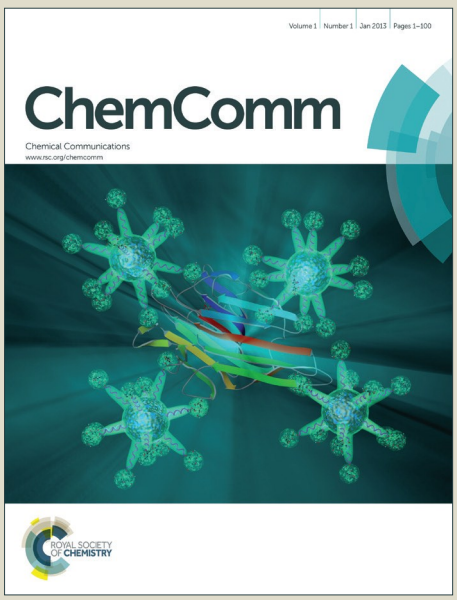
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Journal Name

RSCPublishing

COMMUNICATION

Cite this: DOI: 10.1039/xoxxoooooox

A Coumarin Dimer Probe of Mechanochemical Scission Efficiency in the Sonochemical Activation of Chain-Centered Mechanophore Polymers

Received ooth January 2012,
Accepted ooth January 2012

DOI: 10.1039/xoxxoooooox

www.rsc.org/

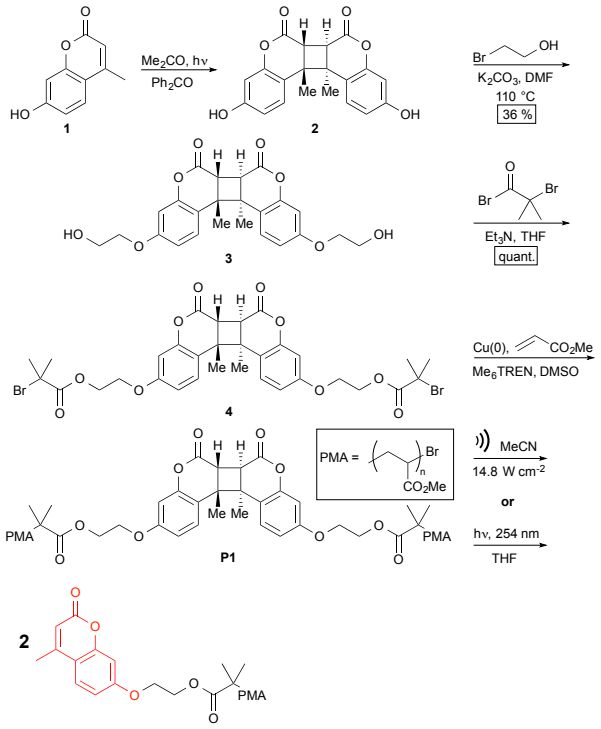
Zachary S. Kean,[a] Gregory R. Gossweiler,[a] Tatiana B. Kouznetsova,[a] Gihan B. Hewage,[a] and Stephen L. Craig[a]

Here we present a coumarin dimer (CD) mechanophore that, when embedded near the mid-chain of poly(methyl acrylate) polymers, activates under pulsed ultrasound conditions to yield coumarin chain-end functional polymers. Quantitative photochemical scission of the CD polymers provides a reference against which the activation efficiency of chain-centered mechanophores in polymers synthesized by controlled/living radical polymerization (CRP) can be assessed. Activation efficiency is characterized with respect to the polymer molecular weight (MW), polydispersity index (PDI), and distribution of mechanophores along the backbone.

The use of force-reactive functional units (mechanophores) has become a promising approach to the development of new stress-responsive polymeric materials.[1-3] To demonstrate the mechanochemical activity of a potential mechanophore, the functional group of interest is often placed at the center of a polymer chain and subjected to activation by pulsed ultrasound. This strategy has become quite common, primarily due to the ease of synthesis of such systems via living/controlled radical polymerization (CRP) methods (most commonly Cu(0)-mediated CRP[4-7]). Sonication of CRP-derived single mechanophore polymers has been used to test the mechanochemical behavior of mechanocatalysts,[8-10] spiropyran-based sensors,[5, 11] and Diels-Alder adducts,[12] and it has seen particularly extensive use in the study of mechanochemically active 4-membered ring systems, including: benzocyclobutenes,[5, 13] cyclobutanes,[14, 15] and cyclobutane derivatives.[16, 17]

