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Anion Recognition by 1,2,3-Triazolium Receptors: Application of Click Chemistry in Anion Recognition

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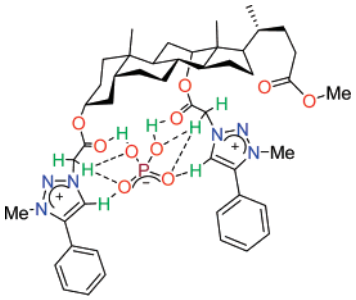
ABSTRACT



Cyclic and acyclic bile acid-based 1,2,3-triazolium receptors which show remarkable ability to recognize anions through C–H···X⁻ hydrogen bond interactions have been synthesized using click chemistry.

The application of click chemistry developed by Meldal[1] and Sharpless[2] involving the Cu(1)-catalyzed 1,3-dipolar cycloaddition of an azide and a terminal alkyne is rapidly growing, especially in the areas of biological, materials, and medicinal chemistry.[3] Besides the advantages of its high efficiency, regioselectivity, and compatibility with reaction conditions, the unique properties of the 1,4-disubstituted 1,2,3-triazole ring in terms of its ability to participate in hydrogen bond and dipole−dipole interactions has made click chemistry even more attractive. The ability of the N(3) atom of 1,2,3-triazole to act as a hydrogen bond acceptor and the polarized C(5) proton as a hydrogen bond donor makes it an amide/peptide bond mimic.[4] Consequently, click chemistry has gained much importance in peptide chemistry for the design of peptide analogues and β-turn peptide mimics.[5]

Recently, the role of 1,2,3-triazole in the formation of stable metal complexes has also been realized and accordingly some triazole-based receptors and dendrimers for the recognition of metals have been reported.[6] Interestingly, the

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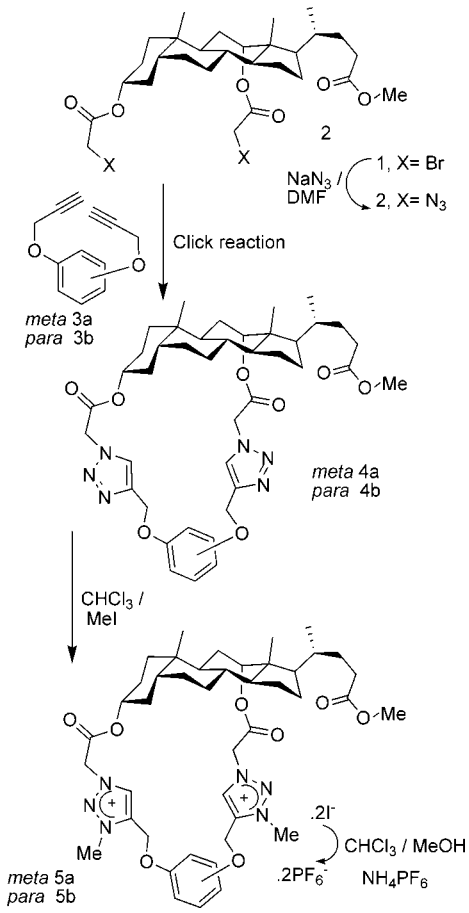
dendrimers developed by Astruc et al.[6g] also showed the ability of binding oxo anions through the 1,2,3-triazole ring localized inside the dendrimers. However, to our knowledge, the potential of the 1,2,3-triazolium ring[7] to act as a hydrogen bond donor for anion recognition has not yet been explored. As compared to 1,2,3-triazole, the 1,2,3-triazolium ring is expected to be a better hydrogen bond donor for anion recognition.

The chemistry of anion recognition has developed rapidly in the past few years due to its biological and medical significance. Many receptors based on different types of sensing moieties involving N−H···X^-, O−H···X^-, and (C−H)$^+$···X^- hydrogen bond interactions have been developed.[8] In recent years, bile acids have attracted considerable interest as building blocks for the construction of receptors for anion recognition because of their unique structural features.[9] Our ongoing interest[9i,j] in developing new types of steroid-based receptors for anion recognition and the interesting properties of the 1,2,3-triazole ring prompted us to design bile acid-based triazolium receptors for anion recognition.

