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Multidentate 1,2,3-Triazole-Containing Chelators from Tandem Deprotection/Click Reactions of (Trimethylsilyl)alkynes and Comparison of Their Ruthenium(II) Complexes

James T. Fletcher,* Benjamin J. Bumgarner, Nicole D. Engels, and David A. Skoglund

Department of Chemistry, Creighton University, Omaha, Nebraska 68178

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Summary: A variation of the copper-catalyzed Huisgen 1,3-dipolar cycloaddition involving a one-pot two-step transformation of trimethylsilyl-protected alkyne reactants was used to prepare multidentate N-heterocyclic chelators containing 1,2,3-triazole rings in high yields. This includes the first reported examples of 1,1′-disubstituted 4,4′-bis(triazole) bidentate chelators derived from click preparations.

The N-heterocyclic chelators 2,2′-bipyridine (bpy) and 2,2′:6′,2″-terpyridine (tpy) have been widely studied, due to their predictable coordination environments and the interesting optoelectronic properties that can result from ligand−metal interactions. Such qualities can be exploited for supramolecular assembly, molecular electronics, and catalysis applications,[1] each often requiring the peripheral incorporation of synthetic handles for physical property manipulation or incorporation into functional systems. Because functionalization of polypyridine-based chelators can be synthetically demanding,[2] it remains important to seek new approaches in the preparation of analogous multidentate chelating motifs that also possess well-defined coordination properties and can be prepared and modified with high efficiency.

The increasingly popular click chemistry approach to covalent modification has demonstrated that 1,2,3-triazole rings can be readily introduced to a wide range of chemical environments.[3] While this has repeatedly proven useful in covalently attaching two organic units in numerous applications, significantly fewer studies have examined physical properties derived from the resulting 1,2,3-triazole ring itself, a nitrogen-containing aromatic heterocycle attractive for chelating applications.[4] Only recently have reports begun to describe the development of organometallic complexes utilizing 1,2,3-triazole rings as chelating components. This includes tridentate 2,6-bis(1,2,3-triazol-4-yl)pyridines, which have been shown to form stable Cu(I), Ru(II), Fe(II), and Eu(III) complexes,[4a,5] as well as bidentate 2-(1,2,3-triazol-4-yl)pyridines, which have been shown to form mixed Ru(II) complexes[6] and display metallochromic properties.[7] As evidenced in the numerous recent reports involving the coordination chemistry of 1,2,3-triazole-containing chelators, using a click approach not only provides access to new chelator identities but also enables the production of such chelators in high yields and facilitates structure−property relationship studies by simple variation of chelator functionalization.

1,2,3-Triazole-containing multidentate chelators are typically prepared from standard aqueous click reaction conditions: a regioselective Cu-catalyzed Huisgen 1,3-dipolar cycloaddition between terminal alkyne and azide reactants. We describe herein the development of a new variation of this click reaction involving a tandem trimethylsilyl-deprotection/click reaction, which not only improves the synthetic efficiency of preparing previously reported bidentate and tridentate chelator motifs but also enables the synthesis of a bis(triazole) bidentate chelator directly from commercially available 1,4-bis(trimethylsilyl)butadiyne, adding a new member to this important family of multidentate chelators.

The chemical orthogonality of the Cu-catalyzed Huisgen 1,3-dipolar cycloaddition makes it amenable to multistep one-pot click reaction development, several examples of which have recently been reported.[8] With the goal of establishing a multistep one-pot approach for preparing 1,2,3-triazole-containing multidentate chelators, it was found that simple addition of K_2CO_3 to standard aqueous click reaction conditions led to the formation of desired chelator products from trimethylsilyl-protected ethynylpyridine reactants (Scheme 1). This tandem deprotection/

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* To whom correspondence should be addressed. E-mail: jamesfletcher@creighton.edu.

