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# Pd(II) catalyzed acetoxylation of arenes with iodosyl acetate

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**Abstract**

$PhI(OAc)_2$ is an effective oxidant in the acetoxylation of arenes with $Pd(OAc)_2$ as catalyst. The data are most easily interpreted in terms of palladation being the step that determines both the rate and the *o/m/p* selectivity, and reductive elimination from a PhPd(IV)(OAc) species being the product forming step.

*Keywords:* Arenes; Acetoxylation; Palladium acetate; Iodosyl acetate; Nuclear oxidation

## 1. Introduction

The catalytic oxidation of arenes to phenols or their esters via Pd(II) catalysis has been well studied [1–4], but none of the catalytic systems have proved to be sufficiently active and selective for practical applications. Such a process would find numerous applications in organic fine chemicals synthesis. Literature precedent suggests that the presence of acids can be helpful [5] and Henry [6] found that dichromate was a particularly suitable ultimate oxidant for favoring nuclear over benzylic acetoxylation. Eberson et al. preferred peroxydisulfate because it gave cleaner reactions [7–9]. A large proportion of *meta* product was observed for toluene [6–11], anisole [7–10] and t-butylbenzene [8–12]. Eberson et al. have argued that this unusual selectivity pattern is the result of addition of Pd–OAc across a C=C bond of the arene [8,9,13] but Stock et al. have instead considered it a result of unselective aromatic substitution [11]. Acetoxylation, which on the Stock mechanism is believed to go via reductive elimination from a Pd(IV)(Ar)(OAc) intermediate, evidently deactivates the arene ring for further substitution and disfavors overoxidation. The formation of biaryls is a common side reaction that lowers selectivity for acetoxylation, however. This arene coupling, which is believed to go via reductive elimination from a $Pd(II)Ar_2$ intermediate, is favored by the presence of chloride ion, Lewis acids, or silver ion. The area has recently been reviewed [14]. In this paper we describe studies using $PhI(OAc)_2$ as the ultimate oxidant.

## 2. Experimental

GC analysis was carried out on a Varian 3300 gas chromatograph (60-m capillary column; methylsilicone, 0.25-mm i.d., 0.25-$\mu$m

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film thickness) with FID detectors and a 4270 Varian integrator. GC–MS studies were conducted on a Hewlett Packard 5890 gas chromatograph (30-m capillary column; SE-30, 0.25-mm i.d., 0.25-$\mu$m film thickness) equipped with a 5971A mass selective detector with 70 eV electron impact ionization. Substrates were used as received from Aldrich Co., Fisher Scientific Co., Matheson Coleman & Bell Manufacturing Chemists, J.T. Baker Inc., Mallinckrodt Specialty Chemicals Co. and Eastman Kodak Co. Products were identified by comparison of retention times in gas chromatography and mass spectra with authentic samples. Some authentic samples which are not commercially available were prepared by the esterification of the appropriate phenols (0.2 $cm^3$) in a mixture of acetic anhydride (0.5 $cm^3$) and pyridine (0.5 $cm^3$).

### 2.1. General acetoxylation method

Substrates (starting number of moles, weight or volume shown for each case) were placed in a pressure-resistant vial with a screw cap unless stated otherwise. After heating (temperatures and times also shown for each case), n-dodecane was added to the mixture as an internal standard for a quantitative GC analysis. The GC sample (0.2 $cm^3$) was diluted with hexanes (1 $cm^3$) and excess $PhI(OAc)_2$ was filtered off. The resulting filtrate was subjected to the GC and GC–MS analysis.

## 3. Results and discussion

$PhI(OAc)_2$ is a powerful oxidant that has been useful in a number of selective oxidation reactions [15]. In contrast to dichromate [6,11], it does not oxidize PhOAc in the absence of a catalyst, however, and is therefore a better system for detailed study.

### 3.1. Benzene

We find that acetoxylation of benzene (Eq. 1) proceeds with good selectivity and rate using $PhI(OAc)_2$, with a 75% yield based on the oxidant and a turnover number (TON) of 37 in 20 h (Table 1, run 1). Unfortunately, the undesired aryl coupling product was formed with a TON of 1.7.

$$PhH + PhI(OAc)_2 \xrightarrow[AcOH,\,\Delta]{cat.\ Pd(OAc)_2} PhOAc + PhI + AcOH \quad (1)$$

Examination of the time course of the reaction showed that acetoxylation was the exclusive initial product, but that biphenyl starts to form after 5 h (Fig. 1). After about 20 h the reaction stops, because metallic palladium precipitates. At that time, about 1.7 turnovers of biphenyl are present.

