Intermolecular Aromatic Substitution by Aryl-nitrenes

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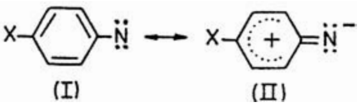
Summary The hypothesis that thermally generated electrophilic aryl-nitrenes should undergo intermolecular aromatic substitution reactions with reactive aromatic substrates has been verified experimentally.

INTERMOLECULAR attack of an aromatic nucleus by ethoxycarbonyl-,[1] sulphonyl-,[2] and cyano-nitrenes[3] is well documented. No analogous reactions of aryl-nitrenes had been reported when this work was initiated, though intramolecular substitutions by aryl-nitrenes and nitrenoids are well known.[4–6] Various explanations are possible. For example, thermal generation of aryl-nitrenes will give the singlet species[4,5] which could undergo singlet→triplet conversion rapidly before attack could take place on the aromatic nucleus, except for an intramolecular process. Triplet phenylnitrene may be involved in intermolecular C–H insertions.[7] Aryl-nitrenes are known to be in equilibrium with a variety of reactive intermediates[8] which probably account for the large amounts of tars formed in the decompositions of aryl azides in aromatic solvents. However, it was unexpected that when phenyl azide was heated in a large excess of benzene that singlet→triplet conversion should take place so rapidly that no diphenylamine was formed[9] (only azobenzene, traces of aniline, and tars were formed), while thermolysis of 2-azidobiphenyl gave high yields of carbazole. This suggested that unlike ethoxycarbonyl-, sulphonyl-, and cyano-nitrene, singlet phenylnitrene was not electrophilic enough to add to benzene. Recent extended Hückel calculations suggest the importance of the delocalisation (I) ⟷ (II) and that singlet phenylnitrene may have substantial nucleophilic properties.[10] If this were so, the introduction of electron-attracting substituents in the aryl-nitrene and electron-donating substituents in the aromatic solvent should result in intermolecular attack being observed. This is indeed the case.



(I) (II)

Thermolysis of *p*-cyanophenyl azide in *NN*-dimethylaniline at 130° gave a mixture of *ortho*-(III) (25·1%) and *para*-(IV) (3·4%) substitution products† together with the hydrogen-abstraction product (X) (20·3%). Aromatic substitution products were also obtained with 1,3,5-trimethoxybenzene (19·2%) and mesitylene (13·2%), but not with benzene, anisole, or *p*-dimethoxybenzene. *p*-Nitro- and *p*-trifluoromethyl-phenylnitrene behaved similarly (Table). Tars were formed in all cases. The biphenyl (XVI) may arise from some *p*-nitrophenyl radicals produced

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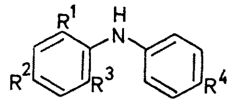
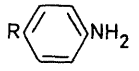
† All new compounds have been fully characterised by i.r., n.m.r., m.s., and micro-analysis.

Products (%) of thermolysis of aryl azides in aromatic solvents

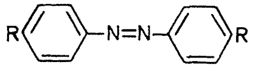
Aryl azide	Solvent	Temp. (°)	Time (h)	% Diphenylamine	% Azo-compound	% Aniline	% Other
p-CN	Benzene	140	45	—	(XII) 25·2	(X) 4·9	—
	Anisole	155	15·5	—	(XII) 2·4	(X) 18·1	—
	p-Dimethoxybenzene	130	50	—	(XII) 3·4	(X) 41·0	—
	1,3,5-Trimethoxybenzene	130	50	(V) 19·2	(XII) 2·0	(X) 13·6	—
	NN-Dimethylaniline	130	48	(III) 25·1; (IV) 3·4	—	(X) 20·3	—
	Mesitylene	165	12	(VI) 13·2	—	(X) 16·4	(XIV) 23·0
p-NO_2	*NN*-Dimethylaniline	130	50	(VII) 13·5	(XIII) 1·0	(XI) 18·3	(XV) 23·7
	1,3,5-Trimethoxybenzene	130	50	(VIII) 18·9	—	(XI) 16·8	(XVI) 3·4
p-CF_3	*NN*-Dimethylaniline	150	16	(IX) 13·4	—	trace	(XV) 9·0



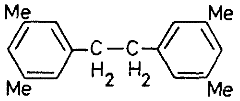
	R^1	R^2	R^3	R^4	M.p.
(III)	NMe_2	H	H	CN	123°
(IV)	H	NMe_2	H	CN	164—165°
(V)	OMe	OMe	OMe	CN	159°
(VI)	Me	Me	Me	CN	liquid
(VII)	NMe_2	H	H	NO_2	121°
(VIII)	OMe	OMe	OMe	NO_2	145°
(IX)	NMe_2	H	H	CF_3	49°



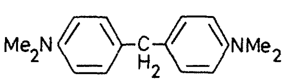
(X); R = CN
(XI); R = NO_2



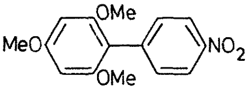
(XII); R = CN
(XIII); R = NO_2



(XIV)



(XV)



(XVI)

by loss of an azide radical from *p*-nitrophenyl azide, a process for which there is some precedent.[11–13] Hydrogen abstraction products and azo-compounds probably come from the triplet nitrene. No side-chain insertion was observed with mesitylene.

Similar results have been obtained in the triethyl phosphite deoxygenation of *p*-nitrosobenzonitrile in dimethylaniline at 0° to give (III) (23·4%), and (IV) (10·6), (XII) (2·6%), and 4,4′-dicyanoazoxybenzene (17·8%). While no evidence has been obtained so far as to whether these are direct electrophilic substitutions, or additions to give aziridine and azepine intermediates followed by ring-opening (*cf.* the sulphonyl-nitrenes[2] and *o*-azidodiphenylmethane[14]), the fact that more (IV) is obtained in the deoxygenations at 0° than in the thermolyses at 130° could be accommodated in an addition–ring-opening pathway in which the azepine leading to (IV) was less stable at higher temperatures than that leading to (III), and went to by-product more readily. On the other hand, the ratio of products observed could just be a reflection of the effect of temperature upon the relative rates of the two substitution processes. The difference observed is not large enough to warrant a conclusion at this time.

Since this work was started Huisgen and von Fraunberg[15] have reported intermolecular aromatic substitutions by 2-pyridyl- and 4,6-dimethyl-2-pyrimidylnitrene into activated substrates. Their results fit well with the concept of the electrophilicity requirement for aryl-nitrenes to undergo such reactions.

The alternative possibility was considered; *i.e.* that there is a change in the mechanism of decomposition with the more electrophilic azides and the more nucleophilic substrates, so that an aryl-nitrene is no longer formed and the reactions are first order in both azide and aromatic substrate. That this was not the case was shown by a study of the kinetics of the decomposition of *p*-cyanophenyl azide in chlorobenzene at 132° with or without *NN*-dimethylaniline. Even with a five-molar excess of amine the rate of decomposition of the azide was unaffected and remained zero order in amine.

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