Synthetic Studies toward Complex Diterpenoids. 12.[1] Stereocontrolled Total Synthesis of Some Gibbane Synthons and Degradation Products of Gibberellins

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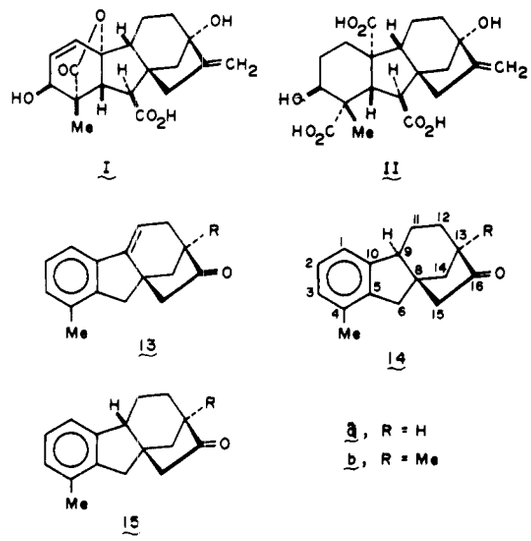
Stereocontrolled total syntheses of (±)-gibberone (**13b**) and (±)-4-methyl-9β,13α-dihydro-16-oxogibba-1,3,5-(10)-triene (**15a**), two degradation products of gibberellins, and a few C-9 epimeric gibbane synthons, **14a,b** and **15b**, are described. The key intermediates, 1,2,3,4-tetrahydro-8-methylfluorene-2-carboxylic acid (**6a**) and its 2-methyl analogue **6b**, prepared by cycloaddition reactions, are converted into the corresponding α′-diazomethyl ketones **11a** and **11b** and are subjected to intramolecular ketocarbenoid addition and boron trifluoride–ether-catalyzed cyclization leading to cyclopropyl ketones **12a,b** and $\Delta^{9,11}$-gibbenes **13a,b**, respectively. Catalytic hydrogenation of the cyclopropyl ketones **12a** and **12b** with palladium-on-charcoal in ethanol proceeded with high stereoselectivity and produced the 9αH epimers **14a** and **14b** containing minor amount of 9βH epimer **15a** in the former case. Under the same conditions reduction of the $\Delta^{9,11}$-gibbenes **13a** and **13b** gave a mixture of the epimeric 9α*H*- and 9β*H*-gibbanes **14a** and **15a** (30–20:70–80) and **14b** and **15b** (~63:37), respectively.

A prodigious number of synthetic routes have been developed[2,3] for tetracyclic gibbane derivatives, including the elegant total synthesis of gibberellic acid (I)[4] and gibberellin-A_{15},[5] two representative members of C_{19} and C_{20} gibberellins. In earlier papers we have reported two simple synthetic approaches to gibbane[6,7] or similar systems[8,9] via intramolecular alkylation of γ,δ-unsaturated α′-diazomethyl ketones.[10] We now describe an extension of these methods leading to a convenient synthesis of gibberone (**13b**),[11] a degradation product of I, in racemic form, stereocontrolled syntheses of some C-9 epimeric gibbane[12] synthons **14a,b** and **15b**, and the first total synthesis of the tetracyclic ketone **15a**, a degradation product of gibberellin-A_{13} (II),[13] in racemic form.



Results and Discussion

The starting γ,δ-unsaturated hydrofluorene acids **6a** and **6b** were prepared by the application of Diels–Alder reaction[6,8,14] (Scheme I).

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(14) (a) The preparations of **6a** and **6b** and several other related hydrofluorene acids were first recorded by us (footnotes, p 548 in ref 1b and p 4656 in ref 6). Subsequent to our publications Mander et al.[2e] reported the preparation of 1,2,3,4-tetrahydro-7-methoxyfluorene-2-carboxylic acid and 1,2,3,4-tetrahydro-2-hydroxy-7-methoxyfluorene-2-carboxylic acid by Diels–Alder reactions of 5-methyl-1-vinylind-1-ene with acrylonitrile and ethyl α-acetoxyacrylate, respectively. (b) For recent applications of vinylindene substrates in cycloaddition reactions, see: Bergamasco, R.; Porter, Q. N. *Aust. J. Chem.* **1977**, *30*, 1061. Bergamasco, R.; Porter, Q. N.; Yap, C. *Ibid.* **1977**, *30*, 1531.

