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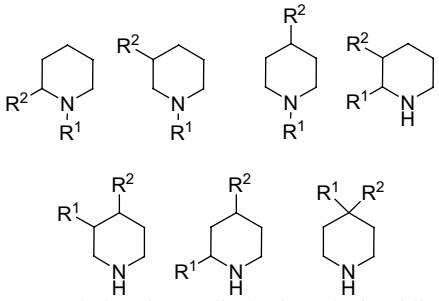
Bioorganic &
Medicinal
Chemistry

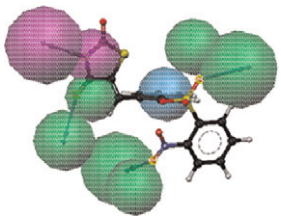
Bioorganic & Medicinal Chemistry Vol. 16, No. 2, 2008

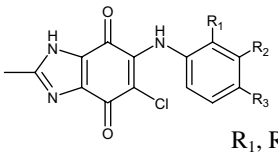
Contents

REVIEW

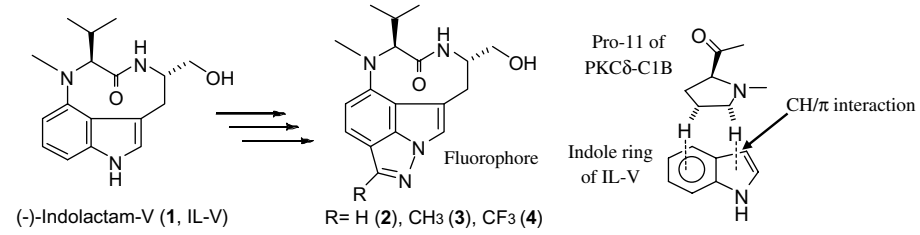


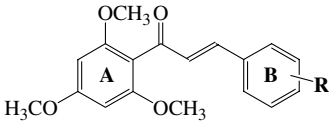
ARTICLES



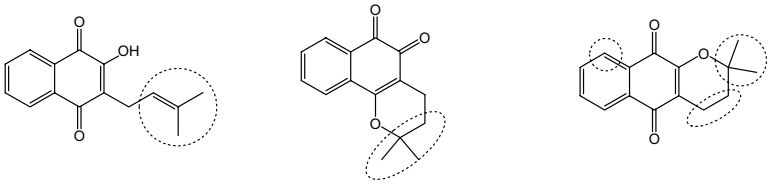


R_1, R_2, R_3 = H

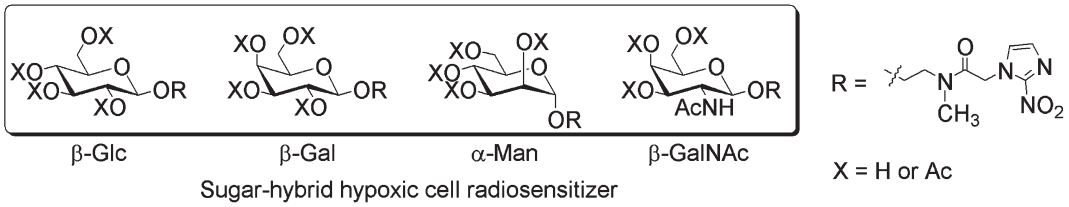


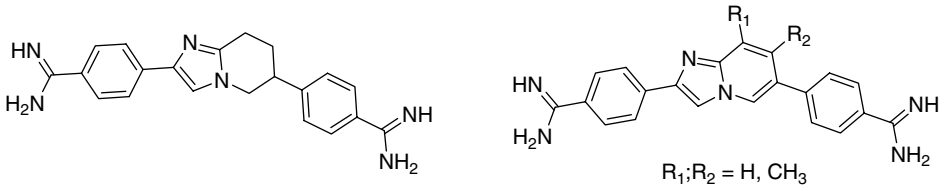


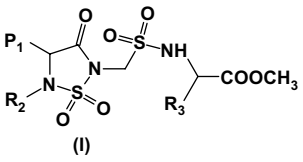
Between 14 chalcones chemically derived from 2,4,6-trimethoxyacetophenone (five of them showed for the first time), eight inhibited the nitrite production in RAW 264.7 cells. Previsions of antiinflammatory activity of other structures were carried out based on QSAR studies.



