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Orientation of the Products from the Nitration of Halopentamethylbenzenes1)

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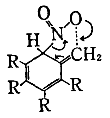
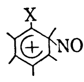
The action of fuming nitric acid upon chloropentamethylbenzene, bromopentamethylbenzene, and iodopentamethylbenzene has been investigated. 5-Halo-2,3,4,6-tetramethyl- and 6-halo-2,3,4,5-tetramethylbenzyl nitrate were the principal products. 4-Halo-2,3,5,6-tetramethylbenzyl nitrate was never formed in any significant amount. The orientation was consistent with the previously suggested mechanistic scheme. PMR spectral data for nine halotetramethylbenzyl chlorides and nitrates have been presented.

Nitration of polyalkylbenzenes by fuming nitric acid often yields unusual products in which a hydrogen atom in one of the alkyl groups has been replaced by $-ONO_2$ group. The formation of such benzyl nitrates was first observed in 1915 by Huender in the nitration of bromopseudocumene.2) Smith and coworkers established that the nitrate formation is a property of the highly alkylated benzenes.3-7) But the mode of peculiar substitution has remained undiscussed for long. Our interest in the side-chain substitution of alkyl aromatics under ionic conditions led us to reinvestigate the nitration of penta-alkylbenzenes. The preferred formation of 2,3,4,5-tetra-alkylbenzyl nitrate was explained by a process similar to that postulated for the unconventional chlorination of hexamethylbenzene8); *i.e.*, a process involving the electrophilic attack of the nitronium ion on the ring, followed by the hyperconjugative release of a proton from the neighboring methyl group and the rearrangement of the unstable intermediate (I) to the benzyl nitrite, which will then be transformed into the nitrate.9)

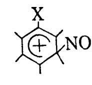
In this connection, the nitration of halopentamethylbenzenes seems to be of special interest. According to the suggested mechanism, four intermediate carbonium ion (II—V) are produced by electrophilic attack of nitronium ion on halopentamethylbenzene.



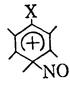
I



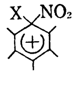
II



III



IV



V

Except for the case where X is the good leaving group, iodine atom, the fourth ion V, is considered to be less important since the electron-attracting halogen atom is bonded direct to the reaction site. Ion III, in which three methyl groups can contribute to the stabilization of the ion by interaction with the positively polarized centers to which they are adjacent, would be more preferable to II and IV, where there are two such methyl groups. Of the other two ions, II is more favorable than IV not only for statistical reason, but also for more effective stabilization by one methyl group in an ortho position and one in para position than two methyl groups in ortho, as IV. Positive charge distribution in the cyclohexadienyl cation system (VI) has been found to be concentrated in the order para>ortho>meta position.10) When the nitronium ion replaces a proton in VI, it follows that an electron-attracting halogen atom should have a more favorable effect on the stability of VII when it is ortho (VII, R_1=halogen) to the entering

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1) The Reaction of Polysubstituted Aromatics. XV. Part XIV: This Bulletin, **43**, 473 (1970).

2) A. Huender, *Rec. Trav. Chim. Pays-Bas*, **34**, 1 (1915). Also *cf.* I. J. Rinkes, *ibid.*, **57**, 1405 (1938); **58**, 538 (1939); **63**, 89 (1944).

3) L. I. Smith and S. A. Harris, *J. Amer. Chem. Soc.*, **57**, 1289 (1953).

4) L. I. Smith and O. Tenenbaum, *ibid.*, **57**, 1293 (1935).

5) L. I. Smith, F. L. Taylor and I. M. Webster, *ibid.*, **59**, 1082 (1937).

6) L. I. Smith and J. W. Horner, *ibid.*, **62**, 1349 (1940).

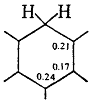
7) L. I. Smith and C. O. Guss, *ibid.*, **62**, 2635 (1940).

8) E. Baciocchi, A. Ciana, G. Illuminati and C. Pasini, *ibid.*, **87**, 3953 (1965). Also *cf.* P. B. D. de la Mare and H. Suzuki, *J. Chem. Soc., C*, **1967**, 1586.

