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RESEARCH ARTICLE

Synthesis of Some New Hydrazide-Hydrazone and Heterocyclic Compounds Thiophene, Imine, Coumarin and Pyrazole Derivatives

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ABSTRACT

A series of new thiophene, imine, coumarin and pyrazole derivatives X4-X16 were synthesized from N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-2-cyanoacetohydrazide X3 as a starting material with different reagents (tetralone, cyclopentanone, cycloheptanone, 2-hydroybenzaldehyde, 2-hydroxy-1-naphthaldehyde, CS_2 and phenylisothiocyanate). The compound X3 was synthesized by the reaction of 4-(benzylsulfonyl)acetophenone with 2-cyanoacetohydrazide under reflux in ethanol. The structures of all synthesized compounds were confirmed by (FT-IR, ^{1}H-NMR, and ^{13}C-NMR).

Keywords: Coumarin, Heterocyclic compounds, Hydrazide-hydrazone, Imine, Pyrazole, Thiophene

Introduction

Hydrazones are considered organic compounds that contain two nucleophilic nitrogen atoms in addition to a double bond (C=N), which has the formula ($R_1HC=NNH_2$).[1] Hydrazones are used in the synthesis of heterocyclic compounds due to their reactions with electrophiles and nucleophiles.[2] Hydrazones were formed by the reactions of an aldehyde or ketone with hydrazine or hydrazine derivatives.[3] Compounds containing the hydrazone group have different biological properties, which have entered into many studies because of their therapeutic value in the development of new agents such as anti-cancer,[4] anti-viral[5] and anti-inflammatory.[6] Thiophene belongs to the class of five-heterocyclic compounds, the structure of thiophene is found in some natural products, and it is also found in many pharmacologically effective compounds, where thiophene is famous in therapeutic applied chemistry, such as anti-inflammatory,[7,8] anti-tumour,[9] antihypertensive[10] and an inhibitor of corrosion of substances.[11] Coumarins are simple and diverse structures of a basic family of natural products found in various microorganisms, where (benzopyrone) is the main structure the natural and synthetic coumarins[12] have received great attention from researchers due to their wide range of biological properties including anti-cancer activities,[13] anti-HIV,[14] anti-inflammatory[15,16] and anticoagulant[17,18] as well as many drugs have been marketed coumarin for the treatment of thrombosis.[12] Pyrazole is a five-membered heterocyclic ring consisting of three carbon atoms with two adjacent nitrogen atoms. Pyrazoles constitute an important class in organic construction, and the presence of the pyrazole nucleus in different structures leads to its use in various fields such as technology, medicine and agriculture[19] as well as in biological activities, including antimicrobial activity,[20–22] antiviral,[23]

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antitumor,[24] antibacterial,[25] and also pyrazole has anti-diabetic activities[26] and the best property of pyrazole is the treatment of infections, especially arthritis.[19]

Materials and methods

Melting points were measured by Electro-thermal SMP30-Stuart melting point apparatus, (uncorrected). (^{1}H-NMR and ^{13}C-NMR) spectra were recorded using Bruker Bio Spin GmbH Spectrophotometer (400 MHz by using TMS as internal standard and using DMSO-d6 as a solvent) [(s) singlet, (d) doublet, (m) multiple]. (FT-IR) spectra were measured using a Japanese-made device (Shimadzu FT-IR-ATR) in a region confined between 400–4000 cm^{-1}. TLC aluminum sheets silica gel 60 F_{254} was used to monitor the progress of all reactions and the homogeneity of the produced compound. As for the used mobile phase, it consisted of a mixture of ethyl acetate and n-hexane in a ratio of (5:5) ml. 4-(benzylthio) acetophenone $\mathbf{X_{1a}}$, 4-benzylsulfonylacetophenone $\mathbf{X_{1b}}$ and 2-cyanoacetohydrazide $\mathbf{X_2}$ were synthesized according to our previously published work.[27]

Preparation of N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-2-cyanoacetohydrazide) (X_3)[2,27,28]

A mixture of (2.74 g, 10 mmol) of 4-(benzylsulfonyl) acetophenone X_{1b} with (1 g, 10 mmol) of cyanoacetohydrazide X_2 in 20 ml absolute ethanol was reflux continued for 3 hours, then cooled, filtered, and recrystallized with ethanol to give the precipitate a light yellow.

Solid (ethanol), (3.22 g, 91%), m.p. = 217–219 °C. IR ν (cm^{-1}): 3029 (NH), 2260 (CN), 1691 (C=O), 1664 (C=N), 1148, 1311 (SO_2). ^{1}H-NMR (DMSO-d6, 400 MHz) δ (ppm): 2.29[s, 3H, CH_3], 4.30[s, 2H, CH_2-SO_2], 4.72[s, 2H, CH_2-CN], 11.25[s, 1H, NH], 7.17–7.97[m, 9H, Ar-H]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 14.80, 25.38, 61.89, 116.68, 127.24, 128.36, 128.6, 128.76, 129.04, 131.46, 139.03, 140.47, 148.53, 160.27.

Preparation of thiophene derivatives (X_4-X_6)[27,28]

A mixture of hydrazide-hydrazone $\mathbf{X_3}$ (0.5 g, 1.4 mmol) with (1.4 mmol) of cyclic ketones (tetralone, cycloheptanone, cyclopentanone), (0.045 gm, 1.4 mmol) of elemental sulfur and (0.056 gm, 1.4 mmol) of sodium hydroxide in 15 ml absolute ethanol, the reaction mixture was refluxed for 6 hrs. (monitored by TLC), and then left to cool at room temperature. then poured onto crushed ice with stirring until the precipitate is formed, filtered, dried and recrystallized with ethanol.

