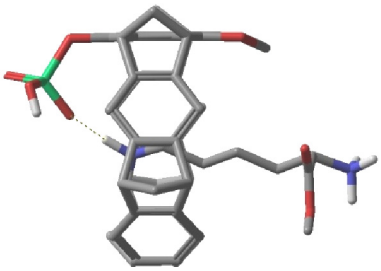
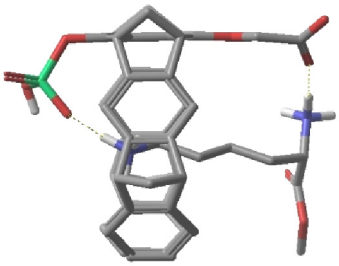


Figure 1. ^{1}H NMR spectra of 1:1 complexes between acetoxy phosphate tweezers **6** and **AcArgOMe** at 0.4 mM in media of increasing polarity (methanol-d_4/ D_2O phosphate buffer mixtures at 10 mM and pH 7.2). Protons of the arginine side chains are assigned by numbers. They are all shifted upfield as the polarity of medium increases. (X^- = Chloride).

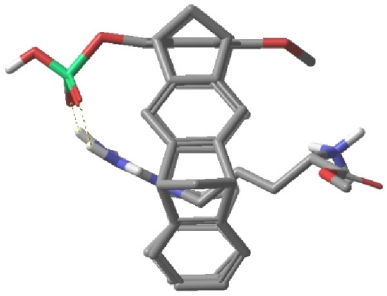
Molecular Modeling



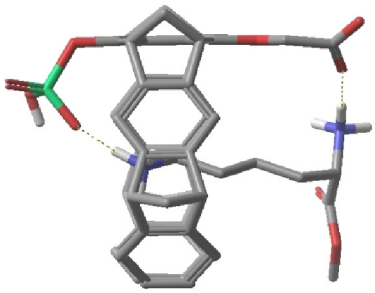
2@HLysOMe



8@HLysOMe

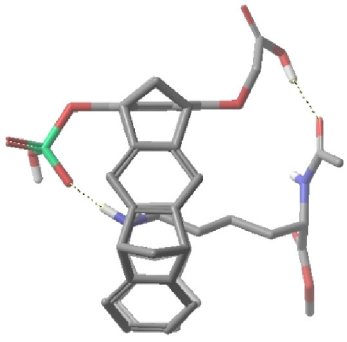


2@HArgOMe

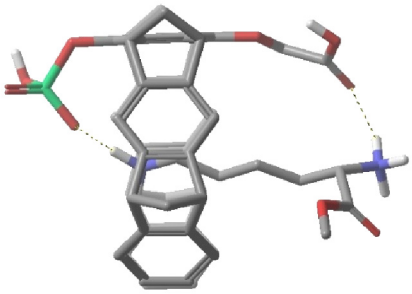


8@HArgOMe

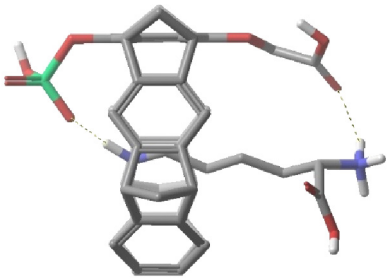
Figure 2. Lowest energy structures from Monte Carlo simulations of complexes between unsymmetrical tweezers **2**/**8** and HLysOMe/HArgOMe (MacroModel 9.2, Conformational Search, OPLS_2005, 5000 steps, water/GBA).



8@AcLysOMe



8@HLysOMe



8@HLysOH

Figure 3. Lowest energy structures from Monte Carlo simulations of complexes between unsymmetrical tweezers **8** andAcLysOMe/HLysOMe/HLysOH at pH 4.0 (protonated carboxylate; MacroModel 9.2, Conformational Search, OPLS_2005, 5000 steps, water/GBA).

Crystal structure

Crystal structure of n-octyl tweezers 3

The crystal was mounted on nylon loops in inert oil. Data were collected on a Bruker AXS D8 Kappa diffractometer with APEX2 detector (mono-chromated $Mo_{K\alpha}$ radiation, λ = 0.71073 Å) at 100 K. The structures were solved by Direct Methods (SHELXS-97)[1] and refined anisotropically by full-matrix least-squares on F^2 (SHELXL-97).[2,3] Absorption corrections were performed semi-empirically from equivalent reflections on basis of multi-scans (Bruker AXS APEX2). Hydrogen atoms were refined using a riding model or rigid methyl groups. The OH hydrogen atoms could not be identified. Because of the limited crystal quality the n-octly chain and one of the water and methanol molecules could not be refined anisotropically to yield a realistic description of a thermal movement or were non-positively defined. In addition C49 of the octyl chain is disordered over two positions.
The crystal diffracted up to θ_{max} = 28.32° however at this resolution ~90% of the reflexes were unobserved (i.e. I < 2σ(I)). R_{int} of the data was 0.0756. In the final refinement R1 = 0.0970 (I > 2σ(I)), wR2 = 0.2908 (all data) and Goof = 1.831 was obtained. The highest peak in the residual electron density was 1.321 e·Å^3 the deepest hole -0.819 e·Å^3. These parameters suggest that the model is qualitatively correct, however one should refrain from a detailed discussion of the structural parameters. The unit cell was found to be a = 40.063(5), c = 11.1451(14) in a tetragonal body-centered lattice with space group $I4_1/c$.

