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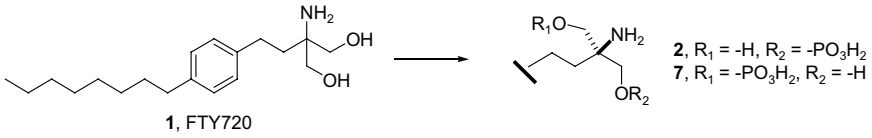
Chemistry

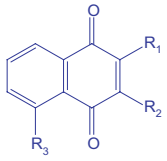
Bioorganic & Medicinal Chemistry Vol. 12, No. 18, 2004

# Contents

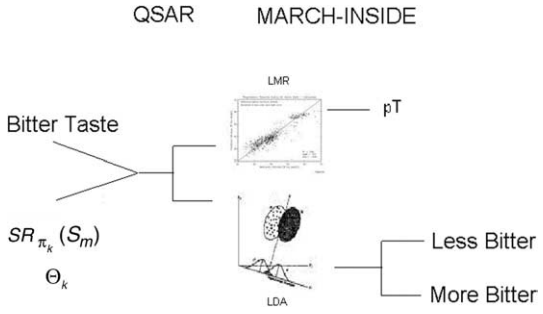
## ARTICLES





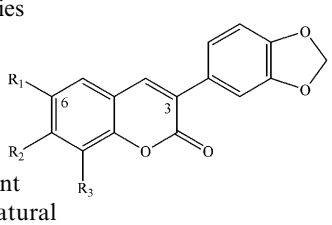





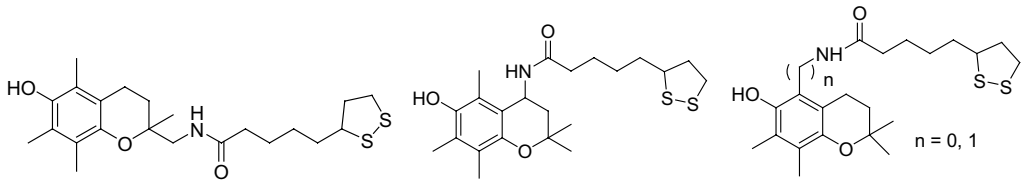





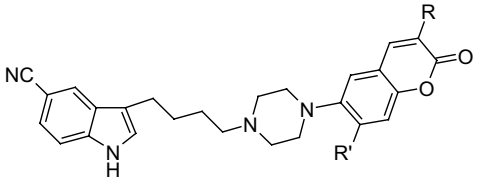

This article describes the synthesis and inhibitory activities of a series of new 3-piperonylcoumarins, designed as inhibitors of glycosomal glyceraldehyde-3-phosphate dehydrogenase (gGAPDH) from *Trypanosoma cruzi*. SAR studies, performed by electronic indices methodology (EIM), clustered the molecules in different groups due to the chemical substitutions regarding the biological activity. Molecular modeling studies by docking suggested a different binding mode for the most active derivatives, when compared to natural hit chalepin. Moreover, the coumarin ring seems to act only as a spacer group.




**2a** $R_1 = NO_2$, $R_2 = R_3 = H$
**2b** $R_1 = OAc$, $R_2 = R_3 = H$
**2c** $R_2 = OAc$, $R_1 = R_3 = H$
**2d** $R_3 = OAc$, $R_1 = R_2 = H$
**2e** $R_1 = R_2 = R_3 = H$
**3b** $R_1 = OH$, $R_2 = R_3 = H$
**3c** $R_2 = OH$, $R_1 = R_3 = H$
**3d** $R_3 = OH$, $R_1 = R_2 = H$
**4** $R_1 = NH_2$, $R_2 = R_3 = H$
**5a** $R_1 = (1E)$-1H-pyrrol-2-ylmethylamino, $R_2 = R_3 = H$
**5b** $R_1 = (1E)$-2-furylmethyleneamino, $R_2 = R_3 = H$
**5c** $R_1 = (1E)$-thien-2-ylmethyleneamino, $R_2 = R_3 = H$
**6** $R_1 = (1E)$-1H-indol-3-ylmethyleneamino, $R_2 = R_3 = H$
**7** $R_1 = (1E)$-pyridin-2-ylmethyleneamino, $R_2 = R_3 = H$

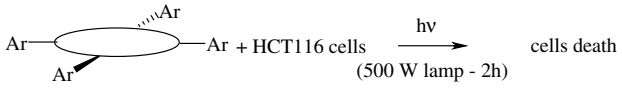





A series of compounds as dual serotonin re-uptake inhibitor and 5-$HT_{1A}$ receptor agonist was found to increase central serotonin levels in rat brain to a greater extent than established antidepressants.



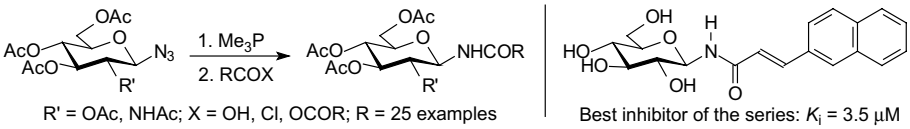



Porphyrins and Chlorins

Ar = 3-methoxyphenyl; 4-methoxyphenyl; 3,4,5,-trimethoxyphenyl; 3-hydroxyphenyl; 4-hydroxyphenyl; 3,4,5-trihydroxyphenyl; 4-solfonamidophenyl.

