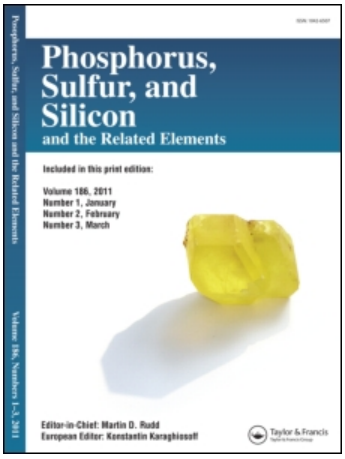

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Toward Chiral Stannane Reducing Agents Derived from Cholic Acid and Cholestanol

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Molecular mechanics studies have identified 3α-(dimethylstannyl)-24-nor-5β-cholane (5α), 7α-(dimethylstannyl)-24-nor-5β-cholane (6α) and 12β-(dimethylstannyl)-24-nor-5β-cholane (7β) to be effective stannanes for use as enantioselective free-radical reducing agents. Synthetic studies toward the preparation of these stannanes as well as 3α-(dimethylstannyl)-5α-cholestane (**21**) are presented together with selected enantioselectivity data.

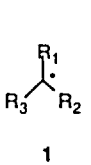
Keywords: stannane; enantioselective; free-radical; cholic acid

INTRODUCTION

Free-radical chemistry has benefited enormously from the invention of stannane-based free-radical chain-carrying reagents.[1] Without doubt tributyltin hydride has been the most studied and utilized stannane,[2] although other stannanes,[3] most noteably triphenyltin hydride,[4] have also been examined for their radical chain-carrying properties. With favorable rate constants for the delivery of hydrogen atom to a variety of alkyl, aryl and other radicals, coupled with useful rate constants for halogen and chalcogen abstraction from organic radical precursors has lead to the positioning of tributyltin hydride at the apex of most useful reagents in radical chemistry.[1]

The synthetic utility of tributyltin hydride in stereo-directed synthesis is somewhat limited; prochiral radicals (**1**) lead to a racemic

mixture of reduced products. Despite considerable efforts toward the construction of suitable chiral, non-racemic Lewis acids to promote the desired stereochemical outcome during radical reactions, it appears that acceptable enantioselectivities can only be obtained through the introduction of chiral ligands on the stannane involved in the radical reduction.



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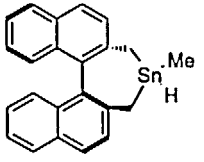

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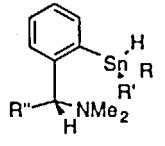

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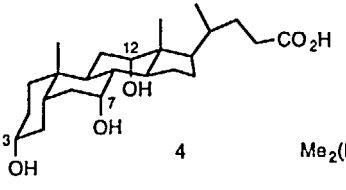
We are not the first group to consider this problem; indeed the groups of Curran and Metzger have independently examined the use of chiral, non-racemic stannanes containing C_2-symmetric binaphthyl ligands (eg. **2**),[5,6] while Metzger has developed some elegant amine-coordinated stannanes (eg. **3**) which have demonstrated enantioselectivities of up to 51% in some radical reduction reactions.[7]



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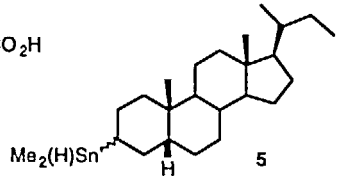

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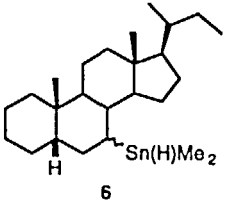

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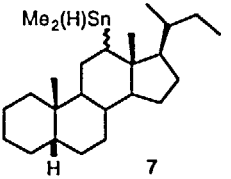

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Our approach to the development of synthetically useful chiral stannanes involves the judicious choice of ligand from the multitude of compounds available in the natural chiral pool. In particular, stannanes derived from steroids are particularly attractive targets. Cholic acid (3α,7α,12α-trihydroxy-5β-cholan-24-oic acid) (**4**) offers a unique concave template for the positioning of a stannane moiety in a chiral enviroment. Accordingly, 3α- and 3β-(dimethylstannyl)-24-nor-5β-cholane (**5**), 7α and 7β-(dimethylstannyl)-24-nor-5β-cholane (**6**), and

12α- and 12β-(dimethylstannyl)-24-nor-5β-cholane (**7**), stannanes that are readily available from **4**, are the targets of current work.

In this paper we report the use of molecular modelling to predict the structure of the most enantioselectively effective stannane (**5–7**) for use in radical reductions. In addition, the syntheses of 7α,12α-diacetoxy-3α-hydroxy-24-nor-5β-cholane (**15**), 7α-acetoxy-12α-hydroxy-24-nor-5β-cholane (**17**) and 7α-hydroxy-24-nor-5β-cholane (**18**), the synthetic precursors of stannanes **5–7**, as well as 3α-(dimethylstannyl)-5α-cholestane (**21**) are also presented.

