Nitration of Aromatic Hydrocarbons and *ipso*-Nitrosodemetallation of Arylmetal Compounds in Sodium Nitrite–Trifluoroacetic Acid

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Treatment of aromatic hydrocarbons with sodium nitrite in trifluoroacetic acid affords nitroarenes in high yields in sharp contrast to a report in which aromatic nitration occurred only slightly in almost the same reaction system. Nitrosodemetallation at the *ipso*-position occurs to give nitrosoarenes in good yields by similar treatment of various arylmetal compounds (metal = Hg, Tl, Si, Sn, Pb, or Bi), nitrodemetallation hardly occurring in this case. The former reaction proceeds through attack of NO_2^+, while NO^+ or its carrier N_2O_3 is the attacking species in the latter reaction.

WE have recently reported that arylthallium(III) compounds react with sodium nitrite in trifluoroacetic acid to give nitroarenes through nitrosodethalliation followed by oxidation of the first-formed nitrosoarenes.[1] We have now found that treatment of aromatic hydrocarbons in a similar reaction system affords nitroarenes directly, whereas nitrosoarenes are formed from various other arylmetal compounds. It was of interest to discover why a mixture of sodium nitrite and trifluoroacetic acid serves as a nitrating agent in one instance and a nitrosating agent in another. It should be noted that our results for aromatic nitration are in sharp contrast to a report by Spitzer and Stewart[2] where the formation of only a small amount of nitroarene was observed for almost the same reaction system, and resemble a report by Norman *et al.* who used nitrogen dioxide instead of sodium nitrite.[3]

RESULTS AND DISCUSSION

Aromatic Nitration.—Addition of solid sodium nitrite to trifluoroacetic acid solutions of benzene, toluene, *o*-xylene, t-butylbenzene, anisole, or halogenobenzenes at 25 °C gave nitroarenes in high yields after stirring the mixture for 3—10 h. From ethylbenzene isomeric nitroethylbenzenes and acetophenone were obtained, the former being predominant, whereas acetophenone and *p*-methylacetophenone were obtained as the only identified product from isopropylbenzene and *p*-cymene, respectively, without any trace of the expected nitro-

arenes. Typical results are shown in Table 1.† No reaction occurred with aromatic compounds with strong electron-withdrawing substituents such as benzonitrile, acetophenone, and nitrobenzene.

Isomer ratios in the nitroarenes are nearly the same as those for normal electrophilic aromatic nitration. Even when the reaction of toluene was stopped after a short time, isomeric nitrotoluenes were still the only products, no formation of nitrosotoluene being observed. For example, the yield of nitrotoluenes $(o : m : p = 57 : 1 : 42)$ was 5% for a reaction time of 5 min at 25 °C. We also confirmed separately that nitrosoarenes cannot be oxidized to nitroarenes under the conditions employed here. These results suggest that the reaction involves direct attack of nitronium ion rather than nitrosonium ion, even though the presence of the latter species in this reaction system has been established by cryoscopic and spectroscopic measurements.[2] This is consistent with the known fact that only highly activated nuclei undergo nitrosation because nitrosating species such as NO^+ or its carrier N_2O_3 are weak electrophiles.[4]

Using sodium nitrate instead of nitrite, nitration also proceeded for all aromatic hydrocarbons examined above. In this case, nitroarene was the sole product in all cases except *p*-cymene from which small amounts of *p*-methylacetophenone and *p*-nitrotoluene were also formed as by-products (see Table 1). Isomer ratios for nitroarenes were nearly the same as those in the case of

† A typical experiment used ArH (2 mmol), $NaNO_2$ (6 mmol), and CF_3CO_2H (200 mmol). When the reaction of toluene was carried out under literature conditions[2] by using ArH (10 mmol), $NaNO_2$ (10 mmol), and CF_3CO_2H (340 mmol), the amount of isomeric nitrotoluenes produced was lower (20%) than that obtained under our conditions, but still higher than the reported yield of *ca.* 2%.

