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Preferential cross-coupling of naphthol derivatives mediated by copper(II)†

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Preferential cross-coupling of differently *N*-substituted amides of 3-hydroxy-2-naphthoic acids 1 and 2 catalyzed by Cu(OH)Cl·TMEDA was observed. The reaction mechanism was investigated using mass spectrometry tools. It was shown that the complexation properties of the *N*-substituent significantly influence the properties of the corresponding copper complexes of the deprotonated compounds ($[(1\text{-H})Cu(TMEDA)]^+$ and $[(2\text{-H})Cu(TMEDA)]^+$). Analysis of the fragmentation patterns of the copper complexes revealed that while the former is prone to the one electron oxidation of $(1\text{-H})^-$, the latter has a larger binding energy between $(2\text{-H})^-$ and copper(II). Interplay between the abundance of the copper complexes and their reactivities explains the preferential cross-coupling. The results are further supported by exploratory density functional theory calculations. Copyright © 2013 John Wiley & Sons, Ltd.
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Keywords: BINOL; copper; cross-coupling; DFT calculations; mass spectrometry; reaction mechanisms

INTRODUCTION

Biaryl compounds, in particular 2,2′-disubstituted 1,1′-binaphthyls, play an important role as ligands in the metal-catalyzed enantioselective synthesis.[1–3] The classical representative of these axially chiral ligands is BINOL (2,2′-dihydroxy-1,1′-binaphthyl).[4] The strategy for the preparation of BINOL and its derivatives often involves oxidative coupling of two naphthol units in the presence of various oxidants based on transition metals ranging from titanium[5] and vanadium[6–12] via iron[13] and manganese[14] to copper[15] complexes. The traditional preparations of BINOL and its derivatives[16] require stoichiometric amounts of oxidants, but also some catalytic processes were developed, usually with oxygen serving as the terminal oxidant.[17–19] Enantiomerically pure binols can be prepared either by resolution of a racemic product[1], or chirality can be induced already during the synthesis in order to directly prepare enantiomerically pure product.[18,20–22] In addition, further asymmetry in binol compounds can be introduced by cross-coupling of different naphthol molecules, which leads to binols with different subunits.[23–26]

Several scenarios have been proposed as the mechanism for the naphthol coupling. While it is broadly accepted that the metal ion is present at the "reaction center" during the whole course of the reaction, the consensus about the particular form of the reaction complex has not been achieved. For the coupling catalyzed by vanadium oxides, it is usually assumed that a binuclear complex is formed, in which two naphthol molecules are bound to two vanadium atoms.[11] On the other hand, for the coupling catalyzed by copper(II), usually a mononuclear complex of the copper ion and a naphtholate ligand is assumed to react with another naphthol molecule from the solution.[27] On contrary, we have recently shown that at least in the gas phase, the copper-mediated naphthol coupling proceeds in binuclear clusters (Scheme 1) analogous to those proposed for vanadium-catalyzed reactions and that the mononuclear clusters do not show any significant reactivity as carbon-centered radicals.[28,29]

Some remarkably selective cross-coupling reactions have been observed for the copper(II)-mediated reactions.[30] For example, a mixture of 2-naphthol and 2-naphthylamine leads preferentially to the cross-coupled product.[20] The available explanation for the observed reactivity is based on the electronic structure of the isolated reactants. It has been suggested that the reactivity is driven by the feasibility of the creating the corresponding naphthoxy radicals and by the relative energies of the highest occupied- and the lowest unoccupied molecular orbital of these radicals.[26] This simple scheme can explain the reactivity in the naphthol cross-coupling to a certain degree and correlates well with some observed selectivities; however, the coordinated copper ion will influence all these properties in that it primarily significantly changes the distribution of the spin density[31] and also the geometry of the naphthoxy radical can be drastically changed. Thus, in the light of the recent mechanistic proposals,

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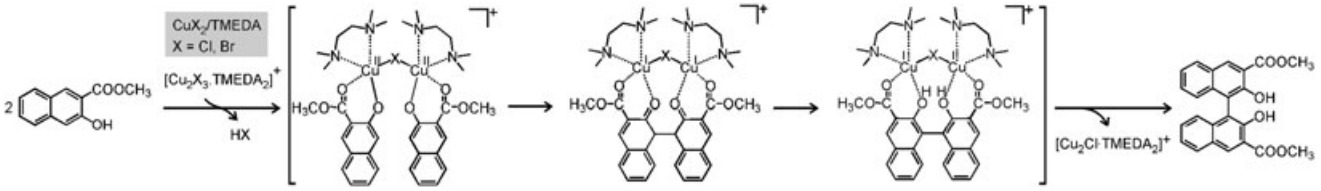
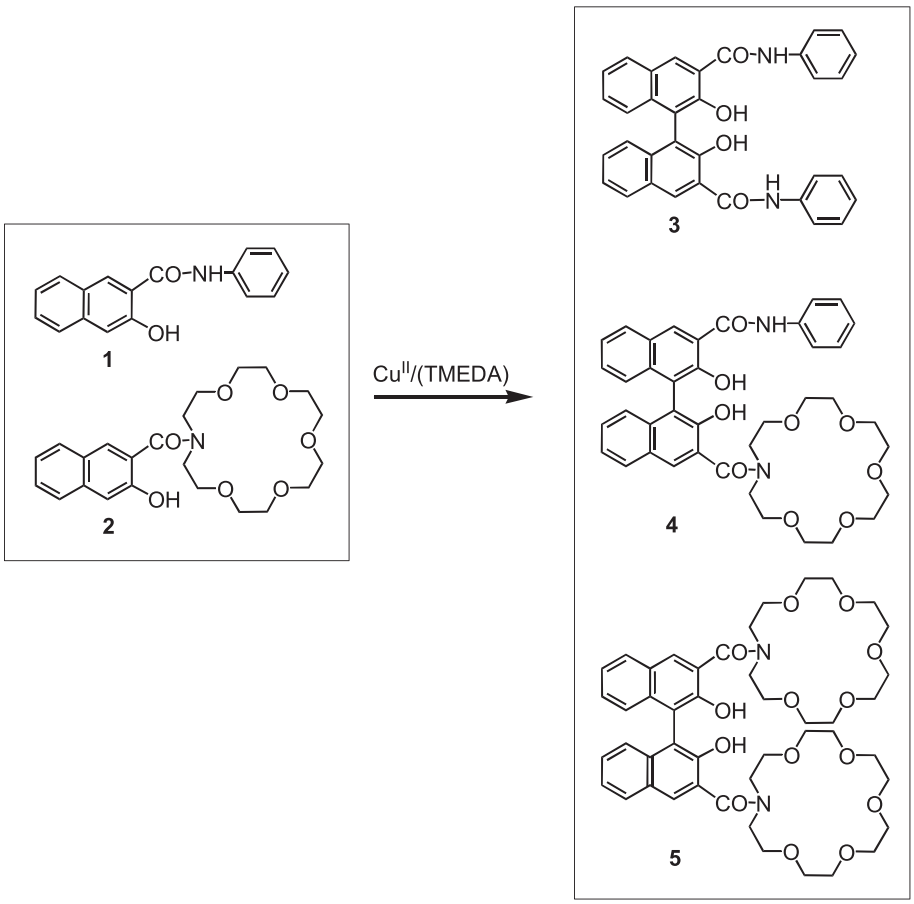


Scheme 1. Proposed mechanism for copper mediated naphthol coupling.



Scheme 2. The investigated reactants and products.

the present work aims in the investigation of the role of the copper ion in the preferential cross-coupling by means of mass spectrometry. Two different amides of 2-hydroxy-3-naphthoic acid **1** and **2** (Scheme 2) were chosen as precursor molecules, because due to the same functionalities at the naphthalene rings, roughly similar electronic properties can be expected, but completely different binding abilities with respect to copper are foreseen.

