## Heterogeneous catalysts for the controlled ring-opening polymerisation of *rac*-lactide and homogeneous silsesquioxane model complexes<sup>†</sup>

Matthew D. Jones,\*<sup>*a*</sup> Matthew G. Davidson,<sup>*a*</sup> Callum G. Keir,<sup>*a*</sup> Ashley J. Wooles,<sup>*a*</sup> Mary F. Mahon<sup>*b*</sup> and David C. Apperley<sup>*c*</sup>

Received 28th March 2008, Accepted 7th May 2008 First published as an Advance Article on the web 29th May 2008 DOI: 10.1039/b805274c

In this communication we report, for the first time, the ring-opening polymerisation in the melt of *rac*-lactide with heterogeneous catalysts. Homogeneous model systems based on silsesquioxanes have been prepared for comparison.

The preparation and characterisation of heterogeneous catalysts has received tremendous attention in recent years.<sup>1</sup> In this paper we report the full characterisation and preparation of Al(III) and Ti(IV) heterogeneous catalysts and silsesquioxane models complexes for the ring-opening polymerisation (ROP) of *rac*lactide (LA). The majority of ROP catalysts are homogeneous and recent examples include aluminium, zinc and group 4 metal centres.<sup>2</sup> The polymers produced *via* traditional organometallic initiators contain heavy metal residues, which can have detrimental effects on polymer performance, especially for drug delivery applications.<sup>3</sup> Heterogeneous catalysts offer the potential to negate this problem and can also offer advantages in polymer processing. Heterogeneous catalysts are dwarfed in the literature by homogeneous examples. However, there are examples of heterogeneous catalysts for the ROP of  $\varepsilon$ -caprolactone and L-lactide.<sup>4</sup> An on-

† Electronic supplementary information (ESI) available: A representative MALDI-TOF mass spectrum of the polymer produced and the solid-state NMR characterisation of Al–SiO<sub>2</sub> are also reported. CCDC reference numbers 683073 & 683074. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b805274c

going strategy to aid the characterisation and understanding of heterogeneous catalysts is to prepare silsesquioxane models.<sup>5</sup> Since the first preparation of silsesquioxanes by Feher *et al.* in the 1980s they have been used extensively as realistic models for heterogeneous catalysts and zeolite materials.<sup>6</sup> For example Feher, Crocker and Johnson *et al.* have prepared titanium silsesquioxane complexes as models for Ti(O'Pr)<sub>4</sub>-supported silica epoxidation catalysts;<sup>6-8</sup> Feher *et al.* have also prepared aluminium, vanadium and boron silsesquioxane complexes;<sup>9</sup> Duchateau *et al.* have prepared Zn–alkysilsesquioxane complexes as model catalysts for the copolymerisation of cyclohexene oxide and CO<sub>2</sub>,<sup>10a</sup> Zr(IV) silsesquioxane complexes as models for alkene polymerisation<sup>10b</sup> and the same group have also prepared Sn(II), Al(III) and Ga(III) complexes;<sup>10c,d</sup> Maschmeyer *et al.* have used silsesquioxanes as solution models for tethered Os(IV) and Rh(II) complexes.<sup>11</sup>

Complex 2 was prepared by the reaction of 1 with an equivalent of AlMe<sub>3</sub> (Fig. 1).‡ Crystals suitable for X-ray diffraction were prepared from a hexane solution and 2 crystallises in the triclinic space group  $P\bar{1}$  with one molecule in the asymmetric unit, see Fig. 2. As expected, the aluminium centres are pseudo-tetrahedral, as exemplified by the O(4A)-Al(1)-O(5) angle of 116.64(13)°. These centres connect two silsesquioxane cubes, with O(4) and O(5) acting as terminal silanols and O(1) bridging the two aluminium centres, and as a consequence has a significantly longer Al–O bond length [1.838(3) Å cf. 1.685(3) Å for Al(1)–O(5)]. The bond lengths and angles are in agreement with the aluminium cyclohexyl silsesquioxane complex previously reported by Feher et al.<sup>12</sup> Silsesquioxane complex 2 was further characterised via <sup>1</sup>H/<sup>13</sup>C/<sup>29</sup>Si NMR spectroscopies which are in agreement with the solid-state structure, for example in the <sup>29</sup>Si NMR (CDCl<sub>3</sub>) five signals were observed in approximately a 1:2:2:1:1 ratio



Fig. 1 Formation of the Al(III) and Ti(IV) silsesquioxane complexes. For 2 and 3 the isobutyl groups have been removed for clarity.

