A Study of the Reaction of Dinitrogen Tetroxide with Aromatic Compounds

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Dinitrogen tetroxide is found to nitrate aromatic hydrocarbons cleanly and in high yield. Some of the characteristics of this reaction have been examined and from competitive rate studies, inferences are drawn as to the mechanism of the reaction.

MUCH of our understanding of physical organic chemistry has its foundations in the investigation of electrophilic aromatic substitutions. Of these studies, none has been more thoroughly documented than the mechanism of nitration. Since agreement on the precise mechanism has not been reached [1] it appears valuable to have another method for examining this reaction.

As part of an unrelated project, we became aware that aromatic hydrocarbons as electron-rich as benzene undergo nitration under mild conditions on treatment with dinitrogen tetroxide (N_2O_4) either in the presence or in the absence [2] of Lewis acid catalysts such as aluminium chloride.[3] This reaction interested us for several reasons. First, from a synthetic point of view, the fact that the reaction went in high yield under mild nonacidic conditions in common organic solvents suggested it was a potentially valuable means of preparing nitrated aromatic compounds inaccessible by conventional techniques. Secondly, in view of the difficulties which have arisen when working with nitronium salts at low concentrations,[4] and the necessity for doing this in order to obtain critical mechanistic information, it appeared that N_2O_4 which could be handled at extremely low pressures on a vacuum line and could therefore be added to the solution as slowly as desired, should prove to be of valuable application. And finally, nitrogen dioxide, NO_2, the stable free radical with which N_2O_4 is known to exist in equilibrium, may be the nitrating species; if such were the case its behaviour would present a valuable counterpoint to the well studied reactions of most free radicals, which by virtue of their instability are normally very reactive and non-selective.[5]

From the studies of Addison and Sheldon [6] it was apparent that N_2O_4 is sufficiently soluble in enough organic solvents to allow a considerable choice of reaction media. Test reactions were therefore carried out using *ca.* 1M solutions of N_2O_4 in chloroform, acetonitrile,

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[1] For recent reviews on electrophilic aromatic substitution in general and aromatic nitration in particular see G. A. Olah, *Accounts Chem. Res.*, 1971, **4**, 240; J. H. Ridd, *ibid.*, p. 248, and references therein.

[2] The reaction in the absence of catalyst is slower than the catalysed reaction by several orders of magnitude, N. A. Valyashko, V. I. Bliznyukov, and A. E. Lutskii, *Trudy Kar'Kov. Kim.-Tekhol. Inst. im. S. Korova*, 1944, No. 4, 48 (*Chem. Abs.*, 1948, **42**, 1218 f).

[3] A. Schaarschmidt, *Chem. Ber.*, 1924, **57**, 2065.

[4] (*a*) W. S. Togyesi, *Canad. J. Chem.*, 1965, **43**, 343; (*b*) G. A. Olah, and B. A. Overchuk, *ibid.*, p. 3279.

[5] J. March, 'Advanced Organic Chemistry: Reaction Mechanisms, and Structure,' McGraw-Hill, New York, 1968.

[6] C. C. Addison and J. C. Sheldon, *J. Chem. Soc.*, 1957, 1397; 1958, 3142.

nitromethane, and pentane. Rapid nitration, accompanied by a colour change to brown or red, occurred in the first three solvents but not in pentane. The *ortho* : *para* ratio of nitroanisoles obtained in the two most convenient solvents, chloroform and nitromethane, is given in Table 1 for different N_2O_4 concentrations. In neither solvent could the *meta*-isomer be detected by n.m.r. spectroscopy and it was therefore assumed to be formed in <1% yield. No dinitroanisole could be detected either by n.m.r. or g.l.c. analysis.

