A Non-acid Methodology for Polynitration of Arenes at Low Temperatures

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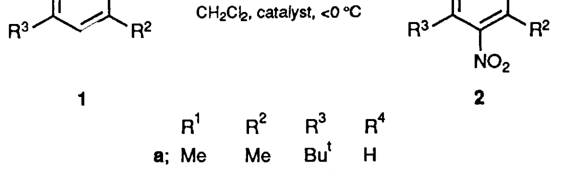
In the presence of ozone and an appropriate catalyst, nitrogen dioxide acts as a powerful nitrating agent at low temperatures, converting arenes into polynitro derivatives in good yields.

The nitro group lowers considerably the reactivity of arenes toward electrophiles, so that the stepwise introduction of multiple nitro groups into the aromatic nucleus offers increasing difficulty as the number of nitro groups increases. Thus, the polynitration of arenes is usually carried out under conditions of strong acid and elevated temperatures.[1] Recently we have observed that lower nitrogen oxides can act as nitrating agents for aromatic systems in the presence of ozone at low temperatures.[2] This finding has now been developed into a novel procedure for aromatic polynitration, which allows the direct conversion of nonactivated arenes into polynitro derivatives under non-acid conditions at low temperatures.

When a stream of ozonized oxygen or air was slowly introduced into a solution of an arene and an excess of nitrogen dioxide in dry dichloromethane below 0 °C, the substrate was easily nitrated on the ring to afford the corresponding polynitro derivative in good yield (Scheme 1). The reaction was often facilitated by the presence of an appropriate catalyst such as boron trifluoride–diethyl ether or methanesulphonic acid. The reaction was clean and no polymeric substances were formed.[3] In the absence of ozone the reaction was quite slow and incomplete, with formation of side products probably arising from addition and abstraction



1 2

	R^1	R^2	R^3	R^4
a;	Me	Me	Bu^t	H
b;	Me	Me	Bu^t	NO_2
c;	Me	Me	Me	NO_2
d;	Bu^t	Bu^t	Bu^t	H

Scheme 1

of hydrogen atom. No polynitration products were obtained in this case.

A typical procedure is exemplified by the preparation of a commercial nitro musk, 2,4,6-trinitro-5-*tert*-butyl-1,3-dimethylbenzene **2b**. Into a solution of 5-*tert*-butyl-1,3-dimethylbenzene (**1a**, 10 mmol) and methanesulphonic acid (1 mmol) in dry dichloromethane (30 ml) kept at between −10 and 0 °C by ice–salt bath, ozonized oxygen and nitrogen dioxide were slowly bubbled through from separate inlet tubes with vigorous stirring. The mixture quickly turned dark and as the reaction progressed, compound **2b** was formed as crystals around the openings of the tubes. After 12 h,† the reaction was quenched by the addition of aqueous sodium hydrogensulphate. Usual workup gave an oily mass, which was crystallized from ethanol to give **2b** in 80% yield. M.p. 114 °C (lit.[4] 110 °C).

Under similar conditions, mesitylene was converted to the 2,4,6-trinitro derivative **2c** in 95% yield, while *m*-xylene gave dinitro and trinitro derivatives in a ratio of 7 : 1 in 70% yield. Polynitration of 1,3,5-tri-*tert*-butylbenzene **1d** with fuming nitric acid or mixed acid usually leads to a complex mixture of products arising from the rearrangement of the intermediate nitrobenzenium ions.[5] Under the present conditions, however, the hydrocarbon underwent smooth nuclear nitration, giving dinitro compound **2d** as the major product in 83% yield. Skeletal rearrangement was not significant. Nitrobenzene itself could be nitrated with the ozone–nitrogen dioxide system to produce a mixture of three isomeric dinitrobenzenes ($o:m:p$ = 8 : 91 : 1) in 99% yield. Attempts to prepare 2,4,6-trinitrotoluene (TNT) by the present procedure proved to be discouraging. 4-Nitrotoluene was efficiently converted into 2,4-dinitrotoluene, which, however, resisted further nitration. Prolonged treatment of the latter compound with the nitrating agent in tetrachloroethane in the presence of molecular sieves 3 Å led to TNT only in less than 10% yield. The substrate was mostly recovered unchanged.[6] The active species responsible for the nitration is not clear at present, although one possibility is a 'hot' dinitrogen pentoxide *in situ* generated from the interaction between nitrogen dioxide and ozone.[7]‡

The present non-acid methodology for aromatic polynitration provides an attractive alternative to the classical procedure based on mixed acid, since it does not require the use of a large excess of nitric acid or the assistance of sulphuric acid/oleum, thus allowing the problem of disposal of spent acids in large quantities to be circumvented.

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† Reaction time is dependent on the efficiency of the ozone generator. An apparatus (Nippon Ozone Co Ltd., type ON-1-2) was used for the generation of ozone. With reactive substrates, ozonized air is preferred to ozonized oxygen.

‡ Aromatic nitrations in dinitrogen tetroxide systems have been reported,[8] in which the isomer distributions of nitro derivatives differ significantly from those obtained in mixed acid systems.