Synthesis of graft copolymers from α-oxanorbornenyl macromonomers

Gaëlle Morandi,[a] Giuseppe Mantovani,[b] Véronique Montembault,[a] David M. Haddleton[b] and Laurent Fontaine*[a]

Received (in Durham, UK) 10th April 2007, Accepted 22nd June 2007
First published as an Advance Article on the web 20th July 2007
DOI: 10.1039/b705245f

α-Oxanorbornenyl macromonomers of poly(solketal methacrylate) were synthesized by ATRP with molar masses ranging from 3500 to 8500 g mol^{-1} and polydispersity indexes (PDi) of 1.22–1.23 prior to being polymerized *via* ROMP. Grubb's second generation catalyst ((IMesH$_2$)(Cy$_3$P)RuCl$_2$(CHPh)) was employed to give complete conversion with PDi of approximately 1.25 obtained. Subsequent hydrolysis led to well-defined polyoxanorbornene-*g*-poly(glycerol methacrylate) copolymers *via* the "grafting through" strategy with number average molar mass of 24 000–37 000 g mol^{-1}. A macromonomer with a molar mass of 6000 g mol^{-1} was the upper limit to obtain a complete conversion under the polymerization conditions employed.

Introduction

Graft copolymers are a class of macromolecular materials of interest due to their specific properties (morphology, phase behaviour, *etc*.) which can be tailored to a certain extent by modification of their structure.[1] Studies focused on their synthesis and on their properties are numerous in the literature.[2] Three different distinct approaches have been applied to the synthesis of graft copolymers.[2] Firstly the "*grafting onto*" strategy, where end-functionalized preformed polymer grafts are linked in a chemical reaction with reactive side chains of a polymer backbone. Secondly, the "*grafting from*" strategy, consists in a polymerization of the grafts from a polymer backbone bearing initiating sites. The last approach is the "*grafting through*" strategy which relies on polymerization of appropriate macromonomers. This latter method has proven to be a most convenient method for preparing well-defined graft copolymers, as it allows better control of grafts, backbone length as well as of the grafting density.[3] The first step of "*grafting through*" strategy involves the synthesis of an α-functional polymer by a controlled polymerization process. In a second step, and according to the nature of the α-functionality, the resulting macromonomer can be polymerized by an appropriate polymerization method such as anionic polymerization, transition-metal-mediated living radical polymerization (TMM LRP, often called ATRP) and ring-opening metathesis polymerization (ROMP).[3] Studies concerning the synthesis of graft copolymers by ROMP of α-norbornenyl macromonomers have already been reported,[4] and we recently reported the synthesis of well-defined polybutadiene-*g*-(polystyrene-*b*-poly(*tert*-butyl acrylate))s from original α-cyclobutenyl macromonomers.[5]

Herein we report the synthesis of well-defined graft copolymers *via* the "*grafting through*" strategy by ROMP of α-oxanorbornenyl macromonomers synthesized by ATRP (Scheme 1). To our best knowledge, ROMP of α-oxanorbornenyl macromonomers has never been described although ROMP of oxanorbornene (7-oxabicyclo[2.2.1]hept-2-ene) derivatives have been widely reported in the literature. Tungsten,[6] molybdenum,[7] or ruthenium based catalysts,[8] have been successfully employed to polymerize various (di)substituted oxanorbornenes which have displayed a comparable behaviour to that of norbornene derivatives. The presence of oxygen atoms in the polymer backbone has allowed some specific applications such as carbohydrate analogue polymers,[9] electrolytes,[10] or neoglycopolymers.[11] Aqueous ROMP[12] or block copolymer synthesis[13] have also been reported in addition to an original study on the polymerization of 7-oxanorbornene monomer substituted with two tapered monodendrons.[14] We focused our study on poly(2,2-dimethyl-1,3-dioxolan-4-yl)methyl methacrylate macromonomers (poly(solketal methacrylate) macromonomers), precursors of poly(glycerol methacrylate)s, a class of polymers employed for the preparation of certain biocompatible materials.[15]

