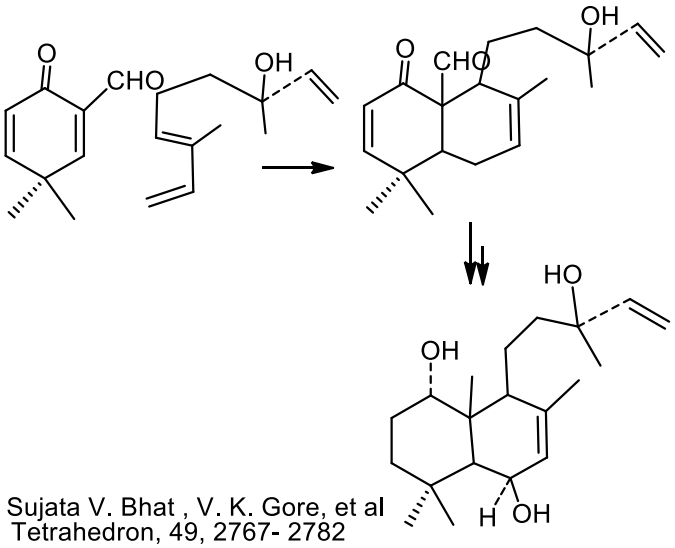
Organic Syntheses

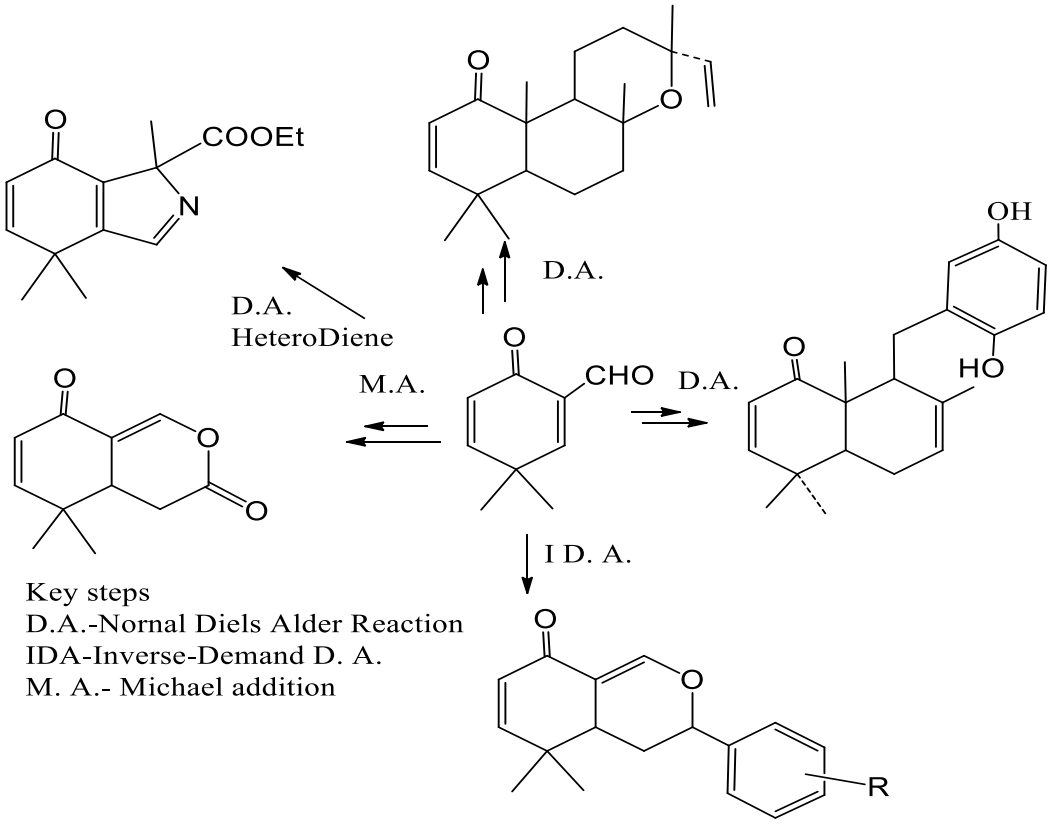
Dr. Bhat has achieved elegant synthesis of Organic molecules with interesting bioactivities. Her synthetic stategies include

- Utility of Formyl-4,4-dimethyl-cyclohexadienone using various condensation reactions to yield a variety of skeletons including dehydroxy-desketo-forskolin, taxadiol, Cinnamolide, Polygodial, Drimenin, Isozonarol, Avarol, heterodecalins, Synthesis of Qussinoid skeleton, etc.
- Green preparation of cyclic ethers using catalysts such as Zeolite, clay, ion-exchange resins.
- Utility of Sulfolene –Regioselective alkylation followed by desulfonation this yielded retinol related polyenes. By altering reaction conditions isomeric polyenes were obtained.
- New retinobenzoic derivatives were synthesized for anti-tumour activity evaluation.
- Amine- peroxides for antimalarial activity evaluations.
- Chiral sulfoxides condensations subsequent manipulations yielded chiral molecules such β-aminoacids, β-phenylethanol-amines, podophyllotoxin.
- Biomimetic cyclization in the presence of Chiral LBA, various tricyclic and teracyclic chiral natural molecules.
- **Zeolite, clay, ion-exchan**ge **resins**- Green preparation of cyclic ethers
- High level of stereoselectivity in the pH sensitive epoxidation and one-pot biomimetic cyclization of olefinic alcohols with camphor and oxone®.

