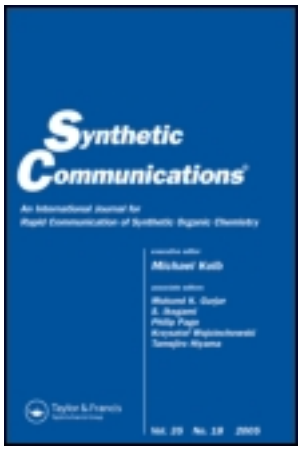

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SILICA CHLORIDE/$NaNO_2$ AS A NOVEL HETEROGENEOUS SYSTEM FOR THE NITROSATION OF SECONDARY AMINES UNDER MILD CONDITIONS

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ABSTRACT

Secondary amines can be readily converted to their corresponding nitroso derivatives with a combination of silica chloride (**I**), wet SiO_2 and sodium nitrite in dichloromethane at room temperature with moderate to excellent yields.

N-Nitrosation chemistry of amines is an important and well-established reaction in organic synthesis.[1] The most general reagent is nitrous acid, generated from sodium nitrite and mineral acid in water or in mixed alcohol–water solvents.[2] Other nitrosating agents, such as Fremy's salt,[3] *bis*(triphenylphosphine)nitrogen(1 +)nitrite,[4] *N*-haloamides

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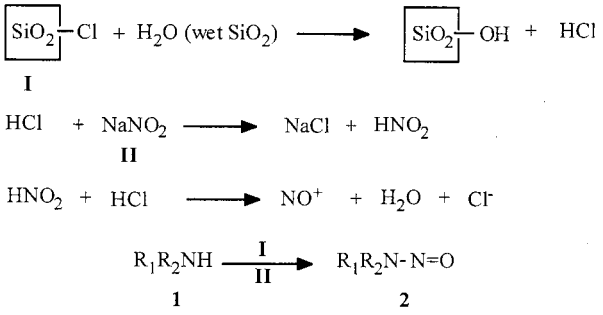
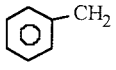
and sodium nitrite under phase-transfer conditions,[5] oxyhyponitrite,[6] dinitrogen tetroxide,[7] solid acids (i.e. oxalic acid dihydrate,[8] inorganic acidic salts[9] and hydrolyzable chloride salts[10]) and sodium nitrite have also been used.

There is intense current research and general interest in heterogeneous systems because of the perceived opportunities such systems present for basic research and because of the unquestioned importance such systems have in industry and in developing technologies.[12,13] In continuation of our studies on the application of inorganic acidic salts[11] we found that the silica chloride[14,15] (**I**) is an excellent source for generation of HCl. It is interesting to note that the addition of wet SiO_2 to the reaction mixture containing silica chloride could generate HCl in situ. Therefore, we were interested in using this reagent (**I**) for the nitrosation of secondary amines via in situ generation of HNO_2 and NO^+ respectively when used in conjunction with $NaNO_2$, wet SiO_2 in organic solvent (Scheme 1). We wish to report a simple



1 or 2	$R_1 = R_2$	1 or 2	$R_1 = R_2$
a	Me	f	$-(CH_2)_2-O-(CH_2)_2-$
b	Et	g	$-(CH_2)_5-$
c	*iso*-Pr	h	
d		i	

Scheme 1.

Table 1. Nitrosation of Secondary Amines (**1**) to Their Corresponding Nitrosoamines (**2**) with a Combination of Silica Chloride (I), $NaNO_2$ (**II**), and Wet SiO_2 (50% w/w) in Dichloromethane at Room Temperature

Entry	Substrate	Product[a]	(Reagent/Substrate)[b] **I** (g)	(Reagent/Substrate)[b] **II** (mmol)	Time (h)	Yield[c] (%)
1	**1a**	**2a**	0.3	1.5	0.75	100[d]
2	**1b**	**2b**	0.3	1.5	0.75	90
3	**1c**	**2c**	0.3	1.5	1	95
4	**1d**	**2d**	0.3	1.5	1.5	98
5	**1e**	**2e**	0.3	1.5	0.75	95
6	**1f**	**2f**	0.3	1.5	0.75	95
7	**1g**	**2g**	0.3	1.5	1.5	98
8	**1h**	**2j**	0.3	1.5	1.5	92

[a]All of the isolated products are known and their spectra and physical data have been reported in the literature; [b]Wet SiO_2: substrate (0.2 g : 1 mmol); [c]Isolated yields; [d]Conversion.

method for the effective nitrosation of secondary amines under mild and heterogeneous conditions.

A range of secondary amines (**1**) was subjected to the nitrosation reaction in the presence of silica chloride (**I**), $NaNO_2$ (**II**) and wet SiO_2 (50% w/w) in dichloromethane (Scheme 1). The nitrosation reactions were performed under mild and completely heterogeneous conditions at room temperature and proceeded in moderate to excellent yields (Table 1).

The nitrosation reaction did not occur in the absence of wet SiO_2. This observation suggests that the water molecule is essential for such processes. The presence of wet SiO_2 thus provides an effective heterogeneous surface area for in situ generation of NOCl[10] (Scheme 1). It also eases the reaction work-up.

In conclusion, the cheapness and the availability of the reagents, easy and clean work-up, make this method attractive for large-scale operations.

EXPERIMENTAL SECTION

General

Chemicals were purchased from Fluka, Merck and Aldrich chemical companies. Yields refer to isolated pure products. The nitrosation products

were characterized by comparison of their spectral (IR, ^{1}H-NMR, ^{13}C-NMR), TLC and physical data with the authentic samples. Silica chloride was synthesized according to the reported procedure.[15]

General Procedure for *N*-Nitrosation of Secondary Amines

A suspension of sodium nitrite, silica chloride (The molar ratio of silica chloride and sodium nitrite to the substrate **1** was optimized Table), amine (**1**, 5 mmol), silica chloride (1.5 g), $NaNO_2$ (0.517 g, 7.5 mmol) and wet SiO_2 (50% w/w) in dichloromethane (10 ml) was vigorously stirred magnetically at room temperature. The progress of the reaction was followed by TLC. The reaction mixture was filtered after completion of the reaction. The residue was washed with CH_2Cl_2 (2×5 ml). Then anhydrous Na_2SO_4 (10 g) was added to the filtrate and filtered after 20 min. The solvent was evaporated and the *N*-nitroso compound (**2**) were obtained (Table 1). If further purification is needed, flash chromatography on silica gel [eluent: acetone/petroleum ether (10 : 90)] provides highly pure **2**.

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