Dynamics of the alkyne → copper(I) interaction and its use in a heteroleptic four-component catalytic rotor†

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The HETPYNE (HETeroleptic Phenanthroline and alkYNE metal) and DABCO (zinc porphyrin) interactions were used to assemble the four-component nanorotor ROT-1 that exhibited a highly dynamic alkyne → copper(I) dissociation (k_{298} = 240 kHz) at 298 K. Quantitative click reaction transformed ROT-1 into the new rotor ROT-2 (k_{298} = 77 kHz) with a triazole → copper(I) linkage thus opening perspectives for bioorthogonal click strategies to biohybrid machinery.

Inspired by nanomechanical motions in biological machines, scientists have developed an enormous interest in the development of artificial molecular devices. Among them, molecular motors, rotors, shuttles, tweezers, turnstiles, muscles, elevators, pumps, walkers etc. are well studied. Though numerous examples of artificial covalent molecular devices are known in the literature, evolution toward multi-component artificial machineries still represents a major challenge due to the limited amount of dynamic orthogonality in hetero-assemblies.

For designing artificial multicomponent rotors, orthogonal dynamic interactions are a key requirement. To the best of our knowledge, all literature known dynamic interactions that have been used to construct artificial multicomponent rotors are derived from H-bonding or N,O-donor metal interactions. Clearly, development of any new dynamic interaction will open further opportunities. Here, we demonstrate for the first time a supramolecular assembly and a rotor built on the dynamic alkyne → copper(I) interaction. Specifically, we designed a four-component supramolecular assembly and nanorotor based on the heteroleptic Cu⁺-phenanthroline alkyne (HETPYNE: HETeroleptic Phenanthroline and alkYNE metal) complexation (Fig. 1). Addition of stoichiometric quantities of azide to the rotor afforded the new class of a Cu⁺-triazole rotor through an in situ copper(I) catalysed click reaction.

For our study, we decided to use the phenanthroline-appended zinc(II) porphyrin ligands or and DABCO (Fig. 1). We performed a few model experiments to evaluate the binding of a terminal ethynyl group to [Cu(phenAr₂)]⁺. Mixing of 4, 5 and [Cu(CH₃CN)₄]PF₆ in 1:1:1 ratio (2.5 mM each) in CD₂Cl₂ accomplished quantitative formation of C1 = [Cu(4)(5)]⁺ (Fig. 2a). In the ¹H NMR, a downfield shift of all phenanthroline protons indicated binding of 5 to [Cu(4)]⁺, for instance, proton 4₀₀-H shifted from 8.67 to 8.74 ppm and 5₀₀-H from...
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8.14 to 8.20 ppm (Fig. 2b). In contrast, protons d'-H (from 6.77 to 6.60 ppm) and e'-H (from 4.68 to 4.09 ppm) of the ethynyl ligand 5 shifted 
upfield upon its complexation to [Cu(4)]+. Due to the shielding of these protons by the π-ring current of the mesityl groups. On the other hand, despite being in the shielding region of a strong π-electron cloud, the downfield shift of proton f'-H (from 5 to C1: 2.58 to 2.68 ppm) validated the ethynyl binding to the Cu center. Single crystal X-ray analysis of C1 revealed a triclinic crystal system with the space group P1 (ESI† Fig. S27). Importantly, it clearly demonstrated the side-on binding of Cu+ to both ethynyl carbons whereas there was no binding visible between oxygen and Cu+ center (Fig. 2c). The solid state structure disclosed the bond lengths of Cu(1)-C(41), Cu(1)-C(42), Cu(1)-N(11) and Cu(1)-N(1) to be 1.958(5) Å, 1.969(4) Å, 2.002(3) Å and 2.013(3) Å, respectively. The angle between the planes defined by N(1)-Cu(1)-N(11) and Cu(1)-C(41)-C(42) was determined as 16°. This geometry around the copper(i) center is not very common. From an NMR titration, the binding constant of 5 to [Cu(4)]+ was determined as log $K = 2.81 \pm 0.16$ (ESI† Fig. S26). We propose to denote the heteroleptic complexation motif between a [Cu(phenAr3)]+ and an alkyn as HETPYNE interaction (vide supra).