3-amino-N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-4,9-dihydronaphtho[2,3-b]thiophene-2-carbohydrazide (X_4)

Solid (ethanol), 50% (0.35 g), m.p. = 255–257°C, R_f = 0.57. IR ν (cm^{-1}): 3333 (NH), 3060, 3030 (NH_2), 1665(C=O), 1601(C=N), 1147, 1313 (SO_2).

3-amino-N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-5,6,7,8-tetrahydro-4-H-cyclohepta[b]thiophenen-2-carbohydrazide (X_5)

Solid (ethanol), 67% (0.45 g), m.p. = 239–241°C, R_f = 0.47. IR ν (cm^{-1}): 3359 (NH), 3063, 3032 (NH_2), 1621(C=O), 1584(C=N), 1148, 1312 (SO_2). ^{1}H-NMR(DMSO-d6, 400 MHz) δ (ppm): 1.58–3.37[m, 10H, 5CH_2-cycloheptane], 2.34 [s, 3H, CH_3], 4.29[s, 2H, NH_2], 4.68[s, 2H, CH_2-SO_2], 7.24–7.34[m, 9H, Ar-H], 8.29[s, 1H, NH].

3-amino-N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-5,6-dihydro-4H-cyclopenta[b]thiophenen-2-carbohydrazide (X_6)

Solid (ethanol), 92% (0.58 g), m.p. = 284–286°C, R_f = 0.51. IR ν (cm^{-1}): 3374 (NH), 3067, 3034 (NH_2), 1624 (C=O), 1586 (C=N), 1146, 1310 (SO_2). ^{1}H-NMR (DMSO-D6, 400 MHz) δ (ppm): 2.32–2.45[m, 5H, CH_3, CH_2-cyclopentane], 3.44–3.48[m, 4H, 2CH_2-cyclopentane], 4.30 [s, 2H, NH_2], 4.69[s, 2H, CH_2-SO_2], 7.17–7.30[m, 9H, Ar-H], 7.98[s, 1H, NH].

Synthesis of imine and coumarin derivatives (X_7-X_{10})[27–29]

The coumarin compounds are prepared in two methods:

Method A

First step: synthesis of imine derivatives X_7, X_9

Equimolar of hydrazide-hydrazone $\mathbf{X_3}$ with 2-hydroxybenzaldehyde or 2-hydroxy naphthaldehyde and 5drops of triethylamine in 15 ml of absolute ethanol. The mixture is refluxed for 5hours (monitored by TLC), and after the end of reflux, the reaction

mixture is left to cool at room temperature, filtered, dried and recrystallized with ethanol.

N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-3-imino-3H-benzo[f]chromene-2-carbohydrazide (X_7)

Green solid (ethanol), 73% (1.1 g), m.p. = 242–244°C, R_f = 0.686. IR ν (cm^{-1}): 3263 (NH), 1690(C=O amide), 1643 (C=N), 1147, 1312 (SO_2) ^{1}H-NMR DMSO-d6, 400 MHz) δ (ppm): 2.35[s, 3H, CH_3], 4.73[s, 2H, CH_2-SO_2], 7.13–8.49[m, 15H, Ar-H], 8.05[s, 1H, CH=C], 9.21[s, 1H, NH], 13.78, [s, 1H, NH-CO]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 61.86, 112.41, 116.29, 124.93, 126.5, 127.46, 128.65, 128.71, 128.79, 128.89, 129.40, 129.48, 130.92, 131.49, 137.87, 138.03, 143.02, 153.97, 153.97, 153.97, 158.96.

N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-2-imino-2H-chromene-3-carbohydrazide (X_9)

Light yellow solid (ethanol), 88% (1.2 g), m.p. = 245–2448°C. IR ν (cm^{-1}): 3300 (NH), 1679 (C=O amide), 1649 (C=N), 1150, 1312 (SO_2).

Second step: synthesis of coumarin derivatives X_8, X_{10}

Dissolves the iminochromene derivative $\mathbf{X_7}$ or $\mathbf{X_9}$ (1 mmol) in HCl (2 ml) and absolute ethanol (10 ml) was refluxed for 4hours (monitored by TLC), leave to cool. The solid was filtered, wished with water, and dried and recrystallized with ethanol.

Method B

To a solution of $\mathbf{X_3}$ (1.056 gm, 3 mmol) in acetic acid (10 ml) containing (0.41 gm, 3 mmol) of sodium acetate, 2-hydroxy naphthaldehyde (0.516 g, 3 mmol) or 2-hydroxy benzaldehyde (0.366 g, 3 mmol) was added. The mixture was heated under reflux for 4 hours (monitored by TLC), after cooling, the formed product was filtered off, dried and recrystallized with ethanol.

N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-3-oxo-3H-benzo[f]chromene-2-carbohydrazide (X_8)

Brown solid (ethanol), 88% (0.45 g), m.p. = 270–273°C, R_f = 0.686. IR ν (cm^{-1}): 3230 (NH), 1704 (C=O lactone) 1679 (C=O amide), 1624 (C=N), 1149, 1343 (SO_2). ^{1}H-NMR (DMSO-d6, 400 MHz) δ (ppm): 2.40[s, 3H, CH3], 4.76[s, 2H, CH_2-SO_2], 7.69–8.12[m, 15H, Ar-H], 7.69[s, 1H, CH=C], 11.01[s, 1H, NH].

N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-2-oxo-2H-chromene-3-carbohydrazide (X_{10})

Yellow solid (ethanol), 87% (0.4 g), m.p. = 261–263°C. IR ν (cm^{-1}): 3210 (NH), 1698(C=O lactone), 1672(C=O amide), 1608(C=N), 1151, 1318 (SO_2).

