Pentacoordinate Organosilicate-Catalyzed Michael Addition of β-Keto Esters to 3-Buten-2-one[‡]

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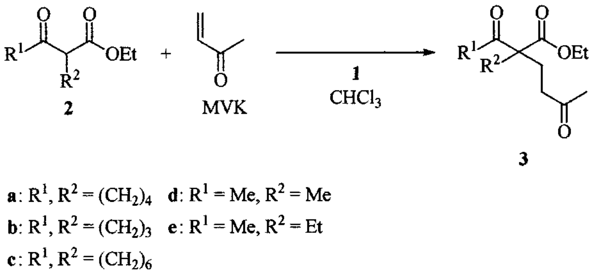
The Michael addition of β-keto esters to 3-buten-2-one (methyl vinyl ketone, MVK) in the presence of a pentacoordinate organosilicate was investigated. Ethyl 2-oxo-1-cyclohexanecarboxylate reacted with MVK in the presence of potassium bis(1,2-benzenediolato)phenylsilicate to furnish ethyl 2-oxo-1-(3-oxo-1-butyl)-1-cyclohexanecarboxylate in 96% isolated yield. Ethyl 2-oxo-1-cyclopentanecarboxylate, ethyl 2-oxo-1-cyclooctanecarboxylate, ethyl 2-methyl-3-oxobutanoate, and ethyl 2-ethyl-3-oxobutanoate also reacted with MVK in the presence of potassium bis(1,2-benzenediolato)phenylsilicate to produce the corresponding 1,4-adduct in moderate to good yields. In these reactions, the silicate might work as both a Lewis acid catalyst and a Brønsted base catalyst at the same time.

Introduction

Organosilicon compounds are essential to modern organic chemistry.[2] In particular, highly coordinate organosilicon compounds such as pentacoordinate organosilicates and hexacoordinate organosilicates are believed to be the keystones in organic synthesis.[3,4] Some pentacoordinate organosilicates have been isolated and found to exhibit oxophilicity or Lewis acidity. The silicates have been used as a reactant with a Lewis acid site in organic synthesis such as chemo- and stereoselective allylations;[4,5] however, to the best of our knowledge, they have not hitherto been used as a Lewis acid catalyst. We focused on pentacoordinate organosilicates as a Lewis acid catalyst. We attempted the Michael addition of β-keto esters to alkenes in the presence of the silicate, and then realized the facile 1,4-addition of ethyl 2-oxo-1-cyclohexanecarboxylate (**2a**) to 3-buten-2-one (methyl vinyl ketone, abbreviated as MVK) in the presence of triethylammonium allylbis(1,2-benzenediolato)silicate (**1d**)[5] (Scheme 1; Table 1, entry 4).



Scheme 1

Results and Discussion

The organosilicate-catalyzed Michael addition of the β-keto ester **2a** to MVK was first investigated under various conditions. Silicates such as potassium bis(1,2-benzenediolato)phenylsilicate (**1a**),[6] triethylammonium bis(1,2-benzenediolato)phenylsilicate (**1b**),[6] (1,4,7,10,13,16-Hexaoxaoctadecane)potassium bis(1,2-benzenediolato)fluorosilicate (**1c**),[7] and **1d**[5a] (Figure 1) were prepared by the previously reported methods, with slight modification. The treatment of a mixture of **2a**, MVK, and chloroform with 10 mol % of **1a** at 40 °C furnished ethyl 2-oxo-1-(3-oxo-1-butyl)-1-cyclohexanecarboxylate (**3a**) regioselectively in 96% isolated yield (Scheme 1; Table 1, entry 1).[8] The reaction proceeded in the presence of **1b** to provide the corresponding 1,4-adduct; however, the reaction was very sluggish. In this case, the adduct **3a** was obtained in 37% isolated yield by increasing the reaction time (Table 1, entry 2). It is worth noting that the catalytic activity of the silicates depended significantly on the counter cation. The silicate **1c** showed a similar reactivity to **1a** to produce the corresponding 1,4-adduct in moderate yield (Table 1, entry 3). The silicate **1d**, which was used as both a Lewis acidic reagent and an allylating agent,[5] also catalyzed the reaction (Table 1, entry 4). In this case, no allylated products were obtained at all. Additionally, the reaction in the absence of the silicate did not proceed (Table 1, entry 5). In the Michael addition with 1.5 mmol of MVK or 5 mol % of **1a**, the adduct **3a** was obtained almost quantitatively (Table 1, entries 6, 9). On the other hand, with 1.2 mmol of MVK, 1 mmol of MVK, or 1 mol % of **1a**, the adduct **3a** was obtained in moderate yields after a prolonged reaction (Table 1, entries 7, 8, 10). As described above, the yield of the adduct depends on the concentration of MVK and the silicate. These results might

