Aerobic Oxidation of Cyclopentane-1,2-diols to Cyclopentane-1,2-diones on Pt/C Catalyst

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Abstract: A new method for the aerobic oxidation of cyclopentane-1,2-diols to corresponding 1,2-diones using heterogeneous Pt/C catalyst in the presence of LiOH is described. Different functional groups tolerate the oxidation conditions. Yields of 1,2-diones up to 76% were achieved.

Key words: diols, ketones, heterogeneous catalysis, oxidation, platinum

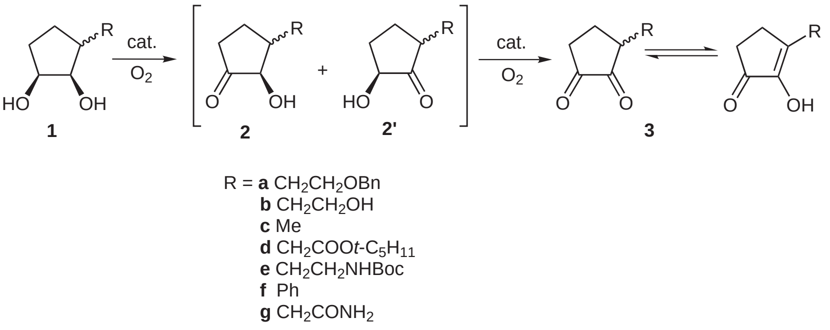
Catalytic dehydrogenation is a common method for the oxidation of alcohols to ketones. The use of atmospheric air oxygen as an oxidant is preferred due to its ‘green’ nature. The first reports on the platinum-metal-catalyzed aerobic oxidations of alcohols date back to the seventies.[1] Since then a variety of such oxidation methods have been developed for the conversion of allylic and benzylic alcohols, as well as of nonactivated primary and secondary aliphatic alcohols, into carbonyl compounds. Both, the homogeneous catalysis using metal complexes in organic solvents[2] or in water[3] and the heterogeneous catalysis using easily recoverable traditional catalysts[4] or metal nanoparticles[5] are used. Oxidation has been carried out in different solvents: common organic solvents,[5a,6] water,[4a,5b] and supercritical carbon dioxide.[7]

There are only a few methods for oxidizing diols to diones[6b,8] and no methods for the catalytic aerobic oxidation of cyclopentane-1,2-diols to the corresponding 1,2-diketones available in literature. Cyclopentane-1,2-diones were of interest to us as substrates for the asymmetric domino oxidation, leading to tertiary hydroxyketones and lactone acids,[9] which are useful as the building blocks for natural compounds.[10]

In the present paper we reveal our results on a new method of aerobic oxidation of vicinal cyclopentane diols to 1,2-diketones using a heterogeneous Pt/C catalyst (Scheme 1).

We have found that aerobic oxidation on a commercially available Pt/C catalyst[11] at 60 °C converts *cis*-1,2-diols **1** into the corresponding 1,2-diones **3**. In our preliminary experiments toluene was used as a solvent for hydrophobic substrates, water for hydrophilic substrates, and a mixture of MeCN and H_2O as a universal medium for both types of substrates. In these cases some amount of hydroxyketone **2** was also isolated, indicating that the oxidation occurred in the succession: diol – hydroxyketone – dione. In the case of **1a** intermediate hydroxy ketone **2a** was isolated and identified by NMR. Presence of a minor amount of the regioisomeric hydroxy ketone **2a′** was also observed in the spectrum.

The process is strongly dependent on the amount of oxygen available to the reaction medium. We established that the amount of oxygen that was present in the solvent and in the catalyst converts approximately 30% of the substrate into the product. Therefore, additional oxygen is needed to complete the process. On the other hand, unrestricted access of air to the reaction system lowers the yield of the product, presumably by overoxidizing the



Scheme 1

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product to carboxylic acids.[8b] Thus, better results were obtained when the reactor was periodically flushed with fresh air (in ca. 4 h intervals) during 16–20 hours. Using this procedure with 10 mol% of Pt/C catalyst, the oxidation of diol **1a** resulted in 76% of dione **3a** in toluene and 66% in acetonitrile–water mixture (1:1), the oxidation of diol **1c** resulted in dione **3c** in 67% in water. It should be noted that solubility of oxygen in these media is different (8.7 mM in toluene and 8.1 mM in acetonitrile compared to 1.3 mM in water at 20 °C[12]). We may suggest that the amount of oxygen in water-containing solvents is not sufficient for the reaction that slightly reduces the yield.