Experimental

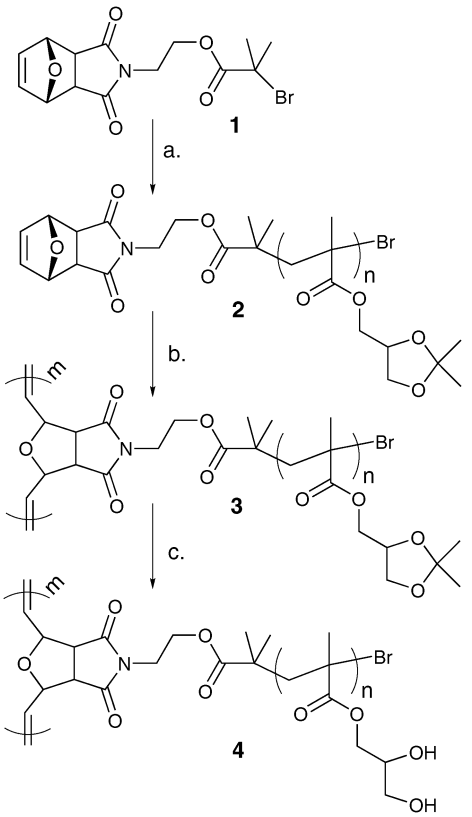
Reagents

α-Oxanorbornenyl poly(solketal methacrylate)s macromonomers were synthesized according to a procedure already described.[16] Grubb's first and second generation catalysts were purchased from Strem Chemicals. All other reagents and solvents were obtained from Aldrich and used without further purification.

Analysis

NMR spectra were recorded on a Bruker AC-400 spectrometer for ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz). Chemical shifts are reported in ppm relative to the deuterated

[a] *LCOM–Chimie des Polymères, UCO2M, UMR CNRS 6011, Université du Maine, Avenue O. Messiaen, 72085 Le Mans Cedex 09, France. E-mail: laurent.fontaine@univ-lemans.fr; Fax: +33 (0)2 43 83 37 54; Tel: +33 (0)2 43 83 33 30*
[b] *Department of Chemistry, University of Warwick, Coventry, UK CV4 7AL*



Scheme 1 Poly(oxanorbornene)-*g*-poly(glycerol)methacrylates synthesis. *Reagents and conditions*: (a) [2,2-dimethyl-1,3-dioxolan-4-yl)-methyl methacrylate] : [**1**] : [Cu(I)Br] : [*N*-(*n*-propyl)-2-pyridylmethanimine] = 30 : 1 : 1 : 2, anisole (70 % v/v), RT; (b) Grubb's II catalyst ([catalyst] : [**2**] = 1 : 10), toluene, 50 °C, 6 h; (c) 1 N HCl / dioxane, 0–25 °C, 24 h.

solvent resonances. Molecular weights and molecular weight distributions were measured using size exclusion chromatography (SEC) on a system equipped with a SpectraSYSTEM AS 1000 autosampler, with a guard column (Polymer Laboratories (PL), PL gel 5 μm guard column, 50 × 7.5 mm) followed by two columns (PL), 2 PL gel 5 μm MIXED-D columns, 2 × 300 × 7.5 mm), with a SpectraSYSTEM RI-150 detector. The eluent used is THF at a flow rate of 1 mL min^{-1} at 35 °C. Polystyrene standards (580–483 × 10^3 g mol^{-1}) were used to calibrate the SEC.

Ring-opening metathesis polymerization

General procedure: polymer (3a). All reactions were carried out either under a dry argon atmosphere or in an inert-atmosphere glove box. Macromonomer (**2a**) (446 mg, 6.9 × 10^{-5} mol) was dissolved in dry and degassed toluene (1 mL) and a precise amount of Grubb's catalyst II in toluene (1.17 mL, C = 0.0059 M) was added. The reaction mixture was heated at 50 °C in a thermostated oil-bath. After 6 h, ethyl vinyl ether was added to deactivate the propagating species. The final polymer was precipitated in cyclohexane, filtered off and dried under vacuum.

Deprotection of the ketal functionality

General procedure: polymer (4a). Polymer (**3a**) (183 mg, 3.0 × 10^{-6} mol) was dissolved in 1,4-dioxane (10 mL) and the solution was cooled to 0 °C. 1 M aqueous HCl (5 mL) was then added dropwise and the resulting turbid solution was stirred at 0 °C for 1 h, then at ambient temperature for 24 h. The final polymer was obtained after removal of the solvent by evaporation.

