FINALREPORT OF THE WORK DONE

IN THE

Major Research Project

Entitled

Synthetic Studies in Terpenoids and Development of Green Synthetic Methodologies

[F. 43 - 221/2014 (SR)]

[Nov. 2015 to June 2018]

Principal Investigator

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OBJECTIVES OF THE PROJECT

The project aims towards the development of ecobenign protocols for the synthesis of molecules of biological importance using inexpensive catalysts to fulfil the demands of green chemistry like atom economy, avoidance of solvent, non-formation of toxic waste, etc. Although the development of totally green methodologies meeting to these requirements is a hypothetical situation for every targeted synthesis / transformation, we wish to direct our efforts to meet with most of the principles of Green Chemistry in a hope that, though small but significant contribution in this context will help in making the stay of human beings comfortable on this planet.

The project also aims at the utilization of the developed methodologies towards the synthesis of a few simple natural products. Synthesis of molecules of biological importance using inexpensive catalysts and in fulfilment of the demands of green chemistry was our basic objective. We started our work on the development of a protocol for the oxidation of sulfides to sulfoxides and sulfones. After that, the synthesized sulfone viz. phenylsulfonyl acetonitrile was used in the synthesis of medicinally prevalent 2-amino-4H-chromenes. As an extension of this work we carried out the synthesis of spirochromenes by three component reaction between isatins, phenylsulfonyl acetonitrile and N-methylquinolone. Based upon the mechanism of the reaction we also developed a protocol for the synthesis of hexahydroxanthenes, bis-coumarins and bis-tetronic acids. In addition we also developed a protocol for the synthesis of easily non-accessible pyridine-3,5-dicarbonitriles.

In addition to this we also accomplished the synthesis of a sesquiterpenoids viz. Solafuranone employing radical cyclization method.

REPORT OF THE WORK DONE
(From: 16 Nov. 2015 to 31 June 2018)

The project was sanctioned to work in two different areas *viz.* ***Synthetic studies in terpenoids and development of green synthetic methodologies***. The progress of the work done in both the areas is summarized below.

SECTION – A
SYNTHETIC STUDIES IN TERPENOIDS

Terpenoids constitutes largest part of naturally occurring compounds and many of them exhibit potential biological activity. Hence, after an adequate literature survey, a few naturally occurring terpenoids were selected for the synthesis. These were Solafuranone, **1A** it's isomer, **1B,** 1-oxo-9-desoxycacalol, **1C,** and Bakuchiol, **1D (Fig. 1).**

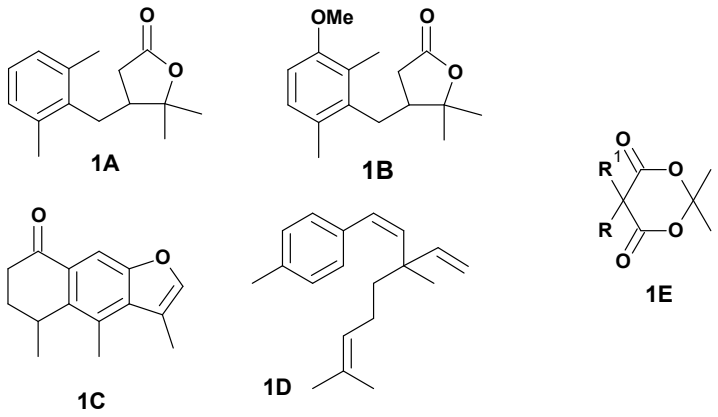
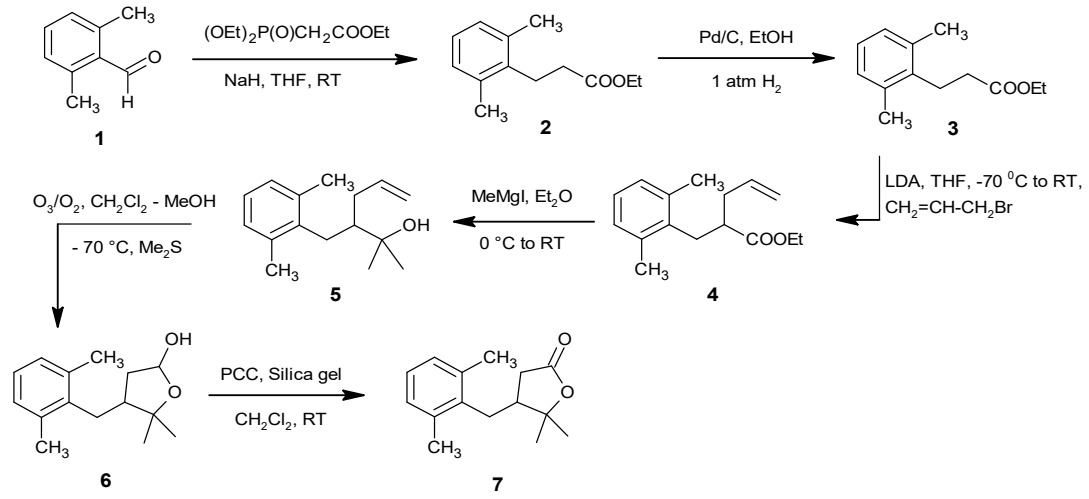


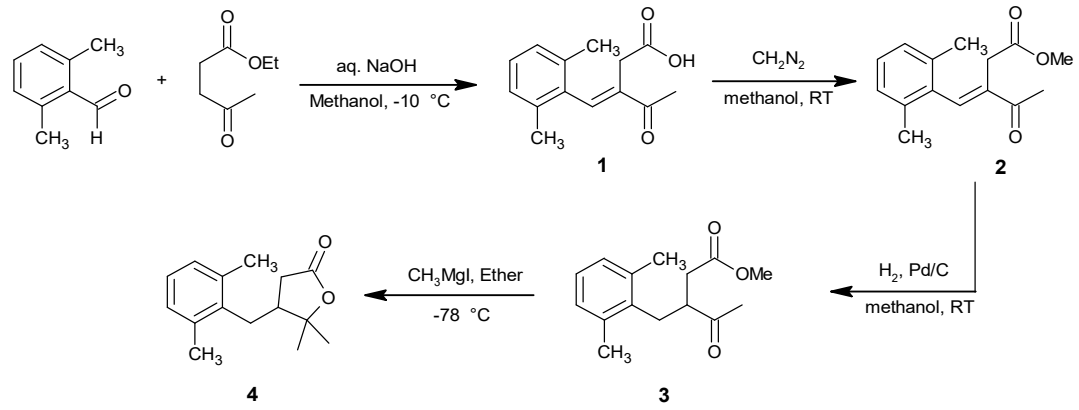
Fig. 1. Structures of few sesquiterpenoids selected for the synthesis

