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New 6-Phenylimidazo[2,1-*b*]thiazole Derivatives: Synthesis and Antifungal Activity

Gültaze Çapan[1,*], **Nuray Ulusoy**[1], **Nedime Ergenç**[1], and **Muammer Kiraz**[2]

[1] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Istanbul, TR-34452 Beyazit, Istanbul, Turkey
[2] Department of Microbiology, Istanbul Faculty of Medicine, TR-34390 Istanbul, Turkey

Summary. New benzylidene-(6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetic acid hydrazides, 4-alkyl-1-((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetyl)-3-thiosemicarbazides, 2-aryl-3-((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetamido)-4-thiazolidinones, and 3-alkyl-2-(((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetyl)-hydrazono)-4-thiazolidinones were synthesized from 6-phenylimidazo[2,1-*b*]thiazole-3-acetic acid hydrazide and evaluated for antifungal activity against three dermatophyte strains using ketoconazole as standard. Several of them were found as effective as the standard against *Trichophyton rubrum* and *Microsporum audounii* ($MIC = 6\ \mu g/cm^3$), whereas the activity of N-benzylidene-(6-phenylimidazo[2,1-*b*]-thiazol-3-yl)-acetic acid hydrazide against *M. audounii* was superior to the standard ($MIC = 3\ \mu g/cm^3$). 2-(4-Methylphenyl)-3-((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetamido)-4-thiazolidinone and 2-(4-chlorophenyl)-3-((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetamido)-4-thiazolidinone showed the highest activity against *Trichophyton mentagrophytes var. erinacei* NCPF-375 ($MIC = 3\ \mu g/cm^3$).

Keywords. Imidazo[2,1-*b*]thiazole; Benzylidenehydrazides; Thiosemicarbazides; 4-Thiazolidinones; Antifungal activity.

Neue 6-Phenylimidazo[2,1-*b*]thiazolderivate: Synthese und fungistatische Aktivität

Zusammenfassung. Ausgehend von 6-Phenylimidazo[2,1-*b*]-thiazol-3-essigsäurehydrazid wurden neue Benzyliden-(6-phenylimidazo-[2,1-*b*]-thiazol-3-yl)-essigsäurehydrazide, 4-Alkyl-1-((6-phenylimidazo[2,1-*b*])thiazol-3-yl)-acetyl)-3-thiosemicarbazide, 2-Aryl-3-((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetamido)-4-thiazolidinone und 3-Alkyl-2-((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetyl)-hydrazono)-4-thiazolidinone dargestellt und hinsichtlich ihrer fungistatischen Aktivität untersucht. Einige der Verbindungen erwiesen sich als aktiv gegen *Trichophyton rubrum* und *Microsporum audounii* ($MIC = 6\ \mu g/cm^3$). Es stellte sich heraus, daß N-benzyliden-(6-phenylimidazo[2,1-*b*]-thiazol-3-yl)-essigsäurehydrazide gegen *M. audounii* aktiver als die Standardsubstanz Ketokonazol ist ($MIC = 3\ \mu g/cm^3$). 2-(4-Methylphenyl)-3-((6-phenylimidazo[2,1-*b*])thiazol-3-yl)-acetamido)-4-thiazolidinon und 2-(4-Chlorophenyl)-3-((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetamido)-4-thiazolidinon zeigen die größte Aktivität gegen *Trichophyton mentagrophytes var. erinacei* NCPF-375 ($MIC = 3\ \mu g/cm^3$).

