TABLE VIII

COMPARISON OF PRODUCTS FROM TOLUENE AND BENZOTRIFLUORIDE WITH NITROBENZENE[a,b]

Products, X = F or H	Rel concn[c] Benzotrifluoride	Rel concn[c] Toluene
Phenol	7	22
Biphenyl	25	42
Nitrobiphenyl	12	...
Trifluoromethylbiphenyl, $C_{13}H_{14}$	100	100
$X_3CC_6H_4C_6H_4CX_3$ and isomers	42	61
Terphenyl	5	5
X_3C-Terphenyl and isomers	21	8
$(X_3C)_2$-Terphenyl and isomers	21	7

[a] Reaction conditions were 600°; contact time, 9.5 sec; and a mole ratio of nitrobenzene to $X_3C-C_6H_5$ of 1:5. [b] The total weight of products from benzotrifluoride was 4.4 g and that from toluene was 6.9 g. [c] From relative intensities in the low-voltage (7.5 V, uncor) mass spectrum, normalized to X_3C–biphenyl = 100.

The product from benzotrifluoride containing two rings and one methyl group was apparently, in view of the retention of all three fluorine atoms, solely trifluoromethylbiphenyl, whereas that from toluene contained a substantial contribution from the isomeric diphenylmethanes. In the product containing two rings and two methyl groups, benzotrifluoride gave only bis(trifluoromethyl)biphenyl; toluene gave bibenzyl and dimethylbiphenyl in almost equal amounts, as well as an appreciable amount of methyldiphenylmethane (Table VI). This difference apparently follows as a consequence of the difference in bond dissociation energies of C_6H_5C-F and C_6H_5C-H,[29] which makes fluorine abstraction unlikely when hydrogen is available in the same molecule. Only in the absence of hydrogen is fluorine abstracted, as in the reaction of nitrobenzene with hexafluorobenzene.[2] Even in the latter case the fluorine was retained to a considerable extent through intramolecular exchange with hydrogen, and hexafluorobiphenyl was formed in about the same concentration as pentafluorobiphenyl.

Registry No.—Nitrobenzene, 98-95-3; toluene, 108-88-3; toluene-α-d_3, 1124-18-1; nitrobenzene-d_5, 4165-60-0.

Acknowledgment.—The authors are greatly indebted to D. K. Albert of the American Oil Co. for his assistance in the gas chromatographic analyses.

[29] C_6H_5C-F, D = 120 kcal/mol;[25] C_6H_5C-H, D = 85 kcal/mol.[26]

Kinetics of the Reversible Reaction of Piperidine with 2,4-Dinitroanisole in Methanol Solution[1]

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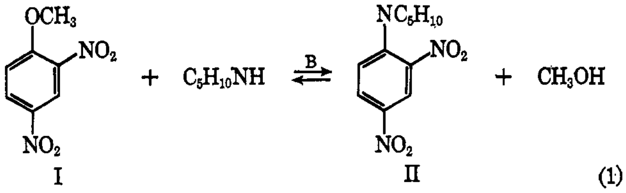
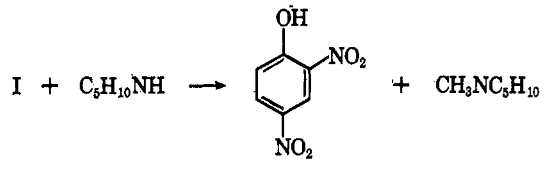
2,4-Dinitroanisole reacts with piperidine in methanol to form 2,4-dinitrophenylpiperidine (eq 1). The reaction is reversible, and the equilibrium constant at 67.9° is about 100 l. mol^{-1}. The reaction rate has been determined in both directions as a function of $NaOCH_3$ concentration. Catalysis by methoxide ion is strong, and the second-order rate coefficient (k_A) for the forward reaction is related to [$NaOCH_3$] in a nearly linear fashion. The forward reaction in the absence of $NaOCH_3$ is catalyzed by methoxide ion generated by the basic dissociation of piperidine in methanol, and probably also by piperidine. A side reaction which produces 2,4-dinitrophenol, *via* S_N2 displacement by piperidine at methyl carbon (eq 2), is important in the absence of $NaOCH_3$; its rate has been estimated.

The reaction of 2,4-dinitrodiphenyl ether with piperidine to form 2,4-dinitrophenylpiperidine is strongly catalyzed by bases.[3,4] The formally similar reaction of ethyl formate with *n*-butylamine to form *n*-butylformamide is also very responsive to base catalysis.[5] We therefore expected that bases would catalyze the reaction of 2,4-dinitroanisole (I) with piperidine to form 2,4-dinitrophenylpiperidine (II). Accordingly, a kinetic investigation of this reaction in methanol solution was undertaken.



