

Redetermination of σ^+ constants for heteroaromatic rings. Oxygen-17 chemical shifts of trifluoroacetyl substituents and solvolytic reactivities of heteroaromatic analogs of 1-*tert*-butylbenzyl halides

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Abstract: The replacement substituent constants σ^+ , for some five-membered heteroaromatic rings were determined from ^{17}O NMR substituent chemical shifts of the carbonyl group in trifluoroacetyl derivatives, and from log *k*s for solvolyses of heteroaryl analogs of 1-*tert*-butylbenzyl bromide and chloride. No agreement with literature values could be found. Preliminary accounts of such observations are given.

Five-membered heteroaromatic rings could be considered to be derived from the replacement of the -CH=CH- moiety in benzene by a specific heteroatom. (1) Heteroaromaticity and heteroaromatic reactivity have long been the theme of continuous interest, as may be exhibited by the appearance of recent reviews(2,3) and communications.(4) Applications of Hammett-type correlation analyses to heterocyclic systems have been reviewed.(1,5,6) The heteroatom in the molecule might be regarded as a substituent, and the replacement substituent constants(1), or aryl values(7), for heteroaryl groups were determined and were compiled(6) nearly twenty years ago. Those values exhibit large variations, e. g., $\sigma^+ = -0.13$ to -1.32 for 2-furyl group, much larger than that has been found for substituent groups in benzene derivatives.(8) The heteroatom is likely to play an important role, and to our knowledge, has not been examined in detail. Therefore, we undertook to redetermine certain σ^+ constants for five-membered heteroaryl groups by using approaches that are differed from those employed by previous authors.

In a previous study we observed an excellent linear correlation of oxygen-17 substituent chemical shifts (SCS) for various trifluoroacetyl derivatives of substituted benzenes with σ^+ constants.(9) A linear relationship was obtained, (eqn. 1) which could be useful in estimating the σ^+ value for heteroaromatic ring systems.

$$\delta = 24.6 \sigma^+ + 556.3 \quad (1)$$

Four trifluoromethyl ketones, namely, 2- and 3-trifluoroacetylfuran (1-2) and 2- and 3-trifluoroacetylthiophene (3-4) were prepared, (10) and the ^{17}O NMR chemical shifts were measured (9) according to literature procedures. The observed $\delta(^{17}\text{O})$ values are listed in TABLE 1. From the chemical shift of carbonyl oxygen σ^+ constants for heteroaryl groups were calculated.

TABLE 1. Oxygen-17 chemical shifts and σ^+ constants for some heteroaromatic compounds.

ArCOCF ₃	Ar	$\delta(\text{C=O})$	$\delta(\text{other})$	$\sigma^+(\text{Calcd})$	$\sigma^+(\text{Lit})$	
					a	b
<u>1</u>	2-furyl	529.6	246.3	-1.09	-0.85	
<u>2</u>	3-furyl	549.2	253.4	-0.29	-0.44	
<u>3</u>	2-thienyl	531.2		-1.02	-0.76	-0.80
<u>4</u>	3-thienyl	543.6		-0.52	-0.44	-0.47

^aRef.11. ^bRef.12

Inconsistency between calculated and literature (6) values is obvious, even for those derived from solvolytic rate constants. (11,12) Since σ^+ constants were first defined from $\log k_s$ for solvolyses of *tert*-cumyl (2-aryl-2-propyl) derivatives, (13) a detailed study on the observed disagreement seemed to be worthwhile.

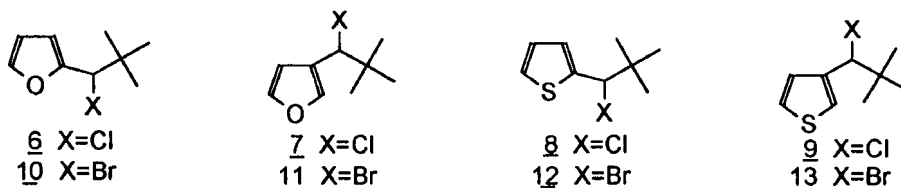
The influence of solvents on chemical phenomena in solution has been studied by quite a number of researchers for many years. (14) Grunwald-Winstein equations (eqns 2 and 3), in which k is the rate constant, Y is the solvent ionizing power and N is the solvent nucleophilicity, have widely been used as mechanistic probes for characterizing solvolytic processes. (15)

$$\log (k/k_0) = mY \quad (2)$$

$$\log (k/k_0) = mY + lN \quad (3)$$

To study the solvolytic mechanism of benzylic substrates, four Y_{BnX} scales have been developed for chlorides (16), bromides (17), *p*-nitrobenzoates (18) and tosylates (19), respectively. Certain advantages of using these new scales, such as the detection of nucleophilic solvent intervention in the solvolysis of some tertiary benzylic systems, have been demonstrated by the observation of deviation from excellent linear correlations ($R \geq 0.99$) in $\log k - Y_{\text{BnX}}$ plots. (20,21) Therefore, it is highly desirable to examine the existence of solvent intervention in solvolysis of 1-arylethyl substrates, from which many literature values of σ^+ constants (6) for heteroaryl groups have been determined. Indeed, a preliminary study on the solvolysis of 1-chloro-1-(2-thienyl)ethane (5) showed dispersion in the plot when eqn. 2 was used, despite the availability of only eight data points due to the high reactivity.

