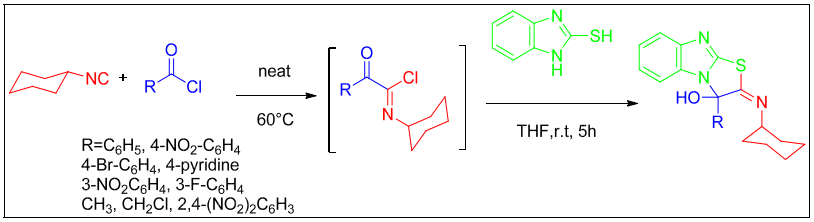
A Simple One-pot Three-component Synthesis of Dihydrobenzo[4,5]imidazo[2,1-*b*]thiazol-3-ols by Reaction of Acyl Chlorides, Isocyanides, and 2-Mercaptobenzimidazoles

Mahdiyeh Talebizadeh, Mohammad Anary-Abbasinejad, and Ali Darehkordi*

Department of Chemistry, Faculty of Science, Vali-e-Asr University of Rafsanjan, Rafsanjan 77176, Iran
*E-mail: adarehkordi@yahoo.com; darehkordi@mail.vru.ac.ir

Received May 2, 2018
DOI 10.1002/jhet.3335
Published online 00 Month 2018 in Wiley Online Library (wileyonlinelibrary.com).



The reactive imidoyl chloride adducts generated *in situ* from the reaction of isocyanide and acyl chlorides were trapped by 2-mercaptobenzimidazole to yield highly functionalized dihydrobenzo[4,5]imidazo[2,1-*b*] thiazoles in excellent yields.

J. Heterocyclic Chem., **00,** 00 (2018).

INTRODUCTION

The benzimidazole nucleus is one of the bioactive heterocyclic compounds that exhibit a range of biological activities [1]. Specifically, this nucleus is a constituent of the vitamin B12 [2].

Also 2-mercaptobenzimidazoles are convenient precursors that have been extensively utilized in the synthesis of compounds containing S–C bonds [3].

Recently, many studies have been focused on the design and synthesis of thiazolo imidazole derivatives, because of their highly significant bioactivities. These compounds have been reported to possess a wide spectrum of biologic activities [4].

Many reactions were developed in the last decades for which the reactivity of 2-mercaptobenzimidazole towards diverse reagents was utilized for the synthesis of nitrogen-bridged and sulfur-bridged heterocycles. From the point of view for biological activities, benzimidazole derivatives are useful intermediates and subunits for the development of molecules having pharmaceutical or biological interests [4–6].

Imidazo[2,1-*b*]thiazoles and their derivatives have attracted more and more research interest since its synthetic utility and occupy a prominent place in medicinal chemistry because of their therapeutic properties. The imidazo[2,1-*b*]thiazole derivatives have emerged as an important target molecules owing to their therapeutic and pharmacological properties such as antibacterial [7], antifungal [8], antihelmintic [9,10], and antitumor [11–15] agents. Also compounds containing this heterocyclic system have been reported as potential acetylcholinesterase and butyrylcholinesterase inhibitors [16].

Previous studies have also showed that some molecules like tricyclic benzimidazole derivatives had anti-HIV activity, which had led to the discovery of 1*H*,3*H*-thiazolo[3,4-*a*]benzimidazoles [4].

The literature describes several methods of synthesis of thiazolo benzimidazoles and their potential biological activities [17,18]. Therefore, the development of more and novel effective thiazolo[3,4-*a*] benzimidazoles is a pharmacological interest.

On the basis of the aforementioned facts and our interest in heterocyclic chemistry, and various imidoyl chlorides reactions, and in order to synthesize bioactive heterocyclic compounds in this project, we decided to synthesize a new series of dihydrobenzo[4,5]imidazo[2,1-*b*]thiazol-3-ols using N,S-bidentate nucleophides such as 2-mercaptobenzimidazole and imidoyl chlorides, which are prepared from a reaction of simple aromatic and aliphatic acyl chlorides with isocyanides without separation and purification (*in situ*).

