

Highly chemoselective, oxyvanadium-catalysed cleavage of α -hydroxy ketones

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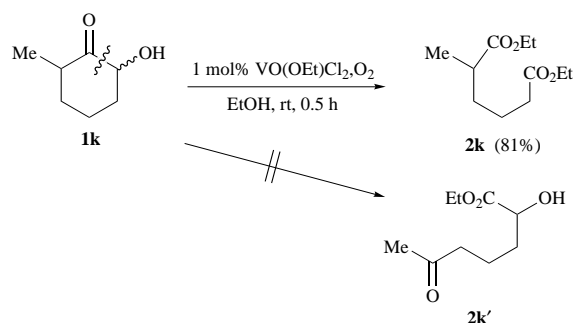
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α -Hydroxy ketones (α -ketols) can be cleaved chemoselectively with a catalytic amount of dichloroethoxyoxyvanadium under an oxygen atmosphere.

The oxidative cleavage of a carbon–carbon bond in α -hydroxy ketones is one of the most important processes in organic synthesis, and several kinds of oxidants are used for this purpose.^{1–6} The most versatile reagents are periodic acid (and its salts),² calcium hypochlorite³ and lead tetraacetate.⁴ Although these reagents cause bond fission effectively in α -hydroxy ketones, a stoichiometric amount of the reagent is required in all cases.

We now report that α -hydroxy ketones can be cleaved efficiently with a catalytic amount of dichloroethoxyoxyvanadium [VO(OEt)Cl₂][†] under an oxygen atmosphere in ethanol. The results are summarised in Table 1.

The oxidation of ketones bearing a secondary α -hydroxy group (**1b–h**) gave diesters (**2b–h**) (entries 2–4), while those with a tertiary hydroxy group (**1i,j**) resulted in the formation of keto esters (**2i,j**) (entries 5 and 6) in moderate to high yields. With **1i,j** other reagents (lead tetraacetate, sodium periodate or calcium hypochlorite) gave the products **2** in poor yields. Although a similar reaction of 2-methylcyclohexanone has been reported to afford ethyl 6-oxoheptanoate,⁷ in the present case reaction of 2-hydroxy-6-methylcyclohexanone **1k** resulted in the regioselective bond-cleavage of C(1)–C(2) (α -cleavage) with complete regioselectivity (Scheme 1).[‡] The high chemoselectivity was



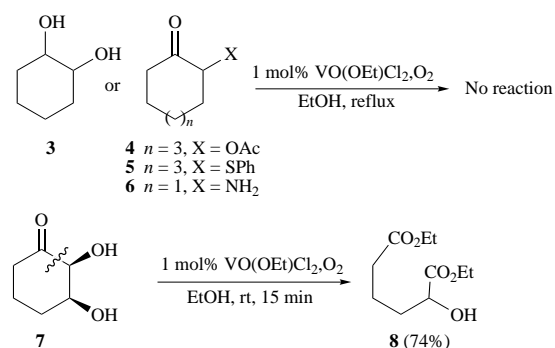
Scheme 1

evidenced by the fact that α -acetoxy- (**4**), α -phenylthio- (**5**) and α -amino-cyclohexanone (**6**) or *cis*- and *trans*-cyclohexane-1,2-diol (**3**) were found to be inert under the conditions examined, and was evidently illustrated by the reaction of an α,β -dihydroxy ketone **7** where only α -cleavage was found to participate (Scheme 2).[§] These results are in contrast to those with other oxidants which cleave both α -hydroxy ketones and 1,2-diols.^{2–6}

[†] Dichloroethoxyoxyvanadium was prepared by a known procedure: see ref. 7.

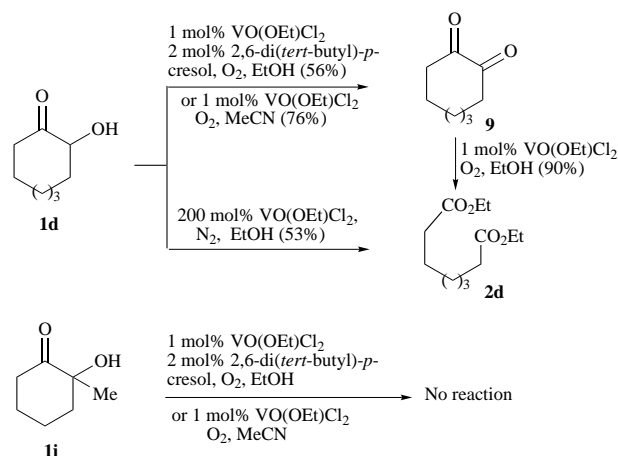
[‡] Diethyl 2-methylhexanedioate **2k** was the only product isolated. Ethyl 2-hydroxy-6-oxoheptanoate **2k'** was not obtained.

[§] The sole product isolated was the hydroxy diester **8**.



Scheme 2

In the presence of a radical inhibitor [2,6-di(*tert*-butyl)-*p*-cresol], the reaction of ketone **1d**, bearing a secondary α -hydroxy group, did not give a diester but the 1,2-diketone **9**. The same result was obtained when acetonitrile was used as solvent instead of ethanol. The 1,2-diketone **9** was cleaved efficiently with VO(OEt)Cl₂ under an oxygen atmosphere. A ketone with a tertiary α -hydroxy group, **1i**, was inert under these reaction conditions. Although the reaction mechanism is unknown, these results suggest that this reaction involves radical intermediates and that ethanol is essential to the cleavage. Molecular oxygen acts as the co-oxidant and reoxidises the low valent vanadium compound formed, thus a stoichiometric amount, or more, of VO(OEt)Cl₂ reacted with **1d** in the absence of oxygen to give **2d** (Scheme 3). The result is in sharp contrast to that



Scheme 3

seen in the reaction of 2-alkylcyclohexanone with VO(OEt)Cl₂, where only a trace amount of the product is obtained in the absence of oxygen.⁷

Further details of the reaction mechanisms are currently under investigation.

Table 1

Entry	Starting material	Conditions	Product	Yield (%)
1		rt, 0.25 h		74
2		rt, 0.5 h		2b n = 1: 55 2c n = 2: 71 2d n = 3: 83 2e n = 7: 87 2f n = 10: 70
3		rt, 1 h		81
4		reflux, 48 h		55
5		reflux, 25 h		64
6		reflux, 48 h		73

All compounds were identified by comparison of their spectral data with those for authentic samples.

Experimental

General procedure for the cleavage of α -hydroxy ketones

A mixture consisting of α -hydroxy ketones (0.4 mmol), VO(OEt)Cl₂ (0.004 mmol) and ethanol (4 ml) was stirred at room temperature (or refluxed) under an oxygen atmosphere for 0.25–48 h. The mixture was quenched with saturated aqueous sodium hydrogen carbonate and extracted with 3 × 20 ml of diethyl ether. The combined organic extracts were washed with brine, dried over magnesium sulfate, and evaporated to afford the crude product. Chromatography on silica gel gave a pure sample.

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