DOI: 10.1002/masy.201100111

Monomer Sequencing in Living Anionic Polymerization Using Kinetic Control

Paul P. Brooks, Adrian Natalello, John N. Hall, E. Alex L. Eccles, Solomon M. Kimani, Karina Bley, Lian R. Hutchings*

Summary: Alternating copolymers containing diphenylethylene (DPE) or diphenylethylene derivatives were prepared by living anionic polymerization using kinetic control. Due to steric hindrance DPE cannot homopolymerize. Therefore alternating copolymers can be prepared by ensuring the rate of cross-propagation (k_{12}) of the co-monomer is favoured over the rate of self-propagation (k_{11}). This reactivity ratio ($r_1 = k_{11}/k_{12}$) can be controlled by many different factors, such as choice of monomer, electron-donating or withdrawing substituents on DPE, choice of solvent, etc. We report our progress on preparing alternating copolymers by varying these factors.

Keywords: alternating copolymers; anionic polymerization; diphenylethylene; monomer sequence; sequence control

Introduction

Whilst natural polymers such as proteins and nucleic acids are constructed with absolute control over co-monomer sequence, controlling the sequence distribution of synthetic polymers is currently much more limited. Sequence controlled copolymers have been prepared by protection-coupling-deprotection reactions but this is an expensive and time consuming process and it is only practical for short sequences. Moreover, there are only a few examples of sequence-controlled chain growth polymerizations in the literature. One elegant approach for the synthesis of oligomers with controlled sequences is to use templates to recognize the incoming monomers.[1–4] This concept was proved by preferentially reacting methacrylic acid in the presence of methyl methacrylate using a bifunctional halide initator to hold methacylic acid in close proximity to the active site with ionic interactions.[1] Lutz[5] has reported a strategy for controlling monomer sequence in the atom transfer radical copolymerization of styrene and a series of *N*-substituted maleimides – the sequence being controlled via a combination of a sequential addition of monomers and a strong preference for cross propagation over self propagation. These (and other current contributions) have been described in more detail in recent reviews.[6,7]

Diphenylethylene (DPE) is a monomer which when used in anionic polymerization behaves similarly to maleic anhydride as a monomer in radical polymerization, in so much that it will not undergo self propagation (because of its steric bulk). It has however been shown to react with a carbanion and 40 years ago was shown to form alternating copolymers with styrene,[8] butadiene[9] and isoprene[10] under optimal conditions. We report here the use of derivatives of diphenylethylene to prepare new alternating copolymers - the simplest example of kinetic control. If we consider two monomers, provided the rate of cross-propagation for both monomers (k_{12} and k_{21}) is much higher than the corresponding rate for self-propagation (k_{11} and k_{22}) then the polymer will tend towards an alternating sequence - diphenylethylene (DPE) and it's derivatives have

---

Department of Chemistry, Durham University, Durham. DH1 3LE, United Kingdom.
Fax: +44 191 3342051
E-mail: p.p.brooks@durham.ac.uk

a self-propagation rate (k_{11}) of 0 due to the steric hindrance preventing the monomer from homopolymerizing. Our research focuses on derivatives of DPE with electron donating or electron withdrawing substituents as a method of controlling monomer sequences.

Experimental Part

Materials

Benzene (Aldrich, HPLC grade >99.9%) and styrene (Aldrich, 99%), were dried with calcium hydride (Aldrich) and degassed by freeze-pump-thaw cycles, and freshly distilled prior to use. Tetrahydrofuran (THF) was dried and degassed over sodium (Aldrich) wire and benzophenone (Aldrich) by freeze-pump-thaw cycles until the solution turned purple, and freshly distilled prior to use. Diphenylethylene (DPE) (Aldrich, 97%) was degassed by freeze-pump-thaw cycles and purified by the drop wise addition of *sec*-butyllithium (Aldrich, 1.4M in cyclohexane) until a deep red colour persisted and freshly distilled prior to use. 1,1-*Bis*-(4-*tert*-butyldimethylsiloxyphenyl)ethylene (DPE-OSi) was synthesised according to the procedue of Quirk and Wang.[11] Diphenylmethylpotassium (DPMK) was synthesized by the reaction of potassium napthalene with diphenylmethane in dry THF according to the previously described procedure.[12] 4-cyanodiphenylethylene (DPE-CN) was synthesised from 4-cyanobenzophenone (Aldrich, 97%) and methyl magnesium bromide (Aldrich, 3M in diethyl ether) according to the previously described procedure.[13]

