p-nitrobenzoate ester and dissolving the ester in 80 ml of absolute ethanol. For the faster runs this ethanol solution was thermostated in a volumetric flask in the temperature bath. To the thermostated solution was added 20 ml of distilled water at temperature, and, after temperature equilibration, aliquots were removed for titration. For the slower runs requiring higher temperatures, a sealed ampoule technique was used.

The aliquots from the kinetic runs were quenched in absolute ethanol and the liberated *p*-nitrobenzoic acid was titrated with *ca.* 0.0075 *M* potassium hydroxide in absolute ethanol on a Metrohm Potentiograph E336-A automatic recording titrator using the first derivative curve.

The solvolysis of 1-(5-methoxy-2-thienyl)ethyl *p*-nitrobenzoate at 13.5° was too rapid to be followed by the titration procedure. Instead an ultraviolet spectrophotometric procedure was used. The ultraviolet spectrum of the ester changed in a first-order manner to that of the reaction products if a slight amount of sodium bicarbonate was present to keep the liberated *p*-nitrobenzoic acid as the anion. A Gilford Model 2000 automatic recording spectrophotometer was used to follow the progress of the reaction. Rates were determined by both the ultraviolet spectrophotometric and titrimetric techniques for the 5-methyl and 5-phenyl compound under conditions which gave half-lives of 0.5 hr or less. The agreement in rates was quite satisfactory.

The rate of solvolysis of 1-(5-methoxy-2-thienyl)ethyl *p*-nitrobenzoate at 0.00° was slow enough to be followed by a titrimetric procedure. About 0.3 g of the ester was dissolved in 0.5 ml of dioxane. The dioxane solution was injected into 25 ml of 80% ethanol equilibrated at 0.00°. The solution was titrated with 0.66 *N* potassium hydroxide in 80% ethanol with a Radiometer SBR2 Titrigraph. The pH was kept constant at 7.6.

Measured rate constants are recorded in Table VI.

Registry No.—2-Acetyl-5-ethoxycarbonylthiophene, 33148-82-2.

Transmission of Substituent Effects in Heterocyclic Systems. The Solvolysis of Substituted 3-Furyl Derivatives[1]

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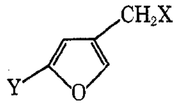
The rate of solvolysis of 2-(5-methyl-3-furyl)-2-propyl *p*-nitrobenzoate is substantially larger than the solvolysis rate for 2-(3-furyl)-2-propyl *p*-nitrobenzoate in 80% ethanol. The correlation of solvolysis rates for other 3-furyl systems is not satisfactory using pseudo meta relationships. However, generally useful and satisfactory correlations are obtained from consideration of CNDO/2 and INDO molecular orbital parameters for these systems. These parameters also provide an excellent basis foı additional predictions.

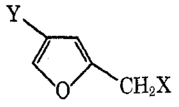
In a previous paper it has been shown that the solvolysis rates of a number of 5-substituted 1-(2-furyl)-ethanol derivatives are satisfactorily correlated by the Hammett relationship, using Brown's $\sigma_p{}^+$ substituent constants.[3] Notable was the high sensitivity of the furan ring to the electronic effect of the substituent in such a correlation, with ρ being -8. These observations were largely limited to 5-substituted 2-furyl systems, because of the generally difficult accessibility of β-substituted furans. The 5-Y-2-furyl relationship may be thought of as a normally "conjugating" relationship as exemplified by consideration of valence bond resonance structures.

It was of interest to extend these observations on the mode of transmission of substituent effects to "nonconjugating" relationships in the furan system. Such systems, A and B, pose some problems in synthesis; as a consequence, we have therefore obtained a somewhat limited amount of information. Nonetheless, the pattern which emerges is quite clear, and points to some particularly interesting general conclusions.

Yur'ev, Gal'bershtam, *et al.*,[4,5] have reported that the rate of methanolysis of 2,5-dimethyl-3-chloromethylfuran is 18 times that of 2-methyl-3-chloromethylfuran. This striking rate increase for introduction of a methyl group in a "nonconjugating" position (*i.e.*, position 5) is unusual; it is to be contrasted with the effect of a methyl group introduced in the meta position in benzene systems. For benzyl systems $k_{m\text{-Me}}/k_{\text{H}}$ ratios are typically 2 or 3.[6]



A



B

Our results show that this high ratio is characteristic of the furan system, and is not a singular or fortuitous result, due perhaps to ortho substitution. We have observed similar high rate ratios in both simple secondary and tertiary systems. From the results given in Table I, for the secondary systems **1** and **2**, the rate ratio $k_{\text{Et}}/k_{\text{H}}$ is 8.85; in the tertiary systems, **3** and **4**, the rate ratio $k_{\text{Me}}/k_{\text{H}}$ is 6.0.

