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MINI REVIEW

Ethnobotanical Uses, Phytochemistry, Biological Potential and Structural Modification of Himachalane Present in *Cedrus deodara*

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Cedrus deodara, often known as "deodara," is native to the Western side of the Himalayas. It is a medicinal herb, with a wide range of pharmacological activities that have proven to be beneficial in treating various health problems. The demand for essential oils is growing at a rapid pace. The leaves and wood of *Cedrus deodara* contain a variety of essential oils. The three components are α-himachalene, β-himachalene and γ-himachalene. *Cedrus deodara* essential oils have more applications, particularly in stress-related diseases. The main purpose is to collect and report all the essential information about various Himachalene in *Cedrus deodara*. An exhaustive literature search was undertaken to construct this study, utilizing linked publications published in various journals. This mini review's findings compile the chemical modification and synthesis of different Himachalene in *Cedrus deodara*. This study brings together and gives an up-to-date evaluation of important sesquiterpenes isolated from cedar essential oil, a family of plentiful and accessible natural materials.

Keywords: Anti-microbial activity, *Cedrus deodara*, Chemical synthesis, Essential oils, Himachalene.

INTRODUCTION

Plants have traditionally been an important source of medicinal substances. Herbal plants are used to treat most of the world's population [1]. To uncover new compounds with unique biological capabilities, the modern pharmaceutical business relies heavily on the variability of secondary metabolites [2]. Pharmaceutical agents have always been prominent in medicinal plants. Herbal plants have supplied a rich source of important components such as polyphenoles and nitrogen containing compounds, many of which have anti-inflammatory, anticancer, antibacterial [3] and other properties [4]. Chemists, biochemists and pharmacists are now engaged in herbal plants. Long-term ambitions include using medicinal chemistry approaches to uncover and develop novel chemotherapeutic medicines based on plant-derived molecular leads. [5]. These studies are essential for discovering and creating a new natural treatment that has fewer side effects while still being effective [6]. The plant is an important supplier of commercial lumber in Western Himalaya region in addition to its therapeutic benefits [7]. It's wood is of exceptional quality and its durability and resistance to rot. The facility produces many building materials and serves as a fuel supply.

The Himalayan regions are one of the world's best biodiverse areas and it encompasses the world's highest topographical region, which includes the majority of the world's main peaks. Gymnosperms are an important part of the Himalayan plant biodiversity [8]. *Cedrus deodara*, a gymnosperm native to the Himalayas, is one such example. It is a huge evergreen tree that grows to be 40 to 50 m tall [9]. The stem is branched and branches emerge from the stem in an uneven pattern, slightly rising or descending [10].

Taxonomy of *Cedrus deodara*: *Cedrus deodara* is a huge evergreen tree and is a monoecious species [11]. Vertical and diagonal fissures run through the bark, which is grey to radish brown. Female cones have a barrel form and are grown singly at the tip of dwarf shoots [12]. Fruits are oval, 3 to 6 inches long, mostly brown and have a dry outer covering. Autumn flowers are bisexual and appear in October month. Solitary, upright and pale green to purplish, male blooms is solitary and upright

[13]. Female cones are barrel-shaped, measuring 7 to 13 cm in length and 5 to 9 cm wide and when fully developed, they disintegrate, releasing winged seeds. The botanical description is shown as below:

Kingdom: Plantae	Clade: Tracheophytes
Division: Pinophyta	Class: Pinopsida
Order: Pinales	Family: Pinaceae
Genus: Cedrus	Species: Deodara

Phytochemistry: A large amount of phytoconstituents, including terpenoids [14], flavonoids and other miscellaneous compounds, have been extracted and acknowledged from various sections of *C. deodara* [15]. Sesquiterpenes is the main ingredient of the oil [16]. It contains α-himachalene (12.5%) and β-himachalene (43%), both of which are sesquiterpenes alcohols (himachalol, allohimachalol, isocentdarol and centdarol) [17]. Three high-antioxidant-activity compounds were isolated in large quantities from the plants' dried heartwood powder and identified using spectroscopic techniques [18]. *C. deodara* is responsible for 78.66% of overall phytoconstituents extracted and known from various classes of chemicals [19]. Phytochemical screening of the leaves part reveals the existence of flavonoids, tannins and saponins. Cedeodarin, cedrin, dihydromyricetin and cedrinoside have also been isolated from cedar wood [6].

Ethnobotanical uses: Local inhabitants in the Himalayan region utilize *C. deodara* widely [19]. The plant is mostly utilized for thatching, sheltering and building houses, temples and bridges [20]. In some areas, plants are also utilized as timber, torchwood and fuel wood in some areas [21]. Fever, diabetes, intestinal parasites, pulmonary difficulties and urinary illnesses are all treated with this wood, which possesses carminative, diuretic and diaphoretic qualities. The plants' resin has anticancerous qualities and is used in the treatment of rheumatism [22].

Geographical distribution: Cedar is a genus of Pinaceae family. This species of tree has been around since the tertiary period. *Cedrus brevi-folia, Cedrus deodara, Cedrus libani* and *Cedrus atlantica* are the four species known [23]. The Atlas cedar is only found in the Northern part of Africa [22]. With an estimated size of 500,000 hectares, the Himalayan cedar (*Cedrus deodara*) remains the most abundant species [24]. It is found in the Himalayan regions from Afghanistan to the western side of Nepal [25]. *Cedrus libani*, Lebanon's national tree, covers vast swaths of northern and central Lebanon's mountains [9].

