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Synthesis, antibacterial and antifungal activities of electron-rich olefins derived benzimidazole compounds

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Abstract

New benzimidazole derivatives were synthesised by electron-rich olefines (**7**, **8** and **9**) with appropriate reagents. The compounds synthesised were identified by ^{1}H NMR, ^{13}C NMR, FT-IR spectroscopic techniques and elemental analysis. All compounds studied in this work were screened for their in vitro antimicrobial activities against the standard strains: *Enterococcus faecalis* (ATCC 29212), *Staphylococcus aureus* (ATCC 29213), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853) and the yeasts *Candida albicans* and *Candida tropicalis*. Eleven of the compounds inhibited the growth of gram-positive bacteria (*E. faecalis* and *S. aureus*) at MIC values between 50 and 400 μg/ml. None of the compounds exhibit antimicrobial activity against Gram-negative bacteria (*E. coli* and *P. Aeruginosa*) at the concentrations studied (6.25–800 μg/ml). Nine of the tested compounds showed an antifungal activity with a range of the MICs between 50 and 400 μg/ml.

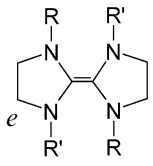
Keywords: Benzimidazole derivatives; Antibacterial activities; Antifungal activities; In vitro studies; Electron-rich olefins

1. Introduction

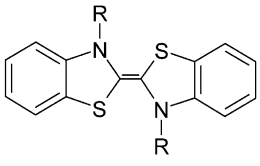
Electron-rich olefins (ero) are very versatile reagents and highly reactive. Eros have been used as powerful reducing agents [1–3], sources of carbene transition metal complexes [4,5], catalyst for acyloin type C–C coupling reactions [6,7]. They have an extensive organic chemistry, particularly ero that contain imidazolidine (**I**) [8–11] or benzothiazolidine (**II**) [12,13] moiety have long been known, but there is limited information about ero contain benzimidazolidine (**III**) [4,5,14–16] moiety.

In previous studies, we have synthesised eros such as **III** (R, R′ = Me, Et or CH_2Ph) and used them as a starting compounds to obtain versatile benzimidazole derivatives and some rhodium [4] and ruthenium [5] complexes (Scheme 1).

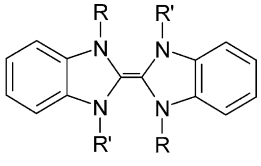
On the other hand, benzimidazole derivatives constitute an important class of heterocyclic compounds for their versatile pharmacological activities such as antibacterial, antifungal, antihelmintic, antiallergic, antineoplastic, local analgesic, antihistaminic, vasodila-



