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A synthetic approach to (±)-forskolin. Part I. Preparation of key hydrobenzofuran intermediates

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Summary — In a synthetic approach to (±)-forskolin **1**, a stereoselective preparation of the unsaturated lactone **2** was envisaged. Propargylic derivatives **18a–c** were prepared from available α-ionone **5** and treated with Bu_3SnH/AIBN to give the bicyclic vinylstannanes **19a–c** in high yield. From these compounds we then performed transmetallation reactions to obtain the **21a–c** and **22b** homologous derivatives. The two enyne compounds **29** and **30** were then prepared by our previous approach to lactone **2** involving a radical C7-C8 bond formation. In a second radical approach promoted by SmI_2, the diol **10**, was used to synthesize a potential precursor of the dialdehyde **9**.

forskolin / tributylstannane / radical cyclization / transmetallation / vinylstannane / vinyl iodide / Pd(0) coupling reaction

Résumé — Approche de synthèse de la (±)-forskoline. Partie I: préparation des intermédiaires clés hydrobenzofuraniques. Pour une approche de synthèse de la (±)-forskoline **1** nous avons envisagé la préparation stéréospécifique de la lactone insaturée **2**. À partir de l'α-ionone **5** commerciale, les dérivés propargyliques **18a–c** ont été préparés et traités avec Bu_3SnH/AIBN pour obtenir avec de très bons rendements les vinylstannanes **19a–c**. Sur ces composés, nous avons réalisé des réactions de transmétallation pour accéder aux homologues **21a–c** et **22b**. À partir des dérivés **21a–c**, les deux énynes **29** and **30** ont été préparées en vue d'une première voie d'approche de la lactone **2** par fermeture de la liaison C7-C8. La seconde voie d'accès envisagée pour la préparation de **2** fait intervenir une autre réaction de cyclisation radicalaire par utilisation de SmI_2. Le diol **10** précurseur du dialdéhyde **9**, produit clé dans cette approche, a également été synthétisé avec de bons rendements.

forskoline / tributylstannane / cyclisation radicalaire / transmétallation / vinyl stannane / vinyl iodure / couplage Pd(0)

Introduction

The diterpenic compound forskolin **1**, isolated from the roots of the Indian plant *Coleus forskohlii* [1], has shown many interesting biological activities and presents a complex polyoxygenated tricyclic structure. Forskolin **1** was proved to activate adenylate cyclases [2], to inhibit platelet aggregation in vitro and in vivo, and to have therapeutic potential toward bronchial asthma [3], congestive heart failure [4] and glaucoma [5]. Due to its activity, forskolin still represents a synthetic challenge for organic chemists [6, 7] and at present four total syntheses of (±)-forskolin **1** have been reported [7], together with many synthetic approaches [6].

Our synthetic approach to (±)-forskolin **1** is based on the crucial B ring closure either by a C6-C7 or a C7-C8 bond formation for an access to the unsaturated lactone **2**, the key intermediate developed by Ziegler, Ikegami and Corey (scheme 1) [7]. In this new strategy, and for the construction of the *trans* decalinic AB ring system, we planned the synthesis of the bicyclic derivative **3** via the hydrobenzofuran precursor **4**.

In preliminary work we described a radical cyclization of the model enyne **7** using Bu_3SnH into the *trans* decalinic compound **6**, via a 6-endo-trig process (scheme 2) [8]. In a second approach we reported another radical cyclization [9], which yielded the bicyclic 6β,7β-diol **8** in a SmI_2 reaction on the dialdehyde **9** derived from diol **10**. After that a formal synthesis of forskolin **1** was reported from the bicyclic 6β,7β-diol **8** [10].

This paper deals with the preparation of the key intermediates **29** and **10** involved in the two radical approaches considered for the synthesis of the racemic lactone **2**.

Preparation of the hydrobenzofuran core 4

The preparation of the hydrobenzofuran derivatives **4** involved controlling the *cis* junction between the

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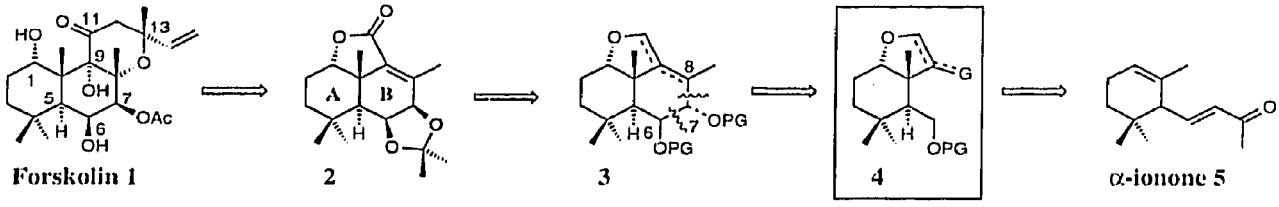
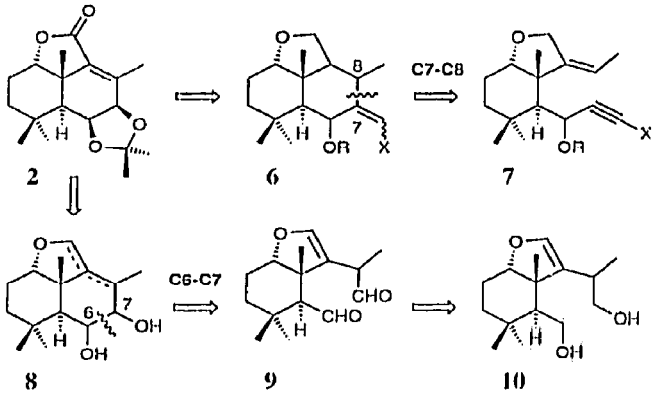


Forskolin 1 — 2 — 3 — 4 — α-ionone 5

Scheme 1



Scheme 2

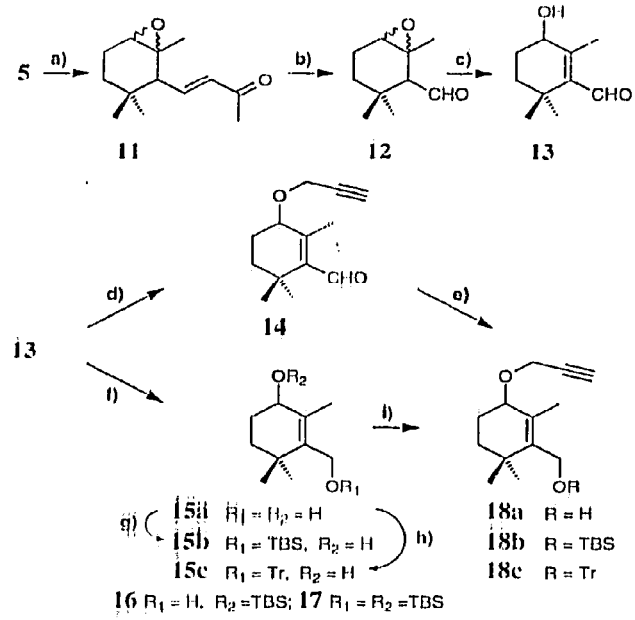
six- and five-membered rings. We decided to carry out a radical cyclization of the enyne compounds **18a–c** induced by Bu_3SnH [11].

The known hydroxyaldehyde **13** [12] was prepared from commercial α-ionone **5** after oxidation of the non-conjugated double bond to give **11** and then ozonolysis of the remaining double bond and basic treatment of the resulting epoxyaldehyde **12** (scheme 3). The hydroxyaldehyde **13** could be directly etherified with propargyl bromide into compound **14**, which was subsequently reduced ($NaBH_4$/MeOH) to afford the expected enynol **18a** (R = H).

Reduction of the hydroxyaldehyde **13** gave the diol **15a** which was selectively protected on the primary hydroxyl group either by a silyl or a trityl group leading to compounds **14b** and **14c**, respectively. A further etherification reaction then gave the corresponding propargyloxy derivatives **18b** and **18c** in good yields.

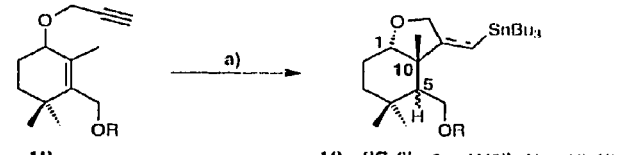
Once we had prepared the enynes **18a–c**, we turned to the radical cyclization involved in our strategy for the construction of the *cis*-hydrobenzofuran precursor **4**. Treatment of the enynes **18a–c** in 10^{-2} M solution in toluene with Bu_3SnH/AIBN resulted in a 5-*exo*-trig process and formation of the expected vinylstannanes **19a–c** in high yields (scheme 4). Compounds **19a–c** were identified as mixtures of epimers at the C5 position [13], whereas the junction of the bicyclic derivatives **19a–c** was found to be *cis* and the vinylstannyl was shown to be exclusively *Z* [14].

Vinylstannanes are known to be good precursors for the preparation of the corresponding lithio derivatives by transmetallation or to undergo Pd(0)-catalyzed vinyl-vinyl coupling reactions with vinylhalides [15]. We used this reactivity to generate the homologous derivatives of vinylstannanes products **19a–c** under mild conditions [16].



a) *m*-CPBA, CH_2Cl_2, 0 °C, 82%. b) (i) O_3, −78 °C, CH_2Cl_2. (ii) Zn, 50% aqueous AcOH, 86%. c) Pyrrolidine, Et_2O, 20 °C, 83%. d) NaOH/H_2O 60% weight, cat Bu_4NI, propargyl bromide, toluene, 20 °C, 17 h, 99%. e) $NaBH_4$, MeOH, 0 °C, 1 h, → **18a** 75%. f) $NaBH_4$, MeOH, 0 °C, 1 h, → **15a** 75%. g) TBSCl, Im, DMF, 0 °C, 4 h, → **15b** 61%, → **16** 9%, → **17** 11%. h) TrCl, NEt_3, DMAP, CH_2Cl_2, Δ, → **15c** 77%. i) NaOH/H_2O 60% weight, cat Bu_4NI, propargyl bromide, toluene, 20 °C, 17 h, **15b** → **18b** 97%, **15c** → **18c** 87%.

Scheme 3



a) Bu_3SnH (1.7 equiv, 0.05 M in toluene), AIBN 10% mol, reflux 2 h, **18a** → **19a** 88% (5α-H/5β-H = 60:40), **18b** → **19b** 98% (5α-H/5β-H = 70:30), **18c** → **19c** 90% (5α-H/5β-H = 50:50).

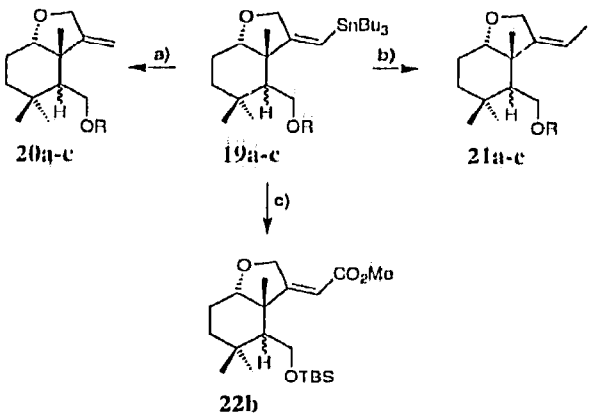
Scheme 4

Homologation of the vinylstannanes 19a–c

In a preliminary experiment the stannanes **19a–c** were treated in acidic media and the protodestannylated derivatives **20a–c** were obtained in quantitative yield

(scheme 5). Transmetallation of **19b,c** was achieved with *n*-BuLi/THF at −78 °C [17] to give the methylidene derivatives **20b,c** (95 and 90% yields, respectively) after quenching with NH_4Cl, or the ethylidene homologous compounds **21b,c** in 87 and 80% yields with MeI. This homologation reaction was required for the construction of **7** in a synthetic approach of forskolin via the C7-C8 bond formation (see scheme 2)

In an approach involving the formation of diol **10** (scheme 2), **19b** was converted into the conjugated methyl ester **22b** by treatement with *n*-BuLi/THF at −78 °C and with $ClCO_2Me$ at 0 °C. The ester **22b** was thus obtained in 85% yield (scheme 5).



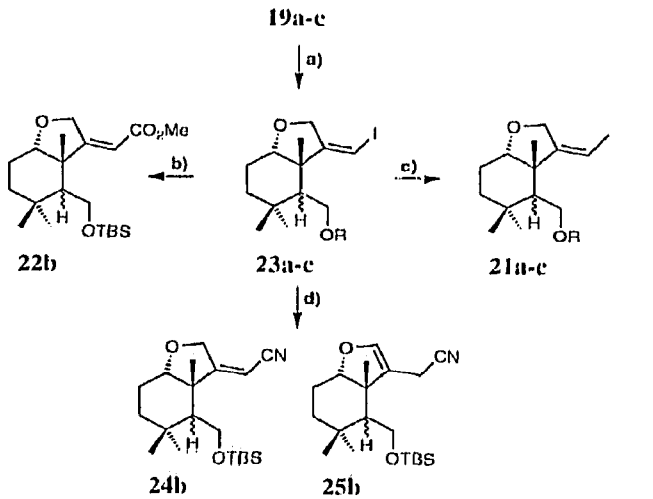
a) HCl 1 N, THF 1:1, 20 °C, **19a–c** → **20a–c** 95% or *n*-BuLi, THF, −78 °C, NH_4Cl, THF, 0 °C, **19b** → **20b** 95%, **19c** → **20c** 90%. b) *n*-BuLi, THF, −78 °C, MeI, −78 °C, **19b** → **21b** 76% **19c** → **21c** 75%. c) *n*-BuLi, THF, −78 °C, $ClCO_2Me$, THF, 0 °C, **19b** → **22b** 85%.

Scheme 5

In order to prevent the protodestannylation reaction of stannanes **19a–c**, we decided to run the homologation reactions from the corresponding vinyl iodides **23a–c**. After a halogen-metal exchange [18] the stannanes **19a–c** were converted into the vinyl iodides **23a–c** in quantitative yield (>95%).

Starting from **23b**, the halogen-metal exchange was carried out with *n*-BuLi/THF at −78 °C, but reaction with $ClCO_2Me$ gave the destannylated compound **20b** in 83% yield and the expected conjugated ester **22b** was isolated in 17% yield (scheme 6). When the halogen-metal exchange was carried out with 2 equiv of *tert*-BuLi in DME at −78 °C, the reaction with $ClCO_2Me$ afforded **22b** in 57% yield together with the methylidene derivative **20b** (34% yield).

For this halogen-metal exchange, we tried to use MeLi instead of *n*-BuLi or *tert*-BuLi. When **23b** was reacted with MeLi (1.5–1.8 equiv) further work-up with NH_4Cl gave the ethylidene compound **21b** in 87% yield (scheme 6). In these conditions the halogen-metal exchange produced the vinyl lithium and 1 equiv of MeI which reacted together to give **21b** in high yield. Thus using MeLi, further reaction with $ClCO_2Me$ led to the conjugated esters **22b** in only 13% yield; the major compound isolated was ethylidene **21b** in 83% yield. The reaction with MeI, generated in situ, was



a) I_2, Et_2O, 20 °C, 3 h, **19a–c** → **23a–c** 95%. b) **23b**, *n*-BuLi (1.1 equiv), THF, −78 °C, 1 h, $ClCO_2Me$ 0 °C → 20 °C, 2 h, → **22b** 17%, → **20b** 83% or **23b**, *tert*-BuLi (2 equiv), DME, −78 °C, $ClCO_2Me$ 0 °C → 20 °C, 2 h, → **22b** 57%, → **20b** 34% or **23b**, MeLi (1.5 equiv), THF, −78 °C, $ClCO_2Me$ 0 °C → 20 °C, 2 h, → **22b** 13%, → **21b** 83%. c) MeLi (1.5 equiv), THF, −78 °C, NH_4Cl, 0 °C → 20 °C, 2 h, **23b** → **21b** 87%, **23c** → **21c** 80%. d) **23b**, $Pd(PPh_3)_4$, 18-crown-6, KCN, benzene, 70 °C → **24b** 47%, → **25b** 16%.

Scheme 6

fast enough to occur to some extent during the halogen-lithium exchange before further addition of $ClCO_2Me$.

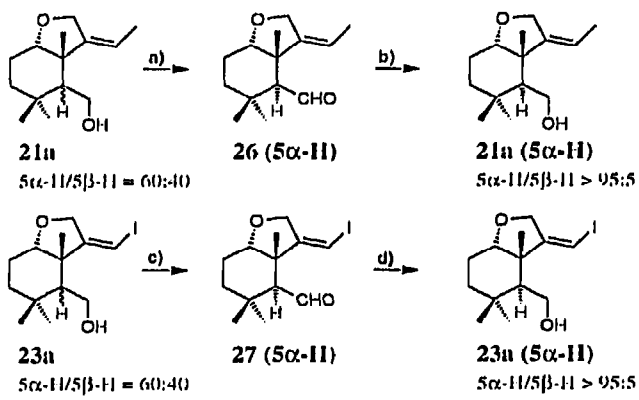
Vinyl iodides undergo Pd(0)-catalyzed reactions with vinylstannanes [19]. More interestingly, we applied the coupling reaction between a vinyl iodide and KCN [20] to our vinyl iodide **23b**. Compound **23b** was treated with KCN in benzene at 70 °C in the presence of $Pd(PPh_3)_4$ and 18-crown-6 and gave the cyano derivatives, isomers **24b** and **25b**, in 47 and 16% yields, respectively. The basic conditions used here led to the isomerization of **24b** into **25b**.

Thus starting from the vinylstannanes **19a–c** or the corresponding iodides **23a–c** we were able to prepare **21a–c**, **22a–c**, **24b** and **25b**, the key intermediates for our synthetic approach to forskolin **1**.

Final preparation of hexahydrobenzofuran derivatives 7 and 10

In this work, the hexahydrobenzofurans **19a–c** were formed via a radical cyclization as a ca 1:1 mixture of the 5α-H and 5β-H epimers. The two isomers were not separately isolated and a synthetic approach of forskolin **1** could not be considered in this way. In order to recover a pure 5α-H hydrobenzofuran isomer we examined the isomerization of compounds derived from **21a** and **23a**.

Starting from a 60:40 mixture of 5α-H and 5β-H **21a**, oxidation of the primary alcohol with the Dess-Martin reagent [21] gave the two isomeric aldehydes **26** (5α-H/5β-H = 60:40) in 99% yield. Equilibration of the mixture of isomers **26** (K_2CO_3, MeOH, Δ) afforded the aldehyde **26** (5α-H) in 94% yield, and further reduction then gave the pure alcohol **21a** (5α-H) in 86% yield.



a) (i) Dess-Martin, CH_2Cl_2, 20 °C, 99%. (ii) K_2CO_3, MeOH, Δ, 94%. b) $NaBH_4$, MeOH, 0 °C, 86%. c) (i) PCC, celite, CH_2Cl_2, 20 °C, 87%. (ii) K_2CO_3, MeOH, Δ, 95%. d) $NaBH_4$, MeOH, 0 °C, 87%.

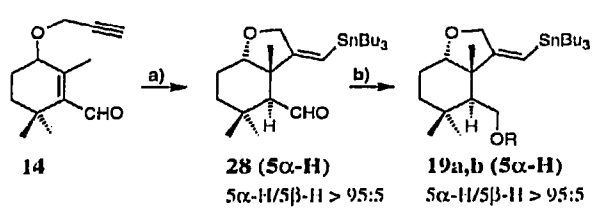
Scheme 7

Using the same method, the 60:40 mixture of 5α-H and 5β-H iodo derivatives **23a** was oxidized using PCC [22] into the aldehydes **27**. These were then isomerized by treatment with base into the expected isomer **27** (5α-H). Iodide **23a** (5α-H) was obtained as the pure 5α-H isomer after $NaBH_4$ reduction of the aldehyde function (scheme 7).

