Rapid and Efficient Microwave-Assisted Synthesis of Some New Triazol-3-one Derivatives

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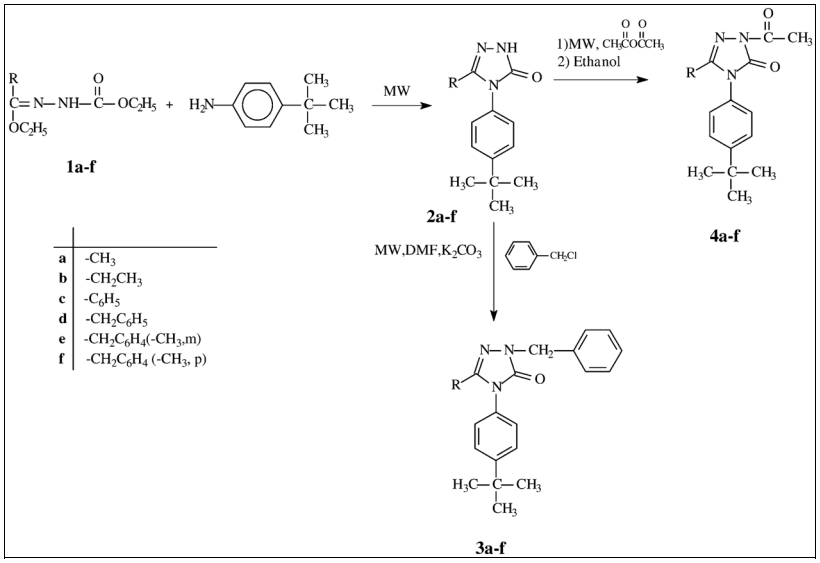


A growing body of literature has shown the effectiveness of using microwaves in chemical reactions. The aim of this study is to demonstrate a rapid and highly efficient synthesis of some new triazol-3-ones via microwave heating using a monomode microwave. Compared with the thermal process, the microwave heating induces a dramatic reduction of the reaction time and improvement of the yields. In this study, rapid *N*-benzylation and *N*-acetylation of triazol-3-ones were achieved by microwave irradiation method for the first time. The newly synthesized compounds showed moderate antimicrobial activity against the standard bacterial and fungal organisms tested.

INTRODUCTION

Microwave-assisted synthesis has become an established tool in organic synthesis [1]. This synthesis technique is much quicker and provides higher yields under microwave irradiation than those of conventional heating. In many cases, reactions that usually require many hours at the reflux temperature under classical condition can be completed within a few minutes in microwave irradiation, even at similar reaction temperatures [2–4]. There is no example of microwave-assisted synthesis of *N*-benzyl and *N*-acetyl derivatives of triazol-3-ones, which has reduced the reaction time dramatically and yielded satisfactory results.

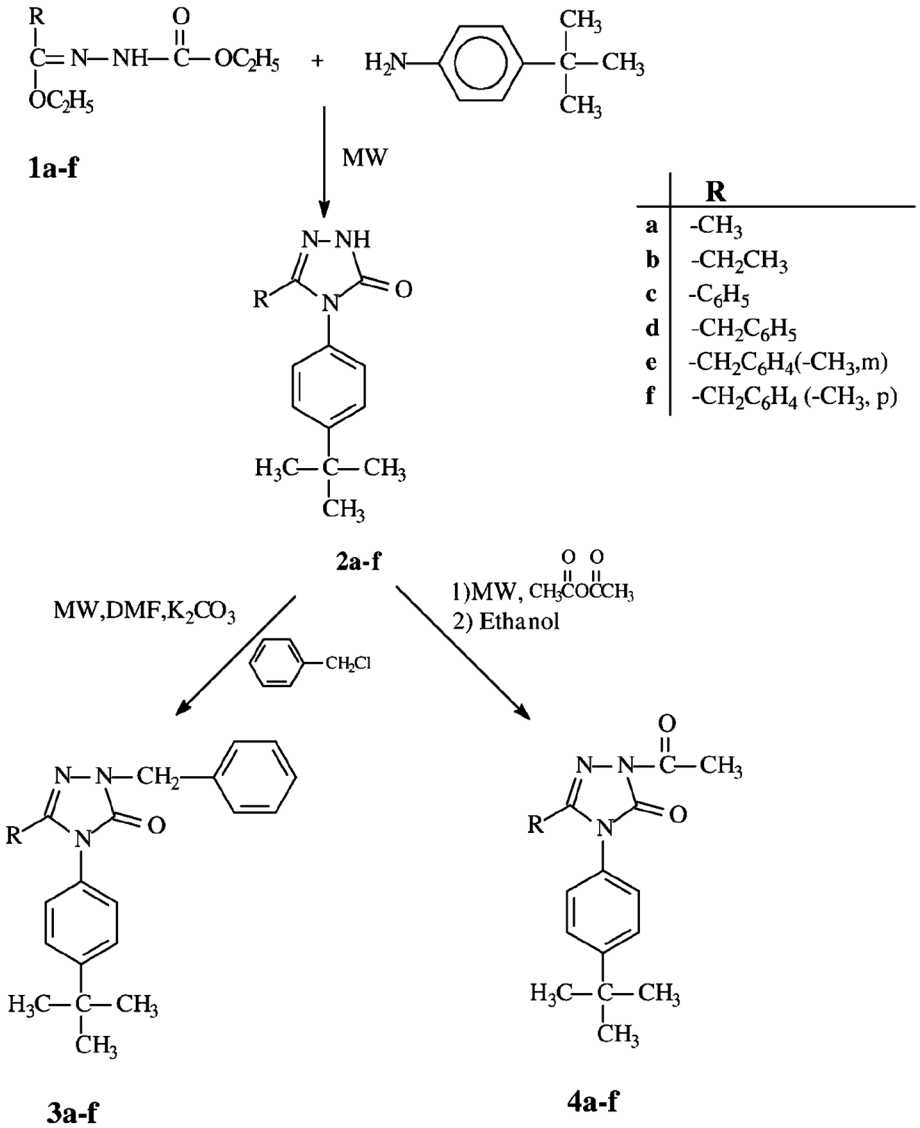
During the last few decades, considerable attention has been devoted to the synthesis of triazol-3-ones derivatives possessing diverse pharmacological properties such as antimicrobial [5], anti-inflammatory [6], analgesic, antitumor, anticonvulsant, and antiviral activities [7–9]. A previous study from our laboratory [10–12] demonstrated a synthesis of a number of triazoles by environmentally friendly microwave methods. Thus, we want to report here a successful microwave-assisted synthesis of *N*-benzyl and *N*-acetyl of some triazol-3-one derivatives with reference to its environmentally friendly, less time-consuming nature and good yields.

