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The Supertristeroids: Large, Chiral, Molecular Bowls Prepared by Trimerization of Pentacyclic Steroidal Ketones

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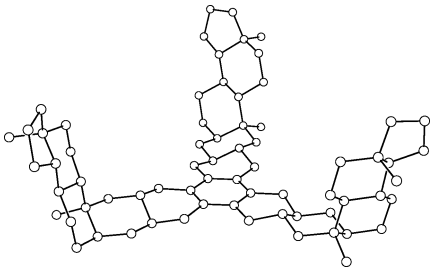
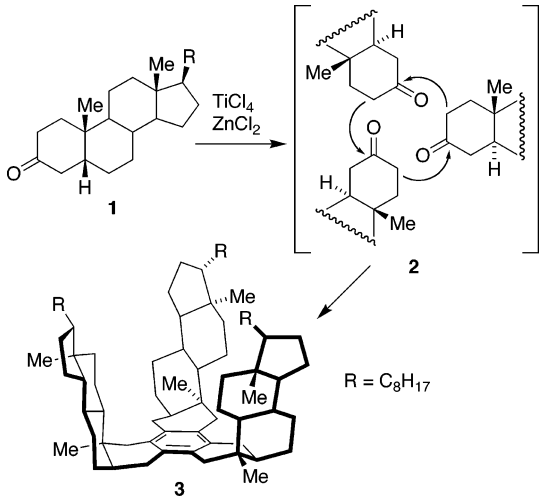


Robinson annulation of coprostanone (**1**) at the 2,3- and 3,4-positions gave two pentacyclic enones (**7** and **10**) that contain A/B-cis-fused ring junctions. Reduction of these enones gave the pentacyclic steroidal ketones 2α,3*β*- (**8**) and 2α,3α-(3′-oxocyclohexano)-5*β*-cholestane (**9**) and 4α,3*β*- (**11**) and 4α,3α-(3′-oxocyclohexano)-5*β*-cholestane (**12**). The structures of compounds **8**, **9**, and **11** were unambiguously established by X-ray analysis. $TiCl_4$-promoted trimerization of compounds **8** and **11** gave the "supertristeroids" **4** and **5**, respectively: large (C_{93}) chiral, hydrocarbon clefts with C_3-symmetric pockets approximately 12 Å in diameter.

Introduction

We have previously reported the synthesis and structure of the chiral molecular cleft **3** by the trimerization of coprostanone (**1**).[1] Provided that an enantiomerically pure ketone is used as the starting material, the inherent directionality of the triple aldol condensation (**2**) assures that only a single trimeric product is formed.

It has been argued that an ideal enantioselective host should not only contain a chiral cavity complementary to only one enantiomer of the guest but also possess a single minimum energy conformation.[2−5] Bowl-shaped steroid trimers such as **3** are conformationally homogeneous[3−5] and might be excellent scaffolds from which to construct such hosts, and they have the practical advantage of very short syntheses. However, ab initio calculations of the structure of **3** indicate that the central cleft is only large enough to hold an *n*-alkane, and in the crystal structure of **3**, the cleft is slightly compressed by packing forces and contains no guest of any kind.[1] In order to accommodate guests of reasonable size, the steroid framework must be expanded. Thus we report herein the synthesis of the two "supertristeroids" **4** and **5** (Scheme 1), hydrocarbon frameworks containing large, C_3-symmetric, chiral cavities, formed by the trimerization of homologated steroidal pentacyclic ketones.