Synthesis of some various compounds and pyrazole derivatives (X_{11}-X_{16})[2,30]

N-(1-(4-(benzylsulfonyl)phenylethylidene)-2-cyano-3-(methlthio)-3-(phenylamino)acrylohydrazid (X_{11})

Adding KOH (0.56 g, 10 mmol) suspended in dry DMF (10 ml), hydrazine-hydrazone $\mathbf{X_3}$ (3.54 g, 10 mmol) was added and continued stirring was done for 30 min. Then phenylisothiocyanate (PhNCS) (1.35 g, 10 mmol) was added gradually to the reaction mixture with continuous stirring for 12 hours at room temperature to form an intermediate compound. Then dimethyl sulfate (1.26 g, 10 mmole) was added to the reaction mixture and stirred for 6 hours. The reaction mixture is poured over crushed ice with stirring, filtered off, dried and recrystallized with ethanol to obtain a dark yellow precipitate.

Yield, 90% (4.44 g), m.p. = 153–155°C. IR ν (cm^{-1}): 3197(NH), 2192(CN), 1681(C=O), 1651(C=N). ^{1}H-NMR (DMSO-d6, 400 MHz) δ (ppm): 2.27[s, 3H, CH_3], 2.63[s, 3H, CH3-S], 4.72[s, 1H, NH], 4.77[s, 2H, CH_2-SO_2], 7.17–8.02[m, 14H, Ar-H], 8.10[s, 1H, NH]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm):14.18, 16.82,61.64, 116.68, 123.53, 125.11, 127.23, 128.43, 128.66, 129.05, 129.21, 128.99, 131.5, 138.9, 140.88, 148.99, 162.78, 168.16.

5-amino-N-(1-(4-(benzylsulfonyl)ethylidene)-3-(phenylamino)-1H-pyrazole-4-carbohdrazid (X_{12})

A mixture of $\mathbf{X_{11}}$ (1.008 gm, 2 mmol) with hydrazine hydrate (0.1 g, 2 mmol) in ethanol (10 ml) was refluxed for 3 hours and allowed to cool. Filtered, dried and recrystallized with ethanol.

Yellow solid (ethanol), 51% (0.5 g), m.p. = 174–177°C. IR ν (cm^{-1}): 3386, 3306 (NH_2), 3219(NH), 1633 (C=O), 1597 (C=N).

5-amino-N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-1-phenyl-3-(phenylamino)-1H-pyrazole-4-carbohdrazide (X_{13})

A mixture of $\mathbf{X_{11}}$ (1.008 gm, 2 mmol) with phenylhydrazine (0.216 gm, 2 mmol) in ethanol (10 ml) was refluxed for 3 hours and allowed to cool. Filtered, dried and recrystallized with ethanol.

Orang solid (ethanol), 62% (0.7g), m.p. = 180–182°C. IR ν (cm^{-1}): 3318, 3253(NH_2), 3060 (NH), 1683 (C=O), 1661 (C=N). ^{1}H-NMR (DMSO-d6,

400 MHz) δ (ppm): 2.27[s, 3H, CH_3], 4.67[s, 2H, CH_2-SO_2], 6.81–7.95[m, 19H, Ar-H], 7.31[s, 2H, NH2], 9.59 [s, 2H, 2NH]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 13.11, 61.32, 62.14, 120.07, 125.70, 128.65, 128.72, 128.81, 129.23, 129.48, 131.47, 136.89, 138.84, 139.68, 144.51, 145.94, 146.21.

N-(1-(4-(benzylsulfonyl)phenyl)ethylidene-2-cyano-3,3-bis(methlthio)acrylohydrazide (X_{14})

Adding KOH (1.12 gm, 20 mmol) suspended in dry DMF (10 ml) with hydrazine-hydrazone **X_3** (3.54 g, 10 mmol). The mixture was cooled in an ice bath, then CS_2 (0.76 gm, 10 mmol) was added to it gradually, with stirring for 6 hours to form the intermediate compound, then dimethyl sulfate (2.52 gm, 20 mmol) was added with continuous stirring for 3 hours, then it is gradually poured over crushed ice containing (10 drops) of conc. HCl with stirring, filtered off, dried and recrystallized with ethanol to obtain a yellow precipitate.

Yield, 58% (2.6 g), m.p. = 135–138°C. IR ν (cm^{-1}): 3192 (NH), 2185 (CN), 1679 (C=O), 1589 (C=N). ^{1}H-NMR (DMSO-d6, 400 MHz) δ (ppm): 2.28[s, 3H, CH_3], 2.62[s, 6H, $2CH_3$-S], 4.76[s, 2H, CH_2-SO_2], 7.28–8.08 [m, 9H, Ar–H], 11.24[s, 1H, NH]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 14.36, 17.38, 61.65, 116.66, 128.42, 128.62, 128.98, 129.04,129.2, 131.50, 138.89, 140.89, 148.99, 166.65.

5-amino-N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-3-methylthio-1H-pyrazol-4-carbohydrazid (X_{15})

A mixture of **X_{14}** (0.5 gm, 1 mmol) with hydrazine hydrate (0.05 gm, 1 mmol) in ethanol (10 ml) was refluxed for 3 hours and allowed to cool. Filtered, dried and recrystallized with ethanol.

Yellow solid (ethanol), 52% (0.5 g), m.p. = 161–163°C. IR ν (cm^{-1}): 3385, 3304 (NH_2), 3218 (NH), 1633 (C=O), 1597 (C=N). ^{1}H-NMR (DMSO-d6, 400 MHz) δ (ppm): 2.03[s, 3H, CH_3], 2.5[s,3H, CH_3-S], 4.64[s, 2H, CH_2-SO_2], 6.84–6.88[m, 3H, NH_2,NH Pyrazole], 7.14–7.76 [m, 10H, Ar-H, NH-CO]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 11.45, 11.72, 61.32, 125.17, 128.53, 128.6, 128.78, 129.24, 131.46, 136.36, 139.69, 140.92, 141.79, 142.7, 145.14.

