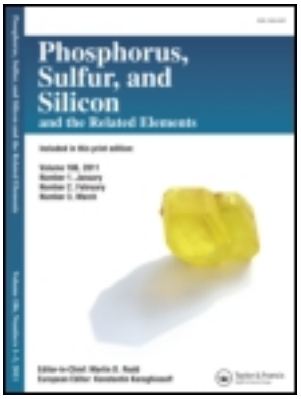

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Synthesis and Screening Antimicrobial Activities of Novel 1,3-Diaryl-3-(Phenylthio)Propan-1-One Derivatives

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SYNTHESIS AND SCREENING ANTIMICROBIAL ACTIVITIES OF NOVEL 1,3-DIARYL-3-(PHENYLTHIO)PROPAN-1-ONE DERIVATIVES

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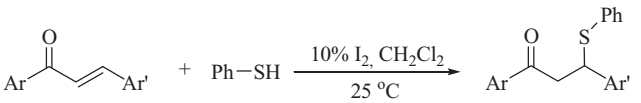
GRAPHICAL ABSTRACT



1a-j **2** **3a-j**

3a; Ar = *o*-OCH_3–Ph	Ar' = Ph	**3f;** Ar = *o*-NO_2–Ph	Ar' = Ph
3b; Ar = Ph	Ar' = *o*-CH_3–Ph	**3g;** Ar = 2-Furyl	Ar' = *p*-OCH_3–Ph
3c; Ar = Ph	Ar' = *m*-CH_3–Ph	**3h;** Ar = 2-Furyl	Ar' = *o*-Cl–Ph
3d; Ar = *p*-Cl–Ph	Ar' = Ph	**3i;** Ar = *p*-OCH_3–Ph	Ar' = 2-Thiophenyl
3e; Ar = Ph	Ar' = *p*-Cl–Ph	**3j;** Ar = *o*-OH–Ph	Ar' = 2-Thiophenyl

Abstract *In this study, a series of novel β-mercapto carbonyl derivatives (**3a–j**) was prepared by addition of thiophenol (**2**) to chalcones (**1a–j**) in the presence of catalytic amount of iodine (10 mol%) in CH_2Cl_2. Antibacterial and antifungal in vitro properties of the synthesized compounds were tested against some human pathogenic microorganisms by employing the disk diffusion technique. For the most active compounds, also minimum inhibitory concentrations (MICs) were determined.*

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords Chalcone; thiophenol; Michael addition; antibacterial and antifungal activity

INTRODUCTION

The preparation of sulfur-containing molecules has long been a mainstay of organic synthesis because of their broad application to organic and medicinal chemistry.[1] Sulfur-containing compounds are known to exhibit various biological activities, such as

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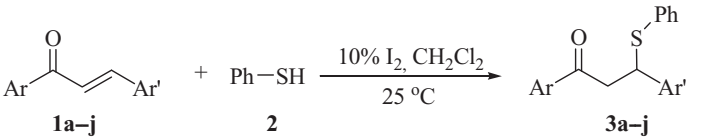
antibacterial,[2–4] antimicrobial,[5,6] antifungal,[7,8] anticancer,[9,10] antithrombotic, antioxidant, antidiabetic effects,[11] and as potential cytotoxic agent.[12] Thia-Michael addition reaction is one of the most fundamental C–S bond-forming reactions in the synthesis of β-mercapto carbonyl derivatives, which have valuable synthetic scaffolds for biological, medicinal, and synthetic organic chemists.[13–16] They are used for the synthesis of various biologically active compounds such as thiochromans,[17,18] thiapyrans,[19] benzothiazapines,[20–23] and 4,5-dihydropyrazoles.[24] On the other hand, chalcones, either natural or synthetic, are known to exhibit various biological activities[25] such as antioxidant,[26] antileishmanial activity,[27] antihyperglycemic activity,[28] antimicrobial activity[29] among others. In addition, chalcones are very important compounds as a Michael acceptor in organic syntheses. Conjugate addition of sulfur-centered nucleophiles to α,β-unsaturated carbonyls such as chalcones serves a powerful synthetic method in this area of sulfur chemistry.[30–32] Traditionally, the 1,4-addition of thiols is catalyzed by strong bases such as alkali metal alkoxides, hydroxides, and amines.[33,34] But in recent years, molecular iodine has been used as a useful catalyst for 1,4-addition of thiols and indoles to enones.[35–37]

