TABLE V

THE CONVERSION OF 1-METHYLCYCLOHEXYL ACETATE INTO 1-METHYLCYCLOHEXENE IN ACETIC ACID SOLUTIONS CONTAINING VARIOUS ADDENDS AT 100°

Base	Acid	Time, hr	1-Methylcyclohexene, %	1-Methylcyclohexyl acetate, %
		1	0	100
		24	91.1	8.9
0.2 M NaOAc	0.1 M TsOH·H_2O	5	45.1	54.9
0.2 M NaOAc	0.1 M TsOH·H_2O	11	83.4	16.6
0.2 M NaOAc	0.1 M TsOH·H_2O	15.5	82.4	17.7
0.2 M Urea	0.1 M TsOH·H_2O	1.5 min	49.1	50.9
0.2 M Urea	0.1 M TsOH·H_2O	10.0 min	98.5	1.5
0.2 M Urea	0.1 M TsOH·H_2O	1	94.8	5.2
0.2 M Urea	0.1 M TsOH·H_2O	2	95.6	4.4
0.2 M Acetamide	0.1 M TsOH·H_2O	1	98.4	1.6

TABLE VI

PRODUCTS OF THE ACETOLYSIS OF 5-HEXENYL p-NITROBENZENESULFONATE IN ACETIC ACID CONTAINING SODIUM ACETATE, UREA, AND SODIUM PERCHLORATE

NaOAc[a,b]	Urea[a]	Temp, °C[c]	Cyclohexene, %	5-Hexenyl acetate, %	Cyclohexyl acetate, %	% cyclohexyl acetate/ % cyclohexene	% cyclic/ % acyclic
	0.2	60	10.4 ± 0.3	69.9 ± 1.0	19.7 ± 0.9	1.9	0.43
0.03	0.2	60	9.7 ± 1.1	66.9 ± 1.7	23.5 ± 2.9	2.4	0.50
0.1	0.1	60	8.2 ± 0.4	77.5 ± 1.9	14.4 ± 1.6	1.8	0.29
0.2		60	4.7 ± 0.3	85.3 ± 2.8	10.3 ± 2.0	2.2	0.18
0.3		60	2.9 ± 0.2	89.6 ± 0.5	6.9 ± 1.1	2.4	0.11
	0.2	100	14.4 ± 0.2	64.6 ± 0.6	21.2 ± 0.4	1.5	0.55
0.03	0.2	100	14.5 ± 0.8	65.4 ± 1.6	20.1 ± 0.7	1.4	0.53
0.1	0.1	100	10.9 ± 0.3	74.8 ± 0.9	14.4 ± 0.8	1.3	0.34
0.2		100	7.1 ± 0.8	80.3 ± 0.8	12.7 ± 1.5	1.7	0.25
0.3		100	5.4 ± 0.4	85.4 ± 0.4	9.0 ± 1.7	1.7	0.17
d	0.2	100	18.3 ± 1.0	60.1 ± 1.0	21.7 ± 0.2	1.2	0.67

[a] In molarity. [b] Two or three runs were made for each determination. [c] Runs at 60° were heated for 22 days. [d] These runs contained 0.2 M sodium perchlorate monohydrate.

drogen phosphate monohydrate is also inferior, since it is not very soluble and must be used as a suspended solid.

Acknowledgment.—The authors are indebted to the National Science Foundation for a postdoctoral fellowship to W. S. Trahanovsky in 1963–1964 and for a research grant, to the National Institutes of Health for a predoctoral fellowship to M. P. Doyle in 1966, and also to the Petroleum Research Fund of the American Chemical Society for support.

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p-Nitrosophenol Chemistry. I. Etherification of *p*-Nitrosophenol

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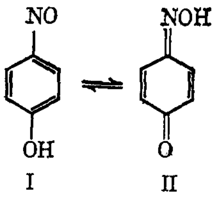
Conversion of *p*-nitrosophenol to its phenolic ethers by reaction with a variety of primary and secondary alcohols is shown to be a superior synthetic method. The equilibrium position in the acid-catalyzed reaction is unfavorable to ether formation but can be shifted toward the ether by use of excess alcohol and by removal of water formed. Careful control of reaction variables has given yields and conversions of ethers up to 98%. This reaction indicates that the recognized activating effect of the nitroso group is enhanced by protonation of *p*-nitrosophenol.

p-Nitrosophenol is a well-known example of tautomerism and is considered to be a mixture of the two forms (I and II).



I II

Although absorption spectra indicate that *p*-nitrosophenol exists predominantly in the quinone oxime form (II) in various solvents[1,2] it undergoes reactions characteristic of both forms. Thus, *p*-nitrosophenol reacts to form the oxime ether in methylation reactions with methyl iodide and alkali and with diazomethane.[3]

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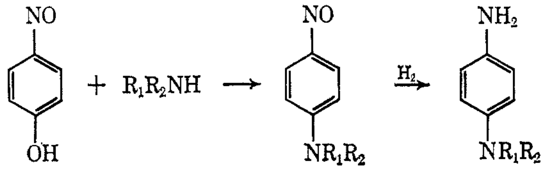
(1) L. C. Anderson and M. B. Geiger, *J. Am. Chem. Soc.*, **54**, 3064 (1932); L. C. Anderson and R. L. Yanke, *ibid.*, **56**, 732 (1934).