I
R,R'= alkyl or aryl



II
R,R'= alkyl or aryl



III

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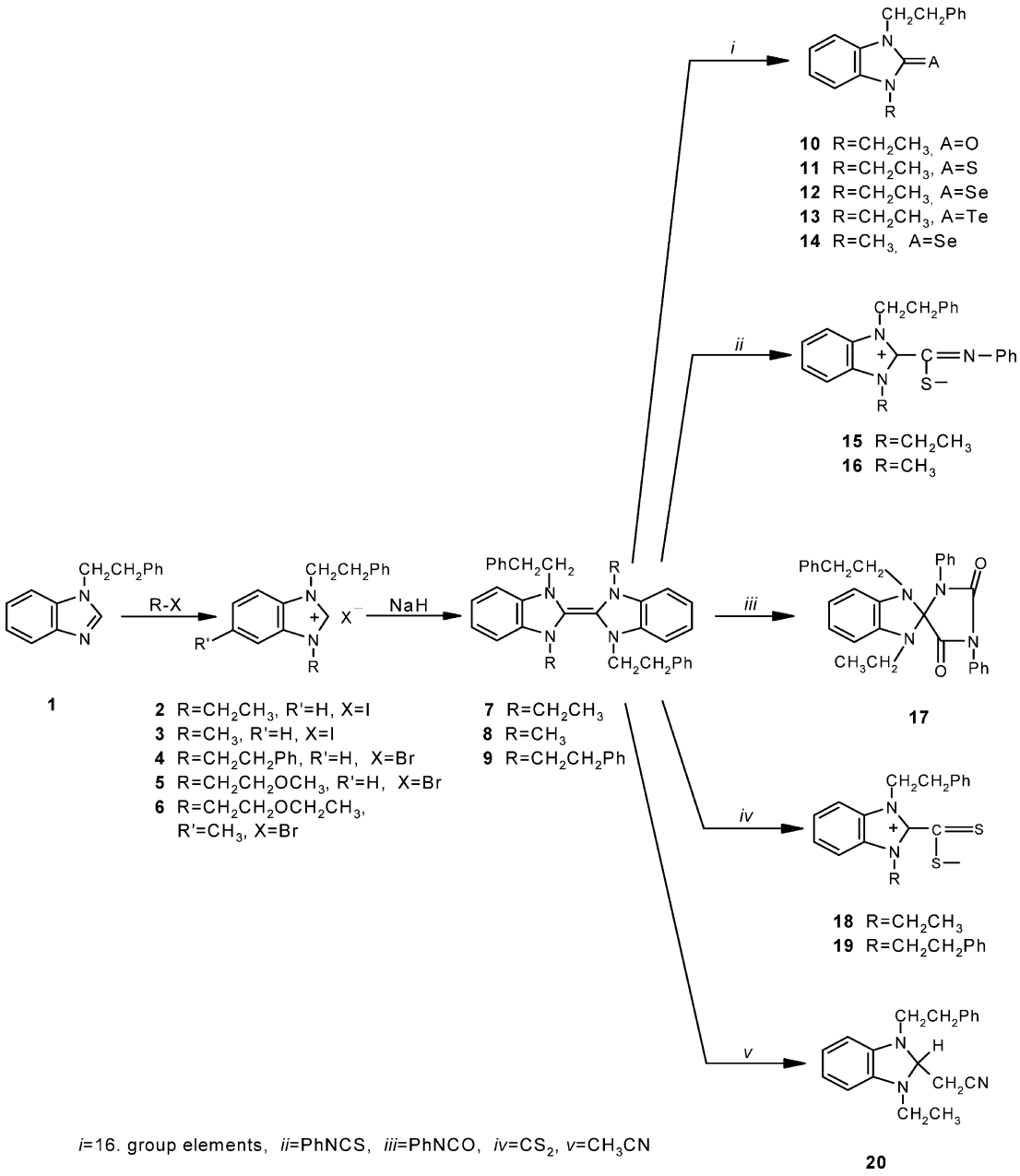

Scheme 1. Synthesis pathways of the new electron-rich olefins and their benzimidazole derivatives.

tive, hypotensive, and spasmolytic activities [17,18]. We also observed that many benzimidazole derivatives and related heterocyclic compounds have shown considerable antimicrobial activities against standard strains; *Enterococcus faecalis* (ATCC 29212), *Staphylococcus aureus* (ATCC 29213), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853) and yeasts *Candida albicans* and *Candida tropicalis* [19–24].

The aim of this study was to synthesise electron rich olefin derived benzimidazole compounds and to study their antibacterial and antifungal activities.

2. Experimental

2.1. Chemistry

All experiments were performed under argon using freshly distilled dry solvents. ^{1}H NMR and ^{13}C NMR spectra were recorded using a Varian ML 60 (Varian Associates Inc., Sunnyvale, CA) and Bruker DPX-400 high performance digital FT NMR (Bruker WM360, Bruker Instruments, Inc., Billercia, USA) spectrometers, respectively. Infrared spectra were recorded as KBr pellets in the range 4000–400 cm^{-1} on an ATI Unicam,

Mattson 1000 (Unicam Ltd. Cambridge, UK) spectrophotometer. Elemental analysis was performed by the elemental analysis laboratory of Tübitak (The Scientific and Technical Research Consul of Turkey) at Ankara (Turkey). Melting points were recorded using an electrothermal melting point apparatus, Electrothermal 9200 (Electrothermal Engineering Ltd., Essex, UK) and are uncorrected.

