Formation of Picric Acid in the Oxidation of *o*-Nitrotoluene with Nitric Acid

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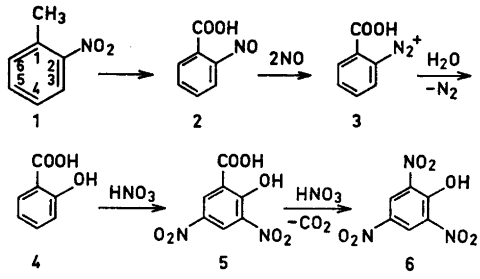
Oxidation of nitrotoluenes with dilute nitric acid at elevated pressure is an established industrial method for the synthesis of *p*- and *m*-nitrobenzoic acids.[1] The yields are good and there are no marked side reactions. With *o*-nitrotoluene, however, the yield of *o*-nitrobenzoic acid is poor, and large quantities of picric acid are formed.[1,2]

The mechanism of this picric acid formation is obscure and has not been subjected to any detailed investigations. However, Askenasy, Elöd and Trogus suggested that the nitro group is reduced and replaced by a hydroxyl group *via* diazotation.[3] Reactions between *o*-nitrobenzaldehyde or *o*-nitrotoluene and nitrogen dioxide lead to diazonium salts, and according to Titov,[3] proceed by intramolecular oxidation of radicals to nitroso compounds which are then diazotised by nitric oxide. Titov also suggested that the formation of picric acid in the oxidation of *o*-nitrotoluene with aqueous nitric acid should proceed through similar stages. Following Titov's suggestions the formation of picric acid should occur by the following path:



If nitroso compounds occur as intermediates, hydroxylation in the *para* position to the nitroso group [4,5] is also a conceivable reaction, especially at high concentrations of nitric acid and low concentrations of nitrous acid.

Thus the formation of picric acid from *o*-nitrotoluene could be expected to occur *via* hydroxylation mainly in the 2- and 5-positions.

The present paper is a preliminary account of an investigation of the oxidation of *o*-nitrotoluene with nitric acid comprising studies of the by-products and some isotopic experiments aimed particularly at the elucidation of the formation of picric acid.

Small scale oxidations of *o*-nitrotoluene with aqueous nitric acid were made in sealed tubes. Typical results are shown in Table 1. Some unexpected products were found, including 2,5-dinitrobenzoic acid, which could be isolated through the slight solubility of its potassium salt in ethanol.

Table 1. Products found from the oxidation of 1 mmole of *o*-nitrotoluene with 3 mmole 35 % nitric acid at *ca.* 190°. The figures are mean values from four runs.

	mmole
o-Nitrobenzoic acid	0.45
Picric acid	0.11
2,5-Dinitrobenzoic acid	0.04
o-Nitrotoluene	0.13
o-Dinitrobenzene	0.004
Nitric acid	0.40
Nitrogen	0.40
Nitrous oxide	0.07
Carbon monoxide	0.07

Oxidations were also performed with an excess of *o*-nitrotoluene over nitric acid. From such an experiment (0.365 mole *o*-nitrotoluene and 0.145 mole of 35 % nitric acid reacted for 30 min at 180° in a 300 ml autoclave) an additional reaction product was isolated and identified as 3,5-dinitrosalicylic acid (*ca.* 1 mmole).

The large amount of nitrogen formed (0.40 mmole) is in accord with the "diazotation" route (*3* → *4*). However, part of the nitrogen was probably formed in the oxidative degradation of picric acid.[6] In separate experiments with picric acid and 35 % nitric acid (molar ratios 1:3 and 1:10, respectively) in sealed tubes for 30 min at *ca.* 200°, considerable amounts of nitrogen were formed (0.30 and 0.14 mmole per mmole of picric acid degraded) and only 30 % and 5 %, respectively, of the picric acid could be recovered. Oxida-

tion of *p*-nitrotoluene, 1 mmole, under comparable conditions gives *p*-nitrobenzoic acid in almost quantitative yield and only 0.04—0.05 mmole nitrogen.

Taking into account the degradation of picric acid during the reaction, the total quantity of picric acid formed could be much larger than the 0.11 mmole found and possibly enough to account for the low yield of other organic products formed.

2,5-Dinitrobenzoic acid is likely to have been formed from *o*-nitrosobenzoic acid by nitration followed by reoxidation of the nitroso group. This was demonstrated by reacting *o*-nitrosobenzoic acid with nitric acid under similar conditions to give a mixture of picric acid, 2,5-dinitrobenzoic acid, and *o*-nitrobenzoic acid. The *para* nitration may be analogous to the *p*-hydroxylation [4,5] mentioned earlier or to the *para*-bromination of nitrosobenzene.[7]

The isolation of 3,5-dinitrosalicylic acid strongly supports the last reaction steps indicated in the reaction scheme. The failure to observe this product unless an excess of *o*-nitrotoluene over nitric acid was used in the reaction is obviously due to the rapid decarboxylation of 3,5-dinitrosalicylic acid in strongly acidic medium.[8]

The *o*-dinitrobenzene (which was also isolated as a by-product in the industrial oxidation of *o*-nitrotoluene with nitric acid) appears to have been formed largely from *o*-nitrobenzoic acid by replacement of the carboxyl group by a nitro group. This was confirmed by treating *o*-nitrobenzoic acid (1 mmole) with nitric acid (3 mmole, 50 %) at 220° for 30 min to give *o*-dinitrobenzene (0.08 mmole) but no *p*-dinitrobenzene. *p*-Nitrobenzoic acid similarly gave 4 % of *p*-dinitrobenzene (1 h at 240°).

