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Fluorous osmium tetraoxide ($^FOsO_4$): a recoverable and reusable catalyst for dihydroxylation of olefins

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Abstract—A fluorous osmium catalyst was firstly developed. It had been effectively used as recoverable and reusable catalyst in the dihydroxylation of olefins.

Osmium tetraoxide (OsO_4) is the most reliable reagent available for the production of *cis*-diols from olefins.[1] Although these reactions have been widely used in the synthesis of pharmaceuticals, fine chemicals, etc., there are few large-scale industrial applications due to the high cost of osmium as well as the high toxicity and volatility of the osmium component.[2] Therefore, catalysts that could be readily separated from the reaction mixture and used are the challenging in the osmium community. A few attempts to address this issue have been made by several groups, achieving varying levels of success. Among these, various strategies to immobilize the osmium tetraoxide on soluble and insoluble supports have been applied.[3]

'Fluorous biphase catalysis (FBC)',[4] a new catalytic procedure, has been developed by Horváth and Rábai in 1994. Since then, this new protocol has been advanced rapidly and a mass of fluorous catalysts[5] and ligands[6] (especially phosphines) are known. FBC is particularly suited for economical and green chemical processes due to the reusable and recoverable of fluorous catalyst and ligands. However, there are hitherto few reports about the application of fluorous catalyst containing toxic metals.[7] Curran and co-workers have developed several fluorous tin reagents[8] with similar reactivity to that of the parent organic reagents. In this letter, we attempted to apply FBC on the toxic, volatile, and expensive catalyst of osmium tetraoxide.

Recently, Jacobs and co-workers have developed a new approach to immobilize the osmium catalyst onto a silica anchored tetrasubstituted olefin by the formation of stable Os-diolate esters.[3e,f] The basic idea[3f] was that these tertiary diolate esters were not hydrolyzed during the reaction, keeping the catalyst immobilized by the support, if the reaction conditions were not too drastic. The *cis*-dihydroxylation reaction could then take place at the remaining free binding sites of the Os center. According to Jacobs' approach, we envisaged to use the fluorous tetramethylethene **1**[9] to anchor the OsO_4 and make it suitable for fluorous biphase catalysis (FBC). An ideal catalytic recycle was proposed in Scheme 1. The added fluorous tetramethylethene **1** was reacted with OsO_4 to form the Os^{VI} monodiolate complex **2**, which could be reoxidized to *cis*-dioxo Os^{VIII} **3** without the release of the diol. The catalytic reaction could then take place at the free coordination sites of Os in **3**.

The fluorous osmium catalyst was prepared in the following procedure: OsO_4 crystal (127 mg, 0.5 mmol) or in 4 wt % of aqueous solution (3.2 mL) was added in FC-77 (perfluoroalkane primarily with eight carbons) (4 mL) at room temperature, and then a solution of fluorous tetramethylethene **1** (576 mg, 0.5 mmol) in FC-77 (8 mL) was added dropwise. After the addition, the reaction mixture was stirred for another 18 h at room temperature. During the reaction, the solution turned black indicating that OsO_4 has been reduced to lower valence osmate complex. The reaction mixture was thoroughly

Keywords: Fluorous synthesis; Dihydroxylation; Osmium tetraoxide.

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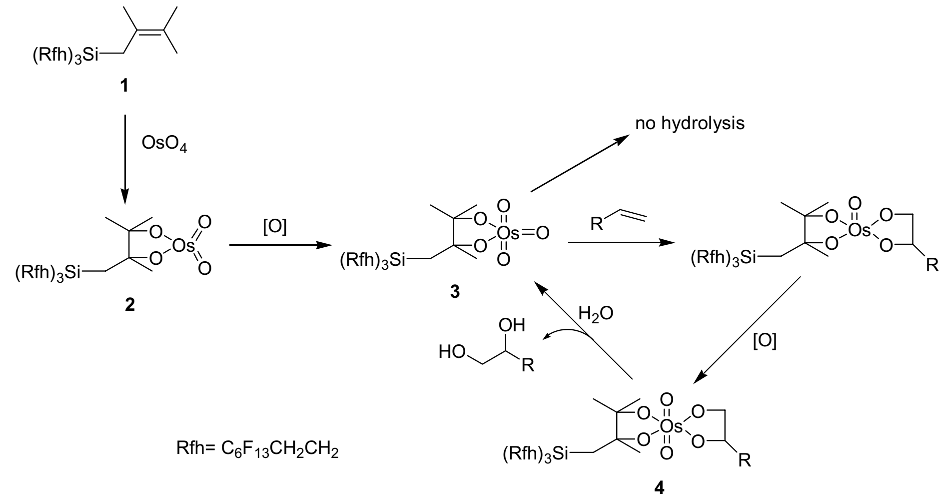


