International Journal of ChemTech Research
CODEN (USA): IJCRGG ISSN: 0974-4290
Vol.7, No.4, pp 1814-1817, 2014-2015

# Synthesis of novel coumarin derivatives with Expected Biological Activity

**Taymaa. ALAwad[1], Farouk. Kandil[2], Sameh Hamo[2]**

**[1]Chemistry Department, Faculty of Science, Damascus University, Syria.**
**[2]Plant Biology Department, Faculty of Science, Damascus University, Syria.**

**Abstract:** Four new coumarin derivatives 6-hydroxy-3-(5-mercapto-4*H*-1,2,4-triazol-3-yl)-2*H*-chromen-2-one, 3-(5-mercapto-4*H*-1,2,4-triazol-3-yl)-8-methoxy-2*H*-chromen-2-one, 6-hydroxy-3-(5-mercapto-4*H*-1,2,4-triazol-3-yl)-4-(phenyldiazenyl)-2*H*-chromen-2-one,and3-(5-mercapto-4*H*-1,2,4-triazol-3-yl)-4-phenyl diazenyl)-2 *H*-chromen-2-one ,were synthesized for the purpose of pharmacological evaluation. Some rep-resentative compounds showed antitumor activity *in vitro* on Ehrlich ascites carcinoma in the preliminary testing.
**Keywords:** Substituted coumarins, mercapto coumarins , synthesis , pharmacological evaluation

## Introduction

The synthesis of coumarin (2-oxo-2H-chromene) derivatives has attracted considerable attention of organic and medicinal chemists as these are widely used as fragrances, pharmaceuticals and agrochemicals [1-4]. Having in mind the wide variety of their usage, we thought it worthwhile to synthesize new coumarin derivatives.

## Materials and Methods

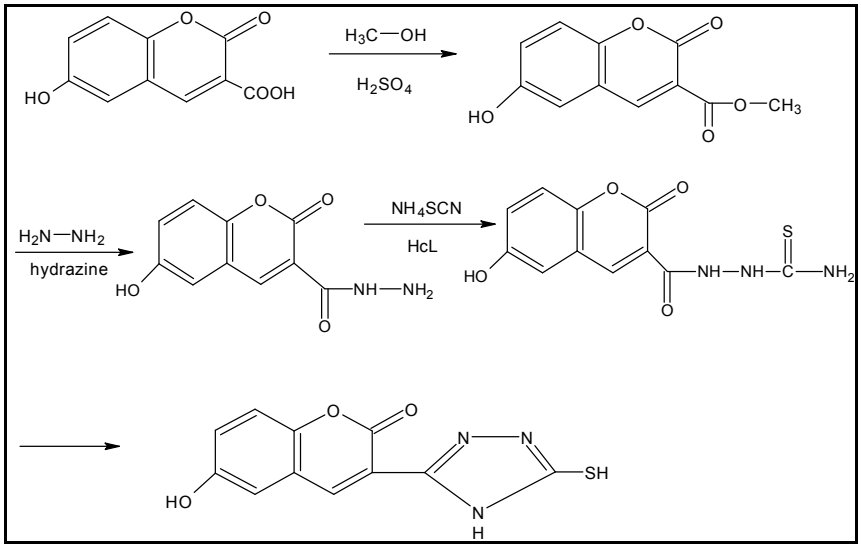
### Chemicals and instruments required

The chemicals are used as of analytical grade i.e. Methanol, Hydrazine, Conc. $H_2SO_4$, Ammonium thiocyanate, Conc. HCl, ethanol. All the melting points were determined in open capillaries, using melting point apparatus, expressed in 0 C. The IR spectra of the compounds were recorded on Shimadzu IR Affinity FTIR spectrophotometer using KBr discs and the values are expressed in $cm^{-1}$. The 1H NMR spectra of compounds were recorded on Bruker Avance Ii 400 MHz NMR spectrophotometer using DMSO as an internal standard and the values are expressed in δ ppm.

