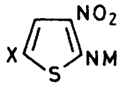
The Protonation of Some 3-Substituted 2-(*N,N*-Dialkylamino)-5-nitrothiophenes

Paolo De Maria and Renato Noto
Dipartimento di Chimica Organica, Università di Palermo, Via Archirafi 20, Palermo 90123, Italy
Giovanni Consiglio and Domenico Spinelli
Dipartimento di Chimica Organica, Università di Bologna, Via S. Donato 15, Bologna 40127, Italy

The protonation of some 3-substituted 2-(*N,N*-dialkylamino)-5-nitrothiophenes (**3**)–(**4**) and some 5-substituted 3-nitro-2-piperidinothiophenes (**2**) has been studied in aqueous perchloric and/or sulphuric acid. pK_{BH^+} values have been calculated according to modified Hammett, Bunnett–Olsen, and Marziano–Yates–Cox methods and the data obtained related to the effect of the substituents. The results obtained have been discussed considering the different interactions that the dialkylamino (*N,N*-dimethylamino or piperidino) group at C-2 can give with the group (nitro-group or variable substituent) present at C-3 (an *ortho*-like position).

In the course of our studies [1] on the effect of substituents on both the reactivities and the equilibrium processes in several derivatives of five-membered heterocyclic compounds we have thoroughly used the Hammett equation [2a,b] or more sophisticated [2c,d] relationships for examining both side-chain and ring reactions. We have paid special attention to the study of S_NAr reactions in thiophene compounds, observing that often these reactions require the use of the so-called σ_p^- values as substituent constants for *para*-substituents.

Since in benzene series the σ_p^- constants have been defined [2b] from acidity constants of substituted phenols and protonated anilines, we have recently determined[3] the protonation constants of some 5-substituted 2-(*N,N*-dimethylamino)-3-nitrothiophenes (**1**) in aqueous perchloric acid as a reference reaction to check the σ_p^- values proposed by us for thiophene S_NAr reactions [piperidino [1f] and/or anilino substitution [1g] in some 5-substituted 2-L-3-nitrothiophenes (L = Cl, Br, I, SO_2Ph, $OC_6H_4NO_2$-*p*)].[1c,e–g]



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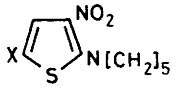

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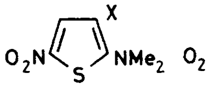

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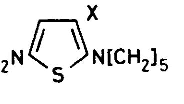

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a; X = Me
b; X = H
c; X = Br
d; X = $CONH_2$
e; X = CO_2Me
f; X = Ac
g; X = SO_2Me
h; X = CN
i; X = NO_2

The obtained pK_{BH^+} values calculated by the modified Hammett[4] method (Hammett acidity functions method: HAFM, *i.e.* using H_0''' as acidity function for tertiary aromatic amines), by the Bunnett–Olsen method (BOM),[5] and by the Marziano–Cox–Yates method [excess acidity method: EAM] [6,7] furnished excellent linear free energy relationships [3] (l.f.e.r.s) with thiophenic σ_p^- values [1f] ($r \geqslant 0.992$, C.L. > 99.9%), showing once more that the electronic interactions between *para* (or *para*-like) substituents and the reaction centre affect in a similar way both the acidity of aromatic (or heteroaromatic) protonated amines and the S_NAr reactivity.

Taking into account our current interest in l.f.e. *ortho*-correlations [1i–r] we now present the results obtained by the pK_{BH^+} determination of some 3-substituted 2-(*N,N*-dialkylamino)-5-nitrothiophenes (**3**)–(**4**) in aqueous perchloric and/or sulphuric acid.

Within the last few years we have pointed out that for several S_NAr reactions of thiophene compounds [*e.g.* piperidino-substitution of some 2-L-5-nitro-3-X-thiophenes (L = Br, SO_2Ph),[1o–q] benzenethiolate debromination of some 3-bromo-4-nitro-2-X-thiophenes and 3-bromo-2-nitro-4-X-thiophenes] [1r] as well as for some reactions occurring in the side-chain of *ortho*-like substituted thiophene derivatives (*e.g.*, pK_a of thiophene-2- or -3-carboxylic acids, alkaline hydrolysis of the corresponding methyl esters, anilinodechlorination of 3-substituted thenoyl chlorides, *etc.*),[1a,b,i–n] it is possible to obtain linear free energy *ortho*-correlations. This behaviour has been related to the favourable geometry of the five-membered ring, where the *ortho*-like substituents give rise to proximity effects smaller than those occurring in six-membered rings. Additionally the rate-determining transition state for the formation of the σ-complex is S_NAr (where the carbon atom of the reaction centre changes its hybridization from sp^2 to sp^3) shows a crowding lower than that present in the starting products and this situation favours the occurrence of l.f.e. *ortho*-correlations.

