Research Article

Microwave-Assisted Regioselective Synthesis and 2D-NMR Studies of New 1,2,3-Triazole Compounds Derived from Acridone

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A simple and mild protocol towards the synthesis of new 1,2,3-triazole compounds derived from acridone has been developed via regiospecific 1,3-dipolar cycloaddition reaction between 10-(prop-2-yn-1-yl)acridone derivatives and aromatic azides using CuI as a catalyst. The cycloaddition reaction has been performed using conventional as well as microwave-assisted methods. Microwave-assisted synthesis caused a significant reduction in the reaction times and improvement in the yields of all the synthesized compounds compared with the conventional method. The structure of the 1,4-disubstituted 1,2,3-triazoles has been elucidated by IR, HRMS, ¹H-NMR, ¹³C-NMR, and 2D NMR (¹H-¹³C HMBC, ¹H-¹H COSY, and ¹H-¹H NOESY) spectroscopies.

1. Introduction

Triazoles derivatives constitute an interesting class of heterocyclic compounds with a wide spectrum of biological activities such as antibacterial [1, 2], antifungal [3], anti-inflammatory [4, 5], tyrosine inhibitors [6], and anticancer [7, 8]. Furthermore, the preparation of 1,2,3-triazole was extensively studied [9–11]. The key for the preparation of these compounds is the 1,3-dipolar cycloaddition reaction between alkynes and azides, first described by Huisgen et al. [12]. This method requires long reaction time and high temperature, and it leads to the formation of two regioisomers 1,4-disubstituted and 1,5-disubstituted triazoles [13]. After, it was reported that the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) makes the reaction of cycloaddition quantitative and selective for the synthesis of 1,4-disubstituted 1,2,3-triazole [14]. This synthetic method is an interesting topic in organic synthesis, since it constitutes a powerful bond forming reaction with many applications including different fields from drug discovery to materials science [15, 16]. On the other hand, the acridone nucleus constitutes an interesting class of natural products that serve as chemical intermediates in the synthesis of several alkaloids [17]. Acridones were

known for their pharmacological activities as antiviral [18, 19], antimicrobial [20–22], antitumor [23, 24], antimalarial [25, 26], and anticancer [27, 28]. Moreover, the fluorescence of acridones allows these molecules to be important chemosensors for selective recognition of metals and pollutants in biological and ecological areas [29].

The microwave-assisted synthesis method has become an interesting tool to preserve the environment by reducing the reaction time, efficient internal heat transfer, as well as increasing the yield of reaction [20]. Numerous reactions have proven to result in selectivity or higher yield under microwave irradiation compared with the conventional method [30–32]. Among these reactions, the copper(I) catalyzed azide-alkyne cycloaddition (CuAAC) [33].

Based on subsequent studies, the 1,2,3-triazole derivatives from acridone are showing an interesting antibacterial activity against pathogenic strains [34]. On the other hand, the flatness of the polycyclic aromatic nucleus in these structures generally allows them easy intercalation between the adjacent base pairs of the double helix of DNA. This interesting property is the cornerstone of some biological activities of these molecules [35, 36]. In this view, we have synthesized new 1,2,3-triazole compounds derived from

acridone via the 1,3-dipolar cycloaddition reaction using an environment friendly method. The synthesized compound was characterized using different spectroscopic methods such as IR, ^1H NMR, ^{13}C NMR, and HR-MS. Also, the regioselectivity of the cycloaddition reaction under microwave irradiation was confirmed by 2D NMR including ^1H - ^{13}C HMBC, ^1H - ^1H COSY, and ^1H - ^1H NOESY.

2. Materials and Methods

2.1. General Details. All materials were purchased from commercial suppliers. The ^1H , ^{13}C , and DEPT-135° NMR spectra were recorded with Bruker Avance 300 MHz. Mass spectrometric measurements were recorded using the Exactive™ Plus Orbitrap Mass Spectrometer. IR spectra were recorded using the JASCO FT-IR 4100 spectrophotometer. Microwave irradiation was carried out with CEM Discover™.

