e-ISSN: 2687-6698 **Research Article**

Turkish Journal of

Analytical Chemistry

TurkJAC

https://dergipark.org.tr/tr/pub/turkjac

New 1H-1,2,3-triazol derivatives: Synthesis, characterization and antioxidant activity

Fatih Çelik

Karadeniz Technical University, Faculty of Sciences, Department of Chemistry, 61080 Trabzon, Türkiye

Abstract

4-bromo-N-(4-((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-methoxy benzylidene) aniline (3), 2-((1-(3-(1,3-dioxoisoindolin-2-yl) propyl)-1H-1,2,3-triazol-4-yl)methoxy) benzaldehyde (6), and 4-((1-(3-(1,3-dioxoisoindolin-2-yl)propyl) -1H-1,2,3-triazol-4-yl)methoxy)-3-methoxybenzaldehyde (8) were synthesized. The compounds were characterized by FTIR, ^{1}H-NMR and ^{13}C-NMR spectroscopic methods. The antioxidant properties of the compounds were evaluated using two widely accepted methodologies assays (DPPH and FRAP). Compound **3** has the highest antioxidant potential among the compounds.

Keywords: 1,2,3-triazole, organic synthesis, antioxidant activity, FRAP assay

1. Introduction

1,2,3-Triazoles are five-membered heterocyclic compounds containing three nitrogen atoms in the ring. These compounds have attracted significant interest due to their extraordinary stability, ease of synthesis, and various biological activities. The triazole ring, in particular, has been incorporated into many drug candidates because of its ability to interact with a variety of biological targets. 1,2,3-Triazoles exhibit antimicrobial, antifungal, anticancer, and anti-inflammatory activities, making them valuable in the development of new therapeutic agents [1–3]. The synthesis of 1,2,3-triazoles has been greatly facilitated with the advent of the concept of "click chemistry." This concept involves the copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction, which efficiently and regioselectively forms 1,2,3-triazole rings, enabling the creation of complex molecules with high yields and minimal side products. Functionalizing the 1,2,3-triazole ring at different positions further enhances their appeal for use in drug design, materials science, and as ligands in coordination chemistry [4–7]. The combination of Schiff bases and 1,2,3-triazoles is an exciting area of research. By synthesizing hybrid molecules that incorporate both the imine group of Schiff bases and the triazole ring, the aim is to combine the distinctive advantages of both structures. These hybrid compounds often exhibit improved biological and chemical properties compared to their individual components. Schiff base-triazole derivatives may demonstrate stronger antimicrobial activity, increased stability, or enhanced metal coordination ability, making them particularly useful in drug development and catalysis. Furthermore, the structural diversity of Schiff bases and the regioselectivity of 1,2,3-triazole formation offer a wide range of possibilities for the creation of compounds with new properties. This opens new avenues for the development of multifunctional agents that can be applied in various fields, such as medicinal chemistry, materials science, and beyond [8–11].

2. Experimental

2.1. Instrumentation

IR spectra of the synthesized compounds were taken on a Perkin Elmer FT-IR 1600 FT-IR (4000-400 cm^{-1}) spectrophotometer device, and ^{1}H-NMR, ^{13}C-NMR spectra were taken on a Bruker brand 400 MHz NMR device with DMSO-d_6 solvent. Antioxidant measurements were made using a Buchi brand spectrophotometer. The solvents and chemicals used in

Citation: F. Çelik, New 1H-1,2,3-triazol derivatives: Synthesis, characterization and antioxidant activity, Turk J Anal Chem, 7(2), 2025, 191–194.

Author of correspondence: fatih.celik502@gmail.com
Tel: +90 (462) 377 25 25 **Fax:** +90 (462) 325 31 96
Received: April 22, 2025 **Accepted:** May 21, 2025
https://doi.org/10.51435/turkjac.1681862

synthesis and structure elucidation were obtained from Fluka, Merck and Aldrich companies, and all solvents were subjected to appropriate purification and drying processes.

