

Title	An Interpretation of the Puzzling Dichotomy of the Reaction Modes Observed during the Side-chain Nitration of Alkylaromatics with $\text{HNO}_3/\text{CH}_2\text{Cl}_2$ and $\text{HNO}_3/(\text{CH}_3\text{CO})_2\text{O}$
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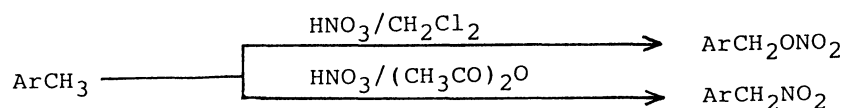
An Interpretation of the Puzzling Dichotomy of the Reaction Modes
Observed during the Side-chain Nitration of Alkylaromatics
with $\text{HNO}_3/\text{CH}_2\text{Cl}_2$ and $\text{HNO}_3/(\text{CH}_3\text{CO})_2\text{O}$

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Nitration of substituted pentamethylbenzenes has been carried out under various conditions using the title nitrating systems in order to elucidate the peculiar dependence of the modes of side-chain substitution on the reagent employed; nitroxylation with $\text{HNO}_3/\text{CH}_2\text{Cl}_2$ and nitration with $\text{HNO}_3/(\text{CH}_3\text{CO})_2\text{O}$. Based on the evidence obtained from product variations with substituents, electrochemical nitrodecarboxylation of arylacetates, and ESR examination of the initial stage of the side-chain reactions, a proposal is made that the side-chain substitution of polysubstituted arenes occurs via a heterolytic path with $\text{HNO}_3/\text{CH}_2\text{Cl}_2$ and via a homolytic path with $\text{HNO}_3/(\text{CH}_3\text{CO})_2\text{O}$.

Reaction of polymethylbenzenes with nitric acid in dichloromethane often results in the side-chain nitroxylation of one of methyl groups to afford benzyl nitrates, whereas the reaction with nitric acid in acetic anhydride in many cases leads to the side-chain nitration to give the corresponding arylnitromethanes.¹⁾ This peculiar dependence of the reaction patterns on the nitrating agents employed cannot yet be accounted for.

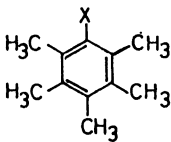
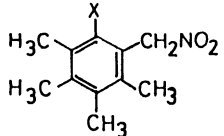
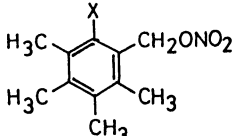


In our continuing interest in the non-conventional nitrations of arenes, we have investigated the side-chain reactions of substituted pentamethylbenzenes with these nitrating systems under various conditions to confirm the dichotomous modes of the reaction. Electrochemical nitrodecarboxylation of arylacetates at anode and ESR responses of the initial stage of the reactions have also been examined. All results we have obtained are wholly consistent with the mechanistic differences between side-chain nitroxylation and nitration referred to herein.

When polymethylated benzophenones, benzoic acid and its ester (**1a-1h**) were reacted with nitric acid in acetic anhydride, the regioselective nitration occurred

at the methyl group adjacent to the electron-withdrawing function to give aryl-nitromethanes (**2a-2h**).²⁾ On prolonged contact with dinitrogen tetroxide in dichloromethane and acetic anhydride, compound **1a** gave side-chain nitration product **2a** though in a low conversion. In contrast, the same substrates **1a-1h** reacted with nitric acid in dichloromethane to produce benzyl nitrates (**3a-3h**), little side-chain nitration products being obtained (Table 1). These results are in accord with our earlier observations.³⁾ Rather surprisingly, however, pentamethylbenzenesulfonyl chloride and fluoride (**1i-1j**), which bear a stronger electron-withdrawing group than acyl or carboxyl groups, were found to afford significant amounts of nitromethanes (**2i-2j**) in addition to the expected nitrates (**3i-3j**).

