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Symposium-in-Print

Tetrahedron Young Investigator Award 2006 Jonathan Ellman

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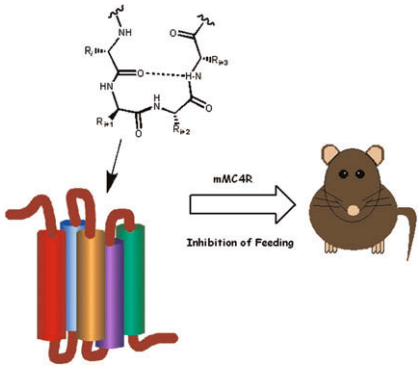

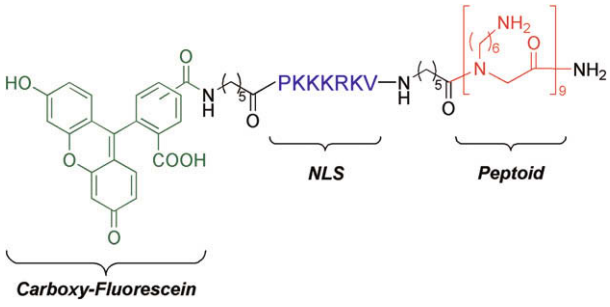

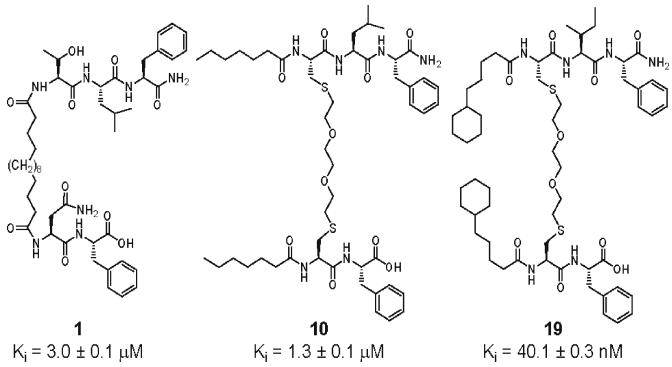

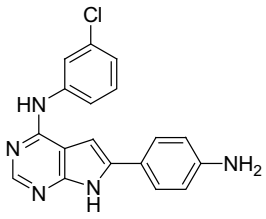

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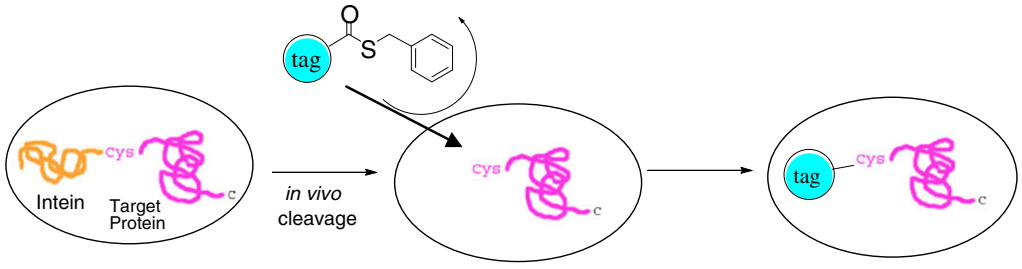
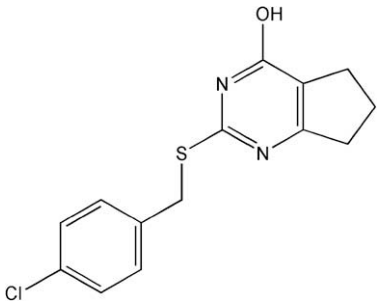
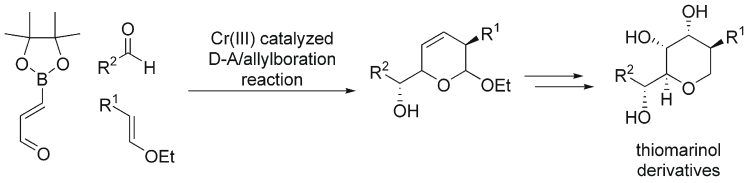
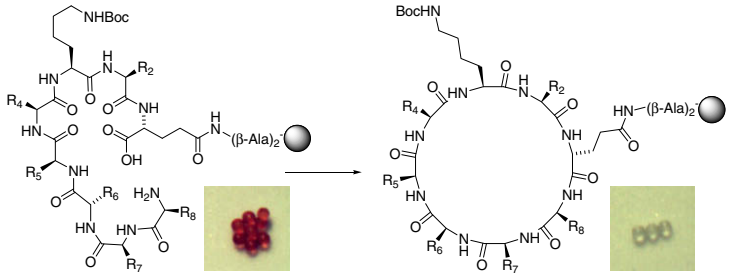
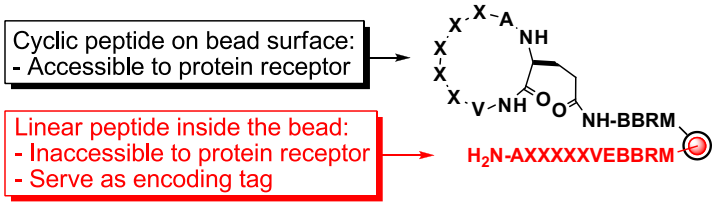




