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Photoinduced Molecular Transformations. Part 150[1]. A New Total Synthesis of (±)-α-Himachalene based on a Sequence involving [2+2] Photoaddition and Regioselective β-Scission of Alkoxyl Radicals generated from the Resulting Cyclobutanols[1]

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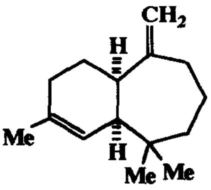
Abstract: A new total synthesis of α-himachalene, a sesquiterpene isolated from essential oil of a Himalayan cedar (Cedrus deodara Loud), has been achieved. It is based on a sequence involving the [2+2] photoaddition of a cyclic enone with a silyl enol ether, followed by a radical-induced ring expansion of the resulting fused cyclobutanol; the [2+2] photoaddition of cyclohexenone with 1-methyl-2-trimethylsiloxy-1-cyclopentene in benzene, followed by a treatment of the resulting photoadducts with acid gave a stereoisomeric mixture of 2-hydroxy-6-methyltricyclo[5.4.0.0^{2,6}]undecan-8-one (33%) accompanied by a product (27%) from a retroaldol reaction of an isomeric photoadduct. The former was transformed into 8-*tert*-butyldimethylsiloxy-6-methyltricyclo[5.4.0.0^{2,6}]undecan-2-ol *via* 3 steps. Irradiation of the hypoiodite generated from this protected fused cyclobutanol in benzene resulted in a β-scission of the ring fusion bond to give a mixture of functionalized bicyclo[5.4.0]undecanes, which was transformed into *cis*-6,6-dimethyl-8-hydroxybicyclo[5.4.0]undecane-2-ones *via* 3 steps. Its methylenation by a Wittig reaction, followed by oxidation of the resulting 2-methylenebicyclo [5.4.0]undecan-8-ol, gave the corresponding bicycloundecan-8-one. Its ethoxycarbonylation, followed by reductive deoxygenation with zirconocene chloride hydride (Cp_2ZrHCl), gave ethyl 6,6-dimethyl-2-methylenebicyclo[5.4.0] undec-8-ene-9-carboxylate. The synthesis of (±)-α-himachalene was achieved by transforming the ethoxycarbonyl group into a methyl group by the standard method; the α,β-unsaturated ester was reduced into the corresponding alcohol with lithium alminium hydride. A reduction of the mesylate of the resulting alcohol with lithium triethylborohydride gave (±)-α-himachalene.

α-Himachalene (**1**) is a representative of a class of sesquiterpenes having a bicyclo[5.4.0]undecane skeleton. This bicyclic sesquiterpene was first isolated from the essential oil of Himalayan cedar (Cedrus deodara Loud) by Dev and colleagues in 1952,[2] and later from Atlas cedar (Cedrus atrantica) and from Cedrus libani by Bredenberg and Erdtman[3].



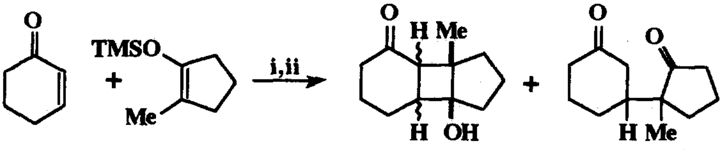
1

α-Himachalene

The structure, including the absolute stereochemistry, was established by Joseph and Dev in 1968.[4] Its total synthesis has been the subject of intensive research by several groups of investigators.[5] Since the first synthesis by de Mayo and colleagues[6a] several total sintheses have been reported.[6] Among these, de Mayo's approach to the synthesis of this molecule involves an ionic ring-expansion of a [2+2] photoadduct obtained from a cyclohexene derivative and the enol acetate of a cyclopentane-1,3-dione (de Mayo reaction).[6a]

We recently reported briefly on a new general synthesis of a functionalized bicyclo[5.4.0]undecane skeleton based on a ring-expansion induced by alkoxyl radicals generated from 2-hydroxytricyclo[5.4.0.$0^{2,6}$]-undecan-8-ones prepared by a [2+2] photoaddition of cyclic enones with the trimethylsilyl enol ethers of cyclic ketones.[7-9]

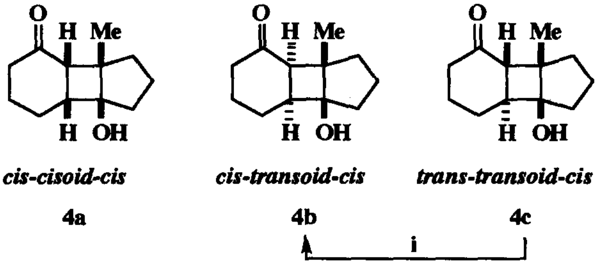
We report here on an application of our radical-induced ring-expansion approach to the total synthesis of α-himachalene. Thus, the [2+2] photoaddition of cyclohexenone **2** with 1-methyl-2-trimethylsiloxy-1-cyclopentene **3** in benzene, followed by a treatment of the resulting photoadducts with diluted hydrochloric acid, gave a stereoisomeric mixture of 2-hydroxy-1-methyltricyclo[5.4.0.$0^{2,6}$]undecan-8-one **4** in 33% yield. A retroaldol product **5** (27%) formed via a de Mayo reaction was an accompanying product (Scheme 1). An isomerization experiment and ^{1}H-NMR spectroscopy indicated that the stereoisomeric mixture **4** comprised *cis-cisoid-cis, cis-transoid-cis,* and *trans-transoid-cis* isomers, **4a**, **4b**, and **4c**, in a ratio of 1, 1.5 and 2.5 (Scheme 2); the ^{1}H-NMR spectrum of the mixture exhibited three signals at δ 1.01, 1.03 and 1.28, which are assignable



2 **3** **4** **5**

Reagents and Conditions: i, hv, benzene ii, HCl-H_2O

Scheme 1



cis-cisoid-cis ***cis-transoid-cis*** ***trans-transoid-cis***

4a **4b** **4c**

Reagents and Conditions: i, 5% KOH-MeOH, r.t.