Despite the pervasiveness of this configuration, the use of a single chain-centered mechanophore generally requires that the mechanophore reside "at or near" the center of the chain where stress tends to accumulate under elongational flow, an observation that is consistent with the well-understood effect of ultrasound on the degradation of homopolymers in solution.[18-22] With few exceptions, however, including a recent report by Church et al.,[12] few studies address how the distribution of molecular weights (i.e., the PDI) of mechanophore-bearing polymers synthesized by CRP affects the spatial distribution of mechanophores along the polymer backbone. Here, we report a mechanophore based on a coumarin dimer (CD) core, and its subsequent mechanochemical activity in pulsed sonication.

Initially, 7-hydroxy-4-methylcoumarin (**1**) was irradiated with a medium pressure mercury arc lamp (450 W) through a pyrex filter in the presence of benzophenone to generate bisphenol (**2**) as previously described.[23] Etherification with 2-bromoethanol afforded diol (**3**) in 36% yield, and subsequent quantitative esterification gave diinitiator (**4**). Subsequent Cu(0)-mediated CRP yields CD chain-centered poly(methyl acrylate) **P1** (M_N = 121, PDI = 1.12, Scheme 1 and Table 1).



Scheme 1 Synthesis of poly(methyl acrylate) chain-centered coumarin dimer and cleavage under mechanochemical or photochemical conditions.

P1 was tested for mechanochemical reactivity under pulsed ultrasound at various sonication times (2 mg mL^{-1}, MeCN, 14.8 W cm^{-2}). We followed molecular weight degradation and generation of free coumarin chain ends using gel-permeation chromatography (GPC) with in-line light scattering, refractive index (RI, Fig. 1a), and UV absorbance detection (330 nm, Fig. 1b), showing monotonic increase in integral absorbance due to the presence of free coumarin (Fig. 1c). Several pieces of evidence directly confirm the formation of coumarin. For instance, the fluorescence emission (excitation 320 nm) and absorbance spectra of the sonicated product were consistent with that of free coumarin (Fig. 1d). Additionally, the aryl protons on both chain-centered CD and chain-end coumarin products can be characterized by standard ^{1}H NMR spectroscopy (Fig. S2). To ensure that the process was mechanochemical in nature, a low molecular weight control polymer was synthesized (M_N = 28, PDI = 1.04) and subjected to identical sonication conditions, showing no apparent coumarin resonances by ^{1}H NMR and minimal change in the GPC-UV trace (supporting Fig. S3 and S4).

We next used the well-known photochemical cleavage of CD units[24-27] to generate a polymer sample representing the desired "model" sonochemical product that would result if every chain were to break at, and only at, the CD mechanophore. Irradiation with short wave (254 nm) UV light resulted in quantitative cleavage of the main chain CDs to yield coumarin end-functionalized polymers with a M_n half that of the parent polymer (M_n = 61, PDI = 1.12, Table 1 (UV)). The fluorescence and emission spectra matched that of the post-sonicated **P1** and the complete disappearance of CD units was confirmed by ^{1}H NMR (see Fig. S1). We used this to our advantage in determining the conversion [%] of CD mechanophores to coumarin chain ends by integration of the GPC-UV traces (normalized based on injected mass), taking that of photolyzed **P1** to be representative of complete conversion, to generate the red curve shown in Fig 1b.

Table 1 Parameters of chain-centered CD PMA polymers and derivatives after photolysis.

Entry	Mn[a] [kDa]	PDI[a]	Efficiency[b] [%]	CDs @ Center[c] [%]	M_n (UV)[d] [kDa]	PDI (UV)[d]
P1	121	1.12	35 ± 5	47	61	1.12
P2	127	1.09	48 ± 6	63	66	1.07
P3	99	1.10	71 ± 10	74	51	1.08
P4	146	1.10	62 ± 12	67	74	1.06

[a] Parameters of polymers as synthesized (**P1**) or after fractionation by preparatory GPC (**P2-P4**). [b] Determined as the slope of the plots of [%] conversion (CD) vs. B as shown in Fig. 3a. Error is based on 95% confidence interval for the slope based on the linear regression. [c] Percentage of CD units in the center 15% of the PMA chain based on distribution of photolytically generated "half fragments." (Fig. 3b) [d] After cleavage of CD moiety by irradiation at 254 nm.

