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# Intermediate Stages of the Nitration of Hexamethylbenzene to Dinitroprehnitene[1]

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A syrupy substance formed in quantity during the nitration of hexamethylbenzene to dinitroprehnitene has been found to be a complex mixture of varying amounts, depending markedly on the conditions, of 2,3,4,5,6-pentamethylbenzyl nitrate, 5,6-bis(nitrooxymethyl)-1,2,3,4-tetramethylbenzene, nitropentamethylbenzene, 6-nitro-2,3,4,5-tetramethylbenzyl nitrate, 2,3,4,5,6-pentamethylphenylnitromethane, bis(2,3,4,5,6-pentamethylbenzyl) ether, pentamethylbenzaldehyde, and several other unidentified carbonyl compounds, nitrite esters, and aliphatic nitro compounds. On the basis of the products isolated, a possible path by which hexamethylbenzene can be converted into dinitroprehnitene has been suggested.

Electrophilic attack on hexaalkylbenzenes usually leads to the replacement of alkyl groups by the attacking reagent.[2] However, some instances are known in which the result is the side-chain sub-

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[1] The Reaction of Polysubstituted Aromatics. XVI, Part XV: This Bulletin, **43**, 481 (1970).

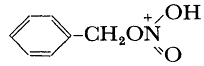
[2] K. Galle, *Ber.*, **16**, 1744 (1883); P. Jannasch and A. Bartels, *ibid.*, **31**, 1716 (1898); L. I. Smith and C. O. Guss, *J. Amer. Chem. Soc.*, **62**, 2635 (1940); H. Hopff and A. K. Wick, *Helv. Chim. Acta*, **43**, 1473 (1960); *ibid.*, **44**, 19 (1961).

stitution, and the replacement of alkyl group by nitro group during the nitration of polyalkylbenzenes has been suggested to proceed through the intermediacy of the nitrate.[3] Recently, Illuminati and co-workers explained the side-chain chlorination of hexamethylbenzene in acetic acid by stating that the attacking reagent undergoes the rearrangement from nucleus to side chain to yield a benzylic compound.[4] An extension of this idea to the nitration and sulfonation of polyalkylated benzenes has been presented.[5,6] In this connection, hexamethylbenzene seems to be a convenient substrate for investigating the mode of alkyl replacement since there is no nuclear hydrogen atom to be replaced and all the methyl groups are equivalent. The reduced complexity of the products is expected—a very considerable advantage over the other polyalkylated systems.

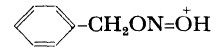
Hitherto little has been reported on the direct nitration of hexamethylbenzene. Willstätter and Kubli treated hydrocarbon with benzoyl nitrate in carbon tetrachloride and obtained bis(2,3,4,5,6-pentamethylbenzyl) ether and a bis(nitromethyl)-tetramethylbenzene in an unspecified yield.[7] No mention was made on the details of the reaction. Smith and Harris carried out nitration with fuming nitric acid in the presence of sulfuric acid and obtained as much as 22% yield of dinitroprehnitene (5,6-dinitro-1,2,3,4-tetramethylbenzene).[8] However, a significant proportion of the starting material remained unaccounted for. The present study was undertaken in order to separate and identify the various intermediate products formed when hexamethylbenzene is nitrated to dinitroprehnitene.

