Baghdad Science Journal

Volume 22 | Issue 6 Article 7

6-17-2025

Synthesis and Antioxidant Evaluation of Urea, Carbamate, and Triazole Derivatives of (2-(6-Methoxynaphthalen-2-yl) propanoyl) glycinoyl azide

Jihan A. Mustafa
Department of Chemistry, College of Science, University of Duhok, Duhok, Iraq, jihan.ahmed@uod.ac

Huda A. Basheer
Department of Chemistry, Faculty of Science, University of Zakho, Duhok, Iraq, huda.basheer@uoz.edu.krd

Parween H. Saleem
Department of Chemistry, College of Science, University of Duhok, Duhok, Iraq, parween.saleem@uod.ac

How to Cite this Article

Mustafa, Jihan A.; Basheer, Huda A.; and Saleem, Parween H. (2025) "Synthesis and Antioxidant Evaluation of Urea, Carbamate, and Triazole Derivatives of (2-(6-Methoxynaphthalen-2-yl) propanoyl) glycinoyl azide," *Baghdad Science Journal*: Vol. 22: Iss. 6, Article 7.
DOI: https://doi.org/10.21123/2411-7986.4957

BAGHDAD SCIENCE JOURNAL 2025;22(6):1815–1828

Scan the QR to view the full-text article on the journal website

RESEARCH ARTICLE

Synthesis and Antioxidant Evaluation of Urea, Carbamate, and Triazole Derivatives of (2-(6-Methoxynaphthalen-2-yl) propanoyl) glycinoyl azide

Jihan A. Mustafa [1,*], **Huda A. Basheer** [2], **Parween H. Saleem** [1]

[1] Department of Chemistry, College of Science, University of Duhok, Duhok, Iraq
[2] Department of Chemistry, Faculty of Science, University of Zakho, Duhok, Iraq

ABSTRACT

In this study, a novel series of compounds, derived from the drug naproxen, was synthesized, this series includes carbamates, ureas, semicarbazides, and 1,2,4-triazole derivatives, and the synthesis was achieved through a multi-step synthetic approach. Initially, hydrazide (1) was prepared by reacting naproxen amino acid ester with hydrazine hydrate, followed by its conversion to naproxen glycine azide (2) through treatment with sodium nitrite in hydrochloric acid. Azide (2) was then subjected to thermal decomposition via Curtius rearrangement to yield isocyanate (3). Isocyanate (3) was subsequently reacted with various reagents, such as water, alcohol, amine, concentrated hydrochloric acid, hydrazine, and naproxen hydrazide, resulting in the formation of symmetrical urea (4), carbamates (5a-e), ureas (6a-d), hydrochloride salt (7) semicarbazides (8), and (11). Furthermore, compound (9) was synthesized by refluxing semicarbazide (8) with acetyl chloride, and both compounds (9 and 11) were subsequently converted into 1,2,4-triazol-5-one derivatives (10 and 12) through a cyclization reaction. In a parallel line of research, nucleophilic substitution reactions were performed on hydrazide (1) using acetyl chloride, aryl sulfonyl chloride (benzene or toluene), and terephthaloyl chloride, yielding substituted hydrazide derivatives (13, 15a-b, and 16), respectively. Diamide compounds (13, 16) were further cyclized with ammonium acetate to produce 1,2,4-triazole derivatives (14, 17). The progression of these chemical reactions were monitored using thin-layer chromatography (TLC), and synthesized compounds were identified using IR, 1H NMR, and 13C NMR spectroscopy. The antioxidant properties of these compounds were extensively assessed, contributing to the development of novel derivatives with potential applications in pharmacology and medicinal chemistry.

Keywords: Antioxidants activity, Carbamate, Curtius rearrangement, Triazole, Urea

Introduction

Naproxen, a propionic acid derivative, belongs to the family of nonsteroidal anti-inflammatory drugs and has been the subject of extensive research on its chemical derivatives.[1–3] These derivatives exhibit various biological activities, including potential anti-inflammatory,[4,5] antimicrobial,[6] antibacterial,[7] anticancer activity.[8–10] Compounds containing nitrogen, such as amines, amides, ureas, acyl ureas, and carbamates, are prevalent in natural products, agricultural chemicals, and pharmaceutical substances. They hold significance in biological and commercial contexts, making synthesizing diverse nitrogen-containing compounds a significant objective in organic chemistry.[11]

The Curtius rearrangement is a reaction characterized by the thermal decomposition of an acyl

Received 18 October 2023; revised 15 March 2024; accepted 17 March 2024.
Available online 17 June 2025

* Corresponding author.
E-mail addresses: jihan.ahmed@uod.ac (J. A. Mustafa), huda.basheer@uoz.edu.krd (H. A. Basheer), parween.saleem@uod.ac (P. H. Saleem).

https://doi.org/10.21123/2411-7986.4957

azide to yield an isocyanate.[12] This reaction is valuable for generating isocyanate and isocyanate-derived compounds, including carbamates, ureas, amides, and amines.[13] The Curtius rearrangement has found broad applications in synthesizing various natural products and important biomolecules.[14] Given the pivotal role of amines and amine-derived functional groups, such as ureas and urethanes, in medicinal chemistry, the Curtius rearrangement is increasingly employed in drug discovery and producing potential pharmaceutical candidates.[15]

The remarkable reactivity and adaptability of azides have stimulated extensive reviews within the research community. Scholars such as D. G. Jo et al.[16] M. Baumann et al.[17] and H. Choi et al.[18] have contributed insightful review articles on the subject of organic azides. Additionally, M. Balci[19] provided a comprehensive review in 2018.

Researchers have made noteworthy advancements in the synthesis of acyl azides. In 2020, M. Baumann et al.[20] reported their work, while C. R. Sagandira and P. Watts[21] detailed their findings in 2017. Their methodologies involved the use of flow apparatus coupled with automated extraction, facilitating efficient and controlled acyl azide synthesis.

A. Mata and colleagues[22], devised a method employing acyl azides for peptide synthesis, effectively circumventing side reactions such as epimerization while preserving chiral integrity. In a separate study, W. Yang et al.[23] used acyl azides for preparing of spirocyclic lactams via a one-pot cascade reaction. Accordingly, we describe here an approach to the synthesis of some new urea, carbamate and triazole derivatives in a goal increased antibiological activity by introducing naproxen moiety. Scheme 1, Scheme 2.

Experimental

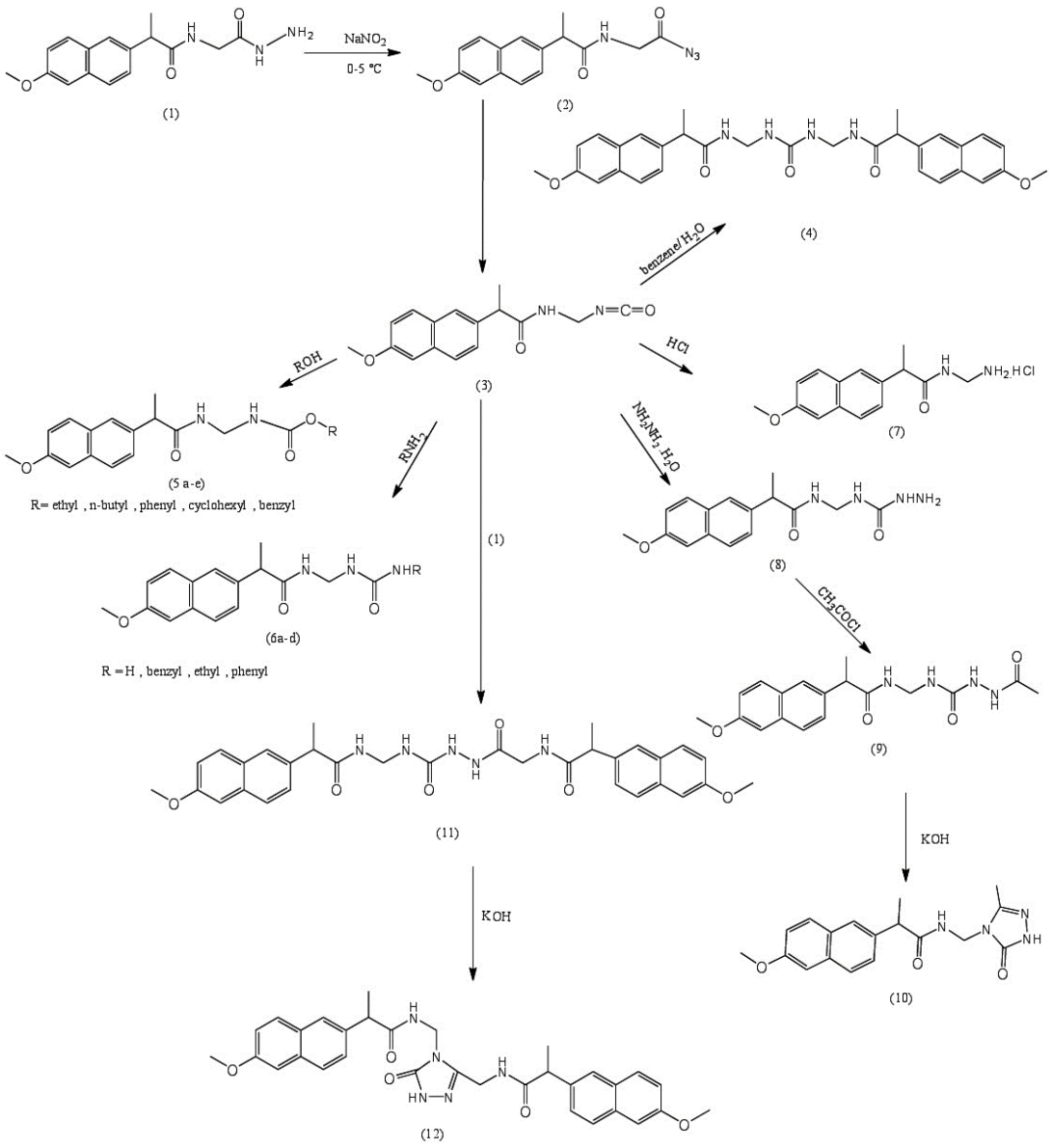
Uncorrected melting points were measured using bibby scientific SMP10 apparatus; IR spectra were measured by IR Affinity-1, Shimadzu spectrophotometer values were represented in cm^1. ^{1}HNMR was carried out on a Bruker 400 MHz spectrometer with TMS as internal standard. Furthermore, ^{13}CNMR was recorded on Bruker (100 MHz). The progress and completion of all reactions was monitored using TLC on Whitman Silica Gel 60 F254 aluminum-backed plates and ultraviolet light detection for reaction materials that are UV-active. Compound (1) N-(2-hydrazineyl-2-oxethyl)-2-(6-methoxy-naphalen-2-yl)propanamide was prepared according to literature procedure.[24,25]

