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

(1) Supported in part by a grant from the National Science Foundation, GP-6133X.

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TABLE I

RATES OF SOLVOLYSIS OF SUBSTITUTED 2-(PYRIDYL)-2-CHLOROPROPANES IN 80% ETHANOL

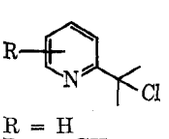
Substituent	Compd	Temp, °C	σ^+	k_1, sec^{-1}	Log k/k_H	Calcd Log k/k_H[a]	Δ log k[b]
			A. Substituted 2-Pyridyl Systems				
H	1	75.0	0.00	1.51×10^{-3} [c]	0.00	0.00	0.0
4-CH_3	3	60.0		6.22×10^{-4}			
		75.0	−0.066	2.52×10^{-3}	0.22	0.264	−0.04
5-CH_3	5	25.0		1.36×10^{-4}			
		45.0		1.30×10^{-3}			
		60.0		5.70×10^{-3}			
		75.0	−0.311	2.13×10^{-2}	1.15	1.24	−0.09
4-Cl	7	75.0	0.399	5.38×10^{-5} [d]	−1.45	−1.59	+0.14
5-Cl	9	45.0	0.114	7.04×10^{-5}			
		75.0		1.13×10^{-3}	−0.13	−0.45	+0.32
4-Cl, 5-OCH_3	11	25.0		7.53×10^{-4}			
		45.0		6.42×10^{-3}			
		60.0		2.63×10^{-2}			
		75.0	−0.379	9.80×10^{-2} [e]	1.81	1.51[f]	+0.31
5-OCH_3	13	0.12		5.30×10^{-3}			
		9.1		1.54×10^{-2}			
		25.0		8.7×10^{-2} [e]			
		75.0	−0.778	7.2×10^{-2} [e]	3.67 ± 0.3	3.11	0.5
			B. Substituted 3-Pyridyl Systems				
H	14	75.0		1.08×10^{-2} [c]	0.00	0.00	0.00
			0.00	1.04×10^{-2} [d]			
5-CH_3	17	25.0		1.20×10^{-4}			
		45.0		1.16×10^{-3}			
		60.0		5.15×10^{-3}			
		75.0	−0.066	1.80×10^{-2}	0.22	0.264	−0.04
5-Br	19	45.0		3.09×10^{-5}			
		75.0	0.405	6.47×10^{-4}	−1.22	−1.62	0.40
6-CH_3	21	25.0		1.38×10^{-3}			
		45.0		1.26×10^{-2}			
		75.0	−0.311	2.14×10^{-1} [e]	1.29	1.24	0.05
			C. 6-Substituted 2-Pyridyl Systems				
6-CH_3	23	45.0		3.77×10^{-4}			
		60.0		1.76×10^{-3}			
		75.0	−0.066	6.28×10^{-3}	0.62	0.264	0.36
6-OCH_3	25	25.0		1.15×10^{-4}			
		45.0		1.17×10^{-3}			
		75.0	0.047	1.52×10^{-2}	1.003	−0.19	−1.19
6-OC_2H_5	27	25.0		1.15×10^{-4}			
		45.0		1.09×10^{-3}			
		75.0		1.55×10^{-2}	1.01	−0.19	1.20
6-C_6H_5	29	75.0	0.109	2.54×10^{-3}	0.23	−0.44	0.67
6-Cl	31	75.0	0.399	2.14×10^{-4}	−0.85	−1.59	0.74

[a] Calculated using $\rho = -4.00$; *cf.* ref 11. [b] Column 5 − column 6. [c] From ref 11. [d] Not at constant pH; using ampoules. [e] Extrapolated from data at lower temperatures. [f] Assuming additivity of substituent constants.

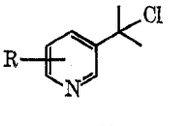
these results is with the $\mathcal{F}$ and $\mathcal{R}$ values for substituents, introduced by Swain and Lupton.[12] This approach quantifies the greater response of the methyl 6-X-picolinates to resonance than of the methyl 4-X-picolinates.

We have examined our data from this point of view (which is closely related, of course, to that used by Charton[13]) and note that our data imply a resonance component of nearly 60% $\mathcal{R}$ for what is formally a meta relationship between the reaction site and the substituent.