5-amino-N-(1-(4-(benzylsulfonyl)phenyl)ethylidene)-3-methylthio-1-phenyl-1H-pyrazol-4-carbohydrazide (X_{16})

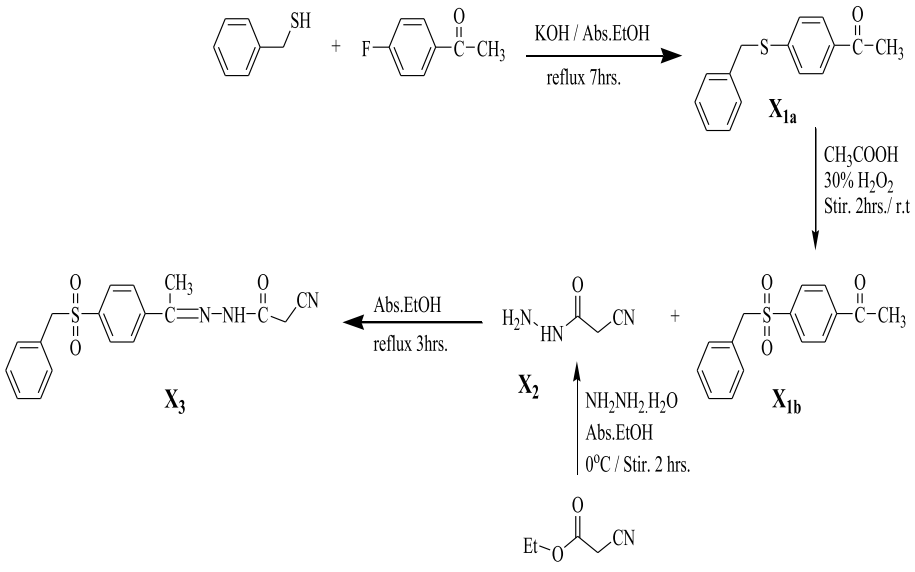
A mixture of **X_{14}** (0.5 gm, 1 mmol) with phenylhydrazine (0.11 gm, 1 mmol) in ethanol (10 ml) was refluxed for 3 hours and allowed to cool. Filtered, dried and recrystallized with ethanol.

Yellow solid (ethanol), 72% (0.7g), m.p. = 175–177°C. IR ν (cm^{-1}): 3343, 3317 (NH_2), 3251 (NH), 1601 (C=O), 1574 (C=N).

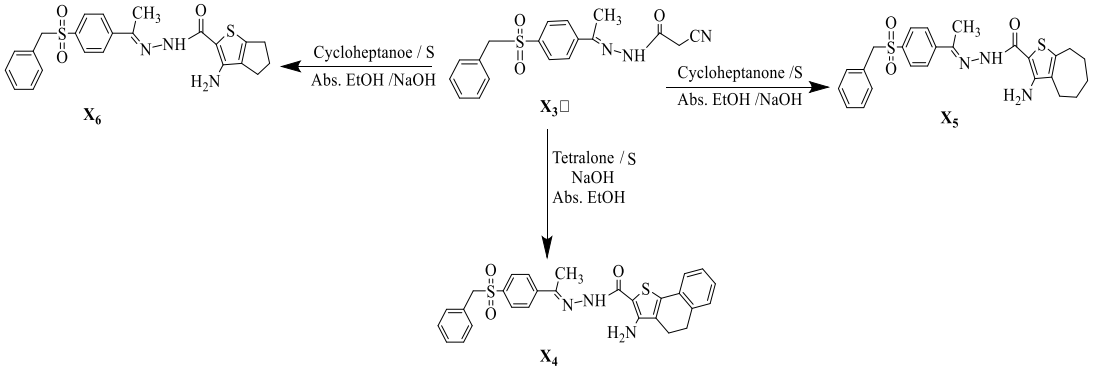
Results and discussion

The hydrazide-hydrazone X_3 was reacted in this investigation in three paths ways to produce several compounds that are predicted to be just as effective biologically as the analogous compounds created in previously published literature.[31] Where the first path includes the synthesis of heterocyclic compounds (thiophene derivatives), the second path includes the synthesis of imine and coumarin derivatives, while the third path includes the synthesis of various heterocyclic compounds and pyrazole derivatives. The 4-(benzylthio)acetophenone **X_{1a}** was prepared by reaction 4-flouro acetophenone with benzylthiol using KOH and absolute ethanol, then oxidation of compound **X_{1a}** using H_2O_2 and acetic acid to give 4-benzylsulfonylacetophenone **X_{1b}** according to the method stated previously. As for 2-cyanoacetohydrazide **X_2** was prepared by reaction of cyanoethylacetate with hydrazine hydrate according to the method listed previously.[27] The starting material hydrazide–hydrazone **X_3** was prepared from reaction 2-cyano acetohydrazide **X_2** with 4-benzylsulfonyl acetophenone **X_{1b}** in refluxing ethanol Scheme 1. The structure of the **X_3** was confirmed by physical and spectroscopic properties (FT-IR, ^{1}H-NMR and ^{13}C-NMR). The FT-IR spectrum showed the bands at 3029 cm^{-1}, 1664 cm^{-1} belonging to the (NH) and (C=N), respectively. In addition, the ^{1}H-NMR the spectrum of compound **X_3** showed (δ, ppm): 11.25 [s, 1H, NH], 7.17–7.97[m, 9H, Ar-H], 2.29 [s, 3H, CH_3], the disappearance of NH_2 bands in IR & ^{1}H-NMR spectrum are excellent evidence of the formation of the compound **X_3**. While its ^{13}C-NMR spectrum showed the following chemical shifts (δ, ppm): 160.27, 148.53, 140.47, 139.03, 131.46, 129.04, 128.76, 128.6, 128.36, 127.24, 116.68, 61.89, 25.38, 14.80, Scheme 1.

