

Nitration of Benzenoid Compounds by Palladium Salts and by Nitrogen Dioxide

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The nitration of benzenoid compounds by palladium nitrate and by a mixture of palladium acetate and sodium nitrite has been studied under a variety of conditions. The latter system yields nitrobenzene semi-catalytically in chloroacetic acid at 100° (ca. 1200% in an oxygen atmosphere), with relatively little by-product (ester) formation. The use of nitrogen dioxide in place of sodium nitrite results in a fully catalytic system. Observations which bear on the mechanisms are discussed. Aromatic nitration has also been effected in good yield by passing nitrogen dioxide into a solution of the aromatic compound in trifluoroacetic acid. In contrast to the reactions involving palladium(II), this is almost certainly an S_N2 process involving the nitronium ion.

THE reports of the reactions of benzenoid compounds with palladium(II) salts¹ include a small number of examples of nitration. Thus, Ichikawa *et al.* found nitro-compounds as by-products in the reactions of benzene, toluene, the xylenes, and mesitylene with palladium nitrate in acetic acid at 90–115°;² Henry obtained some nitrobenzene from benzene with palladium acetate in acetic acid containing methanesulphonic acid at 90° when either sodium nitrite or sodium nitrate was included;³ and Tissue and Downs⁴ obtained nitrobenzene and phenyl acetate, in proportions varying from ca. 1:2 to 2:1 depending on the conditions, by treating colloiddally dispersed Pd⁰ with sodium nitrite, nitrogen dioxide, or nitric oxide and oxygen and then heating with benzene in acetic acid at 100°.

We have explored the possibility of using a palladium(II) salt, preferably in catalytic amount, to effect aromatic nitration in synthetically useful yield and without significant formation of other products such as acetoxy-derivatives. We chose palladium nitrate in an acetic acid medium for our first experiments and, in order to provide an initially homogeneous medium, added

¹ P. M. Maitlis, 'The Organic Chemistry of Palladium,' vol. 2, Academic Press, 1971, p. 160.

² K. Ichikawa, S. Uemura, and T. Okada, *Nippon Kagaku Zasshi*, 1969, **90**, 212.

dimethyl sulphoxide (10%) to the acetic acid. The results of these and related experiments are in Table 1.

TABLE 1

Products from the oxidation of benzene (6.5 mmol) with a palladium(II) salt (0.5 mmol) in a mixture of RCO₂H and dimethyl sulphoxide (10:1 v/v) at 100° with or without sodium nitrite

Experiment	Pd ^{II} salt	Time (h)	Products (mol %) ^b			
			RCO ₂ H	PhNO ₂	PhO-COR	PhPh
1	Nitrate	1	HOAc	3	20	
2		2	HOAc	12	42	
3		5.5	HOAc	13	51	1
4		12	HOAc	15	56	5
5*	Acetate	2	HOAc	16	11	
6*		7	HOAc	28	29	
7		2	CH ₂ Cl·CO ₂ H	25	8	
8*		2	HOAc	15	11	
9*		24	HOAc	49	48	
10*		2	CH ₂ Cl·CO ₂ H	29	7	
11*		8	CH ₂ Cl·CO ₂ H	72	11	
12*	2	Me ₃ C·CO ₂ H	trace	9		

* 2.9 mmol NaNO₂ added. ^b Based on Pd^{II}.

Experiments 1–4 show that the two major products, nitrobenzene and phenyl acetate, accumulate steadily with time, but the latter, unwanted product is throughout the major constituent. However, the yield of

³ P. M. Henry, *J. Org. Chem.*, 1971, **36**, 1886.

⁴ T. Tissue and W. J. Downs, *Chem. Comm.*, 1969, 410.

biphenyl increases sharply after the first few hours, possibly because its formation involves the palladium which is slowly deposited during the reaction. The inclusion of sodium nitrite significantly raises the yield of the nitro-compound relative to the ester, but this ratio is even more effectively increased by the use of chloroacetic acid instead of acetic acid (experiment 7); however, the total yield is depressed for the same reaction time (*cf.* experiment 2). A mixture of palladium acetate and sodium nitrite also gives a higher ratio of nitrobenzene to ester than palladium nitrate, and after 24 h the (stoichiometric) yield is very high. Again, the ratio is increased by replacing acetic by chloroacetic acid, as also is the overall yield in this instance, whereas when pivalic acid is used both ratio and yield are very small.