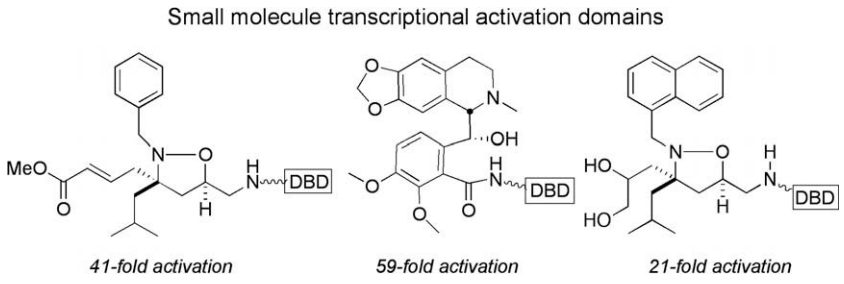


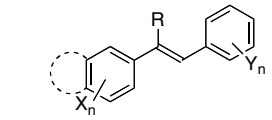
Simplified derivatives of the thiomarinol class of antibiotics were prepared via a catalytic enantioselective inverse electron demand hetero [4 + 2] cycloaddition/allylboration tandem reaction. These analogs were tested for antimicrobial activity using a standard disk diffusion assay.



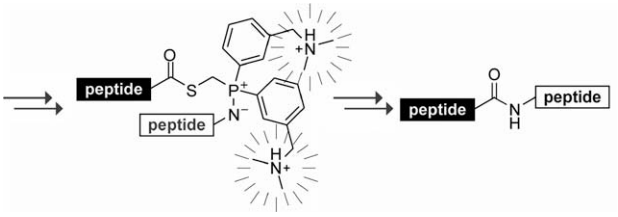


A cyclic peptide library was screened against the extracellular domain of human prolactin receptor and ligands with low-micromolar dissociation constants were discovered.

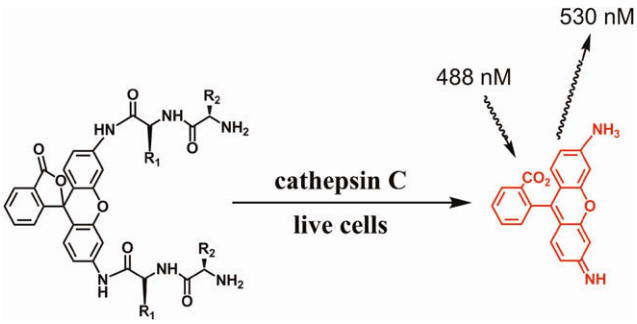


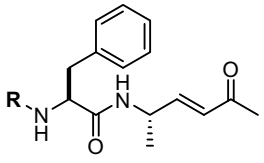


X, Y = *m*-, *p*- OH, OMe, NMe_2, F, CF_3, NO_2
R = H, Me, Et, CF_3



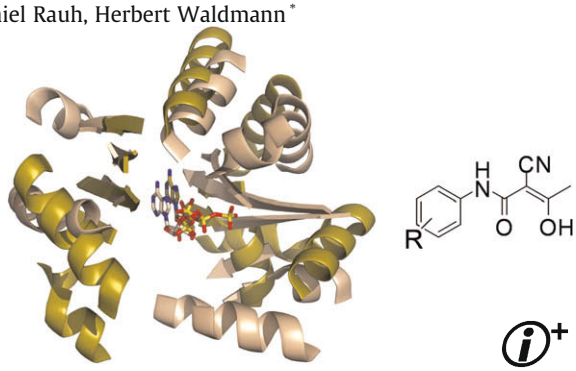
Consideration of Coulombic interactions enables phosphinothiols to mediate a traceless Staudinger ligation efficiently in water.

