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Copper-based ATRP catalysts of very high activity derived from dimethyl cross-bridged cyclam

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Abstract

Dimethyl cross-bridged cyclam (DMCBCy) forms a very reducing Cu^I complex that possesses the highest known catalytic activity to date in atom transfer radical polymerization (ATRP) reactions. The value of the ATRP equilibrium constant in a reaction with methyl chloroacetate for Cu^ICl/DMCBCy is 30-fold larger than for the very active catalyst Cu^ICl/Me_6TREN. The activation rate constant for the DMCBCy-based complex was also determined and is about 1.5 times larger than for Cu^ICl/Me_6TREN. The ATRP of *n*-butyl acrylate mediated by Cu^IBr/DMCBCy was fast even at 30 °C and yielded well-defined polymers when a sufficient amount (about 10 mol% of the total catalyst) of deactivator ($Cu^{II}Br_2$/DMCBCy) was added to the reaction mixture. Side reactions such as electron transfer from the very reducing Cu^IBr/DMCBCy to the electrophilic acrylate radicals most likely account for the observed limited conversions.

Keywords: ATRP; Bridged cyclam; Catalysis; Controlled radical polymerization

1. Introduction

The preparation of well-defined/living polymers via the radical polymerization of vinyl monomers has long been a challenge due to the very fast (diffusion controlled) radical termination reactions. However, it was demonstrated [1] that if an equilibrium between active radicals and dormant species unable to terminate or react with the monomer is established, a living-like radical polymerization proceeds, similar to the living anionic process described in the 1950s [2–4]. All controlled radical polymerization (CRP) methods, including stable free radical-(mostly nitroxide-) mediated polymerization [5,6], atom transfer radical polymerization (ATRP) [7–11], reversible addition-fragmentation chain transfer (RAFT), [12–14] and degenerative group transfer polymerization [15] rely on such an equilibrium.

ATRP, originally reported in 1995, has become one of the most powerful synthetic techniques in polymer science. It allows the synthesis of polymers of various compositions with predetermined molecular weight and narrow molecular weight distribution. The highly chain end functionalized ATRP-prepared polymers can serve as macroinitiators for subsequent chain extension reactions, yielding a large variety of segmented copolymers [16]. In addition, a multitude of telechelic polymers can be conveniently synthesized using either end-group chemistry (mostly nucleophilic substitution or elimination reactions) or functional ATRP initiators, or a combination of both [17]. ATRP (Scheme 1) is a catalytic process based on the reversible reaction of a low-oxidation state metal complex Mt^zL_m (Mt^z represents the metal ion in oxidation state z, and L is a ligand; all charges are omitted for simplicity) with an alkyl halide RX producing radicals and the corresponding higher-oxidation state metal complex with a coordinated halide ligand $XMt^{z+1}L_m$. The "livingness" of this polymerization process can be ascertained from the first-order kinetics of consumption of the monomer M, accompanied by a linear increase in polymer molecular weights with conversion, with a value of the number-average degree of polymerization (DP_n) determined by the ratio of reacted monomer to initially introduced initiator ($DP_n(conv) = conv \times [M]_0/[RX]_0$). Originally, complexes of Cu [7,18] and Ru [9,19,20] were used as ATRP mediators, but many other metal complexes have

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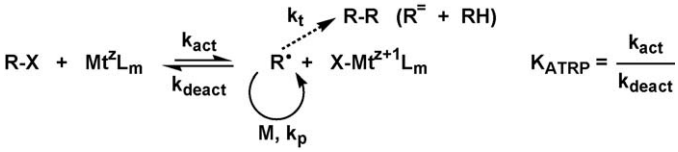


Scheme 1. Atom transfer radical polymerization.

since been used, including Ti [21], Mo [22–25], Re [26], Fe [27–32], Rh [19,33], Ni [34–36], Pd [37], and Os [38]. The copper-mediated reactions have found the most wide-spread application and will be the subject of this work.

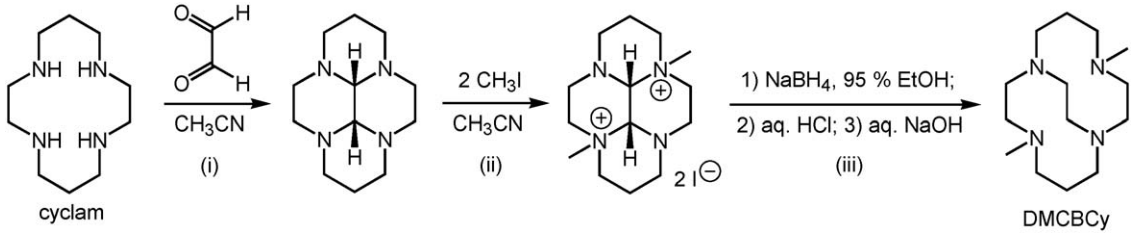
ATRP has already found industrial application [39], and it is envisioned that it will soon emerge as one of the processes of choice for the commercial production of specialty polymers. However, in order to minimize environmental pollution and ensure the success of ATRP in an industrial setting, the development of very active catalysts that can be used at low concentrations while still maintaining acceptable polymerization rates is desired [40]. In addition, catalysts that can perform well in environmentally friendly reaction media, mostly water, are needed. The activity of an ATRP catalyst is reflected by the value of the equilibrium constant $K_{ATRP} = k_{act}/k_{deact}$ (Scheme 1). The first copper-based ATRP catalysts were mostly derived from bidentate ligands such as 2,2′-bipyridine (bpy) [7,18] or its derivatives with alkyl [41–43] or fluoroalkyl [44] substituents (to increase the solubility of the catalyst in nonpolar media or supercritical carbon dioxide, respectively). Other bidentate ligands, including 1,10-phenanthrolines [45,46] and pyridylimine (Schiff bases derived from pyridine 2-carbaldehyde) [47,48] were also used. These complexes possessed satisfactory catalytic activity but still had to be used at relatively high concentrations (typically, 0.5–1 mol% relative to monomer). The produced polymers contained residual copper compounds, which had to be removed using various filtration, extraction, or ion-exchange methods [40,49]. This was one of the driving forces of the search for more active (and, preferably, less expensive) complexes.

