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Immobilisation of ketone catalyst: a method to prevent ketone catalyst from decomposing during dioxirane-mediated epoxidation of alkenes

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Covalent attachment of trifluoromethyl ketone catalyst to a solid support such as silica gel increased the stability of catalyst dramatically, so solving an intrinsic problem of dioxirane-mediated epoxidation of alkenes catalysed by ketones.

Dioxiranes have been shown to be powerful and environmentally safe oxidants, which can be generated *in situ* from ketones and Oxone® ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$).[1] In principle, only a catalytic amount of ketone is required and, moreover, with a chiral ketone there exists the opportunity for catalytic asymmetric epoxidation.[2] However, an intrinsic problem of this catalytic epoxidation procedure is that the turnover number (TON) of ketone catalysts is generally very low owing to their instability under the epoxidation conditions. It has been generally known that ketone catalysts can be destroyed *via* Baeyer–Villiger oxidation and/or formation of 1,2,4,5-tetroxane *etc*.[1]

We proposed that the decomposition of ketone catalysts in the dioxirane-mediated epoxidation of alkenes could be prevented by covalent attachment of ketone catalysts to a suitable solid support,[3] since, as shown in Fig. 1, site isolation of catalytic centres can minimise the possibility of 1,2,4,5-tetroxane formation, and, moreover, the migration of a solid-bound alkyl chain in the Baeyer–Villiger oxidation step may need larger movement energy than that of the homogeneous analogue. Of course, this approach can provide an additional advantage of easy recycling of catalyst.

To test our rationale, we prepared a new silica-bound trifluoromethyl ketone **1** and compared its stability in the dioxirane-mediated epoxidation of alkenes with its homogeneous analogue, 1,1,1-trifluorododecan-2-one **2**. Here we report our preliminary results.

The silica-bound trifluoromethyl ketone **1** was simply prepared by the reaction of 1,1,1-trifluorodode-11-cen-2-one **3**[4] with 3-mercaptopropylsilanised silica gel **4**[5] in the presence of α,α'-azoisobutyronitrile (AIBN) as a radical initiator in acetonitrile (Scheme 1).[6] The fluorine and sulfur analyses of **1** (F, 2.61%; S, 2.90%) indicated that 0.45 mmol g^{-1} of trifluoromethyl ketone moiety was incorporated and the coupling yield of **3** with **4** was 50%. Thus, 0.45 mmol g^{-1} of unreacted thiol groups exist in the silica-bound trifluoromethyl ketone **1**. The attachment of trifluoromethyl ketone moieties to silica gel in the silica-bound ketone **1** was also confirmed *via* IR spectroscopy (1766 cm^{-1} for $\nu_{C=O}$).

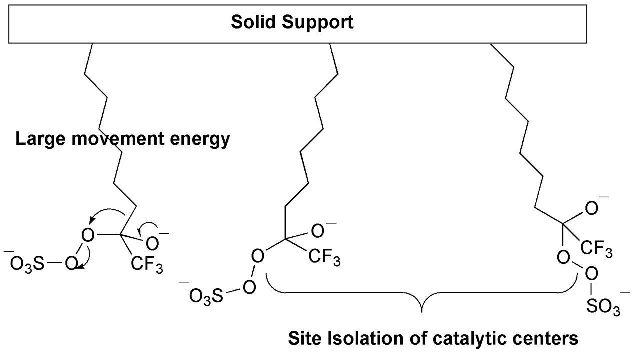
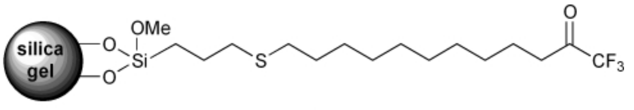


Fig. 1



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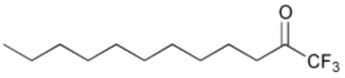
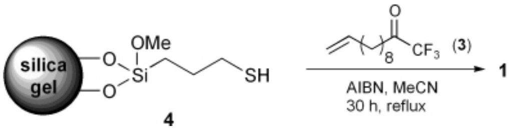


2

In order to compare the catalytic efficiency and stability of silica-bound ketone **1** with its homogeneous analogue **2**, the epoxidation of alkenes were carried out with Oxone® in a MeCN–H_2O solvent system under the modified condition employed by Shi and co-workers.[7] The results are summarised in Table 1.

