Synthesis of chiral tricyclo[3.2.1.0^{2,7}]octanes by an efficient 3-*exo-trig* radical cyclisation reaction[1]

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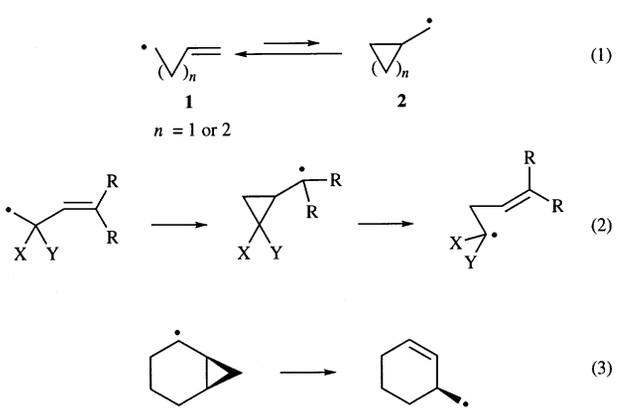
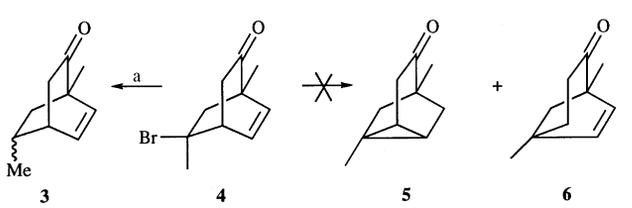
Synthesis of chiral tricyclo[3.2.1.0^{2,7}]octanes by efficient and exclusive *3-exo-trig* radical cyclisation of either a bicyclo[3.2.1]oct-6-en-2-yl radical or a bicyclo[2.2.2]oct-5-en-2-yl radical is described. Reaction of the methoxy enones 7a–c with boron tribromide at low temperature furnishes the bicyclo[3.2.1]octenyl bromides 9a–c and 10a–c along with varying amounts of 8a–c, whereas the methoxy enone 7d provides the unrearranged bicyclo[2.2.2]octenyl bromide 8d. Treatment of the homoallyl bromides 9a–c and 10a–c and 8d with tributyltin hydride and AIBN generates, exclusively, the tricyclic ketones 15a–d.

The use of carbon centred radicals in organic synthesis has increased dramatically within the last 10 to 15 years.[2] By far, the most frequent applications of radical cyclisation in organic synthesis have involved formation of five-membered rings, but larger rings including macrocycles, can also be produced by such reactions. However, for small rings, cyclisation of the but-3-enyl and pent-4-enyl radicals are energetically unfavourable [eqn. (1)]. For example, the rate constant for 3-*exo* cyclisation of the but-3-enyl radical **1** (n = 1) is *ca.* 8000 s^{-1} at 25 °C, whereas the rate constant for ring opening of the cyclopropylmethyl radical **2** (n = 1) is 10^8 s^{-1} at 25 °C.[3] Hence the ring formation is highly unfavoured, and 3-*exo* cyclisations are commonly followed by fragmentation [eqn. (2)][4] that can result in an overall 1,2-vinyl group migration (homoallyl–homoallyl radical rearrangement). Indeed radical chemistry was successfully employed to cleave the cyclopropyl systems to homoallyl systems in a stereo- and regio-selective manner [eqn. (3)].[5] Although



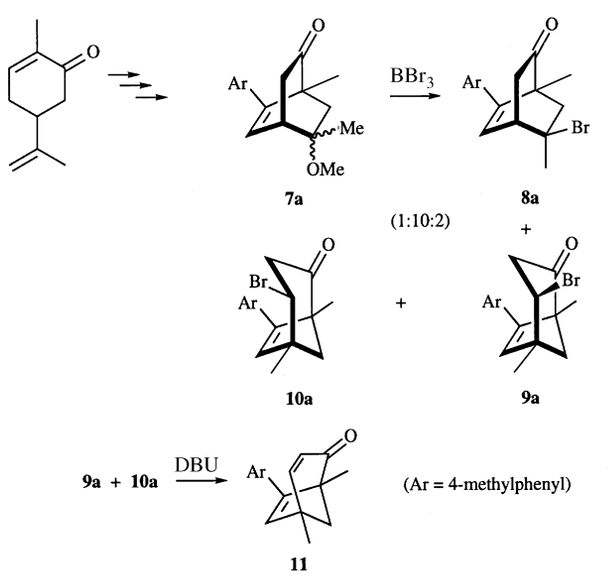
numerous examples have been reported of 1,2- vinyl shifts [eqn. (2)], there are quite understandably, very few reports[6,7] in the literature on the formation of a cyclopropane ring by a 3-*exo trig* radical cyclisation using standard conditions. Here we report the synthesis of chiral tricyclo[3.2.1.0^{2,7}]octanes by efficient



