The hot mixture was filtered and the residue, crude pyruvaldehyde 2,4-DNP was washed with 95% ethanol. The aqueous filtrate on cooling deposited impure yellow crystals of acetone 2,4-DNP. The filtrate which contained acetate ion was processed to give phenacyl acetate in the same way that the lactate containing filtrate was processed to give phenacyl lactate (see above).

To the aqueous solution remaining after the ether extraction was added an excess of barium chloride which precipitated barium sulfate and barium oxalate. The barium oxalate was separated from the sulfate by repeated extraction with hot water.

The products were purified as follows. The pyruvaldehyde di-2,4-DNP was recrystallized twice from nitrobenzene and dried at 60° under vacuum over phosphorus pentoxide for 12 hr., m.p. 295–299°.

The acetone 2,4-DNP was dissolved in benzene and chromatographed over alumina. It was then recrystallized twice from 95% ethanol and dried as above,

m.p. 123–125°. The phenacyl acetate was recrystallized four times from aqueous ethanol and dried at 25°, m.p. 39–40°. The barium oxalate precipitate was dissolved in 20 ml. of 2 M hydrochloric acid and barium ion precipitated with 50% sulfuric acid. The mixture was filtered and brought to pH 2 with potassium hydroxide pellets. Most of the water was removed by heating the solution in a stream of air, and then the residue was triturated with acetone, the acetone solution was filtered and concentrated to 1 ml., from which oxalic acid crystallized. The oxalic acid was sublimed under reduced pressure.

The analyses for C^{14} content were performed by the New England Nuclear Corp. using a liquid scintillation counter and an independent efficiency determination for each sample. The amount of each product was calculated from the observed activity of the product, the activity of the starting acetone, and the amounts of material used.

Kinetics of Reactions of Piperidine with Ethers of 2,4-Dinitrophenol in 10% Dioxane–90% Water. Dependence of Base Catalysis on the Group Displaced[1]

J. F. Bunnett and Claude Bernasconi

Contribution from the Department of Chemistry, Brown University, Providence, Rhode Island. Received July 6, 1965

Rates of reactions of several 2,4-dinitrophenyl ethers with piperidine, to form 2,4-dinitrophenylpiperidine, have been measured as a function of sodium hydroxide concentration. The sensitivity of these reactions to base catalysis varies with the leaving group. When the leaving group is 2,4-dinitrophenoxy or p-nitrophenoxy, catalysis by NaOH is weak. When it is methoxy, catalysis is strong. When catalysis is strong, the second-order rate coefficient (k_A) is curvilinearly related to base concentration; the plot (Figure 1) for 2,4-dinitrophenyl phenyl ether is a good example of this effect. The reaction of 2,4-dinitrophenyl phenyl ether with piperidine is subject to general base catalysis by piperidine, and the plot of k_A vs. piperidine concentration is curvilinear. The solvent deuterium isotope effect on this reaction, as catalyzed by NaOH, changes in direction as the alkali concentration is varied. All these observations are compatible with the intermediate complex mechanism, as sketched in eq. 1, and many of them fulfill specific expectations from it. They constitute important additional evidence for this mechanism. The reaction of 2,4-dinitrophenyl phenyl sulfide with piperidine, under the conditions of our experiments, was only moderately accelerated by sodium hydroxide. Incidentally, our measurements furnished rate coefficients (k_{OH}) for reactions of the several substrates with NaOH to form 2,4-dinitrophenol.

Primary and secondary amines react with many 1-substituted-2,4-dinitrobenzenes to form 2,4-dinitrophenylamines. Some of these reactions are strongly accelerated by bases, but others are insensitive to base catalysis.[2]

In previous papers,[5,6] the susceptibility of such a reaction to catalysis by bases has been associated with the frequency of reversion of intermediate complex I to reactants. The second step of the intermediate complex mechanism of substitution is judged to be

$$(1)$$
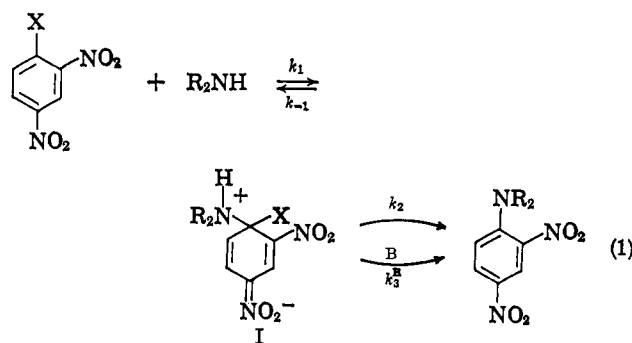
(2) The mild augmentations of second-order rate coefficients for such reactions caused by addition of relatively large amounts of amines and other compounds[3] are of uncertain character,[4] and are not designated as "base catalysis" in the present discussion.

(3) S. D. Ross, *Progr. Phys. Org. Chem.*, **1**, 31 (1963).

(4) J. F. Bunnett and R. H. Garst, *J. Am. Chem. Soc.*, **87**, 3875 (1965).

(5) J. F. Bunnett and J. J. Randall, *ibid.*, **80**, 6020 (1958).

(6) J. F. Bunnett and R. H. Garst, *ibid.*, **87**, 3879 (1965).

sensitive to catalysis by bases, but not the first. Consequently, only when expulsion of the leaving group X from the complex is at least partially rate limiting are reactions of this type subject to catalysis by bases. When formation of the intermediate is fully rate determining, base catalysis is not observable.[2]

Whether or not expulsion of the leaving group is rate limiting depends upon the relative rates of reversion of the intermediate to reactants and progression to products. One expects base catalysis to be observable when the leaving group is relatively slow to separate from carbon and/or when the amine moiety is easily expelled from the complex. In these terms one can understand why no reactions of amines with 2,4-dinitrochloro- or -bromobenzene have been observed to be base catalyzed, whereas reactions of piperidine with 2,4-dinitrophenyl phenyl ether[6] and 2,4-dinitroanisole[7] are strongly catalyzed by bases.

Because introduction of one or more nitro groups *ortho* or *para* in a phenoxy group should facilitate its heterolytic detachment from carbon, we expected that reactions of piperidine with 2,4-dinitrophenyl 4-nitrophenyl ether and bis(2,4-dinitrophenyl) ether should be less sensitive than the reaction of the dinitro ether to catalysis by bases. We set out to test this expectation. We chose 10% dioxane–90% water as reaction medium because this was the most aqueous water–dioxane mixture in which the several reactants and products were sufficiently soluble for kinetic study.

Earlier, Bunnett and Pruitt[8] had observed that reaction of the trinitro ether with piperidine in 50% dioxane was accelerated only about 20% by addition of 0.016 *M* sodium hydroxide.

Experimental Section

Materials. 1,4-Dioxane was purified by the method of Fieser[9] and was stored over lithium aluminum hydride, from which it was distilled as needed. "10% dioxane–90% water" was prepared by diluting one volume of dioxane to a total of ten volumes with distilled water. Commercial piperidine was heated for 12 hr. at reflux with sodium metal and then distilled; the fraction boiling at 105° was taken and stored under nitrogen gas in the dark. Commercial 2,4-dinitrochlorobenzene was twice recrystallized from ethanol, m.p. 52°. Piperidine hydrochloride (m.p. 251°), N-(2,4-dinitrophenyl)piperidine (m.p. 92–93°), 2,4-dinitrophenyl 4-nitrophenyl ether (m.p. 115–116°), bis(2,4-dinitrophenyl) ether (m.p. 197.5–199°), and 2,4-dinitroanisole (m.p. 95–96.5°) had been prepared by Garst[7] and were generously made available to us. 2,4-Dinitrophenyl phenyl ether, m.p. 68–69°, and 2,4-dinitrophenyl phenyl sulfide, m.p. 120–121°, represented samples available in the laboratory further recrystallized in this work.

Rate Measurements. The general photometric procedure developed in earlier investigations[5,10] was employed. Reaction solutions were prepared in thermostated volumetric flasks by combination of appropriate

(7) R. H. Garst, Ph.D. Thesis, Brown University, 1964; *Dissertation Abstr.*, 25, 4404 (1965).

(8) J. F. Bunnett and K. M. Pruitt, *J. Elisha Mitchell Sci. Soc.*, 73, 297 (1957).

(9) L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., D. C. Heath and Co., Boston, Mass., 1957, p. 284.

