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Original article

Microwave assisted one-pot tandem three-component synthesis of 2,4,5-triary1-2-4-dihydro-3*H*-1,2,4-triazol-3-one derivatives

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ABSTRACT

This work described a one-pot tandem three-component synthesis of 2,4,5-triaryl-2,4-dihydro-3*H*-1,2,4-triazol-3-ones using a simple reaction between phenylhydrazines, benzaldehydes and phenyl isocyanates under microwave irradiation and solvent-free conditions in good to excellent yields.

1. Introduction

Multicomponent reaction (MCR) is a chemical reaction where three or more compounds react to form a single product. By definition, MCRs are those reactions whereby more than two reactants combine in a sequential manner to give highly selective products that retain the majority of the atoms of the starting material. In the past decade, multicomponent reactions involving the condensation of three or more reactants either in tandem or in single step have become an integral part of drug discovery [1–9]. The 1,2,4-triazol-3-one (1,2,4-triazolone) ring structure is found in a number of biologically active compounds. Some 1,2,4-triazolones have been shown to be angiotensin II antagonists [10], antimicrobial, antitumor agents [11–13] and anticonvulsants [14]. Several drugs possessing triazole nucleus have been approved for marketing, such as alprazolam (anxiolytic agent, tranquilizer), vorozole (antineoplastics, nonsteroidal competitive aromatase inhibitors), etoperidone (antidepressant), TAK-187 and Syn-2869 (antifungal agents) [15], nefazodone (antidepressant, 5-HT2 A-antagonist), rizatriptan (antimigraine agent), trapidil (hypotensive), trazodone (antidepressant, anxiolytic, selectively inhibits central serotonin uptake) and triazolam (sedative and hypnotic) (Fig. 1) [16].

There are many methods reported for the synthesis of the 1,2,4-triazolone ring [17–21]. The most common synthetic methods involve a cyclization-dehydration sequence of acyl semicarbazides in alkaline solutions [22], reaction between 1,2,4-triazolium salts with aqueous potassium carbonate [23], the condensation of mono Boc-protected hydrazines with acyl isocyanates and the subsequent deprotection and then an intramolecular cyclization of the intermediate [24], a reaction of amidrazones and isocyanate esters and the cyclization of the imidoylsemicarbazide of ethyl chloroformate and *N*-1-tosylamidrazones [25], the cyclization of 1-aryl-1 nitroso-3-(2-pyridylmethyl) ureas [26] and a reaction between thiocarbohydrazide and substituted benzoyl hydrazine [27].

High-speed synthesis promoted by microwaves irradiation has attracted a considerable amount of attention in recent years. Using a microwave oven in microwave-assisted organic synthesis (MAOS), not only reduces chemical reaction time from hours to minutes, but also reduces side reactions, increases the yields, and improves reproducibility. Therefore, many academic and industrial research groups are already using MAOS as a forefront technology for rapid optimization of reactions, for the efficient synthesis of new chemical entities, and for discovering and probing new chemical reactivity [28,29].

As a part of our efforts on the development of simple methods to prepare biologically active organic compounds [30], I used one such simple method for the synthesis of the scaffold (1,2,4-triazole-3-ones). I wish to report the synthesis of a trisubstituted 1,2,4-triazole-3-one derivatives **4** by a tandem three-component condensation of phenylhydrazines **1**, benzaldehydes **2** and phenyl isocyanates **3** (Scheme 1).

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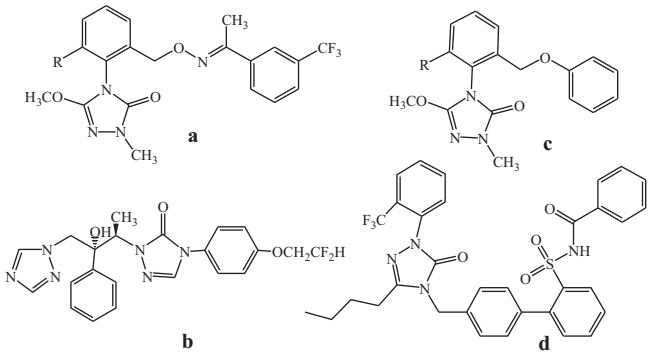


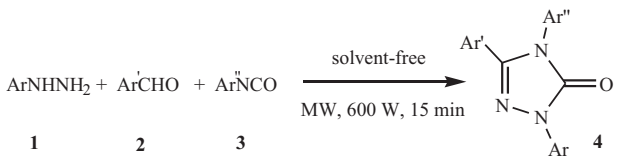
Fig. 1. Examples of biologically active 1,2,4-triazolones: (**a** and **c**) agricultural fungicides, (**b**) TAK-187 (antifungal), and (**d**) AT1-receptor antagonist.

