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Products from the Reaction of Dinitrotetramethylbenzenes with Fuming Nitric Acid. A New Route to Some Polynitro Carbonyl Compounds[1]

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Reaction of dinitrotetramethylbenzenes with fuming nitric acid has been investigated. 5,6-Dinitro-1,2,3,4-tetramethylbenzene undergoes a slow oxidation to give 2,3,4,5-tetranitro-2,3,6,6-tetramethylcyclohex-4-enone in 82—87% yield, which is thermally unstable and upon heating readily converted into 4,5-dinitro-2,3,6,6-tetramethylcyclohexa-2,4-dienone losing two molecules of nitrogen dioxide. 4,6-Dinitro-1,2,3,5-tetramethylbenzene reacts readily with cold fuming nitric acid, giving 2,6-dinitro-3,4,5-trimethylbenzaldehyde in 76—84% yield, together with small amounts of 2,6-dinitro-3,4,5-trimethylphenylnitromethane, 2,6-dinitro-3,4,5-trimethylbenzoic acid, and 2,6-dinitro-3,4,5-trimethylbenzyl alcohol. 3,6-Dinitro-1,2,4,5-tetramethylbenzene is stable towards the action of fuming nitric acid, but is slowly converted into 3,6-dinitro-2,4,5-trimethylbenzyl nitrate on being heated with mixed acid at 40—50°C. The mode of formation of unusual products is briefly discussed.

On treatment with an excess of ordinary nitrating agent, tetraalkylbenzenes give dinitrotetraalkylbenzenes as the final product. Because of good crystallization and moderate melting range, dinitro derivatives are often used for the characterization of liquid hydrocarbons. We have reported that fuming nitric acid nitrooxylated the alkyl side-chain of fully substituted derivatives of polyalkylbenzenes to yield the benzylic compounds.[2] The reaction is of electrophilic character and remarkably retarded by the presence of deactivating substituents such as nitro or carboxyl groups, although pentamethylnitrobenzene and pentamethylbenzoic acid can undergo a slow side-chain nitrooxylation at ortho methyl groups.[3,4] It is expected, therefore, that the doubly deactivated dinitrotetramethylbenzenes are quite stable towards further action of the nitrating agent. However, dinitro derivatives of 1,2,3,4-tetramethylbenzene (prehnitene) and 1,2,3,5-tetramethylbenzene (isodurene) are found to react with fuming nitric acid with moderate ease to produce a tetranitrocyclohexenone or a dinitrobenzaldehyde, respectively, in good yields.

When a solution of 5,6-dinitro-1,2,3,4-tetramethylbenzene (5,6-dinitroprehnitene, DNP) in cold fuming nitric acid (d=1.50) was stood at room temperature for several days, it reacted with the nitrating agent with gentle liberation of nitrogen dioxide. Quenching with water, followed by careful crystallization of the precipitate from a mixture of dichloromethane and light petroleum (bp 40—50°C) gave nearly colorless prisms (I), $C_{10}H_{12}N_4O_9$, in 82—87% yield, which melted at 111—114°C with complete decomposition. Its mass spectrum showed fragment ion peaks derived from the non-detectable molecular ion at m/e 286 ($M-NO_2$), 256 ($M-NO_2-NO$), and 240 ($M-2NO_2$). Its infrared spectrum suggested the formation of an unsaturated nitro carbonyl compound (1742 (C=O), 1674 (C=C), 1540—1580 (NO_2, broad), 1328—1337 (NO_2, broad), and 846 cm^{-1} (NO_2)). Its ^{1}H NMR spectrum (100 MHz, $CDCl_3$) with four singlets at 8.71, 8.51, 8.11, and 7.67 τ indicated the presence of four methyl groups. The possibility of formation of the conjugated carbonyl compound was ruled out by the absence of ultraviolet maximum (in MeOH) above 220 nm.