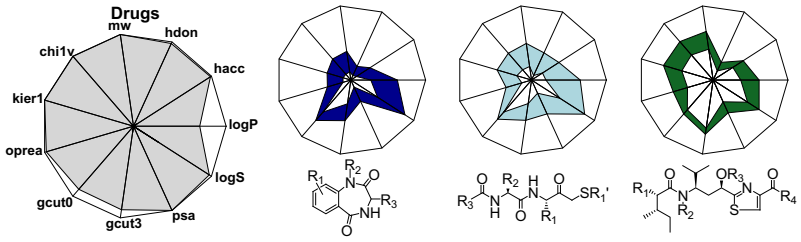




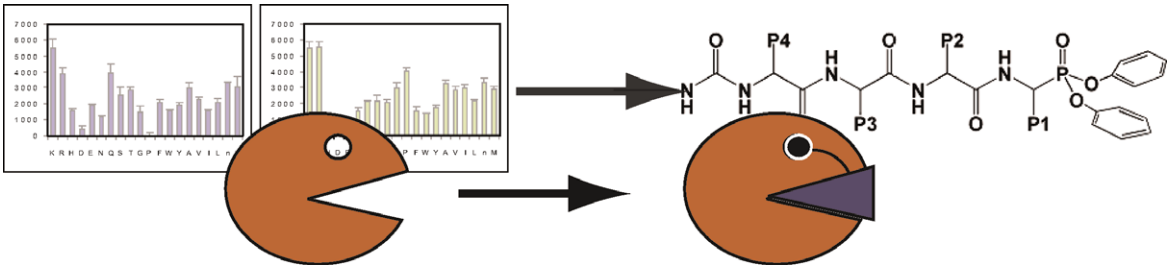
yzm09 R=Cbz
yzm13 R=Biotin-PEO_4
yzm24 R=Bidipy-TMRX

Activity-based probes based on α,β-unsaturated ketone label papain-family cysteine proteases (Cat B and Cat L) in mouse tissue lysates, cell lysate, and intact cells.

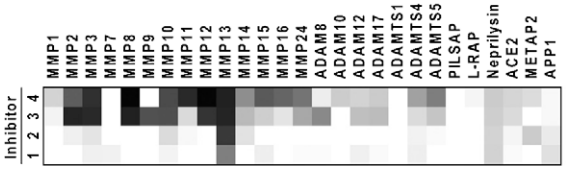




Analysis of the physiochemical properties of eight libraries produced by the Ellman group indicates that they cover a wide span of biologically relevant chemical space.



Library-based approaches for screening the substrate specificity of a protease (shown as 'Pacman') as a strategy to develop specific and potent peptidic and small molecule inhibitors.



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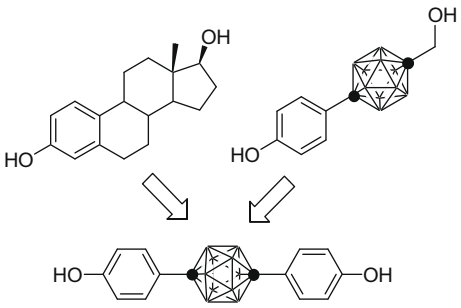
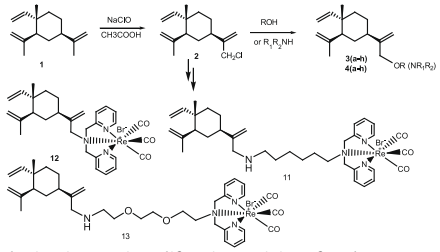
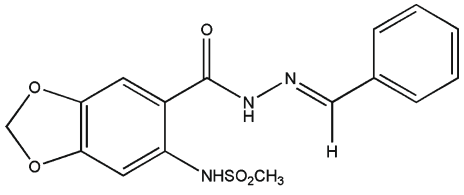