While differences in scission kinetics are generally observable between polymers bearing mechanophores and their mechanophore-free analogues,[12, 14, 28] the true specificity of mechanophore-centered scission is often unclear. The CD system provided us with the ability to generate an "authentic" GPC trace of what a system that undergoes quantitative mechanochemical conversion would look like. Shown in Fig. 1a are the GPC-RI overlays of the starting polymer **P1** (navy), photolyzed (red-dashed), and sonicated to approximately half molecular weight (black). While the MWs of the photolyzed and sonicated (180 min) polymers were nearly identical (61 kDa vs. 57 kDa respectively), the differences in PDI values (1.12 and 1.23 respectively) and the specificity of CD activation differed considerably. Photolysis results in quantitative conversion of CD units to coumarin as evidenced by ^{1}H NMR (supporting Fig S2) and MW, whereas the sonicated polymer only reached 36% conversion after 180 min of ultrasound. Despite the very similar molecular

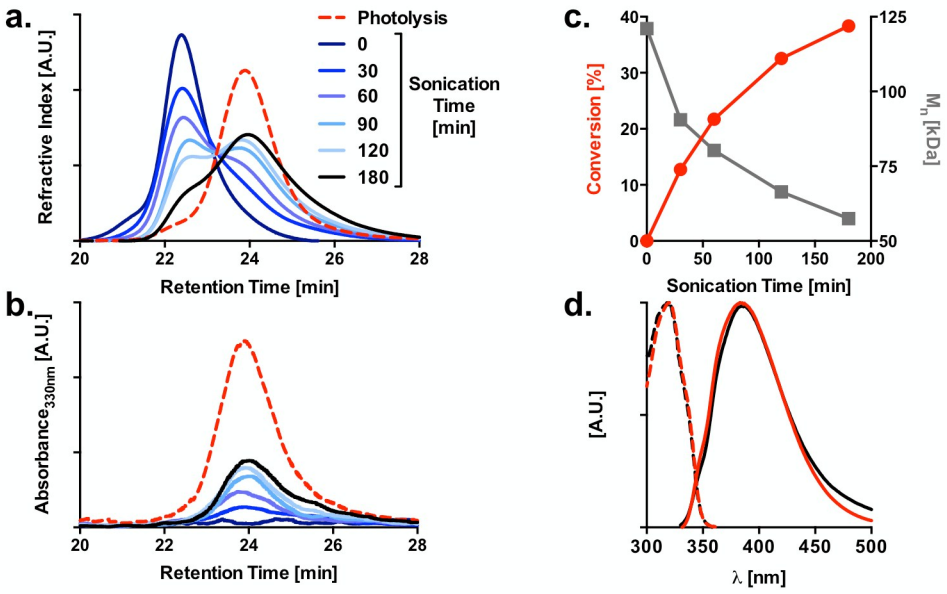


Figure 1 GPC traces of **P1** (dark blue), both during sonication, from 30 min (blue) to 180 min (black, PDI = 1.12) and after photolysis (red, dashed, PDI = 1.23). (a) RI detection showing evolution of molecular weight distribution due to sonication and photolysis. (b) UV detection ($\lambda_{detection}$ = 330 nm) showing the generation of free coumarin chain ends. Conversion as shown in Fig. 1b was calculated by taking the integral of the dashed red curve to equal 100%. (c) Conversion of CD to chain-end coumarin units (red, left axis) and concurrent reduction in MW (grey, right) as a function of sonication time. (d) Normalized absorbance (dashed) and fluorescence emission (λ_{ex} = 320 nm, solid) spectra of **P1** after sonication (black) and photolysis (red).

weights of the sonicated and photolyzed polymers, a comparison of the GPC-RI traces reveals that the sonicated polymer still contains some parent polymer, whose presence is offset by an excess of low molecular weight chains, likely due to the presence of chains in the original polymer that underwent multiple scission events.

We next wanted to examine the effect of M_n and polydispersity on activation efficiency. Even at apparently narrow PDI values, the distribution of chain lengths is significant and small changes in PDI have a dramatic effect on the distribution of chain lengths. **P2** was obtained by fractionating **P1** via preparatory GPC, while **P3** and **P4** were synthesized and fractionated independently (Table 1, supporting Fig. S1). All polymers were then sonicated in a manner identical to that of **P1** with the conversion [%] determined by integration of their respective GPC-UV traces. The average number of breaks per chain (B) was determined according to the following equation:

$$B = \frac{[1/M_n(0)] - 1/M_n(t)]}{1/M_n(0)} \quad (1)$$

where $M_n(0)$ is the initial MW and $M_n(t)$ is the MW after a given sonication time (t). Figure 3a shows the conversion of CD units plotted against B. Linear fitting of all samples resulted in lines with slopes representative of the efficiency of CD activation relative to total scission events (CD-scission and "random" scission) in a given polymer, essentially a modified method to that of Berkowski et al. to determine site-specificity.[29] While our method is likely a simplification and the plots are not strictly linear, the relative efficiencies for P1-P4 remain consistent regardless of the range of B examined (supporting Fig. S5).