Since the limiting S_N1 character for the solvolysis of 1-aryl-2,2-dimethyl-1-propyl substrates has been proved, (19,22) the 1-heteroaryl analogs, 1-(2-furyl)-, 1-(3-furyl)-, 1-(2-thienyl)-, and 1-(3-thienyl)-2,2-dimethylpropyl chlorides (6-9) and the corresponding bromides (10-13) were prepared for the purpose of this investigation. With the exception of 10, which was too reactive to be purified for kinetic study, other halides were found to have acceptable elemental analyses and spectral data in line with the correct structures.



Solvolyses were carried out in various solvent systems and the first order rate constants were measured by conductimetric method at least in duplicate ($\pm 2\%$). Pertinent data at 25°C are given in TABLE 2. Only poor correlations with Y_X values (23) using eqn. 2, $R \leq 0.97$, could be found. There was no improvement even if eqn. 3 was used. However, the plot of $\log k_s$ against Y_{BnCl} (16) or Y_{BnBr} (17) (24) displayed excellent linear correlations in most cases. The results are summarized in TABLE 3.

TABLE 2. Rate Constants (/s) for solvolyses of halides 6-9 and 11-13.

Solvent [#]	Substrate						
	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>	<u>11</u>	<u>12</u>	<u>13</u>
a	4.60×10^{-3}	5.44×10^{-6}	8.04×10^{-4}	2.50×10^{-6}	1.72×10^{-4}	2.45×10^{-2}	7.60×10^{-5}
b	5.75×10^{-2}	6.20×10^{-5}	9.95×10^{-3}	2.69×10^{-5}	1.90×10^{-3}	0.275	7.80×10^{-4}
c	0.261	2.67×10^{-4}	4.48×10^{-2}	1.00×10^{-4}	7.18×10^{-3}		2.81×10^{-3}
d		9.45×10^{-4}	0.201	3.37×10^{-4}	2.35×10^{-2}		8.82×10^{-3}
e	1.10×10^{-3}	1.43×10^{-6}	2.03×10^{-4}	5.50×10^{-7}	6.50×10^{-5}	1.05×10^{-2}	2.34×10^{-5}
f	2.30×10^{-2}	2.26×10^{-5}	4.13×10^{-3}	8.60×10^{-6}	9.44×10^{-4}	0.154	3.38×10^{-4}
g	0.180	1.60×10^{-4}	3.04×10^{-2}	6.00×10^{-5}	5.70×10^{-3}	1.06	2.03×10^{-3}
h		8.57×10^{-4}	0.156	3.05×10^{-4}	2.90×10^{-2}		1.02×10^{-2}
i	8.93×10^{-2}	7.68×10^{-5}	1.85×10^{-2}	3.95×10^{-5}	2.97×10^{-3}		1.21×10^{-3}
j	0.589	4.51×10^{-4}	9.55×10^{-2}	2.00×10^{-4}	1.28×10^{-2}	0.560	5.14×10^{-3}
k		1.50×10^{-3}	0.320	6.50×10^{-4}	3.87×10^{-2}		1.50×10^{-2}
l		1.83×10^{-2}		7.85×10^{-3}			
m		3.95×10^{-2}		2.87×10^{-2}	0.337		0.269
n		5.31×10^{-3}		3.38×10^{-3}	5.06×10^{-2}		3.62×10^{-2}
o		7.42×10^{-4}	0.345	4.58×10^{-4}	1.12×10^{-2}		7.52×10^{-3}
p	0.219	1.50×10^{-4}	4.47×10^{-2}	9.04×10^{-5}	2.94×10^{-3}	0.922	1.59×10^{-3}

[#]For abbreviation of solvent systems: a, 100E; b, 90E; c, 80E; d, 70E; e, 90A; f, 80A; g, 70A; h, 60A; i, 100M; j, 90M; k, 80M; l, 60M; m, 100T; n, 80T20E; o, 60T40E; p, 40T60E; and A, acetone; E, ethanol; M, methanol; T, 2,2,2-trifluoroethanol, the numbers denote the volume percent of the specific solvent in the mixture.

TABLE 3. Correlation analyses (eqn 2) of 6-9 and 11-13 against Y_{BnX} .

Substrate	m	R	SD	n
<u>6</u>	0.967	0.990	0.051	9
<u>7</u>	0.745	0.978	0.044	15
<u>8</u>	0.952	0.992	0.037	13
<u>9</u>	0.789	0.990	0.032	15
<u>11</u>	0.797	0.976	0.049	15
<u>12</u>	1.051	0.997	0.038	7
<u>13</u>	0.864	0.991	0.032	15

Obviously, 3-furyl derivatives are different from others. For 7 and 11 better correlations could be obtained, if eqn. 3 with the use of Y_{BnX} and N_{T} was employed. The improvement, however, is probably an artefact because the bulky tertiary butyl group would make the intervention of nucleophilic solvent less feasible. The representative plots for excellent ($R = 0.997$ for 12) and relatively poor ($R = 0.976$ for 11) correlations are illustrated in FIGURE 1.