Synthesis of Forskolin Skeleton



Sujata V. Bhat , V. K. Gore, et al
Tetrahedron, 49, 2767- 2782
.https://doi.org/10.1016/s0040-4020(01)86353-5



Key steps
D.A.-Nornal Diels Alder Reaction
IDA-Inverse-Demand D. A.
M. A.- Michael addition

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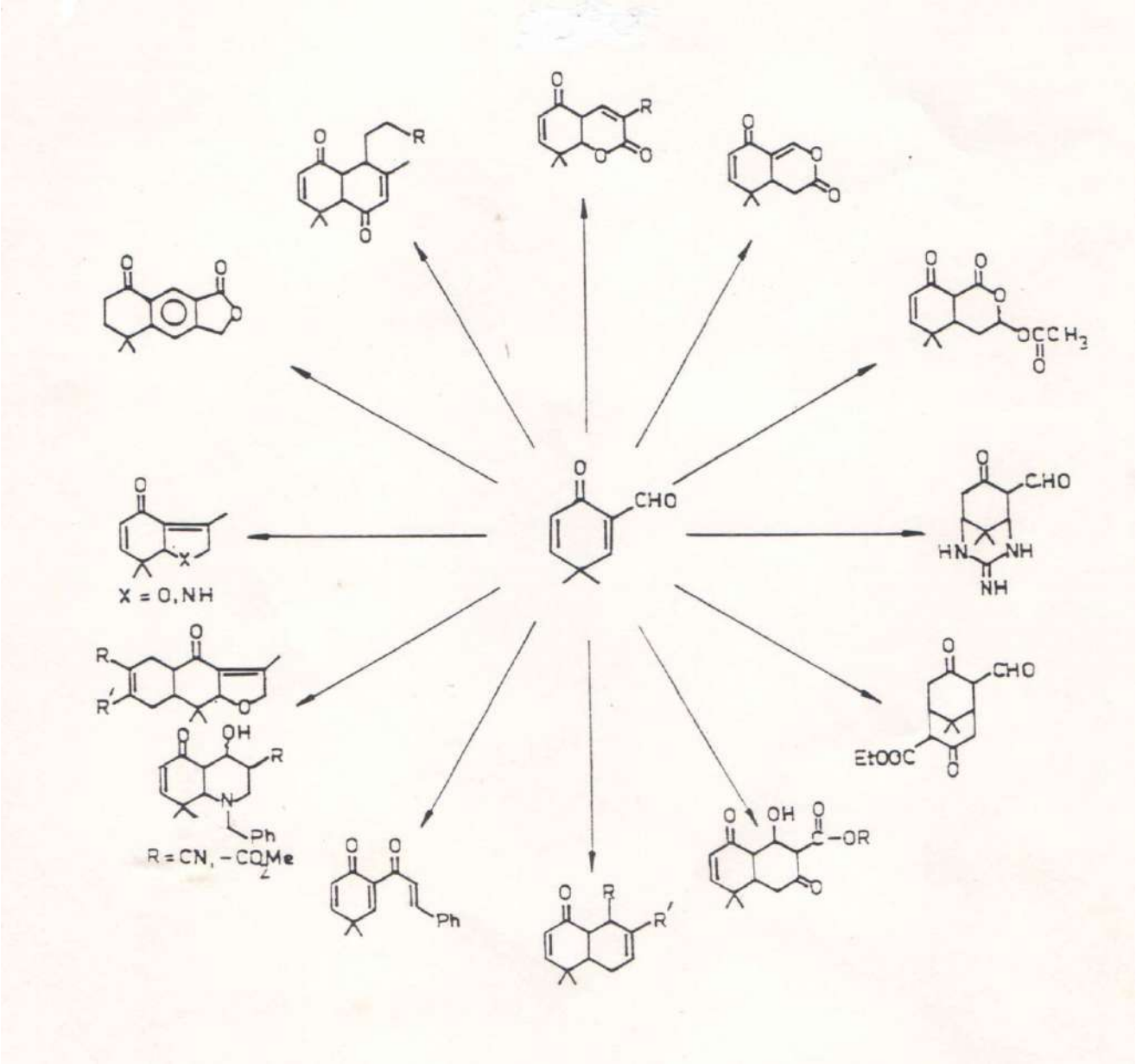
V. K. Gore, S. R. Desai, T. Mayalvaganan, R. Padmakumar, S. B. Hadimani and **Sujata V. Bhat, *Tetrahedron*, 1993**,D. Kalyan Das, U. C. Sinha, *Acta. Cryst. C48, **1992***, *Synthetic communications,* **1992,** S. B. Hadimani, R. Padmakumar and **Sujata V. Bhat**, **1996**,

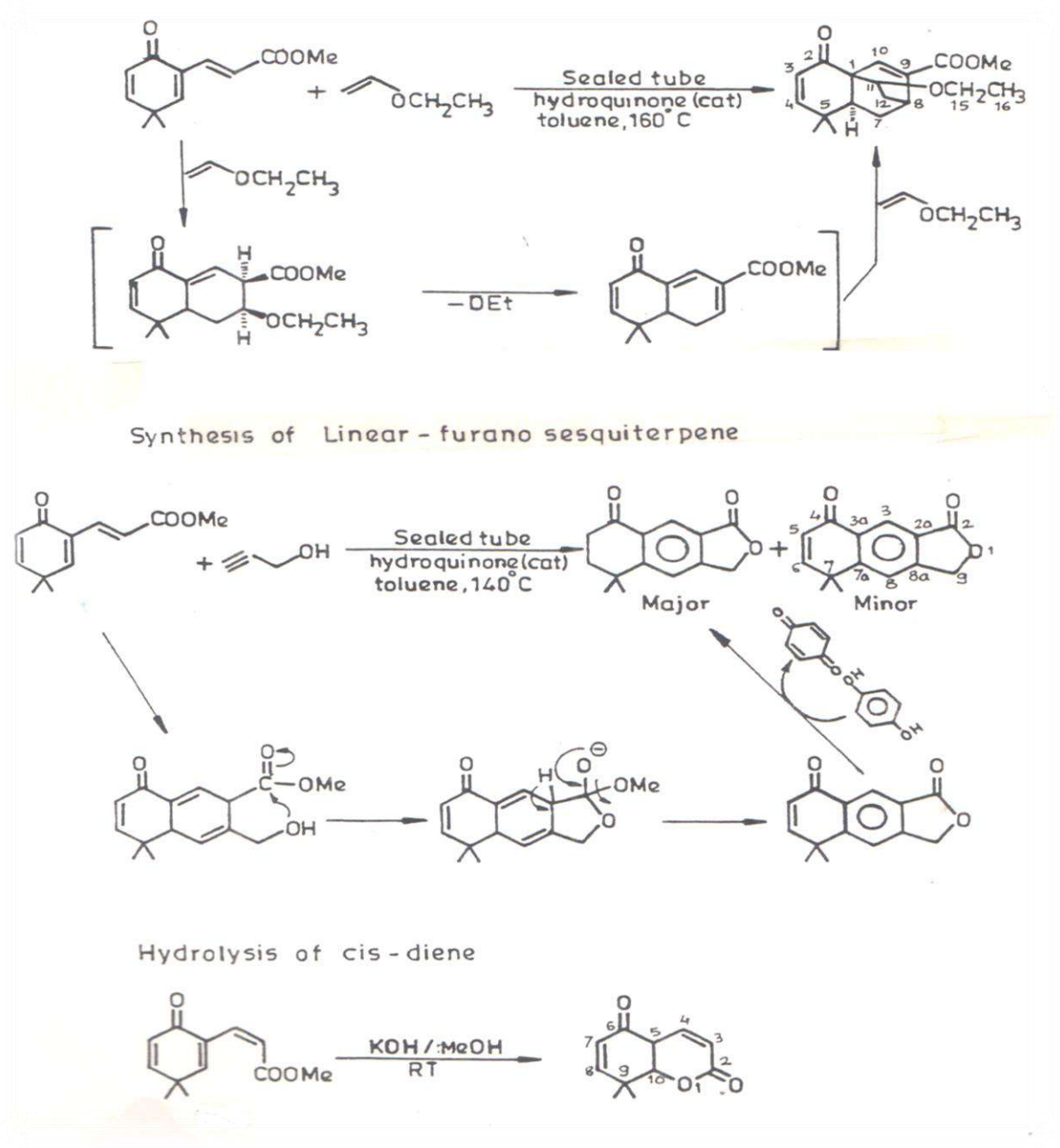
- Convenient synthesis of hetero-decalins, *Synthetic Communications*, 26, 3527-3533; Convenient Synthesis of (l*H*)-Isoindoles and Cyciopenta[e]pyrrole Skeletons, Veera reddy, Sujata Bhat, *Tetrhedron Letters***,1997.** S. B. Hadimani, A. Sivaramakrishnan and **Sujata V. Bhat**, **2001**, A novel approach to decalin synthons of bioactive terpenoids: Inverse electron demand Diels-Alder reactions, *J. Ind. Institute of Science*, 81, 159-163.