Table 1. Nitration of acylpentamethylbenzenes, pentamethylbenzoic acid and its ester, and pentamethylbenzenesulfonyl halides with $\text{HNO}_3/\text{CH}_2\text{Cl}_2$ and $\text{HNO}_3/(\text{CH}_3\text{CO})_2\text{O}$

Arene 1	Reagent a)	Product yield/% ^{b)}	
		Nitromethane 2 ^{c)}	Nitrate 3
			
a	X= CH_3CO	A B	57 -- 81
b	$\text{C}_2\text{H}_5\text{CO}$	A B	53 -- 45
c	$(\text{CH}_3)_2\text{CHCO}$	A B	42 -- 71
d	$\text{C}_6\text{H}_5\text{CO}$	A B	59 -- 80
e	4- FC_6H_4	A B	63 -- 99
f	4- ClC_6H_4	A B	64 -- 73
g	COOH	A B	70 -- 63
h	$\text{CO}_2\text{C}_2\text{H}_5$	A B	90 -- 78
i	SO_2Cl	A B	27 30 -- 24
j	SO_2F	A B	78 (65) ^{d)} -- (35) ^{d)}

a) A: $\text{HNO}_3/(\text{CH}_3\text{CO})_2\text{O}$. B: $\text{HNO}_3/\text{CH}_2\text{Cl}_2$.

b) Yields refer to the isolated ones and are not optimized.

c) Values taken from Ref. 2. Very similar results were obtained by us.

d) Ratio of mixture components estimated from ^1H NMR.

Pentamethylbenzyltrimethylsilane having a good electrofugal silyl function on side-chain reacted very rapidly in dichloromethane at low temperatures to give pentamethylbenzyl nitrate as the sole product.⁴⁾ The reaction with nitric acid in acetic anhydride, however, gave pentamethylphenylnitromethane along with small amounts of benzyl nitrate and acetate. The results obtained in the reaction of cyclopropylmethylpentamethylbenzene were more noteworthy, where cyclopropane ring opened when the reagent was $\text{HNO}_3/\text{CH}_2\text{Cl}_2$ while it remained intact with $\text{HNO}_3/(\text{CH}_3\text{CO})_2\text{O}$. These results strongly suggest the involvement of a homolytic process in the nitration using $\text{HNO}_3/\text{CH}_2\text{Cl}_2$. In order to support this interpretation of the

Table 2. Anodic oxidation of arylacetates in the presence of nitrite ion

$$\begin{array}{ccccccc}
 \text{ArCH}_2\text{CO}_2^- & \xrightarrow{-e} & \text{ArCH}_2\cdot & \xrightarrow{-e} & \text{ArCH}_2^+ & \xrightarrow{\text{NO}_2^-} & \text{ArCH}_2\text{ONO} & \longrightarrow & \text{ArCHO} \\
 \underline{4} & & \underline{5} & & \underline{6} & & \underline{9} & & \underline{10} \\
 & & \swarrow & & \searrow & & & & \\
 \text{NO}_2^- & \xrightarrow{-e} & \text{NO}_2 & \longrightarrow & \text{ArCH}_2\text{NO}_2 & & (\text{ArCH}_2)_2 & & (\text{Ar}=\text{R}-\text{C}_6\text{H}_4) \\
 & & & & \underline{7} & & \underline{8} & &
 \end{array}$$

Arylacetate R	Conversion/%	Product distribution ^{a)}			
		<u>7</u>	<u>8</u>	<u>9</u>	<u>10</u>
NO ₂	8	85	15	0	0
F	9	51	49	0	0
Cl	12	49	31	0	20
CH ₃	19	0	56	0	44
OCH ₃	21	0	6	4	90

a) Based on consumed substrates.

mechanism, the initial phase of the reactions of some pentamethylbenzene derivatives was closely examined by ESR in several solvent systems at low temperatures.⁵⁾ Indeed we detected a characteristic transient signal only when the reactions were carried out in acetic anhydride, where the products were nitromethanes (Fig. 1a). Reactions in dichloromethane, trifluoroacetic acid and its anhydride, and nitromethane, where benzylic esters were main products, the only signal observed was due to nitrogen dioxide (Fig. 1b).

