Nucleophilic Aromatic Substitution during Deoxygenation. Deoxygenation of Nitrosobenzene by Triethyl Phosphite in Alcohols[1a]

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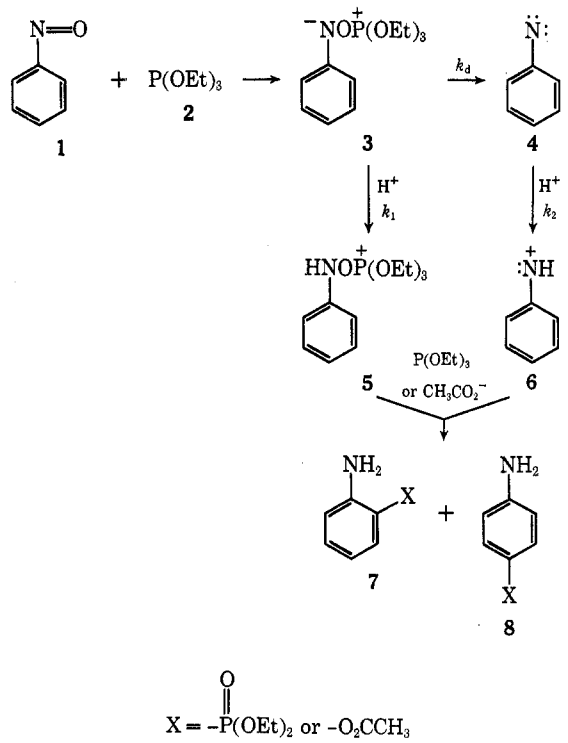
Deoxygenation of nitrosobenzene by triethyl phosphite in methanol has been found to give *o*- and *p*-anisidine in yields up to 70%. Similar deoxygenations in ethanol, 2-methoxyethanol, isopropyl alcohol, and *tert*-butyl alcohol give mixtures of the corresponding *o*- and *p*-alkoxyanilines, but only in the presence of small amounts of acid in the solvent (0.01–1.0 mol % acetic acid). Deoxygenation of *p*-nitrosotoluene in methanol gives 2-methoxy-4-methylaniline and 4-methoxy-4-methyl-2,5-cyclohexadienone. Deoxygenations which lead to aromatic nucleophilic substitution are interpreted in terms of a mechanism which proposes that an intermediate prior to phenylnitrene in the deoxygenation sequence is protonated and undergoes solvolysis leading to the alkoxyanilines.

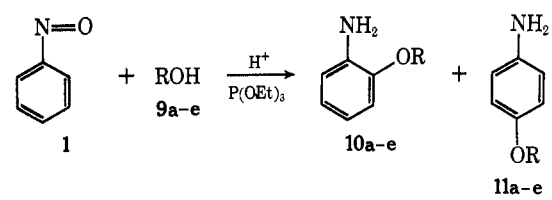
The deoxygenation of nitrosobenzene by trivalent phosphorus compounds has usually been studied in aprotic solvent media. In benzene in the presence of excess nitrosobenzene, a modest yield (21%) of azoxybenzene is formed.[2] In excess triethyl phosphite, deoxygenation occurs, but the products have not proven to be tractable.[2] We have reported that the deoxygenation of nitrosobenzene in triethyl phosphite (TEP) containing 5% by volume acetic acid led to the formation of 2-hydroxyacetanilide and diethyl *o*- and *p*-aminophenylphosphonate.[3] These products, on the basis of their structures, appear to have been formed by a process involving nucleophilic aromatic substitution. We proposed that such products arose as a result of protonation of phenylnitrene or some prior intermediate during the deoxygenation reaction.[3] The addition of a proton to either **3** or **4** would generate an intermediate which would be expected to be attacked by a nucleophile at the ortho and para positions of the ring and thus lead to the observed products.[4] In this paper we present the results of the study of the deoxygenation of nitrosobenzene by TEP in several alcohols. Nucleophilic aromatic substitution has been found to be an important process under these conditions and further evidence has been developed which points to a proton transfer step as being crucial to nucleophilic aromatic substitution under these conditions.

SCHEME I



Results

The deoxygenation of nitrosobenzene was studied using methanol, ethanol, 2-methoxyethanol, isopropyl alcohol, and *tert*-butyl alcohol as solvents. Deoxygenations were also carried out in each alcohol with added amounts of acetic acid in concentrations ranging from 0.01 to 1.0 mol %. The introduction of each of the alcohols as a nucleophile was observed. However, except for methanol, the substitution process was important only in the presence of added acetic acid.



It was possible to isolate samples of the alkoxyanilines **10a–e** and **11a–e** from deoxygenations run on a preparative scale. Each of the anilines was unequivocally identified by preparation of derivatives or by spectral data, as is described fully in the Experimental Section. Quantitative yield data were obtained gas chromatographically using the internal standard method. The data are shown in Table I.

The formation of *o*- and *p*-anisidine in a combined yield of ~60% in the absence of any acid was a reproducible result. Methanol, distilled directly from sodium methoxide under nitrogen and used without exposure to the atmosphere, gave similar yields of anisidines. It, therefore, seems very unlikely that acidic impurities are responsible for the nucleophilic substitu-

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(2) P. J. Bunyan and J. I. G. Cadogan, *J. Chem. Soc.*, 42 (1963).

