Terpenes and Related Systems. IX.[1] A Synthesis of (+)-Himachalene Dihydrochloride and (+)-*ar*-Himachalene

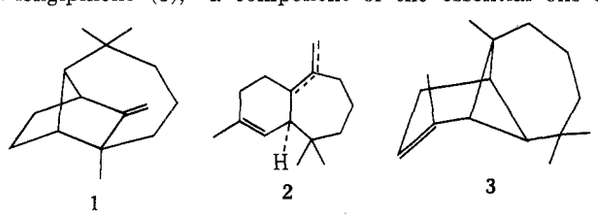
Goverdhan Mehta* and Surinder K. Kapoor[2]

Department of Chemistry, Indian Institute of Technology, Kanpur-208016, U. P., India

Received December 13, 1973

A seven-step synthesis of (+)-himachalene dihydrochloride and (+)-*ar*-himachalene from the tricyclic sesquiterpene *longifolene* is described. The successful route involved the preparation of a key bifunctional longibornane derivative (12) as the initial target. This was obtained from ω-bromolongifolene (9) *via* an acid-catalyzed rearrangement involving an intramolecular 1,5-hydride shift. The bicyclic homodecalinenones **22**, **23**, and **24** were obtained from **12** in a novel base-catalyzed fragmentation reaction that removes the carbon-to-carbon span which gives longibornane its tricyclic bridged structure. Elaboration of β,γ-unsaturated ketone **22** to the title compounds **30** and **31** was achieved through Wolff-Kishner reduction followed by either hydrochlorination or aromatization. Attempts to convert enones **22** and **24** to α-longipinene (**3**) are also included.

The diversity of carbocyclic structures replete with a wide variety of functionalities makes sesquiterpenes attractive and formidable targets of chemical synthesis. It is not surprising, therefore, that intense activity[3] has been witnessed in this area during the past few years. In a majority of the reported syntheses, the C_{15} network of sesquiterpenes has been created by a combination or elaboration of small synthons (fragments) employing routine or novel reactions and reagents. An alternate approach utilizing naturally occurring sesquiterpenes as synthons for complex synthesis, on the other hand, has only received limited attention.[4] Such an approach, besides furnishing optically active compounds, is likely to be economical and would essentially require the reorganization of a carbocyclic network through suitable bond-breaking and -making processes. The efficacy of such a synthetic approach is exemplified here by considering the possibility of employing the readily available tricyclic hydrocarbon longifolene (**1**) for the synthesis of α- and β-himachalenes (**2**),[5] chief constituents of the essential oil of *Cedrus deodar* Loud., and α-longipinene (**3**),[6] a component of the essential oils of

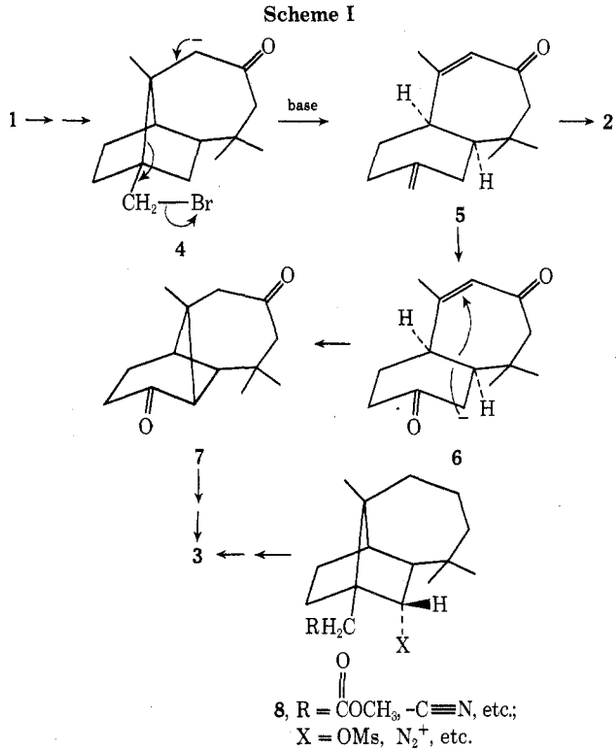


1 2 3

α = exocyclic olefin
β = endocyclic olefin

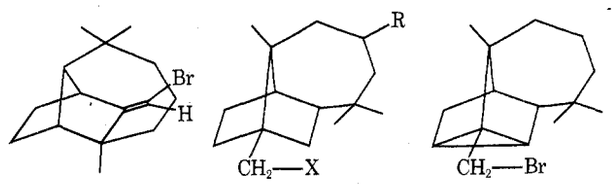
Pinus longifolia Roxb. and *Pinus silvestris* L. The choice of longifolene (**1**) for the contemplated synthesis is dictated by its close biogenetic relationship[7] with **2** and **3**. The synthetic route adopted and executed here constitutes a reversal of the biogenetic pathway in terms of the gross carbocyclic skeletons, *i.e.*, longifolene → longibornane type → himachalene type. The pathways by which **1** can eventuate in **2** and **3** by logical and conceptually plausible steps are shown in Scheme I. The synthetic strategy depicted in Scheme I consists of the preparation of suitably functionalized longibornane precursors **4** and **8** followed by key transformations involving a base-catalyzed fragmentation **4** → **5**,[8,9] an intramolecular Michael addition **6** → **7**,[10] and solvolytic ring contraction **8** → **3**.[11] The other subordinate steps in the scheme are easy to comprehend and can be carried out through well-established reactions. A particularly hopeful feature of the fragmentation of the tricyclic longibornane derivative **4** was the expectation that removal of the carbon bridge would lead to a cis-fused homodecalin corresponding to the stereochemistry of

Scheme I



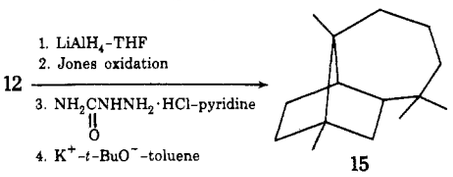
naturally occurring himachalenes. In this paper is described the synthesis of (+)-himachalene dihydrochloride (**30**)[12] and (+)-*ar*-himachalene (**31**)[13] and preparation of synthons related to the synthesis of α-longipinene (**3**) from longifolene through the reaction sequence **1** → **4** → **5** → **30**.

(*E*)-ω-Bromolongifolene (**9**), readily available[1e] from **1**, appeared to be ideally suited as a starting material which has sufficient functionality, properly disposed, for elaboration into bifunctional longibornane derivative **12**. Reac-

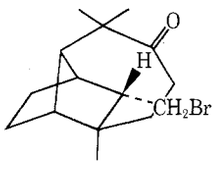


9 10, X = Br; R = OCCF3 11, X = Br; R = OH 12, X = Br; R = =O 13, X = H; R = OH 14

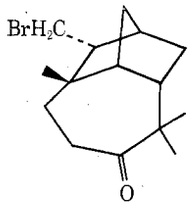
Scheme II



tion of **9** with trifluoroacetic acid (TFA) furnished a complex mixture of hydrocarbons and a trifluoroacetate (**10**). Hydrolysis with alcoholic potassium hydroxide and purification on a silica gel column gave a hydrocarbon fraction followed by the secondary alcohol **11**, mp 65–66°. The hydrocarbon fraction consisted of at least six components and only the major component (~50%) was obtained pure and characterized on the basis of spectral evidence (see Experimental Section) as longicyclenyl bromide (**14**).[15] Oxidation of alcohol **11** with Jones reagent resulted in the isolation of two crystalline ketones, mp 72 and 103°, which could be readily separated by column chromatography. That the low-melting ketone possessed the requisite structure **12** was indicated by its carbonyl absorption in the ir spectrum at 1700 cm^{-1} and signals in the pmr spectrum for three quaternary methyls (δ 0.91, 0.97, and 1.07), a bromomethyl group (δ 3.5, AB quartet, J = 12 Hz), and two deshielded methylene groups flanking the carbonyl (δ 2.4, AB quartet, J = 11 Hz). The structure of this key ketone (**12**) required for the fragmentation reaction was further verified by an unambiguous conversion to the known[16] hydrocarbon longibornane (**15**) through steps outlined in Scheme II. This correlation of **12** with **15** rules out of contention alternate structures **16** and **17** for the