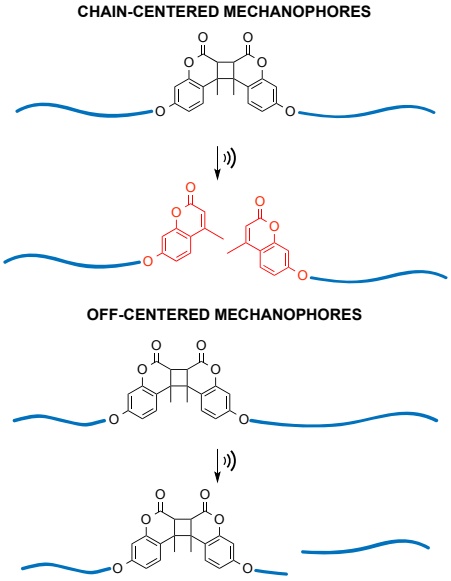


Figure 2 Chains with off-center mechanophores are more likely to undergo non-specific "random" scission, resulting in MW degradation without generating coumarin chain ends.

Interestingly, the fraction of chain scission that occurs at the CD is modest for all polymers tested (35-71%), despite the ostensibly narrow MW distributions. While variations in initial M_n showed no obvious correlation with efficiency, it appeared that the fractionated polymers activated more efficiently regardless of M_n. It is possible that chains with MWs in the highest and lowest portions of the MW distribution are the result of termination processes that result in disproportionately off-center mechanophores. For example, termination by radical combination[30, 31] at high conversions would result in large chains with 2 mechanophores, each approximately 25 % of the total contour length from the chain center. Other termination processes that result in "dead chains"[31] would not be expected to occur consistently on both propagating chains, resulting in smaller chains with an off-center mechanophore. It is likely that not only the PDI but the relative contributions of these termination processes should have a measurable influence on the efficiency of mechanophore targeting.

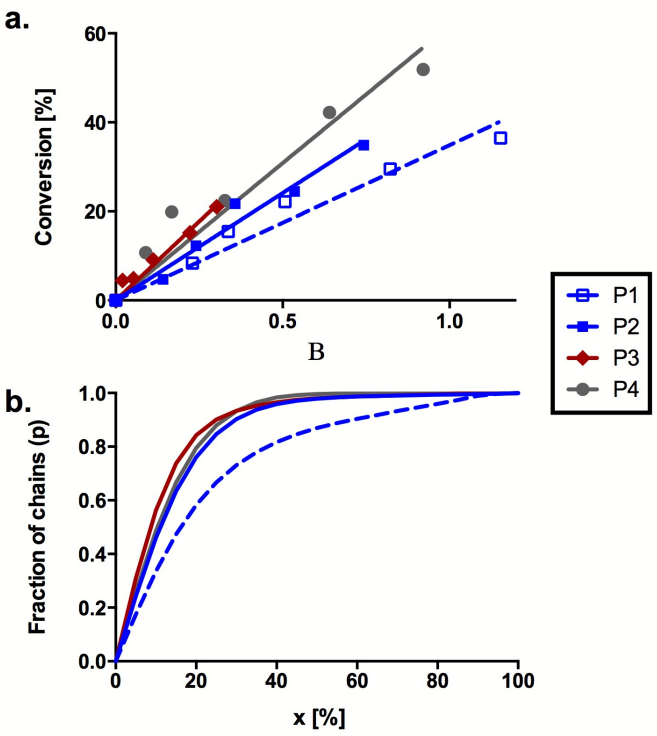


Figure 3 (a) Conversion of CD to coumarin during sonication of polymers **P1-P4** vs. B. The slopes of the linear fits are indicative of selectivity of activation for the given polymer. (b) Simulated distribution of CD units with respect to the chain center. The fraction of the population of chains (p) that reside within a given percentage of the total contour length (x) about the chain center is plotted.

