IMPORTANCE OF PIPERIDONE MOIETY IN PHARMACEUTICAL CHEMISTRY: A REVIEW

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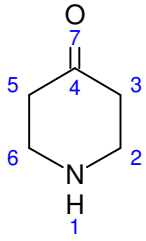
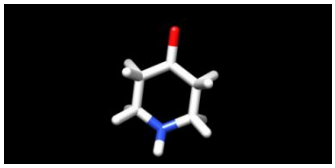
Piperidone heterocycle have gained a considerable attention in the field of drug discovery. The wide range of its therapeutic application paved the way to the researchers to insert the nucleus every now and then in diversified pharmacophore, so as to generate novel therapeutic profile. In this review, we have tried to present various therapeutic applications, which have already been demystified by the researchers. The study may prompt the researcher to generate scaffolds of highest therapeutic efficacy considering the importance of 4- Piperidone nucleus.

Keywords: Piperidone, Analgesic activity, Antidepressant activity, Antifungal activity and Antibacterial activity

INTRODUCTION

4-piperidone is a monocyclic compound with the molecular formula C_5H_9 NO. This heterocyclic amine consists of six member ring containing five methylene units and one nitrogen atom in adjacent position, at no 4th position carbonyl group present and to the unsubstituted parent compound.





Properties

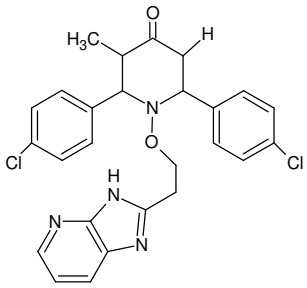
Molecular formula: C_5H_9 NO
Molar Mass: 99.13106 gm/mol

Many substituted piperidone derivatives are acknowledged to possess a wide range of bioactivities as antiviral, antitumor, anti inflammatory, central nervous system depressant, local anaesthetic, anticancer, antidiabetic and antimicrobials. In the foregoing section, we preferentially wanted to shape our study in a manner of target oriented development of piperidones

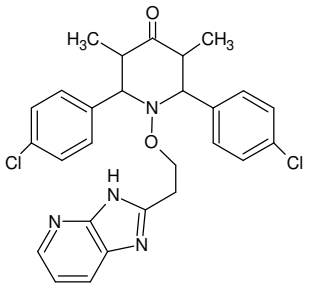
PIPERIDINE MOIETY AS ANTI MICROBIAL AGENTS:

Aridoss[8] *et al* designed, synthesized and evaluated a series of imidazo (4, 5- b) pyridinyl ethoxy piperidones derivatives, which showed good inhibitory activity against bacterial as well as fungal strains.

Among the two derivatives **1b** exerted strong *in vitro* antibacterial activity against *Bacillus subtilis* and *Staphylococcus aureus* whereas, compounds **1a** and **1b** displayed promising antifungal activity against *Aspergillus flavus*.

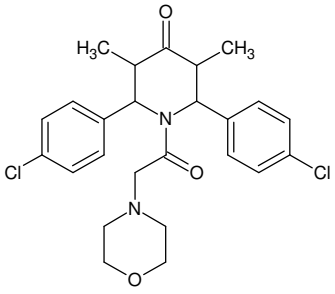


1a

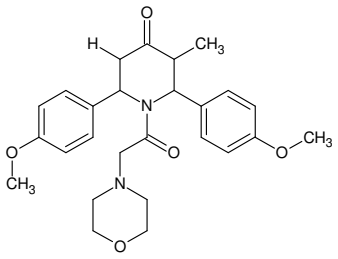


1b

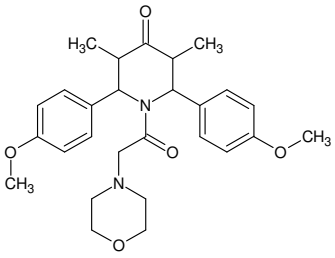
Aridoss[8] *et al* synthesized an array of novel N-morpholinoacetyl-2, 6-diarylpiperidin-4-ones (2) and evaluated there *in vitro* antibacterial and antifungal activity.



