# Nitration of Hexamethylbenzene and Hexamethylbenzene-$d_{18}$ in Acetic Acid. Deuterium Isotope Effect on the Product Distribution. Mechanism of Side-chain Substitution of Arenes[1)]

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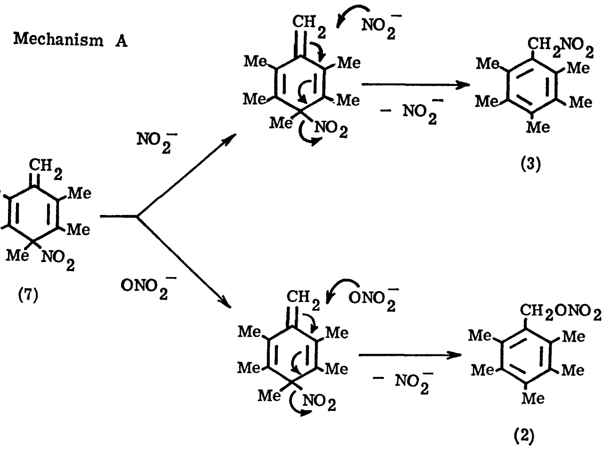
The reaction in acetic acid of hexamethylbenzene and hexamethylbenzene-$d_{18}$ with nitric acid in the dark has been investigated under various conditions using a high-pressure liquid chromatographic method. Pentamethylbenzyl nitrate, pentamethylphenylnitromethane, pentamethylbenzyl acetate, and pentamethylbenzyl alcohol were formed immediately after the mixing of reactants; their relative amounts remained almost unchanged up to nearly 50% conversion. The addition of sodium nitrite gave little influence on the composition of the product mixture, while urea was found to depress somewhat the formation of nitromethane. In the presence of lithium nitrate, the reaction was modestly accelerated and the nitrate formation seems to be slightly favored over the nitromethane formation. Hexamethylbenzene-$d_{18}$ reacted with nitric acid at the same rate as the non-labeled hydrocarbon did, but the benzyl nitrate/phenylnitromethane ratio in the product mixture was considerably higher in the former. Based on the quantitative data obtained, the mechanism for the side-chain substitution has been discussed in terms of the $S_N1'$ pathway: nitronium ion makes an *ipso* attack on the substrate to form the arenium ion, which releases a proton from the activated methyl group *para* to the site of attack to give the 3-methylene-6-nitro-1,4-cyclohexadiene intermediate (**7**). Heterolytic fission of the C–N bond in **7** will form a benzyl cation-nitrite anion pair, which recombines at the benzylic carbon atom *via* a C–N bond or *via* a C–O bond, giving benzyl nitrite or phenylnitromethane, respectively. Benzyl nitrite will be further converted into benzyl nitrate and benzyl alcohol, while benzyl acetate will arise from the incorporation of solvent molecules into the ion-pair.

When treated with an electrophile at low or room temperature, polyalkylated aromatic compounds often undergo substitution on a side-chain to yield benzylic compounds. The recent literature contains a variety of examples of such unusual substitution, which include chlorination,[2,3)] bromination,[4)] nitration,[5)] nitrooxylation,[5)] acetamidation,[6)] sulfonation,[7)] thiocyanation,[8)] and others.[9,10)] Although the first report on the side-chain nitration of polyalkylbenzenes under heterolytic conditions appeared nearly seventy years ago,[11)] the mechanistic aspect of this unique reaction had received little attention until very recently, probably because of the wide-spread misbelief that all the side-chain substitutions of arenes should proceed through the homolytic process. In the past decade, however, increasing attention has been focused on this aspect of non-conventional electrophilic substitutions. The accumulation of experimental evidence now provides substantial support for the view that alkylbenzenes may undergo side-chain substitution through a heterolytic mechanism involving a primary electrophilic attack at the aromatic ring: an *ipso* attack of an electrophile to form a benzenium ion is followed by a proton loss from the alkyl substituent to yield a methylenecyclohexadiene intermediate, which is then transformed into benzylic compounds. This type of reaction usually takes place in competition with the normal ring substitution and could be classified as a branched-off process of the ordinary $S_E2$ reaction.

Based on the product studies and kinetic evidence, several mechanistic propositions have been made for the side-chain substitution,[7,12,13)] but the actual mechanism is not yet fully understood. For *nitration*, the two propositions shown in Schemes 1 and 2, both referring to a methylenecyclohexadiene intermediate (**7**), appear to merit consideration:

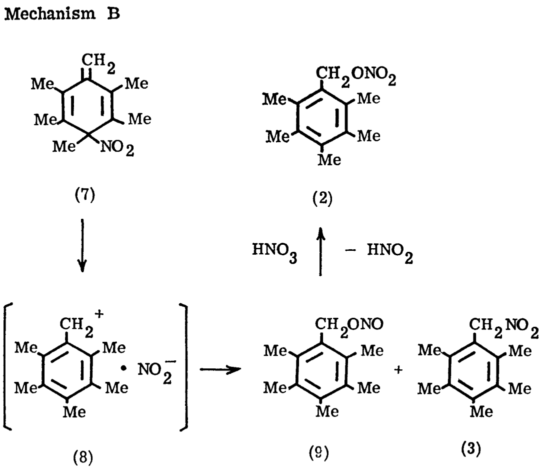
*Mechanism A*:[14)] nucleophilic attack of nitrite or nitrate ions to the terminal methylene carbon atom in **7**, redistribution of electrons to regain the aromatic system, and departure of the nitro group as an anion.



