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# A SYNTHESIS OF (−)HIBAENE

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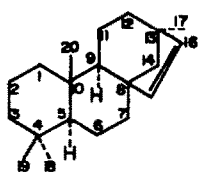
**Abstract**—A total synthesis of (−)hibaene 1 is described. The key steps are a photochemical cycloaddition of vinyl acetate on the α–β unsaturated ketone 2 and a Wagner–Meerwein type rearrangement of the diols 14 and 15, which contain a highly strained cyclobutane ring. A selective esterification of the rearranged diols 22a or 22b leads to intermediates which can conveniently be transformed into (−)hibaene.

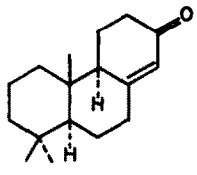
Several total syntheses of racemic podocarp-8(14)-ene-13-one 2 have been described.[1,2] The (+) form of this compound is conveniently available[3] from manöol 3, an abundant natural diterpene.

Photochemical cycloaddition of olefins on the unsaturated ketone 2 leads, with a high selectivity, to the tetracyclic compounds **4a**, **4b**[3] and **4c**,[4,5] containing a cyclobutane ring. These strained substances, which undergo a variety of rearrangements under acidic or basic conditions are useful precursors of many tetracyclic diterpenes.[3-5]

In a previously reported synthesis of (+)hibane,[3] such an intermediate **4b** was used in a process closely related to biogenesis. Thus, a conveniently substituted cyclobutane compound should afford (−)hibaene **1**.‡



1



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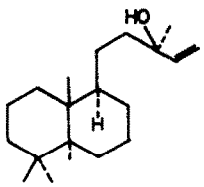

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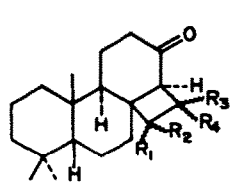


4

| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| **4a:** | Cl | H | Cl | H |
| **4b:** | H | H | H | H |
| **4c:** | H | H | —$CH_2$— | |

*Preparation and structure of the photochemical intermediates*

Photochemical cycloaddition of vinyl acetate on the unsaturated ketone 2 at low temperature, gave an inseparable mixture of four compounds, as judged by its PMR spectrum (4$CH_3CO$–O– peaks). The structures of these compounds were established as follows.

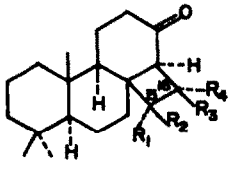
(a) Ketalisation (ethylene glycol/$H^+$) followed by reduction (LAH) led to a mixture from which two major components could be isolated. Compound **A**, an oil, and **B** m.p.: 129°, gave the same cyclobutanone **C** ($\nu_{CO}$: 1770 $cm^{-1}$) by oxidation. Wolff–Kishner reduction of this ketone afforded the crystalline ketal **8**. Its hydrolysis gave the ketone **4b** which is also formed by photochemical cycloaddition of ethylene on **2**.[3] Since it has been converted into (+)hiba-14-one its stereochemistry is well authenticated: the cyclobutane ring is in the β configuration.

(b) Cyclobutanone **C** and compound **9**,[5] the ozonolysis product of **4c**, are different, although the cyclobutane ring is β in both cases. This suggests that **C** is in fact compound **7**.

(c) Acidic treatment of the crude reduction product of the mixture of ketal acetates gave three hydroxy ketones. One of them is the known noratisanone **10**.[4,5] This compound is formed by a retroaldol opening of the strained β-hydroxyketone **11**, followed by cyclisation into the much more stable atisane derivative **10**. Since the two other cyclobutane derivatives are stable toward acidic treatment, they are certainly not β-hydroxyketones, but the γ-hydroxyketones **12** and **13**.

(d) The physical data fit quite well with these conclusions. In particular the cyclobutanone from **A** or **B** exhibits a negative Cotton effect, as expected on the basis of the octant rule. Besides, in the IR spectrum of compound **A**, there is no "free" OH band, in sharp contrast with the isomer **B**. This is indicative of an internal H-bonding in **A**.

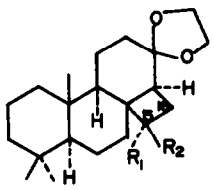
Therefore, compounds **A** and **B** should have structure **6a** and **6b** respectively. Their oxidation product is ketone **7**. The parent acetates[6] are **5a**, **5b** and most probably **5c** and **5d**, which should lead to the same hydroxyketone **10**.



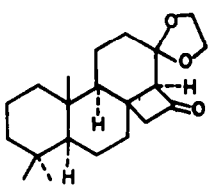
| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| **5a:** | H | OAc | H | H |
| **5b:** | OAc | H | H | H |
| **5c:** | H | H | OAc | H |
| **5d:** | H | H | H | OAc |

†This work was submitted as part of a D.Sc. Thesis (Université de Paris-Sud).

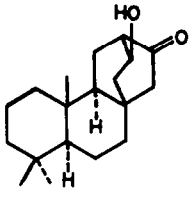
‡A synthesis of (−)hibaene is also a synthesis of (−)kaurene, since these two compounds have been correlated (A. H. Kapadi and S. Dev, *Tetrahedron Letters* 1255 (1965)).



