

Supramolecular fixation of NO<sub>2</sub> with calix[4]arenes

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**Reaction of NO<sub>2</sub> with simple calix[4]arenes in chloroform in the presence of a Lewis acid rapidly results in intense coloration caused by the encapsulation of nitrosonium cation.**

Nitrogen dioxide (NO<sub>2</sub>) is a major component of so-called NO<sub>x</sub> gases.<sup>1</sup> It is a toxic atmospheric pollutant derived from fossil fuel combustion, power plants, and large-scale industrial processes. In combination with nitric oxide (NO), NO<sub>2</sub> is involved in various nitrosation processes in biological tissues.<sup>2</sup> Nitrosative mechanisms have been implicated in ion conductance, signal transduction, glycolysis, apoptosis, and DNA repair. Extensive NO<sub>2</sub> circulation in the atmosphere requires not only its systematic monitoring,<sup>3</sup> but also necessitates the development of improved methods of NO<sub>2</sub> fixation. Here, we describe host–guest complexes, formed upon interaction between NO<sub>2</sub> and simple calix[4]arenes. Our findings offer a novel process of NO<sub>2</sub> utilization and may also lead towards stable, supramolecular nitrosating reagents, nitrogen oxides storing materials, and new visual sensory systems for NO<sub>x</sub>.

Calixarenes are popular building blocks for molecular containers—cavitands, carcerands, and capsules.<sup>4</sup> They provide quite rigid, π-electron rich inner cavities for complexation of electron deficient guest-species. We discovered that tetra-alkylated calix[4]arenes **1**<sup>5</sup> and **2**,<sup>6</sup> possessing *cone* and *1,3-alternate* conformations, respectively, reversibly interact with NO<sub>2</sub> and trap the highly reactive nitrosonium (NO<sup>+</sup>) cation. Bubbling NO<sub>2</sub> through the solutions of **1** and **2** in CHCl<sub>3</sub> resulted in instant, deep coloration. The UV–vis spectra changed accordingly: the broad bands appeared at λ<sub>max</sub> = 560 and 512 nm, respectively. This is in striking contrast to the colorless solutions of **1** and **2**, and the pale yellow solution of NO<sub>2</sub> in CHCl<sub>3</sub>, and implies a charge-transfer. NO<sub>2</sub> is a popular nitrosating/nitrating agent, and its chemistry is well developed. Two molecules of NO<sub>2</sub> exist in equilibrium with N<sub>2</sub>O<sub>4</sub>, which may disproportionate to ionic NO<sup>+</sup>NO<sub>3</sub><sup>−</sup> upon reacting with aromatic compounds.<sup>7</sup>

Interaction of NO<sub>2</sub> with **1** and **2** is very dynamic, and the initial <sup>1</sup>H NMR analysis gave rather complex, quickly changing pictures. The solutions of **1,2** and excess NO<sub>2</sub> bleached within 1–2 h, yielding mixtures of *p*-nitrated calixarenes (TLC, NMR). To slow down the nitration and to identify the involved complexes, solutions of **1,2** and NO<sub>2</sub> in CHCl<sub>3</sub> were treated with SnCl<sub>4</sub>. It is known that Lewis acids stabilize arene-nitrosonium charge-transfer complexes.<sup>8</sup> Subsequent precipitation with hexanes resulted in deeply colored, moisture sensitive solids, assigned to nitrosonium complexes **3** and **4** (> 90% yield, Fig. 1). Compounds **3** and **4** were characterized by UV–vis, FTIR, <sup>1</sup>H NMR spectroscopy in dry chloroform, and CHN elemental analysis.

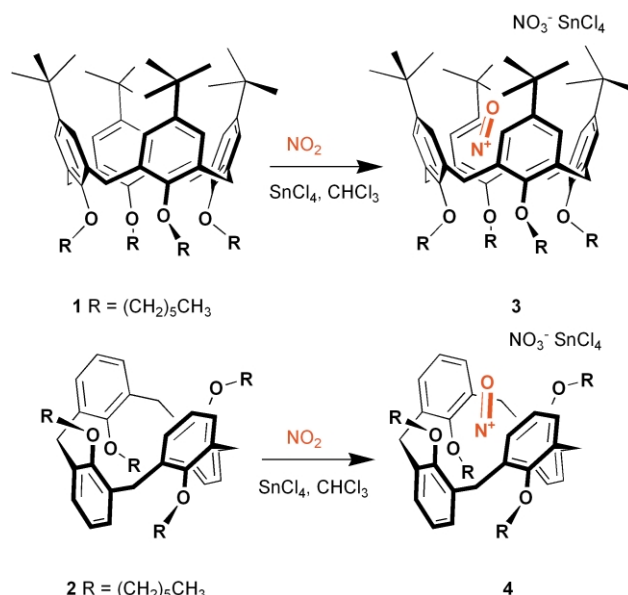
The UV–vis spectra showed broad charge-transfer<sup>7</sup> bands at λ<sub>max</sub> ~ 563 and 524 nm, and the FTIR spectra exhibited characteristic<sup>7</sup> arene-NO<sup>+</sup> stretching at ν = 1923 and 1955 cm<sup>−1</sup> for **3** and **4**, respectively. The <sup>1</sup>H NMR spectra of **3** and **4** showed new sets of the calixarene signals (Fig. 2). In particular, aromatic CH protons of guest-free **1** were seen as a singlet at 6.76 ppm. In nitrosonium complex **3**, these were transformed into a singlet at 7.00 ppm. The methylene bridge CH<sub>2</sub> protons of

