Polymer Chemistry

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Cite this: *Polym. Chem.*, 2018, **9**, 5411

Received 13th September 2018,
Accepted 26th October 2018

DOI: 10.1039/c8py01331d

rsc.li/polymers

Acetone: a solvent or a reagent depending on the addition order in SET-LRP†

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Depending on the order of addition to the reaction mixture during biphasic SET-LRP performed in acetone/water mixtures, acetone can serve as a solvent or as a reagent brominated by $CuBr_2$ to provide the electrophilic bromoacetone initiator as well as aldol condensation products.

Cu(0)-wire and powder mediated single-electron transfer living radical polymerization (SET-LRP) has been shown to be one of the most robust and versatile polymerization tools to obtain well-defined polymers and more complex architectures in very short reaction times at room temperature or below even in the presence of air.[1] The basic pillar of SET-LRP is the selection of the solvent and ligand. This is because the solvent plays an important role during the polymerization, self-regulating the generation of the Cu(0) activator and the Cu(II)X_2 deactivator *via* the solvent–ligand mediated disproportionation of Cu(I)X species.[2] Water,[3] hydrogenated and fluorinated alcohols,[4] dipolar aprotic and cyclic carbonates[5] and their biphasic mixtures[6] have been employed in the past few years and are known to mediate efficient disproportionation of the Cu(I)X generated in the presence of N-ligands.[7] Classic non-polar solvents such as toluene or hexane and some polar solvents such as acetonitrile and acetone are poor disproportionating solvents or do not mediate the disproportionation of Cu(I)X and therefore their use in SET-LRP has been limited for a long time.[8] However, our group recently developed a library of "programmed" multiphasic SET-LRP systems based on mixtures of organic solvents and water to overcome this limitation.[6] This approach is sustained by the disproportionation of Cu(I)X species exclusively in the water phase and the simultaneous partitioning of "nascent" Cu(0) species to the organic phase at the same time that the Cu(II)X_2 generated remains in the aqueous phase. Thus, the application of this methodology allows the use of classical non-disproportionating solvents with excellent results in terms of molecular weight control and chain end functionality.[6a–d]

In this context, acetone has emerged as one of the most appealing solvents to perform SET-LRP due to its very low cost, lack of toxicity and simple recycling. Recently, our group reported the use of acetone–water mixtures as the solvent system for the SET-LRP using Cu(0) nano-particles as a catalyst generated by *in situ* reduction of Cu(II)Br_2 with $NaBH_4$ and non-activated copper wire as the catalyst for methyl acrylate and butyl acrylate monomers, resulting in a quantitative monomer conversion and a high chain end functionality.[6d] Moreover, SET-LRP mediated by tris(2-aminoethyl)amine (TREN) in acetone–water mixtures has also been reported with excellent results for the polymerization of hydrophobic acrylates.[6g] All these results support the use of acetone as a solvent for SET-LRP and other LRP techniques. However, like all other solvents, acetone presents some limitations such as potential side reactions under basic,[9] acidic[10] or redox[11] conditions.

The typical experimental procedure for SET-LRP and biphasic SET-LRP involves the preparation of the polymerization mixture by sequential addition of monomer, solvent, ligand, initiator and finally Cu(II)Br_2 for monophasic SET-LRP and monomer, organic solvent, water containing N-ligand, $CuBr_2$ and initiator for biphasic SET-LRP, in this specific order before the deoxygenation step and the incorporation of the Cu(0) catalyst.[1b] If $CuBr_2$ is added before the ligand, bromination of the monomer will occur.[6d] Here we report that the alteration of the order from that described above to acrylate monomer, acetone and Cu(II)Br_2 leads to an extremely fast Cu(II)Br_2-mediated bromination of acetone, occurring under non-stoichiometric conditions, to yield bromoacetone, Cu(I)Br and HBr (Scheme 1a). Note that the stoichiometric bromination of ketones in the presence of Cu(II)Br_2 has previously been investigated and reported in different solvents such as water,[12] alcohols[13] and dipolar aprotic solvents.[14,15] The HBr resulting

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†Electronic supplementary information (ESI) available. See DOI: 10.1039/c8py01331d

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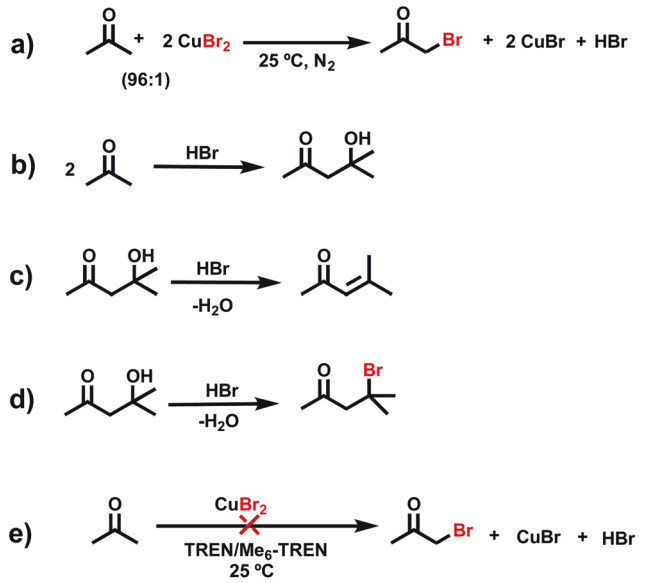

