



Crystal structure of a methimazole-based ionic liquid

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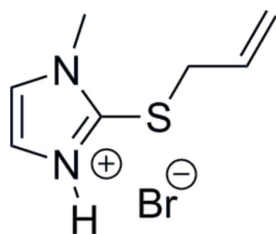
The structure of 1-methyl-2-(prop-2-en-1-ylsulfanyl)-1*H*-imidazol-3-ium bromide, C₇H₁₁N₂S⁺·Br[−], has monoclinic (*P*2₁/*c*) symmetry. In the crystal, the components are linked by N—H···Br and C—H···Br hydrogen bonds. The crystal structure of the title compound undeniably proves that methimazole reacts through the thione tautomer, rather than the thiol tautomer in this system.

Keywords: crystal structure; ionic liquids; methimazole; *S*-allylation; nitrogen heterocycle.

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1. Related literature

For the biological activity of methimazole, see: Rong *et al.* (2013). For its use as a ligand, see: Crossley *et al.* (2006). For a discussion of methimazole-based ionic liquids, see: Siriwardana *et al.* (2008). For reaction chemistry of methimazole, see: Roy & Mughes (2005).



2. Experimental

2.1. Crystal data

C ₇ H ₁₁ N ₂ S ⁺ ·Br [−]	<i>V</i> = 1004.62 (11) Å ³
<i>M_r</i> = 235.15	<i>Z</i> = 4
Monoclinic, <i>P</i> 2 ₁ / <i>c</i>	Mo <i>K</i> α radiation
<i>a</i> = 10.8692 (7) Å	<i>μ</i> = 4.24 mm ^{−1}
<i>b</i> = 7.4103 (5) Å	<i>T</i> = 180 K
<i>c</i> = 12.8551 (9) Å	0.6 × 0.32 × 0.25 mm
<i>β</i> = 104.006 (7)°	

2.2. Data collection

Agilent Xcalibur, Eos diffractometer	7388 measured reflections
Absorption correction: multi-scan (<i>CrysAlis PRO</i> ; Agilent, 2014)	1829 independent reflections
<i>T</i> _{min} = 0.321, <i>T</i> _{max} = 1.000	1558 reflections with <i>I</i> > 2σ(<i>I</i>)
	<i>R</i> _{int} = 0.042

2.3. Refinement

<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)] = 0.030	H atoms treated by a mixture of independent and constrained refinement
<i>wR</i> (<i>F</i> ²) = 0.065	Δ <i>ρ</i> _{max} = 0.34 e Å ^{−3}
<i>S</i> = 1.03	Δ <i>ρ</i> _{min} = −0.38 e Å ^{−3}
1829 reflections	
105 parameters	
1 restraint	

Table 1

Hydrogen-bond geometry (Å, °).

<i>D</i> —H··· <i>A</i>	<i>D</i> —H	H··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> —H··· <i>A</i>
N2—H2···Br1 ⁱ	0.84 (3)	2.46 (3)	3.246 (2)	158 (3)
C2—H2A···Br1 ⁱⁱ	0.93	2.84	3.723 (4)	159
C3—H3···Br1 ⁱⁱⁱ	0.93	2.91	3.757 (3)	152
C4—H4B···Br1	0.96	2.87	3.737 (3)	151
C5—H5B···Br1 ^{iv}	0.97	2.89	3.814 (3)	161

Symmetry codes: (i) *x*, −*y* + ½, *z* − ½; (ii) −*x* + 1, *y* − ½, −*z* + ½; (iii) −*x* + 1, −*y* + 1, −*z* + 1; (iv) −*x* + 2, −*y* + 1, −*z* + 1.

Data collection: *CrysAlis PRO* (Agilent, 2014); cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2* and *publCIF* (Westrip, 2010).

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Supporting information for this paper is available from the IUCr electronic archives (Reference: HG5463).

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S1. Comment

2-Mercapto-1-methylimidazole or methimazole **1** belongs to a class of five-membered heterocyclic nitrogen compounds, which possess various biological activities (e.g. it is a widely used anti-thyroid drug under the name Tapazole), see: Rong *et al.* (2013). Additionally, it has found use as a multidentate ligand in the fields of inorganic and organometallic chemistry, in which the sulfur atom can serve as a soft donor towards a wide variety of transition metals, see: Crossley *et al.* (2006). The alkylation of methimazole with alkyl halides (e.g. iodoethane and chlorobutane) lead to the formation of methimazole-based ionic liquids in high yields, see Siriwardana *et al.* (2008). To date, no methimazole-based ionic liquids have been structurally characterized by X-ray diffraction.