2.2. Synthesis

2.2.1. 10-(Prop-2-yn-1-yl)acridone (1). To a mixture of acridone (0.5 g, 2.5 mmol), potassium carbonate (0.55 g, 3 mmol), and TBAB (0.5 g, 2.5 mmol) in DMF (7 ml), propargyl bromide (0.4 g, 3.6 mmol) was added, and the mixture was then irradiated for 10 min. Microwave irradiation power was set at 200 W maximum. After that, it was poured into water, and the white yellow formed precipitate was recrystallized from methanol-DMF.

White yellow solid; yield: 75%, mp = 206–208°C. IR (KBr): 3208, 3010, 2210, 1638, and 1598 cm^{-1} . ^1H NMR (300 MHz, DMSO- d_6 , 25°C, TMS): δ = 8.34 (d, J = 7.8 Hz, 1H, Ar-H), 8.12 (s, 1H, Ar-H), 7.87–7.86 (m, 4H, Ar-H), 7.37–7.38 (m, 2H, Ar-H), 5.32 (s, 2H, CH₂), 2.41 (s, 1H, CH), 2.38 (s, 3H, CH₃). ^{13}C NMR (75 MHz, DMSO- d_6 , 25°C, TMS) δ 177.18, 141.78, 134.76, 134.47, 127.78, 127.07, 123.37, 122.20, 118.44, 116.35, 79.12, 76.16, 36.12, and 20.18.

2.3. General Procedure for the Synthesis of Acridone-Triazole Derivatives (2a–h)

2.3.1. Conventional Method. A mixture of 10-(prop-2-yn-1-yl)acridone (0.23 g, 1 mmol), CuI (0.02 g, 1 mmol), and TEA (0.14 g, 1.2 mmol) was suspended in 10 mL DMF. To this mixture, aromatic azide (2 mmol) was added at room temperature, and the reaction mixture was stirred at 80°C for 4–8 h. After completion of the reaction, water (25 ml) was added, and the mixture was extracted with chloroform; the organic layer was evaporated in high vacuum, and the obtained product was purified by recrystallization in DMF.

2.3.2. Microwave-Assisted Method. A mixture of 10-(prop-2-yn-1-yl)acridone (0.23 g, 1 mmol), CuI (0.01 g, 0.5 mmol), and TEA (0.07 g, 0.6 mmol) was suspended in 10 mL of solvent in a glass vial equipped with a small magnetic stirring bar. To this, aromatic azide (2 mmol) was added, and the vial was tightly sealed. The mixture was then irradiated for 10 min. Microwave irradiation power was set at 200 W maximum. After completion

of the reaction, water (25 ml) was added, and the mixture was extracted with chloroform; the organic layer was evaporated in high vacuum, and the obtained product was purified by recrystallization in DMF.

2.3.3. 10-((1-(*o*-Tolyl)-1H-1,2,3-triazol-4-yl)methyl)acridine-9(10H)-one (2a). Yellow solid; yield: 90%, mp = 224–226°C. IR (KBr): 3112, 3063, 1638, 1600, and 1502 cm^{-1} . ^1H NMR (300 MHz, DMSO- d_6 , 25°C, TMS) δ 8.62 (s, 1H, CH-triazole), 8.40 (dd, J = 8.0, 1.7 Hz, 2H, Ar-H), 8.05 (d, J = 8.8 Hz, 2H, Ar-H), 7.86 (ddd, J = 8.7, 6.9, 1.8 Hz, 2H, Ar-H), 7.57–7.34 (m, 6H, Ar-H), 5.91 (s, 2H, CH₂), and 2.11 (s, 3H, CH₃). ^{13}C NMR (75 MHz, DMSO- d_6 , 25°C, TMS) δ 176.68, 142.58, 141.91, 136.06, 134.14, 132.95, 131.29, 129.79, 126.90, 126.59, 125.91, 125.19, 121.76, 121.49, 116.39, 41.56, and 17.31. MS (ESI) for C₂₃H₁₈N₄O [M + H]⁺, calcd: 367.1511, found: 367.1511.

