

# SYNLETT Spotlight 206

## Tris(trimethylsilyl)silane (TTMSS)

Compiled by Jean-François Brazeau



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

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### Introduction

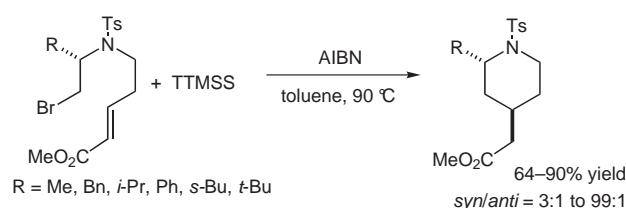
Tris(trimethylsilyl)silane (TTMSS) has been used in many transformations, especially in radical chain reactions. Chatgililoglu et al. demonstrated that this reagent can be a valuable substitute for tin reagents commonly used in radical processes.<sup>1</sup> The Si–H bond dissociation energy in TTMSS of 79 kcal·mol<sup>-1</sup> is very similar to the Sn–H bond dissociation energy of 74 kcal·mol<sup>-1</sup> in Bu<sub>3</sub>SnH.<sup>2</sup> The ease of purification and the low toxicity of TTMSS make it an attractive alternative to tin as a

reducing agent. Interestingly, there are also reports demonstrating that the behavior of TTMSS can be very different from that of tin hydrides.<sup>3</sup>

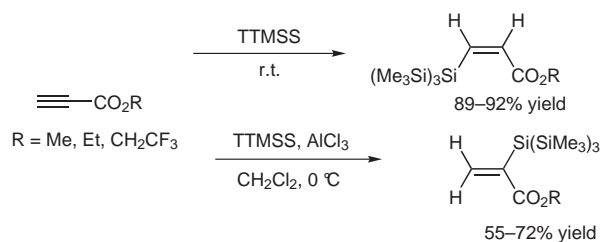
This reagent is commercially available as a colorless liquid.<sup>4</sup> It should be stored under nitrogen because it is sensitive towards oxygen.<sup>5</sup> Reactions such as functional reductions,<sup>6</sup> hydrosilylations,<sup>7</sup> intramolecular cyclizations,<sup>8</sup> intermolecular reactions,<sup>9</sup> and non-radical reactions<sup>10</sup> can be performed with TTMSS.

### Abstracts

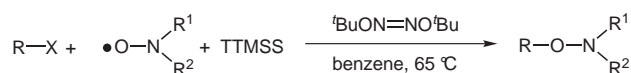
(A) Recently, Gandon et al. have reported a novel approach to 2,4-disubstituted piperidines.<sup>11</sup> This strategy involved the radical cyclization of 7-substituted 6-aza-8-bromo-2-enoates. Cyclization with TTMSS and azobisisobutyronitrile (AIBN) led to *trans* piperidines with diastereomeric ratios of up to 99:1 in particular cases.



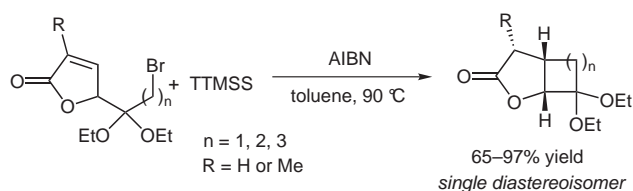
(B) Various propiolate esters and TTMSS without solvent were stirred at room temperature overnight to give  $\beta$ -silicon-substituted *Z*-alkenes in high yields.<sup>12</sup> Interestingly, in CH<sub>2</sub>Cl<sub>2</sub>, the reaction of propiolate ester and TTMSS in the presence of Lewis acid AlCl<sub>3</sub> at 0 °C afforded exclusively the  $\alpha$ -silicon-substituted alkenes. The regioselectivity observed was explained by two competitive mechanisms: a free radical and an ionic one.



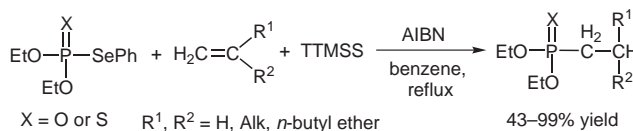
(C) Braslau et al. reported an efficient strategy for the preparation of *N*-alkoxy amines.<sup>13</sup> Alkyl halides (X = Cl, Br) were treated with TTMSS in the presence of *tert*-butyl hyponitrite (TBNH) in combination with various nitroxides to allow the clean generation of *N*-alkoxy amines that are inaccessible by standard methods. The resulting products can be used as initiators in free radical polymerization.



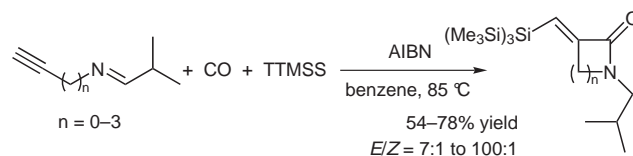
(D) Maulide and Markov reported a new strategy that involves a TTMSS-mediated cyclization to generate functionalized bicyclo[3.n.0]lactones in high yields.<sup>14</sup> A Thorpe–Ingold effect induced by the ketal substituent facilitates the radical-mediated cyclization. Importantly, the contiguous stereogenic centers were generated with complete diastereocontrol.



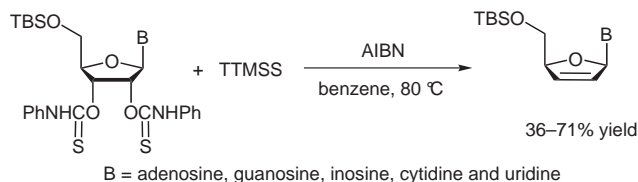
(E) The radical addition of dialkyl selenophosphates and selenophosphorothioates to electron-rich alkenes was described by Lopin et al.<sup>15</sup> The corresponding adducts were generated in fair to excellent yields. AIBN and TTMSS were used as a radical initiator and a hydrogen donor source, respectively. This approach led to phosphonates and phosphonothioates, which can be interesting in the field of nucleotide analogues.



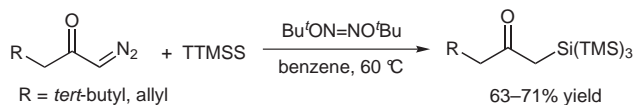
(F) Free-radical-mediated cyclizative carbonylations of azaenynes were also carried out using TTMSS.<sup>16</sup> The reactions afforded  $\alpha$ -silylmethylene lactams having four- to seven-membered rings in good yields. The excellent *E*-diastereoselectivity observed in the TTMSS-mediated reaction was explained by the steric effect due to the bulky (TMS)<sub>3</sub>Si group. On the other hand, *Z*-selectivity of the resulting vinylsilane moiety was obtained during the analogous carbonylation using tributyltin hydride.



(G) Bis(*O*-thioxo)carbamate derivatives of vicinal diols were reduced with TTMSS in the presence of AIBN to afford the corresponding olefins in good yields.<sup>17</sup> Ribonucleoside analogues of adenosine, guanosine, inosine, cytidine, and uridine were prepared using this approach.



(H) The reaction of TTMSS with the  $\alpha$ -diazo ketones was carried out at 60 °C in benzene in presence of *tert*-butyl hyponitrite to give the corresponding  $\alpha$ -silyl ketones.<sup>18</sup> It is important to note that the  $\alpha$ -silyl ketone does not isomerize to the more stable silyl enol ether under the reported reaction conditions.



## References

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