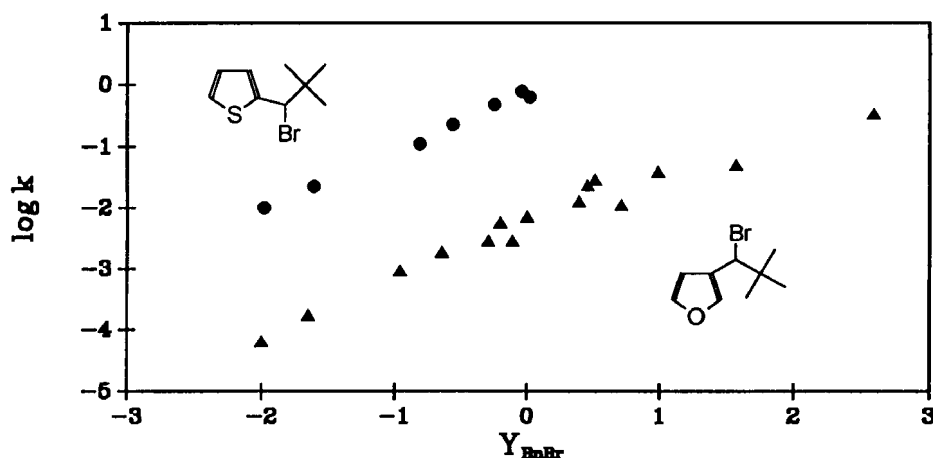


FIGURE 1. Correlations of $\log k$ against Y_{BnBr} .

The σ^+ constants for heteroaryl rings could thus be determined by using 6-9 and 11-13 as references, in which no significant solvent intervention would be present in the solvolysis. The rate constants for the solvolysis of several 1-aryl-2,2-dimethyl-1-propyl chlorides (14) (25) and bromides (15) (26) have already been measured, and could be used for this purpose. From the plots of $\log k$ s for 1-(4-methoxyphenyl)-, 1-(4-methylthiophenyl)-, 1-(4-methylphenyl)- and 1-(3,5-dimethylphenyl)-2,2-dimethyl-1-propyl bromides versus σ^+ constants, good linear correlations ($R \geq 0.998$) were observed in many solvents. Similar results were also obtained from 1-(4-methoxyphenyl)-, 1-(4-methylthiophenyl)-, and 1-(4-methylphenyl)-2,2-dimethyl-1-propyl chlorides. The ρ values are very much alike in different cases. (TABLE 4) Hence, the

TABLE 4. Estimation of σ^+ constants for some heteroaryl groups.

Reference	Solvent [#]	ρ -value	σ^+ constant			
			<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
<u>14</u>	80E	-7.43	-1.03	-0.629	-0.929	-0.572
	70E	-7.30		-0.628	-0.947	-0.566
	70A	-7.78	-1.03	-0.638	-0.931	-0.583
	60A	-7.73		-0.643	-0.935	-0.585
	90M	-7.33	-1.03	-0.605	-0.922	-0.557
	80M	-7.34		-0.597	-0.920	-0.564
<u>15</u>	80E	-7.39		-0.612		-0.557
	70E	-7.57		-0.613		-0.557
	80A	-7.18		-0.618	-0.926	-0.556
	60A	-7.54		-0.622		-0.562
	90M	-7.45		-0.584		-0.531
	80M	-7.47		-0.572		-0.517

[#]See TABLE 2.

new σ^+ constants for 2-furyl, 3-furyl, 2-thienyl and 3-thienyl groups were obtained from the corresponding log k_s by extrapolation. (TABLE 4) The mean value of σ^+ for 2-furyl is -1.03 from chloride, for 3-furyl is -0.623 from chloride or -0.606 from bromide, for 2-thienyl is -0.930 from chloride or -0.926 from bromide, for 3-thienyl is -0.568 from chloride or -0.549 for bromide.

Consequently, the σ^+ constants for the four heteroaryl groups from solvolyses can be redetermined as the average of the two data obtained. The comparison of the σ^+ constants derived from oxygen-17 NMR chemical shifts and from solvolyses is shown in TABLE 5.

TABLE 5. Comparison of σ^+ constants for heteroaryl groups 1-4.

Method	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
¹⁷ O NMR	-1.09	-0.29	-1.02	-0.52
solvolysis	-1.03	-0.615	-0.928	-0.559

The significant difference exhibited in the case of 3-furyl group is remarkable. It should also be noted from TABLE 3 that poor linear correlation with Y_{BnBr} was realized for 3-furyl substrates 7 and 11. The low aromaticity for furan molecule(2,4) might be relevant to these phenomena. Further study is in progress.

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