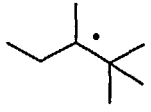
RESULTS AND DISCUSSION

Molecular Modelling Studies

In order to gain insight into the performance of stannanes (**5–7**) as enantioselective radical reducing agents, we chose to model the lowest energy conformers of the transition states involved during the delivery of hydrogen atom from the stannanes in question to the 2,2,3-trimethyl-3-pentyl radical (**8**) which we chose as the prototypical prochiral radical in our modelling studies. In all, three low-energy staggered conformations for each transition state (**9 – 11**) involved in the delivery of hydrogen atom to each face of **8** were considered. Transition states (**9 – 11**) were modelled in a similar manner to that published for intramolecular free-radical addition reactions (Beckwith-Schiesser model) and that for intramolecular homolytic substitution at selenium.[8,9] To that end the array of reacting centres in each transition state was fixed at the geometry of the transition state determined by *ab initio* (MP2/DZP) molecular orbital calculations for the attack of methyl radical at trimethyltin hydride (*viz.* $r_{Sn\text{-}H} = 1.81$Å; $r_{C\text{-}H} = 1.69$Å; $\theta_{Sn\text{-}H\text{-}C} = 180°$).[10] The remainder of each structure (**9 – 11**) was optimized using molecular mechanics (MM2) in the usual way.[11]

Table 1 lists the MM2-calculated difference in energy ($\Delta E^{\ddagger}_{re} - \Delta E^{\ddagger}_{si}$) between the lowest energy *re* and *si* transition states determined for delivery of hydrogen atom from stannanes (**5 – 7**) to the *re* and *si* faces of the prochiral radical (**8**) respectively. Predicted enantioselectivities have been determined using the Arrhenius expression and assuming similar entropy (logA) terms for reactions leading to hydrogen transfer to the *re* and *si* faces of **8** for each stannane considered. It should be remembered that these MM2-calculated energy differences will provide insight into the strain-energy

component of the activation energies associated with these reactions and make no allowance for changes in electronic factors. Despite this deficiency, these calculations should still provide a qualitative picture of the outcome of the reactions in question as steric factors appear to have the greatest influence on the energy of the transition state for hydrogen transfer from tin to carbon.[3]



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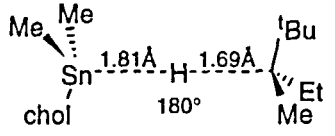


9 chol = 24-nor-5β-cholan- 3 -yl

10 chol = 24-nor-5β-cholan- 7 -yl

11 chol = 24-nor-5β-cholan- 12 -yl

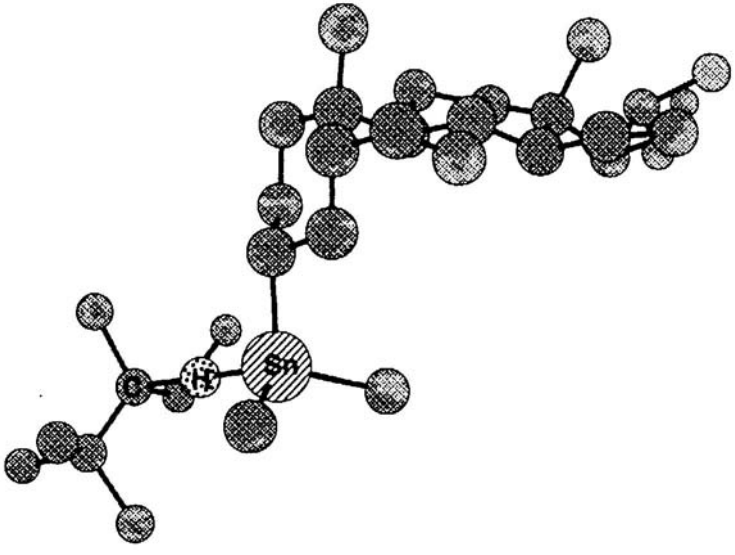
TABLE 1. Calculated enantioselectivity date for the reactions of stannanes (**5** – **7**) with the 2,2,3-trimethyl-3-pentyl radical (**8**). (Energies are in kJ.mol^{-1}).

Stannane	$\Delta E^{\ddagger}_{re} - \Delta E^{\ddagger}_{si}$	%ee (-78°)	%ee (80°)
5α (3α-Sn)	1.13	95	83
5β (3β-Sn)	-0.56	81	69
6α (7α-Sn)	-1.39	97	88
6β (7β-Sn)	-0.56	81	69
7α (12α-Sn)	1.26	96	86
7β (12β-Sn)	-4.95	>99	>99

A typical transition state ($\mathbf{9}_{si}$) as calculated for the reaction involving stannane (5α) with the *si* face of **8** is displayed in Figure 1.

