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Oxidative Cyclizations. VIII*
Mechanisms of Oxidation of *ortho*-Substituted Benzenamines and Improved Cyclizations by Bis(acetato-*O*)phenyliodine

Leonard K. Dyall,[A,B] *Jacqueline J. Harvey*[A] *and Tony B. Jarman*[A]

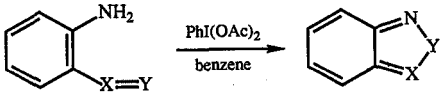
[A] Department of Chemistry, University of Newcastle, Callaghan, N.S.W. 2308.
[B] Author to whom enquiries should be addressed.

Abstract

Published reports describe the oxidative cyclization of suitable *ortho*-substituted arenamines to form such products as 2,1-benzisoxazoles, benzofurazan 1-oxides and benzotriazoles, by using bis(acetato-*O*)phenyliodine at room temperature. However, the reactions are often inconveniently slow. We now report attempts to achieve short reaction times with more powerful iodine(III) oxidants. These often failed to give cyclic products, but the results enable us to argue that the reaction competing with cyclization involves the arenaminyl cation ArN^+H. When such cations are predicted to be relatively unstable, the parent arenamine can be rapidly cyclized in high yield by oxidation with bis(acetato-*O*)phenyliodine in boiling benzene.

Introduction

Bis(acetato-*O*)phenyliodine has been reported[1–6] to oxidatively cyclize a wide range of arenamines with α,β-unsaturated *ortho*-substituents (Scheme 1).



Scheme 1

Typically, the reaction has been carried out in benzene solution at room temperature, though acetone solvent[7] has been used for less soluble substrates. Yields of oxidatively cyclized products are usually excellent, but weakly nucleophilic arenamines involve such long reaction times (days and even weeks[2]) that this method of synthesizing heterocycles has not been widely used. The more active oxidant, tetra(acetato-*O*)lead(IV) ('lead tetraacetate') fails to bring about oxidative cyclization,[8] except when the *ortho* substituent is arylazo[8] or *N*-arylmethyleneamino.[9]

* Part VII, *Aust. J. Chem.*, 1984, **37**, 2013.

[1] Pausacker, K. H., and Scroggie, J. G., *J. Chem. Soc.*, 1954, 4499.
[2] Dyall, L. K., and Pausacker, K. H., *Aust. J. Chem.*, 1958, **11**, 491.
[3] Boulton, A. J., and Middleton, D., *J. Org. Chem.*, 1974, **39**, 2956.
[4] Boulton, A. J., Malls, P. J., and Katritzky, A. R., *J. Chem. Soc. B*, 1970, 636.
[5] Takakis, I. M., and Hadjimihalokis, P. M., *J. Heterocycl. Chem.*, 1990, **27**, 177.
[6] Dyall, L. K., and Kemp, J. E., *Aust. J. Chem.*, 1967, **20**, 1625.
[7] Eatough, J. J., Fuller, L. S., Good, R. H., and Smalley, R. K., *J. Chem. Soc. C*, 1970, 1874.
[8] Dyall, L. K., *Aust. J. Chem.*, 1979, **32**, 643.
[9] Stephens, F. F., and Bower, J. D., *J. Chem. Soc.*, 1949, 2971.

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We now report attempts to bring about oxidative cyclizations of arenamines with iodine(III) oxidants of greater power than bis(acetato-*O*)phenyliodine. While these oxidants did not produce useful procedures for the synthesis of heterocycles, the results shed considerable light on the oxidative pathways which compete with cyclization. Procedures, using bis(acetato-*O*)phenyliodine, have been developed for successful oxidative cyclization in short reaction times.

Discussion

For the purposes of this paper, the usual abbreviations[10,11] for common iodine(III) oxidants will be used: pia (phenyliodoso acetate) for bis(acetato-*O*)phenyliodine and pifa (phenyliodoso trifluoroacetate) for phenylbis(trifluoroacetato-*O*)iodine.

Table 1. Data for oxidation of solvents by iodine(III) oxidants
Oxidant consumption was measured by iodometric titration

Oxidant	Solvent	Temp. (°C)	Time (h)	Oxidant consumed (%)
pia	benzene	50	22	0
		80	48	9[A]
	toluene	50	1	9
	acetone	30	48	3
		56	8	14[B]
	methanol	30	24	10
	pyridine	25	24	34[C]
	dmso	25	24	97[C]
pifa	benzene	50	23	0[A]
	dichloromethane	30	22	66

[A] The i.r. spectrum of the solution did not change during the experiment.
[B] A white precipitate appeared at 8 h. After 3 days the titre dropped by 76%.
[C] Data from ref. 6.

Table 2. Oxidative cyclizations of 2-nitrobenzenamine to benzofurazan 1-oxide with pia in various solvents at 30°
Initial concentrations: 1·1 mmol oxidant and 1·0 mmol amine in 10 ml solvent. Product abbreviations: bfo, benzofurazan oxide; azo, 2,2′-dinitroazobenzene; amine, 2-nitrobenzenamine

Solvent	Time (h)	Product(s)	Yield (%)
Benzene	37	bfo	95
Dichloromethane	120	bfo	82
Acetone	17	bfo	97
Methanol	23	bfo	35
		azo	9
		amine	12

[10] Varvoglis, V., *Synthesis*, 1984, 709.
[11] Varvoglis, V., *Chem. Soc. Rev.*, 1981, **10**, 377.