Solafuranone, **1A**, along with it's structural isomer, **1B,** are the naturally occurringsesquiterpenoids isolated from Chinese folk medicine. Amongst these two terpenoids, **s**ynthesis of Solafuranone **(Fig. 1A)**, has been reported earlier by Srikrishna*et. al.***(Scheme A)**and Mahajan*et. al.* [1, 2]**(Scheme B).** Both the reported synthesis are bit complicated and not green. Based upon our earlier studies on the synthesis of mixed dialkylated Meldrum's acid **(Fig. 1E)**, we surmised that, synthesis of Solafuranone can be executed by much simpler and green route **(Scheme 1).** We are indeed happy to disclose that, we have recently completed the synthesis of Solafuranone, **1A (Scheme C),** and we have also accomplished the synthesis of ofit's isomer **(Fig. 1B)**employing another route **(Scheme 1B)**.

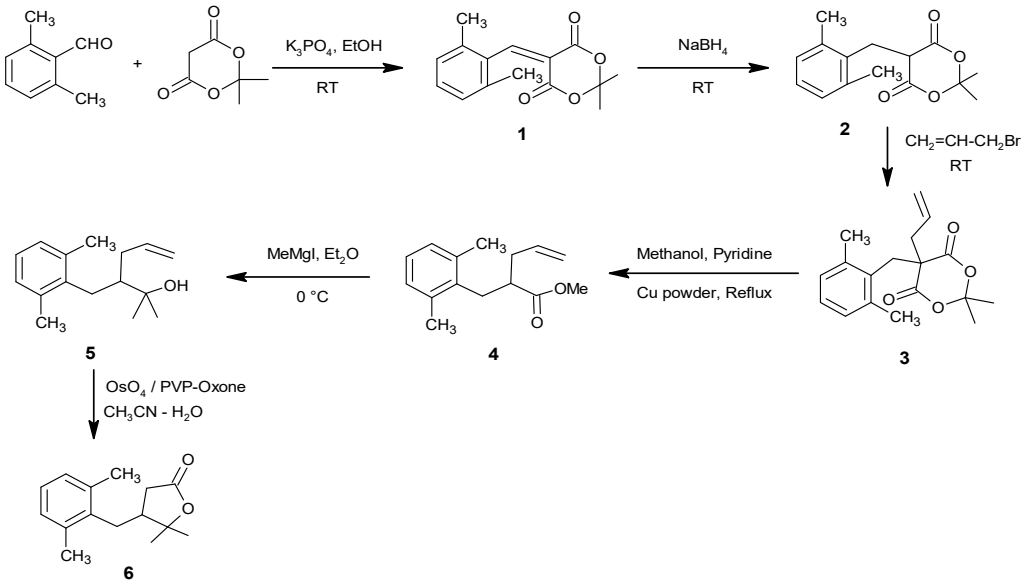
Scheme A. Srikrishna's approach for the synthesis of solafuranone



Scheme B. Mahajan's approach for the synthesis of Solafuranone

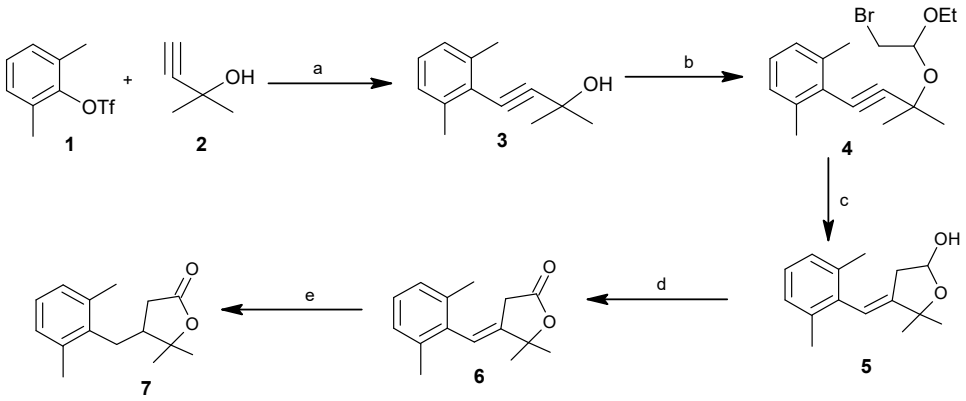


In our laboratory, we have developed earlier very simple protocol for the synthesis of Solafuranone, **2**. Strategically it is very much similar to that described by Srikrishna*et al.* The main difference in the approach developed by us and that described by Srikrishna*et al.* involves the preparation of ester, **4, (Scheme 2).** In our approach the samehas been prepared by ring opening of mix-dialkylated Meldrum's acid, which itself was prepared by sequential, one-pot procedure **(Scheme3).**[7]



Scheme C: Desai's approach for three step, sequential, one pot synthesis of mixed dialkylated Meldrum's acid

Another approach for synthesis of Solafuranone has been developed in which starting material is 2,6 dimethyl phenol which is inexpensive and commercially available. The scheme for the same explained as below.