TABLE I

RATE CONSTANTS FOR SOLVOLYSIS OF SOME SUBSTITUTED FURAN DERIVATIVES IN 80% ETHANOL

Compound solvolyzed	Temp, °C	k, sec^{-1}
1-(3-Furyl)ethyl *p*-nitrobenzoate (**1**)	75.00	8.18×10^{-6}
1-(5-Ethyl-3-furyl)ethyl *p*-nitrobenzoate (**2**)	75.00	7.24×10^{-5}
2-(3-Furyl)-2-propyl *p*-nitrobenzoate (**3**)	25.00 25.00	4.57×10^{-4} 4.66×10^{-4}
2-(5-Methyl-3-furyl)-2-propyl *p*-nitrobenzoate (**4**)	25.00	2.75×10^{-3}

A rational explanation of these observations comes

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[2] Graduate Fellow on the University of California–Chile Cooperative Program from funds provided by the Ford Foundation, 1966–1970.

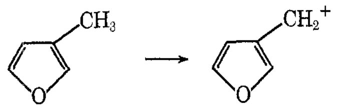
[3] D. S. Noyce and G. V. Kaiser, *J. Org. Chem.*, **34**, 1008 (1969).

[4] Y. K. Yur'ev, M. A. Gal'bershtam, and A. F. Prokof'eva, *Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Tekhnol.*, **7**, 598 (1964); *Chem. Abstr.*, **62**, 3897*i* (1965).

[5] M. A. Gal'bershtam, G. T. Khachaturova, N. E. Bairamova, K. Y. Novitskii, and Y. K. Yur'ev, *Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Tekhnol.*, **11**, 1395 (1968); *Chem. Abstr.*, **71**, 21307b (1969).

[6] Exemplary are the following: cumyl chlorides, 2.0, 2.28 [Y. Okamoto, T. Inukai, and H. C. Brown, *J. Amer. Chem. Soc.*, **80**, 4972 (1958)]; benzhydryl chlorides, 2.1 [J. F. Norris and J. T. Blake, *ibid.*, **50**, 1808 (1928)]; benzyl tosylates, 2.65 [A. Streitwieser, *et al.*, *ibid.*, **92**, 5141 (1970)].

from consideration of the change in charge density at various positions within a heterocyclic nucleus which are induced by the change from a nonalternant hydrocarbon to the related cation, C → D.



C D

Discussion

It should be noted initially that furan represents a nonalternant hydrocarbon; as such, the charge density about the ring in the parent hydrocarbon is not equal at various carbon atoms, in contrast to benzene or other condensed polynuclear aromatic hydrocarbons. Hence any studies of the relationship of molecular orbital parameters with activity at these systems must consider the *change* in charge density at position *i*.

The availability of standard programs for CNDO/2 and for INDO calculations now make it feasible to carry out such calculations with reasonable facility. This we have done.[7,8] It has been recently shown by Streitwieser, *et al.*,[9] that the CNDO/2 method is superior to SCF-π and HMO methods for correlating the acetolysis rates of arylmethyl tosylates with ΔE values calculated for the transformation $ArCH_3 \rightarrow ArCH_2^+$. We have also compared CNDO/2 and INDO calculations concurrently. The pertinent results of these calculations of the change in regional charge,[10] Δq, are listed in Table II.

TABLE II

CHARGE DENSITIES AT VARIOUS POSITIONS FROM CNDO/2 AND INDO CALCULATIONS

System	Position	CNDO/2 Δq	INDO Δq	r^a	% ℛ calcd (INDO)
Toluene → benzyl cation	4	0.2114	0.2109	2.00	65
	3	0.0368	0.0353	1.732	30
2-Methylfuran → furfuryl cation	5	0.2763	0.2726	1.571	66
	4	0.0642	0.0696	1.605	39
3-Methylfuran → 3-furylmethyl cation	5	0.1076	0.1150	1.605	49

[a] Distance (in units of standard benzene bond length, 1.39 Å) from aromatic carbon to which side chain is attached to numbered carbon bearing substituent.