The success of pia in achieving high yields in oxidative cyclizations of appropriate *ortho*-substituted benzenamines is so well known[1–7] that this reagent provides the obvious starting point in a search for improved reaction conditions. Our approaches have involved either modification of the structure of the oxidant, or changes in the conditions under which it is used. Reactions were monitored by iodometric titration of the iodine(III) oxidant.

(i) *Effect of Variation of Solvent*

This approach to speeding up the reaction is limited, because many of the solvents undergo considerable attack by the pia oxidant (see Table 1).

Attempted oxidative cyclizations of 2-nitrobenzenamine by pia in a range of solvents are summarized in Table 2. Reaction times are not greatly shortened by changing the solvent from benzene to a more polar one (acetone) or to a hydroxylic one (methanol). The last solvent introduces the competing reaction of azo compound formation. In this respect it is similar to acetic acid[6] in which the oxidation is reported to produce 24% of the azo compound and only 2% of the cyclic product benzofurazan 1-oxide.

Although acetone does not greatly shorten the reaction time, its ability to dissolve some of the less soluble substrates led us to explore its use (Table 3). To our surprise, 3-methyl-2-nitrobenzenamine was successfully cyclized by pia in this solvent, whereas in benzene the cyclization has to compete with azo compound formation. Our attempts to oxidatively cyclize other sterically hindered 2-nitrobenzenamines in acetone were not, however, successful. High recoveries of the amines indicated that most of the oxidant had been consumed in attack on the solvent.

Table 3. Oxidative cyclizations of *ortho*-substituted arenamines by bis(acetato-*O*)phenyliodine in benzene or acetone solvent at 30°

Initial concentrations: 1·0 mmol amine and 1·1 mmol oxidant in 10 ml solvent

Arenamine	Solvent	Time (h)	Product(s)	Yields (%)
3-Methyl-2-nitro-benzenamine	benzene[2]	140	cyclic	42
			azo	28
	acetone[A]	5	cyclic	92
4-Methyl-3-nitro-pyridin-2-amine	benzene	21	cyclic	96
	acetone[A]	7	cyclic	84
6-Methyl-2-nitro-benzenamine	benzene[2]	168	cyclic	0
			azo	0
			amine	53
	acetone[A]	96	cyclic	0
			azo	4
			amine	29
6-Methyl-2,4-dinitro-benzenamine	acetone[B]	530	cyclic	9
			amine	87
2,6-Dinitro-benzenamine	acetone	528	cyclic	18
			amine	78

[A] A finely divided white precipitate appeared after 1·5 h.
[B] Undissolved amine was present throughout this oxidation run.

(ii) *Effect of Ring Substitution in Bis(acetato-O)phenyliodine*

In earlier (unpublished) work[12] we examined the effect of substituting the phenyl ring in pia, but nothing useful was achieved. While the oxidation of 2-nitrobenzenamine with these modified pia reagents did yield the cyclized product benzofurazan 1-oxide, the variations in half-lives for pia and its 4-methyl, 4-methoxy and 3-chloro derivatives did not exceed 2·4-fold at 30° in toluene solution (see Experimental). This approach not only failed to reduce the reaction times significantly, but also resulted in troublesome separations of the cyclized product from the aryl iodides which are the reduction products of these reactions. Nitro derivatives of pia were not sufficiently soluble to be useful.

(iii) *Effects of Carboxylate Exchange in pia*

The alternative modification of the pia oxidant is to exchange the acetate ligands for those of a stronger acid. This exchange is known[13] to be achieved simply by adding the stronger acid to a solution of pia (Scheme 2).

$$PhI(OAc)_2 + 2RCOOH \rightleftharpoons PhI(OCOR)_2 + 2AcOH \qquad \text{Scheme 2}$$

Exchanges of acetate in pia for chloroacetate, formate and trifluoroacetate were carried out, and the modified oxidants were used on 2-nitrobenzeneamine (see Table 4). Reaction times were shortened with respect to pia but no oxidative cyclization was achieved. The observed products (azo compounds and mixtures of oligimers) will be discussed later.

The pifa oxidant did, however, achieve oxidative cyclization with 2,4-dinitrobenzenamine (47% yield at 50°, with 52% amine recovered) (see Experimental). While the high consumption of oxidant by attack on solvent makes this an unsatisfactory preparative procedure, the fact that oxidative cyclization is the exclusive reaction of this amine is a key mechanistic point to be discussed later.

Arenamines with *ortho*-phenylazo groups are oxidatively cyclized by all the modified oxidants (see Table 5), and the cyclization by pia is effective even in acetic acid solvent where it is known to fail with 2-nitrobenzenamine.[6] There is, however, no preparative advantage in using modified oxidants with these phenylazo-substituted arenamines, the yields of triazoles being significantly lower than with the pia reagent.

(iv) *Use of pia at Elevated Temperatures*

In view of the lack of success of any of the above measures to achieve high yields in oxidative cyclizations with short reaction times, it was clear that the unmodified pia reagent should be used, in benzene solution, at above ambient temperatures.

[12] Evans, J. O. M., Honours Thesis, University of Newcastle, 1964.
[13] Merkushev, E. B., Novikov, A. N., Marachenko, S. S., and Matykov, N. E., *Chem. Abstr.*, 1977, **86**, 171041u.