(2) E. Havinga and A. Schors, *Rec. Trav. Chim.*, **69**, 457 (1950).

(3) N. V. Sidgwick, "The Organic Chemistry of Nitrogen," revised and rewritten by T. W. J. Taylor and W. Baker, Oxford University Press, New York, N. Y., 1937, p 222.

Similarly, it reacts as a ketone with hydroxylamine to give quinone dioxime.[4,5] In acetic acid, *p*-nitrosophenol reacts as a typical aromatic nitroso compound in yielding *p*-hydroxyazobenzene by reaction with aniline;[6] with strong sulfuric acid, it reacts with N,N-dimethylaniline to form an indoaniline.[7] While *p*-nitrosophenol has strongly acidic properties due to the activated phenolic group,[8] O-substituted *p*-nitrosophenols have not been prepared and isolated as such by direct methods.

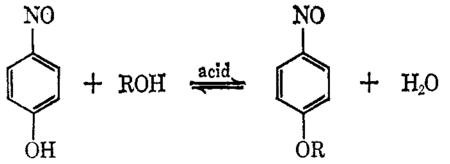
We became interested in *p*-nitrosophenol as the key intermediate in a new synthetic route from phenol to *p*-phenylenediamine derivatives. This route involves replacement of the phenolic hydroxyl group with an amino group. This synthesis requires that the typical aromatic nitroso reactions of *p*-nitrosophenol and the ready formation of high molecular weight products[9] be avoided. The reaction of *p*-nitrosophenol with the ketone reagents cited and its conversion to *p*-nitrosoaniline by reaction with ammonium salts[10] suggested that the desired reaction with amines might be feasible.



We have been successful in carrying out this type of reaction,[11] but have found that ethers of *p*-nitrosophenol undergo the desired displacement reaction much more readily than *p*-nitrosophenol itself. The practical preparation of *p*-nitrosophenol ethers thus became an essential step in the over-all synthesis of *p*-phenylenediamine derivatives.

This paper will be concerned with preparation of the ethers. Reaction with amines will be covered in the second and in subsequent papers in this series.

Etherification. Scope and Reaction Variables.—*p*-Nitrosophenol reacts with alcohols in the presence of an acid catalyst to form the corresponding *p*-nitrosophenyl alkyl ethers. This is a general reaction, offering a direct synthesis of these ethers which is much superior to previous routes based on reduction of ethers of *p*-nitrophenol.[12] The following equilibrium is set up.



(1)

The equilibrium is unfavorable to ether formation. Stoichiometric equilibrium constants, $K_{eq} = [p\text{-ROC}_6\text{H}_4\text{NO}][\text{H}_2\text{O}]/[p\text{-HOC}_6\text{H}_4\text{NO}][\text{ROH}]$ at 25°, with the reacting alcohol as solvent, are approximately 0.06 for methanol and 0.03 for 1-butanol. However, by using a large excess of the alcohol (*i.e.*, as the solvent medium), conversions of *p*-nitrosophenol to the ether at equilibrium are approximately 50–70% at room temperature for low molecular weight primary alcohols.

The nature of the alcohol affects both the position of equilibrium and the rate at which it is reached, as shown in Table I. While these data are not strictly comparable, because the solvent medium is not constant, the solvent changes are small and the large effect of the nature of the alcohol is clearly indicated. Thus, the equilibrium conversions to ether decrease in the order methyl > other primary > secondary ≫ tertiary. *p*-Nitrosophenol has also been shown spectroscopically to form ethers with a variety of primary and secondary alcohols, including allyl, benzyl, cyclohexyl, and 2-octyl.

TABLE I

EFFECT OF NATURE OF ALCOHOL ON THE ETHERIFICATION OF *p*-NITROSOPHENOL[a]

Alcohol	Conversion to ether at equilibrium, %	Fraction of equilibrium ether concn at 20 min, %
Methyl	71	89
Ethyl	58	50
1-Propyl	54	. .
1-Butyl	53	25
Isopropyl	31	10
t-Butyl	0	

[a] Alcohol/*p*-nitrosophenol mole ratio of 40:1, H_2SO_4/*p*-nitrosophenol mole ratio of 0.07:1, solvent/excess alcohol; temperature 30 ± 2°.

In addition to the structure of the alcohol, the nature and concentration of the acid catalyst, temperature, and reaction time are important variables. A strong acid catalyst is required for the etherification; *p*-toluenesulfonic and sulfuric acids were generally used in our work. Hydrogen chloride and boron trifluoride also gave high conversions to ether, while trichloroacetic and phosphoric acids were less active. Essentially no reaction occurred in the absence of added acid catalyst. An acid to *p*-nitrosophenol mole ratio of about 0.05 is sufficient to provide a reasonable rate of reaction.

