Nitration of Pentamethylnitrobenzene, Pentamethylbenzoic Acid and Its Methyl Ester, Pentamethylacetanilide, and Pentamethylphenol and Its Methyl Ether. Orienting Effect of the Substituents for the Side-chain Nitrooxylation[1]

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The nitration of a series of the titled pentamethylbenzene derivatives has been investigated in order to know the orienting effect of substituent groups for the side-chain nitrooxylation. The nitrooxylation was found to occur almost exclusively at the methyl groups adjacent to the electron-withdrawing substituents (NO_2, COOH, and $COOCH_3$), while with the compounds containing electron-donating groups (OH and OCH_3) the main reaction led to the conversion into cyclohexadienone, with the concomitant formation of small amounts of meta-nitrooxylated product. Pentamethylacetanilide underwent side-chain nitrooxylation along with some deacetylation. The location of the nitrooxymethyl group seems to be most likely ortho and meta, the latter being predominant.

Polyalkylated aromatic compounds often suffer side-chain substitution to give benzyl nitrates when they are treated with fuming nitric acid at low temperature. A particularly important feature of this unusual reaction is the peculier orientation and high positional selectivity. Nitration of pentamethylbenzene, for example, gives 2,3,4,5-tetramethylbenzyl nitrate as the major product,[2] while halopentamethylbenzenes yield comparable amounts of 5-halo-2,3,4,6-tetramethylbenzyl nitrate and 6-halo-2,3,4,5-tetramethylbenzyl nitrate.[3] Other isomeric products were never formed in any significant amounts. Such high positional selectivity seems to make this reaction an attractive pathway for the synthesis of the otherwise with difficulty accessible polysubstituted aromatic compounds, because the nitrooxymethyl group is known to be quite versatile for various transformations. To obtain a further information about the character of this reaction, especially the orienting effect of substituent groups, the action of fuming nitric acid upon pentamethylnitrobenzene (I), pentamethylbenzoic acid (II) and its methyl ester (III), pentamethylphenol (IV) and its methyl ether (V), and pentamethylacetanilide (VI) has been studied.

Pentamethylnitrobenzene (I) was comparatively stable towards nitric acid, and remained essentially unchanged under the conditions successfully employed for halopentamethylbenzenes. However, by treating with a large excess of fuming nitric acid at somewhat elevated temperature, it gave a light yellow half-crystalline solid with infrared bands characteristic of nitrobenzyl nitrates, at 876, 1277, 1535, and 1636 cm^{-1}. This was shown by TLC and PMR spectroscopy to contain five components, the principal of which was readily identified as 6-nitro-2,3,4,5-tetramethylbenzyl nitrate (VII) by the comparison of its infrared spectrum with that of an authentic specimen, prepared by the chloromethylation of 5-nitro-1,2,3,4-tetramethylbenzene and the subsequent treatment of the benzyl chloride with silver nitrate in acetonitrile. A close spectroscopic inspection confirmed the formation of some 5-nitro-2,3,4,6-tetramethylbenzyl nitrate (VIII, less than 5% of the total nitrate), but 4-nitro-2,3,5,6-tetramethylbenzyl nitrate (IX) could not be detected. The products were usually accompanied by some dinitroprehnitene. The anisotropic effect of the adjacent nitro group makes the methylene protons of VII to absorb considerably at high-field (4.68 τ) as compared to VIII (4.32 τ) and IX (4.30 τ). A minor peak at 4.70 τ which might arise from 6-nitro-2,3,4,5-tetramethylphenylnitromethane was also observed. VII could be isolated from the reaction mixture by chromatography on a short alumina column, followed by fractional crystallization from light petroleum. When refluxed with excess of dilute hydrochloric acid, the reaction product was converted into a light brown solid, from which 6-nitro-2,3,4,5-tetramethylbenzyl alcohol was obtained as a light yellow prisms.