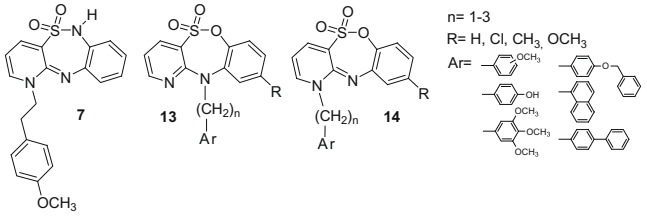


β-Elemene monosubstituted derivatives were synthesized. The in vitro anti-proliferative activity of β-elemene monosubstituted amine and $Re(CO)_3$-β-elemene derivatives in human cervix epitheloid carcinoma HeLa cells were improved significantly compared with both of ether derivatives and parent β-elemene. These derivatives could reduce Rb phosphorylation and cyclin D_1 protein expression to arrest the cell cycle at G_1 phase.

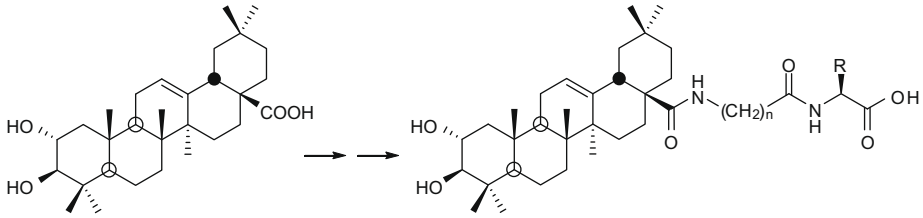


LASSBio-930 (1c)

We describe herein the discovery of NAH-derivative LASSBio-930 (**1c**) as a novel in vivo anti-inflammatory and anti-hyperalgesic prototype, that acts as non-selective COX inhibitor.

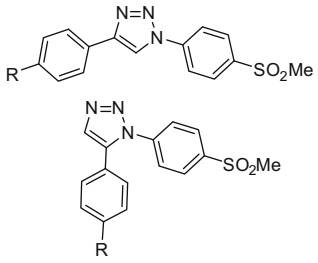


Herein, we describe the structure–activity relationship study of a new 1-(arylalkyl)-11*H*-benzo[*f*]-1,2-dihydropyrido[3,2,*c*][1,2,5]oxathiazepine 5,5-dioxide series of antimitotic agents. The pharmacological results obtained from previous works allowed us to identify compound **1** as a new cytotoxic agent inhibiting tubulin polymerization. We have undertaken the synthesis of its non-methylated analogue **7** and have extended our investigations to a novel, structurally related benzopyridooxathiazepine dioxide series **9** and **10**.

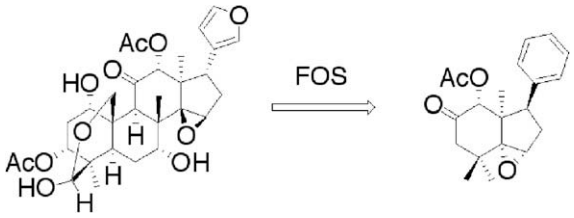


A solid-phase method for the preparation of maslinic acid derivatives has been described, to achieve derivatives that are not cytotoxic and show potent anti-HIV activity.

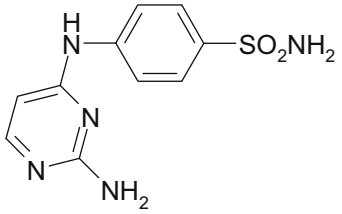
1,4- and 1,5-diaryl substituted 1,2,3-triazoles were synthesized by either Cu(I)-catalyzed or Ru(II)-catalyzed 1,3-dipolar cycloaddition reactions between 1-azido-4-methane-sulfonylbenzene and a panel of various *para*-substituted phenyl acetylenes (4-H, 4-Me, 4-OMe, 4-NMe_2, 4-Cl, 4-F). All compounds were used in in vitro cyclooxygenase (COX) assays to determine the combined electronic and steric effects upon COX-1 and COX-2 inhibitory potency and selectivity.