2.1.1. Preparation of 1-(2-phenylethyl)benzimidazole (**1**)

Benzimidazole (2 g, 16.95 mmol) and 2-bromoethylbenzene (2.5 ml, 18.30 mmol) were added to a solution of KOH (1.43 g, 25.54 mmol) in 20 ml of ethanol and the mixture was refluxed 3 h. The mixture was then cooled, after which potassium bromide was filtered, washed with a little ethanol, and the solvent was removed from the filtrate in vacuo. The residue was treated with chloroform (10 ml), and the chloroform extract was washed with NaOH solution, then with water, and dried over anhydrous sodium sulphate overnight. The sodium sulphate was then filtered off and the oily residue was crystallised from toluene/*n*-hexane (2:1) after removal of the all volatiles in vacuo. Yield: 2.89 g, 77%; m.p.: 77–78 °C.

^{1}H NMR (TFA): δ 2.2 (t, CH_2CH_2Ph, 2H), 3.9 (t, CH_2CH_2Ph, 2H), 6.0–6.9 (m, Ar–*H*, 9H), 7.3 (s, C*H*, 1H). ^{13}C NMR ($CDCl_3$): δ 36.59, 47.05, 110.06, 120.76, 122.58, 123.36, 129.05, 129.25, 133.94, 137.94, 143.42. *Anal.* Calc. for $C_{15}H_{14}N_2$: C, 81.08; H, 6.31; N, 12.61. Found: C, 80.91; H, 6.31; N, 12.87%.

2.1.2. Preparation of 1-ethyl-3-(2-phenylethyl)benzimidazolium bromide (**2**)

A mixture of 1-ethylbenzimidazole (4 ml, 34.24 mmol) and 2- bromoethylbenzene (5.00 ml, 36.61 mmol) was heated on water bath at 90–95 °C for 2 h. The solution was cooled to room temperature (r.t.) and Et_2O (5 ml) was added. The precipitate was then crystallised from EtOH/Et_2O (2:1). Yield: 11.1 g, 98%; m.p.: 108–109 °C. Similarly compounds **3**–**6** were synthesised from appropriate benzimidazole derivatives and alkyl halides.

^{1}H NMR (TFA): δ 1.5(t, CH_2CH_3, 3H), 3.2 (t, CH_2CH_2Ph, 2H), 4.4(t, CH_2CH_2Ph, 2H), 4.5 (q, CH_2CH_3, 2H), 6.9–7.8 (m, Ar–*H*, 9H), 8.4 (s, C*H*, 1H). ^{13}C NMR ($CDCl_3$): δ 15.14, 35.78, 42.16, 48.95, 113.52, 113.55, 127.38, 127.42, 127.45, 129.10, 129.14, 131.02, 131.43, 136.47, 141.82. $\nu_{(\text{amine salt}):\ 2720\ \text{cm}-1}$.

2.1.3. 1-Methyl-3-(2-phenylethyl)benzimidazolium iodide (**3**)

Yield: 84%, m.p.: 104–105 °C. ^{1}H NMR (TFA): δ 2.2 (t, CH_2CH_2Ph, 2H), 2.9 (s, NCH_3, 3H), 3.7 (t, CH_2CH_2Ph, 2H), 6.0–6.6 (m, Ar–*H*, 9H), 7.4 (s, *CH*, 1H). ^{13}C NMR ($CDCl_3$): δ 34.35, 35.88, 49.00, 113.30, 113.46, 127.33, 127.44, 129.09, 129.17, 131.26, 131.90, 136.56. $\nu_{(\text{amine salt})}$: 2950 cm^{-1}.

2.1.4. 1,3-Di(2-phenylethyl)benzimidazolium bromide (**4**)

Yield: 68%, m.p.: 100–101 °C. ^{1}H NMR (TFA): δ 2.7(t, CH_2CH_2Ph, 2H), 4.2 (t, CH_2CH_2Ph, 2H), 6.5–7.1 (m, Ar–*H*, 9H), 7.7 (s, C*H*, 1H). ^{13}C NMR ($CDCl_3$): δ 35.16, 49.08, 113.37, 127.39, 129.13, 129.25, 131.23, 136.36, 142.00. $\nu_{(\text{amine salt})}$: 2750 cm^{-1}. *Anal.* Calc. for $C_{23}H_{23}N_2Br$: C, 67.81; H, 5.65; N, 6.88. Found: C, 68.45; H, 5.78; N, 7.06%.

