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## Dynamics of the alkyne $\rightarrow$ copper(I) interaction and its use in a heteroleptic four-component catalytic rotor<sup>†</sup>

Suchismita Saha,<sup>a</sup> Sohom Kundu,<sup>a</sup> Pronay Kumar Biswas,<sup>a</sup> Michael Bolte<sup>b</sup> and Michael Schmittel<sup>\*</sup>

The HETPYNE (HETeroleptic Phenanthroline and alkYNE metal) and DABCO (zinc porphyrin)<sub>2</sub> interactions were used to assemble the four-component nanorotor ROT-1 that exhibited a highly dynamic alkyne  $\rightarrow$  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  $\rightarrow$  copper(i) linkage thus opening perspectives for bioorthogonal click strategies to biohybrid machinery.

Inspired by nanomechanical motions<sup>1</sup> in biological machines,<sup>2–4</sup> scientists have developed an enormous interest in the development of artificial molecular devices.<sup>5–8</sup> Among them, molecular motors,<sup>9–11</sup> rotors,<sup>12</sup> shuttles,<sup>13–15</sup> tweezers,<sup>16–18</sup> turnstiles,<sup>19</sup> muscles,<sup>20</sup> elevators,<sup>21</sup> pumps,<sup>10</sup> walkers<sup>22</sup> *etc.*<sup>5–8</sup> are well studied. Though numerous examples of artificial covalent molecular devices are known in the literature,<sup>5–8</sup> evolution toward multicomponent artificial machineries still represents a major challenge due to the limited amount of dynamic orthogonality in hetero-assemblies.<sup>23,24</sup>

For designing artificial multicomponent rotors, orthogonal dynamic interactions are a key requirement.<sup>25</sup> 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<sup>19</sup> metal interactions.<sup>26-30</sup> 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  $\rightarrow$  copper(i) interaction.<sup>31,32</sup> Specifically, we designed a four-component supramolecular assembly and nanorotor based



Fig. 1 (a) Chemical structure and cartoon representation of the ligands 1,
2, 3 and DABCO. (b) Cartoon representation of the four-component assembly ASB-1 and nanorotor ROT-1.

on the heteroleptic Cu<sup>+</sup>-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<sup>+</sup>-triazole rotor through an *in situ* copper(I) catalysed click reaction.

For our study, we decided to use the phenanthrolineappended zinc( $\pi$ ) porphyrin ligands 1 or 2 as stator. Bulky aryl groups<sup>33</sup> at the 2,9-position of the phenanthroline phenAr<sub>2</sub> are essential to avoid the unwanted formation of the corresponding homoleptic Cu<sup>+</sup> complexes.<sup>34–36</sup> In order to design rotator 3, we performed a few model experiments to evaluate the binding of a terminal ethynyl group to [Cu(phenAr<sub>2</sub>)]<sup>+</sup>. Mixing of 4, 5 and [Cu(CH<sub>3</sub>CN)<sub>4</sub>]PF<sub>6</sub> in 1:1:1 ratio (2.5 mM each) in CD<sub>2</sub>Cl<sub>2</sub> accomplished quantitative formation of C1 = [Cu(4)(5)]<sup>+</sup> (Fig. 2a). In the <sup>1</sup>H NMR, a downfield shift of all phenanthroline protons indicated binding of 5 to [Cu(4)]<sup>+</sup>, for instance, proton 4"-H shifted from 8.67 to 8.74 ppm and 5"-H from

<sup>&</sup>lt;sup>a</sup> Center of Micro and Nanochemistry and (Bio)Technology, Organische Chemie I, Universität Siegen, Adolf-Reichwein-Str. 2, Siegen D-57068, Germany.

E-mail: schmittel@chemie.uni-siegen.de; Tel: +49(0) 2717404356

<sup>&</sup>lt;sup>b</sup> Institut für Organische Chemie und Chemische Biologie, Johann Wolfgang Goethe-Universität, Max-von-Laue Strasse 7, Frankfurt am Main D-60438, Germany

<sup>&</sup>lt;sup>†</sup> Electronic supplementary information (ESI) available: Experimental procedures, compound characterizations, spectral data, NMR titration, and VT<sup>-1</sup>H-NMR kinetics. CCDC 2199510. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d2cc04497h



Fig. 2 (a) Formation of model complex C1. (b) Partial <sup>1</sup>H NMR (400 MHz, 298 K) of  $[Cu(4)]^+$ , 5 and C1 in  $CD_2Cl_2$  (2.5 mM). (c) X-ray crystal structure of complex C1. Carbons are shown in light grey; H, light green; N, blue; O, red; Cu<sup>+</sup>, cyan and I, violet.

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  $\pi$ -ring current of the mesityl groups. On the other hand, despite being in the shielding region of a strong  $\pi$ -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<sup>+</sup> 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<sup>+</sup> to both ethynyl carbons whereas there was no binding visible between oxygen and Cu<sup>+</sup> 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 C(41)-Cu(1)-C(42) was determined as 16°. This geometry around the copper(1) 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,<sup>†</sup> Fig. S26). We propose to denote the heteroleptic complexation motif between a [Cu(phenAr<sub>2</sub>)]<sup>+</sup> and an alkyne 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 zinc(II) porphyrin and propargyl bromide in presence of base furnished ligand **3** in 85% yield. Protons e-H of **3** appear in the <sup>1</sup>H NMR well separated from other proton signals and should serve 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  $[Cu(CH_3CN)_4]PF_6$  in a 1:1:1:2 ratio in CD<sub>2</sub>Cl<sub>2</sub> (Fig. 3a). Two characteristic multiplets for the CH<sub>2</sub>-units of DABCO in the negative region of the <sup>1</sup>H NMR indicated quantitative formation of the hetero-sandwich complex (Fig. 3b).<sup>37</sup> Significant changes at all phenanthroline protons in the <sup>1</sup>H NMR upon moving from  $[Cu_2(1)]^{2+}$  to **ASB-1** supported the binding of **3** to the copper(1)-loaded phenanthroline stations (Fig. 3c and d).