2.2. Synthesis of 4-bromo-N-(4-((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-methoxybenzylidene)aniline (3)

Acetylene derivative 4-bromo-N-(3-nitro-4-(prop-2-yn-1-yloxy)benzylidene) aniline (1) (1 mmol) with 1-(azidomethyl)-4-bromobenzene (2) (1 mmol) was stirred in a water/acetone (1:4) mixture at room temperature in a 100 mL flask. Then, copper sulfate pentahydrate (1/20 mol) and sodium ascorbate (1/10 mol) were added to the reaction mixture in the specified proportions and refluxed for 18 hours. At the end of the reaction, the contents of the flask were poured into the ice-water mixture, and a solid was obtained, which was filtered and washed with water. It was crystallized with DMF-water and then dried over $CaCl_2$ in a desiccator (Scheme 1).

Yield: 96.72%; m.p.253-255°C; IR (ν,cm^{-1}): 1576 (CH=N), 1267 (C-O); ^{1}H-NMR (δ ppm): 3.81 (s, 3H, OCH_3), 5.27 (s, 2H, OCH_2), 5.63 (s, 2H, NCH_2), Arom. [7.22 (bs, 3H, CH), 7.31 (bs, 4H, CH), 7.59 (bs, 4H, CH)], 8.36 (s, 1H,1,2,3-trz.CH), 8.53 (s,1H, N=CH); ^{13}C-NMR (δ ppm): 52.46 (OCH_2), 55.99 (OCH_3), 61.86 (NCH_2), Arom. C [113.04(CH), 113.28 (CH), 123.66 (CH), 129.55(C), 149.65(C), 153.23(C), 4-Br-Ph_1C (124.60(CH), 132.19(CH), 118.54 (C), 151.04(C)), 4-Br-Ph_2C C(130.74 (CH), 132.49 (CH), 122.06 (C), 135.69 (C))], 126.24 (1,2,3-trz.(CH)), 135.84 (1,2,3-trz.(C)), 161.54 (N=CH)

2.3. Synthesis of 1,2,3-triazole derivatives 6

Azide derivative 2-(3-azidopropyl)isoindoline-1,3-dione (4) compound (1 mmol) and acetylene derivative 2-(prop-2-yn-1-yloxy)benzaldehyde (5) and 3-methoxy-4 –(prop-2-yn-1-yloxy)benzaldehyde (7) compounds (1 mmol) were mixed separately in water/acetone (1:4) in a 100 mL flask. Then, copper sulfate pentahydrate (1/20 mol) and sodium ascorbate (1/10 mol) were added to the reaction mixture in the specified proportions and refluxed for 18 hours. At the end of the reaction, the contents of the flask were poured into the ice-water mixture, and a solid was obtained, which was filtered and washed with water. It was crystallized with DMF-water and then dried over $CaCl_2$ in a desiccator (Scheme 1). Compounds **1,2, 5** and **7** were synthesized from literature [12,13].

2.3.1. 2-((1-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1H-1,2,3-triazol-4-yl)methoxy)benzaldehyde (6):

Yield: 86.48%; m.p.184-186°C; IR (ν,cm^{-1}): 1719 (C=O), 1600 (C=C), 1242 (C-O) ; ^{1}H-NMR (δ ppm): 2.20 (bs, 2H, CH_2), 3.63 (t, 2H, NCH_2), 4.44 (t, 2H, NCH_2), 5.32 (s, 2H, OCH_2), Arom. [7.12 (bs, 1H, CH), 7.44 (bs, 1H, CH), 7.68 (bs, 2H, CH), 7.84 (bs, 4H, CH)], 8.33 (s, 1H,1,2,3-trz.CH), 10.35 (s,1H, HC=O); ^{13}C-NMR (δ ppm): 29.08 (CH_2), 35.33 (NCH_2), 47.80 (NCH_2), 62.72 (OCH_2), Arom. C [114.62(CH), 121.57 (CH), 134.75 (CH), 136.83(CH), 124.90©, 160.87©, 4-Br-Ph_1C (123.43(CH), 128.04(CH), 132.20 ©)], 125.24 (1,2,3-trz.(CH)), 132.20 (1,2,3-trz.(C)), 168.32 (C=O), 189.65 (HC=O).

