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Atom Transfer Radical Polymerization of Methyl Methacrylate Initiated by Alkyl Bromide and 2-Pyridinecarbaldehyde Imine Copper(I) Complexes

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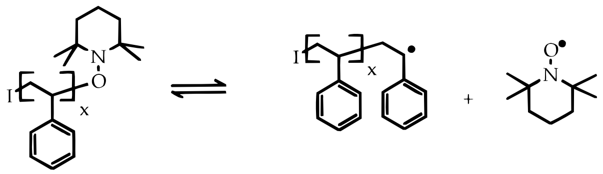
The controlled/"living" polymerization of methacrylates is the object of intense activity.[1] The discovery of group transfer polymerization (GTP) by DuPont has initiated many investigations into this area with one of the primary objectives being a commercially viable process giving access to the wealth of novel polymer architecture and polymer properties afforded by controlled synthesis.[2] As pointed out by one of the inventors of GTP, perhaps the ultimate goal in this area is a truly living free radical process[3] which will be compatible with protic solvents, functional monomers, and "non-activated" monomers. A number of advances in this area have recently been made. The use of stable organic free radicals such as nitroxides to end cap propagating styryl radicals, Scheme 1, enables the synthesis of narrow molecular weight distribution and controlled M_n polystyrene and polystyrenes at elevated temperatures over prolonged reaction times in the absence of solvent.[4−12] However, this is not applicable to other vinyl monomers such as methacrylates and acrylates. The position of the equilibrium in Scheme 1 is controlled by the strength and nature of the polymer−nitroxide bond and the stability of the polymer radical. The stability of the polymer radical is a fixed parameter, and it is difficult to exercise control over the polymer−nitroxide bond due to the inherent nature of the stable nitroxide species.

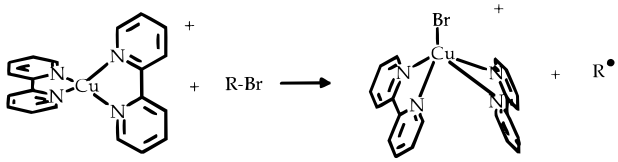
Scheme 1



Scheme 2

$$M(n) + R\text{-}X \leftrightharpoons M(n+1)\text{-}X + R^{\bullet}$$

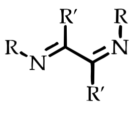
Scheme 3



Recently, independently from each other, Matyjaszewski[13,14] and Sawamoto[15] reported the use of atom transfer radical addition chemistry, as developed for carbon−carbon bond formation in organic synthesis, to mediate atom transfer radical polymerization (ATRP) for the controlled/"living" polymerization of vinyl monomers. In both cases the chemistry can be described by the equilibrium in Scheme 2, where X = Br or Cl and M = Cu(I) or Ru(II) in the case of Matyjaszewski and Sawamoto, respectively. In both cases R represents both the initiator species and the polymer radical where the initiating alkyl halide is chosen so as to give a primary radical of similar type to the propagating polymer radical. Sawamoto utilizes $Ru(PPh_3)_3Cl_2/CCl_4$ for polymerization of methyl methacrylate. However, in order to achieve acceptable rates of polymerization a sterically hindered aluminum alkyl or $Al(O^iPr)_3$ is used as co-catalyst, thus limiting the choice of solvents and of certain functional monomers that are prone to reaction with such species.[15] Percec has offered an alternative type of initiator based on aryl sulfonyl chlorides.[16] Matyjaszewski has described the use of Cu^IX(X = Br, Cl) with 2,2′-bipyridine, bpy, as a "solubilizing" ligand. The active species has been described as "CuBr·bpy". This system is active toward styrene, acrylates, and methacrylates under the appropriate conditions.[14] Percec has also described the role of bpy as partially solubilizing the Cu(I)/Cu(II) catalyst.[16b] The role of the bpy will be to co-ordinate to Cu(I) to give a *pseudo*-tetrahedral Cu(I) center in solution, Scheme 3.