Reagents: a, Bu_3SnH, AIBN

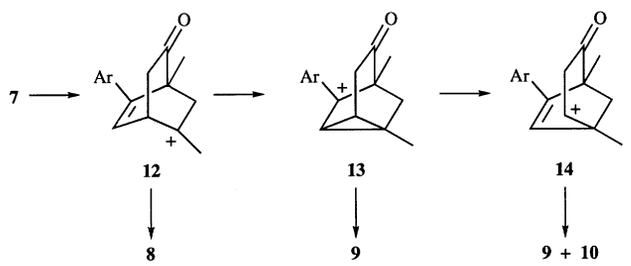
and exclusive 3-*exo-trig* radical cyclisation of either bicyclo-[3.2.1]oct-6-en-2-yl or a bicyclo[2.2.2]oct-5-en-2-yl bromides.[8]

In line with the earlier reports, reaction of the bicyclooctenyl bromide **4** with tributyltin hydride and AIBN gave an epimeric mixture of the reduction product **3**, neither the cyclised product **5** nor the rearranged product **6** being formed. However, it was expected that the presence of an electron-withdrawing group on the olefin might change the course of the radical reaction. The ready accessibility of the 6-aryl-8-methoxybicyclo[2.2.2]oct-5-en-2-ones **7** from *S*-carvone,[10] prompted us to choose compound **7** as starting material for the generation of the radical precursors. Reaction of the epimeric mixture of the methoxy enone **7a** with boron tribromide[11] in CH_2Cl_2 at low temperature, contrary to expectation, furnished a mixture (≈1:2:10 by NMR) of bromides, with the bromo ketone **9a** as the major product and its epimer **10a** and the unrearranged bromo ketone

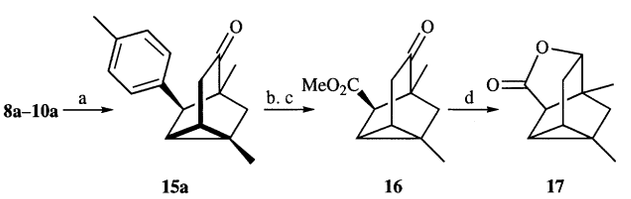


8a as minor components. The structure of the major bromide was established as the bicyclo[3.2.1]octenyl bromide **9a** from the spectral data. The dehydrobromination of the bromo ketone **9a** using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) furnished the dienone **11** in >85% yield and thus confirming the structure of the bromo ketone **9a**. Formation of the bromide **9a** from the methoxy enone **7a** can be rationalised as depicted below. Cleavage of the methoxy group generates the initial tertiary carbonium ion **12**, trapping of which by bromide would have resulted in the bromo ketone **8a**. Interaction of the styrenic double bond with the carbonium ion transforms the ion **12** into the cyclo-

propyl benzyl carbonium ion **13**. Either opening of the cyclopropane bond to form the secondary carbonium ion **14**, followed by attack of bromide from *exo* face, or the attack of bromide on the cyclopropane carbon along with the cleavage of the cyclopropane bond, results in the bromide **9a**.



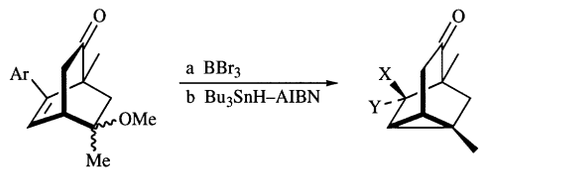
The bicyclo[3.2.1]oct-6-en-2-yl bromide **9a** which is also a homoallyl bromide with an aryl group on the olefin, was subjected to 3-*exo-trig* radical cyclisation. Refluxing a 0.02 M benzene solution of the mixture of the bromides **8a**–**10a** with 1.1 equiv. of tributyltin hydride in the presence of a catalytic amount of AIBN furnished, stereoselectively the 3-*exo-trig* cyclised product **15a** (>90% yield), whose structure rests secured on the basis of its spectral characteristics. The *endo* stereochemistry of the tolyl group was deduced from the coupling constant (2.8 Hz) of the benzylic proton. It was established,[12] on the basis of the dihedral angles, that in tricyclo[3.2.1.$0^{2,7}$]octan-4-one $J_{6\text{-}exo,7}$ and $J_{6\text{-}endo,7}$ will be in the order of 2 and 0 Hz, respectively. Final confirmation of the stereochemistry of the aryl group was achieved by degradation of the aryl moiety. The ruthenium chloride-catalysed oxidation[13] of the tricyclic ketone **15a** followed by esterification of the resultant keto acid generated the keto ester **16**. Stereospecific reduction of the keto ester **16** with sodium borohydride directly furnished the γ-lactone **17**, unambiguously establishing