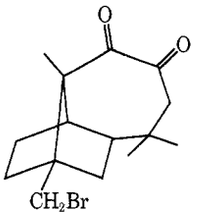


16

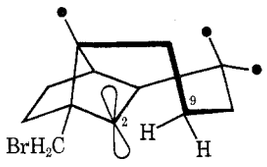


17

low-melting ketone.[17] The high-melting ketone analyzed for $C_{15}H_{21}O_2Br$ and showed ir absorption due to carbonyl group at 1720 cm^{-1} (broad). Its pmr spectrum exhibited quaternary methyl singlets at δ 1.01, 1.1, and 1.14, a bromomethyl as a doublet of doublets at δ 3.60 (J = 10 Hz), and another doublet of doublets due to methylene flanking the carbonyl at δ 2.51 (J = 12 Hz). This spectral data clearly indicated a diketone structure (**18**) for the high-



18

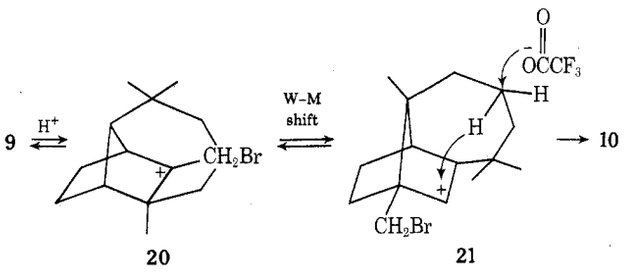


19, —●, CH_3 groups

melting ketone and was fully supported[18] by an independent X-ray crystal structure determination.

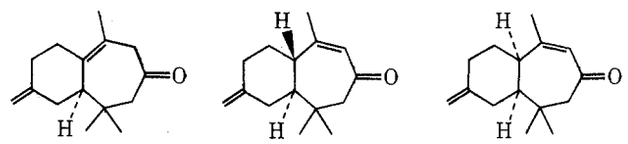
The formation of trifluoroacetate **10** from the rearrangement of ω-bromolongifolene (**9**) in TFA can be rationalized in terms of the protonation of **9** to equilibrating ions **20** and **21** followed by a precedented[1b,19] transannular 1,5-hydride migration and capture by the nucleophile (Scheme III). This intramolecular hydride shift is facilitated by the favorable conformation (**19**) of the eight-membered ring resulting in the proximity of the hydrogen at C_9 with the sp^2 center at C_2. Proton loss from ions **20** and **21** accounts for the formation of the tetracyclic bromide **14**.

Scheme III



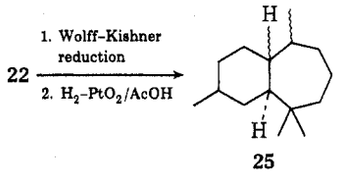
20 21

With the structure of longibornane precursor **12** firmly established and its adequate supply assured, we turned our attention toward the key fragmentation step (Scheme I), which to our expectation proved extremely facile and easy to execute. Indeed, exposure of **12** to methylsulfinyl carbanion[20] at room temperature and quenching with water resulted in the formation of three ketones A, B, and C in a ratio of 15:4:1 in 96% yield. The major ketone A could be conveniently isolated by column chromatography and is formulated as the unconjugated homodecalin ketone (**22**).[21] The structure of this product is indicated by



22 23 24

the lack of uv absorption, the presence of unconjugated carbonyl (1705 cm^{-1}) and terminal methylene (3100, 1600, 890 cm^{-1}) in the ir spectrum, and the pmr absorption (Figure 1, two quaternary methyls, a vinylic methyl, and two olefinic protons). The ketone B was clearly an α,β-unsaturated ketone, as revealed by its uv spectrum [λ_{max} (MeOH) 244 nm] and exhibited complimentary carbonyl absorption (1640 cm^{-1}) in the ir spectrum. The pmr spectrum (Figure 2, two quaternary methyls, a vinylic methyl, two terminal methylene protons, and a vinylic proton) was fully consistent with the gross structure **23**. The trans stereochemistry at the ring junction in **23** was established through equilibration studies (*vide infra*). The minor ketone C which had earlier[1d] eluded isolation but whose presence was vital to our contemplated internal Michael addition (Scheme I) in fact turned out to be the cis-fused α,β-unsaturated ketone **24**. Its structure follows from its uv spectrum [λ_{max} (MeOH) 244 nm], carbonyl (1650 cm^{-1}) and terminal methylene absorption in the ir spectrum, and pmr data (Figure 3, two quaternary methyls, a vinylic methyl, two terminal methylene protons, and a vinylic proton). The gross carbocyclic structure of the ketones **22**, **23**, and **24** was ascertained by the transformation of the major ketone **22** into the saturated hydrocarbon **25** *via* Wolff-Kishner reduction and catalytic hydrogenation. The compound **25** was found to be similar to the parent hydrocarbon himachalane[5] obtained from the reduction of natural β-himachalene.



25

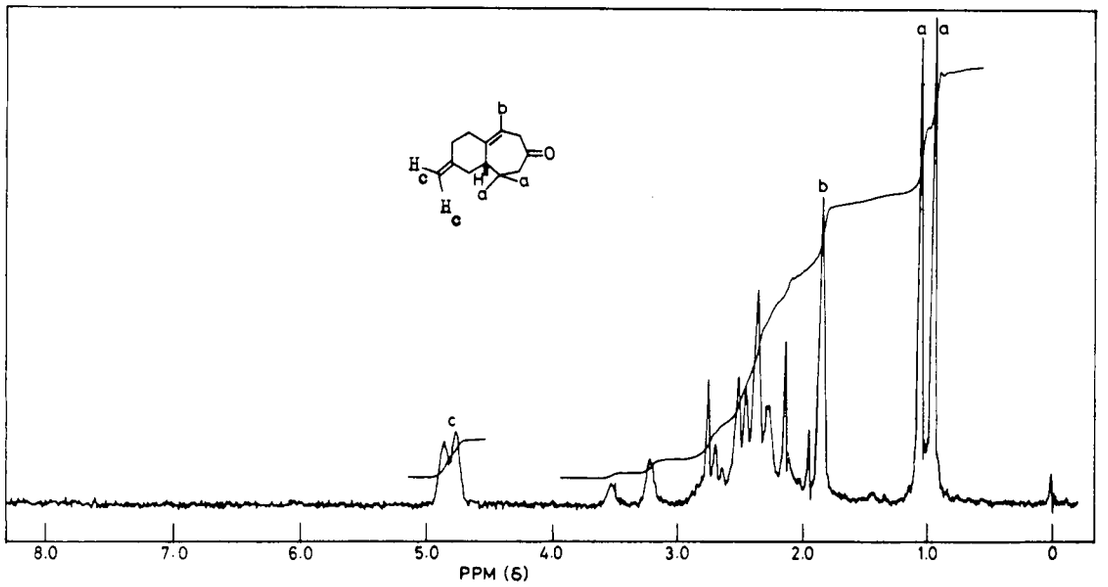


Figure 1. Pmr spectrum (60 MHz) of β,γ-unsaturated ketone **22**.

