NMR SPECTROSCOPIC STUDIES OF THIALENE (CYCLOPENTA[*b*]THIAPYRAN) AND ISOTHIALENE (CYCLOPENTA[*c*]THIAPYRAN)

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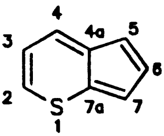
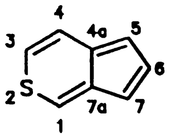
^{1}H and ^{13}C NMR spectral parameters are reported for the S-pseudoazulenes thialene (cyclopenta[*b*]thiapyran) (*I*) and isothialene (cyclopenta[*c*]thiapyran) (*II*). Both compounds display complex first order spectra, with thialene having 10 and isothialene 14 of 15 possible coupling constants. Complete unambiguous assignments of all protons and non-quaternary carbons were made via 2-dimensional NMR techniques and PPP-SCF π-electron density/chemical shift and π-bond order/vicinal coupling constant correlations.

Thialene[1,**] (cyclopenta[*b*]thiapyran) (*I*) and isothialene[2] (cyclopenta[*c*]thiapyran) (*II*) are iso-π-electronic S-heteroanalogues of azulene (*III*) (hence the general classification[3] "pseudoazulenes") and may be viewed as the non-benzenoid isomers of benzo[*b*]thiophene (*IV*). As such, both compounds have attracted considerable interest in heteroaromaticity and molecular orbital studies[1,3].



I



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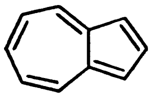

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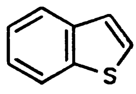

IV

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[**] This article includes a comprehensive review of the parent N, O, and S-pseudoazulenes and contains extensive pertinent references.

NMR has been extensively utilized in determination of aromaticity[4,5]. Previous NMR studies of *I* (ref.[1]) and *II* (refs [2,6,7]) verified sustained ring currents (based on chemical shifts) and firmly established both compounds as aromatic based on a diatropic definition[5,8 – 10]. However, these studies were either accomplished at low field and/or were only tentatively assigned. In particular, the elucidation of coupling constants was hampered by the nearly coincident chemical shifts of several coupled protons, resulting in pronounced second order effects and virtually uninterpretable fine structure.

The recent advent of high field NMR spectrometers and concurrent development of two-dimensional NMR experiments[11,12] has allowed for nearly routine solutions of highly complex compounds. Herein, we report a comprehensive NMR study of *I* and *II*.

EXPERIMENTAL

Thialene (*I*) and isothialene (*II*) were prepared as previously described[1,2]. All NMR solvents were products of MSD Isotopes and were purified via column chromatography over aluminum oxide and saturated with nitrogen prior to use. NMR samples were prepared under nitrogen and kept at dry ice or liquid nitrogen temperatures prior to use. Proton and carbon spectra were obtained with 1 and 5% solutions, respectively (see Tables I – IV).

Most 1-D and all 2-D NMR spectra were run on a Bruker AM-300 WB NMR spectrometer operating at 300.1 MHz for ^1H and 75.5 MHz for ^{13}C. All 2-D experiments (COSY-45, COSY-LR, JRES and HETEROCOSY) were run and processed using standard Bruker software. For thialene, the ^1H NMR spectra was obtained at 600.6 MHz using the experimental spectrometer at The NMR Facility for Biomedical Studies, Carnegie-Mellon University, Pittsburg, PA (U.S.A.). The 75.47 MHz ^1H decoupled ^{13}C NMR spectra of thialene was obtained on a General Electric GN-300 WB NMR spectrometer. All spectra were obtained at –20 °C (except the 600.6 MHz ^1H NMR of thialene, obtained at 20 °C) and were calibrated using internal tetramethylsilane. Standard acquisition parameters were utilized for all 1- and 2-D experiments.