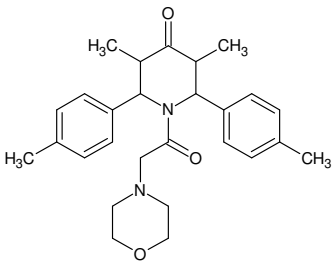
2a



2b



2c



2d

Among the four derivatives the compounds **c** and **d** exerted excellent antibacterial activity against all the bacterial strains

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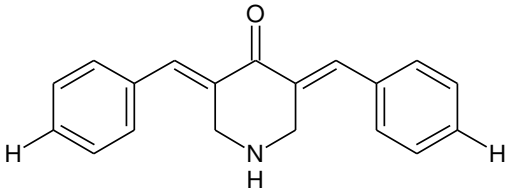
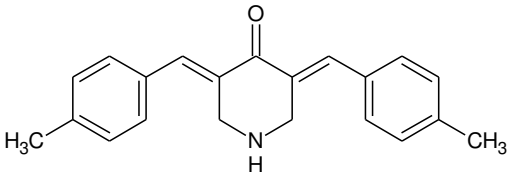
used except **d** against *S. aureus*. against *C. Albicans* and *A. flavus*, compound **a** recorded excellent antifungal activities, compound **b** showed potent activities.

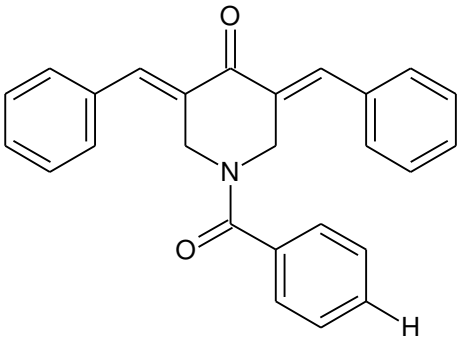
Das[9] *et al* designed, synthesized & evaluated the cytotoxic properties of some 1-[4-(2-alkylaminoethoxy)phenylcarbonyl]-3,5-bis(arylidene)-4-piperidones(3,4,5) and related compounds



3a



3b



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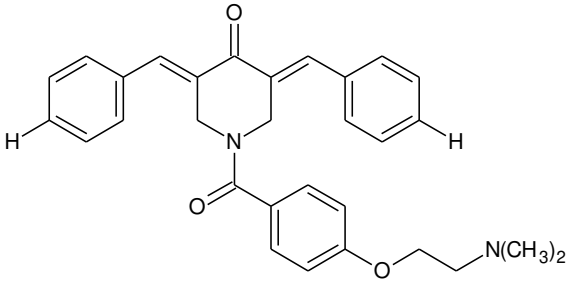
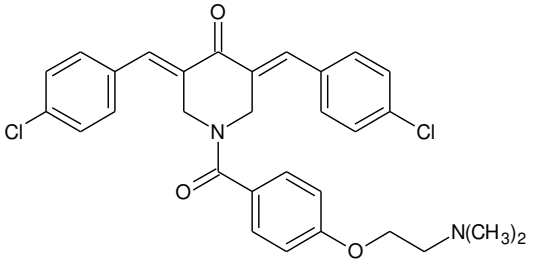
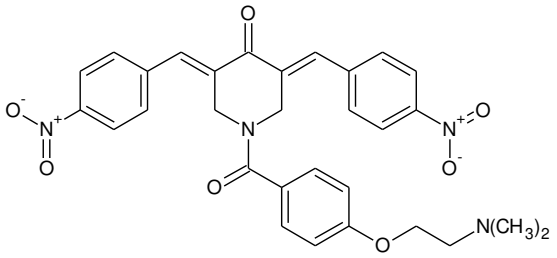


5a



5b



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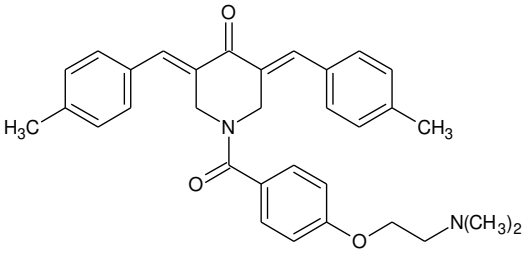
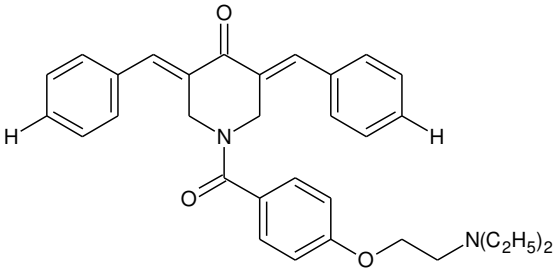
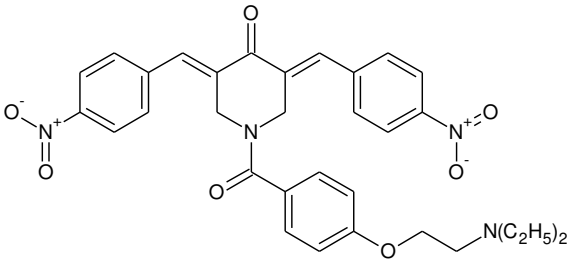