The present study of the protonation reaction of the amines was undertaken to test whether or not the variable substituents at C-3, which have very different steric requirements, are able to affect the equilibrium reaction by effects that can be evaluated by substituent constants (thiophenic σ_p^- values) [1f] which depend only on electronic effects (*i.e.* free from steric effects). Therefore we have studied two series of tertiary amines (dimethylaminothiophenes in aqueous perchloric acid and piperidinothiophenes in aqueous sulphuric acid: some amines of the two series have been tested with both acids) to gain information about the influence on the pK_{BH^+} values of: (i) the structure of the amines, (ii) the nature of the acid used (according to the definition of pK_{BH^+} the values obtained should be independent of the nature of the acid used, but often this is not the case [8] if pK_{BH^+} is calculated by EAM), and (iii) the calculation method used.[9,10]

Moreover we have studied the protonation reaction of some 5-substituted 3-nitro-2-piperidinothiophenes (**2**), a series of compounds where the variable substituent is at C-5 (*i.e.* far from

Table 1. pK_{BH^+} values of 5-substituted 3-nitro-2-piperidinothiophenes (**2a**–i) in aqueous sulphuric acid.

		HAFM			BOM			EAM			
Compound	X	$-pK_{BH^+}$	*m*	*r*	$-pK_{BH^+}$	$-\varphi$	*r*	$-pK_{BH^+}$	*m**	*r*	σ_p^- [a]
(**2a**)	Me	0.65	1.01	0.999	0.71	0.73	0.997	0.64	1.72	0.999	−0.10[b]
(**2b**)	H	1.07	1.03	0.998	1.07	0.76	0.998	1.06	1.78	0.998	0.00
(**2b**)	H[c]	1.00	1.00	0.999	1.00	0.86	0.997	0.90	1.70	0.998	0.00
(**2c**)	Br	2.05	0.94	0.992	1.94	0.39	0.982	2.02	1.55	0.986	0.35
(**2d**)	$CONH_2$	3.30	0.93	0.998	3.04	0.30	0.994	2.99	1.28	0.996	0.55
(**2e**)	CO_2Me	3.90	1.11	0.998	3.71	0.72	0.995	3.58	1.68	0.997	0.71
(**2f**)	Ac	4.08	0.95	0.993	3.57	0.22	0.994	3.64	1.25	0.989	0.85
(**2g**)	SO_2Me	4.46	0.99	0.999	3.97	0.29	0.995	4.01	1.31	0.997	0.85
(**2h**)	CN	4.43	0.96	0.998	3.85	0.20	0.998	4.00	1.27	0.998	0.92
(**2i**)	NO_2	6.66	1.04	0.987	7.07	0.58	0.987	6.55	1.53	0.986	1.27
(**2i**)	NO_2[c]	6.83	1.00	0.990	7.03	0.64	0.980	6.73	1.52	0.994	1.27

[a] Values from ref. 1(*f*). [b] Value from ref. 1(*o*). [c] In aqueous perchloric acid.

Table 2. pK_{BH^+} values of 3-substituted 2-(*N*,*N*-dimethylamino)-5-nitrothiophenes (**3a**–**g**) and (**3i**) in aqueous perchloric acid.