<sup>&</sup>lt;sup>a</sup>Department of Chemistry, University of Bath, Claverton Down, Bath, U. K. BA2 7AY. E-mail: mj205@bath.ac.uk; Fax: +44 (0)1225 386231; Tel: +44 (0)1225 384908

<sup>&</sup>lt;sup>b</sup>Bath Chemical Crystallography Unit, Department of Chemistry, University of Bath, Claverton Down, Bath, U. K. BA2 7AY

<sup>&</sup>lt;sup>e</sup>Durham University, Department of Chemistry, Solid State NMR Service, Durham, U. K. DH1 3LE



**Fig. 2** The molecular structure of **2**; the isobutyl groups have been omitted for clarity. Selected bond lengths [Å] and angles [°] are: Al(1)–O(1) 1.838(3), Al(1)–O(5) 1.685(3), Al(1)–O(4A) 1.687(3), Al(1)–O(1A) 1.830(3), O(4)–Si(3) 1.603(3), O(5)–Si(7) 1.604(3), O(1)–Si(1) 1.662(3). O(4A)–Al(1)–O(5) 116.64(13), O(4A)–Al(1)–O(1) 113.59(13). Labels with suffix A relate to those in the asymmetric unit by the -x, -y + 1, -z + 1 symmetry operation.

as expected for the  $C_{2h}$  symmetry present in **2**. This is consistent with previously characterised analogous Al–silsesquioxane complexes.<sup>12</sup> The titanium complex **3** was characterised *via* single-crystal X-ray diffraction (Fig. 3); in the solid-state **3** exists as a dimer.§ The bond lengths and angles reported are comparable to those reported by Johnson *et al.*, for a similar methoxide-bridged dimer, and structures reported by Crocker *et al.*<sup>7,13</sup> The synthesis of complex **3** has been previously reported by Abbenhuis and coworkers.<sup>14</sup> In a freshly prepared <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) of **3** one isopropoxide methine resonance was detected at 4.56 ppm,



Fig. 3 The molecular structure of 3; the isobutyl groups have been omitted for clarity. Selected bond lengths [Å] and angles [°] are: Ti(1)–O(4) 1.7949(18), Ti(1)–O(1) 1.8206(18), Ti(1)–O(8) 1.8118(17), Ti(1)–O(13) 1.9227(17), Ti(1)–O(14) 2.1261(16). O(1)–Ti(1)–O(14) 167.90(8), O(1)–Ti(1)–O(13) 96.01(8), O(1)–Ti(1)–O(4) 98.64(9).

Table 1	Catalytic data	for the melt ROP	of rac-LA
---------	----------------	------------------	-----------

and in the <sup>29</sup>Si NMR three major resonances were detected in a 3:1:3 ratio, consistent with the  $C_{3\nu}$  symmetry of the monomeric species present in solution. In the <sup>29</sup>Si NMR a minor series was observed for the  $C_{2h}$  symmetric dimer, as observed previously by Crocker *et al.* for the cyclohexane silsesquioxane derivative.<sup>13</sup> Variable-temperature <sup>1</sup>H NMR (C<sub>6</sub>D<sub>5</sub>CD<sub>3</sub>, -60 to + 80 °C) only afforded one septet at 4.42 ppm.

