Reaction of Tetrachloroxylenes with Fuming Nitric Acid.[1] Side-chain Nitrooxylation and Quinol Nitrate Formation

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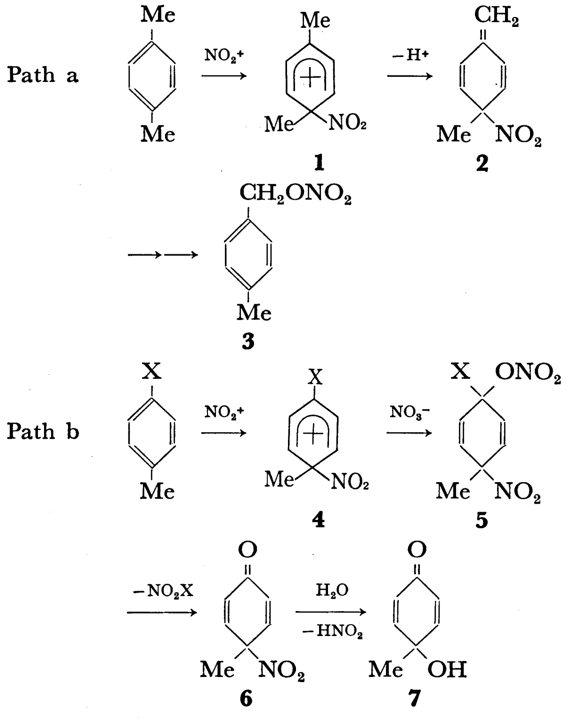
Direct action of fuming nitric acid upon tetrachloro-*o*- and -*m*-xylenes at room temperatur led to the formation of 3,5,6-trichloro-1,2-dimethyl-4-oxocyclohexa-2,5-dienyl nitrate and 2,5,6-trichloro-1,3-dimethyl-4-oxocyclohexa-2,5-dienyl nitrate, respectively, as the major products. In contrast, tetrachloro-*p*-xylene was simply converted into 2,3,5,6-tetrachloro-4-methylbenzyl nitrate. Plausible reaction sequences as well as criteria as a basis for predicting the propensity of polysubstituted alkylaromatics towards unusual nitration have been discussed.

Action of nitrating agent upon lightly substituted alkylbenzenes usually results in the replacement of one of the ring hydrogen atoms by nitro group. The increase in number of alkyl groups, however, tends to divert the reaction from the normal course into branch pathways leading to the production of unexpected products.[2] The most typical of these anomalous nitrations are the side-chain nitrooxylation (path a) and oxidation to unsaturated cyclic ketones (path b).

With substituted polymethylbenzenes these two processes are often in competition and as far as the substrate contains two methyl groups in *para* relationship, preference for the side-chain substitution dominates. We have previously suggested that the dichotomy of the reaction would presumably be determined by the structure of a benzenium ion intermediate;[3]

i) If the ion has the structure **1** in which the nitro group is attached to the nuclear carbon atom bearing a methyl group which is *para* to another methyl group, proton release would occur from the latter group to give a nitromethylene cyclohexadiene (**2**) which could be transformed into benzyl nitrate (**3**) (path a).

ii) If the ion has the structure **4** in which the nitro group is attached to the ring carbon atom bearing a methyl group which is *para* to a halogen atom, capture of the nitrate ion by the halogen-bearing carbon would occur to give an addition product (**5**), which will then be converted to the unsaturated carbonyl compound (**6**), usually isolated as *p*-quinol (**7**) (path b).



Scheme 1.

In order to test the reliability of the above criteria as a basis for predicting the propensity of polysubstituted alkylaromatics towards unusual nitration, as well as to obtain further insight into factors involved in the competition between side-chain substitution and nuclear oxidation, our studies were extended to the reaction of tetrachloroxylenes with fuming nitric acid.

