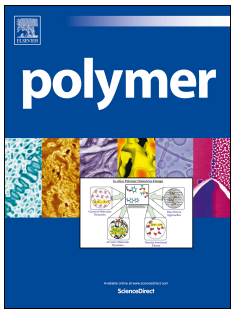
Accepted Manuscript



Atom Transfer Radical Addition (ATRA) Catalyzed by Copper Complexes with *N*,*N*,*N'*,*N'*-tetrakis(2-pyridylmethyl)ethylenediamine (TPEN) Ligand

Aman Kaur, Erin E. Gorse, Thomas G. Ribelli, Callista C. Jerman, Tomislav Pintauer

PII: S0032-3861(15)00172-X

DOI: 10.1016/j.polymer.2015.02.021

Reference: JPOL 17634

To appear in: *Polymer*

Received Date: 19 December 2014

Revised Date: 2 February 2015

Accepted Date: 14 February 2015

Please cite this article as: Kaur, A, Gorse, EE, Ribelli, TG, Jerman CC, Pintauer T, Atom Transfer Radical Addition (ATRA) Catalyzed by Copper Complexes with *N*,*N*,*N'*,*N'*-tetrakis(2-pyridylmethyl)ethylenediamine (TPEN) Ligand, *Polymer* (2015), doi: 10.1016/j.polymer.2015.02.021.

Atom Transfer Radical Addition (ATRA) Catalyzed by Copper Complexes with *N,N,N',N'*-tetrakis(2-pyridylmethyl)ethylenediamine (TPEN) Ligand

Aman Kaur,[a] Erin E. Gorse,[a] Thomas G. Ribelli,[b] Callista C. Jerman[b] and Tomislav Pintauer[a]*

[a*]Department of Chemistry and Biochemistry, Duquesne University, 600 Forbes Avenue, 308 Mellon Hall, Pittsburgh, Pennsylvania, 15282, USA. Tel: 412-396-1626, Fax: 412-396-5683, E-mail: pintauert@duq.edu

[b]Department of Chemistry, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, Pennsylvania, 15213, USA.

KEYWORDS. Tris(2-pyridyl)methyl amine, copper, homogeneous catalysis, multidentate N-donor ligand, ATRA.

ABSTRACT. Synthesis, characterization, electrochemical studies and ATRA activity of copper complexes with *N,N,N',N'*-tetrakis(2-pyridylmethyl)ethylenediamine (TPEN) ligand in the presence of ascorbic acid as a reducing agent were reported. $[Cu^{II}(TPEN')Br][Br]$ (TPEN' denotes tetracoordinated ligand) catalyst showed a very low activity in ATRA of CBr_4 to 1-octene, methyl methacrylate, methyl acrylate and styrene in methanol, which is a typical solvent used for ATRA reactions employing ascorbic acid. On the contrary, the yields and stereoselectivity towards monoadduct formation were dramatically increased in slightly polar but aprotic acetone. Based on molecular structures of isolated $[Cu^{II}(TPEN)][BPh_4]$ and $[Cu^{II}(TPEN')Br][Br]$ complexes, as well as UV-Vis and cyclic voltammetry studies, an equilibrium was proposed involving inactive $[Cu^{II}(TPEN)]^{2+}$ and ATRP active $[Cu^{II}(TPEN')Br]^{+}$ cations The halidophilicity of the bromide-based deactivating complex ($[Cu^{II}(TPEN')Br][Br]$) decreased approximately 750 times upon changing the solvent from acetone (K_{Br} =3000±230) to methanol (K_{Br} =4.1±0.1), explaining poor catalytic activity in methanol. In acetone, $[Cu^{II}(TPEN')Br][Br]$ complex was nearly as active in ATRA reactions employing ascorbic acid as previously reported $[Cu^{II}(TPMA)Br][Br]$.

INTRODUCTION AND BACKGROUND

Over the past several decades, copper complexes have attracted a considerable interest as catalysts for carbon-carbon bond forming reactions, in particular atom transfer radical addition (ATRA)[1-5] and polymerization (ATRP).[6-12] Mechanistically, in both processes, the copper(I) complex homolytically cleaves a carbon halogen bond from alkyl halide to generate the corresponding radical and copper(II) halide (Scheme 1). The radical then adds across a carbon-carbon double bond of an alkene or monomer to generate the secondary radical, which is rapidly trapped by copper(II) halide to form the desired monoadduct (ATRA). This step also regenerates the activator or copper(I) complex. ATRP is mechanistically very similar to ATRA with the

[Insert Scheme 1]

exception that the activation-addition-deactivation cycles are repeated many times resulting in polymers with well-defined molecular weights and narrow molecular weight distributions ($Đ=M_w/M_n$).

Recent advances in the area of catalyst regeneration in transition metal catalyzed ATRA and ATRP reactions not only enable the approach of the equilibrium from the right-hand side (Scheme 1), but also a significant decrease in the catalyst concentration.[1,3,6,13-27] In such processes, the activator (transition metal complex in the lower oxidation state) that is responsible for homolytic

cleavage of carbon-halogen bond is continuously regenerated from the deactivator (transition metal complex in the higher oxidation state) in the presence of reducing agents such as free-radical diazo initiators, tin(II) 2-ethylhexanoate, glucose, phenols, ascorbic acid, magnesium and metallic copper.[1,2,6,13-21,23,28,29] Transition metal complexes in the higher oxidation states are

typically air stable and therefore their use surpasses otherwise necessary deoxygenation techniques.

Electrochemical measurements are commonly used to predict the activity of copper complexes in atom transfer radical processes, namely ATRA and ATRP.[30-37] Generally, for a given alkyl halide, the equilibrium constant for atom transfer ($K_{ATRP}=k_a/k_d$) can be directly correlated with $E_{1/2}$ values provided that the halidophilicity of the copper complex ($X^- + [Cu^{II}L_m]^{2+} \rightleftharpoons [Cu^{II}L_mX]^+$, K_X, X=Br or Cl) remains constant. As a result, for copper complexes with neutral nitrogen based ligands commonly used in ATRA and ATRP, a linear correlation between $\ln(K_{ATRP})$ and $E_{1/2}$ values is typically observed.[34,38,39] Another method of predicting the activity of copper catalysts in ATRP is to directly compare the stability constants of Cu^{II} and Cu^{I} complexes with the particular ligand

$$\beta^m = \frac{[Cu^mL_n]}{[Cu^m][L]^n}; \text{ m=I or II, n=1 or 2} \qquad [1]$$

(β^{II} and β^{I}, respectively, Eq [1]). Both β^{II} and β^{I} should be large in order to eliminate or suppress possible concurrent reactions such as coordination of monomer and/or polymer, which are typically present in large excess relative to the catalyst. Generally, a copper complex with a low reduction potential should be more stable in its oxidized form (i.e. Cu^{II} should be more stable than Cu^{I}) in order to achieve high catalytic activity.[35,36]

With the recent discovery indicating that the reducing agents can significantly reduce the amount of copper complexes in ATRA and ATRP,[14] a significant effort has been devoted towards development of more active catalysts that could be used at even lower concentrations, and potentially enable controlled radical polymerization of α-olefins. The research in this area is significantly focused on ligand design, which can be used to tailor electronic properties of the

copper(I) center. Currently, tetradentate neutral nitrogen based ligands tris(2-pyridyl)methyl amine (TPMA) and tris[2-(dimethylamino)ethyl]amine (Me_6TREN) are among the most active

[Insert Scheme 2]

ligands in copper catalyzed ATRA and ATRP (Scheme 2). They form very stable copper(I and II) complexes and more importantly are very reducing (-0.25 mV<$E_{1/2}$<-0.30 mV, v.s. SCE, Scheme 3).[39] Recently, a new class of multidentate nitrogen based ligands such as *N*,*N*,*N'*,*N'*-tetrakis(2-pyridylmethyl)ethylenediamine (TPEN) have been shown to be quite promising in copper catalyzed ATRP of acrylic, methacrylic, and styrenic monomers at very low concentrations and in the absence of a reducing agent.[40] For example, $Cu^{I}Br$/TPEN catalyst mediated ATRP at a catalyst/initiator molar ratio of 0.005 and produced polymers with well-controlled molecular weights and low polydispersities. ATRP also occurred even at a catalyst/initiator molar ratio as low as 0.001 with copper concentration in the produced polymers as low as 6-8 ppm (catalyst/ monomer molar ratio = 10^{-5}). Inspired by these results, we reverted our attention to potential use of TPEN ligand in copper catalyzed ATRA.