The Cedrus genus has been studied as a possible curative preparation since ancient times. Ayurveda recognized therapeutic concoctions based on *C. deodara* [26]. Since antiquity, essential oils extracted from therapeutic plants have been acknowledged to exhibit antibacterial, fungal and antioxidant characteristics [27,28]. Essential oils have been extracted from a variety of plant parts, such as flowers, roots, leaves, seeds, stems, bark and wood (Table-1). These essential oils are frequently employed in medicines as medicine product ingredients (Table-2). Due to its extensive use, *C. deodara* has become a study subject of considerable interest.

Structure of some chemical constituents in cedar oil: Much chemical research has been conducted on Pinaceae species, but only a few have focused on *C. deodara* [39]. Three species, atltatica, deodara and libani, are categorized according to their chemical composition. Grimal [40] isolated ketone **1** for the first time in 1902, when he was working on the essential oils of cedar oil. Planttier & Pfau [41] discovered two sesquiterpenes ketones α-atlantone (**2**) and γ-atlantone (**3**). Thopate [17] also found additional sesquiterpenoid compounds, including allohimachalol (**4**) as well as (+)-longiborneol (**5**). Rao *et al.* [42] identified two bicyclic optically active sesquiterpenes hydrocarbons termed α-himachalene (**6**) and β-himachalene (**7**).

TABLE-1
PHYTOCHEMISTRY OF DIFFERENT CONSEQUENTS OF CEDAR OIL AND THEIR IDENTIFICATION

Class of compound	Constituents	Extract	Methods used	Ref.
Terpenoids	Himachalol	Needle oil, wood	Column chromatography	[22]
	2-β,7-β-Dihydroxyhimachalene	Wood	NMR spectroscopy	
	β-Himachalene (1.90%)	Wood essential oil	Column chromatography	[29]
	Atlantone, himaphenolone	Wood/chloroform extract	Column chromatography	[30]
	E-γ-Atlantone	Dried wood Powder	Column chromatography	[31]
	α-Himachalene (1.40%)	Wood	Column chromatography	[31]
	β-Himachalene (1.90%)	Heartwood, wood oil, needle essential oil	Column chromatography & GC-MS	[32]
Flavonoids	Cedeodarin, dihyromyricetin, cedrin, cedrinoside	Wood	NMR spectroscopy	[9]
	Myrecetin-3-O-(6"-O-E-*p*-coumaroyl)-α-D-glucopyranoside	Needles	Gel-chromatography	[33]
	3',4',5'6-Tetrahydroxy-8-methyl-dihydroflavonol	Needle oil, stem bark	Column chromatography	[31]
Lignans	Wikistromol, (-)-matairesinol benzyrolactol, nortrachelogin	Heartwood powder/chloroform extract	Column chromatography	[32]
Sterols	β-Sterol	Stem bark	Column chromatography	[33]
Saturated acid	Palmitoleic acid (40.15%), linoleic acid (9.5%)	Seed oil	Column chromatography	[34]
Diterpenoids	De-hydro-epitodomatuic acid, delta, 7-de-hydrotodomatoic acid	Wood	Column chromatography, high-performance liquid chromatography	[24]

TABLE-2
USES OF CEDAR OIL

Traditional uses	Part used	Preparation	Dose	Region	Ref.
Skin diseases					
Scabies	Wood	Oil	4-5 drops are applied	Western Nepal	[23]
Itching	Bark oil	Extract	5 mL of oil is applied topically	Niti Valley, Central Himalayas	[24]
Joint disorder					
Rheumatoid arthritis	Wood oil	Extract	A small quantity of oil extract is applied externally	Uttarakhand/India (Kalimath Valley)	[12]
Arthralgia	Bark	Paste	Applied topically	Uttarakhand/India (Kedarnath Valley)	[2]
	Wood oil	Extract	A small quantity of oil extract is applied	Uttarakhand/India (Kalimath Valley)	[35]
	Stem, bark	Oil	A small quantity of oil is massaged	Jammu and Kashmir (Shankaracharya Hills)	[36]
Microbial infection					
Bacterial infection	Heartwood	Powder	3-6 g Powder intake with water	Utrakhand/India	[25]
Boils	Bark	Paste	The bark is boiled and ground to make a paste to be applied	Chamba district, Himachal Pradesh	[37]
Fungal disease	Needles	Extract		Russi	[38]

Other compounds include, γ-atlantone (**8**), acetyldipentene (**9**), deodarone (**10**), dehydroxy-7,8-ar-himachalene (**11**), limonene carboxylic acid (**12**), α-torsol (**13**) [8] and palmitoleic acid (**14**) are also isolated. The structure of the isolated compounds are shown in Fig. 1.

Synthesis of α- and β-himachalene: Wenkert & Naemura carried out the synthesis [43], which is based on a Lewis acid-catalyzed intramolecular Diels-Alder cycloaddition of trienone (**15**). In nine stages, this derivative was synthesized from 3,3,6-trimethyl-5-heptenal (**16**) [44,45]. Compound **28** was reacted