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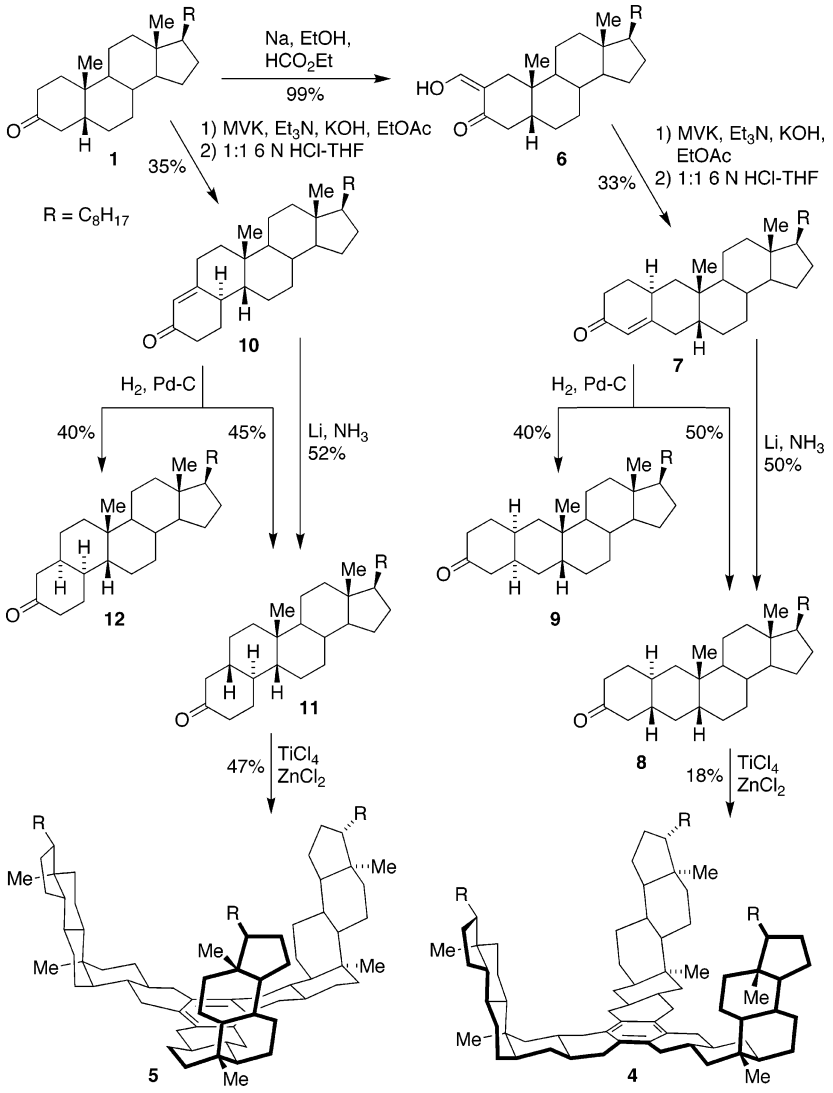
SCHEME 1



Results and Discussion

Synthesis of 2,3- and 3,4-Annulated Steroid Pentacycles. The supertristeroid **4** (Scheme 1), a triple homologue of compound **3**, was our first target, and its synthesis from pentacyclic ketone **8** was judged likely to succeed. However, the construction of the precursor **8** with some confidence in the regio- and stereochemistry of the additional ring was a more challenging task. Pentacyclic steroid homologues with trans A/B ring fusions have been known for almost 50 years,[6−9] but we know of no comparable A/B-cis-fused pentacycles such as **8**. (In this paper, the four original steroid rings are designated A−D, as is conventional; the extra ring of the pentacycle that is fused to ring A is designated E.)

Our first attempts to adapt the literature methods for Robinson annulation of cholestanone (A/B-trans) to coprostanone (A/B-cis) were failures. The initial formylation of coprostanone (**1**) to give the 2-hydroxymethylene derivative **6** worked well, but the subsequent Michael addition of methyl vinyl ketone (MVK) was very sensitive to conditions. Frequently, the reactions succeeded with model compounds but failed when applied to **6**. Several traditional bases were examined, including KO*t*Bu/*t*BuOH,[10] Triton B/MeOH,[11] NaOEt/EtOH, and NaH/THF, but without success. Ultimately, the use of a mixture of triethylamine and KOH in ethyl acetate[12] was found to give reasonable amounts of the desired Michael adduct. The crude acyclic adduct formed under these conditions readily closes upon treatment with 1:1 6 N HCl−THF to give pentacyclic enone **7** in ca. 30% overall yield from **1**. This modest but easily reproducible yield of **7** was sufficient for our purposes because of the easy availability of coprostanone by the Raney nickel-catalyzed isomerization of cholesterol.[13]

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(13) Forsek, J. *Tetrahedron Lett.* **1980**, *21*, 1071−1074.