Reagents: a, Bu_3SnH–AIBN; b, $RuCl_3{\cdot}3H_2O$, $NaIO_4$; c, CH_2N_2; d, $NaBH_4$

the stereochemistry of **15a**. It was expected that it might be possible to generate the tricyclic ketone **15a** from the dienone **11** by reductive cyclisation, since the intermediacy of a radical (at the β carbon) anion in the reduction of enones with alkali metal in liquid ammonia is well established. Thus, reaction of dienone **11** with lithium in liquid ammonia and THF furnished the cyclised product **15a**.

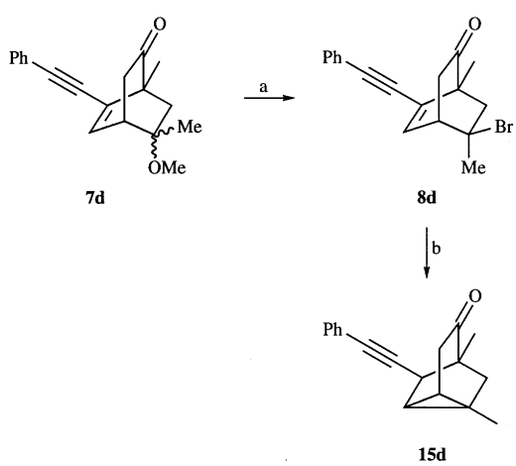
The observed ready and exclusive formation of the cyclopropane ring by 3-*exo-trig* radical cyclisation (**9a**→**15a**) established that the presence of the tolyl group on the homoallyl system in bicyclo[3.2.1]octenes enhances the cyclisation rate to a value much higher than that of the ring cleavage. The sequence was carried out with other derivatives. Thus, whilst reaction of the epimeric mixture of the methoxy enone **7b** with boron tribromide in CH_2Cl_2, analogous to that of tolyl compound **7a**, furnished the bicyclo[3.2.1]octenyl bromides **9b** and **10b** as major products along with traces of the unrearranged bromide **8b**, the epimeric mixture of the methoxy enone **7c** provided a ≈1:1 mixture of the bromides **10c** and **8c** along with a trace of **9c**.[14] Radical cyclisation of the mixture of the bromo enones **9b**–**10b** with tributyltin hydride (1.1 equiv.) in the presence of a catalytic amount of AIBN, furnished cleanly the tricyclic compound **15b** in a stereoselective manner by 3-*exo-trig* cyclisation, whereas radical cyclisation of the mixture of the bromo enones **8c**–**10c** furnished an epimeric mixture (at the benzylic carbon) of the tricyclic ketone **15c** and **18**. The structures of all compounds were established on the basis of spectral results particularly by comparison with these with those of tolyl compounds. The structure of the epimeric tricyclic ketone **18** was deduced from the singlet (*vide supra*) benzylic proton resonance at 3.62 ppm in the ^{1}H NMR spectrum.



7b Ar = 4-$MeOC_6H_4$
7c Ar = 2-$MeOC_6H_4$

15b X = 4-$MeOC_6H_4$, Y = H
15c X = 2-$MeOC_6H_4$, Y = H
18 X = H, Y = 2-$MeOC_6H_4$

As an alternative to the aryl moiety for stabilisation of the product radical in the 3-*exo-trig* radical cyclisation and for the generation of the bicyclo[2.2.2]octenyl bromide, we thought that phenylethynyl might be a possibility; thus, we allowed an epimeric mixture of the methoxy enone **7d** to react with boron tribromide. In contrast to the aryl derivatives, this reaction generated stereoselectively the bicyclo[2.2.2]octyl bromide **8d** with only trace of rearranged product. The bicyclo[2.2.2]oct-5-en-2-yl radical, generated from the bromo enone **8d** under standard conditions, underwent clean 3-*exo-trig* radical cyclisation to furnish stereoselectively the tricyclic compound **15d**.



