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Triazole-based chromogenic and non-chromogenic receptors for halides

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ABSTRACT

We designed and synthesized a series of triazole-based receptors for anion recognition. Our studies demonstrated that an amide-linked triazole unit is a promising moiety for anion recognition. We synthesized various chromogenic and non-chromogenic receptors based on this moiety. Receptor **11** binds very strongly ($K = 102{,}750\ M^{-1}$) to fluoride. Receptor **18** changes color from faint yellow to orange upon binding to fluoride.

The design of anion receptors is an area of intense research interest, owing to their biological, medical, and chemical applications. Anions and cations are important players in living systems and therefore their transport across the cell membrane has high therapeutic significance.[1] Synthetic ligands with cation-binding properties are common, but less effort has been devoted to the design and synthesis of anion receptors, in spite of their significance and potential applications.[2] For example, a defect in chloride ion transport leads to cystic fibrosis; synthesized anion receptors could contribute to a cure for this disease.[3] Fluoride ions are commercially used in toothpaste industries; excess fluoride in the body can lead to fluorosis.[4] Chemists are interested in the design of anion receptors and have produced novel receptors with many intricate structures.[5] These receptor molecules display good binding ability and selectivity for anions.[6]

There are several positively charged synthetic anion receptors. Their binding efficacy is mainly due to Coulomb interactions that contribute to the attractive force.[7] Neutral receptors bind anions through interactions weaker than Coulomb interactions. Therefore, preorganization and the introduction of several binding sites are the salient features of neutral anion receptor design. The use of non-conventional H-bonding moieties is an additional advantage in the design of anion receptors. The crystallographic evidence of CH···X (X = N, O) hydrogen bonds was first proposed by Taylor and Kennard in 1982.[8] A number of studies later demonstrated their existence, after notable developments in crystal engineering.[9] In recent years, the design of receptors that use non-conventional hydrogen bonding interactions has gained importance. CH···X hydrogen bonding is an additional attractive interaction that chemists can employ in isolation or with other attractive interactions in the design of receptors.

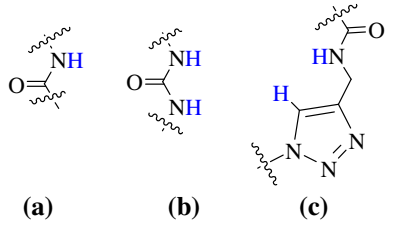

Figure 1. Comparison of anion binding motifs (a) amide; (b) urea and; (c) amide-linked triazole unit. The colored protons are the potential hydrogen bond donors.

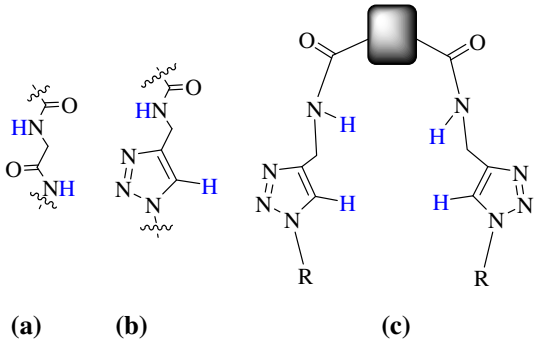

Figure 2. Comparison of two peptide linkages with an amide-linked triazole. The trans arrangement of hydrogen bond donors (a and b). Co-facially oriented amide-linked triazole on a scaffold (c).

