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FEATURES OF THE REACTION OF UNSYMMETRICAL 2-MERCAPTO-IMIDAZOLES WITH AROMATIC AND ALIPHATIC KETONES

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The cyclization of unsymmetrical 2-mercaptoimidazoles with aliphatic and aromatic ketones has been studied. Using ^{1}H NMR and X-ray analysis it has been shown that 4-R^1-1H-2-mercaptoimidazoles undergo selective oxidative cyclization to the corresponding 3-R^3-2-R^2-6-R^1-imidazo[2,1-b][1,3]thiazoles while 6-R^4-1H-2-mercaptobenzo[d]imidazoles give a mixture of 6-R^4-3-R^2-2-R^3-benzo[4,5]imidazo[2,1-b][1,3]thiazole and 7-R^4-3-R^2-2-R_3-benzo[4,5]imidazo[2,1-b][1,3]thiazole in the ratio 1 : 1.

Keywords: 6-R^4-3-R^2-2-R^3-benzo[4,5]imidazo[2,1-*b*][1,3]thiazole, 7-R^4-3-R^2-2-R^3-benzo[4,5]imidazo [2,1-*b*][1,3]thiazole, 3-R^3-2-R^2-6-R^1-imidazo[2,1-*b*][1,3]thiazoles, 6-R^1-1H-2-mercaptobenzo[d]imidazoles, 4-R^1-1H-2-mercaptoimidazole, X-ray analysis, selectivity.

2-Mercaptoimidazoles are highly active in reactions with different electrophilic reagents. Analysis of the literature data [1-5] has shown that imidazo[2,1-*b*][1,3]thiazoles obtained in this case prove to have high anti-inflammatory, antibacterial, antipsychotic, and antiallergic activity as inhibitors of cyclooxygenase 2 and dopamine D3 antagonists.

The synthesis of imidazo[2,1-*b*][1,3]thiazoles has been reported only for symmetrical 2-mercaptoimidazoles and the reaction course in the case of unsymmetrical structures has not been determined [1-3]. With the aim of studying the reaction of 2-mercaptoimidazoles with aromatic and aliphatic ketones we prepared a series of novel imidazo[2,1-*b*][1,3]thiazoles **4**.

The starting 2-mercaptoimidazoles were synthesized by a known methods. The 4-aryl-1H-imidazo-2-thiols **1** were prepared by a Markwald reaction from phenacylamines with potassium thiocyanate and the 1H benzimidazo-2-thiols **2** by heating *o*-phenylenediamines with potassium *n*-butyl xanthate in alcohol [6, 7].

Refluxing compounds **1a-c** with the corresponding ketones in glacial acetic acid in the presence of sulfuric acid gave the 3-R^3-2-R^2-6-R^1-imidazo[2,1-*b*][1,3]thiazoles **4a-e** in 36-71% yield and their ^{1}H NMR spectrum showed the absence of the imidazole NH group proton signal.

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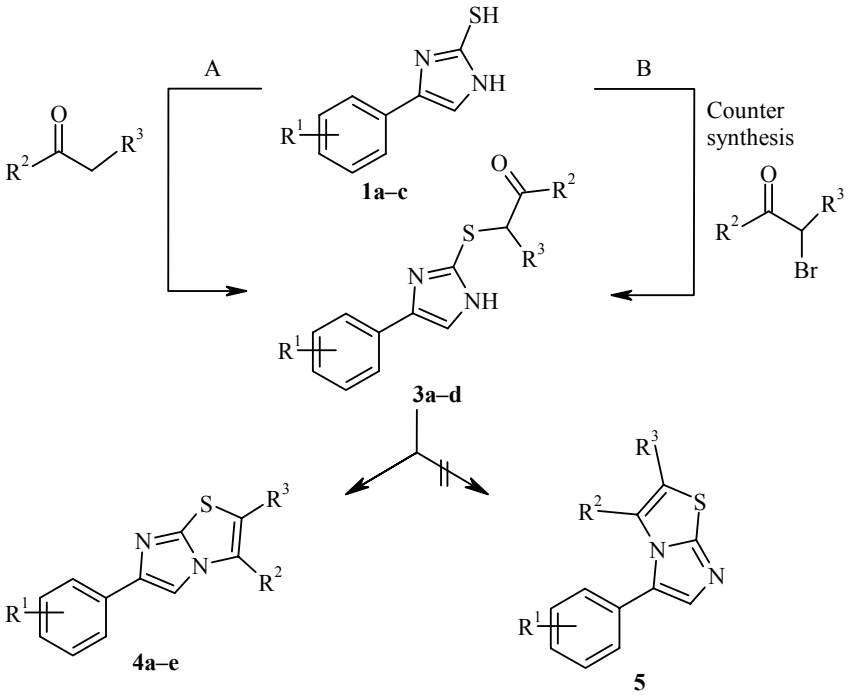
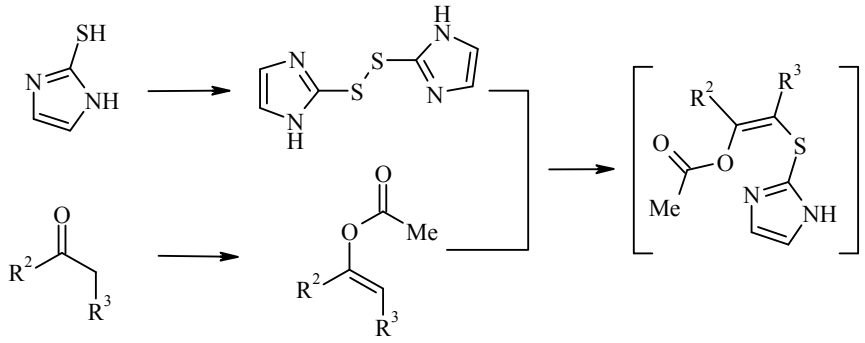