(2-(6-methoxynaphalen-2-yl)propanoyl)glycinoyl azide (2)

A cold solution of sodium nitrite (3.88 g, 0.056 moles) in 5 ml of water was introduced dropwise with continuous stirring into a cold mixture of hydrazide (1) (0.6 g, 0.002 moles) in 10 ml of 25% HCl over a 15-minute period. The stirring process was sustained for 1 hour at 0 ˚C. Subsequently, the reaction mixture was carefully refrigerated overnight.[26] Confirmation of the successful formation of the azide compound was achieved through thin-layer chromatography (TLC), employing a 1:1 hexane:ethyl acetate solvent system (Rf = 0.60). The resultant mixture was then diluted with water, inducing the precipitation of a yellowish solid. This precipitate was meticulously isolated by filtration and subjected to thorough washing with a combination of water and ethanol.Yield: 72%; mp: 98–100˚C; yellowish solid; ^{1}H-NMR (DMSO-d_6) δ (ppm):1.35 (d, J = 8 Hz, 3H) $CH\underline{CH_3}$, 3.73 (q,J = 8 Hz,1H) $\underline{CH}CH_3$, 3.85 (s,3H) OCH_3, 4.12(s,2H) $NH\underline{CH_2}CO$, 7.13–7.78 (m,6H) Ar-H, 8.70 (b,1H)NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): δ 19.00 $CH\underline{CH_3}$, 43.74 $\underline{CH}CH_3$, 45.10 $NH\underline{CH_2}CO$, 55.60 OCH_3, 106.13, 119.07, 125.92, 126.97, 127.05, 128.82, 129.57, 133.60, 137.32, 157.44 (10C) Ar-C, 174.64, 177.93 (2C = O); IR (KBr), ν (cm^{-1}) 3280, 2146, 1699, 1649, 1606, 1267.

N-(isocyanatomethyl)-2-(6-methoxynaphthalen-2-yl)propanamide (3)

A quantity of 3.01 grams (0.01 moles) of Azide (2) was meticulously dissolved in dry toluene (25 ml) and subjected to reflux conditions for 48 hours.[27] The progression of the reaction was vigilantly monitored via thin-layer chromatography (TLC), using a hexane:ethyl acetate mixture in a 1:1 volume ratio as the eluent (Rf = 0.47). Subsequently, the solvent was efficiently removed under reduced pressure. The resulting residue was subjected to a purification process using a combination of petroleum ether and diethyl ether, yielding a beige precipitate of isocyanate. This precipitate was further subjected to recrystallization, employing a solvent system of dimethyl sulfoxide (DMSO) and water. Yield: 88%; mp: 238–239˚C; beige solid; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.32 (d, J = 8 Hz, 3H) $CH\underline{CH_3}$, 3.70 (q, J = 8 Hz, 1H) $\underline{CH}CH_3$, 3.86 (s,3H) OCH_3, 4.32(s,2H) $NH\underline{CH_2}N$, 7.12–7.82 (m,6H) Ar-H, 8.63 (b,1H) NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.87 $CH\underline{CH_3}$, 45.00 $\underline{CH}CH_3$, 49.01 $NH\underline{CH_2}N$, 55.60 OCH_3, 106.10, 119.03, 125.80, 126.98, 127.02, 128.81, 129.55, 133.59, 137.61, 157.44 (10C) Ar-C,

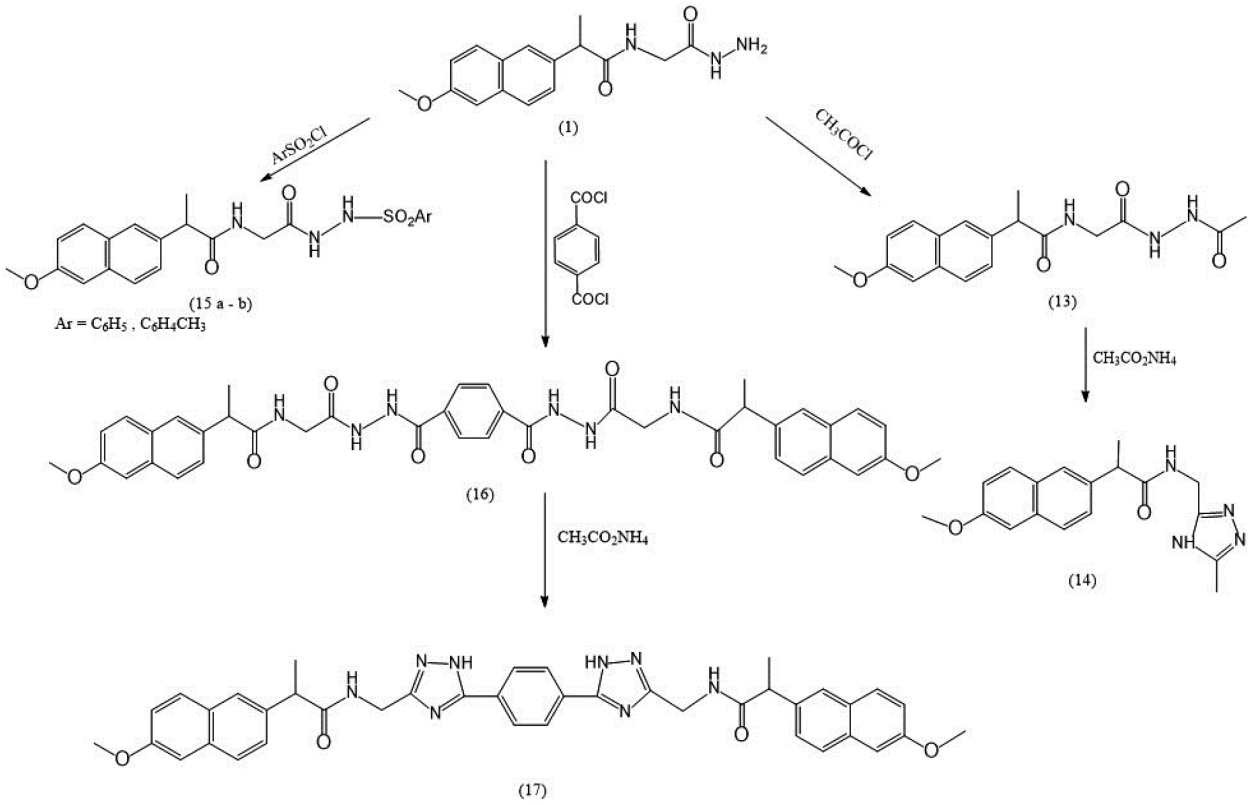


Scheme 1. Curtius rearrangement and its reactions.

157.58, 174.59 (2C = O); IR (KBr), ν (cm^{-1}) 3307, 2249, 1647,1606,1265.

N,N'-((carbonylbis(azanediyl))bis(methylene))bis(2-(6-methoxynaphthalen-2-yl)propan-amide (4)

A solution of Isocyanate (0.852 grams, 0.003 moles) in benzene (20 ml) was augmented with 2 ml of water. The resulting reaction mixture was subjected to reflux conditions for a duration of 48 hours.[28] To assess the reaction's progress, a thin-layer chromatography (TLC) analysis was performed using a hexane: ethyl acetate mixture in a 1:1 volume ratio as the eluent, yielding an Rf value of 0.87. Following this, the reaction mixture was allowed to cool to room temperature. Subsequent to the evaporation of the solvent, the remaining solid was subjected to a diethyl ether wash. Finally, the residue was meticulously recrystallized using a solvent system composed of methanol /water. Yield: 77%; mp: 148–150°C; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.37 (d, J = 8 Hz,6H) 2CH$\underline{CH_3}$, 3.73 (appearant q, J = 8 Hz, 2H) 2$\underline{CH}CH_3$, 3.86(s,6H) 2OCH_3, 4.29 (s,4H) 2NH$\underline{CH_2}$NH, 7.09–7.85 (m,12H) 2Ar-H, 6.65, 8.60 (b,4H) 4NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.86 (2C) 2CH$\underline{CH_3}$, 45.03(2C) 2$\underline{CH}CH_3$, 46.59 (2C) 2NH$\underline{CH_2}$NH, 55.59 (2C) 2OCH_3, 106.11, 119.02, 125.80, 126.97, 127.03, 128.81, 129.54, 133.59, 137.60, 157.44 (20C) 2Ar-C,



Scheme 2. Reactions of naproxen glycine hydrazide.

157.61(C = O),174.62 (2C = O). 7; IR (KBr), ν (cm^{-1}) 3354, 3296, 1704, 1651, 1606, 1265.

