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Note

Substituent effects on ^{15}N and ^{13}C NMR chemical shifts of 5-phenyl-1,3,4-oxathiazol-2-ones: a theoretical and spectroscopic study

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The synthesis and assignment of ^{15}N and ^{13}C NMR signals of the 1,3,4-oxathiazol-2-one ring in a series of *para*-substituted 5-phenyl derivatives are reported. DFT calculations of ^{15}N and ^{13}C chemical shifts correspond closely to observed values. Substituent effects are interpreted in terms of the Hammett correlation and calculated bond orders. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: ^{13}C NMR; ^{15}N NMR; chemical shifts; DFT calculations; electronic effects; Hammett correlation; 5-phenyl-1,3,4-oxathiazol-2-ones

INTRODUCTION

The transmission of substituent effects in selected azole systems has been studied by a combination of ^{15}N NMR and ^{13}C chemical shift data for 3-phenylisoxazoles[1] and 2-phenyl-1,3,4-oxadiazoles.[2] Hammett correlations established the nature of electronic delocalization, and density functional theory calculations predicted chemical shifts and heterocyclic ring bond orders. We report, herein, the application of these methods to 5-phenyl-1,3,4-oxathiazol-2-ones (**1a–1h**), for which substituent effects have not previously been assessed. These compounds are used in antimicrobial, herbicidal, and polymer cross-linking applications,[3] and they are the precursors of choice for the generation of benzonitrile *N*-sulfides.[4] The synthesis of the desired series was carried out by a standard procedure (Scheme 1).[5]

RESULTS AND DISCUSSION

^{15}N NMR chemical shift analysis

The calculated and experimentally determined ^{15}N chemical shifts for compounds **1a–1h** are listed in Table 1, arranged according to σ_p values.[6] A set of calculated chemical shifts, determined for geometry-optimized compounds, and referenced to the calculated chemical shift of CH_3NO_2 (see experimental section for complete details) are also included in this table. The calculated and experimental ^{15}N shifts fit the relation,

$$\delta_{calcd} = (1.28 \pm 0.03)\delta_{expt} + (52.3 \pm 4.1)$$
$$N = 8, R^2 = 0.999 \quad (1)$$

Consistent with our previous studies of substituted 3-phenylisoxazoles,[1] the range of chemical shifts is fairly narrow (calculated: 22.2 ppm; experimental: 17.1 ppm) and the trend in shifts is consistent with the electron-releasing or electron-withdrawing ability of the phenyl *para* substituent (Y). In keeping with expected electronic effects, electron-withdrawing groups cause ^{15}N signals to appear more deshielded (i.e. less negative values, since CH_3NO_2 is the chemical shift reference) while electron-releasing groups cause ^{15}N signals to appear more shielded. Also consistent with our earlier work, the calculated chemical shifts are regularly higher than the experimental values ($\Delta\delta_{ave.} = 7.28$) but their variation is small ($\Delta\delta_{st.dev} = 1.51$). In accordance with the work of Cheeseman *et al.*,[7] this small systematic deviation derives from the calculated chemical shift of the reference compound (CH_3NO_2), but does not compromise the excellent correlation between theory and experiment. Likewise, the calculated natural charge of the 1,3,4-oxathiazol-2-one ring nitrogen (N-4) is entirely consistent with the increasing electron-donating ability of the Y group and mirrors the observed (and calculated) chemical shifts nicely.

The ^{15}N chemical shifts in Table 1 also display the expected response to σ_p Hammett values and fit the relation,

$$\delta_{expt.} = (14.48 \pm 1.22)\rho - (162.02 \pm 0.45)$$
$$N = 8, R^2 = 0.97 \quad (2)$$

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The strongly positive ρ value is entirely consistent with our observation that ^{15}N chemical shifts are highly sensitive to the electronic nature of the Y group.[8]

These results are congruent with our results for 3-phenylisoxazoles,[1] while also showing some important differences. In the 3-phenylisoxazoles, the polarizing effects of the Y group are attenuated by the isoxazole ring oxygen, resulting in a smaller range of ^{15}N chemical shifts (9.0 ppm) than in the 5-phenyl-1,3,4-oxathiazol-2-ones (17.1 ppm). We attribute this to an increase in the N–O bond order in the 3-phenylisoxazoles as supported by Wiberg bond index calculations.[1]

^{13}C NMR chemical shift analysis

The data presented in Table 2 for the corresponding ^{13}C chemical shifts of compounds **1a–1h** indicate that, once again, the calculated and experimental ranges of chemical shifts agreed closely. Although the range of ^{13}C shifts observed is small, the correlation between the measured chemical shifts and the Hammett σ_p constants for phenyl *para* substituents is good (R^2: C-2, 0.87) or excellent (R^2: C-5, 0.99), with electron-withdrawing substituents causing increased deshielding at both C-2 and C-5, as expected. However, as with the 1,3,4-oxathiazol-2-one ring nitrogen, C-2 and C-5 are more strongly affected by the Y group. In an attempt to understand some of these trends, we performed Wiberg bond index calculations (Table 3).

