

Surface-mediated Solid Phase Reaction. Part 6.¹ Mukaiyama–Michael Addition of Silyl Enol Ethers to Alkyl Vinyl Ketones on the Surface of Alumina: a Simple and Convenient Method for the Synthesis of 1,5-Diketones

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Michael addition of silyl enol and dienol ethers to alkyl vinyl ketones occurs in high yield through a simple solvent-free reaction on the surface of anhydrous zinc chloride-impregnated alumina to give 1,5-diketones.

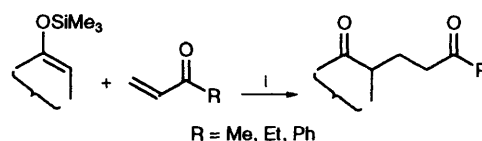
Reactions using reagents or reactants on insoluble inorganic supports such as zeolites, aluminas or silica gels are of considerable interest.² With a modification of this technology, the surface-mediated solid-phase reaction,³ we have achieved remarkable improvements in reactions^{3j} such as Michael addition,⁴ alkylation of 1,3-dicarbonyl compounds,⁵ and the aldol reaction of silyl enol ethers with aldehydes.¹ Recently⁶ we disclosed that anhydrous zinc chloride-impregnated alumina efficiently activates Mukaiyama–Michael addition of silyl enol ethers to methyl vinyl ketone. Here we report the full details of these reactions demonstrating further the scope and generality of this procedure for a variety of silyl enol ethers and alkyl vinyl ketones.

Michael addition of silyl enol ethers to α,β -unsaturated ketones in the presence of TiCl_4 ,⁷ is an important carbon–carbon bond-forming reaction.⁸ Various Lewis acids (e.g. SnCl_4 ,^{9a} BiCl_3 ,^{9b} $\text{BF}_3 \cdot \text{Et}_2\text{O}$,^{9c} ZnCl_2 ,^{9d} and Me_2AlCl ^{9e}) have been used to catalyse this reaction, although they rarely show a uniform scale of efficiency, possibly because of large differences in reactivity between the various types of silyl enol ethers and reagents. Further, since most of these Lewis acids have serious limitations with acid-sensitive substrates, particularly vinyl ketones because of their tendency to polymerise under acidic conditions,¹⁰ masked vinyl ketones have been used.^{10,11} Salts such as TrClO_4 ,^{12a} $\text{Zn}(\text{OTf})_2$,^{12b} $\text{Bu}_2\text{Sn}(\text{OTf})_2$,^{12c} $\text{Sc}(\text{OTf})_3$,^{12d} $\text{BiCl}_3 \cdot x\text{MIn}$ ^{12e} and tris(pentafluorophenyl)boron^{12f} have also been used to catalyse the reaction in attempts to overcome this problem. Also, highly reactive silyl enolates have been reported to accelerate this reaction without any catalysts.¹³ In spite of this, however, since many of these reagents have practical disadvantages, being toxic or not readily available, there is still a need for a convenient procedure to effect additions to unmasked vinyl ketones.

Results and Discussion

The experimental procedure is very simple: alumina impregnated with anhydrous zinc chloride was added to a cooled and stirred mixture of silyl enol ether and alkyl vinyl ketone (Scheme 1). The results are presented in Table 1.

Several trimethylsilyl enol ethers underwent clean addition to either methyl, ethyl or phenyl vinyl ketone by this procedure to produce the corresponding 1,5-diketone. The addition was found to be uniform towards all types of silyl enol ethers and alkyl vinyl ketones with no side product. The conjugated trimethylsilyloxydienes (entries 15–18) were also found to undergo addition with methyl vinyl ketone, although the yields were less satisfactory than with silyl enol ethers. The lower yield may be due to polymerisation of the more reactive siloxydienes and tarry materials were also isolated. However, isolation of



Scheme 1 Reagents and conditions: i, Al_2O_3 – ZnCl_2 , room temp.

only one regioisomeric addition product in the reaction of 4-trimethylsilyloxybuta-1,3-diene (entry 16) indicates that addition of methyl vinyl ketone occurs preferentially or predominantly at the α -position of the parent carbonyl compound. These addition products from conjugated siloxydienes have considerable synthetic potential.^{14a,b}