This study reports the addition of thiophenol to chalcones in the mild conditions in the presence of catalytic amount of molecular iodine. This reaction occurs in short reaction time at room temperature and result in high yield.[14,38] In additional, the antimicrobial activities of the 1,3-diaryl-3-(phenylthio)propan-1-one derivatives (**3a–j**) were investigated against the 10 different human pathogen microorganisms.

RESULTS AND DISCUSSION

The addition of thiophenol with chalcone was explored in order to search for the optimal conditions, such as catalysts and solvent. The reaction did not take place when it was carried out separately in ethanol or methanol with solid I_2 and ethanol or methanol with NaOH. A longer reaction time would be necessary and lower yield was obtained with CH_2Cl_2 and solid I_2. The best results were obtained using CH_2Cl_2 and dissolved I_2 in CH_2Cl_2 for about 3 h.

Treatment of chalcone derivatives (**1a–j**) with thiophenol (**2**) and a solution of 10 mol% iodine in CH_2Cl_2 at room temperature for 3 h yielded 1,3-diaryl-3-(phenylthio)propan-1-one derivatives (**3a–j**) (Scheme 1), which were purified by silica gel column and crystallization. The final yield of the obtained derivatives was in the range of 74%–94% (Table 1). The compounds (**3a–j**) have been characterized by IR, ^{1}H and



1a–j **2** **3a–j**

3a; Ar = *o*-OCH_3–Ph	Ar' = Ph	**3f;** Ar = *o*-NO_2–Ph	Ar' = Ph
3b; Ar = Ph	Ar' = *o*-CH_3–Ph	**3g;** Ar = 2-Furyl	Ar' = *p*-OCH_3–Ph
3c; Ar = Ph	Ar' = *m*-CH_3–Ph	**3h;** Ar = 2-Furyl	Ar' = *o*-Cl–Ph
3d; Ar = *p*-Cl–Ph	Ar' = Ph	**3i;** Ar = *p*-OCH_3–Ph	Ar' = 2-Thiophenyl
3e; Ar = Ph	Ar' = *p*-Cl–Ph	**3j;** Ar = *o*-OH–Ph	Ar' = 2-Thiophenyl

Scheme 1

^{13}C NMR, and elemental analyze data. In the ^{1}H NMR spectrum of **3a–j**, the protons of PhCO$\underline{CH_2}$ led to an AB system that is characteristic to these compounds;[39] part A of the AB system was shown as a doublet of doublet at $\delta = 3.80$–3.52 ($J = 17.4$–16.4, 8.6–7.0 Hz) and that of part B as a doublet of doublet at $\delta = 3.66$–3.47 ($J = 17.4$–16.4, 7.6–5.8 Hz). Moreover, in the ^{1}H NMR spectrum of **3a–j** the protons of PhCOCH$_2\underline{CH}$ led to a doublet of doublet at $\delta = 5.42$–4.89 ($J = 8.4$–8.0, 6.6–5.6 Hz). All of the spectral data are consistent with the proposed compounds.

Comparison of activity of the compounds with the standard antibiotic SCF is presented in Table S1 (Supplemental Materials). Compounds **3f**, **3h**, and **3j** have significantly and/or remarkable activity against *Proteus vulgaris* KUEN 1329, *Candida utilis* KUEN 1031, *Bacillus cereus* DSM 4312, *Salmonella enteridis* ATCC 13076, and *Candida albicans* ATCC 1213. Compounds **3a**, **3d**, and **3i** showed moderate activity against *Escherichia coli* 111 while the other compounds showed very low activity or not activity. Only compounds **3j** showed significantly activity against *Bacillus cereus* DSM 4312. All compounds demonstrated low activity against *Pseudomonas aeruginosa* ATCC 9027, *Bacillus subtilis* ATCC 6633, and *Staphylococcus aureus* ATCC 29213.

