Supramolecular fixation of NO₂ with calix[4]arenes

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Reaction of NO₂ 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 (NO₂) is a major component of so-called NO$_x$ gases.[1] It is a toxic atmospheric pollutant derived from fossil fuel combustion, power plants, and large-scale industrial processes. In combination with nitric oxide (NO), NO₂ is involved in various nitrosation processes in biological tissues.[2] Nitrosative mechanisms have been implicated in ion conductance, signal transduction, glycolysis, apoptosis, and DNA repair. Extensive NO₂ circulation in the atmosphere requires not only its systematic monitoring,[3] but also necessitates the development of improved methods of NO₂ fixation. Here, we describe host–guest complexes, formed upon interaction between NO₂ and simple calix[4]arenes. Our findings offer a novel process of NO₂ utilization and may also lead towards stable, supramolecular nitrosating reagents, nitrogen oxides storing materials, and new visual sensory systems for NO$_x$.

Calixarenes are popular building blocks for molecular containers—cavitands, carcerands, and capsules.[4] 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**[5] and **2**,[6] possessing *cone* and *1,3-alternate* conformations, respectively, reversibly interact with NO₂ and trap the highly reactive nitrosonium (NO⁺) cation. Bubbling NO₂ through the solutions of **1** and **2** in CHCl₃ resulted in instant, deep coloration. The UV–vis spectra changed accordingly: the broad bands appeared at λ_{max} = 560 and 512 nm, respectively. This is in striking contrast to the colorless solutions of **1** and **2**, and the pale yellow solution of NO₂ in CHCl₃, and implies a charge-transfer. NO₂ is a popular nitrosating/nitrating agent, and its chemistry is well developed. Two molecules of NO₂ exist in equilibrium with N₂O₄, which may disproportionate to ionic NO⁺NO₃⁻ upon reacting with aromatic compounds.[7]

Interaction of NO₂ with **1** and **2** is very dynamic, and the initial ¹H NMR analysis gave rather complex, quickly changing pictures. The solutions of **1,2** and excess NO₂ 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 NO₂ in CHCl₃ were treated with SnCl₄. It is known that Lewis acids stabilize arene-nitrosonium charge-transfer complexes.[8] 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, ¹H NMR spectroscopy in dry chloroform, and CHN elemental analysis.

The UV–vis spectra showed broad charge-transfer[7] bands at λ_{max} ~ 563 and 524 nm, and the FTIR spectra exhibited characteristic[7] arene-*NO⁺* stretching at ν = 1923 and 1955 cm⁻¹ for **3** and **4**, respectively. The ¹H 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 CH₂ 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⁺ cation in both structures.

Independent structural evidence came from the complexation experiments between calixarenes **1**,**2** and commercially available NO⁺SbF₆⁻ salt (CDCl₃, 295 K). The corresponding UV–vis, FTIR and ¹H 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 NO₂. Moreover, when mesitylene-derived, Pappalardo's calixarenes,[9] with sterically *blocked* cavities, were tested, no coloration was observed either; there was no indication for strong complexation in the UV–vis and ¹H NMR spectra. These experiments emphasize the importance of the calixarene cavities in the described transformations and rule out the possibility of the NO⁺ coordination outside the cavity.† According to molecular modeling, *only one* NO⁺ can fit inside the cavities of **1** and **2**.

Recently, Rathore, Kochi and co-workers described charge-transfer complexes between NO⁺ and structurally similar calix[4]arenes.[10] 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 NO₂ may disproportionate to NO⁺NO₃⁻, we thus
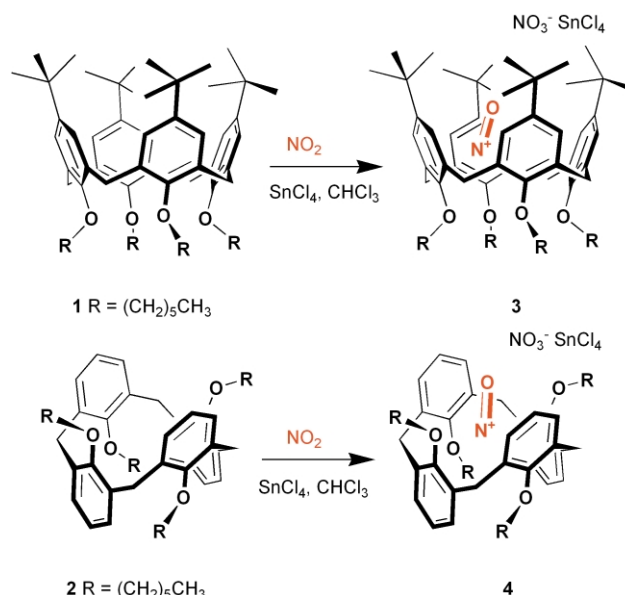

Fig. 1 Chemical fixation of NO₂ with calix[4]arenes. Formation of nitrosonium complexes.

conclude that *reaction between NO$_2$ and calix[4]arenes lead to NO$^+$ encapsulation*.