Scheme 1A. Synthesis of Solafuranone**1B**

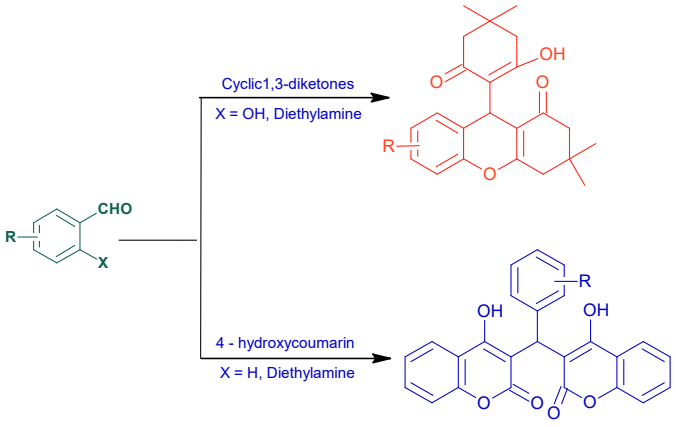
SECTION – B

DEVELOPMENT OF GREEN SYNTHETIC METHODOLOGIES

Part - I: Green synthesis of 1-oxo-hexahydroxanthenes and bis-coumarins

The main issue in the synthesis of complex organic molecules is currently aimed at improvement of efficiency, avoidance of toxic reagents, reduction in waste and responsible utilization of natural sources. In this context, use of Domino reactions is of relevance both, from economical and ecological point of view. Amongst these, Knoevenagel – Michael domino reactions have emerged asa powerful strategy in the synthesis of various oxa- as well as aza- heterocycles.

In recent years, construction of xanthenes scaffold has attracted much attention of organic chemists due to their importance in the field of medicine as well as material science. Two important class of compounds containing xanthene structural motif are 1,8-octahydroxanthenes and 1-oxo-hexahydroxanthenes. Amongst these 1-oxo-hexa-hydroxanthenes are of particular interest to synthetic organic chemists due to their important pharmacological properties such as, anti-estrogenic, anti-bacterial, anti-microbial as well as hypoglycemic activities. They also exhibit thrombin-inhibitory activity and serve as neuropeptide YY5 receptor antagonist. Alike 1-oxo-hexahydroxanthenes, bis - coumarins are also known to exhibit important biological activities like, urease inhibitor, anti-coagulant as well as snake venom inhibitor activity. There are several reports on the synthesis of 1-oxo-hexahydroxanthenes as well as bis – coumarins. However, the mechanistic details of their synthesis have not been explored fully. Based upon the mechanism of the reaction, we have developed diethylaminecatalyzed protocol for the synthesis of 1-oxo-hexahydroxanthenes as well as bis-coumarins. Perhaps this is the simplest and most green protocol developed for the synthesis of 1-oxo-hexahydroxanthenes as well as bis - coumarins target molecules **(Scheme 2).**



Scheme 2. Diethylaminecatalyzed synthesis of 1-oxo-hexahydroxanthenes and bis - coumarins

Published in "Res. Chem. Intermed. 2016, 42, 6313 – 6319"

Part - II: ***Sulfamic acid catalyzed eco-benign synthesis of bis-coumarins and bis-tetronic acids***

Knoevenagel-Michael domino reactions have emerged as a very powerful strategy in the synthesis of heterocycles as well as structurally diverse organic compounds having promising synthetic as well as biological potential.Tetraketones, bis-indolylalkanes, bis-uracils, bis-Meldrum's acid, bis-pyrazoles and, bis-coumarins are a few such heterocycles with important biological properties **(Fig. 2).** These compounds could be prepared by using either acid or base catalyst.

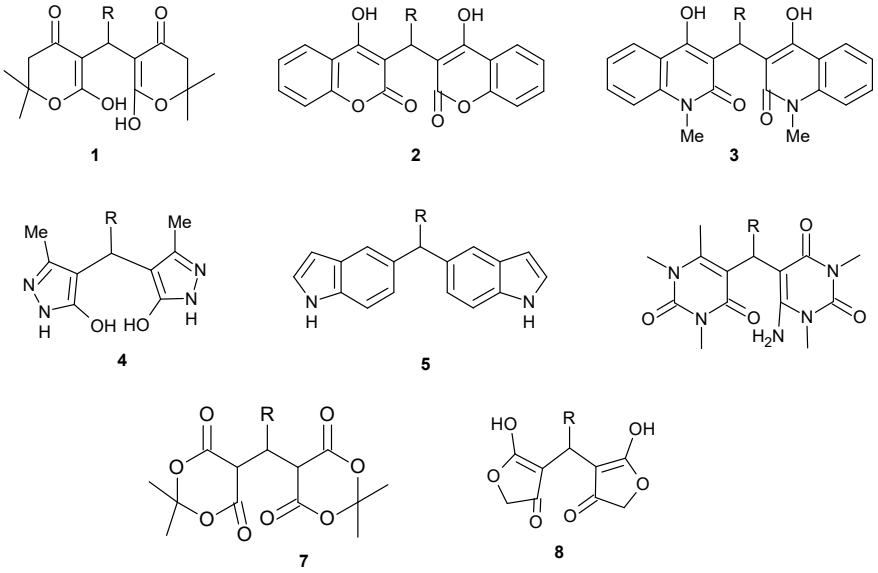
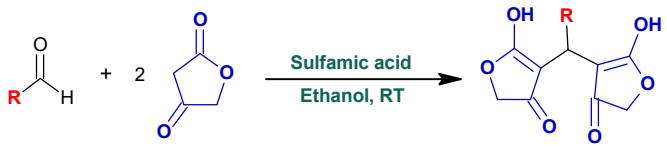


Fig. 1. Structures of few bioactive molecules resulting through Domino reaction

Encouraged by the success in diethylaminecatalyzed synthesis of bis- coumarins, we had anticipated that, synthesis of bis- tetronic acids could be executed easily employing diethylamine or other base catalyst. The main objective to undertake the synthesis of these molecules was twofold. i) There exists only one earlier report on their synthesis using Electrogenerated base as the catalyst and, ii) these compounds being structurally similar to bis – coumarins, they should also exhibit urease inhibitor activity. During optimization of the reaction conditions it was noticed that, the synthesis of bis – tetronic acids could be executed using sulfamic acid as the commercially available, least expensive and biodegradable catalyst **(Scheme 3).** During screening of their urease inhibitor activity, these compounds were found to have moderate urease inhibitor activity.