Measurements

Molecular weight analysis was carried out by size exclusion chromatography (SEC) on a Viscotek TDA 302 with refractive index (660 nm source), viscosity and light scattering (690 nm wavelength laser) detectors. 2 × 300 mm Plgel 5μm mixed C columns (with a linear range of molecular weight from 200 to 2,000,000 g mol^{-1}) were used, and THF was used as the eluent with a flow rate of 1.0 mL/min at 35 °C. In all cases except the styrene/DPE-CN copolymers, molecular weights were obtained by triple detection SEC with light scattering, using a value of 0.185 (obtained from Viscotek) for the dn/dc. This is the dn/dc for polystyrene in THF and as such all quoted data were generated assuming the copolymer is polystyrene. In the case of the low molecular weight styrene/DPE-CN oligomers, molecular weight data were generated using refractive index data and a conventional calibration curve generated by a series of narrow polystyrene standards (Polymer-Labs) with molecular weights in the range of 580–1,112,000 g mol^{-1}.

^{1}H NMR spectra were measured on either a Varian VNMRS 700 MHz, Varian Inova-500 MHz or Bruker DRX-400 MHz spectrometer using either $CDCl_3$ or acetone-d6 as solvents.

Copolymerization Reactions

All copolymers were synthesised using living anionic polymerization using standard high vacuum techniques, highly purified (dried and degassed) solvents and monomers and trap to trap distillation.

Copolymerization of Styrene and DPE-OSi

A typical copolymerization was carried out as follows. DPE-OSi (1.0 g, 2.3 mmol) was added to the reaction vessel which was subsequently sealed and evacuated overnight. Approximately 20 mL of dry benzene was distilled into the vessel, dissolving the DPE-OSi. The benzene was then removed from the vessel by distillation and replaced with a further 20 mL of dry benzene. This process was repeated one more time to azeotropically dry the DPE-OSi. Benzene (50 mL) was then distilled into the reaction vessel to dissolve the DPE-OSi. The reaction vessel was raised to atmospheric pressure with dry nitrogen, and *sec*-butyllithium added drop wise (to titrate out any residual impurities) until the red colour of living DPE-OSi persisted. At this point the required amount of *sec*-butyllithium to initiate the polymerization was injected –

0.41 mL of 1.4 M solution for a target molecular weight of 10,000 g mol^{-1}–followed by styrene (4.74 g, 45.6 mmol). The polymerization was allowed to proceed overnight although samples collected at intermediate times suggested that the reaction was complete in a few hours. The reaction was terminated with nitrogen spareged methanol, precipitated into excess methanol, collected by filtration and dried to constant mass in vacuo. Yield 5.1 g (89%). SEC (THF): $M_w = 10{,}000$ g mol^{-1}, $M_n = 9{,}500$ g m-9,500 g mol^{-1}, 700 MHz ^{1}H NMR ($CDCl_3$): 0.0–0.2 (12H, -$Si(\mathbf{CH_3})_2C(CH_3)$), 0.9–1.1 (18–$Si(CH_3)_2C(\mathbf{CH_3})_3$) ppm. A series of analogous copolymers with different feed ratios of styrene and DPE-OSi was made by the method described above. A second series of anaolgous polymers was made by the described method with the exception of using THF as the polymerization solvent in place of benzene and DPMK (1.0 M in THF) as the initator in place of butyllithium (Table 1).

