Chiral synthons from carvone. Part 50. † Enantiospecific approaches to both enantiomers of bicyclo[4.3.0]nonane-3,8-dione derivatives

A. Srikrishna* and T. Jagadeeswar Reddy

Department of Organic Chemistry, Indian Institute of Science, Bangalore, 560 012, India. E-mail: ask@orgchem.iisc.ernet.in; Fax: 91-80-3600683

Received (in Cambridge, UK) 15th May 2001, Accepted 2nd July 2001 First published as an Advance Article on the web 7th August 2001

Enantiospecific synthesis of both enantiomeric forms of bicyclo[4.3.0]nonane-3,8-dione derivatives has been described starting from (R)-carvone employing two different cyclopentannulation methodologies. Thus, in the first methodology, carveol (5) was converted into tricyclic ketone 4 employing a Claisen rearrangement and intramolecular diazo ketone cyclopropanation reactions. Degradation of the isopropenyl group followed by cyclopropane cleavage and cuprate addition generated the dione (-)-12a. Whereas, a Wacker mediated cyclopentannulation of (R)-carvone via the dione 15 furnished the enone 17. Functional group manipulation including the degradation of isopropenyl group transformed the enone 17 into the dione (+)-12a, which on regioselective ketalisation generated the ketoketal (+)-2.

The creativity of Nature in devising varied molecular architectures is revealed through the isolation of a wide range of natural products with remarkable skeletal build-up and multifarious functionality.1 Development of methodologies for the total synthesis of natural products with diverse architecture and varying degrees of complexity is an area that has inspired and attracted several generations of organic chemists.² Particularly in the last three decades, dramatic advances were made in the development of new synthetic methodologies with high regio-, stereo- and enantiocontrol. Monoterpenes are being widely used as chiral auxiliaries but their potential as chiral synthons has not been properly exploited.³ The overwhelming emphasis on carbohydrates as chirons⁴ in natural product synthesis has somewhat marginalised the importance of the abundantly available monoterpenes as chiral building blocks for the synthesis of natural products in their optically active form. This has come about despite the fact that monoterpenes are cheap, readily available (in several cases, in both enantiomeric forms unlike carbohydrates and amino acids) and are endowed with only one or two chiral centres with modest functionality, which means that it does not require recourse to wasteful manoeuvres to dispense with excess chirality or functionality as in carbohydrate based approaches. More interestingly, terpenes can be readily restructured into cyclic and acyclic fragments that can be directly incorporated into carbocyclic frameworks of complex target molecules.

Functionalised bicyclo[4.3.0]nonanes (hydrindane systems), in particular with a substituent at one of the ring junction positions, or as part structures are present in many biologically important natural products, *e.g.* picrotoxinin, bakkenolides, homogynolides, palmosalide, zizaenes, neopupukenanes, *etc.* Our interest in the synthesis of sesquiterpene natural products containing a hydrindane framework led us to investigate new approaches for the construction of bicyclo[4.3.0]nonanes in optically active form. The readily available monoterpene carvone (1) is an excellent chiral starting material in the synthesis of natural products.³ (S)-Carvone has been exploited by de Groot and coworkers for the construction of several

2040 J. Chem. Soc., Perkin Trans. 1, 2001, 2040–2046

functionalised decalin systems⁵ and their conversion to a variety of natural products. We have employed (*R*)-carvone as the chiral starting material for the synthesis of a variety of bridged systems and sesquiterpenoids.^{6,7} In continuation of our interest in the development of enantiospecific methodologies for the generation of both enantiomers of a particular carbon framework, starting from a single enantiomer of carvone,^{6c,e,7} herein we describe details of our investigation on the synthesis of both enantiomers of the bicyclo[4.3.0]nonane based ketoketal **2** employing two different cyclopentannulation methodologies.⁸



The isopropenyl group in carvone 1 was readily recognised as a masked hydroxy group. To begin with, for the enantiospecific synthesis of the (-)-ketoketal 2 an orthoester Claisen rearrangement-intramolecular diazo ketone cyclopropanation based approach was chosen starting from (*R*)-carvone 1. The retrosynthetic pathway for the (-)-ketoketal 2 is depicted in Scheme 1. It was anticipated that conjugate addition of a methyl group followed by regio-selective ketalisation could transform the enedione 3 into the ketoketal 2, and degradation of the isopropenyl group followed by acid catalysed ring opening of cyclopropane could transform the tricyclic ketone 4 into the

DOI: 10.1039/b104253j

[†] For parts 49 and 48, see: references 6a and 6b, respectively.



enedione **3**. A stereospecific Claisen rearrangement and intramolecular diazo ketone cyclopropanation could be exploited for the conversion of carveol (**5**) into the tricyclic ketone **4**.

Synthesis of the tricyclic ketone 4 is depicted in Scheme 2.



Scheme 2 (a) LAH; (b) MeC(OEt)₃, Hg(OAc)₂, Δ ; (c) NaOH; (d) (COCl)₂, CH₂N₂; (e) CuSO₄.

Lithium aluminium hydride (LAH) reduction of (R)-carvone (1) in ether at -90 °C furnished carveol (5), the precursor for the projected Claisen rearrangement, in quantitative yield with a very high degree of stereoselectivity. The syn relationship between the hydroxy and isopropenyl groups in carveol was well established.9 An orthoester variant of the Claisen rearrangement, developed¹⁰ by Johnson et al. was used for the stereospecific introduction of the acetate side chain. Thus, thermal activation (180 °C) of a solution of carveol (5), triethyl orthoacetate and a catalytic amount of mercuric acetate in a sealed tube furnished the γ , δ -unsaturated ester **6** in 70% yield, whose structure was established from its spectral data. The stereochemistry of the ester side chain was assigned based on the well-established stereospecificity of the Claisen rearrangement. The ester 6 was transformed into the tricyclic ketone 4 via an intramolecular diazo ketone cyclopropanation¹¹ strategy. Thus, hydrolysis of the ester 6 using 15% aqueous sodium hydroxide and methanol furnished the acid 7. Treatment of the acid 7 with oxalyl chloride in benzene furnished the acid chloride, which on addition to an excess of ethereal diazomethane furnished the diazo ketone 8. Anhydrous copper sulfate catalyzed decomposition of the diazo ketone 8 in refluxing cyclohexane using a tungsten lamp led to the intramolecular insertion of the intermediate ketocarbenoid into the ring olefin in a regioand stereospecific manner, resulting in the formation of the cyclopropyl ketone 4 in 50% yield (from the acid 7). The cis stereochemistry of the ring junction was a consequence of the insertion of the intermediate ketocarbenoid from the preferred syn face of the olefin.