During this study for obtaining the desired 5α-H configuration of the hydrobenzofuran derivatives **4** we examined the radical cyclization of aldehyde **14** (Bu_3SnH/AIBN/toluene/Δ). The cyclization of **14** into *cis*-hydrobenzofuran **28** occurred in 87% yield and after reduction of **28** ($NaBH_4$/MeOH) the alcohol **19a** (5α-H) was obtained pure in 85% yield (scheme 8). This sequence gave us an efficient access to the hydrobenzofuran derivatives **4**, **21a–c**, **23a–c**, **24b** and **25b** as pure 5α-H isomers.

Having solved the problem of the 5α-H configuration of the synthetic intermediates, we started the synthesis of the ethylidene compound **7**. Starting from the pure aldehyde **26** (5α-H) addition of lithium acetylide ethylenediamine complex gave **29** in 70% yield. Addition of lithiotrimethylsilylacetylene to aldehyde **26** provided **30** in 84% yield. For the two derivatives **29** and **30** the configuration at the C6 center was shown [23] to be opposite to the required configuration of forskolin **1**.

In order to prepare the 6β-OH isomer **7**, the oxidation of **29** with the Dess–Martin reagent gave ketone **31** which was reduced by $NaBH_4$/MeOH. Surprisingly,



a) Bu_3SnH (1.7 equiv, 0.05 M in toluene), AIBN 10% mol, reflux 2 h, 87% (5α-H/5β-H = 98:2). b) $NaBH_4$, MeOH, 0 °C, 85%.

Scheme 8

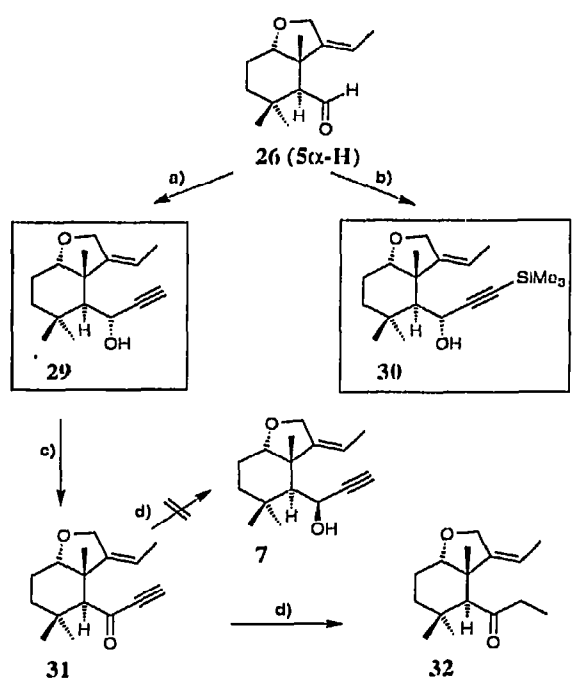
the alcohol **7** was not obtained; $NaBH_4$ reacted with **31** to give the ethyl ketone **32** in 74% yield via a bis-1,4-reduction (scheme 9). The formation of **32** only may reflect steric hindrance at C6 which disfavors 1,2-addition at the 6 position.

In spite of this disappointing result, we decided to pursue our scheme and the previous synthetic approach of forskolin **1** via C7-C8 bond formation (see scheme 2) was performed with derivatives **29** and **30**. We envisaged an inversion of the 6α-OH function later in the synthesis.

For the synthetic approach involving C6-C7 bond formation, the derived enolate of **22b** (LDA/HMPA/THF, −78 °C) was then quenched with MeI to cleanly afford the expected dihydrofuran **33b** in 95% yield (scheme 10a).

Application of this sequence to the cyano compound **24b** also provided the deconjugated derivative **34b** in 84% yield. For the two compounds **33b** and **34b**, introduction of the methyl group in the C8 position was stereospecific, probably due to the bent structure of the *cis*-hexahydrobenzofurans during the quenching of the lithio intermediate in an *exo* less hindered pathway.

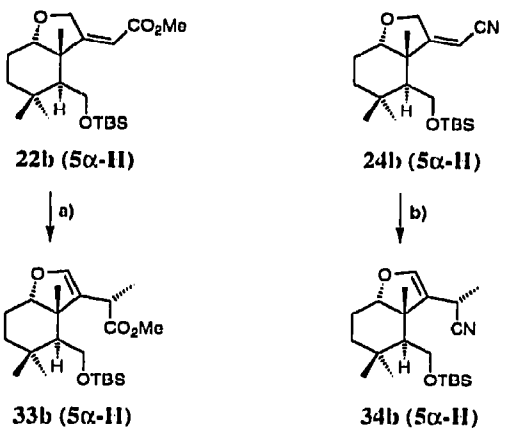
The diol **10** was prepared from compound **33b** (5α-H). Removal of the silyl group afforded the lactone **35** in 95% yield. A further reduction of **35** gave the expected diol **10** (5α-H) in 91% yield. The diol **10** (5α-H) was also obtained in 60% overall yield by an alternate sequence: reduction of the ester into **36b** (5α-H), and further removal of the silyl group (scheme 10b).



a) C≡CLi·TMEDA, THF, 0 °C, 70%. b) $Me_3SiC{\equiv}CLi$, THF, 0 °C, 84%. c) Dess–Martin, CH_2Cl_2, 20 °C, 85%. d) $NaBH_4$, MeOH, 0 °C, → **32** 74%.

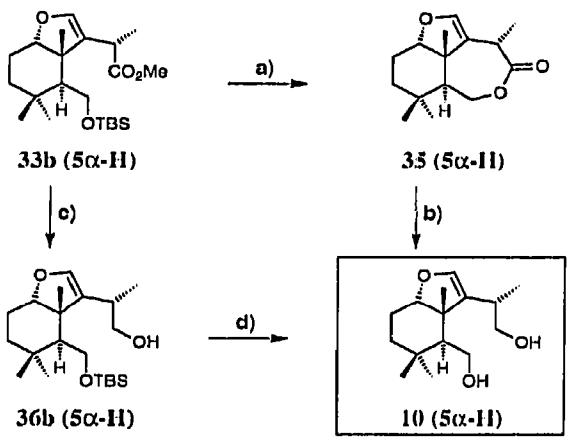
Scheme 9

a



a) LDA, HMPT, THF, −78 °C, MeI, −78 °C → 20 °C, 95%. b) LDA, HMPT, THF, −78 °C, MeI, −78 °C, 84%.

b



a) TBAF, THF, 20 °C, 12 h, 95%. b) LAH, THF, 0 °C, 1 h, 91%. c) LAH, Et_2O, 0 °C, 1 h, 70%. d) TBAF, THF, 20 °C, 18 h, 83%.

Scheme 10

Conclusion

During this work an efficient radical cyclization promoted by Bu_3SnH was used for the preparation of *cis*-hydrobenzofuran derivatives **4** as versatile key intermediates for a synthetic approach to forskolin **1**. Transmetallation and Pd(0)-catalyzed coupling reactions of stannyl compounds **19a–c** allowed us to prepare the suitable functionalized compounds **29**, **30** and **10** which were used in radical cyclization reactions for the synthesis of the AB ring system of (±)-forskolin **1**.

Experimental section

Physical data and spectroscopic measurements

Melting points were determined with a Reichert apparatus and are uncorrected. Boiling points are uncorrected. Infrared spectra were obtained on a Perkin-Elmer FT 1600 instrument using either NaCl salt plates (film) or NaCl cells (in the specified solvent) and are reported in terms of frequency of absorption (ν, cm^{-1}).

^1H NMR spectra were recorded with a Bruker WP 200 (200 MHz) or a Bruker AM 400 (400 MHz) instrument. The solvent and the instrument are specified for each product. The chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform at 7.28 ppm. Data are reported as follows: chemical shift, multiplicity (recorded as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet)), integration, coupling constants (J) in hertz (Hz) and assignment. $^1H,^1H$-COSY and $^1H,^1H$-NOESY experiments were routinely carried out to ascertain ^1H-^1H connectivities and configuration assignments, respectively.

^{13}C NMR spectra were recorded with the same instruments at 50.3 and 100.6 MHz respectively. The chemical shifts are given in parts per million (ppm), the central peak of deuterochloroform being referenced at 77.14 ppm. J-modulated spin-echo technique (J-mod) experiments were used for the determination of CH multiplicities. When necessary, ^{13}C NMR spectra were assigned with the aid of HETCOR experiments.

Mass spectra were obtained with a Hewlett Packard HP5989B spectrometer via either direct introduction or GC-MS, by chemical ionization (CI) with ammonia (NH_3) or methane (CH_4) or by electronic impact (EI). Microanalyses were performed by the analytical laboratory of the Institut de chimie des substances naturelles in Gif-sur-Yvette.

Usual procedures

All non-aqueous reactions were conducted under argon, in oven (120 °C) or flame-dried glassware.

Organolithium reagents were titrated using the procedure of SC Watson and JF Eastham [24]. The solution to be titrated was added dropwise via a syringe at 0 °C in a well-dried 25 mL round-bottomed flask containing a well-stirred solution of 1,2-phenanthroline or 2,2'-biquinoline (ca 5 mg), THF or diethyl ether (10 mL) and anhydrous benzyl alcohol (0.5 mL, 4.8 mmol). The addition was stopped after the colorless mixture turned dark-red.

Bulb-to-bulb distillations were performed with a Buchi GKR 51 Kugelrohr apparatus.

Solvent distillation

THF, diethyl ether, benzene and toluene were distilled over sodium benzophenone. Dichloromethane and amines were distilled over calcium hydride. DMF was distilled from magnesium sulfate under reduced pressure. Ethanol and methanol were distilled over magnesium.

Chromatography

Thin layer chromatography (TLC) was performed on precoated plates of silica gel 60F 254 (Merck). Visualization was accomplished with UV light then 7–10% ethanolic phosphomolybdic acid solution followed by heating was used as developing agent.

Flash chromatography was performed on silica gel Merck SI 60 (0.040–0.063 mm). The solvents used were not distilled except petroleum ether.

^1H and ^{13}C NMR of organostannyl compounds

For large Sn-^1H or Sn-^{13}C coupling constants (250–450 Hz), the central signal was associated with two close pairs of satellites corresponding to both ^{117}Sn and ^{119}Sn isotopes; in this case two different coupling constants were reported. For small Sn-^1H and Sn-^{13}C (<100 Hz), the two pairs

of satellites collapse and only one coupling constant was observed.

Nomenclature

IUPAC nomenclature is used for all compounds. Because racemic derivatives are described the relative stereochemistry is expressed using asterisks, and the first stereocenter is assigned as R^*. In some cases and to be in agreement with the forskolin numbering, 5α-H and 5β-H assignments are used.

[3E(1R,2R*S*,3R*S*)]-4-(2,3-Epoxy-2,6,6-trimethylcyclohexyl)but-3-en-2-one* **11**

To a solution of commercial α-ionone **5** (15 g, 78 mmol) in CH_2Cl_2 (200 mL) at 0 °C was added *m*-chloroperbenzoic acid (86%, 23 g, 93 mmol, 1.2 equiv). The reaction mixture was stirred at 0 °C for 4 h and filtered. The white solid was washed with CH_2Cl_2 (2 × 200 mL). The resulting organic phases were washed with a saturated aqueous $NaHCO_3$ solution (3 × 100 mL), then brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo to furnish a 8:2 mixture of diastereomeric epoxides **11** (13.3 g, 82% yield) which were used in the next step without further purification.

IR (NaCl) ν 2 960, 1 723, 1 670, 1 622, 1 436, 1 365, 1 253, 1 224, 1 094, 990, 901.

• *Major isomer: [3E(1R*,2S*,3R*)]-4-(2,3-epoxy-2,6,6-trimethylcyclohexyl)but-3-en-2-one*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.67–2.04 (m, 4H, H_2-4′, H_2-5′), 0.68, 0.86 and 1.18 (3s, 9H, $3CH_3$, CH_3-2′, $2CH_3$-6′), 2.03 (d, J = 10.0 Hz, 1H, H-1′), 2.23 (s, 3H, CH_3, CH_3-1), 3.04 (broad s, 1H, H-3′), 6.03 (d, J = 16.0 Hz, 1H, H-3), 6.7 (dd, J = 16.0, 10.0 Hz, 1H, H-4).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.7 (C-5′), 24.0 (CH_3), 26.4 (CH_3), 27.4 (CH_3), 27.8 (CH_3), 28.5 (C-4′), 31.2 (C-6′), 52.4 (C-1′), 59.4 (C-3′), 58.7 (C-2′), 133.9 (C-3), 146.3 (C-4), 198.5 (C-2).

• *Minor isomer: [3E(1R*,2R*,3S*)]-4-(2,3-epoxy-2,6,6-trimethylcyclohexyl)but-3-en-2-one*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.82 and 0.88 (2s, 6H, $2CH_3$, $2CH_3$-6′), 1.21 (s, 3H, CH_3, CH_3-2′), 1.00–2.01 (m, 5H, H-1′, H_2-4′, H_2-5′), 2.31 (s, 3H, CH_3, H_3-1), 3.03 (t, J = 3.0 Hz, 1H, H-3′), 6.11 (d, J = 18.0 Hz, 1H, H-3), 6.72 (dd, J = 18.0, 10.0 Hz, 1H, H-4).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.5 (C-5′), 23.4 (CH_3), 27.2 (CH_3), 28.5 (C-4′), 29.5 (CH_3), 32.0 (CH_3), 32.5 (C-6′), 48.0 (C-1′), 54.1 (C-3′), 59.7 (C-2′), 134.1 (C-3), 145.1 (C-4), 198.5 (C-2).

MS (CI, NH_3) m/z 226 ($MH^+ + NH_3$), 209 (MH^+), 191, 179, 165, 163, 151, 139, 123, 109, 95, 81, 79.

(1R,2R*S*,3R*S*)-2,3-Epoxy-2,6,6-trimethylcyclohexane-1-carbaldehyde* **12**

A solution of the mixture of diastereomeric epoxides **11** (13.3 g, 64 mmol) in CH_2Cl_2 (180 mL) and MeOH (20 mL) was treated with a stream of ozone at −78 °C until it turned blue. Oxygen was then bubbled through the solution until the blue color disappeared and then the solution was flushed with argon. The reaction mixture was treated with a 50% aqueous acetic acid solution (60 mL) and Zn powder (7 g, 100 mmol, 1.3 equiv) was added cautiously at −78 °C and the heterogeneous mixture was stirred for 4 h at 20 °C. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 200 mL). The combined organic phases were washed with a saturated aqueous $NaHCO_3$ solution (3 × 100 mL), then brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give an 8:2 mixture of diastereomeric epoxyaldehydes **12** (9.2 g, 86% yield) as an oily residue which was used in the next step without further purification.

IR (CH_3Cl) ν 2 959, 2 736, 1 718, 1 674, 1 448, 1 381, 1 368, 1 232, 1 180, 1 145, 1 101, 806, 736.

• *Major isomer: (1R*,2S*,3R*)-2,3-epoxy-2,6,6-trimethylcyclohexane-1-carbaldehyde*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.93–2.42 (m, 5H, H-1, H_2-4, H_2-5′), 0.93, 0.93 and 1.30 (3s, 9H, $3CH_3$, CH_3-2, $2CH_3$-6), 3.04 (broad s, 1H, H-3), 9.63 (d, J = 5.0 Hz, 1H, C*H*O).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.3 (C-5), 24.3 (CH_3), 26.4 (CH_3), 27.7 (CH_3), 28.9 (C-4), 30.0 (C-6), 57.4 (C-1), 59.0 (C-3), 57.0 (C-2), 203.4 (CHO).

• *Minor isomer: (1R*,2R*,3S*)-2,3-epoxy-2,6,6-trimethylcyclohexane-1-carbaldehyde*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.88–2.42 (m, 5H, H-1, H_2-4, H_2-5), 1.03, 1.10, and 1.11 (3s, 9H, $3CH_3$, CH_3-2, $2CH_3$-6), 3.0 (broad s, 1H, H-3), 9.73 (d, J = 5.4 Hz, 1H, C*H*O).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.4 (C-5), 22.3 (CH_3), 22.8 (CH_3), 27.8 (CH_3), 29.1 (C-4), (C-6, not observed), (C-1, not observed), 61.6 (C-3), (C-2, not observed), 202.8 (CHO).

MS (CI, NH_3) m/z 186 ($MH^+ + NH_3$), 169 (MH^+), 151, 123, 107, 95, 79.

(±)-3-Hydroxy-2,6,6-trimethylcyclohex-1-ene-1-carbaldehyde **13**

Pyrrolidine (12 mL, 140 mmol, 2.5 equiv) was added to a solution of epoxyaldehydes **12** (9.2 g, 55 mmol) in diethyl ether (50 mL). The reaction mixture was stirred at 20 °C for 3 h and then partitioned between a 1 N aqueous hydrochloric acid solution (50 mL) and ethyl acetate (50 mL). The phases were separated and the aqueous phase was extracted with 3 × 100 mL ethyl acetate. The combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo to give hydroxyaldehyde **13** (7.6 g, 83% yield), which was obtained as an oily residue and used in the next step without further purification.

IR ($CHCl_3$) ν 3 414, 2 939, 2 867, 1 674, 1 606, 1 455, 1 380, 1 299, 1 123, 1 079, 1 041, 667.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.92–1.19 (m, 4H, H_2-4, H_2-5), 1.13 and 1.18 (2s, 6H, $2CH_3$, $2CH_3$-6), 2.16 (s, 3H, CH_3, CH_3-2), 3.10 (m, 1H, OH), 4.08 (t, J = 5.6 Hz, 1H, H-3), 10.12 (s, 1H, C*H*O).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 15.6 (CH_3-2), 27.3 (CH_3-4), 27.5 (CH_3-4), 28.1 (C-5), 33.6 (C-6), 36.0 (C-4), 70.7 (C-3), 141.4 (C-1), 153.9 (C-2), 193.8 (CHO).

MS (CI, NH_3) m/z 186 ($MH^+ + NH_3$), 169 (MH^+), 168, 151, 139, 123, 107, 93, 72.

(±)-3-(Prop-2-ynyloxy)-2,6,6-trimethylcyclohex-1-ene-1-carbaldehyde **14**

To a solution of the crude hydroxyaldehyde **13** (10 g, 59 mmol) in propargyl bromide (80% weight in toluene, 16.4 mL, 147 mmol, 2.5 equiv) was added a 60% aqueous NaOH solution (250 mL), followed by $Bu_4N^+I^-$ (2.2 g, 5.9 mmol, 0.1 equiv). The resulting brown solution was stirred for 17 h at 20 °C and then diluted with diethyl ether (250 mL). The phases were separated and the aqueous layer

was extracted with diethyl ether (3 × 100 mL). The combined organic phases were washed with a 6 N aqueous HCl solution (3 × 50 mL), then with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave compound **14** (12.1 g, 99% yield) as a yellow oil.

IR ($CHCl_3$) ν 3 300, 2 938, 2 867, 2 250, 1 674, 1 610, 1 456, 1 346, 1 265, 1 059, 915.

^1H NMR ($CDCl_3$, 200 MHz) δ 1.03–1.78 (m, 4H, H_2-4, H_2-5), 1.10, 1.14, 2.11 (3s, 9H, $3CH_3$, CH_3-2, $2CH_3$-6), 2.44 (t, J = 2.4 Hz, 1H, H-3'), 3.90 (t, J = 4.8 Hz, 1H, H-3), 4.13 (dd, J = 16.0, 2.4 Hz, 1H, Ha-1'), 4.25 (dd, J = 16.0, 2.4 Hz, 1H, Hb-1'), 10.08 (s, 1H, CHO).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 15.7 (CH_3-2), 27.1 and 27.7 ($2CH_3$-5), 23.3 (C-5), 33.5 (C-6), 35.8 (C-4'), 56.5 (C-1'), 74.6 (C-3'), 76.5 (C-2'), 76.8 (C-1), 142.6 and 150.4 (C-2, C-3), 193.2 (*C*HO).

