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Medicinal
Chemistry

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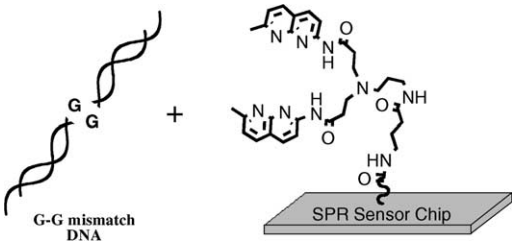
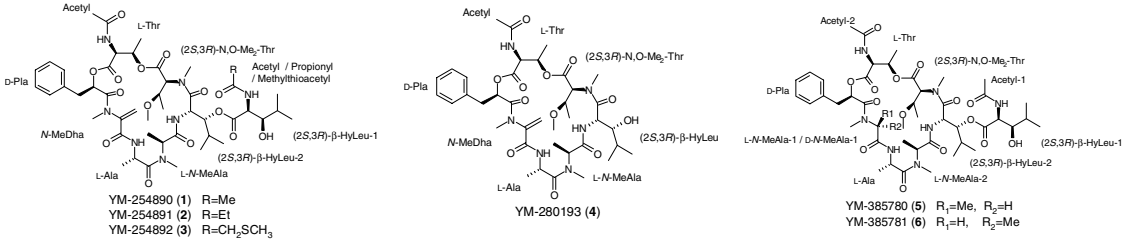
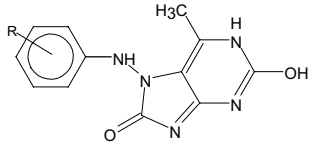
Contents

ARTICLES

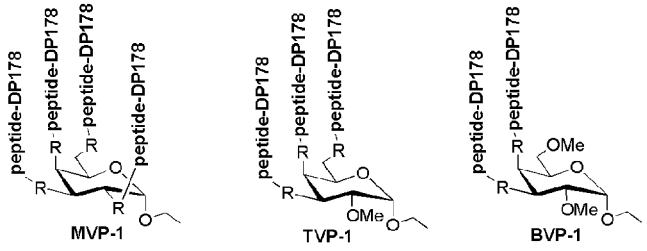


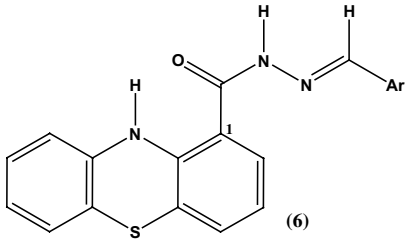
The kinetics for the binding of the G–G mismatch to the naphthyridine dimer was investigated by surface plasmon resonance assay.





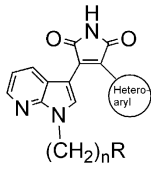
A series of 2-hydroxy-6-methyl-7-(arylamino)-1,7-dihydropurin-8-ones have been synthesized. Their chemical structures were confirmed by spectral and elemental analysis data. These synthesized compounds were subjected to antibacterial activity against Gram-positive and Gram-negative bacteria using a reference antibiotic drug purinthol as control. Molecular refractive index parameters (M_R) and Hammett substituent constant (σ) have also been calculated to study quantitative structure–activity relationship.

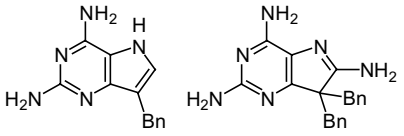


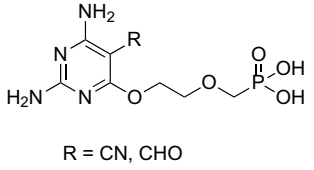


The synthesis and pharmacological evaluation of new 10*H*-phenothiazine-1-acylhydrazone derivatives (**6**) is reported.