Scheme 1.

*Mechanism B*:[15)] heterolytic fission of the C–N bond in **7** to form a benzyl cation-nitrite anion pair (**8**) and subsequent recombination of these ions at the benzylic carbon atom either *via* a C–N bond or *via* a C–O bond.

In order to differentiate between these two possibilities, we have reinvestigated the nitration of hexamethylbenzene (**1**) and its perdeuterated derivative using the high-pressure liquid chromatographic method and now present the first quantitative data, which provide support for the mechanism B in which the side-chain substituted products are formed from the methylenecyclohexadiene intermediate through the intervention of an ion-pair.



Scheme 2.

## Experimental

All melting points were taken on a hot stage apparatus and are uncorrected. The IR, PMR, UV, and mass spectra were obtained using the same procedure and apparatus described in the previous paper[20] of this series, unless otherwise stated.

Acetic acid and nitric acid ($d$=1.5) of guaranteed grade were dried over phosphorus pentaoxide and carefully redistilled before use. Hexamethylbenzene (**1**; mp 163—164 °C),[21] pentamethylbenzyl nitrate (**2**; mp 95—97 °C),[22] pentamethylphenylnitromethane (**3**; mp 86—88 °C),[22] pentamethylbenzyl acetate (**4**; mp 84—86 °C),[23] and pentamethylbenzyl alcohol (**5**; mp 160—161 °C)[23] were prepared as described in the literature. Pentamethylbenzyl nitrite (**9**; mp 23.5—24 °C; bp 88 °C/3 mmHg)[24] was obtained by the reaction of alcohol **5** with nitrosyl chloride in pyridine.

*Hexamethylbenzene*-$d_{18}$ was prepared according to the procedure of Koptyug and Shubin[25] with the indicated modification; a solution of 1,2,4,5,6,6-hexamethyl-3-methylene-1,4-cyclohexadiene (1.5 g)[26] in trifluoroacetic acid-*d* (10 ml) was allowed to stand at 70 °C for 15 min under nitrogen and then the solvent was removed under reduced pressure. A fresh 10 ml portion of trifluoroacetic acid-*d* was added to the solid residue and the solution was again worked up in a similar manner. This process was repeated until a total of seven exchanges had been performed. The progress of the isotopic exchanges was monitored by PMR spectroscopy. The solution was then diluted with deuterium oxide (6 ml) and kept under nitrogen for 72 h. The resulting oil was extracted with benzene and the organic layer was washed with saturated aqueous sodium carbonate and water, dried over sodium sulfate, and the solvent removed under reduced pressure. The crude solid obtained was placed on the top of an alumina column and eluted with light petroleum. Evaporation of the early eluate followed by recrystallization of the residue from methanol gave perdeuterated hydrocarbon as colorless plates, 0.16 g (10%). The deuterium content determined by mass spectroscopy was 99.3 atom %. Mp 165—166 °C. IR (Nujol): $\nu_{\max}$ 2240, 2190, 2110, 2070, 1410, 1030, and 900 cm$^{-1}$.

*Product analyses* were performed with a high-pressure liquid chromatograph JASCO Model FLC A-700, equipped with a UV detector (Model UVIDEC-100) and a maximum 700 kg/cm$^2$ solvent delivery system with constant-flow capacities. The separations were made on a 500×2 mm stainless-steel column packed with JASCO-Pack SS-05 (available from Japan Spectroscopic Co., Hachioji, Tokyo). A computerized reporting integrator, Hewlett-Packard Model 3380-A, was used to estimate the concentration of each component. The eluting solvent was a water-saturated mixture of dichloromethane and hexane; the flow rate was 1.0 ml/min at a pressure of 180 kg/cm$^2$; the column temperature was ambient; and the injection volume was 2 μl. A 10 μl precision sampling pressure-lock syringe was used for sample injection. Determinations were made at 275 nm with UV units full scale. The difference in absorbance between the ordinary and fully deuterated compounds was negligible. Minor peaks which appeared at higher conversion were neglected.

All *kinetic measurements* were started by adding 10 ml of a solution of nitric acid (0.20 M) in acetic acid at 15 °C to 10 ml of a solution of hexamethylbenzene (0.02 M) and 3,5,6-trinitro-1,2,4-trimethylbenzene as internal standard (0.001 M) in the same solvent preequilibrated to the same temperature. The mixture was left at 15.0±0.1 °C for a suitable time which depended on the reaction rate. The products of reaction were identified by isolation and direct comparison with the authentic specimens. All products are known.

