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Toward Synthetic Tubes for NO_2/N_2O_4: Design, Synthesis, and Host−Guest Chemistry

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Abstract: Design of molecular nanotubes is proposed for entrapment and conversion of NO_2/N_2O_4 gases. Synthesis of 1,3-alternate bis-calix[4]arene tube **3** of 5 × 11 Å internal dimensions is presented, and its reversible reactions with NO_2/N_2O_4 in solution are studied. Exposure of **3** to NO_2/N_2O_4 in chlorinated solvents results in the rapid encapsulation of nitrosonium (NO^+) cations within its interior. Mono- and dinitrosonium complexes **4** and **5**, respectively, were isolated and characterized by UV−vis, FTIR, and ^{1}H NMR spectroscopies, and also molecular modeling. The NO^+ entrapment process is reversible, and addition of water quickly recovered starting tube **3**. Encapsulated within the tube NO^+ species act as nitrosating agents for secondary amides. These findings open wider perspectives toward NO_2/NO_x storing and converting materials and also offer a promise for further development of supramolecular chemistry of synthetic nanotubes.

Introduction

Recent studies have revealed that gases can be stored inside single-walled carbon nanotubes (SWNTs). This is exciting. Entrapping isotopes of noble gases by SWNTs may improve their use in medical imaging, where it is desirable to physically confine the gas before injection.[1] SWNTs encapsulate N_2, O_2, NO, and CF_4.[2] They have been shown to effectively detect O_2, NH_3, and NO_2.[3] Upon exposure to gaseous molecules the electrical resistance of SWNTs dramatically changes. Storage of H_2 in SWNTs is extremely promising in the design of energy-rich fuel-cell electric devices.[4] Synthetic nanotubes are rare,[5] and their chemistry with gases is not known. This is surprising. Organic synthesis permits much greater structural variations and control over the tube length/diameter, which is important for the gas dynamics and for the design of potential gas storing chambers and conversion/catalytic vessels. In this paper, we present the design of synthetic tubes for NO_2/N_2O_4 fixation, which is based on calixarenes (Figure 1, Figure 2).

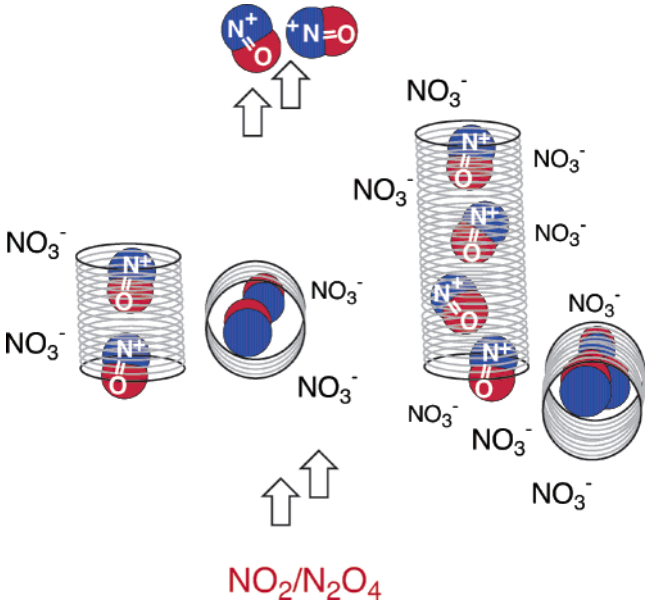

Figure 1. Molecular tubes for NO_2/N_2O_4 fixation, a schematic representation. Upon exposure to polyaromatic surfaces of the tubes, N_2O_4 disproportionates to $NO^+NO_3^-$. Nanotubes encapsulate NO^+ within their interiors. In and out exchange of trapped NO^+ species is possible, and this can be applied for nitrosation reactions.

Starting here with the first generation, we disclose the synthesis and unique host−guest chemistry between NO_2/N_2O_4 and tube **3**, and also chemical reactions with thus-obtained encapsulating complexes **4** and **5**. Nitrogen dioxide (NO_2) and its dimer—dinitrogen tetroxide (N_2O_4)—belong to the family of NO_x gases.[6] These are toxic environmental pollutants, originated in large quantities from fuel combustion and large-scale industrial processes. Their extensive circulation requires not only the systematic monitoring but also necessitates the development of

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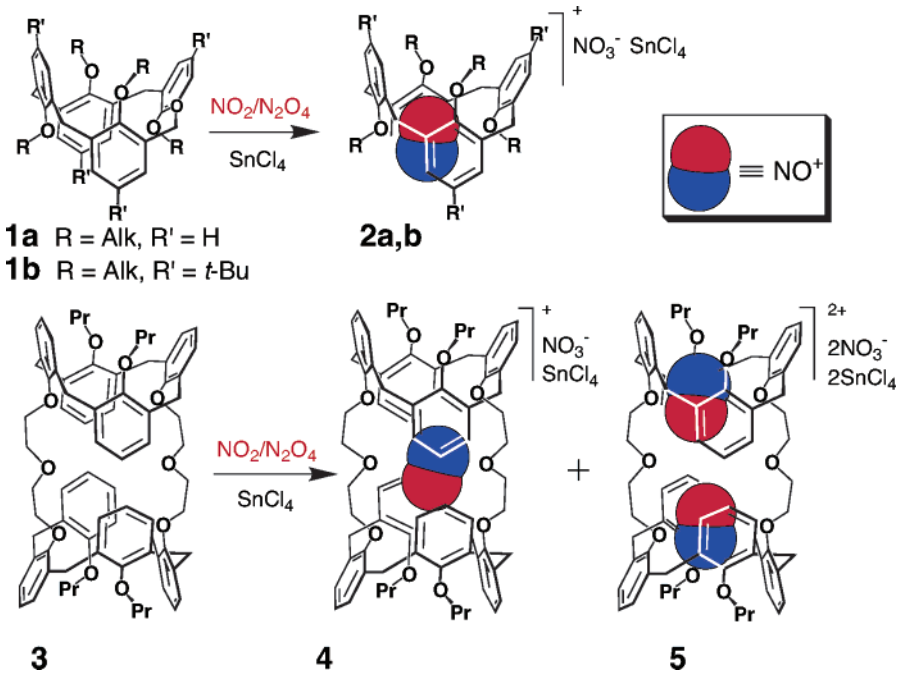


Figure 2. Calix[4]arenes **1a,b** and tube **3** and their nitrosonium complexes **2a,b**, **4**, and **5**.

improved methods of their fixation. In addition, we feel that our approach may lead to further progress in supramolecular chemistry of synthetic nanotubes, especially multiple guest encapsulation, their dynamics, and relations within enclosed spaces.