There is a slight difference in the reactivity of *all-cis* and *cis*-diol-*trans*-alkyl compounds. In the case of **1d** we observed that *cis*-diol-*trans*-alkyl compounds react slower.

Inorganic base additives to the oxidation system have been recommended by Bäckvall for heterogeneous catalytic dehydrogenations[13] and Mueller et al. for aerobic oxidations.[14] In our case the addition of alkali significantly influenced the process by considerably increasing the reaction rate. This enabled us to reduce the amount of catalyst to 5 mol%. It is noteworthy that in the presence of base hydroxyketone **2** was no longer detected among the reaction products. Thus, in acetonitrile–water without alkali, the yields of **2a** and **3a** were 16% and 60%, respectively, within 16 hours, while in the presence of one equivalent of alkali the only reaction product was **3a** in 70% yield within four hours. We may suggest that in the presence of alkali the conversion of **2** into **3** is faster than the conversion of **1** into **2**. In the presence of base the process was also less sensitive to the oxygen concentration. A part of this effect can probably be caused by the complex nature of the oxidation process, as discussed by Steinoff and Stahl.[12b] By adding LiOH we achieved a stable process in acetonitrile–water when access of atmospheric air was not restricted.

In order to establish the necessary amount of alkali, substrate **1a** was oxidized in a 1:1 mixture of acetonitrile–water in the presence of different amounts of LiOH. The obtained results are presented in Figure 1. We can note that already starting from 0.5 equivalent of LiOH the yields of the isolated product are close to maximum (ca. 70%).

Using a reactor with unrestricted air access through an open condenser, acetonitrile–water (1:1) as a solvent and LiOH as an additive, we performed the aerobic oxidation of alkyl, substituted alkyl, and aryl diols **1a**–**g**[15] on the Pt/C catalyst. The obtained results are presented in Table 1.[16]

In most cases 1,2-diones **3**[17] were obtained in good yield (around 70%). There are some exceptions: hydroxyalkyl substrate with unprotected OH group **1b** resulted in a modest yield of **3b** (49%, Table 1, entry 6). It is also noteworthy that only the secondary OH groups of the substrate were oxidized leaving the primary alcohol group untouched. The oxidation of *tert*-amylcarbonyloxy diol (**1d**) proceeded quickly over about one hour, until a yield of **3d** of 28% was reached and then the reaction stopped (Table 1, entry 8); diol **1g**, which bears an amido group, did not afford the expected dione **3g**. At the same time Boc-aminoalkyl substrate **1e** resulted in the best isolated yield of dione **3e** (76%, Table 1, entry 9). In all these cases no hydroxyketone intermediates **2** were observed.

When the catalyst was filtered from the reaction mixture and reused for the oxidation of diol **1a**, only a minor decrease in the yield was observed and the product dione **3a** was isolated in 68% yield (Table 1, entry 5). Thus the catalyst can be reused at least once without noticeable decrease in the catalyst activity and the TON for a batch remains approximately 14.

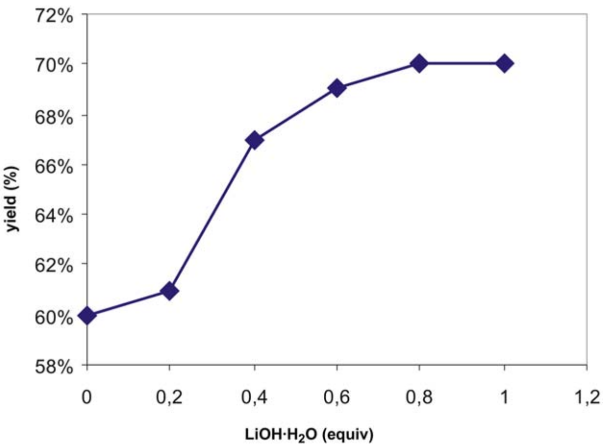

Figure 1 The effect of different amounts of LiOH·H_2O on the isolated yield of **3a**. *Reaction conditions*: MeCN–H_2O (1:1); 60 °C; 4 h; 5 mol% Pt/C catalyst.

