An Approach toward the Triquinane-Type Skeleton via Reagent-Controlled Skeletal Rearrangements. A Facile Method for Protection−Deprotection of Organomercurials, Tuning the Selectivity of Wagner−Meerwein Migrations, and a New Route to Annulated Lactones†

Pavel Kočovský,*,‡ Victoria Dunn,‡ Adolf Gogoll,§ and Vratislav Langer||

Department of Chemistry, University of Leicester, Leicester LE1 7RH, U.K., Department of Organic Chemistry, University of Uppsala, Box 531, S-75121 Uppsala, Sweden, and Department of Inorganic Chemistry, Chalmers University of Technology and University of Göteborg, S-41296 Göteborg, Sweden

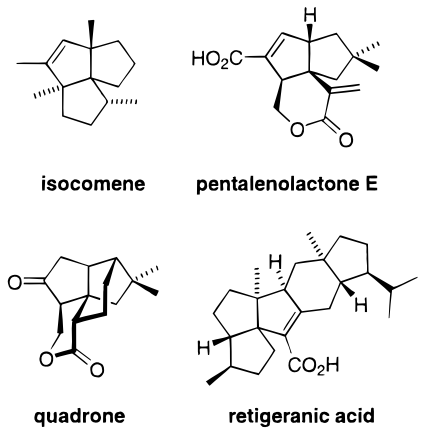
Received July 2, 1998

Nonlinear triquinane-type building blocks have been synthesized using three strategic steps, namely, (1) Hg^{2+}-mediated opening of a cyclopropane ring involving a skeletal rearrangement (**3** → **8**), (2) an intramolecular organometallic addition across a C=O bond triggered by activation of the C−HgX group by means of Me_3CuLi_2 (**14** → **26**), and (3) selective, reagent-controlled skeletal rearrangements (**43** → **47** with Tl^{3+} or Hg^{2+}; **43** → **51** + **52** with Pd^{2+}; **44** → **47** with Pd^{2+}). A new method for protection/deprotection of organomercurials has been developed, which allows selective reduction of a carbonyl group with $NaBH_4$ and other hydrides (**8** → **14** → **16** → **20**) and Tebbe methylenation (**14** → **31** → **32**). Oxidative demercuration (**8** → **11** + **28**) and Pd^{2+}-catalyzed carbonylation of organomercurials (**20** → **53**) allowed syntheses of γ- and δ-lactones.

Introduction

The structural complexity and fascinating compactness of naturally occurring triquinanes[1] has inspired numerous research groups. Synthetic approaches to the nonlinear triquinanes,[2] such as isocomene, pentalenolactones, quadrone, retigeranic acid, etc. (Chart 1), encompass cyclizations via intramolecular radical additions,[3] vinylcyclopropane rearrangements,[4] carbene insertions,[5] cycloadditions,[6] Pauson−Khand reaction,[7] electrophilic cyclizations,[8] cascade rearrangements,[9] and other methods.[10−12] Herein we report on model experiments aimed at the construction of various triquinane-type building blocks annulated to a steroid skeleton. Our methodology is based on (1) a unique, metal-mediated skeletal rearrangement, triggered by opening of a cyclopropane ring in the isosteroid **3**, (2) an intramolecular organometallic addition across a C=O bond, and (3) selective, reagent-controlled Wagner−Meerwein-type expansion of a cyclobutane ring.

Chart 1



Results and Discussion

The "iso-steroid" rearrangement,[13] a textbook example of the kinetically controlled solvolysis with neighboring

† Dedicated to Drs. Václav Černý and Jan Fajkoš in acknowledgment of their life-long contribution to steroid chemistry and on the occasion of their 76th (V. Č.) and 75th (J. F.) birthdays.

* Corresponding author: e-mail, PK10@Le.ac.uk.
‡ University of Leicester.
§ University of Uppsala.
|| Chalmers University of Technology and University of Göteborg.

(1) For overviews, see: (a) Paquette, L. A. *Top. Curr. Chem.* **1979**, *79*, 41. (b) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1. (c) Hanson, J. R. *Nat. Prod. Rep.* **1992**, *9*, 481. For classification of pentalenolactones, see: (d) Cane, D. E.; Shong, J. K.; Williard, P. G. *J. Org. Chem.* **1992**, *57*, 844. For listing of the biological activities (anticancer, antibacterial, antiviral, cardiotoxic, enzyme inhibition, etc.) see, e.g., refs 4a.

(2) Kočovský, P.; Tureček, F.; Hájíček, J. *Synthesis of Natural Products: Problems of Stereoselectivity*; CRC: Boca Raton, FL, 1986; Vols. I and II. For references covering synthetic work, see also ref 4.

(3) For reviews, see: (a) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (b) Curran, D. P. *Synlett* **1991**, 63. (c) Curran, D. P.; Sisko, J.; Yeske, P. E.; Liu, H. *Pure Appl. Chem.* **1993**, *65*, 1153. (d) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307. See also: (e) Pattenden, G.; Teague, S. J. *Tetrahedron* **1987**, *43*, 5637. (f) Curran, D. P.; Kuo, S.-C. *Tetrahedron* **1987**, *43*, 5653. (g) Meyers, A. I.; Lefker, B. A. *Tetrahedron* **1987**, *43*, 5663. (h) Curran, D. P.; Sisko, J.; Balog, A.; Sonoda, N.; Nagahara, K.; Ryu, I. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1591. (i) Rawal, V. H.; Dufour, C.; Eschbach, A. *J. Chem. Soc., Chem. Commun.* **1994**, 1797. (j) Hollingworth, G. J.; Pattenden, G.; Schulz, D. J. *Aust. J. Chem.* **1995**, *48*, 3811. (k) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1996**, *118*, 4059.

