ORGANIC
LETTERS

1999
Vol. 1, No. 4
583−585

Oxidation of Phosphines by Supercritical Nitrous Oxide

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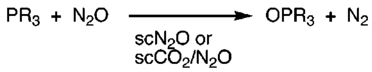
Received May 27, 1999

ABSTRACT



$$PR_3 + N_2O \xrightarrow[scN_2O \text{ or } scCO_2/N_2O]{} OPR_3 + N_2$$

Despite its reputation for lack of reactivity at moderate temperatures, nitrous oxide is capable of oxidizing at least one class of organic compounds, the phosphines, at temperatures at or below 100 °C. The use of supercritical N_2O as both the solvent and the reactant simplifies the isolation of the products and allows one to avoid the use of flammable liquid solvents.

Nitrous oxide (N_2O) is an under-utilized byproduct of chemical processes involving nitric acid. Scrubbing of N_2O emissions from nylon manufacture has been adopted in recent years[1] in order to combat its contribution to the greenhouse effect.[1−3] Although much of the waste N_2O is destroyed, one of the more attractive options for recycling N_2O is its use as an oxidant for organic chemistry. From the point of view of "green" chemistry, nitrous oxide would be preferable to many other oxidants because the only byproduct is N_2. The most dramatic result of efforts in academia and industry in this direction is the recently announced Monsanto process for the high-temperature heterogeneously catalyzed oxidation of benzene to phenol.[4,5] However, there is almost no information in the literature on low-temperature oxidation of organic functional groups by N_2O.

Oxidations of most organic compounds by nitrous oxide are thermodynamically favorable but are reputed to be extremely slow except at high temperatures.[6] Buckley et al.[7−9] found that alkenes and alkynes were oxidized by N_2O, but the reactions required temperatures of at least 200 °C. Ohtani et al. found that 2-propanol and, to a lesser extent, other small secondary alcohols and primary amines in water were oxidized by N_2O at room temperature in the presence of platinum "black".[10] The low-temperature oxidation of inorganic compounds by N_2O has been more fully explored. For example, catalyzed oxidations of CO[11−13] and NF_3,[14] and especially the uncatalyzed oxidations of low-valent organometallic complexes,[15−20] have been well investigated.

Supercritical N_2O (scN_2O) or scN_2O/CO_2 mixtures offer several advantages as media for the study of N_2O chemistry. Nitrous oxide is supercritical at temperatures and pressures

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10.1021/ol9906918 CCC: $18.00

above its critical point of 36.4 °C and 72.5 bar.[21] Depending on the exact conditions, the density is high enough for the scN_2O to act as a solvent for many nonpolar organic compounds, in the same manner as supercritical carbon dioxide (scCO_2). *The reader should peruse the safety warnings in the footnotes.*[22] In the past, the few low-temperature oxidations with N_2O that have been reported were performed in either organic solvents or water. Using the supercritical fluid as the solvent allows one to avoid the use of a flammable liquid solvent and also to dissolve substrates too hydrophobic to dissolve in water. A second advantage is the facile separation of the product from the solvent.[23] The use of scN_2O as both solvent and oxidant for organic functional group transformations has not been reported previously.

During tests of the effect of scN_2O on various compounds, we found that attempting to dissolve PPh_3 in scN_2O at 100 °C and 100−140 bar resulted in its rapid oxidation to phosphine oxide (Table 1 and eq 1).[24] The N_2 byproduct is assumed but was not experimentally confirmed.

$$PPh_3 + N_2O \rightarrow OPPh_3 + N_2 \tag{1}$$

The reaction can also be achieved at 65 °C, but it is somewhat slower at this temperature. The pressure of the N_2O must be supercritical or it will be unable to dissolve the phosphine. For example, the oxidation of PPh_3 at 65 °C proceeds readily at 100 to 140 bar but the starting material was recovered entirely unreacted after an experiment at 10 bar. Note that PPh_3 at this temperature is a solid. Methyldiphenylphosphine, tricyclohexylphosphine, and triethylphosphine are oxidized more rapidly by scN_2O than is PPh_3. Triethylphosphine (470 μmol) was 43% oxidized after 90 min in a mixture of N_2O (6 bar, ca. 40 mmol) and CO_2 (total pressure 100 bar) at 50 °C. The same experiment but with only CO_2 and no N_2O gave 0% oxidation.

This oxidation of PR_3 requires no added catalyst, although catalysis by the vessel walls cannot be ruled out. In contrast to the present results, previously reported examples of the oxidation of PPh_3 by N_2O have involved metal complexes as catalysts or promoters; the complexes were $CoH(N_2)(PPh_3)_3$ (6 mol $OPPh_3$ per mol catalyst, 62% isolated yield, −5 to 20 °C)[16,25] and $[MoO(CN)_5]^{3-}$ (0.5 mol $OPPh_3$ per mol catalyst, room temperature, 48 h).[26] Presumably the lack of a requirement for a catalyst in the present system is due to the higher temperature and the higher concentration of N_2O in the reaction phase.

Table 1. Oxidation of Phosphines to Phosphine Oxides by N_2O

substrate	T, °C	SCF	P_{total}, bar	time, h	% convn
PPh_3	65	N_2O	10	2	0
PPh_3	65	N_2O	100	2	43
PPh_3	65	N_2O	140	2	34
PPh_3	100	N_2O	130	0.5	66
PPh_3	100	N_2O	140	3	100
PPh_3	100	CO_2[a]	100	0.5	0
$PMePh_2$	64	N_2O	140	2	71
$PMePh_2$	65	N_2O	140	4	100
PCy_3	70	N_2O	140	4	100
PEt_3	50	CO_2[b]	100	1.5	43
PEt_3	50	CO_2	100	1.5	0

[a] 1 bar of air added. [b] 6 bar of N_2O added.