Scheme 1 (a) Non-stoichiometric Cu(II)Br_2-mediated bromination of acetone at 25 °C, (b) HBr-catalyzed aldol condensation of acetone, (c) HBr-mediated dehydration of DAA, and (d) HBr-mediated bromination of DAA. (e) No Cu(II)Br_2-mediated bromination of acetone was observed in the presence of TREN or hexamethylated tris(2-aminoethyl)amine (Me_6-TREN).

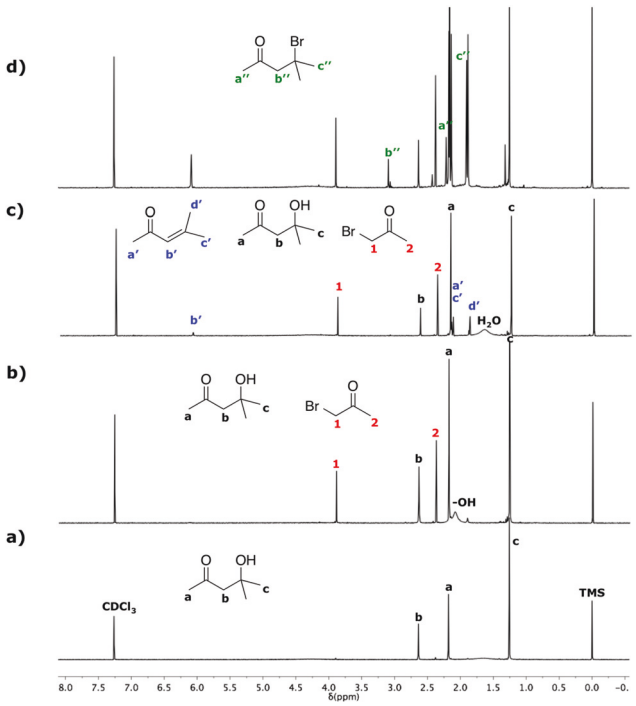

Fig. 1 ^{1}H-NMR spectra recorded during the Cu(II)Br_2-mediated bromination of commercial acetone: (a) 4 minutes, (b) 10 minutes, (c) 30 minutes, and (d) 4 hours.

from this reaction catalyzes the aldol condensation of acetone to form diacetone alcohol (DAA) (Scheme 1b). Finally, the HBr-mediated dehydration of DAA resulted in the formation of mesityl oxide (Scheme 1c). Note that the alteration of the order of addition of reagents from that described above can also lead to the Cu(II)Br_2-mediated dibromination of acrylate monomers as was reported in a previous publication.[16]

First, we investigated the Cu(II)Br_2-mediated bromination of acetone at room temperature using a large excess of commercially available acetone to mimic SET-LRP conditions in which Cu(II)Br_2 is catalytically present with respect to the organic solvent. This reaction was monitored for 4 hours by ^{1}H-NMR (Fig. 1).

Shortly after mixing acetone and Cu(II)Br_2 three characteristic singlets of DAA were detected (Fig. 1a). Next, we observed the formation of bromoacetone after 10 min through the appearance of the characteristic signal **1** corresponding to methylene protons adjacent to the bromo position at 3.8 ppm (Fig. 1b). The ratio between both products was determined to be 30 : 70 bromoacetone : DAA (Fig. 2a).

The visualization of the reaction mixture at this point showed the precipitation of the white Cu(I)Br powder (Fig. 3b). After 30 minutes, the ratio of bromoacetone : DAA increased to 50 : 50. Meanwhile, mesityl oxide was also detected in the reaction mixture, which was also confirmed by the appearance of the signal **b′** at 6.0 ppm, corresponding to the olefinic proton (Fig. 1c). Note that at longer reaction times, we also detected the formation of 4-bromo-4-methylpentan-2-one, the halogenation product of DAA (Scheme 1d), by the appearance of the characteristics signals **a″**, **b″** and **c″** (Fig. 1d) in a ratio of bromoacetone : 4-bromo-4-methylpentan-2-one of 45 : 20 (Fig. 2a). Moreover, the increase of the ratio of bromoacetone : mesityl oxide to 40 : 20 and the decrease of the ratio of bromoacetone : DAA to 40 : 30 were observed and were attributed to the dehydration of DAA to form mesityl oxide (Fig. 2a).

