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

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Abstract

The scope for *n*-Bu_3SnH-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**, |allyl-cyclohexanols **11a**,**b**, **12a**, **18a**,**b**, **32**, **36a**,**b** and butenylcyclohexanols **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* cyclization[7–14] 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 (Bu_3SnH)-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]

† Dedicated to Prof. S. C. Bhattacharyya.

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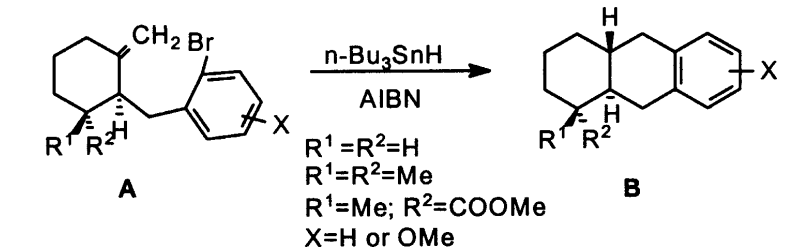
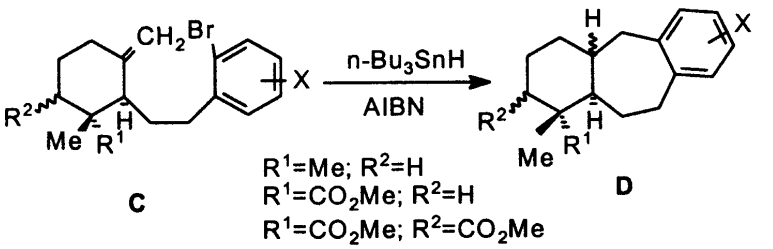
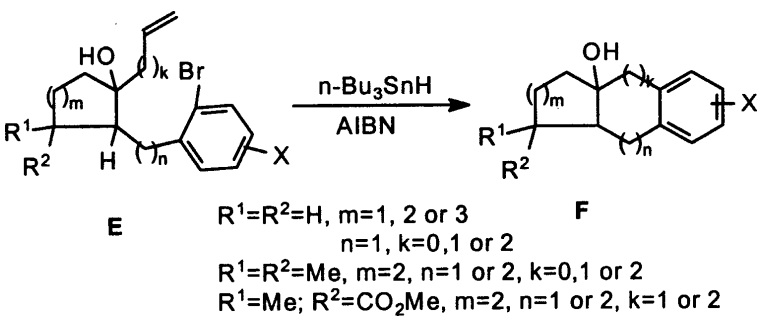
As a prelude to our systematic study, we demonstrated[23] in 1991 an exclusive regio- and stereoselective 6-*endo*-aryl radical cyclization in some 2-(2-bromobenzyl)methylenecyclohexanes **A** to the respective *trans*-octahydroanthracenes **B**, through preferred radical attack at the least substituted exocyclic methylene carbon centre (eqn 1).[24] In the following year the implementation of a regioselective 7-*endo-trig*-aryl radical cyclization of 2-(2-bromoarylethyl)-1-methylenecyclohexanes **C** to the corresponding *trans* and *cis*-octahydro-l*H*-dibenzo[*a*,*d*]cycloheptenes **D** with Bu_3SnH in good yields (eqn 2) was recorded.[25,26] Although organotin hydride-mediated ring closures have been reported to a limited extent to construct seven-membered hetero-ring structures,[21,22] a hetero atom replacing a methylene group in the newly formed ring, the examples of carbocyclics formations by carbon-centered radicals are only few.[27] 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 Bu_3SnH-induced highly regioselective 7-*endo*-,[25,26] 8-*endo*-[28] and 9-*endo-trig*[29] 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-



[eqn 1]



[eqn 2]

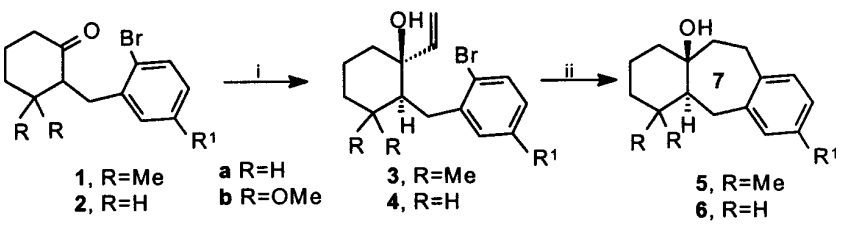


[eqn 3]

sized ring-fused structures[22] which still remain a challenging problem.[22,30–34,36] While there are a few reports on the formation of eight-membered ring,[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.[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 vinylcyclohexanols **3a,b** and **4a**,**b** (Scheme 1).



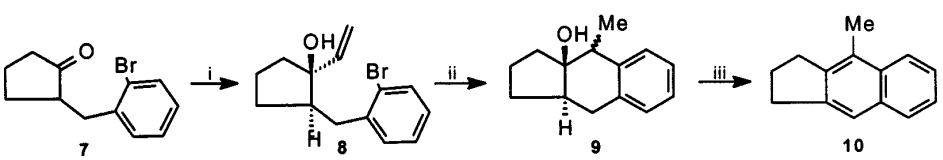
Reagents: i) CH_2=CHMgBr, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.

Scheme 1.

The cyclohexanols **3a**,**b** and **4a**,**b** were obtained as a single epimer in each case, in excellent yields, by condensation with the easily accessible[24] cyclohexanones **1a**,**b** and **2a**,**b** with vinylmagnesium bromide in THF. The stereostructures assigned are based upon analogy.[38] The radical cyclization of the vinylcyclohexanols **3a**,**b** in refluxing benzene with Bu_3SnH and a catalytic amount of azoisobutyronitrile (AIBN) afforded the alcohols **5a**,**b** in 68–70% yields, as the only isolable pure compounds. The radical cyclizations of unsubstituted cyclohexanols **4a**,**b** under the same condition gave the respective cyclized alcohols **6a**,**b**, in good yields. The assigned structure for each of the products resulting from 7-*endo-trig* 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**[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 $FeCl_3$-silica gel[39] giving the benz[*f*]indene derivative **10** in 72% yield (Scheme 2).

