

Palladium on Charcoal-catalysed Arylation of Methyl Vinyl Ether with 4-Bromonitrobenzene

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Palladium on charcoal has been used as a catalyst in the reaction of 4-bromonitrobenzene with methyl vinyl ether to give 81% of the desired (*E*)- and (*Z*)-methyl 2-*p*-nitrophenylvinyl ether. In addition, methyl 1-*p*-nitrophenylvinyl ether, isolated as 4-nitroacetophenone, was formed in 10% yield. The dependence of these yields on solvent, temperature, and reaction time has been studied. Reaction in toluene at 120 °C for 16 h in the presence of triethylamine gave the best results. The *E* to *Z* ratios were approximately constant.

The palladium acetate-catalysed reaction of iodobenzene with ethyl vinyl ether has been reported to give low yields of ethyl phenylvinyl ethers.¹ However, we found that much higher yields were obtained when the halogenobenzenes contained a *p*-nitro group. The ratio of 1-arylvinyl to 2-arylvinyl ether adducts was 5.2:1 and was found to be dependent on the reaction temperature. The presence of triphenylphosphine, surprisingly, was found to decrease the yield drastically and also to have an influence on the regioselectivity.² Therefore, we assumed that this reaction would be quite sensitive to the nature of any components of the reaction mixture which could act as ligands towards palladium. The present paper describes the effects of various amine bases and solvents on yields and regioselectivity. Substitution of palladium on charcoal for the palladium acetate is also described. The optimum reaction time and temperature were determined.

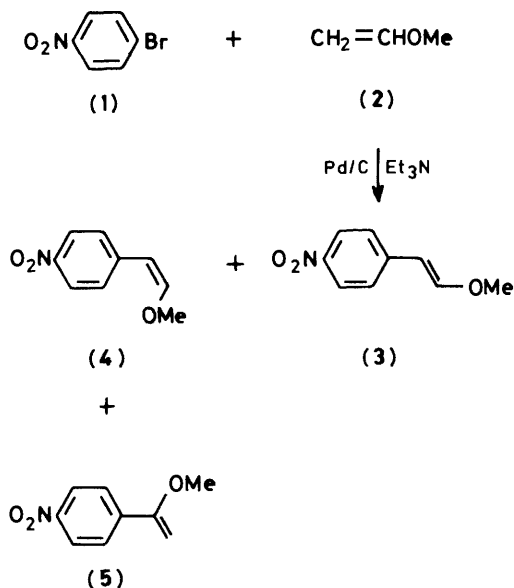
Results and Discussion

The importance of the basicity and bulk of the amine base used in the palladium acetate-catalysed reaction of 4-bromonitrobenzene with methyl vinyl ether in acetonitrile was first studied. Compared to the result with triethylamine, the reaction was slower when the somewhat bulkier tributylamine was used. It should be pointed out, however, that, unlike triethylamine, tributylamine was not completely soluble in the reaction mixture. With dimethylaniline, sterically not too different from triethylamine, but a much weaker base, only traces of the desired products (*E*)- and (*Z*)-methyl 2-*p*-nitrophenylvinyl ether were formed.

At this state of the investigation, it was found that the more convenient palladium on charcoal (Pd/C) could be substituted for palladium acetate, resulting in somewhat higher yields and ratios of 1-arylvinyl to 2-arylvinyl product. In the further optimization of reaction conditions described in this paper, Pd/C was therefore used as the catalyst.

Further amine bases were tested using toluene as solvent. Pyridine, which is a weak base but of low bulk, was completely ineffective, and so was 2,4,6-trimethylpyridine, intermediate both in bulk and in base strength between triethylamine and pyridine. 1,4-Diazabicyclo[2.2.2]octane, which is similar in base strength to triethylamine, but less bulky, gave a slow conversion into the desired product. Thus, a high base strength of the amine appears to be essential, while steric factors are less important.

In order to investigate the importance of solvent in the Pd/C-catalysed reaction in the Scheme, a series of small-scale experiments in sealed tubes were performed. The *E* to *Z* ratios



Scheme.

were approximately constant (1:1) but the ratio of 1-arylvinyl to 2-arylvinyl substitution in the ether produced was dependent on the solvent (see Table 1).

