microenvironments and that hydroxide-mediated cleavages of the differentially bound substrate molecules are kinetically separable. This kinetic separability appears to be a general property of functional or nonfunctional vesicles, at least when the rate of the observed reaction is comparable to or faster than the rate of *substrate* permeation through vesicular membranes,[2a,4a,19] so that differentially bound substrate molecules kinetically reflect their specific microenvironments.

Experimental Section

Materials. Substrate **3** was prepared by literature methods.[20] Surfactant **2** (16_2OH) was prepared from *N*-methyl-2-aminoethanol by successive cetylations with cetyl bromide.[9] The experimental details of this preparation appear in another publication.[21] Surfactant **3** (16_2) was a gift from Professor T. Kunitake. Indigo (carmine) disulfonate was obtained from Aldrich Chemical Co.

Kinetic Studies. Vesicular solutions were prepared by injection or sonication.[12] In the injection technique,[22] usually 0.25 mL of $\sim 10^{-3}$ M ethanolic solutions of surfactant (or surfactant + substrate) were injected into 3 mL of various aqueous solutions held at $\sim$60 °C during injection. The injection syringe was fitted with a capillary tapering to a 100–200-nm exit aperture. Specific details of reactant concentrations, experimental method, and additives appear in Table I.

Reactions were followed with a Durrum Model D-130 stopped-flow spectrophotometer equipped with a Beckman DU-2 monochromator and a Tektronix Model 5103N/D15 storage oscilloscope. The oscilloscope trace was photographed for permanent recording. A constant-temperature circulating bath maintained the reaction temperature at 25 ± 0.2 °C. All buffers or other aqueous solutions were prepared from nitrogen-purged steam-distilled water and were purged again immediately before use.

Rate constants were obtained from computer-generated correlations of log $(A^{\infty} - A^{t})$ with time in the standard manner. For studies of biphasic kinetics, reactions were monitored with oscilloscope time bases of 0.1 or 0.2 s/div $(k_{\psi}{}^{f})$ or 2.0 or 5.0 s/div $(k_{\psi}{}^{s})$. Rate constants were calculated from the appropriate traces. First-order kinetic behavior was observed for fast and slow reactions, with correlation coefficients >0.999 and >0.99, respectively. "Crossover", or contributions of the $k_{\psi}{}^{f}$ process to the absorbance belonging to the $k_{\psi}{}^{s}$ process (and vice versa) was usually <0.5% of the total absorbance change, and never more than 3%, i.e., of the order of the experimental error in reading the oscilloscope photographs.

Acknowledgment. This work was supported in part by the U.S. Army Research Office and the National Science Foundation. We are grateful to these agencies. We also thank Ms. L. Flores and Professor V. Stoller (Rutgers Medical School, UMDNJ) for electron microscopy.

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Mechanism of the Apparent Electron-Transfer Reaction between *tert*-Butoxide Ion and Nitrobenzene

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Abstract: Potassium *tert*-butoxide reacts with nitrobenzene in tetrahydrofuran to produce *tert*-butoxynitrobenzenes. During the reaction at least 2 equiv of the potassium salt of nitrobenzene radical anion precipitates per equivalent of substitution products. The reaction is first order in nitrobenzene and second order in *tert*-butoxide. When a mixture of deuterated and undeuterated nitrobenzene is used, the substitution reaction is selective for the undeuterated reagent. In the presence of molecular oxygen, the nitrobenzene radical anion does not form but the substitution reaction proceeds at the same rate. The isotopic selectivity is undiminshed by the presence of molecular oxygen, demanding that the hydrogen-transfer step occur prior to the electron-transfer steps. These experimental observations demonstrate that substitution occurs by dianion formation followed by electron transfer.

Replacement of hydrogen by nucleophilic substitution in aromatic nitro compounds is not a frequently encountered reaction despite being known since 1899.[1] Nitrobenzene, $PhNO_2$, has been shown to react with both oxygen and nitrogen nucleophiles to produce substitution products although usually in low yield.[2]

Several of our publications[3] have dealt with processes requiring both alkoxide and $PhNO_2$ to be present for the production and oxidation of carbanions. In addition we have studied the potassium *tert*-butoxide, *t*-BuOK, catalyzed hydrogen–deuterium exchange reaction of $PhNO_2$ in *tert*-butyl alcohol-*d*.[4] In connection with running controls for these reactions, we became interested in the sometimes-observed background process in which $PhNO_2$ is consumed through direct reaction with alkoxide.

