Screening of Biological Activities of a Series of Chalcone Derivatives against Human Pathogenic Microorganisms

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In an effort to develop new antimicrobial agents, a series of chalcone derivatives, **3**–**60**, were prepared by *Claisen*–*Schmidt* condensation of appropriate acetophenones and 2-furyl methyl ketones with appropriate aromatic aldehydes, furfural, and thiophene-2-carbaldehyde in an aqueous solution of NaOH and EtOH at room temperature. The synthesized compounds were characterized by means of their IR- and NMR-spectral data, and elemental analysis. All compounds were tested for their antibacterial and antifungal activities by the disc diffusion method. For the most active compounds, also minimum inhibitory concentrations (*MIC*s) were determined.

Introduction. – Besides their importance as intermediates for the synthesis of a large number of heterocyclic systems, such as benzothiazepines [1][2], benzodiazepines [1], benzoxazepines, pyrimidines [3], pyrazoles [4][5], and oxazoles [6], chalcones are also of interest due to their interesting biological properties. Indeed, various substituted chalcones possess antioxidant [7], radical-scavenging, anticancer [8][9], antileishmanial [10], antimalarial [11], cytotoxic, antimitotic, and antibacterial properties, as well as P-glycoprotein-mediated multidrug resistance. Furthermore, many chalcone-based drugs are passing through pre-clinical trials for the development of antimalarial and antileishmanial drugs [10][11].

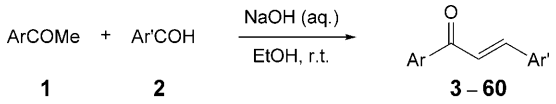
Ansari et al. [12] have screened 120 variously substituted chalcones for their antibacterial activities against six bacterial strains, *viz.*, three *Gram*-positive ones (*Bacillus subtilis* ATCC 6633, *Micrococcus leuteus*, and *Staphylococcus aureus* ATCC 6538) and three *Gram*-negative ones (*Escherichia coli* ATCC 1522, *Enterobacter aerogenes* ATCC 13048, and *Salmonella setubal* ATCC 19196). They have observed that the chalcones were active against *S. aureus*, *B. subtilis*, and, very weakly, against *E. coli*, but inactive towards the other three strains.

Therefore, this study focuses on the synthesis of further chalcone derivatives with various substituents, *e.g.*, furan and thiophene rings, and the determination of their activities against 13 human pathogenic microorganisms.

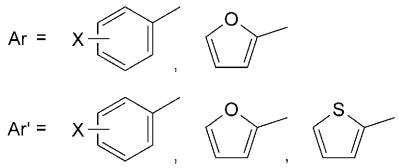
Results and Discussion. – *Chemistry.* The general synthetic strategy for the preparation of the chalcone derivatives **3**–**60** was based on *Claisen*–*Schmidt* condensation [13]. As shown in the *Scheme*, a series of 58 chalcone derivatives were prepared by base-catalyzed condensation of appropriately substituted acetophenone

and 2-furyl methyl ketones with substituted benzaldehydes, furfural, and thiophene-2-carbaldehyde in aqueous EtOH.

Scheme. *Synthesis of Chalcone Derivatives* **3**–**60**



1 **2** **3**–**60**



X = H, Cl, OH, MeO, Me, NH_2, NO_2

After purification of the crude products, chalcone derivatives **3**–**60** (*Scheme* and *Table 1*) were obtained in yields of 69–97%. According to our literature survey [14–18], the chalcone derivatives are known, except compounds **12**, **13**, **23**, **24**, **28**, **32**, **34**, **35**, **37**, **40**, **42**, **47**, **48**, **50**, and **51**. The structures of all the synthesized chalcone derivatives were assigned on the basis of IR, ^{1}H-NMR, and ^{13}C-NMR data, elemental analysis, and comparison with published data. The results are in agreement with the proposed structures.

Biology. Determination of Inhibition Zones. The antimicrobial activity of 30 chalcones, **3**–**32**, and 28 chalcone-like compounds, **33**–**60**, against 13 microorganisms, *i.e.*, two yeasts (*Candida albicans* ATCC 1213 and *Candida utilis* KUEN 1031), five *Gram*-positive bacteria (*Streptococcus hominis*, *Bacillus cereus* DSM 4312, *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 29213, and *Streptococcus pyogenes* ATCC 176), and six *Gram*-negative bacteria (*Proteus vulgaris* KUEN 1329, *Escherichia coli* 111, *Pseudomonas aeruginosa* ATCC 9027, *Salmonella enteridis* ATCC 13076, *Enterococous faecalis* ATCC 29122, and *Pseudomonas aeruginosa* ATCC 27859), was determined with the disc diffusion method. SCF (30 μg sulbactam +75 μg cefoperazone) and MeOH were used as positive and negative controls, respectively. Inhibition zones produced by each compound were determined in triplicate and the means are given in *Table 1*.

Chalcone-like compounds substituted with a thionyl ring, *i.e.*, **39**–**43**, showed weak or no antimicrobial activity. On the other hand, chalcone derivatives with OH, Cl, and, particularly, furyl substituents were found to be active against the majority of the tested bacteria. Among them, **7**, **18**, **35**, and **54** were found to have a good antifungal activity against both yeasts tested. Compounds **45**, **54**, and **58** showed a particularly high activity against *Pseudomonas aeruginosa* ATCC 9027 and **18**, **35**, and **54** against *Candida albicans* ATCC 1213. Further, **7**, **35**, **54**, and **58** were found to be more effective against *Salmonella enteritidis* ATCC 13076 than other chalcones and **54** and **58** against *Streptococcus pyogenes* ATCC 176.