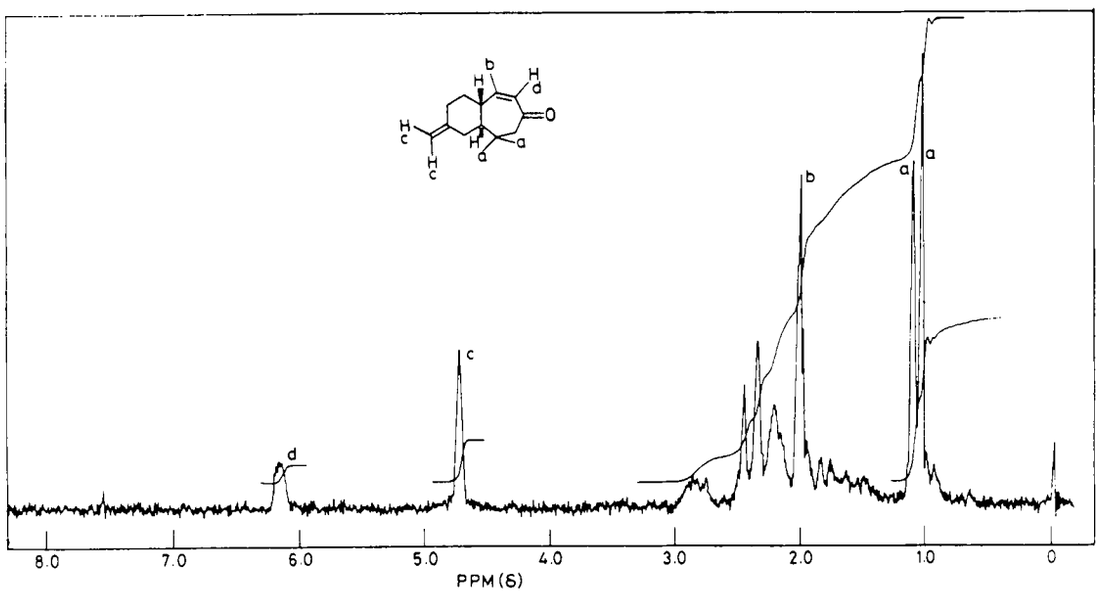


Figure 2. Pmr spectrum (60 MHz) of trans α,β-unsaturated ketone **23**.

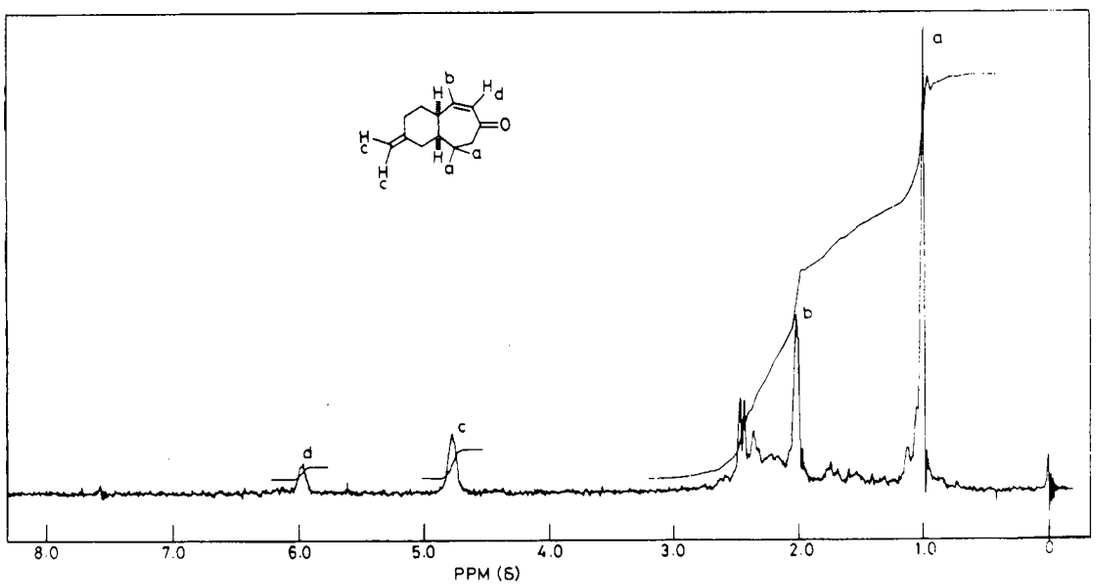
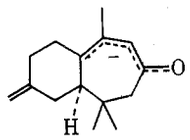


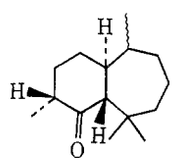
Figure 3. Pmr spectrum (60 MHz) of cis α,β-unsaturated ketone **24**.

The formation of structurally related ketones **22**, **23**, and **24** in the fragmentation reaction suggests that they are derived from **26** through the base-catalyzed equilibra-

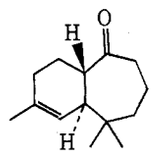


26

tion under experimental conditions. This contention is substantiated by the fact that when pure ketones **22**, **23**, or **24** or their mixtures were equilibrated with methylsulfinyl carbanion in DMSO, the product consisted of the three ketones in the same ratio in which they were originally isolated from the fragmentation reaction. In the light of these equilibration studies, the α,β-unsaturated ketone **23** predominating under equilibrium conditions is assigned the more stable trans stereochemistry at the ring junction. The greater stability of *trans*-perhydrobenzosuberone over the corresponding cis isomer has been experimentally established.[22] In the himachalene series itself the trans isomers **27** and **28** have been shown[12b,23,24] to



27

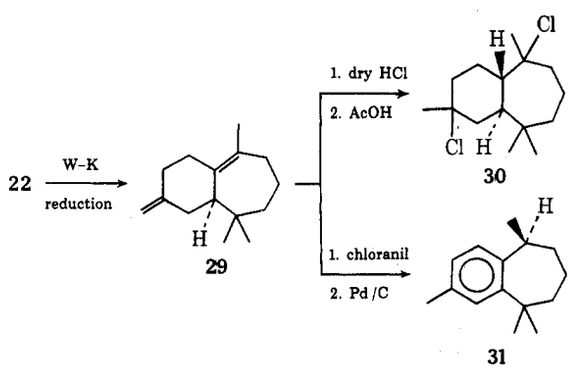


28

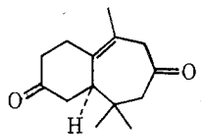
predominate over their cis isomers under equilibrium. The conjugated ketone **24** present in trace amounts only is, therefore, recognized as the less stable cis isomer.

