Direct liquid-phase side-chain oxidation of alkylbenzenes over [Pd(phen)(OAc)$_2$] catalyst

Shannonmarie D. George, Sheldon C. Sherman, Alexei V. Iretskii and Mark G. White *

School of Chemical Engineering, Georgia Institute of Technology, Atlanta, GA 30332-0100, USA
E-mail: mark.white@che.gatech.edu

Received 19 October 1999; accepted 9 February 2000

Only the side-chain oxidation of alkylbenzenes (R–C$_6$H$_3$–R′–R″; R = H, Me, Et, Pr^i; R′ = H, Me; and R″ = H, Me) by oxygen (35–50 atm, 200 °C) is promoted in the presence of [Pd(phen)(OAc)$_2$].

Keywords: alkylbenzene, toluene, ethylbenzene, xylene, mesitylene, *p*-ethyltoluene, cumene, *p*-cymene, oxidation, palladium, 1,10-phenanthroline

The oxidation of some alkyl arenes over a transition metal catalyst (usually Co) is known to proceed by a radical mechanism [1–3] and shows that the formation of the aldehyde from the arene can occur without the formation of alcohol as the intermediate product. The aldehyde is further converted to the acid. Unlike cobalt, palladium catalyzes the aromatic carbon oxidation in preference to the benzyl carbon for alkyl aryl substrates [4,5]. Our previous results showed the low-temperature oxidative coupling over a Pd^{2+} catalyst in superacidic media [6]. Subsequent research for the coupling of methyl benzoate showed the benefit of using different ligands with the Pd^{2+} catalysts [7]. This communication discusses the rather surprising result that the [Pd(phen)(OAc)$_2$] catalyst, which successfully couples methyl benzoate [7] and dimethyl phthalate [8], shows a high activity towards oxidation of the aryl methyl group and only a very low activity towards ring activation.

The catalyst may be prepared either *in situ* or *ex situ*. All reactions were completed in 50 ml Parr autoclaves using pressurized, artificial air (50 mol% O$_2$) as the oxidant. In a typical reaction 1 mmol of Pd(OAc)$_2$ was used with an equimolar amount of 1,10-phenanthroline and 200 mmol of substrate; the reaction temperature was set at 120–200 °C and samples were taken in regular intervals for the reaction times up to 24 h.

We examined this reaction for the following substrates: toluene, ethylbenzene, *o*-xylene, *m*-xylene, *p*-xylene, mesitylene, *p*-ethyltoluene, cumene, and *p*-cymene. A radical scavenger, 2,6-di-*tert*-butyl-4-methylphenol (BHT), was used to determine if a radical intermediate is produced. All samples were mixed with an internal standard (20–200 μl per 0.75 ml of internal standard and 1 ml of acetone) and analyzed on HP 5890 series II GC/HP 5972 MS. The internal standard was prepared by combining 200 μl of tridecane with 99.8 ml of hexane/acetone (50 vol% each). The partitioning agent was a Supelco SPB-5 column (30 m × 0.25 mm × 0.5 μm).

In the presence of [Pd(phen)(OAc)$_2$] the methyl group of toluene is oxidized to produce benzyl alcohol, benzaldehyde, and benzoic acid, whereas, benzyl benzoate is the final product (table 1). Activation of the ring carbons is minimal ($<1\%$). The composition of the reaction mixture changes with time (figure 1), as for all other substrates. In a separate test at the same reaction conditions, under 50 bars of artificial air but without the Pd catalyst, benzyl alcohol, and benzaldehyde were reacted to produce benzyl benzoate. Thus, the following reaction network (scheme 1) may explain these results. When the substrate was *o*-xylene, after 60 min the following products were found: 2-methylbenzyl alcohol (32%), 2-methylbenzoic acid (56%), and 2-methylbenzoic acid 2-methylbenzoic ester (11%) with combined turnover numbers (TON) up to 19. However, we did not observe 2-methylbenzaldehyde. Small amounts of the coupled product 3,4,3′,4′-tetramethylbiphenyl were also found. Phthalide was observed in modest yields (∼1 turnover) at each reaction time. This product may be the result of the following reaction path (scheme 2) involving the condensation of an acid with an alcohol.

The oxidation products in significant yields (combined TON = 43) from *p*-xylene after 4 h at 200 °C include 4-methylbenzyl alcohol (8.3%), 4-methylbenzaldehyde (29.5%), 4-methylbenzoic acid (50.7%) and the ester (11.2%). The kinetic yields of these products suggest that they are intermediates to the final product, which is 4-methylbenzoic acid 4-methylbenzoic acid ester. Minor products include the coupled products and terephthalaldehyde. The reaction pathway for the major products and intermediates of *p*-xylene oxidation is similar to the network described earlier for *o*-xylene. Terephthalaldehyde is the result of oxidizing both methyl groups of the *p*-xylene. In the case of mesitylene as the substrate, the primary products were 3,5-dimethylbenzyl alcohol and 3,5-

---

[*] To whom correspondence should be addressed.

© J.C. Baltzer AG, Science Publishers

Table 1
Comparison of oxidations of aryls over Pd^{2+} catalysts.

