d_6) δ 4.55 (s, 2 H), 7.28 (m, 10 H), 9.08 (s, 1 H), and 10.3 (s 1 H).

N-Phenyl-1,2-thiazetidin-3-one 1-Oxide (13).—In a reaction cell, 0.5 g (3.7×10^{-3} mol) of pure sulfinylaniline was dissolved in 25 ml of dry acetone. The mixture was cooled to −195° and the vessel was evacuated to a pressure of less than 10^{-3} mm on the vacuum system. Ketene was generated, collected, and purified as previously described. The pure ketene was distilled into the reaction cell. The temperature of the mixture was slowly raised to −78°. The solution was stirred at this temperature for 2 hr. During this period, the orange solution became colorless and a white solid formed. The reaction mixture was slowly warmed to room temperature. The solid decomposed with evolution of ketene. The acetone was evaporated under reduced pressure and the resulting oil was chromatographed on a dry column of silica gel with benzene. Only sulfinylaniline and polymeric materials were isolated.

Interception of N-Phenyl-1,2-thiazetidin-3-one 1-Oxide (13) with Aniline and p-Toluidine.—A sample of *N*-phenyl-1,2-thiazetidin-3-one 1-oxide (**13**) was prepared as described above. A solution of aniline (1.0 g) in 10 ml of dry acetone was cooled to −78° and then added slowly to the reaction mixture. The solution was allowed to stand at −78° overnight. It was then warmed to room temperature and the white solid was collected by filtration. The solid was recrystallized from methanol. The yield of 2-(phenylsulfinamoyl)acetanilide was 463 mg (45.8%): mp 172–173° dec (lit.[2] mp 167–168° dec); ir (KBr) 3280, 3250 (>NH), 1655 (>C=O), and 1062 cm^{-1} (>S=O); nmr (DMSO-d_6) δ 4.55 (s, 2 H), 7.28 (m, 10 H), 9.08 (s, 1 H), and 10.3 (s, 1 H).

A second sample of **13** prepared as described above was treated with a solution of *p*-toluidine (1.0 g) dissolved in 10 ml of dry acetone. The yield of 2-(phenylsulfinamoyl)-*p*-acetotoluidide (**14**) was 1.45 g (58.3%): mp 181–182° dec; ir (KBr) 3225, 3185 (>NH), 1650 (>C=O), and 1049 cm^{-1} (>S=O); nmr (DMSO-d_6) δ 2.27 (s, 3 H), 4.12 (s, 2 H), 7.25 (m, 9 H), 9.23 (s, 1 H), and 10.3 (s, 1 H).

Anal. Calcd for $C_{15}H_{16}N_2SO_2$: C, 62.48; H, 5.59; N, 9.71; S, 11.12. Found: C, 62.70; H, 5.82; N, 9.58; S, 11.05.

Reduction of 2-(Phenylsulfinamoyl)-p-acetotoluidide (14).—A solution of 70 mg (2.4×10^{-4} mol) of 14 dissolved in 30 ml of absolute ethanol was placed in a 50-ml, round-bottomed flask, fitted with a condenser. Raney nickel W-4 (500 mg) was added to the solution. The reaction mixture was heated under reflux overnight. The hot solution was filtered to remove the catalyst. The ethanol was evaporated under reduced pressure and the residue was chromatographed on a preparative alumina thin layer plate with ether. The major band (R_f 0.49) was isolated and the alumina was leached with acetone. The acetone was evaporated under reduced pressure and the resulting white solid was recrystallized from chloroform. The yield of *N*-(*p*-tolyl)-acetamide was 16 mg (44.5%): mp 155–156° (lit.[13] mp 155–156°); ir (KBr) 3215 (>NH) and 1660 cm^{-1} (>C=O); nmr (CDCl$_3$) δ 2.12 (s, 3 H), 2.30 (s, 3 H), 7.09 (d, 2 H, J = 8.0 Hz), 7.39 (d, 2 H, J = 8.0 Hz), and 8.05 (s, 1 H).