MS (CI, NH_3) m/z 224 ($MH^+ + NH_3$), 207 (MH^+), 184, 168, 151, 140.

(±)-3-(Hydroxymethyl)-2,4,4-trimethylcyclohex-2-en-1-ol **15a**

To a cooled solution (0 °C) of crude hydroxyaldehyde **13** (7.6 g, 45 mmol) in methanol (100 mL) was added sodium borohydride (430 mg, 11.3 mmol, 0.25 equiv). After 30 min, a further 0.25 equiv of sodium borohydride was added to complete the reaction. The reaction mixture was treated 30 min later with of a 1 N aqueous hydrochloric acid solution (20 mL) and concentrated in vacuo. The mixture was partitioned between water (50 mL) and ethyl acetate (100 mL), the phases were separated and the aqueous phase was extracted with ethyl acetate (3 × 100 mL). The combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave diol **15a** (5.8 g, 75% yield) as a white solid.

Mp: 109 °C.

IR (KBr) ν 3 259, 2 932, 1 486, 1 360, 1 030, 1 001, 869.

^1H NMR ($CDCl_3$, 200 MHz) δ 0.70–1.88 (m, 6H, H_2-5, H_2-6, 2OH), 0.98 and 1.09 (2s, 6H, $2CH_3$, $2CH_3$-4), 1.86 (s, 3H, CH_3, CH_3-2), 3.95 (t, J = 4.7 Hz, 1H, H-1), 4.08 (d, J = 12.5 Hz, 1H, Ha-1'), 4.12 (d, J = 12.5 Hz, 1H, Hb-1').

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 16.7 (CH_3-2), 27.3 (CH_3-4), 28.2 (C-5), 28.6 (CH_3-4), 34.7 (C-4), 34.9 (C-6), 59.1 (C-1'), 70.2 (C-1), 134.6, 141.5 (C-2, C-3).

MS (CI, NH_3) m/z 188 ($MH^+ + NH_3$), 171 (MH^+), 170, 153, 109, 95.

Anal calc for $C_{10}H_{18}O_2$, 170.24: C, 70.54; H, 10.66. Found: C, 70.66; H, 10.65.

(±)-3-{[(tert-Butyldimethylsilyl)oxy]methyl}-2,4,4-trimethylcyclohex-2-en-1-ol **15b**, *(±)-3-[(tert-butyldimethylsilyl)oxy]-2,6,6-trimethylcyclohex-1-ene-1-methanol* **16** *and (±)-6-[(tert-butyldimethylsilyl)oxy]-2-{[(tert-butyldimethylsilyl)oxy]methyl}-1,3,3-trimethylcyclohexene* **17**

To a cooled solution (0 °C) of diol **15a** (1.0 g, 5.9 mmol) and imidazole (1.0 g, 14 mmol, 2.5 equiv) in 2 mL of DMF was added dropwise a solution of *tert*-butyldimethylsilyl chloride (980 mg, 6.5 mmol, 1.1 equiv) in 2 mL of DMF. After stirring at 0 °C for 4 h, the reaction mixture was allowed to warm up to room temperature and stirred overnight at 20 °C. The reaction mixture was partitioned between 10 mL of a 1 N aqueous hydrochloric acid solution and 50 mL of ethyl acetate. The phases were separated and the aqueous layer extracted with 3 × 50 mL of ethyl acetate. The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave the expected monoprotected alcohol **15b** (1.02 g, 61% yield), the isomeric derivative **16** (151 mg, 9% yield), disilylated compound **17** (266 mg, 11% yield) and starting material **15a** (88 mg, 9% yield).

- *Compound* **15b**

IR ($CHCl_3$) ν 3 382, 2 928, 2 244, 1 660, 1 470, 1 361, 1 255, 1 056, 909, 835, 774, 734, 648.

^1H NMR ($CDCl_3$, 200 MHz) δ 0.09 [s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.91 [s, 9H, $3CH_3$, $SiC(CH_3)_3$], 0.91–1.98 (m, 5H, H_2-5, H_2-6, OH), 1.00, 1.06 and 1.81 (3s, 9H, $3CH_3$, CH_3-2, $2CH_3$-4), 3.94 (t, J = 4.5 Hz, 1H, H-1), 4.08 (broad s, 2H, H_2-1').

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.5 [$2CH_3$, $Si(CH_3)_2$], 16.4 (CH_3-2), 18.3 [C, $SiC(CH_3)_3$], 26.0 [$3CH_3$, $SiC(CH_3)_3$], 27.3 (CH_3-4), 28.2 (CH_3-4), 28.6 (C-5), 34.4 (C-4), 34.8 (C-6), 59.1 (C-1'), 69.9 (C-1), 133.2 and 140.7 (C-2, C-3).

MS (CI, CH_3) m/z 302 ($MH^+ + NH_3$), 284 (M^+), 267.

Anal calc for $C_{16}H_{32}O_2Si$, 284.50: C, 67.54; H, 11.34. Found: C, 67.44; H, 11.22.

- *Compound* **16**

IR ($CHCl_3$) ν 3 385, 2 930, 2 240, 1 665, 1 470, 1 365, 1 265, 1 105, 905, 845, 778, 735, 658.

^1H NMR ($CDCl_3$, 200 MHz) δ 0.10 [s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.91 [s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.01–1.92 (m, 5H, H_2-4, H_2-5, OH), 1.03, 1.07 and 1.78 (3s, 9H, $3CH_3$, CH_3-2, $2CH_3$-6), 4.0 (t, J = 5.7 Hz, 1H, H-3), 4.09 (d, J = 10.0 Hz, 1H, H-1'a), 4.16 (d, J = 10.0 Hz, 1H, H-1'b).

MS (CI, CH_3) m/z 302 ($MH^+ + NH_3$), 284 (MH^+), 267.

- *Compound* **17**

IR ($CHCl_3$) ν 2 955, 2 856, 1 660, 1 471, 1 462, 1 360, 1 253, 1 048, 834, 772.

^1H NMR ($CDCl_3$, 200 MHz) δ 0.09, 0.10, 0.10 and 0.10 [4s, 12H, $4CH_3$, $2Si(CH_3)_2$], 0.91 [s, 18H, $6CH_3$, $2Si(CH_3)_3$], 0.84–1.89 (m, 4H, H_2-4, H_2-5), 1.01, 1.03 and 1.73 (3s, 9H, $3CH_3$, CH_3-1, $2CH_3$-3), 4.02 (d, J = 10.7 Hz, 1H, Ha-1'), 4.03 (m, 1H, H-6), 4.15 (d, J = 10.7 Hz, 1H, Hb-1').

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.2, −4.4 and −3.9 [$4CH_3$, $2Si(CH_3)_2$], 16.2 (CH_3-1), 18.3 and 18.5 [2C, $2SiC(CH_3)_3$], 26.1 [$6CH_3$, $2SiC(CH_3)_3$], 28.1 and 28.3 ($2CH_3$-3), 29.7 (C-4), 34.8 (C-3), 36.8 (C-5), 59.4 (C-1'), 71.8 (C-6), 134.6 and 139.1 (C-1, C-2).

MS (CI, NH_3) m/z 399 (MH^+), 385, 341, 267, 265, 135.

(±)-2,4,4-Trimethyl-3-{[(triphenylmethyl)oxy]methyl}-cyclohex-2-en-1-ol **15c**

To a solution of diol **15a** (6.0 g, 35 mmol) in dry CH_2Cl_2 (30 mL) was added triethylamine (18 mL, 130 mmol, 3.7 equiv) followed by triphenylmethyl chloride (10.8 g, 38.8 mmol, 1.1 equiv) and DMAP (310 mg, 18 mmol, 0.05 equiv). The resulting solution was stirred at reflux for 3 h and after cooling to 0 °C, the reaction was quenched with a 2 N aqueous HCl solution (50 mL). The phases were separated and the aqueous phase extracted with diethyl ether (3 × 100 mL). The combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and

concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave the monoprotected diol **15c** (11.2 g, 77% yield).

IR ($CHCl_3$) ν 3 337, 3 058, 2 917, 1 597, 1 446, 1 366, 1 132, 1 044, 898, 699.

^1H NMR ($CDCl_3$, 200 MHz) δ 0.97–1.96 (m, 4H, H_2-5, H_2-6), 1.01, 1.01, 1.78 (3s, 9H, $3CH_3$, CH_3-2, $2CH_3$-4), 2.2 (s, 1H, OH), 3.69 (d, J = 10.0 Hz, 1H, Ha-1′), 3.76 (d, J = 10.0 Hz, 1H, Hb-1′), 3.98 (t, J = 4.5 Hz, 1H, H-1), 7.24 (m, 9H, Ar-H), 7.62 (m, 6H, Ar-H).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 16.9 (CH_3-2), 27.8 (CH_3-4), 28.7 (CH_3-4), 29.0 (C-5), 34.9 (C-4), 35.7 (C-6), 60.4 (C-1′), 70.7 (C-1), 87.4 [*C*($Ph)_3$], 127.0 (3CH, Ar), 127.7 (6CH, Ar), 129.3 (6CH, Ar), 134.5, 139.1 (C-2, C-3), 144.3 (3C, Ar).

MS (Cl, NH_3) m/z 413 (MH^+), 298, 258, 244, 165, 105, 35.

Anal calc for $C_{29}H_{32}O_2$, 412.55: C, 84.42; H, 7.82. Found: C, 84.38; H, 7.85.

(±)-2-Hydroxymethyl-1,3,3-trimethyl-6-[(prop-2-ynyl)-oxy]cyclohexene **18a**

• *Procedure A*

To a solution of aldehyde **14** (7.6 g, 37 mmol) in methanol (100 mL) at 0 °C was added sodium borohydride (340 mg, 9.0 mmol, 0.25 equiv). After 30 min, the same amount of sodium borohydride was added to complete the reaction and the reaction mixture was treated 30 min later with a 1 N aqueous hydrochloric acid solution (20 mL) and concentrated in vacuo. The mixture was partitioned between water (50 mL) and ethyl acetate (100 mL), the phases were separated and the aqueous phase was extracted with ethyl acetate (3 × 100 mL). The combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and the resulting mixture was concentrated in vacuo. Purification by flash chromatography on silica gel gave alcohol **18a** (5.8 g, 75% yield) as a colorless oil.

• *Procedure B*

To a solution of silyl ether **18b** (see below, 1.0 g, 3.1 mmol) in acetonitrile (15 mL) at 20 °C was added a 48% aqueous solution of HF (5 mL). The resulting cloudy mixture was stirred at 20 °C for 1.5 h and quenched with a saturated aqueous $NaHCO_3$ solution (75 mL). The phases were separated and the aqueous layer was extracted with diethyl ether (3 × 75 mL). The combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave alcohol **18a** (432 mg, 67% yield) as a colorless oil.

• *Procedure C*

To a solution of **18c** (see below, 590 mg, 1.3 mmol) in THF (5 mL)/H_2O (2 mL)/AcOH (4 mL) at 20 °C was added TsOH (25 mg, 0.1 mmol, 0.1 equiv). The resulting mixture was stirred at 65 °C for 3 h, cooled at 20 °C and then the reaction was quenched with a saturated aqueous $NaHCO_3$ solution (25 mL) and diluted with diethyl ether (50 mL). The phases were separated and the aqueous layer was extracted with diethyl ether (3 × 25 mL). The combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave alcohol **18a** (130 mg, 48% yield) as a colorless oil.

IR ($CHCl_3$) ν 3 441, 3 303, 2 933, 1 263, 1 632, 1 446, 1 362, 1 349, 1 244, 1 060, 916, 850, 732.

^1H NMR ($CDCl_3$, 200 MHz) δ 1.05–1.78 (m, 5H, H_2-4, H_2-5, OH), 0.94, 1.01 and 1.78 (3s, 9H, $3CH_3$, CH_3-1, $2CH_3$-3), 2.39 (t, J = 2.4 Hz, 1H, CC*H*), 3.76 (t, J = 4.5 Hz, 1H, H-6), 4.07 (m, 2H, H_2-1″), 4.09 (dd, J = 15.7, 2.4 Hz, 1H, Ha-1′), 4.19 (dd, J = 15.7, 2.4 Hz, 1H, Hb-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 16.6 (CH_3-2), 28.1, 26.9 ($2CH_3$-4), 23.4 (C-5), 34.3 (C-6), 34.6 (C-4), 58.5 (C-1″), 56.0 (C-1′), 74.4 (C-3′), 76.2 (C-1), 80.4 (C-2′), 132.2 and 142.4 (C-2, C-3).

MS (Cl, NH_3) m/z 226 ($MH^+ + NH_3$), 208, 191, 170, 153, 135, 123, 109, 95.

Anal calc for $C_{13}H_{20}O_2$, 208.29: C, 74.96; H, 9.68. Found: C, 74.88; H, 9.52.

(±)-2-{[(tert-Butyldimethylsilyl)oxy]methyl}-6-[(prop-2-ynyl)oxy]-1,3,3-trimethylcyclohexene **18b**

To a solution of alcohol **15b** (1.0 g, 3.5 mmol) in propargyl bromide 80% weight in toluene (980 μL, 8.9 mmol, 2.5 equiv) was added a 60% aqueous NaOH solution (25 mL), followed by $Bu_4N^+I^-$ (130 mg, 0.35 mmol, 0.1 equiv). The resulting brown solution was stirred for 17 h at 20 °C and diluted with diethyl ether (10 mL). The phases were separated and the aqueous layer extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with an aqueous 6 N HCl solution (50 mL), then with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave compound **18b** (1.1 g, 97% yield) as a yellow oil.

IR ($CHCl_3$) ν 3 331, 2 955, 2 928, 2 856, 1 471, 1 361, 1 255, 1 056, 836, 774, 665.

^1H NMR ($CDCl_3$, 200 MHz) δ 0.06 [s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.89 [s, 9H, $3CH_3$, $SiC(CH_3)_3$], 0.90–1.81 (m, 4H, H_2-4, H_2-5), 1.02, 1.04, 1.77 (3s, 9H, $3CH_3$, CH_3-1, $2CH_3$-3), 2.38 (t, J = 2.4 Hz, 1H, CCH), 3.63 (t, J = 4.6 Hz, 1H, H-6), 4.06 (d, J = 7.4 Hz, 1H, Ha-1″), 4.11 (d, J = 7.4 Hz, 1H, Hb-1″), 4.15 (dd, J = 15.9, 2.4 Hz, 1H, Ha-1′), 4.25 (dd, J = 15.9, 2.5 Hz, 1H, Hb-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.3 [$2CH_3$, $Si(CH_3)_2$], 18.3 [C, $SiC(CH_3)_3$], 16.6, 28.2, 27.3 (CH_3-1, $2CH_3$-3), 23.7 (C-4), 26.1 [$3CH_3$, $SiC(CH_3)_3$], 34.6 (C-3), 35.2 (C-5), 56.0 (C-1′), 59.2 (C-1″), 73.9 (*C*CH), 76.8 (C-1), 81.8 (*C*CH), 131.1 and 141.8 (C-1, C-2).

MS (Cl, NH_3) m/z 340 ($MH^+ + NH_3$), 323 (MH^+).

Anal calc for $C_{19}H_{34}O_2Si$, 322.52: C, 70.74; H, 10.62. Found: C, 70.56; H, 10.56.

(±)-1,3,3-Trimethyl-6-[(prop-2-ynyl)oxy]-2-{[(triphenylmethyl)oxy]methyl}cyclohexene **18c**

To a solution of alcohol **15c** (11 g, 27 mmol) in propargyl bromide 80% weight in toluene (7.4 mL, 67 mmol, 2.5 equiv) was added a 60% aqueous NaOH solution (200 mL), followed by $Bu_4N^+I^-$ (990 mg, 2.7 mmol, 0.1 equiv). The resulting brown solution was stirred for 17 h at 20 °C. The phases were separated and the aqueous layer was extracted with diethyl ether (3 × 200 mL). The combined organic phases were washed with an aqueous 6 N HCl solution (2 × 100 mL), then with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave compound **18c** (10.5 g, 87% yield) as a yellow oil.

IR ($CHCl_3$) ν 3 301, 3 058, 2 993, 1 596, 1 526, 1 490, 1 448, 1 343, 1 264, 1 132, 1 151, 1 044, 705, 632.

^1H NMR ($CDCl_3$, 200 MHz) δ 0.80–1.76 (m, 4H, H_2-4, H_2-5), 0.83, 0.88 and 1.51 (3s, 9H, $3CH_3$, CH_3-1, $2CH_3$-3), 2.32 (t, J = 2.4 Hz, 1H, CC*H*), 3.53 (d, J = 10.0 Hz, 1H, Ha-1″), 3.60 (d, J = 10.0 Hz, 1H, Hb-1″), 3.74 (t, J = 4.2 Hz, 1H, H-6), 4.05 (dd, J = 15.9, 2.4 Hz, 1H, H-1′a), 4.17 (dd, J = 15.9, 2.4 Hz, 1H, H-1′b), 7.11 (m, 9H, Ar-H), 7.48 (m, 6H, Ar-H).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 17.0 (CH_3-1), 24.0 (C-4), 27.7 and 28.5 ($2CH_3$-3), 34.7 (C-3), 35.7 (C-5), 56.0 (C-1′), 60.3 (C-1″), 73.8 (*C*CH), 77.1 (C-6), 80.9 (C-2′), 87.2 [*C*(Ph)$_3$], 126.9 (3CH, Ar), 127.6 (6CH, Ar), 129.6 (6CH, Ar), 132.7 and 140.0 (C-1, C-2), 144.3 (3C, Ar).

MS (Cl, NH_3) *m/z* 428, 411, 391, 369, 329, 299, 258, 244, 183, 153, 135, 105.

Anal calc for $C_{32}H_{34}O_2$, 450.59: C, 85.29; H, 7.61. Found: C, 85.12; H, 7.58.

(3Z,3aR,4R*S*,7aR*)-4-Hydroxymethyl-3-[(tributylstannyl)methylidene]-3a,5,5-trimethyl octahydrobenzofuran* **19a**

To a solution of compound **18a** (1.3 g, 6.2 mmol) in 620 mL of toluene was added AIBN (102 mg, 0.62 mmol, 0.1 equiv) and Bu_3SnH (2.84 mL, 10.5 mmol, 1.7 equiv). The mixture was stirred at reflux for 3 h. The oily residue obtained on removing toluene under reduced pressure was purified by flash chromatography on basic silica gel (pretreated with $NaHCO_3$) to give a 60:40 mixture of 5α-H and 5β-H diastereoisomeric compounds **19a** (2.72 g, 88% yield).

