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Formation of 4-Halo-4-nitrocyclohexa-2,5-dienones on Nitration of *p*-Halophenols and *p*-Halophenyl Acetates.

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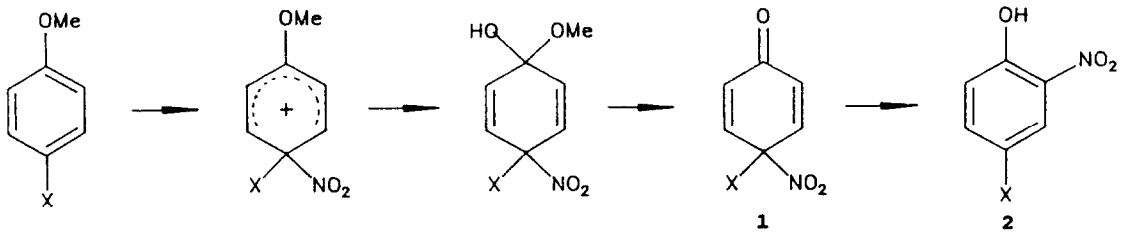
Abstract: Nitration of *p*-chloro-, *p*-fluoro-, and *p*-bromo-phenol or the corresponding *p*-halophenyl acetates at -40 °C and below gives the 4-halo-4-nitrocyclohexa-2,5-dienones in addition to the 4-halo-2-nitrophenols. The dienones isomerize to the nitrophenols at temperatures between -40 °C and 0 °C. Nitration of 4-chloro-2-methylphenol or its acetate gives both 4-chloro-2-methyl-4-nitrocyclohexa-2,5-dienone and 4-chloro-6-methyl-6-nitrocyclohexa-2,4-dienone. 4-Chloro-3-methylphenol and its acetate give 4-chloro-3-methyl-4-nitrocyclohexa-2,5-dienone.

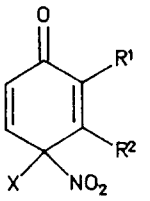
Introduction

Nitration of *p*-cresol gives 4-methyl-4-nitrocyclohexa-2,5-dienone as a result of nitration *ipso* to the methyl group, as well as the expected 4-methyl-2-nitrophenol. Nitration *ipso* to halogen is well established[1-4] but the formation of dienones from the *p*-halophenols has not been observed previously, although in the naphthalene series 1-chloro-1-nitro-2-oxo-1,2-dihydronaphthalene and the corresponding bromo compound were obtained 76 years ago by nitration of the respective 1-halo-2-naphthols.[1] Nitration of *p*-chloro- and *p*-fluoro-anisole in aqueous sulfuric acid or in aqueous acetic acid gives the 4-halo-2-nitrophenol in addition to the expected 4-halo-2-nitroanisole. The formation of the halonitrophenol is indicative of the intermediate formation of the 4-halo-4-nitrocyclohexa-2,5-dienone (**1**) and thus of *ipso* attack at the halogen of the *p*-haloanisole (Scheme I).[3,5] The previous workers did not observe **1a**, **1b** nor any precursor intermediate. We have now established conditions for the formation of 4-halo-4-nitrocyclohexa-2,5-dienones (**1**) from both *p*-halophenols and *p*-halophenyl acetate precursors. We have isolated 4-chloro- (**1a**), 4-fluoro- (**1b**) and 4-chloro

Scheme I

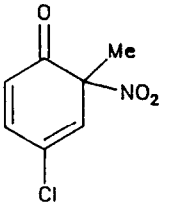


-3-methyl-4-nitrocyclohexa-2,5-dienone (**1e**) and have observed in solution 4-bromo- (**1c**), 4-chloro-2-methyl-4-nitrocyclohexa-2,5-dienone (**1d**), and 4-chloro-6-methyl-6-nitrocyclohexa-2,4-dienone (**3**).