The presence of DAA as the only product at short reaction times led us to think about the possibility of the presence of this compound as an initial impurity in commercial acetone. This was indeed confirmed by ^{1}H-NMR. In order to clarify the order of formation of the products during the reaction and the possible mechanism, acetone was freshly distilled and used immediately to carry out the bromination reaction using $CuBr_2$. In this case, bromoacetone was the first identified product (ESI, Fig. 1b†). No DAA formation was observed, while the precipitation of Cu(I)Br was observed. After 15 minutes, the formation of DAA was clearly observed in a ratio of bromoacetone : DAA of 90 : 10 (Fig. 2b and ESI Fig. 1c†). After 30 minutes, the ratio of DAA increased to 60 : 35 bromoacetone : DAA (Fig. 2b) and after 4 hours the formation of mesityl oxide was observed in a ratio of 50 : 10 bromoacetone : mesityl oxide (Fig. 2b and ESI, Fig. 1e†). The ^{1}H NMR spectrum after 17 hours still showed the coexistence of the abovementioned three compounds (ESI, Fig. 1f†). These observations suggest, as expected, that first the bromination of acetone takes place *via* copper-bound enolate, generating bromoacetone, hydrobromic acid and Cu(I)Br (Scheme 1a), followed by the acid catalyzed aldol condensation of acetone to

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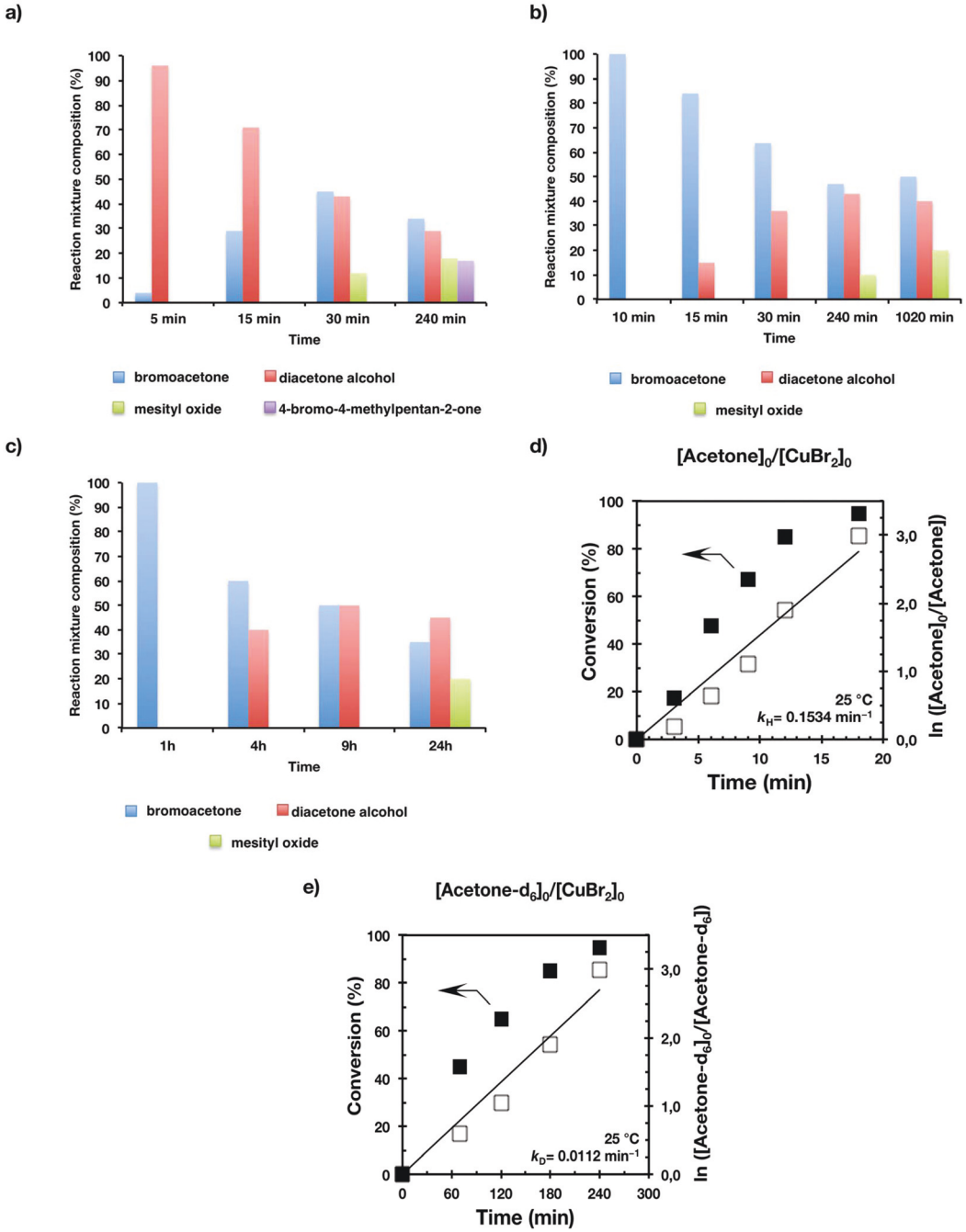