IR ($CHCl_3$) ν 3 453, 2 955, 2 869, 1 616, 1 456, 1 375, 1 149, 1 077, 1 042, 1 019, 946, 875, 801, 753.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.80–1.78 (m, 6H, H-4, H_2-6, H_2-7, OH), 0.78 (s, 3H, CH_3), 0.87 {t, J = 6.0 Hz, 9H, $3CH_3$, Sn[$(CH_2)_3CH_3$]$_3$}, 0.90 [t, J = 6.0 Hz, 6H, $3CH_2$, Sn(CH_2-)$_3$], 0.97 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 1.30–1.50 {m, 12H, $6CH_2$, Sn[$CH_2(CH_2)_2CH_3$]$_3$}, 3.46 (broad s, 1H, H-7a), 3.61 (dt, J = 12.0, 7.0 Hz, 1H, Ha-1″), 3.70 (dt, J = 12.0, 7.0 Hz, 1H, Hb-1″), 4.14 (dd, J = 13.2, 2.6 Hz, 1H, Ha-2), 4.58 (dd, J = 13.2, 2.6 Hz, 1H, Hb-2), 5.74 (t, J = 2.6 Hz, 1H, H-1′, J H-^{117}Sn = J H-^{119}Sn = 60.0 Hz).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.8 [$3CH_2$, Sn(CH_2-)$_3$, J C-^{117}Sn = 350.0 Hz, J C-^{119}Sn = 340.0 Hz], 14.0 {$3CH_3$, Sn[$CH_2(CH_2)_3CH_3$]$_3$}, 17.5 (CH_3), 23.6 (C-6), 26.3 (CH_3), 26.8 [$3CH_2$, Sn($CH_2CH_2CH_2CH_2$)$_3$, J C-^{117}Sn = J C-^{119}Sn = 57.0 Hz], 29.1 [$3CH_2$, Sn($CH_2CH_2CH_2CH_3$)$_3$, J C-^{117}Sn = J C-^{119}Sn = 26.0 Hz], 31.7 (C-5), 33.1 (CH_3), 35.2 (C-7), 45.3 (C-3a, J C-^{117}Sn = J C-^{119}Sn = 56.0 Hz), 48.2 (C-4), 61.0 (C-1″), 71.3 (C-2, J C-^{117}Sn = J C-^{119}Sn = 24.0 Hz), 84.5 (C-7a), 115.7 (C-1′), 168.7 (C-3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.80–1.78 (m, 5H, H_2-6, H_2-7, OH), 0.80 (s, 3H, CH_3), 0.87 {t, J = 6.0 Hz, 9H, $3CH_3$, Sn[$(CH_2)_3CH_3$]$_3$}, 0.90 [t, J = 6.0 Hz, 6H, $3CH_2$, Sn(CH_2-)$_3$], 0.98 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.30–1.50 {m, 12H, $6CH_2$, Sn[$CH_2(CH_2)_2CH_3$]$_3$}, 2.5 (m, 1H, H-4), 3.58 (t, J = 5.0 Hz, 1H, H-7a), 3.90 (dt, J = 11.7, 3.8 Hz, 1H, Ha-1″), 4.00 (dt, J = 11.7, 3.2 Hz, 1H, Hb-1″), 4.21 (dd, J = 12.5, 2.5 Hz, 1H, Ha-2), 4.30 (dd, J = 12.5, 2.5 Hz, 1H, Hb-2), 5.66 (t, J = 2.5 Hz, 1H, H-1′, J H-^{117}Sn = J H-^{119}Sn = 60.0 Hz).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.9 [$3CH_2$, Sn(CH_2-)$_3$, J C-^{117}Sn = 350.0 Hz, J C-^{119}Sn = 340.0 Hz], 13.8 {$3CH_3$, Sn[$(CH_2)_3CH_3$]$_3$}, 24.0 (C-6), 26.5 (CH_3), 27.3 [$3CH_2$, Sn($CH_2CH_2CH_2CH_2$)$_3$, J C-^{117}Sn = J C-^{119}Sn = 61.0 Hz], 28.8 (CH_3), 29.6 [$3CH_2$, Sn(CH_2CH_2-)$_3$, J C-^{117}Sn = J C-^{119}Sn = 28.0 Hz], 32.0 (CH_3), 33.7 (C-5), 35.4 (C-7), 50.6 (C-3a, J C-^{117}Sn = J C-^{119}Sn = 45.0 Hz), 56.4 (C-4), 62.7 (C-1″), 72.4 (C-2, J C-^{117}Sn = J C-^{119}Sn = 24.0 Hz), 85.8 (C-7a), 116.8 (C-1′), 165.9 (C-3).

MS (Cl, NH_3) *m/z* for major ^{120}Sn isotope 518 (MH^+ + NH_3), 501 (MH^+), 291.

(3Z,3aR,4R*S*,7aR*)-4-{[(tert-Butyldimethylsilyl)oxy]methyl}-3-[(tributylstannyl)methylidene]-3a,5,5-trimethyl octahydrobenzofuran* **19b**

To a solution of compound **18b** (6.0 g, 19 mmol) in 1.5 L of toluene were added AIBN (310 mg, 1.9 mmol, 0.1 equiv) and Bu_3SnH (8.5 mL, 32 mmol, 1.7 equiv). The mixture was stirred at reflux for 3 h. The oily residue obtained on removing toluene under reduced pressure was purified by flash chromatography over basic silica gel to give a 70:30 mixture of 5α-H and 5β-H diastereomeric compounds **19b** (11.2 g, 98% yield).

IR ($CHCl_3$) ν 2 955, 2 927, 2 854, 1 616, 1 462, 1 379, 1 254, 1 066, 836, 774, 735.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.02, 0.03 [2s, 6H, $2CH_3$, Si(CH_3)$_2$], 0.89 [s, 9H, $3CH_3$, SiC(*C*H_3)$_3$], 0.90 {t, J = 6.0 Hz, 9H, $3CH_3$, Sn[$(CH_2)_3CH_3$]$_3$}, 0.91 {t, J = 6.0 Hz, 6H, $3CH_2$, 3 Sn[$CH_2(CH_2)_2CH_3$]$_3$}, 0.90–1.82 (m, 4H, H_2-6, H_2-7), 1.03, 1.03 and 1.06 (3s, 9H, $3CH_3$), 1.30–1.50 [m, 12H, $6CH_2$, Sn($CH_2CH_2CH_2CH_3$)$_3$], 1.83 (m, 1H, H-4), 3.49 (t, J = 2.7 Hz, 1H, H-7a), 3.75 (dd, J = 10.7, 6.2 Hz, 1H, Ha-1″), 3.86 (dd, J = 10.7, 2.4 Hz, 1H, Hb-1″), 4.19 (dd, J = 13.1, 2.1 Hz, 1H, Ha-2), 4.69 (dd, J = 13.1, 2.5 Hz, 1H, Hb-2), 5.65 (dd, J = 2.4, 2.1 Hz, 1H, H-1′, J H-^{117}Sn = J H-^{119}Sn = 58.0 Hz).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.2 and −5.3 [$2CH_3$, Si(CH_3)$_2$], 9.9 [$3CH_2$, Sn(CH_2-)$_3$, J ^{13}C-^{117}Sn = 342.0 Hz, J ^{13}C-^{119}Sn = 339.0 Hz], 13.8 {$3CH_3$, Sn[$(CH_2)_3CH_3$]$_3$}, 17.7 (CH_3), 18.2 [C, Si*C*(CH_3)$_3$], 22.4 (CH_3), 22.8 (CH_2-6), 26.1 [3 CH_3, SiC(*C*H_3)$_3$], 27.4 [$3CH_2$, Sn($CH_2CH_2CH_2CH_3$)$_3$, J ^{13}C-^{117}Sn = J ^{13}C-^{119}Sn = 58.0 Hz], 29.4 [$3CH_2$, Sn($CH_2CH_2CH_2CH_3$)$_3$, J ^{13}C-^{117}Sn = J ^{13}C-^{119}Sn = 23.0 Hz], 33.5 (C-5), 33.8 (CH_3), 36.1 (C-7), 47.6 (C-4), 48.7 (C-3a, J C-^{117}Sn = J C-^{119}Sn = 42.0 Hz), 60.6 (C-1″), 71.6 (C-2, J C-^{117}Sn = J C-^{119}Sn = 31.0 Hz), 85.2 (C-7a), 115.8 (C-1′), 166.9 (C-3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.09 [s, 6H, $2CH_3$, Si(CH_3)$_2$], 0.87 {t, J = 6.0 Hz, 9H, $3CH_3$, Sn[$(CH_2)_3CH_3$]$_3$}, 0.89 [s, 9H, $3CH_3$, SiC(CH_3)$_3$], 0.90 [t, J = 6.0 Hz, 6H, $3CH_2$, Sn(CH_2-)$_3$], 1.02 (s, 6H, $2CH_3$), 1.04 (s, 3H, CH_3), 0.91–1.42 (m, 5H, H-4, H_2-6, H_2-7), 1.30–1.50 {m, 12H, $6CH_2$, Sn[$CH_2(CH_2)_2CH_3$]$_3$}, 3.64 (dd, J = 9.2, 6.1 Hz, 1H, H-7a), 3.95 (dd, J = 15.8, 10.2 Hz, 1H, Ha-1″), 4.20 (dd, J = 10.2, 2.2 Hz, 1H, Hb-1″), 4.32 and 4.38 (2dd, J = 13.5, 2.5 Hz, 2H, H_2-2), 5.65 (t, J = 2.0 Hz, 1H, H-1′, J H-^{117}Sn = J H-^{119}Sn = 60.0 Hz).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.2 and −5.3 [$2CH_3$, Si(CH_3)$_2$], 9.9 [$3CH_2$, Sn(CH_2-)$_3$, J C-^{117}Sn = 342.0 Hz, J C-^{119}Sn = 338.0 Hz], 13.8 {$3CH_3$, Sn[$(CH_2)_3CH_3$]$_3$}, 18.2 [C, Si*C*(CH_3)$_3$], 23.0 (CH_3), 25.0 (C-6), 26.0 [$3CH_3$, SiC(CH_3)$_3$], 26.1 (CH_3), 27.6 [$3CH_2$, Sn($CH_2CH_2CH_2CH_3$)$_3$, J ^{13}C-^{117}Sn = J ^{13}C-^{119}Sn = 58.0 Hz], 29.4 [$3CH_2$, Sn($CH_2CH_2CH_2CH_3$)$_3$, J ^{13}C-^{117}Sn = J ^{13}C-^{119}Sn = 23.0 Hz], 30.0 (CH_3), 32.5 (C-5), 38.2 (C-7), 51.3 (C-3a, J C-^{117}Sn = J C-^{119}Sn = 56.0 Hz), 56.8 (C-4), 61.5 (C-1″), 72.0 (C-2, J C-^{117}Sn = J C-^{119}Sn = 30.0 Hz), 87.3 (C-7a), 116.2 (C-1′), 163.8 (C-3).

MS (Cl, NH_3) *m/z* for major ^{120}Sn isotope 615 (MH^+), 571, 556, 501, 405, 356, 339, 308, 291, 249, 193, 137, 91.

(3Z,3aR,4R*S*,7aR*)-3-[(Tributylstannyl)methylidene]-3a,5,5-trimethyl-4-{[(triphenylmethyl)oxy]methyl} octahydrobenzofuran 19c*

To a solution of compound **18c** (2.3 g, 5.2 mmol) in 520 mL of toluene were added AIBN (43 mg, 0.26 mmol, 0.05 equiv) and Bu_3SnH (2.4 mL, 8.9 mmol, 1.7 equiv). The mixture was stirred at reflux for 3 h. The oily residue obtained on removing toluene under reduced pressure was purified by flash chromatography on basic silica gel to give a 50:50 mixture of 5α-H and 5β-H diastereomeric compounds **19c** (3.47 g, 90% yield).

IR ($CHCl_3$) ν 3 085, 3 058, 3 022, 2 955, 2 870, 1 630, 1 490, 1 463, 1 376, 1 056, 743, 703.

• *5α-H isomer*

^1H NMR ($CDCl_3$, 400 MHz) δ 0.65 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 0.87 {t, J = 6.0 Hz, 9H, $3CH_3$, $Sn[(CH_2)_3CH_3]_3$}, 0.90 [t, J = 6.0 Hz, 6H, $3CH_2$, $Sn(CH_2\text{-})_3$], 1.15 (s, 3H, CH_3), 0.91–1.40 (m, 4H, H_2-6, H_2-7), 1.30–1.50 {m, 12H, $6CH_2$, $Sn[CH_2(CH_2)_2CH_3]_3$}, 1.60 (m, 1H, H-4), 2.96 (dd, J = 9.5, 7.5 Hz, 1H, Ha-1″), 3.35 (dd, J = 9.5, 4.0 Hz, 1H, Hb-1″), 3.33 (broad s, 1H, H-7a), 4.07 (dd, J = 12.9, 2.5 Hz, 1H, Ha-2), 4.57 (dd, J = 12.9, 2.5 Hz, 1H, Hb-2), 5.27 (t, J = 2.5 Hz, 1H, H-1′, J H-^{117}Sn = J H-^{119}Sn = 58.0 Hz), 7.32 (m, 9H, Ar-H), 7.51 (m, 6H, Ar-H).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.9 [$3CH_2$, $Sn(CH_2\text{-})_3$, J C-^{117}Sn = 345.0 Hz, J C-^{119}Sn = 338.0 Hz], 13.8 {$3CH_3$, $Sn[(CH_2)_3CH_3]_3$}, 17.5 (CH_3), 23.0 (C-6), 22.4 (CH_3), 27.3 [$3CH_2$, $Sn(CH_2CH_2CH_2CH_3)_3$, J C-^{117}Sn = J C-^{119}Sn = 61.0 Hz], 29.3 [$3CH_2$, $Sn(CH_2CH_2CH_2CH_3)_3$, J C-^{117}Sn = J C-^{119}Sn = 26.0 Hz], 33.5 (C-5), 34.2 (CH_3), 36.2 (C-7), 48.0 (C-4), 48.5 (C-3a, J C-^{117}Sn = J C-^{119}Sn = 43.0 Hz), 62.0 (C-1″), 72.0 (C-2, J C-^{117}Sn = J C-^{119}Sn = 32.0 Hz), 85.2 (C-7a), 87.3 [C(Ph)$_3$], 117.0 (C-1′), 127.0 (3CH, Ar), 127.7 (6CH, Ar), 129.0 (6CH, Ar), 144.4 (3C, Ar), 167.0 (C-3).

• *5β-H isomer*

^1H NMR ($CDCl_3$, 400 MHz) δ 0.55 (s, 3H, CH_3), 0.87 {t, J = 6.0 Hz, 9H, $3CH_3$, $Sn[(CH_2)_3CH_3]_3$}, 0.90 [t, J = 6.0 Hz, 6H, $3CH_2$, $Sn(CH_2\text{-})_3$], 0.93 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 0.90–1.41 (m, 4H, H_2-6, H_2-7), 1.30–1.50 {m, 12H, $6CH_2$, $Sn[CH_2(CH_2)_2CH_3]_3$}, 1.80 (m, 1H, H-4), 3.12 (dd, J = 9.5, 6.3 Hz, 1H, Ha-1″), 3.59 (dd, J = 10.0, 5.7 Hz, 1H, H-7a), 3.66 (dd, J = 9.5, 1.8 Hz, 1H, Hb-1″), 4.13 (dd, J = 13.3, 2.5 Hz, 1H, Ha-2), 4.19 (dd, J = 13.3, 2.5 Hz, 1H, Hb-2), 5.11 (t, J = 2.4 Hz, 1H, H-1′, J H-^{117}Sn = J H-^{119}Sn = 58.0 Hz), 7.31 (m, 9H, Ar-H), 7.52 (m, 6H, Ar-H).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.9 [$3CH_2$, $Sn(CH_2\text{-})_3$, J C-^{117}Sn = 345.0 Hz, J C-^{119}Sn = 338.0 Hz], 13.8 {$3CH_3$, $Sn[(CH_2)_3CH_3]_3$}, 22.5 (C-6), 25.0 (CH_3), 27.3 [$3CH_2$, $Sn(CH_2CH_2CH_2CH_3)_3$, J C-^{117}Sn = J C-^{119}Sn = 60.0 Hz], 29.4 [$3CH_2$, $Sn(CH_2CH_2CH_2CH_3)_3$, J C-^{117}Sn = J C-^{119}Sn = 28.0 Hz], 30.0 (CH_3), 33.2 (C-5), 34.0 (CH_3), 38.6 (C-7), 46.5 (C-3a, J C-^{117}Sn = J C-^{119}Sn = 41.0 Hz), 54.0 (C-4), 62.5 (C-1″), 71.9 (C-2, J C-^{117}Sn = J C-^{119}Sn = 32.0 Hz), 87.3 [C(Ph)$_3$], 87.3 (C-7a), 116.1 (C-1′), 127.0 (3CH, Ar), 127.7 (6CH, Ar), 129.0 (6CH, Ar), 144.4 (3C, Ar), 163.0 (C-3).

MS (CI, NH_3) m/z for major ^{120}Sn isotope 760 ($MH^+ + NH_3$), 743 (MH^+), 143, 291.

(3Z,3aR,4R*S*,7aR*)-4-(Hydroxymethyl)-3a,5,5-trimethyl-3-methylidene octahydrobenzofuran 20a*

• *Procedure A*

To a solution of the crude stannane **19a** (5α-H/5β-H = 60:40, 2.0 g, 4.0 mmol) in THF (20 mL) was added a 1 N HCl aqueous solution (6 mL). The reaction mixture was stirred at 20 °C for 3 h, partitioned between diethyl ether (50 mL) and water (10 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (2 × 100 mL) and the organic phases were washed with brine, then dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 60:40 mixture of 5α-H and 5β-H isomers **20a** (800 mg, 95% yield) as a yellow oil.

• *Procedure B*

To a solution of silyl compound **20b** (see below, 5α-H/5β-H = 70:30, 3.0 g, 9.2 mmol) in CH_3CN (19 mL) at 20 °C was added a 48% aqueous HF solution (1 mL). The reaction mixture was stirred at this temperature for 1 h and partitioned between diethyl ether (100 mL) and a saturated aqueous $NaHCO_3$ solution (20 mL). The aqueous phase was extracted with diethyl ether (3 × 100 mL) and the combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H isomers **20a** (1.55 g, 80% yield) as a yellow oil.

IR ($CHCl_3$) ν 3 434, 2 936, 2 870, 1 660, 1 455, 1 389, 1 369, 1 248, 1 079, 1 019, 944, 888.

• *5α-H isomer*

^1H NMR ($CDCl_3$, 200 MHz) δ 0.78–1.91 (m, 6H, H-4, H_2-6, H_2-7, OH), 0.80 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 3.45 (t, J = 2.5 Hz, 1H, H-7a), 3.75 (m, 2H, H_2-1″), 4.23 (dt, J = 14.5, 2.5 Hz, 1H, Ha-2), 4.85 (t, J = 2.5 Hz, 1 H, Ha-1′), 4.57 (dt, J = 14.5, 2.5 Hz, 1H, Hb-2), 4.88 (t, J = 2.5 Hz, 1H, Hb-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 16.8 (CH_3), 21.7 (CH_3), 22.1 (C-6), 28.6 (CH_3), 33.0, (C-5), 35.2 (C-7), 46.1 (C-3a), 49.1 (C-4), 60.9 (C-1″), 69.7 (C-2), 84.3 (C-7a), 104.1 (C-1′), 159.0 (C-3).

• *5β-H isomer*

^1H NMR ($CDCl_3$, 200 MHz) δ 0.81–1.89 (m, 5H, H-4, H_2-6, H_2-7), 0.88 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.40 (m, 1H, OH), 3.57 (t, J = 5.8 Hz, 1H, H-7a), 3.92 (m, 2H, H_2-1″), 4.35 (dt, J = 14.0, 2.5 Hz, 1H, Ha-2), 4.48 (dt, J = 14.0, 2.5 Hz, 1H, Hb-2), 4.81 (t, J = 2.5 Hz, 1H, Ha-1′), 4.91 (t, J = 2.5 Hz, 1H, Hb-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 23.7 (C-6), 25.3 (CH_3), 28.6 (CH_3), 31.9 (CH_3), 33.2 (C-5), 35.8 (C-7), 48.0 (C-3a), 55.9 (C-4), 62.2 (C-1″), 70.5 (C-2), 85.4 (C-7a), 104.5 (C-1′), 155.8 (C-3).

MS (CI, NH_3) m/z 228 ($MH^+ + NH_3$), 211 (MH^+).

Anal calc for $C_{13}H_{22}O_2$, 210.31: C, 74.24; H, 10.54. Found: C, 73.93; H, 10.79.

(3Z,3aR,4R*S*,7aR*)-4-{[(tert-Butyldimethylsilyl)oxy]methyl}-3a,5,5-trimethyl-3-methylidene octahydrobenzofuran 20b*

• *Procedure A*

To a solution of the crude stannane **19b** (5α-H/5β-H = 70:30, 6.0 g, 9.8 mmol) in THF (50 mL) was added a

1 N HCl aqueous solution (20 mL). The reaction mixture was stirred at 20 °C for 3 h, partitioned between diethyl ether (100 mL) and water (30 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (2 × 100 mL) and the organic phases were washed with brine, then dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H isomers **20b** (3.02 g, 95% yield) as a yellow oil.

