Synthetic Studies
To implement the theme depicted in Scheme 20 and to demonstrate its
generality, we selected 1-methylcyclohexene, 1-phenylcyclohexene, 1-methyl
cyclopentene, 1,5-cyclooctadiene and (+)-Δ₃-carene as the precursor
olefins.24 All the five olefins 71-75 were routinely transformed into their α,α-
dichloroketene adducts 76-80 Scheme 22. The method of choice for this
purpose involved trichloroacetyl chloride and off-the-shelf zinc dust in the
presence of ultrasound irradiation. Under these conditions, cleaner products
were realised and reaction times were considerably shortened. All the ketene
adducts 76-80 were duly characterised on the basis of their spectral
characteristics.

The ketene adducts 76-80, thus obtained, were subjected to the ring-
contraction-rearrangement reaction. Treatment of the adducts 76-80 with
excess of sodium methoxide in methanol under reflux, furnished the
corresponding cyclopropyl esters 81a,b-85a,b as diastereomeric mixtures in
good yields (60-80%). This was a pleasing outcome and set the stage for the
next key step. Although the mixture of the esters 81a,b-85a,b was separated
for the sake of characterization, the stereo structures to the individual
compounds could not be assigned unambiguously based on the spectral data.
The chemical shift changes were too small for a clear cut distinction.
However, for the contemplated sequence, it was not considered necessary to
separate the diastereomers. Therefore, the mixture of diastereomeric
cyclopropyl ester was carried as such for the next step.
Scheme 22

Reagents and conditions: (a) CCl₃ COCl, Zn, Et₂O, sonication.
Reagents, conditions and yields: (a) NaOMe 5eq., MeOH, Δ, 10-30 min. (b) DIBAL-H 2 eq., DCM, -78°C, 20-60 min. (c) MsCl 1.2 eq., Py. 0°C-R.T., 15min.; 35% HClO₄, Et₂O, 0°C, 30 min. (E=COOMe and X=CH₂OH)
The next key operation in this sequence was in set up the cyclopropylcarbinyl-homoallylic rearrangement in the activated "push-pull" cyclopropyl carbinol derivatives. For this purpose, the ester moiety in 81a,b-85a,b was reduced using Dibal-H at low temperatures, to furnish the corresponding cyclopropyl carbinols 86-90, respectively, as diastereomeric mixtures. The spectral data of the mixtures enabled their gross characterization.

Having obtained the required cyclopropyl carbinols 86-90 the objective now was to carry-out a fragmentation sequence to access the desired α-vinyl ketones by activating the hydroxyl group. To execute this protocol, the carbinols 86-90 were reacted with methanesulphonyl chloride in pyridine, to obtain the corresponding "push-pull" mesylates. Not surprisingly, the mesylates were not isolated but instead we directly obtained the α-vinyl ketones 91-95. However, the α-vinyl ketones 62 were found to be contami-
nated with the enol ethers 96 formed concomitantly during the reaction of carbinols 61 with methanesulfonyl chloride in pyridine, Scheme 24. Therefore, the reaction product obtained from methanesulfonyl chloride-pyridine reaction was briefly exposed to aq. perchloric acid (to hydrolyse the enol ether) and α-vinyl ketones 91-95 were isolated in good (40-75%) yield. All the α-vinyl ketones (Fig. 1-10) obtained in this sequence were duly characterised (IR, 1H and 13C NMR) and the data is presented in the experimental section.

This simple and short protocol for the synthesis of α-vinyl ketones 62, from olefins 58 prompted us to seek further applications in the synthesis of terpenes, particularly those bearing a quaternary carbon centre. The high regio- and stereoselectivities in the addition of the dichloroketene was expected to influence the stereochemical outcome of the α-vinyl ketones, leading to the formation of a single diastereomer and paving the way for the enantioselective synthesis of (+)-α–elemene and other useful carbocyclic skeleta starting from the monoterpene chiral pool.

First Enatioselective Synthesis of (+)-α–Elemene

Elated by the success in the development of a new protocol for the generation of α-vinyl ketones, from the corresponding olefin equivalents, it was considered essential to demonstrate its practical utility to the synthesis of some structurally related natural product skeleta. In this pursuit, the elemene group of sesquiterpenes (Chan 225a-f with the vinyl and the methyl groups
strategically placed at the quaternary centre, attracted our immediate attention. In this section is reported the first enantioselective synthesis of (+)-α-elemene 97 using the aforementioned protocol, from readily available R-(+)-limonene,

Chart 2

(+)-α-elemene 97, a sesquiterpene hydrocarbon, was first isolated by Ivanov et al., in 1955 from the oil of *Bulgarian zdravets*. The structural evidence of (+)-α-elemene 97, the main product obtained in the dehydration of elemol, was provided by Paknikar *et al.*, on the basis of degradative and NMR studies. In 1977, Vig and his co-workers have reported the synthesis
of racemic \( \alpha \)-elemene. However, the enamioselective synthesis of \((+)-\alpha\)-Elemene 97 has not been reported in the literature.

Terpenes, among the "chiral pool", continue to attract attention in the enantioselective synthesis of complex natural products. They can be conveniently homologated, annulated and restructured into useful natural product skeleta through simple chemical transformations.\(^\text{29}\) The readily available chiral monoterpane \( \text{R-}(+)-\text{limonene} \) 106 with pre-installed isopropyl and

**Scheme 25**
methyl groups in 1,4-relationship, as present in the elemene group of sesquiterpenes and our target molecule 97, led us in select it as the starting material. Through the recognition of structural patterns present in limonene and the target structure 97, and keeping in mind our two carbon methodology for generating the α-vinyl ketone moiety, a retrosynthetic strategy could be formulated as shown in Scheme 25.

The α-vinyl ketone 64 and the enone 104 were identified as the advanced intermediates for the synthesis of (+)-α-elemene.