A suspension of tetrachloro-*o*-xylene (**8**) in cold fuming nitric acid ($d=1.50$) was set aside with stirring overnight. **8** disappeared slowly to give a clear light brown solution which, on pouring into excess of water, gave a good yield of a pale yellow solid. Chromatography of the product on deactivated alumina resulted in the separation of some unchanged material and two new crystalline compounds melting at 166—167 °C and 145—146 °C, respectively. The high-melting compound had the formula $C_8H_7Cl_3O_2$ and showed mass peaks at *m/e* 240 (M^+), 225 (M^+-Me), and 205 (M^+-Cl). Proton NMR spectrum showed two methyl singlets at δ 1.68 and 2.32 and one hydroxyl peak at *ca.* 2.6 ppm (broad, exchangeable with D_2O). Its infrared spectrum contained carbonyl absorption at 1680 cm^{-1}, carbon-carbon double bond absorptions at 1637 and 1600 cm^{-1}, and hydroxyl absorption at 3400—3200 cm^{-1}, suggesting a cross-conjugated hydroxyketone. Its ultraviolet spectrum exhibited absorption maxima at 251—252 ($\log \varepsilon=4.08$) and 291—292 nm ($\log \varepsilon=3.33$) characteristic of a 2,5-cyclohexadienone system. Thus, the structure of dienone could be either 3,5,6-trichloro-1,2-dimethyl-4-oxocyclohexa-2,5-dienol (**12**) or 2,5,6-trichloro-1,3-dimethyl-4-oxocyclohexa-2,5-dienol (**19**). An unequivocal structure assignment to **12** was obtained by the zinc-acetic acid reduction of the ketone, which resulted in the isolation of a good yield of 2,5,6-trichloro-3,4-xylenol (**15**). The identity of the latter was confirmed by the independent synthesis starting with 3,4-xylenol according to the sequence shown in Scheme 2.[4]

The low-melting product had the formula $C_8H_6Cl_3NO_4$ and showed mass peaks at *m/e* 285 (M^+), 239 (M^+-NO_2), 223 (M^+-NO_3), and 221 (M^+-NO_2-CO). Its infrared spectrum showed prominent bands at 1683 (CO), 1646 (ONO_2), 1600 (C=C), 1292 (ONO_2), 1188, 1140, and 1042 cm^{-1}. The proton NMR spectrum displayed two methyl singlets at δ 1.71 and 2.27 ppm. The ultraviolet spectral pattern with maxima at 254—255 (log ε=4.05) and 286—290 nm (log ε=3.44) was typical of a 2,5-cyclohexadienone system. Given the presence of a cross-conjugated cyclohexadienone skeleton, two methyl groups, three chlorine atoms, and a nitrooxyl group, we could write twenty possible structures, nineteen of which, however, could readily be eliminated on the following chemical and spectral grounds:

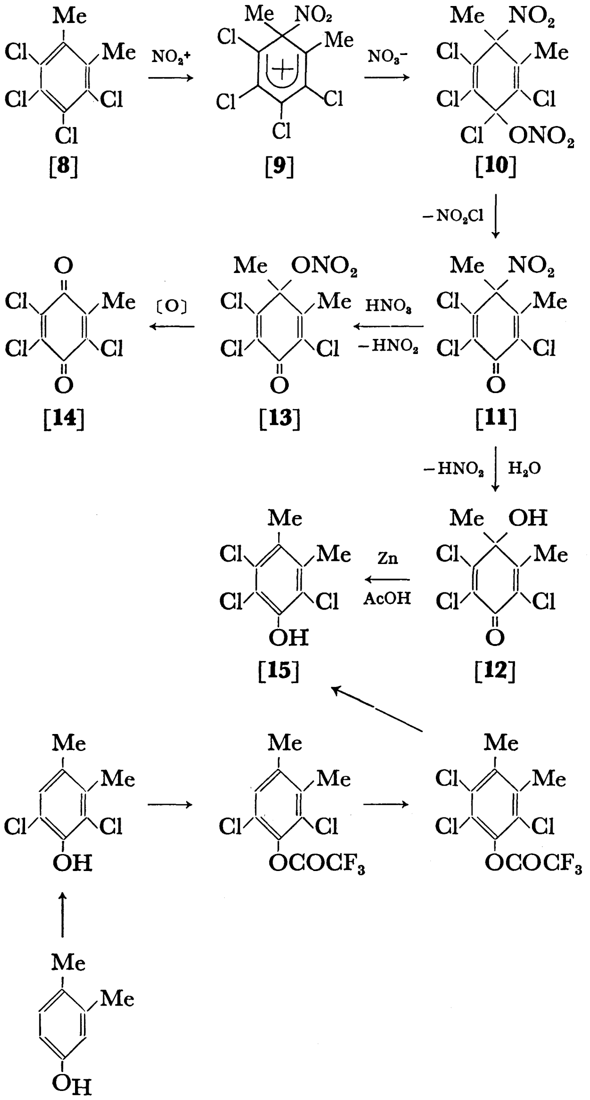
1) Two methyl groups are magnetically non-equivalent.