(3) R. J. Sundberg, R. H. Smith, Jr., and J. E. Bloor, *J. Amer. Chem. Soc.*, **91**, 3392 (1969).

(4) For related examples of nucleophilic aromatic substitution, see (a) P. G. Gassman, G. Campbell, and R. Frederick, *ibid.*, **90**, 7377 (1968); (b) P. A. S. Smith, "Open Chain Nitrogen Compounds," Vol. 2, W. A. Benjamin, New York, N. Y., 1966, pp 225–226; (c) H. J. Shine, "Aromatic Rearrangements," Elsevier, New York, N. Y., 1967, pp 182–190.

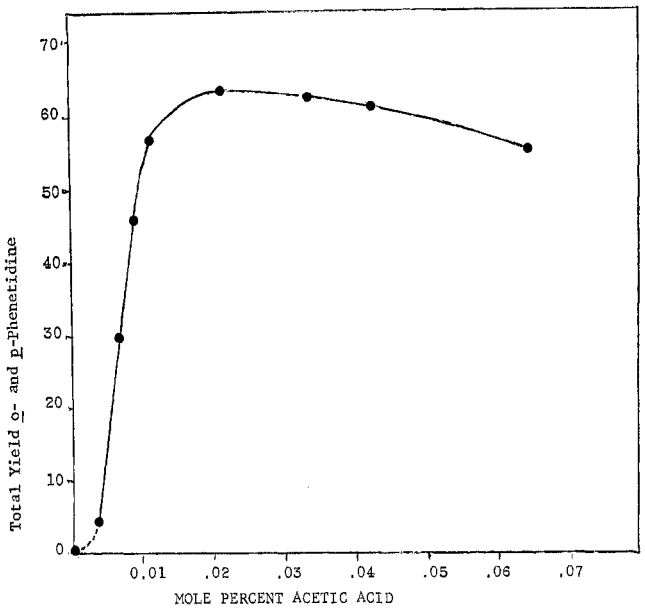


Figure 1.—Yield of phenetidine as a function of acetic acid concentration in ethanol.

TABLE I

ALKOXYANILINES FROM NITROSOBENZENE BY DEOXYGENATION IN ALCOHOLS

Alcohol	R	Mol % acetic acid	% yield[a] 10	11
9a	CH_3	0.00	11	49
9a	CH_3	0.01	11	61
9b	CH_3CH_2	0.00	<1	<1
9b	CH_3CH_2	0.01	12	42
9b	CH_3CH_2	0.02	14	50
9c	$CH_3OCH_2CH_2$	0.00	0	0
9c	$CH_3OCH_2CH_2$	0.01	8	39
9d	$(CH_3)_2CH$	0.01	2	2
9d	$(CH_3)_2CH$	0.10	15	52
9e	$(CH_3)_3C$	0.10	6	4
9e	$(CH_3)_3C$	1.0	13	24

[a] The yields are averages of at least two runs. The absolute yields are reproducible to ±2% for **10** and ±3% for **11**.

tion which is observed in methanol. Indeed, **10a** and **11a** were formed in a combined yield of 27% when a deoxygenation was carried out in methanol containing 1.0 mol % sodium methoxide. The addition of small amounts of acetic acid resulted in a slight increase in the yield of *o*- and *p*-anisidine (12 and 60%, respectively, in methanol containing 0.2 mol % acetic acid).

The extent of nucleophilic aromatic substitution in ethanol was studied as a function of the concentration of added acetic acid. As shown in Figure 1, the yields of *o*- and *p*-phenetidine rise sharply as the amount of acetic acid is increased from 0.004 to 0.02 mol %, but then remain relatively constant and eventually decrease again at higher acetic acid concentrations.

Both anisidines and phenetidines are formed in methanol–ethanol mixtures. The total yield of alkoxyanilines drops with increasing ethanol concentration, but the proportion of the total mixture which is accounted for by **10b** and **11b** increases as the amount of ethanol in the solvent mixture increases. The data are shown in Table II.

Deoxygenation of nitrosobenzene in methanol-*d* gave reproducibly lower yields (8 ± 1 and 47 ± 1%, respectively) of **10a** and **11a** than identical deoxygenations in

TABLE II

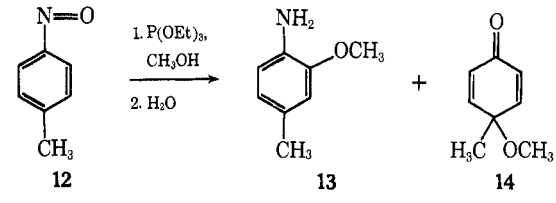
YIELDS OF ALKOXYANILINES IN ETHANOL–METHANOL MIXTURES

Mole % EtOH	% yields[a] 10a	11a	10b	11b	% 10b + 11b of total alkoxyanilines
0	10	49			
10	10	44	1	4	8.5
25	7	32	2	8	20
30	5	21	2	7	26
35	5	22	2	9	29
41	4	14	2	7	33
59	1	5	1	3	40
100			0	0	

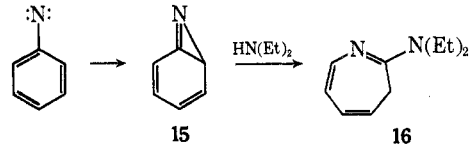
[a] Yields were measured gas chromatographically using the internal standard method.

normal methanol (11 ± 1, 60 ± 2, respectively). Because of slightly modified reaction conditions, these data are not directly comparable to those in Table I.