It is to be noted that the change in regional charge for position 5 in the 3-furylmethyl cation is strikingly larger than in the meta relationship in the case of toluene → benzyl. Hence one should not expect meta substituent constants to correctly represent the mode of response for this furyl system. However, for 2-methylfuran the change in regional charge at position 5 in going to the furfuryl cation is more nearly in accord with the para relationship in the case of toluene to benzyl. Hence, as previously reported,[3] para substituent constants, σ_p^+, should be reasonably good in correctly reproducing the observed results. This is in fact what we observed previously, namely, excellent correlation with σ para plus.[3] In order to relate these results of the change in charge density to substituent effects we need an appropriate method for calculating an effective substituent constant. Substituent constants have been treated as a blend of field and resonance contributions. Dewar and Grisdale[11] have been successful in treating the dissociation constants of naphthalene derivatives in this fashion and more recently Swain and Lupton[12] have shown that separation of substituent constants into ℱ and ℛ components successfully deals with the massive quantities of data in the literature.

Bancroft and Howe[13] have shown that the Dewar–Grisdale equation[11a] when calibrated with Brown's σ^+ constants[14] rather than Hammett σ constants gives greatly improved results in correlating the measured rates of detritiation of substituted naphthalenes. Eaborn and Fischer[15] have extended these observations. We make the further modification of using Δq_{ij} as the coefficient of the resonance term, and thus have the modified Dewar–Grisdale equation (1).

$$(\sigma_{ij}{}^+)_x = F^+{}_x/r_{ij} + \Delta q_{ij}M^+{}_x \tag{1}$$

The $1/r_{ij}$ and Δq_{ij} values for benzyl listed in Table II and the σ^+ values of Brown and Okamoto[14] define the parameters F^+ and M^+ for any substituent when related by eq 1. Thus follow eq 2–5.

$$F^+{}_{\mathrm{INDO}} = 2.039\sigma_m{}^+ - 0.3548\sigma_p{}^+ \tag{2}$$

$$M^+{}_{\mathrm{INDO}} = 5.568\sigma_p{}^+ - 4.822\sigma_m{}^+ \tag{3}$$

$$F^+{}_{\mathrm{CNDO}} = 2.026\sigma_m{}^+ - 0.339\sigma_p{}^+ \tag{4}$$

$$M^+{}_{\mathrm{CNDO}} = 5.546\sigma_p{}^+ - 4.803\sigma_m{}^+ \tag{5}$$

It is to be noted that both the CNDO/2 method and the INDO method give closely similar results.

The F^+ and M^+ substituent parameters then may be directly transcribed to give $\sigma_{ij}{}^+$ values for any heterocyclic system and any substitution pattern for which Δq values have been calculated. It should be noted that this approach does not have any arbitrary parameters introduced, save the standard parameters in the regular CNDO/2 or INDO program.

From the calculated $\sigma_{ij}{}^+$ values, predicted rates of reaction may be obtained from a modified Hammett equation (eq 6), using ρ for the corresponding solvolysis reaction in the benzene series.

$$\log k/k_0 = \rho\sigma_{ij}{}^+ \tag{6}$$

Comparisons involving 3-substituted furans are given in Table III.[16,17] It is evident that this approach

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(7) We wish to express our appreciation to Professor Streitwieser and to Dr. P. Mowery for making available to us the QCPE program 142 suitably modified to use on the CDC 6400, and for counsel in use of this program.

(8) These calculations were carried out by Dr. R. W. Nichols with time donated by the University of California Computer Center. Further details will be available in a forthcoming paper by R. W. Nichols and D. S. Noyce.

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(10) Regional charge: the sum of the charges on a carbon atom and on any hydrogen atoms bonded to it. A. Streitwieser, Jr., and R. G. Jesaitis in "Sigma Molecular Orbital Theory," O. Sinanoglu and K. B. Wiberg, Ed., Yale University Press, New Haven, Conn., 1970, p 197.

(11) (a) M. J. S. Dewar and P. J. Grisdale, *J. Amer. Chem. Soc.*, **84**, 3539, 3548 (1962); (b) M. J. S. Dewar, R. Golden, and J. M. Harris, *ibid.*, **93**, 4187 (1971).