## Experimental

An equimolar quantity of coumaryl-carboxylic acid hydrazide (0.01 mole, 1.26 g), ammonium thiocyanate (0.01 mole, 1.52 g) and hydrocholoric acid (5 mL) in absolute ethanol (50 mL) was refluxed for 4 h. The white solid that appeared on cooling was filtered and the excess solvent was removed by vacuum evaporation. The residue was recrystallised from DMF-ethanol (30-70 v/v), (Yield 90 %; mp: 233-235 C0). This intermediate (0.01 mole 1.85 g) was refluxed in 10 % sodium hydroxide solution (5 mL) for 3 h. The resulting solution was cooled and filtered. The filtrate was acidified with hydrocholoric acid to pH 5-6. The solid which appeared was filtered, dried and recrystallised from dilute ethanol. Yield 75 %; mp: 295

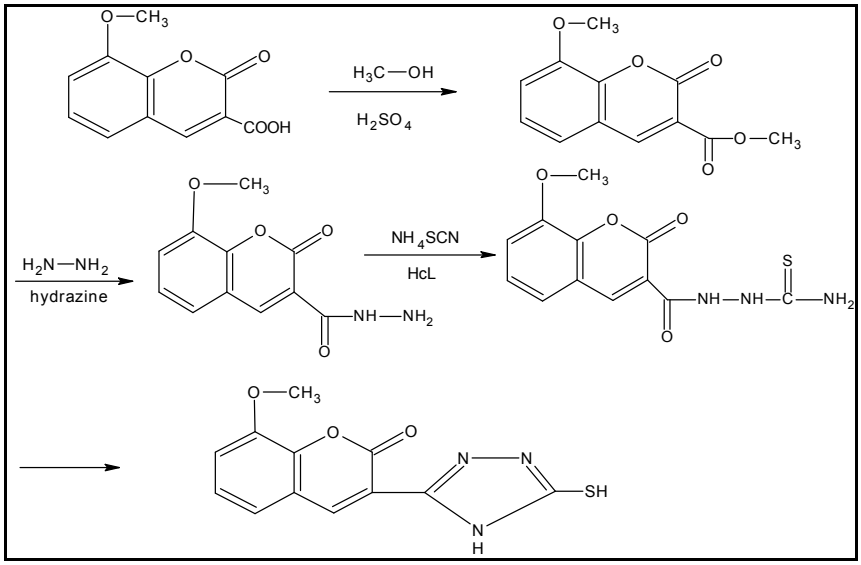
**1)- 5-hydroxy-2-(5-mercapto--1,3,4-triazol-2-yl)-2H-chromen-2-one**




**IR, $cm^{-1}$ : 3356 (NH), 1642 (C=N), 2667(--SH), 1722 (C=O); 3432(-OH), $^{1}$ H-NMR, ppm: 5.10 (s, 1H, NH), 7.5-7.6 ppm (3 H, aromatic protons), 11.6 ppm (1H, SH) and at 11.8 ppm (1H, broad OH).**