In conclusion, an efficient alternate method for synthesis of triazole-3-one derivatives has been proposed. Structure of new compounds was identified by spectroscopic methods using IR, ^{1}H-NMR, ^{13}C-NMR, and elemental analysis.

RESULTS AND DISCUSSION

Chemistry. Ether carbetoxy hydrazones (**1a-f**) can be considered as useful intermediates leading to the formation of some heterocycles such as 5-alkyl(aryl)-1,2,4-triazole-3-ones, which are used in the synthesis of 1,2,4-triazole derivatives that showed pharmacological activities [13,14]. Therefore, treatment of compound **1a-f** with p-*tert*-butylaniline

Scheme 1. The general reactions of triazol-3-one derivatives.



under microwave irradiation resulted in the formation of 2,4-Dihidro-4-[4-(*tert*-butyl)phenyl]- 5-alkyl(aryl)-3H-1,2,4-triazol-3-one. This reaction was carried out under microwave irradiation in ethanol at closed vessels with pressure control.

We now report a simple procedure for the benzylation of triazol-3-one (**3a-f**) under microwave irradiation in the presence of powered K_2CO_3 in DMF solution with pressure control.

In the third step, as a result of the reaction of compounds **2a-f** with acetic anhydride, **4a-f** were obtained under microwave heating using closed vessels with pressure control. When compared with the conventional (thermal) heating method, microwave heating offers more advantages such as reduced reaction time low cost, simplicity in processing, reduced pollution, and high yield. The general reactions representing triazol-3-one derivatives are illustrated in Scheme 1.

Antibacterial activity. The antimicrobial activity results presented in Table 1 revealed that, compounds **4a, 4d, 4e,** and **4f** exhibited antibacterial activity against *Staphylococcus aureus* (*S. aureus*) in 500 μg/mL and **2d, 2e,** and **2f** exhibited antituberculotic activity against *Mycobacterium smegmatis* (*M. smegmatis*) in 62–125 μg/mL concentration. All compounds exhibited high concentration influence to mold fungi.

EXPERIMENTAL

Melting points were determined on Büchi melting-point apparatus, in open capillaries; uncorrected. The IR spectra were recorded for KBr pellets on Perkin-Elmer 100 FTIR spectrophotometer. ^{1}H- and ^{13}C-NMR Spectra: *Varian-200* spectrometer; in DMSO-d_6; chemical shifts δ in ppm rel. to Me_4Si as internal standard and

Table 1

Antimicrobial activity of the compounds (μg).

Comp. No.	Stock solution (μg/mL)	Minimal inhibition concentration values (μg/mL)										
		Ec	En	Yp	Pa	Sa	Ef	Bc	Ms	Ca	Sc	An
2a	10,000	–	–	–	–	–	–	–	–	–	–	1000
2c	10,000	–	–	–	–	–	–	–	–	–	–	1000
2d	10,000	–	–	–	–	–	–	–	62.5	–	–	1000
2e	10,000	–	–	–	–	–	–	–	125	–	–	1000
2f	10,000	–	–	–	–	–	–	–	125	–	–	1000
3a	10,000	–	–	–	–	–	–	–	–	–	–	500
3c	10,000	–	–	–	–	–	–	–	–	–	–	1000
3d	10,000	–	–	–	–	–	–	–	–	–	–	500
3f	10,000	–	–	–	–	–	–	–	–	–	–	500
3e	10,000	–	–	–	–	–	–	–	–	–	–	1000
4a	10,000	–	–	–	–	500	–	–	–	–	–	1000
4c	10,000	–	–	–	–	–	–	–	–	–	–	1000
4d	10,000	–	–	–	–	500	–	–	–	–	–	1000
4f	10,000	–	–	–	–	500	–	–	–	–	–	1000
4e	10,000	–	–	–	–	500	–	–	–	–	–	1000
Amp.	1200	2	2	32	>128	2	2	<1				
Str.									4			
Flu.	2000									<8	<8	ND

Ec, *Escherichia coli* (ATCC 25922); En, Enterobacter *aerogenes* (ATCC 13048); Yp, Yersinia *pseudotuberculosis* (ATCC 911); Pa, Pseudomonas *aeruginosa* (ATCC 27853); Sa, Staphylococcus *aureus* (ATCC 25923); Ef, Enterococcus *faecalis* (ATCC 29212); Bc, Bacillus *cereus* (702 Roma); Ms, Mycobacterium *smegmatis* (ATCC607); Ca, Candida *albicans* (ATCC 60193); Sc, Saccharomyces *cerevisiae* (RSKK 251); An, Aspergillus *niger* (RSKK 4017); Amp, Ampicillin; Str, Streptomycin; Flu, Fluconazole; ND, Not determined; (—), no activity.

coupling constants *J* in Hz. Elemental analyses. *Carlo-Erba-1106-CHN* analyzer; the measured percentages were in agreement (±0.4%) with the calculated ones. The compounds **1a-f** were prepared by published methods [15,16]. A monomode CEM-Discover microwave apparatus was used in the standard configuration as delivered, including its software. All experiments were carried out in microwave process vials (35 mL) with control of the temperature by an IR sensor. The temperature was computer monitored and maintained constant by a discrete modulation of delivered microwave power. After completion of the reaction, the vial was cooled to 60° by air-jet cooling (see also the General procedure below).

