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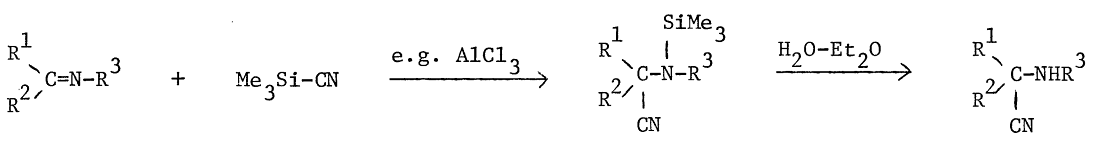
A NEW ROUTE TO AMINONITRILES VIA CYANOSILYLATION OF SCHIFF BASES AND OXIMES

Iwao OJIMA*, Shin-ichi INABA, and Kimiyo NAKATSUGAWA
Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa 229
and Yoichiro NAGAI
Department of Chemistry, Gunma University, Kiryu, Gunma 376

Trimethylsilyl cyanide was found to react with Schiff bases and oximes in the presence of a catalytic amount of Lewis acids to afford N-trimethylsilyl-α-aminonitriles and N-trimethylsilyloxy-α-aminonitriles in excellent yields, which were easily hydrolyzed to the corresponding α-aminonitriles and α-hydroxyaminonitriles.

Recently, it has been shown that trimethylsilyl cyanide (TMSCN) is a good reagent for the preparation of cyanohydrin derivatives which can be used as selective carbonyl protective groups in organic syntheses.[1,2] Thermal and Lewis acid catalyzed reaction of TMSCN with acyl halides or epoxides have been also reported.[2] However, little attention has been drawn to the reaction of TMSCN with carbon-nitrogen double bonds except our recent report on the formation of 5-(TMS-imino)diazolidinediones from TMSCN and isocyanates.[3] Now, we wish to describe in this communication the first examples of the addition reaction of TMSCN to Schiff bases and oximes catalyzed by Lewis acids such as $AlCl_3$, ZnI_2 and $Al(OR)_3$, which demonstrate that TMSCN has a wide potential utility as a safe and versatile hydrogen cyanide substitute.[4]

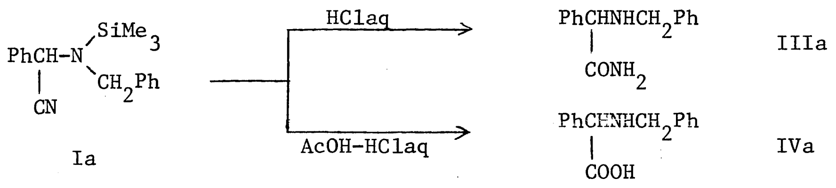
We found that TMSCN smoothly reacted with Schiff bases in the presence of a catalytic amount (0.5-5.0 mol%) of the Lewis acid at 0-40°C to afford N-TMS-α-aminonitriles in high yields. These N-TMS-α-aminonitriles were easily converted to the corresponding α-aminonitriles, α-aminoamides and α-aminoacids by hydrolysis depending upon the reaction conditions.



I

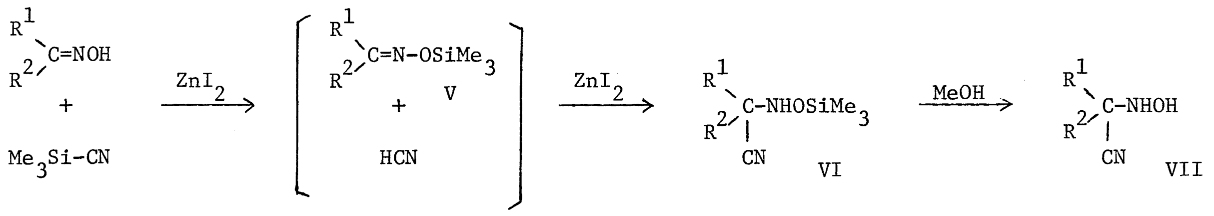
II

In a typical procedure, to a mixture of TMSCN and benzilidenebenzylamine was added 0.5 mol% of aluminum trichloride, and the mixture was stirred at ambient temperature for 6 hr. Then, the reaction was completed, which was checked by means of IR and NMR spectra [α-(N-TMS-N-benzylamino)-α-phenylacetonitrile(Ia): IR(neat) 2220 cm^{-1}(νC≡N), NMR(CDCl$_3$) δ0.06(s, 9H), 3.89(s, 2H), 5.06(s, 1H) and 6.95-7.40 (m, 10H)]. The reaction mixture was hydrolyzed in aqueous ether, and the ether layer was condensed and submitted to column chromatography on silica gel. α-(N-benzylamino)-α-phenylacetonitrile(IIa) was obtained from the benzene eluate in 88 % yield, which was pure enough to satisfy the elemental analysis. The N-TMS-α-aminonitrile Ia was converted to α-(N-benzylamino)-α-phenylacetamide(IIIa) by hydrolysis using hydrochloric acid, and was also hydrolyzed to N-benzylphenylglycine(IVa) using acetic acid-hydrochloric acid (1:1).



