ways of inclusion of **1** namely from the *tert*-butyl side or from the phenyl side. In the inclusion from the *tert*-butyl side the radical can go farther into the cavity than in the inclusion from the phenyl side, which is hindered by another phenyl group. Inspection of the hfs of these two compounds shows that one hfs pair changes only its β-H hfs upon inclusion, while the other changes mainly its N hfs. The solvent effect on hfs of **1** has been investigated in great detail, and the N and H hfs' change in the same direction as a function of solvent polarity.[17] The present results do not fit this tendency suggesting that anomalous solvation occurs. The inclusion from the *tert*-butyl side could include the NO group, and thus the N hfs is smaller than that in water due to the hydrophobic environment of interior β-CD. On the other hand inclusion from the phenyl side changes only the bulkiness of the group attached to α-C thus changing only the β-H hfs (Figure 3). Since the polarities of the *tert*-butyl and phenyl group are not very different, the larger equilibrium constant for the formation of the complex assigned to the *tert*-butyl group inside comes solely from the larger area of interaction, because the inclusion from the phenyl side is hindered by the other phenyl group. The possibility of formation of a complex with two or more CD molecules attached to one radical is not supported by the fact that two species appear even at very low concentration of CD (Figure 3). Also the slowing down of the rotational tumbling motion which is revealed by the weaker intensity of the high field line shows that the molecular size for both species is similar.

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A Symmetrically Hydrogen-Bonded "Binitrosamine Cation" Produced on Protonation of *N*-Nitrosopyrrolidine

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While reinvestigating the acid–base reactions of the carcinogenic nitrosamines as part of a systematic effort to infer possible cancer prevention strategies from data on their chemical and biological properties,[1] we have unexpectedly isolated a salt in which each acid proton is bound to two nitrosamine molecules rather than one, with the biscoordinate hydrogen apparently being symmetrically and collinearly situated between the two nitroso oxygens. The *N*-nitroso group is thus shown to be one of the limited number of functionalities that are capable of exhibiting this form of very strong hydrogen bonding.[2]

We describe herein the preparation and structure of this interesting compound, which appears to be the first in which the position of nitrosamino group protonation has been confirmed by X-ray crystallography. It was isolated by precipitation from ethereal solutions containing both *N*-nitrosopyrrolidine and hexafluorophosphoric acid during evaporation of solvent. After recrystallization by dissolution in dichloromethane followed by addition of ethyl acetate, the material showed mp 128–132 °C and was analytically pure.[3] The structure of the compound was determined by a single-crystal X-ray diffraction study. The results[4] are illustrated in Figures 1 and 2.

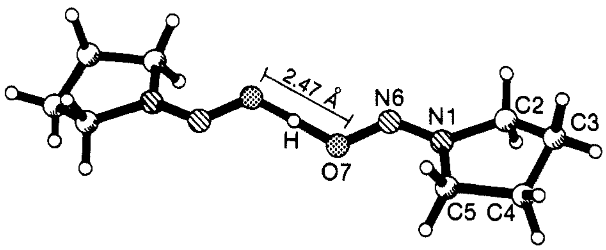

Figure 1. Diagram of the results of the X-ray study. The hydrogen-bonded proton lies on a center of symmetry, with only one of the nitrosamine moieties being crystallographically unique. Bond lengths (Å) and bond angles (deg) are as follows: N1–N6 = 1.270 (6); N1–C2 = 1.454 (7); N1–C5 = 1.475 (7); N6–O7 = 1.276 (6); average C–C = 1.471 (8); O7–N6–N1 = 111.4 (5); N6–N1–C2 = 120.9 (5); N6–N1–C5 = 126.4 (5); C2–N1–C5 = 112.7 (5); average C–C–C = 106.9 (6); average C–C–N 102.9 (7).

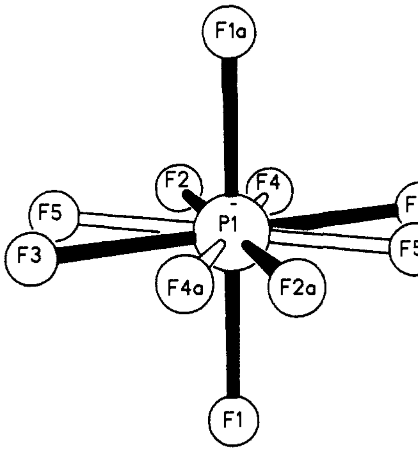

Figure 2. The PF_6^- ion has octahedral symmetry and is disordered such that there are two different positions for the four planar fluorine atoms. The refined ratio for the two positions is approximately 1:1. The phosphorus atom lies on a center of symmetry with only three of the fluorine atoms being crystallographically unique. F1 and F1a are perpendicular to the plane and involved with both sets of disordered fluorine atoms. Bond lengths (Å) and bond angles (deg) are as follows: P1–F1 = 1.558 (4); average for other P–F = 1.508 (13); F1–P1–F1a = 180.0 (0); average for other F–P–F = 90.0 (6).

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[3] Anal. ($C_8H_{17}F_6N_4O_2P$): C, H, N, P.