2. Experimental

All starting materials and solvents were obtained from Merck (Germany) or Fluka (Switzerland) and were used without further purification. The methods used to monitor the reactions were TLC and NMR. Melting points were measured on an Electrothermal 9100 apparatus and were uncorrected. IR spectra were measured on a Jasco 6300 FTIR spectrometer. ^{1}H NMR and ^{13}C NMR spectra ($CDCl_3$) were recorded on a BRUKER DRX-300 AVANCE spectrometer at 300 MHz and 75.5 MHz, respectively. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 70 eV. Preparative layer chromatography (PLC) plates were prepared from Merck silica gel (F254) powder.

General procedure for the preparation of **4a–k**: This reaction was carried out using two protocols, namely microwave and conventional heating methods. Both methods were carried out by first mixing the arylhydrazine **1** and the arylaldehyde **2** at room temperature. After a few minutes and nearly a complete conversion to the corresponding arylhydrazone **5** was achieved, as indicated by TLC monitoring, the isocyanate **3** was added to the reaction mixture and in the first method, the mixture was irradiated under microwave irradiation and in the second method the reaction mixture was heated and stirred on a magnetic stirrer. The workup process of these methods is the same. ^{1}H NMR analysis of the reaction mixtures clearly indicated the formation of 1,2,4-triazol-3-ones **4**. The structures of the isolated products were assigned on the basis of IR, ^{1}H NMR and ^{13}C NMR spectroscopy, mass spectrometry and elemental analysis. The mass spectrum of **4a** displayed the molecular ion (M^+) peak at *m/z* 375, which was consistent with a 1:1:1 adduct of phenylhydrazine, 3-methyl benzaldeyde and 3-chloro-4-methylpenyl isocyanate, losing two hydrogen atoms.

A mixture of phenylhydrazine (0.216 g, 2 mmol) and 3-methylbenzaldehyde (0.240 g, 2 mmol) was stirred at 25 °C for 10 min. Then 3-chloro-4-methylphenylisocyanate (0.335 g, 2 mmol) was added to the reaction mixture and in the first method, the reaction mixture was irradiated (ETHOS 1600 Milestone) in a sealed 5 mL vial at 600 W for 15 min and in the second method, the reaction mixture was heated at 250 °C for 1 h. In both methods, the residue



Scheme 1. One pot synthesis of 2,4,5-triary1-2-4-dihydro -3*H*-1,2,4-triazol-3-ones.

was purified by column chromatography using petroleum ether–ethyl acetate (4:1) as the eluent. The solvent was removed, and the product was obtained as colorless crystals. The characterization data of the compounds are given below.

4-(3-Chloro-4-methylphenyl)-5(3-methylphenyl)-2-phenyl-2,4-dihydro-3*H*-1,2,-triazol-3-one (**4a**): Colorless crystals, the yield was 330 mg (88%), Rf = 0.46 (petroleum ether:ethyl acetate, 4:1), mp 168–169 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.34 and 2.41 (2s, 6H), 7.04 (dd, 1H, *J* = 2.1 and 8.1 Hz), 7.06 (d, 1H, *J* = 7.5 Hz), 7.19 (t, 1H, *J* = 7.6 Hz), 7.24 (d, 1H, *J* = 7.9 Hz), 7.25 (t, 1H, *J* = 7.4 Hz), 7.28 (d, 1H, *J* = 7.8 Hz), 7.37 (d, 1H, *J* = 2.1 Hz), 7.40 (s, 1H), 7.46 (dd, 2H, *J* = 8.4 and 7.4 Hz), 8.10 (d, 2H, *J* = 7.7 Hz); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 19.88 and 21.35 (2C), 118.90, 125.09, 125.52 and 125.59 (4C), 125.94 (1C), 127.76, 128.43, 12,861, 128.99, 131.28 and 131.44 (6C), 132.06, 134.97, 137.09, 137.71 and 138.67 (5C), 145.17 (1C), 151.64 (1C), IR (KBr, cm^{-1}): υ 1709 (C=O), 1637, 1608, 1595, 1556, 1499, 1458, 1418, 1371, 1325, 1184, 1055, 800, 758, MS (*m/z*): 375 (M^+), 327 (11), 208 (20), 149 (8), 91 (100), 69 (23), anal. calcd. for $C_{22}H_{18}ClN_3O$ (375.5): C, 70.30; H, 4.83; N, 11.18. Found: C, 70.15; H, 4.93; N, 11.04.