In addition, among the chalcone-like compounds substituted with a furyl ring, *i.e.*, **44**–**60**, all were found to be active against *Candida albicans* ATCC 1213, all except **46**

Table 1. *Antimicrobial Activities* (inhibition zones [mm]) *of Chalcones* **3**–**60** (105 μg/disc in MeOH). Inhibition zones are given as means ± S.D. ($n = 3$).

Compound	Substituents		Microorganisms[a])												
	Ar	Ar′	A	B	C	D	E	F	G	H	I	J	K	L	M
3	*o*-MeO-C_6H_4	Ph	–[b])	–	–	–	–	11 ± 0.0	9 ± 0.0	–	–	–	9 ± 0.0	7 ± 0.2	n.d.[c])
4	*m*-MeO-C_6H_4	Ph	–	–	–	–	–	11 ± 0.3	9 ± 0.0	–	–	–	9 ± 0.2	8 ± 0.2	n.d.
5	*p*-MeO-C_6H_4	Ph	12 ± 0.2	12 ± 0.0	–	–	13 ± 0.1	–	–	–	13 ± 0.3	9 ± 0.3	–	13 ± 0.0	n.d.
6	*o*-HO-C_6H_4	Ph	–	–	–	–	11 ± 0.0	–	–	–	13 ± 0.4	–	9 ± 0.1	13 ± 0.0	n.d.
7	*p*-HO-C_6H_4	Ph	16 ± 0.0	16 ± 0.3	15 ± 0.2	12 ± 0.5	15 ± 0.3	18 ± 0.7	14 ± 0.2	14 ± 0.1	17 ± 0.3	13 ± 0.2	13 ± 0.4	14 ± 0.1	n.d.
8	*p*-Cl-C_6H_4	Ph	–	–	10 ± 0.0	–	–	12 ± 0.1	–	–	9 ± 0.0	9 ± 0.0	–	–	n.d.
9	*o*-Br-C_6H_4	Ph	–	–	–	–	–	–	–	–	–	–	9 ± 0.2	–	n.d.
10	*m*-Br-C_6H_4	Ph	14 ± 0.0	–	–	–	12 ± 0.2	13 ± 0.4	9 ± 0.3	–	13 ± 0.5	9 ± 0.2	10 ± 0.0	14 ± 0.3	n.d.
11	*p*-Br-C_6H_4	Ph	–	12 ± 0.2	–	–	8 ± 0.2	n.d.	10 ± 0.3	9 ± 0.2	8 ± 0.0	10 ± 0.1	15 ± 0.4	10 ± 0.3	11 ± 0.0
12	*o*-O_2N-C_6H_4	Ph	14 ± 0.4	9 ± 0.0	10 ± 0.2	–	12 ± 0.4	–	–	–	12 ± 0.1	–	9 ± 0.2	13 ± 0.2	n.d.
13	*m*-H_2N-C_6H_4	Ph	13 ± 0.0	14 ± 0.2	11 ± 0.2	11 ± 0.0	11 ± 0.1	n.d.	14 ± 0.3	11 ± 0.2	12 ± 0.0	10 ± 0.3	15 ± 0.2	16 ± 0.4	12 ± 0.2
14	*p*-H_2N-C_6H_4	Ph	10 ± 0.2	–	–	9 ± 0.3	8 ± 0.1	n.d.	9 ± 0.0	9 ± 0.0	9 ± 0.3	10 ± 0.1	11 ± 0.0	10 ± 0.2	–
15	*p*-Me-C_6H_4	Ph	12 ± 0.4	15 ± 0.5	11 ± 0.2	12 ± 0.0	11 ± 0.3	n.d.	9 ± 0.0	9 ± 0.1	10 ± 0.2	12 ± 0.3	10 ± 0.3	12 ± 0.4	11 ± 0.2
16	Ph	*o*-MeO-C_6H_4	–	–	10 ± 0.0	–	–	–	–	–	–	11 ± 0.2	10 ± 0.2	–	n.d.
17	Ph	*p*-MeO-C_6H_4	–	–	–	–	–	13 ± 0.5	9 ± 0.3	–	8 ± 0.1	–	–	–	n.d.