We then sought to determine whether this low efficiency was related to the distribution of mechanophores about the chain center. Because of previous work on chain-centered mechanophores, it is commonly assumed that a mechanophore should reside in the middle 15% of the chain's contour length[22, 32] for activation to occur readily and efficiently. This assumption is certainly not quantitatively general, as demonstrated in the extensive activation of gem-dihalocyclopropane mechanophores,[1, 33] but it provides a convenient reference point for discussing mechanophore distribution. A "low" PDI is often taken as an indicator that the "chain-centered" condition has been fulfilled. It might be expected that polymers with a broader MW distribution might have a greater prevalence of chains with "off-center" mechanophores that undergo non-specific or "random" scission. For the photolyzed derivative of each polymer, the

distribution of s (*n*) vs. MW was generated from the original GPC-MALS-RI traces. We then simulated the reconstruction of the parent polymer distribution (*n* vs. MW) by randomly pairing chains from the set of photolyzed chains. Using this method, we then had knowledge of the MW and location of the CD along the backbone of each chain in the parent polymer. Fig. 3b shows the fraction of chains (p) where the CD mechanophore resides within the middle x ([%]) of its polymer's contour length. The probability of the CD mechanophore being in the middle 15% of the chain correlates well with the efficiency of mechanophore scission. While **P1** has what would be considered a narrow PDI value (1.12), the spatial distribution of CD units along the polymer backbone is quite broad, with only 47% expected to be within the middle 15% of the chain. This percentage increases to between 63 and 74% for polymers **P2-P4**, likely accounting for, at least in part, the observed increases in activation efficiency.

Conclusions

Here we have introduced the coumarin dimer mechanophore as a tool to examine the effect of mechanophore distribution in polymers synthesized by Cu(0) mediated CRP of PMA on their activation efficiency. Activation of the CD by pulsed ultrasound yields coumarin chain-end functionalized polymers, which display enhanced UV absorption as well as fluorescence. Like other cyclobutane mechanophores,[14, 15] the coumarin dimer is obviously more prone to mechanochemical scission than are carbon-carbon bonds along the PMA backbone. Nonetheless, the specificity for scission at the mechanophore, versus scission elsewhere along the polymer backbone, is substantially less than unity (~35 – 71%), and the reduced efficiency is found to correlate with the distribution in the position of CD along the polymer backbone. Just how close to the chain center a mechanophore must be is obviously a function of the relative activation parameters of the mechanophore and the polymer main chain, and we are mindful that no sweeping conclusions as to the necessary level of "chain-centeredness" should be drawn from this work. Rather, the key result stems from our analysis of the distribution of chains obtained by photolysis of the CD mechanophore. This analysis reveals that polymers synthesized by CRP do not necessarily meet the "chain-centered" requirement for nearly quantitative levels of activation to occur, even for polymers of relatively low PDI (although similar polydispersities might be adequate for more easily activated mechanophores). Beyond serving as a caution for the design and interpretation of sonochemical polymer mechanochemistry experiments, the results highlight the value of quantitative measures of activation. It is not clear that mechanochemical activity of the CD mechanophore employed here will allow it to be useful in solid-state applications, but the spectroscopic properties of the system coupled with the photolytic cleavage suggest that CD should at a minimum prove quite useful in further studies of mechanochemical activation by ultrasound.

Notes and references

This material is based on work supported by the NSF (CHE-1124694).

Notes and references

[a]Department of Chemistry, Duke University, French Family Science Center, Durham, NC 27708-0346 (USA)

Electronic Supplementary Information (ESI) available: Detailed experimental procedures, ^{1}H NMR and ^{13}C NMR spectra. See DOI: 10.1039/c000000x/