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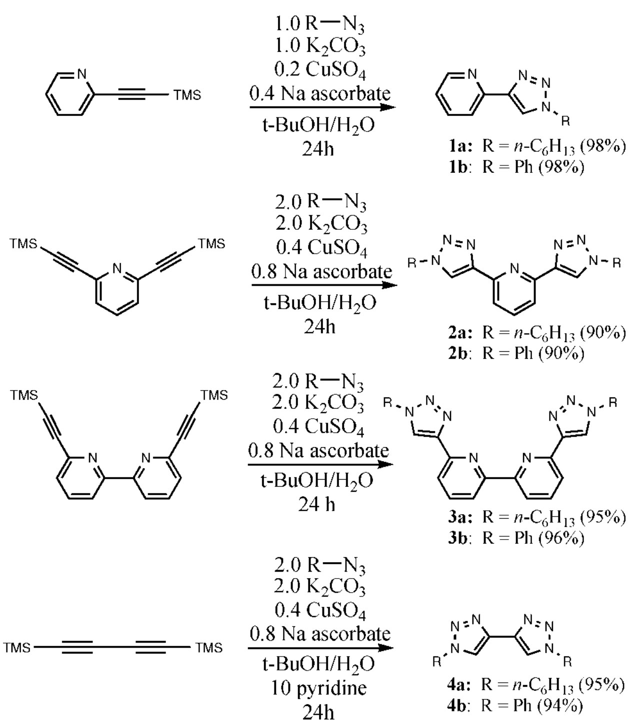
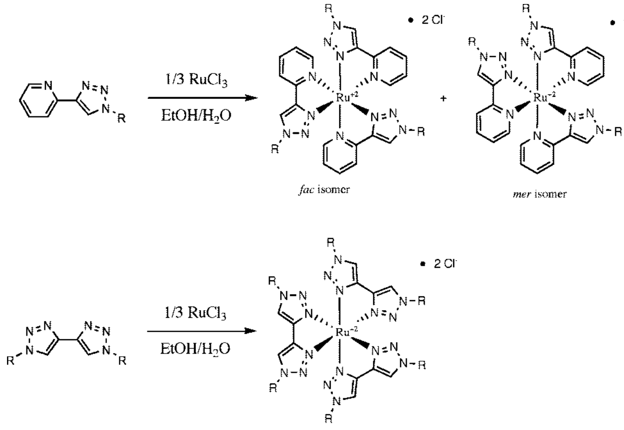
10.1021/om800768k CCC: $40.75

Scheme 1. Chelator Synthesis[9]



Scheme 2. Synthesis of Ru(II) Bidentate Complexes[14]



click transformation utilizes the commonly employed H_2O/t-BuOH solvent system and requires no special exclusion of oxygen. As arylalkynes are commonly prepared from their trimethylsilyl-protected precursors, this method circumvents the need to isolate intermediate alkyne products.

Using this general deprotection/click approach, analogues of previously reported chelator motifs **1** and **2**, as well as the previously unreported tetradentate **3**, were each prepared in near-quantitative yields from multistep one-pot transformations. This simple modification of standard click reaction conditions was successful using both alkyl (derivatives **a**) and aryl (derivatives **b**) azides. (Trimethylsilyl)alkynes have been shown to direct the preferential formation of 1,5-disubstituted 1,2,3-triazoles,[10] but under the tandem deprotection/click reaction conditions no evidence of trimethylsilyl incorporation or 1,5-regioisomer formation was observed. It appears that deprotection is the rate-limiting step of this two-step process, as only triazole product and trimethylsilyl-protected reactants (and not terminal alkyne intermediate products) are observed in incomplete reaction mixtures.