The early work[1,14–16] on amine oxidation by pia was all carried out at or near ambient temperatures, apparently in the belief that the oxidant would decompose if heated. Our data for pia in benzene (see Table 1) indicate that this oxidant

Table 4. Oxidative cyclizations of 2-nitrobenzenamine to benzofurazan 1-oxide with various iodine(III) oxidants at 30°

Initial concentrations and product abbreviations as in Table 2

Oxidant	Solvent	Time (h)	Product(s)	Yield (%)
$PhI(OCOCH_3)_2$	benzene	37	bfo	95
$PhI(OCOCH_2Cl)_2$[A]	benzene[B]	8	bfo	0·03
			azo	25
			amine	6
$PhI(OCHO)_2$[A]	benzene	24	bfo	0
			azo	4
			amine[B]	17[C]
$PhI(OCOCF_3)_2$	benzene[C]	0·3	bfo	0
			azo	23
			amine	9
	dichloro-methane[C]	4	bfo	0
			azo	15
			amine	7

[A] These oxidants were prepared *in situ* from $PhI(OCOCH_3)_2$ by adding the appropriate carboxylic acid (5:1 molar ratio).
[B] This oxidation also gave a 5% yield of *N*-formyl-2-nitrobenzenamine.
[C] These oxidations also yielded mixtures of oligomers.

Table 5. Oxidation of arenamines with *ortho*-phenylazo substituents by iodine(III) oxidants

Initial concentrations: 1·0 mmol amine and 1·1 mmol oxidant in 10 ml solvent, unless otherwise noted

Aren-amine	Oxi-dant	Sol-vent	Temp. (°C)	Time (h)	Cyclic product yield (%)
2-Phenylazo-benzenamine	pia	benzene	25	7	81[A]
	pia	AcOH[B]	25	2	73[A]
	pifa	benzene	15	<0·02	67
2,4-Dibromo-6-phenylazo-benzenamine	pia	benzene[C]	25	140	86[A]
1-Phenylazo-napthalen-2-amine	pia	benzene[D]	30	3	86[A]
	pica[E]	benzene	30	<0·05	73
	pifa	benzene	30	<0·05	50
	pifa	benzene	15	<0·1	60

[A] This is the yield of isolated pure compound.
[B] Initial concentration 1 mmol amine in 30 ml solvent.
[C] Initial concentration 1 mmol amine in 35 ml solvent.
[D] Data from Boshev, G., Dyall, L. K., and Sadler, P. R., *Aust. J. Chem.*, 1972, **25**, 599.
[E] The $PhI(OCOCH_2Cl)_2$ reagent was prepared *in situ* by adding 5 moles chloroacetic acid per mole of pia.

[14] Barlin, G. B., Pausacker, K. H., and Riggs, N. V., *J. Chem. Soc.*, 1954, 3122.
[15] Mitchell, J., and Pausacker, K. H., *J. Chem. Soc.*, 1954, 4502.
[16] Pausacker, K. H., *J. Chem. Soc.*, 1953, 1989.

can be used even at the boiling point of the solvent, provided the reaction time is not too long. The increased solubility of the amines at this temperature is sometimes an advantage.

The results in Table 6 show that judicious choice of reaction temperature can achieve acceptably short reaction times without sacrificing yield of cyclized product. There is a clear correlation of acceptable temperature with the electron-withdrawing nature of the ring substituents. Thus, the ceiling temperature is about 30° for an *ortho* benzoyl substituent, 50° for one *ortho* nitro, but 80° for arenamines with two electron-attracting substituents. By working within these guidelines, the pia reagent can be made to bring about very satisfactory oxidative cyclizations.

Table 6. Optimization of reaction conditions for oxidative cyclization by bis(acetato-*O*)phenyliodine in benzene solution

Initial concentrations: 1·1 mmol oxidant and 1·0 mmol amine in 10 ml benzene

Arenamine	Temp. (°C)	Time (h)	Product(s)	Yield (%)
2-Nitrobenzenamine	30°	37	cyclic	95
	50	5·5	cyclic	93
	80	<1·5	cyclic	67
			azo	2
			amine	0·3
(2-Aminophenyl)-phenylmethanone	30	24	cyclic	80
			amine	9
	50	4	cyclic	63
			azo	5
			amine	1
	80	<2	cyclic	40
			amine	13
2-Nitropyridin-3-amine	80	12·5	cyclic	90
2-Chloro-6-nitro-benzenamine	42	700	cyclic	82[A]
			amine	12
	80	46	cyclic	82[B]
			amine	5
2,4-Dinitrobenzen-amine	50	22	cyclic	98
	80	1	cyclic	95
2,6-Dinitrobenzen-amine	50	190	cyclic	11
			amine	79
	80	35	cyclic	57
			amine	29
6-Methyl,2,4-dinitro-benzenamine	80	24	cyclic	70
			amine	4