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TABLE III

RELATIVE RATES AND SUBSTITUENT CONSTANTS FOR 5-SUBSTITUTED 3-FURYL SYSTEMS

System	Log k/k_0	$(\sigma_{5,3}{}^+)_{\text{INDO}}$	Calcd rate predicted
5-Me (**4**)	0.78[a]	−0.177	0.77[e]
5-Acetyl (**5**)	−2.53[a,b]	0.597[d]	−2.5[e]
5-Et (**2**)	0.95[c]	−0.169	0.96[f]

[a] At 25°. [b] $k = 1.36 \times 10^{-6}$ sec^{-1}, extrapolated. [c] At 75°. [d] $\sigma_p{}^+$ and $\sigma_m{}^+$ from ref 14. [e] Assuming $\rho = -4.34$. [f] Assuming $\rho = -5.7$ (ref 16 and 17).

satisfactorily accommodates the experimental data, both in the nature of the acceleration of rate of solvolysis caused by introduction of a 5-alkyl group and also in showing that this acceleration is greater in primary systems[4,5] than in secondary or tertiary systems.

Two additional features of this approach merit comment. For the effects of substituents in the 5 position in 3-furylmethyl systems, one may now calculate the percentage field and percentage resonance contributions which contribute to the total effect using Swain and Lupton's formulation.

For the three possible patterns of substitution in furan, these are given in the last column of Table II. Notable is the fact that the percentage resonance in 5-substituted furfuryl systems is 67%, almost identical with the corresponding value found by Swain and Lupton for para-substituted benzene derivatives, and defined by $\sigma_p{}^+$. For the 4 position in furfuryl systems, the percentage resonance is much less, but distinctly greater than for a meta position in a benzene ring. For 5-substituted 3-furylmethyl systems, the percentage resonance is 49%, and thus this increased resonance component is responsible for the sharp response of reaction rate to the introduction of a 5-methyl group.

Extending this analysis to an additional substituent, the 5-acetyl group, 2-(5-acetyl-3-furyl)-2-propyl *p*-nitrobenzoate (**5**), we find that the reaction rate is sharply depressed. For these three substituents, the correlation of reaction rate by a modified Hammett relationship is excellent.

Experimental Section[18]

1-(3-Furyl)ethyl *p*-Nitrobenzoate (**1**).—1-(3-Furyl)ethanol has been reported previously.[16,19,20] We observed that 1-(3-furyl)ethanol is conveniently prepared from 3-bromofuran by the halogen metal interchange reaction with *n*-butyllithium at −78° followed by treatment with acetaldehyde, yield 73%, bp 92–93° (18 mm) [lit.[19] bp 55–60° (8 mm)].

To prepare the *p*-nitrobenzoate, the alcohol was converted to the lithium salt (*n*-butyllithium in hexane) and treated with *p*-nitrobenzoyl chloride. The ester was crystallized from hexane: mp 64–65°; ir ($CHCl_3$) 3016 (w), 1723 (s), 1612 (m), 1534 (s), 1277 (s), 873 (s), 660 cm^{-1} (m); nmr ($CDCl_3$) δ 1.68 (d, 3, $J_{CH_3,H}$ = 6.5 Hz, CH_3), 6.12 (q, 1, CHOPNB), 6.43 (dd, 1, 4-H), 7.31 (dd, 1, 5-H), 7.45 (dd, 1, 2-H), 8.15 (s, 4, phenyl H).

Anal. Calcd for $C_{13}H_{11}NO_5$: C, 59.77; H, 4.24; N, 5.36. Found: C, 59.63; H, 4.48; N, 5.32.

4-Bromo-2-acetylfuran.—The preparation of 4,5-dibromo-2-acetylfuran by the method of Gol'dfarb and Tarasova[21] was improved to give a 75% yield using dibromomethane as solvent. Reduction with zinc in aqueous acetic acid afforded 4-bromo-2-acetylfuran in 77% yield, mp 68° (lit.[21] mp 68°).

4-Bromo-2-ethylfuran.—4-Bromo-2-acetylfuran was converted by Wolff–Kishner reduction to 4-bromo-2-ethylfuran in 79% yield: bp 78° (54 mm) [lit.[21] bp 56–57° (23 mm)]; nmr ($CDCl_3$) δ 1.21 (t, 3, J_{CH_3,CH_2} = 7.5 Hz, CH_3), 2.63 (m, 2, CH_2), 6.04 (m, 1, 3-H), 7.28 (d, 1, 5-H).