Pentacyclic enone **7** may be reduced by either of two methods. Reduction by lithium in ammonia gives, as expected,[14] the desired 2α,3β (A/E-trans) isomer **8**. Unfortunately, this reaction is plagued by over-reduction of the ketone to give the corresponding alcohol, and strict control of the amount of lithium used invariably leaves unreacted starting material. In practice, it is simpler to subject **7** to a 1 h catalytic hydrogenation, giving a very clean mixture of A/E-trans **8** and A/E-cis **9** that is easily resolved by column chromatography.

The NMR data for compounds **8** and **9** shed no light on the stereochemical assignments. Compound **8** was suspected to be the A/E-trans isomer on the basis of its formation in the dissolving metal reduction, but X-ray data were needed to confirm this assignment. Fortunately, single crystals of both compounds **8** and **9** were obtained, and their structures were determined. Both the regio- and stereochemistry of the added rings in **8** and **9** are as indicated in Scheme 1, that is, compound **8** possesses an A/E-trans ring junction (2α,3β) and compound **9** has an A/E-cis junction (2α,3α). The molecular structures of both molecules are illustrated in the Supporting Information.

In the synthesis of the 2,3-annulated pentacycles **7**−**9**, the regiochemistry of Robinson annulation was determined by the presence of the 2-hydroxymethylene group of compound **6**. A direct Robinson annulation of coprostanone might be expected to give a mixture of pentacycles. In fact, when compound **1** is treated with MVK, triethylamine, and KOH in ethyl acetate, exactly as for the annulation of **6**, the only pentacyclic enone formed is the 3,4-adduct **10**. The yield of this transformation (35%) is, if anything, slightly higher than that for the synthesis of **7**, and thus we had easy access to the 3,4-annulated pentacyclic ketones.

Lithium/ammonia reduction of **10** gives the A/E-trans ketone **11**, and its structure was confirmed by X-ray analysis (the structure is illustrated in the Supporting Information). However, as before, it proved more convenient to hydrogenate compound **10** to the give a mixture of A/E-trans **11** and A/E-cis **12**, which were then separated chromatographically.

The crystal structures leave no doubt as to the structures of the pentacyclic ketones and their enone precursors, but the easy formation of the step-like, E/A/B-cis,cis isomers **9** and **12** is somewhat surprising. The initial Michael additions give the expected equatorial substitutions at C-2 and C-4 in enones **7** and **10**, respectively. However, these pentacycles are bent by roughly 60° at the cis A/B ring junction, and thus it is hard to imagine how the α-faces of the enones approach the surface of a heterogeneous hydrogenation catalyst in order to give the ketones **9** and **12**! One might have expected the essentially unencumbered β-faces of the enones to be hydrogenated much more rapidly than the α-faces, but the A/E-cis and A/E-trans isomers are formed in roughly equal amounts in both hydrogenation reactions.

Synthesis of the "Supertristeroids" 4 and 5. The trimerization of ketones **8** and **11** to give supertristeroids **4** and **5**, respectively, was conducted in essentially the same manner as the previously reported synthesis of **3**.[1] The ketone was dissolved in hexanes in a screw-capped tube, 1 equiv of $ZnCl_2$ and 3−4 equiv of $TiCl_4$ were added, and the mixture was heated in an oil bath at 140 °C overnight. Yields of the trimers were variable, ranging from 10 to 50%. More highly polar solvents gave inferior yields, and although lower temperatures gave poor results, higher temperatures had little effect.

