Base-Catalyzed Hydrogen–Deuterium Exchange of Nitrobenzene and Related Aromatic Nitro Compounds

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Abstract: Nitrobenzene and other mononitroaromatics have been found to undergo exchange of *ortho* hydrogen for deuterium in *t*-butyl alcohol-O-*d* with potassium *t*-butoxide at 50°. The mechanism involves phenyl anions rather than radical anions or alkoxide adducts. The effects of several substituents cannot be explained entirely on the basis of inductive interactions.

Numerous examples of base-catalyzed isotopic exchange of phenyl hydrogens have been reported.[1] It has also been known for many years that dinitro and trinitro aromatics undergo base-catalyzed hydrogen–deuterium exchange under a variety of conditions[2] and it has been established[3] that phenyl anions are intermediates in the exchange of these compounds. Nitro groups also facilitate the decarboxylation of nitrobenzoate ions.[4] Although it has been shown that *o*-lithionitrobenzene can be prepared at −100°,[5] base-catalyzed isotopic exchange of nitrobenzene has not previously been observed.[6] This paper reports kinetic data for the base-catalyzed exchange of nitrobenzene and some of its substituted derivatives.

Results

The hydrogen–deuterium exchange of nitrobenzene takes place at convenient rates in *t*-butyl alcohol-O-*d* catalyzed by potassium *t*-butoxide at 50°. Incorporation of deuterium was followed by mass spectrometry and rate constants obtained in several ways are displayed in Table I. Runs 2 and 3 were allowed to proceed for more than three half-lives and plots of $-\ln((2D_0 + D_1)/2)$ *vs.* time were not linear after the second half-life. (D_0 and D_1 refer to the fractions of molecules containing 0 and 1 atoms of D.) By assuming that the maximum percentage of molecules containing two atoms of D was less than 100 and treating the data as a first-order approach to equilibrium (plotting $-\ln[((2D_0 + D_1)/2) - ((2D_{0\infty}+D_{1\infty})/2)]$ *vs.* time) good linearity was obtained. The slope in this case is $k_1 + k_{-1}$ where the rate constants refer to replacement of H by D and D by H. The values in Table I can be obtained using the relationship $k_{-1} = k_1[(D_{0\infty} + D_{1\infty}/2)/(1 - (D_{0\infty} + D_{1\infty}/2))]$, solving for k_1 and dividing by the base concentration. For complete rigor, a second-order approach to equilibrium should be assumed to allow for the change in solvent deuterium content with time, but the differences would be minor. The equilibrium values used in runs 2 and 3 (Table I) were selected to give the most linear plots. The values chosen, however, were very close to the sum of the initial fraction of *t*-butyl alcohol-O-*h* and that introduced by exchange. In run 1, where the reaction was only followed into the second half-life, the scatter was too great to justify calculation of an infinity composition. The rate constant in this run was, nevertheless, calculated for both approach to 100 and 95.6% of two atoms of D. The latter value is the expected dilution of the deuterium pool by the two substrates present and presumably gives the more correct rate constant. It will be noted that the difference between rate constants calculated in the two ways is small. Table II gives the results of some reactions carried out at higher temperatures and higher concentrations.

Table I. Exchange of Nitrobenzene[a]

Run no.	$[C_6H_5NO_2]$, *M*	$k_2{}^b \times 10^4$	Number of points	Assumed infinity concn
1[c,f]	0.093	0.661 ± 0.040[d]	8	95.6% of 2D
		0.638 ± 0.046	8	2D
2	0.109	0.688 ± 0.015	5	96.8% of 2D
3	0.234	0.703 ± 0.015	6	93.9% of 2D
4[f]	0.049	0.707	1[e]	2D
5[f]	0.056	0.724	1[e]	2D

[a] In *t*-butyl alcohol-O-*d* with potassium *t*-butoxide (0.43–0.48 *N* at 50.0°). [b] Second-order rate constant in l./mol sec. [c] *p*-Nitroanisole (0.067 *M*) was also present. [d] The standard deviation is used for all error estimates. [e] Reactions carried out in evacuated sealed tubes. [f] Using base-treated and repurified nitrobenzene.

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(1) See for example: (a) J. A. Zoltewicz and J. F. Bunnett, *J. Amer. Chem. Soc.*, **87**, 2640 (1965); (b) J. Hine and P. B. Langford, *J. Org. Chem.*, **27**, 4149 (1962); (c) G. E. Hall, E. M. Libby, and E. L. James, *ibid.*, **28**, 311 (1963); (d) A. I. Shatenstein, *Advan. Phys. Org. Chem.*, **1**, 155 (1963).