[1] S. Uemura, A. Toshimitsu, and M. Okano, *Bull. Chem. Soc. Japan,* 1976, **49,** 2582.
[2] U. A. Spitzer and R. Stewart, *J. Org. Chem.,* 1974, **39,** 3936.
[3] R. O. C. Norman, W. J. E. Parr, and C. B. Thomas, *J.C.S. Perkin I,* 1974, 369.
[4] R. O. C. Norman and R. Taylor, ' Electrophilic Substitution in Benzenoid Compounds,' Elsevier, Amsterdam, 1965, pp. 91—92.

sodium nitrite. This excludes the possibility that nitrite was oxidized by oxygen in the solvent and/or atmosphere to nitrate [5] which then became the sole reactant, since the products and yields were quite different in the cases of ethylbenzene, isopropylbenzene, and p-cymene. This was also confirmed by experiments using nitrite in degassed solution under nitrogen, since almost the same yields of nitroarenes with similar

of such metals as Hg, Si, Sn, Pb, and Bi reacted to give nitrosoarenes in good yields, whereas only a small amount of nitrosobenzene was obtained from triphenyl-antimony and no reaction occurred with triphenyl-phosphine and -arsine. Typical results are shown in Table 2 together with some results for arylthallium(III) compounds. Nitrosodemetallation occurs at the *ipso*-position with p-tolylmercury(II) bromide as in the case

TABLE 1

Aromatic nitration with sodium nitrite or nitrate in trifluoroacetic acid (200 mmol) at 25 °C

Aromatic compound (2 mmol)	NaNO₂ or NaNO₃ (6 mmol)	t/h	Product and yield (%) [a]		Isomer ratio in ArNO₂ [a] (o : m : p)
			ArNO₂	Ketone	
Benzene	NaNO₂	3	68	0	
Benzene	NaNO₂	10	97	0	
Toluene	NaNO₂	0.2	5	0	
Toluene	NaNO₂	3	56	0	
Toluene	NaNO₂	8	100	0	57 : 1 : 42
Toluene [b]	NaNO₂	4	20	0	52 : ~0 : 48
Toluene	NaNO₃	4	100	0	60 : 1 : 39
o-Xylene	NaNO₂	8	61	0	3 : 4 = 53 : 47
o-Xylene	NaNO₃	8	91	0	3 : 4 = 61 : 39
Anisole	NaNO₂	3	72	0	13 : ~0 : 87
Anisole	NaNO₃	3	47	0	25 : ~0 : 75
Ethylbenzene	NaNO₂	8	65	8 [c]	47 : 1 : 52
Ethylbenzene	NaNO₃	8	100	0	48 : 1 : 51
Isopropylbenzene	NaNO₂	8	0	33 [c,d]	
Isopropylbenzene	NaNO₃	8	86	0	25 : 2 : 73
t-Butylbenzene	NaNO₂	8	90	0	13 : 4 : 83
t-Butylbenzene	NaNO₃	8	95	0	13 : 4 : 83
p-Cymene	NaNO₂	7	0	23 [e,d]	
p-Cymene	NaNO₃	8	19	5 [e,f]	2 : 3 = 10 : 90
Chlorobenzene	NaNO₂	10	90	0	33 : ~0 : 67
Bromobenzene	NaNO₂	10	97	0	39 : ~0 : 61
Iodobenzene	NaNO₂	13	77	0	36 : ~0 : 64

[a] Determined by g.l.c. [b] Under the conditions employed by Spitzer and Stewart:[2] toluene (10 mmol), NaNO₂ (10 mmol), CF₃CO₂H (340 mmol) at 25 °C. [c] Acetophenone. [d] Appreciable amounts of tars were also formed. [e] p-Methylacetophenone. [f] Other product, p-nitrotoluene (2%).

isomer ratios were obtained as for reactions in the presence of atmospheric oxygen.