Methimazole exists in two tautomeric forms, equilibrating between the 2-thiol **1a** and 2-thione **1b**, and both N-alkylation and S-alkylation reactions are possible, depending upon the reaction conditions and types of substrates employed, see Roy & Mugesh (2005). They reported that only S-alkylated methimazoles were formed. The product structures were established by NMR spectroscopy, which is elusive in terms of proving the exclusive formation of S-alkylated products over N-alkylated products. Herein, we report the crystal structure of S-allylated methimazolium bromide **2**, which was prepared in quantitative yield (96%) via the reaction of methimazole with allyl bromide in refluxing acetonitrile (Scheme S1). The crystal structure of **2** undeniably proves that methimazole reacts through the 2-thione tautomer **1b**.

S2. Synthesis and crystallization

2-Mercapto-1-methylimidazole (0.57 g, 5 mmol) and allyl bromide (0.85 g, 7 mmol) were dissolved in acetonitrile (5.0 mL) and the mixture refluxed for 48 hours. The solvent and excess allyl bromide were removed under vacuum to afford an off-white solid. The solid was washed with toluene (3 x 10 mL) and then recrystallized in acetonitrile to yield pure product **2** as an off-white solid in 96% isolated yield.

S3. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1. The H-atom (H2) located on N2 was allowed to freely refine (isotropically). The remaining H-atoms were placed in calculated positions and allowed to ride during subsequent refinement, with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ and C—H distances of 0.96 Å for methyl hydrogens, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ and C—H distances of 0.97 Å for the secondary hydrogens, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ and C—H distances of 0.93 Å for all remaining hydrogen atoms.

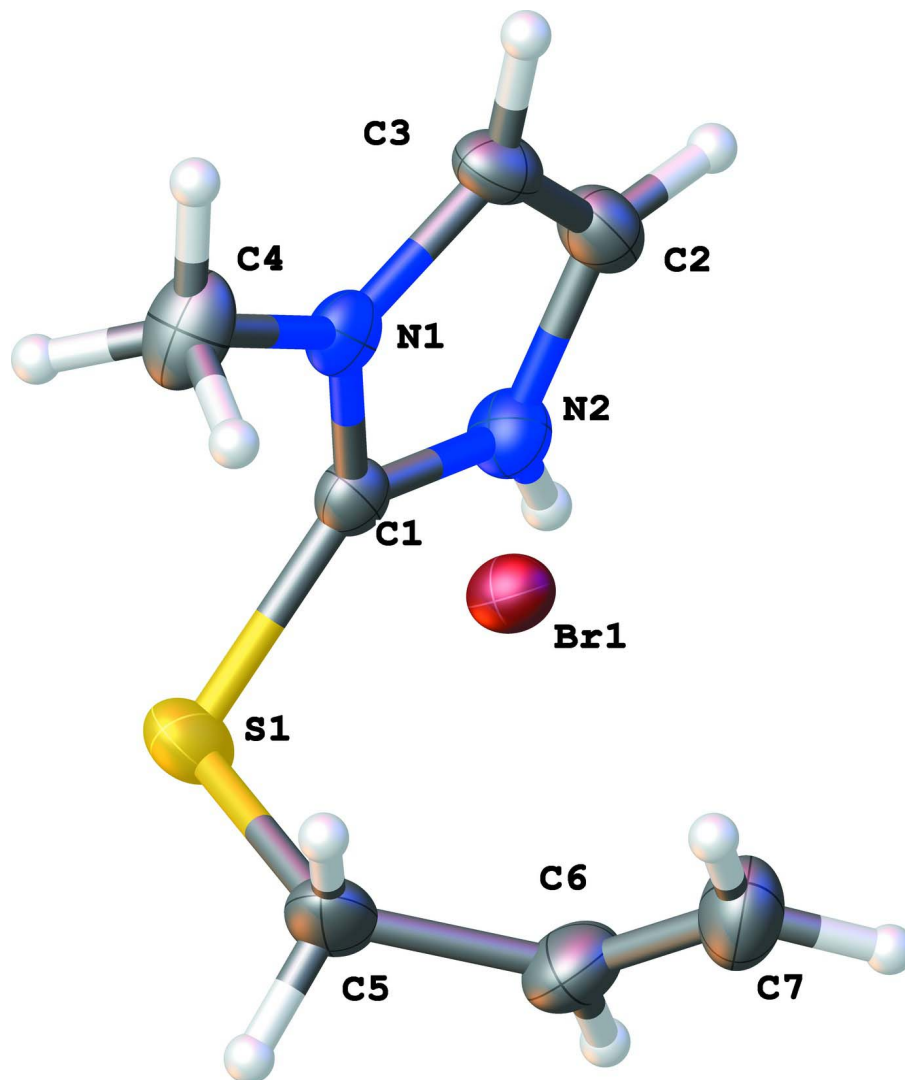


Figure 1

A thermal ellipsoid diagram of the structure of the title compound.



Figure 2

Reaction scheme.

