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An Efficient Synthesis of Some Novel Benzo Coumarin Derivatives Under Solvent Conditions from 2-acetyl-benzo[*f*]chromen-3-one

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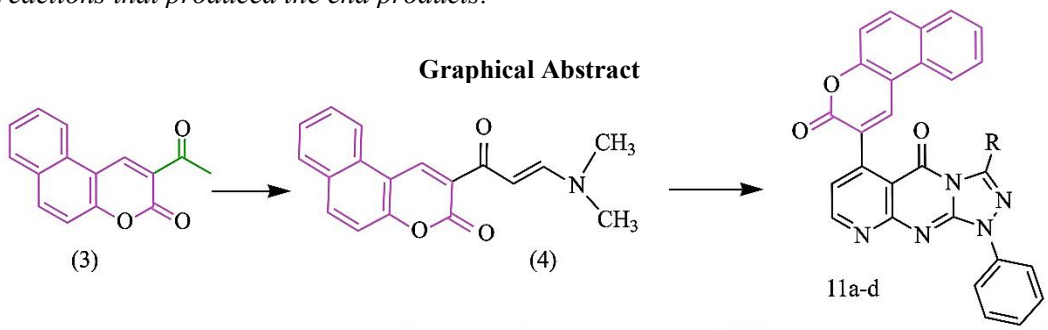
Abstract

The synthesis of the target compounds began with the preparation of 2-(3-(dimethylamino)acryloyl)-3H-benzo[f]chromen-3-one. This intermediate was obtained through the reaction of 2-acetylbenzo[f]coumarin-3-one with N,N-dimethylformamide dimethyl acetal (DMFDMA) under reflux conditions in xylene. The enaminone thus formed was subsequently reacted with 6-aminothiouracil in acetic acid, leading to the formation of 2-thioxo-2,3-dihydro-1H-pyrido[2,3-d]pyrimidin-4-one. This compound served as a pivotal intermediate for the synthesis of a series of pyridotriazolopyrimidinones. These derivatives were synthesized by reacting compound 6 with various hydrazonoyl halides in the presence of triethylamine and dioxane as a solvent. The structures of all the newly synthesized compounds were confirmed through comprehensive spectroscopic techniques, including nuclear magnetic resonance (NMR), infrared (IR) spectroscopy, and mass spectrometry (MS), as well as elemental analysis. There was also discussion and rationalization of the mechanistic elements of the reactions that produced the end products.

Graphical Abstract



Keywords: 2-hydroxynaphthaldehyde, enaminone, hydrazonoyl halides, pyridotriazolopyrimidinones, 2-acetyl-benzo[*f*]chromen-3-one.

INTRODUCTION

Heterocyclic compounds containing nitrogen, oxygen, and sulfur atoms possess various interesting biological activities. Among these compounds, Coumarins which are naturally occurring compounds found in the plant kingdom [1], Coumarin (1) 2*H*-1-benzopyran-2-one, as shown in Figure 1, is an organic compound that belongs to a worthwhile family of heterocycles (benzopyrone family), that exist naturally and/or synthetically. It was isolated for the first time in 1820 by Vogel from tonka beans and synthesized for the first time in 1868 by Perkin. Literature survey showed that coumarin and its diverse derivatives exhibited antimicrobial [2–4], antiviral [5], antitumor [6], anti-HIV [7], analgesic [8], anti-SARS-CoV-2

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agents [9], as well as antioxidant [10] activities. Because coumarins have cytotoxic effects against a variety of cancer cell types, including gastric, liver, colon, breast, and prostate cancer, their activity has drawn a lot of attention [11–19]. In addition, derivatives of coumarin have different biomedical potentials such as antimicrobial [20–24], anticoagulants [25], antioxidant [26–29], anticancer [30–35], and anti-inflammatory [36–38] activities. The isolation, synthesis, and evaluation of coumarins have become a very attractive and rapidly developing field in recent years [39, 40]. Benzocoumarins are a type of extended structure of coumarins in which the coumarin core is fused with the benzene ring at 7,8-, 6,7-, 5,6-, or 3,4-positions. Benzocoumarin derivatives might be classified into four groups: 7,8-benzocoumarin (2) [benzo[*h*]coumarin], 6,7-benzocoumarin (3) [benzo[*g*]coumarin], 5,6-benzocoumarin (4) [benzo[*f*]coumarin], and 3,4-benzocoumarin (5) [benzo[*c*]coumarin], as illustrated in Figure 1 [24], Benzocoumarins have a wide range of applications, especially in organic and pharmaceutical chemistries, which makes them of particular interest.

This paper aimed to describe the utility of 2-acetylbenzo[*f*]coumarin-3-one [3] in the synthesis of pyridotriazolopyrimidinone [11] and their annulated systems through multicomponent reaction of 2-Thioxo 2,3-dihydro-1*H*-pyrido[2,3-*d*]pyrimidin-4-one [6], trimethylamine, and hydrazonoyl halide derivatives (7a-d).

EXPERIMENTAL SETUP

The characterization of the synthesized compounds was carried out using a variety of analytical techniques to ensure the accuracy and reliability of the structural assignments. An electrothermal melting point equipment was used to measure melting points; the results are uncorrected. Infrared (IR) spectra were recorded using a Shimadzu FT-IR 8201 PC spectrophotometer with potassium bromide (KBr) discs as the medium, enabling the identification of key functional groups present in the compounds.

Proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained using two advanced spectrometers, namely, a Varian Gemini operating at 300 MHz and a JNM-LA 400 FT-NMR system operating at 400 MHz. The spectra were recorded in deuterated solvents, specifically chloroform ($CDCl_3$) and dimethyl sulfoxide $(DMSO\text{-}d)_6$, with tetramethylsilane (TMS) used as an internal reference to standardize chemical shift values, which are reported in parts per million (ppm).

Mass spectrometric analysis was performed using a Shimadzu GC-MS QP1000 EX system, allowing for the determination of the molecular weight and fragmentation pattern of the synthesized compounds. Elemental analysis was conducted at the Microanalytical Centre of Cairo University to confirm the elemental composition and purity of the final products. The combined use of these analytical techniques provided comprehensive confirmation of the structures and compositions of the synthesized compounds.

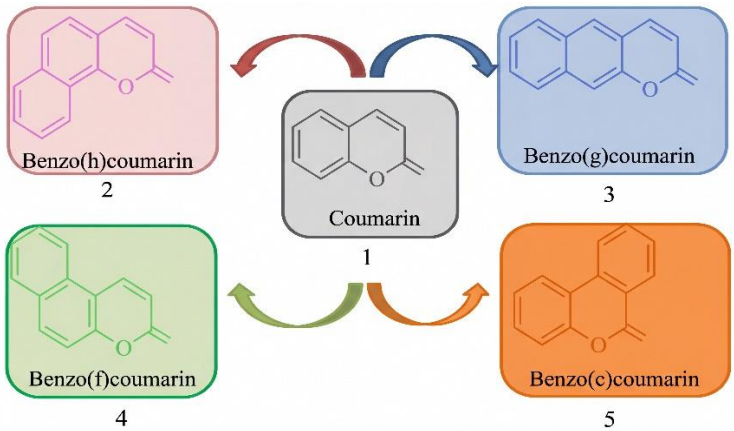


Figure 1. The chemical structures of coumarin and benzocoumarins.

Synthesis of Enaminone [4]

The synthesis of 2-acetylbenzo[f]coumarin-3-one (3) was carried out following a procedure reported in the literature [16]. To obtain the corresponding enaminone, 0.02 moles of compound 3 reacted with an equimolar amount (0.02 moles) of N, N-dimethylformamide dimethyl acetal (DMFDMA) in xylene. To guarantee full conversion, the reaction mixture was refluxed for two hours. The mixture was allowed to cool to room temperature following the reaction period, which caused the xylene to gradually evaporate.

The resulting crude product was treated with petroleum ether to facilitate purification, yielding the desired product with a yield of 40-60%. The melting point of the final product was found to be 200°C, which is consistent with values previously reported in the literature [17]. This approach demonstrates an efficient method for the synthesis of the intermediate enaminone, which plays a crucial role in subsequent reaction pathways.

Synthesis of 2,3-dihydro-5-[3-oxo-3H-benzo[f]chromen-2-yl]-2-thioxo-pyrido[2,3-d]pyrimidin-4(1H)-one [6]

To synthesize 2-thioxo-2,3-dihydro-1H-pyrido[2,3-d]pyrimidin-4-one[6], a mixture of 2-(3-(dimethylamino)acryloyl)-3H-benzo[f]chromen-3-one (4) [2.93 g, 10 mmol] and 6-amino-2-thiouracil (5) (1.43 g, 10 mmol) was prepared in 15 mL of glacial acetic acid. To aid in the synthesis of the intended product, the reaction mixture was exposed to reflux for four hours. A solid product precipitated when the reaction was finished, and the liquid was allowed to cool naturally to room temperature. To improve purity, the material was filtered, cleaned, and then recrystallized from dimethylformamide (DMF). The final product, 2-thioxo-2,3-dihydro-1H-pyrido[2,3-d]pyrimidin-4-one (6), was obtained as an orange solid with a yield of 80% (Figure 2). The compound exhibited a melting point greater than 360°C, indicative of its thermal stability and purity.

Characterization of Substrate 6

Yield and Physical Appearance

Yield: 80%

Physical State: Orange solid

Infrared (IR) Spectroscopy (KBr, cm^{-1})

3314, 3191 cm^{-1}: These peaks correspond to the stretching vibrations of two N-H (amine or amide) groups.

3094, 2965 cm^{-1}: These peaks are attributed to the C-H stretching vibrations, typically observed for aromatic and aliphatic C-H bonds.

1720 cm^{-1}: This peak represents the stretching vibration of a carbonyl (C=O) group, possibly from a ketone, ester, or similar functional group.

1639 cm^{-1}: This is also indicative of C=O stretching, likely corresponding to an additional conjugated carbonyl group.

1600 cm^{-1}: This peak is associated with the C=N (imine or azomethine) bond stretching vibration.

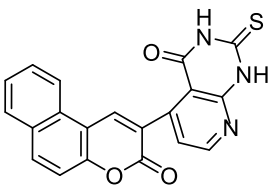


Figure 2. 2,3-dihydro-5-[3-oxo-3H-benzo[f]chromen-2-yl]-2-thioxo pyrido[2,3-d]pyrimidin-4[1H]-one.

