This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
Titanium complexes bearing oxa- and azacalix[4, 6]arenes: structural studies and use in the ring opening homo-/co-polymerization of cyclic esters

Tian Xing, Timothy J. Prior,a Kai Chenb and Carl Redshaw*a

Abstract: Reaction of excess [Ti(OiPr)4] with p-tert-butyltetramethyldioxacalix[6]areneH (L1H2) afforded, after work-up (MeCN), the complex [Ti2(OiPr)8(MeCN)L1]·3.5MeCN (1·3.5MeCN), whilst the oxo complex [Tiμ2-OiPr]2H2O(L1)·MeCN (2·MeCN) was isolated via a fortuitous synthesis involving the use of two equivalents of [Ti(OiPr)4]. Reactions of p-methyl-dimethylidiazacalix[6]areneH (L2H2) with [TiF4] (four equivalents), [TiCl4(THF)]2 (two equivalents) or [TiBr4] (>four equivalents) resulted in the titanium-based azacalix[n]arene complexes [TiF4(L1)2(H2)]·2.5MeCN (3·2.5MeCN), [TiX2(H2)2Cl2L2(H2)] (K = Cl (4·5MeCN), Br (5·4.5MeCN) and [TiBr4L2(H2)]·MeCN) (6·7MeCN), respectively. Reaction of four equivalents of [TiF4] with L1H2 (L1H4 = p-methyl-dimethylidiazacalix[6]areneH2) afforded the product [TiF2L4(L1)2(H2)](SilF5)2·2MeCN (7·2MeCN). These complexes have been screened for their potential to act as pre-catalysts in the ring opening polymerization (ROP) of ε-caprolactone (ε-CL), δ-valerolactone (δ-VL) and rac-lactide (r-LA). Generally, the titanium complexes bearing oxacalixarene exhibited better activities than the azacalixarene-based pre-catalysts. For ε-CL, δ-VL and r-LA, moderate activity at 130 °C over 24 h was observed for 1-6. In the case of the co-polymerization of ε-CL with r-LA, 1-6 afforded reasonable conversions and high molecular weight polymers; 7 exhibited lower catalytic performance due to low solubility. None of the complexes proved to be active in the polymerization of ω-pentadecalactone (ω-PDL) under the conditions employed herein.

Introduction

Calix[n]arenes are a family of macrocyclic molecules consisting of phenol units linked most commonly by methylene (-CH2-) bridges at their ortho positions, and have found widespread use in supramolecular chemistry.1 Investigations into their coordination chemistry have shown that their potential in areas such as catalysis can be greatly improved if the methylene bridges are replaced by heteroatom-containing bridges such as thia (-S-), sulfanyl (-SO-), sulfonyl (-SO2-) or dimethylenoxo (-CH2OCH2-), which can potentially bind to the metal.2 Interestingly, there is a lack of such studies involving dimethylenoxo (-CH2OCH2-) containing calix[n]arenes, where n ≥ 6.3 Moreover, there is even less data on azacalix[n]arenes, where the bridge (-NR-) has an addition group (R) bound to the nitrogen which can potentially be varied to control the steric and/or electronic properties of the system.4 Given this, we have initiated a study of the coordination chemistry of both dimethyloxo- and azacalix[n]arenes with a view to investigating their potential as catalysts for the ring opening polymerization (ROP) of cyclic esters. Given recent successes using titanocalix[n]arenes for ROP (see Chart 1),5 we opted here to focus on titanium-containing dimethyloxo- and azacalixarenes, and have structurally characterized a number of interesting poly-metallic species (see Chart 2). The ability of these complexes to act as pre-catalysts for the ROP of ε-caprolactone (ε-CL), δ-valerolactone (δ-VL) and rac-lactide (r-LA) has been investigated; the copolymerization of ε-CL and r-LA was also investigated.

Results and Discussion

Syntheses and solid-state structures

Dioxacalix[6]arene complexes

Figure 1. Molecular structure of [Ti2(OiPr)8(MeCN)L1]·3.5MeCN (1·3.5MeCN). Solvent molecules and hydrogen atoms omitted for clarity.

---

*a Plastics Collaboratory, Department of Chemistry, University of Hull, Cottingham Road, Hull, HU6 7RX, UK. E-mail: c.redshaw@hull.ac.uk
b Collaborative Innovation Center of Atmospheric Environment and Equipment Technology, Jiangsu Key Laboratory of Atmospheric Environment Monitoring and Pollution Control, School of Environmental Science and Engineering, Nanjing University of Information Science & Technology, Nanjing 210044, P. R. China.
Interaction of an excess (3 equiv.) of [Ti(O\textit{i}Pr)]\textsubscript{4} with p-tert-butyltetrahomodioxacalix[6]arene\textsubscript{H\textdegree} (L\textdegree H\textdegree) in refluxing toluene afforded, after work-up (MeCN), the orange complex [Ti\textsubscript{4}(O\textit{i}Pr)\textsubscript{4}(MeCN)L\textdegree] 3.5MeCN (1:3.5MeCN) in 52% yield. The molecular structure is shown in Figure 1, with selected bond lengths and angles given in the ESI; crystallographic data are given in Table 5. The complex contains two titanium centres, one of which, Ti(1), is distorted octahedral bound by an isopropoxide ligand, an acetonitrile ligand and four calixarene phenoxy oxygens in a square plane, two of which are shared with Ti(2). Ti(2) is five-coordinate and adopts a slightly distorted rectangular pyramidal (τ = 0.015).\textsuperscript{[6]}

