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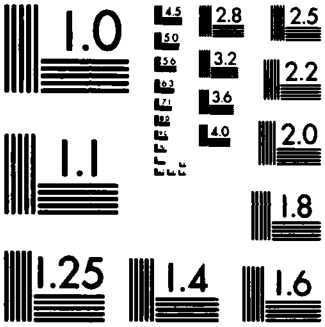

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REACTIVITY OF METAL NITRATES

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July 1982

Final Scientific Report for the period October 1978 through September 1981

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Preparative aromatic nitration, including recently developed methods, is reviewed. Previous attempts to use metal nitrates as nitrating agents are reviewed. The techniques developed for handling anhydrous titanium(IV) nitrate are described. Mechanistic and preparative investigations of titanium(IV) nitrate are described. Results and scope for future investigations are summarised.

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REACTIVITY OF METAL NITRATES

Introduction

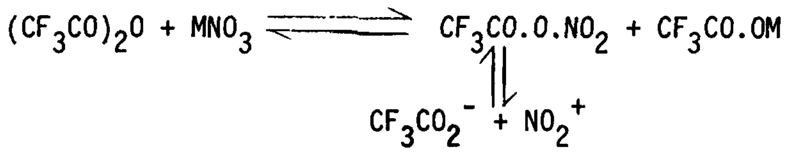
The substitution of aromatic compounds with nitro groups is from both preparative and mechanistic viewpoints one of the most studied[1] reactions of organic chemistry. Electrophilic nitration of aromatic compounds is often thought of, and in teaching used as *the* prototypical aromatic substitution. Despite the enormous effort which has been expended in this area, new mechanistic interpretations[2] are still being suggested, new details of the sequence of events in aromatic nitrations (for example the prevalence of *ipso* substitutions[1a,3a] and the importance of encounter controlled processes in some situations[3b]) continue to be worked out and new practical methods developed. Olah's group has been particularly active in his last area: recently, for example, they have described the use of perfluorinated resinsulphonic acid to catalyse nitrations using butylnitrate or acetone cyanohydrin nitrate[4a] and the use of mercury(II)nitrate - impregnated resinsulphonic acid to catalyse nitration in only 70% aqueous nitric acid with azeotropic removal of water.[4b]

A variety of reagent mixtures have been utilised as sources of the species (most generally the nitronium ion) which attacks the aromatic compound to lead to substitution but most often, mixtures of nitric acid with sulphuric acid, acetic acid or acetic anhydride have been used.[5] Very little indeed was known of the potential of pure anhydrous metal nitrates for this purpose before the commencement of the present study.

Metal nitrates and aromatic nitration - background

The Menke reaction[6a] involves the use of copper(II) nitrate in solution in acetic acid/acetic anhydride; any water added with the salt is removed by reaction with the anhydride. Later investigations[6b] utilised nitrates of iron(III), manganese(II), cobalt(II), nickel(II), mercury(II), silver(I), sodium(I), lithium(I) and bismuth(III), in each case rendered anhydrous by solution in acetic acid/acetic anhydride and reaction of the water with the latter. High yields of nitrated products were implied in some of these studies but this early work did not clarify the role of the metal nitrate, if any, and the observed nitrations could have been effected by nitric acid produced *in situ*. Certainly no comments were made on possible mechanisms and the observed substitution patterns were those to be expected from conventional electrophilic nitration.

In a very recent study,[7] of the use of inorganic nitrates in trifluoroacetic anhydride in chloroform at room temperature, the nitrations were ascribed not to the metal nitrate but to the formation of trifluoroacetyl nitrate as:



$$\begin{tikzcd}[column sep=small] (CF_3CO)_2O + MNO_3 \arrow[r, rightleftharpoons] & CF_3CO.O.NO_2 \arrow[d, shift left] & + CF_3CO.OM \\ & CF_3CO_2^- + NO_2^+ \arrow[u, shift left] & \end{tikzcd}$$

$CF_3CO.O.NO_2$ thus served as a source of nitronium ions. Differences between the various nitrates studied - those with ammonium, sodium(I), copper(II), silver(I), lead(II), cadmium(II) or chromium(III) cations were studied - were ascribed simply to differing solubilites in the medium employed.[7]

The first report[8] of the use of anhydrous titanium(IV) nitrate in nitration appeared in 1973. This preliminary communication described the addition of the solid anhydrous metal nitrate to excess liquid organic substrates (benzene, toluene, chlorobenzene and nitrobenzene) and apparently showed the efficient transfer of two nitro groups from each mol of metal nitrate to benzene to give nitrobenzene. However, only for benzene itself was any comment on yield made, by gas chromatography of the total product mixture.

A more detailed study by Coombes, reported in two papers[9] in 1974, employed titanium(IV) nitrate, zirconium(IV) nitrate, or nitrosonium tetranitratoiron(III) in solution in carbon tetrachloride for 0.5 h. Coombes' results for titanium(IV) nitrate showed only one nitro group per mol of the metal complex to be transferred to substrate. Benzene, toluene and chlorobenzene were examined and efficient formation of nitrobenzene, 2- and 4-mono-nitrotoluenes and 2- and 4-mono-nitrochlorobenzenes were demonstrated by g.c. analysis. No clear results could be obtained using titanium(IV) nitrate with nitrobenzene, anisole or biphenyl.

Coombes showed that the rate of reaction with simple aromatic substrates depended only on the concentration of metal nitrate and accordingly suggested the mechanism of substitution involved initial co-ordination of metal to the aromatic compound and then "intramolecular electrophilic substitution". Coombes also demonstrated a very low yield nitration of pyridine (giving only the 3-nitro-derivative) and of quinoline (giving mainly the analagous 3-nitro-derivative) with titanium(IV) nitrate.

Significant and thus potentially preparatively useful differences were observed with zirconium(IV) nitrate and nitrosonium tetranitratoiron(III), both of which nitrated pyridine at C-4, albeit in low yield, and quinoline, in good yield, at the 7 position.

Aims and brief summary of achievements

The suggestion[2a] that conventional strong acid nitration of *reactive* aromatic substrates may proceed *via* a cation radical was of considerable interest in the light of the earlier suggestion[10] by one of us (CDG) arising out of theoretical considerations, that nitration by anhydrous titanium(IV) nitrate may proceed *via* initial electron transfer from aromatic substrate to the metal i.e. *via* an aromatic cation radical. We speculated that the metal might be able to promote this type of mechanism, even for less reactive aromatic compounds, being well able to accept an electron and that there would certainly be differences in case of reaction and regioselectivity in nitration by this method, as compared to the more conventional methods which centre on attack by NO_2^+.

With this background, we embarked on a detailed investigation of the nitration potential anhydrous titanium(IV) nitrate (planning to move to other anhydrous metal nitrates at a subsequent stage, having established a firm factual framework for the titanium compound) in the hope of: (a) clarifying its mechanism of action, (b) assessing the reagent from the practical nitration standpoint, and (c) searching for novelty, perhaps in being able to nitrate normally inert substrates and/or perhaps in finding non-standard substitution regioselectivity.

Although we initially felt that it would be unnecessary to examine the simpler aromatic compounds which had been reported on previously, certain discrepancies which became apparent forced us in this direction and, in the event, we have now checked most of the literature reports and have enlarged the range of simple aromatic substrates which have been reacted with anhydrous titanium(IV) nitrate.