1547 cm^{-1}: This peak corresponds to the stretching vibration of a conjugated C=C bond, typically found in aromatic or unsaturated systems.

1287 cm^{-1}: This band is characteristic of the C=S (thiocarbonyl) group stretching vibration.

Proton Nuclear Magnetic Resonance (^{1}H NMR) (DMSO-d_6, δ, ppm)

δ 7.41–7.82 (multiplet, 5H): This range corresponds to the aromatic protons, likely from a substituted benzene or similar aromatic system.

δ 8.05 (doublet, 1H, J = 8 Hz): This doublet indicates a proton on an aromatic ring with a coupling constant (J) of 8 Hz, suggesting an ortho-positioned neighboring proton.

δ 8.30 (doublet, 1H, J = 8 Hz): Similar to the previous signal, this peak indicates another proton in an aromatic system with an ortho-coupling of 8 Hz.

δ 8.41 (doublet, 1H, J = 8 Hz): Another doublet, indicating an aromatic proton in proximity to another hydrogen.

δ 9.22 (singlet, 1H): This singlet corresponds to a single isolated proton, possibly on a nitrogen or part of a unique system like an imine (C=NH) or an amidic structure.

δ 12.58 (singlet, 1H, NH, D_2O exchangeable): This singlet represents a hydrogen attached to a nitrogen (N-H) group. Its D_2O exchangeability confirms its identity as an N-H proton (like an amide, imide, or amine).

δ 13.11 (singlet, 1H, NH, D_2O exchangeable): This is another N-H proton, as confirmed by D_2O exchange, indicating the presence of an additional NH-containing functional group, possibly from a pyrimidine, triazole, or thiourea-like structure.

Mass Spectrometry (MS)

Molecular ion (m/z = 373): The observed molecular ion peak corresponds to the molecular mass [M^+] of the compound, confirming its molecular weight as 373 Da.

Elemental Analysis (Calculated vs. Found)

Molecular Formula: $C_{20}H_{11}N_3O_3S$ (molecular weight = 373.38)
Calculated Composition (%):
Carbon (C): 64.33%
Hydrogen (H): 2.97%
Nitrogen (N): 11.25%
Sulfur (S): 8.59%

Experimental Composition (Found, %)

Carbon (C): 64.45%, slightly higher than calculated, within an acceptable range

Hydrogen (H): 2.86% slightly lower, but within the experimental margin of error

Nitrogen (N): 11.12%, slightly lower, but close to the calculated value

Sulfur (S): 8.49% close to the calculated value

Summary

The compound was successfully characterized using IR, NMR, MS, and elemental analysis. The IR data confirmed the presence of N-H, C-H, C=O, C=N, and C=S functional groups, while the NMR spectra revealed the expected proton environments for an aromatic system, N-H protons, and isolated

protons. The molecular mass (373 Da) was confirmed by MS, and the elemental analysis was consistent with the calculated values for the proposed molecular formula ($C_{20}H_{11}N_3O_3S$).

General Method for Synthesis of Pyridotriazolo[4,3-*a*]pyrimidinones *11a-d*

To synthesize the pyridotriazolopyrimidinone derivatives (11a-d), a mixture of compound **6** (0.373 g, 1 mmol) and the corresponding hydrazonoyl halides (7a-d) (1 mmol each was prepared in 10 mL of dioxane). To this reaction mixture, triethylamine (0.14 mL, 1 mmol) was added as a base to facilitate the reaction. The reaction mixture was then subjected to reflux at 101°C, allowing the reaction to proceed until the evolution of hydrogen sulfide gas was no longer observed, indicating the completion of the reaction.

After completion, the reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure. The resulting solid product was collected by filtration and subsequently purified by recrystallization from ethanol, yielding the target pyridotriazolopyrimidinone derivatives (Figure 3) (11a-d).

The yields and physical characteristics of the synthesized compounds are presented in Table 1, providing detailed insights into their purity and structural attributes.

Characterization of Substrates

Physical Appearance and Yield

The compound appears as a yellow solid.

The reaction yielded the product in 70% yield.

The melting point of the compound is recorded in the range of 237-239°C, suggesting its purity and stability.

Infrared (IR) Spectroscopy (KBr, cm^{-1})

3064, 2919 cm^{-1}: These peaks correspond to the stretching vibrations of the C-H bonds, indicating the presence of aromatic and aliphatic C-H groups.

1715 cm^{-1}: This strong band is characteristic of a carbonyl (C=O) group, likely associated with an ester, ketone, or amide functional group.

1609 cm^{-1}: This peak is attributed to the stretching vibration of the (C=N) imine group, confirming the presence of a nitrogen-containing heteroaryl system.

1556 cm^{-1}: This band is assigned to the stretching of C=C bonds present in the aromatic or conjugated system.