TABLE 1

The effect of concentration of dinitrogen tetroxide on the *ortho* : *para* ratio of nitroanisoles. The absolute concentrations have a probable error of ±10% while the relative concentrations are accurate to ±1%. The anisole concentration was 0·46M

$[N_2O_4]$/M	*ortho* : *para* ratio in $MeNO_2$	*ortho* : *para* ratio in $CHCl_3$
1·0	$0{\cdot}5_6 \pm 0{\cdot}02$	$0{\cdot}4_5 \pm 0{\cdot}09$
0·75	$0{\cdot}5_3 \pm 0{\cdot}06$	$0{\cdot}4_6 \pm 0{\cdot}2$
0·5	$0{\cdot}5_9 \pm 0{\cdot}04$	$0{\cdot}7_1 \pm 0{\cdot}2$
0·25	$0{\cdot}5_8 \pm 0{\cdot}05$	$0{\cdot}5_7 \pm 0{\cdot}1$

Nitration in nitromethane gave the most reproducible results and this solvent was used in all subsequent studies. The nitration in both solvents favours the *para*-position. The reasons for the preference for reaction at the *para*-position may be that nitration *via* nitrosation is the major pathway leading to the observed products. This conclusion appears to have been well established by Hoggett *et al.* in studies carried out under somewhat different conditions.[7] It is perhaps worthy of note, however, that the product ratios obtained by this method are very different from those obtained in other aprotic solvents.[8] The positional selectivity is in direct contrast to the known lack of selectivity in normal free radical aromatic substitutions [9] and, as supported by the competitive rate data below, strongly suggests the lack of free radical character in the reaction.

Stoicheiometry.—One mole of dinitrogen tetroxide and one mole of anisole produced one mole of product. Although nitrous acid was not characterized as a product, the only reasonable balanced equation is (1).

$$PhOMe + N_2O_4 \longrightarrow MeOC_6H_4NO_2 + HNO_2 \quad (1)$$

Stoicheiometries were not determined for the other substrates, but were assumed to be the same as for anisole.

Substrate Selectivity: Competitive Nitration Studies.—Competitive nitrations were attempted using mixtures of anisole and mesitylene. This choice was unfortunate, however, since the ratio of nitroanisoles : nitromesitylene formed, changed drastically during the early stages of the reaction (Figure 1). This phenomenon cannot be due to (a) excessive depletion of one of the substrates by the reaction since both were in large excess nor (b) removal of one of the products by further nitration since no dinitro-products could be detected during the runs.

Furthermore, this effect remained unchanged even after rigorous purification of the reactants and it could not be attributed to the formation, during the reaction, of acid, nitrite ion, water, NO, or N_2O_3, since the controlled addition of these possible products did not produce the necessary effect.

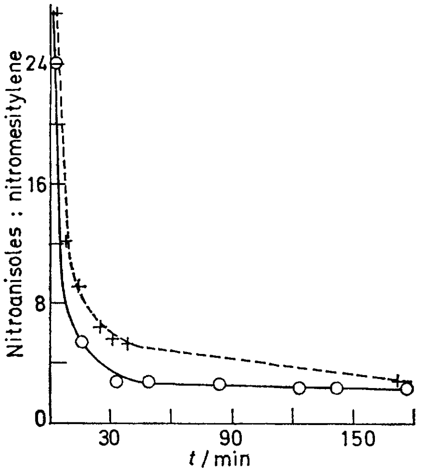

FIGURE 1 Variation of the ratio nitroanisoles : nitromesitylene as a function of time during the reaction of the hydrocarbons with dinitrogen tetroxide

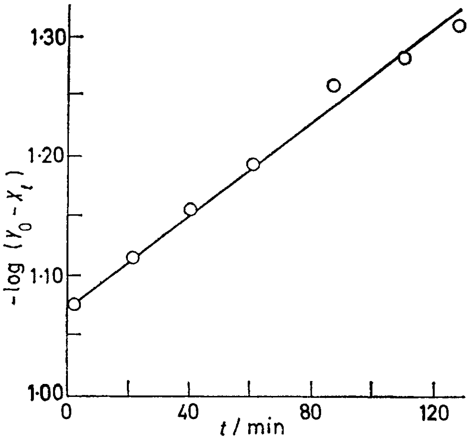

FIGURE 2 —log $(Y_0 - X_t)$ against time. The solid line is the least-squares, best-fit line