Inspection of Table 1 reveals that the dimethylstannyl substituted 24-norcholanes (**5**α, **6**α, **7**α, **7**β) are predicted to the most stereochemically effective stannanes, with predicted enantiomeric excesses (ees) of 95, 97, 96 and > 99% respectively for their reactions with **8** at –78°. It is interesting to note that reactions involving **5**β and **7**α are predicted to proceed with *si*-face selectivity, while the remaining stannanes in this study are predicted to react with *re* selectivity.

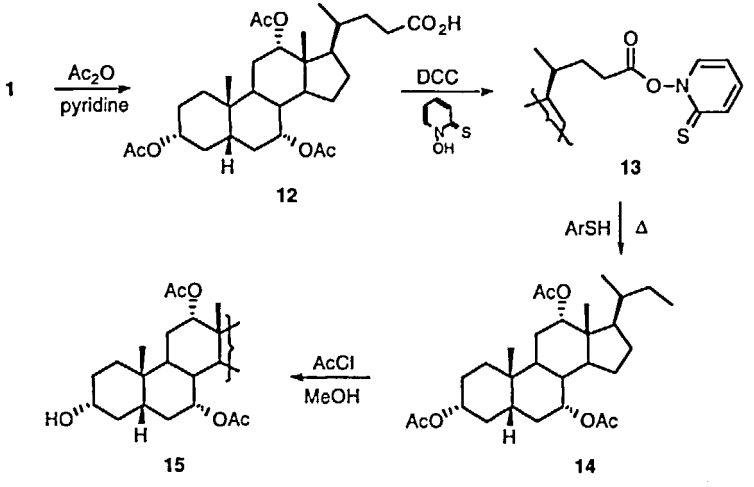
FIGURE 1 Lowest energy transition state (9_{si}) for the delivery of hydrogen atom from stannane **5**α the *si* face of the prochiral radical (**8**). (Hydrogen atoms have been removed for clarity.)



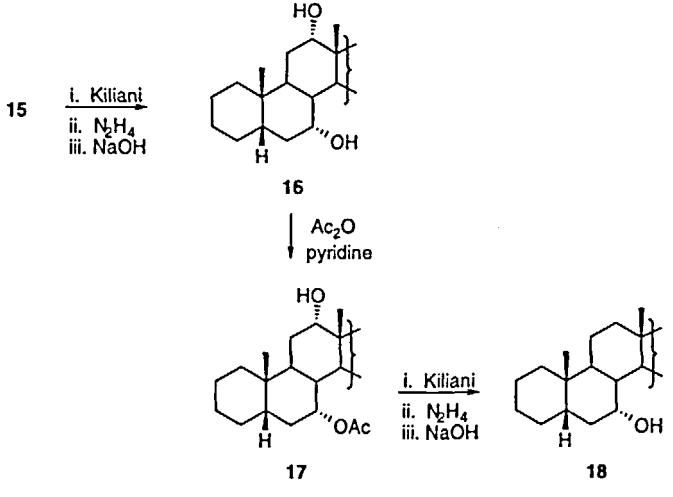
Preparation of Chiral Stannanes

With these computational data in mind, we next set about the preparation of stannanes (**5** – **7**). For ease of synthetic manipulation, the carboxylic acid functionality in cholic acid (**4**) was removed using standard Barton ester methodology (Scheme 1). To that end, cholic acid was peracetylated using acetic anhydride in pyridine to afford the triacetate (**12**) which was converted into the Barton ester (**13**) upon treatment with N-hydroxypyridine-2-thione and DCC in dichloromethane.[12]

Scheme 1



Scheme 2

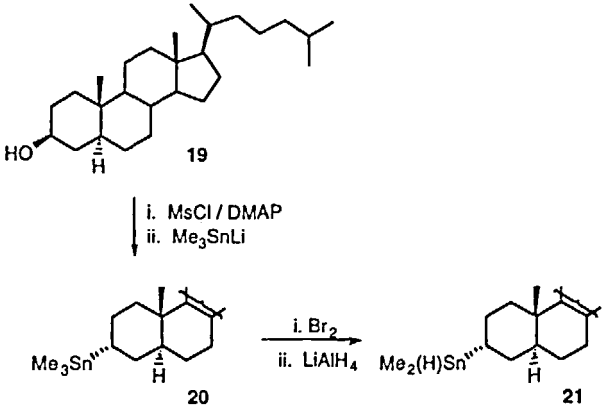


Thermolysis of **13** in the presence of thiocresol resulted in decarboxylation to afford the 24-norcholane (**14**) which was selectively

deprotected through the use of methanolic hydrogen chloride, generated by the slow addition of acetyl chloride to **14** in methanol.