Results and Discussion

Reaction Products. At temperatures above 50 °C, $PhNO_2$ is slowly destroyed by *t*-BuOK in *t*-BuOH.[4] The products include 4-*tert*-butoxynitrobenzene (4-*t*-BuOPhNO$_2$), azoxybenzene, azobenzene, an intractable black resin, and a large balance of unisolated material. We also detected the formation of nitrobenzene radical anion ($PhNO_2^{-}\cdot$). This was demonstrated by the observation of exchange broadening of $PhNO_2$ peaks in the NMR spectrum of the reaction and confirmed by direct ESR measurement. At room temperature, $PhNO_2^{-}\cdot$ reaches a constant concentration after a few hours and remains at this level indefinitely. It may be destroyed by O_2 but reforms on degassing of the solution. This cycle can be repeated indefinitely. Even at 50 °C, however, O_2 consumption is immeasurably small over a period of several days.

The conditions used by Russell and Bemis[5] for the preparation of $PhNO_2^{-}\cdot K^{+}$ suggested that tetrahydrofuran (THF) would be a good choice of solvent in which to examine the details of this reaction. If $PhNO_2^{-}\cdot K^{+}$ is a major product of the reaction between *t*-BuOK and $PhNO_2$, it should precipitate from this solvent. In a typical experiment, 2 mmol of $PhNO_2$ was allowed to react with 2 mmol of *t*-BuOK in 11 mL of THF at 50 °C for 72 h under argon gas. A copious brown precipitate was found to contain 0.93 mmol of $PhNO_2^{-}\cdot K^{+}$ as evidenced by its ESR spectrum in dimethyl sulfoxide (Me_2SO) and determined quantitatively by GC analysis

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Table I. Nitrobenzene Loss and *tert*-Butoxynitrobenzene Formation in the Reaction of 0.20 M Nitrobenzene with 0.32 M Potassium *tert*-Butoxide in THF at 30 °C under Argon

time $\times 10^{-3}$, s	% of $PhNO_2$ lost[a]	% conversion[a] 2-*t*-$BuOPhNO_2$	4-*t*-$BuOPhNO_2$
1.21	3.6	1.1	1.5
2.09	13.3	2.1	2.5
4.81	34	4.3	5.5
8.75	58	5.9	8.7
14.16	76	7.7	11.6
24.9	~95	7.8	13.2
82.3		7.4	11.4
188.2	~99	6.7	7.9

[a] Determined by gas chromatography vs. internal bicyclohexyl. The value listed for $PhNO_2$ represents material still remaining in solution at the time indicated.

Table II. Concentration Dependence of Product Formation Rate in the Reaction of Nitrobenzene with Potassium *tert*-Butoxide in THF at 30 °C under Argon

run no.	$[PhNO_2]_0$, M	$[t\text{-}BuOK]_0$, M	$t \times 10^{-3}$, s	% conversion to 2-*t*-$BuOPhNO_2$	4-*t*-$BuPhNO_2$
1	0.58	0.33	3.60	3.3	4.2
2	0.39	0.33	3.60	3.5	4.2
3	0.20	0.33	3.60	3.4	5.2
4	0.10	0.33	3.60	3.3	4.6
5[a]	0.10	0.33	3.60	3.3	4.0
6	0.05	0.33	3.60	2.9	3.8
7[a]	0.05	0.33	3.60	2.5	3.7
8	0.20	0.33	3.60	4.0	4.0
9	0.10	0.16	3.60	1.2	1.4
10	0.05	0.082	3.60	0.38	0.50
11	0.028	0.047	3.60	0.18	0.20
12	0.22	0.45	1.21	2.5	2.6
13	0.11	0.34	2.10	2.0	2.2
14	0.11	0.22	5.52	2.7	3.6
15	0.088	0.18	7.48	2.6	3.6
16	0.073	0.15	10.8	2.3	3.3
17	0.11	0.113	19.2	2.5	3.6

[a] Reaction run on larger scale than preceding run.

after conversion to $PhNO_2$ with O_2. Ninety percent of the initial $PhNO_2$ is consumed. 2-Nitrophenol, 2-*t*-$BuOPhNO_2$ and 4-*t*-$BuOPhNO_2$ are produced in varying ratios but in a total yield corresponding to conversion of up to 25% of the initial $PhNO_2$ to substitution products. With THF purified by distillation from $LiAlH_4$, the major substitution product is the phenol. With benzophenone ketyl treated THF, the amount of this product is reduced to about 20% of the total substitution products. Under the latter conditions, up to 21% of the initial $PhNO_2$ is converted to the *tert*-butoxy substitution products with the 4 isomer predominating. At least 2 mol of $PhNO_2^{-}\cdot$ are produced per mole of substitution products. The ratio is most nearly two when the phenol is the major product. With very dry THF the *t*-$BuOPhNO_2$ isomers produced do not account for all of the $PhNO_2^{-}\cdot$. This is partly, but probably not entirely, explained by the formation of 2-nitro-5-*tert*-butoxyphenol which was shown to arise from 4-*t*-$BuOPhNO_2$ under the reaction conditions. Traces of azoxybenzene are also found. About 85% of the starting $PhNO_2$ could be accounted for.

