Recep Tayyip Erdoğan Üniversitesi Fen ve Mühendislik Bilimleri Dergisi, 2(1) 1-5 2021
Recep Tayyip Erdogan University Journal of Science and Engineering, 2(1) 1-5 2021
ISSN: 2687-2315 / E-ISSN: 2757-7686

Microwave Assisted Synthesis of Some New Schiff Bases from 2,4-Dihydro-3*H*-1,2,4-Triazol-3-one

Emre MENTEŞE[1]*, Fatih YILMAZ[2], Bahittin KAHVECİ[3]

[1]Recep Tayyip Erdogan University, Art and Science Faculty, Department of Chemistry, Rize, Turkey
[2]Recep Tayyip Erdogan University, Vocational School of Technical Sciences, Department of Chemistry and Chemical Process Technology, Rize, Turkey
[3]Karadeniz Technical University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Trabzon, Turkey

*Sorumlu Yazar/Corresponding Author
E-mail: emre.mentese@erdogan.edu.tr
Orcid ID: 0000-0003-4105-8666

Araştırma makalesi/Research article
Geliş tarihi/Received: 02.11.2020
Kabul tarihi/Accepted: 12.03.2021

ABSTRACT

In this manuscript, a new series of 1,2,4-triazole-3-ones containing imin function was synthesized from 5-(4-bromobenzyl)-4-amino-2*H*-1,2,4-triazol-3(4H)-one and aromatic aldehyde by using microwave irradiation technique via schiff base reaction. Firstly, ethyl imido-p-bromophenylacetate hydrochloride (**2**) was synthesized according to the pinner method in the literature. Then, compound **2** was reacted with ethyl carbazate to synthesized ethyl p-bromophenylacetate etoxycarbonylhydrazone (**3**) compound. Then, 5-(4-bromobenzyl)-4-amino-2*H*-1,2,4-triazol-3(4H)-one (**4**) was synthesized from the reaction of ethyl p-bromophenylacetate etoxycarbonylhydrazone (**3**) with hydrazine monohydrate. Then, it was converted to their corresponding triazole containing Schiff bases (**5a-e**) with the reaction of corresponding aromatic aldehydes in ethanol by using the microwave irradiation method. This microwave technique has some advantages, including rapid and uniform heating, higher product yield and purity, mild reaction conditions, low energy requirement and shorter reaction time. The chemical structures of newly synthesized triazole containing schiff bases were identified using IR, ^{1}H-NMR, and mass spectroscopy data.

Keywords: Triazole, Schiff base, Microwave synthesis, Hydrazine monohydrate

Bazı Yeni Schiff Bazlarının 2,4-Dihidro-3*H*-1,2,4-Triazol-3-on'dan Mikrodalga Destekli Sentezi

ÖZET

Bu çalışmada, imin fonksiyonu içeren bazı yeni 1,2,4-triazol-3-on bileşikleri 5-(4-bromobenzil)-4-amino-2*H*-1,2,4-triazol-3(4H)-on ve karşılık gelen aromatik aldehitlerden Schiff bazı reaksiyonuyla mikrodalga ışıma yöntemiyle sentezlenmiştir. İlk olarak, etilimido p-bromofenilasetathidroklorür (**2**) bileşiği literatürdeki Pinner metoduna göre sentezlendi. Ardından, bileşik **2** etilkarbazat ile etkileştirilerek etil p-bromofenilasetat etoksikarbonilhidrazon (**3**) sentezlendi. Daha sonra, 5-(4-bromobenzil)-4-amino-2*H*-1,2,4-triazol-3(4H)-on (**4**), etil p-bromofenilasetatetoksikarbonilhidrazon (**3**) ile hidrazinhidrat'ın reaksiyonuyla sentezlendi ve mikrodalga ışıma tekniğiyle Schiff bazı reaksiyonuyla karşılık gelen triazol içeren Schiff bazlarına (**5a-e**) dönüştürüldü. Bu mikrodalga tekniği, hızlı ve tek tip ısıtma, yüksek verim ve saflık, ılıman reaksiyon koşulları, düşük enerji gereksinimi ve kısa reaksiyon süresi gibi bir çok avantaj sağlamıştır. Yeni sentezlenen triazol içeren Schiff bazlarının yapıları IR, ^{1}H,NMR ve kütle spektroskopisi yöntemleriyle aydınlatılmıştır.

