STUDIES IN TERPENOIDS FROM TAXACEAE, COMPOSITAE AND MELIACEAE FAMILIES

THESIS
SUBMITTED TO THE
UNIVERSITY OF PUNE

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IN
CHEMISTRY

by
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CERTIFICATE

This is to certify that the work incorporated in the thesis entitled "Studies in Terpenoids from Taxaceae, Compositae and Meliaceae Families" submitted by Mr. Gurunath Suryavanshi was carried out by him at National Chemical Laboratory under my supervision for the Degree of Philosophy in Chemistry of the University of Poona. Such material as has been obtained from other sources has been duly acknowledged in the thesis.

Date: 7, Jan. 2000.

Pune 411 008

Dr. G. T. Panse
(Research Guide)
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Section B: Oxidation of Methyl Ketone to Carboxylic Acids using Rhenium Oxide (Re_2O_7)

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(Suryavanshi Gurunath)

ABBREVIATIONS

Ac	Acetyl
Ar	Aryl
bp	Boiling point
Et	Ethyl
EtOAc	Ethyl acetate
EtOH	Ethyl alcohol
g	Grams
h	Hours
IR	Infra Red
M^+	Molecular Ion
Me	Methyl
MeOH	Methanol
mg	Milligram
min	Minutes
ml	Milliliter
mp	Melting point
Ms	Mass Spectrum
NMR	Nuclear Magnetic Resonance
Pet-ether	Petroleum ether
Ph	Phenyl
RT	Room temperature
TLC	Thin layer chromatography
TBHP	*tert.* Butyl hydrogen peroxide

General Remarks

1. The compound numbers, figure numbers, scheme numbers, charts numbers and reference numbers, etc. given in each chapter refer to that particular chapter only. The references and figures are given at the end of each chapter.
2. All melting points are uncorrected and recorded on Celsius scale
3. All solvents were distilled before use. Petroleum ether refers to the fraction boiling in the range 60-80°C.
4. Organic layers were dried over sodium sulphates.
5. Column chromatographic separations were carried out using the column grade (60-120mesh) silica gel.
6. The thin layer chromatography (TLC) and preparative TLC plates were prepared by spreading an aqueous suspension of silica gel (200-300 mesh) uniformly over glass plates using an applicator. Layer thickness : TLC plates, 0.5 mm; preparative TLC 1.2 mm. After initial drying at room temperature the plates were activated at 100°C for one hour before use.
7. After development, the spot on TLC plates were visualized by exposing them to iodine vapors and /or by spraying with a mixture of H_2SO_4-HNO_3 (1:1) followed by charring in an oven. In case of preparative TLC the band of the compounds (after development) were visualized by spraying a dilute solution of iodine in $CHCl_3$ to the sides (after covering the major central portion) with a glass plate.
8. Optical rotations were measured using sodium light (5893 A°) as the source on a JASCO DIP –181 digital polarimeter.
9. The UV spectrum was recorded in ethanol solution on Shimadzu UV-visible recording spectrometer UV-260
10. The IR Spectrum were recorded on Perkin Elmer 599 B, Perkin –Elmer "Infracord" 137 B model and Perkin – Elmer 1620 FT-IR spectrometers.
11. All the ^{1}H NMR and ^{13}C NMR spectra mentioned were recorded in $CDCl_3$ solution using tetra-methylsilane as internal reference on Bruker AC-200 MHz (50.32 MHz) FT NMR. Other ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker WH-90 FT, MSL-300 and MSL-500 spectrometers wherever mentioned abbreviations viz., s = singlet, d = doublets, t = triplets, q = quartets, dd = doublet of doublet, brs = broad singlet and m = multiplet have used.
12. Mass spectra were recorded on Finnigan Mat – 1020 using direct inlet system at 70 V.

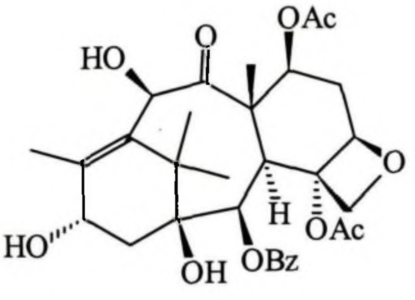
ABSTRACT

The thesis entitled "Studies in Terpenoids from Taxaceae, Compositae and Meliaceae Families" is divided into four chapters.

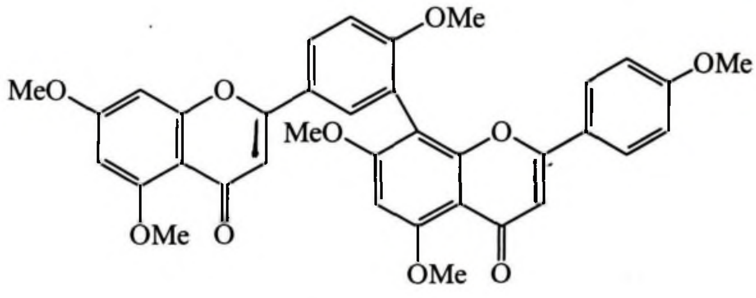
The title of the thesis clearly indicates the objective, which is to interface the isolation and characterization of organic compounds from the naturally occurring sources, particularly plants. Chapter-I describes the *Chemical investigation of Taxus baccata.* Chapter-II presents the *Chemical investigation of Amoora Lawii.* Chapter-III describes the *Chemical investigation of Callicarpa lanata l.* and finally Chapter-IV deals with *Organic Transformations using Alumina (Al_2O_3) and Rhenium oxide (Re_2O_7) as Catalysts.*

Chapter I: ***Chemical investigation of Taxus baccata.***

This chapter describes the isolation and characterization of the 7β - acetyl -10-deacetyl baccatin –III (I) a new compound and isolated a biflavon (IIa) from Taxus



I

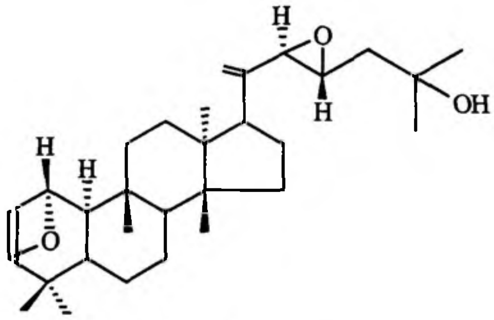


IIa

baccata. It has been isolated from the methanol extract of the needles of the *Taxus baccata.* Spectral methods and critical comparison with the known literature have established the structure of the compound (I) and (II).

Chapter II: ***Chemical investigation of Amoora lawii.***

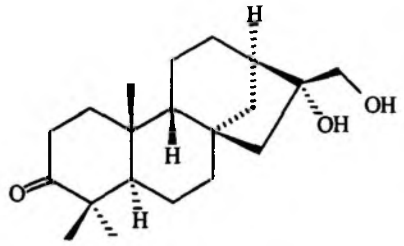
Amoora lawii belongs to the family Meliaceae. Amoora is a monotypic genera which is common in eastern part of India. There is no previous report regarding the chemical **investigation** of this plant. Most of the Meliaceae plants contain tetranortriterpenoids as a markers chemotaxonomically. These tetranortriterpenoids are not present in *Amoora lawii.* A new triterpenoid **(I)** has been isolated from the acetone extract of *Amoora lawii.* The structure of the compound has been deduced mainly by spectral methods.



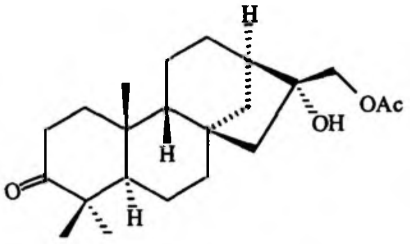
I

Chapter III: Chemical investigation of Callicarpa lanata l.

The species *Callicarpa lanata* belongs to the family Verbenacea. This species generally found in the coastal region of Maharashtra State in India. The chemical investigation of *Callicarpa lanata* gives compounds **I, II** and **III** generally belonging to diterpenoid and triterpenoid groups. The structure of these compounds has been deduced by spectral methods.



I



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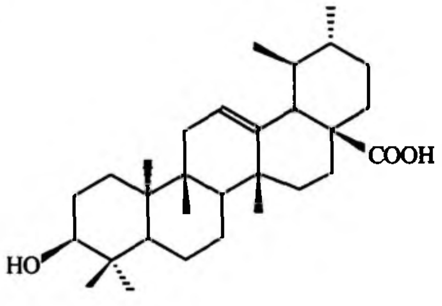
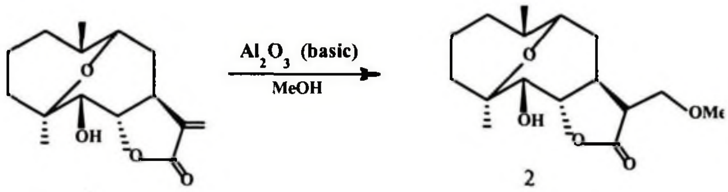


III

Chapter IV: ***Organic Transformations using Alumina (Al_2O_3) and Rhenium Oxide (Re_2O_7) as Catalyst***

Section A: ***Alumina (Al_2O_3) Catalysed Transformations of Naturally Occurring Compounds.***

Sesquiterpene lactones are the characteristic constituents of the plants belonging to the family Compositae. Chemical investigation of the acetone extracts of Cyathocline species i.e. *Cyathocline purpurea* and *Cyathocline lutea* afforded in the isolation of Germacranolides and Guainolides respectively from *C. Purpurea* and *C. lutea* in large quantities. Michael type of addition were carried out on the compounds (1) and (3) by alumina catalysed reactions, to get a new sesquiterpene lactones (2) and (4) which are rarely available in nature itself. The structures of the same (2) and (4) were elucidated by spectral analysis.



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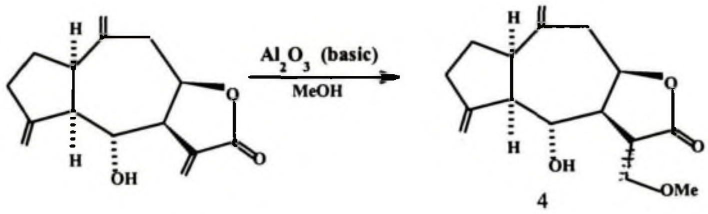

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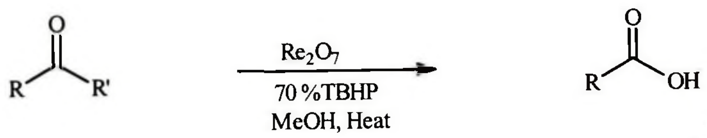
3

Section B: ***Oxidation of Methyl Ketone to Carboxylic Acids using Rhenium Oxide (Re_2O_7)***

A mild and efficient method for oxidation of ketones into corresponding carboxylic acids in good yields are carried out by using Re_2O_7 as a catalyst and 70% *tert.*- butyl hydroperoxide (TBHP) as oxidant



Chapter I

Chemical Investigation of Taxus baccata

7β-Acetoxy-10-deacetyl baccatin III from the needles of *Taxus baccata*

S. R. Rojatkar **S. Gurunath,** D. D. Sawaikar, P. P. Pujar, G. T. Panse and B. A. Nagasampagi

7th International Symposium on Natural Products Chemistry, Dec. 28, 1997, Karachi, Pakistan. Abs. P. 17

1.1 Introduction

Yew trees, valued for centuries for their strong supple wood, poisonous nature and hardy adaptability, have now been found to provide the most promising anticancer agent known: Paclitaxel is mainly concentrated in the bark of the pacific yew (*Taxus bravifolia*) a tree found in the west coast regions of United States.

Taxonomically, different species of yew tree in the genus of Taxus, which are in turn belong to the Taxaceae and consist of much-branched trees or shrubs. Taxaceae is a family of five genera: *Amentotaxus pilger, Austrotaxus compton, Pseudotaxus cheng, Taxus Linn and Torreya Arn*[1]. Family Taxaceae having several species such as *Taxus brevifolia, Taxus wallichiana, Taxus cupsidata, Taxus media, Taxus chinensis, Taxus yunnanensis, Taxus canadensis, Taxus matret, Taxus mairet and Taxus baccata. Taxus baccata* is an evergreen tree usually 6 meters in height and 1.5 to 1.8 meters in girth found in the temperate Himalayas at altitudes between 1800 to 3300 meters[2]. The species of yew tree are also identified by the region of their occurrence i.e. Himalayan yew, European yew and Canadian yew etc. They are widely distributed in northern hemisphere, occurring in Europe, North America, Northern India, China and Japan.

A medicinal tincture made from young shoots of *Taxus baccata* has long been used for the treatment of headache, giddiness, feeble and falling pulse, coldness of extremities, diarrhea and severe boliononess. The leaves are credited with emmenagogue and antispasmodic properties. They are employed for treatment of Cysteria, Epilepsy and nervousness[2].

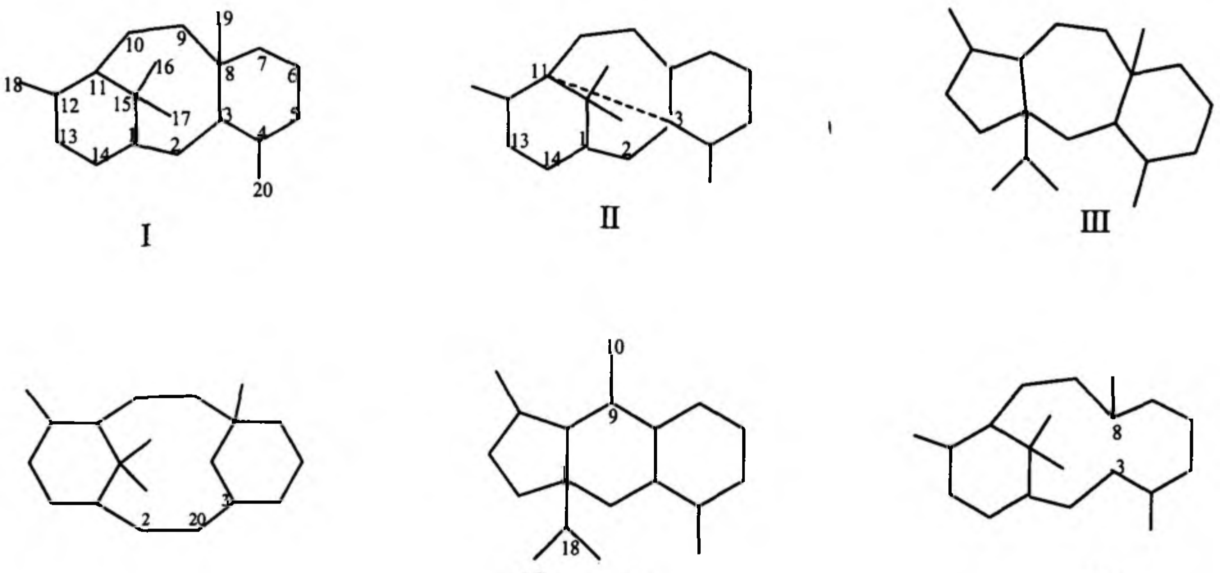
Different Taxus species have proved to be of special significance among phytochemists in recent years because they have been found to posses a number of biological activities[3]. The chemical constituents of the different Taxus species have been studied for over hundred years. Taxane alkaloids, diterpenoids with taxane skeletons are commonly found to occur in this genus. The phytochemistry of genus Taxus has evoked a great deal of interest because of the occurrence of antitumor and antileukemic taxane, moulting hormones, alkaloids, antineoplastic diterpenes and other physiologically important compounds in the various species, in particular because of the world renowned antitumor drug Taxol now being marketed as Paclitaxel. Taxol a novel anticancer drug from natural sources having high impact on human health occur mainly in the barks of Taxus species. Although it shows exceptionally promising antitumor property its use as a drug has been hampered due to its limited availability. Taxol produced by three whole trees is enough for the treatment of one patient[4]. This can be circumvented by semisynthesis from its precursor 10 - deacetyl baccatin III[5, 6] which can be isolated from the renewable resources such as leaves (needles) *Taxus baccata*[7] and other *Taxus* species[7].

Taxol was isolated for the first time from *Taxus brevifolia* by Wani et al[8] in 1971. It was proved by federal drug administration of U. S. A. as a drug in 1992 for the treatment of ovarian cancer. Taxol differs in anticancer activity from other anticancer drug by inhabiting the cell division by unique mechanism. Cell division takes place by duplication of chromosomes, which line up on spindles formed by microtubules during mitosis. Taxol gums up the tubules stopping the formation of the spindles, thus avoiding the cell division due to which the cancerous cells eventually die[4].

Chemical investigation of *Taxus baccata* was carried out in this laboratory during the standardization of the process for the isolation of 10-deacetyl baccatin III from the needles of the plant.

1.2 Review of Literature

Taxol and other taxanes are typical of tricyclic diterpenoids. All the taxanes isolated show different types of skeleton of their structures (Chart - I).



I II III

IV V VI

chart-I

The first category of skeleton shows a eight membered ring sandwiched between two six membered rings **I.** The second type of taxane possessing a rearranged skeleta - 3, 11-cyclotaxanes **II** of an tetracyclic systems with an additional bond between C-3 and C-11. The third category of taxanes shows a seven membered ring sandwiched between five and six membered rings called 11 (15--3) abeotaxane **III**. Six/ten/six ring skeleton system is known as 2 (2--20) abeotaxane **IV**. 11 (15--1) and 11 (10--9) is another class of taxane called bisabeotaxane **V**. The last category of taxanes is referred as pretaxanes because the bond between C-3 and C-8 supposed to be formed **VI**.

Several taxanes have been isolated from *Taxus baccata* along with non-taxoid higher isoprenoids such as flavonoides[9-18], lignans[16, and 19], sugar derivatives, steroids[20], triterpenoids, aromatic compounds[21-23] and fatty acids[24].

1.2.1 Taxanes from *Taxus baccata*

1.2.1.1 Normal Taxanes

The naturally occurring diterpenoids with the taxane skeleton are the typical constituents of *Taxus baccata.* Terpenoids of taxanes group has brought an importance to the phytochemical and synthetic work[25].

Taxanes having typical tricyclic skeleton with C-4 / C-20 double bond having hydroxyl hydrogen or acetoxyl groups at C-13 (1 - 20) have been reported from different parts of the plant. These are listed in chart II (a) and II (b)

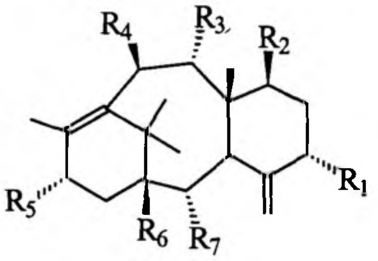
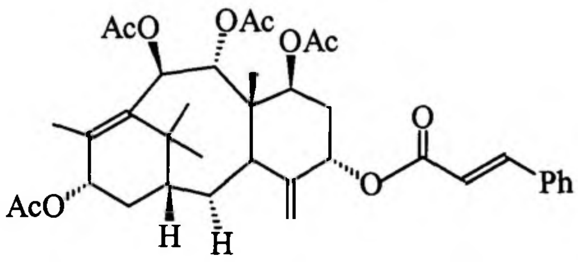


Chart - II (a)

Compound No	R_1	R_2	R_3	R_4	R_5	R_6	R_7	References
1	OH	H	OH	OH	OH	H	H	26, 27
2	OAc	H	OAc	OAc	OAc	H	H	28,29, 30
3	OAc	OAc	OAc	OAc	OAc	H	H	28
4	OAC	H	OAc	OAC	OAc	H	OAc	28
5	OAc	OAc	OAc	OAc	OAc	H	OAC	28
6	OH	OAc	OAc	OAc	H	OAc	H	30
7	OH	OAc	OAc	OAc	OAC	H	H	31
8	OH	OAc	OAc	OAc	OAc	OH	OAc	31
9	OH	H	OAC	OAC	OAc	H	OH	31
10	OH	H	OAc	OAc	OH	H	H	28
11	OH	OAc	OAc	OAc	H	H	$OCOCH(CH_3)C_6H_5$	28
12	OAc	OAc	H	OAc	H	H	$OCOCH(CH_3)C_6H_5$	28



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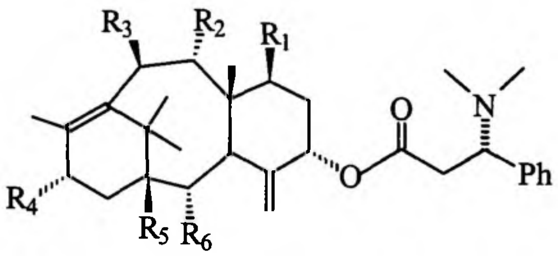
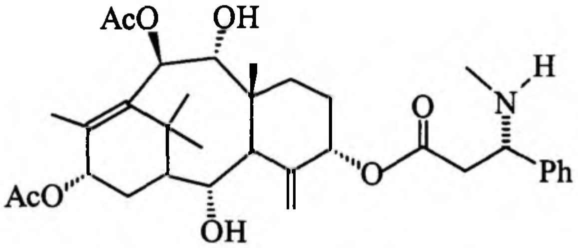


Chart - II (b)

Compound No	R_1	R_2	R_3	R_4	R_5	R_6	References
14	H	OH	OAc	OAc	OH	OH	32
15	H	OH	OAc	OAc	H	OH	32
16	OAc	OAc	OAc	OAc	H	H	33
17	H	OAc	OAc	OAc	OH	OAc	34



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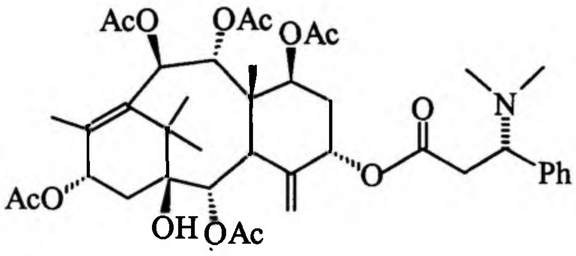

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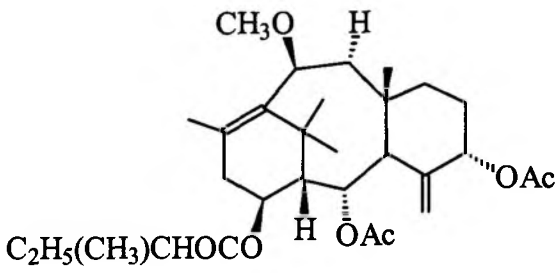
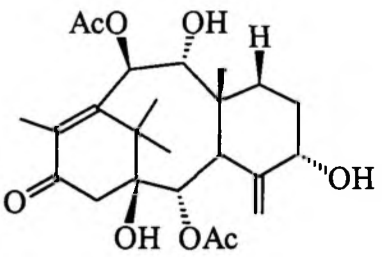


20. Ref. 30

The another class of taxanes with tricyclic skeleton having double bond at C-4 / C-20 and the carbonyl group at C-13 (21 - 36) which have been reported are listed in Chart - III (a) and III (b).



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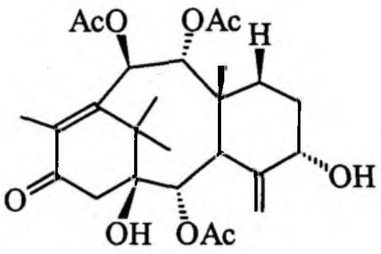

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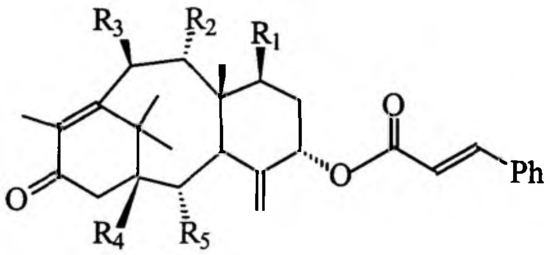
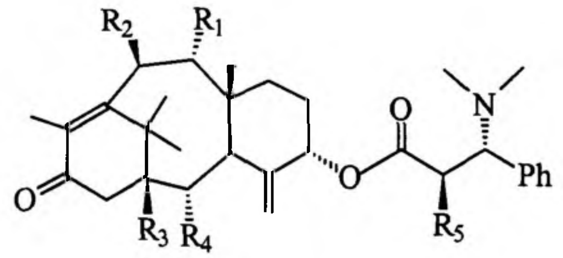


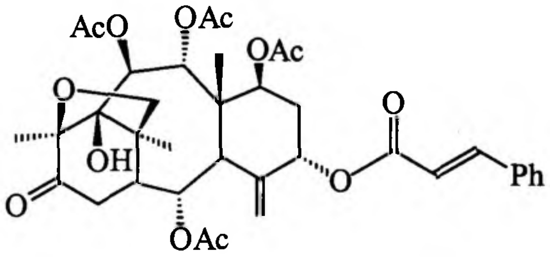
Chart - III (a)

Compound No	R1	R2	R3	R4	R5	References
23	H	OH	OH	OH	OAc	35
24	H	OAc	OAc	OH	OH	36
25	H	OAc	OH	OH	OH	37, 38
26	H	OH	OH	OH	OAc	37, 38
27	H	OAc	OH	H	OH	37
28	H	OH	OAc	H	OH	37

Chart - III (b)



Compound No	R_1	R_2	R_3	R_4	R_5	References
29	OH	OAc	OH	OH	H	39, 40, 41
30	OAc	OAc	H	OAc	H	42
31	OAc	OAc	OH	OAc	H	39, 43, 44
32	OH	OAc	H	OH	H	41
33	OH	OAc	OH	OAc	H	41
34	OAc	OH	H	OH	H	41
35	OAc	OH	OH	OAc	H	41



36. Ref. 27, 45

Few taxanes (37 - 41) obtained from the *Taxus baccata* possessing an epoxide where the exomethylene double bond between C-4 and C-20 has been converted into epoxide have been reported are listed in chart - IV.

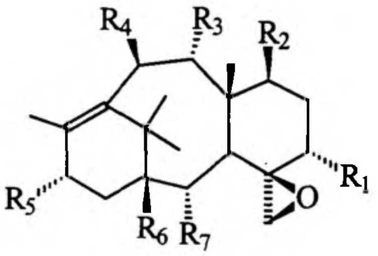
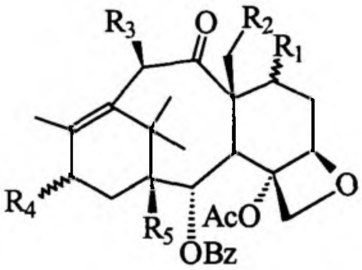


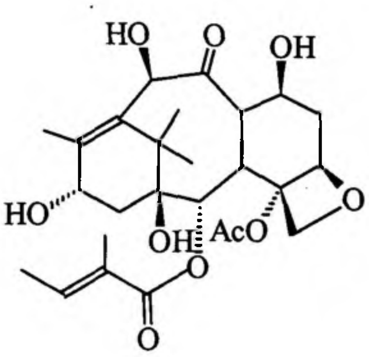
Chart - IV

Compound No	R_1	R_2	R_3	R_4	R_5	R_6	R_7	References
37	OAc	OAc	OAC	OAc	OAc	H	OAc	26, 46
38	OAC	OAc	OAc	OAc	OAc	OH	OAc	46, 47
39	OAc	OH	OAc	OAc	OAc	OH	OAc	48
40	OH	OAc	OAc	OAc	OAc	H	OAc	46
41	OH	OAc	OAc	OAc	OAc	OH	OAc	48

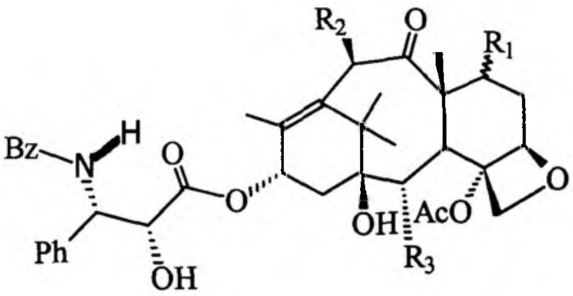
The taxanes (42 – 68) possessing an oxetane ring at C-4 / C-5 are presently important class of taxanes owing to their excellent therapeutic potential. Such compounds from this plant have been listed in chart - V.



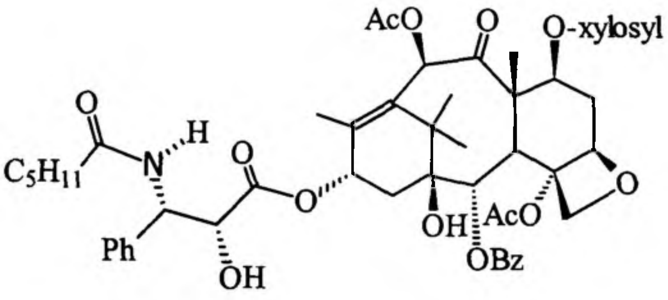
Compound No	R_1	R_2	R_3	R_4	R_5	References
42	β-OH	H	OAc	α-OH	OH	26, 49, 50, &51
43	α-OH	H	OAc	α-OH	OH	52, 53
44	β-OH	OH	OAc	α-OH	OH	27
45	β-OH	H	OH	α-OH	OH	54, 55, 51 & 57
46	β-OH	OH	OH	α-OH	OH	57
47	β-OH	H	OH	β-OH	OH	58



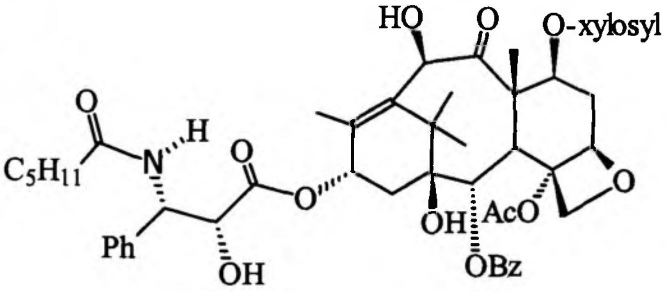
48. Ref. 58



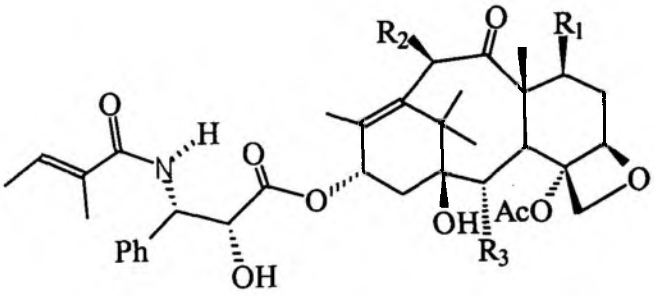
Compound No	R_1	R_2	R_3	References
49	β-OH	OH	OBc	27
50	α-OH	$OCOCH_2(CHOH)CH_3$	OAc	48
51	β-OH	OAc	OBc	8,27,48,59,60,61, 62,55,51,63
52	β-O-xylosyl	OH	OAc	48
53	β-O-xylosyl	OAc	OAc	48
54	α-OH	OH	OBz	63
55	β-O-xylosyl	OH	OAc	33



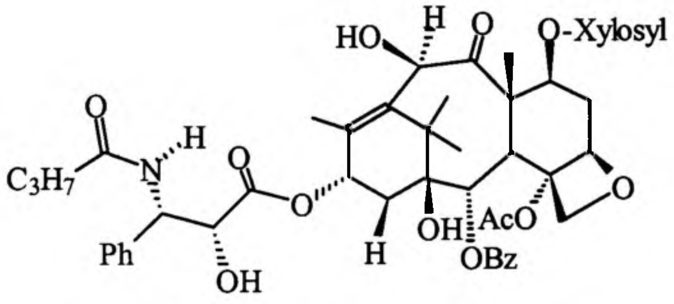
56. Ref. 48



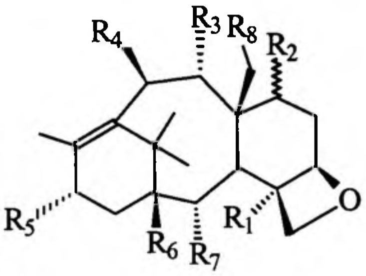
57. Ref. 33, 48



Compound No	R_1	R_2	R_3	References
58	β-OH	OAc	OBz	49, 27, 64, 51, 63
59	β-OH	OH	OBz	27
60	β-OH	$OCOCH_2CH(OH)CH_3$	OAc	48
61	β-O-xylosyl	OH	OAc	48
62	β-O-xylosyl	OAc	OAc	48



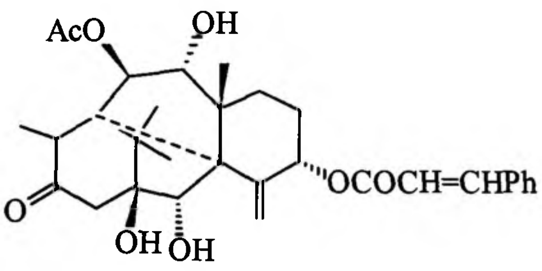
63. Ref. 33



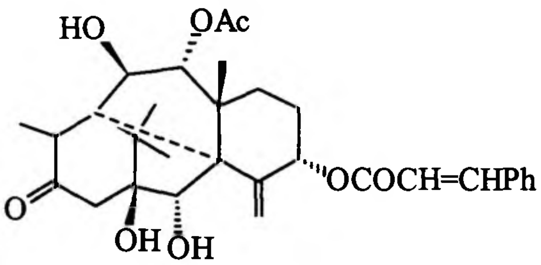
Compound No	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	References
64	OAc	β-OAc	OAc	OAc	OAc	OH	OAc	H	26, 65, 47
65	OAc	β-OAc	OAc	OAc	OAc	OH	OBz	H	65, 48
66	OAc	β-OAc	OAc	OAc	OAc	H	OAc	H	65
67	OAc	β-OH	OH	OH	OH	OH	OBz	OAc	35
68	OH	β-OAc	OAc	OAc	OAc	OH	$OCOC_5H_{11}$	H	65

1.2.1.2 Unusual Taxanes

1. The taxanes (69, 70) are unusual in their structures this category of taxanes possessing a rearranged skeleta 3, 11 – cyclotaxanes of a tetracyclic systems with an additional bond between C-3 / C-11 are as follows.



69. Ref. 66



70. Ref. 35, 38

2 The second category of unusual taxanes has also been reported, where seven membered ring had been sandwiched between five membered and six membered rings. Five, seven and six membered rings fused linearly called 11 (15 – 1 0) abeotaxane (71 – 77) have been listed in chart VI.

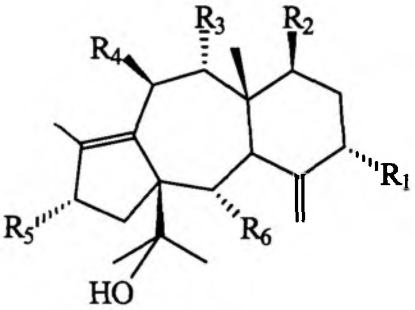
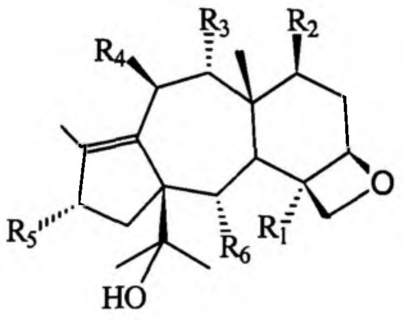


Chart VI

Compound No	R_1	R_2	R_3	R_4	R_5	R_6	References
71	OH	H	OAc	OH	OH	OAc	67, 35
72	OH	OAc	OBz	OH	OH	OAc	33
73	OH	OAc	OAc	OBz	OH	OAc	67, 44
74	$OCOCH_2CH(Ph)NMe_2$	H	OAc	OAc	OAc	OAc	34



Compound No	R_1	R_2	R_3	R_4	R_5	R_6	References
75	OAc	OH	OH	OH	OAc	OBz	36
76	OAc	OAc	OAc	OBz	OH	OAc	68
77	OAc	OAc	OAc	OBz	OAc	OAc	68

There are the abeotaxane from *T. baccata* having six / ten / six membered fused ring system called 2 (3 – 20) abeotaxane. Chart VII

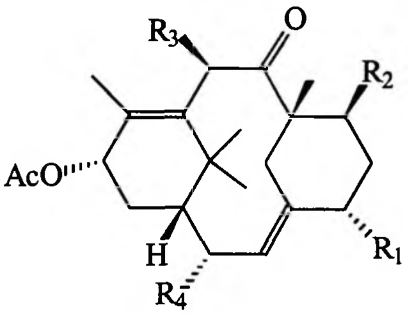


Chart VII

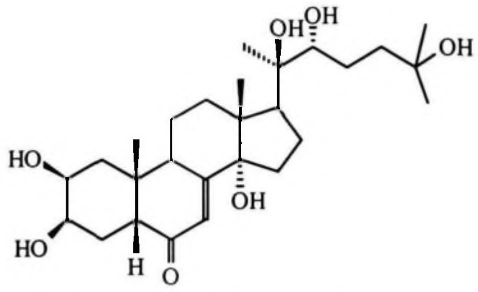
Compound No	R_1	R_2	R_3	R_4	References
78	OH	OH	OH	OAc	36
79	OCOCH(OH)CH(NM_2)Ph	OAc	OH	OAc	31
80	OCOCH(OH)CH(NM_2)Ph	OH	OH	OH	69, 31

1.2.1.3 Non – Taxoides From *T. baccata.*

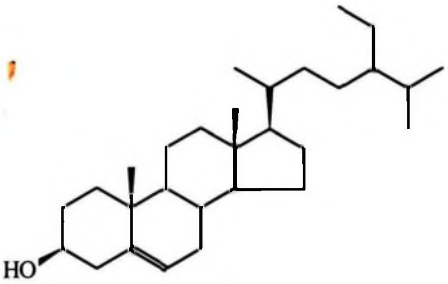
Apart from taxane derivatives it has been found that there are a number of non- – taxoides moieties which have been reported from *T. baccata.* The non-taxoid moieties are isoprenoids, lignans, flavonoids, glycosides and some novel aromatic, cyclic and straight chain compounds (81-145). See chart VIII.