To execute the synthetic plan revealed through the retrosynthetic analysis, R-(+)-limonene 106 was regioselectively hydrogenated over

![Scheme 26](image)

Reagents, conditions and yields: (a) H₂/PtO₂, EtOH, 90% (b) CCl₃ COCl, Zn, Et₂O, sonication, 65%.
platinum oxide to furnish the desired R-(+)-dihydrolimonene 63 in 90% yield. The olefin 63 on reaction with α,α-dichloroketene, generated from trichloroacetyl chloride and zinc dust in the presence of ultrasound irradiation furnished the expected [2+2]-adduct 107 stereoselectively, in 65% yield, Scheme 26. The spectral data of the adduct 107 was in full agreement with its formulation. The IR spectrum showed a strong absorption at 1800 cm⁻¹ due to the presence of the carbonyl moiety and the ¹H NMR spectrum exhibited a characteristic proton resonance at δ 3.70-3.50 (m, 1H) corresponding to the ring junction proton. A 12 line ¹³C NMR spectrum with carbon absorptions at δ 195.3 and 92.1 characteristic of the carbonyl carbon and the carbon attached to the chlorine atoms, further confirmed the formulation of the ketene adduct 107. The formation of a single diastereomer was an expected and satisfying outcome. We had reasoned on the basis of previous precedences that the ketene addition to the visubstituted double bond will occur from the face opposite to the isopropyl group. Having acquired the ketene adduct 107 in good quantities, our next objective was to carry-out the ring contraction-rearrangement protocol to get the cyclopropyl esters 108a,b. Exposure of the ketene adduct 107, to the sodium methoxide-methanol milieu yielded a diastereomeric mixture of "push-pull" cyclopropyl esters 108a,b in 75%, Scheme 27.

The IR spectrum of the mixture 108a,b with a strong absorption at 1720 cm⁻¹, and sharp singlets in ¹H NMR spectrum at δ 3.64 and 3.63 due to carbomethoxy functionality provides strong evidence of its formation. At this
Reagents, conditions and yields: (a) NaOMe-MeOH. Δ, 75%

stage, the mixture was not required to be separated and the same was carried over to the reduction-step. However, the mixture was separated for characterization purpose, and each diastereomer was found to be in agreement with its gross formulation.

The mixture of the esters 108a,b on reduction with Dibal-H, furnished a diastereomeric mixture of bicyclic cyclopropyl carbinols 105 in 80% yield. Scheme 28. A strong absorption at 3350 cm\(^{-1}\) in the IR spectrum established the presence of the hydroxy group. However, reduction of the ester mixture 108a,b with LAH was found to be more efficient, especially for large scale preparation.
Reagents, conditions and yields: (a) Dibal-H, DCM, -40°C, 80% (b) LAH, Et₂O, RX 75%

The crude carbinol mixture 105 obtained, was directly subjected to the key ring-opening reaction to generate the α-vinyl ketone moiety. Brief reaction of the alcohol mixture 105 to methanesulfonyl chloride and pyridine followed by exposure to aq. HCICO₄ resulted in the facile ring opening via the cyclopropylcarbinyl-homoallylic rearrangement to furnish a single diastereomer, the α-vinyl ketone 64, Scheme 29, in 78% yield. A strong carbonyl absorption at 1705 cm⁻¹ in the IR spectrum and the presence of the typical vinyl moiety resonances, between δ 6.2-6.0 and 5.2-4.9, in the ¹H NMR spectrum (Fig. 11), and the signals at δ 214.0, 142.8 and 112.8 characteristic of the carbonyl and the olefinic carbons, respectively, in the ¹³C NMR spectrum (Fig 12) confirmed the identity of its formulation. Later, we found that the 105—>64 transformation involving cyclopropyl cleavage can be carried out more efficiently (90% yield) on exposure to in situ generated
Reagents, conditions and yields: (a) MsCl, Py, 0°C. R.T., 15 min.; 35% aq. HClO₄, ether, 0°C, 30min., 78% (b) Me₃SiI, MeCN. R.T., 90%

trimethylsilyl iodide (TMSI). In this way, further treatment with aq. perchloric acid was not required as the intermediate enol ether of the type 96, if formed was also cleaved by TMSL.

For elaboration to the elemene skeleton, a C₃-unit had to be added to the carbonyl group of C₁₂-ketone 64. For this purpose, addition of isopropenyllithium and isopropyllithium to 64 was attempted. However, the ketone 64 was found to be unreactive, with a portion of it getting convened to either the alcohol 65 or 109 under the reaction conditions and the major portion remaining intact, despite long reaction times. The separation of the alcohols 65 and 109, which were themselves mixtures of diastereomers from the precursor ketone 64 was found to be a tedious exercise and alternative methods to avert this situation were sought.
Reagents, Conditions and Yields: (a) Isopropenyllithium, THF, R.T., sonication, 80%  (b) Isopropyllithium THF, R.T., sonication, 80% (both yields based on recovery of starting material)

The sluggish reactivity of the ketone 64 was attributed to the steric hindrance by the isopropyl group and the quaternary carbon bearing the vinyl group on both the faces of the carbonyl group. To circumvent this problem and to continue with our approach, it was decided to transform the ketone 64 into the enone 104. The carbonyl group of the enone 104 was expected to project outward with the introduction of the unsaturation in the ring system and thus partially relieve the steric hindrance caused by the neighbouring isopropyl substituent.

After considerable trial and error, it was found that, dehydrogenation of the α-vinyl ketone 64 with selenium dioxide in ten.-butanol delivered the required enone 104 in 45% yield (based on the recovery of the starting material) Scheme 31. The formation of the enone 104 was fully consonant
Reagents, conditions and yields; (a) SeO$_2$, Bu$^\dagger$OH, Δ, 45%

with its UV, IR, $^1$H and $^{13}$C NMR spectral data. The IR spectrum showed the presence of the enone carbonyl moiety at 1670 cm$^{-1}$ and the $^1$H NMR spectrum (fig 13) exhibited the presence of the $\alpha$-proton of the enone and characteristic vinylic protons at $\delta$ 5.85 (s, 1H), 5.84 (dd, 1H) and 5.20-4.90 (m, 2H), respectively. In particular, the $^{13}$C NMR spectrum (fig 14) had signals at $\delta$ 202.1, 170.0, 140.9, 122.7, 114.0 corresponding to the carbonyl and four olefinic carbons.

Having acquired the enone 104, our next objective was to implement a 1,2-nucleophilic addition on the carbonyl group of the enone 104, with suitable alkyl lithium reagent. Thus, treatment of the enone 104 with isopropyl lithium in THF, under ultrasound irradiation, furnished a diastereomeric mixture of the carbinols 103.
Reagents, conditions and yields; (a) 2-propyllithium, THF, ultrasound (b) p-TsCl, CHCl₃, R.T., 42% from 104.