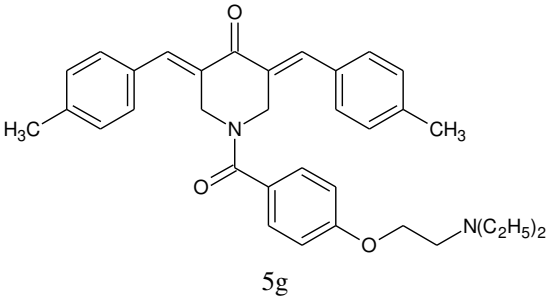
5d



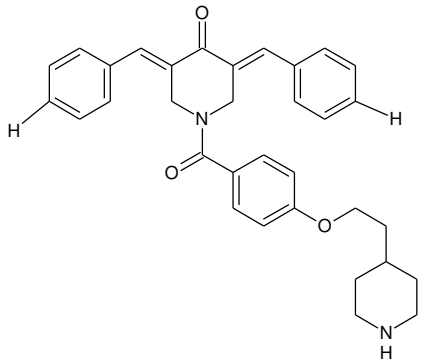
5e



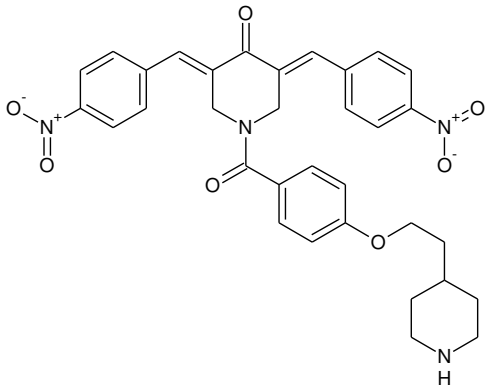
5f



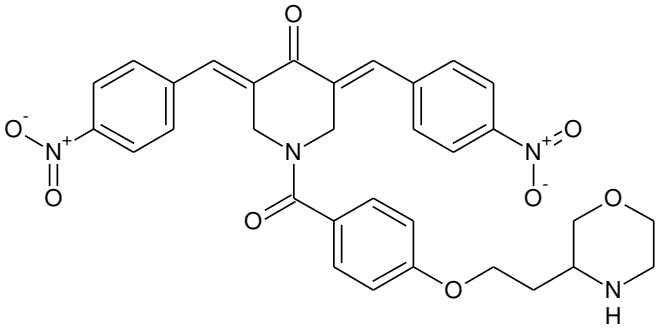
5g



5h



5i



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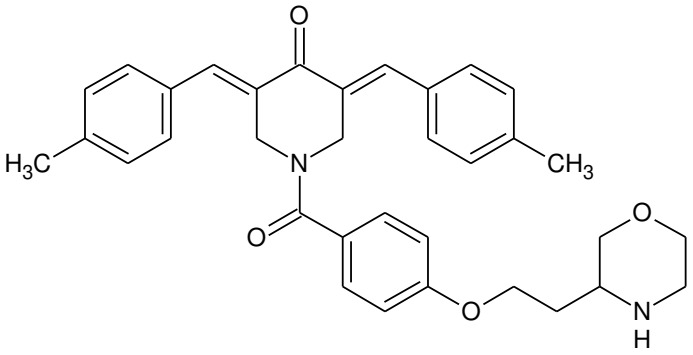