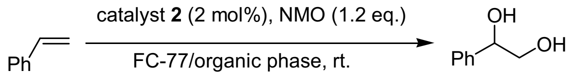
Scheme 1. A plausible reaction pathway of the fluorous osmium catalytic dihydroxylation of olefins.

washed twice with *t*-BuOH/CH_2Cl_2 (v/v = 2:1, 3 mL) to remove trace of unbound OsO_4. Thus, the catalyst **2** in FC-77 solution (calcd Os: 0.042 M in FC-77) was ready for use.

The performance of the fluorous osmium catalyst ($^FOsO_4$) in FBC was investigated using styrene as a test substrate (Table 1). Initially, the reaction was carried out under the standard Upjohn conditions[10] (Table 1, entry 1), using 2 mol% of the $^FOsO_4$ **2** in a biphasic solvent system: *t*-BuOH/H_2O (v/v = 2:1, 3 mL) as organic phase and FC-77 (2 mL) as fluorous phase with *N*-methylmorpholine-*N*-oxide (1.2 equiv) as the secondary oxidizing agent. After stirring 36 h at room temperature, the upper organic phase was removed by a syringe and purified using standard method to afford the pure diol product in a quantitative yield (Table 1, entry 1, run 1). A new batch of olefin and co-oxidant dissolved in organic solvent was added to the remaining FC-77 solution to carry out the second run of the dihydroxylation. It was gratifying that the diol was isolated in 94% yield (Table 1, entry 1, run 2), indicating that the fluorous catalyst was effective and reusable. However, further runs with the remaining FC-77 solution resulted in a dramatic decrease in the yield of the diol. The $^FOsO_4$ catalyst leached significantly. The loss of the catalyst may be attributed to two factors. Firstly, the fluorous osmium monodiolate underwent some hydrolysis to release the osmium during the reaction; secondly, the $^FOsO_4$ went into the organic phase during the separation. In order to minimize the influence of these two factors, the organic solvents used were varied. An addition, the partition of $^FOsO_4$ between organic phase and fluorous phase would be more favored at a lower temperature of separation (from room temperature to 10 or 0 °C). As shown in Table 1, using *t*-BuOH/CH_2Cl_2/H_2O (v/v/v = 10:5:1) and acetone/H_2O (v/v = 10:1) as the organic phase, the results were similar to those using *t*-BuOH/H_2O (v/v = 2:1). The isolated yields of products were also decreased significantly in the third run. Fortunately, when the mixture of *t*-BuOH/acetone/H_2O (v/v/v = 10:5:1) was used as the organic phase, the diol could be isolated in 80% yield even in the fifth run.

Representative results of the $^FOsO_4$-catalyzed dihydroxylation reaction of a range of olefins are summarized in Table 2.[11] Cyclic and acyclic, *exo* and internal olefins including mono-, di-, and trisubstituted aliphatic as well as aromatic underwent the dihydroxylation smoothly at room temperature in the fluorous biphase catalytic system, giving moderate to excellent yields of products over five consecutive runs. In the case of a sterically hindered substrate (entry 3), a moderately elevated temperature was required to afford the product in an excellent yield.

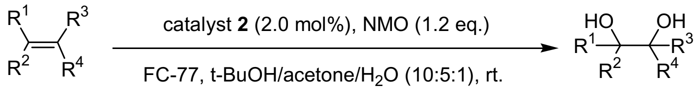
Table 1. Dihydroxylation of styrene using the fluorous osmium catalyst ($^FOsO_4$) in fluorous biphase system[a]

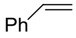
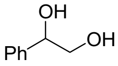
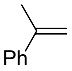
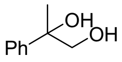
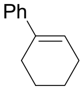
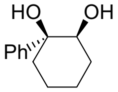
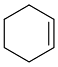
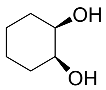
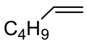
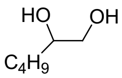
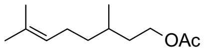
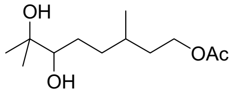
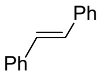
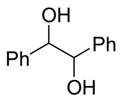


Entry	Organic phase	Yield (%)[b]				
		Run 1	Run 2	Run 3	Run 4	Run 5
1	*t*-BuOH/H_2O (2:1)	100	94	79	55	45
2	*t*-BuOH/CH_2Cl_2/H_2O (10:5:1)	100	98	62	74	52
3	Acetone/H_2O (10:1)	98	92	87	53	53
4	*t*-BuOH/acetone/H_2O (10:5:1)	97	100	95	97	80

[a] All reactions were carried out using $^FOsO_4$ (2 mol%) and NMO in FC-77 (2 mL)/organic solvent (3 mL) at room temperature for 36 h.
[b] Isolated yield.