As seen in Table S2 (Supplemental Materials), most of the compounds showed lower activity than positive controls against *Proteus vulgaris* KUEN 1329, *Candida utilis* KUEN 1031, *Pseudomonas aeruginosa* ATCC 9027, *Staphylococcus aureus* ATCC 29213, and *Streptococcus pyogenes* ATCC 176. Compound **3i** demonstrated low activity than CEF and AMP against *Escherichia coli* 111, better than (MIC: 250 μg/mL) AMP against *Bacillus subtilis* ATCC 6633. Compound **3j** showed the same activity (MIC: 7.8 μg/mL) with the Cs-T, better than CEF (MIC: 125 μg/mL) and AMP (MIC: 500 μg/mL) against *Salmonella enteridis* ATCC 13076.

Concerning SAR, compound **3i** (4-OCH$_3$ on Ar′ ring; Ar = 2-thiophenyl) and **3j** (2-OH on Ar′ ring; Ar = 2-thiophenyl) found to be the most active compounds according to the MIC values. In addition, when the effects of methoxy and nitro substituent on activity were discussed. Compound **3f** (2-NO$_2$ on Ar′ ring) showed better activity than **3a** (2-OCH$_3$ on Ar′ ring). Moreover, compound **3h** (Ar′ = 2-furan; 2-Cl on Ar ring) showed better activity than **3g** (Ar′ = 2-furan; 4-OCH$_3$ on Ar ring) according to the inhibition zones.

According to the results, compounds, containing hydroxyl group and furan ring, show remarkable antibacterial activity.

Table 1 Synthesized 1,3-diaryl-3-(phenylthio)propan-1-one derivatives

Products	Ar	Ar′	Yield (%)	mp (°C)
3a	*o*-OCH$_3$–Ph	Ph	88	86–88
3b	Ph	*o*-CH$_3$–Ph	**88**	85–87
3c	Ph	*m*-CH$_3$–Ph	82	54–56
3d	*p*-Cl–Ph	Ph	91	94–97
3e	Ph	*p*-Cl–Ph	94	88–90
3f	*o*-N0$_2$–Ph	Ph	74	57–59
3g	2-Furyl	*p*-OCH$_3$–Ph	84	94–96
3h	2-Furyl	*o*-Cl–Ph	82	77–79
3i	*p*-OCH$_3$–Ph	2-Thiophenyl	91	72–74
3j	*o*-OH–Ph	2-Thiophenyl	89	77–79

Summary, a series of β-mercapto carbonyl derivatives (**3a–j**) were prepared by iodine-catalyzed addition of thiophenol (**2**) to chalcones (**1a–j**) at room temperature for 3 h. The most active compounds are **3i,j**.

EXPERIMENTAL

Chemistry

Melting points were measured on Electrothermal 9100 apparatus. IR spectrums (KCl disc) were recorded on a Jasco FT/IR-430 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX-400 instrument. As internal standards served TMS (δ 0.00) for ^{1}H NMR and $CDCl_3$ (δ 77.0) for ^{13}C NMR spectroscopy J values are given in Hz. The multiplicities of the signals in the ^{1}H NMR spectra are abbreviated by s (singlet), d (doublet), t (triplet), q (quarted), m (multiplet), br (broad), and combinations thereof. Elemental analyses were obtained from a LECO CHNS 932 Elemental Analyzer. All column chromatographies were performed on silica gel (60–230 mesh, Merck). Anhydrous sodium sulfate was used as a drying agent for the organic phase.

Synthesis of chalcone derivatives (**1a–j**) were carried out through Claisen–Schmidt condensation[29] of substituted acetophenones and 2-furyl methyl ketone with the substituted benzaldehydes and thiophene-2-carbaldehyde using sodium hydroxide as catalyst in ethanol at room temperature. The chalcones were obtained in high yields (>80%).