Scheme 3. Sulfamic acid catalyzed synthesis of bis-tetronic acids

***Published in "Res. Chem. Intermed. 2016, 43,* 143 – 148**".

Part - III: Diversity oriented synthesis of 2 - amino-3 – phenylsulfonyl–4H–chromenes

Chromene moiety often appears as an important structural motif in many naturally occurring compounds with important biological activities [15-16]. Among chromene family members, 2-amino-4H-chromenes 2-amino-4H-benzo[b]pyrans constitutes an important class of compounds customarily used in pigments, cosmetics as well as biodegradable agrochemicals [17-19]. The interest in this class of compounds has rejoiced in last few years due to their wide spectrum of biological activities such as antibacterial, mutageneticidal, antiviral, antihypertensive as well as antitumor activities [20-25]. They also find application as cognitive enhancers in treatment of neodegradable diseases like Alzheimer's disease, insomnia, etc [26-27]. It is a well established fact that, the biological activities of 2-amino-4H chromenes depend upon the nature substituent's in pyran ring as well as in adjacent rings. Thus, variation of substituent's in both the rings results in to a large number of structurally related compounds with important biological activities. The structures of a few biologically active 2-amino-4H-chromenes possessing anticancer activities are summarized in Fig. 1.

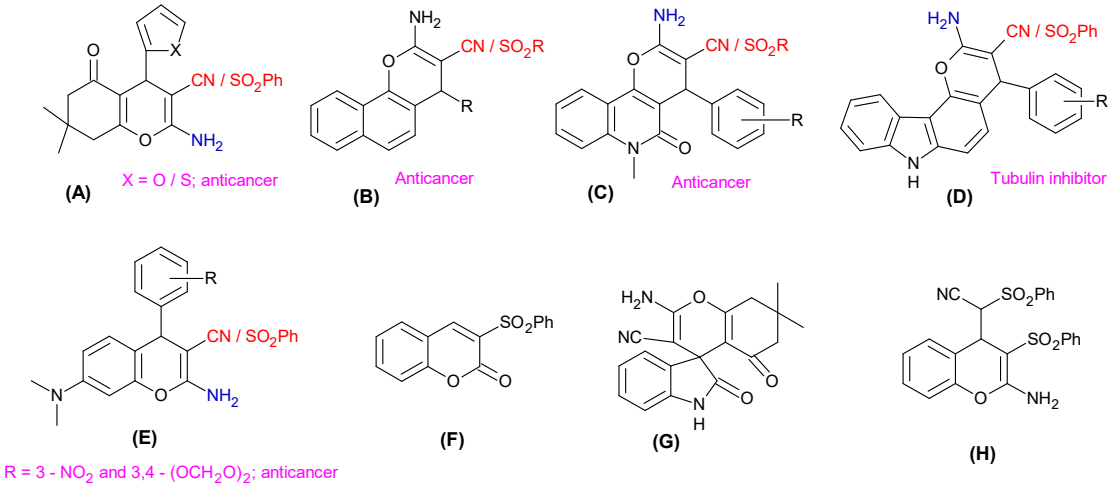
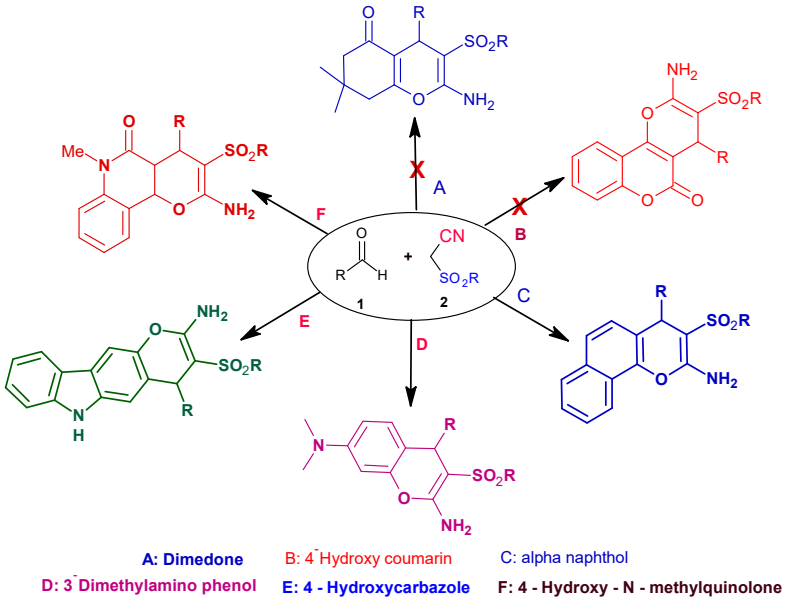


Fig. 2. Structures of few biologically active 2-amino-4H- chromenes

A classical approach in one-pot synthesis of 2-amino-4H-chromenes involves a base catalyzed multicomponent reaction between aldehyde (orisatin) with two different C-H acids. [28] In most of the reported protocols compounds like dimedone, barbituric acid, naphthols,

resorcinol, 4-hydroxycoumarin, 4-hydroxyquinolin-2-one, Kojic acid, 2-hydroxy naphthoquinone, etc. have been used as one of the C-H acid while the choice of other C-H acid has been limited towards the use of malononitrile or alkyl cyanoacetate. More precisely it is interesting to notice that, although many compounds bearing sulfone moiety are known to possess important applications in the field of pharmaceuticals, agrochemicals, polymers, etc. there are only a few reports wherein alkyl / arylsulfonyl acetonitrile has been used as C-H acid. Thus, our attention got focused on the choice of phenylsulfonyl acetonitrile as a C-H acid.