* Corresponding author

Introduction

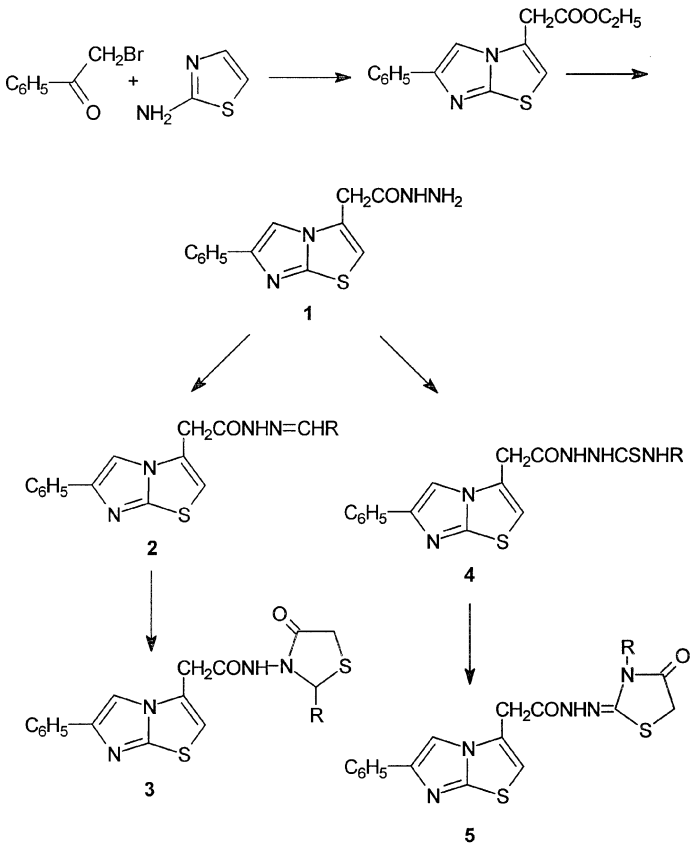
The rapidly expanding population of immunocompromised patients results in a corresponding increase of diseases caused by yeasts and other fungi. Although not life-threatening, superficial mycosis and infections of keratinized tissues such as skin, nails, and hair cause prolonged periods of distress. Dermatophytoses which are most prevalent among superficial mycosis are currently treated by the imidazole derivatives ketoconazole, clotrimazole, miconazole, econazole, and other azole antifungals which interfere with fungal ergosterol synthesis by inhibiting lanosterol 14-demethylase [1]. Derivatives of imidazo-fused heterocycles also show antifungal activity [2, 3]. To provide further insight into the antifungal properties of compounds carrying imidazo-fused systems, the hitherto unreported imidazo[2,1-*b*]thiazole derivatives **2–5** were synthesized from 6-phenylimidazo[2,1-*b*]thiazole-3-acetic acid hydrazide **1** [4] and evaluated for antifungal activity against three dermatophyte strains (*Trichophyton mentagrophytes var. erinacei* NCPF-375, *Trichophyton rubrum*, and *Microsporum audounii*).

Results and Discussion

The target compounds were prepared from 6-phenylimidazo[2-1-*b*]thiazole-3-acetic acid hydrazide (**1**) as outlined in Scheme 1. **1** reacted with aromatic aldehydes to afford substituted N-benzylidene-(6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetic acid hydrazides **2** which furnished 2-aryl-3-((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetamido)-4-thiazolidinones **3** on cyclodehydration with thioglycolic acid. 4-Alkyl-1-((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetyl)-3-thiosemicarbazides **4** were obtained from **1** and the corresponding alkylisothiocyanates. On treatment with ethyl bromoacetate, **4** yielded 3-alkyl-2-(((6-phenylimidazo[2,1-*b*]thiazol-3-yl)-acetyl)-hydrazono)-4-thiazolidinones **5**. The structures of the acyclic adducts **2** and **4** as well as those of 4-thiazolidinones **3** and **5** were assigned by elemental analysis (CHN) and spectroscopic methods (IR, ^{1}H NMR, EIMS).

The IR spectra of **2** showed the N–H and C=O bands at about 3446–3047 and 1697–1673 cm^{-1}. The ^{1}H NMR spectra of **2f** and **2g** revealed the presence of two isomers in a ratio of 2.5:1 in *DMSO*-d_6 as concluded from the NH, N=CH, and CH_2 protons resonating as double singlets at about 11.84–11.83/11.72–11.70, 8.71–8.70/8.24–8.23 and 4.35/3.93–3.92 ppm [5]. It is assumed that the N=CH double bond restricts rotation and gives rise to the formation of *E* and *Z* isomers with the *E* isomer dominating. To overcome the rotational barrier, the ^{1}H NMR spectrum of **2f** was recorded at elevated temperatures. At 90°C, coalescence occurred as expected (NH: $\delta = 11.38$ ppm, N=CH: $\delta = 8.16$ ppm, CH_2: $\delta = 4.21$ ppm).