General Procedure for the Synthesis of 3a–j

To a solution of thiophenol (1.2 mmol) and chalcone (1 mmol) in dichloromethane (15 mL), iodine (10 mol%) solution in dichloromethane (1 mL) was added and the mixture was stirred at room temperature for 3 h. Then, the iodine was removed with diluted $Na_2S_2O_3$ (0.06 M) and washed with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and the solvent removed under reduced pressure. The crude product was purified on a silica gel column eluting with $CHCl_3$/*n*-hexane (4:6) and/or crystallized in $CHCl_3$/*n*-hexane (1:4). According to our literature survey, synthesized compounds (except **3d**,[40] **3e**,[41] and **3g**[42]) are unknown in literature. Spectral data and selected NMR spectra for **3a,j** (Figures S1–S4) are presented in the Supplemental Materials.

Spectral Data

1-(2-methoxyphenyl)-3-phenyl-3-(phenylthio)propan-1-one (3a). Yield 88%; white crystal; mp 86 °C–88 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.55 (dd, J = 7.6, 1.2 Hz, 1H), 7.47–7.42 (m, 1H), 7.33–7.29 (m, 4H), 7.27–7.17 (m, 6H), 6.98–6.93 (m, 2H), 4.89 (dd, J = 7.6, 6.6 Hz, 1H), 3.86 (s, 3H), 3.72 (dd, J = 17.2, 8.2 Hz, 1H, A part of AB system), 3.63 (dd, J = 17.2, 6.4 Hz, 1H, B part of AB system). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 199.4, 158.4, 141.5, 134.5, 133.6, 132.9 (2C), 130.5, 128.7 (2C), 128.3 (2C), 128.0 (2C), 127.9, 127.4, 127.2, 120.7, 111.4, 55.5, 49.8, 48.7. IR (KCl, cm^{-1}): 3056, 3027, 2969, 2937, 2832, 2360, 2341, 1671, 1656, 1596, 1577, 1482, 1454, 1288, 1240, 1164, 1022, 987, 759. Anal. Calcd. for $C_{22}H_{20}O_2S$: C, 75.83; H, 5.79; S, 9.20. Found: C, 75.69; H, 5.62; S, 9.08.

1-phenyl-3-(phenylthio)-3-o-tolylpropan-1-one (3b). Yield 88%; white crystal; mp 85 °C–87 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.91 (d, J = 7.6 Hz, 2H), 7.57 (t,

$J = 7.4$ Hz, 1H), 7.45 (t, $J = 7.6$ Hz, 2H), 7.40–7.37 (m, 2H), 7.35–7.33 (m, 1H), 7.28 (t, $J = 3.0$ Hz, 3H), 7.15 (t, $J = 2.4$ Hz, 3H), 5.22 (dd, $J = 8.4$, 5.6 Hz, 1H), 3.80 (dd, $J =$ 17.4, 8.6 Hz, 1H, A part of AB system), 3.62 (dd, $J = 17.4$, 5.8 H z, 1H, B part of AB system), 2.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): $\delta =$ 197.4, 138.9, 136.7, 136.4, 134.2, 133.3 (3C), 130.6, 128.9 (2C), 128.6 (2C), 128.1 (2C), 127.8, 127.2, 126.5, 126.2, 44.3, 43.9, 19.5. IR (KCl, cm^{-1}): 3064, 3016, 2983, 2958, 2902, 2819, 2360, 2343, 1677, 1579, 1477, 1448, 1322, 1228, 1085, 981, 761, 740, 682. Anal. Calcd. for $C_{22}H_{20}OS$: C, 79.48; H, 6.06; S, 9.64. Found: C, 79.14; H, 6.05; S, 9.43.