(2) (a) J. A. A. Ketelaar, A. Beer, and H. T. Vlaar, *Rec. Trav. Chim.*, **73**, 37 (1954); (b) V. Baliah and B. Ramakrishana, *ibid.*, **73**, 37 (1954); (c) R. Foster and R. K. Mackie, *Tetrahedron*, **16**, 119 (1961).

(3) (a) R. A. Foster and C. A. Fyfe, *J. Chem. Soc., Phys. Org.*, **53**, (1966); (b) M. R. Crampton and V. Gold, *ibid.*, 498 (1966); (c) E. Buncel and A. W. Zabel, *J. Amer. Chem. Soc.*, **89**, 3082 (1967).

(4) F. H. Verhoek, *ibid.*, **61**, 186 (1939).

(5) G. Kobrich and P. Buck, *Angew. Chem. Intern. Ed. Engl.*, **5**, 1044 (1966).

(6) See, however: A. I. Shatenstein, *et al.*, *Dokl. Akad. Nauk SSSR*, **79**, 479 (1951); *Chem. Abstr.*, **46**, 29 (1952). Chemical Abstracts refers to exchange of nitrobenzene in ND_3. This is apparently a misprint and is not mentioned in the original article.

Table II. Exchange of Nitrobenzene at Temperatures above 50° [a]

Run no.	$[C_6H_5NO_2]$, *M*	Temp, °C	Time, sec × 10^{-4}	Per cent				
				D_0	D_1	D_2	D_3	D_4
6	0.36[b]	51.3	0.828	54	39	7	0	0
7	0.38	51.3	1.91	22	50[c]	28[c]	0	0
8	0.47	51.3	6.44	(83% *ortho* D by nmr)				
9	0.38	80.3	2.14	1	17	82	0	0
10	0.38	100.0	5.32	1	13	58	23	4

[a] $[KOC(CH_3)_3]$ = 0.47 *M*. [b] *p*-Nitrotoluene (0.018 *M*) added. [c] Checked by combustion analysis, J. Nemeth, Urbana, Ill.

Run 9 shows that raising the temperature to 80.3° and allowing the reaction to proceed for a length of time roughly equal to the half-life for introduction of 2 atoms of D at 51.3°, leaves 1% D_0 and 17% D_1. These values must represent complete equilibration with solvent and are only slightly higher than those calculated for statistical distribution of available H. This justifies our calculation of infinity concentrations for kinetic runs. Mass spectrometry shows that no more than two atoms of D are introduced and these can be shown by nmr to occupy the positions *ortho* to the nitro group. Not until the temperature was raised to 100.0° (run 10) was an appreciable fraction of molecules containing more than two atoms of D observed.

The introduction of deuterium must proceed according to Scheme I. The fractions of molecules containing one and two deuterium atoms for the various kinetic points of run 1 are given in Table III and are compared to values calculated according to Scheme I.

Scheme I

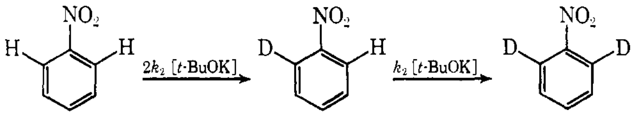

Table III. Distribution of Deuterium in the Exchange of Nitrobenzene[a]

Time, sec × 10^{-4}	Obsd		Calcd		% substrate remaining[b]
	D_1	D_2	D_1	D_2	
0.1572	0.0792	0.000	0.0809	0.002	91
0.4572	0.219	0.005	0.208	0.014	92
0.7380	0.315	0.022	0.300	0.034	91
1.0710	0.398	0.063	0.380	0.065	89
1.3782	0.448	0.102	0.432	0.099	88
2.2152	0.506	0.211	0.496	0.208	75
2.9862	0.505	0.300	0.493	0.313	67
3.8244	0.475	0.399	0.455	0.422	58

[a] Data taken from run 1. [b] By gc comparison with hexadecane, added as an internal standard.

The agreement between experimental and calculated values is generally good although the distribution of D_1 and D_2 favors D_1 by an amount well outside of the standard deviation for the analyses. This almost certainly reflects some systematic error in the mass spectral analysis and was not observed for other runs.

One troublesome problem in the exchange of nitrobenzene under these conditions was a competing loss of substrate. Aside from being usually more severe in runs where aliquots were removed through a septum than in reactions run in sealed ampoules, the phenomenon was not a reproducible one. Run 1 (Table III) represents the greatest loss at 50°. In the other runs listed the loss was less than 25%. Attempts to determine the products of this reaction have had very limited success. Fortunately, the competing loss of nitrobenzene did not appear to affect the exchange rate of nitrobenzene, nor did it affect the exchange of *p*-nitroanisole when this was included as a second substrate (run 1, Table IV).[7] *p*-Nitroanisole was relatively stable under these conditions, the loss of substrate being less than 4% after 5 exchange half-lives. Significant amounts of trideuterated material appeared in the latter points of these runs. In runs 11 and 12, *p*-*t*-butylnitrobenzene was added as a second substrate. Kinetic results for this compound are shown in Table V. *p*-*t*-Butylnitrobenzene was recovered quantitatively from the reaction mixture.