With the successful synthesis of the cyclopropyl ketone 4, attention was turned towards the degradation of the isopropenyl side chain into oxygen functionality, Scheme 3. Since



Scheme 3 (a) HCl; (b) DBU; (c) O_3 , Me_2S ; (d) *p*TSA.

a one-pot conversion of isopropenyl group into an acetoxy group employing a Criegee rearrangement¹² was found to be inefficient, an alternative route was envisaged. Isomerisation of the isopropenyl to the isopropylidene group by an addition–elimination sequence and oxidative cleavage to generate the ketone functionality was contemplated. Thus, treatment of the cyclopropyl ketone **4** with an excess of freshly prepared saturated solution of hydrogen chloride gas in ether generated the dichloride **9** via addition of hydrogen chloride to both olefinic and cyclopropane moieties. Reaction of the dichloride **9** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene at 160 °C in a sealed tube led to double dehydrochlorination to furnish the cyclopropyl ketone **10**. Ozonolysis of the tricyclic ketone **10** in methanol–methylene chloride followed

J. Chem. Soc., Perkin Trans. 1, 2001, 2040–2046 2041

by reductive work up of the ozonide with dimethyl sulfide furnished the dione 11, which was found to undergo partial isomerisation to enedione 3 on a silica gel column. Treatment of the dione 11 with a catalytic amount of toluene-*p*-sulfonic acid (*p*TSA) in methylene chloride brought about the complete isomerisation *via* the cleavage of the cyclopropane ring furnishing the enedione 3, whose structure rests secured from its spectral data.

Addition of lithium dimethylcopper to the enedione 3, furnished a 3:2 epimeric mixture of hydrindanediones 12a,b in 71% yield (Scheme 4). The structures of the diones 12a,b



were established from the spectral data. It was anticipated that protection of the 5-membered ring ketone in enedione **3** as its cyclic ketal might increase the stereoselectivity in the cuprate reaction. Accordingly, regioselective protection of the five membered ketone in the enedione **3** with ethylene glycol in the presence of a catalytic amount of *p*TSA using a Dean–Stark water separator furnished the ketal **13** in 69% yield in a highly regioselective manner. However, reaction of the ketoketal **13** with lithium dimethylcopper followed by hydrolysis of the ketal moiety in the product generated a 2:1 mixture of the diones **12a,b** with only marginal increase in stereoselectivity.

In the second approach, for the generation of enantiomeric compounds, initial introduction of the secondary methyl group and construction of a hydrindane by Wacker mediated cyclopentannulation methodology was envisaged, as depicted in Scheme 5. For the addition of methyl and allyl groups to the enone at the β and α positions, respectively, in a *trans* manner, a cuprate mediated 1,4-addition followed by allyl-

ation of the intermediate enolate was chosen. Thus, addition of lithium dimethylcopper to (R)-carvone 1 followed by quenching of the resultant enolate with allyl bromide in the presence of HMPT provided a 9:1 epimeric mixture of the ketone 14. The stereochemistry of the secondary methyl group in 14 was assigned based on the preferred addition of the nucleophile trans to the isopropenyl group, which has enough precedence in the literature.¹³ Similarly, stereoselective alkylation of the intermediate enolate generates the quaternary carbon as both the secondary methyl at C-3 and the isopropenyl group at C-5 directs the approach of the electrophile trans to the secondary methyl group. The regiospecificity of the Wacker reaction¹⁴ for the oxidation of monosubstituted olefins was exploited for the conversion of the allyl into an acetonyl group for the generation of the 1,4-diketone necessary for cyclopentannulation. Thus, reaction of the allyl compound 14 with palladium chloride and cuprous chloride in a mixture of N,N-dimethylformamide and water in an oxygen atmosphere furnished a 9:1 mixture of the 1,4-diketones 15 and 16, which were separated on a silica gel column. Intramolecular aldol condensation of the major dione 15 using 10% aqueous potassium hydroxide in methanol cleanly furnished the enone 17, whose structure was established from its spectral data. The ¹³C NMR spectrum of the enone 17 exhibited a singlet at δ 207.6 ppm due to the carbonyl carbon, two olefinic carbon resonances at 187.3 and 127.4 typical for a β-substituted cyclopentenone moiety,¹⁵ two olefinic signals at 146.0 and 111.7 ppm due to $C=CH_2$ carbons in addition to aliphatic carbon resonances, confirming the structure of the enone 17.

For further elaboration, regiospecific reduction of the endo cyclic olefin was addressed first, employing electron transfer methodology. Thus, regiospecific reduction of the enone 17 with lithium in liquid ammonia in the presence of tert-butanol (2-methylpropan-2-ol) furnished a ≈ 2 : 1 mixture of the *cis* and trans hydrindanones 18 and 19, which were separated by column chromatography on silver nitrate impregnated silica gel. For the conversion of the isopropenyl moiety into ketone functionality, as in the first approach, the three step sequence was used. Thus, addition of hydrogen bromide followed by DBU mediated dehydrobromination of the resultant tertiary bromide 20 transformed the hydrindanone 18 into the isomerised compound 21 in near quantitative yield. Ozonolysis of the isopropylidene group in 21 followed by reductive work up with triphenylphosphine furnished the dione 12a in 88% yield, whose structure was established from its spectral data. Regioselective protection of the 6-membered ring ketone with 1.0 equivalent of ethylene glycol and pTSA using a Dean-Stark



Scheme 5 (a) Me₂CuLi, CH₂CH=CH₂Br; (b) PdCl₂, CuCl, DMF-H₂O, O₂; (c) KOH; (d) Li, liq. NH₃; (e) HBr, (f) DBU; (g) O₃, Me₂S; (h) (CH₂OH)₂, pTSA.

water separator in refluxing benzene transformed the dione 12a into the (+)-ketoketal 2 in 68% yield, whose structure was established from its spectral data.

In conclusion, employing two different cyclopentannulation methodologies, (*R*)-carvone has been transformed, *via* several useful chiral synthons, into both enantiomeric forms of bicyclo[4.3.0]nonane-3,8-dione derivatives, potential precursors in sesquiterpene synthesis.