2.4. Synthesis of new 1,2,3-triazole derivative compound 8

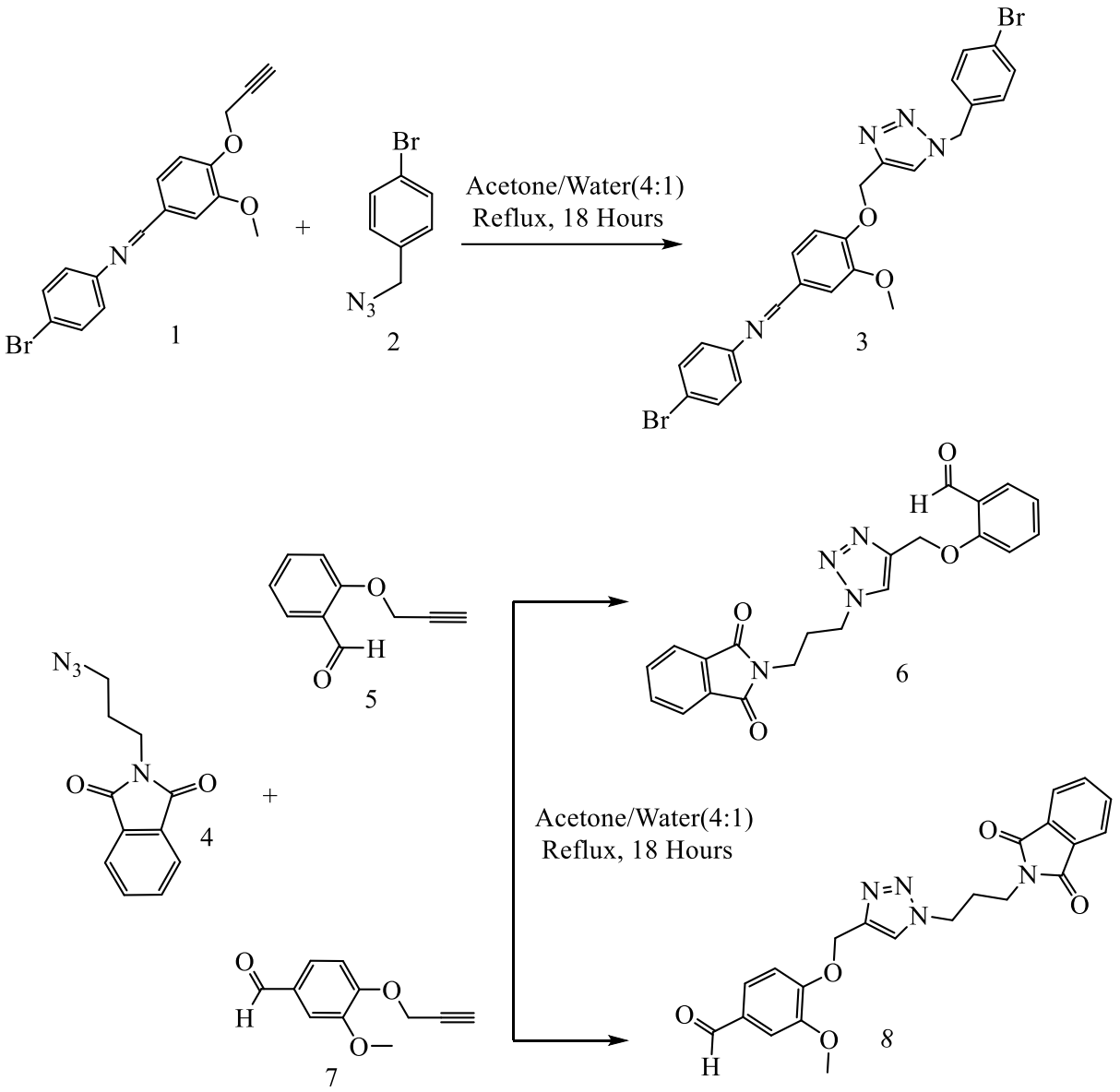
Azide derivative 2-(3-azidopropyl)isoindoline-1,3-dione (4) compound (1 mmol) and acetylene derivative 3-methoxy-4 -(prop-2-yn-1-yloxy)benzaldehyde (7) compounds (1 mmol) were mixed separately in water/acetone (1:4) in a 100 mL flask. Then, copper sulfate pentahydrate (1/20 mol) and sodium ascorbate (1/10 mol) were added to the reaction mixture in the specified proportions and refluxed for 18 hours. At the end of the reaction, the contents of the flask were poured into the ice-water mixture, and a solid was obtained, which was filtered and washed with water. It was crystallized with DMF-water and then dried over $CaCl_2$ in a desiccator (Scheme 1). Compounds **1,2** and **7** were synthesized from literature [12,13].