In 103, with all its carbon atoms placed in requisite positions, functional group fine-tuning was sought to accomplish the total synthesis of (+)-α-elemene 97. A dehydration reaction was, therefore, executed on the alcohol mixture 103 and was found to be very facile. Indeed, traces of dehydration product were noticed even in the ¹H NMR sample prepared in chloroform-d. However, exposure of the carbinol mixture 103, to p-toluencesulphonyl chloride in chloroform and filtration through a column delivered (+)-α-elemene 97, in 42% yield, Scheme 32. The spectral data UV, IR, ¹H & ¹³C NMR of 97 were found to be in full agreement with its formulation. The ¹H NMR spectrum (Fig. 15) clearly exhibited the presence of the α-proton of the diene moiety at δ 6.37 (s, 1H) and the typical vinylic proton resonances at δ 5.78 (dd, 1H) 5.10-4.90 (m, 2H). A 15 line ¹³C NMR spectrum (Fig 16) with the carbon resonances at δ 149.7, 146.3, 128.1, 124.5,
119.7 and 112.4 due to their olefinic moieties, established the structural identity of the natural product.

The specific rotation of the synthetic sample trained by us ([α]_D = +112.5) matches with that of the natural product ([α]_D = +116) supports the

While elucidating the structure of α- elemene 97, Paknikar et. al.\textsuperscript{27} found it difficult to differentiate between the two possible isomeric structures 97 & 110 for this hydrocarbon. Their degradative studies leading to structure 97 for α-elemene, though correct, was not based on unambiguous deductions. Our NOESY spectrum (Fig. 17) settles the structure of 97 unambiguously.
absolute configuration assigned earlier to (+)-α-elemene 97. Thus, the first enantioselective synthesis of (+)-α-elemene 97 was accomplished.

Although the synthesis of (+)-97 was achieved from R-(+)-limonene, the unsatisfactory yield and the difficult chromatographic separation impeded easy access of the enone 104. To circumvent this problem, it was considered appropriate to use an alkene equivalent that can directly furnish the enone 104, during the cyclopropyl ring opening process. In this context, we realised the importance of (+)-2-carene as the chiral synthon for our projected synthesis of (+)-α-elemene 97.

**Scheme 33**

Reagents, conditions and yields: (a) CC13 COC1, Zn, Et₂O, ultrasound, 95%.

The commercially available (+)-2-carene was subjected to the four-step transformation as described earlier for the generation of α-vinyl ketone
moiety. Treatment of (+)-2-carene 111 with α,α- dichloroketene under sonication conditions furnished the required ketene adduct (+)-112, stereoselectively in 95% yield. Scheme 33, and the IR spectrum of the product showed a strong absorption at 1803 cm⁻¹ characteristic of α,α-dichlorocyclobutane. The ¹H NMR spectrum, and in particular, the ¹³C NMR spectrum resonance at 8 196.6 corresponding to the carbonyl carbon atom established the identity of the ketene adduct 112.

Encouraged by the high yield in the dichloroketene adduct formation we turned our attention towards the ring contraction-rearrangement protocol.

**Scheme 34**

Reagents, conditions and yields; (a) NaOMe-MeOH, heat, 63%.

Treatment of the ketene adduct (+)-112, with sodium methoxide in methanol under reflux, gave a diastereomeric mixture of cyclopropyl esters 113a,b in 63% yield. Scheme 34. The IR spectrum showing strong carbonyl absorption
at 1730 cm$^{-1}$ and the sharp singlets in the $^1$H NMR spectrum at $\delta$ 3.65 due to carbomethoxy group confirmed the formulation of 113a,b. For the sake of characterization, 113a and 113b were separated and the spectral data is gathered in the experimental section. However, separation of the mixture was not required at this stage and it was carried over to the next step.

Reduction of the ester moiety in 113a,b with LAH in ether furnished the corresponding diastereomeric mixture of alcohol 114, in 92% yield. A strong infrared absorption at 3372 cm$^{-1}$ confirmed the formation of the cyclopropyl carbinol moiety. Brief exposure of the crude alcohol mixture 114 to TMSI, resulted in a facile fragmentation via cyclopropylcarbinyl-

![Scheme 35](image)

**Scheme 35**

**Reagents, conditions and yields:** (a) LAH, Et$_2$O, R.T., 92% (b) TMSI, MeCN, R.T., 85%.
homoallylic rearrangement to deliver the enone (-)-104 in 85% yield, as a single stereoisomer, Scheme 35. Formation of 104 from 114 is quite interesting as two cyclopropane rings are cleaved regioselectively in a single pot reaction. Whether this cleavage takes place in a concerted manner 115 (higher order fragmentation?) or in a step-wise manner 116 is not clear at this point, Scheme 36.\textsuperscript{34}

Scheme 36

As this enone was identical with the enone 104 obtained from R-(+)-limonene, on the basis of both spectral and optical rotation data, it should be possible to transform this into (+)-\(\alpha\)-elemene 97.
Germacrenes

As a logical continuation to our new protocol, we ventured to pursue the synthesis of medium ring carbocycles. Among the medium ring carbocycles, the germacrane group (Chan 35a-f) comprising of a 10-membered ring occupies a prominent position because of their wide occurrence, biological activity of some of the compounds, e.g., periplanone-A&B and their role as biogenetic precursors of many polycyclic sesquiterpenes, e.g., guaianes and eudesmanes. It is worth noting that germaacranes are biogenetic precursors of many structural types that are

**Chart 3**

<table>
<thead>
<tr>
<th>Chemical Structure</th>
<th>Formula</th>
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<tbody>
<tr>
<td>Germacrene A</td>
<td>117&lt;sup&gt;35a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Germacrone</td>
<td>118&lt;sup&gt;35b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Curdione</td>
<td>119&lt;sup&gt;35c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Germacradiene-11-ol</td>
<td>120&lt;sup&gt;35d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Periplanone A</td>
<td>121&lt;sup&gt;35e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Periplanone B</td>
<td>122&lt;sup&gt;35f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
present among pheromones, antibiotics, cytotoxins and antitumor agents. Consequently, there has been a great deal of interest in the synthesis of germacrane-based sesquiterpene natural products and many new and ingenuous methodologies have been developed.  

The ready availability and the strategic disposition of both the isopropyl and methyl groups in the α-vinyl ketone 64, turned our attention towards the synthesis of deoxycurdione 66, a germacrane type sesquiterpenoid. Our approach towards the synthesis of germacrane ring system through an oxy-Cope pathway is delineated through the retrosynthetic route shown in Scheme 37.

