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Synthesis, spectroscopic, theoretical and structural studies of new trihalomethyl sulphenyl derivatives of 5-methyl-1,3,4-thiadiazole-2-thiol

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ABSTRACT: Although 2-mercapto-5-methyl-1,3,4-thiadiazole (mmtd) is commonly thought of as a thione tautomer, electrophilic substitution occurs on the thiol moiety. The tautomeric ability of mmtd allows a substitution reaction to take place at the sulphur; this is shown by reaction with $Cl_{3-n}F_nCSCl$ compounds ($n = 0$–2) to give perhalomethyldithio thiadiazole derivatives. Three novel perhalomethylsulphenyl compounds, which exhibit a wide range of potentially interesting applications, were obtained and characterized by x-ray crystal diffraction, mass spectrometry, IR and Raman spectroscopy and density functional theory calculations. Copyright © 2002 John Wiley & Sons, Ltd.

KEYWORDS: 5-methyl-1,3,4-thiadiazole-2-thiol; trihalomethyl sulphenyl derivatives; structure; density functional theory

INTRODUCTION

Within the synthesis of heterocyclic sulphur- and nitrogen-containing compounds, 1,3,4-thiadiazoles are substances of great interest because of their wide use in medicine, agriculture and many technological applications.[1] Some of these involve dyes, lubricants, optically active crystals, photographic materials, epoxy resins, etc. Thiadiazoles have been found to have, among other properties hypotensive and anticonvulsive activities.[2] Thiadiazoles having a 2-thio group react with metals as ambident ligands to form complexes widely used as antioxidants. They have also been useful in the synthesis of macrocyclic compounds[3] and 1,3,4-thiadiazolo thia crown ethers have also been reported.[4] 5-Methyl-1,3,5-thiadiazole-2-thiol moieties are found in a great number of β-lactams with antibacterial activity and 5-methyl-2-mercapto-1,3,4-thiadiazole (mmtd) gives, on treatment with butyllithium, a dianion that on reaction with alkyl bromides or iodides yielded the 5-homologated-2-mercaptothiadiazoles.[5]

The heterocyclic compounds that we describe have are characterized by trihalomethylsulphenyl groups: Cl_3CS—, Cl_2FCS— and ClF_2CS—. Compounds with these types of substituents have shown remarkable biological activity, including hypolipidic and anorexic effects.[6,7]

Syntheses, characterizations and structural studies of trichloro-, dichlorofluoro- and chlorodifluoromethylsulphenyl-2-mercapto-5-methyl-1,3,4-thiadiazole derivatives, named cl3cs-mmtd, cl2fcs-mmtd, and clf2cs-mmtd, respectively, were the targets of this work.

RESULTS AND DISCUSSION

Although in 2-mercapto-1,3,4-thiadiazole rings tautomerism may be possible, thione tautomers have been observed to be predominant in several 4-thiazoline-2-thiones.[8] The thione form has also been predicted to be preferred by several theoretical calculations.[9]

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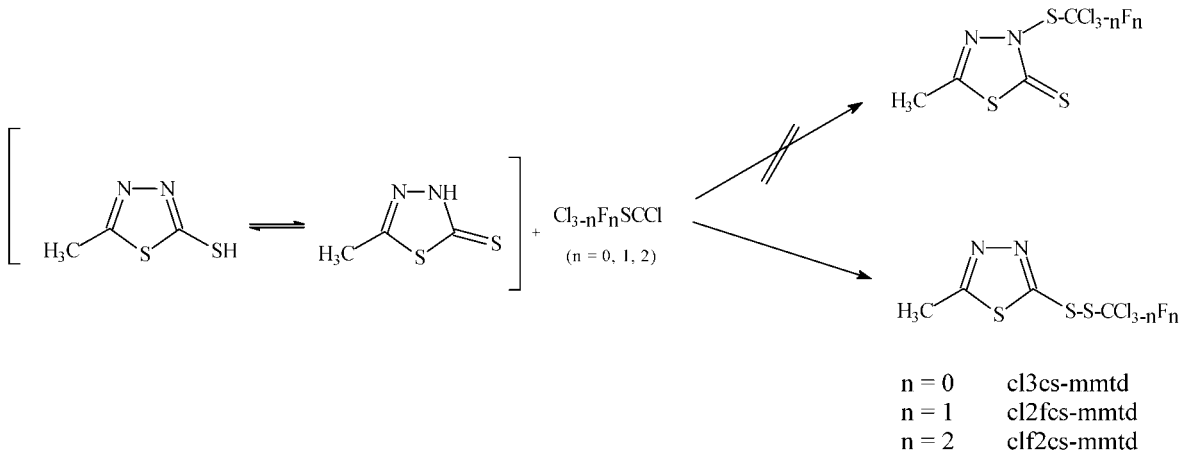


Scheme 1

Substituents at the 2- and 5-positions have a large effect in determining the reactivity of 1,3,4-thiadiazoles. Thus, 2-aminothiadiazoles react electrophilically on both the amino group and the ring nitrogen atom. 2-Mercaptothiadiazoles react similarly to arenethiols, while compounds containing a methyl group on the thiadiazole ring show a reactivity similar to that of picolines.[9]