When hexamethylbenzene was nitrated in methylene chloride with excess of fuming nitric acid ($d=1.5$), at temperatures between $-5$ and 0°C, there resulted a white crystalline product, which showed strong infrared bands at 1272 and 1612 cm$^{-1}$ ($-ONO_2$); PMR peaks at 4.41 $\tau$ ($-CH_2ONO_2$) in accord with the expected formation of 2,3,4,5,6-pentamethylbenzyl nitrate (I) as the initial product. If the dark brown mixture was allowed to stand at room temperature, a further reaction soon took place under active liberation of brown fume to give a slightly pasty, pale yellow solid, the infrared spectrum of which showed strong absorptions at 1277 and 1626 cm$^{-1}$ ($-ONO_2$); PMR peak at 4.36 $\tau$ ($-CH_2ONO_2$). Neglecting the minor peaks due to by-products and comparing it with an authentic specimen, the major product was readily identified as 5,6-bis(nitrooxymethyl)-1,2,3,4-tetramethylbenzene (II). A close inspection of the infrared spectra ruled out the possibility of the concurrent formation in significant amounts of other isomers, 4,6-bis-(nitrooxymethyl)-1,2,3,5-tetramethylbenzene (III) or 3,6-bis(nitrooxymethyl)-1,2,4,5-tetramethylbenzene (IV).

Chromatography of the nitration products on alumina gave an appreciable amount of bis(2,3,4,5,6-pentamethylbenzyl) ether (V) as an early light petroleum eluate. In the presence of a strong acid, the benzyl nitrate or nitrite will form the conjugate acid,[9] VI or VII, which can act as an alkylating agent when there is appropriate nucleophile in the system.



(VI)



(VII)

Thus, V seems to be derived from the nucleophilic displacement of the ester oxygen on the benzylic carbon.[10] A similar case has been reported by Paraille during the decomposition of *p*-nitrobenzyl perchlorate in nitromethane to give bis(*p*-nitrobenzyl) ether.[11] Pentamethylbenzaldehyde (VIII) and other carbonyl compounds were obtained from the late light petroleum eluates, or from the benzene eluates. Nitrate I was hydrolyzed during the elution and appeared as 2,3,4,5,6-pentamethylbenzyl alcohol (IX), but dinitrate II was adsorbed so firmly on alumina that chromatographic treatment did not give satisfactory results at all. Even the prolonged elution with ether gave only small amounts of 5,6-bis(hydroxymethyl)-1,2,3,4-tetramethylbenzene (X) besides some non-crystallizable syrupy substances.

When the reaction mixture was allowed to stand overnight in an ice-bath, a light brown oily solid was obtained. Its PMR spectrum contained six peaks in the nitrooxymethylene proton region. Besides two strong peaks due to I (4.41 $\tau$) and II (4.37 $\tau$), the third peak at 4.31 $\tau$ became prominent. Its infrared spectrum showed an increased broad absorption due to $-NO_2$ group at 1545—1565 cm$^{-1}$, suggesting the presence of some aliphatic nitro

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[3] L. I. Smith and J. W. Horner, *J. Amer. Chem. Soc.*, **62**, 1349 (1940).

[4] E. Baciocchi, A. Ciana, G. Illuminati and C. Pasini, *ibid.*, **87**, 3953 (1965).

[5] H. Suzuki, K. Nakamura and K. Maruyama, This Bulletin, **41**, 1487 (1968).

[6] H. Suzuki and Y. Tamura, *Chem. Commun.*, **1969**, 244.

[7] R. Willstätter and H. Kubli, *Ber.*, **42**, 4151 (1909).

[8] L. I. Smith and S. A. Harris, *J. Amer. Chem. Soc.*, **57**, 1289 (1935).

[9] R. Boschan, R. T. Merrow and R. W. van Dolah, *Chem. Rev.*, **55**, 485 (1955).

[10] Treatment of fully substituted benzyl nitrates with a catalytic amount of sulfuric acid usually gives some bis-benzyl ether. However, if nuclear hydrogen atom is available, preference for the ring substitution is observed. Thus, nitration of pentamethylbenzene yields as by-products 2,2′,3,3′,4,4′,5,5′,6-nonamethyldiphenylmethane and 2,2′,3,3′,4,4′,5,5′-octamethyl-6-nitrooxymethyldiphenylmethane rather than bis(2,3,4,5-tetramethylbenzyl) ether (H. Suzuki and K. Nakamura, This Bulletin, **43**, 473 (1970).

