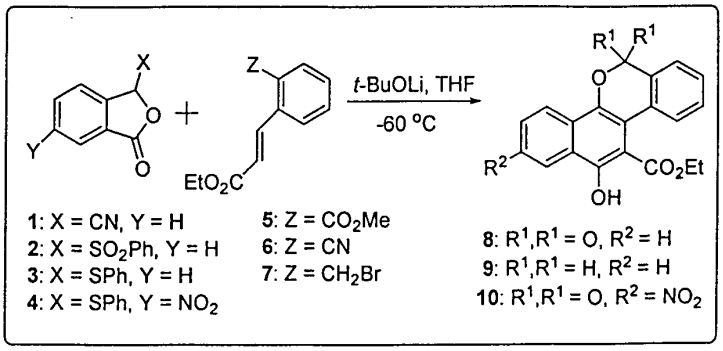
Abstract

This thesis describes the model synthetic studies of aromatic polyketides containing **benzonaphthopyranones, arylnaphthoquinones, quinonoids** and **benzofluorenones** skeletons, and related naturally occurring antibiotics **chartreusins, chrymutasins, hayumicins, gilvocarcins, WS-5995 A, B, C** and **kinamycins.**

The Hauser-Kraus annulation has been demonstrated to be effective for double annulation. The reaction between isobenzofuranones (**1**, **2**, **3** and **4**) and cinnamate derivatives (**5**, **6** and **7**) with an *ortho* appendage in the presence of *t*-BuOLi in THF at –60 °C gave in one pot, benzonaphthopyranes e.g., **8**, **9** and **10** through double annulation. In all the cases studied, the annulated products have been obtained in excellent yields.



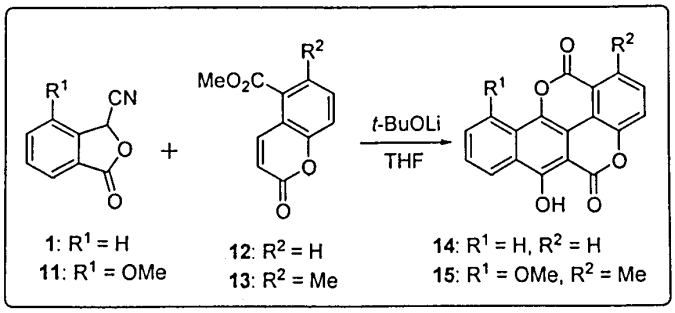
1: X = CN, Y = H
2: X = SO_2Ph, Y = H
3: X = SPh, Y = H
4: X = SPh, Y = NO_2

5: Z = CO_2Me
6: Z = CN
7: Z = CH_2Br

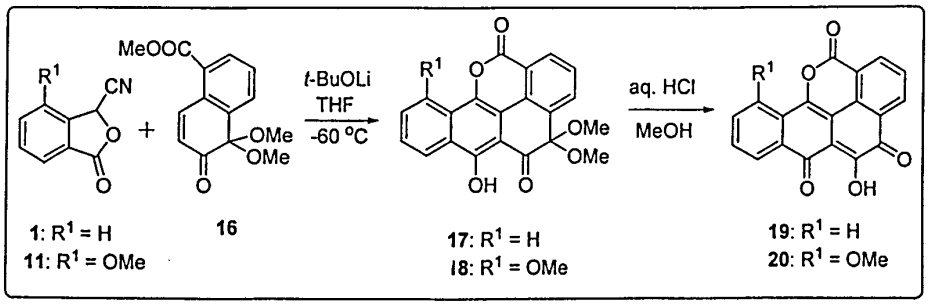
8: R^1,R^1 = O, R^2 = H
9: R^1,R^1 = H, R^2 = H
10: R^1,R^1 = O, R^2 = NO_2

The double annulation route has culminated in a shorter total synthesis of chartreusin aglycon and the synthesis of several chartarin analogs. Thus, 5-substituted coumarin derivatives **12** and **13** underwent double annulation with isobenzofuranones

1 and **11** respectively in the presence of *t*-BuOLi in THF at –60 °C to give benzo[*h*]chromeno[5,4,3-*cde*]chromene-5,12-diones **14** and **15**.