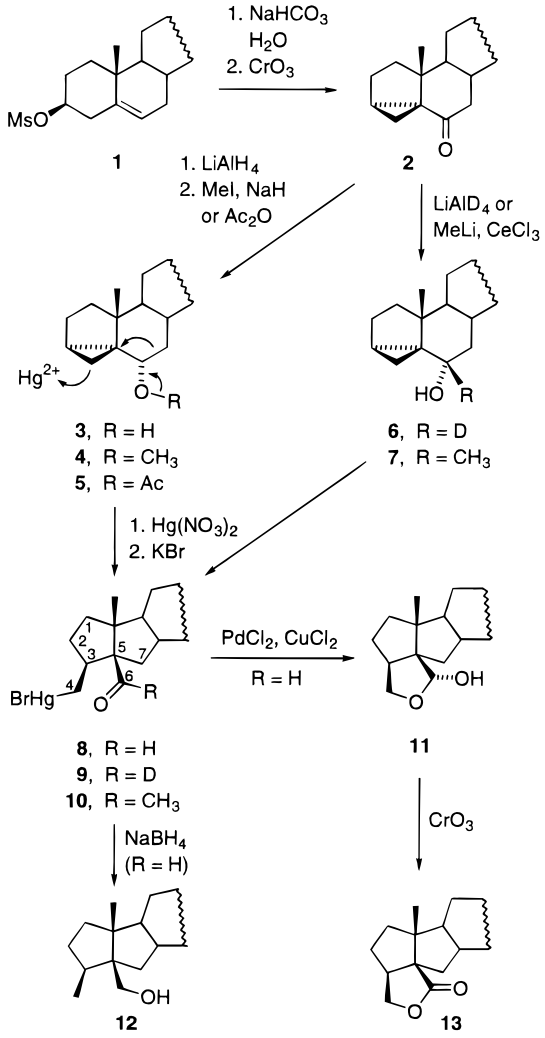
(4) (a) Hudlicky, T.; Sinai-Zingde, G.; Natchus, M. G.; Ranu, B. C.; Papadopolous, P. *Tetrahedron* **1987**, *43*, 5685 and refs cited therein. (b) Hudlicky, T.; Natchus, M. G.; Sinaizingde, G. *J. Org. Chem.* **1987**, *52*, 4641. (c) Wong, H. N. C.; Hon, M. Y.; Tse, W.; Yip, Y. C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165. (d) Hudlicky, T.; Price, J. D. *Chem. Rev.* **1989**, *89*, 1467. (e) Hudlicky, T.; Fleming, A.; Radesca, I. *J. Am. Chem. Soc.* **1989**, *111*, 6691. (f) Hudlicky, T.; Herad, N. E.; Fleming, A. *J. Org. Chem.* **1990**, *55*, 2570. (g) Franck-Neuman, M.; Miesch, M.; Gross, L. *Tetrahedron Lett.* **1992**, *33*, 3879. (h) Enholm, E. J.; Jia, Z. J. *J. Org. Chem.* **1997**, *62*, 174.

(5) (a) Cane, D. E.; Thomas, P. J. *J. Am. Chem. Soc.* **1994**, *106*, 5295. (b) Taber, D. F.; Schuchardt, J. L. *J. Am. Chem. Soc.* **1985**, *107*, 5289; *Tetrahedron* **1987**, *43*, 5677. (c) Mori, K.; Tsuji, M. *Tetrahedron* **1988**, *44*, 2835. (d) Hashimoto, S.; Watanabe, N.; Ikegami, S. *Tetrahedron Lett.* **1992**, *33*, 2709.

10.1021/jo9812882 CCC: $18.00
Published on Web 12/15/1998

group participation,[13] occurs readily under buffered conditions and can be regarded as an expedient construction of a cyclopropane ring. Thus, solvolysis of cholesteryl mesylate **1**, carried out in the presence of $NaHCO_3$ and Et_3N in boiling butanone,[14,15] affords the corresponding, acid-sensitive[13] 3α,5-cyclo-6β-hydroxy derivative which, without proper isolation, can be directly oxidized with Jones reagent[14,15] to give the cyclopropyl ketone **2**[14,16] in 70% overall yield (Scheme 1). Reduction of **2** with $LiAlH_4$ is known to proceed with complete stereoselectivity to produce the equatorial alcohol **3**,[16] which is less acid-sensitive than its axial epimer. Accordingly, the deuterium-labeled alcohol **6** was obtained on reduction of **2** with $LiAl^2H_4$. By analogy, reaction of **2** with MeMgI[17] or MeLi−$CeCl_3$ (THF, 0 °C, 1 h; 73%) furnished exclusively the tertiary alcohol **7**[17] as a result of axial attack from the sterically more hindered β-side, which appears to be a common behavior in this class of compounds, presumably dictated by stereoelectronic effects.[16b,18] While **3** − **5** and their axial epimers have most often been utilized as a means of protection in the AB segment of the steroid skeleton[13,19] and for solvolytic studies,[13c,20] we intended to employ the cyclopropane ring as a synthetic building block in a conceptually different way.

Scheme 1



(6) (a) Wender, P. A.; Singh, S. K. *Tetrahedron Lett.* **1990**, *31*, 2517. (b) Hwang, J.-T.; Liao, C.-C. *Tetrahedron Lett.* **1991**, *32*, 6583. (c) Ihara, M.; Tokunaga, Y.; Taniguchi, N.; Fukumoto, K.; Kabuto, C. *J. Org. Chem.* **1991**, *56*, 5281. (d) Amougay, A.; Pete, J. P.; Piva, O. *Tetrahedron Lett.* **1992**, *33*, 7347. (e) Liu, H. J.; Ulibarri, G.; Browne, E. N. C. *Can. J. Chem.* **1992**, *70*, 1545. (f) Leblanc, S.; Pete, J. P.; Piva, O. *Tetrahedron Lett.* **1993**, *24*, 635. (g) Rawal, V. H.; Dufour, C. *J. Am. Chem. Soc.* **1994**, *116*, 2613. (h) Cheng, K. L.; Wagner, P. J. *J. Am. Chem. Soc.* **1994**, *116*, 7945. (i) Wender, P. A.; Dore, T. M. *Tetrahedron Lett.* **1998**, *39*, 8589.

(7) (a) Gybin, A. S.; Smit, W. A.; Caple, R.; Veretenov, A. L.; Shashkov, A. S.; Vorontsova, L. G.; Kurella, M. G.; Chertkov, V. S.; Carapetyan, A. A.; Kosnikov, A. Y.; Alexanyan, M. S.; Lindeman, S. V.; Panov, N. V.; Maleev, A. V.; Struchkov, Y. T.; Sharpe, S. M. *J. Am. Chem. Soc.* **1992**, *114*, 5555. (b) Rowley, E. G.; Schore, N. E. *J. Org. Chem.* **1992**, *57*, 6853. (c) Becker, D. P.; Flynn, D. L. *Tetrahedron Lett.* **1993**, *34*, 2087. (d) Clive, D. L. J.; Cole, D. C.; Tao, Y. *J. Org. Chem.* **1994**, *59*, 1396.

(8) (a) Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1983**, *24*, 3851. (b) Pattenden, G.; Teague, S. J. *Tetrahedron* **1987**, *43*, 5637.

(9) (a) Kakiuchi, K.; Fukunaga, K.; Jimbo, M.; Yamaguchi, B.; Tobe, Y. *J. Org. Chem.* **1992**, *57*, 1021. (b) Klobus, M.; Zhu, L. J.; Coates, R. M. *J. Org. Chem.* **1992**, *57*, 4327. (c) Willmore, N. D.; Goodman, R.; Lee, H. H.; Kennedy, R. M. *J. Org. Chem.* **1992**, *57*, 1216. (d) Fitjer, L.; Majewski, M.; Monzooltra, H. *Tetrahedron* **1995**, *51*, 8835 and refs given therein. (e) MacDougall, J. M.; Moore, H. W. *J. Org. Chem.* **1997**, *62*, 4554.