If the reaction is conducted in the presence of adventitious oxygen/water and using only two equivalents of [Ti(O\textit{i}Pr)\textsubscript{4}], then the isopropoxide groups are lost and a structure involving a titanium-oxygen Ti\textsubscript{IV}O\textsubscript{3} ladder sandwiched between two oxacalix[6]arenes is formed, namely [Ti\textsubscript{4}(\mu\textsubscript{2}-O)\textsubscript{2}(H\textdegree O)\textsuperscript{L\textdegree} \cdot MeCN (2:MeCN). The molecular structure is shown in Figure 2, with selected bond lengths and angles given in the ESI. The water ligand partially occupies positions at Ti(1) and Ti(1\#) (50:50). We note that calix[8]arene titanium ladder complexes have recently been isolated and utilized for ROP, CO\textsubscript{2} photoreduction and photocatalytic H\textsubscript{2} production.\textsuperscript{[16, 7]}

**Azacalixarene complexes**

Reaction of p-methyl-dimethylidiazacalix[6]arene\textsubscript{H\textdegree} (L\textdegree H\textdegree) with four equivalents of [TiF\textsubscript{4}] in refluxing toluene afforded, following work-up (MeCN), the orange complex [Ti\textsubscript{4}F\textsubscript{14}L\textdegree(H\textdegree)\textsubscript{2}] 2.5MeCN (3:2.5MeCN). The molecular structure is shown in Figure 3, with selected bond lengths and angles given in the ESI. The complex contains four distorted octahedral titanium centres each linked via fluoride bridges to give a central Ti\textsubscript{4}F\textsubscript{14} core. The azacalixarene acts as a bidentate O,O-
chelate to Ti(1) and to Ti(2), leaving two uncoordinated phenolic groups on the macrocycle.

Figure 2. Left: molecular structure of \([\text{Ti}_4(\mu_3-O)_2(H_2O)(L_1)_2]\cdot\text{MeCN}\) (2-MeCN); Right: core of the structure. Solvent molecules and hydrogen atoms omitted for clarity.

Figure 3. Left: molecular structure of \([\text{Ti}_4F_{14}L_2H_2(H)_2]\cdot2.5\text{MeCN}\) (3·2.5MeCN); Right: core of the structure. Solvent molecules and hydrogen atoms omitted for clarity.

Treatment of \(L^2H_2\) with two equivalents of \([\text{TiCl}_4(\text{THF})_2]\) in refluxing toluene afforded, after work-up (MeCN), dark red prisms of \([\text{Ti}_2\text{Cl}_4(H_2O)_2\text{OL}_2H_2(H)_2]\cdot5\text{MeCN}\) (4·5MeCN) in 41% yield. The molecular structure is shown in Figure 4, with selected bond lengths and angles given in the ESI. The complex contains two distorted octahedral titanium centres linked via a near linear oxo bridge \([\text{Ti}(1)-O(7)-\text{Ti}(2)\ 168.84(6)]\). The coordination at each Ti centre is completed by two adjacent phenoxides of the calixarene, a water molecule and two chlorides, one of which is found trans to the oxo bridge. The titanium phenoxide bond lengths are typical \([1.8324(11) - 1.8975(11) \text{Å}]\), whilst those to the water ligands are, as expected, somewhat longer \([2.1445(12)\text{ and } 2.1570(11) \text{Å}]\). Similar treatment of \(L^2H_2\) with two equivalents of \([\text{TiBr}_4]\) resulted in the isostructural complex \([\text{Ti}_2\text{Br}_4(H_2O)_2\text{OL}_2H_2(H)_2]\cdot2\text{MeCN}\) (5·4.5MeCN) in 32% yield. The molecular structure is shown in Figure 5, with selected bond lengths and angles given in the ESI. As in 4, a linear oxo bridge \([\text{Ti}(2)-O(7)-\text{Ti}(1)\ 172.65(17)]\) links the two distorted octahedral centres, and a bromide at each Ti centre can be found trans to the \(\mu_2-O\). The Ti-O bond length range is similar to that in 4.
When \( \text{L}^2 \text{H}_6 \) was treated with four equivalents of [TiF_4], orange prisms were isolated on work-up, albeit in poor yield (< 20%). A crystal structure determination revealed the complex to be [TiF_2(\mu-F)_3L_2(H)(\text{SiF}_5)]·2MeCN (7·2MeCN), see Figure 7. In 7·2MeCN, triply bridging fluorides link two distorted octahedral Ti centers, with a terminal fluoride and two adjacent phenoxides of the macrocycle completing the coordination sphere at each metal centre. The \( \text{SiF}_5^- \) ion is thought to result from the scavenging of HF formed during the reaction. As noted previously, the scavenging of HF can occur via the reaction 5HF + \( \text{SiO}_2 \rightarrow 2\text{H}_2\text{O} + \text{H}^+ + \text{SiF}_5^- \). [9]