Additionally, we have examined several heterocyclic systems since they appeared to offer considerable potential novelty in case of nitration and/or positional selectivity.

A detailed study has been made of the nitration of toluene with titanium(IV) nitrate and several novel aspects of the reactivity of the metal nitrate emerged from this examination.

Therefore, it is now possible to be much clearer as to the potential utility of anhydrous titanium(IV) nitrate for aromatic nitration and also to begin to speculate in some greater authority as to its mode of action.

Techniques for handling and using anhydrous titanium(IV) nitrate

Titanium(IV) nitrate is a highly water-sensitive crystalline solid[11] which was routinely prepared by firstly collecting, at -78°C, dinitrogen pentoxide, produced from fuming nitric acid and phosphorus pentoxide and flushed in an oxygen-ozone stream through phosphorus pentoxide drying tubes; subsequent addition of titanium(IV) chloride, removal of excess dinitrogen pentoxide, followed by sublimations of the metal nitrate allowed the reproducible preparation of *ca.* 4 g samples from one conveniently sized run. The anhydrous metal nitrate was stored in a glove-box maintained water-free by the continuous passage of phosphorus pentoxide-dried, pure nitrogen.

All the early experiments were carried out in the glove-box until (see below) experiment design required otherwise. Normally, work was conducted with a 1:1 molar ratio of reactant and metal nitrate and on a scale corresponding to *ca.* 300 mg of titanium(IV) nitrate (0.001 mol).

In initial experiments only the solid metal nitrate was added to a large excess of substrate, however, it soon became clear that such a technique allowed too little control and in any case would not be generally applicable, for example to solid substrates. Accordingly, the use of inert dry solvents was adopted: carbon tetrachloride, chloroform (alcohol free) and methylene chloride have all been used and shown not to react with the metal nitrate. The solvents were purified, distilled and stored over thoroughly dried (250°C) 4A molecular sieves.

For reactions at room temperature, the entire experiment was carried out in the glove box : the substrate in solution was added to a solution of the metal nitrate stirred magnetically. Working on the scale described above has not revealed any problems associated with exothermicity of mixing or reaction. An (arbitrary) procedure established early in this project was consistently adopted, that is, solutions were separated after the reactants had been in contact for 0.75 h and, unless otherwise stated, the experiments described below can be assumed to be of this duration.

The work-up of solutions and the isolation of products involved the addition of water (outside the glove-box) to the stirred reaction mixture, (including the basification of the resulting aqueous acidic layer, if the substrate structure necessitated this), separation of organic phase and re-extraction with further portions of solvent to give a solution of product(s) and any unchanged starting material. Preparative layer and column chromatography, using appropriate adsorbents and eluants have allowed separation and isolation of products.

It had been the aim at the outset to view each experiment from the preparative chemist's standpoint, i.e. to try and assess ratios of products and yields of products *isolated*, rather than specifying these parameters by analysis (e.g., gas chromatography), since it is what can actually be isolated which is of relevance to the practical chemist. This emphasis on the isolation of products inevitably resulted in a slower rate of progress than would have been allowed by the simple analysis only of total product mixture, as employed by previous investigators.[8,9]

In some experiments, particularly those in which rather complex mixtures were produced, this principle had to be set aside in favour of gas chromatographic analysis of the total unseparated product mixture.

In such cases, where a complex product mixture was not preparatively separated, but analysed only, the technique of gc-ms (gas chromatography linked with mass spectrometry) proved to be extremely powerful. The analytical separation of components was first established in terms of suitable column packing, temperature etc. and then these conditions applied to a column linked directly to a mass spectrometer. The peaks were monitored as they emerged from the chromatography column and a complete mass spectrum of each was recorded. This powerful combination then allowed a statement to be made, not only of the relative quantities (questions of detector response aside) but also (in most instances) a good estimate could be made of the chemical constitution of each fraction, certainly the number of nitro groups which had been substituted was obtained. The availability of authentic samples of the suspected products made verification of product component structure a simple matter.

In cases where authentic samples were not available, a preparative thin-layer chromatographic separation was carried out and each component isolated, purified and identified using, mainly, mass spectrometry and NMR spectroscopy at 90 or 300 MHz, where necessary.

As the range of substrates studied was extended, situations arose where *either* no nitration occurred under the room temperature 0.75 h conditions described above, *or* such a complex mixture of products were produced that no worthwhile products or results could be obtained. It was clearly necessary to study some of the reactions of titanium(IV) nitrate both at higher temperatures and at lower temperatures, respectively. Working in a glove-box does not lend itself easily to either of these modifications and so experiments conducted outside the glove-box were embarked upon.

Surprisingly and encouragingly, it proved to be relatively easy to handle the anhydrous metal nitrate outside the glove-box. Reactions were carried out under a stream of nitrogen and, as before, in rigorously dried solvents and apparatus. The solid metal nitrate itself was handled only in the glove-box and transferred to the reaction vessel only after dissolving in the solvent to be used and using a syringe with introduction through a septum cap on one of the necks of the reaction flask. As before the substrate solution was added to the metal nitrate solution with stirring.

For reactions at low temperature carbon tetrachloride (m.p. -20°C) was abandoned in favour of chloroform (m.p. -63.5°C), with cooling to *ca.* -60°C being achieved using an acetone/solid carbon dioxide bath (the temperature of the bath was monitored). Solutions were stirred at all times: during mixing of reactant and reagent and then continuously throughout the procedure. For reaction at higher temperatures refluxing chloroform (b.p. 61°C) was employed; the absence of any deterioration of titanium(IV) nitrate in refluxing chloroform for 0.75 h was established.

Reaction of titanium(IV) nitrate with aromatic compounds

A broad survey has been conducted on the products formed upon reaction with titanium(IV) nitrate in chloroform solution, for 45 min at room temperature (unless otherwise specified) for a large number of aromatic and heteroaromatic compounds. The percentage conversions of reactant into products were determined by gas chromatography and, in some instances, by isolation using thin-layer chromatography. In the latter case the yields obtained are lower than the former but they are a more realistic assessment of the yields which could be expected on a preparative scale. The results are summarised in Table 1 and described below.

Benzene does not react with titanium(IV) nitrate in chloroform solution at -60°C. At room temperature the smooth formation of nitrobenzene was observed, with a hint that a second nitration was taking place, but at a slower rate. This second nitration was not observed by previous workers[8,9] was confirmed by carrying out the reaction for 24 h at room temperature, whence 23% of *meta*-dinitrobenzene had been produced. This effective dinitration of benzene should be compared with the more vigorous (temperature) conditions necessary to achieve dinitration with conventional nitrating conditions.

The reaction proceeded in at least two phases; on admixture of aromatic and metal nitrate, a yellow colouration was produced which faded after about 15 mins, with the formation of a white precipitate which easily dissolved on aqueous work-up.