Scheme 37

As per this protocol, nucleophilic addition of isopropenyl lithium to the ketone (+)-64, was expected to deliver the 1,2-divinylcyclohexanol 65a,b, An oxy-Cope rearrangement was expected to lead the germacrane skeleton.
The synthetic plan was put into practice by the addition of isopropenyllithium to the α-vinyl ketone (+)-64, under sonication conditions to give a diastereomeric mixture of 1,2-divinylcyclohexanols 65a,b in 80% yield (based on the recovery of the starting material), Scheme 38. The IR spectrum of the mixture of alcohols 65a,b showed a strong absorption at 3475 cm\(^{-1}\) corresponding to the alcohol moiety. At this stage, separation of the alcohol mixture 65a,b was not attempted and the same was carried over to the next step.

The mixture of alcohols 65a,b, thus obtained, was first subjected to a thermal oxy-Cope rearrangement- However, thermal activation up to ~250°C only led to mixtures of dehydration products and no characterizable material could be isolated. Recourse was, therefore, taken to the anionic version of the
oxy-Cope rearrangement. Treatment of the mixture of alcohols 65a,b with KHMDS in the presence of 18-crown-6, furnished the desired ring expanded product 66 \([\alpha]_D -34.6\) (lit.\(^{37}\)[al]_D -50.28) in 60% yield. Scheme 39. The spectral data of the ketone 66 was fully consonant with its formulation, with

Scheme 39

Reagents, Conditions and Yields: (a) KHMDS, 18-crown-6, THF. \(\Delta\), 60%

the \(^1\)H NMR spectrum (Fig. 18) showing an olefinic proton at \(6 4.80-5.00\) (m, 1H) and the \(^{13}\)C NMR spectrum (Fig. 19) exhibiting the presence of carbonyl resonance at \(\delta 215.9\), establishing the formation of deoxycurdione (-)-66. The spectral data for (-)-66 were found to be identical with that reported for this compound in the literature.\(^{37}\) The oxy-Cope process was highly diastereoselective, in the sense that only one diastereomer was produced.

The possibility of constructing a germacrane derivative with additional functionality in the 10-membered ring was also been attempted following a similar synthetic plan, starting from the chiral \(C_{12}\)-enone (-)-104
and involving oxy-Cope process as the pivotal step, Scheme 40. Addition of isopropenyllithium to the enone (-)-104, under sonication conditions smoothly

**Scheme 40**

![Reaction Scheme](image)

Reagents, Conditions and Yields: (a) isopropenyllithium, THF, ultrasound, R.T., 61%.

furnished a diastereomeric mixture of allylic alcohols 123. The IR spectrum of the mixture 123 showed a strong alcohol absorption at 3428 cm$^{-1}$, along with other relevant features. However, efforts to transform the alcohol mixture 123 into the desired 10-membered ring compound 124 under a variety of anionic and thermal reaction conditions were unsuccessful.

**Synthesis of a cis-Diquinane Synthon**

As a part of our ongoing project on the synthetic applications of the alkene to $\alpha$-vinyl ketone transformation protocol, a new approach for the synthesis of cis-diquinane 126 was considered. The ready availability of the enone 104, both from R-(+)-limonene 106 and (+)-2-carene 111, prompted us
to convert it to a diquinane derivative like 126 through an intramolecular [2+2]-photocycloaddition-fragmented on strategy. **Scheme 41**

The *cis*-diquinane frame-work, with a quaternary carbon centre, is an important structural moiety present in a variety of polyquinane based natural product skeleta. Some representative examples of the natural products containing this structural moiety are delineated in Chan 4. These molecules constitute challenging targets for the synthesis because of the dense functionalisation and unusual carbocyclic frame-work.

Synthetic strategies towards these molecules require a simple and rapid assembly of the *cis*-diquinane moiety endowed with a quaternary carbon centre. Although several strategies for the construction of these moieties were reported in the literature, the enantioselective approaches are limited. The following is an account of a novel enantioselective approach for the easy and rapid access of the *cis*-diquinane moiety from readily available chirors R-(+)-limonene 106 and (+)-2-carene 111.
intramolecular [2+2]-Photocycloaddition in the enone 154, effected through irradiation from a 450W Hanovia medium pressure lamp through a pyrex filter, afforded the tricyclic ketone 125 in 87% yield, Scheme 42. The IR spectrum of the product 125 exhibited a strong absorption at 1759 cm⁻¹.
due to a cyclopentanone moiety. The $^1$H NMR spectrum (Fig. 20) signals for the quaternary methyl and isopropyl groups at $\delta$ 1.20 (s, 3H), 0.95 (d, 3H) and 0.88 (d, 3H) respectively, confirmed the formation of the cycloaddition product. In particular, a 12 line $^{13}$C NMR spectrum (Fig. 21) with diagnostic carbon resonance at $\delta$ 218.4 due to carbonyl carbon established the formulation of the ketone 125. Expectedly, both the $^1$H & $^{13}$C NMR spectra were transparent in the olefinic proton and sp$^2$-carbon regions.

The formation of the tricyclic photoproduct 125. in high yield, encouraged us to administer a regiospecific fragmentation reaction. Exposure of the photoadduct 125 to BF$_3$-etherate resulted in a facile fragmentation to give the desired cis-diquinane 135 in 50% yield, Scheme 43, with the spectral data of the product 135 in full agreement with its formulation. The $^1$H NMR
Scheme 43

Reagents, Conditions and Yields: (a) BF$_3$-Et$_2$O, DCM, R.T., 50%.

(Fig. 22) signals at $\delta$ 1.70 (s,3H), 1.63 (s,3H) and 1.08 (s, 3H) due to the isopropylidene and quaternary methyl groups and a 12 line $^{13}$C NMR spectrum (Fig. 23) with characteristic signals at $\delta$ 223.5, 138.6 and 123.7 due to carbonyl and olefinic carbons, established the identity of the compound 135.

Scheme 44

Reagents, Conditions and Yields: (a) O$_3$, DCM, -78°C, 87% or RuCl$_3$,
MeCN-CCl$_4$-H$_2$O, NaIO$_4$, 76%
Having obtained the required cis-diquinane 135 moiety, it was considered necessary to oxidatively cleave the isopropylidene group by either cat.ruthenium oxidation or ozonolysis, to give the bifunctional cis-diquinane dione 126. Ozonolysis of the cis-diquinane 135 proceeded smoothly to give the bifunctional (+)-cis-diquinane dione 126, \( [\alpha]_D^+ +289.45 \), with an angular methyl group, in 87% yield Scheme 44. Catalytic ruthenium oxidation of the cis-diquinane 135 also afforded the cis-diquinane dione in 76% yield. The spectral (Fig. 24 & 25) and analytical data of the dione 126 were in agreement with its formulation. The 9 line \(^{13}\)C NMR spectrum with two carbonyl signals at \( \delta 221.4 \) and 220.0 established the presence of two cyclopentanone rings. The chiral dione 126 with its secured stereochemistry and strategic placement of the functionality in the two rings is a promising starting point for further polyquinane synthesis.