5-(4-Chlorophenyl)-2,4-diphenyl-2*H*-1,2,4-triazol-3(4*H*)-one (**4b**): Colorless crystals, the yield was 319 mg (92%), Rf = 0.65 (petroleum ether:ethyl acetate, 4:1), mp 176–177 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26–7.31 (m, 3H), 7.31 (d, 2H, *J* = 8.8 Hz), 7.36 (d, 2H, *J* = 8.8 Hz), 7.44–7.52 (m, 5H), 8.10 (d, 2H, *J* = 7.6), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 118.86 (1C),124.80 (1C), 125.66, 127.32,128.93, 129.03, 129.08, 129.22 and 129.70 (7C), 133.25, 136.53 and 137.70 (3C), 144.18 (1C), 151.71 (1C), IR (KBr, cm^{-1}): υ 1715 (C=O), 1639, 1619, 1599, 1497, 1427, 1369, 1321, 1150, 1095, 831, 760, MS (*m/z*): 347 (M+), 228 (13), 91 (100), 277 (22), anal. calcd. for $C_{20}H_{14}ClN_3O$ (347.5): C, 69.07; H, 4.06; N, 12.08. Found: C, 68.91; H, 4.12; N, 12.03.

4-(3-Chloro-4-methylphenyl)-2,5-di(4-methylphenyl)-2*H*-1,2,4-triazol-3(4*H*)-one (**4c**): Colorless crystals, the yield was 342 mg (88%), Rf = 0.54 (petroleum ether:ethyl acetate, 4:1), mp 175–177 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.36, 2.38 and 2.42 (3s, 3H), 7.05 (dd, 1H, *J* = 2.1 and 8.1 Hz), 7.15 (d, 2H, *J* = 8.1 Hz), 7.25 (d, 2H, *J* = 7.5 Hz), 7.28 (d, 1H, *J* = 8.3 Hz), 7.31 (d, 2H, *J* = 8.3 Hz), 7.37 (d, 1H, *J* = 2.1 Hz), 7.96 (d, 2H, *J* = 8.5 Hz), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 19.88, 20.97 and 21.41 (3C), 118.88 (1C), 123.28 (1C), 125.58, 127.84, 127.85, 129.36, 129.50 and 131.45 (6C), 132.21, 134.98, 135.22, 135.34, 137.03 and 140.67 (6C), 144.86 (1C), 151.61 (1C), IR (KBr, cm^{-1}): υ 1708 and 1695 (C=O), 1637, 1616, 1512, 1427, 1371, 1326, 1151, 1053, 818, 735, MS (*m/z*): 389 (M^+), 105 (89), 78 (13), anal. calcd. for $C_{23}H_{20}ClN_3O$ (389.5): C, 70.86; H, 5.17; N, 10.78. Found: C, 70.83; H, 5.24; N, 10.73.

4-(3-Chloro-4-methylphenyl)-5-(4-methoxyphenyl)-2-phenyl-2*H*-1,2,4-triazol-3(4*H*)-one (**4d**): Colorless crystals, the yield was 320 mg (82%), Rf = 0.50 (petroleum ether/ethyl acetate, 4:1), mp: 174–175 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.42 (s, 3H), 3.02 (s, 3H), 6.85 (d, 2H, *J* = 8.9 Hz), 7.05 (dd, 1H, *J* = 2.1 and 8.1 Hz), 7.24 (t, 1H, *J* = 7.4 Hz), 7.29 (d, 1H, *J* = 8.1 Hz), 7.36 (d, 2H, *J* = 8.8 Hz), 7.37 (d, 1H, *J* = 2.1 Hz), 7.45 (dd, 2H, *J* = 8.2 and 7.8 Hz), 8.09 (d, 2H, *J* = 8.3 Hz), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 19.90 (1C), 55.33 (1C), 114.14 (1C), 118.33 (1C), 118.79, 125.46, 125.64, 127.89, 128.97, 129.51 and 131.52 (7C), 132.18, 135.02, 137.13, 137.78 and 144.88 (5C), 151.65 (1C), 161.19 (1C), IR (KBr, cm^{-1}): υ 1711 (C=O), 1637, 1610, 1595, 1512, 1500, 1458, 1429, 1373, 1327, 1256, 1179, 1150, 1026, 835, 754, MS (*m/z*): 391 (M^+), 327 (31), 209 (11), 91 (100), 69 (38), anal. calcd. for $C_{22}H_{18}ClN_3O_2$ (391.5): C, 67.43; H, 4.63; N, 10.72. Found: C, 67.34; H, 4.72; N, 10.70.