The thiophene derivatives **X_4-X_6** were prepared from the reaction of the starting material hydrazide-hydrazone **X_3** with cyclic ketones in the presence of elemental sulfur and using absolute ethanol as a solvent and sodium hydroxide as a base as shown in Scheme 2. The structure of the thiophene compound X_5 was confirmed according to physical and spectroscopic methods (FT-IR, ^{1}H-NMR). The FT-IR spectrum showed the bands at 3063, 3032 cm^{-1} for (NH_2). While the ^{1}H-NMR the spectrum of compound X_5 showed signals at 1.58–3.37 ppm [m, 10H, $5CH_2$-cycloheptane], 4.29 ppm [s, 2H, NH_2], the



Scheme 1. Preparation of hydrazide-hydrazone X_3.

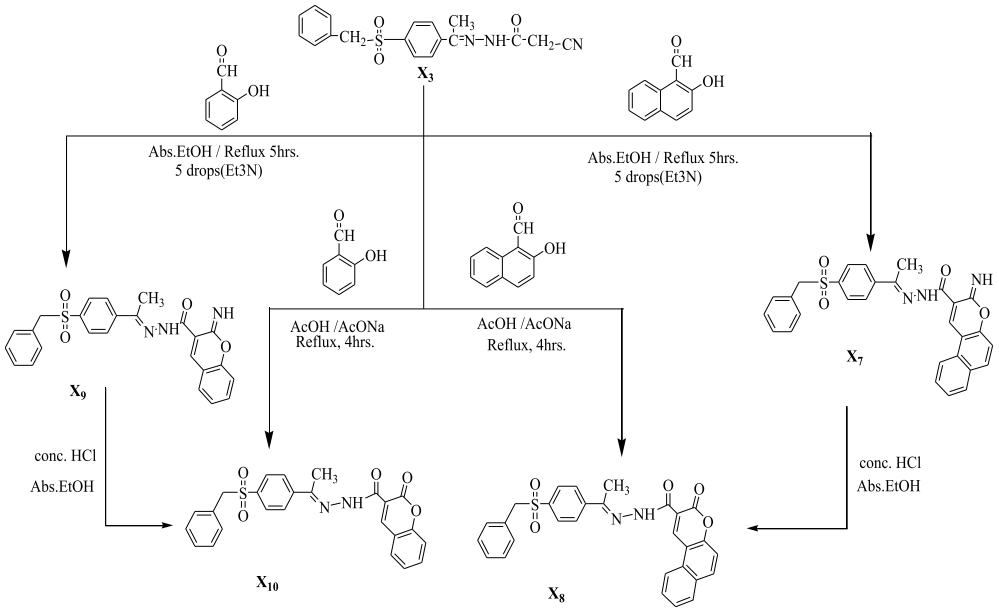


Scheme 2. Synthesis of thiophene derivatives X_4-X_6.

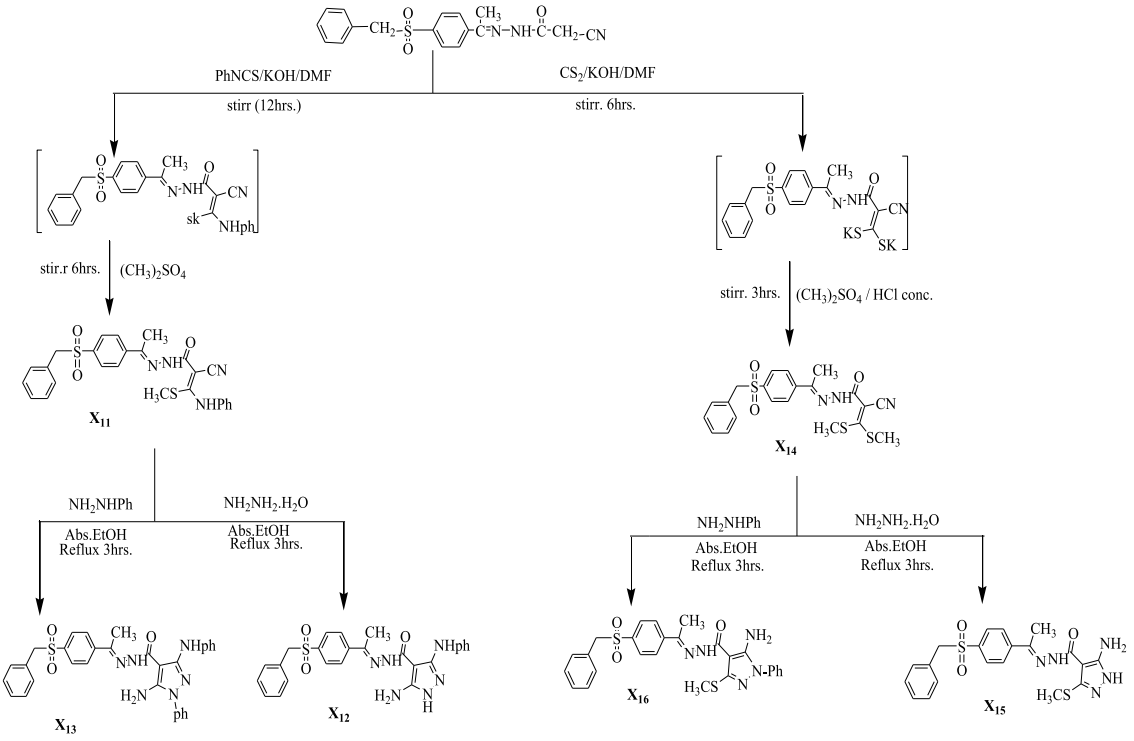
appearance of NH_2 bands and disappearance of nitrile band in IR spectrum and signals for protons NH_2 and cyclic heptane in ^{1}H-NMR spectrum are strong evidence of the formation of the compound **X_5**.