Toluene was also untouched by titanium(IV) nitrate in chloroform at -60°C. However, it reacted faster than benzene at room temperature, thus after 0.75 h the 2:1 mixture of *para*- and *ortho*-mono-substitution products was already being further nitrated: 2,6-dinitrotoluene (5%) and 2,4-dinitrotoluene (45%) being produced. This result is at variance with the earlier reports[8,9] of only mono-nitration of toluene by titanium(IV) nitrate at room temperature. Also, it shows that, whatever the detailed mechanism of action of titanium(IV) nitrate as a nitrating agent, the presence of an alkyl group on the aromatic substrate enhances the rate of substitution. Furthermore, this result demonstrates that each molecule of the metal nitrate must be providing more than one nitro group. This reaction has been studied in considerable detail, see later and Table 2.

As with benzene, an immediate yellow colouration was produced on mixing the reagent and substrate solutions; less time was required for the fading of this colour and the formation of a precipitate.

Xylenes; Ortho, meta and *para* isomers were all nitrated, with some dinitration being observed, by titanium(IV) nitrate at room temperature. None of the *meta* isomer remained after the standard 45 min. reaction period; by this criterion, the *para* isomer was the least reactive. Also, the *para* isomer was the only one of the three for which no dinitration was observed. The major products from *ortho*-xylene were the 3-(20%) and 4-(36%) mono-nitro derivatives but three dinitro derivatives amounted to (16%) in all. The major product from the *meta*-isomer was the 4-nitro derivative (55%) but here two dinitro-derivatives, 2,4-di- and 4,6-di- amounted together to a 41% yield. The introduction of a nitro group in the 2-position between the two methyl groups is noteworthy.

As with the simpler aromatics, the admixture of reactants gave a yellow colour which faded with formation of a precipitate.

Mesitylene produced mono- and disubstitution products in roughly equal proportions after reacting with titanium(IV) nitrate at room temperature for 45 mins. The initial yellow colour was discharged more rapidly than in the reactions described above. The high total yield (99%) of mono and disubstitution products, outlaws the possibility that any appreciable percentage of side-chain substitution occurred (*cf.* Ref. 2b).

t-Butylbenzene like toluene, had all been consumed during the standard reaction time; an appreciable percentage (20%) of 2,4-dinitration accompanied the formation of the main product, the 4-nitro derivative (75%).

1,2-Diphenylethane (bibenzyl). Since appreciable amounts of dinitrated species had been obtained for the aromatic compounds described above, even after a short reaction time with titanium(IV) nitrate, the speculation arose that the aromatic nucleus and the metal nitrate may remain closely associated after a first nitration, thus facilitating a second substitution. The results obtained with bibenzyl seem to support this view for, although an appreciable (13%) amount of unreacted bibenzyl was obtained, 20% of dinitrated species were obtained in addition to the main 2- and 4- mono nitro-products, obtained in 7 and 13% yield, respectively. These yields are minimal, being obtained by a preparative thin-layer chromatographic separation and isolation process once again, in a manner quite comparable to toluene, the initial yellow of the mixed reactant solution faded with precipitation after 5 mins.

Biphenyl, on admixture with the metal nitrate in solution produced not a yellow, but a red colouration which rapidly produced a precipitate. The different colour observed in this case strongly suggests that the colours produced in these nitrations are associated with the aromatic compound. Here again nearly 40% of the product isolated after 45 mins of reaction was dinitrated, with the two nitro groups being introduced on different rings of the mono- nitro biphenyls (53%), on appreciable percentage (17%) was the 2-isomer.

Naphthalene and titanium(IV) nitrate produced an immediate dark brown colour followed rapidly by precipitation. The higher reactivity to conventional electrophilic substitution of the bicyclic system was nitrated in the present study for 45 mins, 64% of 1-nitro naphthalene and 26% of dinitronaphthalene were obtained. Most interestingly, the dinitronapthalene was a single isomer, the 1,8-dinitro-derivative. This result can be taken as further evidence for a close association of the aromatic nucleus and metal nitrate after the initial nitration; indeed, the orientation of the second nitro group would even suggest that very little re-aligning of the aromatic molecule took place between successive nitrations.

Chlorobenzene, which in conventional electrophilic nitration is less reactive than benzene but nonetheless has a tendency to nitrate at *ortho*- and *para*-positions was, like benzene and toluene, unaffected by titanium(IV) nitrate at -60°C. At room temperature a quite clean mixture of mono-substitution products was obtained in 80% yield; this was shown to comprise 2- and 4-nitrochlorobenzene, in a ratio of 1:2.5. Once again an initial yellow colour was observed. No dinitration took place.

Nitrobenzene. Early in our investigations we showed that Amos's observation[8] that neat nitrobenzene is nitrated by the addition of solid titanium(IV) nitrate is valid. We also confirmed that the major nitration product under these conditions was the *meta*-isomer (87%) with smaller amounts of *ortho*- (12%) and *para*-isomers (1%) being produced. However, such a technique allows little control, especially over local temperature rises and since, in any case, we needed to compare the reaction of this substrate with that of benzene the reaction was repeated in chloroform. At room temperature and in agreement with the results obtained with benzene, virtually no *meta*-dinitrobenzene had been formed after 0.75 h; exposure to the reagent for 24 h, however, led to the formation of *meta*-dinitrobenzene in 17% yield.

This much slower nitration of nitrobenzene as compared to benzene is consistent with the observation that the yellow colour of the mixed reactant solution only began to fade after 90 mins, when precipitation also started.

Benzonitrile produced a very surprising result. The first observation was that no yellow colouration resulted from treatment with the metal nitrate. This negative sign was substantiated, for no nitration took place in the standard 45 min. period, nor after 24 h at room temperature, nor indeed when the reactant solution was refluxed.

N,N-Dimethylbenzamide also proved to be completely resistant to nitration by the metal nitrate, 85% being recovered unchanged after one day's exposure.

Benzoic acid. Following the failure to nitrate either benzonitrile or N,N-dimethylbenzamide, it was not surprising that no nitration of benzoic acid occurred at room temperature. However, at reflux in chloroform substitution did occur and, after esterification of the products to facilitate analysis, it was shown that 71% of the *meta*-nitro-acid had been formed, together with small amounts of the two other isomers.

Methyl benzoate nitrates by conventional means to give almost exclusively the *meta*-substitution product. With titanium(IV) nitrate at room temperature there was a yellow colour produced, but no precipitate, after 45 mins. of reaction and no nitration was detected. However, precipitation did start from the reactant solution after about 3 h and after a day, besides 18% of starting material, 44% of methyl *meta*-nitrobenzoate, together with an appreciable amount (33%) of the *para*-isomer had been formed. Alternatively, on bringing the solution of metal nitrate and ester to reflux, precipitation began immediately; after 45 mins. at reflux *meta*- (63 %) and surprisingly *ortho*- (25%) nitrated products had been formed with only a small amount (4%) of the *para*-isomer.

Acetophenone behaved like methyl benzoate in being resistant to titanium(IV) nitrate at room temperature but smoothly nitrated at reflux. No dinitration was observed. The proportion of the 'unconventional' *ortho*-isomer was again high, representing 40% of the nitrated material.

Aniline was the first powerfully activated aromatic examined. On admixture with the metal nitrate, immediate dark colouration occurred and no identifiable products could be isolated. With the idea that part of the difficulty might be associated with presence of N-hydrogens, an N,N-disubstituted derivative was examined.

