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Anion Complexation by Triazolium “Ligands”: Mono- and Bis-tridentate Complexes of Sulfate

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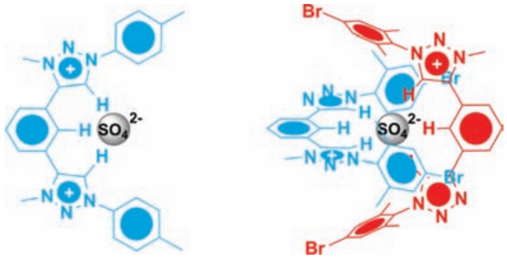
ABSTRACT



By utilizing click chemistry and methylation, the triazolium motif was employed to design tridentate “ligands” that bind by electron acception instead of electron donation. As electronically inverted ligands they are able to complex sulfate ions by hydrogen bonding and electrostatic interactions. The formation of mono- or bis-tridentate complexes could be achieved by controlling the degree of methylation with the appropriate reagents and was proven by NMR spectroscopy and computational methods.

In supramolecular chemistry, pincer-type ligands have attracted particular interest as exemplarily shown by terpyridine. Consequently, the copper(I)-catalyzed azide alkyne 1,3-dipolar cycloaddition (CuAAC)—one of the prime examples of the concept of highly efficient and modular reactions named click chemistry[1]—has been applied in the synthesis of analogous tridentate ligands, the so-called tripy,[2] coordinating metal ions via triazoles. Recently, click chemistry was successfully applied in anion coordination, and the triazole and triazolium moieties have been shown to act as efficient C−H hydrogen bond donors as well.[3] We intended to expand the scope of tridentate “clicked” ligands in terms of anion complexation by hydrogen bonding and electrostatic interactions. Since anions can be structured, biorelevant, and nucleophilic, the respective ligands might have potential for template-directed assembling, sensing and recognition of anions, and organocatalysis.[4] Furthermore, they show a dynamic coordination behavior that allows fast switching processes and stimuli responses, respectively.

So far, triazoles have been employed in anion recognition

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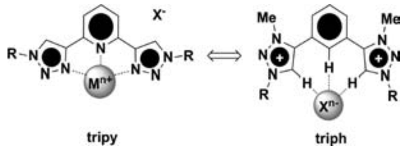
in terms of triazolophanes[3a−c] and triazole foldamers[3d−f] where a lot of weak C−H···X interactions were accumulated. Very recently, the anion binding capacity was enhanced by preorganization to form a neutral tridentate hydrogen bond donor.[5] Alternatively, triazolium salts with strongly increased CH-acidity have been used as anion receptors[6] and within the template synthesis of a [2]rotaxane.[7] Furthermore, a [2]catenane has been synthesized by using pyridinium nicotinamide as hydrogen bond donor and sulfate as the templating anion.[8] Both templates were primarily based on hydrogen bonds as well as electrostatic interactions, but required elegantly designed second sphere interactions such as additional hydrogen bonds and π-stacking.[9] There are further interesting examples of 2:1 sulfate complexes, but the ligand syntheses lack facility.[10]

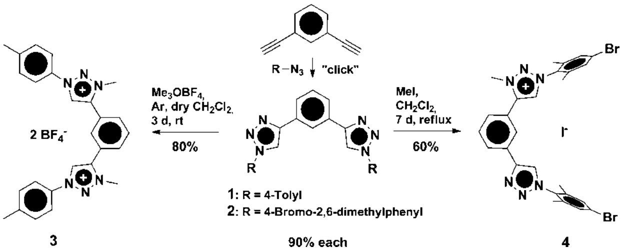
Our approach is to use strong hydrogen bonding as well as electrostatic interactions offered by the triazolium moieties. A direct motivation was to make use of the functional groups that are readily installed within the ligand synthesis by CuAAC, but that point in opposite directions in a metal complex (Scheme 1). Essentially, coordination via the triazole or triazolium protons would lead to functional groups pointing in the same direction and the choice of a tetrahedral anion might allow the formation of an octahedral bis-tridentate complex that can be considered as a *directed* template. Thereby, a singly charged ligand should support the formation of a charge neutral bis-complex with a doubly charged anion.

