Electrogenerated Acid-Catalyzed Michael Reaction of Enol Silyl Ethers and Ketene Silyl Acetals to α,β-Unsaturated Carbonyl Compounds

Tsutomu INOKUCHI, Yuji KUROKAWA, Masahiko KUSUMOTO, Shinichi TANIGAWA, Sadahito TAKAGISHI, and Sigeru TORII*

Department of Applied Chemistry, Faculty of Engineering, Okayama University, Okayama 700

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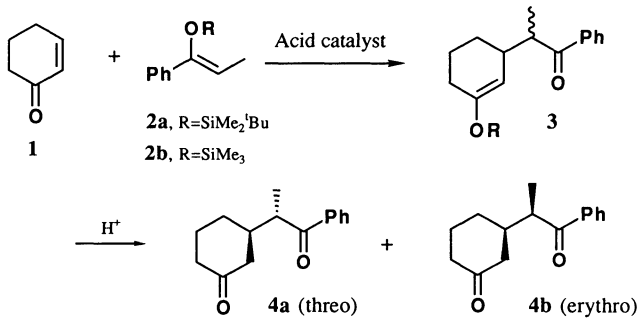
Synopsis. 1,5-Dicarbonyl compounds and their enol silyl ethers were prepared by the reaction of α,β-unsaturated ketones and enol silyl ethers or ketene silyl acetals by using an electrogenerated acid (EG acid) as a catalyst. Similar reaction of 1-trimethylsiloxy-1,3-butadiene with enones produced six-membered adducts as the result of a double-Michael process.

The conjugate-addition of basic enolates to α,β-unsaturated carbonyl compounds (i.e. the Michael reaction) is an important tactics for the preparation of 1,5-dicarbonyl compounds.[1] Recently, the reaction has been greatly improved by using enol silyl ethers as an equivalent of enolates in the presence of a stoichiometric amount of Lewis acids such as $TiCl_4$, $Ti(OC_3H_7\text{-}i)_4$, and $SnCl_4$ (the Mukaiyama-Michael reaction),[2] which may suppress side-reactions, e.g. self-condensation, proton transfer, 1,2-addition, and so on. Cesium fluoride (CsF) can catalyze 1,4-addition of enol silyl ethers in a heterogeneous medium.[3] Besides these reagents, homogeneous catalysts such as tris(dimethylamino)sulfonium difluorotrimethylsiliconate (TAS-F)[4] and a number of triphenylmethyl (trityl) salts[5] have currently been developed in order to achieve the 1,4-addition stereoselectively, giving rise to the adducts as a form of enol silyl ethers.

In the preceding paper, we reported the electrogenerated acid (EG acid)-catalyzed aldol reactions, cyanations, allylations, and hydride additions of organosilicon compounds.[6] In continuation of our study on EG acid-catalyzed carbon-carbon bond making reactions, we describe here the EG acid-catalyzed Michael reaction of α,β-unsaturated kenones with enol silyl ethers or ketene silyl acetals and their stereochemical product distributions.

Procedures employed in the EG acid-catalyzed Michael reaction are as follows: (1) The method A is based on the concurrent electrolysis of enol silyl ethers and enones in a CH_2Cl_2–$LiClO_4$–Bu_4NClO_4–(Pt) system.[6] (2) The method B is relied on the treatment with the pre-generated EG acid in an MeCN–$LiClO_4$–Bu_4NClO_4–(Pt) system.[7] (3) The method C is the reaction catalyzed by the electrochemically prepared trityl perchlorate. Prior to the present study, we have found that trityl perchlorate ($TrClO_4$) can be easily provided by the electrooxidation of phenylthiotriphenylmethane in an MeCN–$LiClO_4$–Bu_4NClO_4–(Pt) system in a divided cell.[8]