2.3.4. 4-(4-((9-Oxoacridin-10(9H)-yl)methyl)-1H-1,2,3-triazol-1-yl)benzoic Acid (2b). Yellow solid; yield: 79%, mp > 300°C. IR (KBr): 3397, 3112, 3063, 1702, 1638, 1600, and 1502 cm^{-1} . ^1H NMR (300 MHz, DMSO- d_6 , 25°C, TMS) δ 8.95 (s, 1H, CH-triazole), 8.41 (dd, J = 8.0, 1.7 Hz, 2H, Ar-H), 8.08–7.95 (m, 6H, Ar-H), 7.87–7.81 (m, 2H, Ar-H), 7.41–7.36 (m, 2H, Ar-H), and 5.92 (s, 2H, CH₂). ^{13}C NMR (75 MHz, DMSO- d_6 , 25°C, TMS) δ 176.73, 164.54, 144.17, 141.89, 139.29, 137.23, 134.24, 132.29, 131.06, 128.08, 126.63, 121.80, 121.68, 121.53, 119.88, 117.18, 116.24, and 41.80. HRMS (ESI) for C₂₃H₁₆N₄O₃ [M + H]⁺, calcd: 397.1255, found: 397.1255.

2.3.5. 10-((1-(*m*-Tolyl)-1H-1,2,3-triazol-4-yl)methyl)acridine-9(10H)-one (2c). Yellow solid; yield: 85%, mp > 300°C. IR (KBr): 3120, 3063, 1637, 1606, 1597, and 1507 cm^{-1} . ^1H NMR (300 MHz, DMSO- d_6 , 25°C, TMS) δ 8.73 (s, 1H, CH-triazole), 8.40 (dd, J = 8.0, 1.7 Hz, 2H, Ar-H), 7.99 (d, J = 8.1 Hz, 2H, Ar-H), 7.83 (t, 2H, Ar-H), 7.70 (d, J = 7.2 Hz, 2H, Ar-H), 7.36 (d, J = 7.2 Hz, 4H, Ar-H), 5.86 (s, 2H, CH₂), and 2.36 (s, 3H, CH₃). ^{13}C NMR (75 MHz, DMSO- d_6 , 25°C, TMS) δ 177.14, 144.10, 142.51, 138.86, 134.62, 130.58, 127.15, 122.42, 121.94, 120.53, 116.65, 42.39, and 20.96. MS (ESI) for C₂₃H₁₆N₄O₃ [M + H]⁺, calcd: 367.1401, found: 367.1404.

2.3.6. 2-(4-((9-Oxoacridin-10(9H)-yl)methyl)-1H-1,2,3-triazol-1-yl)benzoic Acid (2d). Yellow solid; yield: 75%, mp > 300°C. IR (KBr): 3405, 3109, 3053, 1700, 1639, 1602, and 1500 cm^{-1} . ^1H NMR (300 MHz, DMSO- d_6 , 25°C, TMS) δ 8.93 (s, 1H, CH-triazole), 8.37 (dd, J = 8.0, 1.7 Hz, 2H, Ar-H), 8.04–7.98 (m, 3H, Ar-H), 7.69–7.62 (m, 5H, Ar-H), 7.34–7.26 (m, 2H, Ar-H), and 5.84 (s, 2H, CH₂). ^{13}C NMR (75 MHz, DMSO- d_6 , 25°C, TMS) δ 176.85, 161.51, 144.90, 142.50, 140.10, 135.54, 132.97, 128.69, 125.56, 124.11, 121.80, 121.53, 119.87, 117.76, 116.24, and 41.80. MS (ESI) for C₂₃H₁₆N₄O₃ [M + H]⁺, calcd: 397.1507, found: 397.1507.