RESULTS AND DISCUSSION

^1H NMR spectra were run in both tetrachloromethane (a non-polar solvent allowing π-electron density/chemical shift correlations) and hexadeuteriobenzene (an interactive solvent giving dramatic chemical shift differences (vs CCl_4) and thereby aiding generation of first order spectra) (Tables I and III). In the case of *I*, extensive overlap occurred in both solvents at 300.1 MHz, and analysis at 600.6 MHz was utilized in order to (successfully) resolve individual multiplets and minimize second order effects. Coupling constants for *I* (10 non-zero *J*'s) were determined from expansions of individual multiplets and were confirmed via simulation (NMRCAL) (ref.[13]) and COSY-45 and COSY-LR experiments; coupling constants for *II* (14 non-zero *J*'s) were determined from expansions of individual multiplets derived from JRES experiments and were confirmed via COSY-45 and COSY-LR experiments.

Proton assignments in bicyclic wholly aromatic molecules with extensive inter-ring couplings (such as *I* and *II*) offer a significant challenge even to advanced NMR techniques. In *I* there are two separate three proton groupings (H-2 – H-4 and H-5 – H-7) which can be rationally ordered and assigned with reasonable certainty to the six and five membered rings, respectively, based on vicinal coupling constants and chemical shifts. However, differentiation and definitive assignment of H-2 vs H-4 or H-5 vs H-7, respectively, is virtually impossible via inspection or (in this case) even with advanced two-dimensional NMR experiments*. To a lesser extent, similar difficulties are evident in *II*.

TABLE I
^{1}H NMR parameters of thialene (*I*), chemical shifts in ppm (δ-scale), coupling constants (*J*) in Hz

Parameter	Chemical shifts		
	CCl_4[a]	$CDCl_3$[b]	C_6D_6[c]
ν_2	7.61 ddd	7.82	7.03
ν_3	7.11 dd	7.26	6.66
ν_4	7.84 ddddd	8.04	7.61
ν_5	6.79 ddd	6.96	7.12
ν_6	7.30 dddd	7.46	7.59
ν_7	6.82 ddd	6.97	7.06

Parameter	Coupling constants	Parameter	Coupling constants
J(2,3)	8.86	*J*(3,7)	0.00
J(2,4)	0.73	*J*(4,5)	0.41
J(2,5)	0.00	*J*(4,6)	0.43
J(2,6)	0.73	*J*(4,7)	1.20
J(2,7)	0.00	*J*(5,6)	4.61
J(3,4)	7.57	*J*(5,7)	1.29
J(3,5)	0.00	*J*(6,7)	3.29
J(3,6)	0.00		

[a] Obtained at 600.6 MHz in CCl_4 solution; iterated values from 1180 ITRCAL (Nicolet Instrument Corporation, Madison, Wisconsin 1977). [b] Obtained at 300.1 MHz in $CDCl_3$ solution; δ($CHCl_3$) 7.27 ppm. [c] Obtained at 300.1 MHz in C_6D_6 solution; δ(C_6H_6) 7.32 ppm.

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* The low concentrations mandated by thialene's extreme sensitivity preclude carbon–carbon connectivity experiments (e.g., 2D-INADEQUATE); similarly, the extensive variations in carbon–proton couplings (typical of heteroaromatics; see Tables II and IV) preclude tuned relay experiments. If either type experiment could be accomplished, then correlation of the results with a HETEROCOSY esperiment would, of course, give definitive assignments.

TABLE II
^{13}C NMR (in $CDCl_3$ at 75.47 MHz) parameters of thialene (*I*)

Parameter	δ, ppm[a]	Multiplicity[b]	*J*(C-H), Hz
ν_2	129.03	ddd	177, 7, 5
ν_3	116.59	d	165
ν_4	130.90	dd	159.5, 9
ν_{4a}	122.72	m	–
ν_5	110.01	ddd	169.5, 8, 8[c]
ν_6	131.97	ddd	164.5, 5, 5
ν_7	110.13	ddd	170, 5, 5[c]
ν_{7a}	132.09	m	–

[a] Values from ^{1}H-decoupled ^{13}C NMR spectrum; assignments of non-quaternary carbons derived from 2-D HETEROCOSY experiments; quaternary assignments are tentative; δ($CDCl_3$) 77.05 ppm. [b] Derived from Gated Decoupling experiments; [c] C-5 and C-7 are nearly coincident; listed multiplicities and values are approximate.