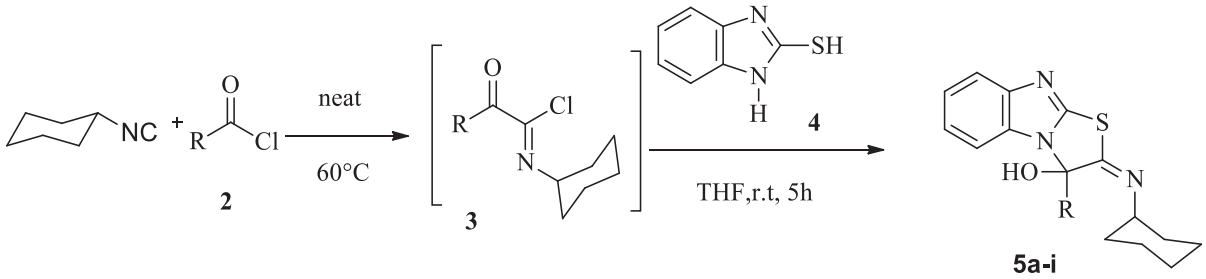
RESULTS AND DISCUSSION

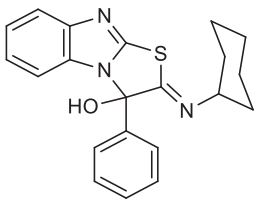
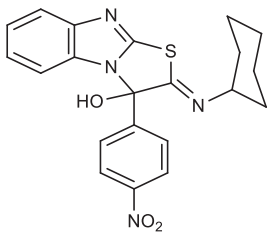
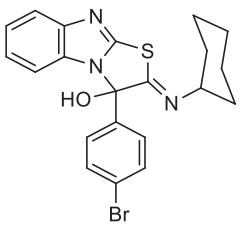
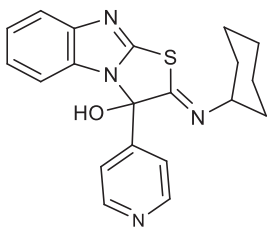
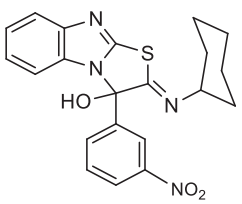
The reaction of isocyanides with acyl chlorides produced reactive imidoyl chlorides, which have been used for the synthesis of a wide variety of organic compounds. They are starting materials or key intermediates in the preparation of heterocyclic compounds and fused analogues [19,20].

The ketoimidoyl chloride adduct **3**, obtained from the reaction of cyclohexyl isocyanide **1** with acyl chlorides **2**, was reacted with 2-mercaptobenzimidazoles **4** at room temperature to give dihydrobenzo[4,5]imidazo[2,1-

Table 1

Reaction of imidoyl chlorides with 2-mercaptobenzimidazole.

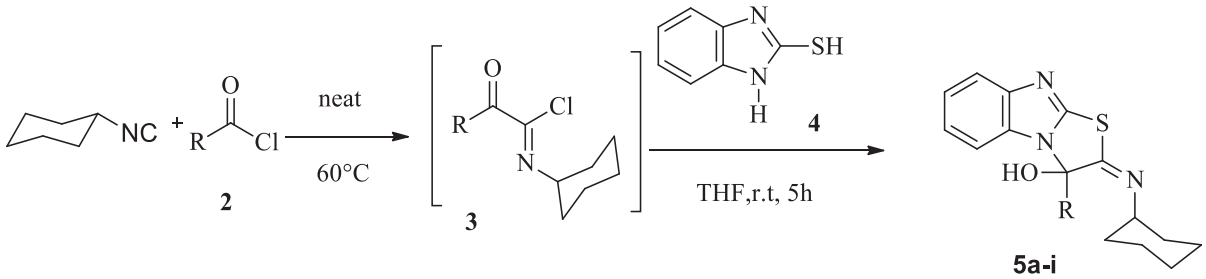


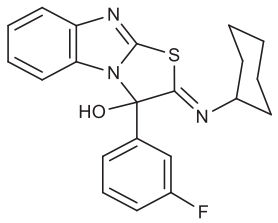
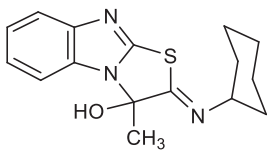
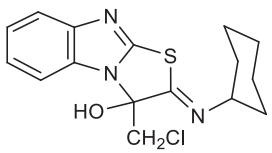
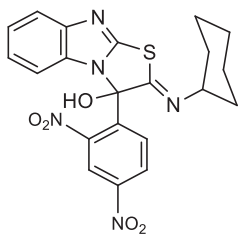
Entry	R	Product	Melting point (°C)	Yield[a] (%)
5a	C_6H_5		145–147	90
5b	4-$NO_2C_6H_4$		188–190	98
5c	4-BrC_6H_4		190–192	96
5d	4-pyridine		191–193	96
5e	3-$NO_2C_6H_4$		189–191	97