		HAFM			BOM			EAM		
Compound	X	$-pK_{BH^+}$	*m*	*r*	$-pK_{BH^+}$	$-\varphi$	*r*	$-pK_{BH^+}$	*m**	*r*
(**3a**)	Me	0.86	0.72	0.972	0.79	0.03	0.984	0.83	1.16	0.960
(**3b**)	H[a]	1.64	0.60	0.999	1.60	−0.35	0.993	1.60	0.72	0.996
(**3c**)	Br	3.06	0.82	0.996	2.85	0.20	0.990	2.75	1.03	0.994
(**3d**)	$CONH_2$	2.80	0.64	0.998	2.70	−0.17	0.994	2.70	0.76	0.996
(**3e**)	CO_2Me	4.21	1.00	0.998	4.09	0.53	0.994	4.08	1.37	0.996
(**3f**)	Ac	4.28	1.00	0.999	4.06	0.51	0.995	4.14	1.40	0.997
(**3g**)	SO_2Me	6.13	1.00	0.996	6.04	0.58	0.989	6.20	1.55	0.991
(**3i**)	NO_2[a]	6.95	0.95	0.999	6.70	0.34	0.986	7.01	1.43	0.999

[a] Data from ref. 3.

Table 3. pK_{BH^+} values of 3-substituted 5-nitro-2-piperidinothiophenes (**4a**–**g**) and (**4i**) in aqueous sulphuric acid.

		HAFM			BOM			EAM		
Compound	X	$-pK_{BH^+}$	*m*	*r*	$-pK_{BH^+}$	$-\varphi$	*r*	$-pK_{BH^+}$	*m**	*r*
(**4a**)	Me	1.02	0.81	0.999	1.04	0.26	0.990	0.96	1.17	0.990
(**4b**)	H	1.92	0.81	0.999	1.93	0.23	0.997	1.87	1.20	0.997
(**4b**)	H[a]	1.75	0.68	0.998	1.73	−0.04	0.994	1.75	0.91	0.997
(**4c**)	Br	2.91	1.01	0.994	2.85	0.60	0.993	2.97	1.80	0.992
(**4d**)	$CONH_2$	2.69	0.87	0.998	2.64	0.30	0.995	2.48	1.22	0.992
(**4e**)	CO_2Me	3.91	1.24	0.999	3.71	0.99	0.999	3.42	1.86	0.999
(**4f**)	Ac	3.48	1.09	0.999	3.32	0.68	0.995	3.09	1.57	0.995
(**4g**)	SO_2Me	6.26	1.30	0.999	6.19	0.98	0.997	6.43	2.11	0.998
(**4i**)	NO_2	6.66	1.04	0.987	7.07	0.58	0.987	6.55	1.53	0.986
(**4i**)	NO_2[a]	6.83	1.00	0.990	7.03	0.64	0.980	6.73	1.52	0.994

[a] In aqueous perchloric acid.

the protonation site) in aqueous sulphuric acid: a comparison between the acidities of 5-substituted 2-(*N*,*N*-dimethylamino)-3-nitro-(**1**) and 3-nitro-2-piperidinothiophenes (**2**) could give information on the influence of the structure of the amino group and of the acid used.

Results

The study of the protonation reaction of some 5-substituted 3-nitro-2-piperidinothiophenes (**2**) has been carried out in aqueous sulphuric acid. Some measurements have also been carried out in aqueous perchloric acid (see Table 1) and the obtained data are much the same within experimental uncertainty, as required by the definition of pK_{BH^+}.[4] The results obtained (Table 1) show a large dependence of the basicity (some six orders of magnitude in K_{BH^+}) on the substituent and give a good l.f.e. correlation [equation (1)] with the thiophenic σ_p^- value.[1f]

$$(pK_{BH^+})_{(2)} = (4.16 \pm 0.23)\sigma_p^- + (0.90 \pm 0.17) \quad (1)$$
$$(r\ 0.989,\ n\ 9,\ \text{C.L.} > 99.9\%)$$

The pK_{BH^+} values used in l.f.e. correlations are those calculated by HAFM. It must be noted that our data analysed by the three classical methods HAFM, BOM, and EAM generally gave nearly coincident results. However, it has been observed that in many cases the pK_{BH^+} values obtained by the HAFM method differ from those obtained by the EAM method, particularly for weak bases. In these cases HAFM often works[8,9] better than EAM or BOM.

The study of the protonation reaction of some 3-substituted 2-(*N*,*N*-dialkylamino)-5-nitrothiophenes (**3**) and (**4**) was carried

Table 4. Physical data for 5-substituted-3-nitro- (**2**) and 3-substituted-5-nitro-(**4**) 2-piperidinothiophenes.