18	Ph	*o*-HO-C_6H_4	13 ± 0.0	14 ± 0.2	16 ± 0.3	15 ± 0.3	12 ± 0.0	n.d.	13 ± 0.2	13 ± 0.3	15 ± 0.4	16 ± 0.3	15 ± 0.2	17 ± 0.5	13 ± 0.3
19	Ph	*o*-Cl-C_6H_4	11 ± 0.2	15 ± 0.3	11 ± 0.4	9 ± 0.2	9 ± 0.3	n.d.	9 ± 0.2	9 ± 0.3	12 ± 0.4	11 ± 0.2	10 ± 0.3	16 ± 1.1	13 ± 0.2
20	Ph	*p*-Cl-C_6H_4	10 ± 0.0	–	10 ± 0.2	–	9 ± 0.2	n.d.	–	–	–	9 ± 0.0	–	9 ± 0.1	11 ± 0.2
21	Ph	*m*-Br-C_6H_4	8 ± 0.2	–	–	–	–	11 ± 0.6	–	–	–	–	–	8 ± 0.4	n.d.
22	Ph	*p*-Br-C_6H_4	8 ± 0.1	12 ± 0.5	–	–	12 ± 0.3	12 ± 0.3	–	–	10 ± 0.0	9 ± 0.2	10 ± 0.2	13 ± 0.0	n.d.
23	Ph	*o*-Me-C_6H_4	–	–	10 ± 0.3	10 ± 0.0	12 ± 0.3	n.d.	10 ± 0.3	10 ± 0.2	8 ± 0.0	–	–	–	–
24	Ph	*m*-Me-C_6H_4	11 ± 0.7	14 ± 0.0	11 ± 0.2	10 ± 0.2	10 ± 0.2	n.d.	9 ± 0.0	9 ± 0.0	11 ± 0.4	11 ± 0.2	10 ± 0.2	14 ± 0.4	11 ± 0.1
25	Ph	*p*-Me-C_6H_4	8 ± 0.0	10 ± 0.1	10 ± 0.2	–	10 ± 0.2	n.d.	10 ± 0.2	–	–	9 ± 0.2	10 ± 0.1	10 ± 0.1	10 ± 0.2
26	*p*-MeO-C_6H_4	*p*-MeO-C_6H_4	–	–	–	–	–	–	–	–	–	–	–	8 ± 0.0	n.d.
27	*p*-Cl-C_6H_4	*p*-Cl-C_6H_4	–	–	10 ± 0.3	–	–	–	9 ± 0.3	10 ± 0.2	13 ± 0.4	–	–	8 ± 0.1	n.d.
28	*p*-Cl-C_6H_4	*p*-MeO-C_6H_4	–	–	9 ± 0.3	–	–	11 ± 0.0	–	–	–	9 ± 0.2	9 ± 0.1	7 ± 0.2	n.d.
29	*p*-MeO-C_6H_4	*p*-Cl-C_6H_4	–	–	–	–	–	–	–	–	8 ± 0.0	10 ± 0.3	10 ± 0.1	–	n.d.
30	*p*-MeO-C_6H_4	*o*-Cl-C_6H_4	–	6 ± 0.0	9 ± 0.0	–	–	12 ± 0.3	–	–	–	–	–	7 ± 0.1	n.d.
31	*p*-H_2N-C_6H_4	*p*-Me-C_6H_4	11 ± 0.0	13 ± 0.2	13 ± 0.0	9 ± 0.3	9 ± 0.0	n.d.	–	9 ± 0.3	14 ± 0.2	11 ± 0.0	13 ± 0.3	14 ± 0.3	14 ± 0.4
32	*m*-H_2N-C_6H_4	*p*-MeO-C_6H_4	8 ± 0.2	13 ± 0.6	12 ± 0.3	9 ± 0.0	11 ± 0.2	n.d.	9 ± 0.1	11 ± 0.1	10 ± 0.1	–	12 ± 0.2	12 ± 0.2	12 ± 0.3
33	Furyl	*o*-MeO-C_6H_4	11 ± 0.2	10 ± 0.0	11 ± 0.0	11 ± 0.2	11 ± 0.1	n.d.	12 ± 0.5	13 ± 0.2	13 ± 0.4	10 ± 0.3	13 ± 0.0	15 ± 0.4	14 ± 0.2
34	Furyl	*p*-MeO-C_6H_4	13 ± 0.3	13 ± 0.4	11 ± 0.1	10 ± 0.0	12 ± 0.4	n.d.	11 ± 0.0	12 ± 0.2	–	10 ± 0.1	12 ± 0.4	10 ± 0.2	14 ± 0.6
35	Furyl	*o*-Cl-C_6H_4	15 ± 0.5	14 ± 0.3	12 ± 0.2	13 ± 0.3	12 ± 0.1	n.d.	9 ± 0.3	13 ± 0.4	17 ± 0.5	15 ± 0.4	14 ± 0.3	19 ± 0.7	17 ± 0.4