General procedure for synthesis of (2a-f). A mixture of 1 (0.01 mol), p-*tert*-butylaniline (0.01 mol) and ethanol (1 mL) was heated under microwave irradiation in closed vessels with pressure control at 185°C for 4 min. (hold time) at 300 W maximum power. At the end of this period, TLC monitoring (AcOEt/hexane 3:1) was conducted to determine if the reaction was over. The reaction mixture was cooled to room temperature and was crystallized from ethanol-water (3:1).

2,4-Dihydro-4-[4-(*tert*-butyl)phenyl]-5-methyl-3H-1,2,4-triazol-3-one [17] (2a). Yield: 75%, m.p. 273–275°C (lit. [17] m.p. 274–275 °C).

2,4-Dihydro-4-[4-(*tert*-butyl)phenyl]-5-ethyl-3H-1,2,4-triazol-3-one (2b). Yield: 77%, m.p. 166–167°C; IR (KBr) (ν_{max}/cm^{-1}): 820 (1,4-disubstituted arom.), 1587 (C N), 1694 (C O), 3182 (N H); ^{1}H-NMR (CDCl$_3$-d_6) δ ppm: 1.10 (3H, t, CH_3, J = 7.2), 1.36 (9H, s, CH_3), 2.42 (2H, q, CH_2, J = 7.2), 7.20 (quasi d, AA′ part of AA′XX′ system, J = 8.6 Hz, 2H, Ar-H), 7.55 (quasi d, AA′ part of AA′XX′ system, J = 8.6 Hz, 2H, Ar-H), 10.20 (1H, s, NH); ^{13}C NMR (50 MHz, DMSO-d_6): 12.40, 30.90, 31.02, 34.06, 126.14, 126.93, 130.34, 143.17, 146.95 (C N), 152.97 (C O). Anal. Calcd. for $C_{14}H_{19}N_3O$: C, 68.54; H, 7.81; N, 17.13. Found: C, 68.50; H, 7.84; N, 17.14.

2,4-Dihydro-4-[4-(*tert*-butyl)phenyl]-5-phenyl-3H-1,2,4-triazol-3-one (2c). Yield: 83%, m.p. 274–275°C; IR (KBr) (ν_{max}/cm^{-1}): 810 (1,4-disubstituted arom.), 1605 (C N), 1701 (C O), 3165 (N H); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.35 (9H, s, CH_3), 7.10–7.45 (9H, m, Ar), 12.05 (1H, s, NH); ^{13}C NMR (50 MHz, DMSO-d_6): 30.96, 34.35, 125.87, 126.91, 127.01, 127.36, 128.29, 129.56, 130.97, 145.11, 150.17 (C N), 154.46 (C O). Anal. Calcd. for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.32. Found: C, 73.65; H, 6.50; N, 14.31.

2,4-Dihydro-4-[4-(*tert*-butyl)phenyl]-5-benzyl-3H-1,2,4-triazol-3-one (2d). Yield: 80%, m.p. 193–195°C; IR (KBr) (ν_{max}/cm^{-1}): 820 (1,4-disubstituted arom.), 1584 (C N), 1703 (C O), 3197 (N H); ^{1}H-NMR (CDCl$_3$-d_6) δ ppm: 1.36 (9H, s, CH_3), 3.78 (2H, s, CH_2), 6.82–7.58 (9H, m, Ar), 10.60 (1H, s, NH); ^{13}C NMR (50 MHz, DMSO-d_6): 30.96, 31.10, 34.33, 125.78, 126.45, 126.87, 128.02, 128.44, 130.08, 134.94, 145.97, 150.89 (C N), 154.32 (C O). Anal. Calcd. for $C_{18}H_{19}N_3O$: C, 74.24; H, 6.89; N, 13.67. Found: C, 74.25; H, 6.82; N, 13.66.

2,4-Dihydro-4-[4-(*tert*-butyl)phenyl]-5-[3-(methyl)benzyl]-3H-1,2,4-triazol-3-one (2e). Yield: 82%, m.p. 159–160°C; IR (KBr) (ν_{max}/cm^{-1}): 822 (1,4-disubstituted arom.), 1605 (C N), 1702 (C O), 3196 (N H); ^{1}H-NMR (CDCl$_3$-d_6) δ ppm: 1.38 (9H, s, CH_3), 2.23 (3H, s, CH_3), 3.76 (2H, s, CH_2), 6.70–7.45 (7H, m, Ar), 10.98 (1H, s, NH); ^{13}C NMR (50 MHz, DMSO-d_6): 21.54, 21.56, 31.68, 32.51, 126.83, 126.52, 128.09, 128.20, 128.88, 129.82, 130.23, 134.30, 138.00, 149.30 (C N), 152.66 (C O). Anal. Calcd. for $C_{20}H_{23}N_3O$: C, 74.74; H, 7.21; N, 13.07. Found: C, 74.75; H, 7.21; N, 13.03.

