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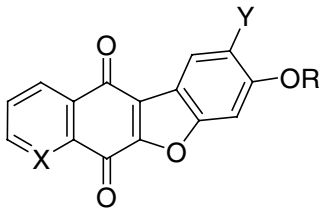
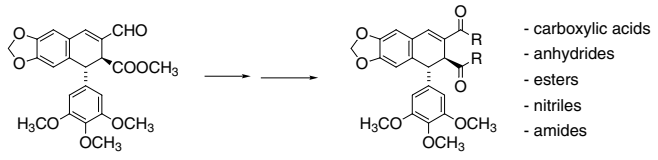
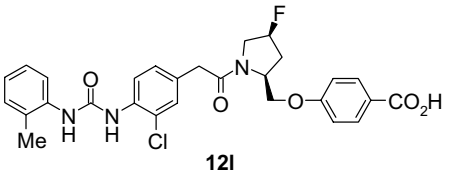
Contents

ARTICLES



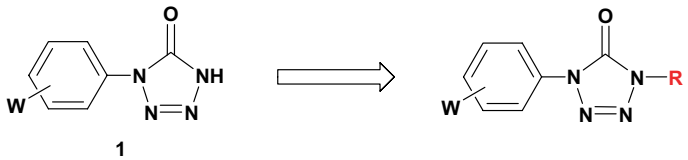


A series of cyclolignans oxidized at C-9 position has been prepared from the cytotoxic and selective podophyllic aldehyde. The functionalities considered at C-9 were carboxylic acids and several derivatives such as anhydrides, esters, nitriles or amides.



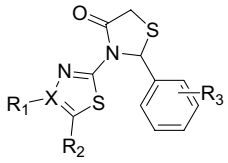
12l

IC_{50} = 0.51 nM
Mouse, CL = 18.5 ml/min/kg, *F* = 28%
Rat, CL = 5.2 ml/min/kg, *F* = 36%
Dog, CL = 3.6 ml/min/kg, *F* = 55%



1

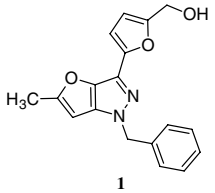
R = structurally diverse substituents, such as alkyl, alkenyl, benzyl, aryl, heterocyclic moiety, etc.



Compounds **1-15**

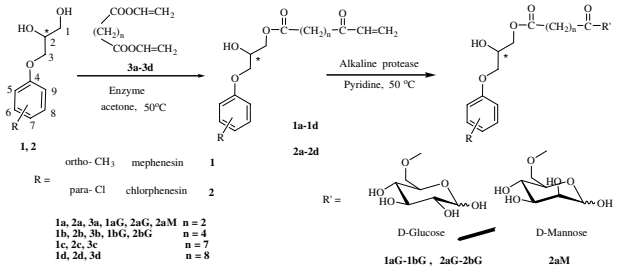
In the present study, 2-aryl-3-heteroaryl-1,3-thiazolidin-4-ones have been assembled by reflux protocol three component reaction of amine, aldehyde and mercapto acetic acid and tested as HIV-RT inhibitors.

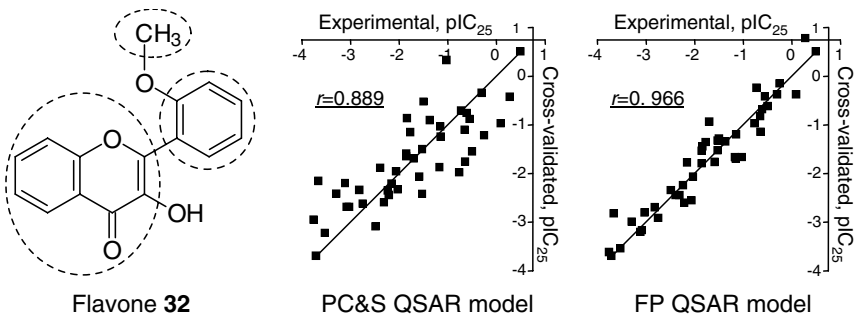
As part of our continuing search for potential anticancer drug candidates in **YC-1** analogs, several 1-benzyl-3-(substituted aryl)-5-methylfuro[3,2-*c*]pyrazoles were synthesized and evaluated for their cytotoxicity against HL-60 cell line. Among these compounds, 1-benzyl-3-(5-hydroxymethyl-2-furyl)-5-methylfuro[3,2-*c*]pyrazole (**1**) showed more potency than **YC-1**. Through investigation of action mechanism, it was found that compound **1** induced terminal differentiation of HL-60 cells toward granulocyte lineage and promoted HL-60 cell differentiation by regulation of Bcl-2 and c-Myc proteins. Meanwhile, compound **1** also demonstrated apoptosis-inducing effect. Such anti-leukemia mechanism of action is apparently different from that of **YC-1** which mainly works by inducing apoptosis, but not cell differentiation. Therefore, compound **1** is identified here as a new lead compound of cell differentiating agent and apoptosis inducer for further development of new anti-leukemia agents.