It was demonstrated that some linear aliphatic amines such as *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDETA) and *N*,*N*,*N*′,*N*″,*N*‴,*N*‴-hexamethyltriethylenetetramine (HMTETA) formed rather active (more active than bpy) Cu^I complexes [50]. Another tridentate ligand with pyridine coordinating groups, 4,4′,4″-tris(5-nonyl)-terpyridine was also used, and it was shown that the catalytic activity of its copper complexes in the ATRP of styrene and methyl acrylate was higher than of those derived from bpy [51]. The linear tridentate ligand with "mixed" N-donor atoms (both pyridine- and aliphatic amine-type), *N*,*N*-bis(2-pyridylmethyl)octylamine (BPMOA), was successfully used in the ATRP of styrene, methyl acrylate, and methyl methacrylate; the polymerization of the last monomer proceeded at a satisfactory rate even at room temperature [52]. Branched *N*-based ligands, such as hexamethylated tris(2-aminoethyl)amine (Me_6TREN) [53,54] and tris(2-pyridylmethyl)amine (TPMA), [52] formed even more active ATRP catalysts. The ATRP of methyl acrylate mediated by the Cu^I complex of Me_6TREN was rather fast even at ambient temperature and at low catalyst concentration (0.05–0.1 mol% relative to initiator) [53,54]. Cyclic aliphatic amines such as Me_4cyclam formed catalytically very active Cu^I complexes [55] (more active than the complex of Me_6TREN [56]). However, despite the fast polymerization rates, the degree of control was not satisfactory due to inefficient radical deactivation by the $Cu^{II}X_2$/Me_4cyclam complex.

The discovery of novel ATRP catalysts of very high activity is extremely important in newly developed processes that use very low (in the ppm-range) concentrations of catalyst such as ARGET ATRP [57]. In addition, it is well known that some monomers can coordinate to Cu^I complexes [58,59] and, especially when used in large excess compared to the ATRP catalyst (as is the case in ARGET ATRP), they can displace the ligand of the catalyst causing a loss of catalytic activity. This unwanted process will be minimized if the ATRP catalyst is kinetically stable towards demetalation.

The redox potential of the couple $Cu^{II}L_m/Cu^IL_m$, which is largely responsible for the catalytic activity in ATRP reactions, depends upon the ratio of the stability constants of the complexes in the two oxidation states, i.e., β^{II}_m/β^I_m [40,60–63]. An appropriate ATRP catalyst of 1:1 stoichiometry is characterized by a large ratio of β^{II}/β^I, with large values of both β^{II} and β^I. If the latter requirement is met, the catalyst will not participate in ligand substitution reactions with monomer, polymer, or solvent, even in dilute solutions with respect to the catalyst and concentrated with respect to the mentioned reaction components. In addition, if the ATRP reaction is to be carried out in aqueous or protic media, the ratio $\beta^{II}/(\beta^I)^2$[L] should be as low as possible in order to prevent disproportionation [40,63]. Most ligands affect the redox potential of the couple $Cu^{II}L/Cu^IL$ through stabilization or destabilization of the Cu^{II} state of the complex [64]. In other words, if a ligand forms very stable Cu^{II} complexes, the corresponding Cu^I complex is likely to be very reducing and therefore catalytically active in ATRP reactions.

It was demonstrated that 4,11-dimethyl-1,4,8,11-tetraazabicyclo[6.6.2]hexadecane (referred to in this text as dimethyl cross-bridged cyclam or DMCBCy; Scheme 2)



Scheme 2. Synthesis of the ligand.

[65,66] forms a Cu^{II} complex that is exceptionally stable, even in acidic solutions such as 1 M $HClO_4$ (half-life of ligand dissociation was estimated as >6 years in this medium) [67]. Since the ligand is very basic ($pK_{a,4}$ of protonated DMCBCy was estimated as >13.5 and $pK_{a,3}$ was estimated as 10.8 [65]), the stability of its complexes in acidic media is a kinetic rather than thermodynamic phenomenon [67]. The formation constant of the parent Cu^{II}-cross-bridged-cyclam ($\log \beta^{II} = 27.1$) has been found to be essentially identical to that of Cu^{II}-cyclam (27.2) [68]. Cyclic voltammetry (CV) analysis of the Cu^{I} complex of DMCBCy demonstrated that it was very reducing [69]. This served as motivation to study the application of Cu^{I}/DMCBCy as an ATRP catalyst.

