# Nitration Studies of 4-Substituted Toluenes, 5-Substituted Hemimellitenes and Acetoxyprehnitene

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#### Abstract

Product distributions are reported for the nitration of 4-methoxy-, 4-bromo- and 4-acetoxy-toluenes, of 5-fluoro- and 5-acetamido-hemimellitenes, and of acetoxyprehnitene. A Hammett  $\rho$  value for *ipso* nitration is estimated from competitive nitrations with a series of 5-substituted hemimellitenes.

# Introduction

*ipso*-Nitration has been shown<sup>1-4</sup> to compete effectively with normal nitration in many substituted benzenes in mixtures of nitric acid and acetic anhydride. The products of ipso nitration are typically nitrocyclohexadienyl acetate adducts or their decomposition products,<sup>1,2</sup> products of nitration in an alkyl side chain,<sup>4</sup> or nitrocyclohexadienones;<sup>3</sup> the formation of any or all of these products constitutes firm evidence for ipso nitration. Nitration at a substituted aromatic position without loss of the substituent has been observed for the following substituents: methyl,<sup>1,2</sup> ethyl,<sup>5</sup> methoxy,<sup>6</sup> neopentyl,<sup>7</sup> and methylene<sup>8</sup> as part of a five- or six-membered fused ring. In any particular system the ratio of *ipso* to normal nitration is determined by the relative reactivities towards electrophilic attack of the various substituted and unsubstituted aromatic positions. For example in toluene,<sup>9</sup> where position 1 is activated only by the *ipso* methyl, only about 3% of the total nitration product is formed by ipso nitration at C1. The addition of one methyl group ortho to C1 (o-xylene)<sup>9</sup> increases the amount of *ipso* product to about 50 %. Although some general conclusions can be drawn about the sensitivity of *ipso* nitration to substituents from data in the literature, no detailed study has been reported. This paper reports results we have

<sup>1</sup> Blackstock, D. J., Fischer, A., Richards, K. E., Vaughan, J., and Wright, G. J., Chem. Commun., 1970, 641.

<sup>2</sup> Blackstock, D. J., Cretney, J. R., Fischer, A., Hartshorn, M. P., Richards, K. E., Vaughan, J., and Wright, G. J., *Tetrahedron Lett.*, 1970, 2793.

<sup>3</sup> Blackstock, D. J., Hartshorn, M. P., Lewis, A. J., Richards, K. E., Vaughan, J., and Wright, G. J., J. Chem. Soc. B, 1971, 1212.

<sup>4</sup> Blackstock, D. J., Fischer, A., Richards, K. E., and Wright, G. J., *Aust. J. Chem.*, 1973, **26**, 775. <sup>5</sup> Clemens, A. H., Hartshorn, M. P., Richards, K. E., and Wright, G. J., *Aust. J. Chem.*, 1977, **30**, 103.

<sup>6</sup> Collins, B. A., Richards, K. E., and Wright, G. J., J. Chem. Soc., Chem. Commun., 1972, 1216.
<sup>7</sup> Reuvers, A. J. M., van Leeuwen, F. F., and Sinnema, A., J. Chem. Soc., Chem. Commun., 1972, 828.
<sup>8</sup> Fischer, A., Greig, C. C., Wilkinson, A. L., and Leonard, D. R. A., Can. J. Chem., 1972, 50, 2211.
<sup>9</sup> Fischer, A., Packer, J., Vaughan, J., and Wright, G. J., J. Chem. Soc., 1964, 3687.

obtained which allow firmer conclusions about *ipso* nitration at a methyl group to be drawn than have previously been possible.

We report product distributions resulting from nitration of *p*-methoxy-, *p*-bromoand *p*-acetoxy-toluene, from 5-fluoro- and 5-acetamido-hemimellitene, and from acetoxyprehnitene.\* We have also carried out competitive nitrations with a series of 5-substituted hemimellitenes which allow us to estimate a Hammett  $\rho$  value for *ipso* nitration.

### Experimental

See the preceding paper for the general experimental information.

#### General Nitration Procedures

(i) Analytical scale.—The aromatic compound (0.5 g) was dissolved in acetic anhydride (2 ml) and the mixture cooled to  $0^\circ$ . Nitric acid (0.1 ml) dissolved in acetic anhydride (1 ml) was added dropwise with stirring and the resultant mixture kept at  $0^\circ$  for 1.5 h. The reaction mixture was then quenched by the addition of water (50 ml) and the aromatic material isolated by means of ether. This product was analysed by g.l.c. An estimate of the amount of the adduct dienes or dienones formed in the nitration was obtained from the n.m.r. spectrum of the crude reaction mixture; this estimate was always in close agreement with the amount of diene or dienone decomposition products indicated by g.l.c. analysis.