Copolymerization of Styrene and DPE-CN

A typical copolymerization was carried out as follows. DPE-CN (0.51 g, 2.5 mmol) was dissolved in 1 mL of THF and added to the reaction vessel which was subsequently sealed and evacuated overnight. Approximately 10 mL of dry benzene was distilled into the vessel, dissolving the DPE-CN. The benzene was then removed from the vessel by distillation and replaced with a further 10 mL of dry benzene. This process was repeated one more time to azeotropically dry the DPE-CN. Dry THF (30 mL) was then distilled into the reaction vessel to dissolve the DPE-CN; the reaction vessel raised to atmospheric pressure with dry nitrogen, and DPMK was added drop wise (to titrate out any residual impurities) until the red colour of DPMK persisted. At this point the reaction vessel was cooled to −78 °C with an acetone/dry ice bath and the required amount of DPMK to initate the polymerization was injected – 0.14 mL of 1.0 M solution for a target molecular weight of 20,000 g mol^{-1}–followed by injection of the styrene (2.33 g, 22.4 mmol). The polymerization was allowed to proceed for 24 hours maintaining a temperature of −78 °C at all times. The polymerization was terminated with nitrogen sparged methanol, but failed to precipitate upon addition to an excess of methanol. The solvents were removed by rotary evaporation, and the resulting gel-like product dried *in vacuo* to yield a few milligrams of product. Further attempts to copolymerize styrene and DPE-CN were made at −30 °C, and also other attempts using *sec*-butyllithium as the initiator instead of DPMK (in THF at −78 °C) using the method described above.

Table 1.

Monomer feed ratio (mole fraction) of styrene (f_1) and DPE-OSi (f_2), mole fraction of styrene in polymer (F_1), reactivity ratio ($r_1 = k_{11}/k_{12}$), weight average molecular weight (M_w) and polydispersity (PDI) for anionic polymerization of styrene and DPE-OSi.

Expt.	f_1	f_2	F_1	r_1	M_w/g mol^{-1}	PDI
1[a]	0.96	0.036	0.99	3.0	56,200	1.02
2[a]	0.95	0.048	0.98	2.4	10,000	1.05
3[a]	0.89	0.110	0.95	2.4	8,000	1.04
4[a]	0.83	0.172	0.94	2.9	9,600	1.05
5[a]	0.74	0.263	0.91	3.4	12,500	1.05
6[a]	0.58	0.417	0.87	4.0	13,600	1.05
7[b]	0.50	0.50	0.87	6.2	16,400	1.65
8[c]	0.50	0.50	0.86	n/a	20,600	1.90
9[d]	0.50	0.50	0.6	n/a	8,300	1.26

[a] Initiated with *sec*-butyllithium in benzene at room temperature. [b] Initiated with DPMK in THF at −78 °C. [c] Initiated with DPMK in THF, styrene added drop wise over 20 min at −78 °C then warmed to room temperature. [d] Initiated with DPMK in THF, styrene added drop wise over 20 min at room temperature.

Terpolymerization of Styrene, DPE, and DPE-OSi

A typical terpolymerization was carried out as follows. DPE-OSi (1.34 g, 3.04 mmol) was added to the reaction vessel which was subsequently sealed and evacuated overnight. Approximately 20 mL of dry benzene was distilled into the reaction vessel, dissolving the DPE-OSi. The benzene was then removed from the vessel by distillation and replenished with a further 20 mL of dry benzene. This process was repeated one more time to azeotropically dry the DPE-OSi. THF (50 mL) was then distilled into the reaction vessel to dissolve the DPE-OSi, before the addition of DPE (1.63 g, 9.06 mmol). The reaction vessel was raised to atmospheric pressure with dry nitrogen and cooled to −78 °C in an acetone/dry ice bath, and *sec*-butyllithium was added drop wise (to titrate out any residual impurities) until the red colour of living DPE/DPE-OSi persisted. At this point the required amount of *sec*-butyllithium to initate the polymerization was injected (0.19 mL of 1.4 M solution for a target molecular weight of 15,000 g mol^{-1}) followed by styrene (0.95 g, 9.13 mmol). The polymerization was then raised to 0 °C and maintained at this temperature using an ice/water bath for the duration of the reaction. Samples were withdrawn periodically for analysis by SEC and NMR until no further change in molecular weight was observed, and the reaction terminated after 70 hours; although SEC data would suggest that the reaction was virtually complete after 18 hours (Figure 6). The reaction was terminated with nitrogen sparged methanol, precipitated into an excess of methanol, redissolved in THF and reprecipitated into methanol in an attempt to wash out any unreacted monomer. The polymer was collected by filtration and dried to constant mass in vacuo. Yield of the final product: 1.8 g (46%). SEC(THF): $M_w = 22{,}600\ g\ mol^{-1}$, $M_n = 20{,}400\ g\ mol^{-1}$. 700 MHz ^1H NMR ($CDCl_3$): 0.0–0.2 (12H, $Si(C\mathbf{H_3})_2C(CH_3)$), 0.9–1.1 (18H, - $Si(CH^3)_2C(C\mathbf{H_3})_3$) ppm. A second terpolymerization was carried out according to the method described above in which the mole ratio of styrene:DPE:DPE-OSi was 4:3:1.