		(**2**)		(**4**)	
Compound	X	Water ε ($\lambda_{max.}$/nm)	Methanol ε ($\lambda_{max.}$/nm)	Water ε ($\lambda_{max.}$/nm)	Methanol ε ($\lambda_{max.}$/nm)
a	Me	6 400(438)	6 020(410)	28 400(463)	14 600(436)
b	H	5 940(422)	5 620(398)	32 600(454), 29 700(480)	31 600(448)
c	Br	6 260(432)	6 030(404)	15 400(474)	12 600(426)
d	$CONH_2$	6 170(416)	5 750(394)	27 600(460)	16 200(432)
e	CO_2Me	5 890(416)	5 750(392)	19 200(448)	16 600(420)
f	Ac[a]	7 300(414)	7 070(388)	19 800(450)	16 700(424)
g	SO_2Me	6 230(404)	6 030(384)	16 500(428)	13 200(404)
h	CN	6 370(410)	6 170(386)		
i	NO_2	14 300(385), 13 400(445)	15 800(380)	14 300(385), 13 400(445)	15 800(380)

[a] (**4f**), orange, m.p. 126 °C (from MeOH) (see also *Materials* in the Experimental section).

out in either aqueous perchloric or sulphuric acid (see above). The results obtained (Tables 2 and 3) show again a large dependence of the measured basicity on the substituent: in fact, all of the 3-substituted compounds containing an electron-withdrawing substituent at C-3 [(**3c**–**g**) and (**4c**–**g**)] are less basic than the unsubstituted 2-(*N*,*N*-dialkylamino)-5-nitrothiophenes (**3b**) and (**4b**). The measured pK_{BH^+} values for amines (**3**) and (**4**) give fair correlations with σ_p^- [1f] [equations (2) and (3)].

$$(pK_{BH^+})_{(3)} = (4.32 \pm 0.56)\,\sigma_p^- + (1.32 \pm 0.40) \quad (2)$$
$$(r\ 0.953,\ n\ 8,\ \text{C.L.} > 99.9\%)$$

$$(pK_{BH^+})_{(4)} = (3.87 \pm 0.76)\,\sigma_p^- + (1.44 \pm 0.53) \quad (3)$$
$$(r\ 0.902,\ n\ 8,\ \text{C.L.} > 99\%)$$

The correlation observed for amines (**3**) is better than for (**4**), as expected on the ground of the smaller steric interactions occurring between the amino group and 3-X substituents in the case of compounds (**3**) as compared with (**4**).

It should be noted that these amines do not all follow the H_0''' acidity function. The expected deviations for the substituents hydrogen (X = H), which offers no steric hindrance, and carboxamide (X = $CONH_2$), for which there might well be some overlap between nitrogen protonation of the amino and oxygen protonation of the amido groups, have been observed. Indeed it is well known that amides are not Hammett bases.[11]

Discussion

The results obtained (Table 1) for the protonation reaction of some 5-substituted 3-nitro-2-piperidinothiophenes (**2**) parallel those observed[3] for the corresponding 2-(*N*,*N*-dimethylamino) compounds (**1**). The trends in the two series are similar, as a good l.f.e.r. between the relevant pK_{BH^+} values indicates (*n* 7, *r* 0.987, C.L. > 99.9%); moreover the slope near to unity (*s* 1.04 ± 0.08) confirms that the effect of the substituent is independent of the nature of the basic nitrogen atom (in both cases tertiary, but one taking part in a ring system and the other not). On the other hand both the value calculated for the intercept (*i* −1.01 ± 0.36) and the direct comparison between amines of the two series containing the same 5-X-substituent (average $|\Delta pK_{BH^+}|$, 0.8) indicate that piperidino derivatives are stronger bases than *N*,*N*-dimethylamino derivatives. This significant difference does not seem to depend on external factors: both classes of compounds show very close m^* values [1.47 ± 0.10 and 1.49 ± 0.21 for (**1**) and (**2**), respectively], indicating that similar solute–solvent interactions[10] occur in the two series. These values of m^* are relatively high, showing low solvation requirements[10] for the conjugate acids, BH^+, of our bases. A comparison with some selected literature m^* values reported in a recent review[10] might be useful. The present m^* values are nearly the same as those reported for pyridinium (1.4) and tertiary ammonium ions (1.4 for Me_3NH^+), as expected. Significantly lower values were reported for anilinium (1.0) and methylammonium (1.0) ions which, of course, are much more strongly solvated by hydrogen bonding. The lowest values are those reported for hydronium (0) or other oxonium ions (0.22 for Et_2OH^+ and 0.14 for $EtOH_2^+$) which are the most strongly solvated ions in aqueous solutions. Considering the fact that the difference in the pK_{BH^+} values[12] between piperidine and dimethylamine is only 0.4 one can suppose that the larger differences observed between piperidino- (**2**) and *N*,*N*-dimethylaminothiophenes (**1**) depend on the differences in proximity effects between amino and nitro groups.