Coumarin was prepared in two methods: the first method is the preparation of imine **X_7**, **X_9** and coumarin **X_8**, **X_{10}** compounds through two steps: the first is the preparation of imine compounds from the reaction of hydrazide-hydrazine **X_3** with 2-hydroxynaphthaldehyde or 2-hydroxybenzaldehyde using absolute ethanol as a solvent and triethylamine as a base in the second step, the coumarin compounds are prepared through addition of HCl to imine compounds, Scheme 3. The structure of the imine compound **X_7** was confirmed according to physical and spectroscopic methods (FT-IR, ^{1}H-NMR, ^{13}C-NMR). The FT-IR spectrum showed the disappearance of nitrile bands. While the ^{1}H-NMR DMSO-d6, 400 MHz) δ (ppm): 7.13–8.49[m, 15H, Ar-H], 8.05[s, 1H, CH=C], 9.21[s, 1H, NH]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 61.86, 112.41, 116.29, 124.93, 126.5, 127.46, 128.65, 128.71, 128.79, 128.89, 129.40, 129.48, 130.92, 131.49, 137.87, 138.03, 143.02, 153.97, 153.97, 153.97, 158.96, in light of the spectrum information, which confirms the formation of the compound **X_7**. For the IR spectrum of the coumarin compound **X_8** showed the stretching absorption bands 1704 cm^{-1} for (C=O lactone). The ^{1}H-NMR (DMSO-d6, 400 MHz) showed signals δ (ppm): 7.69–8.12[m, 15H, Ar-H], 7.69[s, 1H, CH=C]. The appearance of C=O lactone band and disappearance of the nitrile band in IR spectrum and the disappearance signal for proton NH in ^{1}H-NMR spectrum are excellent evidence of the formation of the compound **X_8**.

The second method is to synthesis the coumarin compound by reacting the starting material hydrazide-hydrazone **X_3** once with



Scheme 3. Synthesis of imine X_7, X_9 and coumarin X_8, X_{10}.



Scheme 4. Synthesis of some various compounds and pyrazole derivatives (X_{11}-X_{16}).

2-hydroxy-naphthaldehyde and once with 2-hydroxybenzaldehyde in the presence of sodium acetate and acetic acid Scheme 3.

The new compounds (**X_{11}, X_{14}**) were prepared by reacting **X_3** with KOH suspended in a solvent DMF and adding phenylisothiocyanate or CS_2 to the reaction mixture to form intermediate compounds and then adding dimethyl sulfate $(CH_3)_2SO_4$ to these compounds. The structures of the (**X_{11}, X_{14}**) compounds were confirmed according to physical and spectroscopic methods (FT-IR, ^{1}H-NMR, ^{13}C-NMR). The FT-IR spectrum for **X_{11}** showed the bands at 3197(NH), 2192(CN), 1681(C=O), 1651(C=N). While the ^{1}H-NMR (DMSO-d6, 400 MHz) showed signals at

2.27[s, 3H, CH_3], 2.63[s, 3H, CH3-S], 4.72[s, 1H, NH], 4.77[s, 2H, CH_2-SO_2], 7.17–8.02[m, 14H, Ar-H], 8.10[s, 1H, NH]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 14.18, 16.82, 61.64, 116.68, 123.53, 125.11, 127.23, 128.43, 128.66, 129.05, 129.21, 128.99, 131.5, 138.9, 140.88, 148.99, 162.78, 168.16. While, the FT-IR spectrum for **X_{14}** showed the bands at 3192 (NH), 2185 (CN), 1679 (C=O), 1589 (C=N). ^{1}H-NMR (DMSO-d6, 400 MHz) δ (ppm): 2.28[s, 3H, CH_3], 2.62[s, 6H, $2CH_3$-S], 4.76[s, 2H, CH_2-SO_2], 7.28–8.08 [m, 9H, Ar-H], 11.24[s, 1H, NH]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 14.36, 17.38, 61.65, 116.66, 128.42, 128.62, 128.98, 129.04, 129.2, 131.50, 138.89, 140.89, 148.99, 166.65. On the other hand, compounds (**X_{12}, X_{13}, X_{15}, X_{16}**) were prepared by reacting (X_{11}, X_{14}) once with hydrazine hydrate (99%) and once with phenylhydrazine to form new pyrazole derivatives, Scheme 4. The structure of the pyrazole compound **X_{13}** was confirmed according to spectroscopic methods (FT-IR, ^{1}H-NMR, ^{13}C-NMR). The FT-IR spectrum showed the bands at 3318, 3253(NH_2), 3060 (NH), 1683 (C=O), 1661 (C=N). The ^{1}H-NMR (DMSO-d6, 400 MHz) showed signals at 2.27[s, 3H, CH_3], 4.67[s, 2H, CH_2-SO_2], 6.81–7.95[m, 19H, Ar-H], 7.31[s, 2H, NH2], 9.59 [s, 2H, 2NH]. ^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 13.11, 61.32, 62.14, 120.07, 125.70, 128.65, 128.72, 128.81, 129.23, 129.48, 131.47, 136.89, 138.84, 139.68, 144.51, 145.94, 146.21. The structure of the **X_{15}** compound was confirmed according to physical and spectroscopic methods (FT-IR, ^{1}H-NMR, ^{13}C-NMR). The FT-IR spectrum showed the bands at 3385, 3304 cm^{-1} for (NH_2). While the ^{1}H-NMR (DMSO-d6, 400 MHz) showed signals at 6.84–6.88 ppm [m, 3H, NH_2, NH Pyrazole].^{13}C-NMR (DMSO-d6, 100 MHz) δ(ppm): 11.45, 11.72, 61.32, 125.17, 128.53, 128.6, 128.78, 129.24, 131.46, 136.36, 139.69, 140.92, 141.79, 142.7, 145.14. The appearance of NH_2 bands and disappearance of nitrile band in IR spectrum and the appearance signals for protons NH and NH_2 in ^{1}H-NMR spectrum is excellent evidence of the formation of these compounds, the results were in agreement with those published in previous literature.[27,28]