RESULTS AND DISCUSSION

The preparative cross-coupling of amides **1** and **2** mediated by stoichiometric amount of Cu(OH)Cl·TMEDA [32] leads to a significantly enhanced yield of the mixed product **4** compared to the homo-coupled products **3** and **5**. According to the analysis of the reaction by high pressure liquid chromatography, the ratio of the products **3** : **4** : **5** amounts to 9% : 82% : 9%. The analogous preparative reaction led to the isolated yields of 16%, 73%, and 5%, respectively.[33] These results clearly show that the cross-coupling between the amides **1** and **2** is favored to the homo-coupling. In the following, we aim to answer these questions: (i) Do properties of complexes of **1** and **2** with copper and the nitrogen ligand substantially differ? (ii) Do reactivities of binuclear clusters of copper with the amides **1** and **2** differ? (iii) Is there a special role of TMEDA? To answer these questions, the complexes of naphthols **1** and **2** with Cu^{II} and Cu^{II}·TMEDA are investigated by means of mass spectrometry,[34–38] and the interpretation is supported by exploratory density functional theory (DFT) calculations.

Complexes of 1

In order to discern the effect of the TMEDA ligand, methanolic solutions of **1** with $Cu(NO_3)_2$ and Cu(OH)Cl·TMEDA, respectively, are investigated by means of electrospray ionization (ESI) mass spectrometry, and the formation of various complexes and their

unimolecular behavior are compared. In the absence of TMEDA, the relevant complexes generated upon ESI correspond to [(**1**-H)Cu]$^+$ (*m/z* 325), its methanol adduct [(**1**-H)Cu(CH_3OH)]$^+$ (*m/z* 357), the analogous adduct with naphthol [(**1**-H)(**1**)Cu]$^+$ ion (*m/z* 588), and the binuclear copper complex [(**1**-H)$_2$Cu$_2$(NO_3)] (*m/z* 712) (Fig. S1a, supplementary material). The initial question concerns the structure of the [(**1**-H)Cu]$^+$ ion, because copper may bind to the oxygen atom of the hydroxy group, but the possibilities of binding to the amide nitrogen or the aromatic moiety should be considered as well. Based on the analogy with the complex of Cu^{II} with phenolate,[39–41] it can be expected that copper binds rather to the deprotonated oxygen (or nitrogen) atom rather than to the aromatic moiety. The collision-induced dissociation (CID) of mass-selected [(**1**-H)Cu]$^+$ reveals the formation of PhNHCu$^+$ (Ph = phenyl) as the dominant reaction (Fig. 1a). Another fragmentation channel is represented by a loss of the PhNH$^\cdot$ radical. These experimental results suggest that the naphthol compound **1** is not deprotonated at the nitrogen atom; instead, it is deprotonated at the oxygen site and copper accordingly binds to oxygen.

The CID experiments with [(**1**-H)Cu(CH_3OH)]$^+$ and [(**1**-H)(**1**)Cu]$^+$ show, as expected, dominant losses of the closed-shell ligands CH_3OH and **1**, respectively. In addition, the fragmentation of [(**1**-H)(**1**)Cu]$^+$ leads also to the elimination of the radical (**1**-H)$^\cdot$ as a byproduct in a 1 : 10 ratio with respect to the elimination of **1**. This finding again shows the ability of copper to accept one electron from the naphthoxo ligand (**1**-H)$^\cdot$, thereby undergoing a reduction of Cu^{II} to Cu^{I}.

The localization of the unpaired electron at carbon atoms of the naphthoxy unit of [(**1**-H)Cu]$^+$ was tested in its reactions with 1,4-cyclohexadiene, methyl iodide, and dimethyldisulphide (DMDS). It is expected that carbon centered radicals are able to activate these molecules.[42] All these reactions led only to formations of the corresponding adducts without apparent hints for the occurrence of bond activations. In addition, also analogous reactions of [(**1**-H)Cu(CH_3OH)]$^+$ and [(**1**-H)(**1**)Cu]$^+$ were conducted, and the exchange of closed-shell ligands by the neutral reactant was observed as the exclusive reaction channel.

With regard to the coupling processes, the dissociation of the binuclear complex [(**1**-H)$_2$Cu$_2$(NO_3)]$^+$ is important. It has been proposed that in such complexes, the coupling reaction takes place.[28] However, the CID of [(**1**-H)$_2$Cu$_2$(NO_3)]$^+$ shows the elimination of HNO_3 as the major channel, which has been confirmed by control experiments with other isotopic ions of [(**1**-H)$_2$Cu$_2$(NO_3)]$^+$ (Fig. S2a, supplementary material). This type of fragmentation is observed also for the dissociation of the analogous binuclear complex of methyl-3-hydroxy-2-naphthoate; however, in that case, it represents only a minor channel. Thus, it seems that hydrogen available from the amide group in **1** causes the preference for the elimination of HNO_3 with respect to the coupling reaction. The second most abundant fragmentation of [(**1**-H)$_2$Cu$_2$(NO_3)]$^+$ leads to a cluster cleavage to yield [(**1**-H)Cu]$^+$ and [(**1**-H)Cu(NO_3)], and finally also elimination of the radical (**1**-H)$^\cdot$ can be identified. Thus, it appears that the cross-coupling reaction is too slow to occur in the time-window of the experiment.

ESI of the solution of **1** and Cu(OH)Cl·TMEDA in the mixture methanol/CH_2Cl_2/H_2O yields a variety of ions (Fig. S3, supplementary material), among which a complex with the composition [(**1**-H)Cu(TMEDA)]$^+$ (*m/z* 441) is dominant. Relevant complexes containing two copper ions and two units of **1** are represented by [(**1**-H)$_2$Cu$_2$Cl(TMEDA)]$^+$ (*m/z* 801) and [(**1**-H)$_2$Cu$_2$Cl(TMEDA)$_2$]$^+$ (*m/z* 917). With increasing time of the experiment also, signal corresponding formally to {[(**1**$_2$-3H)Cu(TMEDA)]}$^+$ (*m/z* 702) appears, which most probably represents the complex [(**3**-H)Cu(TMEDA)]$^+$ of the binol **3** formed in the solution.

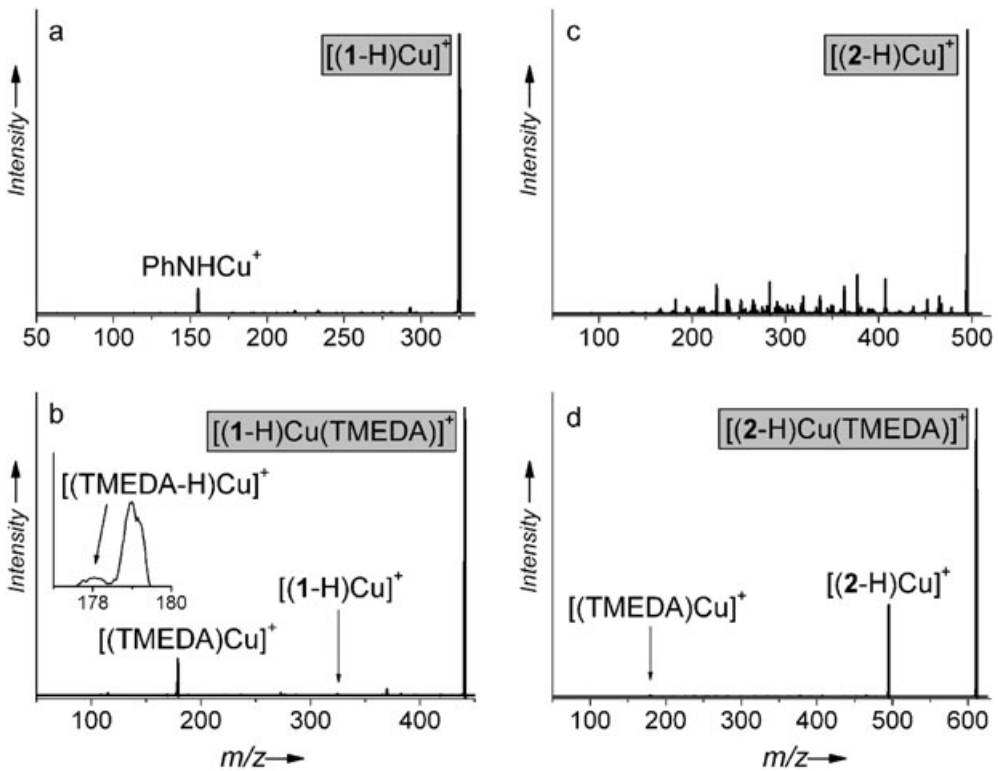


Figure 1. CID spectra of (a) [(**1**-H)Cu]$^+$, (b) [(**1**-H)Cu(TMEDA)]$^+$, (c) [(**2**-H)Cu]$^+$, and (d) [(**2**-H)Cu(TMEDA)]$^+$. Collision energies in the center-of-mass frame were 2.9 eV, 3.4 eV, 3.1 eV, and 2.7 eV, respectively; collision gas: xenon