The heterogeneous catalysts were prepared by reacting silica (with a pore diameter of 40 or 60 Å) with Ti(O<sup>i</sup>Pr)<sub>4</sub> or Al(O<sup>i</sup>Pr)<sub>3</sub> in toluene.¶<sup>15</sup> The <sup>13</sup>C{<sup>1</sup>H} CP/MAS NMR of the Ti–SiO<sub>2</sub> was in agreement with literature precedent; ICP-AES (inductively-coupled plasma–atomic-emission spectroscopy) indicates that the titanium loading was 3.40 wt%.<sup>15</sup> For Al–SiO<sub>2</sub> the <sup>13</sup>C{<sup>1</sup>H} CP/MAS NMR afforded two resonances for the methyl group of the isopropoxide at 23.1 and 24.3 ppm and one resonance for the methine carbon at 63.8 ppm. In the <sup>27</sup>Al NMR three resonances were observed at 50.8, 30.3 and 2.0 ppm for tetrahedral, 5-coordinate and octahedral aluminium environments.† MQMAS confirmed that these are separate environments and not part of a quadrupolar lineshape.

The homogeneous models and heterogeneous catalyst were tested for the ROP of *rac*-LA in the melt at 130 °C (Table 1). Complexes **2** and **3** were both active for the polymerisation, producing a polymer with a very broad molecular weight distribution; this could be due to the production of cyclic polymers. Notably, **3** is more active than **2**. This is presumably due to initiation being faster due to the presence of the Ti–O<sup>i</sup>Pr bond, whereas in **2** initiation is assumed to occur *via* an Al–OSi bond.

The microstructure of the polylactide (PLA) produced from Al-SiO<sub>2</sub> was shown to be predominately isotactic (75% isotactically enriched, as determined by the analysis of the <sup>1</sup>H homonuclear decoupled NMR). The MALDI-TOF mass spectrum of the polymer produced with Al-SiO<sub>2</sub> (entry 7) showed one major series of peaks with a repeat unit of 144 indicating that there is little transesterification present and the MALDI-TOF mass spectrum significantly also showed the presence of the isopropoxide end group and the expected hydroxyl end group.<sup>†</sup> For the heterogeneous titanium catalysts (entries 3-6) it was observed that the yield was higher for the 60 Å support compared to the 40 Å support, presumably as a result of mass transport effects being more significant for the smaller pores. MALDI-TOF mass spectrometry of the polymer produced from the 40 Å after 2 h (entry 5) showed a major series of peaks with a repeat unit of 144 and a minor series with a repeat unit of 72

Entry	Initiator <sup>b</sup>	Time/h	Yield <sup>c</sup>	$M_n^{d}$	$M_{w}{}^{d}$	$M_w/M_n^{d}$	Pr <sup>e</sup>
1	2	48	5	24 500	81 400	3.3	0.5
2	3	0.5	83	200 500	506 200	2.5	0.55
3	$Ti-SiO_2(60)$	2	78	47 950	48 9 50	1.02	0.5
4	$Ti-SiO_2(60)$	6	98	65 650	92 000	1.40	0.5
5	$Ti-SiO_2$ (40)	2	52	14 700	15900	1.08	0.5
6	$Ti-SiO_2$ (40)	6	58	16 550	18 500	1.12	0.5
7	$Al-SiO_2$ (60)	48	10	3000	4050	1.13	0.25

<sup>*a*</sup> Conditions [LA]/[Initiator] = 300:1 for the homogeneous catalysts, for the heterogeneous catalysts 100 mg of solid was used and 2 g of *rac*-LA, temperature = 130 °C. <sup>*b*</sup> The number in brackets represents the pore diameter of the silica used. A polymerisation run with pure silica failed to yield polymer after 48 h under analogous conditions. <sup>*c*</sup> Isolated % yield. <sup>*d*</sup> Determined from GPC (in THF) using polystyrene as the reference. <sup>*e*</sup> Calculated from the <sup>1</sup>H homonuclear decoupled NMR (CDCl<sub>3</sub>) analysis.

indicating that little transesterification occurs and MALDI-TOF also showed the presence of the isopropoxide and hydroxyl end groups. Interestingly the heterogeneous systems are far more well controlled (narrow PDIs) than their homogeneous counterparts. The polymerisation was quenched with the addition of methanol and the residue was dissolved in  $CH_2Cl_2$  and filtered. The residue was analysed *via* ICP-AES; for the Ti–silsesquioxane there was 1110 ppm of Ti in the residue and for the Ti–heterogeneous catalysts (entry 4) there was 15 ppm, indicating that leaching is not significant. These results imply that heterogeneous catalysts could play an important role in ROP catalysts for the production of PLA.