Substrate (catalyst)	Toluene [Pd(phen)$(OAc)_2$]	Toluene [Pd(acac)$(OAc)_2$]	Methyl benzoate [Pd(phen)$(OAc)_2$]
Substrate (mmol)	327	402	257
Pd(II) (mmol)	0.5	0.5	0.5
ligand (mmol)	0.5	0.5	0.5
Reaction time (min)	240	180	180
TOF (h^{-1})	8	13.3	6.4
Yield (%)			
Benzyl alcohol	0.15	0	0
Benzaldehyde	0.85	0	0
Benzoic acid	1.11	0	0
Benzyl benzoate	2.77	0	0
Dimer	0.06	5.0	3.7

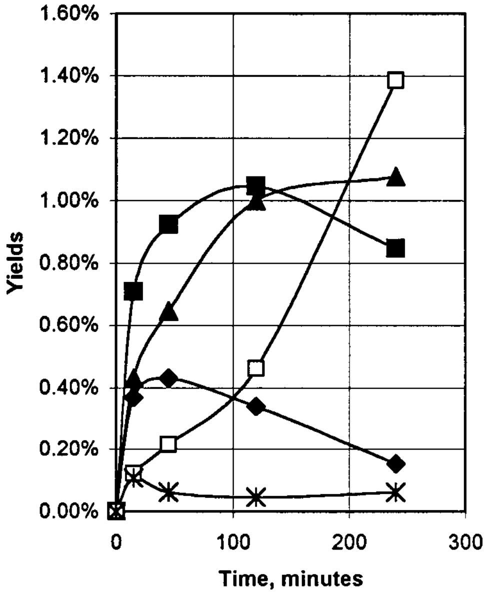
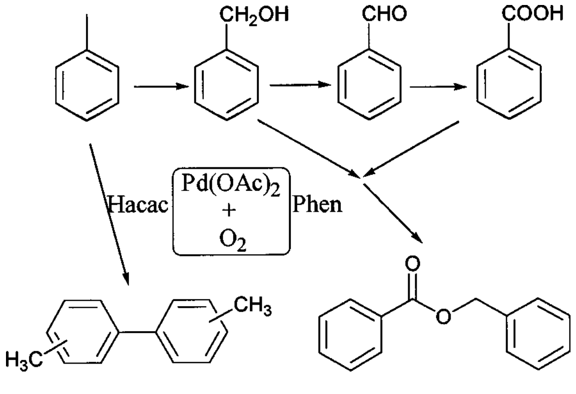
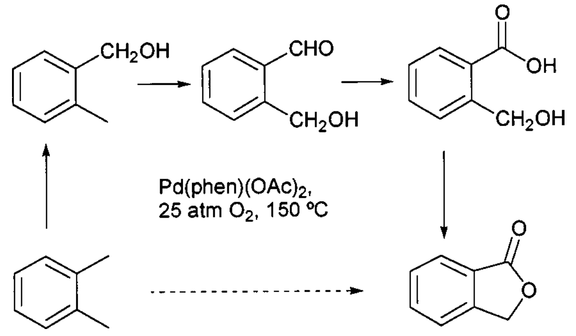


Figure 1. Dynamic yields of products from toluene oxidation: (◆) benzyl alcohol, (■) benzaldehyde, (▲) benzoic acid, (□) benzyl benzoate and (∗) dimer.



Scheme 1.



Scheme 2.

dimethylbenzaldehyde, whereas the minor product is 2,4,6-trimethylphenol.

Only two products were observed in significant yields for the oxidation of m-xylene: 3-methylbenzaldehyde and 3-methylbenzoic acid in 4 : 1 ratio after 15–45 min, 2 : 1 after 2 h and 0.9 : 1 after 4 h. No alcohol or ester was observed.

The oxidation of ethylbenzene gives rise to acetophenone as the major product with TON up to 15 after 24 h. The oxidation of 4-ethyltoluene shows p-methylacetophenone (29%) and p-tolylethanol (70%) as the major products with 4-methylbenzaldehyde and 4-ethylbenzyl alcohol as minor products. Acetophenone and p-methylacetophenone were the major products when the substrates were cumene and p-cymene, respectively.

The same Pd-phen catalyst in the presence of CO activates aromatic C–H bonds and catalyses phenol formation from benzene [9]. Our data for the oxidation of the four methyl-substituted benzenes suggests that the major reaction products are the result of a sequential oxidation of the benzyl carbon in preference to oxidation of phenyl carbons. In the case of di-substituted o- and p-xylene, these reactions show the same network as that described by the oxidation of toluene. These reaction schemes lead to the final product that is an ester. This result suggests that preferentially only one of the benzyl carbons on o- and p-xylenes was oxidized since we observe only small amounts of phthalide and terephthalaldehyde. The reaction pathway for the oxidation of m-xylene and mesitylene is more difficult to describe. For the former, no alcohol product is observed and for the latter no acid has been identified. The absence of either intermediate product precludes the formation of the ester, thus we are not surprised that no ester product is observed for either substrate.