**Reaction of \( \text{L}^2 \text{H}_6 \) with excess [TiBr_4]** led to the isolation of the orange complex [Ti_4Br_12L_2(H)_2(MeCN)_6]·7MeCN (6·7MeCN) in 26% isolated yield. A view of the molecular structure is shown in figure 6, with selected bond lengths and angles given in the ESI. The asymmetric unit of 6·7MeCN contains two independent half molecules each comprising one half a \( p \)-methyldimethyldiazacalix[6]arene and two Ti ions (Ti1 and Ti2 in first half molecule; Ti3 and Ti4 in second half molecule). The complete molecule in each case is generated by the inversion centre. The two half molecules are similar but are not related by symmetry. In each, the two octahedral Ti ions have different environments. One (Ti1 or Ti3) is coordinated by four bromide ions in a square plane, with O from the calix and NCH_3 in trans arrangement. The calixarene is twisted so that the phenoxide points away from the centre of the molecule and places Ti1 and Ti1_i on opposite sides of the plane of the calixarene (symmop \( i = 1-x, -y, -z \)). A very similar arrangement is observed for Ti3 and Ti3_ii (symm. op. \( ii = 2-x, 1-y, 1-z \)). The second Ti ion (Ti2 & Ti4) is coordinated in an 8-membered chelate ring, by two geminal phenoxides from the calixarene, two cis NCH_3 in approximately the same plane, and two trans bromide ions. The twisted orientation of the calixarene allows for the formation of an N–H···Br hydrogen bond from the protonated aza linkage.

**Ring opening polymerization studies**

**General:** The performance of these complexes to act as precatalysts for the ring opening polymerization (ROP) of \( \varepsilon \)-caprolactone (\( \varepsilon \)-CL), \( \delta \)-valerolactone (\( \delta \)-VL) and rac-lactide (r-LA) with one equivalent of benzyl alcohol (BnOH) per titanium...
present, has been investigated. The co-polymerization of ε-caprolactone and rac-lactide (Table 4) has also been investigated.

ε-caprolactone (ε-CL)

Complexes 1-7 were screened for their ability to polymerise ε-caprolactone and the results are collated in Table 1. The polymerization screening indicated that the best conditions were 250 equivalents of ε-caprolactone to titanium at 130 °C. In separate experiments, we re-recorded the 1H NMR spectra of 1 – 7 after prolonged heating at 130 °C to confirm their stability during the ROP conditions. The activity of complex 1 increased with temperature and peaked at 250 equivalents of monomer. Complex 1 was also active at low catalyst loading leading to 80.4% conversion after 8 h for 1000 equivalents of monomer. All polymers obtained were of relatively low polydispersity (PDI < 1.75), which suggested that these polymerizations occurred without significant side reactions. The $M_n$ were found to be much lower than the calculated values. Interestingly, complex 1 proved to be active also under aerobic conditions achieving 84% conversion during 8 h (Table 1, run 7), which may suggest that the dioxcalix[6]arene based complexes 1 and 2 can tolerate air/water during the ROP catalyst.

The screening of complexes 1-7 (Table 1) revealed that the titanium-based L3 complexes namely 1 and 2 herein, exhibited higher activities than other complexes under the conditions employed. After 24 h (Table 1), complexes 3, 4 and 7 afforded relatively lower conversions (<90%), whereas higher conversions (>90%) were reached using complexes 1, 2, 5 and 6, under similar conditions. From a kinetic study (Figure 8), it was observed that the PCL polymerization rate followed the order: 2>1>5=6>4>3>7. Compared with the larger titaniumcalix[6]arene complexes (complexes 1-6), complex 7 was found to be relatively inactive (Table 1, run 12 and 22), presumably due to its low solubility in toluene. The observed activity of complex 2 surpassed that of the other complexes screened herein, and this may be attributed to the arrangement of and distance between the Ti centers.$^{[5b]}$ The higher activity of the chloro- (4) and bromo- (5, 6) azacalixarene titanium complexes compared with that of fluoro- (3) compound can be explained considering the lability of the ligands present. This is in line with our recent study on titanocalix[4]arenes, in which the presence of a labile ligand (i.e. MeCN and H2O) proved beneficial for the catalyst activity.$^{[5]}$ 1H NMR spectra of the PCL indicated the presence of an BnO end group (e.g. Figure S4, ESI), which agrees with the MALDI-ToF mass spectra (e.g. Figure S1, ESI) and indicates that the polymerization proceeded via a coordination insertion mechanism. Indeed, the MALDI-ToF spectrum of the sample displayed a major series of peaks separated by 114 m/z units accountable to two OH terminated PCL n-mers (M = 17 (OH)+ $\delta$H + $n \times 114.14$ (CL) + 22.99 (Na$^+$)) and there is a part of peaks consistent with the polymer terminated by OH and BnO end group (M = $n \times 114.12$ (CL) + 108.05 (BnOH) + 22.99 (Na$^+$)) and cyclic PCL (M = $n \times 114.12$ (CL) +22.99 (Na$^+$))

δ-valerolactone (δ-VL)