In this article, we report on the synthesis, characterization, electrochemical studies and ATRA activity of copper complexes with TPEN ligand in the presence of ascorbic acid as a reducing agent.

EXPERIMENTAL SECTION

General. All chemicals were purchased from commercial sources, and used as received unless otherwise stated. *N*,*N*,*N'*,*N'*-tetrakis(2-pyridylmethyl)ethylenediamine (TPEN) and $[Cu^{II}(TPEN)Br][Br]$ were synthesized according to previously published literature procedures.[38] Cyclic voltammetry experiments were performed under argon. Copper(II) complexes were synthesized under ambient conditions.

Instrumentation and Equipment. ^{1}H NMR spectra were obtained using Bruker 400 MHz spectrometer and chemical shifts are given in ppm relative to residual solvent peaks [$CDCl_3$ δ7.26 ppm; $(CD_3)CO$ δ2.05 ppm; CD_3CN δ1.96 ppm]. IR spectra were recorded in the solid state using Nicolet Smart Orbit 380 FT-IR spectrometer (Thermo Electron Corporation). Elemental analyses for C, H, and N were obtained from Roberston Microlabs, NJ. UV-Vis spectra were recorded using a Beckman DU-530 spectrometer in 1.0 cm path-length airtight quartz cuvettes. All cyclic voltammograms were measured at 25°C with a NuVant potentiostat. Solutions of $Cu^{II}Br_2$ and $Cu^{II}(BPh_4)_2$ complexes with TPEN ligand (1.0 mM) were prepared in the mixture of acetonitrile (4.9 mL) and DMF (0.1 mL) containing 0.1 M NBu_4Br or NBu_4BPh_4 as the supporting electrolyte. Measurements were carried out under argon atmosphere at a scanning rate (ν) of 0.1 Vs^{-1}, using a platinum disk and platinum mesh as the working and counter electrode, respectively. An $Ag|AgI|I^-$ reference electrode was used and potentials were measured relative to a ferrocenium/ferrocene couple, which was used as an internal standard.

X-ray Crystal Structure Determination. The X-ray intensity data were collected at 150 K using graphite-monochromated Mo-K radiation (0.71073 Å) with a Bruker Smart Apex II CCD diffractometer. Data reduction included absorption corrections by the multi-scan method using SADABS.[41] Crystal data and experimental conditions are given in Table 1. Structures were solved

[Insert Table 1]

by direct methods and refined by full matrix least squares using SHELXTL 6.1 bundled software package.[42] The H-atoms were positioned geometrically (aromatic C-H 0.93, methylene C-H 0.97, and methyl C-H 0.96) and treated as riding atoms during subsequent refinement, with U_{iso}(H) = 1.2U_{eq}(C) or 1.5U_{eq}(methyl C). The methyl groups were allowed to rotate about their

local threefold axes. Crystal Maker 8.3 was used to generate molecular graphics. CCDC-1039735 (for [($Cu^{II}Br_2$)$_2$TPEN]) and CCDC-1039736 [Cu^{II}(TPEN)][BPh_4]$_2$ contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/ data_request/cif.

Synthesis of Copper Complexes.

[($Cu^{II}Br_2$)$_2$(TPEN)]. A solution of TPEN (724 mg, 1.7 mmol) in 2.0 mL of dichloromethane was added to a suspension of $Cu^{II}Br$ (763 mg, 3.4 mmol) in 1.0 mL of dichloromethane, resulting in the formation of a green solution. After stirring for 5 min at ambient temperature, [($Cu^{II}Br_2$)$_2$(TPEN)] was precipitated as green powder (yield=1.22 g, 82%). X-ray quality crystals were obtained by crystallization in DMF via slow diffusion of diethyl ether. FT-IR (solid):ν (cm^{-1}) = 2944(m), 1600(m), 1570(s), 1466(m), 1461 (s), 1261(m), 1262(m), 1062(s), 863(m), 670(m), 619(m). Anal. Calcd. for $C_{26}H_{28}Br_4Cu_2N_6$ (871.24): C, 34.84; H, 3.24; N, 9.65. Found: C, 35.50; H, 3.31; N, 8.82.

[Cu^{II}(TPEN)][BPh_4]$_2$. [(Cu^{II}(TPEN')Br][Br] (131.0 mg, 0.203 mmol) was dissolved in solution of methanol and DMF (95/5), and $NaBPh_4$ (138.0 mg, 0.406 mmol) was added. Green powder which precipitated immediately was washed with methanol, collected by filtration, and dried under vacuum to yield (139 mg, 61%) of [(Cu^{II}(TPEN)][BPh_4]$_2$. Crystals of [Cu^{II}(TPEN)][BPh_4]$_2$ suitable for X-ray analysis were obtained in acetone by slow diffusion of diethyl ether. FT-IR (solid): ν (cm^{-1}) = 3054(s), 2998(s), 2923(s), 1694(m), 1580(m), 1477(m), 1427 (m), 1398(m), 1291(m), 1062 (m), 733(s), 702(s), 611(m). Anal. Calcd. for $C_{74}H_{68}B_2CuN_6$ (1126.53): C, 78.90; H, 6.08; N, 7.46. Found: C, 79.16; H, 6.13; N, 7.99.

General Procedure for ATRA reactions. ATRA reactions were performed in 5.0 mm air tight J. Young NMR tubes. In a typical experiment, alkene (1.11 x 10^{-3} mol, V(methyl

acrylate)=100 μL, V(1-octene)=174 μL, V(methyl methacrylate)=120 μL and V(styrene)=127 μL) was dissolved in 400 μL of methanol or acetone. Carbon tetrabromide (CBr_4) was then added to the solution (1.25 eq, 0.455 g), followed by addition of 0.2 mL of ascorbic acid solution (0.25M) in methanol as a reducing agent and 1,4-dimethoxybenzene as internal standard. After the desired amount of copper(II) was added (for 0.01 M $[Cu^{II}(TPEN)Br][Br]$ in methanol or mixture of acetone and methanol (9:1): 1000:1 (V=80 μL), 5000:1 (V=16 μL), 10000:1 (V=8.06 μL) and 20000:1 (V=4.03 μL)), the NMR tube was sealed and placed in an oil bath thermostated at 60 ºC for 24 hours. The conversion of alkene and the percent yield of monoadduct were determined using ^{1}H NMR spectroscopy.

Determination of Halidophilicity Constants (K_{Br})

The equilibrium constant (K_{Br}) for association of Br^- anions to $[Cu^{II}(TPEN)]^{2+}$ cations was determined according to previously published literature procedure.[43] Solutions containing $[Cu^{II}(TPEN)][(OTf)_2]$, (2.5 mM, OTf^- = trifluoromethanesulfonate) were titrated with different amounts of tetrabutylammonium bromide (TBABr) in a given solvent (several methanol-acetone mixtures, as well as pure methanol and acetone). Spectra of the original solution containing no bromide anions and of solutions containing *n* equivalents of Br^- v.s. Cu^{II} were then collected. TBABr was added to the solution until no further changes in the spectra were observed (i.e. all of $[Cu^{II}(TPEN)][BPh_4]_2$ was converted to $[Cu^{II}(TPEN)'Br][Br]$).