Though our data are of somewhat limited extent, they clearly show that a different defined substituent



1, R = H
3, R = 4-CH_3
5, R = 5-CH_3
7, R = 4-Cl
9, R = 5-Cl
11, R = 4-Cl, 5-OCH_3
13, R = 5-OCH_3
23, R = 6-CH_3
25, R = 6-OCH_3
27, R = 6-OEt
29, R = 6-C_6H_5
31, R = 6-Cl



14, R = H
17, R = 5-CH_3
19, R = 5-Br
21, R = 6-CH_3

constant other than σ_m, σ_p, σ_m^+, or σ_p^+ is needed for application to situations where the substituent is adjacent to the pyridine nitrogen. The Swain and

(12) C. G. Swain and E. C. Lupton, Jr., *J. Amer. Chem. Soc.*, **90**, 4328 (1968).

(13) Charton, ref 3, expresses the total substituent effect as $\sigma_T = \lambda\sigma_I + \delta\sigma_R$.

Lupton treatment offers a promising basis upon which to proceed; with the information we have in hand, there is sufficient information for making intelligent projections of solvolysis rates of 2-(2-X-4-pyridyl)-2-chloropropanes. These would be interesting to test.

Experimental Section[14]

Standard Procedures. A. Chloride Formation from Alcohol.—To a stirred solution of the alcohol in methylene chloride a slight excess of thionyl chloride was added dropwise. The solution was stirred for 30 min and the methylene chloride and excess thionyl chloride were removed with a rotary evaporator. The residue 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 solution was dried ($MgSO_4$), filtered, and concentrated. Owing to the instability of the chloride, the resulting oils were used in kinetic measurements without further purification. The contaminant in these oils was olefin, which does not affect the kinetic measurements. The relative concentrations of olefin and chloride were determined by comparison of proton areas of appropriate nmr spectra.

B. Alcohol Formation from Esters.[15]—The ester was added dropwise to a 2.5 *M* excess of methylmagnesium bromide in dry ether. The solution was stirred at room temperature overnight. Saturated ammonium chloride solution was added cautiously. The ether phase was separated and the saturated ammonium chloride solution was extracted with 3 × 200 ml of ether. The combined ether extracts were dried ($MgSO_4$), filtered, and concentrated to yield the desired product.

C. Alcohol Formation from Bromopyridines.—To a stirred solution of the bromopyridine in absolute ether under nitrogen in a Dry Ice–acetone bath was added dropwise a slight excess (*ca.* 5%) of *n*-butyllithium (1.6 *M* in hexane). After the addition was complete the solution was stirred for 15 min and acetone (2.5 *M* excess) was added. The mixture was allowed to warm to room temperature and 100 ml of water was added cautiously. The ether phase was separated, washed twice with 100 ml of water, dried ($MgSO_4$), filtered, and concentrated to yield the desired product.

2-(2-Pyridyl)-2-chloropropane (1) **and 2-(3-pyridyl)-2-chloropropane** (14) have been reported previously.[11]

2-(4-Methyl-2-pyridyl)-2-propanol (2).—The procedure of Emmert and Asendorf[11,16] was used with γ-picoline substituted for pyridine. After work-up in the usual manner, the combined ether extracts were dried ($MgSO_4$), concentrated, and distilled to yield 21% alcohol **2**: bp 65° (0.1 mm);[17] nmr (CCl_4) δ 1.45 (s, 6), 2.30 (s, 3), 4.87 (broad s, 1), 6.80 (d, 1, J = 5.0 Hz), 7.10 (s, 1), and 8.12 (d, 1, J = 5.0 Hz).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.66; N, 9.26. Found: C, 71.63; H, 8.74; N, 9.07.

2-(4-Methyl-2-pyridyl)-2-chloropropane (3).—Chloride **3** was synthesized by standard procedure A. The nmr spectrum of the red oil (2.8 g) showed it to be 50% **3** and 50% 2-(4-methyl-2-pyridyl)propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 1.92 (s), 2.21 (s), 6.85 (d), 7.21 (s), and 8.32 (m), The same spectrum showed resonances for the olefin at δ 2.21 (s), 2.32 (broad), 5.21 (broad, 1), 5.76 (broad, 1), 6.85 (d), 7.55 (s), and 8.32 (m).

2-(5-Methyl-2-pyridyl)-2-propanol (4).—2-Bromo-5-methylpyridine was prepared by the method of Case,[18] from 2-amino-5-methylpyridine in 85% yield, mp 49–50° (lit.[18] mp 49–50°). For the preparation of the alcohol 4, standard procedure C using 2-bromo-5-methylpyridine (17.29 g, 0.10 mol) was followed. Distillation afforded 7 g (47% yield) of alcohol **4** as a viscous, colorless oil: bp 58° (0.1 mm); nmr (CCl_4) δ 1.45 (s, 6), 2.12 (s, 3), 4.78 (s, 1), 7.24 (m, 2), and 8.13 (s, 1).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.66; N, 9.26. Found: C, 71.40; H, 8.90; N, 9.49.