Crystal structure of dimethoxy phosphate octyl tweezers 3a

Crystals of the tweezers **3a** were obtained by dissolving 10 mg **3a** in 3 mL of a methanol/n-pentane mixture (5:1) and allowing the solution to stand at room temperature for 3-5 days. **3a** crystallizes in the monoclinic space group $P2_1/c$ with an asymmetric unit constituted by one tweezers molecule and one methanol molecule, which is - unlike in **3** - not incorporated in the cavity of the tweezers. The cavity is blocked from one side by self-inclusion of one of the phosphate's methyl groups (C44) which forms CH-π with the interior side of the tweezers' π-systems (interaction *i* and *ii*, see Table 3). Unlike in **3** the *n*-octyl residue adopts an orientation pointing away from the core in a straight line leaving the cavity open at this side to receive guest molecules which is in this case the second phosphate methyl group (C43) of a neighbouring tweezers molecule. The resulting stacking (by *c* glide plane symmetry) is supported by a CH-π interaction of this methyl group with the internal tweezers π-system (*iii* and *iv*); similarly, the *n*-octyl moiety interacts with the external tweezers π-system (*v*). They are accompanied by a non-classical hydrogen bond (*vi*). However, this stacking establishes a close packing, rendering it quite unlikely that especially the orientation of the *n*-octyl residue is retained in solution where close packing is no longer energetically favoured. The methanol molecule is firmly attached to the phosphate group via a classical hydrogen bond (*vii*) and is filling gaps in the packing of the tweezer molecules.

The crystals were mounted on nylon loops in inert oil. Data were collected on a Bruker AXS D8 Kappa diffractometer with APEX2 detector (mono-chromated $Mo_{K\alpha}$ radiation, λ = 0.71073 Å) at 100 K. The structures were solved by Direct Methods (SHELXS-97)[1] and refined anisotropically by full-matrix least-squares on F^2 (SHELXL-97).[2,3] Absorption corrections were performed semi-empirically from equivalent reflections on basis of multi-scans (Bruker AXS APEX2). Hydrogen atoms were refined using a riding model or rigid methyl groups. C50 and C51 were disordered over two positions where the main component is occupied by 90%. The position of H60 was taken from the difference Fourier synthesis and constrained. Its thermal parameter was constrained to be 1.5 times the isotropic displacement

parameter of the equivalent U_{ij} of the corresponding oxygen atom. Details of the structure determination are summarized in Tables 6.1 – 6.4.

Table 3. Intermolecular interactions in **3a**. Symmetry operators: #1 *x*, –*y*+3/2, *z*–1/2 , #2 *x*, –*y*+3/2, *z*+1/2, #3 . M: centroid of a phenyl ring, R: best plane of the ring.

	interaction	H···A/M[Å]	D–H···A[°]	H···R[Å]	<(HMR)[°]
i	C44–H44B···M1	3.14	146.8	2.898(2)	67.4
ii	C44–H44B···M2	3.56	126.8	3.321(2)	68.9
iii	C43–H43C···M3$^{\#1}$	3.48	106.8	3.010(2)	59.9
iv	C43–H43C···M4$^{\#1}$	3.44	149.3	3.022(3)	61.1
v	C48–H48A···M5$^{\#2}$	2.72	166.6	2.7124(18)	85.7
vi	C46–H46A···O1$^{\#2}$	2.76	136.8		
vii	O60–H60···O2$^{\#1}$	1.87	169.7		

M1: centroid of C3, C25, C28, C10, C29, C24; M2: centroid of C5, C6, C7, C8, C26, C27; M3: centroid of C21, C37, C32, C14, C33, C36; M4: centroid of C19, C18, C17, C16, C34, C35; M5: centroid of C1, C23, C30, C12, C31, C38.

[1] G. M. Sheldrick, *Acta Crystallogr.* 1990, **A46**, 467.
[2] G. M. Sheldrick, SHELXL-97, Program for the Refinement of Crystal Structures University of Göttingen, Göttingen (Germany) **1997**. (see also: Sheldrick, G. M. Acta Crystallogr. 2008, **A64**, 112).
[3] shelXle, *A Qt GUI for SHELXL*, C. B. Hübschle, G. M. Sheldrick, B. Dittrich, *J. Appl. Cryst.* **2011**, *44*, 1281-1284.