[Insert Table 1]

RESULTS AND DISCUSSION

Copper catalyzed ATRA reactions in the presence of non-radical generating reducing agent such as ascorbic acid are typically conducted in polar protic and aprotic solvents such as MeOH, EtOH and acetone.[44-47] The solubility of ascorbic acid in such solvents is relatively high, as

opposed to conventional non-polar ATRA solvents like anisole or toluene. Shown in Table 2 are the results for ATRA of CBr_4 to various alkenes catalyzed by $Cu^{II}Br_2$/TPEN complex in the presence of

[Insert Table 2]

ascorbic acid as a reducing agent. The results for previously reported [Cu^{II}(TPMA)Br][Br] complex are included for comparison.[44] Interestingly, for all alkenes investigated, the activity of $Cu^{II}Br_2$/TPEN was much lower than that of [Cu^{II}(TPMA)Br][Br]. The differences are particularly noticeable for more active alkenes such as methyl methacrylate and methyl acrylate. It is important to observe that relatively high conversions were achieved for both alkenes at low catalyst loadings. However, the yield of the monoadduct was dramatically decreased. This clearly points to inefficient deactivation, which is not consistent with previously conducted ATRP studies.[40] Hence, our attention shifted towards examining the structures of the deactivator or $Cu^{II}Br_2$/TPEN complex in both the solid state and solution.

In addition to [Cu^{II}(TPEN')Br][Br] (TPEN' denotes tetracoordinated ligand) which was previously isolated directly from ATRP reaction mixture, we were able to isolate and structurally characterize two new complexes, namely [$(Cu^{II}Br_2)_2$(TPEN)] (Figure 1) and [Cu^{II}(TPEN)][BPh_4] (Figure 2). Both complexes indicated that TPEN ligand can also coordinate to the copper(II) center

[Insert Figure 1]

[Insert Figure 2]

in a tridentate and hexadentate fashion, respectively. In previously characterized [Cu^{II}(TPEN')Br][Br][40] the molar ratio of $Cu^{II}Br_2$ to TPEN was 1:1. The TPEN ligand was coordinated to the copper(II) center using four of its six donor nitrogen atoms from pyridine

rings. The fifth nitrogen atom was only weekly coordinated to the Cu^{2+} ion (Cu^{II}-N=2.525(5) Å), resulting in a highly distorted octahedral geometry. The structure of the complex was similar to previously characterized $[Cu^{II}(TPEN)][ClO_4]_2$ in which the metal center was also coordinated by four nitrogen atoms with one pyridyl nitrogen atom involved only in partial coordination.[48] In the molecular structure of $[(Cu^{II}Br_2)_2(TPEN)]$, the stoichiometric ratio between $Cu^{II}Br_2$ and TPEN was found to be 2:1. The hexadentate TPEN ligand was coordinated to two copper(II) centers through two sets of bis(2-pyridylmethyl)amino units. The molecule also contained a two-fold symmetry. Each copper(II) cation was coordinated by two nitrogen atoms from pyridine rings (Cu^{II}-N=1.979(2) Å and 1.989(2) Å), one tertiary amine nitrogen (Cu^{II}-N=1.979(2) Å), and two bromide anions (Cu^{II}-Br=2.4755(4) Å and 2.4844(4) Å) in a highly distorted trigonal bipyramidal geometry (τ=0.67; τ values range between 0 (ideal square pyramidal geometry) and 1 (ideal trigonal bipyramidal geometry)). The structure of $[(Cu^{II}Br_2)_2(TPEN)]$ shared many similar structural features with other ATRA/ATRP active $Cu^{II}Br_2$ complexes containing neutral tridentate nitrogen based ligand such as $Cu^{II}(PMDETA)Br_2$[49] (PMDETA=*N*,*N*,*N'*,*N"*,*N"*-pentamethyldiethylenetriamine) or $Cu^{II}(terpy)Br_2$[50] (terpy=2,2':6',2"-terpyridine). Lastly, crystals of $[Cu^{II}(TPEN)][BPh_4]_2$ suitable for X-ray analysis were obtained in acetone by slow diffusion of diethylether. The corresponding molecular structure is shown in Figure 2. The Cu(II) center adopted distorted octahedral geometry and was coordinated by six nitrogen donor atoms from TPEN ligand. The axial Cu-N_{ax} bond distances (Cu-N_{ax}=2.475(4) Å and 2.210(3) Å) were found to be longer than the equatorial ones (average Cu-N_{eq}= 2.050(6) Å). In a structurally related $[Cu^{II}(TPEN)][PF_6]_2$ complex, the coordination sphere around Cu^{2+} cation was occupied by only five nitrogen atoms from TPEN ligand due to the dissociation of one of the pyridine arms (Cu-N_{py}=5.008Å).

Furthermore, contrary to the octahedral $[Cu^{II}(TPEN)][BPh_4]_2$ complex, the axial bond distances in $[Cu^{II}(TPEN)][PF_6]_2$[48] ($Cu\text{-}N_{ax}$=2.005Å and 1.972Å) were found to be shorter than the equatorial ones ($Cu\text{-}N_{eq}$=2.148Å, 2.029Å and 2.084Å). Apart from $[Cu^{II}(TPEN)][BPh_4]_2$, hexacoordination of TPEN based ligands was also observed in some Fe^{II} and Zn^{II} complexes.[51-53] With these transition metals, TPEN appears to be more strongly coordinating to the metal center as indicated by shorter and nearly equal Mt^{II}-N bond distances (average Fe^{II}-N=1.981 Å and Zn^{II}-N=2.160 Å).

So far, based on the isolation of copper(II)/TPEN complexes discussed above, it appears that the only two possible deactivators in the system include $[(Cu^{II}Br_2)_2(TPEN)]$ and $[Cu^{II}(TPEN')Br][Br]$. Hexacoordinated $[Cu^{II}(TPEN)]^{2+}$ cation can be clearly ruled out since it does not contain coordinated bromide anions. Furthermore, the presence of $[(Cu^{II}Br_2)_2(TPEN)]$ can also be ruled out due to three important experimental observations. Firstly, the ratio of $Cu^{II}Br_2$ to TPEN in $[(Cu^{II}Br_2)_2(TPEN)]$ is 2:1, as opposed to 1:1, which was used experimentally. Secondly, $[(Cu^{II}Br_2)_2(TPEN)]$ complex was virtually insoluble in solvents used for ATRA studies, namely MeOH and acetone. It was only slightly soluble in DMSO and DMF. Also, most importantly, based on cyclic voltammetry studies, $[(Cu^{II}Br_2)_2(TPEN)]$ ($E_{1/2}$=-641 mV v.s. Fc/Fc^+ couple, ΔE_p=124 mV, i_{pa}/i_{pc}= 0.98) was found to be less reducing than $[Cu^{II}(TPEN')Br][Br]$ ($E_{1/2}$=-689 mV v.s. Fc/Fc^+ couple, ΔE_p=100 mV, i_{pa}/i_{pc}= 0.98). Hence, our attention focused on the possibility for the existence of an equilibrium between inactive $[Cu^{II}(TPEN)][Br]_2$ and active ATRA deactivator $[Cu^{II}(TPEN')Br][Br]$. The position of this equilibrium should be very dependent on solvent polarity, with $[Cu^{II}(TPEN)]^{2+}$ cations being more favored in polar protic medium such as MeOH, due to its ability to effectively stabilize Br^-

anions via intermolecular interactions. To further examine this equilibrium, solution studies were conducted using UV-Vis spectroscopy.

