Formation of Cyanonitro-3-cyclohexen-1-ones in the Reaction of Tetramethylbenzonitriles with Fuming Nitric Acid[1)]

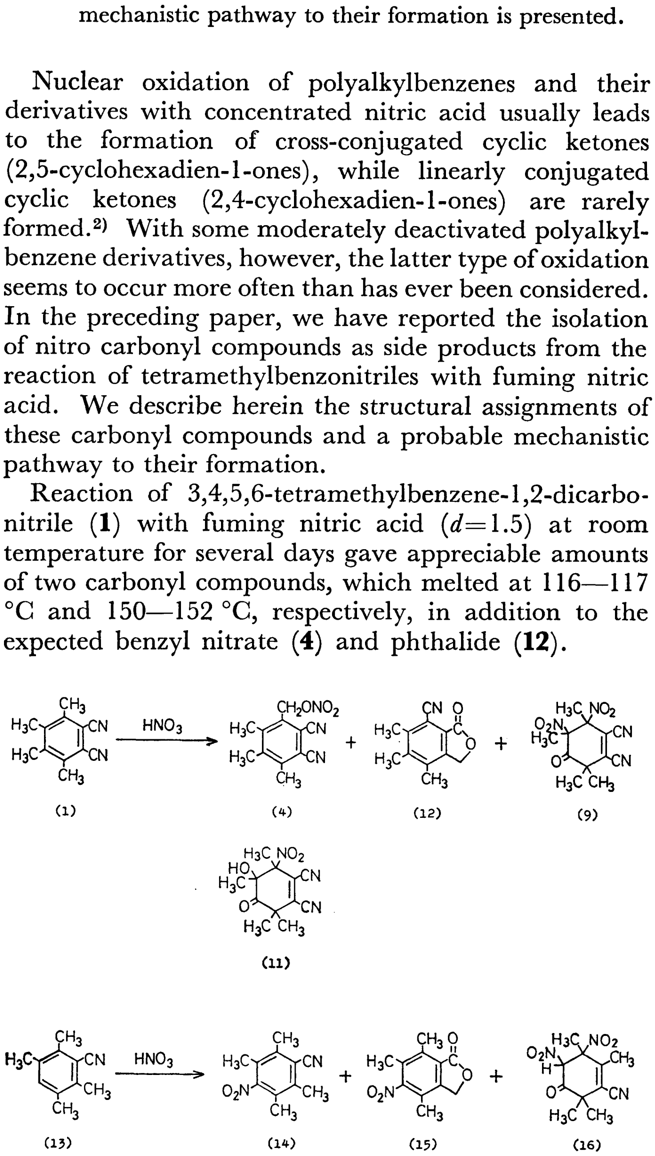
Hitomi SUZUKI, Akiyoshi INOUE, Mamie KOGE, and Terukiyo HANAFUSA
Department of Chemistry, Faculty of Science, Hiroshima University, Higashi-sendamachi, Hiroshima 730

(Received August 31, 1977)

The reaction of 3,4,5,6-tetramethylbenzene-1,2-dicarbonitrile with fuming nitric acid at room temperature yielded appreciable amounts of 3,4-dicyano-5,6-dinitro-2,2,5,6-tetramethyl-3-cyclohexen-1-one and 3,4-dicyano-6-hydroxy-5-nitro-2,2,5,6-tetramethyl-3-cyclohexen-1-one in addition to the expected side-chain substitution products. 2,3,5,6-Tetramethylbenzonitrile similarly gave 3-cyano-5,6-dinitro-2,2,4,5-tetramethyl-3-cyclohexen-1-ones as minor products. The structures of these nitro ketones have been assigned by spectral methods and a probable mechanistic pathway to their formation is presented.