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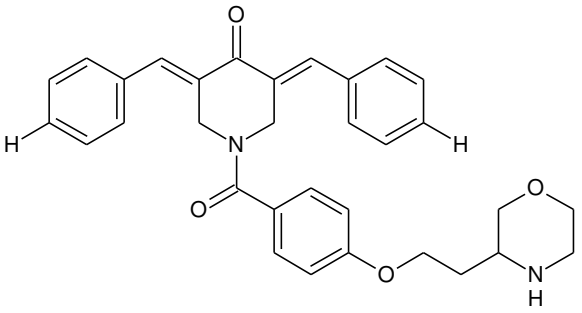
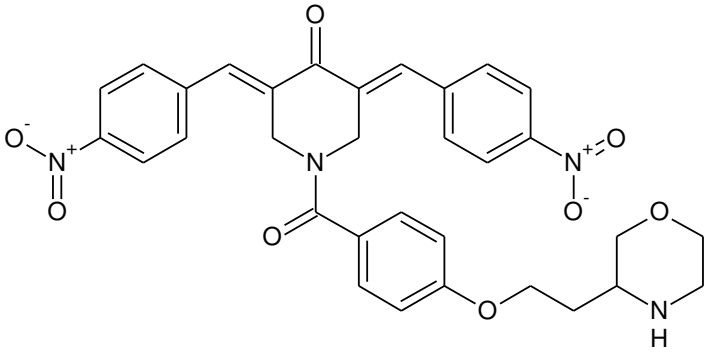


5l

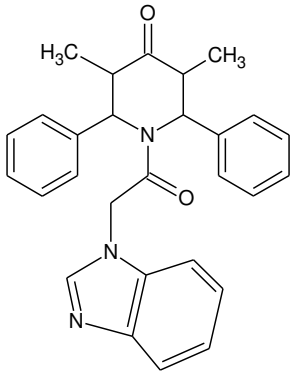


5m

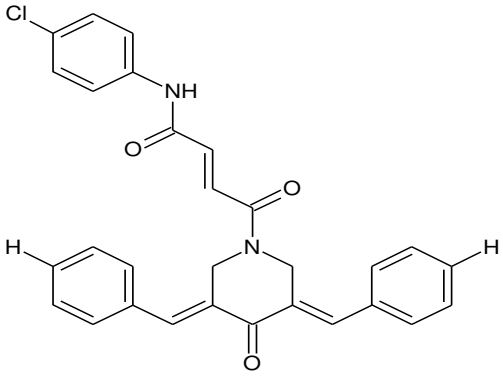
Compounds **3a**, **b**; **4a**; **5a**-**m** were more potent than melphalan. A comparison of the potencies between the compounds in series **3** and the related nonquaternary analogues of series **4** and **5** revealed that in approximately half of the comparisons made, compounds of **4** and **5** series had increased potencies.

Jha[19] *et al* synthesized a series of E, E, E-3, 5-bis (arylidene)-1-(4-arylamino-4-oxo-2-butenoyl)-4-piperidones (6) in order to explore the structural features of the N-acyl group which affects the cytotoxic potency.

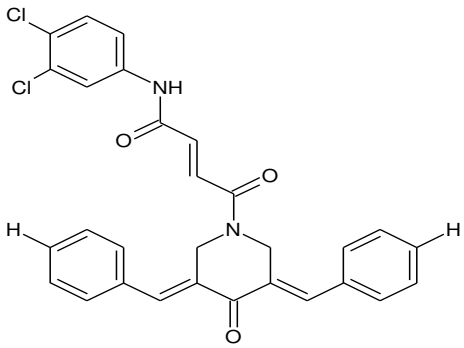
The raise in clinical significance of multidrug-resistant bacterial pathogens has directed, Aridoss[16] *et al* to synthesize 2, 6-diarylpiperidin-4-one and tetrahydropyridin-4-ol based benzimidazole and O-arylsulfonyl derivatives (7, 8).