Results and discussion

The synthesis of poly(solketal methacrylate)s with an α-oxanorbornenyl used as a protecting group has been achieved by ATRP.[16] Such polymers have been employed as useful precursors of maleimide-terminated water-soluble macromolecules that were then successfully conjugated with cysteine-containing (poly)peptide to give a new class of synthetic polymer–protein biohybrid materials. We have applied the same procedure to synthesize well-defined α-oxanorbornenyl poly(solketal methacrylate)s (**2**) from an α-oxanorbornenyl initiator (**1**) and (2,2-dimethyl-1,3-dioxolan-4-yl)methyl methacrylate (Scheme 1) in the presence of Cu(I)Br and an iminopyridine ligand. Well-defined macromonomers were obtained with molar masses ranging from 3500 to 8500 g mol^{-1} and polydispersity indexes (PDi) of 1.22–1.26.

Subsequently we have investigated the ROMP of those macromonomers using Grubb's catalysts, chosen for their stability and excellent tolerance of functional groups. A preliminary study on the reactivity of the ATRP initiator **1** towards Grubb's generation I catalyst (Grubbs I)

Table 1 ROMP of α-oxanorbornenyl initiator **1** and α-oxanorbornenyl macromonomers **2**

								Poly(macromonomer)s	
Run	Monomer	$\overline{M_{n,SEC}}^{a}$/ g mol^{-1}	PDi[a]	$\overline{M_{n,NMR}}^{b}$/ g mol^{-1}	Catalyst[c]	$[M]_0 : [In]_0$ [d]	Solvent, T/°C, t/h	$\overline{M_{n,SEC}}^{a}$/ g mol^{-1}	PDi[a]
1	Initiator **1**				I	10	Dichloromethane, *RT*, 1 h	5500	1.22
2						100	Dichloromethane, *RT*, 1 h	36 700	1.23
3	Macromonomer **2b**	6000	1.24	7160	I	10	Toluene, 50 °C, 24 h	Bimodal distribution	
4	Macromonomer **2a**	3500	1.22	3750	II	10	Toluene, 50 °C, 6 h	11 100	1.25
5	Macromonomer **2b**	6000	1.24	7160	II	10	Toluene, 50 °C, 6 h	24 700	1.56
6	Macromonomer **2c**	8500	1.26	11 350	II	10	Toluene, 50 °C, 6 h	Bimodal distribution	
7	Macromonomer **2a**	3500	1.22	3750	II	20	Toluene, 50 °C, 24 h	Bimodal distribution	
8	Macromonomer **2b**	6000	1.24	7160	II	20	Toluene, 50 °C, 24 h	Bimodal distribution	

[a] Determined by SEC in THF at 35 °C *vs.* polystyrene standards. [b] Determined by ^{1}H NMR with the integration of oxanorbornenyl insaturation signal *vs.* repeating unit signals. [c] I = Grubbs I ($(Cy_3P)_2RuCl_2(CHPh)$), II = Grubbs II ($(IMesH_2)(Cy_3P)RuCl_2(CHPh)$). [d] $[M]_0 : [In]_0$ = concentration of monomer : concentration of initiating species.

(($Cy_3P)_2RuCl_2$(CHPh)) was conducted. Reactions were carried out in dichloromethane (to afford a good solubility of the final polymer in the medium), at ambient temperature, using different monomer-to-catalyst ratios with a reaction time of 1 h (Table 1, runs 1 and 2). Well-defined polyoxanorbornenes with relatively low PDi (1.22–1.23) were obtained. Therefore, the same catalyst has been used for the ROMP of poly(solketal methacrylate) macromonomer with a molar mass of 6000 g mol^{-1} (**2b**) (Table 1, run 3). The resulting copolymer shows a bimodal distribution of the SEC trace consistent with the presence of unreacted macromonomer. Such a phenomenon has already been observed and was ascribed to the steric hindrance effect of the polymeric chains.[4b,5] We then focused our interest on the more reactive Grubbs generation II catalyst (Grubbs II) (($IMesH_2$)(Cy_3P)$RuCl_2$(CHPh)).

The first attempt with Grubbs II and the macromonomer with a molar mass of 6000 g mol^{-1} (**2b**) led to a complete conversion with no residual macromonomer detected by either SEC or ^{1}H NMR (Table 1, run 5). This demonstrates that Grubbs II is a more suitable ROMP catalyst for entangled macromonomers. However, the PDi of the final polyoxanorbornene-*g*-polysolketal (**3**) (Fig. 1) is quite broad (1.56). It should be noticed that the difference in hydrodynamic volumes of poly(macromonomer)s compared to linear polystyrene standards can lead to anomalous elution times and separations of these polymers in SEC.[5,17] It is known in the literature[17] that the measured values for the molecular weights underestimate the true molecular weights of comb polymers by up to a factor of 10.