After establishing the HETPYNE motif, the zinc(II) porphyrin 3 with two ethynyl terminals was designed. To synthesize ligand 3, we first reacted 5,15-di(4-iodophenyl)-10,20-dimesityl zinc(II) porphyrin and 4-ethynylphenol under Sonogashira coupling conditions providing the corresponding diphenol. In the final step, a Williamson ether synthesis between the phenol-substituted phyrin and 4-ethynylphenol under Sonogashira coupling conditions serving as good indicator of any binding.

As expected from the model studies, the four-component self-assembly ASB-1 was quantitatively afforded by mixing DABCO, ligands 1 & 3, and [Cu(CH3CN)4]PF6 in a 1:1:1:1 ratio in CD2Cl2 (Fig. 3a). Two characteristic multiplets for the CH2-units of DABCO in the negative region of the $^1$H NMR indicated quantitative formation of the hetero-sandwich complex (Fig. 3b).† Signiﬁcant changes at all phenanthroline protons in the $^1$H NMR upon moving from [Cu2(1)]2+ to ASB-1 supported the binding of 3 to the copper(i)-loaded phenanthroline stations (Fig. 3c and d). Downfield shift of proton f-H from 2.64 to 3.10 ppm in ASB-1 attested the terminal ethynyl binding of 3 at the Cu+ center of 1 (Fig. 3d). Drastic upfield shifts of proton signal e-H from 4.79 to 3.60 ppm and of d-H from 7.05 to 6.77 ppm along with a downfield shift of proton signal c-H from 7.64 to 7.75 ppm validated the formation of the HETPYNE complex. Furthermore, a single peak in the ESI-MS at $m/z = 1489.1$ confirmed formation of the hetero-assembly (ESI† Fig. S23) and a single diffusion trace in the $^1$H-DOSY NMR representing structure ASB-1 excluded the presence of other undesired assemblies (ESI† Fig. S20).

The clean formation of the heteroleptic sandwich complex encouraged us to test the HETPYNE motif as a dynamic interaction in a multicomponent rotor. To assemble the rotor, we selected zinc(n) porphyrin 2 containing just one phenanthroline station as stator and ligand 3 as rotator. Dissolving the ligands 2, 3, DABCO and [Cu(CH3CN)4]PF6 in a 1:1:1:1 ratio in CD2Cl2 quantitatively furnished rotor ROT-1 irrespective of the sequence of addition (Fig. 4a). As in ASB-1, two broad signals in the negative region corresponding to DABCO and significant shifts of all phenanthroline protons in the $^1$H NMR validated formation of the hetero-assembly (Fig. 4b–d). Upfield shifts of rotator proton signals e-H from 4.79 to 4.19 ppm along with downfield shift of f-H from 2.64 to 2.88 ppm authenticated the rotor structure (Fig. 4c and d). Its formation was further conﬁrmed by DOSY NMR and ESI-MS data (ESI† Fig. S21 and S24).

A single set of $^1$H NMR signals for protons c-H, d-H, e-H and f-H of ROT-1 suggested fast rotation of the rotor on the NMR
time scale (Fig. 4c and d). Comparison of the $^1$H NMR spectra of the free rotator 3, ROT-1 and ASB-1 showed that the proton signals d-H, e-H and f-H of rotor ROT-1 appeared approximately in the averaged position of those of free 3 and ASB-1 (Fig. 5a). Variable temperature (VT) $^1$H NMR of ROT-1 was thus performed to evaluate its dynamic behavior. Upon lowering the temperature, the sharp singlet at 4.19 ppm corresponding to proton e-H broadened and split into two singlets in a 1:1 ratio at $-75 \degree C$ with a coalescence temperature around $-50 \degree C$ (Fig. 5b). The upfield signal at 3.50 ppm was assigned to the HETPYNE-complexed proton e-H and the downfield signal at 4.71 ppm is ascribed to proton e-H at the uncomplexed arm. The rotational frequency of the rotor at different temperatures was evaluated using winDNMR-based spectral simulations. The activation data for the rotation was derived from the Eyring plot (Table 1 and ESI,† Fig. S18). The rotational frequency turned out to be 240 kHz at 25 $\degree C$ and $\Delta G_{298}^\ddagger = 42.5$ kJ mol$^{-1}$.