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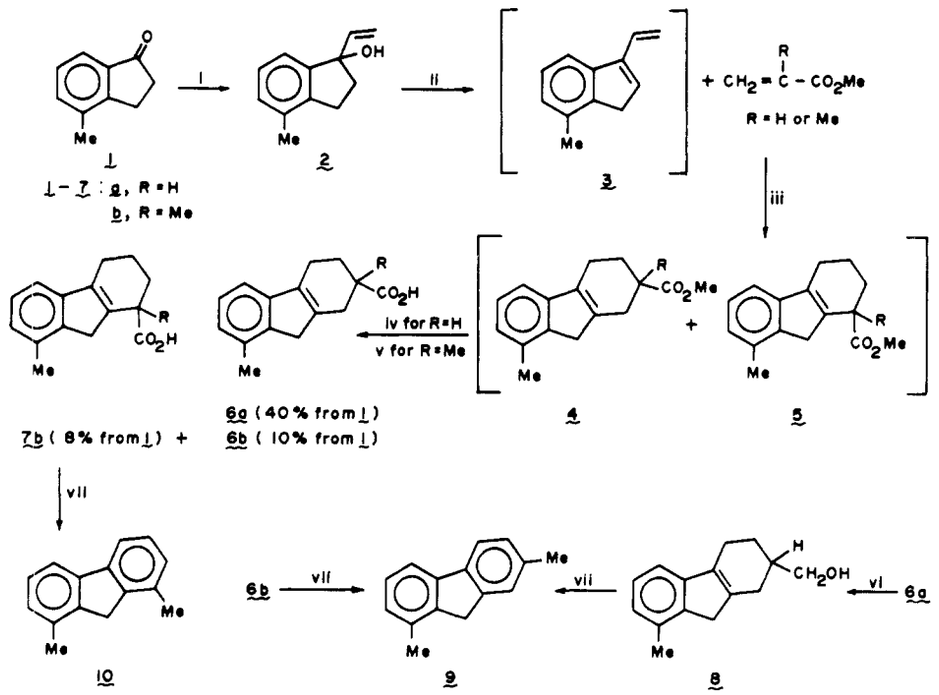
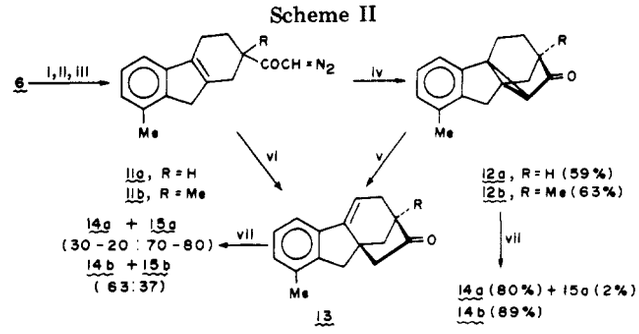
Scheme I



i, CH_2=CHMgBr, THF; ii, quinoline, hydroquinone, I_2, benzene; iii, HCl (g), benzene; iv, KOH, H_2O, EtOH; v, KOH, H_2O, $HOCH_2CH_2OH$; vi, $LiAlH_4$, THF; vii, Pd/C (10%), Δ

Cycloaddition of an excess of methyl acrylate with the vinylidene **3**, generated in situ from the crude carbinol **2** in benzene, prepared by the condensation of vinylmagnesium bromide with 4-methylindanone (**1**), followed by treatment with hydrogen chloride afforded an ester adduct in 62% yield along with a considerable amount of an uncharacterized high-boiling product, possibly originated from the self condensation of the reactive diene.[2e] The ^{1}H NMR spectra of the crude ester adduct and the pure ester **4a** appeared very similar, and its saponification afforded the acid **6a** in 40% overall yield from **1**. No other regioisomeric acid could be isolated from the mother liquor after crystallization of **6a**. The methyl ester **4a** (diazomethane) showed a tetrasubstituted styrenoid band in the UV spectrum. The ^{1}H NMR spectrum of this compound also supported the assigned structure. The structure of **6a** was finally confirmed by its reduction to the carbinol **8a** with lithium aluminum hydride followed by dehydrogenation with palladium-on-charcoal (Pd/C) to 1,7-dimethylfluorene (**9**).[15] Diels–Alder addition of methyl methacrylate to the diene **3** generated in situ from **2**, followed by isomerization of the double bond with hydrogen chloride, afforded a mixture of the esters **4b** and **5b**, along with a high-boiling product. The ratio of **4b** to **5b** was 54:46 as determined from the relative integrations of the corresponding quaternary methyl singlets at δ 1.28 and 1.45 in the ^{1}H NMR spectrum. Saponification of this mixture with potassium hydroxide in ethylene glycol followed by fractional crystallization afforded the pure acids **6b** and **7b** in approximately 10 and 8% overall yields, respectively, from **1**. The methyl esters **4b** and **5b** (diazomethane) showed UV, IR, and ^{1}H NMR spectral data consistent with the assigned structures. The structures of the acids **6b** and **7b** were finally confirmed by dehydrogenation with palladium-on-charcoal, leading respectively to 1,7-dimethylfluorene (**9**) and 1,8-dimethylfluorene (**10**).[16]

Scheme II



i, NaOEt, EtOH; ii, $(COCl)_2$, pyridine, benzene; iii, CH_2N_2, Et_2O, Et_3N; iv, "activated CuO", $h\nu$; v, HCl (g), $CHCl_3$; vi, BF_3·Et_2O, $ClCH_2CH_2Cl$; vii, Pd/C (10%), EtOH, H_2

Although the overall yields of the hydrofluorene acids from the starting indanone are not altogether satisfactory, the simplicity of the reaction provides an easy general route to the difficulty accessible key intermediate hydrofluorene-2-carboxylic acids and to some hydrofluorene-1-carboxylic acids,[17] valuable intermediates for compounds related to gibberellins.