In order to establish to what extent the nitro group of *o*-nitrotoluene is lost in the formation of picric acid, *o*-nitrotoluene was oxidized with $H^{15}NO_3$ and the picric acid as well as the nitrogen formed were analyzed by mass spectrometry. The picric acid contained very little ^{14}N. A separate experiment showed, however, a rapid exchange of nitro groups between picric acid and labelled nitric acid. Consequently, no safe conclusions are possible. The nitrogen formed contained approximately 70 % $^{14}N^{15}N$ and 30 % $^{15}N^{15}N$, indicating that some of it could have been formed *via* "diazotation" of the original nitro group of *o*-nitrotoluene.

The present work thus strongly supports the theory that the picric acid is formed *via* *o*-nitrosobenzoic acid and 3,5-dinitrosalicylic acid.

Experimental. Most of the oxidations were carried out in sealed glass tubes with a volume of approximately 4 ml. A typical charge was 1 mmole of *o*-nitrotoluene and 3 mmole of nitric acid (35 %). Some oxidations were made on a larger scale using a 300 ml titanium autoclave with magnetic stirring.

The tube was suspended in a vibrating device and immersed in a silicone oil bath. The bath temperature was raised at a rate of approximately 5°/min to 190° (reaction started at *ca.* 150°) and was allowed to decrease at a corresponding rate after *ca.* 5 min.

The tube was broken inside a bomb of stainless steel. The gases formed were collected and the neutral gases (N_2, N_2O, and CO) isolated and analyzed by gas chromatography (on an F & M 720 chromatograph programmed from 75 to 200° at 7.5°/min using Linde molecular sieve 5 A and hydrogen as carrier).

The reaction mixture was extracted with 1-pentanol and analyzed by thin-layer chromatography on fluorescent silica gel, using chloroform-ethanol-acetic acid (16:1:1) as developer. The spots were viewed in UV light or were made visible by reduction with stannous chloride followed by coupling with *p*-dimethylaminobenzaldehyde. For positive identification the reaction products were separated by column chromatography using a corresponding system, and IR and mass spectra and melting points recorded.

Picric acid and total carboxylic acids were determined by potentiometric titration of the 1-pentanol extract (after addition of acetone) with KOH in 2-propanol. Individual carboxylic acids were determined by gas chromatography of their methyl esters (after methylation with diazomethane). Nitric acid was determined by acidimetric titration of the aqueous phase after the extraction with 1-pentanol.

For mass spectrometric analysis, the picric acid was isolated from the reaction mixture *via* the slightly soluble tetrammine cupric salt, and the N_2 was purified from N_2O with a cold trap (−190°) and from CO by catalytical combustion and absorption of the CO_2 formed.

Neutral products were isolated from a separate oxidation by extraction with methylene chloride after neutralization with sodium bicarbonate, and determined by gas chromatography (using a Perkin-Elmer F 11 Mark II chromatograph and 15 % SE 30 on Chromosorb W at 110° and nitrogen as carrier gas. *p*-Nitrotoluene was used as internal standard).

The quantitative methods of analysis used were checked and were generally found to be reliable within ± 10 %.

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Interpretation of Proton Magnetic Resonance Spectra of α-Amino Acids in Terms of Rotational Isomers

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α-Amino acids, except glycine, are mixtures of 3 different rotational isomers (I, II, III) generated by rotation about the $C_\alpha - C\beta$ single bond. The life-time of such "rotamers" may be so short that PMR spectra of α-amino acids are effectively averaged at room temperature. In fact, earlier investigators [1-6] have all agreed that one PMR spectrum is observable per α-amino acid, meaning a rapid interconversion between I, II, and III. In a recent paper Aruldhas [7] has analyzed freshly recorded PMR spectra (100 MHz instrumental frequency) of DL-threonine (CH_3-$CHOHCHNH_2COOH$) and DL-valine ($(CH_3)_2CHCHNH_2COOH$) dissolved in D_2O (28°C). Aruldhas believes to have observed 2 superimposed spectra in each of these cases. His interpretation is that two of the rotamers, II and III, are separated by a very large barrier while the remaining barriers of the internal rotation potential function are low, causing the interconversions I → II and I → III to be rapid, while II → III is slow. We are unable to see why this is a satisfactory explanation of the alleged occurrence of 2 spectra since the interconversion II → III could still take place rapidly enough *via* the rotamer I to produce one and only one averaged spectrum per amino acid.

On the experimental side Aruldhas paper is in disagreement with, for example, the results obtained by Taddei and Pratt,[1] not cited by Aruldhas. These authors investigated PMR spectra (at 60 MHz) of DL-threonine and the diastereomeric *allo*-threonine under experimental conditions (pH, solvent, and temperature) similar to Aruldhas'. In separate experiments (as far as can be seen) Taddei and Pratt observed one methyl group spin-doublet for DL-threonine, and one for *allo*-threonine, the chemical shift difference being 0.12 ppm. At 100 MHz (Aruldhas' experiment) this corresponds to a chemical shift difference of 12 cps. Fig. 2(b) of Aruldhas' paper shows that there is a chemical shift difference between his two recorded methyl doublets of 11.5 cps. There can be little doubt, therefore, that Aruldhas' sample of alleged DL-threonine has been contaminated (to 30–40 %) by the *allo* isomer. To exclude any doubt (since the spectra of DL-threonine and *allo*-threonine are only details in the paper by Taddei and Pratt) we have again recorded the PMR spectrum of DL-threonine in D_2O at 60 MHz. The spectrum of the methyl group is a clear-cut doublet (Fig. 1, lines a and b of this paper) in contrast to the triplet to be expected according to Aruldhas.

In the case of DL-valine there is no "*allo*" isomer to complicate matters. Yet, two methyl group spin-doublets were again observed by Aruldhas and the spectrum was tentatively interpreted in anology with DL-threonine. This feature and the re-