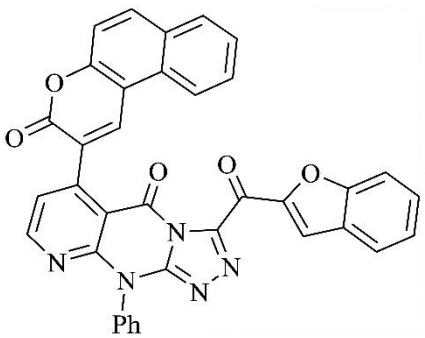


Figure 3. 3-(benzofuran-2-oyl)-6-(3-oxo-3H-benzo[f]chromen-2-yl)-1-phenyl-pyrido[2,3-d][1,2,4] triazolo[4,3-a]pyrimidin-5(1H)-one (11a).

Proton Nuclear Magnetic Resonance (^{1}H NMR), $CDCl_3$, δ, ppm

7.50-7.69 ppm (multiplet, 15H): These signals correspond to protons in an aromatic environment, indicative of multiple aromatic rings or substituted aryl groups.

7.88 ppm (doublet, 1H, J = 8 Hz): This signal corresponds to an aromatic proton with a coupling constant (J) of 8 Hz, suggesting an ortho-coupled system.

8.13 ppm (doublet, 1H, J = 8 Hz): Another doublet at 8.13 ppm is consistent with an ortho-coupled aromatic proton.

8.60 ppm (doublet, 1H, J = 8 Hz): Similar to the previous two doublets, this also suggests an ortho-coupled aromatic proton, indicating symmetry or specific substitution in the aromatic system.

9.23 ppm (singlet, 1H): This singlet likely corresponds to a proton associated with an imine (C=N-H) or an isolated aromatic proton, confirming the structure of a heteroaryl system.

Mass Spectrometry (m/z)

Molecular ion peak (m/z = 601): The molecular ion peak corresponds to the molecular weight [M^+] of 601, confirming the expected molecular formula $C_{36}H_{19}N_5O_5$.

Elemental Analysis

Calculated (%): Carbon (C) = 71.88%, Hydrogen (H) = 3.18%, Nitrogen (N) = 11.64%.

Found (%): Carbon (C) = 71.99%, Hydrogen (H) = 3.27%, Nitrogen (N) = 11.53%.

The experimental values are in close agreement with the theoretical (calculated) values, validating the proposed molecular formula $C_{36}H_{19}N_5O_5$ for the synthesized compound.

Summary

The synthesized compound is a yellow crystalline solid with a melting point of 237–239°C. Spectroscopic data (IR, NMR, and MS) confirm the presence of key functional groups such as C=O, C=N, and C=C, along with multiple aromatic systems. The elemental analysis and molecular ion peak (m/z = 601) support the proposed molecular formula $C_{36}H_{19}N_5O_5$, while the NMR data reveal the presence of specific aromatic and imine protons.

1. *Appearance:* The compound is an off-white solid, obtained with a yield of 70%.
2. *Melting Point:* The substance melts between 200-201°C.
3. *Infrared (IR) Spectrum (cm-1):* 3070, 2980, 2927 cm^{-1} are characteristic of C-H stretching vibrations (alkyl groups).
   1740 and 1645 cm^{-1} indicate the presence of carbonyl (C=O) and imine (C=N) functional groups.

   1602 cm^{-1} corresponds to another C=N stretching, while 1554 cm^{-1} is indicative of C=C (aromatic) stretching (Figure 4).

Proton Nuclear Magnetic Resonance (^{1}H NMR)

1.27 ppm (triplet, 3H, J = 7Hz): This corresponds to a -CH_2CH_3 group (ethyl group).

4.29 ppm (quartet, 2H, J = 7Hz): This is associated with the -CH_2 group of the same ethyl group.
7.27 ppm (singlet, 2H): Aromatic protons.

7.41-7.82 ppm (multiplet, 7H): Additional aromatic protons showing splitting due to the complex structure of the aromatic system.

7.96, 8.10, 8.39, 8.42 ppm (doublets, each 1H, J = 8Hz): These signals correspond to additional aromatic protons, each splitting into doublets with an 8 Hz coupling constant.

9.22 ppm (singlet, 1H): Likely associated with a proton on an electron-rich aromatic ring or an imine proton.

Mass spectrometry: The molecular ion peak (m/z) observed at 529 corresponds to the molecular weight of the compound, confirming its structure.

5. *Elemental Analysis:* The compound's molecular formula is $C_{30}H_{19}N_5O_5$, and the elemental analysis shows a very close match to the theoretical values:
Calculated: C = 68.05%, H = 3.62%, N = 13.23%
Found: C = 68.16%, H = 3.51%, N = 13.34%

   This confirms that the compound's composition is in agreement with its expected molecular formula.

   In summary, these spectroscopic and analytical data confirm the successful synthesis of the compound and provide insights into its molecular structure, purity, and composition.
   7.56-7.67 (m, 7H), 7.74 (t, 1H, *J* = 7.5Hz), 8.00 (d, 1H, *J* = 8Hz), 8.08 (d, 1H, *J* = 8Hz), 8.31 (d, 1H, *J* = 8Hz), 8.66 (d, 1H, *J* = 8Hz), 9.25 (s,1H); MS (m/z): 499. Anal. calcd. for $C_{29}H_{17}N_5O_4$ (499.48): C, 69.74; H, 3.43; N, 14.02; found: C, 69.61; H, 3.32; N, 14.13 (Figure 5).