When uncoordinated, bpy exists predominately in the s-trans conformation in the solid state, in solution there is free rotation with the trans conformation and orthoganal rings are preferred over the cis conformation. Metal complexes contain bpy in a cisoid conformation, forming a planar 5-membered chelating ring. The ligand π* orbitals can accept electron density from the metal thus stabilizing low oxidation states, in particular Cu(I). Abstraction by the $Cu(bpy)_2^+$ cation of halogen atoms from alkyl halides results in oxidation to Cu(II); we have proposed the pentaco-ordinated species shown in Scheme 3 which involves rotation of the bpy ligands away from the tetrahedral and co-ordination of the halide at the Cu center. This has also been proposed by Matyjaszewski.[17] Thus, if this proposed mechanism is correct, the two main roles of the ligand are (i) stabilization of Cu(I) by removal of electron density from the metal and (ii) the ability to interchange between tetrahedral Cu(I) and distorted square based pyramidal Cu(II). Copper(I) halides are very insoluble in organic solvents and monomers, and therefore the concept of solubilizing copper(I) is indeed valid. However, the use of either Cu^IBr or Cu^ICl with bpy under atom transfer radical polymerization conditions results in a very heterogeneous reaction medium with a deep red $Cu(bpy)_2$ complex in solution and insoluble copper halide visible as a pale green solid. Under these conditions the actual concentration of active catalyst is impossible to determine. The system has been modified to give a homogeneous system by the use of bipyridines with alkyl substituents in the 4 position e.g. *tert*-butyl.[18] The use of these homogeneous copper(I) complexes results in a marked lowering of the polydispersity index (PDI) to approximately 1.05.

Bipyridines are α-diimines which have the N=C−C=N skeleton. Two other representatives of this class of ligand are 1,4-diaza-1,3-butadienes, **1**,[19] and 2-pyridinecarbaldehyde imines, **2**.[20] Both **1** and **2** have the



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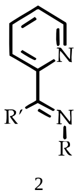

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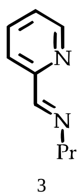

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Table 1. Polymerization of MMA at 90 °C where [3]:[Cu^{I}Br]:[ethyl 2-bromoisobutyrate] (In) = 3:1:1 and [MMA]:[In] = 200:1.

time/min	C_w/%[a]	M_n	M_w/M_n
120	16.47	2380	1.28
240	52.69	5250	1.22
300	61.02	6230	1.18
360	67.56	6740	1.21
485	78.56	7020	1.27

[a] C_w = weight conversion by gravimetry.

capability of accepting electron density into a π^* orbital and have been found to be superior to bpy in stabilizing metals in low oxidation states.[19,20] Ligands of class **1** have recently been used co-ordinated to Ni as very effective ethene polymerization catalysts[21] although neither have been used in atom transfer chemistry. Both **1** and **2** are readily synthesized by the condensation of the appropriate aldehyde, or ketone, with a primary amine. The wide range of R groups that may be introduced, from primary amines and carbonyl compounds, as well as the possibility of substitution on the aromatic pyridyl ring in the case of **2** led us to believe that these classes of ligand may be utilized with Cu(I) for effective atom transfer radical polymerization. The ability to alter the ancillary substituents should give control over the equilibrium shown in Scheme 2. Using electron-donating and -withdrawing groups on the ligand will allow stabilization of Cu(II) and Cu(I), respectively, as well as allowing control over catalyst solubility. Having catalysts with a range of solubility is important in determining the amount of active species present in solution as well as in the subsequent development of this chemistry to heterogeneous polymerization, e.g. miniemulsion. This communication reports the initial results of our study.

Polymerization of methyl methacrylate was carried out in xylene solution at 90 °C using a 3:1:1 ratio of **3**[22]: Cu^{I}Br:ethyl 2-bromoisobutyrate (In) and [MMA]:[In] = 200:1;[23] the results are summarized in Table 1. Figure 1a shows that M_n increases linearly with conversion up to over 70% conversion while the PDI remains consistantly low, PDI broadens at higher conversion. Increasing the [MMA]:[ethyl 2-bromoisobutyrate] ratio results in the expected increase in M_n, Figure 1a. However, it must be noted that while maintaining the [ethyl 2-bromoisobutyrate]:[CuBr] ratio at 1:1 we also change the [MMA]:[ethyl 2-bromoisobutyrate] ratio by the same degree. Figure 1b shows the *pseudo*-first-order kinetic plot for the reaction where [MMA]:[ethyl 2-bromoisobutyrate] = 200:1. The plot is close to linear indicating the number of active species remains constant throughout the reaction; i.e. $k_p[P^*]$ = constant. It is interesting to note that the kinetic plot does not pass through zero time but indicates an induction period of approximately 50 min. The presence of a induction period has been observed over all of our experiments and is ascribed to formation of the active initiator *in situ* from either reaction between the alkyl bromide and copper(I) bromide, from impurities either in the monomer or copper(I) bromide or more probably formation of an active Cu(II) species. This could explain why the PDI is significantly greater than 1.05, and this is currently being investigated in our laboratory. The SEC curve is observed to move to higher mass throughout the course of the reaction, Figure 2. These results are consistent with a "living" atom transfer radical polymerization. The broadening of PDI at higher conversion is indicative of a certain amount of termination occurring and manifests itself as the rate of propagation decreases due to monomer consumption.