Fig. 2 Reaction mixture composition *vs.* time for the Cu(II)Br_2-mediated bromination of acetone using: (a) commercially available acetone, (b) freshly distilled acetone and (c) freshly distilled deuterated acetone. (d) Kinetic plot for the bromination of freshly distilled acetone. (e) Kinetic plot for the bromination of freshly distilled deuterated acetone.

yield DAA, which undergoes dehydration to produce mesityl oxide (Scheme 1b and c).

In order to determine the bromination rate, the above described experiment was carried out in the presence of anisole as an internal standard. Fig. 2d shows the evolution of the conversion of acetone to bromoacetone in time, considering 100% conversion of bromoacetone obtained with respect to the stoichiometric amount of Cu(II)Br_2 used, since acetone is present in a large excess. Note that after 6 min more than 60% of acetone was converted to bromoacetone and, more interestingly, the full conversion of acetone into bromoacetone within 18 min points to the extremely high rate (K_H = 0.1534 min^{-1}) of bromination of acetone even in the presence of a catalytic amount of Cu(II)Br_2.

An additional experiment using freshly distilled acetone-D6 was carried out under the conditions described above in order

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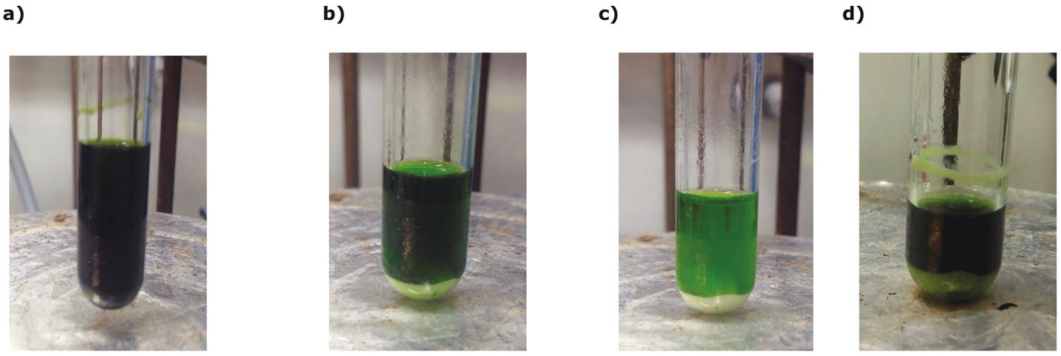

Fig. 3 Visualization of Cu(II)Br_2-mediated bromination of commercial acetone after (a) 4 minutes, (b) 10 minutes, (c) 1 hour and (d) 10 minutes in the presence of Me_6-TREN.

to determine the bromination rate using deuterated acetone and investigate the potential existence of a kinetic isotopic effect (KIE)[18] (Fig. 2c and 4). The first important observation is that in this case, the formation of white Cu(I)Br powder required a longer reaction time (45 min) than when non-deuterated acetone was used (10 min). In this case, the reaction was monitored using D-NMR. As can be seen in Fig. 4a, no products were detected by NMR after 30 minutes. Note that when using non-deuterated acetone, bromoacetone was already detected after 10 min (Fig. 1b and ESI, Fig. 1b†). After 1 h, signals **1** and **2** corresponding to bromoacetone-D5 were already observed (Fig. 4b). After that, the D-NMR analysis of the aliquot corresponding to 4 h reveals the formation of DAA-D12 with the characteristic signals of the products **a**, **b**, and **c** (Fig. 4c) in a ratio of 60 : 40 bromoacetone-D5 : DAA-D12 (Fig. 2c). Finally, the formation of mesityl oxide-D10 was only detected at long reaction times. Fig. 4e shows the D-NMR spectrum after 17 h where the characteristic signals of bromoacetone-D5 and DAA-D12 coexist with the signals of the mesityl oxide-D10 (**a′**, **b′**, **c′**, **d′**). Note that mesityl oxide was detected in the previous experiment already after only 1 hour.

