Tetrahedron Vol. 44, No. 16, pp. 5205 to 5208, 1988
Printed in Great Britain.

0040-4020/88 $3.00 + .00
Pergamon Press plc

EVIDENCE FOR A NON-CHAIN $S_{RN}1$ REACTION OCCURRING ON A NITROARYLHALIDE.[1]

CARLO GALLI

Centro di Studio sui Meccanismi di Reazione del CNR
c/o Dipartimento di Chimica, Università "La Sapienza", 00185 Roma, Italy.

(*Received in UK* 16 *June* 1988)

Abstract - While nitroarylhalides are unreactive in $S_{RN}1$ reactions, o-iodonitrobenzene (1) gives an efficient nucleophilic substitution with pinacolone enolate ion under photostimulation in liquid ammonia. The observed reactivity of (1) confirms the high rate of fragmentation of the C-I bond of this substrate, as determined in the literature by electrochemical measurements. The origin of such reactivity is traced to the steric inhibition of conjugation of the nitro group with the aromatic ring, as due to the presence of the bulky iodine atom in the ortho position.

A key step in the $S_{RN}1$ aromatic nucleophilic substitution is the fragmentation of the carbon-halogen bond in the radical anion deriving from the aryl halide substrate (step M2).[2]

Scheme 1

$$ArX \xrightarrow{(h\nu/Y^-)} [ArX]^{\cdot} \qquad M1$$

$$[ArX]^{\cdot} \longrightarrow Ar\cdot + X^- \qquad M2$$

$$Ar\cdot + Y^- \longrightarrow [ArY]^{\cdot} \qquad M3$$

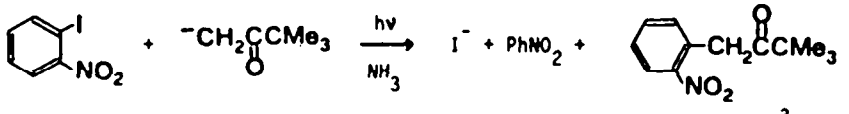
$$[ArY]^{\cdot} + ArX \longrightarrow ArY + [ArX]^{\cdot} \qquad M4$$

Fragmentation of that bond requires population of its σ^* MO. This may occur directly in the photostimulated initiation step or, depending on the energy level of the other antibonding MOs of the molecule, population of the π^* MO may be energetically favoured and take place first. In the latter case, an intramolecular electron transfer must then intervene from $\pi^* \rightarrow \sigma^*$ to cause the fragmentation of the C-X bond.[3]

Among the various possible substituents attached to the aromatic ring, the electron-withdrawing NO_2-group is inimical to the $S_{RN}1$ reaction,[1,2] because it stabilizes so strongly the π^* MO in the radical anion of the starting reagent, that the transfer of the odd electron to the σ^* MO is prevented.[3,4] Nevertheless, Danen *et al.*[5] have reported that the radical anion of o-iodonitrobenzene (1) did fragment at the C-I bond in a chronoamperometric experiment with the conspicuous rate of 8×10^4 s^{-1}, whereas the meta- and para-isomers had much lower rates of fragmentation, i.e., 0.31 and 0.90 s^{-1}, respectively. Analogously, o-bromonitrobenzene fragmented faster (110 s^{-1}) than p-bromonitrobenzene (4×10^{-3} s^{-1}), while both o-chloro- and p-chloronitrobenzene had low rates of fragmentation (ca. 10^{-2} s^{-1}). A steric inhibition of coplanarity of the NO_2-group with the aroma-

tic ring, the greater the larger the halogen atom in the ortho position, was suggested to reduce the stabilization of the π^* MO and to make the population of the σ^* MO of the C-iodine bond, and its concomitant fragmentation, much easier.[5]

The same steric effect could be expected to make then possible a nucleophilic $S_{RN}1$ substitution on 1. To test this hypothesis, 1 has been made to react under typical photostimulation conditions with the enolate ion of pinacolone (2), one of the most common and well behaved nucleophiles in this kind of processes.[1,2] Indeed, the substitution product 3 was obtained in a sa-



1 2 3 (1)

tisfactory yield (66%; expt.1, Table), accompanied by nitrobenzene (20%). The meta- and para-isomers of 1 reacted instead rather badly (expts. 2 and 3). In addition, o-bromo- and o-chloro-nitrobenzene were increasingly less efficient as substrates (expts. 4 and 5). These results confirm the reactivity trend reported by Danen et al. in the chronoamperometric reductive process,[5] and support the steric effect of inhibition of coplanarity of the NO_2-group, the more pronounced the larger the halogen atom, as responsible for an increased reactivity in the substitution reaction.

