A novel route to functionalized linearly benzannulated medium ring carbocyclics through regioselective aryl radical cyclization†

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Abstract
The scope for n-Bu₃SnH-AIBN-mediated regioselective endo-trig aryl radical cyclization processes in elaboration of linearly benzannulated medium ring carbocycles is described. A range of vinylcyclohexanols 3a, b, 4a, b, 28a, b, c and butenylcyclohexanols 11a, b, 12a, 18a, b, 32, 36a, b and allyl-cyclohexanols 11a, b, 12a, 18a, b and 32a, b, 36a, b, 43a, b and 44a, prepared using synthetic sequence based on sound literature precedent, were first examined. Radical cyclization of 3a, b, 4a, b and 28a–c led to the corresponding seven- and eight-membered ring-annulated tricyclic alcohols 5a, b, 6a, b and 13a, b, 14a, b and 30a–c in good yields. Radical cyclization of 11a, b, 12a, 18a, b and 32a, b, 36a, b, 43 a, b and 44a produced the corresponding 8-endo- and 9-endo-trig products 13a, b, 14a, 19a, b and 33, 39a, b, 45a, b and 47a in moderate to good yields, in addition to the respective uncyclized debrominated alcohols. The X-ray crystal structure of the γ-lactones 22a and 42b, derived from the respective hydroxy esters 19a and 39b, have been determined. The ring size of the starting cycloalkanols affecting the propensity of the endo-cyclizations have been examined with the allyl- and butenyl cyclopentanols 23, 49 and the cycloheptanols 26, 52 leading to corresponding eight- and nine-membered ring products 24, 50 and 27, 53. The vinylcyclopentanol 8 produced exclusively the 6-exo-trig products 9, which on oxidative dehydration led to the hydrocarbon 10.

Keywords: Seven-, eight-, nine-membered rings, tributyltin hydride, tertiary alcohol, carbon–carbon bond formation.

1. Introduction
Organotin-mediated intramolecular free-radical cyclization reactions have gained dramatic prominence in the synthesis of carbo- and heterocyclic ring structures.1–6 The mild reaction conditions with these reagents and normally high levels of their chemo-, regio-, and often, stereo-control coupled with functional group tolerance allow radical reactions to serve as a powerful method for carbon–carbon bond formations. While ring closures in alkyl radicals operate readily via 5-exo and 6-exo pathways resulting in the corresponding ring structures, 7-exo cyclization7–14 is less facile. The presence of substituents and other structural features such as ring strain and the reactivities of the radicals may allow the alternative endo trajectories to operate.3–5,15 In contrast to the alkyl radical reactions in organic synthesis, only limited information was available on the rates and regiochemistry of aryl radical ring closure in tri-n-butyltin hydride (Bu₃SnH)-mediated reactions.16–20 Their synthetic applications have also been sparse in comparison to alkyl radical reactions.4, 21 The relatively small steric demand of an aryl radical coupled with its enhanced reactivity in comparison to that of an alkyl radical may render this to enter into intramolecular cyclizations through relatively uncommon endo-ring closures leading to six, seven and medium-sized rings.22

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As a prelude to our systematic study, we demonstrated in 1991 an exclusive regio- and stereoselective 6-endo-aryl radical cyclization in some 2-(2-bromobenzyl)methylene cyclohexanes A to the respective trans-octahydroanthracenes B, through preferred radical attack at the least substituted exocyclic methylene carbon centre (eqn 1). In the following year the implementation of a regioselective 7-endo-trig-aryl radical cyclization of 2-(2-bromoaryl ethyl)-1-methylene cyclohexanes C to the corresponding trans and cis-octahydro-IH-dibenzo[a,d]cycloheptenes D with Bu₃SnH in good yields (eqn 2) was recorded. Although organotin hydride-mediated ring closures have been reported to a limited extent to construct seven-membered hetero-ring structures, a hetero atom replacing a methylene group in the newly formed ring, the examples of carbocyclics formations by carbon-centered radicals are only few. The readiness of the 7-endo-cyclization of C to D suggested that the kinetic preference of an aryl radical attack at the least substituted terminal methylene centre in an easily accessible cycloalkanol, such as E, with varying lengths of the unsaturated and the 2-bromoarylalkyl chains, could lead to the respective seven-, eight- or higher-member benzo-fused ring structures F (eqn 3). Parts of our studies which shed light on the feasibility of such an approach in the synthesis of 6-7-6, 6-8-6 and 6-9-6 benzannulated alcohols through Bu₃SnH-induced highly regioselective 7-endo-, 8-endo- and 9-endo-trig aryl radical cyclizations were reported in mid-90s in several preliminary reports. We present in this paper the detailed results of our study revealing that such a strategy may be employed quite efficiently for a generalized convergent synthesis of benzannulated medium-
sized ring-fused structures\textsuperscript{22} which still remain a challenging problem.\textsuperscript{22,30–34,36} While there are a few reports on the formation of eight-membered ring,\textsuperscript{22,27,35,36} virtually no recorded example of the construction of nine-membered benzo-fused carbocyclic ring structures by a similar carbon-centered aryl radical process exists.\textsuperscript{37}

2. Results and discussion

In order to validate the feasibility of our conceived strategy (eqn 3) and gain understanding of the regiochemistry of an aryl radical cyclization, we first examined the behaviour of the vinyl-cyclohexanols 3\textsubscript{a,b} and 4\textsubscript{a,b} (Scheme 1).

![Scheme 1](image)

Reagents: i) CH\textsubscript{2}=CHMgBr, THF and ii) n-Bu\textsubscript{3}SnH, AIBN, C\textsubscript{6}H\textsubscript{6}.

Scheme 1.

The cyclohexanols 3\textsubscript{a,b} and 4\textsubscript{a,b} were obtained as a single epimer in each case, in excellent yields, by condensation with the easily accessible\textsuperscript{24} cyclohexanones 1\textsubscript{a,b} and 2\textsubscript{a,b} with vinylmagnesium bromide in THF. The stereostructures assigned are based upon analogy.\textsuperscript{38} The radical cyclization of the vinylcyclohexanols 3\textsubscript{a,b} in refluxing benzene with Bu\textsubscript{3}SnH and a catalytic amount of azoisobutyronitrile (AIBN) afforded the alcohols 5\textsubscript{a,b} in 68–70\% yields, as the only isolable pure compounds. The radical cyclizations of unsubstituted cyclohexanols 4\textsubscript{a,b} under the same condition gave the respective cyclized alcohols 6\textsubscript{a,b}, in good yields. The assigned structure for each of the products resulting from 7-endotrig cyclization was based upon spectroscopic data and elemental analyses.

In sharp contrast to the vinylcyclohexanols, radical cyclization of the vinylcyclopentanol 8, prepared by condensation of the cyclopentanone 7\textsuperscript{24} with vinylmagnesium bromide, gave an inseparable mixture (ca 2:1) of the epimeric alcohols 9, the 6-exo-trig products, as the only isolable material in 83\% yield. The alcohols (9) underwent facile dehydration with concomitant oxidative dehydrogenation by treatment with FeCl\textsubscript{3}-silica gel\textsuperscript{39} giving the benz[f]indene derivative 10 in 72\% yield (Scheme 2).

The outcome of the radical cyclization of the vinylcyclohexanol 4\textsubscript{a} and the vinylcyclopentanol 8 leading to the respective 7-endot- and 6-exo products 6\textsubscript{a} and 9, respectively, in good yields is

![Scheme 2](image)

Reagents: i) CH\textsubscript{2}=CHMgBr, THF; ii) n-Bu\textsubscript{3}SnH, AIBN, C\textsubscript{6}H\textsubscript{6} and iii) FeCl\textsubscript{3}/silica gel.

Scheme 2.
noteworthy in several aspects. Although there is a marked proclivity for 6-exo-mode of ring closure in comparison to that of the 7-endo mode for 6-heptenyl radicals, the present results of dramatic difference on the nature of aryl radical cyclization products from 4a and 9 clearly indicate that such inclination is delicately balanced and may be attributed to the variations in the steric and/or tortional strains engendered in accompanying the mandatory dispositions of the radical and the double-bond-reacting centres in the carbon–carbon bond formation process1,3 in the six- and five-membered ring systems.

The relatively efficient production of benzannulated cycloheptene ring system such as 5a,b and 6a,b via 7-endo-trig cyclization by preferred aryl radical attack at the respective terminal vinyl carbon centre led us to extend parallel investigations on similar modes for an ambitious eight-membered ring annulation. The detailed study was first undertaken28 on the radical cyclization of the allylalcohols 11a,b and 12a (Scheme 3).

Barbier reaction40 of 1a,b with allylbromide in THF proceeded smoothly to give the corresponding alcohols 11a,b in 77–80% yield 92–93% (GLC) purity. Column chromatography of the crude products on silica gel gave each of the alcohols 11a and 11b in 96–98% epimeric purity. The assigned stereochemistry of the major epimers is based upon analogy.38, 41 The radical cyclization of ca 96:4 epimeric mixture of 11a gave a mixture of the tricyclic alcohol 13a and the debrominated olefin 15a in a ratio of ca 70:30. Chromatographic separation of the mixture on basic alumina gave the pure cyclized alcohol 13a (62%). Under identical conditions, radical cyclization of 11b (97% epimeric purity) gave a mixture of 8-endo-cyclized alcohol 13b and the debrominated product 15b (ca 64:36). The pure alcohol 13b was separated by chromatography. Similarly, the radical cyclization of the allyl alcohol 12a (ca 95% purity), prepared through Barbier reaction of the ketone 2a, gave ca 3:1 mixture of the corresponding cyclized and uncyclized products 14a and 16a. The pure eight-membered alcohol 14a was obtained in 67% yield. The assigned structure for each of the products resulting from the regioselective 8-endo-trig aryl radical cyclization is based on spectroscopic data and elemental analysis.

With the successful development of a stereoselective synthetic route to linear decahydrodibenz[a, d]cyclooctanols 13a,b and 14a, attention was next turned towards extension of this new methodology to more complex substrates such as the hydroxy ester 18a,b (Scheme 4). Barbier reaction of the keto-esters24 17a,b with allyl bromide and magnesium in THF and rapid filtration through a short wide column of basic alumina gave a mixture of the respective diastereoisomeric hydroxy-esters 18a,b in 73–75% yields. The GLC analyses of these mixtures revealed the presence of ca 72–75% of a major epimer, initially assigned as 18a,b from the analogy.41
Attempted purifications of each of these mixtures through alumina or silica gel columns slowly transformed these to the respective γ-lactones, as evident from the appearance of a strong C=O bands at 1780–1782 cm\(^{-1}\) at the expense of the ester band at 1730 cm\(^{-1}\). Without further purification and characterization, the mixture of \(18a\) and its epimers were subjected to cyclization with \(\text{Bu}_3\text{SnH}\) and a catalytic amount of AIBN in refluxing benzene. Chromatographic separation of the tin compounds from the reaction product gave a mixture of the tricyclic-hydroxy ester \(19a\), the uncyclized debrominated olefins \(20a\) (1H NMR) and other uncharacterized products. The careful rechromatography of this mixture on basic alumina gave the pure 8-endo-product \(19a\), m.p. 143°C in 42% overall yield from the keto-ester \(17a\). Under identical conditions, the hydroxy-ester \(18b\) and its epimers mixture on radical cyclization and purification gave the desired cyclized hydroxy-ester \(19b\), m. p. 116°C. The assigned structures of \(19a\) and \(19b\) resulting from the 8-endo-trig cyclization at \(18a\) and \(18b\) were based upon spectroscopic data. For further characterization, the hydroxy ester \(19a\) was subjected to DMSO-\(\text{BuOK}\)-mediated\(^{43}\) ester cleavage (Scheme 5) to afford the corresponding acid \(21a\) as a gummy solid. A part of this on esterification with diazomethane in ether gave back unchanged \(19a\), thereby establishing that no configurational change had taken place during the ester cleavage. The hydroxy acid \(21a\) was recovered unchanged on treatment with ice-cold 6N-hydrochloric acid, revealing the trans-orientations of the respective hydroxy and carboxyl groups.\(^{42}\) Finally, the treatment of \(21a\) with \(p\)-TsOH in boiling benzene gave the crystalline cis-γ-lactone, in 67% yield. The complete structure and stereochemistry of the γ-lactone \(22a\) has been established\(^{44}\) by an X-ray crystal structure analysis (Fig. I).