The relative rates and partial rate factors for benzene and toluene in both reactions were within the ranges found for nitration by nitronium ion [6] with a slightly large p_f^{Me} values: {for example $k_T/k_B(o_f^{Me}, m_f^{Me}, p_f^{Me})$ is as follows, 39.7 (56.2, 3.8, 119.2) for NaNO₂-CF₃CO₂H at 31 °C, 35.5 (60.2, 1.2, 88.6) for NaNO₃-CF₃CO₂H at 31 °C, 23 (46.5, 2.1, 48.5) [6] for AcONO₂-Ac₂O at 25 °C, and 28 (51.7, 2.18, 60.1) [7] for anhydrous HNO₃-CF₃CO₂H at 25 °C. Upon considering these results together with the isomer distribution for the nitroarenes we can conclude that the attacking entity for aromatic nitration is probably the same in both reactions, probably NO₂⁺.

Nitrosodemetallation.—We have reported [1] that a mixture of sodium nitrite and trifluoroacetic acid serves as a reagent for nitrosodethalliation of arylthallium(III) compounds to afford nitrosoarenes. In order to see whether this nitrosodemetallation occurs with other organometallic compounds, various arylmetal compounds were treated with sodium nitrite in trifluoro-acetic acid. As a result it was found that compounds

of p-tolylthallium(III) compound. The oxidation of the first-formed nitrosoarenes to nitroarenes was observed in the reactions of arylmercury(II) compounds by prolonging the reaction time as also occurs for aryl-thallium(III) compounds,[1] although it was slower in the case of the mercury(II) compound than for the thallium-(III) one. In the reactions with compounds of Si, Sn, Pb, and Bi, lower temperatures and somewhat shorter times were necessary to obtain nitrosobenzene, otherwise polymerized tars were obtained.

Mechanism.—Since a trifluoroacetic acid solution of sodium nitrite can nitrosodemetallate arylmetal compounds on the one hand and nitrate aromatic compounds on the other, it seems reasonable to assume that reactions (1)—(6) are involved in this system. In the case of nitrosodethalliation we have already proposed reactions (1)—(3) for the formation of nitrosonium ion or its carrier dinitrogen trioxide (N₂O₃).[1] The dissociation of N₂O₃ to NO and NO₂ or NO⁺ and NO₂⁻ [reaction (4) and (5)] is known;[4] we have confirmed the presence of NO by mass spectrometry (m/e 30) in the gaseous phase of a reaction flask under nitrogen containing the same amount of sodium nitrite, degassed tri-

[5] It is known that sodium nitrite is slowly oxidized in air to the nitrate. See, for example, 'The Merck Index, 8th edn.', Merck and Co., Rahway, 1968, p. 963; 'Comprehensive Inorganic Chemistry,' eds. J. C. Bailar, jun., H. J. Emeleus, R. Nyholm, and A. F. Trotman-Dickenson, Pergamon, Oxford, 1973, vol. 1, p. 472.
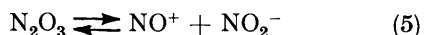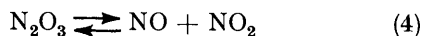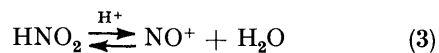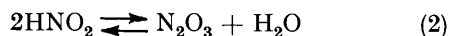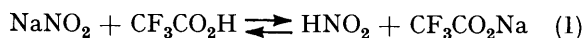
[6] L. M. Stock and H. C. Brown, Adv. Phys. Org. Chem., 1963, 1, 35.
[7] H. C. Brown and R. A. Wirkkala, J. Amer. Chem. Soc., 1966, 88, 1447.

fluoroacetic acid, and toluene as in the actual reaction.* The nitronium ion (NO_2^+) for aromatic nitration can be formed by reaction (6) which has already been postulated for aromatic nitration by nitrogen dioxide in trifluoroacetic acid.[3] In order to confirm that N_2O_3 can, in fact,

$$NaNO_2 + CF_3CO_2H \rightleftharpoons HNO_2 + CF_3CO_2Na \quad (1)$$

$$2HNO_2 \rightleftharpoons N_2O_3 + H_2O \quad (2)$$

$$HNO_2 \overset{H^+}{\rightleftharpoons} NO^+ + H_2O \quad (3)$$

$$N_2O_3 \rightleftharpoons NO + NO_2 \quad (4)$$

$$N_2O_3 \rightleftharpoons NO^+ + NO_2^- \quad (5)$$

$$2NO_2 \rightleftharpoons N_2O_4 \overset{H^+}{\rightleftharpoons} NO_2^+ + HNO_2 \quad (6)$$

nitrate aromatic compounds and also nitrosodemetallate arylmetal compounds, we carried out reactions of N_2O_3, prepared separately, with some aromatic compounds and arylmetal compounds in trifluoroacetic acid at room

dissociation to NO_2, NO, and NO^+, and the ionization of NO_2 to NO_2^+.