Compared to acetonitrile and ethyl acetate (polar aprotic), the aromatic solvents as well as heptane tended to increase the arylation on the methylene carbon atom of the methyl vinyl ether. However, in heptane the total conversion was low. Also in the protic solvent, methanol, the yield was decreased. One reason for this may be that part of the methyl vinyl ether was converted by palladium-catalysed addition of methanol into the dimethyl acetal.^{3,4} To find out if drying of the solvents was critical, water was added to a reaction carried out in toluene. The yield of (*E*)- and (*Z*)-methyl 2-*p*-nitrophenylvinyl ether (3) and (4) decreased markedly and the amount of unidentified products increased. The water may have caused partial hydrolysis of the methyl vinyl ether and/or the vinyl ethers (3) and (4), leading to easily polymerized aldehydes (*cf.* ref. 5). The vinyl ethers would be expected to be stable to hydrolysis under the basic reaction conditions used, but addition of water to their double bonds may well be palladium-catalysed by analogy with the above-mentioned methanol addition.^{3,4}

The presence of triphenylphosphine in a Pd/C-catalysed reaction in toluene, as previously found when palladium acetate in acetonitrile was used,² reduced the yield as well as the ratio of 1-arylvinyl to 2-arylvinyl products.

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Table 1. Influence of solvent on the Pd/C-catalysed reaction of 4-bromonitrobenzene with methyl vinyl ether at 120 °C^a

Solvent	Products ^b					
	(E)- and (Z)- (3) + (4)	(5) ^c + <i>p</i> -NO ₂ C ₆ H ₄ Ac	<i>p</i> -BrC ₆ H ₄ NO ₂	PhNO ₂	Not identified	[(3) + (4)]/(5)
Acetonitrile	68	12	7	6	7	5.7
Ethyl acetate	54	11	11	4	20	4.9
Methanol	26	7	59	6	2	3.7
Toluene	69	11	9	5	6	6.3
Toluene + 10% water	48	10	6	6	30	4.8
<i>o</i> -Xylene	68	11	9	5	7	6.2
Mesitylene	57	9	24	4	6	6.3
Anisole	65	13	14	6	2	5.0
Chlorobenzene	48	8	12	4	28	6.0
Heptane	30	5	49	4	12	6.0

^a A mixture of 4-bromonitrobenzene (5.0 mmol), (Pd/C 5%; 0.05 mmol) triethylamine (5.5 mmol), methyl vinyl ether (7.5 mmol), and solvent (1.0 ml) was heated in a sealed tube for 16 h. ^b G.l.c. yield, %. ^c The presence of this compound was evident from the n.m.r. spectrum of the crude product, *cf.* G. M. Loudon, C. K. Smith, and S. E. Zimmerman, *J. Am. Chem. Soc.*, 1974, **96**, 465.

Table 2. Influence of temperature and reaction time on the Pd/C-catalysed reaction of 4-bromonitrobenzene with methyl vinyl ether in toluene^a

Temp./°C; time	Products ^b					
	(E)- and (Z)- (3) + (4)	(5) ^c + <i>p</i> -NO ₂ C ₆ H ₄ Ac	<i>p</i> -BrC ₆ H ₄ NO ₂	PhNO ₂	Not identified	[(3) + (4)]/(5)
120; 16 h	69	11	9	5	6	6.3
120; 6 h	39	6	50	3	2	6.5
120; 3 d	28	6	10	5	52	4.7
100; 16 h	38	5	43	4	10	7.6
100; 3 d	51	6	7	4	32	8.5
80; 3 d	34	5	41	3	17	6.8

^{a-c} See the corresponding footnotes in Table 1 except for temperature and time.

In a study of the influence of temperature and time on yield and regioselectivity, toluene was selected as solvent. Preliminary experiments had shown that higher temperatures (135–140 °C) than those used above drastically decreased the yield of (3) and (4). Table 2 gives the results of a systematic study; lowering of the temperature from 120 to 100 °C (16 h reaction time) caused an appreciable decrease in conversion. On the other hand, the 1- to 2-arylvinyl ratio was increased. The product distribution after 16 h at 100 °C is in fact similar to that obtained after 6 h at 120 °C. The distributions differed mainly only in the content of unidentified products. It is obvious from Table 2 that prolonged reaction time (3 days) increased the amount of unidentified products, particularly at the higher temperatures. After 16 h at 120 °C, no more starting material was consumed and the only further changes appeared to be due to decomposition reactions.

In the sealed tube experiments described so far, no stirring or shaking was employed. This means that the outcome of the reactions may to some extent have been dependent on diffusion, heat transfers, *etc.* However, our best results obtained in the sealed-tube runs could easily be improved on a large scale in a well stirred autoclave. Thus, a high yield of (2) and (3), 81% (g.l.c.), and 10% (g.l.c.) of 4-nitroacetophenone were obtained (120 °C for 16 h) after acid work-up. The 1- to 2-arylvinyl ratio was remarkably high (see Table 2; 120 °C for 16 h). Obviously the formation of the 1-arylvinyl ether was favoured under the conditions of the large-scale run.