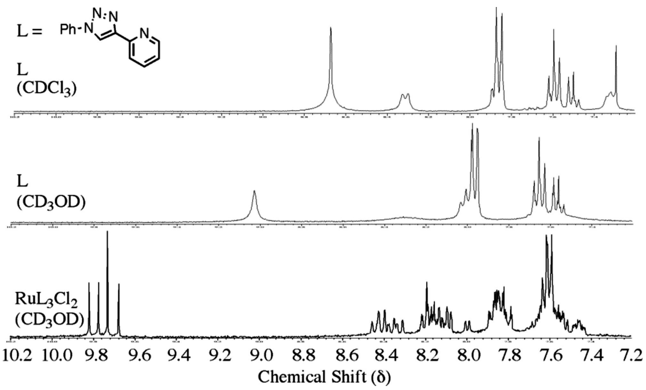


Figure 1. ^{1}H NMR spectra of **1b** and its Ru(II) complex.

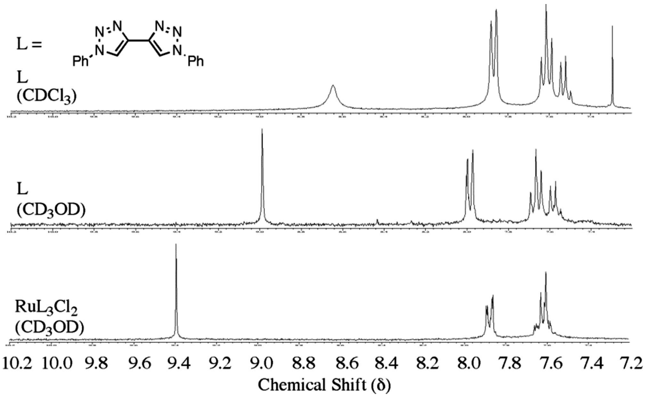


Figure 2. ^{1}H NMR spectra of **4b** and its Ru(II) complex.

While one advantage of this approach is its removal of an intervening step in the synthesis of the desired chelators (particularly pertinent for those analogues not commercially available as terminal alkynes), it also enables the preparation of molecules that would be synthetically impractical using traditional click reaction conditions that employ terminal alkyne reactants. For example, the 4,4′-bis(triazole) analogues **4a**,**b** were prepared in high yields directly from commercially available 1,4-bis(trimethylsilyl)butadiyne. Because this reagent is a solid, it has a practical advantage over its terminal alkyne equivalent, butadiyne, which is a flammable gas under ambient conditions. 1,1′,5,5′-tetrasubstituted 4,4′-bis(triazole) rings have been reported only as minor impurities in organometallic click reactions,[11] while 1,1′,4,4′-tetrasubstituted 5,5′-bis(triazoles) (which are unable to coordinate in a bidentate manner) can also be prepared using modified click conditions.[12] Interestingly, the pyridine ring in each reactant used to synthesize **1**−**3** was essential for promoting the two-step one-pot transformations, as the synthesis of **4** from 1,4-bis(trimethylsilyl)butadiyne was unsuccessful without the addition of pyridine itself to the reaction mixture.

We then sought to compare the coordination properties of **4** with those of the pyridine-containing **1**−**3** and determine how

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(9) Typical chelator synthesis: to a 20 mL screw-top vial was added 2-(trimethylsilylethynyl)pyridine (175 mg, 1.0 mmol), azidobenzene (119 mg, 1.0 mmol), $CuSO_4$ (32 mg, 0.2 mmol), sodium ascorbate (79 mg, 0.4 mmol), K_2CO_3 (136 mg, 1.0 mmol), *tert*-butyl alcohol (5 mL), and H_2O (5 mL). The mixture was stirred rapidly for 24 h and then extracted between CH_2Cl_2 and 5% NH_4OH (aqueous). The organic layer was dried over $MgSO_4$, and gravity-filtered, and the volatiles were removed via rotary evaporation to give **1b** as a white solid (218 mg, 98%).

