One-Pot Microwave-Assisted Solvent Free Synthesis of Simple Alkyl 1,2,3-Triazole-4-carboxylates by Using Trimethylsilyl Azide

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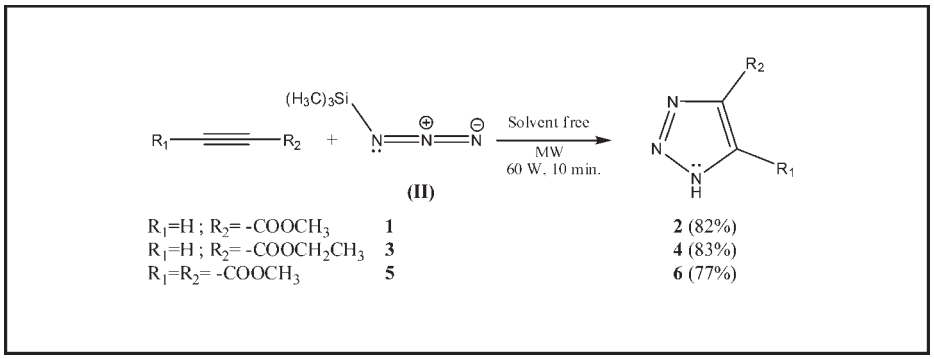

A fast one-pot microwave-assisted solvent free synthesis of simple alkyl 1,2,3-triazole-4-carboxylate derivatives by 1,3-dipolar cycloaddition reactions with trimethylsilyl azide (Me_3Si-N_3) on the alkylpropiolates and DMAD in high yields is described.

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INTRODUCTION

The synthesis of important compounds with many applications in chemistry and medicinal area has been observed in the literature. Microwave-assisted synthesis has been utilized as a powerful and effective technique to promote a group of chemical reactions [1–9]. Since the first publications on the use of microwave irradiation in organic chemistry, the accelerated process described have been a lure for chemists to further apply new reactions to this technology [10]. Huisgen's 1,3-dipolar cycloaddition of alkynes and azides yielding triazoles is, undoubtedly, the premier example of click chemistry reactions [11–21]. This type of reaction is an effective and excellent reaction for preparation of 1,2,3-triazoles. 1,2,3-Triazoles are known to be relatively resilient to metabolic degradation and have known utility in several medicinal chemistry campaigns as isosteres for phenyl rings and carboxyl functionalities [19]. The triazoles may display a wide range of biological activity as anti-HIV and antimicrobial agents, as well as selective β_3 adrenergic receptor agonist and antiallergic agents [20–23]. Additionally, 1,2,3-triazoles are found in herbicides, fungicides, and dyes [14,24].

Because of these interesting activities, fast and new methods for the synthesis of these compounds should be significant. In general, 1,2,3-triazole formation requires harsh conditions, that is, high temperature and longer reaction times. In the original description, the explored examples showed that although these were relatively clean processes, they could take from 12 to 48 h at high temperatures (~110°C) [19]. Several examples of Cu(I)-catalyzed alkyne-azide 1,3-dipolar cycloaddition under milder conditions have been described. The mechanistic proposal of the Cu(I)-catalyzed alkyne-azide 1,3-dipolar cycloaddition was reported and found to involve polar transition states, favorable for microwave activation [25]. These Huisgen 1,3-dipolar cycloaddition of azides and alkynes resulting in 1,2,3-triazoles is one of the most powerful click reactions [14,24–26]. An example of microwave-assisted azide-alkyne cycloaddition was reported by Katritzky and Singh [11]. The reactions involved primary azides and acetylenic amide. Recently, the synthesis of simple alkyl 1,2,3-triazole-4-carboxylate derivatives was reported by reaction between N_3^- and alkylpropyolates [27–30]. The total reaction time was 48 h [29,30]. In another report, the reaction time for synthesis of **2**, **4**, and **6** was 90 h [30].

Here, was reported a fast one-pot microwave-assisted (60 W, 10 min) solvent free synthesis of simple alkyl 1,2,3-triazole-4-carboxylate (**2**, **4**, and **6**) derivatives by 1,3-dipolar cycloaddition reactions with trimethylsilyl

azide **II** (Me_3Si-N_3) on the alkylpropyolates (**1**,**3**) and DMAD (**5**) in high yields.

RESULTS AND DISCUSSION

The results show that the trimethylsilyl (Me_3Si-) was removed at the final simple alkyl 1,2,3-triazole-4-carboxylate (**2**, **4**, and **6**) products. No details are given about the by-products and only the final products are considered.

The ^{13}C NMR results show 4, 5, and 3 C-atom types for **2**, **4**, and **6**, respectively. See results in the Experimental section. The [M^+] for **2**, **4**, and **6**, were 127, 141, and 185, respectively. The percentages of C, H, and N are explained in the Experimental section. In accordance with the results that were shown in the Experimental section the MS (and CI) spectrums and CHN analysis demonstrated that the trimethylsilyl (Me_3Si-) was removed from the products during the synthesis process.