Compound **4** has previously been reported as one component of the mixture resulting from the Emmert reaction on β-picoline.[16,17]

2-(5-Methyl-2-pyridyl)-2-chloropropane (5).—Chloride **5** was synthesized in the usual manner (procedure A). The nmr spectrum of the red oil (1.8 g) showed it to be 60% chloride **5** and 40% 2-(5-methyl-2-pyridyl)propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 1.83 (s), 2.20 (s), 7.30 (m), and 8.10 (broad s). The same spectrum showed resonances for the olefin at δ 2.12 (broad s, 3), 2.20 (s), 5.08 (m, 1), 5.63 (broad s, 1), 7.30 (m), and 8.10 (m).

2-(4-Chloro-2-pyridyl)-2-propanol (6).—Methyl 4-chloropicolinate, prepared by the method of Mosher and Look,[19] was treated with excess methylmagnesium bromide in ether (standard procedure B). Alcohol **6** was isolated in 80% yield: bp 73° (0.2 mm); nmr (CCl_4) δ 1.48 (s, 6), 4.54 (broad s, 1), 7.00 (2 d, 1, J = 2 and 5 Hz), 7.41 (d, 1, J = 2 Hz), and 8.22 (d, 1, J = 5 Hz).

Anal. Calcd for $C_8H_{10}ClNO$: C, 56.00; H, 5.87; N, 8.16; Cl, 20.66. Found: C, 56.03; H, 5.63; N, 8.19; Cl, 20.48.

2-(4-Chloro-2-pyridyl)-2-chloropropane (7).—The standard procedure was followed. The nmr spectrum of the red oil (1.5 g) showed it to be 40% chloride **7** and 60% 2-(4-chloro-2-pyridyl)-propene. The nmr spectrum (CCl_4) of the chloride showed resonances at δ 1.95 (s), 7.07 (m), 7.78 (d, J = 2 Hz), and 8.35 (m). The same spectrum showed resonances for the olefin at δ 2.18 (broad s, 3), 5.28 (broad s, 1), 5.85 (broad s, 1) 7.07 (m), 7.40 (d, J = 2 Hz), and 8.35 (m).

2-(5-Chloro-2-pyridyl)-2-propanol (8).—5-Amino-2-bromopyridine was converted to 2-bromo-5-chloropyridine,[20] mp 69–70° (lit.[21] mp 70–71°). Standard procedure C was followed to afford alcohol **8** in 38% yield: bp 78° (0.2 mm); nmr (CCl_4) δ 1.49 (s, 6), 4.32 (broad s, 1), 7.53 (m, 2), and 8.37 (broad s, 1).

Anal. Calcd for $C_8H_{10}ClNO$: C, 56.00; H, 5.87; N, 8.16; Cl, 20.66. Found: C, 56.22; H, 6.04; N, 7.97; Cl, 20.48.

2-(5-Chloro-2-pyridyl)-2-chloropropane (9).—Standard procedure A yielded 1.1 g of a red oil. The nmr spectrum showed it to be 40% chloride **9** and 60% 2-(5-chloro-2-pyridyl)propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 1.92 (s), 7.60 (m), and 8.42 (m). The same spectrum showed resonances for the olefin at δ 2.17 (broad s, 3), 5.28 (broad s, 1), 5.80 (broad s, 1), 7.60 (m), and 8.42 (m).

Ethyl 4-Chloro-5-methoxypicolinate.—2-Hydroxymethyl-5-methoxy-1,4-pyrone[22] was converted to 2-hydroxymethyl-5-methoxy-4-pyridone.[23] Oxidation to 5-methoxy-4-pyridone-2-carboxylic acid followed the procedure of Beyerman, mp 254–256° (lit.[24] mp 251–253°). Thence treatment with thionyl chloride, followed by ethanol, afforded ethyl 4-chloro-5-methoxypicolinate, mp 147–148° (lit.[24] mp 145–146°).

2-(4-Chloro-5-methoxy-2-pyridyl)-2-propanol (10).—Alcohol **10** was synthesized by procedure B using 7.8 g of ethyl 4-chloro-5-methoxypicolinate. The thick yellow oil was distilled to yield 4.7 g (64%) of alcohol **10**: bp 90° (0.1 mm); mp 71.0–72.5°; nmr (CCl_4) δ 1.45 (s, 6), 3.91 (s, 3), 4.13 (broad s, 1), 7.35 (s, 1), and 7.99 (s, 1).