N,N-Dimethylaniline, upon reacting with titanium(IV) nitrate gave an orange-red colouration, with rapid formation of solid material at room temperature. A similar behaviour was observed even at -60°C but at the lower temperature the reaction products were somewhat less complex; the main products were the *ortho*- (17%) and *para*- (32%) derivatives. Even at -60°C, some dinitration occurred; also some N-demethylation was observed and this was more significant in the reaction at 21°C, where 22% of the products had lost one methyl group. At room temperature, the 2,4-dinitro-derivative was the major product (30%) amongst a complex mixture of products.

This oxidative cleavage of a methyl group from a basic nitrogen atom is of interest in its own right (and reminiscent of the reported[12] oxidation of ethers with anhydrous copper(II) nitrate). In a different context this reaction would be worthy of a separate investigation, perhaps utilising other amines, where nitration would not be a competing process.

Acetanilide. Despite the complexity encountered with aniline, the corresponding amide, acetanilide, though having an N-hydrogen atom, was nitrated without tar formation, although this was not accomplished efficiently. After reaction for 24 h at room temperature, 28% of the starting material remained, together with roughly equal amounts of *ortho-* (28%) and *para-* (31%) mono-substitution products. No dinitration was observed. *N-Methylacetanilide* was examined in the hope that a more efficient substitution would result, as compared to acetanilide, in the absence of a N-hydrogen atom. However, the reverse proved to be the case, for after one day at room temperature nearly 60% of starting material remained, together with approximately equal quantities of the *ortho-* (15%) and *para-* (18%) mono-substitution products. No dinitration was observed.

Pyridine. One of the initial aims of the investigation was to be able to achieve ring-C-nitration of the difficulty substituted π-deficient heterocycles. A previous report[9] seemed to auger well for this hope, however, we found that pyridine could *not* be nitrated at room temperature, even over a long time, or at reflux in chloroform solution, or indeed at reflux in neat pyridine. This was despite the formation of a yellow coloured solution, followed by the appearance of an insoluble colourless gum. Thus, this conclusion is in contrast to the previous report[9] that pyridine could be nitrated with titanium(IV) nitrate albeit in only 6% yield. This contrast is heightened by the fact that, in the present investigation, dinitration of toluene had been easily achieved where the workers describing the nitration of pyridine had *not* reported dinitration of toluene.

Quinoline proved to be more amenable to nitration by titanium(IV) nitrate than did pyridine and this reaction provided the interesting result that substitution occurred only on the pyridine ring and not the benzene ring. From an initial green solution a red insoluble oil was formed of the total product after 45 mins. at room temperature, 50% was unchanged starting material, 8% was 2-nitroquinoline, 16% was 3-nitroquinoline and 28% was 4-nitroquinoline.

Isoquinoline reacted with titanium(IV) nitrate to provide one of the surprises of this investigation. Thus, under the standard reaction conditions, in addition to starting material, only an adduct, 1,2-dihydro-1-hydroxy-2-nitroisoquinoline was obtained. This product was obtained as a crystalline material which could be purified by chromatography, but the material was unstable and slowly decomposed in a flask, even at $0^{o}C$. 4-Nitro-isoquinoline was identified amongst the decomposition products.

Indole and 1-Methylindole. Indole is an example of a heterocyclic aromatic compound of a reactive nature and of the π-excessive type, as opposed to the π-deficient type, pyridine. Indole proved, to be as would be anticipated, much more sensitive to the reaction with the metal nitrate, indeed, from the reactions with simple heterocycle no discrete products could be isolated.

To avoid probable complications associated with the presence of N-hydrogen groups, 1-methylindole was employed. At room temperature, a very complex mixture of compounds was produced in the reaction of 1-methylindole with titanium(IV) nitrate, as assessed by thin-layer chromatographic analysis, such that it was not deemed worthwhile to study further. On reducing the reaction temperature to $-60^{o}C$ a mixture of three compounds, including unchanged starting material (63%) was formed, of which the major component was shown to be a dimer. The formation of indole dimers is well known[14] and is usually catalysed by mineral acids. However, it was shown that aqueous nitric acid of the strength produced during work-up of the attempted nitration with titanium(IV) nitrate was insufficient to bring about the dimerisation of 1-methylindole. It must be concluded that, in this case the dimerisation is catalysed by the metal nitrate, perhaps by its serving as a Lewis acid. Furthermore, a minor component of the reaction products was shown to be a mono-nitrated dimer. In the hope of increasing the yield of this substituted dimer the reaction was repeated at an intermediate temperature, $-5^{\circ}C$; however, neither of the dimers was observed at this temperature and since the complexity of the crude product was equal to that obtained at room temperature, no further investigations were made.

1-Phenylsulphonyl indole was investigated on the basis that the partially reduced nucleophilicity of the heterocyclic ring, carrying as it does the electron withdrawing phenylsulphonyl substituent, might allow for a more controlled nitration, perhaps allowing substitution in both of the aromatic rings. Indeed, this turned out to be the case. At room temperature (a comparable but slower reaction occurred at $-60^{\circ}C$) two mono-nitration products were obtained in 60% yield and in an approximately 1:1 ratio and these were identified spectroscopically as the 3- and 5-mono-nitro derivatives. These structures were confirmed by alkaline hydrolyses, predictably much easier for the 3-nitro-isomer than for the other, to the corresponding 3- and 5-nitroindoles. It is noteworthy that no nitration of the phenylsulphonyl ring was observed.

1,2,3,4-Tetrahydrocarbazole. With the idea that blocking the two reactive positions on the heterocyclic ring might provide a cleaner reaction, the nitration of 1,2,3,4-tetrahydrocarbazole was investigated. However, a complex mixture of products resulted from the treatment of this compound with the metal nitrate.

Pyridine-N-oxide gave some indication that nitration is possible with titanium(IV) nitrate and the 'usual' 4-nitro-derivative was isolated and identified. However, the very poor recovery of the reaction products must leave open the question as to the fate of the bulk of material used.

Titanium(IV) nitrate and toluene - a detailed study. The mechanism of aromatic nitration with titanium(IV) nitrate.

When a chloroform solution of toluene was mixed with a solution of titanium(IV) nitrate, the solution assumed an immediate yellow colour. After about four minutes, a white solid was precipitated and most of the colour faded. After several hours the precipitate was greyish and no colour remained in solution.

During the work-up of products at the 'yellow' stage, the addition of water caused an immediate discharge of the colour. Upon work-up after precipitation, the precipitate dissolved easily in water giving two colourless liquid phases.

A colouration was observed in all cases where nitration of an aromatic compound was achieved; the colour was deeper and more orange or red for these aromatic substrates carrying mesomerically electron releasing substitutents.

This intriguing behaviour, coupled with questions raised by earlier work,[8,9] as to the availability of the four nitrato groups of the metal nitrate, led to a detailed study of the nitration of toluene with titanium(IV) nitrate, the results of which are summarised in Table 2 and presented below. Quantitative analyses were carried out using gas chromatography.

Before the appearance of a precipitate and even with a large excess of metal nitrate, no nitration had occurred and the aromatic substrate could be recovered essentially quantitatively (Runs 1, 5, 9, and 14). However, analysis *immediately after* precipitation had been observed showed that appreciable nitration had occurred. (Runs 2, 6, 10, and 15). Even dinitration had occurred at this stage, when a large excess of metal nitrate was used (Run 15).