Tests of the solubility of PPh_3 in scN_2O were not possible because of the rapid reaction. Instead, observations were made of the solubility of PPh_3 in scCO_2, a supercritical fluid which is quite similar to scN_2O in all of its physical properties. PPh_3 (up to 65 mg) was completely dissolved in the scCO_2 at 150 bar and 65 or 100 °C. Literature measurements of the solubility of PPh_3 in scCO_2 have only been reported for 47 °C and below, but the mole fraction solubility at 150 bar was found to be roughly temperature independent.[27] The mole fraction used in our experiments is an order of magnitude lower than the solubility limit at this pressure.

It is unlikely that the oxygen source was anything other than N_2O. The purity of the N_2O was 99.998%, with less than 2 ppm of O_2 and less than 20 ppm of other impurities. Two different batches of N_2O were tested. Inadvertent admission of air to the vessel could not have caused the oxidation, because there is little reaction between PPh_3 and low concentrations of O_2 under these conditions. A reaction of PPh_3 in scCO_2 with no N_2O present gave 0% oxidation, as did an experiment in scCO_2 with 1 bar of added air. The oxidation of PEt_3 in a N_2O/CO_2 mixture proceeded at a PEt_3:N_2O mole ratio of 1:85, further evidence that the oxidation could not have been caused by the presence of trace

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[22] **SAFETY WARNINGS:** (a) Nitrous oxide is a thermodynamically powerful oxidant. Never mix high concentrations of organic compounds with scN_2O. Explosions have occurred with a 9 vol % solution of ethanol in scN_2O and with a mixture of 1 g of ground coffee in 2.5 mL of scN_2O.[31−33] To minimize the risk, we choose to keep the combustible substrate to microscale quantities and *very low concentrations*. For example, the experiments with triphenylphosphine were typically performed at 0.00018 g substrate per mL of scN_2O. In addition to using microscale quantities of substrate, we employ a burst disk, blast shield, and eye protection in all experiments. Diluting scN_2O with scCO_2 may further enhance the safety. Combustible cosolvents should not be used with scN_2O under any circumstances. (b) Triethylphosphine ignites on exposure to air[34] or pure N_2O.

[23] Jessop, P. G.; Leitner, W., Eds. *Chemical Synthesis using Supercritical Fluids*; VCH/Wiley: Weinheim, 1999.

[24] **General Procedure for the Oxidation of a Phosphine by scN_2O.** A stir bar and 21 mg of PPh_3 were placed in a 160 mL stainless steel vessel while in a glovebox under argon. The vessel cap contains a burst disk, a pressure transducer, a thermocouple, and a valve for N_2O. The vessel was closed, removed from the glovebox, heated to 100 °C, and then pressurized with 140 bar of scN_2O. The temperature was monitored by a thermocouple inside a thermowell. After 3 h, the vessel was cooled to room temperature and then placed in a bath of acetone/dry ice until the internal pressure dropped to zero due to condensation of the N_2O. At this point, the vent valve was opened and the vessel slowly warmed to room temperature, the N_2O venting as it boiled. The vessel was then opened, and the product was recovered from the bottom of the vessel by dissolution in $CDCl_3$ and analyzed by ^1H and $^{31}P\{^1H\}$ NMR spectroscopy without further workup. The product was pure $OPPh_3$ (100% conversion, 94% isolated yield).

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impurities in the N_2O. A possibility that cannot be ruled out is the conversion of the N_2O to other nitrogen oxides, either thermally or as a wall-catalyzed reaction, followed by reaction of those nitrogen oxides with PPh_3. The oxidation of phosphines by NO and N_2O_4 has been reported.[28,29]

Many other classes of organic compounds are *not* oxidized by dissolution in or exposure to scN_2O. For example, the following compounds did not react when kept in scN_2O solution overnight at 90−130 °C: 2-butanol, cyclohexane, cyclododecene, cyclohexanone, triethylamine, and diethyl sulfide. Even aliphatic and aromatic aldehydes were recovered unreacted if air was rigorously excluded at all stages. Thus, aldehydes and phosphines are opposite in their reactivity toward O_2 and N_2O. Aldehydes are easily oxidized by air at room temperature but are resistant to oxidation by N_2O even at 130 °C. Neither triphenylphosphine nor methyldiphenylphosphine in acetonitrile solution is oxidized by exposure to air over 17 h at room temperature, but both are readily oxidized by N_2O at 65 °C. It is not surprising that ease of oxidation by O_2 is not a reliable indicator of ease of oxidation by scN_2O; very different mechanisms must be involved. For oxidation of aldehydes and other substrates by scN_2O, catalysis will be required.[30]

In conclusion, nitrous oxide is capable of oxidizing at least one class of organic compounds, the phosphines, at temperatures well below 200 °C. The use of supercritical N_2O as the solvent and the reactant simplifies the isolation of the products and allows one to avoid the use of flammable liquid solvents. A kinetic investigation of the reaction and tests of the oxidation of other functional groups by scN_2O or scN_2O/CO_2 mixtures, with and without catalysts, are in progress.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

OL9906918

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