Reactions with zinc chloride in tetrahydrofuran (THF) in the absence of alumina are messy, giving unwanted side reactions, whilst in the absence of zinc chloride on an alumina surface they are sluggish. Thus, it seems that the combination of zinc chloride and alumina surface is acidic enough to catalyse the addition to alkyl vinyl ketones but sufficiently moderate to prevent side reactions such as vinyl ketone polymerisation. Although the precise role of alumina to tune the activity of zinc chloride for this reaction is not clear, this is a novel, and to the best of our knowledge, first attempt to control the acidity of a Lewis acid for this type of addition.

Experimental

¹H NMR spectra were recorded at 60 MHz on an EM 360 spectrometer of Varian Associates in CCl_4 solutions with Me_4Si as an internal standard (J values in Hz). IR spectra were recorded on a Perkin-Elmer 298 spectrometer as thin films. Elemental analyses were performed by Mr. S. Sarkar of this laboratory. Thin layer chromatography (TLC) was done on precoated silica gel plates (E. Merck). Alumina, (SRL, India; Aluminium oxide, acidic, Brockmann activity grade 1 for column chromatography) was used in all the reactions. Silica gel (SRL, India: 60–120 mesh) was used for filtration chromatography. All commercial chemicals were distilled before use. Trimethylsilyl enol ethers were prepared following the reported procedure of House.¹⁵ Ethyl¹⁶ and phenyl¹⁷ vinyl ketone were also prepared by reported methods.

General Procedure for Michael Addition.—Alumina (1 g, activated at 200 °C for 4 h *in vacuo* and cooled under nitrogen) was stirred with a solution of anhydrous zinc chloride (1 mmol) in THF (5 cm^3) for 5 min after which the excess of THF was removed under reduced pressure to furnish ZnCl_2 -impregnated alumina as a white powder. This reagent (it can be stored under nitrogen for a few days, if necessary, without loss of activity) was then added to a cooled (0 °C, ice bath) and stirred mixture of