These observations suggest, as expected, that the reaction mechanism follows the same reaction pathways as when non-deuterated acetone was used.[18] However, the much longer reaction time when using acetone-D6 (K_D = 0.0112 min^{-1}, Fig. 2e) in comparison with that when non-deuterated acetone was used (K_H = 0.1534 min^{-1}, Fig. 2d) supports the existence of the KIE derived from the lower mobility and increased stability from the higher dissociation energies of heavier isotopes (D) when compared to compounds containing lighter isotopes (H). Note that the difference in rate (K_H/K_D = 14) indicates the presence of a primary kinetic isotopic effect, which is associated with the labelled bond, which is made or broken in the rate determining step.[17]

It is important to point out that when the reaction was conducted by dissolving Cu(II)Br_2 in acetone containing an equimolar amount of N-ligands such as TREN or Me_6-TREN as the most common ligands for SET-LRP (Scheme 1e), no bromination reaction was observed even after long reaction times (24 hours). Note that the formation of green acetone-insoluble

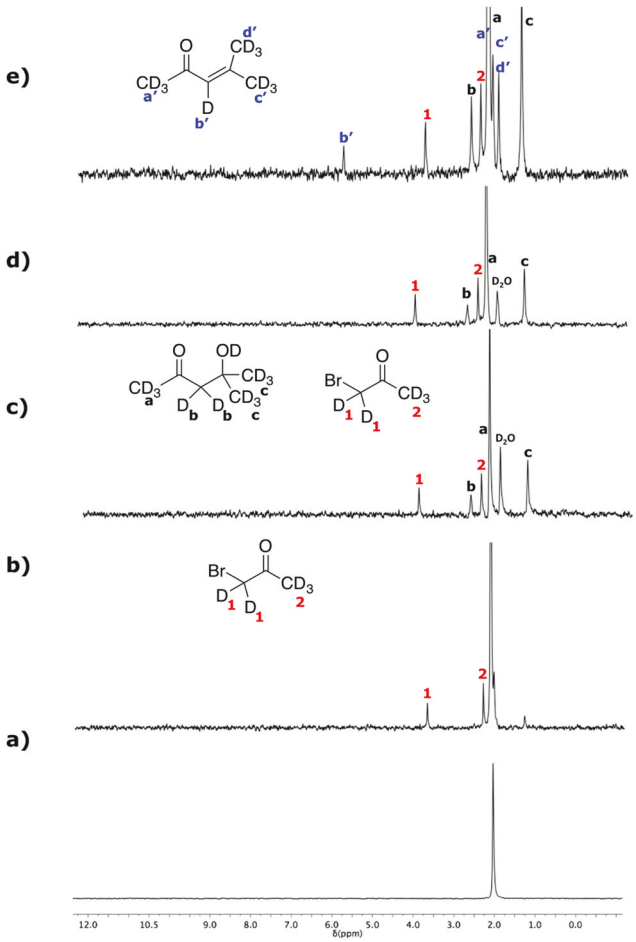

Fig. 4 D-NMR spectra recorded during the Cu(II)Br_2-mediated bromination of freshly distilled acetone-D6: (a) 45 minutes, (b) 4 hours, (c) 9 hours, (d) 12 hours and (e) 17 hours.

crystals of the Cu(II)Br_2/ligand complex was observed in 10 minutes (Fig. 3d). These results indicate the importance of the order of addition of reactants to the reaction mixture using acetone as a solvent for SET-LRP and other LRP techniques. To avoid the formation of bromoacetone during the SET-LRP set-

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up is of crucial importance because it is a highly electrophile reagent that can act as an alkylating agent towards the classical N-ligands used in SET-LRP such as TREN or Me_6-TREN as well as an alternative alkyl initiator during the polymerization process. In addition, mesityl oxide is well known to undergo a wide variety of simple nucleophilic additions at the double bond including amines. Consequently, the addition of N-ligand to mesityl oxide is a non-desirable side reaction that needs to be taken into account and avoided.[18] The bromination of acetone and other ketones mediated by $CuBr_2$ has been reported during the past few years, with the attractive idea of using the brominated analogous ketones to access more complex molecules through the inherent reactivity of the α-brominated position.[19] However, this reaction has never been studied under conditions that can be relevant to SET-LRP or ATRP. The experiments reported here indicate and set up a new and necessary protocol for the addition order of reagents for SET-LRP[6d,g,20] and most probably also for ATRP[21] when acetone is used as a solvent in order to practice a clean and efficient process.

In order to estimate the role of the order of addition of reagents to ATRP experiments performed in the presence of $CuBr_2$, two literature experiments in which the order of addition of the reagents to acetone solvent was incorrect[21a,b] and their initiation step were reinvestigated. In the first case when CuBr, $CuBr_2$, monomer, initiator and ligand was the order of addition, 20% bromoacetone was obtained after 3 min and 45% was obtained after 6 min.[21a] In the second case[21b] 27% bromoacetone was obtained after 4 min and 57% after 6 min.[21b] These simply demonstrate that under incorrect reaction conditions the bromoacetone initiator is generated and acts as a co-initiator for the polymerization while $CuBr_2$ becomes CuBr and acts as a supplementary activator rather than a deactivator. This demonstrates the extremely important role of the order of addition of reagents to metal catalyzed living polymerizations performed in acetone.

