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THE REACTION OF CHROMYL CHLORIDE AND O-SILYLATED ENOLATES: A NOVEL REGIOSPECIFIC ROUTE TO α-HYDROXY KETONES[1].

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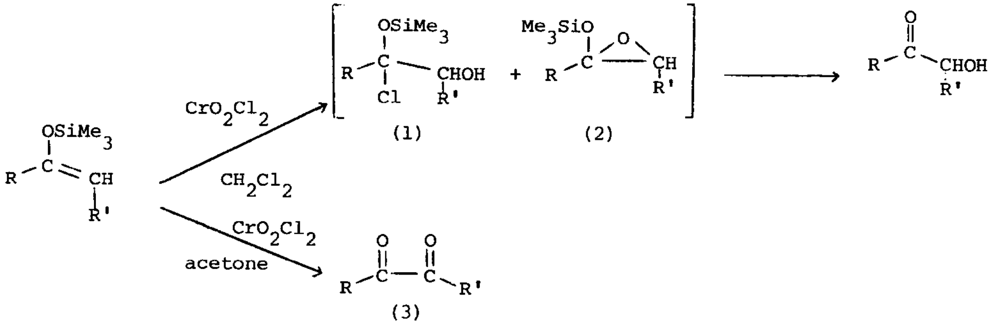
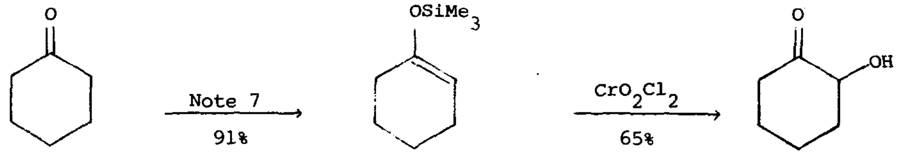
Summary: Chromyl chloride reacts regiospecifically with O-silylated enolates to form α-hydroxy ketones.

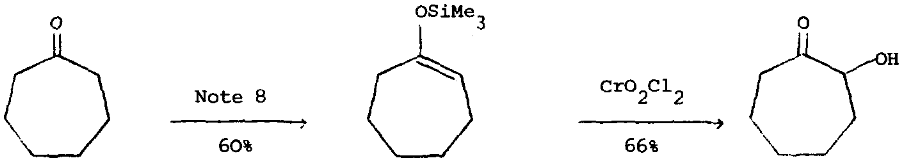
A number of oxo-metal complexes enjoy widespread use in organic synthesis due to their ability to selectively oxidise certain organic substrates[2]. Amongst this number is chromyl chloride which has been shown to add to alkenes at low temperatures to form a mixture of epoxides and chlorohydrins[3].

This stimulated us to investigate the reaction of O-silylated enolates[4] with chromyl chloride in an attempt to extend this reaction to oxygenated alkenes.



Two possible modes of reaction, for the addition of chromyl chloride to O-silylated enolates, would seem to exist. Reaction in methylene chloride would be expected to result in formation of α-hydroxy ketones, via the intermediate chlorohydrin (1) and/or epoxide (2). In contrast, using acetone as solvent may result in formation of α-diketones (3), by analogy to the





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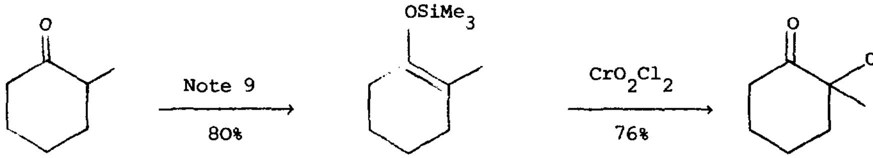
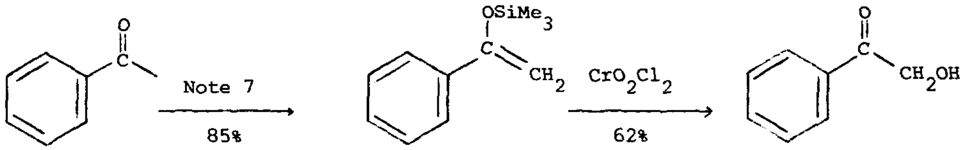
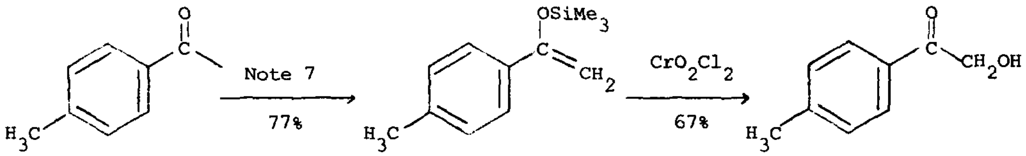
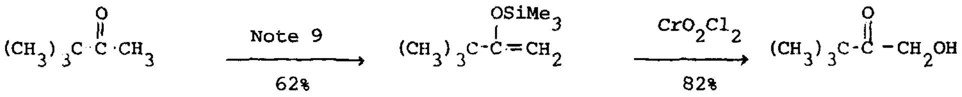


(5)





(6)



$$(CH_3)_3C\cdot\overset{O}{\overset{\|}{C}}\cdot CH_3 \xrightarrow[62\%]{\text{Note 9}} (CH_3)_3C\text{-}\overset{OSiMe_3}{\overset{|}{C}}=CH_2 \xrightarrow[82\%]{CrO_2Cl_2} (CH_3)_3C\text{-}\overset{O}{\overset{\|}{C}}-CH_2OH$$

work of Sharpless[5].

