Poly(methyl methacrylate)s with pendant calixpyrroles: polymeric extractants for halide anion salts†

Abdullah Aydogan,[ab] Daniel J. Coady,[b] Vincent M. Lynch,[b] Ahmet Akar,*[a] Manuel Marquez,[c] Christopher W. Bielawski*[b] and Jonathan L. Sessler*[b]

Received (in Berkeley, CA, USA) 21st November 2007, Accepted 21st December 2007
First published as an Advance Article on the web 25th January 2008
DOI: 10.1039/b718021g

Poly(methyl methacrylate)s containing pendant octamethylcalix[4]pyrrole subunits were prepared and demonstrated to be capable of extracting tetrabutylammonium chloride and fluoride salts from aqueous media.

Octamethylcalix[4]pyrrole (**1**) is a commercially-available anion receptor‡ that recognizes certain anions (*e.g.*, fluoride, chloride, and dihydrogen phosphate) well in organic media (K_a = $>10^4$, 350, and 100 M^{-1}, for the tetrabutylammonium, TBA^+, salts of F^-, Cl^-, $H_2PO_4^-$, respectively, in CD_2Cl_2).[1] The nature of the binding interactions involved, primarily hydrogen bonds, would lead to the expectation, generally supported by experiment, that in highly competitive media this and other neutral pyrrole-derived receptors[2] would display anion affinities that are substantially reduced. However, recent studies wherein pyrrolic systems are either embedded in various types of functional materials, *e.g.*, ion selective electrodes[3] and colorimetric sensors,[4] or covalently attached to solid supports to produce anion-selective HPLC packings,[5] have served to show that ostensibly weak anion binding agents, including calix[4]pyrrole and its derivatives, can be highly effective anion receptors under mixed organic-aqueous interfacial conditions. This has led us to consider that soluble polymeric materials containing calix[4]pyrrole subunits linked directly to the macromolecular backbone (as opposed to covalently attached to a preformed polymer support) should be capable of binding anions. Such materials may find utility in addressing a variety of current challenges, including corrosion prevention (*e.g.*, chloride, carbonate, and sulfate control under conditions of combustion[6]), waste remediation (*e.g.*, sulfate extraction from tank waste[7]), toxin control (*e.g.*, mitigating the effects of overexposure to cyanide[8] or fluoride[9]), and health care (*i.e.*, enhanced phosphate removal under conditions of hemodialysis[10]), to name but a few.

Herein, we report the synthesis and characterization of calixpyrrole **3**, as well as its homopolymer and copolymers with methyl methacrylate (MMA, **4**). In addition, we demonstrate that organic solutions of the calixpyrrole-functionalized copolymer are capable of extracting tetrabutylammonium chloride (TBACl) and tetrabutylammonium fluoride (TBAF) from aqueous solutions significantly more effectively than calixpyrrole **1** and poly(methyl methacrylate) (PMMA). To the best of our knowledge, this is the first example of an anion receptor appended to a PMMA backbone and the first report wherein an anion receptor-based polymeric system of any type has been used to effect anion extraction under interfacial aqueous-organic conditions (Fig. 1).[11]

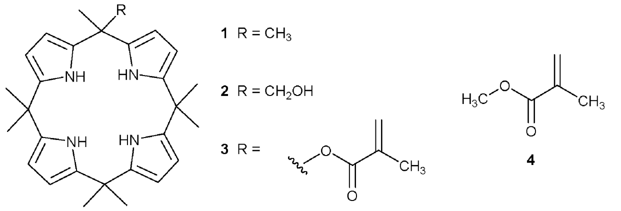

Fig. 1 Structures of octamethylcalix[4]pyrrole (**1**), its functionalized derivatives used in this study (**2** and **3**), and methyl methacrylate (**4**).

