SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NEW CONDENSED COUMARIN 4-ACETOHYDRAZIDE

KAILASH PANCHOLIa, MAHENDRA BORISAGARa* and DENISH KARIYAb

aH. & H. B. Kotak Institute of Science, RAJKOT (Guj.) INDIA
bPatel J. D. K. Davolwala Science College, BORSAD (Guj.) INDIA

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ABSTRACT

Synthesis of a series of 4-(2-(2-(substitutedbenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate (3a-l) was achieved from different substituted 2-(7-Hydroxy-2-oxo-2H-chromen-4-yl) acetohydrazide, acetic anhydride and using few drops H2SO4 added and string with DCM. The structures of the products were supported by FTIR, PMR and mass spectral data.

Key words: 4-(2-(Substitutedbenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate, Different substituted 2-(7-Hydroxy-2-oxo-2H-chromen-4-yl) acetohydrazide, Anhydrous acetic acid, H2SO4 only string.

INTRODUCTION

Coumarin and its derivatives from natural products, either semi-synthetic or synthetic, represent one of the most active classes of compounds exhibiting a wide spectrum of biological activity. Additionally, coumarin derivatives are used as additives in food and cosmetic industry. Due to the significance of these compounds, the quest for efficient syntheses of coumarin ring compounds1 as well as new bioactive derivatives from known coumarins2 is topic.

There are a number of reports that natural and synthetic coumarin derivatives posse’s antimicrobial activity3-6. It was found that when one biodynamic heterocyclic system was coupled with another heterocyclic system, enhanced biological activity was produced. Compounds containing azomethine group (-CH=N-) is known as Schiff bases. Day by day Schiff bases are more frequently applied for the betterment of human welfare. The importance of the Schiff base is due its versatile nature. Literature survey shows that many Schiff bases exhibit biological activities such as antifungal, antibacterial, antitumor, anti-inflammatory, and Anticonvulsant7-11.

To evade these problems, we have developed a new etiquette for the synthesis of novel 4-(2-(2-(substitutedbenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate (3a-l) with the benefit of good quality yield and environmentally friendliness (Scheme 1).
Typical experimental procedure for the synthesis of Coumarin 4-acetohydrazide

In a 50 mL single neck round bottom flask above 0.005 mole hydrazide derivative of coumarine was taken in 20 mL MeOH. To this 0.005 mole of various substituted aldehydes and 2 drops of glacial acetic acid were added, and then the reaction mass was refluxed for two hours. The completion of reaction was monitored by TLC. Reaction mass was cooled to room temperature and obtained solid was filtered and wash with MeOH to give pure product with good yield.

3a. 4-(2-(2-Benzylidenehydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 64%; MP 252-254°C; MS: m/z M+1 365 and M-1 363; IR (cm⁻¹): 3032 (C-H stretching of aromatic ring), 2965 (C-H asymmetrical stretching of alkane group), 1670, 1606 (C=O stretching), 1562 (C=C stretching of aromatic ring), 1394 and 1325 (C-H asymmetrical deformation of CH₃ group), 1263 (C-N stretching), 1143, 1062, 837 (C-O-C stretching); ¹H NMR: 2.28 (s, 3H), 3.21 (s, 2H), 6.10 (s, 1H), 7.00 (s, 1H), 7.11 (d, 1H), 7.39 (d, 2H), 7.73 (s, 1H), 7.90 (d, 2H) 8.20 (d, 1H), 11.49 (s, 1H (NH)), Anal. Calcd. C₂₀H₁₆N₂O₅, C, 65.93; H, 4.43; N, 7.69; Found: C, 65.81; H, 4.29; N, 7.58%.

3b. 4-(2-(2-(2-Bromobenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 56%; MP 240-250°C; MS: m/z 443; IR (cm⁻¹): 3044 (C-H stretching of aromatic ring), 2965 (C-H asymmetrical stretching of alkane group), 1674, 1602 (C=O stretching), 1542 (C=C stretching of aromatic ring), 1384 and 1305 (C-H asymmetrical deformation of CH₃ group), 1260 (C-N stretching), 964 (C-Br stretching), 1153, 1072, 831 (C-O-C stretching); Anal. Calcd. C₂₀H₁₅BrN₂O₅, C, 54.19; H, 3.41; Br, 18.03; N, 6.32; O, 18.05 Found: C, 54.00; H, 3.01; Br, 17.90; N, 6.01; O, 17.75%.