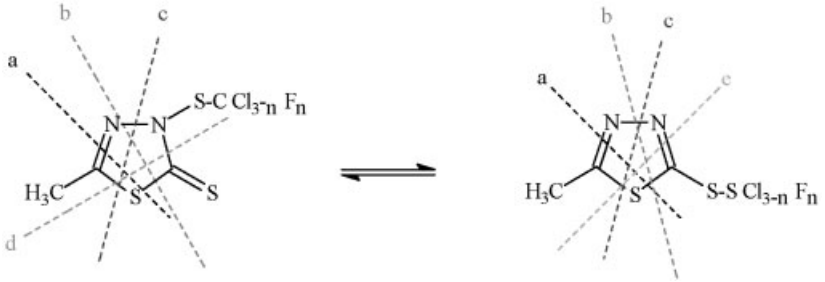
Alkylthio derivatives of 1,3,4-thiadiazoles have been obtained by direct alkylation of 1,3,4-thiadiazolinethiones.[10] In order to obtain trihaloalkylthio-mmtd derivatives, reactions of trichloro-, dichlorofluoro- and chlorodifluoromethylsulphenyl chloride with mmtd have been carried out. No *N*-substituted derivatives are obtained in this way (Scheme 1). The ^{1}H NMR spectrum shows only one signal at about $\delta = 2.76$ ppm that corresponds to the methyl group. This indicates that only one product is formed. The ^{13}C NMR spectrum of cl3cs-mmtd confirms that the substitution occurs at the thiol group, giving rise a signal at $\delta = 166.3$ ppm that may be ascribed to the thiadiazole C-2, while a hypothetical N-3 substitution, yielding the 2-thione derivative, would be characterized by signals whose displacements are expected in the $\delta = 185$–190 ppm region.[11]

Mass spectrometry

The *m/z* values and their relative intensities (*I*) for the ions in the mass spectra of cl3cs-mmtd, cl2fcs-mmtd and clf2cs-mmtd are listed in Table 1.

Table 1. *m/z* values and relative intensities (*I*) as a percentage of I_{max} for the ions in the mass spectra of cl3cs-mmtd-, cl2fcs- and clf2cs-mmtd

	cl3cs-mmtd		cl2fcs-mmtd		clf2cs-mmtd	
Fragment	*m/z*	*I* (%)	*m/z*	I (%)	*m/z*	I (%)
$M^{+\cdot}$	280/282/284/286	5.5:6.0:2.3:0.3	264/266/268	11.3:8.7:2.0	248/250	12.9:5.8
$[M-Cl]^+$	245	1.2	229	<1	213	1.8
$[SSCCl]^+$	—		153/155	2: <1	—	
$[SCCl_nF_{3-n}]^+$	149/151/153/155	<1	133	<1	—	
$[CCl_nF_{3-n}]^+$	117/119/121/123	54:51:16:2	101/103/105	34:21:4	85/87	13:5
$[M-CCl_nF_{3-n}]^+$	163	6	163	7	163	4.3
$[M-SCCl_nF_{3-n}]^+$	131	>1	131	>1	131	4
$[SCCl_2]^+$	114/116	3:2	—		—	
$[CS_3]^+$	108	2	108	<1	108	1
$[M-(S)-(SCCl_nF_{3-n})]^+$	99	6.5	99	9	99	17.8
$[SCCl]^+$	79/81	13:5	79/81	1: <1	—	
$[CS_2]^{+\cdot}$	76	3	76	1.5	76	2
$[CH_2{=}C(N){=}S]^+$ (b)	72	2	72	1.5	72	2.6
S_2^+	64	12.5	64	12.5	64	16
$[SCF]^+$	—		63	15.1	—	
$[CH_2{=}C{=}S]^+/[CH_3{-}C{=}S]^+$ (a)	58/59	32:100	58/59	36:100	58/59	39:100
$[CF_2]^+$	—		—		50	6.6
CCl^+	47/49	17.6:4	—		—	
$[CS]^+$	44	39	44	29	44	25
$[CH_3CN]^{+\cdot}$ (c)	41	40	41	55	41	70



Scheme 2. Possible thiadiazole ring fragmentation scheme for trihalomethylsulphenyl-mmtd derivatives

The mass spectra show similar fragmentation patterns characterized by the loss of halogenated substituents. In all cases, the molecular ion M is observed with the corresponding characteristic natural isotopic abundance. Possible fragmentation paths involving fissions across the ring are illustrated in Scheme 2. Cleavage of 4,5 and 1,2 bonds (path 'a') generates *m/z* 59 $[CH_3C{=}S]^{+\cdot}$ that constitutes the base peak in all three cases. Fragmentation on the substituent occurs, with high relative abundance, producing CCl_3^+, CCl_2F^+ and $CClF_2^+$.

Although fragments $[SSCCl_{3-n}F_n]^+$ have been not detected, $[M-(S{-}SCCl_nF_{3-n})]^+$ (*m/z* 99) is observed with a relative abundance between 6.5 and 17.8. The fragment of *m/z* 108, most likely $[CS_3]^+$, is also detected.

