Heteroaromatic Rings as Substituents. Part IV.[1] The ' Non-constancy ' of the σ_p^+ Constants of the 2-Thienyl and 2-Furyl Groups

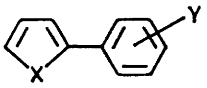
By **Francesco Fringuelli, Gianlorenzo Marino,*** and **Aldo Taticchi,** Istituto di Chimica Organica, Università di Perugia, Via Elce di Sotto 10, 06100 Perugia, Italy

The σ_m^+ and σ_p^+ constants for the 2-thienyl group have been calculated from the rates of solvolysis of 1-(2-thienylphenyl)ethyl acetates in aqueous 30% ethanol. A comparison with the values previously determined from similar reactions shows that, whereas the σ_m^+ value is constant, the σ_p^+ value varies within wide limits. The σ^+ constants for the 2-thienyl and 2-furyl groups have also been calculated from the carbonyl stretching frequencies of thienyl- and furyl-substituted acetophenones by applying the Traylor and Ware correlation. The possible reasons for such ' non-constancy ' of the σ_p^+ values for these ' aromatic ' substituents are discussed.

In a previous paper[2] the σ^+ constants for *para-* and *meta*-2- and 3-thienyl groups were evaluated from the solvolysis of 2-aryl-2-chloropropanes in aqueous 90% acetone, the reference reaction suggested by Brown and Okamoto[3] for the calculation of electrophilic substituent constants. We noted that our σ_p^+ value for the 2-thienyl group (—0·43) disagreed with the value (—0·23) derived from the rate constants for the protodetritiation of [5-^{3}H]2,2′-bithienyl and [2-^{3}H]thiophen.[4] Accordingly, we have studied the effect of the 2-thienyl group on the solvolysis of 1-arylethyl acetates[5] in aqueous 30% ethanol and on the carbonyl stretching frequencies of substituted acetophenones.

RESULTS AND DISCUSSION

Solvolysis of 1-Arylethyl Acetates.—The required 1-arylethyl acetates (3) and (6) (see Experimental section) were synthesized by a procedure analogous to that for the 2-furyl derivatives.[1] Their structures, as well as those of intermediate compounds, were established by spectroscopic data (i.r., u.v., and n.m.r.) and by the well known course of the reactions employed. The purity of the compounds was checked by g.l.c., t.l.c., and elemental analyses. Because of the very different reactivity of the *para-* and *meta*-derivatives, the more reactive *para*-isomer was solvolysed at 80 and 100°, and the *meta*-isomer at 120°. The procedure followed for the determination of the rate of solvolysis was identical to that described by Hill and his co-workers.[5] The first order rate constants are reported in Table 1.



	X	Y
(1)	S	*p*-COMe
(2)	S	*p*-CH(OH)Me
(3)	S	*p*-CH(OAc)Me
(4)	S	*m*-COMe
(5)	S	*m*-CH(OH)Me
(6)	S	*m*-CH(OAc)Me
(7)	O	*p*-COMe
(8)	O	*m*-COMe

TABLE 1

Rate constants for solvolysis of 1-arylethyl acetates in aqueous 30% ethanol

Compound	T/°C	10^6k/s^{-1}
(3)	80	10·4 ± 0·01
(3)	100	63·3 ± 0·10
(6)	120	1·76 ± 0·03
1-Phenylethyl acetate	80	0·224[a]
1-Phenylethyl acetate	100	1·51[a]
1-Phenylethyl acetate	120	8·35 ± 0·1[b]

[a] Extrapolated value. [b] Ref. 5.

The ρ values for the solvolysis of substituted 1-phenylethyl acetates at 80 (—5·05), at 100 (—4·83), and at 120° (—4·65) were calculated from the rate constants for monosubstituted benzenes,[5] extrapolated to the required temperatures. The σ^+ values obtained by dividing $\log k/k_0$ by the appropriate ρ value are reported in Table 2, together with those previously determined from other reactions. The data of Table 2 reveal that, whereas the electronic contribution of a 2-thienyl group from the *meta*-position is substantially constant, the same cannot be said for the effect exerted from the *para*-position. In this case the effects are variable and cannot be adequately described in terms of a unique substituent parameter, valid for all electrophilic reactions. This behaviour is analogous to that of other

---

[1] Part III, F. Fringuelli, G. Marino, and A. Taticchi, *J. Chem. Soc.* (*B*), 1971, 2304.

[2] F. Fringuelli, G. Marino, and A. Taticchi, *J. Chem. Soc.* (*B*), 1971, 2302.

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

[4] A. R. Butler and C. Eaborn, *J. Chem. Soc.* (*B*), 1968, 370.