The acids **6a** and **6b** were converted through their sodium salts to the corresponding acyl chlorides by a standard method[8] (Scheme II), which in turn were treated with an excess of ethereal diazomethane solution in the presence of triethylamine. The diazo ketones **11a** and **11b** obtained in 95 and 92% yields, respectively, were characterized by IR.

Intramolecular keto carbenoid additions of the diazo ketones **11a** and **11b** in the presence of "activated CuO"[1b] in boiling cyclohexane–tetrahydrofuran under irradiation with tungsten lamps afforded the respective cyclopropyl

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(17) Ghatak, U. R.; Dasgupta, R.; Chakravarty, J. *Tetrahedron* **1974**, *30*, 187.

ketones **12a** and **12b** in 59 and 64% yields. By use of anhydrous $CuSO_4$ or copper bronze as catalyst under various conditions,[6] the cyclopropyl ketones were obtained in only 35–45% yields. Fragmentations[6] of the cyclopropyl ketones **12a** and **12b** on exposure to dry hydrogen chloride in chloroform produced the $\Delta^{9,11}$-gibbene **13a**[18] and (±)-gibberone (**13b**)[19] in 90 and 93% yields, which were also obtained in 60 and 80% yields, respectively, by boron trifluoride–etherate-catalyzed cyclizations[6-9] of the corresponding diazo ketones **11a** and **11b** in 1,2-dichloroethane. The structures of these compounds have been confirmed from the UV, IR, and ^1H NMR spectral data. In accord with our previous findings[1b,6,7] with similar systems, the aromatic conjugated cyclopropane σ bond in **12b** underwent rapid and highly stereoselective hydrogenolysis with inversion[20] at the C-9 asymmetric center in the presence of Pd/C (10%) in ethanol, affording the 9α-gibbane derivative **14b** in excellent yield as the only isolable product. Reductive cleavage of the cyclopropyl ketone **12a**, on the contrary, gave a mixture from which the epimeric 9αH and 9βH ketones **14a** and **15a** were isolated in 80 and 2% yields, respectively, by fractional crystallization. While the stereochemistry of **14b** was assigned from analogies,[6,7] the stereochemistries of the epimeric ketones **14a** and **15a** were assigned from ^1H NMR studies. In conformity with our previous findings,[21] the C-6 methylene protons in the 9αH ketone **14a** forming AB quartet [(100 MHz in $CDCl_3$): δ_A 2.82, δ_B 2.70; J_{AB} = 16 Hz] resonate at a higher field than that of the 9βH epimer **15a** [δ_A 3.01, δ_B 2.79; J_{AB} = 16 Hz]. The 9αH epimer **14a** was proved to be identical by mixture melting point, IR, and GLC comparisons with a sample prepared by Mori[18,22] and presumed to have the assigned stereochemistry. The IR (nujol) spectrum of the 9βH epimer **15a** is identical with that of the optically active ketone,[22] obtained by degradation of II,[13] thereby establishing its previously undefined stereochemistry.

Catalytic hydrogenation of $\Delta^{9,11}$-gibbene **13b** in the presence of Pd/C (10%) in ethanol produced a mixture of 9αH and 9βH epimers **14b** and **15b** in a ratio of ~63:27 from which **14b** and presumably the 9βH epimer **15b** were partly separated by fractional crystallization. The preponderance[1b,6,7] of the 9αH epimers in catalytic hydrogenation has been observed in similar $\Delta^{9,11}$-gibbenes. On the other hand the gibbene **13a** under identical conditions produced a mixture of the 9αH and 9βH epimers **14a** and **15a** in a ratio of ~20:80 as determined from the integrations of the C-6 methylene protons in the ^1H NMR (100 MHz) spectrum and also by direct comparisons of ^1H NMR spectra with a known mixture of the epimers. The ratio of the epimers **14a** and **15a** varied from 30:70 to 20:80 with the different samples of the catalyst.

The reversal of the stereoselectivity in the hydrogenation of **13a** (in the Pd/C) leading predominantly to the 9βH epimer **15a** is in contrast to the related hydrogenation results[1b] on similar $\Delta^{9,11}$-gibbenes where 9αH epimer was found to be the major component (~69–75%). That the stereochemical outcome in catalytic hydrogenation of **13a** is also influenced by the nature of the metal catalyst[23] used is evident from the observed[18] formation of mostly the 9αH epimer **14a** in the hydrogenation of **13a** in the presence of Raney Ni catalyst. The effects of the polar C-6 substituents in the gibbenes on the stereoselectivity[2i,k,24] of the hydrogenation of 9,11 double bond have been recorded in several cases. Similar influences by polar angular substituents in controlling the stereochemistry of catalytic reduction in other hydrofluorene systems have also been observed.[25]

So far we have not been able to rationalize the observed stereoselectivity in the reduction of **13a** and other $\Delta^{9,11}$-gibbenes. The present study has thus developed stereocontrolled synthetic routes to the $\Delta^{9,11}$-gibbenes **13a,b** and the 9αH and 9βH gibbanes **14a,b** and **15a,b** by a simple general method.