Side reactions, as well as the rate of etherification, increase with temperature, resulting in reduced yields at temperatures greater than 75°. Furthermore, the reaction mixtures may decompose violently under certain conditions at about 110° (see the Experimental Section). Thus, both for reasons of safety and maximum conversion, the reaction temperature is preferably kept low. A convenient temperature range in the laboratory is about 25–50°.

Closely related to reaction temperature and catalyst concentration is the reaction time. The amount of ether formed reaches a maximum and decreases with time as the result of side reactions. At temperatures >50° and an acid catalyst/*p*-nitrosophenol mole ratio of >1, detectable yield loss takes place within 10 min. At 30° and an acid catalyst/*p*-nitrosophenol mole ratio of about 0.05:1, there is no detectable loss for 2.5 hr. A reasonable reaction period is about 1 hr.

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[4] R. Nietzki and F. Kehrmann, *Ber.*, **20**, 614 (1887); R. Nietzki and A. L. Guiterman, *ibid.*, **21**, 429 (1888).

[5] J. Thiele and W. Barlow, *Ann.*, **302**, 331 (1898). E. H. Rodd, "Chemistry of Carbon Compounds," Vol. IIIA, Elsevier Publishing Co., New York, N. Y., 1954, p 447.

[6] C. Kimich, *Ber.*, **8**, 1027 (1875).

[7] E. H. Rodd, "Chemistry of Carbon Compounds," Vol. IIIB, Elsevier Publishing Co., New York, N. Y., 1956, p 721.

[8] M. M. Fickling, A. Fischer, B. R. Mann, J. Packer, and J. Vaughan, *J. Am. Chem. Soc.*, **81**, 4226 (1959).

[9] O. N. Witt and E. G. P. Thomas, *J. Chem. Soc.*, **43**, 115 (1883).

[10] O. Fischer and E. Hepp, *Ber.*, **20**, 2477 (1887). O. Fischer and E. Schäffer, *Ann.*, **286**, 151 (1895).

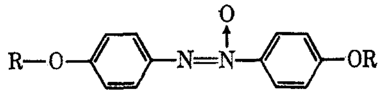
[11] J. T. Hays, H. L. Young, and H. H. Espy, *J. Org. Chem.*, **32**, 158 (1967).

[12] A. Rising, *Ber.*, **37**, 44 (1904).

As is apparent from eq 1, the concentration of water will influence the position of equilibrium. Thus, excess water in the presence of acid was shown to reverse the reaction and convert ether back to *p*-nitrosophenol. Therefore, in addition to the use of a large excess of alcohol, the removal of water can also be used to drive the equilibrium in the direction of ether formation. This method was most effectively applied in the preparation of the 1-butyl ether by passing dry 1-butanol into the system at reduced pressure (~40 mm) and removing wet butanol. Conversions of 95 and yields of 98% have been obtained.

Although the azeotroping capacity of 1-butanol is used in this method to remove the water formed, "sparging" or passing the 1-butanol rapidly through the system was found to give results superior to removal of the azeotrope by careful fractional distillation, because yield losses occur on prolonged exposure of the ether product to elevated temperatures.

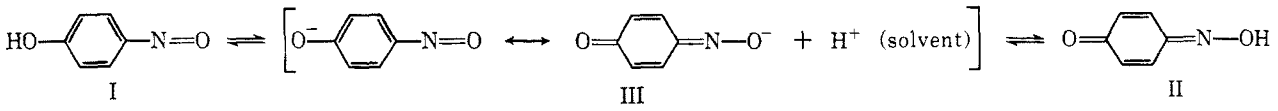
Preparative Methods.—A general method, particularly for the methyl and ethyl ethers from which the water formed is not preferentially removed by distillation, consists of equilibration of *p*-nitrosophenol (~1 *M*) with the alcohol in the presence of about 5 mole % of strong acid at 25–35°. The acid and unreacted *p*-nitrosophenol are then exactly neutralized after 1 hr. [Care must be taken in the neutralization to avoid excess base, which will cause condensation of the ether to the azoxy compound, shown below].



The resulting mixture is distributed between water and pentane. The ether is concentrated in the pentane layer and the alcohol is extracted into the water layer. The pentane layer is separated, dried, and concentrated. The ether can then be isolated by crystallization at low temperatures (−30 to −40°).

For recovery of the excess alcohol and the unreacted *p*-nitrosophenol, an alternative method is to add a hydrocarbon such as toluene or heptane and to remove the alcohol and water by distillation. As the alcohol is removed, the insoluble *p*-nitrosophenol precipitates completely from the hydrocarbon solution.