The β,γ-unsaturated ketone **22** was now converted to the target compounds **30** and **31** through the reaction sequence summarized in Scheme IV. Thus, Wolff-Kishner reduction of **22** and purification ($AgNO_3$–silica gel) gave himachalene isomer **29**. A passage of a stream of dry HCl gas through an acetic acid solution of **29** led to the isolation of (+)-himachalene dihydrochloride (**30**), mp 118–119°, indistinguishable (mixture melting point, ir, $[\alpha]_D$) from the material prepared from natural α- and β-himachalene. Since himachalene dihydrochloride (**30**) has already been converted[12a] into β-himachalene, this also constitutes a formal synthesis of the latter. Dehydrogenation of **29** with chloranil followed by aromatization over Pd/C gave (+)-*ar*-himachalene (**31**) found identical (ir, nmr) with the naturally occurring material. The *S* configuration (**31**) of (+)-*ar*-himachalene at the asymmetric center is based on its $[\alpha]_D$ of +7.7°, which is comparable to the $[\alpha]_D$ of +5.90° of (+)-*ar*-himachalene prepared[14] from (+)-*ar*-turmerone, a compound of well-established absolute stereochemistry.

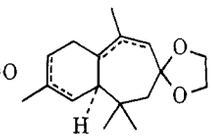
Scheme IV



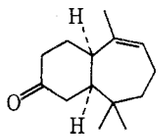
Finally, it was of obvious interest to attempt the transformation of ketones **22**–**24** to α-longipinene (**3**). Several attempts to selectively ozonize the ketone **22** to the enedione **32** required for the internal Michael addition met with failure and resulted in the formation of highly polar, intractable material. Efforts to ketalize the carbonyl function in **22** prior to ozonolysis led to the isomerization of the exocyclic double bond and formation of undesired ketal mixture **33**. Similarly, attempted preparation of enone **34** for a Lewis acid catalyzed Stork–Grieco type[25] cyclization to a bridged cyclobutane derivative also proved futile.



32



33



34

Experimental Section[26]

(*E*)-ω-Bromolongifolene (9). This was prepared according to the previously reported[1c] procedure. The material used for the present investigation had bp 120–125° (6 mm); mp 40–41°; $n^{35}D$ 1.5315; and $[\alpha]_D$ +52.06° (c 1.96).

Rearrangement of (*E*)-ω-Bromolongifolene (9) in Trifluoroacetic Acid. A solution of (*E*)-ω-bromolongifolene (12 g) in 25 ml of methylene chloride was slowly added to a cooled (5–10°) solution of trifluoroacetic acid (50 ml) over a period of 15 min with vigorous stirring. The stirring was continued for 4 hr at room temperature (35°) after which the reddish-brown reaction mixture was quenched by pouring into iced sodium bicarbonate solution. The product was extracted with ether (two 150-ml portions), washed with brine, and dried. Removal of solvent gave 14.8 g of an oily mixture of hydrocarbons and trifluoroacetate **10**, ir 1775 (ester carbonyl) and 1230 cm^{-1}.

Base Hydrolysis of (*E*)-ω-Bromolongifolene Rearrangement Product. The above mixture (14.8 g) was taken up in 40 ml of ethanol and potassium hydroxide (3 g) in 30 ml of water was added. After stirring for 8 hr at ambient temperature the reaction mixture was diluted with water, extracted with ether (three 100-ml portions), washed with brine, and dried and solvent was evaporated to furnish a viscous residue (12 g). This material was adsorbed on a silica gel (200 g) column and readily separated into a hydrocarbon fraction by successive elution with petroleum ether and benzene. Fraction 1 (4 g, 27%), bp 110–115° (2 mm), was revealed to be a mixture of seven components by vpc analysis. The major component (~50%) was isolated by preparative layer chromatography (20 × 20 cm plates, solvent system petroleum ether) and found to be the tetracyclic bromide **14**:[27] $n^{30}D$ 1.5584; ir (neat) (cyclopropane CH) 845 cm^{-1} (tricyclene type nucleus); pmr (CCl_4) δ 0.83 (CCH_3, 3 H, s), 0.88 (CCH_3, 6 H, s), 3.41 (CCH_2Br, 2 H, q, J = 9 Hz), 0.72 (cyclopropane, 1 H, s), 0.95 (cyclopropane, 1 H, s). *Anal.* Calcd for $C_{15}H_{23}Br$; C, 63.60; H, 8.12. Found: C, 63.82; H, 8.54.

Fraction 2 (6 g, 53%) solidified on standing and was twice sublimed at 90° (2 mm) to furnish white, waxy crystals of bromo alcohol **11**: mp 65–66°; $[\alpha]_D$ +23.5° (c 1.47); ir (KBr) 3300 (hydroxyl), 1250, 1060, 1040 cm^{-1}; pmr (CCl_4) δ 0.95 (CCH_3, 6 H, s), 1.03 (CCH_3, 3 H, s), 3.45 (CCH_2Br, 2 H, q, J = 12 Hz), 4.05 (HCOH, 1 H, m), *Anal.* Calcd for $C_{15}H_{25}OBr$: C, 59.80; H, 8.36. Found: C, 59.53; H, 8.05.

Jones Oxidation[29] of Bromo Alcohol 11. A stirred solution of 5.4 g of **11** in 60 ml of acetone was treated dropwise at room temperature with Jones reagent (50 ml) until the brown color persisted. The mixture was stirred for 5 hr, diluted with water, and extracted with ether (two 100-ml portions). The organic layer was successively washed with aqueous sodium carbonate and brine and dried. Removal of solvent gave a semisolid residue (4.7 g) which was adsorbed on a silica gel (200 g) column. Elution with petroleum ether–benzene (60:40) afforded 1.5 g (27%) of the crystalline diketone **18**. Recrystallization from petroleum ether gave pale-colored, stout crystals: mp 103°; $[\alpha]_D$ −47.6° (c 2.99); uv λ_{max} (MeOH) 310 nm (ϵ 52); ir (KBr) 1710 (carbonyl), 995, 800 cm^{-1}; pmr (CCl_4) δ 1.01 (CCH_3, 3 H, s), 1.11 (CCH_3, 3 H, s), 1.14 (CCH_3, 3 H, s), 3.60 (CCH_2Br, 2 H, q, J = 10 Hz), 2.51 [$-C(=O)CH_2-$, 2 H, q, J = 12 Hz]. *Anal.* Calcd for $C_{15}H_{21}O_2Br$: C, 57.52; H, 6.76. Found: C, 57.38; H, 6.5.

The semicarbazone of ketone **18** was prepared by the pyridine method and crystallized from ethanol as colorless needles, mp 218–219°. *Anal.* Calcd for $C_{16}H_{24}O_2N_3Br$: C, 51.89; H, 6.48; N, 11.35. Found: C, 51.75; H, 6.70; N, 11.77. Further elution of the column with petroleum ether–benzene (40:60) afforded 3 g (55%) of crystalline ketone **12**. Recrystallization from petroleum ether gave an analytical sample of bromo ketone **12**: mp 72°; $[\alpha]_D$ +47.7° (*c* 5.33); uv λ_{max} (MeOH) 290 nm (ϵ 46); ir (KBr) 1700 (carbonyl), 1300, 920 cm^{-1}; pmr (CCl_4) δ 0.91 (CCH_3, 3 H, s), 0.97 (CCH_3, 3 H, s), 1.07 (CCH_3, 3 H, s), 3.5 (CH_2Br, 2 H, q, J = 12 Hz). *Anal.* Calcd for $C_{15}H_{23}OBr$: C, 60.21; H, 7.75. Found: C, 60.60; H, 7.31.

A portion of the ketone **12** was converted to the semicarbazone derivative by the pyridine method and recrystallized from ethanol to give colorless, needle-shaped crystals, mp 222–223°. *Anal.* Calcd for $C_{16}H_{26}ON_3Br$: C, 53.93; H, 7.30; N, 11.79. Found: C, 54.36; H, 6.9; N, 11.94.

