S. Afr. J. Chem., 2013, **66**, 72–76,
<http://journals.sabinet.co.za/sajchem/>.

Microwave-Assisted Synthesis of Some 1*H*-1,2,4-Triazol-3-one Derivatives

Nesrin Karaali[a], Emre Menteşe[a,*], Fatih Yılmaz[a], Asu Usta[a] and Bahittin Kahveci[b]

[1]*Department of Chemistry, Faculty of Arts and Sciences, Recep Tayyip Erdoğan University, 53100, Rize, Turkey.*

[2]*Department of Nutrition and Dietetics, Faculty of Health Sciences, Karadeniz Technical University, Trabzon, Turkey.*

Received 7 September 2012, revised 30 November 2012, accepted 26 February 2013.

ABSTRACT

4-Amino-5-(methyl/ethyl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one were synthesized from the reaction of (methyl/ethyl)-ester ethoxycarbonyl hydrazone with hydrazine hydrate and then, converted to corresponding Schiff bases using 9H-fluorene-3-carbaldehyde. Ester, hydrazide and oxadiazole derivatives were synthesized starting from Schiff bases in three steps. All reactions occurred under conventional conditions and microwave irradiation. The obtained results were compared.

KEYWORDS

Triazole, oxadiazole, hydrazine hydrate, microwave irradiation.

1. Introduction

Microwave activation, as an unconventional energy source, has become very popular and useful technology in organic chemistry. It can be used as an alternative to classical methods enabling development of easy and rapid access to new heterocycles.[1–7] The synthesis of 1,2,4-triazol-3-one derivatives have attracted increasing interest over the past decade because of their diverse pharmacological properties, such as antimicrobial,[8–10] antifungal,[11] anti-inflammatory,[12] antihypertensive,[13] anticonvulsant and antiviral.[14]

The main aim of this study is to synthesize the new Schiff base, ester, hydrazide, oxadiazole and acetic acid derivatives of 1,2,4-triazol-3-one by using microwave irradiation and conventional heating. Our research group has previously reported the microwave-assisted synthesis of *N*-benzyl and *N*-acetyl triazole-3-one.[15] In this paper we report the synthesis of some new 1, 2, 4-triazole derivatives with different functional groups. Microwave irradiation was used and the yields of the desired compounds were better than those obtained by conventional heating. The overall time for the synthesis of new 1,2,4-triazole derivatives was considerably reduced and the overall yield was enhanced. The new compounds were characterized by IR, ^{1}H-NMR, ^{13}C-NMR, elemental analysis and mass spectroscopic techniques.

2. Results and Discussion

Synthesis of all compounds was performed according to the reactions outlined in Scheme 1. Firstly, compounds **1(a–b)** were prepared according to the literature[16], then treated with hydrazine monohydrate to obtain compounds **2(a–b)**. The treatment of compounds **2(a–b)** with 9*H*-fluorene-2-carbaldehyde resulted in the formation of 5-methyl/ethyl-4-[(9*H*-fluoren-3-ylmethylidene)amino]-2,4-dihydro-3*H*-1,2,4-triazol-3-one **3(a–b)** which were used as starting materials for the synthesis of all new desired compounds. Ethoxycarbonylmethylation of compounds **3(a–b)** with ethylbromoacetate, in acetone, under microwave irradiation, afforded the ethylacetate derivatives **4(a–b)**. The treatment of compounds **3(a–b)** with chloroacetic acid resulted in the carboxylic acid derivatives **5(a–b)** in good yields. New acetohydrazide derivatives, compounds **6(a–b)** and **7(a–b)**, were synthesized from the reaction of compounds **4(a–b)** with phenylacetohydrazide and hydrazine monohydrate, respectively. Finally, compounds **7(a–b)** were reacted with CS_2 to prepare 1,3,4-oxadiazole derivatives; compounds **8(a–b)**. All reactions were carried out with microwave irradiation and conventional heating, and the results are compared in Table 1.

