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Chemical Proteomics

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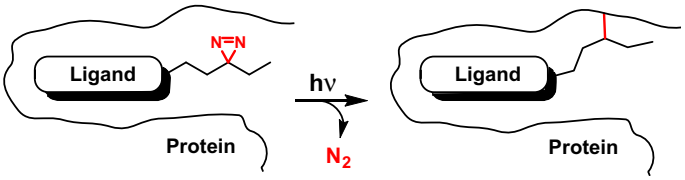
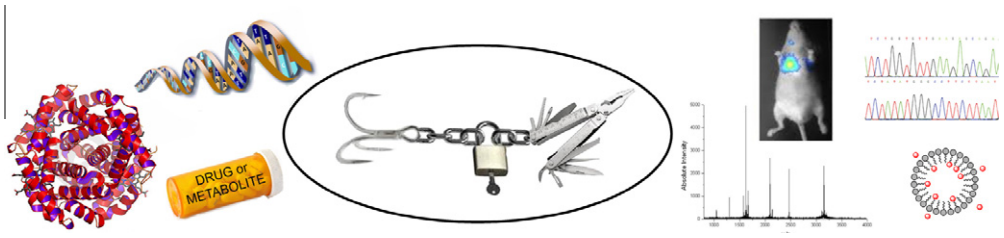
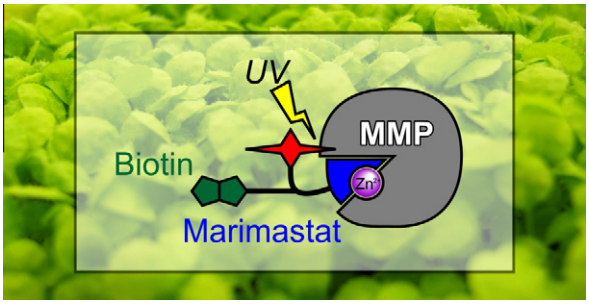
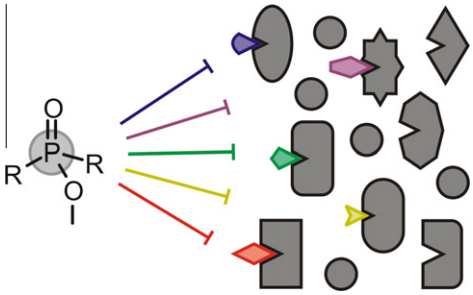
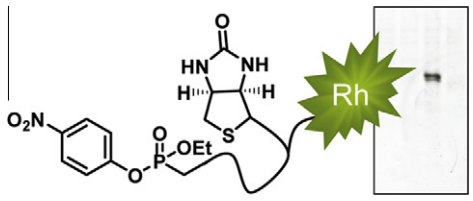


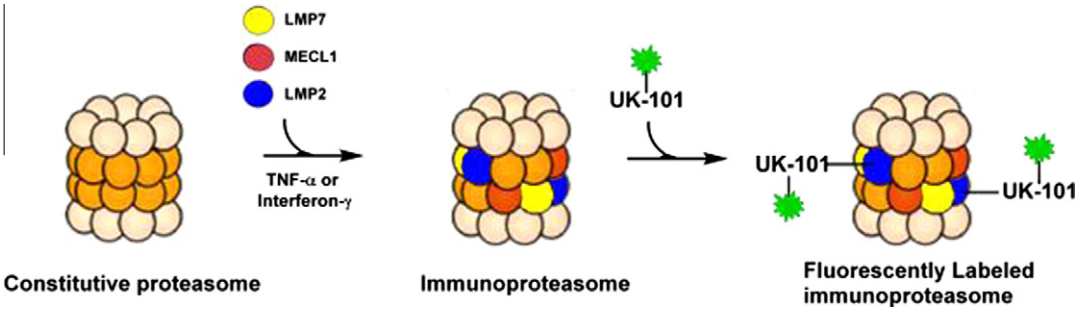
Diazirines are among the smallest photoreactive groups that form a reactive carbene upon light irradiation. This feature has been widely utilized in photoaffinity labeling to study ligand–receptor, ligand–enzyme and protein–protein interactions, and in the isolation and identification of unknown proteins. This review summarizes recent advances in the use of diazirines in photoaffinity labeling.