An ortho-directing effect of electron-attracting groups for side-chain nitrooxylation was further evidenced by the nitration of pentamethylbenzoic acid (II) and its methyl ester (III). II was nitrated with fuming nitric acid in dichloromethane at 0—5°C to yield a white crystalline solid, TLC and PMR spectroscopy of which indicated that it was almost a single compound. Crystallization of the product from dichloromethane - light petroleum mixture gave white fine needles, mp 150—152°C, which had a molecular formula $C_{12}H_{15}NO_5$; PMR peaks at 7.66 (2 Me), 7.72 (2 Me), 4.38 (CH_2), and 2.28 τ (OH, broad); infrared bands at 863, 1272, 1617 (ONO_2), and 1685 cm^{-1} (COOH), consistent with it being a nitrooxymethyltetramethylbenzoic acid. A quite similar result was obtained by the nitration of III. The product was white needles, mp 104—105°C, with a composition $C_{13}H_{17}NO_5$; PMR peaks at 7.84 (Me), 7.77 (2 Me), 7.72 (Me), 6.16 (COOMe), and 4.60 τ (CH_2); infrared bands at 877, 1279, 1613 (ONO_2), 1193, and 1718 cm^{-1} (COOMe), and was readily formulated as methyl nitrooxymethyltetramethylbenzoate. When both products from II and III were heated with concentrated hydrochloric acid, it gave a light brown solid, from which the identical product was obtained as white needles in high yield. This compound, of formula $C_{12}H_{14}O_2$, exhibited PMR peaks at 7.78

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[1] The Reaction of Polysubstituted Aromatics. XX. Part XIX: H. Suzuki, This Bulletin, **43**, 3299 (1970).

[2] H. Suzuki and K. Nakamura, *ibid.*, **43**, 473 (1970).

[3] L. I. Smith and J. W. Horner, *J. Amer. Chem. Soc.*, **62**, 1349 (1940); H. Suzuki, This Bulletin, **43**, 481 (1970).

(Me), 7.70 (2 Me), 7.37 (Me), and 4.92 τ (CH_2); infrared bands at 1123, 1262, and 1735 cm^{-1} ($CO \cdot OCH_2$). No absorption due to hydroxyl group was observed. It did not dissolve into aqueous sodium hydrogen carbonate, but on prolonged heating with dilute sodium hydroxide it slowly went into solution and was again precipitated on acidification. From its mode of reaction and spectral data, therefore, the product was formulated as 3,4,5,6-tetramethylphthalide, the identity of which was further confirmed by preparing the authentic specimen in low yield from the condensation of chloromethyl methyl ether with 2,3,4,5-tetramethylbenzoic acid in the presence of anhydrous zinc chloride. When a methylol or chloromethyl group is located ortho to a carboxyl group, a loss of water or hydrogen chloride usually occurs to produce a phthalide.[4] Since the ortho relationship of carboxyl and methylol groups was established, the original nitrooxylated products were identified as 6-nitrooxymethyl-2,3,4,5-tetramethylbenzoic acid (X) and methyl 6-nitrooxymethyl-2,3,4,5-tetramethylbenzoate (XI), respectively. Further supporting evidence for the predominant ortho substitution was obtained by reducing the product mixtures with lithium aluminum hydride to bis-hydroxymethyl-tetramethylbenzenes, which, after conversion into bis-acetoxymethyl compound, was gas-chromatographed to prove 1,2-bis(acetoxymethyl)-3,4,5,6-tetramethylbenzene as the sole main product.

