Discovery of 5-Benzyl-1,3,4-Oxadiazole/ Thiadiazole-2-Carboxamides as Potential Leads for Selective SIRT2 Inhibition

Mahmut Gozelle[1], Yesim Ozkan[2], Gokcen Eren[1]

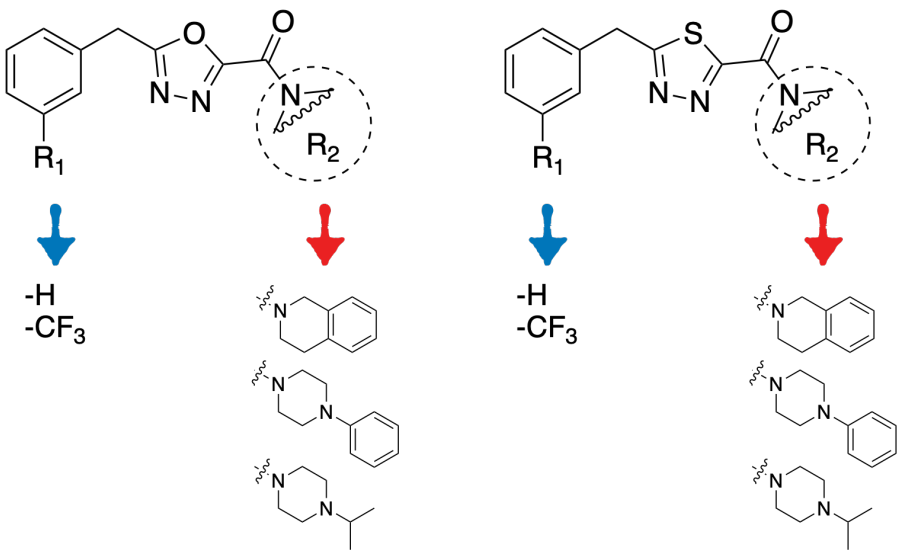
[1]SIRTeam Group, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Gazi University, Ankara, Turkey
[2]Department of Biochemistry, Faculty of Pharmacy, Gazi University, Ankara, Turkey

Introduction

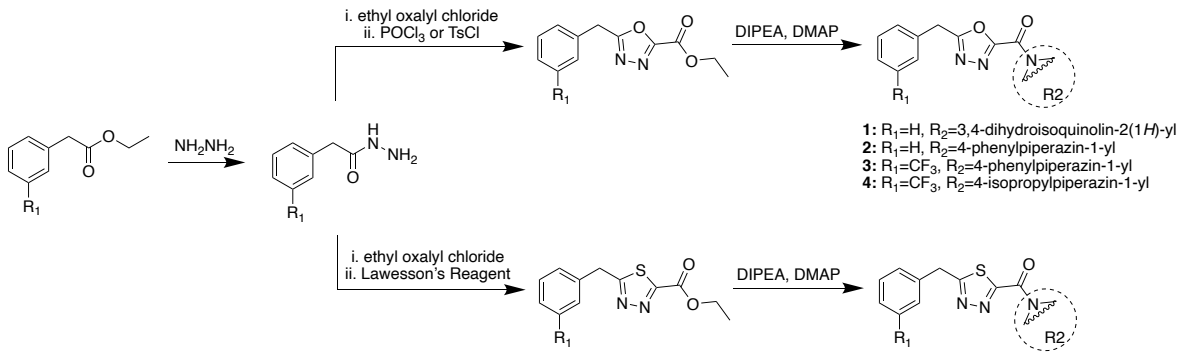
SIRT2 plays a significant role in cancer development since it affects several biological processes;