The functionalized calix[4]pyrrole monomer **3** was prepared in 82% yield from the hydroxylmethyl calixpyrrole derivative **2**§ through treatment with methacryloyl chloride under basic conditions.¶ Monomer **3** contains a methacrylate functionality and proved amenable to polymerization using conventional free radical methods.[12] In initial studies, we prepared homopolymer **5** by dissolving monomer **3** in THF (0.3 M) followed by treatment with 1 mol% of azoisobutyronitrile (AIBN). After stirring at 70 °C for 17 h under an atmosphere of nitrogen, the resulting viscous solution was added dropwise into excess methanol with rapid stirring. This caused precipitation of polymer **5**, which was later isolated *via* filtration in 66% yield. Using gel permeation chromatography (GPC), the polymer was found to have a number-average molecular weight (M_n) of 23 600 Da (relative to PMMA standards) and a polydispersity index (PDI) of 2.3.‖

To tune the physical properties of the calix[4]pyrrole functionalized PMMAs (including their potential ability to serve as anion extractants), a copolymer of methacrylate functionalized calixpyrrole **3** and MMA (**4**) was prepared. Using the conventional free radical polymerization protocol described above, a 77% yield of copolymer **6** was obtained from a 1 : 10 mixture of **3** and MMA. Using GPC, copolymer **6** was found to possess a M_n of 85 500 Da and a PDI of 2.1.** The relatively high molecular weight, compared to **5**, led us to

---

[a] *Department of Chemistry, Faculty of Science and Letters, Istanbul Technical University, 34469 Maslak Istanbul, Turkey. E-mail: akara@itu.edu.tr*
[b] *Department of Chemistry and Biochemistry, The University of Texas at Austin, 1 University Station A5300, Austin TX 78712, USA. E-mail: bielawski@cm.utexas.edu, sessler@mail.utexas.edu*
[c] *Harrington Department of Bioengineering, Arizona State University, Tempe, Arizona 85287, USA*

† Electronic supplementary information (ESI) available: Synthetic procedures, NMR spectra, and thermograms. See DOI: 10.1039/b718021g

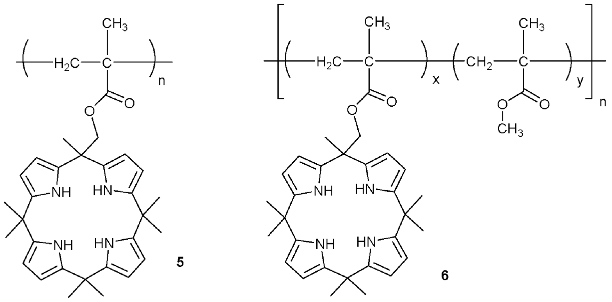

Fig. 2 Structures of homopolymer **5** and copolymer **6**.

conclude that the incipient and/or growing polymer chains may be negatively influenced by the large steric bulk of the calix[4]pyrrole in monomer **3**.†† Regardless, polymer **6** proved to be highly soluble in most common organic solvents, including dichloromethane. ^{1}H NMR spectroscopic analysis (CD_2Cl_2) revealed that there were *ca.* 14 methacrylate units per calixpyrrole unit within **6**. For comparison, a sample of PMMA (M_n = 40 700; PDI = 1.5) was prepared using a procedure analogous to that used to obtain **5** and **6**. Thermal analysis of **6** revealed a decomposition temperature (T_d) at 272 °C, which is intermediate between the respective T_ds found for **5** (270 °C) and the PMMA homopolymer (276 °C) used for comparison.‡‡ Collectively, these results provide support for the proposal that the physical properties of copolymers prepared from MMA and **3** may be tuned through judicious monomer selection (Fig. 2).