Lithium Aluminum Hydride Reduction of Bromo Ketone 12. The bromo ketone (500 mg) in tetrahydrofuran (5 ml) was slowly added to a stirred slurry of lithium aluminum hydride (200 mg) in dry tetrahydrofuran (20 ml). The stirring under reflux was continued for 7 days and the complex was decomposed by careful addition of ice-cold water. The organic product was isolated by extraction with ether (two 50-ml portions), washed with brine, and dried. Removal of solvent gave 350 mg of a viscous oil consisting of an epimeric mixture of longibornan-9-ols.

Longibornane (1,4,4,8-Tetramethyltricyclo[6.3.0.0^{3,9}]undecane 15. To a stirred solution of the above alcohols in 5 ml of acetone was added Jones reagent dropwise till the yellow color persisted. The reaction mixture was further stirred for 0.5 hr and worked up as described above to give a pale yellow oil (350 mg). This material was adsorbed on a silica gel (10 g) column and eluted with petroleum ether–benzene (80:20) to give longibornan-9-one (270 mg, 74%): ir (neat) 1698 cm^{-1} (carbonyl); pmr ($CDCl_3$) δ 0.86 (CCH_3, 3 H, s), 0.88 (CCH_3, 6 H, s), 1.05 (CCH_3, 3 H, s). To a solution of the above ketone (80 mg) in 2 ml of ethanol was added a solution of semicarbazide hydrochloride (50 mg) in 1 ml of water containing a few drops of pyridine. The mixture was left overnight and the solid was filtered. Recrystallization from ethanol gave 60 mg of white needles, mp 213–214°.

The semicarbazone of longibornan-9-one (200 mg) and potassium *tert*-butoxide[30] (250 mg) in dry toluene (10 ml) were refluxed for 24 hr. The reaction mixture was poured into water and the organic layer was separated. Removal of solvent and filteration of a petroleum ether solution through silica gel furnished 70 mg of hydrocarbon longibornane (**15**). The ir spectrum of this material was found indistinguishable from that of an authentic sample[31] of longibornane.

Fragmentation of Ketone 12 with Methylsulfinyl Carbanion. A solution of methylsulfinyl carbanion in 20 ml of DMSO was prepared under nitrogen atmosphere according to Corey's procedure from 2 g of sodium hydride (50% dispersion in mineral oil). To this reagent was added a solution of 5 g of bromo ketone **12** in 20 ml of DMSO with the aid of a hypodermic syringe and the reaction mixture was stirred at room temperature for 0.5 hr. The reaction mixture was diluted with water and extracted with petroleum ether (two 100-ml portions). The organic phase was washed with brine, dried, and freed of solvent to give 3.6 g (96%) of an oily mixture of ketones. This material was adsorbed on a silica gel (100 g) column and chromatographed. Elution with petroleum ether–benzene (60:40) afforded 2.7 g (75%) of the major ketone **22**: bp 110–120° (0.6 mm); $n^{30}D$ 1.5215; $[\alpha]_D$ +12.32° (*c* 2.75); uv λ_{max} (MeOH) 296 nm (ϵ 160); ir (neat) 1705 (unconjugated carbonyl), 3100, 1600, 890 cm^{-1} (terminal methylene); pmr (CCl_4) δ 0.93 (CCH_3, 3 H, s), 1.05 (CCH_3, 3 H, s), 1.84 ($H_3CC{=}C-$, 3 H, s), 4.81 ($H_2C{=}C<$, 2 H, d), 2.0–3.3 (allylic and α to carbonyl, 11 H, m). *Anal.* Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.85; H, 10.15. A portion of the ketone **22** was converted to the semicarbazone derivative by the pyridine method and recrystallized from ethanol to give colorless crystals, mp 115° dec. *Anal.* Calcd for $C_{16}H_{25}ON_3$: C, 69.78; H, 9.15; N, 15.26. Found: C, 69.59; H, 8.8; N, 14.98.

Elution of the column with petroleum ether–benzene (40:60) gave 0.6 g (20% yield) of the α,β-unsaturated ketone **23**: bp 110–120° (0.6 mm); $n^{30}D$ 1.5305; $[\alpha]_D$ −45.8° (*c* 2.10); uv λ_{max} (MeOH) 244 nm (ϵ 10,700); ir 1640 (conjugated carbonyl), 3090, 1630, and 890 cm^{-1} (terminal methylene); pmr (CCl_4) δ 1.06 (CCH_3, 3 H, s), 1.14 (CCH_3, 3 H, s), 2.01 ($CH_3C{=}C<$, 3 H, broad s), 4.76 ($H_2C{=}C<$, 2 H, s), 6.2 ($HC{=}C<$, 1 H, broad s). *Anal.* Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.74; H, 10.25.

A small quantity of the ketone **23** was transformed (pyridine method) into its semicarbazone derivative and crystallized from ethanol to give colorless microcrystals, mp 197–198° dec. *Anal.* Calcd for $C_{16}H_{25}N_3O$: C, 69.78; H, 9.15; N, 15.26. Found: C, 69.90; H, 9.25; N, 15.56. Further elution of the column with benzene gave a fraction containing 105 mg of ketone **24**: bp 110–115° (2 mm); $[\alpha]_D$ −48.3° (*c* 1.61); uv λ_{max} (MeOH) 244 nm (ϵ 9400); ir 1650 (conjugated carbonyl), 3090, 1630, and 895 cm^{-1} (terminal methylene); pmr (CCl_4) δ 0.99 (CCH_3, 6 H, s), 2.01 ($H_3CC{=}C<$, 3 H, s), 4.78 ($H_2C{=}C<$, 2 H, s), 5.96 ($HC{=}C<$, 1 H, broad s). *Anal.* Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.27; H, 10.2.

Equilibration of Ketone 22 with Methylsulfinyl Carbanion. A solution of methylsulfinyl carbanion in 5 ml of DMSO was prepared from 0.5 g of sodium hydride (50% dispersion in mineral oil) as described in the above experiment. To this reagent was added a solution of 0.1 g of β,γ-unsaturated ketone **22** in 5 ml of DMSO with the aid of a hypodermic syringe and the reaction mixture was stirred at room temperature for 0.5 hr. The reaction mixture was worked up as in the above experiment and gave 0.1 g of product, which consisted of the three ketones in the same ratio as in the above reaction.

Similarly experiments were carried out for ketones **23** and **24** and the same mixtures were obtained in the same ratio.

Wolff–Kishner Reduction of β,γ-Unsaturated Ketone 22. To a solution of enone **22** in 15 ml of ethanediol was added 10 ml of hydrazine (80%) under nitrogen atmosphere and the mixture was stirred for 1 hr at 100°. Potassium hydroxide pellets (2.5 g) were then added and stirring was continued for a further period of 2 hr at 200°. The reaction mixture was poured into an ice-cold solution of dilute HCl. Extraction with ether (two 50-ml portions), washing with saturated sodium bicarbonate and brine, and removal of solvent gave 0.26 g of a mixture of hydrocarbons. This material was adsorbed over 15 g of 20% $AgNO_3$-impregnated silica gel. Elution with petroleum ether–benzene (90:10) gave 0.15 g of pure hydrocarbon **29**: bp 110–115° (4 mm); $[\alpha]_D$ +40.76° (*c* 0.85); ir (neat) 3090, 1650, 890 cm^{-1} (terminal methylene); pmr (CCl_4) δ 0.83 (CCH_3, 3 H, s), 0.91 (CCH_3, 3 H, s), 1.76 ($H_3CC{=}C-$, 3 H, s), 4.76 ($H_2C{=}C<$, 2 H, d). *Anal.* Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.06; H, 11.7.