(*Continues*)

Table 1

(*Continued*)



Entry	R	Product	Melting point (°C)	Yield[a] (%)
5f	3-FC_6H_4		184–185	96
5g	CH_3		167–169	95
5h	CH_2Cl		180–182	98
5i	2,4-$(NO_2)_2C_6H_3$		168–169	98

[a]Isolated yields.

b]thiazoles **5** in excellent yields. The results are summarized in Table 1. As shown, the reaction was compatible with different aromatic and aliphatic acyl chlorides. Although both electron-donating and electron-withdrawing groups on the acyl chloride resulted in excellent yields, when electron-poor acyl chlorides were used, the related dihydrobenzo[4,5]imidazo[2,1-*b*]thiazol-3-ol was obtained in higher yields.

The structures of compounds **5a–i** were confirmed by the analytical and NMR and IR spectral data. For example, the ^{1}H-NMR spectrum of **5d** exhibited a singlet at δ = 8.76 due to the OH proton, doublet at δ = 8.62, $^3J_{HH}$ = 5.0 Hz, doublet at δ = 7.65, $^3J_{HH}$ = 8.0 Hz, doublet at δ = 7.49, $^3J_{HH}$ = 5.0 Hz, triplet at δ = 7.22, $^3J_{HH}$ = 7.1 Hz, triplet at δ = 7.10, $^3J_{HH}$ = 7.1 Hz, and doublet at δ = 6.95, $^3J_{HH}$ = 8.0 Hz for aromatic

hydrogens. The multiplet signals are at 1.19–1.76 and at 3.05–3.09 ppm for the cyclohexyl ring. The ^{1}H decoupled ^{13}C-NMR spectrum of **5d** showed 16 distinct resonances in agreement with the suggested structure, with the sulfide (C–S) and imine carbons resonating at 150.60 and 161.16 ppm, respectively.

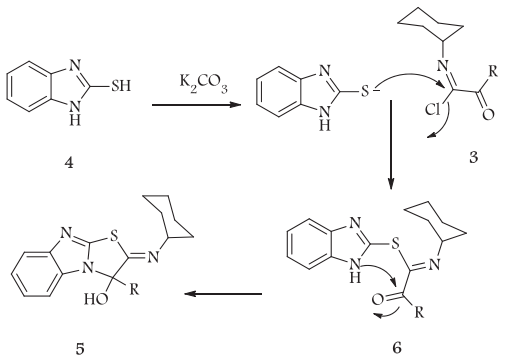
The ^{1}H decoupled ^{13}C-NMR spectrum of **5d** showed 16 distinct resonances in agreement with the suggested structure, with the sulfide (C–S) and imine carbons resonating at 150.60 and 161.16 ppm, respectively. The structure of compound **5f** was finally unambiguously confirmed by X-ray crystallographic analysis (Fig. 1).

Mechanistically, the formation of dihydrobenzo[4,5] imidazo[2,1-*b*]thiazoles **5** can be rationalized by initial formation of the ketoimidoyl chloride adduct **3** from reaction of cyclohexyl isocyanide **1** with acyl chlorides **2**. Then, the intermediate **3** is attacked by 2-mercaptobenzimidazole **4** to form the intermediate **6**, which then undergoes an intramolecular cyclization reaction to afford product **5** (Scheme 1).

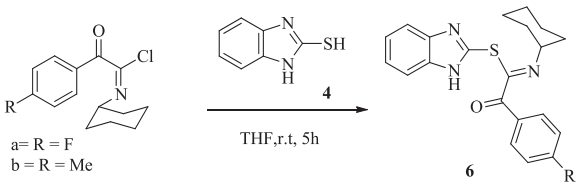
In the aforementioned reaction, when the utilized acyl chloride was not electron poor, the cyclization step did not progress and the intermediate **6** was isolated. Thus, the reaction of 4-fluorobenzoyl chloride and 4-methylbenzoyl chloride with cyclohexyl isocyanide, and 2-mercaptobenzimidazole led to 1*H*-benzo[*d*]imidazol-2-yl-*N*-cyclohexyl-2-oxo-2-phenylethanimidothioate compounds **6a** and **6b** in high yields (Scheme 2). The structures **6a** and **6b** were easily distinguished from compounds **5** by observing the signal related to the carbonyl group at about 190 ppm in ^{13}C-NMR spectra.