With the successful stereoselective generation of linear eight-membered ring from allylcyclohexanols, attention was turned to the aryl radical cyclization of the allylcyclopentanol \(23\) (Scheme 6) [and allylcycloheptanol \(25\) (Scheme 7)]. The allyl cyclopentanol \(23\) of \(ca\) 95% purity was obtained in very good yield through Barbier reaction of the corresponding ketone \(7\). The radical cyclization of allylcyclopentanol gave mixture of the corresponding cyclized products \(24\)
along with the respective debrominated uncyclized alcohol (ca 1:1). After usual work-up and chromatographic purification, 24 was obtained in 40% yield.

Reagents: i) CH$_2$=CHCH$_2$Br, Mg, THF and ii) n-Bu$_3$SnH, AIBN, C$_6$H$_6$.

Scheme 6.

The Barbier reaction of the cycloheptanone 25 gave the alcohol 26 in 80% yield (98% GLC purity). The trans-stereochemistry has been assigned to 26 by analogy. The radical cyclization of the allylcycloheptanol (26) gave the 8-endo product 27 in 82% yield on chromatographic purification. The unusually efficient radical cyclization of 26 to the respective 8-endo-trig product, unlike that of the related allylcyclohexanol 12a and allylcyclopentanol 23 leading to the corresponding eight-membered annulated compounds 14a and 24 in 67% and 40% yields, respectively, is noteworthy. This is possibly due to the flexibility of seven-membered ring in placing the aryl radical to terminal carbon centre of the allyl group in the bond-forming stage with respect to that of the corresponding six- and five-membered analogous 12a and 23. With the success of the eight-membered ring annulation by aryl radical reactions of the aforementioned 1-allyl-2-(2-bromobenzyl)cycloalkanols, we next investigated the effect of increasing the chain
lengths of the aryl group with shortening of the double bond on the cyclization modes of the vinlylcyclohexanols 29a-c (Scheme 8). The cyclohexanols 29a-c were obtained as single diastereoisomers, in each case, in excellent yields by condensation of the cyclohexanones26 28a-c with vinylmagnesium bromide in THF followed by purification by chromatography on silica gel. The stereochemical homogeneity of each of the alcohols followed from 1H NMR spectroscopy and the assigned stereostructure is based upon analogy. Radical cyclization of each of the vinylcyclohexanols 29a-c in refluxing benzene, with Bu₃SnH and a catalytic amount of AIBN furnished a ca 1:1 mixture of the tricyclic alcohols 30a-c and the respective reduced products 31a-c, after separation of the tin compounds by silica gel chromatography. Each of these mixtures was cleanly separated by chromatography on basic alumina affording the pure cyclized products 30a-c in 40–45% yields. The assigned structures of the products resulting from 8-endo-trig cyclization were based upon spectroscopic data.

The relatively favourable disposition of the bond-forming carbon atoms in intermediate oct-7-enyl aryl radicals, which are held in the rigid benzyl side chain as generated from the allylcyclohexanols 11a,b (cf. Scheme 3) compared to that in the flexible 2-phenylethyl side chain from the vinylcyclohexanols 29a-c, are clearly reflected in the substantially higher yields of cyclization products in the former substrates.

The intrinsic preference of an endo-trig aryl radical ring closure at the least substituted olefinic carbon centre45 suggested that the radical site in the aromatic moiety needs only be located close to the terminal double bond for a successful endo cyclization, even in the formation of unfavourable medium ring sizes.30–34 Although no definitive report existed22 for the formation of the nine-membered carbocyclics involving radical cyclization, we first implemented29 such a strategy in several diversified substrates (Scheme 9).

Reagents: i) CH₂=CHMgBr, THF and ii) n-Bu₃SnH, AIBN, C₆H₆.

Scheme 8.

Reagents: i) CH₂=CHCH₂Br, Mg, THF and ii) n-Bu₃SnH, AIBN, C₆H₆.

Scheme 9.
The Barbier reaction of the cyclohexanone 28a gave a mixture of the alcohol 32 and its epimer in ca 93:7 (Scheme 9). Careful silica gel chromatography gave the major epimer assigned as 32 (98% pure) which on radical cyclization furnished a difficultly separable (ca 3:1) mixture of the tricyclic alcohol 33 and the respective debrominated olefinic alcohol 34 in excellent yield, after removal of the tin compounds. Repeated chromatographic purification of the mixture gave the pure nine-membered annulated alcohol 33.

With the successful 9-endo-trig aryl radical cyclization our attention was next focused upon the more complex hydroxy-ester substrates 36a and 36b (Scheme 10). The enolizable keto-ester 35a on Barbier reaction with allyl bromide and magnesium in THF gave a complex mixture comprising at least of three components, the epimeric hydroxy-esters (36a and 37a), and the γ-lactones (38a) in excellent yield. The epimeric mixtures of the hydroxy-esters (36a and 37a) (ca 70:30) separated from the lactones by chromatography on basic alumina, on radical cyclization gave a mixture of the tricyclic alcohol 39a and the debrominated product (40a). Usual work-up and chromatographic separation afforded the cyclized alcohol (39a), m.p. 94ºC in 55% yield as the one isolable product. Similarly, the Barbier reaction of 35b on Barbier reaction with allyl bromide and magnesium in THF gave a complex mixture comprising at least of three components, the epimeric hydroxy-esters (36b and 37b) in a ratio of ca 60:40 in 70% yield, after elimination of the γ-lactones (38b) from the crude reaction products by chromatography. Radical cyclization of the mixture afforded the pure tricyclic hydroxy-ester (39b), as a low-melting solid. The assigned structures of the products resulting from 9-endo-trig cyclization were based upon spectroscopic data. For further characterization, each of the cyclized hydroxy esters (39a,b), was subjected to ester cleavage and lactonization (Scheme 11). The resulting acids (41a,b) on lactonization with p-TsOH in boiling benzene gave respective crystalline γ-lactones (42a,b). An X-ray crystallographic determination established the stereostructure of 42b (Fig. 2) and thereby its congeners.

Scheme 10.

Reagents: i) CH₂=CHCH₂Br, Mg, THF and ii) n-Bu₃SnH, AIBN, C₆H₆.

Scheme 11.

Reagents: i) BuOK, DMSO; ii) CH₃N₂, Et₂O and iii) p-TsOH, C₆H₆.

Scheme 11.
The 9-endo-trig aryl radical cyclization was also successfully extended to the butenyl cyclohexanols (43a,b and 44), with the terminal olefinic moiety placed in a relatively flexible chain (Scheme 12). The cyclohexanols (43a, 43b and 44) were obtained in very good yields, in each case with high stereoselectivity, by condensation of the cyclohexanones (1a,b and 2a), with butenylmagnesium bromide in the presence of CeCl₃ in THF followed by silica gel chromatography. The assigned stereostructures are based upon analogy. Unlike the allylcyclohexanols (32 and 36a,b), the attempted radical cyclizations of the butenylcyclohexanols (43a,b and 44a), under the aforementioned conditions, gave predominantly the uncyclized debrominated compounds (46a,b and 48a) along with only minor amounts of the corresponding cyclized products 45a,b and 47a. We were pleased to find that 9-endo cyclization of these cyclohexanols (43a,b and 44a) could be effected under relatively dilute conditions by very slow addition of a dilute solution of Bu₃SnH in benzene containing catalytic amounts of AIBN, to a gently refluxing solution of each of the substrates. On usual work-up and purifications, the reaction gave the respective tricyclic alcohols (45a,b and 47a), and the uncyclized reduced products (46a,b and 49a) in a ratio of ca 1:1, in each case in 90–95% yields. Separation of each of these mixtures gave the corresponding 9-endo-trig products 45a,b and 47a in 40–50% yields (Fig. 2).

The relatively favourable disposition of the bond-forming carbon atoms in the non-8-enyl aryl radicals generated from the allylcyclohexanols 32a and 36a,b compared to that in the flexible butenyl side chain in the cyclohexanols 43a,b and 44a is reflected in the higher yields of the 9-endo products in the former substrates.

The 9-endo cyclization was further extended to the butenylcyclopentanol (49) (Scheme 13) and the butenylcycloheptanol 52 (Scheme 14). The cyclopentanol (49), prepared in 75% yield by condensation of the cyclopentanone (7) with butenylmagnesium bromide in the presence of CeCl₃ in THF, on radical cyclization with Bu₃SnH under the aforementioned high dilution conditions, gave a mixture which on careful purification furnished 9-endo product (50) and the debrominated alcohol (51), from which 50 was isolated in 36% yield (Scheme 13). The butenylcycloheptanol 52, prepared by stereoselective condensation of the cycloheptanone (25) with butenylmagnesium bromide, on radical cyclization under high dilution furnished a mixture of the tricyclic alcohol (53) and the reduced olefin (54) in a ratio of ca 6:4. The pure cyclized product (53) was obtained

FIG. 2. Perspective view of 42b showing the crystallographic number.44
in 54% yield. In parallel to the similar 8-endo-cyclizations (loc. cit) the favourable disposition of the bond-forming terminal carbon atom of the butenyl moiety in 52, having a relatively flexible seven-membered ring, is clearly reflected in a higher yield of 9-endo product (53) to that observed in the 6-9-6 and 5-9-6 benzannulation reactions on 44a and 49, respectively.

Scheme 12.

Reagents: i) CH$_2$=CHCH$_2$CH$_2$MgBr, CeCl$_3$, THF and ii) n-Bu$_3$SnH, AIBN, C$_6$H$_6$.

3. Conclusion

A conceptually new general and convergent synthetic route to functionalized linear benzannulated cyclohepten-, cycloocten- and cyclononene has been developed using a highly regioselective radical cyclization. The versatility of the endo-trig aryl radical ring closures has been demonstrated in two different types of substrates leading to the stereocontrolled synthesis of partially reduced dibenzo[a,d]- and -[a,e]-cyclooctanols. The generality of the latter route, developed in the eight- and nine-membered ring annulations on a cyclopentane or a cycloheptane ring in the present work, has a broad scope. The reasonably clean stereochemical course in the transformations of suitably substituted cycloalkanones to the respective vinyl-, allyl- or butenyl-cycloalkanols and their radical mediated-cyclizations has a potential as an important synthetic method for condensed polycyclic systems incorporating an eight- or a nine-membered ring which is difficult to
access. While we have extended similar reaction to generate angularly methylated condensed seven- and eight-membered ring-annulated cycloalkenone, a remarkably simple entry to chiral condensed medium ring cyclic ethers has been established through application of regioselective aryl radical cyclization methodology. Investigations are currently in progress to exploit the regio- and stereoselective heteroaryl radical cyclization in the construction of newer condensed systems incorporating six- to nine-membered rings.