The outcome of the radical cycliztion of the vinylcyclohexanol **4a** and the vinylcyclopentanol **8** leading to the respective 7-*endo*- and 6-*exo* products **6a** and **9**, respectively, in good yields is

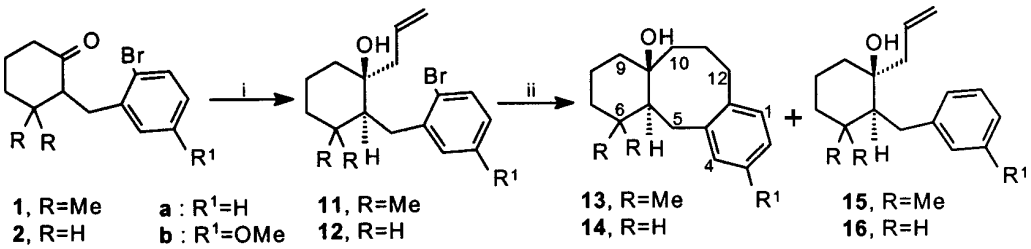


Reagents: i) CH_2=CHMgBr, THF; ii) *n*-Bu_3SnH, AIBN, C_6H_6 and iii) $FeCl_3$/silica gel.

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 process[1,3] 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 undertaken[28] on the radical cyclization of the allylalcohols **11a**,**b** and **12a** (Scheme 3).

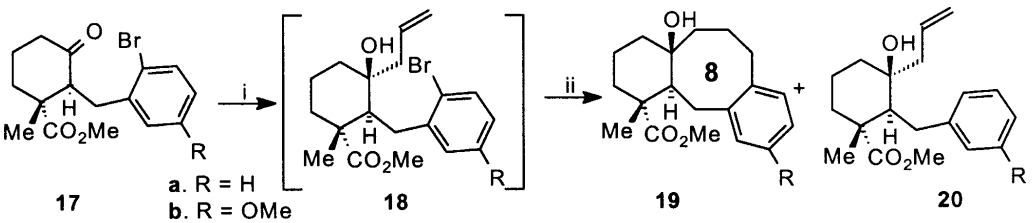


Reagents: i) CH_2=$CHCH_2MgBr$, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.

Scheme 3.

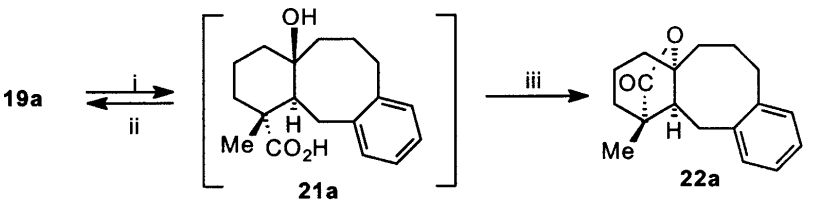
Barbier reaction[40] of **1a**,**b** with allylbromide in THF proceeded smoothly to give the corresponding alcohols **11a**,**b** in 77–80% yield 92–93% (GLC) purity. Column chromatography of the crude products on silica gel gave each of the alcohols **11a** and **11b** in 96–98% epimeric purity. The 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 decahydrodibenzo[*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-esters[24] **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]



Reagents: i) CH_2=$CHCH_2Br$, Mg THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.
Scheme 4.

Attempted purifications of each of these mixtures through alumina or silica gel columns slowly transformed[42] 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 Bu_3SnH 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** (^{1}H NMR) and other uncharacterized products. The careful rechromatography of this mixture on basic alumina gave the pure 8-*endo*-product **19a**, m.p. 143ºC 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. 116ºC. 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-Bu^{t}OK-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 6*N*-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. l).



Reagents: i) Bu^{t}OK, DMSO; ii) CH_2N_2, Et_2O and iii) *p*-TsOH, C_6H_6.
Scheme 5.

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**

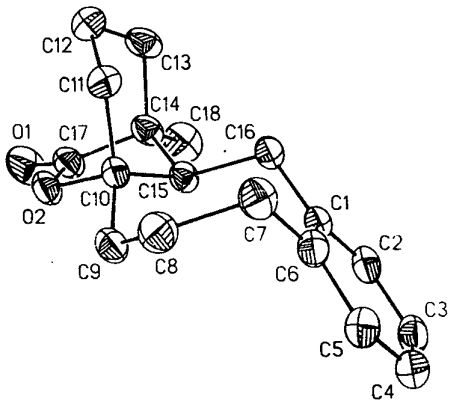
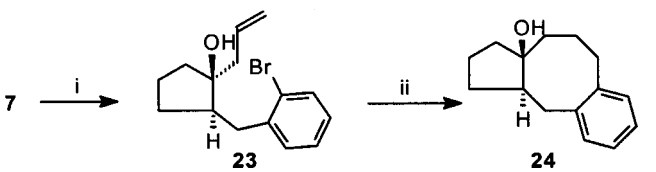


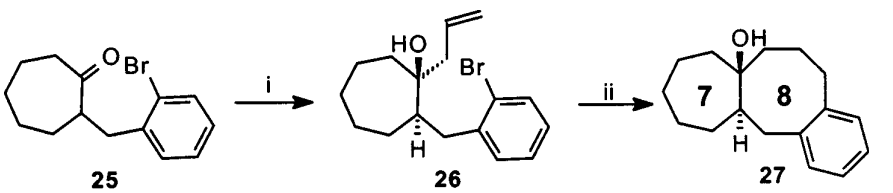
FIG. 1. Perspective view of **22a** showing the crystallographic number.[29]

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=$CHCH_2Br$, Mg, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.