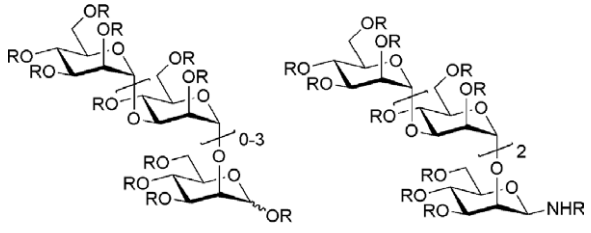
Derivatives obtained by chemical modifications of lapachol, α- and β-lapachones, have been synthesized and their trypanocidal activity evaluated in vitro in *Trypanosoma cruzi* epimastigote and trypomastigote forms.

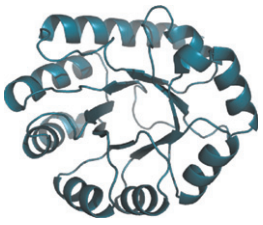


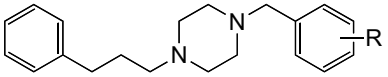




A series of 1,2,5-thiadiazolidin-3-one 1,1 dioxide-based sulfonamides (I) were found to be potent and selective inhibitors of human neutrophil elastase.

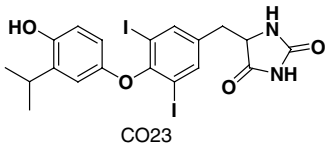




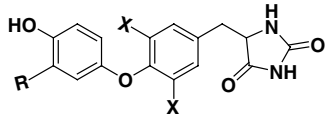


Quantitative structure–activity relationships depended on π_x, MR or E_s, and Hammett σ values. The hydrophobicity term is negative for σ_1 binding but positive for σ_2 binding.

CO23 displays TRα-specificity in vitro and in vivo. Compound **CO23** analogs with greater specificity may prove superior to **CO23** in treating heart disease or as a pharmacological probe of TR biology.

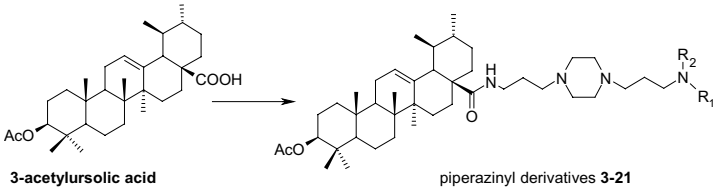


CO23

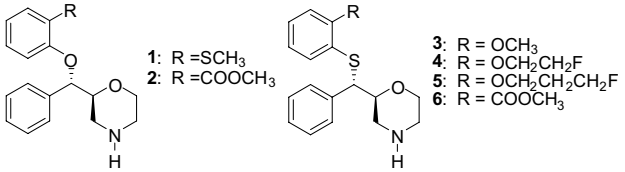


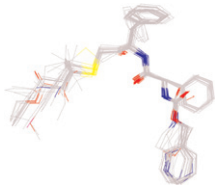
CO23 Analogs

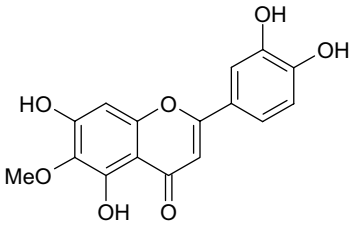
New piperazine derivatives from ursolic acid were designed and synthesized. Seven analogues showed activity in the nanomolar range against *Plasmodium falciparum* FcB1 strain. A possible mechanism of interaction implicating binding of these compounds to β-hematin was supported by in vitro tests and molecular dynamic simulations.

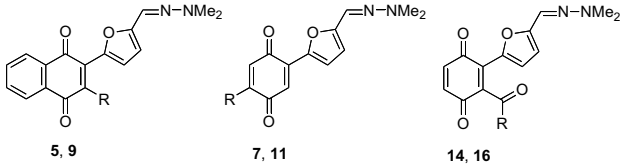


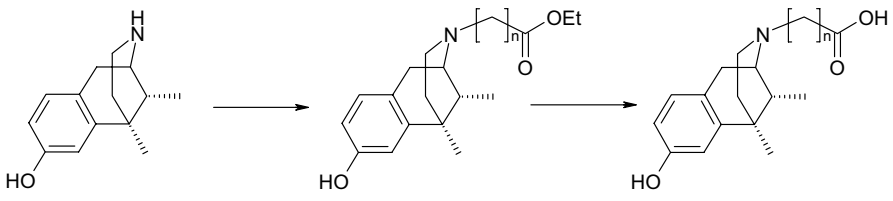
3-acetylursolic acid piperazinyl derivatives **3-21**