4. Experimental

4.1. General methods

IR spectra (neat) were recorded on a Perkin–Elmer model PE 298 spectrometer. 1H NMR spectra were determined at 60, 100, 200 and 400 MHz, 13C NMR spectra were recorded at 100 and 50 MHz. Mass spectra were obtained by El at 70 eV. Analytical GLC was performed on a Shimadzu GC 90 model. Petroleum ether refers to b.p. 60–80°C. Elemental analyses were performed by S. K. Sarkar of IACS.

4.2. (1S*,2S*)-2-(2-Bromobenzyl)-3,3-dimethyl-1-vinylcyclohexanol (3a)

To an ice-cold stirred solution of vinylmagnesium bromide in THF (25 ml) [prepared from Mg (360 mg, 15 mg atom)] was added dropwise a solution of 1a (860 mg, 2.9 mmol) in dry THF (5 ml). The stirring was continued for 1 h at room temperature and refluxed for 4 h. It was quenched with ice-cold aqueous NH4Cl (10 ml) and extracted with Et2O. The organic layer was washed with saturated brine, then dried (Na2SO4) and evaporated in vacuo. The residue was purified by basic alumina column chromatography (Et2O–petroleum ether 1:9) to afford pure vinyl alcohol 3a (730 mg, 78%) as a colourless oil; νmax 3450, 1640 cm–1; δH (200 MHz, CDCl3), 0.82 (3H, s, Me), 1.19 (3H, s, Me), 1.27–1.70 (6H, m), 1.79–1.82 (2H, m), 2.94 (2H, t, J=7 Hz, ArCH2), 4.78 (1H, dd, J=10 and 1 Hz, CH=C H2), 5.19 (1H, dd, J=16 and 1 Hz, CH=C H2), 5.58–5.70 (1H, dd, C H=CH2), 6.99–7.08 (1H, m, ArH), 7.2–7.32 (2H, m, ArH), 7.50 (1H, d, J=8 Hz, ArH). Anal. Calc. for C17H23BrO: C, 63.15; H, 7.17. Found: C, 62.87; H, 7.10.

4.3. (1S*,2R*)-2-(5-Methoxy-2-bromobenzyl)-3,3-dimethyl-1-vinylcyclohexanol (3b)

The ketone 1b (1.30 g, 4 mmol) was converted in the same way as described for 1a to the vinylcyclohexanol 3b (1.12 g, 79%) as a colourless oil after basic alumina column chromatography using Et2O–petroleum ether (1:9). νmax 3420, 1635 cm–1; δH (200 MHz, CDCl3); δ0.88 (3H, s, Me), 1.20 (3H, s, Me), 1.2–1.82 (8H, m), 2.80 (2H, brd, J=7 Hz, ArCH2), 3.78 (3H, s, ArOMe), 4.70 (1H, dd, J=11 and 2 Hz, CH=CH2), 5.05 (1H, dd, J=16 and 2 Hz, CH=CH2), 5.38–5.80 (1H, dd, CH=CH2), 6.68 (1H, dd, J=8 and 2 Hz, ArH), 7.71 (1H, d, J=2 Hz, ArH), 7.24 (1H, d, J=9 Hz, ArH). Anal. Calc. for C18H25BrO2: C, 61.19; H, 7.13. Found: C, 60.84; H, 6.89.

4.4. (1S*,2R*)-2-(2-Bromobenzyl)-1-vinylcyclopentanol (8)

The ketone 7 (880 mg, 3.5 mmol) was converted in the same way as described above for 1a to the vinyl alcohol 8 (660 mg, 68%) as a colourless liquid after basic alumina column chromatography (Et2O–petroleum ether 1:19). vmax 3450, 1640 cm–1; δH (200 MHz, CDCl3), 1.25–2.20 (8H, m), 2.55 (1H, dd, J=14 and 10 Hz, ArCH2), 2.95 (1H, dd, J=14 and 4 Hz, ArCH2), 5.14 (1H, dd, J=10 and 1 Hz, CH=CH2), 5.87–6.04 (1H, dd, CH=CH2), 6.85 (1H, m, ArH), 7.42 (1H, d, J=2 Hz, ArH), 7.24 (1H, d, J=2 Hz, ArH). Anal. Calc. for C14H17BrO: C, 59.79; H, 6.09. Found: C, 59.49; H, 6.01.
4.5. (5aS*,9aS*)-6,6-Dimethyl-5a,6,7,8,9,9a,10,11a-octahydro-5H-dibenzo[a,d]cyclohepten-9a-ol (5a)

Bu₃SnH (1.09 g, 3.49 mmol) was added dropwise over 10 min to a stirred solution of the vinylcyclohexanol 3a (800 mg, 2.87 mmol) and AIBN (20 mg) in refluxing benzene (300 ml) under nitrogen atmosphere and the reaction continued for 7 h. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel using petroleum ether followed by benzene–petroleum ether (1:4) to eliminate most of the tin compounds. Further elution with Et₂O–petroleum ether (1:9) afforded colourless oil consisting of the cyclized alcohol 5a along with a trace of reduced uncyclized product (¹H NMR spectrum). This on chromatography over basic alumina using Et₂O–petroleum ether (1:9) afforded pure 5a (420 mg, 69%); ν max 3425, 1605 cm⁻¹; δH (200 MHz, CDCl₃), 1.04 (s, 3H, CMe), 1.08 (s, 3H, CMe), 1.0–1.9 (m, 9H), 2.35–2.48 (2H, m), 2.68–2.9 (1H, m), 3.08 (1H, dd, J=12 and 8 Hz), 3.30 (1H, dt, J=12 and 2 Hz), 7.04–7.13 (4H, m, ArH). MS (m/z) (relative intensity) 244 (M⁺, 30), 226 (100), 156 (47), 118 (83), 91 (43). Anal. Calc. for C₁₇H₂₄O: C, 83.35; H, 9.89. Found: C, 83.20; H, 9.87.

4.6. (5aS*,9aS*)-3-Methoxy-6,6-dimethyl-5aH,6,7,8,9,9a,10,11-octahydro-5H-dibenzo-[a,d]cyclohepten-9a-ol (5b)

Treatment of a solution of 3b (700 mg, 1.98 mmol) in benzene (220 ml) with Bu₃SnH (750 mg, 2.58 mmol) and AIBN (15 mg), using procedure identical with that described for 5a, gave the pure tricyclic alcohol 5b (370 mg, 68%) m.p. 87°C (MeOH); ν max 3440, 1605 cm⁻¹; δH (200 MHz, CDCl₃), 1.03 (3H, s, CMe), 1.06 (3H, s, CMe), 1.06 (3H, s, CMe), 1.0–1.85 (9H, m), 2.30–2.45 (2H, m), 2.65–2.90 (1H, m), 3.08 (1H, dd, J=11 and 8 Hz), 3.24 (1H, dt, J=11 and 2 Hz), 3.78 (3H, s, ArOMe), 6.55–6.75 (2H, m, ArH), 7.0 (1H, d, J=8 Hz, ArH). Anal. Calc. for C₁₈H₂₆O₂: C, 78.78; H, 9.55. Found: C, 78.64; H, 9.48.

4.7. (5aS*,9aR*)-5a,6,7,8,9,9a,10,11-Octahydro-5H-dibenzo[a,d]cyclohepten-9a-ol (6a)

Bu₃SnH (900 mg, 3.09 mmol) was added to a stirred solution of the alcohol 4a (700 mg; 2.37 mmol) and AIBN (15 mg) in refluxing benzene (300 ml) and the reaction continued for 7 h. After work-up as described for 5a the residual light yellow oil was chromatographed on silica gel using petroleum ether followed by benzene–petroleum ether to eliminate most of the tin compounds. Further elution with Et₂O–petroleum ether (1:9) afforded a colourless liquid consisting of a mixture of the cyclized product 6a and the respective uncyclized debrominated alcohol (¹H NMR spectrum) which on chromatography on basic alumina using petroleum ether–Et₂O (19:1) gave the pure alcohol 6a (350 mg, 68%) as the sole isolable product; ν max 3500, 1600 cm⁻¹; δH (200 MHz, CDCl₃), 0.98–2.10 (11H, m, 5 × CH₂ and OH), 2.35–2.6 (3H, m, CH₃ and methine), 3.25–3.40 (2H, m, CH₂), 7.15–7.25 (4H, m, ArH). MS (m/z) (relative intensity) 216 (M⁺, 34), 198 (100), 129 (68), 117 (58), 91 (60). Anal. Calc. for C₁₅H₂₀O: C, 82.99; H, 9.20.

4.8. (5aS*,9aR*)-9-Methoxy-5a,6,7,8,9,9a,10,11-octahydro-5H-dibenzo[a,d]cyclohepten-9a-ol (6b)

Treatment of a solution of the vinylcyclohexanol (4b) (600 mg, 1.85 mmol) in benzene (250 ml) with Bu₃SnH (670 mg, 2.3 mmol) and AIBN (15 mg), using procedure identical with that described for 5a gave a mixture of the cyclized alcohol 6b and the respective debrominated product in a ratio of ca 3:1 (¹H NMR), which on further chromatography on basic alumina afforded pure
6b (310 mg, 61%); \( \nu_{\text{max}} \) 3425, 1595 cm\(^{-1}\); \( \delta_{\text{H}} \) (60 MHz, CCl\(_4\)), 0.8–2.2 (11H, m, 5 \times \text{CH}_2 \text{ and OH}), 2.3–2.6 (3H, m, \text{CH}_2 \text{ and methine}), 3.2–3.3 (2H, m, CH\(_2\)), 3.8 (3H, s, ArOMe), 6.6–6.8 (2H, m, ArH), 7.05 (1H, d, \( J=9 \) Hz, ArH). MS (\( m/z \)) (relative intensity) 246 (M\(^+\), 53), 228 (61), 213 (37), 159 (37), 148 (100). Anal. Calc. for C\(_{16}\)H\(_{22}\)O\(_2\): C, 78.0; H, 9.0. Found: C, 77.94; H, 8.81.

