

SYNLETT Spotlight 286

Dimethylsulfonium Methylide: A Versatile Reagent

Compiled by Huankai Yao



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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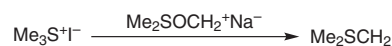
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Introduction

Dimethylsulfonium methylide, Me_2SCH_2 , was reported by Corey and Chaykovsky for the first time in 1962.¹ It is a versatile nucleophile which can insert the methylene unit into certain unsaturated linkages, such as $\text{C}=\text{O}$ and $\text{C}=\text{C}$, to form epoxides and cyclopropanes, respectively.² Utilization of this reagent is a reliable method in many synthetic applications and it has been well-utilized in the synthesis of functional molecules, especially bioactive natural products.

Preparation

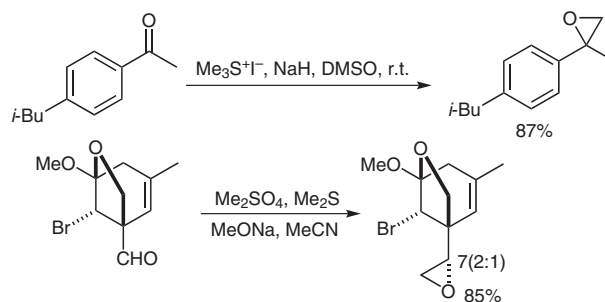
In general, Me_2SCH_2 is prepared from trimethylsulfonium iodide. Addition of a DMSO solution of trimethylsulfonium iodide to an equivalent solution of methylsulfinyl carbanion in THF–DMSO under nitrogen afforded Me_2SCH_2 successfully.² This reagent is decomposable at room temperature with a half-life of a few minutes.² In practice trimethylsulfonium iodide and a strong base are employed directly to produce Me_2SCH_2 .



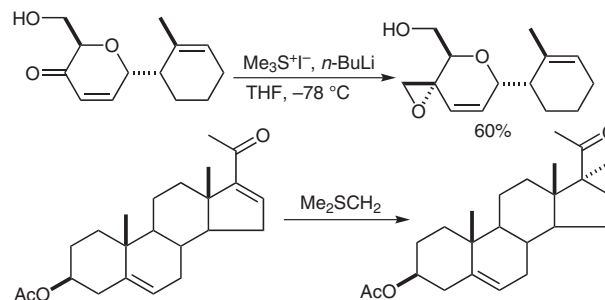
Scheme 1

Abstracts

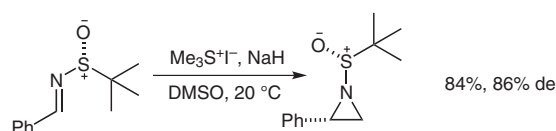
(A) Carbonyl groups of aromatic and nonconjugated aldehydes and ketones can react with dimethylsulfonium methylide to generate corresponding epoxides. Toward the synthesis of quassinoid, the nonconjugated aldehyde was treated with Me_2SCH_2 to give a separable 2:1 mixture of epoxide and its C7 diastereomer in 85% combined yield, respectively.³ In the (*S*)-ibuprofen synthesis the aromatic epoxide can be synthesized from the corresponding acetophenone precursor by the reaction with Me_2SCH_2 .⁴



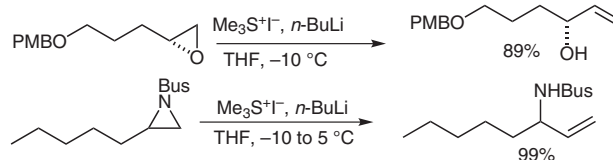
(B) When α,β -unsaturated carbonyl compounds react with dimethylsulfonium methylide, epoxide or cyclopropane derivatives are generated as major products. By the reaction with Me_2SCH_2 , α,β -keto unsaturated *C*-glycosides can be converted into α,β -unsaturated epoxy-*C*-glycosides.⁵ But in the synthesis of D-homo analogues of the natural neurosteroid, cyclopropylketone was obtained by reaction of 16-dehydropregnenolone with Me_2SCH_2 .⁶



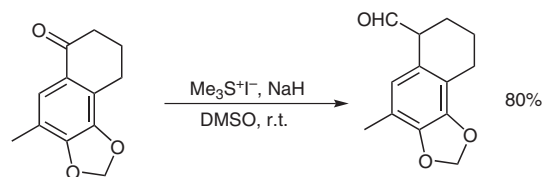
(C) The reaction of benzyl *tert*-butylsulfinyl imine with Me_2SCH_2 led to an aziridine in good yield and with excellent diastereoselectivity.⁷