The promising result from experiment 11 led us to study further the use of palladium acetate and sodium nitrite with chloroacetic acid (Table 2). Dimethyl sulphoxide is not necessary with this system to provide homogeneity at the start of the reaction, and it was therefore omitted. This led to substantial increases in both the total yield and the ratio of nitrobenzene to ester after reaction for the same time at 100° (*cf.* experiments 10 and 13);* since both decreased sharply when the temperature was reduced to 65°, all further reactions were at 100°. Reduction of the concentration of palladium acetate caused a further marked rise in the overall yield (experiment 16) and showed conclusively that reduced palladium(II) was being reoxidised. Since atmospheric oxygen was the likeliest oxidant, reaction was carried out in an atmosphere of oxygen instead of air. Periodic monitoring showed the amount of product increased for about 6 h and then levelled off to give the final yields quoted for experiment 17, by

TABLE 2

Products from the oxidation of benzene (6.5 mmol) with Pd(OAc)₂ in chloroacetic acid containing sodium nitrite (2.9 mmol)

Experiment	Temp. (°C)	Pd(OAc) ₂ (mmol)	Time (h)	Products (mol %) ^d	
				PhNO ₂	PhO-CO-CH ₂ Cl
13	100	0.5	2	110	9
14	80	0.5	5	59	4
15	65	0.5	7	12	22
16	100	0.1	3	490	32
17 ^a	100	1	18	1100	10
18 ^{a,b}	100	1	9	1200	16
19 ^c	100	0.1	2	800	150

^a 0.13 mol Benzene; reaction under oxygen. ^b 5.7 mmol NaNO₂. ^c PhHgOAc in place of PhH. ^d Based on Pd^{II}.

which time most if not all the palladium had been deposited as metal. Little effect was noted when the amount of sodium nitrite was doubled (experiment 18). Phenylmercury(II) acetate was found also to give nitrobenzene efficiently (experiment 19), and since *p*-tolylmercury(II) acetate gave *p*-nitrotoluene but neither the *ortho*- nor the *meta*-isomer whereas toluene gives all three (see later), we infer that protodemercuration does not occur as a first step.

* Only *ca.* 0.1% nitrobenzene was formed when the palladium salt was omitted.

The selectivity of the nitrating agent was examined by treating a large excess of an equimolar mixture of benzene and toluene with palladium acetate in chloroacetic acid containing sodium nitrite at 100° in an oxygen atmosphere. Under these conditions, the amount of each aromatic compound lost was negligible, so that the ratios of the yields of the products correspond to their relative rates of formation. The yields of nitrobenzene and *o*-, *m*-, and *p*-nitrotoluene were, respectively, 113, 11, 50, and 57%, from which the following partial rate factors are derived: *o*-Me, 0.3; *m*-Me, 1.3; *p*-Me, 3.0. (The values were essentially the same for reaction in air.) A similar experiment with benzene and chlorobenzene gave the partial rate factors: *o*-Cl, 0.4; *m*-Cl, 0.3; *p*-Cl, 0.7.

Palladium acetate with sodium nitrite in chloroacetic acid shows some promise as a nitrating agent since the palladium salt is required in much less than stoichiometric quantities. However, although each palladium ion can effect the nitration of up to some twelve molecules of benzene, its use in catalytic quantities has not proved possible since it is eventually lost irreversibly as palladium metal. Now Tisue and Downs noted that when nitrogen dioxide was employed in place of sodium nitrite no palladium metal was deposited and yields, based on palladium, could be as high as 6000%.⁴ However, their acetic acid system suffers from the drawback that a substantial amount of phenyl acetate is also produced. Combining the two systems surmounts this problem. On passing nitrogen dioxide into a solution of benzene in chloroacetic acid containing a catalytic amount of palladium acetate at 100° for 17 h, a yield [based on palladium(II)] of 18,300% of nitrobenzene was obtained, contaminated by only minor amounts of chloroacetate ester. At this stage 48% of the benzene had been nitrated and the system was still catalytically active. In view of the ability of nitrogen dioxide in trifluoroacetic acid to nitrate benzene (see later) it has to be shown that palladium(II) is indeed a necessary ingredient of the system. In the absence of palladium acetate 0.68% of the benzene was nitrated in 3 h. Palladium acetate was then added and $\frac{1}{2}$ h later the yield of nitrobenzene had risen to 9.9%, confirming the catalytic nature of the palladium.

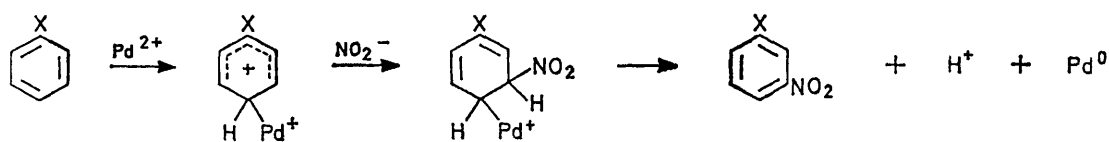
It is not possible to give a full description of the mechanism of the nitration, but three observations are pertinent to the nitrations effected by sodium nitrite. First, for both toluene and chlorobenzene, the *para*-isomer is more reactive than the *meta*-position. This argues against reaction of the benzenoid compound with electrophilic palladium followed by the uptake of nitrite ion and the elimination of palladium, as in Scheme 1, and is in contrast to some reactions of palladium(II) acetate with benzenoid compounds in which *ortho*, *para*-directing substituents induce acetoxylation mainly at the *meta*-position and for which a sequence analogous to that in Scheme 1 has been suggested.⁵

⁵ L. Ebersson and L. Gomez-Gonzales, *Acta Chem. Scand.*, 1973, **27**, 1249, 1255.