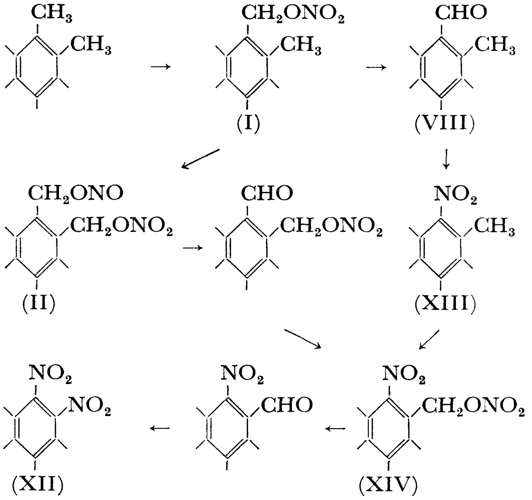
[11] P. F. G. Paraille, *J. Chem. Soc.*, **1957**, 3162.

compounds. If the concentration of the nitrous acid formed was lowered either by passing a gentle stream of dry nitrogen into the mixture, or by using a large excess of nitric acid, the peak could be weakened.

Evidence of nitroalkane formation was obtained by the isolation of a crystalline product. Nitration of hexamethylbenzene in methylene chloride saturated with nitrogen trioxide gave a yellow pasty solid. Chromatography of this product on alumina gave unchanged hydrocarbon and the ether V from the light petroleum eluates; some carbonyl compounds from the benzene eluates; and the alcohol IX from the early ether eluates. Further prolonged elution with ether gave a dark yellow syrup, which gradually separated prisms (mp 80—84°C) and was identified as 2,3,4,5,6-pentamethylphenylnitromethane (XI) by comparison with the authentic specimen. Since the homolytic reaction was less probable under these conditions, aliphatic nitro compounds seem to have been formed by the union of the benzylic portion of the conjugate acid, VI or VII, with the nitrogen atom of the nitrite ion. The process is analogous to that of the Victor Meyer reaction in which phenylnitromethane and benzyl nitrite are formed from benzyl halide and silver nitrite.[12] When the above reaction mixture was kept overnight in an ice-salt bath, to which no further amount of ice was added, there resulted a non-crystallizable, sticky, pale yellow syrup. The mixture was found to contain, in addition to the anticipated products, appreciable amounts of nitrite esters, carbonyl compounds and aliphatic nitro compounds. Chromatographic separation did not give any satisfactory results.

Treatment of hexamethylbenzene with fuming nitric acid alone always gave nitrates as the principal product. Dinitroprehnitene (XII) was not formed in any significant amount. Since XII was obtained by Smith and Harris as much as in 22% yield by carrying out the reaction in presence of a large excess of sulfuric acid,[8] the effect of sulfuric acid on the product composition has been examined. Addition of a small amount of sulfuric acid to the reaction mixture was found to facilitate the side-chain substitution greatly, and the hydrocarbon was readily converted into the mono or dinitrate, depending on the amount of nitric acid used. With the increase of sulfuric acid, the yield of V fell rapidly, while those of nitropentamethylbenzene (XIII), 6-nitro-2,3,4,5-tetramethylbenzyl nitrate (XIV) and XII rose progressively. Carbonyl compounds (aldehyde and carboxylic acid) also increased, but aliphatic nitro compounds diminished. The results are consistent with the proposal by Smith and Horner that the group $-CH_2ONO_2$ can be replaced by a nitro group in the presence of sulfuric acid.[3]

While the results reported here do not provide a basis for describing in a precise way the mode of the alkyl replacement, they seem to provide valuable insights. Noteworthy is the marked increase in the formation of carbonyl compounds, especially aldehyde such as VIII when some sulfuric acid is added to the nitrating system. Considering the ease of electrophilic displacement of the formyl group at suitably activated or blocked positions,[13] a mechanism involving the preliminary transformation of the benzyl nitrate into the aldehyde, followed by the nitrodeformylation now seems worthy of consideration. One of the possible courses which can lead hexamethylbenzene to dinitroprehnitene is shown below:



In fact, a catalytic quantity of sulfuric acid can lead the benzyl nitrate to the benzaldehyde as well as benzoic acid,[14] and the replacement of formyl group by nitro group is a quite common occurrence.[15] The behavior of various polysubstituted benzyl nitrates towards sulfuric and nitric acids are now being investigated. We hope to clarify the role of the aldehyde in these anomalous nitrations in a later paper.