The gradual accumulation of nitrated and dinitrated products after longer reaction times showed that the metal nitrate was capable of donating more than one nitro-group. In the limit, three of the four nitrato groups effected nitration of toluene (Runs 12 and 13). It is also clear that the "second" nitro-group is transferred to the aromatic substrate more slowly than the "first", and the "third" more slowly than the "second". (Compare Runs 10, 11, and 12 and Runs 6, 7 and 8).

In the conventional electrophilic process, nitration of nitro-aromatics is considerably slower than that of the corresponding hydrocarbon; they are 'deactivated'. This proved also to be the case in the titanium(IV) nitrate nitration of toluene (Run 13 and compare Runs 3 and 7 and 7 with 11).

In no instance was any trinitro toluene detected, even when sufficient metal nitrate was used to provide three mole equivalents of the "first" and most potent nitrating nitrato-group. This was true even at reflux (Runs 17 and 23) and in space of the fact that at 21°C dinitration was complete after 45 minutes at 21°C (Run 16).

Since it was clear that nitration continued after formation of a precipitate; it followed that, either a soluble nitrating species remained in solution or that the solid material was capable of nitrating toluene. A sample of the precipitate removed after 45 mins. showed a Ti:N ratio which corresponded to the loss of between one and two nitro groups from the original $Ti(NO_3)_4$ molecule. The precipitate also contained some organic material, not derived from solvent, and corresponding to about $^1/_5$ mole equivalent of aromatic per mole of titanium. No further nitration occurred in the solution after removal of the precipitate. (Compare Runs 11 and 18) and the precipitate was shown to be capable of nitrating toluene (Run 19).

In earlier work,[9] with titanium(IV) nitrate in CCl_4 solution, very little dinitration had been reported. A comparison of chloroform, methylenechloride and carbon tetrachloride showed the first two solvents to be of equal suitability and to be superior to carbon tetrachloride (Runs 20, 21 and 22).

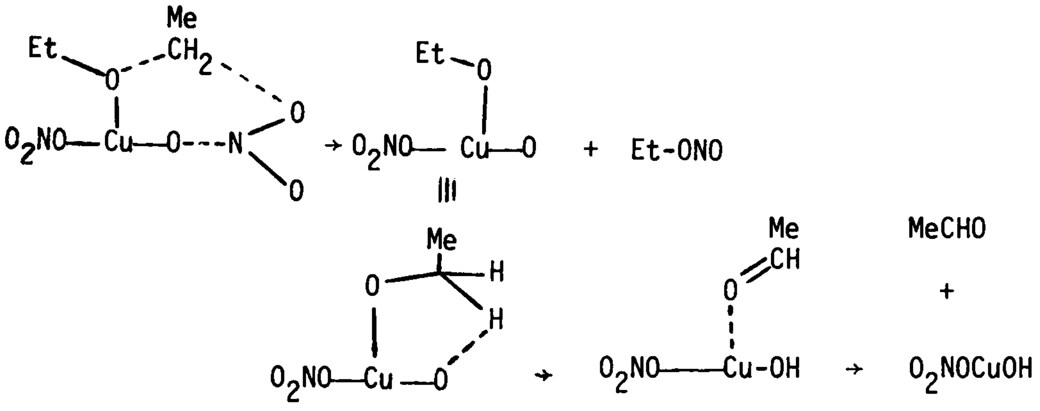
In summary, the nitration of toluene by titanium(IV) nitrate in $CHCl_3$ at 21°C was found to involve an induction period of 3 to 4 mins. the shorter times corresponding to higher metal nitrate concentrations, during which time a distinctive yellow colour present and no nitration occurred. The formation of a precipitate typically after 5 mins. and the fading of the colour appeared to be associated with ring nitration and the loss of the "first" nitro group from reagents; after 45 mins, nearly all of the "second" nitro group had been transferred to toluene and after one day all of the "third" had been utilised. Successive nitrato groups are decreasingly potent as nitrating agents. No evidence for the utilisation of the "fourth" nitrato group was obtained. Titanium(IV) nitrate was not observed to nitrate dinitrotoluene.

The Raman spectrum of a solution of titanium(IV) nitrate in carbon tetrachloride or chloroform solutions showed no evidence for the presence of nitranium (NO_2^+) cations. Since reaction with toluene proceeded rapidly past the 'yellow' stage, and since a comparable colour was produced with methyl benzoate, the yellow-coloured mixture of titanium(IV) nitrate and methyl benzoate was also examined by Raman spectroscopy. Again no evidence for the presence of nitronium ions was found.

Since it had been suggested[10] that titanium(IV) nitrate nitration may involve, as the initial step, electron transfer from an aromatic molecule to the metal nitrate, the thesis emerges that the 'yellow' stage represented just such a charge-transfer complex. This charge-transfer complex would involve the formation of radicals. Accordingly using toluene as the substrate, the 'yellow' solution was frozen by immersion in liquid nitrogen and its electron spin resonance spectrum recorded at 77K. A clear indication of radical formation was obtained; the spectrum contained resonances at g values of1.996 and 1.994 and could be consistent with the formation of a titanium(III) complex. No evidence for the formation of a radical cation deriving from toluene was obtained. Furthermore, some electron spin resonance activity was observed for the solution at 77K, after the frozen solution was allowed to warm to room temperature and the precipitation of the solid had occurred (after *ca.* 10 mins.). Similar electron spin resonance signals were observed for the 'yellow' solutions formed when titanium(IV) nitrate reacted with benzene and methyl benzoate.

Thus, an indication has been obtained that the initial stage, of the reaction between titanium(IV) nitrate and an aromatic molecule, involves radical formation, consistent with the charge-transfer concept,[10] prior to the nitration. Further studies are, however, required to establish the nature of the radical species.

In a nitration by titanium(IV) nitrate, nitrogen-oxygen bonds, of the formally negatively charged nitrato-groups which are utilised, must be broken. Further, it is necessary to envisage a process in which nitrogen and not oxygen becomes linked to the aromatic. The process must be different, then, from that suggested[12] for the oxidative cleavage of di-ethyl ether with copper(II) nitrate which gives ethyl nitrite and acetaldehyde, for in this, the initial co-ordination of ether oxygen to the metal was pictured as being followed by O-N cleavage but with NO_2 *oxygen*, not nitrogen, attack on the atom adjacent to the co-ordinating oxygen.



Any mechanism suggested for the nitration of aromatic systems by titanium(IV) nitrate must take into account the observed similarity, in overall effect, of conventional nitronium ion nitration and titanium(IV) nitrate nitration. Substituents on the aromatic ring have, at least qualitatively the same effects on the metal nitrate and nitronium nitrations, both in terms of activity and deactivating the aromatic substrate and in their directing effects. However, as indicated above, no evidence for the intervention of nitronium ions was obtained for the metal nitrate process and the relatively facile double nitration of benzene by titanium(IV) nitrate, as compared to NO_2^+, argues for a different mechanism.