Deoxygenation of *p*-nitrosotoluene (**12**) in methanol also afforded products characteristic of nucleophilic aromatic substitution. 2-Methoxy-4-methylaniline (**13**) and 4-methoxy-4-methyl-2,5-cyclohexadienone (**14**) were isolated and identified as products. The details of product identification are described in the Experimental Section.



Since the major goals of this study included an effort to establish the stage at which the crucial proton transfer occurs, it was of interest to study some alcohol–amine solvent mixtures. Secondary amines are efficient traps for the bicyclic intermediate **15** which is believed to be rapidly formed from phenylnitrene.[5] The nature



of the products formed in alcohol–amine solvent mixtures should then provide insight into the relative rates of processes leading to **10** and **11** as opposed to those leading to **16** in such solvent mixtures. Figures 2 and 3 record the yields of **11a** and **16** found for deoxygenation in a series of methanol–diethylamine mixtures and for **11b** and **16** in a series of ethanol–diethylamine mixtures. Deoxygenation of nitrosobenzene in methanol–diethylamine also led to the formation of a small amount of 1,1-diethyl-2-phenylhydrazine which was identified by comparison with an authentic sample.[6] The formation of hydrazines from amines and arylnitrenes has

(5) (a) R. Huisgen and M. Appl, *Chem. Ber.*, **91**, 12 (1958); (b) W. von E. Doering and R. A. Odum, *Tetrahedron*, **22**, 81 (1966); (c) R. A. Odum and M. Brenner, *J. Amer. Chem. Soc.*, **88**, 2074 (1966); (d) J. I. G. Cadogan and M. J. Todd, *J. Chem. Soc. C*, 2808 (1969); (e) R. J. Sundberg, B. P. Das, and R. H. Smith, Jr., *J. Amer. Chem. Soc.*, **91**, 658 (1969); (f) R. J. Sundberg, *ibid.*, **88**, 3781 (1966).

(6) K. Kratzl and K. P. Berger, *Monatsh. Chem.*, **89**, 83 (1958).

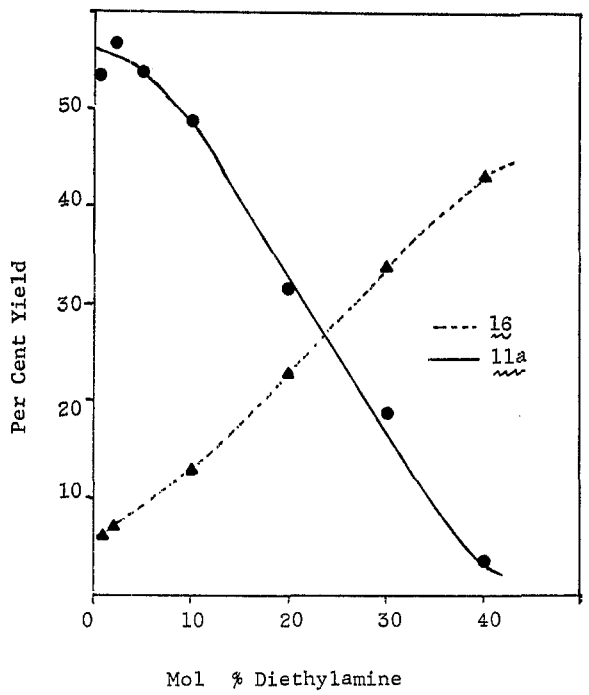


Figure 2.—Product composition in methanol-diethylamine mixtures.

previously been observed with phenylnitrene,[5c] *p*-cyanophenylnitrene,[7a] and 2-pyrimidylnitrene.[7b]

The photolytic decomposition of phenyl azide in certain protic solvents has been found to give products resulting from apparent nucleophilic aromatic substitution.[5b,8] However, the mechanisms by which net nucleophilic substitution occurs in these systems have not been carefully studied. We have photolyzed phenyl azide in solvent systems similar to those employed in the deoxygenation reactions. Since photolysis of phenyl azide is believed to generate phenylnitrene,[9] these experiments permit a test for the existence of the reaction pathway **4** → **6** → **10** + **11** in alcoholic solutions of acetic acid. Photolysis of phenyl azide in methanol, methanol containing 10% acetic acid, ethanol, and ethanol containing 10% acetic acid gave no significant amounts of alkoxyanilines, indicating that the reaction path **4** → **6** + **10** + **11** is inoperative under these conditions. Interestingly, we observed small yields of 2-alkoxy-3*H*-azepines in these reactions. Their formation can be accounted for by a mechanism similar to that invoked for 2-dialkylamino-3*H*-azepines[5] but the alcohols are evidently much poorer "traps" for the intermediate **15** than are amines.