The CID experiment with mass-selected [(**1**-H)Cu(TMEDA)]$^+$ reveals almost exclusive elimination of the (**1**-H)$^\cdot$ radical concomitant with the formation of [Cu(TMEDA)]$^+$ (Fig. 1b). Detailed inspection of the CID spectrum reveals a trace elimination of TMEDA from the parent complex to yield [(**1**-H)Cu]$^+$ ion in a ratio about 1 : 20 with respect to [Cu(TMEDA)]$^+$. Further, also neutral naphthol **1** is eliminated concomitant with the formation of [Cu(TMEDA-H)]$^+$ (insert in Fig. 1b). The degree of localization of the radical site at the carbon atoms is again probed by the reaction with DMDS. The reaction leads dominantly to an exchange of the (**1**-H)$^\cdot$ ligand to form [(DMDS)Cu(TMEDA)]$^+$; as a minor channel, also the adduct [(**1**-H)Cu(TMEDA)(DMDS)]$^+$ is observed. Similar to monocopper complexes without TMEDA, however, no S–S bond activation of DMDS is detected.

As far as the relevant coupling products are concerned, the complex with *m/z* 702, which most probably corresponds to the composition [(**3**-H)Cu(TMEDA)]$^+$, is investigated first. The CID experiment shows a loss of the fragment with $\Delta m/z = 134$, which corresponds to the combined loss of TMEDA and water, as the dominant reaction (Fig. 2a). The so-formed ion (*m/z* 568) can further expel aniline from the amide moiety, which leads to the ion with *m/z* 475. Aniline can also be eliminated in the first step of the fragmentation of the parent ion (formation of the ion with *m/z* 609). In the lower mass region of the CID spectrum, the formation of the complex [Cu(TMEDA)]$^+$ is observed, which corresponds to the loss of the radical (**3**-H)$^\cdot$. All together, the CID spectrum is consistent with the formation of the coupled product **3** in the solution, whose deprotonated form is complexed to copper (Fig. 2a). This suggestion was verified independently by measuring the ESI spectrum of the binol **3** in the presence of Cu(OH)Cl·TMEDA. Thus, the dominant peak in the spectrum corresponds to [(**3**-H)Cu(TMEDA)]$^+$ (*m/z* 702), and the CID spectrum of the mass-selected [(**3**-H)Cu(TMEDA)]$^+$ is identical with that of the corresponding ion generated from the solution of naphthol **1** (Fig. 2a).

For further evaluation of the reactivity, the most important result arises from the comparison of the fragmentations of [(**1**-H)Cu(TMEDA)]$^+$ and [(**3**-H)Cu(TMEDA)]$^+$. While the fragmentation of [(**1**-H)Cu(TMEDA)]$^+$ leads dominantly to the elimination of (**1**-H)$^\cdot$, the coupled product **3** binds much more strongly to the copper center, and the eliminations associated with loss of TMEDA prevail.

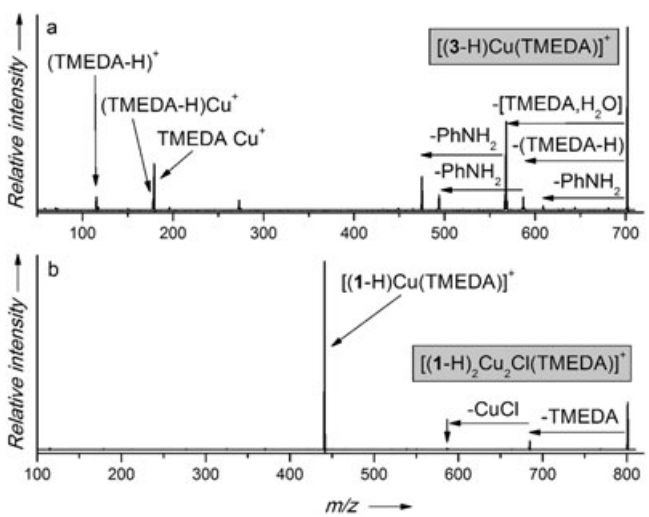


Figure 2. CID spectrum of (a) [(**3**-H)Cu(TMEDA)]$^+$ at $E_{coll} = 3.2$ eV and (b) of [(**1**-H)$_2$Cu$_2$Cl(TMEDA)]$^+$ at $E_{coll} = 1.4$ eV generated by ESI of a $CH_3OH/CH_2Cl_2/H_2O$ solution of **1** and Cu(OH)Cl·TMEDA. Collision energies given in the center-of-mass frame; collision gas: xenon

The complexes [(**1**-H)$_2$Cu$_2$Cl(TMEDA)]$^+$ and [(**1**-H)$_2$Cu$_2$Cl(TMEDA)$_2$]$^+$ have been suggested as those, in which the coupling reaction may proceed.[28,29] The main reactive pathways suggested correspond to eliminations of the corresponding binol and formations of Cu^I complexes [Cu$_2$Cl(TMEDA)]$^+$ and [Cu$_2$Cl(TMEDA)$_2$]$^+$, respectively (Scheme 1). The dominant fragmentation of [(**1**-H)$_2$Cu$_2$Cl(TMEDA)]$^+$ upon CID leads to the cluster cleavage to form [(**1**-H)Cu(TMEDA)]$^+$ and [(**1**-H)CuCl] (Fig. 2b, Scheme 3). This result indicates that the parent ion contains two independent (**1**-H)Cu$^+$ units bound via a chlorine anion and presumably also the TMEDA ligand, but TMEDA can, of course, also bind to one copper center only (only the bridged structure is shown in Scheme 3). The second most abundant peak corresponds to the loss of TMEDA (m/z 686). If the fragmentation would correspond to the uncoupled product, then a loss of (**1**-H)$^\cdot$ should prevail over the loss of TMEDA. We do not observe any loss of (**1**-H)$^\cdot$, and therefore the loss of TMEDA is considered as a sign of the coupling reaction (Scheme 3). In addition, two almost negligible peaks can be discerned *m/z* 587 and m/z 277. The first one corresponds to loss of TMEDA and CuCl, which thus leads to a complex between binol **3** and Cu^I. The second one, even less abundant, corresponds to the formation of [Cu$_2$Cl(TMEDA)]$^+$ (*m/z* 277) and concomitant elimination of the binol **3**.

CID of the larger complex [(**1**-H)$_2$Cu$_2$Cl(TMEDA)$_2$]$^+$ also mainly leads to fragments with only one copper atom, i.e. [(**1**-H)Cu(TMEDA)]$^+$ and [(**1**-H)CuCl(TMEDA)] (Fig. S4 in the Supporting Information). Other channels involve the elimination of the TMEDA ligand, (1-H)$^\cdot$ and the formation of [Cu$_2$Cl(TMEDA)$_2$]$^+$ (*m/z* 393), which most probably reflects the coupling reaction leading to the product **3**.