Results and Discussion

Design and Synthesis. Calixarene-based nanotubes were introduced by Shinkai 10 years ago.[5a] These were designed for small metal ions and represented, probably, the first synthetic nanotubes in molecular recognition. In contrast to cavitands, carcerands, and self-assembling capsules,[7] nanotubes are open from both ends and, besides their larger dimensions, possess different guest dynamics. We recently discovered that simple calix[4]arenes, for example **1a,b** (Figure 2), reversibly interact with NO_2/N_2O_4 and entrap highly reactive nitrosonium (NO^+) cation within their π-electron-rich interiors.[8] NO^+ is generated from N_2O_4, which is known to disproportionate to $NO^+NO_3^-$. Stable nitrosonium complexes **2a,b** were quantitatively isolated upon addition of a Lewis acid $SnCl_4$. Only one NO^+ cation was found per cavity; very high association constants $K_{assoc} \gg 10^6$ M^{-1} were determined.

In the design of nanotubes, several calix[4]arenes should be rigidly connected from both sides of their rims, with at least two symmetrical bridging units. This is possible for a 1,3-alternate conformation. Calix[4]arenes in a 1,3-alternate conformation are much more rigid than other conformers and possess a cylindrical inner tunnel, defined by two cofacial pairs of aromatic rings oriented orthogonally along the cavity axis. According to a number of X-ray studies, this tunnel is ~5−6 Å in diameter. Two pairs of phenolic oxygens are oriented in opposite directions, providing a diverse route to enhance the tube length modularly.

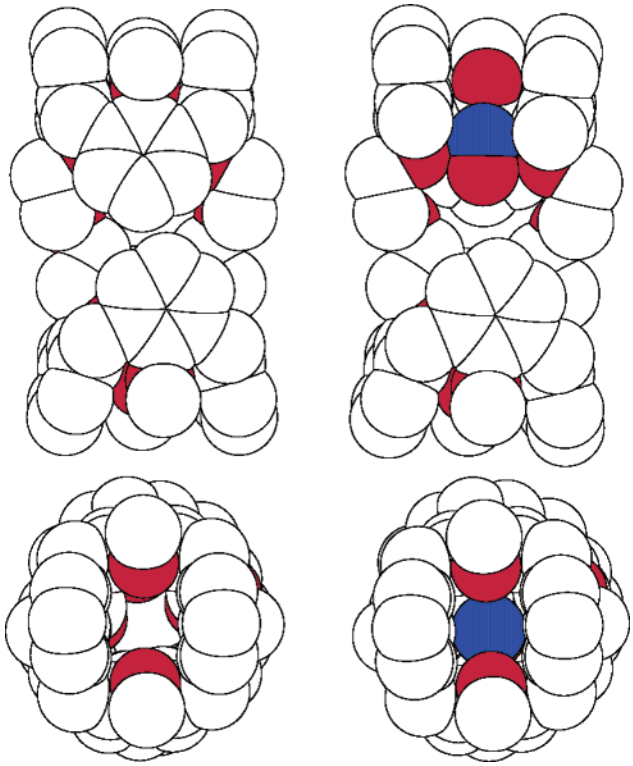
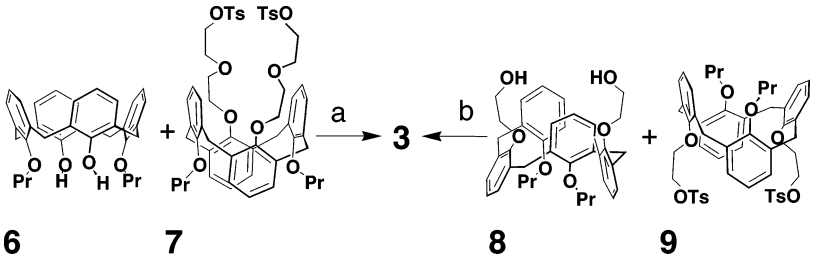


Figure 3. MacroModel 7.1 (Amber* Force Field) representation of tubular stricture **3** and its complex with NO^+, side and top views. The alkyl chains and hydrogens were removed for clarity. In complex **5**, the front aromatic ring is omitted to reveal the encapsulated species.

Described here molecule **3** is a bis-calixarene tube, designed to entrap up to two NO^+, one per each cavity. It possesses the inner tunnel of ~5 × 11 Å dimensions and thus represent a first generation of calixarene nanotubes for NO_2/N_2O_4 fixation and conversion. Two 1,3-alternate calix[4]arenes in **3** are connected via their phenolic oxygens through two diethylene glycol bridges (Figure 3). By our calculations, the bridge length is quite optimal: it not only provides relatively high confor-

(6) U. S. EPA site: http://www.epa.gov./air/urbanair/nox.
(7) Rudkevich, D. M. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 393−413.
(8) (a) Zyryanov, G. V.; Kang, Y.; Rudkevich, D. M. *J. Am. Chem. Soc.* **2003**, *125*, 2997−3007. (b) Zyryanov, G. V.; Kang, Y.; Stampp, S. P.; Rudkevich, D. M. *Chem. Commun.* **2002**, 2792−2793.

Scheme 1. (a) Cs_2CO_3, MeCN, Reflux, 48 H, 9%; (b) NaH, DMF, 80 °C, 48 H, 13%



mational rigidity of the tubular structure but also seals the walls, minimizing the gaps between the calixarene modules.

The synthesis of tube **3** was accomplished by two independent routes—either through alkylation of dipropyloxycalix[4]arene **6**[9] with ditosylate **7** or by coupling of diol **8** and ditosylate **9**[10] (Scheme 1). Ditosylate **7** was prepared in two steps from calixarene **6** and diethylene glycol monotosylate (Cs_2CO_3, MeCN, reflux), followed by the quantitative acylation of the resulting diol with TsCl (NaOH, H_2O−THF (THF = tetrahydrofuran)). Diol **8** was obtained by the basic hydrolysis of known ditosyl derivative **9** (KOH, H_2O−DMSO (DMSO = dimethyl sulfoxide, 110 °C). Preparation of calixarene **1** included the two-step alkylation of de-*tert*-butylated calix[4]arene with *n*-hexyl bromide, using successively K_2CO_3 and then Cs_2CO_3 in boiling MeCN.[8] This was used for comparison and also in the guest exchange experiments.

