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Chemistry

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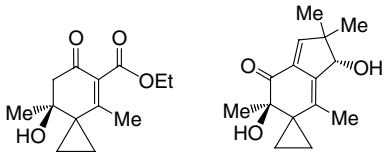
Contents

ARTICLES



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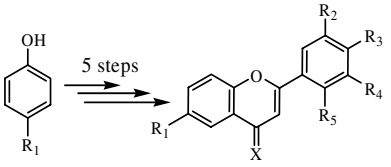
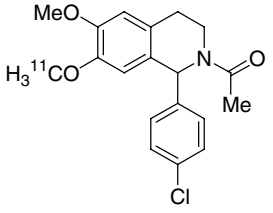
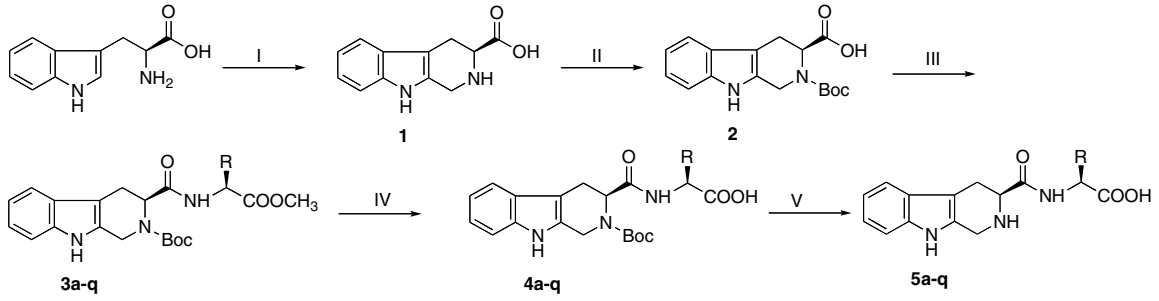
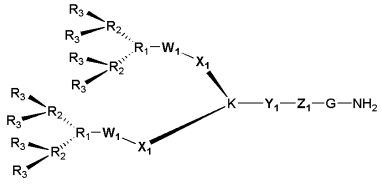


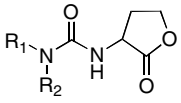
X= O, S, 2,4-DNPH



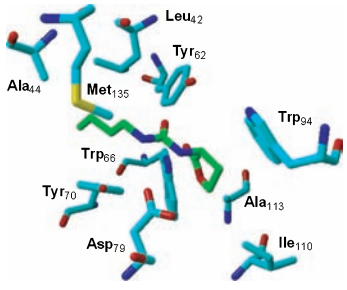


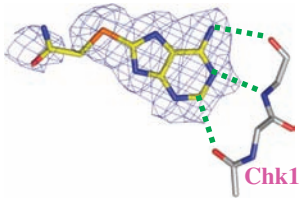


Synthesis of a library of new polycationic dendrimers and their evaluation in downregulation of human vascular endothelium growth factor is presented.

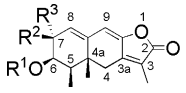


A series of homoserine lactone derived ureas were synthesized and evaluated for their ability to inhibit the quorum sensing in *Vibrio fischeri* bacteria.





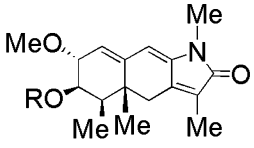
Chk1 structure → virtual screening → binding assay → compound QC → diverse new ligands → crystallography.