2. Experimental

2.1. Materials

Prior to use, *n*-butyl acrylate (*n*BA) was passed through a column filled with basic alumina in order to remove the polymerization inhibitor. CuBr (98%, Aldrich) was purified by washing with glacial acetic acid followed by 2-propanol. CuCl used for kinetic and equilibrium constant measurements was very pure reagent (99.995+%, Aldrich) and was kept in a vacuum desiccator. All other reagents: cyclam (98%, Aldrich), glyoxal (40% aqueous solution, Aldrich), iodomethane (99%, Aldrich), TEMPO (98%, Aldrich), sodium borohydride (98%, granules, Aldrich), $CuBr_2$ (99%, Aldrich), tetrabutylammonium hexafluorophosphate (98%, Aldrich), and the solvents (HPLC grade) were used as received. The initiators, methyl 2-bromopropionate (MBP, 98%, Aldrich) and methyl chloroacetate (MClAc, 99%, Aldrich), the ligands, bridged cyclam (DMCBCy, synthesized as described below) and Me_6TREN (synthesized according to a literature procedure [70]), as well as acetonitrile were purged with nitrogen for at least 6–7 h prior to the experiments.

2.2. Synthetic procedures

2.2.1. Synthesis of DMCBCy

A modification of the literature procedure was used for the synthesis of DMCBCy (Scheme 2) [66].

(i) Cyclam (10 g, 50 mmol) and 8.2 mL 40% aqueous solution of glyoxal were mixed with 830 mL of acetonitrile. The slightly turbid mixture was stirred for 20 h at room temperature, then for 5 h at 60 °C, and was left overnight at room temperature. The solvent was removed and the resulting product was extracted with 600 mL of chloroform for 1 h. The extract was filtered and the solvent was removed. An oil was obtained which was not purified.

(ii) The product from the previous step was mixed with 400 mL of acetonitrile (a turbid solution was obtained) and iodomethane (44 mL) was added over a period of 5 min. In ca. 5 min, crystals of the product started to separate. The reaction mixture was stirred at room temperature for 72 h and the excess of iodomethane and approximately half of the solvent was removed on a rotary evaporator. The obtained crystalline product was filtered and washed with acetonitrile. No further purification was performed.

(iii) 22.6 g of the ammonium salt obtained in the previous step was suspended in 830 mL of 95% ethanol and 15.97 g of sodium borohydride was slowly added. The reaction mixture was stirred at room temperature for 72 h (clear solution was formed) and the excess of borohydride was decomposed by the addition of ca. 500 mL of 10% HCl. The next day (the reaction mixture was noticeably darker), the solvent was removed on a rotary evaporator and the product was dissolved in 240 mL of water. The solution was made strongly basic by the addition of solid NaOH (pH 14) and the amine was extracted with six portions of 100 mL of benzene. The combined extracts were dried over sodium sulfate and the solvent was removed. The final product was distilled under reduced pressure (solid KOH was added to it) to yield 6.25 g (24.6 mmol, 49% overall yield) of pure *N*,*N*′-dimethyl cross-bridged cyclam (DMCBCy). NMR spectra were consistent with those previously reported in literature [66]. GC–MS analysis confirmed the purity of the product, and a molecular ion peak with *m*/*z* equal to 254 (M^+) was observed in the mass spectrum.

2.2.2. Synthesis of $Cu^{II}Br_2$/DMCBCy

The procedure was similar to that reported for $Cu^{II}Cl_2$/DMCBCy [69]. Anhydrous $CuBr_2$ (0.1115 g, 0.5 mmol) was placed in a flask under dry nitrogen and extra dry (5 ppm of water) methanol (10 mL) was added. A solution of DMCBCy (0.127 g, 0.5 mmol) in 5 mL of extra dry methanol was added. A greenish-blue solution was obtained containing a small amount of bluish precipitate. The mixture was stirred for 1 h at room temperature and then at 70 °C for 3 h. The solvent was removed on a rotary evaporator and the complex (0.23 g) was obtained as blue crystals.

2.2.3. ATRP of nBA

To a mixture of *n*BA (10 mL, 0.07 mol), butanone (5 mL), and diphenyl ether (internal standard for determination of conversion) contained in a Schlenk flask, the ligand DMCBCy (33 μL, 0.0356 g, 0.14 mmol, 1/500 versus monomer) was added and the mixture was degassed by five freeze-pump-thaw cycles. The mixture was frozen, the flask was back-filled with nitrogen, and CuBr (0.0201 g, 0.14 mmol) was added. While the reaction mixture was still frozen, the reaction flask was tightly closed and evacuated and back-filled with nitrogen several times. The mixture was allowed to thaw and was then heated in an oil bath to 75 °C. The deoxygenated initiator, MBP (16 μL, 0.14 mmol), was added last. The initially colorless mixture rapidly became heterogeneous and dark green due to the fast formation of Cu^{II} complex of DMCBCy. Samples were periodically withdrawn with a nitrogen-purged syringe for determination of monomer conversion and polymer molecular weights and polydispersities. In another experiment, the total concentration of catalyst was decreased by a factor of four, the solvent was replaced by acetone, and the reaction temperature was lowered to 30 °C. The catalyst consisted of a mixture of $Cu^{I}Br$/DMCBCy (formed in

situ from CuBr and DMCBCy) and $Cu^{II}Br_2$/DMCBCy (synthesized as described above) at a ratio of 9:1. A bulk ATRP of *n*BA was also carried out at 30 °C using Cu^{I}-only containing catalyst.