Scheme 2

to the tertiary methyl group of the three isomers in a ratio of 1, 1.5 and 2.5. Treatment of the mixture **4** with 5% methanolic KOH removed the signal at δ 1.03 and enhanced the area of the signal at δ 1.01. These results indicated that the signal at δ 1.03 is due to the *trans-transoid-cis* isomer **4c** which is isomerized to the more stable *cis-transoid-cis* isomer **4b** by the treatment with a base.[10b] Between isomers **4a** and **4b**, the minor isomer **4a** was assigned to the less stable *cis-cisoid-cis* isomer on the basis of the known stereochemical outcome in the photoadditions of cyclohexenone.[10] Thus, *trans-transoid-cis* isomers are the predominant photoadducts in these photoadditions.[10]

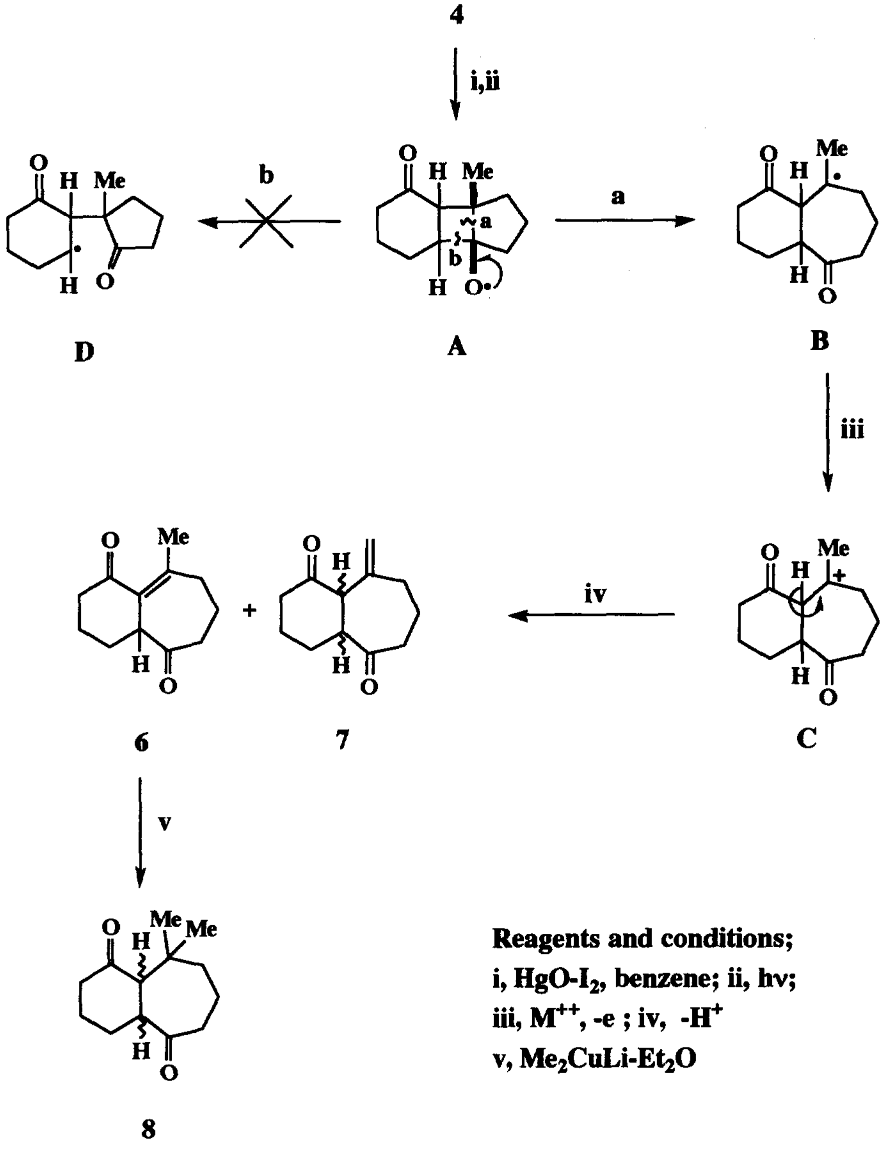
Irradiation of the hypoiodite of cyclobutanols **4**, prepared *in situ* with 2 equivalents of red mercury(II) oxide-iodine in benzene with a Pyrex-filtered light generated by a 100-W high-pressure Hg arc lamp,[11] gave an unstable 1:1 mixture of 6-methylbicyclo[5.4.0]undec-6-ene-2,8-dione **6** and 6-methylenebicyclo[5.4.0]-undecane-2,8-dione **7** in 31% yield (Scheme 3). Bicycloundecenediones **6** and **7** were clearly formed by removing of a proton from cationic intermediates **C** generated by one-electron oxidation of the corresponding secondary carbon radicals **B** formed by cleaving of the ring-fusion bond of the alkoxyl radicals **A** (as outlined in Scheme 3).As reported in our preliminary paper[7], no product(s) derived from a less stabilized secondary radical **D** arising from B-scission of the non-ring junction bond was formed in this ring expansion.

In our first approach to the synthesis of α-himachalene from bicycloundecenedione **6** we attempted a transformation of bicycloundecenedione **6** into 6,6-dimethylbicyclo[5.4.0]undecane-2,8-dione **8**. Treatment of bicycloundecenedione **6** with lithium dimethylcuprate in diethyl ether, however, gave the anticipated gem-dimethylbicyclo[5.4.0]undecane **8** in less than 5% yield (Scheme 3). This approach was therefore abandoned.