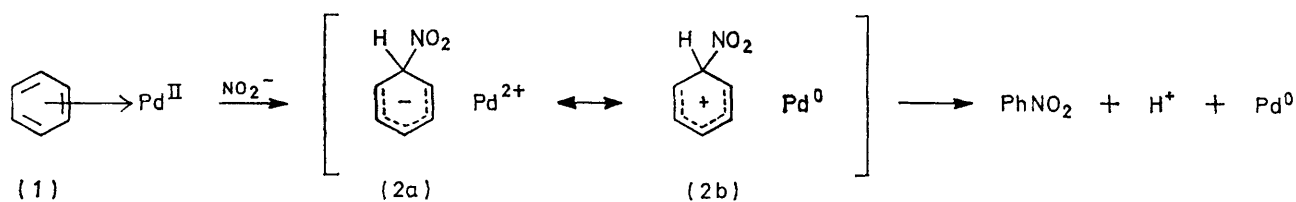
Secondly, the selectivity of the reagent, as revealed by the partial rate factors for toluene and chlorobenzene, is far smaller than for the nitronium ion or carriers of this ion,⁶ and we discount NO_2^+ as the reagent. Nevertheless, the order of partial rate factors, $p\text{-Me} > m\text{-Me} > (\text{H}) > p\text{-Cl} > m\text{-Cl}$, is that for an electrophilic reagent. Thirdly, under otherwise similar conditions, the ratio of the yields of nitrobenzene and ester increases, as the carboxylic acid in the solvent is changed, in the order $\text{Me}_3\text{C}\cdot\text{CO}_2\text{H} < \text{HOAc} < \text{CH}_2\text{Cl}\cdot\text{CO}_2\text{H}$. This is the order in which the acid strength increases and, presumably, the nucleophilicity of the carboxylic acid decreases, and it would be consistent with competitive nucleophilic attack by nitrite ion and the carboxylic acid on the aromatic molecule.

It was found that nitration occurred to a significant extent in the absence of the palladium salt and we studied this system further. Nitration proved to be more efficient when nitrogen dioxide was passed through a solution of the aromatic compound in trifluoroacetic acid, instead of including sodium nitrite in the solvent. We now report briefly on the results of this study, which show that the system may have synthetic utility.

Some of the results are in Table 3; an excess of nitrogen dioxide was passed, and the quoted yield of nitrobenzene is based on benzene. The following features are apparent. Nitration is more rapid at the reflux temperature (*ca.* 70°) than at 0°, as would be expected. However, the conversion, in the same time, is greater still at 50°, possibly because nitrogen dioxide



SCHEME 1



SCHEME 2

The second and third observations are at first sight incompatible. They could, however, be reconciled by a mechanism such as that which we tentatively suggest in Scheme 2. Here, the benzene ring, rendered somewhat electron-deficient by π -complexation to Pd^{II} (other ligands unspecified), is attacked by nitrite ion to form the intermediate (2) which incorporates palladium and from which Pd^0 is then extruded. If the formation of (2) is rate-determining and canonical (2b) is of greater significance than (2a), then the reaction will show the characteristics of electrophilic substitution; but, to the extent that (2a) is also a contributor, the aromatic ring in the intermediate, and the preceding transition state, may have comparatively little positive charge associated with it, in accord with the small selectivity. If this is an adequate description of the mechanism, then it is likely that palladium nitrate acts as a nitrating agent only after nitrate ion has first been reduced to nitrite in the course of reoxidising the Pd^0 formed during the competing acyloxylation. Likewise, nitrogen dioxide may act as a source of nitrite ion through reduction by Pd^0 , but it is not clear why this system is catalytically more efficient than that with sodium nitrite.