The reaction of 2-cyclohexenone (**1**) and 1-*t*-butyldimethylsiloxy-1-phenylpropene (**2a**)[9] was examined with EG acids of methods A—C and the results are shown in Table 1. In each case, the reaction proceeded smoothly at −78°C to give the corresponding 1,4-adducts **3** in good yields. The enol silyl moiety of **3** was subjected to hydrolysis with 10% hydrochloric acid in MeOH–H_2O (1:10 v/v) to give the corresponding 1,5-diketones **4a**, **b**. The anti/syn (threo/erythro)[10] stereochemistry of **4a**, **b** was assigned according to the data reported[5] and then the diastereomeric ratios were estimated by peak areas at δ 1.16, 1.17 and 1.19, 1.21 in ^1H NMR (500 MHz) spectra (Scheme 1). The anti/syn (threo/erythro) ratios of the 1,5-diketones **4a**, **b** are in the range of 76—77:24—23 and these results are virtually same with that[5] obtained with the chemically prepared trityl perchlorate.[11] Similarly, the 1,4-addition of 1-phenyl-1-trimethylsiloxypropene (**2b**)[9] to the enone **1** was attempted with the EG acid (method A) in dichloromethane, giving the corresponding adducts **4a**, **b**, after the hydrolysis of silyl group, in 80% yield with a threo/erythro ratio of 71:29 (Entry 5). In addition to these acid-catalysts, we



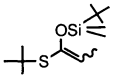
Scheme 1.

Table 1. Michael Reaction of **1** and **2a** to **3**

Entry	Method	Temp(°C)/min	Yield of **3**/%	Threo/Erythro[a]
1	A	−78/30	90	77/23
2	B	−78/20	94	76/24
3	C	−78/90	90	77/23
4	D	−78/90	81	62/38
5[b]	A	−78/60	80	71/29

a) Determined by ^1H NMR (500 MHz). b) Trimethylsilyl ether **2b** was used in place of **2a**.

Table 2. The Reaction of Enones with Enol Silyl Ethers or Ketene Silyl Acetals

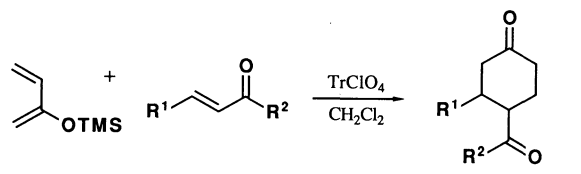
Entry	Enones	Enol silyl ethers	Electricity / F mol^{-1}	Temp / °C	Yield of adducts / %	(Isomer ratio)[a]
1			0.05	0	88	
2			0.05	−78	87	(>98/2)
3			0.10	−78	94	
4			0.10	−78	94	(55/45)
5			0.15	−78	88	

a) Determined by ^{1}H NMR (500 MHz) after hydrolysis to dicarbonyl compounds.

examined triphenylsilyl perchlorate (Ph_3SiClO_4)[12] as an acid-catalyst for the reaction of **1** and **2a** in dichloromethane [method D] and threo/erythro ratio of which has changed to 62:38 [Entry 4] as compared with that obtained by acid-catalysts of Methods A—C.

Among the three different electrochemical procedures, the method A was used for the 1,4-addition of a variety of enones with enol silyl ethers or ketene silyl acetals (Table 2). The reaction of 1-phenyl-2-buten-1-one and enol silyl ether **2a** gave the threo adduct preferentially (Entry 2)[13] in good accordance with the reported trityl cation-catalyzed reaction.[5] Enol silyl ether derived from ethyl acetate and *S*-*t*-butyl thiopropionate added to 2-cyclohexenone (**1**), smoothly.

The reactions of enones **6** with 2-trimethylsiloxy-1,3-butadiene (**5**) as a nucleophile, giving the corresponding six-membered adducts **7** in 51—81% yields by a double-Michael process, were attempted in a CH_2Cl_2–$TrClO_4$ system.[5d,14] Apparently, $TrClO_4$ prepared from stable precursors, e.g. phenylthiotriphenylmethane and lithium perchlorate, by electrolysis can be used for Michael reactions as an effective catalyst as that chemically prepared.



3 **6a**, R^1=Ph, R^2= Me; **6b**, R^1= Me, R^2= Ph

7a 81% (62%)[5d] **7b** 51% (68%)

Experimental

IR spectra were taken on a JASCO FT-IR-5000 spectrometer. NMR spectra were recorded in $CDCl_3$ on a Varian VXR-500 spectrometer.