Nuclear oxidation of polyalkylbenzenes and their derivatives with concentrated nitric acid usually leads to the formation of cross-conjugated cyclic ketones (2,5-cyclohexadien-1-ones), while linearly conjugated cyclic ketones (2,4-cyclohexadien-1-ones) are rarely formed.[2)] With some moderately deactivated polyalkylbenzene derivatives, however, the latter type of oxidation seems to occur more often than has ever been considered. In the preceding paper, we have reported the isolation of nitro carbonyl compounds as side products from the reaction of tetramethylbenzonitriles with fuming nitric acid. We describe herein the structural assignments of these carbonyl compounds and a probable mechanistic pathway to their formation.

Reaction of 3,4,5,6-tetramethylbenzene-1,2-dicarbonitrile (**1**) with fuming nitric acid (d=1.5) at room temperature for several days gave appreciable amounts of two carbonyl compounds, which melted at 116—117 °C and 150—152 °C, respectively, in addition to the expected benzyl nitrate (**4**) and phthalide (**12**).



Scheme 1.

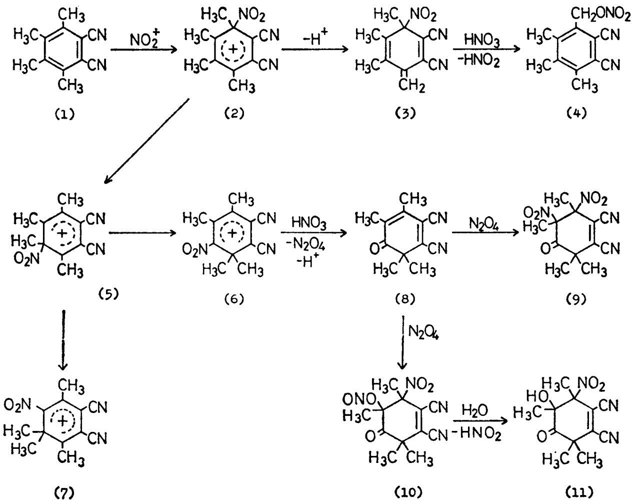
The *low-melting compound (9)* had the formula $C_{12}H_{12}N_4O_5$; its mass spectrum showed peaks at m/e 292 (M^+), 246 (M^+-NO_2), 200 (M^+-2NO_2), 185 ($M^+-2NO_2-CH_3$), 172 (M^+-2NO_2-CO), 157 (base peak; $M^+-2NO_2-CO-CH_3$), and 142 ($M^+-2NO_2-CO-2CH_3$). Its IR spectrum suggested the formation of an unsaturated nitro carbonyl compound with absorption bands due to a nitro group (1560 and 1330 cm^{-1}), a carbonyl group (1745 cm^{-1}), and the carbon-carbon double bond (1635 cm^{-1}). Its PMR spectrum with four singlets at δ 2.27, 2.05, 1.26, and 1.22 indicated the presence of four methyl groups intact. The possibility of the conjugated carbonyl compound was ruled out by the absence of an UV maximum above 220 nm.

This nitro carbonyl compound was thermally unstable and, when heated gently in ligroin, it readily released nitrogen dioxide and was converted into another new ketone (**8**), $C_{12}H_{12}N_2O$, mp 83—84 °C. Its mass spectrum was quite similar to that of the parent compound **9**, except for the lack of two minor peaks at m/e 292 and 246. The high carbon-to-hydrogen ratio of the empirical formula points to an unsaturated cyclic structure. The IR spectrum showed the presence of the cyano group (2210 cm^{-1}) and the conjugated carbonyl group (1670 and 1625 cm^{-1}), but absorptions due to the nitro group were no longer observed. An intense band at 315 nm ($\log\varepsilon=3.61$) in the UV spectrum and a characteristic mass pattern with peak clusters at m/e 102—107, 88—93, and 77—79 were in accord with the presence of a 2,4-cyclohexadien-1-one system. The PMR spectrum consisted of three singlets at δ 2.19, 2.06, and 1.44, with relative areas 1 : 1 : 2. The signal at δ 1.44 obviously represented the *gem*-dimethyl grouping, but exhibited a significant downfield shift as compared to the normal positions of this grouping, δ 1.11—1.28.[3)] If we make a reasonable assumption that the vicinal disposition of the two cyano groups in **1** remains intact during the course of reaction, the *gem*-methyl groups should be placed next to the *vic*-dicyano grouping. These data were consistent with the formulation of this compound as 4,5-dicyano-2,3,6,6-tetramethyl-2,4-cyclohexadien-1-one (**8**). The original nitro carbonyl compound was, therefore, formulated as 3,4-dicyano-5,6-dinitro-2,2,5,6-tetramethyl-3-cyclohexen-1-one (**9**). This structural assignment was further substantiated by the CMR spectrum, which indicated the presence of four methyls (δ 18.6, 18.6, 23.2, and 23.5), two cyano groups (δ 110.8 and 112.0), a carbonyl carbon (δ 200.7), two olefinic carbons (δ 122.1 and 144.1), two sp^3 carbons attached to nitrogen (δ 70.0 and 87.5), and a sp^3 carbon in non-hetero atom function (δ 51.8).