I II (1)



(2)

Subsequent to our work, the same reaction in 10% dioxane–90% water was investigated by Bunnett and Bernasconi[4] and by Bernasconi.[6]

Years ago, Cahn[7] examined the reactions of several nitroanisoles with refluxing neat piperidine. He reported that 2,4-dinitroanisole gave 2,4-dinitrophenylpiperidine quantitatively within 15 min on the water bath. This indicates piperidinodemethoxylation at aromatic carbon, since 2,4-dinitrophenylpiperidine was not formed by heating 2,4-dinitrophenol with piperidine at reflux. In contrast, 2,4,6-trinitroanisole was quantitatively converted to picric acid within 1 min under the same conditions. Also, 2-methyl-4-nitroanisole gave almost 100% of 2-methyl-4-nitrophenol within 1 hr at reflux. The latter two examples suggest that nucleophilic displacement at methyl carbon occurred, although Cahn recognized hydrolysis due to traces of water to be

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(1) (a) Supported, in part, by the National Science Foundation. (b) Based on the Ph.D. Thesis of R. H. Garst, Brown University, June, 1964; *Dissertation Abstr.*, **25**, 4404 (1965).

(2) University of California at Santa Cruz, Santa Cruz, Calif.

(3) J. F. Bunnett and R. H. Garst, *J. Amer. Chem. Soc.*, **87**, 3879 (1965).

(4) J. F. Bunnett and C. Bernasconi, *ibid.*, **87**, 5209 (1965).

(5) J. F. Bunnett and G. T. Davis, *ibid.*, **82**, 665 (1960).

(6) C. F. Bernasconi, *J. Org. Chem.*, **32**, 2947 (1967).

(7) R. S. Cahn, *J. Chem. Soc.*, 1121 (1931).

an alternative possibility. Tertiary amines are known to react with 4-substituted 2,6-dinitroanisoles *via* displacement at the methyl carbon.[8]

Our work indicates that both types of reaction occur between piperidine and 2,4-dinitroanisole in methanol. Displacement at aromatic carbon (eq 1) predominates and can be made nearly quantitative by suitable adjustment of conditions. This reaction is strongly catalyzed by sodium methoxide. Also, the reverse of this reaction can be made to occur quantitatively; it is, of course, also catalyzed by sodium methoxide.

Experimental Section

Materials.—Methanol was purified by the magnesium method.[9] Piperidine was purified as we have previously described.[3] Commercial 2,4-dinitroanisole was recrystallized four times from diethyl ether containing a small amount of petroleum ether (bp 30–60°): mp 94.8–96.5°. N-(2,4-Dinitrophenyl)piperidine, mp 92–94.5°, was crystallized from absolute ethanol. Solutions of sodium methoxide in methanol were prepared and stored after Reinheimer, *et al.*[10] "Quenching solution" was prepared by mixing 1 l. each of distilled water and 95% ethanol with 200 g of concentrated hydrochloric acid solution. N-Methylpiperidine, bp 104° (uncor), n^{20}_{D} 1.4373, was prepared from piperidine by the Leuckart reaction.[11] Proton magnetic resonance and infrared spectra confirmed its structure and high purity.

Spectra of Reactants and Products.—Suitably dilute solutions were prepared in solvents as noted below, and spectra were recorded by means of a Bausch and Lomb Spectronic 505 spectrophotometer. Wavelengths of maximum absorption (mμ) and the associated molar extinction coefficients (ϵ) were as follows: I in CH_3OH, 254 (7190), 293 (10,700); I in quenching solution, 258 (8390), 297 (10,600); 2,4-dinitrophenol in CH_3OH, 355 (14,700); 2,4-dinitrophenol in 0.1 *M* $NaOCH_3$ in CH_3OH, 356 (14,800); 2,4-dinitrophenol in quenching solution, 257 (10,900); II in CH_3OH, 377 (14,700); II in quenching solution, 390 (15,100). Neither I nor 2,4-dinitrophenol absorbs measurably in quenching solution at 390 mμ.

Kinetic Procedure.—Reaction solutions were prepared at room temperature by combination of appropriate volumes of standard methanolic solutions of reactants (or, in some cases, the appropriate weight of pure piperidine), and dilution to the mark in a volumetric flask with methanol. Aliquots were pipetted into nitrogen-filled Pyrex ampoules which were then flushed with nitrogen and sealed with a flame. All the ampoules for a run were immersed in the thermostat at the same time. Ampoules were removed at recorded times and plunged into cold water. They were quickly opened, and the contents were transferred quantitatively to a volumetric flask and diluted to the mark with quenching solution. The absorption at 390 mμ was determined by means of a Beckman Model DU spectrophotometer. Pseudo-first-order kinetics were obeyed in all runs, and the pseudo-first-order rate coefficient (k_ψ) was determined in the usual way from the "infinity" absorbance and the absorbance of samples taken at various times.[12]

The rate of reaction of sodium methoxide with I, to form 2,4-dinitrophenol, was determined in one run.[13] The technique was generally as described above. However, after the ampoules were cooled to room temperature and opened, a 5-cc portion of the reaction solution was diluted to 50 cc with methanol, and the absorbance at 356 mμ was measured. The spectrum of the "infinity" sample between 200 and 500 mμ was recorded; it matched that of 2,4-dinitrophenol in 0.1 *M* $NaOCH_3$ in CH_3OH.