2) Ring carbon atom bearing geminal chlorine atom and nitrooxyl group would be converted into carbonyl group.

3) Chlorine atoms are unable to undergo the intramolecular migration during the course of nitration.

4) Nitrooxyl group placed on a double bond would be subject to a facile nitrogen-oxygen single bond fission in protic acid medium.

5) When dissolved into nitric acid, **12** was converted into this nitrooxyl compound, which on prolonged contact with the nitrating agent was further converted into trichloro-*p*-toluquinone (**14**). These leave the structure 3,5,6-trichloro-1,2-dimethyl-4-oxocyclohexa-2,5-dienyl nitrate (**13**).



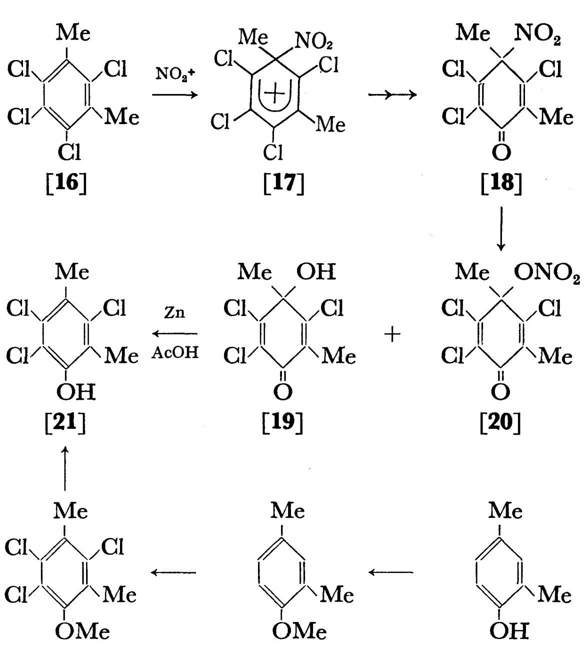
Scheme 2.

When the reaction mixture was quenched immediately after the dissolution of **8** in cold nitric acid, a yellow crystalline solid was obtained. Since this product showed infrared bands at 1690, 1610, and 1570 cm^{-1} and proton NMR peaks at δ 2.10 and 2.19 ppm, and since it gradually converted to **12** and other unidentified substances on standing, it was assigned the structure 2,5,6-trichloro-3,4-dimethyl-4-nitrocyclohexa-2,5-dienone (**11**).

A plausible mechanism to account for the formation of **12** and **13** is outlined in Scheme 2. In this mechanism an electrophilic attack on the methyl-bearing carbon by nitronium ion results in the formation of benzenium ion (**9**) which would take up nitrate anion to form addition product (**10**), from which nitryl chloride is eliminated to yield ketone **11**. The nitro group on the doubly activated allylic carbon atom undergoes a facile solvolytic replacement, yielding **13** as the major product. Minor amount of **12** would arise from the hydrolysis of **11** during aqueous work-up. The possibility of some secondary reactions occurring on the alumina column during elution is excluded since **12** and **13** are also obtained directly from the reaction product by fractional crystallization from ethanol.

A similar treatment of tetrachloro-*m*-xylene (**16**) with nitric acid resulted in the formation of a mixture of two carbonyl compounds **19** and **20** melting at 151—152 °C and 135—136 °C, respectively. Elemental analysis and molecular weight determination revealed that **19** is isomeric with **12** and **20** is isomeric with **13**. The high-melting ketone was uniquely established as 2,5,6-trichloro-1,3-dimethyl-4-oxocyclohexa-2,5-dienol (**19**), since the alternative structure **12** had been assigned to the isomeric product from **8**.

The low-melting ketone with a formula $C_8H_6Cl_3NO_4$ (*m/e*, 285 (M^+)) exhibited two methyl singlet peaks

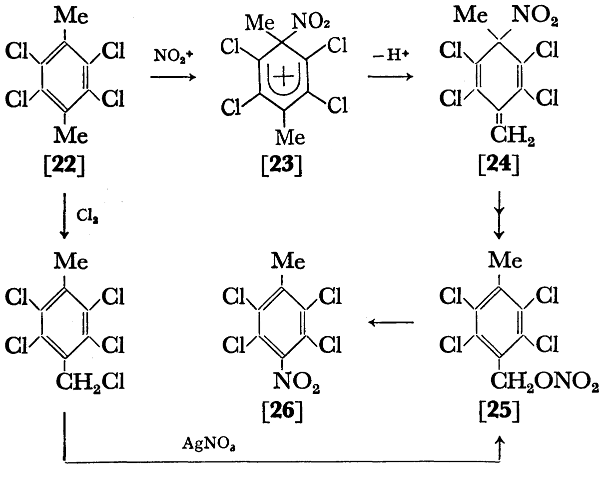


Scheme 3.