Scheme 1. Classical and Electronically Inverted Ligands



The synthesis of the building blocks **1** and **2** could be achieved most easily under click conditions (Scheme 2).[1a]

Scheme 2. Synthesis of the Anion Coordinating Ligands



The "activation" for the sulfate complexation could be performed selectively by choosing the appropriate reagents. Methyl iodide just leads to single methylation, while Meerwein's salt easily affords double methylation.

The degree of methylation of **3** and **4** was proven unambiguously by single crystal X-ray diffraction (Figure 1). In the solid state, no tridentate interactions could be found with the given counterions tetrafluoroborate and iodide, respectively. While ligand **4** features already a *syn-syn* conformation with respect to the potential hydrogen-bonding protons, ligand **3** shows an *anti-syn* conformation but can easily flip in solution since **3** shows at least C_2-symmetry in ^{1}H NMR experiments. However, due to the steric demand in particular of the methyl groups, the triazolium rings are twisted out of plane by 33° for **3** and 38° for **4** in the free ligand, respectively.

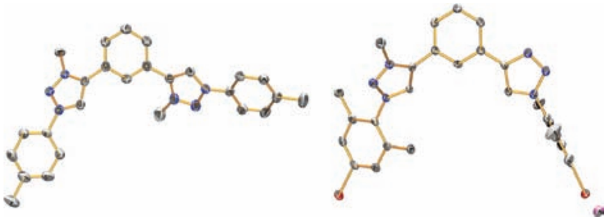


Figure 1. Solid-state structures of **3** (left) and **4** (right) (ellipsoids at 50% propability level; hydrogen atoms, solvents molecules, and tetrafluoroborate anion omitted for clarity).

The anion coordination behavior of **3** and **4** could be determined qualitatively and quantitatively. A continuous variation plot (Job plot) of **3** and tetrabutylammonium sulfate (TBA$_2$SO$_4$) obtained from ^{1}H NMR spectroscopy revealed the formation of a 1:1 complex.[12] For solubility reasons, acetonitrile-d_3/methanol 4:1 was used as solvent mixture with nondeuterated methanol, since the triazolium protons rapidly undergo deuterium exchange as they are strongly CH-acidic. The association constant of the 1:1 complex could be obtained by ^{1}H NMR titration of **3** with TBA$_2$SO$_4$ (Figure 2) and by analyzing the relatively large triazolium proton downfield shift with the WinEQNMR2 software[11] and was

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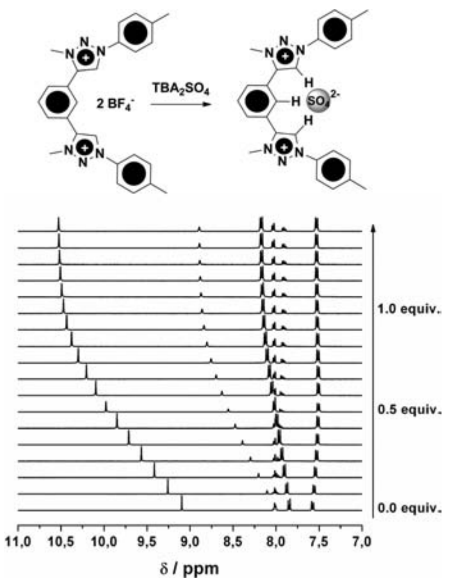

Figure 2. ^{1}H NMR spectra of **3** upon titration with tetrabutylammonium sulfate (TBA$_2$SO$_4$) in acetonitrile-d_3/methanol 4:1 at 298 K.

determined to be log $K = 4.39 \pm 0.28$ or $K \approx 24{,}000$ M^{-1}, respectively.[12]

The concentration-weighted shift of a single signal for the free ligand *and* the complex results from an exchange faster than the NMR time scale. The large binding constant and the fact that the maximum shift, i.e., the full complexation, is nearly reached after the addition of 1 equiv of TBA$_2$SO$_4$ demonstrate a relatively strong sulfate binding even in the presence of methanol. The symmetry within the spectrum and the protons that are involved in the hydrogen bonding indicate a tridentate complexation as depicted in Figure 2.

The Job plot of **4** with sulfate (Figure 3) in acetonitrile-d_3 reveals the formation of a 2:1 complex beside a 1:1 complex.