Chart VIII

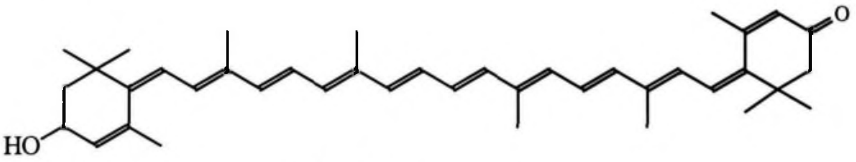
1. Isoprenoids



81. Ref. 70, 71

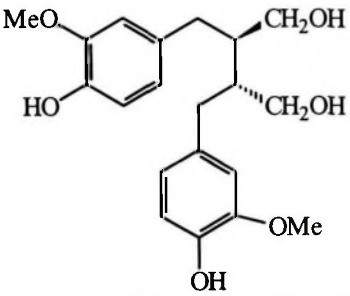


82. Ref. 72

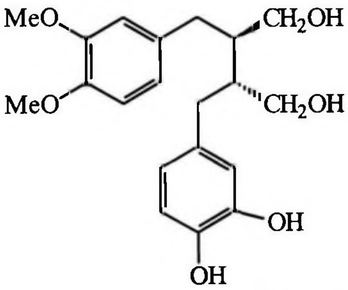


83. Ref. 73

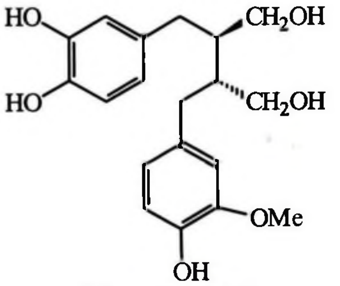
2. Lignans



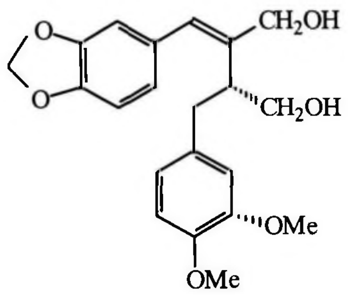
83. Ref. 74, 72, 75, 76



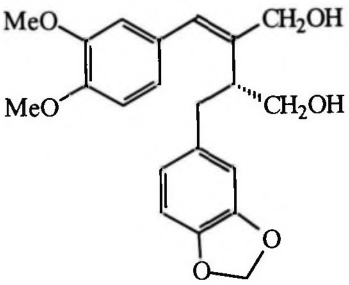
85. Ref. 76



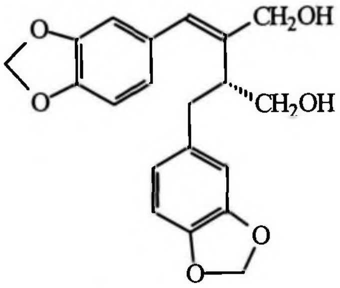
86. Ref. 77



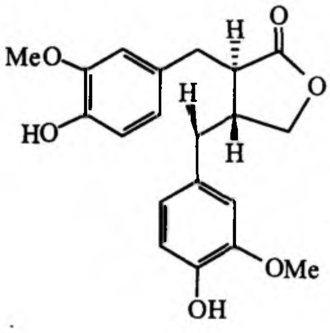
87. Ref. 79



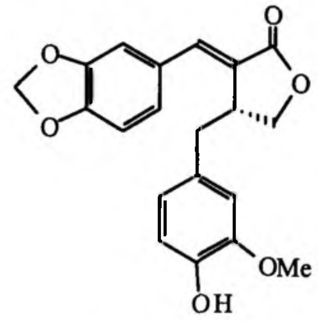
88. Ref. 78



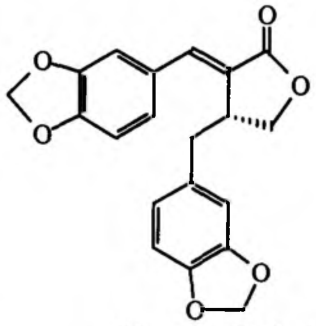
89. Ref. 78



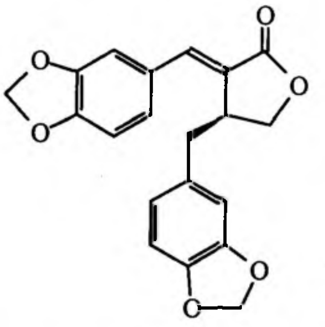
90. Ref. 78



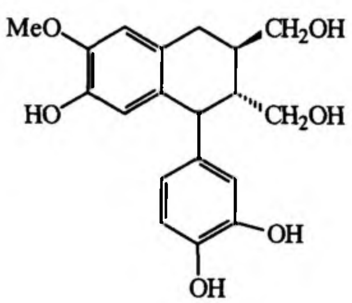
91. Ref. 79



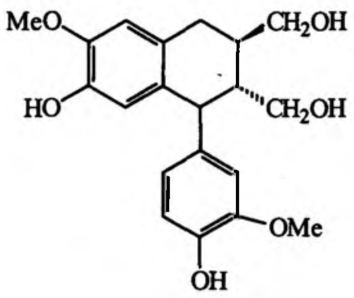
92. Ref. 78



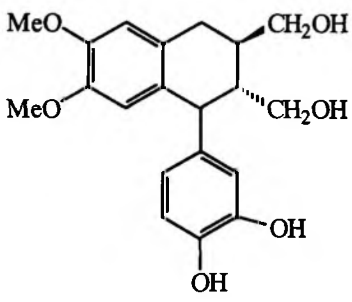
93. Ref. 78



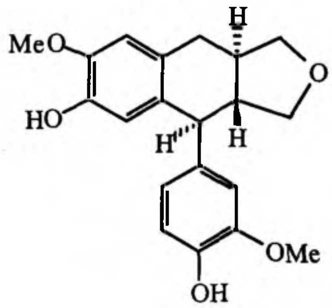
94. Ref. 74, 75, 72, 71



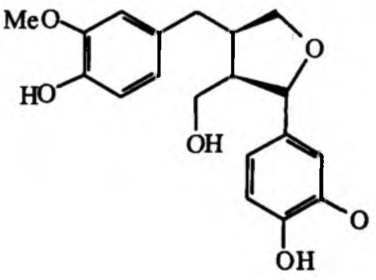
95. Ref. 72, 76



96. Ref. 72

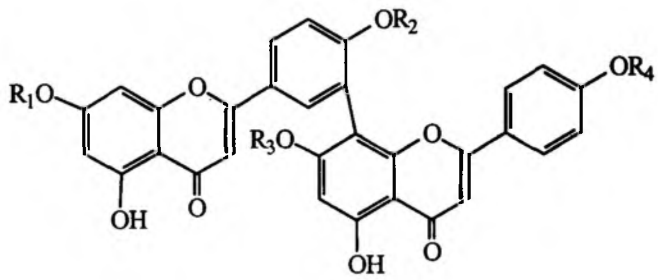


97. Ref. 78



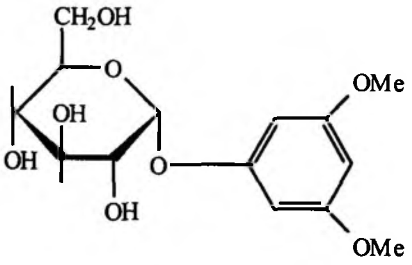
98. Ref. 75

3. Flavonoids

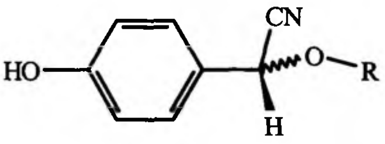


Compound No	R_1	R_2	R_3	R_4	References
99	Me	Me	H	H	80
100	Me	Me	H	Me	80, 81
101	Me	H	H	H	80
102	H	H	Me	H	82, 83
103	H	H	H	H	84
104	Me	Me	Me	H	85
105	Me	Me	Me	Me	85, 84
106	H	Me	Me	H	84

4. Glycosides

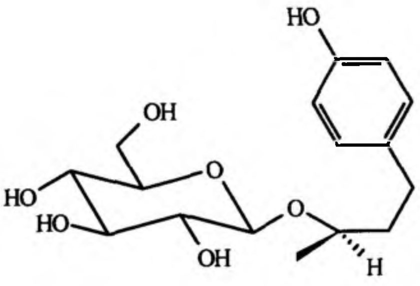


107. Ref. 86, 87, 88, 89

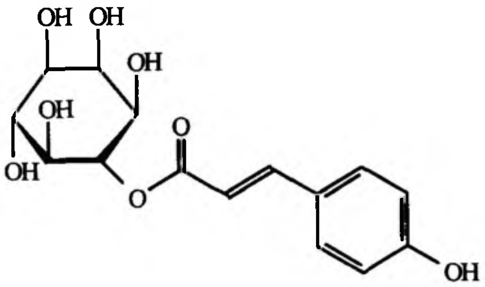


108. R = α - O – Glycosyl, Ref. 90

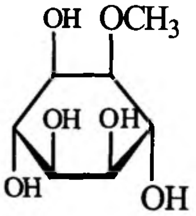
109. R = β - O – Glycosyl, Ref. 90



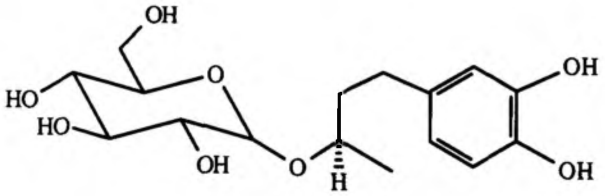
110. Ref. 80, 55, 91



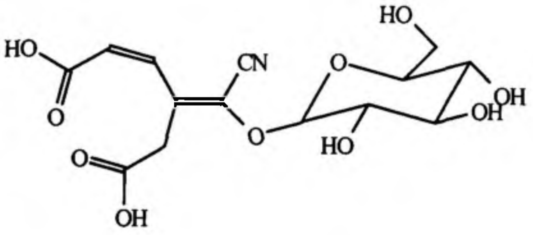
111. Ref. 92, 93



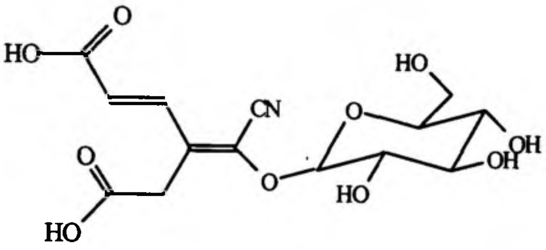
112. Ref. 94



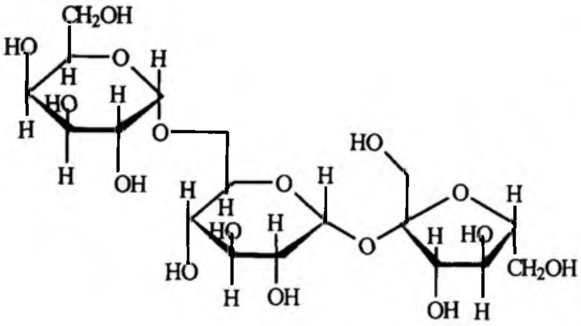
113. Ref. 77, 76



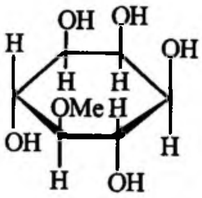
114. Ref. 90



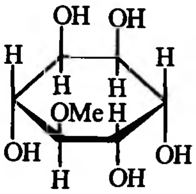
115. Ref. 90



116. Ref. 87, 89

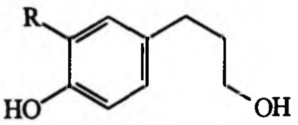


117. Ref. 94



118. Ref. 94

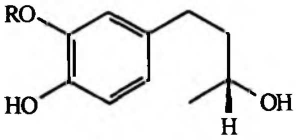
5. Aromatic, Cyclic and Straight Chain Compounds.

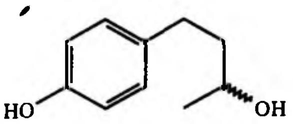


119. R = H, Ref.76

120. R = OH, Ref.76

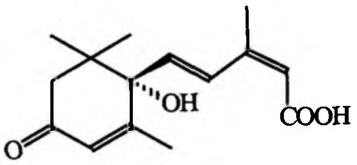
121. R= OMe, Ref.76





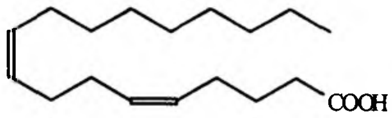
122. R., Ref. 80, 95, 76

123. S, Ref. 96



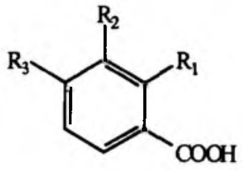
124. R = H, Ref. 95, 76

125. R = Me, Ref. 95, 76



127. Ref. 100

126. Ref. 91, 98, 99

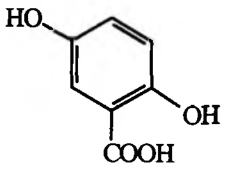


128. R$_1$ = H, R2 = OCH$_3$, R$_3$ = OH, Ref. 101

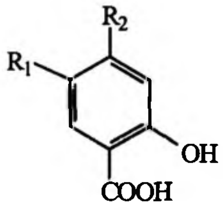
129. R$_1$ = OH, R$_2$ = OH, R3 =H, Ref. 101

130. R$_1$ = H, R2 = OH, R3 = OH, Ref. 101

131. R$_1$ = OH, R$_2$ = OH, R3 = OH, Ref. 101

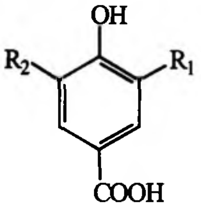


132. Ref. 101



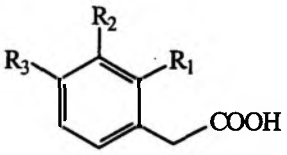
133. R$_1$ = OH, R2 = H, Ref. 101

134. R$_1$ = OH, R$_2$ = OH, Ref. 101



R$_1$ = OH, R$_2$ = OH, Ref. 101

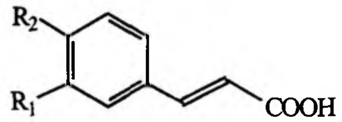
136. R$_1$ = OCH$_3$, R$_2$ = OCH$_3$, Ref. 101



137. R$_1$ = OH, R$_2$ = H, R$_3$ =H, Ref. 101

138. R$_1$ = H, R2 = H, R$_3$ = OH, Ref. 101

139. R$_1$ = H, R$_2$ = OH, R$_3$ =OH, Ref. 101

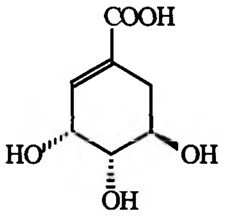


140. R_1 = H, R2 = H, Ref. 101

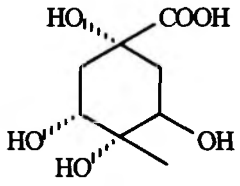
141. R_1 = H, R2 = OH, Ref. 101

142. R_1 = OCH_3, R_2 = OH, Ref. 101

143. R_1 = OH, R_2 = OH, Ref. 101



144. Ref. 102, 101



145. Ref. 101, 102.

1.3 Present work

With the intention to isolate more bioactive compounds from the needles of *Taxus baccata*, further chemical investigation of methanol extract of needles of *T. baccata* was carried out. As a result of this work, the methanol extract, after successive thin layer chromatography, column chromatography and preparative thin layer chromatography over column grade, TLC grade silica gel afforded (i) a new taxane 7-β – acetoxy -10- deacetyl baccatin – III (I). (ii) During the isolation of taxane we get fraction which have comparatively less solubility in solvent. To increase its solubility some of the fraction was methylated with diazomethane and isolated as 7, 7", 5,5", 4', 4"' – hexamethyl amentoflavone (II a). (iii) To confirm the number of hydroxy groups present in the molecule, rest of the fraction was acetylated with pyridine and acetic anhydride and isolated as 7, 7",4',- trimethoxy – 5,5",4"', triacetoxy amentoflavone (II b). This present experimental study of compound (II a) & (II b) gave an idea that the extract had 7, 7", 4'-trimethoxyamentoflavone (II)[85].

1.3.1 Characterization of compound –I

Compound I is obtained as gummy liquid. Its mass spectrum showed a molecular ion peak at m/z 586 in accordance with the molecular formula $C_{31}H_{38}O_{11}$. A prominent fragmentation ion at m/z 568 (M- H_2O)$^+$ and IR (Fig.1) absorption at 3410 cm^{-1} indicated that the compounds contained a hydroxyl group. In addition, the IR spectrum exhibited absorption at 1710, 1740, 1660 & 1240 cm^{-1} revealing the presence of carbonyls and unsaturation in the compound (I).

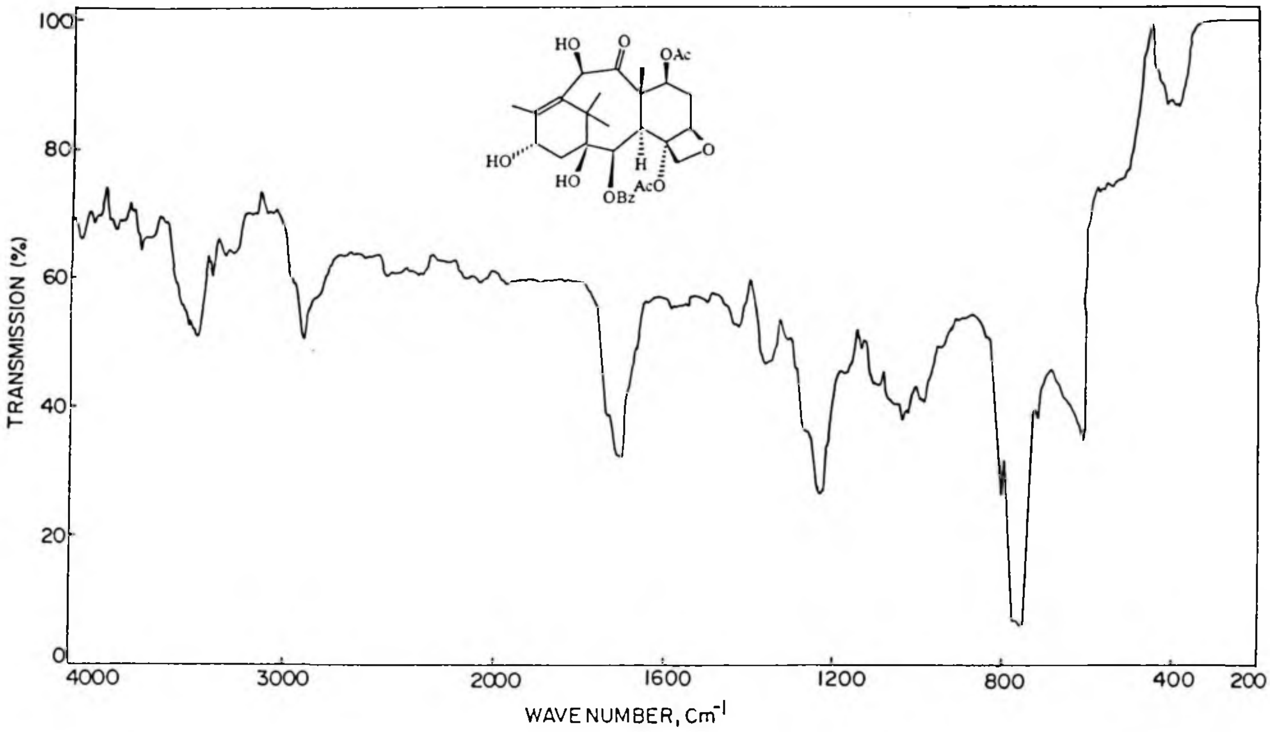


Fig.1. IR Spectra of Compound I

The ^{1}H NMR spectrum (Fig 2; table 1) of the of the compound showed three methyls at δ 1.05 , 1.20, 1.80 as singlets for H-16, H-17 and H-19 respectively and a methyl on double bond at δ 2.14 as doublet (J= 1.0 Hz) for H- 18. This pattern of the tertiary methyl groups indicated that compound (I) belonged to taxane type of compound.

The ^{1}H NMR spectrum of the compound (I) further revealed the presence of two acetyl groups at C- 4 & C – 7 by showing two methyl signals at δ 2.30 and 2.00 as singlets respectively. However the methyl signal at δ 2.00 singlet is a new signal which is not present in 10 – DAB – III from this species. These type of Taxoids were isolated by Kingston etal [103] (1982) from T. brevifolia species.

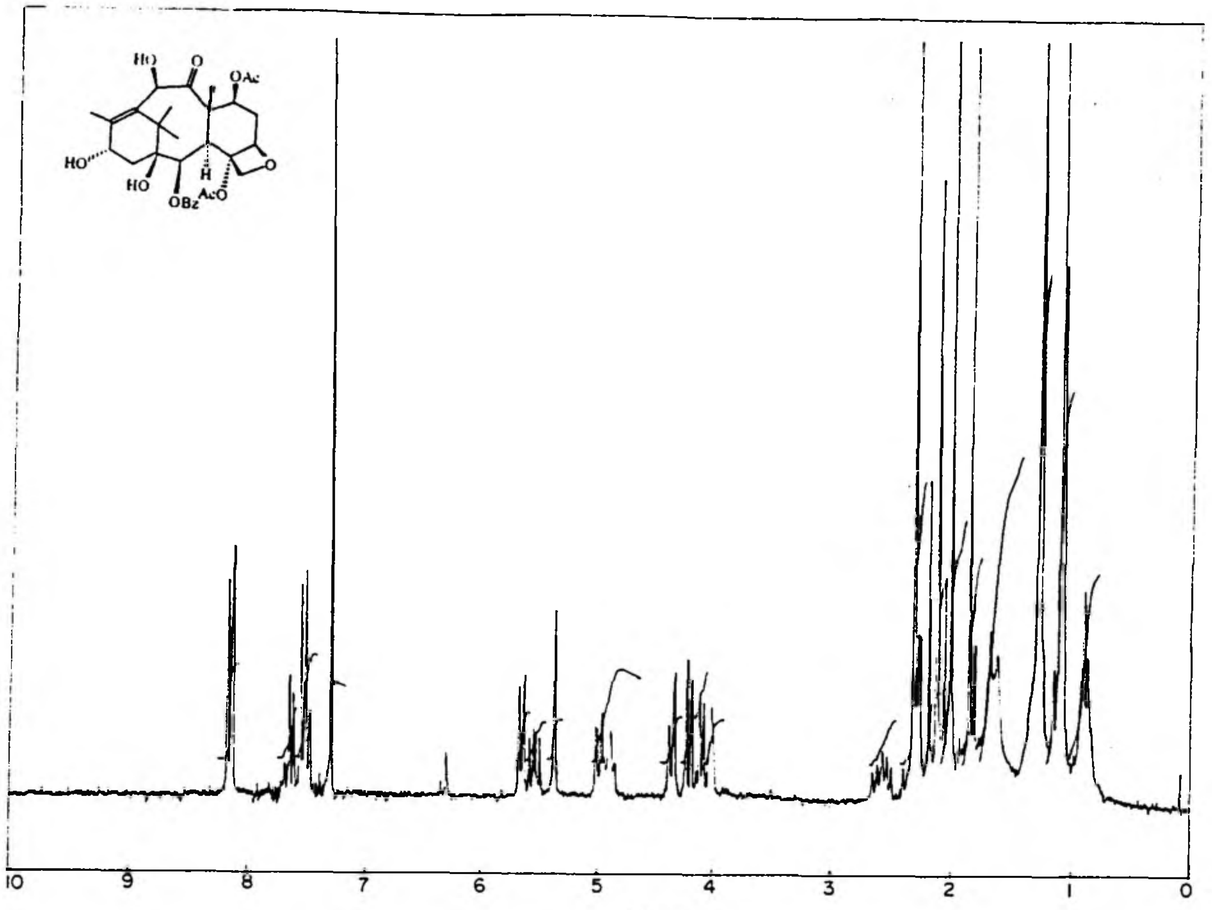


Fig. 2 ^{1}H NMR Spectra of Compound I

It also revealed the presence of a hydroxyl group at C- 1 and a benzoyl group at C- 2 by showing a doublet at δ 5.65 (J = 7Hz) due to H – 2 which couples with H – 3 appearing at δ 4.05 doublet (J = 2 Hz).the coupling constants showed clearly that these protons should be trans to each other i.e. H – 2 as β and H – 3 as α, as in other taxanes.

The ^{1}H – NMR spectrum further showed a singlet at δ 5.35 accounting for one proton which has to be due to H –10 indicating the presence of a carbonyl group at C – 9 and hydroxyl group at C- 10. The chemical shift of acetate methyl at δ 2.30 singlet clearly revealed to be at C- 4 and an oxetane ring present in the molecule. The spectrum showed the typical doublet of doublet as AB quartet for H – 20a and H – 20b of oxetane ring at δ 4.15 as doublet (J = 10.0 Hz) and at δ 4.30 as doublet (J = 10.0 Hz) respectively. The proton at C – 5 also appeared at δ 5.0 as doublet of doublet (J =2, 9 Hz) for H – 5. However the spectrum did not show a multiplet at δ 4.24 for H – 7 as found in 10 – DAB or 10 – Deacetyl taxol. Instead it showed a downfield shift of H – 7 proton as a doublet of doublet at δ 5.50 (J = 7.0, 9.50 Hz) due to acetyl group attached to H – 7 accounting for one proton (H – 7). The spectrum further revealed that a triplet of quartet at δ 4.92 (J = 4.0, Hz) was assigned to C – 13 proton by analogy with other taxane hydroxyls, the smaller coupling constant with the C – 18 methyl group. This proton exhibited signals at δ 7.50m (2H); 7.62 m (1H) and 8.10 (2H) characteristics of the presence of benzoyl side chain at C – 2 in the compound (I). A singlet indicated the presence of another secondary hydroxyl group at δ 5.35 for H – 10, which was shifted to δ 6.30 after acetylation with pyridine and acetic anhydride at room temp.

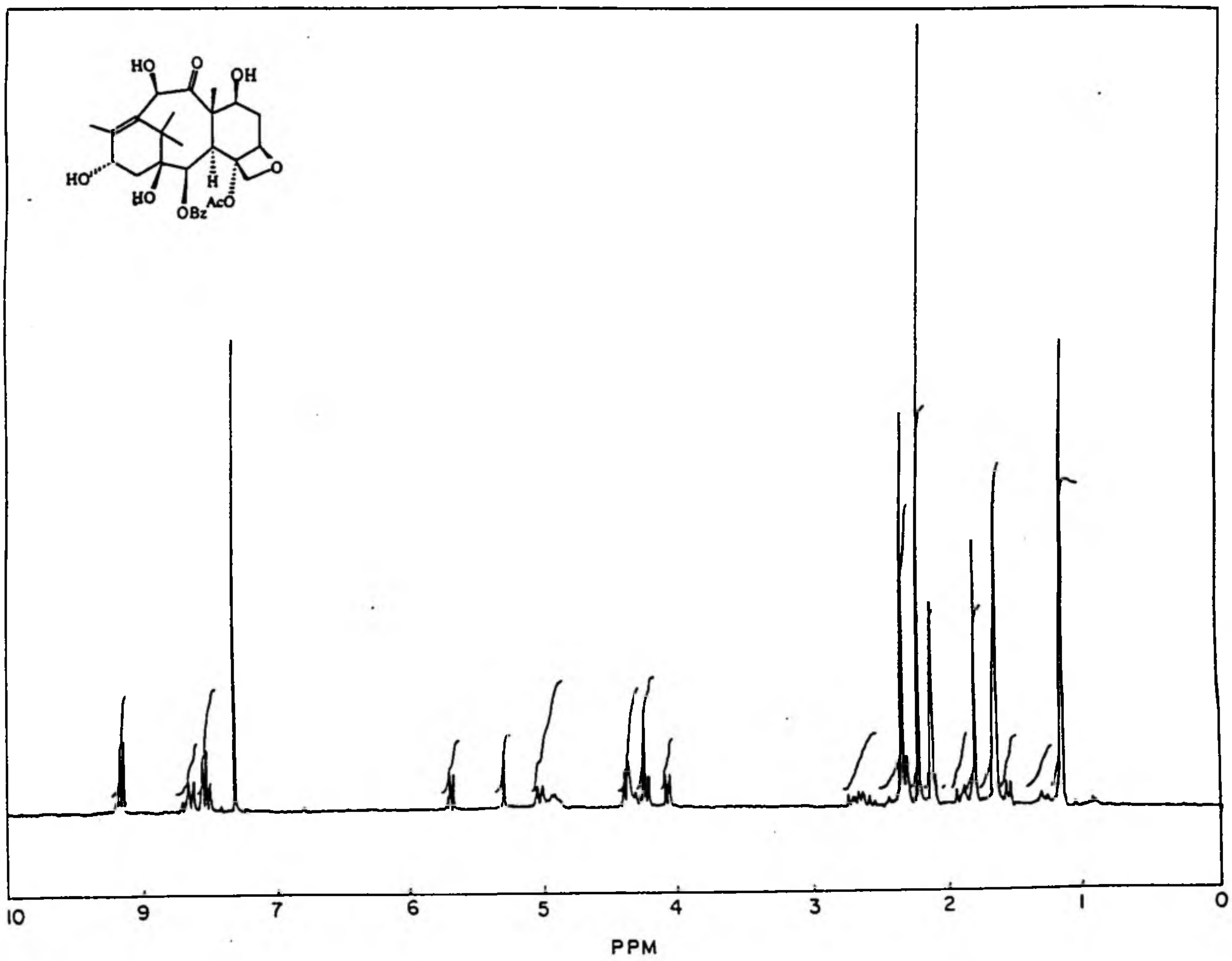


Fig.3 ^{1}H NMR Spectra of Compound I

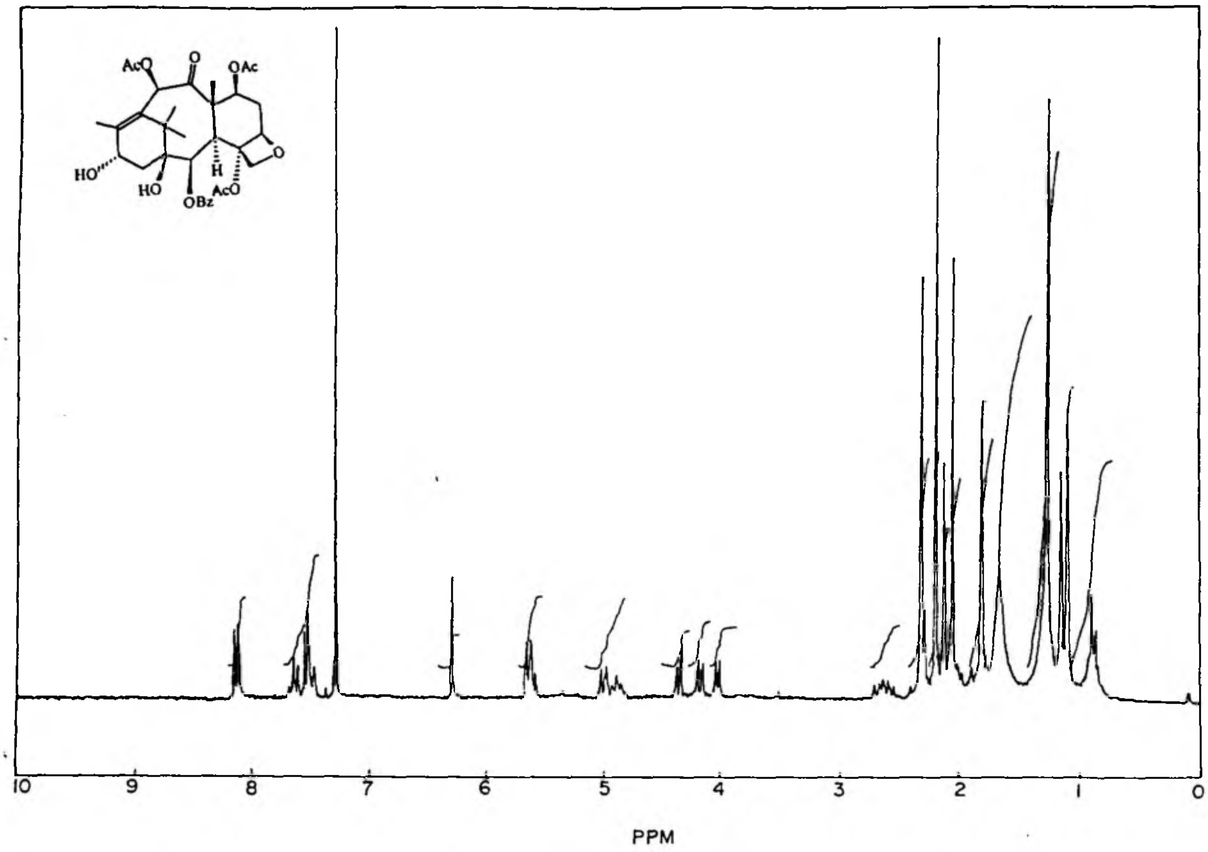
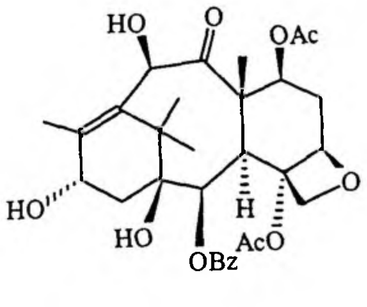


Fig. 4. ^{1}H NMR Spectra of Acetylated 10 DAB

Further comparison of these spectral data with those of 10 – deacetyl baccatin III (Fig.3), and its acetylated product (Table.1, Fig. 4) it became clear that compound (I) was indeed 7. β – Acetoxyl – 10 deacetyl baccatin III. The spectral data (1H – NMR, IR. Mass) of compound (I) was identical to the acetylated product of 10 deacetyl baccatin III in all respect.



[I]

Table 1. : ^{1}H NMR ($CDCl_3$) Spectral data of compound I

Proton	10 – Deacetyl baccatin (10-DAB)		Compound - I		Acetate of 10 –Deacetyl baccatin	
	Chemical Shift δ	Multiplicity	Chemical Shift δ	Multiplicity	Chemical Shift δ	Multiplicity
H-2	5.60	d, J = 7Hz	5.65	d, J = 7Hz	5.65	d, J = 7Hz
H-3	3.96	d, J = 7Hz	4.05	d, J = 7Hz	4.0	d, J = 7Hz
H-5	4.95	d, J = 9Hz	5.0	dd, J = 2, 9Hz	5.0	d, J = 9Hz
H-6	2.26	m	2.30	m	2.30	m
H-7	4.24	m	5.50	dd, J =7, 9.5 Hz	5.60	Overlapped with H-2
H-10	5.25	s	5.35	s	6.30	s
H-13	4.78	br, t, J = 1, 4	4.92	br, t, J = 1, 4	4.92	tq, J = 1, 4Hz
H-14	2.57	m	2.60	m	2.70	m
H-16	1.10	s	1.05	s	1.05	s
H-17	1.10	s	1.14	s	1.10	s
H-18	2.07	br, s	2.10	br, s	2.10	br. d, J = 1.0Hz
H-19	1.75	s	1.80	s	1.85	s
H-20A	4.24	d, J = 9Hz	4.15	d, J = 9Hz	4.15	d, J = 10Hz
H-20B	4.36	d, J = 9Hz	4.30	d, J = 9Hz	4.30	d, J = 10Hz
OBz	7.48	m	7.50	m	7.50	m
	7.68	m	7.60	m	7.62	m
	8.13	dd J = 2, 7Hz	8.10	dd J = 2, 7Hz	8.12	dd J = 2, 7Hz
OAc	2.28	s	2.0	s	2.02	s
			2.30	s	2.15	s
					2.35	s

1.3.2 Characterization of compound (II),

Compound (II a) obtained as methylated product, yellow solid m.p. 212^0 C, showed its UV spectrum λ max at 264 to 322 nm (Fig – 5) suggested a flavone skeleton. It showed in its mass spectrum molecular ion peak at m/e 622, suggesting the molecular formula $C_{36}H_{30}O_{10}$. It showed in its IR spectrum (Fig – 6), the carbonyl at 1720 cm^{-1}, absorption at 1640 cm^{-1} for unsaturation, 1380 cm^{-1} & 1440cm^{-1} for aromatic moiety. ^{1}H NMR spectrum (Table 2, Fig. 7) revealed the presence of six methoxy group at δ 3.80, 3.84, 3.86,3.92, 3.94 and 4.10.

