

A COMPARATIVE STUDY ON THE OXYGEN EXCHANGE OF C-, N-, AND O-NITROSO COMPOUNDS  
WITH  $\text{H}_2^{18}\text{O}$

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Acid-catalyzed oxygen exchange of C-, N-, and O-nitroso compounds with  $^{18}\text{O}$ -enriched water is investigated. The rates of exchange increase in the order of C-, N-, and O-nitroso compounds, and nitrite esters exchange their oxygens with those of  $\text{H}_2^{18}\text{O}$  fairly rapidly.

Although the acid-catalyzed oxygen exchange of carbonyl compounds<sup>1</sup> and sulfinyl compounds<sup>2</sup> are well known, similar oxygen exchange of nitroso or nitro compounds has not been reported except in a paper on oxygen exchange of n-alkyl nitrites with water.<sup>3</sup>

The rates of oxygen exchange of C-, N-, and O-nitroso compounds were determined in  $^{18}\text{O}$ -enriched water ( $^{18}\text{O}$  excess atom %; 1.3, 1.6, or 5.0%) in the presence of some sulfuric acid. The molar ratio of water/nitroso compound was up to 400. Since nitroso compounds are sparingly soluble in water, some dioxane or hexamethylphosphoramide (HMPA) were used for preparing homogeneous solutions. The concentrations of sulfuric acid were determined by titrating such mixed solutions. Oxygen exchange was allowed to proceed at 20.0°C. In the cases of C- and N-nitroso compounds, the samples removed from the constant-temperature bath were neutralized with aqueous (or  $^{18}\text{O}$ -enriched aqueous)  $\text{Na}_2\text{CO}_3$  solutions, and then the nitroso compounds were extracted with ether or dichloromethane, purified by sublimation or chromatography, and then subjected to  $^{18}\text{O}$ -analysis. In the case of nitrite esters, the samples removed from the bath were diluted with water; the esters which separated were dried over anhydrous magnesium sulfate, distilled under reduced pressure, and then were subjected to  $^{18}\text{O}$ -analysis. The  $^{18}\text{O}$ -contents in nitroso compounds were determined by mass-spectrometric analyses of the carbon dioxide formed by pyrolysis of nitroso compounds in the presence of  $\text{Hg}(\text{CN})_2$  and  $\text{HgCl}_2$ .<sup>4</sup>

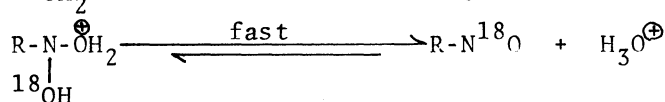
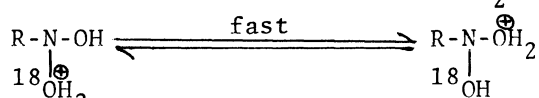
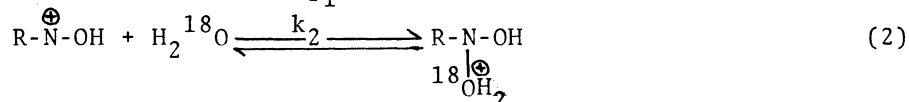
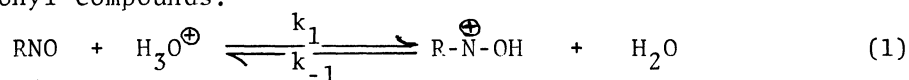
Table 1 shows the data on C-nitroso compounds. Although the aromatic nitroso compounds used are usually dimeric (except p-dimethylaminonitrosobenzene), the reaction solutions showed the greenish blue color characteristic of nitroso monomers and therefore at least a part of these nitroso compounds exists in a monomeric form. Nitrosobenzene and 4-methyl- and 2,4,6-trimethylnitrosobenzene are rather unstable and decomposed at high acid concentrations. p-Iodo- and p-dimethylaminonitrosobenzene are fairly stable; the latter could be recovered in a 60% yield after 45 days in 18 N  $\text{H}_2\text{SO}_4$ , but  $^{18}\text{O}$ -incorporation was very little even after 45 days. Although

the  $^{18}\text{O}$  excess values were very small, they were always positive values over the natural  $^{18}\text{O}$  atom %.

Since aliphatic nitroso compounds possessing  $\alpha$ -hydrogens tautomerize to oximes, only the tertiary alkyl nitroso compounds can be subjected to our  $^{18}\text{O}$  study. The oxygen exchange in 1-nitrosoadamantane was faster than that in nitrosoarenes.