For the formation of aromatic ketones from alkylbenzenes with labile hydrogens such as isopropylbenzene and p-cymene, hydrogen abstraction by radical species such as NO or NO_2 to give cumyl radical may be conceivable, although the details are not yet clear. It is well known that this radical forms hydroperoxide and then alkoxyl radical which breaks down alkyl radical to form ketone or dimerizes to dialkyl peroxide.[8] It is interesting to note, however, that appreciable amounts of ketones were obtained even at low temperature (25 °C), since the breakdown to ketone is usually the main route at higher temperatures.[8]

In the sodium nitrate case aromatic nitration proceeded smoothly without the formation of any appreciable amount of ketone, while both nitroso- and nitro-demetallation scarcely occurred. Therefore, the mechanism seems to be simpler than the nitrite case as shown in reactions (7) and (8), the possibility of the

TABLE 2

Nitrosodemetallation of arylmetal compounds with sodium nitrite in trifluoroacetic acid (200 mmol)

Arylmetal compound (mmol)		$NaNO_2$ (mmol)	$T/°C$	t/min	Product and yield (mmol) [a]	
					ArNO [b]	$ArNO_2$
Ph_2Hg	2	6	0	30	1.65	0.04
PhHgCl	2	6	0	30	1.43	0
PhHgCl	2	6	25	20	1.03	0.03
PhHgOAc	2	6	0	30	1.22	0
PhHgOAc	2	6	25	30	0.81	Trace
$PhTl(OAc)ClO_4H_2O$	2	6	25	10	1.02	0.03
$PhTl(OAc)ClO_4H_2O$ [d]	1	3	25	180	0.27	0.25
$PhTl(OAc)ClO_4H_2O$	1	3	−10	10	0.12	Trace
p-MeC_6H_4HgBr	2	6	25	5	1.10	0.22
p-MeC_6H_4HgBr	2	6	25	30	0.70	0.86
p-MeC_6H_4HgBr	2	6	25	180	0	1.71
p-$MeC_6H_4Tl(OAc)ClO_4H_2O$ [d]	2	6	25	0.5	0.40	0.24
p-$MeC_6H_4Tl(OAc)ClO_4H_2O$ [d]	2	6	25	5	0.23	0.82
Ph_2SiCl_2	1	3	−10	10	0.54	0
Ph_2SiCl_2	1	3	0	10	Trace	0 [e]
Ph_4Sn	1	3	−2	10	1.19	0
Ph_4Sn	1	3	0	60	0.02	0.01 [e]
Ph_4Pb	1	3	−5	10	1.23	0
Ph_4Pb	1	3	25	10	Trace	0.09 [e]
Ph_3Bi	1	3	0	8	1.46	0

[a] Determined by g.l.c. analysis. [b] PhNO and p-MeC_6H_4NO. [c] $PhNO_2$ and p-$MeC_6H_4NO_2$. [d] Ref. 1. [e] Polymerized tars were formed.

temperature. Nitrotoluenes of almost the same isomeric ratio as found in the reaction with sodium nitrite were obtained almost quantitatively from toluene, and only acetophenone was formed from isopropylbenzene as in the sodium nitrite case (see Experimental section). Furthermore, from phenylthallium(III) compounds and p-tolylmercury(II) bromide nitrosobenzene and a mixture of p-nitrosotoluene and p-nitrotoluene, respectively, were obtained (see Experimental section). These facts together with the mass spectral data support the formation of N_2O_3 in $NaNO_2$-CF_3CO_2H, followed by its

* We observed only a trace of NO_2 in the gaseous phase, suggesting that the solubility of NO_2 in the acid is much greater than that of NO. When the same experiment was carried out in the presence of p-tolylmercury(II) bromide instead of toluene, almost no NO and NO_2 was observed probably because of the rapid reaction of the mercury(II) compound with N_2O_3.

presence of N_2O_3 and/or radical species such as NO being very low.

