

THERMAL CYCLISATION OF AROMATIC NITROCOMPOUNDS

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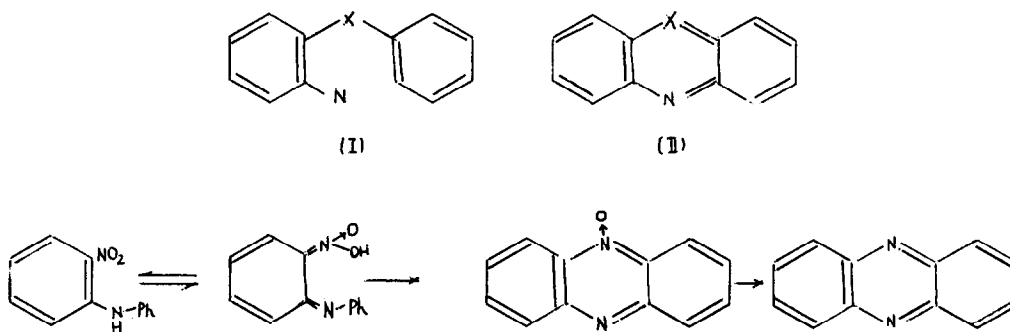
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Intramolecular cyclisation of suitably constituted nitrocompounds to give N-heterocycles has been effected with various reducing agents such as metal oxalates (1), triethyl phosphite (2) and iron pentacarbonyl (3). We have, however, shown that such ring-closures can be carried out by simply heating the appropriate nitrocompound in sand (4) and other workers have subsequently reported that pyrolysis of certain nitrocompounds in diphenyl ether (2c) also produces N-heterocycles. Triethyl phosphite and metal oxalate reactions are held by most authors (2) to involve a nitrene intermediate (R·N·) which by insertion into a favourably positioned C-H bond causes ring-closure with formation of a carbon-nitrogen link (e.g. I → II) although an ionic mechanism cannot always be excluded (2b). The metal oxalates presumably cause deoxygenation of the nitro group to a nitrene at the surface of the reagent or of its breakdown product while trialkyl phosphites are known to accept oxygen readily from nitro- and nitroso-compounds.

For the uncatalysed nitro-cyclisations, however, we demonstrated an alternative mechanism involving the aci-form of the nitro-compound as for instance in the phenazine formation from diphenylamine (scheme 1). More-

over, Smolinsky (2c) has recently suggested that certain nitrocyclisations in diphenyl ether or even in presence of ferrous oxalate may also follow the 'aci-nitroroute'. It thus appears that especially in absence of a