On the other hand, no significant $[M-CS_2]^{+\cdot}$ is observed. This feature would indicate the presence of substitution on the nitrogen that would allows the loss of CS_2 from the molecular ion, according to path 'd'.[12]

Fragments and losses common to all the compounds are $[M-CCl_nF_{3-n}]^+$, $[M-SCCl_nF_{3-n}]^+$, $[M-(S{-}SCCl_nF_{3-n})]^+$, $[CS]^+$ and $[CH_3CN]^{+\cdot}$.

Vibrational analysis

Vibrational spectra were compared with those of related compounds (mercaptothiadiazoles and thiadiazolinethiones).[13,14] Theoretical vibrational spectra were calculated using density functional theory (DFT) methods to assist the assignment (see the Theoretical calculations section). Experimental and calculated wavenumbers for cl3cs-mmtd, cl2fcs-mmtd and clf2cs-mmtd are collected in Table 2.

Methyl group stretching modes, including two $\nu_{as}(CH_3)$ antisymmetric and one $\nu_s(CH_3)$ symmetric mode, are observed between 2990 and 2892 cm^{-1}.[13] The antisymmetric CH_3 bend modes occur at 1474–1441 cm^{-1},[15] therefore bands at 1382 cm^{-1} (Raman) (cl3cs-mmtd), 1385 cm^{-1} (Raman) (cl2fcs-mmtd) and 1423 cm^{-1} (Raman) (clf2cs-mmtd) are assigned to $\delta_s(CH_3)$.[13,15] IR absorptions at 1417, 1394 and 1408 cm^{-1} are assigned to the ν(C2=N2) stretching mode for cl3cs-mmtd, cl2fcs-mtd and clf2cs-mtd, respectively, while the corresponding ν(C1=N1) for clf2cs-mmtd is found at 1545 (IR)–1546 (Raman) cm^{-1}.

The ν(C–F) fundamentals are observed in the IR spectrum of clf2cs-mtd at 1122 and 1064 cm^{-1}, while for cl2fcs-mmtd a band appearing at 1040 cm^{-1} is assigned to the same vibrational mode. Bands found for the three compounds between 851 and 738 cm^{-1} can be assigned to the ν(C–Cl) vibrational modes.[16–18]

Characteristic torsional modes and ring deformation modes are found at wavenumbers lower than 400 cm^{-1}; these modes involve all atoms of the molecule in rather complex movements.

Theoretical calculations

The first step in the study of the structures of these compounds from a theoretical point of view is the investigation of the minima over the potential energy surfaces originated in the variation of the different torsional angles. Initially, we performed this search for clf2cs-mmtd, using the B3LYP/6–31+G* approximation. The molecule has three independent torsions: τS(3)–S(2)–C(2)–N(2), τC(4)–S(3)–S(2)–C(2) and τCl(2)–C(4)–S(3)–S(2). A value of 90° was used as the starting point for τC(4)–S(3)–S(2)–C(2), owing to the characteristic values of the torsional angles for the XSSY compounds. The potential energy curve for the variation of τS(3)—S(2)—C(2)—N(2) was calculated, by varying the values of the corresponding torsional angle between 0° and 360° at intervals of 10°. Two minima were found, as shown in Fig. 1. For each of these conformers the torsion τCl(2)—C(4)—S(3)—S(2) was varied between 0° and 360° at intervals of 10°, with the potential energy curves shown in Figs 2 and 3 for the conformers I and II, respectively. In both cases, we found a minimum at approximately 180°, in a *trans* position with respect to the S—S bond. There are also minima in a *gauche* position, but with an energy difference of approximately 4 kcal mol^{-1} (1 kcal = 4.184 kJ), that we are not taking into account in the further analysis. These two minima were fully optimized using the B3LYP/6–31+G* approximation, with the simultaneous relaxation of all the geometric parameters. The vibrational wavenumbers were calculated to characterize the stationary points as minima.

Table 3 lists the energy differences and the calculated

Table 2. Experimental (IR and Raman) vibrational data and calculated wavenumbers (B3LYP/6–31+G*) for cl3cs-mmtd, cl2fcs-mmtd and cmmtd (cm^{-1})