The fact that the two products are not formed in a constant ratio during the reaction is best explained if the two products are formed by distinct pathways, as suggested by the Stock

Table 1
Pd(II) Catalyzed acetoxylation of benzene with phenyliodosyl acetate [a]

| n | Benzene | $Pd(OAc)_2$ | $PhI(OAc)_2$ | AcOH | Phenyl acetate | | Biphenyl | X-$C_6H_4OAc$ [b] |
|---|---|---|---|---|---|---|---|---|
| | (mmol) | ($\mu$mol) | (mmol) | (ml) | (%) [c] | (TON) [d] | (TON) [d] | (TON) [d] |
| 1 | 22.4 | 45.4 | 2.24 | 2 | 75 | 37 | 1.7 | 1.4 |
| 2 | 11.2 | 223 | 0 | 1 | – | 0.07 | 0.8 | 0 |
| 3 | 11.2 | 0 | 1.12 | 1 | 3.7 | – | 0 | 0 |
| 4 | 0 | 0 | 1.12 | 2 | < 0.6 | – | 0 | 0 |
| 5 | 44.8 | 43.2 | 2.24 | 0 | 51 | 27 | 1.4 | 1.1 |

[a] At 100 ± 2°C, for 20 h.
[b] X = I or AcO.
[c] Based on oxidant.
[d] Turnover number of Pd.

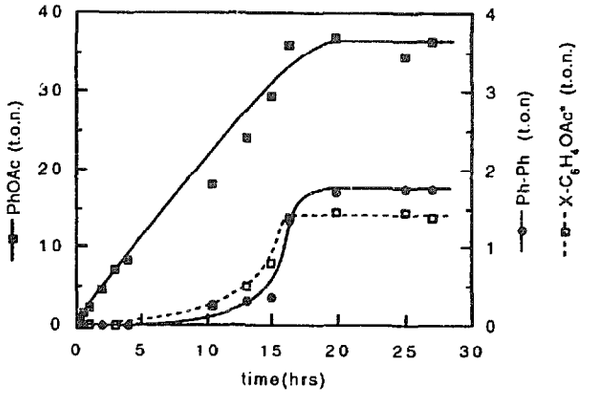


Fig. 1. Time-course of product formation in the Pd(II) catalyzed acetoxylation of benzene. Reaction conditions: benzene (22.4 mmol), $Pd(OAc)_2$ (45.4 μmol), $PhI(OAc)_2$ (2.24 mmol), AcOH 2 ml, 100°C. * X = I or AcO.

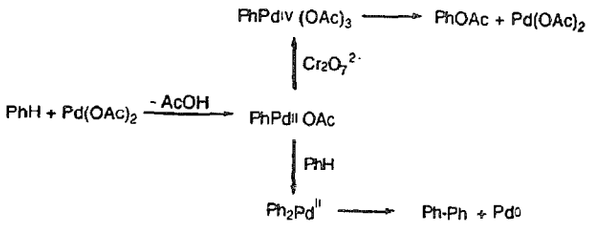


Fig. 2. Reaction mechanism proposed for acetoxylation of benzene using dichromate as the oxidant [1,6,11,14].

mechanism (Fig. 2). This idea is also supported by the finding that without the oxidant, the reaction predominantly gives biphenyl (Table 1, run 2). This suggests that the PhPd(II)OAc intermediate fails to reductively eliminate to form the carbon–heteroatom bond, in contrast to $PhPd(II)NR_2$ and PhPd(II)SR complexes, which do so readily [16]. The new C–O bond is only formed on oxidation, presumably via a reductive elimination from a PhPd(IV)OAc intermediate.

In the absence of the palladium catalyst, phenyl acetate is still formed in small amounts

Table 2
Acetoxylation of a variety of arenes [a]