Furthermore, complexes 1-7 were also evaluated as pre-catalysts in the presence of one equivalent of BnOH for the ROP of δ-VL (Table 2). Using compound 1, the conditions of temperature and [Ti]: [δ-VL] were varied. On increasing the temperature to 130 °C and lowering the monomer to pre-catalyst ratio, best results were achieved at 130 °C using [Ti]:[δ-VL] at 1:250 over 8 h. As in the case of the ROP of ε-CL, kinetic studies (Figure 9) revealed that the catalytic activities followed the order: 2>1>5=6>4>3>7. As for the ROP of ε-CL, nearly all observed $M_n$ values were significantly lower than the calculated values. The MALDI-ToF mass spectra (Figure S2, ESI) exhibited a major family of peaks consistent with BnO end groups (M = 108.05 (BnOH) + $n \times 100.12$ (VL) + 22.99 (Na$^+$)), and a minor family assigned to cyclic PVL. 1H NMR spectra of the PVL also indicated the presence of an BnO end group (e.g. Figure S5, ESI).

Table 1. ROP of ε-CL using 1 – 7.

| Run | Cat. | CL: Ti: BnOH | T/°C | t/h | Conv (%) | $M_n$GPC×10$^{3b}$ | $M_w$×10$^{3b}$ | $M_n$Cal×10$^{3c}$ | PDI$^d$ | TON$^f$ |
|-----|------|----------------|------|-----|-----------|-----------------|-----------------|-----------------|--------|--------|
| 1   | 1    | 500: 1:1       | 130  | 8   | 84.9      | 8.44            | 13.41           | 48.66           | 15.9   | 425    |
| 3   | 1    | 250: 1:1       | 130  | 8   | 92.3      | 10.58           | 18.43           | 26.55           | 1.74   | 231    |
| 4   | 1    | 100: 1:1       | 130  | 8   | 93.4      | 5.04            | 6.54            | 10.87           | 1.30   | 93     |
| 5   | 1    | 250: 1:1       | 100  | 8   | 74.2      | 4.87            | 5.49            | 21.38           | 1.13   | 186    |
| 6   | 1    | 250: 1:1       | 80   | 8   | 28.3      | 2.95            | 3.43            | 8.28            | 1.16   | 71     |
| 7   | 1+   | 250: 1:1       | 130  | 8   | 85.4      | 9.43            | 12.03           | 24.58           | 1.27   | 214    |
| 8   | 2    | 250: 1:1       | 130  | 8   | 93.5      | 12.54           | 15.20           | 26.89           | 1.21   | 234    |
| 9   | 3    | 250: 1:1       | 130  | 8   | 62.3      | 4.37            | 6.43            | 17.99           | 1.47   | 156    |
| 10  | 4    | 250: 1:1       | 130  | 8   | 67.5      | 6.19            | 9.97            | 19.47           | 1.50   | 169    |
| 11  | 5    | 250: 1:1       | 130  | 8   | 77.1      | 8.21            | 12.32           | 22.21           | 1.61   | 193    |
| 12  | 6    | 250: 1:1       | 130  | 8   | 84.2      | 8.84            | 13.09           | 24.10           | 1.48   | 211    |
| 13  | 7    | 250: 1:1       | 130  | 24  | >99       | 11.43           | 16.32           | 28.46           | 1.42   | 248    |
Table 2. ROP of \( \delta \)-VL using using \( 1 \)-7.

| Run | Cat. | VL: Ti: BnOH | T/°C | t/h | Conv\(^a\) (%) | \( M_n,\text{GPC}\times10^{3}\) | \( M_p\times10^{3}\) | \( M_n,\text{Cal}\times10^{3}\) | PDI\(^b\) | TON\(^c\) |
|-----|------|-------------|------|-----|----------------|----------------|----------------|----------------|-------|--------|
| 1   | 1    | 250: 1: 1   | 130  | 24  | >99           | 13.34          | 23.14          | 8.40            | 1.32  | 206    |
| 16  | 3    | 250: 1: 1   | 130  | 24  | 76.4          | 6.78           | 7.93           | 22.01          | 1.17  | 199    |
| 17  | 4    | 250: 1: 1   | 130  | 24  | 82.5          | 8.40           | 11.11          | 23.75          | 1.32  | 206    |
| 18  | 5    | 250: 1: 1   | 130  | 24  | 96.4          | 8.28           | 11.64          | 27.72          | 1.41  | 241    |
| 19  | 6    | 250: 1: 1   | 130  | 24  | >99           | 10.04          | 15.82          | 28.46          | 1.58  | 248    |
| 20  | 7    | 250: 1: 1   | 130  | 24  | 34.6          | 2.28           | 2.63           | 9.98           | 1.15  | 87     |
| 21  | 1    | 250: 1: 0   | 130  | 24  | 71.6          | 4.30           | 5.20           | 20.49          | 1.20  | 179    |
| 22  | 2    | 250: 1: 0   | 130  | 24  | 74.7          | 6.13           | 7.01           | 21.37          | 1.14  | 187    |
| 23  | 3    | 250: 1: 0   | 130  | 24  | 59.1          | 2.38           | 3.62           | 16.92          | 1.52  | 148    |
| 24  | 4    | 250: 1: 0   | 130  | 24  | 63.8          | 3.42           | 5.51           | 18.26          | 1.61  | 160    |
| 25  | 5    | 250: 1: 0   | 130  | 24  | 69.2          | 4.18           | 5.79           | 19.80          | 1.39  | 173    |
| 26  | 6    | 250: 1: 0   | 130  | 24  | 62.8          | 4.85           | 5.78           | 17.97          | 1.19  | 157    |
| 27  | 7    | 250: 1: 0   | 130  | 24  | -             | -              | -              | -              | -     | -      |

