# Use of 1-Methoxy-1-trimethylsilylallene Oxide and Titanium Tetraiodide as a Dianion Synthon of Methoxyacetone

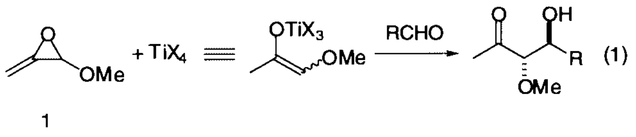
Ryuuichirou Hayakawa, Hiroaki Makino, and Makoto Shimizu*
*Department of Chemistry for Materials, Mie University, Tsu, Mie 514-8507*

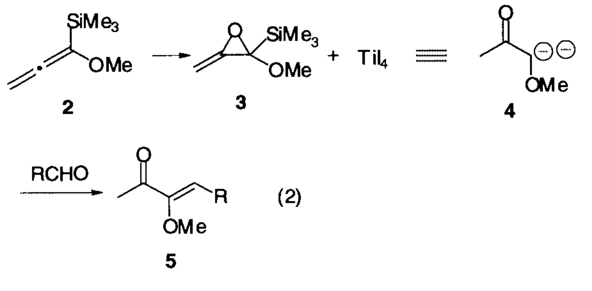
(Received May 17, 2001; CL- 010462)

A dianion equivalent of methoxyacetone was successfully generated using 1-methoxy-1-trimethylsilylallene oxide and titanium tetraiodide and subsequent reaction with acetals or aldehydes gave α-methoxy-α,β-unsaturated ketones in good yields.

---

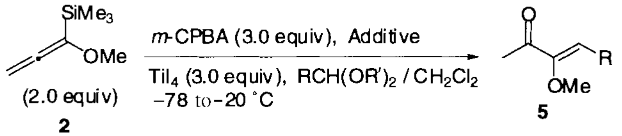
Although interesting species are generated from allene oxide and the subsequent reactions proceed to give several products, these relatively reactive intermediates have not been fully utilized in organic synthesis. We have recently described a useful reaction using methoxyallene[1] oxide and titanium tetraiodide,[2] where reductive formation of the enolate of methoxyacetone led to regioselective aldol reaction, giving α-methoxy-β-hydroxy ketones in good yields with good diastereoselectivity.[3] In an effort to find the utility of derivatives of methoxyallene oxide, silylated species are expected to undergo further Peterson-type olefination[4] with acetals or aldehydes to give α-methoxy-α,β-unsaturated ketones. This report describes a successful generation of a dianion equivalent of methoxyacetone from 1-methoxy-1-trimethylsilylallene oxide and subsequent reaction with acetals or aldehydes.





The starting material, 1-trimethylsilyl-1-methoxyallene **2** was readily prepared according to the reported procedure in good overall yield.[5] The epoxidation of 1-trimethylsilyl-1-methoxyallene **2** was regioselectively carried out at the electron-rich carbon–carbon double bond[6] with *m*-CPBA[7] to give 1-trimethylsilyl-1-methoxyallene oxide **3**. Subsequent treatment of the crude allene oxide with $TiI_4$[8] and acetal or aldehyde gave (*Z*)-α-methoxy-α,β-unsaturated ketone with complete regioselectivity and diastereoselectivity.[9] The results of reaction with acetals are summarized in Table 1.[10]

**Table 1.** Reaction with acetals[a]



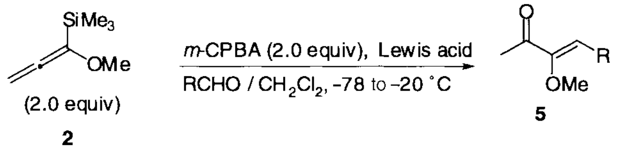
| Entry | R | R' | Additive(equiv) | Time/h | Yield/%[b] |
|---|---|---|---|---|---|
| 1 | Ph | Me | none | 2.0 | 35 |
| 2 | Ph | Me | $ClCH_2CO_2H$(0.5) | 1.8 | 46 |
| 3 | Ph | Me | $PhCO_2H$(0.5) | 2.0 | 49 |
| 4 | Ph | Me | Salicylic acid(0.5) | 1.8 | 38 |
| 5 | Ph | Me | dist $H_2O$ (1.0) | 2.0 | 55 |
| 6 | Ph | Me | dist $H_2O$ (4.0) | 2.3 | 65 |
| 7 | 4-$MeC_6H_4$ | Me | dist $H_2O$ (4.0) | 3.0 | 43 |
| 8 | Ph | Et | dist $H_2O$ (4.0) | 2.2 | 25 |
| 9 | $Ph(CH_2)_2$ | Me | dist $H_2O$ (4.0) | 2.3 | trace |

[a]Reaction was carried out according to the typical procedure.
[b]Isolated yield.