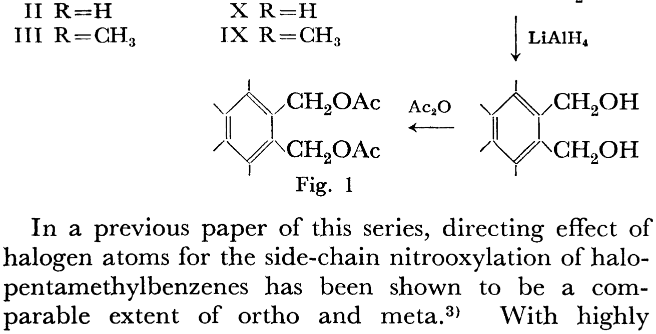

Fig. 1

In a previous paper of this series, directing effect of halogen atoms for the side-chain nitrooxylation of halopentamethylbenzenes has been shown to be a comparable extent of ortho and meta.[3] With highly electron-withdrawing nitro and carboxyl groups, the nitrooxylation was found to occur almost exclusively at ortho methyl groups. From the electronic points of view, therefore, the orientation exhibited by the electron-releasing groups is of special interest. Thus, pentamethylphenol (IV) and its methyl ether (V), and pentamethylacetanilide (VI) were treated with nitric acid. Since fuming nitric acid was found to react with these highly activated aromatic systems destructively under ordinary conditions,[5] the nitration was carried out cautiously in a very dilute methylene chloride solution at −10—−5°C with a limited reaction time. Both IV and V reacted actively with nitric acid to give light brown oil of almost identical composition. The methyl group bonded to the oxygen atom of V was completely cleaved during nitration. These products showed a very weak PMR peak at 4.79 τ (CH_2ONO_2) and infrared bands at 845, 1270, and 1630 cm^{-1} (ONO_2), indicating the formation of a benzyl nitrate only as a minor product. When stored at cool place, the syrupy product partly solidified to a sticky, half-crystalline mass, which could be separated into white prisms (mp 138—140°C) by fractional crystallization from light petroleum and diethyl ether. However, a considerable part of it was lost as a non-crystallizable syrup during recrystallization. The PMR spectrum of the carbon tetrachloride solution showed three methyl signals at 8.63, 8.16, and 7.96 τ of relative intensities 1 : 2 : 2. Its infrared spectrum contained strong bands for unsaturated ketones and hydroxyl group, at 1084, 1613, 1662, and 3390 cm^{-1}, and its ultraviolet spectrum produced a single intense band at 242 mμ ($\log \varepsilon = 4.20$) which is characteristic of cross-conjugated cyclohexadienones.[6] The analysis and spectral data are in agreement with the structure of 4-hydroxy-2,3,4,5,6-pentamethylcyclohexa-2,5-dienone, $C_{11}H_{16}O_2$. The isolation of hydroxycyclohexadienone and the numerous examples of parallel reactions of polysubstituted phenolic systems[7] are, therefore, consistent with the formulation of the major component of the original mixture as 4-nitro-2,3,4,5,6-pentamethylcyclohexa-2,5-dienone (XII). Trituration of the pasty mixture in cold ethanol gave small amounts of white powder, melting with decomposition up to *ca.* 260°C, which had an elemental analysis (C, 64.6; H, 7.4; N, 4.5%) and showed a complicated PMR spectral pattern. It was probably a secondary product from the cyclohexadienone and no further attempt was made to elucidate the structure.

In view of the supposed instability of 2- and 4-hydroxytetramethylbenzyl nitrates and their possible degradation product, quinomethide, the accumulation of these nitrates to any significant amount in the reaction mixture seems very unlikely.[8] Therefore, a small amount of benzyl nitrate found in the nitration product is probably 3-hydroxy isomer. With the aim to confirm this, attempts were made to prepare the authentic 3-hydroxy-2,4,5,6-tetramethylbenzyl nitrate (XIII) from the reaction of the corresponding benzyl chloride with silver nitrate in acetonitrile. The product was unfortunately a yellow to light brown syrupy mixture of several substances, although the nitrate appeared still to be the main component. Since the

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[4] C. A. Buehler, T. A. Powers, and J. G. Michels, *J. Amer. Chem. Soc.*, **66**, 417 (1944); C. A. Buehler, J. O. Harris, C. Shacklett, and B. P. Block, *ibid.*, **68**, 574 (1946); J. C. Overeen and G. J. M. van der Kerk, *Rec. Trav. Chim. Pays-Bas*, **83**, 1023 (1946).