General Procedure for the Reaction of Enol Silyl Ether with α,β-Unsaturated Ketones (Method A). Into the electrolysis vessel[6] were added $LiClO_4$ (17 mg, 0.15 mmol) and Bu_4NClO_4 (17.1 mg, 0.05 mmol) and the resulting mixture was dried at about 100 °C under vacuum for 1 h and then purged with argon. To this mixture was added a solution of 1-*t*-butyldimethylsiloxy-1-phenylpropene (**2a**, 149 mg, 0.6 mmol) and cyclohexenone (**1**, 48 mg, 0.5 mmol) in CH_2Cl_2 (3 ml). The entire mixture was electrolyzed under a constant current of 6.7 mA cm^{-2} (applied voltage: 10—15 V) at −78 °C. The progress of the reaction was monitored by TLC and the reaction was quenched with Et_3N (3 drops) when the starting **1** has completely disappeared (it took about 30 min and 0.2 F (1F=96480 C)mol^{-1} of electricity has been passed). The volatiles were removed on a rotary evaporator and the residue was purified by column chromatography (SiO_2, hexane–AcOEt 20:1) to give 155 mg (90%) of **3a**: bp 117 °C/0.02 Torr (1 Torr≈133.322 Pa); IR (neat) 3040, 1680 (C=O), 1660 (C=C), 1595, 1575, 1445, 1365, 1250, 1200, 1175, 980, 910, 835, and 780 cm^{-1}; ^{1}H NMR (500 MHz) δ=0.13, 0.14 (s, 6, $SiMe_2$), 0.85, 0.92 (s, 9, $SiCMe_3$), 1.14, 1.16 (d, *J*=7 Hz, 3, CH_3), 1.18—1.30 (m, 1, CH_2), 1.50—1.80 (m, 3, CH_2), 1.90—2.04 (m, 2, CH_2), 2.64 (m, 1, CH), 3.40 (m, 1, PhCH), 4.87 (brs, 1, OC=CH), 7.44—7.48, 7.54—7.57, and 7.93—7.95 (m, 5, PhH).

Hydrolysis of Enol Silyl Ether. To a solution of **3a** (34 mg, 0.1 mmol) in a mixed solution of MeOH (1 ml) and H_2O (10 ml) was added 10% HCl (2 drops). The mixture was stirred at room temperature for 1.5 h and extracted with AcOEt. Washing with brine and concentration followed by column chromatography (SiO_2, hexane–AcOEt) gave 21 mg (91%) of **4a**, **b**: bp 94—95 °C/0.4 Torr; IR (neat) 3066, 1713 (C=O), and 1682 (C=O) cm^{-1}; ^{1}H NMR (500 MHz) δ=1.17, 1.20 (d, *J*=7 Hz, 3, CH_3), 1.43 (m, 1), 1.58—1.68 (m, 1), 1.83—1.91 (m, 1), 1.98—2.06 (m, 1), 2.13 (m, 1), 2.20—2.31 (m, 2), 2.38—2.44 (m, 1), 2.49 (m, 1), 3.47 (m, 1, COCH), 7.42 (m, 1, PhH), 7.57 (m, 1, PhH), and 7.93 (m, 2, PhH).

Preparation of Trityl Perchlorate from Phenylthiotriphenylmethane. A Typical Procedure. Into the anodic compartment of a divided cell separated by a Nafion 324 diaphragm was added a solution of phenylthiotriphenylmethane (176 mg, 0.5 mmol), $LiClO_4$ (110 mg, 1.0 mmol), and Bu_4NClO_4 (340 mg, 1.0 mmol) in MeCN (7 ml). The mixture was electrolyzed at a constant current at 20 mA (applied voltage; 10—20 V) with platinum electrodes (1.5 cm^2) at room temperature. When the electrolysis was initiated, yellow color has appeared in the anolyte. The progress of the

reaction was monitored by TLC and the anolyte was transferred to a Schlenk tube when the sulfide was completely consumed (it took about 150 min and 1.87 F mol^{-1} of electricity has been passed). The mixture was concentrated under vacuum at ca. 0.1 Torr at 0 °C and yellow solids left were dissolved in CH_2Cl_2 (5 ml). A 1.0 ml portion of this solution was used for the following Michael reactions.

Michael Reaction by Using Electrochemically Prepared Trityl Perchlorate. To a solution of **2a** (298 mg, 1.2 mmol) and **1** (96 mg, 1.0 mmol) in CH_2Cl_2 (3 ml) was added a solution of the above trityl perchlorate (1.0 ml) at −78 °C and stirring was continued for 30 min. The mixture was treated with Et_3N (0.5 ml), concentrated under vacuum, and purified by column chromatography (SiO_2, hexane–AcOEt) to give 310 mg (90%) of the adducts **3a**.

