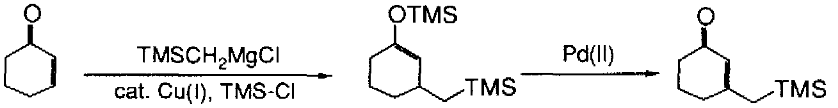
Tetrahedron Letters,Vol.30,No.25,pp 3327-3330,1989 0040-4039/89 \$3.00 + .00
Printed in Great Britain Maxwell Pergamon Macmillan plc

REGIOSELECTIVE SYNTHESIS OF TWO TYPES OF CYCLIC 3-(TRIMETHYLSILYLMETHYL)ENONES

Yoshiaki Horiguchi, Yasuhiro Kataoka, and Isao Kuwajima*
Department of Chemistry, Tokyo Institute of Technology, Meguro, Tokyo 152, Japan

Summary: Two types of cyclic 3-(trimethylsilylmethyl)enones were prepared selectively from the corresponding 1,3-diketones through 3-bromoenones or 3-siloxyenones.

We recently described synthetic utility of 3-(trimethylsilylmethyl)enones for several types of selective carbon-carbon bond formation.1) By utilizing such feature, we attempted to develop a powerful route for direct construction of the medium-sized carbon ring seen in certain terpenoids, e.g. a taxane family, from acetal-containing precursor **A**. Substrates such as **A** were previously prepared from the corresponding enones through TMS-Cl accelerated conjugate addition2) of TMS-methylmagnesium chloride followed by treatment with Pd(II)3) as shown in Eq 1.1)

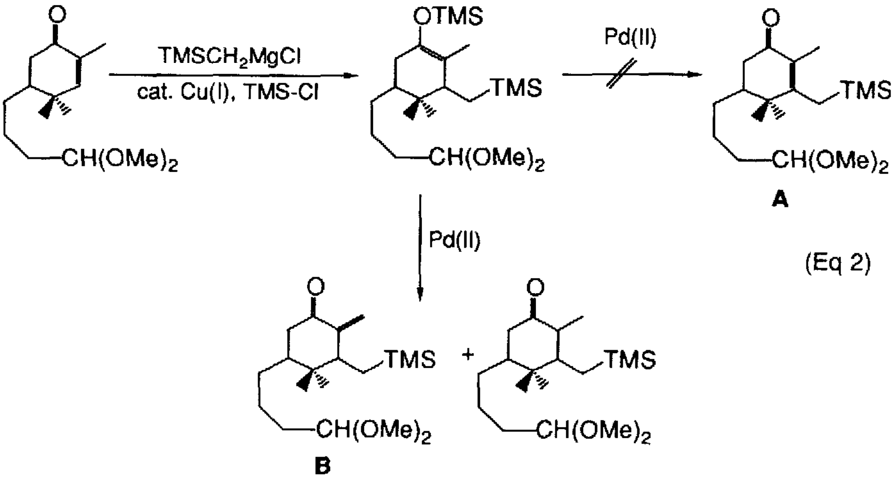


(Eq 1)

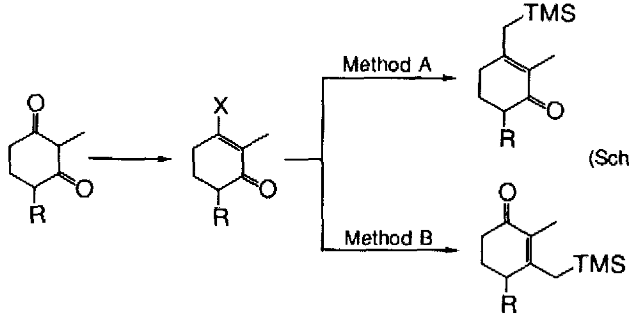
However, application of these procedures to the substituted enol silyl ether failed to give the desired endo-olefinic product **A**, but exo-methylene ketone **B** was formed in ca.30% yield together with predominant formation of the hydrolyzed product (Eq 2).

In connection with such transformation, we investigated alternative methodologies of general use, especially aiming regioselective synthesis of substituted 3-(TMS-methyl)enones.

For synthesis of 3-(TMS-methyl)enones, 1,3-diketone derivatives also seemed to be reasonable precursors. We examined the following two methods (Scheme I): One involves an addition-elimination process (Method A) and the other (X = $OSiR_3$) is based on 1,2-addition of TMS-methyl anionic species followed by 1,4-removal of silanol (Method B). Application of these procedures has allowed us to prepare two types of 3-(TMS-methyl)enones.

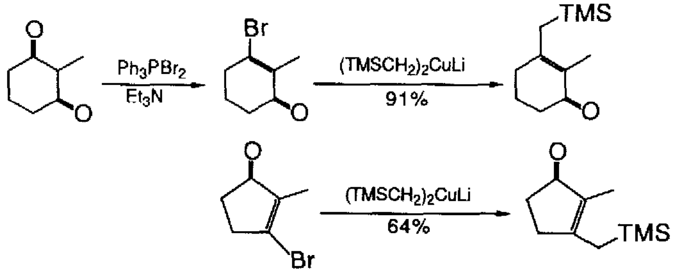


(Eq 2)

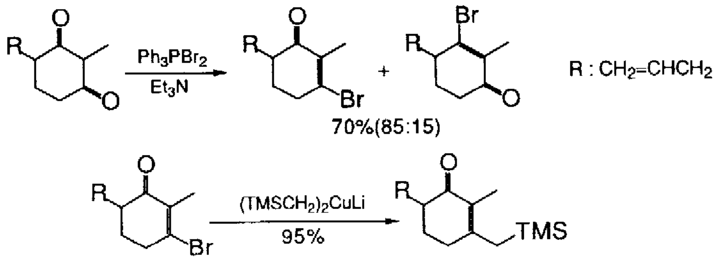


(Scheme I)