Registry No.—**1**, 32720-35-7; **2**, 32720-36-8; **3**, 40328-72-1; **4**, 40328-73-2; **5**, 40328-74-3; **6**, 40328-75-4; **7**, 40328-76-5; **8**, 1888-29-5; **9**, 40328-78-7; **10**, 40328-79-8; **11a**, 27393-94-8; **12**, 23990-58-1; **13**, 40328-82-3; **14**, 40328-83-4; ketene, 463-51-4; diphenylketene-*N*-(*p*-tolyl)imine, 5110-45-2; diphenylketene-*N*-(*p*-bromophenyl)imine, 29376-76-9; diphenylketene-*N*-(*p*-methylthiophenyl)imine, 40328-86-7; diphenylketene-*N*-(*p*-methylsulfonylphenyl)imine, 40328-87-8; diphenylketene-*N*-phenylimine, 14181-84-1; diphenylketene-*N*-*n*-butylimine, 21843-89-0; dimethylketene-*N*-phenylimine, 14016-34-3; isopropylketene-*N*-phenylimine, 34621-16-4; sulfur dioxide, 7446-09-5; *N*-(*p*-tolyl)diphenylacetamide, 4107-01-1; *N*-(*p*-tolyl)-α,α-diphenylacetoacetamide, 40328-93-6; 4,5-dimethyl-*o*-phenylenediamine, 3171-45-7; 3,6-dimethoxy-*o*-phenylenediamine, 40328-95-8; *N*-(*p*-tolyl)acetamide, 103-89-9.

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The Solvolysis of Pyridine Analogs of Cumyl Chloride. The Determination of the Brown Electrophilic Substituent Constants for Pyridine Derivatives[1a]

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Rates of solvolysis in 80% ethanol have been determined for 2-(2-pyridyl)-2-chloropropane, 2-(3-pyridyl)-2-chloropropane, and 2-(4-pyridyl)-2-chloropropane, and for 2-(2-pyridyl)-2-chloropropane *N*-oxide and 2-(4-pyridyl)-2-chloropropane *N*-oxide. From these rates and the rates of solvolysis of cumyl chlorides bearing electron-withdrawing substituents, σ^+ values appropriate for the replacement of the benzene ring by a pyridine moiety have been calculated.

There have been numerous studies in recent years aimed at relating pyridine derivatives to benzene derivatives. As a determination of the Hammett substituent constant, σ, appropriate for substitution of the aza =N for =CH in benzene by the primary defining reaction (ionization of an aromatic carboxylic acid) is fraught with some difficulty because of zwitterion formation, such σ values have generally been evaluated by secondary reactions. A summary by Blanch[2] evaluates a number of such reactions, and lists preferred σ values. A more recent study by Campbell, *et al.*,[3] derives similar though slightly modified values from ester saponification rates. Katritzky and Swinbourne[4] have derived substituent constants for the pyridine *N*-oxide moiety from spectroscopic studies. There has been less attention to determination of Brown's electrophilic substituent constants, σ^+.[5] An early study by Taylor[6] derives σ^+ values from the high-temperature pyrolysis of 1-(X-pyridyl)ethyl acetates. Extensive studies of the nitration, bromination, and hydrogen exchange reactions of pyridine derivatives

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[1] (a) Supported in part by a grant from the National Science Foundation, GP-6133X. (b) National Institutes of Health Predoctoral Fellow, 1970–1973, GM 49,154.

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[5] H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **80**, 4979 (1958).

[6] R. Taylor, *J. Chem. Soc.*, 4881 (1962).

by Katritzky, *et al.*,[7] have led to several derived σ^+ constants for pyridyl moieties.

