



Tetrahedron Letters 44 (2003) 33-36

TETRAHEDRON LETTERS

Synthesis of redox-active biscalix[4]quinones and their electrochemical properties

Kriengkamol Tantrakarn, Chalita Ratanatawanate, Tipsukhon Pinsuk, Orawon Chailapakul and Thawatchai Tuntulani*

Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand

Received 15 September 2002; revised 28 October 2002; accepted 8 November 2002

Abstract—Biscalix[4]arenes, 7 and 8, have been synthesized by a one-pot coupling method and a stepwise approach, respectively. A one-pot reaction in a pressurized vessel resulted in the symmetric biscalix[4]arene 7 in high yield. Oxidation of compounds 7 and 8 by Tl(CO₂CF₃)₃ in CF₃COOH yielded biscalix[4]quinones, 9 and 10, respectively. Preliminary electrochemical studies by cyclic voltammetry of 9 and 10 show significant changes of their voltammograms upon addition of Na⁺. © 2002 Elsevier Science Ltd. All rights reserved.

Sensing technology and sensors have advanced in the past decade.¹ Chemists play a very important role in the development of chemical sensors. Typically, a chemical sensor composes of two important parts: a receptor unit and a signaling unit.² The signaling unit can give either electrochemical or optical responses. The most popular signaling units used by chemists are ferrocene and *p*-quinone.^{3,4} The fabrication of sensory units and sensors can be carried out in a suitable way for sensing metal ions, anions or organic molecules.

Calix[4]arene is one of the most versatile molecular building blocks suitable for attaching both receptor and sensory units to the same molecules. Many calix[4]arene derivatives containing ferrocene³ and p-quinone⁴ have been synthesized and their binding and sensing properties towards metal ions and anions have been studied. However, calix[4]quinones, in particular, are superior to ferrocenes because of the direct involvement of the calixarene framework. Therefore, one can design and construct a molecular sensor from a calix[4]quinone using its available oxygen atoms as donors for binding alkali cations.⁵ This should enhance both the selectivity and sensitivity of the sensors. A number of biscalixarenes have been synthesized and their binding studies with metal ions have been reported.⁶ It is of interest to synthesize different biscalix[4]arenes using ethylene bridges connecting lower rim phenoxy groups. The

substituents at the other *o*-phenoxy groups can also be varied. Upon oxidation, we expect to obtain various kinds of biscalix[4]quinones possessing a different number and various positions for the quinone moieties. This should lead to new selectivity and sensitivity for the compounds.

Biscalix[4]arene 7 has been synthesized in one step. Nucleophilic substitution reactions of *p-tert*-butylcalix[4]arene (1) with bromoethyl tosylate (3) using K_2CO_3 as base yielded compound 7 in 41% yield.⁷ This reaction also produced bisbromoethoxy calix[4]arene in 23% yield. This result implies that the coupling process occurred in a stepwise manner in which bisbromoethoxy calix[4]arene was produced in the first step. Subsequent nucleophilic substitution with another unit of calix[4]arene resulted in 7. Janssen et al. found that the use of pressure for selective alkylation of calix[6]arene resulted in a high yield of the alkylated products.8 Ostaszewski and Jurczak also reported the use of high pressure in the synthesis of simple and chiral bicyclic cryptands and diazacoronands that produced the desired products in high yield.⁹ The highpressure approach was thus used in the synthesis of 7 aiming to increase the cyclization rate. The reaction between 1 and bromoethyl tosylate (3) in acetonitrile in the presence of K₂CO₃ in a pressurized vessel which was compressed with N_2 at 50 psi and heated at 100°C yielded 7 in 69% yield as shown in Eq. (1).¹⁰ Compound 7 was thus obtained in a very high yield upon applying high pressure, and bisbromoethoxy calix[4]arene was not found in the reaction.

Keywords: biscalixarene; quinone; cyclic voltammetry.

^{*} Corresponding author.

