



0031-9422(95)00592-7

## REGIO- AND STEREOSPECIFIC CONSTRUCTION OF VICINAL QUATERNARY CARBONS: TOTAL SYNTHESIS OF (±)-ALBENE

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(Received in revised form 3 July 1995)

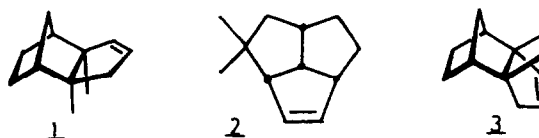
### IN HONOUR OF PROFESSOR ANTONIO G. GONZALEZ

**Key Word Index**—Albene; quaternary carbons; Claisen rearrangement; diazo ketone; cyclopropanation; reductive cyclopropane cleavage; Shapiro reaction.

**Abstract**—A regiospecific and stereoselective total synthesis of the trisnorsesquiterpene (±)-albene, via a prochiral precursor is described. The *ortho* ester Claisen rearrangement of the allyl alcohol, obtained in two regiospecific reactions from a Diels–Alder adduct, followed by hydrolysis of the resultant ester furnished an ene acid in a highly stereoselective manner. Anhydrous copper sulphate catalysed intramolecular cyclopropanation reaction of the diazo ketone derived from the ene acid, generated a cyclopropyl ketone. The regiospecific reductive cleavage of this cyclopropyl ketone resulted in a prochiral ketone. Finally, Shapiro reaction on the tosylhydrazone, derived from the latter ketone, furnished (±)-albene.

### INTRODUCTION

The optically active crystalline hydrocarbon albene (1), a trisnorsesquiterpene containing a unique *exo*-2,6-dimethyltricyclo[5.2.1.0<sup>2,6</sup>]decane carbon framework incorporating two vicinal quaternary carbon atoms, was first isolated in 1962 by Novotny *et al.* [1] from the plant, *Petasites albus*. Later, it was found to be ubiquitous in species of the genera *Petasites* (white pestilence weed) and *Adenostyles*. This deceptively simple looking molecule has an interesting chemical history. The earliest structural studies carried out on albene showed it to be a tricyclic hydrocarbon with a disubstituted double bond in a five membered ring, for which Sorm *et al.* [2] proposed, provisionally the tetrahydrotriquinacene structure 2. In 1972 the tetrahydrotriquinacene structure was revoked [3] based on chemical degradation and correlation with camphene, and the *endo* structure 3 (now referred to as isoalbene) was assigned to albene. Later in 1978, the correct stereostructure of albene as *exo*-2,6-dimethyltricyclo[5.2.1.0<sup>2,6</sup>]undec-3-ene (1) was established conclusively, largely due to the efforts of Kreiser and co-workers [4–6] via the total synthesis of the *endo*-isomer and reinterpretation of earlier results. Since the assignment of correct stereostructure to albene four research groups [7–10], Baldwin (1981), Trost (1982), Dreiding (1983) and Curran (1987) have reported the total synthesis of albene (1), prior to the initiation of work in the authors' laboratory [11, 12]. The unique *exo*-2,6-dimethyltricyclo[5.2.1.0<sup>2,6</sup>]decane skeleton with two

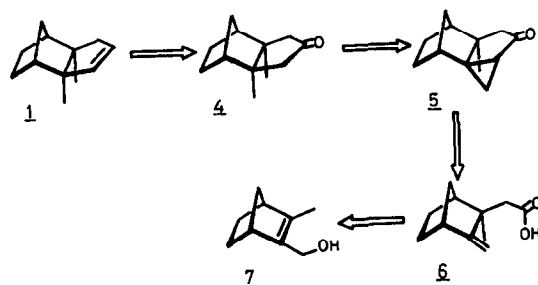


vicinal quaternary carbon atoms makes albene an interesting synthetic target. Herein we report the details of a regiospecific total synthesis of (±)-albene via a prochiral precursor.

### RESULTS AND DISCUSSION

In the authors' laboratory a general methodology was developed [13] for the annulation of a cyclopentane ring with two vicinal quaternary carbon atoms starting from allyl alcohols based on *ortho* ester Claisen rearrangement [14] and diazo ketone cyclopropanation [15] reactions. The presence of two vicinal quaternary carbon atoms with methyl substituents prompted the extension of this methodology for the total synthesis of albene via the prochiral ketone 4. The retro synthetic analysis (Scheme 1) of albene (1) based on the *ortho* ester Claisen rearrangement and intramolecular diazo ketone cyclopropanation reactions readily identified the prochiral ketone 4, cyclopropyl ketone 5 and ene-acid 6 as the requisite precursors. The allyl alcohol 7 [16, 17] was chosen as the starting material in anticipation that the acetate side chain will be introduced from the *exo* face of the norbornane moiety during the Claisen rearrangement which will result in the *endo* orientation for the *tert*-methyl group as required. The allyl alcohol 7