Anahtar Kelimeler: Triazol, Schiff bazı, Mikrodalga sentez, Hidrazin monohidrat

Cite as;
Menteşe, E., Yılmaz, F., Kahveci, B. (2021). Microwave Assisted Synthesis of Some New Schiff Bases from 2,4-Dihydro-3*H*-1,2,4-Triazol-3-one. *Recep Tayyip Erdogan University Journal of Science and Engineering*, 2(1), 1-5.

1. Introduction

Heterocycles having a 1,2,4-triazol-3-one ring is extensively worked compounds, owing to their vital biological properties. Some of these are antibacterial (Milcent and Redeuilh, 1980), anticancer (Flefel et al., 2013), antifungal (Sun et al., 2013), antioxidant (Menteşe et al., 2015), and antiviral activities (El-Sayed et al., 2013). Moreover, several papers (Gokce et al., 2013; Gürsoy-Kol and Ayazoğlu, 2017; Kahveci et al., 2014; Kahveci et al., 2005; Menteşe et al., 2013) reporting the synthesis of some triazole imine derivatives which are different important aspects such as anticonvulsant activities, acidic properties, spectroscopic properties and antimicrobial activities. Recently some Schiff bases containing triazole ring were reported with their enzyme inhibitory properties (Bekircan et al., 2016).

Schiff bases are an essential class of organic chemistry to prepare more bioactive compounds, and they have a wide range of applications. Therefore, they have gained much attention in pharmaceutical chemistry. Apart from this, microwave-assisted organic synthesis has also taken considerable interest in organic synthesis. It has taken some advantages, including rapid and uniform heating, higher product yield and purity, mild reaction conditions, low energy requirement and shorter reaction time for organic synthesis (Kahveci et al., 2014).

In this current study, we have obtained1,2,3-triazol-3-one Schiff bases by using the microwave irradiation technique. The chemical structures of novel triazole derivatives were determined by IR, ^{1}H-NMR, and mass spectroscopy data.

2. Materials and Methods

All the chemicals were supplied by Merck, Aldrich and Fluka. Melting points were determined on capillary tubes on a Büchi oil-heated melting point apparatus and are uncorrected. ^{1}H NMR spectra were performed on the Varian-Mercury 400 MHz spectrophotometer (Varian, Darmstadt, Germany) in DMSO-d6 using TMS as an internal standard. A mono-mode CEM-Discover microwave oven (Lintfort, Germany) was used to carry out microwave reactions in 30 mL microwave process vials with temperature control by an infrared detection temperature sensor.

2.1. Synthesis of 5-(4-bromobenzyl)-4-amino-2*H*-1,2,4-triazol-3(4*H*)-one (4)

This compound was synthesized according to the literature (Kahveci et al., 2012). Compound **3** (0.01 mol) and hydrazine monohydrate (0.012 mol) in pure water (5 mL) were taken in a clossed vessel and stirred for 5 mininutes before microwave irradiation. Then the mixture was irradiated in the microwave at 120 °C for 10 minutes at 300 W maximum power. After the reaction was completed (TLC, ethyl acetate hexane:3:1, monitored it), the product was taken in a beaker with hot water and washed. It was filtrated off, recrystallized from ethylacetate to obtain the pure product.

Yield 85 %, m.p. 183-184 ºC; IR: 3318, 3218 (NH_2), 3170 (NH), 1724 (C=O), 1639 (C=N); ^{1}H-NMR (DMSO-d_6, 200 MHz) δ: 4.06 (2H, s, CH_2), 5.33 (2H, s, NH_2), 7.28 (2H, d, *J=6 Hz,* Ar-H), 7.83 (2H, d, *J=6,* Ar-H), 12.03 (1H, s, NH). LC-MS (m/z): 270.10 $[M+H]^+$.