The literature survey within the frame work of choice of phenyl or alkylsulfonyl acetonitrile revealed that, there are no reports on the synthesis of 2-amino-3-phenyl/alkylsulfonyl-4-aryl-4H-chromenes. In light of promising anticancer activities associated with 2-amino-3-cyano-4H-chromenes **(Fig. 2 A-E)** and the biological activities associated with the compounds containing sulfonyl group we surmised that, the replacement of cyano functionality from 2-amino-3-cyano-4H-chromenes with alkyl or arylsulfonyl group would furnish 2-amino-3-phenyl/alkylsulfonyl-4-aryl-4H-chromenes a novel class of compounds, with promising biological activities. With all these observations in mind, we planned undertake the synthesis of 2-amino-3-phenyl / alkylsulfonyl-4H-chromenes. Following scheme describes our studies on the failure as well as success on the synthesis of few 2-amino-3-alkyl/phenylsulfonyl-4H-chromenes **(Scheme 3).**

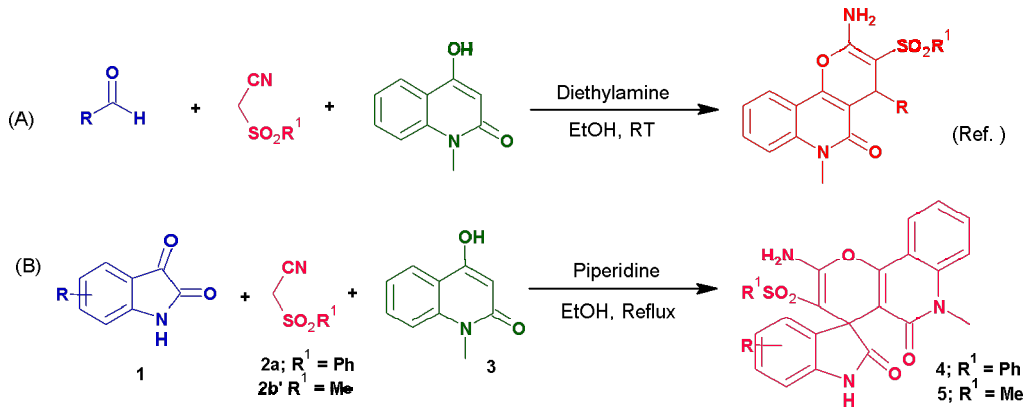


Scheme 4. Diversity oriented synthesis of 2-amino-3-phenylsulfonyl-4H-chromenes

Published in ACS Sustainable Chem. Eng. 2016, 4, 3450 – 3464

Part- IV: One – pot synthesis of 2 - amino-3 – phenylsulfonylspirocyclicoxindoles

The spirooxindole is among the most important class of naturally occurring substances, characterized by highly pronounced biological properties, and is also the core structure of many synthetic pharmaceuticals. Various biological activities of spirooxindole derivatives have attracted much attention of organic chemists, and as a consequence, a number of methods have been reported for the preparation of spirooxindole-fused heterocycles. After having established an environmentally benign protocol for the synthesis of 2-amino-3-phenylsulfonyl-4*H*- chromenes, we planned to replace aldehyde component from the above scheme with isatin. This is because,isatin and its derivatives are the most useful starting materials or precursors in the synthesis spirocyclicoxindoles. Many of our attempts to effect three component condensation between isatin, phenylsulfonyl acetonitrile and dimedone / 4 – hydroxycoumarin / phenol / naphthols were unsuccessful. After repeated trials, we were successful in the synthesis of spirocyclicoxoindole derivatives via piperidinecatalyzed condensation between isatin, phenylsulfonyl acetonitrile and 4- hydroxy–N– methylquinolones**(Scheme 5).**



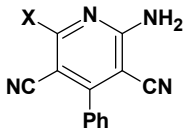
Scheme 5. Multicomponent synthesis of spirochromenes

(Manuscript submitted to Res. Chem. Inter. April 2018)

P*art-V: Problem solving synthesis of densely substituted pyridine 3,5- dicarbonitriles*

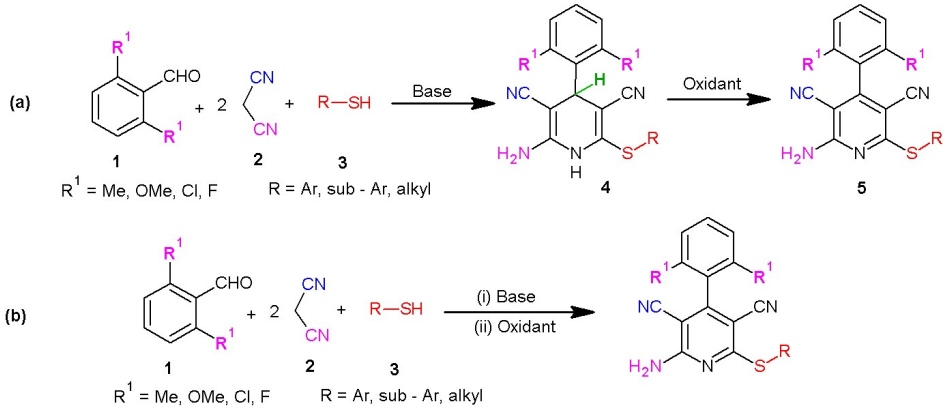
Alike 2-amino-4H-chromenes, pyridine-3,5-dicarbonitriles constitutes one such medicinally privileged scaffold (**A**, Figure 1) and diversifications at positions C_2, C_4, and C_6 of the pyridine core has resulted in a great number of compounds with useful biological activities. For instance, pyridine-3,5-dicarbonitriles with amino and sulfanyl moieties at position C_2 and C_6, respectively and aryl or heteroaryl substitution atC_4 has been found to be