Synthesis of carbamate (5a-e)

General procedure

A suspension of Isocyanate (3) (0.005 moles) in 15 ml of dry toluene was vigorously stirred while introducing 0.005 moles of the respective alcohol (ethanol, 1-butanol, phenol, cyclohexanol, benzyl alcohol). The reaction mixture was subsequently refluxed for a duration of 72 hours.[29] The advancement of each reaction was closely monitored via thin-layer chromatography (TLC), wherein the formation of a distinctive reddish spot on the TLC plate indicated successful carbamate formation for each reaction. Following this, the reaction mixtures were subjected to evaporation under reduced pressure. The resulting residues were thoroughly washed with diethyl ether multiple times and subsequently recrystallized employing ethanol.

ethyl((2-(6-methoxynaphthalen-2-yl)propanamido)methyl)carbamate (5a)

Yield: 80%; mp: 154–156˚C; pale brown needles; eluent: hexane: ethyl acetate 1:1 and R_f = 0.53; ^{1}H-NMR ($CHCl_3$-d) δ (ppm): 1.20 (t, J = 8 Hz,3H) $CH_2\underline{CH_3}$, 1.55 (d, J = 8 Hz,3H) $CH\underline{CH_3}$, 3.67 (q, J = 8 Hz, 1H) $\underline{CH}CH_3$, 3.95(s,3H) OCH_3, 4.05 (q, J = 8 Hz, 2H)$\underline{CH_2}CH_3$, 4.50 (s,2H) $NH\underline{CH_2}NH$, 5.65, 6.40 (b,2H) 2NH, 7.14–7.74(m,6H) Ar-H; ^{13}C-NMR ($CHCl_3$-d) δ (ppm): 14.47 $CH_2\underline{CH_3}$, 18.33 $CH\underline{CH_3}$, 46.49 $\underline{CH}CH_3$, 46.81 $NH\underline{CH_2}NH$, 55.35 OCH_3, 61.12 $\underline{CH_2}CH_3$, 105.61, 119.21, 126.06, 126.14, 127.60, 128.97, 129.23, 133.79, 135.92, 157.77 (10C)Ar-C, 156.81, 175.41 (2C = O); IR (KBr), ν (cm^{-1}) 3313, 1694,1651, 1606,1263.

Butyl((2-(6-methoxynaphthalen-2-yl)propanamido)methyl)carbamate (5b)

Yield: 61%; m.p: 145–146˚C; white solid; eluent: hexane:ethyl acetate 1:1, R_f = 0.73; ^{1}H-NMR (DMSO-d_6) δ (ppm): 0.74 (t, J = 4 Hz,3H) $CH_2\underline{CH_3}$, 1.13–1.21 (m,2H)$CH_2\underline{CH_2}CH_3$, 1.39 (d, J = 8 Hz, 3H) $CH\underline{CH_3}$, 1.51–1.58 (m,2H) $CH_2\underline{CH_2}CH_2$, 3.70 (q, J = 8 Hz, 1H) $\underline{CH}CH_3$, 3.85(s,3H) OCH_3, 4.07 (appearant t, J = 8 Hz, 2H) $O\underline{CH_2}CH_2$, 4.50 (s,2H) $NH\underline{CH_2}NH$, 7.13–7.83 (m,6H) Ar-H, 6.88, 7.29 (b,2H) 2$\underline{NH}$; ^{13}C-NMR (DMSO-d_6) δ (ppm): 13.81$CH_2\underline{CH_3}$, 18.91$CH\underline{CH_3}$, 19.29 $CH_2\underline{CH_2}CH_3$, 30.96 $CH_2\underline{CH_2}CH_2$, 45.30 $\underline{CH}CH_3$, 47.01 $NH\underline{CH_2}NH$, 55.59 OCH_3, 64.89

O$\underline{CH_2}CH_2$, 106.09, 119.04, 125.74, 126.98, 127.01, 128.82, 129.54, 133.57, 138.01, 157.40 (10C) Ar-C, 155.76, 175.87 (2C = O); IR (KBr), ν (cm^{-1}) 3307, 1689, 1643, 1604, 1265.

Phenyl((2-(6-methoxynaphthalen-2-yl)propanamido)methyl)carbamate (5c)

Yield: 58%; mp: 158–160°C; off-white solid; eluent: hexane: ethyl acetate 2:1 with R_f = 0.21; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.33 (d, J = 8 Hz, 3H) CH$\underline{CH_3}$, 3.71 (q, J = 8 Hz, 1H) $\underline{CH}CH_3$, 3.86(s,3H) OCH_3, 4.31(s, 2H) NH$\underline{CH_2}$NH, 7.08–7.85(m,11H) Ar-H, 6.74, 8.51 (b,2H) 2NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.85CH$\underline{CH_3}$, 44.99$\underline{CH}CH_3$, 47.63 NH$\underline{CH_2}$NH, 55.59 OCH_3, 106.09, 119.04, 121.60, 124.52, 125.80, 126.61, 127.03, 128.17, 128.80, 129.57, 133.59, 137.54, 150.54, 157.43 (16C) Ar-C, 157.60, 174.61 (2C = O); IR (KBr), ν(cm^{-1}) 3313, 1712, 1654, 1606, 1263.

Cyclohexyl((2-(6-methoxynaphthalen-2-yl)propanamido)methyl)carbamate (5d)

Yield: 69%; mp: 172–174°C; brown solid; eluent: hexane: ethyl acetate 1:1 and R_f = 0.65; 1H-NMR ($CHCl_3$-d) δ (ppm): 1.28 (d, J = 8, 3H) CH$\underline{CH_3}$,1.48–1.72 (m,6H) Cyclo-H, 1.96–2.29 (m,4H) Cyclo-H, 3.72(q, J = 8 1H) $\underline{CH}CH_3$, 3.90(s,3H) OCH_3, 4.45(s, 2H) NH$\underline{CH_2}$NH, 4.95–5.34 (m,1H) O$\underline{CH}$ Cyclo-H, 5.66, 6.56 (b,2H) 2NH, 7.07–7.78 (m,6H) Ar-H; ^{13}C-NMR ($CHCl_3$-d) δ (ppm): 18.25 CH$\underline{CH_3}$, 23.66 (2C) Cyclo-C, 25.28(1C) Cyclo-C, 31.79 (2C) Cyclo-C, 46.43 $\underline{CH}CH_3$, 46.78 NH$\underline{CH_2}$NH, 55.33 OCH_3, 73.49 O$\underline{CH}$ Cyclo-H, 105.55,119.17,125.16,126.11, 127.58, 128.94, 129.22, 133.75, 135.91, 157.71(10C) Ar-C, 158.63,175.43 (2C = O); IR (KBr), ν (cm^{-1}) 3309, 1667, 1643, 1604, 1265.

Benzyl((2-(6-hydroxynaphthalen-2-yl)propanamido)methyl)carbamate (5e)

Yield: 81%; mp: 198–200°C; off-white solid; eluent: hexane: ethyl acetate 1:1, R_f = 0.5; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.37 (d, J = 8 Hz, 3H)CH$\underline{CH_3}$, 3.71 (q, J = 8 Hz,1H) $\underline{CH}CH_3$, 3.85 (s,3H) OCH_3, 4.29 (s, 2H) NH$\underline{CH_2}$NH, 4.90 (s,2H) O$\underline{CH_2}$-Ar, 7.01–7.94 (m,11H) Ar-H, 6.64, 8.63 (b,2H) 2NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.86 CH$\underline{CH_3}$, 44.99 $\underline{CH}CH_3$, 47.33 NH$\underline{CH_2}$NH, 55.60 OCH_3, 65.77 O$\underline{CH_2}$-Ar, 106.09, 119.03, 125.79, 126.98, 127.03, 127.94, 128.14, 128.80, 129.55, 130.40, 133.59, 136.07, 137.60, 157.43 (16C) Ar-C, 156.93, 174.60 (2C = O); IR (KBr), ν (cm^{-1}) 3305, 1701, 1647, 1604, 1265.

2-(6-methoxynaphthalen-2-yl)-N-(ureidomethyl)propanamide (6a)

To a chilled solution of concentrated ammonium hydroxide (15 ml) within an ice bath, isocyanates (3) (2.84 grams, 0.01 moles) were gradually introduced in portions over a 10-minute duration, with continuous stirring. Subsequently, the cooling bath was removed, and the reaction was brought to a reflux state for 20 hours, as confirmed by thin-layer chromatography (TLC).[30] The resulting reaction mixture was allowed to cool, and the solid product was thoroughly washed with water. A final purification step was executed through recrystallization in ethanol, ultimately yielding a precipitate. Yield: 82%; mp: 212–213°C; beige solid; eluent: hexane ethyl acetate 1:2 and $R_{f=}$ 0.11; ^{1}H NMR (DMSO-d_6) δ (ppm): 1.40(d, J = 8 Hz, 3H) CH$\underline{CH_3}$, 3.76 (appearant q, J = 8 Hz, 1H) $\underline{CH}CH_3$, 3.85 (s,3H) OCH_3, 4.30 (s,2H) NH$\underline{CH_2}$NH, 5.62 (b,2H) NH_2, 7.12–7.79 (m,6H) Ar-H, 6.59, 8.70 (b,2H) 2NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.86 CH$\underline{CH_3}$, 45.00 $\underline{CH}CH_3$, 45.91 NH$\underline{CH_2}$NH, 55.58 OCH_3, 106.08, 119.04, 125.78, 127.00, 127.03, 128.82, 129.57, 133.59, 137.66, 157.43 (10C) Ar-C, 158.72, 174.69 (2C = O); IR (KBr), ν (cm^{-1}): 3454, 3344,3294, 1643, 1608, 1267.

Synthesis of urea (6b-d)

General procedure

A mixture of isocyanate (3) (2.84 grams, 0.01 moles) and an equivalent amount of the respective amine (benzylamine, ethyl amine, aniline) was subjected to reflux in 10 ml of dry toluene for 72 hours, utilizing a sand bath. Subsequently, any excess solvent was efficiently removed under reduced pressure. The resulting residue was meticulously treated with diethyl ether, leading to the formation of a solid product. It was subjected to recrystallization using a suitable solvent to purify the product further.

N-((3-benzylureido)methyl)-2-(6-methoxynaphthalen-2-yl)propanamide (6b)

Yield: 91%, mp: 98–100°C; brown solid; eluent: hexane: ethyl acetate 1:1, R_f = 0.21; ^{1}H NMR ($CHCl_3$-d) δ (ppm): 1.53 (d, J = 8 Hz,3H) CH$\underline{CH_3}$,3.71 (q, J = 8 Hz,1H) $\underline{CH}CH_3$, 3.85 (s,2H) NH$\underline{CH_2}$Ar, 3.90(s,3H) OCH_3, 4.30(s,2H) NH$\underline{CH_2}$NH, 7.09–7.79(m,11H) Ar-H, 6.60,6.89, 8.40 (b,3H) 3NH; ^{13}C-NMR ($CHCl_3$-

d) δ (ppm): 18.27 $CH\underline{CH_3}$,43.36 $\underline{CH}CH_3$, 46.61 $NH\underline{CH_2}NH$, 55.30 OCH_3, 66.04 $NH\underline{CH_2}Ar$, 105.58, 119.19, 125.93, 126.99, 127.43, 127.57, 127.97, 128.60, 128.90, 129.22, 133.74, 137.75, 139.21, 157.70 (16C) Ar-C, 168.81, 175.11(2C = O); IR (KBr), ν (cm^{-1}): 3306, 3200, 1630, 1605, 1264.

