

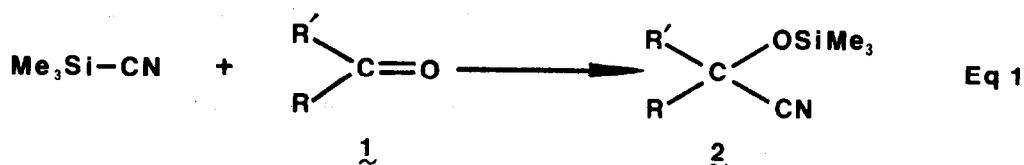
CARBONYL INSERTION REACTIONS OF SILICON PSEUDOHALIDES: CATALYSIS

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(Received in USA 22 August 1973; received in UK for publication 29 October 1973)

Recently the thermal and Lewis acid catalyzed addition of trimethylsilyl cyanide (TMSCN)² to aldehydes, ketones (Eq 1), and acid chlorides has been reported by us and others.^{3,4} In addition to the advantages of utilizing TMSCN as a reagent for the preparation of cyanohydrin derivatives presently inaccessible by other means, the applications of these adducts as selective carbonyl protective groups in organic synthesis appear to be promising. Our recent report on the selective protection of *p*-quinone carbonyl functions bears out this assertion.^{3b}

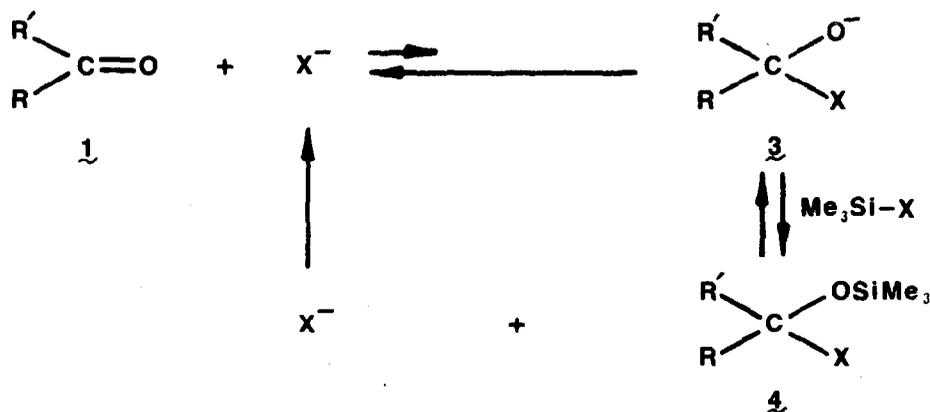


Although there is ample precedent for the Lewis acid catalyzed addition of silicon pseudohalides to aldehydes and ketones,^{3,4,5} no precedent for anionic catalysis has been reported for these reactions. Herein we wish to report our observations on the first examples of anionic catalysis for this carbonyl addition process.

We have found that small amounts (.01-.02 equiv) of cyanide ion are exceptionally mild and efficient catalysts for carbonyl cyanosilylation (Eq 1). Crown ether complexes of alkali metal cyanides, tetra-*n*-butylammonium cyanide, and resin-bound tetraalkylammonium cyanide have each proven effective as catalytic agents.

As illustrated in Scheme I, the presumed mode of catalysis involves carbonyl addition of cyanide ion (X = CN) affording small equilibrium concentrations of **3** which is trapped by subsequent silicon transfer. This catalytic model suggests that any anion, X⁻, which is either capable of carbonyl addition or of effecting ligand exchange on silicon (Eq 2) should initiate catalysis of carbonyl cyanosilylation.

Scheme I.



Examination of the 18-crown-6⁶ complexes⁷ of potassium azide, thiocyanate, and methoxide as initiators for carbonyl cyanosilylation reveals these other anionic reagents, in addition to cyanide ion, are equally effective.



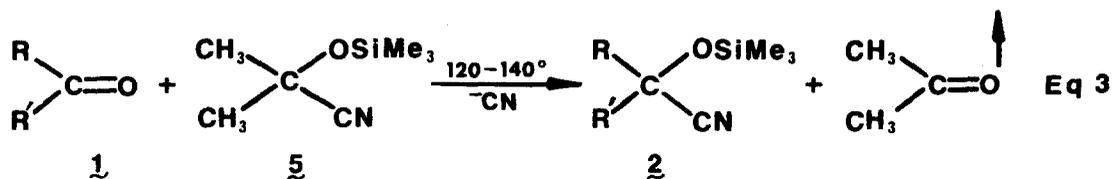
A comparison of four convenient cyanosilylation catalysts (Table I) has shown them to be of comparable efficiency; the only substrate which demonstrated catalyst selectivity was *p*-benzoquinone, which was inert to the Lewis acid catalysts examined.⁸