1

	R^1	R^2	X
a	H	H	Cl
b	H	H	F
c	H	H	Br
d	Me	H	Cl
e	H	Me	Cl



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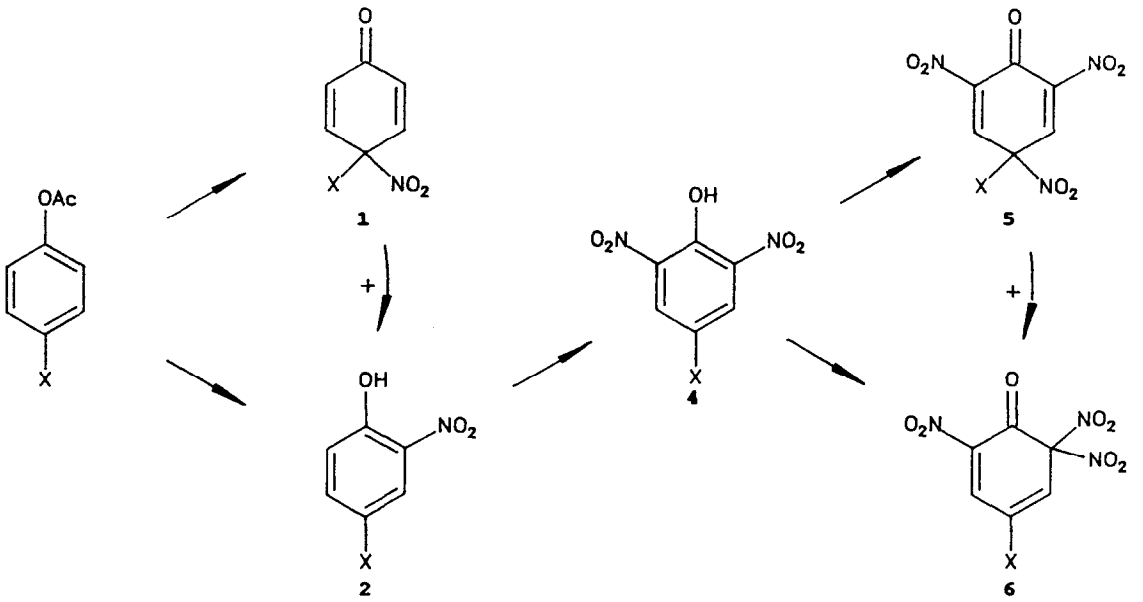
Results

Nitration of *p*-chlorophenol with nitric acid in acetic anhydride at -40 °C gave a mixture of dienone **1a** (20%) and 4-chloro-2-nitrophenol (**2a**, 80%). Dienone **1a** rapidly isomerized to **2a** at 0 °C. Nitration of *p*-chlorophenol with nitric acid in [^{2}H]chloroform at -60 °C also gave a mixture of **1a** and **2a**. The nitrophenol is relatively insoluble in chloroform and thus on cold filtration a solution containing 80% **1a** was obtained. In [^{2}H]chloroform **1a** slowly isomerized to **2a** at -20 °C. The rearrangement is partly intermolecular as shown by the fact that when **1a** was allowed to isomerize in the presence of excess 2,6-dimethylphenol 25% of the dienone was converted into *p*-chlorophenol and 4-nitro-2,6-dimethylphenol was formed. Likewise in the presence of hydroquinone 20% of the dienone was converted into *p*-chlorophenol and benzoquinone was formed.

Attempts to isolate **1a** from the foregoing reactions and from the nitration of *p*-chlorophenyl acetate (below) were only partially successful in that it was possible in to obtain solutions containing mainly **1a** but not possible to obtain solutions containing only **1a**. However we were able to isolate **1a** by nitrating *p*-chlorophenol in ether with trifluoroacetyl nitrate followed by neutralization of the excess acid with N,N,N',N'-tetramethylethylenediamine, filtration of the precipitated salt, and flash chromatography of the filtrate on alumina, all at -78 °C. Crystalline **1a** isomerized to **2a** above -40 °C.

Nitration of *p*-chlorophenyl acetate with nitric acid in trifluoroacetic anhydride and acetic anhydride at -60 °C gave ca. 70% of **1a**. Nitration of *p*-cresyl acetate has been found to give an enhanced yield of the nitrodienone as compared with nitration of the parent phenol[6] and *p*-chlorophenyl acetate behaves similarly. However, **1a** was not observed on nitration of *p*-chlorophenyl acetate with trifluoroacetyl nitrate in [^{2}H]chloroform, presumably because under these stronger acid conditions **1a** isomerized to **2a** (observed) very rapidly and this was followed by nitration of **2a** to 4-chloro-2,6-dinitrophenol (**4a**) (observed) and of the latter to 4-chloro-2,6,6-trinitrocyclohexa-2,4-dienone (**6a**) (Scheme II).

Scheme II



Nitration of **2a** in chloroform is competitive with nitration of the *p*-chlorophenyl acetate since when the nitric acid and trifluoroacetic anhydride were in only slight excess of the acetate a mixture of unreacted acetate and **4a** was obtained. Nitration of **4a** with nitric acid in a mixture of trifluoroacetic anhydride and acetic anhydride in chloroform at -40 °C gave 4-chloro-2,4,6-trinitrocyclohexa-2,5-dienone (**5a**) which rearranged to **6a**. Nitration of **4a** with trifluoroacetyl nitrate in ether gave **6a**. No **5a** was observed but it seems likely that in both this reaction and in the nitration of *p*-chlorophenyl acetate with trifluoroacetyl nitrate **5a** was formed as an intermediate but rearranged rapidly to **6a** in the stronger acid conditions and thus was not detected. Although we were able to isolate crystalline product from the reactions in which **6a** was formed we

were not able to characterize this as the product did not exhibit an nmr spectrum after isolation.