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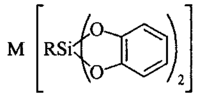
Table 1. Pentacoordinate organosilicate-catalyzed Michael addition of the β-keto ester **2a** to 3-buten-2-one (methyl vinyl ketone, MVK)[a]

Entry	MVK [mmol]	Silicate	[mol %]	Temperature [°C]	Time [h]	Isolated yield of **3a** [%]
1	2	**1a**	10	40	6	96
2	2	**1b**	10	40	24	37
3	2	**1c**	10	40	6	64
4	2	**1d**	10	40	6	14
5	2	–	0	40	18	0
6	1.5	**1a**	10	40	6	94
7	1.2	**1a**	10	40	24	77
8	1	**1a**	10	40	24	73
9	2	**1a**	5	40	6	93
10	2	**1a**	1	40	42	71
11	2	**1a**	10	70	1	94
12	2	**1a**	10	room temp.	24	90

[a] The β-keto ester **2a** (1 mmol) with MVK and the silicate in chloroform (0.2 cm^3) under N_2.

indicate that the interaction between the silicate and MVK plays an important role in this reaction. Reactions at 70 °C and at ambient temperature were completed within 1 h and 24 h, respectively (Table 1, entries 11, 12). The reaction proceeded rapidly at 70 °C, but unidentified tarry products were produced to some extent. The adduct **3a** was produced in good yield in any solvent [e.g. chloroform (isolated yield, 96%), dichloromethane (96%), toluene (96%), THF (95%), methanol (94%), DMF (94%), and HMPA (92%)].



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a: M = K, R = Ph
b: M = [Et$_3$NH], R = Ph
c: M = [18-crown-6]-K, R = F
d: M = [Et$_3$NH], R = allyl

Figure 1. Pentacoordinate organosilicates

In the presence of 10 mol % of **1a**, a similar reaction of **2a** with 1-penten-3-one (ethyl vinyl ketone, abbreviated as EVK) at 40 °C for 6 h furnished ethyl 2-oxo-1-(3-oxo-1-pentyl)-1-cyclohexanecarboxylate in 34% isolated yield. However, the reaction of **2a** with α- or β-substituted α,β-unsaturated ketones such as 3-penten-2-one, 3-methyl-3-buten-2-one, 4-methyl-3-penten-2-one, and 2-cyclohexenone did not proceed. The silicate was found to be very selective for sterically less hindered α,β-unsaturated ketone such as MVK and EVK. Acrylonitrile and α,β-unsaturated esters such as ethyl acrylate and *tert*-butyl acrylate did not react under our conditions.

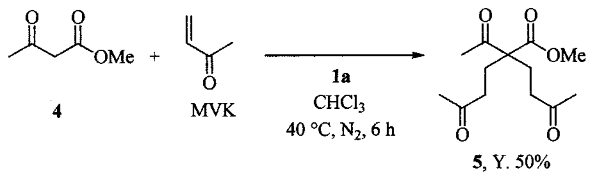
The organosilicate-catalyzed Michael addition of a variety of β-keto esters such as ethyl 2-oxo-1-cyclopentanecarboxylate (**2b**), ethyl 2-oxo-1-cyclooctanecarboxylate (**2c**), ethyl 2-methyl-3-oxobutanoate (**2d**), and ethyl 2-ethyl-3-oxobutanoate (**2e**) to MVK was also carried out. The β-keto ester **2b** reacted with MVK to produce the corresponding 1,4-adduct, ethyl 2-oxo-1-(3-oxo-1-butyl)-1-cyclopentanecarboxylate (**3b**) quantitatively in the presence of any of the silicates **1a**, **1b**, or **1c** (Table 2, entries 1−3). In the presence of **1a**, ethyl 2-oxo-1-(3-oxo-1-butyl)-1-cyclooctanecarboxylate (**3c**), ethyl 2-methyl-3-oxo-2-(3-oxo-1-butyl)-butanoate (**3d**), and ethyl 2-ethyl-3-oxo-2-(3-oxo-1-butyl)-butanoate (**3e**) were obtained in moderate to good yields from the β-keto esters **2c**, **2d**, and **2e**, respectively (Table 2, entries 4, 7, 10). In the same manner as with **2a**, the compounds **2c**, **2d**, and **2e** reacted sluggishly with MVK in the presence of **1b** (Table 2, entries 5, 8, 11). The silicate **1c** also catalyzed the reaction of **2c**, **2d**, and **2e** with MVK to furnish the corresponding 1,4-adduct in moderate to good yields (Table 2, entries 6, 9, 12). The silicate **1a** was found to be the most effective catalyst for these reactions. In the presence of **1a**, methyl 3-oxobutanoate (**4**) reacted with two equivalents of MVK in chloroform at 40 °C for 6 h to produce methyl 3-oxo-2,2-bis(3-oxo-1-butyl)butanoate (**5**) in 50% isolated yield (Scheme 2). In this case, the corresponding mono-adduct was not obtained at all. The silicates were found to be less sensitive to the structure of the β-keto ester since the sterically hindered β-keto esters **2d** and **2e** still reacted efficiently and **4** reacted with two equivalents of MVK. They were applicable to the Michael addition of both cyclic and acyclic β-keto esters.