[5] E. A. Hill, M. L. Gross, M. Stasienwicz, and M. Manion, *J. Amer. Chem. Soc.*, 1969, **91**, 7381.

polarizable groups, especially the 'aromatic' ones, such as the *para*-phenyl[6] and the 3,4-benzo-substituents.[7] However, in our case, contrary to what has been observed for other related groups,[8] the σ_p^+ value does not become increasingly negative as ρ becomes larger (in absolute value); thus the last negative σ^+ value is that derived from the protodetritiation, for which the ρ constant has the largest (negative) value. The apparent anomaly probably disappears if the Yukawa–Tsuno equation[9] is used, since the quantity $1/\rho \log k/k_0$ is linearly correlated[10] with the parameter r of this equation. Moreover, this is one of the cases for which the improvement obtained by the use of the Yukawa–Tsuno treatment relative to the simple Hammett equation, will be particularly remarkable since the difference $(\sigma_p^+ - \sigma_p)$ is large (—0·48) when compared with the σ_p value which is close to zero[7a] (+0·05). Unfortunately, the available data do not permit the calculation of the parameter r for the reactions examined.

TABLE 2

Electrophilic substituent parameters for 2-thienyl and 2-furyl groups from solvolytic and spectroscopic data

	Thienyl		Furyl	
Reaction	σ_m^+	σ_p^+	σ_m^+	σ_p^+
Solvolysis of 1-arylethyl acetates	+0·15	—0·33	+0·10[a]	—0·39[a]
Solvolysis of 2-aryl-2-chloropropanes[b]	+0·16	—0·43		
Protodetritiation[c]		—0·23		
Carbonyl stretching frequencies	+0·15	—0·38	+0·10	—0·45

[a] Ref. 1. [b] Ref. 2. [c] Calculated from data of ref. 4.

I.r. Frequencies of Substituted Acetophenones.—An independent approach to the determination of substituent constants is based on the measurements of spectroscopic quantities. Both i.r. group frequencies and band intensities of groups of aromatic compounds have been correlated with substituent constants (either σ or σ^+).[11] In particular, a good linear relationship has been found between the carbonyl stretching frequencies of *meta*- and *para*-substituted acetophenones and the electrophilic σ^+ constants.[12] The empirical correlation provides an extremely useful way for the determination of new σ^+ values through the use of the formula $\sigma^+ = 0·0877\,[\nu(\mathrm{C{=}O}) - 1691·1]$.

The values of the carbonyl frequencies for *meta*- and *para*-2-thienyl and 2-furyl acetophenones (1), (4), (7), and (8), which were used for the determination of the substituent parameters, are reported in Table 3.

The σ_m^+ values obtained by this procedure are in excellent agreement with the values obtained from the rates of solvolysis, confirming the validity of the empirical approach. The σ^+ value for the 2-thienyl group (—0·38) lies in the range of the values determined from reactivity data (—0·23, —0·33, or —0·43); the σ_p^+ value for the 2-furyl group is quite different (—0·45) from that obtained from the solvolysis of the 1-arylethyl acetates (Table 2). This indicates that for the furyl as for the thienyl group, the electronic effects are variable and are not represented by a single σ_p^+ value, valid for all cases.

TABLE 3

Carbonyl stretching frequencies of substituted acetophenones

Compound	ν(C=O)/cm^{-1}
(1)	1686·8
(4)	1692·8
(7)	1686·0
(8)	1692·3

EXPERIMENTAL

Light petroleum had b.p. 40—60° and ligroin b.p. 100—120°. Neutral alumina (C. Erba) was used for column chromatography and Kieselgel PF_{254} (Merck) for analytical t.l.c. I.r. spectra of alcohols and acetates were measured on a Perkin-Elmer model 257 instrument and u.v. spectra, for n-hexane solutions, on a Beckman DKW 1. N.m.r. spectra were recorded on Varian A100 or JEOL JNM-60 HL spectrometers, with tetramethylsilane as internal standard, for deuteriochloroform solutions. *J* Values are given in Hz. H-3, H-4, and H-5 indicate the hydrogen atoms of 2-thienyl ring.

p-(2-*Thienyl*)*acetophenone* (1).—*p*-Aminoacetophenone (100 g) was diazotized at 0—5° in conc. hydrochloric acid (236 ml) and water (133 ml) with aqueous sodium nitrite (60·5 g). The filtered diazonium solution and then 5N-sodium hydroxide (400 ml) were added to thiophen (500 ml) with vigorous stirring at 0—5°. The mixture was stirred for 5 h at 5—10° and for 48 h at room temperature, then extracted with ether. The combined extracts were washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was extracted with hot ligroin and the combined extracts were concentrated and column-chromatographed, with ligroin as eluant. The crude *product* (14 g) was crystallized twice from light petroleum–ethyl acetate; m.p. 115—116°, $\lambda_{max.}$ 230 (ε 9200) and 308 nm (24,500), τ 7·44 (3H, s, CH_3), 2·92 (1H, q, $J_{4.3}$ 3·5, $J_{4.5}$ 5·0, H-4), 2·64 (2H, m), and 2·35 and 2·06 (each 2H, d, *J* 8, ArH) (Found: C, 71·3; H, 5·1. $C_{12}H_{10}OS$ requires C, 71·25; H, 5·0%).

m-(2-*Thienyl*)*acetophenone* (4).—The above procedure was used to give the *ketone* (4), m.p. 45—47° (from light petroleum), $\lambda_{max.}$ 245 (ε 22,000) and 281 nm (13,900), τ 7·41 (3H, s, Me), 2·96 (1H, q, $J_{4.3}$ 3·5, $J_{4.5}$ 5·0, H-4), 2·62 (3H, m), 2·22 (2H, m), and 1·85 (1H, s) (Found: C, 71·4; H, 4·8%).