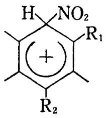
9) H. Suzuki, K. Nakamura and K. Maruyama, This Bulletin, **41**, 1487 (1968).

10) C. MacLean and E. L. Mackor, *Mol. Phys.*, **4**, 241 (1961); J. P. Colpa, C. MacLean and E. L. Mackor, *Tetrahedron*, **19**, 65 (1963).

reagent (NO_2^+) than when it is para (VII, R_2= halogen). Thus it is understandable that the intermediate cation II will be energetically more preferred than IV.

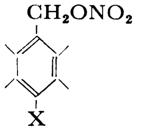


VI[*1]

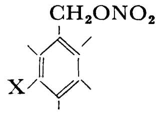


VII

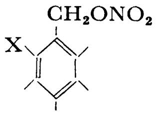
Rearrangement of the ions II and IV according to the suggested sequence will lead to the same nitrate, 5-halo-2,3,4,6-tetramethylbenzyl nitrate (IX). Migration of the nitro group in ion III, however, can occur in two directions, to yield either 4-halo-2,3,5,6-tetramethylbenzyl nitrate (VIII), or 6-halo-2,3,4,5-tetramethylbenzyl nitrate (X). Simple electronic consideration suggests that the hyperconjugative proton release from the methyl group in ortho to the halogen atom would be more preferable than that from the methyl group in a para position, since the former is bonded to the more positively polarized carbon. It follows that the ion III should give rise to X rather than VIII, and if the decomposition of the intermediate benzenonium ion into the side-chain products is quite a slow step, IX and X will be the major products derived from the ordinary nitration of halopentamethylbenzene. The amount of the latter is somewhat greater than that of the former.



VIII



IX



X

Nitration of halopentamethylbenzene has been investigated only by Smith and Horner.[6)] They converted the nitration product from bromopentamethylbenzene into a mixture of the amines and separated them by fractional sublimation, and concluded that the action of fuming nitric acid upon bromopentamethylbenzene produced an inseparable mixture of two benzyl nitrates, 5-bromo-2,3,4,6-tetramethylbenzyl nitrate (IX, X= Br) and 6-bromo-2,3,4,5-tetramethylbenzyl nitrate (X, X=Br) in an approximate ratio 3 : 2. No derivative of durene could be obtained from the mixture. Their result seems to be quite consistent with the above discussion, although their conclusion based on the classical method of separation leaves some uncertainty as to the claimed absence of 4-bromo-2,3,5,6-tetramethylbenzyl nitrate (VIII, X=Br) in the reaction mixture. We have carried out nitration of three halopentamethylbenzenes and investigated the product by means of infrared and PMR spectroscopy. Identity of the product has been confirmed by comparison with the authentic specimen, prepared from the corresponding halotetramethylbenzenes by chloromethylation and subsequent treatment of the chlorides with silver nitrate in acetonitrile. PMR spectral data for the chlorides and nitrates derived from each of the three halotetramethylbenzenes are summarized in Table 1.

Chloropentamethylbenzene was nitrated with fuming nitric acid at −5—0°C in methylene chloride to give pale yellow, half-crystalline solid, the PMR spectrum of which showed two prominent peaks due to $-CH_2ONO_2$ at 4.31 and 4.45 τ with average relative areas of 58 : 42. By comparison with the reference compound, a signal at lower field was readily attributed to 6-chloro-2,3,4,5-tetramethylbenzyl nitrate (X, X=Cl). A signal at higher field may be due to either 4-chloro-2,3,5,6-tetramethylbenzyl nitrate (VIII, X=Cl), or 5-chloro-2,3,4,6-tetramethylbenzyl nitrate (IX, X= Cl), since both nitrates absorb at the same position in this region. On the basis of infrared spectra, the absorption at 4.45 τ was assigned to the 5-chloro isomer. Some minor peaks observed at 5.16, 5.36 and 6.60 τ were not investigated further.