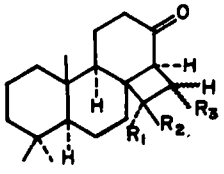
| | $R_1$ | $R_2$ |
|---|---|---|
| 6a: | H | OH |
| 6b: | OH | H |
| 7 | =O | |
| 8 | H | H |



9



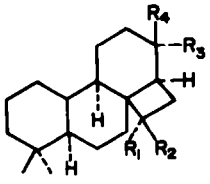
10



| | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| 11: | H | H | OH |
| 12: | H | OH | H |
| 13: | OH | H | H |

*Rearrangement of the photochemical intermediates*

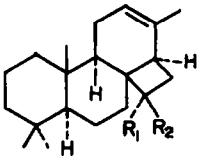
The hydroxyketone 13 was treated with excess methyllithium in diethyl ether. Compound 13 led to a mixture of two diols **14a** (65%) and **14b** (35%). These two diols have also been obtained from 13 and MeMgI in diethyl ether. However, **14a** and **14b** were isolated in 15 and 85% yield respectively.† Compound 12, treated with MeLi gave two diols **15a** and **15b**. However, only one (**15a**) of these diols could be isolated in a pure state. Oxidation of **14a** and **15a** afforded the same hydroxycyclobutanone **16**; **14b** and impure **15b** (contaminated with some starting material) were also oxidized to the same hydroxycyclobutanone **17**.



| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| 14a: | OH | H | OH | Me |
| 14b: | OH | H | Me | OH |
| 15a: | H | OH | OH | Me |
| 15b: | H | OH | Me | OH |
| 16: | =O | | OH | Me |
| 17: | =O | | Me | OH |

†Usually, MeMgI yields a high proportion of axial alcohols. The equatorial isomer is obtained when MeLi is used.[7]

Rearrangement under acidic conditions of the hydroxycyclobutanones **16** and **17** was entirely unsuccessful. In formic acid, dehydration took place, and the unsaturated ketone **18** was obtained. This ketone was recovered unchanged after prolonged treatment with formic acid at room temperature. In trifluoroacetic acid, many compounds were formed. None of them could be identified.[8] Diols **14a**, **14b**, **15a** and **15b** however were rapidly dehydrated in formic acid at room temperature. The resulting hydroxyolefins **19a** and **19b** were smoothly converted in high yield (90%) albeit very sluggishly (one month), into hibane derivatives. Diols **14** gave the diformate **21a**, whereas diols **15** give **21b**. The corresponding hibanediols **22a** and **22b** were formed by LAH reduction of their diformates. The structures of these diols rely on the following evidence.



| | $R_1$ | $R_2$ |
|---|---|---|
| 18: | =O | |
| 19: | —OCHO | H |
| 19: | H | —OCHO |
| 20a: | OH | H |
| 20b: | H | OH |

(a) These diols could be oxidized into a diketone which has the same physical constants as the known hibanedione **23**.[9]

(b) In the PMR spectra of diols **22a**, **22b** and (+)14$\alpha$-hydroxyhibane[3] a singlet at 4.75, 4.60 and 4.46 ppm respectively can be assigned to a 14$\beta$ proton. The 15$\beta$ or 15$\alpha$ proton in **22a** and **22b** respectively gave rise to a signal which can be considered as the X part of an ABX system.

A diol resulting from a reduction of dione **23**, which according to the published data[9] should be **22b**, was transformed into 14$\alpha$-acetoxyhibaene by Wenkert. However, the key step, a pyrolysis of the corresponding diacetate **24**, gave a rather poor yield. We found that oxidation of diol **22a** by silver carbonate on Celite is regioselective. From diol **22a**, ketol **25** was the only detectable oxidation product. This was expected, since proton 15$\beta$ is severely hindered, and the oxidizing solid is far too bulky to allow the assumed transition state to be formed.

On the contrary, in diol **22b**, the 15$\alpha$ proton is readily accessible. The oxidation of diol **22b** yielded a mixture of two compounds: a dione **23** which had been described[9] previously and 14$\alpha$-hydroxyhibaene-15-one **26**. Since the latter hydroxyketone gave dione **23** when treated with excess silver carbonate on Celite, very probably, oxidation of the 15$\alpha$-OH group was more rapid than oxidation of the other secondary alcohol..

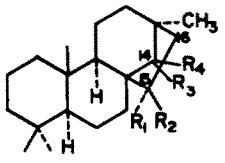
The structure of these hydroxyketones was proved as follows:

(a) In the IR spectrum of **26**, a sharp band is found at 1410 $cm^{-1}$ (scissoring vibration of $CH_2\alpha$ to the CO group).

(b) A singlet at 3.17 ppm is still present in the PMR spectrum of **26**. In the oxidation product of **22a**, **25**, the X part of the mentioned ABX system is observed.

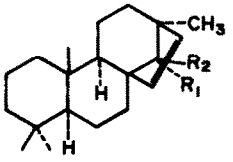
(c) Ketones **25** and **26** exhibit a negative Cotton effect, as predicted on the basis of the octant rule.