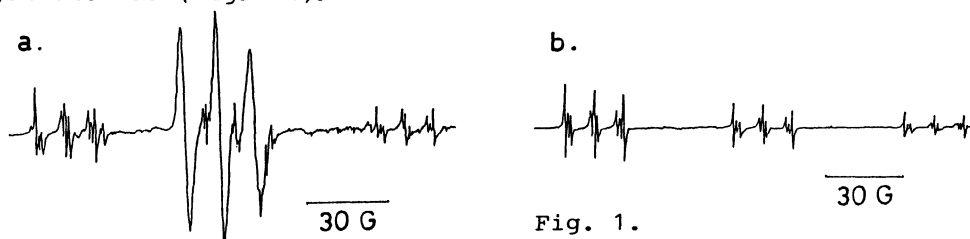
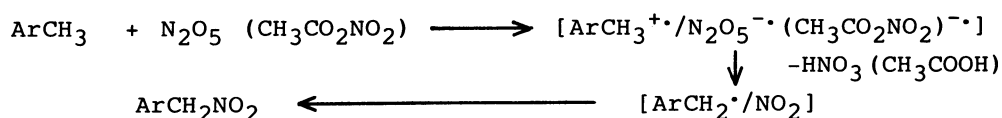


Fig. 1.

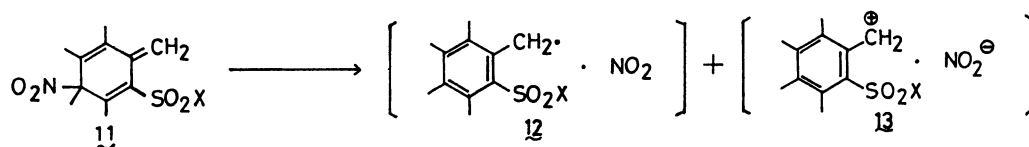
With an intent to obtain further information supporting the involvement of a radical species in the case of $\text{HNO}_3/(\text{CH}_3\text{CO})_2\text{O}$, we carried out the anodic oxidation of sodium arylacetates in the presence of tetrabutylammonium nitrite in 90% tert-butyl alcohol containing tetrabutylammonium perchlorate as supporting electrolyte. From arylacetates (4) with electron-withdrawing groups, arylnitromethanes (7) and 1,2-diarylethanes (8) were obtained, whereas benzaldehydes (10) were the dominant product isolated when arylacetates 4 contain electron-releasing group on the aromatic ring (Table 2). Aldehydes 10 clearly arose from the decomposition of benzyl nitrites initially formed.⁶⁾ These results are in good accordance with the fact that arylacetates with electron-withdrawing group undergo one-electron oxidative decarboxylation at the anode to generate benzyl radical (5), while those with electron-donating group suffer two-electron oxidation with a loss of carbon dioxide to form benzyl cation (6) as the oxidized species.⁷⁾ Thus, arylnitromethanes 2 obtained in the nitration with $\text{HNO}_3/(\text{CH}_3\text{CO})_2\text{O}$ are highly likely to arise from a

homolytic process in which benzyl radical couples with nitrogen dioxide.

Based on the above evidence the puzzling changes of product distributions with the nitrating agents may be rationalized as follows: Arenes with electron-releasing and weakly electron-withdrawing groups react in two different ways depending on the reagent. In dichloromethane the reaction proceeds via benzenium ion and methylenecyclohexadiene intermediates as previously proposed,⁸⁾ and in acetic anhydride nitration takes place via radical cation generated through one-electron transfer between arene and dinitrogen pentoxide and/or acetyl nitrate, the latter species being present as electron-deficient covalent molecules in an equilibrium mixture.



An enigmatic behavior of pentamethylbenzenesulfonyl chloride and fluoride 1i-1j may well be rationalized now by assuming a divergence of mechanisms. A methylenecyclohexadiene intermediate (11) derived from arenes with highly electron-withdrawing group such as sulfonyl halides would undergo a homolytic dissociation in appreciable preference to a heterolytic one at the tertiary carbon-nitrogen bond to give a benzyl radical/nitrogen dioxide pair (12), because the formation of benzyl cation/nitrite ion pair (13) should be less favored by strong electron-withdrawal from sulfonyl group in the vicinity.



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