4-(3-Chloro-4-methylphenyl)-2-phenyl-5-(4-methyl phenyl)-2*H*-1,2,4-triazol-3(4*H*)-one (**4e**): Colorless crystals, the yield was 319 mg (85%), Rf = 0.52 (petroleum ether: ethyl acetate, 4:1), mp 175–177 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.37 and 2.42 (2s, $2CH_3$), 7.05 (dd, CH, *J* = 2.1 and 8.1 Hz), 7.16 (d, 2H, *J* = 8.1 Hz), 7.25 (t, 1H,

J = 7.4 Hz), 7.27 (d, 1H, J = 8.2 Hz), 7.33 (d, 2H, J = 8.2 Hz), 7.38 (d, 1H, J = 2.1 Hz), 7.47 (dd, 2H, J = 8.5 and 7.5 Hz), 8.11 (d, 2H, J = 7.6 Hz), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 19.90 and 21.43 (2C), 118.86 (1C), 123.20 (1C), 125.53, 125.60, 127.85, 127.88, 128.98, 129.40 and 131.49 (7C), 132.14, 135.02, 137.12, 137.76 and 140.79 (5C), 145.09 (1C), 151.67 (1C), IR (KBr, cm^{-1}): υ 1711 (C=O), 1639, 1616, 1599, 1497, 1427, 1373, 1321, 1150, 1051, 824, 750, MS (m/z): 375 (M^+), 327 (17), 149 (32), 91 (71), 81 (46), 69 (100), 57 (55), anal. calcd. for $C_{22}H_{18}ClN_3O$ (375.5): C, 70.30; H, 4.83; N, 11.18. Found: C, 70.33; H, 4.82; N, 11.12.

5-(4-Chlorophenyl)-4-phenyl-2-(4-methylphenyl)-2*H*-1,2,4-triazol-3(4*H*)-one (**4f**): Colorless crystals, the yield was 317 mg (88%), Rf = 0.62 (petroleum ether: ethyl acetate, 4:1), mp 193–195 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H), 7.26 (d, 2H, J = 7.9 Hz), 7.28–7.33 (m, 4H), 7.36 (d, 2H, J = 8.7 Hz), 7.42–7.49 (m, 3H), 7.97 (d, 2H, J = 8.5 Hz), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 20.98 (1C), 118.90 (1C), 124.89 (1C), 127.32, 128.90, 129.01, 129.20, 129.55 and 129.66 (6C), 133.32, 135.29, 135.39 and 136.43 (4C), 143.94 (1C), 151.65 (1C), IR (KBr, cm^{-1}): υ 1709 and 1690 (C=O), 1639, 1610, 1515, 1427, 1377, 1153, 1100, 841, 820, MS (m/z): 361 (M^+), 327 (8), 105 (36), 91 (12), 84 (100), anal. calcd. for $C_{21}H_{16}ClN_3O$ (361.5): C, 69.71; H, 4.46; N, 11.61. Found: C, 69.50; H, 4.43; N, 11.55.

4-Phenyl-2,5-di(4-methylphenyl)-2*H*-1,2,4-triazol-3(4*H*)-one (**4g**): Colorless crystals, the yield was 306 mg (90%), Rf = 0.60 (petroleum ether:ethyl acetate, 4:1), mp 192–194 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.35 and 2.39 (2s, 6H), 7.13 (d, 2H, J = 8.0 Hz), 7.25–7.33 (m, 6H), 7.41–7.48 (m, 3H), 8.00 (d, 2H, J = 8.5 Hz), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 20.99 and 21.41 (2C), 118.88 (1C), 123.56 (1C), 127.38, 127.91, 128.72, 129.26, 129.47 and 129.50 (6C), 133.66, 135.11, 135.50 and 140.50 (4C), 145.10 (1C), 151.79 (1C), IR (KBr, cm^{-1}): υ 1707 and 1695 (C=O), 1637, 1615, 1512, 1427, 1375, 1313, 1151, 966, 816, 733, MS (m/z): 341 (M+), 105 (10), 84 (100), anal. calcd. for $C_{22}H_{19}N_3O$ (341): C, 77.04; H, 5.23; N, 12.84. Found: C, 76.74; H, 5.41; N, 12.66.

