Cofacial Phenylene Donors as Novel Organic Sensors for the Reversible Binding of Nitric Oxide

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The stilbenoid hydrocarbon ligand "venus flytrap" (VFT) forms the basis for the noncovalent binding of nitric oxide by strong charge-transfer (CT) forces.[1] Thus, the green cation radical (VFT[•+]) upon exposure to NO immediately afforded the blue adduct [VFT, NO][+], the molecular structure of which showed nitric oxide to fit neatly within the cleft between the cofacial pentamethylphenyl moieties. The tightly (CT) bound nitric oxide could only be extricated by complete reduction (to rapidly regenerate the neutral VFT and nitric oxide), i.e.

$$[VFT, NO]^+ \xrightarrow{+e} VFT + NO \quad (1)$$

We now confirm the reversible (redox-controlled) binding of NO by cyclic voltammetric analysis of VFT, which undergoes a reversible oxidation to VFT[•+] at $E^o_{ox} = 1.27$ V vs SCE in dichloromethane as presented in Figure 1A. However, the oxidation of VFT in the presence of NO shows an irreversible cyclic voltammogram (Figure 1B) in which the anodic peak ($E^p_{ox} = 1.27$ V vs SCE) corresponds to the oxidation of VFT to VFT[•+], whereas the cathodic peak ($E^p_{red} = 0.57$ V vs SCE)[2] on return scan represents the reduction of [VFT, NO][+], i.e.

$$VFT + NO \underset{-0.57 V}{\overset{+1.27 V}{\rightleftarrows}} [VFT, NO]^+ \quad (2)$$

Such a cyclic voltammogram in Figure 1B can be repeated indefinitely, and this electrochemical behavior is characteristic of chemically reversible (but electrochemically irreversible) redox systems[3] that are relevant to the construction of a variety of molecular sensors, switches, devices, etc.[4]

Contemporary biological interest in NO (as an important intercellular messenger[5] in a variety of physiological processes) prompted us to devise an organic chemical sensor for its reversible binding that can be controlled *thermally.* Indeed, we now identify the triptycene analogues **1**−**3** (Chart 1) with cofacial phenylene units[6] for the binding of nitric oxide. Most importantly, the reversible uptake and release of NO can be readily regulated by a simple temperature modulation, and the cyclic process can be carried out repeatedly. Thus, the highly persistent (bright yellow) dimethoxytriptycene cation radical (**1**[•+])[7] upon exposure to gaseous nitric oxide at −30 °C immediately turns green.
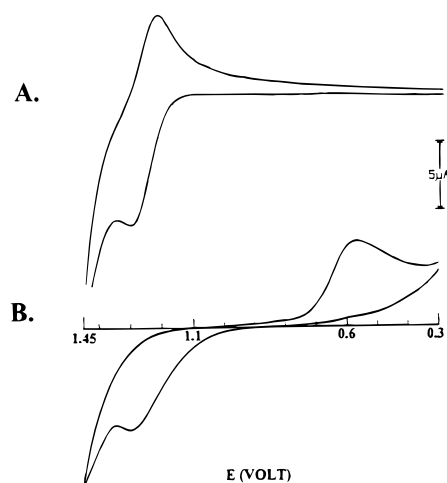
Figure 1. Cyclic voltammograms of (A) 5 mM VFT alone at 25 °C and (B) 5 mM VFT in the presence of NO (in excess) at −10 °C at a ∼1 mm² Pt disk electrode in anhydrous dichloromethane containing 0.2 M *n*-Bu$_4$N$^+$ PF$_6^-$ at a scan rate $\nu = 200$ mV s^{-1}.

Chart 1

	1		**2**		**3**	
E^o_{ox}	1.21		1.34		1.46	(V vs. SCE)
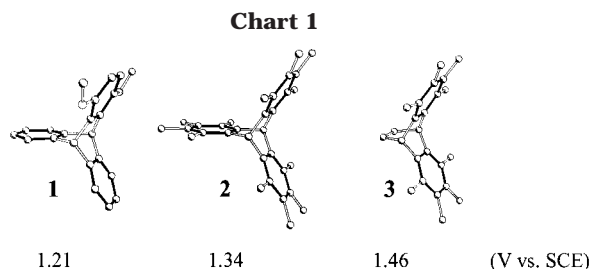
Infrared spectral analysis of the green solution indicated the quantitative entrapment of nitric oxide, as judged by the characteristic IR absorption at 1902 cm^{-1} due to a single N−O stretching frequency.[8] The green adduct [**1**, NO][+] is stable for prolonged periods if protected from air and moisture and spontaneously bleaches to yield the characteristic yellow triptycene cation radical **1**[•+] when it is warmed to room temperature, i.e.[9]