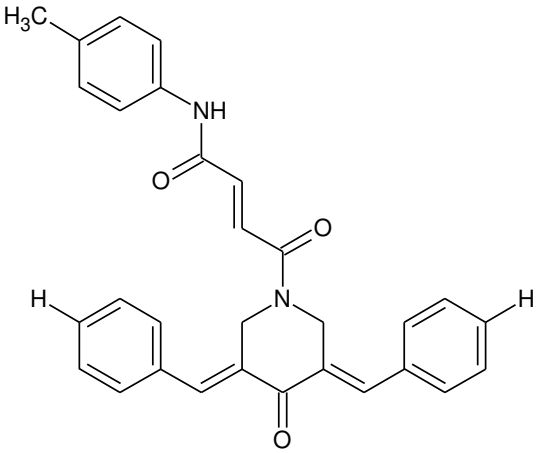
7



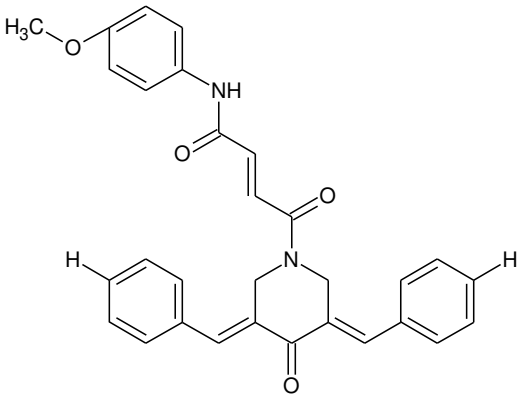
6a



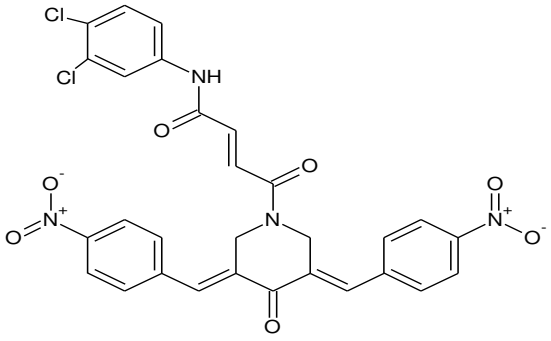
6b



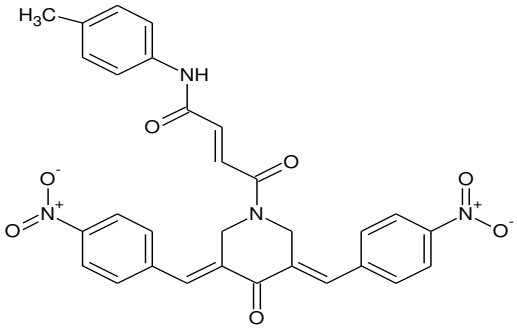
6c



6d



6e



6f

Antibacterial activities have been evaluated against a wide range of bacterial pathogens (both sensitive and multidrug-resistant) revealed that **7a, 8c** against *Staphylococcus aureus*, **8c** against *Enterococcus faecalis*, and **7a, 7b, 8a,** and **8c** against *Enterococcus faecium* are significantly good at lowest MIC (16 µg/ml). Inhibitory power noticed by **8a** against Vancomycin–Linezolid- resistant *E. faecalis* and **8c** against Vancomycin-resistant *E. faecium* are onefold better than the standard Linezolid and Trovafloxacin drugs, respectively. Moreover, antitubercular activity for the selected compounds against *Mycobacterium tuberculosis* H37Rv revealed that compounds **8a, b, c** expressed one fold improved potency compared to the standard Rifampicin drug.

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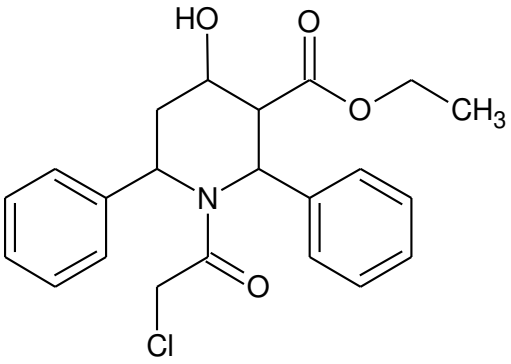
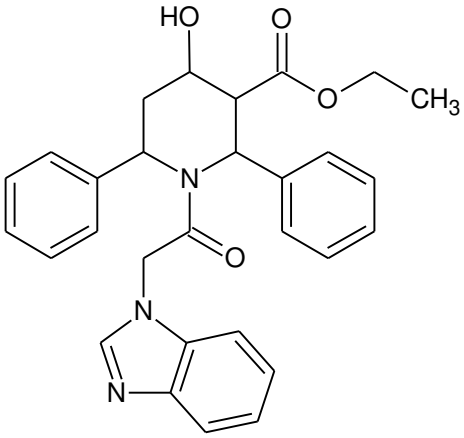
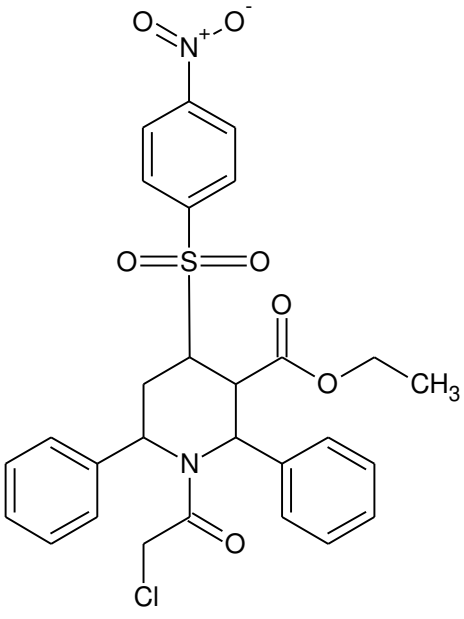