cl3cs-mmtd			cl2fcs-mmtd			clf_2cs-mmtd			Assignment[a]
Calc.	Exp.		Calc.	Exp.		Calc.	Exp.		
	IR	Raman		IR	Raman		IR	Raman	
3155 (2)			3155 (2)			3155 (2)			ν_{as} (CH_3)
3115 (7)		2990 (w)	3116 (5)	2985 (vw)		3116 (6)		2976 (w)	ν_{as} (CH_3)
3058 (12)	2926 (vw)	2932 (m)	3059 (11)	2956 (vw)	2931 (m)	3059 (11)		2917 (m)	ν_s (CH_3)
1536 (15)			1523 (14)			1523 (14)	1545 (m)	1546 (m)	ν (C1=N1)
1500 (12)		1474 (w)	1500 (13)			1500 (13)			δ_{as} (CH_3)
1486 (22)	1441 (s)		1475 (30)	1492 (w)		1475 (30)			δ_{as} (CH_3)
1437 (23)	1417 (s)	1421 (w)	1410 (27)[b]	1394 (s)		1410 (29)[b]	1408 (s)	1410 (m)[b]	ν (C2=N2)
1431 (5)		1382 (s)	1431 (1)[b]		1385 (s)	1431 (1)[b]		1423 (m)[b]	δ_s (CH_3)
1208 (31)	1192 (s)		1217 (38)	1212 (vw)		1217 (31)	1263 (m)		ν (C–C)
1108 (5)	1074 (s)	1076 (s)	1122 (11)	1197 (vw)	1081 (m)	1123 (9)			ν (N–N)
						1105 (226)	1122 (vs)		ν (C–F)
1067 (<1)			1066 (<1)	1090 (s)		1066 (<1)[b]		1025 (m)	ρ (CH_3)
			1043 (148)	1040 (vs)		1080 (162)[b]	1064 (vs)		ν (C–F)
1044 (54)	1070 (s)		1031 (1)	977 (w)		1033 (17)	985 (m)		δ (N1N2C2)
1002 (7)	977 (w)		1001 (8)	917 (w)		1001 (8)			ρ (CH_3)
			804 (222)	849 (vs)	842 (w)	863 (333)	846 (w)	851 (m)	ν (C–C1)
			789 (191)	803 (vs)	800 (w)				ν (C–C1)
762 (2)		790 (m)	760 (1)		749 (w)	761 (<1)			δ (C1N1N2)
752 (104)	791 (vs)	769 (s)							ν (C–C1)
730 (148)	760 (vs)	738 (w)							ν (C–C1)
713 (105)									ν (C–C1)
						652 (2)			δ (CF_2)
642 (8)	642 (w)	652 (s)	651 (5)	651 (w)	689 (m)	651 (5)	675 (m)		ν (C1–S1)
615 (<1)			625 (2)		653 (w)	626 (2)		642 (s)	δ_{oop} (ring)
600 (13)	604 (w)	608 (w)	608 (13)	606 (w)	606 (w)	608 (13)			ν (C2–S1)
552 (1)	544 (w)		562 (1)			562 (2)			δ_{oop} (ring)
			513 (8)						δ ($CC1_2$)
495 (1)		531 (s)	477 (<1)	519 (w)	526 (vs)	479 (1)		481 (s)	ν (S–S)
433 (4)	440 (w)	447 (vs)	424 (9)	402 (w)	408 (w)	438 (5)		401 (vs)	ν (S–CX_3)
413 (3)		408 (w)	389 (4)		393 (m)	425 (9)			Deformation
358 (6)			382 (1)		359 (w)	415 (2)			and torsion
337 (3)		335 (m)	353 (3)		322 (m)	413 (1)			modes
320 (<1)		314 (m)	343 (1)			354 (2)			involving
309 (<1)			321 (1)			340 (1)			movements
286 (2)		269 (m)	249 (2)		239 (w)	299 (<1)		309 (s)	of all atoms
254 (3)		221 (m)	238 (2)			246 (5)		226 (s)	
210 (1)			212 (2)		203 (w)	217 (2)			
201 (<1)		200 (m)	159 (2)		167 (w)	161 (1)			
152 (1)		143 (m)	114 (<1)		127 (w)	121 (<1)			
111 (<1)			97 (<1)		86	97 (<1)			
102 (2)			84 (<1)			85 (<1)			
95 (1)			44 (1)			45 (1)			
37 (<1)			29 (<1)			33 (<1)			
28 (<1)			15 (3)			17 (4)			
19 (5)									

[a] δ, Deformation; ν, stretch; ρ, rock; oop, out-of-plane; ip, in-plane; s, symmetric; as, antisymmetric.
[b] The decreasing order of these pairs of bands has been altered for comparison proposes.

torsional angles for these two conformers. The same procedure was followed for the other two compounds, cl2fcs-mmtd and cl3cs-mmtd, and the results presented in Tables 4 and 5, respectively. Very small energy differences of 0.29 and 0.13 kcal.mol^{-1} were found in favor of conformer I for clf2cs-mmtd and cl2fcs-mmtd, respectively, while conformer II was found to be more stable by 0.37 kcal.mol^{-1} than conformer I for the cl3cs-mmtd molecule. The calculated geometric parameters of the most stable forms of the three compounds are listed in Table 6. The optimized structures are also depicted in Figure 4.

X-ray crystal structure of cl3cs-mmtd

The trihalomethylthio substituent is bonded to the exocyclic sulphur atom, yielding 2-methyl-5-trichloro-

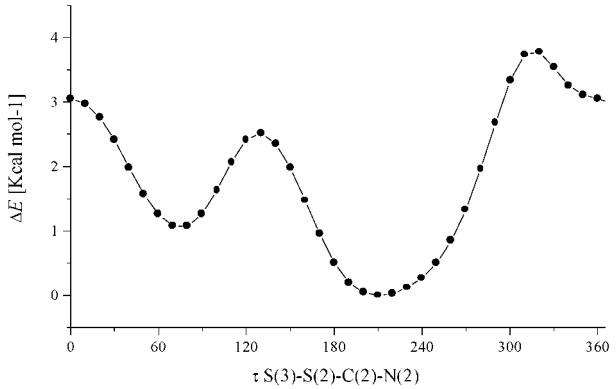


Figure 1. Potential energy curve for ClF_2CS-mmtd as a function of the S(3)—S(2)—C(2)—N(2) torsion angle calculated with the B3LYP/6–31+G* approximation