Host−Guest Chemistry. We found that tube **3** can be used for fixation and conversion of NO_2/N_2O_4. Upon bubbling NO_2/N_2O_4 through the solution of **3** in chlorinated solvents in the presence of $SnCl_4$, two nitrosonium complexes **4** and **5** were identified and subsequently isolated in preparative quantities. When performed in $CHCl_3$, the reaction resulted in instant precipitation of dark-purple solid, assigned as complex **4** (Figure 2). In $(CHCl_2)_2$ solution, complex **5** formed. The use of CH_2Cl_2 resulted in a mixture of **4** and **5**.

Adducts **4** and **5** possess typical features of calixarene−NO^+ complexes.[11] In the UV−vis spectra of **4** and **5** in CH_2Cl_2, broad charge-transfer bands at $\lambda_{max} = 540$ and 515 nm were recorded, respectively, and the FTIR spectra exhibited a characteristic[12] arene−*NO*$^+$ stretching at $\nu = 1932$ and 1948 cm^{-1}, respectively. The ^1H NMR spectra in $(CDCl_2)_2$ produce new sets of signals, different from those of empty tube **3** (Figure 4). In particular, the aromatic protons of free **3** were seen as a pair of doublets at 7.21 and 7.02 ppm and a pair of triplets at 7.00 (overlap) and 6.86 ppm. In complex **4**, these were transformed into a multiplet centered at ~7.1 ppm and a triplet at 6.96 ppm. In complex **5**, these signals appeared as doublets at 7.26 and 7.10 ppm and triplets at 7.35 and 6.29 ppm. The CH_2 methylene bridge, the propyl OCH_2, and the glycol CH_2OCH_2 and $ArOCH_2$ protons of **3** were seen as an apparent singlet and three triplets, 2:1:1:1, at 3.88, 3.26, 3.55, and 2.59 ppm, respectively. In

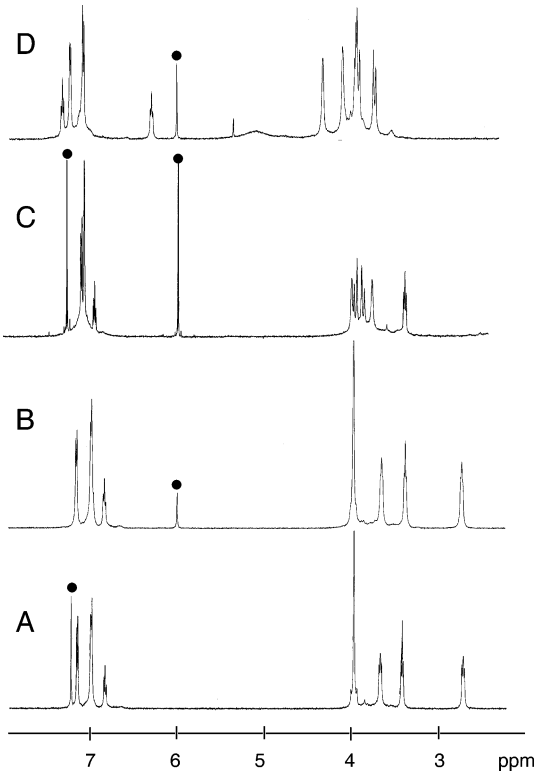


Figure 4. Selected portions of the ^1H NMR spectra (500 MHz, 295 ± 1 K) of (A) calix[4]arene tube **3** in $CDCl_3$, (B) **3** in $(CDCl_2)_2$, (C) mononitrosonium complex **4** in $(CDCl_2)_2$, and (D) dinitrosonium complex **5** in $(CDCl_2)_2$. The residual solvent signals are marked with "•".

complexes **4** and **5**, these changed and shifted. We will inspect their behavior below.

The guest stoichiometry in **4** and **5** was estimated by ^1H NMR through NO^+ exchange in $(CDCl_2)_2$.[13] Specifically, when **5** was mixed with empty **3**, complex **4** formed exclusively. No spectral changes were recorded upon mixing **3** and **4**. Further, when mixed with monomeric calixarene host **1b**, complex **5** generated nitrosonium complexes **2b** and **4**. At the same time, no exchange was observed upon mixing **1b** and **4**. Accordingly, complex **4** possesses one NO^+ guest, and complex **5** encapsulates two of them. Further, upon bubbling NO_2/N_2O_4 through the solution of **4** and $SnCl_4$ in $(CDCl_2)_2$, complex **5** emerges; this process can be clearly followed by ^1H NMR spectroscopy. Higher stoichiometries of NO^+ were ruled out: there is simply no room to accommodate more than two electrostatically repulsive cations.

(9) Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing, M.-J.; Egberink, R. J. M.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767−2777.

(10) Kim, J. S.; Shon, O. J.; Ko, J. W.; Cho, M. H.; Yu, I. Y.; Vicens, J. *J. Org. Chem.* **2000**, *65*, 2386-2392.

(11) Kochi, Rathore, and co-workers generated calix[4]arene•NO^+ complexes from nitric oxide (NO) and calixarene cation radicals and from NO^+SbCl_6 and calixarenes. In the solid state, the NO^+ cation was found tightly encapsulated within the calixarene cavity. See: Rathore, R.; Lindeman, S. V.; Rao, K. S. S. P.; Sun, D.; Kochi, J. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 2123−2127.

(12) Borodkin, G. I.; Shubin, V. G. *Russ. Chem. Rev.* **2001**, *70*, 211−230.

(13) Due to the high thermal and moisture sensitivity, attempts to obtain satisfactory mass-spectrometry data on nitrosonium complexes **4** and **5** have had a limited success. To date, a MALDI-TOF signal for **4** was detected in $(CDCl_2)_2$ at *m*/*z* 1186 ([**3** + NO]$^+$, calcd for $C_{76}H_{84}O_{10}$•NO 1186.6) along with decomposition and nitration products.