An examination of molecular models shows that piperidino is larger than *N*,*N*-dimethylamino, therefore there are larger steric interactions (and consequently smaller electronic interactions) between piperidino and nitro groups than between *N*,*N*-dimethylamino and nitro groups: *i.e.* the 3-nitro group affects (lowers) the basicity of 2-piperidinothiophenes (**2**) less than that of 2-(*N*,*N*-dimethylamino)thiophenes (**1**).*

The above interpretation of $|\Delta pK_{BH^+}|$ is confirmed by the results from an examination of u.v.–visible spectra. 2-(*N*,*N*-Dimethylamino)-5-nitrothiophene (**3b**)[13] and 5-nitro-2-piperidinothiophene (**4b**) (Table 4) show similar values of $\lambda_{max.}$ (444 and 448 nm, respectively) and log ε (4.49 and 4.50, respectively) in MeOH, indicating that the interactions between amino and nitro groups in a quasi-*para* relation are practically the same [*i.e.* when there are no direct steric interactions the chromophore $\overset{+}{\geqslant}N{=}C(2) \longrightarrow C(5){=}NO_2^-$ is not affected by substitution at the nitrogen atom of the amine function]. In contrast 2-(*N*,*N*-dimethylamino)-3-nitrothiophene (**1b**)[13] and 3-nitro-2-piperidinothiophene (**2b**) (Table 4) show a significant difference in log ε (3.81 and 3.75, respectively), indicating that the electronic interactions in the chromophore [$\overset{+}{\geqslant}N{=}C(2) \longrightarrow C(3){=}NO_2^-$] in an *ortho*-relation, due to steric interactions, are not independent of the substituent at the nitrogen atom of the amine function. The more bulky the tertiary amine, the smaller

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* In contrast, the difference in pK_{BH^+} values between 2-(*N*,*N*-dimethylamino)-5-nitrothiophene (**3b**) and 5-nitro-2-piperidinothiophene (**4b**) ($|\Delta pK_{BH^+}| < 0.2$) is lower than that observed between dimethylamine and piperidine, indicating that the electron-withdrawing 5-nitro-2-thienyl group exerts a levelling effect on the acidity.

Table 5. DSP analysis[a] of pK_{BH^+} data for amines (**1**)–(**4**).

Series	$\rho_I \pm s_\rho$	$\rho_R \pm s_\rho$	$i \pm s_i$	n	R	F	C.L.	λ
(**1**)	3.42 ± 0.45	4.75 ± 0.42	1.90 ± 0.17	7	0.9952	209	99.95	1.4
(**2**)	3.96 ± 0.54	4.34 ± 0.51	0.93 ± 0.19	9	0.9895	141	99.95	1.1
(**3**)	5.84 ± 1.12	3.01 ± 1.00	1.15 ± 0.38	8	0.9680	37.2	99.9	0.52
(**4**)	5.98 ± 1.49	2.05 ± 1.33	1.21 ± 0.50	8	0.9362	17.8	99.0	0.34

[a] ρ_I, ρ_R, Susceptibility constants; *i*, intercept; s_ρ and s_i, standard deviations; *n*, number of points; *R*, correlation coefficient; *F*, value for *F*-test; C.L. confidence level; $\lambda = \rho_R/\rho_I$.

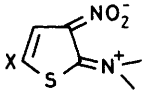
Table 6. Physical data[a] for 3-substituted 2-(*N*,*N*-dimethylamino)-5-nitrothiophenes (**3a**–**g**) and (**3i**).