Results and Discussion

We have investigated the anionic copolymerization of DPE derivatives with styrene. One derivative, DPE-OSi (Figure 1a), contains an electron donating group, which increases the electron density on the vinyl double bond. This serves to retard the reaction with the polystyryl carbanion (k_{12}) whilst accelerating the rate at which the DPE-OSi carbanion reacts with styrene (k_{21}). In contrast the other derivative, DPE-CN (Figure 1b), contains an electron withdrawing cyano group, which activates k_{21}, the rate at which DPE monomer reacts with the polystyryl carbanion, but decreases k_{21}, the rate at which the resulting DPE-CN carbanion reacts with styrene.

Copolymerization of Styrene with DPE-OSi

Copolymerizations of styrene and DPE-OSi were attempted in benzene at room temperature and initiated with *sec*-butyllithium. A range of reactions with varying monomer feed ratios confirmed that styrene preferentially self propagates (Table 1–Expt. 1–6 and Figure 2).

A further reaction using diphenylmethylpotassium (DPMK) as the iniator and THF as the solvent yielded a similar result (Table 1–Expt. 7). However, when styrene was added drop wise to generate starved monomer conditions the incorporation of DPE-OSi was increased to 40 mol-% (Table 1–Expt. 8–9), however it was not possible to obtain a perfectly alternating copolymer.

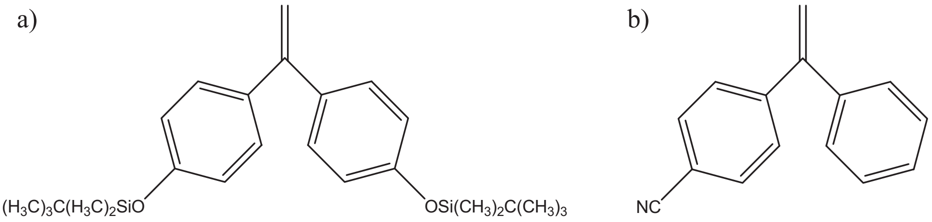


Figure 1.
Structures of (a) 1,1-*Bis*(4-*tert*-butyldimethylsiloxyphenyl)ethylene, (DPE-OSi) and (b) 4-cyanodiphenylethylene (DPE-CN).

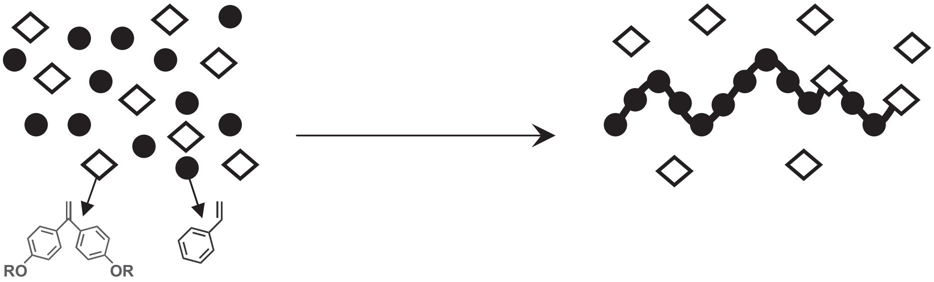


Figure 2.
Schematic representation of a potential polymer chain formed during the anionic polymerization of styrene and DPE-OSi with monomer feed ratio of [Styrene]:[DPE-OSi] = 4:3.