3c. 4-(2-(2-(4-Bromobenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 50%; MP 240-243°C; MS: m/z 443; IR (cm⁻¹): 3067 (C-H stretching of aromatic ring), 2961 (C-H asymmetrical stretching of alkane group), 1671, 1600 (C=O stretching), 1522 (C=C stretching of aromatic ring), 1354 and 1301 (C-H asymmetrical deformation of CH₃ group), 1220 (C-N stretching), 961 (C-Br stretching), 1150, 1012, 866 (C-O-C stretching); Anal. Calcd. C₂₀H₁₅Br₂N₂O₅, C, 54.19; H, 3.41; Br, 18.03; N, 6.32; O, 18.05 Found: C, 53.68; H, 3.11; Br, 17.94; N, 6.10; O, 17.19%.

3d. 4-(2-(2-(2-Chlorobenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 52%; MP 235-240°C; MS: m/z 398; IR (cm⁻¹): 3060 (C-H stretching of aromatic ring), 2960 (C-H asymmetrical stretching of alkane group), 1671, 1608 (C=O stretching), 1528 (C=C stretching of aromatic ring), 1354 and 1301 (C-H asymmetrical deformation of CH₃ group), 1224 (C-N stretching), 868 (C-Cl stretching), 1152, 1014, 860 (C-O-C stretching); Anal. Calcd. C₂₀H₁₅ClN₂O₅, C, 60.23; H, 3.79; Cl, 8.89; N, 7.02; O, 20.06 Found: C, 60.03; H, 3.61; Cl, 8.54; N, 6.87; O, 19.85%. 
3e. 4-(2-(2-(4-Chlorobenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 45%; MP 235-238°C; MS: m/z 398; IR (cm⁻¹): 3089 (C-H stretching of aromatic ring), 2987 (C-H asymmetrical stretching of alkane group), 1675, 1665 (C=O stretching), 1520 (C=C stretching of aromatic ring), 1376 and 1311 (C-H asymmetrical deformation of CH₃ group), 1234 (C-N stretching), 828 (C-Cl stretching), 1159, 1014, 843 (C-O-C stretching); Anal. Calcd. C₂₀H₁₅ClN₂O₅, C, 60.23; H, 3.79; Cl, 8.89; N, 7.02; O, 20.06; Found: C, 60.00; H, 3.41; Cl, 8.50; N, 6.80; O, 19.56%.

3f. 4-(2-(2-(2-Methylbenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 68%; MP 210-212°C; MS: m/z M+1 379 and M-1 377; IR (cm⁻¹): 3058 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of alkane group), 1683, 1648 (C=O stretching), 1467 and 1394 (C-H asymmetrical deformation of CH₃ group), 1267 (C-N stretching), 1147, 1026, 857 (C-O-C stretching); ¹H NMR: 2.027 (s, 3H), 2.241 (s, 3H), 4.215 (s, 2H), 6.238 (s, 1H), 6.785 (m, 2H), 7.256 (t, 2H), 7.602 (m, 3H), 8.017 (s, 1H), 8.198 (s, 1H (NH)), Anal. Calcd. C₂₁H₁₈N₂O₅, C, 66.66; H, 4.79; N, 7.40; Found: C, 66.21; H, 4.53; N, 7.18%.

3g. 4-(2-(2-(4-Methylbenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 64%; MP 208-210°C; MS: m/z M+1 379 and M-1 377; IR (cm⁻¹): 3054 (C-H stretching of aromatic ring), 2974 (C-H asymmetrical stretching of alkane group), 1684, 1644 (C=O stretching), 1464 and 1395 (C-H asymmetrical deformation of CH₃ group), 1267 (C-N stretching), 1144, 1024, 854 (C-O-C stretching); Analyst. Calcd. C₂₁H₁₈N₂O₅, C, 66.66; H, 4.79; N, 7.40; Found: C, 66.24; H, 4.56; N, 7.14%.