➢ **Various bicyclic, tricyclic and tetracyclic molecules were synthesised starting** from 2-formyl-4,4-dimethyl-cyclohexadienone:



S. B. Hadimani, R. Padmakumar and Sujata V. Bhat, **1996**, Convenient synthesis of hetero-decalins, *Synthetic Communications*, 26, 3527-3533

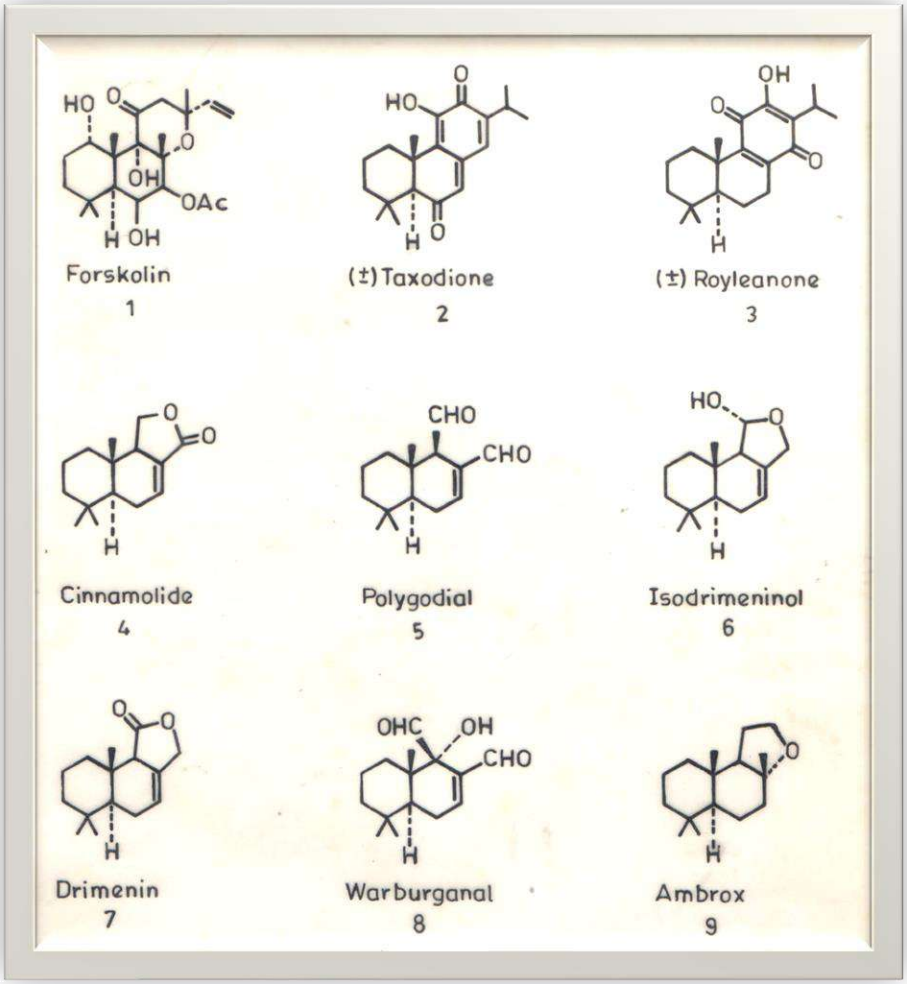
Convenient Synthesis of New tricyclo- [6.2.2.0^{1,6}]dodecanes



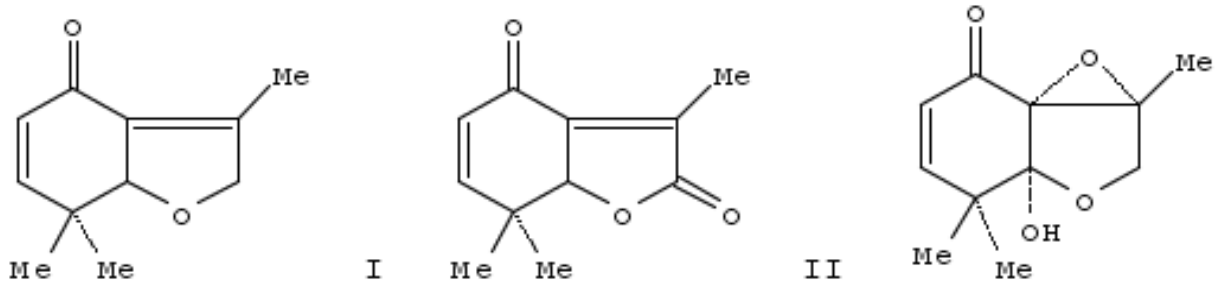
S. B. Hadimani, R. Padmakumar and **Sujata V. Bhat**, **1997**, A novel approach to tricyclo-[6.2.2.0^{1,6}]dodecanes through tandem Diels-Alder reaction, *Ind. J. Chem* 36B, 381-383.