1. Z. S. Kean and S. L. Craig, *Polymer*, 2012, **53**, 1035-1048.
2. A. L. Black, J. M. Lenhardt and S. L. Craig, *J. Mater. Chem.*, 2011, **21**, 1655-1663.
3. M. M. Caruso, D. A. Davis, Q. Shen, S. A. Odom, N. R. Sottos, S. R. White and J. S. Moore, *Chem. Rev.*, 2009, **109**, 5755-5798.
4. G. Lligadas, B. M. Rosen, M. J. Monteiro and V. Percec, *Macromolecules*, 2008, **41**, 8360-8364.
5. S. L. Potisek, D. A. Davis, N. R. Sottos, S. R. White and J. S. Moore, *J. Am. Chem. Soc.*, 2007, **129**, 13808-13809.
6. D. Konkolewicz, Y. Wang, P. Krys, M. Zhong, A. A. Isse, A. Gennaro and K. Matyjaszewski, *Polym. Chem.*, 2014, **5**, 4396-4417.
7. D. Konkolewicz, Y. Wang, M. Zhong, P. Krys, A. A. Isse, A. Gennaro and K. Matyjaszewski, *Macromolecules*, 2013, **46**, 8749-8772.
8. S. Karthikeyan, S. L. Potisek, A. Piermattei and R. P. Sijbesma, *J. Am. Chem. Soc.*, 2008, **130**, 14968-14969.
9. A. Piermattei, S. Karthikeyan and R. P. Sijbesma, *Nat. Chem.*, 2009, **1**, 133-137.
10. R. Groote, R. T. M. Jakobs and R. P. Sijbesma, *Polym. Chem.*, 2013, **4**, 4846-4859.
11. D. A. Davis, A. Hamilton, J. Yang, L. D. Cremar, D. Van Gough, S. L. Potisek, M. T. Ong, P. V. Braun, T. J. Martinez, S. R. White, J. S. Moore and N. R. Sottos, *Nature*, 2009, **459**, 68-72.
12. D. C. Church, G. I. Peterson and A. J. Boydston, *ACS Macro Lett.*, 2014, **3**, 648-651.
13. C. R. Hickenboth, J. S. Moore, S. R. White, N. R. Sottos, J. Baudry and S. R. Wilson, *Nature*, 2007, **446**, 423-427.
14. M. J. Kryger, A. M. Munaretto and J. S. Moore, *J. Am. Chem. Soc.*, 2011, **133**, 18992-18998.
15. M. J. Kryger, M. T. Ong, S. A. Odom, N. R. Sottos, S. R. White, T. J. Martinez and J. S. Moore, *J. Am. Chem. Soc.*, 2010, **132**, 4558-4559.
16. Z. S. Kean, A. L. Black Ramirez, Y. Yan and S. L. Craig, *J. Am. Chem. Soc.*, 2012, **134**, 12939-12942.
17. Z. S. Kean, Z. Niu, G. B. Hewage, A. L. Rheingold and S. L. Craig, *J. Am. Chem. Soc.*, 2013, **135**, 13598-13604.
18. T. Q. Nguyen and H. H. Kausch, *Adv. Polym. Sci.*, 1992, **100**, 73-182.
19. G. J. Price and P. F. Smith, *Polymer*, 1993, **34**, 4111-4117.
20. G. J. Price and P. F. Smith, *Eur. Polym. J.*, 1993, **29**, 419-424.
21. G. J. Price and P. F. Smith, *Polym. Int.*, 1991, **24**, 159-164.
22. P. A. May and J. S. Moore, *Chem. Soc. Rev.*, 2013, **42**, 7497-7506.
23. *United States Pat.*, US 8,258,318 B2, 2012.
24. N. Yonezawa, T. Yoshida and M. Hasegawa, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1083-1086.
25. M. Hasegawa, K. Saigo, H. Katsuki, N. Yonezawa and T. Kanoe, *J. Polym. Sci., Polym. Chem. Ed.*, 1983, **21**, 2345-2362.
26. M. Hasegawa, Y. Suzuki and N. Kita, *Chem. Lett.*, 1972, **1**, 317-320.
27. J. Ling, M. Z. Rong and M. Q. Zhang, *J. Mater. Chem.*, 2011, **21**, 18373-18380.
28. M. V. Encina, E. Lissi, M. Sarasúa, L. Gargallo and D. Radic, *J. Polym. Sci., Polym. Lett. Ed.*, 1980, **18**, 757-760.
29. K. L. Berkowski, S. L. Potisek, C. R. Hickenboth and J. S. Moore, *Macromolecules*, 2005, **38**, 8975-8978.
30. N. H. Nguyen, M. E. Levere and V. Percec, *J. Polym. Sci., Part A: Polym. Chem.*, 2012, **50**, 860-873.
31. B. M. Rosen and V. Percec, *Chem. Rev.*, 2009, **109**, 5069-5119.
32. K. S. Suslick and G. J. Price, *Annu. Rev. Mater. Sci.*, 1999, **29**, 295-326.
33. J. M. Lenhardt, A. L. Black and S. L. Craig, *J. Am. Chem. Soc.*, 2009, **131**, 10818-10819.

