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AN EFFICIENT METHOD FOR N-NITROSATION OF SECONDARY AMINES UNDER MILD AND HETEROGENEOUS CONDITIONS

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Abstract: A combination of inorganic acidic salts or silica gel supported inorganic acids and sodium nitrite in the presence of wet SiO_2 was used as an effective nitrosating agent for the nitrosation of secondary amines to their corresponding nitroso drivatives under mild and heterogeneous conditions in moderate to excellent yields. $Mg(HSO_4)_2$ and $NaHSO_4$ are superior to all the aforementioned reagents in convenience, yield and purity of the isolated nitrosoamines.

N-Nitrosation chemistry of amines is an important and well-established reaction in organic synthesis. Although various nitrosating agents have been reported for this purpose^{1,2} we wish to report a simple, cheap and convenient

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

Different kinds of secondary amines (1) were subjected to nitrosation reaction in the presence of NaNO₂, wet SiO₂ (50% w/w), silica gel supported inorganic acids such as H_2SO_4/SiO_2 and H_3PO_4/SiO_2 or inorganic acidic salts e. g. Mg(HSO₄)₂ and NaHSO₄.H₂O in dichloromethane (Scheme). The nitrosation reactions were performed under mild and completely heterogeneous conditions at room temperature in moderate to excellent yields (Table).



NaHSO₄.H₂O and Mg(HSO₄)₂ are superior to all the above mentioned reagents, in convenience, yield and purity of the isolated nitrosoamines (2).

The present nitrosation reaction can be readily carried out only by placing, $NaNO_2$, solid acid, 1, wet SiO₂ (50% w/w) and CH₂Cl₂ as the inert usable solvent in a reaction vessel and efficiently stirring the resultant heterogeneous mixture at room temperature for and the nitrosoamines (2) can be obtained by simple filtration and evaporation of the solvent. The results and reaction conditions are tabulated in Table.

Reagent	1	2	2 Reag. /Subst. (mmol) ^a		Time	Yields ^b
			I	II	(h)	%
Mg(HSO ₄) ₂	a	a	4	2	1	100 ^e
NaHSO ₄ .H ₂ O	a	a	2	2	1	100 ^e
H ₂ SO ₄ /SiO ₂ ^c	a	a	2	2	0.5	100 ^e
H ₃ PO ₄ /SiO ₂ ^c	a	a	2	2	0.5	100 ^e
Mg(HSO ₄) ₂	b	b	4	2	1	98
NaHSO ₄ .H ₂ O	b	b	2	2	1	90
H ₂ SO ₄ /SiO ₂ ^c	b	b	2	2	1	82
H ₃ PO ₄ /SiO ₂ ^c	b	b	2	2	1	85
Mg(HSO ₄) ₂	c	c	4	2	1	80
NaHSO ₄ .H ₂ O	c	c	2	2	5	93
H ₂ SO ₄ /SiO ₂ ^c	c	c	2	2	5	77
H ₃ PO ₄ /SiO ₂ ^c	c	c	2	2	8	80
Mg(HSO ₄) ₂	d	d	4	2	1	95
NaHSO ₄ .H ₂ O	d	ď	2	2	1	98
H ₂ SO ₄ /SiO ₂ ^c	d	d	2	2	1	97
H ₃ PO ₄ /SiO ₂ ^c	d	d	2	2	8	97
Mg(HSO ₄) ₂	e	e	4	2	1	81
NaHSO ₄ .H ₂ O	e	e	2	2	6	93
H ₂ SO ₄ /SiO ₂ ^c	e	e	2	2	5	80
H ₃ PO ₄ /SiO ₂ ^c	e	e	2	2	5	91
Mg(HSO ₄) ₂	f	f ^d	2	1	2	85
NaHSO ₄ .H ₂ O	f	f ^d	2	_ 2	5	99
H ₂ SO ₄ /SiO ₂ ^c	f	fd	2	2	5	f
H ₃ PO ₄ /SiO ₂ ^c	f	fd	2	2	5	85

Table. Nitrosation of Secondary Amines to Their Corresponding Nitrosoamines (2) with a Combination of NaNO₂ (I), Wet SiO₂ (50% w/w) and Different Reagents (II) in Dichloromethane at Room Temperature.

⁴ Wet SiO₂ : substrate (0.2 g : 1mmol) . ^b Isolated Yields. ^cSilica gel supported inorganic acids [acid : SiO₂ (30% w/w)] were used which were prepared by applying H₂SO₄ (98%) and SiO₂ and H₃PO₄ (85%). ^d These reaction were not completely chemoselective. ^c Conversion. ^f Mixture of products were produced.

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

General Procedure for N-Nirosation of Secondary Amines

A suspension of sodium nitrite, solid acid (The molar ratio of solid acid and sodium nitrite to the substrate 1 was optimized Table) and amine (1, 10 mmol) in dichloromethane (20 ml) was stirred vigorously magnetically at room temperature. The progress of the reaction was followed by TLC. To the reaction mixture silica gel (5 g) and petroleum ether (20 ml) were added, the undesired precipitates were removed by filtration and washing with petroleum ether :dichloromethane (1:1, 20 ml). The solvent was evaporated and the N-nitroso compounds 2 was obtained (Table). If further purification is needed, flash chromatography on silica gel [eluent: acetone / petroleum ether (5:95)] to give extra pure 2.

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