Table 2. Pentacoordinate organosilicate-catalyzed Michael addition[a]

Entry	β-Keto ester	Silicate	Time [h]	Product	Isolated yield [%]
1	**2b**	**1a**	6	**3b**	98
2	**2b**	**1b**	6	**3b**	98
3	**2b**	**1c**	6	**3b**	98
4	**2c**	**1a**	6	**3c**	91
5	**2c**	**1b**	48	**3c**	75
6	**2c**	**1c**	6	**3c**	46
7	**2d**	**1a**	6	**3d**	84
8	**2d**	**1b**	48	**3d**	88
9	**2d**	**1c**	6	**3d**	91
10	**2e**	**1a**	6	**3e**	74
11	**2e**	**1b**	48	**3e**	36
12	**2e**	**1c**	6	**3e**	56

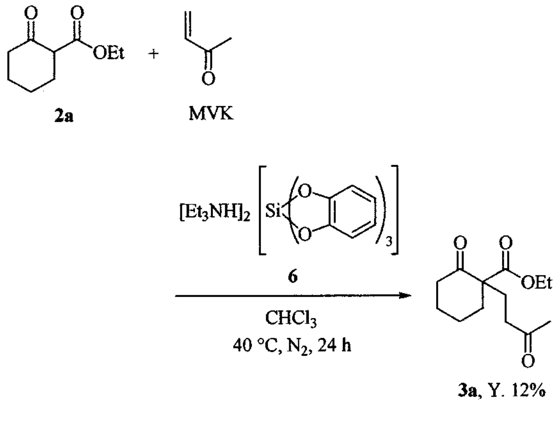
[a] The β-keto ester (1 mmol) with MVK (2 mmol) and the silicate (10 mol %) in chloroform (0.2 cm^3) at 40 °C under N_2.

The Michael addition proceeds in the presence of a Lewis acid catalyst.[9] The silicate **1d**,[5] which has been used as



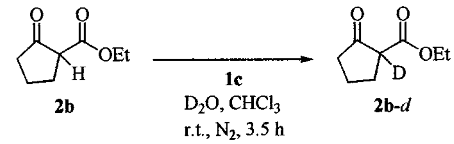
Scheme 2

a Lewis acidic reagent, was found to catalyze the Michael addition of the β-keto ester to MVK (Table 1, entry 4). In order to investigate the Lewis acidic property of the silicates, ^{1}H, ^{13}C, and ^{29}Si NMR spectroscopy and an IR analysis of a mixture of MVK and the silicate **1a**, **1b**, **1c**, or **1d** was attempted. Unfortunately, the obvious interaction of MVK and the silicate was not detected spectroscopically. Furthermore, the reaction with a hexacoordinate organosilicate was performed and compared with that with a pentacoordinate organosilicate. In the presence of bis(triethylammonium) tris(1,2-benzenediolato)silicate **6** (10 mol %),[10] the β-keto ester **2a** was reacted with MVK (2 equivalents) at 40 °C for 6 h to produce the corresponding 1,4-adduct **3a** in 12% isolated yield (Scheme 3). The catalytic activity of **6** was lower than that of **1b** (Scheme 1; Table 1, entry 2). These results may indicate that the pentacoordinate organosilicates such as **1b** and **1d** work as a Lewis acid catalyst and the Lewis acidity accelerates the reaction.