Table 1 Michael addition of silyl enol ethers to alkyl vinyl ketones

Entry	Ether	Ketone	t/min	Product	Yield (%) ^a
1	$\overline{\text{CH}_2(\text{CH}_2)_2\text{C}=\text{OSiMe}_3}$ 1	MVK ^b	5	$\overline{\text{OC}(\text{CH}_2)_3\text{CH}(\text{CH}_2)_2\text{COMe}}$	78
2	1	EVK ^c	5	$\overline{\text{OC}(\text{CH}_2)_3\text{CH}(\text{CH}_2)_2\text{COEt}}$	79
3	1	PVK ^d	90	$\overline{\text{OC}(\text{CH}_2)_3\text{CH}(\text{CH}_2)_2\text{COPh}}$	78
4	$\overline{\text{CH}_2(\text{CH}_2)_3\text{C}=\text{OSiMe}_3}$ 2	MVK	5	$\overline{\text{OC}(\text{CH}_2)_4\text{CH}(\text{CH}_2)_2\text{COMe}}$	72
5	2	EVK	5	$\overline{\text{OC}(\text{CH}_2)_4\text{CH}(\text{CH}_2)_2\text{COEt}}$	77
6	2	PVK	90	$\overline{\text{OC}(\text{CH}_2)_4\text{CH}(\text{CH}_2)_2\text{COPh}}$	80
7	$\overline{\text{CH}_2\text{CH}_2\text{CH}(\text{Bu}^t)\text{CH}_2\text{C}=\text{OSiMe}_3}$ 3	MVK	5	$\overline{\text{OC}(\text{CH}_2)_2\text{CH}(\text{Bu}^t)\text{CH}_2\text{CH}(\text{CH}_2)_2\text{COMe}}$	85
8	3	EVK	5	$\overline{\text{OC}(\text{CH}_2)_2\text{CH}(\text{Bu}^t)\text{CH}_2\text{CH}(\text{CH}_2)_2\text{COEt}}$	84
9	$\text{Me}_3\text{SiOC}(\text{Et})=\text{CHMe}$ 4	MVK	60	$\text{EtCOCH}(\text{Me})(\text{CH}_2)_2\text{COMe}$	70
10	4	EVK	60	$\text{EtCOCH}(\text{Me})(\text{CH}_2)_2\text{COEt}$	72
11	4	PVK	120	$\text{EtCOCH}(\text{Me})(\text{CH}_2)_2\text{COPh}$	67
12	$\text{Me}_3\text{SiOCH}=\text{CHEt}$ 5	MVK	120	$\text{HCOCH}(\text{Et})(\text{CH}_2)_2\text{COMe}$	85
13	$\text{Me}_3\text{SiOCH}=\text{CMe}_2$ 6	MVK	30	$\text{HCOC}(\text{Me}_2)(\text{CH}_2)_2\text{COMe}$	86
14	6	EVK	60	$\text{HCOC}(\text{Me}_2)(\text{CH}_2)_2\text{COEt}$	78
15	4-Trimethylsiloxy-1,2-dihydronaphthalene 7	MVK	30	2-(2-Acetyloethyl)-3,4-dihydronaphthalen-4(3H)-one	82
16	$\overline{\text{CH}_2=\text{CHCH}=\text{CHOSiMe}_3}$ 8	MVK	90	$\overline{\text{CH}_2=\text{CHC}(\text{CHO})(\text{CH}_2)_2\text{COMe}}$	51
17	$\overline{\text{CH}_2(\text{CH}_2)_2\text{C}(\text{Me})=\text{CCH}(\text{CH}_2)\text{OSiMe}_3}$	MVK	60	$\overline{\text{CH}_2(\text{CH}_2)_2\text{C}(\text{Me})=\text{CC}(\text{O})(\text{CH}_2)_3\text{COMe}}$	52
18	3-Trimethylsiloxy-5,6,7,8,9,9a-tetrahydro-1H-benzocyclooctene	MVK	60	2-(2-Acetyloethyl)-5,6,7,8,9,9a-hexahydro-1H-benzocycloocten-3(2H)-one	60

^a Yield calculated on the basis of isolated product after purification. ^b MVK = methyl vinyl ketone. ^c EVK = ethyl vinyl ketone. ^d PVK = phenyl vinyl ketone.

trimethylsilyl enol ether (1 mmol) and alkyl vinyl ketone (1.2 mmol) and stirring was continued at 0–5 °C as required for completion (TLC or ¹H NMR) (Table 1). The solid mass was then eluted with methylene dichloride (25 cm³) and the extract was boiled with a few drops of water for 1 min, dried (Na₂SO₄) and evaporated to furnish the adduct. This was further purified by filtering it through a short column of silica gel. (Gram-scale reactions also afforded the corresponding products in analogously good yields.)

The Michael adducts are mostly known compounds and are easily identified by comparison of ¹H NMR and IR spectral data with those reported. Data below corresponds to entries in Table 1.

1. ^{12c} $\nu_{\text{max}}/\text{cm}^{-1}$ 1720 and 1735; δ 0.76–2.66 (11 H, m) and 2.1 (3 H, s).

2. ^{14d} $\nu_{\text{max}}/\text{cm}^{-1}$ 1715 and 1735; δ 1.03 (3 H, t, J 7) and 1.23–2.7 (13 H, m).

3. ^{14d} $\nu_{\text{max}}/\text{cm}^{-1}$ 1680 and 1735; δ 1.23–2.89 (9 H, m), 3.10 (2 H, t, J 7), 7.23–7.50 (3 H, m) and 7.85–8.06 (2 H, m).

4. ^{12c} $\nu_{\text{max}}/\text{cm}^{-1}$ 1710; δ 1.0–2.66 (13 H, m) and 2.07 (3 H, s).

5. ^{12e} $\nu_{\text{max}}/\text{cm}^{-1}$ 1710; δ 1.0 (3 H, t, J 7) and 1.26–2.6 (15 H, m).

6. ¹⁸ $\nu_{\text{max}}/\text{cm}^{-1}$ 1680 and 1705; δ 1.33–2.56 (11 H, m), 2.70–3.13 (2 H, m), 7.23–7.53 (3 H, m) and 7.73–8.10 (2 H, m).