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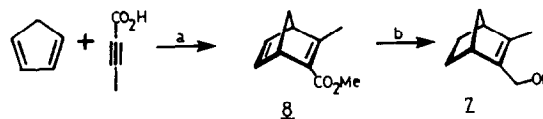


Scheme 1. Retro synthetic analysis of albene.

was prepared in a straightforward manner starting from cyclopentadiene. Since the Diels–Alder reaction of cyclopentadiene with methyl tetrolate resulted in low yield of the adduct **8**, Diels–Alder reaction was carried out using tetrolic acid. Thus reaction of cyclopentadiene and tetrolic acid in a sealed tube at 140° for 5 hr, followed by esterification of the adduct **9** with an excess of ethereal diazomethane furnished the ester **8** in 80% yield. The regiospecific hydrogenation of the less substituted olefin of the ester **8**, using 10%-Pd/C as catalyst in ethyl acetate at atmospheric pressure of hydrogen, furnished the dihydro derivative, the ester **10**. Since the reaction of the ester **10** with LAH was found to generate a mixture of allyl and saturated alcohols, it was reduced with diisobutylaluminium hydride (DIBAH) in toluene at –78° to furnish the allyl alcohol **7**, the requisite starting material for the Claisen rearrangement, in 92% yield (Scheme 2).

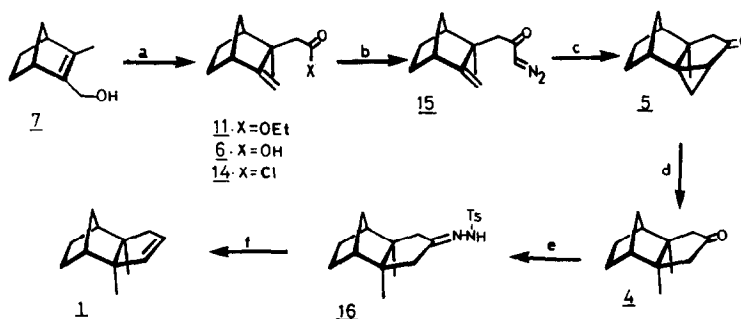
The first quaternary carbon atom of albene was introduced using a highly stereoselective *ortho* ester Claisen rearrangement [14]. Thus, thermal activation of a solution of the allyl alcohol **7** and a catalytic amount of propionic acid in triethyl *ortho*-acetate for 48 hr at 180° generated the ene-ester **11** [16] in 81% yield, whose structure was delineated from its spectral data. The sterically preferred *exo* transition state **12** over the *endo* transition state **13** explains the exclusive formation of the *exo* product **11**. The long reaction time required for this rearrangement was drastically reduced by employing a microwave oven [18]. Thus, microwave irradiation of a solution of the allylic alcohol **7**, triethyl *ortho*-acetate and a catalytic amount of propionic acid in dry DMF in a clean Erlenmeyer flask for 14 min in a commercial microwave oven furnished the ester **11** in 87% yield. Hydrolysis of the ester **11** using 20% aqueous sodium hydroxide in methanol furnished the key intermediate of the sequence, the ene-acid **6**, m.p. 85–87°, 76% yield.

The second quaternary carbon atom was created employing a copper catalysed intramolecular diazo ketone cyclopropanation reaction [15]. Reaction of the acid **6** with oxalyl chloride in benzene at room temperature furnished the acid chloride **14** which on treatment with an excess of freshly prepared ethereal diazomethane at 0° generated the diazo ketone **15**. Anhydrous copper sulphate catalysed decomposition of the diazo ketone **15** in refluxing cyclohexane, using a 100 W tungsten lamp for

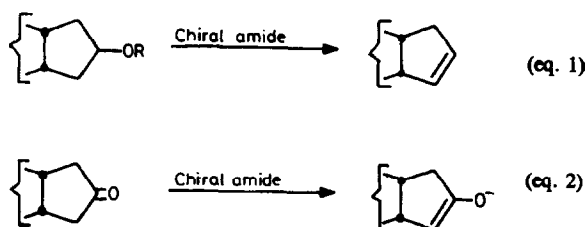
Scheme 2. (a) i 140°, sealed tube, 5 hr; ii CH<sub>2</sub>N<sub>2</sub>, Et<sub>2</sub>O. (b) i H<sub>2</sub>–10% Pd/C, 1 atm, 1.5 hr; ii DIBAH, PhMe, –78°, 1 hr.