^{0040-4039/03/\$ -} see front matter @ 2002 Elsevier Science Ltd. All rights reserved. PII: S0040-4039(02)02520-0



The diethyl ester calix[4]arene **4** was synthesized according to the published procedure with slight modification.¹¹ The reaction of **1** with ethyl bromoacetate (2.5 equiv.) in CH₃CN using K_2CO_3 as base and refluxing for 4 h resulted in compound **4** which can be easily separated from the mixture in 85% yield by addition of

CH₃OH into its CH₂Cl₂ solution. The compound 4 was subsequently reduced with 3 equiv. of LiAlH₄ in dry THF at 0°C to yield the dialcohol 5^{12} in 97% yield. To facilitate the nucleophilic substitution reaction, the -OH groups were changed to methylsufonate (mesyl) groups by the addition of methanesulfonyl chloride (3.0 equiv.) in the presence of Et_3N (3 equiv.) and a catalytic amount of DMAP. The disulfonyl ester 6^{13} was obtained in 96% yield. The compound 6 acts as a building block for constructing both symmetric and unsymmetric biscalix[4]arenes. Finally, the coupling reaction of 1 and 6 in CH_3CN using K_2CO_3 as base resulted in the symmetric biscalix[4]arene 7 in 24% yield. It is clearly seen that in the case of the symmetric biscalix[4]arene, the one-pot synthetic approach gives much higher yields than that of the stepwise synthesis. Nevertheless, the stepwise synthesis is good for preparing unsymmetric biscalixarenes. The coupling reaction of 6 and 2^{14} in THF using NaH as base resulted in the unsymmetric biscalix[4]arene $\mathbf{8}^{15}$ in 18% yield. The oxidation of compounds 7 and 8 using $Tl(CF_3CO_2)_3$ in CF₃COOH resulted in yellowish biscalix[4]tetraquinone, 9 (21%),¹⁶ and biscalix[4]arenediquinone, 10 (56%),¹⁷ respectively.

Echegoyen and co-workers have shown that there are marked perturbations of the quinone redox couples of calix[4]quinones on addition of sodium cations.⁵ We thus investigated the electrochemical properties of com-



Scheme 1.





Figure 1. Voltammogram of **9** in 20% DCM in CH_3CN using tetrabutylammonium tetrafluoroborate (TBABF₄) as supporting electrolyte at a scan rate of 50 mV/s.

pounds 9 and 10 by cyclic voltammetry in 20% DCM in CH₃CN using tetrabutylammonium tetrafluoroborate (TBABF₄) as supporting electrolyte.¹⁸ Compound 9 showed two broad quasi-reversible redox waves 1 and 2 at -1.235 and -1.790 V, respectively (Fig. 1) indicating a complicated electron transfer mechanism which was quite similar to the behavior of the biscalix[4]arene tetraquinone possessing a longer spacer reported by Beer and co-workers.¹⁹ Interestingly, upon addition of 1 equiv. of Na⁺ (ClO₄⁻ as counter cation), a new reversible reduction wave at -0.885 V appears in the voltammogram and the quasi-reversible reduction wave 2 shifts more anodically while wave 1 shifts insignificantly. However, adding excess Na⁺ results in the disappearance of both waves 1 and 2 and the appearance of an irreversible wave at -1.466 V. This may indicate that Na⁺ forms a more stable complex with the reduced form of 9.

Cyclic voltammograms (CV) of compound **10** exhibit three waves 1, 2 and 3 at -1.092, -1.201 and -1.754 V, respectively (Fig. 2). This voltammogram is similar to the calixdiquinone esters and amides reported by Beer and colleagues.²⁰ The first two couples indicate two one-electron transfer processes. Wave 3 is an irreversible wave probably involving a reduction of the quinone to its radical form and subsequent protonation to the hydroquinone. However, upon increasing the scan rate, two new irreversible oxidation waves appear at -0.750and -0.337 V. This may signify that wave 3 represents a two-electron transfer reduction process. The result suggests that **10** undergoes an electron transfer, electron transfer and chemical reaction (EEC) mechanism.



Figure 2. Voltammogram of **10** in 20% DCM in CH_3CN using tetrabutylammonium tetrafluoroborate (TBABF₄) as supporting electrolyte at various scan rates.

On addition of Na⁺ (1 equiv.) to the solution of **10**, a new wave at -0.880 V appears in the voltammogram. However, upon adding excess Na⁺, the current of the wave at -0.880 V increases, waves 1 and 2 disappear and a quasi-reversible wave at -1.334 V appears in the voltammogram (Fig. 3). In addition, wave 3 at -1.754 V becomes reversible. Biscalix[4]quinone **10** thus shows a significant change of its CV waves upon complexing Na⁺.