In conjunction with studies from these laboratories of the transmission of substituent effects in heterocyclic systems,[8] we have had occasion to examine the solvolysis rates of some 2-(pyridyl)-2-chloropropanes. These reactions are easily followed kinetically at constant (and neutral) pH. This provides a much more direct measure of the Brown electrophilic substituent constants for these systems, as there is less need for the severe extrapolations which Katritzky found necessary, and there is no ambiguity about the nature of the species undergoing reaction; it is the neutral species. In order to assign σ^+ constants from these measured rates, it is necessary to determine the ρ value for the solvolysis reaction of the cumyl chlorides at 75°, and to have rates for appropriate cumyl chlorides in 80% ethanol. Okamoto, Inukai, and Brown[9] have reported extensive data for the solvolysis of cumyl chlorides at a number of temperatures. Extrapolating the data for deactivating substituents to 75° gives a ρ in 90% acetone of -4.00. They also report[9b] that ρ is relatively insensitive to the change of solvent to ethanol. However, calculation of expected rates in 80% ethanol by use of mY[10] correlations and the data of Okamoto, Inukai, and Brown[9] proved to be unsatisfactory. Both Fainberg and Winstein[11] and Swain, Mosely, and Bown[12] have noted that mY correlations involving α-phenylethyl chloride and benzhydryl chloride show much dispersion as between aqueous acetone and aqueous ethanol. Rates in aqueous acetone are invariably less than mY correlations predict.

In view of these considerations we have made rate measurements in 80% ethanol on a limited number of cumyl chlorides bearing electron-withdrawing substituents. These rate measurements are summarized in Table I. Rates for cumyl chlorides in 80% ethanol at 75° are satisfactorily predicted by eq 1.

$$\log k = -4.0\sigma^+ + 0.18 \qquad (1)$$

Measured rates for the pyridyl analogs of cumyl chlorides are given in Table II, and Table III summarizes σ^+ values, both as herein determined and related values from other studies.

Although it seemed likely that these were typical solvolytic reactions, we examined the plausible alternative that an intramolecularly assisted E2 pathway was involved in the reaction of 2-(2-pyridyl)-2-chloropropane (**1**). The rate of solvolysis of α-(2-pyridyl)benzyl chloride (**6**) (in which an elimination pathway is impossible) was measured. Compound **6** gave a rate of solvolysis quite comparable to that of **3**, Table IV. As Streitwieser[13] has pointed out, a phenyl group is roughly as effective as two methyl groups in stabilizing a carbonium ion. Additionally, 2-(2-pyridyl)-2-bromopropane (**7**) was solvolyzed, and its rate was 40 times that of compound **1**, again a typical result.[14] Incidentally, Olah and Calin[15] have demonstrated the formation of a number of substituted pyridinylcarbonium ions in superacid solutions, though the cation from 2-(2-pyridyl)-2-propanol was not observed owing to the rapidity of subsequent reactions.

TABLE I

RATES OF SOLVOLYSIS OF SUBSTITUTED *tert*-CUMYL CHLORIDES IN 80% ETHANOL AT VARIOUS TEMPERATURES

Registry no.	Compd	Temp, °C	k, sec^{-1}
14276-98-3	*p*-Br	0.0	$2.18 \pm 0.05 \times 10^{-4}$
		24.96	$4.71 \pm 0.04 \times 10^{-3}$
		75.00[a]	5.92×10^{-1}
40473-10-7	*m*-Cl	44.80	$2.43 \pm 0.02 \times 10^{-3}$
		60.09	$9.92 \pm 0.1 \times 10^{-3}$
		75.00	$3.51 \pm 0.05 \times 10^{-2}$
		75.00[b]	3.54×10^{-2}
2924-89-2	*p*-CF_3	75.0	$5.22 \pm 0.1 \times 10^{-3}$

[a] Extrapolated from rates at lower temperatures. [b] Extrapolated from rates at 45 and 60°.

TABLE II

RATES OF SOLVOLYSIS OF 2-HETEROARYL-2-CHLOROPROPANES IN 80% ETHANOL AT 75.0°

Compound solvolyzed	k, sec^{-1}	k_{rel}
2-(2-Pyridyl)-2-chloropropane (**1**)	1.51×10^{-3}	46.9
2-(3-Pyridyl)-2-chloropropane (**2**)	1.08×10^{-2}	335
2-(4-Pyridyl)-2-chloropropane (**3**)	3.22×10^{-5}	1.0
2-(2-Pyridyl)-2-chloropropane *N*-oxide (**4**)	2.85×10^{-3}	88
2-(4-Pyridyl)-2-chloropropane *N*-oxide (**5**)	2.31×10^{-2}	717

Experimental Section[16]

2-(2-Pyridyl)-2-chloropropane (1).—The preparation of 2-(2-pyridyl)-2-propanol followed the procedure of Emmert and Asendorf[17] incorporating modifications suggested by Bachman and Micucci,[18] mp 49–50° (lit.[18] mp 49–50°).