Experimental Section

The compounds described are all racemates. Melting points, taken in an open capillary, and boiling points are uncorrected. Petroleum ether and petroleum refer to the fractions with boiling points of 40–60 and 60–80 °C, respectively. The homogeneity of all compounds was checked by TLC on silica gel G (Merck, 200 mesh) plates of ~0.2-mm thickness using benzene–ethyl acetate and benzene–methanol systems. The spots were located by exposing the dried plates in iodine vapor. UV spectra were determined in 95% ethanolic solution on a Beckman DU spectrometer, and IR spectra were determined on a Perkin–Elmer 21 or a Beckman IR 20A. ^1H NMR spectra were taken in the indicated solvent on a Varian A-60 (60 MHz) or a HA-100 (100 MHz), and chemical shifts are reported in δ unit from internal Me_4Si standard. Microanalyses were performed by Mrs. C. Dutta of this laboratory.

The term "usual workup" used here refers to the following procedure. The reaction mixture was cooled, diluted with water and extracted several times with the indicated solvent. The combined organic extracts were washed with saturated brine, dried (Na_2SO_4), and concentrated under a water aspirator.

1,2,3,4-Tetrahydro-8-methylfluorene-2-carboxylic Acid (6a). To an ice-cold well-stirred solution of vinylmagnesium bromide under a dry nitrogen atmosphere, prepared through a modified method[8] from 9 g (0.37 g-atom) of magnesium turnings in 60 mL of dry THF and a freshly generated vinyl bromide solution prepared from 113 g (0.6 mol) of 1,2-dibromoethane in 60 mL of dry THF, was added a solution of 30.0 g (205 mmol) of 4-methylindan-1-one (1)[18] in 100 mL of dry THF dropwise over a period of 1 h. The resulting mixture was stirred for an additional 1.5–2 h at room temperature and finally refluxed for 2 h. The THF was recovered (recovered THF can be used after redistillation over lithium aluminum hydride) by distillation on a steam bath. The mixture was cooled, treated with 60 mL of benzene, and decomposed with ice-cold aqueous ammonium chloride. The organic layer was separated, and the aqueous layer was extracted with benzene (3 × 50 mL). The combined extracts were washed with water and dried. This was directly subjected to Diels–Alder reaction.

The benzene solution of the crude vinyl carbinol **2** was refluxed under nitrogen for 10 h with 34.5 g (0.4 mol) of methyl acrylate, a catalytic amount of iodine (2 crystals), 0.5 mL of quinoline, and 30 mg of hydroquinone under a Dean–Stark water separator. The red reaction mixture was then cooled in an ice bath, and a constant stream of dry hydrogen chloride was passed through it for 30 min, and it was left as such for 20 min. The mixture was washed with water, 5% aqueous sodium carbonate, 2% aqueous sodium thiosulfate, and finally with water and dried. Evaporation of the solvent followed by fractional distillation yielded the ester **4a** as a pale yellow gummy solid (31 g, 64%) which distilled at 155–165 °C (0.15 mm): UV 259 nm (log ϵ 4.11); IR ($CHCl_3$) 1728 cm^{-1}.

(18) Mori, K.; Matsui, M.; Sumiki, Y. *Agric. Biol. Chem.* **1961**, *25*, 907.
(19) Kos, Y.; Loewenthal, H. J. E. *J. Chem. Soc.* **1963**, 605.
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(21) Baker, A. J.; Goudie, A. C.; Ghatak, U. R.; Dasgupta, R. *Tetrahedron Lett.* **1972**, 1103.
(22) We thank Professor K. Mori for his help in providing these comparative data and spectra.
(23) For a general discussion see: House, H. O. "Modern Synthetic Reactions", 2nd ed; Benjamin, W. A.: Menlo Park, CA, 1972; pp 19–28.
(24) (a) Grove, J. F.; MacMillan, J.; Mulholland, T. P. C.; Turner, W. D. *J. Chem. Soc.* **1960**, 3049. (b) Loewenthal, H. J. E.; Malhotra, S. K. *Ibid.* **1965**, 990. (c) Cross, B. E.; Markwell, R. E. *J. Chem. Soc. C* **1971**, 2980. (d) Loewenthal, H. J. E.; Schatzmiller, S. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2149.
(25) Thompson, H. W.; Naipawer, R. E. *J. Am. Chem. Soc.* **1973**, *95*, 6379.

A considerable amount of high-boiling products were left as pot residue.

