Synthesis and Reactions of Trimethylsilylmethyl Azide

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Trimethylsilylmethyl azide, prepared quantitatively from trimethylsilylmethyl chloride and sodium azide, could be used for the amination of aryl Grignard reagents or aryl-lithium compounds.

We are currently interested in the reactivity and synthetic utility of silicon compounds containing azido groups. There have been many studies[1] of silyl azides, in which the azido group is directly attached to silicon, whereas azides, having a silicon atom in the α-position are unknown.[2] We now report the synthesis and reactions of trimethylsilylmethyl azide (TMSMA).

A mixture of trimethylsilylmethyl chloride (0.20 mol) and sodium azide (0.24 mol) in dried dimethylformamide was heated at 80 °C for 44 h; distillation under reduced pressure then gave TMSMA [ν_{max} 2100 cm^{-1}, ^{1}H n.m.r. δ 0.12 (s, 9H) and 2.75 (s, 2H); m/z 129 and 73] in 97% yield as a colourless, stable† liquid, b.p. 43 °C at 43 mmHg.

The importance of primary amines, both as synthetic intermediates and as precursors of nitrogen heterocycles, led us to investigate the potential of TMSMA for the amination of organic halides. Silyl azides ($\geqslant$SiN$_3$),[3] sulphonyl azides ($-$SO$_2$N$_3$),[4] and thiomethyl azides ($-$SCH$_2$N$_3$)[5] have been reported to react with Grignard reagents, giving amino compounds. However, the use of these azides required relatively drastic conditions (acidic hydrolysis at elevated temperature,[3] alkaline reducing conditions,[4] or hydrolysis with 50% aq. KOH[5]) in order to obtain the amine.

In a typical procedure, to an ethereal solution of phenyl-magnesium bromide (prepared from 1.0 equiv. of bromo-benzene and 1.2 equiv. of magnesium) at room temperature was added dropwise 1.2 equiv. of TMSMA in ether (1.2 M), and the mixture was stirred for 3 h. After the usual work-up followed by removal of low boiling substances under reduced pressure, the residue contained only aniline (72% yield from bromobenzene) without any purification. Other aromatic bromides reacted with TMSMA similarly (Table 1).

On the basis of the reported study,[5] we suggest that the reaction takes place as in equation (1). In this case, the aniline derivatives were more readily obtained than with other methods[3−5] because the trimethylsilylmethyl group of the intermediate (I) would be a good leaving group; it is not yet clear how this group acts, however.
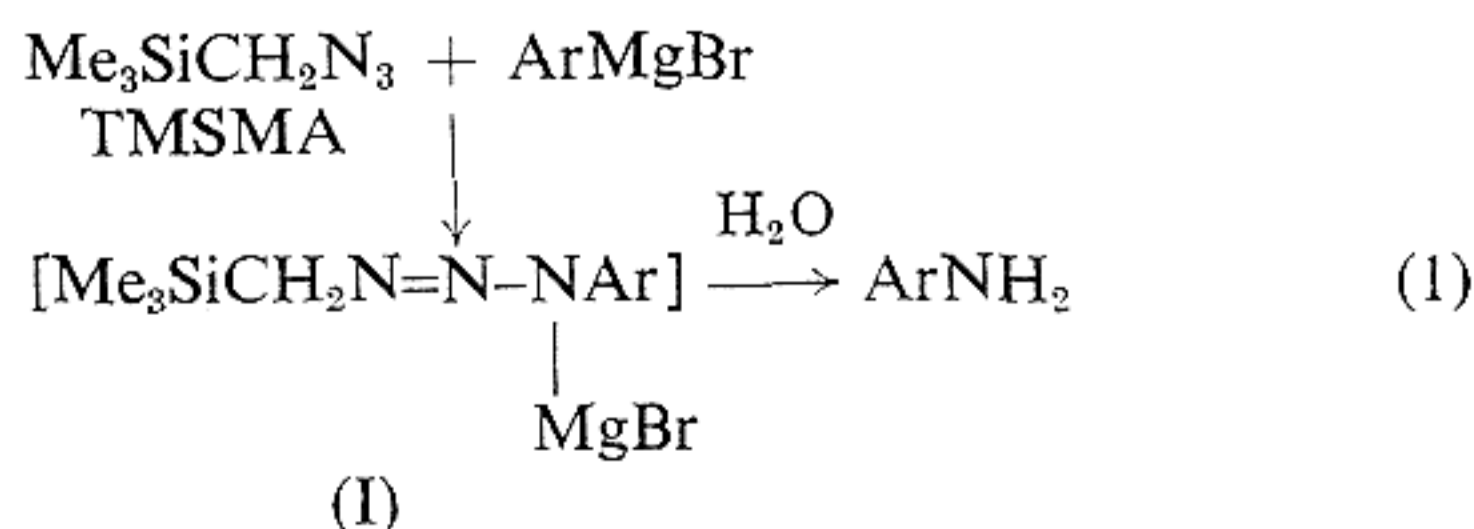
This amination approach offers several advantages. (i) It requires merely neutral hydrolysis to decompose the intermediate [probably the triazene derivative (I), but a silylmethyl amine derivative cannot be excluded[3]] to produce the amino compounds in good yields; (ii) it is easy to introduce the amino group at a sterically hindered position (Table 1, entry 4); (iii) electronic effects of substituents need not be considered; (iv) with aromatic compounds substituted by two or more different halogen atoms, selective amination occurs depending on their reactivity to magnesium (entry 5).