In summary, we have synthesized two new biscalix[4]arenes (7 and 8) and two biscalix[4]quinones (9



Figure 3. Voltammogram of 10 upon addition of Na⁺ in 20% DCM in CH₃CN using tetrabutyl ammonium tetrafluoroborate (TBABF₄) as supporting electrolyte at a scan rate of 50 mV/s.

and 10). We also show that the use of pressure increases the yield of the symmetric biscalix[4]arene 7. Calixquinones 9 and 10 exhibit interesting electrochemical properties and show a promising ability to sense Na⁺. We are currently pursuing electrochemical studies of the compounds synthesized towards other alkali metal ions and the results will be reported in due course.

Acknowledgements

This work was financially supported by the Thailand Research Fund (Grant no. RSA/06/2544). Authors thank Professor Jeremy Kilburn for the ESI MS results.

References

- 1. Cattrall, R. W. Chemical Sensors, Oxford Chemistry Primers; Oxford Science Publisher: Oxford, UK, 1997.
- 2. Beer, P. D. Acc. Chem. Res. 1998, 31, 71.
- (a) Cooper, J. B.; Drew, M. G. B.; Beer, P. D. J. Chem. Soc., Dalton Trans. 2000, 2721; (b) Beer, P. D.; Hesek, D.; Nam, K. C.; Drew, M. G. B. Organometallics 1999, 18, 3933.
- (a) Chung, T. D.; Kang, S. K.; Kim, H.; Kim, J. R.; Oh, W. S.; Chang, S.-K. *Chem. Lett.* **1998**, 1225; (b) Nam, K. C.; Kang, S. O.; Jeong, H. S.; Jeon, S. *Tetrahedron Lett.* **1999**, 40, 7343.
- Gómez-Kaifer, M.; Reddy, P. A.; Gutsche, C. D.; Echegoyen, L. J. Am. Chem. Soc. 1994, 116, 3580.
- 6. Asfari, Z.; Weiss, J.; Vicens, J. Synlett 1993, 719.
- 7. Tomapatanaget, B.; Pulpoka, B.; Tuntulani, T. Chem. Lett. 1998, 1037.
- Janssen, R. G.; Verboom, W.; Reinhoudt, D. N.; Casnati, A.; Freriks, M.; Pochini, A.; Ugozzoli, F.; Ungaro, R.; Nieto, P. M.; Carramolino, M.; Cuevas, F.; Prados, P.; de Mendoza, J. Synthesis 1993, 380.
- Jurczak, J.; Ostaszewski, R. J. Coord. Chem. Part B 1992, 27, 201.
- 10. In a high pressure tube (Ace Glass Co., Catalog No. 8648-29) equipped with valves and pressure gauge, *p*-tertbutylcalix[4]arene, 1, (3.0 g, 4.62 mmol), catalytic amount of 18-crown-6, bromoethyl tosylate, 3, (1.3 g, 4.62 mmol) and K₂CO₃ (1.3 g, 9.24 mmol) were suspended in anhydrous acetonitrile (10 mL). The tube was then pressurized with N_2 at 50 psi. The mixture was stirred and heated at 100°C for 4 days. The solution was allowed to cool to room temperature. The pressure in the tube was then released. The solvent was evaporated to dryness to yield a yellow residue. The residue was dissolved in dichloromethane (100 mL) and an aqueous solution of 3 M hydrochloric acid was subsequently added until the pH of the solution reached pH 1. The mixture was extracted with dichloromethane (3×50 mL). The combined organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated on rotary evaporator to

obtained a white solid of 7. The product was recrystallized in dichloromethane upon addition of methanol to afford a white crystalline solid (2.16 g, 69%). 7: ¹H NMR spectrum (200 MHz, CDCl₃) δ 7.65 (s, 4H, ArOH), 7.00 (s, 8H, *m*-HArOH), 6.82 (s, 8H, *m*-HArOCH₂CH₂ArH), 4.55 (s, 8H, ArOCH₂CH₂OAr), 3.55 and 4.50 (d each, $J_{\text{H-H}}$ =14.0 Hz, 16H, Ar CH₂Ar), 1.25 (s, 36H, HOAr-*t*-C₄H₉), 0.99 (s, 36H, ROAr-*t*-C₄H₉). FAB MS (*m*/*z*): 1367.8 [*M*⁺+NH₄⁺]. Anal. calcd for 7 (C₉₂H₁₁₆O₈): C, 81.86; H, 8.66. Found: C, 81.86; H, 8.86.