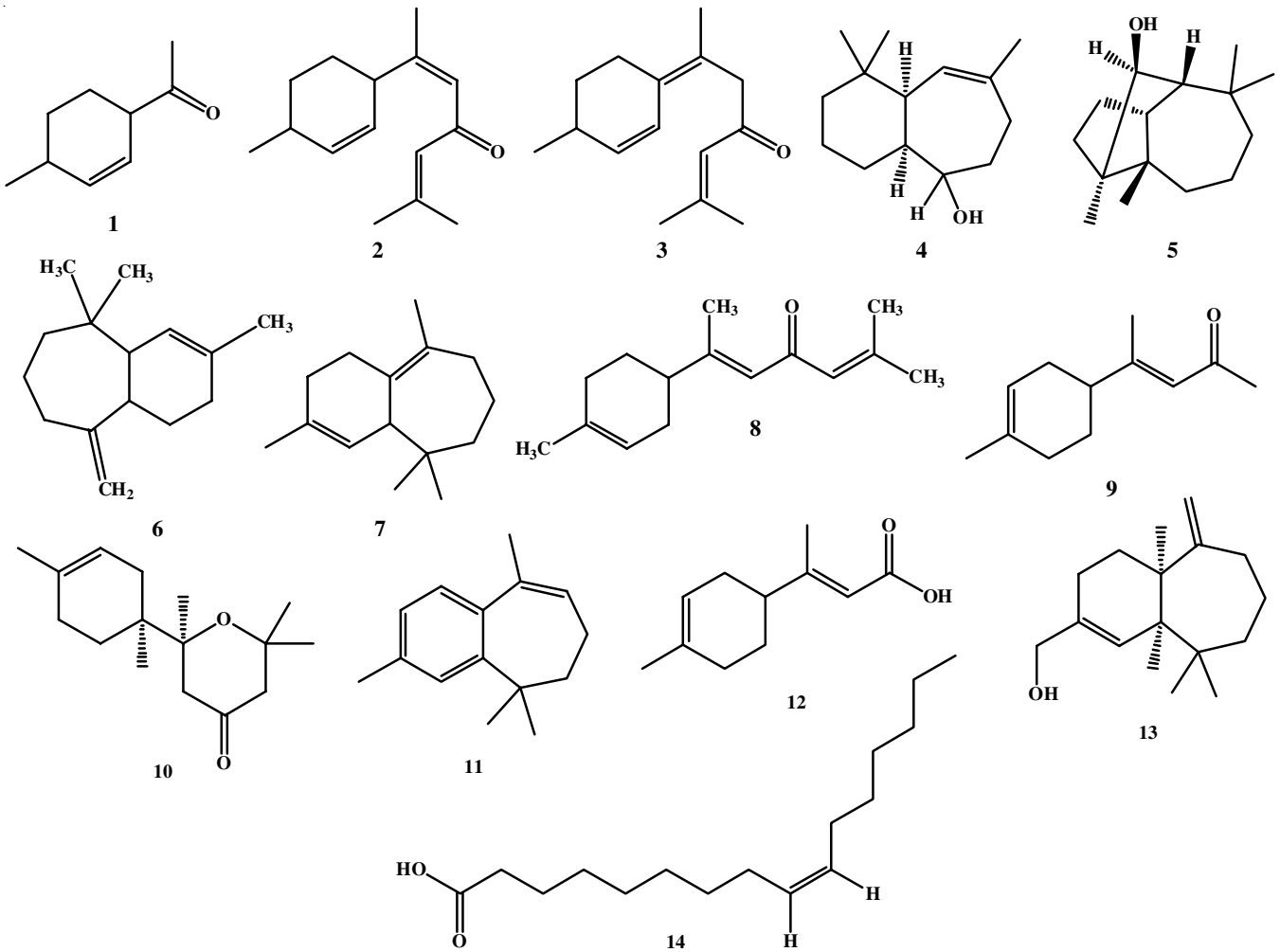


Fig. 1. Chemical constituents present in cedar

with $AlCl_3$ in toluene under reflux for 2 h, to produce octahydrobenzocycloheptanone (**17**), then with methyl lithium to produce 7-isohimachalol (**18**), which was then dehydrated to yield a mixture of bicyclic β-himachalene (**7**) and dienes-α *cis*-himachalene (**19**) [46] (**Scheme-I**).

Another method was utilized by Evans *et al.* [47] to synthesize *cis*-himachalene beginning from a chiral dienimide **20**. This chiral molecule reacts stereoselectively with acrolein to produce allylic alcohol **21**. To synthesize the trienone **22**, the latter underwent Parikh-Doering oxidation [48]. The trienone undergoes intramolecular [4+2] cycloaddition in the presence of $ZnBr_2$, resulting in the formation of product **23**, which uses LiSEt to transform into an *S*-ethyl-ketothioester [49]. The latter is decarboxylated to provide ketone **24** and the synthesis is finished by treating with Tebbe reagent (**Scheme-II**).

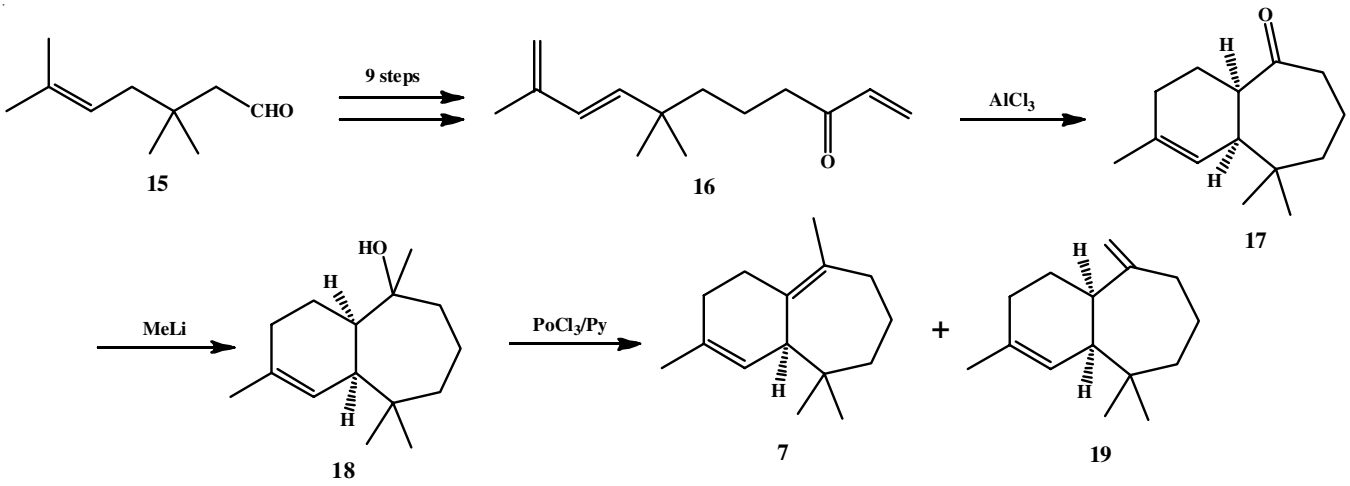
Liu & Browne [50] synthesized α-*cis*-himachalenes (**19**) and β-himachalenes (**7**) from 4,4-dimethyl-2-cyclohexenone in 11 steps with an effective overall yield of 21% *via* an intermolecular Diels-Alder process.