Table IV. Exchange of *p*-Nitroanisole[a]

Run no.	$[CH_3OC_6H_4NO_2]$, *M*	k_2[b] × 10^4	Assumed infinity concentration
1[c]	0.067	1.12 ± 0.07	95.4% 2D
11[c]	0.120	1.08 ± 0.03	100% 2D
12[d]	0.109	1.11 ± 0.04	98% 2D

[a] Carried out in *t*-butyl alcohol-O-*d* with potassium *t*-butoxide (0.43–0.48 *N*) at 50.0°. Eight kinetic points were determined for each run. [b] Second order rate constant in l./mol sec. [c] Nitrobenzene (0.093 *M*) was present. [d] *p*-*t*-Butylnitrobenzene (0.103 *M*) was present.

Table V. Exchange of *p*-*t*-Butylnitrobenzene[a]

Run no.	$[(CH_3)_3CC_6H_4NO_2]$, *M*	k_2 × 10^4	No. of points	Assumed infinity concn
11[b]	0.102	0.301 ± 0.023	8	100% D_2
12[c]	0.103	0.293 ± 0.015	8	100% D_2
		0.296 ± 0.016		98% D_2
13[d]	0.13	0.299	1	100% D_2
14[d]	0.13	0.283	1	100% D_2

[a] Base, solvent, and temperature as in Table IV. [b] *p*-Nitroanisole (0.120 *M*) present. [c] *p*-Nitroanisole (0.109 *M*) present. [d] In sealed ampoule as single substrate.

An attempt was made to study the exchange kinetics of N,N-dimethyl-*p*-nitroaniline. The insolubility of this compound in *t*-butyl alcohol and a competing loss of substrate (greater than 75% after one exchange half-life) make this experimentally difficult. If it is assumed, however, that the loss of substrate is independent of the exchange, a rate constant of (1.7 ± 0.2) × 10^{-5} l./mol sec may be calculated.

In addition to these kinetic runs, an assortment of other nitroaromatics was surveyed as listed in Table VI. Most of these data were obtained at 51.3° and *p*-*t*-butylnitrobenzene (runs 15 and 16) and *p*-nitroanisole (run 25) are included for comparison. Runs 17, 21, and 24 probably represent complete equilibration

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[7] The loss of substrate should not affect the exchange rate provided that the competing reaction is irreversible and does not consume base. In run 3 consumption of an equivalent of base should have noticeably lowered the exchange rate. This was not observed.

Table VI. Exchange of Assorted Aromatic Nitro Compounds[a]

Run no.	Substituent	[ARNO$_2$], M	Temp, °C	Time, sec × 10^{-4}	Per cent				
					D_0	D_1	D_2	D_3	D_4
15	*p*-*t*-Butyl	0.18	51.3	5.80	14	45	41	0	0
16	*p*-*t*-Butyl	0.23	51.3	1.91	48	43[b]	9[b]	0	0
17	*o*-*t*-Butyl	0.21	80.3	8.10	4	96	0	0	0
18	*o*-*t*-Butyl	0.18	51.3	25.04	47	53[b]	0	0	0
19	*m*-Methyl	0.33	51.3	1.75	70	27	3	0	0
20	*m*-Methyl	0.25	51.3	8.68	19	54	26	0	0
21	*p*-Bromo	0.27	51.3	1.75	0	1	9	34	56
22	*p*-Bromo	0.023	28.1	1.69	3	66	26	5	0
23	*m*-Bromo	0.20	51.3	1.09	0	4	55	41	0
24	*p*-Fluoro	0.37	51.3	0.780	0	2	12	34	51
25	*p*-Methoxy	0.20	51.3	1.45	17	47	34	2	0
26	*o*-Methoxy	0.24	51.3	0.672	81	19	0	0	0
27	*o*-Methoxy	0.24	51.3	2.37	49	51	0	0	0

[a] With potassium *t*-butoxide (0.047 M) in *t*-butyl alcohol-O-*d* in sealed tubes. [b] Deuterium content checked by combustion analysis J. Nemeth, Urbana, Ill.