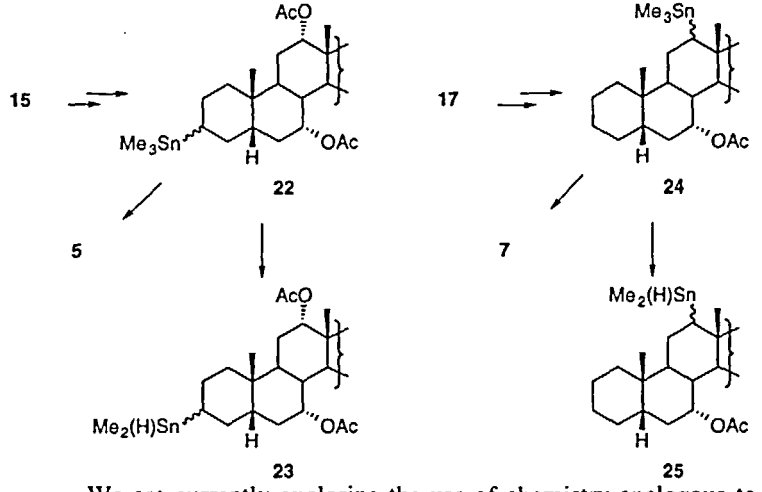
The diacetate (**15**) was further oxidized with Kiliani's reagent followed by standard Wolff-Kischner reduction to provide 7α,12α-dihydroxy-24-nor-5β-cholane (**16**), a key intermediate in this work (Scheme 2). Subsequent selective acetylation, Kiliani oxidation and Wolff-Kischner reduction afforded 7α-hydroxy-24-nor-5β-cholane (**18**), the synthetic precursor of stannanes (**6**).

Scheme 3



With alcohol (**18**) in hand, we began to explore methods for the conversion of steroidal alcohols into the corresponding or epimeric stannanes. In order to determine the optimum conditions for this transformation, we chose to subject the model alcohol, 3β-cholestanol (**19**) to the proposed reaction conditions. Accordingly, **19** was mesylated by reaction with methanesulfonyl chloride followed by treatment with trimethyltin lithium to afford 3α-trimethylstannylcholestane (**20**). Subsequent treatment of **20** with bromine in carbon tetrachloride followed by lithium aluminium hydride reduction gave the required stannane (**21**) as a low-melting solid. The ^{119}Sn NMR spectrum of **21** exhibited a single signal at δ -98.0, with a characteristic Sn-H coupling constant (J_{Sn-H}) of 1564 Hz. To the best of our knowledge, stannane (**21**) represents the first example of a tin hydride derived from a steroid.

Scheme 4

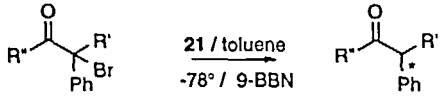


We are currently exploring the use of chemistry analogous to that depicted in Scheme 3 to the preparation of stannanes (**6**). We envisage that stannanes (**5**, **7**) will arise from further synthetic manipulation of the cholane skeleton and application of the same stannylation methodology (Scheme 4). In addition, synthetic intermediates (**15**, **17**) should also allow for some structurally-modified stannanes, such as **23** and **25** to be prepared, as outlined in Scheme 4.

Selected Enantioselectivity Testing

With the preparation of 3α-dimethylstannylcholestane (**21**) complete, it seemed appropriate to determine its effectiveness as a chiral radical reducing agent. In order to provide a direct comparison with our previous work[13] as well as that of Curran[5] and Metzger,[6,7] racemic bromides (**26** – **29**) were reacted with one equivalent of stannane (**21**) in toluene at –78°, initiated by addition of a small amount of 9-BBN[14] to afford the corresponding reduced product (**30**) as a mixture of enantiomers and with enantiomeric excesses of 4, 6, 8 and 9% as determined by chiral-phase gas chromatography of the crude reaction mixtures (Scheme 5). Not surprisingly, the stannane (**21**), derived from 3β-cholestanol, is only able to provide low levels of chiral induction. We hope to be able to provide enantioselectivity data for the other stannanes (**5** – **7**) in this study in the near future.

Scheme 5



26 R' = Me; R* = Ph
27 R' = Me; R* = OMe
28 R' = Et; R* = OMe
29 R' = ^{t}Bu; R* = OMe

30

EXPERIMENTAL

3α,7α,12α-Triacetoxy-5β-cholan-24-ioc acid[15] (12)

