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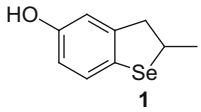
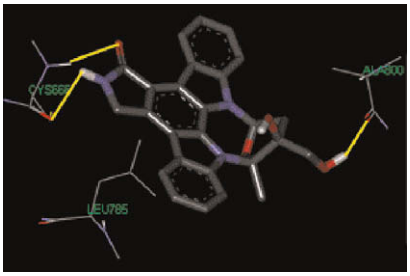
Contents

ARTICLES

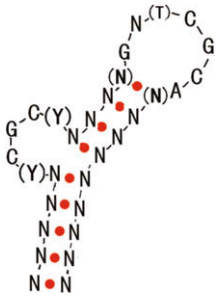


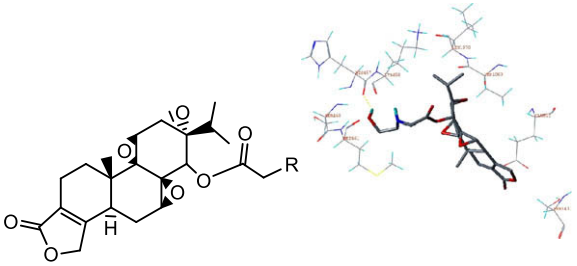
1

Organoselenium antioxidant **1** efficiently quenched ROS production from neutrophils and macrophages. It showed minimal toxicity in five human cell lines and is proposed for antioxidant pharmacotherapy.

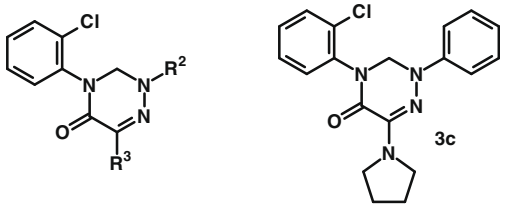


Binding of CEP-701 to the FMS receptor kinase domain is mediated via three hydrogen bonds (yellow lines) and a hydrophobic interaction.



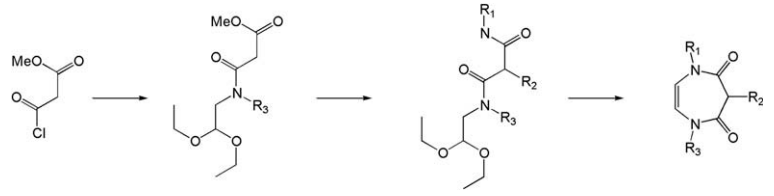


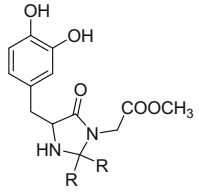
A series of novel derivatives of triptolide were synthesized. In vitro and in vivo antitumor activity was examined. The interaction between compound **9** and RNA polymerase was analyzed with docking.



R^2=C_6H_5; 4-Cl-C_6H_4
R^3= $(CH_3)_2N$; pyrrolidine, piperidine, morpholine

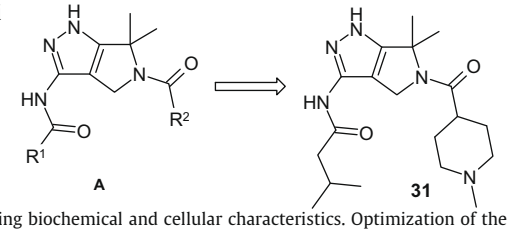
A series of novel 1,2,4-triazin-5-ones was synthesized. Compound **3c** shows promising antiproliferative effects on the human leukemia cell line (K-562), little cytotoxicity against HeLa, and fulfills very well the 'rule-of-five' claims by Lipinski for orally bioavailable drugs.



