SYNLETT
Spotlight 204

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

Tebbe's Reagent

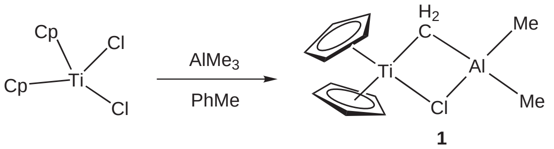
Compiled by Kalpeshkumar C. Rana

Kalpeshkumar C. Rana was born in Vyara, India in 1981. He received his B.Sc. and M.Sc. degrees from North Maharashtra University, Jalgaon, Maharashtra, India in 2002 and 2004, respectively. He joined the Division of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune, India as a CSIR-JRF in 2005 in the group of Dr. Asish K. Bhattacharya. His present research is focused on structure elucidation of biologically active natural products, synthesis of natural product libraries, and development of new synthetic methodologies.

Division of Organic Chemistry: Synthesis, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411008, MS, India
E-mail: kc.rana@ncl.res.in

Introduction

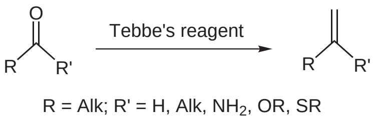
Tebbe's reagent (**1**) is an organometallic compound and has found diverse applications in organic synthesis such as methylenation of carbonyl compounds,[1] synthesis of *C*-glycosides,[2] 1,6-disaccharides[3] and in the synthesis of intermediates, for example vinyl silanes[4] and allenylketenes.[5] It is readily prepared by reacting titanocene dichloride and trimethylaluminum in toluene at r.t. (Scheme 1).[1] When Tebbe's reagent is treated with a Lewis base, for example pyridine or THF, a highly reactive titanocene methylidene is generated. It methylenates a range of carboxylic and carbonic acid derivatives, presumably via oxatitanacyclobutane to furnish alkenes in a short period of time at room temperature and below.[6]



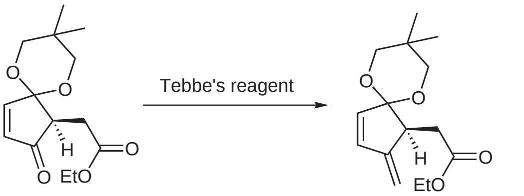
Scheme 1

Abstracts

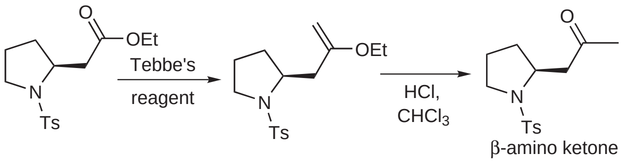
(A) Compounds containing carbonyl groups such as aldehydes, ketones, amides, esters, and thiolactones can be methylenated by using Tebbe's reagent.[1]



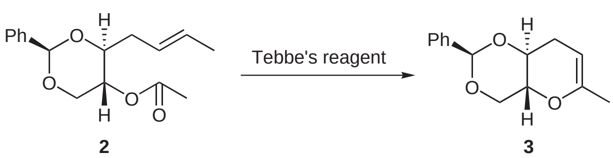
(B) Selective methylenation of aldehydes and ketones in the presence of an ester or amide group can be achieved using Tebbe's reagent.[7a] This regioselectivity is also found in the methylenation of a methyl ester in the presence of a bulky silyl ester group.[7b]



(C) An easy and effective synthesis of enantiomerically pure β-amino ketones and γ-amino alcohols can be achieved by Tebbe methylenation of proline derivatives.[8]

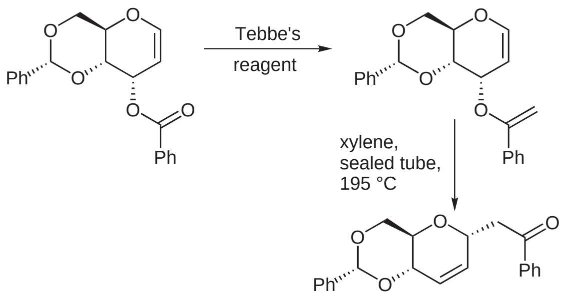


(D) Cyclic enol ether **3** is easily synthesized from olefinic ester **2** by using two equivalents of Tebbe reagent.[9]