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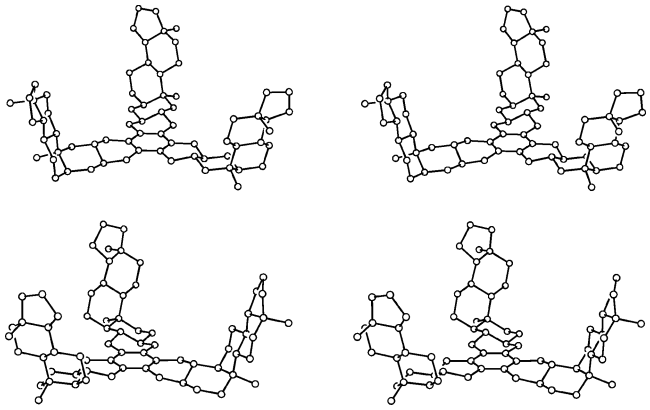

FIGURE 1. Stereoviews of the calculated structures [B3LYP/6-31G-(d)] of the polycyclic cores of supertristeroids **4** (top) and **5** (bottom).

The proton NMR spectra of the trimers **4** and **5** are relatively uninformative, but the C_3-symmetric supertristeroids are easily identified by the presence of two (and only two) aromatic resonances in their ^{13}C NMR spectra near δ 132. The byproducts of the trimerization, for which cyclization is incomplete, are asymmetric and have very complicated ^{13}C NMR spectra. The strong molecular ions in the FAB mass spectra of **4** and **5** confirm their composition.

A great deal of effort was invested in the growth of crystals of compounds **4** and **5**, with the hope of determining their X-ray crystal structures. Both compounds form relatively large hexagonal plates from solutions in chlorinated hydrocarbons, but only inferior crystals are deposited from other solvents. X-ray analysis of large crystals of compound **4** gave a trigonal unit cell [$a = b = 30.3934(5)$ Å, $c = 17.1086(3)$ Å] with *P*3 as the likely space group. This large unit cell must contain at least two independent molecules of **4**, as well as several solvent molecules. Several X-ray data sets were collected, but no solution to the structure has been obtained. In addition, attempts were made to brominate compounds **4** and **5** selectively at the benzylic positions, as well as to displace the bromine atoms with aromatic thiols, in order to generate derivatives that might crystallize more satisfactorily, but only intractable mixtures were obtained (data not shown).

With no crystal structure in hand, the structures of the cores of supertristeroids **4** and **5** (lacking the C_8H_{17} side chains) were calculated at the B3LYP/6-31G(d) level.[15,16] Both molecules possess chiral pockets some 12 Å in diameter, and the calculated molecular structures are illustrated in Figure 1. The structures

(15) Hybrid density functional calculations were performed using Gaussian 03;[16] the built-in default thresholds for wave function and gradient convergence were employed.

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indicate that large, propeller-like guests should fit easily into the clefts. For this reason, cocrystallization experiments with triphenylphosphine, triphenylamine, tris(pentafluorophenyl)-phosphine, and tris(pentafluorophenyl)borane were attempted, but without success. Whether these molecules associate with the supertristeroids in solution is the subject of future experiments.

Conclusion

We have reported very short syntheses (3−4 steps) of two large (C_{93}), chiral, hydrocarbon clefts, containing C_3-symmetric cavities big enough to accommodate guests of moderate complexity. If one employed a similar synthetic strategy with precursors containing polar functionality—perhaps an A/B-cis-fused polyhydroxy steroid such as cholic acid—then chiral clefts with multiple, internally directed polar groups might be prepared.