Nitro carbonyl compound (I) was thermally unstable and, when heated gently in carbon tetrachloride, it readily released nitrogen dioxide and was converted into a bright yellow substance (II), $C_{10}H_{12}N_2O_5$, mp 94—96°C. The mass spectrum was very similar to that of I, except for the lack of two minor peaks at m/e 286 and 256. The peak at m/e 240 indicated the formation of II from I by the loss of two molecules of nitrogen dioxide. Its infrared spectrum showed the conjugated carbonyl bands at 1684, 1644 (C=O), and 1617 cm^{-1} (C=C), and absorption bands due to the conjugated nitro groups at 1533—1543 and 1365 cm^{-1}. The ultraviolet spectrum (in MeOH) had a maximum at 296—298 nm (log ε=3.66) in accord with the

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[1] The Reaction of Polysubstituted Aromatics. XXVII. Part XXVI: This Bulletin, **45**, 1270 (1972). Preliminary account has been published in *Chem. Commun.*, **1972**, 340.

[2] H. Suzuki, This Bulletin, **43**, 879 (1970); H. Suzuki, K. Nakamura, and M. Takeshima, *ibid.*, **44**, 2248 (1971).

[3] H. Suzuki and K. Nakamura, *ibid.*, **44**, 227 (1971).

[4] K. Nakamura, *ibid.*, **44**, 133 (1971).

presence of a 2,4-cyclohexadienone system.[5] The ^{1}H NMR spectrum of II consisted of three singlets at 8.56, 7.94 and 7.81 τ, with relative areas 2: 1: 1. The signal at 8.56 τ was due to the *gem*-dimethyl on C-6. If we make a reasonable assumption that the vicinal disposition of two nitro groups in DNP remains intact during the course of reaction, the two *gem*-methyl groups should be located next to the *vic*-dinitro grouping; otherwise they will absorb at around 8.7—8.9 τ.[6] The significant low-field shift is attributed to the location of the methyl groups in a deshielding region of the neighboring nitro group.[7] The inductive and electric field effects would also contribute. The two signals at 7.81 and 7.94 τ could be assigned to the methyl groups on C-2 and C-3, respectively. Examination of a scale model shows that the most preferred conformation of the two nitro groups in II is the one in which the C-5 nitro group is nearly coplanar with the ring to minimize steric crowding, while the C-4 nitro group is twisted considerably out of the ring plane to decrease unfavorable electrostatic interaction between two polar functionalities.[8] The C-3 methyl will then be placed out of the center of the deshielding region of the C-4 nitro group and be subject to reduced deshielding. The C-2 methyl group would be deeply deshielded by the combined effect of the nitro and carbonyl groups. These spectral evidences allowed for II the formulation of *4,5-dinitro-2,3,6,6-tetramethylcyclohexa-2,4-dienone*. Further proof of the structure is obtained from the mass spectrum, which showed prominent peaks at m/e 194 (M$-$Me$-$NO$-$H), 166 (M$-$Me$-$NO$-$CHO), 152 (M$-$2Me$-$NO$-$CO), 150 (M$-$2Me$-$2NO), 148 (M$-$2NO$_2$), and a peak cluster at m/e 119—124, Very strong peaks at m/e 108, 105, 93, 91, 79, 78, and 77 indicate a structure closely related to the benzenoid compound.

Nitro carbonyl compound (I) was, therefore formulated as *2,3,4,5-tetranitro-2,3,6,6-tetramethylcyclohex-4-enone*, whose most preferred structure was suggested from the molecular model shown in Fig. 1, two molecules of nitrogen dioxide being added to the unsaturated bond of II in a *trans* manner. The marked non-equivalence of the geminal methyl groups at 8.71 and 8.51 τ is probably due to the anisotropic effect of the neighboring carbonyl and nitro groups. The easy elimination of two nitrogen dioxide molecules from I suggests the crowding of the nitro and carbonyl groups in half-chair conformer.

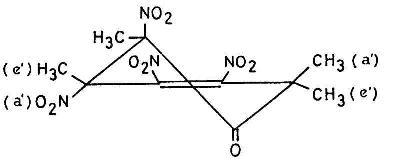
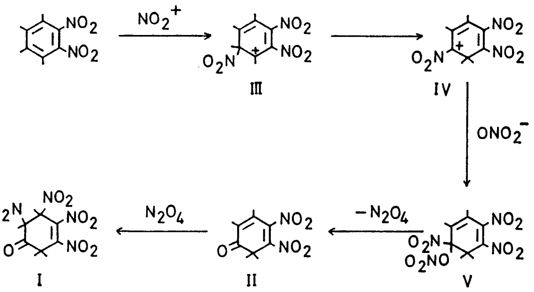


Fig. 1.