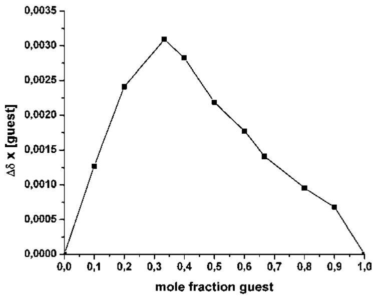

Figure 3. Continuous variation plot (Job plot) of **4** and TBA$_2$SO$_4$ obtained from ^{1}H NMR spectroscopy (aromatic 4-bromo-2,6-dimethylphenyl protons).

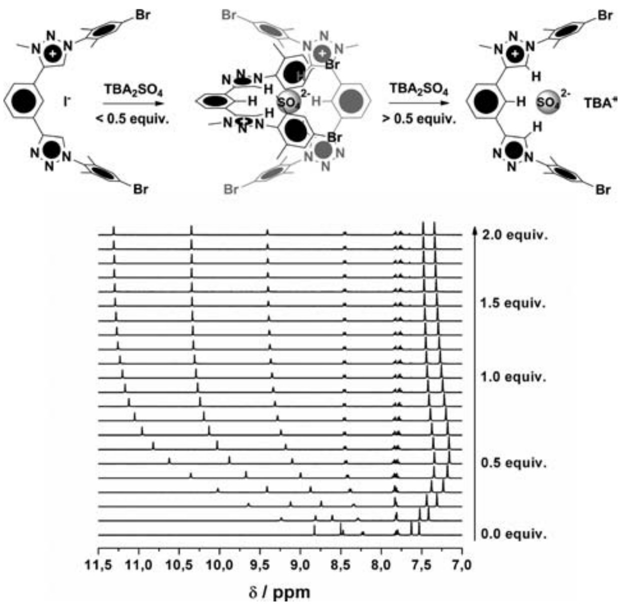

Figure 4. ^{1}H NMR spectra of **4** upon titration with tetrabutylammonium sulfate (TBA$_2$SO$_4$) in acetonitrile-d_3 at 298 K.

The ^{1}H NMR titration experiment (Figure 4) supports these findings: the aromatic protons of the quasi-mesityl substituents are shifted to higher field with a maximum shift at 0.5 equiv of TBA$_2$SO$_4$ and recover in the course of the titration, whereas the triazole, phenyl, and triazolium signals are downfield-shifted only. Obviously, the protons of the outer phenyl rings selectively respond to the complexation in a bis-tridentate fashion and remain nearly unchanged in the free ligand and in the 1:1 complex. The signals involved in the hydrogen bonding respond similarly on both coordination modes, but with a less pronounced downfield shift for the 2:1 complex since the two ligands compete in binding to the same anion. By titration of TBA$_2$SO$_4$ with **4**, the order of the formed complexes is changed, and thus also the shifts of protons participating in hydrogen bonds show a characteristic migration resulting from an initial 1:1 complexation and the successive formation of a 2:1 complex.[12] Again, the set of protons that contribute to the hydrogen bonding can only be explained by a tridentate coordination in each case.

The association constants could be calculated by fitting the titration curve of the aromatic 4-bromo-2,6-dimethylphenyl protons with the WinEQNMR2 software[11] and were determined to be log $K_1 = 3.73 \pm 0.07$ ($K_1 \approx 5{,}400$ M^{-1}), log $K_2 = 3.1 \pm 0.2$ ($K_2 = 1{,}300$ M^{-1}), and log $K_1K_2 = 6.84 \pm 0.15$ ($K_1K_2 \approx 7{,}000{,}000$ M^{-2}).[12] Again, the overall sulfate binding is relatively strong, and the difference of K_1 and K_2 reflects qualitatively the same coordination behavior as in terpyridine complexes of zinc(II), i.e., a 2:1 stoichiometry of host to guest yields a 2:1:1 ratio of 2:1 complex to 1:1 complex to free ligand. With respect to the ligand, the ratio is 4:1:1, and a maximum yield of 70% can be expected from a template synthesis in acetonitrile at a concentration of 10^{-3} M if dynamic effects are negligible as found in the report of Beer and co-workers.[8] This might be improved by removing the iodide with silver sulfate and by using a less polar solvent such as dichloromethane to provoke the formation of the uncharged bis-complex.

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(12) See Supporting Information.