Aromatic lithium derivatives could also be used instead of Grignard reagents; e.g. the lithio derivatives of anisole (entry 6) or benzylamine (entry 7), obtained using n-butyl-lithium reacted with TMSMA in a similar manner, to give the ortho-substituted products regioselectively. However, the yield of the amines was lower compared with the Grignard method because TMSMA was decomposed by Bu^{n}Li under the reaction conditions.

Table 1. Reaction of TMSMA with metallo-aromatic compounds.

$$\text{ArX} \xrightarrow[\text{Method A}]{\text{Mg}} \text{ArM} \xleftarrow[\text{Method B}]{\text{Bu}^n\text{Li}} \text{ArH}$$

$$\downarrow$$

$$\text{ArNH}_2$$

Entry	Substrate	Method[a]	Product	Yield, %
1	PhBr	A	PhNH$_2$	72
2	2-MeOC$_6$H$_4$Br	A	2-MeOC$_6$H$_4$NH$_2$	73
3	4-MeOC$_6$H$_4$Br	A	4-MeOC$_6$H$_4$NH$_2$	69
4	2,6-Me$_2$C$_6$H$_3$Br	A	2,6-Me$_2$C$_6$H$_3$NH$_2$	79
5	4-ClC$_6$H$_4$Br	A	4-ClC$_6$H$_4$NH$_2$	92
6	PhOMe	B	2-MeOC$_6$H$_4$NH$_2$	35
7	PhCH$_2$NMe$_2$	B	2-Me$_2$NCH$_2$C$_6$H$_4$NH$_2$	41

[a] A: Grignard method; B: lithiation method.

$$\text{Me}_3\text{SiCH}_2\text{N}_3 + \text{ArMgBr}$$
$$\text{TMSMA} \quad \downarrow$$
$$[\text{Me}_3\text{SiCH}_2\text{N}=\text{N}-\text{NAr}] \xrightarrow{\text{H}_2\text{O}} \text{ArNH}_2 \qquad (1)$$
$$\underset{\text{MgBr}}{|}$$
$$\text{(I)}$$

References

1 For a recent review, see W. P. Weber, 'Silicon Reagents for Organic Synthesis,' Springer-Verlag, Heidelberg, 1983, and references cited therein.

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† TMSMA was stable to temperatures of at least 120 °C and could be stored in a refrigerator for more than 6 months.