

Novel *cine* Substitution in the Reaction of 2,3-Dinitrophenol with Secondary Amines

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Summary A novel nucleophilic aromatic *cine* substitution has been discovered in the reactions of 2,3-dinitrophenol with secondary amines giving 2-(*NN*-dialkylamino)-5-nitrophenols.

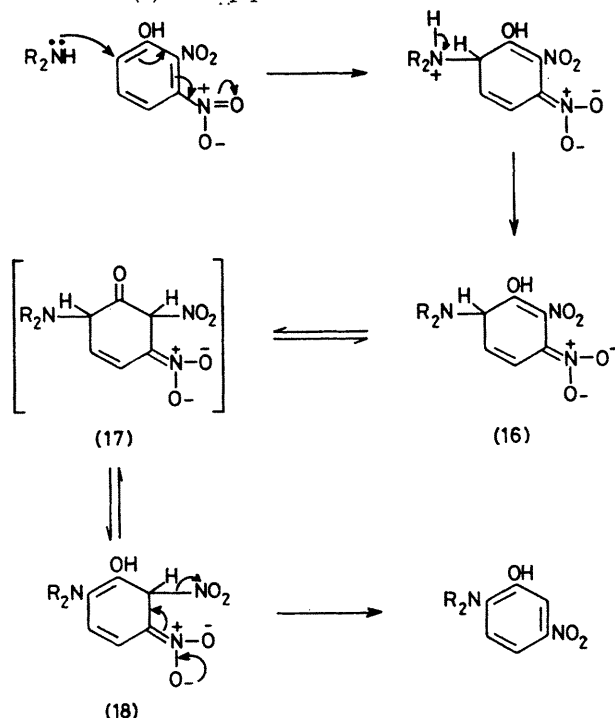
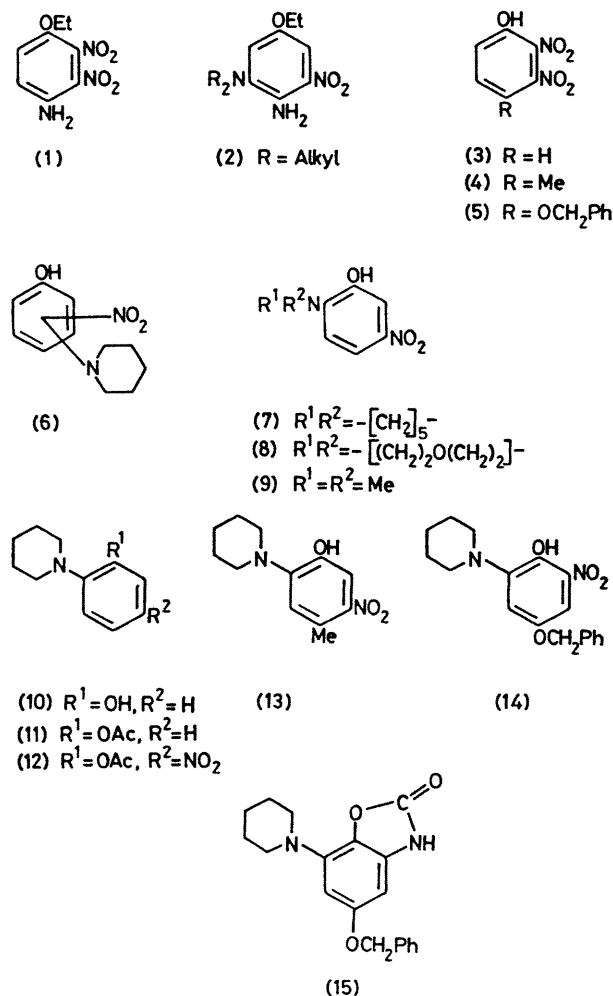
ALTHOUGH nucleophilic substitution reactions of aliphatic amines with 2,4- and 2,6-dinitro aromatic derivatives have been extensively studied,¹ there are few reports of reactions with 2,3-dinitro derivatives. As well as activating an

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aromatic ring for nucleophilic substitution, a nitro group is itself an excellent nucleofuge. 1,2-Dinitrobenzene undergoes substitution reactions with a variety of nucleophiles with the loss of one of the nitro groups.² 4-Ethoxy-2,3-dinitroacetanilide undergoes nucleophilic substitution with secondary amines with direct displacement of the 3-nitro group,³ but the corresponding aniline (1) undergoes *cine* substitution leading to nitroanilines with structure (2).³ In this reaction the incoming amino group is situated *para* to the outgoing nitro group. We now report a novel *cine* substitution in the reactions of 2,3-dinitrophenol (3)⁴ with

secondary amines, in which the incoming amino group is situated *meta* to the outgoing nitro group.