## Experimental

Infrared spectra were run as Nujol mulls on a DS-402G

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[12] N. Kornblum, R. A. Smiley, R. K. Blackland and D. C. Iffland, *J. Amer. Chem. Soc.*, **77**, 6269 (1955); N, Kornblum, J. W. Jones and D. E. Hardies, *ibid.*, **88**, 1704 (1966).

[13] W. M. Suhubert and R. Kintner, "The Chemiistry of the Carbonyl Group," ed. by S. Patai, Interscience Publishers, London (1966), p. 695; J. Strating, L. Thijs and B. Zwanenburg, *Rev. Trav. Chim.*, **85**, 291 (1966).

[14] S. D. Ross, E. R. Coburn and M. Finkelstein, *J. Org. Chem.*, **33**, 585 (1968).

[15] D. V. Nightingale, *Chem. Rev.*, **40**, 117 (1947); P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution, Nitration and Halogenation," Butterworths, London (1959).

spectrophotometer. Only prominent peaks were recorded. PMR measurements were carried out on a Varian A-60A spectrometer with deuteriochloroform as solvent and tetramethylsilane as internal standard. All melting points were determined in hot stage and not corrected.

Hexamethylbenzene was prepared by methylation of commercial xylene mixture and crystallized from ethanol.16) Pentamethylbenzaldehyde (VIII) was prepared from 2,3,4,5,6-pentamethylbenzyl chloride17) by oxidation with 2-nitropropane.18) Bis(2,3,4,5,6-pentamethylbenzyl) ether (V) was prepared from 2,3,4,5,6-pentamethylbenzyl alcohol19) according to Rhoad and Flory.20)

**2,3,4,5,6-Pentamethylbenzyl Nitrate (I).** A solution of silver nitrate (12 g) in acetonitrile (30 m*l*) was added all at once to a solution of 2,3,4,5,6-pentamethylbenzyl chloride (12 g) in acetonitrile (20 m*l*). The mixture was stirred for 5 hr at room temperature. Silver chloride was removed by filtration and the solvent was pumped off. The product was crystallized from light petroleum to yield 12.2 g (90%) of white leaflets, mp 95—97°C. IR: 760, 855, 875, 900, 962, 1272 (-$ONO_2$), 1301, 1612, and 1625 cm$^{-1}$ (-$ONO_2$); PMR (in $CCl_4$), 7.80 (3*1 $CH_3$), 7.72 (2$CH_3$), and 4.42 $\tau$ ($CH_2$).

Found: C, 64.4; H, 7.9; N, 6.0%. Calcd for $C_{12}H_{17}NO_3$: C, 64.6; H, 7.7; N, 6.3%.

**5, 6-Bis(nitrooxymethyl)-1, 2, 3, 4-tetramethylbenzene (II).** A warm solution of silver nitrate (2.0 g) in acetonitrile (10 m*l*) was added all at once with stirring, to a hot solution of 5,6-bis(chloromethyl)-1,2,3,4-tetramethylbenzene (1.5 g, mp 133—137°C; lit,21) 138—139°C) in acetonitrile (30 m*l*). The mixture was stirred for several hours, and silver chloride was separated by filtration. Evaporation of the solvent *in vacuo*, followed by crystallization of the residue from ligroin gave white needles (0.7 g), mp 127—129°C. IR: 697, 732, 755, 859, 876, 954, 964, 1277 (-$ONO_2$), and 1626 cm$^{-1}$ (-$ONO_2$); PMR, 7.74 (2$CH_3$), 7.68 (2*1$CH_3$), and 4.36 $\tau$ ($CH_2$).