Catalytic Hydrogenation of 29 to Tetrahydrohimachalene (Himachalane 25). A solution of 0.1 g of hydrocarbon **29** in glacial acetic acid (5 ml) was hydrogenated over Adams catalyst (20 mg) at room temperature and 1 atm pressure of hydrogen. The catalyst was removed by filtration and the filtrate was poured into 25 ml of water. Extraction with petroleum ether (two 20-ml portions), washing with sodium bicarbonate and brine, and removal of solvent gave 0.1 g of oily material. This was filtered through a 20% $AgNO_3$-impregnated silica gel column with petroleum ether to give **25** as a colorless oil: bp 110–115° (4 mm); ir 1450, 1390, 1380, 870, 860 cm^{-1}. The ir spectrum was found to be similar to that of the material obtained by the catalytic hydrogenation of naturally occurring α- and β-himachalene mixture obtained as described in the literature.[14]

(+)-Himachalene Dihydrochloride (30). An ice-cooled solution of 80 mg of hydrocarbon **29** in glacial acetic acid (1 ml) was saturated with a slow stream of dry hydrogen chloride gas until the solution turned deep brown. This solution was left overnight at −5° and the colorless crystals were collected by filtration. Recrystallization from petroleum ether–benzene gave long, white needles: mp 118–119°; $[\alpha]_D$ +3.4° (*c* 1.62); ir 1440, 1450, 1360, 1100, 840 cm^{-1}. The melting point was undepressed on admixture with an authentic specimen prepared from α- and β-himachalene. The ir spectra of the two were also completely superimposable.

(+)-*ar*-Himachalene (31). A mixture of 0.23 g of hydrocarbon **29** and 0.5 g of chloranil in dry benzene was refluxed for 4 hr under a nitrogen blanket. The reaction mixture was filtered and the precipitate was washed with 10 ml of benzene. The organic phase was concentrated, diluted with petroleum ether, and passed through a silica gel (10 g) column. The petroleum ether eluate on concentration gave 0.23 g of a hydrocarbon mixture.

The above mixture (0.23 g) was refluxed with 200 mg of 10% Pd/C in dry benzene for 12 hr. The reaction mixture was filtered and the precipitate was washed with 10 ml of benzene. Removal of solvent furnished 0.2 g of a pale yellow liquid. This was dissolved in 10 ml of acetone–water (9:1) and stirred with an excess of powdered potassium permanganate to destroy olefinic impurities. The reaction mixture was again filtered and diluted with water. Extraction with petroleum ether (two 25-ml portions), washing with brine, drying, and removal of solvent furnished 120 mg of pure (+)-*ar*-himachalene (**31**): bp 110–115° (2 mm); $n^{35}D$ 1.5249; $[\alpha]_D$ +7.7° (*c* 1.02); ir (neat) 3010, 1620, 1580, 1450, 810

cm^{-1}; pmr (CCl_4) δ 1.26 (CCH_3, 3 H, s), 1.30 (CCH_3, 3 H, s), 1.38 (CCH_3, 3 H, s), 2.26 ($ArCH_3$, 3 H, s), 6.91 (Ar, 1 H, s), 7.03 (ArH, 1 H, s). The literature records[14] $[\alpha]D$ +2.92° (*c* 1.7) for the naturally occurring material and $[\alpha]D$ +5.9° (*c* 1.04) for the (+)-*ar*-himachalene obtained from (+)-*ar*-turmerone. *Anal.* Calcd for $C_{15}H_{22}$: C, 89.04; H, 10.96. Found: C, 89.12; H, 10.4.

Ozonolysis of β,γ-Unsaturated Ketone 22. A 440-mg solution of ketone **22** in ethyl acetate (15 ml) was treated with 0.097 g of ozone generated in a Welsbach ozonizer at −80°. The solvent was then removed under reduced pressure and the residue was treated with aqueous sodium carbonate and a few drops of hydrogen peroxide (30%). Dilution with water, extraction with benzene, and removal of solvent gave 400 mg of glassy residue. Tlc behavior indicated it to be a complex mixture of highly polar material and the ir spectrum displayed multiple carbonyl and hydroxyl absorptions.

Ketalization of Ketones 22, 23, and 24. To a stirred solution of 800 mg of ketones **22, 23,** and **24** in dry benzene (50 ml) was added ethylene glycol (7 ml) and *p*-toluenesulfonic acid in catalytic amounts. The reaction mixture was refluxed for 2 hr and poured into water. Extraction with ether (two 30-ml portions), washing with aqueous sodium bicarbonate and brine, and removal of solvent afforded 1.07 g of **33**: bp 150° (1 mm); $n^{30}D$ 1.5172; uv λ_{max} (MeOH) 208 nm (ϵ 4900); ir no absorption at 890 cm^{-1} due to terminal methylene. *Anal.* Calcd for $C_{17}H_{26}O_2$: C, 77.86; H, 9.92. Found: C, 78.00; H, 10.00.

Acknowledgment. The authors wish to thank Professor Gurubux Singh of Banaras Hindu University and Dr. Nityanand of CDRI, Lucknow, for the pmr spectra of the compounds reported here. We also appreciate the help of Dr. T. S. Santhanankrishnan in obtaining the vpc data on our compounds. One of us (S. K. K.) is grateful to the CSIR for the award of a junior research fellowship.

Registry No.—**9,** 1139-15-7; **11,** 51599-80-5; **12,** 51599-81-6; **12** semicarbazone, 51599-82-7; **14,** 51635-66-6; **15,** 51599-83-8; **18,** 51599-84-9; **18** semicarbazone, 51599-60-1; **22,** 51704-14-4; **22** semicarbazone, 51599-85-0; **23** semicarbazone, 51599-86-1; **24,** 51704-15-5; **25,** 20479-45-2; **29,** 51599-87-2; **30,** 33496-01-4; **31,** 19419-67-1; **33,** 51635-68-8.

References and Notes

(1) For earlier papers in the series, see (a) G. Mehta, *Indian J. Chem.*, **7,** 565 (1969); (b) G. Mehta, *Chem. Ind. (London)*, 1264 (1970); (c) G. Mehta, *J. Org. Chem.*, **36,** 3455 (1971); (d) G. Mehta and S. K. Kapoor, *Tetrahedron Lett.*, 715 (1972); (e) G. Mehta, *Chem. Ind. (London)*, 762 (1972); (f) G. Mehta, N. M. Pattnaik, and S. K. Kapoor, *Tetrahedron Lett.*, 4947 (1972); (g) G. Mehta and S. K. Kapoor, *ibid.*, 497 (1973); (h) G. Mehta and S. K. Kapoor, *ibid.*, 2385 (1973).

(2) Junior Research Fellow of CSIR (1970–present).

(3) Recent reviews in sesquiterpene synthesis: (a) J. M. Mellor and S. Munavalli, *Quart. Rev., Chem. Soc.*, **18,** 270 (1964); (b) G. Mehta and A. Bhattacharyya, *J. Sci. Ind. Res.*, **32,** 118 (1973); (c) G. Mehta, A. Bhattacharyya, and S. K. Kapoor, *ibid.*, **32,** 191 (1973).