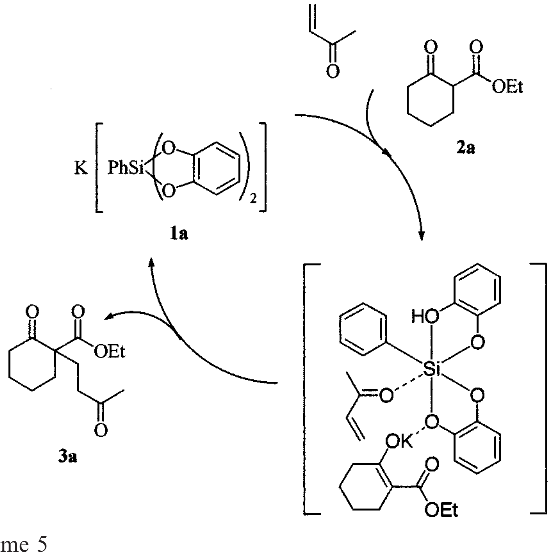
Scheme 3

The Michael addition also proceeds in the presence of a Brønsted base catalyst.[11,12] In order to investigate the Brønsted basic property of the silicates, an H−D exchange reaction with **1c** was tried. The β-keto ester **2b** was treated with **1c** in chloroform at 40 °C then with deuterium oxide at that temperature.[13] As a result, the deuterated compound **2b-*d*** was obtained in 30% isolated yield in 3.5 h (Scheme 4); the reaction in the absence of **1c** did not proceed at all. Therefore, silicate **1c** was revealed to catalyze the H−D exchange reaction. It is difficult to rule out the possibility that the pentacoordinate organosilicates such as **1c** exhibit Brønsted basicity.



Scheme 4

Based on these results, the pentacoordinate organosilicate might act as a Lewis acid catalyst and, at the same time, as a Brønsted base catalyst.[14] Thus, a plausible reaction pathway is as follows, although the details are still unclear (Scheme 5). Initially, the pentacoordinate organosilicate interacts with MVK at its silicon atom as a Lewis acid site, and the hexacoordinate silicate forms. At the same time, the silicate abstracts the α-proton of the β-keto ester with its oxygen atom acting as a Brønsted base site to produce an enolate, which binds to the counter cation of the silicate. The Michael-type addition of the enolate to the activated MVK then proceeds. The resulting enolate is again stabilized by the counter cation of the silicate. Finally, the silicate introduces the proton to the enolate to furnish the corresponding 1,4-adduct. The regenerated silicate then catalyzes the reaction again. The plausible reaction pathway suggests that the Lewis acidity and Brønsted basicity of the silicates are the effective determining factors of the reactivity of the alkenes and the β-keto esters, respectively.



Scheme 5

Conclusion

In conclusion, we have performed the Michael addition of the β-keto esters to MVK in the presence of the pentacoordinate organosilicate to furnish the corresponding 1,4-adducts in moderate to good yields. In particular, the silicate **1a** proved to be the most effective catalyst. The pentacoordinate organosilicates have been used as a reactant with a Lewis acid site in organic synthesis; however, to the best of our knowledge, they have not hitherto been used as a Lewis acid catalyst. In this reaction, the silicate might work both as a Lewis acid catalyst and a Brønsted base catalyst at the same time. We believe that the use of the silicates in these reactions clearly opens up new possibilities in the field of the Michael reaction since the silicates might offer a better environmental compatibility and economy.

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[1] For part 37 see: M. Hojo, Y. Murakami, H. Aihara, R. Sakuragi, Y. Baba, and A. Hosomi, *Angew. Chem. Int. Ed.* **2001**, *40*, 621−623.

[2] For recent reviews on organic chemistry with organosilicon compounds see, for example: M. A. Brook, *Silicon in Organic, Organometallic, and Polymer Chemistry*, Wiley, New York, **2000**.

[3] For reviews on the reactions in the presence of highly coordinated organosilicon compounds see, for example: [3a] K. Akiba, *Chemistry of Hypervalent Compounds*, Wiley-VCH, New York, **1998**. − [3b] C. Chuit, R. J. P. Corriu, C. Reye, J. C. Young, *Chem. Rev.* **1993**, *93*, 1371−1448.

[4] [4a] A. Hosomi, *Rev. Heteroatom Chem.* **1992**, *7*, 214−228 and references cited therein. − [4b] H. Sakurai, *Synlett* **1989**, 1−8 and references cited therein.