The compound was isolated as a brown solid with a yield of 70%. It exhibited a melting point in the range of 270–271°C, indicating its purity and thermal stability. Infrared (IR) spectroscopy analysis revealed characteristic absorption bands at 3059 cm^{-1} and 2920 cm^{-1}, corresponding to C-H stretching vibrations. Strong signals at 1719 cm^{-1} and 1668 cm^{-1} were attributed to carbonyl (C=O) functional groups, while the band at 1556 cm^{-1} indicated the presence of a C=N bond (Figure 6).

Proton nuclear magnetic resonance (^{1}H NMR) spectroscopy performed in DMSO-d_6 showed multiple peaks in the range of δ 7.50–7.71 ppm, corresponding to aromatic protons (15H). Distinct doublets were observed at δ 8.00, 8.31, and 8.66 ppm (1H each) with coupling constants (J) of 8 Hz, indicative of specific proton environments. A singlet at δ 9.25 ppm (1H) further confirmed the structure.

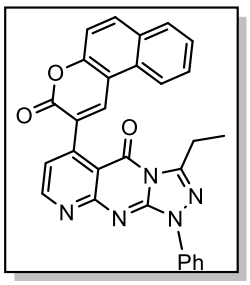
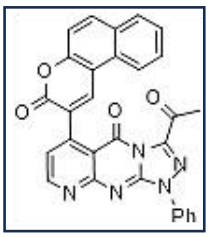


Figure 4. 3-ethyl-6-[3-oxo-3H-benzo[f]chromen-2-yl]-1-phenyl-1, 5-dihydropyrido [2,3-d] [1, 2, 4] triazolo [4,3-a]pyrimidin-5(1H)-one.



Yellow solid in 71% yield; m.p.: 234-235°C; IR (KBr, cm^{-1}): 3072, 2920 (CH), 1720, 1685 (c = 0) , 1602 (C=N), 1547 (C=C); H NMR (DMSO-d_6, 8, ppm):
2.43 (s, 3H, $COCH_3$), 7.43 (t, 1H, J = 7.5Hz),

Figure 5. [3-Acetyl-1-phenyl-1,5-dihydropyrido[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one-6-yl]-3H-benzo[f]chromen-3-one (11c).

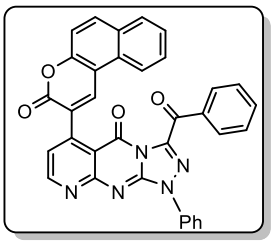


Figure 6. 3-Benzoyl-1-phenyl-1, 5-dihydropyrido[2, 3-d] [1,2,4]triazolo [4,3-a]pyrimidin-5-one-6-yl-3H-benzo[f]chromen-3-one (11d).

Mass spectrometry analysis showed a molecular ion peak at m/z 561, consistent with the molecular formula $C_{34}H_{19}N_5O_4$. Elemental analysis calculated for this formula yielded C: 72.72%, H: 3.41%, and N: 12.47%. The experimental values found were C: 72.60%, H: 3.29%, and N: 12.60%, which closely matched the theoretical predictions, confirming the compound's identity and composition.

General Procedure for the Synthesis of Sulphonamides (13a-d)

A mixture of enaminone (4) (0.322 g, 1 mmol) and sulphadiazine, sulphademidine, sulphadimethoxazine, or sulphaisoxazole in EtOH (10 mL) and acetic acid (5 mL) was refluxed for 3 h. After cooling the reaction mixture, the solid product was filtered out and recrystallized from DMF to yield 13a and 13b, respectively.

13a: The compound was obtained as an orange solid with a high yield of 79% and a melting point of 355°C, suggesting its stability and purity.

NMR Analysis

The proton nuclear magnetic resonance (^{1}H NMR) spectrum recorded at 300 MHz in DMSO-d_6 displayed the following signals:

A singlet at δ 2.27 ppm corresponding to two methyl groups (6H, $2CH_3$).

A singlet at δ 6.10 ppm, indicative of a single proton at the fifth position of the pyrimidine ring (H5-pyrimidine).

Doublets at δ 6.60 ppm, 6.74 ppm, 7.30 ppm, 7.52 ppm, and 8.18 ppm (1H each, J = 8 Hz), corresponding to aromatic protons.

Multiplets were observed between δ 7.61–8.03 ppm and δ 8.22–8.32 ppm, representing overlapping signals for four aromatic protons (2H each).

A doublet at δ 8.57 ppm (1H, J = 8 Hz) and singlets at δ 9.25 ppm and δ 9.39 ppm (1H each) were assigned to distinct aromatic protons.

Two singlets at δ 10.60 ppm and 11.28 ppm indicated the presence of NH protons.

Elemental Analysis

The molecular formula, $C_{28}H_{22}N_4O_3S$, was verified by elemental analysis. The calculated values were:

Carbon (C): 63.87%
Hydrogen (H): 4.21%
Nitrogen (N): 10.64%
Sulfur (S): 62.09%

The experimentally determined values were slightly different but closely matched the theoretical predictions:

C: 63.40%
H: 3.96%
N: 10.02%
S: 61.81%

This confirms the successful synthesis and correct composition of the compound.

13b: The compound was obtained as an orange solid with a yield of 70%, and its melting point was recorded in the range of 289–291°C, suggesting its stability and relatively high purity.