(4) Some of the recent syntheses achieved through sesquiterpene → sesquiterpene transformations and involving alteration of the carbocyclic framework are (a) α-santonin → dihydrocostunolide, E. J. Corey and A. G. Hortmann, *J. Amer. Chem. Soc.*, **85,** 4033 (1963); (b) longifolene → (+)-sativene, P. de Mayo and R. E. Williams, *ibid.*, **87,** 3275 (1965); (c) α-santonin → 1-epicyclocolorenone, G. Buchi, J. M. Kauffman, and H. J. E. Lowenthal, *ibid.*, **88,** 3403 (1966); (d) α-cyperone → cyperolone, H. Hikino, N. Suzuki, and T. Takemoto, *Chem. Pharm. Bull.*, **15,** 1395 (1967); (e) germacatriene → eudesmane types, E. D. Brown, M. D. Solomon, J. K. Sutherland, and A. Torre, *Chem. Commun.*, 111 (1967); (f) β-himachalene → cuparene, H. N. Subba Rao, N. P. Damodaran, and S. Dev, *Tetrahedron Lett.*, 2213 (1968); (g) α-cyperone → α-bulnesene, E. Piers and K. F. Chang, *Can. J. Chem.*, **48,** 2234 (1970); (h) α-santonin → achillin, E. H. White and J. N. Marx, *Tetrahedron,* **25,** 2177 (1969); (i) α-santonin → pseudoguaianolides, J. B. Hendrickson, C. Ganter, D. Dorman, and H. Link, *Tetrahedron Lett.*, 2235 (1968); (j) methyl farnesate → (±)-junenol, M. A. Schwartz, J. D. Crowell, and J. H. Musser, *J. Amer. Chem. Soc.*, **94,** 4361 (1972); (k) thujopsene → cuparene and α-chamigrene, S. Ito, M. Yatagi, and K. Endo, *Tetrahedron Lett.*, 1149 (1971).

(5) J. B-Son Bradenberg and H. Erdtman, *Acta Chem. Scand.*, **15,** 685 (1961); T. C. Joseph and S. Dev, *Tetrahedron,* **24,** 3809 (1968).

(6) H. Erdtman and L. Westfelt, *Acta Chem. Scand.*, **17,** 2351 (1963); L. Westfelt, *ibid.*, **21,** 159 (1967).

(7) J. B. Hendrickson, *Tetrahedron,* **7,** 83 (1959); W. Parker, J. S. Roberts, and R. Ramage, *Quart. Rev., Chem. Soc.*, 331 (1967).

(8) This is a typical example of Grob fragmentation with elimination: C. A. Grob and P. Schiess, *Angew. Chem., Int. Ed. Engl.*, **6,** 1 (1967). For examples of C_1–C_7 bond scission in the bicyclo[2.2.1]heptane system, see P. G. Gassman and J. G. Macmillan, *J. Amer. Chem. Soc.*, **91,** 5527 (1969); D. H. Gustafson and W. F. Erman, *J. Org. Chem.*, **30,** 1665 (1965).

(9) This reaction has been reported in a preliminary communication.[1d]

(10) The examples on which this expectation was based are provided by the work of (a) S. Cannizzaro and F. Sestini, *Gazz. Chim. Ital.*, **2,** 241 (1873); (b) R. B. Woodward, F. I. Brutschy, and H. Baer, *J. Amer. Chem. Soc.*, **70,** 4216 (1948); (c) E. J. Corey, M. Ohno, R. B. Mitra, and P. A. Vatakencherry, *ibid.*, **86,** 478 (1964).

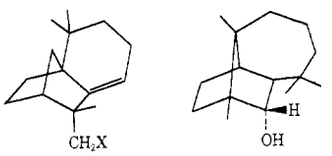
(11) A similar approach for the synthesis of tricyclic sesquiterpene copaene from santonic acid has been considered: A. G. Hortmann and D. S. Daniel, *J. Org. Chem.*, **37,** 4446 (1972). Also see Y. Lin and A. Nickon, *J. Amer. Chem Soc.*, **92,** 3496 (1970); W. Kirmse, G. Arend, and R. Siegfried, *Angew. Chem., Int. Ed. Engl.*, 165 (1970).

(12) For the previously reported synthesis of (±)-himachalene dihydrochloride and (±)-himachalenes, see (a) B. D. Challand, H. Hikino, G. Kornis, G. Lange, and P. de Mayo, *J. Org. Chem.*, **34,** 794 (1969); (b) E. Wenkert and K. Naemura, *Syn. Commun.*, **3,** 45 (1973).

(13) This compound has been found to occur[14] in the essential oil of *Cedrus deodar* Loud. and a synthesis[14] of its racemate along traditional lines has been reported.

(14) R. C. Pandey and S. Dev, *Tetrahedron,* **24,** 3829 (1968).

(15) The complexity of the hydrocarbon mixture and formation of tetracyclic bromide **14** was quite unexpected. The analogous rearrangement[1b] of longifolene (**1**) in trifluoroacetic acid followed by hydrolysis has been shown to give isolongifolene (i, 60%) as the major product, a secondary alcohol (**13,** 35%), and longiborneol (ii, 5%). However, in the rearrangement of **9** no product corresponding



i, X = H
iii, X = Br

ii

to iii was encountered. This substituent-induced dichotomy in the rearrangement of **1** and the total suppression of a pathway leading to iii from **9** has certain mechanistic implications on the longifolene-isolongifolene rearrangement. For relevant discussion see G. Ourisson, *Proc. Chem. Soc.*, 274 (1964); R. Ranganathan, U. R. Nayak, T. S. Santhanakrishnan, and S. Dev, *Tetrahedron,* **26,** 621 (1970); J. A. Berson, J. H. Hammons, A. W. McRowe, R. G. Bergman, A. Remanick, and D. Houston, *J. Amer. Chem. Soc.*, **89,** 2590 (1967); J. E. McMurry, *J. Org. Chem.*, **36,** 2826 (1971).

(16) P. Naffa and G. Ourisson, *Bull. Soc. Chim. Fr.*, 1410 (1954); S. Akiyoshi and H. Erdtman, *Tetrahedron,* **9,** 237 (1960).

(17) Acid-catalyzed rearrangement products from longifolene (**1**) bearing the carbon skeleton of **16** and **17** have been reported: L. Stehelin, J. Lhomme, and G. Ourisson, *J. Amer. Chem. Soc.*, **93,** 1650 (1971); R. Coates and J. P. Chen, *Chem. Commun.*, 1481 (1970).

(18) We wish to thank Dr. K. Venkatesan, Indian Institute of Science, Bangalore, for this information. These results will be published separately.

(19) J. R. Prahlad, U. R. Nayak, and S. Dev, *Tetrahedron,* **26,** 663 (1970); S. G. Patnekar and S. C. Bhattacharyya, *Indian J. Chem.*, **8,** 36 (1970).

(20) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **84,** 866 (1962); E. J. Corey, R. B. Mitra, and H. Uda, *ibid.*, **86,** 485 (1964).

(21) The absolute configuration of bicyclo[5.4.0]undecane derivatives **22–31** follows from the known absolute configuration of longifolene. The absolute configuration of naturally occurring himachalenes (**2**) has been deduced[23] from their correlation with longifolene (**1**); G. Ourisson, *Bull. Soc. Chim. Fr.*, 895 (1954); S. Munavalli and G. Ourisson, *ibid.*, 2825 (1964).

(22) D. Ginsberg and W. J. Rosenfelder, *Tetrahedron,* **1,** 3 (1957).

