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A NEW SYNTHESIS OF α-CYANOAMINES. LEWIS ACID PROMOTED NUCLEOPHILIC SUBSTITUTION OF α-SILOXYAMINES USING TRIMETHYLSILYL CYANIDE

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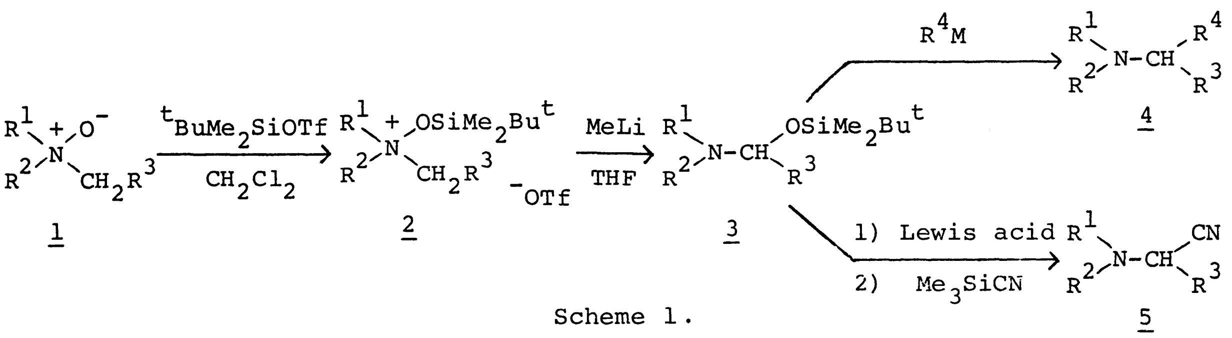
α-Siloxyamines obtained from tertiary amines via their N-oxides were treated with titanium tetrachloride and trimethylsilyl cyanide to give α-cyanated tertiary amines in good yields.

The α-functionalization of amines has been attracting much attention from a viewpoint of the syntheses of nitrogen-containing natural products such as alkaloids. Although the electrophilic α-substitution of amines via dipole-stabilized carbanions and the conventional Mannich type of nucleophilic introduction of α-substituents into primary and secondary amines have been studied extensively,1) the nucleophilic direct α-functionalization of tertiary amines have not been fully investigated.

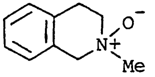
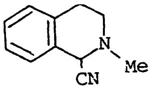
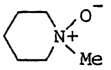
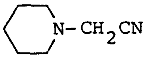
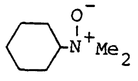
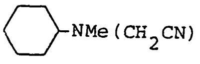
Recently, we have reported a new general α-substitution method of tertiary amines via their N-oxides (1).2) Thus, siloxyammonium salts (2) prepared from 1 and trialkylsilyl trifluoromethanesulfonate rearrange in the presence of alkyllithiums to give α-siloxyamines (3), whose siloxy group undergoes nucleophilic substitution with Grignard reagents or trialkylaluminums to afford new tertiary amines (4) having an α-substituent derived from the organometallics. In this report we delineate Lewis acid promoted nucleophilic substitution of α-siloxyamines (3) with trimethylsilyl cyanide leading to α-cyanation of tertiary amines (Scheme 1). α-Cyanoamines thus obtained are a synthetically useful intermediate in the preparation of important amine derivatives such as aminoacids.3,4)



Scheme 1.

Treatment of 3 (obtained in situ from 1 via 2) with titanium tetrachloride and subsequently with trimethylsilyl cyanide afforded α-cyanated product (5) in good yields. As a Lewis acid titanium tetrachloride was most effective; trimethylsilyl trifluoromethanesulfonate and stannic chloride could be used but the yields of 5 were somewhat diminished. Results obtained from the reactions of several amine N-oxides are summarized in Table 1.5) They suggest that the regioselectivity of this cyanation is controlled by the acidity of α-hydrogen of substituents on the ammonium salt (2) which is deprotonated by the base. In view of ready availability of amine N-oxides and trimethylsilyl cyanide, and the possibility of further functionalization of the newly introduced cyano group, we believe the present one-pot sequence provides a new convenient synthetic method for nitrogen-containing natural products.

Table 1. α-Cyanation of Tertiary Amines via Their N-Oxides

N-Oxide (1)	Product (5)	Yield/%	
		63	
		61	
		71	
$PhCH_2(Me)_2N^+-O^-$	$PhCH(CN)NMe_2$	22	62
	$PhCH_2NMe(CH_2CN)$	40	
$(PhCH_2)_3N^+-O^-$	$(PhCH_2)_2NCH(CN)Ph$	78	

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References

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3) Very recently, different approaches to α-cyanoamines have been reported: K. Mai and G. Patil, Tetrahedron Lett., 25, 4583 (1984); H. Yamanaka, S. Nishimura, S. Kaneda, and T. Sakamoto, Synthesis, 1984, 681.

4) The α-cyanoamines can also be a useful intermediate for the synthesis of α-alkylamines via alkylation-decyanation procedure: G. Stork, R. M. Jacobson, and R. Levitz, Tetrahedron Lett., 1979, 771 ; M. Bonin, J. R. Romeo, D. S. Grieson, and H.-P. Husson, J. Org. Chem., 49, 2392 (1984).

5) A typical example is as follows. N-Methyl-1,2,3,4-tetrahydroisoquinoline N-oxide (1a) (1 mmol) was allowed to react with t-butyldimethylsilyl trifluoromethanesulfonate (1.1 mmol) in dichloromethane at 0 °C to give 2a. After replacement of the solvent by tetrahydrofuran, 2a was treated with methyllithium (1.2 mmol) at 0 °C and then, after once more replacement of the solvent into dichloromethane, with titanium tetrachloride (1.3 mmol) at -78 °C and after stirring 30 min at this temperature was added trimethylsilyl cyanide (1.5 mmol) at -78 °C. The mixture was stirred for further 10 h at room temperature and subjected to alkaline work-up to give the α-cyanated product (5a) exclusively in 63% yield.

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