Side-chain Reactions of 2,4,5-Trimethylneopentylbenzene with Nitric Acid and with Cerium Ammonium Nitrate: Comparison of the Products from Reactions *via* Arenium Ions and *via* Cation Radicals

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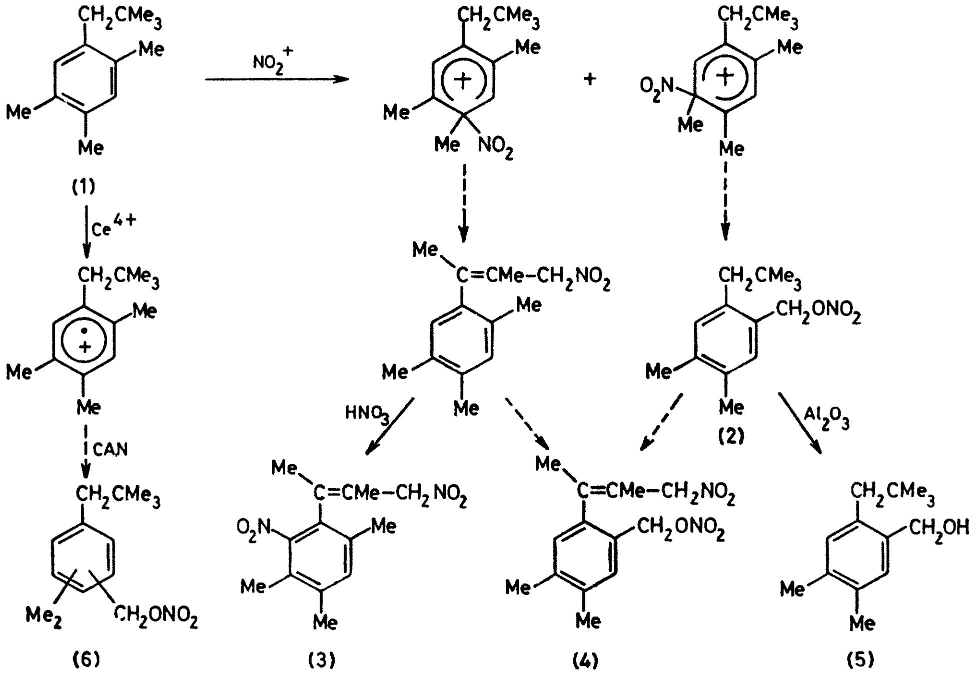
Summary When treated with excess of nitric acid, the title arene underwent both nitro-oxylation of the methyl group and isomerization of the neopentyl group, followed by nitration, giving 3-(4,5-dimethyl-2-nitro-oxymethylphenyl)-2-methyl-1-nitrobut-2-ene as the major product, while with cerium ammonium nitrate it yielded a mixture

of isomeric benzyl nitrates, these results show that side chain substitutions of arenium ions and cation radicals follow different pathways.

THE action of nitrating agents upon polyalkylbenzenes often leads to substitution reactions on the alkyl side-chain, giving the corresponding benzyl nitrates and arylnitromethanes.[1] For these non-conventional nitrations of arenes, we have proposed an ionic mechanism which assumes the conversion of an arenium ion intermediate into a benzyl cation–nitrite anion pair, followed by the recombination of these ionic species at the benzylic carbon atom either *via* C–N or C–O bond formation.[2] An alternative mechanism has been proposed in which electron-transfer occurs from the arene to the nitronium ion to form an arene cation-radical–nitrogen dioxide pair and the subsequent recombination of these species results in the formation of side-chain substitution products.[3]

We have recently reported that 2,3,4-trimethylneopentylbenzene reacts with nitric acid to afford a nitro-olefin through a Wagner–Meerwein type rearrangement of the neopentyl group,[4] this strongly suggests the heterolytic character of the side-chain reaction, since the α-t-butyl-2,3,4-trimethylbenzyl radical itself shows no tendency to isomerize, but dimerizes readily in spite of the highly crowded structure of the product. Further investigations of the nitration of various polymethylneopentylbenzenes revealed that this anomalous behaviour is uncommon, and is dependent on the number and substitution pattern of the ring alkyl groups, *i.e.* it is closely related to the site of attack of the electrophile. In an attempt to distinguish between the two mechanistic alternatives proposed for the side-chain substitution we have compared the product composition from reactions of the cation-radical of arenes with that found in the direct nitration. For this purpose the title hydrocarbon (**1**) proved to be an ideal substrate, because on nitration it undergoes two modes of side-chain substitution in parallel: nitro-oxylation of the methyl group, and isomerization of the neopentyl group followed by nitration of the resulting alkenyl group. Cerium ammonium nitrate (CAN) was used for the generation of the cation radical from (**1**).