4.9. (3aR\(^*\),9aR\(^*\),4R\(^*\)) and (3aR\(^*\),9aR\(^*\),4S\(^*\))-2,3,3a,4,9,9a-Hexahydro-4-methyl-1H-benz[f]inden-3a-ol (9)

The vinylcyclopentanol 8 (1 g, 3.5 mmol) in benzene (400 ml) was refluxed with Bn\(_3\)SnH (1.3 g, 4.46 mmol) and AIBN (20 mg) for 7h. Removal of the solvent under vacuo gave yellow oil which on chromatography over silica gel using petroleum ether and benzene–petroleum ether (1:4) separated all the tin compounds. Further elution with Et\(_2\)O–petroleum ether (1:9) afforded a diastereoisomeric mixture of the cyclized alcohol 9 (600 mg, 83%) as a colourless oil; \( \nu_{\text{max}} \) 3445, 1590 cm\(^{-1}\); \( \delta_{\text{H}} \) (200 MHz, CDC\(_3\)), 1.23 and 1.42 (each d, \( J=7 \) Hz for CMe of the minor and major epimers) in a ratio of ca 1:2, 1.49–3.28 (11H, m), 7.08–7.42 (4H, m, ArH); MS (\( m/z \)) 182 (M\(^+\), 81), 167 (100), 152 (34). Anal. Calc. for C\(_{14}\)H\(_{18}\)O: C, 83.12; H, 8.96; Found: C, 82.98; H, 8.74.

4.10. 2,3-Dihydro-4-methyl-1H-benz[f]indene (10)

After vigorously shaking a mixture of silica gel (16 g, 60–120 mesh) and FeCl\(_3\), 6H\(_2\)O (1.6 g, 5.9 mmol) containing Et\(_2\)O (10 ml), the solvent was evaporated and heated at 70–80°C (0.1 mm Hg) for 2.5 h to afford a dry yellow powder. To this was added the alcohol 9 (300 mg, 1.5 mmol) in Et\(_2\)O (5 ml) with rapid stirring, the solvent was evaporated and kept under vacuo (0.1 mm Hg) for 20 min and the resulting mixture was thoroughly washed with Et\(_2\)O. After removal of Et\(_2\)O, the residue on filtration through a short wide silica gel column in petroleum ether gave the hydrocarbon 10 (190 mg, 70%) as a thick oil; \( \nu_{\text{max}} \) 1630, 1600 cm\(^{-1}\); \( \delta_{\text{H}} \) (200 MHz, CDCl\(_3\)), 2.99–3.10 (4H, m), 7.16–7.23 (1H, m, ArH), 7.38–7.46 (2H, m, ArH), 7.72–7.75 (1H, m, ArH), 7.77–7.97 (1H, m, ArH). MS (\( m/z \)) 182 (M\(^+\), 81), 167 (100), 152 (34). Anal. Calc. for C\(_{14}\)H\(_{16}\): C, 91.24; H, 8.75. Found: C, 91.16; H, 9.44.

4.11. (1S\(^*\),2S\(^*\))-1-Allyl-2-(2-bromobenzyl)-3,3-dimethylcyclohexanol (11a)

To a well-stirred suspension of activated Mg (220 mg, 9.16 mg atom) in dry THF (5 ml) under N\(_2\) atmosphere, 2 drops of allyl bromide were added initially. After the exothermic reaction sets on within 1–2 min, a solution of cyclohexanone (1a) (900 mg, 3 mmol) and allyl bromide (3 ml) in dry THF (10 ml) was added dropwise at 25°C over a period of \( ca 3 \) h at room temperature and then quenched at 0°C with cold aqueous NH\(_4\)Cl (15 ml) and extracted with Et\(_2\)O. The ether extract was washed with brine, dried (Na\(_2\)SO\(_4\)), evaporated and the residual oil was chromatographed on silica gel using Et\(_2\)O–petroleum ether (1:9) as eluant to afford a diastereoisomeric mixture of allylcyclohexanols (11a) (820 mg, 80%) as a colourless oil. GLC analysis showed two epimers in a ratio of \( ca 96:4 \) with \( R_t=6.83 \) and 6.15 min, respectively. \( \nu_{\text{max}} \) 3460, 1635 cm\(^{-1}\); \( \delta_{\text{H}} \) (400 MHz, CDCl\(_3\)), 0.94 (3H, s, Me), 1.10 (3H, s, Me), 1.14–2.20 (10H, m), 2.6–2.94 (1H, s, CH\(_2\)CH=CH\(_2\)), 4.84 (1H, dd, \( J=16 \) and 2 Hz, CH=CH\(_2\), major isomer), 5.02 (1H, dd, \( J=14 \) and 2 Hz, CH=CH\(_2\), major isomer), 5.04–5.2 (m, CH=CH\(_2\), minor isomer), 5.50–5.74 (m, CH=CH\(_2\), major isomer), 5.8–6.0 (m, CH=CH\(_2\), minor isomer), 6.94–7.28 (3H, m, ArH), 7.41 (1H, dd, \( J=8 \) and 2 Hz, ArH), \( \delta_{\text{C}} \) (100 MHz, CDCl\(_3\)), 17.8, 22.1, 30.9, 32.7, 35.0, 38.2, 42.2, 47.0, 52.9, 74.3, 119.0, 125.0, 126.9, 127.3, 129.9, 132.9, 133.6,
143.3. MS (m/z) 295 [(M+1), 51], 293 [(M-1), 51], 169 (75), 171 (75), 95 (61), 69 (100). Anal. Calc. for C_{18}H_{25}BrO: C, 64.09; H, 7.47. Found: C, 63.96; H, 7.48.

4.12. \((1S^*,2S^*)-1\text{-Allyl}-2-(5\text{-methoxy-2-bromobenzyl})-3,3\text{-dimethylcyclohexanol (11b)}\)

The ketone 1b (1.5 g, 4.6 mmol) was converted to a diastereoisomeric mixture of allyl-cyclohexanol (11b) (1.31 g, 77%) following the same procedure as described for 11a. GLC analyses showed a major epimer (97%), and a minor epimer (3%).

\(\nu_{\text{max}} 3500, 1630 \text{ cm}^{-1} ; \delta_{\text{H}} (400 \text{ MHz, CDCl}_3) 0.94 \text{ and } 1.09 \text{ (each s, two CMe for major isomer), } 0.95 \text{ and } 1.08 \text{ (each s, two Me for minor isomer), } 1.18-1.84 \text{ (}1\text{H, m), } 1.85 \text{ (1H, dd, } J=10 \text{ and } 4 \text{ Hz, dt, ArCH}_2), 2.14 \text{ (1H, dd, } J=10 \text{ and } 8 \text{ Hz, ArCH}_2), 2.68 \text{ (2H, dd, } J=16 \text{ and } 2 \text{ Hz, CH}_2\text{-CH=CH}_2), 3.78 \text{ (s, ArOMe, major isomer), } 3.79 \text{ (s, ArOMe, minor isomer), } 4.84 \text{ (dd, } J=16 \text{ and } 2 \text{ Hz, CH=CH}_2, \text{ major isomer), } 5.02 \text{ (dd, } J=14 \text{ and } 2 \text{ Hz, CH=CH}_2, \text{ major isomer), } 5.46-5.72 \text{ (m, CH=CH}_2, \text{ minor isomer), } 6.54-6.7 \text{ (1H, m, ArH), } 6.88 \text{ (1H, s, ArH), } 7.52 \text{ (1H, d, } J=8 \text{ Hz, ArH), } \delta_{\text{C}} (100 \text{ MHz, CDCl}_3) 18.8 (\text{C-6}), 22.0, 31.0, 32.6, 35.0, 38.1 (C-6), 42.1, 46.9, 53.1, 55.3, 74.2, 112.1, 115.6, 116.1, 119.6, 133.2, 133.6, 144.5, 158.8. MS (m/z) 368 [(M+1), 10], 366 [(M+-1), 10], 325 (100), 323 (100), 251 (31), 253 (31), 199 (67), 197 (67), 121 (57). Anal. Calc. for C_{19}H_{20}BrO: C, 62.12; H, 7.40. Found: C, 61.81; H, 7.34.

4.13. \((1S^*,2S^*)-1\text{-Allyl-2-(2-bromobenzyl)cyclohexanol (12a)}\)

The ketone 2a (900 mg, 3.37 mmol) was converted in the same way as described for 10a into a ca 95:5 diastereoisomeric mixture of 12a (820 mg, 79%).

\(\nu_{\text{max}} 3430, 1630 \text{ cm}^{-1} ; \delta_{\text{H}} (60 \text{ MHz, CCl}_4) 1.15-1.75 \text{ (10H, m), } 2.35-2.55 \text{ (2H, m), } 2.64 \text{ (1H, dd, } J=12 \text{ and } 2 \text{ Hz, CH}_2\text{-CH=CH}_2), 3.14 \text{ (1H, dd, } J=8 \text{ Hz, ArH), } 5.55-6.10 \text{ (1H, m, CH=CH}_2, \text{ minor isomer), } 6.84-7.30 \text{ (3H, m, ArH), } 7.50 \text{ (1H, dd, } J=8 \text{ and } 2 \text{ Hz, ArH). Anal. Calc. for C}_{16}H_{21}BrO: C 62.14; H, 6.84. Found: C, 61.83; H, 6.81.

4.14. \((5aS^*,9aS^*)-6,6\text{-Dimethyl-5,5a,6,7,8,9,9a,10,11,12-decahydrodibenzo[a,d]cycloocten-9a-ol (13a)}\)

Cyclization of ca 96:4 diastereoisomeric allyl cyclohexanols 11a (800 mg, 2.37 mmol) in benzene (400 ml) with Bu\textsubscript{3}SnH (1.0 g, 3.4 mmol) and AIBN (20 mg) after work-up and silica gel chromatography as described for 3a gave a mixture of 13a and the uncyclized reduced product 15a in over 90% yield. Separation of the mixture on chromatography over basic alumina using Et\textsubscript{2}O–petroleum ether (1:9) afforded 13a (380 mg, 62%) as a colourless oil; \(\nu_{\text{max}} 3460 \text{ cm}^{-1}; \delta_{\text{H}} (200 \text{ MHz, CDCl}_3) 0.80-0.95 \text{ (1H, m), } 1.04 \text{ (3H, s, CMe), } 1.15 \text{ (3H, s, CMe), } 1.15-2.15 \text{ (11H, m), } 2.55-2.70 \text{ (2H, m), } 2.92 \text{ (1H, dd, } J=11 \text{ and } 13 \text{ Hz), } 3.08 \text{ (1H, dt, } J=8 \text{ and } 13 \text{ Hz), } 7.0-7.25 \text{ (4H, m, ArH). } \delta_{\text{C}} (50 \text{ MHz, CDCl}_3) 18.8 (\text{C-3}), 21.0 (\beta\text{-methyl), } 26.9, 29.7, 31.8, 33.1, 35.3, 38.9, 42.2, 45.2, 59.8, 74.7, 126.3, 126.4, 128.8, 129.1, 140.0, 143.8. Anal. Calc. for C_{18}H_{26}O: C, 83.66; H, 10.14. Found: C, 83.39; H, 10.0.