of the exchangeable hydrogens with solvent. In run 23, the two most acidic hydrogens in *m*-bromonitrobenzene are completely exchanged and a third hydrogen is partially replaced. Nmr study of the product from this run suggests that complete exchange in the two positions *ortho* to the nitro group is followed by exchange of the *para* hydrogen. In all of the other cases, assignment of position of exchangeable hydrogens was conveniently done by nmr, the disappearing hydrogens being those farthest downfield from TMS. The one exception was *o*-*t*-butylnitrobenzene in which the nitro group did not cause the usual downfield shift. An attempt was made to study *o*-fluoronitrobenzene; however, displacement of fluoride by *t*-butoxide proved to be faster than exchange. *t*-Butoxide displacement products were also observed in runs 24 and 27. In both of these cases, the deuterium content of the displacement product was close to that of the recovered starting compound. In the case of run 24, exchange was apparently much faster than displacement. In run 27, the product probably is similar to the starting material in acidity.

For reasons to be discussed, it was desirable to show that the position of the *t*-butoxy group in *o*-*t*-butoxynitrobenzene did not change during the exchange. This compound was prepared from the reaction of *o*-chloronitrobenzene with potassium *t*-butoxide in *t*-butyl alcohol-O-*d* at 75°. The mixture of deuterated 2-*t*-butoxynitrobenzenes obtained was 1% D_0, 21% D_1, 67% D_2, 9% D_3, and 1% D_4. Nmr indicated essentially no hydrogen *ortho* to the nitro group and the spectrum was essentially that for two aromatic protons with an *ortho* relationship. The D_1 material was necessarily 6-deuterated and the D_2 material was either 3,6 or 5,6 dideuterated. When this product was subjected to exchange conditions in protio alcohol designed to remove only the deuterium *ortho* to the nitro group the recovered 2-*t*-butoxynitrobenzene was analyzed as 14% D_0, 66% D_1, and 18% D_2. Nmr analysis indicated that little, if any (less than 5%), of the hydrogen *ortho* to the nitro group was flanked by deuterium. Typical *ortho* and *meta* splittings were observed for this hydrogen but very little *para*-coupled hydrogen was present. It would appear that most of the residual deuterium is in the 3 position.

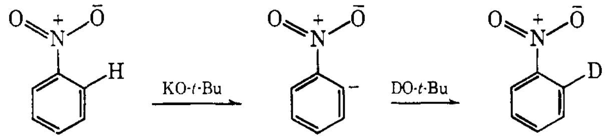
Finally, it was observed that 3,5-dichloronitrobenzene underwent complete exchange of all three hydrogens in potassium *t*-butoxide and *t*-butyl alcohol-O-*d* in 10 min at room temperature. The substrate could be recovered quantitatively from the reaction mixture.

Discussion

Of the functional groups commonly encountered, the nitro group is best at stabilizing negative charge. Despite this and perhaps also because of it, the base-catalyzed chemistry of nitro compounds has been less well understood and generally less useful than that of other, weaker electron-withdrawing substituents such as cyano, keto, halo, etc. A major problem is that nitro compounds exhibit a variety of different types of behavior on treatment with base and results are often unpredictable and mixed. The behavior of aromatic nitro compounds in base is no exception.[8] The case of nitrobenzene is illustrative. With alkoxide bases in primary alcohols, reduction of the nitro group is observed.[9] Even if good leaving groups are not present, results suggestive of nucleophilic addition to the ring by oxygen and nitrogen bases have been obtained[10] and electron transfer from carbon bases is a well-documented phenomenon.[11]

Our observation of hydrogen–deuterium exchange at the *ortho* positions of nitrobenzene is most simply explained in terms of proton removal by potassium *t*-butoxide and subsequent reprotonation by solvent (Scheme II). We feel that the previously mentioned alternative reactions between nitrobenzene and bases are at most side reactions, unrelated to exchange under our conditions. Nevertheless, mechanisms can be written in which nucleophilic addition to the ring and electron transfer reactions are part of the process by

Scheme II



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(8) (a) E. Buncel, A. R. Norris, and K. E. Russell, *Quart. Rev.* (London), **22**, 123 (1968); (b) P. Buck, *Angew. Chem. Intern. Ed. Engl.*, **8**, 120 (1969).

(9) Y. Ogata and J. Mibae, *J. Org. Chem.*, **27**, 2048 (1962).

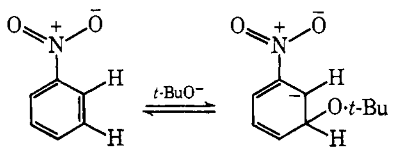
(10) (a) V. Veijola and V. Tolvanen, *Suomen Kemistilehti*, **27B**, 61 (1954); *Chem. Abstr.*, **49**, 13135 (1955); (b) G. de Montmollin and M. de Montmollin, *Helv. Chim. Acta*, **6**, 94 (1923); (c) W. Bradley and F. P. Williams, *J. Chem. Soc.*, 360 (1959).