Experimental

Melting points are recorded using a Tempo melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. ¹H (90, 200 and 270 MHz) and ¹³C NMR (22.5, 50 and 100 MHz) spectra were recorded on JEOL FX-90Q, Bruker ACF-200, WH-270 and AMX-400 spectrometers. The chemical shifts (δ 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 CDCl₃ (for ¹³C). In the ¹³C NMR spectra off-resonance multiplicities, when recorded are given in parentheses. Low and high resolution mass measurements were carried out using 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 CHN analyser. Optical rotations were measured using a Jasco DIP-370 digital polarimeter and $[a]_D$ values are given in the units of $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$. Ozonolysis was carried out using a Penwalt Wallace and Tierman ozonator. Acme's silica gel (100-200 mesh), approximately 15-20 g per 1 g of the crude product, was used for column chromatography. All smallscale dry reactions were carried out using a standard syringeseptum technique. Dry THF was obtained by distillation over sodium-benzophenone ketyl. HBr in ether was prepared by bromination of tetralin with bromine according to the Vogel procedure.

(+)-(1*R*,5*R*)-5-Isopropenyl-2-methylcyclohex-2-enylacetic acid (7)

A solution of carveol 5 (4.0 g, 26.3 mmol), triethyl orthoacetate (25 ml, 136.6 mmol) and mercuric acetate (25 mg) was placed in a sealed tube and heated to 180 °C for 6 days in an oil bath. The reaction mixture was cooled, diluted with ether (90 ml), washed with 1 M HCl, saturated aq. NaHCO₃ and brine, and dried (Na₂SO₄). Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate-hexane (1:40) as eluent furnished the ester 6 (4.1 g, 70%): v_{max} (neat) 1735, 1640, 885 cm $^{-1}$. $\delta_{\rm H}$ (90 MHz, CDCl_3) 5.28 (1 H, m, H-3), 4.55 (2 H, br s, C=CH₂), 3.96 (2 H, q, J 7.2 Hz, OCH₂CH₃), 1.40-2.70 (8 H, m), 1.66 (3 H, s) and 1.58 (3 H, s) $(2 \times \text{olefinic CH}_3)$, 1.20 (3 H, t, J 7.2 Hz, OCH₂CH₃). To a solution of the ester 6 (4.0 g, 18 mmol) in 20 ml methanol was added 15% aq. NaOH (30 ml). The reaction mixture was refluxed for 8 h, cooled to RT and acidified with 3 M HCl. It was then extracted with ether $(3 \times 25 \text{ ml})$. The ether extract was washed with brine and dried (Na₂SO₄). Evaporation of the solvent furnished the acid 7 (3.3 g, 95%) as a yellow oil. $[a]_{\rm D}^{24}$: +21.3 (c 4.0, CHCl₃). $v_{\rm max}$ (neat) 3000, 1707, 1644, 885 cm⁻¹. $\delta_{\rm H}$ (90 MHz, CDCl₃) 11.6 (1 H, br s, COOH), 5.50 (1 H, br s, H-3), 4.64 (2 H, s, C=CH₂), 2.50-2.80 (2 H, m, H- α), 1.00–2.30 (6 H, m), 1.67 (3 H, s) and 1.63 (3 H, s) $(2 \times \text{olefinic CH}_3)$. δ_C (100 MHz, CDCl₃) 179.9 (C=O), 149.6 (C=CH₂), 134.3 (C-2), 123.9 (C-3), 108.8 (C=CH₂), 41.3, 38.8, 37.1, 35.1, 31.1, 21.0, 20.7. Mass: m/z 194 (M⁺, 25%), 151 (15), 134 (55), 126 (37), 119 (60), 105 (67), 93 (70), 84 (45), 81 (100). HRMS: m/z Calcd. for C12H18O2: M 194.1307. Found: M⁺, 194.1299.

(-)-(1*S*,2*S*,4*R*,6*R*,9*R*)-4-Isopropenyl-1-methyltricyclo-[4.3.0.0^{2,9}]nonan-8-one (4)

To a magnetically stirred solution of the acid 7 (3.0 g, 15.46 mmol) in dry benzene (6 ml) was slowly added oxalyl chloride (3.0 ml, 34.9 mmol) and the reaction mixture was stirred for 2 h at RT. Evaporation of benzene and excess oxalyl chloride under reduced pressure furnished the acid chloride, which was taken in dry ether (10 ml) and added dropwise to a cold magnetically stirred ethereal solution of diazomethane (250 ml, prepared from 30 g of N-nitroso-N-methylurea and 260 ml of 60% aq. KOH solution). The reaction mixture was slowly warmed up to RT, stirred for 2 h and the excess diazomethane and ether were carefully evaporated on a water bath. Rapid purification by filtration of the crude product through a silica gel column using ethyl acetate-hexane (1:5) as eluent furnished the diazo ketone **8** (3.0 g) as a yellow oil. v_{max} (neat) 2080, 1640, 890 cm⁻¹. δ_{H} (90 MHz, CDCl₃) 6.50 (1 H, br s, olefinic H), 6.21 (1 H, s, CHN₂), 4.65 (2 H, s, C=CH₂), 2.50–2.80 (2 H, m, H-α), 1.80–2.30 (6 H, m), 1.68 (6 H, s, $2 \times$ olefinic CH₃). To a magnetically stirred, refluxing (by keeping two 100 W tungsten lamps near the flask) suspension of anhydrous copper sulfate (14 g) in 400 ml dry cyclohexane was added, dropwise, a solution of the diazo ketone 8 (3.0 g) in cyclohexane (70 ml) over a period of 2 h and refluxed for 4 h. The reaction mixture was then cooled and copper sulfate was filtered off using a sintered funnel. Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate-hexane (1:20 to 1:5) as eluent furnished the tricyclic ketone 4 (1.46 g, 50% from the acid 7) as a yellow oil. [a]_D²⁴: -100.5 (c 1.9, CHCl₃). v_{max} (neat) 1720, 1640, 890 cm⁻¹. $\delta_{\rm H}$ (200 MHz, CDCl₃) 4.70 (2 H, br s, C=CH₂), 2.73 (1 H, dd, J 19.5 and 12 Hz), 2.50–2.70 (1 H, m), 2.30 (1 H, m), 1.90-2.20 (2 H, m), 1.50-1.80 (3 H, m), 1.68 (3 H, s, olefinic CH₃), 1.35 (3 H, s, tert-CH₃), 1.25 (1 H, dd, J 14.2 and 8.8 Hz), 1.04 (1 H, d of t, J 14.2 and 6.6 Hz). $\delta_{\rm C}$ (100 MHz, CDCl₃) 213.2 (s, C=O), 148.6 (s, C=CH₂), 108.6 (t, C=CH₂), 47.6 (t, CH₂C=O), 40.4 (d), 39.3 (d), 32.8 (d), 30.7 (s, C-1), 28.5 (t), 26.8 (t), 20.1 (d), 22.9 (q), 19.8 (q). Mass: m/z 190 (M⁺, 5%), 162 (10), 147 (20), 133 (25), 107 (60), 93 (60), 79 (100). HRMS: m/z Calcd. for C₁₃H₁₈O: M, 190.1358. Found: M⁺, 190.1353.