It is worth mentioning that all of the 2,3-dihydrobenzo[4,5]imidazo[2,1-*b*]thiazol-3-ol derivatives synthesized by this method were isolated by easily washing the isolated precipitate with diethyl ether. The

Scheme 1. A possible mechanism for the synthesis of dihydrobenzo[4,5] imidazo[2,1-*b*]thiazol-3-ol.



Scheme 2. Synthesis of 1*H*-benzo[*d*]imidazol-2-yl-*N*-cyclohexyl-2-oxo-2-phenylethanimidothioate.



products were characterized by the IR, ^{1}H-NMR, ^{13}C-NMR, and elemental analysis, further confirmed by single-crystal X-ray diffraction determination of compound **5f** (Fig. 1). Crystallographic data for the structure of **5f** reported in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication with CCDC No. 1476856. Structural parameters for **5f**: data collection; crystal size: 0.30 × 0.10 × 0.08 mm^3; $C_{21}H_{20}FN_3OS$, M_r = 381.47,

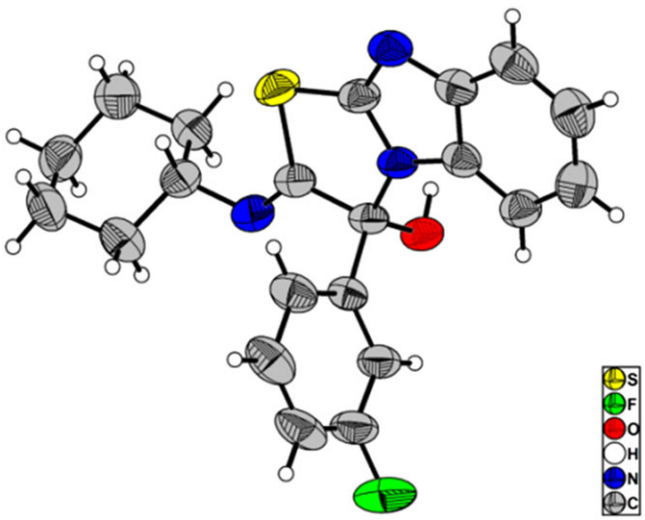


Figure 1. The ORTEP diagram of **5f**. [Color figure can be viewed at wileyonlinelibrary.com]

orthorhombic system, space group $P2_12_12_1$, a = 8.3242 (17), b = 12.107 (2), c = 20.597 (4) Å; V = 2075.8 (7) Å^3, Z = 4.

CONCLUSIONS

In summary, the reaction of ketoimidoyl chlorides with 2-mercaptobenzimidazoles provides a facile and efficient route for synthesis of dihydrobenzo[4,5] imidazo[2,1-*b*]thiazol-3-ol derivatives in excellent yields. The advantages of this method are simply available starting materials, neutral and easy reaction condition, and also very simple purification method.

EXPERIMENTAL

All of the chemicals and solvents were purchased from commercial sources and used without further purification unless otherwise stated. Melting points were determined on a Melt-Temp II melting point apparatus (Merck, Tehran, Iran) and are uncorrected. Elemental analyses were performed at analytical laboratory of Islamic Azad University, Yazd Branch, using a Costech ECS 4010 CHNS–O analyzer. IR spectra were obtained on a Mattson 1000 Fourier transform IR spectrometer. Peaks are reported in wave numbers (cm^{-1}). All of the NMR spectra were recorded on a Bruker model DRX-400 Avance (^{1}H, 400; ^{13}C, 100) NMR spectrometer (Bruker Corporation, Billerica, MA). Chemical shifts of ^{1}H-NMR and ^{13}C-NMR are reported in parts per million (ppm) from tetramethylsilane as an internal standard in DMSO-d_6 or $CDCl_3$ as a solvent.

General procedure for the synthesis of compounds 5a–i. In a typical experimental procedure, a dry, two-necked, 50-mL round-bottom flask was charged with 1.0 mmol of acyl chloride derivatives and 1.0 mmol of cyclohexyl isocyanide and was heated at 60°C for 1 h. Then a mixture of 2-mercaptobenzothiazole (1.0 mmol) and K_2CO_3 (1.0 mmol) in tetrahydrofuran (10 mL) was added. The reaction mixture was stirred at room temperature for 5 h and then was filtered. After removing the solvent under reduced pressure, the crude product was purified by washing with diethyl ether. The products may be further purified by crystallization from absolute ethanol.