**MS : m/z 261,257**

**2)- 2-(5-mercapto-4H-1,3,4-triazol-2-yl)-7-methoxy-2H-chromen-2-one**



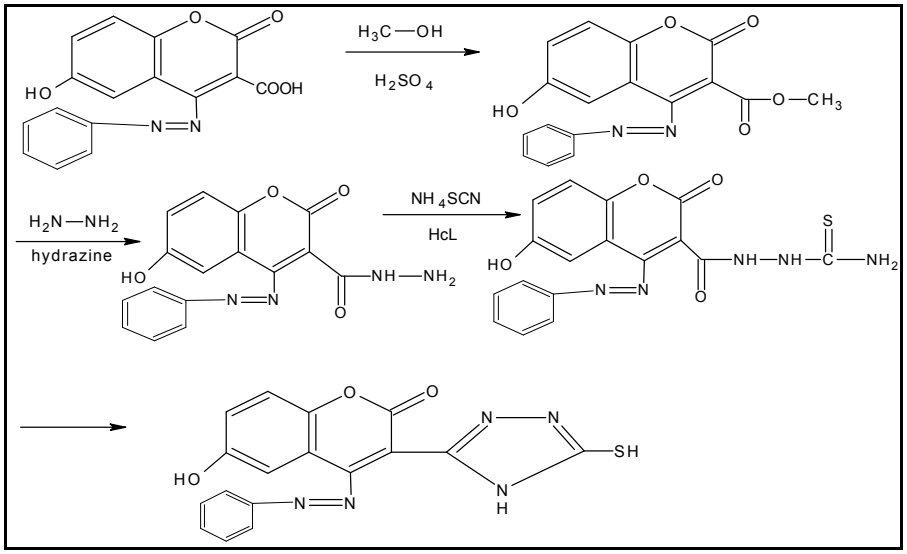

**IR, $cm^{-1}$ : 3378 (NH), 1645(C=N), 2522(-SH); 1720 (C=O); $^{1}$ H-NMR, ppm: 5.22 (s, 1H, NH) , 7.4-7.6 ppm (3 H, aromatic protons), and 11.7 ppm (1H, SH). MS : m/z 275,284**

**Antibacterial studies**

Condensation products of some active group with coumarin-derivatives, (Rabarova et al, Lacova et al [5,6 ] found to possess antimicrobial *Staphylococcus aureus*, as Gram-positive bacteria. Nutrient agar plates were seeded using 0.1 of overnight cultures. Cylindrical plugs were removed from the agar plates using a sterile cork borer and 100 µL of the tested compound (50µg/ml, 100µg/mlEtOH) were added to the well in triplicates. Blank solvent was used as control. Plates inoculated with tested bacteria were incubated a37˚c, while those of Fungi were incubated at30˚c. Results were taken after 24 h of incubation and were recorded as average

diameter of inhibition zone in mm. All the newly synthesized compounds were subjected to antimicrobial screening by in vitro Cup plate technique,using positive controls Nystatine.

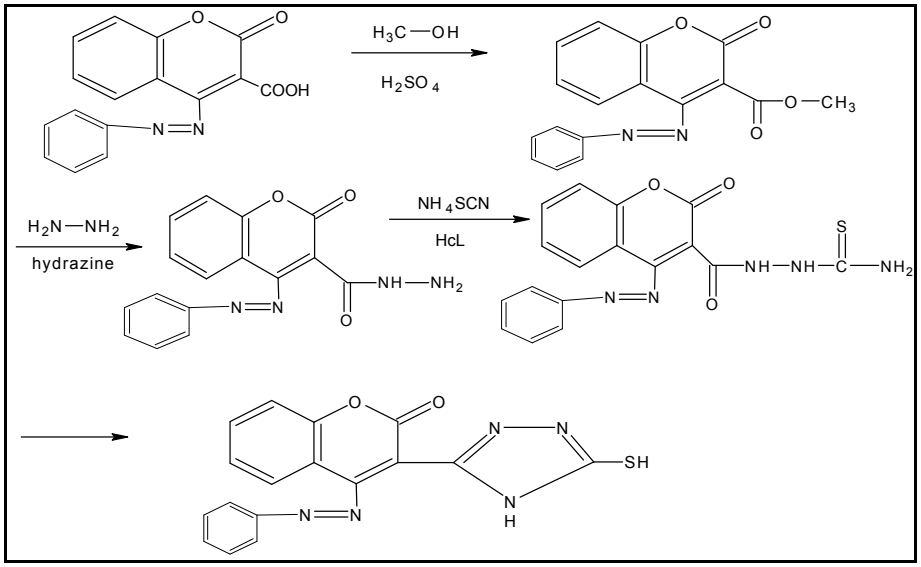
**3)- 5-hydroxy-2-(5-mercapto-4H-1,3,4-triazol-2-yl)-3-(phenyldiazenyl)-2H-chromen-2-one**




**IR, $cm^{-1}$ : 32681 (NH), 1630(C=N), 2541(-SH); 1730 (C=O); 3425(-OH), $^1$H-NMR, ppm: 5.20 (s, 1H, NH), , 7.3-7.7 ppm (3 H, aromatic protons), 11.3 ppm (1H, SH) and at 11.4 ppm (1H, broad OH).**