Some considerations about the possible mechanism of reaction 1 are necessary. The substitution product (3) is a pure ortho-substituted compound, thus excluding an aryne mechanism which would have mainly afforded a meta-substituted product. Against the involvement of a S_NAr mechanism are i) the halogen mobility trend obtained (I>Br>Cl), which is opposite to the one expected for reactions occurring by that mechanism,[6] but is typical of $S_{RN}1$ processes,[2] and ii) the unreactivity of the para-isomer of 1.

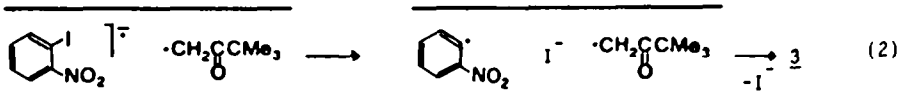
Table. Reactions of Potassium Pinacolone Enolate (2) with Nitroarylhalides in Liquid Ammonia at -33 °C.

expt no.	substrate ($O_2NC_6H_4X$)	reaction time	conditions	yield (%)[a] X^-	ArX	$PhNO_2$	3
1	X=o-I (1)	8 min	hν	93	0	20	66
2	=m-I	35 min	hν	22	40	2	0.4[b]
3	=p-I	35 min	hν	24	35	1	0
4	=o-Br	8 min	hν	15	16	0.2	5
5	=o-Cl	8 min	hν	3	17	0	0
6	1	15 sec (1.5 min overall)[c]	hν	-[d]	11	18	61
7	1	1.5 min	dark	-[d]	30	17	33
8	1	15 sec	hν,12% inhibitor[e]	-[d]	-[d]	-[d]	39
9	1	15 sec (1.5 min overall)[c]	hν,33% inhibitor[e]	-[d]	51	16	32
10	1	1.5 min	dark,33% inhibitor[e]	-[d]	55	19	17

[a] Determined either by titration of X^- or by GLC. [b] Meta-substituted product. [c] Real time elapsed while the reaction flask was introduced into the Rayonet photochemical reactor for the 15 sec irradiation. [d] Not determined. [e] Di-t-Butylnitroxide.

What is in favour of the $S_{RN}1$ mechanism? Common clues are that "dark" reaction conditions, or addition of free radical scavengers, depress dramatically the reactivity in such chain process.[2,3] Accordingly, it was observed here that absence of photostimulation provoked indeed less substitution (expt. 7) with respect to the normal conditions of expt. 6, although a rather significant spontaneous substitution did occur all the same, possibly due to the high electron affinity[4a] of substrate 1, and to the resulting efficiency of the initiation step. Addition of a 12% molar amount of di-t-butylnitroxide, a quantity well sufficient in general to depress severely the $S_{RN}1$ propagation chain,[7] did only lower the yield of product 3 to 39% (expt. 8). Even a higher amount of scavenger (a 33% molar amount) did not suppress completely the substitution process (expt. 9). The same amount of scavenger did depress as well the reactivity of the "dark" experiment, but again not exhaustively (expt. 10). Hence it is inferred that two kinds of pathways lead to product 3 in reaction 1 : the normal $S_{RN}1$ chain process, which is inhibited by the radical scavenger, and a non-chain process, which is not inhibited.