3-Phenyl-2-(phenylimino)-2,3-dihydrobenzo[4,5] imidazo[2,1-b]thiazol-3-ol (5a). Colorless crystals, mp: 145–147°C. Yield: 90%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 3060 (OH), 1671 (C═N). Elemental analysis: Calcd. for ($C_{21}H_{21}N_3OS$): C, 69.39; H, 5.82; N, 11.56%. Found: C, 69.44; H, 5.71; N, 11.43%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.30–2.05 (10H, m, 5CH_2 of cyclohexyl), 2.91 (1H, brond, CHN), 7.15–7.17 (3H, m, HAr), 7.23–7.25 (1H, m, HAr), 7.37–7.38 (3H, HAr), 7.46–7.48 (2H, m, HAr). 8.81 (1H, s, OH). ^{13}C-NMR (100 MHz, DMSO-d_6) δ: 24.15, 24.39, 25.36, 31.80, 32.41, 69.28 (C–N-cyclo), 91.47 (C–OH), 112.04, 115.39, 116.22, 124.21, 124.29, 125.66, 128.66, 129.39, 130.24, 131.65, 138.24 (C–S), 151.14 (C–N-cyclo).

3-(4-Nitrophenyl)-2-(phenylimino)-2,3-dihydrobenzo[4,5] imidazo[2,1-b]thiazol-3-ol (5b). Yellow crystals, mp: 188–190°C. Yield: 98%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 3072 (OH), 1670 (C═N). Elemental analysis: Calcd. for ($C_{21}H_{20}N_4O_3S$): C, 61.74; H, 4.92; N, 13.72%. Found: C, 61.51; H, 4.67; N, 13.75%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.22–1.77 (10H, m, 5CH_2 of cyclohexyl), 3.05–3.1 (1H, m, CHN), 6.94 (1H, d, $^3J_{HH}$ = 8.1 Hz, HAr), 7.09 (1H, t, $^3J_{HH}$ = 8.1 Hz, HAr), 7.22 (1H, t, $^3J_{HH}$ = 8.1 Hz, HAr), 7.69 (3H, m), 8.26 (2H, d, $^3J_{HH}$ = 8.1 Hz, HAr), 8.8 (1H, s, OH). ^{13}C-NMR (100 MHz, DMSO-d_6): δ: 23.92, 24.01, 25.39, 32.25, 32.36, 68.14 (C–N-cyclo), 89.59 (C–OH), 110.63, 119.38, 123.11, 123.21, 124.25, 127.18, 131.17, 146.58 147.08, 148.24, 150.43 (C–S), 163.31 (C–N-cyclo).

3-(4-Bromophenyl)-2-(phenylimino)-2,3-dihydrobenzo[4,5] imidazo[2,1-b]thiazol-3-ol (5c). Colorless crystals, mp: 190–192°C. Yield: 96%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 3422 (OH), 1668 (C═N). Elemental analysis: Calcd. for ($C_{21}H_{20}BrN_3OS$): C, 57.02; H, 4.56; N, 9.50%. Found: C, 57.13; H, 4.46; N, 9.38%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.20–1.75 (10H, m, 5CH_2 of cyclohexyl), 3.06–3.09 (1H, broad, CHN), 6.96–7.25 (3H, m, HAr), 7.32 (2H, d, $^3J_{HH}$ = 8.0 Hz, HAr), 7.58–7.60 (3H, m, HAr), 8.57 (1H, s, OH). ^{13}C-NMR (100 MHz, DMSO-d_6): δ: 23.97, 24.04, 25.42, 32.11, 32.40, 68.06 (C–N-cyclo), 89.97 (C–OH), 110.74, 119.25, 122.76, 122.94, 123.03, 128.41, 131.92, 139.35, 147.05, 150.30 (C–S), 161.52 (C═N-cyclo).