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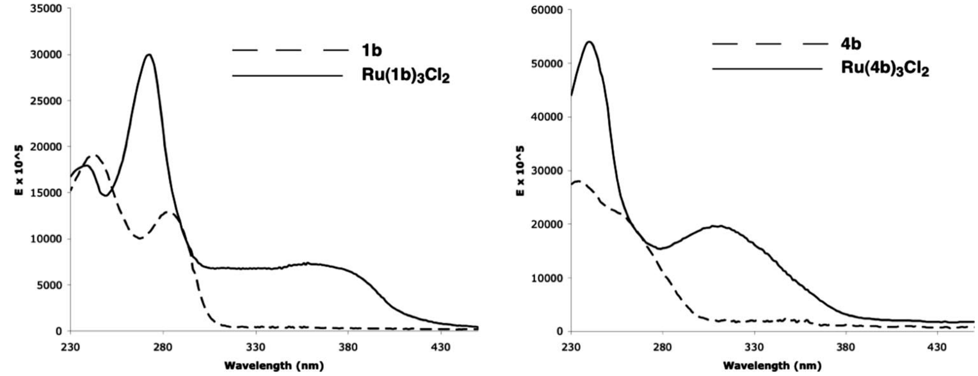

Figure 3. UV−visible absorption spectra in methanol of chelators **1b** and **4b** (dashed lines) and their Ru(II) dichloride complexes (solid lines).

chelator identity influences the physical properties of Ru(II) complexes within this family of 1,2,3-triazole analogues. Each chelator was refluxed with a requisite stoichiometry of $RuCl_3$ in $EtOH/H_2O$. Tridentate chelators **2a**,**b** each formed octahedral Ru(**2**)$_3$Cl$_2$ products analogous to similar tridentate Ru(II) complexes previously reported.[5] Chelators **3a**,**b** did not cleanly form 1:1 ruthenium coordination complexes but, rather, produced insoluble black precipitates indicative of oligomerization products, a common problem for tetradentate chelators such as 2,2′:6′,2″:6″,2‴-quaterpyridine due to rotation about the bipyridyl bond during complexation.[13] Future studies will examine the ability of motif **4** to serve as a bis-bidentate chelating bridge.

Surprisingly, while mixed-chelator complexes of **1** are known,[6] symmetrical Ru(**1**)$_3^{2+}$ complexes have not yet been described. Both Ru(**1**)$_3$Cl$_2$ complexes were prepared in high yield via simple reflux of 3:1 chelator−$RuCl_3$ mixtures (Scheme 2).[14] On examination of the ^{1}H NMR spectra of Ru(**1a**)$_3$Cl$_2$ and Ru(**1b**)$_3$Cl$_2$, it is evident that two different complexes are formed, due to the asymmetry of the bidentate chelator **1**. The ratio of isomers is most readily measured by the ratio of the triazole ring singlets (a set of three unique triazole signals from the *mer* coordination complex versus one signal from the *fac* coordination complex) (Figure 1). For both alkyl- and aryl-substituted complexes of **1**, an essentially statistical mixture of the two complexes was obtained. In contrast, Ru(**4a**)$_3$Cl$_2$ and Ru(**4b**)$_3$Cl$_2$ show simple sets of peaks indicative of the presence of only a single coordination environment, with the triazole singlet simply shifting downfield upon Ru(II) complexation (Figure 2).[15]

The optoelectronic properties of the octahedral Ru(II) complexes in this series were found to be sensitive to the iteration of 1,2,3-triazole and pyridine units. Relative to the chelators themselves, the complexes display lower energy absorption bands indicative of metal−ligand electronic communication between metal d and chelator π* orbitals (Figure 3).[16] These bands appear at significantly higher energies than for analogous Ru(bpy)$_3^{2+}$ and Ru(tpy)$_2^{2+}$ complexes. Unlike bpy and tpy derivatives, none of the complexes examined are strongly colored, nor do they display measurable fluorescence signals at room temperature.