(11) G. A. Russell and E. G. Janzen, *J. Amer. Chem. Soc.*, **86**, 1807 (1964).

which the *ortho* hydrogens are replaced and we have made an effort to rule these out.

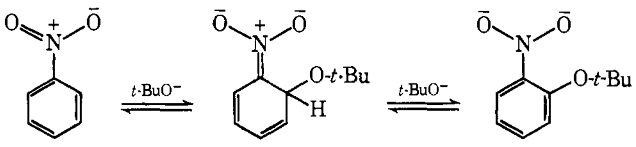
The simplest addition mechanism for exchange of nitrobenzene would involve reversible addition of base at the *meta* position (Scheme III) followed by reversible protonation at the *ortho* position. Clearly, the *meta* adduct would be less stable than the *ortho* or *para* adducts because charge can not be as thoroughly delocalized into the nitro group. Although some inductive stabilization would be operative, it seems extremely doubtful that this could sufficiently compensate for the loss of aromaticity. It has been shown that nucleophilic displacement in *meta*-halogenated nitrobenzenes is a slow reaction.[12] Our observation that 3,5-dichloronitrobenzene undergoes exchange without loss of chloride rules out Scheme III at least for this one example.

Scheme III



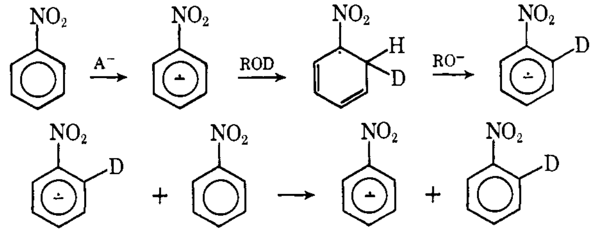
Addition in the *ortho* or *para* positions is known to be a facile reaction. In the case of polynitroaromatics, the adducts are often quite stable.[13] Crampton and Gold[3b] have shown that, in the case of the methoxide adduct of 1,3-dinitrobenzene, proton removal is slower than proton removal from 1,3-dinitrobenzene itself. To show that this was also true in our case (to rule out the mechanism of Scheme IV), we carried out the exchange of what proved to be essentially 3,6-dideuterio-2-*t*-butoxynitrobenzene. The fact that exchange of this compound in protio alcohol gave little or no 5-deuterated product eliminates Scheme IV from consideration. If Scheme IV were operative, the dianion obtained would be the 2,6-di-*t*-butoxy dianion in which the 3 and 5 positions are equivalent. Reversal of the steps leading to its formation would produce 5-deuterated material.

Scheme IV



A possible radical anion mechanism for exchange is illustrated in Scheme V, where A⁻ is formed by some reaction of nitrobenzene with base or arises from trace impurities. An analogous situation was observed by Streitwieser and Lawler[14] when the exchange of anthracene was carried out in the presence of 9,10-dihydroanthracene. Russell and Janzen[15] have associated a red color with the formation of nitrobenzene radical anion. In most of our runs some reddish color was present from the start, but this could be essentially eliminated by treating the nitrobenzene with potassium *t*-butoxide in *t*-butyl alcohol, followed by distillation or gas chromatographic purification. The runs carried out with substrate purified in this manner (runs 1, 4, and 5) did not give significantly different results (see Table I). In one run (6) *p*-nitrotoluene was added. The second-order rate constant calculated for this run is 0.79 × 10^{-4} l./mol sec which is slightly lower than the value of 0.84 × 10^{-4} l./mol sec calculated for run 7. Russell and Janzen[15] have shown that *p*-nitrobenzyl anion will react to give nitrobenzene radical anion under conditions similar to those of run 6. Their description of the appearance of the reaction mixture fit ours as well, and we conclude that the addition of nitrobenzene radical anion had no effect on the exchange rate. This observation is somewhat surprising and suggests that Scheme V is not a practical exchange mechanism. We suspect the troublesome step is the protonation at a ring carbon with its attendant loss of aromaticity. Either protonation is restricted to oxygen or does not occur at all for this radical anion under these conditions. The lack of dependence on nitrobenzene concentration or on the concentration of other added nitroaromatics and the slightly greater exchange rate constant for *p*-nitroanisole, a poorer electron acceptor,[16] would eliminate most kinetic variations of Scheme V from consideration.