Shown in Figure 3 are UV-Vis spectra of $[Cu^{II}(TPEN)][OTf]_2$ complex in acetone and methanol in the absence and presence of externally added tetrabutylammonium bromine (2.0 eq. relative to Cu^{II} complex). In methanol and acetone, the UV-Vis spectra of $[Cu^{II}(TPEN)][OTf]_2$ are nearly identical, with strong absorption band and shoulder appearing at 684 and 960 nm, respectively. The addition of 2.0 eq. of TBABr in acetone gives rise to a completely different UV-Vis spectrum with an absorption band centered around 744 nm. Interestingly, only slight changes were observed in methanol indicating that the predominant species in solution were still $[Cu^{II}(TPEN)]^{2+}$ cations.

[Insert Figure 3]

Furthermore, very small changes were also observed in methanol solution containing as much as 100 eq. of TBABr relative to starting $[Cu^{II}(TPEN)][OTf]_2$ complex. This experimental results clearly confirm that the predominant species in methanol include hexacoordinated $[Cu^{II}(TPEN)]^{2+}$ cations. In acetone, on the other hand, bromide anions readily displace one of the coordinated pyridine arms to form active deactivator or $[Cu^{II}(TPEN')Br]^{+}$ species. The equilibrium constant for association of Br^- anions to $[Cu^{II}(TPEN)]^{2+}$ cations was further quantified in different mixtures of acetone and methanol using UV-Vis spectroscopy. Data were analyzed using previously published procedures.[43] The halidophilicity (K_{Br}) values in different MeOH/acetone mixtures are listed in Table 3. The halidophilicity of the bromide-based deactivating complex ($[Cu^{II}(TPEN')Br][Br]$) approximately decreased 750 times upon changing the solvent from

[Insert Table 3]

acetone (K_{Br} =3000±230) to methanol (K_{Br} =4.1±0.1), clearly indicating that a predominant species in methanol were deactivation inactive $[Cu^{II}(TPEN)]^{2+}$ cations, which clearly explains very poor results for ATRA studies summarized in Table 1. The results in methanol could be improved by externally adding the source of Br^- anions. However, as indicated in Table 3, under normal ATRA conditions, as much as 2400 equivalents would be needed to insure quantitative formation of the deactivator or $[Cu^{II}(TPEN')Br][Br]$. Alternatively, a much more useful solution would be to conduct experiments in slightly polar but aprotic acetone. Indeed, as indicated in Table 4, a dramatic improvement in catalytic performance was observed. For 1-octene (entries 1 and 2), the

[Insert Table 4]

desired monoadduct was formed in very high yields using catalyst loadings as low as 0.01 mol-% (relative to alkene). Furthermore, at catalyst loadings between 0.02 and 0.1 mol-% relative to alkene high yields of the monoadduct were also observed in the case of more active methyl methacrylate (entries 3 and 4), methyl acrylate (entries 6 and 7) and styrene (entries 9 and 10). The yields slightly decreased at lower ratios of alkene to copper catalyst (10000:1, entries 5, 8 and 11). What is even more important to notice, particularly in the case of MMA, MA and styrene, is that the stereoselectivity towards monoadduct formation was dramatically increased in acetone when compared to methanol due to an increase in deactivation efficiency. Based on the results presented in Table 4, the activity of $[Cu^{II}(TPEN')Br][Br]$ complex in ATRA reactions in the presence of ascorbic acid as a reducing agent was nearly as high as the one obtained previously with $[Cu^{II}(TPMA)Br][Br]$.[44]

CONCLUSIONS

In summary, synthesis, characterization, electrochemical studies and ATRA activity of copper complexes with TPEN ligand in the presence of ascorbic acid as a reducing agent were reported. $[Cu^{II}(TPEN'Br][Br]$ (TPEN' denotes tetracoordinated ligand) catalyst showed a very poor performance in ATRA of CBr_4 to 1-octene, methyl methacrylate, methyl acrylate and styrene in MeOH, which is a typical solvent used for ATRA reactions employing ascorbic acid. On the contrary, the yields and stereoselectivity towards monoadduct formation were dramatically increased in slightly polar but aprotic acetone. Based on molecular structures of isolated $[Cu^{II}(TPEN)][BPh_4]$ and $[Cu^{II}(TPEN')Br][Br]$ complexes, as well as UV-Vis and cyclic voltammetry studies, an equilibrium was proposed involving inactive $[Cu^{II}(TPEN)]^{2+}$ and deactivation active $[Cu^{II}(TPEN'Br]^{+}$ cations The halidophilicity of the bromide-based deactivating complex ($[Cu^{II}(TPEN')Br][Br]$) approximately decreased 750 times upon changing the solvent from acetone (K_{Br} =3000±230) to methanol (K_{Br} =4.1±0.1), explaining poor catalytic activity in methanol. In acetone, the activity of $[Cu^{II}(TPEN')Br][Br]$ complex in ATRA reactions that utilize ascorbic acid as a reducing agent was nearly as high as the one obtained previously with $[Cu^{II}(TPMA)Br][Br]$.

ACKNOWLEDGMENT

Financial support from the National Science Foundation (CHE-0844131 and CHE-1360886) is greatly acknowledged. Part of the data reported in this manuscript were obtained in the Department of Chemistry at Carnegie Mellon University while the corresponding author was on a sabbatical leave. TP wishes to express his gratitude to Prof. Krzysztof Matyjaszewski and his group members for their hospitality.

REFERENCES

(1) Eckenhoff, W. T.; Pintauer, T. *Cat. Rev. Sci. Eng.* **2010**, *52*, 1-59.

(2) Pintauer, T. *ACS Symp. Ser.* **2009**, *1023*, 63-84.

(3) Pintauer, T. *Eur. J. Inorg. Chem.* **2010**, 2449-2460.

(4) Severin, K. *Curr. Org. Chem.* **2006**, *10*, 217-224.

(5) Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519-564.

(6) Wang, J.-S.; Matyjaszewski, K. *J. Am. Chem. Soc.* **1995**, *117*, 5614-5615.

(7) Kamigaito, M.; Ando, T.; Sawamoto, M. *Chem. Rev.* **2001**, *101*, 3689-3745.

(8) Kato, M.; Kamigaito, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1995**, *28*, 1721-1723.

(9) Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921-2990.

(10) Matyjaszewski, K. *Curr. Org. Chem.* **2002**, *6*, 67-82.

(11) Matyjaszewski, K.; Davis, T. P. *Handbook of Radical Polymerization*; Wiley: Hoboken, 2002.

(12) Matyjaszewski, K.; Gnanou, Y.; Leibler, L. *Macromolecular Engineering-Precise Synthesis, Materials Properties, Applications*; Willey-VCH: Weinheim, 2007.

(13) Matyjaszewski, K.; Jakubowski, W.; Min, K.; Tang, W.; Huang, J.; Braunecker, W. A.; Tsarevsky, N. V. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 15309-15314.

(14) Pintauer, T.; Matyjaszewski, K. *Chem. Soc. Rev.* **2008**, *37*, 1087-1097.

(15) Jakubowski, W.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 4139-4146.

(16) Jakubowski, W.; Matyjaszewski, K. *Angew. Chem. Int. Ed.* **2006**, *45*, 4482-4486.

(17) Jakubowski, W.; Min, K.; Matyjaszewski, K. *Macromolecules* **2006**, *39*, 39-45.

(18) Matyjaszewski, K.; Dong, H.; Jakubowski, W.; Pietrasik, J.; Kusumo, A. *Langmuir* **2007**, *23*, 4528-4531.

(19) Min, K.; Gao, H.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2005**, *127*, 3825-3830.