2.3.7. 2-Methyl-10-((1-(*o*-tolyl)-1*H*-1,2,3-triazol-4-yl)methyl)acridine-9(10*H*)-one (2e). Yellow solid; yield: 89%, mp > 300°C. IR (KBr): 3110, 3065, 1637, 1610, 1601, and 1502 cm⁻¹. ¹H NMR (300 MHz, DMSO-*d*₆, 25°C, TMS) δ 8.59 (s, 1H, CH-triazole), 8.38 (d, *J* = 7.9 Hz, 1H, Ar-H), 8.25–8.12 (m, 1H, Ar-H), 8.01 (dd, *J* = 19.3, 8.7 Hz, 2H, Ar-H), 7.83 (t, *J* = 7.9 Hz, 1H, Ar-H), 7.68 (d, *J* = 8.7 Hz, 1H, Ar-H), 7.58–7.25 (m, 5H, Ar-H), 5.89 (s, 2H, CH₂), 2.46 (s, 3H, CH₃), and 2.10 (s, 3H, CH₃). ¹³C NMR (75 MHz, DMSO-*d*₆, 25°C, TMS) δ 176.50, 141.75, 140.03, 136.06, 135.43, 133.94, 132.94, 131.28, 130.68, 129.79, 126.89, 126.61, 125.90, 125.82, 125.13, 121.64, 121.21, 116.40, 116.24, 41.44, 20.18, and 17.31. MS (ESI) for C₂₄H₂₀N₄O [M + H]⁺, calcd: 381.1669, found: 381.1669.

2.3.8. 2-Methyl-4-(4-((9-oxoacridin-10(9*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl)benzoic Acid (2f). Yellow solid; yield: 82%, mp > 300°C. IR (KBr): 3398, 3110, 3063, 1700, 1638, 1609, and 1502 cm⁻¹. ¹H NMR (300 MHz, DMSO-*d*₆, 25°C, TMS) δ 8.93 (s, 1H, CH-triazole), 8.40 (s, 1H, Ar-H), 8.14 (s, 1H, Ar-H), 8.04–7.95 (m, 5H, Ar-H), 7.87–7.82 (m, 2H, Ar-H), 7.37 (t, *J* = 7.4 Hz, 2H, Ar-H), 5.90 (s, 2H, CH₂), and 2.29 (s, 3H, CH₃). ¹³C NMR (75 MHz, DMSO-*d*₆, 25°C, TMS) δ 176.55, 164.99, 144.24, 141.72, 139.98, 139.27, 135.52, 134.03, 130.72, 126.64, 125.86, 121.68, 121.24, 116.25, 116.07, 41.65, and 20.18. MS (ESI) for C₂₄H₁₈N₄O₃ [M + H]⁺, calcd: 411.1403, found: 411.1408.

2.3.9. 2-Methyl-10-((1-(*m*-tolyl)-1*H*-1,2,3-triazol-4-yl)methyl)acridin-9(10*H*)-one (2g). Yellow solid; yield: 81%, mp > 300°C. IR (KBr): 3112, 3063, 1638, 1600, and 1502 cm⁻¹. ¹H NMR (300 MHz, DMSO-*d*₆, 25°C, TMS) δ 8.70 (s, 1H, triazole), 8.33 (d, *J* = 7.2 Hz, 1H, Ar-H), 8.14 (s, 1H, Ar-H), 7.94–7.53 (m, 6H, Ar-H'), 7.33 (d, *J* = 7.2 Hz, 3H, Ar-H), 5.78 (s, 2H, CH₂), 2.42 (s, 3H, CH₃), and 2.32 (s, 3H, CH₃). ¹³C NMR (75 MHz, DMSO-*d*₆, 25°C, TMS) δ 177.01, 144.22, 142.22, 140.49, 138.80, 135.99, 134.51, 131.17, 130.60, 127.11, 126.32, 122.14, 121.83, 121.70, 120.36, 116.81, 116.64, 42.67, 21.00, and 20.68. MS (ESI) for C₂₄H₂₀N₄O [M + H]⁺, calcd: 381.1669, found: 381.1660.

