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Supramolecular, Calixarene-Based Complexes That Release NO Gas

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Dedicated to Prof. Dr. David N. Reinhoudt on the occasion of his honourable retirement

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Calix[4]arenes and nanotubes based on them convert NO_2/N_2O_4 gases into nonvolatile NO^+ species and encapsulate them. In a one-electron reduction scheme with hydroquinone, the complexed NO^+ transforms into NO gas. While NO is released, calixarenes are regenerated and can be loaded again. Supramolecular materials for generation, storage and release of NO can be potentially created, with high-capacity calixarene nanotubes holding a special promise.

Introduction

The well-documented biological importance of nitric oxide (NO) includes protective, regulatory, and deleterious functions.[1] To control the gas release, compounds have been developed that deliver NO by their thermochemical or photochemical decomposition.[2,3] At the same time, there are only very few examples of *supramolecular* systems that have the capability to reversibly trap, store and release NO.[4]

We recently described synthetic, molecular containers for NO_2/N_2O_4 gases, which are based on calix[4]arenes.[5] These reversibly react with NO_2/N_2O_4 with the quantitative formation of stable calixarene–nitrosonium (NO^+) complexes. NO^+ is generated from N_2O_4 upon its disproportionation to $NO^+NO_3^-$. In this communication, we further extend the supramolecular chemistry between calixarenes and NO_x gases and demonstrate their use for the effective generation of NO, in a simple and reliable protocol.

Results and Discussion

While there are several available agents, capable of clean, one-electron reduction of NO^+,[6–8] we identified commercially available hydroquinone as the most suitable. Hydroquinone quantitatively reduces NO^+ with the formation of NO and benzoquinone.[6] We found, that when mixed with hydroquinone in apolar, chlorinated solution, calixarene–NO^+ complexes smoothly react and release NO.

Preliminary experiments started with the simple calix[4]arene **1** (Figure 1). Bubbling NO_2/N_2O_4 gas through the $CDCl_3$ solution of the tetrakis(*O*-*n*-hexyloxy)calix[4]arene **1** led to the rapid, quantitative formation of the calixarene–NO^+ complex **2** (Figure 1). In complex **2**, NO^+ is tightly encapsulated inside a π-electron-rich calix[4]arene tunnel with a remarkably high $K_{assoc} >> 10^6$ M^{-1}. Calixarene–NO^+ complexes were originally prepared from calix[4]arenes and nitrosonium salts,[5,9] calix[4]arenes and NO_2/N_2O_4[5] or calix[4]arene cation radicals and free NO.[9] In the ^1H NMR

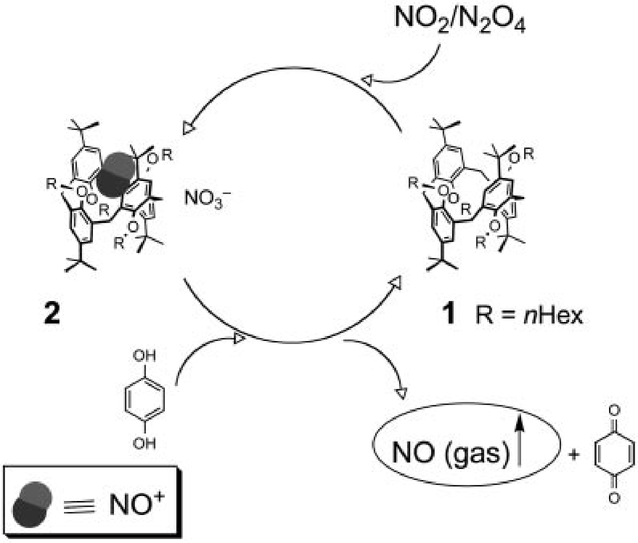

Figure 1. Calixarene-nitrosonium complex **2** is obtained from calixarene **1** and NO_2/N_2O_4 and used to generate NO gas.

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spectrum of **1** in $CDCl_3$ the aromatic protons were recorded as a singlet at δ = 6.95 ppm (Figure 2). In nitrosonium complex **2**, it was transformed into a singlet at δ = 7.02 ppm. The CH_2 bridge protons of **1** give rise to a singlet at δ = 3.74 ppm. In complex **2**, this was observed at δ = 3.60 ppm. The OCH_2 protons in **1** were recorded at δ = 3.39 ppm, and they characteristically shifted to δ = 3.77 ppm in complex **2**.

