Iminophthalans (Imino-1,3-dihydroisobenzofurans) from the Nitration of Some *p*-Xylonitrile Derivatives

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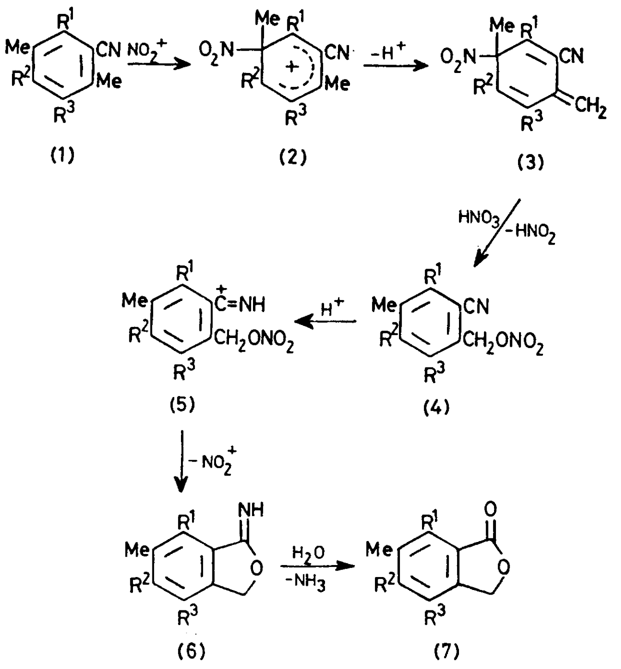
Summary On treatment with conc. nitric acid at room temperature, some substituted *p*-xylonitriles undergo an easy oxidative cyclisation as the unusual consequence of *ipso* attack, giving 1-iminophthalans in modest to good yields.



Scheme

	R¹	R²	R³
a;	Me	Me	H[a]
b;	Me	H[a]	Me
c;	CN	Me	Me
d;	Me	CN	Me
e;	Me	Me	CN

[a] NO_2 in (**6**) and (**7**)

NITRATION of aryl cyanides usually leads to the expected products of substitution and addition, the CN group remaining intact.[1] However, some *p*-xylonitrile derivatives are found to undergo an easy oxidative cyclisation during nitration, giving 1-iminophthalans (1-imino-1,3-dihydroisobenzofurans) in modest to good yields.

The nitrile (**1a**) was dissolved in nitric acid (*d* 1·5) at temperatures below −10 °C and the mixture was set aside at room temperature for several days. Dilution with water, followed by immediate neutralization of the aqueous filtrate† with $NaHCO_3$ gave the iminophthalan (**6a**), yellow needles, m.p. 185—190 °C with sintering and gradual decomposition, in 23—52% yield. When the aqueous filtrate was set aside overnight without neutralization, the phthalide (**7a**) was precipitated, white needles, m.p. 191—194 °C. Compounds (**1b**—**e**) under similar conditions gave (**6b**—**e**) in 18—85% yields, or (**7b**—**e**) in 20—96% yields;‡ no effort was made to maximize the yields.

Few cyclic imino-ethers of this type have been described, most being obtained in unspecified yields by heating *o*-halogenomethylbenzamides at high temperatures.[2] Formation of (**6a**—**e**) can be explained by a sequence involving the *ipso* attack of a nitronium ion at the site *meta* to the cyano group in (**1**) to form the ion (**2**), which releases a proton from the activated methyl group *para* to the site of attack to give the methylene-cyclohexadiene (**3**),[3] which is then transformed into the benzyl nitrate (**4**); in moderately strong protogenic acidic media, the nitrate (**4**) undergoes intramolecular ring closure through nucleophilic attack of the ester oxygen on the electron-deficient carbon of the nitrilium ion (**5**), giving (**6**) (Scheme).

Iminophthalan formation is limited to those nitriles having at least one pair of methyl groups *para* to each other; others are simply nitrated on the ring or recovered unchanged. In contrast to the nitration of polymethylbenzenes in acetonitrile in which *N*-(polymethylbenzyl)-acetamides are obtained,[4] no Ritter-type reaction leading to phthalimidines[5] was observed. To our knowledge, the reaction seems to be the first example in which the electrophilic carbon of the nitrilium ion displaces the acyl component on the ester oxygen, giving imino-ethers as stable products. It may also have synthetic potential as a new route to some substituted iminophthalans and phthalides.

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† Insoluble part was mainly composed of 2,3,4,6-tetramethyl-5-nitrobenzonitrile and 2-cyano-3,4,5-trimethyl-6-nitrobenzyl nitrate

‡ The isolated products were characterized by their analytical and spectral data. The melting ranges of the iminophthalans varied depending on the rate of heating.

[1] For a review of nitrile chemistry, see 'Chemistry of the Cyano Group,' Ed. Z. Rappoport, Interscience, London, 1970; adduct formation has been reported by A. Fischer and C. C. Greig, *Canad. J. Chem.*, 1974, **52**, 1231.

[2] S. Gabriel, *Ber.*, 1887, **20**, 2235; S. Gabriel and W. Landsberger, *ibid.*, 1898, **31**, 2732; G. Berti, *Gazzetta*, 1957, **87**, 707; L. M. Yagupol'ski and R. V. Belinskaya, *Zhur. obshchei Khim.*, 1966, **36**, 1414. The alternative route involves the reaction of *o*-lithiobenzonitrile with ketones; W. E. Parham and L. D. Jones, *J. Org. Chem.*, 1976, **41**, 1187.

[3] H. Suzuki, H. Yoneda, and T. Hanafusa, *Bull. Chem. Soc. Japan*, 1975, **48**, 2116; and other papers in the series. For a review of non-conventional processes which occur as a consequence of *ipso* attack, see S. R. Hartshorn, *Chem. Soc. Rev.*, 1974, **3**, 167; B. Moodie and K. Schofield, *Accounts Chem. Res.*, 1976, **9**, 287; H. Suzuki, *Synthesis*, 1977, in the press.

[4] E. Hunziker, J. R. Penton, and H. Zollinger, *Helv. Chim. Acta*, 1971, **54**, 2043; H. Suzuki and T. Hanafusa, *Bull. Chem. Soc. Japan*, 1973, **46**, 3607.

[5] L. I. Krimen and D. J. Cota, *Org. Reactions*, 1969, **17**, 213.