New C=O bands (1727–1717 cm^{-1}) in the IR spectra of 4-thiazolidinones **3** provided confirmatory evidence for ring closure [6, 7]. Further support was obtained from the ^{1}H NMR spectra of **3f** and **3g** which showed the resonance of the C–H proton at position 2 of the 4-thiazolidinone ring at 5.85 and 5.83 ppm. The upfield shift observed here is consistent with the change in the hybridization state of the involved carbon atom brought about by the addition of the SH function to the N=CH bond of **2** [8, 9]. The methylene ring protons absorbed as a doublet (**3f**:



Scheme 1

$\delta = 3.95$ ppm, $J = 16.5$ Hz; **3g**: $\delta = 3.95$ ppm, $J = 16.0$ Hz) and a multiplet (**3f**: $\delta = 3.84$–3.74, **3g**: $\delta = 3.85$–3.74 ppm). The appearance of the latter was affected by the exocyclic methylene resonance located within the second doublet of the non-equivalent geminally interacting methylene protons [10].

The IR spectra of **4** displayed bands at about 3302–3106 and 1693–1690 cm^{-1} associated with the N–H and C=O functions. The three resonances located in the region of 10.14–8.08 ppm were assigned to the NH resonances of the thiosemicarbazides and supported the structures of **4a** and **4b** [6].

Additional C=O absorptions (1733–1717 cm^{-1}) in the IR spectra of **5** confirmed ring closure. The exocyclic and ring methylene protons of **5a** and **5b** displayed two singlets at $\delta = 4.05$ and 3.87 ppm with unequal integrals (**5a**: 1.73:1, **5b**: 1.62:1), indicating both the presence of two isomers in unequal proportions in *DMSO*-d_6 and the coincidence of the related split signals. This may be explained on the basis of the difference in the relative stability of the *E* and *Z* isomers formed due to the rotational restriction about the exocyclic N=C bond at position 2 of the 4-thiazolidinone ring. Coalescence in the ^{1}H NMR spectrum of **5a** was observed at 110°C.

EIMS of compounds **2g**, **3g**, **4a**, and **5a** displayed molecular ions which confirmed their molecular weights. The major fragmentation pattern involved the

Table 1. Antifungal activity of **2–5** (*MIC*/$\mu g \cdot cm^{-3}$); A = *Trichophyton mentagrophytes var. erinacei* NCPF-375, B = *Trichophyton rubrum*, C = *Microsporum audounii*

	A	B	C		A	B	C
2a	6	6	3	**3g**	25	25	25
2b	6	6	6	**4a**	25	25	25
2c	12.5	12.5	12.5	**4b**	25	25	25
2d	>25	6	6	**4c**	12.5	12.5	12.5
2e	12.5	25	25	**4d**	6	6	6
2f	6	6	6	**4e**	12.5	25	12.5
2g	6	6	6	**5a**	25	25	25
3a	25	25	12.5	**5b**	12.5	12.5	12.5
3b	3	12.5	6	**5c**	25	25	25
3c	12.5	12.5	12.5	**5d**	6	6	6
3d	12.5	12.5	12.5	**5e**	12.5	25	12.5
3e	12.5	25	12.5	Ketoconazole	1.6	6	6
3f	3	12.5	12.5				

cleavage of the CH_2–CO, CO–NH, and NH–N bonds of the side chain, yielding common fragments at $m/z = 213/214$, 241, and 257. Further spectroscopic details are presented in the experimental part.

Compounds **2–5** were evaluated for *in vitro* antifungal activity [11] against the three dermatophyte strains *Trichophyton mentagrophytes var. erinacei* NCPF-375, *Trichophyton rubrum* and *Microsporum audounii*. As can be seen in Table 1, compounds **2b**, **2d**, **2f**, **2g**, **4d**, and **5d** were as effective as the standard against *T. rubrum* and *M. audounii* ($MIC = 6\ \mu g/cm^3$), whereas the activity of **2a** against *M. audounii* was superior to the standard ($MIC = 3\ \mu g/cm^3$). Compounds **3b** and **3f** showed the highest activity against *T. mentagrophytes var. erinacei* NCPF-375 ($MIC = 3\ \mu g/cm^3$). These promising results make compounds **2** potential candidates for further investigations.