As shown in Table 1, the silica-bound ketone **1** exhibited comparable catalytic activity with that of its homogeneous analogue **2**. In a ratio of ketone : olefin of 0.5 : 1 at room temperature, epoxidation of alkenes using 2.07 equiv. of Oxone® and 8.7 equiv. of K_2CO_3 was complete within 5 min after addition of Oxone® and K_2CO_3, and afforded the corresponding epoxides in very high yield.[8] Most of the oxidised products were obtained in nearly pure form by simple filtration of the ketone **1**, followed by extraction of organic product and evaporation of the solvent. The observed results suggest that trifluoromethyl ketone moiety on silica gel remains highly exposed to the reactants and thus substrates can access to the catalytic sites easily.

The silica gel supported trifluoromethyl ketone **1** could be easily recovered after reaction by simple filtration and the recovered ketone **1** was reused several times without any significant loss of activity. All epoxidations of *trans*-β-methylstyrene using the recycled ketone **1** afforded *trans*-β-methylstyrene oxide in nearly quantitative yield, even after tenth use.[9] As we proposed, the retainment of the catalytic activity during several cycles can be explained by that the decomposition of the supported ketone catalyst **1** *via* Baeyer–Villiger oxidation and/or 1,2,4,5-tetroxane formation[10] proceeds much more slowly than that of its homogeneous analogue **2**. We could not find any carbonyl peak of the Baeyer–Villiger oxidation product (ester) in the IR spectrum of **1** recovered after



Scheme 1

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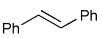
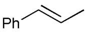
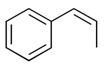
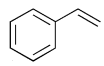
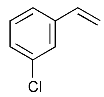
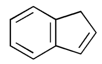
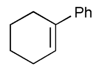
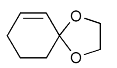
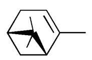
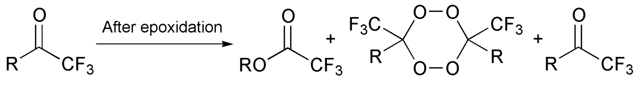
Table 1 Epoxidations of alkenes with Oxone® catalysed by silica-bound ketone **1** or its homogeneous analogue **2**[a]

Entry	Alkene	Yield (%)[b] Using catalyst **1**	Yield (%)[b] Using catalyst **2**
1		94	93
2		>98	>98
3		>98	>98
4		>98	>98
5		>98	>98
6		>98	>98
7		>98	>98
8		71	67
9		>98[c]	>98[d]

[a] The reaction conditions were not optimised: substrate (1 equiv.), ketone catalyst (0.5 equiv.) Oxone® (2.07 equiv.) and K_2CO_3 (8.7 equiv.) in MeCN–aqueous EDTA (4×10^{-4} M) (1.5/1, v/v) at room temperature. Under such conditions, the blank reaction (the epoxidation of *trans*-β-methylstyrene only with Oxone®) gave the epoxide only up to 16% yield. [b] Yields were determined by GC and ^{1}H NMR analysis of crude products. [c] 93% of α-pinene oxide and *ca.* 5% of α-campholenic aldehyde. [d] 84% of α-pinene oxide and *ca.* 15% of α-campholenic aldehyde.



2 (R = $C_{10}H_{21}$) **5** (8%) **6** (77%) **2**

Scheme 2

10 runs. In contrast to the silica-bound catalyst **1**, *ca.* 85% of its homogeneous analogue **2** was decomposed after a first run of the epoxidation of *trans*-β-methylstyrene. The main decomposed products were ester **5** (*ca.* 8%) and 1,2,4,5-tetroxane **6** (*ca.* 77%) (Scheme 2). The structure of **6** was assigned by NMR and HRMS analyses.[11]