**1** were recorded as doublets at 4.41 and 3.12 ppm (*J* = 12.5 Hz). In complex **3**, these were seen as doublets at 4.39 and 3.43 ppm (*J* = 12 Hz). The aromatic protons of free **2** were seen as a doublet and a triplet, 2 : 1, at 7.00 and 6.68 ppm, respectively (*J* = 7.5 Hz). In nitrosonium complex **4**, these were transformed into a triplet and a doublet, 1 : 2, at 7.17 and 7.08 ppm, respectively (*J* = 7.5 Hz). Elemental analysis of extremely moisture sensitive **3** and **4** proved to be difficult but reproducibly showed CHN ratios corresponding to the presence of *only one* NO<sup>+</sup> cation in both structures.

Independent structural evidence came from the complexation experiments between calixarenes **1,2** and commercially available NO<sup>+</sup>SbF<sub>6</sub><sup>−</sup> salt (CDCl<sub>3</sub>, 295 K). The corresponding UV–vis, FTIR and <sup>1</sup>H NMR complexation induced changes were in agreement with the data presented above for complexes **3,4**.

In the control experiments with non-cyclic anisole (*e.g.*, methoxybenzene), only weak coloration was observed upon exposure to NO<sub>2</sub>. Moreover, when mesitylene-derived, Pappalardo's calixarenes,<sup>9</sup> with sterically *blocked* cavities, were tested, no coloration was observed either; there was no indication for strong complexation in the UV–vis and <sup>1</sup>H NMR spectra. These experiments emphasize the importance of the calixarene cavities in the described transformations and rule out the possibility of the NO<sup>+</sup> coordination outside the cavity.† According to molecular modeling, *only one* NO<sup>+</sup> can fit inside the cavities of **1** and **2**.

Recently, Rathore, Kochi and co-workers described charge-transfer complexes between NO<sup>+</sup> and structurally similar calix[4]arenes.<sup>10</sup> The cation was indeed found encapsulated within the cavity (X-ray analysis). Our spectral data are in agreement with these data. Owing to the fact, that two molecules of NO<sub>2</sub> may disproportionate to NO<sup>+</sup>NO<sub>3</sub><sup>−</sup>, we thus



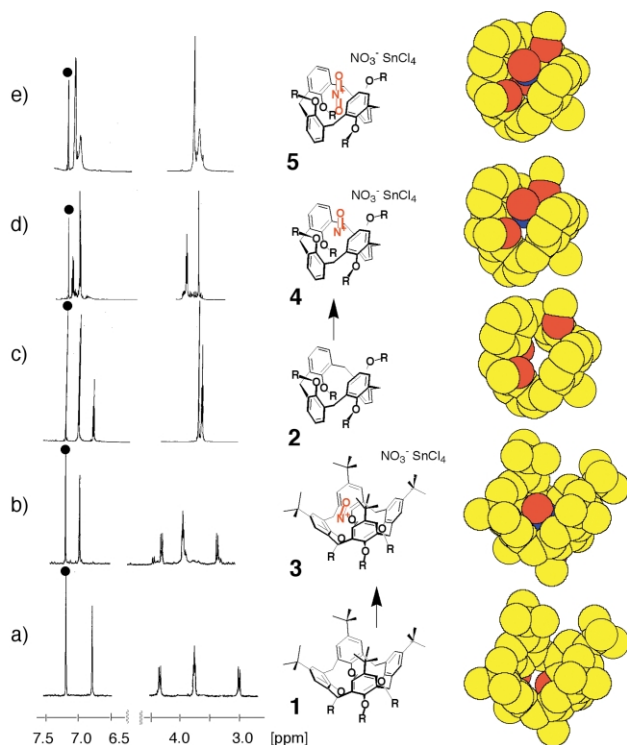
**Fig. 1** Chemical fixation of NO<sub>2</sub> with calix[4]arenes. Formation of nitrosonium complexes.

conclude that reaction between  $\text{NO}_2$  and calix[4]arenes lead to  $\text{NO}^+$  encapsulation.