Whilst the self-propagation constant for DPE-OSi, k_{22} is 0, in this case the self-propagation constant for styrene, k_{11} is greater than the cross-propagation constant k_{12}. An alternative approach is to use a DPE derivative with an electron-withdrawing substituent which should increase k_{12}.

Copolymerization of Styrene with DPE-CN

Copolymerization reactions of styrene and DPE-CN were initiated with DPMK and carried out in THF at −78 °C to avoid potential side reactions involving DPE-CN.[14] Whilst it had been expected that propagation would be reasonably rapid even at −78 °C, the size exclusion chromatography (SEC) data showed that even after 24 h only oligomers had formed (Figure 3 and 4). During the initation step, due to the steric bulk of the initator it is most likely that DPMK reacts exclusively with styrene instead of DPE-CN. The cyano group will cause a strong activation effect on the DPE vinyl double bond which would then be expected to react quickly with the styryl carbanion (i.e. an increase in k_{12} as predicted). However, the cyano group then deactivates the DPE-CN carbanion

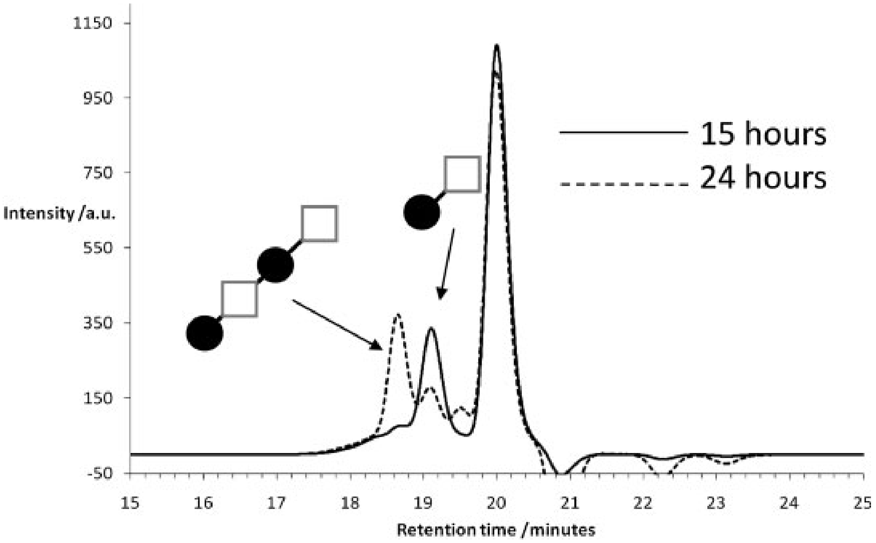


Figure 3.
Size exclusion chromatography (RI) data for copolymerization of styrene (circles) and DPE-CN (squares) after 15 h (solid line) and 24 h (dashed line).

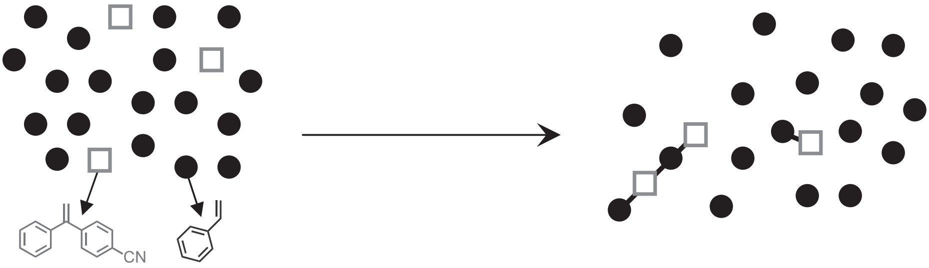


Figure 4.
Schematic representation of an anionic polymerization of styrene and DPE-CN.