In the experiments between calixarene **2**, SnCl$_4$ and a larger (~50-fold) excess of NO$_2$, one more prereactive complex was detected, which we assigned to nitronium species **5** (Fig. 2). In the UV–vis spectrum, a broad charge-transfer band at $\lambda_{max} = 512$ nm was recorded. The FTIR spectrum showed stretches at $\nu = 2356$ cm^{-1}, characteristic[8] for NO$_2^+$ species. In the ^{1}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 π-complexes have been isolated to date,[11] and we attribute the stability of **5** to the encapsulation effects.

Complex **4** can be converted to **5** when a larger excess of NO$_2$ is employed. As one possible scenario, initially formed nitrosonium complex **4** yields the electron transfer complex [**2**$^{+\bullet}$·NO]NO$_3^-$ and releases NO. The resulting cation-radical **2**$^{+\bullet}$NO$_3^-$ reacts with an excess of NO$_2$, producing [**2**$^{+\bullet}$·NO$_2$]NO$_3^-$ and further charge-transfer nitronium complex **5** ([**2**·NO$_2^+$]NO$_3^-$). Bent NO$_2$ cannot fit inside **2**, but linear NO$_2^+$ can. Judging from the intense coloration, the calixarene walls in **5**, most probably, encapsulate 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 NO$_2^+$SbF$_6^-$ salt in CDCl$_3$. The obtained UV–vis, FTIR and ^{1}H NMR spectra were similar to those of complex **5**.

We then reexamined the reaction between **1,2** and NO$_2$, in the absence of SnCl$_4$. As an excess NO$_2$ was passed through the solution of **1**, spectral features of nitrosonium complex [**1**·NO$^+$]NO$_3^-$ were recorded (UV–vis, ^{1}H NMR), along with the nitration products. For **2**, no signals for nitrosonium complex [**2**·NO$^+$]NO$_3^-$ were seen, but nitronium complex [**2**·NO$_2^+$]NO$_3^-$ was detected. Apparently, while formed the nitrosonium species quickly react with excess NO$_2$. Both reactions subsequently yield *p*-nitrated calixarenes.
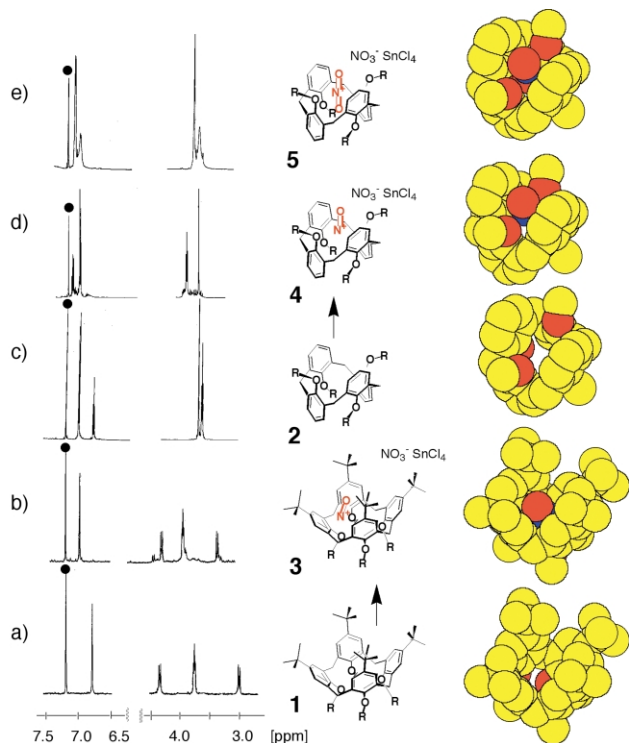
Addition of H$_2$O or alcohols to the freshly prepared CHCl$_3$ solutions of **3–5** resulted in the complete dissociation and recovery of calixarenes **1,2** (TLC, UV–vis, ^{1}H NMR). Significantly, H$_2$O decolorizes **4** within seconds, but takes several minutes to decompose complex **3**. Apparently, *t*-Bu groups at the upper rim of the latter pose significant steric hindrances and protect the encapsulated NO$^+$ species. Such stability of the arene-NO$^+$ complex is without precedent.[7]

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

In summary, a novel 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 NO$_2$ binding *via* visible light signals. The described charge-transfer interactions are unique for NO$_2$ and would guarantee its detection in the presence of such gases as H$_2$O, O$_2$, HCl, SO$_x$, NH$_3$, and even NO. These findings open wider possibilities towards more sophisticated NO$_2$/NO$_x$ sensing materials, including peptide-based nanostructures. The latter may be useful to detect NO$_x$ species in biological fluids, provided that the complexes with sterically hindered calixarenes are quite stable in water.

Notes and references

† Even slight excess of NO$^+$SbF$_6^-$ results in complete complex formation in CDCl$_3$, and no free calixarenes **1,2** were observed after equilibration; $K_{ass} > 10^6$ M^{-1} for both complexes was estimated. The experimental details will be given in a full paper.
‡ Spectral data for the obtained *N*-nitrosoamides are in agreement with those published, see ref. 12. Mixing nitronium complex **5** and AlkC(O)NH$_2$ (Alk = Me, *t*-Bu) in MeCN at 295 K resulted in the nitro derivatives AlkC(O)NHNO$_2$ (^{1}H NMR analysis).

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