Towards the Synthesis of AB Rings of Taxol 136 (Paclitaxel®)

Having successfully applied the olefin 58 -> αvinylketone 62 methodology to the enantioselective synthesis of (+)-α-elemene, germacrane and diquinane skeleta, we considered further opportunities in the synthesis of more complex molecules like taxol 136.

Taxol 136 is a densely functionalized, tetracyclic diterpenoid isolated from the Western Yew (Taxus brevifolia) by Wall, Wane and co-workers in 1971.\(^{39}\) Its proven efficacy as an anti-cancer drug, has elicited a great deal of biochemical attention from both clinical perspective and medicinal chemistry
point of view Despite its clinical activity against ovarian, breast and several other cancer cell lines, the sources of its supply remains limited.

Structure

The paucity of the material being a major impediment for its successful usage in clinical trials, the demand for its supply can only be achieved by a semi- or total synthesis. So far, only three successful total syntheses of taxol have been reported in literature as a result of massive efforts and their accomplishment is regarded as major milestone in contemporary organic synthesis. The semi-synthesis of taxol has been projected as an attractive alternative, as the lengthy total syntheses have received little interest from commercial considerations. Various research groups have since been engaged in the investigation of a pro-drug version of taxol for their successful application in clinical usage. Presently, the focus of attention is directed towards the development of improved analogue of the drug.
While the successful syntheses of taxol have been few, the number of methodologies and strategies evolved for the construction of various ring fragments and substitution patterns is very large and impressive and reflect the ongoing world-wide interest in this molecule.\textsuperscript{40}

We recognised the importance of our newly developed protocol in the context of taxol, and began a model study on the construction of AB ring portion 137 of its tetracyclic framework- A retrosynthetic approach invoking the aforementioned methodology is represented in the Scheme 45.

As indicated in the retrosynthetic analysis, the $\alpha$-vinyl ketone 68, was identified as an advanced precursor in the construction of AB rings of taxol. The $\alpha$-vinyl ketone 68 can be readily accessed from (-)-pinene 67 via the protocol evolved during the present study through the formation of the "push-pull" bicyclic $\beta$-methoxy cyclopropylester 138a,b. When treated with a suitable nucleophile the ketone 68, with a strategically positioned olefin, can be used to generate an oxy-Cope system 69. The oxy-Cope transformation on the alcohol 69 can be expected to lead to the formation of the ketone 70 which can be further transformed into the AB rings of taxol 137 through a light irradiated [1.3] sigmatropic alkyl shift.

As a first step towards the synthesis of the framework 137, the synthesis of the $\alpha$-vinyl ketone 68 was attempted. For this purpose, the cheap
and commercially available monoterpen e (-)-α-pinene was chosen as the starting material to prepare optically active α-vinyl ketone 68,
Addition of $\alpha,\alpha$-dichloroketene, generated in situ from trichloroacetyl chloride and zinc, to (-)-$\alpha$-pinene, under ultrasound initiation, preceded in

**Scheme 46**

![Scheme 46](image)

**Reagents, Conditions and Yields; (a) CCl$_3$COCl, Zn, Ether. ultrasound, 30 min., 40%.

modest yield to give the ketene [2+2]-adduct (+)-139 in 40% yield. Scheme 46. The spectral data of the ketene adduct was in full agreement with the reported values. The steric hindrance of the olefin in the rigid tricyclic system was found to be the main reason for the low yield in the ketene addition reaction. However, the ready availability of the (-)-$\alpha$-pinene allowed us to prepare ketene adduct (+)-139 on multigram scale. The stereochemistry of the ketene addition follows from the expected addition from the *endo-face* opposite to the *gem*-dimethyl bearing methano-bridge.

Having accessed the ketene adduct (+)-139 in good quantities, our next objective was to effect the ring contraction-rearrangement step. The
ketene adduct (+)-139 was subjected to sodium methoxide mediated rearrangement in methanol to deliver a diastereomeric mixture of cyclopropyl esters 138a,b in 73% yield, Scheme 47. The IR spectrum of the mixture of isomers exhibited a strong carbonyl absorption at 1750 cm\(^{-1}\). The sharp resonances at \(\delta 3.67\) and 3.66 in the \(^1\)H NMR spectrum due to carbomethoxy functionality in 138a,b confirmed their formulation.

**Scheme 47**

![Scheme 47](image)

**Reagents, conditions and yield:** (a) NaOMe (5 eq.), MeOH, \(\Delta\), 30 min., 73%.

However, separation of the diastereomer mixture was not required and the same was carried over to the reduction step. Reduction of the ester moiety present in 138a,b, with DIBAL-H, furnished the required cyclopropyl carbinol 140, again as a mixture of diastereomers, Scheme 48. A strong absorption at 3376 cm\(^{-1}\) in the IR spectrum due to the presence of hydroxy group established the identity of the carbinol 140.
Reagents, conditions and yields: (a) DIBAL-H, DCM. -78°C 30 min., 72%.

Satisfied by the high yields in the ring contraction-rearrangement and the subsequent reduction steps, the cyclopropylcarbinyl-homoallylic rearrangement was now attempted. The crude carbinol mixture 140 on treatment with methanesulphonylchloride in pyridine, yielded the enol ether 141, Scheme 49. The spectra IR, $^1$H & $^{13}$C NMR of the enol ether were in agreement with its formulation. The resonances at $\delta$ 5.77(dd, 1H), 5.04(d, 1H), 4.99 (d, 1H) and 4.86(d, 1H) in the $^1$H NMR spectrum established the presence of the vinyl protons and the proton on the enol ether functionality.

The enol ether 141 was hydrolysed with aq. 35% perchloric acid at 0°C to furnish the desired (-)-$\alpha$-vinyl ketone 68 in 65% yield as a single stereoisomer. The IR spectrum showed the presence of the carbonyl moiety at 1720 cm$^{-1}$ and the characteristic vinylic proton pattern was observed in the
Reagents, conditions and yields: (a) Py, MsCl, 0°C, 30 min. 89% (b) 35% HClO₄(aq.), Ether, 0°C, 65%.