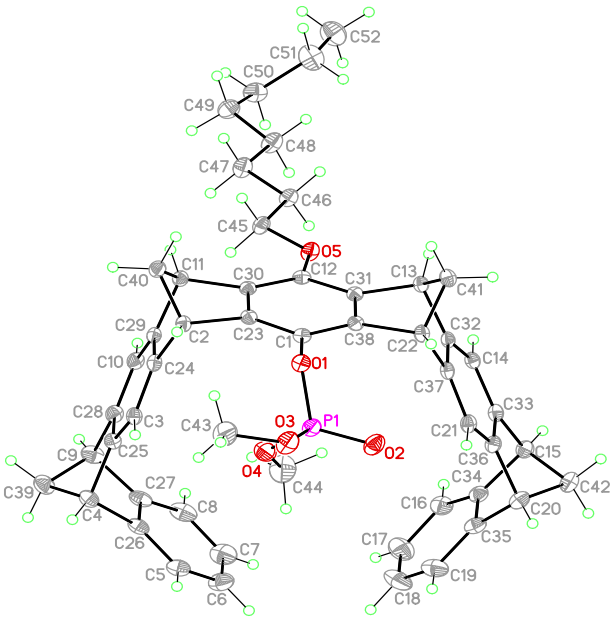
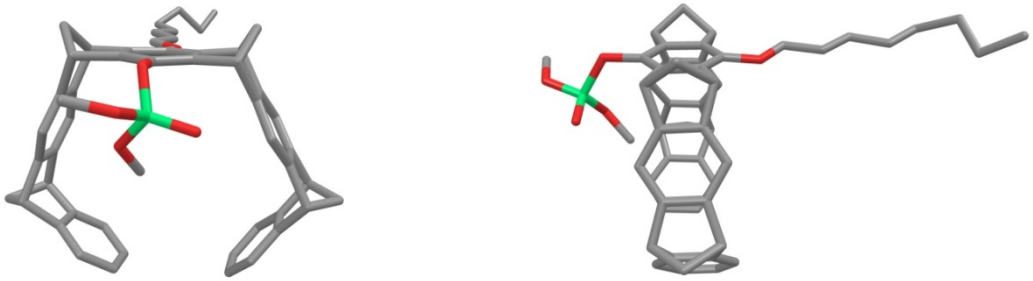
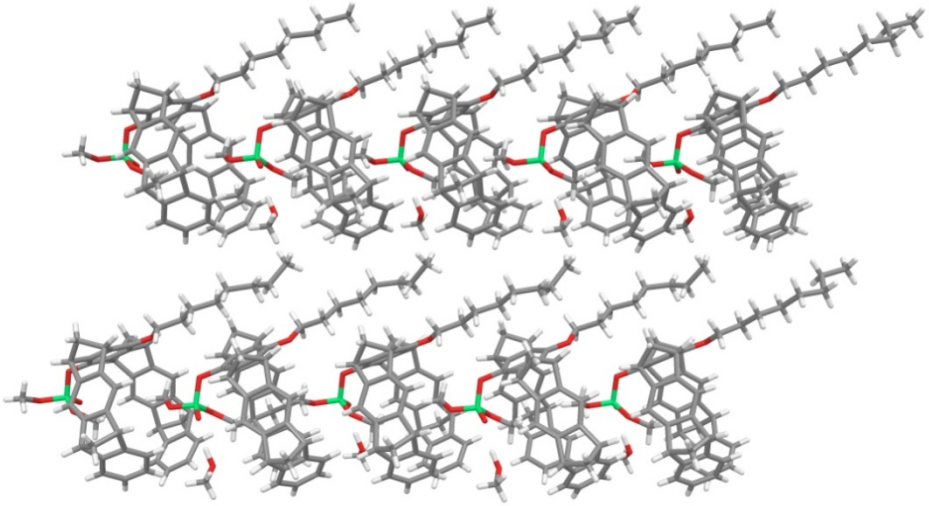


Figure 4. Asymmetric unit of **3a**; thermal ellipsoids at 50% probability levels.



3a
Cavity view

3a
Side view



Crystal packing of tweezer **3a**

Figure 5. Top: cavity and side view. Bottom: crystal packing view of the stacked phosphate methyl ester octyl tweezers **3a**.

Crystal data and structure refinement for the tweezer 3a

Identification code	sd_182p1
Empirical formula	$C_{52}\ H_{51}\ O_5\ P * C\ H_4\ O$
Formula weight	818.94 Da
Density (calculated)	1.261 g cm^{-3}
F(000)	1744
Temperature	100(1) K
Crystal size	0.32 x 0.12 x 0.07 mm
Crystal color	colourless
Crystal description	needle
Wavelength	0.71073 Å