All of the synthesized compounds were characterized by their spectral data. The IR spectra of all compounds showed the strong band between 1710–1690 cm^{-1} for C = O of the triazole ring and 1640–1600 cm^{-1} for the C = N band of the triazole ring and Schiff base. ^{1}H-NMR and ^{13}C-NMR spectra of all compounds exhibited the suitable signals with proposed structures. NH, NH_2 and SH signals were removed by D_2O wash. Treatment of compounds **4(a–b)** with 2-phenylacetohydrazide and hydrazine monohydrate resulted in their acetohydrazide derivatives, compounds **6(a–b)** and **7(a–b)**, respectively. In the ^{1}H-NMR spectra of compounds **6(a–b)** and **7(a–b)**, disappearance of OCH_2CH_3 showed the removal of this group; also new NH and NH_2 signals showed that the hydrazide formation had been successful. In the ^{13}C-NMR spectra of these compounds, no signals were evident for the OCH_2CH_3 carbons; in addition, a new CH_2 signal, at about 63 ppm, and the presence of additional aromatic carbons proved this reaction successful for compounds **6(a–b)**.

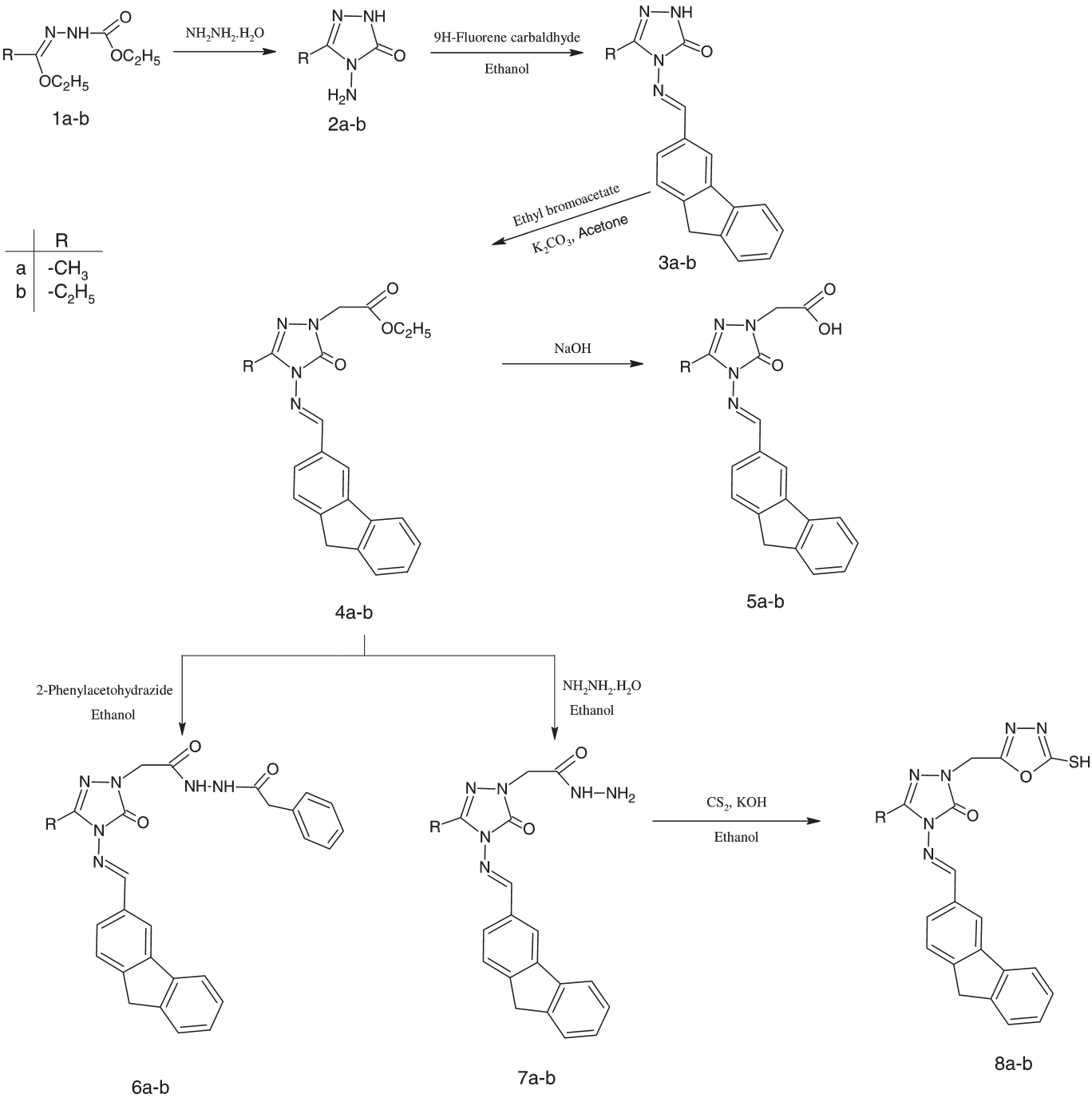
Treatment of compounds **7(a–b)** with CS_2 in absolute ethanol in the presence of KOH solution resulted in the formation of compounds **8(a–b)**. The NH and NH_2 signals were no longer observed due to oxadiazole formation, while a new SH signal was evident at about 14 ppm in the ^{1}H-NMR spectra of these compounds. Also, no signal was apparent for the C=O carbons in the ^{13}C-NMR spectra of compounds **8(a–b)**.