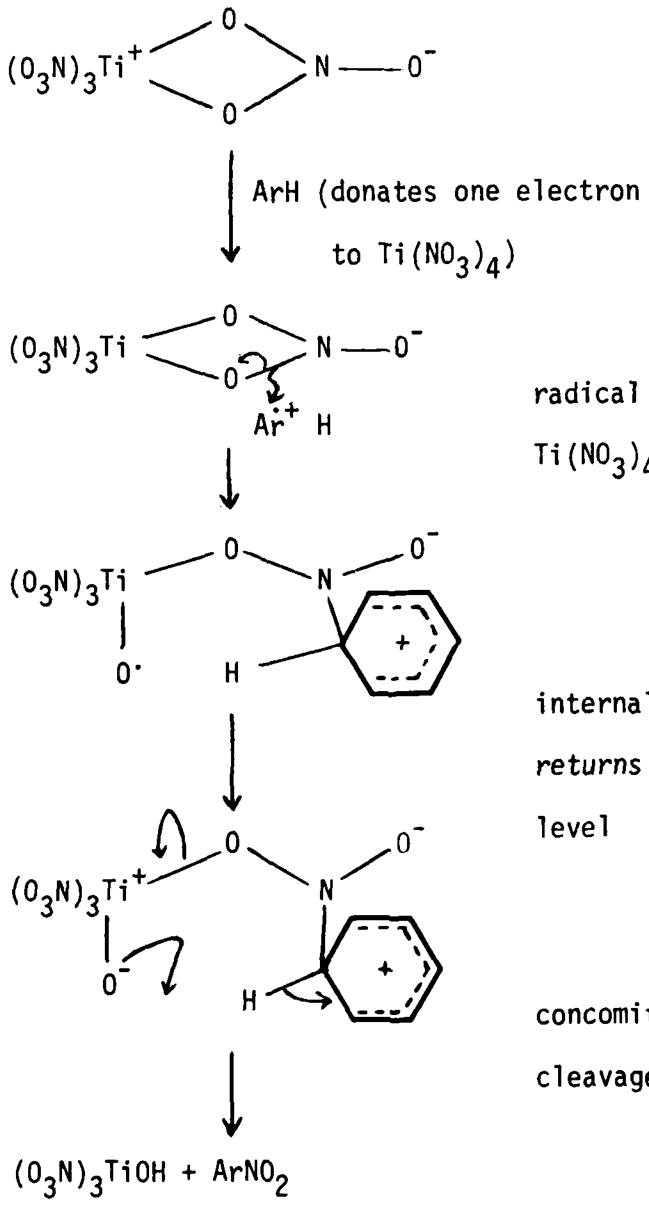
Generally speaking, aromatic substitution by a radical process, such as that involving the formation of an initial charge-transfer complex,[10] would produce the same type of activation and regio selective picture as electrophilic substitution : the recent reports[13] of $Mn(III)_2$ and Ce(IV) promoted nitro methylations illustrate this, where the metal converts nitromethane into a nitro methyl radical which attacks the aromatic system.

Ridd's experiments,[26] in which reaction of mesitylene with ceric ammonium nitrate in acetonitrile was studied, gave *only* side-chain nitrite *via*, it was assumed, the aromatic cation radical. Reaction with ceric ammonium nitrate in the presence of added N_2O_4 gave a 3:1 mixture of ring-*nitrated* material and side-chain nitrite. No side-chain nitrite was observed in the present work in the efficient ring nitration of mesitylene by titanium(IV) nitrate.

Also of relevance is the side-chain acetoxylation of alkyl benzenes with ceric ammonium nitrate in acetic acid, a process believed to involve the reduction of Ce(IV) to Ce(III) and the concomitant the formation of an aromatic cation radical.[15] With mesitylene and anisole, only ring acetoxylation was observed[16] and again it was assumed that a cation radical is involved.

At this stage, the available facts are consistent with the original postulate[10] that the titanium(IV) nitrate nitration process is initiated by electron together from aromatic to metal. It seems likely that aromatic cation radical and metal nitrate remain closely associated whilst electron and bond reorganisation takes place. The scheme below is an attempt to represent this process in a step-wise manner. For simplicity, only one of the four nitrato groups is represented in detail:

Scheme for the nitration of aromatic molecules by $Ti(NO_3)_4$



radical cation reacts with $Ti(NO_3)_4$ via N-O bond cleavage

internal redox process, titanium returns to original oxidation level

concomitant Ti-O and C-H bond cleavage, with O-H bond formation

Conclusions and scope for future investigations

The work described above has defined, to a considerable extent, the potential and some limits of the utility of titanium(IV) nitrate as a nitrating agent, in particular for the introduction of nitro groups onto aromatic molecules. We have found that the compound is reasonably readily prepared from inexpensive starting materials, is conveniently stored and handled, provided that its sensitivity to moisture is recognised. Reactions are usually accomplished in a short time (one or more hours) at ambient temperature in a suitable solvent (chloroform) and product isolation is a relatively straightforward procedure. Titanium(IV) nitrate is more potent than conventional nitrating agents and can lead to a more rapid double nitration (e.g. with benzene) of aromatic molecules, however, the regioselectivity observed generally corresponds to that of conventional nitration. Some instances of novel substitution were observed, in particular for polycyclic benzenoid and heteroaromatic systems.

Extensions of this study would include the following:

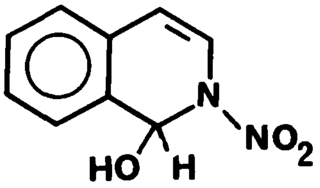
(1) A more systematic investigation of the value of controlling the reaction temperature to achieve an improvement of the yield and/or a simplification of the product distribution. This would also involve the use of molten titanium(IV) nitrate at *ca.* 50^{o}C to obtain vigorous nitrating conditions.

(2) Further investigations of the nitration of polycyclic benzenoid and heteroatomic systems to further define novel substitutions observed with these molecules.

(3) Systematic investigations of the reaction of titanium(IV) nitrate with ethers or amines in the absence of aromatic rings. Thus, there were indications during the above study that interesting interactions were

taking place the formation of 1,2-dihydro-1-hydroxy-2-nitroisoquinoline (1) as an entirely unanticipated product provokes speculation as to the sort of structures which might be produced, in analogy, from quinazoline (2) (? → (3)), 1,3,5-triazine (4) (? → (5)), or even 1,3,4-triazole (6) (? → (7)).