(10) (a) Marino, J. P.; Silveira, C.; Comasseto, J.; Petragnani, N. *J. Org. Chem.* **1987**, *52*, 4139. (b) Piers, E.; Renaud, J. *J. Chem. Soc., Chem. Commun.* **1990**, 1324. (c) Wu, Y.-J.; Burnell, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 764. (d) Oppolzer, W.; Xu, J.-Z.; Stone, C. *Helv. Chim. Acta* **1991**, *74*, 465. (e) Franck-Neumann, M.; Miesch, M.; Gross, L. *Tetrahedron Lett.* **1991**, *32*, 2135. (h) Piers, E.; Renaud, J. *Synthesis* **1992**, 74. (i) Negishi, E. *Pure Appl. Chem.* **1992**, *64*, 323. (j) Paquette, L. A.; Meister, P. G.; Friedrich, D.; Sauer, D. R. *J. Am. Chem. Soc.* **1993**, *115*, 49 and refs cited therein. (k) Hirst, G. C.; Johnson, T. O.; Overman, L. E. *J. Am. Chem. Soc.* **1993**, *115*, 2992. (l) Xy, F. U.; Kubiak, G.; Zhang, W. J.; Han, W. C.; Gupta, A. K.; Cook, J. M. *Tetrahedron* **1993**, *49*, 1511. (m) Ihara, M.; Fukumoto, K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1010. (n) Norris, D. J.; Corrigan, J. F.; Sun, Y.; Taylor, N. J.; Collins, S. *Can. J. Chem.* **1993**, *71*, 1029. (o) Vittoz, P.; Bouyssi, D.; Traversa, C.; Goré, J.; Balme, G. *Tetrahedron Lett.* **1994**, *35*, 1871. (p) Maki, S.; Toyota, K.; Mori, T.; Kosemura, S.; Yamamura, S. *Tetrahedron Lett.* **1994**, *35*, 4817. (q) Wu, Y. J.; Zhu, Y. Y.; Burnell, D. J. *J. Org. Chem.* **1994**, *59*, 104. (r) Tinawooldrich, L. V.; Moeller, K. D.; Hudson, C. M. *J. Org. Chem.* **1994**, *59*, 2381. (s) Saitoh, F.; Mori, M.; Okamura, K.; Date, T. *Tetrahedron* **1995**, *51*, 4439. (t) Meyer, C.; Marek, I.; Normant, J.-F. *Tetrahedron Lett.* **1996**, *37*, 857. (u) Singh, V.; Prathap, S.; Porinchu, M. *J. Org. Chem.* **1998**, *63*, 4011.

(11) Vo, N. H.; Snider, B. B. *J. Org. Chem.* **1994**, *59*, 5419.

(12) (a) Kates, S. A.; Dombroski, M. A.; Snider, B. B. *J. Org. Chem.* **1990**, *55*, 2427. (b) Curran, D. P.; Morgan, T. M.; Schwartz, C. E.; Snider, B. B.; Dombroski, M. A. *J. Am. Chem. Soc.* **1991**, *113*, 6667. (c) Snider, B. B.; Merritt, J. E.; Dombroski, M. A.; Buckman, B. O. *J. Org. Chem.* **1991**, *56*, 5544. (d) Snider, B. B.; McCarthy, B. A. *J. Org. Chem.* **1993**, *58*, 6217. (e) Snider, B. B.; Vo, N. H.; Foxman, B. M. *J. Org. Chem.* **1993**, *58*, 7228.

(13) (a) Fieser, L. F.; Fieser, M. *Steroids*; Reinhold: New York, 1959. (b) Fried, J.; Edwards, J. A. *Organic Reactions in Steroid Chemistry*; Van Nostrand: New York, 1972. (c) Kirk, D. N.; Hartshorn, M. P. *Steroid Reaction Mechanisms*; Elsevier: Amsterdam, 1968.

(14) (a) Aburatani, M.; Takeuchi, T.; Mori, K. *Synthesis* **1987**, 181. (b) Kondo, M.; Mori, K. *Agric. Biol. Chem.* **1983**, *47*, 97.

(15) The advantage of using butanone rather than the more conventional acetone is its immiscibility with water, which allows an expedient workup, followed by direct Jones oxidation in the same solution.

(16) (a) Wagner, A. F.; Wallis, E. S. *J. Am. Chem. Soc.* **1950**, *72*, 1047. (b) Just, G.; Richardson, K. S. *Can. J. Chem.* **1964**, *42*, 456.

(17) (a) Davis, M.; Julia, S.; Summers, G. H. R. *Bull. Soc. Chim. Fr.* **1960**, 742. (b) Just, G.; Lee-Ruff, E. *Can. J. Chem.* **1966**, *44*, 2587.

(18) (a) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; J. Wiley: New York, 1994. (b) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon: Oxford, 1983.

(19) For selected examples, see: (a) Partridge, J. J.; Toome, V.; Uskoković, M. *J. Am. Chem. Soc.* **1976**, *98*, 3739. (b) Thoa, H. K.; Procházka, Ž.; Buděšínský, M.; Kočovský, P. *Collect. Czech. Chem. Commun.* **1978**, *43*, 2305. (c) Fung, S.; Siddall, J. B. *J. Am. Chem. Soc.* **1980**, *102*, 6580. (d) Mariono, J. P.; de Dios, A.; Anna, L. J.; Fernández de la Pradilla, R. *J. Org. Chem.* **1996**, *61*, 109. (e) Kabat, M. M.; Kiegiel, J.; Cohen, N.; Toth, K.; Wovkulich, P. M.; Uskoković, M. R. *J. Org. Chem.* **1996**, *61*, 118.

(20) (a) Kosower, E. M.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 4347. (b) Winstein, S.; Kosower, E. M. *J. Am. Chem. Soc.* **1959**, *81*, 4399.