Nitration of p-fluorophenol with nitric acid in acetic anhydride at -40 °C gave a mixture of 4-fluoro-4-nitrocyclohexa-2,5-dienone (**1b**) (19%) and 4-fluoro-2-nitrophenol (**2b**) (81%). The dienone isomerized slowly to the nitrophenol at 0 °C. Nitration of *p*-fluorophenol with nitric acid in chloroform at -50 °C likewise gave **1b** and **2b**. Work-up of the reaction mixture by extraction with cold aqueous ammonia gave a mixture containing 70% **1b** with isomerization of **1b** to **2b** again occurring at 0 °C. As in the case of **1a** isomerization in the presence of 2,6-dimethylphenol or hydroquinone resulted in the trapping of a portion (45%, 30%) of the migrating nitro group. Pure **1b** was isolated from the nitration of *p*-fluorophenol with trifluoroacetyl nitrate in ether, as described for **1a**. It isomerized rapidly above -25 °C

Nitration of p-fluorophenyl acetate with nitric acid in trifluoroacetic anhydride and acetic anhydride gave **1b** (56%) and 4-fluoro-2,6-dinitrophenol (**4b**) (44%). The further nitration of **4b** was also investigated. Nitration with nitric acid in a mixture of trifluoroacetic anhydride and acetic anhydride in chloroform at -50 °C gave 4-fluoro-2,4,6-trinitrocyclohexa-2,5-dienone (**5b**). At -20 °C **5b** gave a product which was not identified. Nitration of **4b** with nitric acid and acetic anhydride in [^{2}H]chloroform at -30 °C also gave **5b**.

Nitration of *p*-bromophenol with nitric acid in [^{2}H]chloroform at -60 °C gave approximately equal amounts of 4-bromo-4-nitrocyclohexa-2,5-dienone (**1c**) and 4-bromo-2-nitrophenol (**2c**). Nitration of the acetate with nitric acid and trifluoroacetic anhydride in acetic anhydride at -40 °C gave a mixture of **1c** (75%) and **2c** (25%). When the reaction mixture was carefully warmed to ambient temperature the dienone isomerized to **2c** as well as forming other products.

p-Iodophenol was too insoluble for its nitration to be studied by nmr. *p*-Iodophenyl acetate was nitrated with nitric acid and trifluoroacetic anhydride in acetic anhydride at -60 °C. The aromatic quartet of the acetate disappeared over 30 min and it was replaced by a quartet at lower field. When the mixture was worked up by washing with cold aqueous ammonia *p*-iodophenyl acetate was the major component of the product mixture. This behaviour parallels that of iodoarenes on nitration, for which it has been shown that oxidation to the iodine(III) state occurs and that this is reversed on work-up.[7] A small amount of *p*-nitrophenyl acetate was also obtained. This is an *ipso* nitration product and it should be noted that de-iodination is faster than loss of acetyl from the acetate group of the intermediate carbocation to give the dienone - otherwise *p*-nitrophenol would have been obtained as the product rather than the acetate. Clearly dienone formation is precluded in this system.

Nitration to nitrophenols occurred when *o*-chloro-, 2,4-dichloro-, and 2,6-dichloro-phenol were used as substrates. *o*-Fluorophenol appeared to give the expected 6-fluoro-6-nitrocyclohexa-2,4-dienone. 2,4-Dichlorophenyl acetate gave 2,4-dichloro-5-nitrophenyl acetate. In the last case the chlorine substituents control the orientation of the entering nitro group whereas in the corresponding phenol the hydroxy group determines the orientation giving the 2,4-dichloro-6-nitrophenol.

Nitration of 4-chloro-2-methylphenol and its acetate gave the dienones **1d** and **3** as well as a minor amount of substitution product. The dienones selectively isomerized to 4-chloro-2-methyl-6-nitrophenol, **3** at -30 °C and **1d** at -20 °C. Nitration of 4-chloro-3-methylphenol in acetic anhydride at -60 °C or in chloroform at -60 °C gave **1e** in addition to 4-chloro-5-methyl- and 4-chloro-3-methyl-2-nitrophenol. Nitration of the acetate with trifluoroacetyl nitrate in [^{2}H]chloroform, and also with nitric acid and trifluoroacetic anhydride in acetic anhydride, at -40 °C, gave **1e** in 80% yield in each case. Pure **1e** was isolated by taking the reaction mixture from nitration of the phenol with nitric acid in [^{2}H]chloroform, containing dienone and nitrophenols, and passing it through a column of deactivated alumina at -70 °C. On warming a solution of **1e** in chloroform to ambient temperature the isomeric nitrophenols were formed in approximately equal amounts.