(ii) *Preparative scale.*—In these reactions more nitric acid was used, usually to give a nitric acid/ aromatic substrate molar ratio of 2:1. The aromatic products were isolated from the reaction mixture by one, or both, of two methods:

(A) Removal of solvent from the reaction mixture at reduced pressure at or below 20° normally gave a residual yellow oil, the components of which were separated by chromatography on alumina or silica.

(B) The reaction mixture was quenched with carbon tetrachloride (200 ml for 5 g aromatic substrate), the resulting solution washed with water and dried, and the carbon tetrachloride removed under vacuum at  $20^{\circ}$ . The components of the residue were separated by chromatography.

#### Nitration of 4-Methoxytoluene (Preparative)

4-Methoxytoluene (2.5 g) was nitrated and the crude product, isolated by method (B) above, adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 4-methoxy-3,5-dinitro-toluene as colourless crystals, m.p. 122-123° (lit.<sup>10</sup> 123-124°) (Found: M<sup>+</sup>, 212.0434. Calc. for C<sub>8</sub>H<sub>8</sub>N<sub>2</sub>O<sub>5</sub>: M<sup>+</sup>, 212.0433).  $\nu_{max}$  (KBr) 1525, 1330, 980, 730 cm<sup>-1</sup>; n.m.r. (CDCl<sub>3</sub>)  $\delta$  2.50 (s. 3H, ArCH<sub>3</sub>), 4.05 (s, 3H, ArOCH<sub>3</sub>), 7.84 (s, 2H, ArH).

Elution with light petroleum/ether (25:1) gave 4-methyl-4-nitrocyclohexa-2,5-dien-1-one as a yellow oil (Found: M<sup>+</sup>, 153.0429. C<sub>7</sub>H<sub>7</sub>NO<sub>3</sub> requires M<sup>+</sup>, 153.0426).  $\nu_{max}$  (liq. film) 1670, 1635, 1610, 1545, 1365 cm<sup>-1</sup>,  $e_{max}$  (at 220 nm in trifluoroethanol) 15700; n.m.r. (CDCl<sub>3</sub>)  $\delta$  1.95 (s. 3H, ArCH<sub>3</sub>), 5.66 (d, J 10 Hz, 2H, H2 and H6), 6.53 (d, J 10 Hz, 2H, H3 and H 5).

#### Nitration of 4-Bromotoluene (Preparative)

4-Bromotoluene (3 · 5 g) was nitrated and the crude product, isolated by method (B) above, adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 4-bromo-3-nitrotoluene as colourless crystals, m.p.  $32-33^{\circ}$  (lit.<sup>11</sup>  $30 \cdot 2-31 \cdot 2^{\circ}$ ) (Found: M<sup>+</sup>, 214 · 9584. Calc. for C<sub>7</sub>H<sub>6</sub><sup>79</sup>BrNO<sub>2</sub>: M<sup>+</sup>, 214 · 9582).  $\nu_{max}$  (Nujol) 1540, 1355, 880 cm<sup>-1</sup>; n.m.r. (CCl<sub>4</sub>)  $\delta 2 \cdot 53$  (s, 3H, ArCH<sub>3</sub>), 7 · 10–7 · 62 (m, 2H, ArH), 7 · 98 (d, J 2 Hz, 1H, ArH).

Continued elution with light petroleum gave a gum which appeared (g.l.c.) to be a mixture of at least three compounds. A bromodinitrotoluene (Found:  $M^+$ , 259.9430. Calc. for  $C_7H_5^{79}BrN_2O_4$ :

\* Concerning nomenclature, see footnote to preceding paper, p. 105.

<sup>10</sup> Bunnett, J. F., Moe, H., and Knutson, D., J. Am. Chem. Soc., 1954, 76, 3936.

<sup>11</sup> Berliner, E., and Monack, L. C., J. Am. Chem. Soc., 1952, 74, 1574.