The *high-melting compound (11)* was a slightly water-soluble, crystalline solid, which was obtained by extracting with ether the aqueous solution from which **4** and **12** separated out. Elemental analysis and mass spectrum established its molecular composition to be

$C_{12}H_{13}N_3O_4$, suggesting an unsaturated cyclic structure similar to **9**. The IR spectrum showed absorptions due to the hydroxyl and carbonyl groups at 3470 and 1720 cm^{-1}, respectively, in addition to those for the cyano group (2230 cm^{-1}), the carbon-carbon double bond (1640 cm^{-1}), and the nitro group (1570, 1340, and 850 cm^{-1}). A moderate fall of the carbonyl stretching frequency as compared to that in **9** suggested the location of the hydroxyl group in the vicinity of the carbonyl group. The PMR spectrum exhibited resonances for four methyl groups (δ 1.18, 1.30, 1.88, and 2.00). The CMR spectrum (in $CDCl_3/(CD_3)_2SO$ (5: 1)) indicated the presence of four methyls (δ 17.2, 18.0, 22.5, and 22.5), two cyano groups (δ 111.1 and 112.0), a carbonyl carbon (δ 200.3), two olefinic carbons (δ 120.2 and 138.7), two sp^3 carbons adjacent to nitrogen and oxygen (δ 68.9 and 94.3, respectively), and a sp^3 carbon in non-hetero atom function (δ 48.6). The UV spectrum showed no maximum above 220 nm, ruling out the possibility of a conjugated ketone. On the basis of the spectral data and reasoning similar to that used to arrive at the structures **8** and **9**, the compound was assigned the structure, 3,4-dicyano-6-hydroxy-5-nitro-2,2,5,6-tetramethyl-3-cyclohexen-1-one (**11**).

On a similar treatment, 2,3,5,6-tetramethylbenzonitrile (**13**) gave a nitro ketone (**16**) along with the expected ring and side-chain products (**14** and **15**).



Scheme 2.

Formation of these nitro ketones can be explained by a sequence of reactions involving addition-elimination and alkyl migration, as exemplified by the conversion of **1** to **9** and **11** (Scheme 2). Thus, electrophilic attack of nitronium ion on **1** will occur at C-3 position to form the arenium ion (**2**), which could react in either of the two competing pathways: proton release from the activated methyl group in **2** to form the triene intermediate (**3**) will give the nitrate (**4**), whereas the 1,2-migration of nitro group in **2** followed by the 1,2-migration of the *ipso* methyl group in ion (**5**) to form ion (**6**) will lead to the formation of the carbonyl compounds **9** and **11**.[4] In the latter path, methyl migration in **5** will occur in one preferred direction to yield **6**, since the latter ion would be more effectively stabilized by the substituent groups than that (**7**) formed by the migration in the other direction. Capture of **6** by nitric acid or nitrate ion will lead to unstable *gem*-nitro nitrate, from which nitrogen dioxide is eliminated to yield the ketone **8**. Addition of nitrogen dioxide to **8** will give **9** as the final product. The alternative mode of the addition of nitrogen dioxide to **8** will produce an unstable adduct (**10**), which on hydrolysis will give the ketone **11**.