1-Methyl-2-(prop-2-en-1-ylsulfanyl)-1H-imidazol-3-ium bromide

Crystal data

$C_7H_{11}N_2S^+ \cdot Br^-$

$M_r = 235.15$

Monoclinic, $P2_1/c$

$a = 10.8692 (7) \text{ \AA}$

$b = 7.4103 (5) \text{ \AA}$

$c = 12.8551 (9) \text{ \AA}$

$\beta = 104.006 (7)^\circ$
 $V = 1004.62 (11) \text{ \AA}^3$
 $Z = 4$
 $F(000) = 472$
 $D_x = 1.555 \text{ Mg m}^{-3}$
 Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$

Cell parameters from 2203 reflections
 $\theta = 3.9\text{--}27.0^\circ$
 $\mu = 4.24 \text{ mm}^{-1}$
 $T = 180 \text{ K}$
 Prism, colourless
 $0.6 \times 0.32 \times 0.25 \text{ mm}$

Data collection

Agilent Xcalibur, Eos
 diffractometer
 Radiation source: Enhance (Mo) X-ray Source
 Graphite monochromator
 Detector resolution: $16.0514 \text{ pixels mm}^{-1}$
 ω scans
 Absorption correction: multi-scan
 (CrysAlis PRO; Agilent, 2014)
 $T_{\min} = 0.321, T_{\max} = 1.000$

7388 measured reflections
 1829 independent reflections
 1558 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.042$
 $\theta_{\max} = 25.3^\circ, \theta_{\min} = 3.2^\circ$
 $h = -13 \rightarrow 13$
 $k = -8 \rightarrow 8$
 $l = -15 \rightarrow 15$

Refinement

Refinement on F^2
 Least-squares matrix: full
 $R[F^2 > 2\sigma(F^2)] = 0.030$
 $wR(F^2) = 0.065$
 $S = 1.03$
 1829 reflections
 105 parameters
 1 restraint
 Primary atom site location: structure-invariant
 direct methods

Secondary atom site location: difference Fourier
 map
 Hydrogen site location: inferred from
 neighbouring sites
 H atoms treated by a mixture of independent
 and constrained refinement
 $w = 1/[\sigma^2(F_o^2) + (0.027P)^2]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.001$
 $\Delta\rho_{\max} = 0.34 \text{ e \AA}^{-3}$
 $\Delta\rho_{\min} = -0.38 \text{ e \AA}^{-3}$

Special details

Experimental. CrysAlis Pro (Agilent, 2014) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R -factors(gt) etc. and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
Br1	0.70880 (3)	0.66161 (4)	0.53045 (2)	0.02621 (12)
N2	0.6562 (2)	0.0414 (3)	0.2392 (2)	0.0273 (6)
N1	0.6302 (2)	0.1226 (3)	0.39296 (18)	0.0233 (6)
C2	0.5297 (3)	0.0739 (4)	0.2258 (3)	0.0316 (8)
H2A	0.4669	0.0623	0.1625	0.038*
C3	0.5134 (3)	0.1262 (4)	0.3221 (3)	0.0285 (7)
H3	0.4371	0.1587	0.3376	0.034*

C1	0.7171 (3)	0.0704 (4)	0.3410 (2)	0.0234 (7)
S1	0.87834 (8)	0.04183 (11)	0.39532 (7)	0.0373 (2)
C4	0.6547 (4)	0.1637 (4)	0.5076 (2)	0.0370 (9)
H4A	0.5756	0.1749	0.5278	0.055*
H4B	0.7009	0.2750	0.5221	0.055*
H4C	0.7037	0.0681	0.5481	0.055*
C6	0.9092 (3)	0.3747 (4)	0.3027 (3)	0.0410 (9)
H6	0.9450	0.3274	0.2498	0.049*
C5	0.9322 (3)	0.2790 (4)	0.4066 (3)	0.0405 (9)
H5A	0.8889	0.3429	0.4532	0.049*
H5B	1.0223	0.2818	0.4401	0.049*
C7	0.8417 (3)	0.5215 (5)	0.2809 (3)	0.0436 (9)
H7A	0.8047	0.5719	0.3323	0.052*
H7B	0.8305	0.5758	0.2141	0.052*
H2	0.689 (3)	0.007 (4)	0.190 (2)	0.049 (11)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Br1	0.02573 (18)	0.0284 (2)	0.02529 (19)	-0.00350 (13)	0.00772 (13)	-0.00185 (13)
N2	0.0309 (15)	0.0295 (16)	0.0227 (15)	0.0016 (12)	0.0088 (13)	-0.0005 (12)
N1	0.0304 (15)	0.0165 (13)	0.0238 (14)	-0.0003 (11)	0.0081 (12)	0.0002 (10)
C2	0.0256 (17)	0.030 (2)	0.0354 (19)	-0.0008 (14)	-0.0003 (15)	0.0026 (15)
C3	0.0190 (16)	0.0255 (18)	0.041 (2)	0.0028 (13)	0.0064 (14)	0.0023 (15)
C1	0.0253 (17)	0.0180 (17)	0.0264 (17)	-0.0015 (13)	0.0057 (14)	0.0027 (13)
S1	0.0229 (4)	0.0335 (5)	0.0518 (6)	0.0031 (4)	0.0019 (4)	0.0112 (4)
C4	0.059 (2)	0.028 (2)	0.0254 (18)	-0.0016 (16)	0.0128 (17)	-0.0035 (14)
C6	0.039 (2)	0.045 (2)	0.044 (2)	-0.0026 (17)	0.0186 (18)	0.0108 (18)
C5	0.0249 (18)	0.040 (2)	0.051 (2)	-0.0105 (15)	-0.0023 (16)	0.0134 (17)
C7	0.049 (2)	0.042 (2)	0.037 (2)	0.0000 (18)	0.0056 (18)	0.0126 (17)