Other Schiff bases reacted with TMSCN in a similar manner. The results are summarized in Table 1.[5]

Next, we performed a cyanosilylation of oximes. The reaction of oximes with TMSCN in the presence of a catalytic amount of zinc iodide was found to afford N-trimethylsilyloxy-α- aminonitriles in high yields. In these cases, the reaction seems to proceed via silylation of hydroxy group followed by addition of *in situ* generated hydrogen cyanide to the carbon-nitrogen double bond.



In fact, the initialy formed O-TMS-oximes(V) could be detected by means of glpc analysis and also be isolated. The N-trimethylsilyloxy-α-aminonitriles(VI) were easily converted to the corresponding α-hydroxyaminonitriles(VII) by the action of methanol. Results are summarized in Table 2.[6]

A further investigation and an application to the asymmetric reactions are now in progress.

Table 1. Cyanosilylation of Schiff Bases

	R^1	R^2	R^3	Catalyst	Amount of Cat. (Mol%)	Conditions	Yield[a] (%)
a	Ph	H	$PhCH_2$	$AlCl_3$	1.0	r.t., 6 hr	98
				ZnI_2	5.0	r.t., 6 hr	88
				$Al(OPr^i)_3$	1.0	50°C, 24 hr	85
b	Ph	H	Ph	$AlCl_3$[b]	1.0	r.t., 12 hr	81
c	Ph	H	Me	ZnI_2	2.5	5-10°C, 5 hr	86
d	Ph	Me	$PhCH_2$	$AlCl_3$[b]	1.0	r.t., 5 hr	87
e	Ph	Ph	H	ZnI_2[b]	5.0	r.t., 6 hr	91
f	$-(CH_2)_5-$		$PhCH_2$	$AlCl_3$	5.0	10°C, 2 hr	82
				ZnI_2	5.0	r.t., 24 hr	89
				$Al(acac)_3$[c]	1.0	r.t., 24 hr	96
				$TiCl_4$	2.0	r.t., 24 hr	81
g	$^nC_3H_7$	H	$PhCH_2$	ZnI_2	5.0	r.t., 1 hr	82

[a] Isolated yield of II based on the Schiff base. [b] Benzene was used as a solvent. [c] $Al(acac)_3$: tris(acetylacetonato)aluminum.

Table 2. Cyanosilylation of Oximes

	R^1	R^2	Catalyst	Amount of Cat. (Mol%)	Conditions	b.p.[a] (°C/mmHg)	Yield[b] (%)
a	CH_3	H	ZnI_2	1.0	r.t., 48 hr	83/13	81
b	$^nC_3H_7$	H	ZnI_2	1.0	r.t., 48 hr	73/0.9	77
c	CH_3	CH_3	ZnI_2	1.0	r.t., 48 hr	89/13	66
d	$-(CH_2)_5-$		ZnI_2	1.0	r.t., 48 hr	95-96/1.0[c]	70

[a] boiling point of VI. [b] Isolated yield of VII based on the oxime.
[c] m.p. 53-55°C.

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4. As for the formation of α-aminonitriles by the addition of hydrogen cyanide to Schiff bases and oximes, see: G. E. P. Smith, Jr., and F. W. Bergstrom, J. Amer. Chem. Soc., 56, 2095 (1934); R. Tiollais, Bull. Soc. Chim. Fr., 959 (1947); A. Dornow and S. Lüpfert, Chem. Ber., 89, 2718 (1956); G. H. Harris, B. R. Harriman, and K. W. Wheeler, J. Amer. Chem. Soc., 68, 846 (1946); J. Collazos, Chim. Ind. (Paris), 86, 47 (1961); F. Adlickes, J. Prakt. Chem., 161, 271 (1943); C. C. Porter and L. Hellerman, J. Amer. Chem. Soc., 61, 754 (1939); H. A. Lillevik, R. L. Hossfeld, H. V. Lindstrom, R. T. Arnold, and R. A. Gortner, J. Org. Chem., 7, 164 (1942); C. C. Porter and L. Hellerman, J. Amer. Chem. Soc., 66, 1652 (1944); C. D. Hurd and J. M. Longfellow, J. Org. Chem., 16, 761 (1951).
5. The structures of N-TMS-α-aminonitriles were confirmed on the basis of NMR and IR spectra, and by hydrolysis to the α-aminonitriles whose structures were elucidated on the basis of NMR and IR spectra and elemental analyses.
6. The NMR and IR spectra and elemental analyses of N-trimethylsilyloxy-α-aminonitriles and α-hydroxyaminonitriles well corresponded to the assigned structures.

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