\(^a\) Determined by \(^1\)H NMR spectroscopy. \(^b\) \( M_n,\text{GPC}\) values corrected considering Mark–Houwink factor (0.56) from polystyrene standards in THF. \(^c\) Calculated from \([(\text{monomer})_0/Ti] \times \text{conv (%)} \times \text{monomer molecular weight (} M_n=114.14\text{) + Molecular weight of BnOH.}\) From GPC. \(^d\) Reaction performed in air. \(^e\) Turnover number (TON) = number of moles of \( \epsilon\)-CL consumed/ number of moles Ti.

Table 3. ROP of rac-lactide using complexes 1-7.

| Run | Cat. | LA: Ti: BnOH | T/°C | t/h | Conv\(^a\) (%) | \( M_n,\text{GPC}\times10^{3}\) | \( M_p\times10^{3}\) | \( P_I\times10^{3}\) | \( M_n,\text{Cal}\times10^{3}\) | PDI\(^e\) | TON\(^c\) |
|-----|------|-------------|------|-----|----------------|----------------|----------------|----------------|----------------|-------|--------|
| 1   | 1    | 250: 1: 1   | 130  | 24  | 75.4          | 5.98           | 10.27          | 0.52           | 27.16          | 1.72  | 189    |
| 2   | 2    | 250: 1: 1   | 130  | 24  | 78.1          | 7.32           | 8.23           | 0.40           | 28.14          | 1.12  | 195    |
| 3   | 3    | 250: 1: 1   | 130  | 24  | 36.9          | 5.86           | 8.75           | 0.58           | 13.29          | 1.49  | 92     |
| 4   | 4    | 250: 1: 1   | 130  | 24  | 54.3          | 5.10           | 7.57           | 0.39           | 19.56          | 1.43  | 136    |
| 5   | 5    | 250: 1: 1   | 130  | 24  | 59.1          | 4.98           | 7.02           | 0.46           | 21.29          | 1.41  | 148    |
| 6   | 6    | 250: 1: 1   | 130  | 24  | 62.6          | 4.38           | 5.39           | 0.41           | 22.66          | 1.05  | 157    |
| 7   | 7    | 250: 1: 1   | 130  | 24  | 25.6          | 3.46           | 4.86           | 0.42           | 9.33           | 1.18  | 64     |

\(^a\) Determined by \(^1\)H NMR spectroscopy on crude reaction mixture. \(^b\) \( M_n,\text{GPC}\) values corrected considering Mark–Houwink factor (0.58) from polystyrene standards in THF. \(^c\) From 2D \( J \)-resolved \(^1\)H NMR spectroscopy. \(^d\) Calculated from \([(\text{monomer})_0/Ti] \times \text{conv (%)} \times \text{Monomer molecular weight (} M_n=144.13\text{) + Molecular weight of BnOH.}\) From GPC. \(^e\) Turnover number (TON) = number of moles of rac-LA consumed/ number of moles Ti.
Table 4. ROP of co-polymer (r-LA + ε-CL) using 1-7.

| Run*  | Cat. | LA: CL: Ti: BnOH | t/h | T/°C | Conva (%) | M_n,GPC×10^{3,cd} | M_w×10^{3,cd} | PDI  |
|-------|------|------------------|-----|------|-----------|-------------------|----------------|------|
| 1     | 1    | 250: 250: 1: 1   | 130 | 24   | 80.2      | 14.16            | 26.71          | 1.88 |
| 2     | 2    | 250: 250: 1: 1   | 130 | 24   | 85.1      | 16.44            | 32.07          | 1.95 |
| 3     | 3    | 250: 250: 1: 1   | 130 | 24   | 72.4      | 9.48             | 14.23          | 1.50 |
| 4     | 4    | 250: 250: 1: 1   | 130 | 24   | 75.9      | 10.63            | 17.37          | 1.63 |
| 5     | 5    | 250: 250: 1: 1   | 130 | 24   | 82.7      | 14.42            | 21.98          | 1.52 |
| 6     | 6    | 250: 250: 1: 1   | 130 | 24   | 80.1      | 15.01            | 22.88          | 1.52 |
| 7     | 7    | 250: 250: 1: 1   | 130 | 24   | 33.8      | 2.35             | 2.75           | 1.16 |

*RDP of r-LA

Selected complexes were also employed as pre-catalysts in the ROP of r-LA (Table 3). Best conversion was achieved in the presence of 2 (78.1%, run 2). The M_n of the polymer was lower than the calculated value albeit with narrow molecular weight distribution (7320 and 1.12, respectively). In the case of systems 1-7, all polymers obtained were of low polydispersity (PDI < 1.75), which suggested that there was reasonable control for polymerization. However, 7 only allowed for 25.6% monomer conversion affording low molecular weight species.