2,4-Dihydro-4-[4-(*tert*-butyl)phenyl]-5-[4-(methyl)benzyl]-3H-1,2,4-triazol-3-one (2f). Yield: 85%, m.p. 186–188°C; IR (KBr) (ν_{max}/cm^{-1}): 805 (1,4-disubstituted arom.), 1582 (C N), 1703 (C O), 3169 (N H); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.28 (9H, s, CH_3), 2.20 (3H, s, CH_3), 3.71 (2H, s, CH_2), 6.79 (quasi d, AA′ part of AA′XX′ system, J = 7.8 Hz, 2H, Ar-H), 6.99 (quasi d, AA′ part of AA′XX′ system, J = 7.8 Hz, 2H, Ar-H), 7.10 (quasi d, AA′ part of AA′XX′ system, J = 8.6 Hz, 2H, Ar-H), 7.45 (quasi d, AA′ part of AA′XX′ system, J = 8.6 Hz, 2H, Ar-H), 11.69 (1H, s, NH); ^{13}C NMR (50 MHz, DMSO-d_6): 21.28, 31.72, 32.18, 35.12, 126.64, 127.69, 129.16, 129.48, 130.91, 132.69, 136.29, 146.87, 151.74 (C N), 155.18 (C O). Anal. Calcd. for $C_{20}H_{23}N_3O$: C, 74.74; H, 7.21; N, 13.07. Found: C, 74.71; H, 7.23; N, 13.05.

General procedure for synthesis of (3a-f). The compounds **2a-f** (0.01 mol), benzyl chloride (0.013 mol), DMF (10mL), and K_2CO_3 (0.04mol) were added in a 35-mL closed vessel. The mixture was stirred and microwave was irradiated with pressure control at 170°C for 4 min (hold time) at 300 W maximum power. After the completion of the reaction (TLC monitoring AcOEt/hexane 3:1), the mixture was poured into the water and allowed to stand. The precipitate was filtered and recrystallized from ethyl acetate-petroleum ether (1:1).

2-Benzyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-methyl-3H-1,2,4-triazol-3-one (3a). Yield: 82%, m.p. 128–129°C; IR (KBr) (ν_{max}/cm^{-1}): 740, 659 (monosubstituted arom.), 1581 (C N), 1707 (C O); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.34 (9H, s, CH_3), 2.10 (3H, s, CH_3), 4.90 (2H, s, CH_2), 7.25–7.67 (9H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6): 13.10, 31.10, 34.17, 49.18, 126.70, 126.96, 127.50, 128.40, 130.61, 134.70, 146.20 (C N), 152.13 (C O). Anal. Calcd. for $C_{20}H_{23}N_3O$: C, 74.74; H, 7.21; N, 13.07. Found: C, 74.69; H, 7.22; N, 13.09.

2-Benzyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-ethyl-3H-1,2,4-triazol-3-one (3b). Yield: 87%, m.p. 122–123°C; IR (KBr) (ν_{max}/cm^{-1}): 706, 654 (monosubstituted arom.), 1660 (C N), 1707 (C O); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.10 (3H, t, CH_3, J = 7.2 Hz), 1.35 (9H, s, CH_3), 2.40 (2H, q, CH_2, J = 7.2 Hz), 4.92 (2H, s, CH_2), 6.59–7.65 (9H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6): 19.10, 23.87, 30.90, 31.70, 49.20, 126.23, 126.79, 127.48, 128.14, 128.44, 130.60, 134.67, 146.91 (C N), 152.98 (C O). $C_{21}H_{25}N_3O$: C, 75.19; H, 7.51; N, 12.53. Found: C, 75.21; H, 7.55; N, 12.50.

2-Benzyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-phenyl-3H-1,2,4-triazol-3-one (3c). Yield: 95%, m.p. 171–172°C; IR (KBr) (ν_{max}/cm^{-1}): 710, 669 (monosubstituted arom.), 1606 (C N), 1714 (C O); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.35 (9H, s, CH_3), 4.90 (2H, s, CH_2), 6.90–7.60 (14H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6): 31.60, 35.20, 50.01, 125.27, 126.70, 128.01, 128.24, 128.80, 129.30, 129.90, 135.17, 137. 40, 137. 96, 146.20 (C N), 152.13 (C O). $C_{25}H_{25}N_3O$: C, 78.30; H, 6.57; N, 10.96. Found: C, 78.32; H, 6.55; N, 10.94.

2-Benzyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-benzyl-3H-1,2,4-triazol-3-one (3d). Yield: 90%, m.p. 132–133°C; IR (KBr) (ν_{max}/cm^{-1}): 704, 690 (monosubstituted arom.), 1587 (C N), 1706 (C O); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.34 (9H, s, CH_3), 3.82 (2H, s, CH_2), 4.92 (2H, s, CH_2), 6.85–7.47 (14H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6): 30.88, 31.59, 34.34, 50.14, 125.91, 126.56, 126.89, 127.40, 128.14, 128.44, 130.01, 134.70, 136.91, 145.01 (C N), 152.73 (C O). $C_{26}H_{27}N_3O$: C, 78.56; H, 6.85; N, 10.57. Found: C, 78.50; H, 6.85; N, 10.58.

2-Benzyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-[3-(methyl) benzyl]-3H-1,2,4-triazol-3-one (3e). Yield: 95%, m.p. 105–107°C; IR (KBr) (ν_{max}/cm^{-1}): 705, 690 (monosubstituted arom.), 1600 (C N), 1701 (C O); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.34 (9H, s, CH_3), 2.19 (3H, s, CH_3), 3.79 (2H s, CH_2), 4.92 (2H, s, CH_2), 6.59–7.45 (13H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6):21.55, 31.71, 32.37, 35.18, 51.01, 125.17, 126.71, 126.90, 127.78, 128.01, 128.23, 128.89, 129.27, 128.01, 128.23, 128.89, 129.27, 129.98, 135.38, 137.78, 137.96, 146.70 (C N), 153.57 (C O). $C_{27}H_{29}N_3O$: C, 78.80; H, 7.10; N, 10.21. Found: C, 78.81; H, 7.14; N, 10.18.