highly useful pattern. Literature survey revealed that such pentasubstituted pyridines exhibit diverse medicinal properties, such as antibacterial, anticancer, potassium channel opener for the treatment of urinary incontinence, anti hepatitis B virus (HBV) infection, Parkinson's disease, hypoxia, asthma, cancer and kidney diseaseetc. **(Fig. 3)**. Such a wide range of applications of pyridine-3,5–dicarbonitriles have inspired many researchers to develop efficient methods for their synthesis. A classical approach for their synthesis involves base catalyzed one –pot, three component condensation between an aldehyde, malononitrile and thiol**(Scheme 4A).** A variety of catalysts have been reported for the synthesis of this class of compounds. At the same time it is worthy to note that, the reaction fails to furnish desired pyridine-3,5–dicarbonitriles with the choice of 2,6-disubstituted aldehydes as the aldehyde component. In fact, the reaction remains arrested to yield corresponding dihydropyridine as the final product **(A, Scheme 4).** Consequently, there are only two reports on their synthesis. This prompted us to develop a new protocol for their synthesis. During the course of this investigation we have found that, diethylamine – Oxone serves as an efficient catalyst – oxidant combination in the synthesis of densely substituted pyridine 3, 5-dicarbonitriles**(Scheme 4B).**



X = OH / NH_2 /SR

Fig. 3. *Pyridine-3,5-dicarbonitriles*



Scheme. 6. Two step, and sequential, one–pot, two-step synthesis of pyridine 3,5–dicarbonitriles

Published in "RSC Advances 2017,7,38877 – 38883"

Part–VI:Catalyst-free oxidation of sulfides to sulfoxidesand diethylaminecatalyzed oxidation of sulfides to sulfones using Oxone as an oxidant

Modern chemistry has been invariably linked with sustainable chemistry, and, in an over-polluted world, its implementation has become a practical need both from socio and economic points of view. Consequently, in recent years, the development of sustainable, atom-economical, operationally simple, scalable, and catalyst-free protocols for the synthesis of pivotal intermediates useful in chemistry as well as biology has become the focal point of research.

Sulfoxides and sulfones are two important classes of compounds which find wide applications as intermediates in chemistry as well as biology. Controlled and chemoselective oxidation of sulfides is one of the rational pathways for the synthesis of sulfoxides and a great number of oxidizing agents have been reported for their synthesis. With our continued interest in Oxone chemistry, we have developed an ecobenign, catalyst-free, and scalable protocolfor the chemoselective oxidation of sulfides to sulfoxides using commerciallyavailable Oxone as an oxidant.

Alikesulfoxidessulfones are also known to play a prominent role in the field of organic synthesis, pharmaceuticals, and agrochemicals as well as polymers and there is an urgent need for the development of a scalable protocol for the synthesis of sulfones. With our continued interest in the development of base catalyzed protocol, We have also developed a chemoselective, chromatography-free and scalable protocol for the oxidation of sulfides to sulfones using diethylamine–Oxone as a unique catalyst–oxidant combination. To the best of our knowledge, the literature to date contains no precedent for such a simple, energy-efficient, functional group compatible and scalable protocol for the oxidation of sulfides to sulfoxides and sulfones**(Scheme 7).**

Scheme 7. Oxidation of sulfides to sulfoxides and sulfones using Oxone as an oxidant

Published in "Res. Chem. Inter. 2017, 43, 6875–6888"

Part- VII: Tris-hydroxymethylaminomethane (THAM) as an efficient organocatalyst in diversity oriented and environmentally benign synthesis of spirochromenes

Most ubiquitous heterocyclic moiety present in a large number of bioactive natural products is indole.It is also known that, sharing of indole 3 - carbon atom in the formation of spiroindolines and the presence of carbonyl group at C-2 in spiroindolines generate spiro-2-oxindoles [spirooxindoles] which occupy a special place in organic as well as medicinal chemistry. Many compounds containing spirooxindole as the structural unit of natural as well as synthetic origin are known to exhibit anti-microbial, anti-oxidant, anti-inflammatory, anti-tubercular, anti-cancer, anti–HIV as well as anti-inflammatory activity **(Fig. 1)**. Furthermore, Sharing of C-3 in spirooxindoles with pyran ring generates pyran annulated spirooxindoles (spiropyrans or spirochromenes) which are also known to exhibit useful biological properties like anticoagulant, spasmolytic, diuretic, anticancer as well as anti-anaphylactic activities. The biological potential of spirochromenes has always been the driving force for the chemists to develop efficient protocols for the synthesis.