Scheme 6.

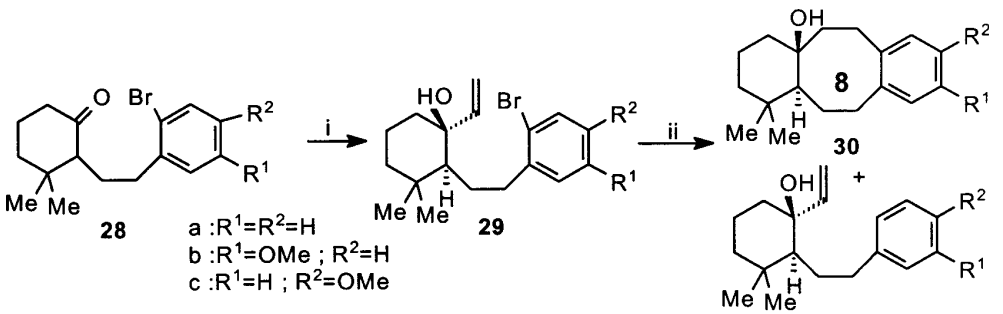


Reagents: i) CH_2=$CHCH_2Br$, Mg, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.

Scheme 7.

The Barbier reaction of the cycloheptanone **25**[24] gave the alcohol **26** in 80% yield (98% GLC purity). The *trans*-stereochemistry has been assigned to **26** by analogy.[41] 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 vinylcyclohexanols **29a-c** (Scheme 8). The cyclohexanols **29a-c** were obtained as single diastereoisomers, in each case, in excellent yields by condensation of the cyclohexanones[26] **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 ^{1}H NMR spectroscopy and the assigned stereostructure is based upon analogy. Radical cyclization of each of the vinylcyclohexanols **29a-c** in refluxing benzene, with Bu_3SnH 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.

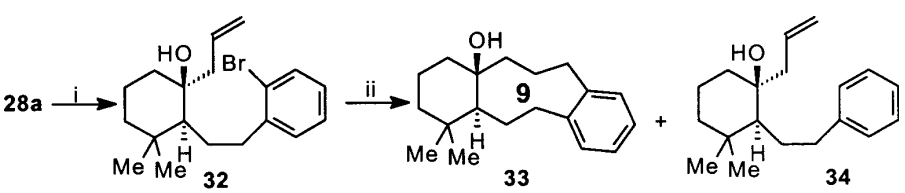


Reagents: i) CH_2=CHMgBr, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.

Scheme 8.

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 centre[45] 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 existed[22] for the formation of the nine-membered carbocyclics involving radical cyclization, we first implemented[29] such a strategy in several diversed substrates (Scheme 9).

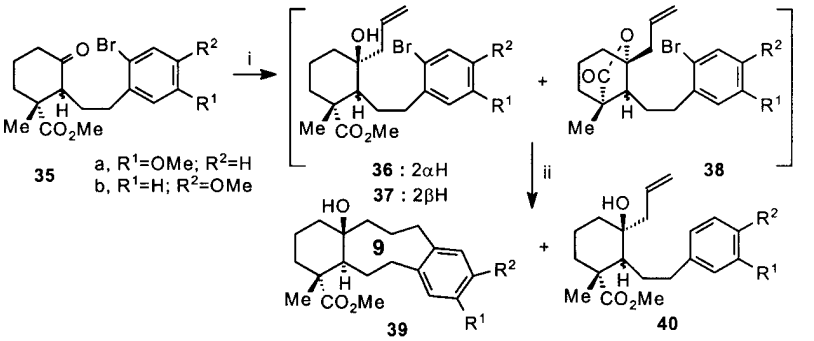


Reagents: i) CH_2=$CHCH_2Br$, Mg, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.

Scheme 9.

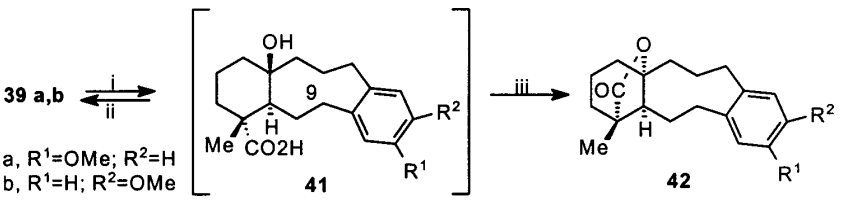
The Barbier reaction of the cyclohexanone **28a** gave a mixture of the alcohol **32** and its epimer in *ca* 93:7 (Scheme 9). Careful silica gel chromatography gave the major epimer assigned as **32** (98% pure) which on radical cyclization furnished a difficultly separable (*ca* 3:1) mixture of the 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**[26] 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 raction of **35b**[26] gave a mixture of 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[29] the stereostructure of **42b** (Fig. 2) and thereby its congeners.



Reagents: i) CH_2=$CHCH_2Br$, Mg, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.

Scheme 10.



Reagents: i) Bu^tOK, DMSO; ii) CH_2N_2, Et_2O and iii) *p*-TsOH, C_6H_6.

Scheme 11.

