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A New Mild Oxidation of Amines to Aldehydes and Ketones. Part II

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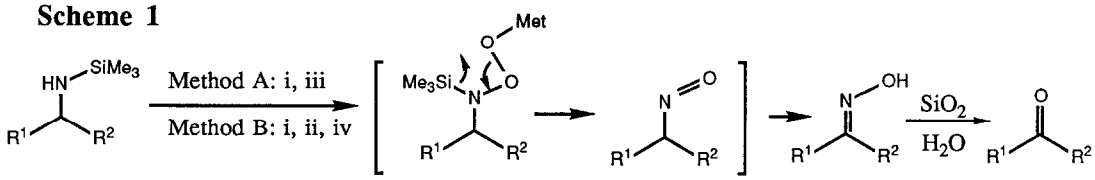
Summary: The silylamines **1**, after conversion into their lithium or zinc salts, were readily oxidized by dry air under very mild conditions (-60° C to -20° C; 5-45 min.) into the corresponding aldehydes or ketones **2** in good yields. Our reaction conditions tolerate the presence of other oxidation sensitive functional groups like a phosphine, a thioether or a tertiary amine.

Recently we reported that 1,1-diorganometallics of tin, silicon and zinc are readily oxidized by dry air into aldehydes and ketones in good yields[1]. We found that this reaction could be extended to metallated silylamines (see Scheme 1).

Scheme 1



1 **3** : Met = Li or ZnBr **4** **5** **2**

i. BuLi, -78°C; ii. $ZnBr_2$; iii. dry air, -60°C to -40°C; iv. dry air, -20°C.

Thus if silylamines[2] of type **1** are first deprotonated by BuLi (1.02 eq.; -78° C; 30 min.) and the reaction flask is then connected to a balloon filled with dry air (-40° C; 5-30 min.), a rapid oxidation occurs which affords after work-up and flash chromatography the ketones or aldehydes **2** in good yields (Method A; see Scheme 1 and Table I). We noticed that a transmetallation of the lithiated silylamine to the corresponding zinc derivative prior to oxidation leads in some cases to slightly higher yields (Method B). We believe that oxygen inserts first between the N-Li or N-Zn bond leading to an intermediate of type **3** which eliminates $Me_3SiOMet$ and gives the nitroso compound **4**. After tautomerization, the oximes **5** are formed and conveniently converted after a flash chromatographic purification into aldehydes or ketones. This new oxidation reaction[3] shows an interesting chemoselectivity and N-trimethylsilylaminodiphenylmethane could be oxidized into benzophenone in over 80% yield in the presence of 1 eq. of triphenylphosphine, thioether or N,N-dimethylbenzylamine. In each of these experiments, the phosphine, thioether and the tertiary amine could be recovered in 83%, 94% and 100% respectively.

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Table I. Preparation of Aldehydes and Ketones **2** From the Silylamines **1**.

Silylamine **1**	Method	T (°C)	Time (min.)	Aldehyde or Ketone **2**	Yield (%)[a]
N-trimethylsilylcyclohexylamine	A	-40	10	cyclohexanone	87
	B	-20	20		86
N-trimethylsilylcyclopentylamine	A	-40	15	cyclopentanone	84
	B	-20	30		87
N-trimethylsilylcyclohexanemethylamine	A	-60	10	cyclohexanecarboxaldehyde	89
	B	-20	45		91
N-trimethylsilyl-2-aminoheptane	A	-60	20	2-heptanone	81
	B	-20	30		85
N-trimethylsilylbenzylamine	A	-60	5	benzaldehyde	74
	B	-20	45		71
N-trimethylsilyl-1-phenylethylamine	A	-60	10	acetophenone	72
	B	-20	30		76
N-trimethylsilylcyclooctylamine	A	-60	25	cyclooctanone	89
	B	-20	40		84
N-trimethylsilyl-2-aminonorbornane	A	-40	30	norbornanone	85
	B	-20	60		81
N-trimethylsilyl-4-aminoheptane	A	-60	20	4-heptanone	82
	B	-20	35		81
N-trimethylsilylaminodiphenylmethane	A	-40	30	benzophenone	85
	B	-20	60		82

[a] All indicated yields are isolated yields. Satisfactory spectral data (IR, ^{1}H and ^{13}C-NMR, mass spectra) were obtained for all compounds.

References

1. A Mild Oxidation of 1,1-Diorganometallics to Ketones and Aldehydes. A New Stereoselective Approach to Aldol Products. Part I. Preceding publication.

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3. For oxidation of primary amines to aldehydes or ketones see: (a) Kahr, K.; Berther, C. Chem. Ber. **1960**, 93, 132; (b) Lee, G.A.; Freedman, H.H. Tetrahedron Lett. **1976**, 1641; (c) Hoffman, R.V.; Kamar, A. J. Org. Chem. **1984**, 49, 4011 and references cited.

4. Typical procedure: **Method A**: To a solution of N-trimethylsilyl-2-aminonorbornane (1.0 g; 5.45 mmol) in 10 ml of THF was added at -78° C (3.5 ml; 5.6 mmol) of BuLi (1.6 M in hexane). After 30 min., the reaction flask was connected to a balloon filled with dry air and the reaction mixture warmed up to -50° C. After 25 min. at this temperature the reaction was worked up as usual. The crude product was purified by flash chromatography (hexane-ether) to give 2-norbornanone (0.51 g; 85%) as white crystals (m.p. 92-93° C). **Method B**: A solution of $ZnBr_2$ (1.35 g; 6.0 mmol) in 5 ml of THF was added to the lithiated silylamine prior to the oxidation which was performed at -20° C for 35 min. and afforded 0.48 g (81%) of pure norbornanone.

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