resulting in a greatly reduced cross-propagation back to styrene (i.e. a large decrease in k_{21}). Whilst this was anticipated, it was not expected to be a problem since the carbanion on the cyano DPE propagating species has ‘‘nowhere else to go’’ except to react with styrene – k_{22} will be zero! Initial reactions contained a molar feed ratio of monomers of styrene:DPE-CN of 9:1 and even with a large excess of styrene it was found that, such was the deactivating effect of the CN group on k_{21}, that the propagation reaction barely proceeded at all. Moreover, it was found that when (eventually) styrene did react it was immediately capped by DPE-CN, thereby halting the reaction once more and low yields of oligomers resulted. The evidence and rationale for this supposition is discussed in detail elsewhere.[13]

However when the monomer feed ratio styrene:DPE-CN was increased from 10:1 to 100:1, quantitative conversion of monomer to polymer resulted. The same result was observed for ratios of 50:1, 25:1 and 18:1. This suggests that when the ratio of styrene is sufficiently high, the concentration of styrene can overcome the low rate of cross-propagation (k_{21}) from DPE-CN to styrene and high molar mass polymer results or alternatively some chains contain no DPE-CN and styrene homopolymerizes unhindered.

Further attempts to copolymerize styrene with DPE-CN were attempted using *sec*-butyllithium as the initator (still in THF at $-78\,^{\circ}\mathrm{C}$). As the smaller lithium counterion is more easily solvated by THF, the rate of propagation was expected to increase.[15] Indeed, SEC analysis of a copolymerization with a molar feed ratio of styrene:DPE-CN 10:1 did suggest that the reaction had proceeded further than when DMPK was used as the initator. The product, a mixture of oligomers, was still recovered in low yields. Assuming the same rationale as previously discussed,[13] SEC results suggest the presence of dimer, tetramer, hexamer and octamer species present (Figure 5).

Simultaneous Terpolymerization of Styrene, DPE and DPE-OSi

We subsequently investigated a more complicated example of kinetic control involving the simultaneous copolymerization of three monomers – styrene (monomer 1), DPE (monomer 2) and DPE-OSi (monomer 3). Whilst there are now nine kinetic propagation rate constants it is only the relative magnitude of k_{11}, k_{12} and k_{13} we are concerned about (k_{22}, k_{33}, k_{23} and k_{32} are zero, and DPE and DPE-OSi can only cross-propagate back to styrene, k_{21} and k_{31}). As discussed earlier DPE-OSi is a deactivated monomer (i.e. $k_{13} < k_{12}$), so we would expect styrene and DPE to initially form an alternating copolymer until all the DPE has been consumed at which point DPE-OSi may begin to be incorporated. This hypothesis was verified by a simultaneous terpolymerization with a molar ratio of [Styrene]:[DPE]:[DPE-OSi] = 3:3:1. If the hypothesis is correct styrene and DPE should form a near-alternating sequence and DPE-OSi should be excluded from the reaction. The

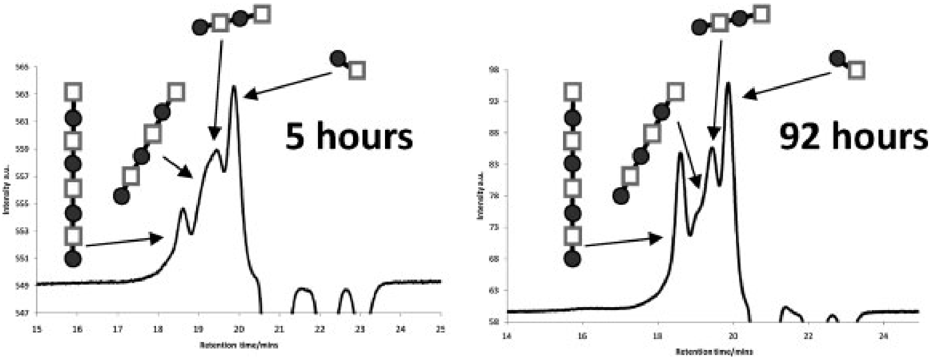
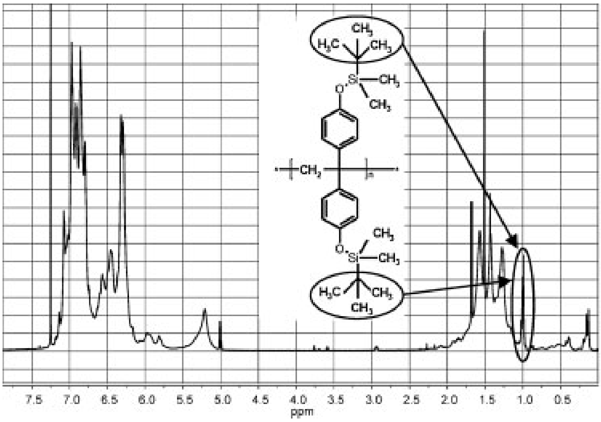