[5] Kolka and Vogt claimed the unusual chemical stability of V, which was recovered according to their experiment after heating with fuming nitric acid and concentrated sulfuric acid for two hours on a water bath.[15] However, their V was recently proved to be 2,3,4,4,5,6-hexamethylcyclohexa-2,5-dienone.[16]

[6] H. H. Jaffé and M. Orchin, "Theory and Application of Ultraviolet Spectroscopy," Wiley, New York (1962), p. 204.

[7] G. M. Sharma and P. R. Burkholder, *Tetrahedron Lett.*, **1967**, 4147; D. H. R. Barton, A. K. Ganguly, R. H. Hesse, S. N. Loo, and M. M. Rechet, *Chem. Commun.*, **1968**, 806; G. Antinori, E. Baciocchi, and G. Illuminati, *J. Chem. Soc.*, *B*, **1969**, 373; J. C. Richer and A. Rossi, *Can. J. Chem.*, **47**, 3935 (1969).

[8] The synthesis and property of these polysubstituted benzyl nitrates will be described in detail in a later paper. For quinomethide, *cf.* A. B. Turner, *Quart. Rev.* (London), **28**, 347 (1964).

amount was very small, the identity of this nitrooxy compound was inferred by indirect means of spectral comparison of the product mixture with the above impure reference compound. It revealed, in fact, that all the major peaks belonging to the impure XIII were contained in the spectra of the nitration products from IV and V. When the syrupy product from IV was treated with cold concentrated hydrochloric acid for some days, a pale yellow pasty solid was obtained, PMR spectrum of which showed several new prominent peaks in the methylene protons region (4.32, 4.72, and 5.25 τ).

Pentamethylacetanilide (VI) underwent the nitration under similar condition much more smoothly than did IV and V. A light brown gummy product with ordor of acetic acid showed prominent PMR peaks due to $-CH_2ONO_2$ at 4.48 and 4.43 τ; infrared bands at 876, 1280, 1613 (ONO_2), 1645 (CONH), and 3220 cm^{-1} (NH), indicating the formation of benzyl nitrate and the partial deacetylation. Several crystallization of the product from dichloromethane - light petroleum mixture gave the major component as white needles, which was identified by analysis, infrared and PMR spectroscopy as a nitrooxymethyltetramethylacetanilide. The minor nitrate with the benzylic protons signal at lower field of 4.43 τ could not be isolated. Because of the difficulty involved in the preparation of the authentic samples, a firm structural assignment for these nitrooxy compounds has not been made yet. However, it is expected that the acetamido group will exhibit anisotropic deshielding effect on the benzylic protons at the ortho positions, but will exert a net shielding effect on these at meta and para positions. Considering the appearance of the methylene protons signal of the minor nitrate at lower field, the orientation of these nitrate seems most likely to be ortho and meta substituted, the latter outweighing the former in its amount.

The nitration of acetanilides has been known to involve the interaction of *p*- or π-electron on nitrogen or carbonyl oxygen with the nitrating species, leading to the formation of XIV as the most readily accessible σ-complex (Fig. 2). The observed partial deacetylation would probably arise from such interaction. When this special effect was superimposed with ordinary ortho and para activating and somewhat meta deactivating effect of acetamido group, the most favored intermediates will be ions XIV and XV, which, according to the previously suggested cyclic process for side-chain nitrooxylation,[2)] will form the meta substituted nitrate as the most preferred isomeride. The minor nitrate is probably ortho-substituted and would be derived from the less important contributor XVI (Fig. 2), in which the preferred proton release will occur from the methyl groups adjacent to the acetamido group ($X=NHCOCH_3$), because the protons of these groups are more positively polarized and the transition state for the migration of the nitro group to the neighboring side-chain will be stabilized more effectively, as in XVII (Fig. 3), through the electron supply from the methyl group meta to the attacking site as well as through the polar interaction between the *p*-electrons on carbonyl oxygen and the leaving hydrogen atom. In the case of para substitution, the conjugative electron release from the acetamido group is greatly disturbed by the methyl groups on both sides, and so the former group will act in an opposite way during the electron-redistribution, by increasing the electron deficit at the attacking site and thus rendering the departure of the nitro group with its unshared electron pair more difficult, as depicted in XVIII (Fig. 3). In view of the almost exclusive ortho substitution for I, II and III, and a comparable extent of ortho and meta substitution for halopentamethylbenzenes, this interpretation seems quite reasonable.