[4] The compound, $C_8H_{17}N_4O_2^+PF_6^-$, crystallizes in the monoclinic space group, $P2_1/c$, with cell dimensions a = 6.035 (2) Å, b = 10.218 (2) Å, c = 12.136 (3) Å, β = 101.1 (2)°, V = 734.4 (3) Å^3, Z = 2 (1/2 formula unit per asymmetric unit), d_{calcd} = 1.56 g/cm^3, fw = 346.21, and μ = 0.26 mm^{-1}. The data were collected on a Nicolet R3M diffractometer with X-radiation (λ = 0.71073 Å) at −65 °C. Because the material had some tendency to decompose, the crystals were kept at <0 °C prior to data collection. The data crystal was then mounted on a glass rod in a hydrocarbon grease in a cold room (~4 °C) and transferred immediately to the cold nitrogen gas stream on the diffractometer. The crystal remained stable long enough to collect a data set of 1207 reflections by using the $\theta/2\theta$ scan technique with $2\theta_{max}$ = 45° at speeds ranging from 10°/min to 30°/min depending upon reflection intensity. The structure was solved by direct methods, and the 119 parameters were refined by full-matrix least-squares techniques to a conventional R-factor of 0.076 [R_w = 0.068 and S (goodness of fit parameter) = 1.91] by using the 627 data for which $|F_o| > 3\sigma|F_o|$. All non-hydrogen atoms were refined anisotropically. All hydrogens on carbon atoms were put in at calculated positions and allowed to ride on covalently bonded carbons, C–H distance set at 0.96 Å and coordinate shifts of carbon atoms also applied to H-atoms, with fixed thermal parameters. The thermal parameter for the hydrogen bonded H-atom, which sits on a center of symmetry, fixing its coordinates, was refined isotropically. In addition, F···F distances in the PF_6^- ion were constrained to be close to 2.169 (3) Å.

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The bonding arrangement in the O–H–O system is strongly reminiscent of the proton-to-heteroatom attachment in the bifluoride ($F-H-F^-$)[5] and bihydroxide ($H-O-H-O-H^-$)[6] ions, suggesting the designation, "binitrosamine", for ions of the sort described here. The O···O separation of 2.47 (1) Å for the binitrosamine ion is similar to those for other very strong, symmetrical or nearly symmetrical O–H–O bonds (typically 2.4–2.5 Å) and considerably shorter than the 2.6–2.9 Å O···O distances seen for most asymmetric H-bonds.[2,7,8] Additionally, while the graph of O–H distance versus O···O separation for the vast majority of previously studied hydrogen bonds is a monotonically decreasing curve, the plot for those that are very strong and symmetrical is a short line of opposite slope;[8] the measurements for the binitrosamine cation (Figure 1) place it squarely on the latter straight line, indicating that the nitrosamino group belongs with the carboxylates, oximes, *N*-oxides, and a few other (mostly inorganic) species in a select set of functional groups capable of serving as oxygen donors in such very strong hydrogen bonds.[2,7,8]

Isolation of a stable species in which attachment of a proton to such a weak base is strong enough to bind not just one but two nitrosamine molecules is the more remarkable because the mixture from which the 2:1 complex was initially crystallized contained equimolar amounts of *N*-nitrosopyrrolidine and HPF_6, leaving unused acid in the supernatant ether solution. It may also be significant that the isolated salt is much less hygroscopic than the 1:1 acid/nitrosamine adducts we have prepared,[1b] suggesting that water is no more able than ether or excess hexafluorophosphoric acid to dislodge either nitrosamine molecule from its position on the crystal lattice. Added evidence that the binitrosamine cation might exist as such in solution can be found in the chemical shift of the O–H proton, which in dichloromethane-d_2 appeared at 17.0 ppm. This value is at substantially lower field than those of the simple *N*,*N*-dialkyl-*N*′-hydroxydiazenium ions, whose O–H protons resonate at 13–16 ppm.[9] Such deshielding appears to be characteristic of strongly bonded, biscoordinate hydrogen.[10]

The *N*-nitrosopyrrolidine salt described above is not unique in its stoichiometry. Preliminary results show that hexafluorophosphoric acid also forms a 1:2 complex with *N*-nitrosothiomorpholine. Further study of this novel compound type may provide insight into the origins of the surprising stability that these binitrosamine cation complexes display.

Warning! The strong toxicity of the materials used in this investigation demands that they be handled, stored, and discarded with due respect for the possible hazards involved.[11]

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Supplementary Material Available: Tables of atomic coordinates and full listings of bond lengths and angles (2 pages); listing of observed and calculated structure factors (3 pages). Ordering information given on any current masthead page.

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Ligand Assisted Nucleophilic Additions. Control of Site and Face Attack of Nucleophiles on 4-Oxidoenones†

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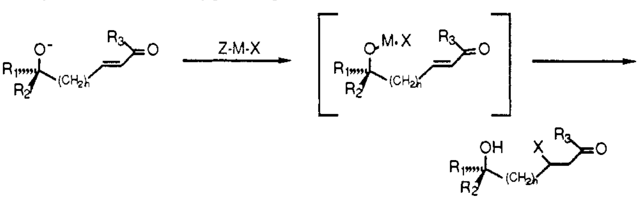
A properly positioned alkoxide–metal complex, possessing a transferable ligand, can exert a high degree of regio- and stereocontrol on the delivery of that ligand to a second reactive site. While the literature is replete with examples of this sort of directing effect where the complex is electrophilic and the second reactive site is electron-rich, little general information is available about the opposite situation, i.e., intramolecular reactions of nucleophilic complexes with electron-deficient functionalities (see generalized depiction in eq 1).[1-6] Herein, we report the results of a systematic study of the latter type of process.[7]



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† Dedicated to Professor Edward C. Taylor on the occasion of his 65th birthday.

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