Mercury(II)-Mediated Cyclopropane Ring-Opening and Rearrangement. We have recently described[21] the stereospecific, "corner-type" cyclopropane ring-opening in the cyclopropyl alcohol **3** with $Hg(NO_3)_2$ (DME-MeCN, room temperature (rt), 1 h),[21] that leads, after quenching with KBr, to the stable organomercurial **8** (90%).[21−23] By analogy, the deuterated alcohol **6** was converted into the expected aldehyde **9**. In this unique reaction, part of the driving force must be the conversion of the OH group in **3** into the C═O functionality in the product **8** along with the relief of cyclopropane ring strain. It was therefore of interest to establish whether the less labile groups, such as OCH_3 or OAc, would retard the reaction. To this end, we have prepared the corresponding derivatives **4**[24] and **5**[16a,20,24] using conventional methods (MeI/NaH and Ac_2O/pyridine, respectively). By contrast with the alcohol **3**, which reacts at room temperature within 1 h, its methyl ether **4** turned out to require 24 h for ∼90% conversion, and the acetate **5** proved to be practically inert.[25]

The latter rearrangement **3** → **8** is unique to Hg(II) and can be attributed to the very soft character of this cation.[21] The isoelectronic Tl(III) is the only other electrophile found to react in the same way;[26] however, in this instance, the primarily formed organothallium species, analogous to **8**, is unstable and undergoes an instantaneous conversion into the lactol **11** (66%).[26] All other electrophiles examined in our previous studies, including a number of standard Brønsted and Lewis acids, preferentially attack the OH group (the harder center) to trigger the "retro-iso-steroid rearrangement," producing cholesterol-type structures; even relatively soft electrophiles, such as Pd(II), followed this pattern.[21,22,27] The organomercurial **8** can be converted into the lactol **11** on a catalytic reaction with Pd(II)/Cu(II) in 87% yield,[21,28] thus making the Hg(II) and Tl(III) routes convergent, but with the former being cleaner. Subsequent Jones oxidation of the lactol **11** to lactone **13** is practically quantitative.[21,26]

Since **3** is a secondary equatorial alcohol, it was of interest to establish the reactivity of the related tertiary alcohol **7**, also possessing an equatorial OH group.[29] Treatment of **7** with $Hg(NO_3)_3$, followed by quenching with KBr, led to a facile reaction at room temperature but, by contrast to **3**, gave rise to a mixture of at least five products, which we failed to fully separate. Although the expected bromomercurio ketone **10** was identified in the crude mixture by ^{1}H NMR spectroscopy and by GCMS,[30] this synthetic route was not investigated further.

Protection−Deprotection of the Organomercurio Group and Selective Reactions of the Carbonyl Group. Although organomercurials are relatively stable[31] so that this functional group can, in principle, survive a variety of functional group interconversions, they are easily reduced,[31] which does limit their synthetic applications. Our bromomercurio aldehyde **8** proved to be no exception and, as expected, its reduction with $LiAlH_4$, $NaBH_4$, or even Bu_3SnH led to the fully reduced product **12**.[22] The question arises as to whether the mercurio group could be protected to allow preferential reduction of other functional groups.

We have shown earlier that halomercurials R−HgX (X = Cl, Br) undergo an instantaneous methylation on treatment with MeCu.[21,22,32] We have now found[33] that the resulting methylmercurio derivatives R−HgMe[34] are stable to a number of hydrides and that the halomercurio functionality can be regenerated by treatment with HgX_2 (X = Cl, Br). Thus, **8** and **9** were converted into the respective methylmercurio derivatives **14**[21] and **15** (MeCu, THF, −78 °C, 5 min; 98%) in practically quantitative yields (Scheme 2). Reduction of **14** with $NaBH_4$, $LiAlH(OBu^t)_3$, L-Selectride, or superhydride gave the methylmercurio alcohol **16** in high yields. On the other hand, $LiAlH_4$ gave the fully reduced product **12**, demonstrating an interesting selectivity. Treatment of **16** with $HgBr_2$ (DME, rt, 2 h) gave rise to the bromomercurio alcohol **20** (90%). Since the water-soluble CH_3HgBr is formed as a bypoduct in the latter exchange reaction, the aqueous layer from the workup should be treated with $NaBH_4$ to eliminate the environmental risks.

Reduction of the aldehyde group in **14** proved to be Re-face stereoselective, as demonstrated by reduction with $LiAl^2H(OBu^t)_3$, which afforded **17** as the main epimer (85:15);[35] super deuteride exhibited an almost identical stereoselectivity (87:13), as revealed by the ^{1}H NMR spectroscopy. In a complementary experiment, the deuterated aldehyde **15** was reduced with $LiAlH(OBu^t)_3$ to afford **18** (84:16). The configuration at the newly formed center C(6) was established as follows: the unlabeled bromomercurio alcohol **20**, obtained from **16** by the $HgBr_2$-mediated deprotection (vide supra), was converted into the rigid tetrahydrofuran derivative **22** on treatment

(21) Kočovský, P.; Šrogl, J.; Pour, M.; Gogoll, A. *J. Am. Chem. Soc.* **1994**, *116*, 186.

(22) Kočovský, P.; Šrogl, J. *J. Org. Chem.* **1992**, *57*, 4565.

(23) For other examples of application of the Hg(II)-mediated cyclopropane opening, see, e.g.: (a) Collum, D. B.; Still, W. C.; Mohamadi, F. *J. Am. Chem. Soc.* **1986**, *108*, 2094. (b) Barrett, A. G. M.; Tam, W. *J. Org. Chem.* **1997**, *62*, 4653.

(24) (a) Shoppee, C. W.; Rees, R. W.; Summers, G. H. R.; Phillips, G. D. *J. Chem. Soc.* **1959**, 2786. (b) Shoppee, C. W.; Connick, W.; Davies, R. H. *J. Chem. Soc.* **1960**, 4857. (c) Pusset, J.; Beugelmans, R. *Tetrahedron* **1976**, *32*, 797. (c) Portella, C.; Deshayes, H.; Pete, J. P.; Scholler, D. *Tetrahedron* **1984**, *40*, 19.

(25) In fact, a very slow conversion has been observed for **5** as well; however, this is likely to be due to the gradual hydrolysis of **5** to **3**, followed by a prompt rearrangement.

(26) Kočovský, P.; Pour, M.; Gogoll, A.; Hanuš, V.; Smrčina, M. *J. Am. Chem. Soc.* **1990**, *112*, 6735.

(27) For discussion of hard and soft Lewis-acidic metals, see: (a) Fleming, I. *Frontier Orbitals and Organic Reactions*; J. Wiley: London, 1976. (b) Klopman, G. *J. Am. Chem. Soc.* **1968**, *90*, 223. (c) Ho, T.-L. *Hard and Soft Acids and Bases Principle in Organic Chemistry*; Academic: New York, 1977.

(28) (a) Kočovský, P.; Šrogl, J.; Gogoll, A.; Hanuš, V.; Polášek, M. *J. Chem. Soc., Chem. Commun.* **1992**, 1086. (b) For other examples of Hg → Pd transmetalation, see, e.g.: (b) Heumann, A.; Bäckvall, J.-E. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 207.

(29) Note that the axial epimer of **3** gives cholesterol via the "*retro-iso*-steroid" rearrangement even with Hg(II) and Tl(III) salts.[21,22]

(30) An authentic sample of **10** was prepared in three steps from **14** (Scheme 3).