4.15. \((5aS^*,9aS^*)-3\text{-Methoxy-6,6-dimethyl-5,5a,6,7,8,9,9a,10,11,12-decahydrodibenzo[a,d]cycloocten-9a-ol (13b)}\)

Cyclization of the ca 97:3 diastereoisomeric mixture of allyl cyclohexanols 11b (600 mg, 1.63 mmol) in benzene (400 ml) with Bu\textsubscript{3}SnH (1.0 g, 3.4 mmol) and AIBN (20 mg) as described for 11a on chromatography over silica gel gave a mixture of the tricyclic alcohol 13b and the reduced product 15b. This on rechromatography over basic alumina using Et\textsubscript{3}O–petroleum ether (1:9) afforded 13b (290 mg, 62%) as a colourless oil; \(\nu_{\text{max}} 3500, 1595 \text{ cm}^{-1}; \delta_{\text{H}} (200 \text{ MHz, CDCl}_3)\)
0.70–0.98 (1H, m), 1.03 (3H, s, CMe), 1.14 (3H, s, CMe), 1.15–2.10 (11H, m), 2.45–2.65 (2H, m), 2.85 (1H, dd, J=15 and 11 Hz), 2.94 (1H, dt, J=7 and 14 Hz), 3.78 (3H, s, ArOMe), 6.67 (1H, dd, J=8 and 2 Hz, ArH), 6.73 (1H, d, J=2 Hz, ArH), 6.98 (1H, d, J=8 Hz, ArH). δ C (50 MHz, CDCl₃), 18.3 (C-3), 21.9 (β-methyl), 27.0, 29.9, 30.9, 33.1 (α-methyl), 35.3, 39.0, 42.2, 45.2, 55.4, 59.7, 74.6, 111.2, 115.0, 129.6, 132.3, 145.1 and 158.3. MS (m/z) 288 (M⁺, 98), 270 (100), 255 (80), 242 (97), 227 (50), 199 (75), 173 (97), 121 (95). Anal. Calc. for C₁₉H₂₁O₂: C, 79.12; H, 9.78. Found: C, 79.04, H, 9.61.

4.16. (5aS*,9aR*)-5,5a,6,7,8,9,9a,10,11,12-Decahydrodibenzo[a,d]cycloocten-9a-ol (14a)

Cyclization of 12a (500 mg, 1.6 mmol) in benzene (250 ml) with Bu₃SnH (700 mg, 2.4 mmol) and AIBN (20 mg) under the same conditions as described for 11a afforded a mixture of the cyclized and the reduced product, 14a and 16a, in over 90% yield after silica gel chromatography. Separation of this mixture by basic alumina column chromatography using Et₂O–petroleum ether (1:9) afforded 14a (250 mg, 67%). ν max 3455, 1600 cm –1; δ H (100 MHz, CDCl₃), 0.85–1.00 (1H, m), 1.12–2.15 (12H, m), 2.55–2.72 (2H, m, ArCH₂), 3.0–3.30 (2H, m, ArCH₂), 7.15–7.35 (4H, m, ArH). Anal. Calc. for C₁₆H₂₂O: C, 83.42; H, 9.62. Found: C, 83.21; H, 9.16.

4.17. Methyl (4R*,4aS*,12aR*)-4-methyl-12a-hydroxy-1,2,3,4,4a,5,10,11,12,12a-decahydro-dibenzo[a,d]cyclooctene-4-carboxylate (19a)

To an ice-cold stirred suspension of activated Mg turnings (150 mg, 6.25 mg atom) in dry THF (5 ml), 2 drops of allyl bromide was added. After the exothermic reaction sets on within 1–2 min, a solution of the keto-esters 17a (900 mg, 2.65 mmol) and allyl bromide (2 ml) in THF (10 ml) was added at 0°C over a period of 15–20 min. The reaction mixture was stirred at ca 0–10°C for 2 h, decomposed with cold aqueous NH₄Cl and extracted with Et₂O. The extract was washed with brine, water, dried (Na₂SO₄) and evaporated to yield a thick oil. This was dissolved in petroleum ether and rapidly chromatographed on a short wide column of basic alumina and eluted with Et₂O–petroleum ether (1:9) to afford a mixture of the hydroxy ester 18a and other epimers (765 mg, 75%) as a colourless oil. The product showed the presence of two major compounds in ca 3:1 ratio (95% purity), presumably 18a and its C-4 epimer, along with three other minor components (GLC); ν max 3460, 1735, 1635 cm –1; δ H (200 MHz, CDCl₃), 1.45 (s, CMe), 1.45–2.7 (m, CH₂, CHOH), 3.39 (s, CO₂Me), 4.90–5.28 (m, CH=CH₂), 5.55–5.93 (m, CH=CH₂), 7.18–7.23 (m, ArH). Attempted purification of this mixture on alumina (basic or neutral) or silica gel chromatography gave γ-lactone and ester mixtures as revealed by C=O bands at 1780 and 1730 cm–1 in IR spectrum. This was directly subjected to radical cyclization reaction.

Treatment of the hydroxyester mixture (500 mg, 1.3 mol) in benzene (280 ml) with Bu₃SnH (600 mg, 2 mmol) and AIBN (15 mg) according to procedure described for 11a gave a mixture of 19a and the debrominated esters 20a (360 mg). This was chromatographed on basic alumina and eluted with Et₂O–petroleum ether (25:75) to give the cyclized product 19a as a thick gum (220 mg, 42% based on 17a), which solidified on standing, m.p. 140–142°C (Et₂O–petroleum ether). The analytical sample was obtained after filtration of the crude solid in Et₂O–petroleum ether (1:9) through basic alumina as rectangular prisms, m.p. 143°C; ν max 3570, 1730 cm –1; δ H (200 MHz, CDCl₃), δ 1.1–1.25 (1H, m), 1.43 (3H, s, CMe), 1.45–2.15 (11H, m), 2.55–2.70 (2H, m), 2.54–2.68 (1H, m), 3.03 (1H, dd, J=6 and 13 Hz), 3.09 (1H, dt, J=11 and 14 Hz), 3.82 (3H, s, CO₂Me), 6.89–7.12 (4H, m, ArH). MS (m/z) 302 (M⁺, 13), 284 (61), 256 (60), 243 (64), 224
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4.18. Methyl (4R*,4aS*,12aR*)-12a-hydroxy-7-methoxy-4-methyl-1,2,3,4,4a,5,6,7,12,12a decahydrodibenzo[a,d]cyclooctene-4-carboxylate (19b)

Barbier reaction of the keto-ester 17b (550 mg, 1.45 mmol) with Mg (100 mg, 4.16 mg atom) and allyl bromide (3 ml) in dry THF and purification of the resulting product according to procedure described for the preparation of 18a and epimeric mixture gave the hydroxyester 18b and its C−1 epimer in ca 78:22 ratio (95% purity) (450 mg, 73%); νmax 3530, 1725, 1635 cm−1; δH (100 MHz, CDCl3) 1.47 (s, CMe), 3.48 (s, CO2Me), 3.78 (s, ArOMe), 4.92–5.15 (m, CH=CH2), 5.60–5.89 (m, CH=CH2), 6.7 (dd, J=8 and 2 Hz, ArH), 7.05 (d, J=2 Hz, ArH), 7.38 (d, J=8 Hz, ArH).

The radical cyclization of the crude hydroxy-ester 18b (600 mg, 1.45 mmol) in benzene (400 ml) with Bu3SnH (900 mg, 3.09 mmol) and AIBN (20 mg) according to the procedure described for the preparation of 19a gave the crude product (430 mg) as a thick liquid. This was rechromatographed on basic alumina and eluted with Et2O–petroleum ether (3:7) to give 19b as a white solid (270 mg, 45% based on 17b) m.p. 116°C (Et2O–petroleum ether); νmax 3440, 1730 cm−1; δH (200 MHz, CDCl3) 1.40 (3H, s, CMe), 1.03–1.92 (11H, m), 2.01–2.12 (2H, m), 2.5–2.65 (1H, m), 2.88–3.18 (2H, m), 3.75 (3H, s, OMe), 3.85 (3H, s, CO2Me), 6.55–6.70 (2H, m, ArH), 6.92 (1H, d, J=9 Hz, ArH). MS (m/z) 332 (M+, 61), 314 (20), 300 (60), 286 (100), 257 (47), 283 (26), 185 (48). Anal. Calc. for C20H28O4: C, 72.25; H, 8.48. Found: C, 71.96; H, 8.44.

4.19. (4R*,4aS*,12aS*)-12a-Hydroxy-4-methyl-1,2,3,4,4a,5,10,11,12,12a-decahydrodibenzof[a,d]cycloocten-4,12a-carbolactone (22a)

The tricyclic hydroxyester 19a (100 mg, 0.33 mmol) was treated with KOBu’ (200 mg, 1.8 mmol) in dry DMSO (4 ml). The mixture was stirred at room temperature for 4 h. It was diluted with ice water, acidified with cold 6N HCl, extracted with Et2O, washed separately with aqueous NaHCO3 solution (5%) followed by brine and dried (Na2SO4). The alkaline washings were combined together, acidified with cold 6N HCl, extracted with Et2O, washed with brine, and dried (Na2SO4). Removal of the solvent afforded the acid 21a (80 mg) as a gummy solid, a small portion of which was esterified with diazomethane in Et2O to give the ester 19a, m.p. 143°C alone or on admixed with the starting ester. The crude acid (50 mg) was refluxed for 4 h with PTSA (10 mg) in benzene (20 ml). It was cooled, diluted with Et2O (20 ml), washed with cold NaOH solution (2%) and brine, dried (Na2SO4) and concentrated. The crude product was purified by chromatography over neutral alumina and eluted with Et2O–petroleum ether (1:4) to afford the γ-lactone (21a) (30 mg, 67%), m.p.138°C (Et2O–petroleum ether). νmax (KBr) 1780 cm−1; δH (200 MHz, CDCl3), 1.25 (3H, s, CMe), 1.4–2.1 (11H, m), 2.56 (1H, brd, J=14 Hz), 2.90 (1H, dd, J=14 and 11 Hz), 2.68–2.81 (2H, m), 7.04–7.28 (4H, m, ArH). MS (m/z) 270 (M+, 36), 260 (12), 242 (70), 227 (16), 201 (56), 155 (33), 129 (50), 115 (48), 105 (27), 91 (100). Anal. Calc. for C18H22O2: C, 79.96; H, 8.24. Found: C, 79.74; H, 8.04.

4.20. (1S*,2R*)-1-Allyl-2-(2-bromobenzyl)cyclopentanol (23)

Barbier reaction of cyclopentanone 7 (800 mg, 3.16 mol) with Mg (220 mg, 9.16 mg atom) and allyl bromide (3 ml) in THF (10 ml) according to the procedure described for 10a gave the cyclopentanol 23 (730 mg, 78%) as a colourless oil after chromatography over silica gel using Et2O–petroleum ether eluants. νmax 3425, 1635 cm−1; δH (60 MHz, CCl4) 1.1–2.9 (12H, m), 4.7–
5.10 (2H, m, CH=CH₂), 5.46–6.15 (1H, m, CH=CH₂), 6.71–7.10 (3H, m, ArH), 7.41 (1H, dd, J=8 and 2 Hz, ArH). Anal. Calc. for C₁₅H₂₂BrO: C, 60.61; H, 7.12. Found: C, 60.82; H, 6.41.

4.21. (3aR*,11aS*)-2,3,3a,4,9,10,11,11a-Octahydro-1H-benzo[a]cyclopenta[d]cycloocten-11a-ol (24)

The allylcyclopentanol 23 (600 mg, 2 mmol) on radical cyclization with Bu₃SnH (900 mg, 3 mmol) and AIBN (10 mg) in benzene following the procedure as described for 11a afforded the tricyclic alcohol 24 (190 mg, 44%) after chromatography on basic alumina using Et₂O–petroleum ether (1:9) as eluant. ν_max 3445, 1605 cm⁻¹; δ_H (100 MHz, CDCl₃) 0.9–1.09 (1H, m), 1.1–2.2 (10H, m), 2.5–3.45 (5H, m), 7.1–7.3 (4H, m, ArH). Anal. Calc. for C₁₅H₂₀O: C, 83.28; H, 9.31. Found: C, 82.91; H, 9.25.