Predominant ortho directing effect of nitro, carboxyl and methoxyl groups probably involves a similar mechanism. Strongly electron-attracting nitro group or carboxyl group will direct the entering nitronium ion at the meta position to yield the benzenonium ion XVI ($X=NO_2$ or COOH) as the most stable intermediate species, which has three methyl groups at the most favorable position to delocalize the positive charge. Methyl protons next to the nitro or carboxyl group are subject to the further activation due to the nitronium ion introduced at the another neighboring position. Hyperconjugative proton release from this highly activated methyl group, followed by the migration of the nitro group to this side-chain according to the outlined sequence will result in the expected ortho-substitution (Figs. 2 and 3).

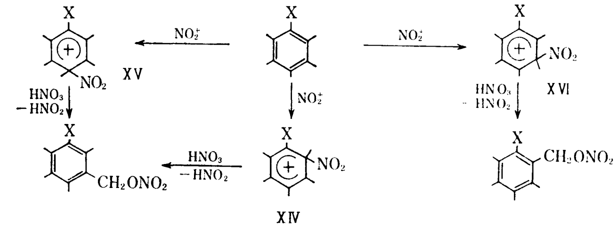

Fig. 2

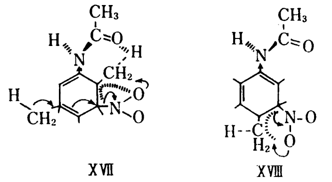

Fig. 3

A small amount of meta-substituted product would arise from the less stabilized ion XIV, in which only two methyl groups can contribute to the stabilization.

The methoxyl cleavage and subsequent meta-nitrooxylation observed in the nitration of pentamethylanisole (V) may be rationalized on a similar basis:

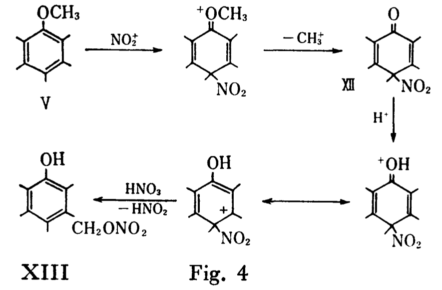

Fig. 4

Initial step of the reaction would be the attachment of nitro group at 4-position, and the methyl group is rapidly cleaved from the oxygen atom to form a dienone XII, which will be partly protonated on the oxygen atom to give the hydroxybenzenonium ion and then transformed into meta-substituted benzyl nitrate XIII (Fig. 4).

Experimental

Melting points were determined on a hot stage apparatus and were uncorrected. Infrared spectra were measured with a KBr disc on a Jasco DS-402 G spectrophotometer, and ultraviolet spectra were recorded in methanol solution with a Shimadzu QV-50 spectrophotometer. PMR spectra were obtained in carbon tetrachloride and deuteriochloroform with a Varian A-60A spectrometer and with a Jeolco 3H-60 spectrometer against internal TMS.

Materials. Pentamethylnitrobenzene (I, mp 158—159°C),[2] pentamethylbenzoic acid (II, mp 210—211°C) and its methyl ester (III, mp 68—69°C),[9,10] and pentamethylacetanilide (VI, mp 212—214°C)[11] were prepared as described in the literatures.

Most of the previously reported synthetic methods for pentamethylphenol (IV) were found to be not entirely satisfactory as a simple laboratory procedure, owing to a difficult access for the material, low yield, or the laborious procedure involved in the synthesis and purification processes.[11,12] A simple and rapid synthesis of pure IV (mp 126—128°C) was accomplished by reducing 3,5-bis(chloromethyl)-2,4,6-trimethylphenol,[13] readily prepared from mesitol by chloromethylation in acetic acid, with lithium aluminum hydride in anhydrous tetrahydrofuran, followed by the purification through steam-distillation. *O*-Methylation of IV required quite long time and was still incomplete.