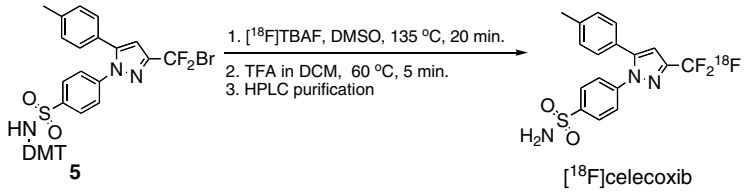
1

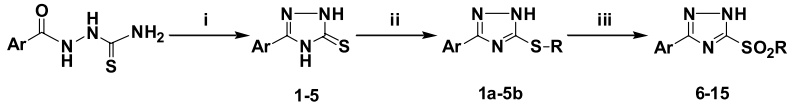
A facile, regioselective enzymatic synthesis procedure for the preparation of a series of amphipathic drug–saccharide derivatives of mephenesin and chlorphenesin was developed by two step sequential acylation.





Flavone **32** PC&S QSAR model FP QSAR model

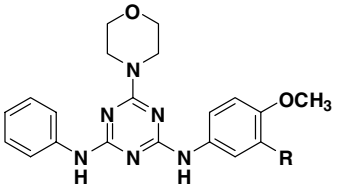




i: 1.KOH 10%; 2. HCl; **ii:** CH_3-/C_2H_5I in 1 M NaOH; 64-93%; **iii:** $KMnO_4$ in AcOH, 20 °C; 22-94%

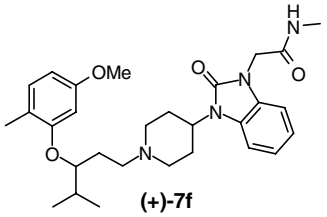
A series of 5-aryl-3-alkylthio-1,2,4-triazoles (**1a**–**5b**) and corresponding sulfones (**6**–**15**) were prepared. The compounds were evaluated for their antiinflammatory and analgesic activity as well as the ulcerogenic risk and acute toxicity.

By structural modification of the screening hit (4,6-bis(*N*-morpholino)-[1,3,5]triazin-2-yl)-phenylamine (**5a**), four compounds exhibited higher inhibition activities against HCT-116 with IC_{50} values below 5 μM. Compounds **6l** and **6o** were most prominent against HCT-116, with IC_{50}s of 0.76 and 0.92 μM, respectively.



6l: R = H
6o: R = OCH_3

A series of N-3 substituted phenoxypropyl piperidine benzimidazol-2-one analogues were prepared and evaluated as NOP agonists. The selective NOP agonist (+)-**7f** showed antinociceptive properties in the mouse formalin paw test (ED_{50} = 1.03 μmol/kg, for second phase) and potent anaesthetic activity in the LRR assay.



(+)-7f

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Terfenadine (an antihistamine pulled from the market in 1997) bound to a model of an open form of the homo-tetrameric pore domain of hERG, produced using Schrödinger's "Induced Fit Docking" technology [Farid, R.; Day, T.; Friesner, R. A.; Pearlstein, R. A. *Bioorg. Med. Chem*. **2006,** *14*, 3160–3173].

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