5 hr, generated the cyclopropyl ketone **5** in 53% yield (from acid **6**) via the intramolecular insertion of the resultant keto carbenoid into the *exo*-methylene whose structure rests secured from its spectral data (Scheme 3). The preferential formation of the cyclopropyl ketone **5** was a consequence of the insertion of the ketocarbene from the *exo* face of the molecule as it cannot approach from the other face of the double bond. This forces the cyclopropyl methylene to occupy the *endo* position, namely *cis* with respect to the *endo tert*-methyl group, thus creating the two quaternary centres in a highly stereoselective manner. The cyclopropyl ketone **5** was then transformed into the prochiral ketone **4**, by the regiospecific cleavage of the C<sub>3</sub>–C<sub>4</sub> bond of the cyclopropane ring. Thus, reduction of the cyclopropyl ketone **5** using lithium in liquid ammonia for 15 min at –33°, regiospecifically furnished the prochiral ketone **4** in 81% yield generating the second *endo tert*-methyl group. Both the <sup>1</sup>H and <sup>13</sup>C NMR (seven lines) spectra clearly revealed the presence of a plane of symmetry in the molecule. The regiospecificity in the cyclopropane ring cleavage can be readily explained [19] as it is well established that in the reduction of cyclopropyl ketones with lithium in liquid ammonia, of the two possibilities, the cyclopropane bond which is having maximum overlap with the *p*-orbital of the carbonyl system will be cleaved. Alternate to the reduction with lithium in liquid ammonia, catalytic hydrogenation (40 psi (≈ 276 kPa), H<sub>2</sub>–10% Pd/C, methanol, 5 hr) of the less substituted cyclopropane bond also transformed the cyclopropyl ketone **5** into the prochiral ketone **4** in quantitative yield.

The last phase in the synthesis, i.e. conversion of the ketone **4** into albene, requires the transformation of a cyclopentanone to a cyclopentene. For this purpose, a Shapiro reaction [20, 21] on the corresponding tosylhydrazone was adopted. Thus, treatment of the ketone **4** with tosylhydrazide in refluxing ethanol for four hours formed the tosylhydrazone **16**, m.p. 162°, in 86% yield. Finally, treatment of the tosylhydrazone **16** in *N,N,N',N'*-tetramethylethylenediamine (TMEDA) and ether with an excess of *n*-butyllithium furnished (±)-albene (**1**), m.p. 110–115° (lit. [1] 110–115°) in 65% yield. The <sup>1</sup>H and <sup>13</sup>C NMR spectra of our synthetic albene were found to be identical with those reported [5] in the literature for the natural product.



Scheme 3. (a) i  $\text{MeC}(\text{OEt})_3$ ,  $\text{EtCOOH}$ ; sealed tube,  $180^\circ$ , 48 hr or DMF, microwave irradiation, 14 min. (b) i Aq.  $\text{NaOH}$ ,  $\text{MeOH}$ ,  $70^\circ$ , 6 hr; ii  $\text{C}_6\text{H}_6$ ,  $(\text{COCl})_2$ , RT, 2 hr. iii  $\text{CH}_2\text{N}_2$ ,  $\text{Et}_2\text{O}$ , 2 hr. (c) Anhydrous  $\text{CuSO}_4$ ,  $\text{c-C}_6\text{H}_{11}$ , W-lamp, 5 hr. (d) Li-liquid  $\text{NH}_3$ , 15 min or  $\text{H}_2$ -10%  $\text{Pd/C}$ , 40 psi, 5 hr. (e)  $\text{NH}_2\text{NH-Ts}$ ,  $\text{EtOH}$ , reflux, 4 hr. (f)  $n\text{-BuLi}$ ,  $\text{Et}_2\text{O}$ ,  $\text{TMEDA}$ ,  $0^\circ$ , 6 hr.



In conclusion, a stereoselective and regiospecific total synthesis of (±)-albene (1) was achieved via the prochiral ketone 4 using the *ortho* ester Claisen rearrangement and intramolecular diazo ketone cyclopropanation reaction as key steps for the construction of the two vicinal quaternary carbons. It is evident from the foregoing discussion that if a methodology is available for the conversion of a prochiral cycloalkanone to a chiral cycloalkene, the ketone 4 can serve as a precursor to chiral albene. Recent reports on the conversion of prochiral ketones to chiral alkenes employing chiral amides [22] either for elimination [23] (equation 1) or generation of chiral enolates [24] (equation 2), enhanced the significance of the present synthesis, as a potential route to chiral albene.

