# Radical Annulation Strategy to Chiral Pupukeanones: Total Synthesis of (+)-10-*exo*-(1-Naphthyl)pupukean-9-one and (+)-10-*exo*-(1-Naphthyl)-5-epipupukean-9-ones[1]

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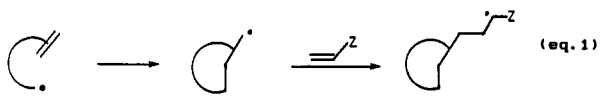
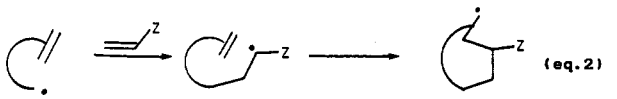
Intramolecular alkylation reaction of the bromoenone **12**, obtained from *S*-carvone in three steps, furnished the bicyclo[2.2.2]octenone **13**. Contrary to the anticipated radical annulation reaction, the bicyclic bromides **14** and **15**, obtained from the enone **13**, generated exclusively the cyclopropane product **18** via a 3-*exo-trig* radical cyclization on reaction with $^{n}Bu_3SnH$ and AIBN, even in the presence of a large excess of a radicophile. On the other hand, bromoenone **24**, synthesized from *R*-carvone via *S*-naphthylcarvone **21**, underwent radical annulation reaction in the presence of radicophiles to furnish the isotwistanes **25–28** in a regio- and stereospecific manner. Hydrogenation of the olefin **34**, obtained from the diketone **27** via a regiospecific Wittig reaction, furnished the naphthyl-5-epipupukean-9-one **33**, whereas stereoselective hydrogenation of the enone **36**, prepared from the keto ester **25** via a Grignard reaction and dehydration sequence, generated the naphthylpupukeanone **32**.

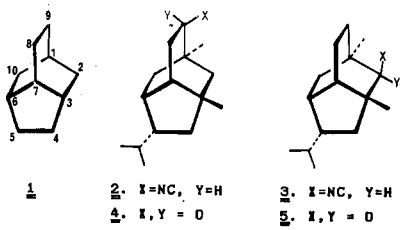
In the last decade, there has been an upsurge of interest in the application of free-radical reactions in organic synthesis. Both inter- and intramolecular radical additions to olefinic and acetylenic systems have been employed for the synthesis of various functional moieties and also to a variety of natural products.[2] A combination of inter- and intramolecular radical additions in a single sequence, to achieve highly functionalized molecules, is appealing from a synthetic standpoint. The most straightforward approach involves sequencing of a rapid intramolecular addition, i.e., radical cyclization, followed by an intermolecular trapping of the cyclized radical (eq 1). On the




other hand, the reverse sequence, i.e., an intermolecular addition of a radical onto a radicophile followed by a radical cyclization (eq 2) can provide functionalized ring systems from acyclic precursors, and overall sequence results in an annulation.[3] However, in the design of such processes, reactivity and selectivity requirements for each intermediate radical must be carefully assessed.

The tricyclic sesquiterpenes, pupukeananes, contain the unique tricyclo[4.3.1.$0^{3,7}$]decane (isotwistane (**1**)) carbon framework. The first members of this class, 9-isocyanopupukeanane (**2**) and 2-isocyanopupukeanane (**3**), were isolated in 1975 from the nudibranch *Phyllidia varicosa* and from its prey, a sponge, *Hymeniacidon* species by Scheuer et al.[4] The structures as well as the absolute configuration were established by chemical degradation

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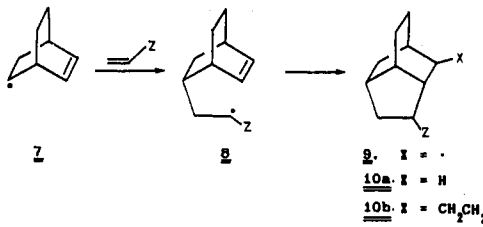
via the corresponding ketones 4 and 5 and from the single-crystal X-ray analysis of 2 and 3. Since then, several other pupukeananes were isolated from various sources.[4] The presence of a novel and unique isotwistane (1) ring system made pupukeananes attractive synthetic targets.[5] Synthesis of pupukeananes in chiral form has not been accomplished so far. In continuation of our interest in the synthesis of chiral bridged systems using radical cyclization reactions,[1,6,7] a radical annulation strategy has been planned for the synthesis of chiral pupukeananes starting from carvone (6), and herein we describe the regio- and stereospecific total synthesis of naphthyl-substituted analogues of the pupukean-9-one (4).[7]

It was anticipated that an intermolecular Michael addition of the bicyclo[2.2.2]oct-5-en-2-yl radical (7) onto a radicophile followed by 5-*exo-trig* cyclization of the resultant radical 8 would lead to the formation of the tricyclo[4.3.1.0$^{3,7}$]decane system 10, (eq 3). However, the

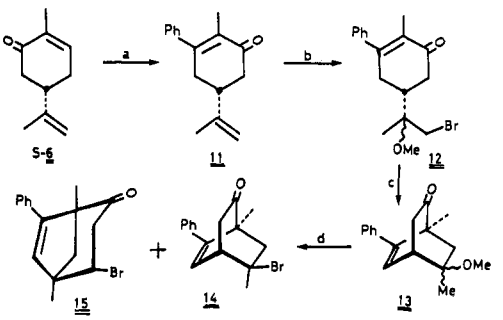


(eq. 3)

7 8 9, X = · 10a, X = H 10b, X = $CH_2CH_2Z$

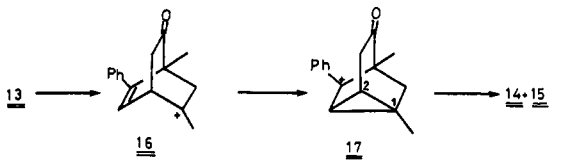
relative reactivity of the initial radical 7 and the final cyclized radical 9 toward the radicophile is comparable, since both are nucleophilic in nature, and hence it is difficult to stop the addition of the radical 9 onto one more molecule of the radicophile leading to the diadduct 10b. On the other hand, the presence of an electron-withdrawing group on the olefin (at C-5) will change the course of the reaction as it results in an electrophilic cyclized radical and thereby eliminate the possibility of second addition of the radicophile. In addition, this also enhances the regioselectivity in the radical cyclization step. To begin with, a phenyl group was opted because of the ready accessibility[1] of the necessary precursor starting from carvone. An intramolecular alkylation reaction strategy[8] was adopted for the generation of the requisite bicyclo-[2.2.2]octenyl system containing the two methyl groups and the ketone moiety suitably positioned for further elaboration to pupukean-9-ones (Scheme I). Thus, 1,2-addition of phenylmagnesium bromide to *S*-carvone ((*S*)-6) followed by oxidation of the resultant allylic alcohol with PCC–silica gel furnished the *R*-phenylcarvone (11) in 85% overall yield.[1] The regiospecific bromoetherification reaction on the electron-rich double bond of 11 with *N*-bromosuccinimide (NBS) in methylene chloride–methanol medium generated the epimeric mixture of the bromoenone 12, the precursor for the intramolecular alkylation reaction. Generation of the thermodynamic dienolate of the bromoenone 12 with $K^+$–O$^t$Bu in $^t$BuOH–

**Scheme I**[a]



[a] Key: (a)[1] (i) PhMgBr, $Et_2O$; (ii) PCC, silica gel, $CH_2Cl_2$, 85%; (b)[1] NBS, $CH_2Cl_2$–MeOH, 75%; (c) $K^+$–O$^t$Bu, THF–$^t$BuOH, 0.05 M, rt, 12 h, 75%; (d) $BBr_3$, $CH_2Cl_2$, –60 °C, 1 h, 78%, 14:15 = 3:1.

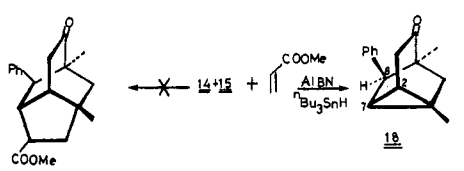
THF brought about the intramolecular alkylation and furnished an epimeric mixture of the enone 13 in 75% yield, whose structure was established from its spectral data (see Experimental Section). Treatment of the epimeric mixture of the enone 13 with boron tribromide in methylene chloride[9] generated an inseparable mixture (3:1) of the bicyclic bromides 14 and 15, in 78% yield. Both the $^1$H and $^{13}$C NMR spectra exhibited two sets of signals due to the bromoenones 14 and 15 [a major set at $\delta$ 6.37 (d, olefinic), 2.01 (s, BrC*Me*), 1.05 (s, bridgehead methyl group) in the $^1$H NMR spectrum and at 67.5 (s, CBr), 36.5 (q, *C*H$_3$CBr) ppm in the $^{13}$C NMR spectrum for 14; a minor set at $\delta$ 5.98 (s, olefinic), 4.46 (d, CHBr), 1.42 and 1.23 (2 × s, bridgehead methyl groups) in the $^1$H NMR spectrum and at 60.5 (s) and 52.8 (s) (bridgehead carbons), 56.3 (d, CHBr) ppm in the $^{13}$C NMR spectrum for 17. Formation of the two products 14 and 15 can be explained[9b] by the stabilization of the initial carbonium ion 16 by styrene moiety leading to the cyclopropyl benzyl carbonium ion 17 and the attack of the bromine at either C-1 or C-2 of 17 (eq 4). As the separation of the bromides 14 and



(eq. 4)

16 17

15 was found to be difficult, radical annulation reaction was attempted with the mixture of 14 and 15. Contrary to expectations, reaction of the mixture of the bromides 14 and 15 with $^n$Bu$_3$SnH (1.1 equiv), methyl acrylate (5 equiv), and AIBN (catalytic) in refluxing benzene (0.02 M) furnished the single product, the cyclopropyl ketone 18, in 85% yield, without incorporating the radicophile.