Discussion

The results of this study have provided a new example of nucleophilic aromatic substitution during deoxygenation reactions. The type of nucleophiles which have been demonstrated to effect substitution of the aromatic ring during deoxygenation processes now include triethyl phosphite,[3] acetic acid or acetate ion,[3] hydrogen fluoride,[10] and primary, secondary, and tertiary alcohols. The isolation of the cyclohexadienone **14** from deoxygenation of *p*-nitrosotoluene in methanol provides further support for the interpretation of the overall reaction as a process involving nucleophilic aromatic substitution. The acid-catalyzed rearrangement of para-substituted phenylhydroxylamines has been shown to provide products related to **14**, as in the case of 2,4-dimethylphenylhydroxylamine.[4c,11]

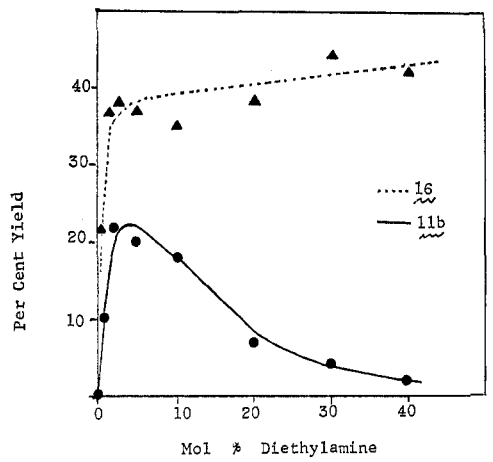
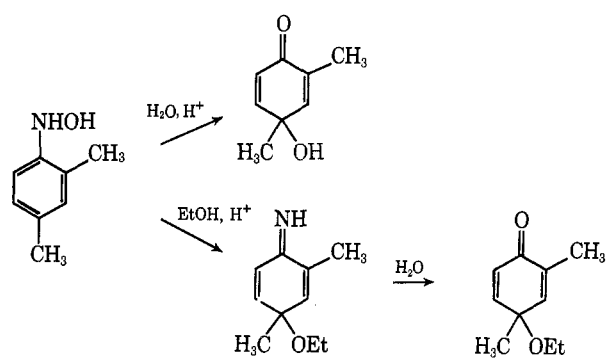


Figure 3.—Product composition in ethanol–diethylamine mixtures.



Several of the qualitative results of our work support the proposal[3] that nucleophilic aromatic substitution occurs when some intermediate in the deoxygenation sequence is protonated. The sharp rise in yields of phenetidines when acetic acid is added to ethanol suggests that protonation is crucial to nucleophilic substitution. The difference in product yield in methanol-*d* *vs.* methanol can be interpreted on the basis of a decreased rate of protonation in the deuterated solvent. If the yield of **10a** and **11a** depends upon the relative magnitudes of k_d and k_1 (Scheme I), the magnitude of the solvent isotope effect can be estimated by assuming that the total yield of **10a** and **11a** reflects the fraction of the intermediate **3** which is converted to **5** rather than **4**. In methanol, $k_1 = 71/29\ k_d$. For methanol-*d*, $k_{1'} = 56/44\ k_{d'}$. Assuming k_d is identical in the two solvents, $k_1 = 1.9\ k_{1'}$. This solvent isotope effect could reflect either a kinetic isotope effect on the rate of proton transfer or the diminished extent of autoprotolysis of the deuterated solvent.

The results in the methanol–diethylamine system are

(7) (a) R. A. Odum and A. M. Aaronson, *J. Amer. Chem. Soc.*, **91**, 5681 (1969); (b) R. Huisgen and K. v. Fraunberg, *Tetrahedron Lett.*, 2595 (1969).

(8) T. Shingaki, *Sci. Rep. Coll. Gen. Educ. Osaka Univ.*, **11**, 93 (1963); *Chem. Abstr.*, **60**, 6734 (1964).

(9) G. L'abbé, *Chem. Rev.*, **69**, 345 (1969).

(10) P. H. Scott, C. P. Smith, E. Kober, and J. W. Churchill, *Tetrahedron Lett.*, 1153 (1970).

(11) E. Bamberger and F. Brady, *Chem. Ber.*, **33**, 3642 (1900); E. Bamberger, *ibid.*, **40**, 1906, 1918 (1907); see also the related work of P. G. Gassman and G. A. Campbell, *Chem. Commun.*, 427 (1970).

in accord with treating nucleophilic aromatic substitution as a process which competes with formation of phenylnitrene. As shown in Figure 2 the yield of the azepine **16**, which is derived from the nitrene, is greatly diminished in the methanol-rich mixtures which facilitate nucleophilic aromatic substitution. In ethanol, which does not favor nucleophilic aromatic substitution, the yield of azepine is roughly constant over the rage 2–40 mol % diethylamine.

A final qualitative conclusion which can be drawn from the results involves the identity of the species which is protonated. The fact that the nucleophilic aromatic substitution products found from deoxygenations in alcohols are not found when phenyl azide is photolyzed in the same solvents leads to the conclusion that nucleophilic aromatic substitution involves an intermediate which is unique to the deoxygenation reaction. Since currently available evidence[2,5c-f] indicates that phenylnitrene is the earliest intermediate common to both deoxygenation and azide photolysis, we conclude that it is the zwitterion **3** which acts as the proton acceptor and leads to nucleophilic aromatic substitution in deoxygenation reactions. It is entirely reasonable that the conjugate acid **5** would solvolyze in alcohols to give **10** and **11**, since **5** is an aniline derivative with an excellent leaving group, triethyl phosphate, bonded to nitrogen by a relatively weak N–O bond. We, therefore, propose the sequence **1** → **3** → **5** → **10** + **11** as the mechanism by which the formation of alkoxyanilines occurs during deoxygenation.