A pale yellow oily solid obtained from the nitration of bromopentamethylbenzene showed two methylene peaks at 4.25 and 4.43 τ, to which 6-bromo-2,3,4,5-tetramethyl- and 5-bromo-2,3,4,6-tetramethylbenzyl nitrates respectively, were readily assigned. Of three isomeric nitrates, 4-bromo-2,3,5,6-tetramethylbenzyl nitrate absorb at the highest field, 4.46 τ, and the lack of observable peak at this position excludes the possibility of the formation of this isomer in any significant amount, in line with the previous findings.[6)] The ratio of the two nitrates was 56 : 44, which was just opposite to the reported value of 2 : 3, but can be rationalized in terms of the difference in the contribution of the benzenonium intermediates, II and III. Several minor peaks at 5.31, 5.54, an 6.61 τ were not assigned.

Nitration of iodopentamethylbenzene proceeded somewhat differently from that of the other two halopentamethylbenzenes. The reaction was always accompanied by nitrodeiodination. PMR spectra of an oily solid, dark-brown with liberated iodine, showed two sharp methylene signals at 4.19 and 4.37 τ, each attributable to 6-iodo-2,3,4,5-tetramethylbenzyl nitrate (X, X=I) and 5-iodo-2,3,4,6-tetramethylbenzyl nitrate (IX, X=I). The relative intensity of two signals was 53 : 47 on an average. A very weak signal which might arise from 4-iodo-2,3,5,6-tetramethylbenzyl nitrate (VIII, X=I) was also observed at 4.42 τ, but its amount was insignificant as compared with that of the other two isomers. Minor peaks observed below 7 τ were at 4.61, 5.28, 5.50, 6.58, and 6.61 τ.

The orientation of the products is in good agree-

[*1] Figures refer to π-electron deficiencies in benzenonium ion calculated from PMR proton shift.

Table 1. PMR spectral data for halotetramethylbenzyl chlorides and nitrates

Compound		Mp °C	PMR spectra (in CCl_4, τ)	
			CH_2	CH_3*
6-Halo-2,3,4,5-tetramethylbenzyl series				
Chloride	6-Chloro,	100—101	5.31	7.63 (2), 7.76 (1), 7.79 (1)
	6-Bromo,	114—116	5.25	7.57 (1), 7.61 (1), 7.73 (1), 7.79 (1)
	6-Iodo,	110—111	5.24	7.50 (1), 7.60 (1), 7.72 (1), 7.82 (1)
Nitrate	6-Chloro,	81— 82	4.30	7.62 (1), 7.67 (1), 7.73 (1), 7.78 (1)
	6-Bromo,	91— 93	4.29	7.56 (1), 7.65 (1), 7.70 (1), 7.79 (1)
	6-Iodo,	98—100	4.18	7.44 (1), 7.61 (1), 7.64 (1), 7.78 (1)
5-Halo-2,3,4,6-tetramethylbenzyl series				
Chloride	5-Chloro,	111—112	5.45	7.51 (1), 7.62 (1), 7.66 (1), 7.75 (1)
	5-Bromo,	113—115	5.43	7.47 (1), 7.56 (1), 7.68 (1), 7.73 (1)
	5-Iodo,	110—112	5.37	7.39 (1), 7.47 (1), 7.71 (2)
Nitrate	5-Chloro,	100—101	4.44	7.52 (1), 7.59 (1), 7.68 (1), 7.74 (1)
	5-Bromo,	105—107	4.43	7.48 (1), 7.53 (1), 7.72 (2)
	5-Iodo,	106—108	4.39	7.38 (1), 7.42 (1), 7.68 (2)
4-Halo-2,3,5,6-tetramethylbenzyl series				
Chloride	4-Chloro,	92— 93	5.49	7.65 (4)
	4-Bromo,	105—107	5.50	7.60 (2), 7.64 (2)
	4-Iodo,	100—101	5.42	7.48 (2), 7.60 (2)
Nitrate	4-Chloro,	112—114	4.47	7.64 (2), 7.68 (2)
	4-Bromo,	113—114	4.46	7.57 (2), 7.65 (2)
	4-Iodo,	116—118	4.44	7.42 (2), 7.57 (2)

* Numerals in parentheses refer to the number of methyl groups.