2.1.5. 1-(2-Methoxyethyl)-3-(2-phenylethyl)benzimidazolium bromide (**5**)

Yield: 79%, m.p.: 94–95 °C. ^{1}H NMR (TFA): δ 3.2(s, CH_3, 3H), 3.8 (m, CH_2CH_2Ph, 2H), 4.0 (t, CH_2CH_2O, 2H), 4.7 (m, NCH_2CH_2–, 4H), 6.7–7.6 (m, Ar–*H*, 9H), 9.3 (s, C*H*, 1H). $\nu_{(\text{amine salt})}$: 2790 cm^{-1}.

2.1.6. 1-(2-Etoxyethyl)-5-methyl-3-(2-phenylethyl)benzimidazolium bromide (**6**)

Yield: 97%, m.p.: 152–153 °C. ^{1}H NMR (TFA): δ 1.2 (t, CH_3, 3H), 2.6 (s, CH_3, 3H), 3.3 (m, CH_2CH_2Ph, 2H), 3.8 (q, CH_2CH_3, 2H), 4.1 (t, CH_2CH_2O, 2H), 4.8 (m, NCH_2CH_2–, 4H), 6.9–7.8 (m, Ar–*H*, 8H), 8.8 (s, *CH*, 1H). $\nu_{(\text{amine salt})}$: 2950 cm^{-1}.

2.1.7. Preparation of bis[1,3-di-(2-phenylethyl)benzimidazolidine-2-ylidene] (**9**)

A mixture of 1,3-bis(2-phenylethyl)benzimidazolium bromide (5 g, 12.28 mmol) and NaH (0.34 g, 14.16 mmol) in tetrahydrofuran (50 ml) was stirred for 3 h at r.t. and then for further 1 h at 50 °C. The solvent was extracted with hot toluene (30 ml) and the extract filtered when hot. The yellow filtrate was concentrated (to ca. 15 ml), *n*-hexane (15 ml) was added and the solution was cooled to −20 °C to yield the crystalline yellow compound **9**. Yield: 3.20 g, 80%; m.p.: 156–157 °C.

^{1}H NMR ($CDCl_3$): δ 2.3 (t, CH_2CH_2Ph, 4H), 3.0 (t, CH_2CH_2Ph, 4H), 6.1–6.7 (m, *Ph*, 28H). ^{13}C NMR ($CDCl_3$): δ 34.05, 44.79, 105.64, 117.25, 120.66, 126.94, 129.11, 129.17, 130.26, 139.23. $\nu_{(C=C)}$: 1710 cm^{-1}.*Anal.* Calc. for $C_{46}H_{44}N_4$: C, 84.66; H, 6.75; N, 8.59. Found: C, 84.76; H, 6.76; N, 9.01%.

Similar to compound **9**, compounds **7** and **8** were synthesised from appropriate benzimidazolium salts and NaH. Although the crystallisation of the compound **7** and **8** were not achieved, but some of their derivatives were synthesised successively.

2.1.8. Preparation of 1-ethyl-3-(2-phenylethyl)benzimidazole-2-selenone (**12**)

A mixture of **8** (1.0 g, 2.11 mmol) and selenium (0.33 g, 4.24 mmol) in toluene (10 ml) was heated under reflux

for 2 h. Then the mixture was filtered to remove unreacted selenium and all volatiles were removed in vacuo (0.02 mmHg). The crude product was crystallised from alcohol upon cooling to −30 °C. Yield: 1.16 g, 87%, m.p.: 103–104 °C.