In conclusion, we report the preparation and full characterisation of two novel silsesquioxane complexes; both structures exist as dimers in the solid state. These catalysts act as models for heterogeneous systems; both homogeneous and heterogeneous systems have shown to be active for the ROP of *rac*-LA under melt conditions, with the homogeneous systems being more active. Work is on-going to prepare further heterogeneous systems and realistic silsesquioxane models for the aluminium system by modifying the silsesquioxane to allow the incorporation of an isopropoxide group on the aluminium centre.

## Acknowledgements

The EPSRC is acknowledged for an RCUK fellowship to MDJ, a case studentship to CGK, and the University of Bath for AJW. Dr John Lowe is gratefully acknowledged for recording <sup>29</sup>Si{<sup>1</sup>H} NMR spectra. The EPSRC national solid-state NMR and mass spectrometry service centres are gratefully acknowledged. We thank Johnson Matthey for the ICP-AES measurements.

## Notes and references

‡ Synthesis and characterisation of complex 2: Isobutyl silsesquioxane (1) (1.76 g, 2.22 mmol) was dissolved in THF (15 ml), to which 2.0 M trimethylaluminium solution in hexane (1.11 ml, 2.22 mmol) was added. The reaction was stirred under argon for 1 h, the solvent removed under reduced pressure, the product dissolved in 10 ml of hot hexane, and left to recrystallise at room temperature. After 2 days crystals suitable for a diffraction had formed. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $0.54(12H, dJ = 7.0 \text{ Hz}, \text{SiCH}_2)$ , 0.60 (12H, d J = 7.0 Hz, SiCH<sub>2</sub>), 0.75 (4H, d J = 7.0 Hz, SiCH<sub>2</sub>), 0.96 (84H, m, CH<sub>3</sub>), 1.84 (12H, sept J = 7.0 Hz, CH), 2.01 (2H, sept J = 7.0 Hz, CH).<sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>) 22.4, 22.5, 22.9, 23.2 (CH<sub>2</sub>), 23.2 (CH), 23.4 (CH<sub>2</sub>), 23.9, 24.0, 24.1 (CH), 25.6, 25.6, 25.7, 25.7, 25.9, 25.9, 26.0 (CH<sub>3</sub>). <sup>29</sup>Si{<sup>1</sup>H} (CDCl<sub>3</sub>) -63.0, -64.0, -66.5, -67.0, -70.5 in a 1:2:2:1:1 ratio. Elemental analysis: calc. for  $C_{56}H_{126}Al_2O_{24}Si_{14}$ : C, 41.24; H, 7.79. Found C, 40.7; H, 7.78. Crystal data for **2**:  $C_{28}H_{63}AlO_{12}Si_7$ , M = 815.39, colourless block,  $0.15 \times 0.10 \times 0.10$  mm, triclinic, space group  $P\overline{1}$ , a =11.8430(5), b = 14.2230(6), c = 15.3430(7) Å, a = 112.420(2),  $\beta = 90.025(2)$ ,  $γ = 112.209(2)^\circ$ , V = 2180.03(16) Å<sup>3</sup>, Z = 1,  $D_c = 1.242$  g cm<sup>-3</sup>,  $F_{000} = 876$ , Mo Kα radiation, λ = 0.71073 Å, T = 150(2) K,  $2θ_{max} = 50.2^\circ$ , 19 937 reflections collected, 7624 unique ( $R_{int} = 0.0429$ ). Final GoF = 1.058,  $R_1 =$ 0.0534,  $wR_2 = 0.1349$ , R indices based on 5938 reflections with  $I > 2\sigma(I)$ (refinement on  $F^2$ ), 606 parameters, 0 restraints,  $\mu = 0.289 \text{ mm}^{-1}$ .†