(10) J. F. Bunnett, E. W. Garbisch, Jr., and K. M. Pruitt, *J. Am. Chem. Soc.*, 79, 385 (1957).

volumes of thermostated standard solutions of the several ingredients; the resulting concentrations are noted in the tabular presentation of data below. Aliquots were removed at measured times, released into an excess of "quenching solution" (approximately 1 *M* hydrochloric acid in 50% ethanol–50% water) and diluted to standard volume with quenching solution. Absorbance at 390 mμ was measured[10a]; in most cases, the absorbance of the infinity sample fell between 0.32 and 0.80. In runs with 2,4-dinitrophenyl phenyl sulfide, solubility considerations required smaller concentrations to be used and infinity absorbances were up to 0.070.

It was conceivable that part of the reaction of 2,4-dinitrophenyl 4-nitrophenyl ether with piperidine might have occurred at C-1 of the *p*-nitrophenyl group, forming *p*-nitrophenylpiperidine and 2,4-dinitrophenol. However, the visible–ultraviolet spectrum of the product solution from this reaction in the presence of piperidine hydrochloride was fully consistent with formation of 2,4-dinitrophenylpiperidine and *p*-nitrophenol. There was no indication of *p*-nitrophenylpiperidine formation.

In all cases, plots of log $(A_\infty - A_t)$ vs. time were linear; thus pseudo-first-order kinetics were obeyed.

Rate coefficients are symbolized, and were computed, as follows: k_ψ, pseudo-first-order coefficient for the sum of all reactions consuming the substrate, reckoned as -2.30 times the slope of the foregoing plot; k_A^*, pseudo-first-order coefficient for formation of 2,4-dinitrophenylpiperidine, k_A^* = (fractional yield of 2,4-dinitrodiphenylpiperidine) $\times k_\psi$; k_A, second-order coefficient for formation of 2,4-dinitrophenylpiperidine, $k_A = k_A^*/[C_5H_{10}NH]_{\text{eff}}$, where $[C_5H_{10}NH]_{\text{eff}}$ is the corrected concentration of piperidine (see below); k_{OH}^*, pseudo-first-order coefficient for formation of 2,4-dinitrophenol, $k_{OH}^* = k_\psi - k_A^*$; k_{OH}, second-order coefficient for formation of 2,4-dinitrophenol, $k_{OH} = k_{OH}^*/[OH^-]_{\text{eff}}$.

Reference is also made to the following conceptual rate coefficients: k_1, k_{-1}, and k_2, coefficients for individual steps of the mechanism presented as eq. 1; k_3^B, coefficient for transformation of intermediate I to products, as catalyzed by base B (see eq. 1); k_3^P, k_3^B for the case of base piperidine; k_3^{OH}, k_3^B for the case of base hydroxide ion.

The reproducibility of measurements may be judged by comparison of supposedly identical runs in Table I, part C1, and in Table IV.

Correction of Concentrations for the Piperidine–Piperidinium Ion Equilibrium. The equilibrium reaction of piperidine with water was appreciable in many of our reaction solutions. Because it consumed piperidine and produced hydroxide ion, both of which were important reactants, it was necessary to correct the concentrations of these species.

Corrections were calculated by means of a K_b value estimated for piperidine in 10% dioxane at ionic strength 0.2, namely, 1.3×10^{-3}. In estimating this value, we took account of the pK_a of piperidine in water at infinite dilution (11.06)[11] and the likelihood

(10a) Note Added in Proof. We note that Bunnett and Garst[4,6] did not specify the wave lengths used in their photometric kinetic determinations. They were 405 mμ for reactions forming N-(*n*-butyl)-2,4-dinitroaniline, 390 mμ for reactions forming 2,4-dinitrophenylpiperidine, and 380 mμ for reactions forming 2,4-dinitrodiphenylamine (except 360 mμ for runs in *t*-butyl alcohol solvent).

Figure 1. Reaction of 2,4-dinitrophenyl phenyl ether with piperidine, catalyzed by NaOH; data from Table I, part C1.
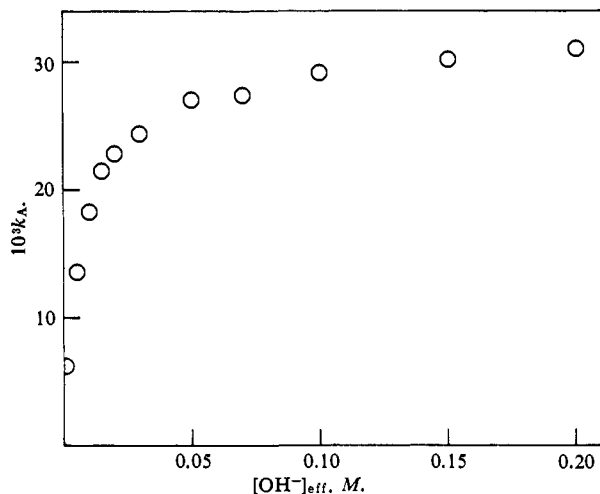

Figure 2. Reaction of 2,4-dinitrophenyl 4-nitrophenyl ether with piperidine, catalyzed by NaOH; data from Table I, part B.

that it diminishes by about 0.1 unit in changing the solvent to 10% dioxane.[12] We estimated pK_w for water in 10% dioxane to be 14.15,[13] subtracted the estimated pK_a in 10% dioxane at zero ionic strength (10.96), and then estimated the effect of increasing the ionic strength to 0.2.[11] The resulting K_b value was 1.3×10^{-3}; it is considered to be valid to $\pm 50\%$.

K_b for piperidine in 10% dioxane–90% deuterium oxide at ionic strength 0.2 was estimated to be 5×10^{-4}. This estimate takes account of the *ca.* six-fold smaller K_w for D_2O than H_2O and the fact that pK_a values of ammonium type acids are greater by about 0.5 in D_2O than in H_2O.[14]

In the tabular presentation of results, $[C_5H_{10}NH]_{eff}$ and $[OH^-]_{eff}$ represent concentrations of these species after correction for piperidinium hydroxide formation.

Reactions in 10% Dioxane–90% Deuterium Oxide. Reaction solutions were prepared in substantially the usual way. Ordinary reagent grade sodium hydroxide and piperidine were used as sources of NaOD and $C_5H_{10}ND$. O–H and N–H bonds are known to exchange rapidly with D_2O under basic conditions, and the amount of protium introduced into the D_2O by exchange was too small to change the deuterium content of the medium appreciably. The usual kinetic procedure was employed, but on a smaller scale in the interest of economy.

Reactions of 2,4-Dinitrochlorobenzene with Sodium Hydroxide. Reactions were carried out in a spectrophotometer cuvette in the (thermostated) cell compartment of a Beckman Model DU spectrophotometer. Absorbance at 365 mμ was measured; it reported directly the formation of 2,4-dinitrophenoxide ion.

Results

Our kinetic determinations are presented in Tables I–V. These tables present for each run the observed pseudo-first-order rate coefficient (k_ψ), the per cent

(11) W. F. K. Wynne-Jones and G. Salomon, *Trans. Faraday Soc.*, 34, 1321 (1938).

(12) J. C. James and J. G. Knox, *ibid.*, 46, 254 (1950).

(13) H. S. Harned and L. D. Fallon, *J. Am. Chem. Soc.*, 61, 2374 (1939).

(14) E. Högfeldt and J. Bigeleisen, *ibid.*, 82, 15 (1960); A. O. McDougall and F. A. Long, *J. Phys. Chem.*, 66, 429 (1962).
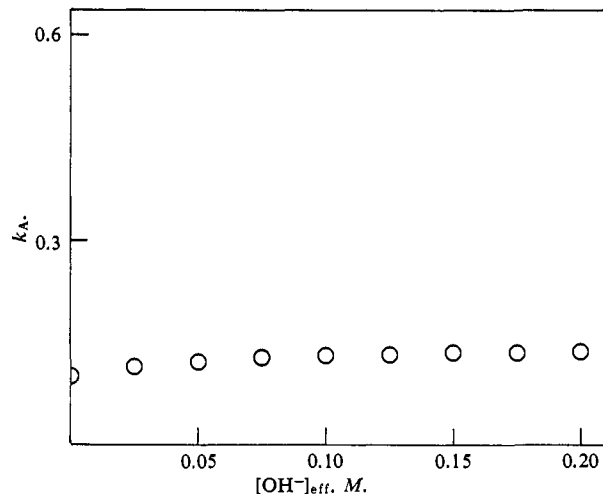
yield of 2,4-dinitrophenylpiperidine (as determined photometrically), and various rate coefficients for parts of the reaction reckoned as described in the Experimental Section. We shall be chiefly interested in k_A and k_{OH}, second-order coefficients for formation of 2,4-dinitrophenylpiperidine and 2,4-dinitrophenol, respectively.