2.2. Synthesis of compounds 5a-e

This compound were synthesized according to the literature (Yilmaz et al., 2013). Compound **4** (0.01 mol) and corresponding aromatic aldehyde (0.012 mol) in ethanol (10 mL) were taken in a clossed vessel and stirred for 5 minutes before the reaction. It was irradiated in the microwave at 120 °C for 10 min, at 300 W maximum power. After the reaction was completed (it was monitored by TLC, ethyl acetate hexane:3:1), the product was taken in a beaker with ethanol. It was left to cool to room temperature, and a solid appeared. This

product was filtrated off, recrystallized from ethanol to obtain the pure product.

2.2.1. 5-(4-Bromobenzyl)-4-(benzylidene amino)- 2,4-dihydro-3*H*-1,2,4-triazol-3-one (5a)

Yield 90 %, m.p. 243-244 ºC; IR: 3162 (NH), 1708 (C=O), 1595, 1588 (C=N); ^{1}H-NMR (DMSO-d_6, 200 MHz) δ: 4.05 (2H, s, CH_2), 7.27-7.81 (9H, m, Ar-H), 9.69 (1H, s, N=CH), 12.00 (1H, s, NH). LC-MS (m/z): 358.30 $[M+H]^+$.

2.2.2. 5-(4-Bromobenzyl)-4-(4-chlorobenzy lideneamino)-2,4-dihydro-3*H*-1,2,4-triazol-3-one (5b)

Yield 96 %, m.p. 206-207 ºC; IR: 3171 (NH), 1704 (C=O), 1593, 1587 (C=N); ^{1}H-NMR (DMSO-d_6, 200 MHz) δ: 4.05 (2H, s, CH_2), 7.27-7.84 (8H, m, Ar-H), 9.70 (1H, s, N=CH), 12.03 (1H, s, NH). LC-MS (m/z): 392.71 $[M+H]^+$.

2.2.3. 5-(4-Bromobenzyl)-4-(3,4-dihydroxy benzylideneamino)-2,4-dihydro-3*H*-1,2,4-triazol-3-one (5c)

Yield 97 %, m.p. 278 ºC (dec.); IR: 3551, 3517 (OH), 3162 (NH), 1713 (C=O), 1595, 1585 (C=N); ^{1}H-NMR (DMSO-d_6, 200 MHz) δ: 4.00 (2H, s, CH_2), 6.81-7.53 (7H, m, Ar-H), 9.42 (1H, bs, OH), 9.44 (1H, s, N=CH), 9.71 (1H, bs, OH), 11.93 (1H, s, NH). LC-MS (m/z): 390.23 $[M+H]^+$.

2.2.4. 5-(4-Bromobenzyl)-4-(2,3-dihydroxy benzylideneamino)-2,4-dihydro-3*H*-1,2,4-triazol-3-one (5d)

Yield 88 %, m.p. 275 ºC (dec.); IR: 3486 (OH), 3206 (NH), 1715 (C=O), 1600, 1595 (C=N); ^{1}H-NMR (DMSO-d_6, 200 MHz) δ: 4.02 (2H, s, CH_2), 6.67-7.52 (7H, m, Ar-H), 9.75, 9.90 (2H, bs, 2OH), 9.92 (1H, s, N=CH), 11.97 (1H, s, NH). LC-MS (m/z): 390.22 $[M+H]^+$.

2.2.5. 5-(4-Bromobenzyl)-4-(3,4,5-trimethoxybenzylideneamino)-2,4-dihydro-3*H*-1,2,4-triazol-3-one (5e)

Yield 87 %, m.p. 201-202 ºC; IR: 3165 (NH), 1698 (C=O), 1586, 1571 (C=N), 1125 (C-O); ^{1}H-NMR (DMSO-d_6, 200 MHz) δ: 3.72 (3H, s, OCH_3), 3.83 (6H, s, $2OCH_3$), 4.06 (2H, s, CH_2), 7.06 (1H, s, Ar-H), 7.29 (2H, d, J=8 Hz, Ar-H), 7.48 (2H, d, J= 8 Hz, Ar-H), 9.56 (1H, s, N=CH), 12.00 (1H, s, NH). LC-MS (m/z): 448.33 $[M+H]^+$.