Table 2 summarizes the results with N-nitrosoamines. The oxygen exchange in N-nitrosoamines is much faster than that in C-nitroso compounds. Table 3 shows the results with nitrite esters. The oxygen exchange is much faster than that in C-nitroso or N-nitroso compounds. Among the nitrite esters the rates decrease in the order of primary > secondary > tertiary.

As the mechanism for the acid-catalyzed oxygen exchange in nitroso compounds, the following mechanism is plausible, which is analogous to that in the case of carbonyl compounds.



$$\begin{aligned} \frac{d[\text{R}-\overset{\oplus}{\text{N}}-\text{OH}]}{dt} &= k_1[\text{RNO}][\text{H}_3\text{O}^+] - k_{-1}[\text{R}-\overset{\oplus}{\text{N}}-\text{OH}] - k_2[\text{R}-\overset{\oplus}{\text{N}}-\text{OH}][\text{H}_2^{18}\text{O}] = 0 \\ \frac{d[\text{RN}^{18}\text{O}]}{dt} &= k_2[\text{R}-\overset{\oplus}{\text{N}}-\text{OH}][\text{H}_2^{18}\text{O}] = \frac{k_1 k_2 [\text{RNO}][\text{H}_3\text{O}^+][\text{H}_2^{18}\text{O}]}{k_{-1} + k_2[\text{H}_2^{18}\text{O}]} \quad (3) \end{aligned}$$

Protonation ( $k_1$ ) and deprotonation ( $k_{-1}$ ) are probably rapid. Since the rates of oxygen exchange observed are generally very small, we may assume that  $k_{-1} \gg k_2[\text{H}_2^{18}\text{O}]$ . Then we have


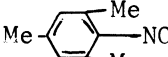
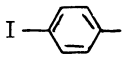

$$\frac{d[\text{RN}^{18}\text{O}]}{dt} = \frac{k_1 k_2}{k_{-1}} [\text{RNO}][\text{H}_3\text{O}^+][\text{H}_2^{18}\text{O}] \quad (4)$$

Therefore, when oxygen exchange was carried out at a constant acid concentration in the presence of excess  $\text{H}_2^{18}\text{O}$ , the determination of the rates of  $^{18}\text{O}$ -incorporation into RNO yield the values of  $k_1 k_2 / k_{-1}$ , which are shown in Table 1-3.

When the  $k_{\text{obs}}$  values shown in Table 1-3 are divided by the acid concentrations used ( $[\text{H}_3\text{O}^+]$ ), the rates of exchange under the normalized conditions ( $[\text{H}_3\text{O}^+] = 1 \text{ M}$ ) can be calculated. Table 4 compares such  $k$  values. It is clear that rates of oxygen exchange increase in the order of C-, N-, and O-nitroso compounds, and those of O-nitroso compounds are comparable to those of sulfoxides and carbonyl compounds.

The smaller rates of exchange in C- and N-nitroso compounds can be explained as follows. Both the nitrogen and oxygen atoms in nitroso groups are basic and can be protonated as described in the equation. However, the N-protonation appears to be more favorable than O-protonation, since nitrogen is more basic than oxygen.

Table 1. Oxygen Exchange in C-Nitroso Compounds

Substrate	$[H_3O^+]$ (M)	Reaction Time (hr)	Excess $^{18}O$ Atom % in Recovered R-NO	$k_{obs}^{**} (=k_1k_2[H_3O^+]/k_{-1})$ ( $sec^{-1}$ )
 -NO	{ 0.17 0.21	{ 3.0 24.0	{ 0.011 0.014	
 -NO	2.75	48.1	0.008	
p-MeC <sub>6</sub> H <sub>4</sub> -NO	1.63	42.1	0.064	$(3.1 \times 10^{-7})$
I-  -NO	{ 5.5 5.5 5.5 5.5	{ 24 48 72 120	{ 0.023 0.026 0.036 0.040	$(1.2 \times 10^{-7})$
Me <sub>2</sub> N-  -NO	{ 18 18 18 4*** 4	{ 96 192 1080 96 192	{ 0.016 0.017 0.0185 0.019 0.020	{ $(1.8 \times 10^{-8})$   $(3.0 \times 10^{-8})$
1-nitroso-adamantane	{ 1.5 1.5	{ 24 48	{ 0.045 0.066	$3.3 \times 10^{-7}$

\*The error range in oxygen-18 determinations were  $\pm 10\%$ .

\*\* $k_{obs}$  values were calculated for the sake of rough comparison. The values in parentheses should be regarded as upper limit values. \*\*\*Solvent: HMPA.