$$[\textbf{1}, NO]^+ \text{ (green)} \qquad \textbf{1}^{+\bullet} \text{ (yellow)} \quad (3)$$
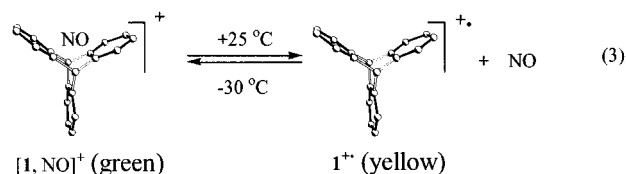
Moreover, the green color is completely restored upon recooling the solution to −30 °C, as monitored by UV−vis spectroscopy,[10] and this dramatic color change is completely

(1) Rathore, R.; Lindeman, S. V.; Kochi, J. K. *Angew. Chem., Int. Ed. Engl.* **1998,** *37,* 1585. Compare: Kim, E. K.; Kochi, J. K. *J. Am. Chem. Soc.* **1991,** *113,* 4962.

(2) An electrochemical reduction potential of $E^o_{red} = 0.58$ V vs SCE was independently measured for the blue adduct [VFT, NO][+] (2 mM) by cyclic voltammetry in dichloromethane (containing 0.2 M tetra-*n*-butylammonium hexafluorophosphate as supporting electrolyte).

(3) (a) Suzuki, T.; Kondo, M.; Nakamura, T.; Fukushima, T.; Miyashi, T. *J. Chem. Soc., Chem. Commun.* **1997,** 2325. (b) Suzuki, T.; Takahashi, H.; Nishida, J.; Tsuji, T. *J. Chem. Soc., Chem. Commun.* **1998,** 1331. (c) Philp, D.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1996,** *35,* 1154 and references therein.

(4) Fabbrizzi, L.; Poggi, A. *Chem. Soc. Rev.* **1995,** 198. Also see: Feringa, B. L.; Jager, W. F.; de Lange, B. *Tetrahedron* **1993,** *49,* 8267.

(5) (a) Feldman, P. L.; Griffith, O. W.; Stuehr, D. J. *Chem. Eng. News* **1993,** Dec. 20, 26. (b) Culotta, E.; Koshland, Jr., D. E. *Science* **1992,** *258,* 1862 and references therein. (e) Keefer, L. K. *CHEMTECH* **1998,** *28,* 30.

(6) (a) The molecular structures of the rigid triptycene donors in Chart 1 are presented with the aid of the QUANTA graphics (Molecular Simulation Inc., 16 New England Executive Park, Burlington, MA 01803). (b) Donors **2** and **3** were prepared from triptycene (Aldrich) and 9,10-dihydro-9,10-ethanoanthracene (Wong, H. N. C.; Sondheimer, F. *Tetrahedron* **1981,** *37*(S1), 99), respectively, by repeated bromomethylation (van der Made, A. W.; van der Made, R. R. *J. Org. Chem.* **1993,** *58,* 1262) followed by hydrodebromination with lithium aluminum hydride. Donor **2:** yield 64%; mp >300 °C (EtOH); ^{1}H NMR (CDCl₃) δ 2.16 (s, 18H), 2.54 (s, 18H), 6.47 (s, 2H); ^{13}C NMR (CDCl₃) δ 15.63, 16.49, 44.18, 127.44, 130.95, 141.83; GC−MS *m/z* 422 (M$^+$), 422 calcd for C₃₂H₃₈. Anal. Calcd for C₃₂H₃₈: C, 90.94; H, 9.06. Found: C, 90.63; H, 8.87. Donor **3:** yield 92%; mp 211−213 °C (EtOH); ^{1}H NMR (CDCl₃) δ 1.79 (br s, 4H), 2.28 (s, 12H), 2.49 (s, 12H), 5.11 (s, 2H); ^{13}C NMR (CDCl₃) δ 15.54, 16.73, 25.60, 36.94, 127.42, 131.67, 140.09; GC−MS *m/z* 318 (M$^+$), 318 calcd for C₂₄H₃₀. Anal. Calcd for C₂₄H₃₀: C, 90.51; H, 9.49. Found: C, 90.32; H, 9.21.