 $M^+$ , 259.9433) was separated from the mixture by further chromatography on 10% deactivated alumina. The residual mixture appeared (mass spectrum) to consist mainly of dibrominated products. Elution with light petroleum/ether (32:1) gave 4-methyl-4-nitrocyclohexa-2,5-dien-1-one, iden-

Eithen with light periode infertion (52, 1) give a methyla interpretation with right periode infertion (52, 1) give a methyla interpretation of p-methoxytoluene.

Elution with light petroleum/ether (10:1) gave 2-nitro-*p*-cresol as yellow crystals, m.p.  $32-33^{\circ}$  (lit.<sup>12</sup> 32°);  $\nu_{max}$  (Nujol) 3250, 1540, 1355, 825 cm<sup>-1</sup>. This compound was formed by aromatization of the nitrodienone on the chromatography column.

#### Nitration of 4-Acetoxytoluene (Preparative)

4-Acetoxytoluene (3 g) was nitrated and the crude product isolated by methods (A) and (B). The yellow-red oily residue that resulted in each case was adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 4-acetoxy-3-nitrotoluene as an oil (Found: M<sup>+</sup>, 195.0531. C<sub>9</sub>H<sub>9</sub>NO<sub>4</sub> requires M<sup>+</sup>, 195.0524).  $\nu_{max}$  (liquid film) 1775, 1535, 1335, 1175 cm<sup>-1</sup>; n.m.r. (CDCl<sub>3</sub>)  $\delta 2.33$  (s, 3H, ArOCOCH<sub>3</sub>), 2.42 (s, 3H, ArCH<sub>3</sub>), 7.33 (m, 2H, ArH), 7.95 (s, 1H, ArH).

Elution with light petroleum/ether (36:1) gave a mixture of 4-acetoxy-3-nitrotoluene and 4-acetoxy-2-nitrotoluene. Hydrolysis of the mixture with aqueous sulphuric acid gave 3-nitro-*p*-cresol (m.p. 78–79°; lit.<sup>13</sup> 79°) in addition to 2-nitro-*p*-cresol.

Elution with light petroleum/ether (22:1) gave 4-methyl-4-nitrocyclohexa-2,5-dien-1-one, identical with the sample isolated from the nitration of *p*-methoxytoluene.

Elution with light petroleum/ether (8:1) gave 2-nitro-*p*-cresol, identical with the sample isolated from the nitration of *p*-bromotoluene.

#### Nitration of 5-Fluorohemimellitene (Preparative)

5-Fluorohemimellitene (3 g) was nitrated and the crude product, isolated by method (B) above, adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 5-fluoro-4-nitrohemimellitene as colourless crystals, m.p. 38-39° (Found: M<sup>+</sup>, 183.0700. C<sub>9</sub>H<sub>10</sub>FNO<sub>2</sub> requires M<sup>+</sup>, 183.0696).  $\nu_{max}$  (KBr) 1530, 1345, 1080 cm<sup>-1</sup>; n.m.r. (CDCl<sub>3</sub>)  $\delta$  2.15 (s, 3H, ArCH<sub>3</sub>), 2.20 (s, 3H, ArCH<sub>3</sub>), 2.27 (s, 3H, ArCH<sub>3</sub>), 6.83 (d, J 10 Hz, 1H, ArH).

Elution with light petroleum/ether (36:1) gave 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one, identical with an authentic sample.<sup>3</sup>

Elution with light petroleum/ether (2:1) gave 3,4,5-trimethyl-2-nitrophenol.

#### Nitration of 5-Acetamidohemimellitene (Preparative)

5-Acetamidohemimellitene (3.5 g) was nitrated and the crude product, isolated by method (B) above, adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 5-acetamido-4-nitrohemimellitene as orange crystals, m.p. 176–179° (Found: M<sup>+</sup>, 222·1010.  $C_{11}H_{14}N_2O_3$  requires M<sup>+</sup>, 222·1004).  $v_{max}$  (KBr) 3400, 1680, 1540, 1360, 1085 cm<sup>-1</sup>; n.m.r. (CDCl<sub>3</sub>)  $\delta$  2·10 (s, 3H, ArNHCOCH<sub>3</sub>), 2·16 (s, 6H, ArCH<sub>3</sub>), 2·21 (s, 3H, ArCH<sub>3</sub>), 6·33 (s, 1H, ArNHCOCH<sub>3</sub>), 7·15 (s, 1H, ArH).