Finally, the results are complemented by the DFT calculations of complexes containing one copper atom (Fig. 3). For the bare complex [(**1**-H)Cu]$^+$, the most stable structure located indeed corresponds to the isomer with copper bound to both oxygen atoms. The alternative isomer with copper bound to the oxygen atom and the nitrogen atom lies 0.67 eV (65 kJ mol^{-1}) higher in energy. This finding is thus consistent with the interpretation based on the experimental results. Further, we have shown previously that the coordination of copper(II) to phenolate leads to a transfer of an electron and formation of a complex between copper(I) and the phenoxy radical.[31,39] In agreement, all structures located for the [(**1**-H)Cu]$^+$ complex have a negligible localization of an unpaired electron at copper, and the radical site is localized at the naphthoxy unit.

In order to facilitate the computations, we have replaced the TMEDA ligand by ethylene diamine (en) in the theoretical studies. The coordination of the bidentate base to the copper atom of [(**1**-H)Cu]$^+$ is associated with 3.23 eV (312 kJ mol^{-1}) binding energy and leads to a complete change of the electronic structure of the complex. The unpaired electron is localized mostly at copper, whereas the spin density at the aromatic moiety is only negligible. This phenomenon has been shown already earlier for the complex of the phenoxy ligand and copper ([(PhO)CuL$_n$]$^+$). The number *n* of additional ligands L crucially influences the electronic structure of the complex.[40] If copper bears only one additional monodentate ligand, then the complex contains copper(I) and the phenoxy radical. Coordination of more ligands, i.e. ligand field effect, leads to the stabilization of copper (II). Here, copper is coordinated formally from two sides already in the bare complex [(**1**-H)Cu]$^+$, and therefore any additional ligand (or a solvent molecule) will induce the electronic change and diminishment of the radical site at the aromatic ring.[40] This

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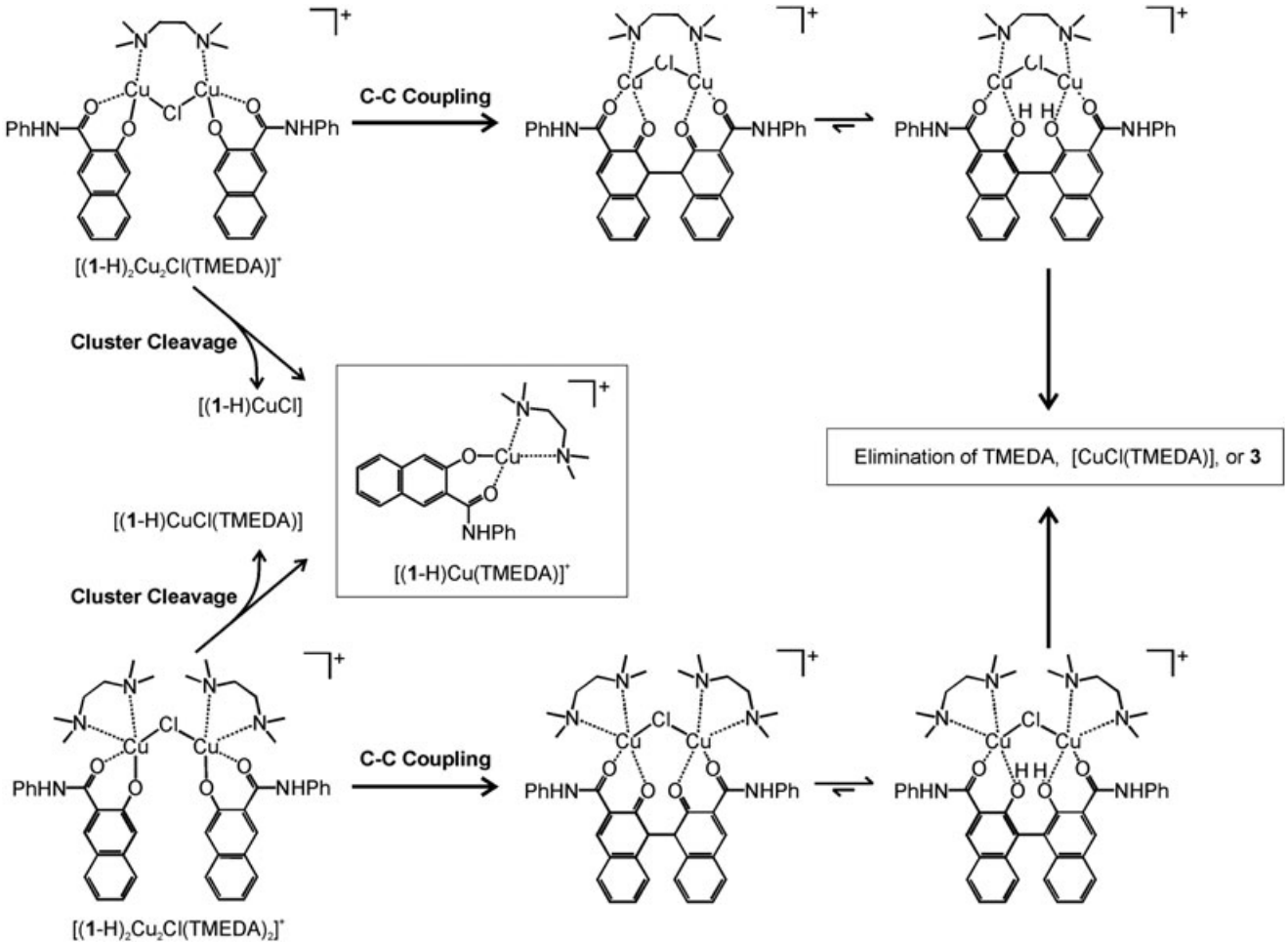

Scheme 3. Fragmentation pathways of $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)]^+$ and $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)_2]^+$. Note that TMEDA can act as a chelating or bridging ligand; only one variant is shown here, but we do not intend to exclude the other possibility

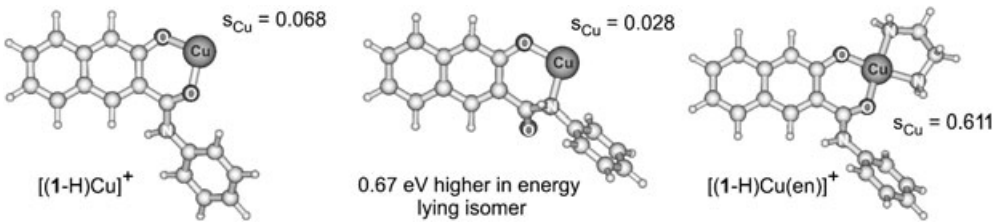

Figure 3. B3LYP/SDD optimized structures of $[(\mathbf{1}\text{-H})Cu]^+$ ($E^{0K} = -1057.028983$ hartree), its isomer lying 0.67 eV (65 kJ mol^{-1}) higher in energy, and the $[(\mathbf{1}\text{-H})Cu(en)]^+$ complex ($E^{0K} = -1247.527204$ hartree)

explains why the complexes of a naphtholate, copper(II), and an additional ligand do not react as carbon-centered radicals.

As mentioned above, the bare complex $[(\mathbf{1}\text{-H})Cu]^+$ also does not show any reactivity as a carbon-centered radical although the theoretical results show that there is a significant carbon-radical character. It can be simply explained by a facile association of the other reactant (e.g. DMDS) to copper, which induces electronic changes and diminishes the spin density at the aromatic moiety. It has to be noted that copper(I) is ideally coordinated by two ligands in the linear arrangement, which cannot be achieved in $[(\mathbf{1}\text{-H})Cu]^+$ simply due to the geometry of **1**. The copper center is therefore in energetically disfavored geometry, and consequently the affinity for additional ligands is high as evidenced by the rather high binding energy with ethylenediamine.