**MS : m/z 365,367**

**4)- 2-(5-mercapto-4H-1,3,4-triazol-2-yl)-3-(phenyldiazenyl)-2H-chromen-2-one**




**IR, $cm^{-1}$ : 33542 (NH), 1641(C=N), 2522(-SH); 1728(C=O) , $^1$H-NMR, ppm: 5.22 (s, 1H, NH), 7.5-8.6 ppm (3 H, aromatic protons), and 11.81 ppm (1H, SH). MS : m/z 349,367**

Compounds I showed remarkable activity towards the gram positive bacteria Staphylococcus and gram negative Pseudomonas , Salmonella sp and E.Coli but Klebsiella sp not yet effect with this comps while compound III(100µg) appear to have remarkable activity negative and positive gram bacteria.

The Gram Negative bacteria Klebsiella sp proved to be sensitive toward compound III(50µg). All prepared compounds showed very good activity toward the tested strains Staphylococcus aureus , Compound III proved to be the most active broad spectrum antimicrobial agents in this study. In conclusion this

study revealed that the heterocyclic system bearing coumarin moiety could be useful as template for future, development through modification or derivatization to design a more potent antimicrobial agents.

| | *S. aureus* | | | *Sal* | | | *K* | | | *Ps* | | | *E. coli* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **I** | 41 | 40 | 40 | 25 | 25 | 24 | 0 | 0 | 0 | 26 | 25 | 26 | 9 | 9 | 9 |
| **IV** | 40 | 40 | 41 | 27 | 25 | 25 | 10 | 10 | 10 | 16 | 16 | 16 | 9 | 9 | 9 |

Gram Negative bacteria: *Escherichia coli , Pseudomonas aeruginosa , Klebsiella sp. Salmonella sp.*

Gram positive bacteria: Staphylococ*cus aureus*

## Results and Discussion

## Conclusions

The main aim of the present study is to synthesize and investigate the antimicrobial activity of new The characterization data of compounds are given in the Experimental section. All the newly synthesized compounds gave satisfactory analyses for the proposed structures, which were confirmed on the basis of their IR and $H^1$-NMR spectral data. The IR spectra of these compounds showed moderately strong bands around3100-3360 $cm^{-1}$, 1600-1650 $cm^{-1}$ and 2500-2600 $cm^{-1}$, characteristic of the-OH, NH, C=N and S-H groups, respectively. In the H-NMR spectra, a characteristic signal due to the -N-CH -N- protons appeared at 5.00-6.05. The signal due to the NH protons appeared at 5.50-5.52. The signals due to the aromatic protons appeared as multiplets at 6.50-8.40heterocyclic derivatives containing five ring with the hope of discovering new structures serving as potential broad spectrum antimicrobial agents,we have successfully synthesized new four coumarin derivatives. Compound (IV) is most potent against bacterial, it's showed good antimicrobial activity. The prepared compounds were characterized by spectral FTIR, $^1$H-NMR and MS methods.

## Acknowledgements

Authors, express thanks to the Administration of this journal for providing required facilities to support this work.

## References

1. R. O'Kennedy and R. D. Thornes, Coumarins - Biology, Applications and Mode of Action, John Wiley &Sons, Chichester, UK, 1997.
2. R. Anschutz, Ber. Dtsch. Chem. Ges., 36 (1), 463-466 (1903).
3. S. Chechi, L. Pecori-Vettori and M. Mambagiotti-Alberti, Gazz. Chim. Ital., 98, 1448-1761 (1968).
4. V. Kaljaj, M. Trkovnik and L. Stefanović-Kaljaj, J. Serb. Chem. Soc., 52, 183 (1987).
5. Zhang X, Chao W, Chuai Y, Ma Y, Hao R, Zou D, Wei Y, Wang Y. A new N-type organic semiconductor synthesized by knoevenagelcondensation of truxenone and ethyl cyanoacetate. Organic. Letters, 8, 2006, 2563.
6. Kwak V, Fujiki M. Synthesis of polyelectrolyte gels with embedded voids having charged walls. Macromolecules, 37, 2004, 20-21.

*****