Reaction temperature for all runs was 67.9°. Rate coefficients are symbolized, and were reckoned, as follows: $k^*_{\mathrm{r}} = k_\psi$ for the special case of reaction 1, reverse; $k_{\mathrm{r}} = k^*_{\mathrm{r}}/[OCH_3^-]$, second-order rate coefficient for reaction 1, reverse; k^*_{f} = pseudo-first-order rate coefficient for reaction 1, forward, reckoned as $(A_\infty/A_{\mathrm{quant}})\cdot k_\psi$, where A_∞ is the observed infinity absorbance and A_{quant} is the infinity absorbance calculated for quantitative conversion of I to II; $k_{\mathrm{A}} = k^*_{\mathrm{f}}/[C_5H_{10}NH]$, second-order rate coefficient for reaction 1, forward; k^*_{P} = pseudo-first-order rate coefficient for side reaction(s) to reaction 1, forward, in absence of $NaOCH_3$, reckoned as $k_\psi - k^*_{\mathrm{f}}(1 + K_{\mathrm{e}}\cdot[C_5H_{10}NH])/(K_{\mathrm{e}}[C_5H_{10}NH])$ (K_{e} is the equilibrium constant for reaction 1); $k_{\mathrm{P}} = k^*_{\mathrm{P}}/[C_5H_{10}NH]$, second-order rate coefficient for side reaction(s) to reaction 1, forward.

Our method for reckoning the last four coefficients calls for comment. When piperidine is in large excess, eq 1 and 2 constitute a system of the type

$$\mathrm{A} \underset{k_{\mathrm{b}}}{\overset{k_{\mathrm{a}}}{\rightleftharpoons}} \mathrm{B} \tag{3}$$

$$\mathrm{A} \xrightarrow{k_{\mathrm{c}}} \mathrm{C} \tag{4}$$

For reaction 3 alone, it is known[15] that the slope in a plot of ln $(A_\infty - A)$, where A_∞ is the final (equilibrium) absorbance, *vs.* time is $k_{\mathrm{a}} + k_{\mathrm{b}}$, and that k_{a} can be reckoned as $A_\infty/A_{\mathrm{quant}}$ times said slope (if the absorbance measured is due only to B). Moreover, if reactions 3, forward, and 4 are competitive irreversible reactions, it is known that the slope in a plot of ln $(A_\infty - A)$ *vs.* time is $k_{\mathrm{a}} + k_{\mathrm{c}}$, and that k_{a} can be reckoned as $A_\infty/A_{\mathrm{quant}}$ times said slope.[16]

The procedure we have used for evaluating k^*_{f} and k^*_{P} (above) represents amalgamation of these two familiar procedures. It is not rigorous, for the true "infinity" value for reactions 3 and 4 in competition will represent complete conversion of A and B into product C. On the other hand, if the equilibrium concentration of reactant A is small and k_{c} is small, the condition of equilibrium between A and B will not drift rapidly toward C and a "quasi-infinity" condition will be attained after eight or ten half-lives of reaction 3. The chief intrusion of reaction 4 will then be direct competition with reaction 3 as the initial state progresses to the "quasi-infinity" state. Under such conditions, which prevailed in most of our experiments concerning reaction 1, forward, the treatment we have used is approximately correct.

Detection of 2,4-Dinitrophenol as a By-product.—"Infinity" samples from reactions of I with 0.2, 0.4, and 0.6 *M* piperidine (without piperidine hydrochloride) were examined. It was assumed that 2,4-dinitrophenol was the by-product containing 2,4-dinitrophenyl groups. On the basis of this assumption, solutions were prepared mimicking the "infinity" solutions from these runs; these solutions contained 2,4-dinitrophenylpiperidine in the concentrations indicated by the absorbance at 390 mμ of acid-quenched "infinity" samples plus 2,4-dinitrophenol as needed to account for the rest of the starting 2,4-dinitroanisole. The spectra of all six solutions, the three actual "infinity" solutions and the three mimics, as diluted with methanol and as diluted with *ca.* 1 *M* HCl in 47% ethanol, were determined between 200 and 500 mμ. In all six cases there was an appreciable difference in the spectra of the methanol-diluted and the acid-diluted samples, and each pair of actual and mimic "infinity" solutions showed qualitatively and quantitatively the same spectra when diluted in a given way. This substantiates the assumption which was made.

We now consider the possibility that 2,4-dinitrophenol was formed by reaction of methoxide ion with 2,4-dinitroanisole. Methoxide ion is generated by the basic dissociation of piperidine in methanol, for which K_{b} is 7.3×10^{-6}.[17] For the piperidine concentrations represented in Table II, $[OCH_3^-]$ is reckoned to range from 0.85×10^{-3} to 2.1×10^{-3} (except in the presence of piperidine hydrochloride). Making use of the probable second-order rate coefficient for the dinitroanisole–methoxide reaction

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[8] M. Kohn and F. Grauer, *Monatsh. Chem.*, **34**, 1751 (1913); E. Hertel and H. Lührmann, *Z. Elektrochem.*, **45**, 405 (1939).

[9] L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed, D. C. Heath and Co., Boston, Mass., 1941, p 360.

[10] J. D. Reinheimer, W. F. Kieffer, S. W. Frey, J. C. Cochran, and E. W. Barr, *J. Amer. Chem. Soc.*, **80**, 164 (1958).