Crystal system	monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 14.804(3) Å α = 90°
	b = 18.391(3) Å β = 103.622(8)°
	c = 16.298(3) Å γ = 90°
Volume	4312.7(12) $Å^3$
Z	4
Cell measurement reflections used	9887
Cell measurement theta min/max	2.39° to 27.08°
Diffractometer control software	Bruker AXS APEX 2 Vers.3.0/2009
Diffractometer measurement device	Bruker D8 KAPPA series II with
	APEX II area detector system
Diffractometer measurement method	Data collection strategy APEX 2/COSMO
Theta range for data collection	1.80° to 27.11°
Completeness to theta = 27.11°	99.3 %
Index ranges	-18<=h<=18, -23<=k<=23, -19<=l<=20
Computing data reduction	Bruker AXS APEX 2 Vers.3/2009
Absorption coefficient	0.116 mm^{-1}
Absorption correction	Semi-empirical from equivalents
Empirical absorption correction	Bruker AXS APEX 2 Vers.3/2009
Max. / min. transmission	0.75 / 0.66
R(merg) before/after correction	0.0777 / 0.0394
Computing structure solution	Bruker AXS SHELXTL Vers. 2008/4/(c) 2008
Computing structure refinement	Bruker AXS SHELXTL Vers. 2008/4/(c) 2008
Refinement method	Full-matrix least-squares on F^2
Reflections collected	78132
Independent reflections	9461 [R(int) = 0.0375]
Data / restraints / parameters	7636 / 0 / 549
Goodness-of-fit on F^2	1.033
Weighting details	$w = 1/[\sigma^2 (Fo^2)+ (0.0597*P)^2+2.6078*P]$
	where $P = (Fo^2+2Fc^2)/3$
Final R indices [I>2sigma(I)]	$R1$ = 0.0414, $wR2$ = 0.1067
R indices (all data)	$R1$ = 0.0573, $wR2$ = 0.1187

Largest diff. peak and hole	0.358 and -0.418 eÅ^{-3}
Treatment of hydrogen atoms	Riding model on idealized geometries with the 1.2 fold isotropic displacement parameters of the equivalent Uij of the corresponding carbon atom. The methyl groups are idealized with tetrahedral angles in a combined rotating and rigid group refinement with the 1.5 fold isotropic displacement parameters of the equivalent Uij of the corresponding carbon atom. Hydrogen atom position H(60) taken from a Fourier-map and also refined as riding group with the 1.5 fold isotropic displacement parameters of the equivalent Uij of the corresponding oxygen atom.
Disorder	Octoxy carbon atoms C(50, 51) disordered over two sites with SOF 0.9 and 0.1 together with the riding hydrogen atoms Methyl hydrogen atoms H(52A to H52C) disordered over two sites with SOF 0.9 and 0.1

Table 6.1 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for sd_182p1. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
P(1)	1802(1)	6862(1)	4694(1)	18(1)
O(1)	706(1)	6958(1)	4567(1)	15(1)
O(2)	2165(1)	6154(1)	5026(1)	25(1)
O(3)	1932(1)	7008(1)	3791(1)	27(1)
O(4)	2239(1)	7531(1)	5241(1)	25(1)
O(5)	-809(1)	7302(1)	7396(1)	18(1)
C(1)	334(1)	7061(1)	5281(1)	13(1)
C(2)	26(1)	8464(1)	4988(1)	14(1)
C(3)	1609(1)	9185(1)	5565(1)	15(1)
C(4)	3070(1)	9914(1)	6481(1)	18(1)
C(5)	4363(1)	8951(1)	7181(1)	22(1)
C(6)	4711(1)	8555(1)	7923(1)	28(1)
C(7)	4338(1)	8639(1)	8622(1)	30(1)
C(8)	3608(1)	9122(1)	8612(1)	26(1)
C(9)	2474(1)	10057(1)	7640(1)	21(1)
C(10)	862(1)	9403(1)	7016(1)	16(1)
C(11)	-593(1)	8684(1)	6116(1)	15(1)
C(12)	-474(1)	7290(1)	6679(1)	13(1)
C(13)	-258(1)	5862(1)	6885(1)	13(1)
C(14)	1191(1)	5454(1)	8104(1)	14(1)
C(15)	2821(1)	4988(1)	9036(1)	17(1)
C(16)	3792(1)	6141(1)	9736(1)	22(1)
C(17)	4482(1)	6630(1)	9644(1)	32(1)
C(18)	4916(1)	6562(1)	8980(1)	35(1)
C(19)	4668(1)	6007(1)	8382(1)	29(1)
C(20)	3534(1)	4880(1)	7944(1)	20(1)
C(21)	2080(1)	5282(1)	6730(1)	16(1)
C(22)	432(1)	5677(1)	5788(1)	14(1)
C(23)	10(1)	7737(1)	5443(1)	13(1)
C(24)	732(1)	8932(1)	5597(1)	14(1)
C(25)	2095(1)	9572(1)	6264(1)	16(1)
C(26)	3644(1)	9431(1)	7171(1)	18(1)