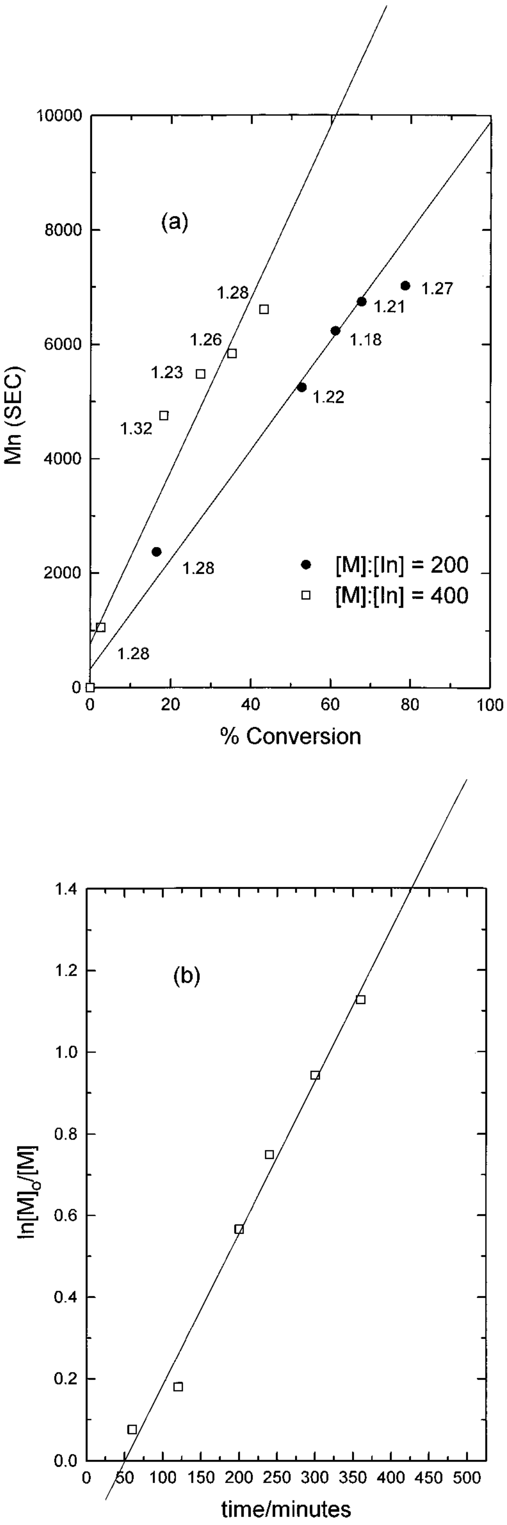


Figure 1. (a) Molecular weight dependance on percent conversion at 90 °C where [**3**]:[CuBr]:[ethyl 2-bromoisobutyrate] = 3:1:1, [CuBr]:[ethyl 2-bromoisobutyrate] = 1:1, and [MMA]:[ethyl 2-bromoisobutyrate] = 200:1 and 400:1. PDI of each sample is shown in the figure. (b) *Pseudo*-first-order kinetic plot at 90 °C where [**3**]:[CuBr]:[ethyl 2-bromoisobutyrate] = 3:1:1, [MMA]:[ethyl 2-bromoisobutyrate] = 200 at 33% v/v in xylene solution.