At predetermined times, each aliquot (5 ml) was drawn from the kinetic sample and transferred to a 50 ml separatory funnel containing ether (20 ml); the mixture was immediately washed with two 20 ml portions of cold distilled water, a suspension of calcium carbonate (*ca.* 0.5 g) in water (20 ml), and again distilled water (20 ml). The organic layer was separated and dried over anhydrous sodium sulfate, and the solvent was removed by flash rotary evaporation. The residual oil was dissolved in 4 ml of a 4:6 mixture of dichloromethane and hexane. An aliquot of the solution was withdrawn and injected immediately for analysis. This procedure should be carried out as quickly as possible to minimize errors arising from partial hydrolysis of the prod-

TABLE 1. CORRECTION FACTORS FOR THE PRODUCT DETERMINATION

| Compound | Relative molar extinction coefficient at 275 nm[a] | Relative extraction efficiency |
|---|---|---|
| Hexamethylbenzene | 0.13 | 1.61 |
| Pentamethylbenzyl nitrate | 0.61 | 1.04 |
| Pentamethylphenylnitromethane | 0.67 | 1.05 |
| Pentamethylbenzyl acetate | 0.41 | 1.06 |
| Pentamethylbenzyl alcohol | 0.36 | 0.813 |
| 3,5,6,-Trinitro-1,2,4-trimethylbenzene[b] | 1.00 | 1.00 |

a) In a water-saturated 4:6-mixture of dichloromethane and hexane. b) Of over fifty compounds examined, this compound was found to be best as the internal standard for liquid chromatography, since it satisfied the following requirements: to be soluble in reaction medium, extracting solvent, and eluant; to be stable throughout the reaction and work-up; to have no effect on the course of the reaction; to be well resolved from all the components of the product mixture on the chromatogram and have an elution order which promotes accuracy in the determination with two different solvent systems; and to have an appropriate intensity of UV absorption at the wavelength used for determination.

ucts. When a kinetic sample to be analyzed was first discharged into water and the products were extracted with ether from the aqueous layer, significant amounts of nitrate were hydrolyzed to alcohol. All the determinations were checked against the control experiments.

Appropriate corrections were made for the errors arising from the difference in loss of each component during the sample preparation, the correction factors being determined using the mixed standard solutions of authentic specimens. The relative molar extinction coefficient at 275 nm and the relative extraction efficiency of each component are shown in Table 1, with the internal standard as unity.

## Results and Discussion

Before beginning our work, we made a systematic search for a substrate and an analytical method which could afford reliable quantitative data for side-chain nitrations of arenes. From the many alkyl aromatics examined, hexamethylbenzene (**1**) was chosen as the best, since it was found to give a clean, simple product mixture at low conversion. For the quantitative determination of the nitration product from **1**, the high-pressure liquid chromatographic method was found to be best; none of the other chromatographic procedures, such as GLC, TLC, and column, was found to give reliable and reproducible data, owing to the side reactions which inevitably took place during the separation.

Several reports have appeared on the nitration of **1**, but quantitative data are not yet available. Willstätter and Kubli treated **1** with benzoyl nitrate in carbon tetrachloride and obtained bis(pentamethylbenzyl) ether (**12**) and a bis(nitromethyl)tetramethylbenzene in an unspecified yield.[11] Smith and Harris carried out the nitration of **1** with fuming nitric acid in the presence of sulfuric acid and obtained as much as 22% yield of 5,6-dinitro-1,2,3,4-tetramethylbenzene (**14**).[27] A significant proportion of the starting material that had remained unaccounted for in their work was found by one of the present authors to be a complicated mixture of **2**, **3**, nitropentamethylbenzene (**13**), 6-nitro-2,3,4,5-tetramethylbenzyl nitrate (**14**), 5,6-bis(nitrooxymethyl)-1,2,3,4-tetramethylbenzene (**16**), pentamethylbenzaldehyde (**17**), and several other unidentified carbonyl compounds, nitrites, and aliphatic nitro compounds.[22] Illuminati and his coworkers nitrated **1** in acetic acid and obtained a mixture of **2**, **3**, and pentamethylbenzyl acetate (**4**).[28] Detsina and Koptyug reported the formation of 2,3,-4,5,6,6-hexamethyl-2,4-cyclohexadien-1-one (**18**) from the reaction of **1** with nitric acid in fluorosulfuric acid at −70 °C.[10] Fischer and his coworkers investigated the nitration of **1** in acetic anhydride at low temperature and obtained, besides various aromatic products, several extremely labile addition products, one of which was identified as 1,2,3,4,5,6-hexamethyl-3,6-dinitro-1,4-cyclohexadiene (**19**).[29]

The reaction of **1** with an excess of nitric acid was carried out in acetic acid at 15.0 °C in the dark. After aqueous work-up a mixture of nitrate **2**, nitromethane **3**, acetate **4**, and alcohol **5** was obtained as initial products. All these four products were formed immediately after the mixing of reactants and their relative amounts studied as a function of time remained almost unchanged up to nearly 50% conversion (Fig. 1). The sum of the concentration of **1** and these four products accounted for nearly all of the stoichiometric concentration, showing that even if some products other than **2** to **5** were formed, their concentrations were very small. The relative distribution of the products is given in Table 2. At higher conversions, these