The reduction of a 1:4 mixture of *cis-cisoid-cis* and *cis-transoid-cis* isomers of 2-hydroxy-6-methyl-tricyclo[5.4.0.0^{2,6}]undecan-8-ones (**4a** and **4b**) in methanol with $NaBH_4$ at room temperature gave the corresponding tricycloundecane-2,8-diols. The hydroxyl group attached to C-8 of the resulting diols was then protected by treatment with *tert*-butyldimethylsilyl chloride in dichloromethane containing 4-dimethylamino-pyridine and triethylamine at room temperature.

A mixture of *cis-cisoid-cis* and *cis-transoid-cis*8-*tert*-butyldimethylsiloxy-6-methyltricyclo[5.4.0.0^{2,6}] undecan-2-ols **9** obtained in 47% yield was then transformed into the corresponding hypoiodite in benzene with two equivalents each of HgO and I_2. Irradiation of the solution with Pyrex-filtered light gave an inseparable mixture of isomeric products in 40% yield. An analysis of the product mixture by IR and ^{1}H NMR spectroscopy as well as mass spectrometry showed that the products were a 1.5 : 1 : 3 mixture of three functionalized bicycloundecenones **10**, **11**, and **12** arising from a cleavage of the fusion-bond of tricycloundecan-2-ol. (see Experimental for the datails of the analysis). Removal of the protecting group from a mixture of bicycloalkenes **10**, **11**, and **12** with tetrabutylammonium fluoride in THF at room temperature gave a mixture of the corresponding hydroxy bicycloalkenes **13**, **14**, and **15** in 69% yield (Scheme 4).

The mixture of bicycloundecenes and a 6-methylenebicycloundecane **13**, **14**, and **15** in diethyl ether was then treated with diethylzinc and diiodomethane at room temperature to give a mixture of three tricyclododecan-2-ones **16**, **17**, and **18** in 43% yield. The mixture of tricyclododecan-2-ones **16** and **18** and bicyclo[5.4.0]-undecan-2-one **17** in acetic acid was then hydrogenated in the presence of Adams platinum oxide as a catalyst at atmospheric pressure and room temperature to give **19** as a *single* product in 71% yield. The spectral data of the product **19** were in full agreement with 6,6-dimethyl-8-hydroxybicyclo[5.4.0]undecan-2-one. The Wittig methylenation of bicyclo[5.4.0]undecan-2-one **19** by the standard method gave 6,6-dimethyl-2-



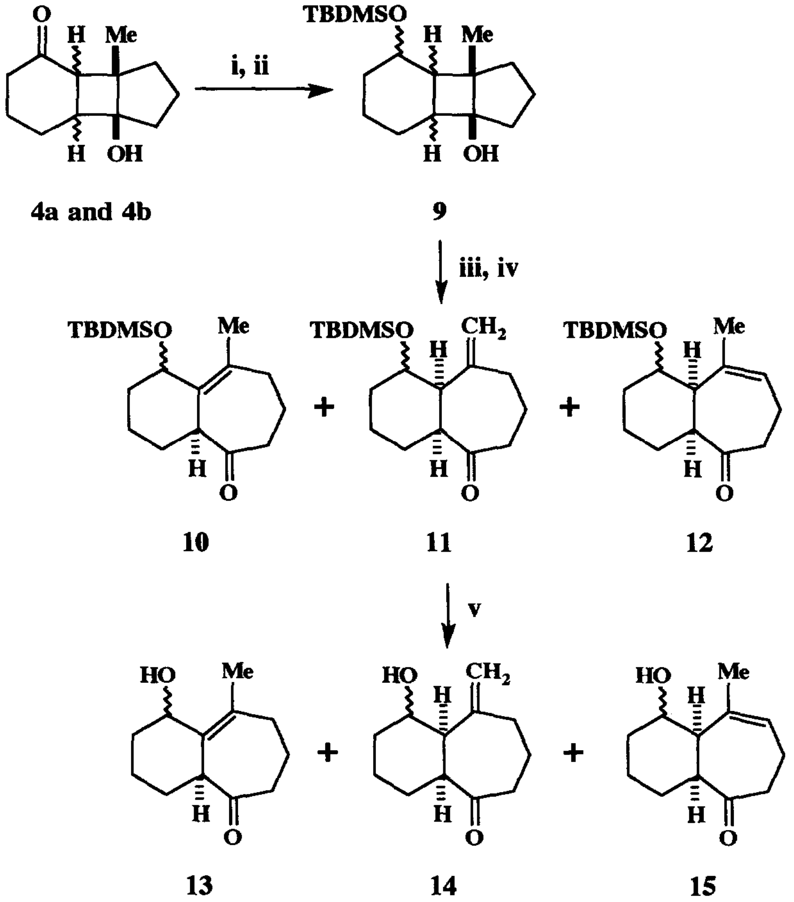
Reagents and conditions;
i, HgO-I$_2$, benzene; ii, hv;
iii, M^{++}, -e ; iv, -H$^+$
v, Me$_2$CuLi-Et$_2$O

< 5% yield

Scheme 3

methylenebicyclo[5.4.0]undecan-8-ol **20** (47% yield), which was then oxidized with PCC in dichloromethane to furnish 6,6-dimethyl-2-methylene-8-oxobicyclo[5.4.0]undecan-8-one **21** in 78% yield (Scheme 5).