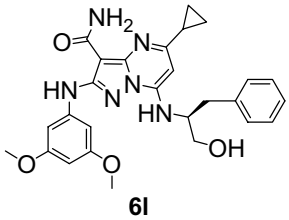






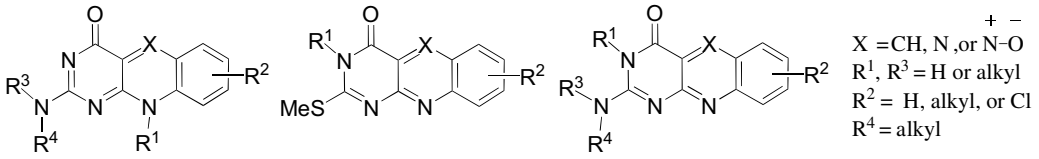






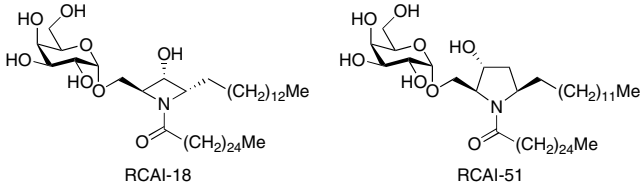
6l

We prepared pyrazolo[1,5-*a*]pyrimidine derivatives that were potent c-Src kinase inhibitors. Modification of the ethylenediamino group at the 7-position of the lead compound **1a** to an amino alcohol group resulted in reduced I_{Kr} channel inhibition. In particular, **6l** showed significant neuroprotective effects in a stroke model.



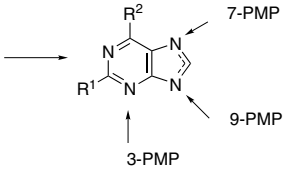
The correlation between the binding free energies (ΔG_b) docked into the c-kit PTK and the growth inhibitory activities (IC_{50}) against CCRF-HSB-2 and KB tumor cells for novel 2-substituted flavin and alloxazine analogs was investigated.

The aminoethyl carbamate structure enabled the convenient purification of amino-modified oligonucleotides with a reverse phase column and increased the labeling efficiency with active esters in aqueous solution.

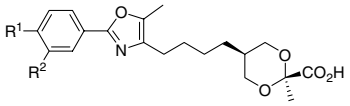


RCAI-18 RCAI-51

These are inducers of cytokine production by mouse NKT cells

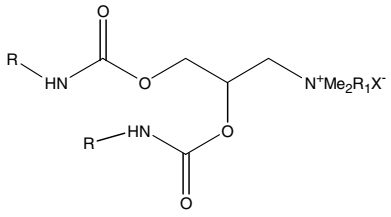


R^1 = guanidino, NH_2, H
R^2 = guanidino, NH_2, H
PMP - (R or S)-[2-(phosphonomethoxy)propyl]



14d (NS-220): R^1 = Me, R^2 = H
14i: R^1 = Me, R^2 = Me

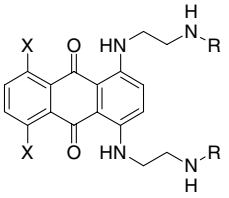
The 1,3-dioxane-2-carboxylic acids **14d** (NS-220) and **14i** were identified as highly potent and selective human PPARα agonists. These compounds showed excellent hypolipidemic activity in type 2 diabetic KK-A^y mice.