#### EXPERIMENTAL

Melting points are not corrected. The chemical shifts ( $\delta$  ppm) and coupling constants (Hz) in  $^1\text{H}$  (60 and 90 MHz) and  $^{13}\text{C}$  NMR (22.5 MHz) spectra are reported with reference to either internal tetramethylsilane (for  $^1\text{H}$ ) or central line (77.1 ppm) of  $\text{CDCl}_3$  (for  $^{13}\text{C}$ ). In the  $^{13}\text{C}$  NMR spectra off-resonance multiplicities, when recorded are given in parentheses. Low- and high-resolution mass measurements were carried out using a direct inlet mode. Relative intensities of the ions are given in parentheses. Elemental analyses were carried out using a Carlo Erba 1106 analyser. Acme's silica gel (100–200 mesh) was used for column chromatography. Cyclopentadiene was freshly prepared by cracking dicyclopentadiene at  $180^\circ$ . Tetrolic acid and *N*-nitroso-*N*-methylurea were prepared according to the reported procedures [25].

#### Methyl 3-methylbicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (8)

(1) *Diels-Alder reaction*. A solution of tetrolic acid (5 g, 59 mmols), freshly distilled cyclopentadiene (5 g, 75 mmols) and a catalytic amount of hydroquinone in toluene (10 ml) was taken in a Carius tube in  $\text{N}_2$  and heated at  $140^\circ$  for 5 hr. The Carius tube was cooled, saturated solution of aqueous  $\text{NaHCO}_3$  (50 ml) was added to the reaction mixture and washed with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 30$  ml) to remove the dicyclopentadiene and other oligomers. The aqueous phase was acidified with 10% aqueous  $\text{HCl}$  and extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 30$  ml). The  $\text{CH}_2\text{Cl}_2$  layer was washed with water and brine, and dried ( $\text{Na}_2\text{SO}_4$ ). Evaporation of the solvent and filtration of the residue through a silica gel (5 g) column using  $\text{CH}_2\text{Cl}_2$  as eluant furnished the adduct 9 ( $\approx 8$  g) as a dark low melting solid.  $^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.92 and 6.72 (2H, *d* of AB *q*,  $J_{5,6} = 4.5$  Hz,  $J_{1,6} = J_{4,5} = 3$  Hz, H-5 and 6), 3.90 (1H, *br s*, H-4), 3.41 (1H, *br s*, H-1), 2.29 (3H, *s*, olefinic  $\text{CH}_3$ ), 2.31 and 1.99 (2H, *t* of AB *q*,  $J_{7a,7b} = 9$  Hz,  $J_{1,7} = J_{4,7} = 2$  Hz, H-7).

(2) *Esterification*. The acid 9, obtained above, was taken in ether (25 ml) and treated with freshly prepared [25] ethereal diazomethane (from 10 g of *N*-nitroso-*N*-methylurea and 100 ml of 50% aqueous  $\text{KOH}$ ). Careful evaporation of the solvent and excess diazomethane followed by purification of the residue over a small silica gel (5 g) column using hexane as eluant furnished the ester 8 (7.75 g, 80%) as an oil [17]. IR (neat):  $\nu_{\text{max}}$   $\text{cm}^{-1}$  3070 ( $=\text{C-H}$ ), 1713 ( $\text{C=O}$ ), 1635 ( $\text{C=C}$ ), 1437, 1341, 1320, 1296, 1239, 1194, 1101, 1068.  $^1\text{H}$  NMR (60 MHz,  $\text{CCl}_4$ ):  $\delta$  6.60–7.00 (2H, *m*, olefin), 3.90 (1H, *br s*, H-4), 3.72 (3H, *s*,  $\text{O-CH}_3$ ), 3.40 (1H, *br s*, H-1), 2.23 (3H, *s*, olefinic  $\text{CH}_3$ ), 2.00 (2H, *m*, H-7).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  169.5 (*s*,  $\text{O-C=O}$ ), 165.8 (*s*, C-3), 143.8 (*d*) and 140.1 (*d*) (C-5 and 6), 137.9 (*s*, C-2), 70.7 (*t*, C-7), 57.8 (*d*, C-4), 50.8 (*q*,  $\text{O-CH}_3$ ), 50.5 (*d*, C-1), 16.9 (*q*,  $\text{C}_3\text{-CH}_3$ ).