1-(5-Ethyl-3-furyl)ethanol.—To a solution of 4-bromo-2-ethylfuran (7.3 g) in 100 ml of anhydrous ether at −78° was added 1 equiv of *n*-butyllithium, precooled to −78°, over 30 min. After the addition was over the reaction mixture was stirred for 20 min at −78°. To this solution 5 ml of cold acetaldehyde was added by syringe. The reaction mixture was stirred for an additional 1 hr at −78°, the contents of the flask were poured over 400 ml of ice-cold water, and the mixture was carefully neutralized with 15% sulfuric acid. After work-up in the usual fashion, 1-(5-ethyl-3-furyl)ethanol (3.87 g, 66%) was obtained as a colorless liquid: bp 94–95° (14.5 mm); ir (CCl_4) 3571 (m, sh), 3436 (broad), 2985 (s), 1550 (m), 921 cm^{-1} (s); nmr ($CDCl_3$) δ 1.21 (t, 3, J_{CH_3,CH_2} = 7.5 Hz, CH_3CH_2), 1.42 (d, 3, $J_{CH_3,H}$ = 6.5 Hz, CHOHC**H**$_3$), 2.42 (s, 1, OH), 2.62 (q, 2, C**H**$_2$CH$_3$), 4.76 (q, 1, CHOH), 6.00 (d, 1, 4-H), 7.18 (d, 1, 2-H).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.86; H, 8.55.

1-(5-Ethyl-3-furyl)ethyl *p*-Nitrobenzoate (**2**).—From 1-(5-ethyl-3-furyl)ethanol and *p*-nitrobenzoyl chloride in the usual fashion,[3] **2** was obtained as white crystals from cold hexane: mp <25°; ir ($CHCl_3$), 1724 (s), 1610 (w), 1524 (s), 1337 (m), 1271 (s), 1117 (m), 1110 cm^{-1} (m); nmr ($CDCl_3$) δ 1.32 (t, 3, J_{CH_3,CH_2} = 7.5 Hz, CH$_2$C**H**$_3$), 1.82 (d, 3, $J_{CH_3,H}$ = 6.5 Hz, C**H**$_3$-CHOPNB), 2.80 (q, 2, C**H**$_2$CH$_3$), 6.15 (q, 1, CH$_3$C**H**), 6.40 (m, 1, 4-H), 7.44 (d, 1, 2-H), 8.10 (s, 4, phenyl H).

Anal. Calcd for $C_{15}H_{15}NO_5$: C, 62.27; H, 5.23; N, 4.84. Found: C, 61.98; H, 4.97; N, 4.98.

2-(3-Furyl)-2-propanol.—From methylmagnesium iodide and methyl 3-furoate the tertiary alcohol was obtained as a colorless liquid: bp 98° (19.5 mm) [lit.[19] bp 53–58° (8 mm)]; nmr (CCl_4) δ 1.48 (2, 6, CH_3), 2.69 (s, 1, OH), 6.32 (m, 1, 4-H), 7.25 (m, 2, 2-H and 5-H).

2-(3-Furyl)-2-propyl *p*-Nitrobenzoate (**3**).—From 2-(3-furyl)-2-propanol and *p*-nitrobenzoyl chloride in pyridine, **3** was obtained in the usual fashion as slightly yellow crystals from petroleum ether (bp 30–60°): mp 99.5–100.5°; ir ($CHCl_3$) 3021 (w), 1726 (s), 1610 (m), 1529 (s), 1351 cm^{-1} (s); nmr (CCl_4) δ 1.82 (s, 6, CH_3), 6.32 (m, 1, 4-H), 7.26 (m, 1, 2-H), 7.37 (m, 1, 5-H), 8.07 (d, 4, phenyl H).

Anal. Calcd for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 60.96; H, 4.50; N, 5.22.

4-Bromofurfural.—Bromination of furfural by the method of Gol'dfarb, *et al.*,[22] afforded 4,5-dibromofurfural, which was reduced with zinc dust in aqueous acetic acid[21] to 4-bromofurfural, mp 54.0–54.5° (lit.[23] mp 54°).

2-Methyl-4-bromofuran.—Wolff–Kishner reduction of 4-bromofurfural afforded 2-methyl-4-bromofuran in 61% yield: bp 132–134° [lit.[24] bp 60–62° (60 mm)]; nmr (CCl_4) δ 2.26 (d, 3, $J_{CH_3,3H}$ = 1 Hz, CH_3), 5.95 (m, 1, 3-H) 7.19 (d, 1, 5-H).

