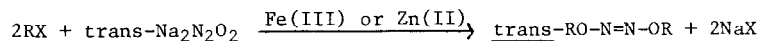# THE LEWIS ACID CATALYZED REACTION OF TRANS-HYPONITRITE ION WITH ALKYL HALIDES

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Summary:  Sodium and other inorganic trans-hyponitrites afford tert-alkyl hyponitrites
in good yield from the corresponding alkyl bromide or chloride in the presence
of weak Lewis acids.

Tertiary alkyl hyponitrites have been widely used to initiate free-radical chains in auto-oxidation and polymerization reactions,[1] most recently in systems designed to mimic autoxidation processes in vivo.[2,3] This class of initiators is often preferred because the decomposition rates show little solvent-dependence and negligible induced decomposition even at high concentrations.[1,4] Alkyl hyponitrites are also convenient photochemical sources of radicals.[5]

Trans-tertiary hyponitrites are usually prepared from a tertiary halide and dry silver trans-hyponitrite.[1,4] The latter can be precipitated from aqueous solutions of hyponitrite ion, usually introduced as the sodium salt, with $Ag^+$ under controlled conditions.[6] Silver hyponitrite is however usually light-sensitive, and it is often unstable to storage when incompletely purified. We have discovered a convenient way to esterify sodium hyponitrite directly with alkyl halides in the presence of ferric or zinc halides:

$$2RX + \underline{\text{trans-}}Na_2N_2O_2 \xrightarrow{\text{Fe(III) or Zn(II)}} \underline{\text{trans-}}RO\text{-}N\text{=}N\text{-}OR + 2NaX$$

A typical procedure is as follows:  Anhydrous ferric chloride (0.6 g, 3.7 mmol) was added with swirling to a mixture of tert-butyl bromide (4 mL) and ether (4 mL).  The dark, multiphase mixture was treated during five minutes with sodium hyponitrite (0.4 g, 3.8 mmol, dried at 1 torr to constant weight) with swirling and occasional cooling to maintain the temperature below 45°C.  The reaction mixture was allowed to stand 75 minutes at room temperature, and then overnight (convenience) at 5°C.  The inorganic salts were removed by filtration followed by several aqueous washes.  Concentration of the $Na_2SO_4$-dried solution under reduced pressure gave an off-white solid, 0.5 g (82%) which showed a single $^1$H-NMR resonance at $\delta$ 1.3 ($CDCl_3$) and other spectral properties identical to those reported for trans-di-tert-butyl hyponitrite.[1]

The new reaction was singularly unsuccessful with cumyl, benzyl, cyclohexyl (<0.01% by HPLC), isopropyl, or methyl halides and ferric or zinc halide catalysts.  The benzylic halides underwent visible changes in the presence of Lewis acids, but the delocalization of charge into the aromatic ring apparently reduces the alkylating ability of the system.  Calcium or tetra-n-butylammonium hyponitrite could replace sodium hyponitrite but offered no particular advantage, since they were prepared in turn from the silver salt.

Trials with other catalysts, substrates, and solvents are summarized in Table 1.  It is interesting that the catalytic activity of the salts does not parallel the usual order in Friedel-Crafts reactions.  The success of the reaction appears to depend on the particular ability of a catalyst to produce a reactive alkylating agent from the halide, as well as to interact with the inorganic hyponitrite.  The reaction must also proceed at a sufficient rate that a

mono-alkylated hyponitrite intermediate does not decompose. In addition to these restrictions, we found that the use of 1,2-dimethoxyethane instead as solvent in the above procedure gave no hyponitrite (HPLC method) from tert-butyl chloride and ferric chloride.

Table 1. Yields of Alkyl Hyponitrites from Metal Salt-Catalyzed Reactions.

| Metal salt, g | $Na_2N_2O_2$, g | RX, mL | Reaction time, min. | Yield of hyponitrite |
|---|---|---|---|---|
| $AlCl_3$, 1.1 | 0.80 | $t-C_4H_9Br$, 8.0 (ether, 8.0 mL) | 40 | < 8% (none isolated) |
| $SnCl_4$, 1.0 | 0.4 | $t-C_4H_9Br$, 4 (pentane,[b] 10 mL) | 30 | 9%[a] |
| $CdCl_2$, 0.73 | 0.4 | $t-C_4H_9Br$, 4 (tetrahydrofuran, 4 mL) | 60 | < 2%[a] |
| $FeCl_3$, 0.28 | 0.2 | $t-C_4H_9Cl$, 2 (ether, 2 mL) | 70 | 88%[a] |
| $ZnBr_2$, 0.9 | 0.40 | $t-C_4H_9Br$, 4.0 (ether, 4.0 mL) | 30 | 45%[a] |
| $ZnCl_2$, 0.68 | 0.53 | $t-C_4H_9Br$, 5 (ether, 4 mL) | 35 | 90%[c] |
| $FeCl_3$, 2.8 | 2.0 | $t-C_5H_{11}Cl$, 15 (ether, 20) | 20 | 60%[c,d] |
| $FeCl_3$, 0.6 | 0.4 | 1-Methylcyclohexyl chloride, 5 (ether, 4 mL) | 15 | 62%[c,e] |

a. Yields by high pressure liquid chromatography (HP 79916B RP-18 10µ column, isopropanol/hexane, 254 nm detection).

b. Ether formed an insoluble complex with $SnCl_4$.

c. Crude, isolated material.

d. Reference 7.

e. Mp 69.5-70°C (dec.) after crystallization from methanol. Exact mass (CIMS) 255.2021 (calc., 255.2072 for M + $H^+$).

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