Reagents: a, BBr_3; b, Bu_3SnH, AIBN

Experimental

IR spectra were recorded on Perkin-Elmer 781 and Hitachi 270-50 spectrophotometers. ^{1}H (60, 90 and 270 MHz) and ^{13}C NMR (22.5 MHz) spectra were recorded on Varian T-60, Jeol FX-90Q and Brucker WH-270 spectrometers using $CDCl_3$ as solvent. The chemical shifts (δ ppm) and the coupling constants (Hz) are reported in the standard fashion with reference to either internal tetramethylsilane (for ^{1}H) 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. Optical rotations, measured at VMSRF, Bangalore and the School of Chemistry, University of Hyderabad using a Jasco DIP-303 polarimeter are recorded in

units of 10^{-1} deg cm^2 g^{-1}. Acme's silica gel (100–200 mesh) was used for column chromatography. All small-scale dry reactions were carried out using standard syringe-septum techniques. Low-temperature reactions were conducted in an ethanol–liquid nitrogen bath. In order to dry it benzene was washed with H_2SO_4, distilled over sodium and stored over pressed sodium wire; CH_2Cl_2 was distilled from P_2O_5. Bu_3SnH, DBU, $RuCl_3 \cdot 3H_2O$ and BBr_3 were obtained from Fluka and were used as such. AIBN was recrystallised from methanol and stored in the dark.

(1*S*,4*S*,5*R*)-4-Bromo-1,5-dimethyl-7-(4-methylphenyl)-bicyclo[3.2.1]oct-6-en-2-one 9a

To a cold (≈ −60 °C), magnetically stirred solution of the epimeric mixture of the methoxy enone[10] **7a** (1.35 g, 5 mmol) in CH_2Cl_2 (10 cm^3) was added BBr_3 (0.5 cm^3, 5 mmol). The reaction mixture was stirred for 1.5 h at the same temperature and then quenched with saturated aq. $NaHCO_3$ (10 cm^3) and diluted with CH_2Cl_2 (20 cm^3). The CH_2Cl_2 layer was separated, washed with water and brine, dried (Na_2SO_4) and evaporated. Purification of the residue on a silica gel (50 g) column using EtOAc–hexane (1:20) as eluent furnished a ≈10:2:1 mixture of the bromides **9a**, **10a** and **8a** (0.8 g, 50%) as a viscous oil; ν_{max}(neat)/cm^{-1} 1728, 1629, 1512, 1380, 1113, 1068, 840, 813 and 609; δ_H(90 MHz, peaks due to the major bromide **9a**) 7.1 (4 H, s, Ar=H), 6.08 (1 H, s, olefinic H), 4.32 (1 H, t, *J* 7.2, CHBr), 3.1 (2 H, d, *J* 7.2, CH_2C=O), 2.36 (3 H, s, Ar-CH_3), 2.36 and 1.92 (2 H, AB q, *J* 12, 8-H), 1.48 (3 H, s, ^{5}-CH_3) and 1.0 (3 H, s, ^{1}-CH_3); *m*/*z* 318 (M$^+$, 90%), 320 (M$^+$ + 2, 90), 238 (80), 211 (65), 197 (90), 196 (85), 184 (100), 183 (45), 181 (44), 165 (40) and 105 (38) (Found: M$^+$, 318.0643. $C_{17}H_{19}BrO$ requires *M*, 318.0600).

(–)-(1*S*,5*S*)-1,5-Dimethyl-7-(4-methylphenyl)bicyclo[3.2.1]octa-3,6-dien-2-one 11

To a magnetically stirred solution of the mixture of bromides **9a**, **10a** and **8a** (225 mg, 0.7 mmol) in dry CH_2Cl_2 (3 cm^3) was added DBU (0.2 cm^3, 1.4 mmol). The reaction mixture was stirred at room temp. for 12 h, diluted with CH_2Cl_2 (8 cm^3), washed with 2% aq. HCl and brine, dried (Na_2SO_4) and evaporated. Purification of the residue on a silica gel (8 g) column using EtOAc–hexane (1:50) as eluent furnished the dienone **11** (160 mg, 85%) as an oil; $[\alpha]_D^{25}$ −194 (*c* 2.3, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1680, 1515, 1380, 1368, 1152, 1110, 1065, 852, 810 and 708; δ_H(90 MHz) 7.2 (1 H, dd, *J* 10 and 2, H-4), 7.1 (4 H, s, aromatic H), 6.27 (1 H, s, H-3), 5.46 (1 H, d, *J* 10, H-6), 2.6 (1 H, $\frac{1}{2}$ ABq, *J* 10) and 2.4 (1 H, dd, *J* 10 and 2) (H-8), 2.3 (3 H, s, Ar-CH_3), 1.4 (3 H, s) and 1.32 (3 H, s) (2 × *tert*-CH_3); δ_C(22.5 MHz) 201.8 (s), 160.2 (d), 149.6 (s), 141.7 (d), 136.9 (s), 133.3 (s), 129.0 (2 C, d), 126.8 (2 C, d), 121.8 (d), 64.7 (t), 61.3 (s), 46.8 (s), 21.9 (q), 17.9 (q), 21.2 (q); *m*/*z* 238 (M$^+$, 20%), 150 (90), 123 (35), 119 (100) and 91 (40) (Found: M$^+$, 238.1362. $C_{17}H_{18}O$ requires *M*, 238.1358).