Experimental

All melting points were taken on a hot stage apparatus and are uncorrected. The IR, PMR, and mass spectra were obtained using the same procedures and apparatus described in the preceding paper, unless otherwise stated. The CMR spectra were determined on a Hitachi R-26 spectrometer by Dr. M. Mishima of Kyushu University. The UV spectra were recorded on a Hitachi 124 spectrophotometer in methanol solutions.

Reaction of Tetramethylbenzonitriles with Fuming Nitric Acid.

a) 3,4,5,6-Tetramethylbenzene-1,2-dicarbonitrile (1). Dinitrile **1** (1.10 g; 6 mmol) was dissolved in fuming nitric acid (*d*=1.5; 20 g) and the mixture was allowed to stand at room temperature (20—30 °C) for several days, during the course of which the solution became dark red and nitrogen dioxide was liberated. On diluting with water, a yellow pasty precipitate (0.84 g) was obtained, which was dissolved in a minimum amount of dichloromethane and fractionally precipitated by dropwise addition of pentane. A nitro carbonyl compound was obtained as an early precipitate (0.48 g; 28%) and a nitrate (0.21 g; 14%) was also obtained from the mother liquor. These products were identified as *3,4-dicyano-5,6-dinitro-2,2,5,6-tetramethyl-3-cyclohexen-1-one (9)* and *5,6-dicyano-2,3,4-trimethylbenzyl nitrate (4)*, respectively, on the basis of elemental analyses and spectral data. **9**: Mp 116—117 °C. Found: C, 49.9; H, 4.2; N, 18.9%. Calcd for $C_{12}H_{12}N_4O_5$: C, 49.3; H, 4.1; N, 19.2%. **4**: Mp 105—106 °C. PMR: δ 2.45 (s, 3H), 2.57 (s, 3H), 2.57 (s, 3H), and 5.52 (s, 2H); IR: ν_{max} 2220 (CN), 1640, 1280, and 840 cm^{-1} (ONO_2). Found: C, 58.5; H, 4.3; N, 17.4%. Calcd for $C_{12}H_{11}N_3O_3$: C, 58.8; H, 4.5; N, 17.1%.

Heating the ketone **9** in ligroin readily eliminated nitrogen dioxide, giving a new ketone melting at 83—84 °C; this was identified as *4,5-dicyano-2,3,6,6-tetramethyl-2,4-cyclohexadien-1-one (8)*. Found: C, 71.8; H, 6.3; N, 13.6%. Calcd for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0%.

The aqueous part was set aside overnight and afforded a white precipitate (0.23 g; 19%), which was collected by filtration and crystallized from aqueous ethanol to give *7-cyano-4,5,6-trimethylphthalide (12)*, mp 286—287 °C (sublim.).[5] Found: C, 71.3; H, 5.4; N, 7.4%. Calcd for $C_{12}H_{11}NO_2$: C, 71.6; H, 5.5; N, 7.0%.

The mother liquor was further extracted with ether and the combined extract was washed successively with aqueous sodium hydrogencarbonate and water, and evaporated *in vacuo* to yield a yellow syrup (0.38 g), from which *3,4-dicyano-6-hydroxy-5-nitro-2,2,5,6-tetramethyl-3-cyclohexen-1-one (11)* slowly separated out as fine needles, mp 150—152 °C. Found: C, 54.6; H, 5.0; N, 16.0%. Calcd for $C_{12}H_{13}N_3O_4$: C, 54.8; H, 5.0; N, 16.0%.