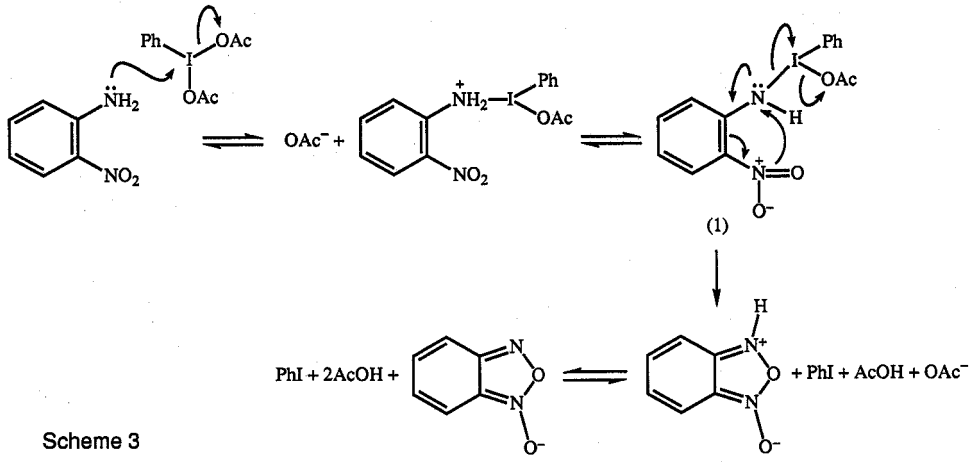
[A] Isolation of a 66% yield was achieved by crystallization from methanol. The chlorofurazan oxide had m.p. 75·5–76·0° (lit. 77°).
[B] Isolated yield, after crystallization from petrol.

Mechanisms of Oxidative Cyclization and Competing Reactions

In our earlier work[17] we used a combination of titrimetric and infrared spectroscopic data to deduce that the first step in the pia oxidation of 2-nitrobenzenamine is a ligand exchange (amine for acetate), and we argued

[17] Dyall, L. K., Evans, J. O. M., and Kemp, J. E., *Aust. J. Chem.*, 1968, **21**, 409.

that this is followed by a neighbouring-group displacement of iodobenzene (see Scheme 3).



Scheme 3

Similar evidence was found for 2,4-dinitrobenzenamine and (2-aminophenyl)-phenylmethanone.[18] Furthermore, a large family of arenamines with $-M$ type *ortho* substituents (acetyl, arylazo, formyl) must oxidize through this common mechanism, because their activation parameters are found to obey an isokinetic relationship.[19] The neighbouring groups in these reactions are the same ones which greatly accelerate the thermolysis of aryl azides.[20] These mechanistic conclusions for the oxidative cyclization are consistent with all the results reported in this present paper.

The competing reaction (which produces azo compound and high molecular weight material) was seen by us[6] in 1967 to involve homolysis of the nitrogen–iodine bond in the intermediate (1) in Scheme 3, to produce the arenamino radical $ArN^{\bullet}H$. This latter species [in equilibrium with its conjugate acid $(ArNH_2)^{\bullet}$] has also been postulated as an intermediate in the oxidation of arenamines by lead tetraacetate.[8] The results obtained in our present work call for a reexamination of the nature of this competing reaction.

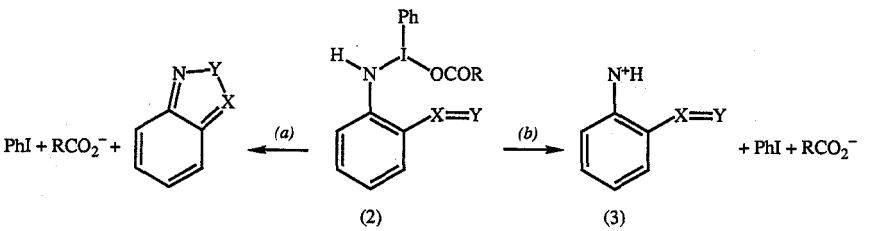
The two competing reactions, one of cyclization and the other involving formation of azo compound and high molecular weight material, are seen to be in a state of delicate balance. The cyclization pathway is known to be disadvantaged in compounds where the neighbouring-group effect would be sterically inhibited.[2] In 4-methoxy-2-nitrobenzenamine, the presence of the electron-releasing 4-substituent results in no formation of the benzofurazan 1-oxide under conditions where 2-nitrobenzenamine is quantitatively cyclized.[1] Even with 2-nitrobenzenamine, the oxidative cyclization by pia is inhibited by such hydroxylic solvents as methanol (Table 2) and acetic acid,[6,14] and none of the stronger iodine(III) oxidants achieves any oxidative cyclization of it even in suitable solvents (Table 4). Some of the

[18] Dyall, L. K., *Aust. J. Chem.*, 1973, **26**, 1969.
[19] Dyall, L. K., *Aust. J. Chem.*, 1973, **26**, 2665.
[20] Dyall, L. K., in 'The Chemistry of Functional Groups, Supplement D' (Eds S. Patai and Z. Rappoport) p. 287 (John Wiley: Chichester 1983).

successful cyclizations, moreover, work less well when the temperature is raised (see Table 6).

On the other hand, *ortho*-nitrobenzenamines with an additional electron-attracting substituent are cyclized even at high temperatures, and 2,4-dinitrobenzenamine follows the oxidative cyclization pathway even when the strongest oxidant (pifa) is used.