The crude ester adduct was hydrolyzed by refluxing for 4 h under nitrogen with a solution of 10 g (0.17 mol) of potassium hydroxide in 8 mL of water and 92 mL of ethanol. After the removal of ethanol under reduced pressure, the solution was diluted with 100 mL of water, and the neutral fraction was removed by extraction with ether. The aqueous alkaline layer was acidified with 6 N hydrochloric acid, and precipitated acid was extracted with ethyl acetate. The ethyl acetate layer was washed with brine, dried, and evaporated to afford 24.8 g (94%) of the crude acid **6a**, mp 145–157 °C. It was recrystallized three times from ethyl acetate to afford 18.3 g (40% overall yield from 1), mp 199–200 °C, as pale yellow needles: UV 262 nm (log ϵ 4.20); IR ($CHCl_3$) 1700, 1600 cm^{-1}. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.91; H, 7.36.

From the dark brown mother liquor, no other pure isomeric acid could be isolated.

Methyl ester **4a** prepared from the pure acid **6a** (diazomethane method) was recrystallized from methanol: mp 83–84 °C; UV 259 nm (log ϵ 4.12); IR ($CHCl_3$) 1728 cm^{-1}; NMR ($CDCl_3$) δ 1.03–3.0 (m, 10 H with $ArCH_3$'s at 2.34), 3.20 (br s, 2 H, $ArCH_2$), 3.73 (s, 3 H, $COOCH_3$), 7.15 (m, 3 H, ArH). Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.10; H, 7.50.

Lithium Aluminum Hydride Reduction of 6a Followed by Dehydrogenation to 1,7-Dimethylfluorene (9). A solution of 200 mg (0.87 mmol) of the acid **6a** was reduced in 15 mL of dry THF by refluxing for 4 h with 100 mg (2.6 mmol) of lithium aluminum hydride. The reaction mixture was cooled, decomposed with 10 mL of saturated aqueous sodium sulfate, and filtered. Most of THF was distilled off under reduced pressure, and the residue was extracted with ether to afford 200 mg (99%) of the crude carbinol **8** as a light yellow solid, mp 86 °C. This was mixed with 200 mg of 10% Pd/C and heated on a metal bath at 300–320 °C for 15 h in a sealed tube. Chromatography of the crude product on basic alumina in petroleum–benzene followed by recrystallization of the white solid, 120 mg (60%), from methanol afforded **9**, mp and mmp 107 °C (lit.[15] mp 107–107.5 °C).

1,2,3,4-Tetrahydro-2,8-dimethylfluorene-2-carboxylic Acid (6b) and 1,2,3,4-Tetrahydro-1,8-dimethylfluorene-1-carboxylic Acid (7b). The crude vinyl carbinol **2**, prepared from 30 g of **1** on Diels–Alder reaction with 45 g (45 mmol) of methyl methacrylate, iodine (2 crystals), 0.5 mL of quinoline, and 30 mg of hydroquinone under the conditions described for **6a** yielded 12.6 g (24%) of a mixture of the regioisomeric adducts **4b** and **5b** as a light yellow oil: bp 158–167 °C (0.1 mm), UV 259 nm (log ϵ 4.15); IR ($CHCl_3$) 1730 cm^{-1}.

The ratio of **4b** and **5b** in the mixture was found to be 54:46 by the relative peak integrations of the quaternary Me singlets in the NMR ($CDCl_3$). The high-boiling pot residue was not investigated further. Saponification of the ester mixture with 10 g (0.17 mol) of potassium hydroxide in 8 mL of water and 92 mL of ethylene glycol by refluxing for 5 h under nitrogen afforded 10.4 g (88%) of the mixture of **6b** and **7b**, as a light brown solid. Fractional crystallization from ethyl acetate yielded 4.40 g (~10% based on **1**) of the less soluble acid **6b** in light yellow needles: mp 217 °C, UV 260 nm (log ϵ 4.19); IR (nujol) 1690, 1595 cm^{-1}. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.37; H, 7.67.

Methyl ester **4b** (diazomethane) was crystallized from methanol: mp 78–79 °C; UV 259 nm (log ϵ 4.19); IR ($CHCl_3$) 1730 cm^{-1}; NMR ($CDCl_3$) δ 1.28 (s, 3 H, $>CCH_3$), 1.62–2.93 (m, 9 H with $ArCH_3$'s at 2.31), 3.11 (m, 2 H, $ArCH_2$), 3.65 (s, 3 H, $COOCH_3$), 7.05 (m, 3 H, ArH).

The mother liquors after separation of **6b** afforded the isomeric acid **7b** as a colorless powder, 3.84 g (~8% based on **1**), mp 180 °C, after two crystallizations from ether–petroleum ether: UV 260 nm (log ϵ 4.2); IR ($CHCl_3$) 1690, 1590 cm^{-1}. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.13; H, 7.74.

Methyl ester **5b** (diazomethane) was purified by evaporative distillation at 140 °C (0.1 mm): UV 259 nm (log ϵ 4.20); IR ($CHCl_3$) 1730 cm^{-1}; NMR ($CDCl_3$) δ 1.45 (s, 3 H, $>CCH_3$), 1.5–2.61 (m, 9 H with $ArCH_3$'s at 2.33), 3.25 (m, 2 H, $ArCH_2$), 3.65 (s, 3 H, $COOCH_3$), 7.05 (m, 3 H, ArH).