This was further proved by the formation of the same product 18 when the reaction was carried out in the absence of a radicophile. The structure of the product 18 was delineated from its spectral data. The mass spectrum

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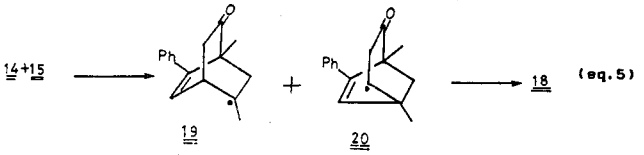
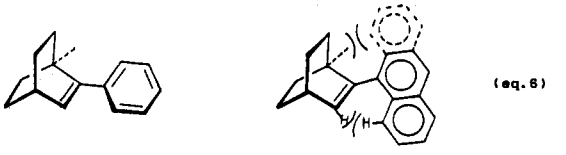
showed the molecular ion at $m/e$ 226 ($C_{16}H_{18}O$). The absence of olefinic proton and olefinic carbons (other than aromatic) in the $^1H$ and $^{13}C$ NMR spectra suggested the tricyclic nature of the product. The presence of two high-field protons at $\delta$ 1.49 and 1.19 due to cyclopropane, a doublet at 3.45 due to the cyclopropyl benzylic proton, and two singlets at 1.35 and 1.1 for the two tertiary methyl groups, AB part of an ABX spin pattern at 2.68 and 2.53 due to $COCH_2$, and an AB quartet at 1.93 and 1.99 ppm for the isolated methylene protons in the $^1H$ NMR spectrum established the structure. The $^{13}C$ NMR spectrum exhibited resonances at $\delta$ 210.9 (s, C=O), 55.9 (s, C-5), 53.7 (d, *C*HPh), 43.2 (t, $COCH_2$), 34.8 (t, C-8), 26.7 (d, C-7), 20.2 (s, C-1), 19.5 (q, cyclopropyl Me), 18.2 (d, C-2), and 17.3 ppm (q, $C_5$-Me) in addition to aromatic resonances, confirming the structure. The endo stereochemistry of the phenyl group was deduced from the coupling constants of the benzylic proton. It was established[10] that in tricyclo[3.2.1.$0^{2,7}$]octan-4-ones the $J_{6endo,7}$ is $\approx$0 and $J_{6exo,7}$ is $\approx$2 Hz. The 2.5-Hz coupling observed in the present case confirmed the presence of exo proton and hence the endo phenyl group at C-6. The cyclopropane product **18** was obviously formed via a 3-*exo-trig* cyclization of either the tertiary **19** or the secondary **20** radicals onto the styrene moiety (eq 5). The cyclization was found to




19 20

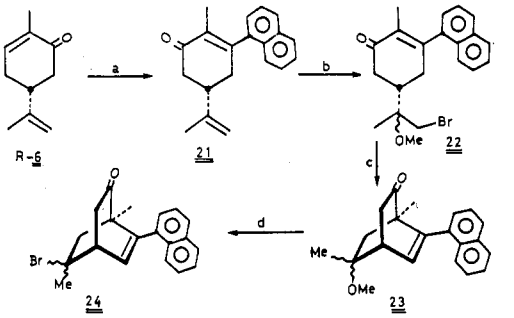
be very facile in that even the presence of 20 equiv of methyl acrylate was not able to trap the initial radical and prevent the formation of **18**. Interestingly, this was found to be the first example of an exclusive formation of a cyclopropane system from a homoallyl system under radical conditions.[11]

To overcome the cyclopropane formation, the phenyl group was replaced by the bulky 1-naphthyl group, in anticipation that the electrophilic nature of the olefin will be decreased. Because of lack of coplanarity between the olefin and aromatic systems due to steric reasons (between the peri hydrogen and the olefinic hydrogen on one side and the bridgehead methyl group on the other side), the olefin moiety may not be able to conjugate with the aromatic system reducing the electrophilic nature of the olefin (eq 6). However, the naphthyl group stabilizes the




resultant radical and inhibits the second addition of the radicophile. To this end, reactions were carried out with $\beta$-(1-naphthyl)carvone (Scheme II). Thus, 1,2-addition of 1-naphthyllithium to (*R*)-carvone ((*R*)-**6**) followed by oxidation of the resultant tertiary alcohol with PCC–silica gel produced the naphthylcarvone (*S*)-**21**, mp 102–104 °C, in over 85% yield. Regiospecific bromomethoxylation of **21** with NBS in the presence of methanol furnished the epimeric mixture of the bromoenone **22**, mp 108–110 °C,

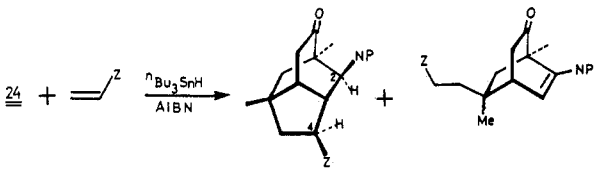
**Scheme II**[a]




[a] Key: (a) (i) 1-bromonaphthalene, $^n$BuLi (1.5 M in hexanes), THF, −70 °C to rt, 6 h; (ii) PCC, silica gel, $CH_2Cl_2$, 6 h, 85%; (b) NBS, $CH_2Cl_2$–MeOH, rt, 12 h, 83%; (c) $K^+$-O$^t$Bu, THF–$^t$BuOH, 0.05 M, rt, 12 h, 75%; (d) $BBr_3$, $CH_2Cl_2$, −60 °C, 1 h, 78%.

in 83% yield. Intramolecular alkylation reaction of the epimeric bromoenone **22** with $K^+$-O$^t$Bu in $^t$BuOH–THF generated the bicyclic enone **23**, mp 116–118 °C, in 75% yield as a 2:1 mixture of epimers. Unlike in the case of phenyl series, reaction of the bicyclic enone **23** with boron tribromide in methylene chloride gave only the epimeric mixture (2:1) of the bromoenone **24**, mp 114–116 °C, without any rearranged product, in 78% yield, clearly indicating the difference in the nature of olefin in both the systems. The presence of resonances at $\delta$ 6.49 and 6.52 (d, olefinic), 2.11 and 2.26 (s, $CH_3CBr$), and 0.82 ppm (s, bridgehead methyl group) in the $^1H$ NMR spectrum established the structure as well as epimeric nature of the bromoenone **24**. The $^{13}C$ NMR spectrum exhibited carbon resonances at $\delta$ 210.1 and 208.9 (s, C=O), 67.7 and 67.3 (s, CBr), 36.6 (q, *Me*CBr), and 14.9 (q, bridgehead methyl group) ppm for the two epimers, confirming the structure.

As expected, radical annulation of the bromoenone **24** with $^n$$Bu_3SnH$ (1.1 equiv), methyl acrylate (20 equiv), and AIBN (catalytic) in refluxing benzene (0.02 M) furnished, regio- and stereospecifically, the isotwistane **25**, 164–166 °C, in 50% yield. The structure of the keto ester **25** was




**25**. Z=COOMe **28**. Z=COOMe
**26**. Z=CN **30**. Z=CN
**27**. Z=COMe **31**. Z=COMe
**28**. Z=Ph

delineated from the spectral data. The presence of a molecular ion at $m/e$ 362 ($C_{24}H_{26}O_3$), the absence of olefinic proton and carbon resonances (other than aromatic signals), and the presence of a COOMe group at $\delta$ 3.61 in the $^1H$ and at 175.9 (s, OCO), 51.6 ppm (q, $OCH_3$) in the $^{13}C$ NMR spectra established the radical annulation reaction. The presence of a doublet at $\delta$ 3.58 due to the benzylic proton and doublet carbon resonances at 51.6 (*C*H-naphthyl) and 43.6 ppm (C-3) established the regiospecificity of the cyclization. The exo,exo stereochemistry at C-2 and -4 was assigned based on the weak coupling[12] (2.1 and 0 Hz) of the C-2 and -4 endo protons with the bridgehead proton at C-3; based on the dihedral angles the exo C-2 and -4 protons (i.e., if the substituents

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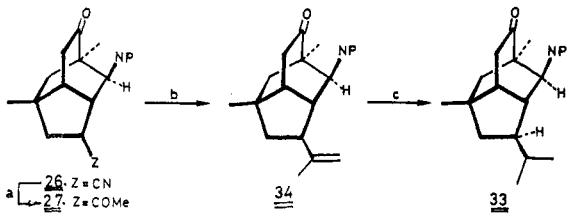
Table I. Chiral Isotwistanes via Radical Annulation

| Z | product | yield (%) | mp (°C) | $[\alpha]^{26}_D$ |
|---|---|---|---|---|
| COOMe | 25 | 50[a] | 164–166 | +96.3 |
| CN | 26 | 58[b] | 218–220 | +99.8 |
| COMe | 27 | 30[c] | 196–198 | +92.3 |
| Ph | 28 | 60 | 158–160 | +117 |

[a] In addition, 20% of the uncyclized adduct **29** was also formed. [b] In addition, 15% of the uncyclized adduct **30** was also formed. [c] Reaction time 2 h with addition of extra $^nBu_3SnH$ and AIBN every half hour. In addition, 20% of the uncyclized adduct **31** was also formed.

**Scheme III**[a]




[a] Key: (a) MeMgI, $Et_2O$–$C_6H_6$, reflux, 6 h, 60%; (b) $Ph_3P^+CH_3$–Br, $K^+$–$O^t$Am, $C_6H_6$–$^t$AmOH, rt, 5 h, 65%; (c) $H_2$–10% Pd/C, EtOAc, 1 atm, 4 h, 92%.

