BINOL and triazole containing cyclic and 29-8-29 membered ladder-type siloxanes: Application for the fluorescence sensing of anions

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Abstract: Tetrachloro- and tetraazide-substituted all-*cis* tetraphenylcyclotetrasiloxanes (all-*cis*-T$_4$) **2** and **3** were synthesized in high yields and were fully characterized. Then the precursor **3** underwent CuAAC click reaction with monopropargyl BINOL **4** and dipropargyl BINOL **6** to give the novel BINOL and triazole containing all-*cis*-T$_4$ **5** and the 29-8-29 membered-ring ladder-type siloxane **7**. The sensing ability of compound **5** and **7** towards anions were studied as well and it was observed that **7** could selectively recognize iodides through synergistic C-H···I hydrogen bonding, resulting in an impressive fluorescence quenching with K$_{sv}$ of 8.10×10^4.

The recognition of anionic species through molecular receptors is a key research field due to the essential role of anions in a variety of chemical, biological, and industrial processes.[1] This is especially true for halide anions, such as fluorides, chlorides, bromides, and iodides, which are essential components for human beings.[2] Excess or deficient amount of halide anions in human body has considerable effects on human health, therefore the highly efficient and selective detection of halide anions becomes crucial.[2] Fluorescence spectroscopy is one of the most powerful methods amongst the numerous analytical techniques for sensing halide anions due to its rapidity, high sensitivity and specificity, excellent resolution and low cost.[3] To date, numerous organic molecules used as fluorescent sensors to detect halide anions have been developed and generally they recognize halides through a combination of strong hydrogen bonding and ion pairing.[4] Among the halides, iodides are the most important elements for various biological activities, like neurological and thyroid functions.[5] However, compared to the other halides, the larger size, lower charge density, and weaker hydrogen-bonding ability of iodides limit the efficiency of the organic-based

sensors to selectively bind them.[2] The design and synthesis of novel host molecules for iodides with suitable host-guest properties remain challenging and are in high demand.

In recent decades, silsesquioxanes (SQs), hybrid silicon compounds consisting of a central inorganic skeleton and peripheral organic fragments, have been extensively studied in various application areas.[6] Currently, three distinct types of well-defined SQs have been reported, including completely condensed SQs (cages like T_8, T_{10} and T_{12}),[7] incompletely condensed SQs (partial cages),[8] and ladder-type SQs.[9] All-*cis* cyclic silanols containing four T-unit silicon atoms are efficient precursors for the preparation of cage- and ladder-type SQs. Functionalization of all-*cis* cyclic silanols through the hydroxy groups, accessing to well-defined all-*cis* cyclic tetrasiloxanes (all-*cis*-T_4, also named as "Janus rings") bearing a variety of reactive functional groups, has been intensively reported during the last decade.[10] Functionalized all-*cis*-T_4 have potential in different application fields such as coating materials, photoactive and optical materials.[11] Very recently, two pyrene-substituted all-*cis*-T_4 were proved to be selective sensors for detection of gold ions and L-cysteine.[12] However, all-*cis*-T_4 used for sensing anions have not been reported yet. It is well-known that 1,2,3-triazole groups possess the ability to associate with the guest anions through both electrostatic force and C-H···X type hydrogen bond.[13] Taking the concept of using siloxane to control physical properties while preserving the inherently useful electronic properties of the organic fragments,[14] we aimed at the creation of well-defined hybrid siloxanes containing triazole and 1,1'-bi-2-naphthol (BINOL) units for the detection of anions.