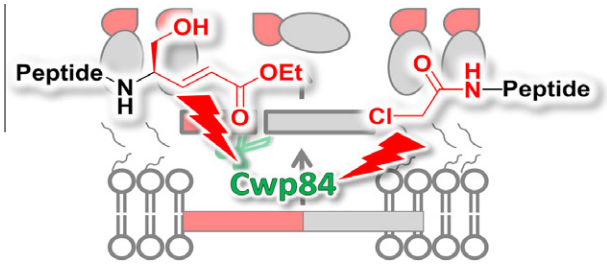


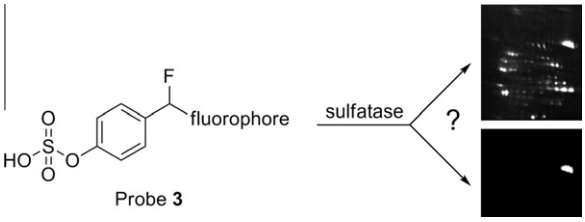


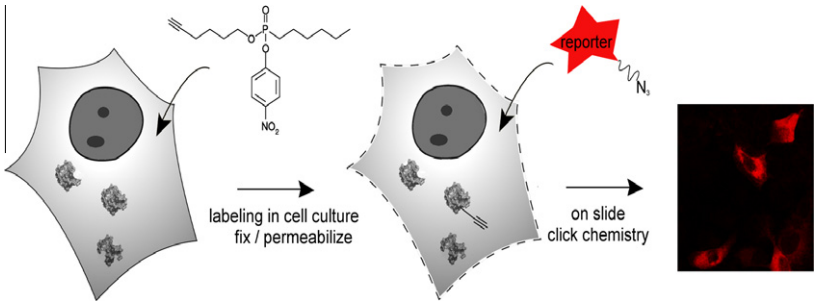


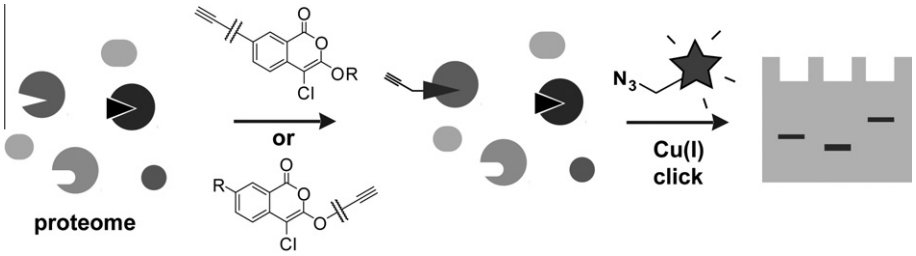


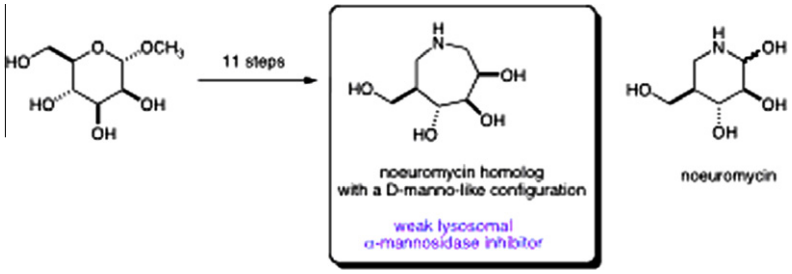


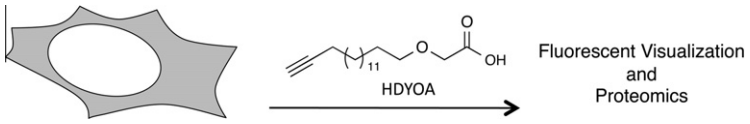


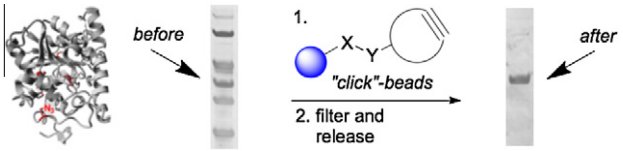


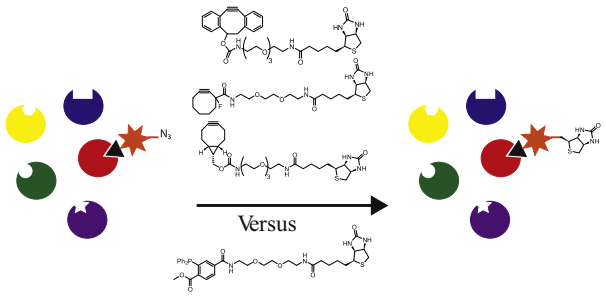


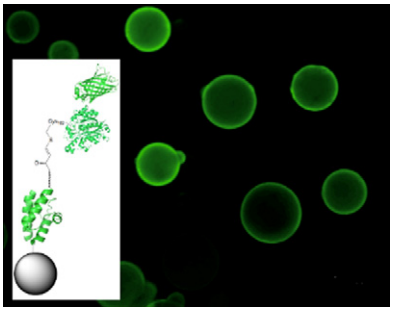


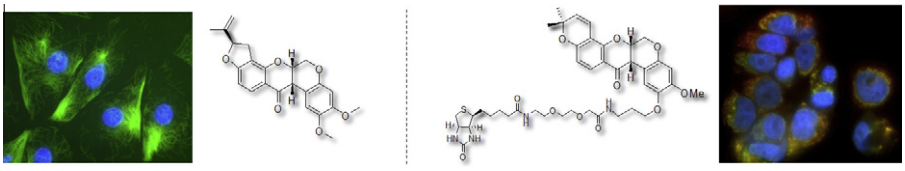




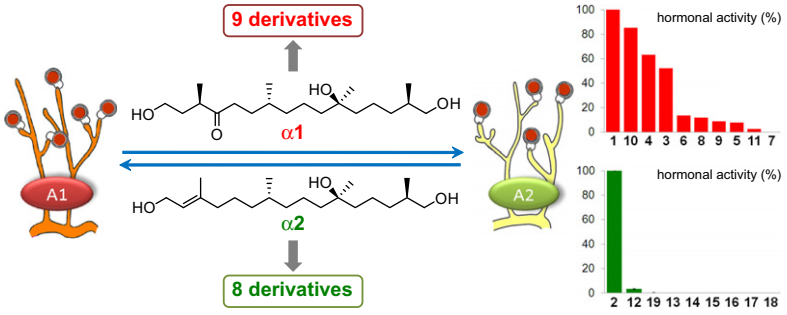