N-((3-ethylureido)methyl)-2-(6-methoxynaphthalen-2-yl)propanamide (6c)

Yield: 72%, mp: 110–112°C; pale brown solid; eluent:(hexane: ethyl acetate 2:1) R_f = 0.31; ^{1}H NMR (DMSO-d_6) δ (ppm): 0.98 (t, J = 8 Hz, 3H)$CH_2\underline{CH_3}$, 1.39 (d, J = 8 Hz, 3H) $CH\underline{CH_3}$, 2.97–3.09 (m,2H) $\underline{CH_2}CH_3$, 3.66 (q, J = 8 Hz, 1H) $\underline{CH}CH_3$, 3.85(s,3H) OCH_3, 4.30(s,2H) $NH\underline{CH_2}NH$, 7.12–7.78(m,6H) Ar-H, 6.65,6.88,8.65(b,3H) 3NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 15.14 $CH_2\underline{CH_3}$, 19.05 $CH\underline{CH_3}$, 33.90 $O\underline{CH_2}CH_3$, 44.99 $\underline{CH}CH_3$, 45.50 $NH\underline{CH_2}NH$, 55.59 OCH_3, 106.09, 119.03, 125.74, 126.98, 127.02, 128.80, 129.54, 133.58, 138.01, 157.43 (10C) Ar-C, 157.40, 175.89 (2C = O); IR (KBr), ν (cm^{-1}): 3345, 3261, 1643, 1604, 1265.

2-(6-methoxynaphthalen-2-yl)-N-((3-phenylureido)methyl)propanamide (6d)

Yield: (55%); mp: 205–206°C; off-white solid; (eluent: hexane: ethyl acetate 4:1) R_f = 0.21; ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.43 (d, J = 8 Hz, 3H) $CH\underline{CH_3}$, 3.71 (q, J = 8 Hz, 1H) $\underline{CH}CH_3$, 3.89 (s,3H) OCH_3, 4.29 (s,2H) $NH\underline{CH_2}NH$, 7.11–7.76 (m,11H) Ar-H, 7.03, 7.37, 8.44 (b,3H) 3NH; ^{13}C-NMR (DMSO-d_6) δ (ppm):18.87 $CH\underline{CH_3}$, 44.12 $\underline{CH}CH_3$, 45.00 $NH\underline{CH_2}NH$, 55.60 OCH_3, 106.11, 119.02, 121.31, 125.79, 127.02, 127.04, 127.94, 128.81, 129.06, 129.55, 133.59, 137.61, 138.91, 157.44 (16C) Ar-C, 169.18, 174.11 (2C = O); IR (KBr), ν (cm^{-1}) 3362, 3281, 1643, 1604, 1265.

N-(aminomethyl)-2-(6-methoxynaphthalen-2-yl)propanamide hydrochloride (7)

A combination of Isocyanate (3) (2.84 grams, 0.01 moles) and 25% hydrochloric acid (15 ml) was subjected to reflux conditions for 24 hours. The mixture was stirred until the evolution of carbon dioxide (CO2) ceased. Subsequently, the reaction mixture was allowed to cool, resulting in the formation of a precipitate. This precipitate was meticulously filtered, washed with water, and subsequently dried in an oven at 50°C, yielding a pale orange solid product. [31] Further purification was carried out through recrystallization using ethanol; yield 78%; mp: 179–180°C; eluent: hexane: ethyl acetate 1:2, R_f = 0.68; ^{1}H NMR (DMSO-d_6) δ (ppm): 1.36 (d, J = 8 Hz, 3H) $CH\underline{CH_3}$, 3.72 (q, J = 8 Hz, 1H) $\underline{CH}CH_3$, 3.84 (s,3H) OCH_3, 4.14 (s,2H) $NH\underline{CH_2}NH_2$, 4.65 (b,2H) NH_2, 7.11–7.78 (m,6H) Ar-H, 8.67 (b,1H) NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.84 $CH\underline{CH_3}$, 44.99 $\underline{CH}CH_3$, 50.20 $NH\underline{CH_2}NH_2$, 55.60 OCH_3, 106.11, 119.02, 125.79, 126.98, 127.04, 128.80, 129.56, 133.59, 137.60, 157.43 (10C) Ar-C, 174.62 (C = O); IR (KBr), ν (cm^{-1}): 3419, 3329, 3319, 1658, 1598, 1251.

N-((2-(6-methoxynaphthalen-2-yl)propanamido)methyl)hydrazinecarboxamide (8)

A solution of Isocyanate (3) (1.42 grams, 0.005 moles) and (0.05 moles) hydrazine hydrate in 10 ml of ethanol was stirred for 24 hours. Subsequently, the reaction mixture was refluxed for 3 hours, followed by stirring without heating for an additional 24 hours. The solvent was systematically evaporated under reduced pressure, and the resulting solid product was diligently washed with water and subsequently filtered. The resulting brown precipitate underwent purification through recrystallization, employing a mixture of ethanol and water [32]; Yield: 81%; mp: 149–150°C; eluent: hexane: ethyl acetate 1:1, R_f = 0.26; ^{1}H NMR (DMSO-d_6) δ (ppm): 1.35 (d, J = 8 Hz, 3H) $CH\underline{CH_3}$, 3.71 (q, J = 8 Hz, 1H)$\underline{CH}CH_3$, 3.85 (s,3H) OCH_3, 4.10 (s,2H) NH_2, 4.36 (s,2H) $NH\underline{CH_2}NH$, 7.12–7.78 (m,6H) Ar-H, 6.67, 8.20, 8.66 (b,3H)3NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.86 $CH\underline{CH_3}$, 43.68 $\underline{CH}CH_3$, 45.02 $NH\underline{CH_2}NH$, 55.60 OCH_3, 106.11, 119.03, 125.80, 126.96, 127.03, 128.81, 129.54, 133.59, 137.60, 157.44 (10C) Ar-C, 157.62, 174.63 (2C = O); IR (KBr), ν (cm^{-1}): 3415, 3361, 3258, 1643, 1604, 1265.

2-acetyl-N-((2-(6-methoxynaphthalen-2-yl)propanamido)methyl)hydrazine-1-carboxamide (9)

Semicarbazide (8) (2.212 grams, 0.007 moles) was dissolved in a solution composed of pyridine as the solvent and tri-n-butylamine as the base. To this solution, acetyl chloride (0.007 moles) was introduced with continuous stirring. The reaction mixture was subjected to reflux conditions for 24 hours, as confirmed by (TLC). Subsequently, the reaction mixture was allowed to cool and carefully poured over ice water while stirring. The resulting mixture was left at room temperature for an additional 24 hours. The product was meticulously

filtered and subjected to several washes with diethyl ether.[33] Finally, the purified product was recrystallized using ethanol; Yield: 71%; mp: 82–84°C; off-white solid; eluent: hexane: ethyl acetate 2:1, R_f = 0.39; ^{1}H NMR (DMSO-d_6) δ (ppm): 1.29 (d, J = 8 Hz, 3H) CH$\underline{CH_3}$, 1.60 (s,3H) CO$\underline{CH_3}$, 3.61 (q, J = 8 Hz, 1H)$\underline{CH}CH_3$, 3.81 (s,3H) OCH_3, 4.67 (s,2H) NH$\underline{CH_2}$NH, 7.00–7.67 (m,6H) Ar-H,7.39, 7.82, 8.67, 10.02 (b,4H) 4NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.93 CH$\underline{CH_3}$, 20.24 CO$\underline{CH_3}$, 43.27 $\underline{CH}CH_3$, 45.16 NH$\underline{CH_2}$NH, 55.60 OCH_3, 106.12, 119.10, 125.88, 127.09, 128.74, 129.58, 133.61, 136.94, 137.73, 157.35 (10C) Ar-C, 159.43, 170.23, 174.90 (3C = O); IR (KBr), ν (cm^{-1}): 3275, 1705, 1631, 1600, 1261.

N-((2-(methoxynaphthalen-2-yl)propanamido)methyl)-2-((2-(6-methoxy naphthalen-2-yl) propanoyl)glycyl)hydrazine-1-carboxamide (11)

A solution of hydrazide (1) (0.9 grams, 0.003 moles) in tetrahydrofuran (25 ml) was prepared, to which a cold solution of isocyanate (3) (0.85 grams, 0.003 moles) in tetrahydrofuran (25 ml) was added dropwise with continuous stirring. The resulting mixture was subsequently refluxed for a duration of 72 hours; after which it was left at room temperature for an additional 24 hours. The solid product was effectively separated by filtration and underwent three rounds of washing with diethyl ether (3 × 15 ml), resulting in the isolation of an off-white solid product.[32] The purified product was further subjected to recrystallization, employing ethanol; yield 83%; mp: 134–135°C; eluent: hexane: ethyl acetate 1:1, R_f = 0.51; ^{1}H NMR (DMSO-d_6) δ (ppm): 1.41,1.48 (d, J = 8 Hz, 6H)2CH$\underline{CH_3}$, 3.49,3.61 (q, J = 8 Hz, 2H)2$\underline{CH}CH_3$, 3.79,3.82 (s,6H) 2OCH_3, 4.00 (s,2H)CO$\underline{CH_2}$NH, 4.32 (s,2H) NH$\underline{CH_2}$NH, 6.93–7.76 (m,12H) 2Ar-H, 6.43, 6.79, 8.16, 9.31, 9.97 (b,5H) 5NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.96, 19.00(2C) 2CH$\underline{CH_3}$, 42.04 CO$\underline{CH_2}$NH, 45.00, 45.16(2C) 2 $\underline{CH}CH_3$, 46.96 NH$\underline{CH_2}$NH, 55.40, 55.68(2C) 2 OCH_3, 105.92, 106.13, 118.90, 119.01, 125.84, 125.86, 126.98, 127.05, 128.69, 128.81, 129.59, 129.71, 133.77, 133.98, 136.71, 136.81, 138.12, 138.22, 157.19, 157.37 (20C) 2Ar-C, 158.30, 168.25, 173.68, 174.49 (4C = O); IR (KBr), ν (cm^{-1}): 3292, 3185, 1662,1649, 1606, 1265.