• *Procedure B*

To a solution of stannyl compound **19b** (5α-H/5β-H = 70:30, 3.0 g, 4.9 mmol) in dry THF (50 mL) cooled at −78 °C was added a 1.5 M *n*-BuLi solution in hexanes (3.9 mL, 5.87 mmol, 1.2 equiv). The reaction mixture, turned brown, was stirred at this temperature for 1 h. The reaction mixture was poured into a saturated aqueous ammonium chloride solution (20 mL), diluted with diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 100 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H diastereomeric products **20b** (1.5 g, 95% yield).

IR ($CHCl_3$) ν 2 929, 1 659, 1 471, 1 254, 1 091, 836, 774.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.04 and 0.05 [2s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.95 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.00–1.93 (m, 5H, H-4, H_2-6, H_2-7), 0.96, 1.05 and 1.06 (3s, 9H, $3CH_3$, CH_3-3a, 2 CH_3-5), 3.50 (t, J = 2.5 Hz, 1H, H-7a), 3.75 (dd, J = 11.7, 6.3 Hz, 1H, Ha-1″), 3.81 (dd, J = 11.7, 2.5 Hz, 1H, Hb-1″), 4.28 (dt, J = 13.5, 2.5 Hz, 1H, Ha-2), 4.61 (dt, J = 13.5, 2.5 Hz, 1H, Hb-2), 4.81 (t, J = 2.5 Hz, 1H, Ha-1′), 4.93 (t, J = 2.5, 1H, Hb-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.32 [$2CH_3$, $Si(CH_3)_2$], 17.4 (CH_3-3a), 18.1 [C, $SiC(CH_3)_3$], 22.2 (CH_3-5), 22.4 (C-6), 26.0 [$3CH_3$, $SiC(CH_3)_3$], 33.3 (C-5), 33.5 (CH_3-5), 35.8 (C-7), 46.5 (C-3a), 47.5 (C-4), 60.5 (C-1″), 69.8 (C-2), 84.7 (C-7a), 104.1 (C-1′), 158.0 (C-3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.01 [s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.95 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.00–1.93 (m, 5H, H-4, H_2-6, H_2-7), 0.91, 1.04 and 1.05 (3s, 9H, $3CH_3$, CH_3-3a, 2 CH_3-5), 3.65 (dd, J = 9.9, 6.4 Hz, 1H, H-7a), 3.91 (dd, J = 11.7, 6.3 Hz, 1H, Ha-1″), 4.12 (dd, J = 11.7, 2.7 Hz, 1H, Hb-1″), 4.44 (broad s, 2H, H_2-2), 4.82 (t, J = 2.5 Hz, 2H, H_2-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.3 [$2CH_3$, $Si(CH_3)_2$], 18.1 [C, $SiC(CH_3)_3$], 22.8 (CH_3), 24.7 (C-6), 26.0 [$3CH_3$, $SiC(CH_3)_3$], 30.0 (CH_3), 32.4 (CH_3), 34.4 (C-5), 38.2 (C-7), 48.8 (C-3a), 56.5 (C-4), 61.3 (C-1″), 70.5 (C-2), 87.1 (C-7a), 104.0 (C-1′), 154.5 (C-3).

MS (Cl, NH_3) m/z 342 ($MH^+ + NH_3$), 325 (MH^+), 295, 284, 267, 237, 125, 193, 175, 163,132.

Anal calc for $C_{19}H_{36}O_2Si$, 324.56: C, 70.37; H, 11.11. Found; C, 70.47; H, 11.37.

(3Z,3aR,4R*S*,7aR*)-3a,5,5-Trimethyl-3-methylidene-4-{[(triphenylmethyl)oxy]methyl} octahydrobenzofuran 20c*

• *Procedure A*

To a solution of crude stannane **19c** [2.0 g derived from compound **18c** (5α-H/5β-H = 50:50, 1.34 g, 2.9 mmol)] in THF (50 mL) was added a 1 N aqueous HCl solution (30 mL). The reaction mixture was stirred at 20 °C for 3 h and partitioned between diethyl ether (100 mL) and water (20 mL). The phases were separated and the aqueous phase was extracted with diethyl ether (2 × 100 mL). The organic phases were washed with brine, then dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 50:50 mixture of 5α-H and 5β-H isomers **20c** (1.15 g, 95% yield) as a yellow oil.

• *Procedure B*

To a solution of stannane compounds **19c** (5α-H/5β-H = 50:50, 4.0 g, 5.4 mmol) in dry THF (35 mL) cooled at −78 °C was added a 1.5 M *n*-BuLi solution in hexanes (4.3 mL, 6.5 mmol, 1.2 equiv). The reaction mixture, turned brown and was stirred at this temperature for 1 h. The reaction mixture was poured into a saturated aqueous ammonium chloride solution (50 mL), diluted with diethyl ether (100 mL) and the phases were separated. The aqueous layer was extracted with diethyl ether (3 × 150 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave a 50:50 mixture of diastereomeric products **20c** (2.2 g, 90% yield).

IR ($CHCl_3$) ν 2 934, 1 550, 1 448, 1 054, 909, 733, 649.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.70–1.90 (m, 5H, H-4, H_2-6, H_2-7), 0.66 (s, 3H, CH_3), 0.71 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 2.95 (dd, J = 9.0, 7.0 Hz, 1H, Ha-1″), 3.32 (dd, J = 9.0, 2.0 Hz, 1H, Hb-1″), 3.35 (t, J = 2.5 Hz, 1H, H-7a), 4.15 (dt, J = 17.0, 1.5 Hz, 1H, Ha-2), 4.27 (t, J = 1.5 Hz, 1H, Ha-1′), 4.58 (dt, J = 17.0, 1.5 Hz, 1H, Hb-2), 4.62 (t, J = 1.5 Hz, 1H, Hb-1′), 7.30 (m, 9H, Ar-H), 7.46 (m, 6H, Ar-H).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 16.9 (CH_3-2a), 21.9 (CH_3-5), 22.6 (C-6), 33.2 (CH_3-5), 34.2 (C-5), 35.4 (C-7), 42.3 (C-3a), 53.8 (C-4), 61.3 (C-1″), 69.8 (C-2), 85.9 (C-7a), 87.5 [C(Ph)$_3$], 104.8 (C-1′), 127.0 (3CH, Ar), 127.8 (6CH, Ar), 129.0 (6CH, Ar), 144.4 (3C, Ar), 156.8 (C-3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.70–1.90 (m, 5H, H-4, H_2-6, H_2-7), 0.55 (s, 3H, CH_3), 0.93 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 3.17 (dd, J = 10.0, 5.0 Hz, 1H, Ha-1″), 3.55 (m, 1H, H-7a), 3.58 (dd, J = 10.0, 3.0 Hz, 1H, Hb-1″), 4.25 (broad s, 2H, H_2-2), 4.25 (broad s, 1H, Ha-1′), 4.47 (broad s, 1H, Hb-1′), 7.21 (m, 9H, Ar-H), 7.46 (m, 6H, Ar-H).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 22.5 (CH_3), 24.8 (C-6), 30.1 (CH_3), 33.0 (CH_3), 33.9 (C-5), 38.4 (C-7), 49.0 (C-3a), 53.9 (C-4), 62.4 (C-1″), 70.5 (C-2), 87.0 [C(Ph)$_3$], 87.1 (C-7a), 103.9 (C-1′), 127.0 (3CH, Ar), 127.8 (6CH, Ar), 129.9 (6CH, Ar), 144.4 (3C, Ar), 154.0 (C-3).

MS (Cl, NH_3) m/z 470 ($MH^+ + NH_3$), 453 (MH^+).

Anal calc for $C_{32}H_{36}O_2$, 452.61: C, 84.91; H, 8.02. Found; C, 84.85; H, 8.15.

(3Z,3aR,4R*S*,7aR*)-3-Ethylidene-4-hydroxymethyl-3a,5,5-trimethyl octahydrobenzofuran 21a*

To a solution of silyl alcohol **21b** (see below, 5α-H/5β-H = 70:30, 3.1 g, 9.1 mmol) in acetonitrile (9.5 mL) at 20 °C was added a 48% aqueous HF solution (0.5 mL). The resulting cloudy mixture was stirred at 20 °C for 1 h and the

reaction quenched with saturated aqueous $NaHCO_3$ solution (20 mL). The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave a 70:30 mixture of alcohols **21a** (1.86 g, 90% yield).

IR (NaCl) ν 3 423, 2 936, 1 450, 1 383, 1 367, 1 079, 1 050, 1 024, 975, 944.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89, 0.97 and 1.01 (3s, 9H, $3CH_3$, CH_3-3a, $2CH_3$-5), 1.10–1.91 (m, 6H, H-4, H_2-6, H_2-7, OH), 1.53 (dt, J = 6.7, 1.1 Hz, 3H, CH_3-1′), 3.40 (t, J = 2.5 Hz, 1H, H-7a), 3.6 and 3.8 (2dd, J = 13.7, 5.6 Hz, 2H, H_2-1″), 4.35 and 4.56 (ddq, J = 12.7, 2.6, 1.1 Hz, 2H, H_2-2), 5.22 (qd, J = 6.7, 2.6 Hz, 1H, H-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 17.3 (CH_3-1′), 22.2 (C-6), and 26.3 (CH_3), 28.6 (CH_3), 33.3 (C-5), 33.3 (CH_3), 35.5 (C-7), 45.6 (C-3a), 49.8 and (C-4), 61.1 (C-1″), 67.7 (C-2), 84.5 (C-7a), 114.2 (C-1′), 150.1 (C-3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.97, 1.00 and 1.03 (3s, 9H, $3CH_3$, CH_3-3a, $2CH_3$-5), 1.10–1.91 (m, 6H, H-4, H_2-6, H_2-7, OH), 1.53 (dt, J = 6.7, 1.1 Hz, 3H, CH_3, CH_3-1′), 3.50 (t, J = 5.5 Hz, 1H, H-7a), 3.6 and 3.8 (2dd, J = 5.6, 13.7 Hz, 2H, H_2-1″), 4.35 and 4.56 (ddq, J = 12.7, 2.6, 1.1 Hz, 2H, H_2-2), 5.10 (qd, J = 6.7, 2.6 Hz, 1H, H-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 17.3 (CH_3-1′), 21.9 (C-6), 23.4 (CH_3), 28.6 (CH_3), 33.2 (C-5), 31. 8 (CH_3), 35.2 (C-7), 47.0 (C-3a), 56.2 (C-4), 62.5 (C-1″), 68.8 (C-2), 85.0 (C-7a), 114.7 (C-1′), 150.1 (C-3).

MS (CI, NH_3) m/z 242 ($MH^+ + NH_3$), 225 (MH^+), 224.

Anal calc for $C_{14}H_{24}O_2$, 224.33: C, 74.95; H, 10.78. Found; C, 74.89; H, 10.82.

(3Z,3aR,4R*S*,7aR*)-4-{[(tert-Butyltrimethylsilyl)-oxy]methyl}-3-ethylidene-3a,5,5-trimethyl octahydrobenzofuran* **21b**

• *Procedure A*

To a solution of stannyl compound **19b** (5α-H/5β-H = 70:30, 7.4 g, 12 mmol) in dry THF (50 mL) cooled to −78 °C was added a 1.5 M *n*-BuLi solution in hexanes (9.62 mL, 14.4 mmol, 1.2 equiv). The reaction mixture turned brown and was stirred at this temperature for 1 h. Methyl iodide (2.3 mL, 36 mmol, 3 equiv) was then added and the solution allowed to warm to 20 °C over 1 h. The reaction mixture was poured into a saturated aqueous ammonium chloride solution (100 mL), diluted with diethyl ether (150 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 150 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H diastereomeric products **21b** (3.1 g, 76% yield).

• *Procedure B*

To a solution of iodo compound **23b** (see below, 5α-H/5β-H = 70:30, 2 g, 4.4 mmol) in dry THF (50 mL) cooled to −78 °C was added a 1.6 M MeLi solution in diethyl ether (4.9 mL, 7.9 mmol, 1.8 equiv). The reaction mixture was stirred at this temperature for 1 h and was then poured into a saturated aqueous ammonium chloride solution (50 mL), diluted with diethyl ether (100 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 100 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H diastereomeric products **21b** (1.3 g, 87% yield).

IR (NaCl) ν 2 928, 2 856, 1 461, 1 383, 1 362, 1 253, 1 093, 1 065, 836, 774.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.06 [s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.88, 0.92 and 1.29 (3s, 9H, $3CH_3$, CH_3-3a and $2CH_3$-5), 0.94 [s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.55 (dt, J = 6.8, 1.4 Hz, 3H, CH_3, CH_3-1′), 1.10–2.05 (m, 5H, H-4, H_2-6, H_2-7), 3.14 (t, J = 2.8 Hz, 1H, H-7a), 3. 67 (dd, J = 10.8, 6.5 Hz, 1H, Ha-1″), 3.77 (dd, J = 10.8, 2.6 Hz, 1H, Hb-1″), 4.33 and 4.47 (2dd, J = 13.2, 2.6 Hz, 2H, H_2-2), 5.14 (qt, J = 6.8, 2.6 Hz, 1H, H-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.3 [$2CH_3$, $Si(CH_3)_2$], 14.1 (CH_3-1′), 17.5 [C, $SiC(CH_3)_3$], 17.5, 22.1 and 33.6 ($3CH_3$, CH_3-3a, $2CH_3$-5), 22.3 (C-6), 26.0 [$3CH_3$, $SiC(CH_3)_3$], 33.3 (C-5), 38.1 (C-7), 46.1 (C-3a), 56.7 (C-4), 60.6 (C-1″), 67.8 (C-2), 84.7 (C-7a), 114.3 (C-1′), 149.2 (C-3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.02, 0.02 [2s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.87, 0.96 and 1.26 (3s, 9H, $3CH_3$, CH_3-3a, $2CH_3$-5), 0.96 [s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.50 (dt, J = 6.8, 1.1 Hz, 3H, CH_3, CH_3-1′), 1.10–1.82 (m, 5H, H-4, H_2-6, H_2-7), 3.60 (dd, J = 9.1, 6.3 Hz, 1H, H-7a), 3.87 (dd, J = 10.4, 5.8 Hz, 1H, Ha-1″), 4.07 (dd, J = 10.4, 2.4 Hz, 1H, Hb-1″), 4.36 and 4.47 (2dd, J = 10.4, 2.6 Hz, 2H, H_2-2), 5.15 (qt, J = 6.8, 2.6 Hz, 1H, H-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.3 [$2CH_3$, $Si(CH_3)_2$], 14.7 (CH_3-1′), 18.2 [C, $SiC(CH_3)_3$], 23.1, 29.8 and 32.4 (CH_3-3a, $2CH_3$-5), 24.6 (C-6), 26.1 [$3CH_3$, $SiC(CH_3)_3$], 33.7 (C-5), 38.1 (C-7), 48.6 (C-3a), 56.8 (C-4), 61.5 (C-1″), 68.5 (C-2), 86.9 (C-7a), 114.1 (C-1′), 145.6 (C-3).

MS (CI, NH_3) m/z 339 (MH^+), 325, 281, 267, 189, 137, 123, 109, 91, 95, 67, 57.

Anal calc for $C_{20}H_{38}O_2Si$, 338.56: C, 70.95; H, 11.31. Found; C, 70.82; H, 11.42.

(3Z,3aR,4R*S*,7aR*)-3-Ethylidene-3a,5,5-trimethyl-4-{[(triphenylmethyl)oxy]methyl} octahydrobenzofuran* **21c**

• *Procedure A*

To a solution of stannane compounds **19c** (5α-H/5β-H = 50:50, 5.4 g, 7.3 mmol) in dry THF (50 mL) cooled at −78 °C was added a 1.5 M *n*-BuLi solution in hexanes (9.62 mL, 14.4 mmol, 1.2 equiv). The reaction mixture, which turned brown, was stirred at this temperature for 1 h. Methyl iodide (2.3 mL, 36 mmol, 3 equiv) was then added and the solution allowed to warm to 20 °C over 1 h. The reaction mixture was poured into a saturated aqueous ammonium chloride solution (100 mL), diluted with diethyl ether (150 mL) and the phases were separated. The aqueous layer was extracted with diethyl ether (3 × 150 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave a 50:50 mixture of diastereomeric products **21c** (2.5 g, 75% yield).

• *Procedure B*

To a solution of iodo compound **23c** (see below, 5α-H/5β-H = 70:30, 1 g, 1.7 mmol) in dry THF (15 mL) cooled to −78 °C was added a 1.6 M MeLi solution in diethyl ether (2.0 mL, 3.1 mmol, 1.8 equiv). The reaction mixture was stirred at this temperature for 1 h and was then poured into a saturated aqueous ammonium chloride solution (20 mL), diluted with diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 100 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H diastereomeric products **21c** (0.63 g, 80% yield).

IR ($CHCl_3$) ν 3 085, 3 058, 3 022, 2 955, 2 870, 1 490, 1 463, 1 376, 1 056, 743, 703.

^1H NMR ($CDCl_3$, 200 MHz, two isomers) δ 0.71, 0.84, 1.08 1.24, 1.28 and 1.29 (6s, 18H, $2CH_3$-3a, $4CH_3$-5), 1.38 and 1.50 (2d, J = 6.4 Hz, 6H, $2CH_3$-1′), 0.85–1.87 (m, 10H, 2H-4, $2H_2$-6, $2H_2$-7), 3.11 (dd, J = 9.5, 7.5 Hz, 1H, Ha-1″), 3.34–3.75 (m, 5H, Hb-1″, H_2-1″, 2H-7a), 4.37 (m, 4H, $2H_2$-2), 4.80 (m, 2H, 2H-1′), 7.3 (m, 18H, Ar-H), 7.5 (m, 12H, Ar-H).

^{13}C NMR ($CDCl_3$, 50.3 MHz, two isomers) δ 14.5, 15.3, 17.4, 21.9, 22.7, 29.9, 32.9 and 33.7 ($8CH_3$, $2CH_3$-5, $2CH_3$-3a, $2CH_3$-1′), 22.1 and 24.4 (2C-6), 32.6 and 33.7 (2C-5), 34.3 and 38.0 (2C-7), 46.1 and 53.8 (2C-4), 45.9 and 48.6 (2C-3a), 61.4 and 62.3 (2C-1″), 67.7 and 68.3 (2C-2), 84.4 and 86.8 (2C-7a), 87.1 [2*C*(Ph)$_3$], 113.8 and 114.7 (2C-1′), 127.7 (6CH, Ar), 128.9 (12CH, Ar), 127.6 (12CH, Ar), 144.3 and 145.0 (6C, Ar), 144.3 and 145.1 (2C-3).

MS (CI, NH_3) m/z 484 ($MH^+ + NH_3$), 467 (MH^+).

[2Z(3Z,3aR,4R*,7aR*)]-(4-Hydroxymethyl-3a,5,5-trimethyl octahydrobenzofuran-3-ylidene) acetic acid methyl ester* **22a** *5α-H*

To a solution of ester **22b** (see below, 5α-H/5β-H = 70:30, 200 mg, 5.2 mmol) in THF (5 mL) at 20 °C was added a 1 M TBAF solution in THF and the mixture was stirred at this temperature for 12 h. The reaction was quenched with water (10 mL) diluted with diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 25 mL) and the combined organic phases washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave the 5α-H isomer **22a** 5α-H (84 mg, 60% yield) as a yellow oil.

IR ($CHCl_3$) ν 3 464, 2 949, 2 856, 1 708, 1 658, 1 436, 1 350, 1 224, 1 177, 1 047, 1 019, 909, 733, 684.