2-Benzyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-[4-(methyl) benzyl]-3H-1,2,4-triazol-3-one (3f). Yield: 93%, m.p. 85°C; IR (KBr) (ν_{max}/cm^{-1}): 708, 665 (monosubstituted arom.), 1590 (C N), 1709 (C O); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.34 (9H, s, CH_3), 2.20 (3H, s, CH_3), 3.78 (2H, s, CH_2), 4.90 (2H, s, CH_2), 6.60–7.58 (13H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6): 21.70, 30.80, 31.10, 35.40, 51.10,125.91, 126.60, 127.80, 127.90, 128.40, 128.70, 130.01, 132.14, 132.40 148.53 (C N), 152.17 (C O). $C_{27}H_{29}N_3O$: C, 78.80; H, 7.10; N, 10.21. Found: C, 78.85; H, 7.10; N, 10.22.

General procedure for synthesis of (4a-f). The compound **2a-f** (0.01 mol) and acetic anhydride (2 mL) were added in a 35-mL closed vessel. The mixture was heated under microwave irradiation with pressure control at 160°C for 5min (hold time) at 150 W maximum power. After the addition of absolute ethanol (20 mL), the mixture was heated under microwave irradiation with pressure control at 80°C for 5 min (hold time). At the end of the reaction (TLC monitoring AcOEt/hexane 3:1), the resulting solution was evaporated at 40–45°C in vacua and crystallized from ethanol-water (1:2).

2-Acetyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-methyl-3H-1,2,4-triazol-3-one (4a). Yield: 92%, m.p. 138–139°C; IR (KBr) (ν_{max}/cm^{-1}): 830 (1,4-disubstituted arom.), 1610 (C N), 1727, 1780 (C O); ^{1}H-NMR ($CDCl_3$-d_6) δ ppm: 1.38 (9H, s, CH_3), 2.20 (3H, s, CH_3), 2.74 (3H, s, CH_3), 7.24 (quasi d, AA′ part of AA′XX′ system, J = 8.6 Hz, 2H, Ar-H), 7.54 (quasi d, AA′ part of AA′XX′ system, J = 8.6 Hz, 2H, Ar-H); ^{13}C NMR (50 MHz, DMSO-d_6): 12.20, 30.87, 34.44, 34.48, 126.23, 126.89, 129.22, 146.60, 150.65 (C N), 151.65, 166.09 (2 C O). $C_{15}H_{19}N_3O_2$: C, 65.91; H, 7.01; N, 15.37. Found: C, 65.92; H, 7.00; N, 15.39.

2-Acetyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-ethyl-3H-1,2,4-triazol-3-one (4b). Yield: 90%, m.p. 95–96°C; IR (KBr) (ν_{max}/cm^{-1}): 826 (1,4-disubstituted arom.), 1601 (C N), 1730, 1769 (C O); ^{1}H-NMR ($CDCl_3$-d_6) δ ppm: 1.17 (3H, t, CH_3, J = 7.4 Hz), 1.38 (9H, s, CH_3), 2.47(2H, q, CH_2, J = 7.4 Hz), 2.74 (3H, s, CH_3), 7.38 (quasi d, AA′ part of AA′XX′ system, J = 8.6 Hz, 2H, Ar-H), 7.57 (quasi d, AA′ part of AA′XX′ system, J = 8.6 Hz, 2H, Ar-H); ^{13}C NMR (50 MHz, DMSO-d_6): 19.19, 23.38, 30.86, 31.17, 34.44, 126.29, 126.80, 127.11, 129.14, 150.31 (C N), 151.80, 166.02 (2 C O). $C_{16}H_{21}N_3O_2$: C, 66.88; H, 7.37; N, 14.62. Found: C, 66.90; H, 7.35; N, 14.63.

2-Acetyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-phenyl-3H-1,2,4-triazol-3-one (4c). Yield: 93%, m.p. 165–166°C; IR (KBr) (ν_{max}/cm^{-1}): 822 (1,4-disubstituted arom.), 1650 (C N), 1736, 1780 (C O); ^{1}H-NMR ($CDCl_3$-d_6) δ ppm: 1.36 (9H, s, CH_3), 2.74 (3H, s, CH_3) 7.10–7.47 (9H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6): 24.31, 31.66, 35.22, 126.42, 126.74, 126.95, 127.88, 128.19, 128.26, 128.91, 129.20, 129.32, 130.78, 131.62, 147.82 (C N), 152.48, 167.17 (2 C O). $C_{20}H_{21}N_3O_2$: C, 71.62; H, 6.31; N, 12.53. Found: C, 71.60; H, 6.33; N, 12.55.

2-Acetyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-benzyl-3H-1,2,4-triazol-3-one (4d). Yield: 95%, m.p. 112–113°C;

IR (KBr) (v_{max}/cm^{-1}): 819 (1,4-disubstituted arom.), 1601 (C N), 1704, 1782 (C O); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.38 (9H, s, CH_3) 2.50 (3H, s, CH_3), 3.76 (2H, s, CH_2) 6.80–7.65 (9H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6): 25.70, 31.16, 32.18, 34.70, 125.60, 126.45, 126.89, 128.10, 128.44, 130.10, 134.98, 144.76, 150.80 (C N), 154.40, 160.70 (2 C O). $C_{21}H_{23}N_3O_2$: C, 72.18; H, 6.63; N, 12.03. Found: C, 72.15; H, 6.64; N, 12.09.