Analytical Method.—Ultraviolet absorption spectroscopy was employed as the chief analytical tool in this work, and was used to assay the starting *p*-nitrosophenol and the ether products as well as to follow the etherification reaction. The ultraviolet absorption spectrum of *p*-nitrosophenol undergoes a large shift in changing from acidic to basic media.[2] Smaller solvent shifts also occur. The spectrum has been qualitatively explained on the basis of the equilibrium shown in eq 2.[2]



(2)

In aqueous base, the ultraviolet spectrum of *p*-nitrosophenol consists of a major absorption band with a maximum at 395 and a minor absorption band with a maximum at 259 mμ. The absorption is due to the anion (III). In aqueous acid, the spectrum consists of a single absorption band with a maximum at 302 mμ which is due to the equilibrium mixture of the quinone monoxime (II) and the nitrosophenol (I).

Table II summarizes the absorption maxima and molar absorptivities (ε) of *p*-nitrosophenol observed in this work in aqueous and ethanolic media.

Table II

Absorption Bands of *p*-Nitrosophenol

Medium	λ_{max}, mμ	ε
Water, basic[a,b]	395	29,500
	290 (min)	2,460
	259	3,800
Water, acidic[b,c]	302	18,200
95% ethanol, basic[d]	405	32,000
	270	4,300
95% ethanol acidic[c]	302	16,000

[a] Aqueous $NaHCO_3$ (5%), KOH (0.01 *N*), NaOH (0.01 *N*). [b] Literature values:[2] pH 9.53, λ_{max} 398 mμ (ε 26,300); pH 3.82, λ_{max} 300 mμ (ε 17,800). [c] Acetic acid. [d] Alcoholic KOH (0.1%).

The *p*-nitrosophenyl alkyl ether products also absorb in the ultraviolet region, with major absorption maxima at about 330–340 and minor absorption maxima at about 230–240 mμ. The absorption maxima of these compounds undergo small solvent shifts (*i.e.*, from about 330 in isooctane to about 340 mμ in ethanol), but do not shift under acid or basic conditions. The absorption maxima and molar absorptivities in isooctane of the methyl, ethyl, and 1-butyl ethers are closely similar as indicated in Table III.

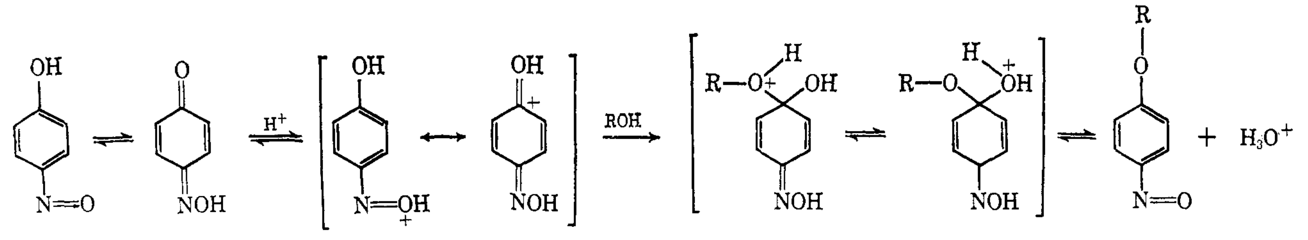
Table III

Absorption Bands of *p*-Nitrosophenyl Alkyl Ethers in Isooctane

Ether	λ_{max}, mμ	ε
Methyl	326	16,700
	236	8,500
Ethyl	329	17,700
	237	8,600
1-Butyl	330	17,900
	238	8,400

The etherification reaction was readily followed by separating the ether product and unreacted *p*-nitrosophenol before obtaining the spectra. This separation was accomplished by partitioning an aliquot of the reaction mixture between isooctane and 5% aqueous $NaHCO_3$; the ethers were extracted into the isooctane phase and the *p*-nitrosophenol was extracted into the aqueous phase. The separations were quantitative (~99%). The concentration of the ethers and of unreacted *p*-nitrosophenol was then determined from the absorption spectra of the appropriate phase.

The ethers of *p*-nitrosophenol are unstable in both acid and alkaline media. Acid media convert the ether back into *p*-nitrosophenol and the alcohol; basic media cause condensation to the corresponding azoxy compound. No significant degradation of the ethers occurred in isooctane, however, even after contact with an acid or alkaline aqueous phase for as long as 1 or



(3)

2 hr. This permitted adequate time to carry out the separations and obtain the spectra.

Mechanism.—The facile equilibrium between *p*-nitrosophenol and its ethers in alcohol solutions presumably depends on the powerful activating effect of the protonated nitroso group. Activated forms of *p*-nitrosophenol may be postulated as reacting with alcohols to give an activated protonated hemiketal, which then forms the *p*-nitroso ether. This is analogous to the mechanism postulated by Bunnett, *et al.*, for the acid-catalyzed formation and hydrolysis of azoaryl ethers.[13] Similarly, Wiberg and Saegebarth[14] have shown that the acid-catalyzed etherification of analogous enol structures proceeds by essentially the same mechanism. (See eq 3.)

The recognized activating effect of the nitroso group[15,16] thus appears to be further enhanced by protonation as shown by the ready etherification of *p*-nitrosophenol as described in this paper and by the amine displacement reactions described in the following paper.