Once polymer **6** was fully characterized, efforts shifted toward exploring its ability to bind anions under interfacial conditions. As shown in Fig. 3, addition of a D_2O solution of tetrabutylammonium fluoride (TBAF, 90 mM) to a CD_2Cl_2 solution of polymer **6** (effective concentration of the calix[4]-pyrrole repeat unit = 6.5 mM) resulted in a substantial downfield shift in the pyrrole NH protons (as typically seen upon anion binding).[1] In addition, peaks ascribable to the methylene units in the TBA^+ counter cation (at δ = 3.2 ppm) were seen, lending support to the notion that both the anion (F^-) and the cation were present in the organic phase. In contrast, no shifts in the NH resonances and no TBA^+-ascribable peaks were observed when a 29 mM solution of octamethylcalix[4]pyrrole (**1**) in CD_2Cl_2 was exposed to aqueous solutions of TBAF. Likewise, no evidence of uptake of TBA^+ into the organic phase (absence of any discernible peak at δ = 3.2 ppm) was seen when analogous experiments were repeated with the MMA homopolymer.§§

The ability of polymer **6** to extract several other TBA^+ salts was also tested. While no extraction was seen in the case of aqueous solutions of tetrabutylammonium dihydrogen phosphate, upon addition of TBACl downfield shifts in the NH proton signals were seen to be greater than those observed with TBAF for analogous anion concentrations (see Fig. 4). Such findings, which are consistent with an enhanced ability to extract chloride relative to fluoride or dihydrogen phosphate, run counter to the relative anion affinities seen in dichloromethane.[1] However, they are in accord with what one would expect based on the so-called Hofmeister bias,[13] namely that a more hydrophobic anion, such as chloride (ΔG_h = −340 kJ mol^{-1}), is extracted more easily than a highly hydrophilic species, such as dihydrogen phosphate (ΔG_h = −465 kJ mol^{-1}), or fluoride (ΔG_h = −465 kJ mol^{-1}).[14] Consistent with this rationale is the finding that both the control MMA homopolymer and calixpyrrole **1** were able to extract TBACl under the aforementioned interfacial conditions, albeit with efficiencies of less than 35% relative to polymer **6** (as calculated from NMR integrations of the MMA methyl ester, β-pyrrolic, and TBA^+ signals, as appropriate). On the other hand, the fact that efficient extraction of TBAF was only seen in the case of polymer **6** (and not the PMMA control or free **1**) underscores the notion that the calixpyrrole receptor appended to the PMMA backbone is playing a critical role

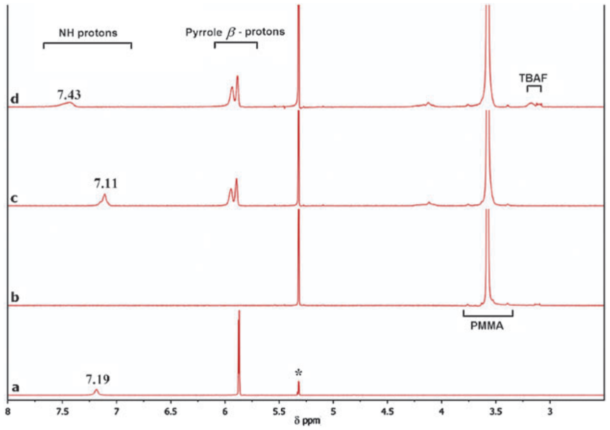

Fig. 3 ^{1}H NMR spectra of CD_2Cl_2 solutions of (a) octamethylcalix[4]pyrrole (**1**) (29 mM) and (b) PMMA (125 mM, based on the repeat unit) after (i) adding 0.5 mL of a D_2O solution of TBAF (90 mM), (ii) shaking the tube vigorously, and (iii) allowing the phases to separate, (c) polymer **6** (effective concentration of the calix[4]pyrrole repeat unit = 6.5 mM), (d) this latter solution of polymer **6** after being subjected to the same treatment applied in the case of (a) and (b). * = residual solvent.