In the experiments between calixarene **2**,  $\text{SnCl}_4$  and a larger (~50-fold) excess of  $\text{NO}_2$ , one more pre-reactive complex was detected, which we assigned to nitronium species **5** (Fig. 2). In the UV-vis spectrum, a broad charge-transfer band at  $\lambda_{\text{max}} = 512 \text{ nm}$  was recorded. The FTIR spectrum showed stretches at  $\nu = 2356 \text{ cm}^{-1}$ , characteristic<sup>8</sup> for  $\text{NO}_2^+$  species. In the  $^1\text{H}$  NMR spectrum, complex **5** exhibits a broader doublet and a triplet, 2:1, at 7.10 and 7.00, respectively (Fig. 2). Due to their extreme reactivity, none of the arene-nitronium  $\pi$ -complexes have been isolated to date,<sup>11</sup> and we attribute the stability of **5** to the encapsulation effects.

Complex **4** can be converted to **5** when a larger excess of  $\text{NO}_2$  is employed. As one possible scenario, initially formed nitronium complex **4** yields the electron transfer complex  $[\text{2}^{+\cdot}\text{NO}]\text{NO}_3^-$  and releases  $\text{NO}$ . The resulting cation-radical  $\text{2}^{+\cdot}\text{NO}_3^-$  reacts with an excess of  $\text{NO}_2$ , producing  $[\text{2}^{+\cdot}\text{NO}_2]\text{NO}_3^-$  and further charge-transfer nitronium complex **5** ( $[\text{2}\text{-NO}_2^+]\text{NO}_3^-$ ). Bent  $\text{NO}_2$  cannot fit inside **2**, but linear  $\text{NO}_2^+$  can. Judging from the intense coloration, the calixarene walls in **5**, most probably, encapsulate  $\text{NO}_2^+$ , however more experiments are needed to further support this. At this stage, the structure of **5** was independently confirmed by complexation between **2** and  $\text{NO}_2^+\text{SbF}_6^-$  salt in  $\text{CDCl}_3$ . The obtained UV-vis, FTIR and  $^1\text{H}$  NMR spectra were similar to those of complex **5**.

We then reexamined the reaction between **1,2** and  $\text{NO}_2$ , in the absence of  $\text{SnCl}_4$ . As an excess  $\text{NO}_2$  was passed through the solution of **1**, spectral features of nitronium complex  $[\text{1}\text{-NO}^+]\text{NO}_3^-$  were recorded (UV-vis,  $^1\text{H}$  NMR), along with the nitration products. For **2**, no signals for nitronium complex  $[\text{2}\text{-NO}^+]\text{NO}_3^-$  were seen, but nitronium complex  $[\text{2}\text{-NO}_2^+]\text{NO}_3^-$  was detected. Apparently, while formed the nitronium species quickly react with excess  $\text{NO}_2$ . Both reactions subsequently yield *p*-nitrated calixarenes.



**Fig. 2** Proposed structures and portions of the  $^1\text{H}$  NMR spectra (500 MHz,  $\text{CDCl}_3$ , 295 K) of: (a) calix[4]arene **1**. (b) nitronium complex **3**. (c) calix[4]arene **2**. (d) nitronium complex **4**. (e) nitronium complex **5**. The residual  $\text{CHCl}_3$  signals are marked '•'. In the MacroModel 7.1 representations, long alkyl chains and hydrogen atoms are omitted for viewing clarity.

Addition of  $\text{H}_2\text{O}$  or alcohols to the freshly prepared  $\text{CHCl}_3$  solutions of **3–5** resulted in the complete dissociation and recovery of calixarenes **1,2** (TLC, UV-vis,  $^1\text{H}$  NMR). Significantly,  $\text{H}_2\text{O}$  decolorizes **4** within seconds, but takes several minutes to decompose complex **3**. Apparently, *t*-Bu groups at the upper rim of the latter pose significant steric hindrances and protect the encapsulated  $\text{NO}^+$  species. Such stability of the arene- $\text{NO}^+$  complex is without precedent.<sup>7</sup>

Primary and secondary amides also bleached the solutions of **3** and **4**. On a preparative scale, *N*-nitrosation of secondary amides  $\text{AlkC(O)NHMe}$  ( $\text{Alk} = n\text{-Pr}, n\text{-Hex}, n\text{-Hept}$ ) by nitronium complex **4** in  $\text{CHCl}_3$  yielded *N*-nitrosoamides  $\text{AlkC(O)N(NO)Me}$ .<sup>‡</sup> This not only provides additional structural evidence for the discovered complexes, but also opens new perspectives to use them as supramolecular/encapsulated<sup>4</sup> nitrosating reagents.