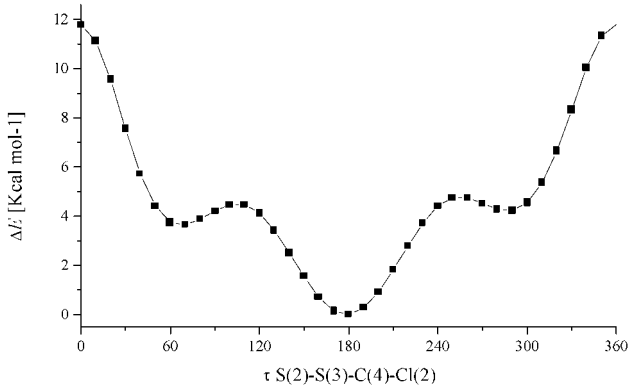


Figure 2. Potential energy curve for conformer I of ClF_2CS-mmtd as a function of the Cl—C(4)—S(3)—S(2) torsion angle calculated with the B3LYP/6–31+G* approximation

methyldithio-1,3,4-thiadiazole (cl3cs-mmtd). This compound crystallized in the space group *Pbca*. The unit cell contains eight molecules, packed in layers, with the

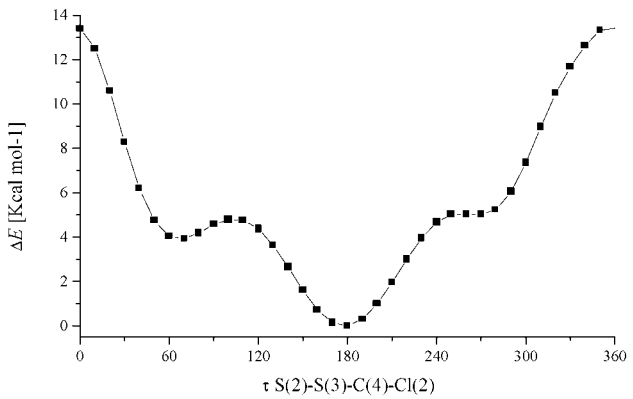


Figure 3. Potential energy curve for conformer II of ClF_2CS-mmtd as a function of the Cl—C(4)—S(3)—S(2) torsion angle calculated with the B3LYP/6–31+G* approximation

Table 3. Calculated energies of the two stable conformers of clf2cs-mmtd using the B3LYP/6–31+G* approximation

Conformer	τS(3)–S(2)–C(2)–N(2) (°)	*E* (hartree)	Δ*E* (kcal mol^{-1})
I	−93.4	−2118.16315931	0.00
II	+148.7	−2118.16270317	0.29

Table 4. Calculated energies of the two stable conformers of cl2fcs-mmtd using the B3LYP/6–31+G* approximation

Conformer	τS(3)–S(2)–C(2)–N(2) (°)	*E* (hartree)	Δ*E* (kcal mol^{-1})
I	−93.4	−2478.50389481	0.00
II	+150.3	−2478.50368616	0.13

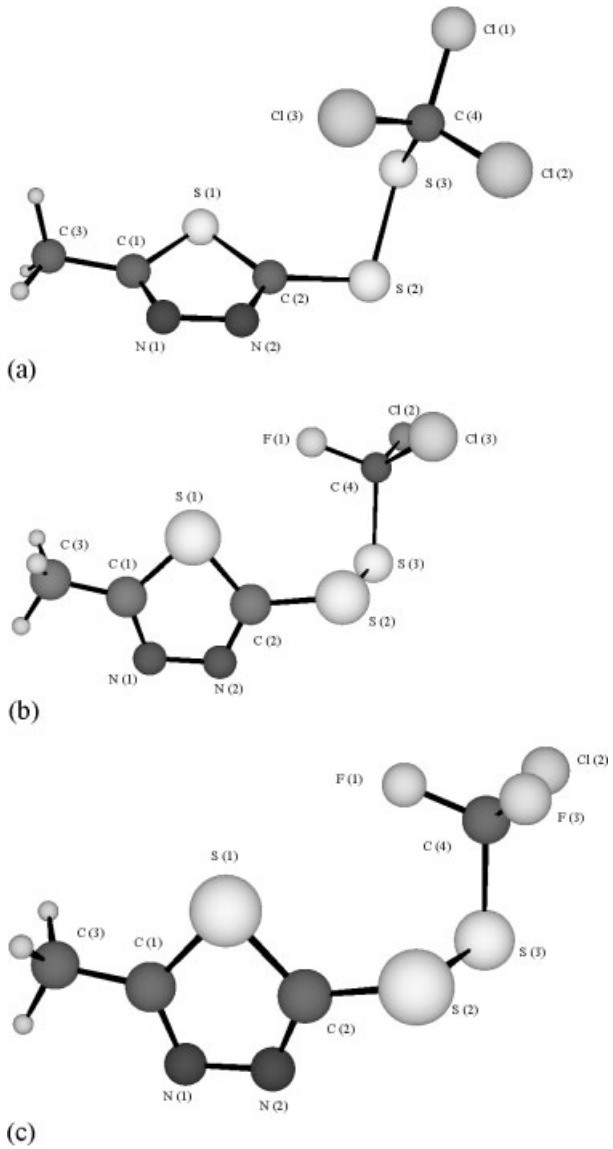


Figure 4. Optimized calculated geometries (B3LYP/6–31+G*) for (a) Cl_3CS-mmtd, (b) Cl_2FCS-mmtd and (c) ClF_2CS-mmtd

Table 5. Calculated energies of the two stable conformers of cl3cs-mmtd using the B3LYP/6–31+G* approximation

Conformer	τS(3)–S(2)–C(2)–N(2) (°)	*E* (hartree)	Δ*E* (kcal mol^{-1})
I	−69.1	−2838.84576016	0.37
II	+144.3	−2838.84635497	0.00

thiadiazole rings oriented in anti-parallel form. Therefore, the endocyclic sulphur of the molecules lies in the upper layer over the two nitrogen atoms of molecules in the layer below. Perpendicular —$SCCl_3$ moieties are arranged in opposite directions.

