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

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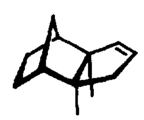
IN HONOUR OF PROFESSOR ANTONIO G. GONZALEZ

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

Abstract—A regiospecific and stereoselective total synthesis of the trisnorsesquiternene (±)-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.$0^{2,6}$]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 In 1972 the tetrahydrotriquinacene structure was revoked [3] based on chemical degradation and correlation with camphene, and the *endo* structure **3** (now referred to as isoalbene) was assigned to albene.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.$0^{2,6}$]undec-3-ene (**1**) was established conclusively, largely due to the efforts of Kreiser and coworkers [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.$0^{2,6}$]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.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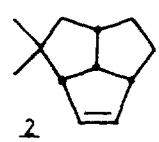
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RESULTS AND DISCUSSION

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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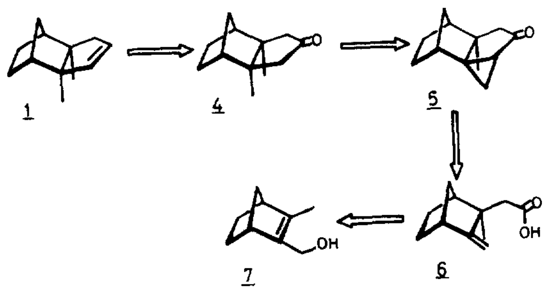
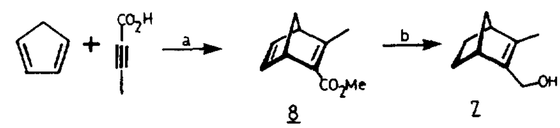
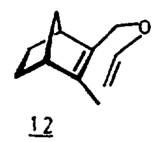
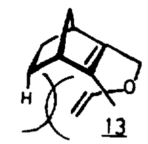


Scheme 1. Retro synthetic analysis of albene.



Scheme 2. (a) i 140°, sealed tube, 5 hr; ii CH_2N_2, Et_2O. (b) i H_2-10% Pd/C, 1 atm, 1.5 hr; ii DIBAH, PhMe, − 78°, 1 hr.



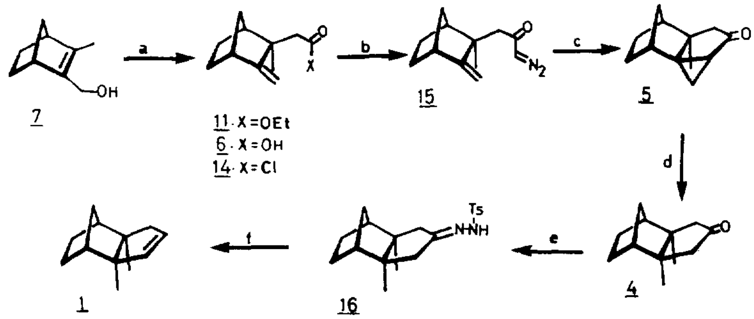


was prepared in a straightforward manner starting from cyclopentadiene. Since the Diels–Alder reaction of cyclopentadiene with methyl tetrolate resulted in low yield of the adduct **8**, Diels–Alder reaction was carried out using tetrolic acid. Thus reaction of cyclopentadiene and tetrolic acid in a 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).