Formation of ketone (I) could be accounted for by the following sequence involving the addition-elimination process and the Wagner-Meerwein migration of methyl group (Scheme 1). Since the *vic*-dinitro grouping deactivates the neighboring positions strongly, the initial attack of the nitronium ion would occur at the 2-position of DNP to form benzenonium ion (III), in which the methyl group at the attacking site will migrate to the more positively charged carbon atom at the 1-position. The nitrate anion will add to ion (IV) thus formed to give an unstable nitro nitrate (V), from which nitrogen dioxide is eliminated to yield ketone (II). Addition of nitrogen dioxide to II, probably in a homolytic fashion, will give I as the final product. This is probably the first example of the intramolecular migration of the ring methyl group observed in nitration. The migration of the methyl group from side-chain to nucleus has been reported by Myhre in the nitration of 1,3,5-tri-*t*-butylbenzene.[9]



Scheme 1.

4,6-Dinitro-1,2,3,5-tetramethylbenzene (4,6-dinitroisodurene, DNI) dissolved in cold fuming nitric acid soon began to react with active liberation of nitrogen dioxide. The major product, mp 163—164°C, had a molecular formula $C_{10}H_{10}N_2O_5$ and was identified as 2,6-dinitro-3,4,5-trimethylbenzaldehyde (XI) on the basis of its spectral data. In addition to XI, small amounts of 2,6-dinitro-3,4,5-trimethylphenylnitromethane (XII), 2,6-dinitro-3,4,5-trimethylbenzoic acid, and 2,6-dinitro-3,4,5-trimethylbenzyl alcohol were obtained as by-products. Aldehyde (XI) might be formed by the acid-catalyzed decomposition of the initially fromed 2,6-dinitro-3,4,5-trimethylbenzyl nitrate (IX). Similar reactions have been observed in our previous work.[10] Several mechanistic routes could explain the fromation of XI, high regio-selectivity suggesting the ionic character of the reaction. One of the possible pathways is shown in Scheme 2.

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5) A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products", Pergamon Press, London (1964).

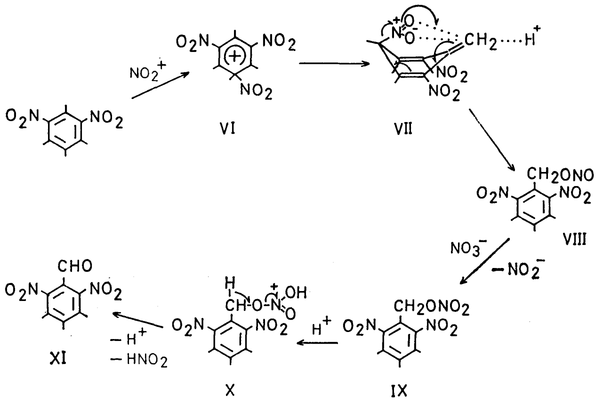
6) Polymethylcyclohexa-2,4-dienones are known to have ^{1}H NMR peaks for 2-methyl at 8.12—8.17, 3-methyl at 7.75—7.98, 4-methyl at 8.12—8.14, 5-methyl at 8.17—8.26, and 6-methyl at 8.72—8.89 τ, respectively. H. Hart, P. M. Collins, and A. J. Waring, *J. Amer. Chem. Soc.*, **88**, 1005 (1966); A. J. Waring, M. R. Morris, and M. M. Islam, *J. Chem. Soc., C*, **1971**, 3274. Reduction of ketone II gave an amino compound, which reacted with 1,2-diketone to form a condensation product of an unidentified structure in accord with the vicinal disposition of two nitro groups.

7) R. W. Frank and S. M. A. Williamson, *J. Org. Chem.*, **31**, 2420 (1966).