C(27)	3273(1)	9517(1)	7884(1)	20(1)
C(28)	1730(1)	9667(1)	6980(1)	17(1)
C(29)	360(1)	9051(1)	6300(1)	14(1)
C(30)	-388(1)	7862(1)	6139(1)	13(1)
C(31)	-187(1)	6606(1)	6476(1)	13(1)
C(32)	733(1)	5609(1)	7275(1)	13(1)
C(33)	2099(1)	5200(1)	8231(1)	15(1)
C(34)	3556(1)	5588(1)	9156(1)	18(1)
C(35)	3994(1)	5519(1)	8480(1)	21(1)
C(36)	2537(1)	5126(1)	7560(1)	16(1)
C(37)	1164(1)	5510(1)	6600(1)	14(1)
C(38)	221(1)	6488(1)	5799(1)	13(1)
C(39)	2876(1)	10556(1)	7042(1)	23(1)
C(40)	-884(1)	8798(1)	5143(1)	16(1)
C(41)	-446(1)	5392(1)	6066(1)	16(1)
C(42)	3350(1)	4387(1)	8666(1)	21(1)
C(43)	1692(1)	7698(1)	3359(1)	33(1)
C(44)	2650(2)	7474(1)	6141(1)	38(1)
C(45)	-1250(1)	7936(1)	7628(1)	17(1)
C(46)	-1600(1)	7726(1)	8397(1)	17(1)
C(47)	-2091(1)	8342(1)	8745(1)	21(1)
C(48)	-2390(1)	8113(1)	9540(1)	22(1)
C(49)	-2936(1)	8695(1)	9890(1)	22(1)
C(50)	-3093(1)	8514(1)	10756(1)	24(1)
C(51)	-3640(2)	7821(1)	10769(1)	31(1)
C(50A)	-3654(11)	8327(9)	10444(10)	18(3)
C(51A)	-3105(13)	7951(10)	11216(12)	27(4)
C(52)	-3924(1)	7688(1)	11608(1)	33(1)
O(60)	4072(1)	8872(1)	949(1)	64(1)
C(61)	4488(2)	9548(1)	920(1)	43(1)

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Table 6.2 Bond lengths [Å] and angles [°] for sd_182p1.

P(1)-O(2)	1.4626(12)	O(3)-C(43)	1.453(2)
P(1)-O(3)	1.5528(12)	O(4)-C(44)	1.453(2)
P(1)-O(4)	1.5662(12)	O(5)-C(12)	1.3737(17)
P(1)-O(1)	1.5961(11)	O(5)-C(45)	1.4291(17)
O(1)-C(1)	1.4118(17)	C(1)-C(23)	1.380(2)

C(1)-C(38)	1.385(2)	C(20)-C(42)	1.560(2)
C(2)-C(24)	1.527(2)	C(21)-C(37)	1.388(2)
C(2)-C(23)	1.5322(19)	C(21)-C(36)	1.391(2)
C(2)-C(40)	1.555(2)	C(22)-C(38)	1.5239(19)
C(3)-C(25)	1.392(2)	C(22)-C(37)	1.531(2)
C(3)-C(24)	1.392(2)	C(22)-C(41)	1.563(2)
C(4)-C(26)	1.526(2)	C(23)-C(30)	1.414(2)
C(4)-C(25)	1.537(2)	C(24)-C(29)	1.401(2)
C(4)-C(39)	1.560(2)	C(25)-C(28)	1.406(2)
C(5)-C(26)	1.380(2)	C(26)-C(27)	1.407(2)
C(5)-C(6)	1.402(2)	C(31)-C(38)	1.395(2)
C(6)-C(7)	1.387(3)	C(32)-C(37)	1.407(2)
C(7)-C(8)	1.396(3)	C(33)-C(36)	1.403(2)
C(8)-C(27)	1.381(2)	C(34)-C(35)	1.410(2)
C(9)-C(27)	1.523(2)	C(45)-C(46)	1.514(2)
C(9)-C(28)	1.525(2)	C(46)-C(47)	1.526(2)
C(9)-C(39)	1.554(2)	C(47)-C(48)	1.524(2)
C(10)-C(29)	1.387(2)	C(48)-C(49)	1.531(2)
C(10)-C(28)	1.389(2)	C(49)-C(50)	1.520(2)
C(11)-C(29)	1.529(2)	C(49)-C(50A)	1.690(16)
C(11)-C(30)	1.5413(19)	C(50)-C(51)	1.513(3)
C(11)-C(40)	1.556(2)	C(51)-C(52)	1.543(3)
C(12)-C(31)	1.393(2)	C(50A)-C(51A)	1.50(2)
C(12)-C(30)	1.396(2)	C(51A)-C(52)	1.573(18)
C(13)-C(32)	1.5279(19)	O(60)-C(61)	1.393(3)
C(13)-C(31)	1.5351(19)		
C(13)-C(41)	1.5605(19)	O(2)-P(1)-O(3)	112.79(7)
C(14)-C(32)	1.391(2)	O(2)-P(1)-O(4)	114.98(7)
C(14)-C(33)	1.391(2)	O(3)-P(1)-O(4)	106.03(7)
C(15)-C(34)	1.530(2)	O(2)-P(1)-O(1)	114.82(6)
C(15)-C(33)	1.535(2)	O(3)-P(1)-O(1)	101.95(6)
C(15)-C(42)	1.557(2)	O(4)-P(1)-O(1)	105.01(6)
C(16)-C(34)	1.376(2)	C(1)-O(1)-P(1)	119.31(9)
C(16)-C(17)	1.397(2)	C(43)-O(3)-P(1)	122.64(11)
C(17)-C(18)	1.386(3)	C(44)-O(4)-P(1)	122.38(11)
C(18)-C(19)	1.401(3)	C(12)-O(5)-C(45)	121.20(11)
C(19)-C(35)	1.380(2)	C(23)-C(1)-C(38)	118.13(13)
C(20)-C(35)	1.525(2)	C(23)-C(1)-O(1)	119.95(12)
C(20)-C(36)	1.529(2)	C(38)-C(1)-O(1)	121.77(12)