1



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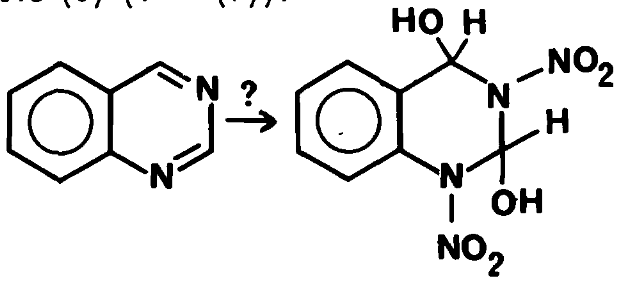

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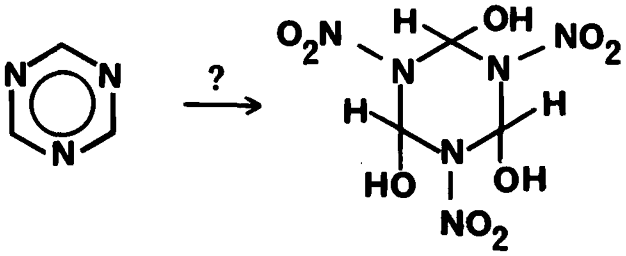

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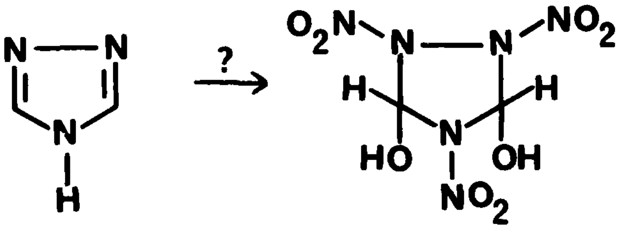

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(4) Although considerably more is now known in mechanistic terms, concerning the mode of action of titanium(IV) nitrate, much more needs to be done; of particular interest is to establish the species formed during the apparent initiation period, during which the reaction mixture becomes coloured but no nitration occurs.

References

1. For recent reviews see (a) R. B. Moodie and K. Schofield, *Accounts Chem. Res.*, 1976, 9, 287; (b) G. A. Olah and S. J. Kuhn, *Friedel-Crafts Relat. React.*, 1964, 3, Part 2, 1393; C. K. Ingold, "Structure and Mechanism in Organic Chemistry", 2nd ed., Cornell University Press, Ithaca, N.Y., 1969, Chapter VI; L. M. Stock, *Prog. Phys. Org. Chem.*, 1976, 12, 21; J. G. Hoggett, R. B. Moodie, J. R. Penton, and K. Schofield, "Nitration and Aromatic Reactivity", Cambridge University Press, 1971; J. H. Ridd, *Acc. Chem. Res.*, 1971, 49, 248; R. Taylor in "Comprehensive Chemical Kinetics", Vol. 13, C. H. Bamford and C. F. H. Tipper, Ed., 1972, pl; S.R. Halartshorn and K. Schofield, *Progress in Organic Chemistry*, 1973, 8, 278; *Advances in Phys. Org. Chem.*, 1978, 16, 1.

2. See for example (a) C. L. Perrin, *J. Amer. Chem. Soc.*, 1977, 99, 5516, and reply by (b) M. R. Draper and J. H. Ridd, *J. C. S. Chem. Comm.*, 1978, 445.

3. (a) K. Fujiwara, J. C. Giffney, and J. H. Ridd, *J. C. S. Chem. Comm.*, 1977, 301; T. Banwell, C. S. Morse, P. C. Myhre, and A. Vollmar, *J. Amer. Chem. Soc.*, 1977, 99, 3042; J. T. Geppert, M. W. Johnson, P. C. Myhre, and S. P. Woods, *J. Amer. Chem. Soc.*, 1981, 103, 7057. (b) J. W. Barnett, R. B. Moodie, K. Schofield, P. G. Taylor, and J. B. Weston, *J. C. S. Perkin II*, 1979, 747.

4. (a) G. A. Olah, R. Malhotne and S. C. Narang, *J. Org. Chem.*, 1978, 43, 4528; G. A. Olah and S. C. Narang, *Synthesis*, 1978, 690; (b) G. A. Olah, V. V. Krishnamurthy and S. C. Narang, *J. Org. Chem.*, 1982, 47, 596.

5. F. Effenberger, *Angew. Chem. Int. Ed. Engl.*, 1980, 19, 151; G. Olah, *Aldrichimica Acta.*, 1979, 12 (3), 43.

6. (a) J. B. Menke, *Rec. Trev. Chim.*, 1925, 44, 141 and 269; (b) G. Bachorach, *J. Amer. Chem. Soc.*, 1927, 49, 1522; L. Spiegel and H. Haymann, *Ber.*, 1926, 59, 202; V. Davey and J. R. Gwilt, *J. C. S.*, 1950, 204 and 3348.

7. J. V. Crivello, *J. Org. Chem.*, 1981, 46, 3056.

8. D. W. Amos, D. A. Baines, and G. W. Flewitt, *Tetrahedron Letters*, 1973, 3191.

9. R. G. Coombes and L. W. Russell, *J. C. S. Perkin I*, 1974, 830 and 1751.

10. C. D. Garner, I. H. Hillier and M. F. Guest, *J. Chem. Soc., Dalton*, 1975, 1934.

11. For discussion of metal nitrate structure see C. C. Addison, N. Logan, S. C. Wallwork and C. D. Garner, *Quart. Rev. Chem. Soc.*, 1971, 25, 239.

12. L. C. Coard and R. E. Powell, *J. Chem. Soc.*, (C), 1967, 296.

13. M. E. Kurz, P. Ngoviwatchai, and T. Tantrarant, *J. Org. Chem.*, 1981, 46, 4668; M. E. Kurz and P. Ngoviwatchai, *ibid.*, 4672.

14. G. F. Smith, *Advances in Heterocyclic Chemistry*, 1963, 2, 287.

15. E. Baciocchi, L. Mandolini, and C. Rol, *Tetrahedron Letters*, 1976, 3343; *idem.*, *J. Org. Chem.*, 1977, 42, 3682.

16. E. Baciocchi, S. Mei, C. Rol, and L. Mandolini, *J. Org. Chem.*, 1978, 43, 2919.

TABLE 1

Products from reaction of titanium(IV) nitrate with aromatic compounds in chloroform solution. Reactants were in a 1:1 molar ratio. Reactions were worked up by addition of water and extraction. All percentages are the average of three preparative runs with analyses by g.c.

Substrate	at -60°C/45 mins.	at 21°C/45 mins.	at 61°C/45 mins.	at 21°C/1140 mins.
benzene	No reaction 85% recovery of starting material	78% nitrobenzene	-	69% nitrobenzene 26% meta-dinitrobenzene
toluene [a]	No reaction	15% ortho nitrotoluene 32% para nitrotoluene 6% 2,6-dinitrotoluene 45% 2,4-dinitrotoluene	-	9% ortho nitrotoluene 23% para nitrotoluene 5% 2,6-dinitrotoluene 57% 2,4-dinitrotoluene
ortho xylene	-	6% starting material 20% 3-nitro-1,2-dimethylbenzene 36% 4-nitro-1,2-dimethylbenzene 3% 4,5-dinitro-1,2-dimethylbenzene 8% 3,6-dinitro-1,2-dimethylbenzene 5% 3,4-dinitro-1,2-dimethylbenzene	-	-
meta xylene	-	55% 4-nitro-1,3-dimethylbenzene 19% 2,4-dinitro-1,3-dimethylbenzene 22% 4,6-dinitro-1,3-dimethylbenzene	-	-
para xylene	-	17% starting material 79% 2-nitro-1,4-dimethylbenzene	-	-

TABLE 1 (Continued)