Table 1 (cont.)

Compound	Substituents		Microorganisms[a])												
	Ar	Ar′	A	B	C	D	E	F	G	H	I	J	K	L	M
36	Furyl	*p*-Br-C_6H_4	–	13±0.2	–	8±0.0	10±0.0	n.d.	–	10±0.1	11±0.1	9±0.2	10±0.2	11±0.2	14±0.2
37	Furyl	*o*-Me-C_6H_4	11±0.2	12±0.4	12±0.2	12±0.3	10±0.1	n.d.	12±0.2	12±0.2	14±0.2	12±0.1	14±0.3	17±0.3	15±0.2
38	Furyl	*p*-Me-C_6H_4	15±0.2	14±0.3	10±0.0	9±0.0	10±0.2	n.d.	10±0.1	11±0.0	10±0.1	11±0.3	14±0.2	15±0.3	10±0.2
39	*p*-MeO-C_6H_4	Thiophenyl	8±0.0	9±0.0	9±0.0	10±0.0	10±0.1	n.d.	–	9±0.2	10±0.1	11±0.0	10±0.2	10±0.1	10±0.2
40	*o*-HO-C_6H_4	Thiophenyl	–	–	9±0.3	–	9±0.0	n.d.	9±0.3	9±0.3	10±0.1	11±0.1	11±0.3	10±0.0	10±0.3
41	*p*-Cl-C_6H_4	Thiophenyl	9±0.2	–	9±0.2	9±0.3	12±0.2	n.d.	9±0.0	9±0.0	8±0.2	–	–	–	–
42	*m*-Br-C_6H_4	Thiophenyl	8±0.0	–	9±0.0	9±0.2	11±0.0	n.d.	9±0.3	10±0.2	9±0.1	–	–	–	–
43	*p*-Br-C_6H_4	Thiophenyl	8±0.2	–	–	–	10±0.2	n.d.	10±0.3	9±0.1	9±0.2	–	9±0.1	–	–
44	*o*-MeO-C_6H_4	Furyl	18±0.5	13±0.2	9±0.1	11±0.2	14±0.4	11±0.1	14±0.2	15±0.2	12±0.2	–	n.d.	16±0.4	n.d.
45	*m*-MeO-C_6H_4	Furyl	16±0.2	14±0.3	10±0.0	13±0.1	18±0.2	–	13±0.3	16±0.3	–	–	n.d.	15±0.2	n.d.
46	*p*-MeO-C_6H_4	Furyl	–	15±0.3	9±0.3	13±0.2	17±0.4	11±0.1	14±0.3	16±0.3	14±0.3	14±0.2	n.d.	14±0.3	n.d.
47	*o*-Cl-C_6H_4	Furyl	16±0.2	13±0.1	9±0.2	14±0.0	15±0.3	12±0.2	13±0.2	15±0.2	14±0.1	14±0.2	n.d.	16±0.3	n.d.
48	*m*-Cl-C_6H_4	Furyl	18±0.4	14±0.1	10±0.0	10±0.2	18±0.5	12±0.2	13±0.4	14±0.3	14±0.3	18±0.8	n.d.	16±0.5	n.d.
49	*p*-Cl-C_6H_4	Furyl	16±0.3	14±0.3	12±0.3	11±0.0	17±0.3	12±0.1	16±0.4	14±0.3	12±0.3	17±0.5	n.d.	16±0.2	n.d.
50	*o*-Br-C_6H_4	Furyl	18±0.2	11±0.2	10±0.4	10±0.3	–	9±0.0	14±0.2	12±0.2	–	14±0.2	n.d.	15±0.3	n.d.
51	*m*-Br-C_6H_4	Furyl	18±0.4	13±0.2	11±0.2	11±0.0	14±0.3	12±0.2	13±0.2	14±0.3	12±0.2	18±0.4	n.d.	15±0.3	n.d.
52	*p*-Br-C_6H_4	Furyl	16±0.2	16±0.0	12±0.2	11±0.0	16±0.3	12±0.2	–	14±0.1	15±0.4	–	n.d.	16±0.6	n.d.
53	*o*-HO-C_6H_4	Furyl	19±0.3	13±0.3	11±0.0	–	17±0.3	11±0.0	14±0.1	15±0.3	12±0.1	19±0.5	n.d.	16±0.3	n.d.
54	*p*-HO-C_6H_4	Furyl	20±0.5	16±0.2	12±0.1	13±0.1	18±0.3	14±0.3	15±0.2	16±0.4	16±0.3	19±0.4	n.d.	17±0.4	n.d.
55	*o*-O_2N-C_6H_4	Furyl	16±0.3	15±0.3	11±0.1	11±0.0	14±0.2	14±0.2	13±0.2	12±0.2	12±0.2	15±0.3	n.d.	15±0.3	n.d.
56	*m*-O_2N-C_6H_4	Furyl	19±0.4	14±0.1	11±0.2	9±0.0	18±0.3	11±0.0	–	–	15±0.4	12±0.0	n.d.	16±0.3	n.d.
57	*p*-O_2N-C_6H_4	Furyl	15±0.2	12±0.2	12±0.3	9±0.0	14±0.2	–	–	–	12±0.2	13±0.2	n.d.	14±0.2	n.d.
58	*m*-H_2N-C_6H_4	Furyl	19±0.7	13±0.0	14±0.3	13±0.0	18±0.3	11±0.1	14±0.1	14±0.4	14±0.2	19±0.3	n.d.	15±0.3	n.d.
59	*p*-H_2N-C_6H_4	Furyl	–	11±0.2	10±0.0	9±0.0	–	12±0.1	14±0.3	12±0.2	–	–	n.d.	12±0.2	n.d.
60	*p*-Me-C_6H_4	Furyl	18±0.2	15±0.2	12±0.0	12±0.2	16±0.3	12±0.1	13±0.0	14±0.3	13±0.2	15±0.3	n.d.	16±0.4	n.d.
SCF[d])			21	20	17	22	24	13	21	20	19	21	22	21	19
MeOH[e])			7	8	8	7	7	7	8	8	7	8	8	6	8

[a]) A: *Proteus vulgaris* KUEN 1329; B: *Candida utilis* KUEN 1031; C: *Escherichia coli* 111; D: *Bacillus cereus* DSM 4312; E: *Pseudomonas aeruginosa* ATCC 9027; F: *Pseudomonas aeruginosa* ATCC 27859; G: *Bacillus subtilis* ATCC 6633; H: *Staphylococcus aureus* ATCC 29213; I: *Salmonella enteritidis* ATCC 13076; J: *Streptococcus pyogenes* ATCC 176; K: *Enterococous faecalis* ATCC 29122; L: *Candida albicans* ATCC 1213; M: *Streptococcus hominis.* [b]) –: Inactive. [c]) n.d.: Not determined. [d]) SCF: Sulbactam (30 μg) + cefoperazone (75 μg) = positive control. [e]) MeOH: Negative control.

and **59** against *Proteus vulgaris* KUEN 1329, all except **44**, **50**, and **59** against *Pseudomonas aeruginosa* ATCC 9027, and all except **45** and **57** against *Pseudomonas aeruginosa* ATCC 27859, respectively. Among all compounds, **54** was found to have the largest inhibition zones against both bacterial and yeast strains.

Minimum Inhibitory Concentrations (*MIC*s). For the most active chalcones, **7**, **18**, **35**, **47**–**49**, **51**, and **53**–**55**, MIC values were determined by the serial microdilution technique in *Mueller–Hinton* broth for bacteria and in *Sabouraud* dextrose broth for yeasts (*Table 2*).

Conclusions. – A series of 58 chalcone derivatives, **3**–**60**, were prepared by *Claisen–Schmidt* condensation and screened for their antimicrobial activities. The presence of substituents as OH, Cl, and NH_2 groups and, in particular, furyl rings resulted in increased antimicrobial activity.