Herein, we report for the first time the synthesis and anion-binding properties of 1,2,3-triazolium-based receptors in which the C-5 proton of the triazolium ring actively participates in the recognition of anions through C−H···X^- hydrogen bond interactions. We used click chemistry involving the 1,3-dipolar cycloaddition of steroidal diazide and alkynes for the construction of cyclic and acyclic triazolium receptors. The synthesis of cyclic receptors **5a** and **5b** based on deoxycholic acid has been outlined in Scheme 1. The steroidal diazido compound, methyl 3α,12α-bis(azidoacetyl)-deoxycholate **2**, was obtained by the treatment of methyl

Scheme 1



3α,12α-bis(bromoacetyl)deoxycholate[9i] **1** with sodium azide in DMF, which on subsequent treatment with *m*-bis(propargyloxy)benzene[10] **3a** and *p*-bis(propargyloxy)benzene[10] **3b** in *t*-BuOH in the presence of $CuSO_4$ and sodium ascorbate (click reaction) gave cycloadducts **4a** and **4b**, respectively, in high yields. The methiodide salts of cyclic receptors **5a** and **5b** were obtained by methylation of **4a** and **4b** with methyl iodide, which were further anion exchanged with NH_4PF_6 in MeOH/$CHCl_3$ to give their PF_6^- salts. The acyclic receptor **7** was synthesized by the reaction of di-azido compound **2** with 2 equiv of phenylacetylene followed by methylation and then anion exchange with NH_4PF_6 in similar reaction conditions (Scheme 2).

The anion binding property of **5a**-$(PF_6)_2$, **5b**-$(PF_6)_2$, and **7**-$(PF_6)_2$ was studied by monitoring the ^{1}H NMR spectral changes caused by the addition of tetrabutylammonium salts of the anions to a $CDCl_3$ solution containing the receptors. Upon addition of Bu_4NX (X = F, Cl, Br, I, CH_3COO, H_2PO_4) to receptors, significant downfield shifts (δ 1.3−0.9 ppm) were observed for the C(5)-H proton of each triazolium moiety suggesting the complexation of the anion with triazolium C(5)-protons by forming C−H···X^- hydrogen bonds. In addition, significant downfield shifts were also

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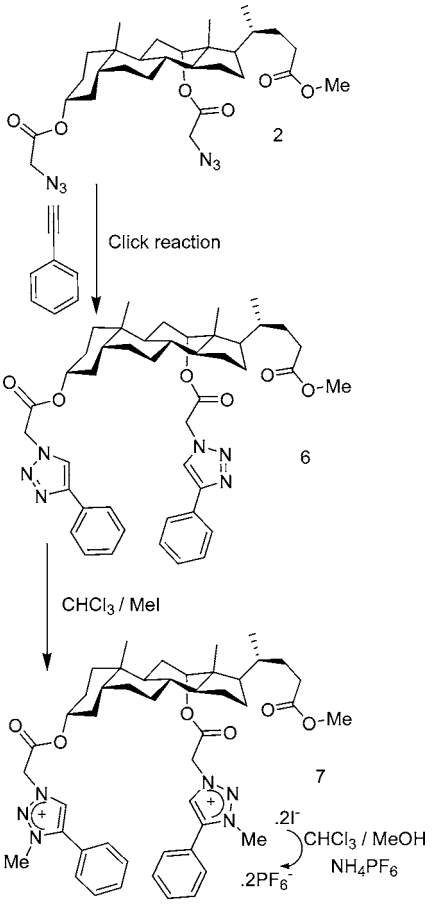
Scheme 2



observed for the bridging methylene protons indicating their participation in hydrogen bonding with anions along with C-5 triazolium protons (Figure 1). The Job's plots analyses

