SYNLETT
Spotlight 443

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Bromotrimethylsilane (TMSBr)

Compiled by Agnieszka Matusiak

Agnieszka Matusiak was born in Łęczyca, Poland in 1986. She graduated from the University of Łódź, Poland in 2010 working in the group of Professor Jarosław Lewkowski. Currently, she is pursuing her Ph.D. in the same group. Her current research is focused on new aminophosphonates, which include heterocyclic aromatic five-membered rings (furans, pyrroles, tiophenes), their cytotoxic and biological properties.

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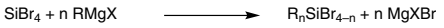
Introduction

Bromotrimethylsilane (TMSBr) is an organosilicon compound, a silyl halide with the formula C_3H_9SiBr. Under standard conditions, it is a colorless liquid, which is stable in the absence of water. It is used as a powerful silylating agent and as a catalyst for the cleavage of ethers[1] and phosphonic/phosphoric acid alkyl esters.

Carbon–Silicon bonds (186 pm) are longer and weaker than carbon–carbon bonds (154 pm), with bond dissociation energies of 451 kJ/mol (C–Si) vs. 607 kJ/mol (C–C). The C–Si bond is polarized towards carbon due to the lower electronegativity of silicon (Si 1.90 vs. C 2.55). Some examples using the bond polarization of organosilanes are the Hosomi–Sakurai reaction,[2] the Hiyama coupling,[3] and the Tamao–Kumada–Fleming oxidation[4,5,6] (certain alkyl silanes can be oxidized to alcohols).

Preparation

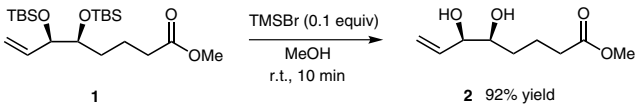
TMSBr can be prepared from silicon tetrabromide by nucleophillic substitution of three of the bromide groups with a nucleophillic methyl source such as methyllithium. Another method uses consecutive Grignard reactions with metal alkyl halides. These are particularly important reactions due to the use in the production of organosilicon compounds, which can be converted into silicones.[7]



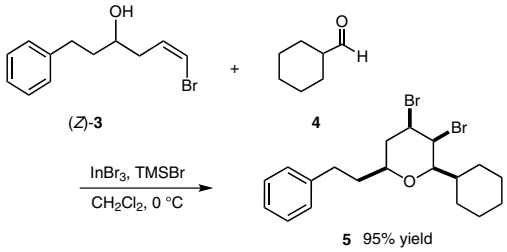
Scheme 1 The Grignard reaction used to prepare TMSBr

Abstracts

(A) The chemoselective and efficient deprotection of (primary, secondary and aromatic) silyl ethers using catalytic amounts of TMSBr in various solvents has been reported.[8] The best results were obtained using methanol as the solvent. A bis-[*tert*-butyldimethylsilyl (TBS)] ether **1** was effectively cleaved to afford the corresponding diol **2** in 92% yield.



(B) An efficient Prins cyclization reaction to construct tetrasubstituted 2,6-*cis*-4,5-dibromo tetrahydropyran (THP) rings with high stereoselectivity in good yields has been developed.[9] The cyclization of γ-brominated homoallylic alcohol (*Z*)-**3** and cyclohexane carboxaldehyde (**4**) proceeded smoothly with 1.2 equivalents of TMSBr to afford **5** in 95% yield as a single isomer. THP product **5** was selected to perform a series functionalizations, such as debromination and further epoxidation or hydroxylation.[10–12]



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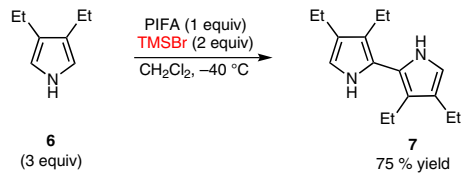
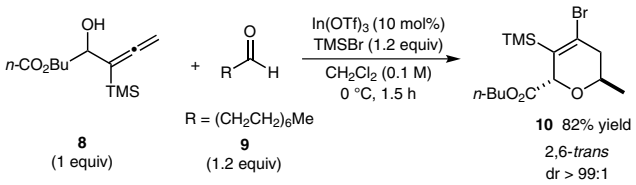
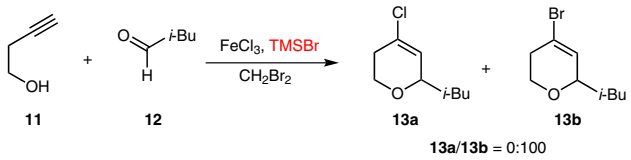
(C) A novel straightforward synthetic method for the selective construction of 2,2′-bipyrroles and even 2,3′-bipyrroles has been developed.[13] An effective oxidative coupling reaction of electron-rich pyrroles was performed using hypervalent iodine(III) reagents, such as phenyliodine bis(trifluoroacetate) (PIFA), and TMSBr. The product **7** was obtained in 75% yield at –40 °C.



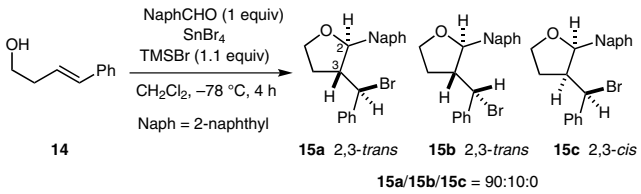
(D) Loh and co-workers[14] reported an efficient synthesis of 2,6-*trans*-pyranyl motifs via Prins cyclization using carboalkoxyl allenic alcohol promoted by indium triflate and TMSBr. When the bulky silicon-substituted allenic alcohol **8** was used under these conditions, the reaction proceeded smoothly to afford the 2,6-*trans* product **10** with excellent diastereoselectivity (>99:1).



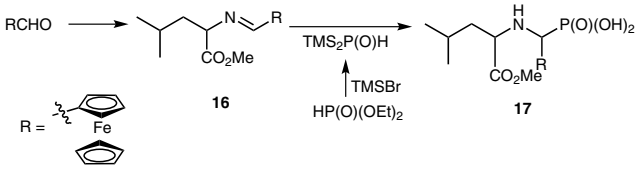
(E) Martín, Padrón and co-workers[15] have developed the first iron-catalyzed oxa- and aza-Prins cyclization of γ,δ-unsaturated alcohols and amines using readily available iron salts [$FeBr_3$, $FeCl_3$ or $Fe(acac)_3$] and trimethylsilyl halides (TMSCl, TMSBr). The use of a combination of $FeCl_3$, TMSBr, and CH_2Br_2 led to the bromotetrahydropyran **13b** in a regioselective and efficient manner.



(F) Spivey[16] and co-workers have reported the diastereoselective synthesis of 2,3-disubstituted THFs using $SnBr_4$-promoted oxonium-Prins cyclizations. (*E*)-4-Phenylbut-3-en-1-ol (**14**) as the homoallylic alcohol component reacted with 2-naphthyl carboxaldehyde as the aldehyde component in the presence of $SnBr_4$ and TMSBr as Lewis acid promotors in CH_2Cl_2. This reaction led to the formation of only two of the three possible isomeric products (**15a** and **b**).



(G) Lewkowski and Karpowicz[17] described the isolation of the main diastereomer of the aminophosphonic acid **17** which was obtained by diastereoselective addition of dialkyl phosphites to the azomethine bond of the chiral Schiff base **16**. This method is based on obtaining silylated esters of phosphonic acid in the reaction of TMSBr and then converting it into the acid. In this case (**17**), the formation of only one diastereomer was observed.



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