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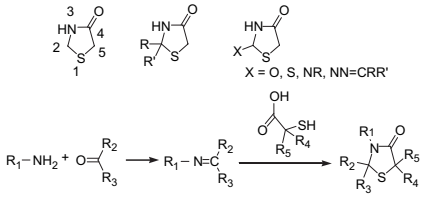
Contents

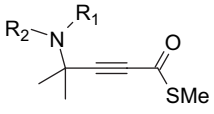
MINI-REVIEW

The broad and potent activity of 4-thiazolidinones has established it as one of the biologically important scaffolds. The article has outlined the chemistry and biological activities of the 4-thiazolidinone scaffold. The synthetic methodologies indicate the simplicity, maneuverability and versatility, which offer the medicinal chemist a complete range of novel derivatives.

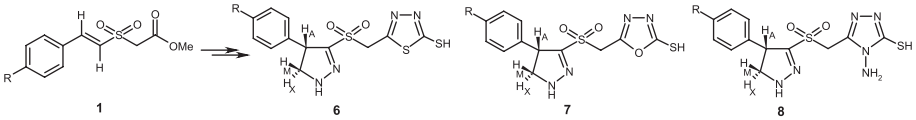


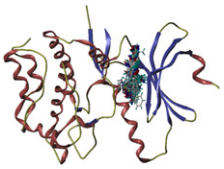
ORIGINAL ARTICLES

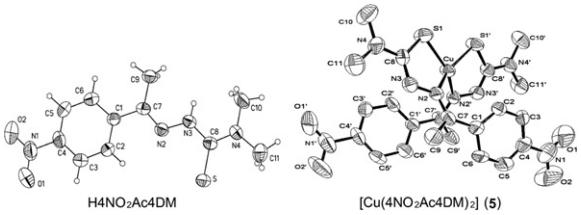
Growth-inhibitory efficacy and selectivity of α,β-acetylenic *N*-substituted aminothiolesters obtained by the pharmacomodulation of the N atom have been addressed. Dimethylamino and morpholino compounds are *reversible* inhibitors of the growth of human prostate epithelial normal cells (HPENC) but *irreversible* inhibitors of the growth of human prostate epithelial cancer cells (DU145).

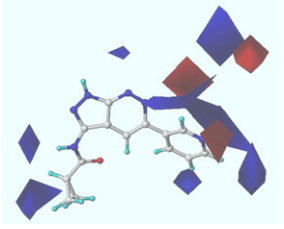


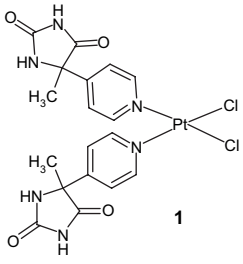
Novel sulfone-linked bis heterocycles pyrazolines in combination with thiadiazoles, oxadiazoles and triazoles were prepared from *E*-styrylsulfonylacetic acid methyl ester and tested for their antimicrobial activity. The compound **8** showed pronounced activity than the compounds **6** and **7**.

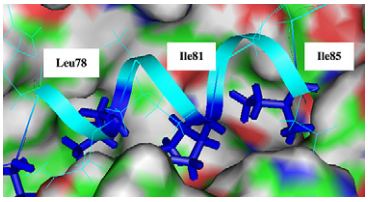


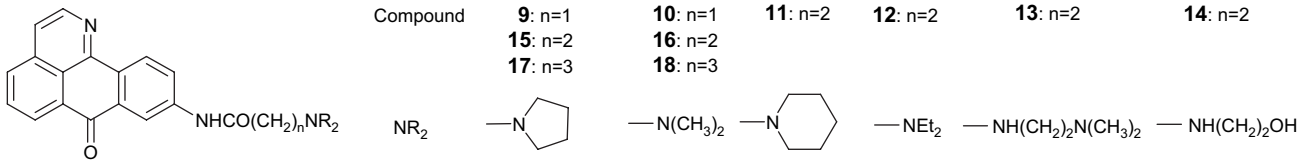




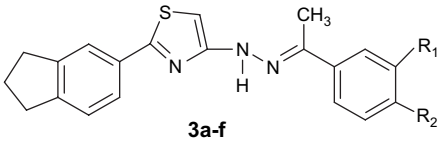






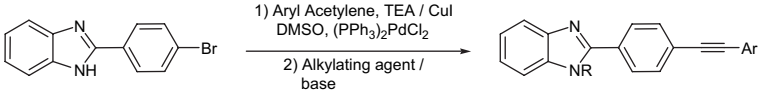


Thiazolylhydrazone derivatives were investigated for antituberculosis activity against *Mycobacterium tuberculosis*. The role of the different substitution on phenyl ring on activity was explored in structure–activity relationship investigations.