When argon was replaced by oxygen as a reaction atmosphere, a precipitate again formed but now contained no radical anion. This precipitate is partially potassium superoxide (KO_2) which is known to form when $PhNO_2^{-}\cdot K^{+}$ reacts with O_2.[5] In contrast to the anaerobic reaction, 72% of the starting $PhNO_2$ is found in the reaction solution. The other products are the same and are formed in similar amounts. In neither case, anaerobic or aerobic, was any significant amount of 4-nitrophenol detected despite quantitative recovery in control experiments.

Kinetics. The reaction did not adapt readily to kinetic analysis for a number of reasons. Chief among these was the difficulty in controlling hydroxide concentration in the solvent–base mixture. Moreover, it seems likely that some hydroxide is generated as the reaction proceeds. Nevertheless, we offer the data of Table I in which a history of the conversion of $PhNO_2$ to 2- and 4-*t*-$BuOPhNO_2$ is presented. It may be seen that, as suggested by the product analysis discussed earlier, $PhNO_2$ is lost at a greater rate than *t*-$BuOPhNO_2$ isomers are formed. For the first 75% of $PhNO_2$ loss, 3–4 equiv of $PhNO_2$ disappears for every equivalent of *t*-$BuOPhNO_2$ formed. For reactions such as that of Table I in which an excess of base was employed, the $PhNO_2$ is completely consumed and this is followed by a slow destruction of the *t*-$BuOPhNO_2$ under the reaction conditions. The destruction is most pronounced for the 4 isomer which gives 2-nitro-5-*tert*-butoxyphenol as mentioned earlier.

Considering the complexity of the latter stages of the reaction, we decided to approach the problem of kinetic order by studying the effect of reagent concentrations on reactions carried out for short time periods as described in Table II. In runs 1–7 the $PhNO_2$ concentration was reduced while holding initial [*t*-BuOK] and reaction time constant. There is no significant variation in the percent conversion to substitution products, showing that the reaction is first order in $PhNO_2$.

In runs 8–11 it can be seen that changes in initial *t*-BuOK concentrations have a greater than first-order effect on the percent $PhNO_2$ converted to substitution products. Changing the [*t*-BuOK] by a factor of 7 changed the yields by a factor of roughly 20, showing clearly that the reaction is greater than first order in *t*-BuOK. Determining a precise order is made difficult by the uncertainty in knowing what value to use for percent conversion at $t = \infty$ and the fact that it is experimentally inconvenient to attain true pseudo-first-order conditions. The first problem would render the rate factor for runs 8–11 larger than 20. The second is minimized by keeping the ratio of *t*-BuOK/$PhNO_2$ constant. Runs 12–17 approach the problem differently. The concentration of *t*-BuOK is lowered but the reaction time is increased in approximate proportion to $1/[t\text{-BuOK}]^2$. It may be seen that there is not much variation in the percent conversion values.

In analysis of the data of Table I, it was noticed that plots of $\ln (P_\infty/(P_\infty - P_t))$ vs. time are nearly linear through the first four to five points (P_t = percent of *t*-$BuOPhNO_2$ at time *t*). The most linear plots were obtained by employing theoretical rather than experimental values for P_∞. This is an unexpected relationship because the disappearance of *t*-BuOK should have produced a rate reduction of at least one-third by the fourth point in Table I. Moreover, $PhNO_2$ loss is greater than calculated from product formation which would further retard the rate. The existence of a simple logarithmic relationship between reaction progress and time could possibly be due to hydroxide-promoted *tert*-butoxide substitution as discussed later.

Regardless of its origin, however, the simple relationship observed provides a vehicle for comparing data obtained at different times, conversions, and base concentrations. Figure 1 is a plot of $(\ln (P_\infty/P_\infty - P_t))/t$ vs. $[t\text{-BuOK}]^2$ for the data of Tables I and II. Considering the scatter in analytical data for ostensibly identical runs, the data points are probably within experimental error of the least-squares line represented. For comparison we offer Figure 2 in which the same measure of reaction progress per unit time is plotted against the first power of [*t*-BuOK]. This second plot shows distinct curvature. It thus appears certain that the rate of production of 2- and 4-*t*-$BuPhNO_2$ has a second-order dependence on initial *t*-BuOK concentration.