TABLE III
^{1}H NMR parameters (300.1 MHz) of isothialene (*II*), chemical shifts in ppm (δ-scale), coupling constants (*J*) in Hz

Parameter	Chemical shifts		Multiplicity
	CCl_4	C_6D_6[a]	
ν_1	8.12	7.59	ddddd
ν_3	6.68	6.22	dddd
ν_4	7.75	7.55	ddddd
ν_5	6.66	6.87	ddddd
ν_6	7.22	7.45	dddd
ν_7	6.62	6.76	ddddd

Parameter	Coupling constants		Parameter	Coupling constants	
	CCl_4	C_6D_6		CCl_4	C_6D_6
J(1,3)	3.03	3.08	*J*(3,7)	0.35	0.37
J(1,4)	0.95	0.95	*J*(4,5)	0.35	0.36
J(1,5)	1.15	1.08	*J*(4,6)	0.12	0.13
J(1,6)	0.45	0.45	*J*(4,7)	0.67	0.72
J(1,7)	0.32	0.34	*J*(5,6)	3.00	2.87
J(3,4)	9.35	9.35	*J*(5,7)	1.33	1.26
J(3,5)	0.55	0.52	*J*(6,7)	4.61	4.61
J(3,6)	0.00	0.00			

[a] δ(C_6H_6) 7.15 ppm.

TABLE IV
^{13}C NMR (at 75.47 MHz) parameters of isothialene (*II*), chemical shifts in ppm (δ-scale)

Parameter	Chemical shifts		$J(C–H)$[c], Hz
	CCl_4[a]	C_6D_6[b]	
ν_1	129.28 dd	131.00	174, 6
ν_3	110.68 ddd	111.95	178, 5, 5
ν_4	124.13 dd	124.91	160, 3
ν_{4a}	136.34 m	137.17	–
ν_5	114.65 dddd	115.41	167, 9, 5.5, 3.5
ν_6	133.37 ddd	134.14	162, 5, 5
ν_7	110.98 dddd	111.98	171, 7, 7, 4.5
ν_{7a}	126.60 m	127.95	–

[a] Co-axial tube containing CD_3SOCD_3 used for deuterium lock. Values from ^1H-decoupled ^{13}C NMR spectrum; assignments of non quaternary carbons derived from 2-D HETEROCOSY experiments; quaternary assignments are tentative; $\delta(CCl_4)$ 96.00 ppm. Multiplicities derived from Gated Decoupling experiments. [b] $\delta(C_6D_6)$ 128.40 ppm. [c] Taken from spectrum measured in CCl_4.

TABLE V
PPP-SCF molecular orbital parameters[14] of thialene (*I*) and isothialene (*II*)

π-Electron densities		π-Bond orders		π-Electron densities		π-Bond orders	
position	q	position	q	position	q	position	q
Thialene (*I*)				Isothialene (*II*)			
1	1.647	*1 – 7a*	0.396	*1*	0.912	*1 – 2*	0.510
2	0.947	*4a – 7a*	0.365	*2*	1.658	*1 – 7a*	0.704
3	1.069	*4 – 4a*	0.669	*3*	1.061	*4a – 7a*	0.352
4	0.903	*3 – 4*	0.601	*4*	0.996	*4 – 4a*	0.497
4a	1.033	*2 – 3*	0.728	*4a*	1.046	*3 – 4*	0.798
5	1.148	*1 – 2*	0.515	*5*	1.120	*2 – 3*	0.410
6	1.022	*4a – 5*	0.524	*6*	1.029	*4a – 5*	0.679
7	1.179	*5 – 6*	0.734	*7*	1.134	*5 – 6*	0.593
7a	1.052	*6 – 7*	0.576	*7a*	1.044	*6 – 7*	0.729
		7 – 7a	0.701			*7 – 7a*	0.516