To a stirred solution of 2-(2-pyridyl)-2-propanol (3.0 g, 0.022 mol) in 100 ml of methylene chloride was added dropwise 5.0 g (0.042 mol) of thionyl chloride. The solution was stirred for 30 min and the methylene chloride and excess thionyl chloride were removed on a rotary evaporator. The oil was redissolved in 100 ml of methylene chloride, washed with aqueous sodium carbonate, and dried ($MgSO_4$). The methylene chloride was removed on a rotary evaporator. The nmr spectrum of the resulting oil showed it to be 50% 2-(2-pyridyl)-2-chloropropane and 50% 2-(2-pyridyl)propene. This mixture of chloride and olefin was used

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[7] (a) C. D. Johnson, A. R. Katritzky, B. J. Ridgewell, and M. Viney, *J. Chem. Soc. B*, 1204 (1967); (b) C. D. Johnson, A. R. Katrizky, N. Shakir, and M. Viney, *ibid.*, 1213 (1967); (c) G. P. Bean and A. R. Katritzky, *ibid.*, 864 (1968); (d) P. Bellingham, C. D. Johnson, and A. R. Katritzky, *ibid.*, 866 (1968); (e) P. J. Brignell, P. E. Jones, and A. R. Katritzky, *ibid.*, 117 (1970).

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[11] A. H. Fainberg and S. Winstein, *J. Amer. Chem. Soc.*, **79**, 1597 (1957).

[12] C. G. Swain, R. B. Mosely, and D. E. Bown, *J. Amer. Chem. Soc.*, **77**, 3731 (1955).

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[15] G. A. Olah and M. Calin, *J. Amer. Chem. Soc.*, **90**, 943 (1968).

[16] Melting points and boiling points are uncorrected. Nmr spectra were recorded using a Varian Associates Model T-60 spectrometer. Elemental analyses were carried out by the Chemical Analytical Services Laboratory, College of Chemistry, University of California, Berkeley, Calif.

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TABLE III

SUBSTITUENT CONSTANTS DETERMINED FOR AZA REPLACEMENT IN BENZENE DERIVATIVES, FOR PYRIDYL, PYRIDINIUM, AND PYRIDYL *N*-OXIDE GROUPS

	2-Py	3-Py	4-Py	2-Py$^+$	3-Py$^+$	4-Py$^+$	2-Py$_{NO}$	3-Py$_{NO}$	4-Py$_{NO}$	Ref
σ	0.71	0.55	0.94	3.11	2.10	2.57				2
σ	0.75	0.65	0.96							3
σ	1.0	0.6	0.8	2.2	1.9	1.3	(1.5)	0.7	0.4	4
σ^+	0.80	0.30	0.87							6
σ^+		0.63						0.8		*a*
σ^+	0.75	0.54	1.16				0.68		0.45	*b*

[a] References 7a, 7d, 7e. [b] This study.

TABLE IV

RATES OF SOLVOLYSIS OF SELECTED PYRIDYLALKYL HALIDES IN 80% ETHANOL

Compound solvolyzed	Temp, °C	*k*, sec^{-1}
1	45.0	$7.45 \pm 0.20 \times 10^{-5}$
	60.0	$3.74 \pm 0.04 \times 10^{-4}$
	75.0[a]	$1.51 \pm 0.03 \times 10^{-3}$
7	25.0	2.53×10^{-4}
	45.0	2.94×10^{-3}
6	45.0	9.80×10^{-5}
	60.0	5.80×10^{-4}
	75.0	1.94×10^{-3}

[a] From Table II.

directly for the kinetic measurements without further purification.

2-(4-Pyridyl)-2-chloropropane (3) and 2-(3-Pyridyl)-2-chloropropane (2).—Reaction of methylmagnesium bromide and methyl isonicotinate afforded 2-(4-pyridyl)-2-propanol, mp 133–134° (lit. mp 132°,[19] 136°[14]). Conversion to a mixture of the chloride, 2-(4-pyridyl)-2-chloropropane (3), and 2-(4-pyridyl)-propene was carried out as above. The nmr spectrum showed that the mixture contained 33% chloride and 67% olefin.

