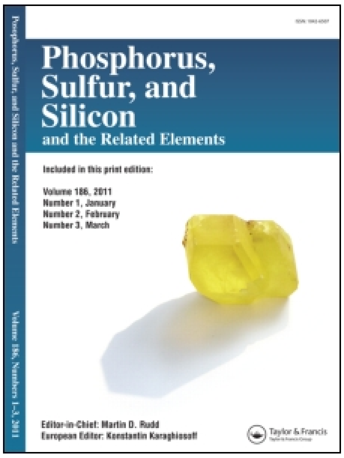

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# Trimethylsilyl Cyanide Addition to Carbonyl Compounds Under Neutral Condition Catalyzed by Iodine

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# TRIMETHYLSILYL CYANIDE ADDITION TO CARBONYL COMPOUNDS UNDER NEUTRAL CONDITION CATALYZED BY IODINE

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*Reaction of trimethylsilyl cyanide with aliphatic or aromatic aldehydes and ketones in the presence of a catalytic amount of elemental iodine produced the corresponding cyanohydrin trimethylsilyl ethers in very short time and high yields.*

*Keywords:* Carbonyl compound; cyanohydrin trimethylsilyl ether; iodine; trimethylsilyl cyanide

Cyanohydrins are valuable intermediates for the synthesis of various chiral compounds such as $\alpha$-hydroxycarbonyl derivatives and $\beta$-aminoalcohols.[1] Although the addition of cyanide to carbonyl compounds is a known reaction, it has been the subject of renewed interest due to the role of cyanohydrin as a versatile intermediate in organic synthesis.

A variety of catalysts has been reported for trimethylsilyl cyanide addition to carbonyl compounds,[2] including different Lewis acids,[3] titanium and ruthenium Schiff base complexes,[4] $Cu(OTf)_2$,[5] 18-crown-6 complexes of potassium and cesium,[6] tetracyano-ethylene,[7] solid acidic montmorillonite, and solid bases such as CaO and MgO.[8] Several optically active catalysts for asymmetric cyanohydrin formation also were used.[9] Although these procedures improved the addition process, in most cases reaction with ketone did not take place or required forceful conditions and prolonged reaction time.

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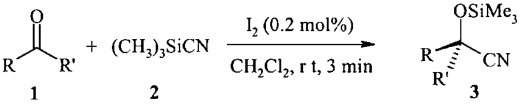
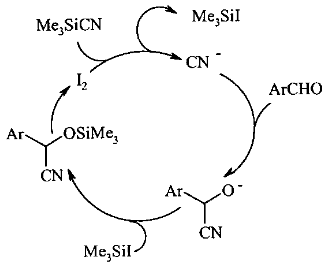
## RESULTS AND DISCUSSION

In connection with our interest for trimethylsilyl cyanide addition to the iminium salts,[10] we now report a new, rapid, convenient, and mild method using iodine as an efficient catalyst for addition of trimethylsilyl cyanide (TMSCN) to the carbonyl functional group. Thus treatment of aldehydes and ketones with TMSCN in the presence of 0.2 equivalents of elemental iodine in dichloromethane afforded the corresponding cyanohydrins in 86–97% yields under neutral and mild condition in a very short time. A wide variety of aldehydes and ketones were caused to react with TMSCN in the presence of a catalytic amount of iodine to produce the corresponding cyanohydrins (Scheme 1). The results are shown in Table I.



SCHEME 1

The data in Table I clearly show that cyclohexanone and different type of aldehydes were converted successfully to the corresponding cyanohydrin trimethylsilyl ethers almost instantly with high to nearly quantitative yields at room temperature. Due to the neutral and exceptionally mild reaction condition, no by-product was observed. Dichloromethane was the best solvent for this reaction. The yields of the cyanohydrin trimethylsilyl ethers in other solvent such as acetonitrile are lower. Both aromatic and aliphatic aldehyds reacted with TMSCN under these conditions to give the corresponding cyanohydrin trimethylsilyl ethers (Table I). The reaction proceeded smoothly at ambient temperature and has the advantages of operational simplicity, improved yields, enhanced rates and simple experimental work up

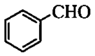
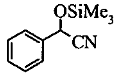
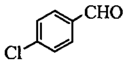
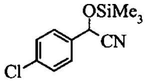
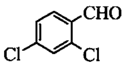
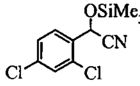
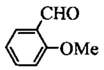
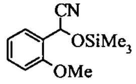
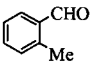
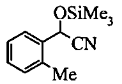
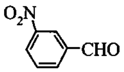
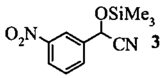
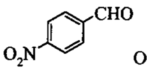
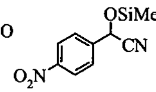
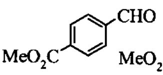
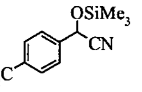
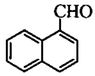
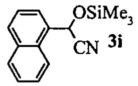
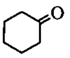
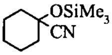
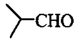
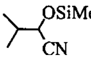


SCHEME 2

procedures. The generality of this reaction is evident from the results summarized in Table I.