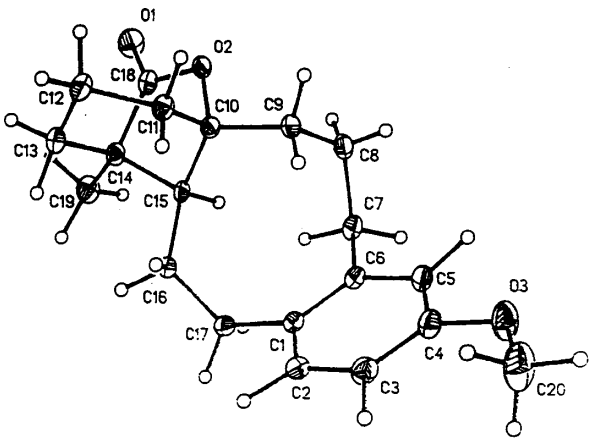
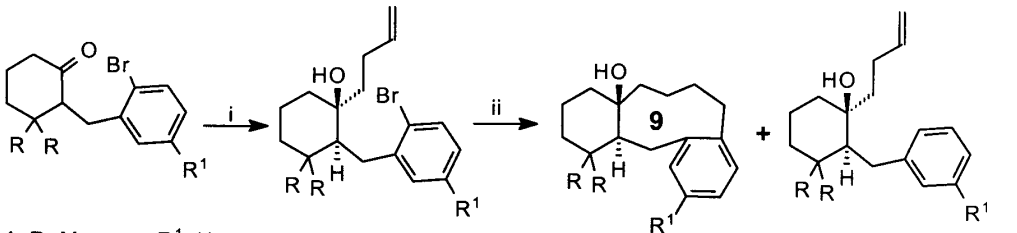


FIG. 2. Perspective view of **42b** showing the crystallographic number.[44]

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[29] of the cyclohexanones (**1a**,**b** and **2a**), with butenylmagnesium bromide in the presence of $CeCl_3$ in THF followed by silica gel chromatography. The assigned stereostructures are based upon analogy.[38] 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 Bu_3SnH 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).

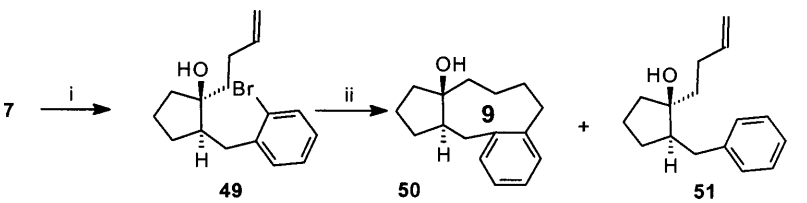
The relatively favourable disposition of the bond-forming carbon atoms in the non-8-enyl aryl radicals generated from the allylcyclohexanols **32a** and **36a**,**b** compared to that in the flexible butenyl side chain in the cyclohexanols **43a**,**b** and **44a** is reflected in the higher yields of 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 $CeCl_3$ in THF, on radical cyclization with Bu_3SnH 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

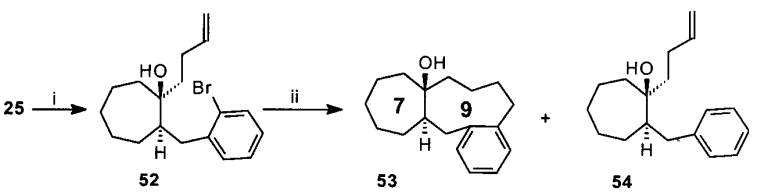


Reagents: i) CH_2=$CHCH_2CH_2MgBr$, $CeCl_3$, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.
Scheme 12.

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.



Reagents: i) CH_2=$CHCH_2CH_2MgBr$, $CeCl_3$, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.
Scheme 13.



Reagents: i) CH_2=$CHCH_2CH_2MgBr$, $CeCl_3$, THF and ii) *n*-Bu_3SnH, AIBN, C_6H_6.
Scheme 14.

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,[46] a remarkably simple entry to chiral condensed medium ring cyclic ethers has been established through application of regioselective aryl radical cyclization methodology.[47] Investigations are currently in progress[48] 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. ^{1}H NMR spectra were determined at 60, 100, 200 and 400 MHz, ^{13}C NMR spectra were recorded at 100 and 50 MHz. Mass spectra were obtained by EI 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 NH_4Cl (10 ml) and extracted with Et_2O. The organic layer was washed with saturated brine, then dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by basic alumina column chromatography (Et_2O–petroleum ether 1:9) to afford pure vinyl alcohol **3a** (730 mg, 78%) as a colourless oil; ν_{max} 3450, 1640 cm^{-1}; δ_H (200 MHz, $CDCl_3$), 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, $ArCH_2$), 4.78 (1H, dd, *J*=10 and 1 Hz, CH=C*H*$_2$), 5.19 (1H, dd, *J*=16 and 1 Hz, CH=C*H*$_2$), 5.58–5.70 (1H, dd, C*H*=CH_2), 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 $C_{17}H_{23}BrO$: 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 Et_2O–petroleum ether (1:9). ν_{max} 3420, 1635 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$); δ 0.88 (3H, s, Me), 1.20 (3H, s, Me), 1.2–1.82 (8H, m), 2.80 (2H, brd, *J*=7 Hz, $ArCH_2$), 3.78 (3H, s, ArOMe), 4.70 (1H, dd, *J*=11 and 2 Hz, CH=C*H*$_2$), 5.05 (1H, dd, *J*=16 and 2 Hz, CH=C*H*$_2$), 5.38–5.80 (1H, dd, C*H*=CH_2), 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 $C_{18}H_{25}BrO_2$: 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 (Et_2O–petroleum ether 1:19). ν_{max} 3450, 1640 cm^{-1}; δ_H (200 MHz, $CDCl_3$), 1.25–2.20 (8H, m), 2.55 (1H, dd, *J*=14 and 10 Hz, $ArCH_2$), 2.95 (1H, dd, *J*=14 and 4 Hz, $ArCH_2$), 5.14 (1H, dd, *J*=10 and 1 Hz, CH=C*H*$_2$), 5.87–6.04 (1H, dd, C*H*=CH_2), 6.98–7.06 (1H, m, ArH), 7.14–7.26 (2 H, m, ArH), 7.50 (1H, d, *J*=8 Hz, ArH). Anal. Calc. for $C_{14}H_{17}BrO$: 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**)*

