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Green Synthesis and Antibacterial Evaluation of Some New 1-Aryl-3-(1-aryl-1*H*-[1,2,3]triazol-4-yl)-propenones[1]

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Abstract—A new series of 1-aryl-3-(1-aryl-1*H*-[1,2,3]triazol-4-yl)propenones (**6a–6j**) was synthesized by condensation of substituted acetophenones (**5a–5c**) with substituted 1-aryl-1*H*-[1,2,3]triazole-4-carbaldehydes (**4a–4d**) in the presence of potassium hydroxide under conditions of grinding and microwave irradiation. All the newly synthesized compounds were characterized by the IR, NMR, and mass spectroscopic analyses and their antibacterial activity against gram-positive and gram-negative bacterial strains was evaluated. Among the compounds synthesized, better activity was exhibited by **6a**, **6c**, **6f**, **6g,** and **6i.**

Keywords: triazole aldehyde, triazole chalcone, antibacterial activity

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INTRODUCTION

Chalcones are a part of selected group of chemical compounds with diverse pharmacological activities. The term chalconoid has been used for the whole family of compounds bearing the 1,3-diarylpropane skeleton, which can be functionalized in the propane chain by the olefinic, keto, and/or hydroxyl groups. Chalcones bearing the 1,3-diaryl-2-propen-1-one carbon framework are the most common and widespread compounds of the chalconoid group [1, 2].

Chalcones are potential compounds owing to their antimalarial [3–6] and anti-tuberculosis [7] activities. The antimictrobial properties of heterocyclic derivatives have been reported in a number of publications [8–11]. Chalcones and their derivatives are polyphenolic compounds of the flavonoids family. They are present in many plants as metabolic precursors of other flavonoids and isoflavonoids [13]. From the viewpoint of synthesis, there is a great interest for the development of structural analogues of chalcones. The Claisen–Schmidt condensation of acetophenone derivatives with benzaldehyde derivatives in the presence of both acid and base catalysts has been by far the leading reaction employed for these compounds.

On the other hand, Green chemistry for chemical synthesis addresses our future challenges in working with chemical processes and products by inventing novel reactions that can maximize the desired products and minimize by-products, by designing new synthetic schemes and apparatus that can simplify a chemical technology, and by searching for environmentally friendly solvents. In continuation of our previous study on the solvent-free organic synthesis [14], we report here a simple, efficient, and solvent-free synthesis of chalcones, including grinding and microwave irradiation. The title compounds, 1-aryl-3-(1-aryl-1*H*-[1,2,3]-triazol-4-yl)propenones (**6a–6j**), were synthesized by the reaction of substituted aceto-phenones **5a–5c** with 1-aryl-1*H*-[1,2,3]triazole-4-carbaldehydes (**4a–4d**) in the presence of potassium hydroxide under conditions of grinding and microwave irradiation.

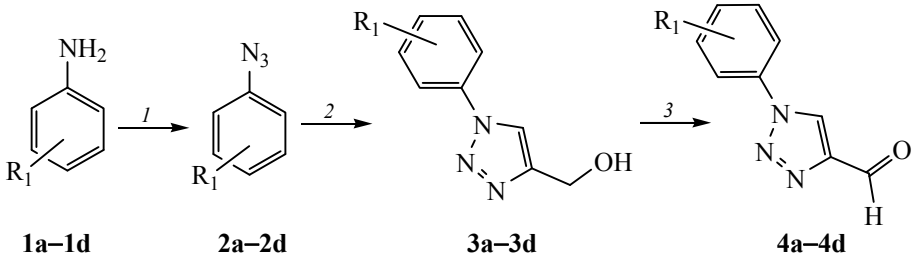
RESULTS AND DISCUSSION

The synthetic route adopted for the title compounds is illustrated in Schemes 1 and 2. First, aromatic azides (**2a–2d**) were synthesized by diazotization [15] of corresponding anilines **1a–1d** and then, (1-phenyl-1*H*-1,2,3-triazol-4-yl)methanol (**3a–3d**) was obtained through Huisgen 1,3-dipolar cycloaddition [16] between an azide and propargyl alcohol. The 4-carboxaldehyde-1,2,3-triazoles (**4a–4d**) were prepared by oxidation of the intermediates (**3a–3d**) in the presence of 2-iodoxy-benzoic acid (IBX) [17].