Experimental Section

***p*-Nitrosophenol.**—*p*-Nitrosophenol may be obtained by the nitrosation of phenol by methods described in the literature[17] or, more conveniently, commercial products may be purified for conversion to ethers.

p-Nitrosophenol (E. I. du Pont de Nemours and Co., technical grade, purity 95%, wet with about 15% water, 150 g) was added to 3 l. of anhydrous ether. The insoluble material was filtered off and the ether solution was dried overnight over 200–250 g of anhydrous sodium sulfate. The ether solution was filtered and concentrated to about half its volume on a steam bath. As the remaining ether was removed it was replaced by hexane, 400 ml being added in 100-ml increments. The concentration was continued until the pot temperature reached 50°. The mixture was cooled to 10° and filtered. The solid product was washed with 200 ml of hexane and dried under vacuum at 35°, yielding 90–100 g, purity >96%.

A satisfactory product was also prepared from the sodium salt of *p*-nitrosophenol (Eastman, No. 2354); 100 g of the salt was dissolved in 1400 ml of distilled water. The solution was acidified to pH 3 by addition of 95% H_2SO_4 at 20°. The resulting precipitate was washed with water and dried to constant weight at 35°. It was screened through a 16-mesh sieve before use.

The values of the melting point of *p*-nitrosophenol reported in the literature vary over the range of 126–138°.[1,18] The samples prepared in this work, in general, began to decompose (*i.e.*, turned brown to black) from 120 to 130°, and melted with decomposition (*i.e.*, melt was black) at about 135°. Consequently, melting point measurements did not appear suitable for characterizing *p*-nitrosophenol. Instead, ultraviolet absorption spectroscopy was employed as an assay tool (see Analytical Procedures).

Safety Considerations in Handling *p*-Nitrosophenol.—*p*-Nitrosophenol is a potentially hazardous material, unstable and spontaneously combustible at elevated temperatures. The danger of detonation is negligible, however; it does not detonate when ignited under pressure.

Our experiments show that at 110°, *p*-nitrosophenol alone or in concentrated solutions in butanol may decompose violently with evolution of gas and liberation of a great deal of heat. The ethers also decompose at elevated temperatures but relatively slowly and uniformly in contrast to *p*-nitrosophenol. Mixtures of *p*-nitrosophenol and its ethers are intermediate in stability.

A series of tests was made by placing a 2.5-g sample of *p*-nitrosophenol, with or without additives, in a glass vessel 1 in. deep and 1 in. in diameter in a thermostated air bath. The temperature of the sample was measured with a 24-gauge chromel–alumel thermocouple coated with silicone varnish. Temperatures developed in the sample over at least a 2-hr period were determined at air temperatures of 75 and 95°. It was observed that no sample of *p*-nitrosophenol of 75% purity or greater decomposed even after several hours at 75° unless it was alkaline. Stable *p*-nitrosophenol wet with a 1% sodium hydroxide solution fumed off at 75°. Alkaline contamination thus appears as the main hazard in drying *p*-nitrosophenol.

Washing with dilute acid to remove any traces of alkali should *always* precede drying of *p*-nitrosophenol. When this is done, drying with circulated air at 50° causes no problems and gives normal drying rates. In view of the properties of *p*-nitrosophenol, no more than 100 g should be dried at one time in the laboratory, and it should not be stored dry. Preferably it should be taken up in alcohol immediately after preparation, or stored with 50% water.

Care should be taken to avoid contact of *p*-nitrosophenol or its ethers with the skin. The use of rubber gloves at all times is recommended. The alkyl ethers are particularly irritating and may cause severe rash with certain individuals.

Analytical Procedures. *p*-Nitrosophenol.—Samples of *p*-nitrosophenol were assayed *via* their ultraviolet absorption spectra by dissolving 0.100 g (8.13×10^{-4} mole) in water, adding 5 ml of 2 *N* NaOH, and diluting to 100 ml in a volumetric flask. This solution was diluted further 1:100 with water for a resultant concentration of 0.0100 g/l. (8.13×10^{-5} *M*). The ultraviolet absorption spectra were recorded and the absorption difference between the maximum at 395 and the minimum at 290 mμ was taken as a measure of the product purity:

$$\text{mole \% purity} = \frac{A_{395} - A_{290}}{8.13 \times 10^{-5} A_1} \times 100$$

where A_1 is the absorptivity ($A_{395} - A_{290} = 27{,}040$) for *p*-nitrosophenol in aqueous base (see Table II).

A standard sample of *p*-nitrosophenol was prepared by acidifying a solution of 14.5 g (0.10 mole) of the sodium salt (Eastman No. 2354) in 200 ml of water with 6.0 g (0.10 mole) of glacial acetic acid. The resulting mixture (a light brown precipitate appeared) was shaken vigorously and extracted with four 100-ml portions of ether. The green ether layer was separated from the dark red-brown aqueous layer, dried over anhydrous sodium sulfate, and filtered. The ether was removed on a steam bath and *p*-nitrosophenol was precipitated by the addition of 250 ml of hexane in 50 ml portions. The mixture was cooled and filtered. The light brown precipitate was washed with hexane and air dried: weight 7.4 g (60%), mp 135–136° dec.