Scheme V



Interpreted on the basis of simple proton removal, the exchange rates of the substituted nitrobenzenes show some interesting effects. The nitro group itself apparently stabilizes negative charge in a predominantly inductive manner. This is suggested by the fact that in run 10 a third and fourth deuterium are being introduced at roughly equal rates. Apparently the *meta* positions are involved. Decomposition of substrate at this temperature prevented more definative investigation. A more clearcut demonstration comes from runs 21 and 23 where the combination of *ortho*-bromo and *meta*-nitro is more acidifying than *ortho*-bromo and *para*-nitro.

The effect of fluorine is highly acidifying as expected.[17] Under the conditions of run 24, the exchange rate constant was too large to be measured. The effect of an *ortho*-methoxy group is roughly equivalent to a temperature difference of 50° (compare runs 10 and 25—significant amounts of D_3 were also present at the end of runs 1, 11, and 12). Shatenstein[1d] has found that at *ortho*-methoxy group raises the exchange rate constant by 5 × 10^2 for substituted benzene in NH_3–KNH_2 which is about the order of magnitude ob-

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[12] C. W. L. Bevan and G. C. Bye, *J. Chem. Soc.*, 3091 (1954).

[13] (a) J. Meisenheimer, *Ann.*, **323**, 205 (1902); (b) K. L. Servis, *J. Amer. Chem. Soc.*, **89**, 1508 (1967); (c) J. H. Fendler, E. J. Fendler, and C. E. Griffin, *J. Org. Chem.*, **34**, 689 (1969); (d) M. I. Foreman and R. Foster, *Can. J. Chem.*, **47**, 729 (1969); (e) A. R. Norris, *J. Org. Chem.*, **34**, 1486 (1969); (f) M. Strauss, *Tetrahedron Lett.*, 2021 (1969); (g) M. R. Crampton in "Advances in Physical Organic Chemistry," Vol. 7, V. Gold, Ed., Academic Press, New York, N. Y., 1969.

[14] A. Streitwieser, Jr., and R. G. Lawler, *J. Amer. Chem. Soc.*, **87**, 5388 (1965).

[15] G. A. Russell and E. G. Janzen, *ibid.*, **89**, 300 (1967).

[16] A. H. Maki and D. H. Geske, *J. Amer. Chem. Soc.*, **83**, 1852 (1961).

[17] (a) A. Streitwieser and F. Mares, *ibid.*, **90**, 644 (1968); (b) A. Streitwieser, Jr., J. A. Hudson, and F. Mares, *ibid.*, **90**, 648 (1968).

served in this study. Relative rates for the exchange of hydrogens *ortho* to the nitro group are given in Table VII. The most notable feature of these data is the general insensitivity of exchange rate to substituents of the electron donation variety. For methoxy and dimethylamino the results are very similar to those obtained by Shatenstein in the absence of the nitro group. It would appear that the groups exert their effects essentially independently. It would have seemed reasonable to find that a nitro group which had its electron deficiency partially satisfied by donation of electrons from an amino or methoxy substituent would be less efficient in inductively stabilizing the phenyl anion. We would be inclined to explain our results this way, were it not for the fact that benzene itself seems to show the same effects. It is clear that the σ and π systems are not completely insulated, otherwise the dimethylamino group would not reduce the rate. Perhaps the situation should be viewed as a change in electron distribution which does not effect the negative charge stabilizing ability of the system as a whole. In other words, electron donation from one substituent to another decreases the electron-withdrawing power of the acceptor but increases that of the donor, the outcome being the same as if the substituents acted independently.

Table VII. Relative Rate Constants for the Exchange of Substituted Nitrobenzenes[a]

Substituent[b]	k_{rel}
H	1
p-CH_3O–	1.6
o-CH_3O–	0.79[d]
p-$(CH_3)_3C$–	0.43
o-$(CH_3)_3C$–	0.076[d]
p-$(CH_3)_2N$–	0.26[c]

[a] In *t*-butyl alcohol-O-*d* with ~0.45 *M* potassium *t*-butoxide. [b] Position relative to the nitro group. [c] Assuming that exchange is independent of loss. [d] Corrected for different number of hydrogens.

An interesting rate reduction is observed when a *t*-butyl group is placed *ortho* to nitro. It is accepted knowledge that the nitro group is inhibited from coplanarity with the ring in such systems[18] and it is possible that a π–σ interaction suffers as a result. Alternatively, the difference in field effect[19] of a nitro which is not coplanar with the ring or solvation differences might explain the results. A specific interaction between the nitro group and the potassium ion is also an interesting possibility.

In considering these results, it is important that the difference between the nature of our medium and that of other investigations be kept in mind. It may be assumed with certainty that our intermediate is tightly ion paired[20] and we are studying the rate of replacement of hydrogen by potassium. We have tried a number of better ionizing media but have encountered serious side reactions.