Bu_3SnH (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 Et_2O–petroleum ether (1:9) afforded colourless oil consisting of the cyclized alcohol **5a** along with a trace of reduced uncyclized product (^{1}H NMR spectrum). This on chromatography over basic alumina using Et_2O–petroleum either (1:9) afforded pure **5a** (420 mg, 69%); ν_{max} 3425, 1605 cm^{-1}; δ_H (200 MHz, $CDCl_3$), 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 $C_{17}H_{24}O$: 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 Bu_3SnH (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}; δ_H (200 MHz, $CDCl_3$), 1.03 (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 $C_{18}H_{26}O_2$: 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**)*

Bu_3SnH (900 mg, 3.09 mmol) was added to a stirred solution of the alcohol **4a** (700 mg; 2.37 mmol) and AIBN (20 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 Et_2O–petroleum ether (1:9) afforded a colourless liquid consisting of a mixture of the cyclized product **6a** and the respective uncyclized debrominated alcohol (^{1}H NMR spectrum) which on chromatography on basic alumina using petroleum ether–Et_2O (19:1) gave the pure alcohol **6a** (350 mg, 68%) as the sole isolable product; ν_{max} 3500, 1600 cm^{-1}; δ_H (200 MHz, $CDCl_3$), 0.98–2.10 (11H, m, 5 × CH_2 and OH), 2.35–2.6 (3H, m, CH_2 and methine), 3.25–3.40 (2H, m, CH_2), 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 $C_{15}H_{20}O$: C, 83.28; H, 9.31. Found: 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 Bu_3SnH (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 (^{1}H NMR), which on further chromatography on basic alumina afforded pure

6b (310 mg, 61%); ν_{max} 3425, 1595 cm^{-1}; δ_H (60 MHz, CCl_4), 0.8–2.2 (11H, m, 5 × CH_2 and OH), 2.3–2.6 (3H, m, CH_2 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_3SnH (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_2O–petroleum ether (1:9) afforded a diastereoisomeric mixture of the cyclized alcohol **9** (600 mg, 83%) as a colourless oil; ν_{max} 3445, 1590 cm^{-1}; δ_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*) 202 (M^+, 10), 1.84 (33), 163 (42), 155 (17), 141 (18), 117 (42), 91 (41), 84 (100). 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 $FeCl_3$, $6H_2O$ (1.6 g, 5.9 mmol) containing Et_2O (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_2O (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_2O. After removal of Et_2O, 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; ν_{max} 1630, 1600 cm^{-1}; δ_H (200 MHz, $CDCl_3$), 2.08–2.16 (2 H, m), 2.58 (3H, s, ArMe), 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* 10 min. The stirring was continued for an additional 3 h at room temperature and then quenched at 0°C with cold aqueous NH_4Cl (15 ml) and extracted with Et_2O. The ether extract was washed with brine, dried (Na_2SO_4), evaporated and the residual oil was chromatographed on silica gel using Et_2O–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. ν_{max} 3460, 1635 cm^{-1}; δ_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, C*H*$_2$CH=CH$_2$), 4.84 (1H, dd, *J*=16 and 2 Hz, CH=C*H*$_2$, major isomer), 5.02 (1H, dd, *J*=14 and 2 Hz, CH=C*H*$_2$, major isomer), 5.04–5.2 (m, CH=C*H*$_2$, minor isomer), 5.50–5.74 (m, C*H*=CH$_2$, major isomer), 5.8–6.0 (m, C*H*=CH$_2$, minor isomer), 6.94–7.28 (3H, m, ArH), 7.41 (1H, dd, *J*=8 and 2 Hz, ArH), δ_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-Allyl-2-(5-methoxy-2-bromobenzyl)-3,3-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%). ν_{max} 3500, 1630 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 0.94 and 1.09 (each s, two CMe for major isomer), 0.95 and 1.08 (each s, two Me for minor isomer), 1.18–1.84 (1H, m), 1.85 (1H, dd, *J*=10 and 4 Hz, dt, $ArCH_2$), 2.14 (1H, dd, *J*=10 and 8 Hz, $ArCH_2$), 2.68 (2H, dd, *J*=16 and 2 Hz, C*H*$_2$-CH=CH_2), 3.78 (s, ArOMe, major isomer), 3.79 (s, ArOMe, minor isomer), 4.84 (dd, *J*=16 and 2 Hz, CH=CH_2, major isomer), 5.02 (dd, *J*= 14 and 2 Hz, CH=C*H*$_2$, major isomer), 5.0–5.22 (m, CH=C*H*$_2$, minor isomer), 5.46–5.72 (m, C*H*=CH_2, major isomer), 5.78–6.02 (m, C*H*=CH_2, minor isomer), 6.54–6.7 (1H, m, ArH), 6.88 (1H, s, ArH), 7.52 (1H, d, *J*=8 Hz, ArH), δ_C (100 MHz, $CDCl_3$), δ_C 17.7, 22.0, 31.0, 32.6, 35.0, 38.1 (C-6), 42.1, 46.9, 53.1, 55.3, 74.2, 112.l, 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-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%). ν_{max} 3430, 1630 cm^{-1}; δ_H (60 MHz, CCl_4), 1.15–1.75 (10H, m), 2.35–2.55 (2H, m), 2.64 (1H, dd, *J*=12 and 2 Hz, C*H*$_2$-CH=CH_2), 3.14 (1H, dd, *J*=12 and 8 Hz, C*H*$_2$-CH=CH_2), 4.85–5.20 (2H, m, CH=C*H*$_2$), 5.55–6.10 (1H, m, C*H*=CH_2), 6.84–7.30 (3H, m, ArH), 7.50 (1H, dd, *J*=8 and 2 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-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_3SnH (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_2O–petroleum ether (15:85) as eluant afforded **13a** (380 mg, 62%) as a colourless oil; ν_{max} 3460 cm^{-1}; δ_H (200 MHz, $CDCl_3$), 0.80–0.95 (1H, m), 1.04 (3H, s, CMe), 1.15 (3H, s, CMe), 1.15–2.15 (11H, m), 2.55–2.70 (2H, m), 2.92 (1H, dd, *J*=11 and 13 Hz), 3.08 (1H, dt, *J*=8 and 13 Hz), 7.0–7.25 (4H, m, ArH). δ_C (50 MHz, $CDCl_3$) 18.8 (C-3), 21.0 (β-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-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_3SnH (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_2O–petroleum ether (l:9) afforded **13b** (290 mg, 62%) as a colourless oil; ν_{max} 3500, 1595 cm^{-1}; δ_H (200 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, $CDCl_3$), 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 $C_{19}H_{21}O_2$: 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 Bu_3SnH (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 Et_2O–petroleum ether (l:9) afforded **14a** (250 mg, 67%). ν_{max} 3455, 1600 cm^{-1}; δ_H (100 MHz, $CDCl_3$), 0.85–1.00 (1H, m), 1.12–2.15 (12H, m), 2.55–2.72 (2H, m, $ArCH_2$), 3.0–3.30 (2H, m, $ArCH_2$), 7.15–7.35 (4H, m, ArH). Anal. Calc. for $C_{16}H_{22}O$: 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-decahydrodibenzo[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 NH_4Cl and extracted with Et_2O. The extract was washed with brine, water, dried (Na_2SO_4) and evaporated to yield a thick oil. This was dissolved in petroleum ether and rapidly chromatrographed on a short wide column of basic alumina and eluted with Et_2O–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, $CDCl_3$) 1.45 (s, CMe), 1.56–2.7 (m, CH_2, CHOH), 3.39 (s, CO_2Me), 4.90–5.28 (m, CH=CH_2), 5.55–5.93 (m, C*H*=CH_2), 7.18–7.23 (m, ArH), 7.42–7.53 (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 Bu_3SnH (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 Et_2O–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 (Et_2O–petroleum ether). The analytical sample was obtained after filtration of the crude solid in Et_2O–petroleum ether (1:9) through basic alumina as rectangular prisms, m.p. 143°C; ν_{max} 3570, 1730 cm^{-1}; δ_H (200 MHz, $CDCl_3$), 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, CO_2Me), 6.89–7.12 (4H, m, ArH). MS (*m*/*z*) 302 (M^+, 13), 284 (61), 256 (60), 243 (64), 224