C(24)-C(2)-C(23)	105.27(11)	C(1)-C(23)-C(30)	121.96(13)
C(24)-C(2)-C(40)	99.03(11)	C(1)-C(23)-C(2)	130.34(13)
C(23)-C(2)-C(40)	98.81(11)	C(30)-C(23)-C(2)	107.66(12)
C(25)-C(3)-C(24)	116.60(13)	C(3)-C(24)-C(29)	121.89(13)
C(26)-C(4)-C(25)	105.11(12)	C(3)-C(24)-C(2)	131.76(13)
C(26)-C(4)-C(39)	98.97(12)	C(29)-C(24)-C(2)	106.24(12)
C(25)-C(4)-C(39)	98.69(12)	C(3)-C(25)-C(28)	121.13(13)
C(26)-C(5)-C(6)	117.96(15)	C(3)-C(25)-C(4)	132.35(14)
C(7)-C(6)-C(5)	120.89(16)	C(28)-C(25)-C(4)	106.37(12)
C(6)-C(7)-C(8)	121.27(16)	C(5)-C(26)-C(27)	120.87(15)
C(27)-C(8)-C(7)	117.71(16)	C(5)-C(26)-C(4)	132.50(14)
C(27)-C(9)-C(28)	105.32(12)	C(27)-C(26)-C(4)	106.55(13)
C(27)-C(9)-C(39)	99.24(12)	C(8)-C(27)-C(26)	121.29(15)
C(28)-C(9)-C(39)	98.87(12)	C(8)-C(27)-C(9)	131.88(15)
C(29)-C(10)-C(28)	116.47(14)	C(26)-C(27)-C(9)	106.75(13)
C(29)-C(11)-C(30)	105.11(11)	C(10)-C(28)-C(25)	122.12(13)
C(29)-C(11)-C(40)	99.28(11)	C(10)-C(28)-C(9)	131.03(14)
C(30)-C(11)-C(40)	99.35(11)	C(25)-C(28)-C(9)	106.79(13)
O(5)-C(12)-C(31)	114.11(12)	C(10)-C(29)-C(24)	121.66(13)
O(5)-C(12)-C(30)	128.99(13)	C(10)-C(29)-C(11)	131.15(13)
C(31)-C(12)-C(30)	116.90(13)	C(24)-C(29)-C(11)	107.04(12)
C(32)-C(13)-C(31)	107.15(11)	C(12)-C(30)-C(23)	120.02(13)
C(32)-C(13)-C(41)	98.40(11)	C(12)-C(30)-C(11)	134.99(13)
C(31)-C(13)-C(41)	97.98(11)	C(23)-C(30)-C(11)	104.93(12)
C(32)-C(14)-C(33)	116.52(13)	C(12)-C(31)-C(38)	122.79(13)
C(34)-C(15)-C(33)	104.93(12)	C(12)-C(31)-C(13)	130.21(13)
C(34)-C(15)-C(42)	98.84(12)	C(38)-C(31)-C(13)	106.99(12)
C(33)-C(15)-C(42)	99.33(12)	C(14)-C(32)-C(37)	121.71(13)
C(34)-C(16)-C(17)	118.41(16)	C(14)-C(32)-C(13)	131.84(13)
C(18)-C(17)-C(16)	120.74(16)	C(37)-C(32)-C(13)	106.39(12)
C(17)-C(18)-C(19)	121.02(16)	C(14)-C(33)-C(36)	121.57(13)
C(35)-C(19)-C(18)	118.13(16)	C(14)-C(33)-C(15)	131.77(13)
C(35)-C(20)-C(36)	105.39(12)	C(36)-C(33)-C(15)	106.60(12)
C(35)-C(20)-C(42)	98.61(12)	C(16)-C(34)-C(35)	120.98(15)
C(36)-C(20)-C(42)	99.12(12)	C(16)-C(34)-C(15)	132.75(15)
C(37)-C(21)-C(36)	116.40(13)	C(35)-C(34)-C(15)	106.19(13)
C(38)-C(22)-C(37)	106.99(11)	C(19)-C(35)-C(34)	120.70(15)
C(38)-C(22)-C(41)	97.98(11)	C(19)-C(35)-C(20)	132.25(15)
C(37)-C(22)-C(41)	98.60(11)	C(34)-C(35)-C(20)	106.96(13)