2-(Phenylimino)-3-(pyridin-4-yl)-2,3-dihydrobenzo[4,5] imidazo[2,1-b]thiazol-3-ol (5d). Colorless crystals, mp: 191–193°C. Yield: 96%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 3422 (OH), 1673 (C═N). Elemental analysis: Calcd. for ($C_{20}H_{20}N_4OS$): C, 65.91; H, 5.53; N, 15.37%. Found: C, 65.78; H, 5.40; N, 15.52%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.19–1.76 (10H, m, 5CH_2 of cyclohexyl), 3.05–3.09 (1H, m, CHN), 6.95 (1H, d, $^3J_{HH}$ = 8.0 Hz, HAr), 7.10 (1H, t, $^3J_{HH}$ = 7.1 Hz, HAr), 7.22 (1H, t, $^3J_{HH}$ = 7.1 Hz, HAr), 7.49 (2H, d, $^3J_{HH}$ = 5.0 Hz, HAr), 7.65 (1H, d, $^3J_{HH}$ = 8.0 Hz, HAr), 8.62 (2H, d, $^3J_{HH}$ = 5.0 Hz, HAr), 8.76 (1H, s, OH). ^{13}C-NMR (100 MHz, DMSO-d_6): δ: 23.91, 23.99, 25.40, 32.25, 32.36, 68.07 (C–N-cyclo), 89.36 (C–OH), 110.62, 119.36, 120.98, 123.07, 123.17, 131.75, 147.05, 148.32, 150.51, 150.60 (C–S), 161.16 (C═N-cyclo).

3-(3-Nitrophenyl)-2-(phenylimino)-2,3-dihydrobenzo[4,5] imidazo[2,1-b]thiazol-3-ol (5e). Colorless crystals, mp: 189–191°C. Yield: 97%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 3088 (OH), 1674 (C═N). Calcd. for ($C_{21}H_{20}N_4O_3S$): C, 61.75;

H, 4.94; N, 13.72%. Found: C, 61.73; H, 4.96; N, 13.70%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.10–1.76 (10H, m, 5CH_2 of cyclohexyl), 3.08–3.09 (1H, m, CHN), 6.96 (1H, m), 7.06 (1H, m, HAr), 7.20–7.24 (1H, m, HAr), 7.64–7.67 (3H, m, HAr), 8.26–8.29 (1H, m, HAr), 8.40 (1H, t, $^2J_{HH}$ = 2 Hz, HAr), 8.85 (1H, s, OH). ^{13}C-NMR (100 MHz DMSO-d_6): δ: 23.88, 23.99, 25.39, 32.04, 32.33, 68.03 (C–N-cyclo), 89.44 (C–OH), 110.70, 119.38, 121.12, 123.13, 123.23, 124.52, 135.92, 131.72, 132.73, 142.00, 147.09, 148.29, 150.52 (C–S), 161.38 (C═N-cyclo).

3-(3-Fluorophenyl)-2-(phenylimino)-2,3-dihydrobenzo[4,5] imidazo[2,1-b]thiazol-3-ol (5f). Colorless crystals, mp: 184–185°C. Yield: 96%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 3059 (OH), 1669 (C═N). Elemental analysis: Calcd. for ($C_{21}H_{20}FN_3OS$): C, 66.12; H, 5.28; N, 11.02%. Found: C, 66.01; H, 5.35; N, 11.19%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.20–1.70 (10H, m, 5CH_2 cyclohexyl), 2.41 (3H, S, CH_3), 3.04–3.09 (1H, m, CHN), 6.97 (1H, d, $^3J_{HH}$ = 8.1 Hz, HAr), 7.05 (1H, d, $^3J_{HH}$ = 8.1 Hz, HAr), 7.19–7.25 (2H, m, HAr), 7.29–7.33 (1H, m, HAr), 7.38–7.44 (1H, m, HAr), 7.64 (1H, d, $^3J_{HF}$ = 8.1 Hz, HAr), 7.99 (1H, m, HAr), 8.83 (1H, s, OH).

3-Methyl-2-(phenylimino)-2,3-dihydrobenzo[4,5] imidazo[2,1-b]thiazol-3-ol (5g). Colorless crystals, mp: 167–169°C. Yield: 95%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 3055 (OH), 1668 (C═N). Elemental analysis: Calcd. for ($C_{16}H_{19}N_3OS$): C, 63.76; H, 6.35, N, 13.94%. Found: C, 63.89; H, 6.24, N, 13.86%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.25–1.94 (10H, m, 5CH_2 of cyclohexyl), 1.94 (3H, S, CH_3), 3.06–3.09 (1H, m, CHN), 7.23–7.25 (2H, m, ArH), 7.62–7.69 (2H, m, ArH), 7.70 (1H, s, OH). ^{13}C-NMR (100 MHz, DMSO-d_6): δ: 24.16 (CH_3), 25.53, 25.95, 32.54, 67.86 (C–N-cyclo), 88.86 (C–OH) 110.85, 119.08, 122.68, 122.74, 132.12, 147.06, 146.68 (C–S), 161.68 (C═N-cyclo).