There are several additional facets of the data which require comment. One of these is the striking contrast in the ability of methanol to promote the formation of aromatic nucleophilic substitution products, as compared to ethanol and the other alcohols studied. Secondly, the data in Figure 2 suggest that the extent of nucleophilic substitution in ethanol rises very sharply over a narrow range of increasing acid concentration. The relative amount of nucleophilic substitution appears to increase by a factor of about five while the acid concentration changes only by a factor of two in the concentration range 0.005–0.010 mol % acetic acid. Finally, as shown in Figure 3, diethylamine in the concentration range 1–30 mol % induces formation of *o*- and *p*-phenetidine.

It is important to consider whether the protonation process **3** → **5** is an equilibrium process under the reaction conditions. A proton transfer to nitrogen from a protic solvent is expected to be rapid. However, decomposition of **3** and **5** by heterolysis of the weak N–O bond may also be fast. Several pieces of data tend to argue against the various solvent effects being reflections of shifts in the position of a **3** ⇌ **5** equilibrium. Extensive nucleophilic aromatic substitution occurs even in the presence of methoxide ion. Under these conditions the equilibrium should be shifted toward **3** unless **3** is a much stronger base than methoxide ion. The induction of nucleophilic aromatic substitution by the base, diethylamine, is also difficult to comprehend in terms of an equilibrium process, since diethylamine could not be expected to shift the equilibrium toward **5**. The present evidence seems more in accord with considering the product-determining protonation step from a kinetic viewpoint and assuming that nucleophilic substitution occurs in solvents in which the protonation step is rapid enough to compete with decomposition of **3** to **4**.

Methanol is a stronger acid than ethanol[12] and the rate of proton transfer to a base is therefore expected to be more rapid for methanol than for ethanol.[13] The rate of dissociation of methanol in autoprotolysis exceeds that of ethanol by a factor of 200.[14] If the rates of protonation of **3** by the two alcohols differed by a comparable magnitude, the observed difference in the extent of nucleophilic substitution in the two alcohols could be readily understood. The magnitude of the rate difference for protonation of **3** by methanol and ethanol would presumably be greatly diminished by a leveling effect if **3** is a very strong base relative to both alcohols. For example, the relative order of protonation of strongly basic aromatic radical anions has been found to fall in the order methanol > ethanol ≈ 1-propanol > 2-propanol, but the protonation rates of methanol and ethanol differ by only a factor of three in this case.[15] The effect of acetic acid in inducing nucleophilic aromatic substitution in ethanol and the other alcohols studied can be interpreted as being the result of an increased rate of proton transfer in the presence of the added acid. We are, however, not able to interpret this effect of the acid concentration in a quantitative way. A simple kinetic scheme which assumes that $k_1 = k_p[HA]$ and that **5** is quantitatively converted to

$$\begin{array}{ccc} & & k_d \\ & \mathbf{3} & \longrightarrow \mathbf{4} \\ & k_p \downarrow & \\ & \mathbf{5} & \end{array}$$

10b and **11b** predicts that the per cent yield of nucleophilic substitution product will be given by

$$\%\ \text{yield} = \frac{100k_p[HA]}{k_p[HA] + k_d}$$

$$\frac{100}{\%\ \text{yield}} = 1 + \frac{k_d}{k_p[HA]}$$

The observed increase in yield of **10b** and **11b** over the range 0.005–0.015 mol % acetic acid is much sharper than predicted by the previous equation.

The extent of formation of *o*- and *p*-phenetidine in diethylamine–ethanol mixtures is surprising. This effect does not appear to be a case of base-catalyzed nucleophilic attack on the intermediate **3** since deoxygenation of nitrosobenzene in ethanol containing sodium ethoxide does not lead to detectable amounts of phenetidines. The possibility that solvolysis of the amine furnishes sufficient $Et_2NH_2^+$ to act as a catalytic species also is unlikely. The dissociation constant of diethylammonium ion in ethanol has been given as $10^{-9.15}$.[16] From this data and the autoprotolysis constant, $10^{-18.9}$,[17] we calculate that $[Et_2NH_2^+]$ in ethanol is 2.0×10^{-5} *M* at $[Et_2NH] = 1$ *M* (~5 mol %). Acetic acid (p*K* = 10 in ethanol)[13b] induces nucleophilic aromatic substitution in 20% yield when present at

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(14) G. Brière and F. Gaspard, *J. Chim. Phys.*, **64**, 1071 (1967).

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(16) P. Rumpf, G. Girault-Vexlearschi, and R. Schaal, *Bull. Soc. Chim. Fr.*, 554 (1955).

(17) K. Bowden, *Can. J. Chem.*, **43**, 2624 (1965).

1×10^{-3} *M*. Thus, it seems unlikely that catalysis by $Et_2NH_2^+$ can be responsible for the effect of diethylamine. In the absence of a satisfactory alternative explanation, we conclude that the solute diethylamine must effect the bulk solvent structure of ethanol in such a way that the solvolytic reaction pathway for **3** is favored relative to pure ethanol.

In conclusion, this work reports a new facet in the study of deoxygenations of aromatic nitroso compounds. While a qualitatively satisfactory mechanistic description of the aromatic nucleophilic substitution process seems to have been developed, several of the details and quantitative aspects of the data must, at present, be ascribed to rather ill-defined solvent effects.

