Aerobic palladium-heteropolyacid-catalyzed allylic acetoxylation of cyclohexene

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Abstract

The heteropolyacid $H_5[PMo_{10}V_2O_{40}]$ is an effective oxygen-activating catalyst in palladium-catalyzed aerobic allylic acetoxylation of cyclohexene.

Keywords: Aerobic allylic acetoxylation; Palladium; Heteropolyacid

1. Introduction

The palladium-catalyzed allylic oxidation of olefins to their corresponding allylic alcohol esters has been developed into a useful method (Eq. 1) [1–8]. In particular, excellent yields and high selectivity have been achieved in systems employing *p*-benzoquinone (BQ) as stoichiometric oxidant, or electron-transfer mediator [1–3,5,6,8] in combination with a stoichiometric oxidant.

(1)
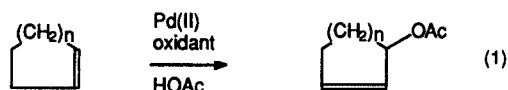
Of great interest for synthetic purposes would be a selective, high-yielding process based on molecular oxygen or air, in combination with a facile work-up procedure. One problem in aero-

bic reactions is dioxygen activation [9]. Aerobic reaction systems for allylic acetoxylation and related reactions employing various organometallic macrocycles such as metalloporphyrins and metallosalenes as oxygen-activating catalysts have been reported [2,10]. The drawback of these systems have been the accessibility and stability of the oxygen-activating catalyst.

Polyoxometalates constitute an interesting group of compounds that include heteropolyacids. They have found use as oxidation catalysts in various reactions [11–17], and some of these compounds catalyze reactions where the stoichiometric oxidant is hydrogen peroxide or molecular oxygen [11,13,15–17]. Some transition metal substituted polyoxometalates have been considered to be inorganic analogues to metalloporphyrins [12,14,15]. Heteropolyacids such as phosphomolybdovanadic acids (HPAs) have found use in oxidation of organic as well as inorganic substrates, for example the oxida-

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tion of zerovalent palladium to divalent palladium in aerobic Wacker-type reactions [11,16,17]. In connection with our studies on palladium- and ruthenium-catalyzed biomimetic aerobic oxidations, [2]a and [10,18] it was of interest to study the use of the robust inorganic polyoxometalates as oxygen-activating agent in the allylic acetoxylation of an internal olefin.

2. Results and discussion

Cyclohexene was treated with oxygen in the presence of catalytic amounts of $Pd(OAc)_2$ and the heteropolyacid $H_5[PMo_{10}V_2O_{40}] \times 34\ H_2O$ [19] (Table 1, entry 1). The progress of the reaction, followed by measurement of the oxygen consumption [20], was slow and 3-acetoxy-1-cyclohexene [21] was obtained after a simple extractive workup procedure. The slow step in this reaction could be either the formation of the intermediate (π-allyl)palladium complex [22,23] or the electron transfer from zerovalent palladium to the oxidized HPA [11,17]. If the latter step is rate-limiting, the addition of an electron transfer mediator such as BQ would result in an increased reaction rate since electron transfer

both from zerovalent palladium to the quinone [24] and from hydroquinone to the heteropolyacid [25] is relatively rapid. Indeed, the addition of p-benzoquinone to the reaction system (Eq. 2) had the expected effect: an increased rate of oxygen consumption, and also an increased yield of the desired product was observed. The amount of quinone added was not highly critical for the rate of the reaction. In fact, it was found that the reaction was slightly faster in the presence of 7 mol% of BQ than with twice the amount (Table 1, entries 2 and 3).
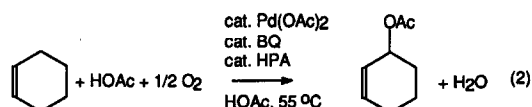
The amount of palladium was found to be a critical factor for the rate of oxygen consumption. In all cases a decreased rate was observed when the amount of palladium was changed from 5 mol% to 2.5 mol% (Table 1). The effect of varying the relative amount of HPA seems to depend on the quality of this catalyst. As can be seen in Table 1 entries 3–6, a doubling of the amount of HPA had almost the same effect on the rate as a doubling of the amount of $Pd(OAc)_2$. However, in experiments carried out employing another batch of HPA the amount of HPA was not significantly important for the rate, whereas the dependence on $Pd(OAc)_2$ was the same as shown in Table 1.

These observations suggest that the slow step in this aerobic allylic acetoxylation could be the first step in the catalytic cycle (Scheme 1), the formation of the (π-allyl)palladium intermediate [22,23]. The steps that follow, (i) activation of the intermediate by quinone coordination [26]; (ii) nucleophilic attack by acetate [27]; and (iii) electron transfer from Pd(0) to coordinated BQ [24], most likely occur faster. The extent to which the steps involving HPA, (iv) reoxidation of hydroquinone, and (v) reoxidation of HPA, are slow seems to depend on the quality of the latter catalyst.