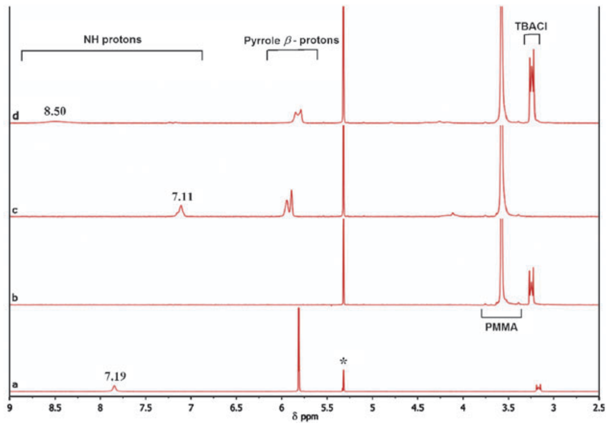

Fig. 4 ^{1}H NMR spectra of CD_2Cl_2 solutions of (a) a mixture of octamethylcalix[4]pyrrole (**1**) (29 mM) and (b) PMMA (125 mM based on the repeat unit) after (i) adding 0.5 mL of a D_2O solution of TBACl (108 mM), (ii) shaking the tube vigorously, and (iii) allowing the phases to separate, (c) polymer **6** (effective concentration of the calix[4]pyrrole repeat unit = 6.5 mM), and (d) this latter solution of polymer **6** after being subjected to the same treatment applied in the case of (a) and (b). * = residual solvent.

in overcoming the Hofmeister bias associated with this highly hydrophilic species.¶¶

Further support for the suggestion that copolymer **6** could bind fluoride and chloride anions came from thermal analyses. Specifically, after independently exposing TBAF or TBACl to **6** as described above, these samples as well as PMMA controls were subjected to thermogravimetric analysis.‡‡ For the sample of **6** exposed to TBAF, a 10% mass loss was observed upon heating to 230 °C, a temperature just below the T_d of the copolymer (262 °C). This compares well with the theoretical mass loss of 11.5% assuming the TBAF became completely volatilized over the aforementioned temperature range and was present in a 1 : 1 stoichiometry relative to each calix[4]pyrrole unit in the polymer chain. In contrast, the sample of **6** exposed to TBACl exhibited a 19% mass loss (theoretical: 12.1%) upon heating to 230 °C. Considering the relative extraction abilities of **6** towards TBACl and TBAF (see above), the observed mass loss was considered reasonable. For comparison, the PMMA controls lost $\leq$2% of their masses prior to polymer decomposition (277 °C), which leads us to conclude that only minimal amounts TBAF or TBACl were present in these samples after extraction.

In conclusion, we have prepared what we believe is the first *bona fide* polymeric systems containing a calixpyrrole anion receptor directly appended to a polymer backbone. One main advantage of these materials is that, at least in principle, other MMA derivatives (*e.g.*, hydroxyethyl methacrylate) could be used to control the solubility, water swellability, thermal- and chemical stability, of the resulting PMMA-type polymers. This versatility leads us to believe that polymers such as **6** could be readily optimized for use in a range of ion binding and extraction applications.

We are grateful to the National Science Foundation (CHE-0645563), the National Institutes of Health (GM 58907), and the INEST Group for support of this work.

Notes and references

‡ Available from Aldrich Chemical Co., catalogue no. 579270.

§ *Characterization data for* **2**: Note: calix[4]pyrrole **2** was prepared from its respective ethyl ester.[15] ^{1}H NMR (500 MHz, CD_2Cl_2) δ: 1.45–1.52 (m, 18H, *meso*-CH_3 protons), 1.87 (dd, 3H, CH_3), 4.34 (s, 2H, CH_2), 5.55 (m, 1H, CH), 5.84–5.92 (m, 8H, pyrrole CH), 5.97 (m, 1H, CH), 7.03 (br s, 2H, NH), 7.11 ppm (br s, 2H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.76, 28.33, 29.45, 41.19, 69.83, 102.65, 102.91, 103.06, 103.37, 134.36, 138.21, 138.46, 138.82 ppm; HRMS (CI) calcd for $C_{28}H_{37}N_4O$ [$M+H^+$]: 445.2967, found: 445.2966. Crystals suitable for X-ray analysis were obtained by vapor diffusion of hexanes into a saturated CH_2Cl_2 solution of **2**.† CCDC 668095. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b718021g