§ Synthesis and characterisation of complex 3: **1** (1.82 g, 2.3 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> to which Ti(O<sup>i</sup>Pr)<sub>4</sub> (0.68 ml, 2.3 mmol) was added; this was stirred for 2 h. After this time the solvent was removed *in vacuo* and the white product was recrystallised in hexane. After 2 days at -20 °C a crop of colourless crystals were obtained which were filtered and dried. <sup>1</sup>H (CDCl<sub>3</sub>) 0.50 (14H, m, SiCH<sub>2</sub>), 0.98 (42H, m, CH<sub>3</sub> silses), 1.30 (6H, d J = 6 Hz, CH<sub>3</sub> isopropoxide), 1.85 (7H, m, CH silses), 4.56 (1H, sept J = 6 Hz,

CH isopropoxide). <sup>13</sup>C{<sup>1</sup>H} (CDCl<sub>3</sub>) 22.3 (CH<sub>2</sub>), 22.6 (CH<sub>2</sub>), 23.9, 25.7, 25.7, 25.8, 79.5 (CH/CH<sub>3</sub>). <sup>29</sup>Si{<sup>1</sup>H} (CDCl<sub>3</sub>) -65.5, -67.9, -68.8 (in a 3 : 1 : 3 ratio). Calc. for C<sub>31</sub>H<sub>70</sub>O<sub>13</sub>Si<sub>7</sub>Ti<sub>1</sub> C, 41.59; H, 7.88. Found C, 41.2; H, 7.75. Crystal data for 3: C<sub>62</sub>H<sub>140</sub>O<sub>26</sub>Si<sub>14</sub>Ti<sub>2</sub>,  $M = 1790.80, 0.25 \times 0.25 \times 0.20$  mm, triclinic, space group *P*1, a = 15.7700(2), b = 17.32200(10), c = 18.9630(2) Å, a = 112.8870(10),  $\beta = 91.380(1)$ ,  $\gamma = 90.600(1)^{\circ}$ , V = 4769.78(8) Å<sup>3</sup>, Z = 2,  $D_c = 1.247$  g cm<sup>-3</sup>,  $F_{000} = 1920$ , MoKa radiation,  $\lambda = 0.71073$  Å, T = 150(2) K,  $2\theta_{max} = 55.0^{\circ}$ , 97 404 reflections collected, 21 875 unique ( $R_{int} = 0.0457$ ). Final GoF = 1.022,  $R_1 = 0.0512$ ,  $wR_2 = 0.1349$ , *R* indices based on 14 926 reflections with  $I > 2\sigma(I)$  (refinement on  $F^2$ ), 1126 parameters, 0 restraints,  $\mu = 0.407$  mm<sup>-1</sup>;†

¶ The heterogeneous catalysts were prepared as follows: SiO<sub>2</sub> (pore diameter either 40 or 60 Å) was dried at 130 °C under vacuum for 5 h. After this time toluene was added and Ti(O'Pr)<sub>4</sub> or Al(O'Pr)<sub>3</sub> (0.8 mmol g<sup>-1</sup> silica) and the mixture heated to 70 °C and stirred for 4 h. The solid was filtered and washed with copious amounts of toluene and diethyl ether and dried under vacuum. Found elemental analysis Ti–SiO<sub>2</sub>(60) C, 4.39; H, 1.23. Ti–SiO<sub>2</sub>(40) C, 4.87; H, 1.36. Al–SiO<sub>2</sub>(60) C, 4.00; H, 1.37.