(23) T. C. Joseph and S. Dev, *Tetrahedron,* **24,** 3841 (1968).

(24) T. C. Joseph and S. Dev, *Tetrahedron,* **24,** 3853 (1968).

(25) G. Stork and P. A. Grieco, *Tetrahedron Lett.*, 1807 (1971).

(26) Melting points and boiling points are uncorrected. Melting points were taken in capillaries on a Fischer-Jones melting point apparatus. Boiling points refer to bath temperature in those cases where short-path bulb-to-bulb distillations were carried out. The petroleum ether corresponds to the fraction of bp 60–80°. All solvent extracts were dried over anhydrous sodium sulfate. Specific rotations were measured in chloroform on a JASCO DIP automatic polarimeter. The ultraviolet spectra were recorded on a Beckman DU spectrophotometer in methanol. Infrared spectra were recorded on a Perkin-Elmer Model 137B spectrophotometer as neat liquids or solids as KBr disks. Pmr spectra were obtained on approximately 10–15% solutions in CCl_4 or $CDCl_3$ on a Varian A-60 spectrometer. The chemical shifts are reported in parts per million downfield from internal tetramethylsilane at δ 0.00 as internal standard. The abbreviations s, d, t, q, and m refer to singlet, doublet, triplet, quartet, and multiplet, respectively. Microanalyses were performed by Mr. A. H. Siddiqui in the microanalytical laboratory of our department.

(27) The structural assignment of **14** is further supported by the fact that the same tetracyclic bromide is also formed on the addition of Br_2 to longifolene (**1**). There is thus, a close analogy[28] in the formation

of 14 from longifolene and the addition of halogens to camphene, the isoprenolog of 1, leading to tricyclene derivatives.
(28) B. H. Jennings and G. B. Herschbach, *J. Org. Chem.*, **30**, 3902 (1965); H. G. Richey, J. E. Grant, T. J. Garbacik, and D. L. Dull, *ibid.*, **30**, 3909 (1965).
(29) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).
(30) M. F. Grunden, H. B. Henbest, and M. D. Scott, *J. Chem. Soc.*, 1855 (1963).
(31) P. Naffa and G. Ourisson, *Bull. Soc. Chim. Fr.*, 1410 (1955).

Syntheses Employing Hexamethyl(Dewar benzene). Reactions of Methyl-Substituted Carbonium Ions with Triethylamine[1]

H. Hogeveen* and P. W. Kwant

Department of Organic Chemistry, The University, Zernikelaan, Groningen, The Netherlands

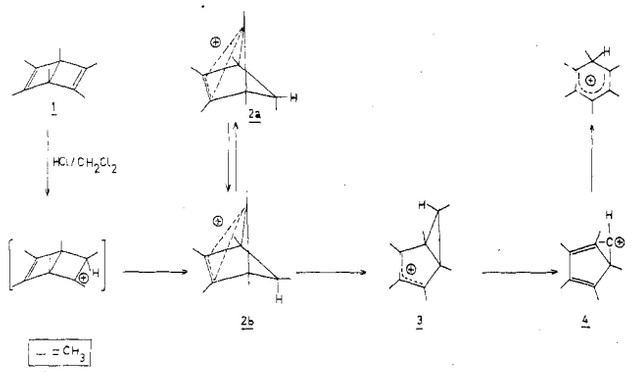
Received March 5, 1974

Syntheses of 1,2,3,5,6-pentamethyl-4-methylenebicyclo[3.1.0]hex-2-ene (**5**), 1,2,4,5,6-pentamethyl-3-methylenetricyclo[2.2.0.0^{2,6}]hexane (**8**), 1,2,5,6-tetramethyl-3,4-dimethylenetricyclo[3.1.0.0^{2,6}]hexane (**9**), and 5-α-chloroethyl-1,2,4,5-tetramethyl-3-methylenecyclopentene (**16**) are reported. These involve proton abstraction by triethylamine from the corresponding carbonium ions. The proton abstraction is proposed to be a kinetically controlled process occurring at the methyl group adjacent to the carbon atom bearing the highest positive charge.

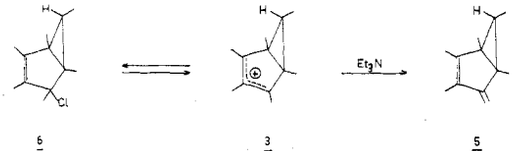
Reactions of hexamethyl(Dewar benzene) (**1**) with acids have been the subject of many investigations in recent years.[2,3] Protonation of **1** followed by rearrangement will give isomers of **1** after subsequent proton abstraction. Triethylamine appeared to be particularly useful for performing these proton abstractions. Some other carbonium ions originating from **1** have been treated in the same way and the low-temperature abstraction of a proton from a methyl-substituted carbonium ion with triethylamine seems to be generally applicable as a good synthetic method for preparing strained compounds with exocyclic methylene groups. The results of this reaction are presented below.

Results and Discussion

It has been shown that the reaction path of **1** with HCl followed by subsequent isomerization is as follows.[2d] The

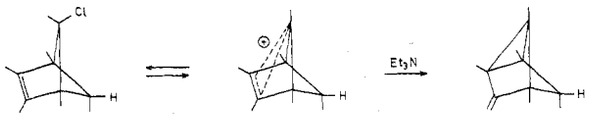


homofulvene **5**, which is an isomer of **1**, was prepared *via* reaction of **1** with HCl at −40° to give **6**. Compound **6** will dissociate to give cation **3**, which then reacts with triethylamine with loss of a proton. The homofulvene **5** was pre-

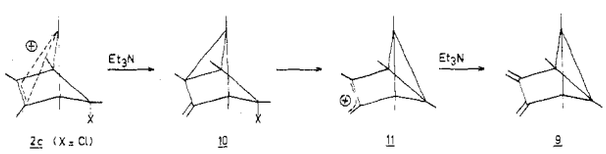


pared previously by a photochemical isomerization of **1**,[4] and also by quenching of a strongly acidic solution of **3** with sodium bicarbonate in methanol.[5] The stereochemistry of **5**, once supposed to be exo-H,[6] is accepted now to be endo-H. The assignment is based on comparison[5,7] of the pmr chemical shifts of **5** and the related ion **3** with those of the homofulvene and the cation with the inverted H and CH_3 configuration.[8]

For the preparation of a tricyclic isomer of **1**, compound **8**, the following procedure was developed. The cation mixture **2a,b** (3:1 in equilibrium[3a]), obtained from reaction of **1** with HCl in methylene chloride at −80°,[2d] was poured into triethylamine at −80°. The pmr spectrum of this mixture indicates that **7**[2d] is formed first; subsequently **7** will dissociate to give ion **2a** and triethylamine will then abstract a proton from the methyl group adjacent to the carbon atom bearing the highest positive charge[9] in ion **2a.**



Another application of the reaction of methyl-substituted carbonium ions with triethylamine is found in the synthesis of **9.** The cations **2c** and **2d,** formed from the reaction of **1** with chlorine and bromine, respectively,[9] give **9** upon proton abstraction with triethylamine. This product can be accounted for by assuming that the proton abstraction to give **10** occurs in the same way as with **2a.** The intermediate **10** will presumably dissociate to give cation **11,** which then undergoes another proton abstraction to give **9.** Compound **9** was obtained also by pouring a solution of



dication $(CCH_3)_6^{2+}$ in a triethylamine solution at low temperature.[10] Structure **9** was assigned on the basis of