As the macromonomer chain length can have an effect on the ROMP efficiency, we then investigated the ROMP of a

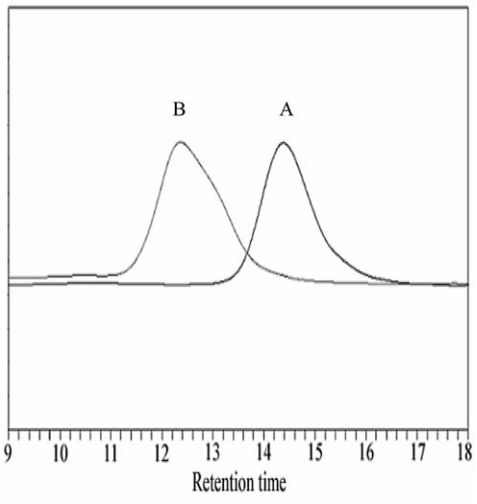


Fig. 1 SEC traces of poly(solketal methacrylate) macromonomer (**2**) (A) and polyoxanorbornene-*g*-poly(solketal methacrylate) (**3**) (B) (Table 1, run 5).

macromonomer with a molar mass of 3500 g mol^{-1} under similar experimental conditions (Table 1, run 4). Complete conversion was observed and a well-defined poly(macromonomer) with a lower PDi (1.25) obtained. Thus macromonomers with molar masses of 3500 and 6000 g mol^{-1} are polymerized with Grubbs II. The PDi of the poly(macromonomer) seems to be dependent on the macromonomer chain length. Therefore, we investigated the ROMP of a macromonomer with a higher molar mass of 8500 g mol^{-1}

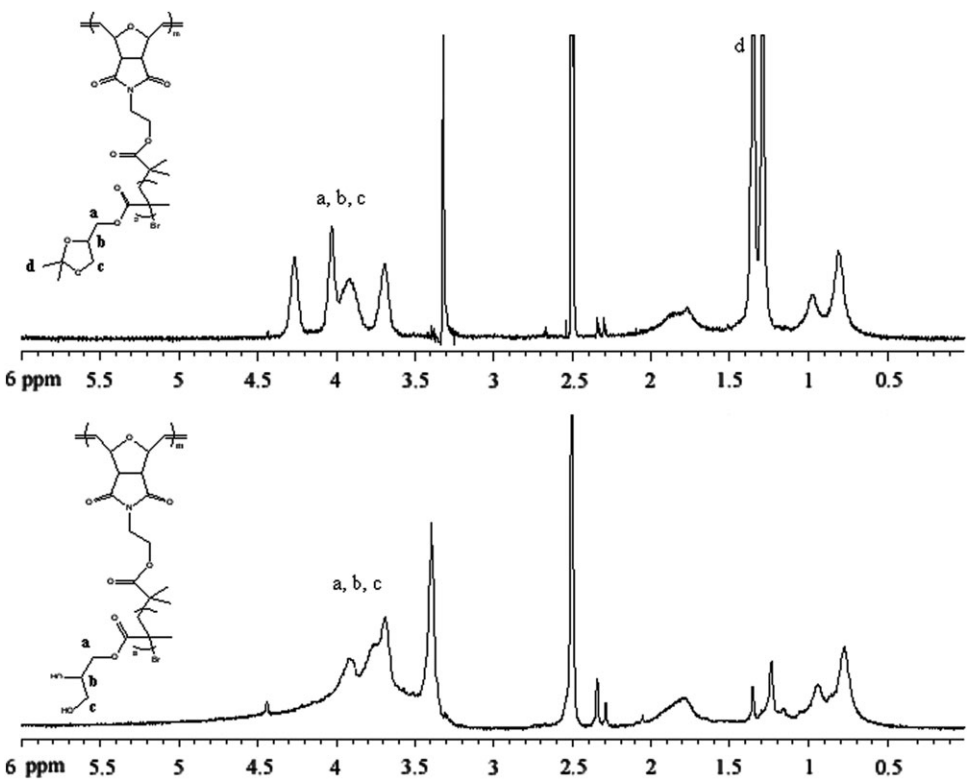


Fig. 2 ^{1}H NMR spectra of the polymers before and after deprotection (DMSO solvent).