Table 2. *cis*-Dihydroxylation of olefins using the reusable and recyclable catalyst[a]



Entry	Olefin	Diol	Yield (%)[b]				
			Run 1	Run 2	Run 3	Run 4	Run 5
1			97	100	95	97	80
2			100	99	94	100	99
3[c]			98	96	95	99	94
4			99	100	83	77	73
5			97	95	94	93	81
6			97	89	95	91	90
7			96	92	71	58	72[d]

[a] All reaction were carried out using $^F OsO_4$ (2 mol%) and NMO in FC-77 (2 mL)/organic solvent (3 mL) at room temperature for 36 h.

[b] Isolated yield.

[c] The reaction was run using t-BuOH/H_2O as organic phase at 60 °C.

[d] The reaction time was prolonged to 48 h.

It should be pointed out that prolonged reaction time in the fifth run resulted in an improved yield (entry 7, runs 4 and 5).

In summary, we have successfully developed a fluorous osmium catalyst according to the Jacobs' approach. This was the first application of FBC with the toxic, volatile, and expensive catalyst of OsO_4. The strategy exerted the advantages of fluorous biphasic catalysis and was demonstrated to be effective and easy to handle. Further optimization of the recyclability of the $^F OsO_4$ is now in progress in our laboratory.

Acknowledgements

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9. Fluorous tetramethylethene **1** was prepared as follow: Bromo-tris-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silane (14 mmol) was added at 0 °C to a freshly prepared 2,3-dimethyl-2-butenylmagnesium bromide (50 mmol) formed from 1-bromo-2,3-dimethylbut-2-ene with magnesium in THF at 0 °C. The reaction mixture was stirred at 0 °C for 4 h, and then was warmed to room temperature and stirred for another 10 h. The reaction mixture was quenched with aqueous NH$_4$Cl. The aqueous phase was further extracted with ether, and the combined organic layer was dried over MgSO$_4$, filtered, and concentrated in vacuo. The crude product was purified by repeated extraction with FC-77/CH$_2$Cl$_2$ to afford the desired product as colorless oil (15.2 g, 94%). ^{1}H NMR δ: 1.95–2.13 (m, 6H), 1.69 (s, 3H), 1.66 (s, 3H), 1.63 (s, 3H), 1.58 (s, 2H), 0.86–0.92 (m, 6H); ^{19}F NMR δ: -81.33 (t, $J = 11.3$ Hz, 9F), -116.81 (t, $J = 15.2$ Hz, 6F), -122.45 (s, 6F), -123.43 (s, 6F), -123.89 (s, 6F), -126.68 (s, 6F); MS (EI, 70 eV, *m/z*): 1152 (M^{+}, 1), 497 (1), 289 (8), 83 (100); IR (thin film): 2929, 1443, 1362, 1240, 1209, 1145, 1070, 904 cm^{-1}; Anal. Calcd for C$_{30}$H$_{23}$F$_{39}$Si: C, 31.26; H, 2.01. Found: C, 31.52; H, 2.27.
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11. General procedure for the dihydroxylation of olefin using ^{F}OsO$_4$: ^{F}OsO$_4$ solution (0.5 mL, 0.042 M in FC-77, 2 mol %) was added to a solution of olefin (1 mmol) and *N*-methylmorpholine-*N*-oxide (NMO) (1.2 mmol) in *t*-BuOH/acetone/H$_2$O (10:5:1) (3 mL) and FC-77 (2 mL), the reaction mixture was stirred for 24–36 h at room temperature and the extent was monitored by thin layer chromatography. The reaction mixture was cooled to 20 °C and the upper organic phase was removed by a syringe and purified by flash column chromatography on silica (EtOAc/hexane 4:1). A new batch olefin and NMO dissolved in organic solvents was then added to the remaining fluorous solution in successive runs. All the products in Table 2 were known compounds. The identity and purity of these diols were secured by ^{1}H NMR and MS data.