Another cloud which hangs over all of the work done in aromatic exchange is the question of internal return raised by Streitwieser.[17] We do not believe that the isotope effect criterion is adequate to demonstrate the phenomenon[21] but if it is important, ionization is not rate determining and interpretation of our relative exchange rates will require the assumption of equal internal return.

We plan future studies in which we will either subject other substituted aromatics to the conditions of this study or find media which will allow direct comparison of the nitro group with other substituents.

Experimental Section

Materials. Most of the nitroaromatics used were commercially available. Solids were purified by recrystallization and sublimation and liquids by distillation or preparative gc. *o-t*-Butylnitrobenzene and *p-t*-butylnitrobenzene were prepared by nitration of *t*-butylbenzene as described by Nelson and Brown[22] and the products separated by preparative gc on a 10 ft × 3/8 in. column of 20% Apiezon L on 60–80 Chromosorb W at 200°. The material of longest retention time was present in the largest amount (79% by peak area, lit.[22] 73%) and had mp 28–30° (lit.[23] mp 28.4 for *p-t*-butylnitrobenzene). The nmr spectrum of this material showed a peak for *t*-butyl hydrogens at δ 1.3 ppm and a typical pattern for *para*-disubstituted aromatics with peaks at 7.39, 7.54, 7.93, and 8.08 ppm. The material of shortest retention time was a liquid (14% of mixture by peak area, lit.[22] 16%). Its nmr spectrum showed *t*-butyl at δ 1.43 ppm and a complex multiplet for the aromatic hydrogens with no peaks downfield from 7.85 ppm. This material was judged to be the *ortho* isomer based on the absence of typically deshielded hydrogens *ortho* to nitro and the agreement of its percentage in the reaction mixture with the literature value.

Preparation of 3,6-Dideuterio-2-*t*-butoxynitrobenzene. *o*-Chloronitrobenzene (241 mg, 1.53 mmol) was sealed in a tube with 5.1 ml of 0.47 *N* potassium *t*-butoxide in *t*-butyl alcohol-O-*d* and the mixture heated at 75.0° for 22 hr, 10 min. The reaction mixture was poured into pentane (50 ml) and water (75 ml) and the pentane layer washed with additional 50- and 30-ml portions of water. Drying (Na_2SO_4, anhydrous) and removal of the pentane by distillation gave a mixture which was found by gc (20 ft × 3/8 in. SE 30 on Teflon at 175°) to contain 12% starting material and 88% of longer retention time material (peak area, not necessarily mol %). The assignment of the *ortho* structure to the compound obtained from these reagents has been made previously.[24] The compound was purified by distillation followed by preparative gc under the above conditions (yield 83%). The nmr spectrum of this compound showed what was essentially a quartet, δ 6.96, 7.09, 7.33, 7.46 ppm (2.0 H), and a singlet, δ 1.36 ppm (9.0 H). The negative ion mass spectrum of this material at 70 eV gave peaks at *m*/*e* 195, 196, 197, 198, 199 the relative intensities of which led to calculation of the isotopic composition given in the results section after comparison with the negative ion spectrum of the completely protio compound obtained from *o*-fluoronitrobenzene and potassium *t*-butoxide in *t*-butyl alcohol.[24] (The positive ion spectrum gave a weak parent ion.)

Exchange of 3,6-Dideuterio-2-*t*-butoxynitrobenzene. A redistilled sample of the title compound (140 mg, 0.71 mmol) was sealed in an evacuated tube with 5.10 ml of 0.431 *N* potassium *t*-butoxide in *t*-butyl alcohol. The mixture was heated at 51.3° for 49 hr and 35 min. Workup as described for the preparation of the starting compound gave 129 mg (92%) exchanged material. The negative ion mass spectrum of this material agreed with the isotopic composition stated in the results section. The nmr spectrum (CCl_4) δ 6.8–7.7 (m, 2.9 H), 1.35 (s, 9.0 H). The aromatic region contained two doublets at 7.51 and 7.63 with slight evidence of additional splitting. The peak separation in each doublet was 2.0 cps. The maximum area for any peaks falling between the two doublets was estimated at 5% of the area of the two doublets.