In conclusion, we have achieved excellent results for the heterogeneous dioxirane-mediated epoxidation of alkenes using silica gel supported trifluoromethyl ketone **1**. This silica-bound ketone was reused ten times without loss of activity. This retainment of the catalytic activity during several cycles was explained by that the decomposition of the supported ketone catalyst **1** *via* Baeyer–Villiger oxidation and/or 1,2,4,5-tetroxane formation[10] proceeds much more slowly than that of its homogeneous analogue **2**. Thus, this type of immobilisation of ketone catalysts will provide a possibility to increase their stability, which is an intrinsic problem of dioxirane-mediated epoxidation catalysed by ketones. The current study will also provide some insight for the development of new chiral ketone catalysts. In the search for efficient ketone catalysts for asymmetric epoxidation, both turnover number and enantioselectivity are crucial issues to be considered.

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Notes and references

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2 Review: S. E. Denmark and Z. Wu, *Synlett*, 1999, 847.

3 Recently, simply for the easy separation of catalyst from the reaction mixture, some polymer-bound ketones have been employed: T. R. Boehlow, P. C. Buxton, E. L. Grocock, B. A. Marples and V. L. Waddington, *Tetrahedron Lett.*, 1998, **39**, 1839; A. Shiney, P. K. Rajan and K. Sreekumar, *Polym. Int.*, 1996, **41**, 377.

4 1,1,1-Trifluorododec-11-en-2-one **3** was synthesised by the published procedure: J. Biovin, L. E. Kaim and S. Z. Zard, *Tetrahedron*, 1995, **51**, 2573.

5 3-Mercaptopropylsilanised silica gel **4** (1.14 mmol of S g^{-1}) was prepared by the reaction of Silica gel 60 (70–230 mesh, Merck) and (3-mercaptopropyl)trimethoxysilane according to the published procedure: C. Rosini, C. Bertucci, D. Pini, P. Altemura and P. Salvadori, *Tetrahedron Lett.*, 1985, **26**, 3361; C. Rosini, P. Altemura, D. Pini, C. Bertucci, G. Zullino and P. Salvadori, *J. Chromatogr.*, 1985, **348**, 79; P. Savadori, C. Rosini, D. Pini, C. Bertucci, P. Altemura, G. Uccello-Barretta and A. Raffaelli, *Tetrahedron*, 1987, **43**, 4969.

6 Some of chiral catalysts have been anchored on silica by same methodology: C. E. Song, J. W. Yang and H.-J. Ha, *Tetrahedron: Asymmetry*, 1997, **8**, 841; D. Pini, A. Mandoli, S. Orlandi and P. Salvadori, *Tetrahedron: Asymmetry*, 1999, **10**, 3883.

7 Z.-X. Wang, Y. Tu, M. Frohn and Y. Shi, *J. Org. Chem.*, 1997, **62**, 2328.

8 The epoxidation of *trans*-stilbene in a MeCN–H_2O solvent system under the same reaction conditions[7] reported by Shi (1.38 equiv. of Oxone®, 5.8 equiv. of K_2CO_3 and 0.5 equiv. of ketone) afforded the corresponding epoxide in *ca.* 76% yield. However, the yield was dramatically increased only by increasing the amount used of Oxone® and K_2CO_3. In a 0.5 : 1 ketone : olefin ratio at room temperature, epoxidation of *trans*-stilbene proceeded completely within 5 min after addition of 2.07 equiv. of Oxone® and 8.7 equiv. of K_2CO_3 and afforded the corresponding epoxide in nearly quantitative yield (Table 1).

9 There was some loss of ketone **1** owing to its slight solubility in the reaction medium and thus, in a each run, the amounts of substrate were used based on the amounts of the recovered ketone **1**.

10 However, our site isolation hypothesis is not very convincing yet since the loading of the ketone catalyst on the silica gel is so high that the interaction between immobilised molecules can not be excluded.

11 *Selected physical data* of **6**: ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 123.24 (q, *J* 285.2 Hz), 94.69 (q, *J* 31.5 Hz), 72.09, 36.09, 32.15, 30.43, 29.64, 26.80, 25.57, 22.98, 18.18, 14.43; FAB-HRMS (M^+ + Na). Calc. for $C_{24}H_{42}O_4F_6Na$: *m/z* 531.2885. Found: 531.2886.