[11] H. T. Clarke, H. B. Gillespie, and S. Z. Weisshaus, *ibid.*, **55**, 4571 (1933).

[12] J. F. Bunnett and J. J. Randall, *ibid.*, **80**, 6020 (1958).

[13] Recently several investigators[14] have studied the kinetics and equilibrium for combination of sodium methoxide with 2,4-dinitroanisole to form the usual Jackson–Meisenheimer complex. Under the conditions of our experiments, the equilibrium concentration of that complex was very small.

[14] (a) C. H. Rochester, *J. Chem. Soc.*, 2404 (1965); J. H. Fendler, *J. Amer. Chem. Soc.*, **88**, 1237 (1966); (b) C. F. Bernasconi, unpublished work.

[15] *Cf.* A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1961, p 186.

[16] J. F. Bunnett, E. W. Garbisch, Jr., and K. M. Pruitt, *J. Amer. Chem. Soc.*, **79**, 385 (1957).

[17] J. R. Schaefgen, M. S. Newman, and F. H. Verhoek, *ibid.*, **66**, 1847 (1944).

determined in this research, we reckon the contribution of this reaction to the pseudo-first-order coefficients in Table II to be not greater than 2.7×10^{-8} sec^{-1}. This is only about one-hundredth the actual magnitude of the side reaction, tabulated as k^*_P in Table II. This is clearly not the principal side reaction.

Detection of N-Methylpiperidine as a By-product.—A solution (75 ml) of I (0.0667 *M*), piperidine (0.4 *M*), and piperidine hydrochloride (0.0667 *M*) in methanol was flushed with nitrogen gas, sealed in a Pyrex tube, and heated 1080 hr at 68°. The tube was cooled to room temperature and opened, and the contents were acidified to pH 1 by dropwise addition of aqueous HCl. The solvents were evaporated by means of a rotary vacuum evaporator, distilled water was added, and the mixture was heated to 60°. The lumps were crushed, and the mixture was cooled and filtered. The collected solids were discarded, and the filtrate was evaporated to dryness as above. The dry residue was treated with 3.0 g of sodium amide in pyridine, and the resulting slurry was filtered under nitrogen pressure through a fritted-glass plate. To a sample of the filtrate, a weighed amount of acetone was added as internal standard, and the mixture was analyzed by glpc, using 10% Carbowax 4000 on 42–60 mesh Johns-Manville C-22 Silocel firebrick. The peak for N-methylpiperidine was sharp; the retention time was the same as that of an authentic sample. The peak area, corrected for molar response, indicated that 0.174 g (36%) of N-methylpiperidine had been formed. Another sample of the pyridine filtrate was subjected to mass spectrometric analysis; peaks at *m/e* 98 (MW − 1 for N-methylpiperidine), 84 (MW − 1 for piperidine), and 79 (pyridine) were strong, and the yield of N-methylpiperidine was indicated to be slightly higher than estimated by glpc.

Concentrations of reactants as listed in the tables refer to room temperature. However, all the second- and third-order rate coefficients given in the tables and in the text have been corrected to take account of solvent expansion between room temperature and 67.9°; the correction factor used was 1.06.

Results and Discussion

Reaction of 2,4-Dinitroanisole with $NaOCH_3$.—A conceivable side reaction was nucleophilic displacement by methoxide ion on methyl carbon of I, forming methyl ether and 2,4-dinitrophenol.[13] Reaction was indeed observed to occur at 67.9°, between 0.10 *M* $NaOCH_3$ and 4.24×10^{-4} *M* 2,4-dinitroanisole, and ultimately the ultraviolet spectrum of the solution matched that of 2,4-dinitrophenol in methanolic $NaOCH_3$. Also, a sample of the "infinity" solution diluted with excess "quenching solution" (*ca.* 1 *M* HCl in 47% ethanol) matched that of 2,4-dinitrophenol in the same solvent.

The rate of this reaction was followed by the increase of absorbance at 356 mμ, an absorption maximum for the 2,4-dinitrophenoxide ion. The pseudo-first-order rate coefficient was 1.2×10^{-6} sec^{-1}. The reaction order in sodium methoxide was not established, although it was found that 2,4-dinitroanisole is stable in methanol free of this base. If the reaction is first order in methoxide ion, the second-order rate coefficient is 1.2×10^{-5} M^{-1} sec^{-1}.

We cannot exclude the possibility that this reaction is hydroxydemethoxylation at aromatic carbon, hydroxide ion having been formed by reaction of methoxide ion with traces of water in the solvent.

Reaction of 2,4-Dinitrophenylpiperidine with Methanol, Catalyzed by Sodium Methoxide.—This tertiary amine was found to be stable in methanol at 67.9°. However, in the presence of sodium methoxide a reaction occurred and ultimately all the 2,4-dinitrophenylpiperidine was destroyed, for the "infinity" solution showed no trace of the characteristic absorption of II at 390 mμ. The ultraviolet spectrum of this solution matched that of 2,4-dinitroanisole in methanol. Thus, the reverse of reaction 1 occurred.