In carrying out and interpreting these experiments, we have been aware of the danger of an order determination for *t*-BuOK under conditions where it is certainly ion paired and possibly aggregated. However, all of the mechanisms considered in this paper would involve processes in which $t\text{-BuO}^-$ reacts to produce more delocalized anions. It seems safe to predict that ion pairing and/or aggregation would reduce the rates of such steps. This being the case, increases in $[t\text{-BuOK}]_0$ which would increase the fraction of total $t\text{-BuO}^-$ present as ion pairs and/or aggregates can be clearly predicted to reduce the dependence of reaction rate

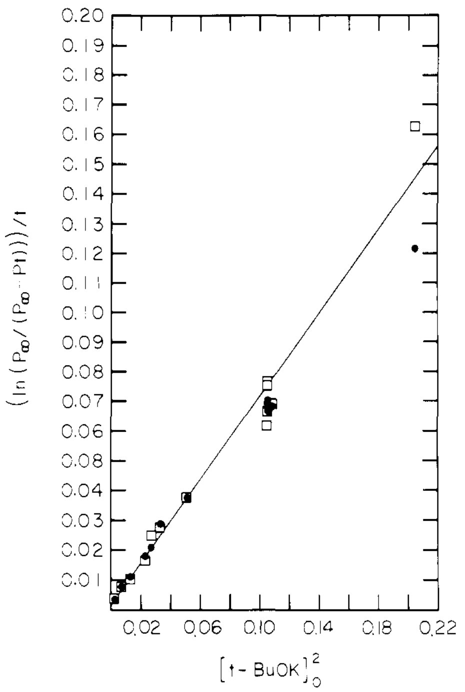


Figure 1. Second-order base-dependence plot for formation of 4-*t*-$BuOPhNO_2$, circles; 2-*t*-$BuOPhNO_2$, squares.

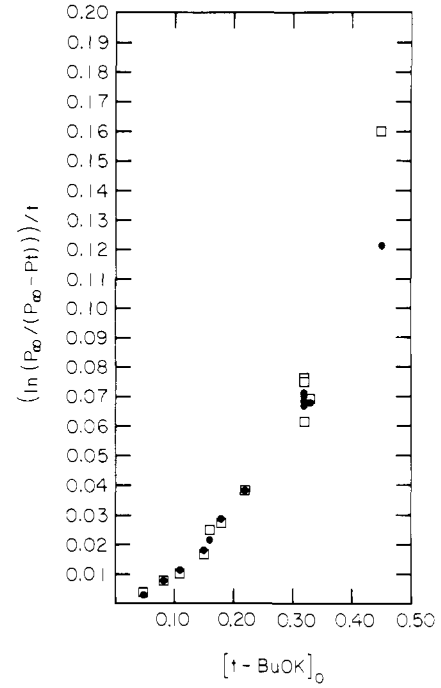


Figure 2. First-order base-dependence plot for formation of 4-*t*-$BuOPhNO_2$, circles; 2-*t*-$BuOPhNO_2$, squares.

on [*t*-BuOK]$_0$. The measured kinetic order thus represents a minimum value. For this reason we feel quite confident that the determined kinetic order may be related to the reaction mechanism in a straightforward manner.

Table III. Effect of Ring Deuteration and Presence of O_2 on Rate of Product Formation in Reaction of 0.2 M Nitrobenzene with Potassium *tert*-Butoxide in THF at 30 °C

run no.	[*t*-BuOK]$_0$, M	O_2[a]	ring,[b] D	$t \times 10^{-3}$, s	% conversion to 2-*t*-$BuOPhNO_2$	4-*t*-$BuOPhNO_2$
1–8	0.33	no	no.	3.60	3.3[d]	4.2[d]
18	0.33	no	yes	3.60	0.60	0.90
19[c]	0.45	no	no	1.20	1.9	2.3
20	0.45	yes	no	1.20	2.1	2.1
21	0.45	no	yes	7.62	1.9	3.5
22	0.45	yes	yes	7.62	2.1	3.0

[a] Reaction carried out under pure O_2. [b] $PhNO_2$-d_5 used. [c] This run was carried out under conditions identical with those of run 12 but is probably a better standard for 20–22 because it was run at the same time under the same analytical conditions. [d] These are average values for eight runs.