Reaction of 1a and 2a by Triphenylsilyl Perchlorate. A solution of **2a** (149 mg, 0.6 mmol) and **1** (48 mg, 0.6 mmol) in CH_2Cl_2 (3 ml) was treated with a 0.2 M Ph_3SiClO_4[11] (1 M=1 mol dm^{-3}) in CH_2Cl_2 (0.3 ml) at −78 °C. After being stirred for 1.5 h at −78 °C, the reaction was quenched with Et_3N (0.3 ml). Concentration under vacuum followed by purification of the residue by column chromatography on SiO_2 (hexane–AcOEt) gave 156 mg (81%) of the adducts **3a** and 12 mg (11%) of the unprotected **4a, b**.

Spectral data of 1,5-dicarbonyl compounds derived from the Michael adducts in Table 2 are as follows.

1,3-Diphenyl-1,5-hexanedione; IR (neat) 1710 (C=O) and 1680 (C=O) cm^{-1}; ^1H NMR (500 MHz) δ=2.00 (s, 3, $COCH_3$), 2.81—2.96 (m, 2, $COCH_2$), 3.26—3.38 (m, 2, $COCH_2$), 3.89 (m, 1, CH), 7.18—7.21, 7.25—7.30, 7.42—7.45, 7.53—7.56, and 7.91—7.92 (m, 10, PhH).

2,3-Dimethyl-1,5-diphenyl-1,5-pentanedione: IR (neat) 3094 and 1682 (C=O) 692 cm^{-1}; ^1H NMR (500 MHz) δ=1.07 (d, J=6.5 Hz, 3, CH_3), 1.23 (d, J=7 Hz, 3, CH_3), 2.70 (m, 1, CH), 2.74 (d, d, J=16, 9.5 Hz, 1, CH_2CO), 3.59—3.65 (m, 1, COCH), 7.39—7.56, and 7.86—7.96 (m, 10, PhH).

Ethyl (3-Oxocyclohexyl)acetate: IR (neat) 1730 (C=O) and 1710 (C=O) cm^{-1}; ^1H NMR (500 MHz) δ=1.25 (t, J=7 Hz, 3, CH_3), 1.41 (m, 1), 1.71 (m, 1), 1.94 (m, 1), 2.02—2.12 (m, 2), 2.21—2.35 (m, 4), 2.38, 2.45 (m, 2, $COCH_2$), and 4.13 (q, 2, OCH_2).

***S-t*-Butyl 2-(3-Oxocyclohexyl)thiopropionate:** IR (neat) 1710 (C=O) and 1670 (COS) cm^{-1}; ^1H NMR (500 MHz) δ=1.09, 1.13 (d, J=7 Hz, 3, CH_3), 1.29—1.42 (m, 1), 1.428, 1.436 (s, 9, $C(CH_3)_3$), 1.55—1.64 (m, 1), 1.90 (m, 1), 1.98—2.08 (m, 2), 2.14 (m, 1), 2.17—2.26 (m, 1), 2.35 (m, 1), and 2.38—2.44 (m, 2).

Ethyl 5-Oxohexanoate: IR (neat) 1730 (COO) and 1710 (C=O) cm^{-1}; ^1H NMR (500 MHz) δ=1.15 (t, J=7 Hz, 3, CH_3), 1.78 (quintet, 2, J=7 Hz, 2, CH_2), 2.04 (s, 3, $COCH_3$), 2.21 (t, J=7 Hz, 2, $COCH_2$), and 2.40 (t, J=7 Hz, 2, $COCH_2$).

Double-Michael Reaction of 2-Trimethylsiloxy-1,3-butadiene (5). To a solution of **5** (284 mg, 2.0 mmol) and the enone **6a** (R^1=Ph, R^2=Me, 146 mg, 1.0 mmol) in CH_2Cl_2 (3 ml) was added a solution of the electrochemically prepared $TrClO_4$ (1.0 ml) in the manner as above at −78 °C. After stirring at −78 °C for 4 h, the mixture was poured into aqueous saturated NH_4Cl and extracted with AcOEt. Usual workup and purification by column chromatography (SiO_2, hexane–AcOEt) gave 174 mg (81%) of 4-acetyl-3-phenylcyclohexanone (**7a**) as solids: mp 63—65 °C (hexane–AcOEt); IR (KBr) 1711 (C=O), 1603 (C=C), and 1584 cm^{-1}; ^1H NMR (500 MHz) δ=1.88 (s, 3, CH_3CO), 1.90—1.98 (m, 1, CH_2), 2.17—2.23 (m, 1, CH_2), 2.45—2.53 (m, 1, CH_2CO), 2.56 (m, 1, CH_2CO), 2.60—2.64 (m, 2, CH_2CO), 3.17 (m, 1, CH), 3.26 (m, 1, CH), and 7.20—7.34 (m, 5, PhH).