In addition, all compounds gave stable M+1 ion peaks and reasonable elemental analysis data.

3. Conclusion

Novel substituted triazol-3-ones were synthesized in good yields and were characterized by spectral and elemental analysis. This work highlights the efficiency of microwave irradiation on the synthesis of this type of compounds.

* Author for correspondence. E-mail: emre.mentese@erdogan.edu.tr



Scheme 1
The synthetic path of the target compounds

4. Experimental

All the chemicals were supplied from Merck, Aldrich and Fluka. Melting points were determined on capillary tubes on a Buchi oil heating melting point apparatus and uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were performed on Varian-Mercury 200 MHz spectrophotometer in DMSO-d_6 using TMS as internal reference. The IR spectra were recorded on a Perkin-Elmer 100 FTIR spectrophotometer as KBr pellets. The elemental compositions were determined on a Carlo Erba 1106 CHN analyzer; the experimental values were in agreement (±0.4 %) with calculated ones. Mass spectra were recorded on a Thermo Scientific Quantum Access max LC-MS spectrophotometer. A mono-mode CEM-Discover microwave oven was used to carry out microwave reactions in 30 mL microwave process vials with temperature control by infrared detection temperature sensor. All reactions were monitored by TLC using pre-coated aluminum sheets (silica gel 60 F 2.54 0.2 mm thickness).

4.1. Synthesis of Compounds 3(a–b)

4.1.1. *Conventional Method*

To a solution of compounds **2(a–b)** (0.01 mol) in dry ethanol (30 mL), 9*H*-fluorene-2-carbaldehyde(0.01 mol) was added and the reaction mixture refluxed for 4 h (monitored by TLC, ethyl acetate: hexane, 3:1). After the mixture was allowed to cool down to room temperature water was added, upon which time a white precipitate was formed. This crude product was filtered, dried and recrystallized from ethanol.