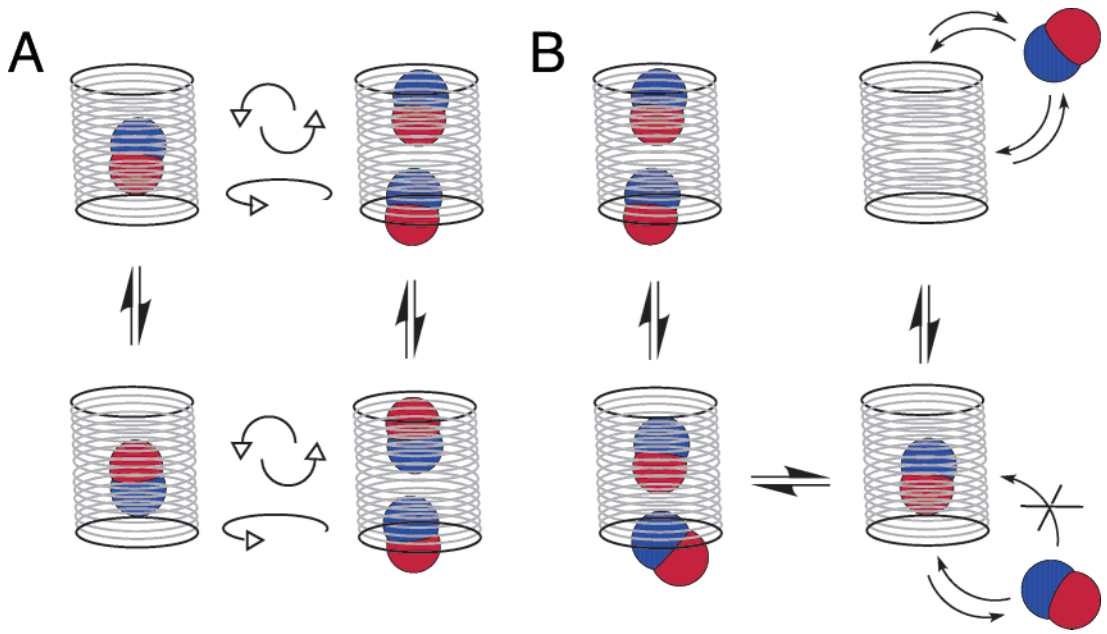


Figure 5. Guest dynamics: (A) rotation and tumbling inside tube **3** and (B) in−out exchange.

For further structural identification, calixarene tube **3** was mixed with the commercially available nitrosonium source, $NO^+SbF_6^-$, in $(CDCl_2)_2$, producing within 1−2 h a mixture of mono- and dinitrosonium complexes, analogous to **4** and **5** (UV−vis, ^{1}H NMR; 295 ± 1 K).

Complexes **4** and **5** are stable in dry solution at room temperature for days but can be readily destroyed with H_2O, quantitatively regenerating free **3**.

^{1}H NMR Spectroscopy. The guest(s) orientation, dynamics, and relations in tube-shaped complexes **4** and **5** were further studied by ^{1}H NMR spectroscopy, which proved to be a very useful and delicate tool. The NO^+ complexation apparently does not influence the symmetry of the host **3** (at 295 ± 5 K). Despite the nonequivalence of the methylene bridge, CH_2 protons becomes more pronounced, the number of the propyl OCH_2, the glycol CH_2OCH_2 and $ArOCH_2$, and the aromatic ^{1}H NMR signals (Figure 4) for **4** and **5** does not change. This implies that the NO^+ guest(s), with the van der Waals dimensions ∼2 Å,[12] freely rotates along the N−O axis and also tumbles within the cavity at room temperatures (Figure 5A). Similar dynamics was previously noticed for simpler calixarene−NO^+ complexes.[8,11]

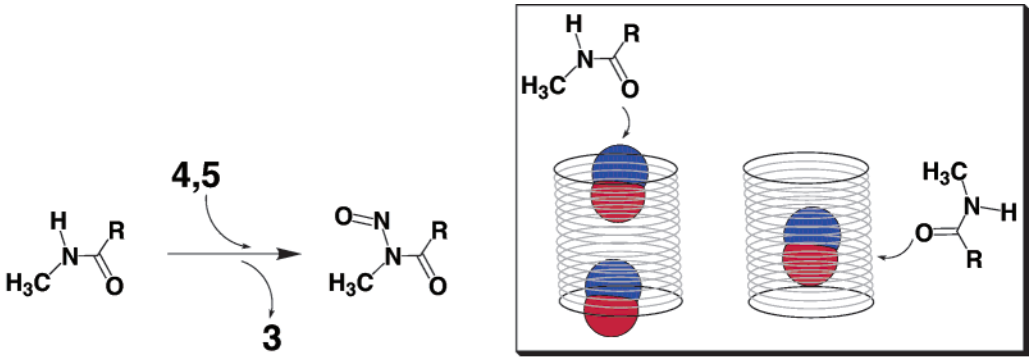
Significant (>1 ppm) downfield shifts of the glycol chain Ar−O−CH_2 and CH_2−O−CH_2 protons in both complexes, compared to empty **3** (Figure 4B−D), imply strong cation−dipole interactions between the glycol oxygens and NO^+. Complexes between NO^+ and simple crown ethers are known.[14−15] Apparently, NO^+ is situated in the middle of structure **4,** simultaneously interacting with the tube benzene edges and the glycol chains. In this arrangement, the propyl Ar−O−CH_2 protons in **4** appear far away from the complexed NO^+ and should not change their chemical shift compared to empty tube **3**. This is indeed the case (Figure 4C) and also suggests that the guest does not freely migrate along the tubular inner space, hopping between two calixarene units.[16]

In dinitrosonium complex **5**, the propyl Ar−O−CH_2 protons are seen downfield from those in empty **3**. Similar shifts were observed for the first generation of calixarene−NO^+ complexes **2a**[8] and **2b**. Obviously, two NO^+ cations in **5** are electrostatically pushed away from each other toward the ends of tube **3** (Figure 5B).

Electrostatic repulsions are most likely responsible for the smooth NO^+ exchange between **5** and **3**, leading to **4**, and between **5** and **1b**, leading to **4** and **2b**. At the same time, mononitrosonium species **4** are more stable and do not visibly exchange with **1b** for days. Accordingly, there is a communication between the two guests within the interior **5**.[17,18]

Upon stepwise addition of $NO^+SbF_6^-$ or NO_2/N_2O_4 to **3** in $(CDCl_2)_2$, ^{1}H NMR signals of **3**−**5** can be seen separately, sharp and in slow exchange. This is typical for the host−guest complexes with high exchange $\Delta G^‡$ barriers (>15 kcal/mol) and/or high K_{assoc} > 10^6 M^{-1} values.[7,19] Molecular modeling suggests that the first NO^+ can enter the tube either through its neck/bottom and then channel to the middle, or through the gate between the two calixarenes (Figure 5B). Complex **4** thus forms. To avoid electrostatic repulsions, the second NO^+ can only enter through the neck/bottom, thus further pushing the first guest toward the tube end. This results in complex **5**. The decomplexation sequence must be similar. Dinitrosonium complex **5** should release one NO^+ through the neck, while the second NO^+ in thus generated complex **4** may exit either through the

