

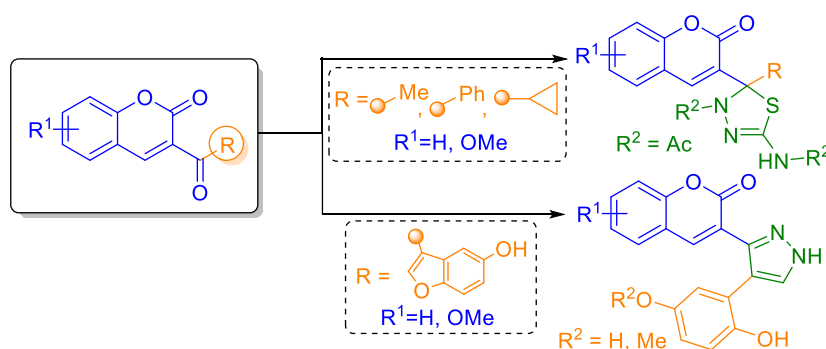
SYNTHESIS OF FUNCTIONALIZED COUMARIN HYBRIDS VIA MOLECULAR HYBRIDIZATION

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Molecular hybridization has emerged as a fundamental and highly effective synthetic strategy in modern medicinal chemistry, enabling the rational fusion of distinct pharmacophoric entities into a unified molecular architecture. This strategy not only facilitates the modulation of physicochemical properties, metabolic stability, and target affinity, but also provides a powerful means for expanding accessible chemical space and generating structurally novel multifunctional scaffolds [1]. Privileged oxygen- and nitrogen-containing frameworks – specifically coumarins, pyrazoles, 1,3,4-thiadiazoles, and benzofurans – possess exceptional biological versatility, exhibiting marked antitumor, anti-inflammatory, and antimicrobial profiles. In this study, 3-acylcoumarins bearing methyl, cyclopropyl, phenyl, or 5-methoxy/hydroxybenzofuran-3-carbonyl substituents at C-3 were successfully employed as central platforms for constructing two distinct classes of hybrid molecules.



First, condensation of 3-acetyl-, 3-benzoyl-, and 3-cyclopropanecarbonylcoumarins with thiosemicarbazide followed by intramolecular heterocyclization in acetic anhydride yielded a library of functionalized 3-(1,3,4-thiadiazol-2-yl)-2*H*-chromen-2-ones [2].

Second, the interaction of 3-(5-hydroxybenzofuran-3-carbonyl)-2*H*-chromen-2-ones (as well as their corresponding 5-methoxy derivatives) with hydrazine hydrate proceeded *via* selective recyclization of the benzofuran core while preserving the lactone ring, affording the corresponding 3-[4-(2,5-dihydroxyphenyl)-1*H*-pyrazol-3-yl]-2*H*-chromen-2-ones and their methoxy-functionalized analogs.

The resulting hybrid systems represent robust, highly adaptable platforms not only for targeted biological screening, but also as versatile synthetic intermediates for further directed chemical modifications in drug discovery.

References:

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2. Ye.Y. Rybina, V.S. Moskvina, V. P. Khilya *Ukr. Bioorg. Acta.* **2025**, *20*, 10–14.