Dehydrogenation of 6b to 1,7-Dimethylfluorene (9). Dehydrogenation of 120 mg (0.49 mmol) of the acid **6b** with 100 mg of 10% Pd/C at 300–320 °C for 13 h in a sealed tube and chromatography of the resulting product on basic alumina in benzene–petroleum gave 50 mg (70%) of a hydrocarbon which on two recrystallizations from methanol afforded **9**, mp and mmp 107 °C (lit.[15] mp 107–107.5°C).

Dehydrogenation of 7b to 1,8-Dimethylfluorene (10). Dehydrogenation of 100 mg (0.41 mmol) of the acid **7b** with 100 mg of 10% Pd/C under the above conditions and purification of the resulting product afforded 56 mg (70%) of **10**: mp 154–155 °C, mmp 152–154 °C with an authentic sample[26] (lit.[16] mp 152–154 °C).

2-(Diazoacetyl)-1,2,3,4-tetrahydro-8-methylfluorene (11a). An adaptation of a previously reported procedure[8] was employed. The acid **6a** (4 g, 0.017 mol) in dry ethanol was neutralized with a dilute solution of sodium ethoxide in ethanol with phenolphthalein as indicator. After removal of the solvent, the residue was freed from ethanol by repeated distillation with dry benzene. The dried sodium salt was suspended in 50 mL of dry benzene and 0.3 mL of dry pyridine, cooled in an ice bath, and treated with 3 mL of oxalyl chloride. The mixture was stirred at 0 °C for 30 min and at room temperature for 30 min and finally warmed at 55–60 °C for 1 h. The precipitate was filtered and the filtrate concentrated under reduced pressure. The crude acid chloride was dissolved in 100 mL of dry ether and added slowly to a stirred solution of an excess of ice-cold ethereal diazomethane containing 1 mL of dry triethylamine. The product was filtered and concentrated, and the crude product was purified by filtration through a short column of neutral alumina (10 g) in ether to afford the diazo ketone **11a** [4.2 g, 95%; mp 118 °C; IR ($CHCl_3$) 2130, 1635 cm^{-1}] which was used for the subsequent reactions without further characterization.

2-(Diazoacetyl)-1,2,3,4-tetrahydro-2,8-dimethylfluorene (11b). By use of the above method, 900 mg (3.7 mmol) of **6b** was converted to the diazo ketone **11b** (900 mg 92%) as a light yellow oil, after purification through chromatography on neutral alumina; IR 2130, 1625 cm^{-1}.

Intramolecular Carbenoid Addition of the Diazo Ketone 11a to the Cyclopropyl Ketone 12a. A solution of 2.52 g (10 mmol) of the diazo ketone **11a** in 350 mL of dry cyclohexane and 150 mL of dry THF was stirred vigorously and refluxed with 9.6 g of "activated CuO"[1b] under irradiation by two 200-W tungsten lamps. The time required for complete decomposition of the diazo ketone was 3 h. The cooled mixture was filtered, and the solvent was removed by distillation under reduced pressure. The resultant semisolid was dissolved in 15 mL of benzene and chromatographed on neutral alumina (40 g). Petroleum eluted the cyclopropyl ketone **12a** (1.35 g, 59%): mp 122 °C, after crystallization from ether–petroleum ether; UV 234 nm (log ϵ 4.07); IR (KBr) 1720, 1590, 1460, 1175, 865, 785, 725 cm^{-1}; NMR ($CDCl_3$) δ 1.47 (s, 1 H), 1.7–2.47 (m; 7 H), 2.21 (s, 3 H, $ArCH_3$), 3.12 (s, 2 H, $ArCH_2$), 7.05 (s, 3 H, ArH). Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.58; H, 7.13.

The diazo ketone **11a** under the above conditions but without irradiation afforded the cyclopropyl ketone **12a** in 35% yield.

Intramolecular Carbenoid Addition of the Diazo Ketone 11b to the Cyclopropyl Ketone 12b. A solution of 2.41 g (913 mmol) of **12b** in 430 mL of 7:3 dry cyclohexane–THF was stirred and refluxed with 9.6 g of "activated CuO" under irradiation as described above. Reaction was completed in 3 h. Usual workup and chromatography on neutral alumina (35 g) in petroleum afforded the cyclopropyl ketone **12b** (1.35 g, 63%): mp 134–135 °C as needles (ether–petroleum ether); UV 238 nm (log ϵ 3.92); IR (KBr) 1720, 1592, 1127, 784 cm^{-1}; NMR ($CDCl_3$) δ 1.03 (s, 3 H, $>CCH_3$), 1.50 (s, 1 H), 2.21 (s, 3 H, $ArCH_3$), 1.34–2.93 (m, 6 H), 3.10 (s, 2 H, $ArCH_2$), 7.03 (s, 3 H, ArH). Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.58; H, 7.89.