When (**1**) was treated with nitric acid (*d* 1·5) in dichloromethane at −5 to 0 °C and the oily product chromatographed over alumina we obtained the ring-nitration product (30%) from hexane–benzene eluates, two crystalline side chain nitration products (**3**) (4%) and (**4**) (16%) from ether eluates and finally an alcohol (**5**) (4%) from methanol eluates (Scheme).† Addition of nitrogen dioxide did not alter the composition of the product. The alcohol (**5**) was presumably derived from an initially formed nitrate (**2**). Compound (**4**) is the first example of a non-conventional nitration product in which one alkyl group suffered nitration and the other nitro-oxylation. Owing to the restricted rotation of the C–C bond imposed by adjacent ring substituent groups, the geminal protons of the nitromethyl group appear as double doublets in the ¹H n.m.r. spectrum.



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† The structures assigned to these side-chain substitution products were consistent with their analyses and spectral data. Yields refer to compounds isolated. Spectral data (**4**) m.p. 74—75 °C ν_{max} (KBr disc) 1610, 1530, 1350, 1260, 960, 880, 840, 790, 750, and 680 cm^{-1}, δ (¹H, CCl$_4$) 1·60 (s, 3H), 2·00 (s, 3H), 2·27 (s, 6H), 4·93 (d, 1H, *J* 14 Hz), 5·20 (s, 2H), 5·23 (d, 1H, *J* 14 Hz), 6·88 (s, 1H), and 7·15 (s, 1H), δ (¹³C, CDCl$_3$) 143·2, 139·0, 138·4, 136·7, 131·7, 130·9, 127·0, 122·6, 78·3, 73·2, 22·8, 20·6, 19·6, and 19·4 p.p.m., M^+ *m/e* 294, (**3**), m.p. 111—112 °C, ν_{max} (KBr disc) 1540, 1510, and 1370 cm^{-1}, δ (¹H, CCl$_4$) 1·63 (s, 3H), 2·00 (s, 6H), 2·17 (s, 3H), 2·30 (s, 3H), 4·93 (d, 1H, *J* 14 Hz), 5·25 (d, 1H, *J* 14 Hz), and 7·02 (s, 1H), M^+—NO$_2$ *m/e* 232.

In contrast, the reaction of (**1**) with CAN in acetonitrile at room temperature in the dark occurred smoothly at the ring methyl groups, (mainly those at the *m*- and *p*-positions) giving a mixture of isomeric benzyl nitrates (**6**) in 20—50% isolated yields. In the presence of nitrogen dioxide, the product was found to contain small amounts of arylnitromethanes which probably arose from the capture of the cation-radical by nitrogen dioxide. Addition of nitric acid merely increased the complexity of the product composition. In no case was the rearrangement of the neopentyl group observed, nor any substitution on that group.

Formation of the nitro-nitrate (**4**) in the direct nitration of (**1**), but not in its reaction with CAN, shows that (**4**) is formed through an arenium ion intermediate, and rules out the formation of a cation radical as an intermediate of the reaction pathway leading to the side-chain substitution of arenes during nitration.

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[1] For a review of non-conventional processes which occur as the consequence of *ipso*-attack of nitronium ions, see H. Suzuki, *Synthesis*, 1977, 217. See also S. R. Hartshorn, *Chem. Soc. Rev.*, 1974, 3, 167.

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[3] J. K. Kochi, *Tetrahedron Lett.*, 1974, 4305.

[4] H. Suzuki, K. Nagae, K. Ohnishi, and A. Osuka, *J. Chem. Soc., Chem. Commun.*, 1980, 245.