- 1 (a) R. Duchateau, Chem. Rev., 2002, **102**, 3525; (b) J. M. Thomas, R. Raja and D. W. Lewis, Angew. Chem., Int. Ed., 2005, **44**, 6456.
- Z. Y. Zhong, P. J. Dijkstra and J. Feijen, Angew. Chem., Int. Ed., 2002, 41, 4510; (b) P. Hormnirun, E. L. Marshall, V. C. Gibson, A. J. P. White and D. J. Williams, J. Am. Chem. Soc., 2004, 126, 2688; (c) M. Cheng, A. B. Attygalle, E. B. Lobkovsky and G. W. Coates, J. Am. Chem. Soc., 1999, 121, 11583; (d) A. J. Chmura, M. G. Davidson, M. D. Jones, M. D. Lunn, M. F. Mahon, A. F. Johnson, P. Khunkamchoo, S. L. Roberts and S. S. F. Wong, Macromolecules, 2006, 39, 7250.
- 3 B. G. G. Lohmeijer, R. C. Pratt, F. Leibfarth, J. W. Logan, D. A. Long, A. P. Dove, F. Nederberg, J. Choi, C. Wade, R. M. Waymouth and J. L. Hedrick, *Macromolecules*, 2006, **39**, 8574.
- 4 (a) T. M. AbdelFattah and T. J. Pinnavaia, *Chem. Commun.*, 1996, 665;
  (b) G. Deshayes, K. Poelmans, I. Verbruggen, C. Camacho-Camacho, P. Degee, V. Pinoie, J. C. Martins, M. Piotto, M. Biesemans, R. Willem and P. Dubois, *Chem.-Eur. J.*, 2005, 11, 4552.
- 5 F. J. Feher, D. A. Newman and J. F. Walzer, J. Am. Chem. Soc., 1989, 111, 1741.
- 6 F. J. Feher, S. L. Gonzales and J. W. Ziller, Inorg. Chem., 1988, 27, 3440.
- 7 M. Crocker, R. H. M. Herold and A. G. Orpen, *Chem. Commun.*, 1997, 2411.
- 8 T. Maschmeyer, M. C. Klunduk, C. M. Martin, D. S. Shephard, J. M. Thomas and B. F. G. Johnson, *Chem. Commun.*, 1997, 1847.
- 9 (a) F. J. Feher and K. J. Weller, Organometallics, 1990, 9, 2638; (b) F. J. Feher and R. L. Blanski, J. Am. Chem. Soc., 1992, 114, 5886; (c) F. J. Feher, T. A. Budzichowski and J. W. Ziller, Inorg. Chem., 1992, 31, 5100.
- 10 (a) R. Duchateau, W. J. van Meerendonkt, S. Huijser, B. B. P. Staal, M. A. van Schilt, G. Gerritsen, A. Meetsma, C. E. Koning, M. F. Kemmere and J. T. F. Keurentjes, Organometallics, 2007, 26, 4204; (b) J. R. Severn, R. Duchateau, R. A. van Santen, D. D. Ellis, A. L. Spek and G. P. A. Yap, Dalton Trans., 2003, 2293; (c) G. Gerritsen, R. Duchateau, R. A. van Santen and G. P. A. Yap, Organometallics, 2003, 22, 100; (d) R. Duchateau, T. W. Dijkstra, J. R. Severn, R. A. van Santen and I. V. Korobkov, Dalton Trans., 2004, 2677.
- 11 (a) M. Nowotny, T. Maschmeyer, B. F. G. Johnson, P. Lahuerta, J. M. Thomas and J. E. Davies, *Angew. Chem., Int. Ed.*, 2001, **40**, 955; (b) P. P. Pescarmona, A. F. Masters, J. C. van der Waal and T. Maschmeyer, *J. Mol. Catal. A: Chem.*, 2004, **220**, 37.
- 12 F. J. Feher, T. A. Budzichowski and K. J. Weller, J. Am. Chem. Soc., 1989, 111, 7288.
- 13 M. Crocker, R. H. M. Herold, A. G. Orpen and M. T. A. Overgaag, J. Chem. Soc., Dalton Trans., 1999, 3791.
- 14 (a) L. Zhang, H. C. L Abbenhuis, G. Gerritsen, N. Ni, Bhriain, P. C. M. M. Magusin, B. Mezari, W. Han, R. A. van Santen, Q. H. Yang and C. Li, *Chem.-Eur. J.*, 2007, **13**, 1210; (b) H. Al Ghatta, H. C. L. Abbenhuis, *World Pat.*, 2008 009 708, publication date 24th January 2008.
- 15 (a) J. M. Fraile, J. I. Garcia, J. A. Mayoral, L. C. Demenorval and F. Rachdi, J. Chem. Soc., Chem. Commun., 1995, 539; (b) P. Iengo, G. Aprile, M. Di, Serio, D. Gazzoli and E. Santacesaria, Appl. Catal., A, 1999, **178**, 97; (c) M. C. Capel-Sanchez, J. M. Campos-Martin and J. L. G. Fierro, J. Catal., 2005, **234**, 488.