Chemical modification of himachalene in cedar oil

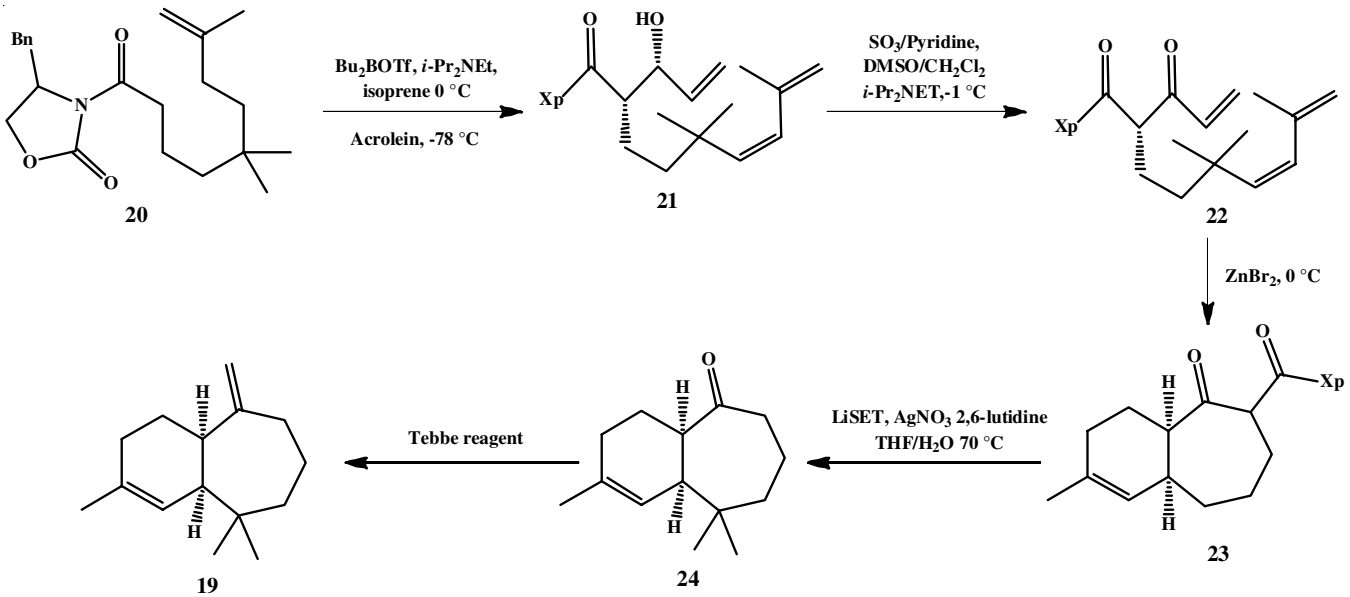
Himachalenes hydrochlorination: Hydrochlorination of himachalene (**19**) provides a mechanism to generate *trans*-himachalene [9,51]. In actuality, hydrochloric acid treatment of a mixture of himachalene yielded 3,7-dichlorohimachalane (**25**), which was subsequently crystallized from methanol to get 3-chloro-7-methylene himachalene (**26**) due to the loss of one HCl molecule [52] (**Scheme-III**).

Himachalenes oxidation with $KMnO_4$: Benharref *et al.* [52] oxidized β-himachalene (**7**) using $KMnO_4$. In this process, the tetrasubstituted double bond interacted quickly with $KMnO_4$. The production of diol **27** was quantified after treating β-himachalene (**7**) with a stoichiometric quantity of $KMnO_4$. Product **28** was regioselectivity generated in 30% yields with an excess of $KMnO_4$ in an acetone/water mixture [17] (**Scheme-IV**).

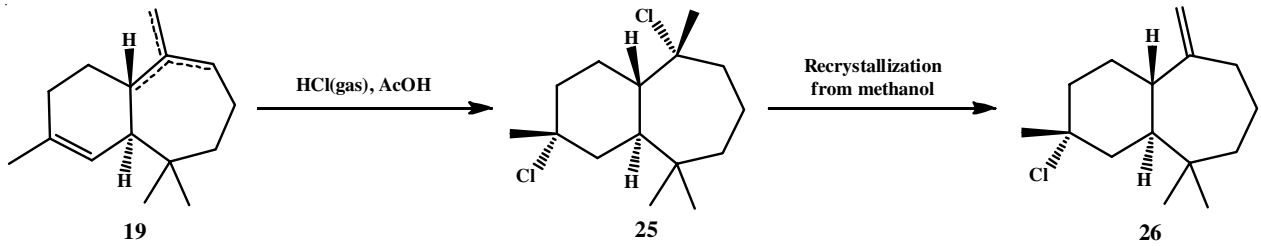
β-Himachalene undergo *gem*-dihalogenocyclopropanation: β-Himachalene (**7**) was used to make several compounds with cyclopropane rings **29**. When it is treated with dichloro-