Here we describe two new tetrachloro and tetraazido-substituted all-*cis*-T_4, prepared following the similar synthetic strategy as our previous work.[15] From the tetraazido-substituted compound, a novel all-*cis*-T_4 bearing BINOL and triazole moieties (**Scheme 1**, A), as well as an innovative 29-8-29 membered tricyclic ladder-type siloxane bearing an all-*cis*-T_4 core and two organic linker (BINOL and triazole units) containing hybrid side macrorings (**Scheme 1**, B), were synthesized via copper-catalyzed Huisgen cycloaddition (CuAAC). The study via fluorescence spectroscopy of these two novel hybrid siloxanes shows the capability of binding halides and the ladder-type one is able to selectively recognize iodide ions.
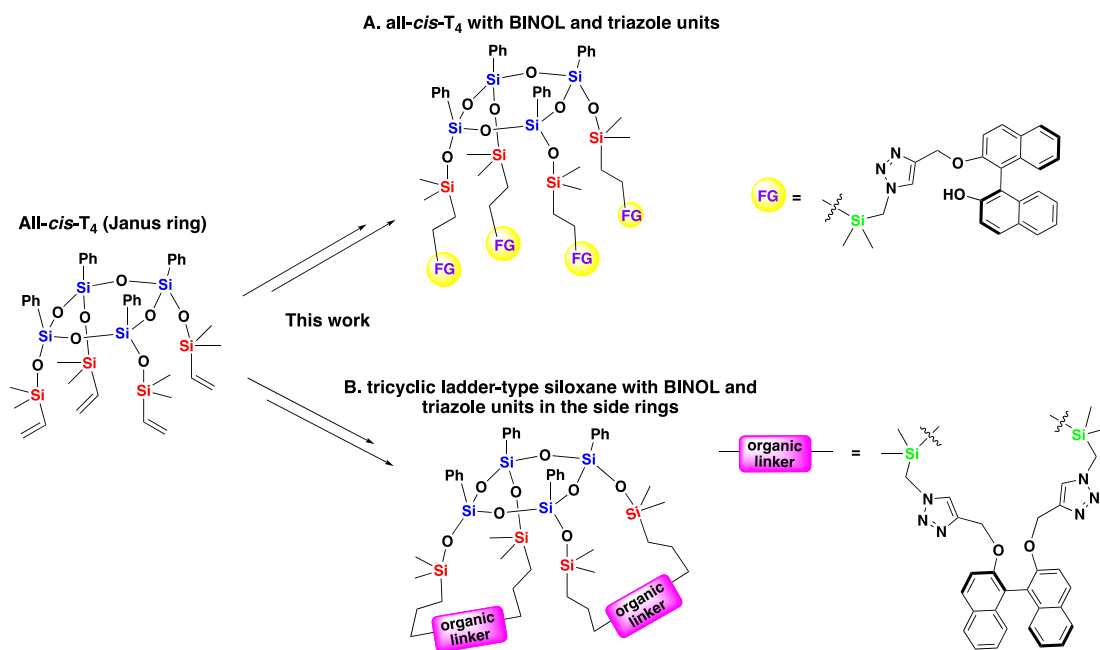
Scheme 1 Synthetic routes to new compounds reported in this work.

As shown in **Scheme 2**, the all-*cis*-T$_4$ (**1**) was allowed to react with (chloromethyl)dimethylsilane in the presence of Karstedt's catalyst at 40 ˚C and the tetrachloromethyl functionalized compound **2** was obtained in a quantitative yield. Subsequently, the chloro substituents of **2** were replaced quantitatively by azido groups using sodium azide in a mixture of THF/DMF. The obtained tetraazido precursor **3** then underwent copper-catalyzed azide-alkyne Huisgen cycloaddition (CuAAC) [16] respectively with pre-prepared monopropargyl BINOL **4**[17] and dipropargyl BINOL **6** (**Scheme 3** and **4**).[18] The CuAAC reaction of compound **3** with 4.4 equivalents of compound **4** proceeded smoothly at room temperature in the presence of CuI and NEt$_3$, resulting in an innovative all-*cis*-T$_4$ (**5**) bearing four BINOL and four triazole groups (66% yield) (**Scheme 3**). On the other hand, the same reaction with 2 equivalents of **6** yielded a new 29-8-29 membered tricyclic ladder-type siloxane (**7**) with two hybrid side rings containing two BINOLs and four triazoles (**Scheme 4**). The low yield (13%) of **7** was due to the low selectivity and several concomitant side reactions, such as the competitive linear intermolecular reaction.
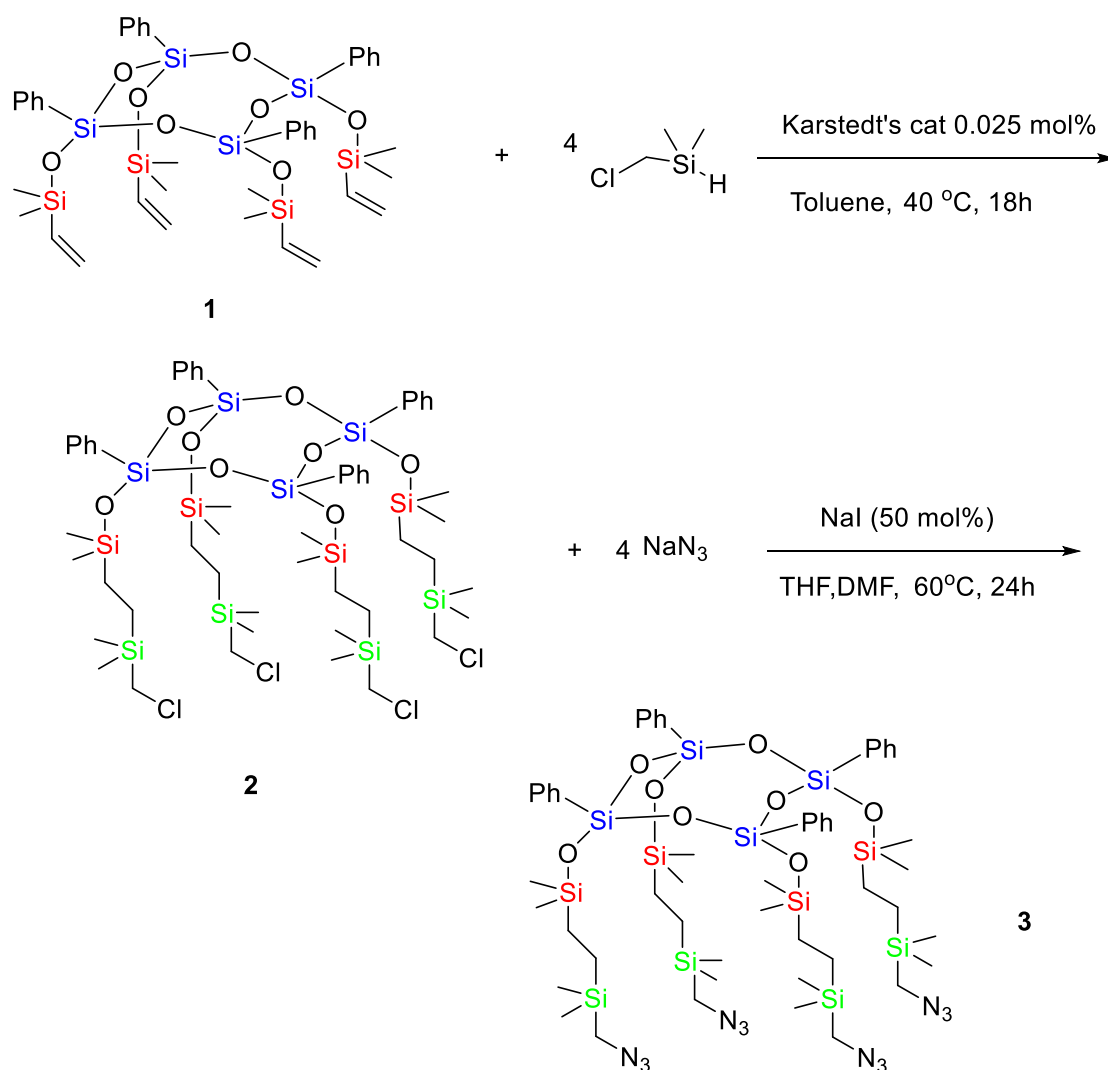
**Scheme 2** Synthesis of the tetrachloro and tetraazido-substituted all-*cis*-T$_4$ (**2**) and (**3**).