7. ^{12c} $\nu_{\text{max}}/\text{cm}^{-1}$ 1710; δ 0.96 (9 H, s), 1.26–2.66 (12 H, m) and 2.06 (3 H, s).

8. $\nu_{\text{max}}/\text{cm}^{-1}$ 1710; δ 0.89 (9 H, s), 0.96 (3 H, t, J 7) and 1.23–2.53 (14 H, m) (Found: C, 75.6; H, 10.9. C₁₅H₂₆O₂ requires C, 75.58; H, 11.00%).

9. ^{11a} $\nu_{\text{max}}/\text{cm}^{-1}$ 1710; δ 1.02 (3 H, t, J 8), 1.09 (3 H, d, J 7), 1.27–2.73 (7 H, m) and 2.10 (3 H, s).

10. ¹⁹ $\nu_{\text{max}}/\text{cm}^{-1}$ 1710; δ 1.0 (6 H, t, J 6), 1.08 (3 H, d, J 6) and 1.50–2.73 (9 H, m).

11. $\nu_{\text{max}}/\text{cm}^{-1}$ 1680 and 1705; δ 1.03 (3 H, t, J 7), 1.15 (3 H, d, J 6), 1.36–3.0 (7 H, m), 7.26–7.5 (3 H, m) and 7.76–8.0 (2 H, m) (Found: C, 76.85; H, 8.3. C₁₄H₁₈O₂ requires C, 77.03; H, 8.31%).

12. $\nu_{\text{max}}/\text{cm}^{-1}$ 1720; δ 0.90 (3 H, t, J 6), 1.26–2.5 (7 H, m), 2.1 (3 H, s) and 9.46 (1 H, d, J 2) (Found: C, 67.2; H, 9.75. C₈H₁₄O₂ requires C, 67.57; H, 9.93%).

13. ²⁰ $\nu_{\text{max}}/\text{cm}^{-1}$ 1710 and 1725; δ 1.1 (6 H, s), 1.56–1.89 (2 H, m), 2.13 (3 H, s), 2.20–2.46 (2 H, m) and 9.36 (1 H, s).

14. $\nu_{\text{max}}/\text{cm}^{-1}$ 1710 and 1720; δ 1.03 (9 H, s and t, J 7); 1.5–1.9 (4 H, m), 2.13–2.56 (2 H, m) and 9.46 (1 H, s) (Found: C, 68.8; H, 10.6. C₉H₁₆O₂ requires C, 69.19; H, 10.32%).

15. $\nu_{\text{max}}/\text{cm}^{-1}$ 1600, 1680 and 1710; δ 1.5–3.15 (9 H, m), 2.10 (3 H, s), 7.06–7.52 (3 H, m) and 7.85–8.06 (1 H, m) (Found: C, 77.6; H, 7.3. C₁₄H₁₆O₂ requires C, 77.75; H, 7.46%).

16. $\nu_{\text{max}}/\text{cm}^{-1}$ 1685 and 1710; δ 1.63–2.50 (5 H, m), 2.15 (3 H, s), 5.82–7.0 (3 H, m) and 9.45 (1 H, d, J 8) (Found: C, 68.3; H, 8.7. C₈H₁₂O₂ requires C, 68.54; H, 8.63%).

17. $\nu_{\text{max}}/\text{cm}^{-1}$ 1610, 1675 and 1710; δ 1.15–2.89 (12 H, m), 2.06 (3 H, s) and 2.13 (3 H, s); *m/z* 194 (M⁺, 41%), 121 (100), 95 (88), 93 (70) and 67 (64) (Found: C, 74.4; H, 9.25. C₁₂H₁₈O₂ requires C, 74.19; H, 9.34%).