All these data can be rationalized in terms of the competing reaction being one of ionization of the intermediate (2) (see Scheme 4). The non-cyclized oxidation products are then derived from the arenaminyl cation (3), a class of reactive intermediate well known from the work of Gassman.[21]



Scheme 4

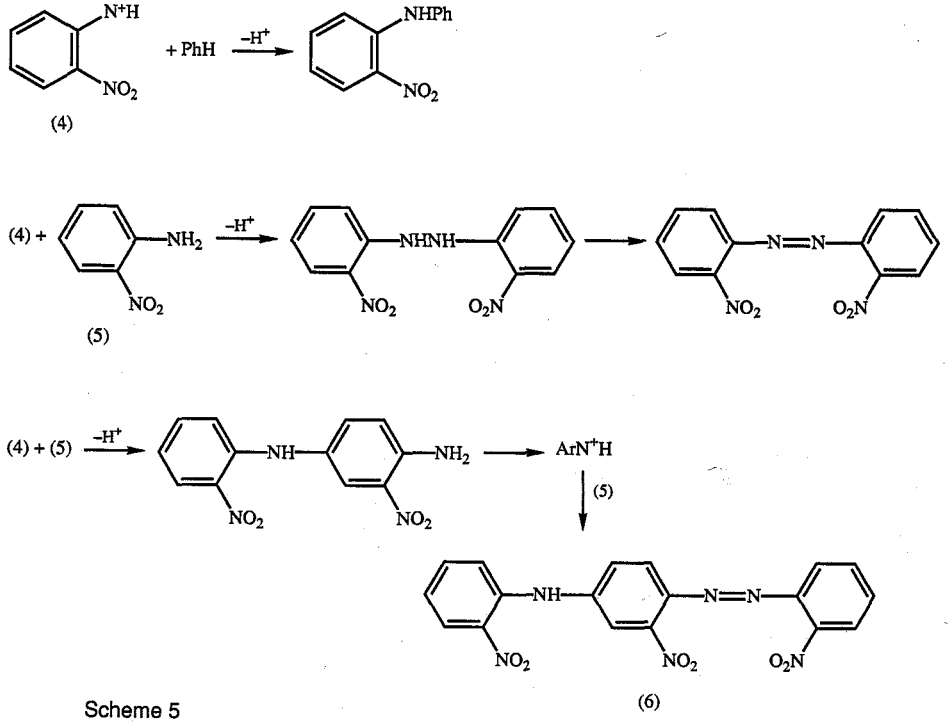
The pathway *(b)* is expected to be favoured by strongly electron-attracting RCO_2 groups, by hydroxylic solvents able to solvate ions, and by electron-releasing substituents in the arenamino ring. On the other hand, when the electronic effect of the X=Y group in (2) is augmented by that of additional electron attractors in the ring (chloro, nitro or pyridyl nitrogen), the formation of the arenaminyl cation (3) is strongly disfavoured. In these cases, raising the temperature does not result in loss of the selectivity for path *(a)* for pia oxidations, but with *ortho*-benzoyl- and *ortho*-nitro-benzenamine the selectivity is partly lost when the temperature is raised (see Table 6). In 2,4-dinitrobenzenamine the formation of an arenaminyl cation is so favourable that the oxidative cyclization path *(a)* is followed exclusively even when the best RCO_2 leaving group (trifluoroacetyl) is involved.

Our earlier version[6] of the non-cyclizing reaction path produced radicals $ArN^{\bullet}H$ and $PhI^{\bullet}(OCOR)$ and drew upon published data which indicated the nitrogen–iodine(III) bond to be weakened by electron-releasing substituents.[22,23] The pifa oxidant should, by this argument, produce an intermediate (2) ($R = CF_3$) *less* prone to bond homolysis. In addition, it is difficult to see why hydroxylic solvents should favour homolysis. The available data fit the heterolysis pathway [Scheme 4, path *(b)*] much more convincingly.

The arenaminyl cation $ArN^{+}H$ is capable of generating the types of product observed by us in pifa oxidation of 2-nitrobenzenanime. 2,2′-Dinitroazobenzene and 2-nitrodiphenylamine were positively identified, and some of the structural features of other (impure) fractions were ascertained (see Experimental). An

[21] Gassman, P. G., Campbell, G., and Frederick, R., *J. Am. Chem. Soc.*, 1968, **90**, 7377; 1972, **94**, 3884; Gassman, P. G., and Campbell, G. A., *J. Am. Chem. Soc.*, 1972, **94**, 3891.
[22] Banks, D. F., *Chem. Rev.*, 1966, **66**, 243.
[23] Bekoe, D. A., and Hulme, R., *Nature (London)*, 1956, **177**, 1230.

oxidative trimer, M = 408, with nitro and secondary amino bands in its i.r. spectrum, is probably (6) in Scheme 5. A fraction of still higher molecular weight (M = 938±129) had two secondary NH bands in both the i.r. and ^{1}H n.m.r. spectra. High molecular weight products from pifa oxidation of 4-chloro-2-nitrobenzenamine were examined in less detail but the i.r. spectra indicated similar structural features.



Scheme 5

Scheme 5 suggests how some of these products might arise in the oxidation of 2-nitrobenzenamine through electrophilic attack and further oxidation. The route shown for azo compound formation has already been suggested for lead tetraacetate oxidations by Rindone and coworkers.[24]

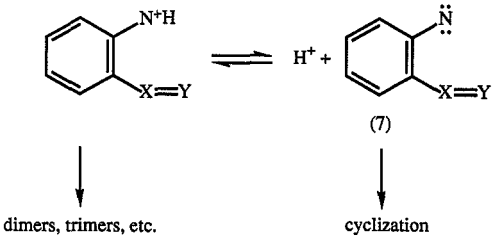
It is not suggested that these products positively identify the cation (4) as the reactive species. These products could equally well be formed from a nitrene species or a free radical ArN•H.