(100), 209 (43), 196 (26), 155 (45), 115 (60), 91 (82). Anal. Calc. for $C_{19}H_{23}O_3$: C, 75.46; H, 8.66. Found: C,75.32; H, 8.61.

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%); ν_{max} 3530, 1725, 1635 cm^{-1}; δ_H (100 MHz, $CDCl_3$) 1.47 (s, CMe), 3.48 (s, CO_2Me), 3.78 (s, ArOMe), 4.92–5.15 (m, CH=CH_2), 5.60–5.89 (m, C*H*=CH_2), 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 Bu_3SnH (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 Et_2O–petroleum ether (3:7) to give **19b** as a white solid (270 mg, 45% based on **17b**) m.p. 116°C (Et_2O–petroleum ether); ν_{max} 3440, 1730 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 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, CO_2Me), 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 $C_{20}H_{28}O_4$: 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-decahydrodibenzo[a,d]cycloocten-4,12a-carbolactone* (***22a***)

The tricyclic hydroxyester **19a** (100 mg, 0.33 mmol) was treated with $KOBu^t$ (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 Et_2O, washed separately with aqueous $NaHCO_3$ solution (5%) followed by brine and dried (Na_2SO_4). The alkaline washings were combined together, acidified with cold 6N HCl, extracted with Et_2O, washed with brine, and dried (Na_2SO_4). Removal of the solvent afforded the acid **21a** (80 mg) as a gummy solid, a small portion of which was esterified with diazomethane in Et_2O to give the ester **19a**, m.p. 143°C alone or on admixtured 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 Et_2O (20 ml), washed with cold NaOH solution (2%) and brine, dried (Na_2SO_4) and concentrated. The crude product was purified by chromatography over neutral alumina and eluted with Et_2O–petroleum ether (1:4) to afford the γ-lactone (**21a**) (30 mg, 67%), m.p.138°C (Et_2O–petroleum ether). ν_{max} (KBr) 1780 cm–^{1}; δ_H (200 MHz, $CDCl_3$), 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 $C_{18}H_{22}O_2$: 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 Et_2O–petroleum ether eluants. ν_{max} 3425, 1635 cm^{-1}; δ_H (60 MHz, CCl_4) 1.1–2.9 (12H, m), 4.7–