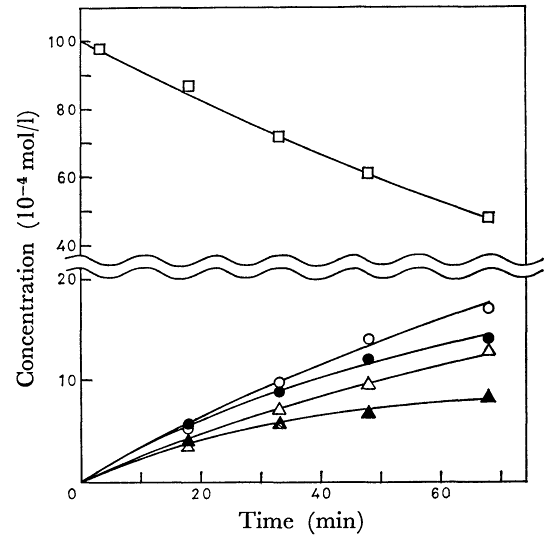


Fig. 1. Reaction of hexamethylbenzene with nitric acid in acetic acid.

□: Hexamethylbenzene,
○: pentamethylbenzyl nitrate,
●: pentamethylbenzyl acetate,
△: pentamethylphenylnitromethane,
▲: pentamethylbenzyl alcohol.

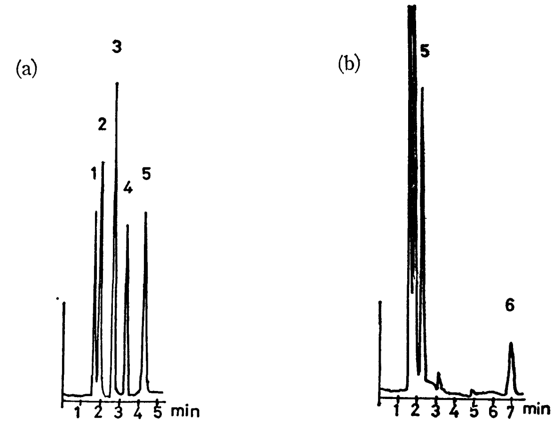


Fig. 2. Liquid chromatograms of the nitration product of hexamethylbenzene.

(a) With a water-saturated 4:6 mixture of dichloromethane and hexane as eluant.

(b) With a water-saturated 8:2 mixture of dichloromethane and hexane as eluant.

1: Hexamethylbenzene,
2: pentamethylbenzyl nitrate,
3: pentamethylphenylnitromethane,
4: internal standard,
5: pentamethylbenzyl acetate,
6: pentamethylbenzyl alcohol.

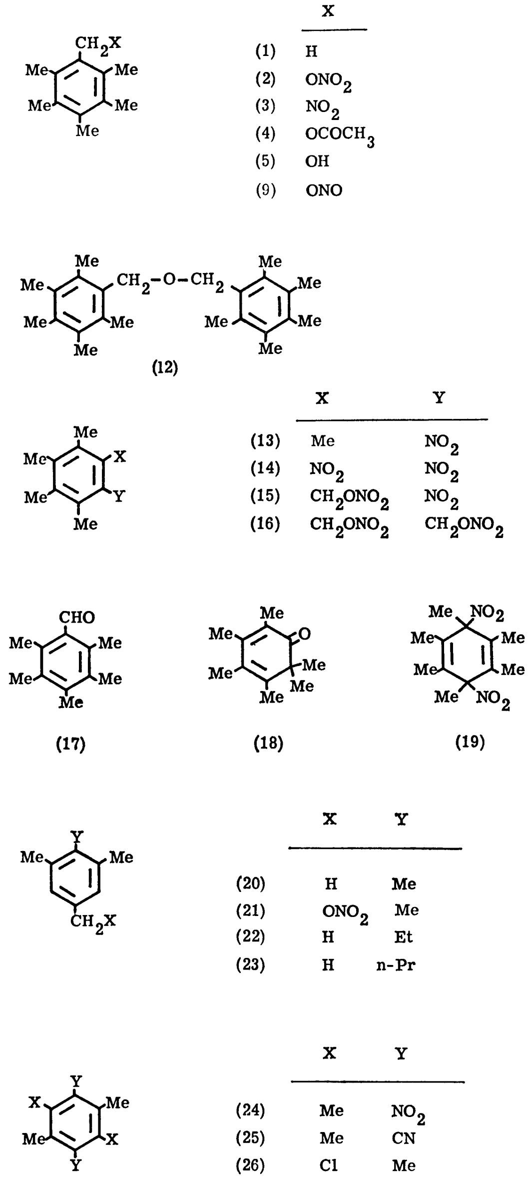
TABLE 2. PRODUCT DISTRIBUTION AND PRODUCT RATIO IN THE REACTION OF HEXAMETHYLBENZENE WITH NITRIC ACID IN ACETIC ACID[a)]