Anal. Calcd for $C_9H_{12}ClNO_2$: C, 53.59; H, 6.00; N, 6.94; Cl, 17.60. Found: C, 53.79; H, 6.12; N, 6.74; Cl, 17.35.

2-(4-Chloro-5-methoxy-2-pyridyl)-2-chloropropane (11).—Alcohol **10** was converted to chloride **11** by procedure A. The nmr spectrum of the red oil (1.7 g) showed it to be 78% chloride **11** and 22% 2-(4-chloro-5-methoxy-2-pyridyl)propene. The nmr spectrum of the chloride showed resonances at δ 1.93 (s), 3.95 (s), 7.85 (s), and 8.02 (s). The same spectrum showed resonances for the olefin at δ 2.16 (broad s, 3), 3.95 (s), 5.16 (broad s, 1), 5.62 (broad s, 1), 7.85 (s), and 8.05 (s).

Ethyl 5-Methoxypicolinate.—Ethyl 4-chloro-5-methoxypicolinate (15.0 g, 0.067 mol) was added to 9.0 g of zinc dust suspended in 75 ml of glacial acetic acid. After a short induction period a vigorous reaction began and the solution was stirred for 1 hr. The solution was heated in an oil bath at 90° for an additional 1 hr. After the mixture cooled to room temperature, the glacial acetic acid was decanted from excess zinc dust onto approximately 200 g of ice. The solution was neutralized with con-

(14) Elemental analyses were determined by the Chemical Analytical Services Laboratory, College of Chemistry, Berkeley, Calif. Melting points and boiling points are uncorrected. Routine infrared spectra were recorded using a Perkin-Elmer Infracord Model 137. Nmr spectra were obtained using a Varian Associates Model T-60 spectrometer.

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(16) E. Emmert and E. Asendorf, *Ber.*, **72**, 1188 (1939).

(17) Lochte, Kruse, and Wheeler report bp 119–121° (23 mm): H. L. Lochte, P. F. Kruse, Jr., and E. N. Wheeler, *J. Amer. Chem. Soc.*, **75**, 4477 (1953).

(18) F. N. Case, *J. Amer. Chem. Soc.*, **68**, 2574 (1946).

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(20) L. C. Craig, *J. Amer. Chem. Soc.*, **56**, 232 (1934).

(21) F. H. Case, *J. Amer. Chem. Soc.*, **68**, 2574 (1946).

(22) K. N. Campbell, J. E. Ackerman, and B. K. Campbell, *J. Org. Chem.*, **15**, 221 (1950).

(23) J. W. Armit and T. J. Nolan, *J. Chem. Soc.*, 3023 (1931).

(24) H. C. Beyerman, *Recl. Trav. Chim. Pays-Bas*, **77**, 249 (1958).

centrated ammonium hydroxide and extracted with 3 × 200 ml of diethyl ether. The combined extracts were dried ($MgSO_4$), filtered, concentrated, and distilled to yield 7.0 g (58%) of ethyl 5-methoxypicolinate: bp 90° (0.3 mm); nmr (CCl_4) δ 1.57 (t, 3), 3.85 (s, 3), 4.30 (q, 2), 7.10 (2 d, 1, J = 10.0 and 2.8 Hz), 7.85 (d, 1, J = 10.0 Hz), and 8.17 (d, 1, J = 2.8 Hz).

2-(5-Methoxy-2-pyridyl)-2-propanol (12).—Ethyl 5-methoxypicolinate (7.0 g, 0.0387 mol) was converted to alcohol **12** by procedure B. The thick yellow oil was distilled to yield 2.2 g (34%) of alcohol **12**: nmr (CCl_4) δ 1.47 (s, 6), 3.75 (s, 3), 4.65 (broad s, 1), 7.23 (m, 2), and 8.10 (d, 1, J = 3 Hz).

Anal. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.83; N, 8.37. Found: C, 64.81; H, 7.60; N, 8.50.

2-(5-Methoxy-2-pyridyl)-2-chloropropane (13).—Alcohol **12** was converted to chloride **13** by procedure A. The nmr spectrum of the red oil (86% yield) showed it to be nearly 100% chloride **13** with only a trace of 2-(5-methoxy-2-pyridyl)propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 1.96 (s, 6), 3.76 (s, 3), 7.03 (2 d, 1, J = 3 and 8.5 Hz), 7.60 (d, 1, J = 8.5 Hz), and 8.08 (d, 1, J = 3 Hz).