18. $\nu_{\text{max}}/\text{cm}^{-1}$ 1610, 1675 and 1710; δ 1.1–2.49 (18 H, m), 2.06 (3 H, s) and 5.56 (1 H, br s); δ_{C} (CDCl₃, 75 MHz) 25.64 (CH₂), 29.34 (CH₂), 29.87 (CH), 30.14 (CH₂), 31.41 (CH₂), 32.77 (CH₂), 33.24 (CH₂), 34.79 (CH₃), 35.16 (CH₂), 41.20 (CH₂), 47.11 (CH), 127.24 (CH), 173.72 (C), 198.79 (C) and 207.67 (C) (Found: C, 76.6; H, 9.3. C₁₅H₂₂O₂ requires C, 76.88; H, 9.46%).

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References

- Part 5, B. C. Ranu and R. Chakraborty, *Tetrahedron*, 1993, **49**, 5333.
- (a) G. H. Posner, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 487; (b) A. McKillop and D. W. Young, *Synthesis*, 1979, 401 and 481; (c) A. Cornellis and P. Laszlo, *Synthesis*, 1985, 909; (d) P. Laszlo, *Acc. Chem. Res.*, 1986, **19**, 121; (e) P. Laszlo and A. Cornellis, *Aldrichim. Acta*, 1988, **21**, 97; (f) T. Morimoto, H. Hitano, Y. Aikawa and X. Zhang, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2423; (g) T. Nishiguchi and H. Taya, *J. Am. Chem. Soc.*, 1989, **111**, 9102; (h) T. Suzuki, K. Wada, M. Shima and Y. Watanabe, *J. Chem. Soc., Chem. Commun.*, 1990, 1059; (i) T. Nishiguchi and M. Bougauchi, *J. Org. Chem.*, 1990, **55**, 5606; (j) E. Garbowski and M. Primet, *J. Chem. Soc., Chem. Commun.*, 1991, 11; (k) G. W. Breton, K. A. Daus and P. J. Kropp, *J. Org. Chem.*, 1992, **57**, 6646; (l) S. Bhat,