(14) Zolfigol, M. A.; Zebarjadian, M. H.; Chehardoli, G.; Keypour, H.; Salehzadeh, S.; Shamsipur, M. *J. Org. Chem.* **2001**, *66*, 3619−3620.
(15) Preliminary account on encapsulated nitrosating reagents, which are produced upon chemical fixation of NO_2/N_2O_4 by calix[4]arenes: Zyryanov, G. V.; Rudkevich, D. M. *Org. Lett.* **2003**, *5*, 1253−1256.
(16) For a detailed discussion of metal cation hopping between two calixarenes within the Shinkai's nanotubes, see ref 5b.
(17) This is in contrast to double-1,3-alternate-calixcrowns, where two calixarene units complex metal ions independently from each other: Kim, S. K.; Vicens, J.; Park, K.-M.; Kim, J. S. *Tetrahedron Lett.* **2003**, *44*, 993−997.
(18) For early examples of a multiple guests' communication inside capsules, see: (a) Tucci, F. C.; Rudkevich, D. M.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 4928−4929. (b) Starnes, S. D.; Rudkevich, D. M.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2001**, *123*, 4659−4669.
(19) Slow exchange in open-ended host−guest complexes with cavitands: (a) Rudkevich, D. M.; Hilmersson, G.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1998**, *120*, 12216−12225. (b) Lücking, U.; Tucci, F. C.; Rudkevich, D. M.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2000**, *122*, 8880−8889.



10a R = $(CH_2)_3CH_3$ **11a** R = $(CH_2)_3CH_3$, R' = CH_3
10b R = $(CH_2)_6CH_3$ **11b** R = $(CH_2)_6CH_3$, R' = CH_3

Figure 6. *N*-Nitrosation of amides **10** with encapsulated reagents **4** and **5**. Right: proposed prereactice complexes for di- and mononitrosonium molecular tubes.

middle gate or through the neck. These unique properties are the direct result of an open-ended tubular structure of **3**.

Chemical Reactions with Encapsulated Nitrosonium. Chemical properties of the encapsulated within **4** and **5** NO^+ species were also tested and found to be *different* from those in bulk solution. They are controlled by the cavity. Highly reactive NO^+ species are protected from the bulk environment. Complexes **4** and **5** are quite stable toward moisture and oxygen, and can be handled, for hours without drybox and/or nitrogen atmosphere. On the other hand, they can be quickly decomposed by addition of large quantities of H_2O, recovering free calixarene **3**. Such stability of arene−nitrosonium complexes is remarkable.[12]

We determined that complexes **4** and **5** may act as mild nitrosating reagents—encapsulated reagents.[15] When added to the equimolar solution of secondary amide **10a,b** in freshly distilled $CHCl_3$, they reacted instantly at room temperature, yielding *N*-nitrosoamides **11a,b** (Figure 6). Complex **4** reacts with lower yields (∼10−15%), and much better results were achieved with complex **5**, where the yields are ∼50%. Dark-purple solutions of **4** and **5** quickly discharged upon addition of **10a,b**, which serves as a visual test for the reaction. In the ^1H NMR spectra of the reaction mixtures, signals for amides **10a,b** and complexes **4** and **5** disappeared and characteristic signals for *N*-nitrosoamides **11a,b** at ∼3.2 ppm (2 H, t, C(O)-CH_2) and ∼3.1 ppm (s, 3 H, N(NO)-CH_3) and for nitrosonium-free calixarene **3** were detected (Figure 7).

Mechanistically, nitrosation of secondary amides incorporates an electrophilic attack of NO^+ on a nucleophilic carbonyl oxygen of the substrate, yielding the corresponding *O*-nitroso species.[20] Rapid deprotonation, rotation around the C−O bond, and inversion through the nitrogen results in the intermediate, in which both the nitrogen lone pair and the NO group are properly oriented for the isomerization to the *N*-nitrosoamide. Substrates **10a,b** thus approach tubes **4** and **5**, facing them with the carbonyl oxygen (Figure 6, right). In complex **4**, the reaction most probably occurs through the middle gate. Otherwise, the NO^+ should migrate first through the tube. In complex **5**, the reaction with the first NO^+ should occur within the neck/bottom

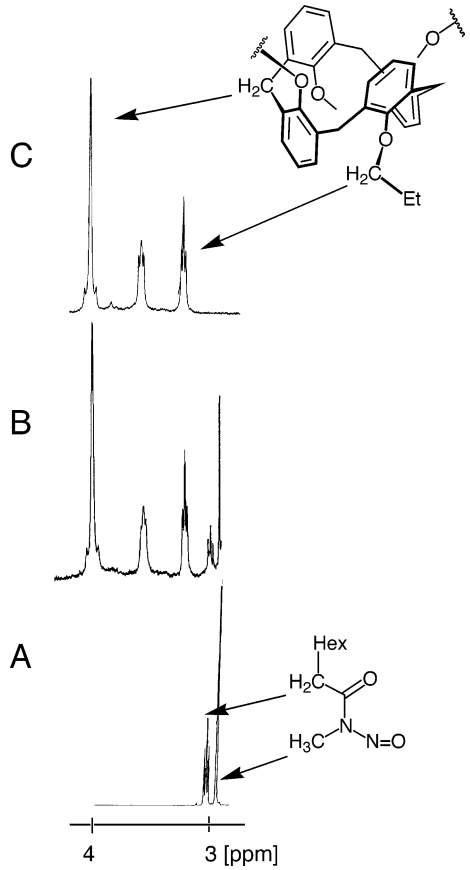


Figure 7. ^1H NMR analysis of a nitrosation reaction (500 MHz, $CDCl_3$, 295 ± 1 K): (A) *N*-nitrosoamide **11b**, independently obtained from amide **10b** and NO_2/N_2O_4 for spectral comparison; (B) reaction mixtures **5** + **10b** after 1 h; (C) guest-free calixarene tube **3**.

of the tube. Such guest dynamics, probably, explains differences between **4** and **5** in the nitrosation yields.

Once formed, the *O*-nitroso intermediate leaves the interior and further collapses in bulk solution, as expected.[20] Due to the extremely strong binding of NO^+ species in **4** and **5**, the rate-limiting formation of the *O*-nitrosation intermediates should take place within the cavity, *prior* to the NO^+ dissociation.