3. Results and Discussion

Our previous studies related to 1,2,4-triazole-3-ones have shown that the microwave technique is very useful process for the synthesis of triazole derivatives (Kahveci et al., 2012). In this work, we synthesized some 1,2,4-triazole compounds containing imin function. Starting materials, iminoester hydrochloride (**2)** and ethoxycarbonylhydrazone (**3)** were prepared according to the known method (Özil et al., 2011). Compound **4** was prepared from the reaction of ester ethoxycarbonylhydrazone (**3**) andhydrazine monohydrate under microwave irradiation. The treatment of compound **4** with the corresponding aldehyde resulted in Schiff's bases of 1,2,4-triazol-3-one (**5a-e**) (Figure 1).

The structure of the synthesized triazole derivatives were identified by using Infrared, ^{1}H-NMR and LC-MS spectral data. The Infrared spectrum data of compounds **5a-e** showed the C=O and NH band between1715-1698 and 3162-3206 cm^{-1}. The ^{1}H-NMR spectrum data of compounds **5a-e** were showed NH signal at 12.03-11.93 ppm. The ^{1}H-NMR signals of -N=CH group for compounds **5a-e** were shown between 9.92-9.44 ppm.

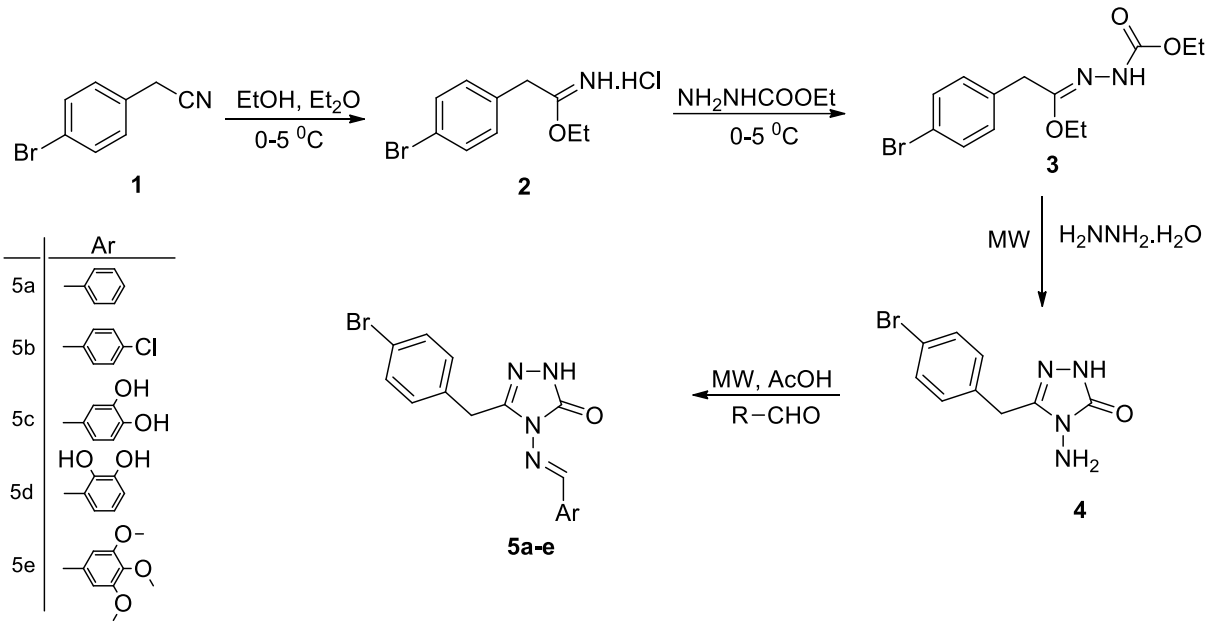

Figure 1. Synthetic pathway for target compounds (**4** and **5a-e**).

4. Conclusion

We have described the microwave-assisted synthesis of some new 1,2,4-triazole-3-one compounds containing imin function. 1,2,4-Triazole is known as an active component found in many drugs and increases biological activity. This method can be applied to synthesize many active triazole compounds.

Author's ORCID ID

Fatih Yılmaz, 0000-0002-6666-3566
Bahittin Kahveci, 0000-0001-7394-0552

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