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ARYLATIONS USING DIAZONIUM TETRAFLUOROBORATE AND PYRIDINE

A CONVENIENT SOURCE OF ARYL RADICALS*

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Abstract—Benzenediazonium tetrafluoroborate together with one equivalent of pyridine provides a convenient source of phenyl radicals *via* the homolysis of N-phenylazopyridinium tetrafluoroborate. Partial rate factors and total rate ratios have been determined for attack of a number of aromatic substrates by phenyl radicals produced in this way and are found to be similar to the values obtained using benzoyl peroxide as the source of phenyl radicals. The ratios of isomers formed in the decompositions in moderate and in large excesses of pyridine differ from one another. The results are discussed.

THE Gomberg-Hey arylation of aromatic compounds is usually carried out by adding an excess of sodium hydroxide or acetate solution to a rapidly stirred mixture of a diazonium salt solution and an aromatic liquid. The mechanism of this reaction has finally been clarified by the elegant work of Rüchardt and Merz:[1] it involves the well-known isomerization of the diazonium salt to the diazo-hydroxide, followed by reaction of the diazotate anion with diazonium ion to give the diazo-anhydride which decomposes to give phenyl and diazo-oxide radicals. The phenyl free radicals attack the aromatic substrate and the diazo-oxide radicals abstract hydrogen from the resulting σ-complex. The pattern of substitution thus obtained is typical of homolytic aromatic arylation reactions.[2]

When pyridine is used as the aromatic substrate it is unnecessary to add alkali to the diazonium salt solution, the pyridine itself acting as the base. The diazonium salt solution is added slowly to the excess pyridine and the resulting solution is heated at 40–100° to complete the reaction. The exact function of the pyridine has not been established unambiguously. It has been suggested[3] that pyridine and water (from the diazonium salt solution) first give rise to some hydroxyl ions (pK_a of pyridine is 5·21) which then convert the diazonium salt to the diazohydroxide:

$$C_5H_5N + H_2O \rightleftarrows C_5H_5NH^+ + OH^-$$
$$ArN_2^+X^- + OH^- \rightleftarrows Ar\text{—}N{=}N\text{—}OH + X^-$$

The mechanism *via* the diazo-anhydride would then follow. Alternatively, pyridine could form a salt (I) with the diazonium salt through its lone pair of electrons;[3,4]

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[*] Aromatic Substitution. Part XII. Part XI in this series: R. A. Abramovitch, J. Roy and V. Uma, *Canad. J. Chem.* submitted.

[1] C. Rüchardt and E. Merz, *Tetrahedron Letters* 2431 (1964).

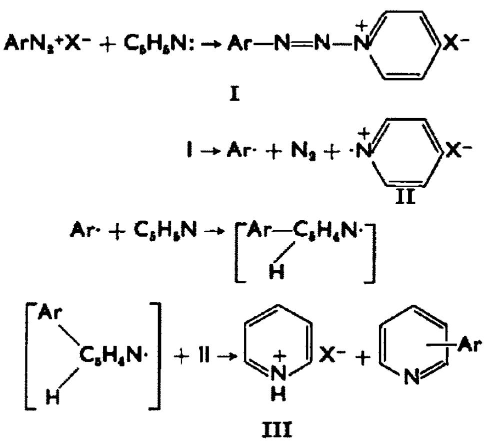
[2] G. H. Williams, *Homolytic Aromatic Substitution* Pergamon Press, London (1960).

[3] J. W. Haworth, I. M. Heilbron, and D. H. Hey, *J. Chem. Soc.* 349 (1940).

[4] R. A. Abramovitch and J. G. Saha, *J. Chem. Soc.* 2175 (1964).

this would undergo homolysis to give a phenyl radical, nitrogen and the pyridinium radical cation (II) which could abstract a hydrogen atom from the σ-complex resulting from attack of the free radical upon another pyridine molecule, as shown in Scheme 1.

Scheme 1



The formation of I finds some support in the fact that no nitrogen is apparently evolved until one equivalent of pyridine has been introduced.[3] Since aqueous solutions of the diazonium salts are usually used it is difficult to differentiate between these two possible mechanisms.