Table 1 Aerobic Oxidation of diols **1** to diones **3** in the Presence of Pt/C Catalyst

Entry[a]	Substrate	LiOH (equiv)	Time (h)	Yield (%)
1	**1a**	0.2	4	61
2[b]	**1a**	0.4	4	67
3	**1a**	0.6	4	69
4	**1a**	1.0	4	70
5[c]	**1a**	1.0	4	68
6	**1b**	1.0	5	49
7	**1c**	1.0	5	74
8	**1d**	1.0	1.3	28
9	**1e**	1.0	4	76
10	**1f**	1.0	3.5	69
11	**1g**	1.0	3	0

[a] All experiments were run at 60 °C with 5 mol% Pt/C catalyst in an open glass reactor equipped with a condenser. MeCN–H_2O (1:1) used as solvent unless stated otherwise.
[b] In toluene.
[c] Regenerated catalyst used in the experiment.

We may conclude that a new, safe, and easy to use Pt/C catalytic aerobic oxidation method for the oxidation of cyclopentane-1,2-diols to the corresponding 1,2-diones was developed. The method is viable in the presence of a variety of functional groups, including benzyl ethers, alkyl-, Boc-amino-, hydroxyl-, and phenyl groups. A wide choice of solvents ranging from toluene to water–acetonitrile mixture to water makes it possible to oxidize many other substrates by this method.

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(15) **Preparation of Substrates**
(a) Substrates **1a**,**b** and **1d**–**f** were prepared from the corresponding alkenes according to the following dihydroxylation procedure: Alkene was dissolved in a H_2O–*t*-BuOH mixture (1:3), and NMO (1.3 equiv) and fiber bound OsO_4 catalyst (0.1 mol%) were added. The reaction mixture was stirred at 60 °C for an appropriate time (the reaction was monitored by TLC), the catalyst filtered, rinsed with EtOAc, and the filtrate quenched with an aqueous solution of $Na_2S_2O_3$ (10%). The aqueous layer was extracted with EtOAc, the organic extracts combined, dried over $MgSO_4$, the solvent evaporated and the crude product purified by flash chromatography, to afford the corresponding diol. Due to the synthetic route always the *cis*-diol was obtained as two isomers at the 3-position and used as a mixture. (b) Diol **1c** is a commercial product[18] and was used without purification. (c) Alkenes preceding diols **1a** and **1b** were prepared from 2-cyclopentene-1-acetic acid.[9a] (d) The alkene preceding diol **1d** was prepared from 2-cyclopentene-1-acetic acid ethyl ester by transesterification, as reported by: Frei, U.; Kirchmayr, R. EP 0278914, **1988**. (e) Alkenes preceding diols **1e** and **1g** were prepared from 2-cyclopentene-1-acetic acid according to: Bertrand, M. B.; Wolfe, J. P. *Tetrahedron* **2005**, *61*, 6447. (f) The alkene preceding diol **1f** was prepared according to: Büchner, I. K.; Metz, P. *Tetrahedron Lett.* **2001**, *42*, 5381.

(16) **General Procedure for the Catalytic Aerobic Oxidation of Diols**
Diol (0.424 mmol), catalyst (5 mol%), $LiOH·H_2O$ (1.0 equiv) and solvent [2 mL, MeCN–H_2O (1:1)] were added to a 10 mL glass reactor, equipped with a condenser and stirred at 60 °C for an appropriate time. Consumption of the substrate was monitored by TLC. When the substrate was consumed the catalyst was filtered, rinsed with EtOAc (15 mL), EtOAc (10 mL) was added and the obtained two-phase solution was washed with 0.025 M HCl aq soln (20 mL). The separated aqueous layer was extracted once with EtOAc (20 mL). The combined extracts were dried over $MgSO_4$ and concentrated in vacuum. The solid crude product was purified by flash chromatography [EtOAc–PE (2.5:10)] to give the diketone as a white crystalline solid.