Ethyl 5-Methylnicotinate (15).—3,5-Lutidine was oxidized to 5-methylnicotinic acid with potassium permaganate.[25] The isolated 5-methylnicotinic acid hydrochloride was directly esterified with ethanol to give **15** in 25% overall yield: bp 76° (0.7 mm); nmr (CCl_4) δ 1.33 (t, 3), 2.28 (s, 3), 4.24 (q, 2) 7.87 (broad s, 1), 8.43 (broad s, 1), and 8.85 (broad s, 1).

2-(5-Methyl-3-pyridyl)-2-propanol (16).—Ester **15** (13.8 g, 0.0838 mol) was converted to alcohol **16** by procedure B. The thick yellow oil was distilled to yield 9.4 g (74%) of alcohol **16**: bp 100° (0.7 mm); nmr (CCl_3) δ 1.50 (s, 6), 2.40 (s, 3), (broad s, 1), 7.55 (broad s, 1), 7.96 (broad s, 1), and 8.24 (broad s, 1).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.66; N, 9.26. Found: C, 71.47; H, 8.45; N, 9.43.

2-(5-Methyl-3-pyridyl)-2-chloropropane (17).—Procedure A was used to yield 1.5 g of a red oil. The nmr spectrum showed it to be 60% chloride **17** and 40% 2-(5-methyl-3-pyridyl)propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 2.00 (s, 6), 2.32 (s), 7.63 (broad s, 1), 8.28 (broad s, 1), and 8.58 (d, 1, J = 2.4 Hz). The same spectrum showed resonances for the olefin at δ 2.15 (broad s, 3), 2.32 (s), 5.12 (broad s, 1), 5.38 (broad s, 1), 8.28 (broad s, 1), and 8.47 (d, 1, J = 3 Hz).

2-(5-Bromo-3-pyridyl)-2-propanol (18).—Ethyl 5-bromonicotinate was prepared form nicotinic acid by the procedure of Bachman and Micucci,[15] and converted to alcohol **18**: bp 110° (0.3 mm) [lit.[15] bp 135–140° (3 mm)]. The nmr spectrum was appropriate for this structure.

2-(5-Bromo-3-pyridyl)-2-chloropropane (19).—Standard procedure A was used. The nmr spectrum of the red oil (1.5 g) showed it to be a mixture of 37% chloride **19** and 63% 2-(5-bromo-3-pyridyl)propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 1.95 (s), 7.92 (m), and 8.50 (m). The same spectrum showed resonances for the olefin at δ 2.15 (broad s, 3), 5.17 (broad s, 1), 5.41 (broad s, 1), 7.78 (m), and 8.50 (m).

2-(6-Methyl-3-pyridyl)-2-propanol (20).—The preparation of ethyl 6-methylnicotinate followed the procedure of Graf[25] involving the oxidation of 5-ethyl-2-methylpyridine and the direct esterification of the crude 6-methylnicotinic acid. Ethyl 6-methylnicotinate was converted to alcohol **20** by procedure B. The thick yellow oil was distilled to yield alcohol **20** in 76% yield: bp 93° (0.5 mm);[26] nmr (CCl_4) δ 1.38 (s, 6), 2.26 (s, 3), 5.16 (very broad s, 1), 6.82 (d, 1, J = 9 Hz), 7.58 (2 d, 1, J = 9 and 1.8 Hz), and 8.20 (broad s, 1).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.66; N, 9.26. Found: C, 71.56; H, 8.66; N, 9.26.

2-(6-Methyl-3-pyridyl)-2-chloropropane (21).—Standard procedure A was used. The nmr spectrum of the red oil (2.9 g) showed it to be 55% chloride **21** and 45% 2-(6-methyl-3-pyridyl)-propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 1.91 (s, 6), 2.45 (s), 7.00 (broad s, 1), 7.61 (m), and 8.59 (d, 1, J = 2.6 Hz). The same spectrum showed resonances for the olefin at δ 2.11 (broad s, 3), 2.45 (s), 4.98 (broad s, 1), 5.23 (broad s, 1), 6.83 (broad s, 1), 7.61 (m), and 8.43 (d, 1, J = 2.0 Hz).

2-(6-Methyl-2-pyridyl)-2-propanol (22) was prepared by the procedure of Emmert and Asendorf,[16] nmr (CCl_4) δ 1.43 (s, 6), 2.49 (s, 3), 4.84 (broad s, 1), and 7.20 (m, 3).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.66; N, 9.26. Found: C, 71.72; H, 8.80; N, 9.41.