8) Analogous situation has been reported for 1,2-dinitrobenzene. K. E. Calderbank, R. J. W. Le Févre, and G. L. D. Ritchié, *J. Chem. Soc., B*, **1968**, 503.

9) P. C. Myhre, M. Beug, K. S. Brown, and B. Östman, *J. Amer. Chem. Soc.*, **93**, 3452 (1971), and previous papers cited therein.

10) H. Suzuki, M. Sawaki, and R. Sakimoto, This Bulletin, **45**, 1515 (1972).

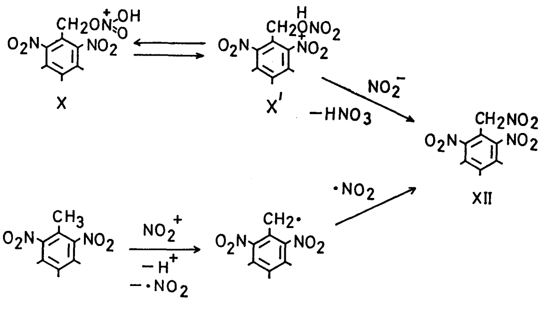


Scheme 2.

The initial attack of the nitronium ion will occur mainly at 2-position of DNI to give ion VI, which can be most effectively stabilized by three methyl groups. Proton release will take place preferentially from the most highly activated C-5 methyl group flanked both sides by nitro groups, leading to the intermediate stage (VII), in which the C-2 nitro group and the C-5 methylene group are not so far apart as to exclude the presence of *any* interaction between the oxygen atom of the C-2 nitro group and the methylene carbon atom. Fission of the C-2–NO_2 bond, followed by the redistribution of electrons in the activated complex will result in the transfer of the nitro group from the C-2 to the methylene carbon, yielding benzyl ester (VIII). Migration of the nitro group to the remote *para* position in preference to the neighboring *ortho* position may be rationalized by assuming that the transition state of the migration resembles the benzylic intermediate rather than the methylenecyclohexadiene, and is stabilized more effectively by the electron-donating methyl group at para position. This interpretation is in agreement with the fact that the nitration of polymethylbenzenes carried out in a dilute acetic acid solution affords a considerable amount of benzyl nitrate along with benzyl acetate at a very early stage of the reaction, and that the ratio of side-chain nitrooxylation and ring nitration is nearly independent of the concentration of nitric acid and added electrolyte.[4] A sort of tight-associated ion-pair may intervene and play some role in the process. The process is formally analogous to the thermal isomerization of 4-methylene-1-ethyl-1,2,3,5,6-pentamethylcyclohexa-2,5-diene to pentamethyl-*n*-propylbenzene, although the latter reaction is known to proceed through radical mechanism.[11] In the presence of excess nitric acid, benzyl nitrite (VIII) is not hightly stable and is readily converted into nitrate (IX). IX will then be protonated to form the conjugated acid (X), in which the fission of the N–O bond will give rise to the formation of benzaldehyde (XI) and the nitrous acid. The sulfuric acid-catalyzed transformation of the benzyl nitrate into the benzaldehyde has been reported to form some amounts of the benzoic acid as a by-product.[12]

Both the ionic mechanism and the one-electron transfer process could explain the formation of phenylnitromethane (XII) (Scheme 3). At present we prefer the view that nitromethane (XII) is derived from the benzyl ester through the nucleophilic displacement on the benzylic carbon of the conjugate acid (X′), although the situation is not clear as yet.[13]

Of three isomeric dinitrotetramethylbenzenes, 3,6-dinitro-1,2,4,5-tetramethylbenzene (3,6-dinitrodurene, DND) was the least soluble in fuming nitric acid. It was quite stable towards the oxidative action of the nitrating agent and mostly recovered unchanged even after a fortnight on being left to stand at room temperature. Protonation of the nitro group seems to have been the major reaction that had occurred. The infrared spectrum of the recovered material indicated the presence of some carbonyl compounds, but the product could not be identified because of the very small quantity. On being heated with a large excess of mixed acid (H_2SO_4:HNO_3=1: 1 v/v) at 40—50°C, DND underwent a slow side-chain nitrooxylation to give 3,6-dinitro-2,4,5-trimethylbenzyl nitrate in good yield. Reduced reactivity of 1,4-dinitro system towards the electrophilic attack was well observed.