NMR Analysis

The ^{1}H NMR spectrum (300 MHz, DMSO-d_6) revealed the following proton signals:
A singlet at δ 3.60 ppm corresponding to two methoxy groups (6H, $2OCH_3$).

Aromatic proton signals included:
Doublets at δ 6.58 ppm, 6.74 ppm, 7.27 ppm, 7.47 ppm, and 8.57 ppm (1H each, J = 8 Hz).

A multiplet between δ 7.60–7.81 ppm representing four aromatic protons.

A doublet at δ 7.88 ppm (1H, J = 8 Hz) and a multiplet between δ 7.94–8.32 ppm indicating two additional aromatic protons.

Singlets at δ 9.25 ppm and δ 9.38 ppm (1H each) are assigned to distinct aromatic protons.

A singlet at δ 10.55 ppm was attributed to an NH proton, confirming the presence of this functional group.

Elemental Analysis

The molecular formula of the compound, $C_{28}H_{22}N_4O_5S$, was supported by elemental analysis. The calculated values were:
Carbon (C): 63.87%
Hydrogen (H): 4.21%
Nitrogen (N): 10.64%
Sulfur (S): 62.09%

The experimentally determined values showed minor deviations but were consistent with theoretical predictions:
C: 63.40%
H: 3.96%
N: 10.02%
S: 61.81%

Additional Products

Further compounds synthesized in this study, along with their corresponding data, are summarized in Table 2 for detailed comparison and reference.

Reaction of Enaminone 1 with Sulpha Drugs

A mixture of enaminone 4 (1 mmol), sulpha drug derivatives 12a–d (1 mmol each), and four drops of acetic acid in ethanol was refluxed for 4–10 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into water, and the resulting solid was filtered, washed with ethanol, dried, and recrystallized from DMF to afford the desired products 13a–d. The results are summarized in Table 2.

Table 1. Preparation of pyrido triazolo[4,3-a] pyrimidiones.

S.N.	R	Product	Time (hr)	Yield(%)	Melting points
					Found
1	benzofuran-2yl	11a	10	70	237–239
2	$CO_2C_2H_5$	11b	9	70	200–210
3	CH_3	11c	8	71	234–235
4	C_6H_5	11d	8	70	270–271

The yield of the isolated products.

Table 2. Synthesis of sulphonamides 13a-d.

S.N.	Ar	Product	Time (hr.)	Yield(%)	Melting points		
					Found	***Reported***	***(Ref.)***
1	2-methyl-4,5-dihydropyrimidine	13a	10	79	355	3620	[18]
2	2,4,6-trimethyl-4,5-dihydropyrimidine	13b	9	70	289-291	290-291	[18]
3	4,6-dimethoxy-2-methyl-4,5-dihydropyrimidine	13c	8	81	264-265	260-261	[18]
4	5-methyloxazole	13d	8	77	261-263	This work	

The yield of the isolated products.

(*E*)-*N*-(oxazol-5-yl)-4-((3-oxo-3-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)prop-1-en-1-yl)amino)benzenesulfonamide

The compound was obtained as orange crystals with an excellent yield of 92%. The melting point was recorded in the range of 261–263°C, indicating high purity and thermal stability.

FT-IR Analysis

The Fourier-transform infrared (FT-IR) spectrum measured with KBr pellets provided the following key absorption bands:

A broad band at 3431 cm^{-1}, characteristic of two NH groups, indicating the presence of amine functionalities.

Peaks at 3062, 2966, and 2924 cm^{-1}, corresponding to C-H stretching vibrations of aromatic and aliphatic groups.

Strong absorptions at 1725 cm^{-1} and 1659 cm^{-1}, indicative of carbonyl (C=O) functional groups.

Bands at 1617 cm^{-1} and 1551 cm^{-1} were attributed to C=N and C=C stretching vibrations, respectively, confirming the presence of aromatic and imine functionalities.

^{1}H NMR Analysis

The proton nuclear magnetic resonance (^{1}H NMR) spectrum (300 MHz, in DMSO-d_6) revealed:

A multiplet between δ 6.76–7.93 ppm, corresponding to 13 aromatic protons (Ar-H), indicative of a richly substituted aromatic framework.

Two distinct singlets at δ 10.6 ppm and δ 11.65 ppm, which were assigned to two NH protons, further support the presence of amine groups in the structure.

This data collectively confirms the successful synthesis and characterization of the compound, with both spectroscopic and melting point data aligning with its expected structure and composition.

RESULTS AND DISCUSSION

Ethyl acetoacetate (2) in pyridine under reflux afforded 3-acetyl benzo coumarin (3). Reaction of compound 3 with dimethylformamide dimethyl acetal (DMFDMA) afforded 2-((E)3(dimethyl amino) acryloyl)-3H-benzo[f]chromen-3-one (4) [16]. The enaminone (4) underwent cyclocondensation with 6-amino-2-thioxo-2,3-dihydropyrimidin-4(1*H)*-one [5] in glacial acetic acid for 4h to give 2,3-dihydro-5-[3-oxo-3H-benzo[f]chromen-2-thioxo-pyrido[3-d] pyrimidin-4[1H]-one (6). The mechanism of the reaction is shown in Figure 2. Spectral data and micro elemental analysis were consistent with the collected product 6 (Figure 7). Its IR spectrum exhibited absorption bands at 3314 and 3191 cm^{-1}, attributable to 2NH groups, in addition to the presence of strong stretching frequencies at 1720, 1639 cm^{-1} due to 2C=O functions, and 1287 cm^{-1} was assignable for C=S group. The 1H NMR spectrum of 6 displayed two new singlet signals at 12.58 ppm and 13.11 ppm. exchangeable with D2O due to 2NH protons.