2,4-Dinitrophenyl Phenyl Ether. The rate of reaction of 2,4-dinitrophenyl phenyl ether with piperidine was determined as a function of sodium hydroxide concentration at two piperidine concentrations. Results are listed in Table I, parts C1 and C2. The k_A values obtained are plotted in Figure 1. k_A rose steeply with increasing sodium hydroxide concentration at low [NaOH], but above 0.1 M NaOH the change was slight. The total acceleration caused by 0.2 M NaOH was three- to sixfold. The curved plots in Figure 1 resemble the corresponding plot for the same reaction in 60% dioxane–40% water observed by Bunnett and Garst[6] and for the reaction of dimethylamine with *p*-nitrophenyl phosphate observed by Kirby and Jencks.[15]

k_{OH} for reaction of 2,4-dinitrophenyl phenyl ether with hydroxide ion varied randomly among the experiments in parts C1 and C2, Table I. When the yield of 2,4-dinitrophenylpiperidine is high, this coefficient represents a small difference between large numbers and as such is not very precise. The variation is much smaller when attention is restricted to experiments in which the yield is less than 80%; the average value of k_{OH} among them is 4.6×10^{-4} l. mole^{-1} sec.$^{-1}$.

2,4-Dinitrophenyl 4-Nitrophenyl Ether. The effect of sodium hydroxide concentration on the rate of reaction of piperidine with this trinitro ether is evident in part B, Table I. Our expectation that this reaction should be less susceptible to base catalysis than the corresponding reaction of the dinitro ether was fulfilled; 0.2 M NaOH causes only a 37% increase in k_A. k_A is plotted *vs.* [NaOH] in Figure 2; the plot is gently curved, again in the sense that the catalytic effect diminishes as alkali concentration increases.

(15) A. J. Kirby and W. P. Jencks, *J. Am. Chem. Soc.*, 87, 3217 (1965).

Table I. Reactions of Piperidine and Sodium Hydroxide with Ethers of 2,4-Dinitrophenol in 10% Dioxane–90% Water at 29.4°[a]

[NaOH]$_{st}$, M	[OH$^-$]$_{eff}$, M	[C$_5$H$_{10}$NH]$_{eff}$, M	$10^4 k_\psi$, sec.$^{-1}$	Yield, %	$10^4 k_A$*, sec.$^{-1}$	$10^3 k_A$, l. mole^{-1} sec.$^{-1}$	$10^5 k_{OH}$*, sec.$^{-1}$	$10^4 k_{OH}$, l. mole^{-1} sec.$^{-1}$
A. Reactions of bis(2,4-dinitrophenyl) ether[b]								
c	0.0012	2.38 × 10^{-3}	15.40	100	15.40	646		
Nil	0.0013	1.23 × 10^{-3}	8.10[d]	100	8.10	658		
0.0010	0.0020	1.50 × 10^{-3}	10.05	100	10.05	670		
0.0050	0.0055	2.01 × 10^{-3}	14.2	99.5	14.1	701		
0.010	0.0103	2.21 × 10^{-3}	16.7	98.6	16.4	744		
0.020	0.0202	2.35 × 10^{-3}	18.0	94.6	17.0	725	10	50
0.050	0.0501	2.44 × 10^{-3}	21.2	86.7	18.3	749	28	57
0.100	0.100	2.47 × 10^{-3}	24.8	77.5	19.2	780	56	56
0.150	0.150	2.48 × 10^{-3}	27.9	68.8	19.2	774	88	58
0.200	0.200	2.48 × 10^{-3}	31.6	61.7	19.5	783	121	60
B. Reactions of 2,4-dinitrophenyl 4-nitrophenyl ether[e]								
c	0.00012	2.38 × 10^{-3}	2.40	100	2.40	101		
0.025	0.251	2.38 × 10^{-3}	3.13	86.8	2.71	114	4.2	16.6
0.050	0.0501	2.44 × 10^{-3}	3.69	80.4	2.97	122	7.2	14.4
0.075	0.0750	2.46 × 10^{-3}	4.24	73.9	3.14	128	11.0	14.7
0.100	0.100	2.47 × 10^{-3}	4.68	69.1	3.23	131	14.5	14.5
0.125	0.125	2.47 × 10^{-3}	5.07	64.4	3.26	132	18.2	14.6
0.150	0.150	2.48 × 10^{-3}	5.52	61.2	3.37	136	21.5	14.3
0.175	0.175	2.48 × 10^{-3}	5.89	57.9	3.40	137	25.0	14.3
0.200	0.200	2.48 × 10^{-3}	6.29	54.7	3.43	138	28.6	14.3
C1. Reactions of 2,4-dinitrophenyl phenyl ether; [C$_5$H$_{10}$NH]$_{st}$ = 2.5 × 10^{-3} M[f]								
g	0.00072	1.78 × 10^{-3}	0.0830	100	0.0830	4.66		
Nil	0.0013	1.23 × 10^{-3}	0.076	100	0.0764	6.23		
0.005	0.0055	2.01 × 10^{-3}	0.295	91.1	0.273	13.6		
0.010	0.0103	2.21 × 10^{-3}	0.458	88.2	0.404	18.3	0.54	5.3
0.015	0.0152	2.30 × 10^{-3}	0.574	86.4	0.495	21.5	0.95	6.2
0.020	0.0202	2.35 × 10^{-3}	0.615	87.6	0.538	22.9	0.77	3.8
0.030	0.0301	2.40 × 10^{-3}	0.739	79.5	0.588	24.5	1.51	5.0
0.050	0.0501	2.44 × 10^{-3}	0.884	74.7	0.659	27.1	2.25	4.5
0.070	0.070	2.46 × 10^{-3}	0.985	68.3	0.672	27.4	3.1	4.5
0.100	0.100	2.47 × 10^{-3}	1.135	63.5	0.720	29.2	4.2	4.2
0.150	0.150	2.48 × 10^{-3}	1.46	51.4	0.749	30.2	7.2	4.8
0.200	0.200	2.49 × 10^{-3}	1.71	45.1	0.771	31.0	9.4	4.7
C2. Reactions of 2,4-dinitrophenyl phenyl ether; [C$_5$H$_{10}$NH]$_{st}$ = 5 × 10^{-2} M[h]								
i	0.0013	4.87 × 10^{-2}	5.89	100	5.89	12.1		
Nil	0.0075	4.25 × 10^{-2}	8.12[d]	100	8.12	19.1		
0.010	0.0142	4.58 × 10^{-2}	10.5	99	10.4	22.7		
0.050	0.0512	4.88 × 10^{-2}	14.0	98	13.7	28.1		
0.100	0.101	4.94 × 10^{-2}	15.2	96.3	14.6	29.7	5.7	5.6
0.200	0.200	4.97 × 10^{-2}	17.4	91.9	16.0	32.1	14.2	7.1
D. Reactions of 2,4-dinitroanisole[j]								
i	0.0013	4.87 × 10^{-2}	0.069	99	0.068	0.139		
Nil	0.0075	4.25 × 10^{-2}	0.269	90.6	0.244	0.574		
0.050	0.0512	4.88 × 10^{-2}	1.40	72.0	1.01	2.07	3.92	7.62
0.100	0.101	4.94 × 10^{-2}	2.03	62.7	1.27	2.58	7.63	7.57
0.200	0.200	4.97 × 10^{-2}	3.43	45.3	1.56	3.14	18.7	9.34
E. Reactions of 2,4-dinitrophenyl phenyl sulfide[k]								
Nil	0.0190	0.281	0.727	97.3	0.707	0.252		
0.030	0.0395	0.290	0.927	94.0	0.871	0.300		
0.050	0.0565	0.294	1.06	91.1	0.969	0.330	0.97	1.7
0.075	0.0798	0.295	1.29	86.0	1.11	0.376	1.80	2.3
0.100	0.104	0.296	1.53	80.8	1.24	0.420	2.9	2.9
0.150	0.152	0.298	1.84	75.3	1.38	0.462	4.6	3.0
0.175	0.177	0.298	2.05	74.3	1.52	0.511	5.3	3.0
0.200	0.202	0.298	2.24	68.9	1.55	0.519	6.9	3.4
F. Reactions of 2,4-dinitrochlorobenzene[l]								
c	0.00012	2.38 × 10^{-3}	1.64	100	1.64	69.0		
0.200	0.200	2.48 × 10^{-3}	2.61	71.2	1.86	74.9	7.5	3.8