(+)-(1*S*,2*S*,4*R*,6*R*)-2-Chloro-4-(2-chloro-2-propyl)-1-methylbicyclo[4.3.0]nonan-8-one (9)

A saturated solution of HCl gas in ether (150 ml) was added to the tricyclic ketone 4 (658 mg, 3.46 mmol) and the reaction mixture was stirred for 36 h under a closed system at RT. It was then diluted with ether (20 ml), washed with water, saturated NaHCO₃ solution and brine, and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1:10 to 1:5) as eluent furnished the dichloride 9 (760 mg, 84%), which was recrystallised from a mixture of hexane and CH₂Cl₂. Mp: 93–95 °C. $[a]_{\rm D}^{24}$: +173 (c 1.2, CHCl₃). v_{max} (Nujol) 1740 cm⁻¹. δ_{H} (200 MHz, CDCl₃) 4.39 (1 H, t, J 2.9 Hz, CHCl), 2.63 (1 H, dd, J 18.7 and 7.1 Hz, H-7a), 2.43 (1 H, d, J 17.8 Hz, H-9a), 2.10-2.35 (3 H, m), 1.85-2.05 (4 H, m), 1.58 (6 H, s, ClC(CH₃)₂), 1.24 (3 H, d, J 1 Hz, C¹-CH₃), 1.03 (1 H, q, J 12 Hz). δ_C (50 MHz, CDCl₃) 216.7 (C=O), 73.2 (C-Cl), 66.6 (CH-Cl), 46.6 (CH₂C=O), 44.9 (CH₂C=O), 42.7 (C-1), 42.1 (CH), 37.8 (CH), 31.9 (CH₂), 31.2 (CH₂), 30.9 (CH₃), 30.8 (CH₃), 27.1 (CH₃). Mass: m/z 262 $(M^+, 25\%), 264 (M^+ + 2, 15\%), 227 (15), 191 (100), 183 (32),$ 149 (28), 121 (25), 109 (50), 107 (48). Anal. Calcd. for C₁₃H₂₀Cl₂O: C, 59.32; H, 7.66. Found: C, 59.06; H, 7.69%.

(-)-(1*S*,2*S*,6*R*,9*R*)-4-Isopropylidene-1-methyltricyclo-[4.3.0.0^{2,9}]nonan-8-one (10)

A solution of the dichloride **9** (208 mg, 0.79 mmol) and DBU (240 mg, 0.236 ml, 1.58 mmol) in dry benzene (2 ml) was heated in a sealed tube at 160 °C for 30 min. The reaction mixture was

then cooled to RT, diluted with ether (10 ml), washed with water, 3 M HCl (5 ml), saturated aq. NaHCO₃ solution and brine, and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1 : 20 to 1 : 5) as eluent furnished the tricyclic compound **10** (116 mg, 77.3%). $[a]_{D}^{23}$: -150 (*c* 0.2, CHCl₃). ν_{max} (neat) 1720 cm⁻¹. δ_{H} (90 MHz, CDCl₃) 1.50–2.60 (9 H, m), 1.60 (6 H, br s, 2 × olefinic CH₃), 1.35 (3 H, s, *tert*-CH₃). δ_{C} (100 MHz, CDCl₃) 215.1 (C, C=O), 126.7 (C) and 123.6 (C) (olefinic C), 44.8 (CH₂, C-7), 41.4 (CH₂), 20.6 (CH₃), 20.2 (CH₃), 20.0 (CH₃). Mass: *m*/*z* 190 (M⁺, 4%), 149 (15), 133 (25), 109 (85), 105 (60), 43 (100). HRMS: *m*/*z* Calcd. for C₁₃H₁₈O: *M*, 190.1358. Found: M⁺, 190.1357.

(-)-(1*S*,6*S*)-6-Methylbicyclo[4.3.0]non-4-ene-3,8-dione (3)

Through a cold $(-70 \,^{\circ}\text{C})$ solution of the compound 10 (400 mg, 2.1 mmol) in methanol (0.1 ml) and NaHCO₃ (catalytic) in 12 ml of CH₂Cl₂ was passed a stream of pre-cooled ozone in oxygen gas until the reaction mixture turned to blue in colour. Excess ozone was flushed off by passing oxygen gas. Dimethyl sulfide (1.1 g, 1.3 ml, 17.8 mmol) was added to the reaction mixture, allowed to warm up to RT and stirred for 10 h. It was then diluted with CH2Cl2, washed with brine and dried (Na₂SO₄). Evaporation of the solvent furnished the dione 11, which was taken in 5 ml CH₂Cl₂ and a catalytic amount pTSA was added and stirred at RT for 8 h. Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate-hexane (1:5 to 2:5) as eluent furnished the enedione **3** (307 mg, 89%) as an oil. $[a]_{D}^{25}$: -55 (c 2.5, MeOH). v_{max} (neat) 1745, 1675 cm⁻¹. δ_{H} (90 MHz, CDCl₃) 6.61 (1 H, d, J 10.2 Hz, H-5), 6.00 (1 H, d, J 10.2 Hz, H-4), 2.00-2.80 (7 H, m), 1.40 (3 H, s, tert-CH₃). δ_C (22.5 MHz, CDCl₃) 214.4 (s, C-8), 196.9 (s, C-3), 154.2 (d, C-5), 128.0 (d, C-4), 51.9 (t), 42.8 (t), 40.7 (d, C-1), 40.4 (s, C-6), 37.4 (t), 25.0 (q). Mass: m/z 164 (M⁺, 48%), 122 (20), 95 (100), 79 (35), 67 (50), 41 (60). HRMS: m/z Calcd. for C₁₀H₁₂O₂: M, 164.0837. Found: M⁺, 164.0818.