Treatment of 6 with different hydrazonoyl halide derivatives (7a-d) in refluxing dioxane in the presence of trimethylamine afforded the corresponding pyrido[2,3-*d*] [1,2,4] triazolo[4,3-*a*] pyrimidinones 11a-d as the end products based on spectral data (Figure 8). The results were summarized in Table 1. The mechanism explained in Figure 8 seems to be the most acceptable pathway for the formation of 11 from the reaction of thione 6 with 7 via two pathways. The first pathway is 1,3-addition of the thiol tautomer to the nitrilimines 7'(synthesized in situ from reaction of 7a-d with triethylamine) to the activated double bond in compound 6, affording 8a-d, which underwent nucleophilic cyclization reaction to give the spiro compounds 9a-d. The cycloadducts 9a-d undergo ring opening to give 10a-d, then cyclize to afford 11a-d through the loss of hydrogen sulfide. Los. The second pathway is the 1,3-cycloaddition reaction of nitrilimines 7' to the (C=S) double bond of 6 to afford 9a-d directly.

The structures of the synthesized products were confirmed by spectroscopic data. The IR spectral analyses for compounds 11a-d revealed the disappearance of bands corresponding to NH and C=S functions. The 1H NMR spectrum of 11b, for example, recorded the appearance of new triplet and quartet signals at δ 1.27 and 4.29 ppm, attributed to the signals of the ester group (Figure 9).

Comp. No. (7, 10)a: benzo furan-2-yl (11a)
Comp. No. (7, 10)b: $CO_2C_2H_5$ (11b)
Comp. No. (7, 10)c: CH_3 (11c)
Comp. No. (7, 10)d: C_6H_5 (11d)

Besides, the reaction of enaminone 4 with sulphadrugs, namely: (sulphadiazine, sulphademi dine, sulphadimethoxazine, or sulphisoxazole) 12a-d was also examined. Thus, condensation of enamine 4 with sulphadrugs by refluxing in ethanol/acetic acid medium afforded benzene sulphonamide derivatives 13a-d with high yield, respectively (Figure 10). Compounds 13a–d's chemical structures

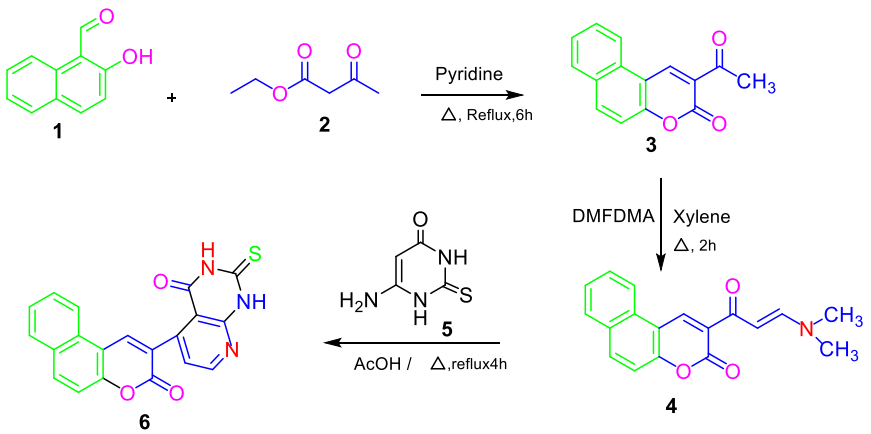


Figure 7. Synthesis of 2-thioxopyridopyrimidone 6.

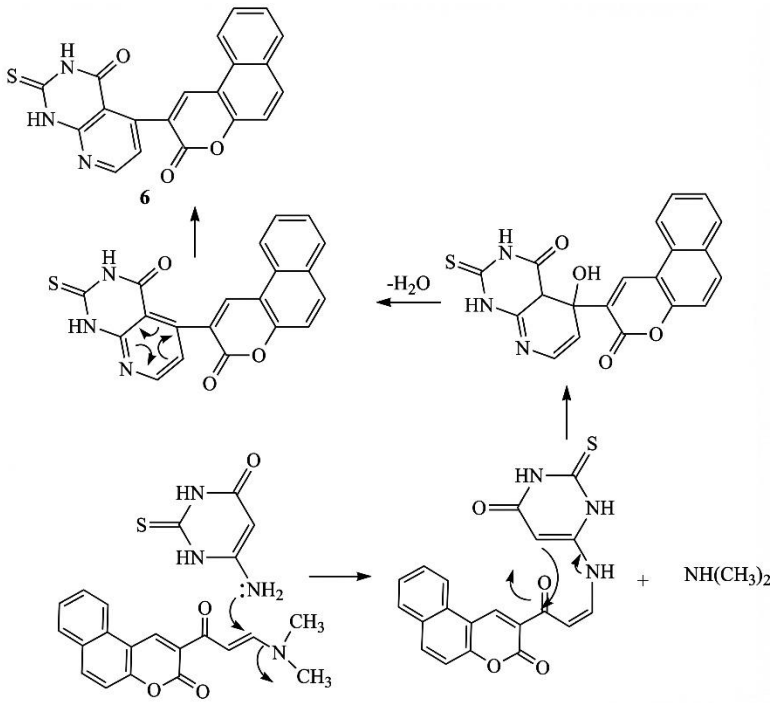


Figure 8. The proposal mechanism for the formation of compound 6.