Ketone **25** was treated in pyridine with *p*-tolylthionocarbonatechloride[10] and the resulting thionocarbonate **27** was heated to 200°. After chromatography, crystalline hibaene-14-one **31** was obtained in nearly quantitative yield. A Wolff–Kishner reduction of this ketone, in the *absence of oxygen*[11] gave (−)hiba-15-ene **1**, whose m.p., IR and PMR data fit quite well with those published in the literature.[12]




| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| **21a:** | —OCHO | H | —OCHO | H |
| **22a:** | OH | H | OH | H |
| **21b:** | H | —OCHO | —OCHO | H |
| **22b:** | H | OH | OH | H |
| **23:** | =O | | =O | |
| **24:** | H | —OAc | —OAc | H |
| **25:** | OH | H | =O | |
| **26:** | =O | | OH | H |
| **27:** | OEst. | H | =O | |
| **28:** | OEst. | H | OH | H |
| **29:** | H | OEst. | OH | H |
| **32:** | OEst. | H | OEst. | H |

Diols **22a** and **22b**, treated with *p*-tolylthionocarbonate chloride[10] gave essentially monothiocarbonates **28** and **29**. Pyrolysis of these two compounds gave the same 14α-hydroxy-hiba-15-ene **30**. Oxidation of this unsaturated alcohol **30**, followed by Wolff–Kishner reduction afforded (−)hiba-15-ene **1** in fair yield.




| | $R_1$ | $R_2$ |
|---|---|---|
| **30:** | OH | H |
| **31:** | =O | |

## EXPERIMENTAL

*General.* M.ps were determined on a Reichert "Kofler" block and are uncorrected. IR spectra were recorded on a Perkin–Elmer Model 577 spectrophotometer. NMR spectra were recorded on a Varian NV 14 NMR spectrometer or a Varian XL 100 FT NMR spectrometer for the 100 MHz spectra. Chemical shifts are expressed in ppm downfield from the signal of TMS which was used as an internal standard. {α} rotatory powers were measured on a Perkin–Elmer Model 241 polarimeter. CD curves were recorded on a Roussel–Jouan Model 185 dichrograph. Microanalysis were carried out by the C.N.R.S. microanalysis laboratory.

*Photo-adducts* **5a, 5b, 5c** *and* **5d**

A soln of **2** (8 g) and 80 ml commercial vinyl acetate in 1 l. purified $CH_2Cl_2$, was irradiated at −70° for 1 hr through a Pyrex filter by a 700 W high pressure mercury lamp. The evolution of the cycloaddition was monitored by IR. The solvent was evaporated under reduced pressure and the crude mixture (9 g) could be used for the next reaction. By fractionated crystallisations in pentane 2.5 g of **5b** could be separated from the mixture.

*Mixture.* IR (film) 1740 $cm^{-1}$ (s, acetate), 1705 $cm^{-1}$ (s, carbonyl groups).

Compound **5b**: m.p. 135°; IR ($CCl_4$) 1740 $cm^{-1}$ (s, acetate), 1705 $cm^{-1}$ (s, C=O); NMR ($CDCl_3$) 0.75, 0.825, 0.88 (each singlet, 3H, Me), 2.07 (singlet, 3H, MeCO–O–), 5.15 (broad signal, 1H, H geminated with –OAc); $\{\alpha\}_{589} = 46.3°$, $\{\alpha\}_{578} = 48.6°$, $\{\alpha\}_{546} = 55.8°$, $\{\alpha\}_{436} = 102.3°$, $\{\alpha\}_{365} = 190.7°$ ($c = 1.05$ in $CHCl_3$); $\Delta\varepsilon = 0.423$ ($\lambda_{max} = 296$ nm, dioxanne). (Found: C, 75.17; H, 9.89; O, 14.94. Calc. for $C_{21}H_{32}O_3$: C, 74.96; H, 10.06; O, 14.98%).

*Cyclobunatols* **6a** *and* **6b**

A soln of the crude photoadducts mixture (6.5 g), *p*-toluensulfonic acid (500 mg) and 10 ml ethylene glycol in 250 ml benzene was refluxed for 12 hr, and water was separated in a Dean–Stark adapter. The cooled soln was extracted in the usual manner. The solvent was removed and the resulting dried material (7.5 g) was used as such for the next step.

A soln of the above mixture of ketals (7.5 g) in 50 ml of dried diethyl ether was added dropwise to a suspension of LAH (3 g) in 250 ml diethyl ether. After 2 hr, stirring at room temp., the mixture was treated with water. After filtration and evaporation of ether, a crystalline mixture was obtained. Samples of the two major products were obtained by preparative TLC on silica gel with 1:1 diethyl ether/petroleum ether as solvent.

*Compound* **6b** ($R_f$: 0.4): oily product; IR($CHCl_3$) 3625, 3475 $cm^{-1}$ (OH); NMR ($CDCl_3$) 0.85, 0.85, 0.85 (each singlet, 3H, Me), 4.32 (triplet, 1H, J = 7.5 Hz, H geminated with OH group), 3.85 (multiplet, 4H, methylenes of ethylene ketal).

*Compound* **6a** ($R_f$: 0.6): m.p. 128–130° ($CH_2Cl_2$–petroleum ether); IR($CHCl_3$) 3474 $cm^{-1}$ (OH, no "free" OH band); NMR ($CCl_4$) 0.85, 0.85, 0.93 (each singlet, 3H, Me), 4.05 (broad signal, 1H, H geminated with OH), 4.07 (multiplet, 4H, methylene of ethylene ketal); $\{\alpha\}_{589} = -27.4°$, $\{\alpha\}_{578} = -28.6°$, $\{\alpha\}_{546} = -31.6°$, $\{\alpha\}_{436} = -48.1°$, $\{\alpha\}_{365} = -55.6°$ ($c = 1.83$ in $CHCl_3$). (Found: C, 75.25; H, 10.42; O, 14.25. Calc. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25; O, 13.50%).