Oxidation of substrates having a secondary carbon in the side chain (ethylbenzene and ethyltoluene) shows its preferential oxidation only in the case of ethylbenzene. However, when the substrate was ethyltoluene, p-tolylethanol was formed favorably to p-methylacetophenone. This result implies that oxidation of a secondary carbon is faster than oxidation of a primary carbon of a *single side chain*. The addition of the p-methyl group to the ring, plays a role in the oxidation of the primary carbon of the other ethyl substituent, and conversely.

The oxidation of an alkyl substituent having a tertiary carbon leads to the formation of the acetophenone when the substrates were cumene and p-cymene. A carbon is lost from the isopropyl group during the oxidation.

The Pd-catalyzed oxidation of toluene shows benzyl alcohol (21%) and benzaldehyde (41%) present at short reaction times (ca. 15 min). It appears that the Pd-catalyzed oxidation of toluene and other substrates produces aryl alcohols in significant quantities and thus the reaction mechanism for this catalysis may be different from the mechanism observed for the process over the Co(III) catalyst. For example, the main products of p-cymene Co-catalyzed oxidation were p-isopropylbenzoic acid (90%) and p-isopropylbenzaldehyde (10%) [10], whereas in our case the major product is methylacetophenone (70%) and the minor products are p-isopropylbenzyl alcohol (9%) and p-isopropylbenzaldehyde (14%).

To examine the new catalysis further, the radical scavenger BHT was added to the ethylbenzene in amounts of 1 and 10 mol% at the beginning of separate experiments. The turnovers to acetophenone decreased by a factor of 2–3, but the oxidation was not suppressed. Whereas the radical catalysis is inhibited by as little as 1 mol% BHT, the new reaction catalysis may involve a mechanism different from that known for traditional chain oxidation.

The present data (table 1) suggest that the Pd(phen)$(OAc)_2$ favorably catalyzes the oxidation of benzyl carbons in preference to the phenyl carbons. We show also data for toluene oxidation using pentanedione as the ligand and for methylbenzoate oxidation with phenanthroline as the ligand. These two control tests show the effects of the ligand on a substrate that has an oxidizable benzylic carbon (toluene) and a substrate that does not (methyl benzoate). Since methyl benzoate has no benzyl carbons *that can be oxidized further*, ring activation is the only possible oxidation reaction. The use of a N-containing ligand in place of an O-containing ligand clearly demonstrates a profound ligand effect in directing the catalysis from ring oxidation to benzylic oxidation.

Acknowledgement

We thank KoSa (Spartanburg, SC) for support.

References

[1] R.A. Sheldon and J.K. Kochi, *Metal-Catalyzed Oxidations of Organic Compounds* (Academic Press, New York, 1981).

[2] W. Partenheimer, Catal. Today 23 (1995) 69.

[3] A.E. Shilov and G.B. Shul'pin, Chem. Rev. (1997) 2879.

[4] J. Tsuji, *Palladium Reagents and Catalysts. Innovation in Organic Synthesis* (Wiley, Chichester, 1997);
J.L. Malleron, J.C. Fiaud and J.Y. Legros, *Handbook of Palladium-Catalyzed Organic Reactions* (Academic Press, San Diego, 1997).

[5] J.M. Davidson and C. Triggs, Chem. Ind. (London) (1967) 1361; J. Chem. Soc. A (1968) 1324, 1331;
H. Itatani and H. Yoshimoto, Chem. Ind. (London) (1971) 674;
H. Iataaki and H. Yoshimoto, J. Org. Chem. 38 (1973) 76;
M. Kashima, H. Yoshimoto and H. Itatani, J. Catal. 29 (1973) 92;
H. Yoshimoto and H. Itatani, J. Catal. 31 (1973) 8; Bull. Chem. Soc. Jpn. 46 (1973) 2490;
A.D. Ryabov, S.A. Deiko, A.K. Yatsimrisky and I.V. Berezin, Tetrahedron Lett. 22 (1981) 3793;
T. Itahara, Chem. Ind. (London) (1982) 599.

[6] B.Q. Xu, D. Sood, A.V. Iretski and M.G. White, J. Catal. 187 (1999) 358.

[7] A.V. Iretskii, S.C. Sherman, M.G. White, J.C. Kenvin and D.A. Schiraldi, J. Catal., submitted.

[8] A. Shiotani, M. Yoshikiyo and H. Itatani, J. Mol. Catal. 18 (1983) 23;
A. Shiotani, H. Itatani and T. Inagaki, J. Mol. Catal. 34 (1986) 57.

[9] T. Jintoku, K. Takaki, Y. Fujiwara, Y. Fuchita and K. Hiraki, Bull. Chem. Soc. Jpn. 63 (1990) 438;
T. Jintoku, K. Nishimura, K. Takaki and Y. Fujiwara, Chem. Lett. (1990) 1687.

[10] A. Onopchenko, J.G.D. Schulz and R. Seekircher, J. Chem. Soc. Chem. Commun. (1971) 939; J. Org. Chem. 37 (1972) 1414;
A. Onopchenko and J.G.D. Schulz, J. Org. Chem. 37 (1972) 2564.