We have now carried out the decomposition of benzenediazonium tetrafluoroborate in aromatic solvents in the presence of one equivalent of dry pyridine per mole of tetrafluoroborate, and present evidence that phenyl radicals are produced in this way. A suspension of benzenediazonium tetrafluoroborate in toluene, bromobenzene, anisole or nitrobenzene was treated with one molar equivalent of pyridine at 75°. Biaryls, pyridinium tetrafluoroborate (III; $X = BF_4$) and nitrogen were the only products detected in these reactions. No phenylpyridines, fluorobenzene or boron trifluoride were formed. This is to be contrasted with the products obtained in the thermal decomposition of benzenediazonium tetrafluoroborate in these solvents in the absence of pyridine:[5] fluorobenzene, the normal Schiemann reaction product, is formed in 90–95% yield, boron trifluoride and nitrogen are copiously evolved, and fluorobiphenyls (0·5–0·8%) and biaryls (3–5%) are usually obtained. Clearly the mechanisms in the presence and absence of pyridine are different. The first step is probably the fast reaction of benzenediazonium tetrafluoroborate with pyridine to form the diazopyridinium salt (I; $Ar = C_6H_6$, $X^- = BF_4^-$). Had this not been a fast step some thermal decomposition of the diazonium salt to give fluorobenzene and boron trifluoride might have been expected. This step is, for the same reason, irreversible to all intents and purposes. The absence of any phenylpyridines in the reaction products eliminates the possibility that any intramolecular rearrangement of the diazopyridinium salt is occurring. The yields of biaryls formed in these reactions were considerably higher (30–40%) than those in the absence of pyridine, and

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[5] R. A. Abramovitch and J. G. Saha, *Canad. J. Chem.* submitted.

compared quite well in most cases with yields obtained using other sources of phenyl radicals.

The intervention of phenyl radicals in the decompositions carried out in the presence of pyridine is indicated quite clearly by the isomer distributions and total rate ratios. The isomer ratios are compared in Table 1 with those obtained in the reactions without pyridine (which probably involve attack by a phenyl diradical cation[5]) and those from phenylations using benzoyl peroxide as the source of phenyl radicals.[2,6] The relative proportions of isomers formed with and without pyridine are appreciably different, particularly in the case where nitrobenzene was the substrate: in the presence of one equivalent of pyridine the isomer ratios are very similar to those obtained from the benzoyl peroxide phenylations. That free radical phenylation is taking place is further indicated (i) by the formation of bibenzyl in nearly 10% yield in the reaction with toluene, and (ii) by the total rate ratios for the phenylation of substituted benzenes compared with benzene itself. The latter are summarized in Table 2, and compared with those determined for phenylations using benzenediazonium tetrafluoroborate alone and using benzoyl peroxide.

TABLE 1. ISOMER RATIOS OBTAINED IN THE PHENYLATION OF AROMATIC SUBSTRATES

Substrate	Position	Isomer ratio for reaction with		
		$C_6H_5N_2^+BF_4^-$ and pyridine[a]	$C_6H_5N_2^+BF_4^-$[b]	$(C_6H_5CO_2)_2$[c]
$C_6H_5CH_3$[e]	*o*-	61·8	57·5	66·5
	m-	21·2	20·0	19·3
	p-	15·0	22·5	14·2
C_6H_5Br	*o*-	55·0	56·1	55·8
	m-	26·2	19·8	27·8
	p-	18·7	24·1	16·5
$C_6H_5OCH_3$	*o*-	61·5	57·5	69·6
	m-	16·5	10·0	14·5
	p-	21·9	32·5	16·0
$C_6H_5NO_2$	*o*-	52·6	19·6	63·1
	m-	14·2	80·4	10·1
	p-	33·2	0	26·9
C_5H_5N	2-		51·8[g] (89·0)[d,g]	54[f]
	3-		32·4 (11·0)	32
	4-		15·7 (0)	14

[a] Reactions carried out at 75°.

[b] Reactions with pyridine were carried out at 40°, the others at 60°.

[c] Reactions with benzoyl peroxide were carried out at 80°.

[d] Using a benzenediazonium tetrafluoroborate: pyridine molar ratio of 1:6.

[e] With benzenediazonium tetrafluoroborate and pyridine a 9·8% yield of bibenzyl was also obtained. No bibenzyl is formed in the absence of pyridine.[5] With benzoyl peroxide a yield of about 13% of bibenzyl is obtained (here hydrogen abstraction by both phenyl and benzoyloxy radicals is taking place).[7]

[f] Reaction carried out at 105°.

[g] Present work.

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[6] R. T. Morrison, J. Cazes, N. Samkoff and C. A. Howe, *J. Amer. Chem. Soc.* **84**, 4152 (1962).

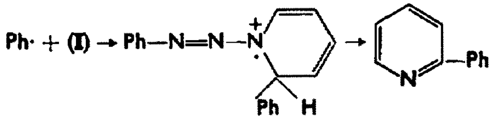
[7] D. H. Hey, H. N. Moulden and G. H. Williams, *J. Chem. Soc.* 3769 (1960).