Experimental Section

Coprostanone (5β-cholestan-3-one), mp 56−58 °C (lit.[17] 60−61 °C) was prepared by the method of Forsek.[13]

2-Hydroxymethylene-5β-cholestan-3-one (6). Sodium (247 mg, 10.7 mmol) and ethyl formate (0.89 mL, 10.7 mmol) were added to a solution of coprostanone (2.08 g, 5.37 mmol) in dry ether (40 mL). The flask was placed in an ice bath, the reaction was initiated by the addition of ethanol (0.4 mL), and the mixture was stirred overnight. Ethanol was added to destroy any excess sodium, and after stirring for 0.5 h, water and 3 N HCl were added. The acidic solution was extracted three times with ether. The combined organic layers were washed twice with brine, dried over Na_2SO_4, and concentrated to give compound **6** (2.21 g, 5.33 mmol, 99%): mp 98−100 °C; ^{1}H NMR ($CDCl_3$) δ 0.63 (s, 3H), 0.84 (d, J = 7 Hz, 6H), 0.86 (d, J = 7 Hz, 3H), 1.03 (s, 3H), 0.90−1.99 (methylene envelope, 26H), 2.29 (dd, J = 20, 8 Hz, 1H), 2.32 (d, J = 16 Hz, 1H), 2.52 (dd, J = 20, 10 Hz, 1H), 8.24 (s, 1H), 14.31 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.0, 18.6, 20.9, 22.2, 22.5, 22.8, 23.7, 24.1, 25.2, 25.3, 27.9, 28.2, 33.8, 34.7, 35.06, 35.14, 35.7, 36.0, 38.4, 39.4, 39.8, 40.4, 42.6, 56.1, 56.2, 107.3, 181.7, 189.3 (28 of 28 expected resonances); MS (EI) m/z 414 (M^+, 10), 386 (M − CO, 22), 316 (53), 81 (100); exact mass 414.3494, calcd for $C_{28}H_{46}O_2$ 414.3498.

2α,3-(3′-Oxocyclohex-4′-eno)-5β-cholestane (7). Triethylamine (2.2 mL, 15.3 mmol) and methyl vinyl ketone (1.9 mL, 23 mmol) were added to a solution of ketone **6** (1.58 g, 3.82 mmol) in ethyl acetate (20 mL). Two pellets of solid KOH were then added, and the reaction mixture was stirred under argon for 24 h at room temperature. Water was added, and the mixture was acidified to pH 2 with 3 N HCl. The aqueous mixture was extracted four times with ether, and the combined organics were washed three times with brine. After drying over Na_2SO_4, removal of the solvent gave a sticky, yellow solid (the crude initial Michael adduct). This material was dissolved in a 1:1 mixture of THF and 6 N HCl (48 mL), and the solution was heated at reflux for 2 h. After cooling, water was added, and the resulting mixture was extracted three times with CH_2Cl_2. The combined organic layers were washed three times with water, and the combined aqueous layers were back extracted with CH_2Cl_2. The combined organics were then washed twice with brine, dried over Na_2SO_4, and concentrated to give a yellow oil. Purification of this material by silica gel column chromatography (solvent, 10:1 hexanes/ethyl acetate) gave pentacyclic ketone **7** (545 mg, 1.24 mmol, 33%): mp 84−87 °C; ^{1}H NMR ($CDCl_3$) δ 0.66 (s, 3H), 0.86 (d, J = 7 Hz, 6H), 0.90 (d, J = 7 Hz, 3H), 0.98 (s, 3H), 1.01−2.07 (methylene envelope, 30H), 2.37 (m, 3H), 2.75 (t, J = 14 Hz, 1H), 5.83 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.0, 18.6, 21.0, 22.5, 22.8, 23.1, 23.8, 24.1, 25.8, 26.2, 27.9, 28.2, 29.2, 32.8, 35.5, 35.7, 35.9, 36.1, 36.6, 39.4, 40.0, 41.0, 42.6, 43.7, 45.4, 56.3, 56.4, 124.0, 168.6, 199.8 (30 of 31 expected resonances); MS (EI) m/z 438 (M^+, 52), 423 (M − CH_3, 19), 316 (37), 81 (100); exact mass 438.3876, calcd for $C_{31}H_{50}O$ 438.3862.

