Nuclear Acetoxylation of Aromatic Compounds by Palladium(II) Acetate: A Reversal of the Usual Isomer Distribution Pattern in Aromatic Substitution

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Summary Palladium(II) acetate acetoxylation of aromatic compounds containing *ortho,para*-directing substituents gives predominantly *meta*-acetoxy-compounds.

PALLADIUM(II) ACETATE is known to oxidize alkylaromatic compounds with formation of benzyl acetates predominantly,[1–4] nuclear acetoxylation being a minor side-reaction.[1] Analogous reactions with olefins give enol and allylic acetates, presumably *via* an oxypalladation mechanism.[5] We now report experimental conditions for this reaction under which *nuclear* acetoxylation of aromatic compounds can be effected, and note the results of a study of the effect of various substituents on the orientation of the incoming acetoxy-group.

The conditions for optimum yields of nuclear acetate were established using *p*-xylene as a model compound. Earlier studies[2–4] had shown that *p*-methylbenzyl acetate (I) and αα'-*p*-xylylene diacetate (II) were the major products in the presence of excess of alkali metal acetate in glacial acetic acid. However, we now have found that nuclear acetoxylation becomes the preferred reaction if excess of acetate is avoided and the reaction is performed under oxygen. The presence of even a small amount of sodium acetate drastically lowers the yield of the nuclear acetoxylation product, 2,5-dimethylphenyl acetate (III), with a concomitant increase in the yield of side-chain acetates (I) and (II). Conducting the reaction in an argon atmosphere has a similar effect.

The reaction can be made catalytic in palladium(II) acetate. Thus, when *p*-xylene was heated at 110° in a solution of $Pd(OAc)_2$ in glacial acetic acid with a slow stream of oxygen bubbling through the mixture, a 70:30 mixture of (III) and (I), respectively, could be isolated in 450% yield [based on $Pd(OAc)_2$] after 150 h.

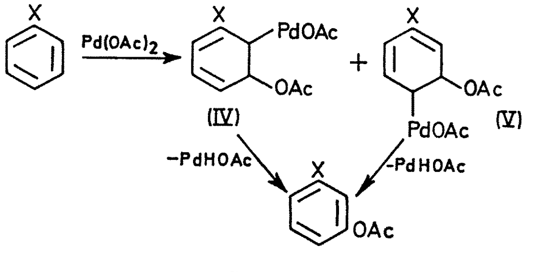
Under these conditions, a number of aromatic compounds

TABLE. *Isomer distributions from* $Pd(OAc)_2$ *or anodic oxidation of aromatic compounds*

		$Pd(OAc)_2$ oxidation[a]			Anodic oxidation[6]	
Compound	*o*(α)	*m*(β)	*p*	*o*(α)	*m*(β)	*p*
t-Butylbenzene	—	95	5	35	22	43
Anisole[b]	1	97	2	67	4	29
Biphenyl	2	98	—	31	1	68
Chlorobenzene	3	88	9	37	5	58
Bromobenzene	5	81	14	30	3	67
Iodobenzene[c]	25	69	6	18	4	78
Naphthalene	50	50	—	96	4	—

[a] Isomer distributions were determined at low conversions; in separate experiments it was established that the acetoxylation products were not oxidized under the reaction conditions used. [b] Small amounts of phenol and acetoxymethyl phenyl ether were also formed. [c] Some biphenyl and di-iodobenzenes were also formed.

were subjected to $Pd(OAc)_2$ oxidation and the isomer distribution of the nuclear acetoxylation product was determined for comparison with another direct acetoxylation process, anodic acetoxylation.[6] These results are given in the Table. The two methods are strikingly different in this respect; the anodic process displays substituent effects analogous to ordinary electrophilic aromatic substitution reactions, whereas the Pd^{II} acetoxylation shows a complete reversal of this orientation pattern, at least for the *ortho,para*-directing substituents chosen here. We suggest that acetoxylation by $Pd(OAc)_2$ takes place as an electrophilic addition process, oxypalladation products being formed as intermediates [*e.g.* (IV) and (V)]. Deoxypalladation of the oxypalladation product would then produce the *meta*-isomer (Scheme).[7]



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