Several interesting features emerge. First, there is a significant bonding interaction between C-2 and S-3 (greater than O-1/C-2) that is consistent with the participation of the sulfur lone pair in the 2-one carbonyl π system, producing an aromatic system (as shown in resonance structure II, Fig. 1). As the Y group becomes increasingly electron-withdrawing, the electron density at sulfur moves toward nitrogen, leading to a slight increase in the S-3/N-4 bond order, a slight decrease in the C-2/S-3 bond order, and a concomitant increase in the C-2/O-6 bonding in the

Table 1. Experimental and calculated ^{15}N NMR chemical shift (δ) data, Hammett substituent constants, and natural atomic charges of N-4 for 5-phenyl-1,3,4-oxathiazol-2-ones **1a–1h**

Compd.	Y	σ_p[a]	Calcd.[b]	Expt.[c]	Natural charge
1a	Ome	−0.27	−162.53	−167.46	−0.645
1b	Me	−0.17	−156.22	−162.90	−0.637
1c	H	0.00	−153.17	−160.67	−0.633
1d	F	0.06	−155.22	−161.69	−0.636
1e	Cl	0.23	−152.35	−159.38	−0.633
1f	Br	0.23	−152.00	−159.02	−0.632
1g	CF_3	0.54	−145.93	−154.49	−0.626
1h	NO_2	0.78	−140.37	−150.39	−0.621

[a] Ref. 6.

[b] B3LYP/6-311++g(2d,2p); relative to calculated CH_3NO_2 = −153.31 ppm.

[c] Relative to CH_3NO_2 = 0.00 ppm.

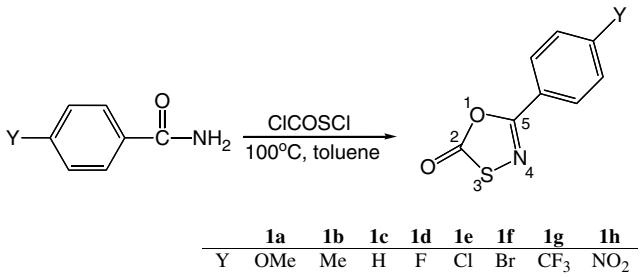
Table 2. Experimental and calculated ^{13}C NMR chemical shift (δ) data and Hammett substituent constants of C-2 and C-5 for 5-phenyl-1,3,4-oxathiazol-2-ones **1a–1h**

			C-2		C-5	
Compd.	Y	σ_p[a]	Calcd[b]	Expt.[c]	Calcd[b]	Expt.[c]
1a	OMe	−0.27	164.03	157.23	181.74	174.13
1b	Me	−0.17	164.40	157.49	181.50	173.94
1c	H	0.00	164.30	157.36	181.27	173.80
1d	F	0.06	163.27	156.39	181.08	173.59
1e	Cl	0.23	163.51	156.41	180.98	173.40
1f	Br	0.23	163.45	156.55	180.90	173.40
1g	CF_3	0.54	163.25	156.01	180.50	173.03
1h	NO_2	0.78	162.85	155.33	180.06	172.60

[a] Ref. 6.

[b] B3LYP/6-311++g(2d,2p); relative to calculated tetramethylsilane = 183.37 ppm.

[c] relative to $CDCl_3$ = 77.00 ppm.



	1a	1b	1c	1d	1e	1f	1g	1h
Y	OMe	Me	H	F	Cl	Br	CF_3	NO_2

Scheme 1. Synthesis of 5-phenyl-1,3,4-oxathiazol-2-ones (**1a–1h**).

Table 3. Calculated Wiberg bond orders of 5-phenyl-1,3,4-oxathiazol-2-ones **1a–1h**

Compd.	Y	σ_p[a]	O-1/C-2	C-2/S-3	S-3/N-4	N-4/C-5	C-5/O-1	C-2/O-6	C-5/C-1′
1a	OMe	−0.27	0.926	1.094	1.008	1.670	0.962	1.762	1.091
1b	Me	−0.17	0.922	1.093	1.009	1.684	0.971	1.770	1.071
1c	H	0.00	0.921	1.091	1.011	1.692	0.973	1.772	1.064
1d	F	0.06	0.920	1.090	1.013	1.695	0.975	1.775	1.060
1e	Cl	0.23	0.916	1.091	1.011	1.693	0.976	1.777	1.062
1f	Br	0.23	0.916	1.090	1.013	1.694	0.977	1.778	1.061
1g	CF_3	0.54	0.916	1.090	1.013	1.694	0.977	1.779	1.060
1h	NO_2	0.78	0.914	1.087	1.015	1.698	0.980	1.783	1.055

[a] Ref. 6.