8a

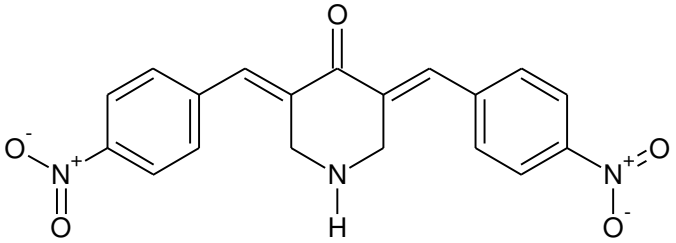


8b

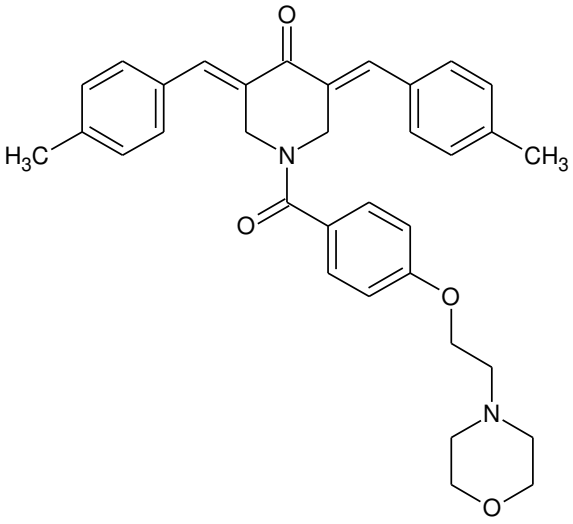


8c

Das[18] *et al* synthesized a number of 3, 5-bis (benzylidene)-4-piperidones and some N-4-(2-aminoethoxy) phenylcarbonyl analogs (9) which display excellent *in vitro* antimycobacterial properties. In particular, **9a** and **9b** are potent antimycobacterials which are well tolerated in mice and are identified as important lead molecules. The nature of both the benzylidene aryl rings and the terminal basic groups which affect the antimycobacterial potencies and the absence of neurotoxic side effects were identified.



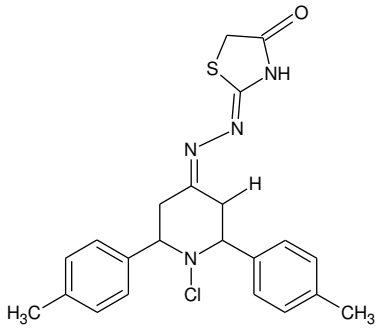
9a



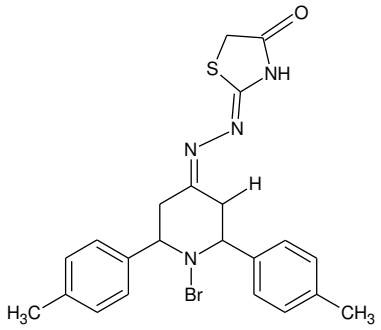
9b

Aridoss[17] et al have a stereo specifically synthesized a series of thiazolidiones and thiazoles based on 3-alkyl-2, 6-diarylpiperidin-4-ones.

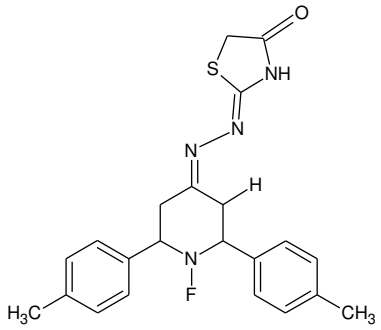
Compounds **10a, b, d, f, g** and **h** exhibited twofold enhanced potency than Rifampicin, a antimycobacterial as well as, compounds **10c** and **10e** have exceptionally promising antimicrobial activities and particularly, **10c** against *Staphylococcus aureus* and, **10d** and **10h** against *Rhizopus* sp. exhibited one fold elevated inhibition potency whereas **10c** against *Klebsiella pneumoniae* showed twofold improved potency than Ciprofloxacin and Amphotericin B.