In summary, a novel  $\text{NO}_2$  fixation process is now available, which employs simple calixarenes. The resulting complexes can be used as stable nitrosating and nitrating reagents. Calixarenes conveniently transmit the information about  $\text{NO}_2$  binding *via* visible light signals. The described charge-transfer interactions are unique for  $\text{NO}_2$  and would guarantee its detection in the presence of such gases as  $\text{H}_2\text{O}$ ,  $\text{O}_2$ ,  $\text{HCl}$ ,  $\text{SO}_x$ ,  $\text{NH}_3$ , and even  $\text{NO}$ . These findings open wider possibilities towards more sophisticated  $\text{NO}_2/\text{NO}_x$  sensing materials, including peptide-based nanostructures. The latter may be useful to detect  $\text{NO}_x$  species in biological fluids, provided that the complexes with sterically hindered calixarenes are quite stable in water.

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## Notes and references

<sup>†</sup> Even slight excess of  $\text{NO}^+\text{SbF}_6^-$  results in complete complex formation in  $\text{CDCl}_3$ , and no free calixarenes **1,2** were observed after equilibration;  $K_{\text{ass}} > 10^6 \text{ M}^{-1}$  for both complexes was estimated. The experimental details will be given in a full paper.

<sup>‡</sup> Spectral data for the obtained *N*-nitrosoamides are in agreement with those published, see ref. 12. Mixing nitronium complex **5** and  $\text{AlkC(O)NH}_2$  ( $\text{Alk} = \text{Me}, t\text{-Bu}$ ) in  $\text{MeCN}$  at 295 K resulted in the nitro derivatives  $\text{AlkC(O)NHNO}_2$  ( $^1\text{H}$  NMR analysis).

- 1 M. T. Lerda, J. W. Mungler and D. J. Jacob, *Science*, 2000, **289**, 2291.
- 2 M. Kirsch, H.-G. Korth, R. Sustmann and H. de Groot, *Biol. Chem.*, 2002, **383**, 389.
- 3 D. Filippini, M. Rosch, R. Aragon and U. Weimar, *Sens. Actuators, B*, 2001, **81**, 83; A. Bradford, P. L. Drake, O. Worsfold, I. P. Peterson, D. J. Walton and G. J. Price, *Phys. Chem. Chem. Phys.*, 2001, **3**, 1750; C. M. Dooling, O. Worsfold, T. H. Richardson, R. Tregonning, M. O. Vysotsky, C. A. Hunter, K. Kato, K. Shinbo and F. Kaneko, *Mater. Chem.*, 2001, **11**, 392.
- 4 D. M. Rudkevich, *Bull. Chem. Soc. Jpn.*, 2002, **75**, 393 (review).
- 5 P. J. A. Kenis, O. F. J. Noordman, H. Schonherr, E. G. Kerver, B. H. M. Snellink-Ruel, G. J. van Hummel, S. Harkema, C. P. J. M. van der Vorst, J. Hare, S. J. Picken, J. F. J. Engbersen, N. F. Van Hulst, G. J. Vancso and D. N. Reinhoudt, *Chem. Eur. J.*, 1998, **4**, 1225.
- 6 A. Casnati, A. Pochini, R. Ungaro, F. Ugozzoli, F. Arnaud, S. Fanni, M.-J. Schwing, R. J. M. Egberink, F. de Jong and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 1995, **117**, 2767.
- 7 E. Bosch and J. K. Kochi, *J. Org. Chem.*, 1994, **59**, 3314; G. I. Borodkin and V. G. Shubin, *Russ. Chem. Rev.*, 2001, **70**, 211 (review).
- 8 J. C. Evans, H. W. Rinn, S. J. Kuhn and G. A. Olah, *Inorg. Chem.*, 1964, **3**, 857.
- 9 S. Pappalardo, G. Ferguson and F. Gallagher, *J. Org. Chem.*, 1992, **57**, 7102.
- 10 R. Rathore, S. V. Lindeman, K. S. S. P. Rao, D. Sun and J. K. Kochi, *Angew. Chem., Int. Ed.*, 2000, **39**, 2123.
- 11 S. V. Rosokha and J. K. Kochi, *J. Org. Chem.*, 2002, **67**, 1727–1737.
- 12 J. Garcia, J. Gonzalez, R. Segura, F. Urpi and J. Vilarrasa, *J. Org. Chem.*, 1984, **49**, 3322.