(±)-4-Methyl-13α*H*-16-oxogibba-1,3,5(10),9(11)-tetraene (13a). Method A: Acid-Catalyzed Fragmentation of the Cyclopropyl Ketone 12a. Through a solution of 120 mg (0.53 mmol) of **12a** in 50 mL of dry chloroform at 0 °C was bubbled a stream of dry hydrogen chloride for 2 h. Removal of solvent under reduced pressure left a solid which was filtered through a short column of alumina in benzene–petroleum to afford the styrenoid ketone **13a** (108 mg, 90%): mp 112 °C (lit.[18] mp 103–105

(26) We thank Professor A. Chatterjee, Jadavpur University, Calcutta, for a generous gift of this sample.

°C), after recrystallization from petroleum; UV 258 (log ε 4.22), 266 (4.16), 287 (3.73); IR (KBr) 1735 cm^{-1}; NMR ($CDCl_3$) δ 2.27 (s, 3 H, $ArCH_3$), 2.8 (m, 1 H), 3.0 (s, $ArCH_2$), 5.8 (br t, 1 H, >C=$CHCH_2$, 7.0–7.34 (m, 3 H, ArH). Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.62; H, 7.48.

Method B: Boron Trifluoride Etherate Catalyzed Intramolecular Alkylation of the Diazo Ketone 11a. To a stirred solution of 500 mg (1.96 mmol) of **11a** in 50 mL of dry 1,2-dichloroethane, cooled in an ice–salt bath (~−10 °C), was added 0.5 mL of freshly distilled boron trifluoride etherate. After 1 h the solution was washed with water, 5% aqueous sodium carbonate solution, and water and dried. Removal of solvent under reduced pressure and chromatography of the residue on neutral alumina (20 g) with petroleum as eluent afforded the ketone **13a** (255 mg, 58%), mp and mmp 112 °C, identical with the sample described above (NMR and IR).

4,13α-Dimethyl-16-oxogibba-1,3,5(10),9(11)-tetraene, [(±)-Gibberone] (13b). Method A: Cleavage of 120 mg (0.5 mmol) of cyclopropyl ketone **12b** with dry hydrogen chloride as in the aforementioned experiment and recrystallization of the crude product from petroleum yielded **13b** (112 mg, 93%): mp 118 °C (lit.[19] mp 118–118.5 °C); UV 260 nm (log ε 4.43); IR (KBr) 1735, 1444, 1094, 777 cm^{-1}; NMR δ 1.20 (s, 3 H, >CCH_3), 2.06 (s, 2 H), 2.3 (s, 2 H, $COCH_2$), 2.25 (s and m, 5 H, $ArCH_3$ and =C-HCH_2C<), 2.96 (br s, 2 H, $ArCH_2$), 5.83 (br t, 1 H, >=$CHCH_2$), 7.13 (m, 3 H, ArH). Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.81; H, 7.85.

Method B: A solution of 2 g (7.5 mmol) of the diazo ketone **11b** in 100 mL of dry 1,2-dichloroethane was reacted with 0.8 mL of boron trifluoride etherate as described above. Usual workup followed by chromatography on 20 g of neutral alumina and elution with petroleum afforded 1.45 g (80%) of **13b**, mp and mmp 118 °C (identical IR and NMR with the sample described above).

(±)-4-Methyl-9α,13α-dihydro-16-oxogibba-1,3,5(10)-triene (14a) and (±)-4-Methyl-9β,13α-dihydro-16-oxogibba-1,3,5-(10)-triene (15a). Method A: Hydrogenolysis of the Cyclopropyl Ketone 12a. The cyclopropyl ketone **12a** (200 mg, 0.89 mmol) in 12 mL of ethanol was hydrogenated over 50 mg of 10% Pd/C at room temperature and atmospheric pressure. Uptake of the calculated amount of hydrogen was complete within 10–15 min. The catalyst was filtered and the solvent evaporated to give the crude product (200 mg, 99%), mp 90–95 °C. This showed a major and a minor component in TLC with very close R_f values in benzene–ethyl acetate (4:1). On crystallization from methanol the mixture gave pure 9α epimer **14a** (160 mg, 80%), mp 109 °C, as colorless square plates: UV 263 nm (log ε 2.59); IR (KBr) 1734, 1584, 779, 739 cm^{-1}; NMR ($CDCl_3$ at 100 MHz) δ 1.33–2.16 (m, 6 H), 2.22–2.54 (m, 6 H with $ArCH_3$ singlet peak at 2.22), 2.58–2.94 (q, $ArCH_2$, J_{AB} = 16 Hz; δ_A 2.82, δ_B 2.70), 3.05 (q, 1 H), 6.84–8.00 (m, 3 H, ArH). Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 84.66; H, 8.14. The ketone **14a** was found to be identical with a sample, mp 102–103 °C, prepared by a different route by Mori et al.,[18] by direct IR and GLC comparisons.[22]

In the concentrated mother liquors after separation of **14a**, a few rectangular prisms were crystallized from petroleum to obtain the 9β epimer **15a** (4 mg, 2%), mp 110–111 °C, identical with the sample described below.