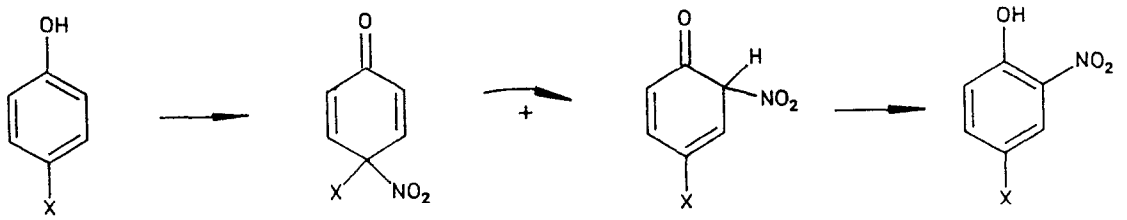
Discussion

Nitration *ipso* to the halogen of the *p*-halophenols and *p*-halophenyl acetates occurs readily and in significant yield. The fact that the resulting dienones have not been observed previously may be attributed to their lability with respect to rearrangement to the nitrophenol. The halodienones are significantly less stable than the alkylnitrodienones. 6-Alkyl-6-nitrocyclohexa-2,4-dienones (from nitration of *o*-alkylphenols) are much more labile than the isomeric 4-alkyl-4-nitrocyclohexa-2,5-dienones.[8] The difference may be attributed to the fact that the *ortho* dienone can rearrange to the 2-alkyl-6-nitrophenol by a process involving a [1,5] sigmatropic shift of the nitro group, whereas the rearrangement of the *para* dienone to a 2-nitro-4-alkylphenol must involve a dissociation-recombination process since the suprafacial [1,3] shift is forbidden. For *para* dienones both uncatalysed and acid-catalysed rearrangement pathways have been observed and these are attributed to dissociation to a radical pair (phenoxy and nitrogen dioxide) and to an encounter pair (phenol and nitronium ion), respectively.[5,9,10] Thus the fact that we did not detect nitration *ipso* to halogen in the *o*-halophenols does not necessarily mean that no such nitration occurred since it seems likely that any *o*-halonitrodienone formed would be even more labile than the *p*-halonitrodienone and thus might rearrange to the 2-halo-6-nitrophenol very rapidly. Similarly the fact that no dienones were observed in

the nitration of 2,4- and 2,6-dichlorophenol likely reflects the lability of the dienones formed rather than the absence of *ipso* attack in these systems. Moodie, Schofield and co-workers have argued for the formation of 2,4-dichloro-4-nitrocyclohexa-2,5-dienone as an intermediate in the nitration of 2,4-dichloroanisole in aqueous acid.[5] Nitration *ipso* to halogen occurred in the very deactivated 4-chloro- and 4-fluoro-2,6-dinitrophenol. Here rearrangement from dienone to phenol does not occur because there is no unsubstituted position *ortho* or *para* to the potential hydroxyl group. Rearrangement to the 4-halo-2,6,6-trinitrodienone did apparently occur.

The formation of secondary nitrodienones (the keto tautomers of the corresponding nitrophenols), in addition to the expected tertiary nitrodienones, has been observed with sufficient generality on the reaction of xylenols with nitrogen dioxide to suggest that the initial molecular product of reaction of a phenol and nitrogen dioxide is the nitrodienone(s), i.e. nitrophenols are only formed by tautomerization of precursor nitrodienones.[11] In electrophilic nitration deprotonation of the carbocation (Wheland intermediate) containing a secondary nitro group should be more rapid at oxygen than at carbon. Secondary nitrodienones have been observed in the acetyl nitrate nitration of 2,3,6-trimethyl- and 2,3,5,6-tetramethyl-phenol and of di-*tert*-butylphenols.[8,12] Thus it has been proposed that generally in electrophilic nitration of phenols also the initial products are the dienones.[11] In those dienones in which the nitro group has been added to an unsubstituted position tautomerization to the nitrophenol is very rapid and the secondary nitrodienone is not normally observed. In dienones in which the nitro group has been added to a substituted position (*ipso*-nitrodienones) the migration of the nitro group to an unsubstituted alternate position will often be slow enough for the original dienone to be observable. The product of this migration will be a secondary nitrodienone which will tautomerize to the nitrophenol (Scheme III).

Scheme III



Nitration of the halophenol with nitric acid and trifluoroacetic anhydride in ether is the preferred method for formation of the halonitrodienone when the latter is to be isolated. Much greater yields of the dienone are obtained when the halophenyl acetate is nitrated but more acidic conditions have to be employed for the less reactive acetate and this proves to be a disadvantage in the

work-up process where it is necessary to neutralize the excess acid. The neutralization of large amounts of acid was usually accompanied by isomerization of the dienone to nitrohalophenol. Although we did not attempt to isolate dienones **1c** and **1d** by nitration of the corresponding phenols in ether it seems evident that this would have been successful.

Experimental

General experimental methods have been described previously.[13,14] Nitration mixtures containing trifluoroacetic anhydride were prepared by the careful addition of trifluoroacetic anhydride to nitric acid at -78 °C followed by careful warming to -40 °C until the mixture became homogeneous. The mixture was then cooled to -78 °C and the solvent (e.g. ether) added.