| Run | Substrate (mmol) | Aryl acetate | | | | By-products (%) [b] |
|---|---|---|---|---|---|---|
| | | % [b] | TON | α:β | o:m:p | |
| 1 | naphthalene (15.0) | 61 | 127 | 57:43 | | PhOAc (1.0) |
| 2 | *p*-xylene (16.3) | 43 | 90 | | | PhOAc (1.0)<br>*p*-methylbenzyl acetate (1.0)<br>*p*-methylbenzaldehyde (1.2) |
| 3 | anisole (18.4) | 40 | 80 | | 44:5:51 | PhOAc (1.5)<br>$PhOCH_2OAc$ (1.0)<br>iodoanisole (5.6) |
| 4 | toluene (18.8) | 39 | 80 | | 43:26:31 | PhOAc (1.1)<br>benzaldehyde (0.5)<br>iodotoluene (1.3) |
| 5 | benzene (22.4) | 39 | 78 | | | biphenyl (0.8)<br>$X\text{-}C_6H_4OAc$ [c] (2.8) |
| 6 [d] | benzene (22.4) | 75 | 37 | | | biphenyl (3.5)<br>$X\text{-}C_6H_4OAc$ (2.9) |
| 7 | phenyl acetate (15.8) | 15 | 31 | | 42:25:33 | $I\text{-}C_6H_4OAc$ (2.8) |
| 8 | chlorobenzene (19.7) | 14 | 27 | | 41:29:30 | PhOAc (1.5) |
| 9 | iodobenzene (17.9) | 12 | 23 | | 39:38:23 | PhOAc (1.4) |
| 10 | mesitylene (14.4) | 9 | 19 | | | PhOAc (1.7)<br>3,5-dimethylbenzaldehyde (2.0)<br>iodomesitylene (6.5) |

[a] Arene 2 ml, AcOH 2 ml, $Pd(OAc)_2$ 22.3 ± 0.9 μmol, $PhI(OAc)_2$ 4.47 mmol, 100 ± 2°C, 21 h.
[b] Based on oxidant.
[c] X = I or AcO.
[d] $Pd(OAc)_2$ 45.4 μmol, $PhI(OAc)_2$ 2.24 mmol.

(run 3). It does not form by a decomposition of $PhI(OAc)_2$ to phenyl acetate and IOAc (run 4), but probably arises via the following pathway:

$$PhI(OAc)_2 + PhH \xrightarrow{-AcOH} Ph_2IOAc \rightarrow PhOAc + PhI \quad (2)$$

The reaction proceeds in good yield even without acetic acid as solvent (run 5), although the use of this solvent is essential with many other oxidants [6].

Since the $PhI(OAc)_2$ oxidant contains an arene ring, we had to consider the possibility that the PhOAc product is derived from the oxidant rather than the benzene substrate. In fact, $PhI(OAc)_2$ is only a minor contributor to the reaction as shown by the results of the reaction of 100% D $C_6D_6$ under the conditions of run 1 of Table 1, which gave a 20:1 mixture of $C_6D_5OAc$: PhOAc.

### 3.2. Other arenes

The reaction was also studied for other arenes (Table 2). Some cases are important in showing the *o-/m-/p*-selectivity and/or in distinguishing between nuclear versus side-chain reaction. The cases of *p*-xylene, anisole and toluene (runs 2–4) show that nuclear substitution is the major product, while side chain oxidation is a very minor pathway. The *o-/m-/p*-selectivity is unusual in that *ortho*-substitution is slightly favored except for the case of anisole. In all the cases but run 6, very little of the aryl coupling products were found, perhaps because use of excess oxidant allows the PhPdOAc intermediate to be rapidly oxidized to the proposed Pd(IV) intermediate.

### 3.3. Additives

Various potential ligands were tried as additives in the hope that these might influence the ratio of acetoxylation to aryl coupling. Table 3 shows that picolinic acid was the most effective of these in suppressing biaryl formation. No ligand was found that favored biaryl presumably because the role of the ligand is to stabilize Pd(IV) and facilitate oxidation.

### 3.4. Kinetics

The kinetics of the acetoxylation of benzene were studied at 100°C. The rate is independent of the $PhI(OAc)_2$ concentration (Fig. 3), but shows a first order dependence on benzene (Fig. 4). The order in $Pd(OAc)_2$ is 0.5 (Fig. 5), implying that the dimeric palladium salt reversibly dissociates into monomers in its active

Table 3
Acetoxylation of benzene with a variety of additives [a]

| Run | Additive | μmol | TON for PhOAc | TON for $Ph_2$ |
|---|---|---|---|---|
| 1 | none | | 15 | 0.86 |
| 2 | acetylacetone | 270 | 9.0 | 0.86 |
| 3 | $Bu^tCOCH_2COBu^t$ | 114 | 7.5 | 0.03 |
| 4 | $Bu^tCOCH_2COBu^t$ | 271 | 7.2 | < 0.02 |
| 5 | hexafluoroacetylacetone | 125 | 14 | 0.89 |
| 6 | hexafluoroacetylacetone | 279 | 12 | 0.87 |
| 7 | picolinic acid | 122 | 12 | 0.17 |
| 8 | picolinic acid | 276 | 1.3 | 0.02 |
| 9 | 2-hydroxypyridine | 126 | 9.4 | 0.42 |
| 10 | 1,10-phenanthroline | 122 | 2.2 | < 0.02 |
| 11 | pyridine | 303 | 6.0 | < 0.02 |
| 12 | triphenylphosphine oxide | 219 | 13 | 0.82 |

[a] In a flask under atmospheric pressure, benzene (11 mmol), AcOH (10 $cm^3$), $Pd(OAc)_2$ (107–116 μmol), $PhI(OAc)_2$ (2.8 mmol), refluxed for 20–21 h.