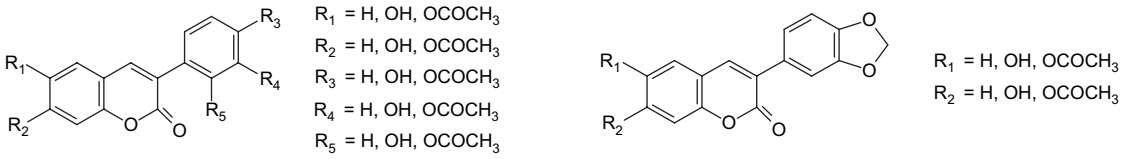


3a-f

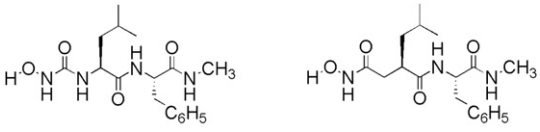
Synthesis of a series of novel and functionalized benzimidazole derivatives by the condensation of OPDA with 4-bromobenzoic acid and subsequent reactions of the product obtained with phenylacetylene and 6-ethynyl-4,4-dimethylthiochroman utilising Sonogashira coupling has been reported. The Sonogashira coupling products were then alkylated at the benzimidazole –NH with different electrophilic reagents leading to functionalized derivatives. All the compounds synthesized were screened for their potential anti-bacterial, anti-asthmatic and anti-diabetic properties, which exhibited moderate activities in screening studies in vitro.

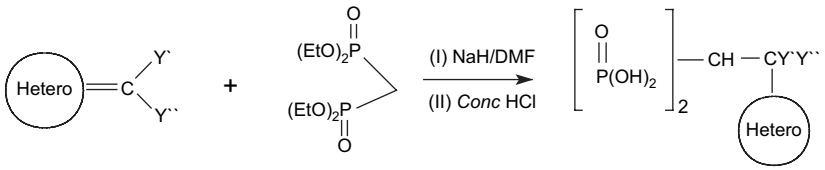


(3) **80 - 95 %** **(4, 6 a - j and 5,7 a - h)**

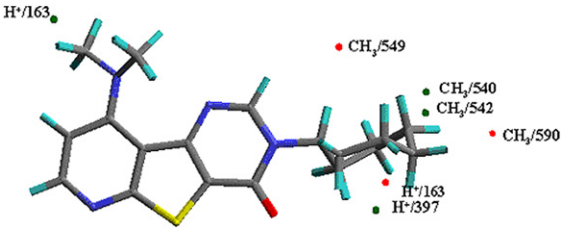


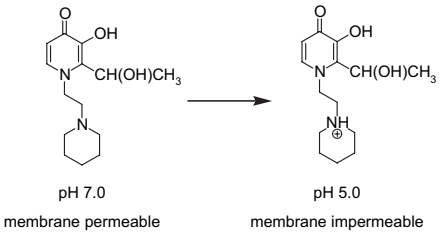
Peptidyl-1-hydroxyureas are easily prepared by *N*-hydroxycarbamoylation of suitable dipeptides. Their potency against six MMPs approaches that of other *N*-hydroxyurea ligands against various zinc metalloenzymes, but is at least 50,000-fold lower than that of their succinylhydroxamate analogues.



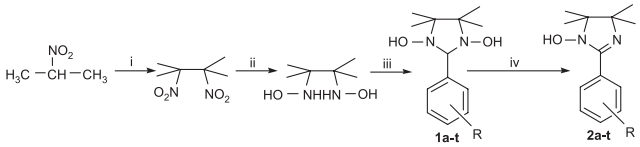


3D-QSAR studies, including MFA and RSA was performed on 46 triazafluorenone derivatives as inhibitors of metabotropic glutamate receptor subtype 1 (mGluR1) to predict the importance of proper steric and electrostatic fragments, which are necessary for higher activity.

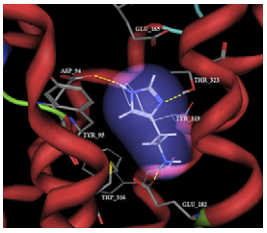




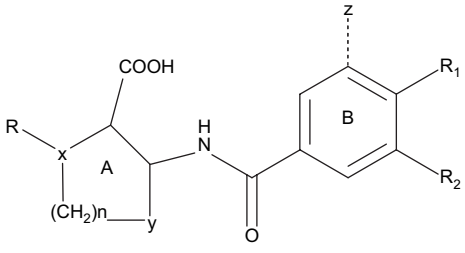
Synthetic route of 1-hydroxyl-2-substituted phenyl-4,4,5,5-tetramethylimidazolines (**2a–t**).



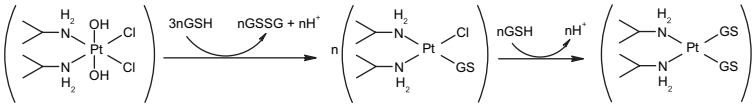
Ligand-supported homology models of the human histamine H4 receptor were developed. Our results suggest a different binding mode of histamine than proposed previously. Enrichment studies demonstrated the suitability of the models for virtual screening.