When the phenol (3) was heated with an excess of piperidine, the product (58% yield after silica gel chromatography) was a nitropiperidinophenol (6). Its u.v. spectrum in 8 M H₂SO₄ [λ_{max} 228, 266, and 322 nm (ϵ 9200, 6650, and 2300, respectively)] indicated⁵ that the phenolic hydroxy and nitro groups were *meta*-orientated, and structure (7) was considered the most likely on the basis of the n.m.r. spectrum [δ {(CD₃)₂SO} 6.74 (1H, d, *J* 10 Hz, 3-H), 7.42 (1H, d, *J* 2 Hz, 6-H), and 7.48 (1H, dd, *J* 10 and 2 Hz, 4-H)]. This structure was confirmed by synthesis. Acetylation of 2-piperidinophenol (10)⁶ afforded the acetate (11) which was nitrated (fuming nitric acid in acetic acid at 15 °C) giving the nitro derivative (12) as the major product (75%). Hydrolysis of (12) (5% sodium hydroxide at 100 °C) gave the phenol (7) (80%), identical with the product from the reaction of (3) with piperidine.



SCHEME

The results of treating several 2,3-dinitrophenols with aliphatic amines are summarised in the Table. In contrast to secondary amines, primary amines were unreactive.

TABLE. Reactions of primary and secondary amines with 2,3-dinitrophenols.^a

Dinitrophenol	Amine	Solvent	Time/h	Product	Yield ^d /%	M.p./°C
(3)	Piperidine	—	2	(7)	58	76—77
(3)	Morpholine	—	4	(8)	64	155—156
(3)	<i>NN</i> -Dimethylamine	MeOH	14	(9)	54	77—78 ^e
(3)	Methylamine	EtOH-Pr ⁱ OH	20	(3) ^b	94	163—165
(3)	Isopropylamine	Pr ⁱ OH	15	(3) ^c	95	126—127
(4)	Piperidine	—	22	(13)	52	86—87
(5)	Piperidine	—	12	(14)	54	88—89

^a Bath temperature 100—110 °C. ^b As methylamine salt. ^c As isopropylamine salt. ^d Yield of purified material after one crystallisation. ^e Lit. m.p. 79 °C (ref. 5).

A 4-methyl substituent [*viz.* compound (4)⁷] had little effect on the reaction, but a 4-benzyloxy substituent [*viz.* compound (5)[†]] changed the course of the reaction giving the phenol (14) [δ (CDCl₃) 6.75 (1H, d, *J* 3 Hz, 5-H) and 7.10 (1H, d, *J* 3 Hz, 3-H)] on reaction with piperidine. Hydrogenation of (14) over Raney nickel, followed by reaction with phosgene in acetic acid furnished the benzoxazolinone (15) (ν_{\max} 1798 cm⁻¹) thus proving that the nitro and phenolic hydroxy groups in (14) were *ortho*-orientated.

A possible mechanism for formation of the 2-(*NN*-di-alkylamino)-5-nitrophenols is outlined in the Scheme. Attack of the amine at C-6 would give the stabilised intermediate (16), which could undergo a 1,3-proton transfer *via* the oxo-tautomer (17). Loss of the 2-nitro group (as

NO₂⁻) from (18) would give the observed products. Evidence for the intermediacy of an oxo-intermediate such as (17), comes from the observation that 2,3-dinitrophenyl ethers do not undergo analogous *cine*-substitution reactions with aliphatic amines. Primary amines cause direct displacement of the 2-nitro group giving high yields of the corresponding 2-alkylamino-3-nitrophenyl ethers,^{8,9} whereas piperidine reacts to give 3-nitro-5-piperidinophenyl ethers.⁹ Satisfactory spectral and analytical data have been obtained for all new compounds.

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[†] Prepared from 4-hydroxy-2,3-dinitrophenylbenzenesulphonate by alkylation with benzyl chloride followed by base hydrolysis [E. M. Kampouris, *J. Chem. Soc. (C)*, 1967, 1235].

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