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Allylic and benzylic oxidation using cobalt(II) alkyl phosphonate modified silica

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Abstract—The allylic and benzylic oxidation of a range of substrates proceeds in good yield using catalytic quantities of cobalt(II) alkyl phosphonate modified silica and *tert*-butyl hydroperoxide.

Allylic and benzylic oxidations are important transformations utilised in the preparation of a range of intermediates and products for various chemical industries. An example of the former is the oxidation of Δ^5 steroids to their corresponding 5-en-7-one derivatives and for the latter the benzylic oxidation of resorcinol to terphthalic acid used in the production of poly(ethylene terephthalate). A variety of chromium reagents have been used for allylic oxidation. Examples include chromium trioxide coupled with a number of bases such as pyridine[1] or 3,5-dimethylpyrazole.[2] In addition a number of chromate reagents have been utilised such as pyridinium chlorochromate[3] or dichromate[4] as well as sodium chromate.[5] Invariably stoichiometric or larger quantities have to be used to complete the oxidation. As a consequence difficulties are usually encountered in working up these reactions and significant quantities of environmentally hazardous chromium residues have to be treated. Alternative oxidation technologies, preferably catalytic and heterogeneous, are needed.

A variety of mainly homogeneous and a few heterogeneous catalytic methods for liquid phase allylic and benzylic oxidation have been reported. Examples primarily involve *tert*-butyl hydroperoxide along with catalytic quantities of metal derivatives such as chromium hexacarbonyl,[6] chromium oxide,[7] 1,3-diol chromate complexes,[8] ruthenium trichloride,[9] copper salts,[10] manganese(II) complexes[11] or cobalt(II) acetate[12] all of which have been reported to effect homogeneous liquid phase benzylic and allylic oxidation. A heterogeneous cobalt(II) acetate *tert*-butyl hydroperoxide derived catalyst has recently been reported for the allylic oxidation of steroids.[12]

We recently reported[13,14] the synthesis and characterisation of the first examples of phosphonate and phosphonic acid modified silicas **1**[15] (Scheme 1). The silica ethyl and propyl phosphonate materials, EPS and PPS, prepared to date have Q:T ratios[16,18] in the range 1:1 to 10:1. In all cases we found the T components to have ca. 66% condensation and Q ca. 90%. Examples from both the ethyl and propyl phosphonate modified silica materials EPS3 and PPS2 with average formulae **2** and **3** were used in this study. Average formulae were derived as previously described.[13] Preparation of these materials **2** and **3** utilised our earlier reported general methodology.[13] We have found that these phosphonic acid modified silica materials can catalyse a wide range of acid catalysed reactions.[17]

A number of metal derivatives of these ethyl and propyl phosphonic acid modified silicas have been prepared[18] and their chemistry and structural characteristics are

1[15] $[O_2Si]_x[O_{3/2}Si(CH_2)_nPO(OR)_2]_y$
R= H, alkyl; n = 2,3; x:y = 1:1 – 10:1

2 EPS3$[(HO)_{0.24}O_{1.88}Si]_{3.2}[(EtO)_{0.79}(HO)_{0.20}O_{0.89}$
$Si(CH_2)_2PO(OH)_2]$[18]

3 PPS2$[(HO)_{0.36}(EtO)_{0.08}O_{1.78}Si]_{1.98}[(HO)_{1.29}O_{0.86}$
$Si(CH_2)_3PO(OH)_2]$

Scheme 1.

Keywords: benzylic; oxidation; steroids; cobalt; phosphonate; silica; immobilised reagents.

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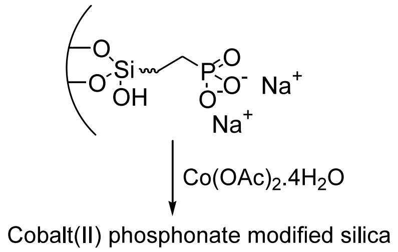
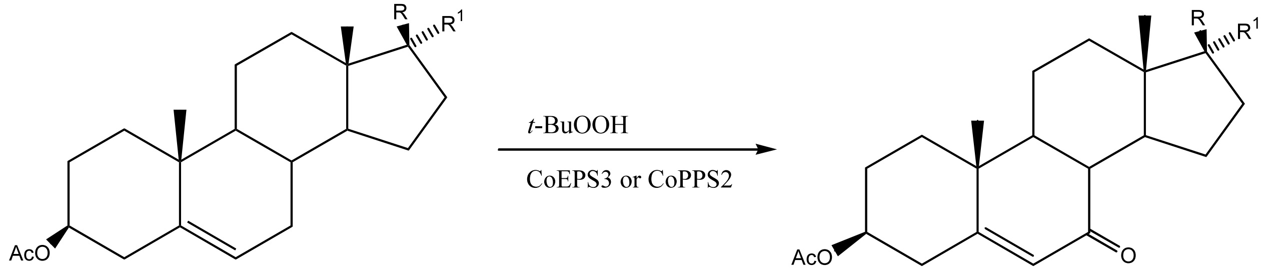