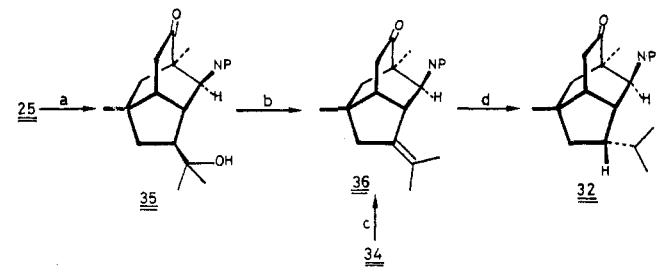
are endo,endo) are expected to have stronger coupling constants (6–10 Hz) with the C-3 proton.

To test the generality, the annulation sequence has been carried out with other radicophiles. Thus, radical annulation reaction of the bromoenone **24** with $^nBu_3SnH$ and AIBN in the presence of acrylonitrile, methyl vinyl ketone, and styrene afforded the annulated products **26**, **27**, and **28**, respectively, and the results are summarized in Table I. In addition to the annulated products, varying amounts of the epimeric mixtures of the uncyclized adducts **29**–**31** were also obtained.

Finally, attention was focused on the synthesis of pupukean-9-one analogues. The tricyclic compounds **25** and **27** were transformed to the analogues of pupukean-9-one **32** and **33**, respectively. First, the tricyclic diketone **27** was converted to an analogue of epipupukeanone **33** in a two-step sequence (Scheme III). The tricyclic diketone **27** was also obtained by a regioselective Grignard reaction (MeMgI, ether, benzene) of the keto nitrile **26** in 60% yield. Regiospecific Wittig reaction on the diketone **27** with methylenetriphenylphosphorane [generated from methyltriphenylphosphonium bromide, $K^+$–$O^t$Am in $^t$-AmOH, benzene][13] furnished the keto olefin **34** in 65% yield. Catalytic hydrogenation of the olefin **34** with 10% Pd–C in ethyl acetate generated the 10-*exo*-(1-naphthyl)-5-epipupukean-9-one (**33**), mp 120–122 °C, in 92% yield. The absence of olefinic proton and carbon resonances in the $^1H$ and $^{13}C$ NMR spectra, the appearance of two doublets at $\delta$ 0.83 and 0.79 ppm due to the diastereotopic isopropyl methyls in the $^1H$ NMR spectrum, and a doublet resonance at 33.2 and quartet resonances at 22.0 and 19.0 ppm in the $^{13}C$ NMR spectrum for the isopropyl group at C-4 confirmed the structure of the epipupukeanone **33**.

The analogue of pupukeanone **32** was obtained from the keto ester **25** (Scheme IV). Grignard reaction of the keto ester **25** with an excess of methylmagnesium iodide provided the tertiary alcohol **35**, mp 166–167 °C, in 86% yield. Dehydration of the tertiary alcohol **35** with PTSA (catalytic) in refluxing benzene led to the formation of the

**Scheme IV**[a]




[a] Key: (a) MeMgI, $Et_2O$–$C_6H_6$, reflux, 4 h, 86%; (b) PTSA, $C_6H_6$, reflux, 30 min, 88%; (c) PTSA, $C_6H_6$, rt, 8 h, 80%; (d) $H_2$–10% Pt/C, MeOH, 2 × 24 h, 50%.

tetrasubstituted olefin **36**, 178–180 °C, in 88% yield. The disappearance of the band due to OH group in the IR spectrum and the presence of quaternary olefinic carbon resonances ($\delta$ 140.7 and 121.9 ppm) in the $^{13}C$ NMR spectrum supported the formation of olefin. The presence of the isopropylidene group was confirmed by the absence of olefinic proton resonances and the appearance of two olefinic methyl singlets at $\delta$ 1.63 and 1.25 in the $^1H$ NMR spectrum and the presence of quartet resonances at 21.3 and 20.7 ppm in the $^{13}C$ NMR spectrum. Further, this compound was found to be identical with the product obtained in the isomerization of the keto olefin **34** with PTSA. Molecular models clearly suggested that the upfield shift of one of the olefinic methyls ($\delta$ 1.25 ppm) is because of the presence of one of the olefinic methyl groups in the shielding zone of the second aromatic ring of the naphthyl group. Hydrogenation[5f] of the keto olefin **36** with 10% Pt–C in methanol at 1 atm pressure yielded, stereoselectively, the 10-*exo*-(1-naphthyl)pupukean-9-one (**32**), mp 164–166 °C.[14] The structure of the product **32** was established from its spectral comparison with its epimer **33**. The endo orientation of the isopropyl group was clearly evident from the presence of two methyl doublets at $\delta$ 0.32 and 0.89 ppm in the $^1H$ NMR spectrum due to the shielding effect of the naphthyl ring.

In conclusion, a radical annulation strategy has been developed for the construction of chiral tricyclo[4.3.1.$0^{3,7}$]-decanes (isotwistanes) with the simultaneous formation of four chiral centers in a stereo- and regiospecific manner. The synthetic application of this annulation methodology has also been illustrated by the synthesis of the chiral pupukeanones **32** and **33**.

## Experimental Section

IR spectra were recorded on Perkin-Elmer 781 and Hitachi 270-50 spectrophotometers. UV spectra were recorded on a Shimadzu UV-190 spectrophotometer. $^1H$ (90, 200, 270 MHz) and $^{13}C$ NMR (22.5 MHz) spectra in $CDCl_3$ were recorded on Jeol FX-90Q, Bruker ACF-200, and Bruker WH-270 spectrometers. The chemical shifts ($\delta$ ppm) and the coupling constants (Hz) are reported in the standard fashion with reference to either internal tetramethylsilane (for $^1H$) or the 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 with a Jeol JMS-DX 303 GC–MS instrument 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. Optical rotations were measured using a JASCO DIP-303 polarimeter. Solvent evaporations were done with either a steam

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(14) Hydrogenation at 30 psi furnished the epimeric mixture of **32** and **33**.

bath or a Buchi rotary evaporator. Analytical thin-layer chromatographies (TLC) were performed on glass plates coated with Acme's silica gel G containing 13% calcium sulfate as binder, and various combinations of ethyl acetate–hexane or ethyl acetate–benzene were used as eluents. Visualization of spots was accomplished by exposure to iodine vapor. Acme's silica gel (100–200) was used for column chromatography. Dry benzene was obtained by washing with $H_2SO_4$ followed by distillation over sodium and stored over pressed sodium wire. Dry ether was obtained by distillation over sodium and stored over sodium wire. Dry THF was obtained by distillation over sodium–benzophenone ketyl. Methylene chloride was distilled from $P_2O_5$. PCC was prepared according to the literature procedure.[15] $^nBu_3SnH$, NBS, and $BBr_3$ were obtained from Fluka and were used without further purification. AIBN was recrystallized from methanol and stored in the dark.

**(−)-(1*S*,4*S*,8*R*)- and (−)-(1*S*,4*S*,8*S*)-1,8-Dimethyl-8-methoxy-6-phenylbicyclo[2.2.2]oct-5-en-2-ones (13).** A solution of the bromoenone[1] **12** (1:1 mixture of epimers, 3.37 g, 10 mmol) in dry THF (15 mL) was added rapidly to an ice-cold, magnetically stirred solution of $K^+$-O$^t$Bu in $^t$BuOH (1 M, 15 mL, 15 mmol). The reaction mixture was stirred at room temperature for 12 h, diluted with ether (20 mL), and washed with 0.5 N aqueous HCl (3 × 10 mL) followed by brine and dried ($Na_2SO_4$). Evaporation of the solvent and purification of the residue over a silica gel (20 g) column with ethyl acetate–hexane (1:4) as eluent furnished a 1:1 mixture of the bicyclooctenones **13** (1.92 g, 75%). Careful separation resulted in the individual epimers. **Compound 13a**: mp 94–95 °C; $[\alpha]^{26}_D$ −224.8° (*c* 2.46; $CHCl_3$); IR ($CCl_4$) $\nu_{max}$ 3028, 1725, 1491, 1452, 1404, 1371, 1329, 1188, 1152, 1131, 1080 cm$^{-1}$; $^1$H NMR (200 MHz) δ 7.2–7.35 (3 H, m) and 7.0–7.1 (2 H, m) (aromatic), 6.34 (1 H, d, *J* = 6.9 Hz, H-5), 3.24 (3 H, s, $OCH_3$), 3.03 (1 H, td, *J* = 6.9 and 2.6 Hz, H-4), 2.68 (1 H, d of $^1/_2$ AB q, *J* = 18.2 and 2 Hz, H-3 a), 2.06 (1 H, d of $^1/_2$AB q, *J* = 18.2 and 3.3 Hz, H-3 b), 1.9 and 1.68 (2 H, AB q, *J* = 14 Hz, H-7), 1.38 (3 H, s, C*H*$_3$COMe), 1.05 (3 H, s, $C_1$-Me); $^{13}$C NMR (22.5 MHz) δ 212.0 (s, C=O), 145.4 (s, C-6), 132.9 (d, C-5), 138.3 (s), 128.1 (2 C, d), 127.9 (2 C, d) and 127.3 (d) (aromatic), 78.4 (s, *C*OMe), 52.7 (s, C-1), 49.7 (q, $OCH_3$), 47.2 (t, CO*C*H$_2$), 41.1 (d, C-4), 34.5 (t, C-7), 25.1 (q, *C*H$_3$COMe), 16.5 (q, $C_1$-Me). **Compound 13b**: $[\alpha]^{26}_D$ −169.4° (*c* 0.71; $CHCl_3$); IR (neat) $\nu_{max}$ 1725, 1452, 1413, 1332, 1284, 1131, 1074, 840, 765, 702 cm$^{-1}$; $^1$H NMR (270 MHz) δ 7.09–7.45 (5 H, m, aromatic), 6.34 (1 H, d, *J* = 6.4 Hz, H-5), 3.23 (3 H, s, $OCH_3$), 3.08–3.1 (1 H, m, H-4), 2.25 (2 H, d, *J* = 2.8 Hz, H-3), 1.95 and 1.63 (2 H, AB q, *J* = 14 Hz, H-7), 1.42 (3 H, s, $C_8$-Me), 1.06 (3 H, s, $C_1$-Me); $^{13}$C NMR (22.5 MHz) δ 211.9 (s, C=O), 143.3 (s, C-6), 132.8 (d, C-5), 138.4 (s), 128.4 (2 C, d), 127.7 (2 C, d) and 127.0 (d) (aromatic), 78.9 (s, *C*OMe), 52.5 (s, C-1), 49.3 (q, $OCH_3$), 47.2 (t, CO*C*H$_2$), 40.9 (d, C-4), 36.1 (t, C-7), 22.3 (q, *C*H$_3$COMe), 16.4 (q, $C_1$-Me). For an epimeric mixture of **13**: mass *m/e* 256 ($M^+$, 20), 241 (20), 185 (40), 184 (100), 183 (60), 182 (55), 167 (20), 156 (21). Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.26; H, 7.92.