The heterocyclic ring is planar within experimental error, and the endocyclic bond lengths C(1)—N(1)=1.282 (9) Å and C(2)—N(2)=1.298 (8) Å clearly indicate C=N double bonds.[19]

The out-of-plane trichloromethyl group has a torsion angle C(2)—S(2)—S(3)—C(4) of 94.11°. Sulphur S(3) lies under the ring plane with S(3)—S(2)—C(2)—S(1) S(3)—S(2)—C(2)—N(2) torsion angles of 6.79° and −175.71°, respectively.

EXPERIMENTAL

mmtd was purchased from Aldrich and used without further purification. Mass spectrometric analyses were performed on a Perkin-Elmer Q Mass 910 quadrupole instrument (electron ionization at 70 eV), coupled to a Perkin-Elmer Model 8000 gas chromatograph, provided with a 30 m × 0.25 mm i.d. column and a 0.25 μm RSL Heliflex stationary phase layer, using an injection split of 100:1 and the temperature programme 2 min at 120 °C, increased from 120 to 230 °C at 15 °C min^{-1}, and held for 12 min at 250 °C. Silica gel (70–230 mesh) was employed for column chromatography. Deuterated solvents were dried and transferred from activated molecular sieves (4 Å). Microanalyses were performed in a Carlo Erba Model 1106 elemental analyser. NMR spectra were recorded in $CDCl_3$ solutions, using Bruker WP 80 (^{1}H) and WM 250 PFT (^{19}F, ^{13}C) instruments, with TMS (^{1}H) and $CFCl_3$ (^{19}F) as internal standards. IR spectra were obtained using a Bruker IFS 113 FT spectrometer (4000–400 cm^{-1}) with KBr pellets. Raman spectra were recorded with a Raman accessory of the Bruker IFS 66 spectrometer equipped with an Nd:YAG laser (3500–100 cm^{-1}). All theoretical calculations were performed using the Gaussian 98 program system[20] under the Linda parallel execution environment using two coupled personal computers.

X-ray crystal structure of cl3cs-mmtd

Data were collected at 293 (±2) K on a Siemens P4 four-circle x-ray diffractometer, using Mo Kα graphite monochromated radiation ($\lambda = 0.71073$ Å). The crystal system is orthorhombic and the space group *Pbca*, $Z = 8$, with unit cell parameters $a = 6.585(2)$ Å, $b = 11.247(5)$ Å, $c = 28.565(10)$ Å, $V = 2115.6(14)$ Å^3, $\rho_{calc} = 1.768$ g cm^{-3}, $\mu = 1.406$ mm^{-1}; 30 reflections were used for the unit cell refinement, 2θ-range reflections $5° \leq 2\theta \leq 20°$; among 2732 measured reflections, 1363 were independent ($R_{int} = 0.0858$).The difference Fourier synthesis on the basis of the final model has a residual electron density with a maximum of 0.333 e Å^{-3} and a minimum of −0.327 e Å^{-3}. The final *R* indices were $R_1 = 0.0613$ and $wR_2 = 0.1601$. *R* indices (all data) are $R_1 = 0.0915$ and $wR_2 = 0.1843$. Bond lengths, angles and torsions are given in Table 7.

Table 6. Selected calculated (B3LYP/6–31+G*) bond lengths (Å) and angles (°) for cl3cs-mmtd, cl2fcs-mmtd and clf2cs-mmtd