5.10 (2H, m, CH=CH_2), 5.46–6.15 (1H, m, CH=CH_2), 6.71–7.10 (3H, m, ArH), 7.41 (1H, dd, J=8 and 2 Hz, ArH). Anal. Calc. for $C_{15}H_{22}BrO$: 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 Bu_3SnH (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 Et_2O–petroleum ether (1:9) as eluant. ν_{max} 3445, 1605 cm^{-1}; δ_H (100 MHz, $CDCl_3$) 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 $C_{15}H_{20}O$: 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 Et_2O–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, CCl_4) 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 $C_{17}H_{23}BrO$: 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 Bu_3SnH (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 Et_2O–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, $CDCl_3$) 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 $C_{17}H_{24}O$: 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 Et_2O–petroleum ether (1:9) as eluant afforded the vinylcyclohexanol **29a** (650 mg, 74%) as a colourless oil. ν_{max} 3445, 1630 cm^{-1}; δ_H (100 MHz, $CDCl_3$) δ 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, $ArCH_2$), 5.1 (1H, dd, J = 18 and 2 Hz, CH=CH_2), 5.24 (1H, dd, J=18 and 2 Hz, CH=CH_2), 5.74–6.04 (1H, dd, CH=CH_2), 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 $C_{18}H_{25}BrO$: 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 vinylcyclohexanol **29b** (580 mg, 77%) in the same way as described for the preparation of **3a**, after silica gel column chromatography using Et_2O–petroleum ether (1:9) as eluant; ν_{max} 3425, 1635 cm^{-1}; δ_H (200 MHz, $CDCl_3$), δ 0.97

(3H, s, Me), 1.01 (3H, s, Me), 1.12–2.0 (10H, m), 2.66 (2H, brt, *J*=9 Hz, $ArCH_2$), 3.76 (3H, s, ArOMe), 5.14 (1H, dd, *J*=10 and 2 Hz, CH=CH_2), 5.26 (1H, dd, *J*=18 and 2 Hz, CH=CH_2), 5.82–5.88 (1H, dd, C*H*=CH_2), 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 $C_{19}H_{27}BrO_2$: 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 Et_2O–petroleum ether (15:85) as eluant. ν_{max} 3440, 1635 cm^{-1}; δ_H (100 MHz, $CDCl_3$); δ 0.97 (3H, s, Me), 1.00 (3H, s, Me), 1.06–2.0 (10H, m), 2.59–2.79 (2H, m, $ArCH_2$), 3.76 (3H, s, ArOMe), 5.12 (1H, dd, *J*=10 and 2 Hz, CH=CH_2), 5.22 (1H, dd, *J*=18 and 2 Hz, CH=CH_2), 5.76–6.04 (1H, dd, *J*=18 and 10 Hz, C*H*=CH_2), 6.78 (1H, dd, *J*=8 and 2 Hz, ArH), 7.02–7.14 (2H, m, ArH). Anal. Calc. for $C_{19}H_{27}BrO_2$: 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 Bu_3SnH (700 mg, 2.4 mmol) and AIBN (15 mg) as described for the preparation of **13a**, on chromatography over silica gel using Et_2O–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 (^{1}H NMR spectrum). This on careful rechromatography on activated basic alumina and elution with Et_2O–petroleum ether (1:19), separated **31a** (*ca* 110 mg) and **30a** (155 mg, 40%) in the latter fractions. ν_{max} 3445, 1605 cm^{-1}; δ_H (100 MHz, $CDCl_3$) 0.66 (3H, s, CMe), 0.94 (3H, s, CMe), 1.01–2.08 (12H, m), 2.24–3.56 (4H, m, 2 × CH_2Ar), 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 $C_{18}H_{26}O$: 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 Bu_3SnH (770 mg, 2.6 mmol) and AIBN (15 mg) as described for **13a** on chromatography on a silica gel column gave a mixture (390 mg) of the cyclized alcohol **30b** and the debrominated product **31b** in a ratio of *ca* 1:1 (^{1}H NMR). This on rechromatograpy over activated basic alumina and elutions with Et_2O–petroleum ether (1:15) separated **31a** (160 mg) and the tricyclic alcohol **30b** (190 mg, 44%). ν_{max} 3425, 1600 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.66 (3H, s, CMe), 0.94 (3H, s, CMe), 1.02–2.10 (12H, m), 2.20–3.48 (4H, m, 2 × CH_2Ar), 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); δ_C (50 MHz, $CDCl_3$) 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 $C_{19}H_{28}O_2$: C, 79.12; H, 9.78. 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 Bu_3SnH (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%); ν_{max} 3425, 1600 cm^{-1}; δ_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 × $ArCH_2$), 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_2O–petroleum ether (1:9) afforded the pure cyclohexanol **32**. ν_{max} 3425, 1635 cm^{-1}; δ_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, $CH_2CH{=}CH_2$), 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_3SnH (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_2O–petroleum ether (1:9) afforded the pure alcohol **33** (215 mg, 55%); ν_{max} 3420, 1600 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.96 (3H, s, CMe), 0.99 (3H, s, CMe), 0.7–2.0 (15H, m), 2.2–2.5 (1H, m), 2.55–3.02 (2H, m), 7.03–7.12 (4H, m, ArH). MS (*m*/*z*) 272 (M^+, 22), 254 (24), 226 (13), 139 (30), 111 (100). 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]cyclononene-7-carboxylate (**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). ν_{max} 3540, 1740, 1635 cm^{-1}; δ_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_2Me for minor epimer), 3.72 (s, CO_2Me 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_3SnH (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_2O–petroleum ether). ν_{max} (KBr) 3550, 1740 cm^{-1}; δ_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_2Me), 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); δ_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 $COOCH_3$), 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 $C_{21}H_{30}O_4$: 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,7,8,9,10,10a,11,12,13-decahydro-5H-dibenzo[a,e]cyclononene-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 (^{1}H NMR). ν_{max} 3425, 1735, 1635 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.34 (s, CMe, minor epimer) and 1.38 (s, CMe, major epimer), 3.69 (s, CO_2Me, minor epimer) and 3.71 (s, CO_2Me, 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 Bu_3SnH (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. ν_{max} 3430, 1735, 1605 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 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, CO_2Me and ArOMe), 6.59–6.71 (2H, m, ArH), 6.97 (1H, d, *J*=8 Hz, ArH). Anal. Calc. for $C_{21}H_{30}O_4$: 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,7,8,9,10,10a,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 $KOBu^t$ (200 mg, 1.8 mmol) in DMSO, as described for **19a**, gave the hydroxy acid **41a** (95 mg) [ν_{max} 3550, 1710, 1605 cm^{-1}]. A small portion of this crude acid was esterified with diazomethane in Et_2O 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 (Et_2O–petroleum ether). ν_{max} (KBr) 1780, 1600 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.96 (3H, s, CMe), 1.26–3.24 (17H, m), 3.86 (3H, s, ArOMe), 6.60 (1H, d, *J*=2 Hz, ArH), 6.73 (1H, dd, *J*=8 and 2 Hz, ArH), 7.06 (1H, d, *J*=8 Hz, ArH). Anal. Calc. for $C_{20}H_{26}O_3$: 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,7,8,9,10,10a,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 $KOBu^t$ (200 mg, 1.8 mmol) and DMSO (4 ml) followed by lactonization of the resulting thick gummy solid acid **41b** (95 mg) with PTSA in benzene afforded the γ-lactone **42b** (81 mg, 64%), m.p. 160ºC (Et_2O–petroleum ether). ν_{max} (KBr) 1775, 1605 cm^{-1}; δ_H (100 MHz, $CDCl_3$) 0.92 (3H, s, CMe), 1.09–3.1 (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). MS (*m*/*z*) 314 (M^+, 67), 162 (31), 121 (100). Anal. Calc. for $C_{20}H_{26}O_3$: 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: $CeCl_3.7H_2O$ (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 0ºC 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 NH_4Cl solution. The suspended solid materials were removed by filtration and the filtrate was extracted with Et_2O. The combined ethereal extract was washed with brine, dried (Na_2SO_4) and evaporated. Chromatography of the oily residue over silica gel and elution with Et_2O–petroleum ether (1:9) afforded **43a** (815 mg, 76%) as a colourless liquid. Attempted GLC analyses in various columns were unsuccessful due to decomposition. ν_{max} 3445, 1635 cm^{-1}; δ_H (100 MHz, $CDCl_3$) 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, -C*H*$_2$-CH=CH$_2$), 3.18 (1H, dd, *J*=8 and 14 Hz, C*H*$_2$-CH=CH$_2$), 3.54 (1H, brs, OH), 4.58–5.05 (2H, m, CH=C*H*$_2$), 5.38–5.62 (1H, m, C*H*=CH$_2$), 6.99–7.45 (3H, m, ArH), 7.62 (1H, dd, *J*=8 and 2 Hz, ArH). Anal. Calc. for $C_{19}H_{27}BrO$: 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 Et_2O–petroleum ether (15:85) as eluant. ν_{max} 3400, 1630 cm^{-1}; δ_H (60 MHz, CCl_4) 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, C*H*=C*H*$_2$), 6.35–6.9 (2H, m, ArH), 7.4 (1H, d, *J*=8 Hz, ArH). Anal. Calc. for $C_{20}H_{29}BrO_2$: 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 Et_2O–petroleum ether (1:9) as eluant. ν_{max} 3440, 1635 cm^{-1}; δ_H (100 MHz, $CDCl_3$) 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 $C_{17}H_{23}BrO$: 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 Bu_3SnH (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 *ca* 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) eliminated most of the tin compounds. Further elution with Et_2O–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 (^{1}H NMR). It was carefully chromatographed on activated basic alumina and eluted with Et_2O–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 Et_2O–petroleum