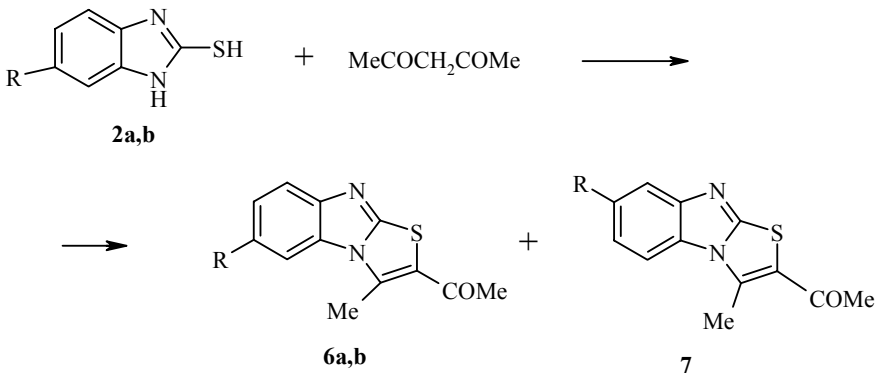
1 a R^1 = H, **b** R^1 = 4-Cl, **c** R^1 = 4-Br; **3 a** R^1 = 4-Br, R^2 = 4-MeC_6H_4, **b** R^1 = 4-Br, R^2 = 2,5-$F_2C_6H_3$, **c** R^1 = 4-Me, R^2 = Ph, **d** R^1 = 4-Cl, R^2 = 4-$O_2NC_6H_4$, **a–d** R^3 = H; **4 a** R^1 = H, R^2 = Me, R^3 = COMe, **b** R^1 = 4-Cl, R^2+R^3 = $(CH_2)_4$, **c** R^1 = 4-Cl, R^2+R^3 = [$CH_2CH(t\text{-}Bu)(CH_2)_2$]; **d** R^1 = 4-Cl, R^2+R^3 = [$CH_2CH(Me)(CH_2)_2$], **e** R^1 = 4-Br, R^2 = 4-MeC_6H_4, R^3 = H

The mechanism we have proposed is based on generalized data [4, 8] and gives the following:



As evidence, in the case of acetophenones it was possible to separate the intermediate 2-(alkylthio)-1H-imidazoles **3a-d**. Their ^{1}H NMR spectra showed the absence of a proton signal for the thiazole fragment and the presence of methylene group and imidazole ring NH proton signals. Subsequent refluxing of intermediates **3** under the same conditions led to a selective conversion (overall 54-72% yield) to the 3,6-diarylimidazo[2,1-*b*][1,3]thiazoles **4a-e** described above, as evidenced by their X-ray structural analytical data. Formation of the alternative 3,5-diarylimidazo[2,1-*b*][1,3]thiazole **5** was not observed.

The reaction of 6-R^4-1H-benzimidazole-2-thiols with ketones in acetic acid in the presence of sulfuric acid under the same reaction conditions gives a mixture of the two isomers 6-R^4-3-R^2-2-R^3-benzo[4,5]imidazo[2,1-*b*][1,3]thiazole **6** and 7-R^4-3-R^2-2-R^3-benzo[4,5]imidazo[2,1-*b*][1,3]thiazole **7** in the ratio 1 : 1 as indicated by their ^{1}H NMR spectroscopic data.