The reaction with benzaldehyde dimethylacetal in the absence of additives gave (*Z*)-3-methoxy-4-phenyl-3-buten-2-one **5** in low yield (entry 1). As in the cases with the results previously reported,[3] the addition of carboxylic acid or water improved the product yields. Among the carboxylic acids examined, the addition of benzoic acid improved the yield up to 49% (entries 2–4). The best result was obtained using distilled water (4.0 equiv) as an additive (entry 6). In the case of *p*-tolualdehyde dimethylacetal, the yield was lower than that of benzaldehyde dimethylacetal. One of the roles of the added water may be that of increasing the solubility of *m*-chlorobenzoic acid formed as a by-product in the oxidation of allene and to facilitate the oxonium ion formation in the reaction with acetals. However, only a small amount of the adduct was obtained in the reaction with aliphatic aldehyde dimethyl acetal. We then turned our attention to the use of aldehydes, and the results are summarized in Table 2.[11]

When the reaction was carried out in the presence of $TiI_4$ or $AlI_3$, the desired adduct **5** was obtained in low yields (entries 1 and 2). In order to improved the product yield several Lewis acids were added. Among the Lewis acids screened borontrifluoride etherate was not effective to give the adduct in low yield (entry 3), whereas the use of trimethylsilyl trifluoromethanesulfonate effectively improved the yield (entry 5). The best result was obtained using *m*-CPBA (2.0 equiv) and subsequently $TiI_4$ (2.0 equiv)–TMSOTf (1.5 equiv), and the enone **5** was obtained in 73% yield (entry 6), in which the use of trimethysilyl trifluoromethanesulfonate also promoted Peterson elimination reaction. Under the optimum conditions the reaction of 1-trimethylsilyl-1-methoxyallene oxide with various aldehydes was carried out. Although aliphatic and α,β-unsaturated aldehydes did not give the desired adduct, aromatic counterparts underwent addition–elimination to give the enones **5** in good yields, showing that the present reaction is suitable for the

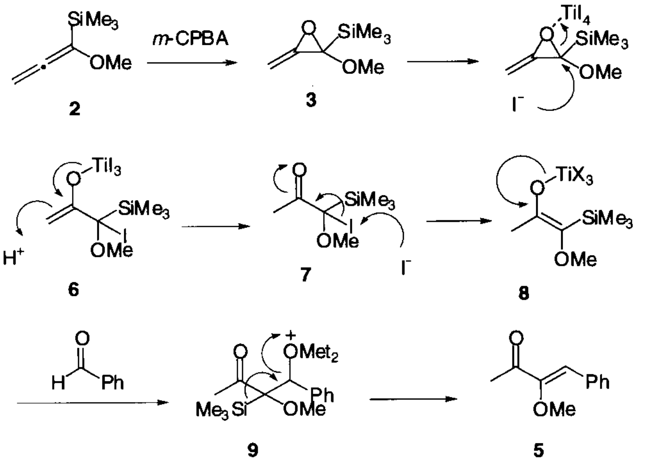
**Table 2.** Reaction with aldehydes[a]



| Entry | R | Lewis acid(equiv) | Time/h | Yield/%[b] |
|---|---|---|---|---|
| 1 | Ph | $TiI_4$(3.0) | 2.0 | 30[c] |
| 2 | Ph | $AlI_3$(3.0) | 2.0 | 5 |
| 3 | Ph | $TiI_4$(2.0)-$BF_3$•$Et_2O$(1.0) | 2.3 | 19[c] |
| 4 | Ph | $TiI_4$(2.0)-TMSOTf(1.0) | 2.8 | 40[c] |
| 5 | Ph | $TiI_4$(2.0)-TMSOTf(1.5) | 2.5 | 50[c] |
| 6 | Ph | $TiI_4$(2.0)-TMSOTf(1.5) | 2.3 | 73 |
| 7 | 1-Naphthyl | $TiI_4$(2.0)-TMSOTf(1.5) | 2.0 | 45 |
| 8 | $PhCH_2CH_2$ | $TiI_4$(2.0)-TMSOTf(1.5) | 2.2 | trace |
| 9 | (*E*)-PhCH=CH | $TiI_4$(2.0)-TMSOTf(1.5) | 1.7 | trace |
| 10 | 4-$ClC_6H_4$ | $TiI_4$(2.0)-TMSOTf(1.5) | 2.3 | 30 |
| 11 | 4-$MeOC_6H_4$ | $TiI_4$(2.0)-TMSOTf(1.5) | 2.0 | 53 |
| 12 | 4-$MeC_6H_4$ | $TiI_4$(2.0)-TMSOTf(1.5) | 2.2 | 76 |
| 13 | 3-$MeC_6H_4$ | $TiI_4$(2.0)-TMSOTf(1.5) | 2.3 | 63 |
| 14 | 2-$MeC_6H_4$ | $TiI_4$(2.0)-TMSOTf(1.5) | 3.2 | 46 |

[a] Reaction was carried out according to the typical procedure. [b] Isolated yield. [c] *m*-CPBA (3.0 equiv) was used.

addition to relatively reactive aldehydes. Regarding the reaction mechanism, the present reaction most probably proceeds via the following pathways.