2.3.10. 2-(4-((2-Methyl-9-oxoacridin-10(9*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl)benzoic Acid (2h). Yellow solid; yield: 78%, mp > 300°C. IR (KBr): 3400, 3121, 3052, 1704, 1640, 1605, and 1501 cm⁻¹. ¹H NMR (300 MHz, DMSO-*d*₆, 25°C, TMS) δ 8.92 (s, 1H, CH-triazole), 8.39 (d, *J* = 7.9 Hz, 1H, Ar-H), 8.15 (s, 1H, Ar-H), 7.96–7.87 (m, 2H, Ar-H), 7.69–7.61 (m, 5H, Ar-H), 7.31–7.26 (m, 2H, Ar-H), 5.81 (s, 2H, CH₂), and 2.44 (s, 3H, CH₃). ¹³C NMR (75 MHz, DMSO-*d*₆, 25°C, TMS) δ 176.01, 166.96, 142.46, 141.71, 140.56, 138.37, 136.61, 134.89, 133.01, 129.82, 126.74, 125.82, 121.75, 120.80, 116.35, 115.06, 41.93, and 20.37. MS (ESI) for C₂₄H₁₈N₄O₃ [M + H]⁺, calcd: 411.0883, found: 411.0884.

3. Results and Discussion

3.1. Synthesis. The new 1,2,3-triazole compounds derived from acridone were synthesized under mild conditions via a two-step reaction. The first step was the *N*-alkylation of

acridone ring. The tautomerism of acridone nucleus contributes to the low basicity of the nitrogen, so the *N*-alkylation of the acridone nucleus is a relatively difficult reaction. However, the use of a strong base such as potassium carbonate in an anhydrous medium is required for the deprotonation of acridone ring. The preparation of 10-(prop-2-yn-1-yl)acridone derivatives (1) was achieved by *N*-propargylation of acridone under microwave irradiation using solid-liquid phase transfer catalyst. A mixture of acridone (1 equiv) with propargyl bromide (1.5 equiv), anhydrous potassium carbonate (1.2 equiv), and tetra-*n*-butylammonium bromide (TBAB) (1 equiv) in DMF was reacted under microwave irradiation during 10 min, after completion of the reaction compound (1) was isolated in good yield (70%) (Scheme 1).

The second step was the 1,3-dipolar cycloaddition between 10-(prop-2-yn-1-yl)acridone derivatives (1) and aromatic azides. 2-Azidotoluene, 3-azidotoluene, 2-azidobenzoic acid, and 4-azidobenzoic acid were prepared from *o*-toluidine, *m*-toluidine, and *p*-anthranilic acid, respectively, by diazotization of amine function followed by nucleophilic substitution reaction with sodium azide (NaN₃). The new 1,2,3-triazole compounds were prepared using microwave-assisted synthesis (MW) and conventional heating methods, which include the cycloaddition reaction between 10-(prop-2-yn-1-yl)acridone derivatives and a variety of substituted aromatic azides in the presence of copper iodide (CuI) as source of Cu(I) and triethylamine. First, our investigation focused on exploring the 1,3-dipolar cycloaddition reaction using the conventional heating method, and the reaction was realized in the presence of CuI (1 equiv) and triethylamine (1.2 equiv) in DMF for 4–8 h at 80°C. In these conditions, the compounds (2a–h) were obtained in 48–62% yields.

In the view, to obtain 1,2,3 triazoles derivatives with excellent yield and shorter reaction times under mild reaction conditions, we have used the microwave-assisted synthesis method. The cycloaddition reaction between 2-azidotoluene and 10-(prop-2-yn-1-yl)acridone 1a was used as a model reaction to study the effect of reaction parameters such as solvents (tert-butanol (t-BuOH), *N,N*-dimethylformamide (DMF), chloroform (CHCl₃), and methanol (CH₃OH)), copper salt (CuI (0.1–1 equiv)), microwave exposure time (2–15 min), and microwave power (60–200 W) were investigated in order to get optimum conditions. Figure 1 and Table 1 present the effect of various reaction parameters on cycloaddition reaction efficiency.