(–)-(1*S*,2*S*,5*S*,6*S*,7*S*)-1,5-Dimethyl-6-(4-methylphenyl)-tricyclo[3.2.1.0^{2,7}]octan-4-one 15a

A solution of the mixture of the bromo ketones **9a**, **10a** and **8a** (319 mg, 1 mmol), Bu_3SnH (0.30 cm^3, 1.1 mmol) and AIBN (10 mg) in C_6H_6 (55 cm^3) was refluxed for 1.5 h and then washed with 1% aq. NH_4OH (2 × 10 cm^3) and brine, dried (Na_2SO_4) and evaporated under reduced pressure. Purification of the residue on a silica gel (10 g) column using EtOAc–hexane (1:50) as eluent furnished the tricyclic ketone **15a** (224 mg, 93%) as a colourless oil; $[\alpha]_D^{25}$ −153 (*c* 0.6, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1720, 1515, 1380, 1325, 1285, 1120, 1085, 1030, 820 and 800; δ_H(270 MHz) 7.05 and 6.99 (4 H, AB q, *J* 8.1 ArH), 3.33 (1 H, d, *J* 2.8, H-6), 2.58 and 2.44 (2 H, d of AB q, *J* 18 and 2, H-3), 2.21 (3 H, s, Ar-CH_3), 1.9 and 1.84 (2 H, AB q, *J* 13, H-8), 1.38 (1 H, dd, *J* 7 and 2.8, H-7), 1.27 (3 H, s, ^{1}-CH_3), 1.1 (1 H, m, H-2) and 1.02 (3 H, s, ^{5}-CH_3); δ_C(22.5 MHz) 211.2 (s), 136.1 (s), 129.0 (2 C, d), 128.6 (s), 127.4 (2 C, d), 56.0 (s), 53.5 (d), 43.3 (t), 34.9 (t), 21.0 (q), 20.2 (s), 26.7 (d), 18.3 (d), 19.6 (q) and 17.4 (q); *m*/*z* 240 (M$^+$, 100%), 171 (50), 144 (40), 129 (30), 105 (43) and 96 (40) (Found: M$^+$, 240.1500. $C_{17}H_{20}O$ requires *M*, 240.1514).

Reduction of the dienone 11 with lithium in liquid ammonia

To magnetically stirred, freshly distilled (over sodium) ammonia (50 cm^3) was added the dienone **11** (238 mg, 1 mmol) in dry THF (1 cm^3) followed by lithium metal (≈28 mg, 4 mmol). The reaction mixture was stirred for 0.5 h at −33 °C and then quenched with solid NH_4Cl (5 g); ammonia was allowed to evaporate over a period of 1 h. The residue was taken up in water (10 cm^3) and extracted with ether (3 × 5 cm^3). The extract was washed with brine, dried (Na_2SO_4) and evaporated. Purification of the residue on a silica gel (5 g) column using EtOAc–hexane (1:50) as eluent furnished the tricyclic ketone **15a** (170 mg, 70%) which was identified by comparison (TLC, IR and ^{1}H NMR spectra) with the sample obtained by radical cyclisation of the bromo enone **9a**.

(+)-(1*S*,3*S*,4*S*,5*S*,7*S*,8*R*)-5,7-Dimethyl-10-oxatetracyclo-[5.3.0.0^{3,5}.0^{4,8}]decan-9-one 17