Anal. Calcd for C_5H_5BrO: C, 37.30; H, 3.13; Br, 49.63. Found: C, 37.31; H, 3.20; Br, 49.52.

2-(5-Methyl-3-furyl)-2-propanol.—To a solution of 14.3 g of 2-methyl-4 bromofuran in 200 ml of ether at −78° was added a precooled hexane solution of *n* butyllithium (1 equiv) over a period of 30 min. After an additional 30 min at −78° acetone (15 ml) was added, and the resulting mixture was maintained at −78° for 2 hr and then allowed to warm to room temperature. After working up in the usual fashion, there was obtained 9.3 g (74%) of 2-(5-methyl-3-furyl)-2-propanol as a colorless liquid: bp 58–60° (1 mm); nmr (CCl_4) δ 1.38 [s, 6, $(CH_3)_2$], 2.20 (d, 3, 5-CH_3), 2.45 (s, 1, OH), 5.88 (m, 1, 4-H), 7.02 (d, 1, 2-H).

2-(5-Methyl-3-furyl)-2-propyl *p*-Nitrobenzoate (**4**).—The above alcohol was converted directly to the ester using the pyridine method.[3] The crude ester, contaminated with *p*-nitrobenzoic acid, was used directly for kinetic measurements.

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(18) Melting points and boiling points are uncorrected. Analyses are by the Microanalytical Laboratory, University of California, Berkeley. Spectra were recorded using Perkin-Elmer Model 237 (ir) or Varian A-60 (nmr) spectrometers.

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2-Acetyl-4-bromofuran Diethyl Ketal.—To a stirred solution of 2-acetyl-4-bromofuran (50.0 g) in 50 ml of absolute ethanol was added triethyl orthoformate (75.0 g) and 25 ml of a 9% (w/w) solution of dry hydrochloric acid in absolute ethanol. The reaction mixture was stirred at room temperature for 24 hr and, after it was neutralized with sodium ethoxide, the mixture was distilled to 85° to remove excess ethanol and ethyl formate. The residual dark liquid was distilled under reduced pressure. A forerun of triethyl orthoformate was collected and 63.0 g (90%) of 2-acetyl-4-bromofuran diethyl ketal was obtained as a colorless liquid: bp 119° (16 mm); bp 95° (3 mm); ir (CCl_4) 3155 (w), 2994 (s), 1370 (m), 1271 (s), 901 (s), 860 (s), 691 cm^{-1} (m) nmr (CCl_4) δ 1.13 (t, 6, J_{CH_3,CH_2} = 7 Hz, CH_2CH_3), 1.54 (s, 3, $=CCH_3$), 3.32 (dq, 4, CH_2), 6.34 (d, 1, $J_{3,5}$ = 0.9 Hz, 3-H), 7.40 (d, 1, 5-H).

2-(5-Acetyl-3-furyl)-2-propanol.—In a nitrogen-swept flask, immersed in an acetone–Dry Ice bath, was placed a solution of 2-acetyl-4-bromofuran diethyl ketal (26.3 g, 0.1 mol) in 250 ml of anhydrous ether. A precooled hexane solution of *n*-butyllithium (62.2 ml, 0.1 mol) was added over a period of 30 min. After the addition was complete the mixture was stirred at −78° for 1 hr and then 15 ml of acetone was added. The reaction mixture was stirred for 3 hr at −78° and for 2 hr at room temperature. The contents of the flask were poured into cold water and the mixture was extracted with ether. The ethereal solution was transferred to a flask, the ether was removed on a rotary evaporator, and the residual oil was hydrolyzed with 150 ml of water containing 3 ml of 3 *N* hydrochloric acid, at room temperature for 2 hr. The reaction mixture was extracted with ether. The ethereal solution was washed with 5% sodium bicarbonate and water, dried over anhydrous magnesium sulfate, and filtered. After removal of the ether on a rotary evaporator, 11.5 g (68%) of crude 2-(5-acetyl-3-furyl)-2-propanol remained as a pale yellow oil: ir (CCl_4) 3436 (broad), 2976 (m), 1681 (s), 1504 (m), 909 cm^{-1} (s); nmr (CCl_4) δ 1.46 (s, 6, CH_3), 2.34 (s, 3, $COCH_3$), 3.63 (s, 1, OH), 7.04 (d, 1, $J_{3,4}$ = 0.7 Hz, 4-H), 7.38 (d, 1, 2-H).