reversible over multiple cooling/warming cycles. The same adduct [**1**, NO]$^+$ can also be obtained by mixing dimethoxy-triptycene **1** with a nitrosonium (NO$^+$) salt in dichloromethane at -30 °C, and when the green solution is warmed to room temperature it yields the characteristic yellow cation-radical **1**$^{•+}$ (see eq 3). The quantitative analysis of the head gas confirms the liberation of nitric oxide by the diagnostic N–O stretching band at 1876 cm^{-1} in the IR spectrum,[8] as well as the characteristic absorptions at $\lambda_{max} = 204, 214, 222$ nm in the UV spectrum.[11] Furthermore, in vacuo removal of the gaseous nitric oxide and solvent quantitatively leads to the yellow crystalline cation radical [**1**$^{•+}$ SbCl$_6^-$], the molecular structure of which was established by X-ray crystallography.[7] In other words, dimethoxytriptycene (**1**) readily binds NO by treatment of either (a) the cation-radical **1**$^{•+}$ with gaseous NO or (b) the neutral donor **1** with the nitrosonium (NO$^+$) salt;[12] their interconversion can be readily modulated thermally (see eq 3). A similar treatment of permethylated triptycene **2** (E^0_{ox} = 1.35 V vs SCE) with NO$^+$ salt at ~0 °C leads to the purple adduct [**2**, NO]$^+$, which upon warming to 25 °C simply affords the increasing amounts of cation-radical **2**$^{•+}$.[13]

To ascertain the structure of NO bound to the cofacial phenylene donors, we isolated a single crystal of the purple [**3**, NO]$^+$ from a mixture of dichloromethane and hexane at -23 °C.[15] X-ray crystallography[16] establishes a single molecule of nitric oxide to nestle between two cofacial phenylene rings, as shown by the space-filling representation in Figure 2. The N–O bond distance of 1.098 Å in [**3**, NO]$^+$ is consistent with a noncovalently bonded nitric oxide.[17] Moreover, the "tightness" of such a noncovalent (charge-transfer) binding[1] of nitric oxide is shown by the N and O thermal ellipsoids (relative to those of methyl carbons) in Figure 3.[18] On the basis of structural rigidity of the neutral
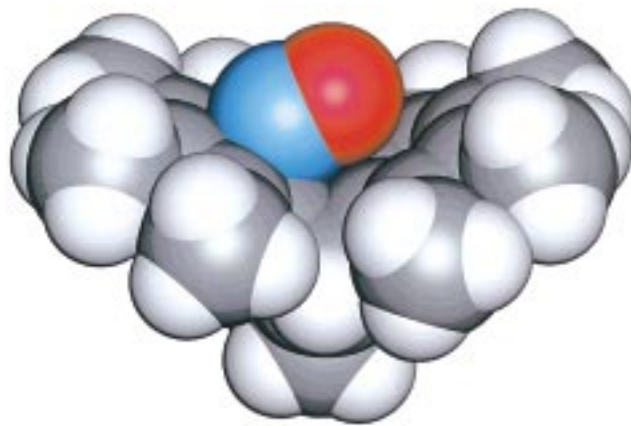
Figure 2. Space-filling representation of [**3**, NO]$^+$ showing the entrapped NO nestled within the cavity of cofacial phenylene donor.
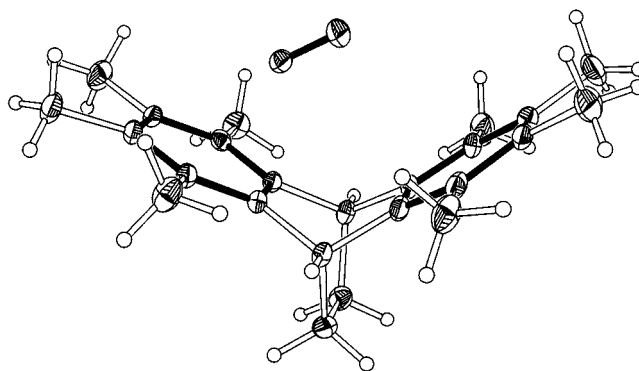
Figure 3. ORTEP diagram showing the tight CT binding and limited libration of the noncovalently bound nitric oxide in the [**3**, NO]$^+$ complex.

triptycene donors **1**–**3**, we believe that the molecular association of NO with **1** and **2** is similar to that observed for [**3**, NO]$^+$.

It is noteworthy that the temperature-dependent release and uptake of NO by triptycene donors stands in sharp contrast to the behavior of VFT, which only releases its NO upon complete reduction. As such, we have successfully demonstrated that triptycene donors with cofacial phenylene groups can be efficiently utilized as sensors for the reversible binding of nitric oxide at specified temperatures. The mechanism of the temperature-dependent binding of NO to various organic cation radicals and the isolation of crystalline adducts for solid-state sensors is currently under investigation.[19]

(7) For the ready preparation of cation radical **1**$^{•+}$ as the hexachloroantimonate salt, see: Rathore, R.; Kumar, A. S.; Lindeman, S. V.; Kochi, J. K. *J. Org. Chem.* **1998**, *63*, 5847.