To a magnetically stirred solution of sodium periodate (430 mg, 2 mmol) and the tricyclic ketone **15a** in a 1:1:1 mixture of CCl_4, MeCN and water (3 cm^3) was added $RuCl_3 \cdot 3H_2O$ (3 mg). The reaction mixture was stirred for 4 h at room temperature after which it was diluted with CH_2Cl_2 (10 cm^3), washed with water and brine, dried (Na_2SO_4) and evaporated. The resultant keto acid (40 mg) was treated with an excess of freshly prepared ethereal diazomethane for 15 min. Careful evaporation of the excess of diazomethane and solvent followed by purification of the residue on a silica gel (5 g) column using EtOAc–hexane (1:10) as eluent furnished the keto ester **16** (35 mg, 35%) [ν_{max}/cm^{-1} 1731; δ_H(90 MHz) 3.66 (3 H, s, $COOCH_3$), 3.06 (1 H, d, *J* 3.6, H-6), 2.66 (2 H, brs, H-3), 2.84 (2 H, s, H-8), 1.46 (1 H, dd, *J* 7.2 and 3.4, H-7), 1.1 (1 H, m, H-2), 1.28 (3 H, s, ^{1}-CH_3) and 1.12 (3 H, s, ^{5}-CH_3)]. To an ice-cold, magnetically stirred solution of the keto ester **16** (31 mg, 0.15 mmol) in MeOH (2 cm^3) was added $NaBH_4$ (17 mg, 0.45 mmol). The mixture was stirred for 4 h at room temperature after which a few drops of acetone was added to it to consume the excess reagent; it was then evaporated under reduced pressure. The residue was taken up in water (3 cm^3) and the solution extracted with ether (2 × 3 cm^3). The extract was washed with water and brine, dried (Na_2SO_4) and evaporated. Purification of the residue on a silica gel (4 g) column using EtOAc–hexane (1:10) as eluent furnished the lactone **17** (22 mg, 82%) which was crystallised from hexane; mp 72 °C; $[\alpha]_D^{24}$ 258 (*c* 0.48, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1759, 1200 and 1030; δ_H(270 MHz) 4.15 (1 H, d, *J* 4.6, H-1), 2.49 (1 H, d, *J* 4.3, H-8), 1.99 and 2.08 (2 H, d of AB q, *J* 15 and 4.3, H-2), 1.58 and 1.68 (2 H, AB q, *J* 13, H-6), 1.38 (1 H, dd, *J* 7.3 and 4.2, H-4), 1.2 (3 H, s) and 1.15 (3 H, s) (2 × *tert*-CH_3) and 0.84–0.88 (1 H, m, H-3); δ_C(22.5 MHz) 178.5 (s), 83.1 (d), 50.4 (s), 49.6 (d), 37.8 (t), 24.7 (d), 24.3 (t), 20.8 (q), 19.3 (q) and 16.4 (d); *m*/*z* 178 (M$^+$, 10%), 134 (70), 119 (100), 105 (40), 92 (40) and 91 (65) (Found: M$^+$, 178.0986. $C_{11}H_{14}O_2$ requires *M*, 178.0994).

(1*S*,4*S*,5*R*)-4-Bromo-1,5-dimethyl-7-(4-methoxyphenyl)bicyclo-[3.2.1]oct-6-en-2-one 9b

Reaction of the epimeric mixture of the bicyclooctenones[10] **7b** (1.43 g, 5 mmol) with BBr_3 (0.5 cm^3, 5 mmol) in dry CH_2Cl_2 (10 cm^3) at ≈−50 °C for 1.5 h and purification of the product on a silica gel (30 g) column using EtOAc–hexane (1:20) as eluent furnished the bicyclic bromide **9b** (1.3 g, 78%), containing minor amounts of the bromides **8b** and **10b**, as a viscous liquid; ν_{max}(neat)/cm^{-1} 1716, 1677, 1602, 1512, 1248, 1173, 1029 and 831; δ_H(90 MHz, for the major isomer **9b**) 7.12 (2 H, d, *J* 7.2) and 6.84 (2 H, d, *J* 7.2) (ArH), 6.02 (1 H, s, H-6), 4.32 (1 H, t, *J*

7.2, CHBr), 3.84 (3 H, s, OCH_3), 3.1 (2 H, d, *J* 7.2, H-3), 2.38 and 1.94 (2 H, AB q, *J* 12.6, H-8), 1.48 (3 H, s, ^{5}-CH_3) and 1.2 (3 H, s, ^{1}-CH_3); *m*/*z* 334 (M^+, 10%), 336 (M^+ + 2, 10), 273 (15), 272 (20), 254 (40), 150 (100) and 135 (70) (Found: M^+, 334.0593. $C_{17}H_{19}BrO_2$ requires *M*, 334.0569).

(–)-(1*S*,2*S*,5*S*,6*S*,7*S*)-1,5-dimethyl-6-(4-methoxyphenyl)-tricyclo[3.2.1.0^{2,7}]octan-4-one 15b

