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LETTERS

Catalytic aerobic oxidative decarboxylation of α-hydroxy-acids. Methyl mandelate as a benzoyl anion equivalent

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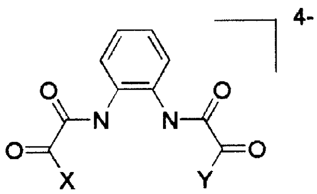
Abstract

The monomeric square-planar cobalt(III) complex of bis-*N,N'*-disubstituted oxamides catalyses the oxidative decarboxylation of α-hydroxy acids with molecular oxygen/pivalaldehyde with very good yields. This reaction offers an interesting alternative in the use of methyl mandelate as a convenient benzoyl anion equivalent.

Keywords: Oxidation; decarboxylation; cobalt; catalysis

Much attention has been recently focused on the aerobic oxidation of a great variety of organic substrates (alkenes, aldehydes, silyl enol ethers, silyl ketene acetals, ketones, lactams, and alkanes) in the presence of aldehydes, with various transition-metal complexes as catalytic systems (Mukaiyama's conditions) [1,2].

In this context we have reported [3] on the synthesis of the monomeric square-planar Co(III) complexes with bis-*N,N'*-disubstituted oxamides and related ligands, of general formula $(NMe_4)[CoL]\cdot 2H_2O\cdot CH_3CN$, where NMe_4 is the tetramethylammonium cation and L stands for *ortho*-phenylenebis(oxamate) (opba) **1**, *ortho*-phenylene(*N'*-methyloxamidate)oxamate (Meopba) **2** and *ortho*-phenylenebis(*N'*-methyloxamidate) (Me_2opba) **3**. The use of this kind of



X	Y	Ligand
O	O	opba
O	NCH_3	Meopba
NCH_3	NCH_3	Me_2opba

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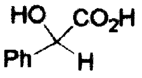
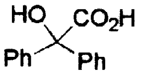
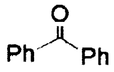
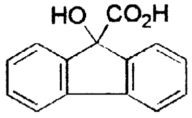
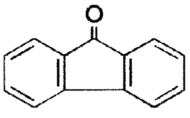
polychelating amido ligands, which have large donor capacities due to the presence of the deprotonated amido groups, allows that unusually high oxidation state complexes of later first row transition metal ions can be attained [4], which is not possible with simpler Co compounds. We have used these complexes as catalysts in the epoxidation of olefins [3] and in the oxidation of secondary alcohols to the corresponding carbonyl compounds with oxygen/pivalaldehyde (or isobutyraldehyde)[5].

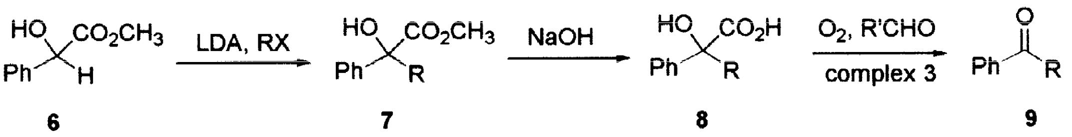
In this *Letter* we report on the oxidative decarboxylation of α-monosubstituted and α,α-disubstituted α-hydroxy acids (**4**) to give carboxylic acids or ketones (**5**) respectively in the presence of an aldehyde and catalytic amounts of complex **3**, under very mild conditions (Table 1). Although the oxidative decarboxylation of α-hydroxy acids to carbonyl compounds can be achieved with various oxidizing agents, such as lead tetraacetate [6], periodates [7], *N*-halogenosuccinimides [8], copper (II) bromide-lithium *tert*-butoxide [9] or by flash vacuum pyrolysis of its ethyl esters [10], these methods require stoichiometric amounts of oxidizing reagents or very high temperatures. The present procedure provides a very convenient method using a cheap and environmental acceptable oxidant such as molecular oxygen in the presence of an aldehyde and only a catalytic amount of a metal complex.