Complexes of 2

ESI of the naphthol **2** and $Cu(NO_3)_2$ dissolved in a mixture of methanol and water yields $[(\mathbf{2}\text{-H})Cu]^+$ (*m/z* 495) as the dominant ion (Fig. S1b, supplementary material). Other relevant ions correspond to the protonated naphthol $\mathbf{2}H^+$, the complex $[(\mathbf{2}\text{-H})(\mathbf{2})Cu]^+$ (*m/z* 928), and finally the binuclear copper complex $[(\mathbf{2}\text{-H})_2Cu_2NO_3]^+$ (*m/z* 1052). The CID of the major ion $[(\mathbf{2}\text{-H})Cu]^+$ shows fragmentation of the crown substituent, in which subsequent losses of C_2H_4 and CH_2O units can be traced out (Fig. 1c). CID of the bisligated ion

$[(\mathbf{2}\text{-H})(\mathbf{2})Cu]^+$ shows exclusive elimination of the neutral naphthol **2** and in contrast to the fragmentation of the analogous complex of **1**, no expulsion of the radical $(\mathbf{2}\text{-H})^{\cdot}$ is observed. The reactions of mass-selected $[(\mathbf{2}\text{-H})Cu]^+$ with CH_3I and CH_3SSCH_3, respectively, lead to only negligible amount of adduct formation without any evidence for the presence of a carbon-centered radical.

The fragmentation of the binuclear copper complex $[(\mathbf{2}\text{-H})_2Cu_2NO_3]^+$ preferentially leads to the cluster cleavage yielding $[(\mathbf{2}\text{-H})Cu]^+$ concomitant with neutral $[(\mathbf{2}\text{-H})CuNO_3]$ (Fig. S2b, supplementary material). Elimination of HNO_3 constitutes a negligible channel, which supports the rationale that the dominance of this channel in the fragmentation of $[(\mathbf{1}\text{-H})_2Cu_2NO_3]^+$ is caused by the hydrogen atom of the amide group of **1**. Finally, again, no indications for the occurrence of the coupling reaction are obtained.

The presence of TMEDA in the mixture leads to an ESI spectrum with TMEDA adducts of $[(\mathbf{2}\text{-H})Cu]^+$, $[(\mathbf{2}\text{-H})Cu(TMEDA)]^+$ (*m/z* 611), and binuclear complex $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)]^+$ (*m/z* 1141) as the dominant signals (Fig. S3b). In addition, also signals corresponding to $[(\mathbf{2}_2\text{-3H})Cu(TMEDA)]^+$ (*m/z* 1042) and $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)_2]^+$ (*m/z* 1257) are observed. At the first sight, the fragmentation of the TMEDA complex $[(\mathbf{2}\text{-H})Cu(TMEDA)]^+$ (Fig. 1d) is fundamentally different from that of the analogous ion $[(\mathbf{1}\text{-H})Cu(TMEDA)]^+$ (Fig. 1b). Elimination of TMEDA is observed as the almost exclusive fragmentation, and only traces of $[(TMEDA)Cu]^+$ can be identified at *m/z* 179. This finding implies that (**2**-H) is much more strongly bound to copper than (**1**-H). It can be explained by a participation of the crown substituent in the bonding of the ligand to copper. In the reactions of $[(\mathbf{2}\text{-H})Cu(TMEDA)]^+$ with CH_3I and CH_3SSCH_3, respectively, not only no bond activation is observed, but the complex even does not form any adducts on contrary to the other studied ions (see above).

The fragmentation of $[(\mathbf{2}_2\text{-3H})Cu(TMEDA)]^+$ exclusively leads to the elimination of TMEDA. In analogy to $[(\mathbf{1}_2\text{-3H})Cu(TMEDA)]^+$, the $(\mathbf{2}_2\text{-3H})$ unit most probably corresponds to the deprotonated coupling product **5**. Fragmentation of the bicopper complex $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)]^+$ leads to a dominant cluster cleavage to form neutral $[(\mathbf{2}\text{-H})CuCl(TMEDA)]$ and $[(\mathbf{2}\text{-H})Cu(TMEDA)]^+$, respectively; the latter ion can subsequently further lose TMEDA (Fig. 4). Other channel leads to the elimination of TMEDA, which however here cannot be ascribed to the coupling reaction, because the uncoupled product also preferentially eliminates the TMEDA ligand. The only channel indicating the coupling reaction thus remains formation of $[(\mathbf{2}\text{-H})_2Cu]^+$ (i.e. $[(\mathbf{5})Cu]^+$), which contains reduced copper(I). The putative dicopper cluster $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)_2]^+$ was not produced in an amount sufficient for studying the mass-selected ions.

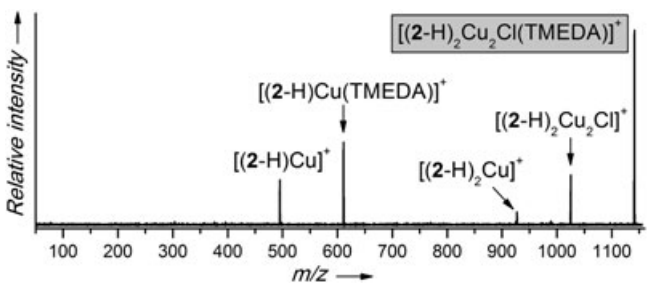

Figure 4. CID spectrum of $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)]^+$ at $E_{coll} = 1.0$ eV (center-of-mass frame) generated by ESI of a $CH_3OH/CH_2Cl_2/H_2O$ solution of **2** and Cu(OH)Cl·TMEDA. Collision gas: xenon

The computational results provide a clear rationale for the observed dramatic differences between the complexation properties of $(\mathbf{1}\text{-H})^-$ and $(\mathbf{2}\text{-H})^-$ toward copper(II). In the most stable geometry found for the $[(\mathbf{2}\text{-H})Cu]^+$ complex, the crown substituent participates in the complexation of copper (Fig. 5) and provides thus a ligand field which stabilizes the whole complex. Due to the coordination from four sides, the copper center stays in the oxidation state II (spin localization on copper amounts to 0.646). For comparison, the most stable isomer, in which the crown substituent does not participate in the complexation of copper, lies 1.74 eV (168 kJ mol^{-1}) higher in energy. As expected for the copper ion being bound only to two oxygen atoms, it is in the reduced + I oxidation state, and the radical site is located at the naphthoxy unit.

Several isomers of $[(\mathbf{2}\text{-H})Cu(en)]^+$ have been found very close in energy. Most interestingly, the additional coordination of copper by the crown substituent does not bring substantial stabilization and is even disfavored entropically (the crown-coordinated isomer is in comparison to the other isomer depicted in Fig. 5 by 0.04 eV (4 kJ mol^{-1}) more stable at 0 K, but 0.11 eV (11 kJ mol^{-1}) less stable at 298 K considering the Gibbs energies). If we consider the high-energy lying isomer of $[(\mathbf{2}\text{-H})Cu]^+$ (the crown substituent does not coordinate to copper), the binding energy to ethylenediamine amounts to 2.93 eV (283 kJ mol^{-1}). Thus, it is slightly smaller than that found for the binding between ethylenediamine and $[(\mathbf{1}\text{-H})Cu]^+$, but in the same energy range. However, if we include the participation of the crown substituent, then the binding energy drops to only 1.19 eV (115 kJ mol^{-1}). Thus, the ability of the crown substituent to coordinate to copper decreases the binding energy of the copper complex to the diamine by about two thirds.