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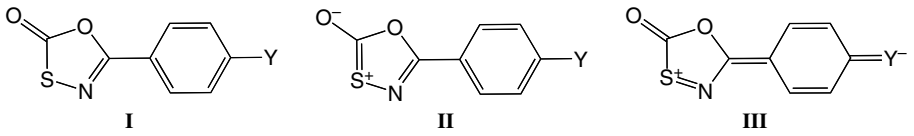

Figure 1. Resonance effects in 5-phenyl-1,3,4-oxathiazol-2-ones.

carbonyl group (structure III). As the 1,3,4-oxathiazol-2-one ring becomes increasingly electron-deficient, the remaining ring bonds, N-4/C-5 and C-5/O-1, show a bond order increase that is significant in magnitude.[9] Although this increase, particularly for N-4/C-5, is not what might be expected from a simple resonance picture (Fig. 1), it is consistent with an overall ring contraction arising from a lowering (by induction) of the C-5 orbital energy, thus enhancing the π character of the N-4/C-5 (and C-5/O-1) bonds. Moreover, this pattern was observed in our studies on 3-phenylisoxazoles.[1] However, unlike the 3-phenylisoxazole ring, which attenuates both electron-donating and -withdrawing substituents, the bond orders in the 1,3,4-oxathiazol-2-one ring system change monotonically over the range of Y groups we studied. For this reason, all of the chemical shifts (^{15}N and ^{13}C) of the oxathiazol-2-one ring system are more profoundly influenced by the nature of the phenyl substituent.

EXPERIMENTAL

Melting points were determined on a MelTemp apparatus. Extracts were dried over Na_2SO_4, and solvents were removed by rotary evaporation at reduced pressure. Product purities were determined by gas chromatography–mass spectrometry analysis on a Hewlett Packard HP 6890 system equipped with a HP-5MS cross-linked diphenyl (5%) dimethyl (95%) polysiloxane capillary column (30 m × 0.25 mm × 0.25 μm film), a 5973 mass selective detector, and a HP Kayak XA computer.

Compounds

*Preparation of 5-phenyl-1,3,4-oxathiazol-2-ones (**1a–1h**)* 5-Phenyl-1,3,4-oxathiazol-2-ones were prepared by a standard procedure employing treatment of substituted benzamides with chlorocarbonylsulfenyl chloride; compounds **1a–1h** have been reported previously.[5] They were purified by recrystallization from an appropriate solvent; their physical constants and spectral data matched literature values.

NMR spectroscopy

NMR spectra were measured at 298 K with a Bruker Avance DRX 500 MHz NMR spectrometer operating at frequencies of 500.630 (^1H), 125.884 (^{13}C), and 50.748 (^{15}N) using a standard 5 mm broadband multinuclear (PABBO) probehead (90° pulse widths: ^1H, 11.5 μs; ^{13}C, 6.0 μs; ^{15}N, 6.0 μs).

Chemical shifts (ppm) were measured relative to internal Me_4Si (^1H) or internal $CDCl_3$ (^{13}C); ^{15}N chemical shifts were measured relative to an external solution of neat CH_3NO_2 in a 1 mm diameter coaxial insert tube. Samples were prepared with concentrations ranging from 14 mg (Y = NO_2) to 63 mg (Y = CH_3) per 400 μl of $CDCl_3$ as solvent. ^{15}N data were acquired at natural abundance. ^{15}N chemical shifts were measured directly using a standard inverse gated decoupling pulse sequence (zgig), while ^{13}C chemical shifts were measured using a standard power gated decoupling pulse sequence (zgpg30), both from the Bruker pulse sequence library.

Spectral windows were set at 240 ppm for ^{13}C and 500 ppm for ^{15}N. For ^{15}N acquisitions, a total of *ca.* 15 k scans of 16 k data points were collected and then zero-filled to 32 k points prior to Fourier transformation (FT). The recycle delay (*D*1) was set at 5 s, and total acquisition time per sample was *ca.* 21 h. ^{13}C acquisitions collected a total of *ca.* 300 scans of 32K data points and then zero-filled to 64K points prior to FT. The recycle delay (*D*1) was set at 2 s. Chemical shift measurement accuracy for all experiments was estimated at ±0.1 ppm.

Computational methods

All computations were carried out using the Gaussian 03 program[10] and employed the B3LYP functional.[11] Substituted 5-phenyl-1,3,4-oxathiazole geometries were optimized in the gas phase using the very tight convergence criteria (the 6-311++g(2d,2p) basis set was used for all models) and with an ultrafine integration grid. Frequency calculations were performed to demonstrate that the structures represented the minimum energy (no imaginary frequencies were observed). ^{15}N and ^{13}C chemical shifts were calculated using the GIAO method[12–15] and were referenced to the calculated chemical shift of nitromethane (−153.31 ppm) or tetramethylsilane (183.37) optimized at the same level of theory. Wiberg Bond indices[16] and Natural Population Analysis Charges[17] were calculated using NBO 3.1.[18]

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