Figure 5.
Size exclusion chromotography (RI) data for copolymerization of styrene and DPE-CN after 5 hours and 92 hours (initiated with *sec*-butyllithium).

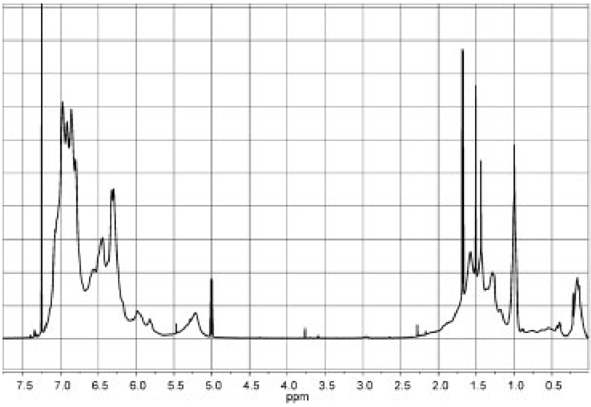
reaction was followed by ^{1}H NMR and SEC, which showed that the reaction was complete after 18 h. NMR analysis indicated a mole ratio of [Styrene]:[DPE]:[DPE-OSi] = 59:52:1 in the final polymer (Figure 6). The incorporation of a single DPE-OSi unit is unsurprising since upon consumption of DPE and styrene, any chain that ends in a styrene unit will then react with the only remaining monomer, DPE-OSi.

The terpolymerization was then repeated with a molar feed ratio of [Styrene]:[DPE]:[DPE-OSi] = 4:3:1, which would potentially allow DPE-OSi to be incorporated after the alternating block of Styrene-DPE. Once again the reaction was followed by SEC and ^{1}H-NMR. SEC data showed that the reaction was approaching completion after 7 hours. Moreover, ^{1}H NMR after 7 hours shows virtually no DPE-OSi has been incorporated and the copolymer at this point has a comonomer composition of [Styrene]:[DPE]:[DPE-OSi] equal to 47: 35: 1. However, after a further 12 hours, whilst the molecular weight had only increased slightly (from 18,500 to 20,500 g mol^{-1}) as the reaction proceeded to completion, the mole ratio of the three monomers in the polymer had



Time/hr	Mn	PDI
1	5400	1.18
3	9700	1.20
18	20200	1.09
69.5	20400	1.11

Figure 6.
^{1}H NMR spectra of polymer formed after 69.5 hours from the simultaneous terpolymerization of styrene, DPE and DPE-OSi with monomer feed ratio of 3:3:1.



Time/hr	Mn	PDI
3	8200	1.16
4	13700	1.14
7	18500	1.11
19	20400	1.14
52	20500	1.14

Figure 7.
^{1}H NMR spectra of polymer formed after 52 hours from the simultaneous terpolymerization of styrene, DPE and DPE-OSi with monomer feed ratio of 4:3:1.

changed rather more significantly to 17: 13.5: 1 (Figure 7). By comparing the data after 24 hours to the data obtained after 7 hours, it is clear that the ratio of DPE-OSi has increased significantly. This is to be expected, since when all the DPE has been consumed, the excess styrene will continue to react and as it does so it can copolymerize with the DPE-OSi. What is also clear about this reaction is that DPE-OSi becomes incorporated during the latter stages, and only during the latter stages of the polymerization. The terpolymer is likely to contain an alternating block of styrene and DPE, and a statistical block containing styrene and DPE-OSi (Figure 8).[13]