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Experimental Part

General. Column chromatography (CC): silica gel (SiO_2; 60–230 mesh; *Merck*). M.p.: *Electrothermal 9100* apparatus. IR Spectra: *Jasco FT/IR-430* spectrometer in KBr disks or $CHCl_3$; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *Bruker Avance DPX-400* instrument, at 300 and 75 MHz, resp., in $CDCl_3$; δ in ppm rel. to int. Me_4Si or solvent signals ($CDCl_3$, δ(C) 77.0), J in Hz. Elemental analysis: *LECO CHNS 932* instrument.

General Procedure for the Synthesis of Chalcone Derivatives **3**–**60**. To a soln. of a acetophenone derivative (1 mmol) in EtOH (20 ml) was added furfural (1 mmol) and NaOH (2.5M, 8 ml) at r.t. The mixture was stirred for 3 h, neutralized with dil. HCl, and extracted with $CHCl_3$. The org. layer was dried (Na_2SO_4) and evaporated. The residue was purified by CC ($CHCl_3$/hexane 3:7) and/or crystallized in $CHCl_3$/hexane (3:7).

*(*E*)-1-(2-Nitrophenyl)-3-phenylprop-2-en-1-one* (**12**). Yield: 79%. Brown crystals. M.p. 125–127°. IR (KBr): 3083, 3043, 1654, 1527, 1448, 1342, 1280, 1203, 1105, 973, 867, 763, 701. ^{1}H-NMR: 8.19 (*dd*, J = 8.1, 0.9, 1 H); 7.78 (*dt*, J = 7.5, 1.2, 1 H); 7.71–7.64 (*m*, 1 H); 7.55–7.48 (*m*, 3 H); 7.42–7.35 (*m*, 3 H); 7.26, 7.03 (*AB*, J = 16.2, 2 H). ^{13}C-NMR: 193.0 (C=O); 146.7; 146.4; 136.3; 134.1; 133.9; 131.1; 130.6; 129.0 (2 C); 128.8; 128.6 (2 C); 126.4; 124.6. Anal. calc. for $C_{15}H_{11}NO_3$: C 71.14, H 4.38, N 5.53; found: C 71.24, H 4.45, N 5.56.

*(*E*)-1-(3-Aminophenyl)-3-phenylprop-2-en-1-one* (**13**). Yield: 94%. Orange crystals. M.p. 115–118°. IR (KBr): 3467, 3365, 3023, 2881, 2834, 1658, 1589, 1334, 1307, 1186, 977, 759, 688. ^{1}H-NMR: 7.82, 7.51 (*AB*, J = 15.6, 2 H); 7.68–7.62 (*m*, 2 H); 7.46–7.38 (*m*, 3 H); 7.36–7.25 (*m*, 3 H); 6.91 (*ddd*, J = 7.9, 2.4, 0.9, 1 H); 3.88 (*s*, NH_2). ^{13}C-NMR: 190.8 (C=O); 146.9; 144.6; 139.3; 135.0; 130.5; 129.5; 129.0 (2 C); 128.5 (2 C); 122.4; 119.5; 118.8; 114.4. Anal. calc. for $C_{15}H_{13}NO$: C 80.69, H 5.87, N 6.27; found: C 80.74, H 5.91, N 6.30.

*(*E*)-3-(2-Methylphenyl)-1-phenlylprop-2-en-1-one* (**23**). Yield: 90%. Viscous oil. IR (KBr): 3060, 3023, 2971, 1662, 1594, 1448, 1330, 1214, 1016, 979, 750, 692. ^{1}H-NMR: 8.15, 7.49 (*AB*, J = 15.6, 2 H); 8.09–8.04 (*m*, 2 arom. H); 7.73 (br. *d*, J = 7.8, 1 arom. H); 7.64–7.52 (*m*, 3 arom. H); 7.35–7.23 (*m*, 3 arom. H); 2.51 (*s*, Me). ^{13}C-NMR: 190.5 (C=O); 142.5; 138.4; 138.4; 133.9; 132.8; 130.9; 130.3; 128.6 (2 C); 128.5 (2 C); 126.4; 126.3; 123.1; 19.9. Anal. calc. for $C_{16}H_{14}O$: C 86.45, H 6.35; found: C 86.50, H 6.42.

*(*E*)-3-(3-Methylphenyl)-1-phenlylprop-2-en-1-one* (**24**). Yield: 90%. Yellow crystals. M.p. 57–59°. IR (KBr): 3056, 3031, 2965, 1656, 1598, 1575, 1446, 1315, 1213, 1016, 991, 771, 682. ^{1}H-NMR: 8.06 (*d*, J = 7.2, 2 H); 7.83 (*d*, J = 15.9, 1 H); 7.64–7.46 (*m*, 6 H); 7.33 (*t*, J = 7.8, 1 H); 7.25 (br. *d*, J = 7.5, 1 H); 2.43 (*s*, Me). ^{13}C-NMR: 190.6 (C=O); 145.1; 138.6; 138.3; 134.8; 132.8; 131.5; 129.1; 128.8; 128.6 (2 C); 128.5 (2 C); 125.8; 121.9; 21.4. Anal. calc. for $C_{16}H_{14}O$: C 86.45, H 6.35; found: C 86.53, H 6.38.

Table 2. *Minimum Inhibitory Concentrations* [μM] *of the Most Active Chalcones.* MIC are given as means ± S.D. ($n=3$).