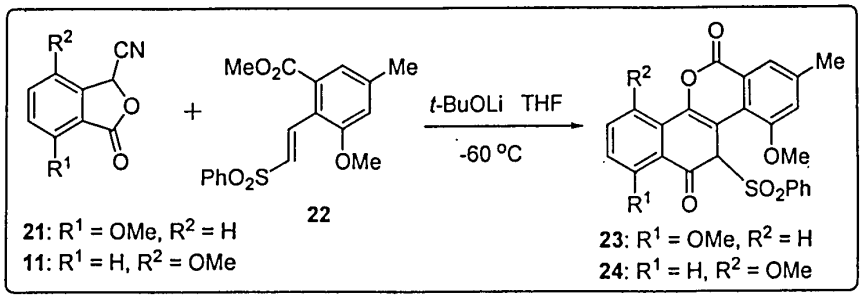


This methodology has been extended to the synthesis of chrymutasin and hayumicin scaffolds. Methyl 5,5-dimethoxy-6-oxo-5,6-dihydronaphthalene-1-carboxylate (**16**) underwent double annulation with cyanophthalides **1** and **11** in the presence of *t*-BuOLi in THF at –60 °C to give pentacyclic quinone monoketal compounds **17** and **18** respectively in high yields. Acid promoted deketalisation of the annulated products provided pentacyclic compounds **19** and **20**, the chromophoric structure of chrymutasin aglycon.

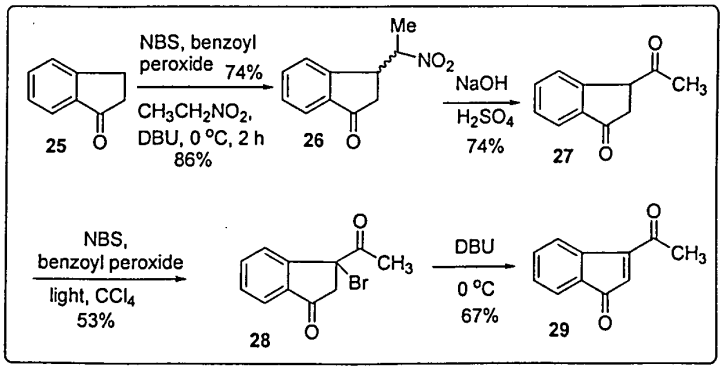


The methodology has also been applied to the synthesis of defucogilvocarcins and WS-5995 A, B, C antibiotics. Vinyl sulfone and styryl sulfones have been shown

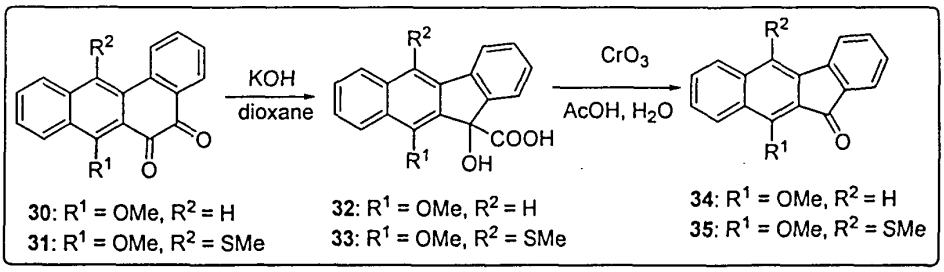
to undergo annulation with isobenzofuranones in the presence of *t*-BuOLi in THF at -60 °C to furnish benzo[*d*]naphtho[1,2-*b*]pyran-6-ones in excellent yields (5 examples). Compound **23** on desulfonylation gave the complete core structure of gilvocarcin chromophore.



In a study directed towards total synthesis of isoprekinamycin, we have synthesized several functionalized 3-substituted indanone derivatives from indanone in good yields. The synthesis of unstable 3-acetylindenone (**29**) required as key reactions: DBU-catalyzed Michael addition of nitroethane, Nef reaction, benzylic bromination with NBS and dehydrohalogenation. The instability of **29** thwarted the progress towards the synthesis of isoprekinamycin.



Benzo[*a*]anthracene-5,6-dione derivatives **30** and **31** have been prepared in regiospecific manner by annulation between appropriate 1,4-dipolar synthons and quinone monoketal. They have been shown to undergo benzil-benzilic acid rearrangement in the presence of KOH to provide benzo[*b*]fluorenone carboxylic acids **32** and **33** respectively, which on oxidative decarboxylation gave benzo[*b*]fluorenones **34** and **35**, representing the skeleton structure of prekinamycin antibiotic.



30: R^1 = OMe, R^2 = H
31: R^1 = OMe, R^2 = SMe

32: R^1 = OMe, R^2 = H
33: R^1 = OMe, R^2 = SMe

34: R^1 = OMe, R^2 = H
35: R^1 = OMe, R^2 = SMe