2,4-Diphenyl-5-(2-methylphenyl)-2*H*-1,2,4-triazol-3(4*H*)-one (**4h**): Colorless crystals, the yield was 267 mg (82%), Rf = 0.66 (petroleum ether:ethyl acetate, 4:1), mp: 177–179 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H), 7.11 (d, 1H, J = 7.3 Hz), 7.18 (t, 1H, J = 7.5 Hz), 7.22 (d, 1H, J = 8.0 Hz), 7.28 (d, 1H, J = 7.3 Hz), 7.30 (dd, 1H, J = 7.9 and 1.7 Hz), 7.37 (s, 1H), 7.44 (m, 4H), 7.48 (dd, 2H, J = 7.6 and 8.3 Hz), 8.16 (d, J = 8.8 Hz, 2H), ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 21.34 (1C), 118.89, 125.17 and 125.50 (3C), 126.24 (1C), 127.36, 128.36, 128.68, 128.80, 129.01, 129.48 and 131.11 (7C), 133.54, 137.89 and 138.50 (3C), 145.39 (1C), 151.83 (1C), IR (KBr, cm^{-1}): υ 1705 (C=O), 1593, 1555, 1495, 1456, 1416, 1373, 1319, 1148, 806, 756, 690, MS (m/z): 327 (M^+), 208 (23), 91 (98), 77 (18), anal. calcd. for $C_{21}H_{17}N_3O$ (327): C, 77.04; H, 5.23; N, 12.84. Found: C, 76.74; H, 5.41; N, 12.66.

2,4-Diphenyl-5-(4-methylphenyl)-2*H*-1,2,4-triazol-3(4*H*)-one (**4i**): Colorless crystals, the yield was 297 mg (91%), Rf = 0.68 (petroleum ether:ethyl acetate, 4:1), mp 165–166 °C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.33 (s, 3H), 7.11 (d, 2H, J = 8.0 Hz), 7.23 (t, 1H, J = 7.4 Hz), 7.27–7.30 (m, 4H), 7.40–7.47 (m, 5H), 8.12 (d, 2H, J = 8.1 Hz), ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 21.38 (1C), 118.84 (1C), 123.49 (1C), 125.41, 127.38, 127.91, 128.76, 128.95, 129.26 and 129.47 (7C), 133.60, 137.91 and 140.57 (3C), 145.31 (1C), 151.85 (1C), IR (KBr, cm^{-1}): υ 1718 (C=O), 1637, 1613, 1597, 1499, 1425, 1373, 1320, 1148, 966, 824, 755, MS (m/z): 327 (M^+), 312 (19), 211 (29), 119 (79), 105 (31), 91 (91), 77 (16), anal. calcd. for $C_{21}H_{17}N_3O$ (327): C, 77.04; H, 5.23; N, 12.84. Found: C, 77.05; H, 5.21; N, 12.76.

5-(4-Methoxyphenyl)-4-phenyl-2-(4-methylphenyl)-2*H*-1,2,4-triazol-3(4*H*)-one (**4j**): Colorless crystals, the yield was 298 mg (87%), Rf = 0.48 (petroleum ether:ethyl acetate, 4:1), m.p. 173–174 °C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.78 (s, 3H), 6.81 (d, 2H, J = 8.7 Hz), 7.22 (t, 1H, J = 7.4 Hz), 7.29 (d, 2H, J = 7.1 Hz), 7.33 (d, 2H, J = 8.7 Hz), 7.39–7.46 (m, 5H), 8.10 (d, 2H, J = 8.3 Hz), ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 55.28 (1C), 114.01 (1C), 118.66 (1C), 118.79, 125.34, 127.43, 128.77, 128.93, 129.49 and 129.53 (7C), 133.64 and 137.92 (2C), 145.10 (1C), 151.83 (1C), 161.08 (C–O), IR (KBr, cm^{-1}): υ 1707 (C=O), 1639, 1614, 1512, 1375, 1258, 1177, 1028, 966, 837, 760, MS (m/z): 343 (M^+), 224 (10), 209 (12), 149 (26), 91 (69), 81 (50), 69 (100), 57 (69), anal. calcd. for $C_{21}H_{17}N_3O_2$ (343): C, 73.45; H, 4.99; N, 12.24. Found: C, 73.51; H, 4.82; N, 12.28.