| Reaction | Reaction time (min) | Conversion (%) | Product distribution (%)[b)] | | | Product ratio | |
|---|---|---|---|---|---|---|---|
| | | | Nitrate **2** and alcohol **5** | Nitromethane **3** | Acetate **4** | (**2**+**5**)/**3** | (**2**+**3**+**5**)/**4** |
| Standard[c)] | 60—73 | 61—68 | 44.3±2.0 | 26.0±2.2 | 29.8±1.3 | 1.74±0.25 | 2.35±0.17 |
| Sodium nitrite added | | | | | | | |
| 0.0039 M | 70 | 70 | 44 | 27 | 30 | 1.6 | 2.4 |
| 0.0143 M | 70 | 69 | 44<br>(43)[d)] | 26<br>(27) | 30<br>(30) | 1.7<br>(1.6) | 2.3<br>(2.3) |
| Urea added | | | | | | | |
| 0.0127 M | 72 | 61 | 50 | 17 | 33 | 2.9 | 2.0 |
| 0.0507 M | 72 | 52 | 52<br>(44) | 15<br>(26) | 33<br>(30) | 3.5<br>(1.7) | 2.0<br>(2.3) |
| Lithium nitrate added | | | | | | | |
| 0.200 M | 66 | 81 | 48<br>(44) | 23<br>(28) | 29<br>(28) | 2.1<br>(1.6) | 2.4<br>(2.6) |
| Other solvent added | | | | | | | |
| 12% Acetic anhydride | 30 | 93 | 38 | 29 | 33 | 1.3 | 2.0 |
| 20% Dichloromethane | 73 | 65 | 49 | 28 | 23 | 1.8 | 3.3 |
| 40% Dichloromethane | 73 | 50 | 53<br>(45) | 29<br>(25) | 18<br>(30) | 1.8<br>(1.8) | 4.6<br>(2.3) |
| Hexamethylbenzene-$d_{18}$[e)] | 60 | 66<br>(65) | 55<br>(42) | 14<br>(28) | 31<br>(30) | 3.9<br>(1.5) | 2.2<br>(2.3) |
| | 90 | 73<br>(72) | 57<br>(42) | 12<br>(27) | 32<br>(31) | 4.8<br>(1.6) | 2.1<br>(2.2) |

a) Hexamethylbenzene, 0.01 M; nitric acid, 0.10 M; reaction temperature, 15.0±0.1 °C. b) Mole percentages determined by high-pressure liquid chromatography using digital integration. c) Averaged value of eight runs. d) Numerals in parentheses refer to the values obtained by control experiments. e) Control experiments demonstrated that deuterium was not exchanged with solvent under any reaction conditions employed.

initial products gradually underwent further reaction with the reagent or solvent. Mechanism A requires that the nitro compound **3** be formed as the main product at sufficiently high nitrous acid concentration; that is, the amount of **3** would be multiplied during the progress of the reaction, as nitrous acid accumulates. According to Scheme 1, the increase in the concentration of nitrite ions in the reaction system is expected to favor the formation of nitromethane **3**. Added sodium nitrite, however, gave little influence on the composition of the product mixture. The role of urea as an added material was somewhat perplexing. Although the yellow coloration of the reaction mixture due to the liberated nitrogen dioxide was suppressed by the addition of small amounts of urea, the product composition remained little affected. However, in the presence of large amounts of urea, the nitrate formation seems to be favored, as shown in Table 2. Urea itself or its salt might be involved in the reaction process, but the situation is not clear at present.

Added lithium nitrate in low concentrations has little effect on the product composition. However, in the presence of large amounts of lithium nitrate (>0.1 M), the reaction was modestly accelerated and the nitrate formation seems to be favored over the nitromethane formation. These findings are not consistent with mechanism A, which assumes the reaction of triene intermediate **7** with external nitrate and nitrite ions for the respective formation of benzyl nitrate and phenylnitromethane. Mechanism B assumes the recombination of a benzyl cation with an ambident nitrite ion in the ion-pair. Thus, replacement of protium by deuterium in the cationic portion of the ion-pair is expected to increase the localized positive charge at the benzylic carbon atom due to the decrease in hyperconjugative electron release, as well as due to the more electronegative character of the perdeuteriomethyl group as compared to methyl group. Such an effect will favor the recombination at the oxygen atom of the ambident nitrite ions, leading to the preferential formation of benzyl nitrate or nitrite, while the secondary isotope effect would be of less significance in the product determination step in the mechanism A. In order to use the deuterium labeling as a probe into the ion-pair intermediate **8**, hexamethylbenzene-$d_{18}$ was prepared from 1,1,2,3,4,5,6-heptamethylbenzenium chloride[26)] by the exchange of hydrogens with trifluoroacetic acid-*d* and subjected to nitration under the same conditions as applied to **1**. The perdeuterated hydrocarbon reacted with the reagent



| | X |
|---|---|
| (1) | H |
| (2) | $ONO_2$ |
| (3) | $NO_2$ |
| (4) | $OCOCH_3$ |
| (5) | OH |
| (9) | ONO |

(12)

| | X | Y |
|---|---|---|
| (13) | Me | $NO_2$ |
| (14) | $NO_2$ | $NO_2$ |
| (15) | $CH_2ONO_2$ | $NO_2$ |
| (16) | $CH_2ONO_2$ | $CH_2ONO_2$ |

(17) (18) (19)

| | X | Y |
|---|---|---|
| (20) | H | Me |
| (21) | $ONO_2$ | Me |
| (22) | H | Et |
| (23) | H | n-Pr |

| | X | Y |
|---|---|---|
| (24) | Me | $NO_2$ |
| (25) | Me | CN |
| (26) | Cl | Me |

Scheme 3.