(1*R*,5*S*,6*R*) and (1*R*,5*R*,6*R*)-5,6-Dimethylbicyclo[4.3.0]nonan-3,8-diones (12a and b)

To a cold (-5 °C) magnetically stirred solution of lithium dimethylcopper (0.92 mmol) in ether [prepared from CuI (174 mg, 0.913 mmol) and MeLi (1.97 ml of a 0.93 M solution in ether, 1.83 mmol)] was slowly added a solution of the enedione 3 (50 mg, 0.305 mmol) in 1 ml of dry ether. The reaction mixture was slowly warmed up to RT and stirred for 3 h. It was then quenched with 5% aq. ammonia solution and extracted with ether $(3 \times 5 \text{ ml})$. The ether extract was washed with brine and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate-hexane (1:5 to 2:5) as eluent furnished a 3:2 mixture of epimers of the diketone 12a,b (39 mg, 71%) as an oil. v_{max} (neat) 1740, 1710 cm⁻¹. $\delta_{\rm H}$ (270 MHz, CDCl₃, 3 : 2 diastereomeric mixture) 1.80-2.80 (10 H, m), 1.27 and 1.18 (3 H, s, tert-CH₃), 0.97 and 1.02 (3 H, d, J 6.6 Hz, sec-CH₃). δ_C (100 MHz, CDCl₃): For the major isomer 12a: 215.8 (C, C-8), 210.3 (C, C-3), 51.9 (CH₂), 45.5 (CH), 44.9 (CH₂), 42.0 (CH₂), 40.7 (2 C, C and CH₂), 35.7 (CH), 18.7 (CH₃), 16.6 (CH₃). For the minor isomer 12b: 217.0 (C, C-8), 209.6 (C, C-3), 45.2 (CH₂), 45.1 (CH₂), 44.6 (CH), 42.3 (CH₂), 40.8 (C), 26.2, 17.8. Mass: m/z 180 (M⁺, 27 %), 137 (12), 111 (20), 109 (18), 96 (26), 69 (100). HRMS: m/z Calcd. for C₁₁H₁₆O₂: M, 180.1150. Found: M⁺, 180.1140.

(-)-(1*R*,6*S*)-8,8-Ethylenedioxy-6-methylbicyclo[4.3.0]non-4-en-3-one (13)

A magnetically stirred solution of the enedione **3** (180 mg, 1.1 mmol), ethylene glycol (72 μ l, 1.3 mmol) and a catalytic amount

of pTSA in 35 ml of dry benzene was refluxed using a Dean-Stark water separator for 3.5 h. It was cooled, washed with saturated aq. NaHCO3 and brine, and dried (Na2SO4). Evaporation of the solvent under reduced pressure and purification of the product on a silica gel column using ethyl acetate-hexane (1:5 to 2:5) as eluent furnished the ketoketal 13 (124 mg, 54%, 63% based on consumed starting material). $[a]_{\rm D}^{25}$: -26.3 (c 3.8, CHCl₃). v_{max} (neat) 1675 cm⁻¹. δ_{H} (270 MHz, CDCl₃) 6.60 (1 H, d, J 9.9 Hz, H-5), 5.92 (1 H, d, J 9.9 Hz, H-4), 3.86 (4 H, s, OCH₂CH₂O), 2.62 (1 H, dd, J 17.9 and 6.0 Hz), 1.90-2.45 (5 H, m), 1.83 (1 H, dd, J 13.6 and 10.7 Hz), 1.29 (3 H, s, tert-CH₃). $\delta_{\rm C}$ (22.5 MHz, CDCl₃) 197.7 (s, C=O), 156.3 (d, C-5), 126.5 (d, C-4), 115.1 (s, O-C-O), 64.0 (t) and 63.7 (t) [OCH₂CH₂O], 50.8 (t), 42.4 (d, C-1), 41.7 (2 C, s and t), 37.2 (t), 24.9 (q, CH₃). Mass: m/z 208 (M⁺, 5%), 164 (17), 112 (28), 99 (17), 95 (35), 86 (100). Further elution of the column furnished the unreacted starting material 3 (25 mg, 14%).

(1*R*,5*S*,6*R*) and (1*R*,5*R*,6*R*)-5,6-Dimethylbicyclo[4.3.0]nonan-3,8-diones (12a,b)

Reaction of the ketal **13** (50 mg, 0.24 mmol) in 1 ml of ether with lithium dimethylcopper [prepared from CuI (136 mg, 0.72 mmol) and MeLi (2 ml of a 0.7 M solution in ether, 1.4 mmol)], as described earlier, for 3 h furnished 50 mg of the product, which was taken up in 1.5 ml of THF and 3 M aq. HCl (1.0 ml) and stirred for 5 h at RT. It was then extracted with ether (3 × 5 ml), washed with water, saturated NaHCO₃ solution and brine, and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1 : 5 to 2 : 5) as eluent furnished a 2 : 1 epimeric mixture of the diketones **12a,b** (31 mg, 70%).

(2*S*,3*R*,5*R*) and (2*R*,3*R*,5*R*)-2-Allyl-5-isopropenyl-2,3dimethylcyclohexanones (14)

To a cold (-10 °C), magnetically stirred solution of lithium dimethylcopper [prepared from cuprous iodide (1.9 g, 10 mmol) and methyllithium in ether (20 mmol, 26 ml of a 0.765 M solution in ether)] was added a solution of (R)-carvone (1, 1.0 g,6.66 mmol) in dry ether (15 ml) over a period of 15 min. The reaction mixture was stirred for 30 min at RT, and a mixture of allyl bromide (8.0 g, 5.6 ml, 66.1 mmol) and HMPT (1.43 g, 1.4 ml, 8 mmol) was added over 5 min. It was stirred for 24 h at RT, quenched with 25% aq. NH4Cl solution and extracted with ether $(3 \times 15 \text{ ml})$. The ether extract was washed with brine and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue on a silica gel column, using ethyl acetate-hexane (1:48) as eluent, furnished a 9:1 epimeric mixture of the product 14 (1.22 g, 89%) as pale yellow oil. Partial purification on a long silica gel column furnished a small amount of major epimer of the product 14. $[a]_{D}^{24}$: +37 (c 1.2, CHCl₃). v_{max} (neat) 1705, 1640, 910, 890 cm⁻¹. $\delta_{\rm H}$ (200 MHz, CDCl₃) 5.63 (1 H, t of dd, J 17.5, 9.5 and 7.3 Hz, H-2'), 5.08 (1 H, d, J 17.5 Hz) and 5.07 (1 H, d, J 9.5 Hz) [H-3'], 4.79 (1 H, s) and 4.72 (1 H, s) [C=CH₂], 2.30-2.70 (5 H, m), 1.90-2.20 (2 H, m), 1.60-1.70 (1 H, m), 1.75 (3 H, s, olefinic CH₃), 1.00 (3 H, s, tert-CH₃), 0.91 (3 H, d, J 7.2 Hz, sec-CH₃). $\delta_{\rm C}$ (22.5 MHz, CDCl₃) 213.4 (s, C=O), 146.8 (s, C=CH₂), 133.2 (d, CH=CH₂), 117.0 (t, CH= CH₂), 109.7 (t, C=CH₂), 51.1 (s, C-2), 42.2, 41.3, 39.9, 36.0 (d), 32.2 (t), 20.4 (q), 18.3 (q), 15.3 (q). Mass: m/z 206 (M⁺, 10%), 191 (20), 163 (30), 123 (25), 109 (40), 95 (95), 41 (100). HRMS: m/z Calcd. for C14H22O: M, 206.1671. Found: M⁺, 206.1679.