We have no completely satisfactory explanation for these results, but since the two compounds are obviously unsuited for competitive nitration studies, they were no longer used. Evidently anisole is the 'abnormal' substrate in the above reactions, since subsequent studies using other methylbenzenes did not lead to the same complications. We note in conclusion that anomalous behaviour of anisole has been reported in other studies also, and though these refer particularly to changes in the *ortho* : *para* distribution [8,10] the explanation that nitrosa-

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[7] J. G. Hoggett, R. B. Moodie, and K. Schofield, *Chem. Comm.*, 1969, 605.

[8] K. Halvarson and L. Melander, *Arkiv. Kemi*, 1957, **11**, 77.

[9] G. H. Williams, 'Homolytic Aromatic Substitution,' Pergamon, New York, 1960, p. 68.

[10] (*a*) P. H. Griffiths, W. A. Walkey, and H. R. Watson, *J. Chem. Soc.*, 1934, 631; (*b*) K. Halvarson and L. Melander, *Arkiv. Kemi*, 1958, **11**, 77.

tion is an intermediate step in the nitration of anisole, whereas it may be of perhaps lesser importance in the case of mesitylene, could account for these observations.

The rate of nitration was shown to be first order in mesitylene by a linear plot (Figure 2) of log $(Y_0 - X_t)$ against time, where Y_0 is the initial concentration of mesitylene and X_t is the concentration of nitromesitylene at time *t*. The order of the reaction in aromatic substrate was assumed to be first order for the other compounds studied. Similar studies using the same concentration of mesitylene but different concentrations of N_2O_4 showed that the rate of the reaction was dependent upon $[N_2O_4]^{1.77 \pm 0.10}$.

In order to obtain information on the amount of charge build-up in the transition state for the rate-determining step in this reaction, competitive nitration of a series of methyl substituted benzenes was studied. Table 2 gives the data for these studies along with a selection of other pertinent information. From the Table no clear cut decision can be made on the nature of the electrophile in this reaction. For the first five entries in the Table, the electrophile is of comparable selectivity to the nitronium ion while for the more reactive substrates, nitration *via* nitrosation assume increasing importance.

TABLE 2

Relative rates and stabilities of σ and π complexes for the methylbenzenes

Substituent	Relative σ [a] complex stability	Relative π [a] complex stability	Relative rate [a, b] nitration	Relative rate [c] nitration, N_2O_4
None	1	1	1	1
Methyl	7	1·51	25	19
p-Dimethyl	11	1·65	$1·3 \times 10^2$	44
o-Dimethyl	12	1·85	$1·39 \times 10^2$	48
m-Dimethyl	$2·9 \times 10^2$	2·06	$1·46 \times 10^2$	57
1,2,4-Trimethyl	$7·0 \times 10^2$	2·23		$2·2 \times 10^2$
1,2,3-Trimethyl	$7·7 \times 10^2$	2·40		$1·8 \times 10^2$
1,2,3,4-Tetramethyl	$4·4 \times 10^3$	2·68		$2·2 \times 10^3$
1,3,5-Trimethyl	$1·45 \times 10^5$	2·60	$4·0 \times 10^2$	$8·7 \times 10^3$
1,2,4,5-Tetramethyl	$1·78 \times 10^5$	2·74		$7·0 \times 10^4$

[a] R. Breslow, 'Organic Reaction Mechanisms,' Benjamin, New York, 1969, p. 169. [b] Kinetic measurements in 15% aqueous nitromethane. [J. G. Hoggett, R. B. Moodie, and K. Schofield, *J. Chem. Soc.* (*B*), 1969, 1]. [c] This work.