^1H NMR ($CDCl_3$, 200 MHz) δ 0.7–1.8 (m, 6H, H-4′, H_2-6′, H_2-4′, OH), 0.90, 1.0 and 1.03 (3s, 9H, $3CH_3$, CH_3-3′a, $2CH_3$-5′), 3.42 (t, J = 2.5 Hz, 1H, H-7′a), 3.62 (s, 3H, CH_3, CO_2CH_3), 3.70 (m, 2H, H_2-1″), 4.68 (dd, J = 17.5, 2.5 Hz, 1H, Ha-2′), 4.88 (dd, J = 17.5, 2.5 Hz, 1H, Hb-2′), 5.60 (t, J = 2.5, 1H, H-2).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 16.3 (CH_3-3′a), 20.7 (C-6′), 21.1 (CH_3-5′), 32.2 (C-5′), 32.5 (CH_3-5′), 34.2 (C-7′), 47.2 (C-3′a), 48.0 (C-4′), 50.5 (CH_3, CO_2CH_3), 59.4 (C-1″), 69.4 (C-2′), 82.3 (C-7′a), 110.2 (C-2), 165.8 (C-3′), 171.5 (C-1, CO_2CH_3).

MS (CI, NH_3) m/z 286 ($MH^+ + NH_3$), 269 (MH^+), 254, 181, 167, 153, 137, 123, 52.

Anal calc for $C_{15}H_{24}O_4$, 268.34: C, 67.13; H, 9.02. Found; C, 67.55; H, 9.38.

[2Z(3Z,3aR,4R*S*,7aR*)]-(4-{[(tert-Butyldimethylsilyl)oxy]methyl}-3a,5,5-trimethyl octahydrobenzofuran-3-ylidene) acetic acid methyl ester* **22b**

• *Procedure A*

To a solution of stannyl compounds **19b** (5α-H/5β-H = 70:30, 10 g, 16 mmol) in THF (75 mL) cooled to −78 °C was added dropwise a 1.5 M *n*-BuLi solution in hexanes (12 mL, 18 mmol, 1.1 equiv). The reaction mixture was stirred at this temperature for 1 h and then transferred via cannula to a cooled solution (0 °C) of methyl chloroformate (6.3 mL, 82 mmol, 5 equiv) in 30 mL of THF. The mixture was stirred at this temperature for 1 h and was allowed to warm to 20 °C. After stirring for another hour at 20 °C, the reaction was quenched with water (20 mL), diluted with diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H isomeric ester **22b** (5.3 g, 85% yield) as a yellow oil.

• *Procedure B*

To a solution of iodo compound **23b** (see below, 5α-H/5β-H = 70:30, 1.0 g, 2.2 mmol) in THF (10 mL) cooled to −78 °C was added dropwise a 1.5 M *n*-BuLi solution in hexanes (2.2 mL, 3.2 mmol, 1.2 equiv). The reaction mixture was stirred at this temperature for 1 h and then transferred via cannula to a cooled solution (0 °C) of methyl chloroformate (0.85 mL, 11 mmol, 5 equiv) in THF (2 mL). The reaction was stirred at this temperature for 1 h, allowed to warm to 20 °C over 1 h and quenched with water (5 mL). The resulting solution was diluted with diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with 3 × 50 mL of diethyl ether and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H isomeric esters **22b** (145 mg, 17% yield) as a yellow oil and a 70:30 mixture of 5α-H and 5β-H isomeric derivatives **20b** (592 mg, 83% yield).

• *Procedure C*

To a solution of iodo compound **23b** (see below, 5α-H/5β-H = 70:30, 2.2 g, 4.9 mmol) in DME (20 mL) cooled to −78 °C was added dropwise a 1.5 M *t*-BuLi solution in hexanes (7.2 mL, 11 mmol, 2.2 equiv). The reaction mixture was stirred at this temperature for 1 h and then transferred via cannula to a cooled solution (0 °C) of methyl chloroformate (1.9 mL, 24 mmol, 5 equiv) in DME (5 mL). The reaction was stirred at this temperature for 1 h, allowed to warm to 20 °C over 1 h and quenched with water (20 mL). The resulting solution was diluted with diethyl ether (100 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H isomeric esters **22b** (1.05 g, 57% yield) as a yellow oil and a 70:30 mixture of 5α-H and 5β-H isomeric derivatives **20b** (0.54 g, 34% yield).

• *Procedure D*

To a solution of iodo compound **23b** (see below, 5α-H/5β-H = 70:30, 1.2 g, 2.7 mmol) in THF (20 mL) cooled to −78 °C was added dropwise a 1.6 M MeLi solution in diethyl ether (2.5 mL, 4.1 mmol, 1.5 equiv). The reaction

mixture was stirred at this temperature for 1 h and then transferred via cannula to a cooled solution (0 °C) of methyl chloroformate (1.1 mL, 13.5 mmol, 5 equiv) in THF (5 mL). The reaction was stirred at this temperature for 1 h, allowed to warm to 20 °C over 1 h and quenched with water (20 mL). The resulting solution was diluted with diethyl ether (100 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H isomeric esters **22b** (135 mg, 13% yield) as a yellow oil and a 70:30 mixture of 5α-H and 5β-H isomeric derivatives **21b** (760 mg, 83% yield).

IR ($CHCl_3$) ν 2 951, 2 856, 1 716, 1 659, 1 461, 1 434, 1 385, 1 354, 1 305, 1 256, 1 220, 1 175, 1 056, 1 020, 950, 836, 775.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.01, 0.02 [2s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.78 (s, 3H, CH_3), 0.80 (s, 3H, CH_3), 0.86 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 0.86 (s, 3H, CH_3), 1.08–1.79 (m, 5H, H-4′, H_2-6′, H_2-7′), 3.7 (t, J = 2.5 Hz, 1H, H-7′a), 3.7 (m, 2H, H_2-1″), 3.7 (s, 3H, CH_3, CO_2CH_3), 4.75 (dd, J = 17.8, 2.5 Hz, 1H, Ha-2′), 4.93 (dd, J = 17.8, 2.5 Hz, 1H, Hb-2′), 5.62 (t, J = 2.5, 1H, H-2).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.4 [$2CH_3$, $Si(CH_3)_2$], 17.5 (CH_3-3a), 18.1 [C, $SiC(CH_3)_3$], 21.7 (CH_3-5′), 22.5 (C-6′), 23.4 (C-5′), 25.9 [$3CH_3$, $SiC(CH_3)_3$], 33.5 (C-5), 33.7 (CH_3-5′), 35.5 (C-7′), 48.4 (C-3′a), 51.3 (C-4′), 60.1 (C-1″), 70.3 (C-2′), 83.56 (C-7′a), 111.2 (C-2), 166.7 (C-3′), 172.3 (C-1, CO_2CH_3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.09 [2s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.91 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.0, 1.03 and 1.13 (3s, 9H, $3CH_3$, CH_3-3′a, $2CH_3$-5′), 1.21–1.66 (m, 5H, H-4′, H_2-6′, H_2-7′), 3.61 (dd, J = 9.9, 5.8 Hz, 1H, H-7′a), 3.67 (s, 3H, CH_3, CO_2CH_3), 3.90 (dd, J = 10.4, 5.6 Hz, 1H, Ha-1″), 4.05 (dd, J = 10.4, 3.2 Hz, 1H, Hb-1″), 4.88 (d, J = 2.5 Hz, 2H, H_2-2′), 5.75 (t, J = 2.5 Hz, 1H, H-2).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.3 [$2CH_3$, $Si(CH_3)_2$], 18.1 [C, $SiC(CH_3)_3$], 23.0 (CH_3), 24.0 (C-6′), 26.0 [$3CH_3$, $SiC(CH_3)_3$], 29.7 (CH_3), 31.9 (CH_3), 33.7 (C-5′), 37.8 (C-7′), 50.9 (C-3′a), 51.2 (CH_3, CO_2CH_3), 56.4 (C-4′), 60.9 (C-1″), 70.8 (C-2′), 85.5 (C-7′a), 110.8 (C-2), 166.7 (C-3′), 170.3 (C-1, CO_2CH_3).

MS (Cl, NH_3) m/z 400 ($MH^+ + NH_3$), 383 (MH^+), 367, 353, 325, 311, 267, 132, 184, 154, 132, 108, 91, 72, 52.

Anal calc for $C_{21}H_{38}O_4Si$, 382.59: C, 65.92; H, 10.01. Found; C, 65.66; H, 10.07.

(3Z,3aR,4R*S*,7aR*)-4-Hydroxymethyl-3-iodomethylidene-3a,5,5-trimethyl octahydrobenzofuran* **23a**

To a solution of a crude mixture of stannyl derivatives **19a** (5α-H/5β-H = 60:40, 5.9 g, 11.9 mmol) in diethyl ether (30 mL) was added dropwise a solution of iodine (5.1 g, 20 mmol, 1.5 equiv) in diethyl ether (50 mL). After 15 min, the mixture was treated with an aqueous KF solution (30 mL, 1 g/10 mL) and stirred for 1 h. The phases were then separated and the aqueous phase extracted with diethyl ether (3 × 150 mL). The combined organic phases were washed with an aqueous $NaHSO_3$ solution, then brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 60:40 mixture of 5α-H and 5β-H isomers **23a** (3.8 g, 95% yield) as a yellow oil.

IR ($CHCl_3$) ν 3 423, 2 936, 2 867, 1 628, 1 454, 1 369, 1 245, 1 166, 1 079, 1 049, 1 021, 999, 945, 768, 676.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.96, 1.06 and 1.06 (3s, 9H, $3CH_3$, CH_3-3a, 2 CH_3-5), 1.15–1.75 (m, 6H, H-4, H_2-6, H_2-7, OH), 3.77 (t, J = 2.5 Hz, 1H, H-7a), 3.78 (m, 2H, H_2-1″), 4.22 (dd, J = 14.7, 2.5 Hz, 1H, Ha-2), 4.46 (dd, J = 14.7, 2.5 Hz, 1H, Hb-2), 5.95 (t, J = 2.5, 1H, H-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 16.4, 21.7 and 33.1 ($3CH_3$, CH_3-3a, 2 CH_3-5), 22.1 (C-6), 34.9 (C-5), 39.2 (C-7), 48.5 (C-4), 52.0 (C-3a), 60.3 (C-1″), 68.6 (C-7a), 74.4 (C-2), 85.3 (C-1′), 160.6 (C-3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.98, 1.05 and 1.36 (3s, 9H, $3CH_3$, CH_3-3a, $2CH_3$-5), 1.1–1.8 (m, 5H, H-4, H_2-6, H_2-7), 2.4 (m, 1H, OH), 3.77 (dd, J = 7.2, 5.6 Hz, 1H, H-7a), 3.85 (m, 1H, Ha-1″), 3.96 (m, 1H, Hb-1″), 4.26 (dd, J = 15.0, 2.5 Hz, 1H, Ha-2), 4.36 (dd, J = 15.0, 2.5 Hz, 1H, Hb-2), 5.88 (t, J = 2.5 Hz, 1H, H-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 23.5 (C-6), 25.2 (CH_3-3a), 28.1 and 31.7 ($2CH_3$, $2CH_3$-5), 34.5 (C-5), 35.7 (C-7), 52.1 (C-3a), 55.8 (C-4), 61.9 (C-1″), 68.6 (C-7a), 75.8 (C-2), 87.9 (C-1′), 158.3 (C-3).

MS (Cl, NH_3) m/z 337 (MH^+), 319, 301, 235, 209, 191, 163, 137.

Anal calc for $C_{13}H_{21}O_2I$, 336.22 C, 46.43; H, 6.29. Found; C, 46.61; H, 6.37.

(3Z,3aR,4R*S*,7aR*)-4-{[(tert-Butyldimethylsilyl)-oxy]methyl}-3-iodomethylidene-3a,5,5-trimethyl octahydrobenzofuran* **23b**

To a solution of stannyl derivatives **19b** (5α-H/5β-H = 70:30, 7.0 g, 11 mmol) in diethyl ether (20 mL) was added dropwise a solution of iodine (4.34 g, 17.1 mmol, 1.5 equiv) in diethyl ether (30 mL). After 15 min an aqueous KF solution (30 mL, 1 g/10 mL) was added and the reaction mixture stirred for 1 h. The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 100 mL). The combined organic phases were washed with a saturated aqueous $NaHSO_3$ solution, then with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave a 70:30 mixture of 5α-H and 5β-H isomeric compounds **23b** (4.9 g, 95% yield) as a yellow oil.

IR ($CHCl_3$) ν 2 955, 2 927, 2 854, 1 616, 1 462, 1 379, 1 253, 1 066, 836, 774, 734.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.06 [2s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.86 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 0.99, 1.00 and 1.05 (3s, 9H, $3CH_3$, CH_3-3a, $2CH_3$-5), 1.08–1.79 (m, 4H, H_2-6, H_2-7), 1.22 (dd, J = 5.8, 2.9 Hz, 1H, H-4), 3.57 (t, J = 2.5 Hz, 1H, H-7a), 3.68 (dd, J = 11.6, 5.8 Hz, 1H, Ha-1″), 3.73 (dd, J = 11.6, 2.9 Hz, 1H, Hb-1″), 4.17 (dd, J = 14.7, 2.5 Hz, 1H, Ha-2), 4.38 (dd, J = 14.7, 2.5 Hz, 1H, Hb-2), 5.84 (t, J = 2.5 Hz, 1H, H-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.2 [$2CH_3$, $Si(CH_3)_2$], 17.5 (CH_3-3a), 22.3 and 33.5 ($2CH_3$-5), 18.3 [C, $SiC(CH_3)_3$], 22.6 (C-6), 26.1 [$3CH_3$, $SiC(CH_3)_3$], 33.5 (C-5), 35.7 (C-7), 47.9 (C-4), 51.0 (C-3a), 60.7 (C-1″), 68.3 (C-7a), 74.7 (C-2), 86.1 (C-1′), 160.9 (C-3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89 [2s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.91 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 0.90, 0.97 and 1.35 (3s, 9H, $3CH_3$, CH_3-3a, $2CH_3$-5), 1.21–1.66 (m, 5H, H-4, H_2-6, H_2-7), 3.84 (dd, J = 10.0, 5.9 Hz, 1H, H-7a), 3.89 (dd, J = 10.6, 5.1 Hz, 1H, Ha-1″), 4.01 (dd, J = 10.6, 3.1 Hz, 1H, Hb-1″), 4.36 (d, J = 2.3 Hz, 2H, H_2-2), 6.01 (t, J = 2.3 Hz, 1H, H-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.4 [$2CH_3$, $Si(CH_3)_2$], 18.1 [C, $SiC(CH_3)_3$], 23.0, 29.3 and 32.1 ($3CH_3$, CH_3-3a, $2CH_3$-5), 24.4 (C-6), 25.9 [$3CH_3$, $SiC(CH_3)_3$], 33.5 (C-5), 38.0 (C-7), 52.4 (C-3a), 56.0 (C-4), 61.2 (C-1″), 68.5 (C-7a), 75.9 (C-2), 88.6 (C-3), 157.0 (C-1′).

MS (Cl, NH_3) m/z 451 (MH^+), 323, 265, 191.

Anal calc for $C_{19}H_{35}O_2SiI$, 450.45: C, 50.66; H, 7.83. Found; C, 50.28; H, 7.92.

(3Z,3aR,4R*S*,7aR*)-3-Iodomethylidene-3a,5,5-trimethyl-4-{[(triphenylmethyl)oxy]methyl} octahydrobenzofuran* **23c**

To a solution of a mixture of the stannyl compounds **19c** (5α-H/5β-H = 50:50, 660 mg, 0.9 mmol) in diethyl ether (5 mL) was added iodine (160 mg, 1.4 mmol, 1.5 equiv) in diethyl ether (2 mL). The resulting brown mixture was stirred at room temperature for 1 h and then treated with a KF aqueous solution (10 mL, 2 g/mL). The aqueous phase was extracted with diethyl ether and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave 495 mg (95% yield) of a 50:50 mixture of 5α-H and 5β-H isomeric compounds iodo derivatives **23c**.

IR ($CHCl_3$) ν 3 032, 2 935, 2 857, 1 645, 1 624, 1 453, 1 166, 1 072, 1 044, 946, 769.

• *5α-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.92–1.51 (m, 5H, H-4, H_2-6, H_2-7), 0.54 (s, 3H, CH_3), 0.65 (s, 3H, CH_3), 0.80 (s, 3H, CH_3), 2.89 (dd, J = 10.0, 7.5 Hz, 1H, Ha-1″), 3.19 (dd, J = 10.0, 5.0 Hz, 1H, Hb-1″), 3.30 (broad s, 1H, H-7a), 4.00 (dd, J = 15.0, 2.5 Hz, 1H, Ha-2), 4.29 (dd, J = 15.0, 2.5 Hz, 1H, Hb-2), 5.04 (t, J = 2.5 Hz, 1H, H-1′), 7.31 (m, 9H, Ar-H), 7.52 (m, 6H, Ar-H).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 17.6 (CH_3), 22.3 (CH_3), 22.3 (C-6), 33.6 (C-5), 34.0 (CH_3), 35.4 (C-7), 46.0 (C-4), 50.7 (C-3a), 61.0 (C-1″), 70.0 (C-7a), 74.9 (C-2), 85.8 (C-1′), 87.3 (*C*-(Ph)$_3$), 127.0 (3CH Ar), 127.9 (6CH Ar), 128.9 (6CH Ar), 144.0 (3C Ar), 159.5 (C-3).

• *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.78–1.91 (m, 5H, H-4, H_2-6, H_2-7), 0.50 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 3.12 (dd, J = 9.5, 5.5 Hz, 1H, H-1″a), 3.40 (dd, J = 9.5, 3.0 Hz, 1H, H-1″b), 3.77 (dd, J = 9.7, 5.9 Hz, 1H, H-7a), 4.13 (d, J = 2.5 Hz, 2H, H_2-2), 5.25 (t, J = 2.5 Hz, 1H, H-1′), 7.31 (m, 9H, Ar-H), 7.62 (m, 6H, Ar-H).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 22.6 (CH_3), 24.4 (C-6), 29.8 (CH_3), 32.7 (CH_3), 33.6 (C-5), 38.0 (C-7), 52.5 (C-3a), 53.7 (C-4), 62.5 (C-1″), 68.0 (C-7a), 76.1 (C-2), 87.7 (*C*-(Ph)$_3$), 88.7 (C-1′), 127.2 (3CH, Ar), 127.8 (6CH, Ar), 129.0 (6CH, Ar), 144.2 (3C, Ar), 156.9 (C-3).

MS (Cl, NH_3) m/z 579 (MH^+).

(3Z,3aR,4R*,7aR*)-4-{[(tert-Butyldimethylsilyl)oxy]-methyl}-3-cyanomethylidene-3a,5,5-trimethyl octahydrobenzofuran* **24b** *(5α-H) and (3aR*,4R*,7aR*)-4-{[(tert-butyldimethylsilyl)oxy]-methyl}-3-cyanomethyl-3a,5,5-trimethyl-3a,4,5,6,7,7a-hexahydrobenzofuran* **25b** *(5α-H)*

A solution of KCN (180 mg, 2.8 mmol, 2 equiv) and 18-crown-6 ether (30 mg, 0.01 mmol, 0.08 equiv) in toluene was concentrated in vacuo and dried at 50 °C under 0.1 mmHg pressure for 2 h. Tetrakis(triphenylphosphine) palladium (50 mg, 0.04 mmol, 0.03 equiv) and vinyl iodide **23b** (5α-H/5β-H > 95:5, 610 mg, 1.4 mmol, 1 equiv) in benzene (20 mL) was added to the KCN and 18-crown-6 ether. The resulting mixture was stirred at 20 °C for 20 min under argon and heated to 70–75 °C for 12 h. After cooling to 20 °C, the mixture was poured into water (10 mL) and diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 25 mL) and the combined organic phases washed with brine and concentrated in vacuo. Purification by flash chromatography on silica gel gave a mixture of the 5α-H isomer **24b** (5α-H) (225 mg, 47% yield) and the 5α-H isomer **25b** (5α-H) (79 mg, 16% yield).

IR ($CHCl_3$) ν 2 930, 2 897, 2 856, 2 219, 1 667, 1 645, 1 470, 1 461, 1 385, 1 255, 1 099, 1 074, 1 059, 814.