PF1092C: R^1 = H, R^2 = OH, R^3 = H
8b: R^1 = EtCO, R^2 = EtCOO, R^3 = H
19i: R^1 = cyclopropyl-NHCO, R^2 = H, R^3 = MeO

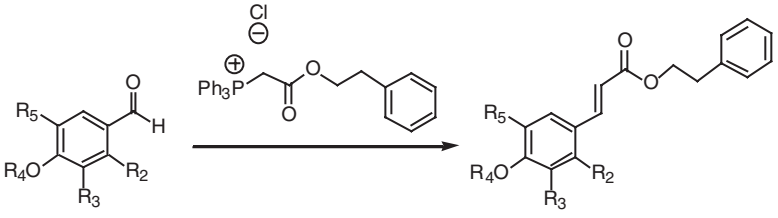
Tetrahydronaphthofuranones, based on the fungal metabolite PF1092C, was synthesized and evaluated for progesterone receptor (PR) binding affinities. Compounds **8b** and **19i** exhibited high affinity and acted as selective PR antagonists.

We have developed a new lead compound, tetrahydrobenzindolone, possessing a lactam ring, which shows sufficient stability for easy modification at the 6- and/or 7-positions. We succeeded in separating the agonistic and antagonistic activities by choosing suitable substituent groups at the 6- and/or 7-position(s) of the tetrahydrobenzindolone.



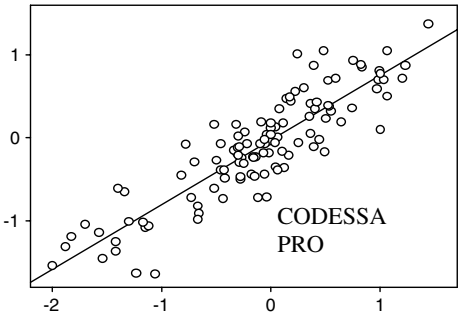
tetrahydrobenzindolone deriv.

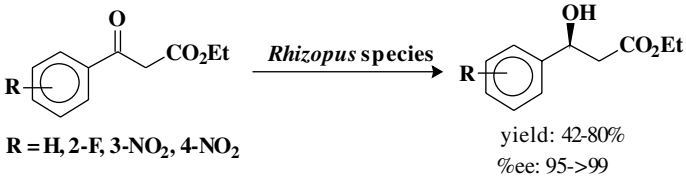
PR agonist: R = *n*-PrNHCO
R = Me_2NCO
PR antagonist: R= $(CH_3)_2CH(CH_2)_2$-

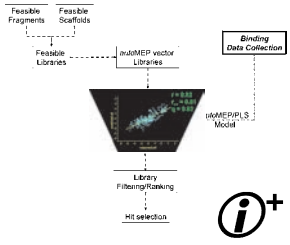


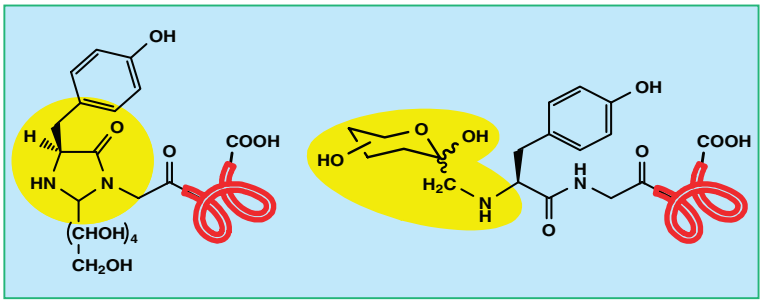
R_2 = H, **F**
R_3 = H, OH, OMe
R_4 = H, Me
R_5 = **F**, OH, OMe

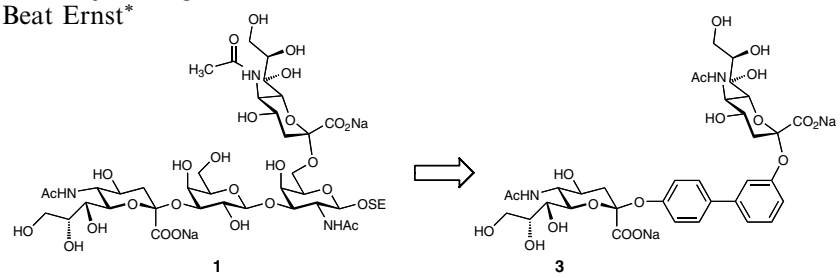
QSAR models of log BB for a diverse set of 113 drug molecules were developed employing structural descriptors using CODESSA-PRO and ISIDA approaches. The models were successfully validated using the central nervous system activity data of an external test set of 40 drug molecules.