4.22. (1S*,2R*)-1-Allyl-2-(2-bromobenzyl)cycloheptanol (26)

Barbier reaction of cycloheptanone 25 (1.2 g, 4.27 mmol) using Mg (320 mg, 13.3 g atom) and allyl bromide (4 ml) in THF (16 ml) as described for the preparation of 3a, followed by chromatography of the product on silica gel using Et₂O–petroleum ether (1:9) eluant gave 26 (1.1 g, 80%) as a colourless oil; (98% purity in GLC). ν_max 3560, 1635 cm⁻¹; δ_H (60 MHz, CCl₄) 1.08–3.22 (16 H, m), 4.82–5.24 (2H, m), 5.52–6.25 (1H, m), 6.84–7.2 (3H, m, ArH), 7.52 (1H, dd, J=8 and 2 Hz, ArH). Anal. Calc. for C₁₇H₂₃BrO: C, 63.15; H, 7.17. Found C, 62.94; H, 7.08.

4.23. (5aS*,10aR*)-5a,6,7,8,9,10,10a,11,12,13-Decahydro-5H-benzo[a]cyclohepta[d]cycloocten-10a-ol (27)

Cyclization of 26 (800 mg, 2.47 mmol) with Bu₃SnH (1.0 g, 3.4 mmol) and AIBN (15 mg) in benzene (400 ml) as described for 11a on chromatography over silica gel using petroleum ether–benzene as eluant followed by rechromatography on basic alumina with Et₂O–petroleum ether (1:9) gave the cyclized alcohol 27 (502 mg, 82%) as a colourless oil. ν_max 3460, 1600 cm⁻¹; δ_H (200 MHz, CDCl₃) 0.92–1.05 (4H, m), 1.15–2.0 (12H, m), 2.05–2.25 (2H, m), 2.88–3.0 (2H, m), 7.15 (4H, brs, ArH). MS (m/z) 244 (M⁺, 12), 201 (51), 187 (63), 153 (25), 121 (14), 109 (24), 91 (100). Anal. Calc. for C₁₇H₂₄O: C, 83.55; H, 9.89. Found: C, 88.28; H, 9.83.

4.24. (1S*,2S*)-1-Vinyl-2-[2-(2-bromophenyl)ethyl]-3,3-dimethylcyclohexanol (29a)

The ketone 28a (800 mg, 2.6 mmol) in THF was reacted with vinylmagnesium bromide prepared from Mg (200 mg, 8.3 mg atom) as described for 1a; chromatography of the crude condensation product on silica gel using Et₂O–petroleum ether (1:9) as eluant afforded the vinlylcylohexanol 29a (650 mg, 74%) as a colourless oil. ν_max 3445, 1630 cm⁻¹; δ_H (100 MHz, CDCl₃) 0.96 (3H, s, Me), 1.02 (3H, s, Me), 1.06–2.0 (10H, m), 2.72 (2H, dd, J=8 and 12 Hz, ArCH₂), 5.1 (1H, dd, J=18 and 2 Hz, CH=CH₂), 5.24 (1H, dd, J=18 and 2 Hz, CH=CH₂), 5.74–6.04 (1H, dd, CH=CH₂), 6.81–7.32 (3H, m, ArH), 7.52 (1H, d, J=8 Hz, ArH). MS (m/z) 318 and 316 [(M⁺+2) and (M⁺) 20], 171 (55), 169 (55), 136 (70), 83 (100). Anal. Calc. for C₁₈H₂₅BrO: C, 64.09; H, 7.47. Found: C, 63.76; H, 7.43%.

4.25. (1S*,2S*)-1-Vinyl-2-[2-(2-bromo-5-methoxyphenyl)ethyl]-3,3-dimethylcyclohexanol (29b)

The ketone 28b (695 mg, 2 mmol) was converted to the vinylic cyclohexanol 29b (580 mg, 77%) in the same way as described for the preparation of 3a, after silica gel column chromatography using Et₂O–petroleum ether (1:9) as eluant; ν_max 3425, 1635 cm⁻¹; δ_H (200 MHz, CDCl₃), δ 0.97
(3H, s, Me), 1.01 (3H, s, Me), 1.12–2.0 (10H, m), 2.66 (2H, brt, J=9 Hz, ArCH₂), 3.76 (3H, s, ArOMe), 5.14 (1H, dd, J=10 and 2 Hz, CH=CH₂), 5.26 (1H, dd, J=18 and 2 Hz, CH=CH₂), 5.82–5.88 (1H, dd, CH=CH₂), 6.62 (1H, dd, J=8 and 2 Hz, ArH), 6.72 (1H, d, J=2 Hz, ArH), 7.45 (1H, d, J=8 Hz, ArH). MS (m/z) 368 and 366 [(M+2) and (M+) 20], 350 (10) and 348 (10), 199 (53), 197, 121(100). Anal. Calc. for C₁₉H₂₇BrO₂: C, 62.12, H, 7.40. Found: C, 61.91; H, 7.31.

4.26. (1S*,2S*)-1-Vinyl-[2-(2-bromo-4-methoxyphenyl)ethyl]-3,3-dimethylcyclohexanol (29c)

The ketone 28c (800 mg, 2.3 mmol) was converted to the vinylcyclohexanol 29c (580 mg, 67%) as a colourless oil in the same way as described for 3a after silica gel chromatography using Et₂O–petroleum ether (15:85) as eluant. νmax 3440, 1635 cm⁻¹; δH (100 MHz, CDCl₃); δ 0.97 (3H, s, Me), 1.00 (3H, s, Me), 1.06–2.0 (10H, m), 2.59–2.79 (2H, m, ArCH₂), 3.76 (3H, s, ArOMe), 5.12 (1H, dd, J=10 and 2 Hz, CH=CH₂), 5.22 (1H, dd, J=18 and 2 Hz, CH=CH₂), 5.76–6.04 (1H, dd, J=18 and 10 Hz, C=CH₂), 6.78 (1H, dd, J=8 and 2 Hz, ArH), 7.02–7.14 (2H, m, ArH). Anal. Calc. for C₁₉H₂₇BrO₂: C, 62.12, H, 7.40. Found: C, 61.81; H, 7.37.

4.27. (4aS*,12aS*)-1,1-Dimethyl-1,2,3,4,4a,5,6,11,12,12a-decahydrodibenzo[a,e]cycloocten-4a-ol (30a)

Cyclization of the vinylcyclohexanol 29a (500 mg, 1.48 mmol) in benzene (300 ml) with Bu₃SnH (700 mg, 2.4 mmol) and AIBN (15 mg) as described for the preparation of 13a, on chromatography on silica gel using Et₂O–petroleum ether (1:4) eluant gave a thick gum (350 mg) containing the cyclized product 30a and the reduced product 31a in a ratio of ca 1:1 (1H NMR spectrum). This on careful rechromatography on activated basic alumina and elution with Et₂O–petroleum ether (1:19), separated 31a (ca 110 mg) and 30a (155 mg, 40%) in the latter fractions. νmax 3445, 1605 cm⁻¹; δH (200 MHz, CDCl₃) 0.66 (3H, s, CMe), 0.94 (3H, s, CMe), 1.01–2.10 (12H, m), 2.20–3.48 (4H, m, 2×CH₂Ar), 6.97–7.24 (4H, m, ArH); MS (m/z) 257 (M+-1, 22), 237 (13), 211 (12), 157 (14), 145 (29), 131 (50), 117 (31), 111 (100). Anal. Calc. for C₁₈H₂₆O: C, 86.66; H, 10.14. Found: C, 83.36; H, 9.91.

4.28. (4aS*,12aS*)-1,1-Dimethyl-9-methoxy-1,2,3,4,4a,5,6,11,12,12a-decahydrodibenzo[a,e]cycloocten-4a-ol (30b)

Cyclization of the vinylcyclohexanol 29b (550 mg, 1.5 mmol) in benzene (330 ml) with Bu₃SnH (770 mg, 2.6 mmol) and AIBN (15 mg) as described for 13a on silica gel chromatography gave a mixture (390 mg) of the cyclized alcohol 30b and the debrominated product 31b in a ratio of ca 1:1 (1H NMR). This on rechromatography over activated basic alumina and elutions with Et₂O–petroleum ether (1:15) separated 31b (160 mg) and the tricyclic alcohol 30b (190 mg, 44%). νmax 3425, 1600 cm⁻¹; δH (200 MHz, CDCl₃) 0.66 (3H, s, CMe), 0.94 (3H, s, CMe), 1.02–2.10 (12H, m), 2.20–3.48 (4H, m, 2×CH₂Ar), 3.77 (3H, s, ArOMe), 6.56 (1H, d, J=2 Hz, ArH), 6.66 (1H, dd, J=8 and 2 Hz, ArH), 6.97 (1H, d, J=8 Hz, ArH); δC (50 MHz, CDCl₃) 17.7, 22.3, 29.2, 31.4, 32.3, 33.3, 34.3, 42.2, 43.2, 43.4, 54.3, 59.5, 74.7, 110.8, 113.9, 115.4, 131.3, 141.5, 157.7; MS (m/z) 288 (M⁺, 33), 276 (77), 255 (18), 201 (32), 185 (8), 160 (10), 147 (100). Anal. Calc. for C₁₉H₂₈O₂: C, 79.12; H, 10.14. Found: C, 78.94; H, 9.51.

4.29. (4aS*,12aS*)-1,1-Dimethyl-8-methoxy-1,1-dimethyldecahydrodibenzo[a,e]cycloocten-4a-ol (30c)

Cyclization of the vinylcyclohexanol 29c (650 mg, 1.77 mmol) in benzene (400 ml) with Bu₃SnH (900 mg, 3.0 mmol) and AIBN (20 mg) as described for 13a on silica gel chromatography gave a
mixture (450 mg) of the cyclized product 30c and the debrominated alcohol 31c in a ratio of ca 1:1. It was rechromatographed on basic alumina to afford the pure tricyclic alcohol 30c (210 mg, 41%); $\nu_{\text{max}}$ 3425, 1600 cm$^{-1}$; $\delta_{\text{H}}$ (200 MHz, CDCl$_3$) 0.66 (3H, s, CMe), 0.96 (3H, s, CMe), 1.02–2.10 (12H, m), 2.24–3.44 (4H, m, 2 $\times$ ArCH$_2$), 3.77 (3H, s, ArOMe), 6.62 (1H, d, $J=2$ Hz, ArH), 6.73 (1H, dd, $J=8$ and 2 Hz, ArH), 6.90 (1H, d, $J=8$ Hz, ArH). Anal. Calc. for C$_{19}$H$_{28}$O$_2$: C, 79.12%; H, 9.78. Found: C, 78.91; H, 9.53.