[a] Total electrolyte concentration maintained at 0.2 M by addition of sodium chloride as required. [b] [Substrate]$_0$ = 1.23 × 10^{-5} M, [C$_5$H$_{10}$NH]$_{st}$ = 2.50 × 10^{-3} M. [c] Piperidine hydrochloride = 2.5 × 10^{-2} M, instead of NaOH. [d] Average of two runs. [e] [Substrate]$_0$ = 4.8 × 10^{-5} M, [C$_5$H$_{10}$NH]$_{st}$ = 2.50 × 10^{-3} M. [f] [Substrate]$_0$ = 9.71 × 10^{-5} M. [g] Piperidine hydrochloride = 2.5 × 10^{-3} M, instead of NaOH. [h] [Substrate]$_0$ = 1.47 × 10^{-4} M. [i] Piperidine hydrochloride = 5.0 × 10^{-2} M, instead of NaOH. [j] [Substrate]$_0$ = 2.42 × 10^{-4} M, [C$_5$H$_{10}$NH]$_{st}$ = 5.0 × 10^{-2} M. [k] [Substrate]$_0$ = 1.55 × 10^{-5} M, [C$_5$H$_{10}$NH]$_{st}$ = 0.30 M; the quenching solution was 2 M HCl in 50% ethanol. [l] [Substrate]$_0$ = 1.02 × 10^{-5} M, [C$_5$H$_{10}$NH]$_{st}$ = 2.5 × 10^{-3} M.

Figure 3. Reaction of bis(2,4-dinitrophenyl) ether with piperidine, catalyzed by NaOH; data from Table I, part A.

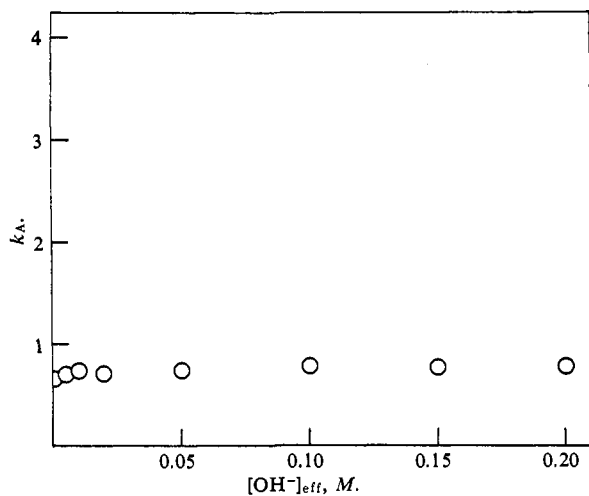Figure 4. Reaction of 2,4-dinitroanisole with piperidine, catalyzed by NaOH; data from Table I, part D.

k_{OH} for the reaction of hydroxide ion with the trinitro ether is substantially constant among experiments in which the yield of 2,4-dinitrophenylpiperidine was less than 80%. The average value of k_{OH} among them is 1.44×10^{-3} l. mole^{-1} sec.$^{-1}$.

Bis(2,4-dinitrophenyl) Ether. As shown in Table I, part A, and in Figure 3, sodium hydroxide has a still smaller effect on k_A for reaction of the tetranitro ether with piperidine. The over-all acceleration caused by 0.2 M NaOH is 21%, and most of this increase is realized when [NaOH] has attained 0.01 M.[16]

The average value of k_{OH}, for reaction of hydroxide ion with the tetranitro ether, is 5.8×10^{-3} l. mole^{-1} sec.$^{-1}$ among the experiments in which the yield of 2,4-dinitrophenylpiperidine was less than 80%.

2,4-Dinitroanisole. The reaction of this substrate with piperidine was relatively slow, and was strongly catalyzed by sodium hydroxide (see Table I, part D). k_A was increased 23-fold by 0.2 M NaOH. As shown in Figure 4, the response of k_A to sodium hydroxide concentration is not entirely linear; the slope decreases as alkali concentration increases, but the reaction does not become even approximately immune to base catalysis within the range of concentrations studied.[17]

Only three runs afforded values of k_{OH} for reaction of 2,4-dinitroanisole with hydroxide ion. The average value is 8.2×10^{-4} l. mole^{-1} sec.$^{-1}$.

2,4-Dinitrochlorobenzene. Only two runs on the reaction of this substrate with piperidine were performed (see Table I, part F). In the presence of 0.2 M NaOH, k_A was only 9% higher than in the presence of 0.025 M piperidine hydrochloride, which reduced hydroxide ion concentration to a very low level. Such meager accelerations, scarcely greater than experimental error, have been observed before.[4,8,18] Whether they repre-

(16) The early k_A values in Table I, part A, are subject to some uncertainty. This is partly because traces of carbon dioxide may disturb the titer of very dilute sodium hydroxide solutions and partly because the corrections for the piperidine–piperidinium ion equilibrium which considerably affect k_A, are inexact insofar as our estimate of K_b for piperidine in this medium is inexact.

(17) Garst[7] has shown that the reaction of 2,4-dinitroanisole with piperidine in methanol is strongly catalyzed by sodium methoxide; the plot of k_A vs. [NaOCH$_3$] is nearly linear, being slightly concave downwards.

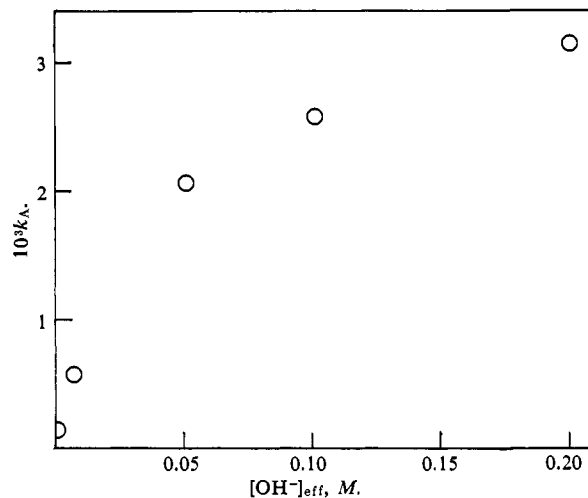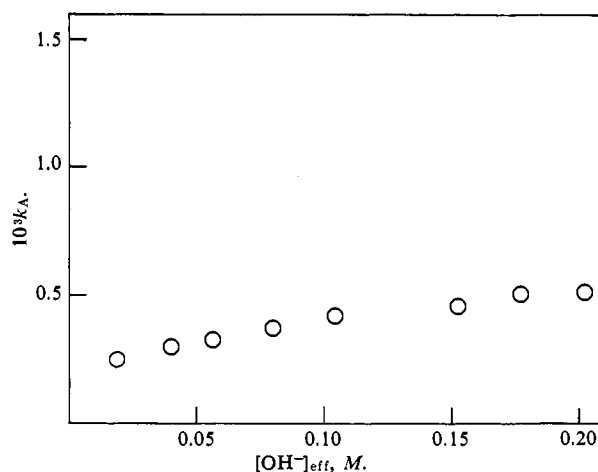(18) S. D. Ross, *J. Am. Chem. Soc.*, **80**, 5319 (1958).

Figure 5. Reaction of 2,4-dinitrophenyl sulfide with piperidine, catalyzed by NaOH; data from Table I, part E.

sent a mild base catalysis by hydroxide ion or some other type of kinetic effect is not clear.[4]

2,4-Dinitrophenyl Phenyl Sulfide. This substrate is less reactive with piperidine than is the corresponding oxygen ether.[19,20] In order to attain adequately rapid over-all reaction rates in the presence of sodium hydroxide, we had to employ a rather high piperidine concentration, 0.3 M, which is six to about one hundred times greater than used with the other substrates.[21]

A moderate degree of dependence of k_A on hydroxide ion concentration is evident in Table I, part E, and in Figure 5. k_A is somewhat more than doubled by 0.2 M NaOH. The plot of k_A vs. [NaOH] is roughly linear; there is a suggestion of downward curvature.

We do not know whether this thio ether reaction is really but moderately sensitive to base catalysis, or whether perhaps it is very sensitive. It is conceivable

(19) L. Bartolotti and A. Cerniani, *Boll. sci. fac. chim. ind. Bologna*, **14**, 33 (1956).

(20) In contrast, ethyl p-nitrothiolbenzoate is much more reactive than the corresponding oxygen ester with n-butylamine: K. A. Connors and M. L. Bender, *J. Org. Chem.*, **26**, 2498 (1961).