4-Benzoyl-3-methylcyclohexanone (7b): mp 58—59 °C (hexane–AcOEt); IR (KBr) 1711 (C=O), 1676, and 1599 (C=C) cm^{-1}; ^1H NMR (500 MHz) δ=0.98 (d, J=6.5 Hz, 3, CH_3), 1.87—1.95 (m, 1, CH), 2.17—2.22 (m, 2, CH_2), 2.38—2.57 (m, 4, CH_2CO), 3.45—3.50 (m, 1, CHCO), 7.50—7.53 (m, 2, PhH), 7.61 (m, 1, PhH), and 7.94—8.01 (m, 2, PhH).

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References

1) E. D. Bergmann, D. Ginsburg, and R. Pappo, "Organic Reactions," Vol. 10, p. 179 (1959); H. O. House, "Modern Synthetic Reactions," 2 nd ed, W. A. Benjamin, Menlo Park, California (1972), p. 595.

2) K. Narasaka, K. Soai, and T. Mukaiyama, *Chem. Lett.*, **1974**, 1223; K. Narasaka, K. Soai, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **49**, 779 (1976); K. Saigo, M. Osaki, and T. Mukaiyama, *Chem. Lett.*, **1976**, 163; C. H. Heathcock, M. H. Norman, and D. E. Uehling, *J. Am. Chem. Soc.*, **107**, 2797 (1985).

3) J. Boyer, R. J. P. Corriu, R. Perz, and C. Reye, *Tetrahedron*, **39**, 117 (1983).

4) T. V. RajanBabu, *J. Org. Chem.*, **49**, 2083 (1984).

5) a) S. Kobayashi, M. Murakami, and T. Mukaiyama, *Chem. Lett.*, **1985**, 953; b) T. Mukaiyama, M. Tamura, and S. Kobayashi, *ibid.*, **1986**, 1017; c) T. Mukaiyama, M. Tamura, and S. Kobayashi, *ibid.*, **1986**, 1817; d) T. Mukaiyama, S. Sagawa, and S. Kobayashi, *ibid.*, **1986**, 1821; e) T. Mukaiyama, M. Tamura, and S. Kobayashi, *ibid.*, **1987**, 743.

6) S. Torii, T. Inokuchi, S. Takagishi, H. Horike, H. Kuroda, and K. Uneyama, *Bull. Chem. Soc. Jpn.*, **60**, 2173 (1987).

7) T. Inokuchi, S. Takagishi, K. Ogawa, Y. Kurokawa, and S. Torii, *Chem. Lett.*, **1988**, 1347.

8) Preparation and characterization of trityl salt by the electrolysis will be reported in detail.

9) Enol silyl ethers were prepared by the reaction of the parent ketones or esters with LDA followed by trapping of the enolates with trialkylsilyl chlorides. The compounds **2a** and **2b** were assigned to be more than 99% (*Z*)-isomers, respectively, by ^1H NMR (500 MHz).[15]

10) a) R. Noyori, I. Nishida, and J. Sakata, *J. Am. Chem. Soc.*, **105**, 1598 (1983). b) M. A. Brook, *J. Chem. Educ.*, **64**, 218 (1987).

11) H. J. Dauben, Jr., L. R. Honnen, and K. M. Harmon, *J. Org. Chem.*, **25**, 1442 (1960).

12) G. K. S. Prakash, S. Keyaniyan, R. Aniszfeld, L. Heiliger, G. A. Olah, R. C. Stevens, H.-K. Choi, and R. Bau, *J. Am. Chem. Soc.*, **109**, 5123 (1987).

13) No appreciable amount of stereoisomer has been observed in its ^1H NMR spectra (500 MHz) and stereochemical purity of product was estimated to be more than 98%.

14) M. Ihara and K. Fukumoto, *Yuki Gosei Kagaku Kyokai Shi*, **44**, 96 (1986).

15) P. Brownbridge, *Synthesis*, **1983**, 1.