In an analogous fashion methyl nicotinate afforded 2-(3-pyridyl)-2-propanol.[20] Conversion to the chloride with thionyl chloride as above gave a mixture, which was shown by nmr to consist of 63% 2-(3-pyridyl)-2-chloropropane and 37% 2-(3-pyridyl)propene. The mixture of chloride and olefin was used without further purification for the kinetic measurements.

2-(2-Pyridyl)-2-propanol *N*-Oxide.—To a stirred solution of 10.0 g (0.073 mol) of 2-(2-pyridyl)-2-propanol in 20 ml of acetic acid, 30 ml of 40% peracetic acid was added dropwise. After the solution was stirred for 15 min at room temperature the mixture was heated at 45° for 20 hr and then at 75° for 5 hr. After cooling, the solution was poured over crushed ice and made alkaline with a concentrated aqueous solution of sodium hydroxide. The aqueous solution was extracted with 3 × 150 ml of methylene chloride. The combined extracts were dried ($MgSO_4$, plus a small amount of Na_2CO_3), filtered, and concentrated. The resulting colorless oil was shaken with 25 ml of mixed hexanes and the *N*-oxide was crystallized. There was isolated 7.6 g (68%) of 2-(2-pyridyl)-2-propanol *N*-oxide: mp 68–71°; ir (neat) 3400 (s), 1295 (m), 965 (m), 972 (m), and 783 cm^{-1} (s); nmr (CCl_4) δ 1.57 (s, 6), 7.33 (m, 4), and 8.10 (m, 1).

2-(2-Pyridyl)-2-chloropropane *N*-Oxide (4).—A solution of 2-(2-pyridyl)-2-propanol *N*-oxide (1.0 g, 0.007 mol) and phosphorus pentachloride (1.36 g, 0.007 mol) in 200 ml of methylene chloride was stirred for 5 days. The solution was concentrated on a rotary evaporator. The oil was redissolved in 100 ml of methylene chloride, and sodium carbonate and water were added to form a slurry. After stirring for 15 min the methylene chloride was dried ($MgSO_4$), filtered, and concentrated. The oil was dissolved in 100 ml of mixed hexanes and cooled in the refrigerator for 4 hr. The mixed hexanes solution was decanted from a small amount of residue and concentrated on a rotary evaporator to yield 0.80 g (67%) of 2-(2-pyridyl)-2-chloropropane *N*-oxide: nmr (CCl_4) δ 2.15 (s, 6), 7.34 (m, 2), 7.87 (m, 1) and 8.16 (m, 1).

Anal. Calcd for $C_8H_{10}ClNO$: C, 56.00; H, 5.83; N, 8.16; Cl, 20.69. Found: C, 56.20; H, 5.83; N, 8.29; Cl, 20.52.

2-(4-Pyridyl)-2-propanol *N*-Oxide.—A solution of 10.0 g (0.073 mol) of 2-(4-pyridyl)-2-propanol in 35 ml of 40% peracetic acid was heated at 75° for 12 hr. The reaction mixture was neutralized by dissolving the mixture in 300 ml of methylene chloride and adding water and sodium carbonate in small portions to form a slurry (note: the *N*-oxide is very soluble in water). After stirring for 1 hr, the methylene chloride was dried ($MgSO_4$), filtered, and concentrated to yield a white solid. The solid was washed with CCl_4 to yield 4.0 g (37%) of 2-(4-pyridyl)-2-propanol *N*-oxide: nmr (CCl_4) δ 1.55 (s, 6), 4.54 (broad s, 1), 7.40 (broad d, 2, J = 6.2 Hz), and 8.02 (broad s, 2, J = 6.2 Hz).

Anal. Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.25; N, 9.15. Found: C, 62.62; H, 7.12; N, 9.05.