Pentamethylanisole (V, mp 62—63°C)[14] was similarly prepared by the reduction of the bischloromethylation product from 2,4,5-trimethylanisole. Direct methylation of anisole with boron trifluoride - methanol complex according to the Kolka and Vogt's procedure[15] was found unsatisfactory since the major product of the reaction was not the expected V, but the 2,3,4,4,5,6-hexamethylcyclohexa-2,5-dienone,[16] although some V could be isolated from the reaction mixture. The reaction could hardly be controlled to stop at the stage of pentamethylation, and it always went too far to yield the dienone as the final stable product.

Tetramethylbenzyl nitrates used as a reference compound were prepared in 70—85% yield by treating the corresponding benzyl chlorides[17] with silver nitrate in acetonitrile, and recrystallized from *n*-hexane.

6-Nitro-2,3,4,5-tetramethylbenzyl Nitrate (VII): mp 102—103°C. IR, 707, 758, 842, 876, 974, 1277 (ONO_2), 1535 (NO_2), and 1637 cm^{-1} (ONO_2); PMR, 7.84 (Me), 7.72 (2 Me), 7.67 (Me), and 4.68 τ (CH_2).

Found: C, 52.0; H, 5.8%. Calcd for $C_{11}H_{14}N_2O_5$: C, 52.0; H, 5.6%.

5-Nitro-2,3,4,6-tetramethylbenzyl Nitrate (VIII): mp, 132—134°C. IR, 705, 756, 838, 871, 967, 1281 (ONO_2), 1528 (NO_2), and 1638 cm^{-1} (ONO_2); PMR, 7.67 (Me), 7.58 (2 Me), 7.50 (Me), and 4.32 τ (CH_2).

Found: C, 52.0; H, 5.6%. Calcd for $C_{11}H_{14}N_2O_5$: C, 52.0; H, 5.6%.

4-Nitro-2,3,5,6-tetramethylbenzyl Nitrate (IX): mp, 157—158°. IR, 713, 757, 848, 867, 966, 1274 (ONO_2), 1531 (NO_2), and 1633 cm^{-1} (ONO_2); PMR, 7.76 (2 Me), 7.55 (2 Me), and 4.30 τ (CH_2).

Found: C, 52.2; H, 5.6%. Calcd for $C_{11}H_{14}N_2O_5$: C, 52.0; H, 5.6%.

Bis(acetoxymethyl)tetramethylbenzenes were obtaind in 80—90% yield from the bis(chloromethyl)tetramethylbenzenes[18] by treatment with silver acetate in gently refluxing glacial acetic acid, and crystallized from ethanol.

1,2-Bis(acetoxymethyl)-3,4,5,6-tetramethylbenzene: mp, 117—118°C. IR, 906, 954, 1025, 1235 (CO·O, broad), and 1731 cm^{-1} (CO·O); PMR, 7.94 (O·$COCH_3$), 7.68 (Me), 7.65 (Me), and 4.67 τ (CH_2).

Found: C, 69.2; H, 8.2%. Calcd for $C_{16}H_{22}O_4$: C, 69.1; H, 8.0%.

1,3-Bis(acetoxymethyl)-2,4,5,6-tetramethylbenzene: mp, 114—115°C. IR, 912, 958, 979, 1031, 1243 (CO·O, broad), and 1731 cm^{-1} (CO·O); PMR, 7.93 (O·$COCH_3$), 7.68 (Me), 7.62 (2 Me), 7.55 (Me), and 4.82 τ (CH_2).

Found: C, 69.0; H, 8.1%. Calcd for $C_{16}H_{22}O_4$: C, 69.1; H, 8.0%.

1,4-Bis(acetoxymethyl)-2,3,5,6-tetramethylbenzene: mp, 191—192°C. IR, 917, 962, 1027, 1239 (CO·O, broad), and 1732 cm^{-1} (CO·O); PMR, 7.81 (O·$COCH_3$), 7.52 (Me), and 4.68 τ (CH_2).