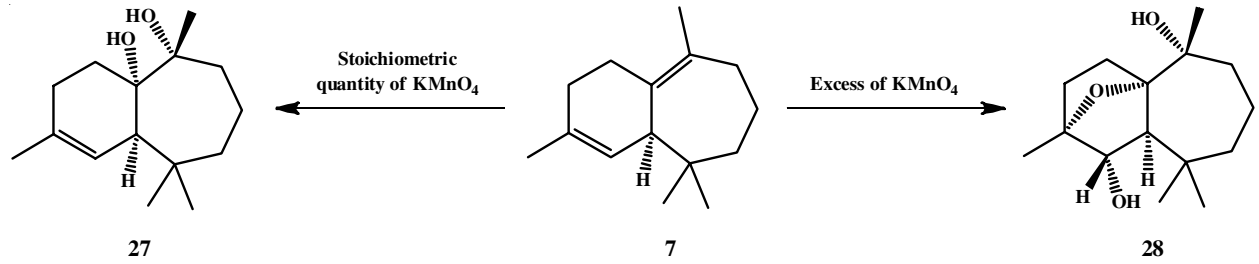
Scheme-I: α-*cis* and β-himachalene synthesis



Scheme-II: Synthesis of α-*cis*-himachalene



Scheme-III: Himachalenes hydro-chlorination



Scheme-IV: Himachalenes oxidation with $KMnO_4$

carbene produced **30** *in situ* from chloroform, whereas NaOH was used as base [50] (**Scheme-V**).

Ar-himachalene derivatives synthesis: The Friedel-Craft acylation of Ar-himachalene **31** [53] was performed with $AlCl_3$ and CH_3COCl has reached room temperature following the dehydrogenation of a mixture of the three isomers α, β and γ-himachalene [54]. The reaction produced only one product under these conditions *e.g.* 1-(3,5,5,9-tetramethyl-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-2-yl)ethanone. The acyl hydroperoxide **32** and **33** formation can be explained by the oxy-functionalization of acyl-Ar-himachalene with molecular O_2 when exposed to air **34, 35** and **36**. Nitration of Ar-himachalene with nitric acid in an acetic anhydride/acetic acid mixture yielded two products **37** and **38**. Only the dinitrate compound was obtained when the reaction was carried out in sulphuric acid medium (**Scheme-VI**).

Synthesis of (*E*)- and (*Z*)-α-altantone: Andrianome & Delmond [55] reported the synthesis of (*Z*)- and (*E*)-α-atlantone (**40** and **41**) from limonene (**39**). The most important phase of the process was synthesis of 10-(trimethyl-stannyl)limonene, which was prepared by metalating using *n*-butyllithium tetramethylethylenediamine complex and trapping with trimethyltin chloride [45]. The necessary extra isoprene unit is introduced during the acylation of stannane with senecoyl chloride [13], resulting in the formation of sesquiterpene ketones (**Scheme-VII**).

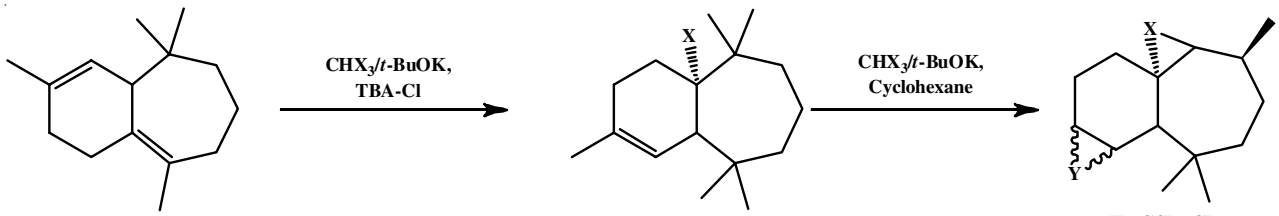
Aerobic oxidation of Ar-himachalene: Ar-Himachalene **42**, a bionature sesquiterpene, was successfully aerobically oxidized using N-hydroxyphthalimide (NHPI), under mild parameters and in the presence of Co^{2+}, yielding the relevant alcohol **43**, aldehyde **44** and COOH **45** in great yield and with great selectively [56] (**Scheme-VIII**).

In order to prepare a unique aerobic oxidation of Ar-himachalene that out performs the traditional auto-oxidants in conversion and selectively, N-hydroxyphthalimide was used as catalyst [57]. This oxidation process gives access to a wide range of important oxygen-containing molecules [33].