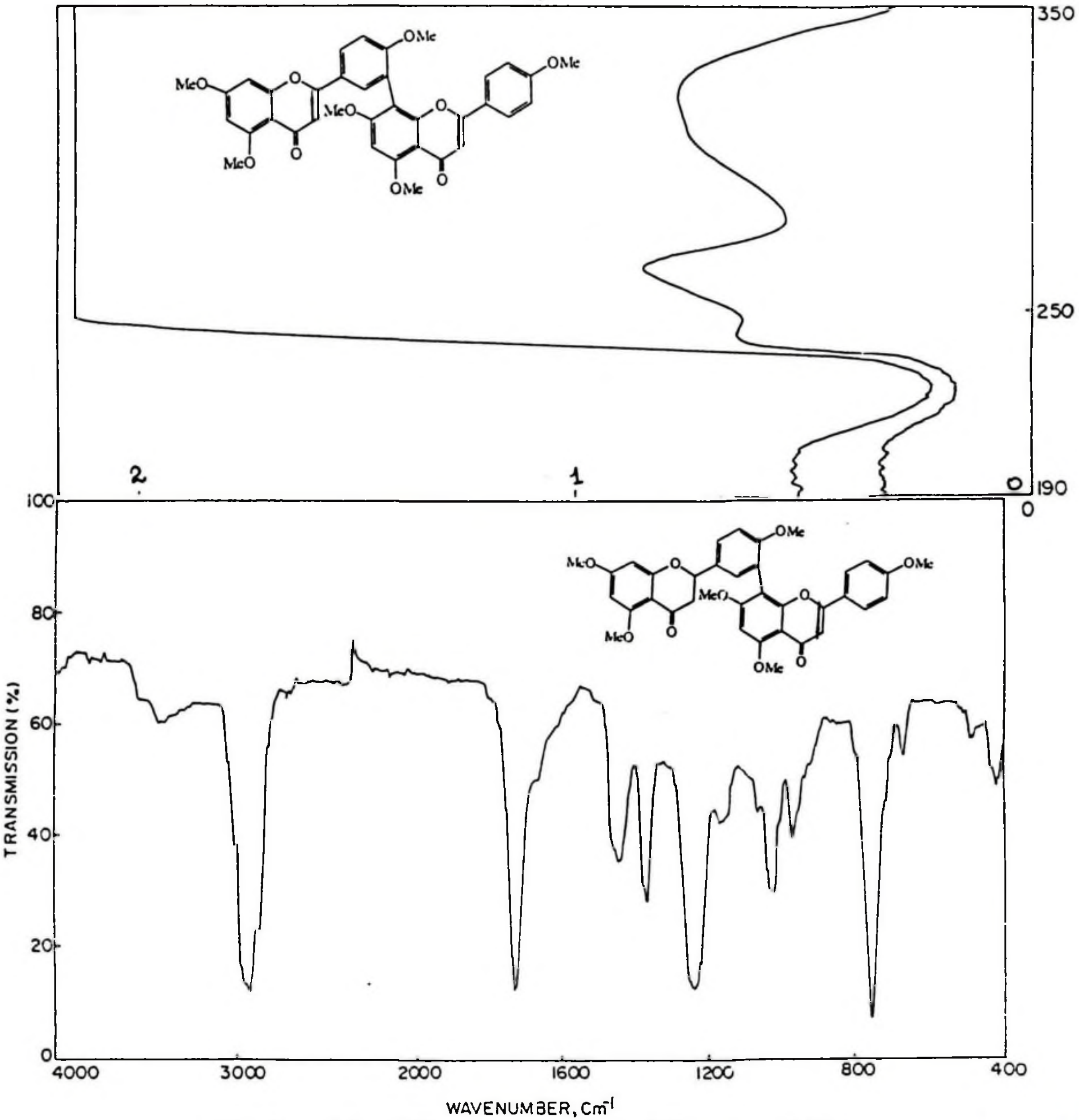


Fig. 5 and 6 . UV and IR Spectra of Compound IIa

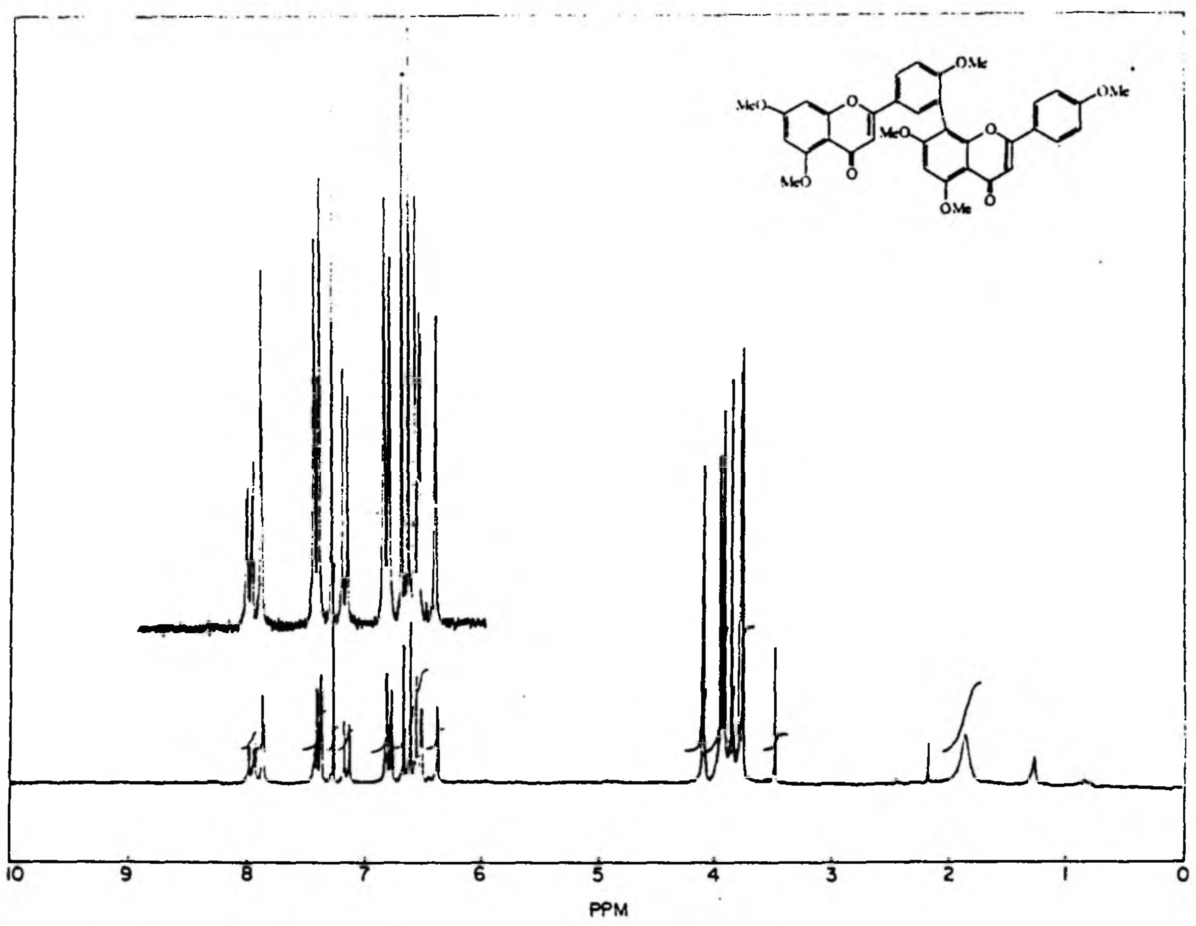
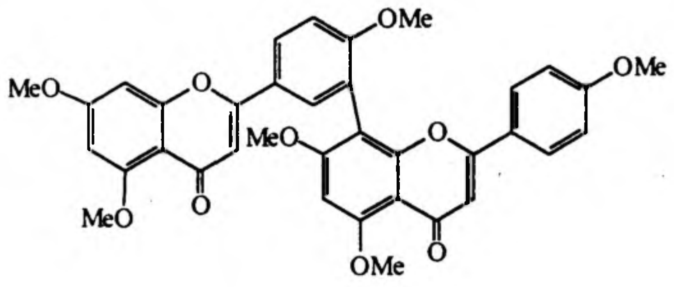


Fig. 7. ^{1}H NMR Spectra of Compound II a

All these features of ^{1}H NMR spectrum of compound (II a) clearly indicated that the molecule must be a biflavone type of compound with A_2 B_2 system, i.e. two doublets at δ 6.80 and δ 7.3 (d, J = 9.0 Hz) for H - 3’’’ (H-5’’’) and H - 2’’’ (H - 6’’’), respectively, while those of the second unit of biflavone exhibited three aromatic protons as (i) doublet at δ 7.13 (d J = 9.0 Hz) for H-5’ indicates the ortho coupling of the proton with H - 6’ (ii) doublet of doublet at δ 7.86 (d J = 9.0 Hz, 2.0 Hz) for H-6’ indicates that the ortho meta coupling of the protons with H-5’.and H-2’ respectively. (iii) A doublet at δ 7. 93 (J = 9.0 Hz) for the proton H-2’ indicates the meta coupling with H-6’. Similarly in case B_2 system the protons H-6’’’ and H-5’’’ resonate at δ 7.37 (dd J =9.0 Hz, 2.0 Hz) and δ 6.80 (d, J=9.0 Hz) respectively due to ortho meta coupling. The fact that the ring A of one flavone unit linked with ring B of the other to have an unsymmetrical biflavone. The structure was further confirmed by appearance of only one metacoupled pair of protons at δ 6.38 doublet of H-6 with proton at δ 6.50 doublet of proton H-8 with the coupling constant of 2.0 Hz in ^1H NMR spectrum of compound (II a). This ^1H NMR spectral data was compared with the ^1H NMR spectral data of similar compound hexamethyl ether of amentoflavone isolated auracuria species[104].

Based on the above spectral data the spectrum of compound (II a) was characterized as amentoflavone hexamethyl ether.



[II a]

The assigned structure of compound (II a) was further supported by critical comparison of ^{13}C NMR (Fig. 8 and 9) spectral data with that of 7, 4', 7" trimethoxy ether of amento flavone (Table.3) isolated from Taxus baccata[85]

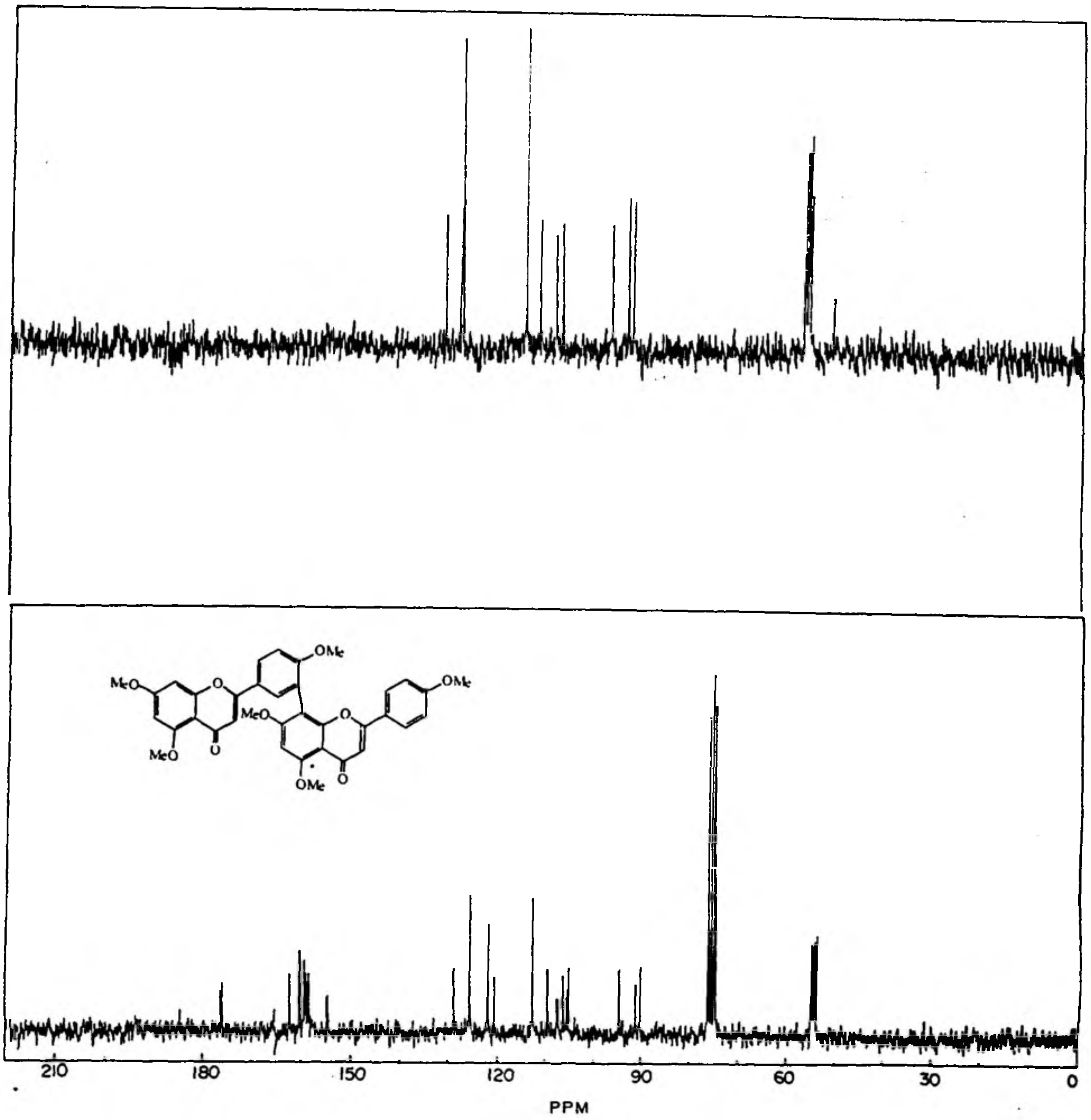


Fig. 8 and 9. ^{13}**C NMR and INEPT Spectra of Compound II a**

The rest of the fraction (which was left during methylation) on acetylation with acetic anhydride and pyridine gave compound (II b), a yellow solid with m.p. 236^0 C. The 1H NMR spectrum (Fig.10) of compound (II b) showed three singlets at δ 2.05, 2.10, and 2.15 for acetoxyl groups and three singlets between δ 3.75, 3.80 and 3.85 for methoxy groups, which clearly indicate that the main fraction (before acetylation as well as methylation) contains biflavone (II) with only three methoxy groups at 7, 7"and 4' positions and three hydroxyl groups at 5, 5", 4"' positions.

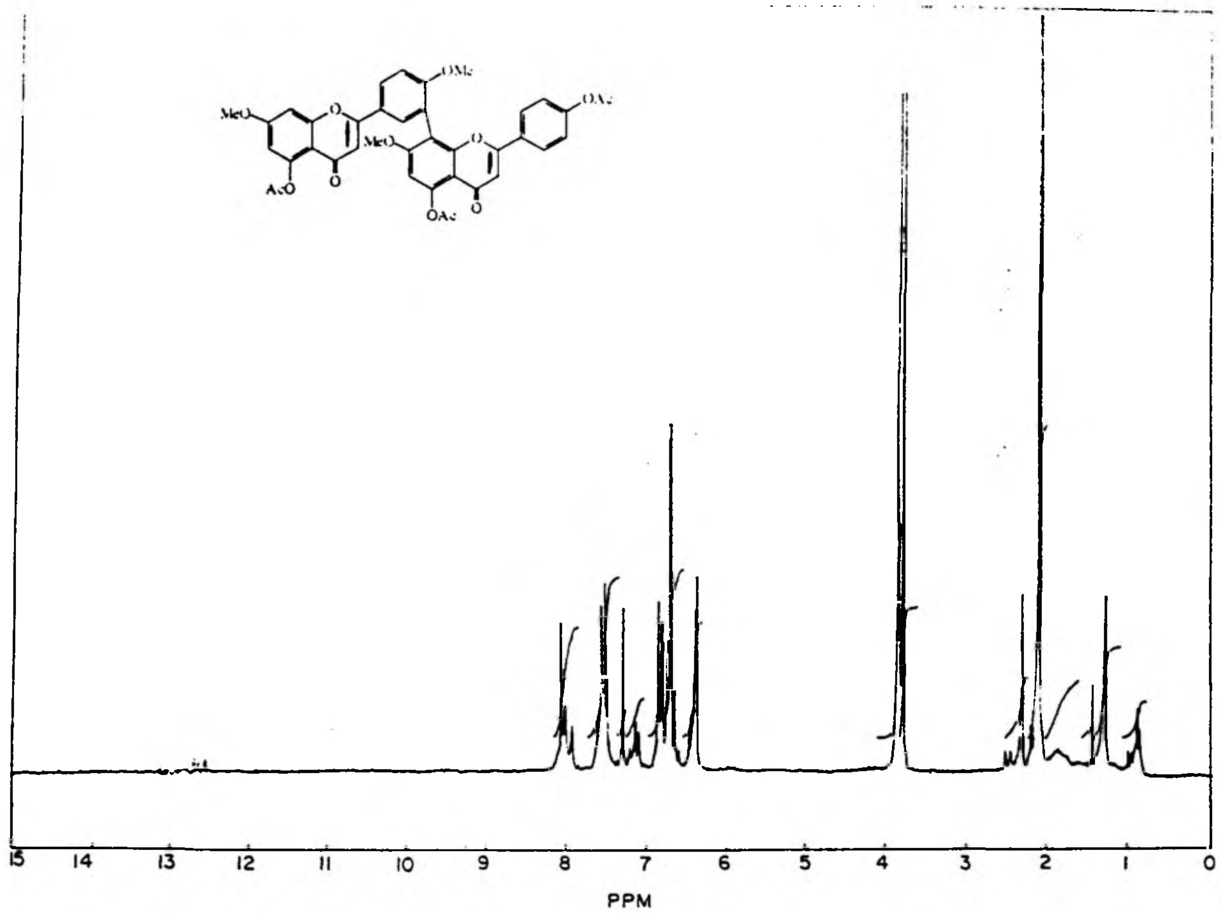
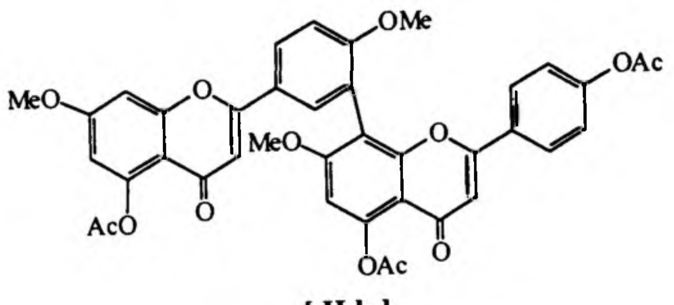
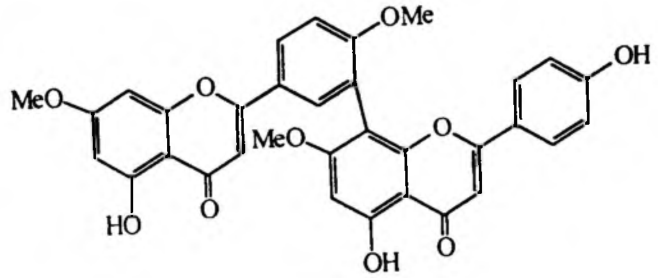


Fig. 10. ^{1}H NMR Spectra of Compound II b



[II b]



[II]

Table 2. : ^{1}H NMR ($CDCl_3$) Spectral data of compound II a

Proton	Chemical Shift δ	Multiplicity	Coupling constant in Hz
H-3	6.62	s, 1 H	--
H-3”	6.55	s, 1 H	--
H-6	6.38	d, 1 H	2.0
H-6”	6.67	s, 1 H	--
H-8	6.50	d, 1 H	2.0
H-2’	7.93	d, 1 H	2.0
H-2’”	7.37	dd, 1 H	9.0, 2.0
H-5’	7.13	d, 1 H	9.0
H-3’”	6.80	dd, 1 H	9.0, 2.0
H-5’”	6.80	d, 1 H	9.0
H-6’	7.86	dd, 1 H	9.0, 2.0
H-6’”	7.37	dd, 1 H	9.0, 2.0
OCH_3	3.80	s	
	3.84	s	
	3.86	s	
	3.92	s	
	3.94	s	
	4.10	s	
OH	--	--	--

Table 3. : ^{13}C NMR ($CDCl_3$) Spectral data of compound II a

Carbon	Chemical shift in delta
C-2	164.15 (s)
C-2"	167.10 (s)
C-3	106.7 (d)
C-3"	107.0 (d)
C-4	177.7 (s)
C-4"	178.1 (s)
C-4a	107.9 (s)
C-4" a	108.9 (s)
C-5	161.1 (s)
C-5"	160.31 (s)
C-6	96.31 (d)
C-6"	93.05 (d)
C-7	168.10 (s)
C-7"	160.66 (s)
C-8	92.04 (d)
C-8"	107.95 (s)
C-8a	160.0 (s)
C-8" a	156.3 (s)
C-1'	122.5 (s)
C-1"'	123.7 (s)
C-2'	130.26 (d)

C-2’’’	127.4 (d)
C-3’	111.27 (s)
C-3’’’	114.4 (d)
C-4’	160.89 (s)
C-4’’’	162.13 (s)
C-5’	123.7 (d)
C-5’’’	114.43 (d)
C-6’	127.6 (d)
C-6’’’	127.4 (d)

1.4 Experimental

The needles of *Taxus baccata* were collected from Darjeeling, West Bengal, India in November 1995. These needles were shade dried and powdered. The powder (5-Kg) was extracted with methanol at room temperature. The extract was filtered and concentrated under reduced pressure to yield dark green mass (165 g). The concentrated extract (65-g) was subjected to column chromatography over silica gel (60 - 120 mesh) using acetone – pet ether as the eluting gradient with increasing proportion of acetone to collect seven fractions (Table 4). Fractions (IV) on repeated column chromatography coupled with preparative TLC yielded compound (I) (Table 5). Half of fractions VII on methylation and its repeated column chromatography coupled with preparative TLC yielded compound (II a) (Table 6). Rest of the fraction (fraction VII) on acetylation with acetic anhydride and pyridine followed by column chromatography coupled preparative TLC yielded compound (II b) (Table 7).

1.4.1 Isolation of compound (I)

Fraction (iii) (3.58 g) of chromatography -2 , (table 5) was purified by repeated preparative TLC using chloroform: methanol (10: 1) as eluents to obtain compound (I) (750mg) as gummy liquid.

$[\alpha]^{25}$: 85^0 ($CHCl_3$) c, 0.4).

IR λmax ($CHCL_3$) : 3410, 1740, 1710 and 1240 cm^{-1} (Fig1).

^1H NMR (2.00 Hz $CDCL_3$) : Table 1., (Fig. 2)

Mass (m/e) : 586 (M^+) (2) ; 568 (12) ; 509 (10); 445 (11) ; 358 (5); 253 (6); 105 (100) and 77 (28).

1.4.2 Isolation of compound (II a)

Half of the fraction (4.5g) (VII) from column chromatography – 1, (table 4) was methylated and isolated the product by column chromatography -3 coupled with repeated preparative TLC using chloroform: methanol (32: 1, 19: 1 and 3:2) as eluent to obtain a mixture of compound to get (1.75 g), Fraction (iii) table 6 on repeated preparative TLC using chloroform: methanol (19:2) as eluents to obtain compound (II a) in pure form (80 mg).

m.p. : 212^0

UV λmax ($CHCl_3$) : 264 to 322nm 9 (Fig : 5)

IR, ($CHCl_3$) :1720, 1640, 1440 and 1380 cm^{-1} (Fig. 6)

1H NMR (200 MHz) $CDCl_3$:Table 2 (Fig. 7)

^{13}C NMR(200 MHz) $CDCl_3$:Table 3 (Fig. 8 and 9)

1.4.3 Isolation of compound (II b)

Remaining part of fraction (4.5g) VII from column chromatography (I) was acetylated and was isolated by column chromatography – 4, and repeated preparative TLC using chloroform: methanol as eluents to obtain compound (II b) in impure form which on repeated preparative TLC using chloroform : methanol (32 : 1) as eluents gave the pure compound (II b) (4 0 mg).

Table 4 : Column chromatography – 1 of methanol extract of *T. baccata.*

Fraction	**Eluent**	**Total volume collected**	**Approx. Wt. In grams**	**Composition**
I	Pet ether	250ml X 4	15.5	Aliphatic compounds
II	PE(90) : Acetone(10)	250ml X 4	7.00	Complex mixture
III	PE(80) : Acetone(20)	250ml X 4	6.30	Mixture of taxanes
IV	PE(70) : Acetone(30)	250ml X 4	8.70	Mixture of 10DAB & Compound I

V	PE(60) : Acetone(40)	250ml X 5	7.50	Mix. of 10 DAB & Aromatic compound
VI	PE(50) : Acetone(50)	250ml X 4	3.0	Aromatic compounds
VII	PE(25) : Acetone(75)	250ml X 4	9.50	flavonoids
VIII	Acetone	500ml X 3	5.60	Mix. of unidentified compounds

Table 5: Column chromatography – 2 of fraction IV of table 4

Fraction	**Eluent**	**Total volume collected**	**Approx. Wt. in grams**	**Composition**
i	PE(90) : Acetone(10)	100ml X 3	1.2	Complex mixture
ii	PE(80) : Acetone(20)	100ml X 4	1.00	Other taxanes
iii	PE(70) : Acetone(30)	100ml X 4	3.50	Compd I and 10DAB
iv	PE(60) : Acetone(40)	1000ml X 3	0.95	10DAB

Table 6 : Column chromatography -3 of fraction VII table 4 (after methylation).

Fraction	**Eluent**	**Total volume collected**	**Approx. Wt. in grams**	**Composition**
i	$CHCl_3$(32) : MeOH(1)	100ml X 2	2.0	Mix. of arom. Complex
ii	$CHCl_3$(19) : MeOH(1)	100ml X 2	1.75	Compound IIa
iii	$CHCl_3$(3) : MeOH(2)	100ml X 3	1.0	Aromatic compounds

Table 7: Column chromatography –4 of fraction VII table 4 (after acetylation)

Fraction	**Eluent**	**Total volume collected**	**Approx. Wt. in grams**	**Composition**
i	$CHCl_3$(32) : MeOH(1)	100ml X 2	1.75	Compound IIb
ii	$CHCl_3$(19) : MeOH(1)	100ml X 2	1.00	Mix. of arom. Compds
iii	$CHCl_3$(3) : MeOH(2)	100ml X 3	1.25	Mix. of Arom. Compds

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Chapter II

Chemical Investigation of Amoora lawii.

2.1 Introduction

The species *Amoora* belonging to the natural order Meliaceae comprising of about 25 species generally found as evergreen trees and distributed mainly in the Ind-Malaya region, tropical and subtropical Asia, Polynesia and Australia[1]. About a dozen species found in India[1], such as *Amoora rohituka (Aphanamixis polystechya); Amoora cullculata; Amoora lawii; Amoora canarana; Amoora wallichi* and *Amoora grandifolia.*

2.2 Review of literature

The detailed survey of literature showed that only few species of genus *Amoora* were chemically investigated so far. Most of the work done so far has been confined to the constituents of the arial parts i.e. leaves and stem. aphanomols, amoorastatin, limonoides, fatty acids, glycerides, sitosterols, amooranin, saponins and ketofatty acids are the major characteristic constituents[2-9] from this genus.

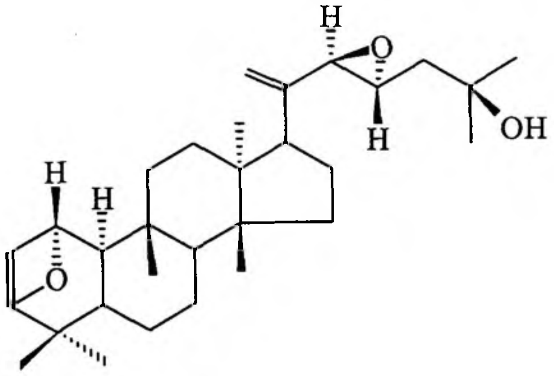
The species of this genus which are chemically investigated so far as *Ammora rohituka (Aphanamixis polystachya), Amoora walllichii* and *Amoora grandifolia*[2-9]. *Amoora rohituka* is the only species that has been chemically investigated in detail and isolated amooranin[7], gedunin[6], limonoides[5], ketofatty acids[9] and saponins[8]. These compounds were biologically tested and found to be the gedunin is active as antimalerial[6] and amooranin showed in vivo antitumor activity against N-nitrosomethyl urea-induced mammary adenocarcinoma in rats[7]. The other two species *Amoora grandifolia* and *Amoora wallichii* on chemical investigation gave aphanomols[2], limonoides[5], amoorastatin[3] and sitosterol[6] respectively.

2.3 Present work

Amoora lawii[10], a moderate sized tree occurring in Konkan area of Maharashtra and North Canara, India, Western Peninsulla. The young branches of the tree lepiodate with yellowish brown scales at length glabrous. Leaves imparipinnate, 6-9 inches long; common petiole short leaflets. Flowers are white, in axillary much branched panicle clothed with yellowish brown scales. Fruits buff colored, pyriform densely lepiodate.

A compound amooranin [7] and gedunin[6] a constituents of *A. rohituka* has been reported to be effective against tumor and malaria respectively. A related species, *A. lawii,* which is commonly available in Maharashtra and Karnataka, India, has not been studied so far from the point of view of its utility as the source of such anticancer and antimalarial drugs. There are no reports on chemical investigation from this species so far therefore the species is monotypic. With a view to explore the possible biologically active compounds similar to amooranin or its precursors, work was undertaken for chemical investigation of the plant of species *A. lawii.*

The Ariel parts of the plant were extracted successively with pet-ether, acetone and methanol. The acetone extract of *A. lawii,* after successive chromatography over column grade silica gel and repeated preparative TLC afforded a new compound (I) a triterpenoid.



[I]

2.4 Characterization of Compound I

Compound I was obtained as a colorless viscous oil, $[\alpha]_D^{25}$ - 5 ($CHCl_3$, c, 0.38), showed in its mass spectrum M^+ at m/e 454 suggesting the molecular formula $C_{30}H_{46}O_3$. Its IR spectrum (Fig.1) showed characteristic bands at 3400cm^{-1} which suggest the presence of hydroxyl group and another band in its IR spectrum at 1665cm^{-1} revealed the presence of unsaturation in the molecule. ^{1}H NMR spectrum (Table.1, Fig. 2) of the compound revealed seven tertiary methyl groups, olefinic proton and exocyclic methylene protons. Its ^{13}C NMR spectrum (Table 2, Fig. 3) along with INEPT experiments (Fig. 4) showed 30 peaks out of which there are seven quartets, eight triplets, eight doublets and seven singlets indicating the number of carbon atoms in the molecule to be 30. Thus the compound may be the triterpene.

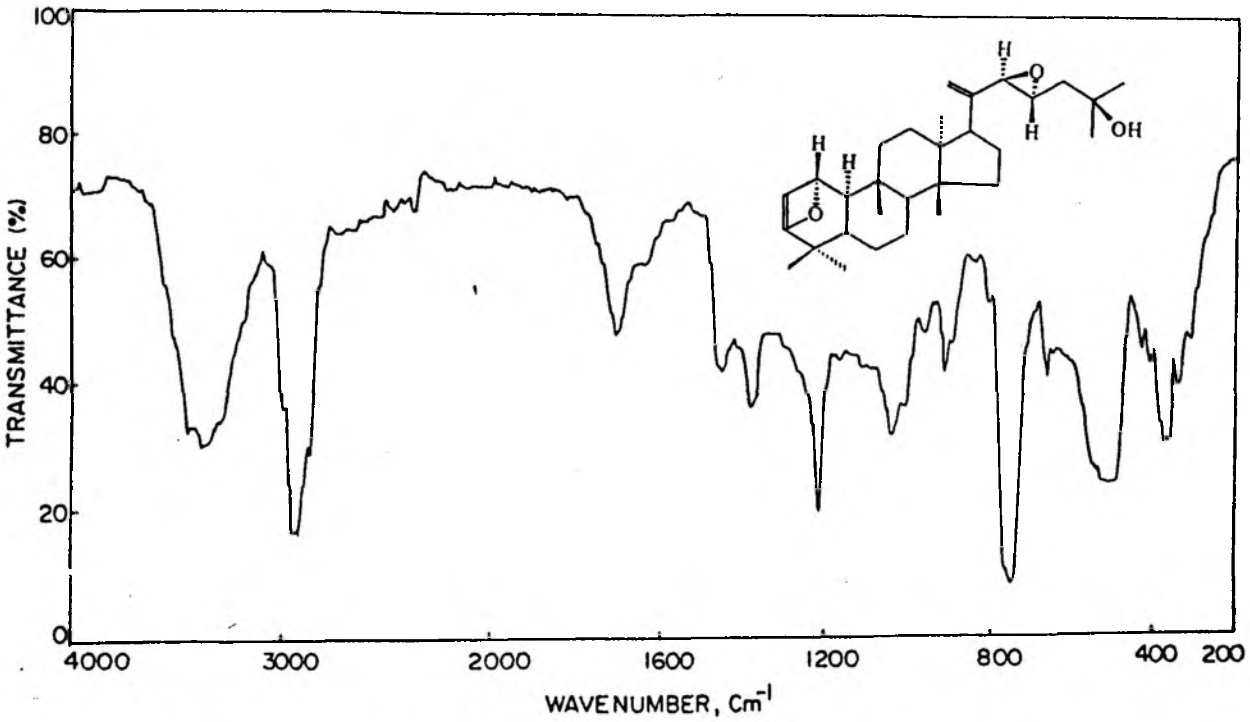


Fig.1. IR Spectra of Compound I

The ^1H NMR spectrum of the compound shows that the signals at δ 0.80, 0.90, 0.92 as a singlets for 3 protons each and a singlet at δ 1.08 for 6 protons revealed that there are five methyl groups present in the upfield region. The downfield methyl signals as singlets at δ 1.15 and δ 1.20 for 3 proton each indicates that these tertiary methyl groups must be attached to oxygenated carbon atom. The ^1H NMR spectrum of the compound further shows that the presence of exocyclic methylene groups appeared as a broad singlets at δ 4.65 and δ 4.75 for one proton each (21-Ha and 21-Hb). The signals at δ 5.85 as doublets (J =5.0 Hz) showed that the presence of the olefinic proton at H-2 in the molecule. In addition to this, the spectrum further showed that the signals as a triplet at δ 3.95 (J = 7.50 Hz); doublet at δ 4.15 (J = 8.0 Hz) and multiplet at δ 3.60 for one proton each reveals that the presence of either secondary hydroxyl group or ether linkage in the molecule which was further confirmed by acetylating the compound I with pyridine and acetic anhydride under normal conditions did not react to form a acetate of compound I. These observations suggested that the instead of secondary hydroxyl group the presence of two ether linkages in the molecule.

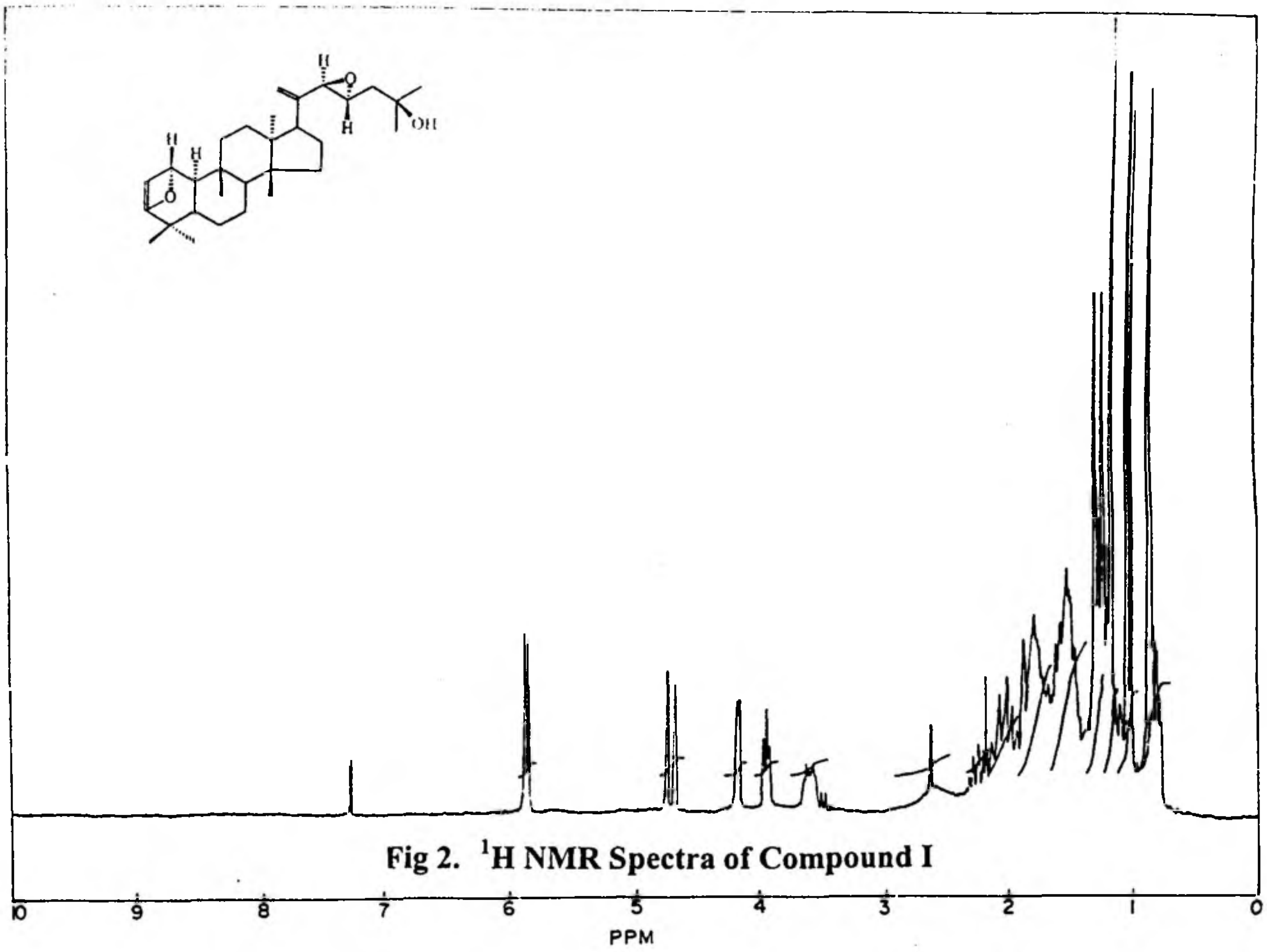


Fig 2. ^1H NMR Spectra of Compound I

Table 1. ^{1}H NMR spectral data of Compound I

Proton.	Chemical shift in δ	Multiplicity	Coupling constant in Hz
H-1	3.95	t, 1H	7.50
H-2	5.85	d, 1H	5.00
H-18	1.08	s, 3H	--
H-19	0.80	s, 3H	--
H-21a	4.65	s, 1H	--
H-21b	4.75	s, 1H	--
H-22	4.15	d, 1H	8.00
H-23	3.60	m, 1H	--
H-26	1.15	s, 3H	--
H-27	1.20	s, 3H	--
H-28	0.92	s, 3H	--
H-29	1.08	s, 3H	--
H-30	0.90	s, 3H	--

On the basis of ^{1}H-^{1}H COSY experiments (Fig. 5) has observed that the signals at δ 3.95 (t, J = 7.50 Hz) couples with the signal at δ 5.85 (d, J = 5.0 Hz) and further the same signal at δ 3.95 (t, J = 7.50 Hz) shows the connectivity with that of H-10 proton appeared as a merged signal at δ 1.55. Secondly the proton signal appeared at δ 4.15 (d, J = 8.00 Hz) shows the connectivity with that of multiplet appeared at δ 3.60 and the same proton signal showed the connectivity with that of the proton signal appeared at δ 1.85 and δ 1.55, which are merged in the multiple's. The COSY experiment further showed that the signal which has appeared as a singlets at δ 4.65 for 21a-H and δ 4.75 for 21b-H has shown long range coupling with signal appeared at δ 2.05 of H-17.