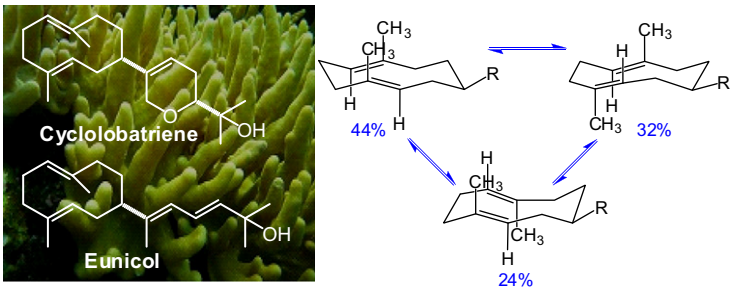


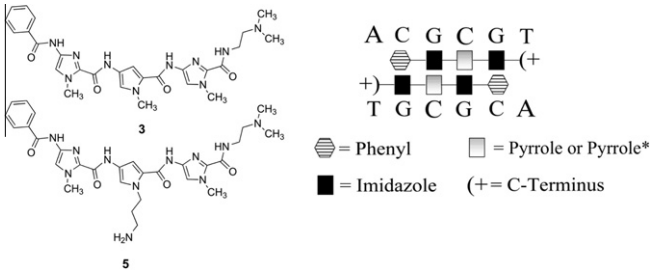


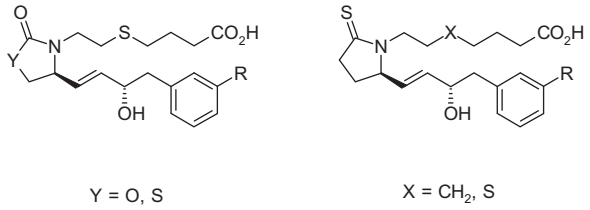


REGULAR ARTICLES

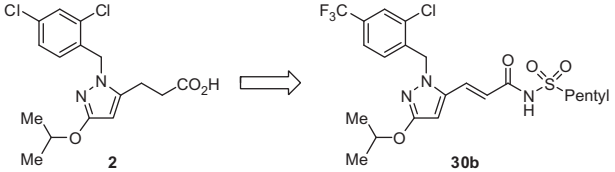


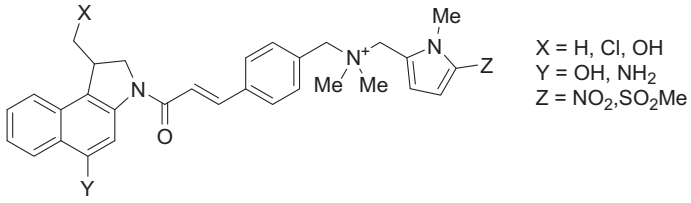


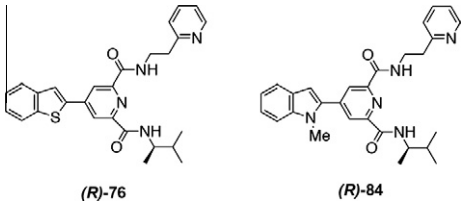


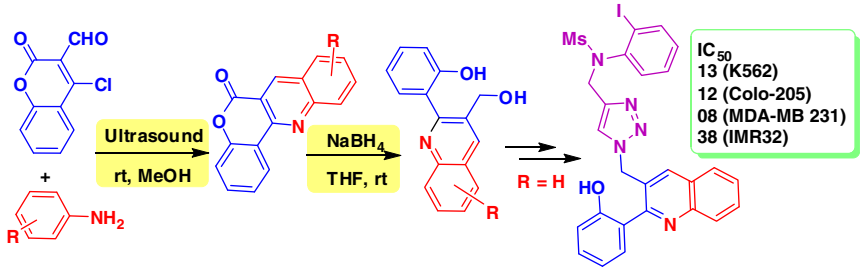


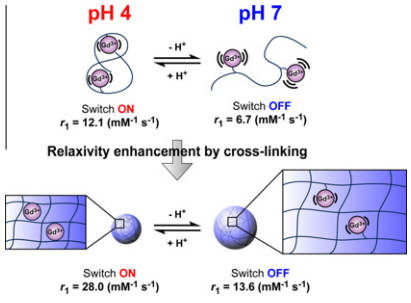
The 2-oxo-1,3-oxazoline, 2-oxo-1,3-thiazolidine and 5-thioxopyrrolidine were identified as new templates for EP4 receptor selective agonists.

