Nitration of 3-Iodoanisole and 2,6-Dimethyl-4-iodoanisole

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Nitration of 3-iodoanisole in the presence of nitrous acid was found to give 3-nitroanisole, 3-iodo-4-nitroanisole, and 3,6-di-iodo-4-nitroanisole. Nitration of 2,6-dimethyl-4-iodoanisole was found to result in the displacement of iodine. The rate of reaction was studied as a function of nitrous acid concentration and acidity. The results confirm the mechanism for nitrodeiodination proposed previously.

NITRATION of both 2- and 4-iodoanisole gives 2-iodo-4-nitroanisole [1] and the mechanism of iodine migration in the latter reaction has been the subject of a previous publication.[2] Further confirmation of the proposed mechanism will be given in this paper but, first, a brief account of a study of the nitration of 3-iodoanisole is presented.

Reaction of 3-iodoanisole with nitric acid in acetic acid solution with added sodium nitrite results in the formation of a series of colours and, although it was found possible to isolate very small quantities of highly coloured products by column chromatography, they were not investigated further. The final product obtained after allowing the reaction mixture to stand for 24 h was examined by t.l.c. and this indicated three products. By direct comparison with authentic samples, two of these were shown to be 3-iodo-4-nitroanisole and 3-nitroanisole. The former is the expected product from the nitration of 3-iodoanisole while the latter results from nitrodeiodination, a process which occurs readily with 4-iodoanisole. Recrystallisation of the crude material from ethanol gave a pure sample of the third, unidentified product. Elemental analysis and mass spectrometry showed that this material is a di-iodonitroanisole. There are fifteen possible isomers of this compound but it was possible to select the correct one with some certainty by a consideration of the n.m.r. spectrum. The positions of the two peaks of the aromatic protons suggest that one is *ortho* to the nitro-group and the other *ortho* to the methoxy-group. The two peaks are not split so that the aromatic protons must be *para* to one another. 3,6-Di-iodo-4-nitroanisole has these characteristics and its formation by the iodination of 3-iodo-4-nitroanisole (by iodine released in the formation of 3-nitroanisole) is readily understood. Thus, the reaction of 3-iodoanisole is, as would be expected, more complicated than those of the other two isomers but raises no new mechanistic problems.

In a previous paper the mechanism of nitrodeiodination was discussed.[2] The substrate used in that study was 4-iodoanisole and the situation is complicated by the fact that the iodine released by nitration re-enters the molecule at the 2-position to give, eventually, 2-iodo-4-nitroanisole. To simplify the situation the nitration of 2,6-dimethyl-4-iodoanisole was examined and here the displaced iodine appears as molecular iodine. The appearance of the colour due to iodine was used to determine the rate of reaction.

In the presence of urea, which destroys nitrous acid, there is no reaction, while sodium nitrite acts as a catalyst. The effect of added sodium nitrite on the rate of reaction is shown in Figure 1. The intercept is not exactly zero as the nitric acid employed contains some nitrous acid as an impurity. Clearly, as was suggested previously,[2] the process of deiodination is nitrosodeiodination and the resulting nitroso-compound is oxidised to the corresponding nitro-compound. Product analysis showed that the final product of reaction is 2,6-dimethyl-4-nitroanisole.

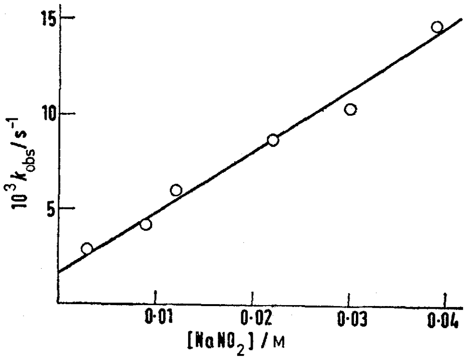

FIGURE 1 Effect of $[NaNO_2]$ on the rate of deiodination of 2,6-dimethyl-4-iodoanisole at 25°: $[substrate]_0 = 2{\cdot}4 \times 10^{-3}$M; $[HNO_3] = 5{\cdot}64$M

The effect of increased nitric acid concentration on the rate of reaction is shown in Figure 2. The value of k_{obs} is proportional to $[HNO_3]$ raised to a power greater than one and this is the sort of behaviour expected if k_{obs} were dependent on the acidity of nitric acid in acetic acid.

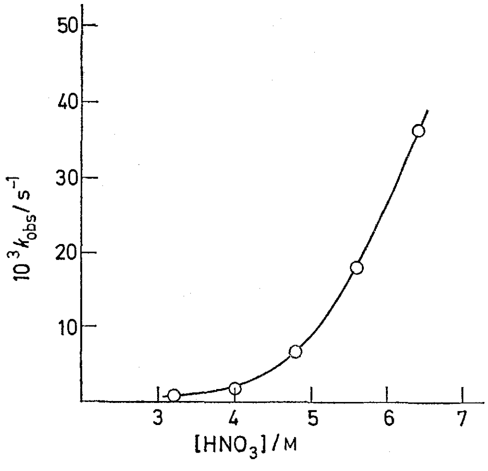

FIGURE 2 Variation of k_{obs} with $[HNO_3]$ for the deiodination of 2,6-dimethyl-4-iodoanisole at 25°: $[substrate]_0 = 2{\cdot}4 \times 10^{3}$M; $[NaNO_2] = 0{\cdot}041$M