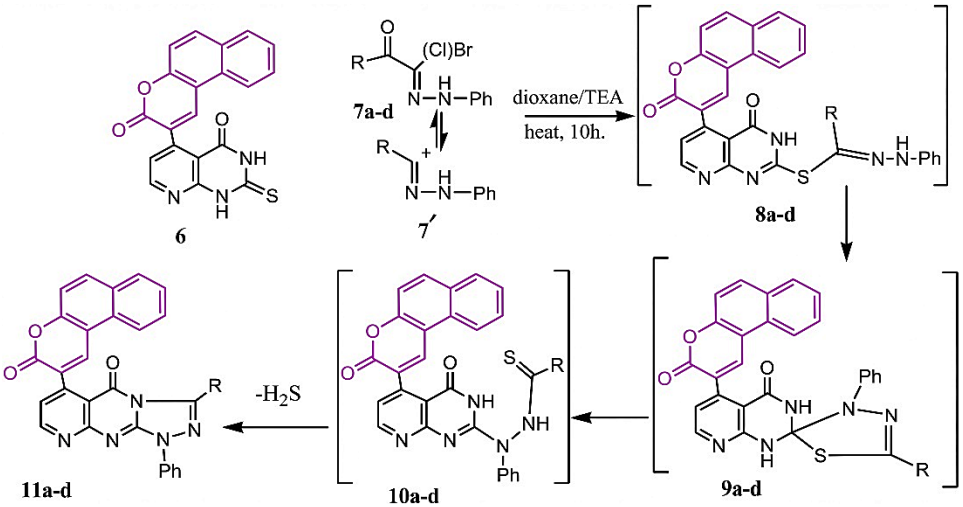


Figure 9. Synthesis of pyridotriazolopyrimidinones 11a-d.

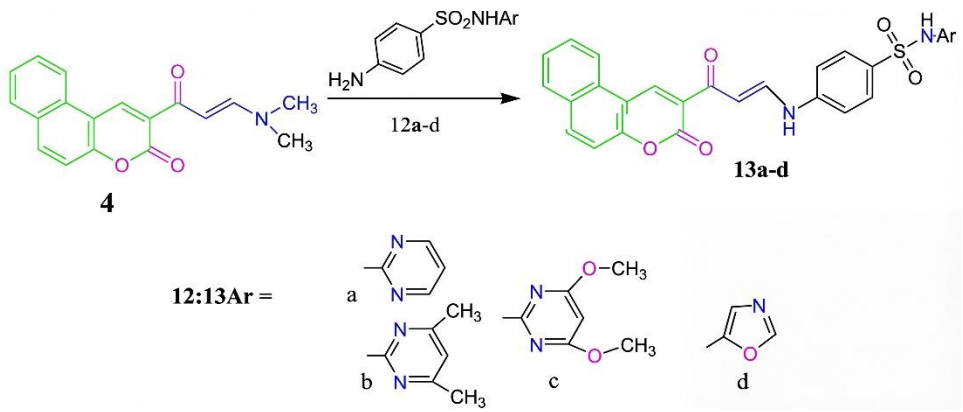


Figure 10. Condensation of enamine with sulphadrugs: synthesis of sulphonamides 13a-d.

were determined using elemental analysis and spectroscopy. The 13b IR spectrum revealed a broad band at 3430 cm^{-1}, which is associated with 2NH groups, and at 1724 cm−1 and 1665 cm−1, which are associated with 2 C=O functional groups. In addition to the aromatic proton signal at δ 6.60–9.25 ppm, the 1H NMR spectrum showed a singlet signal at δ 2.27 ppm that was attributed to two methyl groups.

Additionally the olefinic protons resonated as a doublet one at δ 6.12, the other at δ 7.42ppm respectively, and two singlet signals at δ 11.62 and 11.32 ppm, assignable to two NH protons exchangeable by D_2O.

CONCLUSIONS

In this study, the compound 2-(3-(dimethylamino)acryloyl)-3H-benzo[f]chromen-3-one, referred to as enaminone [4], was employed as a pivotal intermediate in the synthesis of novel heterocyclic frameworks. The reaction between enaminone 4 and 6-aminothiouracil in the presence of acetic acid resulted in the formation of 2-thioxo-2,3-dihydro-1H-pyrido[2,3-d]pyrimidin-4-one (compound 6) with a significant yield. This product was subsequently treated with a range of hydrazonoyl halides in a dioxane medium using triethylamine as a catalyst to synthesize pyridotriazolopyrimidinone derivatives, specifically 11a-d. Furthermore, a separate series of reactions was carried out to produce sulphonamides linked to enaminone 4, expanding the chemical diversity of the synthesized compounds.

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