Experimental

Melting points were determined with a Büchi 530 melting point apparatus and are uncorrected. IR (KBr), ^{1}H NMR (*DMSO*-d_6/*TMS*), and El mass spectra were recorded on Perkin-Elmer 1600 FTIR, Bruker AC 200 (200 MHz)/Bruker DPX 400 (400 MHz), and VG Zab Spec (70 eV) instruments. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer; their results were in good agreement with the calculated values. The starting materials were either commercially available or synthesized according to the references cited.

Substituted benzylidene-(6-phenylimidazo[2,1-b]thiazol-3-yl)-acetic acid hydrazides (**2a–g**); *general procedure*

A solution of 0.005 mol **1** in 30 cm^3 EtOH and 0.005 mol of an appropriate aromatic aldehyde was heated under reflux for 4 h. The precipitate obtained was purified either by recrystallization from EtOH (**2a–c** and **2e–g**) or by washing with hot EtOH (**2d**).

N-Benzylidene-(6-phenylimidazo[2,1-b]thiazol-3-yl)-acetic acid hydrazide (**2a**; $C_{20}H_{16}N_4OS$)

Yield: 45%; m.p.: 223–224°C.

N-(4-Methylbenzylidene)-(6-phenylimidazo[2,1-b]thiazol-3-yl)-acetic acid hydrazide (**2b**; $C_{21}H_{18}N_4OS$)

Yield: 78%; m.p.: 205–206°C.

N-(4-Methoxybenzylidene)-(6-phenylimidazo[2,1-b]thiazol-3-yl)-acetic acid hydrazide (**2c**; $C_{21}H_{18}N_4O_2S \cdot 0.5H_2O$)

Yield: 55%; m.p.: 185–186°C.

N-(2-Nitrobenzylidene)-(6-phenylimidazo[2,1-b]thiazol-3-yl)-acetic acid hydrazide (**2d**; $C_{20}H_{15}N_5O_3S \cdot 0.5H_2O$)

Yield: 74%; m.p.: 253–254°C.

N-(4-Fluorobenzylidene)-(6-phenylimidazo[2,1-b]thiazol-3-yl)-acetic acid hydrazide (**2e**; $C_{20}H_{15}FN_4OS$)

Yield: 94%; m.p.: 230–231°C.

N-(4-Chlorobenzylidene)-(6-phenylimidazo[2,1-b]thiazol-3-yl)-acetic acid hydrazide (**2f**; $C_{20}H_{15}ClN_4OS$)

Yield: 64%; m.p.: 236–237°C; IR (KBr): $\nu = 3127$ (N–H), 1687 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6, 200 MHz, 25°C): $\delta = 11.84$, 11.72 (2s, 1H, NH), 8.71, 8.23 (2s, 1H, N=CH), 8.06 (s, 1H, H-5), 7.92–7.71 (m, 4H, ar), 7.60–7.20 (m, 5H, ar), 7.08 (s, 1H, H-2), 4.35, 3.92 (2s, 2H, CH_2) ppm; ^1H NMR (*DMSO*-d_6, 200 MHz, 90°C): $\delta = 11.38$ (s, 1H, NH), 8.16 (s, 1H, N=CH), 8.11 (s, 1H, H-5), 7.90–7.71 (m, 4H, ar), 7.57–7.21 (m, 5H, ar), 7.03 (s, 1H, H-2), 4.21 (bs, 2H, CH_2) ppm.