2-(5-Acetyl-3-furyl)-2-propyl *p*-nitrobenzoate (**5**) was prepared directly from the crude alcohol and *p*-nitrobenzoyl chloride using the pyridine method.[3] After two recrystallizations from ether–hexane, 2-(5-acetyl-3-furyl)-2-propyl *p*-nitrobenzoate was obtained as very pale yellow crystals: mp 108°; ir ($CHCl_3$) 3012 (w), 1725 (s), 1678 (s), 1613 (m), 1524 (s), 1279 cm^{-1} (s); nmr ($CDCl_3$) δ 1.94 (s, 6, CH_3), 2.48 (s, 3, $COCH_3$), 7.28 (d, 1, 3-H), 7.65 (d, 1, 5-H), 8.22 (d, 4, phenyl H).

Anal. Calcd for $C_{16}H_{15}NO_6$: C, 60.56; H, 4.76; N, 4.42. Found: C, 60.42; H, 4.69; N, 4.27.

Kinetic Methods.—Most of the kinetic procedures have been described previously.[3] Some of the individual experiments with **3** and **4** were carried out by measuring the kinetics at controlled pH, using a Radiometer Titrator (TTTlc), Autoburette (Type ABUlc), and a Titrigraph (Type SBR2c) maintaining the pH at 7.5. Additional kinetic data are recorded in Table IV.

TABLE IV

RATE CONSTANTS UNDER VARIOUS CONDITIONS

Compd	Temp, °C	Solvent	k, sec^{-1}
4	45.00	80% EtOH	$4.49 \times 10^{-3\,a}$
	45.00	70% Dioxane	1.02×10^{-3}
5	75.00	80% EtOH	7.61×10^{-4}
	25.00	80% EtOH	$1.36 \times 10^{-6\,b}$

[a] $\Delta H^{\ddagger} = 20.9$ kcal; $\Delta S^{\ddagger} = -3.7$ eu. [b] Extrapolated assuming $\Delta S^{\ddagger} = -4.0$ eu.

Registry No.—**1,** 34878-28-9; **2,** 34878-29-0; **3,** 34878-30-3; **4,** 34878-31-4; **5,** 34878-32-5; 1-(5-ethyl-3-furyl)ethanol, 34878-33-6; 2-methyl-4-bromofuran, 24666-43-1; 2-(5-methyl-3-furyl)-2-propanol, 34878-35-8; 2-acetyl-4-bromofuran diethyl ketal, 34878-36-9; 2-(5-acetyl-3-furyl)-2-propanol, 34878-37-0.

Notes

Transmission of Substituent Effects in Heterocyclic Systems. The Application of Molecular Orbital Parameters to the Solvolysis of 4-Substituted 1-(2-Furyl)ethyl Systems[1]

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Recent studies from these laboratories[3–5] have shown that advanced molecular orbital calculations employing all-valence electron methods, such as CNDO/2 and INDO, provide a very useful foundation and framework for interpretation of substituent effects in heterocyclic systems.

It was shown[4] that equally good correlations were obtained for the rates of solvolysis of substituted 1-(2-thienyl)ethyl *p*-nitrobenzoates, using either Brown's electrophilic substituent constants[6] or substituent constants determined from CNDO/2 parameters incorporated in a modified Dewar–Grisdale equation. For 1-(3-furyl)ethanol derivatives only the substituent constants derived by the modified Dewar–Grisdale equation adequately accounted for the observed rates of solvolysis,[5] while for 5-substituted 1-(2-furyl)ethyl derivatives, excellent correlations are obtained with both σ^+ constants and CNDO/2 parameters. The modified Dewar-Grisdale approach is also particularly adaptable to predictions for other systems. It is the purpose of the present note to examine 1-(4-X-2-furyl)ethanol derivatives in this context.

The equation (1) first proposed by Nichols[7] leads naturally to the predictions presented below.

$$\sigma_{ij}^{+} = F^{+}/r + \Delta q M^{+} \qquad (1)$$

In eq 1, an electrophilic substituent constant, σ_{ij}^+, is determined for a substituent at a position i in a heterocyclic ring system, with reference to position j as

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