2.2.4. Analyses

Monomer conversions were determined on a Shimadzu GC-14A gas chromatograph equipped with a flame ionization detector and a capillary column (30 m × 0.53 mm × 1.0 μm CEC-Wax column, Chrom Expert Co.) using the signal of the added diphenyl ether as standard. GC for the determination of activation rate constants was performed using a Schimadzu GC-17A, AOC-20i autosampler and J&W Scientific DB 608 column (30 m × 0.53 mm) with an electron capture detector (ECD). The ECD is very sensitive to alkyl halides and governed by radiation (β-ray) from a ^{63}Ni source sealed in the ECD cell ionized by an inert gas (nitrogen). Molecular weight distributions were determined by SEC using a series of Styrogel columns (10^5, 10^3 and 100 Å, PSS) and THF (30 °C) as the eluent, and polystyrene calibration using diphenyl ether as internal standard. The spectroscopic measurements were performed on a Cary 5000 UV/VIS/NIR spectrometer (Varian).

2.2.5. Measurement of activation rate constants (k_{act})

An initiator stock solution was prepared by adding 0.0043 g (0.04 mmol) of MClAc along with 0.0072 g (0.04 mmol) of internal standard, trichlorobenzene, and 0.0625 g (0.4 mmol) of TEMPO in acetonitrile in a 10 mL volumetric flask. Similarly, an 80 mM stock solution of Me_6TREN was prepared in acetonitrile. CuCl (0.0079 g, 0.08 mmol) was added to a Schlenk flask, which was then degassed and back-filled with nitrogen three times. Stock solution of Me_6TREN (1 mL) along with 2 mL of acetonitrile were subjected to freeze-pump-thaw cycle three times and then transferred to the Schlenk flask through a degassed syringe. Then, 1 mL of the stock solution of MClAc, trichlorobenzene, and TEMPO was degassed by freeze-pump-thaw cycle three times and transferred to the Schlenk flask through a degassed syringe. The flask was stirred and a sample was taken immediately for the GC analysis generating the data for time 0. The reaction was carried out at 35 °C under constant stirring. Samples were taken at timed intervals, and the consumption of alkyl chloride with time was monitored by GC. The reaction with the CuCl complex of DMCBCy was performed in a similar manner.

2.2.6. General procedure for the determination of equilibrium constants (K_{ATRP})

CuCl (0.0049 g, 0.05 mmol) was added to a Schlenk flask joined to a quartz UV cuvette and the Schlenk flask was carefully sealed. It was then evacuated and back-filled with nitrogen five times. Deoxygenated MeCN (10 mL) was added through the side arm of the flask via a nitrogen-purged syringe. The ligand, Me_6TREN (13.2 μL, 0.05 mmol) or DMCBCy (13.5 μL, 0.05 mmol), was added using a nitrogen-purged micro-syringe. The contents were stirred for 30–40 min until a yellowish (in the case of Me_6TREN) or colorless (in the case of DMCBCy) solution was obtained. The flask was transferred to a UV/VIS spectrometer and the absorbance of the solution at a wavelength corresponding to the λ_{max} of the Cu^{II}/ligand chloride complex (940 nm for the Me_6TREN ($\varepsilon_{940} = 425\ M^{-1}\ cm^{-1}$) and 670 nm for the DMCBCy complex ($\varepsilon_{670} = 100\ M^{-1}\ cm^{-1}$)) was set to zero. MClAc (purged with nitrogen, 4.38 μL, 0.05 mmol) was then transferred to the Schlenk flask via a N_2-purged microsyringe. The absorbance at a wavelength corresponding to the λ_{max} of the generated X–Cu^{II} complex was monitored at timed intervals. The concentration of the deactivator generated in the system due to the persistent radical effect was calculated using values of the extinction coefficients for the Cu^{II} complexes determined separately in MeCN. Two measurements were performed with each complex and the average value of K_{ATRP} is reported.

2.2.7. Cyclic voltammetry

The voltammograms were recorded on a Perkin-Elmer Potentiostat/Galvanostat 263A. 1.0 mM solutions of $Cu^{II}X_2$/L were prepared in acetonitrile containing 0.1 M Bu_4NPF_6 as the supporting electrolyte. Measurements were carried out at room temperature under nitrogen at a scanning rate of 0.1 V s^{-1} using a platinum disk as the working electrode, a platinum wire as the counter electrode, and an Ag/AgCl reference electrode. The $E_{1/2}$ value of the ferrocene standard was determined in a separate CV experiment; all reported values of $E_{1/2}$ are relative to this standard.