S. B.; Padmakumar, R.; Bhat, Sujata V, Sythetic Communications (1996), 26(19), 3527-3533.

Forskolin related molecules-

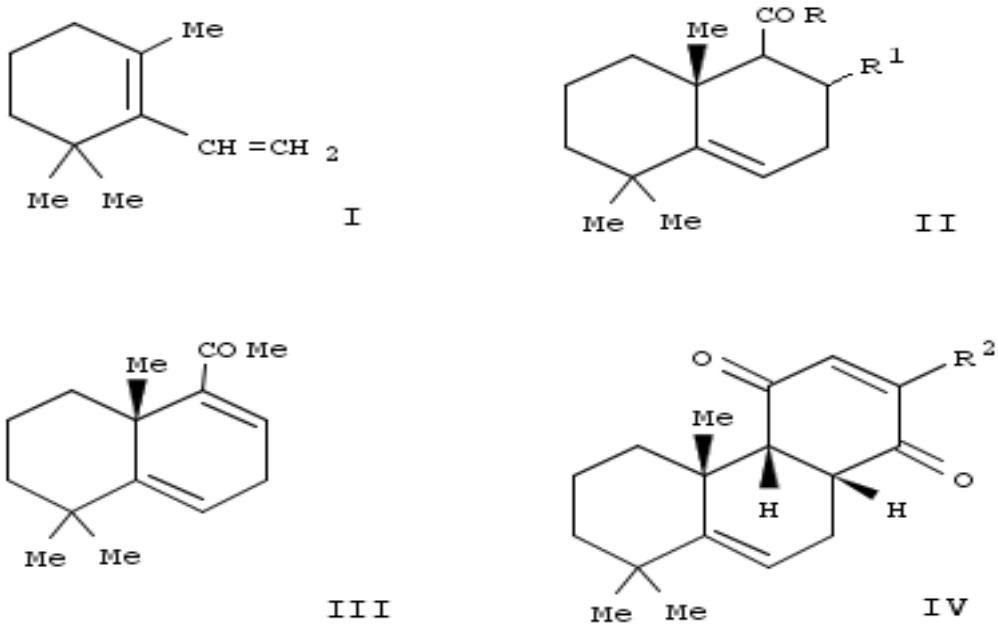


Unprecedented tandem Michael-ene reaction-followed by autooxidation



➢ Desai, Shailesh R.; Gore, Vinayak K.; Bhat, Sujata V., Journal of Organic Chemistry (1992), 57(8), 2467-8

➢ **Synthesis of decalin synthons of bioactive terpenoids: Lewis acid-catalyzed Diels-Alder reactions**