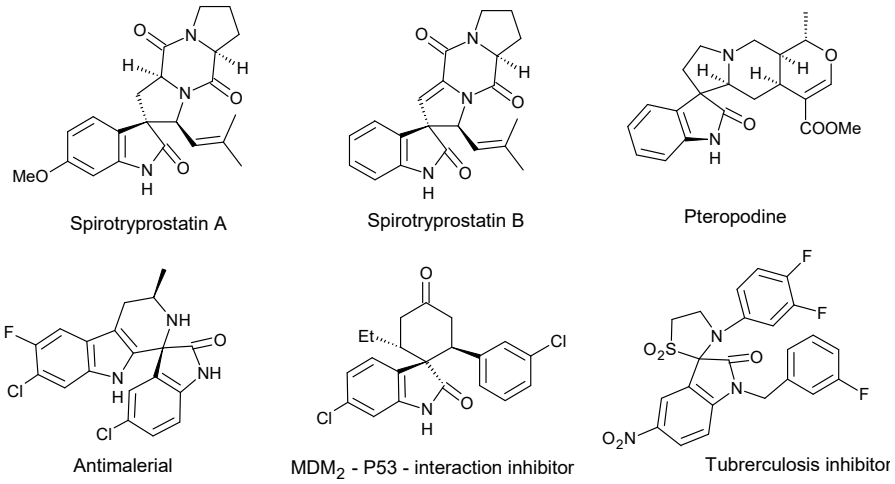


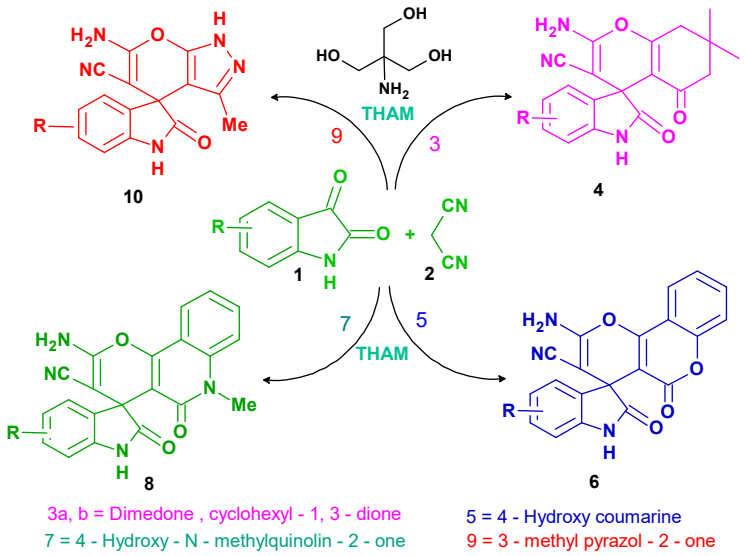
Fig. 4. Representativebiologically active spirooxindoles

Classical synthesis of spirochromenes involve one-pot, three component condensation between isatin, malononitrile and an enolizable C-H acid like dimedone, barbituric acid, naphthols, 4-hydroxycoumarin, etc. and the literature is enumerated with several approaches for their synthesis. A focused literature survey towards enviro-economic protocols developed for the synthesis of spirochromenes revealed that, a few catalyst-free protocols have earlier been reported for their synthesis.Notably, all the catalyst-free protocols developed for the synthesis of spirochromenes require either thermal or electrochemical activation. These reports indirectly project the necessity of a catalyst, an alternate energy source or the reaction medium for the synthesis of spirochromenes at ambient temperature. During our search on protocols operable at ambient temperature it was noticed that, a range

of catalysts as well as reaction media have been reported for their synthesis.Each of the reported method has it's own merits while a few of the reported protocols suffer from the drawbacks as regards the use of expensive or difficult to prepare catalyst or the reaction medium and to the best of our knowledge, there are only a few protocols wherein the problem of economics and environmental protection have been addressed successfully.[18a-c] with our continued interest in the development of organocatalyzed protocols for the synthesis of chromene based heterocycles,we set out to develop an enviro-economic and diversity oriented protocol for the synthesis of spirochromenes.

Tris-hydroxymethylaminomethane, THAM (**Scheme 1**) is a biodegradable, non-corrosive, physiologically inert and thermally stable compound available commercially at extremely low cost.It contains an amino and three primary alcoholic groups and when dissolved in water or water – ethanol medium, it generates basic reaction medium.In the recent past we have reported it's use as an efficient organocatalyst in the diversity oriented synthesis of 2-amino-4*H*-chromenes by multicomponent condensation between aldehydes and two different C-H acids. In continuation of the same, herein we report the use of THAM in diversity oriented synthesis of spirochromenes by three component reaction between isatins, malononitrile and dimedone, 4-hydroxycoumarin, 4-hydroxy-N-methylquinolone and *insitu* generated 2-methylpyrazolon-2-one **(Scheme 8).**

The protocol mainly exhibits remarkable versatility on various substrates to afford the desired products in good to excellent yields. Ambient reaction conditions, simple work-up procedure and avoidance of conventional purification methods have improved the practical utility of the protocol manifold.



Scheme 7. THAM catalyzed synthesis of spirochromenes

Part- VIII: Diversity oriented synthesis of 2-amino-4H-chromenes bt reaction between salicylaldehydes and two different C-H acids

Chromene moiety often appears as an important structural motif in many naturally occurring compounds with important biological activities. Amongst chromene family members, 2-amino-4H-chromenes, (2-amino-4H-benzo[b] pyrans), constitutes an important class of compounds customarily used in pigments, cosmetics as well as biodegradable agrochemicals [6]. Owing to their wide spectrum of biological activities such as antibacterial, mutageneticidal, antiviral, antihypertensive, antitumor activities, etc. these compounds have also attracted the attention of medicinal chemists. They also find application as cognitive enhancers in treatment of neodegradable diseases like Alzheimer's disease, insomnia, etc.[8].

During literature survey on biologically important 2-amino-4*H*-chromenes, it was revealed that, 2-amino-4*H*-chromenes of type **A(e.g. HA-14-1, Fig. 1)** serve as tumor antagonist and family of related alkyl (4H-chromen-4-yl) cyano acetates exhibit binding activity for surface pocket of the cancer-implicated Bcl-2 proteins and induce apoptosis in follicular lymphoma-B cells as well as Leukemia HL-60 cells. On the other hand, compound **D(Fig. 1)** has been found to inhibit mitogen-activated protein kinase-activated protein kinase-2 (MK-2) and to suppress the expression of TNF-α in U 937 cells. A few other compounds containing 2-amino-4*H*-chromene moiety **(B, C, E; Fig. 1)** are also known to exhibit important biological activities.

