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Methyltriphenylphosphonium iodide catalyzes the addition of trimethylsilyl cyanide to aldehydes

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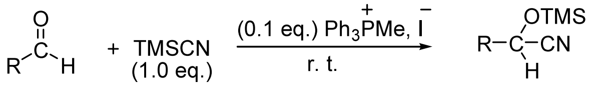
Abstract—Methyltriphenylphosphonium iodide catalyzes the formation of cyanohydrin trimethylsilyl ethers of aliphatic, aromatic and heterocyclic aldehydes.

Cyanohydrin trimethylsilyl ethers are versatile intermediates such as in the synthesis of α-hydroxy acids and β-aminoalcohols.[1] For the synthesis of O-TMS cyanohydrins a plethora of catalytic agents including Zn(II), Ti(IV), Cu(II), Ce(IV), Al(III), In(III) and Sm(III) salts have been used, among others.[2] Several of these methodologies were adapted to the preparation of non-racemic cyanohydrins.[3] Searching for new non-metallic catalysts for this reaction without lack of efficiency, phosphonium salts were used as new catalytic reagents. To the best of our knowledge, the use of phosphines for the trimethylsylil cyanation of aldehydes has been reported in one unique paper applied on an isolated case.[4] Thus, the reaction of 3-phenylpropanal with TMSCN at 0°C gave 96% of the O-TMS cyanohydrin in the presence of 10 mol% of Bu_3P and gave 27% in the presence of Ph_3P. On the other hand, phosphorus(V) reagents did not promote the cyanosilylation.[5] No data on the use of phosphonium salts as catalysts for these reactions has been so far reported. In this paper we wish to describe our findings in this field.

The reaction of aromatic and aliphatic aldehydes (1.0 equiv.) with TMSCN (1.0 equiv.) in the presence of 0.1 equiv. of methyltriphenylphosphonium iodide salt, took place at room temperature to give good yields of the expected cyanohydrins.[6] The results are quoted in Table 1.

Table 1. Synthesis of cyanohydrins by reaction of aldehydes and TMSCN



Entry	Substrate (R)	Isolated yield (%)
1	C_6H_5	70
2	PMeO-C_6H_4	85
3[a]	PNO_2-C_6H_4	81
4	2-Furyl	97
5	3-Furyl	73
6	2-Pyridyl	92
7	3-Pyridyl	92
8	1-Naphthyl	86
9	Isopropyl	86

[a] The reaction mixture was achieved from −78 to 5°C during 24 h.

In the case of aldehydes with OH or NH groups, the reaction with 2.0 equiv. of TMSCN gave the O- or N-protected cyanohydrin for *o*-hydoxybenzaldehyde and 2-pirrolcarboxaldehyde, respectively, and a mixture of N-protected and NH cyanohydrin for 3-indolcarboxaldehyde (Scheme 1).

In the case of α,β-unsaturated aldehydes, the reaction takes place as well. For instance, in the case of acroleyn and cinnamaldehyde, excellent yields of the expected O-TMS cyanohydrins were obtained in 1 h of reaction (Scheme 2).

In summary, the use of methyltriphenylphosphonium iodide as a catalytic reagent for cyanosilylation of aldehydes has been described in this report. The experimental method is very simple and, in some cases, pure

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Keywords: trimethylsilyl cyanide; cyanohydrins; phosphonium salts.

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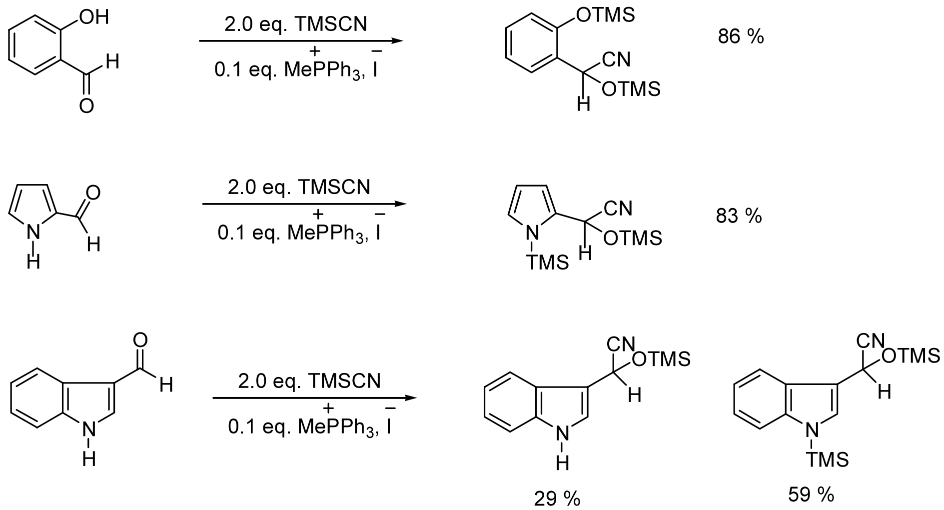
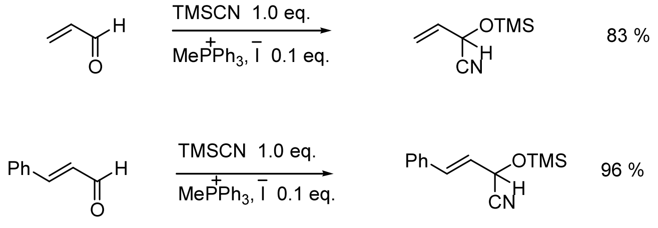


Scheme 1.



Scheme 2.

O-TMS cyanohydrins are isolated by successive washes of the reaction crude with water. On the other hand, the use of chiral phosphonium salts, in order to achieve the enantioselective synthesis of these useful compounds, is now under active research in our laboratory.

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6. **Typical experimental procedure**: To a solution of the phosphonium salt (30 mg, 0.074 mmol) in dry CH_2Cl_2 was added, under argon and at room temperature, the carbonyl compound (0.742 mmol) followed by TMSCN (0.093 mL, 0.742 mmol). The reaction was allowed to progress for 24–72 h. Water (6 mL) was added and the mixture was extracted with CH_2Cl_2. Drying of the combined organic phases with $MgSO_4$ was followed by evaporation of the solvent in vacuo. The products were purified by chromatography on silica gel (ethyl acetate/hexane), and characterized by ^1H and ^{13}C NMR.