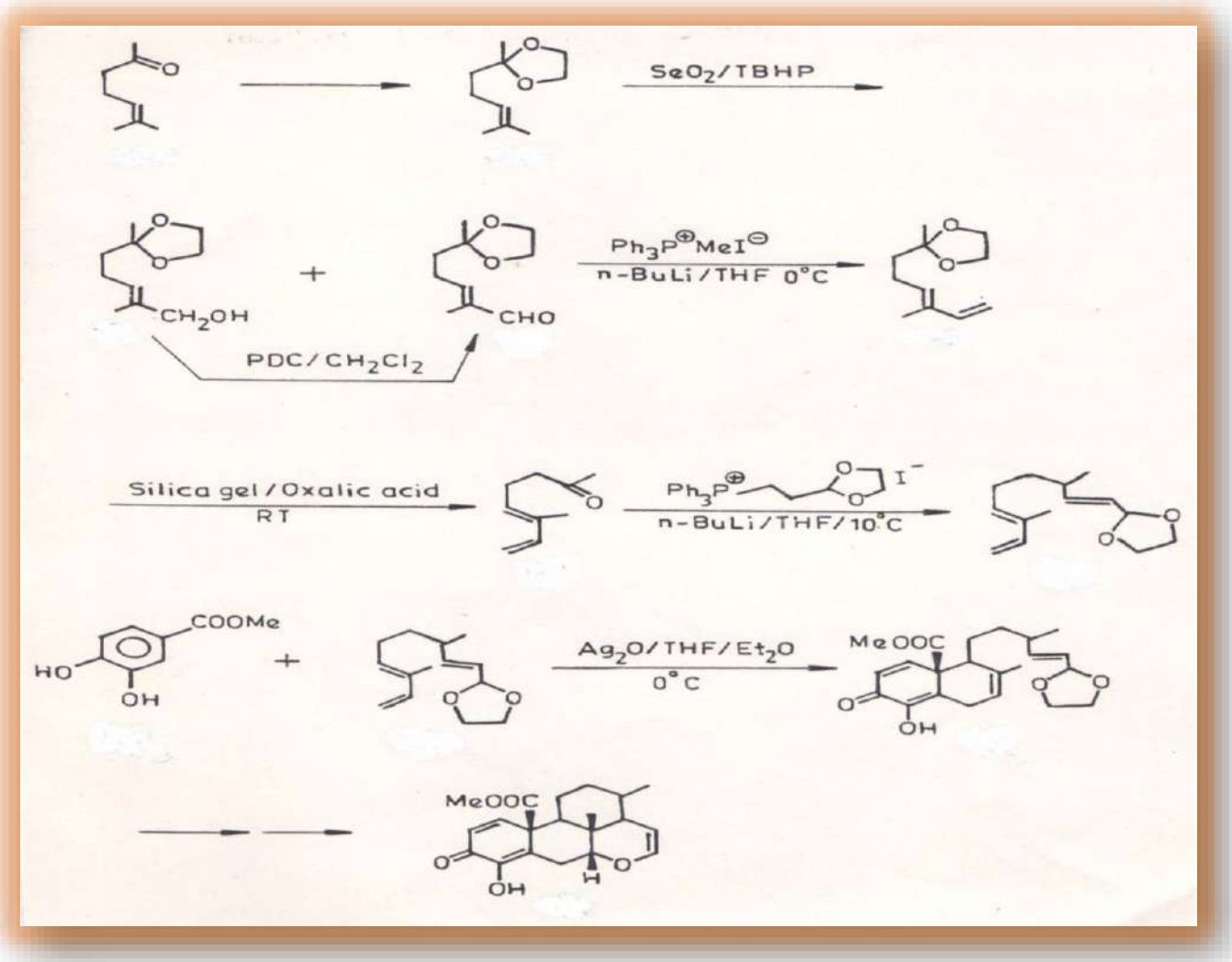


➢

➢ Mayelvaganan, T.; Hadimani, Shreeshailkumar; Bhat, SujaCyclisation

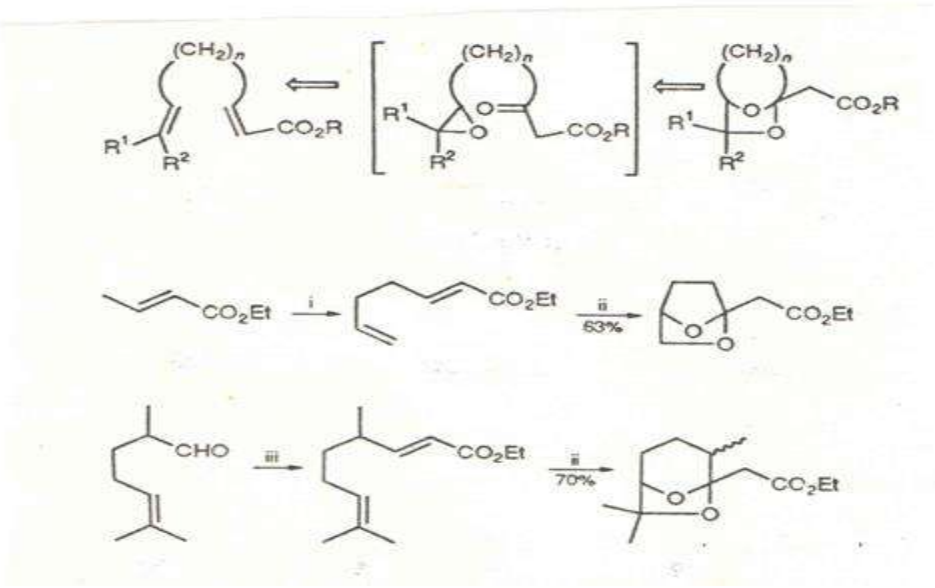
➢ **Quassinoids** are the bitter compounds of the Simaroubaceae family which are a group of structurally complex and highly oxygenated degraded triterpenes. They are divided into five groups according to their basic skeleton: C-18, C-19, C-20, C-22, and C-25. In recent years, attention has been focused on quassinoids because several of them have shown promising biological activities. Some quassinoids present insecticidal and antifeedant effects in insects. Quassin was first used as an insecticide at the end of the seventeenth century, with the application of plant extracts from *Quassia amara*. More recent studies also reveal this activity in other species and/or other quassinoids. Additional bioactivities of quassinoids include antimalarial, antiviral, antitumor etc.

➢ D.r. Bhat's group has synthesisedquassinoid skeleton as described in the following Figure.



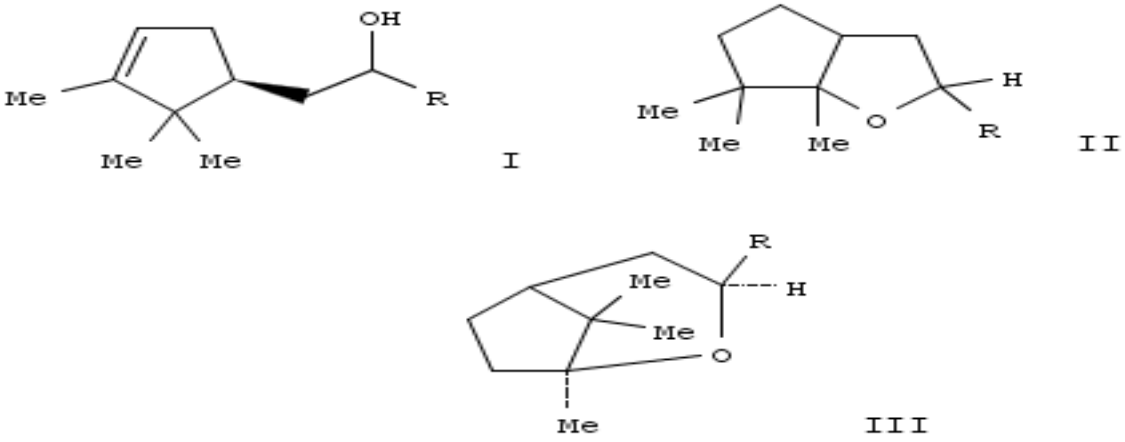
S. V. Bhat, S. S. Hadimani- Dissertation.

- Synthesis of Dioxabicyclo[n.2.n]alkanes through Palladium catalysed oxidative



N. Balu, Sujata V. Bhat J. Chem. Comm. 1994, 903.

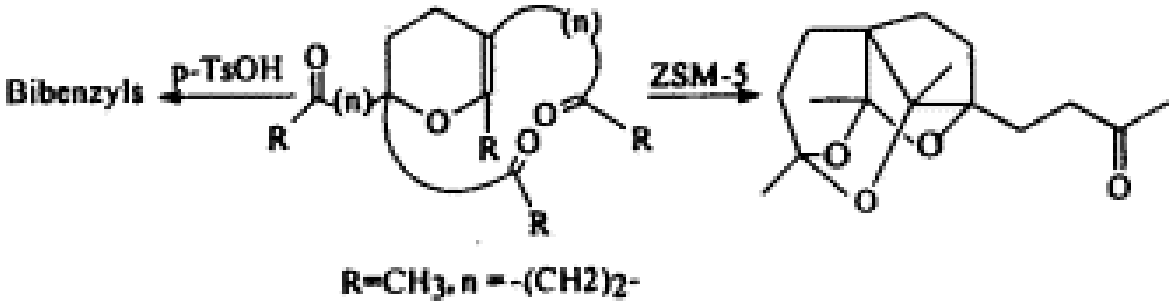
- **Green one pot Synthesis- Clay-10 catalysed cyclisation**