Elution with light petroleum/ether (38:1) gave 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one, identical with an authentic sample.<sup>3</sup>

#### *Nitration of Acetoxyprehnitene (Preparative)*

Acetoxyprehnitene (1 g) was nitrated and the crude product isolated by method (B) above. As the carbon tetrachloride was being removed under vacuum a solid separated from the solution and on crystallization from light petroleum gave 2,3,4,5-tetramethyl-4-nitrocyclohexa-2,5-dien-1-one as colourless crystals, m.p. 82-83° (Found: M<sup>+</sup>, 195.0904. C<sub>10</sub>H<sub>13</sub>NO<sub>3</sub> requires M<sup>+</sup>, 195.0895).  $\nu_{max}$  (KBr) 1680, 1640, 1540, 1365 cm<sup>-1</sup>,  $\varepsilon_{max}$  (at 237 nm in trifluoroethanol) 13560; n.m.r. (CDCl<sub>3</sub>)  $\delta$  1.85 (s, 3H, ArCH<sub>3</sub>), 1.93 (s, 6H, ArCH<sub>3</sub>), 1.95 (s, 3H, ArCH<sub>3</sub>), 6.25 (broad s, 1H, H 6).

The residue, after the separation of the above crystalline material, was a gum (< 3%).

<sup>12</sup> Henry, R. A., J. Org. Chem., 1958, 23, 648.

<sup>13</sup> Holleman, A. F., and Hoeflake, J. M. A., Recl Trav. Chim. Pays-Bas, 1916, 36, 271.

## Rearrangement of 2,3,4,5-Tetramethyl-4-nitrocyclohexa-2,5-dien-1-one

The dienone on rearrangement in methanol solution at 20° gave 2,3,4,5-tetramethyl-6-nitrophenol as colourless crystals, m.p. 89-90° (Found: M<sup>+</sup>, 195 0902.  $C_{10}H_{13}NO_3$  requires M<sup>+</sup>, 195 0895).  $v_{max}$  (KBr) 3300, 1535, 1330 cm<sup>-1</sup>; n.m.r. (CDCl<sub>3</sub>)  $\delta$  2·15 (s, 3H, ArCH<sub>3</sub>), 2·25 (s, 3H, ArCH<sub>3</sub>), 2·33 (s, 3H, ArCH<sub>3</sub>), 2·40 (s, 3H, ArCH<sub>3</sub>), 10·40 (s, 1H, ArOH).

#### Competitive Nitrations

The competitive nitrations were carried out by taking an equimolar mixture of the competing substrates being investigated (see Table 5 below) and adding an amount of nitrating agent (nitric acid/acetic anhydride at  $0^{\circ}$ ) less than the stoichiometric amount. The reaction mixture was analysed by n.m.r. at  $0-3^{\circ}$  at various stages of reaction. Allowance was made for the fact that some of the competing compounds underwent *ipso* nitration to different degrees (see Table 4).

G.l.c. analysis of the final product mixture from the competition nitrations between 5-acetoxyhemimellitene and hemimellitene and between 5-bromo- and 5-acetoxy-hemimellitene showed that the ratio of ipso/normal nitration products was the same as that obtained when each substrate was nitrated individually. It was assumed that this was a characteristic of the other cases also.

The major error in each n.m.r. analysis lay in obtaining an accurate reading of the integral of the reactant's aromatic proton signals; this introduced an error of approximately 10% into the measurements.





Scheme 2

## **Results and Discussion**

# Nitration of para-Substituted Toluenes

Nitration of 4-substituted o-xylenes and 5-substituted hemimellitenes (where the substituents were Br, OMe or OAc) showed<sup>3</sup> that *ipso* nitration at a methyl group in these substrates leads to the formation of nitrocyclohexadienones (e.g., Scheme 1, for 4-substituted o-xylenes). These are generally unstable; they can be isolated from the crude reaction mixture at low temperatures, but at temperatures ranging from 0° to 60° they decompose smoothly to nitrophenols (Scheme 2, for the dienone derived from 4-substituted o-xylene). The formation of either dienone or nitrophenols in nitration by nitric acid in acetic anhydride therefore provides evidence for *ipso* nitration.