¹H NMR spectrum (Fig. 26) at δ 5.63 (dd, 1H), 5.03(d, 1H) and 4.84(d, 1H) confirming the formation of the (-)-α-vinyl ketone 68. A 12 line ¹³C NMR spectrum (Fig. 27) with carbonyl and olefinic carbon resonances at δ 214.8, 143.3 and 113.4 further supported the formulation of (-)-68.

Our next goal was to convert the α-vinyl ketone (-)-68 into a 1,2-divinyl carbinol 69 to carry out the oxy-Cope rearrangement as outlined in the retrosynthetic analysis, Scheme 45. To transform the (-)-α-vinyl ketone 68 to the 1,2-divinyl carbinol 69, a simple vinyl Grignard/alkyl lithium reagent addition to (-)-68 was sought.

Addition of vinyl lithium or vinyl magnesium bromide to the ketone (-)-68 did not give the required 1,2-addition product 69 but resulted either in
the recovery of starting material or some complex and uncharacteristic reaction mixture. Scheme 50.

Attempts to carry out the nucleophilic addition to the ketone (-)-68, under different reaction conditions and with varied reagents, proved to be unsuccessful. Efforts to activate the carbonyl functionality in (-)-68 with reagents like cerium chloride\textsuperscript{42} and lithium perchlorate\textsuperscript{43} were also unsuccessful. The reason for this was attributed to the steric hindrance experienced by the carbonyl group due to the presence of \textit{gem}-dimethyl bearing methano-bridge and the flanking quaternary centre with a methyl and vinyl groups.

Alternate methods to overcome this problem were therefore sought to prepare the 1,2-divinyl carbinol 69. At this stage the use of a sterically less demanding nucleophile, like lithium acetylide, which can probably approach the hindered carbonyl group easily to effect the required nucleophilic addition was considered. This possibility was put into practice and the lithium
Acetylide-ethylene diamine complex was allowed to react with the (-)-α-vinyl ketone 68, Scheme 51. Reaction of lithium acetylide ethylenediamine complex with the ketone (-)-68 resulted in the formation of a diastereomeric mixture of ethynyl vinyl carbinol 142 in 27% yield. A strong absorption at 3400 and 3306 cm\(^{-1}\) in the IR spectrum revealed the presence of the hydroxy and alkyne functionality, respectively. The \(^1\)H NMR spectrum with characteristic vinylic proton pattern at \(\delta 6.30-4.80\) (m, 3H) and the alkyne proton at \(\delta 2.59\) (s, 1H) established the identity of the product 142. The low yield obtained during the lithium acetylide addition further substantiates our earlier finding that the high steric hindrance at the carbonyl site makes the approach of the nucleophile difficult.

**Scheme 51**

Reaction of lithium acetylide ethylenediamine complex with ketone 68 to form 142.

**Reagents, conditions and yields:** (a) Lithium acetylide-EDA, THF

Acetylene, 3-4 h, 27%.

With the ketone (-)-68 resulted in the formation of a diastereomeric mixture of ethynyl vinyl carbinol 142 in 27% yield. A strong absorption at 3400 and 3306 cm\(^{-1}\) in the IR spectrum revealed the presence of the hydroxy and alkyne functionality, respectively. The \(^1\)H NMR spectrum with characteristic vinylic proton pattern at \(\delta 6.30-4.80\) (m, 3H) and the alkyne proton at \(\delta 2.59\) (s, 1H) established the identity of the product 142. The low yield obtained during the lithium acetylide addition further substantiates our earlier finding that the high steric hindrance at the carbonyl site makes the approach of the nucleophile difficult.
The success in getting the ethynyl vinyl carbinol 142, although in poor yields, allowed us to reduce it into the required 1,2-divinyl carbinol 69, through partial hydrogenation of the alkyne functionality, Scheme 52. The carbinol mixture 142, was subjected to semi hydrogenation in the presence of Lindlar catalyst at atmospheric pressure to give the 1,2-divinyl carbinol in 85% yield, again as a diastereomeric mixture. The IR and $^1$H NMR spectra of 69 were in full agreement with its formulation. A strong absorption at 3383 cm$^{-1}$ in the IR spectrum and the resonances at δ 6.20-4.70 (m, 6H) in $^1$H NMR spectra clearly established the formation of 69.

Scheme 52

Reagents, conditions and yields: (a) Lindlar cat., EtOAc, 1 h, 85%.

However, conversion of the carbinol mixture 69 to the corresponding oxy-Cope rearrangement product 70 under a variety of thermal as well as anionic conditions were unsuccessful. Exposure of the 69 to a variety of reagents resulted either in the recovery of the starting material or formation of complex reaction mixture. Efforts to overcome this obstacle and carryout
the rearrangement, using new reagents and micro-wave reaction conditions were also of no avail. It is quite likely that due to the rigidity inherent in the bicyclo[3.1.1]heptane system and the steric congestion present, the required cope transition state (chair or boat) for a [3,3]-sigmatropic rearrangement is difficult to attain. This is probably the reason for our inability to effect the key oxy-Copc rearrangement in 69.

Formal synthesis of "Copa" Sesquiterpenes

The ready access to 108a,b via the ring contraction-rearrangement of [2+2]-ketene adduct 107, in good quantities, encouraged us to consider further restructuring it into a 1,4-dicarbonyl functionality through a ring opening approach. It was realised that 108a,b is a "push-pull" cyclopropane derivative\(^{44}\) in which the cleavage of the cyclopropane bond should generate a

**Chart 5**

\[
\text{copaborneol 143}^{45a} \quad \text{copacamphor 144}^{45b} \quad \text{copacamphene 145}^{45c}
\]

1,4-dicarbonyl derivative. Such 1,4-dicarbonyl derivatives emanating from 108a,b appeared to be useful for the synthesis of tricyclic "copa"
sesquiterpenoid frameworks. Some member of this family of natural products are shown in Chan 5. Among them (+)-copaborneol 143 and copacamphor 144 have been isolated from the wood of Pinus Silvestris and Espeletiopsis guacharaca, respectively. The hydrocarbon copacamphene 145 has been made by chemical transformation from (+)-copaborneol 143. Several synthesis of "copa" sesquiterpenes have been reported in the literature.46

Scheme 53

Reagents, conditions and yields: (a) ref. 46a (b) 2-iodopropionate, Pu'OK, BuOH, 73%; KOH, aq. diethylene glycol; CH$_2$N$_2$-Et$_2$O, 85%
However, the synthesis of these sesquiterpenes by Piers and coworkers.\textsuperscript{46a} Scheme 53, caught our attention as we saw the opportunity to prepare the advanced intermediate employed by them in a short, efficient sequence from readily available chirons. In our scheme of things, the $\alpha$-mcihyl $\gamma$-oxo ester 148 could be prepared from the cyclopropane ester as shown in Scheme 54. Further base catalysed cyclisation in 148 was expected to deliver the tricyclic intermediate, Scheme 54.