N-(4-Bromobenzylidene)-(6-phenylimidazo[2,1-b]thiazol-3-yl)-acetic acid hydrazide (**2g**; $C_{20}H_{15}BrN_4OS$)

Yield: 58%; m.p.: 241–242°C; IR (KBr): $\nu = 3441$, 3047 (O–H/N–H), 1687 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6, 400 MHz): $\delta = 11.83$, 11.70 (2s, 1H, NH), 8.70, 8.24 (2s, 1H, N=CH), 8.05 (s, 1H, H-5), 7.85–7.63 (m, 6H, ar), 7.41–7.36 (m, 2H, ar), 7.26–7.23 (m, 1H, ar), 7.00 (s, 1H, H-2), 4.35, 3.93 (2s, 2H, CH_2) ppm; EIMS: $m/z(\%) = 440$, 438 ($(M+2)^+$, M^+; 51, 52), 398 (10), 382 (6), 344 (75), 314 (10), 257 (22), 249 (71), 241 (100), 234 (10), 214 (94), 205 (10), 183 (20), 175 (37), 169 (12), 147 (15), 130 (16), 117 (16), 111 (12), 102 (24), 95 (28), 89 (26), 75 (16), 63 (28).

2-Aryl-3-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetamido)-4-thiazolidinones (**3a**–**g**); *general procedure*

A mixture of 0.005 mol **2** and 0.005 mol mercaptoacetic acid was refluxed in 30 cm^3 dry benzene using a *Dean-Stark* trap. Excess benzene was evaporated *in vacuo*. The resulting residue was triturated with saturated $NaHCO_3$ solution until CO_2 evolution ceased and was allowed to stand overnight. The solid thus obtained was washed with H_2O, dried, and recrystallized from EtOH/H_2O.

2-Phenyl-3-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetamido)-4-thiazolidinone
(**3a**; $C_{22}H_{18}N_4O_2S_2 \cdot 2H_2O$)

Yield: 99%; m.p.: 89–90°C.

2-(4-Methylphenyl)-3-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetamido)-4-thiazolidinone
(**3b**; $C_{23}H_{20}N_4O_2S_2 \cdot 2H_2O$)

Yield: 97%; m.p.: 95°C.

2-(4-Methoxyphenyl)-3-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetamido)-4-thiazolidinone
(**3c**; $C_{23}H_{20}N_4O_3S_2 \cdot 1.5H_2O$)

Yield: 99%; m.p.: 120–121°C.

2-(2-Nitrophenyl)-3-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetamido)-4-thiazolidinone
(**3d**; $C_{22}H_{17}N_5O_4S_2 \cdot 2H_2O$)

Yield: 98%; m.p.: 139–140°C.

2-(4-Fluorophenyl)-3-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetamido)-4-thiazolidinone
(**3e**; $C_{22}H_{17}FN_4O_2S_2 \cdot H_2O$).

Yield: 84%; m.p.: 135°C.

2-(4-Chlorophenyl)-3-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetamido)-4-thiazolidinone
(**3f**; $C_{22}H_{17}ClN_4O_2S_2 \cdot H_2O$)

Yield: 97%; m.p.: 146–147°C; IR (KBr): $\nu = 3474$, 3177, (O–H/N–H), 1727 (C=O ring), 1673 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6, 400 MHz): $\delta = 10.64$ (s, 1H, NH), 8.04 (s, 1H, H-5), 7.78 (d, $J = 7.8$ Hz, 2H, ar), 7.52–7.25 (m, 7H, ar), 6.98 (s, 1H, H-2), 5.85 (s, 1H, NCHS), 3.95 (d, $J = 16.5$ Hz, 1H, SCH_2), 3.84–3.74 (m, 3H, SCH_2 and CH_2) ppm.

2-(4-Bromophenyl)-3-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetamido)-4-thiazolidinone
(**3g**; $C_{22}H_{17}BrN_4O_2S_2 \cdot H_2O$)

Yield: 95%; m.p.: 150–151°C; IR (KBr): $\nu = 3474$, 3177 (O–H/N–H), 1725 (C=O ring), 1673 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6), 400 MHz): $\delta = 10.64$ (s, 1H, NH), 8.05 (s, 1H, H-5), 7.79 (d, $J = 8.3$ Hz, 2H, ar), 7.57 (d, $J = 8.4$ Hz, 2H, ar), 7.44–7.40 (m, 4H, ar), 7.29–7.26 (m, 1H, ar), 6.98 (s, 1H, H-2), 5.83 (s, 1H, NCHS), 3.95 (d, $J = 16.0$ Hz, 1H, SCH_2), 3.85–3.74 (m, 3H, SCH_2 and CH_2) ppm; EIMS: $m/z(\%) = 514{,}512$ ($(M+2)^+$, M^+; 3,3), 484,482 (6,6), 440,438 (15,15), 398 (6), 291 (18), 275 (38), 257 (14), 248 (100), 241 (38), 214 (64), 185,183 (8,8), 161 (6), 146 (6), 135 (14), 118 (18), 103 (10).