Mixed complexes of 1 and 2

In order to address the questions posed at the outset, mixed complexes of naphthols **1** and **2** generated from their solution with Cu(OH)Cl·TMEDA in methanol/CH_2Cl_2/H_2O were investigated. The relevant mixed complexes obtained correspond to $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-2H})Cu(TMEDA)]^+$ (*m/z* 872), $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)]^+$ (*m/z* 971), and $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)_2]^+$ (*m/z* 1087). The CID spectrum of $\{[(\mathbf{1}\text{-H})(\mathbf{2}\text{-2H})Cu(TMEDA)]\}^+$ reveals a profound loss of the TMEDA ligand, but also a small channel leads to the formation of $[Cu(TMEDA)]^+$. The fragmentation is identical with that of the binol complex $[(\mathbf{4}\text{-H})Cu(TMEDA)]^+$ suggesting again that the coupling reaction takes place in the solution. The spectrum suggests that binol **4** is deprotonated at the unit corresponding to naphthol **2**, and only a small part of ions is deprotonated at the naphthol unit **1** as indicated by a small abundance of $[Cu(TMEDA)]^+$ in the CID spectrum.

The major dissociation of the complex $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)]^+$ corresponds to the formation of $[(\mathbf{1}\text{-H})CuCl]$ and $[(\mathbf{2}\text{-H})Cu(TMEDA)]^+$ (Fig. 6). The second abundant fragmentation leads to the elimination of the $(\mathbf{1}\text{-H})^{\cdot}$ radical from the parent ion. With lower abundances then follow dissociations into $[(\mathbf{1}\text{-H})Cu(TMEDA)]^+$ and $[(\mathbf{2}\text{-H})CuCl]$, $[(\mathbf{1}\text{-H})CuCl(TMEDA)]$, and $[(\mathbf{2}\text{-H})Cu]^+$. This fragmentation pattern demonstrates once more the larger ability of naphthol **2** to bind to copper compared to naphthol **1**. Further, the eliminations of the TMEDA ligand and CuCl(TMEDA) are observed, where the latter witnesses the coupling reaction followed by the cluster cleavage.[43] The loss of TMEDA alone cannot be ascribed to the coupling reaction from the same reason as described above for the

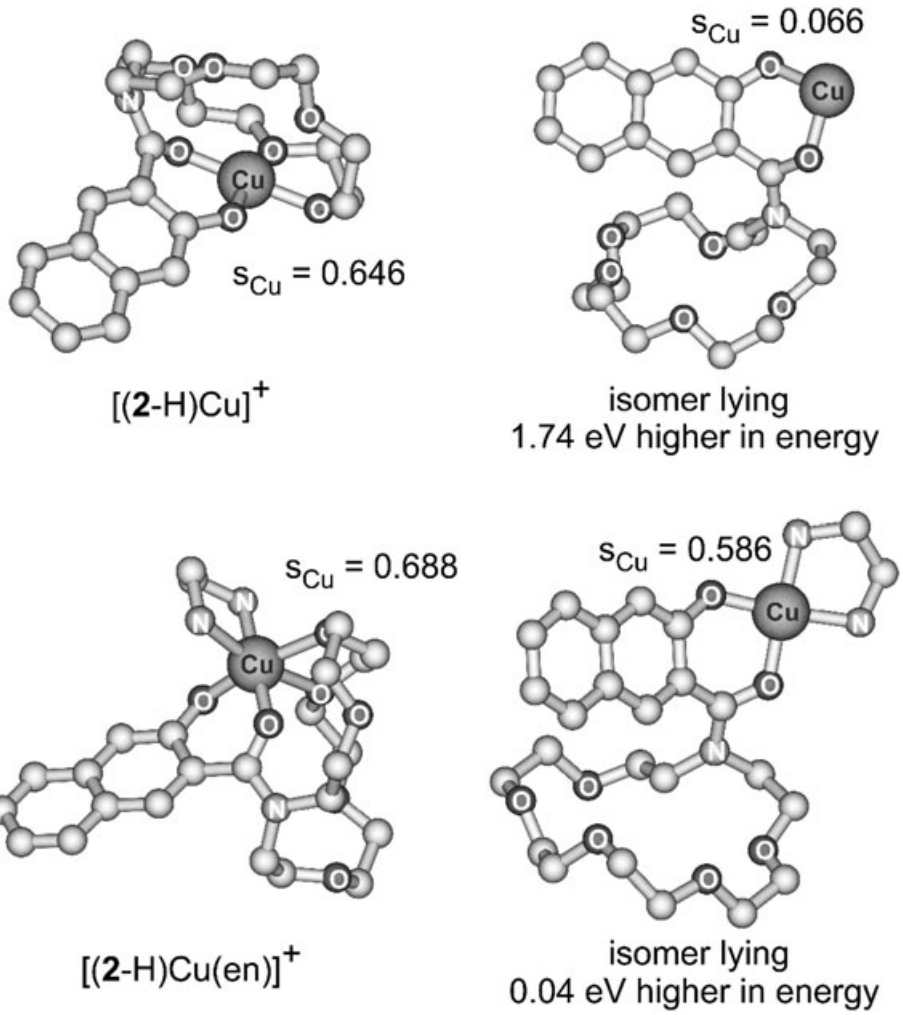

Figure 5. B3LYP/SDD optimized structures of $[(\mathbf{2}\text{-H})Cu]^+$ ($E^{0K} = -1672.276663$ hartree), its isomer lying 1.74 eV (168 kJ mol^{-1}) higher in energy, and their complexes with ethylenediamine $[(\mathbf{2}\text{-H})Cu(en)]^+$ ($E^{0K} = -1862.701699$ hartree). The hydrogen atoms have been removed for the sake of clarity of the figure

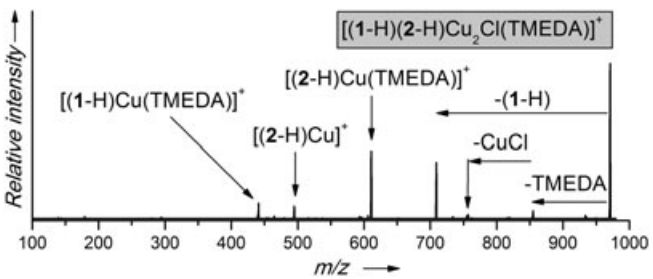

Figure 6. CID spectrum of $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)]^+$ at $E_{coll} = 1.2$ eV (center-of-mass frame) generated by ESI of a $CH_3OH/CH_2Cl_2/H_2O$ solution of **1**, **2**, and Cu(OH)Cl·TMEDA. Collision gas: xenon

fragmentation of $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)]^+$. Fragmentation of the larger complex with two TMEDA ligands, $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)_2]^+$, leads dominantly to the loss of one TMEDA ligand (Fig. S5). Further fragmentation proceeds in analogy to that of $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)]^+$.

Comparison of the spectra of $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)]^+$, $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)]^+$, and $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)]^+$ reveals one major difference observed for the mixed complex. In the homo complexes $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)]^+$ and $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)]^+$, no eliminations of the $(\mathbf{1}\text{-H})^{\cdot}$ and $(\mathbf{2}\text{-H})^{\cdot}$ radicals are observed. From the fragmentation of the mononuclear complex $[(\mathbf{1}\text{-H})Cu(TMEDA)]^+$, we know that the $(\mathbf{1}\text{-H})^{\cdot}$ radical can be formed via the homolytical cleavage of the copper–oxygen bond (see above). For the binuclear complex $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)]^+$, however, the cluster cleavage is more facile than the one-electron oxidation of $(\mathbf{1}\text{-H})^-$, which is hence completely suppressed, and the two electron oxidation leading to the coupling is observed only as a minor channel (eliminations of TMEDA and [CuCl(TMEDA)]). Oxidation of $(\mathbf{2}\text{-H})^-$ is much more difficult, (c.f. Fig. 1d) and again for the binuclear cluster $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)]^+$, only the concerted two electron oxidation evidenced by the elimination of CuCl(TMEDA) is observed.