A subsequent treatment of bicycloundecan-8-one **21** with diethyl carbonate in the presence of NaH in dioxane at 80 °C gave ethyl ester **22** in 62% yield. A transformation of this keto-ester **22** into the corresponding α,β-unsaturated ester **23** was achieved by applying reductive deoxygenation through the hydridozirconium

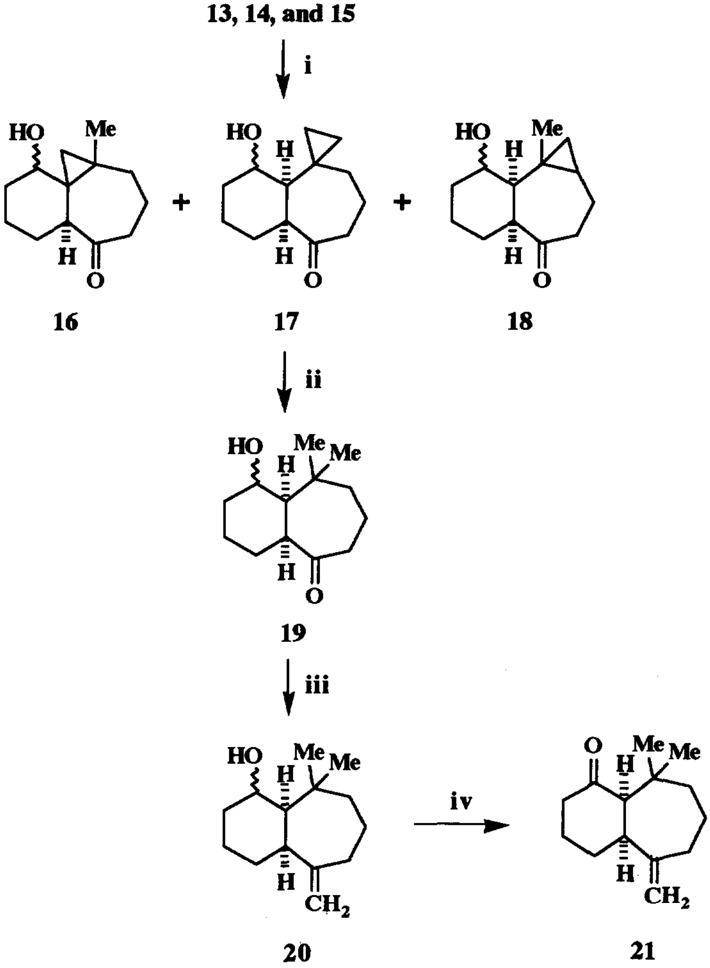


Reagents and Conditions: i, NaBH$_4$-MeOH, r.t.
ii, TBDMSCl-DMAP-Et$_3$N-CH$_2$Cl$_2$, r.t. iii, HgO-I$_2$-benzene
iv, hν > 300 nm v, Bu$_4$NF-THF, r.t.

Scheme 4

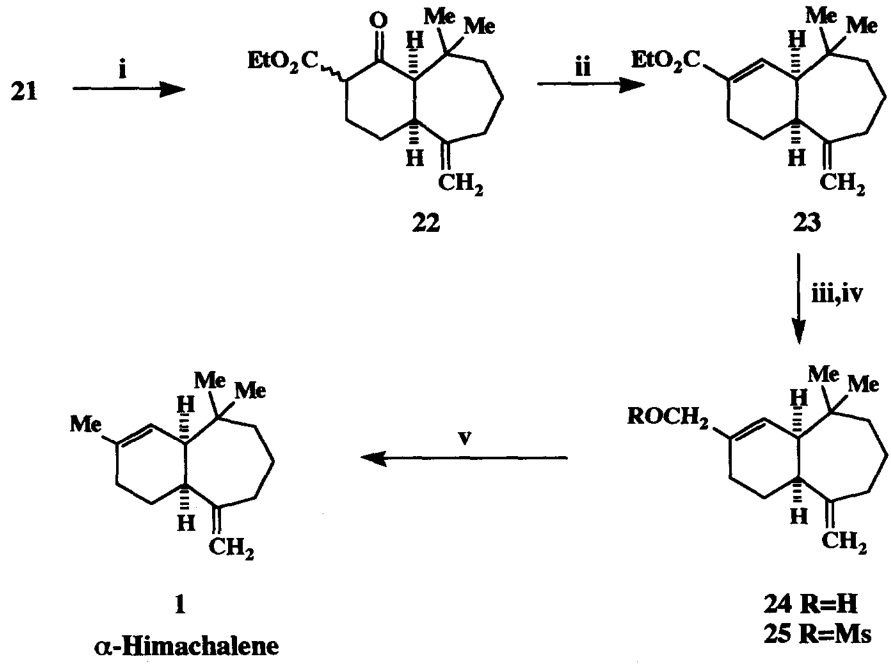
enolate; keto-ester **22** in THF was treated with lithium disopropylamide (LDA) to give the corresponding lithium enolate. The enolate in THF was then treated with chlorobis(cyclopentadienyl)hydridozirconium (Cp$_2$ZrHCl) according to the procedure published by Godfrey and Ganem[12] to give an α,β-unsaturated ester **23** in 42% yield as a single product.

The reduction of α,β-unsaturated ester **23** in diethyl ether with LiAlH$_4$ gave the corresponding alcohol **24** in 99% yield. The crude alcohol **24** was then transformed into the corresponding mesylate **25** (70%) by the standard method. The reduction of mesylate **25** with lithium triethylborohydride in THF at room temperature gave (±)-α-himachalene (1) in 42% yield (Scheme 6). The IR, ^{1}H-NMR, and mass spectra were identical with those of natural α-himachalene recorded in the literature.[4]



Reagents and Conditions: i, CH_2I_2-Et_2Zn-Et_2O, r.t. ii, H_2-PtO_2-AcOH, r.t. iii, Ph_3P^+-CH_3 Br^--BuLi, r.t. iv, PCC-CH_2Cl_2, r.t.

Scheme 5



Reagents and Conditions: i, (EtO)$_2$CO-NaH-dioxane, reflux ii, LDA-Cp$_2$ZrHCl, r.t. iii, LiAlH$_4$-Et$_2$O, r.t. iv, MsCl-Py v, LiEt$_3$BH-THF, r.t.

Scheme 6

EXPERIMENTAL

M.p.s were determined with a Yanagimoto m.p. apparatus. The IR spectra were determined for Nujol mulls with a JASCO IR 810 infrared spectrophotometer. The ^{1}H-NMR spectra were determined in CDCl$_3$ (SiMe$_4$ as internal reference) with a JEOL J-FX 270 spectrometer operating at 270 MHz, or with a Hitachi R-90H spectrometer operating at 90 MHz. The *J* values are in Hz. The high- and low-resolution mass spectra were recorded with a JEOL JMS-DX 303 mass spectrometer at the Faculty of Pharmaceutical Sciences of this University. PLC was carried out on Merck silica gel 60 PF$_{254}$. The photolysis was carried out in a Pyrex tube with a 100-W high-pressure Hg arc lamp.

