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OXIDATIVE CYCLODIMERIZATION OF N,N-DIMETHYLANILINES
A NOVEL CARBON-CARBON BOND FORMATION BY PALLADIUM(II) ACETATE

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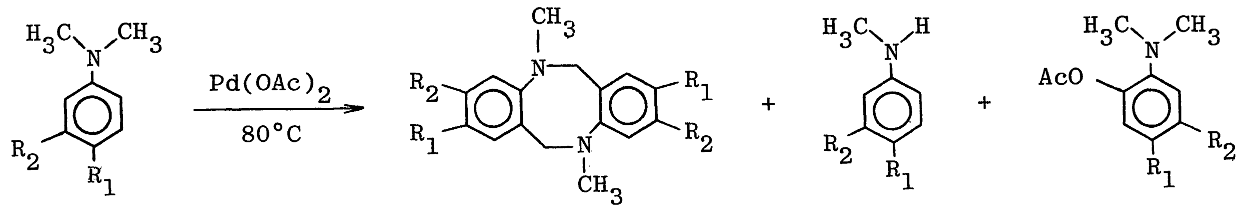
The reaction of N,N-dimethylanilines p-substituted by electron-donating groups with palladium(II) acetate in a mixed solvent of benzene and acetic acid gave cyclodimerized products, i.e. 5,6,11,12-tetrahydrodibenzo[b,f][1,5]diazocine derivatives in good yields, via novel C-C bond formation, along with small amount of acetoxylated or demethylated products. Radical cation species was suggested as a cyclodimerization intermediate.

Palladium(II) salts are known as useful reagents for the C-C bond formation between aromatic rings and other carbon compounds, such as oxidative coupling between aromatic rings,1) aromatic carbonylation with carbon monoxide,2) or aromatic vinylation with olefins.3) However, to our knowledge, the C-C bond formation between aromatic ring and N-methyl carbon is unknown.

In a course of our study on organic transformation of aromatic amines by metal compounds,4) we found that p-substituted N,N-dimethylanilines (1) are transformed to 5,6,11,12-tetrahydrodibenzo[b,f][1,5]diazocine derivatives (2) by palladium(II) acetate in good yields.5) The reaction contains a novel C-C bond formation between aromatic ring and N-methyl carbon, and is interesting from mechanistic and synthetic view points.

In a typical reaction, a mixture of N,N-dimethyl-p-anisidine (1a) (10 mmol), palladium(II) acetate (5.0 mmol), benzene (25 ml), and acetic acid (25 ml) was heated at 80°C under an atmosphere of nitrogen for 5 h. During the reaction, palladium (II) acetate was reduced to metallic palladium and 48.5 % of starting 1a was consumed. The organic products were separated by silica gel column-chromatography and



1 a. R_1= OCH_3, R_2= H
b. CH_3 H
c. CH_3 CH_3
d. Cl H

2 3 4

identified by ir, nmr, mass spectra, and elemetal analysis. After the work-up, 3,8-dimethoxy-5,11-dimethyl-5,6,11,12-tetrahydrodibenzo[b,f][1,5]diazocine (2a) was isolated in a yield of 51.3 %, along with 1.5 % of N,N-dimethyl-o-acetoxy-p-anisidine (4a) and small amount of N-methyl-p-anisidine (3a). 2a was characterized as follows: mp 136.0-137.0°C; nmr ($CDCl_3$, TMS) δ 4.25(s, 4H), 2.84(s, 6H), 3.85(s, 6H); mass (m/e) 298 (M^+); elemental analysis, required C 72.45, H 7.43, N 9.37% ; found C 72.17, H 7.57, N 9.42%. Similar reactions of p-substituted N,N-dimethylanilines with palladium(II) acetate are summarized in Table 1.

As shown in Table 1, some acetoxylated or demethylated anilines (4 or 3) were obtained as by-products. When the reaction of N,N,2,4-tetramethylaniline (1e, 10 mmol) with palladium(II) acetate (5 mmol) was carried out in a mixed solvent (50 ml) of acetic acid and benzene (1:1) at 80°C for 5 h, 52.5 % of 1e was recovered and 4-(N,N-dimethylamino)-3-methylbenzyl acetate (5e, 40.0 %), N,2,4-trimethylaniline (3e, 4.5 %), and N,N,2,4-tetramethyl-6-acetoxyaniline (4e, 3.3 %) were isolated. The cyclodimerization was suppressed by the presence of the ortho substituent, as expected, and the major reaction path was acetoxylation, though it occurred mainly at benzylic position. The steric effect of ortho substituent may also disturb the reactions at ring carbon and N-methyl carbon, causing the preferential p-benzylic acetoxylation. Only an isolated product derived through the reaction on the N-methyl group was the demethylated product (3e). The demethylation may be explained in terms of easy hydrolysis of N-methyl acetoxylated product, followed by deformylation to form 3, during the reaction or the work-up.

In acetic acid in the absence of benzene or toluene, the yield of cyclodimer (2a) was extremely low (2.7 %), while the addition of benzene or toluene gave 2a in good yields (Table 1). The role of benzene or toluene in the cyclodimerization is not clear from the present result. However, the following point was elucidated.