Scheme 3.

The present unusual reaction seems to provide a novel, simple route to some polynitro carbonyl compounds which are otherwise not readily accessible. The reaction is closely dependent on the orientation of the alkyl groups in the ring, and a facile destruction of the aromatic ring upon nitration may be characteristic of the vicinal polyalkylbenzene derivatives.

Experimental

All melting points were determined with a hot-stage apparatus and are uncorrected. Infrared spectra were run as Nujol on a Jasco DS-402G spectrophotometer and only prominent peaks were recorded. ^1H NMR measurements were carried out on a JEOLCO PS-100 spectrometer with deuteriochloroform as solvent and tetramethylsilane as an internal standard. Ultraviolet spectra were recorded in methanol solution of a Shimadzu QV-50 spectrophotometer. The mass spectra were obtained by Dr. A. Ohno of Sagami

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11) R. N. Berezina, V. G. Schubin, and V. A. Koptyug, *Zh. Vses. Khim. Obshchest.*, **1968**, 356; V. G. Schubin, R. N. Berezina, and V. A. Koptyug, *Zh. Org. Khim.*, **6**, 2262 (1970).

12) S. D. Ross, E. R. Coburn, and M. Finkelstein, *J. Org. Chem.*, **33**, 589 (1968).

13) In view of the high propensity that the nitro compounds have to undergo protonation on nitro groups rather than release of one electron from the deactivated nucleus, the intermediary formation of the radical cation from DNI seems to be less probable in the strong protogenic acid medium.

Chemical Research Center, to whom the authors are indebted.

5,6-Dinitro-1,2,3,4-tetramethylbenzene (mp 178—179°C), 4,6-dinitro-1,2,3,5-tetramethylbenzene (mp 181—182°C), and 3,6-dinitro-1,2,4,5-tetramethylbenzene (mp 210—211°C) were prepared from the corresponding hydrocarbons by the ordinary procedure.

Reactions of Dinitrotetramethylbenzenes with Fuming Nitric Acid. 5,6-Dinitro-1,2,3,4-tetramethylbenzene (DNP). DNP (7.5 g) was dissolved in small portions in cold fuming nitric acid (*d*=1.5, 60 m*l*) to give a clear yellow solution. The color of the solution gradually turned dark red and a fume of nitrogen dioxide began to evolve slowly. The mixture was allowed to stand under hood at room temperature for several days, during the course of which the initial dark color faded to a light yellow. On being diluted with an excess of water, a pasty precipitate was obtained which, on being left to stand, gradually solidified to a white crystalline cake. The product was filtered, thoroughly washed with water, and dissolved into a minimum amount of dichloromethane. The solution was warmed at 35—40°C, light petroleum (bp 40—50°C) was added drop by drop until the solution became slightly cloudy, and the solution was left to cool under cover. Care should be taken to avoid excess heating. Faintly yellow prisms soon began to separate (8.8—9.4 g). Any attempt to crystallize the product from the hot solvent led to extensive decomposition of the product. On the basis of elemental analysis, infrared, ultraviolet, ^{1}H NMR, and mass spectral data, the product was formulated as *2,3,4,5-tetranitro-2,3,6,6-tetramethylcyclohex-4-enone (I)*. IR: 697, 732, 763, 785, 824, 846, 912, 976, 995, 1024, 1032, 1066, 1084, 1126, 1155, 1182, 1240, 1328—1337, 1540—1580, 1674, and 1742 cm^{-1}.

Found: C, 36.23; 36.42; H, 3.58; 3.78; N, 16.76; O, 43.37%. Calcd for $C_{10}H_{12}N_4O_9$: C, 36.16; H, 3.64; N, 16.87; O, 43.34%.

The ketone was thermally unstable and melted at 111—114°C with complete decomposition. When crystallization was attempted by dissolving I in hot carbon tetrachloride, nitrogen dioxide was liberated and a bright yellow substance, mp 94—96°C, was obtained. This was identified as *4,5-dinitro-2,3,6,6-tetramethylcyclohexa-2,4-dienone (II)* on the basis of spectral evidences. IR: 714, 736, 777, 849, 999, 1048, 1198, 1245, 1272, 1299, 1533—1540, 1617, 1644, and 1684 cm^{-1}.