The structure of the dendrimer-like compound **5** was verified using ^{1}H, ^{13}C, ^{29}Si NMR and MALDI-TOF mass spectroscopy. The result of ^{1}H NMR reveals four sets of signals (see supporting information **Figure S11**). The first set includes the aromatic protons such as naphthalene, phenyl and triazole moieties at 6.94-7.95 ppm, together with hydroxy protons connected to naphthalene at 8.05 ppm (confirmed by the ^{1}H-^{1}H COSY NMR, see supporting information **Figure S12**). The second set of signals comprises the [CH$_2$O] protons connected to the binaphthol spacers presented as an AB spin signal at 5.11-5.19 ppm, and the [Si-CH$_2$-N] protons attached to the triazole spacers presented as a singlet at 3.74 ppm. The third set corresponds to the protons of [Si-CH$_2$CH$_2$-Si] presented at 0.50 ppm. The fourth set of signals are assigned to Si(CH$_3$)$_2$ adjacent to -O- and Si(CH$_3$)$_2$ near the triazole spacers, both presented as singlets at 0.21

and -0.09 ppm respectively. Additionally, ^{29}Si NMR spectrum (see supporting information **Figure S14)** demonstrated the all-*cis* structure of **5**, with three single peaks. The T-unit silicon atoms (Si in blue) at -78.79 ppm, silicon atoms of carbosilane (Si in green) at 4.86 ppm, and M-unit silicon atoms (Si in red) at 12.08 ppm, which was in accordance with those found in the previous reports.[10,15] In addition, MALDI-TOF mass spectrum confirmed the structure of compound **5** with its ([M+Na]$^+$, 2667.54, calcd 2667.88) peak.