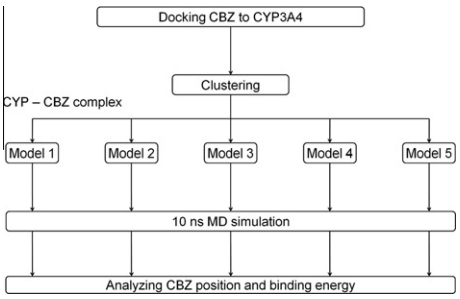


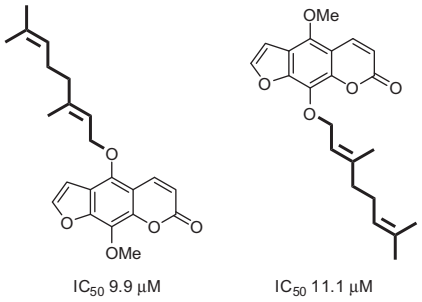


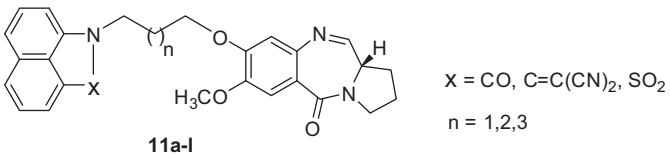






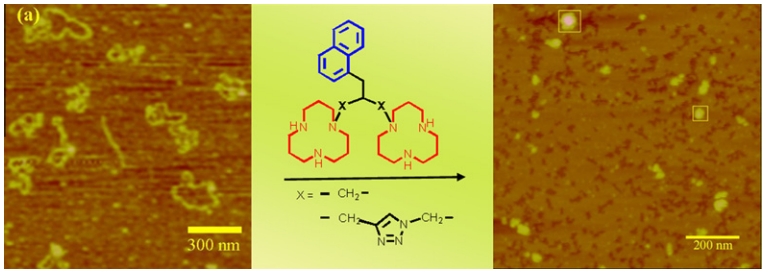




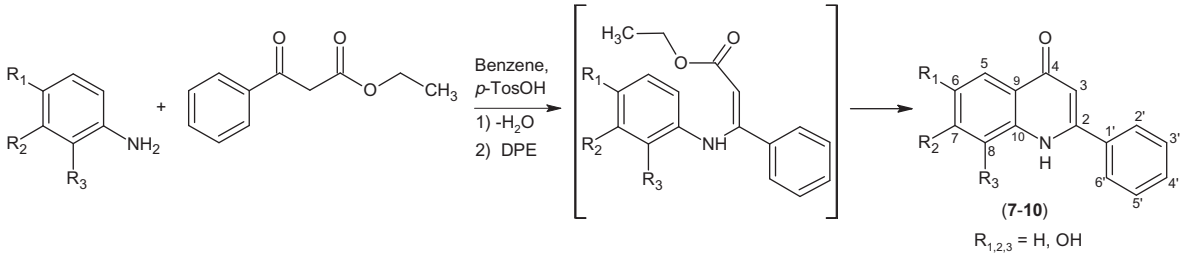


11a-l

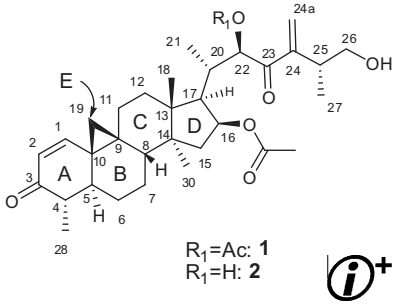
A series of benzo[*c*,*d*]indolone-pyrrolobenzodiazepine conjugates **11a**–**l** have been prepared and evaluated for their anticancer activity.