1,2,4-Triazol-5-one derivatives (10,12)

General method

A mixture of semicarbazide derivatives (9, 11) (0.002 moles in total) was refluxed with 20 ml of a 5% alcoholic potassium hydroxide solution for a period of 48 hours. Subsequently, the reaction solution was carefully neutralized through the gradual addition of 5% acetic acid until a precipitate appeared. The resulting precipitate was meticulously washed with water and subjected to recrystallization using ethanol.[34]

2-(6-methoxynaphthalen-2-yl)-N-((3-methyl-5-oxo-1,5-dihydro-4 H-1,2,4-triazol-4-yl) methyl)propanamide (10)

Yield: 53%; mp: 234–235°C; pale brown solid; eluent: hexane: ethyl acetate 1:1, R_f = 0.53; ^{1}H NMR (DMSO-d_6) δ (ppm): 1.37 (d, J = 8 Hz, 3H) CH$\underline{CH_3}$, 2.25(s,3H) = C$\underline{CH_3}$, 3.56 (q, J = 8 Hz,1H) $\underline{CH}CH_3$, 3.87 (s,3H) OCH_3, 4.75 (s,2H) NH$\underline{CH_2}$N, 7.02–7.82 (m,6H) Ar-H, 8.07, 11.25 (b,1H) 2NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 12.80 = C$\underline{CH_3}$, 18.97 CH$\underline{CH_3}$, 45.17 $\underline{CH}CH_3$, 46.21 NH$\underline{CH_2}$N, 55.61 OCH_3, 106.13, 119.14, 126.01, 126.92, 127.27, 128.86, 129.57, 133.67, 136.96, 157.54 (10C) Ar-C, 144.87 C = N, 158.96, 176.03 (2C = O); IR (KBr), ν (cm^{-1}): 3278, 3190, 1709, 1631, 1604, 1269.

N,N'-((5-oxo-1,5-dihydro-4 H-1,2,4-triazole-3,4-diyl)bis(methylene))bis(2-(6-methoxynaphthalen-2-yl)propanamide (12)

Yield: 63%; mp: 109–110°C; pale orange solid; eluent: hexane: ethyl acetate 1:1, R_f = 0.63; ^{1}H NMR (DMSO-d_6) δ, (ppm): 1.38,1.46 (d, J = 8 Hz, 6H) 2CH$\underline{CH_3}$, 3.65,3.72 (appearant q, J = 8 Hz,2H)2$\underline{CH}CH_3$, 3.81, 3.84 (s,6H) 2OCH_3, 4.06 (s,2H) C$\underline{CH_2}$NH, 4.93 (s,2H) NH$\underline{CH_2}$N, 7.110–7.80 (m,12H) 2Ar-H, 7.37, 8.84, 11.92 (b,3H)3NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 19.24, 19.34 (2C) 2 CH$\underline{CH_3}$, 22.01 C$\underline{CH_2}$NH, 45.78, 45.81 (2C) 2$\underline{CH}CH_3$, 46.96 NH$\underline{CH_2}$N, 55.58, 55.66 (2C) 2OCH_3, 105.99, 106.11, 118.90, 118.99, 125.80, 125.91, 127.03, 127.08, 127.11, 127.16, 128.83, 128.88, 129.53,129.59, 133.56,133.61, 137.75,137.81, 157.42, 157.51 (20C) 2Ar-C, 144.50 C = N, 172.87(C = O),176.38 176.42 (2C = O); IR (KBr), ν (cm^{-1}): 3390, 3270, 1709, 1638, 1604, 1265.

N-(2-(2-acetylhydrazineyl)-2-oxoethyl)-2-(6-methoxynaphthalen-2-yl) propanamide(13)

A procedure akin to that employed for compound (9) was applied here, utilizing 2.107 grams (0.007 moles) of hydrazide (1) and 0.007 moles of acetyl chloride[35], resulting in a yield of 63%; mp:128–129°C; off-white solid; eluent: hexane: ethyl acetate

1:1, R_f = 0.37; ^{1}H NMR (DMSO d_6) δ, ppm: 1.31(d, J = 8 Hz,3H)CH<u>CH</u>$_3$, 1.59 (s, 3H) CO<u>CH</u>$_3$, 3.67 (q, J = 8 Hz,1H) <u>CH</u>CH$_3$, 3.86(s,3H) OCH$_3$, 4.55 (s,2H) NH<u>CH</u>$_2$CO, 6.97–7.71 (m,6H) Ar-H, 7.27, 8.74, 10.09 (b,3H) 3NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.78 CH<u>CH</u>$_3$, 20.91 CO<u>CH</u>$_3$, 43.54 <u>CH</u>CH$_3$, 45.16 NH<u>CH</u>$_2$CO, 55.60 OCH$_3$, 106.11, 119.00, 125.86, 127.02, 127.49, 128.81, 129.57, 133.58, 137.67, 157.56 (10C) Ar-C, 166.72, 168.25, 174.31 (3C = O); IR (KBr), ν (cm^{-1}): 3260, 3110, 1755, 1708, 1631, 1604, 1265.

2-(6-methoxynaphthalen-2-yl)-N-(2-oxo-2-(2-(phenylsulfonyl)hydrazineyl)ethyl) propanamide (15a)

A procedure akin to that employed for compound (9) was applied here, with use of (2.107 g,0.007 mole) of hydrazide (1) and (0.007mole) phenyl sufonyl chloride to obtained brown participate; yield (59%); mp: 163–164˚C; eluent: hexane: ethyl acetate 1:1, R_f = 0.52; ^{1}H NMR (DMSO d_6) δ, ppm: 1.38 (d, J = 8 Hz,3H) CH<u>CH</u>$_3$, 3.79 (q, J = 8 Hz,1H) <u>CH</u>CH$_3$, 3.86 (s,3H) OCH$_3$, 4.03(s,2H) NH<u>CH</u>$_2$CO, 7.13–7.81 (m,11H) Ar-H, 8.23, 9.91, 10.14 (b,3H) 3NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 19.01 CH<u>CH</u>$_3$, 40.72 NH<u>CH</u>$_2$CO, 45.06 <u>CH</u>CH$_3$, 55.60 OCH$_3$, 106.09, 119.01, 125.85, 127.02, 127.62, 127.99, 128.79, 129.32, 129.58, 133.37, 133.59, 137.62, 139.46, 157.43 (16C) Ar-C, 168.47,174.75 (2C = O); IR (KBr), ν (cm^{-1}): 3298, 1708, 1639, 1601, 1338, 1261, 1153.

2-(6-methoxynaphthalen-2-yl)-N-(2-oxo-2-(2-tosylhydrazineyl)ethyl) propanamide(15b)

A similar procedure to (9) was used here, with use of (2.107 g,0.007 mole) of hydrazide (1) and (0.007 mole) toluene sulfonyl chloride to obtain (66 %); mp:158–159˚C; pale brown solid; eluent: hexane: ethyl acetate 1:1, R_f = 0.29; ^{1}H NMR (DMSO d_6) δ, ppm: 1.37 (d, J = 8 Hz,3H) CH<u>CH</u>$_3$, 2.00 (s,3H) Ar-<u>CH</u>$_3$, 3.78 (appearant q, J = 8 Hz,1H) <u>CH</u>CH$_3$, 3.87 (s,3H) OCH$_3$, 4.04 (s,2H) NH<u>CH</u>$_2$CO, 7.12–7.84 (m,10H) Ar-H, 8.25, 9.88, 10.13 (b, 3H) 3NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.80 CH<u>CH</u>$_3$, 20.86 Ar-<u>CH</u>$_3$, 41.17 NH<u>CH</u>$_2$CO, 45.16 <u>CH</u>CH$_3$, 55.60 OCH$_3$, 106.10, 119.09, 125.86, 127.07, 127.33, 128.74, 129.29, 129.57, 133.37, 133.66, 137.06, 137.69, 139.69, 157.43 (16C) Ar-C, 168.25, 174.27 (2C = O); IR (KBr), ν (cm^{-1}): 3282, 1712, 1654, 1604, 1381, 1265, 1157.

N,N'-((terephthaloylbis(hydrazine-2,1-diyl))bis(2-oxoethane-2,1-diyl))bis(2-(6-methoxy-naphthalen-2-yl)propanamide)(16)

A similar procedure to (9) was used here, with use of (2.107,0.007mole) of hydrazide (1) and (0.0035mole) terephthaloyl chloride to obtain (81%); mp: 170–171˚C; off-white solid; eluent: hexane: ethyl acetate 1:1, R_f = 0.40; ^{1}H NMR (DMSO d_6), δ, ppm: 1.38 (d, J = 8 Hz,6H) 2CH<u>CH</u>$_3$, 3.77 (q, J = 8 Hz,2H) 2<u>CH</u>CH$_3$, 3.87(s,6H) 2OCH$_3$, 4.04 (s,4H) 2NH<u>CH</u>$_2$CO, 7.11–7.88(m,16H) Ar-H, 8.20, 9.95, 10.11 (b,6H) 6NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.77 (2C) 2CH<u>CH</u>$_3$, 43.27 (2C) 2NH<u>CH</u>$_2$CO, 45.15 (2C) 2<u>CH</u>CH$_3$, 55.63 (2C) 2OCH$_3$, 106.10, 118.98, 125.86, 126.84, 127.06, 127.94, 128.81, 129.57, 133.03, 133.99, 137.69, 157.43 (26C) Ar-C, 165.68, 168.25, 174.27 (6C = O); IR (KBr), ν (cm^{-1}): 3294, 1695, 1655, 1606, 1265.