(20) Min, K.; Gao, H.; Matyjaszewski, K. *Macromolecules* **2007**, *40*, 1789-1791.

(21) Quebatte, L.; Thommes, K.; Severin, K. *J. Am. Chem. Soc.* **2006**, *128*, 7440-7441.

(22) Eckenhoff, W. T.; Garrity, S. T.; Pintauer, T. *Eur. J. Inorg. Chem.* **2008**, 563-571.

(23) Eckenhoff, W. T.; Pintauer, T. *Inorg. Chem.* **2007**, *46*, 5844-5846.

(24) Pintauer, T.; Eckenhoff, W. T.; Ricardo, C.; Balili, M. N. C.; Biernesser, A. B.; Noonan, S. J.; Taylor, M. J. W. *Chem. Eur. J.* **2009**, *15*, 38-41.

(25) Fernández-Zúmel, M. A.; Thommes, K.; Kiefer, G.; Sienkiewicz, A.; Pierzchala, K.; Severin, K. *Chem. Eur. J.* **2009**, *15*, 11601-11607.

(26) Thommes, K.; Kiefer, G.; Scopelliti, R.; Severin, K. *Angew. Chem. Int. Ed.* **2009**, *48*, 8115-8119.

(27) Muñoz-Molina, J. M.; Belderraín, T. R.; Pérez, P. J. *Adv. Synth. Catal.* **2008**, *350*, 2365-2372.

(28) Konkolewicz, D.; Wang, Y.; Krys, P.; Zhong, M.; Isse, A. A.; Gennaro, A.; Matyaszewski, K. *Polym. Chem.* **2014**, *5*, 4396-4417.

(29) Konkolewicz, D.; Wang, Y.; Zhong, M.; Krys, P.; Isse, A. A.; Gennaro, A.; Matyaszewski, K. *Macromolecules* **2013**, *46*, 8749-8772.

(30) Pintauer, T.; Matyjaszewski, K. *Coord. Chem. Rev.* **2005**, *249*, 1155-1184.

(31) Pintauer, T.; McKenzie, B.; Matyjaszewski, K. *ACS Symp. Ser.* **2003**, *854*, 130-147.

(32) Pintauer, T.; Matyjaszewski, K. *Top. Organomet. Chem.* **2009**, *26*, 221-251.

(33) Braunecker, W. A.; Matyjaszewski, K. *Prog. Polym. Sci.* **2007**, *32*, 93-146.

(34) Tang, W.; Kwak, Y.; Braunecker, W.; Tsarevsky, N. V.; Coote, M. L.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2008**, *130*, 10702-10713.

(35) Tsarevsky, N. V.; Braunecker, W. A.; Matyjaszewski, K. *J. Organomet. Chem.* **2007**, *692*, 3212-3222.

(36) Tsarevsky, N. V.; Braunecker, W. A.; Vacca, A.; Gans, P.; Matyjaszewski, K. *Macromol. Symp.* **2007**, *248*, 60-70.

(37) Tsarevsky, N. V.; Matyjaszewski, K. *Chem. Rev.* **2007**, *107*, 2270-2299.

(38) Tang, W.; Tsarevsky, N. V.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2006**, *128*, 1598-1604.

(39) Qiu, J.; Matyjaszewski, K.; Thounin, L.; Amatore, C. *Macromol. Chem. Phys.* **2000**, *201*, 1625-1631.

(40) Tang, H.; Arulsamy, N.; Radosz, M.; Shen, Y.; Tsarevsky, N. V.; Braunecker, W. A.; Tang, W.; Matyjaszewski, K. *J. Am. Chem. Soc.* **2006**, *128*, 16277-16285.

(41) Sheldrick, G. M. *SADABS Version 2.03*; University of Gottingen: Germany, 2002.

(42) Sheldrick, G. M. *SHELXTL 6.1,Crystallographic Computing System*; Bruker Analytical X-Ray System: Madison, WI, 2000.

(43) Tsarevsky, N. V.; Pintauer, T.; Matyjaszewski, K. *Macromolecules* **2004**, *37*, 9768-9778.

(44) Taylor, M. J. W.; Eckenhoff, W. T.; Pintauer, T. *Dalton. Trans.* **2010**, *39*, 11475-11482.

(45) Ricardo, C.; Pintauer, T. *Eur. J. Inorg. Chem.* **2011**, 1292-1301.

(46) Ricardo, C.; Pintauer, T. *Isr. J. Chem.* **2012**, *52*, 320-327.

(47) Ricardo, C.; Pintauer, T. *ACS Symp. Ser.* **2012**, *1100*, 73-98.

(48) Yoon, D. C.; Lee, U.; Oh, C. E. *Bull. Korean Chem. Soc.* **2004**, *25*, 796-800.

(49) Kickelbick, G.; Pintauer, T.; Matyjaszewski, K. *New. J. Chem.* **2002**, *26*, 462-468.

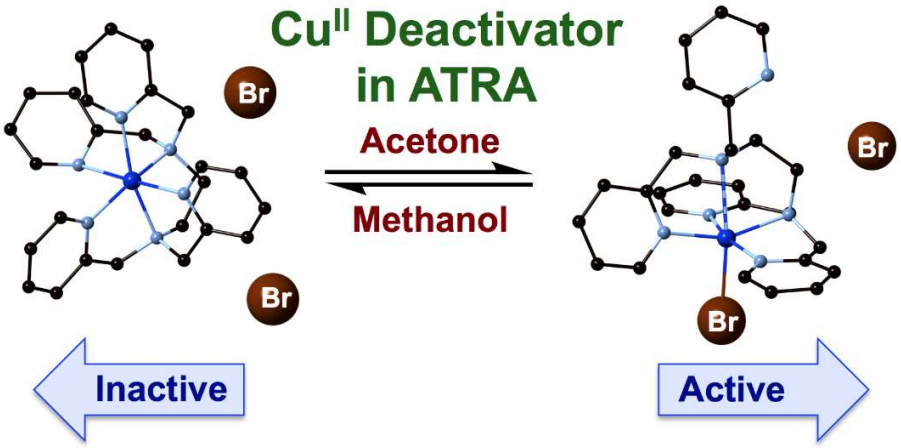
(50) Arriortua, M. I.; Mesa, J. L.; Rojo, T.; Debaerdemaeker, T.; Beltran-Porter, D.; Stratemeier, H.; Reinen, D. *Inorg. Chem.* **1988**, *27*, 2976-2981.

(51) Mikata, Y.; Yamanaka, A.; Yamashita, A.; S., Y. *Inorg. Chem.* **2008**, *47*, 7295-7301.

(52) Thibon, A.; Bartoli, J.-F.; Guillot, R.; Sainton, J.; Martinho, M.; Mansuy, D.; Banse, F. *J. Mol. Cat. A: Chem.* **2008**, *287*, 115-120.

(53) Hazell, A.; Monsted, O.; Rasmussen, J. C.; Toftlund, H. *Acta Cryst. Sec F.* **2008**, *64*, m185-m189.

Graphical Abstract



Captions for Schemes, Figures and Tables

Scheme 1. Proposed mechanism for copper catalyzed ATRA and ATRP.

Scheme 2. Highly active ligands for copper catalyzed ATRA and ATRP.

Scheme 3. Proposed equilibrium between $[Cu^{II}(TPEN)]^{2+}$ and $[Cu^{II}(TPEN')Br^{+}$ species in ATRA (TPEN' denotes tetracoordinated ligand).

