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A Surprisingly Stable *S*-Nitrosothiol Complex

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S-nitrosothiols (RSNOs) have been known from the middle of the nineteenth century, but the first intentional synthesis and identification was described in 1909 by Tasker and Jones.[1] Due to their low stability, RSNOs did not attract much attention until their physiological role, related to NO transport, was discovered.[2] For the same reason, only limited structural data on these species have been reported. The structures of five RSNOs have been crystallographically characterized thus far; they are: triphenylmethylthionitrite (Ph_3C-SNO),[3] *S*-nitroso-*N*-acetylpenicillamine (SNAP),[4] *S*-nitroso-triarylmethylthiol (TRM-SNO),[5] *S*-nitroso-captopril,[6] and *S*-nitrosonitrosylhemoglobin.[7]

Elucidation of the structural features of RSNOs is important for the chemical understanding of these species. A great number of studies on *S*-nitrosothiols have been focused mostly on their biochemical aspects. However, the coordination chemistry of RSNOs may uncover new aspects of nitrosation processes since coordination to metal centers may change their properties considerably.[8]

Several mechanistic studies[9] report that in the presence of a thiolate anion, a great variety of nitrosyl complexes of the general formula type $[(X)_5MNO]^n$, with X comprising ligands of different donor−aceptor abilities and M = Fe, Ru, and Os, are transformed into the *S*-nitrosothiolato-*N* complex via nucleophilic attack of the thiolate on the NO ligand.[10] In most cases the $[(X)_5MN(O)SR]^{n-1}$ complexes are unstable and decompose spontaneously to metal complexes and disulfides, the lifetimes depending strongly on the thiol structure.[11] Olabe et al. has reported the rate constants for reactions of several metal nitrosyls with cysteine in aqueous solution.[12]

Recently, Ashby et al. have described time-resolved IR spectra in solution that for the first time show spectroscopic data other than UV−visible spectra for the transient "red products", the widely postulated adducts that are formed when nitroprusside reacts with thiols in aqueous media.[13] In this work we present for the first time the X-ray structure of a coordinated *S*-nitrosothiol: *trans*-$K[IrCl_4(CH_3CN)N(O)SCH_2Ph]$ (**3**). This surprisingly stable compound could be isolated in high yield (80%) and fully characterized. This complex represents an important starting point to understand the factors that are responsible for the stability and reactivity of biologically relevant RSNOs. Since in the presence of free thiols **3** decomposes producing the corresponding disulfide- and presumably NO or HNO-, in principle it could be used as a water-soluble NO donor in the same way as RSNOs.

When benzylmercaptan is added to an acetonitrile solution of $K[IrCl_5(NO)]$ at room temperature, immediate formation of the corresponding coordinated *S*-nitrosothiol is observed as a green precipitate, eq 1.[14] After a few minutes, this precipitate changes to a dark-red color. Crystals suitable for X-ray diffraction were obtained by recrystallization from CH_3CN (Figure 1). Benzylmercaptan turned out to be a good choice: its complex could be crystallized, probably due to the rigidness provided by the ring. Additionally, being very unstable as an S-nitrosothiol, it resulted in a good example to test the stabilization by coordination.

$$\underset{\mathbf{1}}{K[IrCl_5NO]} + \underset{\mathbf{2}}{PhCH_2SH} \xrightarrow{CH_3CN} \underset{\mathbf{3}}{trans\text{-}K[IrCl_4(CH_3CN)N(O)SCH_2Ph]} + H^+ + Cl^- \quad (1)$$

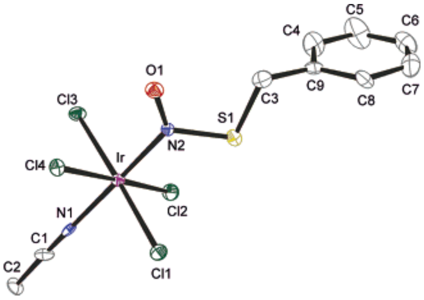

Figure 1. X-ray crystal structure and atom numbering for the anion portion of **3.** Thermal ellipsoids are drawn at the 50% level.