Our strategy for the construction of "copa" sesquiterpenoid intermediate 148 involved a ring opening in the substituted donor-acceptor cyclopropyl ester 108a,b as delineated in Scheme 54.

\begin{scheme}[ht]
\begin{center}
\includegraphics[width=\textwidth]{Scheme_54.png}
\end{center}
\end{scheme}

To demonstrate the above sequence, the ring opening reaction was attempted on the cyclopropyl ester 108a,b. Thus, treatment of the ester
108a,b with trimethylsilyl iodide at ice temperature readily furnished the γ-oxo ester 149 in 64% yield. Scheme 55, The IR. $^1$H and $^{13}$C NMR spectral data were in harmony with its formulation. The proton resonances at δ 3.66 (s,3H), 1.23 (s,3H) and 0.91 (d, 3H) due to the carbomethoxy, quaternary methyl and the isopropyl groups, in the $^1$H NMR spectrum (Fig. 28) clearly established its identity. A 13 line $^{13}$C NMR spectrum (Fig. 29) with characteristic carbon resonances at δ 214.0 and 172.3 due to the ester and ketone carbonyl moieties further confirmed the formation of 149.

Spurred on by the success in the above transformation, a recourse was taken to study the ring opening in the α-substituted cyclopropyl esters, Deprotonation of the ester 108a,b with LDA at low temperature and quenching the anion with methyl iodide furnished the required α-methyl-β-
methoxy cyclopropyl ester 150 in 70% yield, Scheme 56. The IR and $^1$H NMR spectra were in agreement with its formulation. It is interesting to note that only one diastereomer is formed in >90% yield.

Scheme 56

**Reagents, conditions and yields:** (a) LDA, THF, -78°C, Mel, 30 min., 70%.

Having obtained the required $\alpha$-methyl-$\beta$-methoxy cyclopropyl ester 150, the stage was now set for the ring opening strategy to deliver the required $\alpha$-methyl $\gamma$-oxo ester. Trimethylsilyl iodide mediated ring opening of the $\alpha$-methyl cyclopropyl ester 150 in acetonitrile, smoothly furnished the required $\alpha$-methyl $\gamma$-oxo ester 148 (60%) along with the side product, methoxy lactone 151 (20%), Scheme 57. The spectral data of these compounds are in full agreement with their formulations. Strong absorptions at 1740 and 1707 cm$^{-1}$ due to the ketone and the ester moieties in IR spectrum and the proton resonances at $\delta$ 3.65 (s, 3H) and 1.15 (d, 3H) corresponding to the carbomethoxy and the secondary methyl groups
Reagents, conditions and yields: (a) TMSI, R.T., MeCN, 0°C, 30 min., 60%.

in the $^1$H NMR spectrum (Fig. 30) support the identity of the $\gamma$-oxo ester 148, A 14 line $^{13}$C NMR spectrum (Fig. 31) with peaks at 8 215.3 and 176.2 characteristic of the ketone and ester carbonyl carbons further confirm its formulation. The $\alpha$-methyl $\gamma$-oxo ester 148 obtained in this sequence was predominantly a single diastereomer.

The formation of the methoxy lactone 151 in this sequence was evident from its spectral and analytical data. The IR, $^1$H and $^{13}$C NMR spectra of the metnoxy lactone 151 were consonant with its structure. The strong absorption at 1784 cm$^{-1}$ in the IR spectrum showed the presence of a $\gamma$-lactone moiety. The proton resonances at $\delta$ 3.31 (s, 3H) and 1.02 (d, 3H) in the $^1$H NMR spectrum (Fig. 32) exhibited the presence of a methoxy group and a secondary methyl group. The carbon resonances at $\delta$ 179.3 and 109.4
in the $^{13}$C NMR spectrum (Fig 33) due to the lactone carbonyl and an acetal carbon further confirmed the structure of 151.

The stereochemistry of the secondary methyl group with respect to the quaternary methyl and the methoxy group in 148 and 151 was deduced from the correlations in the 2-D NOESY experiment in 151 (fig. 34).

Treatment of the $\gamma$-oxo ester 148 with sodium hexamethyldisilazide (generated from sodamide and hexamethyldisilazane) delivered the hydroxy lactone 152. The expected tricyclic product was not observed probably due to
the preferential hydrolysis of the ester over the condensation under the basic conditions, Scheme 58.

**Scheme 58**

Reagents, conditions and yields, (a) NaNH$_2$, HMDS, DME, D, 1h, 92%.

The formation of the hydroxy lactone in this type of transformation has a precedence in the literature and expected to be in equilibrium with the corresponding acid, Scheme 59.
The hydroxy lactone fragment 152 is an important functional moiety present in a number of biologically active diterpenes e.g. myrocone C 153 and its 11-oxo derivative 154. These molecules have interesting biological activity against gram-positive bacteria and show \textit{in vivo} inhibitory activity against Ehrlich ascites carcinoma. The same moiety is also present in gibberellin precursor 156. A structurally related form of myrocin, LL-S491β 155 which was obtained by fermentation of the fungus \textit{Aspergillus chenalieri} also exhibits significant antibacterial activity, Chart 6.

The γ-oxo ester 148 was a single diastereomer, whereas the advanced intermediate in the Piers synthesis of "Copa" sesquiterpenes (Scheme 53) was a mixture of diastereomers. Our preparation of 148 in a sense constitutes a formal enantioselective synthesis of "Copa" sesquiterpenes.
Towards the synthesis of eudesmane sesquiterpenes

The methylation of β-methoxy cyclopropyl ester 157 and its subsequent ring opening protocol resulting in the formation of γ-oxo-α-methyl ester, en route to the formal synthesis of "copa" sesquiterpenoids has been illustrated in the earlier section. A more general version of this sequence i.e allylation of the ester 108a,b. followed by ring opening and further fine tuning of the resulting α-allyl-γ-oxo-ester 157 can be exploited for the synthesis of fused bicyclic systems. In Scheme 60 is illustrated the possible realisation of this theme leading to the synthesis of eudesmane framework. Some of the sesquiterpenes belonging to the eudesmane-type are depicted in Chart 7. The formation of the α-allyl-γ-oxo-cyclopropylester 157 could easily be envisaged from the routine alkylation-ring opening sequence of the β-methoxy cyclopropyl ester 108a,b. Oxidation of the olefinic moiety in the ester 157, followed by aldol type cyclisation was expected to deliver the desired eudesmane frame-work. Scheme 60.
In practice, deprotonation of the β-methoxy cyclopropyl ester 108ab with LHMDS and subsequent quenching of the anion with allyl bromide furnished the desired α-allyl-β-methoxy cyclopropyl ester 162 in 90% yield.