Preparation of 2-Hydroxy-6-methyltricyclo[5.4.0.0^{2,6}]undecan-8-one* 4 *by [2+2] Photocycloaddition of Cyclohexenone* 2 *with 1-Methyl-2-trimethylsiloxy-1-cyclopentene* 3*, followed by Acid Hydrolysis. —— A solution of silyl enol ether **3** (2.01 g, 11.8 mmol) in benzene (14 mL) in a Pyrex vessel was flushed with nitrogen. To this solution was added enone **2** (0.14 mL); the solution was then irradiated for 12 h with a 500-W high-pressure Hg arc (EIKOSHA) while the solution was being cooled by water. At each 12 h interval additional enone **2** (each 0.14 mL; 4 times; total amounts; 0.7 mL) was added.

After removing the solvent from the solution, the residue was subjected to acid hydrolysis (as described above). A mixture of the obtained products was subjected to PLC (3:1 benzene-ethyl acetate) to give two fractions. The more mobile fraction (357 mg, 27%) was 3-(1'-methyl-2'-oxocyclopentyl)-cyclohexanone **5**. ν_{max}/cm^{-1} (neat) 1711 (6-membered ring C=O) and 1733 (5-membered ring C=O); δ (270MHz) 0.99 (3H, s, Me); *m/z* 194 (M^+, 3.7), 179 [$(M\text{-}Me)^+$, 5.1], 111 (24.8), 98 (100), 83 (35.6) and 55 (32.0%); (Found; M^+, 194.1295. $C_{12}H_{18}O_2$ requires *M*, 194.1307).

The less mobile fraction (438 mg, 33%) was 2-hydroxy-3-methyltricyclo$[5.4.0.0^{2,6}]$undecan-8-one **4**, which was an inseparable 1 : 1.5 : 2.5 mixture of *cis-cisoid-cis, cis-transoid-cis, and trans-transoid-cis* isomers. ν_{max}/cm^{-1} (neat) 3412 (OH) and 1703 (6-membered ring C=O); δ (270MHz) 1.01 (0.6H, s, Me), 1.03 (0.9H, s, Me), and 1.28 (1.5H, s, Me); *m/z* 194 (M^+, 3.7), 179 [$(M\text{-}Me)^+$, 2.3], 177 [$(M\text{-}OH)^+$, 2.4], 98 (100), 97 (49.7), and 41 (60.2%); (Found; M^+, 194.1334. $C_{12}H_{18}O_2$ requires *M*, 194.1307).

An Isomerization of the Isomeric Mixture of 2-Hydroxy-6-methyltricyclo$[5.4.0.0^{2,6}]$undecan-8-one 4 by aq. Potassium Hydroxide. —— To the isomeric mixture of [2+2] photoadducts **4** (872 mg, 4.49 mmol) in methanol (10 mL) was added a 5% methanolic potassium hydroxide solution (5 mL). The solution was stirred for 1.5 h at room temperature. Removal of the solvent by rotary evaporator gave a residue which was treated with water and 2N hydrochloric acid (pH 3-4). The mixture was extracted 5 times with diethyl ether. The combined ether solution was washed with water, brine, and dried over anhydrous Na_2SO_4. Removal of the solvent gave a 1:4 mixture of *cis-cisoid-cis* and *cis-transoid-cis* adducts. δ (270MHz) 1.01 (2.4H, s, Me of *cis-cisoid-cis*) and 1.28 (0.6H, s, Me of *cis-transoid-cis*).

β-Scission of the Alkoxyl Radicals generated from 2-Hydroxy-6-methyltricyclo$[5.4.0.0^{2,6}]$-undecan-8-one 4; A Ring Expansion. —— To a solution of cyclobutanol **4** (542 mg, 2.79 mmol) in benzene (120 mL) were added red mercury (II) oxide (1.24 g, 5.86 mmol) and iodine (1.47 g, 5.86 mmol). This solution was flushed with nitrogen and irradiated for 3 h (as described above). The photolyzed solution was worked up as described above to give a mixture of the products which was subjected to PLC (4:1 benzene-ethyl acetate) to give a 1:1 inseparable mixture of 6-methylbicyclo[5.4.0]undec-6-ene-2,8-dione **6** and 6-methylenebicyclo[5.4.0]undecane-2,8-dione **7** (167 mg, 31%). ν_{max}/cm^{-1} (neat) 1596 and 1677 (C=C-C=O), and 1709 (7-membered ring C=O); δ (270 MHz) 1.57 (1.5H, s, 6-Me), 4.81 (1H, s, one of the exomethylene protons), and 5.15 (1H, s, one of the exomethylene protons); *m/z* 192 (M^+, 68.1), 177 [$(M\text{-}Me)^+$, 26.6], 164 (45.2), 149 (45.8), 136 (50.6), 121 (54.4) 108 (100), 93 (66.5) and 79 (75.1%); (Found; M^+, 192.1123. $C_{12}H_{16}O_2$ requires *M*, 192.1150).