Pyridine (30 mL) and 4-(N,N-dimethylamino)pyridine (DMAP) (1.80g, 1.47 mmol) was added to a cooled suspension of cholic acid (10g, 24.5 mmol) in acetic anhydride (20 mL) and the resulting solution was stirred for 4 h at room temperature. The solvent was removed *in vacuo*, the residue diluted with ether and washed with brine, 10% HCl (3x), sat. $NaHCO_3$ and water. The solution was dried ($MgSO_4$) and the solvent evaporated to give *crude* **12** as a white solid (12.4g, 95%) of sufficient purity for further use. ^{1}H NMR ($CDCl_3$) δ 0.74 (s, 3H), 0.82 (d, 3H, J=1.2 Hz), 0.92 (s, 3H), 1.02 – 2.04 (m, 25 H), 2.04 (s, 3H), 2.08 (s, 3H), 2.14 (s, 3H), 4.59 (m, 1H), 4.91 (q, 1H, 2.7 Hz), 5.10 (t, 1H, 2.7 Hz). ^{13}C NMR ($CDCl_3$) δ 12.2, 17.5, 21.4, 21.5, 22.5, 22.8, 25.6, 26.8, 27.1, 28.9, 30.0, 31.2, 32.2, 34.3, 34.4, 34.6, 34.7, 37.7, 40.9, 43.4, 45.1, 47.4, 70.7, 74.1, 75.3, 170.5, 180.8.

3α,7α,12α-Triacetoxy-23-(2'-pyridinethioneoxycarbonyl)-24-nor-5β-cholane (13)

N-Hydroxypyridine-2-thione (3.15g, 24.8 mmol) and N,N-dicyclohexylcarbodiimide (DCC) (5.2g, 25.6 mmol) were added to a stirred solution of **12** (12.4g, 25.3 mmol) in dichloromethane (70 mL) at 0°, shielded from background light. The solution was stirred at 0° for 4 h and then placed in a freezer overnight. Taking care to exclude background light, the solution was filtered and the solid washed with ice-cold dichloromethane (2x). The solvent was removed *in vacuo*, (< 40°) to give **13** as a yellow solid, of sufficient purity for further use.

3α,7α,12α-Triacetoxy-24-nor-5β-cholane (14)

p-Thiocresol (3.27g, 26.3 mmol) was added to a stirred solution of **13** in toluene (300 mL) and the solution refluxed for 4 h. Evaporation of the solvent *in vacuo* and column chromatography (80 : 3, dichloromethane : ethyl acetate) gave **14** as a thick clear gum (8.08g, 71%). ^{1}H NMR ($CDCl_3$) δ 0.73 (s, 3H), 0.79 (s, 1H), 0.81 (d, 3H, J = 1.5Hz), 0.84 (s, 1H), 0.92 (s, 3H), 0.93–2.01 (m, 23H), 2.05 (s, 3H), 2.09 (s, 3 H), 2.14 (s, 3H), 4.58 (m, 1H), 4.91 (q, 1H J = 2.7 Hz), 5.10 (t, 1H, J = 2.7 Hz). ^{13}C NMR ($CDCl_3$) δ 10.2, 12.1, 17.2, 21.3, 21.4, 21.5, 22.5, 22.8, 25.5, 26.8, 27.1, 28.0, 28.8, 31.2, 34.3, 34.6, 34.6, 36.2, 37.7, 40.9, 43.3, 44.9, 47.2, 70.7, 74.0, 75.5, 170.3, 170.4. 170.5. IR ν_{max} 3450, 1732. MS *m/z* (70 eV) : 430 (M- CH_3COOH, 1.1), 370 (100), 313 (51), 310 (86), 295 (18), 253 (57). HRMS. Calcd. for $C_{29}H_{46}O_6$ (ESI M^+): 490.3294. Found: 490.3296

7α,12α-Diacetoxy-3α-hydroxy-24-nor-5β-cholane (15)

Following the method of Dias and coworkers[16] acetyl chloride was added dropwise to a vigorously stirred solution of **14** (5.31g, 10.8 mmol) in methanol (50 mL) at 0° such that the temperature did not exceed 5°. The solution was warmed to room temperature and stirred for 13 h. The solvent was removed *in vacuo* and the solid recrystallized from methanol/water to give **15** (4.82g, 99 %) as a white solid (mp=187 – 189°). ^{1}H NMR ($CDCl_3$) δ 0.72 (s, 3H), 0.78 (s, 1H), 0.80 (d, 3H, J = 2.4 Hz), 0.83 (s, 1H), 0.90 (s, 3H), 0.9 –2.0 (m, 24 H), 2.10 (s, 3H), 2.12 (s, 3H), 3.50 (m, 1H), 3.49 (q, 1 H, J = 2.7), 5.09 (t, 1H, J = 2.7Hz). ^{13}C NMR ($CDCl_3$) δ 9.8, 11.8, 16.8, 21.1, 21.4, 22.1, 22.4, 25.1, 26.7, 27.6, 28.5, 29.7, 30.9, 33.8, 34.4, 35.8, 37.3, 37.8, 40.6, 42.9, 44.5, 46.7, 70.5, 71.6, 75.1, 170.3. IR ν_{max} 3517, 1735. MS *m/z* (70 eV): 328 (100), 313 (25), 310 (41), 295 (27), 271 (80), 253 (61). Anal. Calcd for $C_{27}H_{44}O_5.H_2O$: C, 69.5; H 9.8. Found C, 69.5; H, 9.4