Table 1. Reaction of p-Substituted N,N-Dimethylanilines with Palladium(II) Acetate

Reactants			Conversion of 1[a] (%)	Products (%)[b]		
				2	3	4
1a,	benzene,	AcOH[d]	48.5	2a (51.3)	3a (sm)[d]	4a (1.5)
1b,	benzene,	AcOH	66.1	2b (52.4)	3b (5.0)	4b (trace)
1b,	toluene,	AcOH	59.2	2b (50.0)	ND[d]	ND
1b,		AcOH	68.9	2b (2.7)	ND	ND
1c,	benzene,	AcOH	49.8	2c (43.2)	3c (trace)	4c (trace)[c]
1d,	benzene,	AcOH	87.3	2d (10.3)	2d (17.0)	4d (trace)

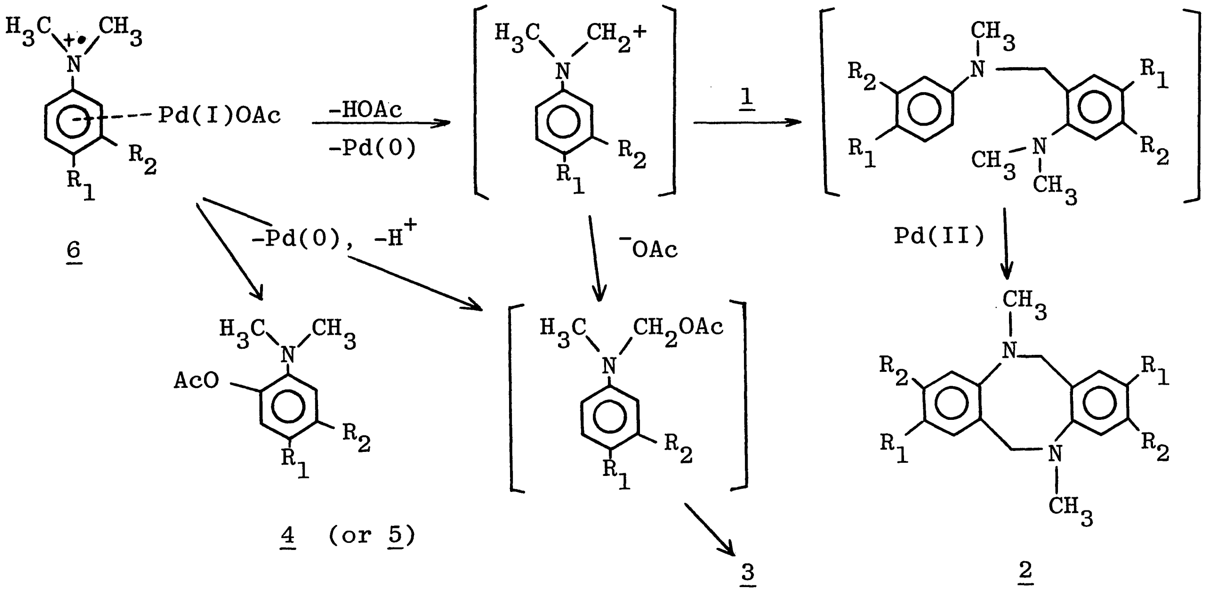
a. Conversion calculated from recovered 1.
b. Yields of isolated products based on consumed 1.
c. A small amount of N,N-dimethylaminobenzyl acetates was isolated.
d. Abbreviation: sm; small amount, ND; not determined, Ac; CH_3CO

Notwithstanding the fact that benzene and toluene react with palladium(II) acetate to give biphenyls and acetoxyphenyls at 80°C in acetic acid,[1b)] these products were not detected in the present reactions on the glc of product mixtures. On the other hand, a similar reaction of N,N-dimethylamino-p-acetophenone (1f) in a mixed solvent of benzene and acetic acid (1:1) resulted in almost quantitative recovery of the starting material (1f), although palladium(II) acetate was completely reduced to metallic palladium. A major product in the reaction was diphenyl (35 %). The fact may show that palladium(II) acetate very rapidly or selectively reacts with N,N-dimethylanilines p-substituted by electron-donating groups, which have lower oxidation potentials than those p-substituted by electron-attracting groups.

On the basis of these observations, it is likely that cyclodimerization, acetoxylation, and demethylation may occur through a common intermediate.

In the previous report,[4b)] it was suggested from the observation of the visible absorption spectra of the reactive intermediate that the reaction of N,N-dimethylanilines with palladium(II) compounds in acetic acid proceeds via a radical cation intermediate. The p-substituted N,N-dialkylanilines with lower oxidation potentials may be expected similarly to undergo one electron oxidation by palladium(II) acetate. The probable radical cation intermediate (6), generated from the reaction of 1 with palladium(II) species, may take place the subsequent reqctions as shown in Scheme 1.

Further investigation on these reactions is now in progress.



Scheme 1

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References and Notes

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