Experimental Section

Procedure for Quantitative Glpc Analyses.—Quantitative analysis of product mixtures was carried out on a Varian Aerograph 204-1C instrument using a 10-ft copper column (1/8-in. o.d.) of 5% Apiezon L–5% potassium hydroxide on Chromosorb G. Column temperature was programmed 160–200° at 15° per min. The internal standard method of analysis was employed and detector responses for the various alkoxyanilines *vs.* biphenyl were determined experimentally with the following exceptions. The internal standard for the reaction in 2-methoxyethanol was *n*-amylbenzene. In the case of *o*-phenetidine, β-methoxy-*o*-phenetidine, *o*-isopropoxyaniline, and *o*-*tert*-butoxyaniline the yields were calculated using the detector responses obtained for the respective para isomers.

Deoxygenation of Nitrosobenzene (1) in Methanol.—A solution of 1 (2.0 g, 18.7 mmol) in benzene (80 ml) was added dropwise over a period of 3 hr to a cooled (0°) solution of TEP (9.4 mol, 55 mmol) in methanol (600 ml) under nitrogen. The methanol and benzene were then removed using a rotary evaporator, the residue was diluted with ether, and an aliquot was removed for quantitative glpc analysis. This analysis indicated yields of *o*- and *p*-anisidine of 10 and 49%, respectively. The main portion of the ether solution was extracted with dilute hydrochloric acid. The acidic extract was made alkaline with dilute sodium hydroxide and extracted with ether. After drying, concentration and chromatography on silicic acid (benzene-ether mixtures were used as the eluent solvent), there was obtained *o*-anisidine (0.14 g, 1.1 mmol, 7%) and *p*-anisidine (0.79 g, 6.4 mmol, 38%). Both compounds were identified by spectral comparison with authentic samples.

Deoxygenation of Nitrosobenzene in Ethanol.—The procedure was analogous to that described above for methanol. Quantitative glpc indicated no trace of *o*- or *p*-phenetidine under analytical conditions capable of detecting a 0.5% yield. Chromatography afforded no characterizable products.

Repetition of the experiment by adding nitrosobenzene (0.90 g, 8.4 mmol) in benzene (140 ml), dropwise over 2 hr, to TEP (4.2 ml, 24 mmol) in ethanol–acetic acid (272 ml, 1.0% acetic acid by volume) followed by the work-up described for methanol gave a glpc yield of 40% *p*-phenetidine. Chromatography on silicic acid using benzene-ether mixtures gave *o*-phenetidine (0.11 g, 0.8 mmol, 10%) and *p*-phenetidine (0.39 g, 2.8 mmol, 34%). Both compounds were identified by spectral comparison with authentic samples.

Deoxygenation of Nitrosobenzene in Methanol–Acetic Acid, Ethanol–Acetic Acid, and Methanol–Ethanol Mixtures.—The yield data for the solvent systems described in Figure I and Table II were obtained as follows. A solution of nitrosobenzene (0.45 g, 4.2 mmol) in benzene (20 ml) was added dropwise over a period of 1 hr to TEP (2.1 ml, 22 mmol) dissolved in the appropriate solvent (136 ml) at 0° under nitrogen. The solvent was then removed using a rotary evaporator and the residue was dissolved in ether and analyzed by glpc using the internal standard technique.

Solvent Isotope Effect in Methanol-*d*.—Two series consisting of three runs each were carried out, one series using methanol and the other using methanol-*d*. A solution of TEP (0.2 ml, 1.2 mmol) in methanol (8 ml) was cooled to 0°. A solution of nitrosobenzene (45 mg, 0.42 mmol) in methanol (5.6 ml) was added in one portion. The solution was then stirred for **1.5 hr. The** solvent was evaporated and the residue was dissolved in ether and analyzed by glpc. The yield data for the individual runs are shown in Table III.

TABLE III
ANISIDINE YIELDS IN METHANOL AND METHANOL-*d*

Solvent	% yield *o*-Anisidine	% yield *p*-Anisidine
Methanol	10	60
Methanol	10	59
Methanol	11	62
Methanol-*d*	8	48
Methanol-*d*	8	46
Methanol-*d*	9	48

Deoxygenation of Nitrosobenzene in Methanol Containing Sodium Methoxide.—A solution of nitrosobenzene (0.45 g, 4.2 mmol) in benzene (20 ml) was added dropwise over a period of 1 hr to a cooled (0°) solution of TEP (2.1 ml) in 1.0 mol % methanolic sodium methoxide (prepared by adding 0.78 g of metallic sodium to 136 ml of methanol). The reaction mixture was concentrated and analyzed by glpc. The yield of *o*-anisidine was 5% and that of *p*-anisidine was 22%.

Deoxygenation of Nitrosobenzene in Other Alcohols.—In each case a solution of nitrosobenzene (0.45 g, 4.2 mmol) in benzene (15 ml) was added dropwise over a period of 1 hr to a cooled (0°) solution of TEP (2.1 ml, 12 mmol) in the alcohol (136 ml) containing acetic acid in the amounts shown in Table I. The solvents were removed using a rotary evaporator and the residues were analyzed by glpc. Yield data are shown in Table I. Product identification procedures are given below for each alcohol.