2-(6-Methyl-2-pyridyl)-2-chloropropane (23).—Standard procedure A was used. The nmr spectrum of the crude product showed it to be 50% chloride **23** and 50% 2-(6-methyl 2-pyridyl)-propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 1.88 (s), 2.40 (s), 6.75 (m), and 7.24 (m). The same spectrum showed resonances for the olefin at δ 2.09 (broad s, 3), 2.40 (s), 5.03 (broad s, 1), 5.61 (broad s, 1), 6.75 (m), and 7.24 (m).

2-Bromo-6-methoxypyridine.—The method of Den Hertog and Wibaut[27] was used with methanol substituted for ethanol. The reaction yielded a mixture containing 20% 2,6-dimethoxypyridine and 80% 2-bromo-6-methoxypyridine. Separation by distillation was incomplete; hence, the mixture was used directly for the following reaction with *n*-butyllithium, as the 2-(6-methoxy-2-pyridyl)-2-propanol and 2,6-dimethoxypyridine were found easier to separate.

2-(6-Methoxy-2-pyridyl)-2-propanol (24).—The mixture above was used in procedure C. From 13.9 g of crude 2-bromo-6-methoxypyridine, containing about 2.1 g of 2,6-dimethoxypyridine, there was obtained 6.1 g (49%) of alcohol **24**: bp 95° (0.5 mm); nmr (CCl_4) δ 1.55 (s, 6), 3.90 (s, 3), 4.33 (s, 1), 6.50 (d, 1, J = 8 Hz), 6.95 (d, 1, J = 8 Hz), and 7.43 (t, 1, J = 8 Hz).

Anal. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.37. Found: C, 64.75; H, 7.68; N, 8.62.

2-(6-Methoxy-2-pyridyl)-2-chloropropane (25).—Alcohol **24** was converted to chloride **25** by procedure A. The nmr spectrum of the red oil (2.0 g) showed it to be 48% chloride **25** and 52% 2-(6-methoxy-2-pyridyl)propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 1.90 (s), 3.87 (s), 6.55 (d), 7.23 (m), and 7.40 (m). The same spectrum showed resonances for the olefin at δ 2.15 (broad s, 3), 5.18 (broad s, 1), 4.87 (broad s, 1), 6.55 (d), 6.95 (m), and 7.40 (m).

2-(6-Ethoxy-2-pyridyl)-2-propanol (26).—2-Bromo-6-ethoxypyridine[27] (7.0 g, 0.347 mol) was converted to alcohol **26** by procedure C. The colorless oil was distilled to yield 3.0 g (48%) of alcohol **26**: bp 72° (0.2 mm); nmr (CCl_4) δ 1.31 (t, 3), 1.39 (s, 6), 4.18 (broad s, 1 H), 4.28 (q, 2), 6.40 (d, 1, J = 8 Hz), 6.83 (d, 1, J = 8 Hz), and 7.40 (t, 1, J = 8 Hz).

Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.28; H, 8.33; N, 7.73. Found: C, 66.53; H, 8.43; N, 7.95.

2-(6-Ethoxy-2-pyridyl)-2-chloropropane (27).—Chloride **27** was synthesized by procedure A. The nmr spectrum of the red oil (2.0 g) showed it to be 40% chloride **27** and 60% 2-(6-ethoxy-2-pyridyl)propene. The nmr spectrum of the chloride (CCl_4) showed resonances at δ 1.34 (t), 1.90 (s), 4.32 (q), 6.44 (d), 6.82 (m), and 7.32 (m). The same spectrum showed resonances for the olefin at δ 1.34 (t), 2.13 (broad s, 3), 4.32 (q), 5.10 (broad s, 1), 5.82 (broad s, 1), 6.44 (d), 6.82 (m), and 7.32 (m).

2-(6-Phenyl-2-pyridyl)-2-propanol (28).—The procedure of Case and Kasper[28] was followed for the preparation of 2-bromo-6-phenylpyridine. Reaction with butyllithium followed by treatment with acetone afforded crude **28** as a pale yellow oil, bp 98–139° (0.2 mm). The nmr showed an excess of aromatic protons and the oil was chromatographed on a silica gel column using mixed hexanes followed by a 2% solution of ether–mixed hexanes which eluted 4.3 g (49%) of alcohol **28**: nmr (CCl_4) δ 1.51 (s, 6), 5.83 (s, 1), 7.30 (m, 6), and 8.85 (m, 2).