TABLE 2. TOTAL RATE RATIOS FOR THE PHENYLATION OF C_6H_5X

Substrate	$^{C_6H_5X}_{C_6H_6}K$		
	$PhN_2^+BF_4^-$ with pyridine	$PhN_2^+BF_4^-$ [5]	$(C_6H_5CO_2)_2$ [6,8]
$C_6H_5CH_3$	1·20	0·72	1·23
C_6H_5Br	1·27	0·31	1·14
$C_6H_5OCH_3$	1·50	1·44	2·0
$C_6H_5NO_2$	2·72	0·35	2·9

Two comments may be made at this time concerning the isomer ratios.

(i) The ratio of isomers obtained with pyridine at high dilution (1:250) is the same as that obtained using an aqueous solution of benzenediazonium chloride under standard Gomberg-Hey conditions.[4] If, however, a much larger proportion of diazonium salt to pyridine is used (1:6) the isomer ratio changes drastically, the 2-isomer now being the predominant product (89%), only 11% of the 3-isomer being formed, and none of the 4-isomer. Similar results were obtained independantly by Lynch and Chang[9] (who did not resolve the mixture of 3- and 4-phenylpyridines and therefore did not detect the absence of the 4-isomer under these conditions). These authors suggested that when pyridine was not present in excess phenylation of I rather than of pyridine took place (Eq. i): the phenylazopyridinium cation was thought to be more susceptible to free radical attack than pyridine itself as predicted by molecular orbital calculations (using a Coulomb integral parameter h for $\overset{+}{N}H$ equal to 2·0) of atom localization energies.[10] The latter suggested that attack at C_2 would be favoured over attack at C_3 and C_4. More recent calculations (using $h = 1{\cdot}0$[11] and $h = 2{\cdot}0$[12]) have predicted almost equal reactivities for C_2 and C_4 in the pyridinium ion towards free radical attack with a slight preference for attack at C_2. If, indeed,



(i)

free radical phenylation of I is occurring as illustrated by Eq. (i), the reactivity of the 2-position in I must be very much higher than that in pyridine, as suggested by Lynch and Chang,[9] since more than five molecules of pyridine are available per molecule of I present to compete with it for the available radicals (some phenylazopyridium salt must be decomposing to produce the necessary phenyl radicals). Even then, however, it is quite hard to explain the absence of a measurable amount of 4-phenylpyridine compared with the amount of 3-isomer obtained since the radical localization energies calculated by Brown and Heffernan[10] for the pyridinium ion actually predict a slightly greater reactivity for C_4 than for C_3. An alternative to the Lynch and Chang

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[8] G. H. Williams, *Chem. & Ind.* 1285 (1961).

[9] B. M. Lynch and H. S. Chang, *Tetrahedron Letters* 2965 (1964).

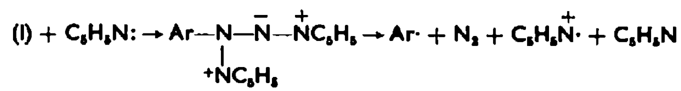
[10] R. D. Brown and M. L. Heffernan, *Austral. J. Chem.* **9**, 83 (1956).

[11] R. A. Barnes, *J. Amer. Chem. Soc.* **81**, 1935 (1959).

[12] R. Zahradník and C. Párkányi, *Coll. Czech. Chem. Comm.* **30**, 355 (1965).

proposal would be that the diazopyridinium complex (I) was undergoing intramolecular attack by the phenyl group, thus leading mainly to the 2-substituted product for geometric reasons. One could also visualize intra- and inter-molecular attack taking place simultaneously to varying extents. It is to be noted that at diazonium salt:pyridine ratios of 1:6 the mixture was heterogeneous initially. At the higher dilutions, however, the mechanism is undoubtedly as in Scheme 1. An induced decomposition of I by pyridine (as in Scheme 2) is also a possibility at higher dilutions in pyridine as solvent. It is rather unlikely, however, in the cases where substituted benzenes are the substrates since only one molar equivalent of pyridine is used and pyridinium tetrafluoroborate is formed (unless one assumes the formation of I to be reversible, in which case the absence of any fluorobenzene in the product is difficult to account for). An induced decomposition would also not explain the absence of any 4-phenylpyridine from the reaction products.