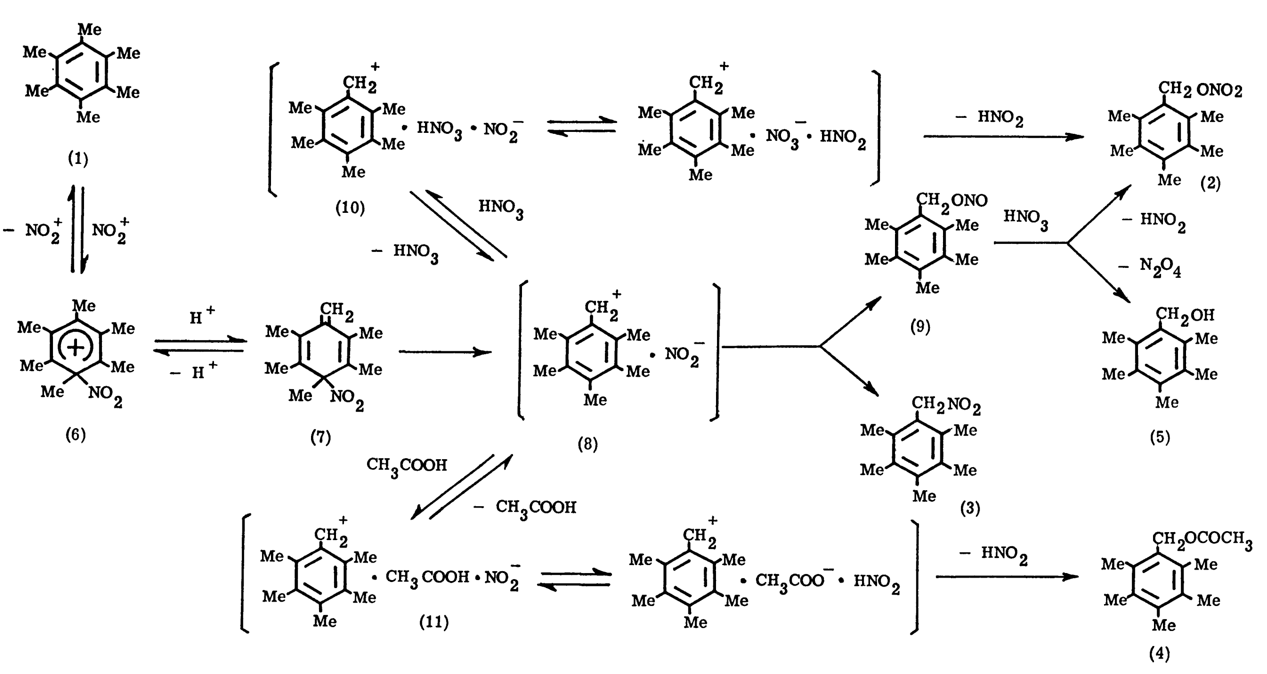
at the same rate as the non-labeled one did. In this case, however, the amount of nitrate was found to increase considerably at the expense of nitromethane, while the amount of acetate did not change very much (Table 2). These results are compatible with Scheme 2, but not with Scheme 1.

It is noteworthy that the molar ratio of acetate **4** to the sum of other three products (**2**+**3**+**5**) remains almost unaffected by the presence of sodium nitrite, urea, and lithium nitrate, as well as by the replacement of protium in **1** by deuterium. Similarly, the molar ratio of nitromethane **3** to the sum of nitrate and alcohol (**2**+**5**) is not very much affected. These trends may be taken to indicate that recombination of initially formed intermediates in **8** is a major pathway to nitrate and nitromethane, while acetate is formed through the nucleophilic capture of carbenium ion intermediate by solvent, possibly *via* a solvent-separated ion-pair (**11**). Pentamethylbenzyl nitrite (**9**) is known to be readily converted into a mixture of nitrate and alcohol in the presence of nitric acid.[24] Part of the nitrate may arise also from the reaction of ion-pair **8** with nitric acid, possibly *via* ion-pair (**10**), since the increase in the concentration of lithium nitrate was found to have a positive effect on the nitrate formation.[30] Alcohol **5** is probably formed partly from the reaction of **9** with nitric acid and partly from the hydrolysis of **2** and **9** during the aqueous work-up. Polymethylbenzyl nitrites are not highly stable and readily undergo hydrolysis to benzyl alcohols in aqueous media. However, they solvolyse quite slowly in anhydrous acetic acid.