Figure 1. Molecular structure of $[(Cu^{II}Br_2)_2(TPEN)]$ at 150 K shown with 30% probability displacement ellipsoids. H-atoms have been omitted for clarity. Symmetry codes used to generate equivalent atoms: (1) -x+2,-y+1, -z+2. Selected bond distances [Å] and angles (°): Cu1-N1 2.119(2), Cu1-N2 1.979(2), Cu1-N3 1.989(2), Cu1-Br1 2.4755(4), Cu1-Br2 2.4844(4), N1-Cu1-N2 82.16(8), N1-Cu1-N3 81.42(9), N2-Cu1-N3 163.15(9), N2-Cu1-Br1 94.73(6), N1-Cu1-Br1 118.43(6), N2-Cu1-Br1 94.73(6), N3-Cu1-Br1 96.39(7), N1-Cu1-Br2 118.81(6), N2-Cu1-Br2 93.37(6), N3-Cu1-Br2 91.22(6).

Figure 2. Molecular structure of $[Cu^{II}(TPEN)][BPh_4]_2$ at 150 K shown with 30% probability displacement ellipsoids. H-atoms, counterion BPh_4^- and solvent molecule (acetone) have been omitted for clarity. Selected bond distances [Å] and angles (°): Cu1-N1 2.050(3), Cu1-N2 2.024(3), Cu1-N3 2.210(3), Cu1-N4 2.063(3), Cu1-N5 2.475(4), Cu1-N6 2.067(3), N1-Cu1-N2 112.72(12), N1-Cu1-N4 81.27(11), N1-Cu1-N6 165.61(11), N2-Cu1-N3 96.71(11), N2-Cu1-N4,159.08(12), N2-Cu1-N5 87.48(12), N2-Cu1-N5 87.48(12), N3-Cu1-N6 80.83(11), N4-Cu1-N6 85.36(11), N4-Cu1-N5 78.00(11).

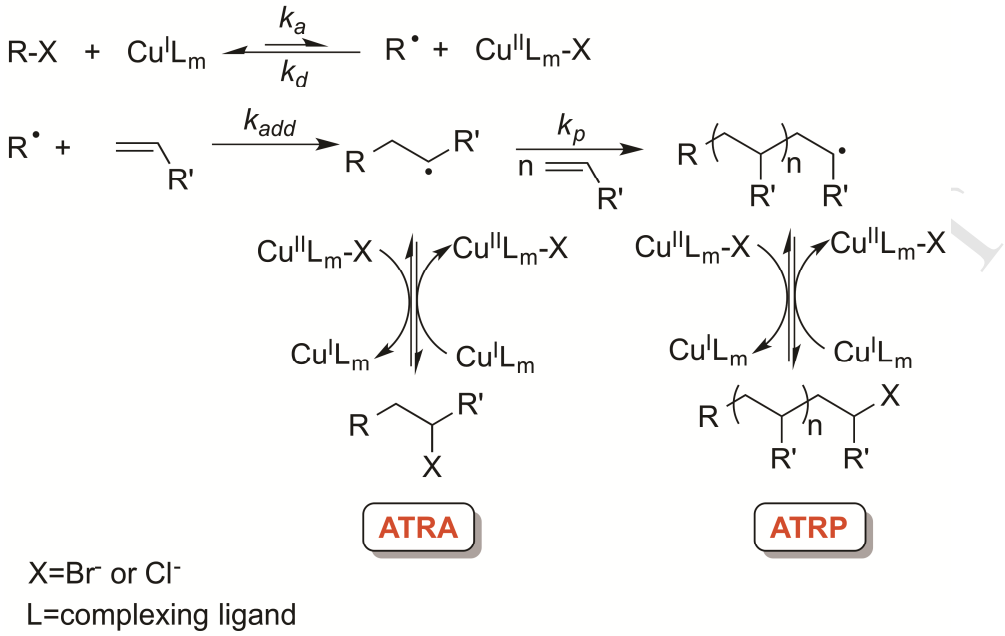
Figure 3. UV-Vis spectra of $[Cu^{II}(TPEN)][OTf]_2$ complexes in acetone and methanol in the absence and presence of externally added tetrabutylammonium bromide (TBABr).

Table 1. Crystallographic data and experimental details for $[(Cu^{II}Br_2)_2(TPEN)]$ and $[Cu^{II}(TPEN)][BPh_4]_2$.

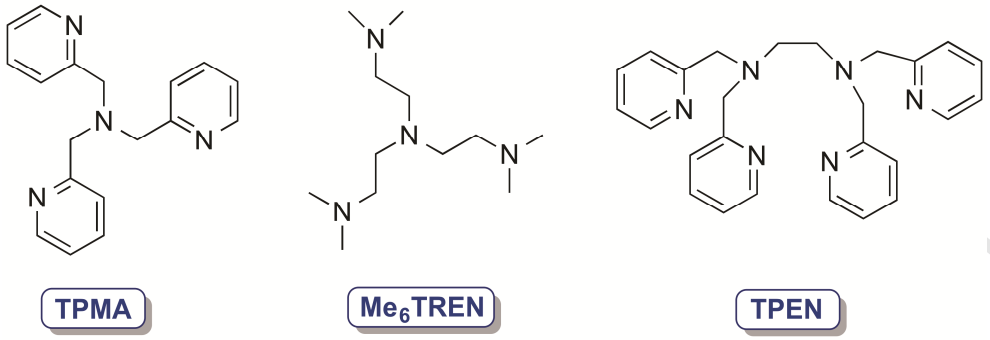
Table 2. ATRA of CBr_4 to alkenes catalyzed by $[Cu^{II}(TPEN')Br][Br]$ and $[Cu^{II}(TPMA)Br][Br]$ complexes in methanol in the presence of ascorbic acid as a reducing agent.[a]

Table 3. Association constants (K_{Br}) for $[Cu^{II}(TPEN)]^{2+}$ with Br^- Anions in Acetone/Methanol Solutions Determined Spectrophotometrically at Ambient Temperature.

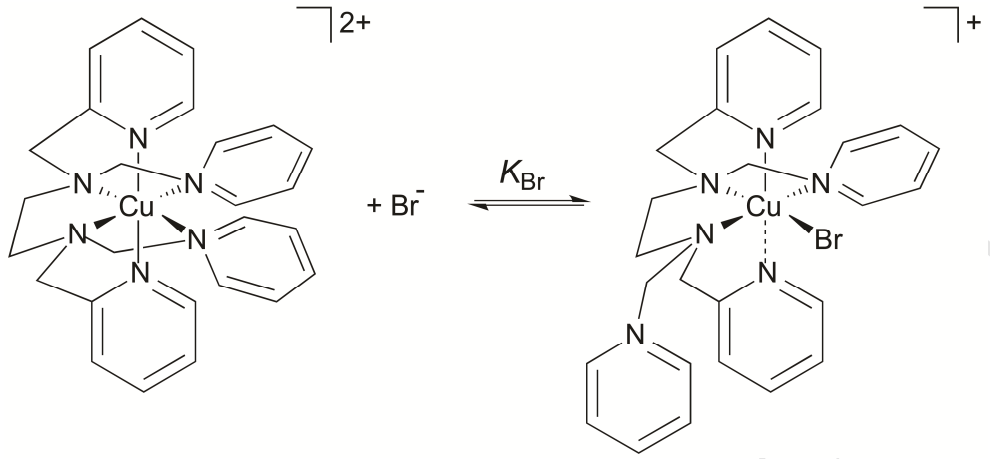
Table 4. ATRA of CBr_4 to alkenes catalyzed by $[Cu^{II}(TPEN')Br][Br]$ in acetone in the presence of ascorbic acid as a reducing agent.[a]



Scheme 1. Proposed mechanism for copper catalyzed ATRA and ATRP.



Scheme 2. Highly active ligands for copper catalyzed ATRA and ATRP.



Scheme 3. Proposed equilibrium between $[Cu^{II}(TPEN)]^{2+}$ and $[Cu^{II}(TPEN')]Br^{+}$ species in ATRA (TPEN' denotes tetracoordinated ligand).