For the mixed complex $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)]^+$, the second most abundant channel corresponds to the elimination $(\mathbf{1}\text{-H})^{\cdot}$. This evidences a larger stability of the mixed binuclear complex compared to $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)]^+$. We note in passing that the stability of the binuclear clusters have a correlation with the yield in the coupling reaction and can hence contribute here to the preferential cross-coupling reaction.[28]

If we take into the account also binuclear complexes with two TMEDA ligands, then the elimination of the (**1**-H)· radical is observed also for $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)_2]^+$ and $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)_2]^+$ (Figs. S4 and S5). The homonuclear $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)_2]^+$ cluster appears as the most reactive towards the coupling reaction among the investigated complexes as we observe not only the one-electron oxidation of the substrate, but also direct elimination of (**1**-H)$_2$ (i.e. **3**) from the cluster (i.e. two-electron oxidation) as a significant channel. Hence, next to the electronic and stability properties of the clusters, also other factors have to play a role in the preferential cross-coupling reaction. We have clearly shown that naphthol **2** has a substantially larger affinity to copper ions than naphthol **1**. Thus, in an equimolar mixture of **1**, **2**, and Cu(OH)Cl·TMEDA, most of the copper ions will be complexed by **2**. For the occurrence of the coupling reaction, a binuclear cluster has to be formed. Formation of binuclear clusters $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)]^+$ will be statistically disfavored, because most of the copper ions are bound to **2**. On the other hand, formation of $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)]^+$ in solution may be slowed down due to the steric reasons and the cluster is little reactive. As a result, the mixed binuclear clusters $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)]^+$ may represent a compromise in the abundance and the reactivity, which finally leads to the preferential cross-coupling.

CONCLUSIONS

It is shown that the complexation properties of deprotonated amides of 2-hydroxy-3-naphthoic acids **1** and **2** toward copper completely differ. The naphtholate (**1**-H)$^-$ binds to copper(II) as a bidentate ligand via both oxygen atoms. On the other hand, due to the crown substituent of (**2**-H)$^-$, copper(II) binds not only to the two oxygen atoms of the naphtholate moiety, but it is also coordinated by the crown backbone. Consequently, the binding of (**2**-H)$^-$ to copper(II) is much stronger than that of (**1**-H)$^-$.

The reactivities of the copper complexes $[(\mathbf{1}\text{-H})Cu(TMEDA)]^+$ and $[(\mathbf{2}\text{-H})Cu(TMEDA)]^+$ differ. While the former is prone to the one-electron oxidation, the latter is not. This is also reflected in the reactivities of the binuclear clusters $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)_x]^+$, $[(\mathbf{2}\text{-H})_2Cu_2Cl(TMEDA)]^+$, and $[(\mathbf{1}\text{-H})(\mathbf{2}\text{-H})Cu_2Cl(TMEDA)_x]^+$ ($x = 1,2$). The homonuclear $[(\mathbf{1}\text{-H})_2Cu_2Cl(TMEDA)_2]^+$ complex appears as the most reactive one. The preferential cross-coupling can hence be explained based on an interplay between the larger abundance of the copper complexes $[(\mathbf{2}\text{-H})Cu(TMEDA)]^+$ (based on the larger binding energy) and the larger reactivity of $[(\mathbf{1}\text{-H})Cu(TMEDA)]^+$.

The effect of TMEDA consists in a strong binding to the complexes of copper and the naphtholates. The coordination of TMEDA to copper stabilizes its oxidation state + II (i.e. the unpaired electron is localized at copper) and thereby decreases the reactivity of the copper complexes of naphtholates for the reactions as carbon-centered radicals. Hence, it suppresses the reactivity of $[(\mathbf{1}\text{-H})Cu(TMEDA)]^+$ which thus does not react directly with another naphthol molecule present in the reaction mixture (i.e. formation of statistical distribution of products would be expected), but instead implies a necessity of formation of *ad hoc* binuclear clusters in order to promote the coupling reaction. As explained above, the necessity of cluster formation results in the preferential cross-coupling for this reaction system.

METHODS

Mass-spectrometric experiments

The experiments were performed with a TSQ Classic mass spectrometer which has been described previously.[44,45] Briefly, the TSQ Classic consists of an ESI source combined with a tandem mass spectrometer of QOQ configuration (Q stands for quadrupole and O for octopole). The investigated ions were generated by ESI of solutions of the precursor naphthols in CH_2Cl_2/CH_3OH, to which either Cu(OH)Cl·TMEDA or $Cu(NO_3)_2$ dissolved in water was added. The first quadrupole was used as a mass filter to scan the spectrum of the ions produced upon ESI or to select particular ions of interest. The Q1-selected ions were then guided through the octopole serving as a collision chamber followed by mass analysis of the ionic reaction products by means of the second quadrupole and subsequent detection. Reagent or collision gases were leaked into the octopole at typical pressures in the order of 10^{-4} mbar. The origin of the collision energy scale was determined using retarding potential field analysis.[45]

Computational details

The computational DFT study was performed using the B3LYP[46–49] functional together with the SDD basis set as implemented in the Gaussian 03 package.[50–53] For all optimized structures, frequency analyses at the same level of theory are used in order to assign them as genuine minima or transition structures on the potential-energy surface as well as to calculate zero-point vibrational energies. The relative energies refer to energies at 0 K. The search for the minima has been restricted to several conformers. We intend to show the trends here rather than an exhaustive conformational search for global minima, which would be rather demanding for the given system. The reported spin localizations at copper atoms were obtained from Mulliken population analysis.

Preparative experiment

To a mixture of amide **1** (60.4 mg; 2.3×10^{-4} mol) and amide **2** (99.5 mg; 2.3×10^{-4} mol) in dichloromethane (10 ml), Cu(OH)Cl·TMEDA (53.3 mg; 2.3×10^{-4} mol) was added, and the mixture was stirred for 71 h at room temperature under the oxygen atmosphere. The mixture was washed with 6 M-HCl, water, and 5% aqueous $NaHCO_3$, and the dichloromethane solution was dried over $MgSO_4$. The drying agent was filtered off, and the solvent was evaporated. The residue was subjected to a column chromatography (SiO_2; eluent: ethylacetate-acetone-ethanol-water 19:3:2:1) giving products **3** (20 mg; 16%), **4** (116 mg; 73%), and **5** (11 mg; 5%). The characterization of the compounds is given in the Supporting Information.

Analytical experiment

Prior to the analytical study, high-performance liquid chromatography (HPLC) analytical conditions for separation of compounds **1–5** were optimized, and absorption coefficients of all compounds at $\lambda = 254$ nm were obtained in order to be able to re-calculate a peak area into a compound quantity. A reaction was monitored by means of HPLC on a Discovery C18 column using an eluent gradient from the methanol – water 70:30 mixture to neat methanol (flowrate 1 ml/min).

To a solution of equimolar mixture of amides **1** and **2** (1.5×10^{-5} mol) in dichloromethane (7 ml), one molar equivalent

of Cu(OH)Cl·TMEDA was added, and the reaction mixture was stirred at room temperature under the oxygen atmosphere. A sample of reaction mixture (2 mg) was diluted with methanol (1 ml), and this solution (10 μl) was injected onto the HPLC column. A progress of the reaction was monitored until the starting amides disappeared. The reaction was finished after 20 h with the products molar ratios **3** : **4** : **5** = 9 : 82 : 9.