Table IV. Deuterium Content of Products from Reaction of Equimolar Mixtures of $PhNO_2$ and $PhNO_2$-d_5 with *t*-BuOK in THF in the Absence and Presence of O_2[a]

run	d_n[b]	product, mole fraction d_n[b] $PhNO_2$[c]	$PhNO_2^{-\cdot}$[d]	$2HOPhNO_2$	2-*t*-$BuOPhNO_2$	4-*t*-$BuPhNO_2$
A	d_0	0.395			0.792	0.727
B		0.188	0.341	0.449	0.395	0.306
C		0.168		0.332	0.398	0.319
A	d_1	0.038			0.072	0.068
B		0.214	0.127	0.098	0.261	0.348
C		0.194		0.138	0.244	0.365
A	d_2	0.00			0.007	0.008
B		0.073	0.032	0.023	0.021	0.198
C		0.065		0.024	0.012	0.195
A	d_3	0.00			0.011	0.032
B		0.214	0.092	0.150	0.193	0.107
C		0.235		0.211	0.214	0.088
A	d_4	0.084			0.118	0.165
B		0.236	0.175	0.280	0.130	0.041
C		0.263		0.294	0.131	0.033
A	d_5	0.483				
B		0.074	0.233			
C		0.076				

[a] In run A, $[PhNO_2]_0$ = 0.49 M, mol % $PhNO_2$-d_5 = 51.3, [*t*-BuOK]$_0$ = 0.45 M at 30 °C for 1 h. In run B, $[PhNO_2]_0$ = 0.14 M, mol % $PhNO_2$-d_5 = 49.5, [*t*-BuOK]$_0$ = 0.137 M at 50 °C for 37 h. In run C, $[PhNO_2]_0$ = 0.14 M, mol % $PhNO_2$-d_5 = 50.9, [*t*-BuOK]$_0$ = 0.164 M at 50 °C for 45 h under an atmosphere of O_2. [b] Fraction of total molecules containing the stated number of deuterium atoms determined by mass spectrometry. [c] Unreacted $PhNO_2$ in solution. [d] Analyzed as $PhNO_2$ after O_2 treatment.

Isotope Effects. The kinetic effect of deuterium substitution was determined by comparing reactions run with $PhNO_2$-d_5 as substrate to those carried out with undeuterated material. It will be seen by comparing the first two entries of Table III that under otherwise identical conditions the yield of 2-*t*-$BuOPhNO_2$ is reduced by a factor of approximately 5.5 and the yield of 4-*t*-$BuOPhNO_2$ is reduced by a factor of 4.7 when $PhNO_2$-d_5 is used. It should also be noted that for runs 21 and 22 in which $PhNO_2$-d_5 is used, the time required to produce a 2% conversion to *o*-*t*-$BuOPhNO_2$ was 7.6 × 10^3 s whereas with undeuterated substrate, runs 19 and 20, only 1.2 × 10^3 s was required to accomplish the same conversion under the same initial conditions. A very important feature of the data in Table III is that in runs 20 and 22, which were carried out under an atmosphere of O_2, the results are not significantly different from those observed under anaerobic conditions. Moreover, the kinetic isotope effect evidenced by comparison of runs 20 and 22 is not appreciably changed from that obtained by comparison of runs 19 and 21. Thus the magnitude of the kinetic isotope effect is not influenced by the presence of O_2. The approximate values calculated from these runs are k_H/k_D = 6.4 (for 2-substitution) and k_H/k_D = 4.2 (for 4-substitution).

A more precise estimate of the isotope effect was obtained from deuterium analyses of products and reactants by mass spectrometry. These results are presented in Table IV. Three separate runs were carried out. In run A, an equimolar mixture of $PhNO_2$ and $PhNO_2$-d_5 (0.49 M total concentration) was allowed to react with 0.45 M *t*-BuOK in THF for 60 min at 30 °C. Deuterium analysis of the products shows that the 2-*t*-$BuOPhNO_2$ produced from this mixture originates mainly from undeuterated $PhNO_2$. The ratio of d_0 plus d_1 material to d_4 plus d_5 material is a factor of 6.7. In the case of 4-*t*-$BuOPhNO_2$ the corresponding ratio is 4.0. These values represent our best estimates of k_H/k_D for 2- and 4-substitution, respectively, and agree reasonably well with the values obtained above by rate comparisons.