We now report some preliminary observations which show that chromyl chloride does add, under mild conditions (-78°C in CH_2Cl_2), to the double bond of O-silylated enolates to form α-hydroxy ketones, in moderate yields. The reactions studied did not produce, under the conditions used, any isolable products arising from further oxidation, as may have been expected. However, unless low temperat ures are used the product is contaminated with some of the starting ketone, derived, presumably, from decomposition of the O-silylated enolate.

In these reactions we have not observed the formation of any α-chloro ketones, due to direct dichlorination, but have still to completely exclude this possibility[6].

The reaction proceeds with various O-silylated enolates including (5) which shows that the method is regiospecific[11]. In addition, the O-silylated enolate (6), which posseses a methyl group bonded to an aromatic ring, undergoes a smooth chemoselective reaction with no oxidation of the methyl group in an Etard type of reaction[12]. This is presumably a reflection of the greater reactivity of the oxygen substituted alkene and the fact that Etard type of reactions normally proceed at higher temperatures[12].

The method provides an alternative to the use of peracids[13] or osmium tetroxide/ N-methylmorpholine-N-oxide[14] for the conversion of O-silylated enolates to α-hydroxy ketones. The use of acetone as solvent[5] resulted in the formation of α-hydroxy ketones and the starting ketone only. However, we are still studying this type of transformation and will report our results shortly.

In a typical procedure, chromyl chloride (0.54g; 3.53mmoles) in dry dichloromethane (5 ml) was added to a stirred solution of the O-silylated enolate (0.5g; 2.71mmoles) in dry dichloromethane (5 ml) at -78°C under nitrogen. After 30 mins at -78° the dark red-brown mixture was added to a cold aqueous solution of $NaHSO_3$ and stirred for 15 mins. The green solution was neutralized with $NaHCO_3$ solution, filtered, extracted with dichloromethane and the organic lay- was dried (Na_2SO_4). Column chromatography afforded pure α-hydroxy ketone[15].

NOTES AND REFERENCES

1 This work was supported by the Science and Engineering Research Council. We thank them for their assistance.

2 For example see:- *Oxidation in Organic Chemistry*. Part A. Wiberg. K.B.(Ed). Academic Press (1965).

3 Sharpless, K.B.,Teranishi, A.Y.,Backvall,J-E., *J.Amer.Chem.Soc.*,(1977),99,3120.

4 Fleming,I.,*Comprehensive Organic Chemistry*. Vol 3, p.584. Pergammon Press (1979).

5 Sharpless, K.B.,Teranishi, A.Y., *J.Org.Chem.*,(1973),38,185.

6 In one case, (4), we observed trace amounts of what may have been an α-chloro ketone, but this result was not reproducible.

hese O-silylated enolates were prepared by treating the ketone with 1.1 equivalent of LDA in THF at -78°C, followed by 1.1 equivalents of Me_3Sicl from -30° to room temperature, non-aquepus work-up and distillation.

8 This O-silylated enolate was prepared by treating the ketone in CH_3CN with 1.1 equivalents of Et_3N, 1.1 equivalents of Me_3SiCl and a catalytic amount of $ZnBr_2$, followed by non-aqueous work-up and distillation.

9 These O-silylated enolates were prepared: Me_3SiCl, Et_3N, DMF, reflux, with a neutral aqueous work-up and distillation[10].

10 House,H.O.,Czuba,L.J.,Gall,M.,Olmstead,H.D.,*J.Org.Chem.*,(1969),34,2324.

11 Used as a 91:9 mixture with its regioisomer. The ratio of the starting enols and of the products were determined by gc and nmr.

12 Hartford,W.H.,Darrin,M.,*Chem. Revs.*,(1958),58,1.

13 Hassner,A.,Reuss,R.H.,Pinnick,H.W.,*J.Org.Chem.*,(1975),40,3427.

14 McKormick,J.P.,Tomasik,W.,Johnson,M.W.,*Tetrahedron Letters*,(1981),22,607.

15 The products agreed in every respect with the reported values of ir, nmr, ms, and where appropriate, m.p. The products were most easily purified using flash chromatography[16].

16 Clark Still,W.,Kahn,M.,Mitra,A.,*J.Org.Chem.*,(1978),43,2923.

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