The effect of time reaction was examined by changing time interval from 2 min to 15 min keeping the stoichiometric quantity of 10-(prop-2-yn-1-yl)acridone (1 mmol), 2-azidotoluene (2 mmol), CuI (0.5 mmol), Et₃N (0.6 mmol) with microwave power (max 200 W), and the total reaction volume of 10 mL. The results are displayed in Figure 1(a). The yield of cycloaddition reaction was increased from 12% to 90%, with increased exposure time from 2 min to 10 min in DMF. Whereas, a modest increase in the yield of product (2a) in methanol was observed with 38%; this is probably due to the low solubility of 10-(prop-2-yn-1-yl)acridone in methanol.

SCHEME 1: The synthetic route of 1,2,3-triazole derivatives from acridone.

FIGURE 1: Optimization of cycloaddition reaction by varying (a) MW exposure time, (b) MW power, and (c) CuI (%).

TABLE 1: Optimization of reaction condition 2a.

Entry	Copper salt	Base	Solvent	Time	Yields (%)
1 ^a	CuI	Et ₃ N	t-BuOH	10 min	52
2 ^a	CuI	Et ₃ N	DMF	10 min	90
3 ^a	CuI	Et ₃ N	CHCl ₃	10 min	62
4 ^a	CuI	Et ₃ N	MeOH	10 min	38
5 ^a	CuI	Et ₃ N	DMF	15 min	92
6 ^b	CuI	Et ₃ N	DMF	10 min	94
7 ^c	CuI	Et ₃ N	DMF	4 h	62

^aReaction conditions: 10-(prop-2-yn-1-yl)acridone (1 mmol), 2-azidotoluene (2 mmol), copper iodide (0.5 mmol), Et₃N (0.6 mmol), and MW 200 W maximum. ^bReaction conditions: 10-(prop-2-yn-1-yl)acridone (1 mmol), 2-azidotoluene (2 mmol), copper iodide (1 mmol), Et₃N (1.2 mmol), and MW 200 W maximum. ^cReaction conditions: 10-(prop-2-yn-1-yl)acridone (1 mmol), 2-azidotoluene (2 mmol), copper iodide (1 mmol), and Et₃N (1.2 mmol) at 80°C (conventional heating).

The effect of microwave power on cycloaddition reaction was studied by altering microwave power from 60 W to 200 W, at fixed stoichiometric quantity of 10-(prop-2-yn-1-yl)acridone (1 mmol), 2-azidotoluene (2 mmol), CuI (0.5 mmol), Et₃N (0.6 mmol) with exposure time (10 min), and the total reaction volume of 10 mL. The results are shown in Figure 1(b). The yield of cycloaddition reaction increased almost linearly from 42% to 90%, with augmentation of microwave power from 60 W to 180 W in DMF. Also, an interesting increase in the yield of product (2a) in chloroform with 70% in 10 min was observed. The reason of this performance is attributed to the thermal and nonthermal microwave effects. The thermal effects in these reactions involve selective heating in solution and accumulation of heat in polar species. The nonthermal effects are due to a specific contribution of electrostatic field resulting from dipoles-dipoles interactions between polar molecules and the electric field, which lead to the polarizability and the stabilization of transition states under microwave irradiation.

The percentage of copper salt and triethylamine was examined by varying the initiator concentration from 0.1 to 1 equivalent for CuI and from 0.12 to 1.2 equivalent for Et₃N at fixed stoichiometric quantity of 10-(prop-2-yn-1-yl)acridone (1 mmol), 2-azidotoluene (2 mmol) with exposure time (10 min), microwave power (max 200 W), and the total reaction volume of 10 mL; the results are shown in Figure 1(c). It was found that the yield of the cycloaddition reaction was increased from 43% to 90% with increased percentage of copper salt from 0.1 to 0.5 equivalent in DMF. While a weak increase in the yield of compound (2a) in t-BuOH was observed, the yield of cycloaddition reaction was improved from 0% to 40% with increased percentage of copper salt from 0.1 to 0.5 equivalent. The direct use of copper salt in its oxidation state (I), brought in the form of copper iodide (CuI) in an inert medium (N₂), allowed to obtain the new 1,4-disubstituted 1,2,3-triazoles with good yields. The use of triethylamine (Et₃N) was necessary to stabilize Cu(I) against oxidation; moreover, triethylamine facilitates deprotonation of CuI-acetylide.