(**2c**), under similar experimental conditions. The bimodal SEC trace shows an incomplete conversion of the macromonomer (Table 1, run 6). An increase of the reaction time from 6 to 8 h did not improve the monomer conversion. The macromonomer chain length seems to be a critical factor towards the conversion, probably due to the limiting effect of the macromonomer steric hindrance during the propagation step. Furthermore the rich-oxygen macromonomers could give competitive coordination with the ruthenium with the result of lowering the rate of polymerization. Indeed, the trapping of catalyst has already been described for poly(ethylene oxide) macromonomers.[18] Macromonomer (**2b**) with a molar mass of 6000 g mol^{-1} was the upper limit to obtain a complete conversion under the polymerization conditions employed.

To complete this study, we investigated the influence of the backbone length on the polymerization. Macromonomers (**2a**) and (**2b**), were engaged in ROMP with a macromonomer-to-catalyst ratio = 20 (Table 1, runs 7 and 8). Both macromonomers, independently of their molar masses, led to incomplete conversions as observed by SEC. Steric hindrance from the growing poly(macromonomer) is probably the limiting factor of the polymerization. As the backbone length increases, the reactivity of the propagating center decreases, making tough the incorporation of new macromonomers. Feast *et al*. have demonstrated that the ROMP at high molar ratio of macromonomer to initiator ceases as a consequence of steric hindrance.[4f]

Poly(macromonomer)s (**3**) (Table 1, runs 4 and 5) were then subjected to ketal deprotection under acidic conditions to give the expected poly(oxanorbornene)-*g*-poly(glycerol methacrylate)s (**4**) (Fig. 2). The total disappearance of the isopropylidene group signals at 1.3 ppm in the ^{1}H NMR spectrum and the appearance of the hydroxyl absorption band on IR spectrum (ν = 3400 cm^{-1}) confirmed that the deprotection was successful.

Conclusion

In summary, poly(oxanorbornene)-*g*-poly(glycerol methacrylate) copolymers have been successfully synthesized by ROMP of α-oxanorbornenyl macromonomers, using a Grubbs II ruthenium catalyst. ROMP of macromonomers featuring different molar masses indicates the existence of an upper limit to the length of poly(solketal methacrylate) grafts ($\overline{M_n} \leq 6000$ g mol^{-1}) and to the length of poly(oxanorbornene) backbone (macromonomer-to-catalyst ratio ≤ 10) attainable under the polymerization conditions employed in this study. This study constitutes a new contribution to the use of macromonomers. The successful synthesis of well-defined poly(oxanorbornene)-*g*-poly(glycerol methacrylate) copolymers from low molar masses α-oxanorbornenyl macromonomers proves the interest and versatility of the "*grafting through*" strategy. The development of more active ruthenium catalysts[19] will probably give a pathway to higher molecular weight poly(macromonomers).

Acknowledgements

The authors thank Dr Sagrario Pascual (UCO2M) for helpful discussions. CNRS, French Ministry of Research, the EU for funding Supramolecular and Macromolecular FP5 Marie Curie Training Site HPMT-CT-2001-00365 and the University of Warwick are acknowledged for support of this research.