SCHEME 2



$$(\mathrm{I}) + \mathrm{C_5H_5N}: \rightarrow \mathrm{Ar{-}\underset{\underset{^{+}NC_5H_5}{|}}{N}{-}\overset{-}{N}{-}\overset{+}{N}C_5H_5} \rightarrow \mathrm{Ar}\cdot + \mathrm{N_2} + \mathrm{C_5H_5\overset{+}{N}}\cdot + \mathrm{C_5H_5N}$$

(ii) In all the cases studied, the amount of *o*-substituted isomer was somewhat smaller than in the corresponding phenylation using benzoyl peroxide. It is suggested that this might be due to a steric effect which could arise if the phenyl radical and pyridinium radical cation (II), formed by homolysis of I, had not diffused apart appreciably before attack of C_6H_5X took place. This would have the effect of increasing the apparent size of the phenyl radical and lead to steric hindrance to attack *ortho* to the substituent X, as envisaged by Hey *et al.*[7] for *ortho*-substituted phenyl radicals.

Partial rate factors for the three modes of phenylation discussed in this paper are compared in Table 3. Possible ambiguities as to how meaningful the values calculated for the phenylations using benzenediazonium tetrafluoroborate alone are have already been discussed.[5] The partial rate factor of less than unity for the *meta* position of

TABLE 3. PARTIAL RATE FACTORS FOR THE PHENYLATION OF C_6H_5X

Compound	Position	F_r		
		$C_6H_5N_2^+BF_4^-$ and pyridine	$(C_6H_5CO_2)_2$	$C_6H_5N_2^+BF_4^-$
$C_6H_5CH_3$	*o*-	2·22	2·5	1·24
	m-	0·76	0·71	0·43
	p-	1·08	1·0	0·96
C_6H_5Br	*o*-	2·09	1·91	0·52
	m-	1·00	0·95	0·18
	p-	1·42	1·12	0·45
$C_6H_5OCH_3$	*o*-	2·76	4·17	2·49
	m-	0·74	0·87	0·43
	p-	1·97	1·92	2·81
$C_6H_5NO_2$	*o*-	4·3	5·48	0·20
	m-	1·16	0·88	0·84
	p-	5·42	4·68	—

toluene has been noted before and is difficult to reconcile with the accepted electrical effect of a methyl group. On the other hand, Murrell and McEwen[13] have suggested a -I effect for methyl to explain the observed shifts in the UV absorption spectra of some substituted benzenes: ${}^{\mathrm{CH_3}}F_m$ then becomes understandable if $C_6H_5\cdot$ has some electrophilic character (as is also indicated by ${}^{\mathrm{CH_3O}}F_m$, but not by ${}^{\mathrm{NO_2}}F_m$ in the present case). There is, however, quite a large body of chemical and physical evidence which indicates that alkyl groups have a +I effect, so that no explanation can be presented at this time to account for this observation.

EXPERIMENTAL

Reagents. AnalaR thiophene-free benzene was dried, distilled and kept over Na-wire. Toluene, bromobenzene, anisole, notrobenzene, pyridine and aniline were purified by standard procedures and had the b.ps reported in the literature.

Reference compounds. The isomeric methyl-, bromo- and nitrobiphenyls were obtained from commercial sources and purified. The isomeric methoxybiphenyls were prepared from the appropriate diazotized anisidine and benzene and the product purified by chromatography on alumina followed by distillation. The isomeric phenylpyridines were prepared as described previously.[4] The purity of each of the reference compounds was checked by gas-chromatography.

Benzenediazonium tetrafluoroborate was prepared from diazotized aniline and sodium tetrafluoroborate following Roe's general procedure.[14] Only freshly prepared and well-dried samples of benzenediazonium tetrafluoroborate were used. All solvents were de-gassed by passing O_2-free N_2 through them before they were introduced into the reaction flask.

General procedure for the decompositions

Benzenediazonium tetrafluoroborate (0·8 g, 0·00417 mole) was added to an excess of the dry solvent (or mixture of solvents in the case of competitive reactions) and dry pyridine (0·33 g, 0·00417 mole) was added slowly to the mixture with vigorous stirring. The reaction flask was then placed in a thermostat maintained at 75 ± 0·1° and the mixture stirred vigorously for 8 hr. The phenylazopyridinium tetrafluoroborate gradually dissolved while pyridinium tetrafluoroborate separated out. The mixture was filtered through a weighed sintered glass funnel to remove the pyridinium tetrafluoroborate which was washed with dry ether and weighed. The combined filtrates were distilled through a 36 cm fractionating column packed with glass helices to remove most of the solvent. The residue (2–5 ml) was analysed directly by gas chromatography to determine the isomer ratio, total rate ratio (if applicable) and yield.