(31) (a) Larock, R. C. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 27. (b) Larock, R. C. *Organomercury Compounds in Organic Synthesis*; Springer: Berlin, 1985. (c) Larock, R. C. *Solvomercuration−Demercuration in Organic Synthesis*; Springer: Berlin 1986. (d) Larock, R. C. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G.; McKillop, A., Eds; Pergamon Press: Oxford, 1995; Vol. 11, Chapter 9.

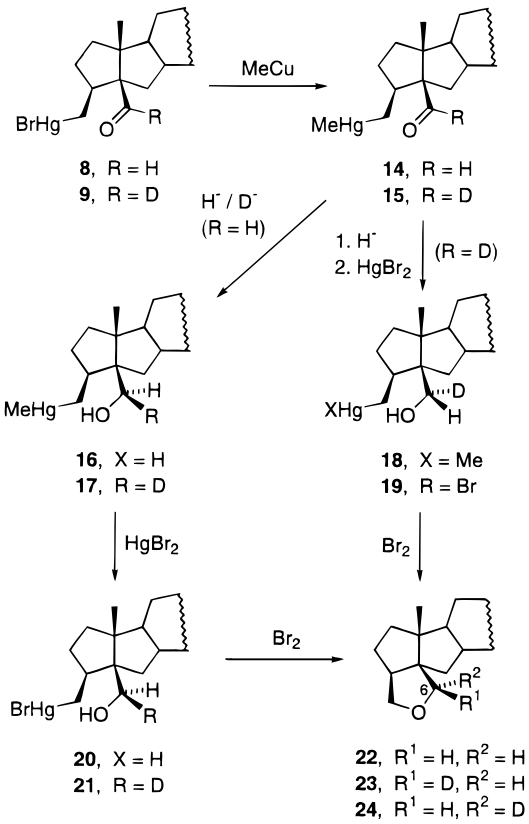
(32) Kočovský, P.; Grech, J. M.; Mitchell, W. L. *J. Org. Chem.* **1995**, *60*, 1482.

(33) For a preliminary account, see: Kočovský, P.; Dunn, V.; Grech, J. M.; Šrogl, J.; Mitchell, W. L. *Tetrahedron Lett.* **1996**, *37*, 5585.

(34) The diagnostic feature for MeHg group is a singlet (83%) and a doublet (17%) of the methyl group in the ^{1}H NMR spectrum, which appear at ∼0.22 ppm; the doublet ($J \cong 102$ Hz) corresponds to the coupling of H with the less abundant ^{199}Hg isotope.

(35) Si-Face selectivity is characteristic for reduction of 10β-CH═O steroids, with 70:30 ratio for NaB^2H_4 and 85:15 for $LiAlH(OBu^t)$. See ref 21 and the following: Arigoni, D.; Battaglia, R.; Akhtar, M.; Smith, T. *J. Chem. Soc., Chem. Commun.* **1975**, 185.

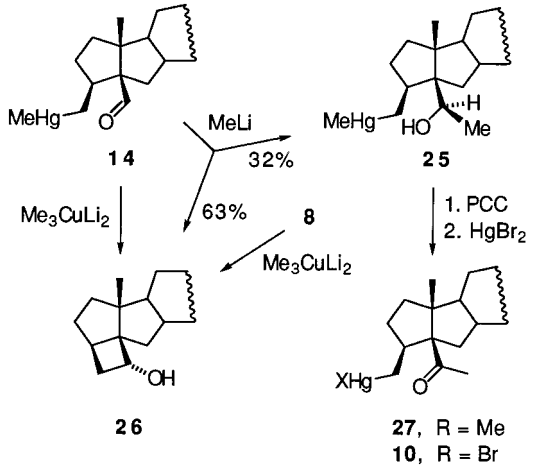
Scheme 2



with bromine[36] (DME, rt, 5 h; 86%), in which the signals of individual protons of the CH_2-O-CH_2 unit in the ^1H NMR spectrum were identified by NOE.[37] Analogous transformations in both deuterated series, i.e., **17** → **21** → **23** and **18** → **19** → **24**, allowed the assignment of the configuration at C(6) by comparison of the ^1H NMR spectra of the ring-closed products **22**, **23**, and **24**.

Since methylation served as an effective means of protecting the organomercurials toward reduction, it was of interest to establish its utility in additions of highly reactive organometallic reagents, such as alkyllithium, cuprates, etc. To this end, methylmercurio aldehyde **14** (Scheme 3) was first treated with methyllithium (Et_2O, −78 °C, 1 min). Analysis of the product mixture revealed a relatively clean reaction with two major products formed, namely, the alcohol **25** (32%),[38] resulting from the "normal" addition of MeLi across the C=O group, and the cyclobutane derivative **26** (63%), arising via activation of the methylmercurio moiety toward an intramolecular addition. By contrast, MeMgI gave an intractable mixture of a number of products, whereas standard cuprates, such as Me_2CuLi and $Me_2Cu(CN)Li_2$, proved inert. On the other hand, Me_3CuLi_2 (generated from 3 equiv of MeLi and 1 equiv of CuI)[39] transformed **14** cleanly into the cyclobutyl derivative **26** (98%) at −78 °C in 5 min. The latter reaction can also be performed with the bromomercurio aldehyde **8** (Et_2O-THF, −78 °C, 5 min; 97%).[40−44]

Scheme 3



The alcohol **25** was oxidized with PCC to give ketone **27** (CH_2Cl_2, rt, 3 h; 93%), which was deprotected on treatment with $HgBr_2$ to afford the bromomercurio ketone **10** (82%), whose unsuccessful preparation in pure form was referred to above.

Oxidative Reactions of Bromomercurials. Reduction of halomercurials R−HgX with $NaBH_4$ proceeds via a radical mechanism, as evidenced, for instance, by the addition to methyl acrylate.[31,45,46] Alternatively, the incipient radical can be trapped by oxygen bubbled through the reaction mixture to generate peroxide R−OOH, which is further reduced by the hydride present to the corresponding alcohol.[31d,45−47] Application of this protocol (O_2, $NaBH_4$, DMF, rt, 15 min) to the bromomercurial **8** (Scheme 4) produced a mixture of the fully reduced alcohol **12** (2%), the expected diol **28** (49%), and the lactol **11** (37%). Formation of the latter byproduct demonstrates that removal of the HgBr group is faster

(36) For halogenation of halomercurials, see ref 31d and the following: (a) Bloodworth, A. J.; Chan K. H.; Cooksey, C. J. *J. Org. Chem.* **1986**, *51*, 2110. (b) Kabalka, G. W.; Varma, R. S. *Tetrahedron* **1989**, *45*, 6601. (c) Martin, O. R.; Xie, F.; Kakarla, R.; Benhamza, R. *Synlett*, **1993**, 165.