*Ketols* **12, 13** *and* **10**

A soln of the preceding mixture (5.5 g) in 150 ml $CHCl_2$ was treated with 150 ml 3N HCl at room temp. for 3 hr. The soln was extracted with $CH_2Cl_2$ and the extracts were worked up with sat $NaHCO_3$ aq and water. A part of the crude mixture (4.2 g) was insoluble in diethyl ether (ketol **10**, 150 mg). Products **12** and **13** were separated by chromatography on a column of silica gel.

*Compound* **10**. m.p. 203° ($CH_2Cl_2$–petroleum ether); IR ($CHCl_3$) 3600, 3420 $cm^{-1}$ (OH) 1715 $cm^{-1}$ (C=O); NMR ($CDCl_3$) 0.85, 0.885, 0.95 (each singlet, 3H, Me), 4.13 (broad signal, 1H, H geminated with OH); $\{\alpha\}_{589} = 50.9°$, $\{\alpha\}_{578} = 53.3°$, $\{\alpha\}_{546} = 61.0°$, $\{\alpha\}_{436} = 111.0°$, $\{\alpha\}_{365} = 205.8°$ ($c = 0.55$ in $CHCl_3$); $\Delta\varepsilon = 0.266$ ($\lambda_{max} = 298$ nm, dioxanne). (Found: C, 78.72; H, 10.50; O, 10.78. Calc. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41; O, 10.78%).

*Compound* **13**: m.p. 176–178° ($CH_2Cl_2$–petroleum ether); IR ($CHCl_3$) 3600, 3450 $cm^{-1}$ (OH) 1680 $cm^{-1}$ (C=O); NMR ($CDCl_3$) 0.85, 0.885, 0.96 (each singlet, 3H, Me), 4.33 (broad signal, 1H, H geminated with OH); $\{\alpha\}_{589} = 16.4°$, $\{\alpha\}_{578} = 17.8°$, $\{\alpha\}_{546} = 21.0°$, $\{\alpha\}_{436} = 50.4°$, $\{\alpha\}_{365} = 141.7°$ ($c = 0.56$ in $CHCl_3$); $\Delta\varepsilon = 1.89$ ($\lambda_{max} = 298$ nm, dioxanne). (Found: C, 78.70; H, 10.30; O, 11.25. Calc. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41; O, 10.78%).

*Compound* **12**: m.p. 153–155° ($CH_2Cl_2$–petroleum ether); IR ($CHCl_3$) 3600, 3450 $cm^{-1}$ (OH), 1680 $cm^{-1}$ (C=O); NMR ($CDCl_3$) 0.885, 0.916, 1.02 (each singlet, 3H, Me), 4.25 (broad signal, 1H, H geminated with OH); $\{\alpha\}_{589} = -9.6°$, $\{\alpha\}_{578} = -9.2°$, $\{\alpha\}_{546} = -7.9°$, $\{\alpha\}_{436} = +16.9°$, $\{\alpha\}_{365} = +160.8°$ ($c = 0.54$ in $CHCl_3$); $\Delta\varepsilon = 0.73$ ($\lambda_{max} = 300$ nm, dioxanne). (Found: C, 78.35; H, 10.60; O, 10.70. Calc. for $C_{19}H_{30}O$: C, 78.57; H, 10.41; O, 11.02%).

*Cyclobutanone* **7**

Compound **6a** or **6b** (150 mg) were added to a magnetically stirred soln of $CrO_3$ (300 mg), pyridine (0.5 ml) and $CH_2Cl_2$ (6 ml). The reaction was stirred under an anhydrous atmosphere for 30 mn. Extraction (diethyl ether) led to crude **7**, purified by crystallisation (diethyl ether), yield: 115 mg.

*Compound* **7**: m.p. 95° (diethyl ether); IR ($CHCl_3$) 1770 $cm^{-1}$ (C=O); NMR ($CDCl_3$) 0.82, 0.82, 0.95 (each singlet, 3H, Me), 3.92 (broad singlet, 4H, ethylene ketal); $\{\alpha\}_{589} = 4.78°$, $\{\alpha\}_{578} = 4.54°$, $\{\alpha\}_{546} = 3.94°$, $\{\alpha\}_{436} = -10.9°$, $\{\alpha\}_{365} = -99.4°$ ($c = 0.84$ in $CHCl_3$); $\Delta\epsilon = -0.985$ ($\lambda_{max} = 311$ nm, dioxanne). (Found: C, 75.19; H, 10.0; O, 14.71. Calc. for $C_{21}H_{32}O_3$: C, 74.96; H, 10.06; O, 14.98%).

*Ketone* **4b**

A mixture of **7** (150 mg) and 4 ml hydrazine hydrate in 15 ml diethylene glycol was refluxed for 1 hr. KOH (300 mg) was then added, and some water and hydrazine were distilled off until a reflux temp. of 210° had been reached. The mixture was refluxed for an additional 10 hr. The cooled soln was diluted in water and extracted with diethyl ether. The crude **8** was crystallised from pentane, yield: 70%.

*Compound* **8**: m.p. 112–114° (pentane); IR ($CCl_4$) 1115 $cm^{-1}$ (ethylene ketal). (Found: C, 78.99; H, 10.70; O, 10.31. Calc. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; O, 10.05%).

A soln of **8** (90 mg) in 10 ml of $CH_2Cl_2$ was treated with 5 ml 3N HCl at room temp. for 3 hr. The soln was extracted with diethyl ether. The crystallisation from pentane gave 70 mg of **4b**.