Compound	Microorganisms[a])										
	A	B	C	D	E	F	G	H	I	J	K
7	1.10 ± 0.19	2.20 ± 0.10	4.40 ± 0.21	1.10 ± 0.19	2.20 ± 0.10	1.10 ± 0.19	2.20 ± 0.10	–[b])	4.40 ± 0.21	–	n.d.[c])
18	0.14 ± 0.03	2.20 ± 0.10	1.10 ± 0.19	–	–	n.d.	2.20 ± 0.10	4.40 ± 0.21	2.20 ± 0.10	1.10 ± 0.19	n.d.
35	1.00 ± 0.26	2.10 ± 0.18	–	–	–	n.d.	–	–	2.10 ± 0.18	1.00 ± 0.26	n.d.
47	2.60 ± 0.31	2.10 ± 0.18	1.00 ± 0.26	0.53 ± 0.03	2.10 ± 0.18	1.00 ± 0.26	2.10 ± 0.18	0.53 ± 0.03	2.10 ± 0.18	2.60 ± 0.31	2.10 ± 0.18
48	0.53 ± 0.03	4.30 ± 0.03	–	–	4.30 ± 0.03	1.00 ± 0.26	–	–	4.30 ± 0.03	–	0.53 ± 0.03
49	1.00 ± 0.26	–	4.30 ± 0.03	4.30 ± 0.03	2.10 ± 0.18	2.10 ± 0.18	2.10 ± 0.18	–	–	–	0.53 ± 0.03
51	2.20 ± 0.22	0.90 ± 0.02	–	–	1.80 ± 0.39	1.80 ± 0.39	1.80 ± 0.39	–	–	–	2.20 ± 0.22
53	0.58 ± 0.02	2.30 ± 0.12	4.60 ± 0.24	4.60 ± 0.24	2.30 ± 0.12	2.30 ± 0.12	2.30 ± 0.12	4.60 ± 0.24	2.30 ± 0.12	2.30 ± 0.12	0.58 ± 0.02
54	0.58 ± 0.02	4.60 ± 0.24	4.60 ± 0.24	2.30 ± 0.12	–	4.60 ± 0.24	4.60 ± 0.24	4.60 ± 0.24	4.60 ± 0.24	2.30 ± 0.12	0.58 ± 0.02
55	1.00 ± 0.95	2.00 ± 0.19	4.10 ± 0.49	2.00 ± 0.19	4.10 ± 0.49	2.00 ± 0.19	2.00 ± 0.19	4.10 ± 0.49	4.10 ± 0.49	2.00 ± 0.19	1.00 ± 0.95
CS-T[d])	7.00 ± 0.12	2.80 ± 0.48	2.80 ± 0.48	1.40 ± 0.02	1.10 ± 0.86	1.10 ± 0.86	2.20 ± 0.17	2.20 ± 0.17	1.10 ± 0.86	1.10 ± 0.86	2.80 ± 0.48
MeOH[e])	–	–	–	–	–	–	–	–	–	–	–

[a]) A: *Proteus vulgaris* KUEN 1329; B: *Candida utilis* KUEN 1031; C: *Escherichia coli* 111; D: *Bacillus cereus* DSM 4312; E: *Pseudomonas aeruginosa* ATCC 9027; F: *Pseudomonas aeruginosa* ATCC 27859; G: *Bacillus subtilis* ATCC 6633; H: *Staphylococcus aureus* ATCC 29213; I: *Salmonella enteritidis* ATCC 13076; J: *Streptococcus pyogenes* ATCC 176; K: *Enterococous faecalis* ATCC 29122. [b]) –: Inactive. [c]) n.d.: Not determined. [d]) CS-T: Tetracycline = positive control. [e]) MeOH: Negative control.

(E)-1-(4-Chlorophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (**28**). Yield: 92%. Yellow crystals. M.p. 119–123°. IR (KBr): 3068, 2973, 2838, 1656, 1594, 1511, 1295, 1257, 1168, 1029, 991, 811. ^{1}H-NMR: 7.95, 7.46 (*AA′BB′*, *J* = 8.4, 4 H); 7.79, 7.37 (*AB*, *J* = 15.6, 2 H); 7.59, 6.93 (*AA′XX′*, *J* = 8.7, 4 H); 3.85 (*s*, MeO). ^{13}C-NMR: 189.3 (C=O); 162.0; 145.4; 139.1; 137.0; 130.5 (2 C); 130.0 (2 C); 129.0 (2 C); 127.6; 119.2; 118.7; 114.6; 55.6. Anal. calc. for $C_{16}H_{13}ClO_2$: C 70.46, H 4.80; found: C 70.52, H 4.92.

*(*E*)-1-(3-Aminophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one* (**32**). Yield: 89%. Orange crystals. M.p. 122–125°. IR (KBr): 3461, 3363, 2965, 2933, 2840, 1654, 1577, 1509, 1454, 1321, 1259, 1174, 991, 827, 788. ^{1}H-NMR: 7.78 (*d*, *J* = 15.6, 1 H); 7.59, 6.94 (*AA′XX′*, *J* = 8.7, 4 H); 7.42–7.24 (*m*, 4 H); 6.91–5.71 (*m*, 1 H); 3.88 (br. *s*, NH_2); 3.85 (*s*, MeO). ^{13}C-NMR: 190.8 (C=O); 161.6; 146.9; 144.4; 139.6; 130.2 (2 C); 129.4; 127.8; 120.0; 119.3; 118.7; 114.4 (3 C); 55.4. Anal. calc. for $C_{16}H_{15}NO_2$: C 75.87, H 5.97, N 5.53; found: C 75.94, H 5.99, N 5.58.

*(*E*)-1-(Furan-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one* (**34**). Yield: 87%. Yellow crystals. M.p. 72–75°. IR (KBr): 3097, 3079, 2879, 2798, 1635, 1587, 1540, 1417, 1373, 1278, 1216, 1168, 1039, 970, 825, 694. ^{1}H-NMR (400 MHz): 7.82 (*d*, *J* = 15.6, 1 H); 7.62 (*s*, 1 H); 7.58, 6.97 (*AA′BB′*, *J* = 8.0, 4 H); 7.31 (br. *d*, *J* = 16.0, 2 H); 6.56 (*t*, *J* = 1.6, 1 H); 3.81 (*s*, MeO). ^{13}C-NMR (100 MHz): 178.1 (C=O); 161.7; 146.4; 143.7; 130.3 (2 C); 127.4; 118.8; 117.2; 114.4; 114.3 (2 C); 112.5; 55.4. Anal. calc. for $C_{14}H_{12}O_3$: C 73.67, H 5.30; found: C 73.75, H 5.42.