The new 1,2,3-triazolo chalcone derivatives (**6a–6j**) were synthesized by reacting 1-aryl-1*H*-[1,2,3]triazole-

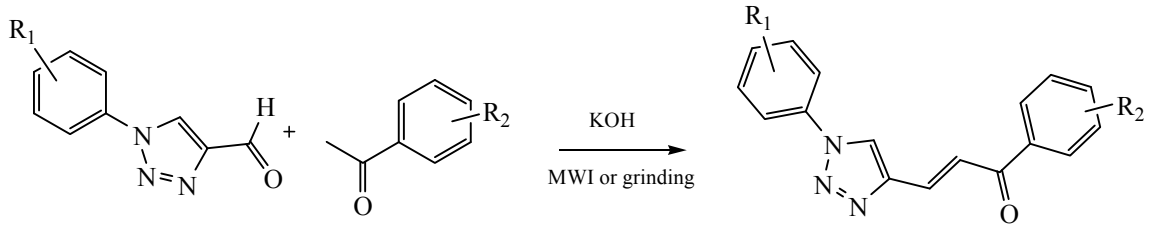
[1] The text was submitted by the authors in English.

Scheme 1. Synthesis of 1-aryl-1*H*-[1,2,3]triazole-4-carbaldehydes (**4a–4d**).



R_1 = H, 2-OMe, 2-Cl, 4-Cl. Reagents and conditions: (*1*) $NaNO_2$, HCl 10%; NaN_3, reaction time 2–4 h; (*2*) propargyl alcohol, $CuSO_4 \cdot 5H_2O$, sodium ascorbate, H_2O : DMF (1 : 2), reaction time 3 h; (*3*) IBX/DMSO, reaction time3 h.

Scheme 2. Synthesis of 1-aryl-3-(1-aryl-1*H*-[1,2,3]triazol-4-yl)-propenones (**6a–6j**).



6a: R_1 = H, R_2 = H, **6b**: R_1 = 20OMe, R_2 = H, **6c**: R_1 = 2-Cl, R_2 = H, **6d**: R_1 = 4-Cl, R_2 = H, **6e**: R_1 = H, R_2 = 4-Me, **6f**: R_1 = 2-OMe, R_2 = 4-Me, **6g**: R_1 = 2-Cl, R_2 = 4-Me, **6h**: R_1 = 4-Cl, R_2 = 4-Me, **6i**: R_1 = H, R_2 = 4-Br, **6j**: R_1 = 2-OMe, R_2 = 4-Br. Reaction time 3 h.

4-carbaldehyde (**4a–4d)** with the substituted acetophenones (**5a–5c)** in the presence of potassium hydroxide under conditions of grinding and microwave irradiation. The synthesis of title compounds under microwave irradiation gave excellent yields in short reaction time. The newly synthesized compounds were characterized by the NMR and mass spectrometric analyses. The ^{1}H NMR spectrum of compound **6j** contains a characteristic doublet of the C^{α}–H proton at δ = 7.08–7.11 (*J* = 14.8 Hz) and a singlet of the triazole proton at δ = 8.28. In the ^{13}C NMR spectrum, peak due to the carbonyl carbon is present at 190.1 ppm. The LCMS spectrum has $[M + 2]^+$ peak at *m/z* 385. Thus, on the basis of the above studies **6j** was identified as 1-(4-bromo-phenyl)-3-[1-(2-methoxy-phenyl)-1*H*-[1,2,3]triazol-4-yl]propenone.

Antibacterial activity. All the synthesized compounds were screened *in vitro* for their antibacterial activity against two gram +ve bacterial strains, *Staphylococcus aureus* (ATCC-9144) and *Bacillus cereus* (ATCC-11778), and two gram –ve bacterial strains, *Escherichia coli* (ATCC-8739) *and Proteus vulgaris* (ATCC-29213). The antibacterial activity was evaluated by cup-plate agar diffusion method at the concentrations 25, 50, and 100 μg/mL. The zone of inhibition (in mm) was compared with that of the standard drug Ampicillinum. The compounds **6a, 6c, 6f, 6g**, and **6i** are more potent than the standard drug.

EXPERIMENTAL

Melting points were determined in an open glass capillary tube on a Gallenkamp MFB-595 apparatus and are given uncorrected. IR spectra of samples (KBr tablets) were recorded on a Perkin-Elmer FT-IR-8400s spectrometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were measured on a Bruker Avance II 400 spectrometer with $CDCl_3$, DMSO as solvent and TMS as internal standard; chemical shifts are given in ppm. Mass spectra were measured on a SHIMADZU LCMS 2020 mass spectrometer. The progress of reactions was monitored by thin layer chromatography (Silica Gel 60 F254 Aluminum Sheet, Merck). Elemental analysis was done on a Perkin Elmer CHN-2400 analyzer. Microwave reactions were carried out in a Milestone multiSYNTH microwave system.