2.4.1. 4-((1-(3-(1,3-dioxoisoindolin-2-yl)propyl)-1H-1,2,3-triazol-4-yl)methoxy)-3-methoxybenzaldehyde (8):

Yield: 93.20%; m.p.195-197°C; IR (ν,cm^{-1}): 1704 (C=O), 1587 (C=C), 1259 (C-O) ; ^{1}H-NMR (δ ppm): 2.21 (bs, 2H, CH_2), 3.64 (t, 2H, NCH_2), 4.48 (t, 2H, NCH_2), 3.81 (s, 3H, OCH_3), 5.25 (s, 2H, OCH_2), Arom. [7.40 (bs, 2H, CH), 7.55 (bs, 2H, CH), 7.86 (bs, 3H, CH)], 8.29 (s, 1H,1,2,3-trz.CH), 9.85 (s,1H, HC=O); ^{13}C-NMR (δ ppm): 29.32 (CH_2), 35.18 (NCH_2), 47.78 (NCH_2), 55.91 (OCH_3), 62.19 (OCH_2), Arom. C [109.92(CH), 113.13 (CH), 123.46 (CH), 130.35(C), 149.89(C), 153.28(C), 4-Br-Ph_1C (126.38(CH), 134.94(CH), 142.02 (C))], 125.40 (1,2,3-trz.(CH)), 132.22 (1,2,3-trz.(C)), 168.46 (C=O), 192.04 (HC=O).

2.5. Antioxidant activity

The antioxidant properties of the compounds were evaluated using two widely accepted methodologies: the DPPH and FRAP assays, renowned for their effectiveness in gauging the antioxidant potential of diverse compounds. The DPPH assay, adapted from [14] measures the compounds' ability to scavenge the DPPH radical. This method relies on the decolorization of the purple DPPH solution upon interaction with antioxidants. Absorbance changes at 517 nm, recorded spectrophotometrically, indicate the degree of radical scavenging activity. Results, reported as SC_{50} values (mg of sample per mL), delineate the concentration required for a 50% reduction in the DPPH radical compared to the standard Trolox.



Scheme 1. Synthetic pathway for the preparation of compounds 3,6 and 8

Concurrently, the antioxidant capacity was determined through the FRAP method, following the protocol described by [15]. This approach involves the reduction of the Fe^{3+} -TPTZ complex to the Fe^{2+} -TPTZ complex in the presence of antioxidants. Spectrophotometric readings at 593 nm after a 4-minute incubation period elucidate the compounds' ability to reduce ferric ions. Results are expressed as μM Trolox equivalent per milligram of compound, where higher Trolox equivalent values denote elevated FRAP and hence increased antioxidant efficacy.