2, 6 a R = H, **b** 6-Br; **7** R = 7-Br

The direction of the cyclization reaction was confirmed by X-ray structural analytical data for 2-(4-chlorophenyl)-5,6,7,8-tetrahydrobenzo[*d*]imidazo[2,1-*b*][1,3]thiazole (**4b**) (Fig. 1) and 6-(4-bromophenyl-3-(4-methylphenyl)imidazo[2,1-*b*][1,3]thiazole (**4e**) (Fig. 2).

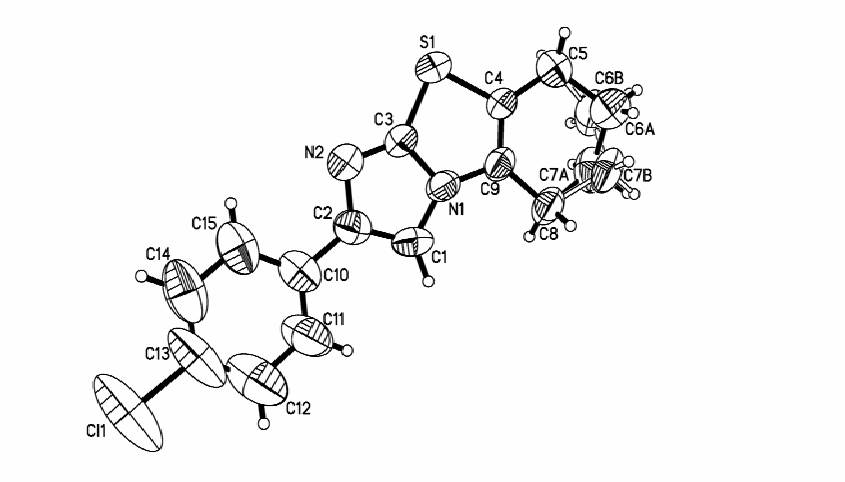


Figure 1. Structure of compound **4b**

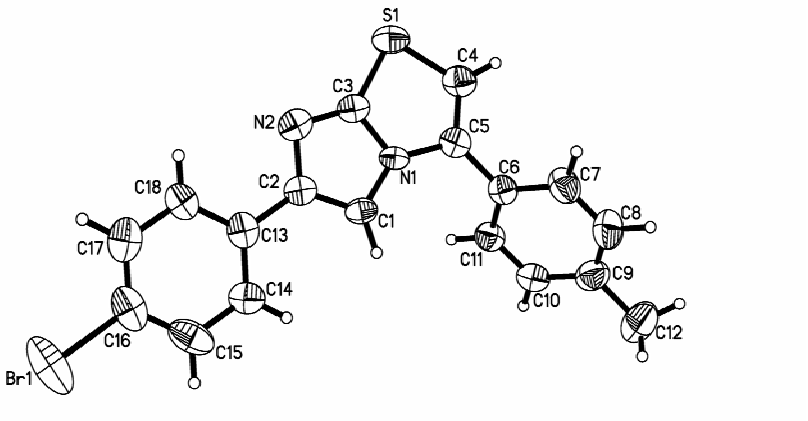


Figure 2. Structure of compound **4e**

TABLE 1. Bond Lengths (d) in Structure **4b**

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
$Cl_{(1)}$–$C_{(13)}$	1.753(6)	$C_{(8)}$–$C_{(9)}$	1.490(5)	$C_{(4)}$–$C_{(5)}$	1.494(5)
$S_{(1)}$–$C_{(4)}$	1.749(4)	$C_{(10)}$–$C_{(15)}$	1.389(7)	$C_{(5)}$–$C_{(6B)}$	1.530(5)
$N_{(1)}$–$C_{(1)}$	1.376(5)	$C_{(12)}$–$C_{(13)}$	1.33(1)	$C_{(7A)}$–$C_{(8)}$	1.530(5)
$N_{(2)}$–$C_{(3)}$	1.303(5)	$C_{(14)}$–$C_{(15)}$	1.391(7)	$C_{(7B)}$–$C_{(8)}$	1.528(5)
$C_{(1)}$–$C_{(2)}$	1.367(6)	$S_{(1)}$–$C_{(3)}$	1.732(5)	$C_{(10)}$–$C_{(11)}$	1.359(7)
$C_{(4)}$–$C_{(9)}$	1.317(5)	$N_{(1)}$–$C_{(3)}$	1.358(5)	$C_{(11)}$–$C_{(12)}$	1.382(8)
$C_{(5)}$–$C_{(6A)}$	1.526(5)	$N_{(1)}$–$C_{(9)}$	1.398(5)	$C_{(13)}$–$C_{(14)}$	1.39(1)
$C_{(6A)}$–$C_{(7A)}$	1.526(5)	$N_{(2)}$–$C_{(2)}$	1.378(5)		
$C_{(6B)}$–$C_{(7B)}$	1.528(5)	$C_{(2)}$–$C_{(10)}$	1.453(6)		