In nitrosodemetallation there may be another route

$$NaNO_3 + CF_3CO_2H \rightleftharpoons HNO_3 + CF_3CO_2Na \quad (7)$$

to nitrosoarene than that involving the attack of NO^+ or N_2O_3. Attack of NO formed in reaction (4) is one possibility, since it is known that the reactions of some

$$2HNO_3 \rightleftharpoons NO_2^+ + NO_3^- + H_2O \quad (8)$$
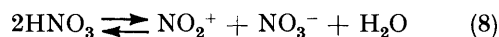
organometallic compounds with NO in nonpolar solvents give N-nitrosohydroxylamine derivatives such as $[RN(NO)O]_nM$ through insertion of NO into the C–M

[8] See, for example, E. S. Gould, 'Mechanism and Structure in Organic Chemistry,' Holt, Rinehart, and Winston, New York, 1959, pp. 710—711.

bond [9,10] and that a small amount of trifluoronitroso-methane was formed when tris(trifluoromethyl)arsine and NO are heated together at 70 °C for five days.[11] There is also the comment [12] that the reactions of Grignard reagents with NO [9] may be potential examples of homolytic substitution at magnesium. However, we can rule out this possibility in our case as follows. First, no N-nitroso-N-phenylhydroxylamine was detected in the products and it was confirmed separately that phenylhydroxylamine which may be derived from the N-nitrosoamine † was not converted into nitroso-benzene under our conditions. Secondly, the reactions of phenyl-mercury(II) and -thallium(III) compounds with commercial NO in trifluoroacetic acid at 0—25 °C gave almost no nitrosobenzene irrespective of the rate of introduction of NO or the concentration of organo-metallic compound. Several attempts using e.s.r. spectroscopy failed to detect the intermediate which would be formed if stepwise S_H2 reaction between NO and the arylmetal compound or electron transfer from NO to arylmetal compound had occurred; i.e., $Ar_nM(NO)X_m$, $Ar_n\bar{M}X_m$, etc.‡ Therefore the attacking entity in nitrosodemetallation is NO^+ [reactions (3) or (5)] or its carrier N_2O_3 and not NO. A recent report [13] on the reaction of p-tolylmercury(II) acetate with $NO^+BF_4^-$ in sulpholan should be noted in which p-nitrosotoluene was obtained in good yield, NO^+ clearly being the attacking entity.

EXPERIMENTAL

N.m.r. spectra were taken with a Varian EM-360 spectrometer (CCl_4 as solvent) and mass spectra with Hokushin time-of-flight type spectrometer. E.s.r. spectra were taken with a JEOL-PE-2X spectrometer. G.l.c. analyses were carried out with a Shimadzu 5APTF apparatus [PEG 6000 (25%)–Chromosorb W (1 or 3 m) and Apiezon L (30%)–Celite (1 m) columns (N_2 as carrier gas)]. Organic materials were used after distillation; commercial inorganic materials were used without further purification. Phenyl- and p-tolyl-thallium(III) acetate perchlorate mono-hydrates,[14] p-tolylmercury(II) bromide,[15] and tetraphenyl-lead [16] were prepared by reported methods. Other organo-metallic compounds were commercial products and used

† $[PhN(NO)O]_nM \xrightarrow{H^+} PhN(NO)OH \xrightarrow[-NO^+]{H^+}$

$PhNHOH \xrightarrow{[O]} PhNO$
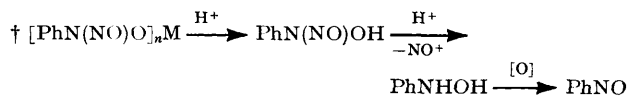
‡ See ref. 12, ch. 1. We have tried to detect intermediates such as $PhM(NO)X_m$ or $Ph\bar{M}X_m$ (X = Ph or suitable ligand) or phenyl radical by e.s.r. measurements in the cases of phenyl-mercury(II) acetate, phenylthallium(III) acetate perchlorate monohydrate, and tetraphenyl-lead(IV) in $NaNO_2$–CF_3CO_2H at −10 to +25 °C in the presence or absence of a spin trap, but no spectrum was observed under our conditions.