1H NMR spectra of the PLA indicated the presence of an BnO end group (e.g. Figure S6, ESI), which agrees with the MALDI-ToF mass spectra in positive-linear mode, the sample was analysed with a Mark–Houwink factor M_n/w, GPC = [(M_n/w measured × 0.56 × (1-%CL) + M_w/w measured × 0.58 × (1-%LA)].

Co-polymerization of r-LA and ε-CL

The co-polymerization of r-LA and ε-CL was next investigated (Table 4). The complexes exhibited moderate conversions, with complex 2 performing best (85.1%), and with 1 and 3-6 also producing conversions > 70%. In general, the systems appeared to be relatively well behaved with PDIs in the range 1.16-1.95; 1H NMR spectra were consistent with the presence of BnO and OH end groups (Figure S7, ESI). The composition of the copolymer was further investigated by 13C NMR spectroscopy. In fact, diagnostic resonances belonging to CL–CL–CL, LA–CL–CL, CL–CL–LA, LA–LA–CL, LA–LA–LA, and LA–LA–LA dyads can be observed in the region between δ 173.6 and 169.6 ppm (Figure S9, ESI). Based on the current results, the number-average sequence length was found to be 1.18 and 5.10 for CL and LA, respectively (Figure S9, Equations 1-2, ESI). Furthermore, no peaks corresponding to the CL-LA-CL triad at 171.1 ppm was observed. Such signals arise from the transesterification of the cleavage of the lactyl-lactyl bond in the lactidyl unit.
Kinetics

From a kinetic study of the ROP of ε-CL using 1-7, it was observed that the polymerization rate exhibited first-order dependence on the ε-CL concentration (Figure 8(a)), and the conversion of monomer achieved over 420 min was >25%. The activity trend in this case revealed that 2 was the most active and then 1>5≈6>4>3>7. An induction period of 2 hours observed for complexes 1-6 could be ascribed to the longer time required for the formation of the catalytically active species. A similar result was also observed in the polymerization of δ-VL (Figure 9).

The dependence of the \( M_n \) and molecular weight distribution on the monomer conversion in the reactions catalyzed by 1, 3, 5 with BnOH was also investigated (Figure 10). For the ROP of ε-CL, the polymer \( M_n \) was shown to increase linearly with the conversion, which suggested that the polymerization was well controlled (Figure 10, left). A similar outcome was also observed in the reaction involving δ-VL (Figure 10, right).

**ROP of ω-pentadecalactone**

To enhance the thermal properties of the polymers obtained herein, we also investigated the ROP of the ω-pentadecalactone. Unfortunately, none of the systems herein proved to be effective as catalysts for the ROP of ω-pentadecalactone either in solution at high temperatures (130 °C) or as melts.

**Conclusions**

In this work, we report rare examples of metal (here titanium) complexes of larger dioxacalix[6]arenes and extend the work to include even rarer examples of titanium complexes bearing azacalixarenes. The molecular structures reveal how these macrocycles can support multiple metal centres which adopt some interesting structural motifs. The complexes are active for the ring opening polymerization of ε-caprolactone (ε-CL), δ-valerolactone (δ-VL) and rac-lactide (r-LA) but not ω-pentadecalactone. In all cases, the oxo complex [Ti(OH)(L)3]·MeCN (2·MeCN) proved to be the most active with first order kinetics.

**Experimental**

**General**

All reactions were conducted under an inert atmosphere using standard Schlenk techniques. Toluene was dried from sodium, acetonitrile was distilled from calcium hydride, diethyl ether was \( \text{MeCN} \) proofed to be effective as catalysts for the ROP of ω-pentadecalactone either in solution at high temperatures (130 °C) or as melts.
distilled from sodium benzenophene, and all solvents were degassed prior to use. The dioxa[6]arene and azaxalixaresene were prepared according to the literature methods.\textsuperscript{13} All other chemicals were purchased from commercial sources. IR spectra (nujol mulls, KBr windows) were recorded on a Nicolet Avatar 360 FT IR spectrometer; \textsuperscript{1}H NMR spectra were recorded at room temperature on a Varian VXR 400 S spectrometer at 400 MHz or a Gemini 300 NMR spectrometer or a Bruker Advance DPX-300 spectrometer at 300 MHz. The \textsuperscript{1}H NMR spectra were calibrated against the residual protio impurity of the deuterated solvent. Elemental analyses were performed by the elemental analysis service at the University of Hull. Matrix Assisted Laser Desorption/Ionization Time of Flight (MALDI-TOF) mass spectrometry was performed in a Bruker autoflex III smart beam in linear mode, and the spectra were acquired by averaging at least 100 laser shots. 2,5-Dihydroxybenzoic acid was used as the matrix and THF as solvent. Sodium chloride was dissolved in methanol and used as the ionizing agent. Samples were prepared by mixing 20 \textmu L of matrix solution in THF (2 mg·mL\textsuperscript{-1}) with 20 \textmu L of matrix solution (10 mg·mL\textsuperscript{-1}) and 1 \textmu L of a solution of ionizing agent (1 mg·mL\textsuperscript{-1}). Then 1 mL of these mixtures was deposited on a target plate and allowed to dry in air at ambient temperature.