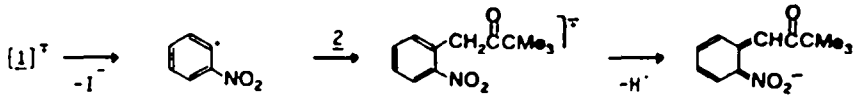
A possibility for the non-chain process may be represented by a combination in the cage, where



(2)

a step-wise substitution occurs and no radical intermediates are left free in solution. Katritzky et al.[8] have similarly suggested a non-chain cage process for a C-alkylation of a nitronate anion, to explain i) the partial inhibition by scavengers and ii) the absence of entrainment.[2] A non-chain $S_{RN}1$ process had also been invoked by Russell et al.[9] in the case of an acetylenide anion reacting with 2-chloro-2-nitropropane, and by Ciminale et al.[10] for PhS^- ion in reaction with 5-halogeno-2H,3H-benzo[b]thiophene-2,3-diones. Recently, a similar non-chain mechanism of substitution has been suggested for the reaction of α-substituted 2-methyl-5-nitrofurans with thiolate anion.[11]

On the other hand, it seems conceivable that in $[3]^{\cdot-}$, which is formed in step M3, the nitro group suffers to a lower extent from steric inhibition of conjugation, due to the smaller dimension of the pinacolone moiety,[12] with respect to the iodine atom. The resulting stronger conjugation would be responsible for a higher stability of radical anion $[3]^{\cdot-}$, presenting the odd electron mainly localized in the NO_2-group.[4b] This would make more difficult the electron transfer to another molecule of substrate (step M4), and would cut off dramatically the efficiency of the propagation steps (and the possibility of interception with a scavenger). Furthermore, termination steps could compete more favourably for the rather stable $[3]^{\cdot-}$: a $H^{\cdot}$ loss could occur, for instance, to give the highly stabilized conjugated anion of 3, which is unproductive for the propagation.



(3)

The loss of $H^{\cdot}$ would be possibly responsible for the reduction of some of the intermediate $PhNO_2^{\cdot}$ to $PhNO_2$, a reaction product that can not be accounted for easily by the cage hypothesis or by the normal $S_{RN}1$ scheme.

In conclusion, an efficient substitution process, partially consistent with the $S_{RN}1$ reaction scheme, appears to be feasible with o-iodonitrobenzene, in agreement with the high rate of fragmentation of the radical anion $[1]^{\cdot-}$ reported in the literature.[5] However, in addition to the effect of steric inhibition of conjugation in the ortho position, another suggestion could be offered to explain that high rate of fragmentation. Danen et al.[5] measured a C-I fragmentation rate of

2.5×10^2 s^{-1} for 2,6-dimethyl-4-iodonitrobenzene, which presents a nitro-group hindered on both sides by methyl groups. This is a fast rate, but not as fast as that of 1. The reason could be that in $[1]^{\cdot}$ the odd electron is transferred directly from the nitro group to the d orbitals of iodine, due to a convenient spatial array of the orbitals of the two adjacent groups.[13] Such structural feature would make the fragmentation of the C-I bond of $[1]^{\cdot}$ to occur even more easily than for the steric hindrance effect only.[14] Evidence for similar intramolecular through space electron transfer has been reported elsewhere.[15]

EXPERIMENTAL

A Rayonet RPR-100 photochemical reactor with 16 "350 nm" lamps was employed. A 25 m quartz capillary column of methyl silicone fluid was used in the GLC analyses.

o-Nitro-phenylpinacolone (3). The following reaction conditions are typical.[1] Treatment of 1.6 g of 1, 1.5 g pinacolone and 2.2 g sublimed t-BuOK in 150 ml distilled NH_3, under photostimulation for 8 min, released 93% I^- and gave a brown oil after a normal work-up. It was chromatographed on silica gel with benzene and then distilled, bp 117 °C (0.35 Torr). IR(CCl_4) $\nu_{C=O}$ 1720 cm^{-1}. ^{1}H-NMR (CCl_4) δ 7.8-7.5 and 7.3-6.8 (bm,4H,aromatic protons),4.1 (s,2H,$ArCH_2CO$),1.2 (s,9H,CMe_3). MS: 222 (M^++1),206(M^+-CH_3),164(M^+-CMe_3),136(M^+-Me_3CCO),120,85(Me_3CCO^+),57(Me_3C^+). Retention time 7.6 min at 100 °C on the capillary column. Anal.Calcd for $C_{12}H_{15}NO_3$: C,65.13; H,6.85; N,6.32. Found: C,65.05; H,7.02; N,6.09.