4-(3-Chloro-4-methylphenyl)-5-(4-chlorophenyl)-2-(4-methylphenyl)-2*H*-1,2,4-triazol-3(4*H*)-one (**4k**): Colorless crystals, the yield was 339 mg (83%), Rf = 0.56 (petroleum ether: ethyl acetate, 4:1), mp 194–195 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 and 2.43 (2s, 6H), 7.04 (dd, 1H, J = 2.0 and 8.1 Hz), 7.27 (d, 2H, J = 8.5 Hz), 7.28 (t, 1H, J = 7.2 Hz), 7.32–7.40 (m, 5H), 7.94 (d, 2H, J = 8.5 Hz), ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 19.91 and 20.99 (2C), 118.90 (1C), 124.63 (1C), 125.50, 127.79, 129.03, 129.15, 129.56 and 131.64 (6C), 131.87, 135.17, 135.21, 135.50, 136.61 and 137.42 (6C), 143.71 (1C), 151.47 (1C), IR (KBr, cm^{-1}): υ 1697 (C=O), 1636, 1605, 1504, 1427, 1377, 1151, 918, 825, 727, MS (m/z): 409 (M^+), 327 (13), 208 (3), 105 (23), 84 (100), anal. calcd. for $C_{22}H_{17}Cl_2N_3O$ (409): C, 64.40; H, 4.18; N, 10.24. Found: C, 64.32; H, 4.27; N, 10.18.

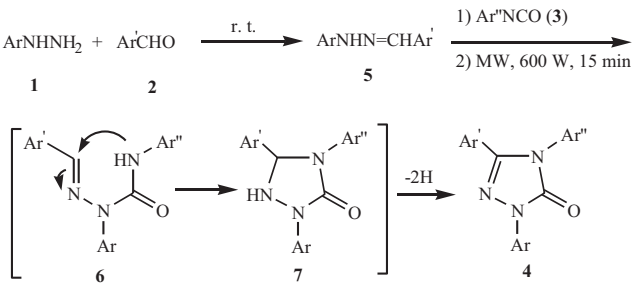
Table 1
Synthesis of 3*H*-1,2,4-triazol-3-ones **4a–k** using microwave irradiation and conventional heating methods.

Product	Ar	Ar′	Ar″	Yield (%)	
				Microwave[a]	Conventional[b]
4a	Ph	2-MePh	3-Cl-4-MePh	88	–
4b	Ph	4-ClPh	Ph	92	8
4c	4-Meph	4-MePh	3-Cl-4-MePh	88	–
4d	ph	4-MeOPh	3-Cl-4-MePh	82	–
4e	ph	4-MePh	3-Cl-4-MePh	85	–
4f	4-MePh	4-ClPh	Ph	88	–
4g	4-MePh	4-MePh	Ph	90	–
4h	Ph	2-MePh	Ph	82	5
4i	Ph	4-MePh	Ph	91	7
4j	Ph	4-MeOPh	Ph	87	2
4k	4-Me Ph	4-ClPh	3-Cl-4-MePh	83	–

[a] Yields of microwave irradiation's method.
[b] Yields of conventional heating's method.

3. Results and discussion

Arylhydeazines, benzaldehydes and arylisocyanates undergo a simple reaction under microwave irradiation and solvent-free conditions producing 2,4,5-triary1-2-4-dihydro-3*H*-1,2,4-triazol-3-ones **4a–k** in 82%–92% yields. This reaction proceeded better under microwave irradiation (the first method), compared to the conventional heating (the second method) in 250 °C for 1 h whose yields are less than 10% and the main product in this method was (*E*)-1,2,4-triarylesemicarbazides **6** (Table 1), (Scheme 2).



Scheme 2. A possible mechanism for the formation of products **4.**

Mechanistically, it is reasonable to assume that the first step may involve the condensation of arylhydrazine **1** and arylaldehyde **2** to form hydrazone **5** *in situ* and then the addition of one molecule of isocyanate **3** leads to the formation of semicarbazone **6**, which is cyclized to produce 1,2,4-triazolan-3-one **7**. Intermediate **7** was finally oxidized under the reaction conditions to produce 2,4-dihydro-3*H*-1,2,4-triazol-3-ones **4** (Scheme 2).

4. Conclusion

The method reported here offers a simple tandem three-component reaction under microwave irradiation and solvent-free conditions for the preparation of 1,2,4-triazol-3-ones of synthetic and pharmacological interest. The use of commercial starting materials, good yields of the products and fairly short reaction times are the main advantages of this method.

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