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Products from the Reaction of Nitrobenzene with Potassium *t*-Butoxide in *t*-Butyl Alcohol. In an attempt to identify the products of nitrobenzene's decomposition under these conditions, a mixture of nitrobenzene (368 mg, 2.99 mmol) and bicyclohexyl (164 mg, 0.99 mmol) was treated with 10.2 ml of a 0.466 *N* solution of potassium *t*-butoxide in *t*-butyl alcohol. The mixture was degassed by the freeze–thaw technique and sealed in an evacuated tube. The tube was heated at 80.0° for 137 hr and 17 min. The mixture was poured into 150 ml of pentane–150 ml of H_2O. The aqueous extract was continuously extracted with ether. Evaporation of the ether and *t*-butyl alcohol gave 1 ml of an aqueous mixture which was extracted with two 5-ml portions of ether. Evaporation of the ether gave 4 mg of a liquid which showed no significant peaks in gc at 223° and 200 cc/min on the Teflon column (above). Acidification of the aqueous extract with HCl followed by continuous ether extraction gave an amber ether solution which was dried (Na_2SO_4). Evaporation of the ether (rotary evaporation) gave black solids (34.4 mg) which would not redissolve in common organic solvents including ether. In other experiments, attempts to concentrate the ether-soluble material in $CDCl_3$ without completely removing the solvent caused precipitation of black material at concentrations which were lower than required for spectral analysis.

The pentane extract was dried (Na_2SO_4, anhydrous) and the pentane partially removed by distillation. Gc analysis under the conditions described above showed 40% loss of nitrobenzene but only traces of other gc observable substances. Materials with retention times identical with azobenzene, azoxybenzene, and *p*-*t*-butoxynitrobenzene were found and compared, after gc collection, to authentic samples by ir, mass spectrum, or melting point. The total area of these peaks represented less than 3% of the starting area of the nitrobenzene peak. It was shown that *o*-*t*-butoxynitrobenzene and 2,2′-dinitrobiphenyl were not present in any significant amount. Column chromatography on silica gel gave, in addition to nitrobenzene and bicyclohexyl, an orange solid, 19 mg, mp 108–110° after recrystallization from ethanol–water. The structure of this compound is being investigated. The chromatographic recovery was 90%. Most of the loss of nitrobenzene is still unaccounted for.

Purification of Nitrobenzene. This could be carried out by essentially the procedure described above with substitution of distillation and preparative gc for column chromatography.

Procedure for Kinetic Runs. The reaction vessels were small pear-shaped flasks with one standard taper joint and a side arm with a stopcock. The side arm was flanged to accept a rubber septum. The flask was evacuated through the ground joint, flamed, and filled with nitrogen which had been purified by passage over copper turnings at 600°, silica gel and ascarite. The substrate(s) and standard (either hexadecane or bicyclohexyl) were introduced by syringe when possible as was the solvent–base mixture. In some cases the mixture was degassed, but this did not make any noticeable difference in the results. The reaction vessel was then placed in a constant-temperature bath. Sampling was carried out by removal of an aliquot through the septum after the same volume of nitrogen had been injected. Reaction mixtures were normally 10 or 15 ml and aliquots were 1–2 ml. Aliquots were quenched in 20–30 ml of pentane and 30 ml of water. The pentane layer was washed with 15 ml of additional water and dried (Na_2SO_4, anhydrous). The pentane solution was concentrated by distilling off the pentane through a short Vigreux column and the resultant solution analyzed by gc. (A variety of columns and conditions were used during the course of this investigation. All were either SE 30 or SF 96 on either Teflon or Chromosorb W at temperatures near 200°.) Samples for deuterium analysis were collected from the gc effluent. In reaction mixtures containing N,N-dimethyl-*p*-nitroaniline, ether was substituted for pentane and in some other cases it was necessary to add ether to the concentrated pentane solutions to keep the samples homogeneous.

Sealed Tube Reactions. The procedure for sealed tube reactions was essentially the same as for kinetic runs except that the reagents were introduced into the tube through a threeway stopcock with a septum inlet. The reagents could be degassed (freeze–thaw) through the stopcock without pumping against the punctured septum and the tube sealed under vacuum. Reaction mixtures were normally 5 ml in volume. Workups were the same as for kinetic points with roughly double the solvent volumes.

Solvent–Base Mixture. *t*-Butyl alcohol-O-*d* was prepared by a literature method[25] and more recently by a new procedure[26] based on the hydrolysis of *t*-butyl orthoborate. Solvent–base mixtures were prepared by dissolving potassium in the alcohol and solutions were titrated with aqueous HCl to bromocresol green–methyl red.

Deuterium Analyses. Unless otherwise stated, deuterium analyses were carried out at 70 eV (low-voltage measurements gave the same results for nitrobenzene) on a Hitachi Model RMU 6-E double-focusing mass spectrometer. At least five scans of the parent region were made and the average relative intensities converted to isotopic composition after correction for natural abundance of ^{13}C, etc. In most cases nmr data were also obtained using either Varian Associates HA-60-IL or T-60 models. Rate constants listed for kinetic runs were calculated as the average slope for all pairs of points (28 values for 8 points). The standard deviation was based on all values.

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