(21) 2,4-Dinitrophenylpiperidine is slowly hydrolyzed by hydroxide ion in 10% dioxane. If the over-all reaction rate is too low, this post-reaction can complicate the kinetic determination. Under the conditions of our experiments, this complication was of no consequence.
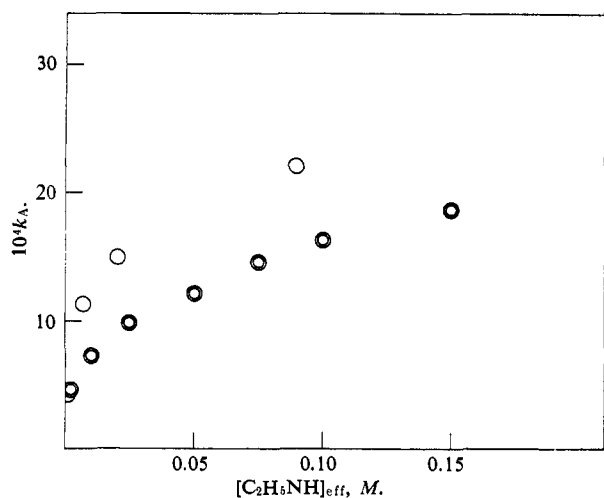
Figure 6. Reaction of 2,4-dinitrophenyl phenyl ether with piperidine, catalyzed by piperidine: open circles, without piperidine hydrochloride; bull's-eyes, with $[C_5H_{10}NH_2Cl] = [C_5H_{10}NH]$. Data from Table II.
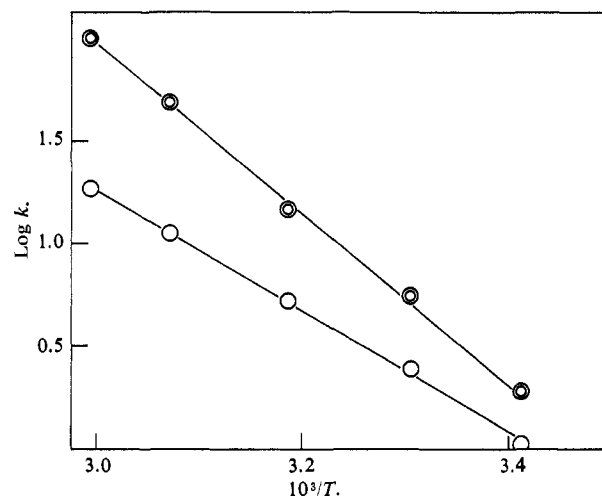

Figure 7. Reactions of 2,4-dinitrophenyl phenyl ether with piperidine, in the presence of 0.03 M NaOH, and with NaOH. Arrhenius plots: open circles, log k_A + 2 (piperidine reaction); bull's-eyes, log k_{OH} + 4 (NaOH reaction). Data from Table III.

that the true plot of k_A vs. base concentration has a shape similar to that (Figure 1) for reaction of the corresponding oxygen ether, but that the 0.3 M piperidine present had, even in the absence of NaOH, already carried the plot past the region of steep rise. If that is the case, only the latter portion of the curve is revealed by our experiments.

The average value of k_{OH}, for reaction of the thio ether with hydroxide ion, is 3.1×10^{-4} l. mole^{-1} sec.$^{-1}$ among reactions in which the yield of 2,4-dinitrophenylpiperidine is less than 80%.

Catalysis by Piperidine. The dependence of k_A on piperidine concentration was investigated in the case of 2,4-dinitrophenyl phenyl ether. Results are set forth in Table II (the runs without $C_5H_{10}NH_2{}^+Cl^-$)

Table II. Reactions of Piperidine with 2,4-Dinitrophenyl Phenyl Ether in 10% Dioxane–90% Water at 29.4°[a]

$[C_5H_{10}-$ $NH]_{st}$,[b] M	$[C_5H_{10}-$ $NH]_{eff}$, M	$[C_5H_{10}-$ $NH_2{}^+Cl^-]_{st}$, M	10^3 $[OH^-]_{eff}$, M	10^4k_ψ, sec.$^{-1}$	10^3k_A, l. mole^{-1} sec.$^{-1}$
0.0025	0.00123	Nil	1.27	0.074	6.23
0.0025	0.00178	0.0025	0.72	0.083	4.66
0.0025	0.00238	0.025	0.12	0.072	3.00
0.010	0.00696	Nil	3.04	0.784	11.2
0.010	0.00894	0.010	1.06	0.653	7.31
0.025	0.0199	Nil	5.1	2.98	15.0
0.025	0.0238	0.025	1.21	2.34	9.86
0.050	0.0488	0.050	1.24	5.92	12.2
0.075	0.0737	0.075	1.26	10.8	14.6
0.100	0.0894	Nil	10.6	19.8	22.1
0.100	0.0987	0.100	1.27	16.1	16.3
0.150	0.149	0.150	1.28	27.4	18.7

[a] Initial substrate concentration, 1.0×10^{-4} M; total electrolyte concentration maintained at 0.20 M by addition of NaCl as required. All reactions formed 2,4-dinitrophenylpiperidine quantitatively. [b] Stoichiometric piperidine concentration.

and are plotted in Figure 6 (the open circles). k_A is higher at higher piperidine concentrations; 0.1 M piperidine causes a 3.5-fold increase in k_A over 0.0025 M piperidine. However, part of the catalytic effect should

be ascribed to the hydroxide ion present through formation of piperidinium hydroxide.

It is interesting that the plot of k_A vs. piperidine concentration is curved in resemblance to Figures 1 and 4. The corresponding plot for the same reaction in 60% dioxane–40% water is linear.[6]

Although it had previously been established that the acetate catalysis of the reaction of N-methylaniline with 2,4-dinitrofluorobenzene in ethanol[5] and the piperidine catalysis of the reaction of piperidine with 2,4-dinitrophenyl phenyl ether in 60% dioxane[6] represented general base catalysis, in neither case was this demonstrated in the classical way. The classical experiment involves determination of rate (k_A in the present case) as a function of buffer concentration in a series of buffers of constant buffer ratio, at constant ionic strength.[22]

We have now performed the classical experiment; 2,4-dinitrophenyl phenyl ether was allowed to react with a series of piperidine–piperidine hydrochloride buffers at ionic strength held constant at 0.20 by compensation with sodium chloride. Results are set forth in Table II and they are plotted in Figure 6 (the bulls-eyes). The fact that k_A rises with increase in buffer concentration shows that general base catalysis prevails.[23] It should be noted that the piperidine-catalyzed reaction is not linearly dependent on piperidine concentration; the curved plot resembles Figures 1 and 4.[24]

(22) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 215.

(23) (a) Kirby and Jencks[15] have observed general base catalysis of the reaction of p-nitrophenyl phosphate with dimethylamine. (b) That the rise in k_A in Figure 6 is not due to general acid catalysis by piperidinium ion is shown, among others, by the first three experiments in Table II. Progressive *increases* in piperidinium ion concentration cause k_A to *decrease*, owing to repression of hydroxide ion formation.

(24) It may seem contradictory that we recognize the present acceleration by piperidine as base catalysis, but withold this designation from the k_A-enhancing effect of amines in related reactions of 2,4-dinitrochlorobenzene. Our reasons are twofold. First, the present accelerations by amines are orders of magnitude greater. Second, the present reactions are even more strongly accelerated by hydroxide ion, whereas the reactions of 2,4-dinitrochlorobenzene with amines are accelerated to more or less the same meager extent by substances as different in basicity as hydroxide ion, amines, and m-dinitrobenzene. The latter characteristics do not exclude the possibility that some or all of these species

Table III. Reactions of Piperidine with 2,4-Dinitrophenyl Phenyl Ether in the Presence of 0.03 M NaOH in 10% Dioxane–90% Water. Temperature Dependence of Reaction Rate[a]

Temp., °C.	$10^4 k_\psi$, sec.$^{-1}$	Yield, %	$10^4 k_A$*, sec.$^{-1}$	$10^3 k_A$, l. mole^{-1} sec.$^{-1}$	$10^5 k_{OH}$*, sec.$^{-1}$	$10^4 k_{OH}$, l. mole^{-1} sec.$^{-1}$
20.0	0.312	81.9	0.255	10.6	0.57	1.9
29.4	0.750	78.0	0.583	24.4	1.65	5.5
40.7	1.76	70.2	1.28	51.5	5.25	14.7
52.5	4.10	64.3	2.66	111	14.6	48.5
60.9	7.44	59.5	4.43	184	30.1	100

[a] Initial concentrations: substrate, 8.66×10^{-5} M; piperidine, 2.5×10^{-3} M; NaCl, 0.17 M.