ether (1:9)]; ν_{max} 3440, 1600 cm^{-1}; δ_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_3SnH (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 uncyclized 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 (8:92)]. ν_{max} 3445, 1595 cm^{-1}; δ_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, 7.42; H, 9.99. Found: C, 79.23; H, 9.69.

4.41. *(5aS*,9aR*)-5a,6,7,8,9,9a,10,11,12,13-decahydro-5H-dibenzo[a,d]cyclononen-9a-ol (**47a**)*

Radical cyclization of the cyclohexanol **44a** (400 mg, 1.24 mmol) with Bu_3SnH (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. ν_{max} 3445, 1600 cm^{-1}; δ_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 $C_{17}H_{24}O$: 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_2O–petroleum ether (5:95) as eluant. ν_{max} 3430, 1635 cm^{-1}; δ_H (60 MHz, CCl_4) 0.90–3.12 (14H, m), 4.75–5.30 (2H, m, CH=CH_2), 5.55–6.05 (1H, m, C*H*=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, 62.14; H, 6.84. 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_3SnH (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_2O–petroleum ether (1:9) as eluant. An analytical sample was prepared by preparative TLC [silica gel, eluant Et_2O–petroleum ether (15:85)]. ν_{max} 3440, 1595 cm^{-1}; δ_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. ν_{max} 3420, 1640 cm^{-1}; δ_H (60

MHz, CCl_4) 0.7–3.2 (18H, m), 4.0–6.1 (3H, C*H*=CH_2), 6.5–7.2 (3H, m, ArH), 7.5 (1H, d, *J*=8 Hz, ArH). Anal. Calc. for $C_{18}H_{25}BrO$: 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 Bu_3SnH (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 Et_2O–petroleum ether (1:9) as eluant. ν_{max} 3440, 1605 cm^{-1}; δ_H (100 MHz, $CDCl_3$) 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 $C_{18}H_{26}O$: C, 83.66; H, 10.14. Found: C, 83.42; H, 9.98.

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