^{1}H NMR (TFA): δ 0.4(t, CH_3, 3H), 2.0 (t, CH$_2$CH_2Ph, 2H), 3.4 (q, CH_2CH$_3$, 2H), 3.7 (t, CH_2CH$_2$Ph, 2H), 5.8–6.2 (m, Ar–H, 4H), 6.7 (s, Ar–H, 5H). ^{13}C NMR (CDCl$_3$): δ 13.72, 34.70, 41.96, 43.05, 109.90, 110.00, 123.62, 123.63, 127.20, 129.10, 129.42, 132.80, 133.46, 138.39, 165.31. $\nu_{(C=Se)}$: 1487 cm^{-1}. *Anal.* Calc. for $C_{16}H_{16}N_2Se$: C, 60.95; H, 5.08; N, 8.85. Found: C, 60.76; H, 5.08; N, 9.03%.

Similarly compounds **10**, **11**, **13** and **14** were synthesised from appropriate benzimidazole derivatives and Group 16 elements.

2.1.9. 1-Ethyl-3-(2-phenylethyl)benzimidazole-2-one (**10**)

Yield: 71%, m.p.: 94–95 °C. ^{1}H NMR (TFA): δ 0.9(t, CH$_2$CH_3, 3H), 2.6 (t, CH$_2$CH_2Ph, 2H), 4.0 (t,CH_2CH$_2$Ph, 2H), 4.1 (q, CH_2CH$_3$, 2H), 6.5–6.9 (m, Ar–H, 9H). $\nu_{(C=O)}$: 1690 cm^{-1}.

2.1.10. 1-Ethyl-3-(2-phenylethyl)benzimidazole-2-thione (**11**)

Yield: 65%, m.p.: 88–89 °C. ^{1}H NMR (TFA): δ 1.0 (t, CH$_2$CH_3, 3H), 2.9 (t, CH$_2$CH_2Ph, 2H), 4.2 (q, CH_2CH$_3$, 2H), 4.5 (t, CH_2CH$_2$Ph, 2H), 6.4–7.1 (m, Ar–H, 4H), 7.3 (s, Ar–H, 5H). $\nu_{(C=S)}$: 1456 cm^{-1}.

2.1.11. 1-Ethyl-3-(2-phenylethyl)benzimidazole-2-tellurone (**13**)

Yield: 78%, m.p.: 127–128 °C. ^{1}H NMR (TFA): δ 1.0 (t, CH$_2$CH_3, 3H), 2.8 (t, CH$_2$CH_2Ph, 2H), 4.1 (q, CH_2CH$_3$, 2H), 4.3 (t, CH_2CH$_2$Ph, 2H), 6.4–6.9 (m, Ar–H, 9H). ^{13}C NMR (CDCl$_3$): δ 14.22, 35.22, 45.42, 51.59, 110.73, 110.78, 124.10, 124.12, 127.31, 129.14, 129.47, 133.84, 134.57, 138.12, 143.47. $\nu_{(C=Te)}$: 1468 cm^{-1}. *Anal.* Calc. for $C_{17}H_{18}N_2Te$: C, 54.02; H, 4.77; N, 7.42. Found: C, 54.09; H, 4.56; N, 7.54%.

2.1.12. 1-Methyl-3-(2-phenylethyl)benzimidazole-2-selenone (**14**)

Yield: 81%, m.p.: 103–104 °C. ^{1}H NMR (TFA): δ 3.2 (t, CH$_2$CH_2Ph, 2H), 4.0 (s, CH_3, 3H), 4.6 (t, CH_2CH$_2$Ph, 2H), 7.1–7.4 (m, Ar–H, 9H). ^{13}C NMR (CDCl$_3$): δ 33.59, 34.70, 48.60, 109.87, 109.91, 123.67, 123.71, 127.21, 129.10, 129.41, 133.21, 133.80, 138.37, 166.38. *Anal.* Calc. for $C_{16}H_{16}N_2Se$: C, 60.95; H, 5.08; N, 8.85. Found: C, 61.46; H, 4.72; N, 9.01. $\nu_{(C=S)}$: 1485 cm^{-1}.