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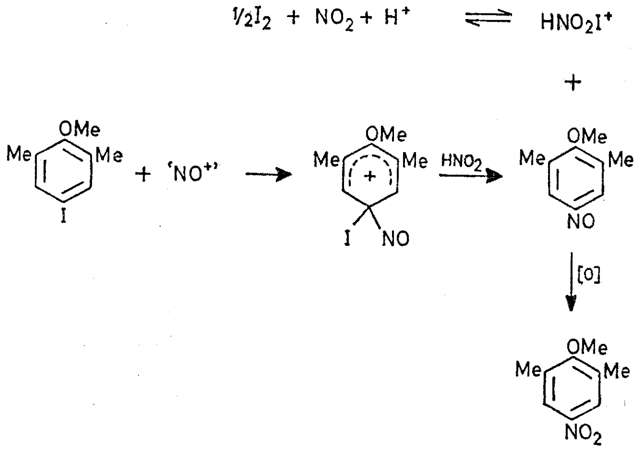
[1] F. Reverdin, *Ber.*, 1896, **29**, 997; G. M. Robinson, *J. Chem. Soc.*, **1916**, **109**, 1078.

[2] A. R. Butler and A. P. Sanderson, *J.C.S. Perkin II*, 1972, 989.

Unfortunately, values of h_0, or any other acidity function, for the relevant range of nitric acid concentrations are not available, but the pattern of dependence is similar to that observed[3] in aromatic iodination by iodine and nitric acid, where the rate was shown to be a linear function of h_0 for nitric acid. The rate of deiodination, therefore, depends upon the rate of nitrosation by some species, the concentration of which is proportional to the acidity of the reaction medium. This is similar to the general mechanism reported by Challis and Lawson[4] for the nitrosodeprotonation of phenols and indoles.

The results described above, and the evidence presented previously, lead us to propose a mechanism for nitrodeiodination shown in the Scheme, where 'NO^+' represents an acid-dependent nitrosating species. The step which is shown as removal of I^+ from the Wheland intermediate by HNO_2 to give HNO_2I^+ and subsequent decomposition to molecular iodine, may be spontaneous loss of I^+, which is then reduced to molecular iodine by the action of the nitrous acid present. Under the experimental conditions employed the nitroso-compound formed initially would be oxidised to the corresponding nitro-compound. The presence of a methoxy-group has an effect on substrate reactivity which is difficult to explain. In this investigation, and in the previous study of the nitration of 2- and 4-iodoanisole,[2] we obtained no evidence for nitrodeiodination: no displacement of iodine occurs in the absence of nitrous acid. However, in the nitration of 1,4-dibromobenzene,[5] iodomesitylene,[6] and 4-bromo-2,6-dimethylanisole[7] there is good evidence for nitrodehalogenation and nitrous acid is not necessary for reaction to occur. At the moment we can offer no explanation for this effect.



SCHEME

EXPERIMENTAL

Materials.—3-Iodoanisole was distilled before use and 3-nitroanisole was recrystallised from ethanol. Nitric acid, sodium nitrite, and acetic acid were AnalaR grade. 3-Iodo-4-nitroanisole was prepared by the method of Hodgson and Moore.[8]

2,6-Dimethylanisole (2·44 g) was added to thallium(III) trifluoroacetate (10 g) in trifluoroacetic acid (25 ml) and stirred for 15 min. KI (13 g) in water (25 ml) was added and the mixture stirred for a further 15 min. The solution was made alkaline with NaOH and extracted with ether. After washing with water and drying ($MgSO_4$), the ether was removed to give 2,6-*dimethyl*-4-*iodoanisole* (70%), which was purified by distillation, b.p. 74—76° at 0·4 mmHg (lit.,[9] 87° at 1·0 mmHg). The material had the anticipated elemental analysis.

Product Analyses.—3-Iodoanisole (2 g) was added to a solution of sodium nitrite (0·08 g) in acetic acid (25 ml) and nitric acid (25 ml). After standing for 24 h the mixture was poured into cold water (75 ml) and the product extracted with ether. After washing with water and dilute Na_2CO_3 and drying (Na_2SO_4), the ether was removed by evaporation to give a yellow solid. Examination of this material by t.l.c. (CCl_4) indicated three products, two of which were shown to be 3-nitroanisole and 3-iodo-4-nitroanisole by comparison with authentic samples. Two crystallisations of the product from ethanol gave a pure material, m.p. 182°, which corresponded to the third, unidentified product. Mass spectrometry, M^+ 405, and elemental analysis indicated that the material was a di-iodonitroanisole (Found: C, 20·9; H, 1·2; N, 3·4; I, 62·8. $C_7H_5I_2NO_3$ requires C, 20·7; H, 1·2; N, 3·5; I, 62·7%), τ 6·00 (3H, s, Me) and 1·78 and 2·21 (each 1H, each s, ArH). This spectrum is that expected for 3,6-*di-iodo*-4-*nitroanisole*.

2,6-Dimethyl-4-iodoanisole (0·5 g) was added to a mixture of acetic acid (10 ml) and nitric acid (10 ml) containing $NaNO_2$ (0·05 g) and allowed to stand for 2 h. After pouring into water (35 ml) the product was extracted with ether. The ether extract was washed with water, dilute Na_2CO_3, dilute KI, and water and then dried ($MgSO_4$). The solvent was removed by evaporation and the residue crystallised from methanol. The material had m.p. 88° (lit.,[10] 91°) and elemental analysis corresponding to 2,6-dimethyl-4-nitroanisole.

Kinetic Method.—The reactants were mixed in a cell contained in the thermostatted cell holder of a Unicam SP 500 spectrophotometer. The appearance of iodine was monitored by measuring the absorbance at 475 nm as a function of time. All the runs were first order over at least two half-lives.

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