7α,12α-Diacetoxy-24-nor-5β-cholan-3-one

Following the method of Sato and coworkers[17] Kiliani's reagent[18] (12 mL) (prepared by the portionwise addition of chromium trioxide (5.3g) to a stirred solution of sulfuric acid (8g) water (40 mL) at 0 °C) was added dropwise to a stirred solution of **15** (5.31g, 11.9 mmol) in acetone (50 mL) at room temperature, until a dark permanent orange

color persisted. The solution was stirred for further 30 min at which time it was diluted with water (20 mL) and extracted with dichloromethane (2x) and washed with 10% sodium metabisulfite until a colorless solution was obtained. The organic layer was dried (Na_2SO_4) and the solvent removed *in vacuo* to give the title compound (5.02g, 95 %). as a white solid (mp = 203-204.5° (MeOH)).)). ^{1}H NMR ($CDCl_3$, 25 °C): δ 0.765 (s, 3H), 0.78 (m , 5H), 1.01 (s,3H), 1.25 (s, 3H), 1.26-2.59 (series of multiplets, 18H), 2.07 (s, 3H), 2.11 (s, 3H), 2.18 (s, 2H), 5.0 (q, 1H, J=2.7), 5.13 (t, 1H, J=2.7 Hz). ^{13}C NMR ($CDCl_3$): δ 10.2, 12.2, 17.2, 21.2, 21.4, 21.6, 22.7, 25.7, 27.0, 28.0, 29.7, 30.8, 34.3, 36.0, 36.1, 36.5, 37.7, 42.1, 43.1, 44.5, 47.1, 70.6, 75.3, 170.1, 170.4, 212.1. IR ν_{max} 3433, 1732. MS *m/z* (70 eV): 326 (79), 269 (100), 242 (20), 203 (17).

7α,12α-Dihydroxy-24-nor-5β-cholane (16)

Following the modified Wolff-Kishner reduction of Huang and Minlon.[19] 7α,12α-Diacetoxy-24-nor-5β-cholan-3-one (5.0g, 11.2 mmol) was added to a solution of potassium hydroxide (10.4 g), hydrazine hydrate (100%, 20 mL) in water (4 mL) and triethylene glycol (90 mL). The reaction mixture was heated at 110° for 90 min. The reflux condenser was removed and the solution gradually heated to 195°, the condenser was replaced and the mixture heated at reflux for 4 h. After cooling, the solution was poured into ice-water (500 mL) and acidified. The resulting white precipitate was collected, washed with copious amounts of water and recrystallized from methanol to give **16** (2.90g, 74%) as fine white needles. (mp = 196 – 197°). ^{1}H NMR ($CDCl_3$): δ 0.70 (s, 3H), 0.83 (s, 1H), 0.84 (s, 3H), 0.86 (s, 1H), 0.90 (s, 3H), 0.96 (s, 1H), 0.98 (s, 1H), 1.10–2.23 (m, 25H), 3.85 (q, 1H, 2.7Hz), 4.00 (t, 1H, J = 3.0 Hz). ^{13}C NMR ($CDCl_3$) δ 10.5, 12.5, 17.1, 21.3, 23.2, 23.4, 26.7, 27.4, 27.7, 28.2, 29.7, 30.5, 35.1,35.5, 36.8, 37.5, 39.6, 42.0, 43.2, 46.5, 47.2, 68.7, 73.1. IR (cm^{-1}) ν_{max} 3500. MS *m/z* (70 eV): 312.2 (M- 2(H_2O), 42.52), 297.1 (M-2(H_2O)-CH_3, 28.52), 255.1 (2(H_2O)-C_4H_9, 100), 228.0 (26.94), 203.1 (29.07). Anal. Calcd for $C_{23}H_{40}O_2$: C, 79.2; H, 11.6. Found C, 79.2; H, 11.5.

7α-Acetoxy-12α-hydroxy-24-nor-5β-cholane (17)

Following the method of Fieser and Rajagopalan.[20] Acetic anhydride (1.2 mL) was added to a stirred solution of **16** (1.13g, 3.25 mmol) in

benzene (16 mL) and pyridine (1.2 mL). The solution was stirred overnight at 20-25°, diluted with dichloromethane and washed with brine, 10% HCl (3x), sat. $NaHCO_3$.and water. The solution was dried (Na_2SO_4) and the solvent removed *in vacuo*. The residue was purified via flash chromatography (dichloromethane) to give **17** (1.13g, 89 %). as a white solid which was further recrystallized from methanol/water (mp =131.5 – 133.5°). ^{1}H NMR ($CDCl_3$) δ 0.69 (s, 3H), 0.82 (s, 1H), 0.84 (s, 3H), 0.87 (s, 1H), 0.88 (s, 3H), 0.96 (s, 1H), 0.98 (s, 1H), 0.99 – 0.22 (m, 29H), 1.99 (s, 3H), 4.01 (t, 1H, J = 2.7 Hz), 4.86 (q, 1H, 2.7 Hz). ^{13}C NMR ($CDCl_3$) δ 10.2, 12.3, 16.9, 21.2, 21.4, 22.9, 23.3, 27.2, 27.5, 28.0, 28.1, 28.4, 29.4, 31.5, 35.0, 36.6, 37.2, 38.0,42.0, 42.8, 46.3, 47.0, 71.2, 72.7, 170.4. IR ν_{max} 3537, 1711. MS *m/z* (70 eV): 313 (40), 312. (79), 297 (33), 255 (100), 228 (28), 203 (34).). Anal. Calcd for $C_{27}H_{48}O_3$: C, 77.1; H 11.5. Found C, 77.0; H 11.5.