Julia *et al.*⁶ reported that 4-chloronitrobenzene could be coupled with styrene using Pd/C as the catalyst and sodium carbonate as the base if methanol or ethylene glycol were used as the solvents. We tried to apply these conditions to methyl vinyl ether instead of styrene, without success. Addition of triethylamine did not improve the result. Of course, addition of

glycol solvent to the vinyl ether double bond (as discussed above for methanol, *cf.* refs. 3 and 4) may well have been faster than the slow (relative to 4-bromonitrobenzene) palladiation of 4-chloronitrobenzene.

We have reported² that 4-iodoanisole reacts with methyl vinyl ether in the presence of palladium acetate and triethylamine to give 4-methoxyacetophenone as the only isolated product (55%). A somewhat lower yield was obtained using palladium on charcoal as the catalyst.

We are at present not able to give a satisfactory explanation of the fact that the heterogeneous reaction gives a regioselectivity which differs from that of the homogeneous reaction starting from 4-bromonitrobenzene. We are continuing our studies of these effects.

Experimental

N.m.r. spectra were recorded on a Varian T 60 spectrometer. Quantitative gas chromatographic analyses utilized a Perkin-Elmer Sigma 1 (Sigma 10 Data System) gas chromatograph equipped with a 2 m column of 10% OV 101 on Chromosorb WHP, 80–100 mesh, and a flame ionization detector. Phenanthrene was used as internal standard. 4-Chloronitrobenzene (KEBO), 4-bromonitrobenzene (Fluka AG), methyl vinyl ether (Merck), and palladium on charcoal (Engelhard) were used without purification. The amine bases and solvents were used as received.

General Procedure for Palladium-catalysed Arylation of Methyl Vinyl Ether.—(A) *Sealed tube experiments.* A mixture consisting of 4-bromonitrobenzene (1.01 g, 5.0 mmol), triethylamine (0.76 ml, 5.5 mmol), palladium on charcoal (5%;

106 mg, 0.05 mmol), and the solvent (1.0 ml) in a glass tube was cooled below 0 °C. Methyl vinyl ether (0.56 ml, 7.5 mmol) was added and the tube was sealed. After heating, the mixture was diluted with methylene chloride, and analysed by gas chromatography.

The effect of different bases on the reaction is shown by comparison of different reaction conditions:

Pd(OAc)₂, acetonitrile, 6 h: triethylamine, (1) 42%, (3) and (4) 23%; tributylamine, (1) 58%, (3) and (4) 17%; dimethylaniline, (1) 87%, (3) and (4) 0.5%.

Pd/C, toluene, 16 h: triethylamine, (1) 9%, (3) and (4) 69%; pyridine, (1) 93%, (3) and (4) 1%; 2,4,6-trimethylpyridine, (1) 93%, (3) and (4) 1%; 1,4-diazabicyclo[2.2.2]octane (1) 71%, (3) and (4) 7%.

(B) *Autoclave experiments.* 4-Bromonitrobenzene (48.5 g, 0.24 mol), triethylamine (38.8 ml, 0.28 mol), Pd/C (5%; 2.4 g, 1.1 mmol), and toluene (50 ml) were added to an ice-cold autoclave (Parr, 250 ml, Hastelloy B). After addition of methyl vinyl ether (28.5 ml, 0.38 mol) the autoclave was closed and heated to 120 °C. After reaction with vigorous stirring for 16 h and cooling, the reaction mixture was poured into ice-cold 10% hydrochloric acid-methylene chloride. After thorough shaking and filtration, the organic layer was separated. The aqueous phase was extracted twice with methylene chloride and the combined organic phases were washed once with water. After drying (Na₂SO₄), the methylene chloride was removed by evaporation. Gas chromatographic analysis of the residue showed that it contained (*E*)- and (*Z*)-methyl 2-*p*-nitrophenylvinyl ether (81%) and 4-nitroacetophenone (10%). For separation and structure analysis, see ref. 2.

Comparative runs with palladium-free carbon gave only starting materials indicating that palladium is essential.

The attempted arylation of methyl vinyl ether by analogy with the preparation of 4-nitrostilbene from 4-chloronitrobenzene and styrene⁶ was performed as just described starting with a mixture of 4-chloronitrobenzene (15.8 g, 0.10 mol), sodium carbonate (10.6 g, 0.10 mol), Pd/C (5%; 4.0 g, 1.9 mmol), methyl vinyl ether (8.3 ml, 0.11 mol), ethylene glycol (20 ml), and dioxane (40 ml). N.m.r. analysis of the crude product showed that it contained only traces of (3) and (4) and a large amount of starting material. When the experiment was repeated in the presence of triethylamine (15.3 ml, 0.11 mol), (3) and (4) could not be detected, but the starting material had been converted into unidentified products.

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