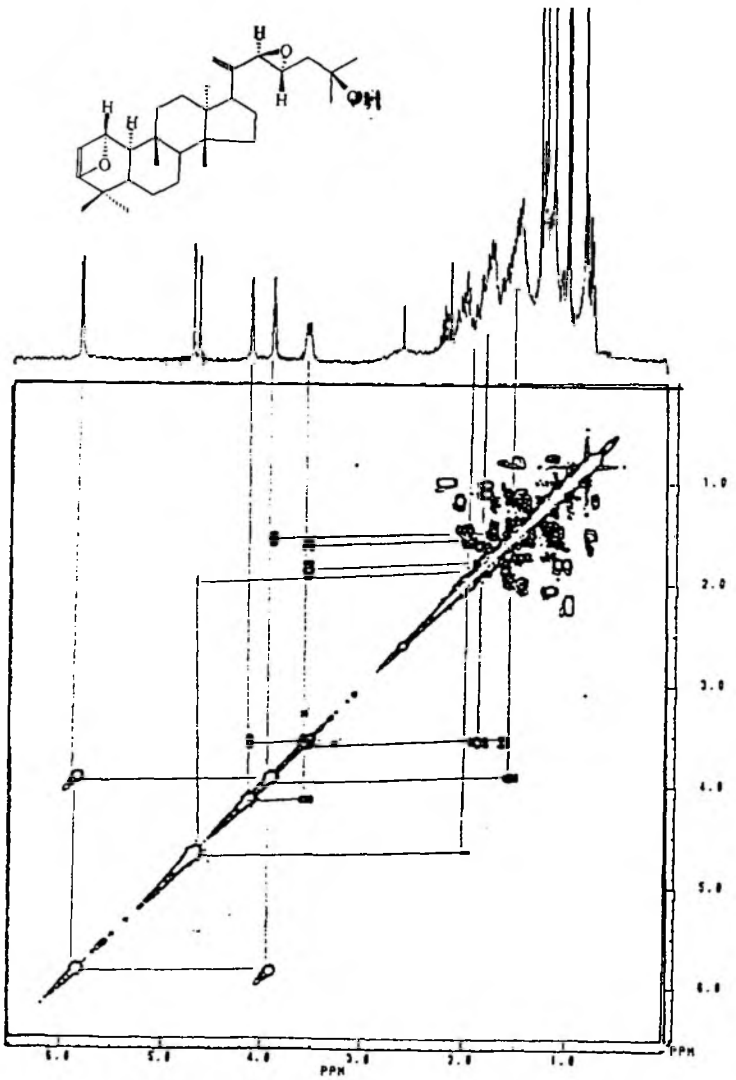


Fig. 5. $^1H - ^1H$ COSY Spectra of Compound I

On the basis of above discussions it has clearly indicated that the presence of olefinic protons at δ 5.85 (d, J =5.00 Hz) must be at C-2 and alternately the proton signal at δ 3.95 (d, J = 7.50 Hz) must be at C-1. The proton signal appeared as doublet at δ 4.15 (J = 8.00 Hz) must be at H-22 whereas the multiplet at δ 3.60 must be located at C-23. There are two possible positions to fix the exomethylene double bond in the molecule i.e. at C-21 and at C-25, but the position C-25 has ruled out due the absence of signal for methyl on double bond in the spectrum of the molecule. Therefore the correct position of the exomethylene group must be at C-21. This was further confirmed by the presence of long range coupling of exomethylene protons with H-17 in COSY experiment.

These conclusions are further supported by ^{13}C NMR spectrum (Table. 2, Fig.3 and 4) appeared at δ 75.04 (d) for C-1; δ 129.52 (d) for C-2; δ 156.22 (s) for C-20; δ 106.26 (t) for C-21; δ 72.06 (d) for C-22; and δ 65.12 (d) for C-23. The stereochemistry for H-1, H-22 and H-23 in the molecule has been derived on the basis of their coupling constants.

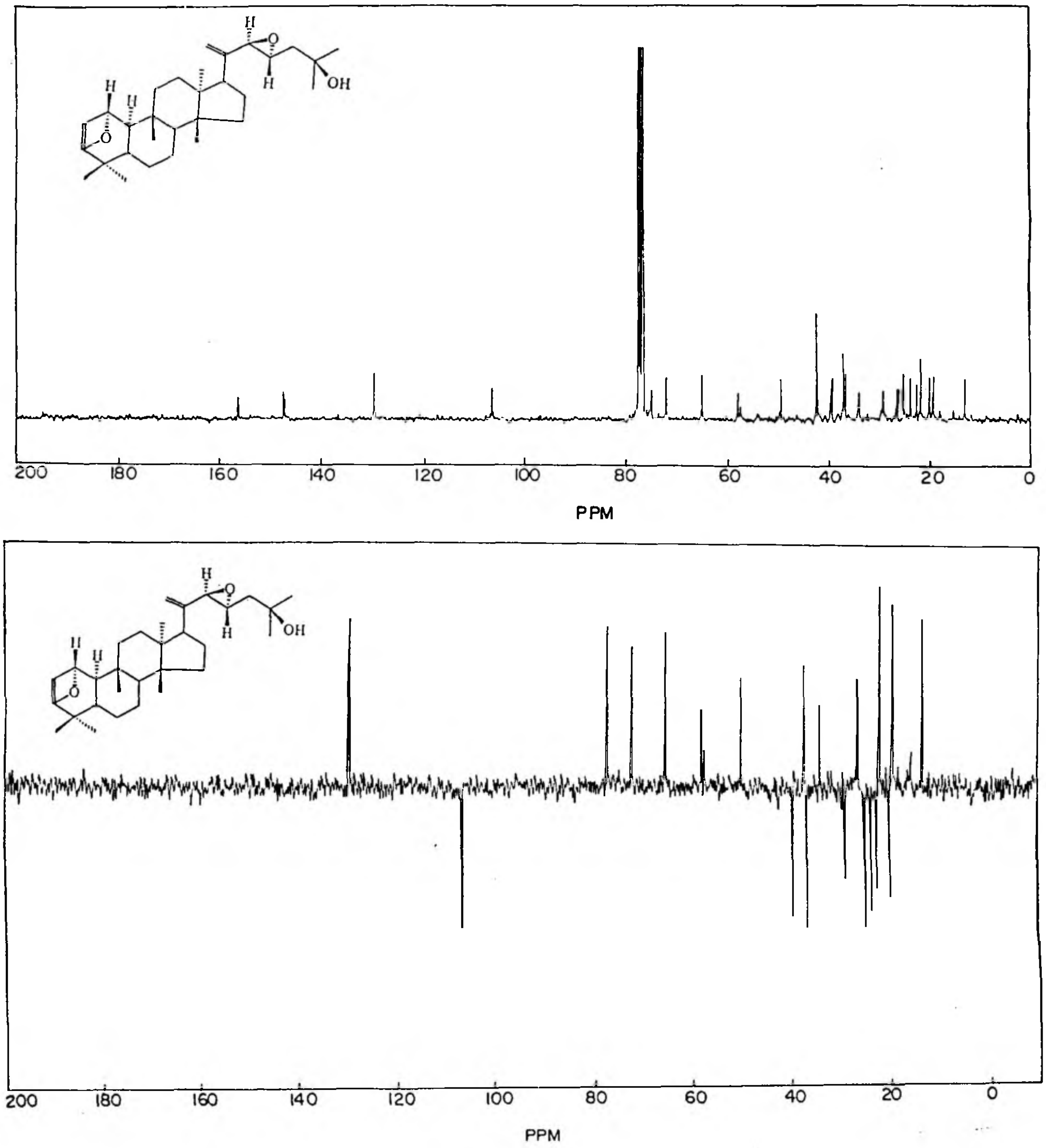


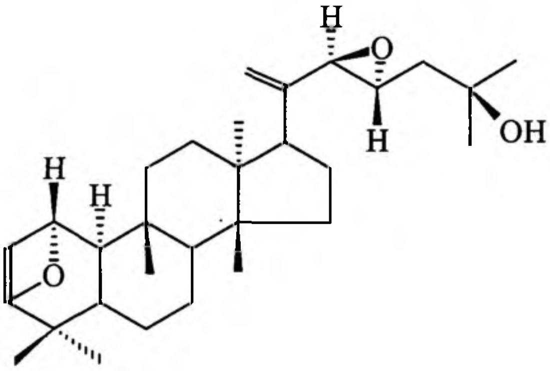
Fig. 3 and 4. ^{13}C and DEPT Spectra of Compound I

Table 2. ^{13}C NMR spectral data of Compound II

S. No.	Carbon	Chemical shift in δ	Multiplicity
1	C-1	75.04	d
2	C-2	129.52	d
3	C-3	147.06	s
4	C-4	28.92	s
5	C-5	57.34	d
6	C-6	19.98	t
7	C-7	22.48	t
8	C-8	49.51	d
9	C-9	42.48	s
10	C-10	37.05	d
11	C-11	23.76	t
12	C-12	25.09	t
13	C-13	42.48	s
14	C-14	42.48	s
15	C-15	28.98	t
16	C-16	36.69	t
17	C-17	57.83	d
18	C-18	13.24	q
19	C-19	19.31	q
20	C-20	156.22	s
21	C-21	106.26	t
22	C-22	72.06	d
23	C-23	65.12	d

24	C-24	39.44	t
25	C-25	75.12	s
26	C-26	33.94	q
27	C-27	26.24	q
28	C-28	21.84	q
29	C-29	26.44	q
30	C-30	21.84	q

Based on the available above spectral data, the probable structure of the compound I was ~~characterized~~ proposed as 19(10 – 9 β) abeo - 10α - lanostane[11] of cucurbitane skeleton.



[I]

The assigned positions of the functional group~~s~~ in the structure of the compound I further supported by the critical comparison of the reported spectral data with that of similar compounds [11, 12, 13] found in various species of cucurbitaceous plants.

2.5 Experimental

The leaves of *A. lawii* were collected from the Mahabaleshwar region of Maharashtra, India in March 1997. The leaves were shade dried and powdered. The course powder (3-kg) was extracted successively with pet-ether, acetone and methanol. The extract was concentrated separately under reduced pressure to yield pet-ether extract (6.0g); acetone extract (8.0g) and methanol extract (30.0g).

The acetone extract (9.0g) was subjected to column chromatography over silica gel (60-120 mesh). The elution was started with pet-ether and continued with the mixture of acetone: pet-ether (5 : 95) and than with successive increase in the percentage of acetone. The fractions showing similar pattern on TLC were combined to obtained 8 fractions (Table 3)

2.5.1 Isolation of compound I

Fraction IV was purified by preparative TLC using benzene : ethyl acetate (80 : 20) as eluent to obtain compounds I in fairly pure form.

$[\alpha]_D^{25}$	: - 5 ($CHCl_3$)
IR ($CHCl_3$, cm^{-1})	: 3400, 1665 (Fig.1)
^1H NMR (200 MHz, $CDCl_3$)	: Table 1, Fig. 2
^{13}C NMR (90 MHz, ($CDCl_3$)	: Table 2. Fig. 3 and 4.
MS : m/e	: 454 (M^+)

Table 3: Column chromatography of acetone extract (9g, silica gel, 250g)

Fraction	Eluent	Total volume	Weight in g	Approximate Composition
I	pet ether	100mlX3	0.940	St. chain Compds
II	pet- ether (95) : acetone (5)	100mlX4	1.610	Unidentified Compds.

III	pet- ether (90) : acetone (10)	100mlX4	0.960	Unidentified Compds.
IV	pet- ether (85) : acetone (15)	100mlX4	0.250	Compound impu and I.
V	pet- ether (75) : acetone (25)	100mlX3	0.300	Complex mix.
VI	pet- ether (60): acetone (40)	100mlX3	1.800	Complex mix.
VII	pet- ether (50): acetone (50)	100mlX3	1.200	Glycosides
VII	pet- ether (75): acetone (25)	100mlX3	1.500	Glycosides

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Chapter III

Chemical Investigation of Callicarpa lanata l.

3.0 Introduction

The genus *Callicarpa lanata* belongs to the family *Verbenacea* . About 120 species of this family are generally found as trees or as shrubs. The characteristic of this genus is its flower, which are axially sessile many flowered cymes. It is a bisexual family. The main centers of distribution of this genus are both tropical & subtropical regions of Eastern Asia. Malaya, Australia and the specific islands of America. Near about more than 10 species are found in India[1] such as *Callicarpa arborea*, C. *americana,* C. *bodineri,* C. *cana* (*C. candicans*), C *formosana,* C. *integerima,* *C. japonica, C. lanata, C. lonifolia, C. maingyi and C. macrophylla.*

3.1 Review of Literature

Not more than 9% of the approximately 120 species of this genus have been investigated chemically. Most of the work done so far has been confined to roots, leaves and bark constituents[1] only. So far steroids, fatty acids, amino acids, sugars, Kaurane type of diterpenes, flavones and related constituents are reported from roots, leaves and bark of this genus. As a result, the information on distribution of Kaurane type of diterpenes and flavonoids is very spotty[2].

So far chemically investigated species of this family are *C. arborea*, C. *bodineri,* C. *cana* (C. *candicans*). C *formosana,* C. *integerima, C. japonica, C. lonifolia, C.. maingyi & C. macrophylla.* The different constituents obtained from the species mentioned above are listed below in table 1.

Table: 1

S. No.	Species	Constituents and their uses	Ref.
1	***C. arborea***	A : Masonic, oleolinic, ursolic acid leupeol acetate, β-amyrin acetate, β- sitisterol, Dihydroxy terpene mono acetate carboxylic acid	2, 3
		B : M. butelinate, β- sitisterol acetate & borneol	4
		C: The amino acids 1 (+) – 9- β-methoxy phenyl propeonic acid.	5
2	***C. bodineri***	Anthocynins glycones, pelumedon, cyanidins, peomidins.	6
3	*C. cana* *(C. candicans)*	Callicarpone, calliterpenones	7
4	*C. formosana*	3,4', 5,7-tetramethoxy flavones; 3,3', 4’, 5,7-pentamethoxy flavones; 5- hydroxy 3,4’, 7- trimethoxy flavones; 5- hydroxy 3,3’, 4, 7 -tetramethoxy flavones; ursolic acid; 2 α, 3 α -dihydroxy urs – 12 en, 28 one acid etc.	8
5	*C. integerima.*	Triacantane; 3', 4’, 6,7 - tetramethoxy flavones; β-sitisterol; 3', 4’, 5,7 - tetramethoxy flavones; Salicylic; Vanillic and Syringic acid.	9
6	*C. japonica*	Reducing sugars, pectins, 5, 6, 7 - tetramethoxy flavones; 4', 5, 6, 7 - tetramethoxy flavones; 7 – fatty acids and 5 amino acids. The extract of this species has got Anti – HIV activity.	10

7	*C. longifolia.*	Calliterpenone and its monoacetate; ursoliic acid; 5 – hydroxy – 3, 7, 3' -trimethoxy flavones.	11
8	*C.. maingyi*	Maingyic acid and its structure determination.	12
9	*C. macrophylla*	A Calliterpenone, its monoacetate and its structure determination. B: Terpenoids & flavones, ursolic acid, structure and absolute configuration. C: Calliterpenone as3 – oxo – 13 - β - kaurane, catagolic acid, amino acids, and ursolic acid.	13

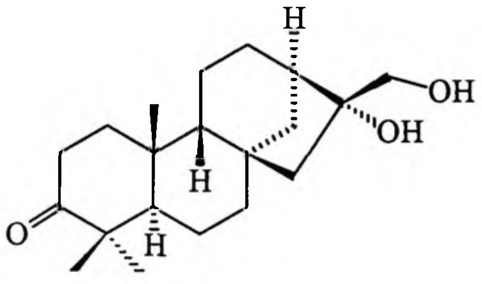
3.2 Present work

Callicarpa lanata, *Linn*[14] is tall shrub or sometimes a small tree occurring throughout the Deccan Peninsula and Sri Lanka. The young branches are stout, cylindrical. Leaves crowed at the end of the branches. Leaves are 3" – 4" in size, ovate dark green with dense stellate tomentin beneath. Flowers sessile, divericately branched, shortly pedunculate densely stelletely tomentosa axillary cymes.

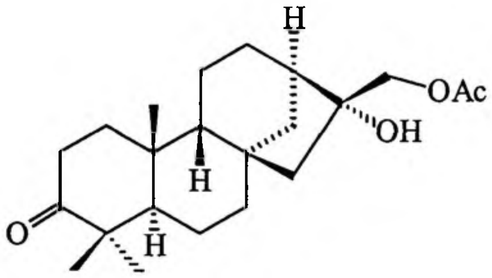
The wood has good working properties and suitable for carving. The bark chewed like betel in Sri Lanka and some parts of South India. A decoction of the bark and root is beneficial for fevers, hepatic obstructions and in skin diseases. The leaves boiled in milk are used as a wash for aphthae of mouth.

Since the species *C. lanata L* is a monotypic and there are no reports on chemical investigation of this species so far. With an intention to isolate the possible biologically active compounds we undertook the chemical investigation of this plant. The Ariel parts of the plant were extracted with acetone. The successive chromatographic separation of acetone extract of *C. lanta L* over column grade silica gel (60-120 mesh)and repeated preparative TLC afforded three compounds (**chart I**). Compound I was Calliterpenone and compound II was its monoacetate which are Kaurane type of diterpenes where as compound III is a ursolic acid. The compound I, II and III are already reported from the other species of the same family.

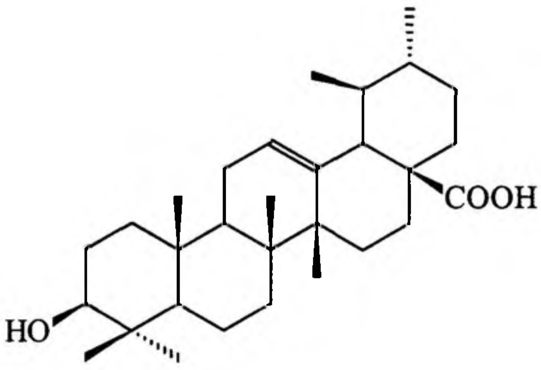
CHART I



[I]



[II]



[III]

3.3 Characterization of compound I

Compound I was obtained as crystalline solid, m.p. 154°C 1. , $[\alpha]^{25}$ + 32 [CHCl$_3$]. It showed its mass spectrum M^+ at m/e 320, suggesting molecular formula $C_{20}H_{32}O_3$. IR spectrum (Fig .1) of the compound should characteristic broad band in the region 3300 –

3400 cm^{-1} and 1710 cm^{-1} revealing the presence of primary and tertiary hydroxy and carbonyl groups respectively. ^{1}H NMR spectrum (Fig. 2) of the compound revealed the presence of three tertiary methyl groups and downfield protons as a doublets of remaining CH$_2$ protons. Its 13 C NMR spectrum (Fig-3 and 4; Table:2) showed twenty peaks indicating to be a diterpene. All these facts showed that compound (I) was a diterpenoid with Kaurane type of skeleton system.

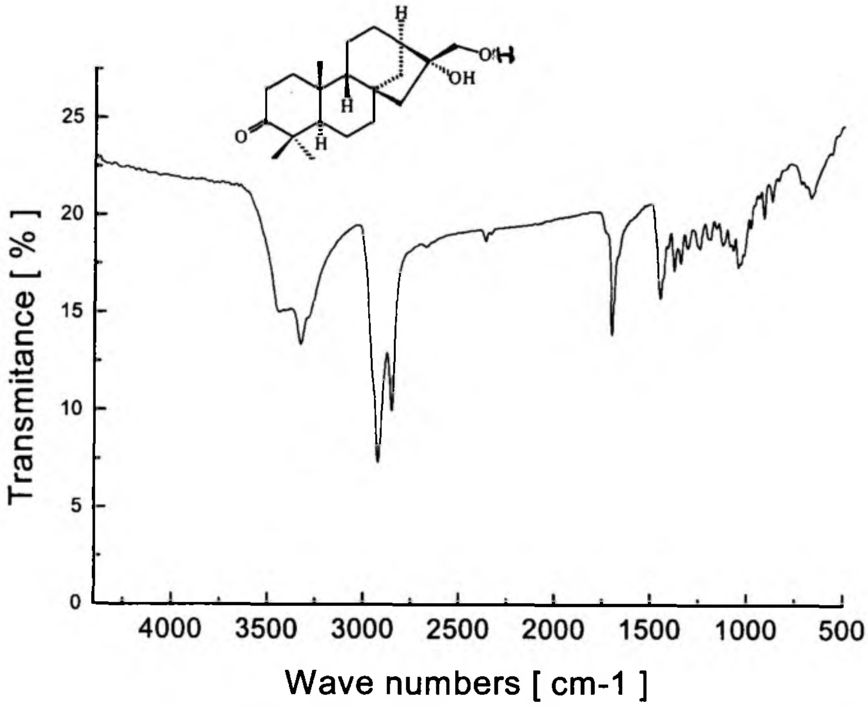


Fig. 1. IR Spectra of Compound I

The presence of a hydroxyl group was further confirmed by mass spectrum, which showed a peak at m/e 302 (M – 18) (7 %). Attempts to acetylate the compound using pyridine and acetic anhydride at room temperature was successful, revealing the nature of one primary or secondary hydroxyl group. ^{1}H NMR spectrum shows the presence of three tertiary methyl groups as singlets at δ 0.97; δ 1.01 & δ 1.06 for 3 protons each. The doublets at δ 3.62 & δ 3.80 (J = 11 Hz) each corresponds to one proton are attributed to methylene protons of hydroxy methyl group (- CH_2OH). A complex multiplet at around δ 2.50 integrating for four protons were associated with two –OH protons & two protons of methylene group at C – 15 (H – 15).

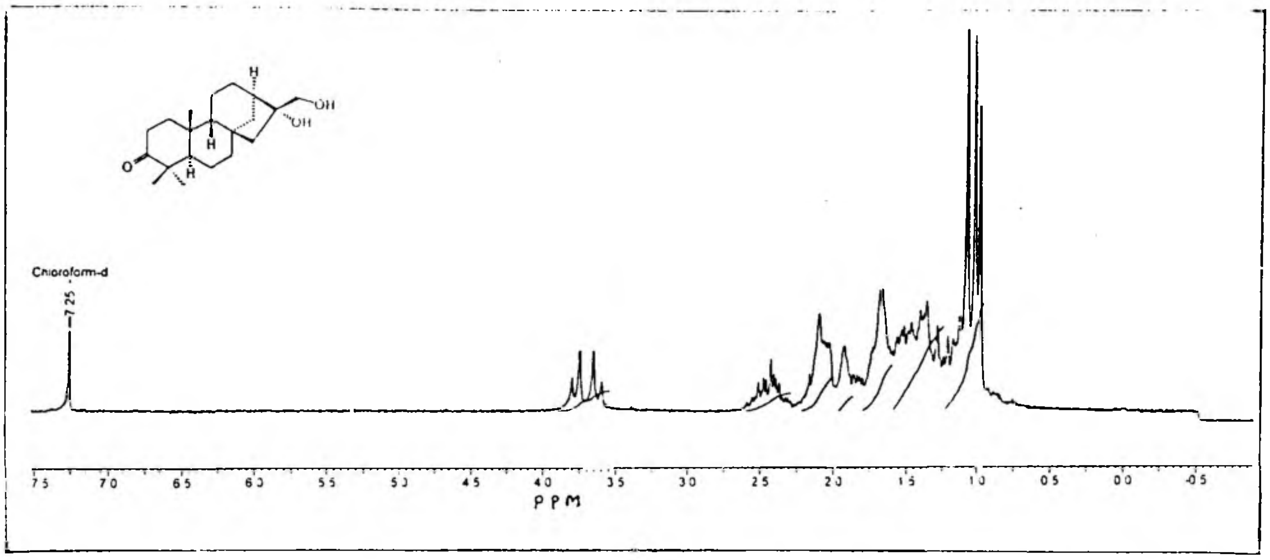


Fig. 2. ^{1}H NMR Spectra of Compound I

This was further confirmed on disappearance of OH protons on deuteration and the spectrum shows a multiplet integrating only for two protons at C – 15 (H – 15) in the same magnetic environment.

The presence of primary hydroxy at C – 17 was further confirmed with ^{1}H NMR spectrum of acetylated product of compound (I) shows sharp singlet at δ 4.21 for protons of $C\underline{H}_2OCOCH_3$ and another singlet at δ 2.10 for acetoxy (- $OCOC\underline{H}_3$) protons.

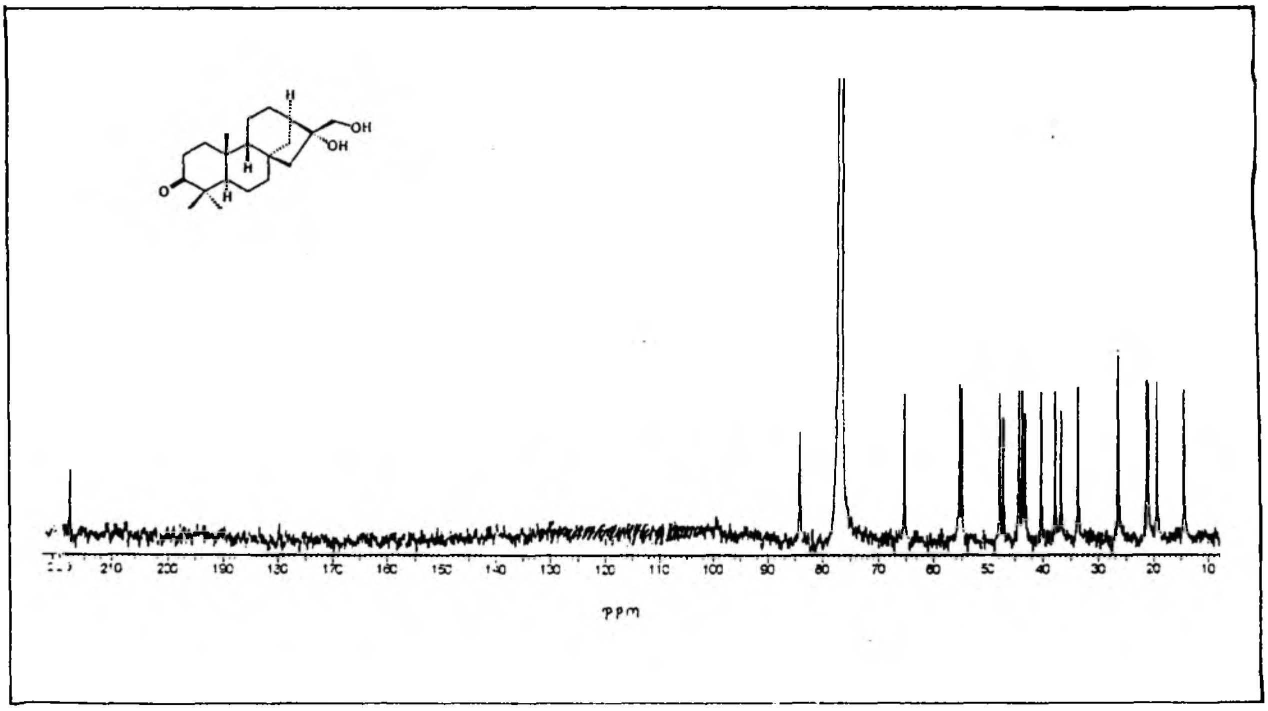


Fig. 3. ^{13}C NMR Spectra of Compound I

^{13}C NMR spectrum (Fig.3 and 4 ; Table. 2) of the compound (I) showed the presence of twenty signals confirming the twenty carbon atoms in the molecule, out of which three signals as quartets at δ 14.57, δ 21.29 and δ 26.54 for tertiary methyl groups at C – 18, C-19, C–20.

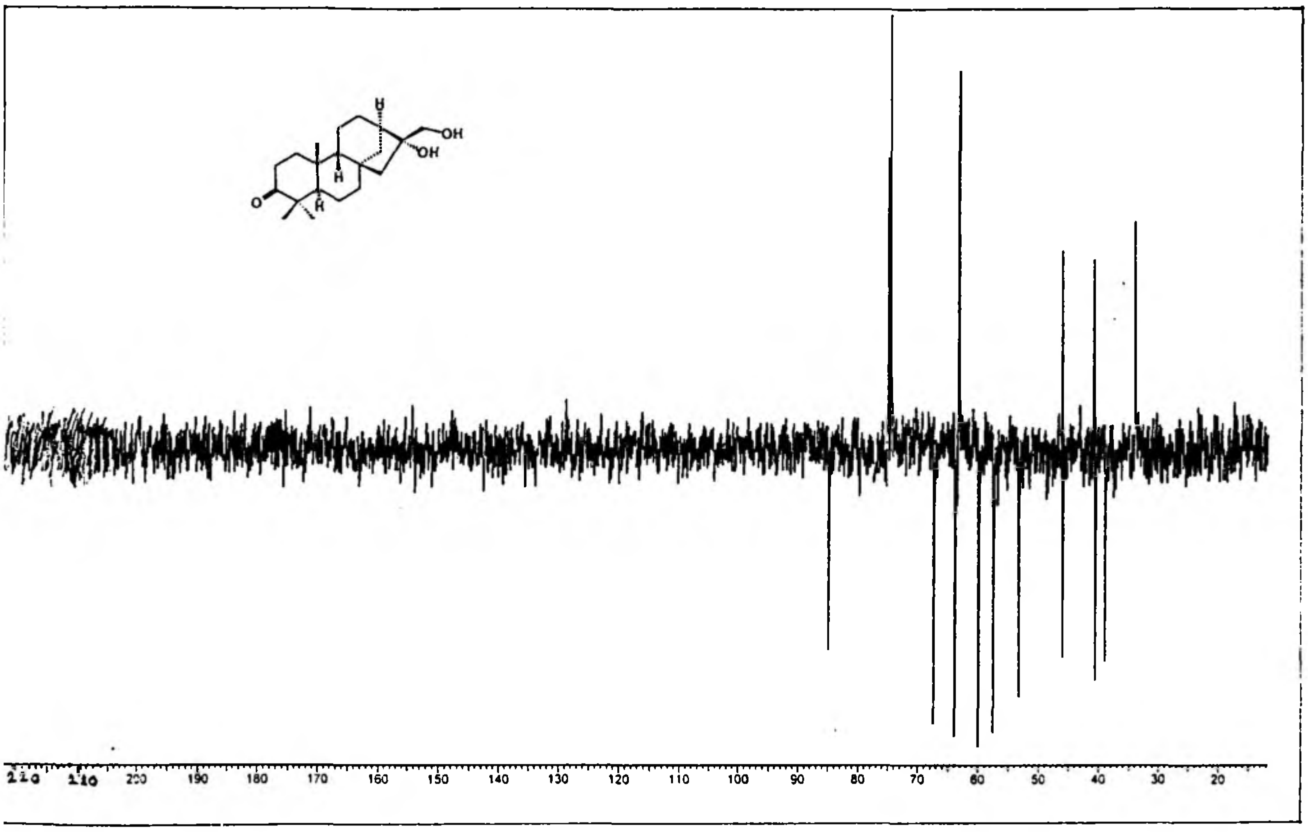
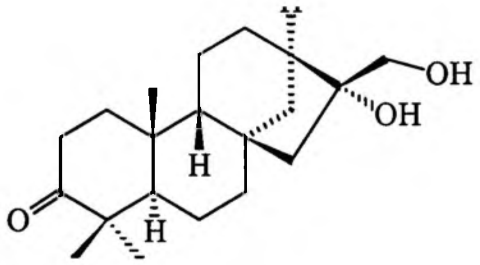


Fig. 4. Spectra of DEPT Experiment of Compound I

The spectrum further reveals that there are nine triplets at δ 14.93, δ 49.45, δ 40.19, δ 37.66, δ 33.57, δ 26.23, δ 21.01, δ 19.55 and δ 64.58 at C – 1, C – 2, C – 6, C – 7, C – 11, C – 12, C – 14, C – 15, C – 17 respectively confirms that there are nine methylene groups present in the molecule. It further shows that there are three doublets at δ 56.62, δ 54.60, and δ 42.35 for C – 5, C – 9, and C – 13 confirms the presence of three – CH groups in the molecule. The presence of four singlets at δ 46.74 of C-4; δ36.64 of C-8; δ42.19 of C-10 and δ 83.25 of C-16 confirms that there are four tetra substituted carbon atoms present in the molecule. The downfield singlet at δ 214.59 shows that C-3 is oxygenated in the form of carbonyl carbon. From all these facts the compound I is under discussion was deduced as



[I]

The compound I, Calliterpenone has been earlier reported from the other *Callicarpa* species such as *C. microphylla*[13]; *C. candicans*[7]; *and C. longifolia*[11]. On direct comparison of the spectral data and the physical constants of the compound I were found to be identical with those reported in literature.

Table 2. **^{13}C NMR spectral data of Compound I**

S. No.	Carbon	Chemical shift in δ	Multiplicity
1	C-1	43.93	t
2	C-2	47.45	t
3	C-3	214.59	s
4	C-4	46.74	s
5#	C-5	56.62	d
6*	C-6	40.19	t
7*	C-7	37.66	t
8	C-8	36.64	s
9#	C-9	54.60	d
10	C-10	42.19	s
11*	C-11	33.57	t
12*	C-12	6.13	t
13#	C-13	42.35	d
14*	C-14	21.01	t

15•	C-15	19.55	t
16	C-16	83.25	s
17	C-17	64.58	t
18	C-18	14.57	q
19	C-19	21.29	q
20	C-20	26.54	q

- These assignments are interchangeable

\# These assignments are interchangeable

3.4 Compound II

Compound II was obtained as a solid, m. p. 124° C, $[\alpha]_D^{25}$ + 22.2 ($CHCl_3$), and analyzed by mass spectrum for molecular formula $C_{22}H_{34}O_4$ (M^+ at m/e 362). IR spectrum (Fig. 5) of the compound II showed absorption at 3400cm^{-1}; 1725 cm^{-1}; 1230 cm^{-1} and 1710 cm^{-1} indicating the presence of hydroxyl, carbonyl and an ester group.

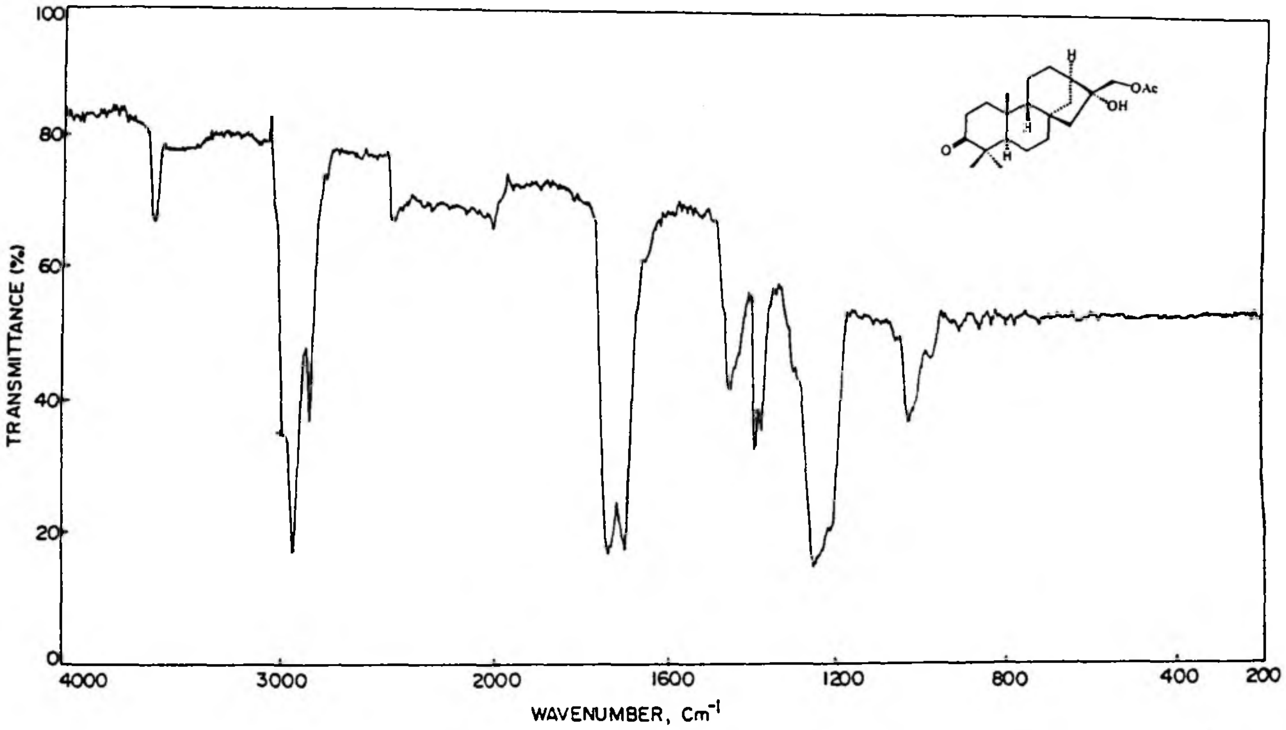


Fig. 5. IR Spectra of Compound II

^{1}H NMR Spectrum (Fig. 6) of the compound II shows that the similar pattern of signals as compound I except two signals of acetoxy and methylene proton attached to ester shows the same diterpenoid having kaurane type of carbon skeleton in the structure of compound II. ^{1}H NMR spectrum of the compound shows the presence of three tertiary methyls at δ 0.98; 1.04 and 1.10 of three protons each. The spectrum of the compound further showed that there was downfield shift of proton as a sharp singlet at δ 4.21 for two protons and another singlet at δ 2.10 of methylene group attached to acetate (-C$\underline{H_2}$ OCOCH$_3$) instead of the doublet at δ 3.62 and 3.80 (J = 11 Hz's) for CH$_2$OH in compound I.