7α-Acetoxy-24-nor-5β-cholan-12-one was prepared from **17** (3.32g, 8.5 mmol) in analogous manner to that described for the preparation of 7α,12α-diacetoxy-24-nor-5β-cholan-3-one to give the title compound in quantitative yield (3.30g) as a white solid (mp = 203–205°(MeOH)). ^{1}H NMR ($CDCl_3$) δ 0.79 (s, 3H), 7.30 (s, 3H), 0.74 (s, 1H), 0.76 (s, 1H), 0.91 (s, 1H), 0.92 (s, 1H), 0.96–2.04 (m, 26 H), 1.88 (s, 3H), 4.93 (q, 1H, J = 2.7). ^{13}C NMR ($CDCl_3$) δ 10.5, 11.1, 18.1, 20.9, 21.1, 22.6, 23.5, 27.1, 27.2, 27.6, 29.3, 31.4, 36.0, 37.0, 37.2, 37.4, 37.6, 37.8, 42.2, 45.9, 52.8, 56.7, 70.7, 169.8, 214.0. IR (cm^{-1}) ν_{max} 3436, 1729. MS *m/z* (70 eV): 327 (39), 326 (98), 269 (92), 256 (27), 242 (26), 91 (100).

7α-Hydroxy-24-nor-5β-cholane (18) was prepared from 7α-acetoxy-24-nor-5β-cholan-12-one (2.35g, 6.0 mmol) via the method for the synthesis of **16**, to give **18** (1.50g, 68%) as fine white needles (mp = 113.5 –114.5° (MeOH)). ^{1}H NMR ($CDCl_3$) δ 0.66 (s, 3H), 0.79 (s, 1H), 0.82 (s, 3H), 0.84 (s , 1H), 0.92 (s, 1H), 0.92–2.20 (m, 30H), 3.84 (q, 1H, J = 3 Hz). ^{13}C NMR ($CDCl_3$ δ 10.2, 11.8, 18.0, 20.6, 21.4, 23.6, 23.8, 27.8, 28.1, 28.3, 30.6, 32.9, 35.0, 35.9, 37.0, 37.6, 39.5, 39.7, 42.6, 43.2, 50.5, 55.6, 68.9. IR (cm^{-1}) ν_{max} 3608. MS *m/z* (70 eV): 332 (M^+, 17), 314 (100), 299 (49), 257 (27), 230 (88), 215 (31). Anal. Calcd for $C_{23}H_{40}O$: C, 83.2; H 12.1. Found C, 83.0; H 12.1.

3α-Trimethylstannyl-5α-cholestane (20)

Pyridine (10 mL), N,N-dimethylaminopyridine (DMAP) (0.08g, 0.68 mmol) and methanesulfonyl chloride (0.66 ml, 8.6 mmol) were added to a solution of dihydrocholesterol (2.22g, 5.70 mmol) in dichloromethane (20 mL) at 0°. The solution was stirred at 0°for 2 h at which time it was warmed to room temperature. The solution was diluted with dichloromethane (30 mL), washed with 10% $NaHCO_3$ (2x), brine (2x), dried (Na_2SO_4) and the solvent removed *in vacuo*, to give 3α-methanesulfonyl-5α-cholestane as a white solid (2.28g, 86 %) and of sufficient purity for further use. ^1H NMR ($CDCl_3$) δ 0.64, (s, 3H), 0.82 –1.99 (m, 43H), 3.00 (s, 3H), 4.61 (m, 1 H). ^{13}C NMR ($CDCl_3$) δ 12.0, 12.1, 18.6, 21.2, 22.5, 22.8, 23.8, 24.1, 28.0, 28.2, 28.4, 28.6, 31.8, 35.1, 35.2, 35.3, 35.7, 36.1, 36.7, 38.8, 39.4, 39.9, 43.5, 44.8, 54.0, 56.2, 56.3, 82.2.