Run B was carried out at 50 °C for 37 h with 0.14 M $PhNO_2$ and 0.14 M *t*-BuOK in THF under argon. Under these more drastic conditions, we observed the expected scrambling of the ortho hydrogens.[4] That this scrambling is confined to the 2- and 6-positions is confirmed by the relatively small amounts of $PhNO_2$-d_2 and the negligible amounts of 2-$ROPhNO_2$-d_2. In order to calculate an isotope effect for the formation of 4-*t*-$BuOPhNO_2$ it must be decided how much of 4-*t*-$BuOPhNO_2$-d_2 is the 2,4 isomer and how much is the 3,5 isomer. This may be done by assuming that the deuterium distribution in the recovered nitrobenzene will be the same as that in the substitution products. More precisely, we assume that 4-*t*-$BuOPhNO_2$-*3,5*-d_2/4-*t*-$BuOPhNO_2$-d_3 = $PhNO_2$-d_3/$PhNO_2$-d_4 and 4-*t*-$BuOPhNO_2$-*2,6*-d_2/4-*t*-$BuOPhNO_2$-d_1 = $PhNO_2$-d_2/$PhNO_2$-d_1. This procedure leads to the calculation of 4-*t*-$BuOPhNO_2$ from $PhNO_2$/4-*t*-$BuOPhNO_2$ from $PhNO_2$-d_5 = 3.2 $\simeq k_H/k_D$. Run C was carried out under an atmosphere of O_2 and the same method of calculation gives k_H/k_D (for 4-substitution) = 4.1.

Thus for 4-*t*-$BuOPhNO_2$ formation the calculated isotope effect is virtually the same for runs A and C. The slightly lower value for run B may or may not be significant. As we have observed some destruction of *t*-$BuOPhNO_2$ after long periods of time at 30 °C, it is possible that this could selectively remove undeuterated *t*-$BuOPhNO_2$ molecules, lowering the apparent selectivity.

Runs B and C are not as useful in determining the isotopic selectivity for 2-*t*-$BuOPhNO_2$ formation except to establish minimum values. In the case of run B (anaerobic), 65.6% of this 2-substitution product arises from $PhNO_2$ and 32.3% arises from $PhNO_2$-d_5 establishing a minimum k_H/k_D = 2.0. Clearly a substantial fraction of the material arising from the $PhNO_2$-d_5 has undergone prior replacement of ortho deuterium by ortho hydrogen via the scrambling process. The minimum k_H/k_D for 2-substitution in run C (aerobic) is 1.9, again confirming that the presence of O_2 does not alter the isotope effect on the substitution rate. It should be pointed out that although run A is carried out under conditions which are somewhat milder than those of runs B or C, the substitution reactions should nevertheless have been at least 60% complete in run A because of the high base concentration employed. The fact that scrambling interferes with measurement of an isotope effect for 2-substitution in runs B and C but not in run A suggests that scrambling has only a first-order dependence on base concentration, rendering it less competitive with substitution at high [*t*-BuOK]. Thus it is probably the low base concentration which makes it difficult to measure isotopic selectivity for 2-*t*-$BuOPhNO_2$ formation in runs B and C and not the higher temperature and longer time.

Interestingly, the 2-$HOPhNO_2$ shows no evidence of isotopic selectivity in its formation despite the fact that the deuterium distribution in this product suggests that it was formed before scrambling was complete. As expected, there is no isotopic selectivity in $PhNO_2^{-}\cdot$ formation. The deuterium distribution in this material shows that most of the salt precipitates before scrambling has become complete. The salt apparently does not equilibrate to any great extent with $PhNO_2$ in solution.

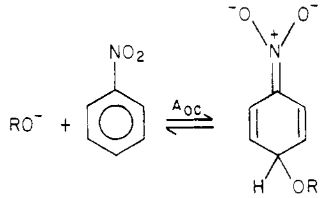
Mechanism. The results presented allow us to draw some detailed conclusions about the mechanism of the reaction between $PhNO_2$, an apparent one-electron acceptor, and tertiary alkoxide, a two-electron donor. We have shown that the ultimate reduction product is $PhNO_2^{-}\cdot$ and the oxidized species are mainly alkoxy- and hydroxy-de-hydro-substitution products. Clearly, if $PhNO_2^{-}\cdot$ is the only reduction product formed in significant quantity, 2 equiv must be produced. This is what we observe.

If *t*-BuO^- and $PhNO_2$ produce $PhNO_2^{-}\cdot$ a single-electron transfer must occur at some stage in the process. The simplest but least likely possibility is direct transfer from alkoxide to $PhNO_2$. This is unlikely because, as pointed out by Buncel,[6] such a reaction should be energetically unfavorable to the extent of about 3 eV. We are not sure this estimate is applicable to our solvent system, but approximate thermochemical calculations show that direct oxidation of *t*-BuO^- is at the very least an appreciably more endergonic proces than those discussed below. A more reasonable first step would entail nucleophilic attack by alkoxide (A_{OC}).[7]

This is, of course, a well-precedented substitution route for aromatic nitro compounds in which the ring atom attacked carries a nucleofugic group (A_{OC} + D_{XC}). The A_{OC} process can also lead to stable adducts in polynitro compounds with poorly nucleofugic substituents.[8] It seems reasonable to assume that such a process occurs when alkoxide and $PhNO_2$ react although the adduct would be present in low concentration.