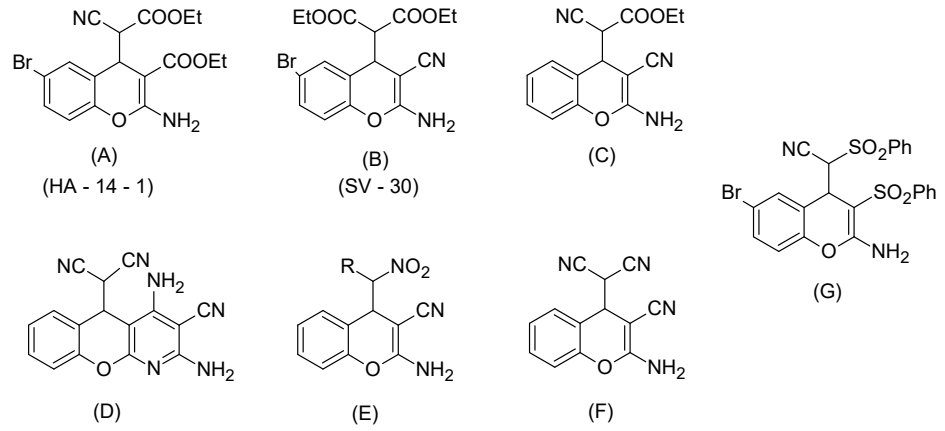


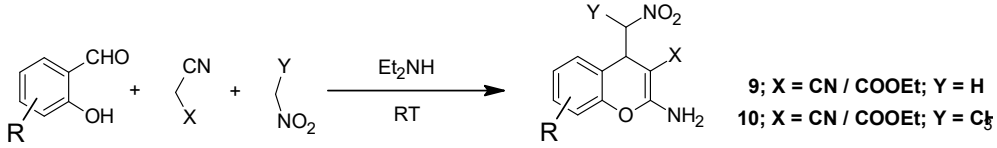
Fig.1: Structures of few biologically active 2-amino-4H-chromene derivatives

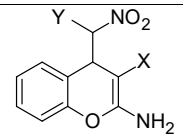
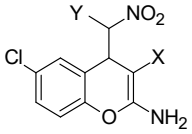
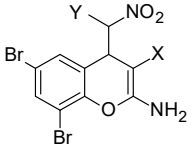
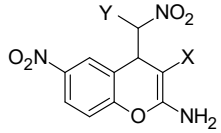
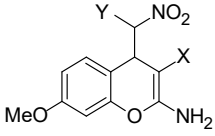
As regards synthesis of 2-amino-4*H*-chromene of type **A, F** and **G** is concerned, they can be prepared by the reaction of salicylaldehyde with two equivalents of active methylene compounds like ethyl cyanoacetate, malononitrile, or phenylsulfonyl acetonitrile, respectively. We have earlier reported the synthesis of **A, F** and **G by** using the aforesaid reactants and

diethylamine as the catalyst. This success prompted us to undertake the synthesis of **E (Fig. 1**) which involves the reaction of salicylaldehyde with two different C-H acids *viz.*malononitrile and nitromethane (or nitroethane) and we are happy to disclose that, synthesis of compounds of type **E** could easily be achieved by simple stirring together an equimolar mixture ofsalicylaldehyde, malononitrile and nitromethane (or nitroethane) in the presence of diethylamine as the catalyst.

During the studies on mechanism of the reaction, we have carried out the synthesis of same chromene derivatives using THAM as a very organobasic catalyst. All the synthesized compounds were screened for their anti-oxidant as well as anti-bacterial activity. Few of the synthesized compounds were found to have promising anti-oxidant activity.

Table 2: Diethyl amine catalyzed synthesis of 2-amino-4H-chromenes, 9 /10.



No.	Product		X	Y	dr[b] =	Time (h)	Yield[c] (%)
1		**9a**	CN	H	----	1	94
2		**9b**	COOEt	H	----	1.5	95
3		**10a**	CN	CH_3	60 : 40	1	96
4		**10b**	COOEt	CH_3		0.5	94
5		**9c**	CN	H	----	6	96
6		**9d**	COOEt	H	----	3	96
7		**10c**	CN	CH_3	60 : 40	5	92
8		**10d**	COOEt	CH_3	75 : 25	1	96
9		**9e**	CN	H	----	3.5	96
10		**9f**	COOEt	H	----	4	95
11		**10e**	CN	CH_3	65 : 35	2	93
12		**10f**	COOEt	CH_3	70 : 30	1	92
13		**9g**	CN	H	----	2.5	97
14		**9h**	COOEt	H	----	4	95
15		**10g**	CN	CH_3	75 : 25	2.5	92
16		**10h**	COOEt	CH_3	60 : 40	1	94
17		**9i**	CN	H	----	6	91
18		**9j**	COOEt	H	----	5	94
19		**10i**	CN	CH_3	70 : 30	7	90
20		**10j**	COOE	CH_3	80 : 20	1	94

a: Reaction conditions: Salicylaldehyde, malononitrile / ethyl cyanoacetate and nitroalkane (2 mmol, each), ethanol (3 mL), diethylamine (10 mol %), RT; b: from ^{1}H NMR; c: Isolated yields

PUBLICATIONS	***(Reprints attached)***
1	Diethylamine-catalyzed environmentally benign synthesis of 1-oxo-hexahydroxanthenes and bis-coumarins at ambient temperature ***Res. Chem. Intermed. 2016, 42, 6313 – 6325.***
2	Sulfamic acid-catalyzed, environmentally benign synthesis of bis-tetronic acids at ambient temperature ***Res. Chem. Intermed. 2017, 43, 141 – 146***.
3	Problem solving and environmentally benign approach toward diversity oriented synthesis of novel 2‑amino-3-phenyl (or Alkyl) sulfonyl-4H‑chromenes ***ACS Sustainable Chem. Eng. 2016, 4, 3450 – 3464***.
4	DiethylamineDess–Martin periodinane: an efficient catalyst–oxidant combination in a sequential, one- pot synthesis of difficult to access 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines at ambient temperature ***RSC Adv., 2017, 7, 38877 – 38883***.
5	Catalyst-free oxidation of sulfides to sulfoxides and diethylaminecatalyzed oxidation of sulfides to sulfones using Oxone as an oxidant ***Res. Chem. Intermed. 2017, 43, 6875 – 6888***.
6	Tris-hydroxymethylaminomethane (THAM) as an efficient organocatalyst in diversity oriented and environmentally benign synthesis of spirochromenes ***C. R. Chimie, April 2018 (Accepted for publication)***
	COMMUNICATED PAPERS
1	Highly rapid and extremely simple protocol for the oxidation α-hydroxyphosphonates to α-ketophosphonates using Dess-Martin periodinane ***Phosphorus, Sulfur, Silicon and related elements, April 2018.***
2	Multicomponent synthesis of novel spirooxindoles by the reaction between isatins, phenyl (or alkyl) sulfonyl acetonitrile and 4-hydroxy-N-methylquinolin-2-one ***Res. Chem. Intermed. April 2018***