Finally, it must be remarked that one could explain nearly all the above results of arenamine oxidation in terms of the intermediate ArN^+H and the singlet nitrene (7) with which it is in protic equilibrium (Scheme 6).

Many of the observed steric effects of flanking substituents, and all of the electronic effects of ring substituents which have been discussed above, can be accounted for in terms of their influence on the basicity of (7). Scheme 6 can also explain why the change of solvent from benzene to acetic acid prevents virtually all the cyclization of 2-nitrobenzenamine.[6] In particular, it offers a

[24] Catto, A., Corboni, F., Rindone, B., and Scolastico, C., *Tetrahedron Lett.*, 1973, 2723.

ready explanation of why the cyclization fails when the oxidant produces strong acids which will drive the equilibrium to the left. Only the deleterious effect of methanol on the oxidative cyclization of 2-nitrobenzenamine (Table 2) is not readily explained.



Scheme 6

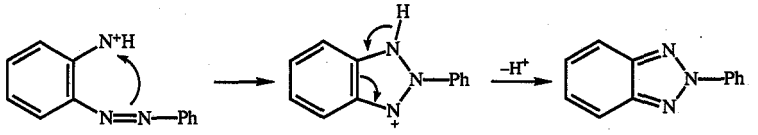
While many arenaminyl cations are well documented, the only previous report of the nitro-substituted cation (4) known to us is our own work[8] in which we believed we had generated it by treating *N*-chloro-2-nitrobenzenamine with silver trifluoroacetate. In that experiment, most of the *N*-chloro compound cyclized to benzofurazan 1-oxide, with rearrangement reactions also occurring. However, now that we know[25] the merest trace of base can cyclize these *N*-chloro-2-nitrobenzenamines, it is doubtful if the cation (4) was involved. We have in the present work attempted a direct test of the Scheme 6 hypothesis, by oxidizing 2-nitrobenzenamine with pifa in the presence of solid sodium hydrogen carbonate so that no acidity would develop. The presence of the mild base made no difference to the products, with no evidence for any cyclization being obtained. On this basis, we cannot support Scheme 6.

Cyclization of *ortho*-Phenylazoarenamines

These amines all undergo oxidative cyclization, even with the most powerful iodine(III) oxidant (pifa) or in a hydroxylic solvent (see Table 5). Although the arylazo group is the best of the known neighbouring groups in azide pyrolysis,[20] its effect there is very much reduced by the steric effect of a naphthyl *peri*-hydrogen.[26] In 1-phenylazo-2-naphthalenamine, the neighbouring-group effect should be only one-fifth that operating in 2-nitrobenzenamine. Nevertheless, this naphthalenamine gives fair yields of cyclized product with pica or pifa (Table 5), whereas 2-nitrobenzenamine does not undergo oxidative cyclization by these reagents (Table 4). The outcome of these oxidative cyclizations of *ortho*-phenylazoarenamines is not, then, controlled by neighbouring-group effects.

A reasonable explanation is outlined in Scheme 7. The internal electrophilic substitution is feasible for arylazo groups but not for a nitro group. In effect, this cyclization is proceeding through path *(b)* of Scheme 4. We have suggested this mechanism previously.[8]

[25] Chapman, K. J., Dyall, L. K., and Frith, L. K., *Aust. J. Chem.*, 1984, **37**, 341.
[26] Boshev, G., Dyall, L. K., and Sadler, P. R., *Aust. J. Chem.*, 1972, **25**, 599.



Scheme 7

Experimental

Apparatus and Instrumentation

Infrared spectra were recorded on chloroform solutions, by using a BioRad FTS-7 F.t.-i.r. spectrometer. Ultraviolet spectra were measured with either a Hitachi U-2000 or a GBC u.v./vis. 911 spectrometer. Mass spectra were measured on either a Kratos MS-30 instrument or the Flinders University of South Australia Kratos 25 instrument, in both cases under electron impact at 70 eV. The ^{1}H n.m.r. spectrum was recorded at 300 MHz by the Brisbane N.M.R. Centre.

Plate chromatograms (p.l.c.) were run on silica gel type G, spread in a layer 1 mm thick. Fractions were recovered by repeated extraction with hot ethyl acetate. Thin-layer chromatograms (t.l.c.) were run over Kodak Eastman 13181 silica gel type G.

Vapour-pressure osmometry was performed with a Hewlett–Packard 302 instrument.

Materials

Solvents were of A.R. grade, and were dried over Linde type 4A molecular sieves. Petroleum was a fraction b.p. 40–70°.

The arenamines either were purified commercial samples or were synthesized by standard methods, and were pure according to both m.p. and t.l.c. Bis(acetato-*O*)phenyliodine (pia) was a commercial sample purified by recrystallization from benzene. Phenylbis(trifluoroacetato-*O*)iodine (pifa) was synthesized from pia by carboxylate exchange,[27] and was 97% pure by iodometric titration.

General Procedure for Oxidations and Product Isolation

The powdered amine (1·0 mmol) was added to a solution of the oxidant (1·1 mmol) in the chosen solvent (10 ml), more solvent being added if required to obtain complete dissolution. This reaction mixture was then boiled under reflux, or stoppered and kept in a thermostatted bath. Progress of the reaction was monitored by adding a 1 ml aliquot to acidified KI and titrating the liberated iodine with 0·050 M $Na_2S_2O_3$ (starch indicator). When 1 mmol of oxidant had been consumed, the products were examined by t.l.c. to determine which of the following two methods for identifying products was appropriate.