• *Compound* **24b** *(5α-H)*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.04 [2s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.88 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.00, 1.02 and 1.15 (3s, 9H, CH_3-3a, $2CH_3$-5), 1.19–1.86 (m, 4H, H_2-6, H_2-7), 1.27 (t, J = 4.4 Hz, 1H, H-4), 3.58 (t, J = 2.5 Hz, 1H, H-7a), 3.72 (d, J = 4.4 Hz, 2H, H_2-1″), 4.57 (dd, J = 16.4, 2.4 Hz, 1H, Ha-2), 4.77 (dd, J = 16.4, 2.4 Hz, 1H, Hb-2), 5.14 (t, J = 2.4 Hz, 1H, H-1′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.3 [$2CH_3$, $Si(CH_3)_2$], 17.1 (CH_3, CH_3-3a), 18.2 [C, $SiC(CH_3)_3$], 21.8 (C-6), 22.4 and 33.2 ($2CH_3$-5), 26.0 [$3CH_3$, $SiC(CH_3)_3$], 33.4 (C-5), 35.3 (C-7), 47.5 (C-4), 48.8 (C-3a), 60.4 (C-1″), 69.8 (C-2), 84.9 (C-7a), 90.4 (C-1′), 115.9 (CN), 176.9 (C-3).

• *Compound* **25b** *(5α-H)*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.05 [s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.8–1.8 (m, 4H, H_2-6′, H_2-7′), 0.90 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.10 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.76 (m, 1H, H-4′), 3.09 (dd, J = 15.1, 3.1 Hz, 1H, Ha-2), 3.21 (dd, J = 15.1, 3.1 Hz, 1H, Hb-2), 3.81 (dd, J = 11.2, 4.9 Hz, 1H, Ha-1″), 3.87 (dd, J = 11.2, 2.6 Hz, 1H, Hb-1″), 3.95 (t, J = 4.1 Hz, 1H, H-7′a), 6.35 (s, 1H, H-2′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.4 [$2CH_3$, $Si(CH_3)_2$], 18.1 [C, $SiC(CH_3)_3$], 22.2 (CH_3), 23.0 (CH_3), 23.8 (C-6′), 26.0 [$3CH_3$, $SiC(CH_3)_3$], 32.6 (C-5′), 33.7 (CH_3-5′), 36.2 (C-2), 36.2 (C-7′), 48.2 (C-3′a), 54.4 (C-4′), 61.4 (C-1″), 90.5 (C-7′a), 116.8 (CN), 128.0 (C-2), 142.7 (C-3).

MS (Cl, NH_3) m/z 384 (MH^+ + $2NH_3$), 367 (MH^+ + NH_3), 350 (MH^+), 339, 309, 150, 131.

Anal calc for $C_{20}H_{35}NO_2Si$, 349.55: C, 68.72; H, 10.09; N, 4.01. Found; C, 68.65; H, 10.12; N, 4.08.

(3Z,3aR,4R*S*,7aR*)-3-Ethylidene-3a,5,5-trimethyl-octahydrobenzofuran-4-carbaldehyde* **26** *(5α-H)*

A solution of alcohols **21a** (5α-H/5β-H = 60:40, 1.9 g, 8.5 mmol) in dichloromethane (10 mL) at 20 °C was added to a solution of the Dess–Martin reagent (3.87 g, 9.12 mmol, 1.1 equiv) in dichloromethane (20 mL). The reaction was

stirred at 20 °C for 1 h, quenched with a saturated Na_2SO_3 aqueous solution (20 mL), diluted with diethyl ether (75 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, then with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave a 60:40 mixture of 5α-H and 5β-H isomeric aldehyde **26a** (1.86 g, 99% yield).

To a solution of the above 60:40 mixture of 5α-H and 5β-H aldehydes **26a** (900 mg, 4 mmol) in methanol (5 mL) was added K_2CO_3 (2.8 g, 20 mmol, 5 equiv) and the resulting suspension was stirred at reflux for 3 h and then cooled to 20 °C. The reaction mixture was partitioned between an aqueous 1 N HCl solution (20 mL) and diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave the pure 5α-H aldehyde **26a** (5α-H) (850 mg, 94% yield).

• *Compound* **26a** *5α-H isomer*

IR (NaCl) ν 2 925, 2 853, 1 718, 1 458, 1 384, 1 077, 1 054.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.95, 1.15 and 1.25 (3s, 9H, $2CH_3$-5, CH_3-3a), 1.52 (dt, J = 6.8, 1.5 Hz, 3H, CH_3, CH_3-1′), 1.01–1.97 (m, 4H, H_2-6, H_2-7), 2.02 (d, J = 3.9 Hz, 1H, H-4), 3.44 (t, J = 2.8 Hz, 1H, H-7a), 4.23 (ddq, J = 12.0, 2.5, 1.5 Hz, 1H, Ha-2) 4.47 (ddq, J = 12.0, 2.5, 1.5 Hz, 1H, Hb-2), 5.05 (tq, J = 2.5, 6.8 Hz, 1H, H-1′), 9.83 (d, J = 3.9 Hz, 1H, H-1″).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.0 (CH_3), 18.2 (CH_3), 22.1 (C-6), 22.2 (CH_3), 32.3 (CH_3), 32.9 (C-5), 35.0 (C-7), 45.2 (C-3a), 59.0 (C-4), 68.0 (C-2), 84.3 (C-7a), 115.4 (C-1′), 147.9 (C-3), 205.5 (C-1″, *C*HO).

• *Compound* **26b** *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.83, 1.06 and 1.28 (3s, 9H, $3CH_3$, $2CH_3$-5, CH_3-3a), 1.52 (dt, J = 6.8, 1.5 Hz, 3H, CH_3, CH_3-1′), 1.0–2.0 (m, 5H, H-4, H_2-6, H_2-7), 3.52 (t, J = 2.8 Hz, 1H, H-7a), 4.21 (m, 2H, H_2-2), 5.20 (m, 1H, H-1′), 9.46 (d, J = 6.3 Hz, 1H, H-1″).

MS (CI, NH_3) m/z 240 (MH^+ + NH_3), 223 (MH^+), 222, 207, 194, 179, 165, 151, 137, 123, 111, 95.

(3Z,3aR,4S*,7aR*)-3-Ethylidene-4-hydroxymethyl-3a,5,5-trimethyl octahydrobenzofuran* **21a** *(5α-H)*

To a solution of aldehyde **26** (5α-H) (120 mg, 0.52 mmol) in MeOH (1 mL) cooled to 0 °C was added $NaBH_4$ (6 mg, 0.1 mmol, 0.25 equiv). The reaction mixture was stirred at this temperature for 1 h and partitioned between diethyl ether (50 mL) and a 0.1 N aqueous HCl solution (10 mL). The aqueous phase was extracted with diethyl ether (3 × 25 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave alcohol **21a** (5α-H) (100 mg, 86% yield) as a yellow oil (see above preparation of **21a**).

(3Z,3aR,4R*,7aR*)-3-Iodomethylidene-3a,5,5-trimethyl octahydrobenzofuran-4-carbaldehyde* **27** *(5α-H)*

To a suspension of PCC (1.5 g, 6.7 mmol, 1.5 equiv) and celite (1.5 g) in dichloromethane (6 mL) was added via cannula a solution of the alcohols **23a** (5α-H/5β-H = 60:40, 1.5 g, 4.5 mmol) in dichloromethane (15 mL). The resulting dark brown solution was stirred at 20 °C for 1.5 h, filtered over celite and concentrated in vacuo. Purification by flash chromatography on silica gel gave a 60:40 mixture of 5α-H and 5β-H isomeric aldehydes **27a** (1.3 g, 87% yield).

To this solution of aldehydes **27a** (600 mg, 1.8 mmol) in methanol (5 mL) was added K_2CO_3 (1.2 g, 9.0 mmol, 5 equiv) and the resulting suspension was stirred at reflux for 3 h and cooled at 20 °C. The reaction mixture was partitioned between an aqueous 1 N HCl solution (10 mL) and diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave the pure 5α-H aldehyde **27a** (5α-H) (570 mg, 95% yield).

• *Compound* **27a** *5α-H isomer*

IR (NaCl) ν 2 934, 2 852, 1 714, 1 634, 1 454, 1 385, 1 368, 1 246, 1 076, 1 054, 887, 774.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.04, 1.23 and 1.34 (3s, 9H, $3CH_3$, $2CH_3$-5, CH_3-3a), 1.00–1.98 (m, 4H, H_2-6, H_2-7), 2.13 (d, J = 3.4 Hz, 1H, H-4), 3.64 (t, J = 2.9 Hz, 1H, H-7a), 4.19 (dd, J = 14.9, 2.4 Hz, 1H, Ha-2), 4.48 (dd, J = 14.9, 2.4 Hz, 1H, Hb-2), 5.88 (t, J = 2.4 Hz, 1H, H-1′), 9.91 (d, J = 3.4 Hz, 1H, H-1″).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 18.0 (CH_3), 22.3 (C-6), 22.3 (CH_3), 32.2 (C-5), 32.3 (CH_3), 34.9 (C-7), 49.2 (C-3a), 58.3 (C-4), 69.8 (C-2), 74.8 (C-7a), 85.6 (C-1′), 159.3 (C-3), 204.3 (C1″).

MS (CI, NH_3) m/z 352 (MH^+ + NH_3), 335 (MH^+), 317, 289, 235, 207, 189, 179, 161, 123.

• *Compound* **27b** *5β-H isomer*

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.89, 1.07 and 1.30 (3s, 9H, $3CH_3$, $2CH_3$-5, CH_3-3a), 1.20–1.93 (m, 4H, H_2-6, H_2-7), 1.95 (d, J = 6.0 Hz, 1H, H-4), 3.74 (t, J = 3.6 Hz, 1H, H-7a), 4.12 (dd, J = 15.2, 2.6 Hz, 1H, Ha-2), 4.19 (dd, J = 15.2, 2.6 Hz, 1H, Hb-2), 5.98 (t, J = 2.6 Hz, 1H, H-1′), 9.59 (d, J = 6.0 Hz, 1H, H-1″).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 23.1 (C-6), 26.1, 28.9 and 30.0 ($3CH_3$, $2CH_3$-5, CH_3-3a), 32.2 (C-5), 31.8 (C-7), 50.1 (C-3a), 66.5 (C-4), 70.9 (C-2), 75.6 (C-7a), 158.5 (C-3), 84.8 (C-1′), 203.4 (C1″).

(3Z,3aR,4R*,7aR*)-4-Hydroxymethyl-3-iodomethylidene-3a,5,5-trimethyl octahydrobenzofuran* **23a** *(5α-H)*

To a cooled solution (0 °C) of aldehyde **27** (5α-H) (750 mg, 2.2 mmol) in methanol (5 mL) was added sodium borohydride (21 mg, 0.55 mmol, 0.25 equiv). A further equal amount of sodium borohydride was added 30 min later to complete the reaction and the reaction mixture was treated with a 1 N aqueous HCl solution (20 mL), concentrated in vacuo and partitioned between water (10 mL) and diethyl ether (75 mL). The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave compound **23a** (5α-H) (653 mg, 87% yield, see above preparation of **23a**).

(3Z,3aR,4R*,7aR*)-4-{[(tert-Butyldimethylsilyl)oxy]-methyl}-3-iodomethylidene-3a,5,5-trimethyl octahydrobenzofuran* **23b** *(5α-H)*

To a cooled solution of alcohol **23a** (5α-H) (1.98 g, 5.9 mmol) and imidazole (1.0 g, 14 mmol, 2.5 equiv) in DMF (2 mL) was added dropwise a solution of *tert*-butyldimethylsilyl chloride (980 mg, 6.5 mmol, 1.1 equiv) in DMF (2 mL). After stirring at 0 °C for 4 h, the reaction mixture was allowed to warm up to room temperature and stirred overnight at 20 °C. The reaction mixture was partitioned between a 1 N aqueous hydrochloric acid solution (10 mL) and ethyl acetate (50 mL). The phases were separated and the aqueous layer extracted with ethyl acetate (3 × 50 mL). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave the tittle compound **23b** (5α-H) (2.27 g, 85% yield).

(3Z,3aR,4R*,7aR*)-3-[(Tributylstannyl)methylidene]-3a,5,5-trimethyl octahydrobenzofuran-4-carbaldehyde* **28** *(5α-H)*

To a solution of compound **14** (2.0 g, 9.7 mmol) in toluene (480 mL) were added AIBN (160 mg, 1.0 mmol, 0.1 equiv) and Bu_3SnH (4.4 mL, 17 mmol, 1.7 equiv). The mixture was stirred at reflux for 3 h. The oily residue obtained on removing toluene under reduced pressure was purified by flash chromatography over basic (pretreated with $NaHCO_3$) silica gel to give a 98:2 mixture of 5α-H and 5β-H diastereoisomeric compounds **28** (5α-H) (4.2 g, 87% yield).

IR ($CHCl_3$) ν 2 948, 2 926, 1 732, 1 616, 1 462, 1 368, 1 251, 1 053, 836, 777.

^1H NMR ($CDCl_3$, 200 MHz) δ 0.75–1.51 (m, 5H, H-4, H_2-6, H_2-7), 0.78 (s, 3H, CH_3), 0.87 {t, J = 6.0 Hz, 9H, $3CH_3$, $Sn[(CH_2)_3CH_3]_3$}, 0.90 [t, J = 6.0 Hz, 6H, $3CH_2$, $Sn(CH_2)_3$], 0.97 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 1.30–1.50 {m, 12H, $6CH_2$, $Sn[CH_2(CH_2)_2CH_3]_3$}, 3.66 (t, J = 4.3 Hz, 1H, H-7a), 4.22 (m, 2H, H-2), 5.78 (t, J = 2.6 Hz, 1H, H-1′, J H-^{117}Sn = J H-^{119}Sn = 60.0 Hz), 9.61 (d, J = 6.24 Hz, 1H, CHO).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 9.7 [$3CH_2$, $Sn(CH_2)_3$, J C-^{117}Sn = 350.0 Hz, J C-^{119}Sn = 340.0 Hz], 13.3 {$3CH_3$, $Sn[CH_2(CH_2)_3CH_3]_3$}, 23.2 (CH_3), 26.8 (C-6), 27.0 (CH_3), 27.3 [$3CH_2$, $Sn(CH_2CH_2CH_2CH_2)_3$, J C-^{117}Sn = J C-^{119}Sn = 57.0 Hz], 29.2 [$3CH_2$, $Sn(CH_2CH_2CH_2CH_3)_3$, J C-^{117}Sn = J C-^{119}Sn = 26.0 Hz], 31.8 (C-5), 32.1 (CH_3), 35.2 (C-7), 48.4 (C-3a, J C-^{117}Sn = J C-^{119}Sn = 56.0 Hz), 66.8 (C-4), 72.1 (C-2, J C-^{117}Sn = J C-^{119}Sn = 29.0 Hz), 83.5 (C-7a), 119.5 (C-1′), 165.0 (C-3), 204.5 (C-1″, CHO).

MS (CI, NH_3) m/z for major ^{120}Sn isotope 516 ($MH^+ + NH_3$), 499 (MH^+).

(3Z,3aR,4S*,7aR*)-4-Hydroxymethyl-3-[(tributylstannyl)methylidene]-3a,5,5-trimethyl octahydrobenzofuran* **19a** *(5α-H)*

To a cooled solution (0 °C) of aldehyde **28** (5α-H) (350 mg, 0.7 mmol) in methanol (5 mL) was added sodium borohydride (7 mg, 0.18 mmol, 0.25 equiv). A further equal amount of sodium borohydride was added 30 min later to complete the reaction and the reaction mixture was concentrated in vacuo and partitioned between water (10 mL) and diethyl ether (75 mL). The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave compound **19a** (5α-H) (297 mg, 85% yield, see above preparation of **19a**).

(3Z,3aR,4S*,7aR*)-4-{[(tert-Butyldimethylsilyl)oxy]-methyl}-3-[(tributylstannyl)methylidene]-3a,5,5-trimethyl octahydrobenzofuran* **19b** *(5α-H)*

To a cooled solution (0 °C) of alcohol **19a** (5α-H) (250 mg, 0.5 mmol) and imidazole (85 mg, 1.25 mmol, 2.5 equiv) in DMF (2 mL) was added dropwise a solution of *tert*-butyldimethylsilyl chloride (90 mg, 0.55 mmol, 1.1 equiv) in DMF (2 mL). After stirring at 0 °C for 4 h, the reaction mixture was allowed to warm up to room temperature and stirred overnight at 20 °C. The reaction mixture was partitioned between a saturated aqueous NH_4Cl solution (10 mL) and ethyl acetate (50 mL). The phases were separated and the aqueous layer extracted with ethyl acetate (3 × 50 mL). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave the title compound **19b** (5α-H) (245 mg, 80% yield, see above preparation of **19b**).

[1R(3Z,3aS*,4S*,7aS*)]-1-(3-Ethylidene-3a,5,5-trimethyl octahydrobenzofuran-4-yl)prop-2-yn-1-ol* **29**

To a solution of lithium acetylide/ethylenediamine complex (4.29 g, 46.7 mmol, 6 equiv) in THF (20 mL) cooled to 0 °C was added aldehyde **26** (5α-H) (1.7 g, 7.6 mmol) in THF (5 mL). The reaction mixture was stirred at this temperature for 3 h and then at 20 °C for 12 h. The reaction was quenched with 1 mL of a saturated aqueous NH_4Cl solution and diluted with diethyl ether (50 mL). The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave alcohol **29** (1.35 g, 70% yield).

IR (NaCl) ν 3 301, 3 052, 2 980, 2 937, 2 857, 1 448, 1 385, 1 265, 1 051, 738, 705.

^1H NMR ($CDCl_3$, 200 MHz) δ 1.24, 1.35 and 1.58 (3s, 9H, $2CH_3$, $2CH_3$-5′, CH_3-3′a), 1.01, 2.50 (m, 4H, H-4′, H_2-6′, H_2-7′), 1.59 (dt, J = 6.8, 1.3 Hz, 3H, CH_3-1″), 2.55 (d, J = 2.5 Hz, 1H, H-3), 2.25 (m, 1H, OH), 3.38 (dd, J = 2.5, 3.2 Hz, 1H, H-1), 3.45 (t, J = 3.1 Hz, 1H, H-7′a), 4.36 (dd, J = 12.5, 2.4 Hz, 1H, Ha-2′) 4.49 (dd, J = 12.5, 2.4 Hz, 2H, Hb-2′), 5.4 (qt, J = 6.8, 2.4 Hz, 1H, H-1″).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.1 (C-2″), 18.00, 23.7 and 33.7 ($3CH_3$, $2CH_3$-5′, CH_3-3′a), 22.3 (C-6′), 34.8 (C-5′), 37.8 (C-7′), 47.6 (C-3′a), 50.1 (C-4′), 61.5 (C-1), 67.4 (C-2′), 73.2 (C-3), 85.0 (C-7′a), 87.7 (C-2), 115.9 (C-1″), 150.0 (C-3′).

MS (CI, NH_3) m/z 266 ($MH^+ + NH_3$), 249 (MH^+), 248, 233, 215, 203, 176, 161, 147, 135, 121, 105, 91.

Anal calc for $C_{16}H_{24}O_2$, 248.35: C, 77.37; H, 9.74. Found; C, 77.52; H, 9.77.

[1R(3Z,3aS*;4S*,7aS*)]-1-(3-Ethylidene-3a,5,5-trimethyl octahydrobenzofuran-4-yl)-3-(trimethylsilyl)prop-2-yn-1-ol* **30**

To a solution of (trimethylsilyl)acetylene (120 μL, 0.84 mmol, 2.1 equiv) in THF (1 mL) cooled to −78 °C

was added a 1.5 M *n*-BuLi solution in hexanes (540 mL, 0.82 mmol, 2 equiv). The reaction mixture was warmed to 0 °C for 15 min whereupon aldehyde **26** (5α-H) (90 mg, 0.4 mmol) in THF (2 mL) was added via cannula. The reaction was stirred at this temperature for 3 h and quenched with a saturated aqueous NH_4Cl solution (1 mL). The mixture was diluted with diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave alcohol **30** (109 mg, 84% yield).