Found: C, 50.9; H, 5.8%. Calcd for $C_{12}H_{16}N_2O_6$: C, 50.7; H, 5.6%.

A product of low purity first separated as an oil from the solution and gradually turned into a powder-like solid. Repeated recrystallization gave no improved result.

The above procedure applied to 4,6-bis(chloromethyl)-1,2,3,5-tetramethylbenzene (mp 115—117°C)20) and 3,6-bis(chloromethyl)-1,2,4,5-tetramethylbenzene (mp 194—196°C)20) gave *4,6-bis(nitrooxymethyl)-1,2,3,5-tetramethylbenzene (III,* mp 126—128°C) and *3,6-bis(nitrooxymethyl)-1,2,4,5-tetramethylbenzene (IV,* mp 203—205°C), respectively. IR: (III), 694, 757, 818, 873, 950, 1275 (-$ONO_2$), and 1622 cm$^{-1}$ (-$ONO_2$); (IV), 727, 759, 871, 895, 964, 1014, 1274 (-$ONO_2$), 1297, 1614, and 1625 cm$^{-1}$ (-$ONO_2$). PMR: (III), 7.78 ($CH_3$), 7.68 (2$CH_3$), 7.60 ($CH_3$), and 4.44 ($CH_2$); (IV), 7.70 (4$CH_3$) and 4.43 $\tau$ ($CH_2$).

**2,3,4,5,6-Pentamethylphenylnitromethane (XI).** A solution of 2,3,4,5,6-pentamethylbenzyl chloride (4 g) in acetonitrile (10 m*l*) was poured into a stirred mixture consisting of silver nitrite (5 g), a small amount of calcium carbonate, and acetonitrile (30 m*l*). After 5 hr, the reaction mixture was worked up as usual, and the residue obtained after removal of the solvent was taken up in ethanol and boiled for some minutes to destroy the accompanying nitrite ester. The solution was evaporated to dryness *in vacuo* and the residue was extracted with three portions each of 20 m*l* cold light petroleum to separate from the less soluble alcohol IX. Spontaneous evaporation of the combined extracts gave XI as large plates, and recrystallization from light petroleum gave prisms (0.6 g),22) mp 86—88°C. IR: 711, 764, 834, 1065, 1271, 1304, 1369 (-$NO_2$), and 1547 cm$^{-1}$ (-$NO_2$); PMR, 7.78 (3$CH_3$), 7.73 (2$CH_2$), and 4.46 $\tau$ ($CH_2$).

Found: C, 69.8; H, 8.3%. Calcd for $C_{12}H_{17}NO_2$: C, 69.6; H, 8.2%.

**5,6-Bis(hydroxymethyl)-1,2,3,4-tetramethylbenzene (X).** 5, 6-Bis(chloromethyl)-1, 2, 3, 4-tetramethylbenzene was converted into the diacetate,20) which without further purification was saponified by refluxing in 10% ethanolic potassium hydroxide for several hours. The product was recrystallized from benzene-ligroin mixture to give white needles, mp 174—175°C.

Found: C, 74.1; H, 9.2%. Calcd for $C_{12}H_{18}O_2$: C, 74.2; H, 9.3%.

**Nitration of Hexamethylbenzene.** Typical examples are shown below. Products were identified by spectral comparison and mixed melting as far as the authentic specimens were available.