(8) Note that the free NO absorbs at ν_{NO} = 1875 cm^{-1}. See: (a) Fateley, W. G.; Bent, H. A.; Crawford, B., Jr. *J. Chem. Phys.* **1959**, *31*, 204. (b) Laane, J.; Ohlsen, J. R. *Prog. Inorg. Chem.* **1980**, *27*, 465.

(9) The *p*-methoxy groups in triptycene donor **1** are omitted due to the ambiguous location of NO in adduct [**1**, NO]$^+$. An X-ray structural study in progress should establish this point.

(10) The characteristic absorption spectrum of the green adduct showed a maximum at λ_{max} = 440 nm and a broad band at λ_{max} = 640 nm.

(11) Bosch, E.; Rathore, R.; Kochi, J. K. *J. Org Chem.* **1994**, *59*, 2529.

(12) As hexachloroantimonate salt.

(13) The purple solution at 25 °C contained ~10% of triptycene cation-radical[14] **2**$^{•+}$ admixed with [**2**, NO]$^+$, as judged by the UV–vis absorption spectroscopy. However, prolonged heating of the purple solution (at >40 °C) led to the irreversible bleaching of the color.

(14) The same yellow-green cation-radical of permethylated triptycene **2** (λ_{max} = 348, and a very broad and intense band at >1100 nm) was obtained either electrochemically at E^0_{ox} = 1.34 V vs SCE or by chemical oxidation with a mixture of chloranil and methanesulfonic acid in dichloromethane (Rathore, R.; Kochi, J. K. *Acta Chem. Scand.* **1998**, *52*, 114).

(15) Note that the intense purple adduct [**3**, NO]$^+$, with UV–vis absorption bands at λ_{max} = 365 and 560 (br) nm, did not release its bound NO at room temperature.

(16) Crystal Data for [Octamethyl-9,10-dihydro-9,10-ethanoanthracene (**3**), NO]$^+$ [(C$_{24}$H$_{30}$)$^+$ NO·SbCl$_6^-$]. An X-ray quality crystal (0.3 × 0.15 × 0.1 mm) was obtained from a slow diffusion of hexane into a dichloromethane solution of [**3**, NO] $^+$ at -23 °C: MW = 682.94, triclinic, space group P1̄, *a* = 9.6158(1) Å, *b* = 12.6372(1) Å, and *c* = 13.2094(2) Å, α = 80.083(1)°, β = 71.311(1)°, γ = 70.09°; D_c = 1.590 Mg m^{-3}, V = 1426.64(3) Å^3, Z = 2. Data collection was carried out on a Siemens SMART diffractometer equipped with a CCD detector, using Mo Kα radiation (λ = 0.710 73 Å), at -150 °C. The total number of reflections measured was 18 044, of which 12 339 reflections were symmetrically nonequivalent. The structure was solved by direct methods and refined by a full-matrix least-squares procedure. Final residuals were $R1$ = 0.0554 and w$R2$ = 0.1370 for 12 339 reflections with $I > 2\sigma(I)$. [Note that the X-ray structure of [**3**, NO]$^+$ SbCl$_6^-$ was also determined at -30 °C, and details are on deposit and can be obtained from the Cambridge Crystallographic Data Center].

(17) (a) Keck, D. B.; Hause, C. D. *J. Mol. Spectrosc.* **1968**, *26*, 163. (b) Also note that the positive charge largely resides on the aromatic carbons as judged by the significant lengthening of the average C$_{ar}$–C$_{ar}$ distance (1.414 Å).

(18) Quantitatively, the limited NO libration is evident from a comparison of the magnitudes of the isotropic equivalent thermal parameters (U_{eq}) of N (0.017) and O (0.030) relative to those of methyl carbons (0.039).

(19) The thermally reversible binding of NO$^+$ as described in eq 3 is also observed with electron-rich aromatic donors (other than triptycene **1**–**3**) such as CRET,[20] tetraalkylated naphthalenes,[7] anthracenes, and triphenylenes[21] with reversible oxidation potentials generally in the range 1.0 < E^0_{ox} < 1.4 V vs SCE. In this regard, the temperature-independent binding of NO$^+$ by VFT with E^0_{ox} = 1.27 V is the clear exception, and the unique effect of the cofacial pentamethylphenyl rings[22] merits further scrutiny.

(20) Rathore, R.; Bosch, E.; Kochi, J. K. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1157.

(21) Rathore, R. To be published.

(22) For example, the bis-tolyl, anisyl, mesityl, and 2,6-dimethylanisyl analogues of VFT with E^0_{ox} = 1.36, 0.98, 1.40, and 1.21 V vs SCE, respectively, show temperature-dependent binding of NO analogous to that described in eq 3 (except at lower temperatures of <-50 °C).