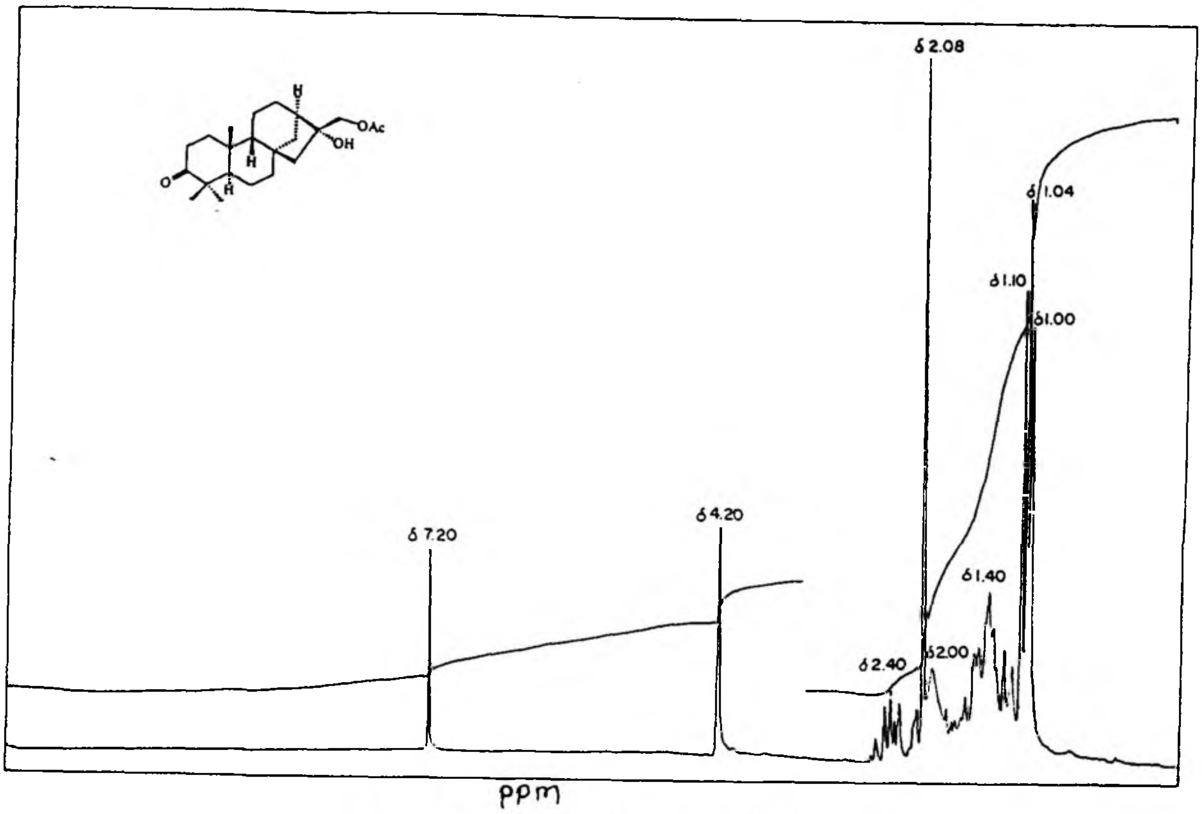
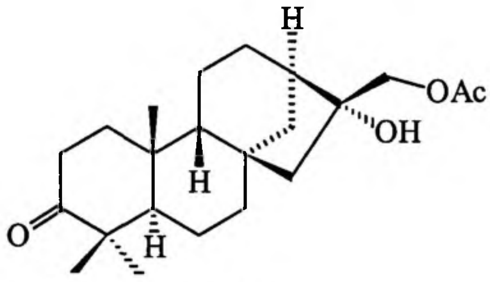


Fig. 6. ^{1}H NMR Spectra of Compound II

The ^{1}H NMR spectrum of compound II was further compared with the acetylated product of compound I which was found that compound II was identical with acetate of compound I in all respect (m.p., IR, NMR, Ms). From all these facts the structure of the compound II was deduced as monoacetate of calliterpenone.



[II]

The compound II has been earlier reported from other *Callicarpa* species such as *C. microphylla*[13]; *C. candicans*[7] *and C. longifolia*[11]. The spectral data and the physical characteristic of compound II was confirmed by critical comparison with reported literature.

3.5 Compound III

Compound III, a crystalline solid, m. p. 289° C, $[\alpha]_D^{25}$ +68 (EtOH), showed its mass spectrum M^+ at m/e 456 suggesting the molecular formula $C_{30}H_{48}O_3$. IR spectrum (Fig. 7) of the compound characteristics bands at 3300cm^{-1} 1720 cm^{-1}, 1245 cm^{-1} and 830 cm^{-1} revealing the presence of hydroxyl, carbonyl and unsaturation functions in the molecule.

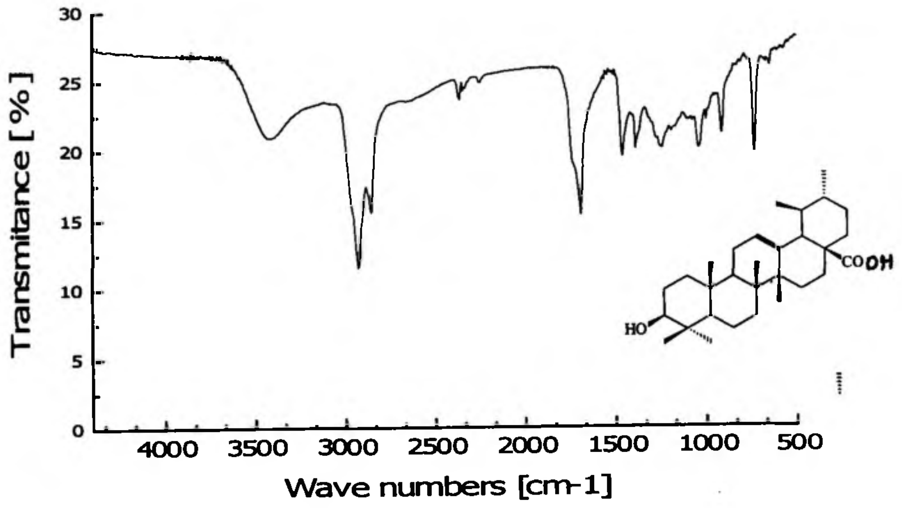


Fig. 7. **IR Spectra of Compound III**

^{1}H NMR spectrum (Fig. 8) of the compound revealed the presence of five tertiary and two secondary methyl groups. The multiplet in the downfield region of the ^{1}H NMR spectrum shows the presence of vinylic proton. And it also shows that the proton H-3 is attached to hydroxyl group.

Considering these observations it can be assumed that the compound III may be pentacyclic triterpene of ursane class. The presence of carboxylic group in the compound III was further confirmed by mass spectrum, which showed a peak at m/e 411 (M - COOH). Compound III on methylation gave a methyl ester, which further confirmed the presence of carboxyl function in the molecule. An attempt to acetylate the compound III was successful, revealing that there was a hydroxyl group to be present in the molecule.

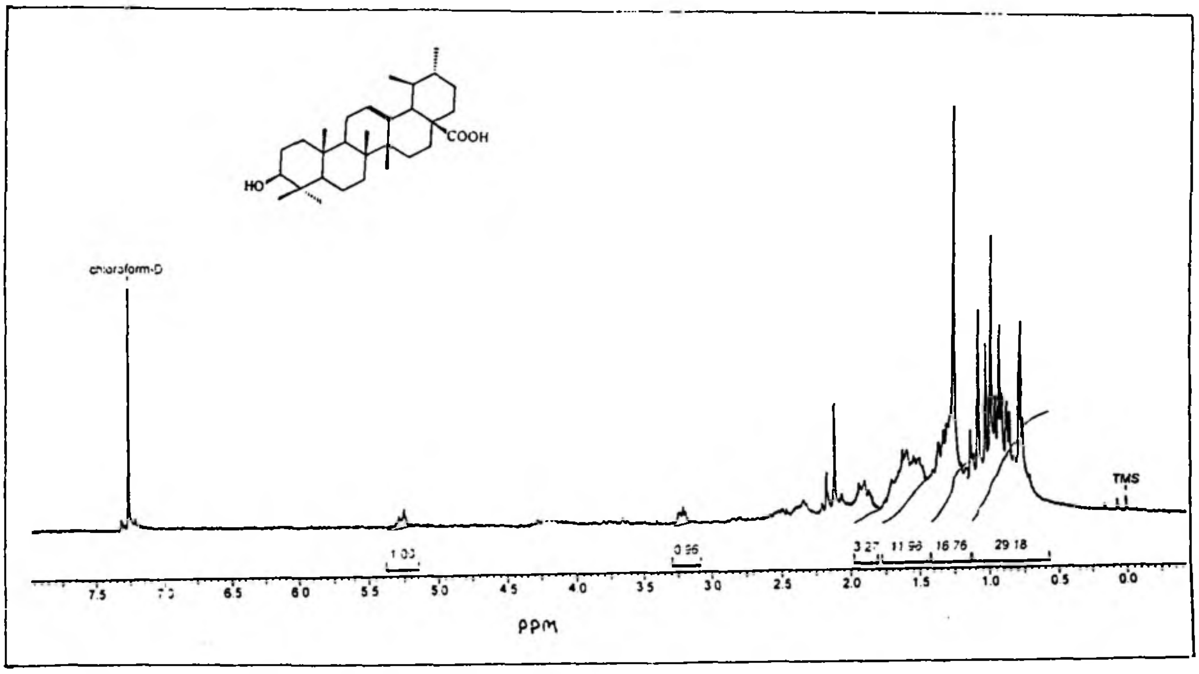


Fig. 8. ^{1}H NMR Spectra of Compound III

^{1}H NMR spectrum shows the presence of five tertiary methyl groups as singlet at δ 0.60, 0.65, 0.75 and 1.21. Singlet at δ 0.75 is for 6 protons while all other protons were for 3 protons each. The presence of two secondary methyl groups appearing as doublets at δ 1.03 (J = 6 Hz's) for 6 protons and one vinylic proton at δ 5.25 as multiplet. A quartet at around δ 3.20 integrating for protons associated with H-3 protons attached to the carbon having hydroxy group ($\text{-C}\underline{H}\text{OH}$) attached to it.

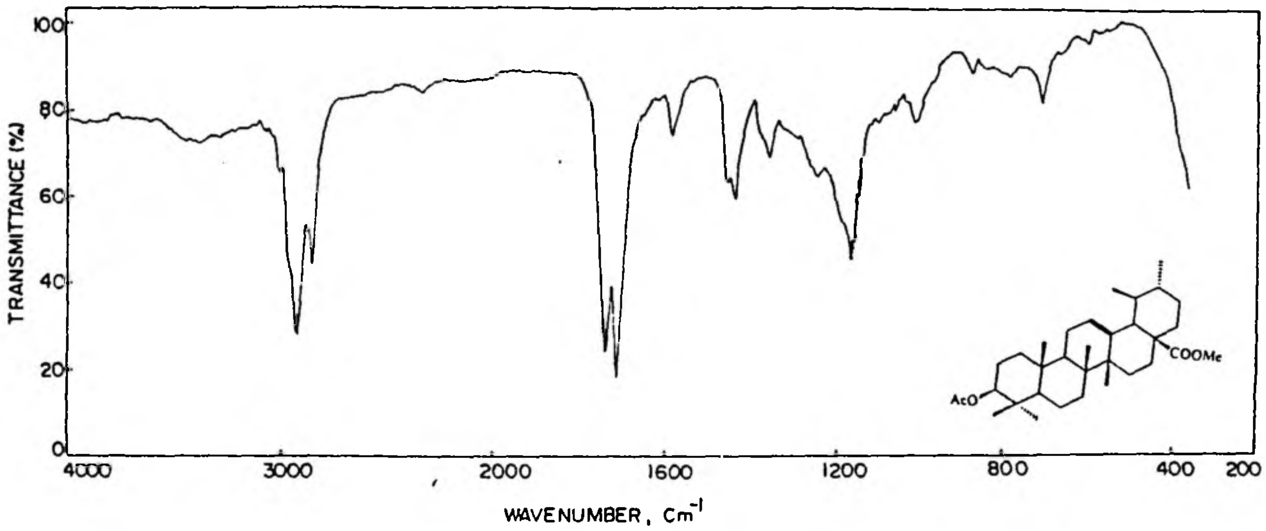


Fig. 9. IR Spectra of Acetoxy methyl Ursolate

The IR Fig (9) and ^{1}H NMR (Fig.10) spectrum of acetate of methyl ester of compound III (Acetoxy methyl ursolate) shows downfield shift from δ 3.20 to δ 4.46 as a triplet for a proton H-3 and a singlet for three protons at δ 2.0 of acetoxy methyl ($\text{-OCOC}\underline{H}_3$) revealed that there was a sec. hydroxyl function at C-3 position

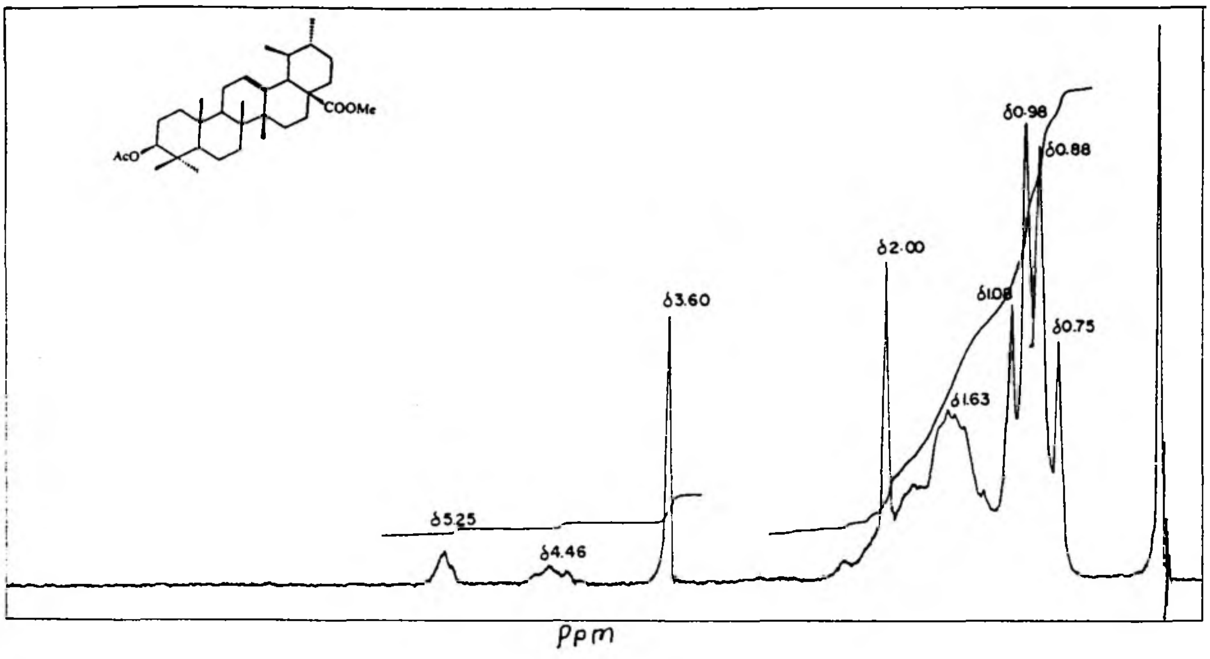
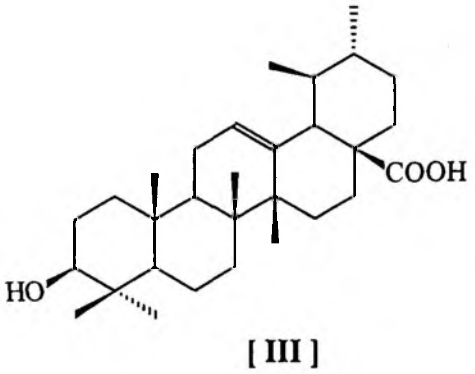


Fig. 10. ^{1}H NMR Spectra of Acetoxy methyl Ursolate

^{1}H NMR spectrum further showed that a singlet at δ 3.6 for three protons of methyl group of carboxyl ester revealed the presence of –COOH group at C-17. From all these facts the compound III must be expected for the urs-12-ene –skeleton with hydroxyl substituents at C-3 position. On the basis of the above observation the structure of the compound III was deduced as



[III]

The compound III , Ursolic acid which has been reported earlier from the other species of *Callicarpa* such as *C. microphylla*[13]; *C. candicans*[7]; *and C. longifolia*[11]. The same compound also reported from *Rhododendron* spp.[15]and *Epigaca asiatica*[15]. The spectral data and other spectral data and other physical characteristic of the compound III was further supported by critical comparison with the reported one.

3.6 Experimental

The plant material of the species *C. lanata L.* were collected from Bhimashankar area of Maharashtra State, India, during September 1995. The arial part of the plant material was shade dried and powered. The powdered plant material (5kg), was extracted with acetone at room temperature. The extract were filtered and concentrated under reduced pressure to yield a green mass (360g). The extract was partitioned into acidic and neutral parts by treating the extract (50g) with saturated sodium bicarbonate solution and the mixture was extracted with $CHCl_3$. The aqueous layer was acidified with 2N HCl to PH 2 and extracted with ethyl acetate. Both organic layers were washed with water, than with brine and dried over anhydrous sodium sulphate and concentrated separately.

3.6.1 Neutral fraction

The neutral chloroform extract (35g), of *C. lanata* was chromatographed over silica gel (60-120 mesh) using pet-ether, pet-ether-acetone in increasing percentage of acetone eluent. The fractions showing similar compositions were combined together to obtain six major fractions (A – F), table 3.

Table 3: Column chromatography of acetone extract (35g, silica gel, 900g)

Fraction	Eluent	Total volume	Weight in g	Composition
A	pet ether	100X5	13.5	St. chain copmds
B	pet- ether (90) : acetone (10)	100X5	7.0	Clear oil ; fatty acids
C	pet- ether (85) : acetone (15)	100X4	3.6	Sterols, other compd.
D_1	pet- ether (75) : acetone (25)	100X5	4.2	Compound I and II
E	pet- ether (50) : acetone (50)	100X3	2.0	Glycosides
F	pet- ether (25): acetone (75)	100X4	1.0	Glycosides

Rechromatography of fraction D

Fraction D (4.2g) was chromatographed by dry column chromatography using pet-ether: acetone (80: 20) as eluent with successive increase in percentage of acetone. Fraction III after repeated preparative TLC afforded compound I in pure form, table 4.

Table 3: Rechromatography of fraction D (4.2g, silica gel, 100g)

Fraction	Eluent	Total volume	Weight in g	Composition
I	pet- ether (85) : acetone (15)	50mlX2	1.8	Unidentified mix.
II	pet- ether (80) : acetone (20)	50mlX2	0.5	Compd. II & impurities
III	pet- ether (75) : acetone (25)	50mlX2	0.2	Compd. I
IV	pet- ether (60) : acetone (40)	50mlX2	1.6	Unidentified mix.

Compound I

The compound I (100mg) obtained in pure form.

M. P. : 154 – 155°C

$[\alpha]_D^{25}$: + 32 ($CHCl_3$, 0·5)

IR ($CHCl_3$, cm^{-1}) : 3300 -3400, 1710 (Fig.1)

^1H NMR (200 MHz, $CDCl_3$) : δ 0.97 (s, 3H); 1.01 (s, 3H); 1.06 (s, 3H); 3.62 (d, 1H, J = 11Hz); 3.80 (d, 1H, J = 11Hz); 2.50 (m, 2H) (Fig. 2)

^{13}C NMR (90 MHz, ($CDCl_3$) : Table 2. Fig. 3 and 4.

MS : m/e : 320 (M^+)

3.6.2 Compound II

Compound II (500mg) was obtained from rechromatography of fraction D, table 4. It was further purified by repeated preparative TLC on silica gel to obtain compound II in pure form (90mg).

M. P. : 124°

$[\alpha]_D^{25}$: + 22.2 ($CHCl_3$; 0·5)

IR ($CHCl_3$, cm^{-1}) : 3400, 1725, 1710, 1230 (Fig.5)

^1H NMR (200 MHz, $CDCl_3$) : δ 0.98 (s, 3H); 1.02 (s, 3H); 1.07 (s, 3H); 4.21 (s, 2H); 2.10 (s, 2H); 2.50 (Fig. 6)

MS : m/e : 362 (M^+)

3.6.3 Acidic fraction

The acidic extract (0.750g) of *C. lanata* was chromatographed over silica gel (60-120 mesh) using pet-ether, pet-ether : ethyl acetate in increased percentage of ethyl acetate as eluent (60 : 40). Fraction after successive chromatography and preparative TLC afforded compound III (0.230 g).

Methylation and acetylation of compound III

Compound III (150mg) was dissolved in cold methanol. To this a cold etheral solution of diazomethane (prepared from 3g of nitrosomethylurea in 25 ml of ether) was added and kept at 5° C overnight. The reaction mixture after usual workup was subjected to preparative TLC to afford a methyl ester of compound III (50mg).

The methyl ester of compound III was acetylated by reacting with pyridine and acetic anhydride and kept it overnight at room temperature. The reaction mixture after usual workup was subjected to preparative TLC to get acetate of methyl ester of compound III (40mg).

	Compound III	**acetylated methyl ester of Compound III**
M.P.	289°	238°
$[\alpha]_D^{25}$	+ 68 (EtOH, 0·5)	+ 58.5 ($CHCl_3$, 0·5)
IR ($CHCl_3$, cm^{-1})	3300, 1720, 1245, 830 Fig.7	1712, 1745 (Fig. 9)
^1H NMR (200 MHz, $CDCl_3$)	δ 0.6 (s, 3H); 0.65 (s, 3H); 0.75 (s, 6H); 1.21 (s, 3H); 1.03(d, 6H, J = 6Hz); 5.25 (m, 1H); 3.20 (q, 1H) Fig.8	δ 0.6 (s, 3H); 0.65 (s, 3H); 0.75 (s, 6H); 1.21 (s, 3H); 1.03(d, 6H, J = 6Hz); 5.25 (m, 1H); **4.46 (t, 1H); 2.0 (s,3H); 3.6(s, 3H)** Fig.10
MS : m/e	456 (M^+)	512 (M^+)

3.7 References

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Chapter IV

Organic Transformations using Alumina (Al_2O_3) and Rhenium oxide (Re_2O_7) as Catalysts.

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4.0 General Introduction

Catalysis plays an important role in a wide range of industrial processes in the manufacture of petroleum and chemical products with end applications in plastics, agrochemicals, fine chemicals, pharmaceuticals and fertilizers[1, 2]. The types of catalyst used in industries are generally classified as heterogeneous and homogeneous depending on the form in which they are used.

Heterogeneous catalysis is perennially relevant, it is endlessly fascinating, and it continues to be deeply enigmatic. More than 90% of the chemical manufacturing processes in use throughout the world utilize catalysis in one form or the other[3]. Much of the food, medicines, fabrics, building materials and fuels are produced by heterogeneously catalyzed reactions. The heterogeneous catalysis is as old as the catalytic concept itself. Faraday was the first scientist to examine the ability of platinum to facilitate oxidation reactions. Many other catalytic processes were subsequently developed that facilitated hydrogenation, dehydrogenation, isomerisation and polymerisation. These catalytic reactions all played a key role in the development of industrial revolution.

The homogeneous catalysts used in the liquid phase have also important application in the industry[4, 5] for example hydroformylation of olefins to aldehydes invented by Rollen made a major impact on application of homogeneous catalyst in chemical industry. The major disadvantage of homogeneous catalysis is that they are not easily separable from the product. However, advantages in high activity, selectivity at mild operating conditions are very significant for many cases. Most of the transition series in the periodic table have proved valuable in forming compounds suitable for homogeneous catalysis. Both salts and complexes of Pd, Pt, Ru, Re, Ir, Rh, Fe, Ni and Co have been used as catalysts.

The application of both type of catalysts in industry are growing due to a strong need for the development of more economical and environmentally cleaner process. Inorganic oxides, plays an important role in catalysis. We carried out simple organic transformations of naturally occurring compounds by using such oxides (Al_2O_3) and also developed a mild and efficient method to get carboxylic acids from methyl ketones by using rhenium oxide (Re_2O_7).

Section A

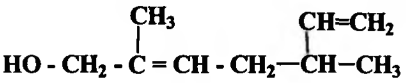
Alumina (Al_2O_3) Catalyzed Transformations of Naturally occurring Compounds.

4.1.0 Introduction

The genus *Cyathocline* class belongs to the tribe *Astereae* of family *Compositae*. The main centers of distribution of this tribe are both America, Southern Africa[6], while the other centers of distribution being Asia, Australia and New Zealand. The total number of *Astereae* is 135 genera with about 2500 species, *purpurea* and *lutea* are one of them. The extract of species purpurea of this class is used for stomach pains. Ethanolic (50%) extracts are used spasmol. Essential oil of this plant has got antimicrobial activity. It acts as antihelmenthis against nodularworms and tapeworms better than piperazine phosphates or hexylresorcinols. It shows hypertension in cats. However, the essential oil of this species is also reported to posses activities such as cardiac depress, spasmol oxytocic[6a].

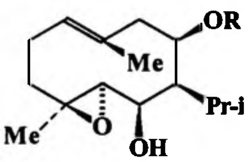
Most of the work done so far has been confined largely to the root constituents[7]; polyacetylenes, polyenes and related substances are characteristic constituents of roots. In certain groups the coumarin are the very characteristics[7]. Less widely distributed are the diterpenes of labdane and clerodane type[8-11]. Epigeal parts have been studied only sporadically; as a result, the information on distribution of flavonoids and other low molecular weight secondary metabolites are very spotty[12-14]. Sequiterpene lactone, alkaloids and sterioisomer coumarin B are the characteristics feature of Haplopappus rigidifolius, is the only sesquiterpene lactone have been found so far[15]. From this genus *Cyathocline* a monoterpene alcohol lyratol (I) has been isolated by Devagan etal[16]. The three sesquiterpenes (II – IV) has been reported from *Echinaceae purpurea*[17].

***Cyathocline purpurea*:** This is an important plant found in western Maharashtra. Various types of compounds have been isolated so far from this species. Four sesquiterpenes lactones, two guainolides (V) and (VI) closely related to each other and two closely related eudesmanolides (VIII) and (IX). In addition to these compounds the other sesquiterpene lactones such as in vangustin (VII) was present as a minor constituent[18].

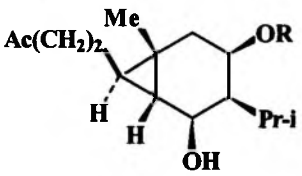


$$HO-CH_2-\overset{CH_3}{C}=CH-CH_2-\overset{CH=CH_2}{CH}-CH_3$$

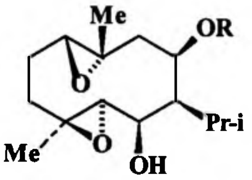
I



II

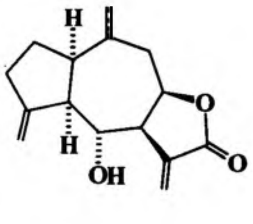


III

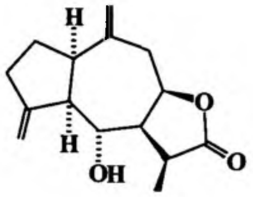


IV

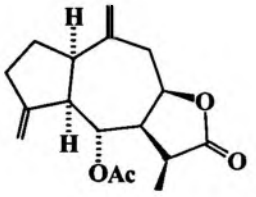
R = arom, acyl, esp.cinnomoyl



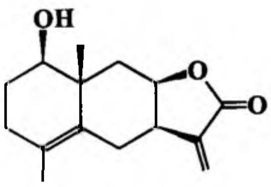
V



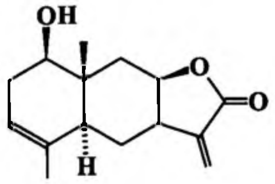
VI



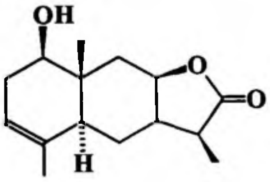
VIa



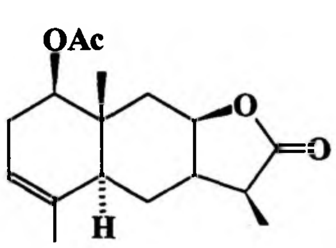
VII



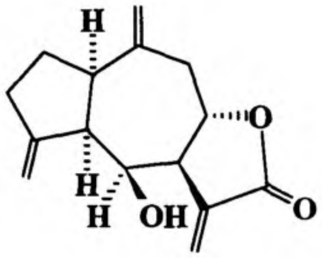
VIII



IX



IXa

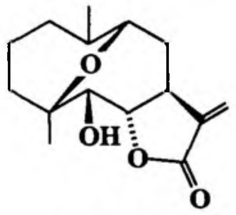


X

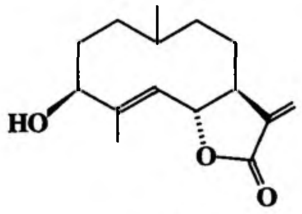
CHART – I

The major compound (V) guainolide is present and its structure was confirmed by Chintalwar et.al[19] by X-ray crystallography as 6α-hydroxy-4- (14), 10 (15)-guainolide, X, and the other sesquiterpene lactones were present as minor constituents. (Chart - I)

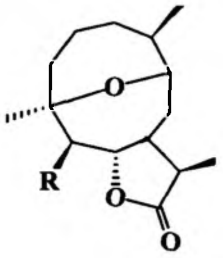
Cyathocline lutea: The compounds isolated from this species so far are sesquiterpenes lactone (XI) and (XII) belongs to the class germacranolides[20]. The compound (XI) was a major one compared to compound (XII). From the same species Rojatkar et. al[21] isolated germacranolide (XIII). (Chart – II).



XI



XII



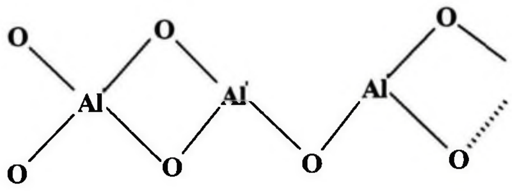
XIII : R = OH,

XIIIa : R = OAc

CHART – II

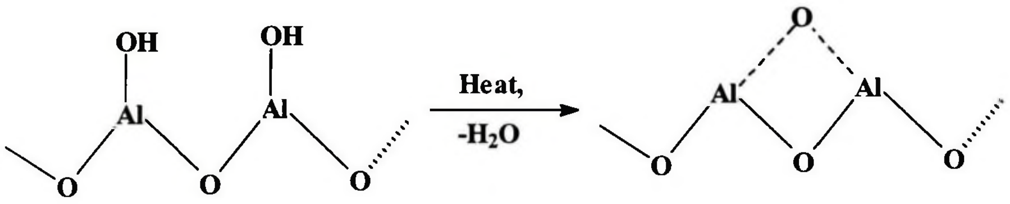
4.1.1 Alumina (Al_2O_3)

It has been generally agreed that Al_2O_3 has dipolar character[22-23]. The presence of two types of acid sites on alumina surfaces the Lewis acid sites and passive Bronsted acid sites. The passivity of Bronsted acids is assumed to arise from the combination of protons with cationic vacancies on the alumina surface. The assumption of the existence of the passive Bronsted acids on alumina surface is compatible with the surface structure of alumina. From the energy considerations it is generally accepted that the outside layer of alumina consists of oxide ions with aluminium ions forming the next lower layer. **(A)**



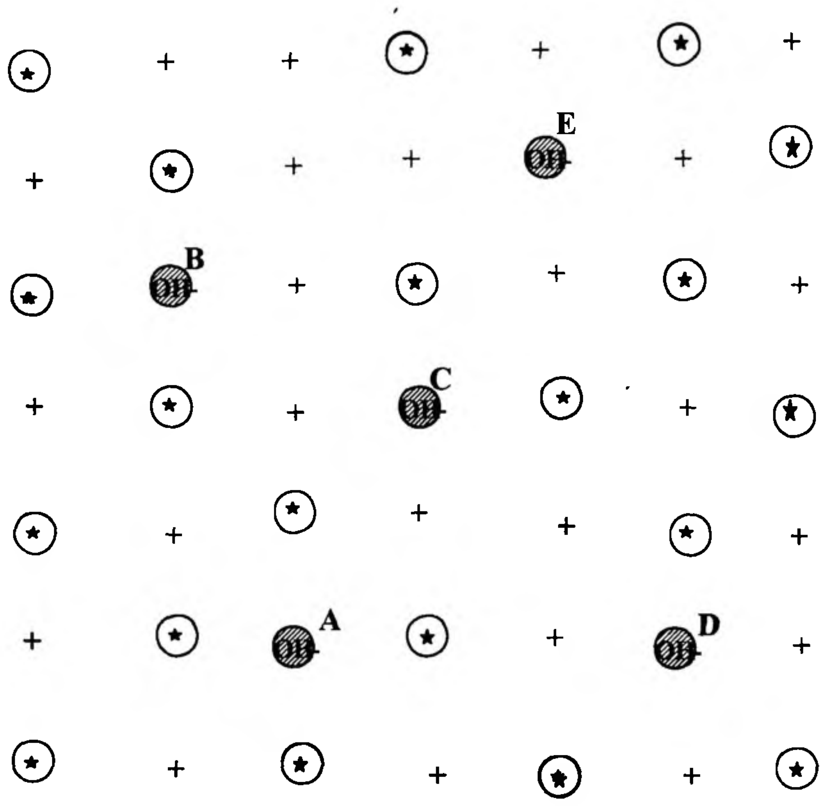
(A)

The electron – doner sites and electron - acceptor sites on the surface of Al_2O_3 plays an very important role in rationalizing the pathways. The surface group on alumina plays important role in the removal of water from the surface of alumina on heating. **(B)**.



(B)

Water removal from the surface of alumina on heat treatment to afford groups at alumina



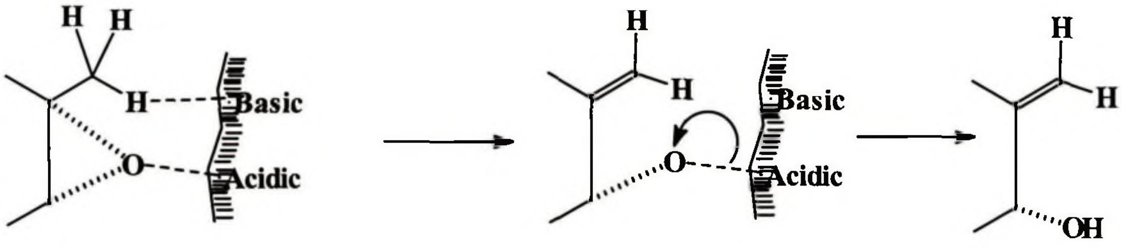
C

Surface and it has been stated that at random removal of all hydroxyl pairs leaves the surface as shown in **(C)**.

The remaining OH^- ions covers about 10% of the alumina surface and have been grouped into fine types A, B, C, D, and E (Fig.1C) having from four to zero nearest oxide neighbors. These four types of OH^- ion sites should vary in chemical properties, site A being the more basic and site E is the most acidic.

4.1.2 The role of alumina in organic reactions:

Sukhdev[23] has suggested that the alumina catalysed conversion of epoxide to allylic alcohols proceed as follows:



1. Co-ordination of epoxy oxygen with an electron acceptor site on Al_2O_3 surface.
2. Oxirane ring cleavage with simultaneous proton elimination and its capture by an electron doner site. However, the exact function of alumina in various reactions is still unknown. It has been suggested that alumina brings together the substrate and the reagent in a proper orientation for chemical reaction [24] and it probably activates the reactant and / or the reagent [25]. The activation of the reagent is probably brought about by cleavage by H-heteroatom bond with attachment of the nucleophilic group to alumina surface. Co-ordination of the heteroatom of the reactant to one of the acidic aluminium atoms on alumina may lead to activation of the reactant.

4.1.3 Applications of alumina :

Recently many heterogeneous chemical reactions effected by reagents immobilized on porous solid supports have been reported. Mckillop and young[26] have reviewed the synthetic applications of various supported reagents such as silver carbonate or Collin's reagent on celite, ozone and water on silica gel, sodium borohydrate on alumina, thallium nitrate on K10 Montmorillonite clay, $SbCl_3$ intercalated in graphite etc. Reactions using supported reagents have attracted the attention of synthetic organic chemists because they are more selective, milder and more easier to operate as compared to the corresponding conventional as well as homogeneous reactions. Further in most of the cases, these reactions gave good yields of the converted products. Since the reagents and the products are often strongly adsorbed on to the inorganic support, the chances of contamination of the organic products or solvents by inorganic materials is less. In some cases, it is even possible to regenerate the active reagent directly from the support by standard organic reactions.