As observed from Figure 1, the optimum reaction conditions for synthesis of 10-((1-(o-tolyl)-1H-1,2,3-triazol-4-yl)methyl)acridone (2a) were obtained in DMF as solvent and

with stoichiometric quantities of 10-(prop-2-yn-1-yl)acridone (1 mmol), 2-azidotoluene (2 mmol), CuI (0.5 mmol), and Et₃N (0.6 mmol) at 200 W with exposure time of 10 min. After optimizing the conditions of the cycloaddition reaction, we applied these conditions to the 10-(prop-2-yn-1-yl)acridone derivatives used as dipolarophiles with the different aromatic azides used as dipoles, in the presence of the catalytic system CuI/Et₃N in DMF. After 10 min, the conversion of the starting product is generally complete, and the purification of the product was carried out by successive washings with dichloromethane and water, followed by a recrystallization in DMF/methanol mixture.

Comparative study results obtained by microwave-assisted synthesis versus the conventional heating method showed that the conventional heating required more reaction time (4–8 h); however, all the reactions were completed within 10 min under the microwave irradiation method which caused significant reduction in the reaction times, and the yields have been improved from 48–62% (conventional heating) to 75–90% (microwave-assisted reaction) (Table 2). This procedure of click chemistry allowed us to obtain only the 1,4-disubstituted regioisomer.

3.2. Characterization of Synthesized Compound (2a–h). The structures of the 1,4-disubstituted triazoles (2a–h) synthesized using the synthetic protocol described above were fully characterized by NMR, IR and HRMS analyses.

3.2.1. FTIR Spectroscopy. To confirm the structure of synthesized compounds, the reactions were monitored by FTIR; the IR spectrum of compounds 2a–h shows the disappearance of the vibration bonds of the alkyne group in the region of 2110 cm⁻¹ and 3210 cm⁻¹ confirmed the formation of the synthesized compounds. Moreover, the FTIR spectra displayed characteristic absorption bands in the region of 1640–1630 cm⁻¹ assigned to the bond (C=O) of the acridone ring, and characteristic bands of triazole ring were detected in the range of 1500–1300 cm⁻¹ corresponding to N=N and C=C bonds. In addition, compounds 2b, 2d, 2f, and 2h showed bands around 3400 cm⁻¹, 3010–2920 cm⁻¹, and 1700 cm⁻¹, demonstrating characteristic stretching vibration of O-H, aromatic and aliphatic C-H, and carbonyl (C=O) of the carboxylic acid group, respectively.

3.2.2. NMR Analyses. In order to confirm the synthesized compounds 2a–h, NMR spectroscopic analysis was investigated. The ¹H NMR spectra showed aromatic protons between 8.95 ppm and 7.25 ppm. We also noticed the presence of signals between 5.92 ppm and 5.85 ppm attributable to the protons of the methylene group (N-CH₂), in addition to a singlet at 8.95–8.59 ppm attributable to the proton of the triazole nucleus. In the ¹H NMR spectrum of compound 2e, the characteristic signal of triazole was observed at 8.59 ppm. The signal at 5.89 ppm attributed to the hydrogens of the methylene group (N-CH₂), and the signals of the methyl group were observed at 2.46 ppm and 2.10 ppm (Figure 2).

TABLE 2: Synthesized compounds (2a-h).

Compounds	R1	R2	Yield (%) microwave method	Yield (%) conventional method
2a	H	o-CH ₃	90	62
2b	—	p-COOH	79	50
2c	—	m-CH ₃	85	58
2d	—	o-COOH	75	48
2e	CH ₃ —	o-CH ₃	89	60
2f	—	p-COOH	82	51
2g	—	m-CH ₃	81	60
2h	—	o-COOH	78	48

FIGURE 2: ¹H NMR and ¹³C NMR spectra of compound 2e in DMSO-d₆.

