Tetrahedron Letters,Vol.29,No.20,pp 2471-2474,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

STUDIES ON THE TWO -PHASE NITRATION OF SELECTED PHENOLS

Malcolm J.Thompson * and Petrus J.Zeegers

School of Physical Sciences,The Flinders University,
Bedford Park, S.A., 5042, AUSTRALIA.

Summary: The two phase nitration of several phenols by aqueous acid, sodium nitrate and diethyl ether, yielded as well as the expected nitro-phenols, a benzoquinone. A variable induction period was observed which could be significantly reduced by added sodium nitrite.

Recently Kagan [1] described a two-phase system comprising aqueous hydrochloric acid, sodium nitrate and diethyl ether for the mono nitration of phenols.Lanthanum nitrate was added for its presumed catalytic properties. Kagan found that the nitration of m-cresol by the two-phase system gave only two nitrated products, the predominant one being the 6-nitro and the minor product the 2-nitro isomer as well as 14% unreacted starting material.

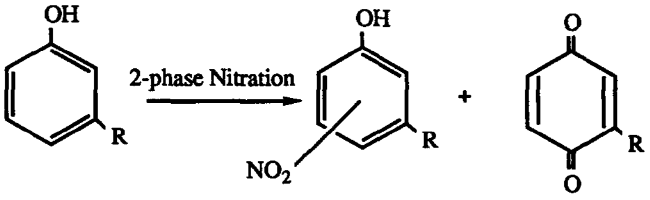
Gaude[2] later showed that the lanthanum nitrate did not act as a catalyst in the nitration of a series of phenols (excluding m-cresol), but did not comment on the induction period (or its cessation) which caused Kagan to propose the catalysis by the lanthanum.

We support the general findings of Gaude in that we find lanthanum has no catalytic influence, but we have observed a variable induction period the significance of which will be elaborated upon later .We find that m-cresol ,with or without, added lanthanum nitrate, consistently gave four nitration products. The major product (see table 1) was the 4-nitro isomer, followed by the 6-nitro, the 2-nitro isomer and 2-methyl-1,4-benzoquinone (5-8%).These findings also contrast with the isomer ratios found by Coombes, Golding and Hajigeorgiou[3] using H_2SO_4 and excluding any nitrous acid. They are also not consistent with the products expected from prior nitrosation followed by oxidation.[4,5] We believe that the analytical method of Kagan probably did not separate the nitro-phenol products sufficiently.

A similar product distribution was observed for the nitration of 3-ethylphenol and, allowing for steric factors, for 3-t-butylphenol (see table 1). It is worth noting that in the presence of the bulky t-butyl group, the least hindered 6 position shows the greatest degree of substitution, at the expense of the 4-nitro but not the 2-nitro isomer. Phenol was included as a point of reference and to demonstrate the high ortho/para ratio of the procedure.

Table 1

Product isomer ratios of 3-Substituted Phenols



Nitration Products, % G.L.C.

R	Quinone	$2NO_2$	$6NO_2$	$4NO_2$
H	2.0	55.7 (53.2)	-----	41.3 (46.6)
Methyl	7.3	22.5 (23.3)	27.9 (28.9)	41.0 (47.8)
Ethyl	5.6	20.5 (23.9)	29.9 (28.3)	41.4 (47.7)
t-Butyl	2.9	19.3 (24.1)	40.7 (28.0)	34.8 (47.9)

Figures in ( ) are predicted values based on the unpaired electron spin density of the phenoxy radical

In each instance the products were confirmed by G.L.C. against purified reference materials and also by ^1H and ^{13}C-N.M.R. analysis of the total product. All products were isolated and purifed by column chromatography. The quinones were also analysed by mass spectrometry.

The formation of a benzoquinone in the nitration of m-cresol has also been observed by us using other nitrating procedures : dilute HNO_3, HNO_3 / AcOH, clay supported $Cu(NO_3)_2$ [6], and NO_2 / CH_2Cl_2 . No quinone was observed when the nitration was achieved using 70% H_2SO_4 / HNO_3 at 0°, a medium in which NO_2^+ is the dominant nitrating species[3]. We have also found a quinone when the following phenols were nitrated by the two phase procedure at 2 M HCl acid concentration : phenol, o-cresol, 3-ethylphenol , 3-t-butylphenol , 2-ethylphenol and 2-t -butyl phenol . At an acid concentration of 6 M HCl the quinone adds HCl to give a chlorohydroquinone which is oxidised to a quinone , which in turn can add the elements of HCl again. It proved difficult to detect the quinone by G.L.C. in that circumstance.

Using a small excess (<10%) of sodium nitrate, 3M H_2SO_4, and a catalytic amount of nitrite, the two-phase procedure proved to be an excellent method for the mono nitration of simple phenols.