Table 1 shows the products obtained from nitration of *p*-substituted toluenes in nitric acid/acetic anhydride. A major product from each substrate, isolated by column chromatography of the crude mixtures, is 4-methyl-4-nitrocyclohexa-2,5-dienone (1); this product provides direct evidence for *ipso* nitration at the methyl group of all three *para*-substituted toluenes. The data for 4-acetoxytoluene (Table 1) show that 2-nitro-*p*-cresol is formed by decomposition of dienone (1); this was established for each crude reaction mixture, and for the isolated dienone, which decomposed quantitatively to 2-nitro-*p*-cresol at 25°. Diene (1) is therefore behaving in exactly the same way as the dienones isolated in our earlier study of 4-substituted *o*-xylenes and 5-substituted hemimellitenes.<sup>3</sup>

Table 1.	Product distributions from nitration of 4-bromo-, 4-methoxy- and 4-acetoxy-
	toluene in HNO <sub>3</sub> /Ac <sub>2</sub> O at 0°

Substrate	Product	P <sub>tot</sub>		
4-Bromotoluene	48±4 <sup>B</sup>			
	2-nitro-p-cresol	40 <u>+</u>	-4 <sup>в</sup>	
	others <sup>A</sup>	12±	2 <sup>в</sup>	
4-Methoxytoluene	$80 \pm 5^{B}$			
	2-nitro-p-cresol	20 <u>+</u>	<u>-</u> 5 <sup>в</sup>	
4-Acetoxytoluene	4-methyl-4-nitrocyclohexa-2,5-dienone	$47 \pm 5^{\circ}$	0	
	4-acetoxy-2-nitrotoluene	1 50 1 50	$30\pm5^{\mathrm{b},\mathrm{d}}$	
	4-acetoxy-3-nitrotoluene	s0±5° ع	$20\pm5^{\mathrm{B},\mathrm{D}}$	
	2-nitro-p-cresol	$3\pm5^{\circ}$	$50 \pm 5^{B,D}$	

$P_{tot}$ ,	percentage	of total	product

<sup>A</sup> A mixture of products containing at least one bromodinitrotoluene and dibromo compounds.

<sup>B</sup> G.l.c. analysis of reaction mixture after aqueous workup.

<sup>c</sup> N.m.r. analysis of crude reaction mixture after pump-down.

 $^{\rm D}$  N.m.r. analysis of decomposed reaction mixture after pump-down followed by warming.

Table 2.	Proportion of dienone decomposition product from reaction of 4-X-toluene,
	4-X-o-xylene and 4-X-hemimellitene with HNO <sub>3</sub> /Ac <sub>2</sub> O

Substrate	$P_{\rm tot} ({\rm X} = {\rm OMe})$	$P_{\rm tot} ({\rm X} = {\rm Br})$	$P_{\rm tot} ({\rm X} = {\rm OAc})$
4-X-toluene	20	40	50
4-X-o-xylene <sup>3</sup>	12	46	67
5-X-hemimellitene <sup>3</sup>	23	60	73

The proportion of *ipso* nitration at the methyl group *para* to the ketone-forming position of the aromatic ring follows the same pattern in the toluenes as it does in the substituted *o*-xylenes and hemimellitenes (Table 2). For the highest yield of dienone, AcO is the preferred substituent; MeO gives mainly ring nitrated products. No evidence for *ipso* nitration at either MeO or AcO was found in these substrates; *ipso* nitration at MeO would certainly not be expected because an earlier study showed<sup>6</sup> that such nitration required the carbon carrying the MeO group to be highly activated towards electrophilic attack. The product from nitration of 4-bromotoluene contained 12% of a mixture of compounds which could not be separated or identified. The mass

spectrum of the mixture established that it contained a dibromotoluene. We believe this arises from nitration at the bromine followed by loss of bromine, which is in turn captured by aromatics in the reaction mixture. We have established such a nitro-debromination process in the nitration of bromopolymethylbenzenes.<sup>14</sup>



Nitration of 5-Fluoro- and 5-Acetamido-hemimellitene and Acetoxyprehnitene

These three substrates were required for the competitive nitration studies. Their behaviour with nitric acid/acetic anhydride mixtures has not been reported previously; Table 3 summarizes the results of our study. The two hemimellitene derivatives show extensive *ipso* nitration at the central methyl group to give 3,4,5-trimethyl-4-nitro-cyclohexa-2,5-dienone (2), identical with the dienone isolated from the nitration of 5-bromo-, 5-methoxy- and 5-acetoxy-hemimellitenes;<sup>3</sup> this dienone decomposes quantitatively to 3,4,5-trimethylnitrophenol. Formation of the dienone from 5-acet-amidohemimellitene may proceed by the usual pathway shown in Scheme 1, or by an alternative pathway involving formation and hydrolysis of the imine (3). Such imines are known<sup>15</sup> to be unstable and hydrolyse rapidly in water, but we could find no evidence for such an imine in our study.