at δ 1.66 and 2.16 ppm. Its infrared spectrum showed absorptions at 1650, 1604, 1296, 1169, and 1051 cm^{-1}, and its ultraviolet spectrum with maxima at 255 (log ε=4.15) and 289—290 nm (log ε=3.46) indicated the presence of a 2,5-cyclohexadienone structure. Thus, the ketone is presumed to be a trichlorodimethyl-4-oxocyclohexa-2,5-dienyl nitrate and a similar consideration made for **13** allowed for **20** the structure 2,5,6-trichloro-1,3-dimethyl-4-oxocyclohexa-2,5-dienyl nitrate possible. Conclusive proof that the low-melting ketone has structure **20** was obtained through its transformation into 3,5,6-trichloro-2,4-xylenol (**21**) and comparing melting point, infrared spectrum and proton NMR spectrum of the latter with those of the authentic specimen prepared from 2,4-xylenol according to the sequence shown in Scheme 3.[4)]

When the reaction mixture was worked up several minutes after mixing the reactants at room temperature, the predominant constituent of the product was an unstable nitroketone (**18**) which, however, could not be separated in pure form.

Tetrachloro-*p*-xylene (**22**) was treated with excess of nitric acid at room temperature to give a single clean product, which was isolated in 82% yield and identified as 4-methyl-2,3,5,6-tetrachlorobenzyl nitrate (**25**) by comparison with the authentic specimen. When the reaction mixture was allowed to stand for several weeks, initial product **25** was completely converted into 4-nitro-2,3,5,6-tetrachlorotoluene (**26**). Scheme 4 outlines the pathway from **22** to **26**. Attack on **22** by nitronium would result in the formation of a benzenium ion **23**, which would be converted to the expected nitrate **25** *via* diene **24**.



Scheme 4.

The presence of a pair of methyl group in *para* relationship is critical for the facile formation of benzyl nitrates. **22** with a pair of *para* methyl groups undergoes side-chain nitrooxylation to form benzyl nitarte **25**, whereas **8** and **16** both bearing no paired methyl groups in *para* positions undergo only nuclear oxidation to give unsaturated cyclic carbonyl compounds **12** and **13**, or **19** and **20**, respectively. No side-chain substitution was observed with the latter two substrates. Thus, the present results serve to reinforce the previous suggestion and augment the applicability of the above-mentioned guides *i* and *ii* as a basis for foreseeing the predisposition of substituted polyalkylaromatics towards the unusual nitration: electrophilic attack of the nitronium ion on three isomeric tetrachloroxylenes **8**, **16**, and **22** will lead to the formation of benzenium ions **9**, **17**, and **23**, respectively. Ion **23** satisfies the requirement *i* to follow the path a, giving the side-chain substitution product, while ions **9** and **17** comply with the requirement *ii* to follow the addition-elimination sequence (path b), resulting in the formation of unsaturated cyclic ketones. Our result, in addition to its mechanistic interest, provides a novel method for the synthesis of quinol nitrates. Further works to extend the method as an easy entry to quinols and related compounds are now in progress.

Experimental

All melting points were determined on a hot-stage apparatus and are uncorrected. Infrared spectra were obtained in Nujol mulls with a Jasco 402G spectrophotometer. Ultraviolet spectra were recorded in methanol on a Shimadzu QV-50 spectrophotometer. Proton NMR spectra were taken using a Varian T-60 instrument. All measurements were made on 5—10% deuteriochloroform solutions using TMS as an internal reference at probe temperature. Mass spectra were obtained on a Hitachi RMS-4 spectrometer.

Three tetrachloroxylene isomers were prepared by the chlorination of the corresponding hydrocarbons and purified through alumina chromatography.

Procedure for the Nitration of Tetrachloroxylenes. The procedures used for tetrachloro-*o*-xylene (**8**) and tetrachloro-*m*-xylene (**16**) were essentially the same and the only one experiment shall be reported here.