(37) In the ^1H NMR spectrum of **22**, the signal at δ 3.38 (d, $J = 9.1$ Hz) was assigned to 6α-H and that at 3.97 (d, $J = 9.1$ Hz) to 6β-H by using NOE; see the Experimental Section for details.

(38) In this case, configuration at C(6) could not be rigorously established since the attempted cyclization to the corresponding tetrahydrofuran derivative (see Scheme 2) was unsuccessful. However, in view of the prevailing Re-face selectivity (**14** → **17**) observed for hydride reductions, it can be assumed to be (6*R*).

(39) (a) We have recently shown[32] that the reaction, in fact, requires "Me_3CuLi_2" rather than the originally reported[21] "excess" of Me_2CuLi. The error in our earlier work originated from not rigorously establishing the concentration of MeLi solutions used for generating the cuprate reagent. (b) For a reliable method of titrating alkyllithiums, see: Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.

(40) While Ashby[41] proposed Me_3CuLi_2 as a realistic structure, Lipshutz[42] argued that this reagent actually exists as a mixture of Me_2CuLi and MeLi. However, the latter argument is based on a study under the iodide-free conditions. In our experiments, LiI (which is known to have a dramatic influence on the structure of organocuprates[42]) was present and proved to have a beneficial effect on the selectivity of the reaction. Furthermore, if free MeLi were present in our reaction mixture, a similar outcome could be expected as that for the reaction of **14** with pure MeLi (i.e., formation of a 1:2 mixture **25**/**26**; vide supra), since **14** is inert to Me_2CuLi. For the effect of various Cu/Li ratios on the cuprate structure, see, e.g., refs 42 and 43.

(41) Ashby, E. C.; Watkins, J. S. *J. Chem. Soc., Chem. Commun.* **1976**, 784.

(42) Lipshutz, B. H.; Kozlowski, J. A.; Breneman, C. M. *J. Am. Chem. Soc.* **1985**, *107*, 3197.

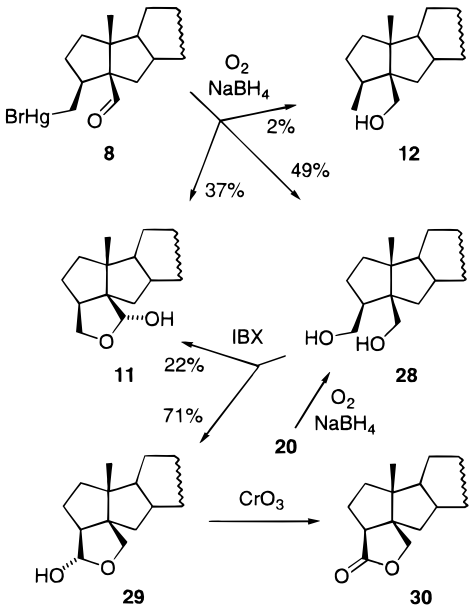
(43) Hauser, F. M.; Mal, D. *J. Am. Chem. Soc.* **1984**, *106*, 1862.

(44) The detailed structuture of the intermediate arising from the reaction of Me_3CuLi_2 with methylmercurio derivatives is unknown; a cluster-type species R-[Hg,Cu,Li] has been proposed: Bergbreiter, D. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 4937.

(45) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Pergamon: Oxford, 1986.

(46) Pasto, D. J.; Gontarz, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 719.

Scheme 4

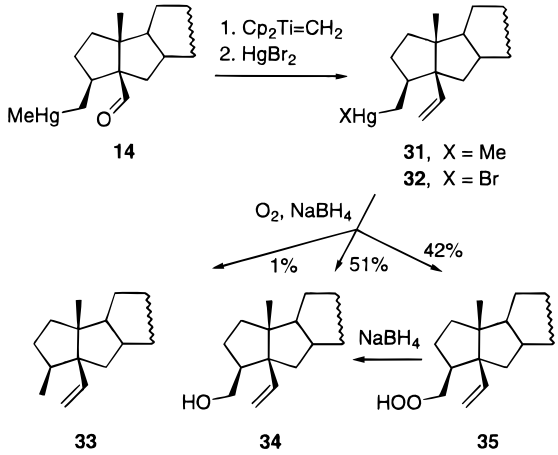


than the reduction of the aldehyde moiety. Pure diol **28** was obtained under the same conditions from the alcohol **20** (84%).

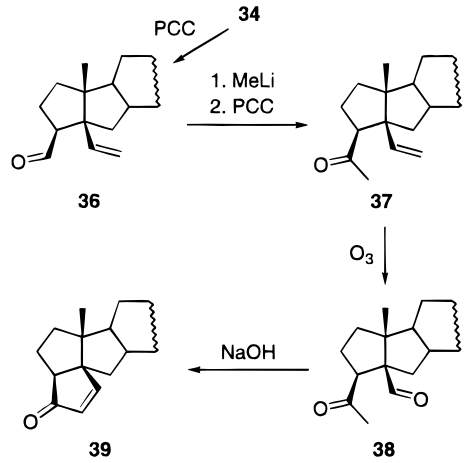
Since this strategy represented an expedient approach to bisoxygenated species, we further explored the selective oxidation of one of the two primary hydroxyl groups in **28** with a view to preparation of the corresponding lactone.[48] While the classical Fetizon reagent (Ag_2CO_3 on Celite),[49] originally designed to oxidize primary alcohols in the presence of secondary hydroxyls, was capricious and not sufficiently selective, Dess−Martin reagent (iodoxybenzoic acid, IBX)[50] proved to oxidize the less hindered hydroxyl preferentially (in DMSO, rt, 45 min), giving a mixture of regioisomeric lactols **29** (71%) and **11** (22%). The former lactol, formed as a single anomer, was oxidized by Jones reagent to the lactone **30** (98%), regioisomeric with **13**, which, in turn, was prepared previously in two steps (Scheme 1), relying either on the thallium(III)-mediated rearrangement **3** → **11** or on the Pd(II)-catalyzed ring-closure **8** → **11** followed by oxidation (**11** → **13**).

By contrast to this straightforward method, ketone **10** gave a mixture of several compounds when treated with $NaBH_4$ and oxygen, which was not further analyzed. On the other hand, the vinyl derivative **32** (Scheme 5), obtained by Tebbe reaction[51,52] **14** → **31** (2 equiv of the reagent, toluene, THF, rt, 1 h; 98%),[53] followed by deprotection (**31** → **32**) with $HgBr_2$ (DME, rt, 2 h; 96%), afforded on treatment with $O_2/NaBH_4$ (DMF, rt, 15 min) a mixture of the demercurated hydrocarbon **33** (1%), the expected alcohol **34** (51%), and the third product, which

Scheme 5



Scheme 6



was identified as the hydroperoxide **35** (42%) on the basis of its IR spectrum[54] and its ready reduction to alcohol **34** by $NaBH_4$ or $LiAlH_4$.