Fig. 3 (a) Cartoon representation of the four-component self-assembly leading to the formation of **ASB-1**. (b) DABCO-H signal of **ASB-1** in <sup>1</sup>H NMR (CD<sub>2</sub>Cl<sub>2</sub>, 400 MHz, 298 K). Partial <sup>1</sup>H NMR (CD<sub>2</sub>Cl<sub>2</sub>, 400 MHz, 298 K) of **1**,  $[Cu_2(1)]^{2+}$ , **3** and **ASB-1** showing the (c) aromatic and (d) aliphatic region.

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<sup>+</sup> 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 <sup>1</sup>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(II) porphyrin 2 containing just one phenanthroline station as stator and ligand 3 as rotator. Dissolving the ligands 2, 3, DABCO and  $[Cu(CH_3CN)_4]PF_6$  in a 1:1:1:1 ratio in  $CD_2Cl_2$ 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 <sup>1</sup>H NMR validated formation of the heteroassembly (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 <sup>1</sup>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



Fig. 4 (a) Cartoon representation of the self-assembly of rotor **ROT-1** from four components. (b)  $(CH_2)_{DABCO}$  signal of **ROT-1** in the <sup>1</sup>H NMR ( $CD_2Cl_2$ , 400 MHz). Partial <sup>1</sup>H NMR ( $CD_2Cl_2$ , 400 MHz, 298 K) of **2**,  $[Cu(2)]^+$ , **3** and **ROT-1** in the (c) aromatic and (d) aliphatic region.



Fig. 5 (a) Partial <sup>1</sup>H NMR ( $CD_2Cl_2$ , 400 MHz, 298 K) of 3, ROT-1 and ASB-1. (b) VT-<sup>1</sup>H NMR ( $CD_2Cl_2$ , 600 MHz) of ROT-1 exhibiting the splitting of proton signal e-H into a 1:1 set and the corresponding rotational frequency at different temperatures.

time scale (Fig. 4c and d). Comparison of the <sup>1</sup>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) <sup>1</sup>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 °C with a coalescence temperature around -50 °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.<sup>38</sup> 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 °C and  $\Delta G_{298}^{\ddagger}$  = 42.5 kJ mol<sup>-1</sup>.

After the clean formation of rotor ROT-1, our next target was the in situ rotor-to-rotor transformation. The presence of a copper(1) 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  $CD_2Cl_2$  (Fig. 6a). To accelerate the reaction, 1  $\mu$ L of Et<sub>3</sub>N was added. After 24 h of heating at 40 °C, the solvent was evaporated to remove NEt<sub>3</sub> and the residue was redissolved in CD<sub>2</sub>Cl<sub>2</sub>. <sup>1</sup>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 5.52 ppm (j-H) corroborated the formation of ROT-2. The broad signal of the DABCO protons at -4.39 ppm confirmed the

Table 1 Exchange frequencies of ROT-1 and ROT-2 along with their activation parameters<sup>a</sup>

Rotor	$k_{298}/\mathrm{kHz}$	$\Delta H^{\ddagger}/kJ  mol^{-1}$	$\Delta S^{\ddagger}/J~\mathrm{K}^{-1}~\mathrm{mol}^{-1}$	$\Delta G_{298}^{\ddagger}/\mathrm{kJ}~\mathrm{mol}^{-1}$
ROT-1 ROT-2	240 77	$\begin{array}{c} 44.0\pm0.2\\ 50.1\pm0.4\end{array}$	$\begin{array}{c} 5.0\pm0.7\\ 16.7\pm0.6\end{array}$	42.5 45.2

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



Fig. 6 (a) *In situ* transformation of **ROT-1** to **ROT-2** upon addition of 2.0 equiv. of benzyl azide. (b) Partial <sup>1</sup>H NMR ( $CD_2CI_2$ , 400 MHz, 298 K) of **ROT-1** and **ROT-2**. (c) VT<sup>-1</sup>H NMR ( $CD_2CI_2$ , 600 MHz) of **ROT-2** showing splitting of the proton signal j-H (1:1 ratio) and the corresponding rotational frequency at different temperatures.

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 <sup>1</sup>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 <sup>1</sup>H NMR the proton signal for j-H split into two singlets in 1:1 ratio at -75 °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.<sup>39</sup>

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 alkyne  $\rightarrow$  copper(i) interactions are well known in the literature,<sup>40</sup> 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<sup>+</sup>-alkyne rotor to a new Cu<sup>+</sup>-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,<sup>35,41</sup> biohybrid materials *via* bioorthogonal functionalization<sup>42</sup> and elsewhere.<sup>43</sup>

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## Conflicts of interest

There are no conflicts to declare.

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