3. Results and discussion

3.1. Electrochemical studies

The rate of ATRP of a monomer *M* is given by [10]

$$R_p = k_p K_{ATRP} \frac{[RX][Cu^{I}L_m]}{[XCu^{II}L_m]}[M] \quad (1)$$

In the above equation, k_p is the propagation rate constant of M. Consequently, the knowledge of the ATRP equilibrium constant and the factors that determine its value are of crucial importance for the development of active ATRP catalysts. The overall atom transfer equilibrium can be presented as a combination of four simpler reversible reactions: (i) oxidation of the $Cu^{I}L_m$ complex (characterized by the equilibrium constant of electron transfer K_{ET}), (ii) reduction of a halogen atom to a halide ion (electron affinity K_{EA} of X), (iii) C–X bond homolysis (K_{BH}), and (iv) association of halide ion to $Cu^{II}L_m$ (termed *halogenophilicity* K_X) as shown in Fig. 1 and Eq. (2) [71].

$$K_{ATRP} = \frac{k_{act}}{k_{deact}} = K_{BH} K_{ET} K_{EA} K_X \quad (2)$$

ATRP is a redox process, and it is natural to correlate the behavior of the copper-based complexes in ATRP reactions with their redox potentials [72–76]. Catalytic activity (i.e., a large value of either k_{act} or K_{ATRP}) is indeed correlated to the reducing power of Cu^{I} complexes. The equilibrium constant K_{ET} (and consequently, K_{ATRP}) is directly related to the redox potential of the

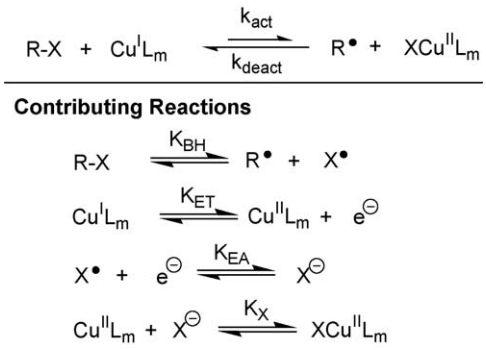


Fig. 1. Representation of atom transfer as a combination of a C–X bond homolysis of alkyl halide (RX), two redox processes, and a heterolytic cleavage of Cu^{II}–X bond. L represents a ligand (adapted from Ref. [71]).

couple $Cu^{II}L_m/Cu^{I}L_m$ [60–62]:

$$E \approx -\frac{RT}{F} \ln K_{ET} \quad (3)$$

More reducing Cu^{I} complexes (higher value of K_{ET}) are catalytically more active. Cyclic voltammograms of $Cu^{II}X_2$/DMCBCy complexes were measured and compared with those of the most active ATRP catalysts known to date, namely these derived from the tripodal tetradentate ligand Me_6TREN. Indeed, the $E_{1/2}$ of $Cu^{II}Cl_2$/DMCBCy was found to be 75 mV more negative than $Cu^{II}Cl_2/Me_6$TREN, while that of the bromide analogue ($Cu^{II}Br_2$/DMCBCy) was 35 mV more negative than $Cu^{II}Br_2/Me_6$TREN (Fig. 2 and Table 1). From Eq. (3), it is expected that the values of K_{ET} and consequently K_{ATRP} in reactions mediated by Cu^{I}Cl/DMCBCy should be slightly more than an order of magnitude higher than those mediated by $Cu^{I}Cl/Me_6$TREN. These results illustrate the considerable reducing power of the Cu^{I}X/DMCBCy catalysts. Based on the electrochemical studies, it is expected that these complexes will be markedly more active catalysts than the most active ones known to date derived from Me_6TREN.

Additionally, the $E_{1/2}$ of $CuCl_2$ complexes of DMCBCy and Me_6TREN are more negative than their bromide analogues by

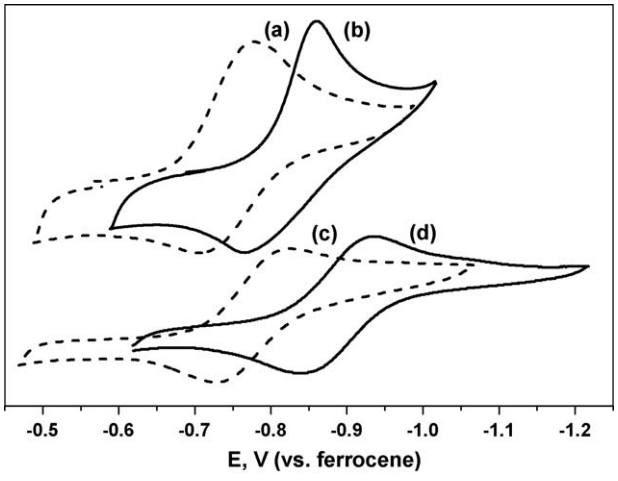


Fig. 2. Cyclic voltammetry of $Cu^{II}X_2/Me_6$TREN (X = (a) Br and (b) Cl) and $Cu^{II}X_2$/DMCBCy (X = (c) Br and (d) Cl) in acetonitrile; 0.1 M Bu_4NPF_6, 1.0 mM $Cu^{II}X_2$/L; scan rate = 0.10 V s^{-1}.

Table 1
Redox potentials of copper complexes measured in acetonitrile at room temperature[a]

Cu^{II} halide	Ligand	$E_{p,a}$ (V)	$E_{p,c}$ (V)	ΔE_p (mV)	$E_{1/2}$ (V)
$CuBr_2$	Me_6TREN	−0.705	−0.777	72	−0.741
$CuCl_2$	Me_6TREN	−0.766	−0.860	94	−0.813
$CuBr_2$	DMCBCy	−0.727	−0.825	98	−0.776
$CuCl_2$	DMCBCy	−0.839	−0.936	97	−0.888

$E_{p,a}$ and $E_{p,c}$ are the peak potentials of the oxidation and reduction waves, respectively. $E_{1/2} = (E_{p,a} + E_{p,c})/2$.
[a] 0.1 M NBu_4PF_6, 1.0 mM Cu^{II} complex, scan rate 0.10 V s^{-1}; potentials reported vs. ferrocene (which was measured as 0.468 relative to Ag/AgCl electrode).