1-[p-(2-*Thienyl*)*phenyl*]*ethyl Alcohol* (2).—Compound (1) (7·3 g) in dry ether (80 ml) was added dropwise and with stirring to lithium aluminium hydride (3·8 g) in dry ether

---

[6] H. C. Brown and L. M. Stock, *J. Amer. Chem. Soc.*, 1962, **84**, 3298.

[7] (*a*) C. Eaborn and R. Taylor, *J. Chem. Soc.*, 1961, 1012; (*b*) R. Taylor and G. G. Smith, *Tetrahedron*, 1963, **19**, 937.

[8] J. R. Knowles, R. O. C. Norman, and G. K. Radda, *J. Chem. Soc.*, 1960, 4885.

[9] Y. Yukawa and Y. Tsuno, *Bull. Chem. Soc. Japan*, 1959, **32**, 971.

[10] Y. Yukawa, Y. Tsuno, and M. Sawada, *Bull. Chem. Soc. Japan*, 1966, **39**, 2274.

[11] C. N. R. Rao, 'Chemical Applications of Infrared Spectroscopy,' Academic Press, New York and London, 1963, p. 568.

[12] T. G. Traylor and J. C. Ware, *J. Amer. Chem. Soc.*, 1967, **89**, 2304.

(70 ml). The mixture was stirred for 4 h, treated with 10% sodium hydroxide, and then worked-up as usual. The crude product (5 g) was crystallized from light petroleum–ethyl acetate; m.p. 84—85°, $\nu_{max.}$ (CCl_4) 3620 (OH), 3120, 850 (thienyl ring), and 1625 cm^{-1} (phenyl ring), $\lambda_{max.}$ 283 nm (ε 18,100), τ 8·52 (3H, d, *J* 6·0, Me), 7·75 (1H, s, OH), 5·15 (1H, q, *J* 6·0, CH), and 2·65 (7H, m) (Found: C, 70·45; H, 5·75. $C_{12}H_{12}OS$ requires C, 70·55; H, 5·9%).

1-[m-(2-*Thienyl*)*phenyl*]*ethyl Alcohol* (5).—The procedure described for compound (2) was used; the crude *alcohol* (5) was purified by distillation at 0·5 mmHg; $\nu_{max.}$ (CCl_4) 3618, 3400 (OH), 3120, 850 (thienyl ring), and 1615 cm^{-1} (phenyl ring), $\lambda_{max.}$ 282 nm (ε 14,200), τ 8·56 (3H, d, *J* 6·3, Me), 7·77 (1H, s, OH), 5·17 (1H, q, *J* 6·3, CH), and 2·70 (7H, m) (Found: C, 70·65; H, 5·9%).

1-[p-(2-*Thienyl*)*phenyl*]*ethyl Acetate* (3).—Acetic anhydride (2 g) was added to a compound (2) (2·8 g) in dry pyridine (20 ml) and the mixture was left at room temperature for 24 h. The usual work-up, followed by column chromatography and distillation at 0·5 mmHg, afforded the *product* (3) (2 g), $\nu_{max.}$ (CCl_4) 3120, 850 (thienyl ring), 1615 (phenyl ring), 1738 (C=O), and 1230 cm^{-1} (C–O) (Found: C, 68·35; H, 5·7. $C_{14}H_{14}O_2S$ requires C, 68·25; H, 5·75%).

1-[m-(2-*Thienyl*)*phenyl*]*ethyl Acetate* (6).—The procedure for compound (3) was used; the *product* (6) was purified by column chromatography and distillation at 0·5 mmHg; $\nu_{max.}$ (CCl_4) 3120, 850 (thienyl ring), 1620 (phenyl ring), 1740 (C=O), and 1230 cm^{-1} (C–O) (Found: C, 68·4; H, 5·75%).

Kinetics.—The solvolyses were carried out at the appropriate temperature (80, 100, or 120° ± 0·05) in aqueous 30% ethanol as previously described.[1,5]

Measurements of Carbonyl Frequencies.—The carbonyl frequencies of the ketones (1), (4), (7), and (8) were measured for carbon tetrachloride solutions (*ca.* 3×10^{-3}M) on a Perkin-Elmer model 521 instrument. The cell thickness was 1 mm. The mid-point of the peak at half its maximum intensity was taken as the position of the absorption maximum.

The uncertainty in the absolute values is *ca.* 0·3 cm^{-1} and the maximum error in σ^+ is $\pm 0{\cdot}025$.

The ketones (7) and (8) were available from a previous study.[1]

We thank the Italian National Council for financial support and Mr. G. F. Conti (Istituto Superiore di Sanità, Roma) for n.m.r. spectra.

[1/1073 *Received, June 28th*, 1971]