4-Alkyl-1-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-3-thiosemicarbazides (**4a–e**); *general procedure*

To a solution of 0.005 mol **1** in 30 cm^3 EtOH, 0.005 mol of an appropriate isothiocyanate were added. The resulting mixture was heated under reflux for 3 h. After cooling, the precipitate was separated and purified either by washing with hot EtOH (**4a–d**) or recrystallization from EtOH (**4e**).

4-Methyl-1-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-3-thiosemicarbazide
(**4a**; $C_{15}H_{15}N_5OS_2$)

Yield: 85%; m.p.: 188–189°C; IR (KBr): $\nu = 3302$, 3216, 3106, (N–H), 1693 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6, 400 MHz): $\delta = 10.14$ (s, 1H, NH), 9.29 (s, 1H, NH), 8.18 (s, 1H, H-5), 8.08 (s, 1H, NH), 7.82 (d, $J = 7.5$ Hz, 2H, ar), 7.47–7.31 (m, 2H, ar), 7.28–7.21 (m, 1H, ar), 7.07 (s, 1H, H-2), 3.82 (s, 2H, CH_2), 2.91 (d, $J = 4.1$ Hz, 3H, NCH_3) ppm; EIMS: $m/z(\%) = 345$ (M^+; 0.1), 327 (100), 311 (6), 294 (16), 272 (12), 257 (9), 241 (18), 214 (34), 213 (36), 200 (3), 186 (3), 176 (10), 169 (8), 159 (11), 153 (8), 142 (7), 140 (6), 134 (7), 128 (8), 116 (13), 103 (20), 89 (10), 77 (10), 63 (6).

4-Ethyl-1-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-3-thiosemicarbazide
(**4b**; $C_{16}H_{17}N_5OS_2$)

Yield: 98%; m.p.: 204–205°C; IR (KBr): $\nu = 3191$, 3107 (N–H), 1690 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6, 400 MHz): $\delta = 10.13$ (s, 1H, NH), 9.51 (s, 1H, NH), 8.19 (s, 1H, H-5), 8.08 (s, 1H, NH), 7.83 (d, $J = 7.4$ Hz, 2H, ar), 7.45–7.39 (m, 2H, ar), 7.33–7.24 (m, 1H, ar), 7.08 (s, 1H, H-2), 3.83 (s, 2H, CH_2), 3.55–3.48 (m, 2H, NCH_2CH_3), 1.09 (t, $J = 6.4$ Hz, 3H, NCH_2CH_3) ppm.

4-(2-Propenyl)-1-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-3-thiosemicarbazide
(**4c**; $C_{17}H_{17}N_5OS_2$)

Yield: 97%; m.p.: 222–223°C.

4-Propyl-1-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-3-thiosemicarbazide (**4d**; $C_{17}H_{19}N_5OS_2$)

Yield: 93%; m.p.: 221–222°C.

4-Butyl-1-((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-3-thiosemicarbazide (**4e**; $C_{18}H_{21}N_5OS_2$)

Yield: 78%; m.p.: 231–232°C.

3-Alkyl-2-(((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)hydrazono)-4-thiazolidinones (**5a–e**); *general procedure*

A mixture of 0.005 mol **4**, 0.005 mol of ethyl bromoacetate, and 0.02 mol of fused sodium acetate in 25 cm^3 anhydrous EtOH was heated under reflux for 3 h. The reaction mixture was cooled, diluted with water, and allowed to stand overnight. The precipitate was filtered, dried, and recrystallized from EtOH.