*i)* Fuming nitric acid (16.8 g, *d*=1.5) was added over a period of thirty minutes to a vigorously stirred solution of hexamethylbenzene (8.1 g) in methylene chloride (50 m*l*), keeping the temperature between −5 and 0°C by the use of an ice-salt bath. The organic layer was separated and washed with dilute sodium bicarbonate and then with water. Removal of the solvent left a white crystalline solid, chromatography of which (5 g) on alumina gave the unchanged hydrocarbon (1.2 g) and V (0.5 g) from the light petroleum eluates; carbonyl compounds (0.3 g) from the benzene eluates; and finally IX (0.8 g) from the ether eluates.

*ii)* Nitration of the hydrocarbon (8.1 g) with the 1 : 1 mixture of fuming nitric acid (23.4 g) and sulfuric acid (23.4 g) under a similar condition gave an orange-yellow pasty solid. The product (5 g) dissolved in a minimum amount of methylene chloride was placed on the top of the alumina column. Elution with light petroleum gave XIII (0.1 g), XIV (0.3 g),5) and XII (0.5 g); and with benzene some carbonyl compounds. Dinitrate II which constituted the bulk of the nitration product could not be eluted successfully even with ether.

*iii)* When the hydrocarbon (8.1 g) was treated with fuming nitric acid (15.8 g) in the presence of an excess of sulfuric acid (48 g), a light brown oily solid was obtained. Because of the difficulties encountered in the

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16) L. I. Smith, "Organic Syntheses," Coll. Vol. 2, p. 248 (1943).

17) F. Bennington, R. D. Morin and L. C. Clark, *J. Org. Chem.*, **23**, 2034 (1958).

18) M. G. Beets, W. Meerburg and H. van Essen, *Rec. Trav. Chim. Pays-Bas*, **78**, 570 (1959).

19) M. S. Newman and N. C. Deno, *J. Amer. Chem. Soc.*, **73**, 3644 (1951).

20) M. J. Rhoad and P. J. Flory, *ibid.*, **72**, 2216 (1950).

21) M. S. Newman, J. R. LeBlanc, H. A. Karnes and G. Axelrad, *ibid.*, **86**, 868 (1964).

*1 Numerals refer to the number of methyl groups.

22) Resourse to chemical separation gave even poorer yield of the product.

chromatographic separation, a part of the product (14.2 g) was fractionally extracted with light petroleum using a Soxhlet's extractor. Each extract was monitored by infrared spectroscopy and those of a similar composition were combined. Chromatography of the earlier extracts on alumina gave, besides some unchanged hydrocarbon, V (0.4 g); VIII (0.4 g); XII (1.9 g); an unidentified carbonyl compound (0.5 g; Found: C, 70.9; H, 7.3%. $C_{12}H_{15}NO_2$ requires C, 70.2; H, 7.3%) which melted partly at 150—153°C, soon solidified in another crystalline form, and remelted at 223—227°C with partial sublimation and decomposition; IX (0.6 g); and an unidentified hydroxy compound (0.6 g; mp 153—154°C; Found: C, 74.6; H, 9.1%; strong IR bands at 993, 1524, and 3310 $cm^{-1}$) as well as a little X. Later extracts were mainly a complicated mixture of several carbonyl compounds (1.5 g). A light brown half-resinous substance (5.2 g) which had broad, deep absorptions due to $-OH$, $>C=O$, and $-NO_2$, was left in the thimble.

iv) A solution of hexamethylbenzene (8.1 g) in methylene chloride (50 m*l*) was saturated with nitrogen trioxide at $-10$—$-5$°C. Fuming nitric acid (15.8 g) was introduced with vigorous stirring over a period of 30 min and the mixture was worked up as usual. A pasty yellow product (5 g) was chromatographed on alumina to give the recovered hydrocarbon (2.5 g), V (0.2 g), aldehydes (0.3 g), and IX (0.7 g). A further prolonged elution with ether gave a yellow syrup, which was dissolved in a small amount of light petroleum and set aside. A solid product (0.2 g, mp 74—84°C) separated out and recrystallized from the same solvent to give prisms, mp 80—84°C, identical with the authentic specimen of XI.