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REFERENCES

[1] J. M. Brunel, *Chem. Rev.* **2005**, *105*, 857 and references therein.
[2] Y. Chen, S. Yekta, A. K. Yudin, *Chem. Rev.* **2003**, *103*, 3155 and references therein.
[3] P. Kočovský, Š. Vyskočil, M. Smrčina, *Chem. Rev.* **2003**, *103*, 3213 and references therein.
[4] R. Noyori, I. Tomino, Y. Tanimoto, *J. Am. Chem. Soc.* **1979**, *101*, 3129.
[5] J. Doussot, A. Guy, C. Ferroud, *Tetrahedron Lett.* **2000**, *41*, 2535.
[6] S.-W. Hon, C.-H. Li, J.-H. Kuo, N. G. Barhate, Y.-H. Liu, Y. Wang, C.-T. Chen, *Org. Lett.* **2001**, *3*, 869.
[7] C.-Y. Chu, D.-R. Hwang, S.-K. Wang, B. J. Uang, *Chem. Commun.* **2001**, 980.
[8] Z. Luo, Q. Liu, L. Gong, X. Cui, A. Mi, Y. Jiang, *Chem. Comm.* **2002**, 914.
[9] Z. Luo, Q. Liu, L. Gong, X. Cui, A. Mi, Y. Jiang, *Angew. Chem. Int. Ed.* **2002**, *41*, 4532.
[10] H. Somei, Y. Asano, T. Yoshida, S. Takizawa, H. Yamataka, H. Sasai, *Tetrahedron Lett.* **2004**, *45*, 1841.
[11] Q.-X. Guo, Z.-J. Wu, Z.-B. Luo, Q.-Z. Liu, J.-L. Ye, X.-W. Luo, L.-F. Cun, L.-Z. Gong, *J. Am. Chem. Soc.* **2007**, *129*, 13927.
[12] S. Takizawa, T. Katayama, H. Somei, Y. Asano, T. Yoshida, C. Kameyama, D. Rajesh, K. Onitsuka, T. Suzuki, M. Mikami, H. Yamataka, D. Jayaprakash, H. Sasai, *Tetrahedron* **2008**, *64*, 3361.
[13] H. Egami, T. Katsuki, *J. Am. Chem. Soc.* **2009**, *131*, 6082.
[14] K. Yamamoto, H. Fukishima, Y. Okamoto, K. Hatada, M. Nakazaki, *J. Chem. Soc., Chem. Commun.* **1984**, 1111.
[15] B. Feringa, H. Wynberg, *Tetrahedron Lett.* **1977**, 4447.
[16] For the case of simplicity, let us use term "binol compounds" for BINOL and also its derivates as well as term "naphthol" for **1** and **2**.
[17] M. Nakajima, I. Miyoshi, K. Kanayanma, S. Hashimoto, M. Noji, K. Koga, *J. Org. Chem.* **1999**, *64*, 2264.
[18] X. Li, J. Yang, M. C. Kozlowski, *Org. Lett.* **2001**, *3*, 1137.
[19] M. Matsushita, K. Kamata, K. Yamaguchi, N. Mizuno, *J. Am. Chem. Soc.* **2005**, *127*, 6632.
[20] M. Smrčina, J. Poláková, Š. Vyskočil, P. Kočovský, *J. Org. Chem.* **1993**, *58*, 4534.
[21] L. Xiaolin, J. B. Hewgley, C. A. Mulrooney, J. Yang, M. C. Kozlowski, *J. Org. Chem.* **2003**, *68*, 5500.
[22] H. Wang, *Chirality* **2010**, *22*, 827.
[23] K. Yamamoto, H. Yumioka, Y. Okamoto, H. Chikamatsu, *J. Chem. Soc., Chem. Commun.* **1987**, *168*.
[24] M. Hovorka, J. Günterová, J. Závada, *Tetrahedron Lett.* **1990**, *31*, 413.
[25] M. Hovorka, R. Scigel, J. Günterová, M. Tichý, J. Závada, *Tetrahedron* **1992**, *48*, 9503.
[26] M. Smrčina, Š. Vyskočil, B. Máca, M. Polášek, T. Claxton, A. P. Abbott, P. Kočovský, *J. Org. Chem.* **1994**, *59*, 2156.
[27] J. B. Hewgley, S. S. Stahl, M. C. Kozlowski, *J. Am. Chem. Soc.* **2008**, *130*, 12232.
[28] J. Roithová, D. Schröder, *Chem. Eur. J.* **2008**, *14*, 2180.
[29] J. Roithová, P. Milko, *J. Am. Chem. Soc.*, **2010**, *132*, 281.
[30] P. Yan, Y. Sugiyama, Y. Takahashi, H. Kinemuchi, T. Temma, S. Habaue, *Tetrahedron* **2008**, *64*, 4325.
[31] P. Milko, J. Roithová, N. Tsierkezos, D. Schröder, *J. Am. Chem. Soc.* **2008**, *130*, 7186.
[32] M. Noji, M. Nakajima, K. Koga, *Tetrahedron Lett.* **1994**, *35*, 7983.
[33] Note that the preparative and analytic experiments were done at different concentrations, which is most probably responsible for different relative yields. Moreover, the preparative experiment is influenced by the efficiency of the product isolation. Products **4** and **5** contain the crown substituent, which might lead to higher losses during the purification of the products.
[34] For selected mass-spectrometric mechanistic studies see: L. S. Santos, C. H. Pavam, W. P. Almeida, F. Coelho, M. N. Eberlin, *Angew. Chem. Int. Ed.* **2004**, *43*, 4330.
[35] For a selected mass-spectrometric mechanistic study see: T. Waters, G. N. Khairallah, S. A. S. Y. Wimala, Y. C. Ang, R. A. J. O'Hair, A. G. Wedd, *Chem. Comm.* **2006**, 4503.
[36] For a selected mass-spectrometric mechanistic study see: B. Chiavarino, R. Cipollini, M. E. Crestoni, S. Fornarini, F. Lanucara, A. Lapi, *J. Am. Chem. Soc.* **2008**, *130*, 3208.
[37] For a selected mass-spectrometric mechanistic study see: S. Torker, D. Merki, P. Chen, *J. Am. Chem. Soc.* **2008**, *130*, 4808.
[38] For a selected mass-spectrometric mechanistic study see: W. Schrader, P. P. Handayani, J. Zhou, B. List, *Angew. Chem. Int. Ed.* **2009**, *48*, 1463.
[39] P. Milko, J. Roithová, D. Schröder, J. Lemaire, H. Schwarz, M. C. Holthausen, *Chem. Eur. J.* **2008**, *14*, 4318.
[40] E. Rezabal, L. Ducháčková, P. Milko, M. C. Holthausen, J. Roithová, *Inorg. Chem.* **2010**, *49*, 8421.
[41] A. M. Lamsabhi, M. Alcamí, O. Mó, M. Yáñez, J. Tortajada, *Chemphyschem* **2004**, *5*, 1871.
[42] K. M. Stirk, J. C. Orlowski, D. T. Leeck, H. I. Kenttämaa *J. Am. Chem. Soc.* **1992**, *114*, 8604.
[43] There is a small interference with the elimination of CuCl(TMEDA) from $[(\mathbf{4}\text{-}2H)Cu_2Cl(TMEDA)]^+$ containing one heavier isotope of Cu or Cl, but the major part of the CuCl(TMEDA) loss evidences the coupling reaction.
[44] J. Roithová, D. Schröder, *Phys. Chem. Chem. Phys.* **2007**, *9*, 713.
[45] L. Ducháčková, J. Roithová, *Chem. Eur. J.* **2009**, *15*, 13399.
[46] S. H. Vosko, L. Wilk, M. Nusair, *Can. J. Phys.* **1980**, *58*, 1200.
[47] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785.
[48] A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098.
[49] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648.
[50] M. J. Frisch, *et al. Gaussian 03, Revision C.02*, Gaussian, Inc., Wallingford CT, **2004**.
[51] For other B3LYP calculations on copper complexes see: M. Alcamí, L. Alberto, O. Mó, M. Yánez, J. Tortajada, B. Amekraz, *B. Chem. Eur. J.* **2004**, *10*, 2927.
[52] For other B3LYP calculations on copper complexes see: J. DeChancie, O. Acevedo, J. D. Evanseck, *J. Am. Chem. Soc.* **2004**, *126*, 6043.
[53] For other B3LYP calculations on copper complexes see: A. Poater, X. Ribas, A. Llobet, L. Cavallo, M. Sola, *J. Am. Chem. Soc.* **2008**, *130*, 17710.