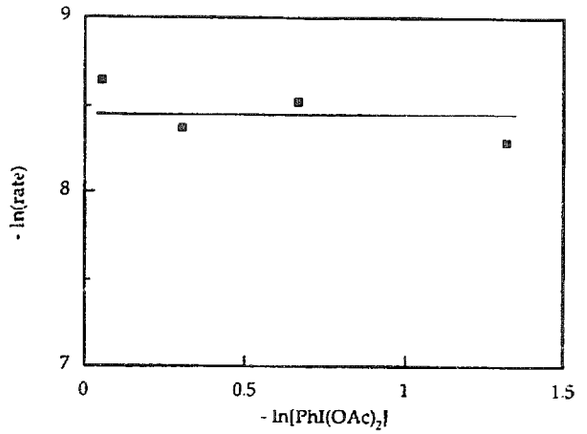


Fig. 3. Dependence of the initial rate for the acetoxylation of benzene on the oxidant concentration. Reaction conditions: $[PhH]_0$ = 5.05 M, $[Pd(OAc)_2]_0$ = 5.02 mM, solvent (acetic acid), 100°C, 3 h.

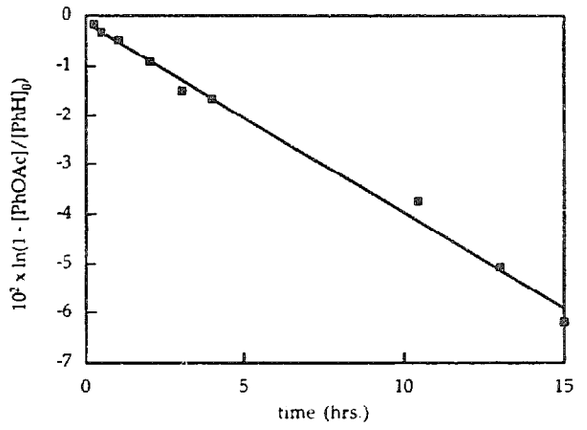


Fig. 4. The first order plots for the acetoxylation of benzene. Reaction conditions: $[PhH]_0$ = 5.14 M, $[Pd(OAc)_2]_0$ = 10.4 mM, $[PhI(OAc)_2]_0$ = 0.514 M, solvent (acetic acid), 100°C.

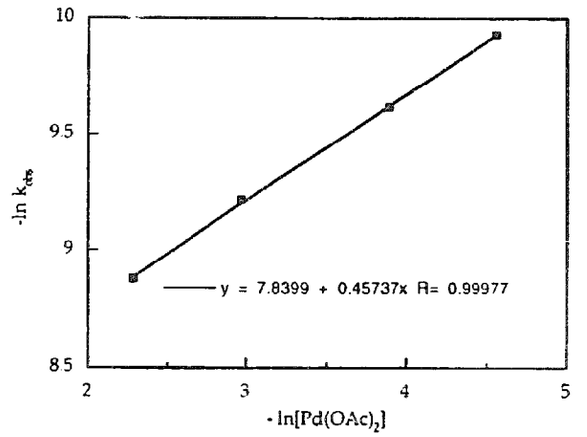


Fig. 5. Dependence of the observed rate constants for the acetoxylation of benzene on the palladium(II) catalyst concentration. Reaction conditions: $[PhH]_0$ = 5.13 M, $[PhI(OAc)_2]_0$ = 0.514 M, solvent (acetic acid), 100°C.

form. These data are consistent with the mechanism of Fig. 2 with the CH activation as the rate determining step. Based on the results of the reactions with benzene and deuterated benzene under identical reaction conditions, a $k_H/k_D$ value of 4.1 was observed. This is consistent with the C–H activation step of Fig. 2 being rate determining.

