Spontaneous and Selective Formation of HSNO, a Crucial Intermediate Linking Nitroso and H$_2$S Chemistries

Matthew J. Nava†, Marie-Aline Martin-Drumel, Christopher A. Lopez, Kyle N. Crabtree, Caroline C. Womack, Thanh L. Nguyen, Sven Thorwirth, Christopher C. Cummins, John F. Stanton and Michael C. McCarthy

†Massachusetts Institute of Technology

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RSNOs in Biology
RSNOs are speculated to be important signaling molecules

\[
\text{O} \quad \text{N} \quad \text{S} \quad \text{R} = \text{S-nitrosothiol}
\]

- HSNO may be responsible for the 'cross talk' between NO and H\textsubscript{2}S
Evidence for the Presence of HSNO Under Biologically Relevant Conditions


-Treatment of red blood cells with GSNO results in S-nitrosated Hb subunit

--> HSNO can diffuse through cell membranes
Literature Precedent for the Existence of HSNO

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Chem. 1987, 91, 5203–5209

\[ 3\text{NH}_3 + \text{OSCl}_2 \rightarrow \text{OSNH} + 2\text{NH}_4\text{Cl} \]

\[ \text{OSNH} \xrightarrow{\text{hv}, 250 \text{ nm}} \text{HSNO} + \text{HOSN} + \text{HONS} \]

-Structural parameters could not be determined

-The existence of HSNO is still disputed in the biology community
Unknown Lines Identified Upon Mixing H$_2$S and NO

\[ \text{NO} + \text{H}_2\text{S} \rightarrow ??? \]

- Discharge diminishes signal
- Lines identified as HSNO

Signal

11762.3  11762.727  11763.3

Frequency (MHz)
Concentration of Relevant Species upon Varying the Amount of H$_2$S

\[ 4 \text{NO} \rightarrow \text{N}_2\text{O} + \text{N}_2\text{O}_3 \]

\[ \text{H}_2\text{S} + \text{N}_2\text{O}_3 \rightarrow \text{HSNO} + \text{HONO} \]

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Calculated Pathway for the Formation of HSNO from H$_2$S and N$_2$O$_3$

Calculated at the CCSD(T)/ANO1 level of theory

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Formation of $\text{N}_2\text{O}_3$ Occurs Through a Metal Surface Catalyzed Disporportionation Reaction

Oxygen can also react with NO to generate NO$_2$

$$3 \text{NO} \xrightarrow{\Delta G=-105\text{kJ/mol}} \text{NO}_2 + \text{N}_2\text{O}_3$$

$$\text{NO} + \text{NO}_2 \leftrightarrow \text{N}_2\text{O}_3$$

$K_{eq}(RT,P) = 0.06$
- Last second mixing enhances HSNO production
- HSNO forms through a surface rx
- SS Mesh just prior to expansion enhances signal
- Premixing NO and O₂ enhances production of HSNO (through N₂O₃)
Concentration of Relevant Species upon Varying the Amount of H$_2$S After Optimization of Conditions

\[ \text{trans-HSNO} \]
\[ \text{cis-HSNO} \times 5 \]
Attempted Preparation of HSN$^{18}$O using $^{18}$O$_2$

Lack of labeled oxygen incorporation into HSNO

\[
\begin{align*}
\text{NO} + \text{NO}_2 & \rightleftharpoons \text{NO}_2\text{NO} \\
K_{eq}(RT,P): 0.06
\end{align*}
\]

\[
\begin{align*}
2 \text{NO} + \text{O}_2 & \rightarrow 2 \text{NO}_2
\end{align*}
\]

\[
\begin{align*}
^{18}\text{O}_2 & \rightarrow \text{HSNO}^{18}\text{O}
\end{align*}
\]
Attempted Preparation of HSN$^{18}$O Using H$_2^{18}$O

Incorporation of labeled oxygen into HSNO

Proceeds through N$_2$O$_4$, which generates NO$^+$ and NO$_3^-$
MW Spectrum of the HSN$^{18}$O Fundamental Line
Acquired with 10 shots

HSN$^{18}$O

$J' \leftarrow J'' = 1 \leftarrow 0$

$F' \leftarrow F'' =$

$0 \leftarrow 1$

$1 \leftarrow 1$

$2 \leftarrow 1$

MHz

11226.416  11226.886  11227.193

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1.345(2) 1.834(1) 1.181(1) 95.2(2) 115.93(6)
1.335(3) 1.852(2) 1.177(2) 90.1(1) 114.63(6)
Histogram of S–N Bond Lengths in the CSD

- All S-N bond lengths
- All S-N bond lengths in RSNO compounds
Concentration of Relevant Species upon Varying the Amount of $\text{H}_2\text{S}$

Excess $\text{H}_2\text{S}$ causes depletion of the HSNO signal
Observation of $N_2^{18}O$ Upon Addition of Excess $H_2S$ to $HSN^{18}O$

Nitroxy (HNO) likely species responsible for formation of labeled $N_2O$

\begin{align*}
\begin{array}{c}
\text{This Work} \\
\text{*Rx not directly confirmed} \\
\text{Known Reaction} \\
*\text{Recall } N_2O \text{ passes through } H_2^{18}O \text{ with } ^{18}O \text{ label incorporation}
\end{array}
\end{align*}
Treatment of $\text{N}_2\text{O}_3$ With $\text{CH}_3\text{SH}$ to Generate $\text{CH}_3\text{SNO}$

Confirm utility of this reaction as well as identify intermediates.
- Existence of HSNO was verified and structural parameters were determined

- In vivo conditions were not used but MW spectroscopy can be used to understand fundamental reaction dynamics

- Verify the presence of HNO, a biologically active cellular redox signaling molecule
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