The intermediacy of nitrosated aromatics may well be feasible under these conditions since nitrosobenzene is converted to nitrobenzene at least 10^3 times faster than the observed rate of formation of the nitrated products. Bonner *et al.* have concluded that the nitration of *p*-dimethoxybenzene with N_2O_4 in carbon tetrachloride takes place primarily by way of a nitroso-intermediate.[11] This is also consistent with the low *ortho* : *para* distribution for the reaction with anisole.

EXPERIMENTAL

Materials.—Dinitrogen tetroxide was obtained from Air Products and Chemicals Inc. (99·5% pure) and was normally used without further purification. Nitric oxide was obtained from the same company (99%) and was used without further purification. When purified N_2O_4 was needed it was obtained by heating dried lead nitrate at 450° in a current of dry oxygen. The gas was then passed through two 14 inch U tubes packed with glass helices and P_2O_5 and was condensed in a tube cooled in ice and salt water. When sufficient liquid had condensed it was then redistilled through another U tube containing P_2O_5. The N_2O_4 prepared in this way was used within 36 h and care was taken to exclude moisture. The results obtained by using the purified N_2O_4 differed insignificantly from those obtained using the commercially obtained material. Nitromethane was purified by drying over calcium hydride for 1 day followed by fractional distillation from calcium hydride. Its purity was monitored by b.p., g.l.c., and n.m.r. spectroscopy. All other organic reagents were commercial and were used without further purification.

Methods.—Preliminary studies in various solvents were made at 25 °C using approximately molar solutions of N_2O_4. The nitrating solution (1 ml) was contained in a flask immersed in a constant temperature oil-bath. Anisole (50 μl) was added to a mixture from a syringe and the mixture was thoroughly mixed. After 5 min intervals aliquot portions (30 μl) were injected into an Auto Prep gas chromatograph fitted with a 9 ft × 1/4 in column packed with UCW 98 packing adsorbed on Chromasorb W. Peaks were identified by comparison of retention times with those of authentic samples. For n.m.r. studies spectra were run within 3 min of sampling.

The studies involving the positional selectivity in anisole were made in a similar manner. The highest N_2O_4 concentration was *ca.* 2M. While the *m*-nitroanisole g.l.c. peak could well have been obscured by the peaks due to the other two isomers 1% of this isomer could readily be detected by n.m.r. spectroscopy. Dinitro-products were not detected either by n.m.r. or by g.l.c.

The determination of stoicheiometry was made by preparing accurately known concentrations of N_2O_4 in nitromethane in tightly stoppered flasks. Appropriate amounts of anisole were then added with stirring * and the flasks were restoppered and left until reaction was complete. After suitable periods the anisole : nitroanisole ratios were determined. In all cases the results were consistent with the given stoicheiometry.

Competitive nitrations were effected at 25 °C using solutions exactly 1M with respect to the two substrates and 0·05M with respect to N_2O_4 and were monitored using an F and M research gas chromatograph model 810 instrument fitted with a 10 ft × 1/8 in column using the packing described above. Temperature programming was frequently necessary to effect suitable separation of the products or starting materials. The following pairs of substrates were used to obtain the data for Table 2: benzene–toluene, *m*-xylene–mesitylene, toluene–*m*-xylene, toluene–*o*-xylene, toluene–*p*-xylene, *m*-xylene-1,2,3-trimethylbenzene, *m*-xylene-1,2,3,4-tetramethylbenzene, 1,2,3-trimethylbenzene–1,2,3,4-tetramethylbenzene, 1,2,3,4-tetramethylbenzene–

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* The slow rate of reaction, and the apparent invariance of product composition with stirring rate indicate that adequate mixing was achieved.

[11] (*a*) T. G. Bonner and R. A. Hancock, *Chem. Comm.*, 1967, 780; (*b*) T. G. Bonner, R. A. Hancock, G. Yousif, and F. R. Rolle, *J. Chem. Soc.* (*B*), 1969, 1237.

mesitylene, mesitylene–1,2,4,5-tetramethylbenzene, and 1,2,4,5-tetramethylbenzene–pentamethylbenzene.

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