¶ *Characterization data for* **3**: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.48–1.54 (m, 18H, *meso*-CH_3), 1.90 (s, 3H, CH_3), 4.38 (s, 2H, CH_2), 5.55 (m, 1H, CH), 5.89–5.93 (m, 8H, pyrrole CH), 6.01 (m, 1H, CH), 7.07 (br s, 2H, NH), 7.16 ppm (br s, 2H, NH);^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.40, 28.92, 29.27, 33.34, 39.43, 70.59, 102.74, 102.88, 103.08, 104.18, 133.18, 138.31, 138.51, 138.86, 191.65 ppm; HRMS (CI) calcd for $C_{32}H_{41}N_4O_2$ [$M+H^+$]: 513.3230, found: 513.3232. Crystals suitable for X-ray analysis were obtained by slow diffusion of a saturated CH_2Cl_2 solution of **3**. CCDC 668096. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b718021g

‖ *Additional characterization data for* **5**: ^{1}H NMR (500 MHz, CD_2Cl_2) δ: 0.34–0.95 (br s, 2H, polymer backbone CH_2), 1.25–1.85 (br m, 24H, *meso*-CH_3 and polymer backbone CH_3), 4.15 (br s, 2H, *meso*-CH_2), 5.89 (br s, 8H, pyrrole CH), 7.12 ppm (br s, 4H, NH).

** *Additional characterization data for* **6**: ^{1}H NMR (500 MHz, CD_2Cl_2) δ: 0.82 (br s, 30H, polymer backbone CH_2), 0.99 (br s, 13.21H, polymer backbone CH_2), 1.52–1.55 (br m, 29.13H, calixpyrrole *meso*-CH_3), 1.80–1.88 (br m, 25.76H, MMA CH_3), 3.58 (br s, 43.57H, MMA CH_3), 4.11 (br s, 2H, calixpyrrole *meso*-CH_2), 5.89–5.95 (br m, 8H, pyrrole CH), 7.11 ppm (br s, 4H, NH).

†† Although the ratio of **3** : MMA observed (1 : 14) in copolymer **6** was slightly higher than the monomer feed ratio (1 : 10), ^{1}H NMR analysis of **6** leads us to suggest that the microstructure of this material is largely random and not a block copolymer of MMA and polymerized **3**. Specifically, two signals attributed to the methyl ester of MMA were found at δ = 3.3 and 3.4 ppm (C_6D_6) in relative integrals of 2 : 1.

‡‡ All thermal analyses were performed under an atmosphere of nitrogen at a scan rate = 10 °C min^{-1}.

§§ Preliminary experiments suggest that **5** exhibits anion recognition abilities comparable to those of **6** on a per calix[4]pyrrole basis.

¶¶ As expected for an extraction-based process where hydrophobicity effects are important, little evidence of extraction was seen when the hydrophobic TBA$^+$ cation was replaced by Na$^+$ in any of these studies. Efforts toward developing polymeric extractants for K$^+$ and Na$^+$ salts are underway.

1 (*a*) P. A. Gale, J. L. Sessler, V. Král and V. M. Lynch, *J. Am. Chem. Soc.*, 1996, **118**, 5140–5141; (*b*) J. L. Sessler, P. A. Gale and W. S. Cho, *Synthetic Anion Receptor Chemistry*, Royal Society of Chemistry, 2006, ch. 5.

2 (*a*) S. Camiolo and P. A. Gale, *Chem. Commun.*, 2000, 1129–1130; (*b*) F. P. Schmidtchen, *Org. Lett.*, 2002, **4**, 431–434.

3 (*a*) V. Král, J. L. Sessler, T. V. Shishkanova, P. A. Gale and R. Volf, *J. Am. Chem. Soc.*, 1999, **121**, 8771–8775; (*b*) T. V. Shishkanova, R. Volf, V. Král, J. L. Sessler, S. Camiolo and P. A. Gale, *Anal. Chem. Acta*, 2007, **587**, 247–253.