(2*S*,3*R*,5*R*) and (2*R*,3*R*,5*R*)-5-Isopropenyl-2,3-dimethyl-2-(2-oxopropyl)cyclohexanones (15) and (16)

A suspension of palladium chloride (61 mg, 0.34 mmol) and cuprous chloride (500 mg, 5 mmol) in DMF (2.5 ml) and water (0.5 ml, 27.8 mmol) was magnetically stirred in an oxygen atmosphere, created *via* evacuative displacement of air using an

oxygen balloon, for 1 h at RT. A solution of the 9:1 mixture of the allyl compound 14 (1.03 g, 5 mmol) in 1 ml of DMF was then added, and the reaction mixture was stirred for 24 h at RT in the oxygen atmosphere. 3 M HCl (5 ml) was added to the reaction mixture and extracted with ether $(3 \times 10 \text{ ml})$. The ether layer was washed with saturated aq. NaHCO3 solution followed by brine and dried (Na₂SO₄). Evaporation of the solvent and careful chromatography of the residue on a silica gel column using ethyl acetate-hexane (1:20 to 1:10) as eluent, furnished the diketone 16 (86 mg, 7.7%) as oil and 15 (775 mg, 70%) as a white solid, which was recrystallised from hexane. For the minor *diketone* **16**: v_{max} (neat) 1700, 1640, 885 cm⁻¹. δ_{H} (90 MHz, CDCl₃) 4.77 (2 H, br s, C=CH₂), 2.10–2.90 (5 H, m), 2.17 (3 H, s, CH₃C=O), 1.74 (3 H, s, olefinic CH₃), 1.60–1.85 (3 H, m), 1.41 (3 H, s, tert-CH₃), 0.86 (3 H, d, J 7.0 Hz, sec-CH₃). δ_C (22.5 MHz, CDCl₃) 212.1 (s, ring C=O), 205.7 (s, MeC=O), 146.6 (s, C=CH₂), 109.2 (t, C=CH₂), 49.9 (s, C-2), 45.1 (t, CH₂C=O), 41.1 (t, C-6), 40.2 (d), 37.3 (d), 32.1 (t), 30.7 (q), 21.7 (q), 19.9 (q), 15.5 (q). For the major diketone **15**: mp: 53–54 °C. $[a]_{D}^{23}$: +6.1 (c 1.14, CHCl₃). v_{max} (neat) 1710, 1700, 1650, 895 cm⁻¹. δ_{H} (90 MHz, CDCl₃) 4.83 (1 H, s) and 4.75 (1 H, s) (C=CH₂), 2.78 (2 H, br s), 2.56 (2 H, br s), 2.20-2.50 (1 H, m), 2.12 (3 H, s, COCH₃), 1.65–1.85 (3 H, m), 1.72 (3 H, s, olefinic CH₃), 1.02 (3 H, s, tert-CH₃), 0.88 (3 H, d, J 7.2 Hz, sec-CH₃). δ_C (22.5 MHz, CDCl₃) 211.8 (s, ring C=O), 205.5 (s, MeC=O), 146.3 (s, C= CH₂), 109.6 (t, C=CH₂), 49.4 (s, C-2), 49.1 (t, CH₂COCH₃), 41.1 (t, C-6), 39.5 (d, C-5), 34.4 (d, C-3), 31.7 (t, C-4), 30.2 (q, COCH₃), 20.0 (q), 17.8 (q), 14.4 (q). Mass: m/z 222 (M⁺, 5%), 165 (90), 109 (22), 95 (25), 43 (100). Anal. Calcd. for C14H22O2: C, 75.63; H 9.97. Found: C, 75.74; H 10.19%.

(+)-(1*S*,2*R*,4*R*)-4-Isopropenyl-1,2-dimethylbicyclo[4.3.0]non-6en-8-one (17)

To a solution of the diketone 15 (686 mg, 3.09 mmol) in 1 ml of methanol was added 10% aq. KOH (1.73 ml, 3.71 mmol), and the reaction mixture was refluxed for 3 h. It was cooled and extracted with ether $(3 \times 10 \text{ ml})$. The ether extract was washed with water followed by brine and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue on a silica gel column, using ethyl acetate-hexane (1:6) as eluent furnished the enone 17 (600 mg, 95%) as an oil. $[a]_{D}^{25}$: +44.2 (c 1.0, CHCl₃). v_{max} (neat) 1700, 1620, 888 cm⁻¹. δ_{H} (200 MHz, CDCl₃) 5.80 (1 H, s, H-7), 4.73 (1 H, s) and 4.84 (1 H, s) [C=CH₂], 2.50-3.10 (3 H, m), 2.20 (2 H, s, H-9), 1.50-1.80 (3 H, m), 1.70 (3 H, s, olefinic CH₃), 1.12 (3 H, s, tert-CH₃), 0.91 (3 H, d, J 6.1 Hz, sec-CH₃). δ_C (50 MHz, CDCl₃) 207.6 (C=O), 187.3 (C-6), 146.0 (C=CH₂), 127.4 (C-7), 111.7 (C=CH₂), 50.6 (C-9), 46.7 (C-1), 40.5, 36.4, 31.4, 30.0, 22.5, 18.5, 16.6. Mass: m/z 204 (M⁺, 28%), 189 (20), 162 (100), 147 (31), 134 (62), 119 (40), 105 (33), 95 (29). HRMS: m/z Calcd. for C14H20O: M, 204.1514. Found: M⁺, 204.1514.