Table 1 Comparison of conventional and microwave conditions of the compounds

Product	Melting point/°C	Conventional heating		Microwave irradiation	
		Reaction time/h	Yield/%	Reaction time/min	Yield/%
3a	238–240	4	83	10	95
3b	212–215	4	88	10	97
4a	208–210	12	76	10	87
4b	198–200	12	80	10	89
5a	246–248	4	58	15	79
5b	230–231	4	61	15	89
6a	141–142	8	67	20	90
6b	135–136	8	70	20	94
7a	255–257	6	65	10	84
7b	230–231	6	60	10	79
8a	278–280	8	56	10	75
8b	200–201	8	60	10	79

4.1.2. *Microwave Method*

Compounds **2(a–b)** (0.01 mol) and 9H-fluorene-2-carbaldehyde (0.01 mol) in dry ethanol (10 mL) were taken in a closed vessel. The mixture was irradiated in a microwave oven at 125 °C for 10 min with pressure control. After the reaction was completed (monitored as stated above), the mixture was cooled to room temperature, transferred to a beaker and a white solid appeared on addition of water. This crude product was filtered and purified as before.

Methyl-4-[(9*H*-fluoren-3-ylmethylidene)amino]-2,4-dihydro-3*H*-1,2,4-triazol-3-one **(3a)**: IR (KBr): ν = 3183 (NH), 3054 (ArCH), 1688 (C=O), 1649 (C=C), 1594 (C=N), ^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.89 (1H, s, NH), 8.94 (1H, s, N=CH), 8.00–7.26 (7H, m, Ar-H), 3.98 (2H, s, CH_2), 1.58 (3H, s, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 155.25, 153.67, 150.48, 145.10, 144.76, 143.98, 143.30, 133.90, 131.97, 128.56, 127.33, 127.03, 124.60, 120.51, 120.10, 37.54, 19.29 ppm; LC-MS: m/z = 291(m+1). Anal. Calcd. for $C_{17}H_{14}N_4O$: C,70.33; H, 4.86; N, 19.30 Found: C,70.37; H, 4.82; N, 19.31 %.

Ethyl-4-[(9*H*-fluoren-3-ylmethylidene)amino]-2,4-dihydro-3*H*-1,2,4-triazol-3-one **(3b)**: IR (KBr): ν = 3197 (NH), 3060 (ArCH), 1685 (C=O), 1651 (C=C), 1604 (C=N), ^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.53(1H, s, NH), 8.99 (1H, s, N=CH), 8.10–7.21 (7H, m, Ar-H), 3.89 (2H, s, CH_2), 2.18 (2H, q, J = 7.0, CH_2), 1.50 (3H, t, J = 7.0, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 157.85, 152.77, 150.98, 147.10, 145.70, 143.18, 141.00, 135.51, 133.37, 129.01, 127.91, 125.70, 124.63, 121.13, 120.16, 37.54, 19.29, 12.43 ppm; LC-MS: m/z = 305(m+1). Anal. Calcd. for $C_{18}H_{16}N_4O$: C,71.04; H, 5.30; N, 18.41 Found: C,71.06; H, 5.28; N, 18.44 %.

4.2. Synthesis of Compounds 4(a–b)

4.2.1. *Conventional Method*

Dry K_2CO_3 (0.025 mol) was added to a solution of compounds **3(a–b)** (0.01 mol) in acetone (30 mL) and stirred for 30 min. Then, ethyl bromoacetate (0.012 mol) was added and stirred for 12 h. After the reaction was complete (monitored by TLC, ethyl acetate: hexane, 3:1), the product was precipitated by addition of water. It was filtered, dried and recrystallized by ethanol to obtain the desired product.

4.2.2. *Microwave Method*

Dry K_2CO_3 (0.025 mol) was added to a solution of compounds **3(a–b)** (0.01 mol) in acetone (10 mL). Then, the mixture was taken in a closed vessel and irradiated in a microwave oven at 90 °C for 5 min with pressure control. Then, the mixture was cooled to room temperature and ethyl bromoacetate (0.012 mol) was added. Again, it was irradiated in a microwave at 90 °C for 10 min at 300 W maximum power. After the reaction was completed (monitored as stated above), the mixture was cooled to room temperature, transferred to a beaker and the product was precipitated by addition of water. The product was purified as described above.