(17) All products have been fully characterized by ^1H NMR and ^{13}C NMR. The analyses of known compounds are in agreement with published data. The characteristics of compounds are as follows:
Compound **2a**: ^1H NMR (800 MHz, $CDCl_3$): $\delta = 7.48$ (m, 4 H, Bn *o*-, *m*-), 7.43 (m, 1 H, Bn *p*-), 4.67 and 4.65 (2d, $J = 11.8$ Hz, 2 H, Bn CH_2O), 3.74 (dd, $J = 1.8$, 10.9 Hz, 1 H, H-2), 3.69 (td, $J = 2 \times 5.0$, 9.6 Hz, 1 H, H-7), 3.65 (ddd, $J = 4.5$, 8.5, 9.6 Hz, 1 H, H-7), 2.41 (ddddd, $J = 0.6$, 1.4, 1.9, 9.2, 19.6 Hz, 1 H, H-5), 2.20 (dddd, $J = 0.4$, 9.6, 11.0, 19.6 Hz, 1 H, H-5), 2.09 (ddddd, $J = 0.5$, 1.4, 6.2, 9.6, 13.1 Hz, 1 H, H-4), 1.97 (m, 2 H, H-3,6), 1.86 (m, 1 H, H-6), 1.51 (dddd, $J = 9.1$, 11.0, 11.6, 13.1 Hz, 1 H, H-4). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 216.4$ (C-1), 137.6 (C-9), 128.3 (C-11), 127.7 (C-10, C-12), 81.1 (C-2),73.1 (C-8), 68.9 (C-7), 42.5 (C-3), 34.2 (C-6), 34.0 (C-5), 23.3 (C-4). This structure was confirmed by 2D FT correlation diagrams and ^1H–^1H coupling constants from H-2 and H-5 (19.6 Hz geminal coupling). The assignment of *trans*-configuration results from the comparison of ^{13}C chemical shifts with *cis*- and and *trans*-isomers of 3-[2-(benzyloxy)ethyl]cyclopentane-*cis*-1,2-diol.

Compound **2a′**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.34 (m, 5 H, Bn *o*-, *m*-, *p*-), 4.46 (s, 2 H, H-8), 4.01 (tdd, $J = 2 \times 0.5$, 8.3, 11.8 Hz, 1 H, H-5), 3.57 and 3.54 (m, 2 H, H-7), 2.37 and 1.60 (m, 2 H, H-4), 2.30 (m, 1 H, H-2), 2.15 and 1.49 (m, 2 H, H-3), 2.02 and 1.75 (m, 2 H, H-6). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 219.6 (C-1), 138.1 (C-9), 128.2 (C-11), 127.4 (C-10, C-12), 75.5 (C-5), 72.7 (C-8), 67.3 (C-7), 43.3 (C-2), 30.2 (C-6), 29.3 (C-4), 22.9 (C-3). Large coupling constants of C-5 carbinol proton point to a methylene group bonded to C-5.

Compound **3a**: data available in ref. 9a. Compound **3b**: data available in ref. 9a. Compound **3c**: data are in accordance with commercial compound purchased from Aldrich.

Compound **3d**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.85 (s, 1 H, OH), 3.38 (s, 2 H, CH_2CO), 2.53 (m, 2 H, H-5), 2.43 (m, 2 H, H-4), 1.75 (q, J = 7.3 Hz, 2 H, CH_2CH_3), 1.42 (s, 6 H, $(CH_3)_2$, 0.86 (t, J = 7.3 Hz, 3 H, CH_2CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.16 (C-3), 168.80 (COO), 150.04 (C-2), 138.61 (C-1), 84.24 [O*C*(Me)$_2$], 35.42 (*C*H$_2$CO), 33.36 (*C*H$_2$CH$_3$), 32.01 (C-4), 25.36 [OC*Me*$_2$ and C-5], 8.09 (*C*H$_3$CH$_2$). IR: ν = 3315, 2979, 2937, 2885, 1727, 1699, 1665, 1465, 1386, 1193, 1149 cm^{-1}.

Compound **3e**: ^{1}H NMR [500 MHz, $CDCl_3$, broadened spectrum (*E*/*Z* exchange of Boc)]: δ = 6.40 (br s, 1 H, OH), 4.89 (br s, 1 H, NH), 3.41 (br m, 2 H, H-7), 2.59 (t, $J = 2 \times 6.6$ Hz, 2 H, H-6), 2.47 (br m, 2 H, H-5), 2.41 (br m, 2 H, H-4), 1.41 (br s, 9 H, H-11). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.21 (C-3), 155.96 (C-9), 149.57 (C-2), 144.18 (C-1), 79.33 (C-10), 37.82 (C-7), 31.90 (C-4), 29.88 (C-6), 28.32 (C-11), 25.51 (C-5). IR: ν = 3371, 3326, 3008, 1689, 1657, 1524, 1451, 1393, 1367, 1249, 1169, 1119 cm^{-1}.

Compound **3f**: Ramage, R.; Griffiths, G. J.; Shutt, F. E. *J. Chem. Soc., Perkin Trans. 1* **1984**, *7*, 1531.

(18) 3-Methylcyclopentane-1,2-diol was purchased from Alfa Aesar as a mixture of diastereomers, 95%.