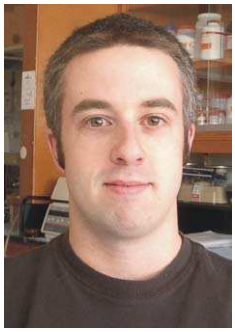
SYNLETT
Spotlight 206

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

Tris(trimethylsilyl)silane (TTMSS)

Compiled by Jean-François Brazeau



Jean-François Brazeau was born in 1978 in Hull, Canada. He received his B.Sc. in Chemistry (2002) from UQAM, Québec, Canada. Then he joined the Institut de recherches cliniques de Montréal (IRCM) where he completed his M.Sc. (2004) under the supervision of Prof. Yvan Guindon, Université de Montréal. As a recipient of a NSERC scholarship, he is currently pursuing his Ph.D. in the same laboratory. His current research focuses on the development of new synthetic methodologies employing free radical intermediates.

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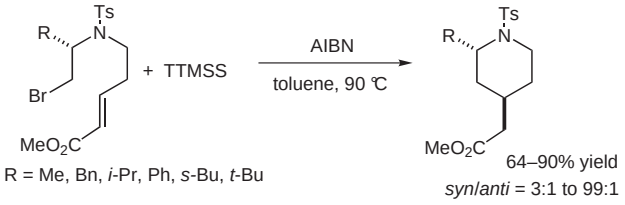
Introduction

Tris(trimethylsilyl)silane (TTMSS) has been used in many transformations, especially in radical chain reactions. Chatgilialoglu et al. demonstrated that this reagent can be a valuable substitute for tin reagents commonly used in radical processes.[1] The Si–H bond dissociation energy in TTMSS of 79 kcal·mol^{-1} is very similar to the Sn–H bond dissociation energy of 74 kcal·mol^{-1} in Bu_3SnH.[2] 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.[3]

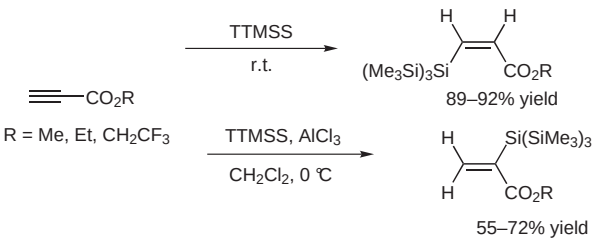
This reagent is commercially available as a colorless liquid.[4] It should be stored under nitrogen because it is sensitive towards oxygen.[5] Reactions such as functional reductions,[6] hydrosilylations,[7] intramolecular cyclizations,[8] intermolecular reactions,[9] and non-radical reactions[10] can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

Abstracts

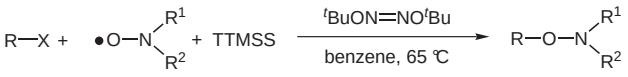
(A) Recently, Gandon et al. have reported a novel approach to 2,4-disubstituted piperidines.[11] This strategy involved the radical cyclization of 7-substituted 6-aza-8-bromooct-2-enoates. Cyclization with TTMSS and azobisisobutyronitrile (AIBN) led to *trans* piperidines with diastereomeric ratios of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



(B) Various propiolate esters and TTMSS without solvent were stirred at room temperature overnight to give β-silicon-substituted *Z*-alkenes in high yields.[12] Interestingly, in CH_2Cl_2, the reaction of propiolate ester and TTMSS in the presence of Lewis acid $AlCl_3$ at 0 °C afforded exclusively the α-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.[13] 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.



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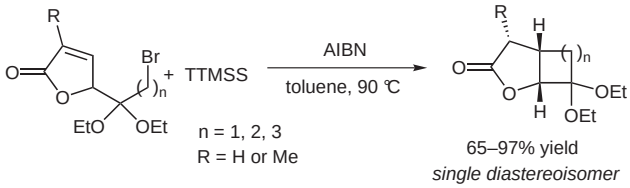
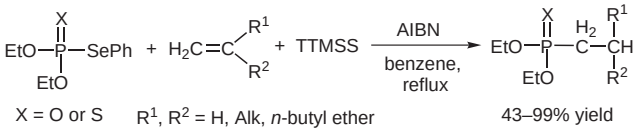
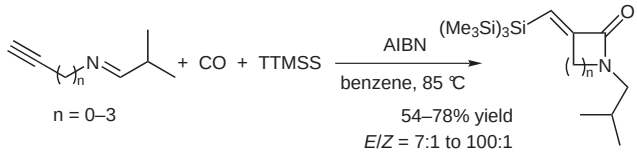
(D) Maulide and Markov reported a new strategy that involves a TTMSS-mediated cyclization to generate functionalized bicyclo[3.*n*.0]lactones in high yields.[14] A Thorpe–Ingold effect induced by the ketal substituent facilitates the radical-mediated cyclization. Importantly, the contiguous stereogenic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