Nitration of p-chlorophenol in ether. The phenol (5.14 g, 40 mmol) in ether (20 cm^3) was added over 30 min to a solution of nitric acid (3.78 g, 60 mmol) and trifluoroacetic anhydride (8.00 cm^3, 57 mmol) in ether (20 cm^3) at -78 °C. After a further 1 h at -78 °C the yellow crystalline precipitate that had formed was filtered off. A solution of N,N,N',N'-tetramethylethylenediamine (14.0 cm^3, 93 mmol) in ether (20 cm^3) was added to the filtrate and the insoluble material that formed was filtered off. The filtrate was passed through basic alumina (25 g) at -78 °C and eluted with ether (200 cm^3). The ether was evaporated under reduced pressure at -50 °C leaving colourless crystals of **1a** (0.62 g, 9%), ^1H nmr ($CDCl_3$, 90 MHz) δ: 6.50 (2H, d, J = 10 Hz, 2-H and 6-H), 7.25 (2H, d, J = 10 Hz, 3-H and 5-H); ^{13}C nmr ($CDCl_3$, 62.9 MHz) δ_C: 89.9 (C-4), 130.1 (C-2 and C-6), 138.3 (C-3 and C-5), 182.7 (C-1). The initial precipitate was redissolved in ether, the solution was washed with water, dried ($MgSO_4$) and the ether evaporated to give **2a** (4.61 g, 66%), yellow crystals (from ether), mp 87 °C (lit.[15a] mp 87 °C); ^1H nmr ($CDCl_3$, 90 MHz) δ: 7.10 (1H, d, J = 9 Hz, 6-H), 7.51 (1H, dd, J = 9 Hz, 3 Hz, 5-H), 8.07 (1H, d, J = 3 Hz, 3-H); ^{13}C nmr ($CDCl_3$, 62.9 MHz) δ_C: 121.3 (C-6), 124.0 (C-3), 129.6 (C-4), 137.7 (C-5), 138.8 (C-2), 153.3 (C-1).

Nitration in chloroform (or [^2H]chloroform). *p*-Chlorophenol (20 mmol) in chloroform (4 cm^3) at -60 °C was added to a mixture of nitric acid (30 mmol) in chloroform (12 cm^3) at -60 °C. The mixture was stirred for 15 min while yellow crystals of **2a** formed and then poured into ether (200 cm^3) at -60 °C. Aqueous ammonia (4 cm^3, 30 mmol) at -60 °C was added and the mixture stirred for 15 min. The ether layer was decanted from the solid material and the ether evaporated at -50 °C. The residue was extracted with ether (20 cm^3) at -60 °C and the solution filtered at -78 °C. The filtrate contained **1a** (80%) and **2a** (20%).

Nitration in acetic anhydride. *p*-Chlorophenol (25 mmol) was added to nitric acid (37.5 mmol) in acetic anhydride (0.5 cm^3) at -40 °C. After 30 min **1a** and **2a** were obtained in a 1:5 ratio.

Dinitrophenol **4a** was prepared by nitration of *p*-chlorophenol (0.1 mol) with nitric acid (0.25 mol) in dichloromethane (100 cm^3) at ambient temperature for 45 min and was recrystallized from ether-pentane to give yellow crystals, mp 87 °C (lit.[15b] mp 86-87 °C); ^{1}H nmr ($CDCl_3$, 90 MHz) δ: 8.30 (2H, s, 3- and 5-H), 11.27 (1H, br s, OH); ms (70 ev) *m/z* (relative intensity) 220 (33), 217.980 (100, $M_r(^{12}C_6{}^1H_3{}^{35}Cl{}^{14}N_2{}^{16}O_5)$ = 217.973).

Nitration of p-*fluorophenol* followed the procedures described above. Dienone **1b** (2.88 g, 11%) was obtained from the nitration in ether as colourless crystals and had ^{1}H nmr (CDCl3, 90 MHz) δ: 6.66 (2H, d, J = 10 Hz, 2-H and 6-H), 6.98 (2H, dd, J = 10 Hz, 6 Hz, 3-H and 5-H); ^{13}C nmr ($CDCl_3$, 62.9 MHz) δ_C: 107.8 (d, $^1J_{CF}$ = 231 Hz, C-4), 134.4 (d, $^3J_{CF}$ = 8 Hz, C-2 and C-6), 134.9 (d, $^2J_{CF}$ = 26 Hz, C-3 and C-5), 183.0 (C-1). Yellow crystals of **2b** (from ether) had mp 74 °C (lit.[16] mp 73.5-74 °C); ^{1}H nmr ($CDCl_3$, 90 MHz) δ: 7.12 (1H, dd, J = 9 Hz, 4 Hz, 6-H), 7.35 (1H, ddd, J = 9 Hz, 8 Hz, 3 Hz, 5-H), 7.78 (1H, dd, J = 8 Hz, 3 Hz, 3-H); ^{13}C nmr ($CDCl_3$, 62.9 MHz) δ_C: 110.3 (d, $^2J_{CF}$ = 28 Hz, C-3), 121.1 (d, $^3J_{CF}$ = 7 Hz, C-6), 125.8 (d, $^2J_{CF}$ = 22 Hz, C-5), 132.0 (d, $^3J_{CF}$ = 9 Hz, C-2), 151.1 (C-1), 154.2 (d, $^1J_{CF}$ = 242 Hz, C-4).

Dinitrophenol **4b** was prepared as described for **4a** and obtained as yellow needles, mp 49-50 °C (lit.[15c] mp 50 °C); ^{1}H nmr ($CDCl_3$, 90 MHz) δ: 8.09 (2H, d, J = 8.5 Hz, 3- and 5-H), 11.14 (1H, s, OH); ms (70 ev) *m/z* (relative intensity) 202.003 (70, $M_r(^{12}C_6{}^1H_3{}^{19}F{}^{14}N_2{}^{16}O_5)$ = 202.003).