In organic chemistry, nitrosation holds a special place. Alkyl nitrites, nitrosamines/amides, and nitrosothiols are used in

(20) Darbeau, R. W.; Pease, R. S.; Perez, E. V. *J. Org. Chem.* **2002**, *67*, 2942−2947, and references therein.

biomedicine as NO-releasing drugs.[21] In total synthesis and methodology, −N═O is an important activating group, allowing elegant transformations of amides to carboxylic acids and their derivatives.[22] In addition, nitrosation mimics interactions between biological tissues and environmentally toxic NO_x gases.[23] Tube **3** thus converts NO_2/N_2O_4 into mild and effective nitrosating reagents. Tight but reversible encapsulation of NO^+ species should offer regioselectivities and size−shape selectivities, previously unknown for existing, more aggressive nitrosating agents (e.g., NO^+ salts, N_2O_3, NO_2/N_2O_4, NO/O_2, HNO_2, etc.).[15]

Conclusions and Outlook

Synthetic nanotubes can now be prepared for chemical entrapment and conversion of NO_2/N_2O_4. These are based on calix[4]arenes and take advantage of their extremely diverse chemistry. Such nanotubes may act as encapsulated nitrosating reagents, thus opening a novel opportunity for NO_2/N_2O_4 utilization. There is also a potential sensory application, since dramatic color changes are involved. Finally, in contrast to cavitands, carcerands, and capsules,[7] supramolecular chemistry of synthetic nanotubes is unexplored. We are now utilizing our design and strategy for the preparation of longer calixarene tubes for supramolecular gas storage and fixation.[24] We are also exploring regio- and stereoselective nitrosation processes with encapsulated nitrosonium guests.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded at 295 ± 1 °C on a JEOL Eclipse 500 MHz spectrometer. Chemical shifts were measured relative to residual nondeuterated solvent resonances. FTIR spectra were recorded on a Bruker Vector 22 FTIR spectrometer. UV−vis spectra were measured on a Varian Cary-50 spectrophotometer. MALDI-TOF mass spectra were recorded on a delayed-extraction MALDI-TOF mass spectrophotometer Voyager DE (Applied Biosystems). HRMS MALDI spectra were obtained on an Ion Spec Ultima FTMS. Elemental analysis was performed on a Perkin-Elmer 2400 CHN analyzer. All experiments with moisture- and/or air-sensitive compounds were run under a dried nitrogen atmosphere. For column chromatography, Silica Gel 60 Å (Sorbent Technologies, Inc.; 200−425 mesh) was used. Parent tetrahydroxycalix[4]arene[25] was prepared according to the published procedures. NO_2/N_2O_4 was generated from copper and concentrated HNO_3. Molecular modeling was performed using commercial MacroModel 7.1 with Amber* Force Field.[26]

Caution 1: NO_2 has an irritating odor and is very toxic! Caution 2: *N*-Nitrosoamides are carcinogens[27] and should be treated with extreme care!

5,11,17,23-Tetra-*t*-butyl-25,26,27,28-tetrakis(*n*-hexyloxy)calix[4]arene, 1,3-Alternate (1b). Prepared by the two-step alkylating procedure described in details in the previous studies.[8] Yield 42%, mp 232 °C; ^{1}H NMR ($CDCl_3$) δ 6.95 (s, 8 H), 3.73 (s, 8 H), 3.38 (t, J = 7.5 Hz, 8 H), 1.28 (s, 36 H), 1.25−1.1 (m, 32 H), 0.86 (t, J = 7.5 Hz, 12 H); ^{13}C NMR ($CDCl_3$) δ 154.8, 143.4, 133.1, 126.0, 70.8, 39.0, 33.9, 32.0, 31.8, 31.7, 29.7, 25.6, 23.0, 14.2; MALDI-TOF, *m*/*z* 985.71 ($[M + H]^+$; calcd for $C_{68}H_{105}O_4$, 985.80), 1007.93 ($[M + Na]^+$; calcd for $C_{68}H_{104}O_4Na$, 1007.78).

25,27-Bis(hydroxy(ethyloxyethyl)oxy)-26,28-bis(1-propyloxy)-calix[4]arene, 1,3-Alternate. 25,27-Dihydroxy-26,28-bis(1-propyloxy)-calix[4]arene (**6**;[9] 1 g, 1.96 mmol), diethylene glycol monotosylate (1.53 g, 5.88 mmol), and Cs_2CO_3 (9.59 g, 30 mmol) in MeCN (100 mL) were refluxed under nitrogen for 24 h. The solution was evaporated to dryness, diluted with CH_2Cl_2 (100 mL), and neutralized with 5% aqueous HCl (100 mL). The organic layer was separated, washed with water (3 × 100 mL), and evaporated. Column chromatography ($CHCl_3$−acetone, 8:2) afforded the product (R_f = 0.21) as a colorless oil. Yield 0.13 g (10%); ^{1}H NMR ($CDCl_3$) δ 7.07 (d, J = 7.5 Hz, 4 H), 7.03 (d, J = 7.5 Hz, 4 H), 6.79 (t, J = 7.5 Hz, 2 H), 6.74 (t, J = 7.5 Hz, 2 H), 3.79−3.76 (m, 8 H), 3.67 (2 × d, J = 15.0 Hz, 8 H), 3.61−3.58 (m, 8 H), 3.52 (t, J = 7.8 Hz, 4 H), 1.59−1.52 (m, 4 H), 0.87 (t, J = 7.5 Hz, 6 H); ^{13}C ($CDCl_3$) δ 156.6, 155.9, 133.9, 130.4, 130.2, 122.7, 122.4, 73.0, 72.8, 71.3, 70.1, 61.7, 37.0, 23.2, 10.3; MALDI−FTMS 707.3540 ($[M + Na]^+$; calcd for $C_{42}H_{52}O_8Na$, 707.3554).