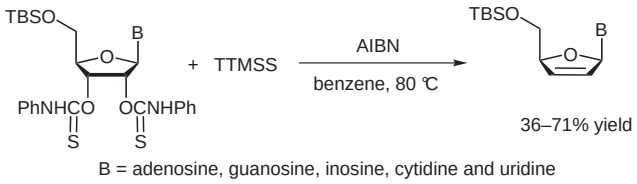
(E) The radical addition of dialkyl selenophosphates and selenophosphorothioates to electron-rich alkenes was described by Lopin et al.[15] The corresponding adducts were generated in fair to excellent yields. AIBN and TTMSS were used as a radical initiator and a hydrogen donor source, respectively.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



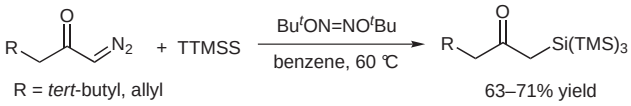
(F) Free-radical-mediated cyclizative carbonylations of azaenynes were also carried out using TTMSS.[16] The reactions afforded α-silylmethylene lactams having four- to seven-membered rings in good yields. The excellent *E*-diastereoselectivity observed in the TTMSS-mediated reaction was explained by the steric effect due to the bulky $(TMS)_3Si$ 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.[17] Ribonucleoside analogues of adenosine, guanosine, inosine, cytidine, and uridine were prepared using this approach.



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



References

(1) (a) Chatgilialoglu, C. *Organosilanes in Radical Chemistry: Principles, Methods and Applications*; John Wiley & Sons: Chichester, **2004**, 49–227. (b) Chatgilialoglu, C. In *Radicals in Organic Synthesis*, Vol. 1; Renaud, P.; Sibi, M. P., Eds.; Wiley-VCH: Weinheim, **2001**, 28–49.

(2) Kanabus-Kaminska, J. M.; Hawari, J. A.; Griller, D.; Chatgilialoglu, C. *J. Am. Chem. Soc.* **1987**, *109*, 5267.

(3) (a) Some examples: Curran, D. P.; Keller, A. I. *J. Am. Chem. Soc.* **2006**, *128*, 13706. (b) Yamaguchi, K.; Kazuta, Y.; Abe, H.; Matsuda, A.; Shuto, S. *J. Org. Chem.* **2003**, *68*, 9255. (c) Lee, E.; Park, C. M.; Yun, J. S. *J. Am. Chem. Soc.* **1995**, *117*, 8017. (d) Apeloig, Y.; Nakash, M. *J. Am. Chem. Soc.* **1994**, *116*, 10781.

(4) Procedure for the preparation of TTMSS: Dickhaut, J.; Giese, B. *Org. Synth.* **1991**, *70*, 164.

(5) Chatgilialoglu, C.; Guarini, A.; Guerrini, A.; Seconi, G. *J. Org. Chem.* **1992**, *57*, 2207.

(6) Giese, B.; Damm, W.; Dickhaut, J.; Wetterich, F.; Sun, S.; Curran, D. P. *Tetrahedron Lett.* **1991**, *32*, 6097.

(7) Kopping, B.; Chatgilialoglu, C.; Zenhder, M.; Giese, B. *J. Org. Chem.* **1992**, *57*, 3994.

(8) Usui, S.; Paquette, L. A. *Tetrahedron Lett.* **1999**, *40*, 3495.

(9) Schneider, H.; Fiander, H.; Harisson, K. A.; Watson, M.; Burton, G. W.; Arya, P. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 637.

(10) Watanabe, H.; Araki, K. I.; Matsumoto, H.; Nagai, Y. *J. Organomet. Chem.* **1974**, *69*, 389.

(11) Gandon, L. A.; Russell, A. G.; Guveli, T.; Brodwolf, A. E.; Kariuki, B. M.; Spencer, N.; Snaith, J. S. *J. Org. Chem.* **2006**, *71*, 5198.

(12) Liu, Y.; Yamazaki, S.; Yamabe, S. *J. Org. Chem.* **2005**, *70*, 556.

(13) Braslau, R.; Tsimelzon, A.; Gewandter, J. *Org. Lett.* **2004**, *6*, 2233.

(14) Maulide, A.; Markov, I. E. *Chem. Commun.* **2006**, 1200.

(15) Lopin, C.; Gouhier, G.; Gautier, A.; Piettre, S. R. *J. Org. Chem.* **2003**, *68*, 9916.

(16) Tojino, M.; Noboru, O.; Fukuyama, T.; Matsubara, H.; Schiesser, C. H.; Kuriyama, H.; Miyazato, H.; Minakata, S.; Komatsu, M.; Ryu, I. *Org. Biomol. Chem.* **2003**, *1*, 4262.

(17) Oba, M.; Suyama, M.; Shimamura, A.; Nishiyama, K. *Tetrahedron Lett.* **2003**, *44*, 4027.

(18) Dang, H. S.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 1* **1996**, 769.

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