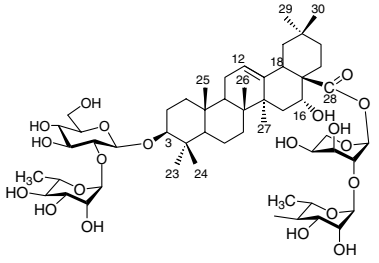
A series of tetraaryl porphyrins and chlorins were synthesized and tested for photodynamic activity in human colon adenocarcinoma cells.



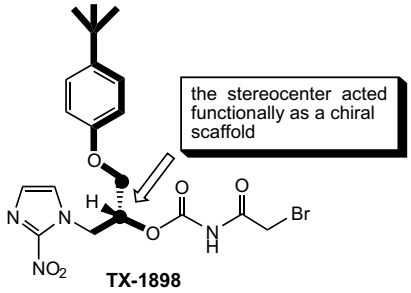



R' = OAc, NHAc; X = OH, Cl, OCOR; R = 25 examples

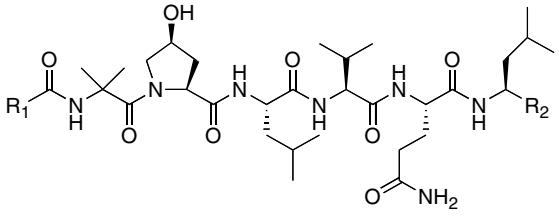
Best inhibitor of the series: $K_i$ = 3.5 μM



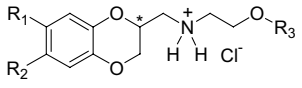






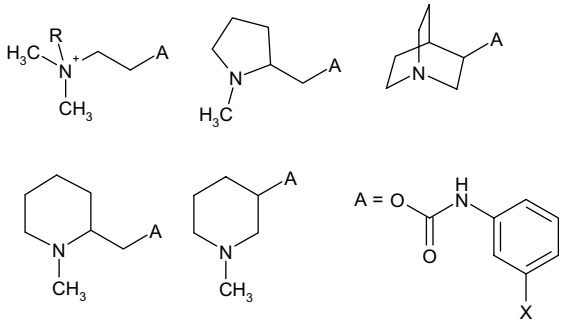





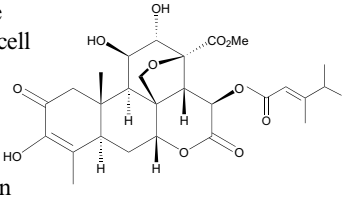


**1** (WB-4101: $R_1$=$R_2$=H, $R_3$=2,6-dimethoxyphenyl)

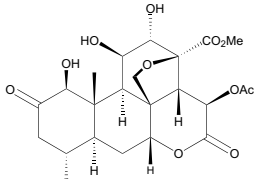
| | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| **2** | -(CH=CH)$_2$- | | 2,6-dimethoxyphenyl |
| **3** | -(CH$_2$-CH$_2$)$_2$- | | " |
| **4** | H | H | 1-naphthyl |
| **5** | H | H | 2-naphthyl |
| **6** | H | H | 2-methoxy-1-naphthyl |
| **7** | H | H | 1-methoxy-2-naphthyl |
| **8** | H | H | 3-methoxy-2-naphthyl |





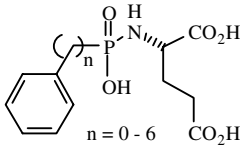




**9**




**24**

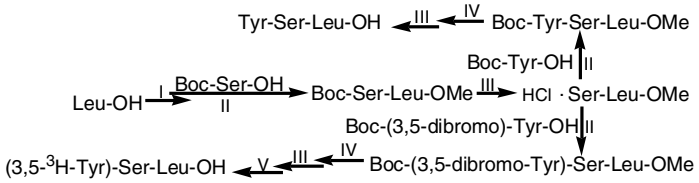





**1a-1g**

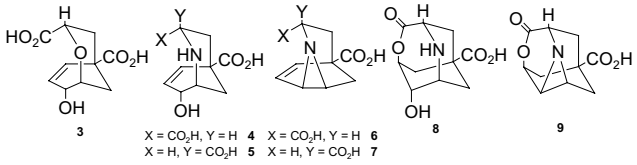
A series of phenylalkylphosphonamidate derivatives of glutamic acid were synthesized and evaluated for their inhibitory potencies against PSMA. The greatest inhibitory potency was observed for the inhibitors **1f** ($n = 5$) and **1g** ($n = 6$) suggesting the presence of a hydrophobic binding register remote from the substrate recognition architecture in the active site of PSMA.






(I) HCl/$CH_3OH$; (II) DCC/HOBt/NMM with corresponding carboxyl component; (III) HCl/$CH_3CO_2C_2H_5$ (6 mol/L); (IV) NaOH/$H_2O$/$CH_3OH$; (V) $^3H_2$ and 10% Pd/C.






The detailed information pertaining to this panel of aza inhibitors is presented.

## OTHER CONTENTS



*Corresponding author

## 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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