2.1.13. Preparation of mercapto-N-phenylformimidoyl-1-ethyl-3-(2-phenylethyl)-benzimidazolinium inner salt (**15**)

To a solution of **7** (0.5 g, 1.00 mmol) in toluene (15 ml) PhNCS (0.3 ml, 2.49 mmol) was added. When the mixture was stirred at r.t., an exothermic reaction took place shortly. All volatiles were then removed in vacuo and the yellow crude product 0.5 g; 76%, m.p.: 114–115 °C.

^{1}H NMR (CDCl$_3$): δ 1.7 (t, CH$_2$CH_3, 3H), 3.4 (t, CH$_2$CH_2Ph, 2H), 4.8 (t, CH_2CH$_2$Ph, 2H), 4.9 (q, CH_2CH$_3$, 2H), 7.2–7.7 (m, Ar–H, 14H). ^{13}C NMR (CDCl$_3$): δ 15.03, 35.95, 41.68, 47.82, 112.80, 112.90, 122.86, 124.25, 126.55, 127.56, 129.13, 129.28, 129.39, 130.05, 130.81, 137.48, 150.00, 151.17, 166.33. *Anal.* Calc. for $C_{24}H_{23}N_3S$: C, 74.81; H, 5.97; N, 10.91. Found: C, 74.61; H, 6.08; N, 10.84%.

Similarly, compound **16** was synthesised from bis[1-methyl-3-(2-phenylethyl)-benzimidazolidine-2-ylidene], **8** and PhNCS. Yield: 89%, m.p.: 133–134 °C.

2.1.14. Mercapto-N-phenylformimidoyl-1-methyl-3-(2-phenylethyl)benzimidazol-inium inner salt (**16**)

Yield: 89%, m.p.: 133–134 °C. ^{1}H NMR (CDCl$_3$): δ 3.5 (t, CH$_2$CH_2Ph, 2H), 4.1 (s, CH_3, 3H), 4.8 (t, CH_2CH$_2$Ph, 2H), 7.2–7.7 (m, Ar–H, 14H). ^{13}C NMR (CDCl$_3$): δ 32.24, 36.03, 47.99, 112.67, 112.76, 122.87, 124.38, 126.63, 126.69, 127.60, 129.17, 129.31, 129.41, 130.54, 137.43, 150.11, 151.01, 166.47. *Anal.* Calc. for $C_{23}H_{21}N_3S$: C, 74.39; H, 5.66; N, 11.32. Found: C, 74.77; H, 5.88; N, 10.88%.

2.1.15. Preparation of 2,4-dioxy-1,3-diphenyl-7,8-benzo-6-ethyl-9-(2-phenylethyl)-1,3,6,9-tetrazaspiro[4.4]nonane (**17**)

To a solution of **7** (0.5 g, 1.00 mmol) in toluene (15 ml) PhNCO (0.5 ml, 4.60 mmol) was added and the resulting mixture was refluxed for 1 h. All volatiles were then removed in vacuo and residue was crystallised from CHCl$_3$–Et$_2$O mixture (3:1). Yield: 0.67 g, 69%, m.p.: 167–168 °C.

^{1}H NMR(CDCl$_3$): δ 1.1 (t, CH$_2$CH_3, 3H), 2.7 (t, CH$_2$CH_2Ph, 2H), 3.2 (t, CH_2CH$_2$Ph, 2H), 3.3 (q, CH_2CH$_3$, 2H), 6.1–7.4 (m, Ar–H, 19H). ^{13}C NMR (CDCl$_3$): δ 13.65, 38.30, 42.33, 45.93, 104.41, 104.47, 119.09, 119.33, 124.62, 126.74, 129.13, 129.17, 129.26, 129.63, 129.83, 152.57, 167.24. $\nu_{(C=O)}$: 1720 cm^{-1}. *Anal.* Calc. for $C_{31}H_{28}N_4O_2$: C, 78.09; H, 6.23; N, 11.38. Found: C, 78.02; H, 6.23; N, 11.47%.

