Participation by the Nitro-group in the Ring-opening Reactions of Substituted *o*-Nitrophenylethylene Oxides

By T. W. M. SPENCE and G. TENNANT*

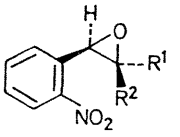
(*Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh* EH9 3JJ)

Summary Ethereal hydrogen chloride converts substituted *o*-nitrophenylethylene oxides into products identified as tautomeric 3,4-dihydro-1,3-dihydroxy-4-oxoquinoline derivatives: a course for these reactions involving participation by the nitro-group in the acid-catalysed opening of the epoxide ring is discussed.

THERE is now ample evidence for the ability of an aromatic nitro-group to function as the electrophile in intramolecular aldol-type condensations.[1] The dipolar nitro-group is also a potential nucleophile but reactions in which it functions as such are rare.[2] The most clear-cut examples are found in reactions of nitrobenzene derivatives which involve intramolecular oxygen transfer between the nitro-group and an *ortho*-side-chain.[2,3] Recent interest in this type of neighbouring-group interaction has centred on the ability of an aromatic nitro-group to participate in the solvolytic reactions of *ortho*-substituents.[4] We now report acid-catalysed reactions of substituted *o*-nitrophenylethylene oxides which are explicable by a course involving participation by the nitro-group in the opening of the epoxide ring.

Treatment of the *trans*-epoxides (**1a**) and (**1c**) with ethereal hydrogen chloride afforded high-melting acidic products $C_{15}H_{10}ClNO_3$ (43%) and $C_{10}H_8ClNO_3$ (20%) subsequently identified as the tautomeric 1-hydroxyquinolones (**2c**) and (**2d**). Formation of these heterocycles from the epoxides (**1a**) and (**1c**) finds analogy in the synthesis of chlorinated *N*-hydroxyquinolones by condensation

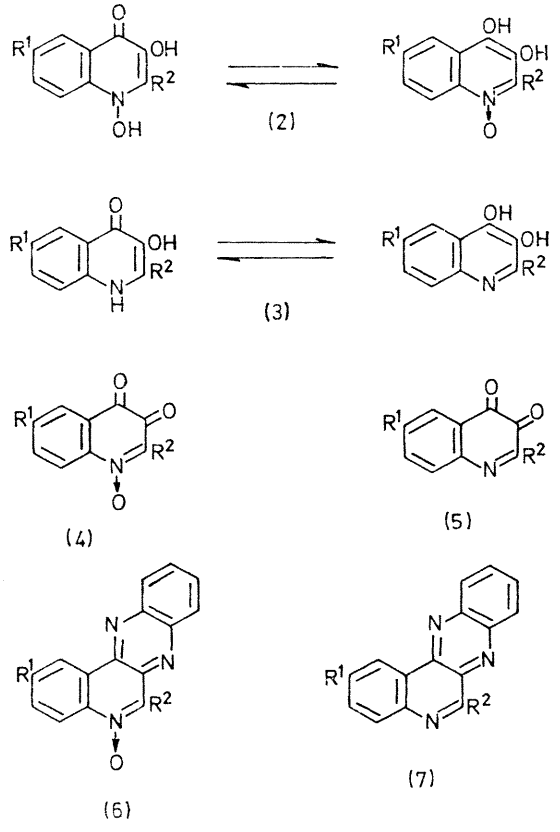
of *o*-nitrobenzaldehyde with β-dicarbonyl compounds in ethereal hydrogen chloride.[5] As in these reactions,[6]



(1)

	R^1	R^2
a;	Bz	H
b;	H	Bz
c;	Ac	H
d;	Bz	Ac
e;	Ac	Ac

ethereal hydrogen chloride in the presence of hydroquinone converted the epoxides (**1a**) and (**1c**) into the chlorine free products (**2a**) and (**2b**), respectively. These reactions are