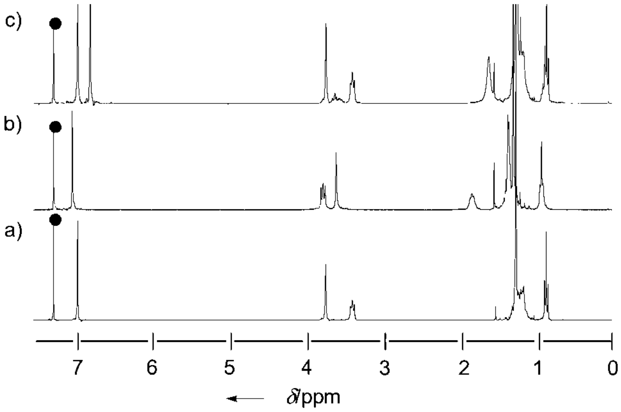

Figure 2. Selected portions of the ^1H NMR spectra (300 MHz, $CDCl_3$, 295 K) of: a) calixarene **1**. b) calixarene–NO^+ complex **2** prepared from calixarene **1** and NO_2/N_2O_4. c) same as b) after mixing with hydroquinone; the benzoquinone singlet is situated at δ = 6.78 ppm. The residual solvent signals are marked (●).

In a typical NO generating experiment, a ca. 20-fold excess of hydroquinone was added to a $CHCl_3$ (or $CDCl_3$) solution of complex **2** and shacked vigorously. At this point, the NO gas release could be detected with a naked eye, and the solution color changed from deep-purple to yellow.[10] The former color belongs to the charge-transfer complex **2**, while the latter reflects the formation of 1,4-benzoquinone. The released NO gas was identified by UV spectrophotometry, showing the fine vibrational structure of three sharp absorption peaks at λ_{max} = 204, 214 and 226 nm (Figure 3). This is in agreement with the previously published absorption data for the identification of NO.[6,11] In addition, the ^1H NMR spectrum clearly showed the quantitative (>95%) regeneration of free calixarene **1** (Figure 2). Noteworthy, NO itself has no affinity to calix[4]arenes.[9]

The calix[4]arene cavity is too narrow for hydroquinone, and the electron-transfer reaction, most probably, occurs outside, in the bulk solution. The encapsulated NO^+ must be released first. While the equilibrium between calixarene **1** and its complex **2** provides only small (<<1%) quantities of free NO^+ for the outside reaction, hydroquinone may facilitate the NO^+ release. Electron-rich aromatic molecules are known to form strong complexes with NO^+.[12] In a model experiment, 1,4-*O*,*O*-dimethylated hydroquinone was mixed with complex **2**. Indeed, the NO^+ release was observed and free calixarene **1** was also regenerated.

To explore our findings, we tested recently prepared calixarene-based synthetic nanotubes.[13] These nanotubes are several nanometers long and can reversibly interact with NO_2/N_2O_4 with the formation of complexes with multiple NO^+. Accordingly, the nanotubes **3** and **4** were filled with NO^+ species by simply bubbling NO_2/N_2O_4 gases through their $(CDCl_2)_2$ solutions (Figure 4). The deep-purple compexes **5** and **6** quantitatively formed, which entrap two and three NO^+ cations, respectively. They were identified by ^1H NMR and absorption spectroscopy (Figure 5).[13] For example, the propyl Ar–O–C*H*$_2$ protons in **5** and **6** were both seen at δ ca. 3.85 ppm, which is significantly downfield comparing to empty tubes **3** and **4** ($\delta \approx 3.26$ ppm). Similarly, downfield shifts ($\Delta\delta > 1$) were observed for the Ar–O–C*H*$_2$ and C*H*$_2$–O–C*H*$_2$ protons in filled tubes **5** and **6**.

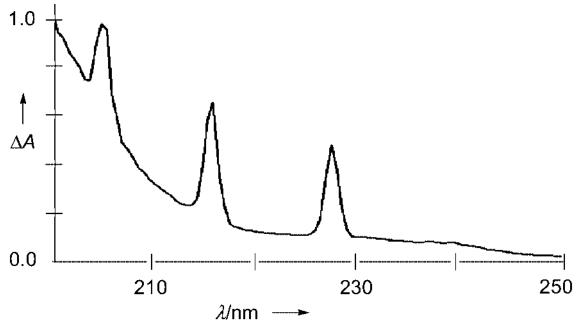

Figure 3. The UV spectrum (gas phase, 295 K) of NO gas generated from calixarene–NO^+ complex **2** and hydroquinone.