25,27-Bis(2-*p*-toluenesulfonyl(bisoxyethyl)oxy)-26,28-bis(1-propyloxy)calix[4]arene, 1,3-Alternate (7). A solution of NaOH (1.96 g, 49 mmol) in water (10 mL) was added dropwise to the mixture of the above-described compound (1.34 g, 1.96 mmol) and TsCl (1.86 g, 9.8 mmol) in THF (100 mL), upon cooling on an ice bath. After 24 h of stirring at room temperature, the solvents were evaporated. Column chromatography on silica gel (EtOAc−hexane, 1:1) afforded product **7** (R_f = 0.6) as a colorless oil. Yield 1.95 g (>95%); ^{1}H NMR ($CDCl_3$) δ 7.80 (d, J = 8.5 Hz, 4 H), 7.31 (d, J = 8.5 Hz, 4 H), 6.98 (d, J = 7.5 Hz, 4 H), 6.96 (d, J = 7.5 Hz, 4 H), 6.69 (t, J = 7.5 Hz, 2 H), 6.61 (t, J = 7.5 Hz, 2 H), 4.17 (t, J = 7.0 Hz, 4 H), 3.64, 3.61 (2 × t, J = 7.0 Hz, 8 H), 3.59 (2 × d, J = 15.0 Hz, 8 H), 3.50, 3.45 (2 × t, J = 7.0 Hz, 8 H), 1.61−1.55 (m, 4 H), 0.89 (t, J = 7.5 Hz, 6 H).

(25,27-Bis(2-hidroxyethyloxy)-26,28-bis(1-propyloxy)calix[4]-arene, 1,3-Alternate (8). 25,27-Bis(2-*p*-toluenesulfonyloxyethyloxy)-26,28-bis(1-propyloxy)calix[4]arene (**9**;[10] 1.2 g, 1.3 mmol) was dissolved in DMSO (45 mL), KOH (1.54 g, 27.4 mmol), and water (10 mL). The reaction mixture was heated at 110 °C for 2−4 h and monitored by thin-layer chromatography (TLC) (hexanes−EtOAc, 5:1), then diluted with CH_2Cl_2 (100 mL), and cooled to −5 °C, after which 5% aqueous HCl (100 mL) was added. The organic layer was separated, washed with water (3 × 100 mL), and evaporated. The residue was passed through the column with silica gel (hexanes−EtOAc, 5:1) to

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afford **8** as a colorless oil. Yield 0.72 g (90%); ^{1}H NMR ($CDCl_3$) δ 7.05 (d, $J = 7.5$ Hz, 4 H), 7.01 (d, $J = 7.5$ Hz, 4 H), 6.82 (t, $J = 7.0$ Hz, 2 H), 6.78 (t, $J = 7.0$ Hz, 2 H), 3.83 (2 × d, $J = 16.5$ Hz, 8 H), 3.58−3.61 (m, 4 H), 3.40 (t, $J = 7.0$ Hz, 8 H), 3.02−2.99 (m, 4 H), 1.31−1.27 (m, 4 H), 0.68 (t, $J = 7.5$ Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 157.1, 156.2, 133.9, 133.7, 129.5, 129.4, 122.9, 122.8, 72.0, 71.1, 61.3, 38.3, 22.3, 10.0; MALDI−FTMS, *m*/*z* 619.3061 ([M + Na^+]; calcd for $C_{38}H_{44}O_6Na$, 619.3030).

Calix[4]arene Tube (3). (A) Procedure A. A mixture of 25,27-dihydroxy-26,28-bis(1-propyloxy)calix[4]arene (**6**; 1 g, 1.96 mmol), 25,-27-bis(2-*p*-toluenesulfonyl(bis(oxyethyl))oxy)-26,28-bis(1-propyloxy)-calix[4]arene (**7**; 1.95 g, 1.96 mmol) and Cs_2CO_3 (9.59 g, 30 mmol) in MeCN (100 mL) was refluxed under nitrogen for 36−48 h. The solvent was evaporated, and the residue was diluted with CH_2Cl_2 (100 mL) and 5% aqueous HCl (100 mL). The organic layer was then separated, washed with water (3 × 100 mL), and evaporated. Column chromatography (EtOAc−hexanes, 1:10) afforded product **3** ($R_f = 0.15$) as a white crystalline solid. Yield 0.2 g (9%); mp > 250 °C; ^{1}H NMR ($CDCl_3$) δ 7.18 (d, $J = 7.5$ Hz, 8 H), 7.03−6.99 (d + t, 12 H), 6.84 (t, $J = 7.5$ Hz, 4 H), 3.89 (2 × d, $J = 17.0$ Hz, 16 H), 3.57 (t, $J = 7.0$ Hz, 8 H), 3.31 (t, $J = 7.0$ Hz, 8 H), 2.58 (t, $J = 7.5$ Hz, 8 H), 1.09−1.05 (m, 8 H), 0.56 (t, $J = 7.0$ Hz, 12H); ^{13}C NMR ($C_2D_2Cl_4$) δ 157.5, 156.2, 134.2, 134.1, 123.3, 122.3, 120.0, 72.0, 71.6, 69.2, 66.5, 38.3, 30.3, 22.8, 10.5; MALDI−FTMS, *m*/*z* 1179.5939 ([M + Na^+]; calcd for $C_{76}H_{84}O_{10}Na$, 1179.5956).

(B) Procedure B. 25,27-Bis(2-hydroxyethyloxy)-26,28-bis(1-propyloxy)calix[4]arene (**8**; 0.8 g, 1.3 mmol) was dissolved in dry DMF (100 mL), after which NaH (60% suspension in mineral oil, 0.127 g, 5.2 mmol) was added. 25,27-Bis(2-*p*-toluenesulfonyloxyethyloxy)-26,-28-bis(1-propyloxy)calix[4]arene (**9**; 1.2 g, 1.3 mmol) was separately dissolved in dry DMF (100 mL). Thus-prepared solutions of **8** and **9** were added dropwise to dry DMF (200 mL) at 60−70 °C in a 30 min period under nitrogen. The reaction mixture was stirred at 80−90 °C for an additional 48 h, evaporated to dryness, suspended in CH_2Cl_2 (100 mL), and neutralized at −10 °C with 5% aqueous HCl (100 mL). The organic layer was separated, washed with water (3 × 100 mL), and evaporated. Crystallization from MeCN afforded product **3** as a white crystalline solid. Yield 0.2 g (13%).

Mononitrosonium Complex (4). To a solution of **3** (0.005 g, 4 μmol) in dry, freshly distilled $CHCl_3$ (1 mL), $SnCl_4$ (0.005 g, 20 μmol) was added, and NO_2 was bubbled for 25−40 s, until purple precipitate formed. This was filtered, washed with $CHCl_3$ (2 × 1 mL), and dried under nitrogen flow. Yield >95%; ^{1}H NMR ($C_2D_2Cl_4$) δ 7.12−7.08 (m, 20 H), 6.96 (t, $J = 6.5$ Hz, 4 H), 4.01 (m, 8 H), 3.92, 3.86 (2 × d, $J = 16.5$ Hz, 16 H), 3.79 (m, 8 H), 3.34 (t, $J = 7.5$ Hz, 8 H), 1.05−1.01 (m, 8 H), 0.72 (t, $J = 8.0$ Hz, 12 H); ^{13}C NMR ($C_2D_2Cl_4$) δ 156.0, 134.3, 133.4, 130.9, 130.2, 124.4, 72.2, 71.0, 38.5, 29.9, 22.2, 10.0; UV−vis (CH_2Cl_2) λ_{max} 540 nm; FTIR ($C_2D_2Cl_4$) ν 1932 cm^{-1} (NO^+).