A portion (5.0 g) of the above product was taken up in 250 ml of ether and precipitated at room temperature by the addition of 600 ml of hexane. The mixture was filtered to recover 1.3 g of brown crystals, mp 134°. The filtrate was concentrated to one-half of its initial volume on the steam bath; a second crop (2.1 g) of light brown crystals was recovered, mp 135°. The

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[13] J. F. Bunnett, E. Buncel, and V. K. Nahabedian, *J. Am. Chem. Soc.*, **84**, 4136 (1962).

[14] K. B. Wiberg and K. A. Saegebarth, *J. Org. Chem.*, **25**, 832 (1960).

[15] J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 308 (1951).

[16] R. J. W. LeFevre, *J. Chem. Soc.*, **134**, 810 (1931).

[17] T. S. Donovan and L. J. Behrndt (to Eastman Kodak Co.), U. S. Patent 2,234,692 (1939).

[18] H. H. Hodgson and F. H. Moore, *J. Chem. Soc.*, **127**, 2260 (1925); H. H. Hodgson, *ibid.*, 520 (1937); 89 (1943).

remaining mother liquor stood at room temperature for several days; a third crop of crystals slowly separated. The light yellow-brown solid was collected and dried at 55° under reduced pressure: weight 0.7 g, mp 136°. This third crop of crystals was taken as the spectral standard for *p*-nitrosophenol.

Ether Products.—The *p*-nitrosophenol alkyl ether products were also assayed by their ultraviolet absorption spectra. Solutions in isooctane of approximately 0.01 g/l. were prepared and the spectra recorded. Product purity was estimated as

$$\text{mole \% purity} = \frac{A_{330}}{A_2C} \times 100$$

where A_2 is the absorptivity of the ether and C is the concentration in moles/l.

Spectral standards were obtained by recrystallizing the ether products from an aliphatic hydrocarbon (*n*-pentane, *n*-hexane, or *n*-heptane) at low temperatures (−30 to −40°).

Etherification.—The etherification reaction was followed spectroscopically by separating the *p*-nitrosophenyl ether product from unreacted *p*-nitrosophenol. The general procedure for these analyses was as follows. A 1-ml aliquot portion of the reaction mixture was partitioned between 50 ml of Spectrograde isooctane and 49 ml of 5% aqueous $NaHCO_3$ by vigorous agitation. After the two layers separated, the aqueous phase was diluted 1:100 with 5% aqueous $NaHCO_3$ and the isooctane phase was diluted 1:100 with isooctane. The ultraviolet absorption spectra of each diluted solution was then obtained with the appropriate solvent as a blank. The concentrations were calculated as follows.

For the aqueous phase

$$[\text{PNP}] = \frac{A_{395} - A_{290}}{A_1} \times F$$

where [PNP] is the concentration of *p*-nitrosophenol in moles/l., A_{395} is the absorption at the maximum at 395 mμ, A_{290} is the absorption at the minimum at 290 mμ, A_1 is the absorptivity, $A_{395} - A_{290} = 27{,}040$ (see Table II), and F is the dilution factor.

For the isooctane phase

$$[\text{ether}] = \frac{A_{330} - A_{360}}{A_4} \times F$$

where [ether] is the concentration of the ether in moles/l., A_{330} is the absorption at the maximum at ~330 mμ, A_{360} is the absorption at the minimum at ~360 mμ, and A_4 is the absorptivity, $A_{\sim 330} - A_{\sim 360}$, for the ether in isooctane solution.

The absorption difference between a maximum and a minimum was used in both calculations rather than simply the absorptions at the maxima; this procedure minimized errors due to the absorption from species formed from minor side reactions.

All spectra were obtained in the 220- to 400-mμ range with a Cary Model 11 recording spectrophotometer operated at a scanning speed of 40 A/sec and with the slit width set at 0.1 mm at 270 mμ. Silica cells (1 cm) were employed.

Reaction of *p*-Nitrosophenol with Alcohols.—Stoichiometric equilibrium constants and conversions for various alcohols were determined by placing 0.030 mole (3.69 g) of purified *p*-nitrosophenol, 0.002 mole sulfuric acid, and various amounts of the alcohols studied in 125-ml crown-capped bottles and heating them for various times at various temperatures. The bottles were flushed with nitrogen and magnetically stirred. Unreacted *p*-nitrosophenol and ether were determined spectroscopically as described in the preceding section. Water was determined by the Karl Fischer method, for calculation of equilibrium constants.

Data on the effect of the nature and concentration of the acid catalyst were obtained by placing 6.15 g (0.05 mole) of purified *p*-nitrosophenol in a three-necked, 250-ml, stirred flask along with most of the alcohol to be used. Solution was effected by stirring and the temperature was adjusted to 20–30°. The acid catalyst was dissolved in the remainder of the alcohol, the temperature being kept below 20°. The catalyst–alcohol solution was then quickly added to the solution of *p*-nitrosophenol in alcohol and the solution was maintained at 30 + 2°. One-milliliter samples were taken for ultraviolet analysis.