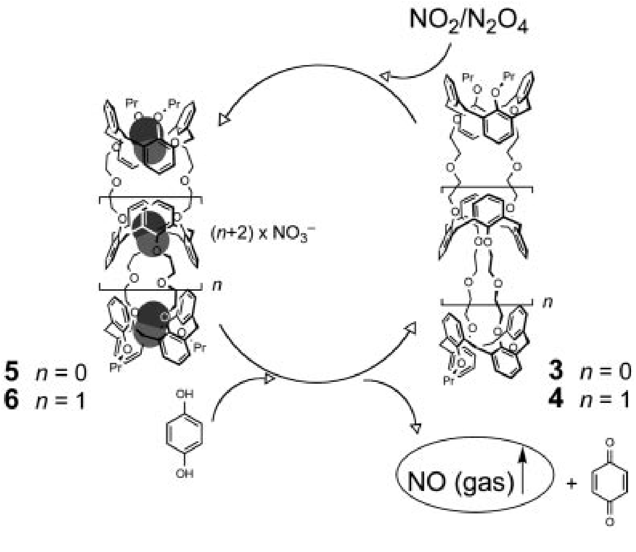

Figure 4. Filling of calixarene-based nanotubes with nitrosonium and generation of NO gas.

When a ca. 20-fold excess of hydroquinone was added to the $(CDCl_2)_2$ solutions of **5** and **6**, the color changed from deep-purple to yellow. The ^1H NMR spectrum clearly showed the quantitative (>95%) regeneration of free nanotubes **3** and **4** (Figure 5). The NO release could be visually detected and identified by UV spectrophotometry. The use of calixarene nanotubes, capable of storing *multiple* NO^+ species, could potentially lead to interesting NO releasing materials with the high gas capacity.

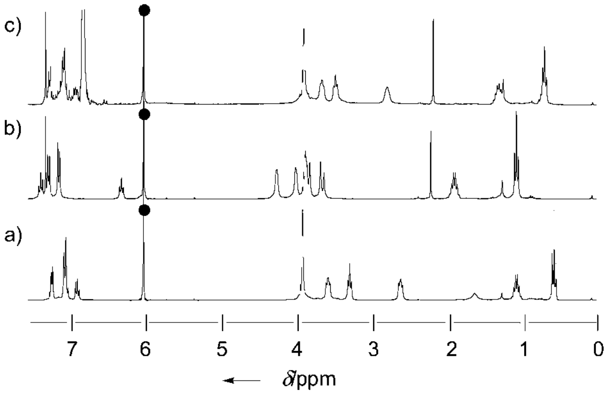

Figure 5. Selected portions of the ^1H NMR spectra [300 MHz, $(CDCl_2)_2$, 295 K] of: a) calixarene-based tube **3**; b) nitrosonium complex **5**, prepared from **3** and NO_2/N_2O_4. c) same as b) after mixing with hydroquinone; the benzoquinone singlet is situated at δ = 6.78 ppm. The residual solvent signals are marked "•".

Conclusions

In conclusion, novel supramolecular systems are now available for the generation of NO gas, which are based on calix[4]arenes. The gas is safely stored in the form of NO^+, which is not volatile and strongly bound within the calixarene cage. The NO^+ is produced from higher NO_x, namely NO_2/N_2O_4. In a one-electron reduction scheme involving calixarene–NO^+ complexes and simple hydroquinone, NO is smoothly released and free calixarenes are quantitatively regenerated, which can be reloaded using NO_2/N_2O_4. The reversibility can also be achieved through spontaneous, atmospheric oxidation of the newly generated NO to NO_2/N_2O_4. There is the possibility to modify the cage structure through conventional calixarene syntheses. We are currently preparing calixarene-based materials for the production of NO gas.

Experimental Section

In a preparative procedure, the calix[4]arene **1** (0.5 g, 0.5 mmol) was dissolved in $CHCl_3$ (1.5 mL) and NO_2/N_2O_4 gas was passed through the solution for 30 s. Complex **2** formed (>95%, NMR). Dry N_2 was then bubbled through the resulted purple solution for 3 min to remove any dissolved gases.[14] The solution was added into the vial with solid hydroquinone (0.5 g, 5 mmol) under dry nitrogen and the mixture was vigorously stirred for 5 min. The evolved NO gas (ca. 11 mL, 0.5 mmol) was collected by a syringe or over cold water and identified by UV spectroscopy; yield >95%, λ_{max} = 204, 214, 226 nm (gas phase). The empty calixarene **1** was quantitatively (>95%) regenerated and identified by ^1H NMR spectroscopy. In addition, newly formed benzoquinone was identified; δ = 6.78 ppm (^1H NMR in $CDCl_3$).