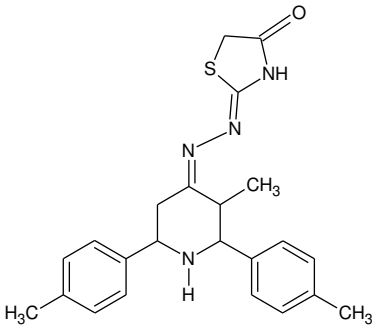
10a



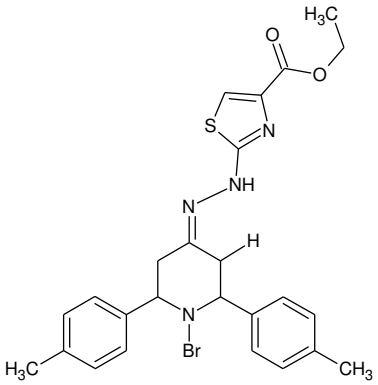
10b



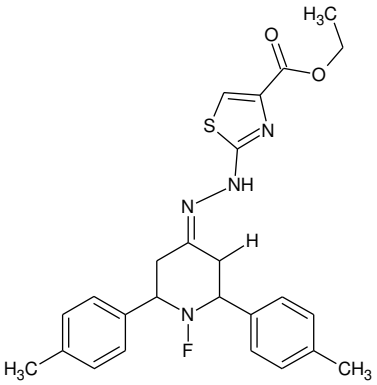
10c



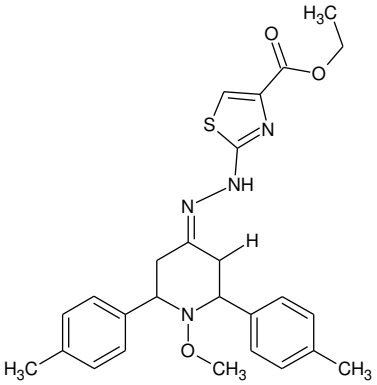
10d



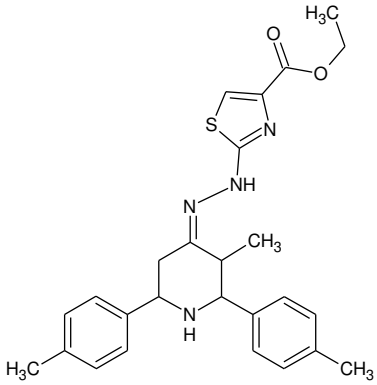
10e



10f



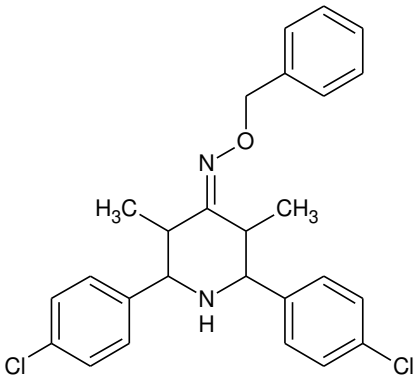
10g



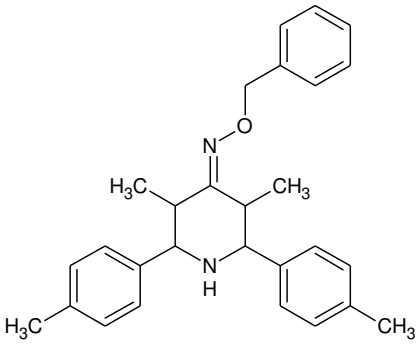
10h

Parthiban[20] *et al* synthesized three series of oxime ethers viz, 2, 6-diarylpiperidin-4-one O-benzyloximes, 2, 6-diaryltetrahydropyran- 4-one O-benzyloximes and 2, 6-diaryltetrahydrothiopyran-4-one O-benzyloximes (11) and stereochemistry were established by their spectral and single crystal analysis. A SAR study had carried out for the above oxime ethers against a panel of antibacterial and antifungal agents respectively, using Ciprofloxacin and Amphotericin B as standards.