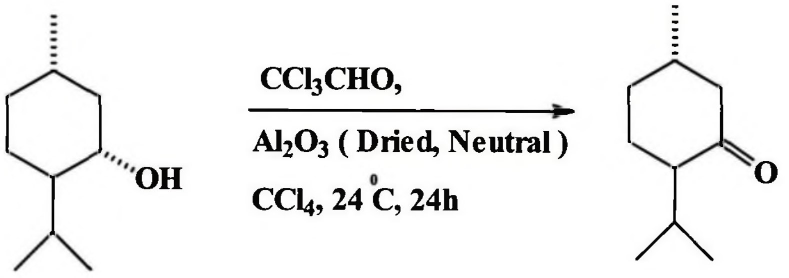
Among the various porous solid supports being used to carry out chemical reactions, alumina has gained importance in recent years probably because of the diversity of chemical reagents effected by it, while γ -alumina itself can catalyze many chemical reactions of the adsorbed organic molecules, alumina deliberately impregnated with the different chemical reagents can be used to effect a variety of chemical reactions heterogeneously. Many organic reactions which do not take place or proceed very slowly with low yields under homogeneous conditions can be effected by alumina in much shorter time and in good yields. Further, these alumina-catalyzed reactions are more selective and milder so that a desired transformations of a compound can be brought about without affecting other labile groups or centers of its molecules. These reactions are easy to perform because they generally involve only stirring with alumina at room temperatures or some times on reflux temperatures and further filtration and solvent evaporation to obtain the product.

A large number of reactions effected on alumina surface have been reported especially during seventies[27]. Some of these reactions came to light during separation and purification of the compound through alumina columns which leads to unexpected transformations. Since it is beyond the scope of this introduction to review all the alumina-catalysed reactions, only a few significant examples will be mentioned here. The different reactions have been broadly classified and need not have any bearing on the mechanism involved.

4.1.3.1 Oxidations:

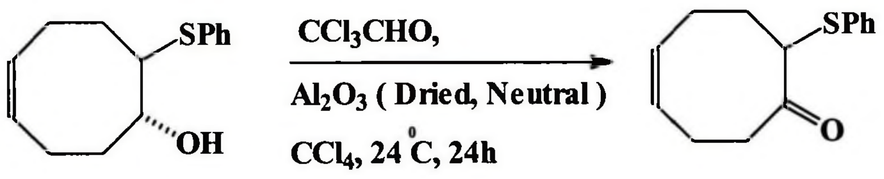
Alcohols to Carbonyl compounds:

Chloral on activated Woelm-200 neutral alumina has been found to oxidize secondary alcohols selectively in presence of primary alcohols[28, 29]. The latter either don't react or react very slowly. The mild and selective nature of this reagent allow the oxidation of secondary alcohols without affecting other labile functional groups such as esters, lactones, ethers, nitro groups, benzylic chlorides etc. Even very sensitive compounds which are prone to polymerize, epimerize or decompose can be successfully oxidized to the corresponding ketones by chloral on alumina, For example, substituted cyclohexanol **(1)** can be oxidized to corresponding ketones **(2)** without epimerization.



1 **2**

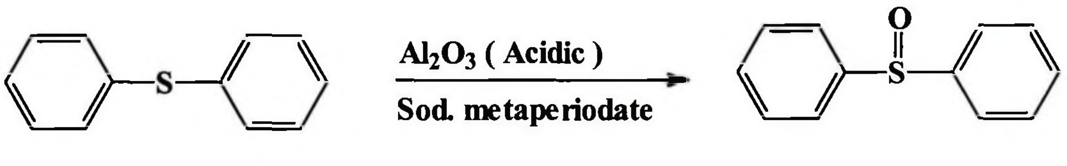
Similarly, allylic alcohols can be oxidized to corresponding vinyl ketones and β-hydrosulfides of type **(3)** can be converted to the corresponding β-ketosulfides **(4)**.



3 **4**

Sulfides to Sulfoxides :

Liu and Tong[30] have reported that sodium metaperiodate impregnated on alumina oxidizes some organic sulfides **(5)** to corresponding sulfoxides **(6)** in excellent yields. Use of acidic alumina and two equivalents of the oxidants are found to be optimum for these reactions.



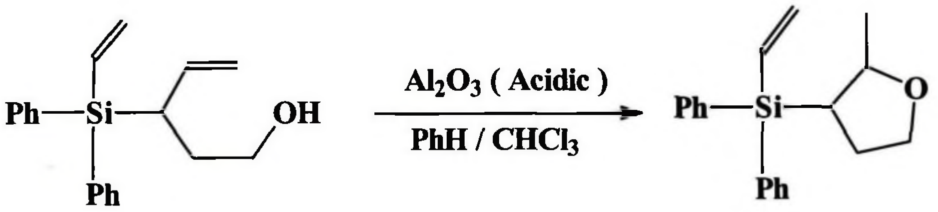
5 **6**

Epoxidation :

Hydrogen peroxide or t-*butyl hydroperoxide* in contact with basic alumina has been reported to oxidize some olefinic compounds abet in low yields[31]. The peroxide probably reacts with alumina to form surface bound hydroperoxide[32] which in turn convert the olefins to epoxides.

4.1.3.2 Intramolecular ether bridge formation:

There are few reports of alumina – catalysed ether bridge formation by intramolecular addition of OH groups across isolated or carbonyl conjugated olefinic bonds[33-35] **(7 –12)**.



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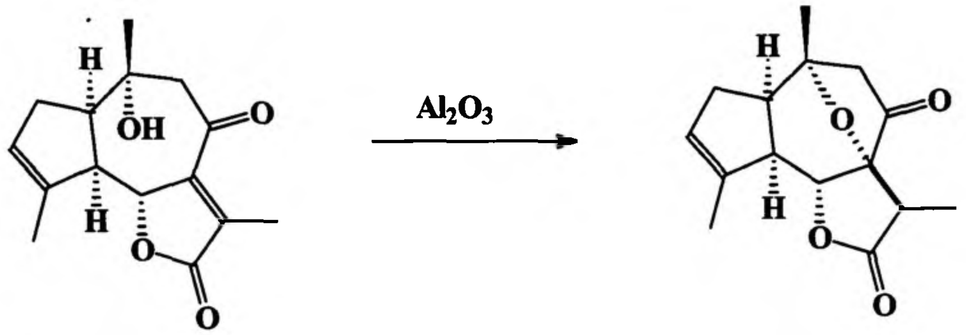
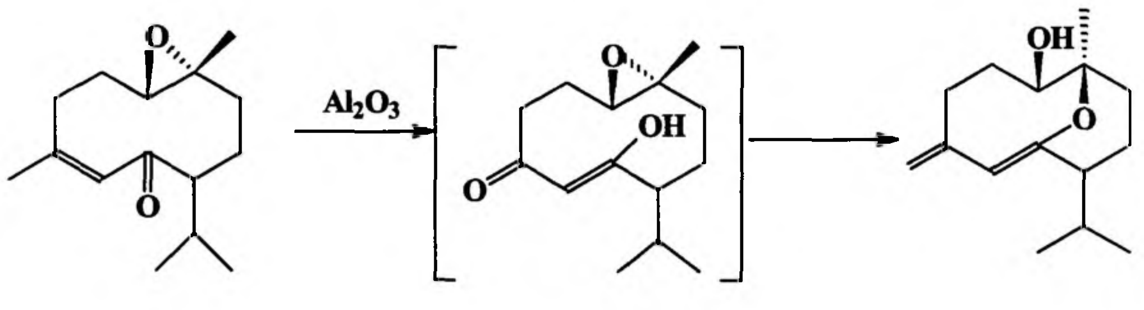


9 10

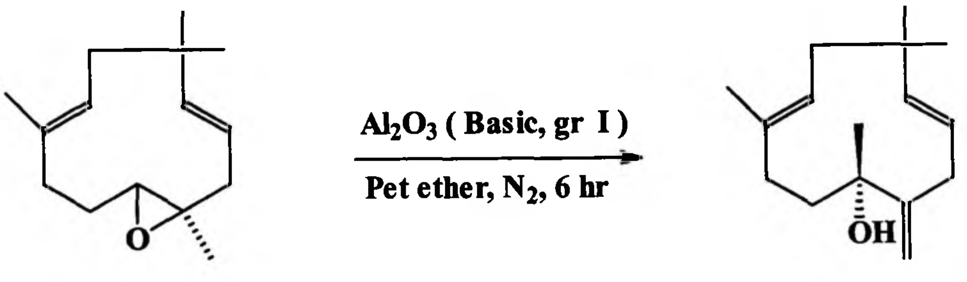


11 12

4.1.3.3 Epoxide Cleavage:

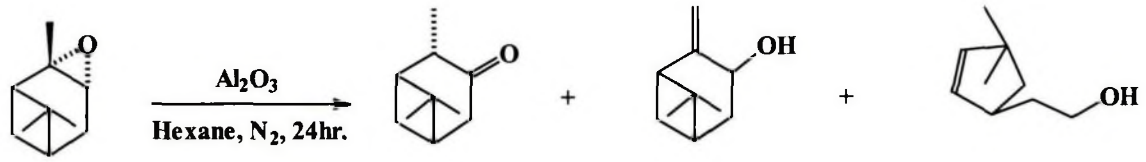
Sukhdev and co-workers[36-39] have reported the alumina-induced rearrangements of a number of terpenoid epoxides. Alumina cleaves the oxirane ring of these compounds and in most of the cases is converted into the corresponding allylic alcohols, glycols, ketones etc.

i. Humulene epoxide – II **(13)** isomerised to humulenol – II **(14)** in 60% yield on treatment with grade-I alumina at room temp[36].



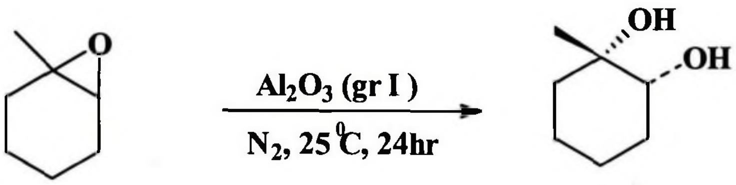
13 14

ii. 2-α, 3α-Epoxy pinene **(15)** with alumina yielded a 1:4:2 mixture of pinocamphene **(16)**, *trans* pinacarveol **(17)** and α-pinocamoholenic alcohol **(18)**[38] .



15 **16** **17** **18**

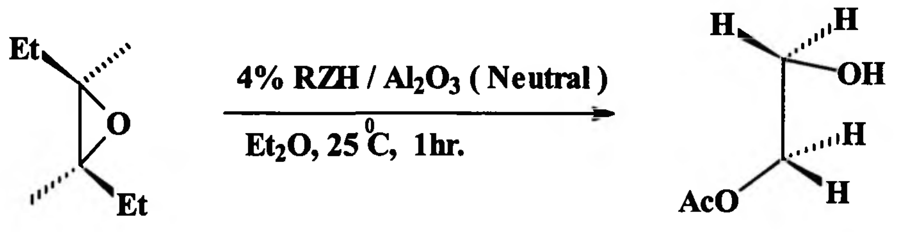
iii. The alumina induced reactions of 1-methyl-1, 2-epoxy cyclohexane **(19)** gave 1-methyl-trans-cyclohexane -1, 2-diol **(20)** as the major product[23].



19 **20**

Joshi and Sukhdev[39] have studied the reaction of terpenoid epoxides with alumina – alkali and alumina alkali halide reagent and observed that with the former reagent rearrangement of the epoxide to allylic alcohol predominates and with the latter isomerisation to ketone is favored.

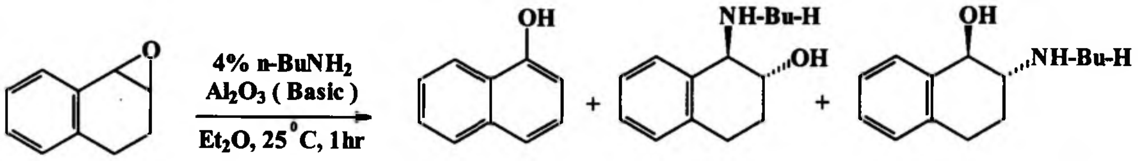
Posner and Rogers [40] have studied the alumina – catalysed nucleophilic opening of many structurally diverse epoxide by alcohols, thiols, amines, acetic acid, benzene selusol etc. Chromatographic neutral alumina impregnated with a few equivalents of the above mentioned nucleophilic reagents open many alkenes, cycloalkenes and steroidal oxides stereospecifically i.e. trans and regioselectively with the preferential attachment of the nucleophile to the less substituted carbon atom **(21) to (22).**



Trans   Erythro

21   22

Treatment with amine impregnated alumina is the only known method of the opening of a naphthalene-1, 2-epoxide by a weak nitrogen[41] nucleophile so far.

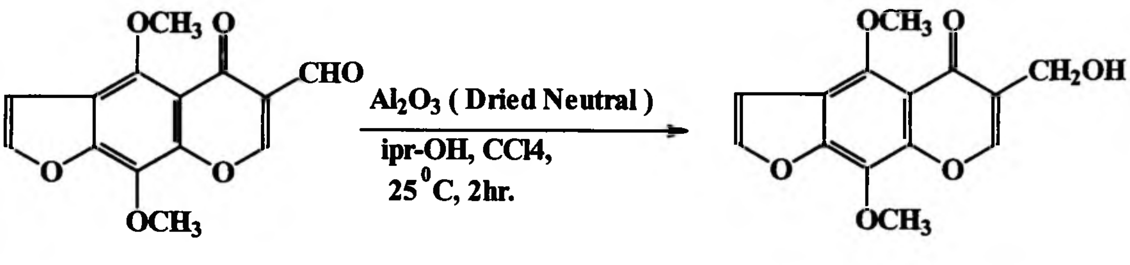


23   24   25   26

4.1.3.4 Reduction :

There are number of reports on catalytic hydrogenation of olefinic bonds by various metals supported on alumina[42]. Sodium borohydrate impregnated on alumina has been found to be an efficient reducing agent to convert carbonyl group to alcohol, especially in alkali sensitive compounds[43]. Further the reaction with this reagent can be carried out even in nonpolar solvents such as benzene.

Posner et.al[44] have developed isopropanol impregnated on Woelm-200-N- Vacuum dehydrated alumina as a mild and selective reducing agent suitable for general synthetic application. The major advantage of this reagent is that it can selectively reduce aldehydes and α, β-unsaturated aldehydes cleanly and rapidly into the corresponding alcohols even in the presence of some keto groups and other sensitive functional groups. For example, the chromone derivative (27) that contains aldehyde, ketone and methoxy functions have been selectively reduced at the aldehyde group by isopropanol-alumina reagent to the corresponding allylic alcohol **(28)**[44].



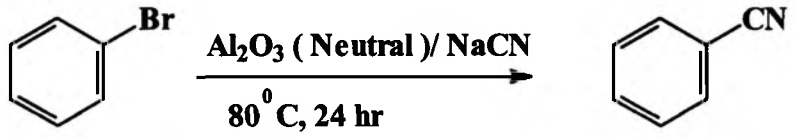
27 **28**

The reagent also reduces the steroidal 3, 6; 3, 17-and 3, 20- diones selectively at the 3 positions. The isopropanol reagent is stable for months together if preserved in sealed vials.

2, 4-Dimethyl-3-pentanol on alumina is another reagent suggested for carbonyl reductions especially to selectively reduce an aliphatic aldehyde in presence of an unhindered cyclohexanone[44]. It has been established that the reduction of carbonyl groups by derived from alcohols.[45, 46].

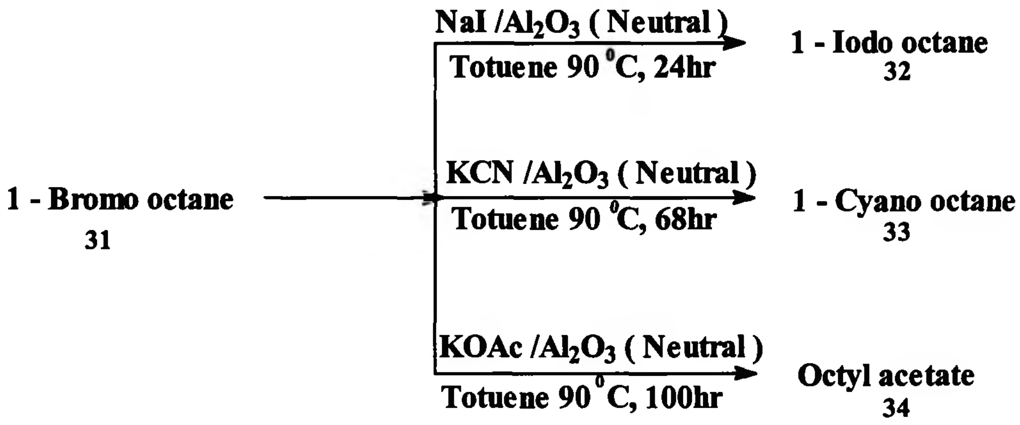
4.1.3.5 Displacement Reactions :

Regen et.al [47, 48] have reported that neutral alumina impregnated with sodium cyanide can effectively displace halogen atoms from alkyl and aryl halide **(29)** giving good yields of the corresponding cyanides **(30)**.



29 **30**

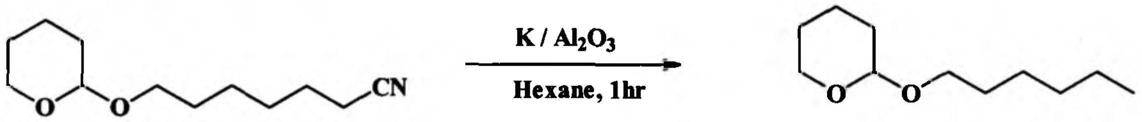
The extension of this method to other nucleophilic reagents such as chloride, iodide, acetate etc. has lead to the development of alumina as a solid –liquid-solid triphase catalyst[49] for the displacement of bromine or iodine from the corresponding octyl halides.



The intimate physical contact between the alumina and the reagent is found to be necessary for these displacement reactions. It was observed that 1-bromo octane is more reactive than 1-iodo octane towards these alumina-catalysed displacements. The major advantages of these reactions are their simplicity, avoidance of highly toxic solvents, aqueous work up and extraction steps with good yields.

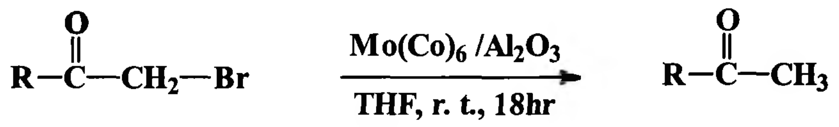
4.1.3.6 Elimination Reactions:

i. **Dehydration:** Highly dispersed potassium metal on neutral alumina has been found to effect reduction cleavage of the cyano group in alkyl nitriles[50]. The K/Al_2O_3 reagent is prepared by melting potassium over neutral alumina in an inert atmosphere. The decyanation is carried out in hexane solution at room temperature gives 70-90% yield **(35 & 36).** The hydrogen incorporated into the alkene might have derived from OH group of alumina or from the solvent.



35 **36**

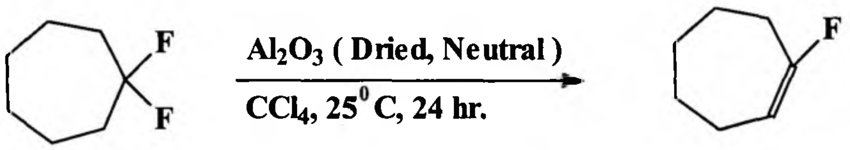
ii. Dehalogenation and Dehydrohalogenation : Molybdenum hexacarbonyl adsorbed on alumina is reported to effect dehalogenation of α-haloketones like **(37)** in tetrahydrofuran at room temperature to give corresponding ketone like **(38)** in good yields[51].



$$R-\overset{\overset{O}{\|}}{C}-CH_2-Br \xrightarrow[\text{THF, r. t., 18hr}]{Mo(Co)_6\,/Al_2O_3} R-\overset{\overset{O}{\|}}{C}-CH_3$$

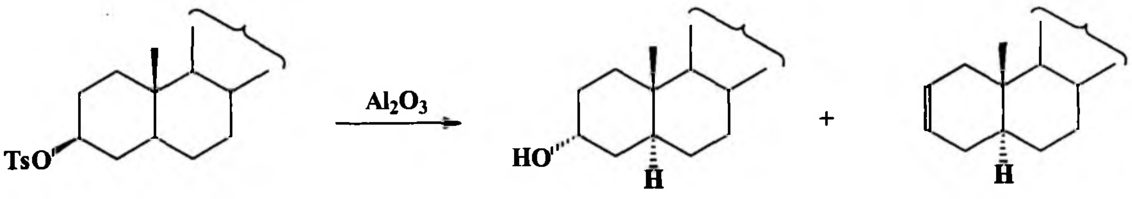
37 **38**

Alkyl halides are comparatively stable to alumina at room temperature. However, gem-difluorides like **(39)** undergo dehydrofluorination in presence of vacuum dehydrated alumina to form monofluorolfines like **(40)**.



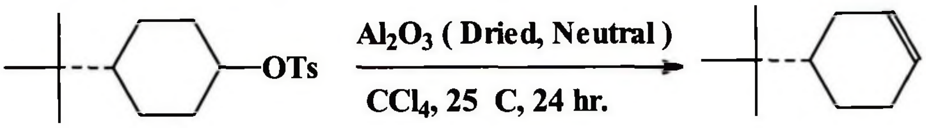
39 **40**

iii. Desulfonation and dehalosulfonation; Alumina has been shown to posses ability to simultaneously hydrolyse and eliminate sulfonate ester to form mixtures of the corresponding hydroxy compounds and olefins [52-54] **(41, 42, 43)**.



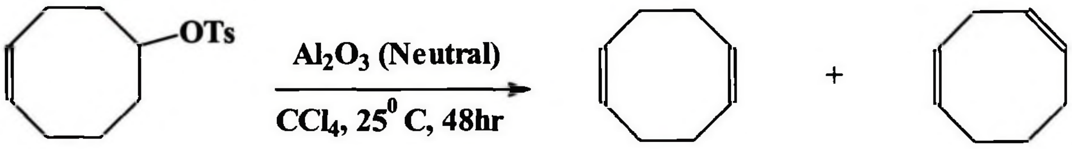
41 **42** **43**

Secondary cyclic and acyclic sulfonates esters having β-hydrogen atoms can be successfully dehydrosulfonated with activated neutral alumina[52] **(44, 45).**



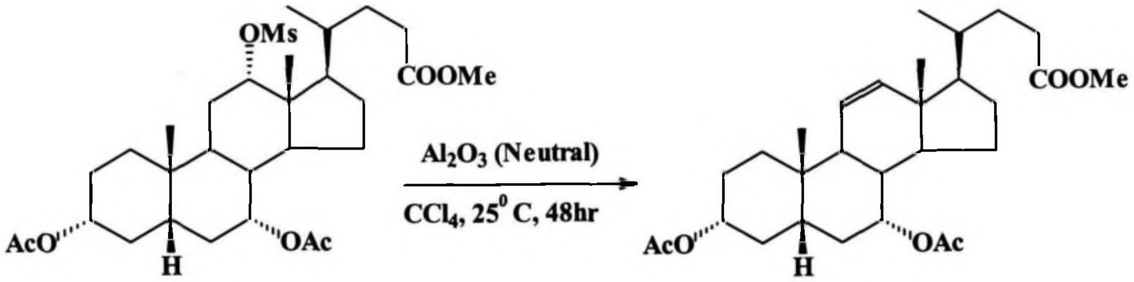
44 45

Dehydrotosylation of cyclooctenyl tosylate **(46)** with neutral inactivated alumina yielded a mixture of the monocyclic dienes. **(47, 48).**



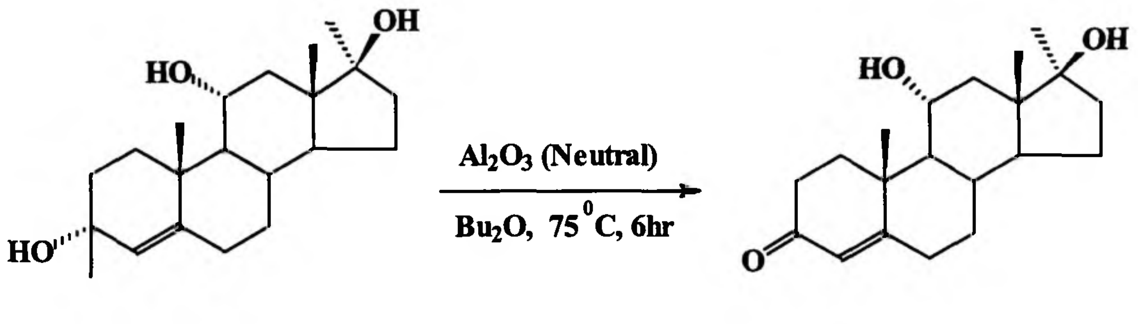
46 47 48

Posner et.al[52] have discussed in detail the applicability of alumina – catalysed dehydro-sulphonation in specific cases and have also highlighted its merits over homogeneous methods. Since alumina-catalysed dehydrosulphonation is concerted elimination, no simultaneous skeletal rearrangements are observed. Further the alertness of alumina towards sensitive functional groups make it a very useful reagent for the introduction of double bonds to polyfunctional and labile compounds like **(49, 50).**



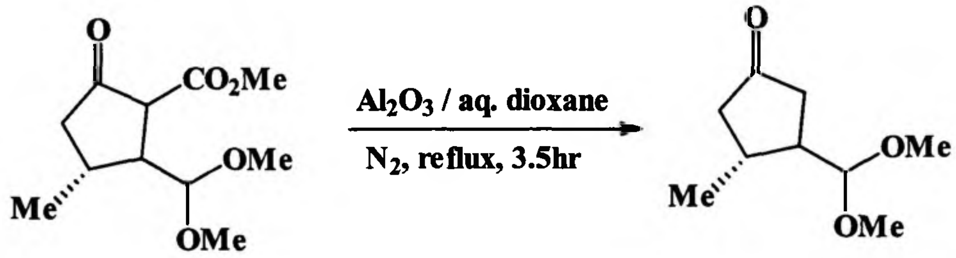
49 50

iv. Dehydration : Dehydration of some nonvolatile terpenes alcohols can be effected by heating them to ~200°C with alumina doped with pyridine or quinoline [55]. however, this method is drastic, nonvolatile and in many cases the compound may decompose at that temperature. More recently Posner[27] has reported a mild relative dehydration of a steroidal triol **(51, 52)** Woelm – 200 –N-alumina at 75°C using dibutyl ether as the solvent.



51 **52**

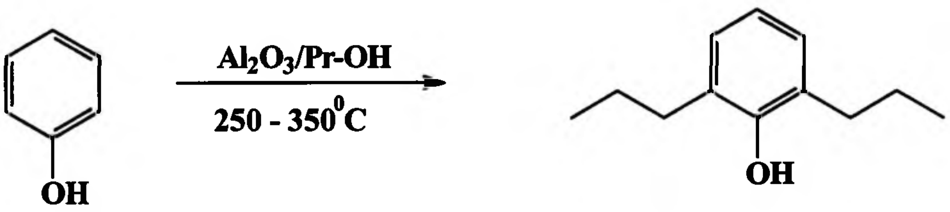
v. **Elimination of ester from β-ketoesters :** Esters groups from β-ketoesters **(53)** have been eliminated by refluxing with alumina in 1.5- % aq. dioxane[56]. The reaction probably proceeds through alumina – catalysed hydrolysis of the ester group followed decarbonylation of the resulting ketoacid.



53 **54**

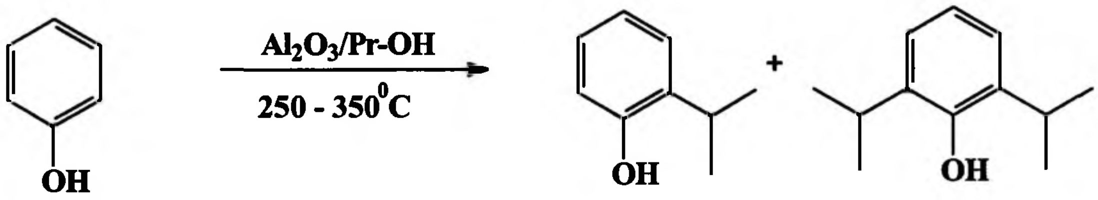
4.1.3.7 Addition Reactions :

i. **C – Alkylation :** Klemm and Taylor [57, 58] have reported the alumina catalysed additions of n-propyl [57] and isopropyl[58] groups to phenol. **(55)** reacts with excess of t-propanol at 250 - 300°C in presence of alumina to form a mixture consisting mainly the C-alkylated product mono to penta n- propyl phenols, 2, 6-di-n-propyl phenol **(56)** being the major product (25-50%) .



55 **56**

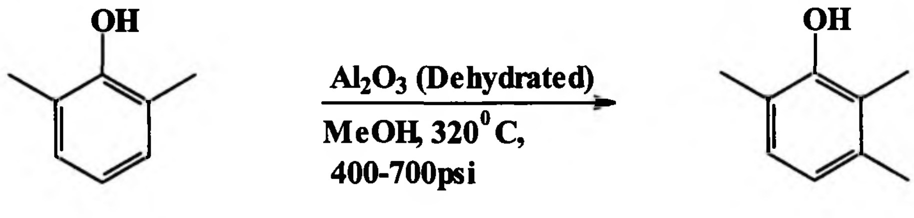
A similar reaction of phenol **(55)** with excess of 2-propanol in presence of alumina gave a mixture of 2-isopropyl-phenol **(57)** and 2, 6-diisopropyl phenol **(58)**



55 **57** **58**

These reactions were carried out by passing a solution of phenol in the alcohol dropwise through a column of alumina material at a constant specified temperature. It has been suggested that the C-alkylated phenols are formed by an SN^2 type reaction of an adsorbed n-phenoxide or n-isopropoxide respectively[57, 58].

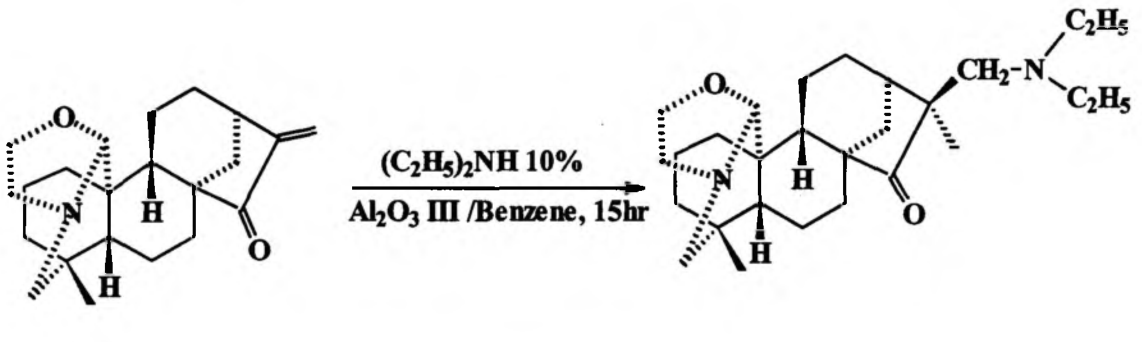
In contrast to the ortho – para substitution reactions mentioned above, Leach[59] has reported an unexpected meta-methylation in the reaction of 2, 6-xylenol **(59)** with methanol over dehydrated alumina to form 2, 3, 6 – trimethyl phenol **(60)**.



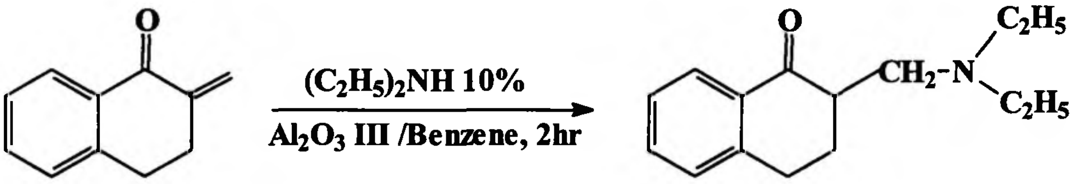
59 **60**

ii. Michael Addition to α, β - unsaturated ketones :

Alumina of Brockmann activity III has been found to catalyse the Michael addition of secondary amine to few exocyclic α, β - unsaturated ketones like Viacchinone **(61)** and 2-methyl –1-tetralone **(63)** giving the corresponding amine adducts (**62** and **64)** in quantitative yields [60].



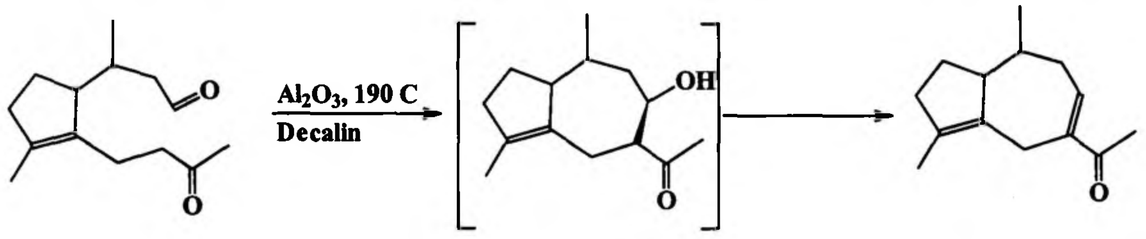
61 **62**



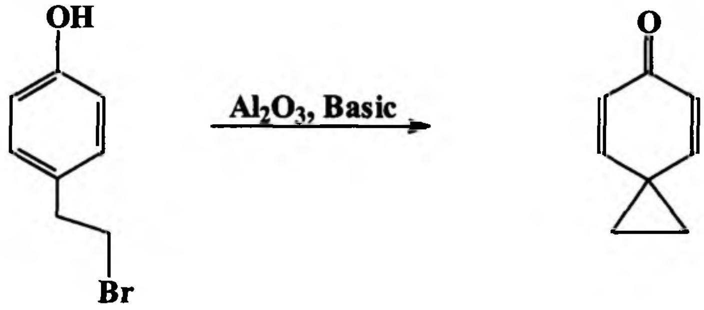
63 **64**

4.1.3.8 Carbocyclisation:

Alumina is known to catalyse intramolecular aldol condesation in some diketones. The reaction proceeds through alumina catalysed enolisation of one carbonyl group followed by addition of the acidic carbon atom of the enol to the nonenolised carbonyl group resulting in the formation of a carbocyclic ring[61]. (e.g.**65, 66**). This method is especially useful in constructing 5, 7-membered carbocyclic rings. Another example of cyclasation by C-C bond formation catalysed by alumina is the conversion of 4-(bromoethyl) phenol **(67)** to spirodienone **(68)** through intramolecular displacement of bromide ion[62].



65 **66**

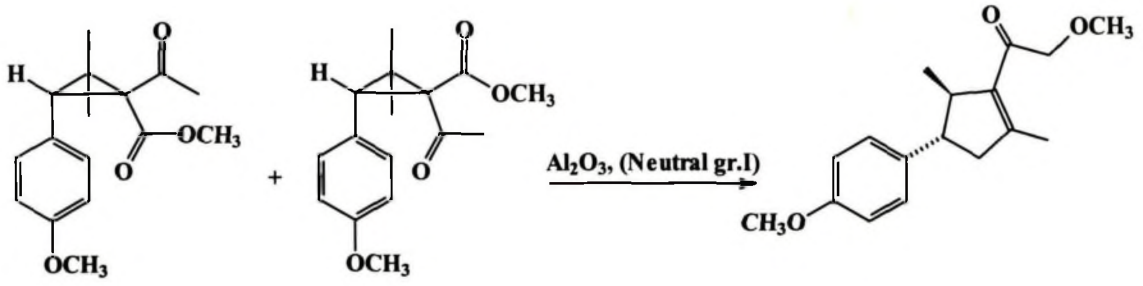


67 **68**

4.1.3.9 Skeletal Rearrangements:

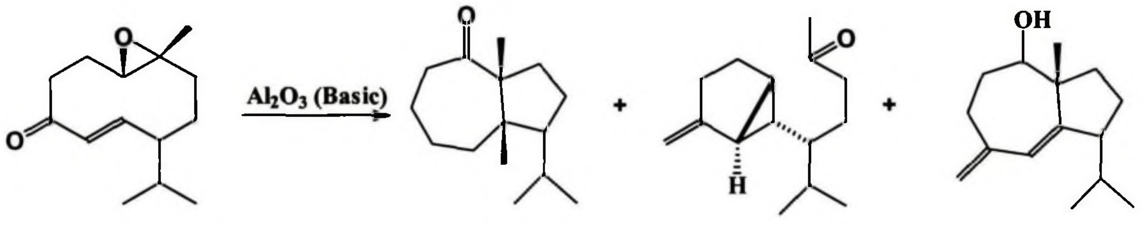
Alumina is known to cause a number of diversified skeletal rearrangement of the compounds adsorbed or in close contact with it. Many of the skeletal rearrangement are thus observed during the separation and the purification of the compounds over alumina columns. Since the alumina – catalysed skeletal rearrangements are too many, only two illustrative examples as.

i. A mixture of the stereoisomeric cyclopropyl ketones **(69 and 70)** underwent a stereospecific rearrangement to the tetrahydrofuran derivative **(71)** when treated with chromatographic neutral alumina at room temperatures[63].



69 **70** **71**

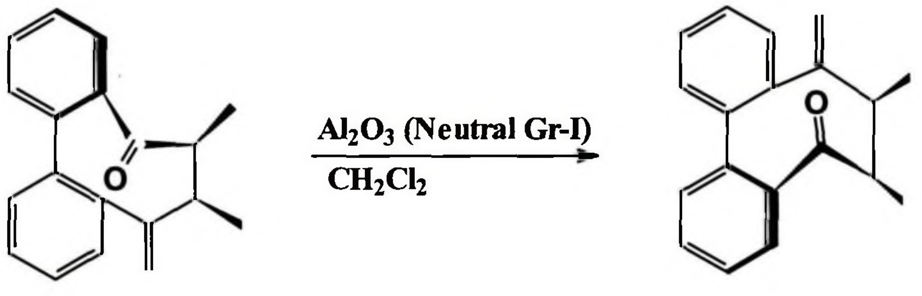
ii. Epoxy germacrine-D **(72)** on treatment with basic alumina underwent a biomematic reaction to form a mixture of **(73, 74,** and **75)**[64]



72 **73** **74** **75**

4.1.3.10 Rotational Isomerisation:

Bridged biphenyls of the type **(76)** have been found to undergo rotational isomerisation when adsorbed on alumina[65].