Radical cyclisation of the mixture of bromides **9b** and **10b** (335 mg, 1 mmol) with Bu_3SnH (0.30 cm^3, 1.1 mmol) and AIBN (10 mg) in benzene (55 cm^3) for 1.5 h followed by purification of the product on a silica gel (10 g) column using EtOAc–hexane (1:50) as eluent furnished the tricyclic ketone **15b** (221 mg, 85%) as a colourless oil; $[\alpha]_D^{25}$ −97.3 (*c* 0.67, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1716, 1614, 1581, 1515, 1380, 1248, 1173, 1026 and 828; δ_H(270 MHz) 7.16 (2 H, d, *J* 8.6) and 6.8 (2 H, d, *J* 8.6) (ArH), 3.76 (3 H, s, OCH_3), 3.39 (1 H, d, *J* 2.5, H-6), 2.67 and 2.51 (2 H, d of AB q, *J* 20.5 and 2.4, H-3), 1.94 (2 H, close AB q, *J* 14, H-8), 1.46 (1 H, dd, *J* 7.2 and 2.5, H-7), 1.34 (3 H, s, ^{1}-CH_3), 1.15–1.2 (1 H, m, H-2) and 1.09 (3 H, s, ^{5}-CH_3); δ_C(22.5 MHz) 211.3 (s), 158.5 (s), 131.2 (s), 128.4 (2 C, d), 113.8 (2 C, d), 56.0 (s), 55.1 (q), 53.2 (d), 43.1 (t), 34.9 (t), 26.9 (d), 20.2 (s), 19.6 (q), 18.3 (d) and 17.4 (q); *m*/*z* 256 (M^+, 100%), 213 (15), 187 (30), 160 (40) and 121 (40) (Found: M^+, 256.1452. $C_{17}H_{20}0_2$ requires *M*, 256.1463).

(1*S*,4*R*,5*R*)-4-Bromo-1,5-dimethyl-7-(2-methoxyphenyl)-bicyclo[3.2.1]oct-6-en-2-one 10c and (1*S*,4*S*,8*R*)-8-bromo-1,8-dimethyl-6-(2-methoxyphenyl)bicyclo[2.2.2]oct-5-en-2-one 8c

Reaction of a mixture of the epimeric methoxy enones[10] **7c** (1.43 g, 5 mmol) with BBr_3 (0.5 cm^3, 5 mmol) in dry CH_2Cl_2 (10 cm^3) at ≈−50 °C for 1 h, and purification of the product on a silica gel (20 g) column using EtOAc–hexane (1:20) as eluent furnished a 1:1 mixture of the bicyclic bromides **10c** and **8c** (0.92 g, 55%), containing a minor amount of the bromide **9c** as a viscous oil; ν_{max}(neat)/cm^{-1} 1719 and 1392; δ_H(60 MHz, CCl_4, ≈1:1 mixture of **8c** and **10c**) 6.8–7.4 (4 H, m, ArH), 1.8–3.2 (4 H, m, H-3 and 8); signals due to **8c** 6.3 (1 H, d, *J* 7, H-5), 3.7 (3 H, s, OCH_3), 3.2 (1 H, m, H-4), 2.0 (3 H, s, ^{8}-CH_3), 0.83 (3 H, s, ^{1}-CH_3); signals due to **10c** 5.8 (1 H, s, H-6), 4.4 (1 H, dd, *J* 7.2 and 1.8, H-3a), 3.56 (3 H, s, OCH_3), 1.37 (3 H, s, ^{5}-CH_3) and 0.97 (3 H, s, ^{1}-CH_3); δ_C(22.5 MHz, ≈1:1 mixture of the bromides **10c** and **8c** 210.0 (s), 207.0 (s), 156.9 (s), 156.1 (s), 152.9 (s), 143.1 (s), 135.9 (d), 131.6 (d), 129.7 (d), 129.2 (d), 127.4 (s), 125.2 (s), 120.5 (d), 110.2 (d), 68.6 (s), 61.5 (s), 58.0 (d), 55.1 (q) and 54.4 (q), 53.6 (s), 52.9 (t), 50.3 (t), 49.6 (s), 47.4 (d), 46.9 (t), 39.0 (t), 36.6 (q), 24.0 (q), 16.2 (q), 14.6 (q); *m*/*z* 334 (M^+, 40%), 336 (M^+ + 2, 40), 255 (35), 227 (40), 213 (95), 212 (100) and 197 (25) (Found: M^+, 334.0565. $C_{17}H_{19}BrO_2$ requires *M*, 334.0569).

(1*S*,2*S*,5*S*,6*S*,7*S*)- and (1*S*,2*S*,5*S*,6*R*,7*S*)-1,5-Dimethyl-6-(2-methoxyphenyl)tricyclo[3.2.1.0^{2,7}]octan-4-ones 15c and 18