2.1.16. Preparation of 1,3-di(2-phenylethyl)benzimidazole-2-dithiote (**19**)

To a solution of **9** (0.5 g 0.77 mmol) in toluene (15 ml) was added CS_2 (0.1 ml, 1.65 mmol). A red precipitate was formed instantly. The red compound was washed

Table 1
The MICs (μg/ml) of the tested compounds

Comp. no.	*Enterococcus faecalis* (ATCC 29212)	*Staphylococcus aureus* (ATCC 29213)	*Escherichia coli* (ATCC 25922)	*Pseudomonas aeruginosa* (ATCC 27853)
Ampicillin	0.78	0.39	3.12	> 75
1	400	400	800	800
2	800	400	> 800	> 800
3	> 800	> 800	> 800	> 800
4	400	200	> 800	> 800
5	800	> 800	> 800	> 800
6	800	> 800	800	> 800
10	800	800	> 800	> 800
11	200	200	800	800
12	50	50	800	800
13	200	200	50	50
14	50	100	800	800
15	400	400	> 800	> 800
16	800	800	> 800	> 800
17	200	200	> 800	> 800
18	800	800	> 800	> 800
19	400	400	800	800
20	200	50	800	800

twice with Et_2O and dried in vacuo. Yield: 0.45 g, 73%, m.p.: 191–192 °C.

^{1}H NMR ($CDCl_3$): δ 2.9 (t, CH_2CH_2Ph, 4H), 4.2 (t, CH_2CH_2Ph, 4H), 6.7-7.2 (m, Ar–*H*, 14H). ^{13}C NMR ($CDCl_3$): δ 35.83, 47.73, 112.70, 126.42, 127.65, 129.29, 129.40, 130.29, 137.29, 152.78, 224.60. *Anal.* Calc. for $C_{24}H_{22}N_2S_2$: C, 71.64; H, 5.47; N, 6.96. Found: C, 71.48; H, 5.43; N, 6.89%.

Similarly, compound **18** was synthesised from **7** and CS_2.

Yield: 82%, m.p.: 201–202 °C. ^{1}H NMR ($CDCl_3$): δ 1.1 (t, CH_2CH_3, 3H), 2.9 (t, CH_2CH_2Ph, 2H), 4.1 (t, CH_2CH_2Ph, 2H), 4.2 (q, CH_2CH_3, 2H), 6.9–7.2 (m, Ar–*H*, 9H). ^{13}C NMR ($CDCl_3$): δ 14.81, 35.84, 41.44, 47.66, 112.69, 112.86, 126.51, 127.61, 129.81, 129.34, 129.91, 130.68, 137.29, 152.88, 224.56. *Anal.* Calc. for $C_{18}H_{18}N_2S_2$: C, 66.26; H, 6.75; N, 8.59. Found: C, 66.43; H, 6.80; N, 8.06%.

2.1.17. Preparation of 2-cyanomethyl-1-ethyl-3-(2-phenylethyl)benzimidazolidine (**20**)

To a solution of bis[1-ethyl-3-(2-phenylethyl)benzimidazolidine-2-ylidene] (**7**) (0.75 g, 1.50 mmol) in toluene (10 ml) was added acetonitrile (0.2 ml, 3.75 mmol) and heated at reflux for 2 h. All volatiles were then driven off in vacuo, the crude product was crystallised from toluene/*n*–hexane mixture (2:1). Yield: 0.48 g; 83%, m.p.: 82–83 °C. ^{1}H NMR ($CDCl_3$): δ 1.1 (t, CH_2CH_3, 3H), 2.6 (*d*, CH_2CN, 2H), 3.0 (t, CH_2CH_2Ph, 2H), 3.2 (t, CH_2CH_2Ph, 2H), 3.3 (q, CH_2CH_3, 2H), 5.0 (t, C*H*, 1H), 6.4–6.8 (m, Ar–*H*, 4H), 7.2 (s, Ar–*H*, 5H). $\nu_{(CN)}$: 2210 cm^{-1}. *Anal.* Calc. for $C_{19}H_{21}N_3$: C, 78.35; H, 7.22; N, 14.43. Found: C, 78.32; H, 7.22; N, 14.44%.