2-(4-Pyridyl)-2-chloropropane *N*-Oxide (5).—A solution of 1.7 g (0.011 mol) of 2-(4-pyridyl)-2-propanol *N*-oxide and 2.31 g (0.011 mol) of phosphorus pentachloride in 100 ml of methylene chloride was stirred for 5 days. The methylene chloride was removed on a rotary evaporator. The oil was redissolved in 100 ml of methylene chloride, and sodium carbonate and water were added to form a slurry. After the mixture was stirred for 15 min the methylene chloride was dried ($MgSO_4$), filtered, and concentrated. The nmr spectrum of the red oil showed that the 2-(4-pyridyl)-2-chloropropane *N*-oxide was mixed with 2-(4-pyridyl)propene *N*-oxide. The nmr spectrum of the mixture (CCl_4) showed resonances at δ 1.96 (s), 7.42 (m), and 8.20 (m) for the chloride and resonances for the olefin at δ 2.13 (broad s, 3), 5.25 (broad s, 1), 5.53 (s, 1), 7.42 (m), and 8.20 (m).

The mixture was used for the kinetic measurements without further purification.

α-(2-Pyridyl)benzyl Chloride (6).—The procedure of Tilford, Shelton, and Van Campen,[21] which is a modification of that of Emmert and Asendorf,[17] was followed for the preparation of α-(2-pyridyl)benzyl alcohol, bp 120° (0.7 mm) [lit.[21] bp 127–129° (0.3 mm)], mp 70–72° (lit.[21] mp 76–78°).

Phosphorus pentachloride (3.4 g, 0.016 mol) was added in small portions to a stirred solution of α-(2-pyridyl)benzyl alcohol in 100 ml of methylene chloride. After the solution was stirred for 30 min, 300 ml of diethyl ether was added. The solution was extracted with 3 × 100 ml of aqueous sodium carbonate. The ether was dried over anhydrous magnesium sulfate and removed on a rotary evaporator. The residual oil was purified by chromatography on a silica gel column using initially 1 l. of mixed hexanes followed by 10% ether–90% hexane, which eluted 2.16 g (71%) of α-(2-pyridyl)benzyl chloride (6): ir (neat) 3010 (w), 1695 (m), 1430 (m), 748 (m), and 696 cm^{-1} (m); nmr (CCl_4) δ 6.06 (s, 1 H), 7.37 (m, 8 H), and 8.35 (m, 1 H).

Anal. Calcd for $C_{12}H_{10}NCl$: C, 70.78; H, 4.91. Found: C, 70.66; H, 5.16.

2-(2-Pyridyl)-2-bromopropane (7).—Bromine (1.3 ml, 0.025 mol) was added dropwise to a stirred solution of phosphorus tribromide (2.4 ml, 0.025 mol) in 300 ml of methylene chloride. The mixture was stirred for 5 min and 2-(2-pyridyl)-2-propanol (1.0 g, 0.0073 mol) was added dropwise. After the addition was complete, 20 ml of pyridine was added very cautiously owing to a very exothermic reaction. The solution was stirred for 2 days and the liquid was decanted from a trace of solid material into 500 ml of mixed hexanes. Anhydrous magnesium sulfate and

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[20] H. C. Brown and W. A. Murphey, *J. Amer. Chem. Soc.*, **73**, 3308 (1951).

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3 ml of water were added and the solution was stirred until it became clear (5 min). The solid was removed by filtration and the solvent was removed on a rotary evaporator to yield 0.65 g (45%) of 2-(2-pyridyl)-2-bromopropane (**7**): nmr (CCl_4) δ 2.16 (s, 6 H), 7.04 (m, 1 H), 7.60 (m, 2 H), and 8.38 (m, 1 H). Upon attempted distillation of the bromide, hydrogen bromide was eliminated; hence the crude bromide was used directly for the kinetic measurements.

Kinetic Measurements.—Rate measurements were made using a Radiometer automatic titration assembly as has been described previously[8d] at constant pH (apparent pH 7.5 in 80% ethanol).