Anal. Calcd for $C_{14}H_{15}NO$: C, 78.85; H, 7.08; N, 6.57. Found: C, 78.67; H, 7.05; N, 6.56.

2-(6-Phenyl-2-pyridyl)-2-chloropropane (29.)—Standard procedure A was used. A nmr spectrum of the red oil showed it to be a mixture of 37% chloride **29**, 52% 2-(6-phenyl-2-pyridyl)-propene, and 11% of the initial 2-(6-phenyl-2-pyridyl)-2-propanol (**28**). The nmr spectrum of the chloride (CCl_4) showed resonances at δ 2.00 (s), 7.30 (m), and 7.95 (m). The same spectrum showed resonances for the olefin at δ 2.24 (broad s, 3), 5.23 (broad s, 1), 5.87 (broad s, 1), 7.30 (m), and 7.95 (m).

2-(6-Chloro-2-pyridyl)-2-propanol (30).—Methyl 6-chloropicolinate, mp 95–96° (lit.[29] mp 96–97°), was prepared by the

(25) R. Graf, *J. Prakt. Chem.*, **133**, 19 (1932).

(26) Oparina reports mp 61–62° for alcohol **20**: M. P. Oparina, *J. Russ. Phys. Chem. Soc.*, **61**, 2011 (1929); *Chem. Abstr.*, **24**, 4785 (1930).

(27) H. J. Den Hertog and J. P. Wibaut, *Recl. Trav, Chim. Pays-Bas*, **52**, 126 (1933).

(28) F. H. Case and T. J. Kasper, *J. Amer. Chem. Soc.*, **78**, 5842 (1956).

(29) M. P. Cava and N. K. Bhattacharya, *J. Org. Chem.*, **23**, 1287 (1958).

method of Cava and Bhattacharya,[29] involving diazotization (HCl) of 6-amino-2-methylpyridine, permanganate oxidation to 6-chloropicolinic acid, and esterification. The ester was treated with methylmagnesium bromide to afford **30** in 85% yield: bp 82–84° (2 mm); nmr (CCl_4) δ 1.52 (s, 6), 4.07 (s, 1), and 7.40 (m, 3).

Anal. Calcd for $C_8H_{10}ClNO$: C, 56.00; H, 5.87; N, 8.16; Cl, 20.66. Found: C, 55.89; H, 5.87; N, 7.94; Cl, 20.80.

2-(6-Chloro-2-pyridyl)-2-chloropropane (31).—Chloride **31** was synthesized by procedure A. The nmr spectrum of the red oil (2.5 g) showed it to be 30% chloride **31** and 70% 2-(6-chloro-2-pyridyl)propene. The nmr spectrum (CCl_4) showed resonances at δ 1.91 (s) and 8.31 (m). The same spectrum showed resonances for the olefin at δ 2.15 (broad s, 3 H), 5.21 (broad s, 1 H), 5.81 (broad s, 1 H), and 8.31 (m).

Kinetic Procedures.—Kinetic procedures have been reported previously.[11,30]

Registry No.—**1**, 6581-08-4; **2**, 40472-49-9; **3**, 40472-50-2; **4**, 40472-51-3; **5**, 40472-75-1; **6**, 40472-76-2; **7**, 40472-77-3; **8**, 40472-78-4; **9**, 40472-79-5; **10**, 40472-80-8; **11**, 40472-81-9; **12**, 40472-82-0; **13**, 40472-83-1; **14**, 40472-84-2; **15**, 20826-02-2; **16**, 40472-86-4; **17**, 40472-87-5; **18**, 40472-88-6; **19**, 40472-89-7; **20**, 40472-90-0; **21**, 40472-91-1; **22**, 40472-92-2; **23**, 40472-93-3; **24**, 40472-94-4; **25**, 40521-10-6; **26**, 40521-11-7; **27**, 40521-12-8; **28**, 40472-95-5; **29**, 40472-96-6; **30**, 40472-97-7; **31**, 40472-98-8; 2-bromo-5-methylpyridine, 3510-66-5; methyl 4-chloropicolinate, 24484-93-3; 2-bromo-5-chloropyridine, 40473-01-6; ethyl 4-chloro-5-methoxypicolinate, 40473-02-7; ethyl 5-methoxypicolinate, 40473-03-8; 5-methylnicotinic acid hydrochloride, 40473-04-9; ethyl 5-bromonicotinate, 20986-40-7; ethyl 6-methylnicotinate, 21684-59-3; 2-bromo-6-methoxypyridine, 40473-07-2; 2-bromo-6-ethoxypyridine, 4645-11-8.