1-phenyl-3-(phenylthio)-3-m-tolylpropan-1-one (3c). Yield 82%; yellow crystal; mp 54 °C–56 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): $\delta = 7.94$ (d, $J = 7.6$ Hz, 2H), 7.57 (t, $J = 7.0$ Hz, 1H), 7.47–7.41 (m, 4H), 7.30–7.21 (m, 6H), 7.07 (br, d, $J = 6.4$ Hz, 1H), 5.42 (dd, $J = 8.0$, 6.0 Hz, 1H), 3.74 (dd, $J = 17.2$, 8.0 Hz, 1H, A part of AB system), 3.64 (dd, $J = 17.2$, 6.0 Hz, 1H, B part of AB system), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): $\delta =$ 197.1, 141.1, 138.1, 136.8, 134.6, 133.3, 132.7 (2C), 129.0 (2C), 128.7 (2C), 128.6, 128.5, 128.3, 128.2 (2C), 127.5, 124.9, 48.2, 44.8, 21.5. IR (KCl, cm^{-1}): 3056, 2996, 2902, 2360, 2341, 1679, 1558, 1540, 1475, 1417, 1326, 1220, 1085, 979, 738, 684. Anal. Calcd. for $C_{22}H_{20}OS$: C, 79.48; H, 6.06; S, 9.64. Found: C, 79.34; H, 5.92; S, 9.51.

1-(2-nitrophenyl)-3-phenyl-3-(phenylthio)propan-1-one (3f). Yield 74%; brown crystal; mp 57 °C–59 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): $\delta = 8.07$ (d, $J = 8.0$ Hz, 1H), 7.62–7.52 (m, 2H), 7.33–7.24 (m, 10H), 7.04 (dd, $J = 6.8$, 1.2 Hz, 1H), 4.84 (t, $J =$ 7.2 Hz, 1H), 3.54–3.43 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): $\delta =$ 199.7, 145.4, 140.5, 137.7, 134.2, 133.8, 132.8 (2C), 130.6, 128.9 (2C), 128.6 (2C), 127.8 (2C), 127.7, 127.6, 127.5, 124.3, 48.8, 48.5. IR (KCl, cm^{-1}): 3100, 3068, 3025, 3004, 2856, 2360, 2341, 1695, 1565, 1521, 1438, 1342, 1230, 1025, 860, 763, 746, 700, 613. Anal. Calcd. for $C_{21}H_{17}NO_3S$: C, 69.40; H, 4.71; N, 3.85; S, 8.82. Found: C, 69.29; H, 4.61; N, 3.73; S, 8.71.

3-(2-chlorophenyl)-1-(furan-2-yl)-3-(phenylthio)propan-1-one (3 h). Yield 82%; yellow crystal; mp 77 °C–79 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): $\delta = 7.49$ (s, 1H), 7.42 (d, $J = 7.6$ Hz, 1H), 7.36–7.33 (m, 3H), 7.23–7.12 (m, 6H), 6.48 (br, s, 1H), 5.45 (t, $J = 7.4$ Hz, 1H), 3.52 (dd, $J = 16.4$, 7.0 Hz, 1H, A part of AB system), 3.47 (dd, $J = 16.4$, 7.6 Hz, 1H, B part of AB system). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): $\delta =$ 185.5, 152.5, 146.6, 138.3, 133.7, 133.6, 133.1 (2C), 129.8, 128.9 (2C), 128.7, 128.6, 127.9, 127.0, 117.5, 112.5, 44.5, 43.8. IR (KCl, cm^{-1}): 3120, 3085, 3060, 3021, 2931, 2360, 2341, 1671, 1565, 1465, 1328, 1245, 1079, 1035, 1016, 898, 765, 744, 682, 595. Anal. Calcd. for $C_{19}H_{15}ClO_2S$: C, 66.56; H, 4.41; S, 9.35. Found: C, 66.47; H, 4.29; S, 9.28.