Triquinane-Type Structure Synthesized by an Intramolecular Aldol Condensation. We envisaged an entry into the triquinane realm via an intramolecular aldol condensation of a keto-aldehyde, such as **38** (Scheme 6) or its positional isomer. After numerous unsuccessful attempts,[55] the dicarbonyl derivative **38** was synthesized from the olefinic alcohol **34**, whose vinylic substituent served as a masked form of the aldehyde group: oxidation

(47) Barluenga, J.; Yus, M. *Chem. Rev.* **1988**, *88*, 487.

(48) For an overview of lactone syntheses, see: Ogliaruso, M. A.; Wolfe, J. F. *Synthesis of Lactones and Lactams*; J. Wiley: Chichester, 1993.

(49) (a) Fetizon, M.; Golfier, M.; Louis, J.-M. *Tetrahedron* **1975**, *31*, 171. (b) Boekman, R. K.; Thomas, E. W. *Tetrahedron Lett.* **1976**, *17*, 4045. (c) Morgans, D. J., Jr., *Tetrahedron Lett.* **1981**, *22*, 3721.

(50) Preparation of IBX: (a) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277. (b) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. Oxidation of diols by IBX: (c) Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35*, 8019. Application of IBX in lactone synthesis: (d) Corey, E. J.; Palani, A. *Tetrahedron Lett.* **1995**, *36*, 3485, 7945.

(51) (a) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611. For modifications, see: (b) Bertini, F.; Grasselli, P.; Zubiani, G.; Cainelli, G. *Tetrahedron* **1970**, *26*, 1281. (c) Canizzo, L. F.; Grubbs, R. H. *J. Org. Chem.* **1985**, *50*, 2316, 2386.

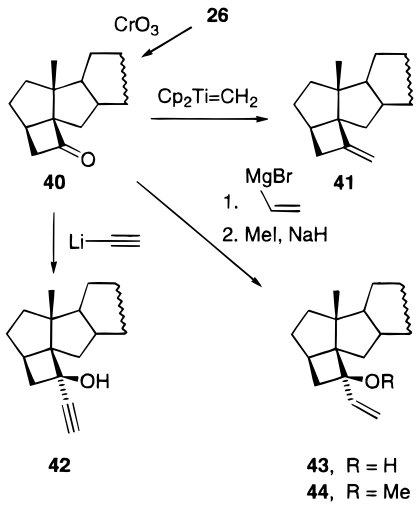
(52) Attempted Wittig olefination with $Ph_3P{=}CH_2$ was unsuccessful in this severely hindered position and so was the reaction with "modified" Tebbe's reagent, i.e., $Cp_2Ti{=}CH_2$ and ZnX_2; for the latter method, see: Eisch, J. J.; Piotrowski, A. *Tetrahedron Lett.* **1983**, *24*, 2043.

(53) Addition of Cp_2TiMe_2 (3 equiv), generated from Cp_2TiCl_2 and MeLi, and pyridine (1 equiv) to a THF solution of **14**, followed by heating at 65 °C for 24 h, produced **31** in 69% yield. For the method, see: (a) Claus, K.; Bestian, H. *J. Liebigs Ann. Chem.* **1962**, *654*, 8. (b) Petasis, N. A.; Fu, D.-K. *Organometallics* **1993**, *12*, 3776. (c) Petasis, N. A.; Lu, S.-P.; *Tetrahedron Lett.* **1995**, *36*, 2393. (d) Petasis, N. A.; Hu, Y.-H.; Fu, D.-K. *Tetrahedron Lett.* **1995**, *34*, 6001.

(54) Characteristic ν_{max}(O−O) at 855 cm^{-1} was identified in the IR spectrum of **35**.

(55) Attempts relying on the reaction of lactone **30** with MeLi or Tebbe reagent, which should, in principle, eventually lead to **38**, were unsuccessful. For successful examples, see, e.g.: (a) Trost, B. M.; Shuey, C. D.; DiNinno, F., Jr.; McElvain, S. S. *J. Am. Chem. Soc.* **1979**, *101*, 1284. (b) Pine, S. H.; Zahler, R.; Evans, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 3270.

Scheme 7

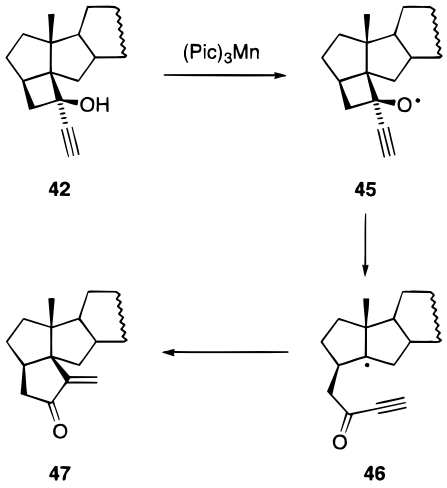


of **34** with PCC (CH_2Cl_2, rt, 2.5 h) afforded aldehyde **36** (82%), whose reaction with MeLi (Et_2O, −78 °C, 15 min) produced a pair of epimeric alcohols, which were directly oxidized by PCC (rt, 2 h) to the single methyl ketone **37** (88% overall). Ozonolysis of the latter product (CH_2Cl_2, −35 °C, 1 h) furnished the required keto-aldehyde **38** (65%), whose intramolecular aldol condensation (NaOH, THF, H_2O, rt, 45 min) produced the triquinane-type structure **39** (34%).[56,57]

Triquinane-Type Structures Synthesized by Ring-Expansion of Cyclobutane Derivatives via Radical Reactions. The extremely facile, intramolecular organometallic addition across a carbonyl bond **14** → **26**[21,39a] represents an interesting approach to annulation of the cyclobutane ring to an existing skeleton in its own right. Furthermore, the four-membered ring can be viewed as a potential synthon for an annulated cyclopentane, provided a suitable and regioselective method for expansion of this "5,5,4" tricyclic block to a "5,5,5" system is identified.[58] We envisioned the cyclobutanone derivative **40** (Scheme 7), prepared from the alcohol **26** by Jones oxidation (95%),[21] as a suitable precursor for ring expansion.

The carbonyl group of the ketone **40** is extremely hindered, as evidenced, e.g., by the failure of attempted Wittig reaction and Peterson olefinations.[21,22] On the other hand, reaction with the Tebbe reagent[51] (Cp_2TiCl_2, Me_3Al, toluene−THF, 65 °C, 2 h) afforded the alkene **41** (87%). Although analogous, less hindered *exo*-methylene cyclobutane derivatives have been reported to ring-expand when treated with Pd(II),[59] **41** proved to be resistant to treatment under similar conditions, presumably owing to steric hindrance; under harsher conditions, slow decomposition of **41** was observed.