Conclusions

Cu(II)Br_2 brominates acetone at 25 °C, yielding bromoacetone in a few minutes and a mixture of DAA and mesityl oxide thereafter. This bromination reaction can be suppressed in the presence of N-ligands such as TREN or Me_6-TREN. Bromoacetone is known to be a reactive electrophile that acts as an N-alkylating agent towards primary amino groups at room temperature or even below and also as a good initiator for all metal catalyzed radical polymerizations. This side reaction, together with the additional side reactions recently reported by our laboratory,[6d,16] must be taken into account during the practice of current SET-LRP and other metal-catalyzed LRPs using acetone as a solvent.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

The financial support from the National Science Foundation (DMR-1066116, DMR-1120901 and DMR-1807127) and the P. Roy Vagelos Chair at the University of Pennsylvania is greatly acknowledged. G. L. and M. G. acknowledge support from the Spanish Ministerio de Economía y Competitividad (MINECO) through project MAT2017-82669-R. G. L. also thanks the Serra Húnter Programme. A. M. was supported by an FPI grant (BES-2015-072662) and a mobility grant (BES-2015-072) from the MINICO.

References

1 (*a*) B. M. Rosen and V. Percec, *Chem. Rev.*, 2009, **109**, 5069–5119; (*b*) G. Lligadas, S. Grama and V. Percec, *Biomacromolecules*, 2017, **18**, 2981–3008; (*c*) G. Lligadas, S. Grama and V. Percec, *Biomacromolecules*, 2017, **18**, 1039–1063; (*d*) A. Anastasaki, V. Nikolau, G. Nurumbetov, P. Wilson, K. Kempe, J. F. Quinn, T. P. Davis, M. R. Whittaker and D. M. Haddleton, *Chem. Rev.*, 2016, **116**, 835–877; (*e*) C. Boyer, N. A. Corrigan, K. Jung, D. Nguyen, N. N. Adnan, S. Oliver, S. Shanmugam and J. Yeow, *Chem. Rev.*, 2016, **116**, 1803–1949; (*f*) A. Anastasaki, V. Nikolaou and D. M. Haddleton, *Polym. Chem.*, 2016, **7**, 1002–1026; (*g*) R. B. Grubbs and R. H. Grubbs, *Macromolecules*, 2017, **50**, 6979–6997; (*h*) S. Fleischmann, B. M. Rosen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 1190–1196; (*i*) S. Fleischmann and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 2243–2250; (*j*) N. H. Nguyen, X. Leng, H.-J. Sun and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2013, **51**, 3110–3122; (*k*) N. H. Nguyen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2013, **49**, 4756–4765; (*l*) E. Liarou, R. Whitflied, A. Anastasaki, N. G. Engelis, G. R. Jones, K. Velonia and D. M. Haddleton, *Angew. Chem., Int. Ed.*, 2018, **29**, 8998–9002; (*m*) M. Vorobii, O.-P. Georgievski, A.-S. Pereira, N. Y. Kostina, R. Jezorek, Z. Sedlákova, V. Percec and C. R. Emmenegger, *Polym. Chem.*, 2016, **7**, 6934–6945; (*n*) A. Simula, G. Nurumbetov, A. Anastasaki, P. Wilson and D. M. Haddleton, *Eur. Polym. J.*, 2015, **62**, 294–303; (*o*) A. Anastasaki, C. Waldron, P. Wilson, C. Boyer, P. B. Zetterlund, M. R. Whittaker and D. M. Haddleton, *ACS Macro Lett.*, 2013, **2**, 896–900.

2 (*a*) M. E. Levere, N. H. Nguyen, X. Leng and V. Percec, *Polym. Chem.*, 2013, **4**, 1635–1647; (*b*) N. H. Nguyen, H.-J. Sun, M. E. Levere, S. Fleischmann and V. Percec, *Polym. Chem.*, 2013, **4**, 1328–1332.

3 (*a*) Q. Zang, P. Wilson, Z. Li, R. McHale, J. Godfrey, A. Anastasaki, C. Waldron and D. M. Haddleton, *J. Am. Chem. Soc.*, 2013, **135**, 7355–7363; (*b*) V. Nikolaou, A. Simula, M. Droesbeke, N. Risangud, A. Anastasaki, K. Kempe, P. Wilson and D. M. Haddleton, *Polym. Chem.*, 2016, **7**, 2452–2456; (*c*) S. R. Samanta, V. Nikolaou, S. Keller, M. J. Monteiro, D. A. Wilson, D. M. Haddleton

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and V. Percec, *Polym. Chem.*, 2015, **6**, 2084–2097; (*d*) M. Gavrilov, Z. Jia, V. Percec and M. J. Monteiro, *Polym. Chem.*, 2016, **7**, 4802–4809; (*e*) M. Gavrilov, T. J. Zerk, P. V. Bemhardt, V. Percec and M. J. Monteiro, *Polym. Chem.*, 2016, **7**, 933–939.