Dinitrosonium Complex (5). To a solution of **3** (0.005 g, 4 μmol) in $(CDCl_2)_2$ (2 mL), $SnCl_4$ (0.005 g, 20 mmol) was added, and NO_2/N_2O_4 was bubbled for 40 s. ^{1}H NMR ($C_2D_2Cl_4$) δ 7.35 (t, $J = 7.5$ Hz, 4 H), 7.26 (d, $J = 7.0$ Hz, 8 H), 7.10 (d, $J = 8.0$ Hz, 8 H), 6.29 (t, $J = 7.5$ Hz, 4 H), 4.25 (m, 8 H), 4.02 (m, 8 H), 3.86 (t, $J = 7$ Hz, 8 H),), 3.83, 3.64 (2 × d, $J = 14$ Hz, 16 H), 1.91−1.87 (m, 8 H), 1.07 (t, $J = 7.5$ Hz, 12 H); ^{13}C NMR ($C_2D_2Cl_4$) δ 162.0, 152.6 133.6, 133.0, 132.9, 132.4, 129.1, 75.4, 75.2, 71.3, 36.6, 29.9, 24.0, 10.6; UV−vis (CH_2Cl_2) λ_{max} 515 nm; FTIR ($C_2D_2Cl_4$) ν 1948 cm^{-1} (NO^+).

Preparation of Nitrosonium Complex (2b). (A) Procedure 1. NO_2/N_2O_4 gas was bubbled for 20 s through the solution of calixarene **1b** (25 mg, 2.5×10^{-5} mol) and $SnCl_4$ (3 mL, 2.6×10^{-5} mol) in dry $CHCl_3$ (0.5−1.0 mL). The solvent was evaporated under the steam of dry nitrogen. The dark-blue precipitate was dissolved in dry $CHCl_3$ (0.5−1.0 mL) and used for further reactions.

(B) Procedure 2. A stock solution of NO_2 (~3 equiv) in $CHCl_3$ was added to the solution of **1b** (1 equiv) and $SnCl_4$ (1.5 equiv) in $CHCl_3$ at room temperature. After 1 h, complex **2b** was precipitated upon addition of hexanes, filtered off, washed with hexanes (2×), and dried in vacuo. Yield >95%; ^{1}H NMR δ 7.02 (s, 8 H), 3.77 (t, $J = 7.5$ Hz, 8 H), 3.60 (s, 8 H), 1.38 (m, 32 H), 1.30 (s, 36 H), 0.92 (t, $J = 7.5$ Hz, 12 H); UV−vis ($CDCl_3$) $\lambda_{max} = 578$ nm; FTIR ($CDCl_3$) ν (NO^+) = 1934 cm^{-1}. Anal. Calcd for $C_{68}H_{104}Cl_4N_2O_8Sn$: C, 61.04; H, 7.83; N, 2.09. Found: C, 60.96; H, 7.88; N, 2.09.

Nitrosation Procedure with Nitrosonium Complexes. Typical nitrosation protocol with calixarene−nitrosonium complexes is described previously.[15] Complex **4** or **5** (1 equiv) was added to a solution of amide **10a,b** (3−5 equiv) in freshly distilled $CHCl_3$, and the reaction mixture was stirred at room temperature for 2−3 h. The solvent was evaporated, and the residue was analyzed by ^{1}H NMR spectroscopy. All runs were performed at least in duplicate. The yields of *N*-nitroso amides **11a,b** were 10−15% for complex **4** as a nitrosating agent and 45−50% for complex **5** as a nitrosating agent. The spectral data for thus-obtained *N*-nitroso amides **11a,b** were identical with those independently obtained from amides **10a,b** and NO_2/N_2O_4 in $CHCl_3$ (>95% yields) following the literature protocols.[28] The starting amides **10a,b** were synthesized by the textbook procedure upon mixing equimolar amounts of the corresponding amines and acid chlorides in 1:1 H_2O−EtOAc in the presence of K_2CO_3 and purified by recrystallization from MeOH. No traces of the solvent were present in samples used for nitrosation (^{1}H NMR, $CDCl_3$).

(A) *N*-Methylvalerylamide (10a). Yield 62%; ^{1}H NMR δ 6.43 (bs, 1 H, NH), 2.69 (d, 3 H, $J = 5$ Hz, NCH_3), 2.09 (t, 2 H, $J = 7.5$ Hz, CH_2), 1.48−1.54 (m, 2 H, CH_2), 1.22−1.28 (m, 2 H, CH_2), 0.81 (t, 3 H, $J = 7.5$ Hz, CH_3).

(B) *N*-Methyloctanoylamide (10b). Yield 66%; ^{1}H NMR δ 6.13 (bs, 1 H, NH), 2.73 (d, 3 H, $J = 5$ Hz, NCH_3), 2.12 (t, 2 H, $J = 7.5$ Hz, CH_2), 1.53−1.58 (m, 2 H, CH_2), 1.22−1.28 (m, 8 H, 4 × CH_2), 0.83 (t, 3 H, $J = 7.5$ Hz, CH_3).

(C) *N*-Methyl-*N*-nitrosovaleramide (11a).[29] ^{1}H NMR d 3.17 (t, 2 H, $J = 8$ Hz, $CH_2C(O)$), 3.10 (s, 3 H, $N(NO)CH_3$), 1.75−1.81 (m, 2 H, CH_2), 1.40−1.47 (m, 2 H, CH_2), 0.95 (t, 3 H, $J = 8$ Hz, CH_3).

(D) *N*-Methyl-*N*-nitrosooctanoylamide (11b).[29,30] ^{1}H NMR d 3.19 (t, 2 H, $J = 7.5$ Hz, $CH_2C(O)$), 3.12 (s, 3 H, $N(NO)CH_3$), 1.72−1.81 (m, 2 H, CH_2), 1.26−1.41 (m, 8 H, $(CH_2)_4$), 0.86 (t, 3 H, $J = 7.5$ Hz, CH_3).

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