The role of iodine could be the formation of trimethylsilyl iodide[11] or $[ArCH{=}OSiMe_3]^+$ in the initial step and subsequently producing a weakly solvated anion, which displays high reactivity toward the carbonyl group in aldehyde or ketone. A plausible mechanism for this transformation is shown in Scheme 2.

**TABLE I** Cyanosilylation of Aldehydes and Ketons in the Presence of Element Iodine

| Entry | Substrate | Product | Yield (%)[a] |
|---|---|---|---|
| 1 |  |  **3a** | 95 |
| 2 |  |  **3b** | 97 |
| 3 |  |  **3c** | 94 |
| 4 |  |  **3d** | 92 |
| 5 |  |  **3e** | 89 |
| 6 |  |  **3f** | 94 |
| 7 |  |  **3g** | 94 |
| 8 |  |  **3h** | 90 |
| 9 |  |  **3i** | 90 |
| 10 |  |  **3j** | 86 |
| 11 |  |  **3k** | 88 |

[a] isolated yields.

## CONCLUSION

In conclusion, the iodine as catalyst is an efficient, mild, readily available, and cheap reagent for TMSCN addition to aliphatic or aromatic aldehydes and ketones. The reaction condition is neutral and exceptionally mild with no by-product and with high yields of the cyanohydrin trimethylsilyl ethers. Both aromatic and aliphatic aldehydes reacted with TMSCN under these conditions and at ambient temperature.

## EXPERIMENTAL

### General

All the yields refer to isolated products. All compounds were characterized on the basis of their spectroscopic data (IR, NMR) and by comparison with those reported in the literature.[2a,8b] IR spectra were taken on a Matt Son 1000 Unicam FTIR, $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker AC 80 or Bruker 500 MHz Ultra Shield. Mass spectra were obtained on Fisson 800 Trio, and GC-Mass HP 5973 MSD. All reactions were performed under argon. Most aldehydes were distilled before use. Chemicals were purchased from Fluka or Merck.

### *General Procedure for Trimethylsilyl Cyanide Addition to Carbonyl Compounds*

Iodine (0.2 mmol) was added to the mixture of aldehyde (1 mmol) and TMSCN (1.3 mmol) in dry $CH_2Cl_2$ and the mixture was stirred at room temperature for 3 min. Then the resulting mixture was quenched quickly with aqueous sodium thiosulphate and extracted with ethyl acetate (2 × 15 ml), the combined organic layers washed quickly with a 5% solution of $NaHCO_3$ and dried over anhydrous sodium sulphate. Solvent was evaporated under reduced pressure and the crude material was purified by chromatography on silica gel eluting with petroleum ether/ethyl acetate, or washing with petroleum ether if needed. All compounds were characterized on the basis of their spectroscopic data (IR, NMR) and by comparison with those reported in the literature.[2a,8b] The prolonged washing with 5% solution of $NaHCO_3$ produced the corresponding cyanohydrins.

*Selected spectroscopic data:* Cyanohydrin trimethylsilyl ether **3a**, $^1H$ NMR (500 MHz, $CDCl_3$), $\delta$, 0.23 (s, 9H), 5.54 (s, 1H), 7.28–7.92 (m, 5H); $^{13}C$ NMR (125 MHz, $CDCl_3$), $\delta$, 0.1 ($CH_3$), 64.1 (CH), 119.4 (CN), 126.8 (CH), 127.12 (CH), 129.4 (CH), 136.7 (C); IR, ($CH_2Cl_2$), $\nu$, 2248 (CN), 1072 (C—O) $cm^{-1}$. Cyanohydrin trimethylsilyl ether **3d**, $^1H$ NMR

(500 MHz, $CDCl_3$) $\delta$, 0.22 (s, 9H), 3.82 (s, 3H), 5.46 (s, 1H), 6.90 (m, 2H) 7.40 (m, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$), $\delta$, 0.1 ($CH_3$), 55.6 ($CH_3$), 63.2 (CH), 114.7 (C), 119.9 (CN), 128.3 (CH), 128.8 (CH), 132.1 (CH), 160.2 (C); IR, ($CH_2Cl_2$), $\nu$: 2232 (CN), 1160 (C—O) $cm^{-1}$.

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