The structure of compound **7** was confirmed in a similar way. The ^{1}H NMR spectrum of the ladder-type compound **7** (see supporting information **Figure S15**) also shows four sets of signals. The first set observed at 7.00-7.99 ppm corresponds to the aromatic protons for naphthalene, phenyl and triazole moieties, in which two single peaks around 7.40 ppm can be assigned to triazoles (confirmed by the ^{1}H-^{1}H COSY NMR, see supporting information **Figure S16**). The second set is composed of two AB spin system protons, one is attributed to the [CH$_2$O] protons (δ = 5.03-5.23 ppm) adjacent to the binaphthol spacers, and the other to the [Si-CH$_2$-N] protons (δ = 3.79-3.88 ppm) connected to the triazole spacers. The third set consists of multiple peaks at 0.53-0.59 ppm, which belong to the [Si-CH$_2$CH$_2$-Si] protons. The fourth set includes the Si(CH$_3$)$_2$ protons close to -O- (methyl groups on the M-unit Si atoms) display four singlets (0.12-0.26 ppm) due to the axial chirality from BINOLs and the restriction of free rotation from (Me$_2$)Si-O bonds, and similarly the Si(CH$_3$)$_2$ protons near the triazole spacers also appear as four single peaks (-0.03, -0.06, -0.08 and -0.11 ppm). The ^{29}Si NMR spectrum (see supporting information **Figure S18**) displays three signals, respectively corresponding to the T-unit silicon atoms (Si in blue, -78.84 ppm), silicon atoms of carbosilanes (Si in green, 4.95 ppm), and M-unit silicon atoms (Si in red, 12.05 ppm). Moreover, the MALDI-TOF mass spectrum of compound **7** clearly shows intense signals for the [M+Na]$^+$ (2096.85, calcd 2096.69). The combination of the multinuclear NMR data and MALDI-TOF mass result firmly confirms the 29-8-29 membered-ring ladder-type structure of compound **7**.
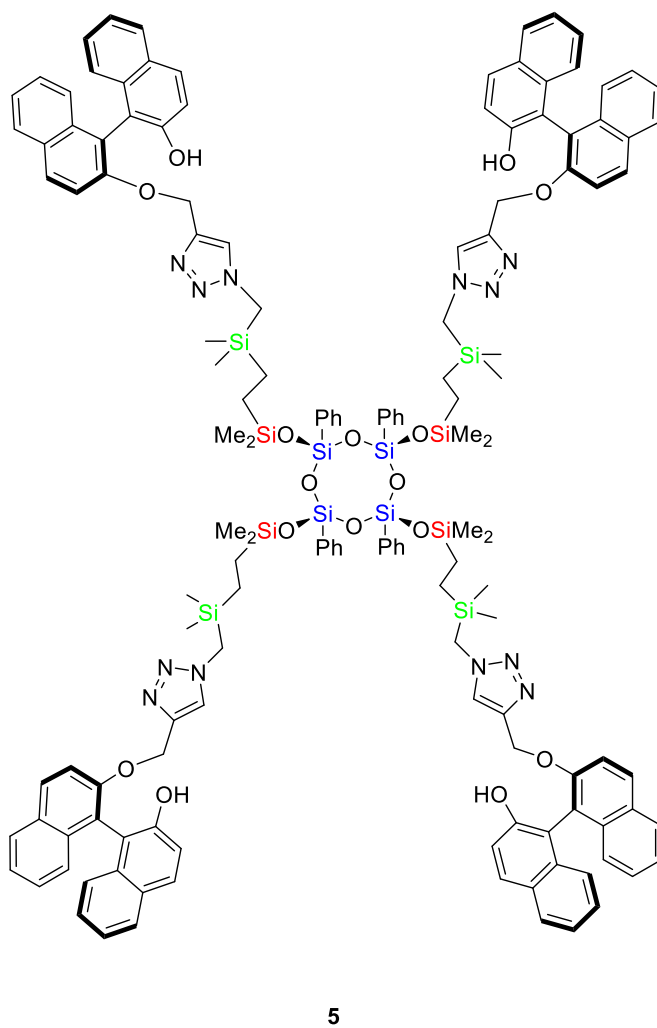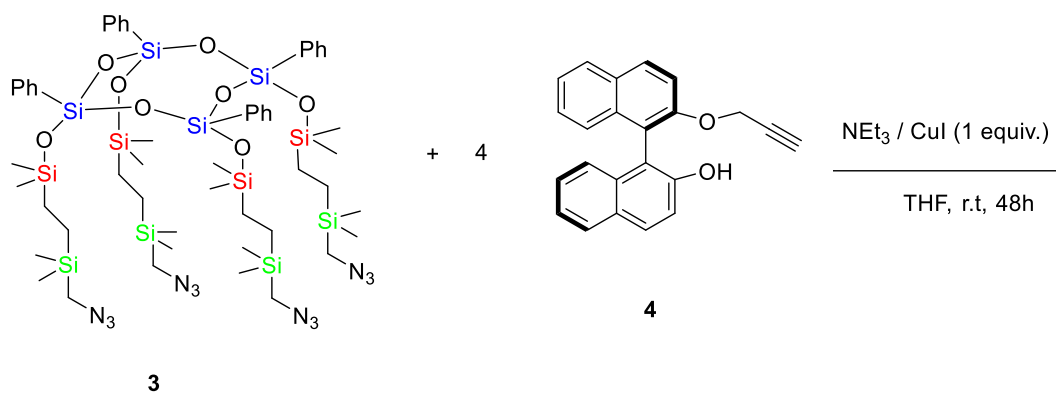
Scheme 3 Synthesis of the BINOL and triazole containing all-*cis*-T$_4$ (**5**)
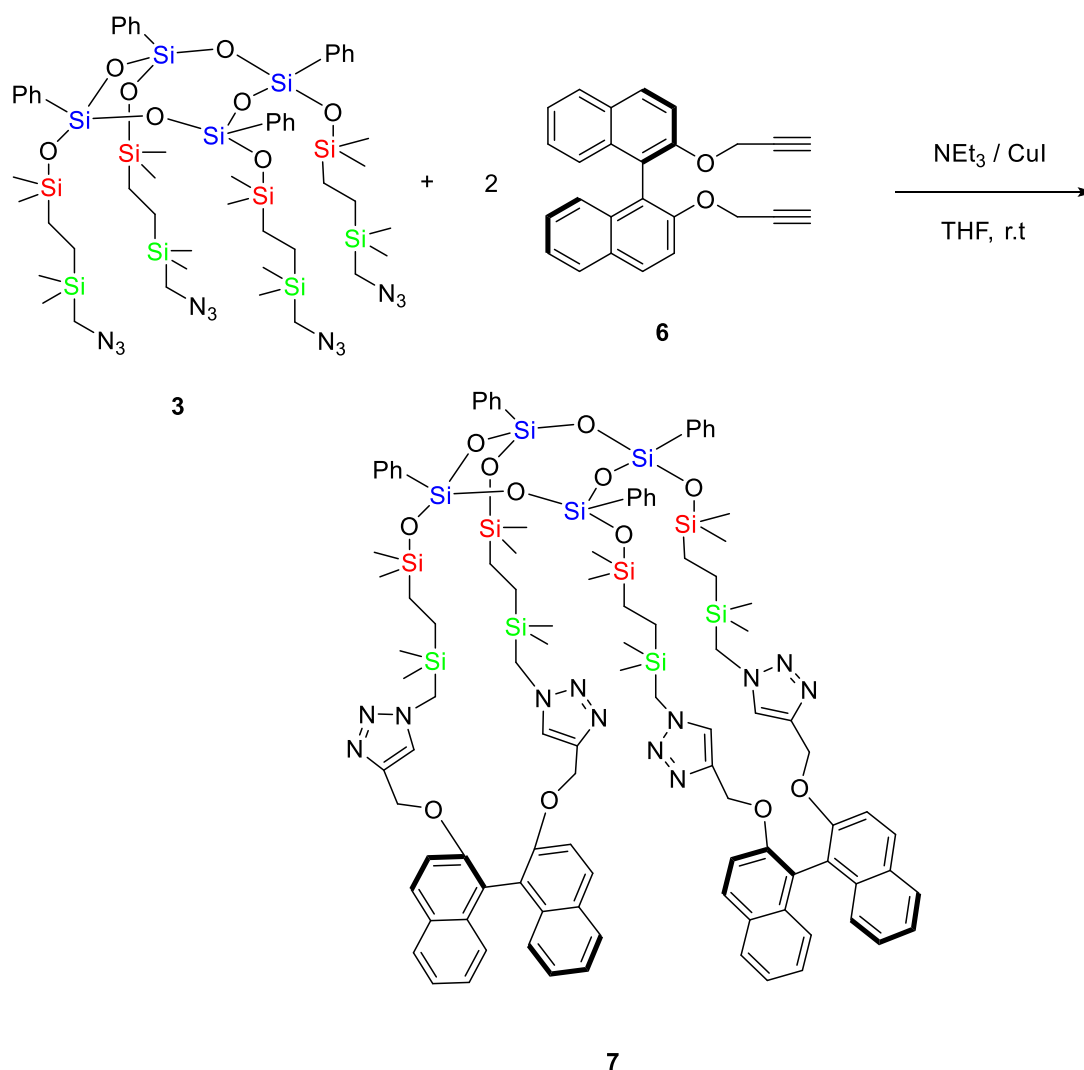
Scheme 4 Synthesis of the BINOL and triazole containing 29-8-29 membered-ring ladder-type siloxane compound **7**.