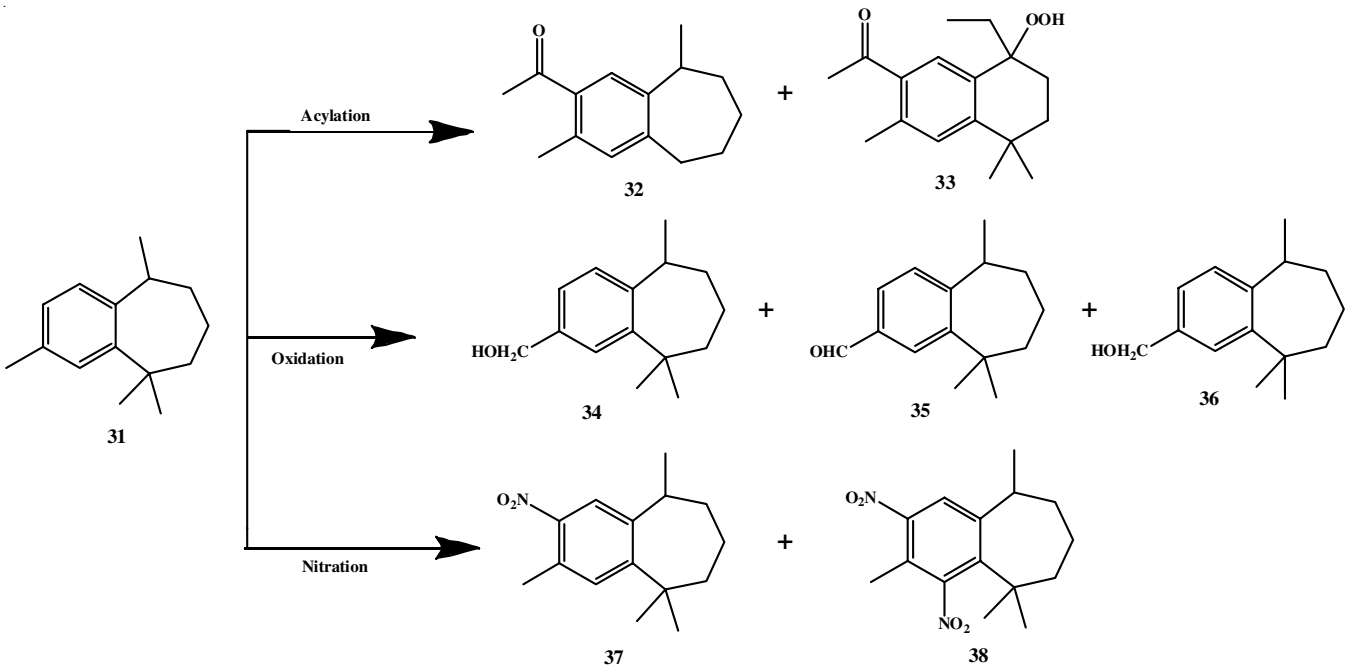
Future prospectives: Despite the plant having undergone a great deal of earlier study, scientific validation for the majority of diseases is still in a nascent stage. Compounds such as himachalol, cedrin and atlantone, for example, have been frequently described in various plant sections of *C. deodara* and identified as critical components liable for a wide range of biotic effects [24]. A thorough examination of *C. deodara* many therapeutic applications and the presence of essential bioactive components implies that the plant should be investigated right away to be developed by using thorough systematic non-clinical research as a potential candidate as well as clinical trials.

Conclusion

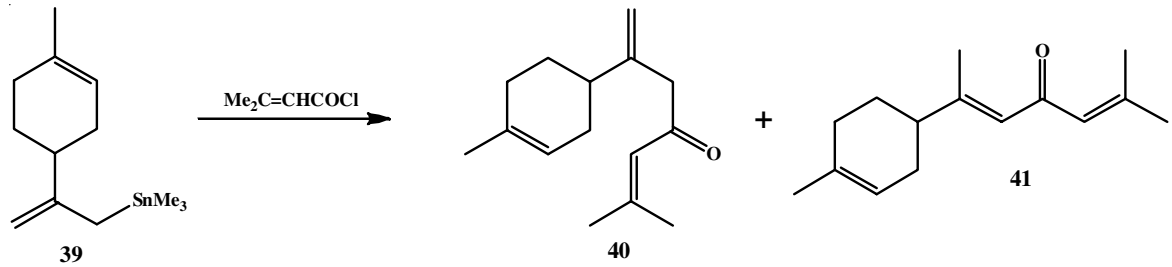
Modification of himachalene has provided a lot of pharmaceutical applications. Chemist has a strong desire to learn about the compounds that nature supplies, but to do so, they must



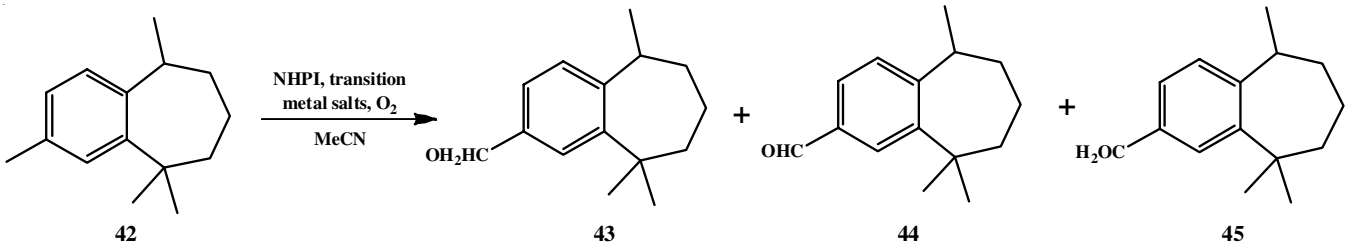
Scheme-V: β-Himachalene undergo *gem*-dihalogenocyclopropanation