*(*E*)-3-(2-Chlorophenyl)-1-(furan-2-yl)prop-2-en-1-one* (**35**). Yield: 68%. Yellow crystals. M.p. 117–119°. IR (KBr): 3143, 3129, 3116, 3056, 3021, 2973, 1652, 1594, 1457, 1334, 1045, 1012, 975, 790, 759, 728. ^{1}H-NMR (400 MHz): 8.24 (*d*, *J* = 16.0, 1 H); 7.76–7.72 (*m*, 1 H); 7.65 (*s*, 1 H); 7.44–7.38 (*m*, 2 H); 7.35–7.25 (*m*, 3 H); 6.58 (*dd*, *J* = 3.2, 1.2, 1 H). ^{13}C-NMR (100 MHz): 177.6 (C=O); 153.5; 146.7; 139.6; 135.6; 132.9; 131.3; 130.3; 127.8; 127.1; 123.8; 117.9; 112.6. Anal. calc. for $C_{13}H_9ClO_2$: C 67.11, H 3.90; found: C 67.40, H 3.92.

*(*E*)-1-(Furan-2-yl)-3-(2-methylphenyl)prop-2-en-1-one* (**37**). Yield: 71%. Yellow crystals. M.p. 74–75°. IR (KBr): 3430, 3100, 3085, 3070, 3023, 2904, 1637, 1560, 1482, 1299, 1207, 1147, 1022, 973, 836, 763, 707. ^{1}H-NMR (400 MHz): 8.17, 7.38 (*AB*, *J* = 15.6, 2 H); 7.70 (*d*, *J* = 7.2, 1 H); 7.65 (br. *s*, 1 H); 7.35–7.20 (*m*, 4 H); 6.59 (*dd*, *J* = 3.6, 1.6, 1 H); 2.47 (*s*, Me). ^{13}C-NMR (100 MHz): 178.0 (C=O); 153.7; 146.6; 141.5; 138.5; 133.7; 130.9; 130.4; 126.5; 126.3; 122.2; 117.6; 112.6; 19.88. Anal. calc. for $C_{14}H_{12}O_2$: C 79.22, H 5.70; found: C 79.40, H 5.92.

*(*E*)-1-(2-Hydroxyphenyl)-3-(thiophen-2-yl)prop-2-en-1-one* (**40**). Yield: 82%. Brown crystals. M.p. 96–98°. IR (KBr): 3127, 3112, 3072, 2998, 2973, 2942, 2838, 1654, 1598, 1465, 1396, 1294, 1247, 1170, 1047, 987, 817, 755. ^{1}H-NMR (400 MHz): 12.9 (*s*, OH); 8.04, 7.47 (*AB*, *J* = 15.2, 2 H); 7.87 (*d*, *J* = 8.0, 1 H); 7.52–7.38 (*m*, 3 H); 7.12–7.10 (*m*, 1 H); 7.02 (*d*, *J* = 8.4, 1 H); 6.94 (*t*, *J* = 8.0, 1 H). ^{13}C-NMR (100 MHz): 193.1 (C=O); 163.5; 140.1; 137.8; 136.4; 132.8; 129.6; 129.5; 128.5; 119.9; 118.8; 118.7; 118.6. Anal. calc. for $C_{13}H_{10}O_2S$: C 67.80, H 4.38, S 13.92; found: C 67.92, H 4.43, S 13.96.

*(*E*)-1-(3-Bromophenyl)-3-(thiophen-2-yl)prop-2-en-1-one* (**42**). Yield: 73%. Yellow crystals. M.p. 99–102°. IR (KBr): 3095, 3066, 2871, 1658, 1592, 1558, 1415, 1282, 1207, 1039, 970, 796, 709, 671. ^{1}H-NMR (400 MHz): 8.12 (*s*, 1 H); 7.95, 7.24 (*AB*, *J* = 15.2, 2 H); 7.91 (*d*, *J* = 7.6, 1 H); 7.69 (br. *d*, *J* = 8.0, 1 H); 7.44 (*d*, *J* = 4.8, 1 H); 7.40–7.34 (*m*, 2 H); 7.10 (*t*, *J* = 4.4, 1 H). ^{13}C-NMR (100 MHz): 188.3 (C=O); 140.1; 139.9; 138.0; 135.6; 132.6; 131.4; 130.2; 129.4; 128.5; 126.9; 123.0; 120.0. Anal. calc. for $C_{13}H_9BrOS$: C 53.26, H 3.09, S 10.94; found: C 53.42, H 3.24, S 10.96.

*(*E*)-1-(2-Chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one* (**47**). Yield: 91%. Viscous oil. IR (KBr): 3126, 2925, 2852, 1621, 1598, 1301, 1284, 1016, 752. ^{1}H-NMR (400 MHz): 7.53–7.31 (*m*, 4 arom. H, H–C(2)); 7.24 (*d*, *J* = 15.7, H–C(7)); 7.02 (*d*, *J* = 15.7, H–C(6)); 6.70 (*d*, *J* = 3.5, H–C(4)); 6.49 (*dd*, *J* = 3.4, 1.8, H–C(3)). ^{13}C-NMR (100 MHz): 193.30; 151.01; 145.59; 139.02; 132.03; 131.40; 131.26; 130.30; 129.30; 126.86; 123.58; 116.88; 112.85. Anal. calc. for $C_{13}H_9ClO_2$: C 67.11, H 3.90; found: C 67.40, H 3.92.