{4-[(9*H*-fluoren-3-ylmethylidene)amino]-3-methyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl}acetate (**4a**): IR (KBr): ν = 3054 (ArCH), 1742, 1705 (C=O), 1649 (C=C), 1594 (C=N), 1280 (C-O),^{1}H NMR (200 MHz, DMSO-d_6): δ = 9.87 (1H, s, N=CH), 7.80–7.17 (7H, m, Ar-H), 4.56 (2H, s, NCH_2), 4.25 (2H, q, J = 7.2, OCH_2), 3.95 (2H, s, CH_2), 2.53 (3H, s, CH_3), 1.35 (3H, t, J = 7.2, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 168.12, 154.90, 152.60, 148.19, 146.73, 145.36, 142.11, 140.90, 132.00, 130.67, 129.00, 127.13, 125.06, 121.49, 120.01, 119.50, 61.21, 46.58, 37.54, 19.29, 13.88 ppm; LC-MS: m/z = 377(m+1). Anal. Calcd. for $C_{21}H_{20}N_4O_3$: C, 67.01; H, 5.36; N, 14.88 Found: C, 67.05; H, 5.37; N, 14.85 %.

{4-[(9*H*-fluoren-3-ylmethylidene)amino]-3-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl}acetate (**4b**): IR (KBr): ν = 3029 (ArCH), 1748, 1700 (C=O), 1648 (C=C), 1589 (C=N), 1273 (C-O),^{1}H NMR (200 MHz, DMSO-d_6): δ = 9.80 (1H, s, N=CH), 7.85–7.12 (7H, m, Ar-H), 4.73 (2H, s, NCH_2), 4.37 (2H, q, J = 7.1, OCH_2), 4.01 (2H, s, CH_2), 2.97 (3H, q, J = 7.0, CH_3), 2.65 (3H, t, J = 7.0, CH_3), 1.35 (3H, t, J = 7.1, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 167.31, 155.51, 153.90, 149.73, 146.75, 144.66, 144.91, 142.50, 135.80, 133.97, 129.90, 128.73, 125.96, 123.41, 124.01, 121.50, 62.80, 48.98, 38.94, 20.49, 16.16, 13.43 ppm; LC-MS: m/z = 391(m+1). Anal. Calcd. for $C_{22}H_{22}N_4O_3$: C,67.68; H, 5.68; N, 14.35 Found: C,C, 67.70; H, 5.65; N, 14.33 %.

4.3. Synthesis of Compounds 5(a–b)

4.3.1. *Conventional Method*

Compounds **4(a–b)** (0.01 mol) was refluxed with 1 equiv. of NaOH in absolute ethanol for 4 h. Then, the mixture was cooled at room temperature , poured into cold water and acidified to pH 5 with conc. HCl. The precipitate was filtered off, washed with H_2O and recrystallized from ethanol-water (3:1).

4.3.2. *Microwave Method*

The mixture of compounds **4(a–b)** (0.01 mol) and NaOH (0.1 mol) in ethanol was taken in a closed vessel and exposed to

microwave irradiation at 110 °C for 15 min. Then, the mixture was cooled to room temperature, poured into cold water and acidified to pH 5 with conc. HCl. The precipitate was filtered off, washed with H_2O. This crude product was recrystallized from ethanol-water (3:1).

{4-[(9*H*-Fluoren-3-ylmethylidene)amino]-3-methyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl} acetic acid (**5a**): IR (KBr): ν = 3431 (OH), 3057 (ArCH), 1692, 1663 (C=O), 1610 (C=N), 1292 (C-O),^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.81 (1H, s, COOH), 9.75 (1H, s, N=CH), 8.03–7.62 (7H, m, Ar-H), 4.23 (2H, s, NCH_2), 3.91 (2H, s, CH_2), 2.25 (3H, s, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 170.27, 158.90, 152.35, 148.23, 147.21, 145.12, 144.11, 142.62, 137.72, 134.27, 131.53, 126.31, 124.27, 124.01, 122.22, 121.00, 50.10, 36.20, 22.69 ppm; LC-MS: m/z = 349 (m+1). Anal. Calcd. for $C_{19}H_{16}N_4O_3$: C, 65.51; H, 4.63; N, 16.08 Found: C, 65.55; H, 4.66; N, 16.04 %.