General procedure for synthesis of 1-aryl-3-(1-aryl-1*H*-[1,2,3]triazol-4-yl)propenones (6a–6j). *a. Microwave method.* A mixture of 1-aryl-1*H*-[1,2,3]-

triazole-4-carbaldehydes (**4a–4d**) (0.01 mol) and substituted acetophenones (**5a–5c)** (0.01 mol) in a powdered potassium hydroxide (0.02 mol) was subjected to microwave irradiation at 180 W for 1–2 min (see the table). The reaction progress was monitored by TLC. After the reaction was complete, the reaction mixture was poured into water and a dilute HCl was added to it to neutral pH. The solid precipitate was filtered, washed with water, dried, and recrystallized from ethanol to give 1-aryl-3-(1-aryl-1*H*-[1,2,3]triazol-4-yl)propenones (**6a–6j**).

b. Grinding method. A mixture of 1-aryl-1*H*-[1,2,3]-triazole-4-carbaldehydes (**4a–4d**) (0.01 mol) and substituted acetophenones (**5a–5c)** (0.01 mol) in a powdered potassium hydroxide (0.02 mol) was inserted into a mortar and ground for 5–9 min (see the table). Progress of the reaction was monitored by TLC. After completing the reaction, crushed ice was introduced and a dilute HCl was added to neutral pH. The solid precipitate was separated by filtration and recrystal-lized from ethanol to give 1-aryl-3-(1-aryl-1*H*-[1,2,3]-triazol-4-yl)propenones (**6a–6j**).

The yield for compounds **6a–6j** synthesized under different conditions

Product	Grinding method		Microwave method	
	time, min	yield, %	time, min	yield, %
6a	6	85	1.0	95
6b	5	80	1.0	92
6c	8	81	1.5	90
6d	6	80	1.0	95
6e	7	85	1.5	94
6f	9	82	2.0	92
6g	5	80	1.0	94
6h	8	83	2.0	95
6i	7	85	1.5	95
6j	6	84	1.0	92

1-Phenyl-3-(1-phenyl-1*H*-[1,2,3]triazol-4-yl)-propenone (6a). Yield 92%, mp 178–180°C. IR spectrum (KBr), ν, cm^{-1}: 1630 (C=O). ^{1}H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm: 8.25 s (1H, triazole H), 7.92–8.00 m (3H, Ar-H, H^{β}), 7.72–7.86 m (5H, Ar-H), 7.29–7.30 d (1H, *J* = 15.2 Hz, H^{α}), 7.14–7.19 m (3H, Ar-H). ^{13}C NMR spectrum (DMSO, 100 MHz), δ, ppm: 189.0, 160.9, 147.2, 140.2, 136.8, 132.1, 129.2, 127.6, 126.7, 125.7, 122.8, 121.9; *M* 276 $[M + H]^+$. Found, %: C 73.59; H 4.24; N 14.40. $C_{17}H_{13}N_3O$. Calculated, %: C 74.17; H 4.76; N 15.26.

3-[1-(2-Methoxyphenyl)-1*H*-[1,2,3]triazol-4-yl]-1-phenyl-propenone (6b). Yield 92%, mp 190–192°C. IR spectrum (KBr), ν, cm^{-1}: 1636 (C=O). ^{1}H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm: 8.51 s (1H, triazole H), 8.13–8.16 m (6H, Ar-H, H^{β}), 7.85–7.88 m (1H, Ar-H), 7.45–7.49 d (1H, *J* = 14.9 Hz, H^{α}), 7.15–7.18 m (3H, Ar-H), 3.95 s (3H, O-CH_3). ^{13}C NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 190.1, 161.2, 147.5, 140.4, 135.9, 132.1, 129.2 127.8, 126.7, 125.6, 122.8, 122.5, 121.9, 55.6; *M* 306 $[M + H]^+$. Found, %: C 69.93; H 4.69; N 12.89. $C_{18}H_{15}N_3O_2$. Calculated, %: C 70.81; H 4.95; N 13.76.