[5] [5a] A. Hosomi, S. Kohra, K. Ogata, T. Yanagi, Y. Tominaga, *J. Org. Chem.* **1990**, *55*, 2415−2420. − [5b] A. Hosomi, S. Kohra, Y. Tominaga, *J. Chem. Soc., Chem. Commun.* **1987**, 1517−1518.

[6] D. F. Evans, A. M. Z. Slawin, D. J. Williams, C. Y. Wong, J. D. Woollins, *J. Chem. Soc., Dalton Trans.* **1992**, 2383−2387. For the preparation of **1a** we employed potassium *tert*-butoxide instead of potassium metal. Thus, the silicate **1a** was prepared with trimethoxyphenylsilane, catechol, potassium *tert*-butoxide, and ethanol at ambient temperature. The silicate **1b** was prepared with trimethoxyphenylsilane, catechol, and triethylamine at ambient temperature. Triethylamine was used as the reactant as well as the solvent.

[7] U. Dettlaff-Weglikowska, E. Hey-Hawkins, H. G. von Schnering, *Z. Naturforsch., B: Chem. Sci.* **1991**, *46*, 609−614.

[8] A mixture of the β-keto ester **2a** (170.4 mg, 1.00 mmol), MVK (140.3 mg, 2.00 mmol), chloroform (0.2 cm^3), and the silicate **1a** (36.0 mg, 0.10 mmol) was magnetically stirred at 40 °C under N_2 for 6 h. After cooling to room temperature, ether (5 cm^3) was added to the mixture which was then filtered to remove the resulting precipitate. The filtrate was concentrated and the residue was subjected to column chromatography on silica gel [eluents: hexane and hexane/ethyl acetate (v/v = 9:1)] to furnish the 1,4-adduct **3a** as a colorless oil (229.5 mg, 0.96 mmol, 96%). A minimum amount of chloroform was added for smooth stirring of the reaction mixture.

[9] See, for example: [9a] E. Keller, B. L. Feringa, *Tetrahedron Lett.* **1996**, *37*, 1879−1882. − [9b] H. Kotsuki, K. Arimura, *Tetrahedron Lett.* **1997**, *38*, 7583−7586. − [9c] E. Keller, B. L. Feringa, *Synlett* **1997**, 842−844. Ytterbium triflate in combination with water or silica gel catalyzes the Michael addition of a β-keto ester to an α,β-unsaturated ketone.

[10] The silicate **6** was similarly prepared from triethoxysilane or tetramethoxysilane, catechol, and triethylamine at room temperature.

[11] M. E. Jung, in *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming, M. F. Semmelhack), Pergamon, Oxford, **1991**, vol. 4, chapter 1.1, p. 1−67.

[12] A mixture of tetraalkoxysilane and cesium fluoride is known to promote stoichiometrically the Michael addition of an alkyl ketone to an α,β-unsaturated ketone. − [12a] J. Boyer, R. J. P. Corriu, R. Perz, C. Reye, *J. Chem. Soc., Chem. Commun.* **1981**, 122−123. − [12b] J. Boyer, R. J. P. Corriu, C. Reye, *Tetrahedron* **1983**, *39*, 117−122.

[13] To a dispersion of the silicate **1c** (56.7 mg, 0.10 mmol) and chloroform (1.0 cm^3) was added the β-keto ester **2b** (148 μL, 1.00 mmol) at ambient temperature under N_2 and mixed at that temperature for 1.5 h with magnetic stirring. To the mixture was added deuterium oxide (360 μL, 20.00 mmol) and then stirred at that temperature for 3.5 h. Ether (5 cm^3) was then added, the resulting mixture dried over Na_2SO_4, and passed through filter paper. The filtrate was concentrated and dried in vacuo to provide a colorless oil, which was analyzed by ^{1}H NMR spectroscopy (150.8 mg, 0.97 mmol, 97%, **2b**:**2b**-*d* = 70:30).

[14] Multi-functional lanthanide catalysts providing a Brønsted base site as well as a Lewis acid site. See, for example: [14a] H. Sasai, T. Arai, Y. Satow, K. N. Houk, M. Shibasaki, *J. Am. Chem. Soc.* **1995**, *117*, 6194−6198. − [14b] H. Sasai, E. Emori, T. Arai, M. Shibasaki, *Tetrahedron Lett.* **1996**, *37*, 5561−5564.

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