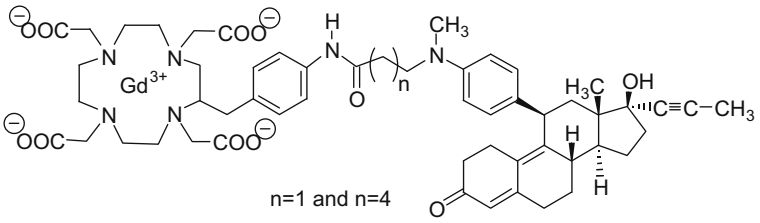


a R=Me; **b** R=Et

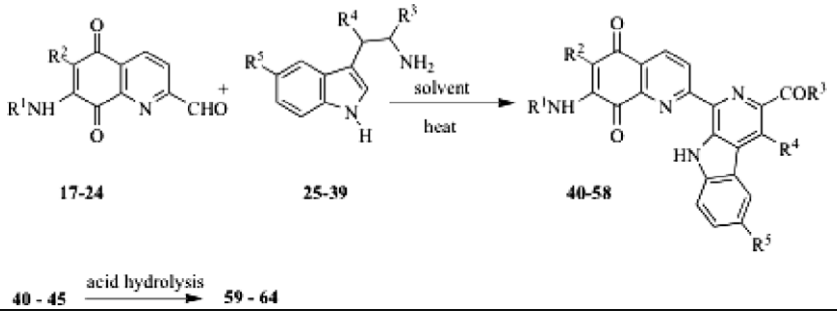
With the aim to increase the bioavailability after oral administration, we designed a multi-protected L-DOPA prodrugs able to release the drug by both spontaneous chemical or enzyme catalyzed hydrolysis. The new compounds have been evaluated for their water solubility, log *P*, chemical stability, and enzymatic stability. The ability of the new prodrugs to increase basal levels of striatal DA, and influence brain neurochemistry, as well as their radical-scavenging activity against DPPH are reported.

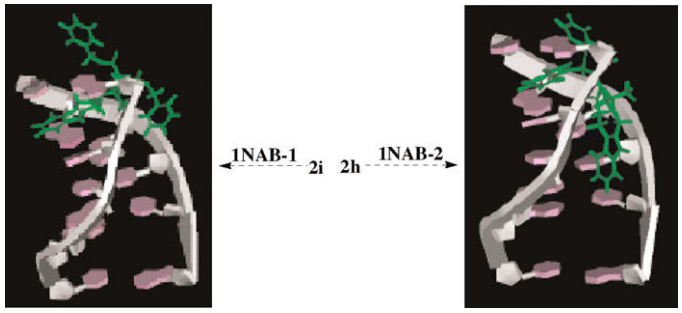


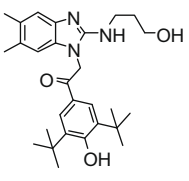
We describe the synthesis of compounds with interesting biochemical and cellular characteristics. Optimization of the physico-chemical properties led to the identification of highly potent compound **31** (PHA-793887), which presents remarkable in vivo efficacy.



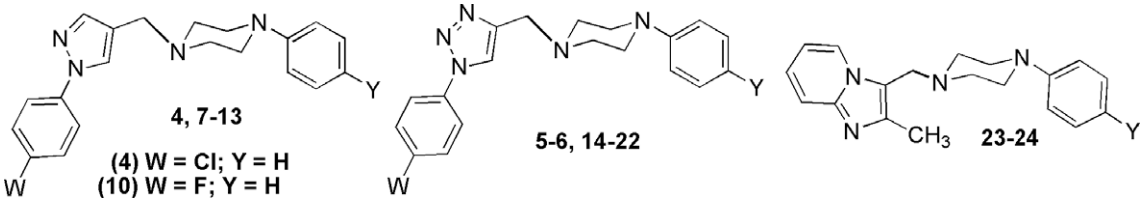
Syntheses of gadolinium containing mifepristone conjugates, in vitro progesterone receptors affinity and estimation of binding sites using the conjugates in human breast cancer cells are described.



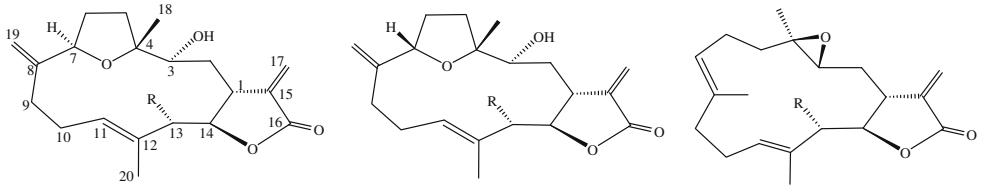




1
IC_{50} =70 nM



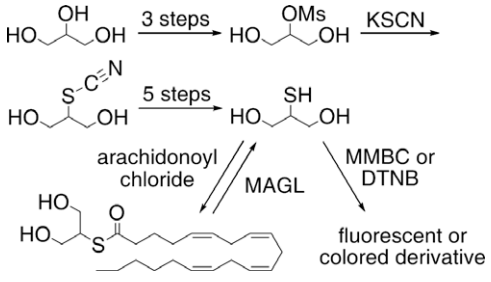
This work describes the synthesis and pharmacological evaluation of heteroarylazole *N*-phenylpiperazines **4–24** as multi-target ligands potentially useful for the treatment of schizophrenia. Among the compounds studied, **4** (LASSBio-579) and **10** (LASSBio-664) exhibited an adequate binding profile and a potential for schizophrenia positive symptoms treatment without cataleptogenic effects.