**Scheme 1.**

The titanium enolate **6** is formed via ring-opening reaction of the methoxyallene oxide **3** with titanium tetraiodide and undergoes protonation with 3-chlorobenzoic acid to give iodo ketone **7**. The iodo ketone **7** is then transformed into the titanium enolate **8** via reduction of the iodide with the iodide anion, and the subsequent reaction with aldehyde followed by the Peterson olefination reaction under the acidic conditions[12] gives the enone **5**.

In conclusion, we have found that 1-trimethylsilyl-1-methoxyallene oxide **3** behaves as a dianion equivalent of methoxyacetone under the influence of $TiI_4$–TMSOTf. Since various alkoxyallene derivatives are readily available from the corresponding propargyl ethers, the present procedure offers a good method for the generation of enolate from methoxyacetone in a regioselective manner.

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, of the Japanese Government.

## References and Notes

1 S. Hoff, L. Brandsma, and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **87**, 916 (1968).

2 a) R. Hayakawa and M. Shimizu, *Chem. Lett.*, **2000**, 724. b) M. Shimizu, K. Shibuya, and R. Hayakawa, *Synlett*, **2000**, 1437. c) R. Hayakawa, T. Sahara, and M. Shimizu, *Tetrahedron Lett.*, **41**, 7939 (2000).

3 R. Hayakawa and M. Shimizu, *Org. Lett.*, **2**, 4079 (2000).

4 P. F. Hudrlik and D. Peterson, *J. Am. Chem. Soc.*, **97**, 1464 (1975).

5 a) M. A. Tius, in "Encyclopedia of Reagents for Organic Synthesis," ed. by L. A. Paquette, John Wiley & Sons, Chichester (1995), Vol. 7, pp 5274–5276. b) J.-C. Clinet and G. Linstrumelle, *Tetrahedron Lett.*, **21**, 3987 (1980).

6 a) J. K. Crandall and W. H. Machleder, *J. Am. Chem. Soc.*, **90**, 7347 (1968). b) R. L. Camp and F. D. Greene, *J. Am. Chem. Soc.*, **90**, 7349 (1968).

7 For reproducible results, purified *m*-CPBA was used. See, N. N. Schwartz and J. H. Blumbergs, *J. Org. Chem.*, **29**, 1976 (1964).

8 Titanium tetraiodide was purified by sublimation (180 °C / 0.8 mmHg).

9 Determined by NOE.

10 A typical procedure is as follows: To a suspension of *m*-CPBA (186 mg, 1.1 mmol) and distilled water (26 mg, 1.4 mmol) in $CH_2Cl_2$ (0.5 mL) was added a solution of 1-trimethylsilyl-1-methoxyallene (102 mg, 0.72 mmol) in $CH_2Cl_2$ (1.0 mL) at 0 °C under an argon atmosphere. After stirring for 30 min, the mixture was transferred into a solution of $TiI_4$ (600 mg, 1.1 mmol) and benzaldehyde dimethylacetal (55 mg, 0.36 mmol) in $CH_2Cl_2$ (2.0 mL) with the aid of $CH_2Cl_2$ (1.5 mL). After being stirred at –78 °C to –20 °C for 2.3 h, the reaction was quenched with sat. aqueous $NaHCO_3$, aqueous 5% $NaHSO_3$ and triethylamine. The mixture was filtered through a Celite pad. The layers were separated and the aqueous layer was extracted with ethyl acetate (10 mL × 3). The combined organic extracts were washed with sat. aqueous $NaHCO_3$ and brine, and then dried over anhydrous $Na_2SO_4$. Purification on preparative silica gel TLC gave the adduct (41 mg, 65%) as a colorless oil.

11 A typical procedure for the reaction of aldehydes is as follows: To a suspension of *m*-CPBA (124 mg, 0.72 mmol) in $CH_2Cl_2$ (0.5 mL) was added a solution of 1-trimethylsilyl-1-methoxyallene (102 mg, 0.72 mmol) in $CH_2Cl_2$ (0.8 mL) at 0 °C under an argon atmosphere, and the resulting mixture was stirred for 30 min at 0 °C. The solution of the epoxidation reaction mixture was transferred into a mixture of $TiI_4$(400 mg, 0.72 mmol), TMSOTf (120 mg, 0.54 mmol) , and *p*-tolualdehyde (43 mg, 0.36 mmol) in $CH_2Cl_2$ (2.7 mL) at –78 °C with the aid of $CH_2Cl_2$ (1.0 mL), and the reaction was conducted and worked up as in the case with acetals. Purification on preparative silica gel TLC gave the adduct (52 mg, 76%) as a colorless oil.

12 I. Matsuda and Y. Izumi, *Tetrahedron Lett.*, **22**, 1805 (1981).