The substitution pattern in our reaction products strongly supports this interpretation. Burdon and co-workers have shown that for perfluoronitrobenzene, 4-substitution predominates over 2-substitution with non-hydrogen-bonding nucleophiles such as methoxide.[9] Moreover, with nucleophiles which can form hydrogen bonds (such as lithium anilide) nearly exclusive 2-substitution is observed.[10] Moreover Wohl's initial report[1] indicates predominant ortho attack by hydroxide. These facts provide a convincing parallel to our finding of predominant 4-substitution by *t*-BuO^- and exclusive 2-substitution by hydroxide.

The first step therefore appears to be an A_{OC} process as shown in eq 1 for the case of 4-substitution. Our experimentally observed products must then be formed from **1** and its ortho analogue. A possible route is the sequence of eq 2 and 3. This has been suggested earlier by Russell to explain the formation of $PhNO_2^{-}\cdot$ when $PhNO_2$ reacts with *t*-BuOK/Me_2SO.[11]



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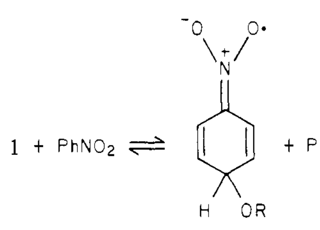
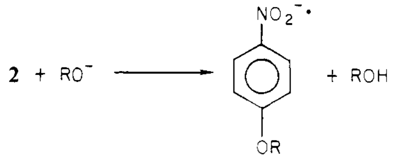


2

(2)



(3)

In a preliminary presentation of this work,[12] we also favored the analysis of eq 1, 2, and 3. However, certain features of this explanation have continued to trouble us. One of these was a doubt about the effectiveness of **1** as an electron donor. It seemed clear that the formation of **1** should be an energetically uphill process.

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(6) Buncel, E.; Menon, B. C. *J. Am. Chem. Soc.* **1980**, *102*, 3499.

(7) A = association, D = dissociation. The first subscript is the nucleophilic atom. See: Guthrie, R. D. *J. Org. Chem.* **1975**, *40*, 402.

(8) See ref 6 (ref 2–9).

(9) Allen, J. G.; Burdon, J.; Tatlow, J. C. *J. Chem. Soc.* **1965**, 1045.

(10) Burdon, J.; Westwood, W. T. *J. Chem. Soc. C* **1970**, 1271.

(11) Russell, G. A.; Janzen, E. G.; Strom, E. T. *J. Am. Chem. Soc.* **1964**, *86*, 1807.

(12) Guthrie, R. D.; Nutter, D. E. "Abstracts of Papers, 28th Southeastern Regional Meeting of the American Chemical Society, Gatlinburg, TN, September, 1976; American Chemical Society: Washington, DC, 1976.

As **1** is a conjugated version of a nitroalkane carbanion and these were observed by Russell[11] to be marginally capable of nonphotochemical electron donation to $PhNO_2$ even at high concentration, this path seems likely to involve a sequence of two rather endergonic steps. Moreover as described above, we found that there is a significant isotope effect on formation of the *tert*-butoxy adducts which, in the context of the explanation under evaluation, demands that the process of eq 3 be at least partially rate determining. This is especially difficult to accept when it is realized that **2** is a conjugate acid of the radical anion of 4-*t*-$BuOPhNO_2$. The conjugate acid of $PhNO_2^{-}\cdot$ is reported to have a pK_a of 3.2[13] even when the most stable tautomer is being considered. We would expect **2** to have a significantly lower pK_a and to react extremely rapidly with *t*-BuOK. For this reason the process of eq 3 seems unlikely to be slower than the reverse of step 2 especially in view of the low concentration of $PhNO_2^{-}\cdot$ in solution compared to *t*-BuOK.

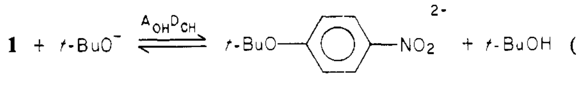
Although these arguments simply weaken the case for the sequence of eq 1, 2, and 3, our observation of an undiminished isotope effect in the presence of O_2 strikes a mortal blow. The reaction of $PhNO_2^{-}\cdot$ with O_2 is known to be fast,[5,14] and the presence of O_2 would render step 2 irreversible with hydrogen removal not occurring until step 3. Such irreversibility would leave step 2 rate determining and remove the isotope effect.