Synthesis of 1,2,4-triazole (14,17)

General procedure

A solution comprising 0.0016 moles of diamide (Compound 13, 16) was prepared in 20 mL of methanol. Subsequently, a separate solution containing 0.0032 moles of ammonium acetate (0.05 g) in 15 mL of methanol was added gradually under continuous stirring. The resulting reaction mixture was subjected to reflux conditions for 48 hours, as confirmed by TLC utilizing a hexane: ethyl acetate solvent system in a 2:1 ratio. Following the completion of the reaction, the solid product was isolated, subjected to three consecutive washes with diethyl ether (3 × 15 mL), and subsequently dried. The isolated product was further purified by recrystallization in ethanol. [36]

2-(6-methoxynaphthalen-2-yl)-N-((3-methyl-1 H-1,2,4-triazol-5-yl)methyl) propanamide (14)

Yield: (68%); mp: 100–102˚C; beige solid; eluent: hexane: ethyl acetate 2:1, R_f = 0.18; ^{1}H NMR (DMSO d_6), δ, ppm: 1.36 (d, J = 8 Hz, 3H) CH<u>CH</u>$_3$, 2.79 (s,3H) = C<u>CH</u>$_3$, 3.62 (q, J = 8 Hz, 1H) <u>CH</u>CH$_3$, 3.83 (s,3H) OCH$_3$, 4.83 (s,2H) NH<u>CH</u>$_2$, 6.96–7.71 (m,6H) Ar-H, 8.06, 10.31(b,2H)2NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 10.64 C<u>CH</u>$_3$, 18.91 CH<u>CH</u>$_3$, 32.49 NH<u>CH</u>$_2$, 45.05<u>CH</u>CH$_3$, 55.62 OCH$_3$, 106.15, 119.17, 126.04, 126.88, 127.32, 128.87, 129.58, 133.70, 136.79,157.57 (10C) Ar-C, 153.67, 154.71 (2C) C = N, 175.97 C = O; IR (KBr), ν (cm^{-1}): 3271, 3172, 1712, 1658, 1604, 1265.

N,N'-((1,4-phenylenebis(1 H-1,2,4-triazole-5,3-diyl))bis(methylene))bis(2-(6-methoxy-naphthalen-2-yl)propanamide(17)

Yield: (68%); mp: 116–118°C; beige solid; eluent: hexane: ethyl acetate 2:1, $R_f = 0.37$; ^{1}H NMR (DMSO d_6), δ, ppm: 1.39 (d, J = 8 Hz, 6H) 2CHC$\underline{H}_3$, 3.77 (q, J = 8 Hz, 2H) 2C$\underline{H}$CH$_3$, 3.86 (s,6H) 2OC$\underline{H}_3$, 4.37 (s,4H) 2NHC$\underline{H}_2$C, 7.10–7.91 (m,16H) Ar-H, 8.32, 9.95 (b,4H) 4NH; ^{13}C-NMR (DMSO-d_6) δ (ppm): 18.99(2C) 2CH$\underline{C}$H$_3$, 35.70(2C) 2NH$\underline{C}$H$_2$C, 45.16(2C) 2$\underline{C}$HCH$_3$, 55.59(2C) 2O$\underline{C}$H$_3$, 106.08, 119.09, 125.86, 126.41, 127.02, 127.06, 128.25, 128.80, 129.57, 133.59, 137.67, 157.42 (26C) Ar-C, 155.84, 158.69 (4C) C = N, 174.29 (2C = O); IR (KBr), ν (cm^{-1}): 3318, 3260, 1656, 1607, 1265.

Antioxidants activity

The antioxidant potential of the synthesized compounds (denoted as compounds 1–17) was evaluated employing the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical assay method, as previously described in the literature.[37–39] To prepare stock solutions of the compounds at a concentration of 200 ppm, 0.001 g of each synthetic compound was dissolved in the minimal volume of dimethyl sulfoxide (DMSO) and subsequently diluted to 5 mL with absolute ethanol. Working solutions were prepared at various concentrations (20 ppm, 40 ppm, and 60 ppm) by dilution of the stock solutions with absolute ethanol. Ascorbic acid was employed as a reference standard. Subsequently, 0.5 mL of a 0.5 mM DPPH solution in ethanol was added to 1.5 mL of the prepared sample solutions at the different concentration levels. The resulting solution was vigorously mixed and allowed to incubate in darkness at room temperature for 30 minutes. The reduction of DPPH, evident by a color change from deep violet to light yellow, was indicative of antioxidant activity.[40,41] The absorbance of the solutions was measured at 517 nm using a UV-Vis spectrometer, and the percentage of DPPH inhibition, denoting the antioxidant activity, was calculated using the following Eq. (1):

$$Inhibition\ (\%) = A_{control} - A_{sample} / A_{control} \times 100 \quad (1)$$

Where A $_{control}$ represents the absorbance of the DPPH solution without any sample. The IC_{50} value, indicating the concentration of the compound required to scavenge (reduce) 50% of the DPPH radicals, was determined from the data as shown in Table 1.

Table 1. The in vitro antioxidants activity of compounds (1–17).

Compound	DPPH inhibition (%)			
	60%	40%	20%	IC50
Ascorbic acid	98	97	97	30
Naproxen	44	20	10	68
1	86	71	49	35
2	51	30	19	59
3	34	14	4	89
4	27	11	6	112
5a	29	24	5	105
5b	27	14	9	113
5c	30	20	8	100
5d	34	4	3	88
5e	20	16	8	147
6a	27	21	15	113
6b	27	23	12	113
6c	25	10	7	122
6d	39	15	12	76
7	50	29	8	60
8	81	73	68	37
9	32	27	22	93
10	36	18	11	84
11	73	61	45	41
12	23	18	10	130
13	24	23	17	123
14	43	22	20	70
15a	75	64	51	40
15b	64	41	39	47
16	62	58	22	49
17	66	54	36	45

Result and discussion

Azide compound (2) was identified by IR spectra which showed the main absorption band at 2146 cm^{-1} for N = N = N stretching absorption. ^{1}HNMR and ^{13}C NMR spectra of the product further confirmed the successful formation of azide in a good yield. Azide (2) undergo thermal decomposition in toluene to give isocyanates (Curtius rearrangement), which on reaction with water or alcohol or amine or hydrazine lead to the formation of symmetrical urea (4) carbamate(5a-e), urea(6a-d) and semicarbazide (8) respectively. Azide (2) was heated at reflux in toluene gave isocyanate (3). Successful conversion to isocyanate (3) was supported by IR, ^{1}HNMR and ^{13}CNMR spectra. Symmetrical urea (4) was synthesized by refluxing of isocyanate (3) with water. The structure of compound (4) was confirmed by IR which showed the disappearance of N = C = O of isocyanate in addition to strong (C = O) bands at 1704, 1651 cm^{-1}. The symmetrical urea (4) was confirmed by IR, ^{1}HNMR and ^{13}CNMR spectra as shown in experimental part. Carbamate (5a) was prepared by the reaction of isocyanate (3) with ethanol under refluxed for three days. The absence of an isocyanate band at 2249 cm^{-1} and the presence of C = O bands at

1694, 1651 cm^{-1} in its IR spectrum is evidence for the rearrangement of isocyanate to carbamate. The ^1H NMR spectrum show and indicate the presence of the ethyl group at 1.16–1.24ppm for CH_3 and 4.00–4.10 for CH_2 and all packs for naproxen. A series of carbamates (5b-e) were prepared using aliphatic and aromatic alcohols. All these compounds were verified by their spectral data. Another reaction of isocyanate (3) in presence of aliphatic and aromatic amines gives the corresponding ureas (6a-d). The IR spectral data for compounds (6a-d) showed absorption bands at 3362-3306 cm^{-1}, 3294–3200 cm^{-1} and 1643–1630 cm^{-1} due to the presence of N-H and C = O respectively. ^1H NMR spectral analyses of compounds (6a-d) exhibited aromatic protons in the expected range (7.83–7.08 ppm), and other signals were observed at appropriate places. Decarboxylation of isocyanate (3) by heating with 25% hydrochloric acid afforded the hydrochloride salt (7).

In another reaction, isocyanate (3) on refluxing with hydrazine hydrate and naproxen hydrazide (1) gives the corresponding semicarbazide (8) and substituted semicarbazide (11) respectively.[42] Their structures were verified by IR spectra which showed signals at 1662–1643 cm^{-1} for C = O, 3361–3185 cm^{-1} stretching absorption for NH. ^{13}C NMR showed the carbonyl carbon signal at 157.6–158.3 ppm. ^1H NMR spectra appeared signal at 4.1 ppm for NH_2, compound (8) and peaks at 9.31, 9.97 for NH, compound (11). Compound (9) was synthesized by refluxing of semicarbazide (8) with acetyl chloride. The IR spectrum showed the disappearance peak at 3415 $cm^{-1}$for NH_2, while ^1H and ^{13}C NMR spectra showed signals at 1.6 ppm and 20.24 ppm due to $COCH_3$ respectively. Compounds (9 and 11) were converted to1,2,4-triazol-5-one (10 and 12), respectively by a cyclization reaction via refluxing with alcoholic potassium hydroxide. Compounds (10 and 12) were confirmed in ^{1}HNMR by disappearance of two NH signals from corresponding semicarbazide (9 and 11) and absence of one carbonyl signal in addition to appear signals at 144.87–144.5 ppm belong to C = N in ^{13}CNMR.

In the next part the hydrazide (1) undergo nucleophilic substitution with acetyl chloride, aryl sulfonyl chloride (benzene or toluene) and terephthaloyl chloride to give the substituted hydrazide (13, 15a-b and 16) respectively.[43] Their structures were verified by IR spectra which showed signals 3298–3110 cm^{-1} for NH stretching absorption. And the proof of the reaction product was made using ^{13}C and ^1H NMR. Diamide compounds (13, 16) with ammonium acetate underwent cyclization through dehydration to afford 1,2,4-Triazole derivatives (14, 17). The IR spectra of Triazole (14, 17) display absorption bonds at (1607–1604) cm^{-1} attributed to C = N. The ^{1}H-NMR results of compounds (14, 17) show signals at 10.31–9.95 ppm due to (NH) of triazole ring.