Reaction rate was determined as a function of sodium methoxide concentration, the decrease in absorption at 390 mμ being followed. Our data are presented in Table I. The rate was higher at higher methoxide concentrations, but the second-order rate coefficient (k_r) diminished somewhat as the base concentration increased.

Table I

Reaction of 2,4-Dinitrophenylpiperidine with Methanol, Catalyzed by Sodium Methoxide[a] at 67.9°

$[NaOCH_2]$, *M*	$10^6 k^*_r$, sec^{-1}	$10^4 k_r$, l. mol^{-1} sec^{-}
0.0145	3.88	2.83
0.036	8.84	2.56
0.073	16.9	2.46
0.109	24.2	2.32
0.146	30.2	2.19
0.218	40.5	1.96
0.328	54.9	1.77

[a] Initial substrate concentration in all runs: 1.92×10^{-4} *M*.

Reaction of 2,4-Dinitroanisole with Piperidine (without $NaOCH_3$).—The reaction velocity was determined as a function of piperidine concentration; results are presented in Table II. The kinetics are complicated by three factors: (i) the reaction progresses to a state of equilibrium which, at low piperidine concentrations, provides an appreciable amount of unreacted 2,4-dinitroanisole; (ii) there is a side reaction which consumes 2,4-dinitroanisole forming something other than 2,4-dinitrophenylpiperidine, as shown by the fact that "infinity" concentrations of the latter are considerably less than called for by the equilibrium constant; and (iii) the formation of 2,4-dinitrophenylpiperidine is catalyzed by base, certainly by methoxide ion and probably also by piperidine.

The side reaction is that of piperidine with 2,4-dinitroanisole to form N-methylpiperidine and 2,4-dinitrophenol, *via* S_N2 attack of piperidine on methyl carbon. The formation of 2,4-dinitrophenol was demonstrated by the ultraviolet spectra of product mixtures, and N-methylpiperidine was detected as a product by gas–liquid partition chromatography (glpc) and by mass spectrometric analysis.

In a situation of competing reversible and irreversible reactions, as represented by eq 1 and 2, "infinity" conditions are attained only when all the reactants have been transformed into the products of the irreversible step. However, if the irreversible reaction is slow and there is but little of the common reactant present at equilibrium, conditions which are fulfilled in the present work, the system may be treated approximately as competing independent first-order reactions. This question is discussed in detail in the Experimental Section. By this treatment, pseudo-first-order coefficients (k^*_P) for the side reaction were computed, and they were converted into second-order coefficients (k_P) by dividing by the piperidine concentration.

The k_P values (Table II) differ considerably. We are inclined to think that the variation is not real, and that the proper value of this coefficient is best indicated by the first experiment in Table II, a run in which piperidine hydrochloride was present. Under the conditions of that run, equilibrium lay strongly on the side of 2,4-dinitrophenylpiperidine and the side reaction accounted for nearly half of the products formed. In the other

Table II

Reaction of 2,4-Dinitroanisole with Piperdine in Methanol at 67.9°

[Substrate]$_0$ × 10^4, *M*	[$C_5H_{10}NH$]	Yield, %	Cor yield,[a] %	10^6k_ψ, sec^{-1}	$10^6k^*_f$, sec^{-1}	10^6k_A, M^{-1} sec^{-1}	$10^6k^*_P$, sec^{-1}	10^6k_P, M^{-1} sec^{-1}
2.87	0.600[b]	55.8	56.8	9.55	5.6	8.9	4.1	7.1
5.00	0.600	92.3	94.0	45.3	44	69.7	2.7	4.8
2.87	0.600	93.0	94.5	45.0	44	69.7	2.5	4.3
5.00	0.400	86.9	89.0	22.0	20	47.8	2.4	6.3
2.87	0.399	87.3	89.5	26.5	24	58.0	2.8	7.4
17.9	0.250	78.2	81.3	10.8	8.9	33.8	2.0	8.6
5.00	0.200	73.9	77.6	9.54	7.4	35.2	2.1	11.3
17.9	0.100	59.6	65.6	3.13	2.0	18.7	1.08	11.4

[a] "Cor yield" is the yield of 2,4-dinitrophenylpiperidine (from photometric data) plus the amount of 2,4-dinitroanisole which should be in equilibrium with it. [b] Piperidine hydrochloride (0.102 *M*) also present.

Table III

Reaction of 2,4-Dinitroanisole with Piperidine, Catalyzed by Sodium Methoxide, in Methanol at 67.9° [a]

[$NaOCH_3$], *M*	[Substrate]$_0$, × 10^4, *M*	10^4k_ψ, sec^{-1}	Yield, %	Cor yield,[b] %	10^4k_A, M^{-1} sec^{-1}	$10^2k_A/[OCH_3^-]$, M^{-2} sec^{-1}	K_e,[c] M^{-1}
0.010	8.98	0.735	91	96	3.70	3.91	136
0.010	3.59	0.812	92	97	4.08	4.31	150
0.030	3.59	1.82	90	95	9.16	3.23	127
0.050	3.59	2.54	98	103	12.8	2.71	108
0.070	1.80	2.87	90	95	14.4	2.18	89
0.100	1.44	4.54	97	102	22.8	2.41	103
0.130	1.44	5.45	98	103	27.4	2.23	99
0.182	1.44	7.37	97	102	37.1	2.16	105
0.327	1.44	11.2	96	101	53.9	1.74	98

[a] Piperidine 0.20 *M* in all runs. [b] See footnote *a*, Table II. [c] Computed from kinetic data.

experiments with 0.6 *M* piperidine, the side reaction was a very small percentage of the whole and its rate, being reckoned as a difference between large quantities, could not be estimated very precisely. In the experiments at low piperidine concentrations, the approximate kinetic analysis employed is somewhat less justified.