Definitive proton assignments were therefore made via PPP-SCF molecular orbital calculations (Table V). For both compounds, plots of π-electron densities vs chemical shifts show excellent linear correlations[15 - 18] (*I* (Fig. 1): r = 0.9905; *II* (Fig. 2): r = 0.9487); the correlation for *I* is, we believe, the highest ever observed for an aromatic heterocycle. Assignments of H-2 vs H-4 and H-5 vs H-7 in *I* and H-5 vs H-7 in *II* were further confirmed via vicinal coupling constant/π-bond order correlations (*I*: $J(3,4)/J(2,3)$ = 0.854, p_d/p_e = 0.826; $J(6,7)/J(5,6)$ = 0.714, $p_{6,7}/p_{5,6}$ = 0.785; *II*: $J(5,6)/J(6,7)$ = 0.651, $p_{5,6}/p_{6,7}$ = 0.813)[4,18 - 22]. The results confirm partial π-bond localization*, as is similarly observed in benzenoid [4.3.0] heteroaromatics[25]. All results were completely internally self-consistent.

Definitive assignments of all non-quaternary carbons were routinely made via proton/carbon HETEROCOSY experiments (Tables II and IV); the results correct numerous previously reported misassignments for both molecules[1,2,6,7]. Quaternary carbons remain tentatively assigned; in *I*, assignments were based on correlation of the *ortho* (ν_2 = 129.03 ppm; assigned ν_{7a} = 132.09 ppm) and *meta* carbons (ν_3 = 116.59 ppm; assigned ν_{4a} = 122.72 ppm). In *II*, assignments were similarly based on correlation of the *meta* carbons (ν_4 = 124.13 ppm; assigned ν_{7a} = 126.60 ppm) and comparison of the *meta* vs *para* carbons in *I* (suggesting that the *para* carbon in *II* should be approximately 10 ppm downfield of the *meta* carbons; assigned ν_{4a} = 136.34 ppm).

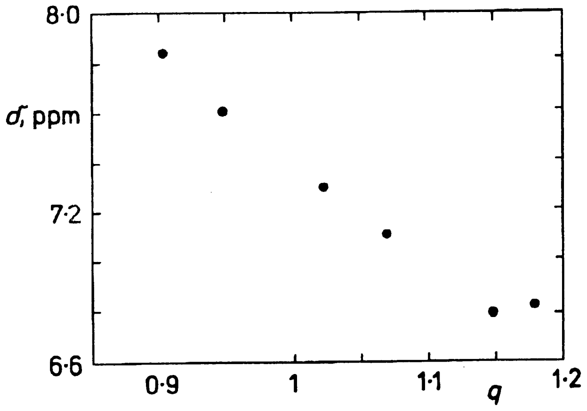

FIG. 1
PPP-SCF-MO calculated π-electron densities (q) vs iterated 600.6 MHz ^{1}H NMR of thialene (*I*) in CCl_4

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* Compared with completely delocalized (0.500) or completely fixed (1.000). Constancy of $J_{(ORTHO)}$ is utilized as an aromaticity criterion, see refs[23,24].

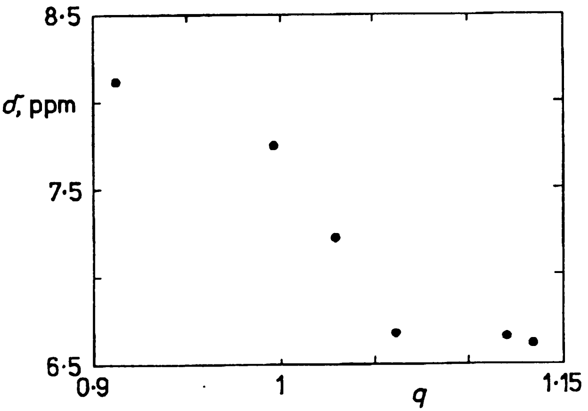

FIG. 2
PPP-SCF-MO calculated π-electron densities (q) vs 300.1 MHz ^{1}H NMR of isothialene (*II*) in CCl_4

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