Table IV. Solvent Deuterium Isotope Effects in Reactions of Piperidine and Sodium Hydroxide with 2,4-Dinitrophenyl Phenyl Ether in 10% Dioxane–90% H_2O vs. 10% Dioxane–90% D_2O, at 29.4°[a]

Solvent component	[NaOH]$_{st}$ or [NaOD]$_{st}$, M	[OH$^-$]$_{eff}$ or [OD$^-$]$_{eff}$, M	[C$_5$H$_{10}$NH]$_{eff}$ or [C$_5$H$_{10}$ND]$_{eff}$, M	$10^5 k_\psi$, sec.$^{-1}$	Yield, %	$10^5 k_A$*, sec.$^{-1}$	$10^3 k_A$, l. mole^{-1} sec.$^{-1}$	$k_A(H)/k_A(D)$	$10^5 k_{OH}$*, sec.$^{-1}$	$10^4 k_{OH}$, l. mole^{-1} sec.$^{-1}$
H_2O	Nil	0.00127	0.00123	0.728	100	0.728	5.91 ⎱	1.46[b]		
D_2O	Nil	0.00090	0.0016	0.590	100	0.590	3.68 ⎰			
H_2O	0.0100	0.0103	0.00221	4.79	90.1	4.32	19.5 ⎱	1.39	0.47	4.6
D_2O	0.0100	0.0101	0.00238	3.93	84.8	3.33	14.0 ⎰		0.60	5.9
H_2O	0.0500	0.0501	0.00244	8.61	74.2	6.39	26.2 ⎱	0.98	2.22	4.4
D_2O	0.0500	0.0500	0.00248	9.29	70.8	6.60	26.7 ⎰		2.69	5.4
H_2O	0.200	0.200	0.0025	16.8	45.1	7.56	30.2 ⎱	0.86	9.19	4.59
D_2O	0.200	0.200	0.0025	23.1	37.9	8.75	35.0 ⎰		14.4	7.18

[a] Initial concentrations: substrate, 8.25×10^{-5} M; C$_5$H$_{10}$NH or C$_5$H$_{10}$ND, 2.5×10^{-3} M. Total electrolyte concentration maintained at 0.20 M by addition of NaCl as required. [b] To estimate $k_A(H)/k_A(D)$, in the absence of NaOH(NaOD), $k_A(D)$ was corrected to [OD$^-$]$_{eff}$ 0.00127 with reference to Figure 1.

Table V. Reactions of Sodium Hydroxide with 2,4-Dinitrochlorobenzene in 10% Dioxane–90% Water at 29.4°[a]

[NaOH], M	$10^5 k_\psi$, sec.$^{-1}$	$10^4 k_{OH}$, l. mole^{-1} sec.$^{-1}$
0.05	1.60	3.21
0.10	3.12	3.12
0.15	4.68	3.13
0.20	6.42	3.21

[a] Initial substrate concentration, 6.3×10^{-5} M; total electrolyte concentration maintained at 0.20 M by addition of NaCl as required.

Dependence of Rate on Temperature. The influence of temperature was determined only for reaction of 2,4-dinitrophenyl phenyl ether with piperidine in the presence of 0.03 M NaOH. Results are presented in Table III. Arrhenius plots concerning k_A and k_{OH} are shown in Figure 7. For the piperidine reaction, ΔH^* is 12.8 ± 0.3 kcal./mole and ΔS^* is −24 e.u. For the hydroxide reaction, ΔH^* is 18.1 ± 0.4 kcal./ mole and ΔS^* is −14 e.u.

Solvent Hydrogen Isotope Effect. The kinetic effect of changing the solvent from 10% dioxane–90% water to 10% dioxane–90% deuterium oxide was studied in the case of the 2,4-dinitrophenyl phenyl ether–piperidine reaction as a function of NaOH (or NaOD) concentration. Results are presented in Table IV.

k_A was greater in light than in heavy water in the absence of alkali and at 0.01 M NaOH or NaOD. However, in 0.2 M NaOH or NaOD k_A was 14%

act catalytically *as bases*, but they do raise doubts as to whether those mild accelerations may be properly identified as base catalysis.

larger in the heavy-water medium. Thus the direction of the solvent isotope effect changes within this range of alkali concentrations.

The hydrolytic side reaction forming 2,4-dinitrophenol is throughout faster in the deuterium oxide medium. The average value of k_{OD}/k_{OH} is 1.36 ± 0.14.

Reaction of 2,4-Dinitrochlorobenzene with NaOH. The rate of this reaction was studied as a function of NaOH concentration for the purpose of estimating medium effects on the activity coefficient of the hydroxide ion or, more rigorously, on the activity coefficient ratio, $f_S f_{OH}$-$/f$*. Sodium hydroxide concentration was varied fourfold, at constant ionic strength. The second-order rate coefficient (k_{OH}) was unchanged within experimental error[25] (see Table V). This shows that the medium effect on the present activity coefficient ratio is negligible, and suggests that it is not a major factor in any of the reactions we have studied. The average value of k_{OH} is 3.17×10^{-4} l. mole^{-1} sec.$^{-1}$.

Discussion

Base Catalysis and the Leaving Group. Our expectation was that base catalysis should diminish as the leaving group were more prone to separate from carbon. The mathematical basis of this expectation is a kinetic expression derived with reference to eq. 1 by means of the usual steady-state assumption.[26]

$$k_A = \frac{k_1 k_2 + k_1 \Sigma k_3{}^B[B]}{k_{-1} + k_2 + \Sigma k_3{}^B[B]} \quad (2)$$

When $(k_2 + \Sigma k_3{}^B[B]) \gg k_{-1}$, eq. 2 simplifies to

$$k_A = k_1 \quad (3)$$

When $k_{-1} \gg (k_2 + \Sigma k_3{}^B[B])$, eq. 2 becomes

$$k_A = \frac{k_1 k_2}{k_{-1}} + \Sigma \frac{k_1 k_3{}^B[B]}{k_{-1}} \quad (4)$$

(25) Cf. J. F. Bunnett and G. T. Davis, *J. Am. Chem. Soc.*, 76, 3011 (1954).

(26) Equation 2 differs slightly from the corresponding equation as presented in previous papers.[5,6] The differences are, first, that specific provision is made for catalysis of the second step by each base present in the system and, second, that k_2 is now restricted to the uncatalyzed (or solvent catalyzed) component of the second step. In previous usage, k_2 also embraced catalysis by any base present in constant amount through a series of kinetic runs, *e.g.*, the amine reagent in a series of hydroxide-catalyzed runs.

When the leading group is a "good" one, prone to separate from carbon, or when it is a moderately good one and there is a high concentration of an effective base, the former inequality is likely to be satisfied. In that case, eq. 3 prevails; the over-all reaction is not catalyzed by bases. But when the leaving group is a poor one or when it is moderately good but $\Sigma k_3^B[B]$ is small, eq. 4 obtains and k_A is linearly dependent on base concentration. If the leaving group is moderately good and the concentration of catalyzing base is varied among a set of runs, linear dependence of k_A at low base concentrations (eq. 4) should gradually yield to immunity at high concentrations of base (eq. 3); thus an over-all curved response should be observed.[27]

In the present work, a "good" leaving group is approximated by 2,4-dinitrophenoxy; the plot of k_A vs. [NaOH] (Figure 3) is nearly flat as called for by eq. 3. Phenoxy is a moderately good leaving group; the plot of k_A vs. [NaOH] (Figure 1) so beautifully demonstrates the predicted change of slope that it is recommended to authors of textbooks. A "poor" leaving group is methoxy; as expected, the plot of k_A vs. [NaOH] (Figure 4) shows less tendency to flatten out at higher base concentrations.

Thus the dependence of the form of base catalysis on leaving group characteristics is in excellent accord with the mechanism of eq. 1.

Base Catalysis and the Solvent. The reaction of piperidine with 2,4-dinitrophenyl phenyl ether, catalyzed by piperidine and by hydroxide, has now been studied in two solvents. For the piperidine-catalyzed reaction, the plot of k_A in 60% dioxane–40% water against [$C_5H_{10}NH$] is linear in obedience to eq. 4.[6] But the corresponding plot for 10% dioxane–90% water (Figure 6) is curved. For the hydroxide-catalyzed reaction, the plots for both solvents are curved but that for 10% dioxane (Figure 1) is more nearly flat at higher hydroxide ion concentrations.

The reaction of 2,4-dinitroanisole with piperidine as catalyzed by the lyate ion has also been studied in two solvents. In methanol, the plot of k_A vs. [NaOCH$_3$] is nearly linear, showing a slight tendency toward lesser slope at higher methoxide concentrations.[7] In 10% dioxane (Figure 4), there is appreciable curvature.