[9] J. Sand and F. Singer, Annalen, 1903, 329, 190; E. Müller and H. Metzger, Chem. Ber., 1956, 89, 396.

without further purification. Dinitrogen trioxide (N_2O_3) was prepared from arsenic trioxide and nitric acid.[17] All nitro compounds, ketones, and nitroso compounds were available either commercially or from previous studies.[1]

Aromatic Nitration.—A typical procedure is given. To a stirred solution of toluene (0.184 g, 2 mmol) in trifluoro-acetic acid (15 ml) was added solid sodium nitrite (0.414 g, 6 mmol) in one portion at 25 °C. The resulted dark brown mixture was stirred for 8 h at 25 °C during which period the mixture turned orange, water (100 ml) was added, and the solution was extracted with benzene (3 × 50 ml). The benzene extract was washed with aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4), and concentrated to ca. 10 ml. G.l.c. analysis of this residue with biphenyl as internal standard revealed the presence of 2 mmol (100%) isomeric nitrotoluenes ($o : m : p =$ 57 : 1 : 42). Reactions with sodium nitrate were carried out similarly. Nitrosodemetallation was carried out as described before.[1]

Reaction of Aromatic Compound with Dinitrogen Trioxide in Trifluoroacetic Acid.—To a solution of toluene (0.184 g, 2 mmol) in trifluoroacetic acid (10 ml) was added a dark green solution of N_2O_3 [17] (0.228 g, 3 mmol) in the same acid (5 ml) dropwise at 25 °C and the resulting brown solution was stirred for 8 h followed by addition of 100 ml of water to stop the reaction. The work-up procedure was as described above. G.l.c. analysis of the organic residue showed the presence of isomeric nitrotoluenes (2 mmol, 100%; $o : m : p = 58 : 0.5 : 41.5$). Similar treatment of isopropylbenzene as substrate afforded only acetophenone (0.32 mmol, 16%).

Reaction of p-Tolylmercury(II) Bromide with Dinitrogen Trioxide in Trifluoroacetic Acid.—To a suspension of p-tolylmercury(II) bromide (0.742 g, 2 mmol) in trifluoro-acetic acid (10 ml) was added a dark green solution of N_2O_3 (0.228 g, 3 mmol) in the same acid (5 ml) at 25 °C dropwise and the resulting dark brown solution was stirred for 0.5 h followed by the same work-up procedure as above. G.l.c. analysis of the organic residue showed the presence of p-nitrosotoluene (0.68 mmol, 34%) and p-nitrotoluene (0.70 mmol, 35%).

We thank Mr. S. Mori for mass spectral measurements and Dr. T. Kawamura for e.s.r. measurements and both for helpful discussions.

[10] M. H. Abraham, J. H. N. Garland, J. A. Hill, and L. F. Larkworthy, Chem. and Ind., 1962, 1615, and references herein.

[11] W. R. Cullen, Canad. J. Chem., 1963, 41, 317.

[12] K. U. Ingold and B. P. Roberts, ' Free-radical Substitution Reactions,' Wiley–Interscience, New York, 1971, p. 21.

[13] L. M. Stock and T. L. Wright, J. Org. Chem., 1977, 42, 2875.

[14] K. Ichikawa, S. Uemura, T. Nakano, and E. Uegaki, Bull. Chem. Soc. Japan, 1971, 44, 545.

[15] O. Itoh, H. Taniguchi, A. Kawabe, and K. Ichikawa, Kogyo Kagaku Zasshi, 1966, 69, 913.

[16] H. Gilman and J. Robinson, J. Amer. Chem. Soc., 1927, 49, 2315.

[17] P. W. Schenk, ' Handbook of Preparative Inorganic Chemistry,' ed. G. Braner, Academic Press, New York, 1963, vol. 1, p. 487.