Conclusion

This study used straightforward and basic working procedures, simple reaction conditions and inexpensive chemicals. Important compounds have been synthesized including hydrazide-hydrazone derivatives, thiophene, imine and Coumarin derivatives and some various compounds and pyrazole derivatives. It is believed to have biological value and medicinal applications depending on published literature. Therefore, this research focused on these derivatives.

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Author's declaration

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

Authors' contribution statement

I. M. contributed to implementation of the research project and interpretation of analytical data. A.H. contributed to the suggestion of the project idea, writing the manuscript and proofreading of research.

References

1. Boulebd H, Zine Y, Khodja IA, Mermer A, Demir A, Debache A. Synthesis and radical scavenging activity of new phenolic hydrazone/hydrazide derivatives: Experimental and theoretical studies. J Mol Struct. 2022;1249:131546. https://doi.org/10.1016/j.molstruc.2021.131546.
2. Hassan RA, Al-Sabawi AH. Synthesis and spectral study of some new α, β-unsaturated carbonyl compounds and pyrazole derivatives. Rafi J Sci. 2023;32(1):138–148. https://doi.org/10.33899/rjs.2023.177296.
3. Mohammed SJ, Sheat AM, Abood SA, Yahya OM. Using microwave and ultrasound to prepare of substituted Bis-acyl hydrazone derivatives. Egypt J Chem. 2021;64(11):6423–6427. https://doi.org/10.21608/ejchem.2021.78532.3842.
4. Şenkardeş S, Han MI, Kulabaş N, Abbak M, Çevik Ö, Küçükgüzel L, *et al.* Synthesis, molecular docking and evaluation of novel sulfonyl hydrazones as anticancer agents and COX-2 inhibitors. Mol Divers. 2020;24:673. https://doi.org/10.1007/s11030-019-09974-z.
5. Houssem B, Yasmine Z, Imene K, Arif M, Adem D, Abdelmadjid D. Synthesis and radical scavenging activity of new phenolic hydrazone/hydrazide derivatives: Experimental and theoretical studies. J Mol Struct. 2022;1249(1):131546. http://dx.doi.org/10.1016/j.molstruc.2021.131546.