Scheme 2.

currently being investigated. We have reported[19] recently the use of cerium(IV) immobilised on similar alkyl phosphonate modified silica for the effective catalytic oxidation of a wide range of alcohols with sodium bromate as the re-oxidant. In this paper we wish to report our initial work on the catalytic allylic and benzylic oxidation of a variety of substrates utilising cobalt(II) immobilised on ethyl and propyl phosphonate modified silicas, CoEPS3 and CoPPS2 (Scheme 2).

As far as we are aware no cobalt(II) phosphonate based homogeneous or heterogeneous reagent for liquid phase catalytic allylic and benzylic oxidation has been reported. Both the CoEPS3 and CoPPS2 materials were prepared[20] by treating the corresponding disodium silica phosphonates with an aqueous solution of cobalt(II) acetate (Scheme 2). The filtered solid was washed extensively with water and then with ether and finally dried at 100°C and 0.01 torr. The cobalt(II) loading was determined by atomic absorption following treatment of the CoEPS3 and CoPPS2 materials with concentrated nitric acid to liberate the cobalt.

Given the biological importance of steroid derivatives we investigated the allylic oxidation of a number of unsaturated derivatives **4**–**7**. The results are shown in



4 $R = C_8H_{17}$; $R^1 = H$ **8**
5 $R = COCH_3$; $R^1 = H$ **9**
6 $R = H$; $R^1 = H$ **10**
7 $R = O$ $R^1 = O$ **11**

Table 1.

Substrate[a]	Product	Catalyst[b] (mmol Co)	Time (h)	Temp. (°C)	Isolated yield (%)
4[c]	**8**	CoEPS3 (0.068)	20	55	61
4[c]	**8**	CoPPS2 (0.096)	20	70	80
4[c]		0[d]	24	70	0
5	**9**	CoEPS3 (0.068)	24	50	90
5	**9**	CoEPS3[e] (0.068)	24	50	87
5	**9**	CoEPS3[e] (0.068)	24	50	87
5	**9**	CoEPS3[e] (0.068)	24	50	88
5	**9**	CoEPS3 (0.058)	24	50	94
5	**9**	CoPPS2 (0.096)	24	50	97
5	**9**	CoPPS2[e] (0.096)	24	50	95
5	**9**	CoEPS3 (0.058)	1	50	78[f]
5		0[d]	24	50	0
6	**10**	CoPPS2 (0.096)	24	50	70
6	**10**	CoEPS3 (0.058)	24	50	89
7	**11**	CoPPS2 (0.096)	48	50	86

[a] All reactions were conducted in acetonitrile on a 1 mmol scale unless otherwise indicated.

[b] Co^{2+} concentration was determined by atomic absorption after the metal ion was liberated by treatment of the CoEPS3 or CoPPS2 with concentrated nitric acid.

[c] Reaction conducted in benzene and 2 mmol of **4** was used.

[d] No CoEPS3 or CoPPS2 catalyst was used, 2 mmol of substrate and *tert*-butyl hydroperoxide in decane (12 mmol).

[e] Recycled catalyst; the catalyst was filtered, washed well with water and diethyl ether and then dried at 100°C and 0.01 torr.

[f] The standard test for catalyst leaching, was applied and no further conversion was observed in hot filtrates of the reaction mixture after a further 24 h.

Table 1. Apart from cholesterol acetate **4** where the reaction was conducted in benzene, all other reactions were performed in acetonitrile. Like the allylic oxidations using the homogeneous metal derivatives mentioned above we used an excess of *tert*-butyl hydroperoxide as the re-oxidant. In the absence of the cobalt(II) catalysts, CoEPS3 and CoPPS2, no oxidation was observed.