Aromatic Nitration by Nitrogen Dioxide in Trifluoroacetic Acid.—During the investigation described above, the use of trifluoroacetic acid as a solvent for nitration by palladium acetate and sodium nitrite was explored.

is too rapidly lost from the refluxing solution. Chloroacetic acid is a much less satisfactory medium than trifluoroacetic acid, and in both cases the yield of nitrobenzene is considerably depressed by the inclusion of a small proportion of dimethyl sulphoxide in the

TABLE 3

Formation of nitrobenzene from benzene with nitrogen dioxide in trifluoroacetic acid

Experiment	Temp. (°C)	PhH (mmol)	Time (h)	Yield of PhNO_2 (mol %)
20	0	6.4	5	29
21	Reflux	6.4	1	37
22	Reflux	3.2 ^a	1	2
23	50	12.8	1	54
24	50	12.8 ^b	1	99
25	100	6.4 ^{a,c}	2	0.5

^a 10% Dimethyl sulphoxide included in the solvent. ^b Urea (1.2 g) added. ^c Chloroacetic acid in place of trifluoroacetic acid.

solvent. However, in trifluoroacetic acid, the inclusion of urea leads to an essentially quantitative conversion at 50°.

Four other benzenoid compounds were nitrated under the conditions of experiment 24 (Table 4). In addition, equimolar mixtures of benzene and toluene, and of benzene and chlorobenzene, were nitrated under these conditions except that nitrogen dioxide was passed

⁶ L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, 1963, 1, 35.

TABLE 4

Nitration under the conditions of experiment 24

Aromatic compound	Yield of mononitro-products (mol %)	Isomer distribution		
		<i>o</i>	<i>m</i>	<i>p</i>
PhMe	76	55	2	43
PhCl	100	36		64
PhOMe	50	37.5		62.5
PhCHO	0.3		100	

for only a short time in order to keep the extent of conversion to only *ca.* 5%. The relative yields of nitrobenzene and the appropriate monosubstituted derivative could then be taken as measures of relative nitration rates, from which the following partial rate factors were derived: *o*-Me, 41; *m*-Me, 1.3; *p*-Me, 60; *o*-Cl, 0.05; *p*-Cl, 0.2.*

The isomer distributions in Table 4 are typical of those for electrophilic aromatic substitution, and the partial rate factors for toluene and chlorobenzene are within the ranges found for nitration by the nitronium ion.^{6,7} There is thus no reason to doubt that this is an S_E2 reaction. Trifluoroacetic acid may act to aid ionisation of the N_2O_4 as in reaction (i), and urea presumably functions by removing nitrous acid.



EXPERIMENTAL

Gas chromatography was performed on a Pye instrument (series 104, model 24), using a 6 ft \times 1/4 in column packed with a 10% coating of diethylene glycol adipate on Celite. Products were identified by comparison of retention times and of mass spectra, obtained on an A.E.I. MS12 spectrometer coupled to the chromatograph *via* a heated capillary,

* The isomer distribution and hence the partial rate factors were found to vary somewhat depending on the rate of introduction of nitrogen dioxide. The figures quoted above were obtained at low flowrate. Increasing this led to a reduction in selectivity.

with those of authentic samples. For quantitative work bibenzyl was employed as internal standard.

Materials.—Palladium acetate and nitrate (Johnson Matthey reagents) and phenylmercury(II) acetate (B.D.H. laboratory reagent) were used without further purification. Trifluoroacetic and chloroacetic acids were B.D.H. reagents and nitrogen dioxide was obtained from Cambrian Chemicals Ltd. The nitrotoluenes and chloronitrobenzenes were available within the department. Phenyl chloroacetate, prepared by the method of Mannich and Drauzburg,⁸ had m.p. 42–44° (lit.,⁸ 45°).

Oxidations.—A catalytic quantity of palladium acetate or nitrate was added to a solution of benzene (6.5 mmol) in a mixture (10 ml) of the appropriate carboxylic acid and dimethyl sulphoxide (10 : 1 v/v). Sodium nitrite (2.9 mmol) was added in most cases but in a number of experiments employing chloroacetic acid the dimethyl sulphoxide was omitted. The solutions were heated for various times as set out in Tables 1 and 2, cooled, and poured into water, and the ether extracts were washed (NaHCO₃ and water), dried (MgSO₄), and evaporated. The resultant oils were analysed by g.l.c. Oxidations employing nitrogen dioxide were conducted similarly except that this compound was continuously bubbled through the heated solution.

The Nitrogen Dioxide-Trifluoroacetic Acid System.—Nitrogen dioxide was bubbled through a solution of the appropriate aromatic substrate in trifluoroacetic acid (or chloroacetic acid) as set out in Tables 3 and 4. The cooled solution was poured into water, and the ether extracts were washed (NaHCO₃ and water), dried (MgSO₄), and evaporated. The product was analysed as before.

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⁷ R. G. Coombes and L. W. Russell, *J. Chem. Soc. (B)*, 1971, 2443; S. R. Hartshorn, R. B. Moodie, K. Schofield, and M. J. Thompson, *ibid.*, p. 2447.

⁸ C. Mannich and W. Drauzburg, *Arch. Pharm.*, 1912, 250, 532.