The pseudo-first-order coefficients for reaction 1 in the forward direction are given (Table II) as k^*_f, and the corresponding second-order coefficients ($k^*_f/[C_5H_{10}NH]$) are tabulated as k_A. It is obvious that k_A increases with piperidine concentration, except that it is much lower in the presence of piperidine hydrochloride. Since a principal effect of the latter salt is to repress basic dissociation of piperidine to form methoxide ion, we conclude that the increase in k_A with piperidine concentration is mainly due to catalysis by methoxide ion. This conclusion is supported by the fact that one can approximate the k_A values in Table II by multiplying the catalytic coefficient for methoxide ion (see below) by the methoxide ion concentrations reckoned from the K_b value. Reaction 1, forward, may also be catalyzed by piperidine, but our data are not suitable for estimating the magnitude of such catalysis.

It is interesting that the enhancement of k_A for reaction 1, forward, by piperidine in methanol is mainly due to catalysis by methoxide ion. In contrast, the augmentation of k_A for the analogous reaction of piperidine with 2,4-dinitrodiphenyl ether in 60% dioxane–40% water, on addition of excess piperidine, is mainly due to catalysis by the amine itself.[3] Also, reaction 1 in 10% dioxane–90% water is strongly catalyzed by piperidine.[6]

Reaction of 2,4-Dinitroanisole with Piperidine, Catalyzed by $NaOCH_3$.—In a series of kinetic runs, sodium methoxide concentration was varied as piperidine concentration was held constant at 0.2 *M*. Under these conditions, one can estimate from the equilibrium constant for reaction 1 (*ca.* 100) that the ratio of I to II at equilibrium should be 1:20. The observed photometric yields of 2,4-dinitrophenylpiperidine (Table III) were multiplied by $^{21}/_{20}$ in order to obtain "corrected yields," which represent the per cent of the starting dinitroanisole accounted for by photometric analysis of the "infinity" solutions. With but three exceptions, the corrected yields are 100 ± 3%. This testifies to the magnitude of experimental error in our product analysis. Yields lower than 97% tend to occur at lower methoxide concentrations where side reactions as discussed above are relatively more serious.

The k_A values for reaction 1, forward, rise with increase in sodium methoxide concentration. The relationship is plotted as Figure 1. The third-order catalytic coefficient, $k_A/[OCH_3^-]$, diminishes as the base concentration augments (Table III). A similar effect was observed in respect to the reverse reaction; see Table I.

The fact that the "corrected yields" of 2,4-dinitrophenylpiperidine in Table III are near to 100% shows that side reaction 2 is insignificant at higher $NaOCH_3$ concentrations. It does not respond, or responds very weakly, to catalysis by bases. Recently Gregory and Bruice[18] have reported that the SN2 reactions of several amines with methyl iodide in water show simple second-order kinetics, with no evidence of base catalysis by the amines, and it has been known for some time that reactions of amines with 2,4-dinitrochlorobenzene and several other aromatic substrates in protic solvents are not base-catalyzed.[19] It appears that nucleophilic *attack* by amines in such solvents is not assisted by bases, and that catalysis when observed involves rate-limiting steps following the initial attack.

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[19] J. F. Bunnett and R. H. Garst, *ibid.*, **87**, 3875 (1965).

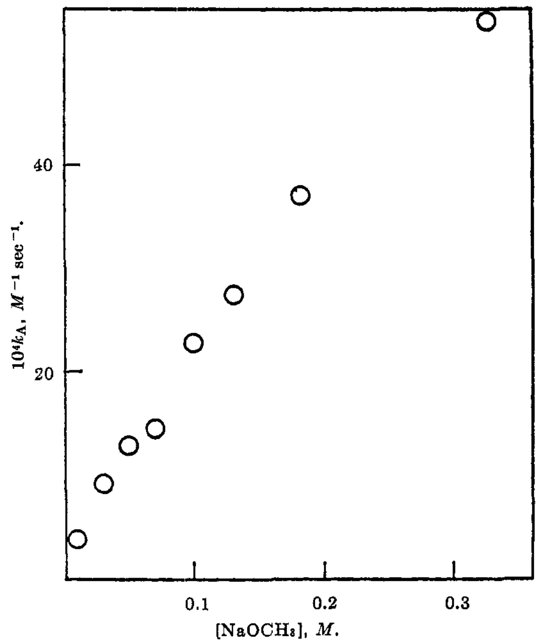


Figure 1.—Dependence of second-order rate coefficient (k_A) for the forward reaction on NaOCH$_3$ concentration; data of Table III.