3-(Chloromethyl)-2-(phenylimino)-2,3-dihydrobenzo[4,5] imidazo[2,1-b]thiazol-3-ol (5h). Colorless crystals, mp: 180–182°C. Yield: 98%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 3057 (OH), 1672 (C═N). Elemental analysis: Calcd. for ($C_{16}H_{18}ClN_3OS$): C, 57.22; H, 5.40, N, 12.51%. Found: C, 57.17; H, 5.32; N, 12.46%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.29–1.82 (10H, m, 5CH_2 of cyclohexyl), 3.12–3.17 (1H, m, CHN), 4.20 (1H, d, $^2J_{HH}$ = 11.1 Hz, CH_2), 4.68 (1H, d, $^2J_{HH}$ = 11.1 Hz, CH_2), 7.26 (2H, m, HAr), 7.62–7.65 (1H, m, HAr), 7.74–7.77 (1H, m, HAr), 8.50 (1H, s, OH). ^{13}C-NMR (100 MHz, DMSO-d_6): δ: 24.03, 25.52, 32.32, 32.54, 47.19, 67.80 (C–N-cyclo), 90.00 (C–OH), 90.10 (C–Cl), 110.87, 119.23, 123.01, 123.18, 131.88, 146.97, 131.07 (C–S), 159.86 (C═N-cyclo).

3-(2,4-Dinitrophenyl)-2-(phenylimino)-2,3-dihydrobenzo[4,5]imidazo[2,1-b]thiazol-3-ol (5i). Yellow crystals, mp: 168–169°C. Yield: 98%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 3089 (OH), 1672 (C═N). Elemental analysis: Calcd. for ($C_{21}H_{19}N_5O_5S$): C, 55.62; H, 4.22, N, 15.44%. Found: C, 55.55; H, 4.35, N, 15.24%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.22–1.77 (10H, m, 5CH_2 of cyclohexyl), 3.03–3.12 (1H, m, CHN), 7.03–7.15 (3H, m, HAr), 7.24 (1H, m, HAr), 7.68 (1H, d, $^3J_{HH}$ = 8.0 Hz, HAr), 8.36 (1H, d, $^3J_{HH}$ = 8.0 Hz, HAr), 8.56 (1H, S, HAr), 9.17 (1H, s, OH).

1H-Benzo[d]imidazol-2-yl(Z)-N-cyclohexyl-2-(4-fluorophenyl)-2-oxoethanimidothioate (6a). Colorless crystals, mp: 155–156°C. Yield: 95%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 1673 and 1614 (C═O and C═N). Elemental analysis: Calcd. for ($C_{21}H_{20}FN_3OS$): C, 66.12; H, 5.28; N, 11.02%. Found: C, 66.15; H, 5.41; N, 10.88%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ: 1.15–1.84 (10 H, m, 5 CH_2 of cyclohexyl), 3.73–3.76 (1H, m, CHN), 7.43 (2H, t, $^3J_{HH}$ = 8.0 Hz, HAr), 7.60 (2H, dd, $^3J_{HF}$ = 9.1 Hz, $^3J_{HH}$ = 3.6 Hz, HAr), 7.48 (2H, dd, $^3J_{HF}$ = 9.1 Hz, $^3J_{HH}$ = 3.6 Hz, HAr), 7.89 (2H, m, HAr), 9.64 (1H, s, NH). ^{13}C-NMR (100 MHz, DMSO-d_6): δ: 24.98, 25.51, 32.48, 48.23, 114.93, 116.59, 126.6, 130.21 (d, $^4J_{CF}$ = 3.1 Hz), 133.28 (d, $^3J_{CF}$ = 9.0 Hz), 140.164 (C–S), 164.47 (C═N, cyclo), 164.89 (d, $^2J_{CF}$ = 41.0 Hz), 166.41 (d, $^1J_{CF}$ = 280.1 Hz), 189.5 (C═O).