76 **77**

4.1.4 Present work

With an intention to isolate the possible new sesquiterpene lactones, we undertook the chemical investigation of *Cyathocline purpurea* and *Cyathocline lutea.* The aerial parts of this plant were extracted successively with pet ether and acetone. The acetone extract, after successive chromatography over column grade silica gel (60-120mesh) and repeated preparative TLC afforded the known compounds (**V** - **XII**). Out of this the compound **V** and compound **XI** were found in large quantity. As many other sesquiterpene lactones, the biological activities of this plant mainly due to sesquiterpenes lactones with α-methelene γ-lactone and cyclopentenone moiety. With an objective of modifying its activity, the chemical transformations of sesquiterpene lactones **V** and **XI** with alumina have been carried out. Since the alumina and silica gel is industrially important and enter into verity of catalytic processes, especially in the petrochemical industry. The only use to which this alumina is put in the laboratory is in the chromatographic separations of the compounds. During such application, it was observed that they undergo some chemical changes, possibly catalysed by alumina. This was prompted us for further study of these reactions catalysed by alumina and were extended to the sesquiterpene lactone **V** and **XI.**

As already described in the types of reactions catalysed by chromatography grade alumina is reported to effect verity of chemical reactions. One of the example is intramolecular addition reaction of OH group across isolated or carbonyl-conjugated olefinic bongs with the formation of an ether linkage[27]. Further, the Michael type of addition of methanol to the methelene group of α-methelene γ-lactone[66,] under basic conditions and same Michael type of addition of methanol to the double bond of an α, β-unsaturated ketones [67, 68] , have been reported. The same types of reactions under the same conditions were performed by the addition of water and methanol also instead of only methanol[69]. However, during the present study we observed that the sesquiterpenes lactones **V** and **XI** which were isolated from *C. purpurea,* and *C. lutea* respectively in large quantities were shown the same Michael type of addition of methanol and water catalysed by basic alumina.

The present study was conducted under the reflux temperature (65°C) with stirring and the ratio of alumina to that of sesquiterpene lactone used in methoxylation experiments were 100:1 for both the compounds **V** and **XI**. A methanolic solution of sesquiterpene lactones (**V** and **XI**) and the activated (Brockmann grade – IV) alumina were used for the same. This reaction was too slow at the room temperature and refluxing conditions gave the best yields of methoxylated products **XIV** and **XV**. The methoxylations were carried out using acidic, basic and neutral alumina and quantitative study of the products formed was made. The results are summerised in Table : 1. The structures of the methoxylated products **XIV** and **XV** in Chart III.

XIV **XV**

Chart: III

Table 1 : Methoxylation of V and XI by methanol on alumina (Reflux, 24 hrs.)

S. No	**Alumina**	**Compound V**			**Compound XI**		
		Product	**Yields %**	**Unreacted %**	**Product**	**Yields %**	**Unreacted %**
1	Acidic PH~6.5	XIV	10	90	XV	10	90
2	Basic PH~7.5	XIV	85	15	XV	80	20
3	Neutral PH~7.0	XIV	30	70	XV	25	75

It is evident that the results shown in Table : 1, all three types of alumina i.e. acidic, basic and neutral gave the same methoxylated products **XIV** and **XV** in the alumina – catalysed reaction though in varying yields. However, during methoxylation with basic alumina, it is quite likely that the basicity of the alumina might be responsible for the addition to the exocyclic methelene bond of the α, β- unsaturated lactones with the formation of new sesquiterpene lactones **XIV** and **XV.** The products obtained after the methoxylation are very rare in nature. Such type of compound reported for the first time from *Sphaeranthus indicus*[70]. The structures of all alumina – catalysed addition products were elucidated from their spectral characteristics that will be described subsequently.

4.1.5 Results and Discussions:

4.1.5.1 Characterization of Compound [XIV].

The compound obtained after purification by preparative TLC with acetone petrol (40 : 60) as eluent a gummy liquid showed its mass spectrum M^+ at m/e 278 suggesting the molecular formula $C_{16}H_{22}O_4$. The IR spectrum (Fig.1) of the compound showed characteristic band at 3390 cm^{-1}, 1770 cm^{-1} and 660 cm^{-1} revealing the presence of hydroxy, saturated γ-lactone and unsaturation in the molecule respectively.

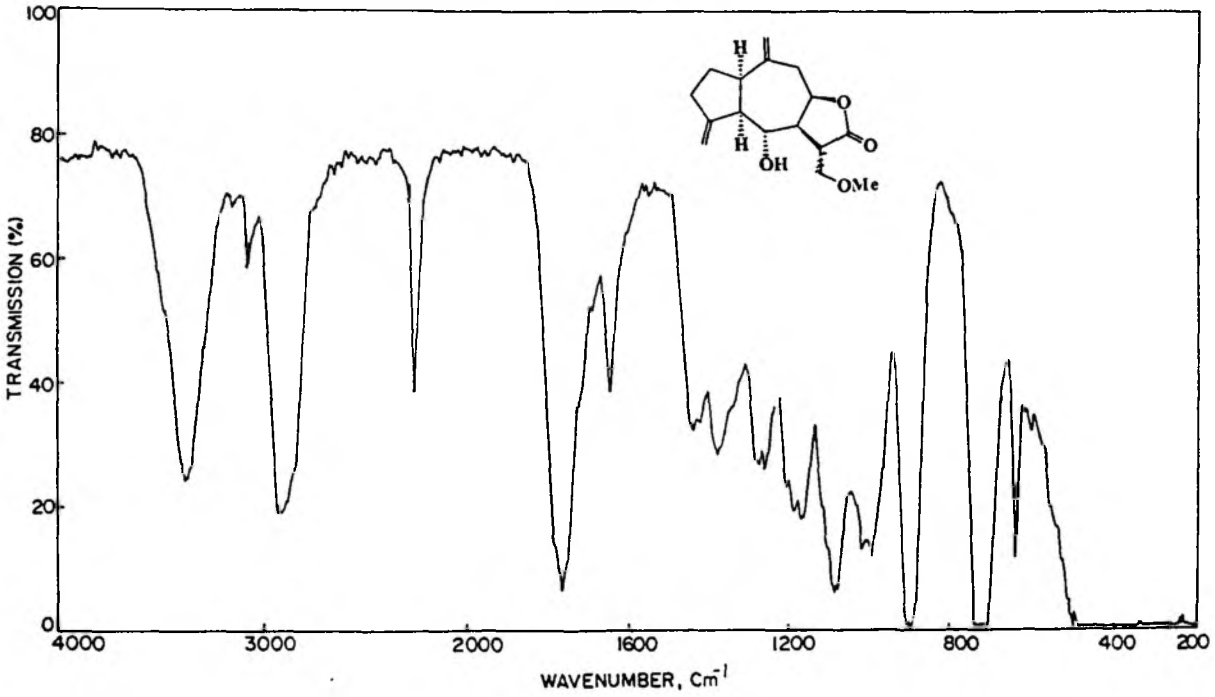


Fig 1. IR Spectra of Compound XIV

^{1}H NMR spectrum (Table:2; Fig. 2) of the compound shows the characteristic doublets of doublet at δ 3.50 (J = 9.5, 2.0 Hz) and δ 3.57 (J = 9.5, 2.0 Hz) accounting for one proton each. And a singlet at δ 3.42 for three protons of methoxy group which clearly indicates that the presence of 11, 13–dihydro–13–methoxy grouping in the compound **XIV**. The presence of two exocyclic methelene groups was indicated by broad singlets at δ 4.93 for two protons at C-14 and singlets at δ 5.05 and δ 5.30 for two protons at C-15. The appearance of doublets of doublet at δ 3.95 (J = 10.0, 10.0 Hz) for H-6 which shows downfield. The multiplet at δ 3.10 for H – 7 and also the downfield shift of shows the doublet of doublet of doublet at δ 4.50 (J = 9.0, 11.0, 4.0 Hz) for H – 8. The downfield shifts of H – 6, and H – 8 must be due the presence of oxygenated functions attached to them.

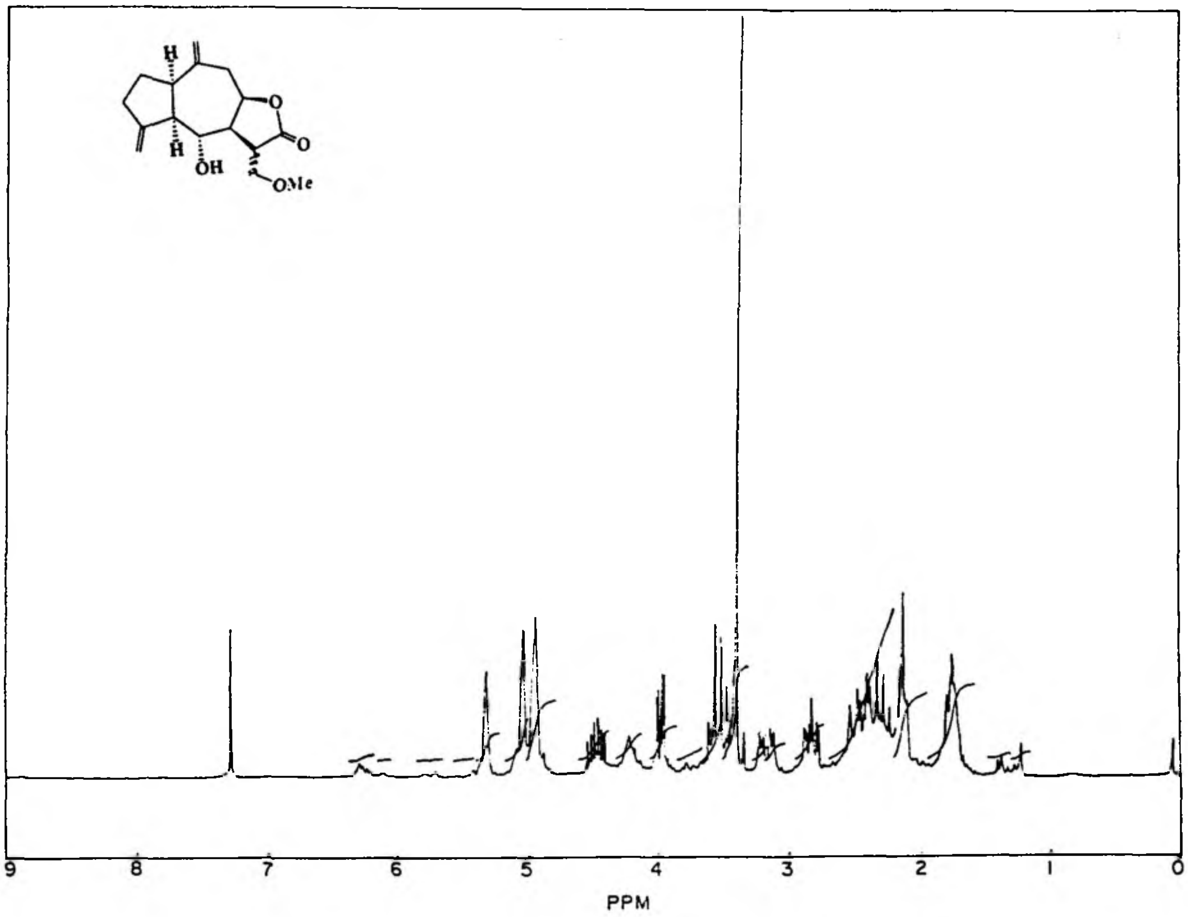


Fig.1 ^{1}H NMR Spectra of Compound XIV

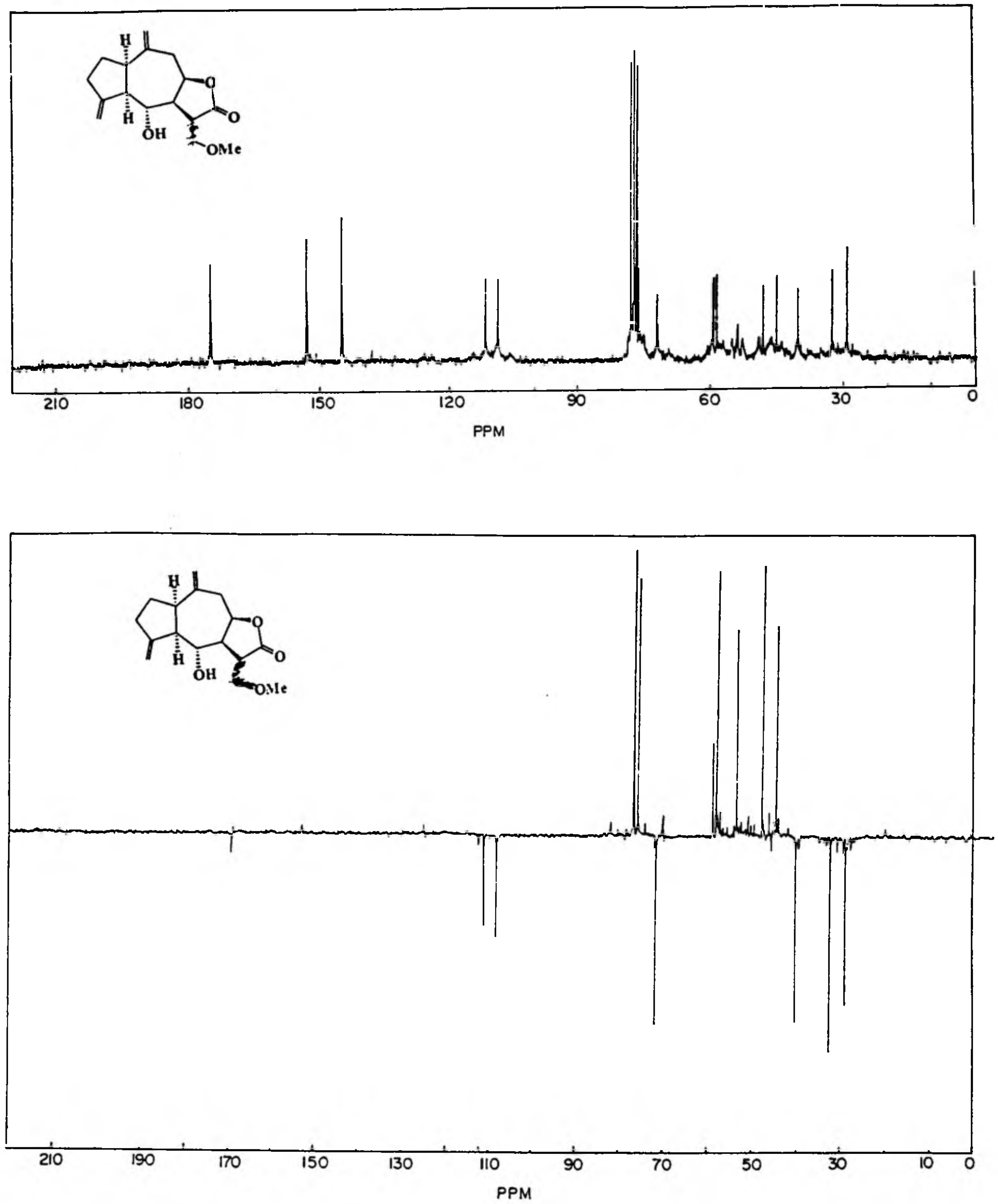


Fig. 3. & 4. ^{13}C NMR and INEPT of Compound XIV

The structure was supported by ^{13}C NMR signals (Table.3, Fig.3 and 4) shows a doublets at δ76.4 ; δ 58.2 and δ 77.6 .

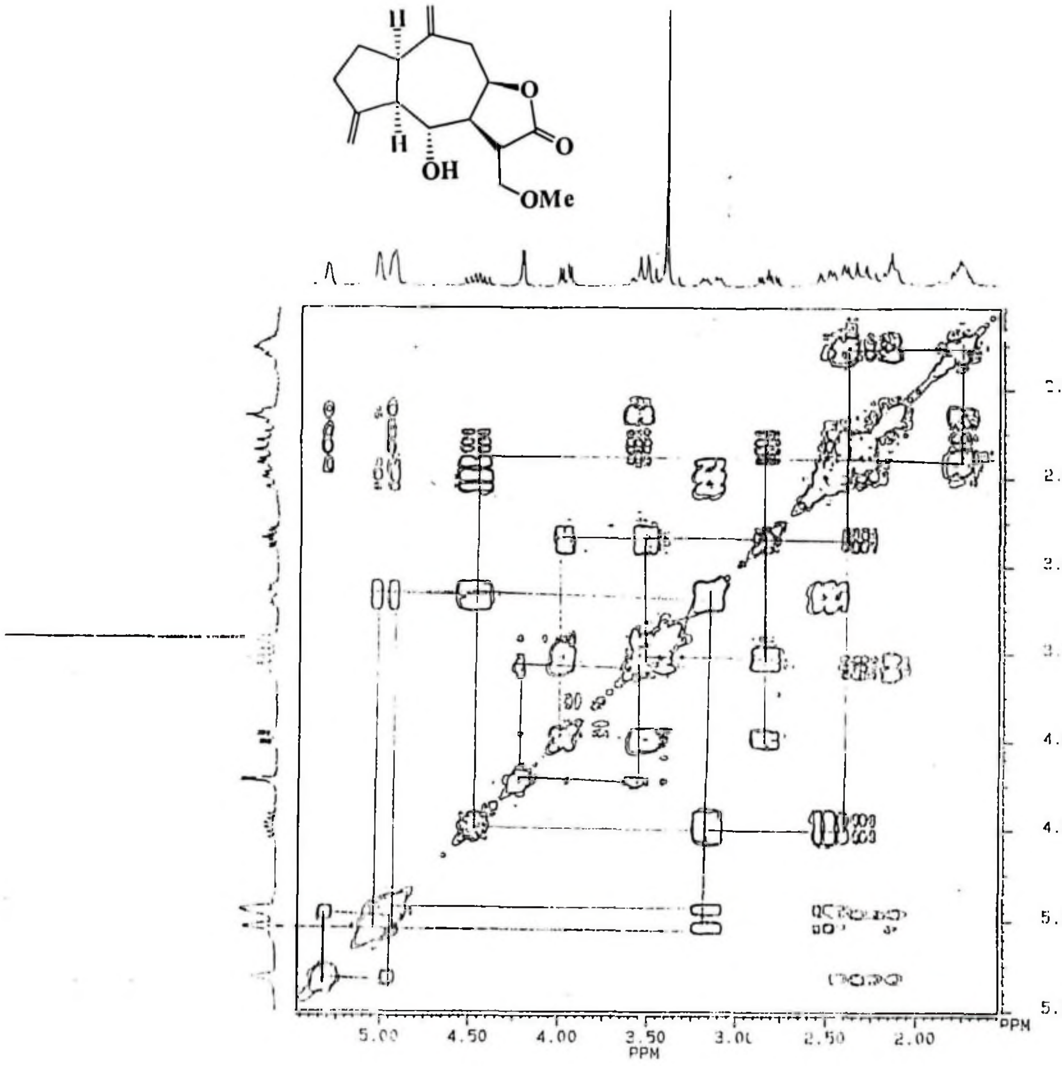


Fig. 5. Spectra of ^{1}H-^{1}H Homonuclear decoupling

The structure was further supported by assignment of the protons were achieved by ^{1}H – ^{1}H homonuclear decoupling (Fig.5) and all multiplicities in ^{13}C NMR were determined by INEPT technique and critical comparison with reported ^{1}H NMR spectral data of compound V (Fig.6). There is a single product isolated from the starting material V though there are three exomethelene double bonds present in the molecule because the addition takes place only in α, β - unsaturated ketones.

From NMR it is clear that H-7 is coupling with the three protons (H-6, H-8 and H-11). The coupling constants showing that there is one strong cis coupling of H-7 with H-8 (J=14 Hz) and another two weak trans couplings of H-7 with H-6 and H-11 (J=~5.0 Hz each). As H-6 and H-8 are fixed (H-6 cis to H-7 and H-8 trans to H-7). Therefore another weak coupling must be from a trans proton H-11. So the center at C-11 must be "S"

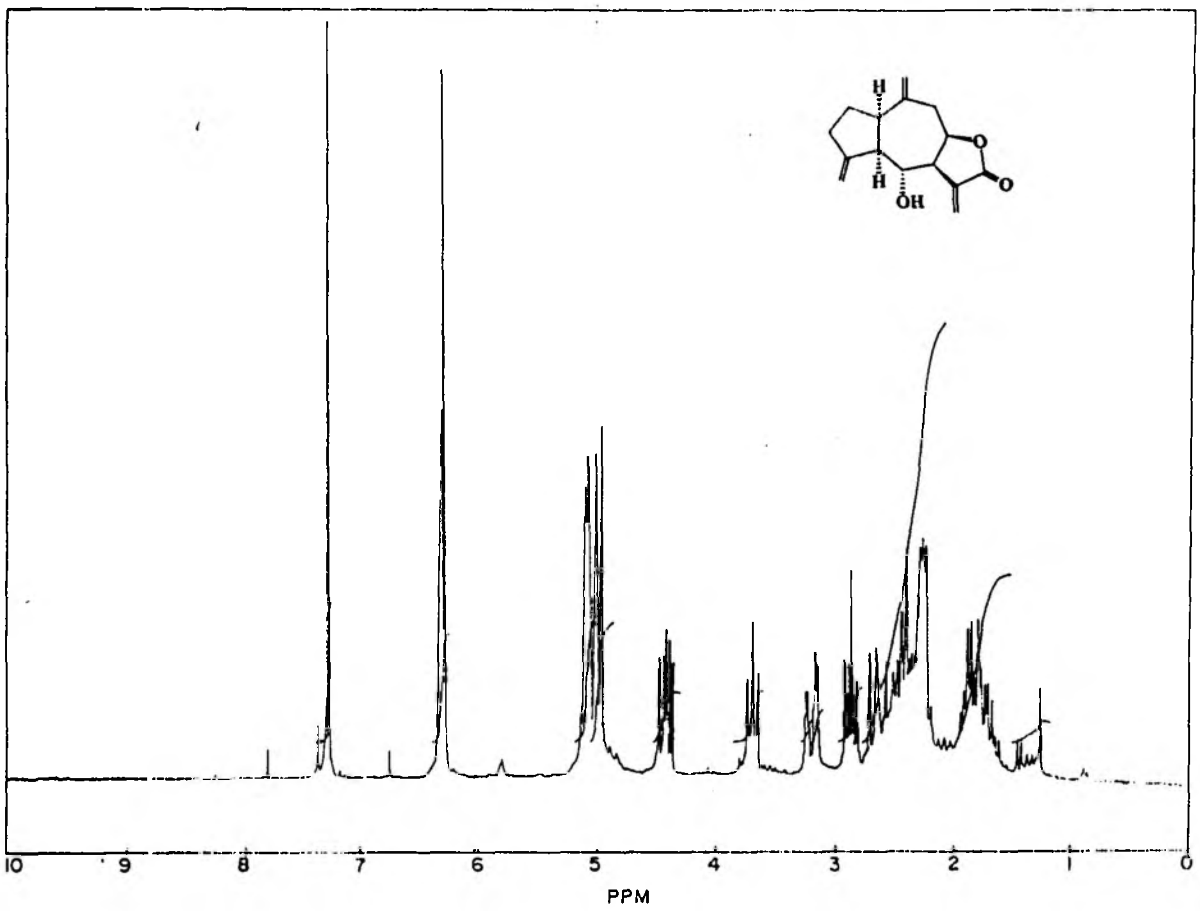
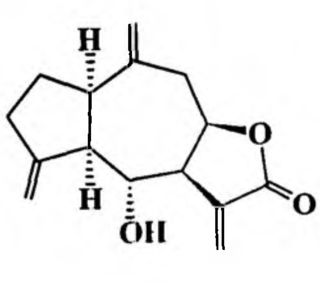
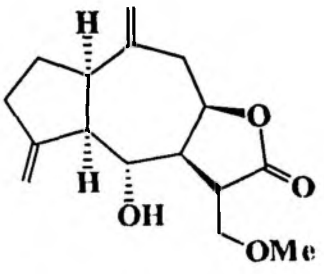


Fig. 6. ^{1}H NMR Spectra of Compound V



V



XIV

Table : 2 ^{1}NMR ($CDCl_3$) spectral data of compound V and XIV

Proton	**Compound V**			**Compound XIV**		
	Chemical Shift in δ	**Multip-licity**	**Coupling constant in Hz**	**Chemical Shift in δ**	**Multip-Licity**	**Coupling constant in Hz**
H –1	2.50	m	--	2.47	m	--
H – 2α	1.60	m	--	1.65	m	--
H – 2β	1.85	m	--	1.75	m	--
H – 3	2.30	m	--	2.35	m	--
H – 5	2.35	m	--	2.38	m	--
H – 6	3.75	dd	10.0, 10.0	3.95	dd	10.0 10.0
H – 7	3.20	m	--	3.10	m	--
H – 8	4.40	ddd	9.0, 11.0, 4.0	4.50	ddd	9.0, 11.0, 4.0
H – 9	--	--	--	--	--	--
H – 11	--	--	--	--	--	--
H – 13a	6.36	Br. s	--	3.50	dd	9.5, 2.0
H –13b	4.95	Br. s	--	3.57	dd	9.5 2.0
H – 14	5.00	Br. s	--	4.97	Br. s.	--
H – 15a	5.05	Br. s	--	5.05	Br. s	--
H – 15b	5.10	Br. s	--	5.30	Br. s	--
OMe	--	--	--	3.42	s	--

Table : 3 ^{13}C NMR ($CDCl_3$) Spectral data of compound XIV

Carbon	Chemical Shift in δ	Multiplicities
C-1	45.0	t
C-2	29.7	t
C-3	32.9	t
C-4	144.8	s
C-5	48.8	d
C-6	76.4	d
C-7	58.2	d
C-8	77.6	d
C-9	40.5	t
C-10	152.2	s
C-11	53.2	d
C-12	174.3	s
C-13	71.5	t
C-14	108.5	t
C-15	122.2	t
OMe	59.2	q

4.1.5.2 Characterization of Compound XV.

Compound XV obtained as a viscous liquid showed a mass spectrum M^+ at m/e 298 suggesting the molecular formula $C_{16}H_{26}O$. Its IR spectrum (Fig.7) showed a characteristic bands at 3420 cm^{-1} and 1775 cm^{-1} revealing that the presence of hydroxy group and saturated γ-lactone moiety in the structure.

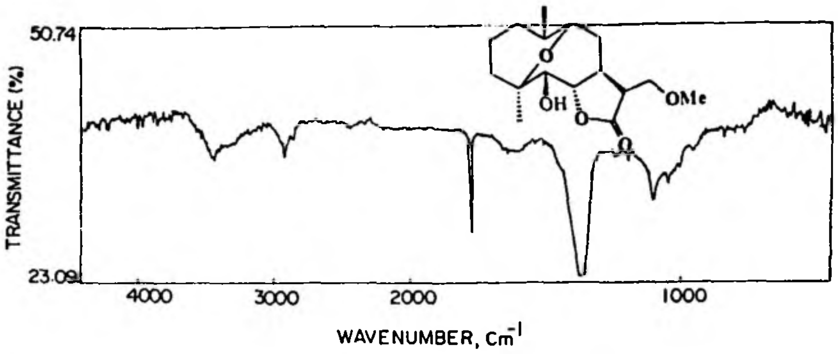


Fig. 7 IR Spectra of Compound XV

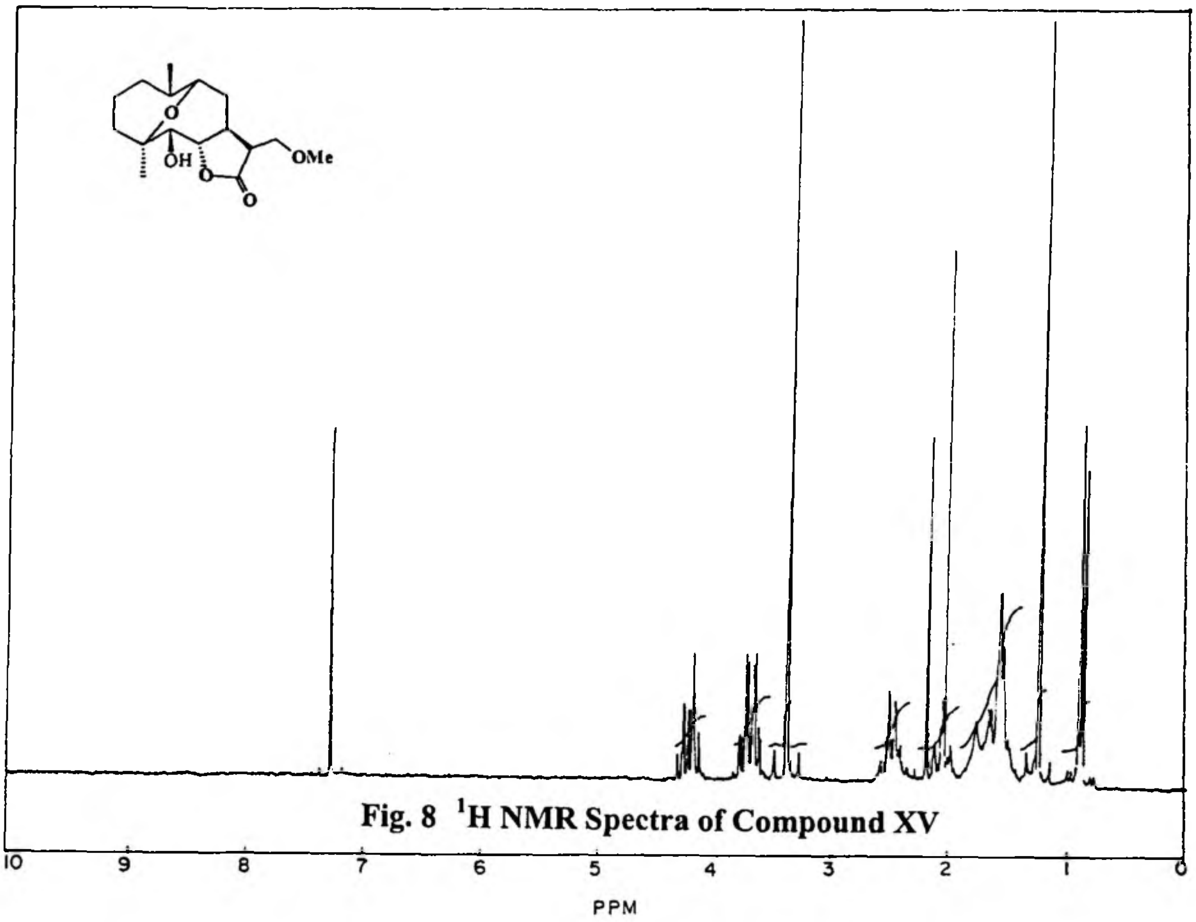


Fig. 8 ^{1}H NMR Spectra of Compound XV

^{1}H NMR spectrum (Table.4, Fig. 8) of the compound shows the characteristic doublet of doublet at δ 3.70 (J = 9.5 , 3.0 Hz.) and δ 3.60 (J = 9.5, 3.0 Hz.) accounting for three protons in methoxy group which clearly indicates that the presence of one 11, 13-dihydro –13-methoxy grouping in the lactone ring of the product XV. The presence of secondary and tertiary methyl group are the evident from a doublet at δ 0.90 (J = 6.8 Hz) and singlet at δ 1.20.

Further the C-6 proton appeared as a double doublet at δ 4.16 (J = 9.5, 9.5 Hz) and single doublet at δ 4.12 (J = 9.5 Hz) suggested a position of lactone ring and secondary hydroxy group. The structure and stereochemistry of the compound **XV** were determined by the critical comparison with reported ^{1}H NMR spectral data of compound **XI** (Fig. 9).

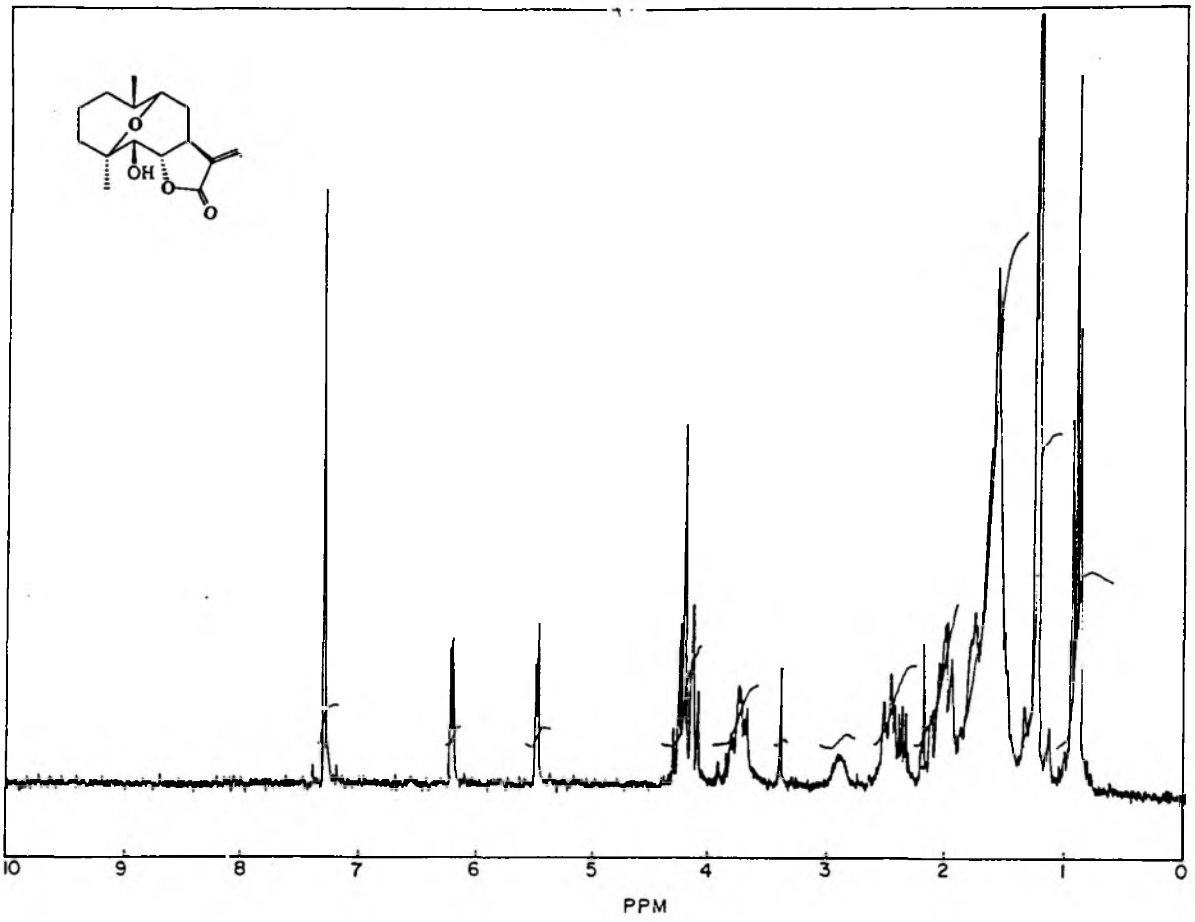
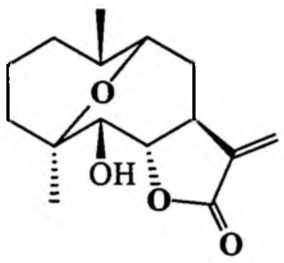
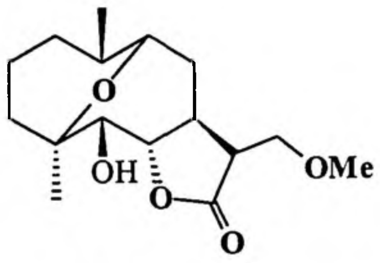


Fig. 9 ^{1}H NMR Spectra of Compound XI



XI



XV

Table : 4 ^{1}NMR ($CDCl_3$) spectral data of compound XI and XV

Proton	**Compound XI**			**Compound XV**		
	Chemical Shift in δ	**Multiplicity**	**Coupling Constant in Hz**	**Chemical shift in δ**	**Multiplicity**	**Coupling Constant in Hz**
H – 1	--	--	--	--	--	--
H – 2α	--	--	--	--	--	--
H – 2β	--	--	--	--	--	--
H – 3	--	--	--	--	--	--
H – 5	4.12	d	9.5	4.12	d	9.5
H – 6	4.15	dd	9.5, 9.5	4.16	dd	9.5, 9.5
H – 7	2.5	m	--	2.65	m	--
H – 8	--	--	--	--	--	--
H – 9	3.7	m	--	3.80	m	--
H – 11	--	--	--	2.45	m	--
H – 13a	5.41	d	3.0	3.60	dd	9.5, 3.0
H –13b	6.13	d	3.2	3.70	dd	9.5 3.0
H – 14	0.88	d	6.8	0.90	d.	6.8
H – 15a	1.20	s	--	1.20	s	--
H – 15b	--	--	--	--	--	--
OMe	--	--	--	3.40	s	--

4.1.6 Experimental

4.1.6.1 Compound XIV

4.1.6.1.1 Isolation of compound V

Compound **V** used in alumina –a catalysed reaction was isolated from the acetone extract of *C. purpurea*. Shade dried plant material coarsely powdered and extracted with acetone. The acetone extract was subjected to repeated chromatography over a column grade silica gel columns using acetone pet. Ether mixture as the eluent and the compound further purified by preparative TLC using different solvent systems.

4.1.6.1.2 Processing of the alumina to get Brockmann Grade IV alumina

The alumina used in these reactions was column chromatographic grade (60- 120-mesh particle size). The acidic, neutral and basic alumina used were approximately of pH 6.5, 7.0 and 7.5 respectively. The pH in each case was measured approximately on 10% w/v aqueous suspension using pH meter. The grades of alumina mentioned refer to Brockmann activity. Grade I alumina was prepared by activating the alumina at 600°C for 5 hours. Further, this alumina was converted to grade IV adding 7.5-ml water per 100g of alumina and mixing thoroughly on a mixing roller for 6 hours. The solvents used in the reactions were distilled ones but were not dried.