# Table 3. Products from reaction of 5-fluoro- and 5-acetamido-hemimellitene and acetoxyprehnitene with $HNO_3/Ac_2O$

Products determined by g.l.c. analysis of the reaction mixture after aqueous workup, except where stated

Substrate	Product	P <sub>tot</sub>		
5-Fluorohemimellitene	3,4,5-trimethyl-2-nitrophenol	$67 \pm 3$	$5\pm5^{A}$	
	5-fluoro-4-nitrohemimellitene	$33 \pm 3$	$35 \pm 5^{A}$	
	3,4,5-trimethyl-4-nitrocyclohexa-2,5-dienone	0	$62\pm5^{A}$	
5-Acetamidohemimellitene	3,4,5-trimethyl-2-nitrophenol	$55 \pm 4$		
	3,4,5-trimethyl-2-nitroacetanilide	$45 \pm 4$		
Acetoxyprehnitene	2,3,4,5-tetramethylnitrophenol	97		

<sup>A</sup> Products determined by n.m.r. of the crude reaction mixture after pump-down.

Acetoxyprehnitene undergoes nitration almost entirely at the methylated ring position *para* to the acetoxy group to give 2,3,4,5-tetramethyl-4-nitrocyclohexa-2,5-dienone (4), which decomposes quantitatively to 2,3,4,5-tetramethylnitrophenol. This is in contrast to the behaviour of prehnitene itself, which undergoes 75% *ipso* nitration, of which at least one-third must be at an outside methyl group (hence the observed 21% 2,3,4-trimethylphenylnitromethane).<sup>4</sup>

<sup>14</sup> Clemens, A. H., Ph.D. Thesis, University of Canterbury, 1975.

<sup>15</sup> March, J., 'Advanced Organic Chemistry' p. 658 (McGraw-Hill: New York 1968).

# Competitive Nitrations

Study of substituent effects on the *ipso* nitration process in mixtures of nitric acid in acetic anhydride is complicated by several factors. The reactions show an apparent zero-order in substrate,<sup>16</sup> although it now seems likely that this arises from a medium effect rather than conventional rate-determining formation of the electrophile.<sup>17</sup> Most substrates give several products through a variety of competing processes of which the most important are shown (Scheme 3), and a change in substituent may well open up a new pathway for reaction. The partitioning between normal nitration (pathway A, Scheme 3) and *ipso* nitration (pathway B) will be affected by the lability of group X, and will presumably be determined by a very large number of factors unless pathways A and B are slower than subsequent steps.



For this first attempt to determine the sensitivity of the *ipso* nitration process to substituent effects we chose for study the series of 5-X-hemimellitene derivatives (5), for X = F, Br, OAc, OMe and NHAc. This and an earlier study<sup>3</sup> have shown that in all these compounds *ipso* nitration occurs only at the central methyl group to give dienone (2) which decomposes on g.l.c. analysis to 3,4,5-trimethylnitrophenol. The only reaction accompanying *ipso* nitration is ring nitration *ortho* to the group X. The series can be extended to X = H (hemimellitene), since here again, although *ipso* nitration occurs at both central and flanking methyl groups,<sup>2</sup> the two processes can be clearly separated, from each other and from the formation of 4- and 5-nitrohemimellitenes by normal nitration. This means that for all these substrates (5) the partitioning between pathways A and B (Scheme 3) can be determined by analysis of the

<sup>16</sup> Fischer, A., Read, A. J., and Vaughan, J., J. Chem. Soc., 1964, 3691.

<sup>17</sup> Marziano, N. C., Rees, J. H., and Ridd, J. H., J. Chem. Soc., Perkin Trans. 2, 1974, 600.

reaction mixture; *ipso* nitration is measured by the extent of formation of diene (X = H) or dienone, and the only possible complicating factor is the 1,2-nitro shift from *ipso* carbonium ion to ring nitro products (Scheme 3), a process for which no evidence has been found under the reaction conditions used in these studies. The ratio  $F_X$  of (*ipso* nitration at the central methyl group)/(total *ipso*+ring nitration ortho to X) for each substrate is as follows:

X	F	OAc	Br	NHAc	OMe	Н
$F_{\mathbf{X}}$	67%	72 %	65%	55%	31 %	43%

We used a competition method to determine the relative rates of total nitration of the substrates (5). This method is reliable only if the reaction is first order in substrate and if the reaction of the nitrating species with each reactant is not affected by the presence of the other reactant. Because of the peculiarities of the nitric acid-acetic anhydride medium the first point must be assumed.<sup>17</sup> The second requirement was tested by showing that nitration of a mixture of acetoxy- and bromo-hemimellitene, and a mixture of acetoxyhemimellitene and hemimellitene, gave the same product distributions for each aromatic as nitration of that aromatic alone. When these two requirements are met the ratio r of specific rate constants for total nitration (of the central methyl group and the position *ortho* to X) in any pair of substrates (5), A and B, is given<sup>18,19</sup> at any time after the start of reaction by the expression\*

 $r = \log(\text{fraction of A remaining})/\log(\text{fraction of B remaining})$ 

A necessary requirement for this method of analysis to be satisfactory is that r values are constant throughout the reaction. Within the limits set by the errors inherent in n.m.r. analysis of a complex mixture and the considerable difference in reactivity between most pairs of substrates, r values were constant during the reactions, and were in fact derived from the slopes of plots of log(fraction of A remaining) against log(fraction of B remaining). A typical plot is shown (Fig. 1), and the values of r are given in Table 4. When the ratio of rate constants is greater than 10 it is difficult to obtain an accurate value for r because most of the more reactive substrate disappears before a measureable amount of the less reactive has reacted. When r is greater than 30 its value cannot be estimated by this method.

The values of r can be combined with the fraction of *ipso* nitration for each substrate to give the ratio  $r_i$  of the specific rate constants for *ipso* nitration at the central methyl group:  $r_i = r(F_A/F_B)$ . These values allow the Hammett  $\rho$  for *ipso* nitration to be estimated. For a substituted and unsubstituted hemimellitene respectively the Hammett equation for *ipso* nitration is

$$\log(k_{\rm X}/k_{\rm H}) = \rho_i \sigma_{\rm X}^{+}$$

Since  $r_i = \log(k_{\rm X}/k_{\rm H})$  (reactant B = hemimellitene) this becomes

$$\log r_i = \rho_i \sigma_X^+$$

\* For this equation to hold, the ratio of concentrations of the reactants A and B must be uniform throughout the reaction mixture, and this in turn requires adequate mixing. The values of r were shown to be independent of stirring speed and of the initial concentrations of A and B; these are sufficient tests for the uniformity of mixing.

<sup>18</sup> Francis, A. W., Hill, A. J., and Johnston, J., J. Am. Chem. Soc., 1925, 47, 2211.
 <sup>19</sup> Ingold, C. K., and Smith, M. S., J. Chem. Soc., 1938, 905.

The usefulness of this analysis is limited by the competition method for measuring  $r_i$ , which allows the use of only four points on the Hammett plot (X = F, H, Br, OAc), which span only a narrow reactivity range  $(0.23\sigma^+)$ . Nevertheless the data allow us to place the  $\rho$  value for *ipso* nitration between -8 and -12. Support for this conclusion is found from the result of the competition nitration for which 4-acetoxyhemimellitene and 4-acetoxyprehnitene were used; the latter compound has an additional methyl group *meta* to the site of *ipso* nitration. Since  $\sigma_{m-Me}^+$  and  $\sigma_{p-F}^+$  are the same, we expect, if our analysis is satisfactory, that  $r_i$  derived from this competition reaction should be the same as that for 4-fluorohemimellitene and hemimellitene. The  $r_i$  values obtained are the same within experimental error (15.5, 16.3).



Fig. 1. Competition nitration of hemimellitene against 5-acetoxyhemimellitene (r = 18).

Table 4.	Ratios r of	specific rate	constants	for	competition	nitration	in
		HNO	) <sub>3</sub> /Ac <sub>2</sub> O				

Competing substrates (first-named compound is more reactive)		
Hemimellitene, 5-acetoxyhemimellitene	18	
Hemimellitene, 5-bromohemimellitene	16	
5-Fluorohemimellitene, hemimellitene	10	
5-Bromohemimellitene, 5-acetoxyhemimellitene	1	
Acetoxyprehnitene, 5-acetoxyprehnitene	7	

These results provide very satisfying evidence that the *ipso* nitration process is essentially the same as that of the accepted electrophilic substitution reaction leading to the formation of ring nitro products.

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