1H-Benzo[d]imidazol-2-yl(Z)-N-cyclohexyl-2-oxo-2-(p-tolyl) ethanimidothioate (6b). Colorless crystals, mp: 145–146°C. Yield: 96%. IR (KBr) ($\overline{\upsilon}_{max}$, cm^{-1}): 1671 and 1604 (C═O and C═N). Elemental analysis: Calcd. for ($C_{22}H_{23}N_3OS$): C, 70.00; H, 6.14; N, 11.13%. Found: C, 69.83; H, 6.04; N, 11.22%. ^{1}H-NMR (400 MHz, DMSO-d_6): 1.12–1.85 (10H, m, 5 CH_2 of cyclohexyl), 2.41 (3H, s, CH_3), 3.73–3.75 (1H, m, CHN), 7.40 (2H, d, $^3J_{HH}$ = 8.1 Hz, HAr), 7.62 (2H, dd, $^3J_{HH}$ = 6.0 Hz, $^3J_{HH}$ = 3.0 Hz, HAr), 7.85 (2 H, d, $^3J_{HH}$ = 8.1 Hz, HAr), 7.89 (2H, $^3J_{HH}$ = 6.0 Hz, $^3J_{HH}$ = 3.0 Hz, HAr), 9.62 (1H, s, NH). ^{13}C-NMR (100 MHz, DMSO-d_6): δ: 21.83 (CH_3), 24.99, 25.53, 32.54, 48.13 (C–N-cyclo), 114.94, 126.61, 127.20, 130.02, 130.19, 130.87, 130.97, 141.00, 145.71 (C–S), 165.13 (C═N-cyclo), 190.87 (C═O).

REFERENCES AND NOTES

[1] Akpa, S. J.; Zoakouma, R. S. P.; Say, V. M.; Ouattara, M.; Kone, M. W.; Sissouma, D.; Adjou, A. Int J Biol Chem Sci 2016, 10, 1403.

[2] O'Neil, M. J.; Smith, A.; Heckelman, E. The Merck Index, 13th ed.; Merck & Co Inc, 2001; Vol 1785, p. 10074.

[3] Abou ECFotooh, O.; Nabii, M. Y. J Chem Eng Data 1982, 27, 207.

[4] Al-Rashood, K. A.; Abdel-Aziz, H. A. Molecules 2010, 15, 3775.

[5] Mavrava, A. T.; Anchina, K. K.; Vuchev, D. I.; Tesnove, J. A.; Kondeva, M. S.; Miteka, K. M. Bioorg Med Chem 2005, 13, 5550.

[6] Yildiz-Oren, I.; Yalcin, I.; Aki-Sener, E.; Ukarturk, N. Eur J Med Chem 2004, 39, 291.

[7] Mohan, J. Indian J Chem 1991, 30B, 898.

[8] Gupta, G. D.; Jain, K. K.; Gupta, R. P.; Pujari, H. K. Indian J Chem 1983, 22B, 268.

[9] Robert, J. F.; Xicluna, A.; Panouse, J. J Eur J Med Chem Chim Ther 1975, 10, 59.

[10] Amarouch, H. P.; Loiseau, R.; Bacha, C.; Caujolle, R.; Payard, M.; Loiseau, P. M.; Bories, C.; Gayral, P. Eur J Med Chem 1987, 22, 463.

[11] Andreani, A.; Bonazzi, D.; Rambaldi, M. Il Farmaco Ed Sci 1980, 35, 896.

[12] Andreani, A.; Bonazzi, D.; Rambaldi, M. Arch Pharm (Weinheim) 1982, 315, 451.

[13] Andreani, A.; Rambaldi, M.; Andreani, F.; Bossa, R.; Galatulas, I. Eur J Med Chem 1988, 23, 385.

[14] Andreani, A.; Rambaldi, M.; Locatelli, A.; Bossa, R.; Fraccari, A.; Galatulas, I. Pharm Acta Helv 1993, 68, 21.

[15] Andreani, A.; Rambaldi, M.; Locatelli, A.; Bossa, R.; Fraccari, A.; Galatulas, I. J Pharm Belg 1993, 48, 378.

[16] Andreani, A.; Burnelli, S.; Granaiola, M.; Guardigli, M.; Leoni, A.; Locatelli, A.; Morigi, R.; Rambaldi, M.; Rizzoli, M.; Varoli, L.; Roda, A. E. J Med Chem 2008, 43, 657.

[17] Chimiri, A.; Monforte, P.; Musumeci, L.; Rao, A.; Zappala, M.; Monforte, A. M. Arch Pharm 2001, 334, 203.

[18] Mavrova, A. T.; Wesselinova, D.; Anichina, K. J Chem Technol Metall 2016, 51, 660.

[19] Nef, J. U. Justus Liebigs Ann Chem 1892, 270, 267.

[20] La Spisa, F. G.; Tron, C.; El Kaïm, L. Synthesis 2014, 46, 829.