4.30. (1S*,2S*)-1-Allyl-2-[2-(2-bromophenyl)ethyl]-3,3-dimethylcyclohexanol (32)
Barbier reaction of cyclohexanone 28a (800 mg, 2.6 mmol) using Mg (250 mg, 10.4 mg atom) and allyl bromide (3 ml) in THF (15 ml) as described for 3a gave the condensed product (725 mg, 80%). The GLC analyses showed the presence of the alcohol 32 and presumably its epimer in a ratio of 93:7. Silica gel chromatography of the mixture using Et$_2$O–petroleum ether (1:9) afforded the pure cyclohexanol 32. $\nu_{\text{max}}$ 3425, 1635 cm$^{-1}$; $\delta_{\text{H}}$ (200 MHz, CDCl$_3$), 0.96 (3H, s, Me), 0.98 (3H, s, Me), 1.02–1.94 (10H, m), 2.1–2.6 (2H, m, ArCH$_2$), 2.62–2.92 (2H, m, CH$_2$CH=CH$_2$), 5.04–5.22 (2H, m, CH=CH$_2$), 5.75–6.02 (1H, m, CH=CH$_2$), 6.94–7.12 (1H, m, ArH), 7.14–7.32 (2H, m, ArH), 7.56 (1H, d, $J=8$ Hz, ArH). Anal. Calc. for C$_{19}$H$_{27}$BrO: C, 64.95; H, 9.74. Found: C, 64.73; H, 7.68.

4.31. (6aS*,10aS*)-1,1-Dimethyl-6,6a,7,8,9,10,10a,11,12,13-decahydro-5H dibenzo[a,e]cyclononen-10a-ol (33)
Radical cyclization of the allylcyclohexanol 32 (500 mg, 1.42 mmol) in benzene (300 ml) with Bu$_3$SnH (700 mg, 2.4 mmol) and AIBN (20 mg) as described for 5a gave a mixture of the tricyclic alcohol 33 and the reduced alcohol 34 in a ratio of ca 3:1 ($^1$H NMR). This on careful rechromatography on activated basic alumina using Et$_2$O–petroleum ether (1:9) afforded the pure alcohol 33. $\nu_{\text{max}}$ 3420, 1635 cm$^{-1}$; $\delta_{\text{H}}$ (200 MHz, CDCl$_3$) 0.96 (3H, s, Me), 0.99 (3H, s, Me), 1.02–1.94 (10H, m), 2.1–2.6 (2H, m, ArCH$_2$), 2.62–2.92 (2H, m, CH$_2$CH=CH$_2$), 5.04–5.22 (2H, m, CH=CH$_2$), 5.75–6.02 (1H, m, CH=CH$_2$), 6.94–7.12 (1H, m, ArH), 7.14–7.32 (2H, m, ArH), 7.56 (1H, d, $J=8$ Hz, ArH). Anal. Calc. for C$_{19}$H$_{28}$O: C, 83.76%; H, 10.35. Found: C, 83.48; H, 10.12.

4.32. Methyl (6aS*,7R*,10aR*)-10a-hydroxy-3-methoxy-7-methyl-6,6a,7,8,9,10,10a,11,12,13-decahydro-5H dibenzo[a,e]cyclononen-10a-ol (39a)
The keto-ester 35a (575 mg, 1.5 mmol) on Barbier reaction using Mg (120 mg, 5.0 mg atom), allyl bromide (3 ml) in THF (15 ml) following the procedure described for 17a gave a mixture of the epimeric hydroxy esters 36a and 37a (490 mg, 77%) in a ratio of ca 7:3 ($^1$H NMR). $\nu_{\text{max}}$ 3540, 1740, 1635 cm$^{-1}$; $\delta_{\text{H}}$ (200 MHz, CDCl$_3$) 1.37 (s, C-Me for major epimer), 1.38 (s, C-Me for minor epimer), 3.70 (s, CO$_2$Me for minor epimer), 3.72 (s, CO$_2$Me for major epimer), 3.78 (s, OMe for major epimer), 3.85 (s, OMe for minor epimer).
Radical cyclization of this mixture (470 mg, 1.1 mmol) in benzene (280 ml) with Bu$_3$SnH (600 mg, 2 mmol) and AIBN (15 mg) following the procedure described for 19a after chromatographic purification gave a gum (310 mg) containing the cyclized product 39a and the reduced hydroxy ester 40a. Rechromatography on basic alumina gave the pure tricyclic product 39a (148 mg, 55% based upon 35a) m.p. 94ºC (Et$_2$O–petroleum ether). $\nu_{\text{max}}$ (KBrs) 3550, 1740 cm$^{-1}$; $\delta_{\text{H}}$ (200 MHz, CDCl$_3$) 0.78–1.0 (1H, m), 1.31 (3H, s, CMe), 1.34–2.2 (16H, m), 3.52 (1H, brs, OH), 3.78 (6H, s, ArOMe and CO$_2$Me), 6.58 (1H, d, $J=2$ Hz, ArH), 6.72 (1H, dd, $J=8$ and 2 Hz, ArH), 7.0 (1H, d, $J=8$ Hz, ArH); $\delta_{\text{C}}$ (90 MHz, CDCl$_3$) 16.9 (C-Me), 17.1, 28.4, 36.85 (8, CH$_2$ carbon in
a ratio of 3:1:4), 51.75, 55.1 (ArOMe and COOCH₃), 74.1, 111.7 and 114.9, 130.3, 157.9, 178.9.

MS (m/z) 346 (M⁺, 30), 328 (10), 300 (12), 160 (85), 148 (100). Anal. Calc. for C₂₁H₃₀O₄: C, 72.80; H, 8.72. Found: C, 72.58; H, 8.68.

4.33. Methyl (6aS*,7R*,10aR*)-10a-hydroxy-2-methoxy-7-methyl-6,6a,7,8,9,10,11,12,13-decahydro-5H-dibenz[a,e]cyclonone-7-carboxylate (39b)

The ketoester 35b (590 mg, 1.54 mmol) on Barbier reaction using Mg (130 mg, 5.41 mg atom) and allyl bromide (3 ml) in THF (15 ml), as described for 35a, after chromatographic separations gave the epimeric hydroxy esters 36b and 37b (460 mg, 70%) in a ratio of 3:2 (1H NMR). νmax 3425, 1735, 1635 cm⁻¹; δH (200 MHz, CDCl₃) 1.34 (s, CMe, minor epimer) and 1.38 (s, CMe, major epimer), 3.69 (s, CO₂Me, minor epimer) and 3.71 (s, CO₂Me, major epimer), 3.78 (s, ArOMe, major epimer), 3.85 (s, ArOMe, minor epimer).

Radical cyclization of a 3:2 mixture of 36b and 37b (580 mg, 1.66 mmol) in benzene (350 ml) with Bu₃SnH (800 mg, 2.75 mmol) and AIBN (20 mg) followed by purification, as described for the preparation of 39a, gave the tricyclic alcohol 39b (150 mg, 53% based on 36b) as a thick liquid. νmax 3430, 1735, 1605 cm⁻¹; δH (200 MHz, CDCl₃) 0.72–1.09 (1H, m), 1.32 (3H, s, CMe), 1.38–2.9 (16H, m), 3.56 (1H, s, OH), 3.78 (6H, s, CO₂Me and ArOMe), 6.59–6.71 (2H, m, ArH), 6.97 (1H, d, J= 8 Hz, ArH). Anal. Calc. for C₂₁H₃₀O₄: C, 72.80; H, 8.72. Found: C, 72.62; H, 8.64.

4.34. (6aS*,7R*,10aS*)-10a-Hydroxy-4-methoxy-7-methyl-6,6a,7,8,9,10,11,12,13-decahydro-5H-dibenzo[a,e]cyclononen-7,10a-carbolactone (42a)

Reaction of the tricyclic hydroxy ester 39a (114 mg, 0.33 mmol) with KOBu⁻ (200 mg, 1.8 mmol) in DMSO, as described for 19a, gave the hydroxy acid 41a (95 mg) [νmax 3550, 1710, 1605 cm⁻¹]. A small portion of this crude acid was esterified with diazomethane in Et₂O to give the ester 39a, m.p. 94ºC, alone or admixed with the starting sample. The crude acid 41a (70 mg) was lactonized with PTSA in benzene (20 ml) and worked up as described for 19a to give the γ-lactone 42a (49 mg, 61%) m.p. 155ºC (Et₂O–petroleum ether). νmax (KBr) 1780, 1600 cm⁻¹; δH (200 MHz, CDCl₃) 0.96 (3H, s, CMe), 1.26–3.1 (17H, m), 3.81 (3H, s, ArOMe), 6.55 (1H, dd, J= 8 and 2 Hz, ArH), 6.80 (1H, d, J= 2 Hz, ArH), 7.05 (1H, d, J= 8 Hz, ArH). Anal. Calc. for C₂₀H₂₆O₃: C, 76.39; H, 8.33. Found: C, 76.12; H, 8.12.

4.35. (6aS*,7R*,10aS*)-10a-Hydroxy-3-methoxy-7-methyl-6,6a,7,8,9,10,11,12,13-decahydro-5H-dibenzo[a,e]cyclononen-7,10a-carbolactone (42b)

The cleavage of the tricyclic hydroxy ester 39b (140 mg, 0.4 mmol) with KOBu⁻ (200 mg, 1.8 mmol) in DMSO, as described for 19a, gave the hydroxy acid 41b (95 mg) [νmax 3550, 1710, 1605 cm⁻¹]. A small portion of this crude acid was esterified with diazomethane in Et₂O to give the ester 39b, m.p. 94ºC, alone or admixed with the starting sample. The crude acid 41b (70 mg) was lactonized with PTSA in benzene (20 ml) and worked up as described for 19a to give the γ-lactone 42b (49 mg, 61%) m.p. 155ºC (Et₂O–petroleum ether). νmax (KBr) 1780, 1600 cm⁻¹; δH (200 MHz, CDCl₃) 0.96 (3H, s, CMe), 1.26–3.24 (17H, m), 3.81 (3H, s, ArOMe), 6.55 (1H, dd, d=2 Hz, ArH), 6.80 (1H, d, d=2 Hz, ArH), 7.05 (1H, d, d=8 Hz, ArH). Anal. Calc. for C₂₀H₂₆O₃: C, 76.39; H, 8.33. Found: C, 76.12; H, 8.12.

4.36. (1S*,2S*)-1-(3-Butenyl)-2-(2-bromobenzyl)-3,3-dimethylcyclohexanol (43a)

Typical procedure: CeCl₃.7H₂O (1.8 mg, 4.8 mmol) was dried in vacuo at 150–160ºC for 4 h and kept under dry argon atmosphere. To the resulting dry white powder, cooled to 0ºC, freshly dis-
tilled anhydrous THF (10 ml) was added and the mixture was stirred for 14 h at room temperature followed by the addition of the cyclohexanone 1a (900 mg, 3 mmol) in THF (5 ml) and the stirring continued for an additional 1 h. The mixture was cooled to 0°C and butenylmagnesium bromide, prepared from Mg (160 mg, 6.6 mmol) and butenyl bromide (4 ml) in THF (12 ml) was added and stirred in the cold for 3 h. It was then decomposed with ice-cold aqueous NH₄Cl solution. The suspended solid materials were removed by filtration and the filtrate was extracted with Et₂O. The combined ethereal extract was washed with brine, dried (Na₂SO₄) and evaporated. Chromatography of the oily residue over silica gel and elution with Et₂O–petroleum ether (1:9) afforded 43a (815 mg, 76%) as a colourless liquid. Attempted GLC analyses in various columns were unsuccessful due to decomposition. νmax 3445, 1635 cm⁻¹; δH (100 MHz, CDCl₃) 1.0 (3H, s, CMe), 1.09 (3H, s, CMe), 1.3–2.5 (11H, m), 2.70 (1H, dd, J=14 and 2 Hz, -CH₂-CH=CH₂), 3.18 (1H, dd, J=8 and 14 Hz, CH₂-CH=CH₂), 3.54 (1H, brs, OH), 4.58–5.05 (2H, m, CH=C₆H₅), 5.38–5.62 (1H, m, CH=CH₂), 6.99–7.45 (3H, m, ArH), 7.62 (1H, dd, J=8 and 2 Hz, ArH). Anal. Calc. for C₁₉H₂₇BrO: C, 64.95; H, 7.74. Found: C, 64.62; H, 7.67.