Nitration of p-*bromophenol* gave **1c**, ^{1}H nmr (90 MHz) δ: 6.48 (2H, d, J = 9 Hz, 2-H and 6-H), 7.39 (2H, d, J = 9 Hz, 3-H and 5-H); ^{13}C nmr (62.9 MHz) δ_C: 77.7 (C-4), 128.7 (C-2 and C-6), 139.4 (C-3 and C-5), 183.0 (C-1), and **2c**, isolated and crystallized, (ether-pentane), mp 89-92 °C (lit.[17] mp 92 °C); ^{1}H nmr ($CDCl_3$, 90 MHz) δ: 7.13 (1H, d, J = 9 Hz, 6-H), 7.73 (1H, dd, J = 9 Hz, 3 Hz, 5-H), 8.32 (1H, d, J = 3 Hz, 3-H); ^{13}C nmr ($CDCl_3$, 62.9 MHz) δ_C: 111.7 (C-4), 121.7 (C-6), 127.3 (C-3), 134.2 (C-2), 140.3 (C-5), 154.1 (C-1).

Nitration of o-*chlorophenol* (5 mmol) with nitric acid (15 mmol) in acetic anhydride at -60 °C gave, over 15 min, 2-chloro-6-nitrophenol (72%) (δ: 7.05 (1H, dd, J = 9 Hz, J = 9 Hz, 4-H), 7.79 (1H, d, J = 9 Hz, 3-H) 8.07 (1H, d, J = 9 Hz, 5-H)) and 2-chloro-4-nitrophenol (28%) (δ: 7.05 (1H, 6-H), 8.05 (1H, 5-H) 8.20 (1H, d, J = 3 Hz, 3-H)). On warming the solution the 4-nitro isomer (at -20 °C) and the 6-nitro isomer (at 0 °C) were further nitrated to 2-chloro-4,6-dinitrophenol (8.60 (1H, d, J = 3 Hz, 3-H) 8.88 (1H, d, J = 3 Hz, 5-H)). Similar results were obtained in chloroform.

Nitration of o-fluorophenol in acetic anhydride at -60 °C gave a species, assigned as 6-fluoro-6-nitrocyclohexa-2,4-dienone, with broad doublets (J = 10 Hz) at δ: 6.30 and 6.55 and which survived until the solution was warmed to -20 °C. However the complications of overlapping spectra and the complex splitting patterns resulting from H-F coupling make the identification tentative. The major species present was 2-fluoro-6-nitrophenol (δ: 7.01 (1H, ddd, J = 9 Hz, 9 Hz, 5 Hz, 4-H), 7.55 (1H, ddd, J = 9 Hz, 2 Hz, 8 Hz, 3-H) 7.91 (1H, ddd, J = 9 Hz, 2 Hz, 2 Hz, 5-H)) and the minor species was 2-fluoro-4-nitrophenol (δ: 7.17 (1H, m, 6-H), 7.95 (1H, m, 3-H) 8.02 (1H, m, 5-H)). On warming to -40 °C 2-fluoro-4,6-dinitrophenol was slowly formed. In chloroform the two mononitrophenols and a little of the dinitrophenol were obtained.

2-Fluoro-4,6-dinitrophenol was prepared as described for **4a** and had mp 101-102 °C (lit.[15c] mp 102 °C); ^{1}H nmr ($CDCl_3$, 90 MHz) δ: 8.29 (1H, dd, J = 9 Hz, 2.5 Hz, 3-H), 8.88 (1H, dd, J = 3 Hz, 2.5 Hz, 5-H), 10.98 (1H, br s, OH); ms (70 ev) m/z (relative intensity) 202.005 (100, $M_r(^{12}C_6{}^1H_3{}^{19}F^{14}N_2{}^{16}O_5)$ = 202.003).

Nitration of 2,4-dichlorophenol in acetic anhydride at -60 °C gave 2,4-dichloro-6-nitrophenol. Minor peaks at δ 6.67 and 7.6, which subsequently disappeared, could have reflected the formation of dienone(s). 2,4-Dichloro-6-nitrophenol was also obtained from nitration in chloroform and had mp 128-129 °C (lit.[15d] mp 124-125 °C); ^{1}H nmr ($(CD_3)_2CO$, 90 MHz) δ: 7.70 (1H, d, J = 3 Hz, 3-H), 8.05 (1H, d, J = 3 Hz, 5-H).

Nitration of 2,6-dichlorophenol both in acetic anhydride and in chloroform, at -60 °C, gave 2,6-dichloro-4-nitrophenol, mp 120-124 °C (decomp.) (lit.[18] mp 127 °C); ^{1}H nmr ($CDCl_3$-$(CD_3)_2CO$, 90 MHz) δ: 8.18 (s); ms (methane CI) m/z 250 (M+41), 248 (M+41), 238 (M+29), 236 (M+29), 212 (10, M+1), 210 (61, M+1), 208 (100, M+1).