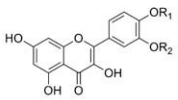
R = Me, OMe, Me_2N, F, H, Cl



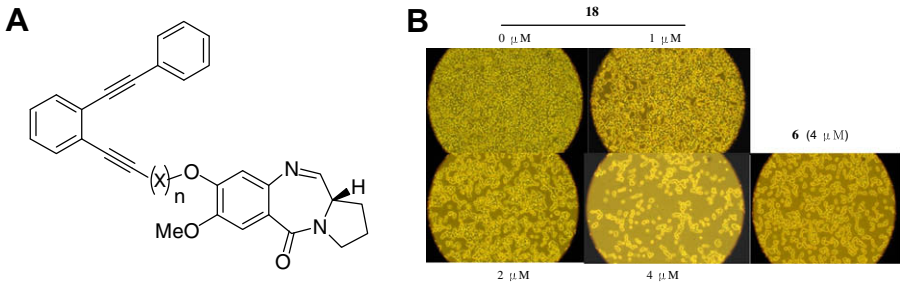
Botulinum neurotoxins (BoNTs) are the most lethal poisons known, while the natural product toosendanin has demonstrated efficacy against the BoNTs. To unravel toosendanin's efficacy, Function-Oriented Synthesis (FOS) was examined.



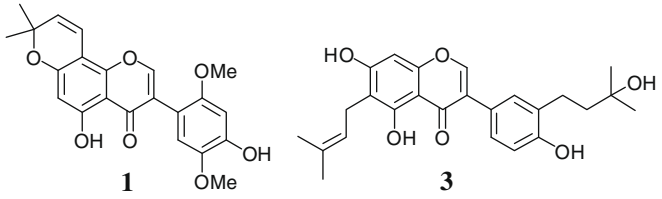
Ki (scCA) = 15.1 nM; Ki (hCA I) = 109 nM; Ki (hCA II) = 33 nM



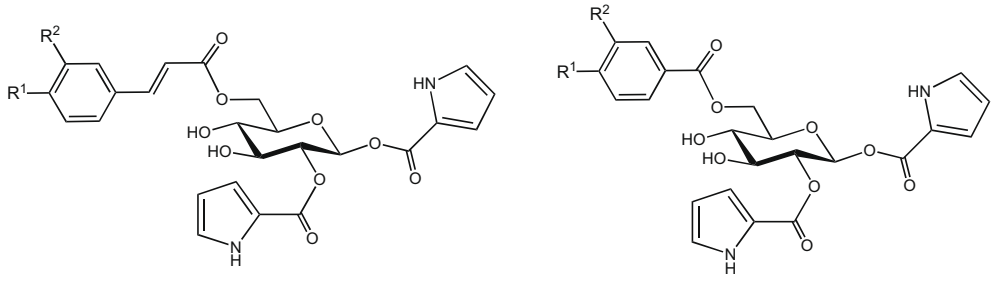
		Quercetin (Qu)	Qu-E
Structure		$R_1 = R_2 = H$	R_1 = (*S*)-CONHCH($CH_2CH_2CO_2H$)CO_2H, $R_2 = H$ / $R_1 = H$, R_2 = (*S*)-CONHCH($CH_2CH_2CO_2H$)CO_2H
Solubility in water (μM)		50	2649
Stability ($t_{1/2}$)	PBS buffer	–	> 17 h
	Cell lysate	–	180 min
Relative cell permeability		1.0	5.2

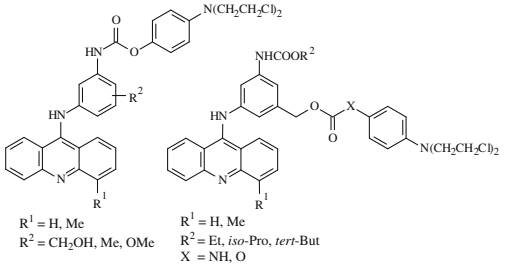


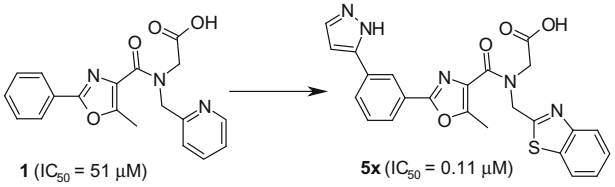
(A) Structure of the enediyne-PBD conjugate agents. (B) The apoptotic morphology after treatment with compound (**6**, **18**) on 293T.