112 and 72 mV, respectively. This difference reflects the stronger affinity of the moderately hard Cu^{II} Lewis acid for the chloride ions compared to bromide, since the former anions are harder bases [77]. The magnitude of this shift is consistent with the trend observed [73] for other Cu-based ATRP catalysts in non-protic solvents. (In protic solvents, the chlorophilicity and bromophilicity of the Cu^{II} complexes of bpy are very close [78].)

3.2. ATRP equilibrium constants

To evaluate the catalytic activity of the Cu^{I}X/DMCBCy complexes in ATRP and compare it to the very active catalysts derived from Me_6TREN, the experimental values of K_{ATRP} should be determined. This can be accomplished using an equation describing the time dependence of accumulation of deactivator due to the persistent radical effect. In early works, the linear dependence of $[XCu^{II}L_m]$ on the cube root of time, proposed by Fischer and Fukuda [79–81] was used for this purpose. This method is useful for reactions that reach equilibrium rapidly, and then only for relatively low conversions of both activator ($Cu^{I}L_m$) and alkyl halide. A modification of this approach was recently proposed [82] that is useful for high conversions and especially for active catalysts. More precise equations describing the persistent radical effect were derived that take into consideration that the concentrations of neither the activator nor the initiator remain constant during the experiment [82]. If the activator and initiator are mixed in a 1:1 molar ratio, the reaction stoichiometry requires that $[RX]_0 - [RX] = [Cu^{I}L_m]_0 - [Cu^{I}L_m] = [XCu^{II}L_m]$. Using the assumption (justified by simulations) that the rate of generation of deactivator exceeds significantly the rate of consumption of radicals, new equations correlating $[XCu^{II}L_m]$ and time were obtained. For the simple 1:1 stoichiometry ($[Cu^{I}L_m]_0 = [RX]_0$), the values of a function $F([XCu^{II}L_m])$ defined in Eq. (4) are plotted against time, and the equilibrium constant K_{ATRP} is obtained from the slope.

$$F([XCu^{II}L_m]) = \frac{[Cu^{I}L_m]_0^2}{3([Cu^{I}L_m]_0 - [XCu^{II}L_m])^3} - \frac{[Cu^{I}L_m]_0}{([Cu^{I}L_m]_0 - [XCu^{II}L_m])^2} + \frac{1}{[Cu^{I}L_m]_0 - [XCu^{II}L_m]} = 2k_t K_{ATRP}^2 t + \frac{1}{3[Cu^{I}L_m]_0} \quad (4)$$

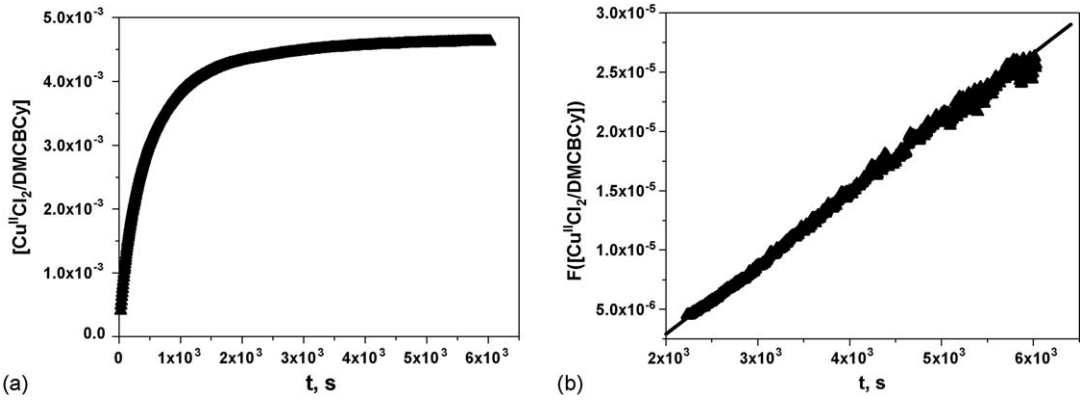


Fig. 3. Determination of K_{ATRP} for the reaction of Cu^ICl/DMCBCy (5 mM) with MClAc (5 mM) in MeCN: (a) accumulation of deactivator with time; (b) plot of $F([Cu^{II}Cl_2/DMCBCy])$ against time (equilibrium reached in ca. 2000 s).

To determine K_{ATRP}, a Cu^I complex is reacted with an alkyl halide, and the increase of deactivator concentration is monitored as a function of time (e.g., by electronic spectrophotometry as shown in Fig. 3a). In Eq. (4), the only variable is the deactivator concentration. If this is known, a plot of $F([XCu^{II}L_m])$ against time should yield a straight line after equilibrium had been reached, and K_{ATRP} can be determined as $K_{ATRP} = \sqrt{\text{slope}/2k_t}$ (Fig. 3b). The wide applicability of this approach was demonstrated [82].