Table 1. Crystallographic data and experimental details for $[(Cu^{II}Br_2)_2(TPEN)]$ and $[Cu^{II}(TPEN)][BPh_4]_2$.

Name	**$[(Cu^{II}Br_2)_2(TPEN)]$**	**$[Cu^{II}(TPEN)][(BPh_4]_2$**
Formula	$C_{26}H_{28}Br_4Cu_2N_6 \cdot {}_2(C_3H_7NO)$	$C_{26}H_{28}CuN_6 \cdot 2(C_{24}H_{20}B) \cdot (C_3H_6O)$
Color	Green	Green
Shape	Cubic	Cubic
Formula Weight	1017.44	1184.59
Crystal System	Triclinic	Triclinic
Space Group	P-1	P-1
Temp (K)	150	150
Cell Constants		
a, Å	8.2417(1)	11.586(1)
b, Å	10.5925(1)	13.581(1)
c, Å	12.0617(1)	23.002(2)
α, deg	95.074(1)	75.197(2)
β, deg	107.344(1)	78.967(2)
γ, deg	101.917(1)	67.586(2)
V, $Å^3$	970.68(2)	3217.2(6)
Formula units/unit cell	1	2
Dcal'd, gcm^{-3}	1.74	1.223
Absorption coefficient, mm^{-1}	5.25	0.39
F(000)	504	1564
Diffractometer	Bruker Smart ApexII	Bruker Smart ApexII
Radiation, graphite monochr.	Mo $K_ʎ$ (ʎ =0.71073 Å)	Mo $K_ʎ$ (ʎ =0.71073 Å)
Crystal size, mm	0.28 × 0.14 × 0.09	0.50 × 0.29 × 0.18
θ range, deg	2.3< θ <27.4	0.9< θ <23.1
Range of h,k,l	±12, ±15, ±18	±12, ±15, ±25
Reflections collected/unique	17444/4815	22249/9092
R_{int}	0.02	0.04
Refinement Method	multi-scan	multi-scan
Data/Restraints/Parameters	6513/0/219	9058/0/786
GOF on F^2	0.9	1.02
Final R indices [I>2σ(I)]	0.034	0.05
R indices (all data)	0.132	0.157
Max. Resid. Peaks ($e*Å^{-3}$)	1.26 and -1.10	0.59 and -0.35

Table 2. ATRA of CBr_4 to alkenes catalyzed by [Cu^{II}(TPEN')Br][Br] and [Cu^{II}(TPMA)Br][Br] complexes in methanol in the presence of ascorbic acid as a reducing agent.[a]

Entry	Ligand	Alkene	$[Alk]_0:[Cu^{II}]_0$	Conv.[%]/Yield[%][b]	TON[c]
Solvent=Methanol					
1	TPEN	1-octene	5000:1	45/45	2250
2	TPMA[d]			90/90	4500
3	TPEN		10000:1	39/39	3900
4	TPMA			85/85	8500
5	TPEN	MMA	1000:1	90/29	290
6	TPMA			~100/~100	1000
7	TPEN		5000:1	78/28	1400
8	TPMA			~100/86	4300
9	TPEN		10000:1	67/32	3200
10	TPMA			99/57	5700
11	TPEN	MA	1000:1	~100/15	150
12	TPMA			~100/~100	1000
13	TPEN		5000:1	~100/12	600
14	TPMA			98/85	4250
15	TPEN		10000:1	~100/26	2600
16	TPMA			99/64	6400
17	TPEN	Styrene	1000:1	97/61	610
18	TPEN		5000:1	90/60	3000
19	TPEN		10000:1	76/18	1800

[a]All reactions were performed in methanol 60 ºC for 24h with $[alkene]_0:[CBr_4]_0:[ascorbic\ acid]_0$=1:1.25:0.07, [alkene]=1.34M. [b]The yield is based on the formation of monoadduct and was determined using ^{1}H NMR spectroscopy (relative errors ±10%). [c]TONs for all reactions were calculated taking into account the percent yield of monoadduct. [d]Data for [Cu^{II}(TPMA)Br][Br] complex were taken from Ref. [44].

Table 3. Association constants (K_{Br}) for $[Cu^{II}(TPEN)]^{2+}$ with Br^- Anions in Acetone/Methanol Solutions Determined Spectrophotometrically at Ambient Temperature.

MeOH/ACTN. (% v/v)	**[MeOH] (M)**	**K_{Br}**	**Equiv. of TBABr for complete (99.999%) association of Br^-**
0/100	0	3000±230 (3)[a]	33
20/80	4.9	450±50 (6)	220
40/60	9.9	45±8 (5)	2200
60/40	14.8	28±6 (5)	3600
80/20	19.8	16±2 (6)	6400
100/0	24.7	4.1±0.1 (5)	2400

[a]The number in parentheses after each value of K_{Br} indicates the number of spectra used for the calculation of the association constant (halidophilicity).

Table 4. ATRA of CBr_4 to alkenes catalyzed by [Cu^{II}(TPEN')Br][Br] in acetone in the presence of ascorbic acid as a reducing agent.[a]

Entry	Alkene	$[Alk]_0:[Cu^{II}]_0$	Conv.[%]/Yield[%][b]	TON[c]
Solvent=Acetone				
1	1-octene	5000:1	84/84	4200
2		10000:1	73/73	7300
3	MMA	1000:1	98/73	730
4		5000:1	71/62	3100
5		10000:1	63/44	4400
6	MA	1000:1	~100/~100	1000
7		5000:1	98/82	4100
8		10000:1	82/64	6400
9	Styrene	1000:1	~100/87	870
10		5000:1	~100/78	3900
11		10000:1	82/47	4700

[a]All reactions were performed in acetone 60 ºC for 24h with $[alkene]_0:[CBr_4]_0:[ascorbic\ acid]_0$=1:1.25:0.07, [alkene]=1.34M. [b]The yield is based on the formation of monoadduct and was determined using ^{1}H NMR spectroscopy (relative errors ±10%). [c]TONs for all reactions were calculated taking into account the percent yield of monoadduct.