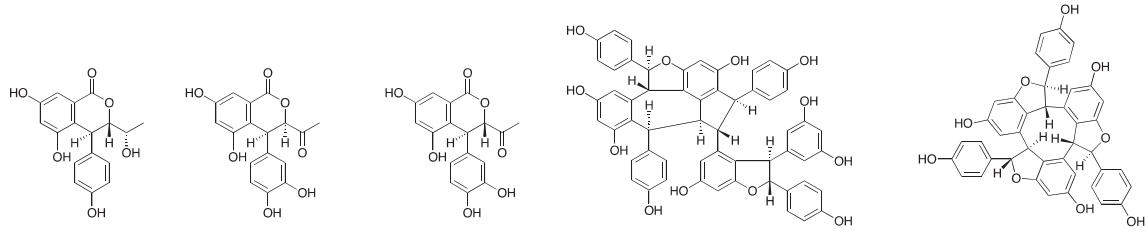
Bifunctional molecules containing naphthyl and macrocyclic polyamine [12]aneN$_3$ moieties have been synthesized and successfully applied in DNA condensation.



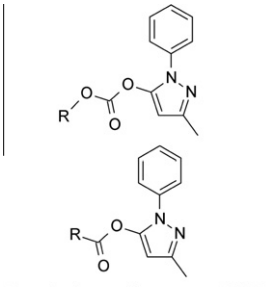
A series of synthesised 4-quinolones (**7**–**10**) were evaluated for antioxidant activity and compared to structurally related quinolines and flavones as potential neuroprotective agents.

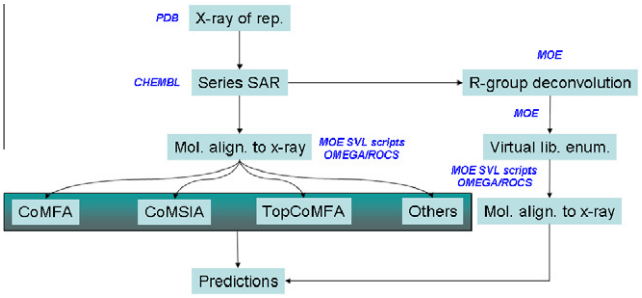


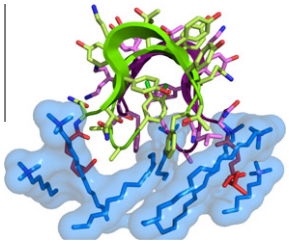
Structures of neoboutomellerones isolated from *Neoboutonia melleri*.

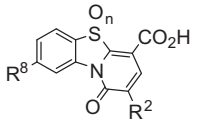


A new class of co-drugs obtained by joining antioxidant edaravone with a vasodilating substructure containing NO-donor functions, is presented. These compounds, characterized by a good gastrointestinal absorption, afford edaravone and the related NO-donor moieties when incubated in human serum and in rat liver homogenate. The title products are potentially useful for treating ROS-related conditions accompanied by decreased NO availability.



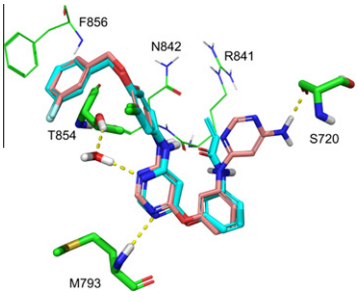


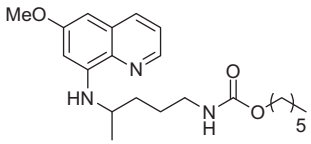




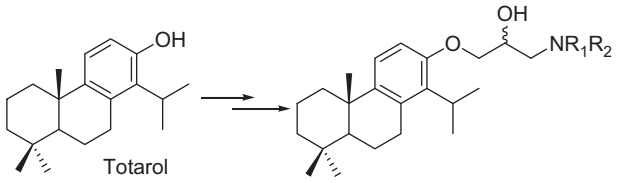
general structure of compounds realized in this study

A series of 4,6-disubstituted pyrimidines derivatives were designed and synthesized as dual EGFR/ErbB-2 inhibitors. 4-[3-Chloro-4-(3-fluorobenzyloxy)anilino]-6-(3-acrylamidophenoxy)pyrimidine and 4-[3-chloro-4-(3-fluorobenzyloxy)anilino]-6-{3-[6-(4-amino)pyrimidinyl]amino)phenoxy}pyrimidine had the best biological activities in vitro. Docking simulation was performed to explore the binding model of these compounds with EGFR.