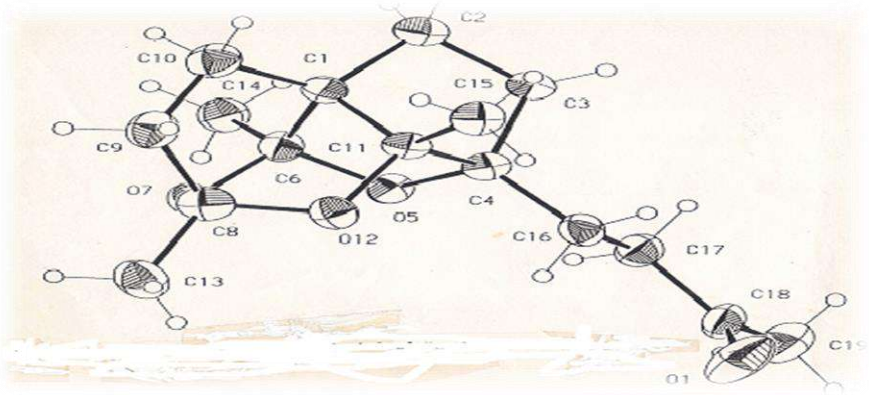


Gupta, Vijaykumar; Kabiraj, Shilpi; Rane, Monica; Bhat, Sujata V., RSC Advances (**2015**), 5(29), 22951-22956.

- Zeolite mediated cyclisation

Methyl Vinyl Ketone on heating in the presence of ZSM-5 undrergoes teramerization followed by cyclization to yield interesting trioxatetracyclo[5.3.2.$0^{4,9}$.$0^{4,11}$]dodecane.





P. Veera Reddy, T. Manisekaran and **Sujata V. Bhat**, **1998**, Novel synthesis of trioxatetracyclo[5.3.2.$0^{4,9}$.$0^{4,11}$]dodecane and bibenzyl skeletons: *Tetrahedron Letters.* 39, 1629-1631

Sulfolene Alkylation and Desulfonation

Using this approach her group achieved the synthesis of Retinol related polyenes, Senensal related Pheromones etc was achieved through sulfolene alkylations followed by desulfonylation. She developed convenient and practical Method for desulfonylation. Hence this method for synthesis of polyenes is practical.

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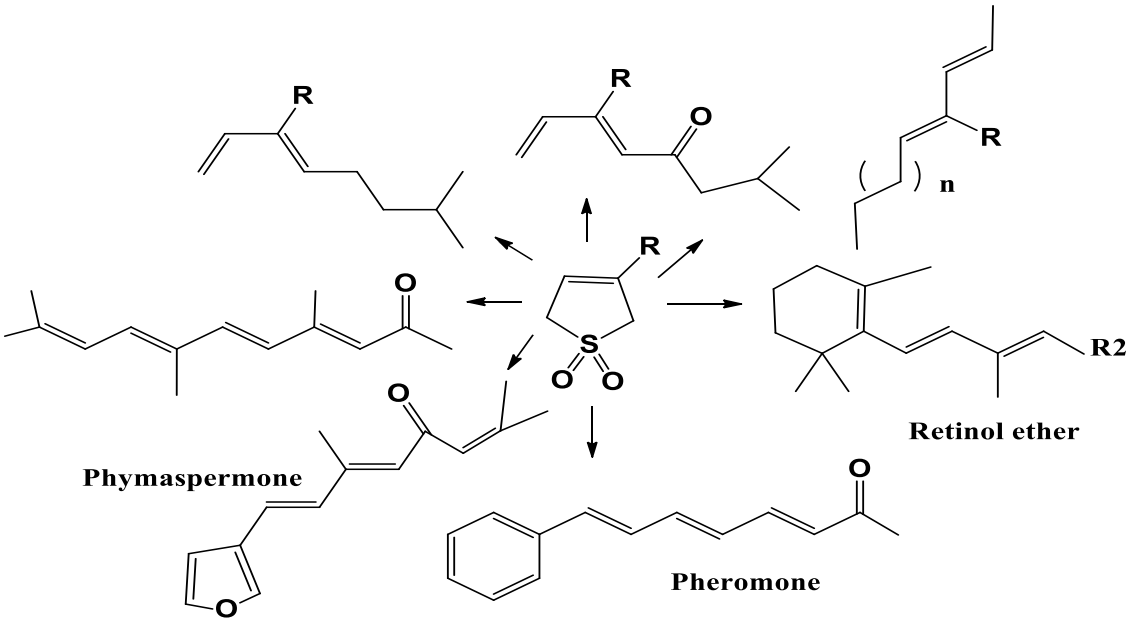
Syntheses of Natural-1,3-dienes derivarives through Alkylations and Thermolysis of 3-Sulfolenes