Division of the present third-order catalytic coefficients by k_r values at corresponding NaOCH$_3$ concentrations should give K_e, the equilibrium constant for reaction 1 in the forward direction. The necessary k_r values were interpolated graphically from data in Table I, and the resulting K_e values are presented in Table III. Among the last six values, the average K_e is 100 ± 5 l. mol^{-1}. The larger estimates of K_e at lower methoxide concentrations possibly are due to the incursion of side reactions, especially in the forward rate determination.

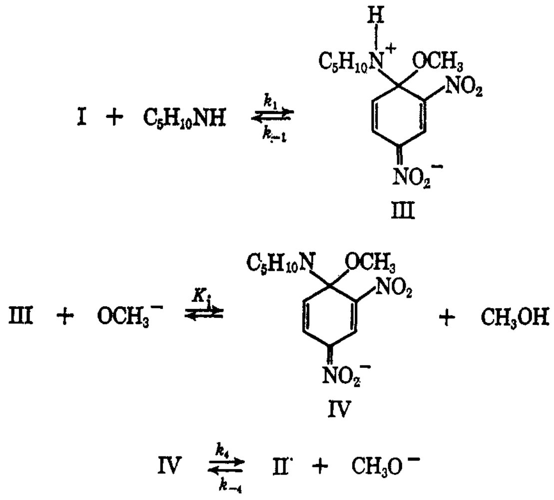
Equilibrium Measurement.—The equilibrium constant, K_e, for eq 1 was also estimated directly from measurement of absorption at 390 mμ after equilibrium had been attained. Because of the side reactions of 2,4-dinitroanisole, it was necessary that equilibrium be attained quickly. Also, the extent of side reactions could be minimized by having a rather high concentration of piperidine which would drive the reaction to the right as written. On the other hand, if it were driven too far to the right, the equilibrium constant could not be measured accurately.

In our experiments, solutions 9.58×10^{-5} *M* in 2,4-dinitroanisole and of various known concentrations of NaOCH$_3$ and piperidine were prepared and, in sealed ampoules with a nitrogen gas atmosphere, were allowed to react at 67.9° for ten half-lives, as indicated by rate measurements. The ampoule contents were then diluted to standard volume with *ca.* 1 *M* HCl in 47% ethanol, and absorption at 390 mμ was measured. With 0.1 *M* piperidine, K_e was 105, 119, and 109, respectively, with [NaOCH$_3$] 0.05, 0.10, and 0.20 *M*. With 0.05 *M* piperidine, K_e was 83, 86, and 81, at the respective NaOCH$_3$ concentrations. These estimates confirm in a general way the K_e (100 l. mol^{-1}) of kinetic origin, which we consider to be more reliable.

The K_e of 100 M^{-1} corresponds to $\Delta G°$ of −3100 cal.

Reaction Mechanism.—Several aromatic nucleophilic substitution reactions involving amine reagents have now been found to be base catalyzed.[3,4,6,12,20,21] The mechanism indicated by those studies is written in Chart I in the form most suitable for the present reaction. The second step of this mechanism is a fast proton-transfer equilibrium with equilibrium constant K_i. We have omitted from Chart I a step commonly included in such a mechanism, namely, the uncatalyzed or solvent-catalyzed transformation of intermediate complex III to products. It is omitted only because we have no evidence for it from the present study.

Chart I



The general expression for k_A in terms of rate coefficients for specific steps[12] is written for the mechanism of Chart I as eq 5. This expression calls for k_A to be

$$k_A = \frac{k_1K_ik_4[\mathrm{OCH_3^-}]}{k_{-1} + K_ik_4[\mathrm{OCH_3^-}]} \qquad (5)$$

linearly dependent on [OCH$_3^-$] when $k_{-1} \gg K_ik_4$[OCH$_3^-$], independent of [OCH$_3^-$] when K_ik_4[OCH$_3^-$] $\gg k_{-1}$, and curvilinearly dependent on [OCH$_3^-$] with ever-diminishing slope when neither inequality is extreme.

The dependence of k_A on methoxide concentration found in the present work (Figure 1) is nearly linear, but the plot is slightly curved in a sense allowed by eq 5. The form of the plot suggests that k_{-1} is larger than K_ik_4[OCH$_3^-$] but not so much larger that the latter term may be dismissed from the denominator. This interpretation means that step 4 is almost wholly rate limiting, in either direction, at low NaOCH$_3$ concentrations, but that rate limitation is increasingly shared with step 1 as the methoxide concentration increases.

An alternative interpretation of the decrease in k_r in Table I and of k_A/[OCH$_3^-$] in Table III is that sodium methoxide exerts a negative salt effect on the reaction in both directions, but this seems unlikely in view of Bernasconi's discovery that the rate coefficient for attack of NaOCH$_3$ on 2,4-dinitroanisole, to form the usual Jackson-Meisenheimer complex, increases as the NaOCH$_3$ concentration increases.[14b]

Another mechanistic possibility is that methoxide ion catalyzes the first step of the intermediate complex mechanism, I and piperidine and CH$_3$O$^-$ reacting in

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one concerted step to form IV and CH_3OH. A linear dependence on methoxide ion concentration would be expected, except as it might be modified by salt effects. We cannot exclude this possibility on the basis of our present results, but we consider it unlikely because no strong catalysis of this type has been encountered in other aromatic nucleophilic substitutions involving amine reagents.