#### Methyl 3-methylbicyclo[2.2.1]hept-2-en-2-carboxylate (10)

To a solution of the ester 8 (6 g, 36.5 mmol) in  $\text{EtOAc}$  (15 ml) was added 10%- $\text{Pd/C}$  (60 mg) and stirred under

hydrogen atmosphere (balloon) for 1.5 hr. The reaction mixture was then filtered through a small silica gel (5 g) column. Evaporation of the solvent furnished the hydrogenated ester **10** (6 g, 99%) as an oil. IR (neat):  $\nu_{\max}$   $\text{cm}^{-1}$  1713 (C=O), 1632 (C=C), 1437, 1359, 1281, 1257, 1203, 1161, 1092, 1056.  $^1\text{H}$  NMR (60 MHz,  $\text{CCl}_4$ ):  $\delta$  3.63 (3H, s, O-CH<sub>3</sub>), 3.15 (1H, br s, H-4), 2.75 (1H, br s, C-1), 2.16 (3H, s, olefinic CH<sub>3</sub>), 0.95–1.90 (6H, m, H-5, 6 and 7).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  165.8 (s, O-C=O), 160.0 (s, C-3), 131.8 (s, C-2), 50.4 (q, O-CH<sub>3</sub>), 49.9 (d, C-4), 45.9 (t, C-7), 43.1 (d, C-1), 26.2 (t) and 24.4 (t) (C-5 and 6), 14.4 (q, olefinic CH<sub>3</sub>).

(3-Methylbicyclo[2.2.1]hept-2-en)-2-methanol (**7**). To a cold ( $-78^\circ$ ) magnetically stirred solution of the ester **10** (5.5 g, 33 mmol) in dry toluene (25 ml) was added a solution of DIBAL-H (1.2M in toluene, 30 ml, 36 mmol) and the reaction was allowed to attain room temperature over a period of 1 hr. The reaction was then quenched with water. The solids were filtered off and the residue was washed with ether (25 ml). The combined organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and the solvent was evaporated. Purification of the residue on a silica gel (15 g) column using EtOAc-hexane (1:9) as eluant furnished the alcohol **7** (4.2 g, 92%) as an oil [17]. IR (neat):  $\nu_{\max}$   $\text{cm}^{-1}$  3340 (OH), 1692, 1446, 1278, 993.  $^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.21 and 4.00 (2H, ABq,  $J = 12.6$  Hz,  $\text{CH}_2\text{OH}$ ), 2.90 (1H, br s) and 2.60 (1H, br s) (H-1 and 4), 1.68 (3H, s, olefinic CH<sub>3</sub>), 0.90–1.70 (6H, m, H-5, 6 and 7).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  140.0 (s) and 139.1 (s) (olefinic), 57.4 (t,  $\text{CH}_2\text{OH}$ ), 47.8 (d) and 43.5 (d) (C-1 and 4), 46.6 (t, C-7), 26.6 (t) and 25.3 (t) (C-5 and 6), 11.8 (q, CH<sub>3</sub>). EIMS:  $m/z$  138 (37%,  $\text{M}^+$ ), 121 (50), 110 (70), 95 (100), 91 (46).

*Ethyl exo-(2-methyl-3-methylenebicyclo[2.2.1]heptane)-2-acetate (11)*

**Method A.** A solution of the allylic alcohol **7** (4 g, 28.9 mmol), triethyl orthoacetate (6 ml, 32.8 mmols) and a catalytic amount of propionic acid were taken in a Carius tube in  $\text{N}_2$  and heated at  $180^\circ$  for 48 hr. The reaction mixture was cooled, diluted with ether (30 ml), washed with 0.5 M HCl followed by saturated  $\text{NaHCO}_3$  solution and brine, and dried ( $\text{Na}_2\text{SO}_4$ ). Evaporation of the solvent and purification of the residue on a silica gel (20 g) column using EtOAc-hexane (1:40) as eluent furnished the ester **11** (4.9 g, 81%) as an oil [16].

**Method B.** A solution of the alcohol **7** (110 mg, 0.8 mmol), triethyl orthoacetate (3 ml, 16.4 mmol) and propionic acid (catalytic) in dry DMF (3 ml) in a 25 ml flask was placed in a microwave oven and irradiated for 14 min. After the completion of the irradiation, work-up and purification as described above furnished the ester **11** (144 mg, 87%).