(-)-(1*S*,2*R*,4*R*,6*S*) and (-)-(1*S*,2*R*,4*R*,6*R*)-4-Isopropenyl-1,2dimethylbicyclo[4.3.0]nonan-8-ones (18) and (19)

To a dark blue coloured solution of lithium (190 mg, 27.3 mmol) in 400 ml of freshly distilled ammonia was added, dropwise, a solution of the enone **17** (1.5 g, 7.35 mmol) and *tert*butanol (0.6 ml, 6.4 mmol) in 20 ml of dry THF over a period of 15 min. The reaction mixture was stirred for 50 min and then quenched with ammonium chloride. Ammonia was evaporated, it was diluted with water and extracted with ether (3 × 25 ml). The ether extract was washed with brine and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue over a silver nitrate impregnated silica gel column using ethyl acetate–hexane (1 : 50 to 1 : 10) as eluent furnished the *trans*hydrindanone **19** (305 mg, 20%), *cis*-hydrindanone **18** (650 mg, 43%) and the unreacted starting material **17** (300 mg, 20%). For the *trans* isomer **19**: $[a]_{2}^{24}$: -186 (*c* 2.7, CHCl₃). v_{max} (neat) 1745, 1640, 888 cm⁻¹. δ_{H} (200 MHz, CDCl₃) 4.93 (1 H, s) and 4.84 (1

H, s) [C=CH₂], 2.43 (1 H, m, H-4), 1.50–2.20 (10 H, m), 1.76 (3 H, s, olefinic CH₃), 0.83 (3 H, d, J 6.3 Hz, sec-CH₃), 0.79 (3 H, s, tert-CH₃). δ_C (22.5 MHz, CDCl₃) 215.6 (s, C=O), 146.6 (s, C= CH₂), 110.0 (t, C=CH₂), 53.3 (t, CH₂C=O), 42.1 (s, C-1), 40.6 (d, C-4), 40.0 (d), 38.7 (d), 37.4 (t), 31.7 (t), 25.5 (t), 22.2 (q), 16.6 (q), 10.6 (q). Mass: m/z 206 (M⁺, 15%), 178 (11), 163 (35), 149 (11), 135 (15), 123 (40), 121 (50), 109 (30), 107 (35), 96 (100). HRMS: m/z Calcd. for C14H22O: M, 206.1671. Found: M⁺, 206.1658. For the cis isomer **18**: $[a]_{\rm D}^{26}$: -100.4 (c 2.5, CHCl₃). $v_{\rm max}$ (neat) 1740, 1640, 890 cm⁻¹. $\delta_{\rm H}$ (270 MHz, CDCl₃) 4.69 (1 H, s) and 4.72 (1 H, s) [C=CH₂], 2.54 (1 H, dd, J 18.7 and 8.5 Hz, H-7a), 1.95 and 2.52 (2 H, 2 × d, J 18.5 Hz, H-9), 1.40-2.30 (8 H, m), 1.72 (3 H, s, olefinic CH₃), 1.06 (3 H, d, J 7.1 Hz, sec-CH₃), 1.03 (3 H, s, tert-CH₃). δ_C (22.5 MHz, CDCl₃) 219.2 (s, C=O), 149.4 (s, C=CH₂), 108.5 (t, C=CH₂), 48.1 (t, C-9), 44.8 (t, C-7), 40.5 (s, C-1), 38.6 (d), 37.1 (d), 34.6 (t), 33.8 (2 C, d & t), 25.4 (q), 21.0 (q), 16.0 (q). Mass: m/z 206 (M⁺, 22%), 163 (35), 149 (25), 109 (55), 95 (55), 40 (100). HRMS: m/z Calcd. for C₁₄H₂₂O: M, 206.1671. Found: M⁺, 206.1688.

(-)-(1*S*,2*R*,6*S*)-4-Isopropylidene-1,2dimethylbicyclo[4.3.0]nonan-8-one (21)

To an ice cold magnetically stirred saturated solution of HBr in dry ether (50 ml) [by dissolving HBr gas, generated by bromination of tetralin, in ether] was added the hydrindanone 18 (400 mg, 1.94 mmol) in 2 ml of dry ether. The reaction mixture was stirred at the same temp for 6 h, diluted with ether (30 ml), washed with water, aq. NaHCO₃ and brine, and dried (Na₂SO₄). Evaporation of the solvent furnished the tertiary bromide 20. A solution of the bromide 20 and DBU (0.347 ml, 2.3 mmol) in 5 ml of benzene was taken up in a sealed tube and heated at 130 °C for 30 min. The reaction mixture was then cooled to RT, diluted with water and extracted with ether $(3 \times 10 \text{ ml})$. The ether extract was washed with 3 M HCl, saturated NaHCO₃ solution and brine, and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate-hexane (1:20) as eluent furnished the isopropylidene compound 21 containing a trace amount of the starting material 18 (390 mg, 97.5% in two steps). $[a]_{\rm D}^{26}$: +79.1 (c 2.73, CHCl₃). $v_{\rm max}$ (neat) 1740 cm⁻¹. $\delta_{\rm H}$ (90 MHz, CDCl₃) 2.35 (1 H, d, J 18 Hz), 2.16 (2 H, s, CH₂C= O), 1.93 (1 H, d, J 18 Hz), 1.60-2.60 (6 H, m), 1.68 (3 H, s), 1.63 (3 H, s), 1.10 (3 H, s, tert-CH₃), 0.85 (3 H, d, J 6.3 Hz, sec-CH₃). $\delta_{\rm C}$ (22.5 MHz, CDCl₃) 218.7 (s, C=O), 127.1 (s) and 123.9 (s) [olefinic C], 52.4 (t, CH₂C=O), 45.0 (d), 40.8 (s, C-1), 40.4 (t), 35.3 (d), 33.8 (t), 28.3 (t), 19.7 (2 C, q), 18.7 (q), 16.1 (q). Mass: m/z 206 (M⁺, 80%), 163 (40), 149 (45), 121 (75), 110 (40), 109 (100), 107 (50). HRMS: m/z Calcd. for C14H22O: M, 206.1671. Found: M⁺, 206.1668.

(+)-(1*S*,5*R*,6*S*)-5,6-Dimethylbicyclo[4.3.0]nonan-3,8-dione (12a)

Ozonolysis of the enone **21** (390 mg, 1.89 mmol), in CH₂Cl₂ (10 ml) and methanol (0.4 ml), as described for the compound **10**, followed by reductive work up with triphenylphosphine (500 mg, 1.9 mmol) for 4 h at RT and purification of the product over a silica gel column using ethyl acetate–hexane (1 : 5 to 2 : 5) as eluent furnished the dione **12a** (300 mg, 88%). $[a]_D^{24}$: +88.4 (*c* 1.9, CHCl₃). v_{max} (neat) 1740, 1710 cm⁻¹. δ_H (200 MHz, CDCl₃) 1.70–2.80 (10 H, m), 1.21 (3 H, s, *tert*-CH₃), 0.90 (3 H, d, *J* 6.6 Hz, *sec*-CH₃). δ_C (100 MHz, CDCl₃) 215.9 (C), 210.4 (C), 51.9 (CH₂), 45.5 (CH), 45.0 (CH₂), 42.0 (CH₂), 40.7 (2 C, C & CH₂), 35.7 (CH), 18.7 (CH₃), 16.6 (CH₃). Mass: *mlz* 180 (M⁺, 25 %), 111 (10), 69 (100). HRMS: *mlz* Calcd. for C₁₁H₁₆O₂: *M*, 180.1150. Found: M⁺, 180.1143.