**(−)-(1*S*,4*S*,8*R*)-8-Bromo-1,8-dimethyl-6-phenylbicyclo[2.2.2]-oct-5-en-2-one (14) and (1*S*,4*S*,5*R*)-4-Bromo-1,5-dimethyl-7-phenylbicyclo[3.2.1]oct-6-en-2-one (15).** To a cold (−70 °C, ethanol–liquid $N_2$ bath), magnetically stirred solution of the bicyclooctenone **13** (1:1 epimeric mixture, 1.28 g, 5 mmol) in dry $CH_2Cl_2$ (10 mL) was added boron tribromide (0.6 mL, 6 mmol) dropwise. The reaction mixture was stirred at −60 °C for 1 h and quenched with an ice-cold aqueous $NaHCO_3$ solution (5 mL). The organic layer was separated, and the aqueous layer was extracted with $CH_2Cl_2$ (3 × 20 mL). The combined organic extract was washed with aqueous saturated $NaHCO_3$ solution followed by brine and dried ($Na_2SO_4$). Evaporation of the solvent and purification of the residue over a silica gel (10 g) column with ethyl acetate–hexane (1:9) as eluent furnished a 3:1 mixture of the bicyclic bromides **14** and **15** (1.2 g, 78%) as red oil: $[\alpha]^{26}_D$ −272.6° (*c* 5.46; $CHCl_3$); IR (neat) $\nu_{max}$ 3040, 1720, 1495, 1450, 1410, 1380, 1080, 1055, 760, 700 cm$^{-1}$; $^1$H NMR (270 MHz) δ 7.0–7.4 (5 H, m, aromatic); peaks due to **14** 6.37 (1 H, d, *J* = 6.8 Hz, olefinic), 3.24–3.3 (1 H, m, H-4), 3.11 (1 H, d of $^1/_2$AB q, *J* = 18.8 and 1.8 Hz, H-3 a), 2.37 (1 H, d of $^1/_2$AB q, *J* = 18.6 and 3.3 Hz, H-3 b), 2.61 and 2.08 (2 H, AB q, *J* = 14.9 Hz, H-7), 2.01 (3 H, s, BrCC*H*$_3$), 1.05 (3 H, s, $C_1$-Me); peaks due to **15** 5.96 (1 H, s, olefinic), 4.46 (1 H, d, *J* = 7 Hz, CH-Br), 3.56 (1 H, d of $^1/_2$AB q, *J* = 18 and 7 Hz, H-3 ax), 2.92 (1 H, d, *J* = 18 Hz, H-3 eq), 2.67 and 2.1 (2 H, AB q, *J* = 12 Hz, H-8), 1.42 (3 H, $C_5$-Me), 1.23 (3 H, s, $C_1$-Me); $^{13}$C NMR (22.5 MHz) δ 137.4 (s), 128.3 (d), 127.8 (2 C, d), 127.4 (d) and 127.0 (d) (aromatic); peaks due to **14** 209.1 (s, C=O), 144.5 (s) and 131.7 (d) (olefinic), 67.5 (s, CBr), 47.0 (d, C-4), 52.8 (s, C-1), 50.7 (t, CO*C*H$_2$), 38.5 (t, C-7), 36.5 (q, BrC*C*H$_3$), 15.8 (q, $C_1$-Me); peaks due to **15** 207.1 (s, C=O), 151.4 (s) and 135.1 (d) (olefinic), 60.5 (s, C-5), 56.3 (d, CHBr), 52.8 (s, C-1), 50.7 (t, CO*C*H$_2$), 23.7 (q, $C_5$-Me), 16.3 (q, $C_1$-Me). For a mixture of **14** and **15**: mass *m/e* 304 ($M^+$, 30), 306 ($M^+$ + 2, 29), 224 (32), 197 (35), 183 (70), 182 (100), 181 (40), 170 (72), 155 (30), 91 (35); HRMS *m/e* calcd for $C_{16}H_{17}BrO$, 304.0463, found 304.0462.

**(−)-(1*S*,2*S*,5*S*,6*S*,7*S*)-1,5-Dimethyl-6-phenyltricyclo-[3.2.1.0$^{2,7}$]octan-4-one (18).** A solution of the 3:1 mixture of bicyclic bromides **14** and **15** (305 mg, 1 mmol), $^nBu_3SnH$ (0.3 mL, 1.1 mmol), and AIBN (catalytic) in dry benzene (55 mL) was refluxed for 1 h. The reaction mixture was cooled, washed with aqueous 1% $NH_4OH$ solution (2 × 10 mL) followed by brine, and dried ($Na_2SO_4$). Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel (10 g) column with ethyl acetate–hexane (1:9) as eluent furnished the tricyclooctanone **18** (185 mg, 85%): $[\alpha]^{26}_D$ −140° (*c* 1.1; $CHCl_3$); IR (neat) $\nu_{max}$ 3060, 1720, 1500, 1090, 1035, 760, 710 cm$^{-1}$; $^1$H NMR (270 MHz) δ 7.25 (5 H, br s, aromatic), 3.45 (1 H, d, *J* = 2.5 Hz, C*H*Ph), 2.68 (1 H, d of $^1/_2$AB q, *J* = 20.5 and 2.2 Hz) and 2.53 (1 H, d of $^1/_2$AB q, *J* = 20.5 and 2.7 Hz) (CO$CH_2$), 1.93 and 1.99 (2 H, AB q, *J* = 12.9 Hz, H-8), 1.49 (1 H, dd, *J* = 7.3 and 2.9 Hz, H-7), 1.35 (3 H, s, $C_1$-Me), 1.19 (1 H, m, H-2), 1.1 (3 H, s, $C_5$-Me); $^{13}$C NMR (22.5 MHz) δ 210.9 (s, C=O), 139.1 (s), 128.1 (2 C, d), 127.5 (2 C, d) and 126.8 (d) (aromatic), 55.9 (s, C-5), 53.7 (d, *C*HPh), 43.2 (t, CO*C*H$_2$), 34.8 (t, C-8), 26.7 (d, C-7), 20.2 (s, C-1), 19.5 (q, $C_1$-Me), 18.2 (d, C-2), 17.3 (q, $C_5$-Me); mass *m/e* 226 ($M^+$, 100), 198 (18), 184 (28), 183 (32), 169 (35), 157 (47), 129 (32), 115 (33), 107 (25), 96 (89), 91 (61); HRMS *m/e* calcd for $C_{15}H_{18}O$, 226.1358, found 226.1362. Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 85.53; H, 8.00.

**(+)-(*S*)-5-Isopropenyl-2-methyl-3-(1-naphthyl)cyclohex-2-en-1-one (21).** To a cold (−70 °C, ethanol–liquid $N_2$ bath), magnetically stirred solution of 1-bromonaphthalene (6.6 mL, 48 mmol) in dry THF (60 mL) was added $^n$BuLi (1.5 M in hexanes, 30 mL, 45 mmol) and the resulting mixture stirred at the same temperature for 1 h. To the solution of 1-naphthyllithium thus formed was added (*R*)-carvone (**6**, 4.5 g, 30 mmol) in one portion. The reaction mixture was stirred at room temperature for 6 h and poured into ice-cold phosphate buffer (pH = 7, 50 mL). The organic layer was separated, and the aqueous phase was extracted with ether (3 × 30 mL). The combined ether extract was washed with brine and dried ($Na_2SO_4$). Evaporation of the solvent furnished the tertiary alcohol as a pale yellow oil (8 g).

To a magnetically stirred suspension of PCC (13 g, 60 mmol) and silica gel[15] (13 g) in dry $CH_2Cl_2$ (50 mL) was added a solution of the tertiary alcohol obtained above, in dry $CH_2Cl_2$ (50 mL) in one portion. The reaction mixture was stirred at room temperature for 6 h and passed through a silica gel (80 g) column and eluted with more $CH_2Cl_2$. Evaporation of the solvent furnished the naphthylcarvone **21** (7.04 g, 85%), which was recrystallized from hexane: mp 102–104 °C; $[\alpha]^{26}_D$ +122.5° (*c* 1.9; $CHCl_3$); UV ($CH_3OH$) $\lambda_{max}$ 282 nm (ε = 8700); IR ($CCl_4$) $\nu_{max}$ 3052, 1671, 1635, 1437, 1380, 1338, 1317, 1290, 1161, 897 cm$^{-1}$; $^1$H NMR (90 MHz) δ 7.1–8.0 (7 H, m, aromatic), 4.82 (2 H, br s, C=C$H_2$), 2.4–3.1 (5 H, m), 1.78 (3 H, s, $C_2$-Me), 1.52 (3 H, br s, $C_8$-Me). Anal. Calcd for $C_{20}H_{20}O$: C, 86.92; H, 7.29. Found: C, 86.71; H, 7.33.