To gain preliminary insight into the interaction between anions and compound **5** and compound **7**, ^{1}H NMR titrations in acetone-d_6 were carried out. As illustrated in **Figure 1**, after the addition of tetrabutylammonium chloride (TBACl), tetrabutylammonium bromide (TBABr), and tetrabutylammonium iodide (TBAI) respectively, the binaphthyl protons of compound **5** don't show any obvious variation in chemical shift, while the triazole protons slightly shifted to downfield due to the weak C-H···X hydrogen bonding, and the strong O-H···X hydrogen bonding lead to a significantly downfield movement for the phenol protons. For example, the protons of hydroxy groups shifted from 8.05 ppm to 11.06 ppm in the presence of TBACl (**Figure 1**, b)), and to 9.03 ppm in the presence of TBABr (**Figure 1**, c)). However, no significant change for hydroxy protons was observed in the presence of TBAI (**Figure 1**, d)). In a

similar way, the binaphthyl protons of ladder-like compound **7** maintained their chemical shifts in the presence of Cl⁻, Br⁻, I⁻, and only the triazole protons shifted marginally to the lower magnetic field as well, because of the weak C-H···X hydrogen bonding (**Figure 2**). For example, the two singlets for triazole protons split into a single peak at 8.24 ppm and two singlets at 7.47, 7.49ppm due to different binding modes when TBACl was added (**Figure 2**, b)). In comparison, the two singlets from triazole protons were not split further into multiple peaks when TBABr and TBAI were added (**Figure 2**, c) and d)), indicating that all four triazole groups were synergistically involved in the binding with Br⁻ and I⁻, respectively. This suggests that the preorganized ladder-like compound **7** may be a good receptor candidate for bromide or iodide ions.
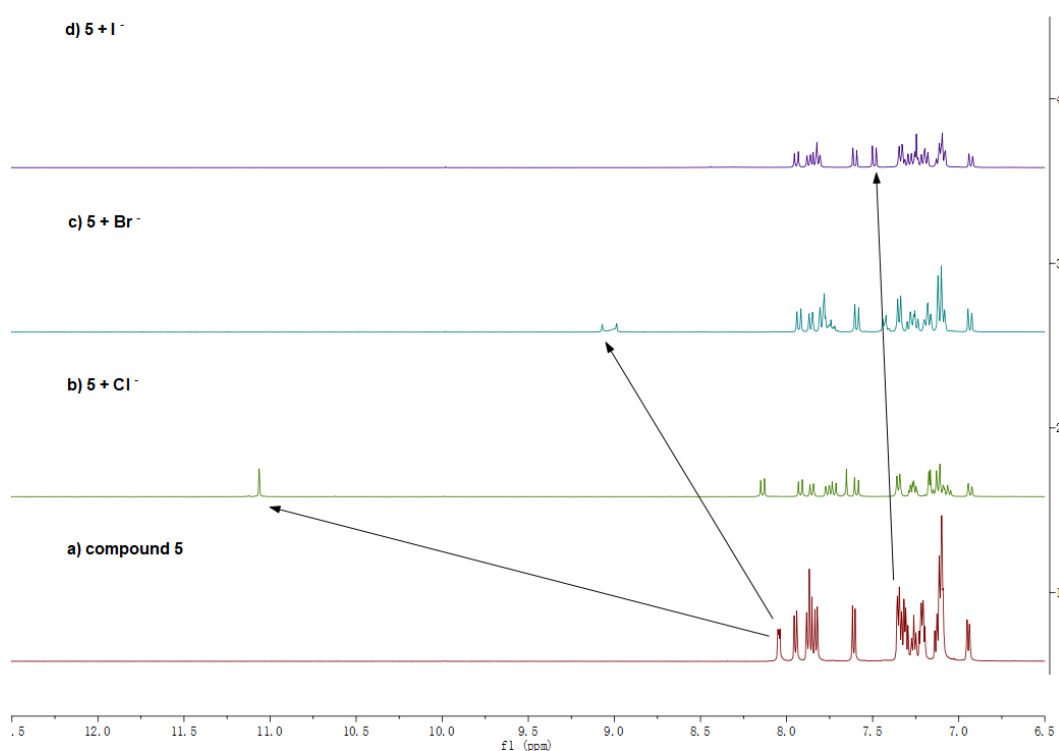

Figure 1 ¹H NMR titrations partial spectra of compound **5** in the presence of 10 equivalents of Cl⁻, Br⁻, and I⁻ respectively

The study of photophysical properties of compounds **5** and **7** were performed. To our delight, it was found that both of compounds **5** and **7** gave strong fluorescent emissions at around 333-422 nm. We then examined their fluorescence in the presence of various biologically and environmentally relevant anions. Unfortunately, the fluorescence intensity of compound **5** hardly decreased when 20 equivalents of F⁻, Cl⁻,

Br$^-$, I$^-$, NO$_3^-$ and SO$_4^{2-}$ were even added respectively (see supporting information **Figure S1**). In contrast, compound **7** displayed a high sensitivity towards iodide ions, with a remarkable fluorescence quenching at about 355 nm (**Figure 3**). The fluorescence intensity of **7** could be quenched by almost 91% with the addition of 100 equivalents of I$^-$. However, the addition of 100 equivalents of F$^-$ led to only half quenching, and little quenching of fluorescence intensity was observed under the similar conditions with the other anions such as Cl$^-$, Br$^-$, NO$_3^-$ and SO$_4^{2-}$.
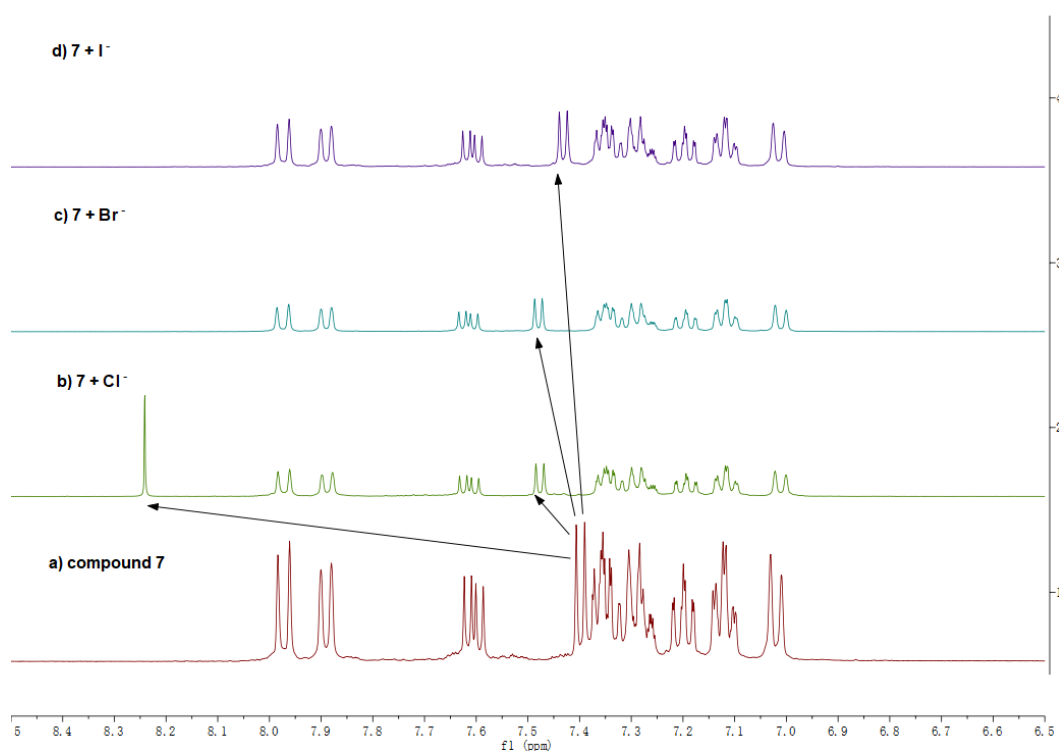