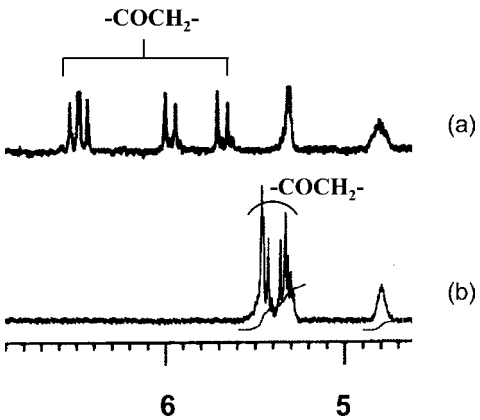


Figure 1. Partial ^{1}H NMR spectra of (a) **7**-2PF_6 + 2.5 equiv of TBACl and (b) **7**-2PF_6.

showed the formation of 1:1 complexes. The association constants were determined by using WinEQNMR software[11] and are presented in Table **1**. Receptor **5a** showed the highest

Table 1. Association Constant (K_a)[a] for 1:1 Complexes of Hosts with Anions in $CDCl_3$ at 298 K

	K_a [M^{-1}]		
anions[b]	receptor **5a**	receptor **5b**	receptor **7**
F^-	560	370	360
Cl^-	270	690	390
Br^-	220	450	200
I^-	100	200	110
$CH_3CO_2^-$	60	25	30
$H_2PO_4^-$		1100	1920

[a] Estimated error <10%. [b] Anions were used as tetrabutylammonium salts.

affinity for fluoride ion with an association constant of 560 M^{-1}. The observed selectivity trend was $F^- > Cl^- > Br^- > I^- > CH_3COO^-$. No significant binding was observed with $H_2PO_4^-$ ion in this case. However, receptor **5b** showed considerable affinity for the $H_2PO_4^-$ ion with a binding constant of 1100 M^{-1}, which may be due to the larger cavity size of the receptor because of the para-substituted benzene ring. The observed selectivity trend was $H_2PO_4^- > Cl^- > Br^- > F^- > I^- > CH_3COO^-$. Interestingly, the acyclic receptor **7** showed much higher affinity and selectivity toward $H_2PO_4^-$ ion as compared to the cyclic receptor **5b**, having a binding constant of 1920 M^{-1}. The selectivity trend was $H_2PO_4^- > Cl^- > F^- > Br^- > I^- > CH_3COO^-$. The higher affinity of the acyclic receptor for $H_2PO_4^-$ ion as compared to the cyclic receptor **5b** may be attributed to the greater flexibility of the acyclic receptor for adapting the suitable geometry required for the binding of a tetrahedral $H_2PO_4^-$ anion (Figure 2).

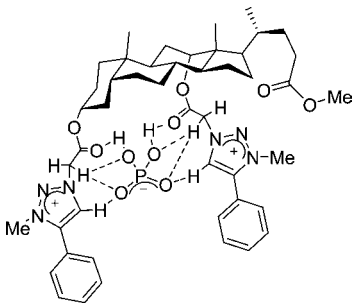


Figure 2.

As there has been much interest[12] in recent years in designing artificial receptors for the $H_2PO_4^-$ ion due to its biological importance, the present work will be of great significance. More importantly, it also establishes the potential of the 1,2,3-triazolium system as an anion-sensing moiety and the importance of click chemistry for anion recognition.

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In summary, we have synthesized bile acid-based cyclic and acyclic 1,2,3-triazolium systems using the click chemistry of 1,3-dipolar cycloaddition of an azide and an alkyne. These receptors display the remarkable ability of the 1,2,3-triazolium ring to act as an anion-sensing moiety. The acyclic receptor has been found to show very high selectivity for the $H_2PO_4^-$ ion with respect to halide and acetate ions.

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Supporting Information Available: Experimental details, analytical data for compounds, and binding isotherms. This material is available free of charge via the Internet at http://pubs.acs.org.

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