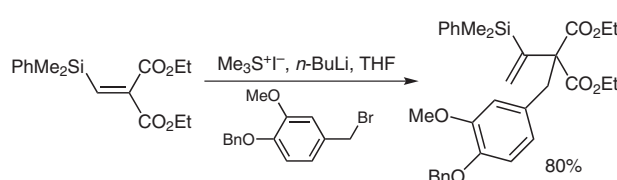
(D) Epoxides and aziridines, when subjected to dimethylsulfonium methylide, can provide corresponding allyl alcohols and allylic amines. In the asymmetric synthesis of (*S*)-vigabatrin Sudalai and co-workers used this regiospecific ring opening of an epoxide with Me_2SCH_2 to produce the allyl alcohol in good yield.⁸ Using Me_2SCH_2 , one-carbon homologation of *N*-sulfonylaziridine to allylic amine could be carried out successfully.⁹



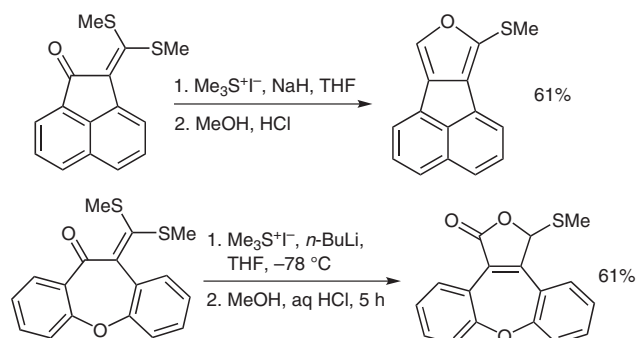
(E) Treating tetralone with dimethylsulfonium methylide, Plumet and co-workers afforded the corresponding aldehyde toward the synthesis of hydrophenalene ring system of pseudopterosins.¹⁰



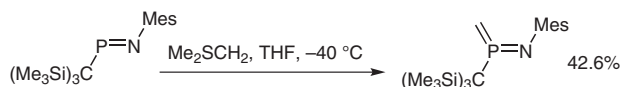
(F) When silylalkylidene malonate was added to Me_2SCH_2 and then quenched with benzyl bromide the desired vinylsilane was provided in high yield.¹¹



(G) Oxoketene dithioacetal was exposed to Me_2SCH_2 followed by acid workup, which gave rise to 7-(methylthio)acenaphtho[1,2-*c*]furan in good yield.¹² If the treatment of ketene dithioacetal with Me_2SCH_2 was followed by acid workup, cyclocondensation led to the formation of an unexpected lactone.¹³



(H) A THF solution of the iminophosphane was added to an equimolar quantity of Me_2SCH_2 to produce methylenephosphorane.¹⁴



References

- (1) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1962**, *84*, 3782.
- (2) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.
- (3) Cwynar, V.; Donahue, M. G.; Hart, D. J.; Yang, D. *Org. Lett.* **2006**, *8*, 4577.
- (4) Cleij, M.; Archelas, A.; Furstoss, R. *J. Org. Chem.* **1999**, *64*, 5029.
- (5) Herscovici, J.; Uriel, C.; Uriel, J.; Antonakis, K. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 421.
- (6) Di Chenna, P.; Ghini, A. A.; Burton, G. *Molecules* **2000**, *5*, 447.
- (7) Morton, D.; Pearson, D.; Field, R. A.; Stockman, R. A. *Synlett* **2003**, 1985.
- (8) Raj, I. V. P.; Sudalai, A. *Tetrahedron Lett.* **2008**, *49*, 2646.
- (9) Hodgson, D. M.; Fleming, M. J.; Stanway, S. *J. Org. Lett.* **2005**, *7*, 3295.
- (10) Benoit-Marquie, F.; Csáký, A. G.; Esteban, G.; Martínez, M. E.; Plumet, J. *Tetrahedron Lett.* **2000**, *41*, 3355.
- (11) Singh, R.; Singh, G. C.; Ghosh, S. K. *Eur. J. Org. Chem.* **2007**, 5376.
- (12) Panda, K.; Venkatesh, C.; Ila, H.; Junjappa, H. *Eur. J. Org. Chem.* **2005**, 2045.
- (13) Kumar, S.; Ila, H.; Junjappa, H. *Tetrahedron* **2007**, *63*, 10067.
- (14) Schinkels, B.; Ruban, A.; Nieger, M.; Niecke, E. *J. Chem. Soc., Chem. Commun.* **1997**, 293.