Preparation of *p*-Nitrosophenetole.—*p*-Nitrosophenol (123 g, 0.9 mole, Du Pont, 90% purity) was placed in a 2-l. resin flask equipped with thermometer, sparge tube, stirrer, sample port, and vacuum distillation take off. Five hundred milliliters of 2BA ethanol[19] was added along with 4.75 g (0.025 mole) of *p*-toluenesulfonic acid hydrate. The system was heated at 45° for 1 hr. The reaction mixture was then neutralized with alcoholic KOH and the volume was reduced to 200 ml under vacuum (*ca.* 140 mm). The remaining solution was treated with 500 ml of heptane and the volume was reduced to 300 ml under vacuum. An additional 250 ml of heptane was introduced and the volume again was taken down to 300 ml. The unreacted *p*-nitrosophenol was filtered off and washed with heptane to give 360 ml of solution. Ultraviolet analysis at this point indicated a practically quantitative yield at a conversion of about 50%.

The solution was cooled to −40°. Beautiful green crystals formed and were separated, yield 54 g (0.28 mole). A sample was recrystallized from heptane, mp 34–35°.[12]

Anal. Calcd for $C_8H_9NO_2$: C, 63.6; H, 6.00; N, 9.28; mol wt, 151.2. Found: C, 63.7, H, 6.04; N, 9.23, mol wt, 152.

Conversion of *p*-Nitrosophenetole into *p,p'*-Diethoxyazoxybenzene.—Purified *p*-nitrosophenol (3.6 g, 0.03 mole) was dissolved in 50 ml of ethanol. Sulfuric acid (0.4 ml of 3 *M*, 0.0012 mole) was added and the mixture was stirred under nitrogen at room temperature for 2 hr. The system was made basic with 25 ml of 1.5 *M* (0.038 mole) of aqueous sodium hydroxide. After 1 additional hr, the system was extracted with pentane and with water. The insoluble product was filtered off and dried (1.68 g); uncorrected melting point to a cloudy liquid was 134.5–135.5°, and to a clear point was 165.2–165.5°. Literature values are 137.4–137.9° and 168–168.5° for this characteristic double melting point.[10]

The same product was obtained in 90% yield by action of 60% KOH on pure *p*-nitrosophenetole in ethanol.

Anal. Calcd for $C_{16}H_{18}N_2O_3$: C, 67.2; H, 6.34; N, 9.80. Found: C, 67.3; H, 6.33; N, 10.35.

On catalytic reduction at 60 psi with 5% palladium-on-carbon catalyst, the azoxy compound yielded *p*-phenetidine, identified by its ultraviolet spectrum.

Preparation of *p*-Nitrosoanisole (with Recycle of *p*-Nitrosophenol and Recovery of Methanol).—*p*-Nitrosophenol (123 g, 0.9 mole, 90% Du Pont) was placed in a 2-l. resin kettle equipped with thermometer, sparge tube, stirrer, sample port, and a vacuum distillation take off. Methanol (35.5 ml) and 145 ml of toluene were added (the azeotropic composition). The system was brought to 45° under nitrogen, and 1.0 ml (0.018 mole) of concentrated H_2SO_4 was added. After 52 min the system was neutralized with 13 ml of 1.5 *N* aqueous sodium hydroxide and diluted with 500 ml of toluene. Methanol and water were removed by vacuum distillation of the toluene azeotropes. The reaction mixture was filtered and the *p*-nitrosophenol filter cake was washed three times with toluene. The process was then repeated after addition of 55 ml of methanol, 70 g of *p*-nitrosophenol, and 145 ml of toluene. The process was carried through four cycles. A total of 2.7 moles of *p*-nitrosophenol was used. In the last cycle, the concentration of catalyst was doubled (0.036 mole). The volumes of the product solutions varied somewhat (700, 605, and 533 ml). Analyses showed that the purity of the recovered *p*-nitrosophenol decreased on the average about 5% per cycle. The average conversion to *p*-nitrosoanisole was 55%. The average yield was 88%. The toluene solutions were combined and the toluene was stripped off under vacuum. The residue was taken up in two volumes of pentane; the solution was filtered and cooled to −40°. Beautiful blue-green crystals separated: first crop, 173 g, mp 25°;[12] second crop, 19 g; total, 192 g (1.40 moles) of *p*-nitrosoanisole.

Preparation of 1-Butyl Ether of *p*-Nitrosophenol.—Purified *p*-nitrosophenol (99%, 61.5 g, 0.5 mole), sulfuric acid catalyst (0.01 mole, 96%), and dry 1-butanol (230 ml, 2.5 moles) were heated at 50° and 40 mm for 15 min in a distilling flask. During heating, all the material went into solution; about half the reaction mixture was then distilled off in an additional 15 min. The reaction was about 60% complete at this point. Over the next 45 min, 2.2 moles of dry 1-butanol was added and the distillation was continued at such a rate as to keep the volume constant. The final temperature in the distillation flask was 55–56°. A conversion of 95% and a yield of 98% were indicated by ultraviolet analysis.