*(*E*)-1-(3-Chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one* (**48**). Yield: 78%. M.p. 52–54°. IR (KBr): 3120, 3068, 2923, 2848, 1679, 1569, 1421, 1284, 1245, 1197, 1010, 730. ^{1}H-NMR (400 MHz): 7.98 (*t*, *J* = 1.8, 1 H); 7.89 (*dt*, *J* = 1.3, 1 H); 7.51 (*dd*, *J* = 2.1, 1.1, 1 H); 7.54 (*d*, *J* = 3.5, 1 H); 7.61 (*d*, *J* = 15.3, 1 H); 7.43 (*t*, *J* = 7.7, 1 H); 7.38 (*d*, *J* = 15.3, 1 H); 6.73 (*d*, *J* = 3.4, 1 H); 6.52 (*dd*, *J* = 3.4, 1.7, 1 H). ^{13}C-NMR (100 MHz): 188.34; 151.46; 145.25; 139.71; 134.90; 132.66; 131.30; 129.94; 128.49; 126.48; 118.57; 116.90; 112.84. Anal. calc. for $C_{13}H_9ClO_2$: C 67.11, H 3.90; found: C 67.81, H 3.97.

*(*E*)-1-(2-Bromophenyl)-3-(furan-2-yl)prop-2-en-1-one* (**50**). Yield: 70%. Viscous oil. IR (KBr): 3116, 3048, 3008, 1646, 1624, 1600, 1301, 1282, 1014, 970, 754. ^{1}H-NMR (400 MHz): 7.45–7.06 (*m*, 4 arom. H); 7.35 (*d*, *J* = 1.5, H–C(2)); 7.03 (*d*, *J* = 15.8, H–C(7)); 6.80 (*d*, *J* = 15.8, H–C(6)); 6.51 (*d*, *J* = 3.5, H–C(4)); 6.31 (*dd*, *J* = 3.4, 1.8, H–C(3)). ^{13}C-NMR (100 MHz): 194.03; 150.89; 145.71; 140.98; 133.42; 132.36; 131.41; 129.10; 127.42; 123.37; 119.43; 117.03; 112.95. Anal. calc. for $C_{13}H_9BrO_2$: C 56.34, H 3.27; found: C 56.62, H 3.56.

*(*E*)-1-(3-Bromophenyl)-3-(furan-2-yl)prop-2-en-1-one* (**51**). Yield: 79%. M.p. 60–63°. IR (KBr): 3122, 2981, 2896, 1698, 1683, 1558, 1540, 1508, 1488, 773, 418. ^{1}H-NMR (400 MHz): (*t*, *J* = 1.7, H–C(14)); 7.89 (*dt*, *J* = 1.5, H–C(10)); 7.67 (br. *dd*, *J* = 1.9, 1.1, H–C(12)); 7.59 (*d*, *J* = 15.3, H–C(7)); 7.53 (br. *d*, *J* = 0.6, H–C(2)); 7.36 (*t*, *J* = 7.7, H–C(11)); 7.35 (*d*, *J* = 15.7, H–C(6)); 6.73 (*d*, *J* = 3.1, H–C(4)); 6.50 (*dd*, *J* = 1.8, 3.4, H–C(3)). ^{13}C-NMR (100 MHz): 188.18; 151.44; 145.27; 139.89; 135.56; 131.41; 131.30; 130.19; 126.92; 122.97; 118.51; 116.93; 112.86. Anal. calc. for $C_{13}H_9BrO_2$: C 56.34, H 3.27; found: C 56.35, H 3.46.

Preparation of Microorganisms. Eleven bacterial and two fungal strains were used in this study (*Table 1*). Bacteria were grown by incubation for 24 h at 36° in *Mueller–Hinton* broth (*Merck*) and *C. albicans* and *C. utilis* by incubation for 24 h at 25° in *Sabouraud* dextrose broth (*Merck*).

Disc Diffusion Assay. Inhibition zones were determined by the disc diffusion method [19][20] using 100 µl of suspension containing 10^8 CFU/ml of bacteria and 10^6 CFU/ml of yeasts spread on nutrient agar (NA), *Sabouraud* dextrose agar (SDA), and potato dextrose agar (PDA) medium. The blank discs (6 mm diameter, *Oxoid*) were impregnated with 20 µl of each test compound dissolved in MeOH (105 µg/disc) and placed on the inoculated agar. MeOH was used as negative control and sulbactam (30 µg) + cefoperazone (75 µg) as positive reference standard to determine the sensitivity of the microorganisms tested. The inoculated plates were incubated at 36° for 24 h for clinical bacterial strains and for 48 h for yeast strains. Antimicrobial activity was evaluated by measuring the zone of inhibition against the test organisms. Each assay was done in triplicate.

Microdilution Assay. MIC Values of chalcone derivatives against bacterial and yeast strains were determined with a micro-well dilution method [21]. The inocula of microorganisms were prepared using 12 h broth cultures, and suspensions were adjusted to 0.5 McFarland standard turbidity. Test compounds and the positive control (tetracycline) dissolved in MeOH were first diluted to the highest concentration tested (1000 µg/ml), and then serial twofold dilutions were made (concentration range 7.8–1000 µg/ml) in sterile 10-ml test tubes containing nutrient broth. 96-Well plates were prepared by dispensing 95 µl of nutrient broth and 5 µl of the inoculums into each well. Then, 100 µl of compound solns. were added. Wells containing 195 µl of nutrient broth without compound and 5 µl of the inoculums were used as negative control. The final volume in each well was 200 µl. The 96-well plates were incubated at 36° for 24 h. The assay was performed in triplicate.

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