Both Cu^IX/Me_6TREN and Cu^IX/DMCBCy react very rapidly with active alkyl halide ATRP initiators and, in order to be able to measure and compare the values of K_{ATRP} for these catalysts, an alkyl halide of relatively low activity, namely MClAc, was studied. The results are shown in Table 2; as expected based on the CV measurements presented above, the activity of the DMCBCy-based catalyst is more than an order of magnitude higher than that of Cu^ICl/Me_6TREN.

3.3. Activation and deactivation rate constants

To evaluate the performance of an ATRP catalyst, knowledge of not only K_{ATRP} but also of the deactivation rate constant k_{deact} is required. While K_{ATRP} determines the polymerization rate (*vide supra*), k_{deact} is mainly responsible for the polymerization control. The polydispersity index (PDI) of the polymers produced in ATRP is given by a relationship, originally derived for living ionic polymerisation [83,84], later [85] modified to describe living radical polymerization, and eventually generalized for all polymerizations involving exchange processes between species of different activities [86]:

$$\text{PDI} = \frac{M_w}{M_n} \approx 1 + \left(\frac{k_p[RX]_0}{k_{deact}[XCu^{II}L_m]}\right)\left(\frac{2}{\text{conv}} - 1\right) \quad (5)$$

The value of k_{deact} can be determined using the clock reaction in which the radicals are simultaneously trapped by TEMPO and the deactivator $XCu^{II}L_n$ [74] or from analysis of the initial degrees of polymerization with no reactivation, end groups, and molecular weight distributions [87–89]. Alternatively, k_{deact} can be determined indirectly from known values of K_{ATRP} and k_{act}. The rate constant k_{act} can be determined by reacting an alkyl halide with an excess (often 20-fold to provide pseudo-first order kinetic conditions) of the Cu^I complex, and trapping the formed radicals by agents such as nitroxides. The consumption of alkyl halide (monitored by spectroscopic or chromatographic techniques) is described by a first-order kinetics law: $\ln([RX]_0/[RX]) = k_{act}[Cu^IL_n]_0 t$, and k_{act} is obtained from the slope of this linear dependence [90–94]. The alkyl halide used in this study was again MClAc. The determined values of k_{act} for both Cu^ICl/DMCBCy and Cu^ICl/Me_6TREN are given in Table 2.

The value of k_{act} for the complex Cu^ICl/DMCBCy is higher than for Cu^ICl/Me_6TREN, which, again, reflects the very high catalytic ATRP activity of the former complex. It should be noted, however, that although the values of K_{ATRP} for the two catalysts differ by a factor of 30, these of k_{act} differ by a factor of only ca. 1.5. This means that the complex $Cu^{II}Cl_2$/DMCBCy is a slower ATRP deactivator than the corresponding Me_6TREN-based Cu^{II} complex (k_{deact} of the former being lower by about a factor of 20). It is therefore expected that although ATRP reactions mediated by Cu^IX/DMCBCy will be very fast and the complex can be used at very low concentrations, the polymerization control may be worse than with Cu^IX/Me_6TREN catalysts.

Table 2
Comparison of the activity of Cu^ICl/DMCBCy and Cu^ICl/Me_6TREN as ATRP catalysts[a]

Catalyst	K_{ATRP} (22 °C)	k_{act} (M^{-1} s^{-1}) (35 °C)
Cu^ICl/DMCBCy	9.9×10^{-5}	0.42
Cu^ICl/Me_6TREN	3.3×10^{-6}	0.27

[a] Reactions were performed using MClAc as the initiator in MeCN.

3.4. ATRP of nBA mediated by Cu^IBr/DMCBCy

The first results from the solution ATRP of *n*BA mediated by Cu^IBr/DMCBCy and initiated by MBP showed that the catalyst was very active. When a degree of polymerization of 500 (i.e.,

Table 3
ATRP of *n*BA mediated by $Cu^{I}Br$/DMCBCy

#	Rection conditions	*t* (min)	Conversion	M_n (g/mol)	PDI
1	[*n*BA]:[MBP]:[$Cu^{I}Br$/DMCBCy] = 500:1:1, 75 °C, in butanone (33 vol.%)	90	0.33	20700	1.64
		300	0.43	25300	1.85
2	[*n*BA]:[MBP]:[$Cu^{I}Br$/DMCBCy] = 730:1:1, 30 °C, bulk	45	0.15	12000	1.30
		140	0.21	19900	1.31
		245	0.24	22900	1.40
		600	0.45	26000	1.60
3	[*n*BA]:[MBP]:[$Cu^{I}Br$/DMCBCy]:[$Cu^{II}Br_2$/DMCBCy] = 500:1:0.225:0.025, 30 °C, in acetone (33 vol.%)	60	0.10	3000	1.26
		285	0.18	5200	1.20

$[nBA]_0/[MBP]_0 = 500$) was targeted and the catalyst was used at a 1:1 molar ratio to the initiator, the conversion reached 43% in 5 h at 75 °C (Table 3). The polydispersities of the polymers were relatively high, most likely due to the large number of dead chains produced at the beginning of the polymerization, as a result of the presence of large concentration of the very active catalyst. This is confirmed by the noticeable tailing of the SEC traces of the polymers towards the low molecular weights (Fig. 4 and entry 1 in Table 3). It should be noted that molecular weights increase with conversion, indicating the controlled/living nature of the process.