**Synthesis of [Ti\textsubscript{3}(OIPr)\textsubscript{6}](MeCN)\textsubscript{3}**. 3.5MeCN (1.35MeCN).

To \text{[Ti(OIPr)\textsubscript{4}]} (0.43 g, 1.50 mmol) and \text{L\textsubscript{3}H\textsubscript{4}} (0.50 g, 0.49 mmol) was added toluene (30 mL) and then the system was refluxed for 12 h. On cooling, the volatiles were removed in vacuo, and the residue was dissolved in MeCN (30 mL). On prolonging standing at 0 °C, an orange crystalline material formed (Figure S10, ESI), yield 0.32 g, 52%. Anal. Cald for \text{C\textsubscript{52}H\textsubscript{44}N\textsubscript{14}O\textsubscript{15}Ti\textsubscript{3}} sample dried in vacuo for 12 h, - 3.5MeCN: C, 71.60; H, 7.06; found C, 71.92; H, 7.28%. IR (nujol mull, KBr): 3213w, 2923s, 2853s, 2349w, 1641w, 1461w, 1433w, 1377m, 1303w, 1260s, 1212w, 1092s, 1019s, 863w, 799s. \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \delta: 6.86-7.32 (m, 12H, HarylH), 5.44 (m, 2H, -OCH\textsubscript{2}CH\textsubscript{2}Ti), 5.04-5.21 (m, 4H, -OCH\textsubscript{2}Ti), 4.87 (d, J = 4.8 Hz, 4H, -OCH\textsubscript{2}Ti), 4.48 (m, 4H, -CH\textsubscript{2}H), 3.40 (d, J = 12.4 Hz, 4H, -CH\textsubscript{2}H), 2.03 (s, 3H, MeCN), 1.56 (m, 12H, -OCH\textsubscript{2}CH\textsubscript{2}Ti), 2.03 (s, 3H, HarylH), 1.21-1.34 (m, 54H, -C(CH\textsubscript{3})\textsubscript{3}). Mass Spec (EI): 1267.6 [M+Na\textsuperscript{+}-3.5MeCN].

**Synthesis of [Ti(μ-O\textsubscript{2})(H\textsubscript{2}O)(L\textsubscript{2})\textsubscript{2}]MeCN (2-MeCN).**

As for 1, but using [Ti(OIPr)\textsubscript{4}] (0.29 g, 1.00 mmol) and \text{L\textsubscript{3}H\textsubscript{4}} (0.50 g, 0.49 mmol) affording 2 as orange prisms. Single orange prisms were grown from a saturated MeCN (30 mL) solution at 0 °C (yield 0.25 g, 44%). Anal. Cald for \text{C\textsubscript{10}H\textsubscript{14}O\textsubscript{2}Ti\textsubscript{2}} sample dried in vacuo for 12 h - MeCN: C, 71.54; H, 7.29; found C, 71.91; H, 7.38 %; IR (nujol mull, KBr): 2292 w, 2283 w, 1693 w, 1645 m, 1567 w, 1546 s, 1377s, 1308w, 1295w, 1094m, 1019m, 927w, 856m, 800s. \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \delta: 6.80-7.38 (m, 12H, HarylH), 3.97 (m, 8H, -CH\textsubscript{2}H), 3.52 (m, 8H, -CH\textsubscript{2}H), 2.83 (s, 6H, -NCH\textsubscript{2}), 2.22 (m, 18H, -CH\textsubscript{2}H, 1.95 (s, 12H, MeCN).
2.34(s, 6H, -C$_6$H$_4$-), 3.72 (m, 4H -C$_6$H$_4$-), 3.46 (m, 8H, -NC$_6$H$_4$-), 2.34(s, 6H, -CH$_3$) 1.99 (s, 12H, -NCH$_2$). $^1$H NMR (CDCl$_3$) δ: 6.98-7.50 (m, 8H, aryl) 7.70 (d, J = 8.0 Hz, 2H), -107.27 (bs, 5F), -82.16 (bs, 3F), -72.06 (bs, 2F). Mass Spec (EI): 879 [M-2MeCN]$_{-}$.

### Procedure for ROP of ε-caprolactone, δ-valerolactone and rac-lactide

A toluene solution of pre-catalyst (0.010 mmol, 1.0 mL toluene) was added into a Schlenk tube in the glove-box at room temperature. The solution was stirred for 2 min, and then the appropriate equivalent of BnOH (from a pre-prepared stock solution of 1 mmol BnOH in 100 mL toluene) and the appropriate amount of ε-CL, δ-VL or r-LA along with 1.5 mL toluene was added to the solution. The reaction mixture was then placed into an oil/sand bath pre-heated at 130 °C, and the solution was stirred for the prescribed time (8 or 24 h). The polymerization mixture was quenched on addition of an excess of glacial acetic acid (0.2 mL) into the solution, and the resultant solution was then poured into methanol (200 mL). The resultant polymer was then collected on filter paper and was dried in vacuo.

