

Cyano-*O*-silylhydroxylamines as Nitron Blocking Groups

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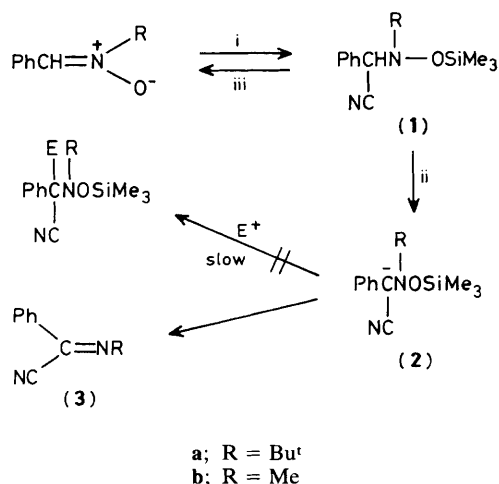
Addition of trimethylsilyl cyanide to *N*-alkyl-*C*-phenylnitrones affords cyano-*O*-silylhydroxylamines; reaction of these species with silver fluoride regenerates the nitron in quantitative yield thereby providing a useful nitron blocking group.

The addition of trimethylsilyl cyanide to carbonyl compounds represents a convenient route for preparation of the corresponding cyanohydrin trimethylsilyl ethers.¹ These compounds serve not only as protected analogues of aldehydes and ketones but also as intermediates for the synthesis of cyanohydrins,² α -hydroxyamides,³ α,β -unsaturated nitriles,⁴ and β -aminoalcohols.⁵ It occurred to us that the reaction of trimethylsilyl cyanide with nitrones should give rise to cyano-*O*-silylhydroxylamines.⁶ The possible use of these cyano derivatives as carbanion equivalents of nitrones would be especially interesting for systems not otherwise readily available. Accordingly, this work was undertaken to synthesize and investigate the chemistry of cyano-*O*-silylhydroxylamines.

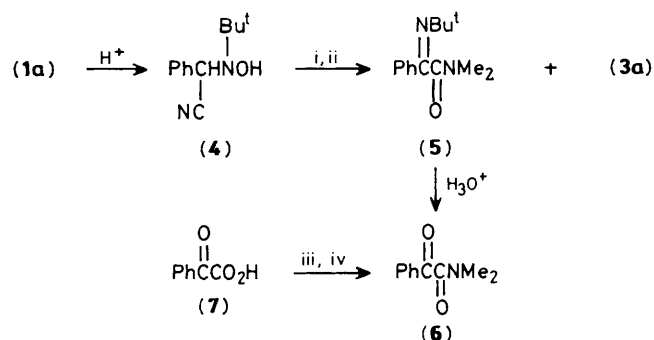
We found that Me₃SiCN reacted smoothly with either *N*-*t*-butyl- or *N*-methyl-*C*-phenylnitron in the presence of a catalytic amount of zinc iodide at 80 °C to give the α -cyano-*O*-silylhydroxylamines (**1**) in 95% yield. The *t*-butyl derivative (**1a**) was isolated as a crystalline solid [m.p. 75–76 °C, ¹H n.m.r. (CCl₄, 90 MHz) δ 0.01 (s, 9H), 1.50 (s, 9H), 5.23 (s, 1H), and 7.43–7.77 (m, 5H)] whereas the methyl derivative (**1b**) was obtained as a clear oil [¹H n.m.r. (CCl₄, 90 MHz) δ 0.02 (s, 9H), 2.40 (s, 3H), 4.80 (s, 1H), and 7.32–7.60 (m, 5H)]. The propensity of silicon to react with fluoride ion⁷ as well as the fact that cyanomethylamines can function as convenient iminium precursors^{8,9} strongly implied that treatment of (**1**) with silver fluoride would regenerate the nitron. This prediction was indeed shown to be valid. Thus, heating an acetonitrile solution of (**1**) with an equivalent quantity of silver fluoride at 80 °C resulted in the formation of the starting nitron in quantitative yield. While nitrones are versatile synthetic intermediates, especially useful for 1,3-dipolar cycloaddition reactions,¹⁰ they are prone to undergo numerous side reactions. The thermal cycloreversion of isoxazol-

idines represents one method that has been successfully utilized for nitron protection.¹¹ In certain cases, however, drastic conditions are required for the thermal fragmentation reaction to proceed.¹² These cyano-*O*-silylhydroxylamines should prove to be valuable as nitron blocking groups.

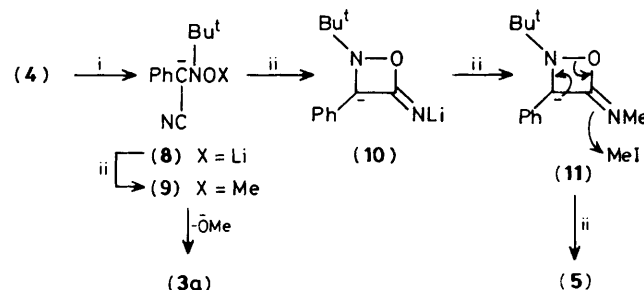
Treatment of compounds (**1**) with lithium diisopropylamide (LDA) at –78 °C generated carbanion (**2**) which failed to react with a variety of electrophilic reagents. Instead, the only material isolated in 90% yield corresponded to cyanoimine (**3**) (Scheme 1). Apparently, elimination of the trimethylsilyloxy group occurs at a faster rate than the bimolecular alkylation reaction. In order to retard the elimination, compound (**1a**) was converted to the corresponding hydroxylamine (**4**) with aqueous acid. Treatment of (**4**) with two equivalents of LDA followed by reaction with an excess of methyl iodide afforded *N,N*-dimethyl- α -(*t*-butylimino)benzeneacetamide (**5**) in 64% yield [¹H n.m.r. (CCl₄, 90 MHz) δ 1.27 (s, 9H), 2.70 (s, 3H), 2.95 (s, 3H), and 7.2–7.5 (m, 5H); u.v. (95% ethanol) 251 nm (ϵ 18000); *m/z* 232 (*M*⁺), 160 and 77]. Subjection of this material to an aqueous hydrolysis produced *N,N*-dimethyl benzoylformamide (**6**). The structure of (**6**) was unequivocally established by comparison with an independently synthesized sample pre-



Scheme 1. Reagents and conditions: i, Me₃SiCN, ZnI₂, 80 °C; ii, lithium diisopropylamide (LDA), –78 °C; iii, AgF, 80 °C.



Scheme 2. Reagents: i, LDA (2 equiv.); ii, excess of MeI; iii, SOCl₂; iv, Me₂NH.



Scheme 3. Reagents: i, LDA (2 equiv.); ii, MeI.

pared by treating benzoylformic acid (7) with thionyl chloride followed by reaction with dimethylamine. In addition to (5), cyanoimine (3a) was also isolated (36%) from the reaction of (4) with LDA and methyl iodide (Scheme 2).

Although information on the mechanistic details of this reaction is minimal, a tentative yet reasonable rationale can be advanced. Thus, the first step involves formation of dianion (8). Reaction of (8) with methyl iodide at oxygen furnishes (9) which can readily undergo elimination of methoxide ion to give the cyanoimine (3a). In addition, attack of the alkoxide portion of the dianion onto the nitrile group results in the formation of a four-membered ring transient [*i.e.* (10)]. Alkylation on nitrogen gives (11) which undergoes a subsequent ring opening and methylation reaction to furnish iminoamide (5) (see Scheme 3).

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