Substrate	at -60°C/45 mins.	at 21°C/45 mins.	at 61°C/45 mins.	at 21°C/1140 mins.
mesitylene	-	51% 2-nitro-1,3,5-trimethylbenzene 48% 2,4-dinitro-1,3,5-trimethylbenzene	-	-
tert butylbenzene	-	75% 4-nitro-*t*-butylbenzene 20% 2,4-dinitro-*t*-butylbenzene	-	-
1,2-diphenylethane[b]		13% starting material 7% 1-(2-nitrophenyl)-2-phenylethane 13% 1-(4-nitrophenyl)-2-phenylethane 7% 1,2-di-(2-nitrophenyl)ethane 12% 1-(2-nitrophenyl)-2-(4-nitrophenyl)ethane 1% 1-(2,4-dinitrophenyl)2-(4-nitrophenyl)ethane	-	-
biphenyl	-	17% 2-nitrophenyl 36% 4-nitrobiphenyl 17% 2,2'-dinitrobiphenyl 22% 2,2'-dinitrobiphenyl	-	-
naphthalene	-	64% 1-nitronaphthalene 26% 1,8-dinitronaphthalene	-	-
chlorobenzene	No reaction	63% *ortho* nitrochlorobenzene 26% *para* nitrochlorobenzene	-	-
nitrobenzene	-	No reaction 88% recovery of starting material	-	69% starting material 17% *meta* dinitrobenzene

TABLE 1 (Continued)

Substrate	at -60°C/45 mins.	at 21°C/45 mins.	at 61°C/45 mins.	at 21°C.1140 mins.
benzonitrile	-	No reaction 94% recovery of starting material	No reaction 89% recovery of starting material	No reaction 99% recovery of starting material
benzoic acid[c]	-	No reaction	6% starting material 3% *ortho* nitrobenzoic acid 1% *para* nitrobenzoic acid 71% *meta* nitrobenzoic acid	-
methyl benzoate	-	No reaction	7% starting material 25% methyl *ortho* nitrobenzoate 4% methyl *para* nitrobenzoate 58% methyl *beta* nitrobenzoate	18% starting material 33% methyl *para* nitrobenzoate 44% methyl *meta* nitrobenzoate
N,N-dimethylbenzamide	-	No reaction 85% recovery of starting material	-	No reaction 85% recovery of starting material
acetophenone	-	No reaction 95% recovery of starting material	21% starting material 23% *ortho* nitroacetophenone 33% *meta* nitroacetophenone	-
phenol	-	Very complex mixture Not investigated further	-	-
anisole[d]	Qualitatively similar to 21°C but cleaner	3% starting material 21% *ortho* nitroanisole 26% *para* nitroanisole	-	-
aniline	-	Very complicated mixture. Not investigated further	-	-

TABLE 1 (Continued)

Substrate	at -60°C/45 mins.	at 21°C/45 mins.	at 61°C/45 mins.	at 21°C/1140 mins.
N,N-dimethylaniline[e]	9% starting material 17% ortho nitro-N,N-dimethylaniline 3% para nitro-N-methylaniline 32% para nitro-N,N-dimethylaniline 5% 2,4-dinitro-N,N-dimethylaniline	3% starting material 4% ortho nitro-N,methylaniline 7% 2,6-dinitro-N,N-dimethylaniline 6% para nitro-N-methylaniline 30% 2,4-dinitro-N,N-dimethylaniline 18% 2,4-dinitro-N-methylaniline	-	-
acetanilide	-	41% starting material 29% ortho nitroacetanilide 17% para nitroacetanilide	-	28% starting material 28% ortho nitroacetanilide 31% para nitroacetanilide
N-methylacetanilide	No reaction 96% recovery of starting material	55% starting material 17% ortho nitrio-N-methylacetanilide 19% para nitro-N-methylacetanilide	-	58% starting material 15% ortho nitro-N-methylacetanilide 18% para-nitro-N-methylacetanilide trace acetanilide
pyridine	-	No reaction	No reaction[f]	No reaction
quinoline[b]	-	12% starting material 2% 2-nitroquinoline 4% 3-nitroquinoline 7% 4-nitroquinoline	-	-
isoquinoline	-	30% starting material 40% 2-nitro-1-hydroxy-1,2-dihydroisoquinoline	-	-
indole	-	Complex mixture, not further investigated	-	-

TABLE 1 (Continued)

Substrate	at -60°C/45 mins.	at 21°C/45 mins.	at 61°C/45 mins.	at 21°C/1140 mins.
1-methylindole	63% starting material 1% x-nitro-1-methylindole 10% 1-methylindole dimer 2% x-mono nitro-1-methylindole dimer	Complex mixture not further investigated	-	-
1,2,3,4-tetrahydrocarbazole	-	Complex mixture not further investigated	-	-
1-phenylsulphonylindole	48% starting material 15% 3-nitro-1-phenylsulphonylindole 18% 6-nitro-1-phenylsulphonylindole	29% 3-nitro-1-phenylsulphonylindole 35% 6-nitro-1-phenylsulphonylindole	-	-
pyridine-N-oxide	-	3% starting material 1% 4-nitridopyridine-N-oxide	-	-

Footnotes for Table 1

a See also Table 2

b Yields from preparative t.l.c. isolation

c Yields by gc after esterification of total product

d O-demethylation may have occurred

e Note extensive N-demethylation co-occurring

f Also no reaction by refluxing titanium(IV) nitrate in neat pyridine.

TABLE 2

Products obtained from the Reaction between Titanium(IV) Nitrate and Toluene in Chloroform at 21°C.

Run No.	Ratio of $PhCH_3$ to $Ti(NO_3)_4$	Reaction time (mins.)	% $PhCH_3$	% mono-nitrotoluenes	*o/p* ratio	% di-nitrotoluenes	2,6-di/2,4-di-ratio	%
1	1:1	2	95	—	—	—	—	95
2	1:1	5	—	95	0.93:1	—	—	95
3	1:1	45	—	47	0.45:1	50	0.13:1	97
4	1:1	1440	—	32	0.39:1	62	0.09:1	94
5	2:1	2	86	—	—	—	—	86
6	2:1	5	55	36	0.89:1	—	—	91
7	2:1	45	24	58	0.95:1	7	0.04:1	89
8	2:1	1440	1	82	0.91:1	12	0.06:1	95
9	4:1	2	87	—	—	—	—	87
10	4:1	5	82	16	0.89:1	—	—	98
11	4:1	45	64	32	0.96:1	2	—	98
12	4:1	1440	35	61	0.79:1	2	—	98
13	4:1	5760	31	63	0.82:1	4	—	98
14	1:4	2	87	—	—	—	—	87
16	1:4	5	—	40	0.31:1	54	0.16:1	94
16	1:4	45	—	—	—	82	0.11:1	82
17	1:4	1440	—	—	—	89	0.08:1	89
18[a]	4:1	1440	59	32	—	2	—	93
19[b]	c	1440	75	8	—	2	—	85
20	1:1	30	—	59	0.69:1	24	0.10:1	83
21[d]	1:1	30	—	57	0.85:1	23	0.17:1	80
22[e]	1:1	30	32	47	0.79:1	13	—	92
23[f]	1:3	45	—	—	—	85	0.13:1	85

Footnotes to Table 2

[a] Precipitate removed after 45 mins.

[b] Precipitate from run 18 removed and used as nitrating agent.

[c] Quantity of toluene equivalent to that used in run 18.

[d] In CH_2Cl_2 solvent.

[e] In CCl_4 solvent.

[f] At reflux.