- Collins, E. M.; McKervey, M. A.; Madigan, E.; Moran, M. B.; Owens, M.; Ferguson, G.; Harris, S. J. J. Chem. Soc., Perkin Trans. 1 1991, 3137.
- 12. 5: ¹H NMR spectrum (200 MHz, CDCl₃) δ 9.23 (s, 2H, ArOH), 7.07 (s, 4H, m-HOArH), 7.01 (s, 4H, m-ROArH), 5.2 (s, 2H, -CH₂CH₂OH), 4.29 (t, 8H, ArOCH₂CH₂OH), 3.43 and 4.30 (d, J_{H-H} = 14.0 Hz, 8H, ArCH₂Ar), 1.20 (s, 18H, ROAr-*t*-C₄H₉), 1.19 (s, 18H, HOAr-*t*-C₄H₉).
- 13. 6: ¹H NMR spectrum (200 MHz, CDCl₃) δ 7.06 (s, 4H, ROArH), 6.74 (s, 4H, HOArH), 6.67 (s, 2H, ArOH), 4.64 (m, 4H, MsCH₂CH₂O), 3.36 (m, 8H, ArCH₂Ar and MsOCH₂CH₂O), 4.24 (d, J_{H-H}=13 Hz, 4H, ArCH₂Ar), 3.23 (s, 6H, SO₂CH₃), 1.28 (s, 18H, HOAr-t-C₄H₉), 0.90 (s, 18H, ROAr-t-C₄H₉).
- Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. Y.; Bauer, L. J. *Tetrahedron* 1983, 39, 409.
- 8: ¹H NMR spectrum (200 MHz, CDCl₃) δ 7.09–6.70 (m, 18H, HAr and ArOH), 4.78–4.12 (m, 22H, OCH₂CH₂O, ArCH₂Ar and –OCH₃), 3.40–3.15 (m, 8H, ArCH₂Ar), 1.30 (s, 18H, Ar-t-C₄H₉), 1.25 (s, 18H, Ar-t-C₄H₉), 0.92 (s, 36H, Ar-t-C₄H₉). ESI MS (m/z): 1395.2 (M⁺+NH₄⁺).
- 16. 9: ¹H NMR spectrum (200 MHz, CDCl₃) δ 7.10 (s, 8H, ROAr*H*), 5.86 (s, 8H, H_{quinone}), 4.39 (s, 8H, OC*H*₂C*H*₂O), 4.52 and 3.00 (dd, *J*_{H-H}=13.9 Hz, 16H, ArC*H*₂Ar), 1.33 (s, 36H, Ar-*t*-C₄*H*₉). ESI MS (*m*/*z*): 1203.4 (*M*⁺+4H+NH₄⁺). IR (*v*_{CO}): 1664.86 cm⁻¹. Anal. calcd for 9 (C₇₆H₇₆O₁₂·2H₂O): C, 74.98; H, 6.62. Found: C, 74.99; H, 6.20.
- 17. **10**: ¹H NMR spectrum (200 MHz, CDCl₃) δ 7.15 (br s, 12H, *H*ArOR), 6.50 (s, 4H, H_{quinone}), 4.70–4.40 (m, 16H, OCH₂CH₂O, ArCH₂Ar), 4.15 (s, 6H, -OCH₃), 3.38–3.12 (m, 8H, ArCH₂Ar), 1.30 (s, 36H, Ar-*t*-C₄H₉), 0.80 (s, 18H, Ar-*t*-C₄H₉). ESI MS (*m*/*z*): 1315.8 (*M*⁺+4H+NH₄⁺). IR (*v*_{CO}): 1657.14 cm⁻¹. Anal. calcd for **10** (C₈₆H₁₀₀O₁₀·3H₂O): C, 76.64; H, 7.93. Found: C, 77.20; H, 8.52.
- CV experiments were carried out on an AUTOLAB PGSTAT100 potentiostat using a glassy carbon working electrode, a Ag/AgNO₃ reference electrode and a platinum auxiliary electrode. All experiments were performed under N₂.
- Webber, P. R. A.; Chen, G. Z.; Drew, M. G. B.; Beer, P. D. Angew. Chem., Int. Ed. 2001, 40, 2265.
- Beer, P. D.; Gale, P. A.; Chen, Z.; Drew, M. G. B.; Heath, J. A.; Ogden, M. I.; Powell, H. R. *Inorg. Chem.* 1997, *36*, 5880.