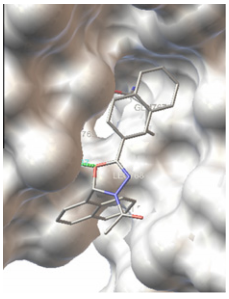


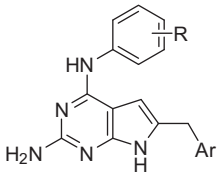


O-Alkyl carbamate derivatives of primaquine were shown to display potent transmission-blocking antimalarial activity.

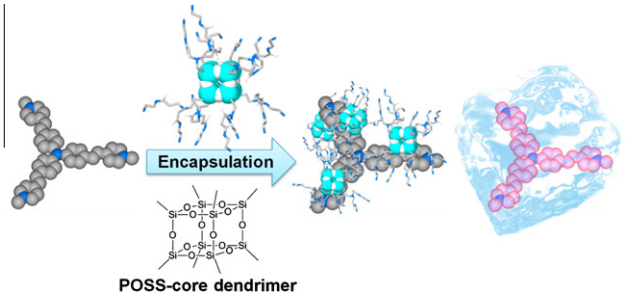


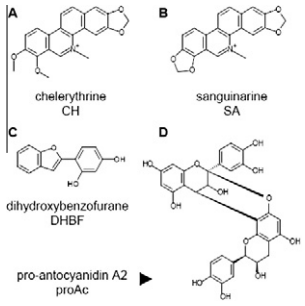
A new series of novel 1,3,4-oxadiazoline analogs (**6a**–**6t**) of combretastatin A-4 with naphthalene ring were designed, synthesized, and evaluated for biological activities as potential tubulin polymerization inhibitors. Among these compounds, **6n** showed the most potent antiproliferative activities against multiple cancer cell lines and retained the microtubule disrupting effects. Docking simulation was performed to insert compound **6n** into the crystal structure of tubulin to determine the probable binding model.

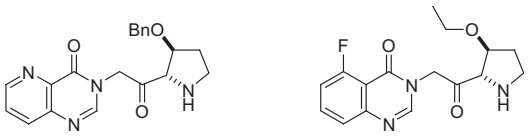


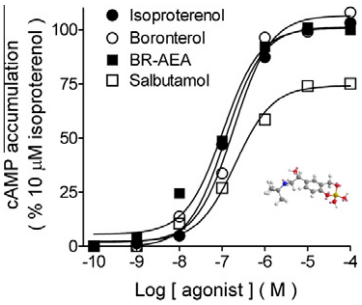


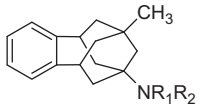
	R	Ar
8	4-Cl, 2-F	2-MePh
9	4-Cl	2-MePh
10	4-Cl, 2-F	2,3-C_4H_4Ph
11	4-Cl	2,3-C_4H_4Ph
12	4-Cl, 2-F	2,5-diOMePh
13	4-Cl	2,5-diOMePh

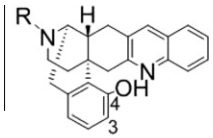








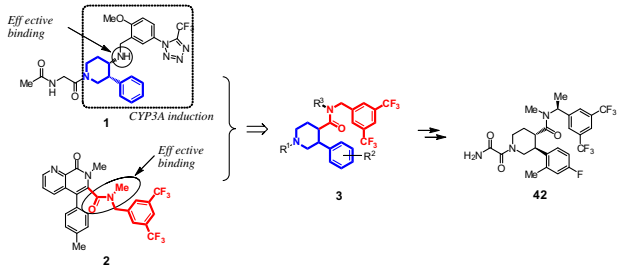


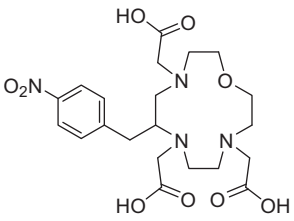


R = isobutyl: SN-24
R = methyl: SN-26
R = cyclopropylmethyl: SN-27

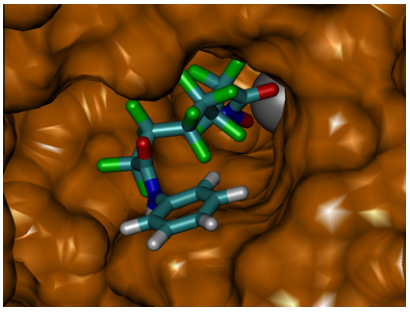
The morphinan derivatives with the 4-hydroxy group (SN-24, 26, 27) showed higher selectivities for the δ receptor over the μ receptor than the corresponding derivatives with the 3-hydroxy group. And they showed high agonist activities for the δ receptor in the [^{35}S]GTPγS binding assay.

