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Novobiocin analogues with second-generation noviose surrogates

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ABSTRACT Hsp90 is a promising therapeutic target for the treatment of cancer. Novobiocin is the first Hsp90 C-terminal inhibitor ever identified and recent structure-activity relationship studies on the noviose sugar identified several commercially available amines as suitable surrogates. In an effort to further understand this region of the molecule, analogues containing various *N'*-amino substituents were prepared and evaluated against two breast cancer cell lines for determination of their efficacy. Compound 37j manifested the most potent anti-proliferative activity from these studies and induced Hsp90-dependent client protein degradation at mid nano-molar concentrations.

KEYWORDS Heat shock protein 90, Hsp90 inhibitors, Novobiocin analogues, Breast cancer

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