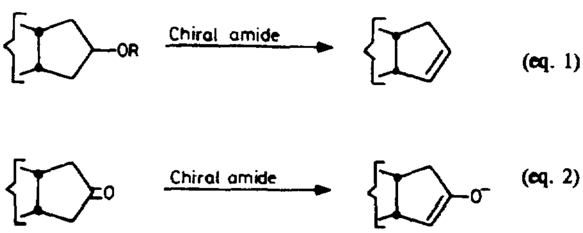
The first quaternary carbon atom of albene was introduced using a highly stereoselective *ortho* ester Claisen rearrangement [14]. Thus, thermal activation of a solution of the allyl alcohol **7** and a catalytic amount of propionic acid in triethyl *ortho*-acetate for 48 hr at 180° generated the ene-ester **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 commerical 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 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 ketocarbenoid 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_3–C_4 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 ^1H and ^{13}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_2-10% 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 ^1H and ^{13}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 $MeC(OEt)_3$, EtCOOH; sealed tube, 180°, 48 hr or DMF, microwave irradiation, 14 min. (b) i Aq. NaOH, MeOH, 70°, 6 hr; ii C_6H_6, $(COCl)_2$, RT, 2 hr. iii CH_2N_2, Et_2O, 2 hr. (c) Anhydrous $CuSO_4$, c-C_6H_{12}, W-lamp, 5 hr. (d) Li-liquid NH_3, 15 min or H_2-10% Pd/C, 40 psi, 5 hr. (e) NH_2NH-Ts, EtOH, reflux, 4 hr. (f) *n*-BuLi, Et_2O, TMEDA, 0°, 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 converison 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 (δ ppm) and coupling constants (Hz) in ^1H (60 and 90 MHz) and ^{13}C NMR (22.5 MHz) spectra are reported with reference to either internal tetramethylsilane (for ^1H) or central line (77.1 ppm) of $CDCl_3$ (for ^{13}C). In the ^{13}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°. 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 N_2 and heated at 140° for 5 hr. The Carius tube was cooled, saturated solution of aqueous $NaHCO_3$ (50 ml) was added to the reaction mixture and washed with CH_2Cl_2 (3 x 30 ml) to remove the dicyclopentadiene and other oligomers. The aqueous phase was acidified with 10% aqueous HCl and extracted with CH_2Cl_2 (3 x 30 ml). The CH_2Cl_2 layer was washed with water and brine, and dried (Na_2SO_4). Evaporation of the solvent and filteration of the residue through a silica gel (5 g) column using CH_2Cl_2 as eluant furnished the adduct **9** ($\approx$ 8 g) as a dark low melting solid. ^1H NMR (90 MHz, $CDCl_3$): δ6.92 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 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 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): ν_{max} cm^{-1} 3070 (=C–H), 1713 (C=O), 1635 (C=C), 1437, 1341, 1320, 1296, 1239, 1194, 1101, 1068. ^1H NMR (60 MHz, CCl_4): δ6.60–7.00 (2H, *m*, olefin), 3.90 (1H, *brs*, H-4), 3.72 (3H, *s*, O-CH_3), 3.40 (1H, *br s*, H-1), 2.23 (3H, *s*, olefinic CH_3), 2.00 (2H, *m*, H-7). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ169.5 (*s*, 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*, O–CH_3), 50.5 (*d*, C-1), 16.9 (*q*, C_3–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 EtOAc (15 ml) was added 10%-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): ν_{max} cm^{-1} 1713 (C=O), 1632 (C=C), 1437, 1359, 1281, 1257, 1203, 1161, 1092, 1056. ^{1}H NMR (60 MHz, CCl_4): δ3.63 (3H, *s*, O–CH_3), 3.15 (1H, *br s*, H-4), 2.75 (1H, *br s*, C-1), 2.16 (3H, *s*, olefinic CH_3), 0.95–1.90 (6H, *m*, H-5, 6 and 7). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ165.8 (*s*, O–C=O), 160.0 (*s*, C-3), 131.8 (*s*, C-2), 50.4 (*q*, O-CH_3), 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_3).

(*3-Methylbicyclo*[2.2.1]*hept-2-en*)*-2-methanol* (**7**). To a cold (–78°) 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 (Na_2SO_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): ν_{max} cm^{-1} 3340 (OH), 1692, 1446, 1278, 993. ^{1}H NMR (90 MHz, $CDCl_3$): δ4.21 and 4.00 (2H, AB*q*, J = 12.6 Hz, C$\underline{H}_2$OH), 2.90 (1H, *br s*) and 2.60 (1H, *br s*) (H-1 and 4), 1.68 (3H, *s*, olefinic CH_3), 0.90–1.70 (6H, *m*, H-5, 6 and 7). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ140.0 (*s*) and 139.1 (*s*) (olefinic), 57.4 (*t*, CH_2OH), 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_3). EIMS: *m/z* 138 (37%, 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 N_2 and heated at 180° for 48 hr. The reaction mixture was cooled, diluted with ether (30 ml), washed with 0.5 M HCl followed by saturated $NaHCO_3$ solution and brine, and dried (Na_2SO_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): ν_{max} cm^{-1} 3070 (=C–H), 1735 (O–C=O), 1662 (C=C), 1230, 1200, 1152, 1134, 1116, 1095, 1030, 880 (C=CH_2). ^{1}H NMR (90 MHz, $CDCl_3$): δ4.78 (1H, *s*) and 4.52 (1H, *s*) (olefinic), 4.12 (2H, *q*, J = 7.2 Hz, O–C$\underline{H}_2$CH$_3$), 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, C$\underline{H}_2$-CO), 1.30–1.90 (6H, *m*, H-5, 6 and 7), 1.26 (3H, *t*, J = 7.2 Hz, O–CH$_2$C$\underline{H}_3$), 1.18 (3H, *s*, *tert*-Me). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ171.7 (*s*, O–C=O), 164.3 (*s*, $\underline{C}$=CH$_2$), 100.8 (*t*, C=$\underline{C}$H$_2$), 59.8 (*t*, O–$\underline{C}$H$_2$CH$_3$), 46.8 (*d*, C-1), 44.8 (*d*, C-4), 45.2 (*t*, $\underline{C}$H$_2$–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$_3$–CH$_3$), 14.3 (*q*, O–CH$_2\underline{C}$H$_3$). EIMS: *m/z* 208 (19%, M$^+$), 134 (20), 121 (84), 120 (70), 105 (40), 93 (100), 91 (70). HRMS: *m/z* 208.1455 (Calcd for $C_{13}H_{20}O_2$: 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° for 6 hr. The reaction mixture was then acidified with 10% HCl and extracted with ether (3 × 30 ml). The ether layer was washed with water followed by brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel (5 g) column using CH_2Cl_2 as eluant gave the acid **6** (2.75 g, 76%) which was recrystallized from hexane–CH_2Cl_2. m.p.: 85–87°. IR (nujol): ν_{max} cm^{-1} 3000 (br, OH), 1707 (O–C=O), 1242, 935, 888 (C=CH_2). ^{1}H NMR (90 MHz, $CDCl_3$): δ4.83 (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, CH_2–CO), 1.30–1.80 (6 H, *m*, H-5, 6 and 7), 1.2 (3H, *s*, *tert*-CH_3). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ179.0 (*s*, O–C=O), 164.5 (*s*, $\underline{C}$=CH$_2$), 101.3 (*t*, C=$\underline{C}$H$_2$), 46.9 (*d*) and 45.0 (*d*) (C-1 and 4), 45.5 (*t*, C-7), 44.2 (*s*, C-2), 37.3 (*t*, $\underline{C}$H$_2$COOH), 29.3 (*t*) and 23.7 (C-1 and C-4), 23.1 (*q*, *tert*-CH_3). (Found: C, 73.46; H, 9.08. $C_{11}H_{16}O_2$ requires C, 73.30; H, 8.95%).