3-[1-(2-Chlorophenyl)-1*H*-[1,2,3]triazol-4-yl]-1-phenyl-propenone (6c). Yield 95%, mp 196–198°C. IR spectrum (KBr), ν, cm^{-1}: 1634 (C=O). ^{1}H NMR spectrum (DMSO, 400 MHz), δ, ppm: 8.20 s (1H, triazole H), 7.98–8.06 m (3H, Ar-H, H^{β}), 7.72–7.80 m (5H, Ar-H), 7.20–7.27 d (1H, *J* = 14.6 Hz, H^{α}), 7.12–7.16 m (2H, Ar-H). ^{13}C NMR spectrum ($CDCl_3$, DMSO, 100 MHz), δ, ppm: 190.0, 161.2, 147.1, 140.5, 135.9, 132.5, 129.3 127.8, 126.7, 125.7, 122.8, 122.6, 121.8; *M* 310 $[M + H]^+$. Found, %: C 65.57; H 3.78; N 13.28. $C_{17}H_{12}ClN_3O$. Calculated, %: C 65.92; H 3.90; N 13.57.

3-[1-(4-Chlorophenyl)-1*H*-[1,2,3]triazol-4-yl]-1-phenyl-propenone (6d). Yield 92%, mp 200–202°C. IR spectrum (KBr), ν, cm^{-1}: 1630 (C=O). ^{1}H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm: 8.17 s (1H, triazole H), 7.95–8.02 m (4H, Ar-H, H^{β}), 7.69–7.75 m (4H, Ar-H), 7.22–7.28 d (1H, *J* = 14.9 Hz, H^{α}), 7.10–7.18 m (2H, Ar-H). ^{13}C NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 190.2, 161.0, 147.5, 140.2, 135.8, 132.7, 129.3 127.8, 126.5, 125.9, 122.8, 122.6, 121.5; *M* 310 $[M + H]^+$. Found, %: C 65.50; H 3.72; N 13.26. $C_{17}H_{12}ClN_3O$. Calculated, %: C 65.92; H 3.90; N 13.57.

3-(1-Phenyl-1*H*-[1,2,3]triazol-4-yl)-1-*p*-tolyl-propenone (6e). Yield 92%, mp 168–170°C. IR spectrum (KBr), ν, cm^{-1}: 1634 (C=O). ^{1}H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm: 8.28 s (1H, triazole H), 7.98–8.05 m (3H, Ar-H, H^{β}), 7.81–7.85 m (3H, Ar-H), 7.40–7.48 m (2H, Ar-H), 7.28–7.33 d (1H, *J* = 15.2 Hz, H^{α}), 7.10–7.16 m (2H, Ar-H), 2.40 s (3H, Ar-CH_3). ^{13}C NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 190.1, 161.6, 147.0, 140.4, 137.0, 131.5, 129.1, 127.6, 126.7, 125.7, 122.9, 120.2, 22.5; *M* 290 $[M + H]^+$. Found, %:

C 74.50; H 5.02; N 14.26. $C_{18}H_{15}N_3O$. Calculated, %: C 74.72; H 5.23; N 14.52.

3-[1-(2-Methoxyphenyl)-1*H*-[1,2,3]triazol-4-yl]-1-*p*-tolyl-propenone (6f). Yield 90%, mp 160–162°C. IR spectrum (KBr), ν, cm^{-1}: 1635 (C=O). ^1H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm: 8.31 s (1H, triazole H), 7.97–8.02 m (3H, Ar-H, H^{β}), 7.81–7.85 m (2H, Ar-H), 7.43–7.48 m (1H, Ar-H), 7.30–7.32 d (2H, J = 15.6 Hz, H^{α}), 7.10–7.15 m (2H, Ar-H), 3.93 s (3H, O–CH_3), 2.44 s (3H, Ar-CH_3). ^{13}C NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 190.2, 161.5, 147.0, 140.5, 137.0, 131.1, 129.2, 127.7, 126.7, 125.7, 122.8, 121.9, 118.3, 116.8, 56.8, 22.7; M 320 $[M + H]^+$. Found, %: C 70.20; H 4.91; N 11.88. $C_{19}H_{17}N_3O_2$. Calculated, %: C 71.46; H 5.37; N 13.16.