Table 1. Selected Bond Lengths (Å) and Angles (deg) for **3** and $PhCH_2$-SNO

	3/X-ray	**3**[a]	$PhCH_2$−SNO[a]
Bond Lengths			
N2−O1	1.22	1.21	1.19
S1−N2	1.73	1.86	1.90
N2−Ir	1.96	1.95	−
N1−Ir	2.03	2.01	−
Angles			
O1−N2−S1	117.05	117.92	117.05
N2−S1−C3	99.70	98.59	101.74
O1−N2−Ir	124.09	126.14	−

[a] Calculated.

A striking fact of this structure is that acetonitrile is coordinated to the trans position, and in contrast to free *S*-nitrosothiols and other metal-coordinated ones, **3** is very stable in aqueous solution.

We have performed density functional theory calculations using the Gaussian98 package[15] at the BPW91[16] level with a 6-31G** basis set for the first-row atoms, combined with quasi-relativistic electron core potentials (LANL2DZ[17]) and the corresponding optimized sets of basis functions for the iridium center. Selected experimental and calculated structural parameters for **3** and free *S*-nitrosobenzylmercaptan ($PhCH_2-SNO$) are shown in Table 1.

The calculated structural parameters shown in Table 1 are in reasonable agreement with the crystallographic ones. As illustrated in Figure 1, the conformational preference for the C−S−N=O moiety in **3** is syn, in good agreement with the results reported by Bartberger et al. for free RSNOs.[6] It can be seen that both the X-ray

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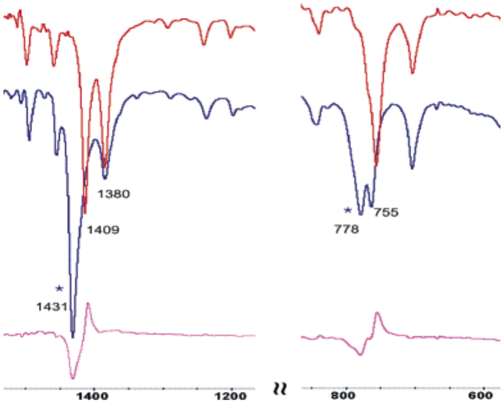

Figure 2. FTIR spectra for the unlabeled (blue) and ^{15}N isotopically labeled (red) complex **3** and difference spectrum (magenta). The bands marked by an asterisk represent those assigned to the −SNO group.

and the optimized N−O bond distances in **3** are longer than the corresponding distances in $PhCH_2$−SNO. Furthermore, the S−N bond distance in **3** is shorter than the same distance in $PhCH_2$−SNO.

An interesting point is to compare the stability of free $PhCH_2$−SNO with that of **3**. Previous works indicate that, when synthesized in situ in oxygen-free CH_3CN, $PhCH_2SNO$ slowly decomposes over a period of 72 h to give mainly the disulfide. On standing under air it decomposes within 2 h at room temperature.[18] Complex **3** is stable in CH_3CN and even in water over periods of weeks.

To characterize **3** we also performed ^{1}H NMR, FTIR, UV−visible spectra, mass spectrometry, and elemental analysis. Complete data are included as Supporting Information.

The UV−visible spectra in acetonitrile shows several intense bands in the UV region: the one at 331 nm (ϵ: 2049 M^{-1} cm^{-1}) was assigned to an allowed $n_O \rightarrow \pi^*$ transition in the ligand. There are two other bands in the visible region, one at 404 nm (ϵ: 3245 M^{-1} cm^{-1}) and the other a weak one at 591 nm (ϵ: 673 M^{-1} cm^{-1}), both assigned to MLCT transitions. This last band is responsible for the color of the *S*-nitrosothiol, in the case of free $PhCH_2$−SNO in aqueous solution, it appears at 530sh (17 M^{-1} cm^{-1}) and 560 (26 M^{-1} cm^{-1}).[8,18,19] These visible bands present some solvent dependence in the case of **3**, shifting to the blue in the presence of polar solvents. This can be ascribed to a donor−acceptor interaction of the chloride ligands with the solvent, as previously suggested for $[Fe(CN)_5NO]^{2-}$.[20] In a similar way, the color change observed in the precipitate described in the previous page may be due to the interaction of two of the chloride ligands with a K^+ counterion in the crystalline form (see Supporting Information).