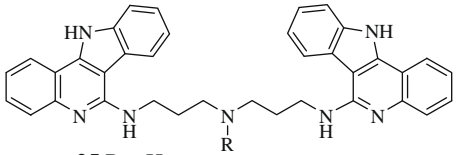


1: R = OAc
3: R = H

2: R = OAc
4: R = H

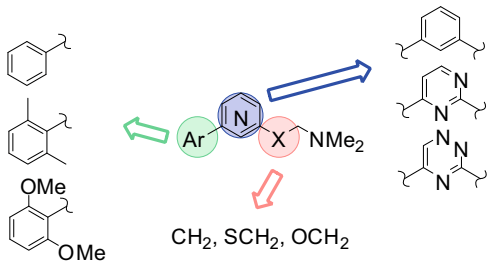
5: R = OCOEt
6: R = H
7: R = OH
8: R = OAc



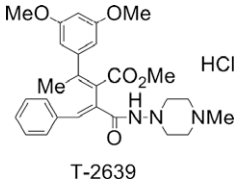


25 R = H
26 R = Me

Mechanism studies indicated **25** can induce caspase-3 activation, γ-H2AX phosphorylation, cleavage of poly (ADP-ribose) polymerase and DNA fragmentation. These results provide evidence that DNA, topo I, and topo II are the primary targets of indolo[3,2-*c*]quinoline derivatives and that consequently inhibits proliferation and causes apoptosis in cancer cells.

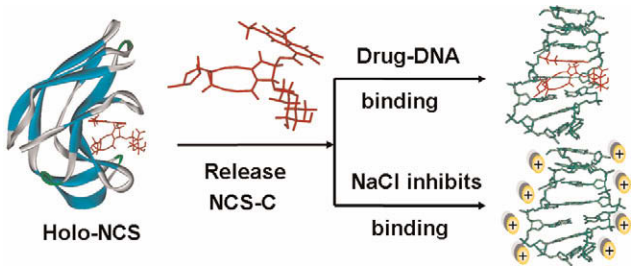


Structure–activity relationships of a series of bis-arylic compounds, investigated as 5-HT$_7$ ligands ligands are reported. A ligand-based pharmacophore model was developed to rationalize the obtained SAR results.

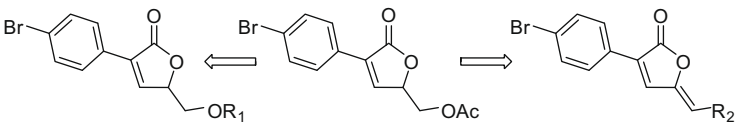


T-2639

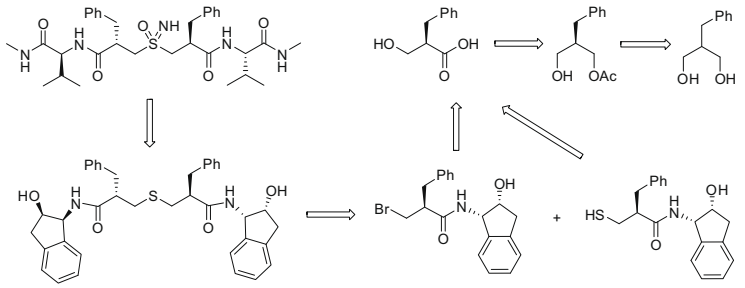
Synthesis and evaluation of T-2639, an orally active inhibitor of PAI-1 production, are reported.

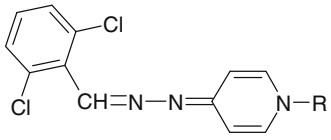


Severe inhibition (up to 85 ± 5%) by the presence of salt on the neocarzinostatin activity was found. Salt interference on the affinity of DNA binding was the main and sole cause of the severe salt inhibition.

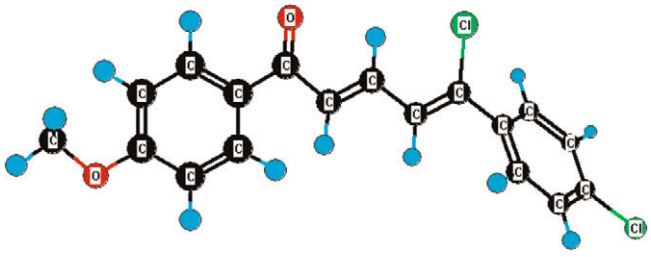


5-Acetoxymethyl-3-(4-bromophenyl)-2,5-dihydrofuran-2-one furnishes highly active 5-methylene derivative (R^2 = H, IC_{80} 0.49–7.81 μmol L^{-1} against *Candida* sp., 1.95 μmol L^{-1} against *Aspergillus fumigatus*) under antifungal assay conditions. 5-Alkoxymethyl furanones are inactive (R^1 = alkyl), 5-aryloxymethylfuranones (R^1 = Ph) also liberate the 5-methylene compound under assay conditions, and the activity of 5-alkylidene furanones is extremely substitution-dependent.





Design of drugs targeting the AChE, BuChE and the the amyloid.



New β-chlorovinyl chalcones were developed and studied as anticancer, anti-inflammatory and antimicrobial agents.

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (http://www.pymol.org). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, *102*, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, *61*(6), 355–360].

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