Both assays serve as robust tools for assessing the antioxidant prowess of compounds, providing valuable insights into their capacity to neutralize free radicals and reduce ferric ions. These standardized methodologies offer a comparative analysis of diverse compounds, enabling a comprehensive evaluation of their antioxidant capabilities.

3. Results and discussion

3.1. Synthesis

Compounds **3, 6** and **8** were synthesized with click reaction in the ^{1}H NMR spectra of compounds **3, 6,** and **8**, C-H proton signal belonging to 1,2,3-triazole ring was seen at 8.29–8.36 ppm as a singlet. Carbon peaks belonging to 1,2,3 triazole rings were observed at 1326.24-135.84 ppm in the ^{13}C-NMR spectra of compounds **3, 6**, and **8**. ^{1}H-, ^{13}C-NMR data confirm the structures of the compounds. The spectral data obtained are in full compliance with the literature. [16].

3.2. Antioxidant activity

The antioxidant capacities of the F-series compounds were investigated using DPPH radical scavenging and FRAP reducing power assays. The results revealed substantial differences among the tested compounds (Table 1).

Table 1. DPPH and FRAP activities of compounds 3, 6 and 8

Compound	DPPH (SC_{50}: mg/mL)	FRAP (µM Trolox Equivalent/mg compound
3	2.27±0.03[d]	278.47±0.42[c]
6	10.81±0.03[b]	28.05±0.82[c]
8	6.620±0.002[a]	No activity
Trolox	0.121±0.000[a]	Not tested

*Same letters in each column were not significantly different at $p < 0.05$ (Tukey's range test). The means of three replicates were given with ± standard deviations.

In the DPPH assay, where lower SC_{50} values indicate higher free radical scavenging activity, compound **3** exhibited the highest antioxidant potential (SC_{50} = 2.27 mg/mL). Compound **8** (SC_{50} = 6.62 mg/mL) showed moderate activity, whereas compound **6** (SC_{50} = 10.81 mg/mL) had the weakest radical scavenging capacity. When compared to Trolox (SC_{50} = 0.121 mg/mL), all tested compounds displayed significantly lower antioxidant efficiency.

The FRAP assay, which measures the ferric ion-reducing ability, showed that compound 3 had the highest reducing power (278.47 µM Trolox equivalent/mg compound), indicating strong electron donation potential. Compound 6 (28.05 µM Trolox equivalent/mg compound) exhibited a relatively weak reduction capacity. Furthermore, compound 8 did not show any detectable activity in the FRAP assay, suggesting its limited ability to reduce ferric ions.

These findings suggest that compound 3 has the highest antioxidant potential among the compounds, demonstrating superior performance in both radical scavenging and reducing power. Compound **8** exhibited moderate activity, while compound **6** had the weakest overall antioxidant efficacy.

Acknowledgment

The author thanks Dr. Ersan Bektaş for antioxidant studies.

References

[1] F. Çelik, Y. Ünver, B. Barut, A. Özel, K. Sancak, Synthesis, Characterization and Biological Activities of New Symmetric Bis-1,2,3-Triazoles with Click Chemistry, Medicinal Chemistry, 2018, 230-241.

[2] E. Düğdü, D. Ünlüer, F. Çelik, K. Sancak, Ş. A. Karaoğlu, A. Özel, Synthesis of Novel Symmetrical 1,4-Disubstituted 1,2,3-Bistriazole Derivatives via 'Click Chemistry' and Their Biological Evaluation, Molecules, 21, 2019, 659-672.

[3] F. Çelik, F. Türkan, A. Aras, M. N. Atalar, H. S. Karaman, Y. Ünver, N. Kahriman, Synthesis of novel 1,2,3 Triazole Derivatives and Assessment of Their Potential Cholinesterases, Glutathione S-transferase Enzymes Inhibitory Properties: An in Vitro and in Silico Study, Bioorganic Chemistry, 107, 2021.