2-Acetyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-[3-(methyl) benzyl]-3H-1,2,4-triazol-3-one (4e). Yield: 95%, m.p. 110–111°C; IR (KBr) (v_{max}/cm^{-1}): 829 (1,4-disubstituted arom.), 1603 (C N), 1714, 1740 (C O); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.30 (9H, s, CH_3), 2.20 (3H, s, CH_3), 2.52 (3H, s, CH_3), 3.79 (2H, s, CH_2) 6.64–7.49 (8H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6):21.53, 24.28, 31.68, 32.51, 35.22, 126.52, 126.83, 128.08, 128.20, 130.23, 134.30, 138.00, 149.30 (C N), 152.66, 166.93 (2 C O). $C_{22}H_{25}N_3O_2$: C, 72.70; H, 6.93; N, 11.56. Found: C, 72.75; H, 6.94; N, 11.58.

2-Acetyl-2,4-dihydro-4-[4-(*tert*-butyl)phenyl]-5-[4-(methyl) benzyl]-3H-1,2,4-triazol-3-one (4f). Yield: 92%, m.p. 115–117° C; IR (KBr) (v_{max}/cm^{-1}): 801 (1,4-disubstituted arom.), 1600 (C N), 1708, 1749 (C O); ^{1}H-NMR (DMSO-d_6) δ ppm: 1.30 (9H, s, CH_3), 2.22 (3H, s, CH_3), 2.49 (3H, s, CH_3), 3.78 (2H, s, CH_2), 6.83–7.45 (8H, m, Ar); ^{13}C NMR (50 MHz, DMSO-d_6): 20.46, 23.42, 30.84, 31.26, 34.38, 35.62, 126.01, 127.17, 127.98, 128.55, 128.69, 128.99, 130.54, 136.40, 148.53 (C N), 152.89, 164.80 (2C O). $C_{22}H_{25}N_3O_2$: C, 72.70; H, 6.93; N, 11.56. Found: C, 72.67; H, 6.97; N, 11.55.

Antimicrobial activity assays. All test microorganisms were obtained from the Hifzissihha Institute of Refik Saydam (Ankara, Turkey) and were as follows: *Escherichia coli* ATCC 25922, *Enterobacter aerogenes* ATCC 13048, *Yersinia pseudotuberculosis* ATCC 911, *Pseudomonas aeruginosa* ATCC \27853, *Staphylococcus aureus* ATCC 25923, *Enterococcus faecalis* ATCC 29212, *Bacillus cereus* 702 Roma, *Mycobacterium smegmatis* ATCC607, *Candida albicans* ATCC 60193, *Saccharomyces cerevisiae* RSKK 251, *Aspergillus niger* RSKK 4017.

The antimicrobial effects of the substances were tested quantitatively by the micro dilution technique in Mueller Hinton broth. The minimal inhibition concentration (MIC) of the extracts was also determined using a twofold dilutions method [18]. The antibacterial and antifungal assays were performed in Mueller-Hinton broth (Difco, Detroit, MI) at pH 7.3 and buffered Yeast Nitrogen Base (Difco, Detroit, MI) at pH 7.0, respectively. The MIC was defined as the lowest concentration that showed no growth.

Brain Heart Infusion agar and broth medium (Difco, Detroit, MI) was used for *M. smegmatis*. The *M. smegmatis* was grown for 3 to 5 days on Brain Heart Infusion agar plates at 35°C. Antituberculois susceptibility test using the minimum inhibitory concentration method as NCCLS was used [19].

Mycelial growth inhibition tests were carried out by the agar diffusion method [20,21]. Five-millimeter mycelial agar disc were placed on potato dextrose agar (PDA) plates containing test compounds. PDA agar without the test compounds were used for control plates. The concentration in the medium was adjusted from 500 to 1000 μg/mL. The plates were incubated at 25°C for 3–5 days. The diameters of the mycelium colonies were then measured to examine the effects of the chemicals on fungal growth. The concentrate value that mycelium colonies were not grown was determined as MIC value. Ampicillin 1.2 mg/mL, Streptomycin 10 mg/mL, and fluconazole 2 mg/mL were used as standard antibacterial and antifungal drugs, respectively. DMSO was used as solvent control. The results are shown in Table 1.

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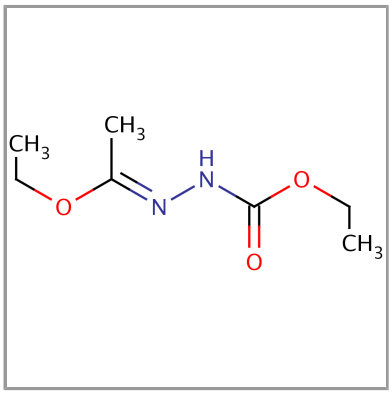

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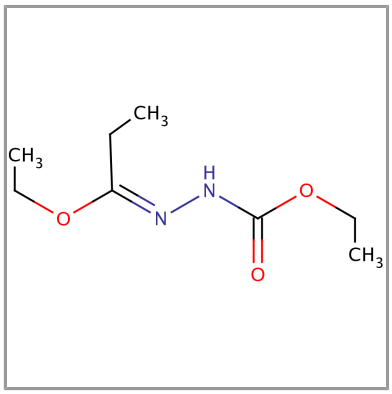

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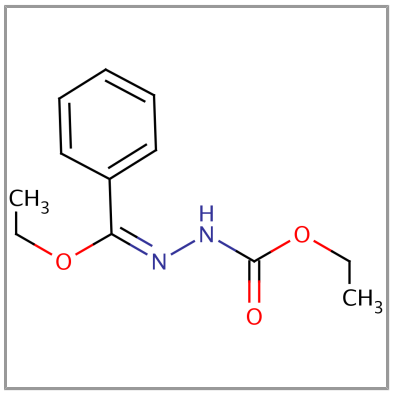