Found: C, 49.92; H, 5.02%. Calcd for $C_{10}H_{12}N_2O_5$: C, 50.00; H, 5.04%.

4,6-Dinitro-1,2,3,5-tetramethylbenzene (DNI). A solution of DNI (7.2 g) in fuming nitric acid (60 m*l*), when stood at room temperature, soon began to liberate red fume. After the cease of reaction, the solution was diluted with water and a white crystalline precipitate was filtered, washed with dilute aqueous sodium hydrogen carbonate, and dissolved in a mixture of dichloromethane and light petroleum, from which the major product was readily separated as large prisms (5.9—6.4 g), mp 163—164°C after recrystallization several times, and identified as *2,6-dinitro-3,4,5-trimethylbenzaldehyde (XI)*. IR: 699, 778, 861, 896, 1023, 1052, 1285, 1359, 1532, and 1712 cm^{-1}; ^{1}H NMR: 7.66 (2 Me), 7.52 (Me), and 0.16 τ (CHO).

Found: C, 50.12; H, 4.29%. Calcd for $C_{10}H_{10}N_2O_5$: C, 50.42; H, 4.23%.

The aldehyde was stable towards spontaneous oxidation, but soon became yellow or light brown on storage under diffused light.

A less soluble minor part was fractionally recrystallized from ligroin to give fine needles (*ca.* 0.5 g), $C_{10}H_{11}N_3O_6$, mp 158—159°C. It showed ^{1}H NMR peaks at 7.65 (2 Me), 7.56 (Me), and 4.58 τ (CH_2), and IR bands at 711, 766, 785, 855, 878, 898, 1057, 1288, 1317, 1360, 1535, and 1567 cm^{-1}, and was identified as *2,6-dinitro-3,4,5-trimethylphenylnitromethane.*

Found: C, 44.69; H, 4.18%. Calcd for $C_{10}H_{11}N_3O_6$: C, 44.61; H, 4.12%.

Another minor product, mp 193—195°C, was *2,6-dinitro-3,4,5-trimethylbenzyl alcohol.* IR: 776, 857, 868, 1010, 1043, 1055, 1365, 1535, and 3530 cm^{-1}.

Found: C, 50.08; H, 5.09%. Calcd for $C_{10}H_{12}N_2O_5$: C, 50.00; H, 5.04%.

The aqueous sodium hydrogen carbonate washing of the product was neutralized with hydrochloric acid to give a white precipitate, which on recrystallization several times from aqueous ethanol gave fine needles (*ca.* 0.5 g), mp 233—236°C with decomposition, and was identified as *2,6-dinitro-3,4,5-trimethylbenzoic acid.* IR: 662, 721, 781, 857, 896, 1168, 1360, 1535, 1753, and 3300 cm^{-1}.

Found: C, 47.43; H, 3.76%. Calcd for $C_{10}H_{10}N_2O_6$:C, 47.25; H, 3.97%.

3,6-Dinitro-1,2,4,5-tetramethylbenzene (DND). DND (4.5 g) was dissolved in a large excess of mixed acid (40 m*l*; H_2SO_4: HNO_3 (*d*=1.5) =1: 1 v/v), and the solution was kept at 40—50°C for several hours and then at around 60°C for 0.5 hr. This was poured onto crushed ice followed by the usual work-up, and gave *3,6-dinitro-2,4,5-trimethylbenzyl nitrate* as pale yellow needles (3.5 g, 61%), mp 139—140°C. IR: 676, 752, 853, 886, 983, 1212, 1222, 1273, 1365, 1535, and 1645 cm^{-1}; ^{1}H NMR (in CCl_4): 7.73 (2 Me), 7.65 (Me), and 4.59 τ (CH_2).

Found: C, 41.93; H, 3.60; N, 14.57%. Calcd for $C_{10}H_{11}N_3O_7$: C, 42.11; H, 3.89; N, 14.73%.