The polymerization was then carried out in bulk at lower temperature while still keeping the same ratios of [*n*BA]:[MBP]:[$Cu^{I}Br$/DMCBCy] as in the previous experiment. The control over polymerization was improved (entry 2 in Table 3). The termination was less pronounced at the lower reaction temperature, which is reflected by the lower values of PDI as well as in the more symmetrical shift of the SEC traces with conversion (Fig. 5). An important side reaction that very likely accounts for the observed relatively low monomer conversions and the slowing down of the polymerization is the electron transfer from the highly reducing $Cu^{I}Br$/DMCBCy to the electrophilic acrylate radical $\sim CH_2–C^{\bullet}H(CO_2C_4H_9)$ [95]. The formed anion leads to the formation of dead polymer chains. Radicals with electron withdrawing α-substituents, such as carbonyl, ester, or nitrile groups, are known to be rather oxidizing [96]. The redox process should be markedly less pronounced in the ATRP of monomers forming less electrophilic radicals, e.g., styrenes. In addition, due to the low redox potential of the catalyst, the reaction mixtures are particularly sensitive to oxygen, and the observed slowing of the polymerization may be partially attributed to the oxidation of the catalyst, which could take place during the sampling.

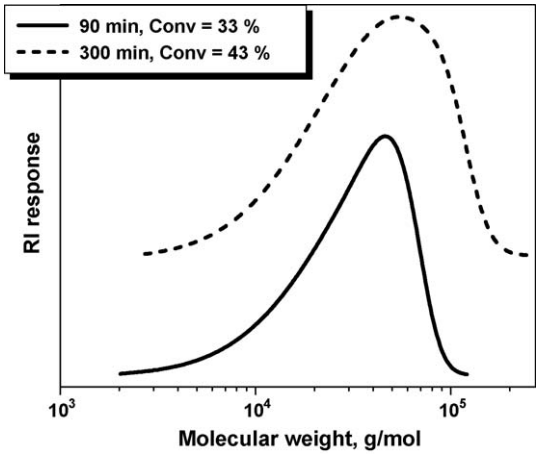


Fig. 4. SEC traces of poly(*n*BA) produced in the solution ATRP of *n*BA using [*n*BA]:[MBP]:[$Cu^{I}Br$/DMCBCy] = 500:1:1 at 75 °C. The amount of butanone was 33 vol.%.

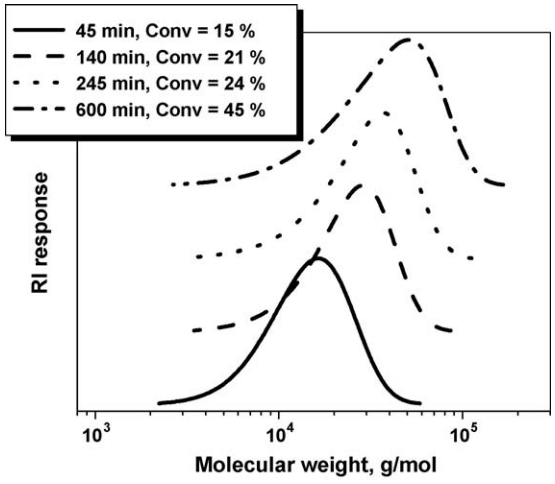


Fig. 5. SEC traces of poly(*n*BA) produced in the bulk ATRP of *n*BA using [*n*BA]:[MBP]:[$Cu^{I}Br$/DMCBCy] = 500:1:1 at 30 °C.

To decrease the polymerization rate even further, the total catalyst concentration was decreased by a factor of four, and, in order to enhance the radical deactivation, the catalyst contained 10 mol% of deactivator ($Cu^{II}Br_2$/DMCBCy). As seen from entry 3 in Table 3, the control over polymerization was improved and polymers of low PDI (which decreased with conversion) were produced. However, the reaction did not proceed to high conversion as a result of the aforementioned redox process with acrylate radicals and/or catalyst oxidation by traces of air introduced in the system.

4. Conclusions

The strongly reducing copper-based ATRP catalyst derived from 4,11-dimethyl-1,4,8,11-tetraazabicyclo [6.6.2] hexadecane (cross-bridged cyclam, DMCBCy) possesses higher activity than any other copper complex known to date. The value of

the ATRP equilibrium constant in a reaction of methyl chloroacetate with $Cu^{I}Cl$/DMCBCy ($K_{ATRP} = 9.9 \times 10^{-5}$) is 30-fold larger than for the very active catalyst $Cu^{I}Cl/Me_6TREN$. The value of the activation rate constant for the DMCBCy complex in a reaction with the same alkyl halide ($k_{act} = 0.42\ M^{-1}\ s^{-1}$) was about 1.5 times larger than for the Me_6TREN-based complex, indicating that the deactivation with the former complex is about 20 times slower. The ATRP of *n*-butyl acrylate mediated by $Cu^{I}Br$/DMCBCy was fast at 30 °C and yielded low-polydispersity polymers especially in the case when sufficient amount of deactivator ($Cu^{II}Br_2$/DMCBCy) had been added to the reaction mixture. The novel complex can be used at low concentration and is thus attractive for the preparation of polymers containing a very low amount of copper impurities. Due to the significant stability of the complex, it can find application in ARGET ATRP as well.

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