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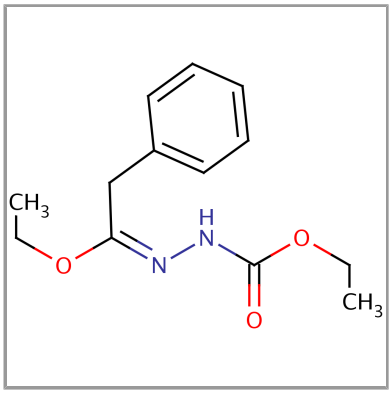

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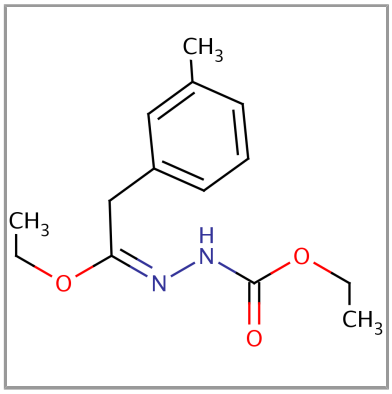

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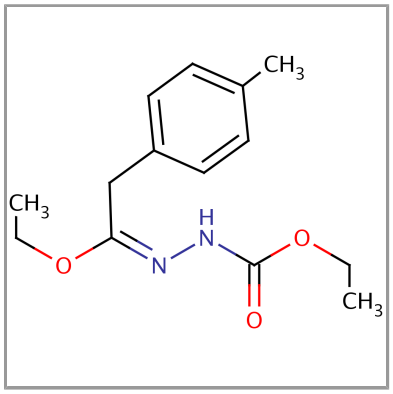

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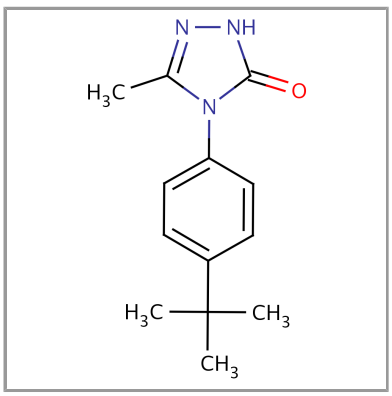

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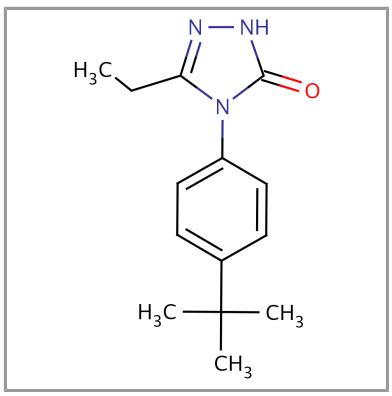

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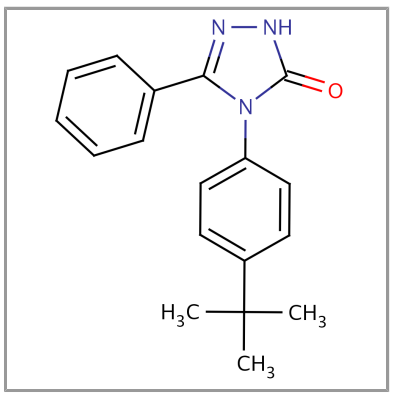

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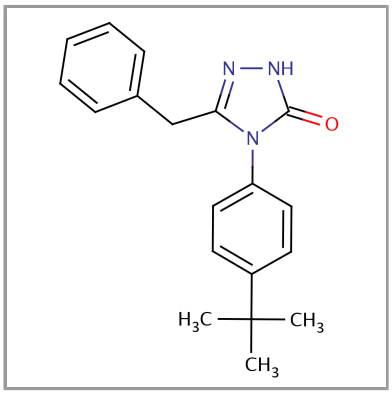

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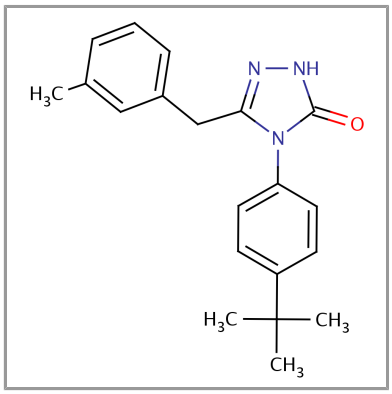

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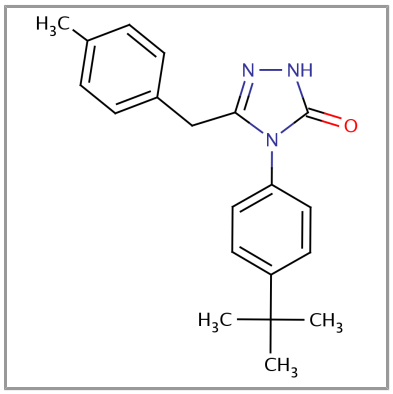

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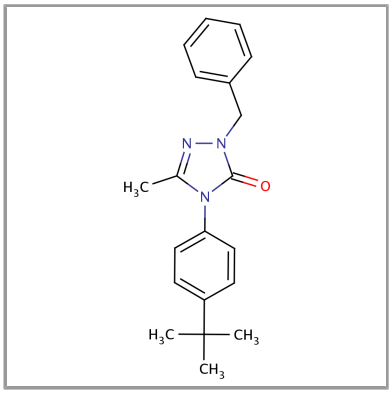

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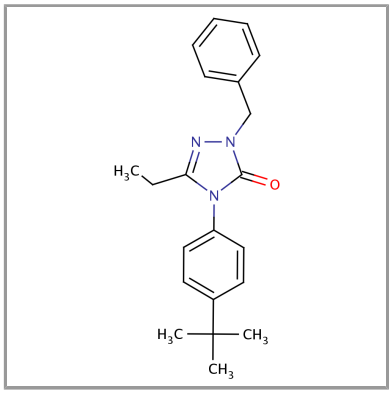