When the polymerization is stopped at relatively low conversion[24] and the resulting polymer isolated MALDI-

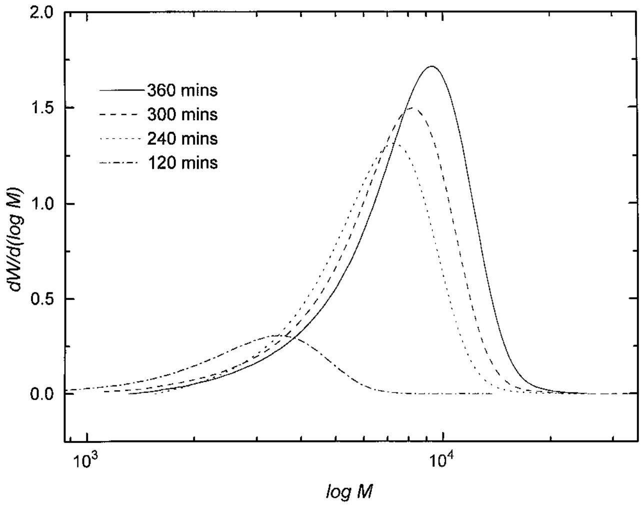


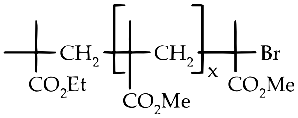
Figure 2. SEC traces of polymerization at 90 °C where [**3**]:[CuBr]:[ethyl 2-bromoisobutyrate] = 3:1:1, [CuBr]:[ethyl 2-bromoisobutyrate] = 1, and [MMA]:[ethyl 2-bromoisobutyrate] = 200 at 33% v/v in xylene solution. Data were normalized for conversion at each time.

Table 2. Polymerization of Methyl Methacrylate with 3/Cu^{I}Br/Ethyl 2-Bromoisobutyrate (In) under Various Conditions[a]

[MMA]/ [In]	[In]/ [CuBr]	temp/ °C	time/ min	M_n (SEC)	PDI	C_w/%
400	1	80	300	3700	1.15	3.1
400	1	90	305	5840	1.28	43.1
400	1	100	330	7600	1.32	48.9
400	1	120	300	18690	1.78	44.5
200	2	90	305	6435	1.19	20.0
200	3	90	305	3671	1.19	12.3
200	4	90	305	2607	1.31	4.2

[a] Data were taken at approximately 5 h; for full data sets, see the Supporting Information.

TOF-MS[25] is consistent with structure **4**. The spectrum



$$\underset{\mathrm{CO_2Et}}{+}\mathrm{CH_2}\left[\underset{\mathrm{CO_2Me}}{+}\mathrm{CH_2}\right]_x\underset{\mathrm{CO_2Me}}{+}\mathrm{Br}$$

4

indicates a relatively simple polymerization mechanism with only one major macromolecular species present where the peaks at 3832 and 3931 Da correspond to **4** where x = 36 and 37 respectively. ^{1}H NMR is also consistent with **4** showing a quartet at δ = 4.05 ppm from the ethyl ester end group and a small singlet at δ = 3.73 ppm from the penultimate methoxy group α to the bromine end group. The ratio of the integrals of 4.05:3.73 ppm is 2.95:1.99 and thus is consistent with very little termination; M_n from NMR is 4620 as compared with 4350 from SEC. The stereochemistry of the polymer is approximately 55% *rr* (from ^{1}H NMR) showing little or no stereocontrol from the propagating end and a statistical stereochemistry consistent with radical polymerization.

When the polymerization is carried out at 80 °C the rate of polymerization decreases dramatically so that after 300 min only 3.1% conversion is reached, Table 2, as compared to 43.1% at 90 °C. The rate of polymerization is increased on raising to both 100 and 120 °C as observed by an increase in M_n after approximately the same reaction time. However, the rate of termination also increases, which is seen as a broadening of PDI and curvature of a pseudokinetic plot at 120 °C. At 80 °C the induction time is increased and the rate of polymerization accelerates after approximately 300 min; it is worth noting that the PDI increases with increasing temperature, over the range studied.

The role of the copper(I) has been investigated by maintaining the ratio [MMA]:[ethyl 2-bromoisobutyrate] = 200:1 at 90 °C and altering the [ethyl 2-bromoisobutyrate]:[Cu(I)] ratio by reducing the amount of Cu(I). As expected the rate of polymerization decreases with a decrease in [Cu(I)] and the induction time increases. Where [ethyl 2-bromoisobutyrate]:[Cu(I)] is increased to 4:1, only very low conversions are observed at long reaction times. In each case M_n increases linearly with conversion and PDI remains less than 1.20 throughout the majority of the reaction. However, we observe an unexpected molecular weight dependence on the [MMA]:[Cu(I)] ratio such that decreasing the level of Cu(I) results in an increase in M_n. This would indicate that the Cu(I) is playing a role in the initiation step as well as catalyzing propagation. This effect is not well understood but is believed to be associated with the observed induction period observed in all experiments. This is currently under investigation.