**(+)-(*S*)-5-[(*R*)- and (*S*)-1-Bromo-2-methoxyprop-2-yl]-2-methyl-3-(1-naphthyl)cyclohex-2-en-1-ones (22).** To an ice-cold magnetically stirred solution of the naphthylcarvone **21** (2.76 g, 10 mmol) in a 3:2 mixture of $CH_2Cl_2$–methanol (20 mL) was added NBS (2.14 g, 12 mmol) in portions over a period of 1 h. The reaction mixture was stirred for 12 h at room temperature, washed with 2% aqueous sodium hydroxide solution and brine, and dried ($Na_2SO_4$). Evaporation of the solvent and purification of the product over a silica gel (60 g) column with ethyl acetate–benzene (1:49) as eluent furnished the bromoenone **22** (1:1 epimeric mixture, 3.2 g, 83%) as a light red solid which was

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recrystallized from hexane: mp 108–110 °C; $[\alpha]^{26}_D$ +100.1° (*c* 1.6; $CHCl_3$); UV ($CH_3OH$) $\lambda_{max}$ 282 nm ($\epsilon$ = 8600); IR ($CCl_4$): $\nu_{max}$ 3058, 1671, 1635, 1434, 1380, 1332, 1101 $cm^{-1}$; $^1H$ NMR (90 MHz, 1:1 epimers) $\delta$ 7.14–8.0 (7 H, m, aromatic), 3.46 (2 H, br s, $CH_2$-Br), 3.28 and 3.24 (3 H, s, $OCH_3$), 2.4–3.0 (5 H, m), 1.56 (3 H, br s, olefinic Me), 1.32 and 1.26 (3 H, s, $CH_3$COMe); $^{13}C$ NMR (22.5 MHz, 1:1 epimers) $\delta$ 199.1 (s, C=O), 156.0 and 154.9 (s, C-3), 139.2 and 138.7 (s, C-2), 133.5 (s), 129.2 (d), 128.6 (d), 127.8 (d), 126.5 (d), 126.2 (d), 125.6 (d), 125.2 (d), 124.6 (s), 124.1 (d) and 123.3 (d) (aromatic), 75.9 (s, COMe), 49.6 (q, $OCH_3$), 40.6 (d, C-5), 38.7 and 38.0 (t, $COCH_2$), 36.6 (t, $CH_2Br$), 34.9 and 33.1 (t, C-4), 18.1 and 17.8 (q, $CH_3$COMe), 12.5 (q, olefinic Me). Anal. Calcd for $C_{21}H_{23}BrO_2$: C, 65.12; H, 5.99. Found: C, 64.88; H, 5.95.

**(+)-(1*R*,4*R*,8*S*)- and (1*R*,4*R*,8*R*)-1,8-Dimethyl-8-methoxy-6-(1-naphthyl)bicyclo[2.2.2]oct-5-en-2-ones (23).** Intramolecular alkylation of the bromoenone **22** (1:1 mixture of epimers, 3.87 g, 10 mmol) with $K^+$-O$^t$Bu (1 M in $^t$BuOH, 15 mL, 15 mmol) in dry THF (15 mL) for 12 h as described for **12** and purification of the product over a silica gel (30 g) column with ethyl acetate–benzene (1:19) as eluent furnished the bicyclooctenone **23** (2:1 mixture of epimers, 2.3 g, 75%) as a pale yellow solid which was recrystallized from hexane: mp 116–118 °C; $[\alpha]^{26}_D$ +272° (*c* 0.6; $CHCl_3$); UV ($CH_3OH$) $\lambda_{max}$ 283 nm ($\epsilon$ = 7500); IR (neat) $\nu_{max}$ 3046, 1725, 1593, 1506, 1452, 1398, 1383, 1329, 1191, 1152, 1131, 1080, 1017, 846, 801, 780 $cm^{-1}$; $^1H$ NMR (270 MHz, 2:1 epimers) $\delta$ 7.6–7.95 (3 H, m), 7.3–7.55 (3 H, m), 7.12 (1 H, d, *J* = 7 Hz) (aromatic), 6.46 and 6.49 (1 H, d, *J* = 7 Hz, olefinic), 3.28 and 3.31 (3 H, s, $OCH_3$), 3.14 (1 H, m, H-4), 2.82 and 2.75 (1 H, d of $^1/_2$AB q, *J* = 18.2 and 2.1 Hz, H-3 a), 2.29 and 2.26 (1 H, d of $^1/_2$AB q, *J* = 18.4 and 3.2 Hz, H-3 b), 1.75 and 2.04 (AB q, *J* = 14 Hz) and 1.96 (s) (2 H, H-7), 1.48 and 1.62 (3 H, s, $CH_3$COMe), 0.81 (3 H, s, $C_1$-Me). Anal. Calcd for $C_{21}H_{22}O_2$: C, 82.32; H, 7.24. Found: C, 82.35; H, 7.28.

**(+)-(1*R*,4*R*,8*S*)- and (1*R*,4*R*,8*R*)-8-Bromo-1,8-dimethyl-6-(1-naphthyl)bicyclo[2.2.2]oct-5-en-2-ones (24).** Reaction of the bicyclooctenone **23** (2:1 mixture of epimers, 3.06 g, 10 mmol) with boron tribromide (1.42 mL, 15 mmol) in dry $CH_2Cl_2$ (30 mL) at –60 °C for 1 h and purification of the product over a silica gel (20 g) column with ethyl acetate–benzene (1:49) as eluent furnished the bicyclic bromide **24** (2:1 mixture of epimers, 2.8 g, 78%) which was recrystallized from hexane: mp 114–116 °C; $[\alpha]^{26}_D$ +254.45° (*c* 1.15; $CHCl_3$); UV ($CH_3OH$) $\lambda_{max}$ 283 nm ($\epsilon$ = 10 370); IR ($CHCl_3$) $\nu_{max}$ 1722, 1593, 1380, 1326, 1140, 1074, 906 $cm^{-1}$; $^1H$ NMR (270 MHz, 2:1 epimers) $\delta$ 7.78–7.9 (2 H, m), 7.3–7.7 (4 H, m) and 7.11 and 6.98 (1 H, d, *J* = 7 Hz) (aromatic), 6.49 and 6.52 (1 H, d, *J* = 6.4 Hz, olefinic), 3.3–3.4 (1 H, m, H-4), 3.26 and 3.19 (1 H, d of $^1/_2$AB q, *J* = 18.7 and 2.4 Hz, H-3 a), 2.67 and 2.2 (AB q, *J* = 15.2 Hz) and 2.74 and 2.47 (AB q, *J* = 15.2 Hz) (2 H, H-7), 2.59 and 2.48 (1 H, d of $^1/_2$AB q, *J* = 18.5 and 3.2 Hz, H-3 b), 2.11 and 2.26 (3 H, s, BrCC$H_3$), 0.82 (3 H, s, $C_1$-Me); $^{13}C$ NMR (22.5 MHz, 2:1 epimers) $\delta$ 210.1 and 208.9 (s, C=O), 143.3 and 143.7 (s, C-6), 135.5 (d, C-5), 133.1 (d), 131.9, 131.7 (s), 128.1 (d), 127.0 (d), 126.3 (d), 125.8 (d), 125.4 (d) and 124.7 (d) (aromatic), 67.7 and 67.3 (s, C-Br), 53.8 (s, C-1), 50.7 and 49.9 (t, $COCH_2$), 47.4 and 46.8 (d, C-4), 39.1 and 38.3 (t, C-7), 36.6 (q, BrCC$H_3$), 14.9 (q, $C_1$-Me). Anal. Calcd for $C_{20}H_{19}BrO$: C, 67.62; H, 5.39. Found: C, 67.82; H, 5.37.

**(+)-Methyl (1*R*,2*R*,3*S*,4*S*,6*R*,7*R*)-1,6-Dimethyl-2-(1-naphthyl)-9-oxotricyclo[4.3.1.0$^{3,7}$]decane-4-carboxylate (25).** A solution of the bicyclic bromide **24** (355 mg, 1 mmol), $^n$Bu$_3$SnH (0.3 mL, 1.1 mmol), freshly distilled methyl acrylate (1.8 mL, 20 mmol), and AIBN (catalytic) in dry benzene (55 mL) was refluxed for 1 h. The reaction mixture was cooled, washed with aqueous 1% $NH_4OH$ solution (3 × 20 mL) and brine, and dried ($Na_2SO_4$). Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel (10 g) column with ethyl acetate–benzene (1:19) as eluent furnished the annulated product **25** (181 mg, 50%) which was recrystallized from hexane: mp 164–166 °C; $[\alpha]^{26}_D$ +96.3° (*c* 1.1; $CHCl_3$); IR ($CCl_4$) $\nu_{max}$ 1728, 1602, 1401, 1365, 1155, 1062, 1023 $cm^{-1}$; $^1H$ NMR (200 MHz) $\delta$ 8.08 (1 H, d, *J* = 7.4 Hz), 7.86 (1 H, dd, *J* = 7 and 2.4 Hz), 7.71 (1 H, d, *J* = 8.2 Hz), 7.45–7.57 (2 H, m), 7.38 (1 H, t, *J* = 8 Hz) and 7.08 (1 H, d, *J* = 7.3 Hz) (aromatic), 3.61 (3 H, s, $COOCH_3$), 3.58 (1 H, d, *J* = 2.1 Hz, C*H*Ar), 3.09 (1 H, dd, *J* = 9.1 and 5.3 Hz, C*H*COOMe), 2.73 (1 H, m, H-7), 2.7 and 2.5 (2 H, d of AB q, *J* = 18 and 3 Hz, $COCH_2$), 2.23 (1 H, d of $^1/_2$AB q, *J* = 13.6 and 9.2 Hz, H-5 a), 2.17 (1 H, m, H-3), 2.06 (1 H, d of $^1/_2$AB q, *J* = 13.6 and 5.4 Hz, H-5 b), 1.69 and 1.84 (2 H, AB q, *J* = 14.4 Hz, H-10), 1.21 (3 H, s, $C_6$-Me), 0.78 (3 H, s, $C_1$-Me); $^{13}C$ NMR (22.5 MHz) $\delta$ 215.6 (s, C=O), 175.9 (s, OC=O), 139.8 (s), 133.8 (s), 132.3 (s), 129.0 (d), 127.1 (d), 125.8 (d), 125.3 (2 C, d), 123.8 (d) and 123.3 (d) (aromatic), 51.6 (2 C, q and d, $OCH_3$ and C-2), 50.7 (2 C, t and d, C-8 and 4), 49.9 (d, C-7), 48.0 (t, C-5), 45.3 (s, C-1), 43.6 (d, C-3), 39.8 (s, C-6), 35.5 (t, C-10), 25.7 (q, $C_6$-Me), 18.6 (q, $C_1$-Me); mass *m/e* 362 ($M^+$, 100), 221 (17), 165 (30), 141 (87). Anal. Calcd for $C_{24}H_{26}O_3$: C, 79.53; H, 7.23. Found: C, 79.71; H, 7.32.