IR (neat):  $\nu_{\max}$   $\text{cm}^{-1}$  3070 (=C-H), 1735 (O-C=O), 1662 (C=C), 1230, 1200, 1152, 1134, 1116, 1095, 1030, 880 (C=CH<sub>2</sub>).  $^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.78 (1H, s) and 4.52 (1H, s) (olefinic), 4.12 (2H, q,  $J = 7.2$  Hz, O-CH<sub>2</sub>CH<sub>3</sub>), 2.70 (1H, br s) and 2.42 (1H, br s) (H-1 and 4), 2.42 and 2.16 (2H, AB q,  $J = 15$  Hz,  $\text{CH}_2\text{-CO}$ ),

1.30–1.90 (6H, m, H-5, 6 and 7), 1.26 (3H, t,  $J = 7.2$  Hz, O-CH<sub>2</sub>CH<sub>3</sub>), 1.18 (3H, s, *tert*-Me).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  171.7 (s, O-C=O), 164.3 (s, C=CH<sub>2</sub>), 100.8 (t, C=CH<sub>2</sub>), 59.8 (t, O-CH<sub>2</sub>CH<sub>3</sub>), 46.8 (d, C-1), 44.8 (d, C-4), 45.2 (t,  $\text{CH}_2\text{-C=O}$ ), 44.0 (s, C-2), 37.0 (t, C-7), 29.2 (t) and 23.5 (t) (C-5 and 6), 22.8 (q, C<sub>3</sub>-CH<sub>3</sub>), 14.3 (q, O-CH<sub>2</sub>CH<sub>3</sub>). EIMS:  $m/z$  208 (19%,  $\text{M}^+$ ), 134 (20), 121 (84), 120 (70), 105 (40), 93 (100), 91 (70). HRMS:  $m/z$  208.1455 (Calcd for  $\text{C}_{13}\text{H}_{20}\text{O}_2$ : 208.1463).

**exo-(2-Methyl-3-methylenebicyclo[2.2.1]heptane)-2-acetic acid (6).** To a solution of the ester **11** (4.2 g, 20.19 mmol) in methanol (20 ml) was added an aqueous solution of NaOH (4 g in 20 ml) and magnetically stirred at  $70^\circ$  for 6 hr. The reaction mixture was then acidified with 10% HCl and extracted with ether ( $3 \times 30$  ml). The ether layer was washed with water followed by brine and dried ( $\text{Na}_2\text{SO}_4$ ). Evaporation of the solvent and purification of the residue over a silica gel (5 g) column using  $\text{CH}_2\text{Cl}_2$  as eluant gave the acid **6** (2.75 g, 76%) which was recrystallized from hexane- $\text{CH}_2\text{Cl}_2$ . m.p.:  $85\text{--}87^\circ$ . IR (nujol):  $\nu_{\max}$   $\text{cm}^{-1}$  3000 (br, OH), 1707 (O-C=O), 1242, 935, 888 (C=CH<sub>2</sub>).  $^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.83 (1H, s) and 4.57 (1H, s) (olefinic), 2.70 (1H, br s, H-4), 2.48 (1H, br s, H-1), 2.48 and 2.27 (2H, AB q,  $J = 16$  Hz,  $\text{CH}_2\text{-CO}$ ), 1.30–1.80 (6 H, m, H-5, 6 and 7), 1.2 (3H, s, *tert*-CH<sub>3</sub>).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  179.0 (s, O-C=O), 164.5 (s, C=CH<sub>2</sub>), 101.3 (t, C=CH<sub>2</sub>), 46.9 (d) and 45.0 (d) (C-1 and 4), 45.5 (t, C-7), 44.2 (s, C-2), 37.3 (t,  $\text{CH}_2\text{COOH}$ ), 29.3 (t) and 23.7 (C-1 and C-4), 23.1 (q, *tert*-CH<sub>3</sub>). (Found: C, 73.46; H, 9.08.  $\text{C}_{11}\text{H}_{16}\text{O}_2$  requires C, 73.30; H, 8.95%).

**7-Methyltetracyclo[6.2.1.0<sup>2,4</sup>.0<sup>2,7</sup>]undecan-5-one (5)**

(1) **Acid chloride (14).** A solution of the acid **6** (2.5 g, 13.8 mmol) and oxalyl chloride (2 ml, 23.2 mmols) in dry benzene (5 ml) was magnetically stirred at room temperature for 2 hr. Evaporation of the solvent and excess oxalyl chloride under reduced pressure afforded the acid chloride **14** which was immediately used for the preparation of the diazo ketone.

(2) **Diazo ketone (15).** A solution of the acid chloride **14**, obtained above, in dry ether (10 ml) was added dropwise with stirring to a cold ethereal solution of diazomethane (excess, prepared from 15 g of *N*-nitroso-*N*-methylurea and 50 ml of 50% aqueous KOH). The reaction mixture was stirred at room temperature for 2 hr, and the ether and excess diazomethane were removed by careful evaporation on a water bath. Filtration of the residue rapidly through a neutral alumina (8 g) column using EtOAc-hexane (1:20) as eluant furnished the diazo ketone **15** (2.2 g, 78%) as a viscous yellow oil. IR (neat):  $\nu_{\max}$   $\text{cm}^{-1}$  3075 (=C-H), 2105 (diazo), 1635 (C=O), 1455, 1359, 1053, 880.  $^1\text{H}$  NMR (60 MHz,  $\text{CCl}_4$ ):  $\delta$  5.08 (1H, s,  $\text{HC=N}_2$ ), 4.65 (1H, s) and 4.41 (1H, s) (olefinic), 2.66 (1H, br s, H-4), 2.50 (1H, br s, H-1), 2.05 and 2.35 (2H, AB q,  $J = 14$  Hz,  $\text{CH}_2\text{-C=O}$ ), 1.00–2.00 (6H, m, H-5, 6 and 7), 1.13 (3H, s, *tert*-CH<sub>3</sub>).