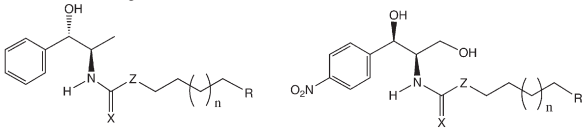
1a: R_1=Me, R=$C_{12}H_{25}$, X^-=I^-
1b: R_1=Me, R=$C_{14}H_{29}$, X^-=I^-
1c: R_1=Me, R=$C_{16}H_{33}$, X^-=I^-
1d: R_1=Me, R=$C_{18}H_{37}$, X^-=I^-
1e: R_1=Et, R=$C_{12}H_{25}$, X^-=I^-
1f: R_1=Et, R=$C_{14}H_{29}$, X^-=I^-
1g: R_1=Et, R=$C_{16}H_{33}$, X^-=I^-
1h: R_1=Et, R=$C_{18}H_{37}$, X^-=I^-
1i: R_1=Me, R=$C_{12}H_{25}$, X^-=Cl^-
1j: R_1=Me, R=$C_{14}H_{29}$, X^-=Cl^-
1k: R_1=Me, R=$C_{16}H_{33}$, X^-=Cl^-
1l: R_1=Me, R=$C_{18}H_{37}$, X^-=Cl^-
1m: R_1=Et, R=$C_{12}H_{25}$, X^-=Cl^-
1n: R_1=Et, R=$C_{14}H_{29}$, X^-=Cl^-
1o: R_1=Et, R=$C_{16}H_{33}$, X^-=Cl^-
1p: R_1=Et, R=$C_{18}H_{37}$, X^-=Cl^-

Cationic lipids **1a**–**p**, with carbamate linkages between hydrocarbon chains and quaternary ammonium heads, were synthesized for liposome-mediated gene delivery, and the biological performance of them was studied.

A focused library of 1,4-bis(2-amino-ethylamino)anthraquinone–amino acid conjugates (BACs) was synthesized. The ability to increase melting temperature of ct-DNA and the cytotoxic activity against human cancer cell lines of these BACs were investigated.



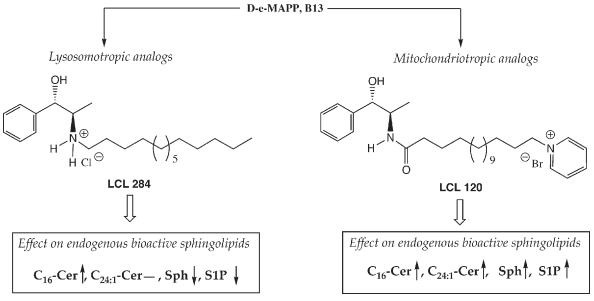
R = L- or D-amino acid residues
X = H or OH

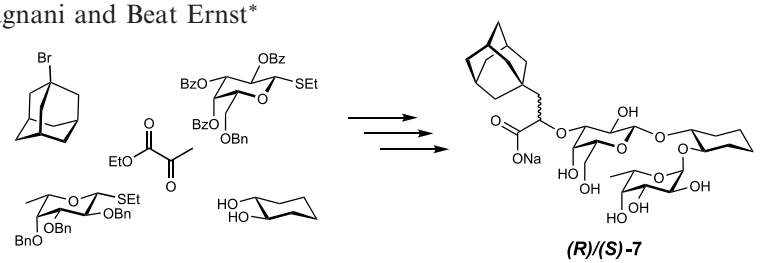


X = O or H_2, Z = NH or CH_2, R = pyridinium bromide or H, n = 8 or 10

	D-MAPP	LCL16	LCL284	LCL120	B13	LCL15	LCL204	LCL85
MCF-7 (IC_{50}/μM)	30.0	16.0	3.5	2.5	14.0	18.0	4.5	2.3
MG MID* $LogGI_{50}$(M)	-4.03	-4.76	-5.75	-5.67	-4.02	-4.84	-5.58	-5.30

*) Based on NCI's 60-human-tumor-cell lines





For the pre-organization of the acid orientation in the bioactive conformation, the selectin antagonists **7** containing (*R*)- and (*S*)-adamantyl-lactic acid were synthesized and biologically evaluated.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Schematic view on the E-selectin - leukocyte interaction during the early steps of the inflammatory cascade: the (S)-configured adamantyllactate analog of sialyl LewisX binds to E-selectin and could therefore inhibit leukocyte extravasation into neighbouring tissue in inflammatory diseases [Titz, A.; Alker, A. M.; Porro, M.; Schwardt, O.; Hennig, M.; Francotte, E.; Magnani, J.; Ernst, B. *Bioorg. Med. Chem.* **2008,** *16,* 1046–1056].

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ISSN 0968-0896