[4] R. P. Frutos, S. Rodriguez, N. D. Patel, D. Reeves, T. Tampone, C.H. Senanayake, A General and Practical Synthesis of N-Aryl-3- 4-(imidazol-4-yl)-1,2,3-triazol-1-yl benzamide Anti-Inflammatory Cytokine Inhibitors, Asian Journal of Organic Chemistry, 3, 2014, 769-772.

[5] R. Jain, P. Gahlyan, S. Dwivedi, R. Konwar, S. Kumar, M. Bhandari, R. Arora, R. Kakkar, R. Kumar, A.K. Prasad, Design, Synthesis and Evaluation of 1H-1,2,3-Triazol-4-yl-methyl Tethered 3-Pyrrolylisatins as Potent Anti-Breast Cancer Agents, Chemistry Select, 19, 2018, 5263-5268.

[6] D. L. Jardim, M. Schwaederle, D. S. Hong, R. Kurzrock, An appraisal of drug development timelines in the Era of precision oncology, Oncotarget, 7, 2016, 53037-53046.

[7] V. Judge, B. Narasimhan, M. Ahuja, D. Sriram, P. Yogeeswari, Isonicotinic Acid Hydrazide Derivatives: Synthesis, Antimycobacterial, Antiviral, Antimicrobial Activity and QSAR Studies, Letters in Drug Design & Discovery, 8, 2011, 792-810.

[8] V. Judge, B. Narasimhan, M. Ahuja, D. Sriram, P. Yogeeswari, E. De Clercq, C. Pannecouque, J. Balzarini, Isonicotinic acid hydrazide derivatives: synthesis, antimicrobial activity, and QSAR studies, Medicinal Chemistry Research, 21, 2012, 1451-1470.

[9] D. Kumar, N.M. Kumar, S. Ghosh, K. Shah, Novel bis(indolyl)hydrazide-hydrazones as potent cytotoxic agents, Bioorganic & Medicinal Chemistry Letters, 22, 2012, 212-215.

[10] K.S. Kumar, S. Mohanty, G.P. Reddy, V. Siddaiah, J.D. Lilakar, G.L. Goud, Synthesis and Antimicrobial Activity of 3-{2-(1-Aryl-1H-1,2,3-triazol-4-yl)methoxy -5-fluorophenyl}isoxazoles, Russian Journal of General Chemistry, 89, 2019, 1221-1224.

[11] S. Kumar, B. Sharma, V. Mehra, V. Kumar, Recent accomplishments on the synthetic/biological facets of pharmacologically active 1H-1,2,3-triazoles, European Journal of Medicinal Chemistry, 212, 2021, 113069.

[12] S. Gallagher, M. Hashemzadeh, L.R. Peyton, Triazole antifungals: A review. Drugs Today, 51, 2015,705-718.

[13] H. H. Renate, M. G. Eric, L. Carmen, J. S. Peter, W. Baojie, G. F. Scott, G. Jiri, J. R. Philip, C. Kelly, Synthesis, antimalarial and antitubercular activity of acetylenic chalcones, Bioorganic & Medicinal Chemistry Letters, 20, 2010, 942-944.

[14] M. Cuendet, K. Hostettmann, O. Potterat, W. Dyatmiko, Iridoid Glucosides with Free Radical Scavenging Properties from Fagraea blumei, Helv Chim Acta, 80, 1997, 1144-1152

[15] I.F. Benzie, J.J. Strain, The ferric reducing ability of plasma (FRAP) as a measure of "antioxidant power": the FRAP assay, Anal Biochem, 239, 1996, 70-76.

[16] F. Çelik, Y. Ünver, B. Barut, A. Özel, K. Sancak, Synthesis, Characterization and Biological Activities of New Symmetric Bis-1,2,3-Triazoles with Click Chemistry, Medicinal Chemistry, 14, 2018, 230-241.