C(21)-C(36)-C(33)	121.96(13)
C(21)-C(36)-C(20)	131.30(14)
C(33)-C(36)-C(20)	106.71(12)
C(21)-C(37)-C(32)	121.74(13)
C(21)-C(37)-C(22)	131.31(13)
C(32)-C(37)-C(22)	106.92(12)
C(1)-C(38)-C(31)	120.07(13)
C(1)-C(38)-C(22)	133.11(13)
C(31)-C(38)-C(22)	106.79(12)
C(9)-C(39)-C(4)	94.15(12)
C(2)-C(40)-C(11)	94.06(11)
C(13)-C(41)-C(22)	93.95(11)
C(15)-C(42)-C(20)	94.10(11)
O(5)-C(45)-C(46)	106.11(12)
C(45)-C(46)-C(47)	113.76(12)
C(48)-C(47)-C(46)	111.63(13)
C(47)-C(48)-C(49)	114.10(13)
C(50)-C(49)-C(48)	113.76(14)
C(48)-C(49)-C(50A)	111.9(5)
C(51)-C(50)-C(49)	113.34(15)
C(50)-C(51)-C(52)	113.78(16)
C(51A)-C(50A)-C(49)	110.4(12)
C(50A)-C(51A)-C(52)	99.6(12)

Table 6.3 Anisotropic displacement parameters ($Å^2 x\ 10^3$) for sd_182p1. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U11 + ... + 2 h k a^* b^* U12]$

	U11	U22	U33	U23	U13	U12
P(1)	20(1)	20(1)	16(1)	4(1)	8(1)	4(1)
O(1)	19(1)	18(1)	10(1)	0(1)	5(1)	1(1)
O(2)	28(1)	25(1)	25(1)	6(1)	13(1)	9(1)
O(3)	34(1)	30(1)	22(1)	8(1)	18(1)	10(1)
O(4)	23(1)	26(1)	25(1)	3(1)	4(1)	-3(1)
O(5)	23(1)	17(1)	15(1)	0(1)	10(1)	4(1)
C(1)	13(1)	16(1)	9(1)	-1(1)	3(1)	-1(1)
C(2)	16(1)	12(1)	13(1)	1(1)	2(1)	0(1)
C(3)	19(1)	13(1)	13(1)	2(1)	4(1)	0(1)
C(4)	18(1)	19(1)	17(1)	-2(1)	4(1)	-5(1)
C(5)	17(1)	29(1)	19(1)	-2(1)	3(1)	-4(1)
C(6)	19(1)	36(1)	28(1)	3(1)	2(1)	3(1)
C(7)	25(1)	42(1)	20(1)	9(1)	-1(1)	-3(1)
C(8)	22(1)	38(1)	16(1)	-2(1)	4(1)	-9(1)
C(9)	20(1)	24(1)	20(1)	-9(1)	5(1)	-5(1)
C(10)	19(1)	14(1)	17(1)	-3(1)	6(1)	2(1)
C(11)	16(1)	13(1)	16(1)	0(1)	4(1)	1(1)
C(12)	12(1)	16(1)	11(1)	-1(1)	2(1)	0(1)
C(13)	16(1)	12(1)	12(1)	0(1)	4(1)	0(1)
C(14)	17(1)	12(1)	14(1)	-1(1)	5(1)	-2(1)
C(15)	18(1)	17(1)	15(1)	1(1)	3(1)	2(1)
C(16)	21(1)	26(1)	18(1)	0(1)	1(1)	-1(1)
C(17)	31(1)	33(1)	28(1)	-5(1)	0(1)	-10(1)
C(18)	27(1)	41(1)	36(1)	1(1)	5(1)	-15(1)
C(19)	20(1)	40(1)	26(1)	3(1)	7(1)	-3(1)
C(20)	19(1)	22(1)	18(1)	0(1)	5(1)	6(1)
C(21)	21(1)	12(1)	15(1)	-2(1)	7(1)	1(1)
C(22)	18(1)	12(1)	12(1)	-1(1)	4(1)	0(1)
C(23)	13(1)	14(1)	12(1)	0(1)	1(1)	-1(1)
C(24)	18(1)	11(1)	14(1)	0(1)	2(1)	1(1)
C(25)	16(1)	15(1)	17(1)	1(1)	3(1)	-1(1)
C(26)	16(1)	22(1)	16(1)	-3(1)	3(1)	-7(1)