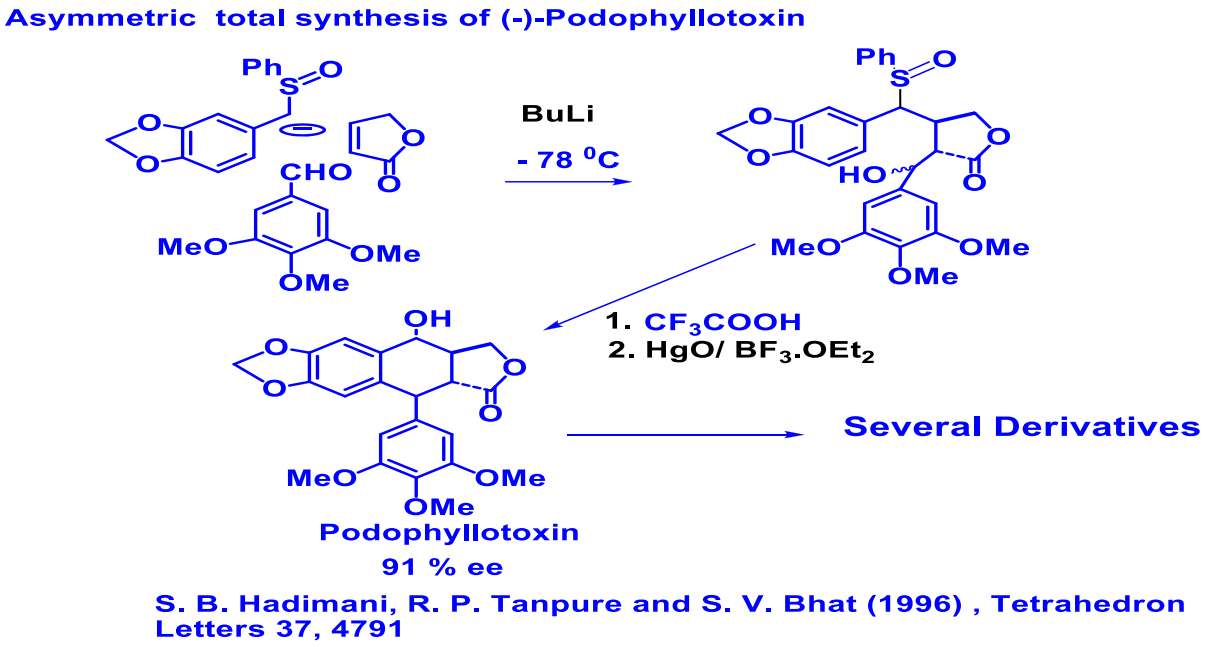


- T. Subramanian, T-S Chou and **Sujata V. Bhat**, **2001**, Convenient synthesis of retinol-related polyenes through hydroxyalkylation of 3-sulfolenes, *Synthetic Communications,* 31, 61-67. DOI:10.1081/SCC-100105327.
- T. Subramanian, R. Padmakumar and **Sujata V. Bhat**, **1997**, Convenient synthesis of 1,3,6-triene systems through alkylation of 3-Methyl-3-Sulfolene, *Synthetic Communications*, 27, 4067-4072. DOI:10.1080/00397919708005452
- T. Subramanian, S. Meenakshi, S. Y. Dange and **Sujata V. Bhat**, **1997**, Facile synthesis of 3-aroyl-3-sulfolenes through cycloadditions of arylnitrile oxide and 3-sulfolene, *Synthetic communications*, 27, 2557-2562. DOI:10.1080/00397919708004123
- T. Subramanian, R. Padmakumar and **Sujata V. Bhat**, **1997**, Short synthetic route to retinoids through dialkylation of 3-Methyl-3-Sulfolene, *Tetrahedron Letters* 38, 2585-86. DOI:10.1016/S0040-4039(97)00459-0
- S. R. Desai, V. K. Gore, T. Mayelvaganan, R. Padmkumar and **Sujata V. Bhat**, **1992**, studies in alkylation of 3-methyl-3-sulfolene and thermolysis of resulting 2-alkyl-3-sulfolene; convenient synthesis of 1,2-disubstituted-1,3-dienes, *Tetrahedron*, 48, 481-485. DOI:10.1016/S0040-4020(01)89010-4

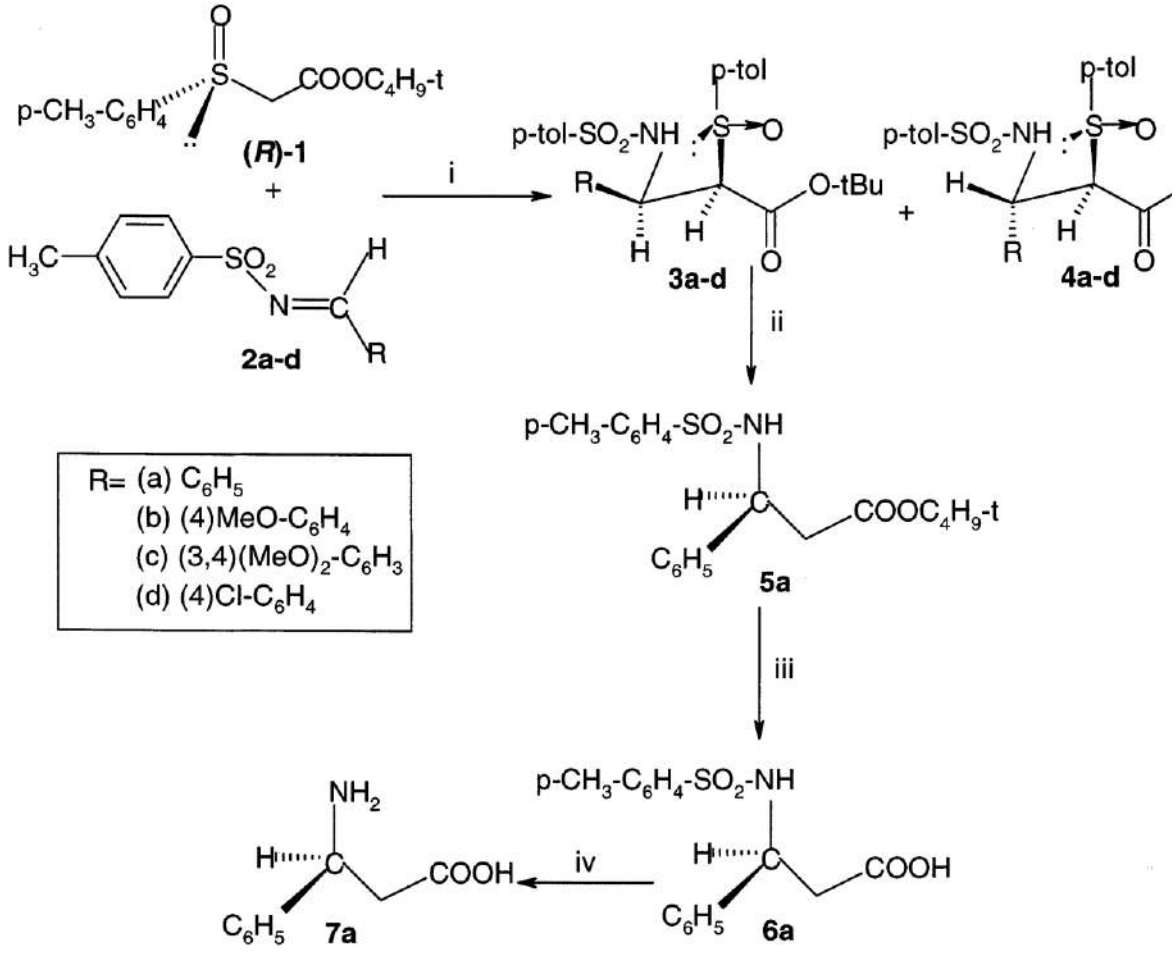
- S. R. Desai, V. K. Gore and **Sujata V. Bhat**, **1990,** Stereoselective synthesis of α-senensal and *trans*-β-ociminal, *Synthetic communications*, 20, 523-527.DOI:10.1080/00397919008244900

• Asymmetric Synthesis

Chirality: It is well known that many pharmaceutical and perfumery molecules have bioactivity difference between enantiomers. Therefore, it is very important to obtain enantiomerically pure compounds. Thus, there is a growing demand for economical methods for asymmetric synthesis or kinetic resolution to obtain enantiomerically pure bioactive molecules. We have developed several methods for asymmetric synthesis of chiral bioactive molecules. Asymmetric synthesis of several bioactive molecules has also been achieved using chiral catalysts, including chiral LBA, chiral acid catalysts, asymmetric sulfoxides, bioconversion and using isolated enzymes. Some methods used are summarized below.



