ipso-Nitration: Formation of Nitronium Acetate Adducts in the Nitration of *p*-Acetamido-, *p*-Halogeno-, and *p*-Methoxy-toluenes, and α-*p*-Tolyloxyisobutyric acid

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Summary Low-temperature nitration of the title compounds in acetic anhydride gives 1,2 nitronium acetate adducts, except *p*-fluorotoluene which gives both 1,2 and 1,4 adducts and α-*p*-tolyloxyisobutyric acid which gives a spiro adduct.

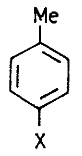
NITRATION of appropriately substituted aromatic compounds in acetic anhydride leads to the formation of nitronium acetate adducts.[1-3] The reaction is initiated by the addition of nitronium ion to an *ipso* position. The great majority of substrates investigated have given 1,4 adducts. However, *p*-t-butyltoluene[4] and 2-nitro-*p*-xylene[5] each give a 1,2 adduct as the major addition product and *p*-cresol,[6] *p*-cresyl acetate,[7,8] *p*-methylanisole,[7] and *p*-bromotoluene[7] are all reported to give 4-methyl-4-nitrocyclohexa-2,5-dienone as the product of *ipso*-nitration. Other phenols and derivatives and halogenoarenes behave similarly,[7,9] although a 1,4 adduct has been detected in the low temperature nitration of 3,4-dimethylanisole.[10] It is evident that the 1-hydroxy-4-methyl-4-nitrocyclohexadienyl cation Wheland intermediate (W_1^{Me})[11] formed by the addition of nitronium ion to *p*-cresol can be readily and rapidly deprotonated to the dienone. It is also now evident that conversion of the 1-X-4-methyl-4-nitrocyclohexadienyl cation (where X is a $+M$ heteroatom substituent other than hydroxy) into the dienone is a more complex process involving other intermediates. Nitration of *p*-bromotoluene, *p*-chlorotoluene, and *p*-methylanisole in aqueous sulphuric acid has been studied by Schofield and his co-workers.[12,13] Their estimates of the extent of attack by nitronium ion at positions *ipso* to methyl are shown in the Table.

TABLE. Yield of nitronium acetate adducts from *p*-X-toluenes.[a]

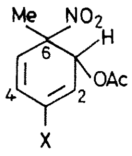
X	F	Cl	Br	OMe	NHAC	$OCMe_2CO_2H$
%[b]	*ca.* 100	72(⩾27)	64(⩾15)	33(38)	27	47

[a] Yields determined by n.m.r. spectroscopy of the reaction mixture and are based on the initial amount of aromatic compound.
[b] Values in parentheses refer to the extent of attack *ipso* to methyl estimated by Schofield and his co-workers (refs. 11—13).

We have nitrated the *p*-halogenotoluenes and some related compounds in acetic anhydride at −40 °C (Table). *p*-Chlorotoluene gave an excellent yield of the 1,2 adduct, acetate (**2a**); m.p. 49—50 °C; ^1H n.m.r. ($CDCl_3$) δ 1·79 (3H, s, Me), 2·00 (3H, s, OAc), 5·54 (1H, dd, $J_{1,2}$ 6, $J_{1,5}$ 1·5 Hz, 1-H), 6·04 (1H, dd, $J_{2,4}$ 1·5, $J_{4,5}$ 10 Hz, 4-H), 6·13 (1H, dd, 2-H), and 6·56 (1H, dd, 5-H); ^{13}C n.m.r. ($CDCl_3$) δ 20·6 (OCO*Me*), 23·2 (Me), 70·2 (C-1), 87·2 (C-6), 118·1 (C-2), 126·1 (C-4), 129·4 (C-5), 133·6 (C-3), and 169·3 p.p.m. (*O*COMe); and, correspondingly, *p*-bromotoluene gave (**2b**) (m.p. 48—49 °C).†



(1)



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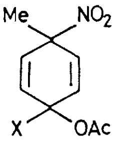
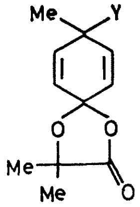


(3)

a; X = Cl
b; X = Br
c; X = OMe
d; X = NHAc
e; X = F
f; X = $OCMeCO_2H$

The two possible nitro-substitution products of *p*-bromo- and *p*-chloro-toluene were also formed. In the ^1H n.m.r. spectra, a characteristic pattern of four sets of doublet of doublets was observed for one allylic and three vinylic protons. ^{13}C n.m.r. spectroscopy also showed four separate signals for one allylic and three vinylic carbons. As in the case of other 1,2 adducts,[4,5] only one diastereoisomer appeared to be formed. *p*-Methylanisole and *p*-methylacetanilide both gave the 1,2 adducts as well as the substitution products. In the case of *p*-fluorotoluene, a mixture of *ca.* 75% of the 1,4 adduct (**3e**) and *ca.* 25% of the 1,2 adduct (**2e**) was obtained. In a separate experiment, when the reaction mixture containing excess of acid was warmed to −20 °C, the adducts were converted into 4-methyl-4-nitrocyclohexa-2,5-dienone. α-*p*-Tolyloxyisobutyric acid gave the spiro adduct (**4a**) on nitration. Corey and his co-workers[14] obtained the related bromo-compound (**4b**) on bromination. Formation of the spiro adduct by capture of the internal nucleophile is favoured, and evidently so much so that it overrides the preference for 1,2 adduct formation.



(4)

a; Y = NO_2
b; Y = Br

We also repeated the nitration of *p*-bromotoluene under the conditions used by Wright and his co-workers.[7] Only 40% of the *p*-bromotoluene reacted and the 1,2 adduct and nitro-substitution compounds were the only products obtained. It seems likely that the nitrodienone product reported previously[7] from nitration of p-bromotoluene was formed from the adduct(s) on column chromatography. In our reactions, we were not able to detect the formation of an adduct from *p*-bromotoluene with nitro *ipso* to bromine nor of any *p*-nitrotoluene which would also result from a W_1^{Br}. It is possible that the W_1^{Br} also rearranged to give (ultimately) either 4-bromo-3-nitrotoluene or 3-bromo-4-nitrotoluene.

Although the adducts of type (**3**) have been postulated as intermediates in the formation of cyclohexadienones,[7] the present work provides the first demonstration of the actual formation of nitronium acetate adducts from aromatic compounds with *para* $+M$ heteroatom substitutents. From the number of different compounds investigated, it appears that the formation of nitronium acetate adducts is a general reaction of aromatic compounds with suitable $+M$ hetero-atom substituents.

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† All the adducts reported here have been isolated and characterized by their ^1H and ^{13}C n.m.r. spectra.

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