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Post-HTS case report and structural alert: promiscuous 4-aroyl-1,5-disubstituted-3-hydroxy-2*H*-pyrrol-2-one actives verified by ALARM NMR

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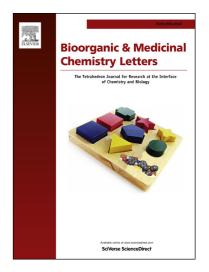
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ACCEPTED MANUSCRIPT

Post-HTS case report and structural alert: promiscuous 4-aroyl-1,5-disubstituted-3-hydroxy-2*H*-pyrrol-2-one actives verified by ALARM NMR

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Keywords | chemical aggregation, drug discovery, high-throughput screening, pan-assay interference compounds, PAINS, structure-activity relationships

Conflicting interests | The authors hereby declare no conflicting interests pertaining to the material in this manuscript.

Abbreviations | Acetyl-CoA, acetyl coenzyme A; ALARM NMR, a La assay to detect reactive molecules by nuclear magnetic resonance; Asf1, anti-silencing function 1; AZ, AstraZeneca; BME, β-mercaptoethanol; BSA, bovine serum albumin; CoA, coenzyme A; CPM, N-[4-(7diethylamino-4-methylcoumarin-3-yl)phenyl]maleimide; dH3-H4; Drosophila histone H3-H4; dimethyl sulfoxide; DNA, deoxyribonucleic acid; DTT, dithiothreitol; EDTA, DMSO. ethylenediaminetetraacetic acid; GSH, glutathione; H3K27, histone H3 lysine 27; H3K27ac, histone H3 lysine 27 acetylation; H3K56, histone H3 lysine 56; H3K56ac, histone H3 lysine 56 acetylation; HAT, histone acetyltransferase; HMQC, heteronuclear multiple quantum coherence; HPLC, high-performance liquid chromatography; HRMS, high-resolution mass spectrometry; HRP-PR, horseradish peroxidase-phenol red; HTS, high-throughput screen or high-throughput screening; IC₅₀, half maximal inhibitory concentration: IPTG. isopropyl

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