TABLE 2. Valence Angles (ω) in Structure **4b**

Angle	ω, deg	Angle	ω, deg.
$C_{(3)}$–$S_{(1)}$–$C_{(4)}$	89.9(2)	$C_{(3)}$–$N_{(1)}$–$C_{(1)}$	105.6(4)
$C_{(3)}$–$N_{(1)}$–$C_{(9)}$	114.7(3)	$C_{(1)}$–$N_{(1)}$–$C_{(9)}$	139.6(4)
$C_{(3)}$–$N_{(2)}$–$C_{(2)}$	104.1(4)	$C_{(2)}$–$C_{(1)}$–$N_{(1)}$	105.9(4)
$C_{(1)}$–$C_{(2)}$–$N_{(2)}$	110.6(4)	$C_{(1)}$–$C_{(2)}$–$C_{(10)}$	127.3(4)
$N_{(2)}$–$C_{(2)}$–$C_{(10)}$	122.1(4)	$N_{(2)}$–$C_{(3)}$–$N_{(1)}$	113.8(4)
$N_{(2)}$–$C_{(3)}$–$S_{(1)}$	135.9(3)	$N_{(1)}$–$C_{(3)}$–$S_{(1)}$	110.3(3)
$C_{(9)}$–$C_{(4)}$–$C_{(5)}$	124.1(4)	$C_{(9)}$–$C_{(4)}$–$S_{(1)}$	113.0(3)
$C_{(5)}$–$C_{(4)}$–$S_{(1)}$	122.9(3)	$C_{(4)}$–$C_{(5)}$–$C_{(6A)}$	110.9(9)
$C_{(4)}$–$C_{(5)}$–$C_{(6B)}$	109(2)	$C_{(7A)}$–$C_{(6A)}$–$C_{(5)}$	110.9(9)
$C_{(6A)}$–$C_{(7A)}$–$C_{(8)}$	114(1)	$C_{(7B)}$–$C_{(6B)}$–$C_{(5)}$	112(1)
$C_{(6B)}$–$C_{(7B)}$–$C_{(8)}$	109(2)	$C_{(9)}$–$C_{(8)}$–$C_{(7B)}$	109.1(9)
$C_{(9)}$–$C_{(8)}$–$C_{(7A)}$	109.0(7)	$C_{(4)}$–$C_{(9)}$–$N_{(1)}$	112.0(3)
$C_{(4)}$–$C_{(9)}$–$C_{(8)}$	126.0(4)	$N_{(1)}$–$C_{(9)}$–$C_{(8)}$	122.0(4)
$C_{(11)}$–$C_{(10)}$–$C_{(15)}$	117.9(5)	$C_{(11)}$–$C_{(10)}$–$C_{(2)}$	122.2(5)
$C_{(15)}$–$C_{(10)}$–$C_{(2)}$	119.9(5)	$C_{(10)}$–$C_{(11)}$–$C_{(12)}$	123.0(7)
$C_{(13)}$–$C_{(12)}$–$C_{(11)}$	118.2(8)	$C_{(12)}$–$C_{(13)}$–$C_{(14)}$	122.2(7)
$C_{(12)}$–$C_{(13)}$–$Cl_{(1)}$	120.4(8)	$C_{(14)}$–$C_{(13)}$–$Cl_{(1)}$	117.4(8)
$C_{(13)}$–$C_{(14)}$–$C_{(15)}$	118.5(7)	$C_{(10)}$–$C_{(15)}$–$C_{(14)}$	120.2(6)