Free radicals are chemical species characterized by one or more unpaired electrons, exhibiting high reactivity. They have the potential to generate additional free radicals by abstracting electrons from other molecules. These species can become toxic when they are present in large quantities in the body, leading to various diseases such as cancer, diabetes, cardiovascular diseases and autoimmune diseases.[44]

The free radical scavenging activity of synthesized compounds (1–17) was assessed in the presence of the stable free radical DPPH, using ascorbic acid as positive control. The DPPH solution has a purple color with a 517 nm absorption, which converts to yellow in the presence of antioxidants. The presence of electron-donating substituents such as the methoxy group in the naproxen ring, enhances its antioxidant activity by providing better radical scavenging ability. The methoxy group can stabilizes the molecule by delocalizing electrons and reducing its reactivity towards free radicals.[45,46] Furthermore, the most active antioxidant compound is the one that has more than one active group (NH_2 or NH), and this addition improves the molecule's capacity to scavenge radicals effectively.[47,48] The amount of antioxidant required to reduce the starting concentration of DPPH by 50% is known as the inhibitory concentration, or IC50, which is how the activity is expressed. The lower the IC50, the higher the antioxidant efficiency. According to the results of the experiments, compounds (1, 8, 15a, 11, 17, 15b, 16) exhibited higher scavenging activity towards DPPH with IC50= 35–49, while compounds (2, 7, 14, 6d, 10, 5d, 3, 9, 5c, 5a) showed moderate activity with IC50 = 59–105, and compounds (4, 5b, 6a, 6b, 6c, 13, 12, 5e) showed lower activity with IC50 = 112–147. Moreover, naproxen is expected to be a promising leader for novel compounds with antioxidant activity.

Conclusion

Despite the Curtius rearrangement having been discovered over a century ago, it continues to be a significant method for creating a diverse range of nitrogen-based compounds in the field of organic synthesis. The compound (2-(6-methoxynaphalen-2-yl) propanoyl) glycinoyl azide serves as a useful intermediate in the synthesis of various organic compounds through its rearrangement to isocyanates. These isocyanates can undergo various reactions

with nucleophiles such as alcohols, amines, and hydrazines forming both acyclic and cyclic compounds. The target synthesized compounds, known for their pronounced antioxidant activity, may enhance the activity of naproxen to different extents depending on the type of nucleophile used in their synthesis. When evaluating the antioxidant effects of the synthesized compounds, it was observed that compounds (1, 8, 15a, 11, 17, 15b, 16) exhibited notably high scavenging activity towards DPPH, with IC50 values ranging from 35 to 49, while the other compounds showed mild and varying activities.

Acknowledgement

The authors express heartfelt thanks to the College of Science at the University of Duhok for generously providing essential resources and laboratory facilities. These contributions played a pivotal role in the successful execution of this research project.

Authors' declaration

- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are ours. Furthermore, any Figures and images, that are not ours, have been included with the necessary permission for republication, which is attached to the manuscript.
- No animal studies are present in the manuscript.
- No human studies are present in the manuscript.
- Ethical Clearance: The project was approved by the local ethical committee at University of Duhok.

Authors' contribution statement

J. A., H. A., and P. H. significantly contributed to the conception, implementation, and analysis of the research, as well as the composition of the manuscript.

References

1. Caglar S, Altay A, Harurluoglu B, Yeniceri EKK, Caglar B, Şahin O. Synthesis, structural characterization and evaluation of anticancer activity of polymeric silver(I) complexes based on niflumic acid/naproxen and picoline derivatives. J Coord Chem. 2022;75(1–2):178–196. https://doi.org/10.1080/00958972.2022.2045586.
2. Zhou J, Bao Z, Wu P, Chen C. Preparation and synthetic application of naproxen-containing diaryliodonium salts. Molecules. 2021;26(11):3240. https://doi.org/10.3390/molecules26113240.
3. Nedeljković N, Dobričić V, Mijajlović M, Vujić Z, Nikolić M. Molecular docking analysis of novel thiourea derivatives of naproxen with potential anti-inflammatory activity. Med Sci Forum. Basel Switzerland: MDPI. 2022;14(1):28. https://doi.org/10.3390/ECMC2022-13279.
4. Shah K, Mujwar S. Delineation of a novel non-steroidal anti-inflammatory drugs derivative using molecular docking and pharmacological assessment. J Pharm Sci. 2022;84(3):642. https://doi.org/10.36468/pharmaceutical-sciences.959.
5. Nedeljković N, Dobričić V, Bošković J, Vesović M, Bradić J, Aniċ M, *et al.* Synthesis and investigation of anti-inflammatory activity of new thiourea derivatives of naproxen. J Pharm. 2023;16(5):666. https://doi.org/10.3390/ph16050666.
6. Han Mİ, Ince U, Gündüz MG, Küçükgüzel ŞG. Synthesis, antimicrobial evaluation, and molecular modeling studies of new thiosemicarbazide-triazole hybrid derivatives of (S)-naproxen. Chem Biodivers. 2022;19(4):e202100900. https://doi.org/10.1002/cbdv.202100900.
7. Nsaif LH, Al-Bayti RI, Kadhem SAb. Synthesis, characterization, and antibacterial, evaluation of new naproxen derivatives. Drug Discov. Today. 2020;13(2):252–264.
8. Han Mİ, Atalay P, Tunç CÜ, Ünal G, Dayan S, Aydın Ö, *et al.* Design and synthesis of novel (S)-naproxen hydrazide-hydrazones as potent VEGFR-2 inhibitors and their evaluation in vitro/in vivo breast cancer models. Bioorg Med Chem. 2021;37:116097. https://doi.org/10.1016/j.bmc.2021.116097.
9. Alam MM, Nazreen S, Almalki ASA, Elhenawy AA, Alsenani NI, Elbehairi SEI, *et al.* Naproxen based 1,3,4-oxadiazole derivatives as EGFR inhibitors: Design, synthesis, anticancer, and computational studies. J Pharm. 2021;14(9):870. https://doi.org/10.3390/ph14090870.
10. Han Mİ, Tunç CÜ, Atalay P, Erdoğan Ö, Ünal G, Bozkurt M, *et al.* Design, synthesis, and in vitro and in vivo anticancer activity studies of new (S)-naproxen thiosemicarbazide/1,2,4-triazole derivatives. New J Chem. 2022;46(13):6046–6059. https://doi.org/10.1039/D1NJ05899A.
11. Gooßen LJ, Rodríguez N, Gooßen K. Carboxylic acids as substrates in homogeneous catalysis. Angew Chem Int Ed Engl. 2008;47(17):3100–3120. https://doi.org/10.1002/anie.200704782.
12. Curtius Th. 20. Hydrazide und Azide organischer Säuren I. Abhandlung. J Prakt Chem. 1894;50(1):275–294. https://doi.org/10.1002/prac.18940500125.
13. Yassine H, Bouali J, Oumessaoud A, Ourhzif EM, Hamri S, Hafid A, *et al.* Synthesis of new dialkyl 2,2'-[carbonylbis(azanediyl)]dibenzoates via Curtius rearrangement. Synth. 2021;53(11):1971–1979. https://doi.org/10.1055/s-0040-1706643.
14. Ghosh AK, Sarkar A, Brindisi M. The Curtius rearrangement: Mechanistic insight and recent applications in natural product syntheses. Org Biomol Chem. 2018;16(12):2006–2027. https://doi.org/10.1039/C8OB00138C.
15. Ghosh AK, Brindisi M, Sarkar A. The Curtius rearrangement: Applications in modern drug discovery and medicinal chemistry. Chem Med Chem. 2018;13(22):2351–2373. https://doi.org/10.1002/cmdc.201800518.
16. Jo DG, Kim C, Lee S, Yun S, Joung S. Synthesis of cyclic N-acyl amidines by [3 + 2] cycloaddition of n-silyl enamines and activated acyl azides. Molecules. 2022;27(5):1696. https://doi.org/10.3390/molecules27051696.
17. Baumann M, Moody TS, Smyth M, Wharry S. Interrupted Curtius rearrangements of quaternary proline derivatives: A