Bond (Å)	cl_3cs-	cl_2fcs-	clf_2cs-	Bond angle (°)	cl_3cs-	cl_2fcs-	clf_2cs-	Torsion (°)	cl_3cs-	cl_2fcs-
S(1)—C(1)	1.757	1.747	1.747	C(1)—S(1)—C(2)	86.0	86.5	86.5	C(2)—S(2)—S(3)—C(4)	89.51	93.14
S(2)—S(3)	2.075	2.091	2.096	S(2)—S(3)—C(4)	105.4	103.8	102.1	C(1)—N(1)—N(2)—C(2)	−0.54	−0.39
S(3)—C(4)	1.866	1.847	1.839	N(1)—N(2)—C(2)	112.9	113.1	113.1	N(2)—N(1)—C(1)—C(3)	177.96	−179.86
N(1)—N(2)	1.369	1.361	1.361	S(1)—C(1)—C(3)	123.1	123.7	123.7	N(2)—N(1)—C(1)—S(1)	−0.97	−0.06
N(2)—C(2)	1.301	1.306	1.306	S(1)—C(2)—S(2)	125.9	124.1	124.1	C(2)—S(1)—C(1)—N(1)	0.85	−0.19
S(1)—C(2)	1.755	1.755	1.755	S(2)—C(2)—N(2)	119.6	122.3	122.3	C(2)—S(1)—C(1)—C(3)	−178.08	179.61
S(2)—C(2)	1.780	1.775	1.775	S(3)—C(4)—Cl(2)	102.8	105.2	107.4	N(1)—N(2)—C(2)—S(1)	−0.14	0.54
X(1)—C(4)[a]	1.793	1.361	1.350	S(3)—C(4)—Y(3)	112.6	114.6	112.4	N(1)—N(2)—C(2)—S(2)	−173.56	176.37
Y(3)—C(4)[b]	1.795	1.790	1.354	Cl(2)—C(4)—Y(3)	109.9	110.9	109.1	C(1)—S(1)—C(2)—N(2)	−0.55	0.41
Cl(2)—C(4)	1.802	1.793	1.788	S(3)—S(2)—C(2)	104.6	104.1	103.8	C(1)—S(1)—C(2)—S(2)	−173.48	176.16
N(1)—C(1)	1.305	1.311	1.311	N(2)—N(1)—C(1)	113.5	113.6	113.6	S(3)—S(2)—C(2)—N(2)	144.28	−93.36
C(1)—C(3)	1.496	1.496	1.496	S(1)—C(1)—N(1)	114.5	113.3	113.3	S(3)—S(2)—C(2)—S(1)	−43.14	91.25
H(13)—C(3)	1.093	1.093	1.093	N(1)—C(1)—C(3)	123.4	123.0	123.0	S(2)—S(3)—C(4)—Y(3)	−64.02	57.73
H(14)—C(3)	1.096	1.096	1.096	S(1)—C(2)—N(2)	114.1	113.5	113.5	S(2)—S(3)—C(4)—Cl(2)	177.74	179.81
H(15)—C(3)	1.096	1.096	1.096	S(3)—C(4)—X(1)	112.5	111.1	112.4	S(2)—S(3)—C(4)—X(1)	59.54	−63.36
				X(1)—C(4)—Cl(2)	109.9	108.2	109.2			
				X(1)—C(4)—Y(3)	108.9	106.8	106.2			

[a] X(1): cl3cs-mmtd, Cl; cl2fcs-mmtd, F; clf2cs-mmtd: F.
[b] Y(3): cl3cs-mmtd, Cl; cl2fcs-mmtd, Cl; clf2cs-mmtd, F.

Table 7. Experimental (x-ray) and calculated (B3LYP/6–31+G*) interatomic bond distances (Å) and bond angles (°) for Cl_3CS-mmtd

Bond distances	Exp.	Calc.	Bond angles	Exp.	Calc.	Torsions	Exp.	Calc.
S(1)—C(1)	1.740 (6)	1.757	C(1)—S(1)—C(2)	86.2 (3)	86.0	C(2)—S(2)—S(3)—C(4)	94.11 (0.37)	89.51
S(2)—S(3)	2.015 (3)	2.075	S(2)—S(3)—C(4)	103.8 (3)	105.4	C(1)—N(1)—N(2)—C(2)	−0.76 (0.80)	−0.54
S(3)—C(4)	1.816 (8)	1.866	N(1)—N(2)—C(2)	109.6 (6)	112.9	N(2)—N(1)—C(1)—C(3)	−179.20 (0.58)	177.96
N(1)—N(2)	1.406 (7)	1.369	S(1)—C(1)—C(3)	122.5 (5)	123.1	N(2)—N(1)—C(1)—S(1)	0.65 (0.72)	−0.97
N(2)—C(2)	1.298 (8)	1.301	S(1)—C(2)—S(2)	126.4 (4)	125.9	C(2)—S(1)—C(1)—N(1)	−0.28 (0.54)	0.85
S(1)—C(2)	1.706 (7)	1.755	S(2)—C(2)—N(2)	116.8 (6)	119.6	C(2)—S(1)—C(1)—C(3)	179.56 (058)	−178.08
S(2)—C(2)	1.768 (6)	1.780	S(3)—C(4)—Cl(2)	112.4 (5)	112.5	N(1)—N(2)—C(2)—S(1)	0.55 (0.77)	−0.14
Cl(1)—C(4)	1.766 (9)	1.802	S(3)—C(4)—Cl(3)	113.3 (4)	112.6	N(1)—N(2)—C(2)—S(2)	−177.29 (0.44)	−173.56
Cl(2)—C(4)	1.749 (9)	1.793	Cl(2)—C(4)—Cl(3)	110.1 (5)	109.9	C(1)—S(1)—C(2)—N(2)	−0.18 (0.59)	−0.55
Cl(3)—C(4)	1.749 (8)	1.795	S(3)—S(2)—C(2)	103.4 (3)	104.6	C(1)—S(1)—C(2)—S(2)	177.42 (0.49)	−173.48
N(1)—C(1)	1.282 (9)	1.305	N(2)—N(1)—C(1)	113.6 (5)	113.5	S(3)—S(2)—C(2)—N(2)	−175.71 (0.51)	144.28
C(1)—C(3)	1.487 (9)	1.496	S(1)—C(1)—N(1)	113.9 (5)	114.5	S(3)—S(2)—C(2)—S(1)	6.79 (0.52)	−43.14
			N(1)—C(1)—C(3)	123.7 (6)	123.4	S(2)—S(3)—C(4)—Cl(3)	−61.07 (0.51)	−64.02
			S(1)—C(2)—N(2)	116.8 (5)	114.1	S(2)—S(3)—C(4)—Cl(2)	62.63 (0.41)	59.54
			S(3)—C(4)—Cl(1)	102.9 (4)	102.8	S(2)—S(3)—C(4)—Cl(1)	−179.82 (0.28)	177.74
			Cl(1)—C(4)—Cl(2)	109.4 (4)	109.9			
			Cl(2)—C(4)—Cl(3)	108.7 (5)	108.9			