^{1}H NMR spectra showed that S-nitrosation and coordination to the metal of benzylmercaptan result in chemical shifts changes for the signals of hydrogen atoms attached to C3 and C5−9 with reference to pure thiol. Signals of protons at the C3 and C5−9 positions are shifted downfield approximately by 1 ppm and 0.1−0.2 ppm respectively (Figures SI 2 and 3 in the Supporting Information).

FTIR spectra obtained in the solid state show two bands characteristic of *S*-nitrosothiols. The assignment of these bands to the −SNO group was confirmed by preparing the ^{15}N-labeled derivative *trans*-$K[IrCl_4(CH_3CN)^{15}N(O)SCH_2Ph]$ (Figure 2). The difference spectra reveals isotope-sensitive vibrations at 1431 cm^{-1} and 778 cm^{-1}. These bands were attributed to υ(NO) and υ(NS) stretching vibrations, respectively. In D_2O, a broad signal due to υ(NO) appears at ca. 1443 cm^{-1} (compare with 1380 cm^{-1} for the reaction of $[Fe(CN)_5NO]^{2-}$).[13] An important observation is the complete loss of the υ(SH) stretch at approximately 2600 cm^{-1} upon the formation of the nitroso complex. (Figures SI 4 and 5 in the Supporting Information)

Because of its instability, free $PhCH_2$−SNO has not ever been isolated, and only the characteristic broad strong IR band at 1500−1530 cm^{-1} has been assigned to the stretching vibration of NO.[8] This υ(NO) stretching vibration becomes 70−100 cm^{-1} lower upon coordination. This trend is well described by the calculations that predict an 89 cm^{-1} shift toward lower frequencies for the υ(NO) stretching vibration and 101 cm^{-1} toward higher frequencies for the υ(SN) stretching vibration. A lower υ(NO) indicates a weakening of the NO bond, whereas a higher υ(SN) points toward a strengthening of the SN bond in **3** compared to free $PhCH_2$−SNO. This fact is consistent with the great stability observed for **3** that allowed isolation of a coordinated *S*-nitrosothiol for the first time; this stabilization is probably due to the electrophilicity of the Ir center, as shown by DFT calculations (see Table 4 in SI).

We are presently studying the chemical behavior of **3** as well as the reactions of other relevant thiols such as L-cysteine-ethyl ester, mercaptosuccinic acid, and phenylthiol with $K[IrCl_5NO]$; all of them exhibit similar stability, and they will be described elsewhere.

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Supporting Information Available: NMR spectra, ESI-MS, ESI MS-MS spectra of the principal ions, optimized geometries, complete FTIR spectra, and UV−visible spectrum are included. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Synthesis of **3**: 27 μL (2.28 × 10^{-2} mmol) of benzylmercaptan (dissolved in 0.25 mL of acetonitrile) was added under Ar atmosphere to 10 mg (2.28 × 10^{-2} mmol) of $K[IrCl_5(NO)]$ in 0.25 mL of acetonitrile The precipitate was separated from the solution by centrifugation, and the solid was dried under vacuum. By slow evaporation of the supernatant, red crystals appeared. Elemental analysis: calculated for $K[Ir(CH_3CN)Cl_4N(O)SCH_2Ph]$. CH_3CN: C, 21.71; N, 6.91; S, 5.27; H, 2.15. Found: C, 21.9; N, 6.5; S, 5.2; H, 2.3.

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