flow route to acyclic ketones and unsaturated pyrrolidines. J Org Chem. 2021;86(20):14199–14206. https://doi.org/10.1021/acs.joc.1c01133.
18. Choi H, Jang H, Choi J, Lee K. Stereoselective synthesis of oxazolidin-2-ones via an asymmetric aldol/Curtius reaction: Concise total synthesis of (−)-cytoxazone. Molecules. 2021;26(3):597. https://doi.org/10.3390/molecules26030597.
19. Balci M. Acyl azides: Versatile compounds in the synthesis of various heterocycles. Synth. 2018;50(07):1373–1401. https://doi.org/10.1055/s-0036-1589527.
20. Baumann M, Leslie A, Moody TS, Smyth M, Wharry S. Tandem continuous flow Curtius rearrangement and subsequent enzyme-mediated impurity tagging. Org Process Res Dev. 2021;25(3):452–456. https://doi.org/10.1021/acs.oprd.0c00420.
21. Sagandira CR, Watts P. Synthesis of amines, carbamates and amides by multi-step continuous flow synthesis. Eur J Org Chem. 2017;2017(44):6554–6565. https://doi.org/10.1002/ejoc.201700906.
22. Mata A, Weigl U, Flögel O, Baur P, Hone CA, Kappe CO. Acyl azide generation and amide bond formation in continuous-flow for the synthesis of peptides. React Chem Eng. 2020;5(4):645–650. https://doi.org/10.1039/D0RE00034E.
23. Yang W, Sun X, Yu W, Rai R, Deschamps JR, Mitchell LA, *et al.* Facile synthesis of spirocyclic lactams from β-keto carboxylic acids. Org Lett. 2015;17(12):3070–3073. https://doi.org/10.1021/acs.orglett.5b01350.
24. Faisal M, Raauf A, Mahdi MF, Raauf AMR, Kadhim FAH. Design, synthesis and acute anti-inflammatory evaluation of new non-steroidal anti-inflammatory agents having 4-thiazolidinone pharmacophore. J Nat Sci. 2015;5(6):21–28. https://www.researchgate.net/publication/274388923.
25. AL-Khazraji SIC, Sadik WM, Ahamed LS. Synthesis and characterization of new 2-amino-5-chlorobenzothiazole derivatives containing different types of heterocyclic as antifungal activity. Baghdad Sci J. 2024;21(3):0962-0974. https://doi.org/10.21123/bsj.2023.8318.
26. Li J, Zhu Y, Liu B, Tang F, Zheng X, Huang W. An atom-economic inverse solid-phase peptide synthesis using bn or bcm esters of amino acids. Org Lett. 2021;23(19):7571–7574. https://doi.org/10.1021/acs.orglett.1c02769.
27. Badran MM, Roshdy SMA, Abd El-Hameid MK. Synthesis of certain fused pyrrolothieno[3, 2-e] pyrazine derivatives with possible anxiolytic activity. Indian J Chemi. 2013;9(11):427–436. https://scholar.cu.edu.eg/sites/default/files/mohkamel/files/02_ocaij_org2634907.pdf.
28. Wolf ME, Vandezande JE, Schaefer HF. Catalyzed reaction of isocyanates (RNCO) with water. Phys Chem Chem Phys. 2021;23(34):18535–18546. https://doi.org/10.1039/D1CP03302F.
29. Jakubkiene V, Kacnova Z, Burbuliene MM, Vainilavicius P. Synthesis of (pyrimidin-4-yloxy)- and (pyrimidin-3-yl)acetyl azides and their rearrangement to carbamates and ureas. ARKIVOC. 2010;2010(11):39–48. https://doi.org/10.3998/ark.5550190.0011.b04.
30. Saraiva Rosa N, Glachet T, Ibert Q, Lohier JF, Franck X, Reboul V. A straightforward synthesis of n-substituted ureas from primary amides. Synthesis (Germany). Georg Thieme Verlag. 2020;52(14):2099–2105. https://doi.org/10.1055/s-0040-1707103.
31. Balci M. Acyl azides: Versatile compounds in the synthesis of various heterocycles. Synth. 2018;50(07):1373–1401. https://doi.org/10.1055/s-0036-1589527.
32. Krátký M, Baranyai Z, Štěpánková Š, Svrčková K, Švarcová M, Stolaříková J, *et al.* N-alkyl-2-[4-(trifluoromethyl)benzoyl]hydrazine-1-carboxamides and their analogues: Synthesis and multitarget biological activity. Molecules. 2020;25(10):2268. https://doi.org/10.3390/molecules25102268.
33. Zarafu I, Matei L, Bleotu C, Ionita P, Tatibouët A, Păun A, *et al.* Synthesis, characterization, and biologic activity of new acyl hydrazides and 1,3,4-oxadiazole derivatives. Molecules. 2020;25(14):3308. https://doi.org/10.3390/molecules25143308.
34. Suaad MHAM, Halah ARI, Yasser AHAI. Synthesis and identification of some new derivatives of ([Benzyl Thio) benzimidazole -N- (Methylene-5-Yl)] - 4,5- di substituted 1,2,4-triazole and evaluation of their activity as antimicrobial and anti-inflammatory agents. Iraqi J Sci. 2021;62(4):1054–1065. https://doi.org/10.24996/ijs.2021.62.4.2.
35. Al-iraqi M, Saad-Aldeen R. Synthesis of new 3-substituted quinazolin-4(3h)-one compounds via linking of some five-membered ring heterocyclic moieties with quinazolin-4(3h)-one nucleus. J Educ Sci. 2021;30(1):158–172. https://doi.org/10.33899/edusj.2020.127904.1101.
36. Avci A, Taşci H, Kandemir Ü, Can ÖD, Gökhan-Kelekçi N, Tozkoparan B. Synthesis, characterization, and in vivo pharmacological evaluation of novel mannich bases derived from 1,2,4-triazole containing a naproxen moiety. Bioorg Chem. Academic Press Inc. 2020;100. https://doi.org/10.1016/j.bioorg.2020.103892.
37. Mustafa AM. Facile synthesis and antioxidant activity of pyrimidine derivatives via thienyl chalcones under phase transfer catalysis method. Int J Drug Deliv Technol. 2022;12(2):558–563. https://doi.org/10.25258/ijddt.12.2.16.
38. Peng Z, Wang G, Zeng Q-H, Li Y, Wu Y, Liu H, *et al.* Synthesis, antioxidant and anti-tyrosinase activity of 1,2,4-triazole hydrazones as antibrowning agents. Food Chem. 2021;341:128265. https://doi.org/10.1016/j.foodchem.2020.128265.
39. Patel KB, Patel D V, Patel NR, Kanhed AM, Teli DM, Gandhi B, *et al.* Carbazole-based semicarbazones and hydrazones as multifunctional anti-alzheimer agents. J Biomol Struct Dyn. 2022;40(20):10278–10299. https://doi.org/10.1080/07391102.2021.1942212.
40. Mustafa YF, Ismael RN, Jebir RM. Natural coumarins from two cultivars of watermelon seeds as biosafe anticancer agents, an algorithm for their isolation and evaluation. J Mol Struct. 2024;1295:136644. https://doi.org/10.1016/j.molstruc.2023.136644.
41. Al-Jeilawi OHR, Oleiwi AQ. Preparation, characterization, antioxidant activity of 1-(2-furoyl) thiourea derivatives and study the molecular docking of them as potent inhibitors of Urease enzyme. Baghdad Sci J. 2023;20(3):994–1011. https://doi.org/10.21123/bsj.2023.7745.
42. Bouchnak H, Ollevier T, Kraïem J. New synthesis of 3-aminohydantoins via condensation of hydrazines with isocyanates derived from α-amino esters. Synopen. Georg Thieme Verlag. 2023;7(4):690–693. https://doi.org/10.1055/a-2217-6821.
43. Sun P, Wang J, Khan KS, Yang W, Wai-Lung Ng B, Ilment N, *et al.* Development of alkylated hydrazides as highly potent and selective Class I histone deacetylase inhibitors with T cell modulatory properties. J Med Chem. 2022;65(24):16313–16337. https://doi.org/10.1021/acs.jmedchem.2c01132ï.

44. Barbuceanu S-F, Ilies D, Saramet G, Uivarosi V, Draghici C, Radulescu V. Synthesis and antioxidant activity evaluation of new compounds from hydrazinecarbothioamide and 1,2,4-triazole class containing diarylsulfone and 2,4-difluorophenyl moieties. Int J Mol Sci. 2014;15(6):10908–10925. https://doi.org/10.3390/ijms150610908.
45. Moazzen A, Öztinen N, Ak-Sakalli E, Koşar M. Structure-antiradical activity relationships of 25 natural antioxidant phenolic compounds from different classes. Heliyon. 2022;8(9):e10467. https://doi.org/10.1016/j.heliyon.2022.e10467.
46. Charlton NC, Mastyugin M, Török B, Török M. Structural features of small molecule antioxidants and strategic modifications to improve potential bioactivity. Molecules. 2023;28(3):1057. https://doi.org/10.3390/molecules28031057.
47. Bendary E, Francis RR, Ali HMG, Sarwat MI, El Hady S. Antioxidant and structure–activity relationships (SARs) of some phenolic and anilines compounds. Ann Agric Sci. 2013;58(2):173–181. https://doi.org/10.1016/j.aoas.2013.07.002.
48. Cetin A, Gecibesler I. Evaluation as antioxidant agents of 1,2,4-triazole derivatives: Effects of essential functional groups. J Appl Pharm Sci. 2015;120–126. https://doi.org/10.7324/JAPS.2015.50620.

تحضير وتقييم مضادات الأكسدة لبعض اليوريا والكاربامات والتريازول المشتقة من (2-(6-ميثوكسي نفثالين-2- يل)بروبانويل)ازايد

جيهان احمد مصطفى[1]، هدى احمد بشير[2]، بروين هاشم سليم[1]

[1] قسم الكيمياء، كلية العلوم، جامعة دهوك، دهوك، العراق.
[2] قسم الكيمياء، فاكولتي العلوم، جامعة زاخو، دهوك، العراق.

الخلاصة

في هذه الدراسة، تم تحضير سلسلة جديدة من المركبات من خلال نهج تخليقي متعدد الخطوات ، مشتقة من دواء النابروكسين، تتضمن كربامات ويوريا وسيميكاربازيدات ومشتقات 1،2،4-تريازول. في البداية، تم تحضير هيدرازيد (1) عن طريق تفاعل إستر الحامض الأميني للنابروكسين مع الهيدرازين المائي، تلاه تحويله إلى أزايد كلاسين النابروكسين (2) عبر معاملته بنترات الصوديوم في حامض الهيدروكلوريك. ثم تم تعريض الأزيد (2) بعد ذلك للتحلل الحراري عبر إعادة ترتيب كورتيوس ليعطي الأيزوسيانات (3). وتم تفاعل الأيزوسيانات (3) بعد ذلك مع مجموعة من العوامل مثل الماء والكحول والأمين وحمض الهيدروكلوريك والهيدرازين وهيدرازيد النابروكسين، مما أدى إلى تكوين اليوريا المتناظرة (4) والكربامات (5a-e) واليوريا (6a-d) وملح الهيدروكلوريد (7) والسيميكاربازيدات (8) و (11). وعلاوة على ذلك، تم تخليق مركب (9) بتصعيد السيميكاربازيد (8) مع كلوريد الأستيل، وتم تحويل المركبين (9 و 11) بعد ذلك إلى مشتقات 1،2،4-تريازول-5-ون (10 و 12) من خلال تفاعل الحولقة. وفي خط موازٍ، تم إجراء تفاعلات الاستبدال النيوكليوفيلي على الهيدرازيد (1) باستخدام كلوريد الأستيل وكلوريد الأريل سلفونيل (البنزين أو التولوين) وكلوريد التيريفثالويل، مما أسفر عن تحضير مشتقات هيدرازيد (13و 15 a-bو 16)على التوالي. ثم تم حولقة المركبات الثنائية الأميد (13 و 16) مع خلات الأمونيوم لإنتاج مشتقات 1،2،4-تريازول (14 و 17). وتم متابعة تقدم هذه التفاعلات الكيميائية باستخدام كروماتوغرافيا الطبقة الرقيقة(TLC) ، وتم تشخيص المركبات المخلقة باستخدام طيف الأشعة تحت الحمراء (IR) والرنين النووي المغناطيسي للبروتونات (1H NMR) والرنين النووي المغناطيسي للكربون-13 .(13C NMR) وتم تقييم الخصائص المضادة للأكسدة لهذه المركبات بشكل شامل، مما ساهم في تطوير مشتقات جديدة ذات تطبيقات محتملة في مجالات الصيدلة والكيمياء الدوائية.

الكلمات المفتاحية: إعادة ترتيب كورتيوس، كربامات، تريازول، يوريا، مضادات الأكسدة.