TABLE 3. Bond Lengths (*d*) in Structure **4e**

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
$Br_{(1)}$–$C_{(16)}$	1.890(5)	$C_{(10)}$–$C_{(11)}$	1.374(6)	$C_{(5)}$–$C_{(6)}$	1.468(6)
$S_{(1)}$–$C_{(4)}$	1.732(5)	$C_{(13)}$–$C_{(14)}$	1.390(6)	$C_{(6)}$–$C_{(7)}$	1.390(7)
$N_{(1)}$–$C_{(1)}$	1.365(5)	$C_{(15)}$–$C_{(16)}$	1.370(8)	$C_{(8)}$–$C_{(9)}$	1.373(7)
$N_{(2)}$–$C_{(3)}$	1.314(6)	$C_{(17)}$–$C_{(18)}$	1.379(7)	$C_{(9)}$–$C_{(12)}$	1.521(8)
$C_{(1)}$–$C_{(2)}$	1.358(6)	$S_{(1)}$–$C_{(3)}$	1.730(5)	$C_{(13)}$–$C_{(18)}$	1.387(7)
$C_{(4)}$–$C_{(5)}$	1.344(6)	$N_{(1)}$–$C_{(3)}$	1.360(5)	$C_{(14)}$–$C_{(15)}$	1.379(7)
$C_{(6)}$–$C_{(11)}$	1.382(6)	$N_{(1)}$–$C_{(5)}$	1.397(6)	$C_{(16)}$–$C_{(17)}$	1.375(7)
$C_{(7)}$–$C_{(8)}$	1.359(7)	$N_{(2)}$–$C_{(2)}$	1.386(5)		
$C_{(9)}$–$C_{(10)}$	1.389(7)	$C_{(2)}$–$C_{(13)}$	1.464(6)		

TABLE 4. Valence Angles (ω) in Structure **4e**

Angle	ω, deg	Angle	ω, deg.
$C_{(3)}$–$S_{(1)}$–$C_{(4)}$	89.7(2)	$C_{(3)}$–$N_{(1)}$–$C_{(1)}$	106.4(4)
$C_{(3)}$–$N_{(1)}$–$C_{(5)}$	115.1(4)	$C_{(1)}$–$N_{(1)}$–$C_{(5)}$	138.4(4)
$C_{(3)}$–$N_{(2)}$–$C_{(2)}$	103.6(4)	$C_{(2)}$–$C_{(1)}$–$N_{(1)}$	105.9(4)
$C_{(1)}$–$C_{(2)}$–$N_{(2)}$	111.1(4)	$C_{(1)}$–$C_{(2)}$–$C_{(13)}$	127.7(4)
$N_{(2)}$–$C_{(2)}$–$C_{(13)}$	121.2(4)	$N_{(2)}$–$C_{(3)}$–$N_{(1)}$	113.0(4)
$N_{(2)}$–$C_{(3)}$–$S_{(1)}$	136.2(4)	$N_{(1)}$–$C_{(3)}$–$S_{(1)}$	110.8(3)
$C_{(5)}$–$C_{(4)}$–$S_{(1)}$	114.1(4)	$C_{(4)}$–$C_{(5)}$–$N_{(1)}$	110.3(4)
$C_{(4)}$–$C_{(5)}$–$C_{(6)}$	127.8(4)	$N_{(1)}$–$C_{(5)}$–$C_{(6)}$	121.8(4)
$C_{(11)}$–$C_{(6)}$–$C_{(7)}$	118.1(4)	$C_{(11)}$–$C_{(6)}$–$C_{(5)}$	120.5(4)
$C_{(7)}$–$C_{(6)}$–$C_{(5)}$	121.2(4)	$C_{(8)}$–$C_{(7)}$–$C_{(6)}$	120.6(5)
$C_{(7)}$–$C_{(8)}$–$C_{(9)}$	121.6(5)	$C_{(8)}$–$C_{(9)}$–$C_{(10)}$	118.3(5)
$C_{(8)}$–$C_{(9)}$–$C_{(12)}$	121.3(5)	$C_{(10)}$–$C_{(9)}$–$C_{(12)}$	120.4(5)
$C_{(11)}$–$C_{(10)}$–$C_{(9)}$	120.4(5)	$C_{(10)}$–$C_{(11)}$–$C_{(6)}$	120.9(4)
$C_{(18)}$–$C_{(13)}$–$C_{(14)}$	117.7(4)	$C_{(18)}$–$C_{(13)}$–$C_{(2)}$	121.1(4)
$C_{(14)}$–$C_{(13)}$–$C_{(2)}$	121.2(4)	$C_{(15)}$–$C_{(14)}$–$C_{(13)}$	120.8(5)
$C_{(16)}$–$C_{(15)}$–$C_{(14)}$	120.5(5)	$C_{(15)}$–$C_{(16)}$–$C_{(17)}$	119.8(5)
$C_{(15)}$–$C_{(16)}$–$Br_{(1)}$	119.5(5)	$C_{(17)}$–$C_{(16)}$–$Br_{(1)}$	120.5(5)
$C_{(16)}$–$C_{(17)}$–$C_{(18)}$	119.8(5)	$C_{(17)}$–$C_{(18)}$–$C_{(13)}$	121.4(5)

EXPERIMENTAL

All solvents and reagents were obtained from commercial sources. Melting points for the compounds synthesized were obtained on a Buchi B-520 instrument (Switzerland). ^{1}H NMR spectra were measured on a Varian WXR-400 spectrometer (200 MHz) using DMSO-d_6 and with TMS as internal standard. The X-ray analysis was carried out on a Siemens P3/PC, four circle diffractometer. The structure was solved by a direct method using the *SHELXTL* program package. Crystals of compounds **4b,e** were grown from solutions in DMF.