- Aging
- Gene transcription
- Inflammation
- Apoptosis
- Metabolism

Design



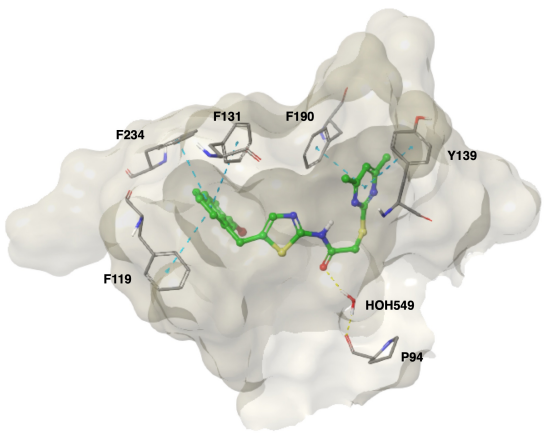
Synthesis



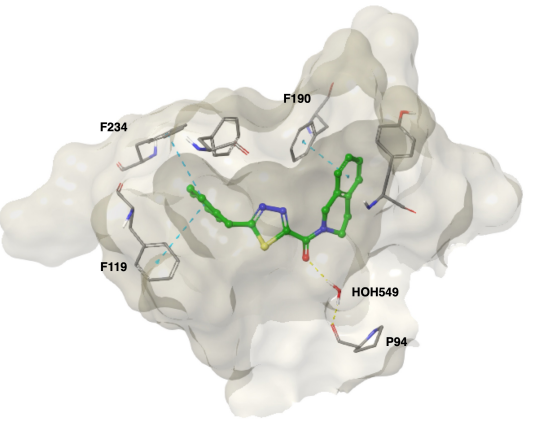
1: R_1=H, R_2=3,4-dihydroisoquinolin-2(1*H*)-yl
2: R_1=H, R_2=4-phenylpiperazin-1-yl
3: R_1=CF_3, R_2=4-phenylpiperazin-1-yl
4: R_1=CF_3, R_2=4-isopropylpiperazin-1-yl

5: R_1=H, R_2=3,4-dihydroisoquinolin-2(1*H*)-yl
6: R_1=H, R_2=4-phenylpiperazin-1-yl
7: R_1=CF_3, R_2=4-phenylpiperazin-1-yl
8: R_1=CF_3, R_2=4-isopropylpiperazin-1-yl

Molecular Docking

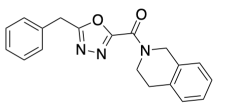
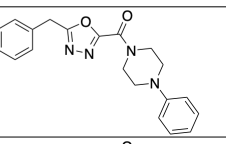
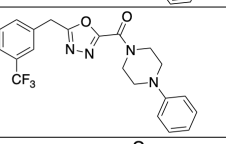
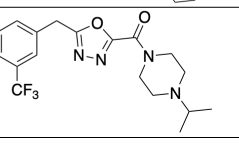
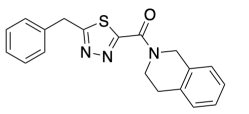
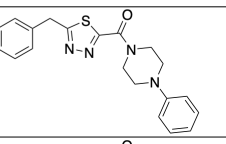
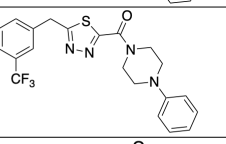
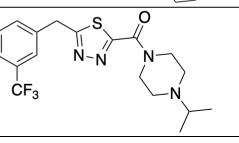


SirReal derivative
PDB: 5DY4



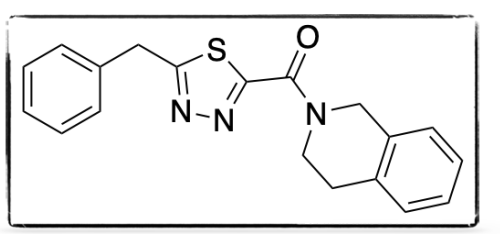
Compound **5**
PDB: 5DY4

Biological Data

ID	Compound	SIRT2 Inh(%) @ 100 µM
1		32.77±1.84
2		n.i.
3		34.98±0.96
4		19.28±0.78
5		76.92±1.85
6		n.i.
7		n.i.
8		23.68±1.05
Suramin		98.37±0.25

Conclusion

The results indicated that 5-benzyl-1,3,4-thiadiazole-2-carboxamides are promising lead compounds for selective SIRT2 inhibition.



IC_{50}= 38.69±0.80 µM

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