EXPERIMENTAL

The simple imides that were synthesized (**2**, **4**, and **6**), are known compounds and those physical data, infrared and ^1H NMR spectra were essentially identical with those of authentic samples [27–30]. The FTIR spectra was recorded as KBr pellets on a Shimadzu FTIR 8000 spectrometer. ^1H NMR spectra was determined on a 300 MHz Brüker spectrometer. The solvent for NMR recording was DMSO. It should be noted that a limited amount of compounds is required for this experiment. Therefore some small quality of vapor is evolved during irradiation. The power generated by the microwave oven was measured before the experiments by the method described in the literature [31].

Caution: For safety reasons all of the experiments should be performed in an efficient hood in order to avoid contact with vapors, as some quantity of substances can be vaporized during irradiation.

Typical experimental procedure for synthesis of methyl-1*H*-1,2,3-triazole-4-carboxylate (2). A mixture of methyl-propiolate 1 (1 g, 1 mL, 0.012 mol) and trimethylsilyl azide (Me_3Si-N_3) II (1.2 g, 1.5 mL, 0.012 mol) was made in a dried heavy wall Pyrex tube. The tube was sealed and then exposed to microwave oven. After 10 min irradiation at 60 W power, the mixture was cooled to room temperature. The residue of compounds was evaporated under air and reduced pressure. An off-white solid was afforded. The product **2** can be re-crystallized from chloroform + acetone and petroleum ether. These stages afforded 0.049 g product (workup yield 82% and GC yield ≈100%).

The amounts of ethylpropiolate **3** and trimethylsilyl azide **II** (Me_3Si-N_3) for synthesis ethyl-1*H*-1,2,3-triazole-4-carboxylate (**4**) are: 0.965 g (1 mL, 0.010 mol) and 1.1 g (1.3 mL, 0.01 mol), respectively. The yield of **4** was 0.054 g, 83%. The amounts of DMAD **5** and Me_3Si-N_3 (**II**) for synthesis dimethyl-1*H*-1,2,3-triazole-4,5-carboxylate (**6**): are: 1.157 g (1 mL, 0.0082 mol) and 1 g (1.2 mL, 0.009 mol), respectively. The yield of **4** was 0.072 g, 77%.

Methyl-1*H*-1,2,3-triazole-4-carboxylate (2). White crystals, mp 127–128°C (lit. 126–128°C) [27–30]. FTIR (KBr): 3150 (N—H), 3138, 3005, 2937, 1708 (C=O), 1660, 1538, 1480, 1432, 1352, 1212, 1116, 1023, 843, 779 cm^{-1}. ^1H NMR δ_H (DMSO): 8.56 (s, 1H), 3.83 (s, 3H). ^{13}C NMR: 161, 138.8, 130.1, and 51.83. MS: *m*/*z* (relative intensity), M_w = 127; 127 (M^+, 8.8), 95 (70.6), 96 (100), 78 (17.6), and 63 (18.5). $C_4H_5N_3O_2$, CHN-analysis; calculated: C (37.80%), H (3.97%), and N (33.06%), experiment: C (37.73%), H (3.95%), and N (33.01%).

Ethyl-1*H*-1,2,3-triazole-4-carboxylate (4). White crystals, mp 102–104°C (lit. 102–104°C) [27–30]. FTIR (KBr): 3224 (N—H), 3167, 2986, 1723 (C=O), 1661, 1533, 1466, 1375, 1332, 1238, 1202, 1114, 1029, 843, 780 cm^{-1}. ^1H NMR δ_H (DMSO): 8.46 (s, 1H), 4.27–4.35 (q, 2H, 7.0 Hz) and 1.27–1.32 (t, 3H, 7.0 Hz). ^{13}C NMR: 160.4, 138.2, 131.4, 60.4, and 14.0. MS: *m*/*z* (relative intensity); M_w = 141; CI = 141 (6.82), 113 (47.73), 95 (100), 71, 68 (78.5), and 44 (34.1). $C_5H_7N_3O_2$, CHN-analysis; calculated: C (42.55%), H (5.00%), and N (29.77%), experiment: C (42.50%), H (5.03%), and N (29.74%).

Dimethyl-1*H*-1,2,3-triazole-4,5-carboxylate (6). White crystals, mp 116–118°C (lit. 117–118°C) [27–30]. FTIR (KBr): 3239 (N—H), 3100, 2996, 2861, 1742 (C=O), 1658, 1519, 1437, 1389, 1304, 1228, 1190, 1084, 990, 833, 767 cm^{-1}. ^1H NMR δ_H (DMSO): 3.87 (s). ^{13}C NMR: 160.2, 131.0, and 52.4. MS: *m*/*z* (relative intensity); M_w = 185; 187 ($M2H^+$, 38.2), 154 (67.65), 124 (58.8), 93, 58, and 43 (100). $C_6H_7N_3O_4$, CHN-analysis; calculated: C (38.92%), H (3.81%), and N (22.70%), experiment: C (38.98%), H (3.85%), and N (22.66%).

The simple one-pot microwave assisted solvent free synthesis of useful alkyl 1,2,3-triazole-4-carboxylate derivatives (**2**, **4**, and **6**) by Huisgen 1,3-dipolar cycloaddition reactions with trimethylsilyl azide (Me_3Si-N_3) on the alkylpropyolates **1**,**3** and DMAD (**5**), in high yields is described. Comparison of this procedure with the other methods confirms the facility and rapidity of this method for synthesis of the alkyl 1,2,3-triazole-4-carboxylate derivatives.

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