Table 2. Oxygen Exchange in N-Nitroso Compounds

Substrate	$[H_3O^+]$ (M)	Reaction Time (hr)	Excess $^{18}O$ Atom % in Recovered R-NO	$k_{obs,1}$ ( $sec^{-1}$ )
Ph <sub>2</sub> N-NO	{ 1.2 1.2	{ 72 144	{ 0.034 0.093	$1.1 \times 10^{-6}$
PhMeN-NO	{ 1.2 1.2	{ 72 144	{ 0.030 0.068	$0.9 \times 10^{-6}$

Table 3. Oxygen Exchange in O-Nitroso Compounds

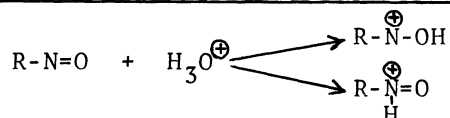
Substrate	$[H_3O^+]$ (M)	Reaction Time (hr)	Excess $^{18}O$ Atom % in Recovered R-NO*	$k_{obs,1}$ ( $sec^{-1}$ )
iso-Amyl-ONO	0.17	2	0.128	$3.4 \times 10^{-6}$
	0.17	4	0.151	
	0.17	12	0.169	
	0.17	24	0.193	
	0.17	36	0.244	
	0.17	48	0.292	
	0.17	72	0.388	
	0.17	96	0.477	
sec-Butyl-ONO	0.17	8	0.071	$2.4 \times 10^{-6}$
	0.17	24	0.157	
	0.17	48	0.231	
	0.17	72	0.270	
tert-Amyl-ONO	0.17	8	0.030	$0.32 \times 10^{-6}$
	0.17	24	0.047	
	0.17	48	0.072	
	0.17	72	0.088	

\*Since nitrites have two oxygen atoms,  $^{18}O$  % for nitroso O alone is twice this value.

Table 4. Comparison of the Rates of Oxygen Exchange at  $[H_3O^+] = 1\text{ M}$ 

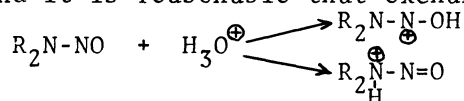
Substrate	$k^*$ ( $\text{sec}^{-1}\text{M}^{-1}$ )	Substrate	$k^*$ ( $\text{sec}^{-1}\text{M}^{-1}$ )
p-Me <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> NO	$(1 \times 10^{-9})$	PhMeN-NO	$0.75 \times 10^{-6}$
p-I-C <sub>6</sub> H <sub>4</sub> NO	$(2 \times 10^{-8})$	Ph <sub>2</sub> N-NO	$0.95 \times 10^{-6}$
p-MeC <sub>6</sub> H <sub>4</sub> NO	$(2 \times 10^{-7})$	tert-Amyl-ONO	$1.9 \times 10^{-6}$
1-NO-adamantane	$0.22 \times 10^{-6}$	sec-Butyl-ONO	$14 \times 10^{-6}$
		iso-Amyl-ONO	$20 \times 10^{-6}$

(\* $k = k_1k_2/k_{-1}$ )



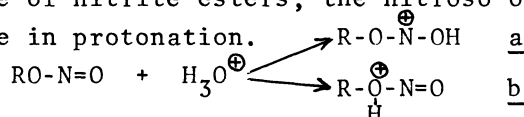
Only the O-protonation can result in oxygen exchange, and the N-protonation is of no use for oxygen exchange. In the case of carbonyl compounds, protonation takes place only on the oxygen atoms, and it is reasonable that the oxygen exchange is rapid.

In the case of N-nitroso compounds, protonation on the amino N atoms probably predominates, and it is reasonable that exchange is slow in this case.



In fact, denitrosation of N-nitrosoamines under acidic conditions proceeds through such nitroso-ammonium ions.

In the case of nitrite esters, the nitroso oxygen and ether oxygen atoms probably compete in protonation.



The conjugate acid a is stabilized by resonance with lone pairs of two adjacent oxygen atoms, whereas b is an oxonium ion containing an electron-withdrawing nitroso group and must be unstable. Thus, RONO is readily protonated with acid, forming a and consequently oxygen-exchanged RO-N<sup>18</sup>O.

The possibility that the oxygen exchange in RONO proceeds through hydrolysis and re-esterification was rejected from our separate finding that almost no ester is formed from ROH and HONO under our reaction conditions with excess water.

Thus, our comparative studies on nitroso compounds show that only O-nitroso compounds form conjugate acids possessing adequate stability for oxygen exchange.

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