In summary we have demonstrated that 2-pyridinecarbaldehyde imines may be used in place of bipyridines in atom transfer radical polymerization in conjunction with copper(I) bromide and alkyl bromides. The presence of a low-lying π^* orbital stabilises Cu(I). The ligands are simple to prepare and allow a wide range of versatility with regards to electron-donating and -withdrawing capability as well as producing soluble Cu(I) species and homogeneous reactions. We have observed an induction period in all reactions and surprisingly a molecular weight dependence on the level of Cu(I).

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Supporting Information Available: Tables of full data sets from seven reactions and figures showing ^{1}H NMR spectra of **3** and **4**, MALDI-TOF-MS of **4**, first order plots at 80, 90, 100 and 120 °C with varying [In]:[Cu] ratios and M_n vs conversion plots. (10 pages). Ordering information is given on any current masthead page.

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(22) Synthesis of 2-pyridinecarbaldehyde *n*-propylimine, **3**. A 1.78 mL sample of pyridine-2-carboxaldehyde (1.87E-2 mol) was dissolved in 30 mL of diethyl ether. Then 1.55 mL of *n*-propylamine was added (1.88E-2 mol) and the solution stirred for 10 min at room temperature prior to the addition of anhydrous magnesium sulfate and stirring for a further 30 min. The magnesium sulfate was removed by filtration, and volatiles were removed under reduced pressure to give the product in quantitative yield as a golden yellow oil. ^{1}H NMR (CDCl$_3$, 373 K, 400.13 MHz): $\delta = 8.51$ (d, $J = 3.5$ Hz, 1H), 8.26 (s, 1H), 7.87 (d, $J = 7.8$ Hz, 1H), 7.59 (d, $J = 7.8$ Hz, 1H), 7.16 (t, $J = 4.6$ Hz, 1H), 3.52 (t, $J = 7.6$ Hz, 2H), 1.63 (sext, $J = 7.3$ Hz, 2H), 0.84 (t, $J = 7.5$ Hz, 3H) (see Supporting Information). ^{13}C (CDCl$_3$, 373K, 100.61 MHz): $\delta = 161.51$, 154.44, 149.18, 136.28, 124.37, 120.97, 63.08, 23.65, 11.65 ppm. IR (NaCl, film), 3053−2830, 1648, 1587, 1566, 772, 742 cm^{-1}. Bp = 218 °C.

(23) Typical polymerization procedure. A 0.1376 g sample of copper(I) bromide (98%, 9.6E-4 mol) was added to 40 mL of xylene and 20 mL of methyl methacrylate (0.187 mol). Then 0.4272 g of **3** (2.89E-3 mol) was added and the mixture deoxygenated by one freeze−pump−thaw cycle prior to the addition of 0.14 mL of ethyl 2-bromoisobutyrate (9.54E-4 mol) at room temperature. The deep red solution was heated at 90 °C for 485 min. At time = 120, 240, 300, 360 and 485 min, 1 mL of reaction mixture was taken and conversion calculated by gravimetry heating to constant weight at 60 °C under vacuum for 300 min. SEC was carried out on the residual polymer; the final product was isolated by precipitation into hexanes.

(24) Synthesis of low molecular mass polymethyl methacrylate for NMR and MALDI-TOF-MS analysis. A 0.1376 g sample of copper(I) bromide (98%, 9.6E-4 mol) was added to 40 mL of xylene and 20 mL of methyl methacrylate (0.187 mol). Then 0.4272 g of **3** (2.89E-3 mol) were added and the mixture deoxygenated by one freeze−pump−thaw cycle prior to the addition of 0.14 mL of ethyl 2-bromoisobutyrate (9.54E-4 mol) at room temperature. The deep red solution was heated at 90 °C for 70 min and was isolated by precipitation into hexanes. The polymer was recovered in 14.4% yield. $M_n = 4050$; PDI = 1.14.

(25) SEC was calibrated with Polymer Laboratories PMMA standards and MMA dimer; the column set consisted of a PL 5 μm guard and 1 PL Mixed-E column (300 × 7.5 mm), elutant was tHF at 1.00 mL min^{-1}. Matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI TOF MS) was carried out on a Kratos MALDI III instrument in the reflection mode. The polymer was deposited onto a stainless steel sample slide with 2,5-dihydroxybenzoic acid as the matrix.

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