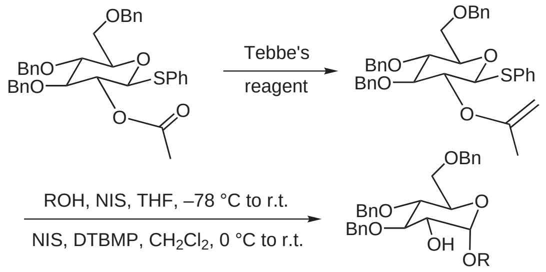


SYNLETT 2007, No. 11, pp 1795–1796
Advanced online publication: 25.06.2007
DOI: 10.1055/s-2007-984505; Art ID: V20706ST

(E) *C*-glycosides[10] can be readily prepared from 3-hydroxyl glycal esters via Tebbe methylenation and subsequent Claisen rearrangement.[2] 1,6-Linked *C*-disaccharides can also be prepared by Tebbe's reagent and Claisen rearrangement.[3]

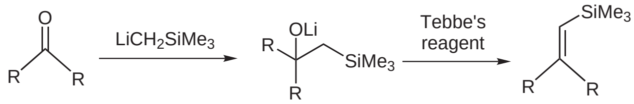


(F) Since 1,2-c*is* glycosides are difficult to prepare, Tebbe methylenation with *N*-iodosuccinimide has been used as intramolecular aglycon delivery to synthesize these.[11]

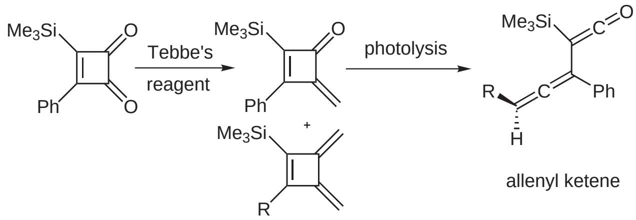


1,2-*cis* glycoside

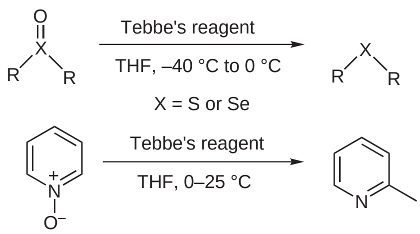
(G) Vinyl silanes play an important role as vinyl anion equivalents for stereospecific electrophilic reactions. They can be readily prepared with the help of Tebbe's reagent.[4]



(H) Allenyl ketene is synthesized from cyclobutenedione by Tebbe methylenation.[5] The allenyl ketene can then undergo different nucleophilic and electrophilic additions and cycloaddition reactions.



(I) Sulfoxides, selenoxides, and pyridinium *N*-oxides can be converted into sulfides, selenides, and 2-methyl pyridines, respectively, on treatment with Tebbe's reagent.[12]



References

(1) (a) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611. (b) Pine, S. H.; Zahler, R.; Evans, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 3270.

(2) (a) Godage, H. Y.; Fairbanks, A. J. *Tetrahedron Lett.* **2000**, *41*, 7589. (b) Godage, H. Y.; Fairbanks, A. J. *Tetrahedron Lett.* **2003**, *44*, 3631.

(3) Chambers, D. J.; Evans, G. R.; Fairbanks, A. J. *Tetrahedron* **2005**, *61*, 7184.

(4) Kwan, M. L.; Yeung, C. W.; Breno, K. L.; Doxsee, K. M. *Tetrahedron Lett.* **2001**, *42*, 1411.

(5) Huang, W.; Tidwell, T. T. *Synthesis* **2000**, 457.

(6) For a review, see: Hartley, R. C.; McKiernan, G. J. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2763.

(7) (a) Göres, M.; Winterfeldt, E. *J. Chem. Soc., Perkin. Trans. 1* **1994**, 3525. (b) Müller, M.; Lamottke, K.; Löw, E.; Magor-Veenstra, E.; Steglich, W. *J. Chem. Soc., Perkin. Trans. 1* **2000**, 2483.

(8) Silva, M. J.; Cottier, L.; Srivastava, R. M.; Sinou, D. *J. Braz. Chem. Soc.* **2005**, *16*, 995.

(9) Nicolaou, K. C.; Postema, M. H. D.; Claiborne, C. F. *J. Am. Chem. Soc.* **1996**, *118*, 1565.

(10) Waldscheck, B.; Streiff, M.; Notz, W.; Kinzy, W.; Schmidt, R. R. *Angew. Chem. Int. Ed.* **2001**, *40*, 4007.

(11) Ennis, S. C.; Fairbanks, A. J.; Slinn, C. A.; Tennant-Eyles, R. J.; Yeates, H. S. *Tetrahedron* **2001**, *57*, 4221.

(12) Nicolaou, K. C.; Koumbis, A. E.; Snyder, S. A.; Simonsen, K. B. *Angew. Chem. Int. Ed.* **2000**, *39*, 2529.