References

1 (*a*) Y. Matsushita, J. Watanabe, F. Katano, Y. Yoshida and I. Noda, *Polymer*, 1996, **37**, 321–325; (*b*) K. Hatada and T. Kitayama, *Polym. Int*., 2000, **49**, 11–47; (*c*) C. Pugh and A. L. Kiste, *Prog. Polym. Sci*., 1997, **22**, 601–691.
2 N. Hadjichristidis, S. Pispas, M. Pitsikalis, H. Iatrou and D. J. Lohse, in Graft Copolymers, in *Encyclopedia of Polymer Science and Technology*, John Wiley & Sons, Inc., Hoboken, New York, 3rd edn, 2004.
3 (*a*) N. Hadjichristidis, M. Pitsikalis, H. Iatrou and S. Pispas, *Macromol. Rapid Commun*., 2003, **24**, 979–1013; (*b*) D. Vlassopoulos, G. Fytas, B. Loppinet, F. Isel, P. Lutz and H. Benoit, *Macromolecules*, 2000, **33**, 5960–5969; (*c*) Y. Tsukahara, S. Namba, J. Iwasa, Y. Nakano, K. Kaeriyama and M. Takahashi, *Macromolecules*, 2001, **34**, 2624–2629.
4 (*a*) J. J. Murphy and K. Nomura, *Chem. Commun*., 2005, **32**, 4080–4082; (*b*) S. Jha, S. Dutta and N. D. Bowden, *Macromolecules*, 2004, **37**, 4365–4374; (*c*) K. Nomura, S. Takahashi and Y. Imanishi, *Macromolecules*, 2001, **34**, 4712–4723; (*d*) H. R. Allcock, C. R. de Denus, R. Prange and W. R. Laredo, *Macromolecules*, 2001, **34**, 2757–2765; (*e*) V. Héroguez, E. Amédro, D. Grande, M. Fontanille and Y. Gnanou, *Macromolecules*, 2000, **33**, 7241–7248; (*f*) W. J. Feast, V. C. Gibson, A. F. Johnson, E. Khosravi and M. A. Mohsin, *J. Mol. Catal. A: Chem*., 1997, **115**, 37–42.
5 G. Morandi, V. Montembault, S. Pascual, S. Legoupy and L. Fontaine, *Macromolecules*, 2006, **39**, 2732–2735.
6 A. D. Benedicto, B. M. Novak and R. H. Grubbs, *Macromolecules*, 1992, **25**, 5893–5900.
7 G. C. Bazan, J. H. Oskam, H. Cho, L. Y. Park and R. R. Schrock, *J. Am. Chem. Soc*., 1991, **113**, 6899–6907.
8 (*a*) B. Chen, K. Metera and H. F. Sleiman, *Macromolecules*, 2005, **38**, 1084–1090; (*b*) J. Vargas, E. S. Colin and M. A. Tlenkopatchev, *Eur. Polym. J*., 2004, **40**, 1325–1335; (*c*) V. Amir-Ebrahimi and J. J. Rooney, *J. Mol. Catal. A: Chem*., 2004, **212**, 107–113.
9 S. Meier, H. Reisinger, R. Haag, S. Mecking, R. Mülhaupt and F. Stelzer, *Chem. Commun*., 2001, 855–856.
10 H. R. Allcock, J. D. Bender, R. V. Morford and E. B. Berda, *Macromolecules*, 2003, **36**, 3563–3569.
11 D. D. Manning, L. E. Strong, X. Hu, P. J. Beck and L. L. Kiessling, *Tetrahedron*, 1997, **53**, 11937–11952.
12 (*a*) M. A. Hillmyer, C. Lepetit, D. V. McGrath, B. M. Novak and R. Grubbs, *Macromolecules*, 1992, **25**, 3345–3350; (*b*) S. Lu, P. Quayle, F. Heatley and C. Booth, *Macromolecules*, 1992, **25**, 2692–2697; (*c*) G. Gangadhara, I. Campistron, M. Thomas and D. Reyx, *J. Polym. Sci., Part A: Polym. Chem*., 1998, **36**, 2807–2821.
13 (*a*) M. Weck, P. Schwab and R. H. Grubbs, *Macromolecules*, 1996, **29**, 1789–1793; (*b*) S. Kanaoka and R. H. Grubbs, *Macromolecules*, 1995, **28**, 4707–4713.
14 V. Percec and D. Schlueter, *Macromolecules*, 1997, **30**, 5783–5790.
15 Y. Ma, Y. Tang, N. C. Billingham, S. P. Armes, A. L. Lewis, A. W. Lloyd and J. P. Salvage, *Macromolecules*, 2003, **36**, 3475–3484.
16 G. Mantovani, F. Lecolley, L. Tao, D. M. Haddleton, J. Clerx, J. J. L. M. Cornelissen and K. Velonia, *J. Am. Chem. Soc*., 2005, **127**, 2966–2973.
17 M. B. Runge, S. Dutta and N. B. Bowden, *Macromolecules*, 2006, **39**, 498–508.
18 V. Héroguez, S. Breunig, Y. Gnanou and M. Fontanille, *Macromolecules*, 1996, **29**, 4459–4464.
19 J. A. Love, J. P. Morgan, T. M. Trnka and R. H. Grubbs, *Angew. Chem., Int. Ed*., 2002, **114**, 4035–4037.