Figure 2 ^{1}H NMR titrations partial spectra of compound **7** in the presence of 10 equivalents of Cl$^-$, Br$^-$, and I$^-$ respectively

In order to further explore the selective sensing properties of compound **7** towards iodide ions, fluorescence titration experiments were carried out. As depicted in **Figure 4**, the fluorescence intensities at 355 nm decreased gradually with the increasing concentrations of I$^-$. The efficiency of quenching was further examined by plotting a Stern-Volmer plot, as shown in the inset of **Figure 4**. This makes it possible to calculate the fluorescent quenching coefficient K$_{sv}$ through the following equation: I$_0$/I = K$_{sv}$[Q]

+ 1, where I_0 and I represent the fluorescence intensity in the absence of I^- and in the presence of I^-, respectively. [Q] is the molar concentration of quencher I^-. According to the Stern-Volmer plot, K_{sv} value of 8.10×10^4 was determined (also see supporting information **Figure S3**). The relatively high value of K_{sv}, as well as the nonlinear behavior, point to the formation of a non-fluorescent complex in the ground state, also known as static quenching.
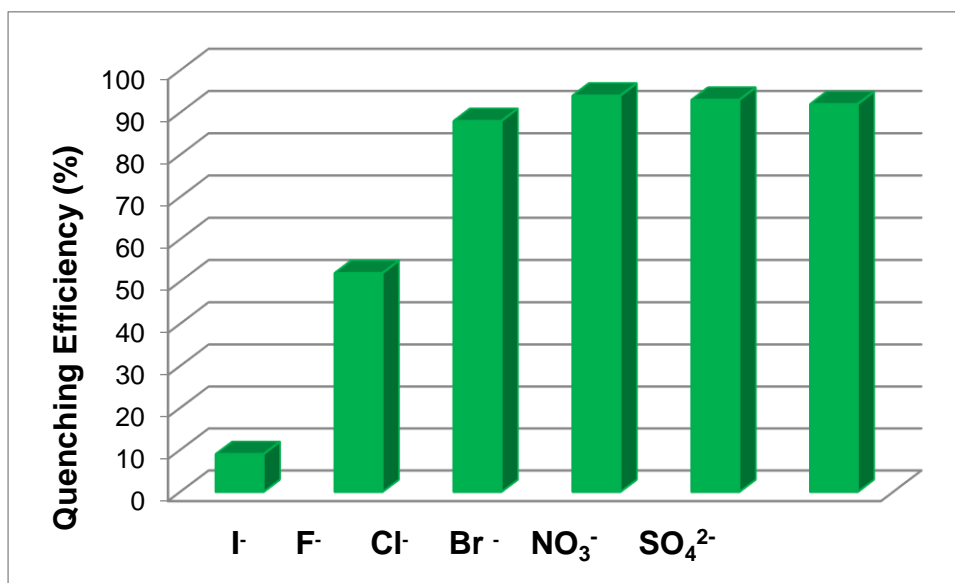

Figure 3 The fluorescence quenching effect of compound **7** in THF (0.5 µM) in the presence of various anions (100 equiv.).
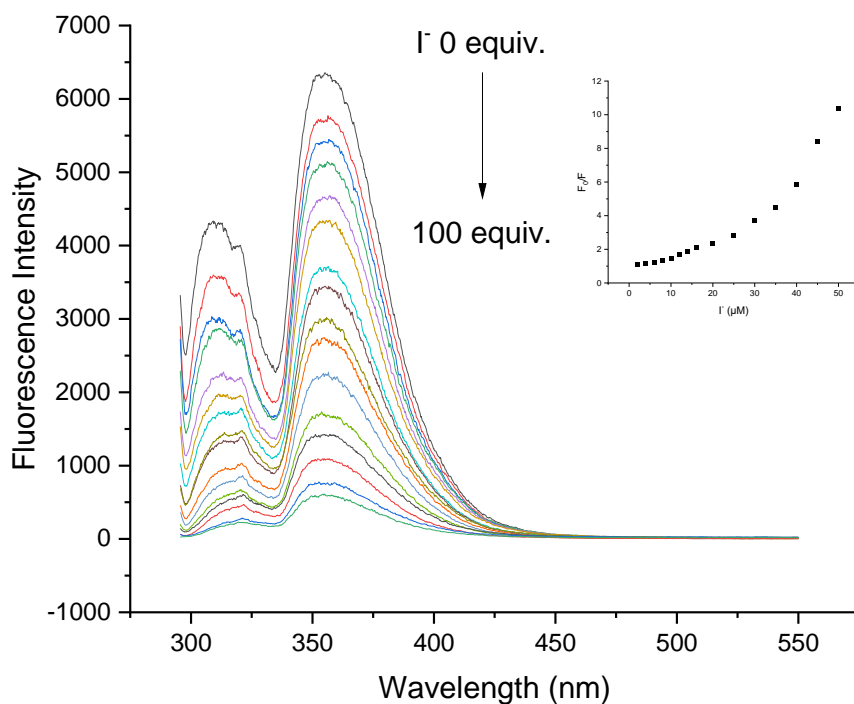
Figure 4 Fluorescence spectra of the solution of compound **7** in THF (0.5μM) with increasing concentration of I $^-$ (source TBAI, 0-100 equiv.).