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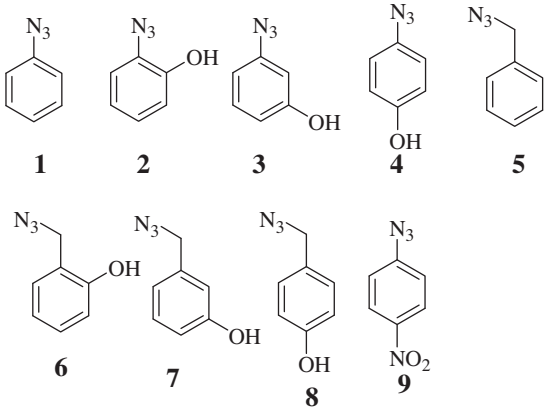
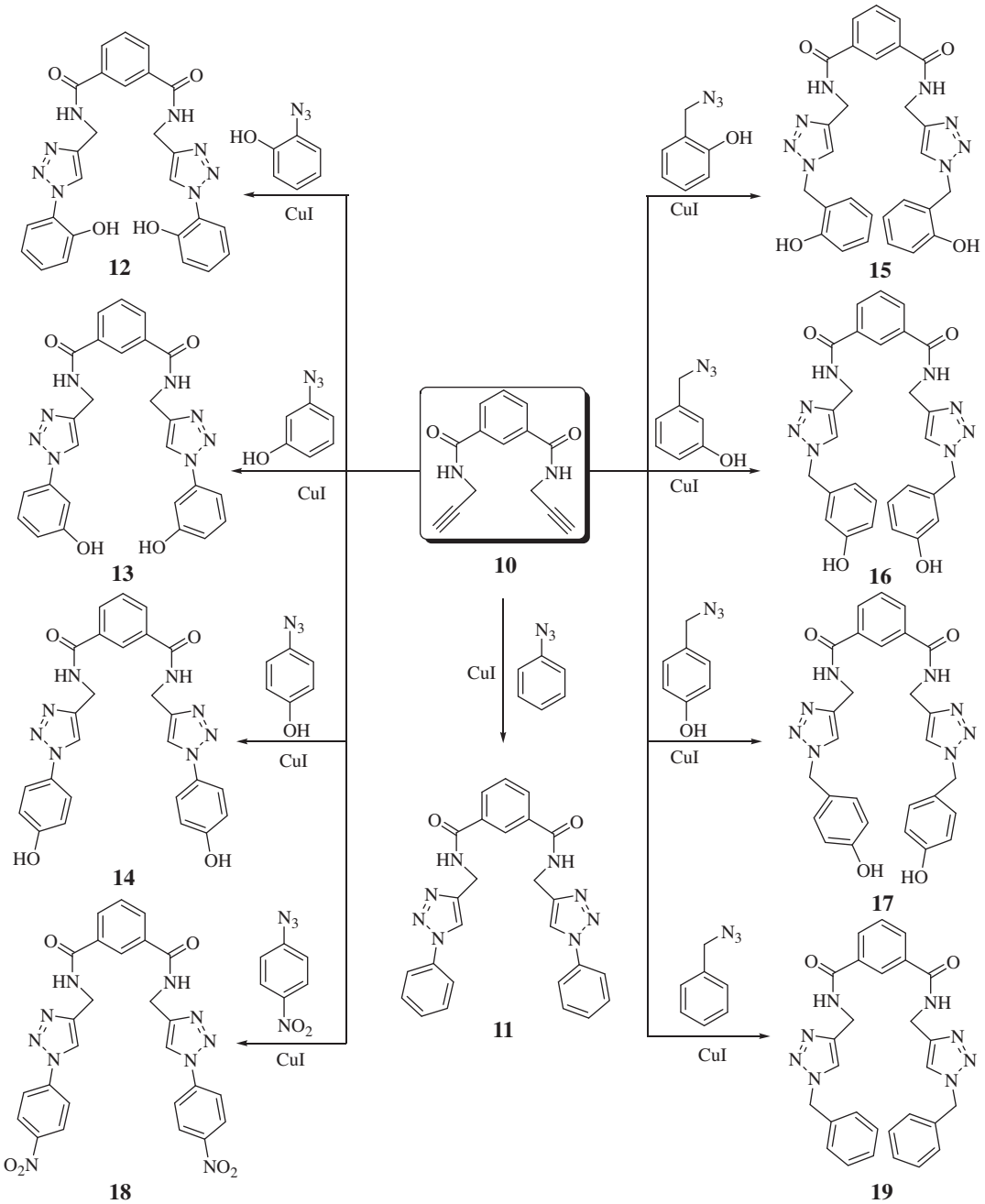


Figure 3. Structure of various azides.

Herein, we report the design and synthesis of anion receptors with remarkable selectivity and binding affinity. Receptors with selectivity for spherical anions like halides are mainly based on cavity size. A cavity decorated with a variety of H-bond donors may show selectivity. Conventional hydrogen bond donors (e.g., amide NHs and urea NHs) are used in typical receptor designs.[10] Urea moieties bind anions, but in most cases fluoride binding involves proton transfer.[11] The use of triazole in the design introduced rigid geometry, as well as an acidic CH capable of H-bonding.[12] Triazole is an excellent amide bond mimic; therefore, we hypothesized that a triazole-amide link would be similar to two consecutive peptide linkages (Fig. 1). Co-facially oriented amide-linked triazole places the H-bond donors on one face and thus is ideal for anion binding (Fig. 1c). A scaffold that can arrange two co-facially orientated amide-linked triazole moieties so that they face each other will favor better binding (Fig. 2).



Scheme 1. Synthesis of triazole-based receptors **11**–**19**.