Table 1. Cyclic Voltammetry Analysis of Ru(L)$_3$Cl$_2$ Complexes[a]

L	$E_{ox,1}$	$E_{red,1}$	$E_{ox,1} - E_{red,1}$
1a	1325	−1820	3145
1b	1390	−1900[b]	3290
4a	1350	<−2300	>3650
4b	1490	<−2300	>3790
bpy	1315	−1345	2660

[a] Conditions: 1 mM in CH_3CN, 0.1 M $TBABF_4$, glassy carbon working electrode, Ag counter electrode, 500 mV/s scan rate. All values are relative to SCE and are given in mV. bpy = 2,2′-bipyridine. [b] Irreversible signal.

The Ru(II) complexes of bidentate chelators **1** and **4** were further analyzed via cyclic voltammetry (Table 1). Ligand-centered reductions for Ru(**1a**)$_3$Cl$_2$ and Ru(**1b**)$_3$Cl$_2$ were observed, while analogous reductions of Ru(**2a**)$_3$Cl$_2$ and Ru(**2b**)$_3$Cl$_2$ were not seen within the electrochemical window of the experiment. As pyridine rings are successively replaced with 1,2,3-triazole rings within the octahedral Ru(II) coordination sphere in this series, the reduction potentials of the complexes occur at much more negative potentials. This can be attributed to the higher π* energy level of the electron-rich 1,2,3-triazole ring relative to pyridine affecting the ligand-centered reductions. The metal-centered oxidations of the complexes were observed within a much narrower range within the series. Notably, the variation of alkyl and aryl substituents on the triazole rings of the bidentate chelators appears to influence the Ru(II)/Ru(III) oxidation potentials, which are shifted on average by +70 mV per replacement of alkyl with aryl units for the bidentate systems examined. Future studies will examine the degree to which the triazole functionality can influence the optoelectronic properties of such complexes.

In conclusion, a family of multidentate chelators comprised of one or more 1,2,3-triazole rings has been synthesized in high yield from trimethylsilyl-protected reactants via tandem deprotection/click transformations. This variation of the aqueous Cu-catalyzed Huisgen 1,3-dipolar cycloaddition relies on simple addition of K_2CO_3 to standard aqueous click reaction media and stands as an additional example of a multistep one-pot transformation employing a click reaction. With the simple addition of pyridine to these reaction conditions, commercially available 1,4-bis(trimethylsilyl)butadiyne was transformed into 1,1′-dialkyl- and 1,1′-diaryl-4,4′-bis(triazole) products. This symmetrical bidentate chelator motif stands as a new, readily accessible addition to this recently established family of 1,2,3-triazole-containing multidentate chelators. All of the bidentate and tridentate chelators examined form stable Ru(II) coordina-

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[14] Typical organometallic preparation: to a 50 mL test tube was added chelator **1b** (67 mg, 0.3 mmol), $RuCl_3 \cdot 2H_2O$ (24 mg, 0.1 mmol), ethanol (6 mL), and H_2O (2 mL). This solution was stirred overnight at 80 °C, during which time the solution color changed from dark brown to yellow. The solvent was then removed via rotary evaporation and the residue purified via passage through a Sephadex-20 column eluted with methanol to give Ru(**1b**)$_3$Cl$_2$ as a tan solid (80 mg, 95%).

[15] It should be noted that each of these bidentate complexes likely exists as a statistical mixture of stereoisomers indistinguishable via NMR analysis.

[16] See the Supporting Information for additional UV−visible absorption spectra.

tion complexes analogous to their polypyridyl counterparts, and the optoelectronic properties of such complexes appear sensitive to chelator identity, where the HOMO/LUMO energy gap of the octahedral Ru(II) complexes increases as the number of triazole rings increases. Ru(II) complexes of 4,4′-bis(triazoles) are coordinatively symmetrical, largely optically transparent, and nonfluorescent, with an oxidation/reduction gap of more than 3.5 V. The combination of modular synthetic efficiency and predictable coordination chemistry promotes this family of "click chelators" as attractive building blocks for the preparation of new organometallic complexes and subunits for supramolecular construction.

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Supporting Information Available: Text and figures giving additional experimental details and characterization data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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