1-(4-methoxyphenyl)-3-(phenylthio)-3-(thiophen-2-yl)propan-1-one (3i). Yield 91%; white crystal; mp 72 °C–74 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): $\delta = 7.92$ (d, $J =$ 8.6 Hz, 2H, AA′ part of AA′XX′ system), 7.41–7.38 (m, 2H), 7.31–7.26 (m, 3H), 7.15 (d, $J = 5.2$ Hz, 1H), 6.93 (d, $J = 8.6$ Hz, 2H, XX′ part of AA′XX′ system), 6.86 (s, 1H), 6.83 (t, $J = 4.2$ Hz, 1H), 5.29 (t, $J = 7.0$ Hz, 1H), 3.86 (s, 3H), 3.65 (dd, $J = 17.2$, 7.8 Hz, 1H, A part of AB system), 3.56 (dd, $J = 17.2$, 6.0 Hz, 1H, B part of AB system). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): $\delta =$ 195.0, 163.7, 145.6, 134.0, 133.0 (2C), 130.5 (2C), 129.7, 128.9 (2C), 127.8, 126.5, 125.5, 124.6, 113.8 (2C), 55.5, 45.3, 43.8. IR (KCl, cm^{-1}): 3099, 3068, 2969, 2933, 2890, 2838, 2360, 2341, 1671, 1600, 1571, 1508, 1419, 1349, 1265, 1226, 1172, 1022, 981, 829, 748, 690. Anal. Calcd. for $C_{20}H_{18}O_2S_2$: C, 67.76; H, 5.12; S, 18.09. Found: C, 67.64; H, 5.01; S, 17.94.

1-(2-hydroxyphenyl)-3-(phenylthio)-3-(thiophen-2-yl)propan-1-one (3j). Yield 89%; yellow crystal; mp 77 °C–79 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): $\delta =$ 12.12

(s, 1H, –OH), 7.71 (d, $J = 8.0$ Hz, 1H), 7.49 (t, $J = 7.4$ Hz, 1H), 7.42–7.40 (m, 2H), 7.31–7.29 (m, 3H), 7.19 (d, $J = 4.4$ Hz, 1H), 6.99 (d, $J = 8.0$ Hz, 1H), 6.93–6.86 (m, 3H), 5.26 (t, $J = 6.8$ Hz, 1H), 3.73 (dd, $J = 17.2$, 8.0 Hz, 1H, A part of AB system), 3.66 (dd, $J = 17.2$, 6.2 Hz, 1H, B part of AB system). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): $\delta = 202.4$, 162.6, 145.0, 136.8, 133.6, 133.2 (2C), 129.8, 129.0 (2C), 128.1, 126.6, 125.6, 124.8, 119.3, 119.1, 118.7, 45.2, 43.6. IR (KCl, cm^{-1}): 3120, 3075, 3048, 2948, 2888, 2842, 2360, 2341, 1641, 1577, 1475, 1436, 1342, 1278, 1207, 1157, 1035, 983, 927, 846, 755, 730, 632. Anal. Calcd. for $C_{19}H_{16}O_2S_2$: C, 67.03; H, 4.74; S, 18.84. Found: C, 66.91; H, 4.63; S, 18.73.

Antimicrobial Activity

The antibacterial activities of 1,3-diaryl-3-(phenylthio)propan-1-one derivatives **3a–j** against 10 microorganisms, i.e., two yeasts (*Candida albicans* ATCC 1213 and *Candida utilis* KUEN 1031), four Gram-positive bacteria (*Bacillus cereus* DSM 4312, *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 29213, and *Streptococcus pyogenes* ATCC 176), and four Gram-negative bacteria (*Proteus vulgaris* KUEN 1329, *Escherichia coli* 111, *Pseudomonas aeruginosa* ATCC 9027, and *Salmonella enteridis* ATCC 13076), were determined with the disc diffusion method[43,44] using 100 mL 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 minimum inhibitory concentration (MIC) values for compounds (**3a, 3f, 3h, 3i, 3j**) defined as the lowest concentration of the compound preventing the visible growth were determined by using the micro dilution method.[45,46]