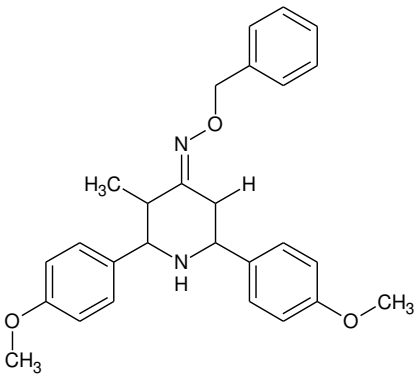
Most of the chloro/methyl/ methoxy substituted compounds exerted moderate to good activity against all the tested organisms; moreover, some compounds **11**(**a, b, c, d, e, f, g, h** and **i**) exhibited promising activity than standard drugs.



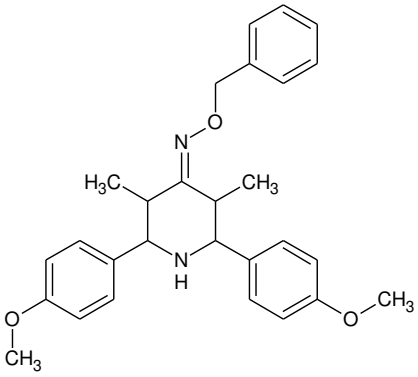
11a



11b



11c



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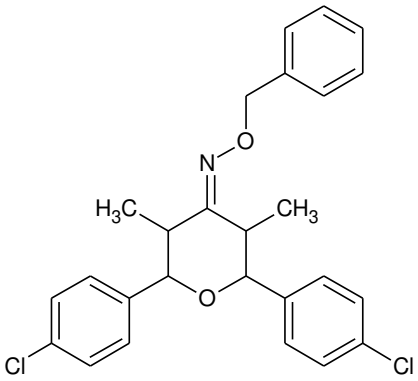

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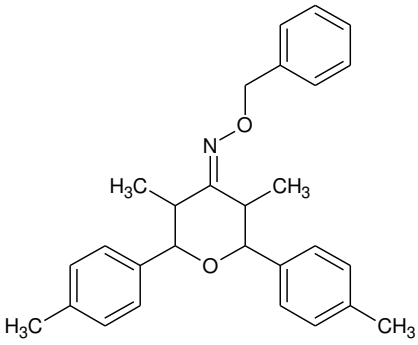

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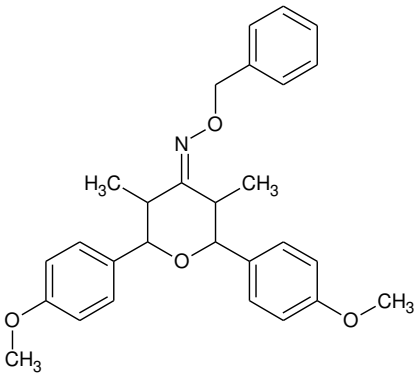

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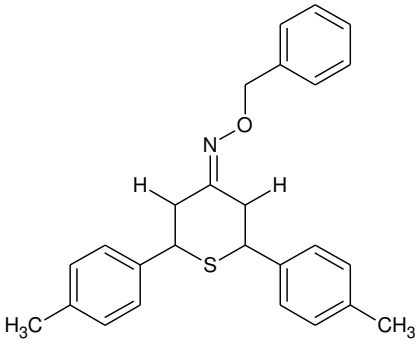

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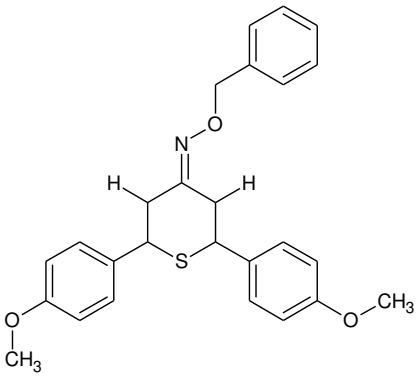

11i

CONCLUSION

The above studies clearly mention the potentiality of piperidone moiety accompanied with other molecular fragments in ameliorating various disease conditions. Owing to its accessibility to various important biogenic residues, it has been included in many xenobiotics. The synthetic feasibility and suitable insertion into many other structural frameworks will surely prompt the researchers to synthesise a huge number of compounds considering piperidone as an effective scaffold, which may demystify various unexplored pathogenic target.

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