Oxidation of a variety of steroids **4**–**7** using either of the catalysts, CoEPS3 or CoPPS2, gave the desired 5-en-7-ones **8**–**11** in good isolated yields. A typical procedure[21] involves stirring a mixture containing the catalyst at concentrations of 3.4–9.66 mol% Co(II) and *tert*-butyl hydroperoxide as the re-oxidant in a suitable solvent at a temperature between 50 and 70°C. Although the reaction is virtually complete within a couple of hours the mixtures were routinely left to run overnight. Both catalysts, CoEPS3 and CoPPS2, can be effectively recycled as the examples with **5** demonstrate, giving similar yields of **9** within experimental error. To check for leaching, the catalyst was filtered, at the reaction temperature, from the oxidation of **5** after one hour and the filtrate was allowed to react for a further twenty four hours. No further oxidation was observed. This suggests that oxidation is occurring at the immobilised cobalt(II). Using a similar procedure these CoEPS3 and CoPPS2 catalysts can be used to oxidise a range of other olefins to their corresponding enones (Table 2). Examples of benzylic oxidation are also given in Table 2. In the examples explored to date no significant difference in reactivity between the CoEPS3 and the CoPPS2 catalysts has been noted. The optimisation of both the reaction conditions and the CoEPS and CoPPS catalyst systems is currently being investigated for both allylic and benzylic oxidations.

In conclusion we have demonstrated that cobalt(II) alkyl phosphonate modified silica can effectively catalyse the allylic and benzylic oxidation of a range of substrates in very good yield without any apparent leaching of the metal.

Acknowledgements

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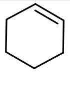
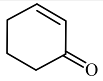
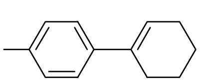
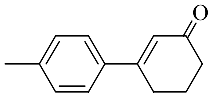
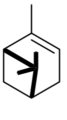
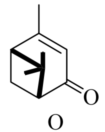
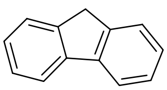
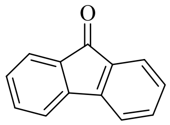
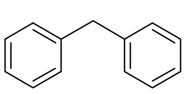
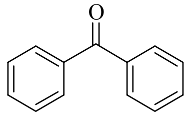
Table 2.

Substrate[a]	Product	Catalyst[b] (mmol Co)	Time (h)	Temp. (°C)	Isolated yield (%)
		CoEPS3 (0.068)	16	70	90
		CoEPS3 (0.068)	24	80	66
		CoEPS3 (0.068)	48	50	88
		CoEPS3 (0.068)	18	40	97[c]
		CoEPS3 (0.068)	24	50	91

[a] All reactions were conducted in acetonitrile at on a 1mmol scale unless otherwise indicated.

[b] Co^{2+} concentration was determined by atomic absorption after the metal ion was liberated by treatment of the CoEPS3 with concentrated nitric acid.

[c] Reaction conducted on a 2 mmol scale.

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20. *Preparation of CoEPS3*: A mixture containing EPS3[18] (1.82 g) was stirred in distilled water (15 ml) for 15 min and then sodium hydroxide (1 M, 9.5 ml) was added dropwise over 30 min. The mixture was stirred for a further 30 min and then filtered. The white solid, $\mathrm{Na_2EPS3}$, was washed well with distilled water and then with ethanol and ether and finally dried under reduced pressure (120°C and 0.01 torr for 12 h). Cobalt(II) acetate tetrahydrate (0.7 g) dissolved in distilled water (15 ml) was added to $\mathrm{Na_2EPS3}$ (1.21 g) and the resultant mixture was stirred for 1 h. The blue purple solid was filtered and washed with distilled water (1.5 L) and then with ethanol and ether and finally dried under reduced pressure, 120°C and 0.01 torr for 12 h, to afford CoEPS (1.13 g).
21. *Typical procedure*: A mixture containing the substrate (1 mmol) dissolved in acetonitrile (6 ml), cobalt(II) alkyl phosphonate silica catalyst (60 mg) and *tert*-butyl hydroperoxide (6 mmol in decane) was heated and stirred under an atmosphere of nitrogen at the temperature and period of time indicated in Tables 1 and 2. On completion the catalyst was filtered and washed well with dichloromethane. The combined filtrate was washed well with an aqueous sodium sulphite solution (10%) and then with water, dried and concentrated under reduced pressure. Purification where necessary, to remove traces of starting material, was by recrystallisation or by column chromatography.