Table 1
Aerobic allylic oxidation of cyclohexene with a triple catalytic system $Pd(OAc)_2$-BQ-HPA [a]

Entry	Oxidation system	% Pd-$(OAc)_2$	Initial O_2 uptake/h (ml) [b]	% yield [c]
1	HPA (1%)	5	1 [d]	30
2	HPA (1%) + BQ (14%)	5	13	73
3	HPA (1%) + BQ (7%)	5	18	76–84 [e]
4	HPA (1%) + BQ (7%)	2.5	16	75–88 [e]
5	HPA (2%) + BQ (7%)	5	26	70–85 [e]
6	HPA (2%) + BQ (7%)	2.5	21	68–76 [e]

[a] The reactions were performed on a 2.3 mmol scale in 10 ml of acetic acid containing 0.1 M of $LiOAc \cdot 2H_2O$ at 55°C. The reaction time was 4 h in all cases. The product was characterized by ^{1}H-NMR spectroscopy [21].
[b] 28 ml of O_2 should be consumed for the oxidation of 2.3 mmol of cyclohexene.
[c] Isolated yield after evaporation of solvents. The product is volatile.
[d] The initial rate was slow in this case but increased to about 4 ml/h after 2 h.
[e] The yields are based on 3–4 experiments.

Of even greater interest would be an efficient large-scale process utilizing only minute amounts of the catalysts. In an attempt to increase the turnover number (TON) on palladium, reactions with large substrate-to-palladium ratios were carried out. The results are summarized in Table 2. With increased substrate: Pd ratios the TON increased, and with a ratio cyclohexene/Pd(OAc)$_2$ of 1000:1 (0.1 mol%) 146 turnovers could be obtained in 6 h. In these semi-preparative reactions, it was found that the concentration of cyclohexene can be increased to 3.2 M with maintained selectivity (Table 2, entry 4 and 5). A further increase to 4.9 M of cyclohexene (cyclohexene/HOAc = 1:1) led to a drop in selectivity and a complex mixture of products was obtained.

It can be concluded that the polyoxometalates constitute an interesting group of biomimetic oxidation catalysts. The heteropolyacid H$_5$[PMo$_{10}$V$_2$O$_{40}$] × 34 H$_2$O is a promising, readily accessible and inexpensive oxygen-activating catalyst with an efficiency comparable to that of the metal-macrocycles previously employed in this group. It has the advantage of not undergoing the oxidative degradation associated with the use of several of the metal-macrocycles in the presence of O$_2$.
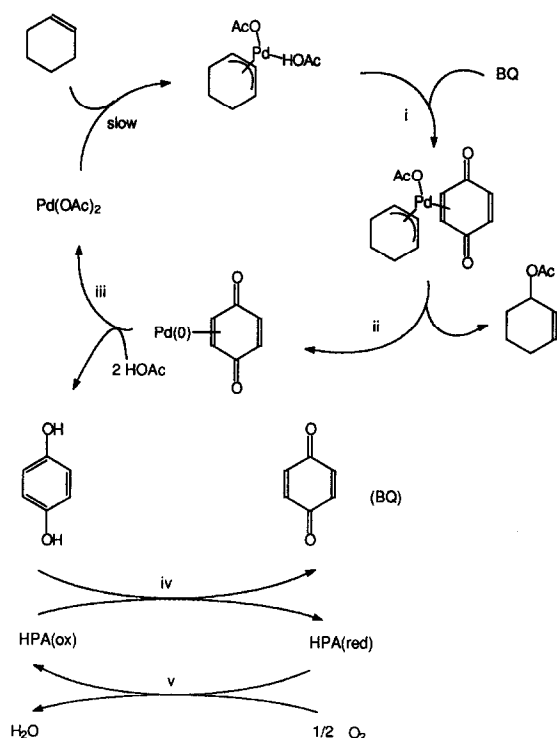
Table 2
Semi-preparative aerobic palladium-catalyzed oxidation of cyclohexene to 3-acetoxy-1-cyclohexene

Entry	Pd/ substrate	[Cyclohexene]	Reaction time	TON on Pd [d]	on HPA [d]
1 [a]	1:20	0.23 M	4 h	16	80
2 [b]	1:40	0.23 M	4 h	32	77
3 [c]	1:100	0.90 M	5 h 30 min	69	140
4 [c]	1:500	3.2 M	6 h	123	246
5 [c]	1:1000	3.2 M	6 h	146	302

[a] From Table 1, entry 3.
[b] From Table 1, entry 4.
[c] The reactions were run with a Pd(OAc)$_2$/BQ/HPA relative ratio of 1:1.25:0.5 in HOAc, 0.1 M in LiOAc at 55°C.
[d] Calculated from the isolated yield of 3-acetoxy-1-cyclohexene.

Acknowledgements

Scheme 1

Scheme 1. Catalytic cycle.

References

[1] (a) A. Heumann and B. Åkermark, Angew. Chem. Int. Ed. Engl., 23 (1984) 453. (b) S. Hansson, A. Heumann, T. Rein and B. Åkermark, J. Org. Chem., 55 (1990) 975. (c) A. Heumann, B. Åkermark, S. Hansson and T. Rein, Organic Synthesis, Vol. 68, p. 109.