6. Łukasz P. Updated Information on Antimicrobial Activity of Hydrazide–Hydrazones. Int J Mol Sci. 2021;22(9389):1–20. https://doi.org/10.3390/ijms22179389.
7. Thibaut B, Alexia B, Jérémy M, Cédric B, Floriane D, Anne B, *et al.* Synthesis and biological evaluation of benzo[*b*]thiophene acylhydrazones as antimicrobial agents against multidrug-resistant *Staphylococcus aureus*. Biomolecules. 2022;12(1):131. https://doi.org/10.3390%2Fbiom12010131.
8. Altaee EA, Al-Sabawi AH. Synthesis and Spectral Study of Some New 4-substituted but-2-enolide derivatives. Egypt J Chem. 2021. 64(12):7117–7122. https://dx.doi.org/10.21608/ejchem.2021.80154.3957.
9. Mishra R, Kumar N, Mishra I, Sachan N. A review on anticancer activities of thiophene and its analogs. Mini Rev Med Chem. 2020;20(19):1944–1965. https://dx.doi.org/10.2174/1389557520666200715104555.
10. Shah R, Verma PK. Therapeutic importance of synthetic thiophene. Chem Cent J. 2018;12(1):1–22. https://doi.org/10.1186/s13065-018-0511-5.
11. Benabdellah M, Aouniti A, Dafali A, Hammouti B, Benkaddour M, Yahyi A, *et al.* nvestigation of the inhibitive effect of triphenyltin 2-thiophene carboxylate on corrosion of steel in 2 M H_3PO_4 solutions. Appl Surf Sci. 2006;252(23):8341–8347. https://doi.org/10.1016/j.apsusc.2005.11.037.
12. Gao L, Wang F, Chen Y, Li F, Han B, Liu D. The antithrombotic activity of natural and synthetic coumarins. Fitoterapia. 2021;154:104947. https://doi.org/10.1016/j.fitote.2021.104947.
13. Wang G, Sun S, Wu B, Liu J. Coumarins as potential anti-drug resistant cancer agents: A mini review. Curr Top Med Chem. 2021;21(19):1725–1736. https://doi.org/10.2174/1568026620999201113110041.
14. Xu Z, Chen Q, Zhang Y, Liang C. Coumarin-based derivatives with potential anti-HIV activity. Fitoterapia. 2021;150(104863):1–10. https://doi.org/10.1016/j.fitote.2021.104863.
15. Saleem M, Asif M, Parveen A, Yaseen HS, Saadullah M, Bashir A, *et al.* Investigation of in vivo anti-inflammatory and anti-angiogenic attributes of coumarin-rich ethanolic extract of Melilotus indicus. Inflammopharmacology. 2021;29:281–293. https://doi.org/10.1007/s10787-020-00703-9.
16. Wang T, Peng T, Wen X, Wang G, Liu S, Sun Y, *et al.* Design, synthesis and evaluation of 3-substituted coumarin derivatives as anti-inflammatory agents. Chem Pharm Bull. 2020;68(5):443–446. https://doi.org/10.1248/cpb.c19-01085.
17. Al-shahwany AG, Omer AO. Synthesis and study some new Schiff Bases derived from pyrazolo-coumarin. Raf J Sci. 2021;30(1):78–90. https://doi.org/10.33899/rjs.2021.167688.
18. Kasperkiewicz K, Ponczek MB, Owczarek J, Guga P, Budzisz E. Antagonists of vitamin K—popular coumarin drugs and new synthetic and natural coumarin derivatives. Molecules. 2020;25(6),1465:1–24. https://doi.org/10.3390/molecules25061465.
19. Ansari A, Ali A, Asif M. Biologically active pyrazole derivatives. New J Chem. 2017;41(1):16–41. https://doi.org/10.1039/C6NJ03181A.
20. Ahmood J, Layth W, Abdullah J. Synthesis, Characterization and biological activityevaluationof some pyrazoles, thiazoles and oxazoles derived from 2-Mercaptoaniline. Baghdad Sci J. 2021;18(1):764–774. https://doi.org/10.21123/bsj.2021.18.1(Suppl.).0764.
21. Hosny MA, Zaki YH, Mokbel WA, Abdelhamid AO. Synthesis, characterization, antimicrobial activity and anticancer of some new pyrazolo[1,5-a]pyrimidines and Pyrazolo[5,1-c]1,2,4-triazines. Med Chem. 2020;16(6):750–760. https://doi.org/10.2174/1573406415666190620144404.
22. Wissam K, Kadir AM, Ibtisam K. Synthesis and characterization of some heterocyclic including oxazoles,Thiazoles, Pyridazines, phthalizines and Pyrazoles with evaluating of biological activity. Baghdad Sci J. 2013;10(3):818–827. https://doi.org/10.21123/bsj.2013.10.3.818-827.
23. Zárate-Zárate D, Aguilar R, Hernández-Benitez RI, Labarrios EM, Delgado F, Tamariz J. Synthesis of α-ketols by functionalization of captodative alkenes and divergent preparation of heterocycles and natural products. Tetrahedron. 2015;71(38):6961–6978. https://doi.org/10.1016/j.tet.2015.07.010.
24. Alsayari A, Asiri YI, Bin Muhsinah A, Hassan MZ. Synthesis of new pyrazole hybrids as potential anticancer agents with xanthine oxidase inhibitory activity. Anticancer Agents Med Chem. 2022;22(12):2303–2309. https://doi.org/10.2174/1871520622666220110162651.
25. Payne M, Bottomley A L, Och A, Asmara A P, Harry E J, Ung AT. Synthesis and biological evaluation of 3, 5-substituted pyrazoles as possible antibacterial agents. Bioorg Med Chem. 2021;48:116401. https://doi.org/10.1016/j.bmc.2021.116401.
26. Nidhar M, Khanam S, Sonker P, Gupta P, Mahapatra A, Patil S, *et al.* Click inspired novel pyrazole-triazole-persulfonimide & pyrazole-triazole-aryl derivatives; Design, synthesis, DPP-4 inhibitor with potential anti-diabetic agents. Bioorg Chem. 2022;120:105586. https://doi.org/10.1016/j.bioorg.2021.105586.
27. Hassan RA, Al-Sabawi AH. Synthesis of some new α,β-Unsaturated carbonyl compounds, thiophene, imine and coumarin derivatives containing hydrazide-hydrazone moiety. Egyp J Chem. 2023;66(6):383–391. https://dx.doi.org/10.21608/ejchem.2022.156323.6764.
28. Al-Sabawi AH, Younis SA, Saeed RA. Synthesis of some novel pyridine, sulfonamide, coumarin and thiophene derivatives. Egyp J Chem. 2023;66(2):349–355. https://doi.org/10.21608/ejchem.2022.135732.5979.
29. Khidre RE, El-Gogary SR, Mostafa MS. Design, synthesis, and antimicrobial evaluation of some novel pyridine, coumarin, and thiazole derivatives. J Heterocycl Chem. 2017;54(4):2511–2519. https://doi.org/10.1002/jhet.2854.
30. Salman AS. Utility of activated nitriles in the synthesis of novel heterocyclic compounds with antitumor activity. Org Chem Int. 2013;1–9. https://dx.doi.org/10.1155/2013/259348.
31. Özkay Y, TunalıY, Karaca H, Işıkdağ I. Antimicrobial activity and a SAR study of some novel benzimidazole derivatives bearing hydrazone moiety. Eur J Med Chem. 2010;45(8):3293–3298. https://doi.org/10.1016/j.ejmech.2010.04.012.

تشييد بعض الهيدرازايد-هيدرازون والمركبات الحلقية غير المتجانسة الجديدة مشتقات الثايوفين، ايمين، كومارين و البيرازول

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الخلاصة

تم تشييد سلسلة من المشتقات الجديدة الثايوفين ، الايمين ، الكومارين و البيرازول X_4-X_{16} باستخدام N – (1- (4- (بنزيل سلفونيل) فينيل) ايثيليدين)-2- سيانو اسيتو هيدرازيد X_3 بوصفه مادة اساسية أولية عن طريق مفاعلتها مع كواشف مختلفة مثل (النترالون ، سايكلو بنتانون ، سايكلو هبتانون ، 2-هيدروكسي بنزالديهايد ، 2-هيدروكسي-1- نفثالديهايد ، كبريتيد ثنائي كاربون و فنيل ايزوثايو سيانيد). تم تحضير المركب X_3 من تصعيد 4-(بنزايل سلفونيل) اسيتوفينون مع 2- سيانو اسيتوهيدرازايد في الايثانول. تم تشخيص تراكيب المركبات المحضرة الجديدة من خلال القياسات الفيزيائية و الطيفية (الأشعة تحت الحمراء والتحليل الطيفي البروتون والكاربون 13 النووي المغناطيسي).

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