*Compound* **4b**: m.p. 74–75°; IR ($CCl_4$) 1703 $cm^{-1}$ (C=O); NMR ($CDCl_3$) 0.72, 0.80, 0.88 (each singlet, 3H, Me); $\{\alpha\}_{589} = 30.0°$, $\{\alpha\}_{578} = 33.5°$, $\{\alpha\}_{546} = 39.0°$, $\{\alpha\}_{436} = 74.0°$, $\{\alpha\}_{365} = 185.6°$ ($c = 0.815$ in $CHCl_3$); $\Delta\epsilon = 0.83$ ($\lambda_{max} = 298$ nm, dioxanne). (Found: C, 82.95; H, 11.12; O, 5.93. Calc. for $C_{19}H_{30}O$: C, 83.15; H, 11.02; O, 5.83%).

*Diols* **14a, 14b** *and* **15a, 15b**

To a soln of **12** or **13** (4 g) in 200 ml diethyl ether, 2M MeLi (120 ml) in diethyl ether was added. The soln was stirred under argon, at room temp., for 2 hr. Then, enough water was added to destroy the reagent, the aqueous layer was separated and extracted with diethyl ether. The combined either extracts were washed with a sat NaCl aq, dried and evaporated. The obtained mixture (4.2 g) which still contained some unreacted ketol was chromatographied on a column of silica gel with 40% diethyl ether in petroleum ether as solvent.†

*From* **13**. **14a**: (65% of the mixture) m.p. 107–110° ($CH_2Cl_2$–hexane); IR ($CCl_4$) 3615, 3450 $cm^{-1}$ (OH); NMR ($CDCl_3$) 0.85, 0.85, 0.95, 1.21 (each singlet, 3H, Me), 4.30 (triplet, 1H, J = 8 Hz, H geminated with sec. OH group); $\{\alpha\}_{589} = 16.5°$, $\{\alpha\}_{578} = 17.0°$, $\{\alpha\}_{546} = 19.2°$, $\{\alpha\}_{436} = 28.15°$, $\{\alpha\}_{365} = 37.0°$ ($c = 0.78$ in $CHCl_3$). (Found: C, 78.32; H, 10.96; O, 10.66. Calc. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18; O, 10.44%).

*Compound* **14b**. (35% of the mixture) m.p. 136–137° ($CH_2Cl_2$, hexane); IR ($CCl_4$) 3616, 3450 $cm^{-1}$ (OH); NMR ($CDCl_3$) 0.83, 0.92, 1.07, 1.63 (each singlet, 3H, Me), 4.22 (triplet, 1H, J = 8 Hz, H geminated with sec. OH group); $\{\alpha\}_{589} = 18.9°$, $\{\alpha\}_{578} = 19.5°$, $\{\alpha\}_{546} = 21.9°$, $\{\alpha\}_{436} = 35.5°$, $\{\alpha\}_{365} = 52.7°$ ($c = 1.25$ in $CHCl_3$). (Found: C, 78.73; H, 11.02; O, 10.44. Calc. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18; O, 10.44%).

*From* **12**. **15a** and **12** could not be separated (same $R_f$).

*Compound* **15b**. (10% of the mixture) m.p. 160–162° ($CH_2Cl_2$); IR ($CCl_4$) 3610, 3450 $cm^{-1}$ (OH); NMR ($CDCl_3$) 0.82, 0.84, 0.95, 1.11 (each singlet, 3H, Me), 4.00 (broad signal, 1H, H geminated with sec. OH group); $\{\alpha\}_{589} = 13.85°$, $\{\alpha\}_{578} = 14.2°$, $\{\alpha\}_{546} = 16.0°$, $\{\alpha\}_{436} = 26.3°$, $\{\alpha\}_{365} = 39.4°$ ($c = 1.10$ in $CHCl_3$). (Found: C, 78.32; H, 10.96; O, 10.72. Calc. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18; O, 10.44%).

*Ketols* **16** *and* **17**

The diols **14a, 14b, 15a** and **15b** were oxidized separately with the $CrO_3$-pyridine complex method as described above. **14a** and **15a** gave the same ketol **16**. **14b** and **15b** gave **17**.

*Compound* **17**. m.p. 133–135° (diethyl ether); IR ($CCl_4$) 3610, 3480 $cm^{-1}$ (OH) 1770 $cm^{-1}$ (C=O); NMR ($CDCl_3$) 0.83, 0.84, 1.00, 1.37 (each singlet, 3H, Me); $\Delta\epsilon = -0.806$ ($\lambda_{max} = 307$ nm, dioxanne). (Found: C, 78.19; H, 10.41; O, 10.69. Calc. for $C_{20}H_{32}O_2$: C, 78.79; H, 10.59; O, 10.51%).

†*Note*. With MeMgI the same products were obtained, but in different proportion (**14a**: 15%, **14b**: 85%).

*Compound* **16**. m.p. 138–140° (diethyl ether); IR ($CCl_4$) 3600, 3500 $cm^{-1}$ (OH) 1778 $cm^{-1}$ (C=O); NMR ($CDCl_3$) 0.82, 0.82, 0.92, 1.20 (each singlet, 3H, Me). (Found: C, 78.31; H, 10.34; O, 10.70. Calc. for $C_{20}H_{32}O_2$: C, 78.79; H, 10.59; O, 10.51%).