Identification of pyridinium tetrafluoroborate

The solid filtered from the above reaction mixtures was dissolved in acetone and precipitated with dry ether and had m.p. 222–224° (dec). The m. p. was undepressed on admixture with an authentic sample of pyridinium tetrafluoroborate, m.p. 223–224° (dec) prepared from an aqueous solution of sodium tetrafluoroborate (4·0 g) which was just acidified with 6 N HCl, and to which was added pyridine (3·5 g). The product which crystallized out was purified by precipitation with dry ether from acetone solution. The IR spectrum of the authentic sample was identical with that of the product isolated from the decomposition reactions.

Quantitative analyses

The products obtained in the phenylation reactions were resolved by gas chromatography and the compounds corresponding to the individual peaks identified by comparing their retention times with those of authentic specimens and by collecting each compound and comparing its IR spectrum with that of the authentic specimen. The molar thermal response factor for each compound was determined by the internal standard method of Chang and Karr.[15] The yields of biaryls were determined by introducing a known amount of the internal standard into the reaction mixture.

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[13] J. N. Murrel and K. L. McEwen, *J. Chem. Phys.* **25**, 1143 (1956).

[14] A. Roe, *Org. Reactions* **5**, 203 (1949).

[15] T. C. Chang and C. Karr, Jr., *Anal. Chem. Acta* **21**, 474 (1959).

Phenylation of toluene

The reactions were carried out with a benzenediazonium tetrafluoroborate: toluene molar ratio of 1:56. The reaction mixtures were best resolved on a 20′ × 1/4″ Cu-tube packed with SE-30 (0·5%) on glass beads using a column temp of 162° and a He carrier gas inlet pressure of 40 p.s.i. The retention times of biphenyl, 2-, 3- and 4-methylbiphenyl and bibenzyl were 23·0, 26·25, 39·5, 41·25 and 46 min, respectively. 2-Bromobiphenyl (retention time 33·25 min) was used as internal standard. The yield of methylbiphenyls was 32–42%.

Phenylation of bromobenzene

The reactions were carried out with a benzenediazonium tetrafluoroborate: bromobenzene molar ratio of 1:57 and analysed on a 10′ × 1/4″ column packed with Apiezon 'L' (25%) on Chromosorb W operated at 215° and 40 p.s.i. He inlet press. The retention times of biphenyl, 2-, 3- and 4-bromobiphenyls were 15·3, 31·0, 49·0, and 52·0 min respectively. Bibenzyl (retention time 26·0 min) was used as the internal standard. The yield of bromobiphenyls was 29–33%.

Phenylation of anisole

The reactions were carried out with a benzenediazonium tetrafluoroborate: anisole molar ratio of 1:60 and analysed on a 10′ × 1/4″ column packed with Apiezon 'L' (25%) on Chromosorb W (45–60 mesh). The column temp was 230° and the He inlet press. 40 p.s.i. The retention times of biphenyl, 2-, 3- and 4-methoxybiphenyls were 13·5, 25·0, 37·0, and 42·0 min, respectively. Bibenzyl (retention time 22·0 min) was used as the internal standard, yield 37%.

Phenylation of nitrobenzene

The benzenediazonium tetrafluoroborate: nitrobenzene molar ratio was 1:50. The reaction products were analysed on a 5′ × 1/4″ column packed with GE–SF–96 (20%) on Gas Chrom P (60–80 mesh) and operated at 182° with a He inlet press. of 40 p.s.i. The retention times of biphenyl, 2-, 3- and 4-nitrobiphenyls were 7·0, 17·0, 25·0 and 29·0 min, respectively. Bibenzyl (retention time 11·6 min) was used as the internal standard.

Phenylation of Pyridine

(i) *Benzenediazonium tetrafluoroborate: pyridine molar ratio of* 1:250. The tetrafluoroborate (0·8 g) was dissolved in pyridine (84·0 ml) and the mixture was heated with stirring at 40 ± 0·1° for 6 hr. The reaction mixture was fractionally distilled until a residue of about 5 ml remained and this was analysed by GLC on a polyester column as previously described.[4]

(ii) *Benzenediazonium tetrafluoroborate: pyridine molar ratio of* 1:6. Benzenediazonium tetrafluoroborate (0·8 g) was added to pyridine (2·75 ml) and the mixture stirred in a bath at 40 ± 0·1°. The reaction mixture was heterogeneous initially but became homogeneous after ½ hr when the reaction was almost over. The reaction was strongly exothermic and the internal temp rose to 90°. The evolution of N_2 was very vigorous for the first 15 min. The mixture was stirred at 40° for 4 hr to complete the decomposition and was then analysed directly by gas chromatography.

Competitive reactions

These were carried out with benzenediazonium tetrafluoroborate: total solvent ratios of 1:100 to 1:150. Equimolar proportions of benzene and the other competing solvent were used and the reaction mixtures were worked up and analysed by the same method as was used in the determination of the isomer ratios.

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