3-Methyl-2-(6-(phenylimidazo[2,1-b]thiazol-3-yl)acetyl)-hydrazono)-4-thiazolidinone
(**5a**; $C_{17}H_{15}N_5O_2S_2$)

Yield: 65%; m.p.: 154–155°C; IR (KBr): $\nu = 3131$ (N–H), 1730 (C=O ring), 1654 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6, 200 MHz, 25°C): $\delta = 10.61$ (s, 1H, NH), 8.19 (s, 1H, H-5), 7.82 (d, $J = 7.4$ Hz, 2H, ar), 7.43–7.15 (m, 3H, ar), 7.04 (s, 1H, H-2), 4.05, 3.87 (2s, 4H, SCH_2 and CH_2), 3.11 (s, 3H, NCH_3) ppm; ^1H NMR (*DMSO*-d_6, 200 MHz, 110°C): $\delta = 10.22$ (s, 1H, NH), 8.07 (s, 1H, H-5), 7.83 (d, $J = 7.4$ Hz, 2H, ar), 7.42–7.21 (m, 3H, ar), 6.97 (s, 1H, H-2), 3.99 (s, 2H, SCH_2), 3.92 (s, 2H, CH_2), 3.13 (s, 3H, NCH_3) ppm; EIMS: $m/z(\%) = 385$ (M^+; 82), 327 (3), 311 (2), 257 (7), 241 (62), 214 (100), 200 (2), 181 (7), 172 (12), 169 (16), 154 (5), 142 (8), 128 (8), 116 (14), 103 (17), 89 (7), 78 (10), 77 (7), 74 (8), 63 (15).

3-Ethyl-2-(((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-hydrazono)-4-thiazolidinone
(**5b**; $C_{18}H_{17}N_5O_2S_2 \cdot 0.5H_2O$)

Yield: 98% m.p.: 193–194°C; IR (KBr): $\nu = 3189$ (O–H/N–H), 1723 (C=O ring), 1684 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6, 400 MHz): $\delta = 10.60$ (s, 1H, NH), 8.22 (s, 1H, H-5), 7.83 (d, $J = 7.7$ Hz, 2H, ar), 7.69–7.42 (m, 3H, ar), 7.05 (s, 1H, H-2), 4.05, 3.87 (2s, 4H, SCH_2 and CH_2), 3.68 (q, $J = 5.8$ Hz, 2H, NCH_2CH_3), 1.12 (t, $J = 6.9$ Hz, 3H, NCH_2CH_3) ppm.

3-(2-Propenyl)-2-(((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-hydrazono)-4-thiazolidinone
(**5c**; $C_{19}H_{17}N_5O_2S_2 \cdot 1.5H_2O$)

Yield: 98%; m.p.: 103–104°C.

3-Propyl-2-(((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-hydrazono)-4-thiazolidinone
(**5d**; $C_{19}H_{19}N_5O_2S_2$)

Yield: 77%; m.p.: 126–127°C.

3-Butyl-2-(((6-phenylimidazo[2,1-b]thiazol-3-yl)-acetyl)-hydrazono)-4-thiazolidinone
(**5e**; $C_{20}H_{21}N_5O_2S_2$)

Yield: 81%; m.p.: 119–120°C.

Antifungal activity

All compounds to be tested were dissolved in *DMSO* at a concentration of 4000 µg/cm^3 and diluted to 200 µg/cm^3 with sterile distilled H_2O. No effect of *DMSO* (5%) was observed upon growth of dermatophytes.

The dermatophyte strains which were grown on slant medium of *Sabouraud* (Difco) were transferred to 3.5 cm^3 nutrient broth (NB, Diagnostic Pasteur) and incubated for three to five days at 25°C. At the end of the incubation period, the strains were transferred into screwcapped bottles containing sterilized beads and shaken for 4–5 min in a vortex (IKA-VF, Germany). The suspensions of the cultures were adjusted to have an absorbance of 0.6 at 450 nm. Eight different dilutions of the test compounds between 25–0.2 µg/cm^3 were prepared in microplates by serial dilutions from top to bottom. Then all the wells except the 12^{th} wells (positive control) were filled with 10 µdm^3 of the standardized strains. These plates were incubated at 25°C for five or six days. The minimum concentration at which no growth was observed was taken as the *MIC* value.

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