The course of the reactions was monitored by TLC on alumina plates coated with Merck Kieselgel 60 F-254 silica gel.

X-ray Structural Analysis of 2-(4-chlorophenyl)-5,6,7,8-tetrahydrobenzo[*d*]imidazo[2,1-*b*][1,3]thiazole (4b). Unit cell parameters and the intensities of 2424 reflections (2423 independent, R_{int} = 0.231) were measured on the Siemens P3/PC (MoKα, graphite monochromator, 2θ/θ scanning, $2\theta_{max}$ = 50°).

The structure was solved by a direct method using the *SHELX97* program package [9]. In the refinement of the structure bond length limits of 1.53 Å were placed on Csp^3–Csp^3 in the disordered fragment. The positions of the hydrogen atoms in the ordered part of the molecule were revealed in electron density difference synthesis and for atoms $C_{(6)}$ and $C_{(7)}$ they were calculated geometrically and refined using the "riding" model with U_{iso} = 1.2U_{eq} for the non-hydrogen atom bound to the given hydrogen atom. The structure was refined by F^2 full matrix least squares analysis in the anisotropic approximation for non-hydrogen atoms to wR^2 = 0.158 for 2382 reflections (R_1 = 0.061 for 1115 reflections with $F > 4\sigma(F)$, S = 0.980).

Crystals are rhombic, $C_{15}H_{13}ClN_2S$, at 20 C: a = 14.433(3) b = 7.504(1), c = 25.641(5) Å, V = 2777.3(9) Å^3, M_r = 288.78, Z = 8, space group *Pbca*, d_{calc} = 1.381 g/cm^3, μ(MoKα) = 0.412 mm^{-1}, F(000) = 1200.

All of the non-hydrogen atoms in the five-membered heterocycles and chlorophenyl substituent lie in a single plane to an accuracy of 0.02 Å and this leads to steric strain between the imidazole ring and the hydrogen atoms of the benzene ring as evidenced by the shortened intramolecular contacts $H_{(1)}\cdots H_{(11)}$ 2.30 (sum of van der Waal radii 2.34 [10]), $H_{(11)}\cdots C_{(1)}$ 2.70 (2.87), and $H_{(15)}\cdots N_{(2)}$ 2.55 Å (2.67 Å).

The tetrahydro ring is disordered into two *half-chair* configurations (**A** and **B**) with a population density of 64 : 36 respectively (folding parameters [11]: $S = 0.74$, $\theta = 35.35$, $\psi = 28.40$ for conformer **A** and $S = 0.80$, $\theta = 35.17$, $\psi = 29.25$ in conformer **B**). The deviations of atoms $C_{(6)}$ and $C_{(7)}$ from the mean square plane of the remaining ring atoms are -0.38 and 0.33 Å in **A** and 0.37 and -0.41 Å in **B** respectively.

The crystal shows shortened intermolecular contacts: $H_{(6ab)}\cdots Cl_1$ (-*x*, -*y*, 1-*z*) 2.95 (sum of van der Waal radii 3.06), $H_{(12)}\cdots Cl_{(1)}$ (0.5-*x*, *y*, *z*) 2.87, $Cl_{(1)}\cdots H_{(5b)}$ (*x*, 0.5-*y*, 0.5+*z*) 3.03, $S_{(1)}\cdots C_{(7b)}$ (*x*, 1+*y*, *z*) 3.44 (3.51), and $S_{(1\}}\cdots H_{(7ba)}$ (*x*, 1+*y, z)* 2.94 Å (2.96 Å) (Tables 1 and 2).

6-(4-Bromophenyl)-3-(4-methylphenyl)imidazo[2,1-*b*][1,3]thiazole (4e). Unit cell parameters and the intensities of 2885 reflections (2671 independent, $R_{int} = 0.072$) were measured on the Siemens P3/PC (MoKα, graphite monochromator, 2θ/θ scanning, $2\theta_{max} = 50°$).

The structure was solved by a direct method using the *SHELXTL* program package [9]. Absorption was allowed for by a semiempirical method from the results of ψ scanning with $T_{min} = 0.329$ and $T_{max} = 0.757$. The positions of the hydrogen atoms were revealed in electron density difference synthesis and refined using the "riding" model with $U_{iso} = 1.2U_{eq}$ for the non-hydrogen atom bound to the given hydrogen atom. The structure was refined by F^2 full matrix least squares analysis in the anisotropic approximation for non-hydrogen atoms to $wR^2 = 0.112$ for 2600 reflections ($R_1 = 0.051$ for 1484 reflections with $F > 4\sigma(F)$, $S = 0.953$).