Method B: Hydrogenation of the Styrenoid Ketone 13a. The ketone **13a** (500 mg, 2.2 mmol) in 25 mL of ethanol was hydrogenated in presence of 10% Pd/C (100 mg). The calculated amount of hydrogen was consumed within 10–15 min. The crude product (490 mg, 98%), mp 75–80 °C, displayed two overlapping spots in TLC in 4:1 benzene–ethyl acetate. NMR ($CDCl_3$ at 100 MHz) showed it to be a mixture of the 9α and 9β epimers **14a** and **15a**, in a ratio of ~20:80 from the relative peak heights of the C-6 $ArCH_2$ quartets by comparison with the mixtures of the pure epimers. Laborious fractional crystallization of this mixture from methanol and mechanical separation of the rectangular prisms (9β epimer) followed by recrystallization from ether–petroleum afforded pure **15a** (180 mg, 36%): mp 110–111 °C; mmp 83–87 °C with the 9α epimer **14a**; UV 264 nm (log ε 2.90); IR (KBr) 1738, 1596, 778, 750 cm^{-1}; NMR ($CDCl_3$ at 100 MHz) δ 1.46–2.14 (m, 6 H), 2.23 (s, 3 H, $ArCH_3$), 2.40 (s, 2 H, >CCH_2CO), 2.68–3.12 (q, 3 H, C-6 $ArCH_2$, J_{AB} = 16 Hz; δ_A 3.01, δ_B 2.79, with a br s at 3.04 for the C-9 benzylic proton), 6.98–7.20 (m, 3 H, ArH). Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 84.96; H, 8.28. The IR spectrum in Nujol[22] of **15a** is identical with that of the optically active ketone, obtained by degradation[13] of gibberallin-A_{13}.

The ratio of the 9α and 9β ketones **14a** and **15a** varied from 30:70 to 20:80 with the different batches of catalyst.

(±)-4,13α-Dimethyl-9αH-16-oxogibba-1,3,5(10)-triene (14b). Hydrogenolysis of the Cyclopropyl Ketone 12b. The cyclopropyl ketone **12b** (120 mg) in 10 mL of ethanol was hydrogenated in presence of 50 mg of 10% Pd/C. The reduction was completed in 10 min. The crude product (120 mg, 99%), mp 86–95 °C, on two recrystallizations from petroleum afforded the ketone **14b** (107 mg, 89%): mp 100 °C; IR (KBr) 1735, 1592, 1090, 688, 645 cm^{-1}; UV 260 nm (log ε 2.92), 265 (2.94), 274 (2.83); NMR ($CDCl_3$) δ 1.10 (s, 3 H, >CCH_3), 1.63–2.00 (m, 7 H), 2.25 (s, 3 H, $ArCH_3$), 2.35–2.97 (m, 4 H), 7.00 (m, 3 H, ArH). Anal. Calcd for $C_{17}H_{20}O$: C, 84.95; H, 8.39. Found: C, 84.77; H, 8.59.

(±)-4,13α-Dimethyl-9βH-16-oxogibba-1,3,5(10)-triene (15b) and 14b. Hydrogenation of the Styrenoid Ketone 13b. The ketone **13b** (500 mg, 2.1 mmol) in 25 mL of ethanol was hydrogenated in the presence of 75 mg of 10% Pd/C, and the reduction was over in 10 min. The crude product (490 mg, 98%), mp 65–70 °C, showed two overlapping spots in TLC in 4:1 benzene–ethyl acetate. NMR ($CDCl_3$) showed two quarternary CH_3 signals at δ 1.0 and 1.1. From the peak heights as well as by direct comparison with the 9α ketone **14b**, the ratio of **14b** and **15b** was estimated as 63:37. The mixture on careful fractional crystallization from petroleum separated the major ketone **14b** (90 mg, 18%), mp and mmp 100 °C. From the mother liquor a very small amount (~4 mg) of 9β epimer **15b**, mp 96–98 °C, was isolated; IR (KBr) 1737 cm^{-1}. The mixture melting point with the 9α epimer was 69–73 °C. Anal. Calcd for $C_{17}H_{20}O$: C, 84.95; H, 8.39. Found: C, 84.70; H, 8.12.

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Registry No. 1, 24644-78-8; (±)-2, 71685-78-4; (±)-4a, 71685-79-5; (±)-4b, 71685-80-8; (±)-5b, 71685-81-9; (±)-6a, 71685-82-0; (±)-6b, 71685-83-1; (±)-7b, 71685-84-2; (±)-8, 71685-85-3; (±)-9, 442-66-0; (±)-10, 1207-11-0; (±)-11a, 50464-35-2; (±)-11b, 50464-37-4; (±)-12a, 50464-40-9; (±)-12b, 50464-42-1; (±)-13a, 50464-45-4; (±)-13b, 7442-69-5; (±)-14a, 50464-50-1; (±)-14b, 50464-49-8; (±)-15a, 50464-51-2; (±)-15b, 50464-54-5; vinyl bromide, 593-60-2; 1,2-dibromoethane, 106-93-4; methyl acrylate, 96-33-3; methyl methacrylate, 80-62-6; diazomethane, 334-88-3; (±)-1,2,3,4-tetrahydro-8-methylfluorene-2-carbonyl chloride, 71685-86-4.