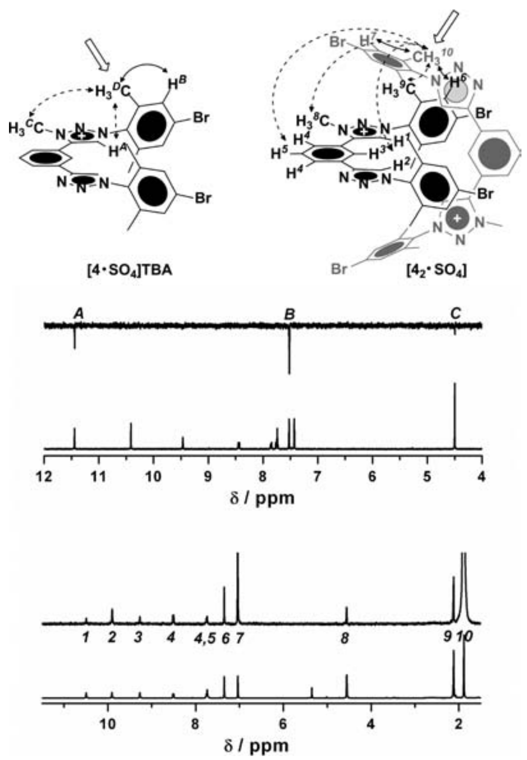

Figure 5. Selective NOESY spectra for [**4**·SO$_4$]TBA (top, acetonitrile-*d*$_3$) and [**4**$_2$·SO$_4$] (bottom, dichloromethane-*d*$_2$) (sulfate omitted; the excited protons are marked with a hollow arrow, and strong and medium NOESY contacts are indicated with solid and dashed arrows, respectively).

To prove a bis-tridentate coordination suitable for templation in solution, selective NOESY experiments were conducted (Figure 5). Therefore, [**4**$_2$·SO$_4$] was prepared using **4**·I and Ag$_2$SO$_4$, whereas [**4**·SO$_4$]TBA was obtained from a 1:10 mixture of **4**·I and TBA$_2$SO$_4$. The methyl groups of the quasi-mesityl substituents, which are not equivalent because of the single site methylation, were excited, and the NOE contacts were recorded.

For the 1:1 complex, only a strong contact to the adjacent aromatic proton and medium contacts to the aromatic and aliphatic triazolium protons on the same side of the molecule were visible. In contrast, the 2:1 complex showed contacts to the central phenyl ring and the other end of the molecule, which is only possible if two ligands arrange in the desired orthogonal fashion. In addition, the phase is inverted due to a doubled molar mass.

To consolidate the indirect image of the bis-tridentate complex obtained by NMR investigations, although crystallization attempts failed, and to exclude packing effects, we conducted DFT calculations (B3LYP/SVP).[12] The results are depicted in Figure 6 and are consistent with the experimental findings of a 2:1 complex. As one could expect from the distortion in the crystal structures of the ligands due to the triazolium methyl groups, the sulfate is complexed less ideally but still in the desired way to serve as template.

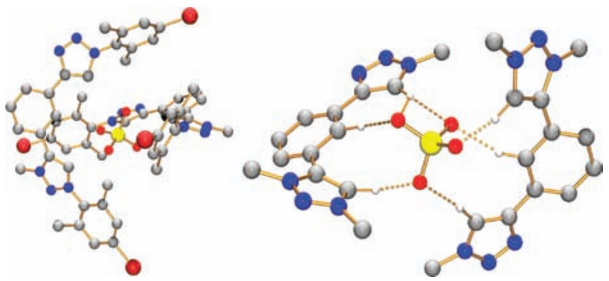

Figure 6. Calculated most stable structure for [**4**$_2$·SO$_4$]. Left: arrangement of the ligands. Right: hydrogen bonds, substituents omitted for clarity.

In conclusion, we applied the facile “click” synthesis with the structural benefits of the triazole and triazolium moieties, respectively, to design tridentate ligands that allow the formation of relatively stable complexes with sulfate ions. The formation of mono- and bis-complexes could be controlled by the number of triazolium moieties within the tridentate ligand. In particular, the formation of a bis-tridentate complex of sulfate could be proven that meets the demands for a [2]catenane template.

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Supporting Information Available: Experimental details, spectral data, NMR spectra, binding studies, X-ray data and DFT calculation data. This material is available free of charge via the Internet at http://pubs.acs.org.

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