{4-[(9*H*-Fluoren-3-ylmethylidene)amino]-3-ethyl-5-oxo-4,5-dihydro-1*H*-1, 2,4-triazol-1-yl}acetic acid (**5b**): IR (KBr): ν = 3455 (OH), 3043 (ArCH), 1699, 1676 (C= O), 1637 (C=N), 1282 (C-O), ^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.93 (1H, s, COOH), 10.09 (1H, s, N=CH), 8.91–7.50 (7H, m, Ar-H), 4.26 (2H, s, NCH_2), 4.21 (2H, s, CH_2), 2.15 (2H, q, J = 7.1, CH_2), 1.43 (3H, t, J = 7.1, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 173.46, 159.42, 154.65, 149.53, 145.86, 144.32, 142.01, 140.32, 139.12, 135.37, 130.11, 125.21, 122.07, 120.81, 119.09, 118.51, 52.08, 39.52, 25.09, 13.34 ppm; LC-MS: m/z = 363(m+1). Anal. Calcd. for $C_{20}H_{18}N_4O_3$: C, 66.29; H, 5.01; N, 15.46 Found: : C, 66.33; H, 5.04; N, 15.43 %.

4.4. Synthesis of Compounds 6(a–b)

4.4.1. *Conventional Method*

A solution of compounds **4(a–b)** (0.01 mol) in ethanol (30 mL) was refluxed with 2-phenylacetohydrazide (0.01 mol) for eight hours. After the reaction was completed (monitored by TLC, ethyl acetate:hexane, 3:1). The mixture was cooled to room temperature and the product was precipitated by addition of water. It was filtered off, washed with water and recrystallized from ethanol.

4.4.2. *Microwave Method*

A solution of compounds **4(a–b)** (0.01 mol) in ethanol (10 mL) and 2-phenylacetohydrazide (0.01 mol) were taken in a closed vessel. The mixture was exposed to microwave irradiation at 300 W, 130 °C for 20 min with pressure control. Then, the mixture was cooled to room temperature and the product was precipitated by addition of water. It was filtered off, washed with water and recrystallized from ethanol.

2-{4-[(9*H*-Fluoren-3-ylmethylene) amino]-3-methyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl}-*N*′-(phenylacetyl) acetohydrazide (**6a**): IR (KBr): ν = 3180, 3060 (NH), 1742, 1703, 1665 (C=0), 1595 (C=N) cm^{-1}, ^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.65 (1H, s, NH), 11.42 (1H, s, NH), 9.70 (1H, s, N=CH), 8.26–7.32 (12H, m, Ar-H), 4.63 (2H, s, NCH_2), 3.98 (2H, s, CH_2), 2.32 (2H, s, CH_2), 1.21 (3H, s, CH_3) ppm;^{13}C NMR (50 MHz, DMSO-d_6): 170.45,166.54, 157.50, 147.22, 144.42, 144.06, 142.19, 137.13, 135.91, 128.97, 127.77, 127.04, 126.92, 125.69, 124.94,123.86, 122.01, 61.96, 46.97, 27.04, 15.76 ppm; LC-MS: m/z = 481(m+1). Anal. Calcd. for $C_{27}H_{24}N_6O_3$: C, 67.49; H, 5.03; N, 17.49 Found: C,67.51; H, 5.00; N, 17.52 %.