Isolated yields of nitration products were routinely 90-95% with no tarry by products.
As mentioned earlier we have noted a variable induction period using the two phase procedure. This "latency " varied with each phenol and is related to temperature and acid concentration. In particular the induction period was increased with lower temperature and lower acid concentration. The induction period could be markedly reduced by the addition of a catalytic amount of sodium nitrite. When m-cresol was nitrated using 6M HCl or 3M H_2SO_4 in the presence of catalytic sodium nitrite the reaction went to virtual completion within 8 minutes, compared to 12 hours with no added nitrite. Some phenols studied, most notably 4-t-butylphenol, showed almost no reactivity toward two phase nitration except on the addition of the nitrite catalyst.
Conversely the latency period could be increased by the addition of urea as a nitrous acid trap: with 1 equivalent of urea nitration was completely supressed.
Nitration is one of the most studied of all organic reactions yet the mechanism continues to be the subject of some controversy[7]. The role of the nitronium ion is well documented but there is growing interest in the involvement of an electron-transfer (ET) process recently rekindled by Perrin[8] and subsequently by others[9]. Associated with this proposed ET mechamism is the role of N(III) species as catalysts, as demonstrated for N,N-dimethyl aniline[4] and phenol[10].
Recent work by Moodie and Al-Obaidi[11] and by Ali, Ridd, Sandall and Trevellick[12] on the nitrous acid catalysed nitration of phenols suggested the existence of phenoxy radicals as one component of a radical pair intermediate.
We thus propose the following mechanism for the two phase nitration procedure, the basis of which is the initial ET step with NO^+ as the transfer agent. The observed induction period can be explained as being due to the slow formation of the transfer agent, by oxidation of the phenol, all subsequent steps are more favourable.

PROPOSED NITRATION MECHANISM

1) $ArOH + NO^+ \longrightarrow ArOH^{+\bullet} + NO^\bullet$

2) $NO^\bullet + NO_3^- \longrightarrow NO_2^\bullet + NO_2^-$

or 3) $NO^\bullet + NO_2^+ \longrightarrow NO^+ + NO_2^\bullet$

then 4) $ArOH^{+\bullet} \longrightarrow ArO^\bullet + H^+$

5) $ArO^\bullet + NO_2^\bullet \longrightarrow NO_2.C_6H_5.O$ (dienone)

6) $NO_2.C_6H_5.O \rightleftharpoons NO_2.ArOH$ (tautomers)

The slow buildup of the ET agent can be circumvented by the addition of NO^+ as NO_2^-,with immediate commencement of the reaction, as indicated by visual colour change to bright red.

We conclude that the product isomer ratios are a result of unpaired electron spin .Table 1 shows the good correlation between the predicted and experimentally found nitro phenols. This is based on the attack by the nitrating species, NO_2, at the sites of highest electron spin density of the phenoxy radical . The phenoxy radical can also undergo a second ET , a thermodynamically feasible process with NO^+, to produce a cation. Nucleophilic attack by water would result in the formation of a hydroquinone.This in turn is readily oxidised to give the observed quinone products.We have observed this oxidation to occur in the nitrating mixture. It is not possible at this stage to predict the amount of quinone product.

We have shown that these proposals can be supported by semi-empirical MO calculations with the Q.C.P.E. program 506 using the AM1 Hamiltonian[13]. We will report our complete findings in the full publication.

ACKNOWLEDGEMENT

We are indebted to the Flinders University Research Fund for financial support

REFERENCES

1. Overtani,M.,Girard,P.and Kagan,H.B., Tetrahedron Let., 23, (42), 4315, (1982)
2. Gaude,D.,LeGoaller,R.and Pierre,J.L., Syn.Comm.,16 (1), 63, (1986)
3. Coombes,R.G.,Golding,J.G.,and Hajigeorgiou, P., J.Chem.Soc. Perkin Trans 2 1451,(1979)
4. Ross,D.S., Hum,G.P.,and Blucher,W.G., J.Chem.Soc. Chem.Comm. 532, (1980)
5. Ross, D.S., Malhotra, R. and Ogier,W.C. , ibid. 1353 ,(1982)
6. Cornelis, A. and Laszlo, P., Synthesis, 908, (1985)
7. Schofield,K.,Aromatic Nitration, Cambridge University Press, Cambridge,1980
8. Perrin,C.L., J.Am.Chem.Soc.,99, 5516,(1977)
9. Eberson,L.and Radner,F., Acc.Chem.Res.,20, 53, (1987)
10. Ridd,J.H.and Giffney,J.C., J.Chem.Soc.Perkin Trans 2, 618, (1979)
11. Usama Al-Obaidi and Moodie,R.B., J.Chem.Soc. Perkin Trans 2, 467,(1985)
12. Mohamed Ali, Ridd,J.H., Sandall,J.P.B.and Trevellick,S., J.Chem.Soc. Chem.Comm . 1168,(1987)
13. Dewar,M.J.S.,Zoebisch,E.G.,Healey,E.F.and Stewart,J.J.P., J.Am.Chem.Soc.107, 3902 (1985)

(Received in UK 9 March 1988)