Compound	X	Crystallization solvent	Colour	M.p./°C
(**3a**)	Me	light petroleum[c]–benzene	red	92–93
(**3b**)	H[b]	benzene	orange	138–139
(**3c**)	Br	methanol	red–orange	114–115
(**3d**)	$CONH_2$	dioxane–methanol	orange	249–250
(**3e**)	CO_2Me	light petroleum–benzene	orange	93–94
(**3f**)	Ac	methanol	yellow	146–147
(**3g**)	SO_2Me	methanol–dioxane	yellow	173
(**3i**)	NO_2[b]	chloroform	orange	153–154

[a] All the compounds gave correct analyses. [b] Data from L. Lunazzi, D. Macciantelli, D. Spinelli, and G. Consiglio, *J. Org. Chem.*, 1982, **47**, 3759. [c] Light petroleum refers to the fraction boiling in the range 40–60 °C.

the electronic interactions: indeed, on going from (**1b**) to (**2b**) a hypsochromic effect ($\Delta\varepsilon$ *ca.* 15%) is observed.

The presence of an electron-withdrawing substituent at C-3 causes an electronic interaction (through-resonance) with the *N*,*N*-dialkylamino group at C-2 [see structures (**5**) and (**6**)], and



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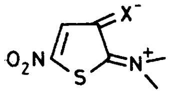

(6)

this interaction is enhanced by the hyper-*ortho* effect.[1i–r] Depending on the bulkiness of the groups at C-2 and C-3 this electronic interaction can or cannot be affected by steric effects (steric inhibition of resonance and/or solvation). Therefore the larger dialkylamino group (piperidino as compared with *N*,*N*-dimethylamino) can give higher steric interactions with the substituent at C-3. With a bulky substituent the steric effects can prevail over the electronic ones in structure (**6**) and as a consequence the statistical parameters improve on exclusion of some substituents from the *ortho*-correlations.

Inspection of Tables 2 and 3 shows that the pK_{BH^+} values calculated for the two series of '*ortho*-like-substituted' amines are generally very similar for a given X, as also supported by the value of the intercept (i 0.11 ± 0.26) and the slope (s 0.93 ± 0.06) obtained by correlating $(pK_{BH^+})_{(4)}$ with $(pK_{BH^+})_{(3)}$ (r 0.987, n 8, C.L. > 99.9%).

This result seems to arise from some balancing between different factors. In fact the compounds of the two series show different m^* values [average values 1.18 ± 0.32 and 1.56 ± 0.35 for (**3**) and (**4**), respectively]; on the other hand the spread of m^* values within each series is rather high. This indicates important differences in solute–solvent interactions.[10]

An examination of the spectroscopic (u.v.–visible) behaviour confirms this interpretation. Data in Table 4 show that compounds (**2a**–**i**) (variable substituent in a *para*-like position) independently of the present substituent show a parallel spectroscopic behaviour in water and in methanol [a blue shift on going from water to methanol, a small difference in ε-values ($\Delta\varepsilon \leqslant 5\%$)]. Moreover in the case of (**2b**) it has been observed that the influence of the solvent is small even on going to very different solvents such as dioxane–water (50:50) mixture or benzene.[14] In contrast, compounds (**4a**–**g**) and (**4i**) (variable substituent in an *ortho*-like position) show a behaviour dependent on the nature of the present substituent. In particular, (**4c**, **e**–**g**) show much the same spectroscopic behaviour as compounds (**2a**–**g**); in contrast (**4a**) and (**4d**) show a large variation in their spectroscopic properties on changing the solvent from water to methanol (in particular very large variations in ε-values). In the case of (**4b**) the spectroscopic properties are largely affected on going from protic solvents (water or methanol) to water–dioxane (50:50) mixture and benzene.[14]

The results observed for compounds (**1**) and (**2**) (average $|\Delta pK_{BH^+}|$ 0.8) would suggest significant differences in the interactions between the dimethylamino group and 3-NO_2 substituent and between the piperidino group and 3-NO_2 substituent (see also above, the discussion of u.v.–visible spectra).

Therefore the close resemblance between pK_{BH^+} measured for compounds (**3**) and (**4**) is probably related to a balance between different external (solvation) and internal factors (electronic effects depending on steric interactions) which causes the observed situation.