Nitration of 4-chloro-2-methylphenol in acetic anhydride at -60 °C gave over 10 min a mixture of **3** (61%), **1d** (18%), and 4-chloro-2-methyl-6-nitrophenol (20%). At ambient temperature (after isomerization of the dienones) further nitration occurred to give a species with singlets at δ 5.86 and 7.20 assigned as either 4-chloro-6-methyl-2,6-dinitrocyclohexa-2,4-dienone or 4-chloro-6-methyl-2,4-dinitrocyclohexa-2,5-dienone. Attempts to isolate the mononitrodienones by chromatography of the reaction mixture at low temperature were unsuccessful. The different thermal stabilities made possible the assignment of both the ^{1}H nmr and the ^{13}C nmr for each dienone. Dienone **3** had ^{1}H nmr δ: 6.27 (1H, d, J = 10 Hz, 2-H), 6.73 (1H, d, J = 3 Hz, 5-H), 7.24 (1H, dd, J = 10 Hz, 3 Hz, 3-H); ^{13}C nmr (62.9 MHz) δ_C: 90.5 (C-6), 124.6 (C-2), 130.4 (C-5), 143.5 (C-3), 189.4 (C-1). Dienone **1d** had ^{1}H nmr δ: 6.47 (1H, d, J = 9 Hz, 6-H), 7.01 (1H, m, 3-H),

7.24 (1H, dd, J = 9 Hz, 3 Hz, 5-H); ^{13}C nmr (62.9 MHz) δ_C: 129.1 (C-6), 132.8 (C-3), 137.7 (C-5). The assignment of the more stable dienone as the *p*-dienone was confirmed by the multiplet for the 3-H at δ 7.01, reflecting the coupling to the adjacent vinylic methyl group. 4-Chloro-2-methyl-6-nitrophenol (from ether-petroleum ether) had mp 105-106 °C (lit.[19] mp 107 °C); ^{1}H nmr ($CDCl_3$, 90 MHz) δ: 2.28 (3H, s, CH_3), 7.37 (1H, m, 3-H), 7.92 (1H, d, J = 2 Hz, 5-H); ^{13}C nmr (62.9 MHz) δ_C: 120.7 (C-5), 122.9 (C-4), 130.8 (C-2), 132.4 (C-6), 136.9 (C-3), 151.5 (C-1). On nitration in chloroform at -60 °C the nitrophenol precipitated.

Nitration of 4-chloro-3-methylphenol in acetic anhydride at -60 °C gave an immediate yellow precipitate of 4-chloro-5-methyl-2-nitrophenol, which was filtered off and recrystallized from ether and had mp 131.5-133 °C (lit.[20] mp 133-134 °C); ^{1}H nmr ($(CD_3)_2CO$), 90 MHz) δ: 2.37 (3H, s, CH_3), 7.14 (1H, br s, 6-H), 8.04 (1H, s, 3-H). The ^{1}H nmr spectrum of the supernatant solution showed **1e** (33%) and 4-chloro-3-methyl-2-nitrophenol (67%). On warming to 0 °C 4-chloro-3-methyl-2,6-dinitrophenol was formed. Nitration in chloroform gave similar results. However, whereas an attempt to isolate **1e** by work-up of an acetic anhydride reaction mixture at -60 °C was unsuccessful, chromatography of a chloroform reaction mixture on alumina (deactivated with 3% of 10% aqueous acetic acid) at -65 °C and elution with ether-petroleum ether gave, after evaporation of the 50% ether fraction at -50 °C, colourless crystals of **1e**, ^{1}H nmr δ: 2.17 (3H, s, CH_3), 6.44 (1H, br s, 2-H), 6.56 (1H, d, J = 10 Hz, 6-H), 7.06 (1H, d, J = 10 Hz, 5-H); ^{13}C nmr (62.9 MHz) δ_C: 18.4 (CH_3), 96.7 (C-4), 129.7 (C-2), 129.8 (C-6), 139.1 (C-5), 147.8 (C-3), 183.7 (C-1).

Nitration in chloroform with a slight excess of nitric acid gave the mononitrophenols after warming to ambient temperature. Most of the less soluble 5-methyl-2-nitro isomer was filtered off and the residue obtained on washing and evaporation of the filtrate (82% 3-methyl-2-nitro isomer) was triturated with ether and the extract chromatographed on silica. Elution with ether-petroleum ether (25:75) gave (after its isomer) 4-chloro-3-methyl-2-nitrophenol, obtained as yellow crystals on recrystallization from petroleum ether, mp 69-71.5 °C, ^{1}H nmr ($CDCl_3$, 90 MHz) δ: 2.55 (3H, s, CH_3), 6.93 (1H, d, J = 9 Hz, 6-H), 7.45 (1H, d, J = 9 Hz, 5-H), 9.28 (1H, br s, OH); ms (70 ev) m/z (relative intensity) 189 (45), 187.000 (100, $M_r(^{12}C_7{}^1H_6{}^{35}Cl{}^{14}N{}^{16}O_3)$ = 187.004), 172 (30), 170 (81).