C(27)	16(1)	26(1)	16(1)	-5(1)	3(1)	-8(1)
C(28)	18(1)	15(1)	17(1)	-4(1)	3(1)	0(1)
C(29)	16(1)	11(1)	17(1)	1(1)	4(1)	2(1)
C(30)	11(1)	14(1)	13(1)	-2(1)	1(1)	0(1)
C(31)	12(1)	15(1)	11(1)	1(1)	1(1)	-1(1)
C(32)	16(1)	9(1)	15(1)	-1(1)	5(1)	0(1)
C(33)	19(1)	12(1)	13(1)	0(1)	2(1)	-1(1)
C(34)	16(1)	20(1)	17(1)	3(1)	0(1)	3(1)
C(35)	16(1)	26(1)	20(1)	2(1)	2(1)	4(1)
C(36)	18(1)	13(1)	17(1)	-2(1)	5(1)	2(1)
C(37)	20(1)	9(1)	13(1)	-1(1)	4(1)	-1(1)
C(38)	13(1)	13(1)	12(1)	-2(1)	2(1)	0(1)
C(39)	23(1)	20(1)	26(1)	-5(1)	4(1)	-6(1)
C(40)	16(1)	15(1)	17(1)	2(1)	2(1)	2(1)
C(41)	19(1)	14(1)	14(1)	-1(1)	3(1)	-2(1)
C(42)	24(1)	18(1)	20(1)	1(1)	3(1)	5(1)
C(43)	37(1)	37(1)	26(1)	16(1)	12(1)	6(1)
C(44)	45(1)	36(1)	27(1)	-2(1)	-8(1)	-1(1)
C(45)	20(1)	16(1)	18(1)	0(1)	7(1)	5(1)
C(46)	20(1)	18(1)	14(1)	1(1)	6(1)	3(1)
C(47)	26(1)	20(1)	18(1)	2(1)	10(1)	5(1)
C(48)	26(1)	24(1)	17(1)	1(1)	8(1)	7(1)
C(49)	22(1)	24(1)	22(1)	-2(1)	7(1)	4(1)
C(50)	23(1)	28(1)	21(1)	-7(1)	7(1)	0(1)
C(51)	40(1)	32(1)	20(1)	-4(1)	8(1)	-6(1)
C(52)	38(1)	35(1)	29(1)	1(1)	12(1)	-5(1)
O(60)	40(1)	52(1)	91(1)	21(1)	-8(1)	-10(1)
C(61)	38(1)	51(1)	39(1)	-1(1)	6(1)	-10(1)

Table 6.4 Hydrogen coordinates (x 10^4) and i displacement parameters (Å^2 x 10^3) for sd_182p1.

___	x	y	z	U(eq)
H(2)	85	8442	4389	17
H(3)	1863	9099	5090	18
H(4)	3349	10041	5997	22
H(5)	4613	8890	6699	26
H(6)	5210	8224	7946	34
H(7)	4584	8363	9117	36
H(8)	3351	9178	9091	31
H(9)	2266	10301	8112	25
H(10)	624	9461	7505	19
H(11)	-1040	8857	6449	17
H(13)	-717	5820	7245	16
H(14)	900	5519	8559	17
H(15)	2579	4854	9539	20
H(16)	3492	6189	10188	27
H(17)	4656	7014	10039	38
H(18)	5389	6898	8932	42
H(19)	4956	5967	7921	34
H(20)	3883	4658	7551	23
H(21)	2380	5236	6278	19
H(22)	546	5475	5252	16
H(39A)	3448	10813	7336	28
H(39B)	2414	10906	6728	28
H(40A)	-1446	8519	4870	20
H(40B)	-962	9317	4981	20
H(41A)	-1035	5519	5661	19
H(41B)	-421	4863	6183	19
H(42A)	2956	3961	8453	25
H(42B)	3929	4229	9066	25
H(43A)	1047	7822	3355	49
H(43B)	1759	7657	2777	49
H(43C)	2107	8079	3653	49
H(44A)	2430	7028	6360	58
H(44B)	2467	7896	6431	58
H(44C)	3328	7459	6238	58
H(45A)	-1774	8088	7161	21

H(45B)	-802	8342	7764	21
H(46A)	-1067	7559	8846	20
H(46B)	-2035	7312	8248	20
H(47A)	-1668	8765	8875	25
H(47B)	-2645	8494	8309	25
H(48A)	-1829	7985	9980	26
H(48B)	-2779	7670	9413	26
H(49A)	-2595	9161	9927	27
H(49B)	-3547	8763	9490	27
H(50A)	-3420	8909	10941	28
H(50B)	-2501	8468	11150	28
H(51A)	-3273	7417	10662	37
H(51B)	-4191	7839	10319	37
H(50C)	-4060	7980	10101	22
H(50D)	-4030	8700	10608	22
H(51C)	-2683	8290	11596	33
H(51D)	-2743	7538	11072	33
H(52A)	-4267	7242	11576	50
H(52B)	-3376	7658	12060	50
H(52C)	-4304	8084	11713	50
H(52D)	-3672	7432	12125	50
H(52E)	-4273	8100	11723	50
H(52F)	-4324	7370	11218	50
H(60)	3431	8857	562	97
H(61A)	4090	9929	1065	65
H(61B)	4573	9634	349	65
H(61C)	5094	9556	1324	65