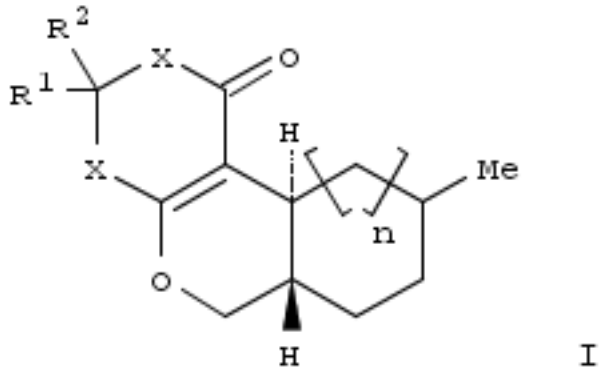
Asymmetric synthesis of β-amino acids through application of chiral sulfoxide



- V. Sivakumar, G. S. Babu and **Sujata V. Bhat, 2001**, Asymmetric synthesis of β-amino acids, *Tetrahedron Asymmetry*, 12, 1095-1099**.** (*) DOI:10.1016/S0957-4166(01)00185-9

- Shivkumar and **Sujata V. Bhat**, **2009,** Asymmetric Synthesis of β-phenylethanol-amines through the applications of chiral sulfoxide, *Synthetic Communications*, 39, 18, 3338-3347**.** DOI:10.1080/00397910902765578

Asymmetric synthesis through Chiral LBA



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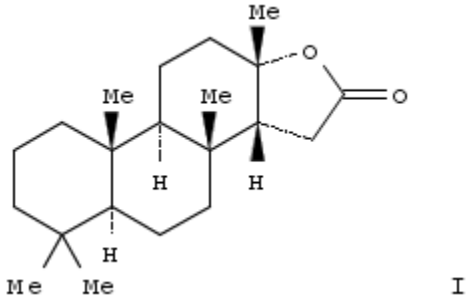
Fernandes, Sylvia; Rajakannu, P.; Bhat, Sujata V., RSC Advances (2015), 5(83), 67706-67711

Facile asymmetric synthesis of spongianone analogue through biomimetic cyclization



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Mishra, Sanjay J.; Upar, Kiran B.; Bhat, Sujata V. Tetrahedron Letters (2009), 50(46), 6402-6403.

K. B. Upar, S. Mishra, R. Khandare, S. P. Nalawade, and **Sujata V. Bhat**, **2009,** Efficient enantioselective synthesis of sclareolide and tetrahydroactinidiolide through biomimetic cyclization, *Tetrahedron Asymmetry*, *20*,1637-1640. DOI:10.1016/j.tetasy.2009.06.020

Amine Peroxides, 3-hydroxyalkyl-2-methylene-propionic acid and aplasmomycin fragment analogue as antimalarials

- N. Sundar, V. T. Jacob, **Sujata V. Bhat**, N. Valecha and S. Biswas, **2001**, Anti-malarial *t*-butyloxyamines, *Bioorganic and Medicinal Chemistry Letters*, 11, 2269-2272.DOI:10.1016/S0960-894X(01)00396-

- 1 N. Balu, J. V. Thomas and **Sujata V. Bhat, 1991,** Monoterpenic fragment analogues of Apalsmomycin as potential antimalarials', *J. Med. Chem*. 34, 2821-2824**.** (*)DOI:10.1021/jm00113a021
- M. K Kundu, N. Sundar, S. K. Kumar, **Sujata V. Bhat**, S. Biswas and N. Valecha, **1999**, Anti-malarial activity of 3-hydroxyalkyl-2-methylene-propionic acid derivatives, *Bioorganic Medicinal Chem. Letters*, 9, 731- 736**.** (*)DOI:10.1016/S0960-894X(99)00057-8

➢ **Rate Enhancements**

Microwave mediated extensive Rate Ehhancementof the Baylis-Hillman Reaction

M. K. Kundu, S. V. Bhat *et al SynLett***, 1994,** 444

Solvent Free Rapid Acetylation

Manisha Gupta, Sujat**a Bhat *et al.*** Procedure, Organic Preparations and Procedures International,**2021**,

Zeolite mediated synthesis of ϒ-alkylidene-butenolides

N. Sundar, M. K. Kundu, P. V. Reddy, G. Mahendra and **Sujata V. Bhat2002**, Zeolite mediated stereoselective synthesis of ϒ-alkylidene-butenolides, *Synthetic Communications*, 32, 1881-1886.

Facile Synthesis of Benzoquinones

• Sujata V. Bhat, R. S. Pawar, P. Rajakannu. **2020**, Facile One-Pot Synthesis and Crystal Structure of 2:1 Adducts of Myrcene (or Ocimene) with Benzoquinones, *Letters in Organic Chemistry*, 17, 624 – 627, doi/10.2174/1570178617666200227110001.

Green Syntheses

- **Sujata V. Bhat et al. 2010,** Amberlyst-15 catalyzed efficient cyclization of unsaturated alcohols: green synthesis of oxygen heterocycles, *Synthetic Communications*, *40*, 74-80. DOI10.1080/00397910902945345.
- Ravindra D. Gaikwad, Shilpi S. Kabiraj, and **Sujata V. Bhat**, **2016**, High level of stereoselectivity in the pH sensitive epoxidation and one-pot biomimetic cyclization of

olefinic alcohols with camphor and oxone®, *Flavor and Fragrance J.***31**, 350-355.DOI:10.1002/ffj.3322

- Sylvia Fernandes and **Sujata V. Bhat**, **2015**, Efficient catalyst for tandem solvent free enantioselective Knoevenagel-formal [3+3] cycloaddition and Knoevenagel-hetero-Diels– Alder reactions, *RSC Advances***, 5**, 67706-67711. DOI:10.1039/C5RA09865C
- Vijaykumar Gupta, Shilpi Kabiraj, Monica Rane and **Sujata V. Bhat**, **2015**, Environmentally benign syntheses of hexahydro-cyclopenta(b)furan and 2-oxabicyclo[3.2.1]octane derivatives, *RSC Advances***, 5**, 22951 – 22956, DOI:10.1039/C4RA14359K.