IR (NaCl) ν 3 444, 2 933, 2 856, 1 462, 1 384, 1 156b, 1 052, 842, 759, 668.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.14 [s, 9H, $3CH_3$, $Si(CH_3)_3$], 1.18, 1.20 and 1.32 (3s, 9H, $3CH_3$, $2CH_3$-5′, CH_3-3′a), 1.02–1.78 (m, 5H, OH, H_2-6′, H_2-7′), 1.57 (dt, J = 6.9, 1.3 Hz, 3H, CH_3, CH_3-1″), 2.29 (d, J = 7.1 Hz, 1H, H-4′), 3.42 (t, J = 3.0 Hz, 1H, H-7′a), 4.33 (ddq, J = 14.9, 2.7, 1.3 Hz, 1H, Ha-2′), 4.46 (ddq, J = 14.9, 2.7, 1.3 Hz, 1H, Hb-2′), 4.84 (dd, J = 7.1, 1.7 Hz, 1H, H-1′), 5.35 (qt, J = 6.9, 2.7 Hz, 1H, H-1″).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −0.3 [$3CH_3$, $Si(CH_3)_3$], 14.1 (C-2″), 18.3, 23.7 and 34.8 ($2CH_3$-5′, CH_3-3′a), 22.3 (C-6′), 33.6 (C-5′), 37.1 (C-7′), 47.8 (C-3′a), 51.0 (C-4′), 62.4 (C-1), 67.5 (C-2′), 85.3 (C-7′a), 81.2 and 109.8 (C-2, C-3), 115.8 (C-1″), 150.5 (C-3′).

MS (CI, NH_3) m/z 338 ($MH^+ + NH_3$), 321 (MH^+), 320, 205, 291, 264, 235, 221, 193, 181.

Anal calc for $C_{19}H_{32}O_2Si$, 320.51: C, 71.20; H, 10.06. Found; C, 71.18; H, 10.13.

(3Z,3aR,4R*,7aR*)-1-(3-Ethylidene-3a,5,5-trimethyl octahydrobenzofuran-4-yl)prop-2-yn-1-one* **31**

A solution of alcohol **29** (180 mg, 0.72 mmol) in dichloromethane (2 mL) at 20 °C was added to a solution of the Dess–Martin reagent (450 mg, 9.1 mmol, 1.5 equiv) in dichloromethane (2 mL). The reaction was stirred at 20 °C for 1 h, quenched with a saturated Na_2SO_3 aqueous solution (5 mL) and diluted with diethyl ether (30 mL). The phases were separated and the aqueous phase extracted with diethyl ether (3 × 25 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, then with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave ketone **31** (149 mg, 85% yield).

IR (NaCl) ν 2 975, 2 942, 2 859, 2 084, 1 690, 1 467, 1 450, 1 091, 1 077, 1 048, 1 029, 879.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.92, 1.05 and 1.15 (3s, 9H, $3CH_3$, $2CH_3$-5′, CH_3-3′a), 1.05–2.01 (m, 4H, H_2-6′, H_2-7′), 1.53 (dt, J = 6.8, 1.4 Hz, 3H, CH_3, CH_3-1″), 2.89 and 3.21 (2s, 2H, H-4′, H-3), 3.49 (t, J = 1.5 Hz, 1H, H-7′a), 4.35 (ddq, J = 13.7, 2.3, 1.4 Hz, 1H, Ha-2′), 4.61 (ddq, J = 13.7, 2.3, 1.4 Hz, 1H, Hb-2′), 5.09 (qt, J = 6.8, 2.3 Hz, 1H, H-1″).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.0 (CH_3, CH_3-1″), 18.0, 21.8 and 32.2 ($3CH_3$, $2CH_3$-5′, CH_3-3′a), 22.1 (C-6′), 34.8 (C-5′), 35.2 (C-7′), 45.9 (C-3a′), 61.6 (C-4′), 68.0 (C-2′), 77.3 (C-3), 84.0 (C-7a′), 85.1 (C-2), 114.9 (C-1″), 147.4 (C-3′), 190.9 (C-1).

MS (CI, NH_3) m/z 264 ($MH^+ + NH_3$), 247 (MH^+).

Anal calc for $C_{16}H_{22}O_2$, 246.34: C, 78.01; H, 9.00. Found; C, 78.25; H, 9.13.

(3Z,3aR,4R*,7aR*)-1-(3-Ethylidene-3a,5,5-trimethyl octahydrobenzofuran-4-yl)propan-1-one* **32**

To a solution of ketone **31** (11 mg, 0.045 mmol) in methanol (1 mL) cooled to 0 °C was added sodium borohydride (4 mg, 0.1 mmol, 2.2 equiv). A further equal amount of sodium borohydride were added 30 min later to complete the reaction and the reaction mixture was stirred for 30 min at 0 °C and then treated with an 1 N aqueous HCl solution (1 mL) and concentrated in vacuo. The mixture was partitioned between water (5 mL) and ethyl acetate (10 mL) and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel (petroleum ether/ethyl acetate 9:1) gave ketone **32** (8 mg, 74% yield).

IR (NaCl) 2 934, 2 854, 1 710, 1 459, 1 387, 1 367, 1 111, 1 077, 1 061, 1 030, 905, 880, 808.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.84, 1.08 and 1.17 (3s, 9H, $3CH_3$, $2CH_3$-5′, CH_3-3′a), 0.92 (t, J = 7.5 Hz, 3H, CH_3, H_3-3), 0.78–1.83 (m, 4H, H_2-6′, H_2-7′), 1.53 (dt, J = 6.8, 1.2 Hz, 3H, CH_3, CH_3-1″), 2.32 (q, J = 7.5 Hz, 2H, H_2-2), 2.59 (s, 1H, H-4′), 3.46 (t, J = 3.3 Hz, 1H, H-7′a), 4.33 (ddq, J = 15.0, 2.5, 1.2 Hz, 1H, Ha-2′), 4.57 (ddq, J = 15.0, 2.5, 1.2 Hz, 1H, Hb-2′), 4.85 (qt, J = 6.8, 2.5 Hz, 1H, H-1″).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 7.0 (C-3), 13.9 (C-2″), 17.9, 21.5 and 32.6 ($3CH_3$, $2CH_3$-5′, CH_3-3′a), 22.1 (C-3′), 33.9 (C-5′), 35.1 (C-7′), 42.3 (C-2), 45.7 (C-3′a), 58.2 (C-4′), 67.9 (C-2′), 84.0 (C-7′a), 113.7 (C-1″), 148.7 (C-3′), 213.78 (C-1).

MS (CI, NH_3) m/z 268 ($MH^+ + NH_3$), 251 (MH^+).

[2R(3aR*,4R*,7aR*)]-2-(4-{[(tert-Butyldimethylsilyl)-oxy]methyl}-3a,5,5-trimethyl-3a,4,5,6,7,7a-hexahydrobenzofuran-3-yl)propanoic acid methyl ester* **33b** *(5α-H)*

To a 1 M LDA solution in THF (2.3 mL, 2.3 mmol, 1.5 equiv) cooled at −78 °C was added HMPA (410 mL, 3.0 mmol, 1.5 equiv). The reaction mixture was stirred at this temperature for 30 min and then ester **22b** (pure 5α-H, 570 mg, 1.5 mmol) in THF (5 mL) was added via cannula. The reaction mixture was stirred at −78 °C for 15 min and allowed to warm to 0 °C for 15 min. After cooling to −78 °C, MeI (290 μL, 4.5 mmol, 3 equiv) was added and then the mixture allowed to warm to 20 °C over 2 h. The reaction was quenched with an aqueous 1 N HCl solution (3 mL), diluted with diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 25 mL) and the combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel gave the 5α-H isomer **33b** (5α-H) (565 mg, 95% yield) as a yellow oil.

IR (CCl_4) 2 958, 2 930, 1 739, 1 632, 1 470, 1 461, 1 254, 1 138, 1 100, 837.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.08 [s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.73–1.84 (m, 4H, H_2-6′, H_2-7′), 0.90 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.00 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.31 (d, J = 7.0 Hz, 3H, CH_3, CH_3-2), 1.88 (m, 1H, H-4′), 3.30 (q, J = 7.0 Hz, 1H, H-2), 3.70 (s, 3H, CH_3, CO_2CH_3), 3.80 (dd, J = 11.2, 4.9 Hz, 1H, Ha-1″), 3.85 (dd, J = 11.2, 2.6 Hz, 1H, Hb-1″), 3.95 (t, J = 4.3 Hz, 1H, H-7′a), 6.35 (s, 1H, H-2′).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.6 [$2CH_3$, $Si(CH_3)_2$], 18.1 [C, $SiC(CH_3)_3$], 21.0 (CH_3), 22.1 (CH_3), 22.9 (CH_3), 23.0 (C-6′), 26.0 [$3CH_3$, $SiC(CH_3)_3$], 32.3 (CH_3), 32.6 (C-5′), 36.5 (C-2), 35.9 (C-7′), 48.2 (C-3′a), 54.4 (C-4′), 52.4

(CH_3, CO_2CH_3), 61.4 (C-1″), 90.5 (C-7′a), 128.0 (C-3′), 142.7 (C-2′), 175.7 (C-1, CO_2CH_3).

MS (CI, NH_3) m/z 414 ($MH^+ + NH_3$), 397 (MH^+).

Anal calc for $C_{22}H_{40}O_4Si$, 396.62: C, 66.62; H, 10.16. Found; C, 66.54; H, 10.22.

(3aR,4R*,7aR*)-2-(4-{[(tert-Butyldimethylsilyl)oxy]-methyl}-3a,5,5-trimethyl-3a,4,5,6,7,7a-hexahydro-benzofuran-3-yl)propanenitrile* **34b** *(5α-H)*

To a 1 M LDA solution in THF (600 μL, 0.6 mmol, 1.5 equiv) cooled to −78 °C was added HMPA (100 μL, 0.6 mmol, 1.5 equiv). The reaction mixture was stirred at this temperature for 30 min and a solution of cyano compound **24b** (5α-H) (140 mg, 0.4 mmol) in THF (2 mL) was then added via cannula. The reaction mixture was stirred at −78 °C for 15 min and allowed to warm to 0 °C for 15 min. After cooling to −78 °C, MeI (75 mL, 1.2 mmol, 3 equiv) was added and the mixture was allowed to warm to 20 °C over 2 h. The reaction mixture was quenched with a 0.1 N aqueous HCl solution (10 mL), diluted with diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 25 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave **34b** (5α-H) (124 mg, 84% yield) as a yellow oil.

IR ($CHCl_3$) 2 934, 2 897, 2 219, 1 667, 1 623, 1 381, 1 093, 1 064, 864.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.08 and 0.10 [2s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.70–1.84 (m, 5H, H-6′, H-7′, H-4′), 0.90 [3s, 9H, $3CH_3$, $SiC(CH_3)_3$], 1.00 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.41 (d, J = 7.8 Hz, 3H, CH_3-1), 3.68 (dd, J = 11.1, 7.3 Hz, 1H, Ha-1″), 3.78 (dd, J = 11.1, 3.4 Hz, 1H, Hb-1″), 3.95 (q, J = 7.8 Hz, 1H, H-1), 4.05 (t, J = 3.6 Hz, 1H, H-7a′), 6.53 (s, 1H, H-2′).

MS (CI, NH_3) m/z 381 ($MH^+ + NH_3$), 364 (MH^+).

(3R,6aR*,9aR*,9bR*)-3,7,7,9b-Tetramethyl-6a,7,8,8,9,9a,9b-hexahydro-6H-furo[4,3,2-ef][2]-benzoxepin-4(3H)-one* **35**

To a solution of the deconjugated ester **33b** (5α-H) (1 g, 2.5 mmol) in THF (10 mL) at 20 °C was added a 1 M TBAF solution in THF (3.0 mL, 3.0 mmol, 1.4 equiv). The reaction mixture was stirred at this temperature for 17 h, partitioned between brine (15 mL) and diethyl ether (50 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 25 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave lactone **35** (590 mg, 95% yield) as a yellow oil.

IR (CCl_4) ν 2 958, 2 930, 1 705, 1 630, 1 455, 1 250, 1 130, 1 100, 840.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.7–1.9 (m, 2H), 1.65 (d, J = 8.3 Hz, 1H, H-6a), 2.0 (m, 2H), 0.83 (s, 3H, CH_3), 1.01 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.20 (d, J = 6.9 Hz, 3H, CH_3, CH_3-3), 3.18 (qd, J = 6.9, 1.0 Hz, 1H, H-3), 4.15 (d, J = 13.1 Hz, 1H, Ha-6), 4.29 (dd, J = 9.5, 7.4 Hz, 1H, H-9a), 4.41 (dd, J = 13.1, 8.3 Hz, 1H, Hb-6), 6.10 (d, J = 1.0 Hz, 1H, H-2).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 15.4 (CH_3), 22.2 (CH_3), 24.0 (C-8), 24.4 (CH_3), 32.5 (C-3), 29.8 (CH_3), 30.6 (C-7), 33.7 (C-9), 47.5 (C-9b), 48.0 (C-6a), 65.6 (C-6), 88.5 (C-9a), 119.1 (C-2), 141.0 (C-2), 174.4 (C-8).

MS (CI, NH_3) m/z 268 ($MH^+ + NH_3$), 251 (MH^+).

Anal calc for $C_{15}H_{22}O_3$, 250.33: C, 71.97; H, 8.86. Found; C, 71.82; H, 8.93.

[3(1R),3aR*,4R*,7aR*]-4-{[(tert-Butyldimethylsilyl)-oxy]methyl}-3-(2-hydroxy-1-methylethyl)-3a,5,5-trimethyl-3a,4,5,6,7,7a-hexahydro-benzofuran* **36b** *(5α-H)*

To a solution of ester **33b** (5α-H) (pure 5α-H, 1.4 g, 3.5 mmol) in THF (15 mL) cooled to 0 °C was added a 1 M $LiAlH_4$ solution in diethyl ether (3.5 mL, 1 equiv). The resulting solution was stirred for 1 h at this temperature, and the reaction quenched with an 0.5 N aqueous HCl solution (17 mL), diluted with diethyl ether (100 mL) and the phases were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL) and the combined organic phases were washed with brine, then dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave alcohol **36b** (5α-H) (910 mg, 70% yield) as a yellow oil.

IR ($CHCl_3$) ν 3 420, 2 026, 1 642, 1 470, 1 385, 1 362, 1 161a, 1 097, 1 098, 1 030, 836.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.06 [s, 6H, $2CH_3$, $Si(CH_3)_2$], 0.84 [s, 9H, $3CH_3$, $SiC(CH_3)_3$], 0.91 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 1.05 (d, J = 6.5 Hz, 3H, CH_3-1′), 1.11 (s, 3H, CH_3), 1.21–2.20 (m, 6H, H-4, H-6, H-7, OH), 2.46 (m, 1H, H-1′), 3.52 (dd, J = 10.6, 2.5 Hz, 1H, Ha-2′), 3.55 (dd, J = 10.6, 7.3 Hz, 1H, Hb-2′), 3.72 (dd, J = 10.9, 3.5 Hz, 1H, Ha-1″), 3.78 (dd, J = 10.9, 3.5 Hz, 1H, Hb-1″), 3.88 (t, J = 3.6 Hz, 1H, H-7a), 6.19 (s, 1H, H-2).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ −5.4 [$2CH_3$, $Si(CH_3)_2$], 18.3 [C, $SiC(CH_3)_3$], 20.2 (CH_3), 21.8 (CH_3), 22.7 (C-6), 22.7 (CH_3), 26.1 [$3CH_3$, $SiC(CH_3)_3$], 32.2 (C-5), 32.7 (CH_3), 33.4 (C-1′), 36.3 (C-7), 47.7 (C-3a), 54.5 (C-4), 62.0 (C-1″), 67.4 (C-2′), 90.0 (C-7a), 131.7 (C-3), 140.9 (C-2).

MS (CI, NH_3) m/z 386 ($MH^+ + NH_3$), 369 (MH^+).

[3(1R),3aR*,4R*,7aR*]-4-Hydroxymethyl-3-(2-hydroxy-1-methylethyl)-3a,5,5-trimethyl-3a,4,5,6,7,7a-hexahydrobenzofuran* **10**

- *Procedure A*

To a solution of lactone **35** (200 mg, 0.8 mmol) in THF (2 mL) cooled to 0 °C was added a 1 M $LiAlH_4$ solution in THF (0.8 mL, 0.8 mmol, 1 equiv). The reaction mixture was stirred at this temperature for 1 h, quenched with an aqueous 0.1 N HCl solution (10 mL) and diluted with ethyl acetate (50 mL). The phases were separated and the aqueous phase was extracted with ethyl acetate (3 × 25 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave diol **10** (185 mg, 91% yield) as a yellow oil.

- *Procedure B*

To a solution of silyl alcohol **36b** (5α-H) (420 mg, 1.9 mmol) in THF (4 mL) at 20 °C was added a 1 N TBAF solution in THF (2.1 mL, 2.1 mmol, 1.1 equiv). The cloudy reaction mixture was stirred for 17 h, partitioned between brine (15 mL) and ethyl acetate (50 mL) and the phases were separated. The aqueous phase was extracted with ethyl acetate (3 × 25 mL) and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography on silica gel gave diol **10** (240 mg, 83% yield) as a yellow oil.

IR ($CHCl_3$) ν 3 378, 2 953, 1 634, 1 453, 1 383, 1 366, 1 008.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.83 (s, 3H, CH_3), 0.97 (d, J = 6.5 Hz, 3H, CH_3-1′), 0.98 (s, 3H, CH_3), 1.07 (s, 3H,

CH_3), 1.4–1.92 (m, 7H, H_2-6, H_2-7, H-4, 2 OH), 2.65 (m, 1H, H-1′), 3.47 (dd, J = 10.2, 2.4 Hz, 1H, Ha-2′), 3.62 (dd, J = 10.2, 2.4 Hz, 1H, Hb-2′), 3.68 (dd, J = 11.8, 4.5 Hz, 1H, Ha-1″), 3.76 (dd, J = 11.8, 4.5 Hz, 1H, Hb-1″), 3.88 (t, J = 2.9 Hz, 1H, H-7a), 6.21 (s, 1H, H-2).

^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 18.4 (CH_3), 21.3 (CH_3), 22.1 (C-6), 22.3 (CH_3), 32.3 (C-5), 32.3 (CH_3), 35.7 (C-1′), 35.8 (C-7), 46.8 (C-3a), 56.3 (C-4), 61.6 (C-1″), 67.1 (C-2′), 89.9 (C-7a), 132.8 (C-3), 140.3 (C-2).

MS (CI, NH_3) m/z 272 ($MH^+ + NH_3$), 255 (MH^+).

Anal calc for $C_{15}H_{26}O_3$, 254.36: C, 70.83; H, 10.30. Found; C, 70.45; H, 10.05.

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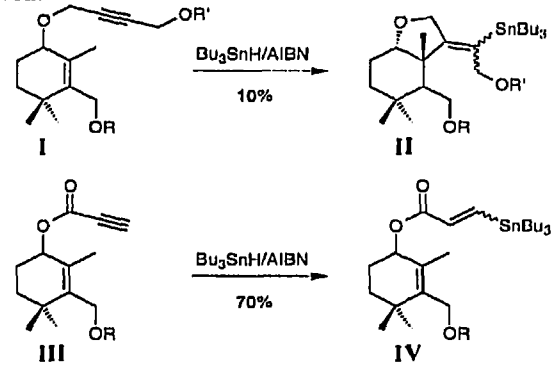
Starting from the enynone **III** in the same conditions used before, the reaction gave a hydrostannylation of the ynone and formation of **IV**, no cyclization was observed.



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