Scheme-VI: Ar-himachalene derivatives-synthesis



Scheme-VII: Synthesis of (E)- and (Z)-α-altantone



Scheme-VIII: Aerobic oxidation of Ar-himachalene

first isolate chemicals from their ordinary sources and regulate their structures. This is rarely a simple operation, particularly when the compound of curiosity is present in a small amount. In this case, both the segregation methods and the accompanying examinations to determine the biological structure demand a high level of competence and technology.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. V.P. Khanduri and C.M. Sharma, *Nord. J. Bot.*, **28**, 119 (2010); https://doi.org/10.1111/j.1756-1051.2009.00335.x
2. K.H. Lee, *J. Nat. Prod.*, **73**, 500 (2010); https://doi.org/10.1021/np900821e
3. S. Parham, A.Z. Kharazi, H.R. Bakhsheshi-Rad, H. Nur, A.F. Ismail, S. Sharif, S.R. Krishna and F. Berto, *Antioxidants*, **9**, 1309 (2020); https://doi.org/10.3390/antiox9121309
4. M. Wink, *Medicines*, **2**, 251 (2015); https://doi.org/10.3390/medicines2030251
5. M.S. Butler, *J. Nat. Prod.*, **67**, 2141 (2004); https://doi.org/10.1021/np040106y
6. A. Sharma, B. Parashar, E. Vatsa, S. Chandel and S. Sharma, *World J. Pharm. Pharm. Sci.*, **5**, 1618 (2021); https://doi.org/10.20959/wjpps20168-7482
7. S.F. Syed Ab Rahman, E. Singh, C.M.J. Pieterse and P.M. Schenk, *Plant Sci.*, **267**, 102 (2018); https://doi.org/10.1016/j.plantsci.2017.11.012