A. 2-Methoxyethanol.—The crude product was chromatographed on silicic acid (50 g). Benzene–ether (9:1) eluted β-methoxy-*o*-phenetidine[18] (30 mg): ir (CCl_4) 3500, 3410 cm^{-1} (NH_2); nmr (CCl_4) δ 3.41 (s, 3 H, OCH_3), 3.50–4.30 (m, 6 H, OCH_2CH_2O and NH_2), and 6.51–6.82 (m, 4 H, C_6H_4); mass spectrum *m/e* 167, 109 (base peak). Benzene–ether (4:1) eluted β-methoxy-*p*-phenetidine (0.21 g): ir (CCl_4) 3490, 3400 cm^{-1} (NH_2); nmr (CCl_4) δ 3.15 (broad s, 2 H, NH_2), 3.38 (s, 3 H, OCH_3), 3.48–4.10 (m, 4 H, OCH_2CH_2O), and 6.35–6.85 (m, 4 H, C_6H_4); mass spectrum *m/e* (relative intensity) 167 (47), 109 (100); hydrochloride mp 180–181 (lit.[19] mp 181°) after recrystallization from methanol-ether; acetyl derivative mp 116–117° (lit.[19] mp 117°) after recrystallization from hexane–ether.

B. 2-Propanol.—The crude product was chromatographed on silicic acid (50 g). Benzene–ether (9:1) eluted *o*-isopropoxyaniline[20] (60 mg): ir (CCl_4) 3500, 3400 cm^{-1} (NH_2); nmr ($CDCl_3$) δ 1.37 (d, 6 H, J = 7 Hz, $CHCH_3$), 3.5 (broad s, 2 H, NH_2), 4.58 [multiplet, $J \approx 7$ Hz, ~1 H, $CH(CH_3)_2$], 6.84 (s, 4 H, C_6H_4); mass spectrum *m/e* (relative intensity), 151 (24), 109 (100). Benzene–ether (4:1) eluted *p*-isopropoxyaniline (0.26 g): ir (CCl_4) 3470, 3390 cm^{-1} (NH_2); nmr ($CDCl_3$) δ 1.29 [d, 6 H, J = 7 Hz, $CH(CH_3)_2$], 3.15 (broad s, ~2 H, NH_2), 4.40 [m, J = 7 Hz, 1 H, $CH(CH_3)_2$], 6.75 (d, 4 H, C_6H_4); mass spectrum *m/e* (relative intensity) 151 (19), 109 (100); acetyl derivative mp 130–131° (lit.[21] mp 131°) after recrystallization from ethanol–water.

C. *tert*-Butyl Alcohol.—The crude product was chromatographed on silicic acid (50 g). Benzene–ether (9:1) eluted *o*-*tert*-butoxyaniline (50 mg): ir (CCl_4) 3480, 3390 cm^{-1} (NH_2); nmr ($CDCl_3$) δ 1.40 [s, 9 H, $C(CH_3)_3$], 3.96 (broad singlet, 2 H, NH_2), and 6.45–7.15 (m, 4 H, C_6H_4); mass spectrum *m/e* 165, 109 (base peak). Treatment with hydrochloric acid (20 min) followed by acetylation gave 2-hydroxyacetanilide, mp 205–206 (lit.[22] mp 209°), identified by spectral comparison with an authentic sample. Benzene–ether (4:1) eluted *p*-*tert*-butoxyaniline (73 mg): mp 64–64.5° (lit.[23] mp 73–74°) after recrystallization from hexane ir (CCl_4) 3480, 3400 cm^{-1} (NH_2); nmr ($CDCl_3$) δ 1.31 [s, 9 H,

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$C(CH_3)_3$]; 3.45 (broad s, ~2 H, NH_2), 6.67 (d, J = 9 Hz, 2 H), 6.93 (d, J = 9 Hz, 2 H); mass spectrum (relative intensity) 165 (6), 109 (100); acetyl derivative mp 131–132° (lit.[23] mp 130°). Treatment of the acetyl derivative with hydrochloric acid gave 4-hydroxyacetanilide, mp 164–165° (lit.[24] mp 166°), which was identified by spectral comparison with an authentic sample.

Deoxygenation of *p*-Nitrosotoluene in Methanol.—A solution of TEP (10.0 ml) in methanol (600 ml) was stirred at room temperature and a solution of *p*-nitrosotoluene (2.0 g, 16.5 mmol) was added dropwise over 3 hr. The solution was then stirred at room temperature for 1 hr followed by addition of water (50 ml). The resulting solution was concentrated at room temperature to about 100 ml with a rotary evaporator. The residue was diluted with water (500 ml) and thoroughly extracted with hexane. Evaporation of the hexane gave a mixture containing 0.3 g (17%) of 2-methoxy-4-methylaniline (**13**) by nmr analysis. A sample purified by glpc using an Apiezon–KOH column gave a pure sample: nmr (CCl_4) δ 2.15 (s, 3 H), 3.45 (broad, 2 H), 3.80 (s, 3 H), and 6.52 (s, 3 H). An acetyl derivative was prepared, mp 127–129° (lit.[25] mp 131°). The water solution remaining after hexane extraction was extracted with ether. Evaporation of the dried ether extract gave a mixture of triethyl phosphate and 4-methoxy-4-methyl-2,5-cyclohexadienone (**14**) containing 0.5 g of **14** (23%) by nmr analysis. Crystallization from hexane gave pure **14**: mp 61–63° (lit.[26] mp 62–63°); nmr (CCl_4) 1.48 (s, 3 H), 3.27 (s, 3 H), 6.35 (d, 2 H), and 6.85 (d, 2 H).