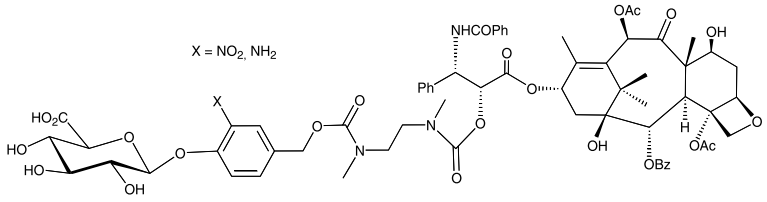




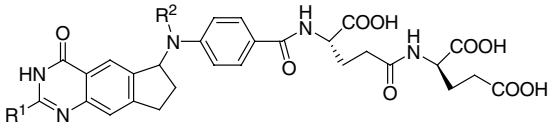


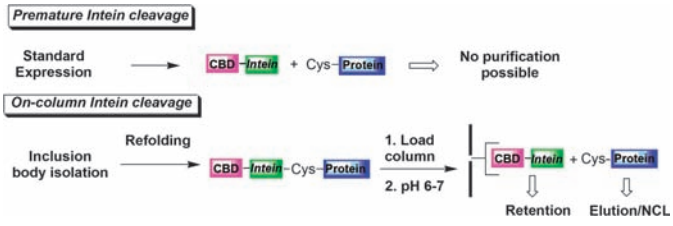


Simplified mimics of tetrasaccharide **1**, where the core disaccharide Galβ(1–3)Gal*N*Ac was replaced with a biphenyl, were synthesized and biologically evaluated as inhibitors of the myelin-associated glycoprotein (MAG).



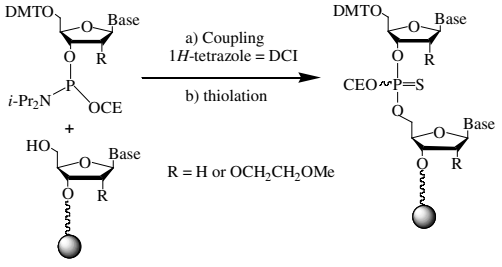
Two new glucuronide paclitaxel prodrugs were synthesized. One of them fulfils all the stability and enzymatic cleavage requirements for an ADEPT or a PMT strategy in cancer chemotherapy.





An amphiphilic N-terminal Cys-protein fragment for NCL, which undergoes premature cleavage from a pH-sensitive intein fusion under standard conditions, has been isolated by expression and refolding of inclusion bodies.

Multiple 2′-O-methoxyethyl modified phosphorothioate oligonucleotides of 18–20-mer in length were synthesized at various scales using 4,5-dicyanoimidazole (DCI) as coupling activator. Extensive synthetic, analytical (using ion-pair LC–MS), and in vivo pharmacological, toxicological studies showed that oligonucleotides made with DCI and 1*H*-tetrazole are chemically and biologically equivalent. This extensive study will help the oligonucleotide therapeutic industry to move from using a potentially explosive activator (1*H*-tetrazole) to a safe activator (DCI).



*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

The figure shows the synthetic approach to 6*RS* CB300945; an inhibitor of thymidylate synthase targeted at α-folate receptor overexpressing tumours. This compound and related derivatives were synthesised via multistep routes [Henderson, E.A.; Bavetsias, V.; Theti, D.S.; Wilson, S.C.; Clauss, R.; Jackman, A.L. *Bioorg. Med. Chem.* **2006**, *14*, 5020].

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