Radical cyclisation of the mixture of bromides **10c** and **8c** (335 mg, 1 mmol) with Bu_3SnH (0.30 cm^3, 1.1 mmol) and AIBN (10 mg) in benzene (55 cm^3) for 1.5 h as described earlier followed by purification of the product on a silica gel (10 g) column using EtOAc–hexane (1:50) as eluent furnished a 3:1 epimeric mixture of the tricyclic ketone **15c** and **18** (153 mg, 63%) as a colourless oil; $[\alpha]_D^{25}$ −117.7 (*c* 2.3, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1719, 1671, 1599, 1491, 1242, 1113, 1026 and 753; δ_H(60 MHz, 3:1 mixture of epimers **15c** and **18**) 6.6–7.4 (4 H, m, ArH), 3.76 and 3.72 (3 H, s, OCH_3), 3.95 (d, *J* 2.5) and 3.62 (s) (1 H, H-5), 2.65 (2 H, d, *J* 3, H-3), 1.95 (2 H, s, H-8), 1.35 and 1.27 (3 H, s, ^{1}-CH_3), 1.03 and 0.92 (3 H, s, ^{5}-CH_3) and 1.0–1.6 (2 H, m, H-2 and 7); δ_C(22.5 MHz, peaks corresponding to major epimer **15c**) 212.5, 157.7, 128.8, 128.0, 127.3, 120.5, 110.4, 56.4, 55.0, 46.9, 43.8, 35.3, 27.3, 20.2, 19.7, 18.3 and 17.4; *m*/*z* 256 (M^+, 100%), 257 (25), 160 (25), 160 (25) and 121 (25) (Found: M^+, 256.1448. $C_{17}H_{20}O_2$ requires *M*, 256.1463).

(1*S*,4*S*,8*R*)-8-Bromo-1,8-dimethyl-6-(2-phenylethynyl)-bicyclo[2.2.2]oct-5-en-2-one 8d

Reaction of the epimeric mixture of the bicyclooctenones[10] **7d** (1.4 g, 5 mmol) and BBr_3 (0.5 cm^3, 5 mmol) in dry CH_2Cl_2 (10 cm^3) at ≈−50 °C for 1.5 h and purification of the product on a silica gel (50 g) column using EtOAc–hexane (1:20) as eluent furnished the bicyclic bromide **8d** (905 mg, 55%) as a viscous liquid; ν_{max}(neat)/cm^{-1} 1728, 1605, 1491, 1380, 1101, 1071, 1017, 756, 711 and 690; δ_H(90 MHz) 7.2–7.6 (5 H, m, ArH), 6.84 (1 H, d, *J* 7.2, H-5), 3.2 (1 H, m, H-4), 3.1 (1 H, dd, *J* 18 and 2, H-3a), 2.26 (1 H, dd, *J* 18 and 3, H-3b), 2.56 and 2.0 (2 H, AB q, *J* 14, H-7), 1.92 (3 H, s, ^{8}-CH_3) and 1.32 (3 H, s, ^{1}-CH_3); δ_C(22.5 MHz) 208.8 (s), 139.2 (d), 131.6 (2 C, d), 128.8 (d), 128.6 (2 C, d), 127.3 (s), 122.7 (s), 94.5 (s), 84.5 (s), 66.8 (s), 52.4 (s), 50.2 (t), 47.7 (d), 38.6 (t), 36.8 (q) and 15.7 (q); *m*/*z* 328 (M^+, 30%), 330 (M + 2, 30), 207 (100), 206 (35), 129 (20) and 115 (35) (Found: M^+, 328.0485. $C_{18}H_{17}BrO$ requires *M*, 328.0463).

(–)-(1*S*,2*S*,5*S*,6*S*,7*S*)-1,5-Dimethyl-6-(2-phenylethynyl)-tricyclo[3.2.1.0^{2,7}]octan-4-one 15d

Radical cyclisation of the bromide **8d** (330 mg, 1 mmol) with Bu_3SnH (0.30 cm^3, 1.1 mmol) and AIBN (10 mg) in benzene (55 cm^3) for 1.5 h followed by purification of the product on a silica gel (10 g) column using EtOAc–hexane (1:50) as eluent furnished the tricyclic ketone **15d** (205 mg, 82%) as a colourless oil; ν_{max}(neat)/cm^{-1} 1725, 1602, 1380, 1344, 1287, 1173, 1074, 756 and 690; δ_H(90 MHz) 7.0–7.4 (5 H, m, ArH), 3.07 (1 H, d, *J* 3.6, H-6), 2.64 (2 H, m, H-3), 1.76 (2 H, s, H-8), 1.2 (3 H, s, ^{1}-CH_3), 1.08 (3 H, s, ^{5}-CH_3) and 1.0–1.56 (2 H, m, H-2 and 7); *m*/*z* 250 (M^+, 20%), 235 (20), 207 (20), 165 (20), 129 (18), 115 (25), 105 (100) and 77 (60) (Found: M^+, 250.1360. $C_{18}H_{18}O$ requires *M*, 250.1358).

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14 Except in the conversion of **7d** into **8d**, in all the reactions with BBr_3, the ratio of the bromides **8**, **9** and **10** varied from batch to batch, perhaps due to variation in the temperature of the reaction.

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