m-Nitro-phenylpinacolone. This compound was independently synthesized to be compared with 3. Reaction of m-bromoaniline and pinacolone enolate in NH_3 under photostimulation (see above) gave m-NH_2-phenylpinacolone, bp 143-145 °C (3 Torr). ^{1}H-NMR (CCl_4) δ 6.9-6.0 (m,4H,aromatic protons), 3.5 (bs,4H,$ArNH_2$ and $ArCH_2CO$),1.1 (s,9H,CMe_3). The diazotised aniline was added portionwise to a warm (60 °C) solution of excess $NaNO_2$ and $NaHCO_3$.[16] After work-up, the crude was flash chromatographed on silica gel (benzene) to obtain the title compound. ^{1}H-NMR (CCl_4) δ 8.0-7.7 and 7.3-7.0 (m,4H,aromatic protons),3.7 (s,2H,$ArCH_2CO$),1.2 (s,9H,CMe_3). MS: 222,136,120,85,57. Retention time 8.6 min on the capillary column under the same conditions of 3. Comparison of GLC retention times and of NMR shifts of the methylenic protons ($ArCH_2CO$) between this and compound 3, allows a clear characterization of 3 as a pure ortho-isomer, free of any meta-isomer contamination.

REFERENCES

1. Described in part in: J.F.Bunnett, E.Mitchel and C.Galli, Tetrahedron, 41, 4119 (1985).
2. J.F.Bunnett, Acc.Chem.Res., 11, 413 (1978).
3. (a) R.A.Rossi, J.Chem.Educ., 59, 310 (1982); (b) M.C.R.Symons, Pure Appl.Chem., 53, 223 (1981).
4. (a) R.F.Nelson, A.K.Carpenter and E.T.Seo, J.Electrochem.Soc., 120, 206 (1973); (b) J.M.Savéant and D.Tessier, Faraday Discuss.Chem.Soc., 74, 57 (1982).
5. W.C.Danen, T.T.Kensler, J.G.Lawless, M.F.Marcus and M.D.Hawley, J.Phys.Chem., 73, 4389 (1969). See also: T.Teherani, A.J.Bard, Acta Chem.Scand.,B37, 413 (1983).
6. J.F.Bunnett, J.Am.Chem.Soc., 79, 5969 (1957).
7. S.Hoz and J.F.Bunnett, J.Am.Chem.Soc., 99, 4690 (1977).
8. A.R.Katritzky, J.L.Chen, C.M.Marson, A.Maia and M.A.Kashmiri, Tetrahedron, 42, 101 (1986).
9. G.A.Russell, M.Jawdosiuk and M.Makosza, J.Am.Chem.Soc., 101, 2355 (1979).
10. F.Ciminale, G.Bruno, L.Testaferri, M.Tiecco and G.Martelli, J.Org.Chem., 43, 4509 (1978).
11. M.C.R.Symons and W.R.Bowman, J.Chem.Soc.,Perkin Trans. 2, 1133 (1987).
12. (a) J.Shorter, Quart.Rev., 24, 433 (1970); (b) M.Charton, Prog.Phys.Org.Chem., 8, 235 (1971).
13. W.L.Jorgensen and L.Salem, "The Organic Chemist's Book of Orbitals", Academic Press, New York (1973).
14. Steric inhibition of conjugation in aromatic nitrocompounds has been often overestimated, see: O.Exner, U.Folli, S.Marcaccioli and P.Vivarelli, J.Chem.Soc.,Perkin Trans. 2, 757 (1983).
15. J.P.Bays, S.T.Blumer, S.Baral-Tosh, D.Behar and P.Neta, J.Am.Chem.Soc., 105, 320 (1983).
16. K.J.Clark and G.I.Fray, J.Chem.Soc., 894 (1960).