2α,3β- (8) and 2α,3α-(3′-Oxocyclohexano)-5β-cholestane (9) by Hydrogenation of 7. Pentacyclic ketone **7** (70 mg, 0.16 mmol) was dissolved in ethanol (20 mL), and 10% Pd on C (10 mg) was added. The mixture was hydrogenated for 1 h at 45 psi. The catalyst was filtered away, and the solvent was removed to give a colorless solid. Silica gel column chromatography (solvent, 30:1 hexanes/ether) gave two new pentacyclic ketones. Compound **8** (35 mg, 0.080 mmol, 50%) eluted first, followed by compound **9** (28 mg, 0.064 mmol, 40%). Subsequent X-ray analysis established the structures of **8** and **9** as the 2α,3β (trans) and 2α,3α (cis) isomers, respectively. Compound **8**: mp 120−122 °C; ^{1}H NMR ($CDCl_3$) δ 0.65 (s, 3H), 0.86 (d, J = 7 Hz, 6H), 0.90 (d, J = 7 Hz, 3H), 0.95 (s, 3H), 0.99−1.70 (methylene envelope, 24H), 1.85 (m, 4H), 2.00 (d, J = 12 Hz, 1H), 2.10 (t, J = 14 Hz, 1H), 2.36 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 12.0, 18.7, 20.9, 22.5, 22.8, 23.8, 23.9, 24.2, 26.5, 26.9, 28.0, 28.3, 33.6, 35.0, 35.8, 35.9, 36.0, 36.2, 39.5, 40.3, 41.6, 41.7, 42.7, 42.8, 43.8, 44.0, 48.3, 56.4, 56.6, 211.8 (30 of 31 expected resonances); MS (EI) m/z 440 (M^+, 29), 425 (M − CH_3, 60), 285 (100); exact mass 440.4020, calcd for $C_{31}H_{52}O$ 440.4018. Compound **9**: mp 155−157 °C; ^{1}H NMR ($CDCl_3$) δ 0.65 (s, 3H), 0.87 (d, J = 7 Hz, 6H), 0.89 (d, J = 7 Hz, 3H), 1.01 (s, 3H), 0.95−2.03 (methylene envelope, 32H), 2.20 (m, 3H), 2.37 (td, J = 14, 7 Hz, 1H), 2.66 (t, J = 14 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 12.0, 18.7, 20.8, 22.5, 22.8, 23.8, 24.2, 24.4, 26.4, 26.5, 28.0, 28.3, 28.5, 31.7, 31.8, 35.5, 35.77, 35.81, 36.2, 36.6, 36.8, 38.0, 39.5, 40.2, 40.7, 42.4, 42.7, 56.4, 56.6, 213.3 (30 of 31 expected resonances); MS (EI) m/z 440 (M^+, 27), 425 (M − CH_3, 58), 285 (100); exact mass 440.4003, calcd for $C_{31}H_{52}O$ 440.4018.

2α,3β-(3′-Oxocyclohexano)-5β-cholestane (8) by Li/NH_3 Reduction of 7. Lithium (23 mg, 3.3 mmol) was added to liquid ammonia (~25 mL) in a three-necked flask topped by a dry ice condenser and a $CaCl_2$ drying tube. After the solution turned dark blue, a solution of pentacyclic ketone **7** (180 mg, 0.411 mmol) in THF (2 mL) was added over 1 h. The solution was stirred for another 2 h, and then solid NH_4Cl was added to quench the reaction. After the ammonia had evaporated, water was added, and the mixture was extracted three times with CH_2Cl_2. The combined organic layers were washed successively with water, saturated $NaHCO_3$, and brine, and then dried over Na_2SO_4. The solution was concentrated to dryness, and the residue was purified by silica gel column chromatography to give compound **8** (90 mg, 50%), identical to that prepared by hydrogenation of **7**.