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[19] 0.5% benzene, absolute ethanol

The reaction mixture was chilled to −40° and the crystalline product was recovered by filtration. The crystals were washed with cold pentane and dried under vacuum, mp −4 to −6°. Recovery (76 g) amounted to 89% of the ether formed; purity, determined by ultraviolet spectroscopy, was 95%.

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p-Nitrosophenol Chemistry. II. Amination of *p*-Nitrosophenol Ethers with Primary Aromatic Amines

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The reaction of alkyl ethers of *p*-nitrosophenol with primary aromatic amines gives *p*-nitrosodiphenylamines in high yields under mild conditions. This reaction is an example of an acid-catalyzed aromatic nucleophilic displacement in which the protonated nitroso group exerts a strong activating effect. Reduction or reductive alkylation of the *p*-nitrosodiphenylamine product provides a simple and unique route to *p*-aminodiphenylamine and its derivatives, currently of commercial importance as antiozonants for rubber.

As indicated in the first paper in this series,[1] the phenolic hydroxyl group of *p*-nitrosophenol can be replaced by an amino group through reaction of its ethers with primary amines. The drastic conditions generally required for direct replacement of a phenolic hydroxyl with an amino group have previously made this type of reaction of little importance in the benzene series.[2] Certain activated phenols (and their ethers) such as those with *o*- and *p*-nitro groups do undergo such replacement reactions.[3,4] Likewise the hydroxyl group of *p*-nitrosophenol has been replaced by fusion with ammonium salts.[5,6] However, according to literature reports, reaction of *p*-nitrosophenol with aniline gives *p*-hydroxyazobenzene in the presence of acetic acid,[7] azophenine on heating with the hydrochloride,[8] or an indoaniline with strong sulfuric acid.[9] These reactions are all avoided and *p*-nitrosodiphenylamines are obtained in high yields under mild conditions when the ethers of *p*-nitrosophenol, presumably in a strongly activated protonated form,[1] react with primary aromatic amines.

$$p\text{-NOC}_6\text{H}_4\text{OR} + \text{H}_2\text{NC}_6\text{H}_4\text{R}' \xrightarrow{\text{H}^+} p\text{-NOC}_6\text{H}_4\text{NHC}_6\text{H}_4\text{R}' + \text{ROH}$$

This reaction is an interesting example of an acid-catalyzed aromatic nucleophilic substitution. Reduction or reductive alkylation of the *p*-nitrosodiphenylamine product provides a simple and unique route to *p*-aminodiphenylamine and its derivatives, currently of commercial importance as antiozonants for rubber.[10]

Our initial attempts to carry out the replacement of the phenolic hydroxyl by direct reaction of *p*-nitrosophenol with amines gave negative results except in alcohol solutions with acid catalysts. Aniline and *p*-nitrosophenol were found to react at room temperature under these conditions to form *p*-nitrosodiphenylamine. Low and variable yields were related to time of contact between *p*-nitrosophenol and acidic alcohol solutions and were then shown to depend on the equilibrium set up between *p*-nitrosophenol and its ethers.[1]

The ether was shown to be the reactive species under these conditions by adding aniline to acidified ethanolic solutions of *p*-nitrosophenol at various times and concentrations. Maximum yields of *p*-nitrosodiphenylamine corresponded to equilibrium concentrations of the ether. Isolation of the pure ether and reaction with aniline gave high yields and conversions to *p*-nitrosodiphenylamine.

Scope of the Amination Reaction.—The replacement of the alkoxy group of a *p*-nitrosophenyl alkyl ether with an amino group has been extended to a variety of ethers of *p*-nitrosophenol and a number of primary aromatic amines. Ultraviolet analysis of reaction mixtures has shown that high conversions (90–95%) to *p*-nitrosodiphenylamine have been obtained by the reaction of aniline with the methyl, ethyl, and 1-butyl ethers (Table I). *p*-Nitrosodiphenylamine has been isolated in conversions of 80–85%. In addition, formation of *p*-nitrosodiphenylamine was qualitatively demonstrated by means of ultraviolet spectra for the reaction of aniline with *p*-nitrosophenol ethers from the following alcohols: 2-octyl, cyclohexyl, 2-ethoxyethyl, oleyl, isoamyl, benzyl, allyl, and cetyl.

Yields and properties of the products of the reaction of the ethyl ether (*p*-nitrosophenetole) with a number of monosubstituted anilines are shown in Table II. Amines with electron-donating substituents gave good yields. Although the products from amines with electron-withdrawing substituents were qualitatively identified, the yields were poor and the products were not completely characterized.

In the absence of acid, little or no reaction takes place. In the presence of acid, the reaction is quite rapid at low temperatures (25–50°). For optimum results an aniline to acid mole ratio of about 10–20:1 is required. The reaction rate increases with acid concentration; however, high acid concentration leads

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