### Kinetic studies

The polymerizations were carried out at 130 °C in toluene (2 mL) using 0.010 mmol of complex. The molar ratio of monomer to initiator to co-catalyst was fixed at 250:1:1, and at appropriate time intervals, 0.5 μL aliquots were removed under N$_2$ and were quenched with wet CDCl$_3$. The percent conversion of monomer to polymer was determined using $^1$H NMR spectroscopy.

### Crystallography

#### Table 5. Crystal structure data for 1:3.5MeCN, 2:MeCN, 3:2.5MeCN, 4:5MeCN, 5:4.5MeCN, 6:7MeCN, 7:2MeCN.

| Compound | 1:3.5MeCN | 2:MeCN | 3:2.5MeCN | 4:5MeCN |
|----------|-----------|--------|-----------|---------|
| Formula  | $\text{C}_{43}\text{H}_{109.5}\text{N}_4\text{O}_{10.5}\text{Ti}_2$ | $\text{C}_{137}\text{H}_{16}\text{NO}_{18}\text{Ti}_{14}$ | $\text{C}_{57}\text{H}_{63.1}\text{F}_1\text{N}_4\text{O}_6\text{Ti}_{14}$ | $\text{C}_{62}\text{H}_{75}\text{Cl}_4\text{N}_6\text{O}_3\text{Ti}_2$ |
| Formula weight | 1426.04 | 2307.30 | 1365.14 | 1299.86 |
| Crystal system | Monoclinic | Monoclinic | Monoclinic | Triclinic |
| Space group | P 21/c | C 2/c | P 21/c | P-1 |
| Unit cell dimensions | | | | |
| a (Å) | 12.0347(2) | 28.1243(7) | 16.1213(2) | 12.6749(8) |
| b (Å) | 28.3198(4) | 17.7721(4) | 22.8130(2) | 14.5410(8) |
| c (Å) | 24.5367(3) | 31.2326(9) | 17.0185(3) | 18.7696(10) |
| α (°) | 90 | 90 | 90 | 111.979 |
| δ (°) | 103.2670(10) | 113.009(3) | 102.381(10) | 95.829 |
| γ (°) | 90 | 90 | 90 | 96.158 |
| V (Å$^3$) | 8140.4(2) | 14369.0(7) | 6113.42(12) | 3151.55(3) |
| Z | 4 | 4 | 4 | 2 |
| Temperature (K) | 100(2) | 100(2) | 100(2) | 100(2) |
| Wavelength (Å) | 1.54184 | 1.54178 | 1.54178 | 1.54178 |
| Calculated density | 1.147 | 1.061 | 1.416 | 1.240 |
| Absorption coefficient | 2.112 | 2.275 | 5.091 | 4.142 |
| Transmission factors | 0.69725 and 1.0000 | 0.52429 and 1.0000 | 0.6143 and 1.0000 | 0.679 and 1.0000 |
| Crystal size (mm$^3$) | 0.200 × 0.120 × 0.040 | 0.160 × 0.030 × 0.010 | 0.150 × 0.080 × 0.050 | 0.090×0.060×0.020 |
| $\vartheta$(max) (°) | 66.6 | 66.5 | 70.4 | 68.2 |
| Reflections measured | 75678 | 46513 | 55482 | 134309 |
| Unique reflections | 14383 | 12487 | 11396 | 11490 |

X-ray Crystallography

In all cases, crystals suitable for an X-ray diffraction study were grown from a saturated MeCN solution at either ambient temperature or 0 °C. Single crystal X-ray diffraction data (except 5) were collected at the UK National Crystallography service using Rigaku Oxford Diffraction ultra-high intensity instruments employing modern areas detectors. X-ray diffraction data for 5-4.5MeCN were collected using a stoe ips2 image plate diffractometer operating with molybdenum radiation. In all cases standard procedures were employed for integration and processing of data. Crystal structures were solved using dual space methods implemented within SHELXT. Completion of structures was achieved by performing least squares refinement against all unique $F^2$ values using SHELXL-2018.[15] All non-H atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed using a riding model. Where the location of hydrogen atoms was obvious from difference Fourier maps, C-H and O-H bond lengths were refined subject to chemically sensible restraints. Minor disorder was treated using standard methods. SQUEEZE[16] was used to model the disordered solvent in structures 1, 3, 4, 5 and 6.
Electronic supplementary information (ESI) available. CCDC 2057320–2057326 (1·3.5MeCN, 2·MeCN, 3·2.5MeCN, 4·5MeCN, 5·4.5, 6·7MeCN, 7·2MeCN) contain the supplementary crystallographic data. For ESI and crystallographic data in CIF or other electronic format see DOI:

Conflicts of interest
There are no conflicts to declare.

Acknowledgements

We thank the China Scholarship Council (CSC) for a PhD Scholarship to TX. The EPSRC Mass Spectrometry Service (Swansea, UK) and the EPSRC National X-ray Crystallography Service (Southampton) are thanked for data collection. CR also thanks the EPSRC (grant EP/S025537/1) for financial support.

References

[1] (a) D. H. Homden and C. Redshaw, Chem. Rev., 2008, 108, 5086-5130; (b) Coordination Chemistry and Applications of Phenolic Calixarene–metal Complexes. Y. Li, K.-Q. Zhao, C. Redshaw, B. A.