4.1.6.1.3 Methoxylation of compound V

Compound **V** was taken 0.5g each in three separate 250 ml round bottom flasks fitted with reflux condensers and added 150-ml methanol to each flask. 50g portions of acidic, basic and neutral alumina (all activated) were added to the three flasks and the contents were refluxed with constant stirring on magnetic stirrers for 24 hours. The reaction product from each flasks was worked up separately by filtering alumina from each flasks through sintered glass funnel and washed thoroughly three to four times with methanol. The filtrate and washing from each flasks were combined and concentrated. The residue in each case was redissolved on each in 10 ml of acetone and filtered through a Watmann No : 1 filter paper to remove traces of alumina. The filtrate from each lot was concentrated and the residues were chromatographed (TLC) showed a spot very much below to that of compound **V**. The compound **XIV** corresponding to this spot as well as the unconverted compound **V** from each lot were separated by preparative TLC with 40% acetone and 60% pet ether as a eluent. This gave compound **XIV** in the yields of 0.050g, 0.423g and 0.150g with acidic, basic and neutral alumina respectively. The obtained product in this experiment was 11, 13-dihydroxy – 13-methoxy guainolide sesquiterpene lactone .

Yield : 85%; 0·423g

IR ($CHCl_3$, cm^{-1}) : 3390, 1770 and 1660. Fig. 1.

^{1}H NMR ($CDCl_3$, 200MHz) : Fig. 2 ; Table : 2

^{13}C NMR ($CDCl_3$,200MHz) : Fig. 3 and 4 ; Table : 3

Mass (m/e, rel. intensities) : 278 (M^+) (2%); 207 (10%); 121 (42%); 117 (10%); 107 (22%); 91 (32%); 79 (20%); 69 (18%) and 55 (15 %)

4.1.6.2 Compound XV :

4.1.6.2.1 Isolation of compound XI

Compound **V** used in alumina –a catalysed reaction was isolated from the acetone extract of *C. lutea*. Shade dried plant material coarsely powdered and extracted with acetone. The acetone extract was subjected to repeated chromatography over a column grade silica gel columns using acetone pet. ether mixture as the eluent and the compound further purified by preparative TLC using different solvent systems.

4.1.6.2.2 **Brockmann Grade IV alumina**

The same Brockmann Grade IV alumina (which was prepared for the Compound **V**) was used for the methoxylation of compound **XI**. The solvents used in the reactions were distilled ones but were not dried.

4.1.6.2.3 **Methoxylation of compound XI**

Compound **XI** was taken 0.5g each in three separate 250 ml round bottom flasks fitted with reflux condensers and added 150-ml methanol to each flask. 50g portions of acidic, basic and neutral alumina (all activated) were added to the three flasks and the contents were refluxed with constant stirring on magnetic stirrers for 24 hours. The reaction product from each flasks was worked up separately by filtering alumina from each flasks through sintered glass funnel and washed thoroughly three to four times with methanol. The filtrate and washing from each flasks were combined and concentrated. The residue in each case was redissolved on each in 10 ml of acetone and filtered through a Watmann No : 1 filter paper to remove traces of alumina. The filtrate from each lot was concentrated and the residue was chromatographed (TLC) showed a spot very much below to that of compound **XI.** The compound **XV** corresponding to this spot as well as the unconverted compound **XI** from each lot were separated by preparative TLC with 40% acetone and 60% pet ether as a eluent (30% EtOAc and 70% benzene as alternative eluent system also tried). This gave compound **XV** in the yields of 0.05g, 0.4g and 0.1g with acidic, basic and neutral alumina respectively. The obtained product in this experiment was 11, 13-dihydro – 13-methoxy germacranolide sesquiterpene lactone .

Yield : 80%; 0·4g

IR ($CHCl_3$, cm^{-1}) : 3420, 1775 Fig. 7.

^1H NMR ($CDCl_3$, 200MHz) : Fig. 8 ; Table : 4

Mass (m/e, rel. intensities) : 298 (M^+) (5%); 280 (2%); 253

(1%); 241 (9%); 107 (22%); 91 (32%); 79 (20%); 159 (27%); 121 (32 %); 95 (42 %); 81 (52%); 71 (56%) and 55 (100 %).

Section B

Oxidations of Methyl Ketones to Carboxylic Acids using Rhenium Oxide (Re_2O_7)

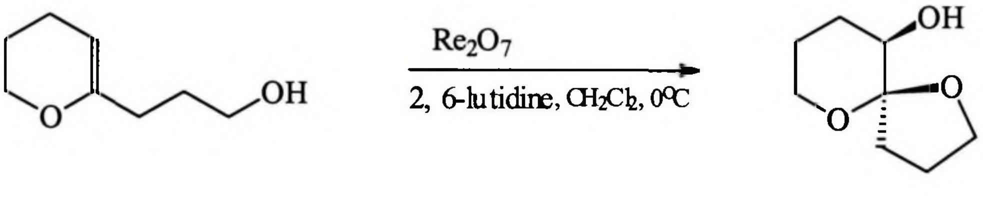
4.2.0 Introduction

Direct carbon-carbon bond cleavage of carbonyl compounds to its corresponding acids is a field of both academic and industrial importance and challenge. Selective oxidations are rapidly gaining importance in organic synthesis. The use of transition metal complexes as catalysts for such reaction is of particular interest. On one hand because of the high selectivity and the versatility of these complexes and on the other hand due to their ability to activate oxidants such as molecular oxygen, H_2O_2[71]. and TBHP[71]. Catalysis by metal complexes plays a central role in selective oxidations of both aliphatic and aromatic ketones to carboxylic acids.

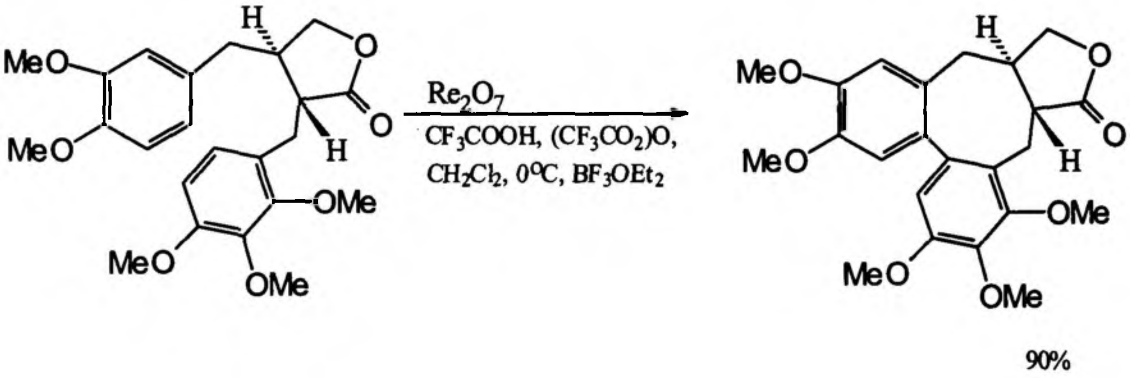
4.2.1 A brief Review of Literature.

Rhenium important transitions metal form which number of oxides has been prepared like Re_2O_7, ReO_2, ReO_3 and ReO. These oxides are used as catalyst in hydrogenation effectively, particularly in the reduction of carboxylic acids to primary alcohols. The rhenium oxides are used very rarely in case of reduction of aromatic, olefinic, carboxyl and nitro groups. Since they are less active than nickel or platinum catalysts[72].

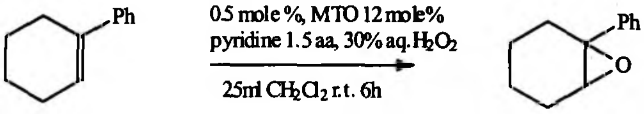
The use of Re_2O_7 had been performed in the studies of spirocyclization of 2- (ω – hydroxy alkyl) – 1 – oxo – 2 – cycloalkenes by using into hydroxy spiroketals[73].



The further utilization of Re_2O_7 has been carried out in synthesis of Bibenzocyclo octadienes. The non-phenolic coupling used in the synthesis of lignans lactones with Re_2O_7 in TFA – TFAA media[74].



The Rhenium compounds such as Re_2O_7 or Re_2O_3 well known to exhibit modest catalytic activity for H_2O_2 based oxidation[75]. However real interest in the potential of Rhenium oxidation catalyst began with an extra ordinary discovery by Hermams group[76]. They found that organometallic oxorhenium (VII) species (species MTO) are powerful epoxidation catalyst with H_2O_2 as oxidant[77].



Oxidation of alkenes with H_2O_2 in the presence of transition metal oxides, such as WO_3, MoO_3 and OsO_4. yielding epoxides or vicinal diols is well known[78] while Rhenium compounds are considered to be poor catalyst[79]. Recently Hermann et.al[76] demonstrated. MTO is an excellent catalyst for not only epoxidation but also for hydroxylation in the system H_2O_2, *tert.* butyl alcohol[80]. Also in this context, Re_2O_7 itself is described to be in

$$R - CH = CH - R^2 \;+\; H_2O_2 \xrightarrow[90^{o}C,\ 1,4\text{-dioxane}]{Re_2O_7} R - CH(OH) - CH(OH) - R^2$$

effective[81] for dihydroxylation of alkenes when used in combination with Me_3SiO $SiMe_3$ and H_2O_2 as oxidants.

4.2.2 Present work.

4.2.2.1 Introduction.

The direct oxidation carbon-carbon bond cleavage of aryl methyl ketone to carboxylic acid by transition metal complexes under mild conditions is an important transformation in organic chemistry. This transformation has greater commercial importance in industry due to the easy accessibility of these ketones by Friedel – Craft acylation[82]. The resulting oxidized products have greater commercial importance in industry due to the variety of substantial benzoic acids which are widely used in the pharmaceutical industry as drug intermediates for the synthesis of anti-rheumatics, anti malarials, tranquilizers etc, in agrochemicals as herbicides and in polymer dye – stuff industries as modifiers for resins and dye sensitizer respectively[83]. The traditional methods for the synthesis of carboxylic acids from methyl ketones are achieved by the oxidative degradation with sodium hypohalides in strongly basic conditions of haloform reactions[84]. The same oxidative degradations were also reported with Cr^{V} and Mn^{VII} reagents under stochiometrc conditions[85]. Lack of selectivity, tedious work up and generation of halo compounds toxic chromium residues as a result of the use of a large excess of chromium reagents are the main disadvantages often encountered in these oxidations. There number of methods to synthesize aromatic carboxylic acids such as

A. p-Methylacetophenone was converted to 1,4-benzene dicarboxylic acid by refluxing it with dilute nitric acid and boiled with aq. NaOH and further treated with Conc. Sulphuric acid[86].

B. Aromatic methyl ketones and iodine was dissolved in pyridine on heating for half an hour and further treated with alc. Sod. Hydroxide which on acidification gave benzoic acid[87].

C. Substituted aromatic acetophenone was heated with sod. Dichromate and acetic acids or sulphuric acids to afford substituted benzoic acid[88].

D. A catalytic amount of manganese triacetate in a stream of oxygen at high temperature to get benzoic acid from acetophenone[89]

E. The conversion of cholest-4-en-3-one and 17β-acetoxyandrost-4-en-3-one to corresponding 4-seco-3-carboxylic acids by treatment of pot. Permanganate and sod. Metaperiodate in water or butanol[90]

F. It was possible to get carboxylic acids by dissolving acetophenone in benzene and water which was on further addition of pentafluoroiodobenzene bis (trifluoroacetate) to get benzoic acids [91].

G. α-Amino ketones when treated with 30% H_2O_2 to get corresponding carboxylic acids was carried out by using liquid phase air oxidation of toluene using cobalt as catalyst.

Most of methods mentioned above are having drawbacks such as there is a use have halogenated oxidants, which are hazardous to environment. The processes are not catalytic and large amounts of waste products with heavy metals (Cr., Mn.,etc) are produced which is difficult to dispose it of. These processes are very inexpensive and are not environmentally friendly. Hence there is a need for cleaner, catalytic alternatives, which do not generate excessive amounts of inorganic salts as by products. In this direction recently the soluble Rhenium heptoxide (Re_2O_7) a homogeneous catalysts are used with the combination of 70% TBHP to get the product.

4.2.2.2 Objective.

As mentioned in the introduction the traditional procedures are usually effective, problems often crop up due to the lack of selectivity in oxidations coupled with safety hazards associated with these of large qualities of toxic chromium and halo compounds. Hence there is a strong need for cleaner and catalytic alternative, which do not generate excessive amounts of byproducts. It is therefore, necessary to provide a single step, simple and easier process for the conversion of methyl ketones to its corresponding carboxylic acids using rhenium (VII) oxide in catalytic amount. Heptavalent rhenium has received attention in recent years in inorganic and organometallic chemistry[77, 92]. Herein we studied efficiency of Re_2O_7 in the carbon-carbon bond cleavage of ketones into carboxylic acids under the homogeneous conditions using 70% aqueous TBHP as secondary oxidants.

4.2.3 Results and discussions:

The study of conversion of methyl ketones to carboxylic acids developed with new catalytic system consists simply of Re_2O_7, 70% TBHP in an organic solvents and totally free from any organic or inorganic halides. We selected 4 – isobutyl – acetophenone as a test substrate and subjected to oxidation with TBHP in various solvents with catalytic quantities of Re – oxides. After some experimentation, we found that that the combination of Re_2O_7 (6 mole%) and 70% TBHP (8 equi.) in acetic acid efficiently catalyses the desired oxidative cleavage of terminal methyl ketones to produce carboxylic acids (Scheme. 1)

$$\underset{R = \text{aryl, alkyl}}{RCOCH_3} \qquad \xrightarrow[\substack{\text{TBHP (8 moles),AcOH,} \\ 100\,^{\circ}\text{C, 5 h}}]{Re_2O_7\text{ (6 mole\%)}} \qquad \underset{25\text{–}72\ \%}{RCO_2H}$$

Scheme. 1

The same procedure we followed for 4-isobutyl acetophenone was subjected to different substrate for the oxidations as mentioned in **table 2** along with the results summarized in the table. A carbon – carbon bond cleavage gives a products were characterized by m.p., IR , ^{1}H NMR and Mass spectral techniques and found in exact agreement with that of the reported spectral values (Fig.10. for 4-Methoxybenzoic acid and Fig 11 for 4-Isobutylbenzoic acid).

Table 1: Re - catalyzed selective oxidation of 4-methoxyacetophenone[a] to 4 methoxybenzoic acid with 70% TBHP

Exp. No.	**Catalyst (moles %)**	**TBHP (equiv.)**	**Solvent (5 ml)**	**Temp. (°C)**	**Time (h)**	**Yield[b] %**
1	Re_2O_7 (10.5)	9.5	MeOH	60	6	41
2	Re_2O_7 (10.5)	9.5	MeOH	60	10	13
3	Re_2O_7 (5.0)	3.0	MeOH	60	15	9[c]
4	Re_2O_7 (3.5)	6.2	t BuOH	90	15	17
5	Re_2O_7 (6.0)	4.0	t BuOH	90	15	20
6	Re_2O_7 (15.2)	6.0	t BuOH	90	20	51
7	Re_2O_7 (6.3)	5.2	AcOH	100	5	33
8	Re_2O_7 (8.0)	8.0	AcOH	100	5	55
9	ReO_3OsiPh_3(4.5)	4.37	AcOH	100	5	10
10	$MeReO_3$ (6.2)	4.37	AcOH	100	5	5[d]

[a] Ketone (5 mmol scale); [b] GLC yield ; the rest is essentially unreacted ketone, [c] additive 4-cyanopyridine added to enhance reaction rate; [d] Baeyer-Villiger rearranged product is the major one.[94]

It has found that **(table 1)** a 55% conversion of ketone to acid was realized in acetic acid in 5 hours when 4-methoxyacetonephenone was reacted with 70%TBHP and catalytic amount of Re_2O_7. Lowering the concentrations of either TBHP or Re_2O_7 lowered the yield of the product. The activity of Re_2O_7 was found to be high in acetic acid as solvent compared to methanol and *t.* butanol. Other rhenium oxides such as ReO_3 $OSiPh_3$[93], and CH_3ReO_3 (methyl rhenium trioxide = MTO) shows less activity and selectivity. In fact, CH_3ReO_3 gave phenyl acetate, the Baeyer-Villiger rearranged product in high yields[94]. Under the conditions employed, a carboxylic acid was not formed in the absence of Re catalyst.

It was further found that the mild reaction conditions are compatible with sensitive functional groups such as phenols, systems having carbon-carbon double bonds etc. The time required for the completion of this reaction is typically 5 hours when 6 mole % of Re_2O_7 is used as catalyst with 8 equivalents of TBHP. A remarkable feature of the Re/TBHP catalytic system is its unusual regioselectivity of the oxidation exhibited towards the methyl and ethyl ketones e.g. 4 - isobutylacetophenone and 4 – phenyl 3 – butene – 2 – one underwent oxidation regioselectively at the methyl group despite the significantly greater oxidizability of the benzylic C-H and C=C bonds respectively (Table 2, entries 7and 13).

Table 2 : Re_2O_7 catalyzed selective oxidative cleavage of ketones to carboxylic acids with 70%TBHP[a]

Exp. No.	**Ketones**	**t/h**	**Carboxylic acids**	**Yield[b] (%)**
1	Acetophenone	5	Benzoic acid	71
2	4-Methylacetophenone	4	4-Methylbenzoic acid	60
3	4-Chloroacetophenone	6	4-Chlorobenzoic acid	61
4	4-Hydroxyacetophenone	5	4-Hydroxybenzoic acid	40
5	4-Nitroacetophenone	8	4-Nitrobenzoic acid	25
6	4-Methoxyacetophenone	4.5	4-Methoxybenzoic acid	55
7	4-Isobutylacetophenone	6	4-Isobutylbenzoic acid	72
8	2,5-Dimethoxyacetophenone	5	2,5-Dimethoxybenzoic acid	55
9	2-Aceto-6-methoxynaphthalene	6	6-Methoxynaphthalene-2-carboxylic acid	40
10	Propiophenone	5	Benzoic acid	55
11	2-Octanone	5	1-Heptanoic acid	30
12	2-Acetylpyrrole	6	Pyrrole-2-carboxylic acid	60
13	Benzalacetone	6	*trans*-Cinnamic acid	52
14	Epoxybenzalacetone	5	Benzoic acid	48
15	Cyclohexanone	9	No reaction	-
16	Androsterone	9	No reaction	-

[a] Ketone (5 mmol), Re_2O_7 (8 mol%), 70%TBHP (40 mmol),AcOH (5 ml) 90°C, 5 h; [b] Isolated yield after chromatographic purification; all acids have been thoroughly characterised by m.p, IR, ^1H & ^{13}C NMR and MS.

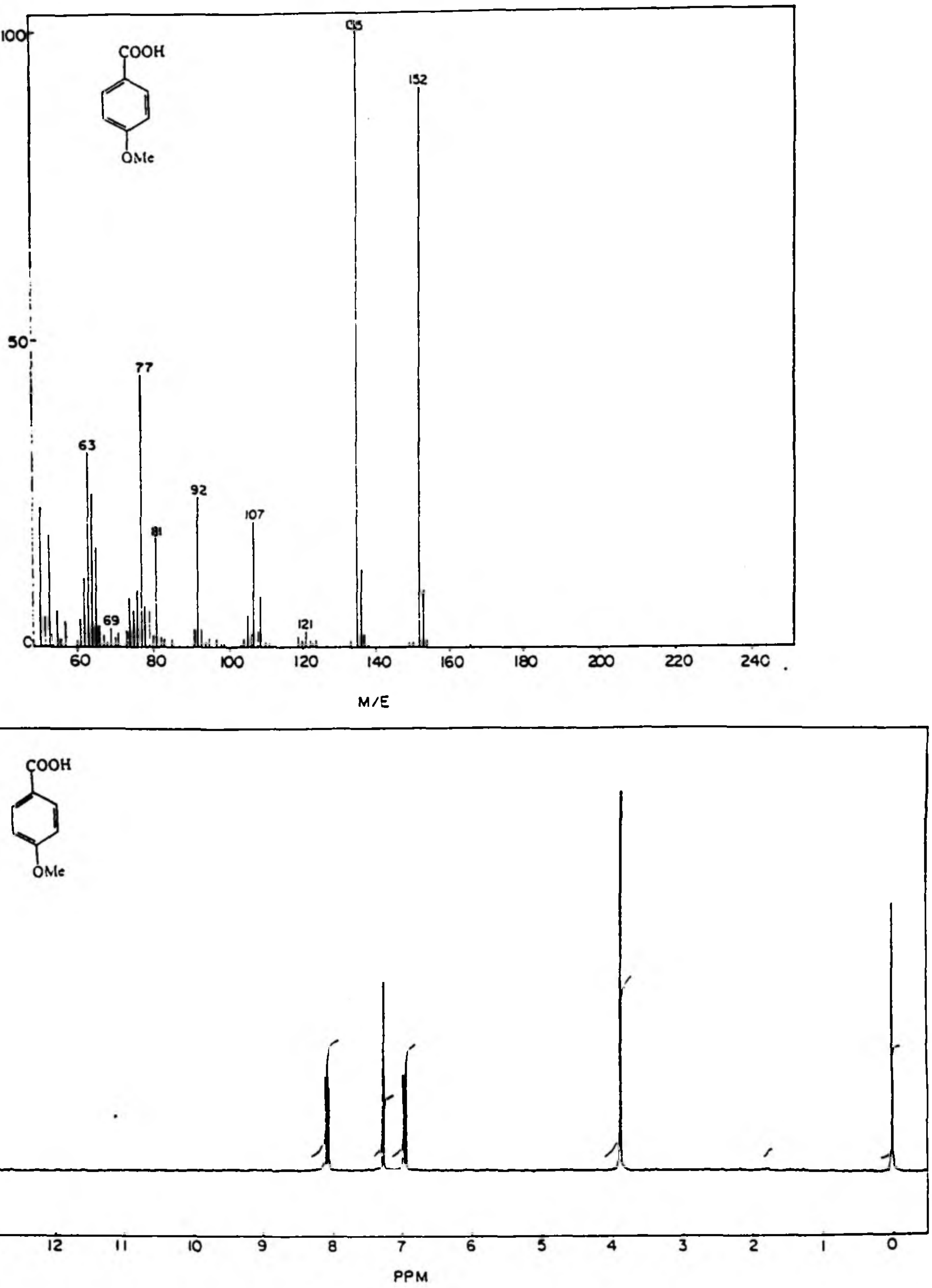


Fig. 10 Mass, ^{1}H NMR Spectra of 4- Methoxybenzoic acid

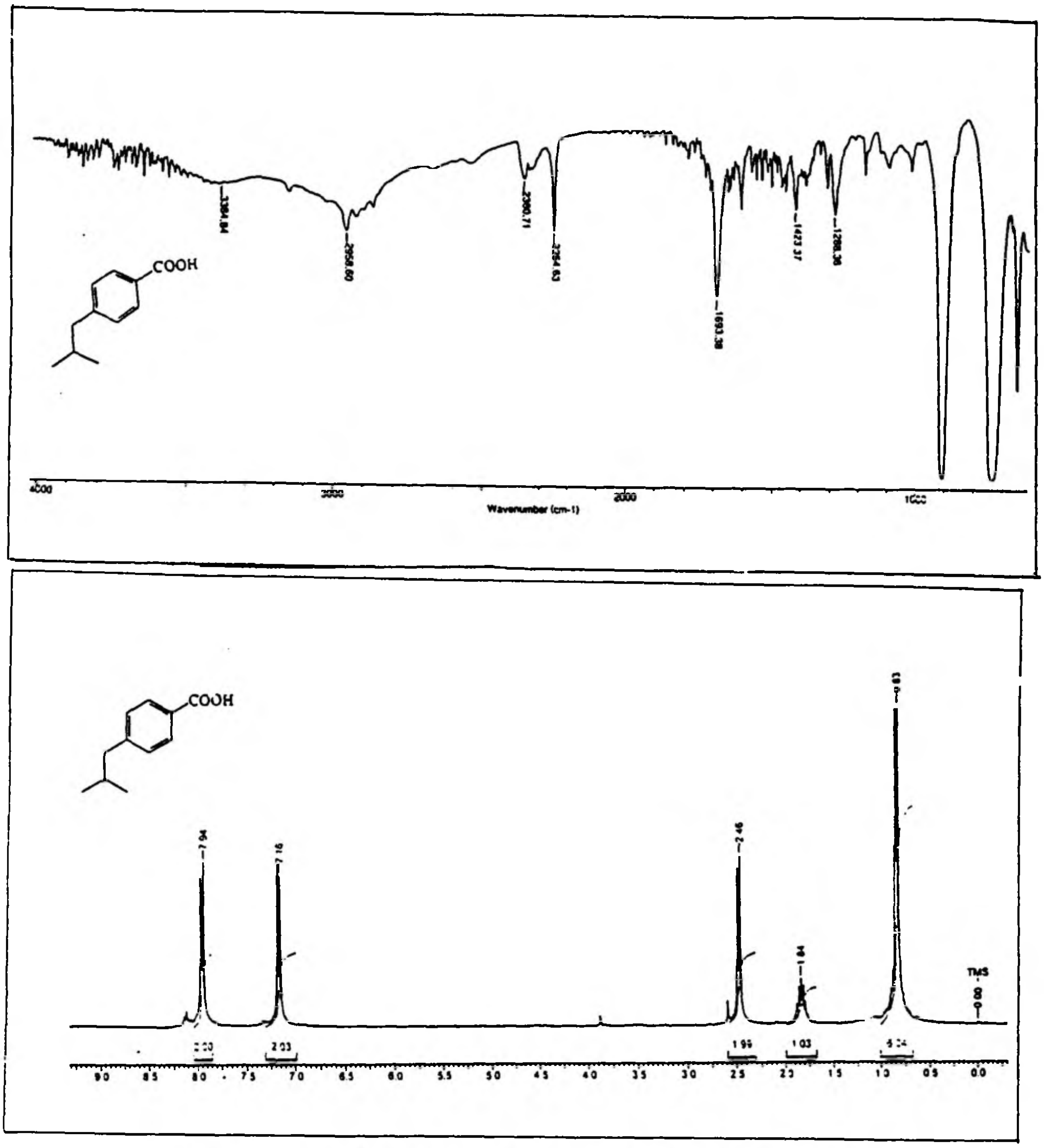


Fig. 11 IR and ^{1}H NMR Spectra of 4- Isobutylbenzoic acid

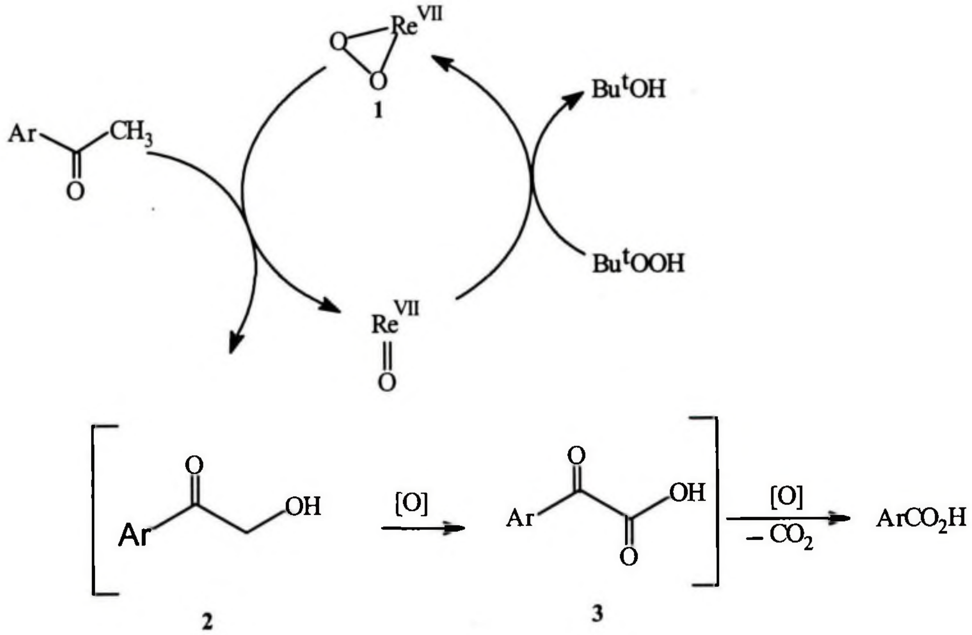
It was interesting to note that even the heterogeneous substrate like 2-acetyl pyrrole underwent oxidative cleavage to afford pyrrole – 2 – carboxylic acid in 60% yield. However, cyclohexanone and naturally occurring compound androsterone (17β-acetoxy androst-4-en-3-

one) failed to undergo oxidation under the same reaction conditions. It was further observed that the reaction failed when we carried out the oxidation of substrates under the test with filtrate of the catalyst at the reaction temperature, confirming that the catalyst is not leached out of the framework to catalyse under homogeneous conditions.

When we used 30 % H_2O_2 as the oxidant instead of 70 % TBHP with Re_2O_7 as a catalyst under the same reaction conditions it was found that the formation of the product was almost negligible. Hence we have demonstrated a catalytic environmentally benign and practical method for the carbon-carbon bond cleavage of the aryl methyl as well as alkyl methyl ketones in good yields under mild conditions.

4.2.4 Mechanism of oxidation

The catalytic cycle for the oxotransfer oxidation or an oxygenation of an organic substrate by the oxygen donor TBHP, catalyzed by transition metal (Re) in the form of its oxide (Re_2O_7) can be written in most general manner as in the scheme **(Scheme 2),** which the possible mechanistic pathway for this reaction.



According to the proposed mechanism, the species (Re^{IV}- O) from Re_2O_7 reacts with TBHP to produce catalytically active highly oxygenated peroxo species 1[95]. This active peroxide species 1, oxidizes the enol form of the ketone[96] at the α - position to give keto alcohol 2, which than subsequently undergoes oxidation to produce the less stable keto acids 3. Oxidation elimination of the CO_2 (which was confirmed by GC analysis) afforded carboxylic acids.

4.2.5 Conclusion

We have developed an elegant method for the direct synthesis of carboxylic acids from ketones using commercially available Re_2O_7 as catalyst and 70% aq. TBHP as oxidant in moderate yields under mild conditions. This process displays good functional group tolerance and high regioselectivity. This method is environmentally friendly and no poisonous or toxic byproducts were formed.

4.2.6 Experimental

General procedure for the preparation of aromatic carboxylic acids from aromatic methyl ketones

The commercially available Re_2O_7 and 70 % TBHP were procured from Aldrich USA. In a typical procedure a mixture of (4-isobutylphenyl) methyl ketone (500 mg, 2.8mmol), 70% TBHP (22.3mmol) and Re_2O_7 (81.31mg, 6mole%) in acetic acid was stirred magnetically at 100°C for 5 hours. The progress of a reaction was monitored by TLC. After 5 hours, the products were analyzed by GLC. The reaction mixture was quenched with water (8ml) and carboxylic acid was isolated by its extraction with ether (4X10ml). Removal of solvent furnished 4-isobutyl benzoic acid (364mg, 72%).

Benzoic acid

IR ($CHCl_3$, cm^{-1}) : 3100, 1708, 1330, 930

^1H NMR ($CDCl_3$, 200 MHz) : δ 7.45,
7.575 ,
8.15

MS: m/z : 122 (M^+), 105, 77

4-Methylbenzoic acid

IR ($CHCl_3$, cm^{-1}) : 3190, 1708, and 1830

^1H NMR ($CDCl_3$, 200 MHz) : δ 2.41 (s, 3H), 7.27 (d, J = 8.0 Hz, 2H),
8.0 (d, J = 8.0 Hz, 2H)

MS: m/z : 136 (M^+), 119, 109, 91

4-Chlorobenzoic acid

IR ($CHCl_3$, cm^{-1}) : 3190, 1710, 1380, 900

^{1}H NMR (CDCl$_3$, 200 MHz) : δ 7.55 (d, J = 9.0 Hz, 2H),
7.95 (d, J = 9.0 Hz, 2H),
MS: m/z : 158/156 (M$^+$)

4-Hydroxybenzoic acid

IR (CHCl$_3$, cm^{-1}) : 3510, 3300, 1700, 1290, 930
^{1}H NMR (CDCl$_3$, 200 MHz) : δ 6.82 (d, J = 7.50 Hz, 2H),
7.82 (d, J = 7.50 Hz, 2H),
MS: m/z : 138 (M$^+$)

4-Nitrobenzoic acid

IR (CHCl$_3$, cm^{-1}) : 3090, 1710, and 1300
^{1}H NMR (CDCl$_3$, 200 MHz) : δ 7.55 (d, J = 9.0 Hz, 2H),
7.95 (d, J = 9.0 Hz, 2H),
MS: m/z : 153 (M$^+$)

4-Methoxybenzoic acid

IR (CHCl$_3$, cm^{-1}) : 3010, 1700, 1310, 920
^{1}H NMR (CDCl$_3$, 200 MHz) : δ 3.98 (s, 2H), 7.0 (d, J = 14.0 Hz, 2H)
8.20 (d, J = 14.5 Hz, 2H)
MS: m/z : 152 (M$^+$), 135, 107, 92,

4-Isobutylbenzoic acid

IR (CHCl$_3$, cm^{-1}) : 3384, 2958, 1693, 1288, 910
^{1}H NMR (CDCl$_3$, 200 MHz) : δ 0.8 (d, 7.0 Hz, 6H), 1.84 (m, 1H), 2.45 (d,
J = 6.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H),
7.94. (d, J = 8.0 Hz, 2H),
MS: m/z : 178 (M$^+$)

2, 5-Dimethoxybenzoic acid

IR ($CHCl_3$, cm^{-1}) : 3180, 1715, and 1380

^1H NMR ($CDCl_3$, 200 MHz) : δ 3.82 (s, 3H), 4.05 (s, 3H), 7.00 (D, J = 7.50 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H),

MS: m/z : 182 (M^+)

6- Methoxynaphthalene-2-carboxylic acid

IR ($CHCl_3$, cm^{-1}) : 3190, 1705, 1385, 950

^1H NMR ($CDCl_3$, 200 MHz) : δ 3.91 (s, 3H), 7.12 (d, J = 3 Hz, 1H), 7.17 (dd, J = 3.0Hz 6.0 Hz), 7.44 (d, J = 6, 4 Hz, 1H), 7.75 (d, J = 3.0Hz, 6.o Hz, 2H), 7.85 (s, 1H)

MS: m/z : 202 (M^+)

1-Heptanoic acid

IR ($CHCl_3$, cm^{-1}) : 3210, 1710

^1H NMR ($CDCl_3$, 200 MHz) : δ 0.88 (t, J = 6.0 Hz, 3H), 1.30 (m, 4H), 1.65 (m, 4H), 2.35 (t, J = 6 Hz, 2H)

MS: m/z : 130 (M^+)

Pyrrole –2 - carboxylic acid

IR ($CHCl_3$, cm^{-1}) : 3080, 1705

^1H NMR ($CDCl_3$, 200 MHz) : δ 6.15 (s, 1H), 6.77 (s, 1H), 6.99 (s, 1H)

MS: m/z : 111 (M^+)

***trans*-2-Cinnamic acid**

IR ($CHCl_3$, cm^{-1}) : 3190, 1720, and 1330

^{1}H NMR ($CDCl_3$, 200 MHz) : δ 6.45 (d br, J = 18.0 Hz, 2H), 7.40 (d, J = 10.0 Hz, 2H), 7.51 (dd, J = 8.0 Hz, 1H), 7.80 (d, J = 10.0 Hz, 2H)

MS: m/z : 148 (M^+)

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List of Publications

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1. Effect of potash application on the yield, disease incidence, quality and essential oil composition of betel leaves (*Piper betel l)*

   S. K. Mishra . A. K. S. Rawat, **S. Gurunath**, R. S. Chourasia and V. R. Balasubramanyan

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2. Quality characteristics of different types of *Piper betel l.* leaves

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3. A. Germacranolide from *Artemesia pallens*

   S. R. Rojatkar, S. S. Pawar, P. P. Pujar, D. D. Sawaikar, **S. Gurunath**, V. T. Sathe and B. A. Nagasampagi

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4. Alumina Catalysed derivatisation of Sesquiterpene lactone

   S. Gurunath, B. R. Patewad, D. D. Sawaikar, G. T. Panse, P. P. Pujar, B. A. Nagasampagi and S. R. Rojatkar

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5. Photo-oxidation of Nimbin

   S. R. Rojatkar, D. D. Sawaikar, **S. Gurunath**, B. R. Patewad, P. P. Pujar and B. A. Nagasampagi

   Natural Products Letters, **11,** 181 (1998)

6. Re_2O_7 – Catalysed carbon-carbon bond cleavage of ketones into carboxylic acids with aq. TBHP.

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7. A New and short enantioselective synthesis of (R) – pantolactone via asymmetric dihydroxylation,

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   Tetrahedron Asymmetry, **10,** 2899 (1999),

Paper at Symposium

7β-Acetoxy-10-deacetyl baccatin III from the needles of *Taxus baccata*

S. R. Rojatkar **S. Gurunath,** D. D. Sawaikar, P. P. Pujar, G. T. Panse and B. A. Nagasampagi

7th International Symposium on Natural Products Chemistry, Dec. 28, 1997, Karachi, Pakistan. Abs. P. 17

Manuscripts ready for Communication

1. A New triterpenoid of cucurbitane class from *Ammora lawii*
   S. Gurunath, G. T. Panse and S. R. Rojatkar
2. Calliterpenone, calliterpenone monoacete and ursolic acid from *Callicarpa lanata*
   S. Gurunath G. T. Panse and S. R. Rojatkar
3. A. short synthesis of Capsaisin
   S. Gurunath and A. Sudalai

Patents Filed

1. A novel heterogeneous catalytic process for production of butenediols.
   Sawaikar D. D., **Suryavanshi G.,** Sudalai
   NF. 273/97 –3068/DEL/98 & NCL No 109/97
2. A improved process for the preparation of carboxylic acids
   Suryavanshi G., D. D. Sawaikar and Sudalai A.
   NF 365/97 , 2706/ DEL/ 98, & NCL No 131/97