Method A

With simple reaction mixtures (up to three components including iodobenzene), the solvent and acetic acid were removed with a rotary evaporator, and the residue was taken up in chloroform accurately delivered by pipette. The F.t.-i.r. spectrum was then compared with spectra of the single components, and the yields were determined by absorbance methods. Each compound was analysed at from two to four frequencies, with the measured yields rarely varying by more than ±2%. Mean values are quoted in Tables 1–6, and have been corrected for the material used up in monitoring the progress of reaction.

When benofurazan 1-oxide was a product, its volatility during distillations of solvent led to losses of the order of several per cent, even after the distillation of solvent from the original reaction mixture had been shortened in time by prior removal of acetic acid by treatment

[27] Loudin, G. M., and Boutin, R. H., *J. Org. Chem.*, 1984, **49**, 4772.

with solid K_2CO_3. The distillates were therefore collected, diluted in ethanol, and analysed by u.v. spectrophotometry (λ_{max} 356, 369 nm).

For each amine in each solvent, the products of at least one run have been isolated by crystallization, chromatography, vacuum sublimation, or combinations of these techniques. Product identities were confirmed by i.r. spectra, m.p. and mixed m.p. with authentic samples, and where appropriate by u.v. and ^1H n.m.r. spectra.

The presence of iodobenzene was not a serious problem in the isolation of products; it was removed during crystallization or chromatography. With the more insoluble products (nitrobenzofurazan 1-oxides and pyridofurazan oxides) the iodobenzene was conveniently removed from the crude reaction mixture by digestion with a small volume of cold petrol.

Method B

The more complicated reaction mixtures were separated by p.l.c., with benzene or chloroform as eluent. The fractions recovered from the chromatogram were then identified and quantified by F.t.-i.r. spectroscopy as described above.

Azo compounds invariably appeared as two bands on the chromatogram, and we attribute these to the *cis* and *trans* isomers. During the subsequent extractions of the silica with hot ethyl acetate, one product isomerized to the other (presumably *trans*).

Examples of Arenamine Oxidations Yielding Non-cyclized Products

Oxidation of 2-Nitrobenzenamine by pifa in Benzene at 30°

2-Nitrobenzenamine (1·38 g, 10 mmol) and pifa (4·30 g, 10 mmol) were dissolved in benzene (200 ml) at 30°. The oxidant was all consumed in 20 min (iodometric titration). The solvent was then removed from the dark red solution to leave a black tar (2·52 g). A u.v. spectrum on the distilled benzene did not detect any benzofurazan oxide.

Virtually all the tar dissolved in boiling chloroform (10 ml). Cooling this extract gave feathery yellow-orange crystals (273 mg) shown by t.l.c., m.p. (211–212°), mass and i.r. spectra to be 2,2′-dinitroazobenzene (lit. m.p. 209–210°). Mass spectrum *m/z* 272 (4·5%, $C_{12}H_8N_4O_4$, M), 150 (100, $C_6H_4N_3O_2$, ArN_2^+).

The mother liquor from this extract was subjected to medium-pressure chromatography over silica (chloroform elution). Iodobenzene eluted first, followed by yellow, orange and some poorly separated red bands. The material from the yellow band proved to be more of the azo compound (38 mg, giving a total yield of 23%), and the orange band which followed it was shown by i.r. spectroscopy to be 2-nitrobenzenamine (123 mg, 9% recovery). The unresolved red bands were combined to give material (633 mg) whose i.r. spectrum showed a complex pattern of N–H and N–O stretching bands.

This red material was subjected to a series of p.l.c. separations, with $CHCl_3$ elution. Resolution on the plates was generally poor, apparently because of the low solubility of most of the material. Eventually three fractions (A, B and C) were isolated and, being homogeneous by t.l.c., were subjected to structure determination. In the event, none of them was a pure compound. There was another interesting component with three N–H stretching bands (3501, 3389 and 3338 cm^{-1}) in its i.r. spectrum, but it could not be separated as a homogeneous fraction.

Fraction A (11 mg, R_F 0·69) crystallized from petrol as orange plates. The i.r. spectrum ($CHCl_3$) of the first crop had bands at 3356, 1617, 1592, 1576, 1503, 1348, 1261 and 1147 cm^{-1}, which matched those of 2-nitrodiphenylamine; however, there was an additional band at 1527 cm^{-1} which suggests 2,2′-dinitroazobenzene. The i.r. spectrum of the second crop was an exact match to that of 2-nitrodiphenylamine.

Fraction B (18 mg, R_F 0·55) crystallized from benzene/petrol as fluffy orange needles. The m.p. (139–143°) was not improved by further crystallization. I.r. ($CHCl_3$) ν_{max} 3357 (secondary NH), 1530, 1349 cm^{-1} (NO_2). Mol. wt (vapour pressure osmometry, CH_2Cl_2 solution): 375±10 a.m.u. Mass spectrum (probe at 100°) *m/z* 272 (6·7%), 150 (100), and all other ions matching those of 2,2′-dinitroazobenzene. This spectrum persisted when the probe temperature was raised to 200°, but disappeared at 250°, when a new spectrum

appeared: *m/z* 408 (39%), 376 (45), 342 (49), 286 (100). The molecular ion of this less volatile component is consistent with the composition $C_{18}H_{12}N_6O_6$ (Found: *m/z* 408·07. Calc. for $C_{18}H_{12}N_6O_6$: 408·08).