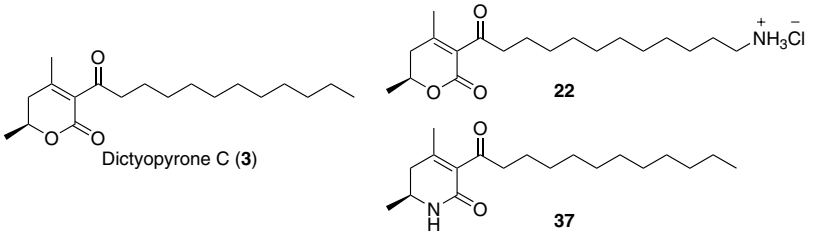
A new CoMFA model of dihydroquinazolinone and tetrasubstituted imidazole compounds with p38 MAPK inhibitory activity is reported.







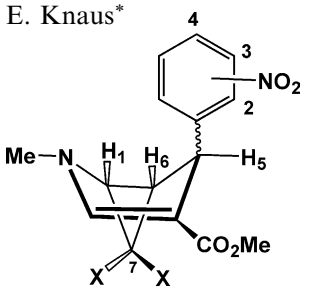
R = CN, CHO



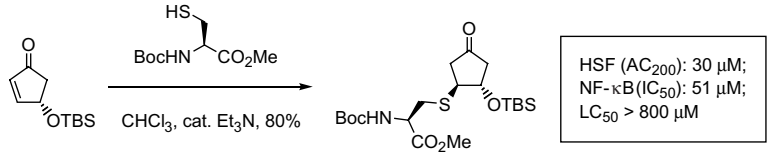
Dictyopyrone C (**3**)

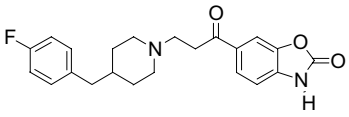
22

37

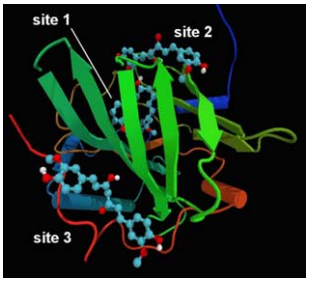


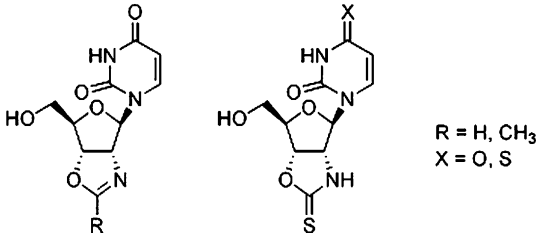
X = Br, Cl



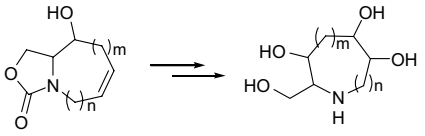


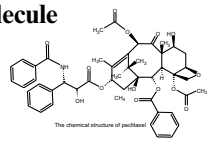
EMD-95885, 6-[3-[4-(4-fluorobenzyl)piperidino]propionyl]-3*H*-benzoxazol-2-one (**1**), a selective NR2B subtype antagonist, has been labelled with carbon-11 ($T_{1/2}$: 20.4 min) and in vivo pharmacologically evaluated as a potential positron emission tomography (PET) radioligand for imaging the NMDA receptor.



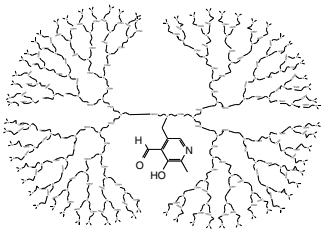


Two novel conformationally restrained alkyl derivatives of 2′,3′-dideoxy-2′,3′-oxazole-β-D-uridine and a novel uridine 2′,3′-thiocarbamate were prepared and conformational parameters determined using MACROMODEL V.6.0 molecular modelling programme. The novel nucleosides were evaluated against a wide range of viral types and strains in cell culture.