4.37. (1S*,2S*)-1-(3-Butenyl)-2-(5-methoxy-2-bromobenzyl)-3,3-dimethylcyclohexanol (43b)

Following the procedure described for 43a, the ketone 1b (910 mg, 2.8 mmol) was transformed to the butenylcyclohexanol 43b (780 mg, 73%), after chromatography on silica gel using Et₂O–petroleum ether (15:85) as eluant. νmax 3400, 1630 cm⁻¹; δH (60 MHz, CCl₄) 0.99 (3H, s, CMe), 1.09 (3H, s, CMe), 0.6–3.42 (14H, m), 3.72 (3H, s, ArOMe), 4.4–5.5 (3H, m, C₆H₅=C₆H₅), 6.35–6.9 (2H, m, ArH), 7.4 (1H, d, J=8 Hz, ArH). Anal. Calc. for C₂₀H₂₉BrO₂: C, 62.98; H, 7.66. Found: C, 62.85; H, 7.38.

4.38. (1S*,2S*)-1-(3-Butenyl)-2-(2-bromobenzyl)cyclohexanol (44a)

Following the procedure as described for 43a, the ketone 2a (510 mg, 1.9 mmol) was transformed to the alcohol 44a (490 mg, 79%) as a colourless oil, after silica gel chromatography using Et₂O–petroleum ether (1:9) as eluant. νmax 3440, 1635 cm⁻¹; δH (100 MHz, CDCl₃) 0.8–2.8 (14H, m), 2.05 (1H, dd, J=12 and 14 Hz), 3.02 (1H, dd, J=14 and 4 Hz), 4.85–5.60 (2H, m), 5.64–6.0l (1H, m), 6.99–7.40 (3H, m), 7.55 (1H, dd, J=8 and 2 Hz). Anal. Calc. for C₁₇H₂₃BrO: C, 63.15; H, 7.17. Found: C, 62.78; H, 6.91.

4.39. Radical cyclization of 43a to (5aS*,9aS*)-6,6-dimethyl-5a,6,7,8,9,9a,10,11,12,13-decahydro-5H-dibenzo[a,d]cyclononen-9a-ol (45a)

**Typical procedure:** To a gently refluxing solution of the butenylcyclohexanol 43a (500 mg, 1.42 mmol) and AIBN (10 mg) in dry benzene (15 ml), a solution of Bu₃SnH (900 mg, 3.09 mmol) and AIBN (15 mg) in dry benzene (400 ml, 0.007 mol dm⁻³ solution) was added dropwise through a capillary dropper over a period of 12 h. After the complete addition, the mixture was finally refluxed for an additional 2 h, the solvent removed under vacuo and the residue was chromatographed on silica gel. The petroleum ether and benzene–petroleum ether (1:4) eluted most of the tin compounds. Further elution with Et₂O–petroleum ether (15:85) gave light yellow oil (360 mg) containing the cyclized product 45a and the uncyclized reduced alcohol 46a in the ratio of ca 1:1 (1H NMR). It was carefully chromatographed on activated basic alumina and eluted with Et₂O–petroleum ether (10–15:85–90) to give the reduced product 46a containing 45a (ca 75 mg) and the tricyclic alcohol 45a (165 mg, 42%) with the increasing polarity of the eluant. The analytical sample was prepared by preparative TLC [silica gel; developer Et₂O–petroleum ether (1:4)].
ether (1:9); \(\nu_{\text{max}}\) 3440, 1600 cm\(^{-1}\); \(\delta_{\text{H}}\) (200 MHz, CDCl\(_3\)) 0.6–0.8 (1H, m), 1.03 (3H, s, CMe), 1.07 (3H, s, CMe), 0.96–1.60 (14H, m), 2.38–2.88 (3H, m), 7.04–7.2 (4H, m, ArH). Anal. Calc. for C\(_{19}\)H\(_{28}\)O: C, 83.76; H, 10.35. Found: C, 83.62; H, 10.17.

4.40. (5aS*,9aS*)-3-Methoxy-6,6-dimethyl-5a,6,7,8,9,9a,10,11,12,13a-decahydro-5H-dibenzo-[a,d]cyclononen-9a-ol (45b)

The butenylcyclohexanol 43b (540 mg, 1.42 mmol) on radical cyclization with Bu\(_3\)SnH (900 mg, 3.09 mmol) in dry benzene in the presence of AIBN (25 mg) under high dilution as described for the preparation of 45a gave a ca 1:1 mixture of the cyclized product 45b and uncydclized alcohol 46b. This on chromatographic separation over basic alumina column gave the reduced alcohol 46b (190 mg) and the tricyclic product 45b (175 mg, 41%). The analytical sample was prepared by preparative TLC [silica gel; developer ethyl acetate–petroleum ether (15:85)]. \(\nu_{\text{max}}\) 3445, 1595 cm\(^{-1}\); \(\delta_{\text{H}}\) (60 MHz, CCl\(_4\)) 1.12 (6H, s, CMe), 0.75–3.25 (18H, m), 3.79 (3H, s, ArOMe), 6.5–6.85 (2H, m, ArH), 7.12 (1H, d, \(J=8\) Hz, ArH). Anal. Calc. for C\(_{20}\)H\(_{30}\)O\(_2\): C, 79.23; H, 9.69.

4.41. (5aS*,9aR*)-5a,6,7,8,9,9a,10,11,12,12a-decahydro-5H-dibenzo[\(a,d\)]cyclononen-9a-ol (47a)

Radical cyclization of the cyclohexanol 44a (400 mg, 1.24 mmol) with Bu\(_3\)SnH (600 mg, 2.06 mmol) and AIBN (20 mg) in benzene under high dilution as described for 45a gave a mixture of the cyclized product 47a and the reduced alcohol 48a (ca 1:1). The separation of the mixture on basic alumina column gave the tricyclic alcohol 47a (135 mg, 45%) as colourless oil. \(\nu_{\text{max}}\) 3445, 1600 cm\(^{-1}\); \(\delta_{\text{H}}\) (100 MHz, CDCl\(_3\)) 0.90–0.99 (1H, m), 1.5–3.2 (15H, m), 2.5–3.2 (4H, m), 7.1–7.25 (4H, m, ArH). Anal. Calc. for C\(_{17}\)H\(_{24}\)O\(_2\): C, 83.55; H, 9.89. Found: C, 83.23; H, 9.72.

4.42. (1S*,2S*)-1-(3-Butenyl)-2-(2-bromobenzyl)cyclopentanol (49)

Following the procedure described for 43a, the ketone 7 (810 mg, 3.2 mmol) was transformed to the alcohol 49 (740 mg, 75%) as a colourless oil, after chromatography on silica gel, using Et\(_2\)O–petroleum ether (5:95) as eluant. \(\nu_{\text{max}}\) 3430, 1635 cm\(^{-1}\); \(\delta_{\text{H}}\) (60 MHz, CCl\(_4\)) 0.90–3.12 (14H, m), 4.75–5.30 (2H, m, CH=C\(_2\)H\(_2\)), 5.55–6.05 (1H, m, CH=CH\(_2\)), 6.85–7.32 (3H, m, ArH), 7.55 (1H, dd, \(J=8\) and 2 Hz, ArH). Anal. Calc. for C\(_{16}\)H\(_{21}\)BrO: C, 61.98; H, 6.70. Found: C, 61.98; H, 6.70.

4.43. (3aS*,12aS*)-1,2,3,3a,4,9,10,11,12,12a-Decahydrobenzo[\(a\)]cyclopenta[\(d\)]cyclononen-12a-ol (50)

Radical cyclization of the cyclopentanol 49 (600 mg, 1.94 mmol) with Bu\(_3\)SnH (900 mg, 3 mmol) and AIBN (25 mg) in benzene under high dilution as described for 45a gave a mixture of the cyclized product 50 and the reduced olefinic alcohol 51. Careful rechromatography of this mixture on activated basic alumina separated the tricyclic alcohol 50 (160 mg, 36%) using Et\(_2\)O–petroleum ether (1:9) as eluant. An analytical sample was prepared by preparative TLC [silica gel, eluant Et\(_2\)O–petroleum ether (15:85)]. \(\nu_{\text{max}}\) 3440, 1595 cm\(^{-1}\); \(\delta_{\text{H}}\) (200 MHz, CDCl\(_3\)) 0.9–1.0 (1H, m), 1.2–3.3 (17H, m), 7.04–7.4 (4H, m). Anal. Calc. for C\(_{16}\)H\(_{22}\)O: C, 83.42; H, 9.62. Found: C, 83.18; H, 9.32.

4.44. (1S*,2S*)-1-(3-Butenyl)-2-(2-bromobenzyl)cycloheptanol (52)

Following the procedure as described for 43a, the ketone 25 (890 mg, 3.16 mmol) was transformed to the alcohol 52 (880 mg, 82.4%) as a colourless liquid. \(\nu_{\text{max}}\) 3420, 1640 cm\(^{-1}\); \(\delta_{\text{H}}\) (60
MHz, CCl₄) 0.7–3.2 (18H, m), 4.0–6.1 (3H, CH=CH₂), 6.5–7.2 (3H, m, ArH), 7.5 (1H, d, J= 8 Hz, ArH). Anal. Calc. for C₁₈H₂₅BrO: C, 64.09; H, 7.47. Found: C, 63.88; H, 7.2.

4.45. (5aS*, 10aR*)-5,5a,6,7,8,9,10,10a,11,12,13,14-dodecahydro-5H-benzo[a]cyclohepta[d]cyclononen-10a-ol (53)

Radical cyclization of the cycloheptanol 52 (480 mg, 1.42 mmol) with Bu₃SnH (700 mg, 2.4 mmol) and AIBN (25 mg) in benzene under high dilution as described for 45a gave a ca 3:2 mixture of the cyclized product 53 and the debrominated alcohol 54 (340 mg). Careful rechromatography of this mixture on basic alumina separated the cyclized product 53 (195 mg, 54%) as a colourless oil using Et₂O–petroleum ether (1:9) as eluant. νₘₐₓ 3440, 1605 cm⁻¹; δH (100 MHz, CDCl₃) 0.78–1.09 (1H, m), 1.25–3.34 (21H, m), 7.18–7.40 (4H, m, 4H); MS (m/z) 240 (M⁺, 20), 201 (67), 167 (11), 149 (24), 130 (36), 91 (100). Anal. Calc. for C₁₈H₂₆O: C, 83.66; H, 10.14. Found: C, 83.42; H, 9.98.

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