This critical observation forced us to think about alternative mechanisms. Specifically, we needed to consider routes by which the adduct, **1**, could lose its hydrogen either prior to or concurrent with the formation of radical anions. One possibility was the hydride transfer of eq 4, $A_{HO}D_{HC}$. However, this is ruled out

$$\mathbf{1} + PhNO_2 \xrightarrow{A_{HO}D_{HC}} t\text{-}BuOPhNO_2 + PhNO_2H^- \qquad (4)$$

because involvement of such a mechanism would render the reaction first order in [*t*-BuOK] and second order in [$PhNO_2$]. Also a hydride-transfer process might be expected to exhibit a smaller isotope effect.[15]

A mechanism which explains all of the observed experimental findings incorporates a step in which the initial adduct **1** reacts with *t*-BuOK by an $A_{OH}D_{CH}$ process to give a dianion, **3**, as shown in eq 5. The conversion to the observed products then proceeds



(5)

3

as shown in eq 6 which of course represents two electron-transfer

$$\mathbf{3} + 2PhNO_2 \rightarrow t\text{-}BuOPhNO_2 + 2PhNO_2^{-}\cdot \qquad (6)$$

steps. The *full mechanism is thus represented by combining eq 1, 5, and 6* and may be symbolized as follows: $A_{OC} + A_{CH}D_{CH} + 2T_e$.[16] Second-order dependence on [*t*-BuOK] and first-order dependence on [$PhNO_2$] are explained. With the process of eq 5 rate determining, the insensitivity of the rate and isotope effect to O_2 is also predicted.

Although the reaction of **1** with *t*-BuOK to form a dianion was not anticipated, the process does not appear to be energetically unreasonable. In studying the electrochemical reduction of $PhNO_2$ in liquid ammonia, Bard[17] has estimated an equilibrium constant of 20–60 for the protonation of $PhNO_2^{2-}$ by isopropyl alcohol. Considering that *t*-BuOK in THF is probably a stronger base than isopropoxide in ammonia and that Bard's calculation deals with oxygen protonation which would be more favorable than the reverse of eq 5, the equilibrium of eq 5 may even lie to the right. Once the dianion, **3**, is generated, its fate would be either protonation on oxygen or electron transfer. The electron-transfer process would clearly be downhill energetically[17] and accounts for the predominant outcome of the reaction. If a competing protonation on oxygen occurs, it could explain the ubiquitous presence of HO^- which would be formed rapidly[17] from the conjugate acid of **3**. It is possible that HO^- might serve more effectively than *t*-BuOK for removal of the sterically protected proton in **1**.

It seems likely that the dianion mechanism for substitution described in this paper is restricted to aromatic nitro compounds because few other functional groups would be likely to provide an accessible dianion. On the other hand it provides one clear example of an apparent electron-transfer reaction proceeding by initial nucleophilic attack.

Experimental Section

Reagents. Commercial (Aldrich) potassium *tert*-butoxide was sublimed and transferred in a glovebox. Tetrahydrofuran was distilled directly into the *t*-BuOK-containing flask from either $LiAlH_4$ or sodium benzophenone ketyl. Solutions prepared by the latter procedure gave relatively more *tert*-butoxy compounds and less nitrophenol. Nitrobenzene was purified as previously described.[4]

Reaction Procedures. The solvent-base solution was transferred by gas-tight syringe to a septum-covered centrifuge tube. A mixture of $PhNO_2$ and either hexadecane or bicyclohexyl was introduced by syringe to start the reaction. Procedures for separating and determining the amount of precipitated $PhNO_2^{-}\cdot K^+$ have been described previously.[18] Workup of the reaction solution was carried out in pentane–water with the acidic fraction being finally extracted into CH_2Cl_2. GC analysis was carried out on either a 17 ft × $^1/_4$ in. column of 10% SF-96 on DCDMS-treated acid-washed Chromosorb W or on a 6 ft × 2 mm column of 3% OV 101 on Partisorb. Products were isolated by condensation of the GC effluent and compared with authentic samples. In the case of 2-nitro-5-*tert*-butoxyphenol, the collected material showed the following: mp 59–60; ^1H NMR ($CDCl_3$) δ 1.2 (9 H, s), 6.2 (1 H, d), 6.4 (1 H, q), 7.8 (1 H, d), 10.6 (1 H, s); MS, *m/e* 211, 196, 155, 57. This compound could also be prepared by treating 4-*tert*-butoxynitrobenzene (136 mg, 0.70 mmol) with 9 mL of 0.102 N *t*-BuOK in $LiAlH_4$-purified THF at 50 °C for 70 h.

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Registry No. 4-*t*-$BuOPhNO_2$, 2109-72-0; 2-*t*-$BuOPhNO_2$, 83747-12-0; potassium *tert*-butoxide, 865-47-4; nitrobenzene, 98-95-3; 2-nitro-5-*tert*-butoxyphenol, 83747-11-9.

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