Supporting Information (see also the footnote on the first page of this article): Experimental details and spectra.

Acknowledgments

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[1] a) S. Pfeiffer, B. Mayer, B. Hemmens, *Angew. Chem. Int. Ed.* **1999**, *38*, 1714–1731; b) *Nitric Oxide: Biology and Pathology* (Ed.: L. J. Ignarro), Academic Press, San Diego, **2000**.
[2] a) C. Napoli, L. J. Ignarro, *Annu. Rev. Pharmacol. Toxicol.* **2003**, *43*, 97–123; b) P. G. Wang, M. Xian, X. Tang, X. Wu, Z. Wen, T. Cai, A. J. Janczuk, *Chem. Rev.* **2002**, *102*, 1091–1134; c) V. G. Granik, N. B. Grigor′ev, *Russ. Chem. Bull, Int. Ed.* **2002**, *51*, 1375–1422; d) J. E. Saavedra, L. K. Keefer, *J. Chem. Educ.* **2002**, *79*, 1427–1434.
[3] a) J. Bordini, P. C. Ford, E. Tfouni, *Chem. Commun.* **2005**, 4169–4171; b) M. C. Frost, M. E. Meyerhoff, *J. Am. Chem. Soc.* **2004**, *126*, 1348–1349; c) A. A. Eroy-Reveles, Y. Leung, P. K. Marscharak, *J. Am. Chem. Soc.* **2006**, *128*, 7166–7167.
[4] a) J. T. Mitchell-Koch, T. M. Reed, A. S. Borovik, *Angew. Chem. Int. Ed.* **2004**, *43*, 2806–2809; b) K. M. Padden, J. F. Krebs, C. E. MacBeth, R. C. Scarrow, A. S. Borovik, *J. Am. Chem. Soc.* **2001**, *123*, 1072–1079; c) X. D. Ding, A. Weichsel, J. F. Andersen, T. K. Shokhireva, C. Balfour, A. J. Pierik, B. A. Averill, W. R. Montfort, F. A. Walker, *J. Am. Chem. Soc.* **1999**, *121*, 128–138.
[5] a) G. V. Zyryanov, Y. Kang, D. M. Rudkevich, *J. Am. Chem. Soc.* **2003**, *125*, 2997–3007; b) Y. Kang, G. V. Zyryanov, D. M. Rudkevich, *Chem. Eur. J.* **2005**, *11*, 1924–1932.
[6] a) E. Bosch, R. Rathore, J. K. Kochi, *J. Org. Chem.* **1994**, *59*, 2529–2536.
[7] G. I. Borodkin, I. R. Elanov, M. M. Shakirov, V. G. Shubin, *Russ. J. Org. Chem.* **2003**, *39*, 1144–1150.
[8] N. G. Connelly, W. E. Geiger, *Chem. Rev.* **1996**, *96*, 877–910.
[9] R. Rathore, S. V. Lindeman, K. S. S. Rao, D. Sun, J. K. Kochi, *Angew. Chem.* **2000**, *112*, 2207–2211; *Angew. Chem. Int. Ed.* **2000**, *39*, 2123–2127.

[10] NO tends to rapidly react with the atmospheric oxygen with the formation of NO_2 and, further, N_2O_3 and N_2O_4. Accordingly, the experiments must be performed under N_2.

[11] F. F. Marmo, *J. Opt. Soc. Am.* **1953**, *43*, 1186.
[12] G. I. Borodkin, V. G. Shubin, *Russ. Chem. Rev.* **2001**, *70*, 211–230.
[13] V. G. Organo, A. V. Leontiev, V. Sgarlata, H. V. R. Dias, D. M. Rudkevich, *Angew. Chem.* **2005**, *117*, 3103–3107; *Angew. Chem. Int. Ed.* **2005**, *44*, 3043–3047.

[14] In the control experiment, involving all the reagents except calixarene **1**, NO gas was not generated (UV measurements). This indicates that no free NO_2/N_2O_4 was present in the bulk solution after bubbling N_2.

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