Bunnett and Bernasconi[4] found reaction 1 in 10% dioxane–90% water to exhibit curvilinear dependence of k_A on hydroxide ion concentration. Their study was conducted at constant ionic strength, and the curvature could not be attributed to a salt effect. Comparison of the two studies shows that the relative rates of reversion of intermediate III to reactants and progression to products are altered by change of solvent and base.

By the principle of microscopic reversibility, the reverse of reaction 1 must occur by the same mechanism, in the other direction. The reverse mechanism in Chart I is a reasonable one.

Registry No.—I, 119-27-7; II, 839-93-0; methanol, 67-56-1; piperidine, 110-89-4; sodium methoxide, 124-41-4.

The Reaction of Diphenylphosphinous Chloride with Benzoyl Peroxide[1]

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The reaction of equimolar quantities of diphenylphosphinous chloride, Ph_2PCl (1), and benzoyl peroxide in refluxing benzene produces a mixture of benzoyl chloride, benzoic anhydride, and diphenylphosphinic anhydride, $Ph_2P(O)OP(O)Ph_2$ (2). In addition, a mixed anhydride, $PhC(O)OP(O)Ph_2$ (3), is detected. The first step of the reaction is an oxygen transfer from peroxide to 1 to form benzoic anhydride and diphenylphosphinyl chloride (4) In a secondary reaction 4 interacts with benzoic anhydride to give a mixture of benzoyl chloride, 3, and benzoic anhydride. Mixed anhydride is thus not a primary product but is formed by a metathesis between benzoic anhydride and 4 or/and by an equilibration of benzoic anhydride with 2.

The reaction between peroxides and trivalent phosphorus compounds may proceed by either a homolytic or a heterolytic route, or by a combination of the two, the products giving some indication of the favored route.[2–4] Thus, the reaction of benzoyl peroxide with triphenyl or tri-*n*-butyl phosphine (eq 1, R = Ph, *n*-Bu)

$$PhC(O)OO(O)CPh + R_3P \longrightarrow PhC(O)O(O)CPh + R_3P \longrightarrow O \quad (1)$$

yields the corresponding phosphine oxide and benzoic anhydride,[5,6] the net effect being the transfer of an oxygen atom to phosphorus. In this case the involvement of ionic intermediates is established.[7,8] However, a radical mechanism is thought to operate in the reaction of phosphorus trichloride with benzoyl peroxide to yield carbon dioxide, benzoyl chloride, and benzene phosphonyl dichloride[9] (eq 2). Benzoyl peroxide and

$$PhC(O)OO(O)CPh + PCl_3 \longrightarrow PhC(O)Cl + PhP(O)Cl_2 + CO_2 \quad (2)$$

triethyl phosphite react in solution by the ionic route to yield benzoic anhydride and triethyl phosphate (eq 1, R = OEt), but the uncontrolled reaction in the absence of a solvent yields in addition to these products diethyl-phenyl phosphonate, $PhP(O)(OEt)_2$, indicating, at least in part, a homolytic route.[10]

Recently, we reported[1b] that the reaction of benzoyl peroxide with diphenylphosphinous chloride (1), although not homolytic, is apparently different from the general ionic type expressed by eq 1. There were isolated benzoyl chloride, and two symmetrical anhydrides, benzoic anhydride and diphenylphosphinic anhydride (2) (eq 3). In addition, a mixed benzoic

$$\underset{\mathbf{1}}{Ph_2PCl} + PhC(O)OO(O)CPh \longrightarrow PhC(O)Cl + {}^1/_2PhC(O)O(O)CPh + {}^1/_2\underset{\mathbf{2}}{Ph_2P(O)O(O)PPh_2} \quad (3)$$

diphenylphosphinic anhydride (3) was detected but was not isolated in pure form. This paper outlines in

$$\underset{\mathbf{3}}{Ph_2P(O)O(O)CPh}$$

greater detail the results of the preliminary communication, and provides further information about the reaction path and the role of 3 in the reaction.

Results

In initial preparative-scale experiments, the reaction between 1 and benzoyl peroxide was carried out in refluxing benzene at molar concentration. Under these conditions and after an isolation procedure involving distillation and recrystallization, the final products were identified as benzoyl chloride, benzoic anhydride, and 2. The stoichiometry corresponds roughly to eq 3. In addition, another material with a characteristic ir absorption band in the carbonyl region at 1740 cm^{-1} (which is not displayed by the other carbonyl-containing materials in the system) was detected in the

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[1] (a) This investigation was supported by a grant from the Public Health Service, U. S. Department of Health, Education, and Welfare (GM 14932-01). The preliminary results (b) were published in *Chem. Ind.* (London), 120 (1967) and (c) were presented in part in a talk at the International Symposium on the Chemistry of Organic Peroxides in Berlin, DDR, Sept 1967.

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