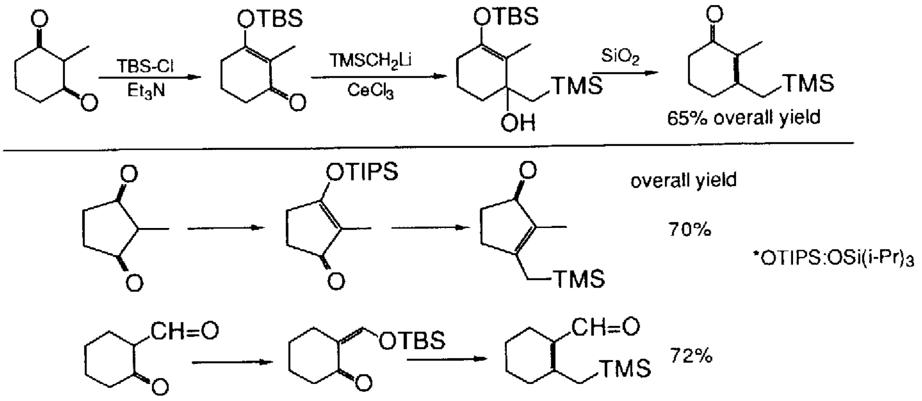
In method A, one of the diketone moieties should be changed into a good leaving group such as halogen. Conversion to the 3-bromoenones has been effected by the reaction with triphenylphosphine-dibromide and triethylamine. Treatment of these bromoenones with lithium bis(trimethylsilylmethyl)cuprate gave the corresponding products in good overall yields.



Unsymmetrically substituted 1,3-diketones usually undergo preferable enolization on less hindered side: [4] 4-substituted cyclohexane-1,3-dione resulted in the predominant formation of 6-substituted 3-bromo-cyclohexenone along with a small amount of 4-substituted isomer. They could be separated by silica gel column chromatography, and the former was converted to the 6-substituted 3-(TMS-methyl)cyclohexenone in good yield.

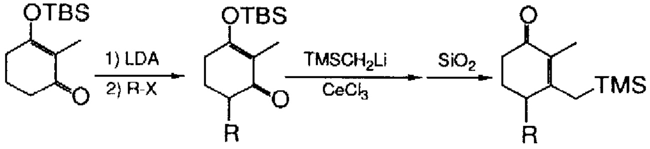


In order to prepare 4-substituted 3-(TMS-methyl)enones (cf. **A**), we next examined the method B. Thus, 1,3-diketones were converted to the corresponding 3-siloxyenones with *t*-butyldimethylsilyl chloride and triethylamine. In the reaction with the siloxyenones, trimethylsilylmethyllithium appears to act preferably as a base rather than a nucleophile to give the addition products in only low yield. Concomitant use of $CeCl_3$[5] efficiently circumvented such problem to afford the desired products. Treatment of these adducts with silica gel induced a facile 1,4-elimination of silanol to give the corresponding 3-(TMS-methyl)enones in good overall yields. Reaction conditions are so mild to induce neither Peterson olefination nor desilylation of the product. Enals bearing TMS-methyl group could also be prepared by similar transformation. *t*-Butyldimethylsilyl group is sometimes so labile to be attacked with TMS-methyllithium. On such occasion, use of tri-*i*-propylsilyl group remarkably improved the product yield as shown in



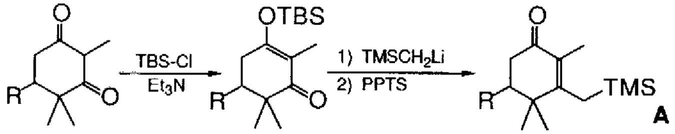
the case of 5-membered ring system.

This method allowed us to introduce several carbon chains at 4-position. Regioselective alkylation of an unsubstituted 3-siloxy-enone and subsequent procedures mentioned above gave the 4-substituted 3-(TMS-methyl)enone in good overall yield.



R-X	overall yield
CH_3-I	83%
CH_2=$CHCH_2$-Br	85%

Applying this method, we could prepare the desired substrate **A** in good overall yield as shown below.



80% overall yield

In conclusion, we developed two methodologies of general use for synthesis of 4- and 6-substituted 3-(TMS-methyl)enones. We are currently studying on the cyclization of 3-(TMS-methyl)enones such as **A**.

Acknowledgment. This work was partially supported by a Grant from the Ministry of Education, Science, and Culture of the Japanese Government.

References

1) Y. Hatanaka and I. Kuwajima, J. Org. Chem., **51**, 1932 (1986).

2) Y. Horiguchi, S. Matsuzawa, E. Nakamura, and I. Kuwajima, Tetrahedron Lett., **27**, 4025 (1986). E. Nakamura, S. Matsuzawa, Y. Horiguchi, and I. Kuwajima, ibid., **27**, 4029 (1986). S. Matsuzawa, Y. Horiguchi, E. Nakamura, and I. Kuwajima, Tetrahedron, in press.

3) Y. Ito, H. Aoyama, T. Hirota, A. Mochizuki, and T. Saegusa, J. Am. Chem. Soc., **101**, 494 (1979). J. Tsuji and I. Minami, Acc. Chem. Res., **20**, 140 (1987).

4) E. Piers, J. R. Grierson, C. K. Lau, and I. Nagakura, Can. J. Chem., **60**, 210 (1982).

5) T. Imamoto, Y. Sugiura, and N. Takiyama, Tetrahedron Lett., **25**, 4233 (1984).

(Received in Japan 13 March 1989)