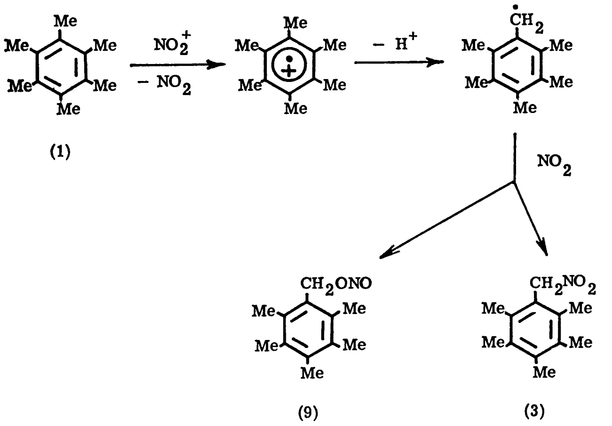
Generally speaking, the side-chain nitration and nitrooxylation of arenes in acetic acid are not sensitive to addenda such as sodium nitrite, urea, and lithium nitrate as long as their concentrations are not very high. In contrast, acetic anhydride exhibited a strong accelerating effect on the reaction and produced a profound effect on the product distribution. Even at the first stages of the reaction, liquid chromatograms of the product revealed a complicated pattern of composition, suggesting the occurrence of various competing side reactions. The addition of dichloromethane to the reaction system, as expected, depressed the acetate formation in favor to the formation of nitrate and nitromethane, leading to the increase in the molar ratio (**2**+**3**+**5**)/**4**. However, the ratio (**2**+**5**)/**3** remained unchanged again. Thus, all the results obtained in our study may be rationalized in terms of the heterolytic mechanism involving the formation of ion-pairs and their conversion to the benzylic compounds, as shown in Scheme 4.

Recently Kochi has made the suggestion of a possible intervention of radical cationic species in the side-chain chlorination of alkyl aromatics, on the basis of his observation of ESR signal during the chlorination of **1**.[13] He extended his idea to the side-chain nitration,[31] suggesting a mechanism in which one electron is transferred from the aromatic substrate to a nitronium ion to form an arene cation radical and nitrogen dioxide (Scheme 5). However, this scheme does not explain the results of our product study: the cation radical derived from 1,2,3,5-tetramethylbenzene (**20**) has a positive charge distribution on the ring carbons in the decreasing order: $C_2 \gg C_5 \gg C_1$, $C_3 > C_4$, $C_6$.[32] Thus, the proton loss should occur preferentially at the 2-methyl group to form 2,4,6-trimethylbenzyl radical and yield its descendents as major products. This is consistent with the result obtained by anodic oxidation of **20** to a mixture of heptamethyldiphenylmethanes,[32] and the results obtained by the reaction of **20** either with *N*-bromosuccinimide under homolytic conditions[33] or with cerium ammonium nitrate in acetic acid.[33] However, it is not consistent with the results obtained by the nitration of **20**, where the only side-chain substituted product was 3,4,5-trimethylbenzyl nitrate (**21**) or its derivative.[34] With 2-ethyl-1,3,5-trimethylbenzene (**22**) and 2-propyl-1,3,5-trimethylbenzene (**23**), side-chain substitution occurs exclusively at the 5-methyl group.[35]

3,6-Dinitro-1,2,4,5-tetramethylbenzene (**24**),[36] 1,2,-



Scheme 4.



Scheme 5.

4,5-tetramethylbenzene-3,6-dicarbonitrile (**25**),[20] and tetrachloro-*p*-xylene (**26**)[37] are all quite stable towards the action of transition metallic oxidizing agents which are thought to react *via* electron-transfer mechanism, but these compounds still undergo a smooth reaction with concentrated nitric acid at room temperature, giving the corresponding benzyl nitrates in good yields. The low efficacy of nitronium tetrafluoroborate to produce side-chain substituted products from **1** provides further evidence against the suggested scheme 5. Therefore, the electron-transfer mechanism does not seem to possess a sound ground on which the formation of a variety of side-chain nitration and nitrooxylation products should be rationalized.

The present findings are highly suggestive of a pathway involving an ion-pair intermediate; nitrate **2** and nitromethane **3** are formed from an intimate ion-pair **8**, and acetate **4** arises from a solvent-separated ion-pair **11**. Full discussion of this problem awaits more detailed data, in particular, direct evidence of isolating the triene intermediate.

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## References

1) The reaction of polysubstituted aromatics. Part LII; Part LI: H. Suzuki, T. Mishina, and T. Hanafusa, *Bull. Chem. Soc. Jpn.*, **51**, 3099 (1978).

2) E. Baciocchi, A. Ciana, G. Illuminati, and C. Pasini, *J. Am. Chem. Soc.*, **87**, 3953 (1965).

3) H. Hart, J. L. Reilly, and J. B.-C. Jiang, *J. Org. Chem.*, **42**, 2684 (1977).

4) P. B. D. de la Mare, N. S. Isaacs, and P. D. McIntyre, *Tetrahedron Lett.*, **1976**, 4835.

5) For reviews see H. Suzuki, *Synthesis*, **1977**, 217; B. Moodie and K. Schofield, *Acc. Chem. Res.*, **9**, 287 (1976).