4α,3-(3′-Oxocyclohex-4′-eno)-5β-cholestane (10). Coprostanone (1.38 g, 3.58 mmol) was subjected to the same two-step procedure used for the preparation of compound **7** from **6**. The crude cyclized product was purified by preparative TLC (solvent, 10:1 hexanes/ethyl acetate) to give pure compound **10** (549 mg, 1.25 mmol, 35%): mp 82−85 °C; ^{1}H NMR ($CDCl_3$) δ 0.64 (s, 3H), 0.84 (d, J = 7 Hz, 6H), 0.88 (d, J = 7 Hz, 3H), 0.96 (s, 3H), 1.20−2.43 (methylene envelope, 33H), 2.65 (t, J = 9 Hz, 1H), 5.82 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.0, 18.6, 21.1, 22.0, 22.5, 22.7, 23.6, 23.7, 24.0, 25.6, 27.2, 27.9, 28.2, 30.6, 35.1, 35.5, 35.67, 35.71, 36.0, 36.7, 36.9, 39.4, 40.0, 41.7, 42.6, 50.3, 56.2, 56.4, 124.5, 168.6, 199.9 (31 of 31 expected resonances); MS (EI) m/z 438 (M^+, 79), 423 (M − CH_3, 36), 329 (47), 175 (100); exact mass 438.3867, calcd for $C_{31}H_{50}O$ 438.3862.

4α,3β- (11) and 4α,3α-(3′-Oxocyclohexano)-5β-cholestane (12) by Hydrogenation of 10. Pentacyclic ketone **10** (90 mg, 0.21 mmol) was hydrogenated and fractionated as described for the preparation of compounds **8** and **9**, to give the saturated ketones **11** (42 mg, 0.095 mmol, 45%) and **12** (37 mg, 0.084 mmol, 40%). Subsequent X-ray analysis established the structure of **11** as the 4α,3β (trans) isomer. Compound **11**: mp 125−127 °C; ^{1}H NMR ($CDCl_3$) δ 0.65 (s, 3H), 0.86 (d, J = 7 Hz, 6H), 0.90 (d, J = 7 Hz,

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3H), 0.95 (s, 3H), 0.99−1.62 (methylene envelope, 26H), 1.70 (m, 2H), 1.82 (m, 3H), 1.98 (d, J = 11 Hz, 1H), 2.14 (t, J = 13 Hz, 1H), 2.30 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 12.1, 18.6, 21.0, 22.1, 22.5, 22.8, 23.8, 24.2, 24.4, 26.0, 28.0, 28.3, 28.8, 30.8, 35.8, 35.9, 36.0, 36.2, 37.0, 37.5, 39.5, 40.3, 41.4, 41.9, 42.7, 44.2, 48.5, 48.7, 56.4, 56.6, 211.9 (31 of 31 expected resonances); MS (EI) m/z 440 (M^+, 33), 425 ($M - CH_3$, 70), 285 (100); exact mass 440.4005, calcd for $C_{31}H_{52}O$ 440.4018. Compound **12**: mp 100−102 °C; ^{1}H NMR ($CDCl_3$) δ 0.65 (s, 3H), 0.86 (d, J = 7 Hz, 6H), 0.89 (d, J = 7 Hz, 3H), 1.02 (s, 3H), 1.03−1.65 (methylene envelope, 26H), 1.80 (m, 3H), 2.00 (m, 2H), 2.13 (m, 2H), 2.25 (m, 3H), 2.68 (t, J = 14 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 12.1, 18.6, 21.1, 21.7, 22.5, 22.8, 23.8, 24.2, 24.8, 25.4, 25.5, 27.6, 28.0, 28.3, 30.2, 30.9, 35.8, 35.9, 36.0, 36.2, 36.3, 38.0, 38.6, 39.5, 40.3, 41.1, 42.5, 42.8, 56.4, 56.6, 213.2 (31 of 31 expected resonances); MS (EI) m/z 440 (M^+, 31), 425 ($M - CH_3$, 56), 386 (16), 285 (75), 81 (100); exact mass 440.4010, calcd for $C_{31}H_{52}O$ 440.4018.