3-[1-(2-Chlorophenyl)-1*H*-[1,2,3]triazol-4-yl]-1-*p*-tolyl-propenone (6g). Yield 93%, mp 195–197°C. IR spectrum (KBr), ν, cm^{-1}: 1635 (C=O). ^1H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm: 8.26 s (1H, triazole H), 7.96–8.02 m (3H, Ar-H, H^{β}), 7.80–7.85 m (4H, Ar-H), 7.26–7.31 d (1H, J = 15.6 Hz, H^{α}), 7.10–7.15 m (2H, Ar-H), 2.44 s (3H, Ar-CH_3). ^{13}C NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 190.0, 161.5, 147.2, 140.6, 137.6, 131.1, 129.2, 127.6, 126.8, 125.5, 122.9, 121.7, 116.8, 22.5; M 324 $[M + H]^+$. Found, %: C 66.77; H 4.18; N 12.62. $C_{18}H_{14}ClN_3O$. Calculated, %: C 66.77; H 4.36; N 12.98.

3-[1-(4-Chlorophenyl)-1*H*-[1,2,3]triazol-4-yl]-1-*p*-tolyl-propenone (6h). Yield 90%, mp 188–190°C. IR spectrum (KBr), ν, cm^{-1}: 1630 (C=O). ^1H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm: 8.21 s (1H, triazole H), 7.95–8.02 m (4H, Ar-H, H^{β}), 7.81–7.86 m (3H, Ar-H), 7.26–7.31 d (1H, J = 15.6 Hz, H^{α}), 7.10–7.14 m (2H, Ar-H), 2.42 s (3H, Ar-CH_3). ^{13}C NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 190.0, 161.6, 147.2, 140.5, 137.7, 131.2, 129.2, 127.5, 126.9, 125.5, 122.7, 121.7, 22.5; M 324 $[M + H]^+$. Found, %: C 66.70; H 4.19; N 12.59. $C_{18}H_{14}ClN_3O$. Calculated, %: C 66.77; H 4.36; N 12.98.

1-(4-Bromophenyl)-3-(1-phenyl-1*H*-[1,2,3]triazol-4-yl)propenone (6i). Yield 95%, mp 164–167°C. IR spectrum (KBr), ν, cm^{-1}: 1635 (C=O). ^1H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm: 8.26 s (1H, triazole H), 7.96–8.02 m (3H, Ar-H, H^{β}), 7.80–7.85 m (3H, Ar-H), 7.26–7.31 t (2H, Ar-H), 7.10–7.15 m (2H, Ar-H), 6.05 d (1H, J = 15.1 Hz, H^{α}). ^{13}C NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 190.0, 161.6, 147.1, 140.7, 137.7, 131.3, 129.1, 127.6, 126.8, 125.5, 122.9, 121.7, 116.8; M 355 $[M + 2]^+$. Found, %: C 57.49; H 3.27; N 11.70. $C_{17}H_{12}BrN_3O$. Calculated, %: C 57.65; H 3.41; N 11.86.

1-(4-Bromophenyl)-3-[1-(2-methoxy-phenyl)-1*H*-[1,2,3]triazol-4-yl]propenone (6j). Yield 90%, mp 178–180°C. IR spectrum (KBr), ν, cm^{-1}: 1632 (C=O). ^1H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm: 8.28 s (1H, triazole H), 7.85–7.89 m (3H, Ar-H, H^{β}), 7.65–7.71 m (2H, Ar-H), 7.40–7.46 m (2H, Ar-H), 7.08–7.11 d (1H, J = 14.8 Hz, H^{α}), 6.95–6.99 m (2H, Ar-H), 3.90 s (3H, O–CH_3). ^{13}C NMR spectrum ($CDCl_3$, 100 MHz), δ, ppm: 190.1, 160.4, 147.5, 140.2, 137.7, 131.5, 129.2, 127.6, 126.9, 125.7, 122.9, 121.7, 116.8, 56.1; M 385 $[M + 2]^+$. Found, %: C 56.10; H 3.54; N 10.81. $C_{18}H_{14}BrN_3O_2$. Calculated, %: C 56.27; H 3.67; N 10.94.

CONCLUSIONS

In conclusion, a convenient, high-efficiency, and environmentally friendly synthetic procedure, including microwave irradiation, was developed for the synthesis of various triazole chalcones (**6a–6j**) and the antibacterial activity of the synthesized compounds was evaluated. It was found that test compounds **6a, 6c, 6f, 6g**, and **6i** have better antibacterial activity against gram-positive and gram-negative bacteria than Ampicillinum. The above results suggest that triazole chalcones, as antibacterial agents, have good potential for further development. The results of this study may be a helpful guide for medicinal chemists engaged in this area.

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