Crystals are triclinic, $C_{(18)}H_{\{13)}BrN_2S$, at 20°C: $a = 7.379(2)$ $b = 7.804(2)$, $c = 14.408(4)$ Å, $\alpha = 76.12(2)^o$, $\beta = 79.57(2)$, $\gamma = 88.22(2)$, $V = 792.1(4)$ Å^3, $M_r = 369.27$, $Z = 2$, space group $P\bar{1}$, $d_{calc} = 1.548$ g/cm^3, $\mu(MoK\alpha) = 2.732$ mm^{-1}, $F(000) = 372$.

The bicyclic fragment is planar to an accuracy of 0.01 Å. The bromophenyl substituent on atom $C_{(2)}$ is virtually coplanar with the bicycle plane ($C_{(1)}$–$C_{(2)}$–$C_{(13)}$–$C_{(14)}$ torsional angle -4.4(7)°) which leads to a shortening of intramolecular contacts $H_{(18)}\cdots N_{(2)}$ 2.58 (sum of Van der Waal radii 2.67 [10]) and $H_{(14)}\cdots C_{(1)}$ 2.72 Å (2.87 Å). The substituent at atom $C_{(5)}$ is twisted relative to the plane of the bicyclic fragment (torsional angle $C_{(4)}$–$C_{(5)}$–$C_{(6)}$–$C_{(7)}$ 54.8(6)).

The crystal shows shortened intramolecular contacts $H_{(14)}\cdots S_{(1)}$ (1+*x*, *y*, *z*) 2.99 (3.01) and $H_{(11)}\cdots N_{(2)}$ (-1-*x*, 1-*y*, 1-*z*) 2.64 Å (2.67 Å) (Tables 3 and 4).

2-(1H-Imidazol-2-ylthio)-1-(R^3-phenyl)ethanones 3 (General Method). A. Sulfuric acid (96%, 3.3 mmol) was added to a solution of 2-mercaptoimidazole (3 mmol) and the corresponding ketone (3.3 mmol) in glacial acetic acid (10-15 ml). The reaction mixture was stirred at 70 C for 15-20 min, cooled to room temperature, and the precipitate formed was filtered off and washed with aqueous alcohol.

B. (counter synthesis). A solution of the corresponding □-bromoacetophenone (3.3 mmol) in ethanol (5 ml) was added to a solution of 2-mercaptoimidazole (3 mmol) in aqueous alcoholic potassium hydroxide solution (10 ml, 3.3 mmol). The product was stirred for 3-5 min to the beginning of crystallization and the precipitate was filtered off and washed with water and then alcohol. Yield 87-95%.

2-{[4-(4-Bromophenyl)-1H-imidazol-2-yl]thio}-1-(4-methylphenyl)ethanone (3a). Mp 155-157 C, yield 97%. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.27 (3H, s, CH_3); 4.90 (2H, s, CH_2); 7.09 (2H, d, $J = 8$, ArH); 7.30-7.55 (4H, m, ArH); 7.60 (2H, d, $J = 10$, ArH); 12.45 (1H, s, NH).

2-{[4-(4-Bromophenyl)-1H-imidazol-2-yl]thio}-1-(2,5-difluorophenyl)ethanone (3b). Mp 143-145 C, yield 92%. ^{1}H NMR Spectrum, δ, ppm (*J*, Hz): 5.05 (2H, s, CH_2); 6.90 (1H, m, ArH); 7.25 (1H, m, ArH); 7.40-7.73 (5H, m, ArH); 7.90 (1H, m, ArH); 12.55 (1H, s, NH).

1-(4-Methylphenyl)-2-[(4-phenyl-1H-imidazol-2-yl)thio]ethanone (3c). Mp 135-137 C, yield 95%. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.20 (3H, s, CH_3); 4.95 (2H, s, CH_2); 6.95-7.20 (3H, m, ArH); 7.25-7.50 (4H, m, ArH); 7.65 (1H, s, CH); 7.75 (2H, d, $J = 10$, ArH); 12.40 (1H, s, NH).

2-{[4-(4-Chlorophenyl)-1H-imidazol-2-yl]thio}-1-(4-nitrophenyl)ethanone (3d). Mp 165-166 C, yield 95%. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.05 (2H, s, CH_2); 7.30-7.65 (5H, m, ArH); 8.10-8.44 (4H, m, ArH); 12.35 (1H, s, NH).