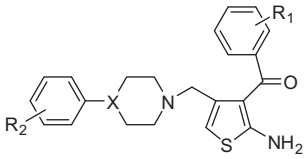
Hybridization of the substructures from two types of tachykinin NK_1 receptor antagonists **1** and **2** generated a novel series of 3-phenylpiperidine-4-carboxamide derivatives **3**. Compound **42** showed high metabolic stability and excellent efficacy in the guinea-pig GR-73637-induced locomotive activity assay at 1 and 24 h after oral administration, exhibited good pharmacokinetic profiles in four animal species, and a low potential in a pregnane X receptor induction assay.



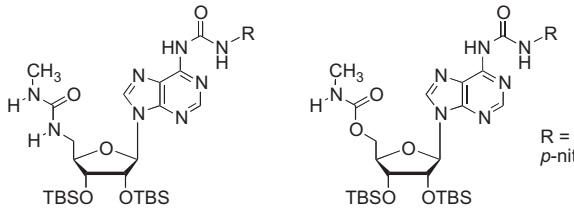


Facile synthetic procedure of the *C*-functionalized ODTA, and its basic study of the complex with ^{111}In are reported.

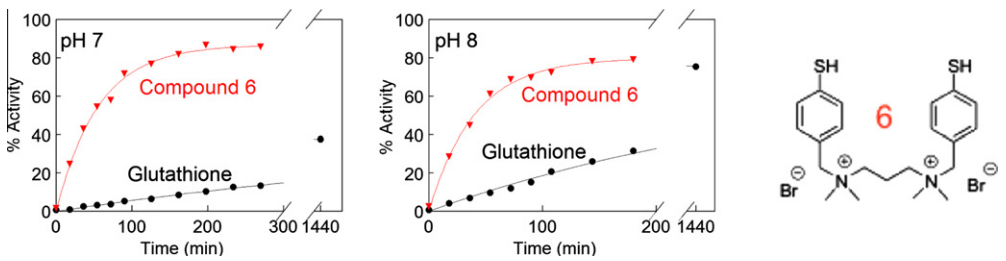


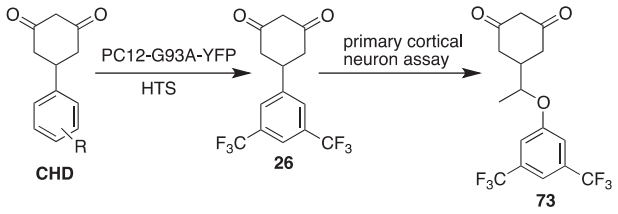


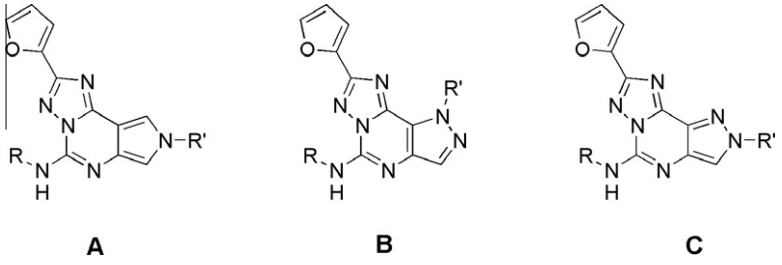
R_1=4-Cl or 3-CF_3
X=N or CH
R_2= one or two EWGs (Cl, F, CF_3 or NO_2)

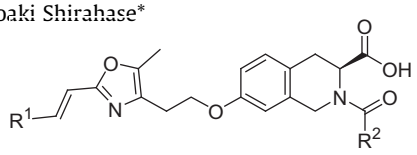


R = Phenyl, *p*-chlorophenyl, *p*-iodophenyl, *m*-iodophenyl, *p*-nitrophenyl, *p*-methoxyphenyl, benzyl, propyl, hexyl, cyclohexyl