In all three examples there is a tendency toward more adherance to eq. 3 and less to eq. 4 in the more polar solvent. This implies that k_{-1} is, relative to ($k_2 + \Sigma k_3^B[B]$), larger in the less polar solvents. Inasmuch as the reverse of the first step involves conversion of the zwitterionic intermediate to neutral reactants, k_{-1} would be expected to increase as the solvent became less polar.[28] Some solvent effect on the rate of progression of intermediate to products is also probable; it is evidently either complementary or of lesser magnitude.

General Base Catalysis and Solvent Isotope Effect. In the present research, we have again demonstrated that it is *general* base catalysis with which we are con-

cerned (see Figure 6). General base catalysis indicates that the catalyzing base is present in the rate-limiting transition state. There being no possibility of nucleophilic catalysis[29] by hydroxide ion[30] or piperidine, the base in the transition state must be engaged in proton transfer. Either it is taking a proton from I or a tautomer thereof, or the conjugate acid of the base is interacting with the conjugate base of I. In either case, the hydrogen being transferred is one rapidly exchangeable with water under basic conditions, and it is deuterium if the reaction medium contains D$_2$O in place of H$_2$O.

Since general acid or general base catalyzed reactions are slower in D$_2$O than in H$_2$O,[31] the reaction of 2,4-dinitrophenyl phenyl ether with piperidine ought to be retarded in 10% dioxane–90% deuterium oxide insofar as the base-catalyzed step is rate limiting. With attention to the curved plot in Figure 1, we should therefore expect k_A(H) to exceed k_A(D) at low NaOH concentrations. At high base concentrations, k_A(H)/k_A(D) should mainly reflect solvent and secondary isotope effects on formation of the intermediate. *A priori*, the latter might be expected to be small or inverse. Over-all, k_A(H)/k_A(D) should decrease as [NaOH] increases.

Our observations (Table IV) match these expectations. k_A(H)/k_A(D) diminishes from 1.46 in the absence of alkali to 0.86 in the presence of 0.2 M NaOH or NaOD.

The inverse isotope effect under the latter conditions is compatible with the view that deuterium has an electron-releasing inductive effect[32] which makes N-deuteriopiperidine a stronger nucleophile. However, $C_5H_{10}ND$ is known to react equally fast as $C_5H_{10}NH$ with aryl halides in hydrocarbon solvents.[33] We therefore judge that the solvent isotope effect contributes importantly toward making formation of the intermediate faster in the heavy-water medium.

Pietra[34] has recently shown the reaction of piperidine with 2,4-dinitrophenyl phenyl ether in benzene to be second order in piperidine. The reaction is thus wholly base catalyzed in benzene solution. The third-order rate coefficient with N-deuteriopiperidine was about 21% less than with piperidine.

Rate Coefficients for Formation and Decomposition of the Intermediate. If eq. 2 be inverted, and k_3^P and k_3^{OH} be allowed to represent k_3^B for the bases piperidine and hydroxide ion, respectively, eq. 5 is obtained. If catalysis by piperidine and by the solvent are very small compared to catalysis by hydroxide ion, eq. 5

$$\frac{1}{k_A} = \frac{k_{-1}}{k_1 k_2 + k_1 k_3^P[C_5H_{10}NH] + k_1 k_3^{OH}[OH^-]} + \frac{1}{k_1}$$

$$(5)$$

simplifies to eq. 6. A plot of $1/k_A$ vs. $1/[OH^-]$ should

(27) These statements imply that changing the leaving group does not change k_{-1}. That cannot be accepted as a general proposition, but is probably approximately true when all the leaving groups have the same first atom, *e.g.*, oxygen.

(28) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 345.

(29) M. L. Bender, *Chem. Rev.*, **60**, 74 (1960).

(30) Hydroxydephenoxylation forms 2,4-dinitrophenol which does not react with piperidine to form 2,4-dinitrophenylpiperidine under the conditions of our experiments.

(31) C. A. Bunton and V. J. Shiner, Jr., *J. Am. Chem. Soc.*, **83**, 3214 (1961); R. Wolfenden and W. P. Jencks, *ibid.*, **83**, 4390 (1961); M. L. Bender, E. J. Pollock, and M. C. Neveu, *ibid.*, **84**, 595 (1962); L. R. Fedor and T. C. Bruice, *ibid.*, **86**, 4117 (1964).

(32) E. A. Halevi, *Progr. Phys. Org. Chem.*, **1**, 180 (1963).

(33) M. F. Hawthorne, *J. Am. Chem. Soc.*, **76**, 6358 (1954); F. Pietra and A. Fava, *Tetrahedron Letters*, 1535 (1963). See also S. D. Ross, M. Finkelstein, and R. C. Petersen, *J. Am. Chem. Soc.*, **81**, 5336 (1959); C. Bernasconi and H. Zollinger, *Tetrahedron Letters*, 1083 (1965).

(34) F. Pietra, personal communication.

be linear, except where the conditions which allow simplification to eq. 6 are not fulfilled. Such a plot,

$$\frac{1}{k_A} = \frac{k_{-1}}{k_1 k_3^{OH}}\frac{1}{[OH^-]} + \frac{1}{k_1} \qquad (6)$$

based on data in Table I, part C1, is presented as Figure 8. It is satisfactorily linear. From the intercept and slope, one may evaluate k_1 and the ratio k_3^{OH}/k_{-1}. Then, from data at low hydroxide ion concentrations, one may reckon $(k_2 + k_3^P[C_5H_{10}NH])/k_{-1}$ by means of a rearranged form of eq. 5.

From data in Table II (the runs with $C_5H_{10}NH_2Cl$ present), one may construct a similar inversion plot. The plot obtained (not shown) is linear with respect to piperidine concentrations 0.05 to 0.15 M. In the manner described, one may estimate k_1, k_3^P/k_{-1} and $(k_2 + k_3^{OH}[OH^-])/k_{-1}$.

If our view of the reaction mechanism is correct, one should obtain the same value for k_1 from either set of data. The k_1 values obtained are 31.1 × 10⁻³ l. mole⁻¹ sec.⁻¹ from the data in Table I, part C1, and 25.4 × 10⁻³ l. mole⁻¹ sec.⁻¹ from the data in Table II. Considering that the latter value represents a rather long extrapolation, we regard the agreement between these two estimates of k_1 as fairly satisfactory.

This is an important result, for it represents fulfillment of another specific requirement of the mechanism presented in eq. 1. Certain alternative interpretations of the curvature in Figures 1, 4, and 6, which have been considered at length elsewhere[6,15] and which are improbable or untenable on other grounds, would not afford such a sameness of intercepts of inversion plots unless there were an extraordinary coincidence of unrelated phenomena.

Equation 5 may be rearranged to the form

$$\frac{k_A}{k_1 - k_A} = \frac{k_2}{k_{-1}} + \frac{k_3^P}{k_{-1}}[C_5H_{10}NH] + \frac{k_3^{OH}}{k_{-1}}[OH^-] \qquad (7)$$

In the runs (Table II) in 1 : 1 piperidine–piperidine hydrochloride buffers, [OH⁻] was essentially constant. Relevant to those runs, eq. 7 has but two unknowns, k_2/k_{-1} and k_3^P/k_{-1}. (k_3^{OH}/k_{-1} has already been determined (from Figure 8) to be 141 l. mole⁻¹.) It is suitable for determination of these unknowns graphically, $(k_A/(k_1 - k_A) - (k_3^{OH}/k_{-1})[OH^-])$ being plotted against $[C_5H_{10}NH]$, or by linear regression analysis. By the latter method, k_2/k_{-1} was reckoned to be 0.02 and k_3^P/k_{-1} to be 9.5 l. mole⁻¹.

Inversion plots were also constructed from the other data in Table I. In all cases these were useful for estimation of k_1 values, but only in the cases of 2,4-dinitroanisole and 2,4-dinitrophenyl phenyl ether were the data judged appropriate for reliable estimation of k_3^{OH}/k_{-1} and $(k_2 + k_3^P[C_5H_{10}NH])/k_{-1}$.

The k_1 values and rate coefficient ratios resulting from these analyses are assembled in Table VI. Also included are k_{OH} values, relating to the side reactions forming 2,4-dinitrophenol.