Table I.⁹ Carbonyl Cyanosilylation Catalysts

1	Catalyst ^a	Adduct 2 ^b
3-Pentanone	ZnI ₂	85%
3-Pentanone	AlCl ₃	84%
3-Pentanone	KCN·18-crown-6	89%
3-Pentanone	Bu ₄ N ⁺ CN ⁻	84%
4- <i>t</i> -butylcyclohexanone	ZnI ₂	97%
4- <i>t</i> -butylcyclohexanone	KCN·18-crown-6	99%
<i>p</i> -Benzoquinone	ZnI ₂	(0%)
<i>p</i> -Benzoquinone	AlCl ₃	(0%)
<i>p</i> -Benzoquinone	KCN·18-crown-6	80% (>95%) ^c
<i>p</i> -Benzoquinone	(115°/2 hr)	(>95%) ^c

^aOne equiv each of TMSCN and 1 and .01-.02 equiv of catalyst were mixed in the absence of solvent at 25°. ^bYields reported in parenthesis were determined by nmr; others refer to isolated adducts. ^cMono adducts.

The potential reversibility of the carbonyl-trimethylsilyl cyanide addition processes suggests that α -silyloxy nitriles can be prepared via the exchange process illustrated in Eq 3.



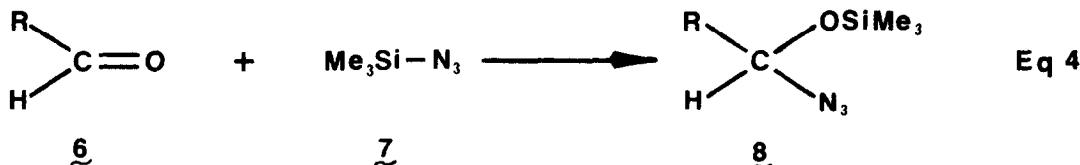
When the α -silyloxyisobutyronitrile 5, readily prepared from acetone cyanohydrin and trimethylsilyl chloride,¹⁰ and *n*-hexanal in equimolar quantities were stirred at 25° for 16 hr in the presence of the KCN·18-crown-6 catalyst (.01-.02 equiv) complete transcyanosilylation occurred. The reaction may be conveniently carried out at elevated temperatures with both aldehydes and ketones where the acetone is distilled from the reaction mixture prior to distillation of the desired carbonyl adduct 2. Table II illustrates the advantage of employing cyanide ion over Lewis acid catalysts for transcyanosilylation in those systems which are prone to undergo acid catalyzed aldol condensation more rapidly than exchange.

Table II. Catalytic Transcyanosilylation (Eq 3)

R	<u>1</u>	R'	Catalyst ^a	Yield, % <u>2</u> ^b
C ₆ H ₁₃		CH ₃	KCN·18-crown-6	95
C ₆ H ₁₃		CH ₃	ZnI ₂	67(100%) ^d
C ₆ H ₁₃		CH ₃	None	0
C ₅ H ₁₁		H	KCN·18-crown-6	76
C ₅ H ₁₁		H	ZnI ₂	0 ^c
C ₅ H ₁₁		H	None	0

^aCatalyst concentrations of .01-.02 equiv employed. ^bYields of isolated product. ^cNo recovered aldehyde. ^dBased on unrecovered starting material.

Extension of the concept of anionic initiated organosilane-carbonyl insertion reactions may prove to be general. We have examined the reaction of aliphatic aldehydes with trimethylsilyl azide (7) catalyzed both by zinc chloride⁵ and with the KN₃·crown complex (Eq 4).⁷



The reaction of both *n*-hexanal and *iso*-butyraldehyde with **7** employing the azide-crown catalyst at room temperature afforded 89% isolated yields of adducts **8**.¹¹ In contrast, the zinc chloride catalyzed reactions with the same aldehydes required heating to effect carbonyl insertion;⁵ furthermore, the yields of adducts **8** are consistently lower employing the acid catalysts. If the catalytic cycle suggested in Scheme I is correct, it thus appears that azide ion is also capable of affording small equilibrium concentrations of azido alkoxide **3** ($X = N_3$). The failure to generate such intermediates would result in the lack of observed anionic catalysis as is the case with both ketones and α,β -unsaturated aldehydes.

All attempts to effect carbonyl insertion with trimethylsilyl thiocyanate¹² employing a variety of acid as well as basic catalysts have proven unsuccessful to date. This result is of some interest in that we have shown that silicon sulfides readily undergo carbonyl insertion with aldehydes specifically with the anionic catalysts.¹³

In summary, there appear to be definite advantages to employing anionic catalysis in effecting organosilane carbonyl addition reactions, particularly when dealing with acid labile carbonyl derivatives. The general scope of other organosilane addition processes will be reported in due course.

Acknowledgement. We wish to thank the Petroleum Research Fund administered by the American Chemical Society for support of this research.

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8. Attempts to add TMSCN to both esters and anhydrides with a variety of catalysts have so far proven unsuccessful thus limiting somewhat the generality of this reaction.
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