ment with the suggested mechanism, involving the migration of the nitro group from the nucleus to the neighboring side-chain.[9] The nitro to nitrite rearrangement is quite reasonable in an activated complex, and may be expressed in a fashion similar to those observed in mass spectrometer or photochemistry.[11] It resembles to some extent the base-catalysed oxidation-reduction mechanism and the photochemical oxygen transfer processes widely observed in ortho nitro compounds.[12] In the benzenonium intermediate, proton release from the adjacent alkyl group and the subsequent redistribution of electrons to give nitrite would proceed in a single continuous process, and it does not seem necessary to postulate a discrete intermediate as I in the reaction sequence. The increasing amount of meta substitution as the atomic number of the halogen increases is explained by the steady growth of the contribution of ion II and IV relative to that of III, and is rationalized on the basis of the change in the inductive effect of the substituent.[13] The radical character of the reaction is ruled out by the high selectivity in orientation and the absence of phenylnitromethane or dibenzyl in the reaction product.

Experimental

IR spectra were measured in Nujol with a DS-402G spectrophotometer, and PMR spectra were obtained with a Varian A-60A spectrometer at 60 Mc/sec. with tetramethylsilane as internal standards.

Materials. *Chloropentamethylbenzene* (mp 155—156°C)[14] and *bromopentamethylbenzene* (mp 159—161°C)[15] were prepared as described in literature. *Iodopentamethylbenzene* was prepared by stirring a mixture of pentamethylbenzene (22.2 g), iodine (15.3 g), and periodic acid dihydrate (6.9 g) in 80% acetic acid (60 m*l*) containing a small amount of sulfuric acid as catalyst, at 70—80°C for about 1 hr until the color of iodine disappeared.[16] The mixture was poured into water, and the solid was removed and recrystallized from ethanol. It weighed 30.4 g (75%) and melted at 140—141°C.[17]

Preparation of Halotetramethylbenzyl Chlorides. A mixture of halotetramethylbenzene, concen-

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[11] O. L. Chapman, D. C. Heckert, J. W. Reasoner and S. P. Thackaberg, *J. Amer. Chem. Soc.*, **88**, 5550 (1966).

[12] J. D. Louden and G. Tennant, *Quart. Rev.*, **18**, 389 (1964).

[13] P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution, Nitration and Halogenation," Butterworth Scientific Publications, London (1959), p. 85.

[14] C. Cook, N. Nash and H. Flanagan, *J. Amer. Chem. Soc.*, **77**, 1783 (1955).

[15] L. I. Smith and J. Nichols, *J. Org. Chem.*, **6**, 489 (1941).

[16] H. Suzuki, K. Nakamura and R. Gotō, This Bulletin, **37**, 1858 (1964).

[17] H. Suzuki, T. Sugiyama and R. Gotō, *ibid.*, **39**, 128 (1966).

trated hydrochloric acid, and an excess of 37%-formalin was stirred vigorously and heated on a water-bath, while a stream of hydrogen chloride was passed through. In due course, the benzyl chloride gradually separated as crystalline solid which was removed, washed with water and crystallized from ligroin. The iodotetramethylbenzenes underwent extensive chloromethyl-deiodonation at elevated temperature and the product was usually accompanied by an appreciable amount of bis-chloromethyltetramethylbenzenes. Satisfactory results were obtained by stirring the mixture at low temperature for prolonged hours, although under these mild conditions iodoisodurene yielded some bis-chloromethyl compound.

Conversion of Benzyl Chlorides into Nitrates. A warm solution of silver nitrate in acetonitrile was added all at once to a magnetically stirred solution of halotetramethylbenzyl chloride in acetonitrile. The mixture was stirred for several hours, and the silver chloride was filtered. After removal of the solvent the residue was crystallized from light petroleum. Physical properties and spectral data of halotetramethylbenzyl chlorides and nitrates are given in Table 1.

Nitration of Halopentamethylbenzenes. Fuming nitric acid (d=1.50, 31.5 g) was added over a period of thirty minutes to a vigorously stirred solution of halotetramethylbenzene (0.1 mol) in methylene chloride (120 ml). During the reaction the temperature was kept at −5—0°C. The mixture was poured into water and the organic layer was washed with water and dilute sodium bicarbonate. Removal of the solvent left an oily solid which was identified as a mixture of halotetramethylbenzyl nitrates by infrared and PMR spectroscopy.