A suspension of **8** (10.0 g, 0.41 mol) in nitric acid (d=1.5, 130 g) was stirred at room temperature for 10 hr. The solid gradually dissolved giving a clear dark brown solution, which was then quenched by pouring into a large excess of ice water. The pale yellow solid precipitate (7.46 g) was collected by filtration, washed with dilute aqueous sodium hydrogen carbonate, and sucked as dry as possible. Aqueous washings were combined and extracted three times with ether and the extract was evaporated to give crude **12** (0.96 g) as pale yellow solid. A part of the product (1.0 g) was placed on the top of alumina column (deactivated by 10% acetic acid) and eluted with light petroleum to give **13** (0.33 g, 33%) as white needles, mp 145—146 °C with decomposition.

Found: C, 33.73; H, 2.05; N, 4.92; O, 22.14; Cl, 36.91%. Calcd for $C_8H_6Cl_3NO_4$: C, 33.54; H, 2.11; N, 4.89; O, 22.34; Cl, 37.12%.

Further elution with light petroleum containing benzene yielded **12** (0.39 g, 33%), which was recrystallized from ethanol to give white prisms, mp 166—167 °C.

Found: C, 40.07; H, 2.91%. Calcd for $C_8H_7Cl_3O_2$: C, 39.79; H, 2.92%.

Direct crystallization of the crude product mixture (3.25 g; air-dried for several weeks) from ethanol gave pure **13** (0.84 g). When a solution of **8** (0.63 g) in cold nitric acid (20 ml) was diluted with water immediately after complete dissolution, nitroketone **11** was obtained as pale yellow precipitate (0.34 g), mp 64—66 °C, which gradually decomposed to **12** and other unidentified substances. Its elemental analysis was not satisfactory.

Found: C, 33.07; H, 2.09; N, 4.90%. Calcd for $C_8H_6Cl_3NO_3$: C, 35.52; H, 2.24; N, 5.18%.

Similar treatment of **16** gave a mixture of several carbonyl compounds, the major components being **19** and **20**, although yields were lower under comparable conditions (20—30 and 15—24%, respectively).

19: mp 151—152 °C. ^{1}H NMR: δ 1.63 (s, 3H), 2.12 (s, 3H), and *ca.* 2.8 ppm (broad, 1H, exchangeable with D_2O); IR: 3400—3200, 1673, 1643, 1606, 1168, and 1070 cm^{-1}; UV: 249—251 (log ε=4.36) and 286—287 nm (log ε=3.75); Mass: *m/e* 240 (M^+), 225 ($M^+ - Me$), and 205 ($M^+ - Cl$).

Found: C, 39.62; H, 2.83%. Calcd for $C_8H_7Cl_3O_2$: C, 39.79; H, 2.92%.

20: mp 135—136 °C. Mass: *m/e* 285 (M^+), 239 ($M^+ - NO_2$), and 223 ($M^+ - ONO_2$).

Found: C, 33.84; H, 2.20; N, 4.59%. Calcd for $C_8H_6Cl_3NO_4$: C, 33.54; H, 2.11; N, 4.89%.

When the reaction mixture was diluted with water several minutes after mixing the reactants, there resulted a precipitate, mp 69—71 °C, which showed infrared bands at 1670, 1605, and 1570 cm^{-1} and proton NMR peaks at δ 2.15 and 2.19 ppm. These features are in line with the structure **18**, but attempt to obtain the ketone in pure form failed. On standing **18** gradually decomposed to **19** and other unidentified substances.

A suspension of tetrachloro-*p*-xylene (**22**; 0.51 g, 0.0021 mol) in nitric acid (13 g) was allowed to stand with stirring overnight. The dark mixture was poured into ice water and the precipitated solid was filtered off, washed with aqueous sodium hydrogen carbonate, and dried. The crude product (0.64 g; mp 69—72 °C) was recrystallized from ethanol to give **25** as white leaflets, mp 80—82 °C. Yield, 0.523 g (82%). IR: 1649, 1620, and 1276 cm^{-1}; ^{1}H NMR; δ 2.67 (s, 3H) and 5.85 ppm (s, 2H).

Found: C, 31.72; H, 1.63; N, 4.65%. Calcd for $C_8H_5Cl_4NO_3$: C, 31.51; H, 1.65; N, 4.59%.

When the reaction mixture was left to stand at room temperature for several weeks, the usual work-up followed by crystallization of the solid precipitate from ethanol gave 4-nitro-2,3,5,6-tetrachlorotoluene as the sole significant product. Mp 156—159 °C. The product was identical with an authentic specimen.[5]

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