[2] (a) J.E. Bäckvall, R.B. Hopkins, H. Grennberg, M.M. Mader and A.K. Awasthi, J. Am. Chem. Soc., 112 (1990) 5160. (b) S.E. Byström, E.M. Larsson and B. Åkermark, J. Org. Chem., 55 (1990) 5674.

[3] A recent extension which allows the use of other carboxylate nucleophiles has further increased the utility of the reaction: B. Åkermark, E.M. Larsson and J.D. Oslob, J. Org. Chem., 59 (1994) 5729.

[4] E.N. Frankel, W.K. Rohwedder, W.E. Neff and D. Weisleder, J. Org. Chem., 40 (1975) 3247.

[5] J.E. McMurry and P. Kocovsky, Tetrahedron Lett., 25 (1984) 4187.

[6] B. Åkermark, S. Hansson, T. Rein, J. Vågberg, A. Heumann and J.E. Bäckvall, J. Organomet. Chem., 369 (1989) 433.

[7] (a) E.M. Larsson and B. Åkermark, Tetrahedron Lett., 34 (1993) 2523. (b) H. Grennberg, unpublished results from our laboratory.

[8] C. Jia, P. Müller and H. Mimoun, J. Mol. Catal., 101 (1995) 127.

[9] L.I. Simàndi, in Catalytic Activation of Dioxygen by Metal Complexes, Vol. 13, R. Ugo, B.R. James (Eds.), Kluwer, Dordrecht 1992.

[10] H. Grennberg, S. Faizon and J.E. Bäckvall, Angew. Chem. Int. Ed. Eng., 32 (1993) 263.

[11] (a) Y. Izumi, K. Urabe and M. Onaka, in Zeolite, Clay and Heteropoly Acid in Organic Reactions, VCH, New York, 1992. (b) G.W. Parshall and S.D. Ittel, in "Homogenous Catalysis", John Wiley & Sons, New York, 1992, p. 141.

[12] M.T. Pope, in Encyclopedia of Inorganic Chemistry, Vol. 6, John Wiley & Sons, LTD, West Sussex, GB, 1994.

[13] R. Neumann and M. Levin, J. Am. Chem. Soc., 114 (1992) 7278.

[14] (a) C.L. Hill and R.B. Brown Jr, J. Am. Chem. Soc., 108 (1986) 536. (b) A.L. Khenkin and C.L. Hill, J. Am. Chem. Soc., 115 (1993) 8178.

[15] (a) R. Neumann and M. Gara, J. Am. Chem. Soc., 116 (1994) 5509. (b) idem, ibid 117 (1995) 5066.

[16] (a) E. Monflier, S. Tilloy, G. Fremy, Y. Barbaux and A. Mortreux, Tetrahedron Lett., 36 (1995) 387. (b) E. Monflier,

E. Blouet, Y. Barbaux and A. Mortreux, Angew. Chem. Int. Ed. Engl., 33 (1994) 2100.

[17] I.V. Kozhevnikov and K.I. Matveev, Russ. Chem. Rev., 51 (1982) 1075.

[18] (a) J.E. Bäckvall, R.L. Chowdhury and U. Karlsson, J. Chem. Soc. Chem. Commun., (1991) 473. (b) G.-Z. Wang, U. Andreasson and J.E. Bäckvall, J. Chem. Soc. Chem. Commun., (1994) 1037.

[19] G.A. Tsigdinos and C.J. Hallada, Inorg. Chem., 7 (1968) 437.

[20] The oxygen uptake is a convenient measure of the progress of the reaction since 1 mole of substrate consumes $1/2$ mole of O_2.

[21] A.J. Pearson and S.Y. Hsu, J. Org. Chem., 51 (1986) 2505.

[22] (a) R.G. Brown, R.V. Chaudhar and J.M. Davidsson, J. Chem. Soc. Dalton Trans., (1977) 176. (b) B.M. Trost and P.J. Metzner, J. Am. Chem. Soc., 102 (1980) 3572. (c) J.E. Bäckvall, K. Zetterberg and B. Åkermark, in Inorganic Reactions and Methods, A.P. Hagen (Ed.), VCH 1991, Vol. 12A (1991) 123.

[23] (a) H. Grennberg, V. Simon and J.E. Bäckvall, J. Chem. Soc. Chem. Commun., (1994) 265. (b) H. Grennberg and J.E. Bäckvall, Manuscript.

[24] H. Grennberg, A. Gogoll and J.E. Bäckvall, Organometallics, 12 (1993) 1790.

[25] K. Bergstad, J.E. Bäckvall and H. Grennberg, Manuscript.

[26] J.E. Bäckvall and A. Gogoll, Tetrahedron Lett., 29 (1988) 2243.

[27] J.E. Bäckvall, R.E. Nordberg and D. Wilhelm, J. Am. Chem. Soc., 107 (1985) 6892.