- N. Chidambaram, S. Chandrasekaran, *J. Chem. Soc., Chem. Commun.*, 1993, 651.
- 3 (a) A. Fadel, R. Yofash and J. Salaun, *Synthesis*, 1987, 37; (b) G. Rosini, R. Galarini, E. Marotta and P. Righi, *J. Org. Chem.*, 1990, **55**, 781; (c) M. Kodomari, T. Sakamoto and S. Yoshitomi, *J. Chem. Soc., Chem. Commun.*, 1990, 701; (d) G. Hondrogiannis, R. M. Pagni, G. W. Kabalka, P. Anosike and R. Kurt, *Tetrahedron Lett.*, 1990, **31**, 5433; (e) B. C. Ranu and A. R. Das, *J. Org. Chem.*, 1991, **56**, 4796; (f) S. Bains, J. Green, L. C. Tan, R. M. Pagni and G. W. Kabalka, *Tetrahedron Lett.*, 1992, **33**, 7475; (g) G. Mehta, F. A. Khan and K. A. Lakshmi, *Tetrahedron Lett.*, 1992, **33**, 7977; (h) F. Toda, *Synlett*, 1993, 303; (i) P. J. Kropp, K. A. Daus, M. W. Tubergren, K. D. Kepler, V. P. Wilson, S. L. Craig, M. M. Baillargeon and G. W. Breton, *J. Am. Chem. Soc.*, 1993, **115**, 3071; (j) B. C. Ranu, S. Bhar, R. Chakraborty, A. R. Das, M. Saha, A. Sarkar, R. Chakraborti and D. C. Sarkar, *J. Indian Inst. Sci.*, in press.
- 4 (a) B. C. Ranu, S. Bhar and D. C. Sarkar, *Tetrahedron Lett.*, 1991, **32**, 2811; (b) B. C. Ranu and S. Bhar, *Tetrahedron*, 1992, **48**, 1327; (c) B. C. Ranu, S. Bhar and R. Chakraborti, *J. Org. Chem.*, 1992, **57**, 7349.
- 5 B. C. Ranu and S. Bhar, *J. Chem. Soc., Perkin Trans. 1*, 1992, 365.
- 6 B. C. Ranu, M. Saha and S. Bhar, *Tetrahedron Lett.*, 1993, **34**, 1989.
- 7 K. Narasaka, K. Soai and T. Mukaiyama, *Chem. Lett.*, 1974, 1223.
- 8 (a) T. Mukaiyama, *Angew. Chem., Int. Edn. Engl.*, 1977, **16**, 817; (b) J. K. Rasmussen, *Synthesis*, 1983, **1**, 85; (c) B. B. Lohray and R. Zimbiniski, *Tetrahedron Lett.*, 1990, **31**, 7273 and refs. cited therein.
- 9 (a) C. H. Heathcock, M. H. Norman and D. E. Uehling, *J. Am. Chem. Soc.*, 1985, **107**, 2797; (b) H. Ohki, M. Wada and K. Akiba, *Tetrahedron Lett.*, 1988, **29**, 4719; (c) P. Duhamel, G. Dujardin, L. Hennequin and J. M. Poirier, *J. Chem. Soc., Perkin Trans. 1*, 1992, 387; (d) B. D. Gray and J. D. White, *J. Chem. Soc., Chem. Commun.*, 1985, 20; (e) H. Hagiwara, A. Okano, T. Akama and H. Uda, *J. Chem. Soc., Chem. Commun.*, 1987, 1333.
- 10 J. W. Huffman, S. M. Potnis and A. V. Satish, *J. Org. Chem.*, 1985, **50**, 4266.
- 11 (a) P. Duhamel, J. M. Poirier and G. Tavel, *Tetrahedron Lett.*, 1984, **25**, 43; (b) A. Rosan and M. Rosenblum, *J. Org. Chem.*, 1975, **40**, 362.
- 12 (a) T. Mukaiyama, M. Tamura and S. Kobayashi, *Chem. Lett.*, 1986, 1817; (b) T. Yura, N. Iwasawa, K. Narasaka and T. Mukaiyama, *Chem. Lett.*, 1988, 1025; (c) T. Sato, Y. Wakahara, J. Otera and H. Nozaki, *Tetrahedron*, 1991, **47**, 9773; (d) S. Kobayashi, I. Hachiya, H. Ishitani and M. Araki, *Synlett*, 1993, 472; (e) C. L. Roux, H. G. Itoughmane, J. Dubac, J. Jaud and P. Vignaux, *J. Org. Chem.*, 1993, **58**, 1835; (f) K. Ishihara, N. Hananki and H. Yamamoto, *Synlett*, 1993, 577.
- 13 S. Kobayashi and K. Nishio, *J. Org. Chem.*, 1993, **58**, 2647.
- 14 (a) H. Hagiwara, T. Akama, A. Okano and H. Uda, *J. Chem. Soc., Perkin Trans. 1*, 1993, 2173; (b) M. P. Sant and W. B. Smith, *J. Org. Chem.*, 1993, **58**, 5479; (c) E. D. Bergmann, D. Ginsburg and R. Pappo, *Org. React.*, 1959, **10**, 179; (d) M. E. Jung, *Tetrahedron*, 1976, **32**, 3; (e) H. Ahlbrecht, M. Dietz and L. Webber, *Synthesis*, 1987, 251; (f) M. Tanaka, H. Suemune and K. Sakai, *Tetrahedron Lett.*, 1988, **29**, 1733.
- 15 H. O. House, L. J. Czuba, M. Gall and H. D. Olmstead, *J. Org. Chem.*, 1969, **34**, 2324.
- 16 B. Byrne and K. J. Wengenroth, *Synthesis*, 1986, 870.
- 17 H. J. Reich, J. M. Renga and I. L. Reich, *J. Am. Chem. Soc.*, 1975, **97**, 5434.
- 18 (a) A. C. Cope and E. C. Hermann, *J. Am. Chem. Soc.*, 1950, **72**, 3405; (b) N. S. Gill, K. B. James, F. Lions and K. T. Potts, *J. Am. Chem. Soc.*, 1952, **74**, 4923.
- 19 K. Schwetlick, J. Jentzsch, R. Kart and D. Wolter, *J. Prakt. Chem.*, 1964, **25**, 95.
- 20 I. Fleming and M. H. Karger, *J. Chem. Soc. C*, 1967, 226.

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