Table 1
Oxidative Decarboxylation of α-Hydroxyacids (4)

Entry	α-Hydroxyacid (4)	Time (h)	Reaction Product (5)	yield(%)[a]
1		6	$PhCO_2H$	98
2		18		86
3		2		98

[a] Yields refer to isolated and chromatographically pure compounds. All compounds exhibited spectral data consistent with their structures

This very easy oxidative decarboxylation of α-hydroxy acids offers an interesting alternative in the use of methyl mandelate (**6**) as a benzoyl anion equivalent, such as it has been very recently reported [10] (Scheme 1): Indeed, methyl mandelate (**6**) can be easily alkylated by using 2 equiv. of LDA and 1 equiv. of alkyl bromides or iodides to give α-alkylated mandelates **7**

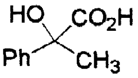
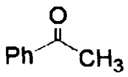
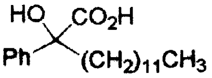
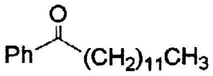
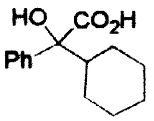
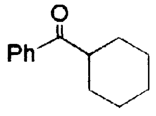
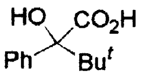
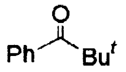
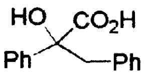
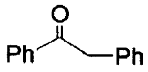
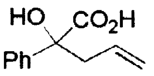
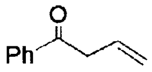
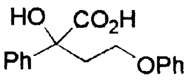
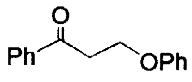
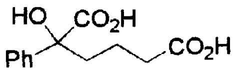
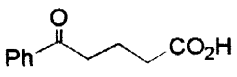


Scheme 1

which after basic hydrolysis and oxidative decarboxylation yield the corresponding carbonyl compounds. The overall process is equivalent to an alkylation of an acyl anion (umpolung).

Following alkylation procedures described in the literature [10,11] we have prepared several α-alkylated mandelic acids (**8**). These compounds were treated with oxygen/pivalaldehyde in the presence of complex **3** (see typical experimental procedure). For simple primary, secondary or even tertiary alkyl groups good yields were obtained in all cases (Table 2, Entries 1-4). Furthermore, substrates with benzyl or allyl substituents, which only gave very low or null yields by flash vacuum pyrolysis [10], underwent the oxidative decarboxylation with very good yields in our conditions (Entries 5-6). Selectivity in the presence of other oxidisable residues, i.e. a double bond [3], can be attained by lowering the temperature at 0 °C (Entry 6).[1] In a similar way,

Table 2
Oxidative Decarboxylation of α-Alkylated Mandelic Acids (**8**)

Entry	α-Alkylated Mandelic Acids (**8**)		Time (h)	Temp (°C)	Reaction Product (**9**)		yield (%)[a]
1	**a**		6	rt	**a**		87
2	**b**		2	rt	**b**		95
3	**c**		2	rt	**c**		94
4	**d**		1	rt	**d**		75
5	**e**		3	rt	**e**		93
6	**f**		6	0	**f**		90
7	**g**		4	0	**g**		96
8	**h**		3	rt	**h**		77

[a] Yields refer to isolated and chromatographically pure compounds. All compounds exhibited spectral data consistent with their structures

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[1] A hydroxyl group is compatible with the decarboxylation conditions at 0°C since the oxidation of alcohols requires room temperature and longer times. Pendent of publication.

substrate **8g** bearing a phenolic ether group gave the corresponding ketone **9g** in good yield at a temperature of 0°C (a complex mixture was obtained at rt). Finally, the presence of an additional carboxylic acid group was also compatible with our conditions and compound **8h** afforded 4-benzoylbutyric acid (**9h**) in 77% yield.

In conclusion, complex **3** catalyses the oxidative decarboxylation of α-hydroxy acids with molecular oxygen/pivalaldehyde with good yields. This reaction offers an interesting alternative in the use of methyl mandelate as a convenient benzoyl anion equivalent (umpolung), a reaction of general interest to synthetic organic chemists.

The use of ring-substituted mandelates and other α-hydroxy acids as well as the use of other electrophyle types are in progress in our laboratory.

Typical experimental procedure: A solution of α-hydroxy acid (0.11 mmol) in 0.2 mL of acetonitrile was added to a stirred mixture of catalyst (6.5 10^{-3} mmol) and pivalaldehyde (0.33 mmol) in 0.2 mL of acetonitrile under dioxygen atmosphere. The mixture was stirred at room temperature for the indicated time in tables 1 and 2, and consumption of the starting α-hydroxy acid and formation of carbonyl compounds were monitored by TLC. The reaction products were purified by flash column chromatography on silica gel.

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