*Unsatured ketone* **18**

A soln of **16** or **17**, (100 mg) in 50 ml formic acid was stirred for 1 hr at room temp. The product **18** which precipitated was filtered off and washed with water. Crystallisation in diethyl ether afforded **18** (75 mg).

*Compound* **18**: m.p. 102–103°; IR ($CS_2$) 1770 $cm^{-1}$ (C=O); NMR ($CDCl_3$) 0.85, 0.85, 1.07, 1.67 (each singlet, 3H, Me), 3.37 (doublet of doublets, 1H, $J_1 = 18$ Hz, $J_2 = 10$ Hz, H14), 5.55 (broad signal, 1H, olefinic proton); $\{\alpha\}_{589} = 42.4°$, $\{\alpha\}_{578} = 42.6°$, $\{\alpha\}_{546} = 47.0°$, $\{\alpha\}_{436} = 67.6°$, $\{\alpha\}_{365} = 62.8°$ ($c = 0.44$ in $CHCl_3$); $\Delta\epsilon = -0.244$ ($\lambda_{max} = 322$ nm, dioxanne). (Found: C, 83.77; H, 10.40; O, 5.86. Calc. for $C_{20}H_{30}O$: C, 83.86; H, 10.55; O, 5.59%).

*Rearranged diols* **22a** *and* **22b**

A soln of **14a** or **14b**, **15a**, **15b**, (500 mg) in 200 ml formic acid was stirred at room temp., under inert atmosphere for one month. After 1 hr the starting material **14a** was converted into the dehydration product **19a**, which rearranged slowly into **21a**. After one month, 80% of **21a** and 20% of **19a** were obtained. Evaporation of the acid gave 550 mg of a crude mixture, whose constituents were separated by TLC on silica gel with 10% ether in pentane as solvent.

The formates were converted into the corresponding alcohols by reduction with a suspension of LAH in diethyl ether.

*From* **14a** *and* **14b**

*Compound* **21a**. Oily product; IR (film) 1730 $cm^{-1}$ (formates); NMR ($CDCl_3$) 0.80, 0.83, 0.93, 1.01 (each singlet, 3H, Me), 4.75 (singlet, 1H, H14), 5.54 (doublet of doublets, 1H, $J_1 = 7$ Hz, $J_2 = 3$ Hz, H15), 8.06, 8.23 (each singlet, 1H, –OCHO).

*Diol* **22a**. m.p. 218–219° ($CHCl_3$–pentane); IR ($CHCl_3$) 3620, 3440 $cm^{-1}$ (OH); NMR ($CDCl_3$) 0.82, 0.88, 0.95, 0.98 (each singlet, 3H, Me), 3.23 (singlet, 1H, H14), 4.40 (doublet of doublets, 1H, $J_1 = 7$ Hz, $J_2 = 3$ Hz, H15); $\{\alpha\}_{589} = 2.07°$, $\{\alpha\}_{578} = 1.50°$, $\{\alpha\}_{546} = 2.83°$, $\{\alpha\}_{436} = 4.15°$, $\{\alpha\}_{365} = 6.6°$ ($c = 0.53$ in $CHCl_3$). (Found: C, 78.02; H, 10.72; O, 10.40. Calc. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18; O, 10.44%).

*Compound* **19a**: oily product, IR ($CS_2$) 1725 $cm^{-1}$ (formate); NMR ($CDCl_3$) 0.75, 0.83, 0.87, 1.56 (each singlet, 3H, Me), 5.00 (triplet, 1H, J = 7.5 Hz, H15), 5.45 (broad signal, 1H, olefinic proton), 8.00 (singlet, 1H, –OCHO).

*Alcohol* **20a**. Oily product, IR ($CCl_4$) 3630, 3480 $cm^{-1}$ (OH), 3040 $cm^{-1}$ (olefinic C–H); NMR ($CDCl_3$) 0.78, 0.78, 0.88, 1.50 (each singlet, 3H, Me), 4.12 (triplet, 1H, J = 7.5 Hz, H15) 5.35 (broad signal, 1H, olefinic proton).

*From* **15a** *and* **15b**

*Compound* **21b**. Oily product; IR (film) 1730 $cm^{-1}$ (formates); NMR ($CDCl_3$) 0.80, 0.84, 0.90, 0.94 (each singlet, 3H, Me), 4.60 (singlet, 1H, H14), 4.94 (doublet of doublets, 1H, $J_1 = 12$ Hz, $J_2 = 6$ Hz, H15), 8.00, 8.15 (each singlet, 1H, –OCHO).

*Diol* **22b**: m.p. 215–216° ($CHCl_3$–pentane); IR ($CHCl_3$) 3620, 3640 $cm^{-1}$ (OH); NMR ($CDCl_3$) 0.80, 0.85, 0.94, 1.00 (each singlet, 3H, Me), 2.92 (singlet, 1H, H14), 3.85 (doublet of doublets, 1H, $J_1 = 10$ Hz, $J_2 = 6$ Hz, H15); $\{\alpha\}_{589} = -37.8°$, $\{\alpha\}_{578} = -39.3°$, $\{\alpha\}_{546} = -45.0°$, $\{\alpha\}_{436} = -78.5°$, $\{\alpha\}_{365} = -125.2°$ ($c = 0.68$ in $CHCl_3$). (Found: C, 78.20; H, 11.58; O, 10.83. Calc. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18; O, 10.44%).