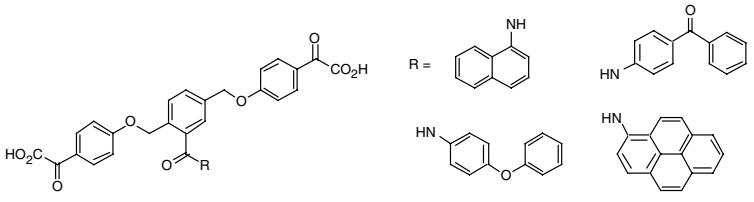


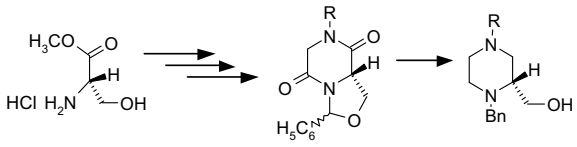


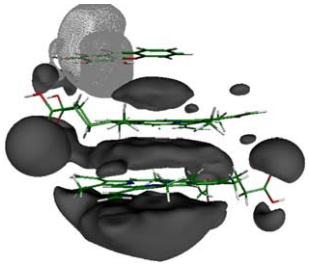
It is used to treat several cancers including tumours of the breast, ovary and lung. The effect of paclitaxel on rapidly dividing cancer cells is based on the ability to bind and stabilize microtubules, thus leading to the block of cell replication in the late G_2–M phase of the cell cycle. In the present work the interaction of paclitaxel with human serum albumin (HSA) in aqueous solution at physiological pH has been investigated through CD, fluorescence spectroscopy and by the antibody precipitate test. Binding of paclitaxel to albumin impact on protein structure and it influences considerably albumin binding of other molecules like warfarin, heme or bilirubin. The paclitaxel–HSA interaction causes the conformational changes with the loss of helical stability of protein and local perturbation in the domain IIA binding pocket. The relative fluorescence intensity of the paclitaxel-bound HSA decreased, suggesting that perturbation around the Trp 214 residue took place. This was confirmed by the destabilization of the warfarin binding site located in subdomain IIA. CD and fluorescence spectroscopic results showed marked reductions (about 50% decrease in the CD Cotton effect intensity, and ~35% decrease of the fluorescence intensity) in the affinity of albumin for bilirubin upon paclitaxel binding. These results suggested that paclitaxel molecule is bound in the vicinity of Trp 214, which forms part of the wall in one of the two main drug-binding cavities of HSA (site I subdomain IIA).

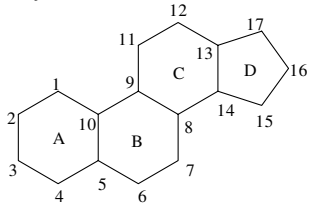


Pyridoxal was covalently attached to polyethylenimine polymers, but the resulting materials were found to degrade rapidly. In comparison, G1 to G6 poly(amidoamine) dendrimers with a pyridoxal core were synthesized and these compounds are relatively stable. Their reactivities in catalyzing racemization and decarboxylation reactions of α-amino acids were studied.

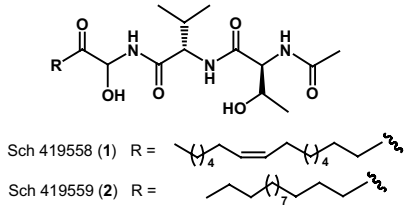








A QSAR study of binding affinity of a series of 30 steroids for corticosteroid-binding globulin was performed using Wang–Ford charges of the non-hydrogen common atoms obtained from molecular electrostatic potential surface of AM1 optimized energy-minimized geometries of the compounds. It was found from the study that the charges of different atoms of the steroid nucleus [atoms 3, 4, 5 (ring A), 8, 9 (fusion points of rings B and C) and 16 (ring D)] contribute significantly to the binding affinity.



Two new RNA polymerase sigma-factor (RpoE) inhibitor, Sch 419558 (**1**) and Sch 419559 (**2**) were discovered from *Pseudomonas fluorescens*. Structures of **1** and **2** were elucidated by spectroscopic data analyses.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

2004: Overlaps of the eight known aldolase alpha-beta barrels in 2-deoxyribose-5-phosphate aldolase (DERA). Ribbon model for DERA is shown in green, with key Lys residues capable of Schiff base formation highlighted in stick figure. Reactive Lys167 is shown in yellow. DeSantis, G.; Liu, J.; Clark, D. P.; Heine, A.; Wilson, I. A.; and Wong, C.-H. *Bioorganic & Medicinal Chemistry* **2003**, *11*, 43–52.

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