8-tert-Butyldimethylsiloxy-6-methyltricyclo$[5.4.0.0^{2,6}]$undecan-2-ol 9. —— To a solution of a 1:4 mixture of *cis-cisoid-cis* and *cis-transoid-cis* isomers of 2-hydroxy-6-methyltricyclo$[5.4.0.0^{2,6}]$undecan-8-one **4** (301 mg, 1.55 mmol) in methanol (10 mL) was added $NaBH_4$ (220 mg, 5.79 mmol). The solution was stirred for 18 h at room temperature. After removing of the solvent diethyl ether was added to the residue. The solution was then filtered, the solvent was removed by evaporation to give an isomeric mixture of 6-methyltricyclo$[5.4.0.0^{2,6}]$undecan-2,8-diols. To a solution of the diols in dichloromethane (10 mL) were added *tert*-butyldimethylsilyl chloride (737 mg, 4.89 mmol), 4-dimethylamino-pyridine (447 mg, 3.66 mmol) and triethylamine (0.29 mL) at room temperature. The solution was stirred for 66 h at room temperature. Removal of the solvent gave a residue which was subjected to PLC (5:1 hexane-ethyl acetate) to give 8-*tert*-butyldimethysiloxyl-6-methyl-tricyclo$[5.4.0.0^{2,6}]$undecan-2-ols **9** (225 mg, 47%). ν_{max}/cm^{-1} 3312 (OH); δ (270 MHz) 0.03 (6H, s, Me_2Si), 0.88 (9H, s, Me_3C), 1.57 (3H, s, 6-Me), and 3.82 (1H, ddd, *J* 11.4, 7.6, and 5.8, 8-H); *m/z* 310 (M^+, 0.26), 295 [$(M\text{-}Me)^+$, 0.48], 277 [$(M\text{-}Me\text{-}H_2O)^+$, 0.29], 253 [$(M\text{-}t\text{-}Bu)^+$, 11.7], 235 [$(M\text{-}t\text{-}Bu\text{-}H_2O)^+$, 2.05], 178 [$(M\text{-}TBDMSOH)^+$, 18.3], 98 (100), 81 (46.0), and 75 (78.9%); (Found: M^+, 310.2355. $C_{18}H_{34}O_2Si$ requires *M*, 310.2328).

β-Scission of the Alkoxyl Radical generated from the Hypoiodite of 8-tert-Butyldimethylsiloxy-6-methyltricyclo[5.4.0.0^{2,6}]undecan-2-ol 9. ——To a solution of 6-methyltricycloundecan-2-ol **9** (158 mg, 0.510 mmol) in benzene (25 mL) were added red mercury(II) oxide (221 mg, 1.02 mmol) and iodine (260 mg, 1.02 mmol). The solution was then flushed with a nitrogen and irradiated with a Pyrex-filtered light generated from a 100-W high-pressure Hg arc lamp for 4.5 h while being stirred and cooled by water. The solution was then filtered and the filtrate was washed with aq. sodium thiosulfate, water, and brine, successively, and dried over anhydrous Na_2SO_4. Removal of the solvent gave a product mixture which was subjected to PLC (4:1 hexane-ethyl acetate) to give a mixture (64 mg, 40%) of 8-*tert*-butyldimethylsiloxy-6-methylbicyclo[5.4.0]undec-6-en-2-one **10**, 8-*tert*-butyldimethylsiloxy-6-methylenebicyclo[5.4.0]undecan-2-one **11**, and 8-*tert*-butyldimethylsiloxy-6-methylbicyclo[5.4.0]undec-5-en-2-one **12**. The ratio of three products **10**, **11**, and **12** determined by ^{1}H NMR spectroscopy was 1.5 : 1 : 3. ν_{max}/cm^{-1} 1702 (C=O) and 1646 (C=C); δ (270 MHz) 0.01, 0.02 and 0.03 (6H, each s, Me_2Si), 0.83, 0.84, and 0.85 (9H, each s, Me_3C), 1.76 (1.65H, s, 6-Me of **12**), 1.83 (0.82H, s, 6-Me of **10**), 4.18 (0.73H, br s, 8-H of **11** and **12**), 4.72 (0.27H, t, *J* 2.54, 8-H of **10**), 4.85 and 4.86 (0.36H, s, C=CH_2 of **11**), and 5.73 (0.55H, br d, *J* 8.25, 5-H of **12**) *m/z* 308 (M^+, 0.28), 293 [$(M-Me)^+$, 2.1], 251 [$(M-Me_3C)^+$, 90.4], 75 (100), and 73 (69.1%); (Found; M^+, 308.2170. $C_{18}H_{32}O_2Si$ requires *M*, 308.2196).

Deprotection of 8-tert-Butyldimethylsilyloxy Group of Bicyclic Compounds 10, 11, and 12. —— To a solution of a mixture (32 mg, 0.103 mmol) of bicyclic compounds **10**, **11** and **12** in tetrahydrofuran (THF) (3 mL) was added a 1.0 M solution of tetrabutylammonium fluoride in THF (1.0 mL, 1.0 mmol). The solution was stirred for 15 h at room temperature. The solution was first washed with water, then brine, and finally dried over anhydrous Na_2SO_4. Removal of the solvent gave a product mixture which was subjected to PLC (3:1 hexane-ethyl acetate) to give a mixture (14 mg, 69%) of 8-hydroxy-6-methylbicyclo [5.4.0]undec-6-en-2-one **13**, 8-hydroxy-6-methylenebicyclo[5.4.0]undecan-2-one **14** and 8-hydroxy-6-methylbicyclo[5.4.0]undec-5-en-2-one **15** in a same ratio as that of the starting mixture. ν_{max}/cm^{-1} (neat) 3378 (OH), and 1701 (C=O); δ (270 MHz) 1.69 (1.65H, s, 6-Me of **13**), 1.81 (0.54H, s, 6-Me of **13**), 3.76 (0.55H, td, *J* 11.4 and 2.64, 8-H of **15**), 4.20-4.26 (0.45H, m, 8-H of **13** and **14**), 4.89 (0.18H, t, *J* 13.0, C=CH_2 of **14**), 5.00 (0.18H, br s, C=CH_2 of **14**), and 5.86 (0.55H, m, 5-H of **15**); *m/z* 194 (M^+, 49.8), 176 [$(M-H_2O)^+$, 55.6], 161 [$(M-H_2O-Me)^+$, 17.5], 123 (78.1), 109 (56.9), 95 (77.4), 91 (70.9), 79 (86.3), 67 (65.8), 55 (61.4) and 41 (100%) (Found; M^+, 194.1306. $C_{12}H_{18}O_2$ requires *M*, 194.1306).