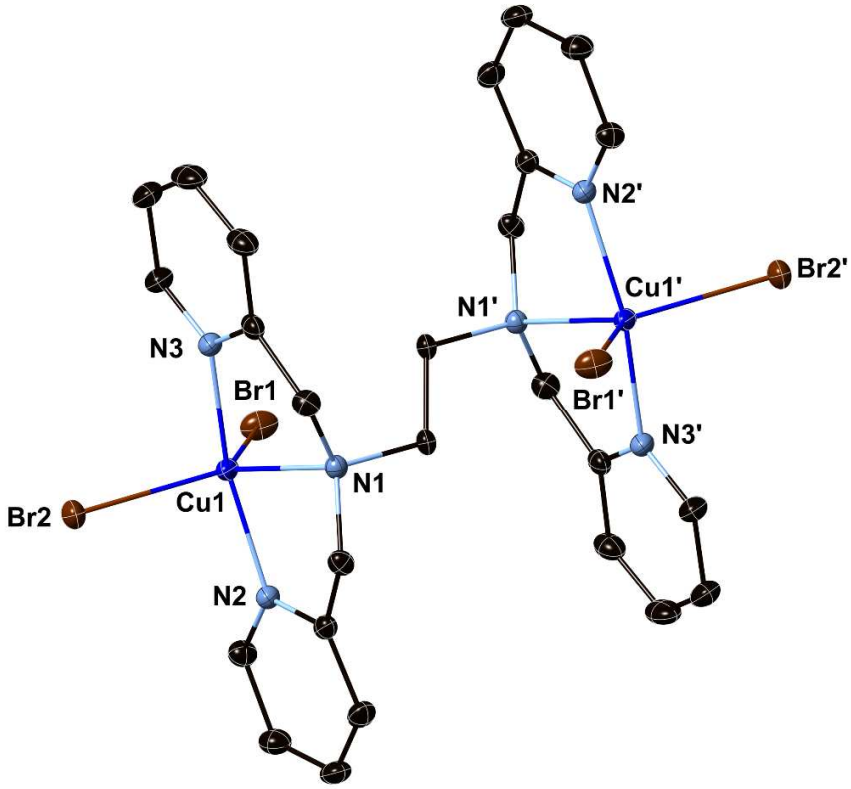


Figure 1. Molecular structure of [($Cu^{II}Br_2$)$_2$(TPEN)] at 150 K shown with 30% probability displacement ellipsoids. H-atoms have been omitted for clarity. Symmetry codes used to generate equivalent atoms: (1) -x+2,-y+1, -z+2. Selected bond distances [Å] and angles (^{o}): Cu1-N1 2.119(2), Cu1-N2 1.979(2), Cu1-N3 1.989(2), Cu1-Br1 2.4755(4), Cu1-Br2 2.4844(4), N1-Cu1-N2 82.16(8), N1-Cu1-N3 81.42(9), N2-Cu1-N3 163.15(9), N2-Cu1-Br1 94.73(6), N1-Cu1-Br1 118.43(6), N2-Cu1-Br1 94.73(6), N3-Cu1-Br1 96.39(7), N1-Cu1-Br2 118.81(6), N2-Cu1-Br2 93.37(6), N3-Cu1-Br2 91.22(6).

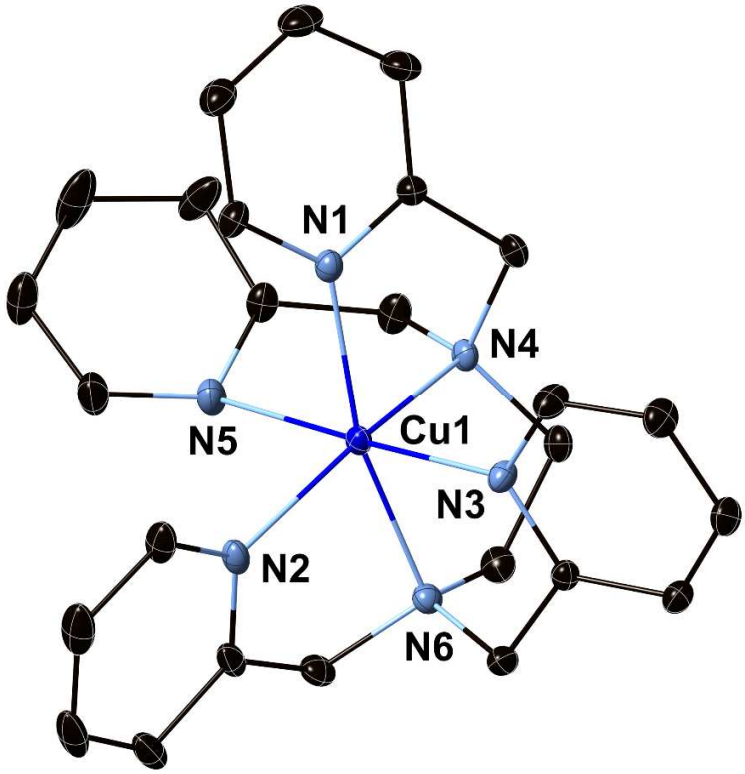


Figure 2. Molecular structure of $[Cu^{II}(TPEN)][BPh_4]_2$ at 150 K shown with 30% probability displacement ellipsoids. H-atoms, counterion BPh_4^- and solvent molecule (acetone) have been omitted for clarity. Selected bond distances [Å] and angles (°): Cu1-N1 2.050(3), Cu1-N2 2.024(3), Cu1-N3 2.210(3), Cu1-N4 2.063(3), Cu1-N5 2.475(4), Cu1-N6 2.067(3), N1-Cu1-N2 112.72(12), N1-Cu1-N4 81.27(11), N1-Cu1-N6 165.61(11), N2-Cu1-N3 96.71(11), N2-Cu1-N4,159.08(12), N2-Cu1-N5 87.48(12), N2-Cu1-N5 87.48(12), N3-Cu1-N6 80.83(11), N4-Cu1-N6 85.36(11), N4-Cu1-N5 78.00(11).

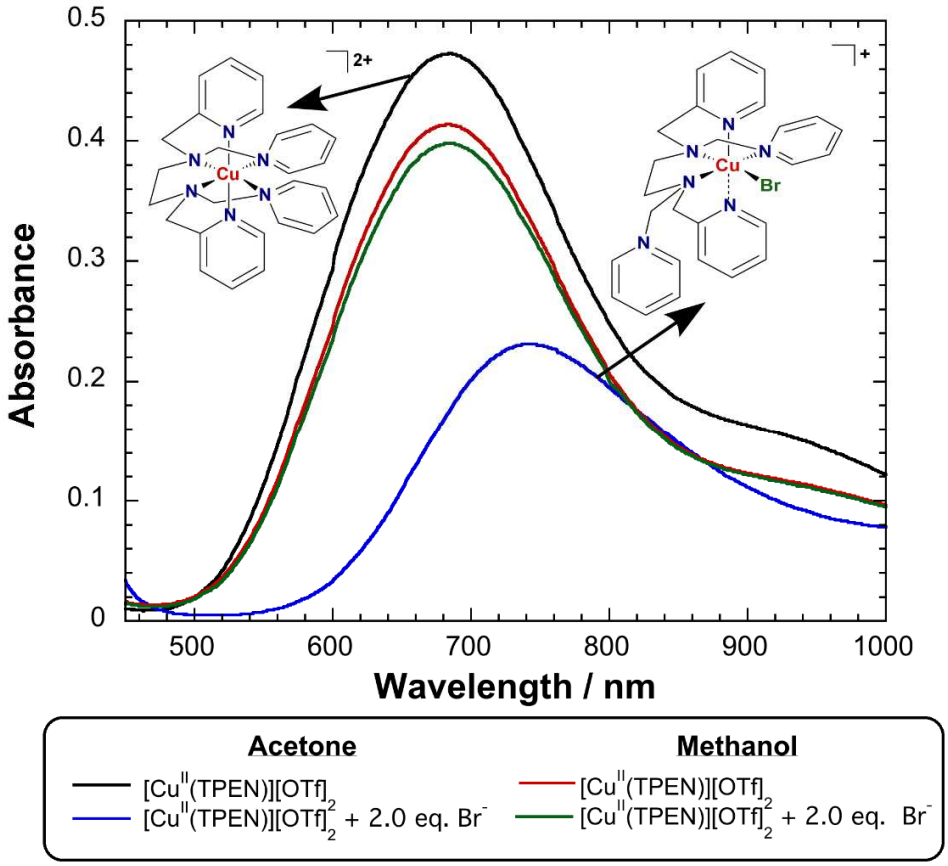


Figure 3. UV-Vis spectra of $[Cu^{II}(TPEN)][OTf]_2$ complex (2.5 mM) in acetone and methanol in the absence and presence of externally added tetrabutylammonium bromide (TBABr).

HIGHLIGHTS

- Copper complexes with TPEN ligand were successfully utilized in ATRA reactions in the presence of ascorbic acid as a reducing agent.
- The yields of the monoadduct were significantly increased in slightly polar but aprotic solvent such as acetone.
- The halidophilicity of the bromide-based deactivating complex, Cu^{II}(TPEN')Br][Br] decreased approximately 750 times upon changing solvent from acetone to methanol, explaining poor catalytic activity in methanol.
- Relevant copper(II) species were successfully isolated and characterized in the solid state and solution.