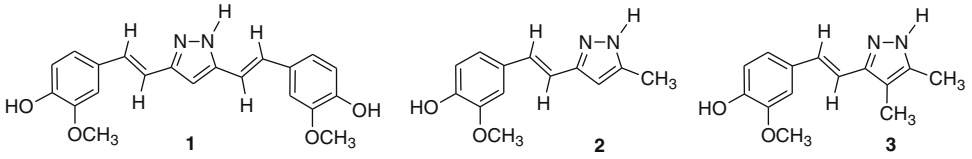
On screening for compounds that enhance DR5 expression, a new isoflavone, coloratanin A (**3**) was isolated from *Ardisia colorata*. In addition, we described that 4′-demethyltoxicarol isoflavone (**1**) sensitized TRAIL-resistant AGS cells to TRAIL-induced apoptosis by up-regulations of DR5 expression.



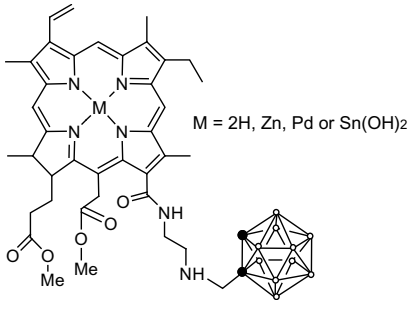




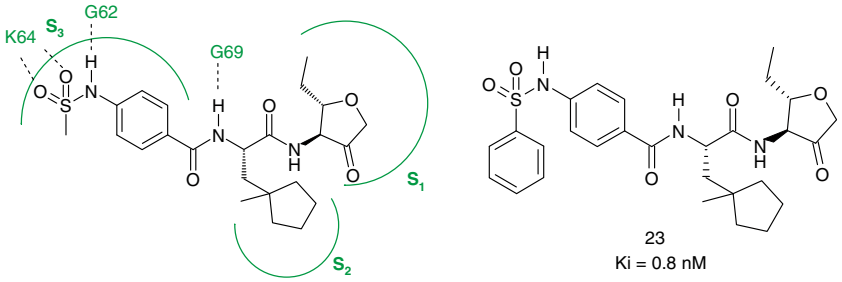
Discovery of new inhibitors of HldE kinase by high throughput screening and structure–activity relationship optimization provided a promising lead series for the development of new Gram-negative antimicrobial agents.

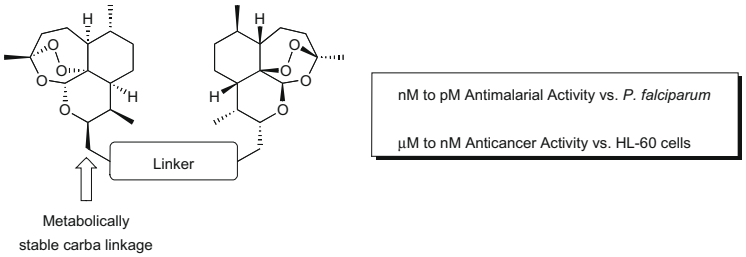


Curcuminoid pyrazoles (**1**–**3**), have demonstrated activity in the biological assays used as models (MMPs inhibition) for inflammatory bowel disease.

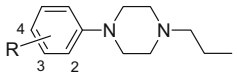


New boronated derivatives of chlorin e_6 for anticancer photodynamic therapy.



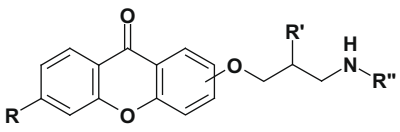


A series of artemisinin dimers incorporating a metabolically stable C-10 carba-linkage have been prepared, several of which show remarkable in vitro antimalarial activity (as low as 30 pM) versus *Plasmodium falciparum* and in vitro anticancer activity in the micromolar to nanomolar range versus HL-60 cell lines.



R= H, CH_3, OCH_3, OH, Cl, CF_3, NO_2, CN, $CONH_2$

$7.59 < pK_a < 8.80$



R = H, Cl
R' = H, OH
R" = allyl, 2-(2-methyl-1-propanol), 2-(2-methyl-1,3-propanediol)

Selected xanthone derivatives, expected to reveal cardiovascular properties, were synthesized and tested for their antiarrhythmic, antihypertensive and anticonvulsive activity, as well as for the α_1- and β_1-adrenoceptor binding affinities.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

A 1.5 Å crystal structure of a small molecule inhibitor identified by the Substrate Activity Screening method in complex with cathepsin S (2H7J). The figure was produced using Pymol (www.pymol.org).

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