2-{4-[(9*H*-Fluoren-3-ylmethylene)amino]-3-methyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl}-*N*′-(phenylacetyl)acetohydrazide (**6b**): IR (KBr): ν = 3187, 3071 (NH), 1745, 1711, 1678 (C= 0), 1601 (C=N) cm^{-1}, ^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.83 (1H, s, NH), 11.49 (1H, s, NH), 9.70 (1H, s, N=CH), 8.26–7.32 (12H, m, Ar-H), 4.63 (2H, s, NCH_2), 3.98 (2H, s, CH_2), 2.32 (2H, q, J = 7.0 CH_2), 1.21 (3H, t, J = 7.0, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 170.05, 168.52, 157.55, 147.19, 144.90, 144.00, 142.29, 137.13, 135.39, 132.97, 128.07, 127.04, 126.92, 126.59, 125.81,124.06, 122.11, 63.02, 48.13, 39.54, 25.90, 15.06 ppm; LC-MS: m/z = 495 (m+1). Anal. Calcd. for $C_{28}H_{26}N_6O_3$: C, 68.00; H, 5.30; N, 16.99 Found: C, 68.03; H, 5.31; N, 17.02 %.

4.5. Synthesis of Compounds 7(a–b)

4.5.1. *Conventional Method*

Hydrazine monohydrate (0.025 mol) was added to a solution of compound **4(a–b)** in dry ethanol (25 mL), an refluxed for 6 h (monitored by TLC, ethyl acetate: hexane, 4:1). After cooling the mixture to room temperature, a white solid appeared. This crude product was filtered, dried and recrystallized from ethanol to yield the pure product.

4.5.2. *Microwave Method*

Solution of compound **4(a–b)** (0.01 mol) in dry ethanol (10 mL) and hydrazine monohydrate (0.025 mol) were placed in a closed vessel. The mixture was irradiated in microwave oven at 130 °C for 10 min at 300 W maximum power. After the reaction was completed (monitored as stated above), the mixture was cooled to room temperature, transferred to a beaker and a white solid appeared. This crude product was filtered and purified as before.

2-{4-[(9*H*-Fluoren-3-ylmethylidene)amino]-3-methyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl} acetohydrazide (**7a**): IR (KBr): ν = 3321,3264 (NH_2), 3150 (NH), 1702, 1654 (C=0), 1604 (C=N) cm^{-1}, ^{1}H NMR (200 MHz, DMSO-d_6): δ = 9.28 (1H, s, NH), 8.81 (1H, s, N=CH), 7.90–6.94 (7H, m, Ar-H), 3.82 (2H, s, NH_2), 3.82 (2H, s, NCH_2), 3.54 (2H, s, CH_2), 1.85 (3H, s, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 168.25, 154.05, 152.61, 148.21, 146.62, 145.06, 143.21, 141.00, 136.20, 135.07, 130.11, 129.01, 127.43, 124.00, 122.61, 120.10, 47.56, 37.54, 19.29 ppm; LC-MS: m/z = 363(m+1). Anal. Calcd. for $C_{19}H_{18}N_6O_3$: C, 62.97; H, 5.01; N, 23.19. Found: C, 63.01; H, 5.00; N, 23.20 %.

2-{4-[(9*H*-Fluoren-3-ylmethylidene)amino]-3-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-1-yl}acetohydrazide (**7b**): IR (KBr): ν = 3357, 3201 (NH_2), 3159 (NH), 1710, 1678 (C=0), 1600 (C=N) cm^{-1}, ^{1}H NMR (200 MHz, DMSO-d_6): δ = 9.47 (1H, s, NH), 8.90 (1H, s, N=CH), 7.99–6.95 (7H, m, Ar-H), 3.92 (2H, s, NH_2), 3.71 (2H, s, NCH_2), 3.54 (2H, s, CH_2), 2.45 (2H, q, J = 7.2, CH_2), 1.27(3H,t, J = 7.2, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 170.05, 157.13, 153.06, 149.22, 145.74, 143.97, 142.75, 142.00, 137.20, 136.97, 132.01, 129.26, 128.03, 124.50, 123.61, 122.10, 49.01, 35.05, 23.81, 13.31 ppm; LC-MS: m/z = 377(m+1). Anal. Calcd. for $C_{20}H_{20}N_6O_3$: C, 63.82; H, 5.36; N, 22.33 Found: C, 63.80; H, 5.41; N, 22.29 %.