Complementary crystallographic data has been deposited at the Cambridge Crystallographic Data Centre (deposition number CCDC 176517).

General procedure for the preparation of 5-methyl-2-trihalomethyldithio-1,3,4-thiadiazole

2-Methyl-5-trichloromethyldithio-1,3,4-thiadiazole (cl3cs-mmtd). A solution of 186 mg (1 mmol) of Cl_3CSCl in 1 ml of dry THF was slowly added to a stirred and cooled (−90 °C) solution of 134 mg (1 mmol) of mmtd in 10 ml of THF. A white solid was formed. When the addition was completed, the mixture, under stirring, was allowed to warm gradually to room temperature overnight. The solid was then dissolved in hexane. The solvent was evaporated *in vacuo* and the residue purified by column chromatography [hexane–ethyl acetate (3:1)]. After solvent evaporation, light yellow crystals were obtained and washed with hexane to give 196 mg of white crystals of cl3cs-mmtd, 70% yield, m.p. 58–59 °C. ^{1}H NMR: δ 2.76 (s, 3H, 2-CH_3). ^{13}C NMR: δ 15.98 (2-CH_3), 99.35 ($SCCl_3$), 166.53 (5-C), 168.31 (2-C). GC–MS: *m/z* 280, 282, 284, 286 (M^+), 163, 117, 119, 121, 123, 114, 108, 99, 79, 81, 76, 72, 64, 58, 59, 47, 49, 44, 41. IR: 3454 (broad), 2926, 1441, 1417, 1192, 1074, 1070, 977, 791, 760, 642, 604, 544, 440 cm^{-1}. Raman: 2990, 2932, 1474, 1421, 1382, 1076, 790, 769, 652, 608, 531, 447, 408, 335, 314, 269, 221, 200, 143 cm^{-1}. Anal. Calcd for $C_4H_3N_2S_3Cl_3$: C, 17.1; H, 1.1; N, 9.9; S, 34.2. Found: C, 17.3; H, 0.7; N, 10.8; S, 34.0%.

2-Dichlorofluoromethyldithio-5-methyl-1,3,4-thiadiazole (cl2fcs-mmtd). This compound was purified by column chromatography [hexane–ethyl acetate (4:1)]. Colorless needles were obtained, yield 84%, m.p. 47–48 °C (hexane). ^{1}H NMR: δ 2.76 (s, 3H, CH_3). ^{19}F NMR: δ − 25.23 (s, $-SCCl_2F$). GC–MS: *m/z* 264, 266, 268 (M^+), 163, 153, 155, 101, 103, 105, 99, 63, 64, 58, 59, 44, 41. IR: 3523, 1492, 1439, 1394, 1197, 1090, 1040, 977, 917, 840, 803, 631, 606, 519, 402 cm^{-1}. Raman: 2931, 1385, 1081, 800, 770, 689, 606, 526, 408, 393, 359, 322, 239, 196, 126 cm^{-1}. Anal. Calcd for $C_4H_3N_2S_3Cl_2F$: C, 18.1; H, 1.1; N, 10.6; S, 36.3. Found: C, 18.2, H, 0.7; N, 11.4; S, 36.8%.

2-Chlorodifluoromethyldithio-5-methyl-1,3,4-thiadiazole (clf2cs-mmtd). This compound was obtained as yellow oil and purified by column chromatography [hexane–ethyl acetate (4:1)]. Yellow crystals were obtained, yield 74%, m.p. 36–37 °C (hexane). GC–MS: *m/z* 248, 250, 163, 131, 99, 85, 87, 76, 72, 64, 58, 59, 50, 44, 41; IR: 3448, 1545, 1408, 1263, 1122, 1064, 985, 846, 675 cm^{-1}. Raman: 3013, 2976, 2917, 1546, 1423, 1410, 1025, 851, 642, 481, 401, 309, 226 cm^{-1}. Anal. Calcd for $C_4H_3N_2S_3Cl_3$: C, 19.3; H, 1.2; N, 11.3; S, 38.7. Found: C, 19.7; H, 0.9; N, 11.9; S, 39.4%.

CONCLUSIONS

The compounds synthesized from the starting material with tested applications may increase their activities after modification of their structures with small groups. This work also offers a sound basis for the study of reactions of mmtd on the basis of the tautomeric thione–thiol equilibrium. Although mmtd is viewed as a thione tautomer, it reacts with perhalomethylsulphenyl derivatives on the thiol moiety to give corresponding disulphur-containing molecules.

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