Further elution of the column with the same solvent furnished the uncyclized adduct **29** (3:2 mixture of epimers, 54 mg, 15%) as a pale yellow oil: $[\alpha]^{26}_D$ +177.7° (*c* 6; $CHCl_3$); IR (neat) $\nu_{max}$ 3040, 1722, 1452, 1437, 1380, 1308, 1263, 1173, 1086, 801, 780 $cm^{-1}$; $^1H$ NMR (90 MHz, 3:2 epimers) $\delta$ 6.88–7.92 (7 H, m, aromatic), 6.5 and 6.52 (1 H, d, *J* = 7.2 Hz, olefinic), 3.68 (3 H, s, $COOCH_3$), 1.62–2.85 (9 H, m), 1.16 and 1.30 (3 H, s, $C_8$-Me), 0.78 (3 H, s, $C_1$-Me); mass *m/e* 362 ($M^+$, 15), 320 (33), 234 (20), 233 (100); HRMS *m/e* calcd for $C_{24}H_{26}O_3$: 362.1882, found 362.1885.

**(+)-(1*R*,2*R*,3*S*,4*S*,6*R*,7*R*)-4-Cyano-1,6-dimethyl-2-(1-naphthyl)tricyclo[4.3.1.0$^{3,7}$]decan-9-one (26).** Radical annulation reaction of the bicyclic bromide **24** (355 mg, 1 mmol) with $^n$Bu$_3$SnH (0.3 mL, 1.1 mmol), freshly distilled acrylonitrile (1.32 mL, 20 mmol), and AIBN (catalytic) in dry benzene (55 mL) for 1 h and purification of the product mixture over a silica gel (10 g) column with ethyl acetate–benzene (1:19) as eluent furnished the tricyclic nitrile **26** (191 mg, 58%) which was recrystallized from carbon tetrachloride: mp 218–220 °C; $[\alpha]^{26}_D$ +99.8° (*c* 1; $CHCl_3$); IR ($CCl_4$) $\nu_{max}$ 2242, 1725, 1599, 1161, 1083 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 7.99 (1 H, d, *J* = 8.1 Hz), 7.89 (1 H, dd, *J* = 7.3 and 1.7 Hz), 7.75 (1 H, d, *J* = 8.2 Hz), 7.53 (2 H, m), 7.42 (1 H, t, *J* = 7.6 Hz) and 7.03 (1 H, d, *J* = 7.3 Hz) (aromatic), 3.51 (1 H, d, *J* = 2.6 Hz, C*H*-Ar), 3.05 (1 H, dd, *J* = 9.3 and 4.0 Hz, CHCN), 2.88 (1 H, m, H-7), 2.78 and 2.65 (2 H, d of AB q, *J* = 20 and 3 Hz, $COCH_2$), 2.46 (1 H, d of $^1/_2$AB q, *J* = 14.1 and 9.3 Hz, H-5 a), 2.32 (1 H, m, H-3), 2.19 (1 H, d of $^1/_2$AB q, *J* = 14.1 and 4 Hz, H-5 b), 1.80 and 1.72 (2 H, AB q, *J* = 14.6 Hz, H-10), 1.28 (3 H, s, $C_6$-Me), 0.71 (3 H, s, $C_1$-Me); $^{13}C$ NMR (22.5 MHz) $\delta$ 213.7 (C=O), 138.7, 133.8, 132.0, 129.3, 127.5, 126.3, 125.6 (2 C), 124.2, 123.0 and 122.5 (aromatic and C≡N), 51.3, 50.4, 50.0, 48.0, 46.6, 43.8, 39.9, 35.1, 34.4, 26.0 ($C_6$-Me), 18.2 ($C_1$-Me); mass *m/e* 329 ($M^+$, 100), 187 (20), 142 (20), 141 (85); HRMS *m/e* calcd for $C_{23}H_{23}NO$ 329.1779, found 329.1779.

Further elution of the column with the same solvent furnished the uncyclized adduct **30** (3:2 mixture of epimers, 66 mg, 20%): $[\alpha]^{26}_D$ +239.1° (*c* 4; $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 2242, 1716, 1602, 1383, 1449, 1086 $cm^{-1}$; $^1H$ NMR (90 MHz, 3:2 epimers) $\delta$ 6.88–7.9 (7 H, m), 6.50 and 6.52 (1 H, d, *J* = 7.2 Hz, H-5), 2.6–2.84 (1 H, m, H-4), 2.2–2.56 (4 H, m), 1.56–2.04 (4 H, m), 1.2 and 1.34 (3 H, s, $C_8$-Me), 0.82 (3 H, s, $C_1$-Me); mass *m/e* 329 ($M^+$, 17), 287 (50), 234 (20), 233 (100); HRMS *m/e* calcd for $C_{23}H_{23}NO$ 329.1779, found 329.1789.

**(+)-(1*R*,2*R*,3*S*,4*S*,6*R*,7*R*)-4-Acetyl-1,6-dimethyl-2-(1-naphthyl)tricyclo[4.3.1.0$^{3,7}$]decan-9-one (27).** Radical annulation of the bicyclic bromide **24** (178 mg, 0.5 mmol) with $^n$Bu$_3$SnH (0.15 mL, 0.55 mmol), freshly distilled methyl vinyl ketone (0.83 mL, 10 mmol), and AIBN (catalytic) in dry benzene (28 mL) for 2 h with the addition of extra $^n$Bu$_3$SnH (0.08 mL) and AIBN (catalytic) every 30 min and purification of the product mixture over a silica gel (5 g) column with ethyl acetate–benzene (1:9) as eluent furnished the tricyclic diketone **27** (53 mg, 30%) which was recrystallized from hexane: mp 196–198 °C; $[\alpha]^{26}_D$ +92.3° (*c* 1; $CHCl_3$); IR ($CCl_4$) $\nu_{max}$ 3010, 1716, 1455, 1425, 1380, 1359, 1083, 927, 663 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 8.08 (1 H, d, *J* = 8.2 Hz), 7.87 (1 H, dd, *J* = 7.4 and 2.2 Hz), 7.72 (1 H, d, *J* = 8.2 Hz), 7.51 (2 H, m), 7.39 (1 H, t, *J* = 7.5 Hz) and 7.09 (1 H, d, *J* = 6.7 Hz) (aromatic), 3.62 (1 H, d, *J* = 2.2 Hz, C*H*-Ar), 3.21 (1 H, dd, *J* = 9.3 and 5.2 Hz, C*H*-Ac), 2.69 and 2.55 (2 H, d of AB q, *J* = 19.8 and 2.9 Hz, $COCH_2$), 2.68 (1 H, m, H-7), 2.17 (1 H, d of $^1/_2$AB q, *J* = 13.4 and 9 Hz, H-5 a), 2.11 (3 H, s, $COCH_3$), 1.98 (1 H, d of $^1/_2$AB q, *J* = 13.4 and 5.3 Hz, H-5 b), 1.96 (1 H, m, H-3), 1.85 and 1.70 (2 H, AB q, *J* = 14.4 Hz, H-10), 1.19 (3 H, s, $C_6$-Me), 0.77 (3 H, s, $C_1$-Me); $^{13}C$ NMR (22.5 MHz) $\delta$ 216.1 (C=O), 209.1

($COCH_3$), 140.1, 133.6, 132.3, 129.4, 127.3, 126.2, 125.7 (2 C), 124.1 and 123.2 (aromatic), 59.2, 51.8, 51.1, 48.5, 44.1, 43.4, 40.2, 35.7, 29.0, 26.0 ($C_6$-Me), 25.2 ($COCH_3$), 18.8 ($C_1$-Me); mass *m/e* 346 ($M^+$, 100), 205 (20), 165 (23), 141 (75). Anal. Calcd for $C_{24}H_{26}O_2$: C, 83.20; H, 7.56. Found: C, 83.11; H, 7.55.

Further elution of the column with the same solvent furnished uncyclized adduct **31** (3:2 mixture of epimers, 35 mg, 20%): $[\alpha]^{26}_D$ +195.8° (*c* 1.57; $CHCl_3$); IR (neat) $\nu_{max}$ 1713, 1593, 1506, 1380, 1164, 1086, 801, 780, 756 $cm^{-1}$; $^1H$ NMR (90 MHz, 3:2 epimers) $\delta$ 6.9–8.0 (7 H, m, aromatic), 6.56 and 6.58 (1 H, d, $J$ = 6.5 Hz, H-5), 2.2–2.85 (3 H, m, C-4 and $COCH_2$), 1.64–2.0 (6 H, m), 2.2 (3 H, s, $COCH_3$), 1.2 and 1.32 (3 H, s, $C_6$-Me), 0.8 (3 H, s, $C_1$-Me); mass *m/e* 346 ($M^+$, 22), 304 (33), 233 (100), 232 (38); HRMS *m/e* calcd for $C_{24}H_{26}O_2$ 346.1933, found 346.1927.