Procedure for Nitration of Pentamethylnitrobenzene (I), Pentamethylbenzoic Acid (II) and Methyl Pentamethylbenzoate (III). Fuming nitric acid (d=1.50, 6.3 g) was added over a period of 30 min to a vigorously stirred solution of II (3.8 g) or III (4.1 g) in dichloromethane (30 m*l*). During the addition, the temperature of the system was kept at −5—0°C. Since I (3.9 g) was recovered mostly unchanged under the same condition, it was treated with a large excess of fuming nitric acid (12.6 g) in dichloromethane (20 m*l*) at somewhat elevated temperature (30—32°C). The mixture was poured into water and the organic layer was washed thoroughly with water. Removal of the solvent left a solid, which was directly subjected to the infrared and PMR spectral determinations.

The nitration product from I showed PMR peaks at 7.76, 7.73, 7.68, and 4.68 τ along with a minor peak at 4.70 τ; infrared bands at 708, 760, 878, 976, 1277, 1535, and 1636 cm^{-1}. On hydrolysis with hydrochloric acid and subsequent recrystallization from ligroin, it gave 6-nitro-2,3,4,5-tetramethylbenzyl alcohol as light yellow prisms, mp 175—176°C. The same compound was obtained from the unsuccessful

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[9] H. Suzuki, *Nippon Kagaku Zasshi*, **91**, 179 (1970).

[10] H. Suzuki, *ibid.*, **91**, 484 (1970).

[11] A. W. Hofmann, *Ber.*, **18**, 1821 (1885).

[12] O. H. Hey, *J. Chem. Soc.*, **1931**, 1581; R. W. Cripps and O. H. Hey, *ibid.*, **1943**, 14; D. E. Winkler and S. A. Ballard, U. S. 2440036, 2448942 (1948); A. Burawoy and J. T. Chamberlain, *J. Chem. Soc.*, **1944**, 624, 626; B. R. M. Monnenberg, A. Ova, and U. Lehmuskoskii, *Paperi ja Puu*, **35**, 8 (1953); *Svensk Paperstidn.*, **56**, 46 (1954); B. R. M. Monnenberg, Swed. 145389 (1953); N. P. Buu-Hoï, G. Lejeune, and M. Sy, *Compt. Rend.*, **240**, 224 (1955); B. V. Gregorovich, K. S. Y. Liang, D. M. Clugston, and S. F. MacDonald, *Can. J. Chem.*, **46**, 3291 (1968).

[13] R. Wegler and E. Regel, *Makromol. Chem.*, **9**, 1 (1952).

[14] G. Vavon, J. Bolle, and J. Calin, *Bull. Soc., Chim. Fr.*, **6**, 1025 (1939).

[15] A. J. Kolka and R. R. Vogt, *J. Amer. Chem. Soc.*, **61**, 1463 (1939).

[16] H. Hart and O. W. Swatton, *ibid.*, **89**, 1874 (1967); B. I. Mokrousov, P. Adomenas, and V. A. Koptyug, *Zh. Org. Khim.*, **3**, 2255 (1967).

[17] H. Suzuki, This Bulletin, **43**, 3299 (1970).

[18] M. J. Rhoad and P. J. Flory, *J. Amer. Chem. Soc.*, **72**, 2216 (1950); M. S. Newman, J. R. LeBlanc, H. A. Karnes, and G. Axelrad, *ibid.*, **86**, 868 (1964).

synthesis of 6-nitro-2,3,4,5-tetramethylphenylnitromethane by treating 6-nitro-2,3,4,5-tetramethylbenzyl chloride with silver nitrite in acetonitrile. PMR, 7.78 (Me), 7.68 (2 Me), 7.56 (Me), and 5.59 τ (CH_2).

Found: C, 63.0; H, 7.3%. Calcd for $C_{11}H_{15}NO_3$: C, 63.2; H, 7.2%.