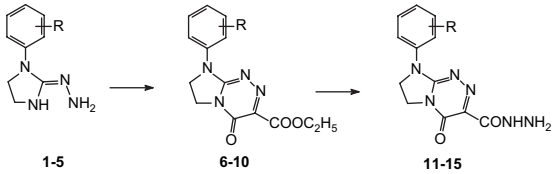
Quantitative structure–activity relationship (QSAR) studies have been carried out on a series of benzoylaminobenzoic acid derivatives as potent inhibitors of FabH and antibacterial activity against *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Neisseria meningitidis* and *Escherichia coli*, which demonstrate FabH inhibitory activity in cell free and whole cell system. The QSAR studies revealed that inhibitory activity increases with increase in hydrophobicity, molar refractivity, aromaticity, and presence of OH group (on *x* position of the nucleus). On the other side presence of hetero-atoms like N, O, or S at R_1 position of the nucleus decreases the inhibitory activity.



SHORT COMMUNICATIONS

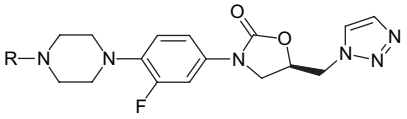


Synthesis, structure elucidation and antitumoural properties of novel fused 1,2,4-triazine aryl derivatives containing the ethoxycarbonyl (**6–10**) and carbohydrazide groups (**11–15**) are presented. Antitumour activities for the heterobicyclic hydrazides of the type **11–14** were evaluated by BrdU method for human LS180, SiHa and T47D carcinoma cells. Amongst them, hydrazide **14** has exhibited remarkable inhibitory effect against SiHa and LS180 cancer cells, and simultaneously was proved to be non-toxic towards the human normal cell line – HSF cells. Beside these, compound **14** in a concentration of 32.6 μM was found to possess efficiency for DNA strand breakage of all the examined cancer cell lines. Furthermore, heterobicyclic hydrazide of the type **14** was able to evoke statistically significant apoptotic effects in human breast cancer (T47D) cells. The antiproliferative properties *in vitro* for heterobicycles **6–14** were evaluated by MTT method for human leukaemic Jurkat cells. Significant viability decreases in Jurkat cells treated with different concentrations of compounds **10** and **11**were observed, suggesting their cytotoxic activities.



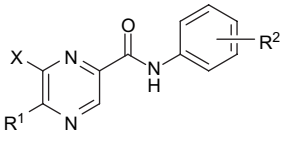
1, 6, 11: R=H; **2, 7, 12**: R=4-CH_3; **3, 8, 13**: R=4-CH_3O; **4, 9,14**: R=3-Cl; **5, 10, 15**: R=3,4-Cl_2

Synthesis of new 5-triazolylmethyl oxazolidinone derivatives, their antibacterial activity and correlation with selected molecular descriptors are presented.



R = alkylcarbonyl: $CH_3(CH_2)_nCO$; where n = 0 to16.
R = bicycloakylcarbonyl

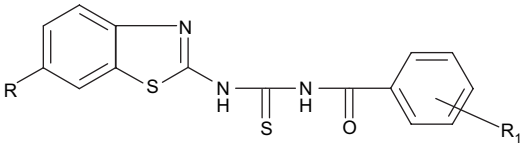
Twenty potential pyrazinamide derivatives were synthesized using modification of currently known synthetic pathways. Substituted anilides of pyrazinecarboxylic acid were investigated for their antimycobacterial, antifungal, photosynthesis-inhibiting activities and their lipophilicity parameters.



R^1 = H, *tert*-butyl
R^2 = 4-CH_3, 3-CF_3, 2-CF_3, 4-F, 2-Cl-5-OH
X = H,Cl

PRELIMINARY COMMUNICATION

A series of 1,3-benzothiazol-2-yl benzamides (**11–30**) were prepared in satisfactory yield and evaluated for their anticonvulsant, neurotoxicity, CNS depressant study and other toxicity studies. All the synthesized compounds were in good agreement with elemental and spectral data. Majority of the compounds were active in MES and scPTZ screen and showed the decrease in the immobility time. None of the compounds had shown neurotoxicity or liver toxicity.



R = Br, Cl, F, NO_2, CH_3, OCH_3
R_1 = H, 2-Cl, 4-Cl, 4-OCH_3

COVER

Overlay of the experimental and docked conformations of the ligand fluorescein in complex with an antifluorescein 4-4-20 Fab fragment (PDB code 1flr, 1.85 Å). The top-scoring conformation (purple) selected by the HINT force field, among the 255 poses generated by AutoDock, nearly overlays the crystallographic structure (yellow), while the conformation selected by the AutoDock scoring function (green) reverses the positions of the carbonyl and hydroxyl groups.
Image provided by Francesca Spyrakis, Alessio Amadasi, Micaela Fornabaio, Donald J. Abraham, Andrea Mozzarelli, Glen E. Kellogg, Pietro Cozzini.

* Corresponding authors.

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