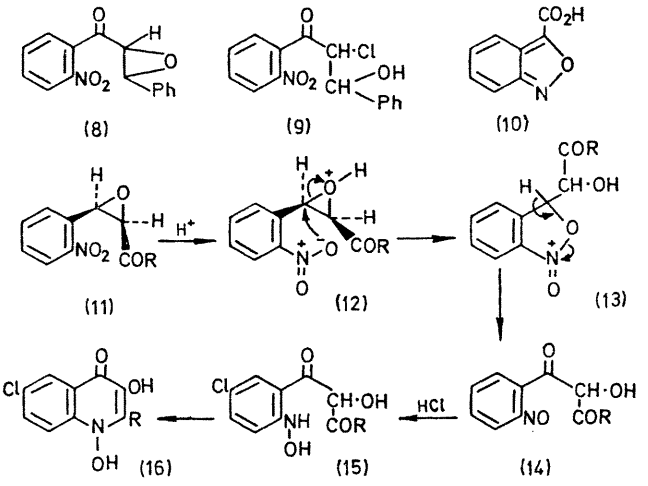


(2) (3) (4) (5) (6) (7)

	R^1	R^2
a;	H	Ph
b;	H	Me
c;	Cl	Ph
d;	Cl	Me

explicable by a course [(**11**) → (**16**)] involving intramolecular nucleophilic attack by the nitro-group on the protonated epoxide. Analogy for the intermediate formation of the nitroso-ketone (**14**) is provided by the acid-catalysed conversion of *o*-nitrophenylethylene oxide into *o*-nitrosobenzoylmethanol.[7] Conversion of the nitroso-intermediate (**14**) into the chlorophenylhydroxylamine (**15**) is in accord with the known[8] reaction of nitrosobenzene with hydrogen chloride to give *p*-chlorophenylhydroxylamine. The formation of chlorine-free products in the presence of a mild reducing agent (*i.e.* hydroquinone) lends further support to a stepwise mechanism involving the reduction of a nitroso-intermediate. Nucleophilic attack by the nitro-group at the benzylic position in the conjugate acid (**12**) rather than at the carbon atom bearing the carbonyl group is indicated by the failure of the nitro-group to participate in ring-opening of the epoxide (**8**)[9] by ethereal hydrogen chloride. The chlorohydrin formed is assigned the structure (**9**) on the basis of its conversion in warm aqueous alkali into a mixture of benzaldehyde and anthroxanic acid (**10**). The latter product is presumably derived by cyclisation[10] of the *o*-nitrophenacyl chloride formed by retro-aldol scission of the chlorohydrin (**9**).

Ethereal hydrogen chloride converted the *cis*-epoxide (**1b**) in high yield (>90%) into the compound (**2c**). High



(8) (9) (10) (11) (12) (13) (14) (15) (16)

yields of the *N*-hydroxyquinolone (**2d**) were similarly obtained from the dicarbonyl derivatives (**1d**—**e**) with concomitant loss of one of the acyl groups. The enhanced yield of cyclised products in these reactions compared with those of the *trans*-epoxides (**1a**) and (**1c**) can be attributed to the steric effect of the *cis*-carbonyl group in the compounds (**1b**) and (**1d**—**e**). Models indicate that this will force the nitrophenyl group into a position favourable for intramolecular attack by the nitro-group on the epoxide ring but at the same time blocking the approach of an external nucleophile (*i.e.* chloride ion).

Treatment of the epoxides (**1a**—**e**) with ethereal hydrogen chloride provides a valuable method for the synthesis of the otherwise inaccessible heterocyclic *N*-oxides (**2a**—**d**) and thence by dithionite reduction the parent bases (**3a**—**d**). In addition, oxidation of the quinolones (**2**) and (**3**) by manganese dioxide affords high yields of the quinoline-3,4-quinones (**4**) and (**5**) which readily condense with

o-phenylenediamine to yield quinolino[3,4-*b*]quinoxaline derivatives (**6**) and (**7**).

We thank Professor J. D. Loudon for helpful discussion and the S.R.C. for a research studentship (to T. W. M. S.).

(*Received, July 16th*, 1970; *Com.* 1152.)

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