Geometric parameters (Å, °)

N2—C2	1.366 (4)	C4—H4A	0.9600
N2—C1	1.334 (4)	C4—H4B	0.9600
N2—H2	0.836 (17)	C4—H4C	0.9600
N1—C3	1.373 (4)	C6—H6	0.9300
N1—C1	1.338 (3)	C6—C5	1.480 (4)
N1—C4	1.465 (4)	C6—C7	1.304 (4)
C2—H2A	0.9300	C5—H5A	0.9700
C2—C3	1.349 (4)	C5—H5B	0.9700
C3—H3	0.9300	C7—H7A	0.9300
C1—S1	1.736 (3)	C7—H7B	0.9300
S1—C5	1.847 (3)		
C2—N2—H2	124 (2)	N1—C4—H4B	109.5
C1—N2—C2	109.9 (3)	N1—C4—H4C	109.5
C1—N2—H2	126 (2)	H4A—C4—H4B	109.5

C3—N1—C4	125.3 (3)	H4A—C4—H4C	109.5
C1—N1—C3	109.0 (2)	H4B—C4—H4C	109.5
C1—N1—C4	125.7 (3)	C5—C6—H6	118.1
N2—C2—H2A	126.7	C7—C6—H6	118.1
C3—C2—N2	106.7 (3)	C7—C6—C5	123.8 (3)
C3—C2—H2A	126.7	S1—C5—H5A	108.8
N1—C3—H3	126.3	S1—C5—H5B	108.8
C2—C3—N1	107.3 (3)	C6—C5—S1	113.8 (2)
C2—C3—H3	126.3	C6—C5—H5A	108.8
N2—C1—N1	107.1 (3)	C6—C5—H5B	108.8
N2—C1—S1	126.0 (2)	H5A—C5—H5B	107.7
N1—C1—S1	126.9 (2)	C6—C7—H7A	120.0
C1—S1—C5	100.68 (14)	C6—C7—H7B	120.0
N1—C4—H4A	109.5	H7A—C7—H7B	120.0
N2—C2—C3—N1	-0.7 (3)	C1—N2—C2—C3	0.7 (4)
N2—C1—S1—C5	104.2 (3)	C1—N1—C3—C2	0.5 (3)
N1—C1—S1—C5	-77.0 (3)	C1—S1—C5—C6	-61.4 (3)
C2—N2—C1—N1	-0.4 (3)	C4—N1—C3—C2	-177.7 (3)
C2—N2—C1—S1	178.7 (2)	C4—N1—C1—N2	178.1 (3)
C3—N1—C1—N2	-0.1 (3)	C4—N1—C1—S1	-0.9 (4)
C3—N1—C1—S1	-179.1 (2)	C7—C6—C5—S1	121.8 (3)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H \cdots <i>A</i>	<i>D</i> —H	H \cdots <i>A</i>	<i>D</i> \cdots <i>A</i>	<i>D</i> —H \cdots <i>A</i>
N2—H2 \cdots Br1 ⁱ	0.84 (3)	2.46 (3)	3.246 (2)	158 (3)
C2—H2A \cdots Br1 ⁱⁱ	0.93	2.84	3.723 (4)	159
C3—H3 \cdots Br1 ⁱⁱⁱ	0.93	2.91	3.757 (3)	152
C4—H4B \cdots Br1	0.96	2.87	3.737 (3)	151
C5—H5B \cdots Br1 ^{iv}	0.97	2.89	3.814 (3)	161

Symmetry codes: (i) $x, -y+1/2, z-1/2$; (ii) $-x+1, y-1/2, -z+1/2$; (iii) $-x+1, -y+1, -z+1$; (iv) $-x+2, -y+1, -z+1$.