8. D. Sinha, *Int. J. Green Pharm*., **13**, 13 (2019); https://doi.org/10.22377/ijgp.v13i01.2331
9. A.M. Saab, R. Gambari, G. Sacchetti, A. Guerrini, I. Lampronti, M. Tacchini, A. El Samrani, S. Medawar, H. Makhlouf, M. Tannoury, J. Abboud, M. Diab-Assaf, A. Kijjoa, R. Tundis, J. Aoun and T. Efferth, *Natural Product Res.*, **32**, 1415 (2018); https://doi.org/10.1080/14786419.2017.1346648
10. A. Kumar, R. Suravajhala and M. Bhagat, *SN Appl. Sci.*, **2**, 1045 (2020); https://doi.org/10.1007/s42452-020-2837-6
11. S. Vidyarthi, S.S. Samant and P. Sharma, *Int. J. Biodiver. Sci. Ecosyst. Serv. Manag*., **9**, 185 (2013); https://doi.org/10.1080/21513732.2013.823113
12. S. Kumar, A. Kumar, H. Pradesh, I.R. Kumar and R. Kumar, *J. Pharmacogn. Phytochem.*, 8, 2228 (2019).
13. U.A. Shinde, A.S. Phadke, A.M. Nair, A.A. Mungantiwar, V.J. Dikshit and M.N. Saraf, *Fitoterapia*, **70**, 333 (1999); https://doi.org/10.1016/S0367-326X(99)00031-3
14. H. Liu, J. Li, P. Gong and C. He, *J. Integr. Plant Biol.*, **65**, 283 (2023); https://doi.org/10.1111/jipb.13351
15. R. Ez-Zriouli, H. ElYacoubi, H. Imtara, A. Mesfioui, A. ElHessni, O. Al Kamaly, S. Zuhair Alshawwa, F.A. Nasr, Z. Benziane Ouaritini and A. Rochdi, *Molecules*, **28**, 2974 (2023); https://doi.org/10.3390/molecules28072974
16. R. Shankaranarayan, S. Krishnappa and S. Dev, *Tetrahedron*, **33**, 885 (1977); https://doi.org/10.1016/0040-4020(77)80040-9
17. T.S. Thopate, *J. Mountain Res*., **13**, 392018 (2018).
18. A. Oukhrib, M. Zaki and A. Benharref, *ARKIVOC*, 134 (2018); https://doi.org/10.24820/ark.5550190.p010.436
19. R. Parveen, M. Ahmed Azmi, R.M. Tariq, S.M. Mahmood, M. Hijazi, S. Mahmud And S.N.H. Naqvi, *Pak. J. Bot.*, **42**, 3645 (2010).
20. G. Tanwar, A.G. Mazumder, V. Bhardwaj, S. Kumari, R. Bharti, Yamini, D. Singh, P. Das and R. Purohit, *Sci. Rep.*, **9**, 7904 (2019); https://doi.org/10.1038/s41598-019-44264-6
21. A. Chaudhary, P. Sharma, G. Nadda, D.K. Tewary and B. Singh, *J. Insect. Sci.*, **11**, 157 (2011); https://doi.org/10.1673/031.011.15701
22. A. Bisht, S. Jain, A. Misra, J. Dwivedi, S. Paliwal and S. Sharma, *J. Ethnopharmacol.*, **279**, 114361 (2021); https://doi.org/10.1016/j.jep.2021.114361
23. K. Kar, V.N. Puri, G.K. Patnaik, B.N. Dhawan, D.K. Kulshrestha, R.N. Sur and R.P. Rastogi, *J. Pharm. Sci.*, **64**, 258 (1975); https://doi.org/10.1002/jps.2600640213
24. S. Kumar, B. Mitra, S. Kashyap and S. Kumar, *Pharmacognosy Res.*, **14**, 181 (2022); https://doi.org/10.5530/pres.14.2.26
25. D.K. Tewary, A. Bhardwaj and A. Shanker, *Ind. Crops Prod.*, **22**, 241 (2005); https://doi.org/10.1016/j.indcrop.2005.01.004
26. S. Raguraman and D. Singh, *Int. J. Pharmacol.*, **35**, 344 (1997); https://doi.org/10.1080/09251619708951280
27. M.A. Ibrahim, P. Kainulainen and A. Aflatuni, *Agric. Food Sci.*, **10**, 243 (2001); https://doi.org/10.23986/afsci.5697
28. X. Shi, D. Liu, J. Zhang, P. Hu, W. Shen, B. Fan, Q. Ma and X. Wang, *BMC Complement. Altern. Med.*, **16**, 245 (2016); https://doi.org/10.1186/s12906-016-1249-z
29. K. Mehta, G. Mehta, and S. K. Kapoor, *J. Org. Chem*., **39**, 2618 (1974); https://doi.org/10.1021/jo00931a038
30. P.K. Agarwal and R.P. Rastogi, *Phytochemistry*, **20**, 1319 (1981); https://doi.org/10.1016/0031-9422(81)80031-3
31. T. C. Joseph and S. Dev, *Tetrahedron*, **24**, 3809 (1968); https://doi.org/10.1016/S0040-4020(01)92589-X
32. A. Chaudhary, P. Kaur, B. Singh and V. Pathania, *Nat. Prod. Commun.*, **4**, 1257 (2009).
33. A. Chaudhary, S. Sood, P. Das, P. Kaur, I. Mahajan, A. Gulati and B. Singh, *EXCLI J.*, **13**, 1216 (2014).
34. J. Bai, Y. Wu, X. Liu, K. Zhong, Y. Huang and H. Gao, *Int. J. Mol. Sci.*, **16**, 27145 (2015); https://doi.org/10.3390/ijms161126015
35. K.J. Singh and A.K. Thakur, *Int. J. Herb. Med.*, **2**, 118 (2014).
36. V.K. Joshi, A. Joshi and K.S. Dhiman, *J. Ethnopharmacol.*, **197**, 32 (2017); https://doi.org/10.1016/j.jep.2016.07.030
36. M.O. F. Health and F. Welfare, "THE AYURVEDIC PHARMACOPOEIA".
37. R.M. Kunwar, R.P. Acharya, C.L. Chowdhary and R.W. Bussmann, *J. Ethnopharmacol.*, **163**, 210 (2015); https://doi.org/10.1016/j.jep.2015.01.035
38. D.P. Semwal, K.C. Bhatt, A. Mamgain, P.L. Uniyal and Y.M. Bahuguna, *Med. Plants-Int. J. Phytomed. Rel. Ind.*, **5**, 223 (2013); https://doi.org/10.5958/j.0975-6892.5.4.036
39. R. Parveen, M.A. Azmi, S.N.H. Naqvi, S.M. Mahmood and I.H. Zaldi, *Trop. J. Pharm. Res.*, **9**, 127 (2010); https://doi.org/10.4314/tjpr.v9i2.53699
40. E. Grimal, *Compt. Rend*., **135**, 582 (1902).
41. P.A. Plattner and A.S. Pfau, *Helv. Chim. Acta*, **20**, 224 (1937); https://doi.org/10.1002/hlca.19370200133
42. G.S.K. Rao, S. Dev and P.C. Guha, *J. Indian Chem. Soc*., **29**, 721 (1952).
43. E. Wenkert and K. Naemura, *Synth. Commun*., **3**, 45 (1973); https://doi.org/10.1080/00397917308062002
44. T.C. Joseph and S. Dev, *Tetrahedron*, **24**, 3841 (1968); https://doi.org/10.1016/S0040-4020(01)92591-8
45. T.-L. Ho and R.-J. Chein, *Helv. Chim. Acta*, **89**, 231 (2006); https://doi.org/10.1002/hlca.200690025
46. Y. Edder, I.A. Lahcen, A. Faris, N. Fdil, B. Boualy and A. Karim, *Org. Prep. Proced. Int.*, **52**, 219 (2020); https://doi.org/10.1080/00304948.2020.1751562
47. D.A. Evans, D.H.B. Ripin, J.S. Johnson and E.A. Shaughnessy, *Angew. Chem. Int. Ed. Engl*. **36**, 2119 (1997); https://doi.org/10.1002/anie.199721191
48. A. Rawat, A. Singh, A.B. Singh, S.N. Gaur, L. Kumar, I. Roy and P. Ravindrun, *Allergy*, **55**, 620 (2000); https://doi.org/10.1034/j.1398-9995.2000.00491.x
49. H. Cetin, Y. Kurt, K. Isik and A. Yanikoglu, *Pharm. Biol.*, **47**, 665 (2009); https://doi.org/10.1080/13880200902918360
50. H.-J. Liu and E.N.C. Browne, *Can. J. Chem.*, **59**, 601 (1981); https://doi.org/10.1139/v81-088
51. S.U. Upadhyay, V.B. Patel, A.A. Patel U.M. Patel and M.N. Patel, *Pharma Sci. Monit.*, **3**, 2085 (2012).
52. A. Benharref, E. Lassaba, D. Avignant, A. Oudahmane and M. Berraho, *Acta Crystallogr. Sect. E Struct. Rep. Online*, **67**, o645 (2011); https://doi.org/10.1107/S1600536811005307
53. D. Canard, O. Perru, V. Tauzin, C. Devillard and J.P. Bonhoure, *Trees*, **11**, 504 (1997); https://doi.org/10.1007/s004680050113
54. I. Hossini, M.A. Harrad, M. Ait Ali, L. El Firdoussi, A. Karim, P. Valerga and M.C. Puerta, *Molecules*, **16**, 5886 (2011); https://doi.org/10.3390/molecules16075886
55. M. Andrianome and B. Delmond, *J. Org. Chem*., **53**, 542 (1988); https://doi.org/10.1021/jo00238a013
56. M. Andrianome, K. Haberle and B. Delmond, *Tetrahedron*, **45**, 1079 (1989); https://doi.org/10.1016/0040-4020(89)80018-3
57. I. Houssini, M. A. Harrad, B. Boualy, and A. Ouahrouch, *Chem. Mater. Res.*, **6**, 110 (2014).
58. W. Partenheimer, *Catal. Today*, **23**, 69 (1995); https://doi.org/10.1016/0920-5861(94)00138-R