b) 2,3,5,6-Tetramethylbenzonitrile (13). A solution of nitrile **13** (1.59 g; 10 mmol) in fuming nitric acid (*d*=1.5; 21 g) was stirred at 30 °C for 3 days, after which the mixture was poured onto crushed ice to give a yellow oily substance (0.99 g). This was triturated with small amounts of cold dichloromethane and the white powder obtained was crystallized from ligroin, giving *3-cyano-5,6-dinitro-2,2,4,5-tetramethyl-3-cyclohexen-1-one (**16a**)* as fine needles (0.13 g; 4.9%), mp 150—151 °C. The dichloromethane solution was evaporated and the residue was fractionally crystallized from benzene/cyclohexane, giving another nitro ketone (**16b**; 0.1 g; 3.8%) isomeric with **16a**, mp 144—147 °C, and *4-nitro-2,3,5,6-tetramethylbenzonitrile* (**14**; 0.17 g; 8.3%), mp 195—198 °C.[5] **16a**: MS: *m/e* 267 (M$^+$), 221, 205, 191, 175 (base peak), 160, and 147; PMR ($(CD_3)_2SO$): δ 1.15 (s, 3H), 1.37 (s, 3H), 2.15 (s, 3H), 2.33 (s, 3H), and 6.10 (s, H); IR: ν_{max} 2230 (CN), 1700 and 1220 (C=O), 1570, 1360, and 1340 cm^{-1} (NO_2); UV: no maximum above 220 nm. Found: C, 49.2; H, 4.9; N, 15.5%. Calcd for $C_{11}H_{13}N_3O_5$: C, 49.4; H, 4.9; N, 15.7%. **16b**: MS: *m/e* 267 (M$^+$), 221, 205, 191, 175, 160, and 147; PMR ($(CD_3)_2SO$): δ 1.13 (s, 3H), 1.18 (s, 3H), 1.93 (s, 3H), 2.47 (s, 3H), and 6.07 (s, 1H); IR: ν_{max} 2240 (CN), 1710 and 1225 (C=O), 1560 and 1340 cm^{-1} (NO_2); UV: no maximum above 220 nm. Found: C, 49.1; H, 4.9; N, 15.2%. Calcd for $C_{11}H_{13}N_3O_5$: C, 49.4; H, 4.9; N, 15.7%.

The aqueous part from which **14** and **16** separated out was set aside overnight, giving *5-nitro-4,6,7-trimethylphthalide (**15**)* as a crystalline precipitate (0.23 g; 10.4%).[5] Mp 203—205 °C. Found: C, 60.0; H, 5.2; N, 6.5%. Calcd for $C_{11}H_{11}NO_4$: C, 59.7; H, 5.0; N, 6.3%.

Acknowledgement is made to the Ministry of Education and the Saneyoshi Scientific Foundation for financial support.

References

1) The reaction of polysubstituted aromatics. Part XLVIII; Part XLVII: H. Suzuki, M. Koge, A. Inoue, and T. Hanafusa, *Bull. Chem. Soc. Jpn.*, **51**, 1168 (1978).

2) For a review of nuclear oxidation which occurs as a consequence of *ipso* nitration, see H. Suzuki, *Synthesis*, **1977**, 217; B. Moodie and K. Schofield, *Acc. Chem. Res.*, **9**, 287 (1976).

3) Polymethyl-2,4-cyclohexadien-1-ones are known to have PMR peaks for 2-methyl at δ 1.83—1.88, 3-methyl at δ 1.02—1.25, 4-methyl at δ 1.86—1.88, 5-methyl at δ 1.74—1.83, and 6-methyl at δ 1.11—1.28, respectively: H. Hart, P. M. Collins, and A. J. Waring, *J. Am. Chem. Soc.*, **88**, 1005 (1966); A. J. Waring, M. R. Morris, and M. M. Islam, *J. Chem. Soc., C*, **1971**, 3274.

4) An interesting example of a multi-step migration of a methyl group has recently been observed in the nitration of pentamethylbenzene with nitric acid in fluorosulfuric acid, and a possible intervention of the electron-transfer process has been suggested for the nuclear oxidation of alkyl aromatics: A. N. Detsina, V. I. Mamatyuk, and V. A. Koptyug, *Zhur. Org. Khim.*, **13**, 130 (1977).

5) Spectral data are given in the preceding paper of this series.