Imidazo[2,1-*b*][1,3]thiazoles 4a-e, 6a,b, 7 (general method). A. Sulfuric acid (96%, 3.3 mmol) was added to a solution of 2-mercaptomidazole (3 mmol) and the corresponding ketone (3.3 mmol) in glacial acetic acid (10-15 ml) and refluxed for 1-1.5 h. The product was cooled to room temperature and diluted with water (5 ml). The precipitate formed was filtered off, washed with water, dissolved in hot alcohol, and the product was precipitated using aqueous ammonia (15%). Yield 36-72%.

B. Sulfuric acid (3 mmol) was added to a solution of 2-(1H-imidazol-2-ylthio)-1-(R^3-phenyl)ethanone (3 mmol) in glacial acetic acid and refluxed for 20-40 min. The product was cooled to room temperature and diluted with water (5 ml). The precipitate formed was filtered off, washed with water, dissolved in hot alcohol, and the product was precipitated using aqueous ammonia (15%). Reaction product yields 41-75%.

1-(3-Methyl-6-phenylimidazo[2,1-*b*][1,3]thiazol-2-yl)ethanone (4a). Mp 191-194°C, yield 68%. ^{1}H NMR spectrum, δ, ppm : 2.15 (3H, s, CH_3); 2.5 (3H, s, Ac); 7.30-7.55 (5H, m, ArH); 8.20 (1H, s, CH).

2-(4-Chlorophenyl)-5,6,7,8-tetrahydrobenzo[*d*]imidazo[2,1-*b*][1,3]thiazole (4b). Mp 180-183 C, yield 58%. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.6 (4H, s, $2CH_2$); 2.65 (4H, m, $2CH_2$); 7.38 (2H, d, *J* = 9, ArH); 7.60 (2H, d, *J* = 9, ArH); 8.18 (1H, s, CH).

7-*tert*-Butyl-2-(4-chlorophenyl)-5,6,7,8-tetrahydroimidazo[2,1-*b*][1,3]benzothiazole (4c). Mp 160-163 C, yield 45%. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.80 (9H, s, $3CH_3$); 1.25-1.70 (3H, m, CH_2); 2.00-2.20 (1H, m, CH); 2.30-2.80 (4H, m, $2CH_2$); 7.40 (2H, d, *J* = 8, ArH); 7.82 (2H, d, *J* = 8. ArH); 8.16 (1H, s, CH).

2-(4-Chlorophenyl)-7-methyl-5,6,7,8-tetrahydrobenzo[*d*]imidazo[2,1-b][1,3]thiazole (4d). Mp 164-165 C, yield 36%. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05 (3H, d, CH_3); 1.50 (1H, m, CH); 1.75-2.10 (2H, m, CH_2); 2.15-2.35 (1H, m, $1/2CH_2$); 2.55-2.80 (3H, m, $3/2CH_2$); 7.40 (2H, d, *J* = 8, ArH); 7.82 (2H, d, *J* = 8, ArH); 8.16 (1H, s, CH).

6-(4-Bromophenyl)-3-(4-methylphenyl)imidazo[2,1-*b*][1,3]thiazole (4e). Mp 216-218°C, yield 55%. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.25 (3H, s, CH_3); 7.18 (1H, s, CH); 7.35 (2H, d, *J* = 10, ArH); 7.53 (2H, d, *J* =8, ArH); 7.70 (2H, d, *J* = 10, ArH); 7.88 (2H, d, *J* = 8, ArH); 8.21 (1H, s, CH).

1-(3-Methylbenzo[4,5]imidazo[2,1-b**][1,3]thiazol-2-yl)-1-ethanone (6a)**. Mp 198-200 C, yield 70%. ^{1}H NMR Spectrum, δ, ppm (*J*, Hz): 2.60 (3H, s, Ac); 3.10 (3H, s, CH_3); 7.34 (2H, m, ArH); 7.69 (1H, d, *J* = 8 ArH); 8.08 (1H, d, *J* = 8, ArH).

1-(6-Bromo-3-methylbenzo[4,5]imidazo[2,1-*b*][1,3]thiazol-2-yl)-1-ethanone (6b) and 1-(7-Bromo-3-methylbenzo[4,5]imidazo[2,1-*b*][1,3]thiazol-2-yl-1-ethanone (7). Yield of the mixture 58%. ^{1}H NMR spectrum, δ, ppm: 2.55 (6H, s, 2Ac); 3.05 (6H, s, $2CH_3$); 7.45-7.55 (4H, m, ArH); 7.87 (1H, s, ArH); 8.00 (1H, s, ArH).

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