Indian Journal of Heterocyclic Chemistry
Vol. 32 - Number 04 (Oct-Dec 2022) 449-453
DocID: https://connectjournals.com/01951.2022.32.449

ISSN (Print) : 0971-1627
ISSN (Online) : 2456-4311

Synthesis, Characterization and Molecular Docking Studies of 4-(5-Alkylsulfanyl-(1,3,4)oxadiazol-2-yl methyl)-7-methyl chromene-2-ones

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ABSTRACT A series of 4-(5-alkylsulfanyl-[1,3,4]oxadiazol-2-ylmethyl)-7-methyl-chromen-2-ones **(5a-d)** was synthesized from (7-methyl-2-oxo-2*H*-chromen-4-yl)-acetic acid **(1)** as starting material. The structures of the synthesized new compounds were confirmed by their ^{1}H-NMR, IR, and mass spectral data. The molecular docking studies of the compounds have been carried out to predict the possible anti-depressant activity.

KEYWORDS Chromens, Condensation and docking studies, Esterification, Oxadiazoles.

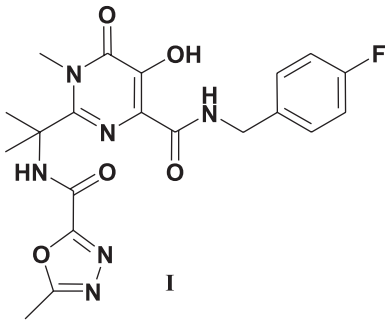
How to cite this article: Gaddam, G.R., Sudugu, R.R., Chittireddy, V.R.R.,Bireddy, S.R., Eppakayala, L. Synthesis, Characterization, and Molecular Docking Studies of 4-(5-Alkylsulfanyl-(1,3,4)oxadiazol-2-yl methyl)-7-methyl chromene-2-ones, *Indian J. Heterocycl. Chem.*, **2022**, *32*, 449–453. (*DocID: https://connectjournals.com/01951.2022.32.449*)

INTRODUCTION

The oxadiazole is known to show broad range of therapeutic activities such as antibacterial,[1] anticonvulsant,[2] anti-cancer,[3] hypoglycemic,[4] antipyretic,[5] anti-tubercular,[6] anti-fungal,[7] immunosuppressive, spasmolytic, and antioxidant,[8] anti-inflammatory,[9] insecticidal,[10] central nervous system stimulant, anti-amoebic, antiemetic, anti-anthelmintic, vasodilator, antimycotic, and antidepressant,[11] and anti-allergic activities.[12] The oxadiazole nucleus with N=C-S linkage exhibits various pharmacological activities.[13]

The stable oxadiazoles are present in various drugs including Fasiplon**(I)** and Fenadiazole **(II)**. The chemistry of oxadiazole has greatly evolved. Many pharmaceuticals have an oxadiazole moiety in connection with various heterocyclic rings.[14,15]

In view of the biological applications of chromes and oxadiazoles, a series of new heterocyclics, 4-(5-alkylsulfanyl-[1,3,4]oxadiazol-2-ylmethyl)-7-methyl-chromen-2-ones **(5a-d)** has been synthesized. The chemical



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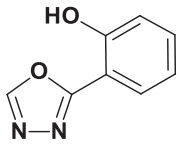

II

structures of these compounds were confirmed by ^{1}H-NMR, IR, Mass, and ^{13}C NMR.

RESULTS AND DISCUSSION

Chemistry

The target compounds **(5a-d)** were synthesized according to the reactions sequence outlined in **Scheme 1** starting from

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(C=N), 1152 (C-O), 677 (C-S) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ ppm 7.74 (s, 1H, Ar-H), 7.65 (s, 1H, =CH), 7.62 (d, 1H, *J* = 7.2 Hz, Ar-H), 7.55 (d, 1H, *J* = 7.2 Hz, Ar-H), 3.66 (s, 2H, CH_2), 2.53 (t, 2H, *J* = 5.0 Hz, CH_2), 2.44 (s, 3H, CH_3),2.36 (m, 2H, CH_2), 1.87 (m, 2H, CH_2), 1.19 (t, 3H, *J* = 5.6 Hz, CH_3).MS: 330 m/z (M^+). Elemental analysis: Calculated for $C_{17}H_{18}N_2O_3S$: C-61.80, H-5.49, N-8.48, O-14.53, S-9.70. Found: C-60.58, H-5.32, N-8.12, O-13.98, S-9.48.

CONCLUSION

4-(5-Alkylsulfanyl-[1,3,4]oxadiazol-2-ylmethyl)-7-methyl-chromen-2-ones **(5a-d)** have been synthesized. All the synthesized compounds exhibited good binding score, according to molecular docking experiments. Molecular studies indicated possible antidepressant activity of all the compounds.

ACKNOWLEDGMENTS

The authors are thankful to Jawaharlal Nehru Technological University Hyderabad, India for providing necessary facilities to carry out this work.

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Received: 19 Jul 2022; Accepted: 07 Sep 2022