Nitration of p-chlorophenyl acetate. The acetate (0.85 g, 5 mmol) was added dropwise to a solution of nitric acid (1.90 g, 30 mmol) in trifluoroacetic anhydride (6.30 g, 30 mmol) and acetic anhydride (3.0 g, 30 mmol) at -40 °C. As soon as the addition of the acetate was complete the solution was cooled to -60 °C and the reaction monitored by nmr. After 40 min the acetate had completely reacted and **1a** (70%) and 4-chloro-2,6-dinitrophenol (30%) were formed. The reaction mixture was added to ether (25 cm^3) at -60 °C and ammonia was condensed

into the solution until it was basic. The ether solution was decanted and evaporated at -50 °C to mixture containing **1a** (70%). When nitration was carried out at -40 °C **1a** formed but eventually reacted further to give first **4a** and then **6a**. Nitration in chloroform at -40 °C was carried out with acetate (2 mmol), nitric acid (6.6 mmol) and trifluoroacetic anhydride (6.6 mmol). The further nitration of **4a** was investigated at -40 °C using nitric acid (3 mmol) and trifluoroacetic anhydride (2 mmol) in acetic anhydride (1 cm^3) and [^{2}H]chloroform (1 cm^3), and also in ether (1 cm^3) with nitric acid (3 mmol) and trifluoroacetic anhydride (6 mmol). Dienone **5a** had ^{1}H nmr δ: 8.07 and **6a** δ: 8.00 and 8.37.

Nitration of p-fluoro-, p-bromo-, 4-chloro-2-methyl-, 4-chloro-3-methyl-, and 2,4-dichloro-phenyl acetate was carried out in trifluoroacetic anhydride and acetic anhydride at -60 °C to -40 °C. 4-Chloro-3-methylphenyl acetate was also nitrated with trifluoroacetyl nitrate in chloroform at -40 °C and on addition of saturated sodium bicarbonate, after the reaction mixture had been warmed to ambient temperature, 4-chloro-3-methyl-2,6-dinitrophenol was precipitated as the red sodium salt. The salt was acidified with hydrochloric acid and the dinitrophenol recrystallized from ether-petroleum ether to give yellow crystals, mp 67-68 °C (lit.[21] mp 69 °C); ^{1}H nmr ($CDCl_3$, 90 MHz) δ: 2.38 (3H, s, CH_3), 8.25 (1H, s, 5-H). The residue from the organic extract was chromatographed on neutral alumina to give 4-chloro-5-methyl-2-nitrophenol which was acetylated via the salt to 4-chloro-5-methyl-2-nitrophenyl acetate, mp 51.5-53.5 °C, ^{1}H nmr ($CDCl_3$, 90 MHz) δ: 2.31 (3H, s, CH_3), 2.40 (3H, s, CH_3), 7.08 (1H, s, 6-H), 8.07 (1H, s, 3-H); ms (70 ev) *m/z* (relative intensity) 231 (3), 229.015 (10, M_r ($^{12}C_9{}^1H_8{}^{35}Cl{}^{14}N{}^{16}O_4$) = 229.014), 189 (60), 187 (100).

Low temperature work up of the 2,4-dichlorophenyl acetate nitration reaction mixture, chromatography of the product on silica, elution of the yellow band with ether-petroleum ether and recrystallization from ether-petroleum ether, gave yellow crystals of 2,4-dichloro-5-nitrophenyl acetate, mp 50-54 °C, ^{1}H nmr ($CDCl_3$), 90 MHz) δ: 2.30 (3H, s, CH_3), 7.60 (1H, s, 3-H), 7.76 (1H, s, 6-H); ms (70 ev) *m/z* (relative intensity) 253 (6), 251 (37), 248.958 (57, M_r ($^{12}C_8{}^1H_5{}^{35}Cl_2{}^{14}N{}^{16}O_4$) = 248.960), 211 (8), 209 (48), 207 (65).

Isomerization and trapping experiments. Isomerization of **1a** in chloroform was carried out in the presence of 2,6-dimethylphenol (0.5 mmol) and of hydroquinone (0.3 mmol) by adding a solution of the reagent at -60 °C to a solution of the dienone (0.2 mmol) in [^{2}H]chloroform (300 mm^3) also at -60 °C and allowing the mixture to warm to ambient temperature, followed by analysis by glc. In the dimethylphenol experiment the ratio of **2a**:*p*-chlorophenol was 75:25 and in the hydroquinone experiment 80:20. Isomerization in the presence of methanol (500 mm^3) gave a 96:4 mixture of **2a** and *p*-chlorophenol. Addition of trifluoromethanesulphonic acid (4 drops) to a solution of **1a** gave only **2a**. Isomeriza-

tion of **1b** in the presence of methanol gave only **2b**. Isomerization in the presence of trifluoromethanesulphonic acid gave **2b**:*p*-fluorophenol = 88:6 and other products (6%).

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