**(+)-(1*R*,2*R*,3*S*,4*R*,6*R*,7*R*)-1,6-Dimethyl-2-(1-naphthyl)-4-phenyltricyclo[4.3.1.0$^{3,7}$]decan-9-one (28).** Radical annulation of the bicyclic bromide **24** (180 mg, 0.51 mmol) with $^nBu_3SnH$ (0.153 mL, 0.56 mmol), freshly distilled styrene (1.2 mL, 10.2 mmol), and AIBN (catalytic) in dry benzene (28 mL) for 1 h and purification of the product over a silica gel (5 g) column with hexane–benzene (1:1) as eluent furnished the tricyclic ketone **28** (115 mg, 60%) which was recrystallized from hexane: mp 158–160 °C; $[\alpha]^{26}_D$ +117° (*c* 1.45; $CHCl_3$); IR ($CCl_4$) $\nu_{max}$ 3028, 1719, 1602, 1455, 1350, 1083, 798, 777, 759, 699 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 8.14 (1 H, d, $J$ = 6.4 Hz), 7.83 (1 H, dd, $J$ = 7.1 and 3.3 Hz), 7.67 (1 H, d, $J$ = 8.2 Hz), 7.43–7.46 (2 H, m), 7.34 (1 H, t, $J$ = 7.6 Hz), 7.06 (1 H, d, $J$ = 7.2 Hz), (naphthyl), 7.12–7.28 (5 H, m, phenyl), 3.76 (1 H, d, $J$ = 1.4 Hz, C*H*-naphthyl), 3.58 (1 H, dd, $J$ = 9 and 5.8 Hz, C*H*-Ph), 2.62 (2 H, d, $J$ = 2.9 Hz, $COCH_2$), 2.49 (1 H, m, H-7), 2.45 (1 H, d of $^1/_2$AB q, $J$ = 13.6 and 9.2 Hz, H-5 a), 2.25 (1 H, m, H-3), 1.92 (1 H, d of $^1/_2$AB q, $J$ = 13.9 and 5.7 Hz, H-5 b), 1.97 and 1.74 (2 H, AB q, $J$ = 14.1 Hz, H-10), 1.25 (3 H, s, $C_6$-Me), 0.90 (3 H, s, $C_1$-Me). Anal. Calcd for $C_{28}H_{28}O$: C, 88.38; H, 7.42. Found: C, 88.74; H, 7.52%.

**Grignard Reaction on the Tricyclic Nitrile 26.** To a freshly prepared magnetically stirred ice-cold suspension of methylmagnesium iodide [prepared from methyl iodide (0.3 mL, 3 mmol) and magnesium (80 mg, 3.3 mmol) in dry ether (5 mL)] was added a solution of the tricyclic nitrile **26** (189 mg, 0.6 mmol) in dry benzene (5 mL). The reaction mixture was refluxed for 6 h, cooled and quenched with ice-cold 10% aqueous $H_2SO_4$ (10 mL), and stirred at room temperature for 20 min. The organic layer was separated, and the aqueous layer was extracted with ether (2 × 10 mL). The combined ether extract was washed with aqueous saturated $NaHCO_3$ solution (2 × 10 mL) followed by brine and dried ($Na_2SO_4$). Evaporation of the solvent and purification of the residue furnished the tricyclic diketone **27** (120 mg, 60%), which was identified by comparison (TLC, IR, $^1H$ NMR spectra) with the sample obtained earlier.

**(+)-(1*R*,2*R*,3*S*,4*R*,6*R*,7*R*)-1,6-Dimethyl-4-(prop-2-yl)-2-(1-naphthyl)tricyclo[4.3.1.0$^{3,7}$]decan-9-one [10-(1-naphthyl)-5-epipupukean-9-one] (33).** To a magnetically stirred suspension of methyltriphenylphosphonium bromide (310 mg, 0.87 mmol) in dry benzene (2 mL) was added at room temperature a 1 M solution of $K^+$-O$^t$Am in $^t$AmOH (0.7 mL, 0.7 mmol), and the solution was stirred at room temperature for 30 min. The Wittig reagent was cooled (0 °C), and a solution of the tricyclic diketone **27** (110 mg, 0.32 mmol) in dry benzene (2 mL) was added. The reaction mixture was stirred at room temperature for 5 h, diluted with ether (10 mL), washed with aqueous 0.5 N HCl (2 × 5 mL) followed by brine, and dried ($Na_2SO_4$). Evaporation of the solvent and purification of the residue over a silica gel (5 g) column with ethyl acetate–benzene (1:19) as eluent furnished the tricyclic olefin **34** (70 mg, 65%) as a pale yellow viscous oil: $[\alpha]^{26}_D$ +48.1° (*c* 0.9; $CHCl_3$); IR (neat) $\nu_{max}$ 3052, 1719, 1644, 1602, 1404, 1380, 1350, 1080, 1020, 885, 795, 780, 759 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 8.09 (1 H, d, $J$ = 9.2 Hz), 7.86 (1 H, dd, $J$ = 9.5 and 3.0 Hz), 7.7 (1 H, d, $J$ = 8.2 Hz), 7.5 (2 H, m), 7.37 (1 H, t, $J$ = 7.7 Hz) and 7.08 (1 H, d, $J$ = 7.2 Hz) (aromatic), 4.77 (1 H, br s) and 4.7 (1 H, br s) (olefinic), 3.59 (1 H, br s, H-2), 2.92 (1 H, dd, $J$ = 8.7 and 6.1 Hz, H-4), 2.59 (2 H, m, $COCH_2$), 2.38 (1 H, br s, H-7), 2.14 (1 H, d of $^1/_2$AB q, $J$ = 13.3 and 9 Hz, H-5 a), 2.02 (1 H, br s, H-3), 1.88 (1 H, d, $J$ = 14.3 Hz, H-10 a), 1.35–1.7 (2 H, m, H-10 b and 5 b), 1.66 (3 H, s, olefinic Me), 1.17 (3 H, s, $C_6$-Me), 0.87 (3 H, s, $C_1$-Me); $^{13}C$ NMR (22.5 MHz) $\delta$ 217.5 (s, C=O), 148.7 (s, *C*=$CH_2$), 140.6 (s), 134.1 (s), 132.4 (s), 129.2 (d), 127.1 (d), 126.0 (d), 125.5 (2 C, d), 123.9 (d) and 123.3 (d) (aromatic), 108.7 (t, C=$CH_2$), 54.5 (d, C-2), 53.5 (d, C-4), 51.3 (t, $COCH_2$), 50.5 (d, C-7), 48.1 (t, C-5), 47.6 (s, C-6), 43.8 (d, C-3), 40.1 (s, C-1), 36.0 (t, C-10), 26.0 (q, $C_6$-Me), 21.6 (q, olefinic Me), 18.9 (q, $C_1$-Me); mass *m/e* 344 ($M^+$, 46), 149 (100), 141 (35); HRMS *m/e* calcd for $C_{25}H_{28}O$ 344.2140, found 344.2135.

A suspension of the tricyclic olefin **34** (60 mg, 0.174 mmol) and 10% Pd–C (10 mg) in ethyl acetate (5 mL) was magnetically stirred under $H_2$ atmosphere (balloon) for 4 h. The reaction mixture was filtered through a silica gel (5 g) column with ethyl acetate–benzene (1:19) as eluent to furnish the epipupukean-9-one **33** (55 mg, 92%) which was recrystallized from hexane: mp 120–122 °C; $[\alpha]^{26}_D$ +78° (*c* 0.155; $CHCl_3$); IR ($CCl_4$) $\nu_{max}$ 3016, 1719, 1455, 1407, 1380, 1203, 1080, 927, 669 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 8.12 (1 H, d, $J$ = 8.2 Hz), 7.85 (1 H, dd, $J$ = 7.4 and 2.3 Hz), 7.69 (1 H, d, $J$ = 8.2 Hz), 7.5 (2 H, m), 7.37 (1 H, t, $J$ = 7.6 Hz) and 7.08 (1 H, d, $J$ = 7.3 Hz) (aromatic), 3.57 (1 H, d, $J$ = 1.3 Hz, *H*C-Ar), 2.66 and 2.55 (2 H, d of AB q, $J$ = 19.8 and 3 Hz, $COCH_2$), 2.34 (1 H, m, H-7), 1.93–2.02 (2 H, m, H-5 b and C*H*($Me_2$), 1.85 (1 H, br s, H-3), 1.82 and 1.64 (2 H, AB q, $J$ = 14.3 Hz, H-10), 1.4–1.64 (2 H, m, H-4 and 5 a), 1.14 (3 H, s, $C_6$-Me), 0.83 (3 H, d, $J$ = 6.6 Hz) and 0.79 (3 H, d, $J$ = 7.1 Hz) (CH*Me*$_2$), 0.81 (3 H, s, $C_1$-Me); $^{13}C$ NMR (22.5 MHz) $\delta$ 217.8 (s, C=O), 140.9 (s), 134.1 (s), 132.5 (s), 129.1 (d), 127.0 (d), 125.8 (d), 125.5 (2 C, d), 124.0 (d) and 123.3 (d) (aromatic), 55.3 (d, C-2), 53.9 (d, C-7), 51.1 (t, $COCH_2$), 49.7 (d, C-4), 48.2 (s, C-6), 46.1 (t, C-5), 43.4 (d, C-3), 39.9 (s, C-1), 36.2 (t, C-10), 33.2 (d, *C*HMe$_2$), 26.5 (q, $C_6$-Me), 22.0 (q), 19.9 (q), 19.0 (q, $C_1$-Me). Anal. Calcd for $C_{25}H_{30}O$: C, 86.65; H, 8.73. Found: C, 86.26; H, 8.78.