(+)-(1*S*,2*R*,6*R*)-4,4-Ethylenedioxy-1,2dimethylbicyclo[4.3.0]nonan-8-one (2)

Regioselective protection of the dione 12a (320 mg, 1.77 mmol)

in 2 ml of dry benzene using ethylene glycol (98 µl, 108 mg, 1.75 mmol) and *p*TSA (catalytic) in 70 ml of dry benzene for 3 h, as described for the ketoketal **13**, and purification of the product over a silica gel column using ethyl acetate–hexane (1 : 5) as eluent furnished the ketoketal **2** (256 mg, 64.5%) as an oil. $[a]_{D}^{25}$: +69.8 (*c* 1.64, CHCl₃). v_{max} (neat) 1730 cm⁻¹. δ_{H} (270 MHz, CDCl₃) 3.85–4.00 (4 H, m, OCH₂CH₂O), 2.93 (1 H, d of t, *J* 16.0 and 7.0 Hz), 1.40–2.50 (9 H, m), 1.06 (3 H, s, *tert*-CH₃), 0.85 (3 H, d, *J* 6.7 Hz, *sec*-CH₃). δ_{C} (50 MHz, CHCl₃ + CDCl₃) 219 (C=O), 109 (O-C-O), 64.4 and 63.5 (OCH₂CH₂O), 58.3, 52.2, 43.5, 41.5, 38.5, 31.8, 31.4, 18.4, 16.0. Mass: *m/z* 224 (M⁺, 5%), 154 (35), 139 (10), 113 (100). HRMS: *m/z* Calcd. for C₁₃H₂₀O₃: *M*, 224.1412. Found: M⁺, 224.1416.

Acknowledgements

We thank the Department of Science and Technology for the financial support and the University Grants Commission for the award of a research fellowship to TJR.

References

- Progress in the Chemistry of Organic Natural Products, eds. W. Herz, H. Falk, G. W. Kirby and R. E. Moore, Springer Wien, New York, vol. 80, 2000; and the earlier volumes in the series.
- 2 *The Total Synthesis of Natural Products*, ed. J. ApSimon, Wiley, New York, vol. 9, 1992; and other volumes in the series.
- 3 T.-L. Ho, *Enantioselective Synthesis: Natural Products from Chiral Terpens*, John Wiley, Chichester, 1992.
- 4 S. Hannessian, Total Synthesis of Natural Products: The Chiron Approach, Pergamon Press, Oxford, 1983.
- 5 H. J. Swarts, A. A. Verstegen-Haaksma, B. J. M. Jansen and A. de Groot, *Tetrahedron*, 1994, **50**, 10083; H. J. Swarts, A. A. Verstegen-Haaksma, B. J. M. Jansen and A. de Groot, *Tetrahedron*, 1994, **50**, 10095; V. N. Zhabinskii, A. J. Minnaard, J. B. P. A.

Wijnberg and A. de Groot, *J. Org. Chem.*, 1996, **61**, 4022; A. J. Minnaard, G. A. Stork, J. B. P. A. Wijnberg and A. de Groot, *J. Org. Chem.*, 1997, **62**, 2344; A. J. Minnaard, J. B. P. A. Wijnberg and A. de Groot, *J. Org. Chem.*, 1997, **62**, 7336; A. J. Minnaard, J. B. P. A. Wijnberg and A. de Groot, *J. Org. Chem.*, 1997, **62**, 7346, see also T. M. Meulemans, G. A. Stork, F. Z. Macaev, B. J. M. Jansen and A. de Groot, *J. Org. Chem.*, 1999, **64**, 9178.

- 6 (a) A. Srikrishna, T. J. Reddy, P. P. Kumar and S. J. Gharpure, Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem., 2001, 40, in the press; (b) A. Srikrishna and S. J. Gharpure, J. Org. Chem., 2001, 66, 4379; (c) A. Srikrishna, P. R. Kumar and S. J. Gharpure, Tetrahedron Lett., 2001, 42, 3929; (d) A. Srikrishna, R. Viswajanani and C. Dinesh, J. Chem. Soc., Perkin Trans. 1, 2000, 4321; (e) A. Srikrishna and S. J. Gharpure, J. Chem. Soc., Perkin Trans. 1, 2000, 3191; (f) A. Srikrishna and D. Vijaykumar, J. Chem. Soc., Perkin Trans. 1, 2000, 2583 and references cited therein.
- A. Srikrishna and P. Hemamalini, Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem., 1990, 29, 152; (b) A. Srikrishna and T. J. Reddy, Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem., 1995, 34, 844; (c) A. Srikrishna and D. Vijaykumar, Tetrahedron Lett., 1998, 39, 5833; (d) A. Srikrishna and T. J. Reddy, J. Chem. Soc., Perkin Trans. 1, 1998, 2137; (e) A. Srikrishna, S. J. Gharpure and P. P. Kumar, Tetrahedron Lett., 2000, 41, 3177.
- 8 For a preliminary communication, see A. Srikrishna, T. J. Reddy and S. Nagaraju, *Tetrahedron Lett.*, 1996, **37**, 1679.
- 9 (a) L. Garver, P. van Eikeren and J. E. Byrd, J. Org. Chem., 1976, 41, 2773; (b) Y.-D. Wu, K. N. Houk, J. Florez and B. M. Trost, J. Org. Chem., 1991, 56, 3656.
- 10 W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T.-t. Li, D. J. Faulkner and M. R. Petersen, J. Am. Chem. Soc., 1970, 92, 741.
- 11 (a) G. Stork and J. Ficini, J. Am. Chem. Soc., 1961, 83, 4678; (b) S. D. Burke and P. A. Grieco, Org. React., 1979, 26, 361; (c) L. N. Mander, Synlett, 1991, 134.
- 12 S. L. Schreiber and W.-F. Liew, Tetrahedron Lett., 1983, 24, 2363.
- 13 B. Hartmann, A. M. Kanazawa, J.-P. Depres and A. E. Greene, *Tetrahedron Lett.*, 1993, 34, 3875.
- 14 J. Tsuji, Synthesis, 1984, 369.
- 15 J. K. Whitesell and R. S. Matthews, J. Org. Chem., 1977, 42, 3878.