A solution of trimethylstannanyl lithium (prepared from lithium metal (0.35g, 0.05 mol), 1M trimethyltin chloride (4.9 mL, 4.9 mmol) in THF (10 mL)) under N_2 was added via cannula, to a rapidly stirred solution of 3α-methanesulfonyl-5α-cholestane (2.28g, 4.9 mmol) in THF (20 mL). The solution was stirred at room temperature for 3 h. Water (10 mL) was added slowly and the mixture extracted with dichloromethane (3x), dried (Na_2SO_4) and the solvent removed *in vacuo*. Purification was achieved by passing the residue through a small column of silica, eluted with petroleum spirits (40 –60°) and recrystallization (ethanol) gave **20** (2.0g, 76%) as fine white crystals (mp = 80.5 –81.5°). ^1H NMR ($CDCl_3$) δ 0.05 (s, 9H, J (^{119}Sn – ^1H) = 49.8 Hz, J (^{117}Sn – ^1H) = 48.0 Hz), 0.80 – 2.01 (m, 47 H). ^{13}C NMR ($CDCl_3$) δ -9.3 (J (^{13}C - ^{119}Sn) = 294.5 Hz, J(^{13}C - ^{117}Sn) = 280.8 Hz), 12.1, 12.5, 18.7, 20.8, 22.6, 22.8, 23.8, 24.2, 25.8, 27.1, 28.0, 28.3, 29.0, 32.3, 32.6, 35.4, 35.8, 36.2, 36.3, 38.1, 39.5, 40.1, 42.6, 46.5, 55.0, 56.3, 56.6. ^{119}Sn NMR ($CDCl_3$,) δ –8.5. MS *m/z* (70 eV) : 538 (M+, 0.2), 86 (67), 85 (27), 84 (100), 51 (75).). Anal. Calcd for $C_{30}H_{56}Sn$: C, 67.3; H 10.6. Found C, 67.4; H 10.6.

3α-(Bromodimethyl)stannyl-5α-cholestane

To a vigorously stirred suspension of **20** (2.0g, 3.70 mmol) in methanol (14 mL) was added a solution of bromine (185 μl, 3.60 mmol) in carbon tetrachloride (2 mL) over 1 h. The solution was stirred for 3 h at which

time the solvent was removed *in vacuo* to give an orange/yellow solid which was recrystallized from hexane to give the title compound (1.68g, 76%) as a fine crystalline solid (mp = 116–117°). ^{1}H NMR ($CDCl_3$) δ 0.65 (s, 6H), 0.72 (s, 3H), 0.73 (s, 3H), 0.83 – 2.36 (m, 41H). ^{13}C NMR ($CDCl_3$) δ -0.95, -0.73, 12.1, 12.5, 18.7, 20.8, 22.6, 24.1, 23.8, 24.1, 25.1, 28.0, 28.2, 28.8, 31.7, 32.1, 35.5, 35.8, 36.2, 36.4, 36.6, 38.4, 39.5, 40.0, 42.6, 47.6, 55.0, 56.3, 56.5. ^{119}Sn NMR ($CDCl_3$,). δ 125.7. MS *m/z* (70 eV) 600 (M+, 1.5), 521 (7), 372 (37), 371 (100), 95 (44). HRMS. Calcd for $C_{29}H_{53}{}^{79}Br^{120}Sn$ (M^+): 600.2353. Found: 600.2314.

3α–Dimethylstannyl-5α-cholestane (21)

3α-(Bromodimethyl)stannyl-5α-cholestane (0.52g, 0.867 mmol) in THF (11 mL) and benzene (5.5 mL) was added via cannula to a suspension of lithium aluminium hydride (0.32g, 8.42 mmol) in THF (6 mL) under N_2. The suspension was stirred for 30 min at which time water (15 mL) was slowly added. The resultant mixture was extracted with ether (2x), dried (Na_2SO_4) and the solvent removed *in vacuo* to give **21** (0.43g, 95%) as a thick clear gum which solidified on standing. ^{1}H NMR (C_6D_6) δ 0.172 (s, 3H, J (^{119}Sn – ^{1}H) = 54.9 Hz, J (^{117}Sn – ^{1}H) = 50.1Hz) 0.180 (s,3H, J (^{119}Sn – ^{1}H) = 27.3 Hz, J (^{117}Sn – ^{1}H) = 24.9 Hz), 0.68 (s, 6H), 0.785 – 2.02 (m, 41H), 5.11 (s, 1H). ^{13}C NMR (C_6D_6) δ11.7, -11.8, 12.4, 12.8, 19.1, 21.2, 22.8, 23.1, 24.4, 24.5, 26.6, 28.4, 28.7, 29.4, 32.5, 33.4, 35.8, 36.3, 36.7, 36.7, 38.2, 40.0, 40.4, 42.9, 46.6, 55.2, 56.6, 56.7. ^{119}Sn NMR (C_6D_6) δ98.0 (d, J (^{119}Sn – ^{1}H) = 1564 Hz). HRMS. Calcd for $C_{29}H_{53}{}^{120}Sn$ (ESI, M-H$^+$): 521.3169. Found: 521.3164.

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