6) H. Suzuki and T. Hanafusa, *Bull. Chem. Soc. Jpn.*, **46**, 3607 (1973); E. Hunziker, J. R. Penton, and H. Zollinger, *Helv. Chim. Acta*, **54**, 2043 (1971).

7) H. Cerfontain, A. Koeberg-Telder, C. Ris, and C. Schenk, *J. Chem. Soc., Perkin Trans. 2*, **1975**, 966.

8) E. Baciocchi, P. Faggioni, and G. Illuminati, *Gazz. Chim. Ital.*, **103**, 1311 (1973).

9) H. Suzuki, *Bull. Chem. Soc. Jpn.*, **42**, 2618 (1969); H. Suzuki and K. Kawamura, *ibid.*, **45**, 1945 (1972); M. M. King and R. H. Brown, *Tetrahedron Lett.*, **1975**, 3995.

10) A. N. Detsina and V. A. Koptyug, *Zh. Org. Khim.*, **8**, 2215 (1972).

11) R. Willstätter and H. Kubli, *Ber.*, **42**, 4151 (1909).

12) For a general review of non-conventional electrophilic aromatic substitution, see S. R. Hartshorn, *Chem. Soc. Rev.*, **3**, 167 (1974).

13) J. K. Kochi, *Tetrahedron Lett.*, **1974**, 4305.

14) A. Fischer and J. N. Ramsay, *J. Am. Chem. Soc.*, **96**, 1614 (1974); *Can. J. Chem.*, **52**, 3960 (1974).

15) H. Suzuki, H. Yoneda, and T. Hanafusa, *Bull. Chem. Soc. Jpn.*, **48**, 2116 (1975), and other papers in the series. While studying the nitration of 4,6-dihalo-[16] and 4,6-dinitro-1,2,3,5-tetramethylbenzene,[17] we noticed the failure of the

original Baciocchi-Illuminati mechanism, which assumes a cyclic intramolecular transfer of an electrophile from ring to an *ortho* side-chain,[2,18] and proposed in 1971 an alternative possibility involving an ion-pair path for the side-chain nitrooxylation of arenes.[16] Later, a similar idea was adopted by Baciocchi and his coworkers in explaining the side-chain chlorination.[19]

16) H. Suzuki, K. Nakamura, and M. Takeshima, *Bull. Chem. Soc. Jpn.*, **44**, 2248 (1971).

17) H. Suzuki and K. Nakamura, *Bull. Chem. Soc. Jpn.*, **45**, 2534 (1972).

18) H. Suzuki, K. Nakamura, and K. Maruyama, *Bull. Chem. Soc. Jpn.*, **41**, 1487 (1968); H. Suzuki and K. Nakamura, *ibid.*, **43**, 473 (1970).

19) E. Baciocchi, L. Mandolini, and A. Patara, *Tetrahedron Lett.*, **1975**, 2268.

20) H. Suzuki, M. Koge, A. Inoue, and T. Hanafusa, *J. Chem. Soc., Chem. Commun.*, **1977**, 341; *Bull. Chem. Soc. Jpn.*, **51**, 1168 (1978).

21) L. I. Smith, *Org. Synth.*, Coll. Vol. II, 248 (1943).

22) H. Suzuki, *Bull. Chem. Soc. Jpn.*, **43**, 879 (1970).

23) O. Jacobsen, *Ber.*, **22**, 1217 (1889).

24) H. Suzuki, K. Nakano, T. Mishina, and T. Hanafusa, *Nippon Kagaku Kaishi*, **1978**, 1049.

25) V. A. Koptyug, V. G. Shubin, and D. V. Korchagina, *Tetrahedron Lett.*, **1965**, 1535.

26) W. von E. Doering, M. Saunders, H. G. Boyton, H. W. Earhart, E. F. Wadley, W. R. Edwards, and G. Laber, *Tetrahedron*, **4**, 178 (1958).

27) L. I. Smith and S. A. Harris, *J. Am. Chem. Soc.*, **57**, 1289 (1935).

28) R. Astolfi, E. Baciocchi, and G. Illuminati, *Chem. Ind. (Rome)*, **53**, 1153 (1971).

29) A. Fischer, personal communication (1977).

30) Nitrations with nitric acid alone, or with nitric acid/dichloromethane and nitric acid/nitromethane, all of these would probably follow a path involving ion-pair **10**, since they afford in most cases benzyl nitrates as the sole side-chain substituted products.

31) J. K. Kochi, personal communication (1977).

32) K. Nyberg, *Acta Chim. Scand.*, **25**, 2499 (1971).

33) E. Baciocchi, L. Mandolini, and C. Rol, *Tetrahedron Lett.*, **1973**, 3787.

34) To be published.

35) H. Suzuki, M. Sawaki, and R. Sakimoto, *Bull. Chem. Soc. Jpn.*, **45**, 1515 (1972).

36) H. Suzuki and K. Nakamura, *Synthesis*, **1972**, 606.

37) H. Suzuki, K. Ishizaki, S. Maruyama, and T. Hanafusa, *J. Chem. Soc., Chem. Commun.*, **1975**, 51; *Bull. Chem. Soc. Jpn.*, **48**, 2112 (1975).