4 (*a*) G. Lligadas and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2008, **46**, 2745–2754; (*b*) S. R. Samanta, A. Anastasaki, C. Waldron, D. M. Haddleton and V. Percec, *Polym. Chem.*, 2013, **4**, 5555–5562; (*c*) S. R. Samanta, H.-J. Sun, A. Anastasaki, D. M. Haddleton and V. Percec, *Polym. Chem.*, 2014, **5**, 89–95; (*d*) S. R. Samanta, A. Anastasaki, C. Waldron, D. M. Haddleton and V. Percec, *Polym. Chem.*, 2013, **4**, 5563–5569; (*e*) S. R. Samanta, M. E. Levere and V. Percec, *Polym. Chem.*, 2013, **4**, 3212–3224; (*f*) N. H. Nguyen, B. M. Rosen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 1752–1763; (*g*) S. R. Samanta, R. Cai and V. Percec, *Polym. Chem.*, 2015, **6**, 3259–3270; (*h*) S. R. Samanta, R. Cai and V. Percec, *Polym. Chem.*, 2014, **5**, 5479–5491; (*i*) A. Moreno, D. Garcia, M. Galià, J. C. Ronda, V. Cádiz, G. Lligadas and V. Percec, *Biomacromolecules*, 2017, **18**, 3447–3456; (*j*) N. Bensabeh, J. C. Ronda, M. Galià, V. Cádiz, G. Lligadas and V. Percec, *Biomacromolecules*, 2018, **19**, 1256–1268.

5 (*a*) N. H. Nguyen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 5109–5119; (*b*) X. Jiang, S. Fleishmann, N. H. Nguyen, B. M. Rosen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 5591–5605.

6 (*a*) R. L. Jezorek, M. Enayati, R. B. Smail, J. Lejnieks, S. Grama, M. J. Monteiro and V. Percec, *Polym. Chem.*, 2017, **8**, 3405–3424; (*b*) M. Enayati, R. L. Jezorek, M. J. Monteiro and V. Percec, *Polym. Chem.*, 2016, **7**, 5930–5942; (*c*) M. Enayati, R. B. Smail, S. Grama, R. L. Jezorek, M. J. Monteiro and V. Percec, *Polym. Chem.*, 2016, **7**, 7230–7241; (*d*) R. B. Smail, R. L. Jezorek, J. Lejnieks, M. Enayati, S. Grama, M. J. Monteiro and V. Percec, *Polym. Chem.*, 2017, **8**, 3102–3123; (*e*) M. Enayati, R. L. Jezorek, M. J. Monteiro and V. Percec, *Polym. Chem.*, 2016, **7**, 3608–3621; (*f*) S. Grama, J. Lejnieks, M. Enayati, R. B. Smail, L. Ding, G. Lligadas, M. J. Monteiro and V. Percec, *Polym. Chem.*, 2017, **8**, 5865–5874; (*g*) A. Moreno, S. Grama, T. Liu, M. Galià, G. Lligadas and V. Percec, *Polym. Chem.*, 2017, **8**, 7559–7574; (*h*) A. Moreno, T. Liu, L. Ding, I. Buzzacchera, M. Galià, M. Möller, C. J. Wilson, G. Lligadas and V. Percec, *Polym. Chem.*, 2018, **9**, 2313–2327; (*i*) A. Moreno, R. L. Jezorek, T. Liu, M. Galià, G. Lligadas and V. Percec, *Polym. Chem.*, 2018, **9**, 1885–1899; (*j*) A. Moreno, T. Liu, M. Galià, G. Lligadas and V. Percec, *Polym. Chem.*, 2018, **9**, 1961–1971.

7 B. M. Rosen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 5606–5628.

8 (*a*) N. H. Nguyen, M. E. Levere, J. Kulis, M. J. Monteiro and V. Percec, *Macromolecules*, 2012, **45**, 4606–4622; (*b*) G. Lligadas, B. M. Rosen, M. J. Monteiro and V. Percec, *Macromolecules*, 2008, **41**, 8360–8364; (*c*) N. H. Nguyen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2011, **49**, 4277–4240.

9 M. D. Waddington and J. E. Meany, *J. Chem. Educ.*, 1978, **55**, 60–70.

10 C. L. Guidry and M. A. F. Walker, *Polymer*, 1970, **11**, 548–552.

11 W. L. Evans and L. B. Sefton, *J. Am. Chem. Soc.*, 1922, **44**, 2276–2283.

12 J. K. Kochi, *J. Am. Chem. Soc.*, 1955, **77**, 5274–5278.

13 (*a*) C. E. Castro, E. J. Gaughan and D. C. Owsley, *J. Org. Chem.*, 1965, **30**, 587–592; (*b*) A. Lorenzini and C. Walling, *J. Org. Chem.*, 1967, **32**, 4008–4010.