On the UV-Vis spectra, ladder-like compound **7** gave an absorption band centered at 237 nm due to a π→π * and n→π * transitions (**Figure 5**). Along with the continuous addition of TBAI, a new peak located at 291 nm appeared, which implies the formation of the ground-state complex between the iodides and the triazole rings, and thus resulting in static quenching of fluorescence in the titration process.
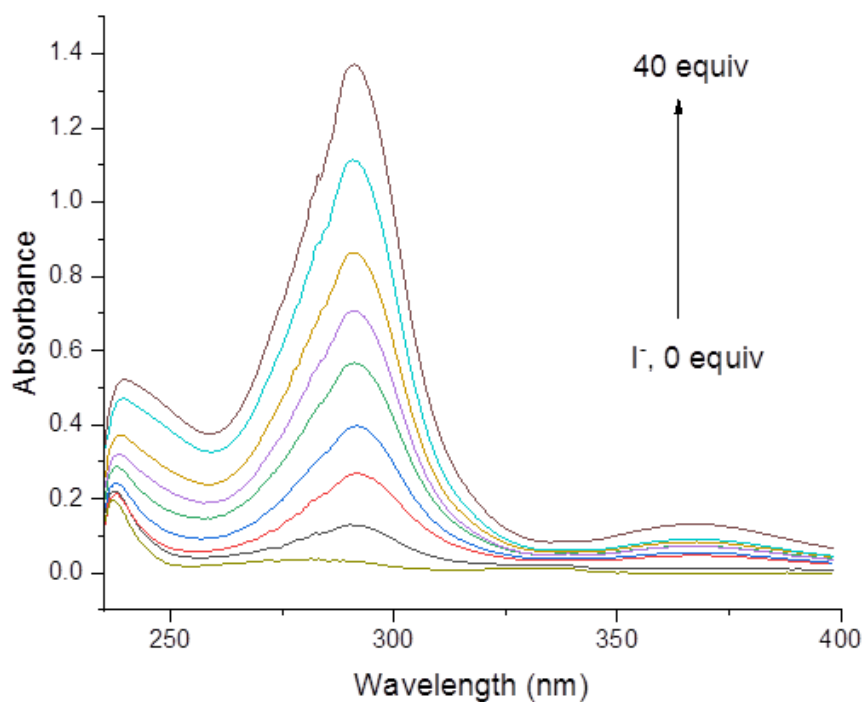
Figure 5 UV-Vis spectra of the solution of compound **7** in THF (1.0 μM) with increasing concentration of I⁻ (source TBAI, 0-40 equiv.).

Based on the above results, an explanation for this quenching phenomenon of compound **7** observed with iodide ions was proposed. Iodide ions could selectively interact with compound **7** via synergistic C⋯I hydrogen bonding during the recognition process. This would then cause the heavy atom effect which increases intersystem crossing to form the non-emissive triplet state, and thus reduce the population of the singlet excited state, leading to a decrease of the overall fluorescence intensity.[19]

In summary, we have synthesized two new all-*cis*-T$_4$ bearing four chloro and four azido groups respectively (compounds **2** and **3**). The tetraazido-substituted compound **3** is a useful precursor for the preparation of new materials because it can react with a wide array of alkynes via CuAAC click reaction. From the intermediate **3** and the pre-prepared BINOL containing alkynes, the unprecedent all-*cis*-T$_4$ (**5**) and tricyclic ladder-type siloxane (**7**) possessing multiple BINOL and triazole units were successfully synthesized. All these new compounds (**2**, **3**, **5**, **7**) were fully characterized. Moreover, the anion binding ability of compounds **5** and **7** was examined by using ¹H NMR, UV-visible and fluorescence spectroscopy. The results showed that both of these two

compounds were able to bind halide anions. And an impressive fluorescence quenching with K_{sv} of 8.10×10^4 demonstrated that ladder-type compound **7** had a strong affinity and selectivity to iodide ions. Further work on exploring the chiral recognition capacity of these compounds are ongoing in our laboratory.

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