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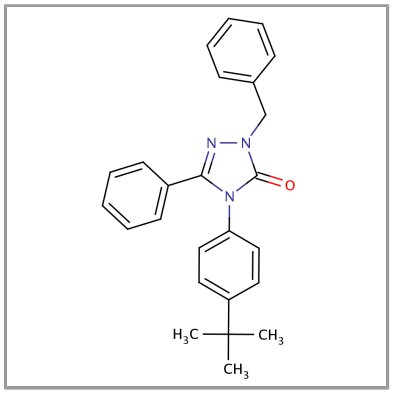

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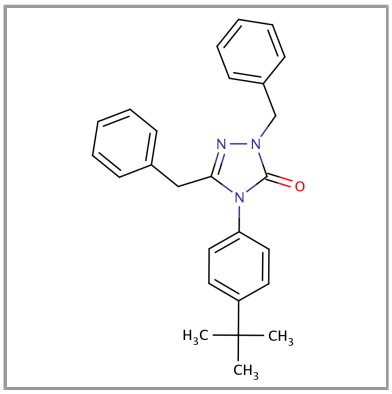

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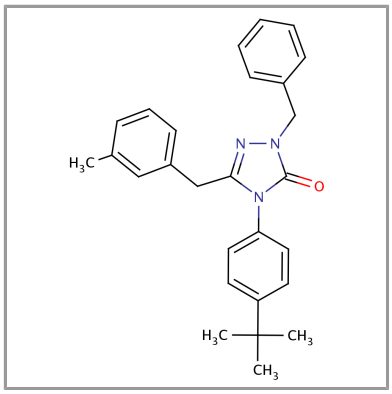

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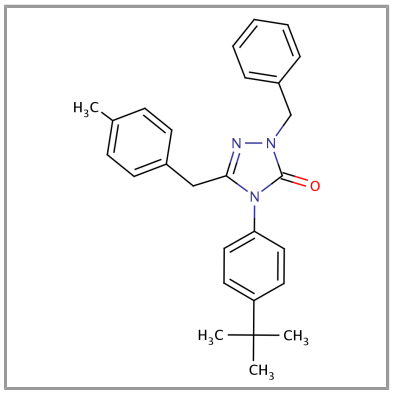

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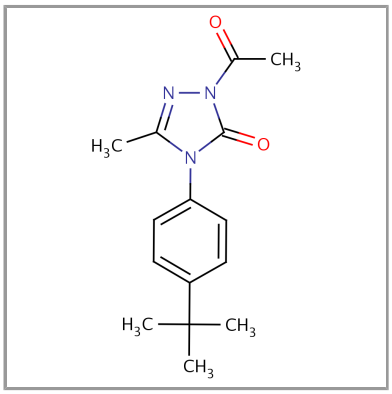

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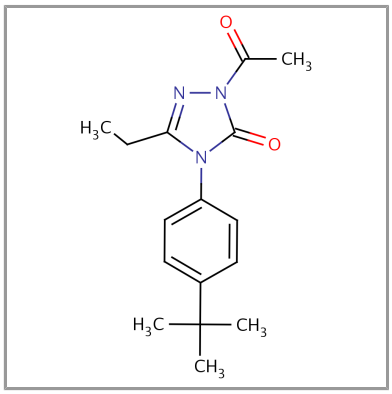

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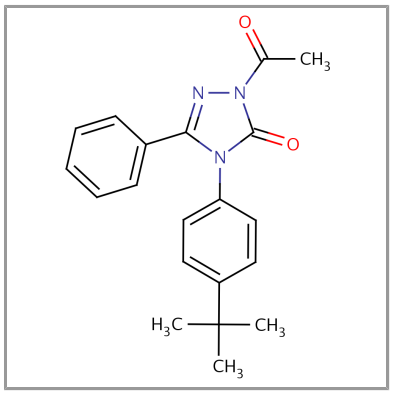

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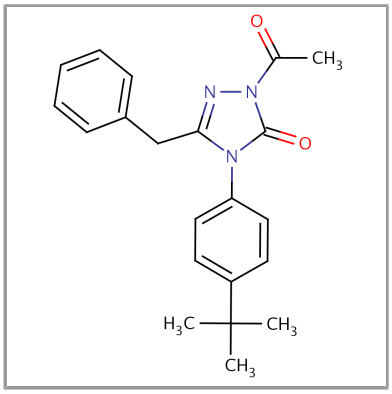

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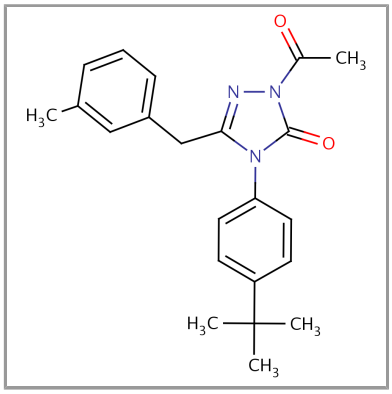

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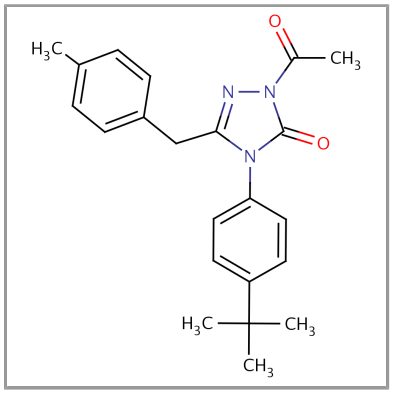

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