2.2. Microbiology

Antimicrobial activities of the compounds were determined by using agar dilution procedure outlined by the National Committee for Clinical Laboratory standards [25,26]. Minimal inhibitory concentrations for each compound were investigated against standard bacterial strains; *E. faecalis* (ATCC 29212), *S. aureus* (ATCC 29213), *E. coli* (ATCC 25922), *P. aeruginosa* (ATCC 27853) and yeast-like fungi; *C. albicans* and *C. tropicalis* obtained from the Department of Microbiology, Faculty of Medicine, Ege University, Turkey. The stock solutions were prepared in dimethyl sulfoxide (DMSO) and DMSO had no effect on the microorganisms in the concentrations studied. All of the dilutions were done with distillated water. The concentrations of tested compounds were 800, 400, 200, 100, 50, 25, 12.5 and 6.25 μg/ml. Ampicilin and flucanazole from FAKO (Istanbul, Turkey) were used as a reference compound for the experimental conditions. A loopfull (0.01 ml) of the standardised inoculum of the bacteria and fungi (10^6 CFUs/ml) was spreaded over the surface of agar plates. All the inoculated plates were incubated at 35 °C and results were evaluated after 16–20 h for bacteria and 48 h for fungi. The lowest concentration of the compounds that prevented visible growth was considered to be minimal inhibitor concentrations (MICs).

3. Results and discussion

The structure of all compounds synthesised were identified by ^{1}H NMR, ^{13}C NMR, FT-IR (Fourier transformation-infrared) and elemental analysis. ^{1}H

Table 2
The MICs (μg/ml) of the tested compounds

Comp. no.	Tested organisms	
	Candida albicans	*Candida tropicalis*
Fluconazole	1.25	1.25
1	400	400
2	> 800	> 800
3	> 800	> 800
4	400	400
5	400	400
10	> 800	> 800
11	> 800	> 800
12	800	800
13	400	400
14	800	800
15	400	400
16	800	800
17	50	50
18	400	400
19	200	200
20	400	400

NMR, ^{13}C NMR, IR, colour, yields, melting points (or boiling points) and analytical data of the newly synthesised compounds are given in experimental section. The antimicrobial and antifungal activity results (MIC values) are given in Tables 1 and 2, respectively. Tables 1 and 2 also contain ampicilin and flucanozole reference compounds results, respectively, for all microorganisms used in this work to compare and the reliability of the method used.

In this study, seventeen new benzimidazole derivatives were tested against standard strains of gram-positive and gram-negative bacteria. As it can be seen in Table 1, the compounds **1**, **2**, **4**, **11**, **12**, **13**, **14**, **15**, **17**, **19** and **20** inhibited the growth of gram-positive bacteria with MICs between 50 and 400 μg/ml. None of the compounds studied here except contain tellurium showed antimicrobial activity against gram negative bacteria. But the antibacterial activity of the compound **13** particularly against gram negative bacteria, *E. coli* and *P. aeruginosa* may not be related to their molecular structure since the compound 13 slightly air sensitive in the solid state and unstable in solution, depositing tellurium. Therefore the antimicrobial activity probably originates from metallic tellurium. Similar observations were also observed in our previously study [23]. As shown in Table 2, the compounds **1**, **4**, **5**, **13**, **15**, **17**, **18**, **19** and **20** also showed activity against *C. albicanis* and *C. tropicalis* with a range of MICs between 50 and 400 μg/ml. Among the tested compounds, **17** was the most effective compound with MIC 50 μg/ml against *C. albicanis* and *C. tropicalis*. The antifungal activity of the compound **17** may relate spiro structure and hydantoin moiety of the compound.

Consideration of the structural formula of the compounds that exhibited some antibacterial activity, the selenium moiety in compounds **12** and **14** may play a role for the activity, and even selenium itself has some biological properties [27]. The compounds tested here generally do not show antimicrobial activity against gram-negative bacteria. The antimicrobial activity against gram-positive bacteria may depend on the difference between cell structures of gram-positive and gram-negative bacteria.

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