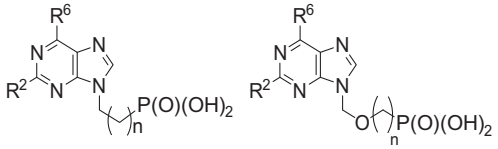




Compound **14i**:
R^1= $(CH_3)_2CHCH_2CH_2$-
R^2= CH_3CH=CH-CH=CH-

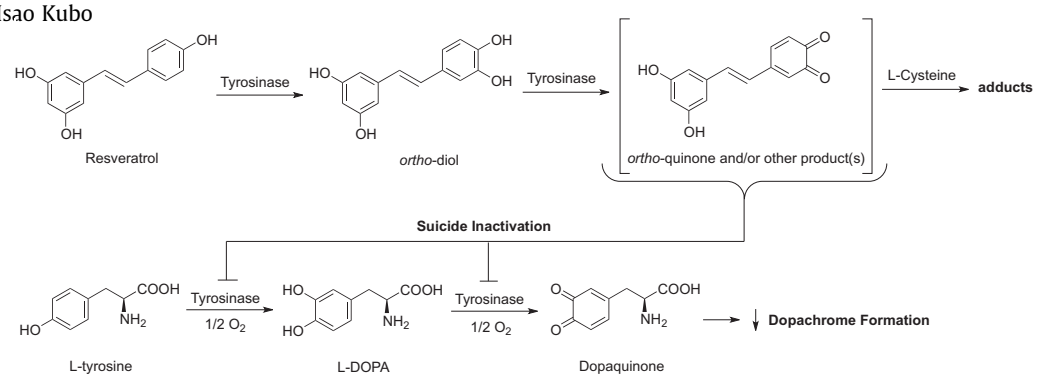
Compound	PPARγ	PTP-1B	Cmax (μM) (10 mg/kg, rats)
	EC_{50}(μM)	IC_{50}(μM)	
14i	0.03	1.18	4.5
Rosiglitazone	0.12	>30	34.7
Ertiprotafib	NT	0.41	NT

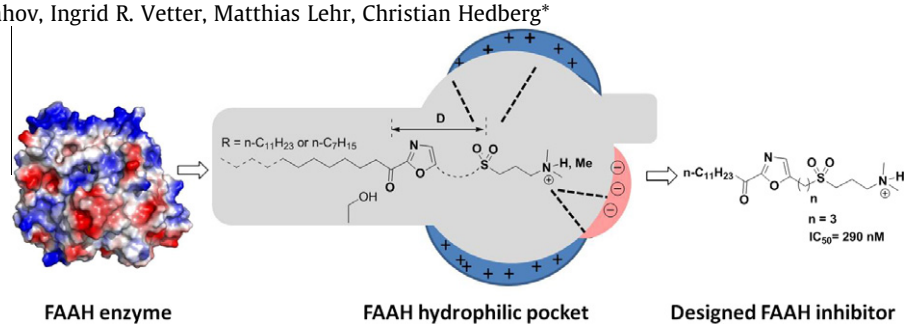
A novel series of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives were synthesized and **14i** was identified as a potent human PPARγ selective agonist and human PTP-1B inhibitor. Compound **14i** is a promising candidate for an efficacious and safe anti-diabetic drug targeting PPARγ and PTP-1B.



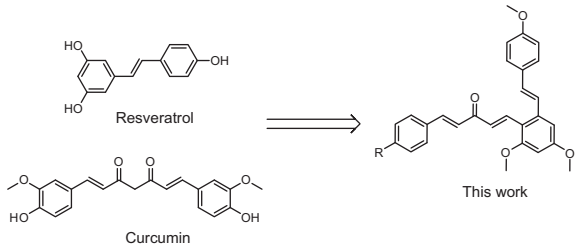
R^2 = H, NH_2, OH
R^6 = OH, Cl, Br
n = 0-6

R^2 = H, NH_2, OH
R^6 = OH, Cl
n = 2-4

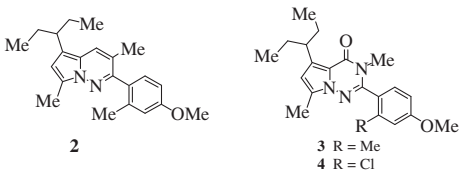


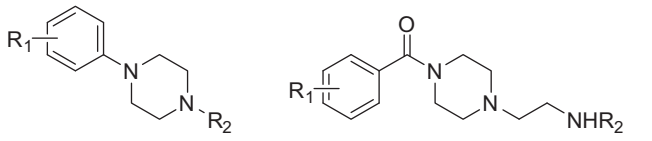


Design of α-keto oxazoles as fatty acid amide hydrolase (FAAH) inhibitors based on the electrostatic potential surface of the enzyme in its hydrophilic pocket.



A series of resveratrol derivatives possessing curcumin moiety were synthesized and evaluated for their antiproliferative and antitubulin activity. Docking simulation was performed to position compound **C5** into the colchicine binding site to determine the probable binding mode.





Arylpiperazine 4-Aminoethylpiperazinyl aryl ketone(**1**)

4-Aminoethylpiperazinyl aryl ketones were designed through homology modeling of 5-HT$_{1A}$R and 5-HT$_7$R, and synthesized compounds showed 5-HT$_{1A}$/5-HT$_7$ selectivity.

*Corresponding author
Supplementary data available via SciVerse ScienceDirect

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Chemical Proteomics (Herman S. Overkleeft, *Bioorg. Med. Chem.* **2012**, *20, 552*).

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