Cyclopropanation of a Mixture of Bicycloundecenes and 6-Methylenebicycloundecane 13, 14 and 15. —— To a solution of mixture (39 mg, 0.20 mmol) of bicyclo[5.4.0]undecenes **13**, **14** and **15** in diethyl ether (1 mL) were added a 1.0 M solution (0.36 mL, 0.36 mmol) of diethylzinc in hexane and diiodomethane (0.09 mL, 1.11 mmol) dropwise under a nitrogen atmosphere. The solution was then stirred for 10 h. The solution was first washed with water, then brine, and finally dried over anhydrous Na_2SO_4. Removal of the solvent gave a product mixture which was subjected to PLC (3:1 hexane-ethyl acetate) to give a mixture of 9-hydroxy-6-methyltricyclo[6.4.0.0^{6,8}]dodecan-2-one **16**, spiro[cyclopropane-1,6'-8'-hydroxybicyclo[5.4.0]-undecan-2-one] **17**, and 9-hydroxy-7-methyltricyclo[6.4.0.0^{5,7}]-dodecan-2-one **18**. The yield of the mixture was 18 mg (43%). ν_{max}/cm^{-1} 3432 (OH) and 1700 (C=O); δ (270 MHz) 0.29 and 0.53 (3H, m, cyclopropane H), 1.01 (3H, s, 6-Me), and 4.08 (1H, m, 9-H of **16** and **18**. 8'-H of **17**); *m/z* 208 (M^+, 6.1), 190 [$(M-H_2O)^+$, 9.1], 175 [$(M-H_2O-Me)^+$, 12.0], 97 (65.2), 79 (81.0), 67 (65.7), 55 (77.1) and 41 (100%); (Found M^+, 208.1465. $C_{13}H_{20}O_2$ requires *M*, 208.1464).

6,6-Dimethyl-8-hydroxybicyclo[5.4.0]undecan-2-one 19. —— A solution of a mixture of tricyclododecan-2-ones and bicyclo[5.4.0]undecan-2-one **16**, **17**, and **18** (21 mg, 0.101 mmol) in acetic acid (3 mL) was hydrogenated in the presence of platinum oxide (20 mg) at atmospheric pressure for 20 h while being stirred at room temperature. The solution was filtered. To the filtrate was added water; the aqueous solution was extracted with diethyl ether, three times. Removal of the solvent gave an oil which was subjected to PLC (3:1 hexane-ethyl acetate) to give 6,6-dimethyl-8-hydroxybicyclo[5.4.0]-undecan-2-one **19** (15 mg, 71%). νmax/cm^{-1} 3344 (OH) and 1704 (C=O); δ (270 MHz) 0.94 (3H, s, 6-Me), 1.05 (3H, s, 6-Me), and 3.80 (1H, m, 8-H); *m/z* 210 (M^+, 13.4), 195 [$(M\text{-}Me)^+$, 58.4], 178 [$(M\text{-}Me\text{-}H_2O)^+$, 12.6], 97 (46.1), 79 (75.3), 67 (63.0), 55 (67.6) and 41 (100%); (Found; M^+, 210,1624. $C_{13}H_{22}O_2$ requires *M*, 210.1620)

***6,6-Dimethyl-2-methylenebicyclo[5.4.0]undecan-8-ol* 20.** —— To methyltriphenylphosphonium bromide (130 mg, 0.364 mmol) in diethyl ether (3 mL) under a nitrogen atmosphere were added 1M hexane solution of butyllithium (0.22 mL, 0.374 mmol) and then bicyclo[5.4.0]undecan-2-one **19** (30 mg, 0.143 mmol) in diethyl ether (1 mL). The solution was stirred for 12 h at room temperature. To the solution was added water; the solution was then filtered. The filtrate was first washed with water, then brine, and finally dried over anhydrous Na_2SO_4. Removal of the solvent gave a residue which was subjected to PLC (5:1 hexane-ethyl acetate) to give 6,6-dimethyl-2-methylenebicyclo[5.4.0]undecan-8-ol **20** (14 mg, 47%). ν_{max}/cm^{-1} 3318 (OH) and 1640 (C=C); δ (270 MHz) 0.93 (3H, s, 6-Me), 1.07 (3H, s, 6-Me), 3.82 (1H, td, *J* 11.5 and 2.64, 8-H), 4.72 (1H, s, one of the $C{=}CH_2$), and 4.79 (1H, s, one of the $C{=}CH_2$) (Found; M^+, 208, 1837. $C_{14}H_{24}O$ requires *M*, 208, 1828).

***6,6-Dimethyl-2-methylenebicyclo[5.4.0]undecan-8-one* 21.** —— To a solution of 6,6-dimethyl-2-methylenebicyclo[5.4.0]undecan-8-ol **20** (31 mg, 0.149 mmol) in dichloromethane (4 mL) was added PCC (86 mg, 0.399 mmol). The solution was stirred for 1 h at room temperature. After removing the solvent diethyl ether was added (5 mL) to the dark residue. The solution was then filtered and the filtrate was first washed with water, then brine, and finally dried over anhydrous Na_2SO_4. Removal of the solvent gave a residue which was subjected to PLC (4:1 hexane-ethyl acetate) to give 6,6-dimethyl-2-methylenebicyclo[5.4.0]undecan-8-one **21** (24 mg, 78%). ν_{max}/cm^{-1} 1701 (C=O) and 1646 (C=C); δ (270 MHz) 0.93 (3H, s, 6-Me), 1.10 (3H, s, 6-Me), 4.70 (1H, s, one of the $C{=}CH_2$), and 4.76 (1H, s, one of the $C{=}CH_2$) (Found; M^+, 206, 1600. $C_{14}H_{22}O$ requires *M*, 206.1671).