Fraction C (56 mg, R_F 0·22) was only sparingly soluble in boiling chloroform, from which it separated as a dark red powder. This material, when heated, began to decompose near 150°, and decrepitated violently at 180°. Attempts to record the e.i. mass spectrum were unsuccessful. I.r. spectrum ($CHCl_3$) ν_{max} 3429, 3307 (NH), 1519, 1344 cm^{-1} (NO_2); other strong bands at 1601, 1588, 1571, 1506, 1301, 1268 cm^{-1}. Mol. wt (vapour pressure osmometry, CH_2Cl_2 solution): 938±129 a.m.u. The ^1H n.m.r. spectrum (300 MHz, $CDCl_3$) had broad singlets at δ 7·8 and 8·6, ascribed to NH, and a complex multiplet at 6·8–8·3. The integral ratio on this very dilute sample is distorted by residual $CHCl_3$ but there are at least 10H in the aromatic proton multiplet (assuming each broad signal is one NH). Among the aromatic proton signals are three well-resolved double doublets at δ 6·83 (*J* 8·0, 1·1 Hz), 6·94 (*J* 8·0, 1·1 Hz), and 8·27 (*J* 8·3, 1·2 Hz). However, a weak extraneous signal on the δ 6·83 double doublet, and two other such signals elsewhere in the aromatic region, indicate that the sample cannot be a pure compound. Consistent with this indication, the microanalysis could not be fitted to a molecular formula (Found: C, 51·1; H, 3·0; N, 18·4%). The material does not contain iodine (sodium fusion).

Oxidation of 2-Nitrobenzenamine by pifa in Benzene with $NaHCO_3$ Present

The amine (13·7 mg, 0·1 mmol) was oxidized with pifa (0·1 mmol) in the presence of finely divided $NaHCO_3$ (0·5 mmol) in dry benzene (2 ml). The mixture was agitated until oxidation was complete. Evaporation of the red solution yielded a red solid product (14 mg). According to t.l.c. and the i.r. spectrum, no 2-nitrobenzenamine remained, but the product mixture was otherwise the same as the one obtained with no $NaHCO_3$ added. No benzofurazan 1-oxide was detected.

Oxidation of 4-Chloro-2-nitrobenzenamine (pifa in Benzene at 25°)

The amine (345 mg, 2·0 mmol) and pifa (946 mg, 2·2 mmol) were mixed in benzene (100 ml) at 25°. After 20 min, the oxidant titre was found to be zero. T.l.c. on the dark red reaction mixture detected six fractions, none of them being 5-chlorobenzofurazan 1-oxide.

Solvent removal left a black tarry residue (640 mg) smelling of iodobenzene. Digestion with hot chloroform left a black solid, which in turn was extracted with boiling benzene. The concentrated benzene extract deposited flaky brown crystals, m.p. 245–246°, identical in i.r. spectrum and mass spectrum to the azo compound isolated below.

The chloroform extract was concentrated and then subjected to p.l.c. (chloroform elution). The pale orange bands at R_F 0·90 and 0·81 both gave the same compound, according to both the i.r. and mass spectra. It crystallized from chloroform as long orange needles, m.p. 247–248°. We identify it as 4,4′-dichloro-2,2′-dinitroazobenzene. Mass spectrum *m/z* 342, 340, (2·0, 5·0%, $C_{12}H_6Cl_2N_4O_4$, M), 186, 184 (27·2, 100, $C_6H_3ClN_3O_2$, ArN_2^+). The i.r. spectrum was identical to that of an authentic sample (m.p. 250–251°) prepared by NaOCl oxidation of 4-chloro-2-nitrobenzenamine.[28]

Further p.l.c. bands at R_F 0·72 and 0·31 gave negligible amounts of material, and a dark yellow band, R_F 0·50, yielded the original amine (4% recovery). The final band (R_F 0·19) gave a red solid which crystallized from ethanol as a red powder (4 mg), m.p. 144° (dec.). I.r. spectrum ($CHCl_3$) ν_{max} 3430, 3390 (NH, both bands very weak), 1570, 1360 cm^{-1} (NO_2). The sample decomposed on a mass spectrometer probe.

Half-Lives of Oxidation of 2-Nitrobenzenamine by Ring-Substituted Phenyliodoso Acetates

The reactions were carried out in toluene solution (initial concentrations of both amine and oxidant 7·77 mM) held at constant temperature (±0·05°). Iodometric titration was used to monitor the progress of reaction, and the $t_{1/2}$ values were read from a plot of thiosulfate titre against time. At 30°, the ring substitutions gave $t_{1/2}$ values (min) as follows: unsubstituted,

[28] Green, A. G., and Rowe, F. M., *J. Chem. Soc.*, 1912, **101**, 2443.

161; 4-methyl, 242; 4-methoxy, 163; 3-chloro, 387. At 40°, the results were: unsubstituted, 59; 4-methyl, 78; 4-methoxy, 53; 3-chloro, 139. All runs were performed in duplicate and the $t_{1/2}$ values were reproduced to ±1 min or better.

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