Registry No.—**1**, 6581-08-4; **2**, 40472-84-2; **3**, 40473-14-1; **4**, 40473-15-2; **5**, 40473-16-3; **6**, 40473-17-4; **7**, 40473-18-5; 2-(2-pyridyl)-2-propanol, 37988-38-8; methylmagnesium bromide, 75-16-1; methyl isonicotinate, 2459-09-8; 2-(4-pyridyl)-2-propanol, 15031-78-4; methyl nicotinate, 93-60-7; 2-(3-pyridyl)-2-propanol, 15031-77-3; 2-(2-pyridyl)-2-propanol *N*-oxide, 40473-22-1; 2-(4-pyridyl)-2-propanol *N*-oxide, 40473-23-2; α-(2-pyridyl)benzyl alcohol, 14159-57-0; bromine, 7726-95-6.

Transmission of Substituent Effects in Heterocyclic Systems. The Solvolysis of Some Substituted Chloroalkylpyridines[1]

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The rates of solvolysis for a number of substituted 2-(pyridyl)-2-chloropropanes have been determined. It is shown that Brown's electrophilic substituent constants give a good representation of the relative reactivities for these compounds, when the substituents are in the 4 and 5 positions in the pyridine ring. The reactivities of 6-substituted pyridines are not satisfactorily correlated with σ^+ constants; it appears that a new set of constants is needed for this structural situation.

The applicability of the Hammett equation to a number of series of pyridine derivatives has been explored by several authors.[2-5] Jaffe and Doak[2] first pointed out that the original Hammett σ constants appropriately reproduce changes in dissociation constants for pyridines and pyridine oxides. Applicability to ester hydrolysis has also been examined more recently.[4] However, when the substituent is adjacent to the nitrogen (*e.g.*, 6-substituted pyridine derivatives), poor correlations result, both with respect to pK_a's[3,5] and with respect to rates of ester hydrolysis.[4]

There has been much less attention given to the application of Brown's electrophilic substituent constants to series of pyridine derivatives. Katritzky[6,7,8] and his coworkers have examined aromatic substitution reactions for a number of pyridine derivatives.

In conjunction with studies from these laboratories of the solvolysis reaction as a probe for the evaluation of the transmission of substituent effects in diverse heterocyclic systems, we have had occasion to determine the rates of solvolysis of a number of substituted pyridine derivatives. We wish to report those results here, and to examine the usefulness of σ^+ constants as applied to pyridine derivatives.

The solvolysis of 2-(2-pyridyl)-2-chloropropane (**1**) is conveniently followed at constant pH in 80% ethanol at somewhat elevated temperatures. Introduction of substituents in the 4 or the 5 position of the pyridine moiety results in sharply modified rates of solvolysis. For a set of such substituted pyridines, the rates which we have measured are recorded in Table I, part A. We compare these rates with the calculated rates, presuming that σ is −4.0, as determined by extrapolation of the data of Brown, *et al.*,[9,10] to 75° and by our independent measurements.[11]

Column 7 of Table I gives the difference between the calculated and the observed rates on this basis.

Likewise for 2-(3-pyridyl)-2-chloropropanes, similar comparative results for a smaller number of compounds are given in Table I, part B. The results for 4- and 5-substituted 2-(2-pyridyl)-2-chloropropanes, compounds **1**, **3**, **5**, **7**, **9**, **11**, and **13**, and for 5-substituted 2-(3-pyridyl)-2-chloropropanes, compounds **14**, **17**, and **19**, show satisfactory correlation with the σ^+ constants.

However, examination of the data for the 6-substituted compounds, compounds **23**, **25**, **27**, **29**, and **31** (Table I, part C), shows that there is little correspondence between the predicted and the observed rate of solvolysis. Each of these compounds shows a very markedly enhanced rate of solvolysis. The set of compounds which we had in hand are all substances where there may be substantial resonance donation to the pyridine nitrogen.

Such a result is perhaps not unexpected. Charton[3] has observed similar "abnormalities" in the pK_a's of pyridine derivatives. Deady, *et al.*,[4] observed that the rates of saponification for 6-substituted pyridine carboxylates deviated from the behavior predicted on the basis of Hammett substituent constants and, moreover, that the magnitude of the deviation was related to σ_{R^0}, *i.e.*, to the resonance capabilities of the substituent.

An alternative and very useful way of correlating

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