14 (*a*) E. M. Kosower, W. J. Cole, G.-S. Wu, D. E. Cardy and G. Meisters, *J. Org. Chem.*, 1963, **28**, 630–633; (*b*) Y. Kojima, K. Usui and S. Kawaguchi, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 3127–3130.

15 (*a*) R. W. Evans, J. R. Zbieg, S. Zhu, W. Lei and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2013, **135**, 16074–16077; (*b*) E. M. Kosower and G.-S. Wu, *J. Org. Chem.*, 1963, **28**, 633–638.

16 A. Moreno, J. Lejnieks, L. Ding, S. Grama, M. Galià, G. Lligadas and V. Percec, *Polym. Chem.*, 2018, **9**, 2082–2086.

17 E. M. Simmons and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2012, **51**, 3066–3072.

18 (*a*) M. Hauser, *Chem. Rev.*, 1963, **63**, 311–324; (*b*) F. H. Westheimer, *Chem. Rev.*, 1961, **61**, 265–273; (*c*) K. B. Wiberg, *Chem. Rev.*, 1955, **55**, 713–743; (*d*) W. F. K. Wynne-Jones, *Chem. Rev.*, 1936, **17**, 115–123.

19 (*a*) B. S. Park, H. M. Lee and S. Cho, *Bull. Korean Chem. Soc.*, 2007, **28**, 871–872; (*b*) H.-J. Yuan, M. Wang, Y.-J. Liu and Q. Li, *Adv. Synth. Catal.*, 2009, **351**, 112–116; (*c*) V. Z. Shirinian, D. V. Lonshakov, V. V. Kachala, I. V. Zavarzin, A. A. Shimkin, A. G. Lvov and M. M. Krayushkin, *J. Org. Chem.*, 2012, **77**, 8112; (*d*) G. Yin, J. Ma, H. Shi and Q. Tao, *Heterocycles*, 2012, **85**, 1941–1948; (*e*) H.-L. Li, X.-L. An, L.-S. Ge, X. Luo and W.-P. Deng, *Tetrahedron*, 2015, **71**, 3247–3252; (*f*) J. K. Mali, D. A. Mali and V. N. Telvekar, *Tetrahedron Lett.*, 2016, **57**, 2324–2326; (*g*) J. S. Sharley, A. C. Pérez, E. E. Ferri, A. F. Miranda and I. R. Baxendale, *Tetrahedron*, 2016, **72**, 2947–2954.

20 (*a*) N. H. Nguyen, B. M. Rosen, X. Jiang, S. Fleischmann and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 5577–5590; (*b*) W. Zhang, J. Zhu and X. Zhu, *J. Polym. Sci., Part A: Polym. Chem.*, 2009, **47**, 6908–6918; (*c*) W. Zhang, Z. Zhang, Z. Cheng, Y. Tu, Y. Qiu and X. Zhu, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 4268–4278; (*d*) D. J. Haloi and N. K. Singha, *J. Polym. Sci., Part A: Polym. Chem.*, 2011, **49**, 1564–1571; (*e*) N. H. Nguyen and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2011, **49**, 4227–4240; (*f*) G. Lu, Y. Li, H. Guo, W. Du and X. Huang, *Polym. Chem.*, 2013, **4**, 3131–3139.

21 (*a*) K. A. Davis and K. Matyjaszewski, *Macromolecules*, 2000, **33**, 4039–4047; (*b*) L.-H. Gan, P. Ravi, B. W. Mao and K.-C. Tam, *J. Polym. Sci., Part A: Polym. Chem.*, 2003, **41**, 2668–2695; (*c*) K. Ibrahim, B. Löfgren and J. Seppälä, *Eur. Polym. J.*, 2003, **39**, 2005–2010; (*d*) U. Chatterjee, S. K. Jewrajka and B. M. Mandal, *Polymer*, 2005, **46**, 1575–1582; (*e*) M. Zhang, L. Liu, C. Wu, G. Fu, H. Zhao and

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B. He, *Polymer*, 2007, **48**, 1989–1997; (*f*) L. M. Van Renterghem, M. Lammens, B. Dervaux, P. Viville, R. Lazzaroni and F. E. Du Prez, *J. Am. Chem. Soc.*, 2008, **130**, 10802–10811; (*g*) G. Hart-Smith, M. Lammens, F. E. Du Prez, M. Guilhaus and C. Barner-Kowollik, *Polymer*, 2009, **50**, 1986–2000; (*h*) D. J. Haloi, S. Ata, N. K. Singha, D. Jehnichen and B. Voilt, *ACS Appl. Mater. Interfaces*, 2012, **4**, 4200–4207; (*i*) J. Lejnieks, A. Mourran, W. Tillmann, H. Keul and M. Möller, *Materials*, 2010, **3**, 3369–3384.