3h. 4-(2-(2,4-Dimethylbenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 62%; MP 200-205°C; MS: m/z M+1 392 and M-1 377; IR (cm⁻¹): 3054 (C-H stretching of aromatic ring), 2978 (C-H asymmetrical stretching of alkane group), 1688, 1647 (C=O stretching), 1464 and 1395 (C-H asymmetrical deformation of CH₃ group), 1260 (C-N stretching), 1140, 1024, 850 (C-O-C stretching); Anal. Calcd. C₂₂H₂₀N₂O₅, C, 67.34; H, 5.14; N, 7.14; O, 20.39; Found: C, 67.22; H, 5.12; N, 7.13; O, 20.36%.

3i. 4-(2-(2,3-Dimethylbenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 55%; MP 199-200°C; MS: m/z M+1 401 and M-1 399; IR (cm⁻¹): 3042 (C-H stretching of aromatic ring), 2945, 2860 (C-H asymmetrical stretching of alkane group), 1647, 1587 (C=O stretching), 1467 and 1394 (C-H asymmetrical deformation of CH₃ group), 1267 (C-N stretching), 1147, 1026, 857 (C-O-C stretching); Anal. Calcd. C₂₀H₁₄F₂N₂O₅, C, 60.00; H, 3.52; F, 9.49; N, 7.00; Found: C, 59.81; H, 3.23; F, 9.67%.

3j. 4-(2-(2,6-Difluorobenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 51%; MP 232-234°C; MS: m/z M+1 409 and M-1 399; IR (cm⁻¹): 3042 (C-H stretching of aromatic ring), 2945, 2860 (C-H asymmetrical stretching of alkane group), 1647, 1587 (C=O stretching), 1467 and 1394 (C-H asymmetrical deformation of CH₃ group), 1267 (C-N stretching), 1147, 1026, 857 (C-O-C stretching); Anal. Calcd. C₂₀H₁₄F₂N₂O₅, C, 59.81; H, 3.23; F, 9.67%; Found: C, 59.81; H, 3.23; F, 9.67%.

3k. 4-(2-(2-(3-Nitrobenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 64%; MP 200-202°C; MS: m/z M+1 409 and M-1 399; IR (cm⁻¹): 3042 (C-H stretching of aromatic ring), 2956 (C-H asymmetrical stretching of alkane group), 1664, 1629 (C=O stretching), 1544 (N-O stretching of NO₂), 1426 and 1345 (C-H asymmetrical deformation of CH₃ group), 1269 (C-N stretching), 1134, 1005, 805 (C-O-C stretching); Anal. Calcd. C₂₀H₁₄N₂O₇, C, 58.68; H, 3.69; N, 10.27; O, 27.36; Found: C, 58.45; H, 3.14; N, 10.12; O, 27.11%.
3l. 4-(2-(2-(4-Nitrobenzylidene)hydrazinyl)-2-oxoethyl)-2-oxo-2H-chromen-7-yl acetate

Yield: 54%; MP 205-210°C; MS: m/z 409; IR (cm⁻¹): 3064 (C-H stretching of aromatic ring), 2957 (C-H asymmetrical stretching of alkane group), 1664, 1629 (C=O stretching), 1548 (N-O stretching of NO₂), 1427 and 1347 (C-H asymmetrical deformation of CH₃ group), 1267 (C-N stretching), 1134, 1005, 805 (C-O-C stretching); Anal. Calcd. C₂₀H₁₅N₃O₇, C, 58.68; H, 3.69; N, 10.27; O, 27.36; Found: C, 58.40; H, 3.04; N, 10.02; O, 27.22%.

Table 1: Antimicrobial activity of compounds 3a-l

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<th>Compound</th>
<th>Antibacterial activity</th>
<th>Antifungal activity</th>
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<tr>
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<td>Gram -ve</td>
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Gentamycin 0.25 0.5 0.05 1 - -
Ampicillin 250 100 100 100 - -
Chloramphenicol 50 50 50 50 - -
Iproflouxacin 50 50 25 25 - -
Norflouxacin 10 10 10 10 - -
Nystatin - - - - 100 100
Greseofulvin - - - - 500 100

CONCLUSION

We have synthesized a library of acylhydrazones using simple and convenient method. This method produces these products in good yields, with a short reaction time and easy workup. Product is isolated by simple vacuum filtration. The isolated products are very pure and do not need any column purification. This study opens up a new area of cost-effective synthesis of potentially biologically active acylhydrazone compounds.
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