***Ethyl 6,6-Dimethyl-2-methylene-8-oxobicyclo[5.4.0]undecane-9-carboxylate* 22.** —— To sodium hydride (60%) (11 mg, 0.275 mmol), washed with hexane, in dioxane (5 mL) was added diethyl carbonate (0.03 mL, 0.25 mmol). The solution was then heated at 80 °C. To this solution was added bicyclo[5.4.0]undecan-8-one **21** (25 mg, 0.12 mmol) in dioxane (2 mL) dropwise. The solution was then heated at 80 °C for 2 h while being stirred. To the solution was added water. The solution was extracted with diethyl ether three times. The combined extracts were first washed with water, then brine, an finally dried over anhydrous Na_2SO_4. Removal of the solvent gave a residue which was subjected to PLC (3:1 hexane-ethyl acetate) to give ethyl 6,6-dimethyl-2-methylene-8-oxobicyclo[5.4.0]undecane-9-carboxylate **22** (21 mg, 62%). ν_{max}/cm^{-1} 1741 (COOEt), 1702 (6-menbered ring C=O), and 1654 (C=C). δ (270 MHz) 0.90 (3H, s, 6-Me), 1.01 (3H, s, 6-Me), 1.23 (3H, t, *J* 6.93, OCH_2*Me*), 3.51 (1H, dd, *J* 8.59 and 2.93, 9-H), 4.10 (2H, q, *J* 6.93, OC*H_2*Me), 4.68 (1H, s, one of $C{=}CH_2$), and 4.75 (1H, s, one of $C{=}CH_2$) (Found; M^+, 278.1897. $C_{17}H_{26}O_3$ requires *M*, 278.1880).

***Ethyl 6,6-Dimethyl-2-methylenebicyclo[5.4.0]undec-8-ene-9-carboxylate* 23.** —— To a solution of diisopropylamine (0.01 mL, 0.071 mmol) in THF (2 mL) was added a 1.7 M hexane solution of butyllithium (0.04 mL, 0.068 mmol) at 0 °C. The solution was stirred for half an hour at 0 °C. To this solution was added ethyl 8-oxobicyclo-[5.4.0]undecane-9-carboxylate **22** (10 mg, 0.036 mmol) in THF (1 mL) at 0 °C. The solution was stirred for 20 min at 0 °C. To this solution was added Cp_2ZrHCl (18 mg, 0.07 mmol) in THF (2 mL) at 0 °C. The solution was then stirred for 2 h at room temperature. To the solution was added hexane

(10mL) and the mixture was filtered. The filtrate was first washed with water, then brine, and finally dried over anhydrous Na_2SO_4. Removal of the solvent gave a residue which was subjected to PLC (3:1 hexane-ethyl acetate) to give ethyl 6,6-dimethyl-2-methylenebicyclo[5.4.0]undec-8-ene-9-carboxylate **23** (4 mg, 42%). ν_{max}/cm^{-1} (neat) 1623 and 1726 (C=C-COOEt) and 1642 (C=C); δ (270 MHz) 0.94 (3H, s, 6-Me), 1.00 (3H, s, 6-Me), 1.23 (3H, t, *J* 6.93, OCH_2*Me*), 4.08 (2H, q, *J* 6.9, OCH_2Me), 4.68 (1H, s, one of the $C=CH_2$), and 6.67 (1H, *J* 5.37, 8-H) (Found; M^+, 262.1946. $C_{17}H_{26}O_2$ requires *M*, 262.1934).

***6,6-Dimethyl-9-hydroxymethyl-2-methylenebicyclo[5.4.0]undec-8-ene* 24.** —— To a solution of bicyclo[5.4.0]undec-8-ene-9-carboxylate **23** (31 mg, 0.096 mmol) in diethyl ether (4 mL) was added $LiAlH_4$ (5 mg, 0.133 mmol). The solution was stirred for 2 h at room temperature. To the solution was first added diethyl ether and then a small amount of aq. sodium thiosulfate. The solution was then filtered; the filtrate was first washed with water, then brine and finally dried over anhydrous Na_2SO_4. Removal of the solvent gave a crude bicyclic alcohol **24** (26 mg, 99%). ν_{max}/cm^{-1} (neat) 3300 (OH). This was immediately subjected to the next step.

6,6-Dimethyl-9-mesyloxymethyl-2-methylenebicyclo-[5.4.0]undec-8-ene 25. ——To a solution of crude bicyclic alcohol **24** in pyridine (4 mL) was added methanesulfonyl chloride (0.03 mL, 0.388 mmol). The solution was stirred for 2 h at room temperature. To the solution was added water; the solution was then extracted with diethyl ether five times. The combined organic layers were washed with 2N hydrochloric acid, water, and brine successively and then dried over anhydrous Na_2SO_4. Removal of the solvent gave a product which was subjected to PLC (10:1 hexane-ethyl acetate) to give mesylate **25** (20 mg, 70%) as a gum. This mesylate was immediately used in the next step.

***(±)-α-Himachalene* 1.** —— To a solution of mesylate **25** (20 mg, 0.067 mmol) in THF (4 mL) was added 1M solution of lithium triethylborohydride (0.1 mL, 0.10 mmol). The solution was stirred for 20 h at room temperature. To the solution was added water; the solution was then extracted with diethyl ether three times. The combined organic layers were first washed with water, then brine, and finally dried over anhydrous Na_2SO_4. Removal of the solvent gave a crude product which was purified by PLC (benzene) to give (±)-α-himachalene (**1**) (6 mg, 42%). The IR, ^{1}H-NMR, and mass spectra of this synthetic α-himachalene were in full agreement with the published spectral data of the natural α-himachalene. δ (270 MHz) 0.99 (3H, s, 6-Me), 1.10 (3H, s, 6-Me), 1.73 (3H, s, 9-Me), 4.70 (2H, br s, $C=CH_2$), and 5.40 (1H, br s, 8-H). (Found; M^+, 204.1870. $C_{15}H_{24}$ requires *M*, 204.1879).

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