The yields of crude products from the nitration of II and III were 70—80% and a single crystallization was usually enough to purify them.

6-Nitrooxymethyl-2,3,4,5-tetramethylbenzoic Acid: mp, 150—152°C.

Found: C, 57.2; H, 5.9; N, 5.3%. Calcd for $C_{12}H_{15}NO_5$: C, 56.9; H, 6.0; N, 5.5%.

Methyl 6-Nitrooxymethyl-2,3,4,5-tetramethylbenzoate: mp, 104—105°C.

Found: C, 58.3; H, 6.6%. Calcd for $C_{13}H_{17}NO_5$: C, 58.4; H, 6.4%.

3,4,5,6-Tetramethylphthalide: mp, 233—235°C.

Found: C, 75.5; H, 7.1%. Calcd for $C_{12}H_{14}O_2$: C, 75.8; H, 7.4%.

Procedure for Nitration of Pentamethylphenol (IV), Pentamethylanisole (V) and Pentamethylacetanilide (VI). A solution of fuming nitric acid (d=1.50, 2.0 g) in dichloromethane (10 m*l*) was added dropwise to a magnetically stirred solution of IV (3.3 g) or V (3.6 g) in the same solvent (25 m*l*) over a period of 20 min. The temperature was cautiously kept at -10—-5°C during the addition. The solution rapidly yellowed, and the color intensified to orange to light brown. VI (4.1 g) reacted less vigorously under the same condition. After the end of the addition, the mixture was diluted with water and the organic part was thoroughly washed with water. After drying over anhydrous sodium sulfate, the solvent was evaporated to give a yellow syrup or a light brown pasty cake, on which infrared, ultraviolet and PMR spectroscopic inspections were performed.

The nitration products (*ca.* 3.5—3.8 g) from IV and V both showed almost identical infrared and PMR spectral pattern. IR: 852, 1002, 1024, 1083, 1272, 1340, 1374, 1445, 1540—1550, 1617—1635, and 1735 cm^{-1}; PMR, 8.79, 8.69, 8.66, 8.88—8.30, 6.58, 5.40, and 4.79 τ. When the syrupy product was dissolved in a minimum amount of light petroleum - ether mixture and set aside in a refrigerator for weeks, it slowly separated crystalline solid of wide melting range (70—90°C), which was purified through fractional crystallization from a mixture of light petroleum and ether to give white prisms (mp 138—140°C) and was formulated as 4-hydroxy-2,3,4,5,6-pentamethylcyclohexa-2,5-dienone on the basis of analysis, infrared, ultraviolet and PMR spectral data.

Found: C, 72.4; H, 8.9%. Calcd for $C_{11}H_{16}O_2$: C, 73.3; H, 8.9%.

A white powder obtained from the above syrup by trituration in cold ethanol melted at up to 260°C with decomposition. It showed infrared bands at 1020, 1074, 1345, 1372, 1540—1545, 1630, and 3420 cm^{-1}, and PMR peaks at 8.79, 8.61, 7.90—8.20 (complicated multiplet), and 6.52 τ.

Found: C, 64.6; H, 7.4, N, 4.5%.

The nitration product (*ca.* 4.2 g) from VI exhibited PMR peaks at 8.73, 8.31, 7.97, 7.86—7.67, 4.48, and 4.43 τ; IR bands at 876, 1280, 1365—1380, 1510, 1613, 1645, 1725, 2900, and 3218 cm^{-1}. Upon crystallization from a mixture of light petroleum and methylene chloride, it gave a nitrooxymethyltetramethylacetanilide, mp 126—127°C, which had PMR peaks at 7.83 (Me), 7.75 (3 Me), 7.66 (COMe), and 4.45 τ (CH_2); IR bands at 877 (ONO_2), 1282 (ONO_2), 1368, 1382, 1613 (ONO_2), 1685 (COMe), and 3220 cm^{-1} (NH).

Found: C, 58.4; H, 7.0; N, 10.3%. Calcd for $C_{12}H_{17}NO_4$: C, 58.6; H, 6.8; N, 10.5%.