7-Methyltetracyclo[6.2.1.0^{2,4}.0^{2,7}]*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): ν_{max} cm^{-1} 3075 (=C–H), 2105 (diazo), 1635 (C=O), 1455, 1359, 1053, 880. ^{1}H NMR (60 MHz, CCl_4): δ5.08 (1H, *s*, $\underline{H}$C=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, C$\underline{H}_2$-C=O), 1.00–2.00 (6H, *m*, H-5, 6 and 7), 1.13 (3H, *s*, *tert*-CH_3).

(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 $CuSO_4$ (4.5 g) in cyclohexane (80 ml), and stirred at reflux for 5 hr. The reaction mixture was cooled and the $CuSO_4$ 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 furnishd the tetracyclic ketone **5** (1.3 g, 53% from acid **6**) as a waxy, low melting solid. IR (neat): ν_{max} cm^{-1} 1730 (C=O), 1470, 1296, 1236, 1206, 957. ^{1}H NMR (90 MHz, $CDCl_3$): δ2.48 and 2.02 (2H, AB *q*, J = 18 Hz, C$\underline{H}_2$–C=O), 2.16 (1H, *br s*, H-4), 1.20–2.00 (10 H, *m*), 0.98 (3 H, *s*, *tert*-CH_3). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ215.1 (*s*, C=O), 56.0 (*t*, $\underline{C}H_2$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_7-Me), 17.2 (*t*, C-3). EIMS: *m/z* 176 (31%, M^+), 148 (45, M^+-CO), 121 (45), 120 (51), 106 (42), 105 (30), 93 (100), 91 (60), 79 (52). HRMS: *m/z* 176.1195. (Calcd. for $C_{12}H_{16}O$ 176.1201).

exo-2,6-*Dimethyltricyclo*[5.2.1.0^{2,6}]*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_4Cl 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_2SO_4). 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_4): ν_{max} cm^{-1} 1737 (C=O), 1404, 1386, 1092, 624. ^{1}H NMR (90 MHz, $CDCl_3$): δ2.32 (4H, *s*, 2 × C$\underline{H}_2$-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_3). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ219.5 (*s*, C=O), 55.4 (2C, *t*, $\underline{C}H_2$–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_3). EIMS: *m/z* 178 (80%, M^+), 150 (30, M^+ − CO), 135 (100), 121 (37), 109 (40), 108 (55), 107 (96), 95 (76), 94 (90), 93 (80). HRMS: *m/z* 178.1364. (Calcd. for $C_{12}H_{18}O$ 178.1358).

exo-2,6-*Dimethyltricyclo*[5.2.1.0^{2,6}]*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_2Cl_2. m.p.: 162° (decomp.). IR (CCl_4): ν_{max} cm^{-1} 3268 (NH), 1680 (C=N), 1467, 1440, 1401, 1341, 1305, 1158, 1086, 1020, 621. ^{1}H NMR (90 MHz, $CDCl_3$): δ7.74 and 7.22 (4H, A_2B_2 *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_3). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ168.5 (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 $NaHCO_3$ and brine, and dried (Na_2SO_4). 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°). ^{1}H NMR (90 MHz, $CDCl_3$): δ5.57 and 5.27 (2H, *t* of AB *q*, $J_{3,4}$ = 7 Hz, $J_{3,5}$ = $J_{4,5}$ = 2Hz, olefinic), 2.23 (2H, *t*, J = 2Hz, C$\underline{H}_2$–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_3). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ139.7 (*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_6-CH_3), 18.2 (*q*, C_2-CH_3).

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