**Scheme 61**

**Reagents, Conditions and Yields:** (a) LHMDS, THF, -78°C, allyl bromide, 1h, 90%.

The IR, $^1$H & $^{13}$C NMR spectra of the allylated product 162 were in agreement with its formulation with strong absorptions in the IR spectrum at...
3076 and 1730 cm$^{-1}$ exhibiting the presence of olefinic and carbonyl moieties and the proton resonances at δ 6.00-5.60 (m, 1H), 5.20-4.90 (m, 2H), 3.64 (s,3H) and 3.35 (s,3H) in the $^1$H NMR spectrum (Fig. 35) indicated the presence of olefinic, carbomethoxy and methoxy group protons of the allyl ester 162. A 17 line $^{13}$C NMR spectrum (Fig. 36) with characteristic carbon resonances at δ 171.6, 136.1 and 116.3 due to the ester carbonyl and olefinic carbons establish the identity of the allylated product 162. Once again during the conditions of kinetic alkylation, only one diastereomer was predominantly formed.

Having obtained the desired allylated ester 162, in good quantities, the next objective was to administer a cyclopropyl ring opening sequence.

**Scheme 62**

Reagents and conditions: (a) TMS1, MeCN, 0°C, 30 min.
Trimethylsilyl iodide mediated ring opening of the \( \alpha \)-allyl-\( \beta \)-methoxy cyclopropyl ester 162 furnished the \( \alpha \)-alkyl-\( \gamma \)-cyclopropylester 157 and the corresponding hydroxy lactone 163 in 63% and 22% yields respectively, Scheme 62. Both the products obtained were characterised analytically and spectroscopically and the data was found to be in good agreement with their formulations. While the ester 157 (Fig. 37 & 38) shows a 16 line \( ^{13} \text{C} \) NMR spectrum with carbonyl carbon resonances at \( \delta \) 214.9 and 175.4 corresponding to the ketone and ester groups, the hydroxy lactone 163 (Fig. 39 & 40) exhibited the lactone carbonyl and the acetal attached carbon at \( \delta \) 178.5 and 107.1, respectively, confirming the assigned structure.

Scheme 63

Reagents, conditions and yields: (a) \( \text{O}_2 \), \( \text{PdCl}_2 \), \( \text{CuCl} \), DMF, \( \text{H}_2\text{O} \), R.T., 6 h, 70% (b) FTS, \( \text{C}_6\text{H}_6 \), \( \Delta \), 2 h, 45%.

As could be envisaged from the Scheme 60 the \( \alpha \)-allyl-\( \gamma \)-oxo-ester 157, was subjected to Wacker-type oxidation following the Tsuji conditions to
set up the aldol condensation reaction for the construction of eudesmane skeleton. Thus, the \( \alpha \)-allyl-\( \gamma \)oxo-ester 157 was subjected to Pd\(^{\text{II}}\) oxidation to yield the diketo ester 164 in 70\% yield. The IR spectrum of the diketo ester 164, with a broad ketone absorption at 1722 cm\(^{-1}\) indicated the presence of the additional carbonyl functionality. At this stage, the aldol ring closure of the diketoester 164 was expected to complete the eudesmane framework synthesis and the cyclisation attempted was under different basic conditions, but all such efforts proved to be unsuccessful. However, treatment of the diketoester 164 with p-toluenesulphonic acid using Dean-Stark water separator delivered the desired bicyclic [4.4.0] framework present in eudesmane sesquiterpenes. The spectral data of the ester 158 was in full agreement with its formulation. A strong absorption at 1667 cm\(^{-1}\) in the IR spectrum and the olefinic proton resonance at \( \delta \) 5.80 (s, 1H) due to \( \alpha \)-proton of the enone functionality, in the \(^1\)H NMR spectrum (Fig. 41) clearly established the identity of the enone 158. D 16 line \(^{13}\)C NMR spectrum (Fig. 42) with characteristic resonances at 197.4 and 172.5 further confirmed the identity of the structure 158.

Having obtained the bicyclo [4.4.0] system 158, efforts were made to refine the framework by decarboxylating the unrequired ester moiety, Scheme 64. Hydrolysis of the ester moiety in 158 with methanolic sodium hydroxide solution furnished the corresponding carboxylic acid 165 almost in quantitative yield. Unfortunately, attempts at the reductive decarboxylation under different radical reaction conditions to give the enone 166 were in vain.
Regents, conditions and yields: (a) 20% NaOH, MeOH, 4h, quant.(b) LAH, Et₂O, 2h, quant, (c) TPAP-NMNO, 10% CHCl₃-DCM, R.T., 30 min.

Similar attempts at oxidative decarboxylation to furnish the cross conjugated dienone were also unsuccessful. A recourse was taken to reduce the ester functionality in 158 to the diol 167 and further oxidise it to give the keto aldehyde 168 for reductive decarbonylation with Rhodium complexes. However, this too proved unsuccessful. In this sequence the keto aldehyde 168 formed was found to be unstable and gave a complex reaction mixture on work-up. Further efforts at the synthesis of eudesmane sesquiterpenes were not pursued.
Conclusions

In summary, a new simple and preparatively useful protocol for the construction of $\alpha$-vinyl ketones, particularly those bearing a quaternary carbon centre from the corresponding alkenes has been developed during the course of this study. The generality of this methodology has been demonstrated with a few representative alkenes. The versatility of the methodology has been established by applying it to the enantioselective synthesis of sesquiterpene (+)-$\alpha$-elemene (starting from R-(+)-limonene and (+)-2-carene). The efficacy of this methodology has been explored to construct an useful diquinane synthon and the framework of germacrane sesquiterpene. Our attempts to synthesise the taxol AB skeleton using this protocol, though looked promising, ultimately proved to be unsuccessful.

The intermediate, $\beta$-methoxy cyclopropyl ester in our newly developed sequence, have been elaborated towards the formal synthesis of copa series of sesquiterpenes. A chiral eudesmane derivative has also been synthesised through the alkylation-ring opening strategy.