Conclusion

We have demonstrated the ability of using kinetics to control the monomer sequences in living anionic polymerizations. In particular we have explored the anionic polymerization of DPE monomers with electron withdrawing or donating substituents. We found that as DPE-OSi is a less reactive monomer than DPE, it has less tendency to form an alternating copolymer with styrene due to a low value of k_{12} relative to k_{11}. However we have used this to our advantage and used DPE-OSi in a simultaneous terpolymerization to prepare a kinetically controlled terpolymer containing one alternating block of styrene

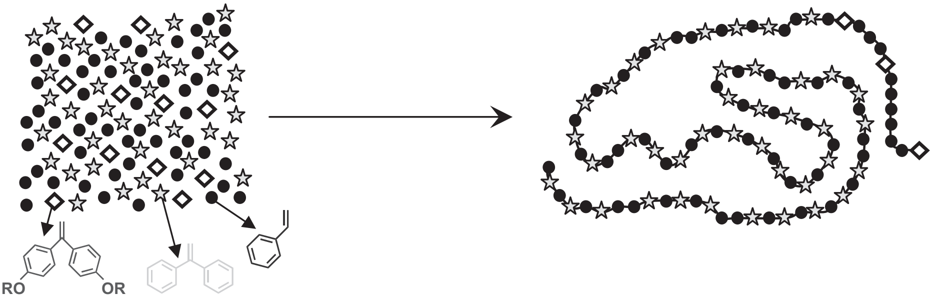


Figure 8.
Schematic representation of a likely polymer chain formed during the anionic terpolymerization of styrene, DPE and DPE-OSi with an initial monomer molar ratio of [Styrene]:[DPE]:[DPE-OSi] = 4:3:1.

and DPE, and one statistical block containing styrene and DPE-OSi. We have also shown that although DPE-CN does form an alternating copolymer with styrene, the reaction is impractically slow. Further research may allow us to prepare a perfectly alternating copolymer using DPE-CN if a more reactive monomer than styrene were to be used instead.

[1] S. Ida, T. Terashima, M. Ouchi, M. Sawamoto, *J. Am. Chem. Soc.*, **2009**, *131*, 10808.
[2] M. Ouchi, T. Terashima, M. Sawamoto, *Chem. Rev.*, **2009**, *109*, 4963.
[3] S. Ida, M. Ouchi, M. Sawamoto, *J. Am. Chem. Soc.*, **2010**, *132*, 14748.
[4] Y. Hibi, M. Ouchi, M. Sawamoto, *Angew. Chem. Int. Ed.*, **2011**, *50*, 7434.
[5] S. Pfeifer, J. F. Lutz, *J. Am. Chem. Soc.*, **2009**, *129*, 9542.
[6] N. Badi, J. F. Lutz, *Chem. Soc. Rev.*, **2009**, *38*, 3383.
[7] J. F. Lutz, *Polym. Chem.*, **2010**, *1*, 55.
[8] H. Yuki, J. Hotta, Y. Okamoto, S. Murhashi, **1967**, **40,** 2659.
[9] H. Yuki, Y. Okamoto, *Bulletin Chem. Soc. Jap.*, **1970**, *43*, 148.
[10] H. Yuki, Y. Okamoto, *Bulletin Chem. Soc. Jap.*, **1969**, *42*, 1644.
[11] R. P. Quirk, C. Y. Wang, *Polym. Int.*, **1993**, *31*, 51.
[12] T. C. Castle, L. R. Hutchings, E. Khosravi, *Macromolecules*, **2004**, *37*, 2035.
[13] A. Natalello, J. Hall, E. Eccles, S. Kimani, L. Hutchings, *Macromol. Rapid Commun.*, **2011**, *32*, 233.
[14] T. Ishizone, K. Sugiyama, A. Hirao, S. Nakahama, *Macromolecules*, **1993**, *26*, 3009.
[15] H. L. Hsieh, R. P. Quirk, *Anionic Polymerization: Principles and Practical Applications*, Marcel Dekker, New York **1996**.