(30) D. S. Noyce and R. W. Nichols, *J. Org. Chem.*, **37**, 4306 (1972).

CNDO–MO Exploration of Concerted and Stepwise Pathways for the Wittig and Peterson Olefination Reactions

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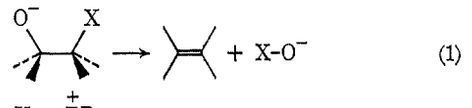
The decomposition of species of the type $XCH_2CH_2O^-$ to XO^- and $CH_2{=}CH_2$ was investigated with the aid of CNINDO calculations for the cases where X is H_3P^+– (Wittig reaction) and H_3Si– (Peterson reaction). Four-center intermediates **2a** (dihydrooxaphosphetane) and **2b** (dihydrooxasiletanide anion) were assumed and energies calculated for these and for the family of structures resulting from cleavage of the C–O and C–X bonds simultaneously (concerted fragmentation) or in separate stages (nonconcerted fragmentation). The calculations indicate that the energy surfaces are sharply skewed with C–X cleavage more advanced than C–O cleavage with the degree of skewing much greater for the Peterson reaction than for the Wittig reaction. The amount of stabilization of **2a** relative to its betaine precursor **1a** is calculated to be greater than that of **2b** relative to its precursor **1b** and it was concluded that dihydrooxaphosphetane **2a** is probably a true intermediate in the Wittig reaction but that dihydrooxasiletanide **2b** may be bypassed in the Peterson process with **1b** going directly to $H_3SiOCH_2CH_2^-$ (**3b**). Examples are given where theory and experiment are in harmony.

Four-center reactions involving intramolecular nucleophilic attack by alkoxide oxygen on a second-row element as a key step are common and provide the basis for a number of mechanistically interesting and synthetically useful olefin syntheses given in general terms by eq 1.



(1)

1a, X = $-\overset{+}{P}R_3$
b, X = $-SiR_3$
c, X = $-S(O)R$

The best known and most widely studied examples of these processes utilize phosphorus as the electrophilic center and include the Wittig reaction and its many modifications.[1] Less well known, but becoming increasingly useful for the synthesis of heteroatom-substituted olefins especially, are the base-catalyzed decomposition reactions of β-hydroxysilanes (the Peterson reaction).[2] In both the silicon and phosphorus cases decomposition of **1** (referred to as the "betaine" intermediate for **1a**) occurs under extremely mild conditions with the thermodynamic driving force being derived, in large part, from the formation of strong phosphorus–oxygen or silicon–oxygen bonds. The decomposition of β-hydroxy sulfoxides has also been observed[3,4] and a method developed for olefin synthesis employing thermal decomposition of β-hydroxy sulfinamides in benzene or toluene at 80–110°.[5] For each of these fragmentations a syn elimination is conceptually the most attractive and is supported by experiment in those cases which have been studied with respect to stereochemistry.[5,6]

An important question regarding the elimination pathways available to **1a–c** remains unanswered despite the number of studies, both synthetic and mechanistic, of the Wittig and related reactions. That question is concerned with whether thermal uncatalyzed decomposition of **1** is concerted or is rather a multistep process proceeding *via* initial formation of a four-membered ring intermediate. Further, if a four-membered ring species is an intermediate, does it

(1) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Inc., Menlo Park, Calif., 1972, pp 682–709, and references cited therein.

(2) (a) D. J. Peterson, *J. Org. Chem.*, **33**, 780 (1968); (b) T. H. Chan, E. Chang, and E. Vinokur, *Tetrahedron Lett.*, 1137 (1970); (c) F. A. Carey and A. S. Court, *J. Org. Chem.*, **37**, 939, 1926 (1972), and references cited therein.

(3) (a) C. Walling and L. Bollyky, *ibid.*, **28**, 256 (1963); (b) E. J. Corey and M. Chaykovsky, *ibid.*, **28**, 254 (1963).

(4) For an analogous process see T. J. Wallace, *ibid.*, **30**, 4016 (1965).

(5) (a) E. J. Corey and T. Durst, *J. Amer. Chem. Soc.*, **90**, 5548, 5553 (1968); (b) T. Durst, *Quart. Rep. Sulfur Chem.*, **3**, 113 (1968).

(6) E. Vedejs and P. L. Fuchs, *J. Amer. Chem. Soc.*, **93**, 4070 (1971).