*Compound* **19b**. Oily product; IR (film) 1725 $cm^{-1}$ (formate); NMR ($CDCl_3$) 0.78, 0.83, 0.83, 1.55 (each singlet, 3H, Me), 4.95 (broad doublet, 1H, H15), 5.48 (broad signal, 1H, olefinic proton). 7.85 (singlet, 1H, –OCHO).

*Alcohol* **20b**. Oily product; IR ($CCl_4$) 3620, 3480 $cm^{-1}$ (OH) 3040 $cm^{-1}$ (olefinic C–H); NMR ($CDCl_3$) 0.90, 0.90, 1.07, 1.66 (each singlet, 3H, Me), 4.05 (broad signal, 1H, H15), 5.58 (broad signal, 1H, olefinic proton).

*Diketone* **23**

Standard Jones reagent (2 ml) was added to a soln of diol **22a**

or **22b** (200 ml) in 40 ml acetone. The soln was stirred for 1 hr. Then 50 ml water were added, and the product was extracted with diethyl ether. The extract was neutralised, dried and evaporated. Crystallisation of the residue from diethyl ether–pentane gave 240 mg of **23**.

*Compound* **23**: m.p. 142–144°; IR ($CCl_4$) 1725 $cm^{-1}$ (C=O, s), 1770 $cm^{-1}$ (C=O, w); NMR ($CDCl_3$) 0.83, 0.88, 0.91, 1.18 (each singlet, 3H, Me), 2.23 and 2.72 (each doublet, 1H, $CH_2$16); $\{\alpha\}_{589} = -31.9°$, $\{\alpha\}_{578} = -34.6°$, $\{\alpha\}_{546} = -41.4°$, $\{\alpha\}_{436} = -99.0°$, $\{\alpha\}_{325} = -304.4°$ ($c = 0.77$ in $CHCl_3$); litt: (9) m.p. (Found: C, 79.75; H, 9.99; O, 10.51. Calc. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00; O, 10.58%).

*Hiba-14-one-15α-ol* **25**

Diol **22a** (200 ml) was refluxed with a suspension of silver carbonate on Celite (10 equivs) in benzene (75 ml). Water was removed in a Dean–Stark adapter. The course of the reaction was followed by analytical TLC. After several days the soln was filtered and evaporated. The product **25** was recrystallised from pentane.

*Compound* **25**. m.p. 195°; IR ($CCl_4$) 3620, 3450 $cm^{-1}$ (OH) 1740 $cm^{-1}$ (C=O); NMR ($CDCl_3$) 0.82, 0.88, 1.02, 1.02 (each singlet, 3H, Me), 4.65 (doublet of doublets, 1H, $J_1 = 8.2$ Hz, $J_2 = 3$ Hz, H15); $\{\alpha\}_{589} = 8.2°$, $\{\alpha\}_{578} = 6.3°$, $\{\alpha\}_{546} = 7.9°$, $\{\alpha\}_{436} = 4.1°$, $\{\alpha\}_{365} = -42.0°$ ($c = 0.60$ in $CHCl_3$); $\Delta\epsilon = -0.75$ ($\lambda_{max} = 299$ nm, dioxanne). (Found: C, 78.47; H, 10.65; O, 10.75. Calc. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59; O, 10.51%).

*Hiba-14α-ol-15-one* **26**

The same procedure applied diol **22b** (200 ml) gave after complete disappearance of starting material: 80 mg of **23** and 60 mg of **26** after separation by TLC on silica gel.

*Compound* **26**. m.p. 199° ($CHCl_3$–petroleum ether); IR ($CCl_4$) 3640, 3450 $cm^{-1}$ (OH), 1735 $cm^{-1}$ (C=O) 1410 $cm^{-1}$ ($CH_2$α to C=O); NMR ($CDCl_3$) 0.82, 0.85, 0.85, 1.05 (each singlet, 3H, Me), 3.17 (singlet, 1H, H14); $\{\alpha\}_{589} = 6.2°$, $\{\alpha\}_{578} = 5.6°$, $\{\alpha\}_{546} = 4.0°$, $\{\alpha\}_{436} = 0.2°$, $\{\alpha\}_{365} = -43.1°$ ($c = 0.63$ in $CHCl_3$); $\Delta\epsilon = -0.19$ ($\lambda_{max} = 314$ nm in dioxanne).

*Hiba-14-one-15α-p-tolylthionocarbonate* **27**

*p*-Tolylthionocarbonatechloride[10] (1.5 ml) was added to a soln of **25** (220 ml). The soln was stirred for 12 hr. Then, 25 ml water was added and the product was extracted with 50 ml benzene. The extracts were washed with a 5% HCl aq. and 10% $NaHCO_3$ aq. After evaporation of the solvent, the crude product was chromatographied on silica gel with a 3–1 cyclohexane–benzene mixture as eluent.

*Compound* **27**. Oily product; IR ($CCl_4$) 1740 $cm^{-1}$ (C=O) 1190, 1220, 1280 $cm^{-1}$ (thionocarbonate); NMR ($CDCl_3$) 0.84, 0.90, 1.10, 1.12 (each singlet, 3H, Me), 2.38 (singlet, 3H, ar. Me), 6.20 (doublet of doublets, 1H, $J_1 = 8$ Hz, $J_2 = 3$ Hz, H15).