FIGURE 3: The ^1H - ^{13}C HMBC spectrum of compound 2a. FIGURE 4: The ^1H - ^1H COSY spectrum of compound 2a.

These structures were further supported by ^{13}C and DEPT NMR spectra, which showed all the expected carbon signals corresponding to acridone-triazole derivatives, especially the aromatic carbons of triazole ring resonating between 125 ppm and 143 ppm and signals of methylene carbons resonated between 50 ppm and 41 ppm. We also noticed the presence of signal between 177 ppm and 176 ppm attributed to the carbonyl ($\text{C}=\text{O}$) of the acridone ring.

The regioselectivity of the cycloaddition reaction under microwave irradiation was confirmed by using 2D NMR. The HMBC experiment is an important tool to identify the structure of synthetic compounds. Therefore, the strategy for identifying above structure is conveniently realized on the basis of long-range connectivities via ^1H - ^{13}C HMBC depending on the correlation between the triazole protons with the adjacent carbons. For instance, in the ^1H - ^{13}C HMBC spectrum of the compound 2a, the protons of the

FIGURE 5: The ^1H - ^1H NOESY spectrum of compound 2a.

FIGURE 6: Synthesis of 1,4-disubstituted triazole.

methylene group (NCH_2) at 5.91 ppm correlates to the triazole carbons at 142.5 ppm ($^2\text{J}_{\text{H-C}}$) (C-17) and 125.1 ppm ($^3\text{J}_{\text{H-C}}$) (C-18); in addition, the proton of triazole ring (H-18) at 8.62 ppm correlates with quaternary carbon of the phenyl group (C-22) at 136 ppm ($^3\text{J}_{\text{H-C}}$) and the carbon of triazole ring (C-17) at 142.5 ppm ($^2\text{J}_{\text{H-C}}$). Also, we notice that the carbonyl functional group at 176.6 ppm correlates to the protons of acridone ring at 8.40 ppm ($^3\text{J}_{\text{H-C}}$) (Figure 3).

Another evidence came from the study of ^1H - ^1H COSY and ^1H - ^1H NOESY spectra of the compound 2a. Accordingly, the ^1H - ^1H COSY spectrum shows correlations

between the proton of triazole ring (H-18) at 8.62 ppm and the protons of the methylene group (NCH_2) (H-16) at 5.91 ppm, in addition to correlations between the protons of acridone ring (H-6, H-14) at 8.40 ppm and the protons (H-1, H-13) at 7.38 ppm (Figure 4). The ^1H - ^1H NOESY spectrum shows correlations between the protons of the methylene group (NCH_2) (H-16) at 5.91 ppm and the protons of acridone ring (H-3, H-11) at 8.05 ppm. Also, we observe that the signal of the proton of triazole ring (H-18) at 8.62 ppm correlate with methyl of the phenyl group (CH_3) at 2.11 ppm (Figure 5).

Therefore, these results confirm the formation of 1,4-disubstituted regioisomer. Thus, the regioselectivity of the 1,3-dipolar cycloaddition reaction between 10-(prop-2-yn-1-yl) acridone derivatives (2) and aromatic azides under microwave irradiation was attained (Figure 6).

4. Conclusion

Facile synthetic routes are designed to synthesis new 1,2,3-triazole compounds derived from acridone via regioselective 1,3-dipolar cycloaddition reaction catalyzed by Cu(I). The microwave irradiation method offered high yields of 1,2,3-triazoles in a short reaction time compared with the conventional method. The structure of the novel compounds was determined by NMR, FTIR spectroscopy, and mass spectrometry. The regioselectivity of the cycloaddition reaction has been confirmed unambiguously by the multi-nuclear NMR (^1H - ^{13}C HMBC, ^1H - ^1H COSY, and ^1H - ^1H NOESY).

Data Availability

The data used to support the findings of this study are included in the supplementary file.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Supplementary Materials

The supplementary data contain IR, ^1H , ^{13}C NMR, and mass spectroscopy charts of the new synthesized compounds. (Supplementary Materials)

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