(3) **Cyclopropyl ketone (5).** A solution of the diazo ketone **15** obtained above was taken in dry cyclohexane

(25 ml) and added dropwise, over a period of 0.5 hr, to a refluxing (using a 100 W tungsten lamp placed at 2" (1" ≈ 25.4 mm) from the reaction flask), magnetically stirred suspension of anhydrous CuSO<sub>4</sub> (4.5 g) in cyclohexane (80 ml), and stirred at reflux for 5 hr. The reaction mixture was cooled and the CuSO<sub>4</sub> was filtered off using a sintered funnel. Evaporation of the solvent and purification of the residue on a silica gel (20 g) column using EtOAc-hexane (1:20) as eluant furnished the tetracyclic ketone **5** (1.3 g, 53% from acid **6**) as a waxy, low melting solid. IR (neat):  $\nu_{\max}$  cm<sup>-1</sup> 1730 (C=O), 1470, 1296, 1236, 1206, 957. <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>):  $\delta$  2.48 and 2.02 (2H, AB *q*, *J* = 18 Hz, CH<sub>2</sub>-C=O), 2.16 (1H, *br s*, H-4), 1.20–2.00 (10 H, *m*), 0.98 (3 H, *s*, *tert*-CH<sub>3</sub>). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>):  $\delta$  215.1 (*s*, C=O), 56.0 (*t*, CH<sub>2</sub>CO), 50.8 (*s*, C-7), 48.2 (*d*) and 42.0 (*d*) (C-1 and 8), 40.5 (*s*, C-2), 37.7 (*t*, C-11), 35.2 (*d*, C-4), 25.0 (2C, *t*, C-9 and 10), 23.1 (*q*, C<sub>7</sub>-Me), 17.2 (*t*, C-3). EIMS: *m/z* 176 (31%, M<sup>+</sup>), 148 (45, M<sup>+</sup>-CO), 121 (45), 120 (51), 106 (42), 105 (30), 93 (100), 91 (60), 79 (52). HRMS: *m/z* 176.1195. (Calcd. for C<sub>12</sub>H<sub>16</sub>O 176.1201).

*exo*-2,6-Dimethyltricyclo[5.2.1.0<sup>2,6</sup>]decan-4-one (**4**).

**Method A.** To a magnetically stirred, freshly distilled ammonia (150 ml) in a three necked flask equipped with a Dewar condenser, was added the cyclopropyl ketone **5** (1.12 g, 6.4 mmol) in dry ether (5 ml), followed by freshly cut lithium (175 mg, 25 mmol). The reaction mixture was stirred at -33° for 15 min, quenched with solid NH<sub>4</sub>Cl and the ammonia was slowly evaporated. The residue was taken in water (30 ml) and extracted with ether (3 × 30 ml). The ether extract was washed with brine and dried (Na<sub>2</sub>SO<sub>4</sub>). Evaporation of the solvent and purification of the residue over a silica gel (15 g) column using EtOAc-hexane (1:20) as eluent furnished the prochiral ketone **4** (908 mg, 81%), as a low melting solid.

**Method B.** A suspension of the cyclopropyl ketone **5** (40 mg, 0.23 mmol) and 10%-Pd/C (10 mg) in methanol (5 ml) was placed in a 250 ml pressure bottle and hydrogenated at 40 psi (≈ 276 kPa) for 5 hr in a Parr-type hydrogenation apparatus. The catalyst was filtered off using a Buchner funnel. Evaporation of the solvent furnished the prochiral ketone **4** (40 mg, 99%).