**(+)-(1*R*,2*R*,3*S*,4*S*,6*R*,7*R*)-1,6-Dimethyl-4-(2-hydroxyprop-2-yl)-2-(1-naphthyl)tricyclo[4.3.1.0$^{3,7}$]decan-9-one (35).** To a freshly prepared magnetically stirred, ice-cold suspension of methylmagnesium iodide [prepared from methyl iodide (0.2 mL, 3 mmol) and magnesium (72 mg, 3 mmol) in dry ether (5 mL)] was added a solution of the tricyclic ester **25** (220 mg, 0.61 mmol) in dry benzene (5 mL). The reaction mixture was refluxed for 4 h, cooled, and quenched with aqueous saturated $NH_4Cl$ solution (10 mL). The organic phase was separated, and the aqueous phase was extracted with ether (3 × 10 mL). The combined organic extract was washed with brine and dried ($Na_2SO_4$). Evaporation of the solvent and purification of the residue over a silica gel (10 g) column with ethyl acetate–hexane (1:9) as eluent furnished the tricyclic tertiary alcohol **35** (190 mg, 86%) which was recrystallized from hexane: mp 166–167 °C; $[\alpha]^{26}_D$ +54.90° (*c* 1.23; $CHCl_3$); IR ($CCl_4$) $\nu_{max}$ 3476 (broad, OH), 3046, 1713, 1602, 1512, 1407, 1380, 1170, 1086, 1035, 942, 837, 777, 735, 675 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 8.17 (1 H, d, $J$ = 8.1 Hz), 7.85 (1 H, dd, $J$ = 7.4 and 1.8 Hz), 7.69 (1 H, d, $J$ = 8.3 Hz), 7.5 (2 H, m), 7.38 (1 H, t, $J$ = 7.6 Hz) and 7.11 (1 H, d, $J$ = 7.3 Hz) (aromatic), 3.63 (1 H, br s, *H*C-Ar), 2.73 and 2.56 (2 H, d of AB q, $J$ = 19.9 and 3.0 Hz, $COCH_2$), 2.31–2.38 (2 H, m, H-5 b, 7), 1.93–2.05 (2 H, m, H-5 a, 3), 1.85 and 1.67 (2 H, AB q, $J$ = 14.3 Hz, H-10), 1.46–1.64 (1 H, m, H-4), 1.58 (1 H, s, OH), 1.17 (3 H, s, $C_6$-Me), 1.13 (6 H, s, $(CH_3)_2$COH), 0.79 (3 H, s, $C_1$-Me); $^{13}C$ NMR (22.5 MHz) $\delta$ 217.5 (s, C=O), 140.6 (s), 134.0 (s), 132.5 (s), 129.1 (d), 127.1 (d), 125.8 (d), 125.5 (2 C, d), 124.0 (d) and 123.5 (d) (aromatic), 72.8 (s, COH), 59.7 (d, C-2), 54.4 (d, C-4), 50.6 (t, $COCH_2$), 48.6 (s, C-1), 47.5 (d, C-7), 44.1 (t, C-5), 44.0 (d, C-3), 39.9 (s, C-6), 36.2 (t, C-10), 28.8 (q) and 27.3 (q) ($Me_2$COH), 26.1 (q, $C_6$-Me), 19.0 (q, $C_1$-Me); mass *m/e* 362 ($M^+$, 100), 344 (12), 304 (26), 220 (11), 165 (29), 141 (93), 123 (12), 59 (73); HRMS *m/e* calcd for $C_{25}H_{30}O_2$ 362.2238, found 362.2241.

**(+)-(1*R*,2*R*,3*S*,6*R*,7*R*)-1,6-Dimethyl-4-isopropylidene-2-(1-naphthyl)tricyclo[4.3.1.0$^{3,7}$]decan-9-one (36).** A solution of the tertiary alcohol **35** (120 mg, 0.33 mmol) and PTSA (catalytic) in dry benzene (5 mL) was refluxed for 30 min. The reaction mixture was cooled, washed with aqueous saturated $NaHCO_3$ solution (2 × 5 mL) followed by brine and dried ($Na_2SO_4$). Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel (5 g) column with ethyl acetate–benzene (1:19) as eluent furnished the tetrasubstituted olefin **36** (100 mg, 86%) which was recrystallized from hexane: mp 178–180 °C; $[\alpha]^{26}_D$ +138.5° (*c* 1; $CHCl_3$); IR ($CCl_4$) $\nu_{max}$ 3042, 1722, 1602, 1380, 1185, 900, 759 $cm^{-1}$; $^1H$ NMR (270 MHz) $\delta$ 8.08 (1 H, d, $J$ = 9.3 Hz), 7.82 (1 H, dd, $J$ = 9.4 and 3.8 Hz), 7.69 (1 H, d, $J$ = 8.2 Hz), 7.44–7.5 (2 H, m), 7.44 (1 H, t, $J$ = 8 Hz), 7.16

(1 H, d, $J$ = 7.2 Hz), 3.72 (1 H, d, $J$ = 1.3 Hz, C*H*-Ar), 3.13 (1 H, d, $J$ = 2.7 Hz, H-3), 2.81 and 2.65 (2 H, d of AB q, $J$ = 20.3 and 3.3 Hz, COC$H_2$), 2.46 and 2.31 (2 H, AB q, $J$ = 16.2 Hz, H-5), 2.01 (1 H, br s, H-7), 1.84 and 1.67 (2 H, AB q, $J$ = 14.3 Hz, H-10), 1.63 (3 H, s) and 1.25 (3 H, s), (2 × olefinic Me), 1.21 (3 H, s, $C_6$-Me), 0.61 (3 H, s, $C_1$-Me); $^{13}$C NMR (22.5 MHz) $\delta$ 215.5 (s, C=O), 140.7 (s) and 121.9 (s) (olefinic), 139.4 (s), 133.8 (s), 132.6 (s), 128.9 (d), 127.1 (d), 125.7 (d), 125.5 (2 C, d), 124.3 (d) and 123.3 (d) (aromatic), 51.3 (d, C-2), 49.8 (t, CO*C*$H_2$), 49.6 (d, C-7), 49.0 (s, C-1), 47.7 (t, C-5), 44.6 (d, C-3), 39.3 (s, C-6), 36.5 (t, C-10), 26.2 (q, $C_6$-Me), 21.3 (q), and 20.7 (q) (olefinic), 18.8 (q, $C_1$-Me); mass $m/e$ 344 ($M^+$, 24), 233 (22), 203 (12), 165 (20), 141 (23), 121 (100), 105 (18), 91 (15); HRMS $m/e$ calcd for $C_{25}H_{28}O$ 344.2133, found 344.2136.

**Isomerization of the Keto Olefin 34.** A solution of the tricyclic olefin **34** (20 mg, 0.06 mmol) and PTSA (catalytic) in dry benzene (2 mL) was stirred at room temperature for 8 h. The reaction mixture was diluted with benzene (2 mL) and washed with aqueous saturated $NaHCO_3$ solution (2 mL) followed by brine and dried ($Na_2SO_4$). Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel (1 g) column with ethyl acetate–benzene (1:19) as eluent furnished the olefin **36** (16 mg, 80%), which was identified by comparison (TLC, $^1$H NMR spectrum) with the sample obtained in the previous experiment.

**(+)-(1*R*,2*R*,3*S*,4*S*,6*R*,7*R*)-1,6-Dimethyl-4-*endo*-isopropyl-2-(1-naphthyl)tricyclo[4.3.1.0$^{3,7}$]decan-9-one [10-(1-Naphthyl)pupukean-9-one] (32).** A suspension of the tricyclic olefin **36** (40 mg, 0.11 mmol) and 10% Pt–C (40 mg) in dry MeOH (5 mL) was magnetically stirred under $H_2$ atmosphere (balloon) for 24 h. The reaction mixture was filtered through a silica gel (5 g) column, solvent was removed under reduced pressure, and the mixture was rehydrogenated with 10% Pt–C (40 mg) in dry MeOH (5 mL) for another 24 h. The reaction mixture was filtered through a silica gel (5 g) column, and the solvent was removed under reduced pressure. Recrystallization of the residue from hexane furnished the pupukeanone **32** (20 mg, 50%): mp 164–166 °C; $[\alpha]^{26}_D$ +43.1° ($c$ 0.8; $CHCl_3$); IR ($CCl_4$) $\nu_{max}$ 3046, 1725, 1677, 1611, 1380, 1122, 1074, cm$^{-1}$; $^1$H NMR (270 MHz) $\delta$ 8.18 (1 H, d, $J$ = 8.2 Hz), 7.84 (1 H, dd, $J$ = 7.7 and 1.7 Hz), 7.68 (1 H, d, $J$ = 8.1 Hz), 7.48 (2 H, m), 7.4 (1 H, t, $J$ = 8 Hz) and 7.05 (1 H, d, $J$ = 7.3 Hz) (aromatic), 3.89 (1 H, d, $J$ = 3.2 Hz, *H*C-Ar), 2.75 and 2.59 (2 H, d of AB q, $J$ = 20 and 3 Hz, H-8), 2.59 (1 H, m, H-7), 2.14 (1 H, dd, $J$ = 12.7 and 9 Hz, H-4), 1.98 (1 H, m, H-3), 1.73 and 1.63 (2 H, AB q, $J$ = 13.5 Hz, H-10), 1.5–1.9 (3 H, m, H-5, $Me_2$C*H*), 1.17 (3 H, s, $C_6$-Me), 0.54 (3 H, s, $C_1$-Me), 0.89 (3 H, d, $J$ = 6 Hz) and 0.32 (3 H, d, $J$ = 6.2 Hz), (CH*Me*$_2$); mass $m/e$ 346 ($M^+$, 100), 233 (10), 219 (5); HRMS $m/e$ calcd, for $C_{25}H_{30}O$ 346.2289, found 346.2272.

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**Supplementary Material Available:** $^{13}$C NMR spectra of **14** + **15**, **26**, **35**, and **36** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.