Finally a comparison between the pK_{BH^+} values calculated for the unsubstituted (X = H) thiophenes (**1b**), (**2b**), (**3b**), and (**4b**) appears interesting. The results obtained are well interpreted taking into account the different steric requirements of the two tertiary amino groups considered. In the case of the relatively small dimethylamino group, *ortho*- (**1b**) and *para*-like (**3b**) isomers show the same pK_{BH^+} value, indicating similar *para*-like and hyper-*ortho* interactions in thiophene compounds. In contrast in the case of the bulky piperidino group the *ortho* and *para*-like isomers show different pK_{BH^+} values ($|\Delta pK_{BH^+}|$ 0.7), indicating steric interactions for the *ortho*-like (**2b**) isomer: in fact these effects do not operate in 5-nitro-2-piperidinothiophene [(**4b**): *para*-like isomer], which shows much the same pK_{BH^+} value as do 2-(*N*,*N*-dimethylamino)-3- (**1b**) and -5-nitrothiophene (**3b**).

Our data allow some final remarks to be made. Following the suggestion of one of the referees, we have treated the pK_{BH^+} data for compounds (**1**)–(**4**) according to the DSP equation (4)[2d]

$$pK_{BH^+} = \rho_I\sigma_I + \rho_R\sigma_R + i \qquad (4)$$

where $\sigma_R = \sigma_p^-$(thiophenic) $- \sigma_I$.

This 'unconstrained' form of the DSP equation allows one to make a homogeneous comparison between the regression parameters obtained by the dual- and single-parameter treatments and to have an unambiguous response as to the statistical improvement of the correlation.

The results of the DSP treatment are reported in Table 5. The confidence levels obtained for all the four DSP correlations indicate that from a statistical point of view there is no real superiority of the DSP over the single-parameter treatment. However, the 'blending coefficients,' $\lambda = \rho_R/\rho_I$, calculated for *ortho*-like substituted compounds (**3**) and (**4**), are *different* from those relative to *para*-like substituted derivatives (**1**) and (**2**). If this difference is not fortuitous, it indicates, as expected, a minor role of resonance as compared with a major role of inductive effects in the *ortho*-like substituted compounds and a minor importance for resonance effects in the more crowded *ortho*-like substituted 2-piperidino- as compared with 2-(*N*,*N*-dimethylamino) derivatives.

Experimental

Materials.—Compounds (**3a–g**) and (**3i**) and (**4f**) were prepared and purified according to the general methods previously reported.[3,15] The relevant physical data are reported in Tables 4 and 6.

pK_{BH^+} *measurements.*—Perchloric (or sulphuric) acid–water mixtures were prepared by dilution of commercial concentrated acids with redistilled water and titrated with standard borax and/or sodium hydroxide.

When an aqueous solution of aminothiophene (B) was diluted without due caution with conc. $HClO_4$ (or H_2SO_4) to make up a solution suitable for spectral measurements, in some cases there was evidence of a relatively fast decomposition of B (or BH^+). The samples were therefore prepared by dilution of equivalent small portions (0.1–1 cm^3) of an aqueous solution of B with the appropriate acid solution. Solutions > 3 mol dm^{-3} in $HClO_4$ (or H_2SO_4) were cooled in an ice-bath before and during the addition. The resulting cold solution was then thermostatted to 25 ± 0.1 °C and the volumetric flask was eventually filled to the mark with water. The solutions were then transferred into 10 mm glass cells and the spectra recorded against acid solutions of the same molarity. Ionization ratios, calculated at least at three wavelengths within the range $\lambda = (\lambda_{max.})_B \pm 20$ nm (see Table 4), were shown to be independent of λ. In spite of the above precautions the absorbance of B, at a fixed λ, was not independent of time for substrates where X = Me and X = H and Br in $HClO_4$ (or H_2SO_4) > 4 mol dm^{-3} and >6 mol dm^{-3}, respectively. In these cases the protonation reactions were followed only up to 4 and 5 mol dm^{-3} acid, respectively. We conclude from this and previous[3] evidence that the decomposition reaction of B (or BH^+) is important (only above a definite acid concentration) when the nitro group is in position 5 and X is not a strong electron-withdrawing group.

Data treatments (according to HAFM, BOM, and EAM methods) and corrections were made as previously described.[3]

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