4α,3β-(3′-Oxocyclohexano)-5β-cholestane (11) by Li/NH_3 Reduction of 10. Compound **10** (73 mg, 0.167 mmol) was subjected to Li/NH_3 reduction, as described above for the reduction of **7**, to yield compound **11** (38 mg, 0.087 mmol, 52%), identical to that prepared by hydrogenation of **10**.

Trimerization of Compound 8 to Give the "2,3-Supertristeroid" 4. Pentacyclic ketone **8** (247 mg, 0.56 mmol) was dissolved in hexanes (15 mL) in a 15 mm × 150 mm screw-capped tube. Anhydrous $ZnCl_2$ (76 mg, 0.56 mmol) and $TiCl_4$ (0.2 mL, 1.8 mmol) were added to give a brown mixture. The bottom of the tube was placed in an oil bath heated to 140 °C, and it was left overnight. After cooling, water was added, and the mixture was extracted three times with CH_2Cl_2. The combined organic layers were washed three times with water, dried over Na_2SO_4, and concentrated to give a light yellow solid. Purification by silica gel column chromatography (solvent, hexanes) gave trimer **4** as a white solid (43 mg, 18%): mp >300 °C; ^{1}H NMR ($CDCl_3$) δ 0.68 (s, 9H), 0.85 (3 overlapping d's, 27H), 0.97 (s, 9H), 0.94−1.62 (methylene envelope, 81H), 1.76−2.04 (m, 15H), 2.18 (m, 3H), 2.51 (d, J = 16 Hz, 3H), 2.63 (d, J = 16 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 12.2, 18.7, 19.1, 20.8, 22.5, 22.8, 23.8, 24.0, 24.3, 26.8, 27.3, 28.0, 28.4, 32.0, 35.0, 35.78, 35.84, 35.9, 36.2, 36.3, 38.5, 39.5, 41.6, 42.8, 42.9, 45.1, 56.0, 56.8, 131.6, 132.1 (30 of 31 expected resonances); MS (FAB) m/z 1267 (M^+ [$^{13}C_1$], 38), 460 (100).

Trimerization of Compound 11 to Give the "3,4-Supertristeroid" 5. Pentacyclic ketone **11** (85 mg, 0.193 mmol) was trimerized by treatment with $ZnCl_2$ (26 mg, 0.19 mmol) and $TiCl_4$ (0.07 mL, 0.6 mmol) as described above to give compound **5** as a white solid (38 mg, 47%): mp >300 °C; ^{1}H NMR ($CDCl_3$) δ 0.65 (s, 9H), 0.85 (3 overlapping d's, 27H), 0.98 (s, 9H), 0.94−1.60 (methylene envelope, 81H), 1.70−2.02 (m, 15H), 2.26 (m, 3H), 2.64 (d, J = 16 Hz, 3H), 2.83 (d, J = 16 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 12.1, 18.7, 21.0, 22.0, 22.6, 22.8, 23.8, 24.2, 24.5, 26.1, 28.0, 28.3, 29.7, 33.2, 34.1, 35.8, 35.9, 36.2, 36.8, 38.4, 39.5, 40.2, 41.9, 42.8, 50.0, 56.3, 56.7, 131.86, 131.89 (29 of 31 expected resonances); MS (FAB) m/z 1268 (M^+ [$^{13}C_2$], 20), 447 (100).

General X-ray Crystallographic Procedures. X-ray data for compounds **8**, **9**, and **11** were collected at 200 K using graphite monochromated Mo Kα radiation (λ = 0.71073 Å) on a Nonius KappaCCD diffractometer. All diffraction data were processed using the program DENZO.[18] All structures were solved by direct methods using Siemens SHELXTL,[19] and all were refined by full-matrix least-squares on F^2 using SHELXTL. All non-hydrogen atoms were refined anisotropically, and hydrogens were included with a riding model. Specific crystal, reflection, and refinement data are contained in the CIF files in the Supporting Information.

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Supporting Information Available: NMR spectra of compounds **4**−**12**; Cartesian coordinates of the DFT-computed structures; three crystallographic information files (CIF); and three Ortep drawings for compounds **8**, **9**, and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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