4 G. V. Zyryanov, M. A. Palacios and P. Anzenbacher, Jr, *Angew. Chem., Int. Ed.*, 2007, **46**, 7849–7852.

5 J. L. Sessler, P. A. Gale and J. W. Genge, *Chem.–Eur. J.*, 1998, **4**, 1095–1099.

6 K. Schofield, *Energy & Fuels*, 2003, **17**, 191–203.

7 (*a*) B. A. Moyer, L. H. Delmau, C. J. Fowler, A. Ruas, D. A. Bostick, J. L. Sessler, E. Katayev, G. D. Pantos, J. M. Llinares, M. A. Hossain, S. O. Kang and K. Bowman-James, *Advanced Inorganic Chemistry*, ed. R. Eldik and K. Bowman-James, Academic Press, 2006, vol. 59, pp 175–204; (*b*) L. R. Eller, M. Stępień, C. J. Fowler, J. T. Lee, J. L. Sessler and B. A. Moyer, *J. Am. Chem. Soc.*, 2007, **129**, 11020–11021; (*c*) Correction: L. R. Eller, M. Stępień, C. J. Fowler, J. T. Lee, J. L. Sessler and B. A. Moyer, *J. Am. Chem. Soc.*, 2007, **129**, 14523.

8 P. K. Bhattacharya, *Metal Ions in Biochemistry*, Alpha Science International Ltd, Harrow, UK, 2005.

9 K. L. Kirk, *Biochemistry of the Elemental Halogens and Inorganic Halides*, Plenum Press, New York, 1991.

10 (*a*) F. H. Albaaj and A. J. Hutchinson, *Drugs*, 2003, **63**, 557–596; (*b*) G. Block and F. K. Port, *Sem. Dialysis*, 2003, **16**, 140–147; (*c*) E. M. Spalding, P. W. Chamney and K. Farrington, *Kidney Int.*, 2002, 655; (*d*) P. Messa, M. Gropuzzo, M. L. Cleva, G. Boscutti, G. Mioni, G. A. Cruciatti, S. Mazzolini and M. R. Malisan, *Neph. Dial. Trans.*, 1998, **13**, 43–48.

11 Examples of polymeric anion receptor systems are limited, see: (*a*) D. Aldakov and P. Anzenbacher, Jr, *J. Am. Chem. Soc.*, 2004, **126**, 4752–4753; (*b*) C.-Y. Wu, M.-S. Chen, C.-A. Lin, S.-C. Lin and S.-S. Sun, *Chem.–Eur. J.*, 2006, **12**, 2263–2269; (*c*) A. Kaledkowski and A. W. Trochimczuk, *React. Polym.*, 2006, **66**, 740–746; (*d*) A. Kaledkowski and A. W. Trochimczuk, *React. Polym.*, 2006, **66**, 957–966; (*e*) H. A. Ho and M. Leclerc, *J. Am. Chem. Soc.*, 2003, **125**, 4412–4413; (*f*) M. Takeuchi, T. Shioya and T. M. Swager, *Angew. Chem., Int. Ed.*, 2001, **40**, 3372–3376; (*g*) W. Zhang, E. Rozniecka, E. Malinowska, P. Parzuchowski and M. E. Meyerhoff, *Anal. Chem.*, 2002, **74**, 4548–4557.

12 G. Odian, *Principles of Polymerization*, John Wiley and Sons Inc., 4th edn., 2004, ch. 3.

13 (*a*) R. Custelcean and B. A. Moyer, *Eur. J. Inorg. Chem.*, 2007, 1321–1340; (*b*) F. Hofmeister, *Arch. Exp. Pathol. Pharmakol.*, 1888, **24**, 247–260.

14 Hydration energies were taken from Table 1.1 of B. A. Moyer and P. V. Bonnensen, "Physical Factors in Anion Separations", in *Supramolecular Chemistry of Anions*, ed. A. Bianchi, K. Bowman-James and E. García-España, Wiley-VCH, New York, 1997, p. 6.

15 A. Aydogan, J. L. Sessler, A. Akar and V. Lynch, *Supramol. Chem.*, 2007, in press.