4.6. Synthesis of Compounds 8(a–b)

4.6.1. *Conventional Method*

Solutions of KOH (0.01 mol) in water (20 mL) and CS_2 (0.01 mol) were added to a solution of compounds **7(a–b)** (0.01 mol) in ethanol (20 mL) and then, the mixture was refluxed for 8 h. After the reaction was complete, (monitored by TLC ethyl acetate: hexane, 3:1), the mixture was cooled to room temperature and neutralized with diluted HCl (4N). The mixture was left to cool and the precipitated product was filtered, washed with H_2O and recrystallized from ethanol.

4.6.2. *Microwave Method*

Solutions of compounds **7(a–b)** (0.01 mol) in ethanol (10 mL) and KOH (0.01 mol) in water (5 mL) were placed in a microwave process vial. Then, the mixture was heated under microwave irradiation at 300 W at 100 °C, with stirring and air-jet cooling for 5 min. After the mixture was cooled, CS_2 (0.01 mol) was added to the mixture and it was then heated again 300 W at 100 °C. Completion of the reaction was achieved in 10 min as indicated by TLC. Then, the mixture was neutralized with 4 N HCl and left to cool. The precipitated product was filtered, washed with H_2O and recrystallized from Ethanol.

4-[(9*H*-Fluoren-3-ylmethylidene)amino]-5-methyl-2-[(5-sulfanyl-1,3,4-oxadiazol-2-yl)methyl]-2,4-dihydro-3*H*-1,2,4-triazol-3-one (**8a**): IR (KBr): ν = 3054 (ArCH), 2997 (SH), 1683 (C=O), 1621 (C=C), 1600 (C=N), ^{1}H NMR (200 MHz, DMSO-d_6): δ = 13.45 (1H, br, SH), 11.75 (1H, br, NH), 9.83 (1H, s, N=CH), 8.03–7.39 (7H, m, ArH), 4.94 (2H, s, NCH_2), 3.98 (2H, s, CH_2), 2.39 (3H, s, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 178.96, 156.51, 155.02, 154.02, 153.80, 151.01, 148.91, 145.52, 144.08, 143.91, 135.94, 132.90, 128.06, 125.71, 124.90, 124.01, 121.50, 119.10,39.84, 17.99 ppm; LC-MS: m/z = 405(m+1). Anal. Calcd. for $C_{20}H_{16}N_6O_2S$: C, 59.39; H, 3.99; N, 20.78 Found: C, 59.41; H, 3.97; N, 20.80 %.

4-[(9*H*-Fluoren-3-ylmethylidene)amino]-5-ethyl-2-[(5-sulfanyl-1,3,4-oxadiazol-2-yl)methyl]-2,4-dihydro-3*H*-1,2,4-triazol-3-one (**8b**): IR (KBr): ν = 3090 (ArCH), 2981 (SH), 1694 (C=O), 1620 (C=C), 1578 (C=N), ^{1}H NMR (200 MHz, DMSO-d_6): δ = 14.00 (1H,br,SH), 11.90 (1H, br, NH), 9.71 (1H, s, N=CH), 8.10–7.40 (7H, m, ArH), 4.92 (2H, s, NCH_2), 4.00 (2H, s, CH_2), 2.39 (2H, q, J = 7.1, CH_2), 1.10 (3H, t, J = 7.1, CH_3) ppm; ^{13}C NMR (50 MHz, DMSO-d_6): 177.05, 158.11, 156.82, 154.12, 153.00, 152.41, 149.23, 147.03, 145.58, 144.01, 137.72, 135.00, 129.46, 128.02, 125.00, 123.91, 122.00, 118.16, 40.04, 38.02, 23.11, 13.19 ppm; LC-MS: m/z = 419(m+1). Anal. Calcd. for $C_{21}H_{18}N_6O_2S$: C, 60.27; H, 4.34; N, 20.08 Found: C, 60.29; H, 4.35; N, 20.06 %.

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