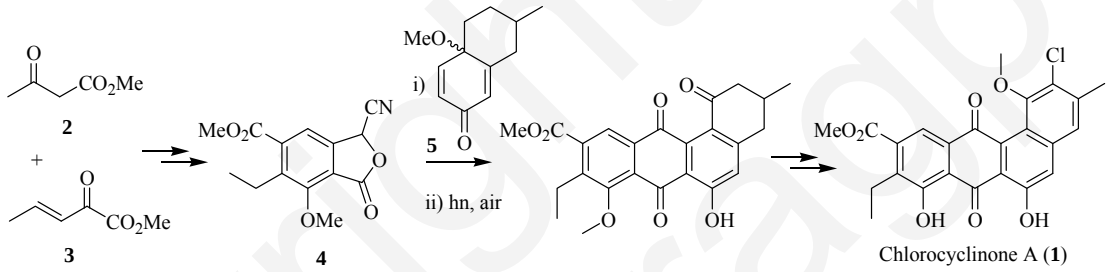
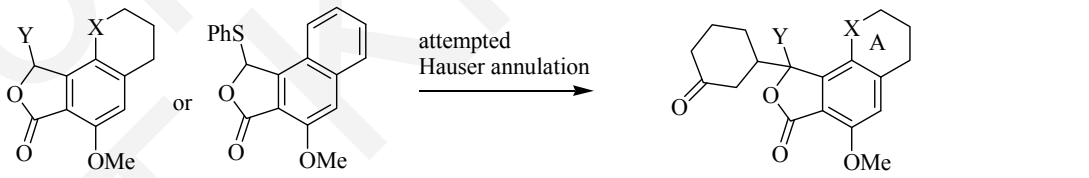
The thesis titled "**Total synthesis of chlorocyclinone A, the first PPAR-gamma antagonist of natural origin; unfolding of Prins reaction, and synthesis of pestacin methyl ethers**" describes total synthesis of chlorocyclinone A, a member of chlorinated angucyclinone natural products. It also illustrates the finding of a new diastereoselective Prins reaction of α-tetralone dimers. Development of synthetic routes to methyl ethers of pestacin, featuring a 1,3-dihydroisobenzofuran moiety is also recorded.

The total synthesis of chlorocyclinone A (**1**) has been achieved in 28 steps in regioselective manner from commercially available starting materials (**2-3**). The key steps are Pd(II)-catalyzed methoxycarbonylation, Hauser annulation between **4** and **5**, Krohn photo-oxidation and regioselective *gem*-dichlorination.



For the model study on the total synthesis of chlorocyclinone A (**1**), model angular phthalides (**6-10**) were synthesized to validate the Hauser annulations methodology. Their reactions with Michael acceptors, however, have been shown to give only 1,4-addition products (**11a-d**).

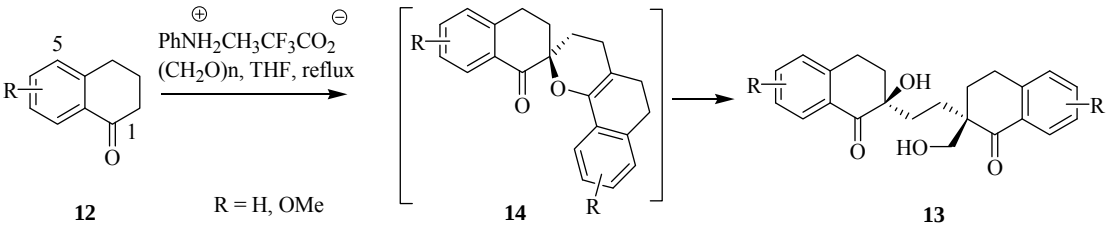


6: X = C=O, Y = SPh
7: X = CH_2, Y = SPh,
8: X = CH_2, Y = SO_2Ph
9: X = CH_2, Y = CN

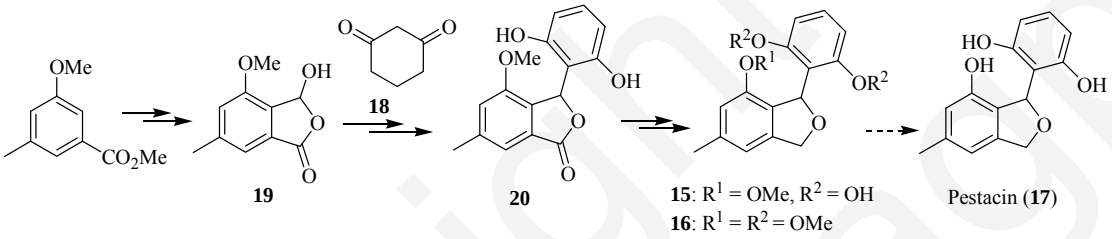
10

11a: X = CH_2, Y = SPh
11b: X = CH_2, Y = SO_2Ph
11c: X = CH_2, Y = CN
11d: X = CH, Y = SPh, A-ring = aromatic

In course of methylenation of tetralone **12**, compound **13** was unexpectedly encountered. The formation of **13** has been studied in detail and established to arise from the Prins reaction of the dimers **14**.



The synthesis of methyl ethers **15** and **16** of pestacin (**17**) has been accomplished in few steps from acetone and diethyl oxalate. The key steps are cyclocondensation of cyclohexane-1,3-dione **18** with a phthalaldehydic acid (**19**), and subsequent aromatization to **20**.



Key Words: Angucyclinones, Hauser annulation, Methoxycarbonylation, *Gem*-dichlorination, Prins reaction, Phthalans, Cycloetherification, Total synthesis.