REFERENCES

1. Li, H.; Zu, L.; Wang, J.; Wang, W. *Tetrahedron Lett.* **2006,** 47, 3145-3148.
2. Rida, S. M.; Labouta, I. M.; Salama, H. M.; A-Ghany, Y. S.; El-Ghazzaui, E.; Kader, O. *Pharmazie* **1986,** 41, 475-478.
3. Bhat, A. R.; Singh, D. *J. Indian Pharm. Sci.* **1988,** 50, 169-171.
4. Pandeya, D.; Nair, K. B. *Pharmazie* **1993,** 48, 414-417.
5. Franchini, C.; Muraglia, M.; Corbo, F.; Florio, M. A.; Di Mola, A.; Rosato, A.; Matucci, R.; Nesi, M.; van Bambeke, F.; Vitali, C. *Arch. Pharm. Chem. Life Sci.* **2009,** 342, 605-613.
6. Ceylan, M.; Gürdere, M. B.; Karaman, İ.; Gezegen, H. *Med. Chem. Res.* 2011, 20, 109-115.
7. Cesur, N.; Cesur, Z.; Ergenç, N.; Uzun, M.; Kiraz, M.; Kasimoglu, Ö.; Kaya, D. *Arch. Pharm.* **1994,** 327, 271-272.
8. Çapan, G.; Ulusoy, N.; Ergenc, N.; Kiraz, M. *Mon. für Chem.* **1999,** 130, 1399-1407.
9. Bhatt, J. J.; Shah, B. R.; Shah, H. P.; Trivedi, P. B.; Undavia, N. K.; Desai, N. C. *Indian J. Chem.* **1994,** 33B, 189-192.
10. Tandon, K. V.; Chhor, R. B.; Singh, R. V.; Rai, S.; Yadav, D. B. *Bioorg. Med. Chem. Lett.* **2004,** 14, 1079-1083.
11. Sheela, C. G.; Augusti, K. T. *Indian J. Exp. Biol.* **1992,** 30, 523-526.
12. Mahmoodi, M.; Aliabadi, A.; Emami, S.; Safavi, M.; Rajabalian, S.; Mohagheghi, M. A.; Khoshzaban, A.; Kermani, A. S.; Lamei, N.; Shafiee, A.; Foroumadi, A. *Arch. Pharm. Chem. Life Sci.* **2010,** 343, 411-416.
13. Clark, J. H. *Chem. Rev.* **1980,** 80, 429-452.
14. Chu, C.-M.; Gao, S.; Sastry, M. N. V.; Yao, C.-F. *Tetrahedron Let.* **2005,** 46, 4971-4974.
15. Trost, B. M.; Keeley, D. E. *J. Org. Chem.* **1975,** 40, 2013-2013.