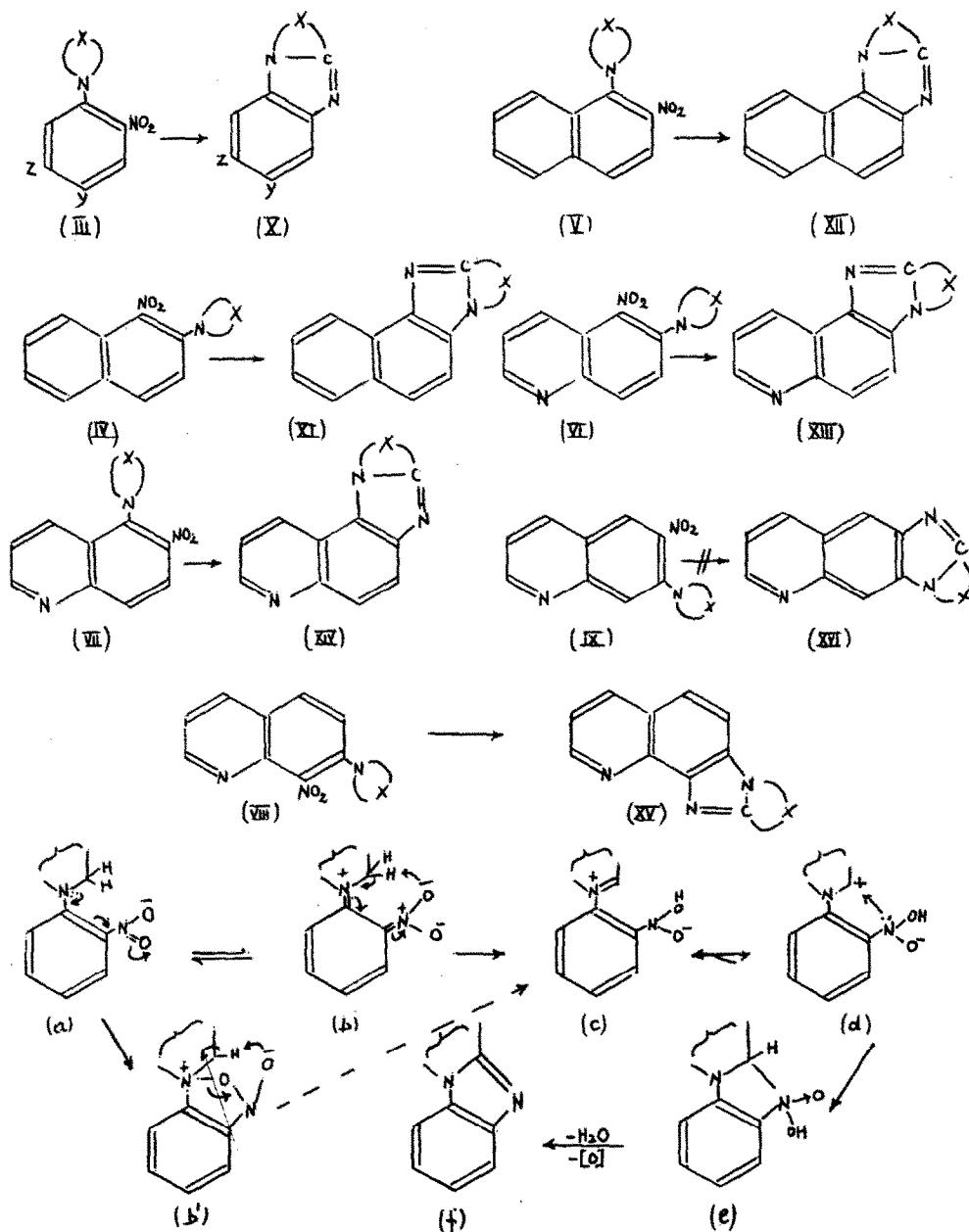


Scheme 1

reducing agent o-nitrocompounds capable of forming aci-tautomers cyclise by this pathway with elimination of water rather than via a nitrene intermediate. We now wish to report further examples of the little explored aci-nitro-mechanism and to quote additional evidence for its operation.

Pyrolysis at 220-240° in sand of the aromatic o-nitrocompounds (III to VIII) possessing an N-heteroparaffinic substituent ($X = [CH_2]_n$) produced the corresponding imidazoles (X to XV) often in excellent yield (cf. table). Substituent effects were studied in the benzene series (III) where it was found that electron withdrawal ($Z = H$; $Y = NO_2, CO_2H, CF_3, Cl$) caused the reaction to be vigorous and complete within 30 minutes. The presence of electron donators (I ; $Y = NHAc, Me$; $Z = H$ or $Y = H$ and $Z = NHAc$) or absence of substituents ($Y = Z = H$) gave lower yields and necessitated

longer heating (1-4 hr.). With morpholine as heterocyclic substituent yields were only moderate. Chromatography on alumina with benzene as



Scheme 2

eluent was used in all cases for final purification. Thermolysis of the nitro-naphthalenes and -quinolines (V—VIII) was also smooth and swift, with the quinolines being slightly less reactive. Similar results were obtained for most of these nitrocompounds in hot diphenyl ether. It is noteworthy that the 6-nitroquinolines (IX) gave even on prolonged heating only starting material.

A nitrene mechanism for these cyclisations is clearly excluded for the following reasons: (a) no primary amines appear as by-products as would be expected from normal nitrene behaviour (5), (b) the *p*-nitro-isomers remain unchanged under the reaction conditions, (c) the quinoline azide (IX; $\text{NO}_2 = \text{N}_3$) decomposes readily - undoubtedly via its nitrene - to give the imidazole (XVI) which is, however, not formed from the appropriate nitro-compound (IX) by pyrolysis and (d) water collects in the reaction vessel which is more compatible with an elimination mechanism (cf. scheme 2 $\text{e} \rightarrow \text{f}$) than with deoxygenation to a nitrene under the reaction conditions.

We propose a reaction mechanism for these uncatalysed benzimidazole formations which involves a nitronic acid intermediate (c) as set out in scheme 2 ($\text{a} \rightarrow \text{f}$). The high yields attending the cyclisation of these *N*-heteroparaffins when compared to their alicyclic analogues e.g. *o*-nitro-phenylcyclohexane (2c; 6) are undoubtedly due to participation of the tertiary nitrogen atom in the reaction. As a result the transient furazanoxide (b') may be formed from which the mesomeric immonium ion ($\text{c} \leftrightarrow \text{d}$) arises in virtue of a 1-6 hydrogen abstraction which is geometrically more favourable than the alternative process in (b). The subsequent changes ($\text{e} \rightarrow \text{f}$) are readily intelligible in terms of elimination of water and deoxygenation for which benzimidazole formation provides the driving force as we have observed in other cyclisation reactions (7).

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TABLE

Imidazoles* (X - XV) Obtained by Heating the Appropriate Nitrocompounds* (III - VIII) in Sand at ca. 240°

Imidazole	X	Y	Z	M.p.	Reaction time (hr.)	Yield (%)
X	[CH ₂] ₄	CO ₂ H	H	298°	0.5	88
X	[CH ₂] ₄	NO ₂	H	209	0.5	82
X	[CH ₂] ₄	Cl	H	152	0.75	70
X	[CH ₂] ₃	CF ₃	H	140	0.5	65
X	[CH ₂] ₄	NHAc	H	222	1	40
X	[CH ₂] ₄	Me	H	126	3	55
X	[CH ₂] ₄	H	H	100	1.5	10
X	[CH ₂] ₄	H	H	100	4	62
X	[CH ₂] ₄	H	NHAc	238	1	60
XI	[CH ₂] ₃	-	-	160	0.25	70
XI	CH ₂ ·O·CH ₂ ·CH ₂	-	-	147	1	8
XI	"	-	-	"	3	32
XII	[CH ₂] ₃	-	-	151	0.25	77
XIII	[CH ₂] ₃	-	-	184	0.5	88
XIV	[CH ₂] ₃	-	-	213	0.5	80
XV	[CH ₂] ₄	-	-	232	0.5	72

* Correct analyses were obtained for all new compounds.

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