IR (CCl<sub>4</sub>):  $\nu_{\max}$  cm<sup>-1</sup> 1737 (C=O), 1404, 1386, 1092, 624. <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>):  $\delta$  2.32 (4H, *s*, 2 × CH<sub>2</sub>-CO), 1.90 (2H, *br s*, H-1 and 7), 1.20–1.80 (6H, *m*, H-5, 6 and 7), 1.12 (6 H, *s*, 2 × *tert*-CH<sub>3</sub>). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>):  $\delta$  219.5 (*s*, C=O), 55.4 (2C, *t*, CH<sub>2</sub>-C=O), 50.5 (2C, *d*, C-1 and 7), 46.2 (2C, *s*, C-2 and 6), 34.8 (*t*, C-10), 23.7 (2C, *t*, C-7 and 8), 21.1 (2C, *q*, 2 × *tert*-CH<sub>3</sub>). EIMS: *m/z* 178 (80%, M<sup>+</sup>), 150 (30, M<sup>+</sup> - CO), 135 (100), 121 (37), 109 (40), 108 (55), 107 (96), 95 (76), 94 (90), 93 (80). HRMS: *m/z* 178.1364. (Calcd. for C<sub>12</sub>H<sub>18</sub>O 178.1358).

*exo*-2,6-Dimethyltricyclo[5.2.1.0<sup>2,6</sup>]dec-4-ene (*albene* **1**).

(1) **Tosylhydrazone (16).** A magnetically stirred solution of the ketone **4** (535 mg, 3 mmol) and tosylhydrazide (600 mg, 3.2 mmol) in ethanol (5 ml) was refluxed for 4 hr. Solvent was then evaporated under reduced pressure and

the crude product was purified on a silica gel (4 g) column using EtOAc-hexane (1:9) as eluant to furnish the hydrazone **16** (890 mg, 86%) which was recrystallized from hexane-CH<sub>2</sub>Cl<sub>2</sub>. m.p.: 162° (decomp.). IR (CCl<sub>4</sub>):  $\nu_{\max}$  cm<sup>-1</sup> 3268 (NH), 1680 (C=N), 1467, 1440, 1401, 1341, 1305, 1158, 1086, 1020, 621. <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>):  $\delta$  7.74 and 7.22 (4H, A<sub>2</sub>B<sub>2</sub> *q*, *J* = 7.5 Hz, aromatic), 2.36 (3H, *s*, Ar-Me), 2.20 (2H, *br s*) and 1.76 (2H, *br s*) (H-3 and 5), 1.00–1.50 (8H, *m*), 0.90 (6H, *s*, 2 × *tert*-CH<sub>3</sub>). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>):  $\delta$  168.5 (C=N), 143.8, 135.7, 129.6 (2C) and 127.9 (2C) (aromatic), 50.5, 50.3 (2C), 49.0, 47.0, 44.9, 34.5, 23.6, 23.4, 21.7, 21.0 (2C).

(2) **Shapiro reaction.** To a magnetically stirred, cold (0°) solution of the tosylhydrazone **16** (800 mg, 2.3 mmol) in dry ether (5 ml) and TMEDA (2.5 ml) was added a solution of *n*-butyllithium (1.6 M in hexanes, 4 ml, 6.4 mmol). The reaction mixture was stirred for 6 hr at 0°, then quenched with wet ether, acidified with HCl (0.5 M) and extracted with ether 3 × 10 ml). The ether extract was washed with saturated aqueous NaHCO<sub>3</sub> and brine, and dried (Na<sub>2</sub>SO<sub>4</sub>). Careful evaporation of the solvent followed by purification of the residue on a silica gel (3 g) column using pentane as eluant furnished (±)-albene (**1**, 245 mg, 65%) as a white solid which was sublimed at 60°/50–60 mm. m.p.: 110–115° (Lit.[1] 110–115°). <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>):  $\delta$  5.57 and 5.27 (2H, *t* of AB *q*, *J*<sub>3,4</sub> = 7 Hz, *J*<sub>3,5</sub> = *J*<sub>4,5</sub> = 2 Hz, olefinic), 2.23 (2H, *t*, *J* = 2 Hz, CH<sub>2</sub>-CH=), 1.80 (2H, *br s*, H-1 and 7), 1.00–1.80 (6H, *m*, H-8, 9 and 10), 0.96 (6H, *s*, 2 × *tert*-CH<sub>3</sub>). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>):  $\delta$  139.7 (*d*, C-3), 128.4 (*d*, C-4), 56.5 (*s*, C-2), 51.9 (*t*, C-5), 50.4 (*d*) and 47.3 (*d*) (C-1 and 7), 46.8 (*s*, C-6), 34.3 (*t*, C-10), 24.0 (2C, *t*, C-8 and 9), 20.8 (*q*, C<sub>6</sub>-CH<sub>3</sub>), 18.2 (*q*, C<sub>2</sub>-CH<sub>3</sub>).

**Acknowledgement**—One of the authors (SN) wishes to thank the Council of Scientific and Industrial Research, New Delhi for the award of a research fellowship.

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