16. Kumar, A.; Salunkhe, R. V.; Rane, R.; Dike, S. Y. *J. Chem. Soc. Chem. Commun.* **1991,** 7, 485-486.
17. Katristzky, A. R.; Button, M. A. C. *J. Org. Chem*. **2001,** 66, 5595-5600.
18. Ram, V. J.; Agarwal, N.; Saxena, A. S.; Farhanullah, S.; Sharon, A.; Maulik, P. R. *J. Chem. Soc. Perkin Trans.* **2002,** I, 1426-1437.
19. van Vliet, L. A.; Rodenhuis, N.; Dijkstra, D.; Wikström, H.; Pugsley, T. A.; Serpa, K. A.; Meltzer, L. T.; Heffner, T. G.; Wise, L. D.; Lajiness, M. E.; Huff, R. M.; Svensson, K.; Sundell, S.; Lundmark, M. *J. Med. Chem.* **2000,** 43, 2871-2882.
20. Tao, G. H.; He, L.; Sun, N.; Kou, Y. *Chem. Commun*. **2005,** 28, 3562-3564.
21. Freemantle, M. *Chem. Eng. News* **1998,** 76, 32-37.
22. Khatik, G. L.; Kumar, R.; Chakraborti, A. K. *Synthesis* **2007,** 4, 541-546.
23. Sharma, G.; Kumar, R.; Chakraborti, A. K. *Tetrahedron Lett.* **2008,** 49, 4269-4271.
24. Zielinska-Blajet, M.; Kowalczyk, R.; Skarzewski, J. *Tetrahedron* **2005,** 61, 5235-5240.
25. Satyanarayana, M.; Tiwari, P.; Tripathi, B. K.; Sriwastava, A. K.; Pratap, R. *Bioorg. Med. Chem.* **2004,** 12, 883-889.
26. Mukherjee, S.; Kumar, N.; Parasad, A. K.; Raj, H. G.; Bracke, M. E.; Olsen, C. E.; Jain, S. C.; Parmar, V. S. *Bioorg. Med. Chem.* **2001,** 9, 337-345.
27. Nazarian, Z.; Emami, S.; Heydari, S.; Ardestani, S. K.; Nakhjiri, M.; Poorrajab, F.; Shafiee, A.; Foroumadi, A. *Eur. J. Med. Chem.* **2010,** 45, 1424-1429.
28. Damazio, R. G.; Zanatta, A. P.; Cazarolli, L. H.; Chiaradia, L. D.; Mascarello, A.; Nunes, R. J.; Yunes, R. A.; Silva, F. R. M. B. *Eur. J. Med. Chem.* **2010,** 45, 1332-1337.
29. Karaman, İ.; Gezegen, H.; Gürdere, M. B.; Dingil, A.; Ceylan, M. *Chem. Biodiv.* **2010,** 7, 400-408.
30. Garg, S. K.; Kumar, R.; Chakraborti, A. K. *Tetrahedron Lett.* **2005,** 46, 1721-1724.
31. Cheng, S.; Cromer, D. D. *Tetrahedron Lett*. **2002,** 43, 1179-1181.
32. Lee, P. H.; Ahn, H.; Lee, K.; Sung, S.; Kim, S. *Tetrahedron Lett.* **2001,** 42, 37-39.
33. Zhu, S.; Cohen, T. *Tetrahedron* **1997,** 53, 17607-17624.
34. Hiemstra, H.; Wiberg, H. *J. Am. Chem. Soc*. **1981,** 103, 417-430.
35. Wang, S.-Y.; Ji, S.-J.; Loh, T.-P. *Synlett* **2003,** 15, 2377-2379.
36. Yadav, J. S.; Reddy, B. V. S.; Sadasiv, K.; Satheesh, G. *Tetrahedron Lett.* **2002,** 43, 9695-9697.
37. Das, B.; Chowdhury, N.; Damodar, K. *Tetrahedron Lett.* **2007,** 48, 2867-2870.
38. Gao, S.; Tzeng, T.; Sastry, M. N. V.; Chu, C.-M.; Liu, J.-T.; Lin, C.; Yao, C.-F. *Tetrahedron Lett.* **2006,** 47, 1889-1893.
39. Ceylan, M.; Gezegen, H. *Turk. J. Chem.* **2008,** 32, 55-61.
40. Shelke, G.; Vikhe, B.; Shivaji, P. *Int. J. Chem. Sci.* **2006,** 4, 409-412.
41. Kumar, A.; Ahmad, I.; Rao, M. S. *J. Sulf. Chem.* **2009,** 30, 570-577.
42. Hakhoechi, H. N. *Kor. Agri. Chem. Biotechnol.* **1994,** 37, 287-294.
43. Karaman, İ.; Sahin, F.; Güllüce, M.; Ogütçü, H.; Sengül, M.; Adigüzel, A. *J. Ethnopharmacol.* **2003,** 85, 231-235.
44. Murray, P. R.; Baron, E. J.; Pfaller, M. A.; Tenover, F. C.; Yolke, R. H. *Manual of Clinical Microbiology*; ASM Press: Washington, DC, 1995, p. 6.
45. NCCLS, *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically. Approved Standard*, 6th ed., NCCLS document M7-A6; NCCLS: Wayne, PA, 2003.
46. NCCLS, *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts. Approved Standart*, NCCLS document M27-A; NCCLS: Wayne, PA, 2000.