After the clean formation of rotor ROT-1, our next target was the in situ rotor-to-rotor transformation. The presence of a copper(i) ion and terminal alkynes in the rotor suggested a conversion of ROT-1 to a triazole rotor through an in situ click reaction. For this purpose, 2.0 equiv. of benzyl azide was added to ROT-1 in CD$_2$Cl$_2$ (Fig. 6a). To accelerate the reaction, 1 $\mu$L of Et$_3$N was added. After 24 h of heating at 40 $\degree C$, the solvent was evaporated to remove NEt$_3$ and the residue was redissolved in CD$_2$Cl$_2$. $^1$H NMR showed quantitative formation of ROT-2 and a disappearance of the proton signal f-H (Fig. 6b). Upon moving from ROT-1 to ROT-2, characteristic shifts for all phenanthroline protons were observed. The downfield shift of proton signal e-H (from 4.19 to 4.81 ppm), upfield shifts of proton signals d-H (from 6.93 to 6.78 ppm) and c-H (from 7.72 ppm to 7.61 ppm) along with the appearance of a new singlet at 5.32 ppm (f-H) corroborated the formation of the ROT-2. The broad signal of the DABCO protons at $-4.39$ ppm confirmed the intactness of the assembly (ESI † Fig. S15). ROT-2 was further characterized by ESI-MS and DOSY NMR data (ESI † Fig. S25 and S22).

A single set of $^1$H NMR signals for protons c-H, d-H, e-H and j-H of ROT-2 indicated a fast rotation on the NMR time scale. Upon performing the VT $^1$H NMR the proton signal for j-H split into two singlets in 1:1 ratio at $-75 \degree C$ (Fig. 6c). Rotational frequencies at different temperature along with activation parameters were calculated (Fig. 6c and Table 1). The facile transformation of the self-catalyzing rotor ROT-1 to rotor ROT-2 opens interesting perspectives to generate biohybrid materials via bioorthogonal click reactions.39

In conclusion, we have synthesized a four-component heterosandwich complex and a four-component rotor based on the dynamic [Cu(phenAr$_2$)(alkyne)]$^+$ motif. Though alkylne $\rightarrow$ copper(i) interactions are well known in the literature,40 for the first time its high dynamics has been determined and used to assemble a high-speed multicomponent rotor. The utility of this dynamic orthogonal motif in supramolecular rotors opens new venues for molecular machines. Furthermore, a successful quantitative transformation of the Cu$^+$-alkyne rotor to a new Cu$^+$-triazole rotor was achieved through in situ click reaction. It is expected that thermal self-catalyzing rotors will find their way into diverse applications, e.g., in catalysis,35,41 biohybrid materials via bioorthogonal functionalization42 and elsewhere.13

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Table 1 Exchange frequencies of ROT-1 and ROT-2 along with their activation parameters

| Rotor | $k_{298}$/kHz | $\Delta H^\ddagger$/kJ mol$^{-1}$ | $\Delta S^\ddagger$/J K$^{-1}$ mol$^{-1}$ | $\Delta G_{298}^\ddagger$/kJ mol$^{-1}$ |
|-------|---------------|---------------------------------|--------------------------------------|---------------------------------|
| ROT-1 | 240           | 44.0 ± 0.2                      | 5.0 ± 0.7                             | 42.5                            |
| ROT-2 | 77            | 50.1 ± 0.4                      | 16.7 ± 0.6                            | 45.2                            |

* The higher $\Delta H^\ddagger$ for ROT-2 than ROT-1 reflects the stronger binding constant of a triazole to [Cu(4)]= (see triazole 6 in ESI, Fig. S27). As often seen in enthalpy–entropy compensation, strong binding leads to higher positive activation entropy.

Conflicts of interest

There are no conflicts to declare.

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