In surveying the dependence of k_1 and k_{OH} upon the leaving group, we first note that neither type of coefficient is much related to the proclivity of the group to separate heterolytically from carbon. Chlorine is probably the best leaving group among the six, but the chloro compound has nearly the lowest k_{OH} and only an intermediate k_1 value. This is further evidence that
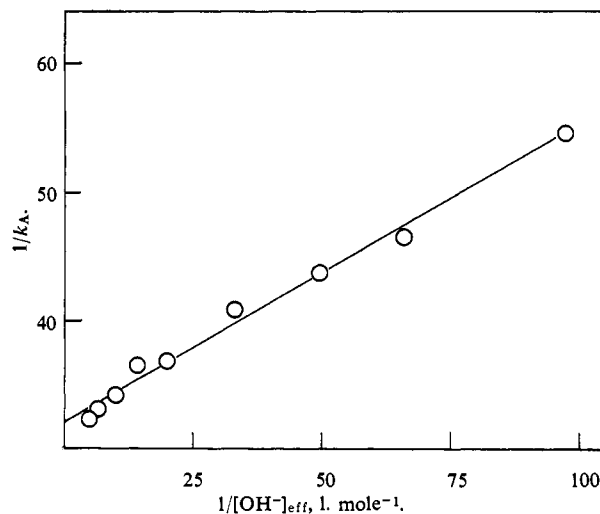

Figure 8. Reaction of 2,4-dinitrophenyl phenyl ether with piperidine, catalyzed by NaOH. "Inversion plot." Data from Table I, part C1.

these two rate coefficients are not concerned with breaking the bond between carbon and the leaving group. The hydroxide reactions occur by the intermediate complex mechanism with the first step rate determining.

Table VI. Reactions of 1-Substituted 2,4-Dinitrobenzenes with Piperidine and Sodium Hydroxide.[a] Dissection of Rate Coefficients

1-Substituent	10^3k_1, l. mole⁻¹ sec.⁻¹	$(k_2 + k_3^P \cdot [C_5H_{10}NH])/ k_{-1}$	k_3^{OH}/ k_{-1}, l. mole⁻¹	10^4k_{OH}, l. mole⁻¹ sec.⁻¹
Chlorine	75			3.17
2,4-Dinitrophenoxy	800[b]			58[b]
4-Nitrophenoxy	150			14.4
Phenoxy	31.1	0.070[c]	141	4.6
Methoxy	3.77	0.014[d]	26	8.2
Thiophenoxy	0.84			3.1

[a] Based on data in Tables I and V; all reactions in 10% dioxane–90% water at 29.4°. [b] Not statistically corrected; divide by two to get rate coefficient per dinitrophenyl group. [c] $[C_5H_{10}NH]$, 2.5 × 10⁻³ M. [d] $[C_5H_{10}NH]$, 5.0 × 10⁻² M.

The inductive effect or electronegativity of the group to be displaced has for some time been considered to be an important factor governing the rate of formation of the intermediate complex.[35,36] Suhr[37] in particular has presented this view forcefully. The electronegativities of the first atoms of the present leaving groups are: oxygen, 3.5; chlorine, 3.0; sulfur, 2.5. The present k_1 and k_{OH} bear some relationship to these electronegativities, though it is not a close correlation. Nitro substituents in a phenoxy group would of course increase the electronegativity of the bridging oxygen atom.

General Remarks. Several kinetic phenomena observed in this work are in full accord with the intermediate complex mechanism, as sketched in eq. 1. These include the incidence of base catalysis as related

(35) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 370.
(36) J. Sauer and R. Huisgen, *Angew. Chem.*, 72, 313 (1960).
(37) H. Suhr, *Chem. Ber.*, 97, 3268 (1964).

to leaving group characteristics, the curvilinear form of plots such as Figures 1, 4, and 6, the demonstration of general base catalysis, the sameness of the intercepts of inversion plots (cf. Figure 8) concerning catalysis by hydroxide ion and by piperidine, and the variation of solvent isotope effect with base concentration. Inasmuch as no conceivable alternative mechanism can accommodate these and other observations recorded in earlier papers, the evidence for this mechanism is compelling.

The Mechanism of Base Catalysis. We have not discussed the question of how a base catalyzes transformation of intermediate I into products. However, this question has been discussed in previous publications.[5,6,15,38] Of several alternative mechanisms which are formally compatible with the observed kinetics, we favor one which itself comprises two steps. In the first step, intermediate I reacts reversibly with base B, losing a proton to it and forming intermediate II as well as the conjugate acid of the base. In the second and rate-limiting step, the conjugate acid (HB) of the

base electrophically assists separation of leaving group X from intermediate II. If this mechanism prevails, each $k_3{}^B$ of eq. 2 represents the product $k'_B K'_B$, where K'_B is the equilibrium constant for reaction of I with base B to form II and HB, and k'_B is the rate coefficient for HB-catalyzed expulsion of leaving group X from II.
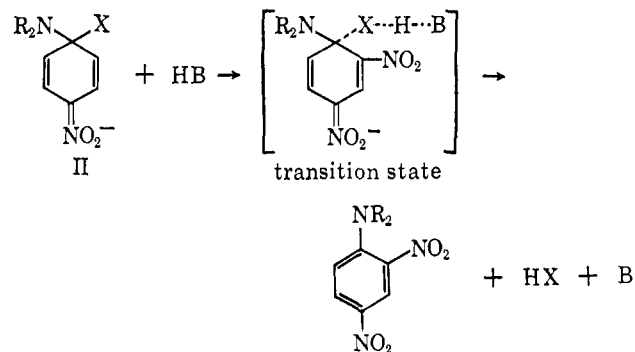
Acknowledgment. We thank Drs. H. Zollinger and R. H. Garst for their friendly interest in this work, and for discussions.

(38) J. F. Bunnett and G. T. Davis, *J. Am. Chem. Soc.*, 82, 665 (1960), footnote 26.

Photochemical Synthesis and Reactions of Carvonecamphor[1]

Jerrold Meinwald and Ronald A. Schneider[2]

Contribution from the Department of Chemistry, Cornell University, Ithaca, New York. Received July 30, 1965

The cyclization of carvone (1) to carvonecamphor (2) can be conveniently carried out using a black-light source. Continued irradiation of the carvonecamphor in alcohol or aqueous dioxane results in a photolytic cleavage, giving an ester (3 or 5) or the corresponding acid (4). Photolyses of α,α-dideuteriocarvonecamphor (11) and of carvonecamphor in dioxane–deuterium oxide support the mechanism established by Quinkert for other saturated ketone photolyses, a mechanism involving intramolecular hydrogen transfer in an intermediate diradical. When 2 is irradiated in benzene-t-butylamine containing oxygen, the expected unsaturated acid (19) and a rearranged unsaturated acid (20) are produced, accompanied by the ketene-derived amide (7). Catalytic reduction of the methyl ester of 19 gives 3 as a minor product, along with its C-5 epimer (22); chemical reduction gives chiefly 3, correlating the two types of photolysis products. The contrast between the solution photolysis of carvonecamphor and of camphor is rationalized by considering steric requirements.
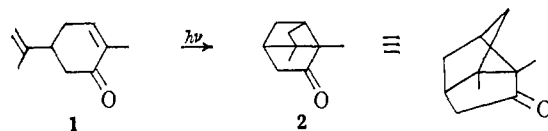
However, the analogous intramolecular photochemical cycloaddition between an isolated double bond and the double bond of an α,β-unsaturated ketone has been effected only in the case of the well-known cyclization of carvone (1) to carvonecamphor (2).[4,5] If this type

of intramolecular reaction were a general one, it would provide a convenient means of synthesizing various bi- and tricyclic small-ring molecules. As a preliminary to investigating such cycloadditions, we sought to maximize the yield of carvonecamphor, and to simplify its method of preparation. In the course of this investigation, a previously undescribed photolytic cleavage of carvonecamphor was discovered and investigated in detail.

Discussion

Carvonecamphor was characterized in 1957 by Büchi and Goldman,[5] who prepared it in 9% yield by irradiation of carvone in sunlight for 6 months, essentially the procedure of Ciamician and Silber.[4] Artifi-

Introduction

The intermolecular photochemical addition of olefins to α,β-unsaturated ketones has recently been shown to be a synthetic reaction of considerable usefulness.[3]

(3) See, for example: (a) P. E. Eaton, *J. Am. Chem. Soc.*, 84, 2454 (1962); (b) E. J. Corey, J. D. Bass, R. LeMahieu, and R. B. Mitra, *ibid.*, 86, 5570 (1964).
(4) G. Ciamician and P. Silber, *Chem. Ber.*, 41, 1928 (1908).
(5) G. Büchi and I. M. Goldman, *J. Am. Chem. Soc.*, 79, 4741 (1957).