*Hibaene-14-one* **31** *by pyrolysis of* **27**

*Compound* **27** (100 ml) was pyrolysed for 30 mn at 200° under vacuum in a sealed tube. Then, the mixture was diluted with diethyl ether and the soln was worked up with a 2N NaOH and water. The solvent was evaporated and the product crystallized from MeOH.

*Compound* **31**. m.p. 98–99°; IR ($CS_2$) 3050 $cm^{-1}$ (olefinic C–H), 1755 $cm^{-1}$ (C=O), 718 $cm^{-1}$ (olefinic C–H); NMR ($CDCl_3$) 0.82, 0.85, 0.85, 1.03 (each singlet, 3H, Me), 5.89 and 6.14 (each doublet, 1H, AB Systems J = 7 Hz, olefinic protons); $\{\alpha\}_{589} = -28.8°$, $\{\alpha\}_{578} = -30.4°$, $\{\alpha\}_{546} = -35.4°$, $\{\alpha\}_{436} = -70.3°$, $\{\alpha\}_{365} = -146.5°$ ($c = 0.79$ in $CHCl_3$); $\Delta\epsilon = -0.69$ ($\lambda_{max} = 287$ nm in dioxanne). (Found: C, 82.33; H, 10.34; O, 6.26. Calc. for $C_{20}H_{30}O$: C, 83.86; H, 10.56; O, 5.59%).

*Hiba-14α-ol-15α-p-tolylthionocarbonate* **28** *and hiba-14α-ol-15β- p-tolylthionocarbonate* **29**

*p*-Tolylthionocarbonatechloride (1 ml) was added to a soln of **22a** or **22b** (500 ml) in 15 ml anhyd pyridine. The soln was stirred for 12 hr. Then, 25 ml water was added and the product extracted 100 ml benzene. The extracts were washed and dried. After evaporation of the solvent, the crude mixture was chromatographied on silica gel with a 6–2–2 pentane–diethyl ether–benzene mixture as solvent.

*Compound* **28**. Oily product; IR (film) 3430 $cm^{-1}$ (OH) 1195, 1225, 1290 $cm^{-1}$ (thionocarbonate); NMR ($CDCl_3$) 0.82, 0.87, 1.00, 1.03 (each singlet, 3H, Me), 2.33 (singlet, 3H, ar. Me), 3.25 (singlet, 1H, H14α), 5.78 (doublet of doublets, 1H, $J_1 = 9$ Hz, $J_2 = 3$ Hz, H15β).†

*Compound* **29**. Oily product; IR (film) 3500 $cm^{-1}$ (OH); 1195, 1225, 1280 $cm^{-1}$ (thionocarbonate); NMR ($CDCl_3$) 0.82, 0.85, 0.96, 1.03 (each singlet, 3H, Me), 2.31 (singlet, 3H, ar. Me), 3.03 (singlet, 1H, H14α), 5.33 (doublet of doublets, 1H, $J_1 = 10.5$ Hz, $J_2 = 5.5$ Hz, H15α).

*Compound* **32**. Oily product; IR (film) 1195, 1225, 1290 $cm^{-1}$ (thionocarbonate); NMR ($CDCl_3$) 0.81, 0.88, 1.06, 1.06 (each singlet 3H, Me), 2.25 and 3.30 (each singlet, 3H, ar. Me), 3.80 (singlet, 1H, H14α), 5.83 (doublet of doublets, 1H, $J_1 = 9$ Hz, $J_2 = 3$ Hz, H15).

*Hibaene-14α-ol* **30**

The same pyrolysis procedure described above gave **30** from **28** and **29**.

*Compound* **30**. Oily product; IR (film) 3440 $cm^{-1}$ (OH) 3040 $cm^{-1}$ (olefinic C–H), 750 $cm^{-1}$ (olefinic C–H); NMR ($CDCl_3$) 0.78, 0.83, 0.85, 0.95 (each singlet, 3H, Me), 3.00 (singlet, 1H, H14α), 5.47 and 5.73 (each doublet, 1H, AB system J = 6.5 Hz, olefinic proton).

*Hibaen-14-one* **31**

It was obtained by Jones oxidation (described above) of hibaenol. The resulting hibaenone has the same physical constants as the compound obtained by pyrolysis of **27**.

*(−)Hibaene* **1**

Hibaenone **31** (70 ml), hydrazine hydrate (1.5 ml) and diethylene glycol (15 ml) and KOH (150 mg) were refluxed *under argon* for 8 hr. The usual working up led to 75 mg of crude hibaene, which was purified by tlc (silica gel impregnated with 8% of $AgNO_3$).

*Compound* **1**. Crystallized on standing m.p. 29° (lit. 29°); IR (film) 3050 $cm^{-1}$ (olefinic C–H) 1385 and 1365 $cm^{-1}$ (gem dimethyl group) 755 $cm^{-1}$ (olefinic C–H); NMR ($CDCl_3$) 0.75, 0.83, 0.88, 0.99 (each singlet, 3H, Me), 5.41 and 5.68 (each doublet, 1H, AB system, J = 6 Hz, olefinic protons); $\{\alpha\}_{589} = -40.4°$, $\{\alpha\}_{578} = -41.9°$, $\{\alpha\}_{546} = -47.8°$, $\{\alpha\}_{436} = -83.1°$, $\{\alpha\}_{365} = -133.8°$ ($c = 0.49$ in $CHCl_3$).

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†*Note*. Only in the case of **28**, traces (30 mg) of the diester **32** of the diol **22a** have been detected.

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