Deoxygenation of Nitrosobenzene in Methanol–Diethylamine Mixtures.—A solution of nitrosobenzene (0.45 g, 4.2 mmol) in benzene (20 ml) was added dropwise over a period of 1 hr to a cooled (0°) solution of TEP (2.1 ml, 12 mmol) in the methanol–diethylamine mixtures indicated in Figure 2. After the reaction was complete, the solvent was removed on a rotary evaporator and the residue was analyzed for *o*-anisidine, *p*-anisidine, and 2-diethylamino-3*H*-azepine by glpc. The glpc analysis indicated the presence of a fourth volatile product which was isolated by preparative glpc using a 5-ft 5% SE-30 on Chromosorb G column. Spectral data indicated this to be 1,1-diethyl-2-phenylhydrazine and the identification was confirmed by comparison with an authentic sample prepared by the procedure of Fratzl and Berger.[6] The hydrazine was not detected at concentrations below 5 mol % diethylamine. The maximum yield observed was 8% at 40 mol % diethylamine.

Deoxygenation of Nitrosobenzene in Ethanol–Diethylamine Mixtures.—The reaction procedure was identical with that described for methanol–diethylamine mixtures. Results of glpc analysis for *p*-phenetidine and 2-diethylamino-3*H*-azepine are shown in Figure 3. Traces of 1,1-diethyl-2-phenylhydrazine were detected by tlc.

Deoxygenation of Nitrosobenzene in Ethanol Containing Sodium Ethoxide.—A solution of nitrosobenzene (0.225 g, 2.1 mmol) in benzene (10 ml) was added slowly to ethanol (67 ml) containing sodium ethoxide (11.7 mmol, prepared by dissolution of 0.27 g of sodium) and TEP (1.0 ml). No *p*-phenetidine was detected by glpc using the standard conditions of analysis.

Photolysis of Phenyl Azide in Methanol, Ethanol, Methanol–Acetic Acid, and Ethanol–Acetic Acid.—A solution of phenyl azide (1.0 g, 8.4 mmol) was irradiated using a 200-W Hanovia mercury lamp (filtered through Pyrex) for 9 hr in 180 ml of the appropriate solvent. More than 90% of the azide decomposed in each run. The solvents were removed using a rotary evaporator and the residue was analyzed by glpc. The results for the four solvent systems are described individually below.

A. Methanol.—No *o*-anisidine or *p*-anisidine was detected. 2-methoxy-3*H*-azepine[27] was formed in 11% yield and identified by spectra data.

B. 9:1 (v/v) Methanol–Acetic Acid.—No *o*-anisidine or *p*-anisidine was detected. A 9% yield of 2-methoxy-3*H*-azepine was indicated by glpc.

C. Ethanol.—No *o*-phenetidine or *p*-phenetidine was detected. A volatile product, tentatively identified as 2-ethoxy-3*H*-azepine, on the basis of spectral data was detected, but the yield was not determined.

D. 9:1 (v/v) Ethanol–Acetic Acid.—No *o*- or *p*-phenetidine was detected. Qualitative glpc indicated that 2-ethoxy-3*H*-azepine had been formed, but the yield was not determined.

Registry No.—**1**, 586-96-9; triethyl phosphite, 122-52-1; **9a**, 67-56-1; **9b**, 64-17-5; **9c**, 109-86-4; **9d**, 67-63-0; **9e**, 75-65-0; **12**, 623-11-0.

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Structure–Reactivity Studies of Deoxygenation Reactions

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The rates of deoxygenation by triethyl phosphite in methanol have been measured for nitrosobenzene, six monosubstituted derivatives, and 2-nitrosomesitylene. The rate of deoxygenation is enhanced by electron-withdrawing substituents and correlated best (ρ = 1.83, r = 0.994) in the Hammett equation using σ^+ substituent constants. Nitrosomesitylene is slightly more reactive than nitrosobenzene and the lack of a steric hindrance to deoxygenation points to nucleophilic attack by phosphorus at oxygen. Rates of deoxygenation of nitrobenzene and eight derivatives are reported. The rate of deoxygenation is enhanced by electron-withdrawing substituents. The question of isolation of triethyl *N*-arylphosphorimidates from thermal deoxygenation reactions is considered in light of these rate data.

The deoxygenation of aromatic nitroso and nitro compounds by trivalent derivatives of phosphorus has attained important synthetic potential for the preparation of a variety of benzoazoles,[1] trialkyl *N*-arylphosphorimidates,[2] dialkyl *N*-arylphosphoramidates,[3] nucleophilic aromatic substitution products,[4] and several types of rearranged heterocyclic nitrogen system.[2,3] During the course of the investigations which have explored the synthetic scope of the deoxygenation reaction, there have been relatively few rate studies which could provide data for more detailed mechanistic discussion of the deoxygenation reaction. Cadogan has reported a comparison of the reactivity of *o*-nitrobiphenyl with its 4-bromo and 4′-methyl derivatives.[5] Half-

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