### 3.5. Mechanism

A radical route can be safely ruled out, and the kinetic isotope effect suggests that CH bond breaking is rate limiting. Net palladation of the arene almost certainly occurs in the first step of the reaction but this could go via a number of pathways: (i) electrophilic attack by Pd; (ii) CH oxidative addition followed by reductive elimination of AcOH, or (iii) by sigma bond metathesis. None of these is definitely excluded by the data. We see no significant acceleration on going from PhH to PhMe and to PhOMe, which argues against (i). Prior results on genuine arene oxidative additions give different selectivity than electrophilic attack. Oxidative addition of anisole to $Cp^*ML$ (M = Rh; L = $PMe_3$) [17] shows an *o:m:p* ratio of 12:76:12, very different from the results obtained in typical electrophilic reactions, which are usually close to 60:0:30. Our results for anisole, 44:5:51, are clearly closer to the electrophilic than the oxidative addition pattern. In collaborative theoretical work with Siegbahn, [18] sigma bond metathesis has been identified as the most probable mechanism in the Shilov reaction, alkane CH activation by Pt(II), so this route is also a possibility here.

## 4. Conclusion

We show that $PhI(OAc)_2$ is a useful oxidant in the Pd catalyzed acetoxylation of arenes, in that it largely avoids biphenyl formation. This is presumably because this oxidant rapidly oxidizes the PhPd(II) intermediate of Fig. 2 and so,

minimizes the side reaction. A number of mechanistic alternatives have previously been considered for this reaction. Although the identity of the rate determining step has been controversial [19], the data obtained to date can best be explained if palladation is rate determining. The *o/m/p* selectivity also seems most easily explained by palladation, rather than by Pd–OAc addition across an arene C=C bond [8,9,13] or simple aromatic substitution [11], but the palladation pathway is still not completely defined.

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## References

[1] R.A. Sheldon and J.K. Kochi, Metal-Catalyzed Oxidations of Organic Compounds, Academic Press, New York, 1981, p. 201.
[2] P.M. Henry, Palladium Catalyzed Oxidation of Hydrocarbons, Reidel, Dordrecht, 1980, p. 310.
[3] J. Tsuji, Synthesis, (1990) 739.
[4] (a) T. Jintoku, H. Taniguchi and Y. Fujiwara, Chem. Lett., (1987) 1865; (b) T. Jintoku, K. Takaki, Y. Fujiwara, Y. Fuchita and K. Hiraki, Bull. Chem. Soc. Jpn., 63 (1990) 438; (c) T. Jintoku, K. Nishimura, K. Takaki and Y. Fujiwara, Chem. Lett., (1991) 193.
[5] J.M. Davidson and C. Triggs, Chem. Ind. (London), (1966) 457.
[6] P.M. Henry, J. Org. Chem., 36 (1971) 1886.
[7] L. Eberson and L. Jönsson, J. Chem. Soc., Chem. Commun., (1974) 885.
[8] L. Eberson and L. Jönsson, Acta Chem. Scand. B, 30 (1976) 361.
[9] L. Eberson and L. Jönsson, Liebigs Ann. Chem., (1977) 233.
[10] L. Eberson and L. Gomez-Gonzales, J. Chem. Soc., Chem. Commun., 1971 (1971) 263.
[11] L.M. Stock, K. Tse, L.J. Vorvick and S.A. Walstrum, J. Org. Chem., 46 (1981) 1757.
[12] L. Eberson and L. Gomez-Gonzalez, Acta Chem. Scand., 27 (1973) 1249.
[13] L. Eberson and L. Gomez-Gonzalez, Acta Chem. Scand., 27 (1973) 1255.
[14] E. Benazzi, C.J. Cameron and H. Mimoun, J. Mol. Catal., 69 (1991) 299.
[15] (a) Y. Kita, H. Tohma, K. Hatanaka, T. Takada, S. Fujita, S. Mitoh, H. Sakurai and S. Oka, J. Am. Chem. Soc., 116 (1994) 3684; (b) O. Prakash and S.P. Singh, Aldrichim. Acta, 27 (1994) 15; (c) A. Varvoglis, Chem. Soc. Rev., 10 (1981) 377; (d) A. Varvoglis, Synthesis, (1984) 709; (e) P.S. Radhakrishnamurti, H.P. Panda and D.C. Pradhan, Indian J. Chem., 26A (1987) 297.
[16] (a) D. Barañano and J.F. Hartwig, J. Am. Chem. Soc., 117 (1995) 2937; (b) M.S. Driver and J.F. Hartwig, J. Am. Chem. Soc., 117 (1995) 4708.
[17] W.D. Jones and F.J. Feher, J. Am. Chem. Soc., 106 (1984) 1650.
[18] P.E.M. Siegbahn and R.H. Crabtree, J. Am. Chem. Soc., (1996) in press.
[19] A.N. Vedernikov, A.I. Kuramshin and B.N. Solomonov, J. Chem. Soc., Chem. Commun., (1994) 121.