Scheme 8. Pic = Picolinate



Since O-radicals[60] generated from cyclobutanol derivatives are known to promptly ring open, generating a C-radical,[45] which can be trapped in a intramolecular fashion, e.g., by addition to a multiple bond,[3,12] we reasoned that radicals generated from **42** or **43** could serve this purpose. Being galvanized by Snider's successful efforts,[11,12] we first synthesized propargylic alcohol **42** via addition of lithium acetylide−ethylenediamine complex to the ketone **40** (THF, rt, 5 min; 62%),[61] the result of an exclusive attack from the convex face (note that the concave side is severely hindered).[21,62] The allylic alcohol **43** was synthesized in a similar way by addition of vinylmagnesium bromide to **40** (THF, 40 °C, 1 h; 97%).

Reaction of the propargylic alcohol **42** with manganese(III) picolinate (DMF, 100 °C, 3 h)[60,63,64] proved moderately successful, giving a complex mixture, from which the major product **47** was isolated in 32% yield (Scheme 8).[65,66] Its formation can be rationalized by generating the O-radical **45**, whose ring-opening can be expected to occur toward the more substituted carbon, followed by capture of the resulting tertiary C-radical **46** by the neighboring triple bond. Although a similar strategy should, a priori, work for the allylic alcohol **43**,[11] in this particular case it led to a complex mixture with no isolable homogeneous product.

(56) For a related strategy, see: Oppolzer, W.; Bättig, K. *Tetrahedron Lett.* **1982**, *23*, 4669.

(57) Synthesis of the regioisomer of **39**, which should be accessible by aldol condensation of the isomer of the keto aldehyde **38**, was unsuccessful since, as mentioned above, its preparation via the oxidative demercuration of **10** (O_2, $NaBH_4$) gave a mixture of a number of products (in contrast to the straightforward reaction of **8** or **32**).

(58) For synthetic strategies employing expansion of cyclobutane rings, see, e.g.: (a) Knapp, S.; Trope, A. F.; Theodore, M. S.; Hirata, N.; Barchi, J. J. *J. Org. Chem.* **1984**, *49*, 608. (b) Corey, E. J.; Desai, M. C.; Engler, T. A. *J. Am. Chem. Soc.* **1985**, *107*, 4330. (c) Abraham, W. D.; Bhupathy, M.; Cohen, T. *Tetrahedron Lett.* **1987**, *28*, 2203. (d) Annis, G. D.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4509. (e) W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923. For a related expansion of cyclopropanes, see: (f) Trost, B. M. *Acc. Chem. Res.* **1974**, *7*, 85.

(59) Boontanonda, P.; Grigg, R. *J. Chem. Soc., Chem. Commun* **1977**, 583.

(60) de Klein, W. J. In *Organic Synthesis by Oxidation with Metal Compounds*; Mijs, W. J., de Jonge, C. R. H., Eds.; Plenum Press: New York, 1986; p 216. For recent examples, see refs 11 and 12.

(61) Starting material (14%) was recovered.

(62) Reduction of **40** with $LiAlH_4$ also occurs exclusively from the convex side.[21] On the other hand, according to Snider's report,[11] similar "5,5,4" ketone lacking the angular methyl gave a 2:1 mixture of the corresponding *exo*- and *endo*-epimers on reaction with HC≡CLi.

(63) For the preparation of $(Pic)_3Mn$, see: (a) Ray, M. M.; Adnya, J. N.; Biswas, D.; Poddar, S. N. *Aust. J. Chem.* **1966**, *19*, 1737. For its application to generate *O*-radicals, see refs 11, 12d, and: (b) Iwasawa, N.; Hayakawa, S.; Funahashi, M.; Isobe, K.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 819.

(64) Unlike other Mn(III) salts, the picolinate does not require the presence of Cu(II) to reduce the radicals arising from the addition since the picolinate moiety itself is capable of the reduction, serving as a hydrogen donor.[12d]

(65) For a similar system, Snider reported 46% and 58% yield with $(AcO)_3Mn$ and $(Pic)_3Mn$, respectively.[11]

(66) Other Mn(III) salts, such as $(AcO)_3Mn$, reacted sluggishly and produced more complex mixtures. For examples of successful application, see ref 12 and the following: (a) Wu, Y.-J.; Zhu, Y. Y.; Burnell, D. J. *J. Org. Chem.* **1994**, *59*, 104. Cobalt(III) was also unsuccessful; for its application, see, e.g.: (b) Pattenden, G. *Chem. Soc. Rev.* **1988**, *17*, 361.

Table 1. Metal-Mediated/Catalyzed Rearrangements of 43 in THF at Room Temperature (Scheme 9)

entry	reagent or catalyst	amount of the reagent	**47**	**50**	**51**	**52**	other (%)	path ratio a/b
1	$Tl(NO_3)_3$	1.1 equiv[a]	76	12				6.3:1
2	$Hg(NO_3)_2$	1.1 equiv[a]	52	13			**49c** (23)	1.4:1
3	$Pd(NO_3)_2$	1.1 equiv[a]	36	2	2	54		1:1.6
4	$Pd(NO_3)_2$	5 mol %[b,c]	13	2	1	60		1:4.8
5	$Pd(NO_3)_2$	5 mol %[d,e,f]				30		
6	$PdCl_2$	5 mol %[b,g]	11	3	28	33		1:5.8
7	$(PhCN)_2PdCl_2$	1.1 equiv[a]	27	1	53	14		1:2.5
8	$(PhCN)_2PdCl_2$	8 mol %[b,h]	12	2	72	11		1:7.1
9	$(MeCN)_2PdCl_2$	7 mol %[b,h]	18	2	56	17		1:4.2

[a] 15 min. [b] 15 h. [c] $Cu(NO_3)_2$ (2 equiv) used to reoxidize Pd(0) to Pd(II). [d] 10 days. [e] O_2 (~1.1 atm) used as oxidant. [f] In DMF. [g] $CuCl_2$ (2 equiv) used as oxidant. [h] *p*-Benzoquinone used as oxidant.

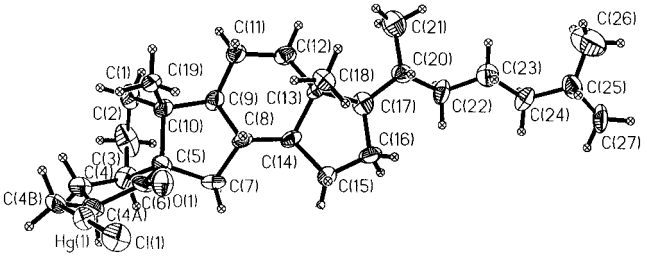
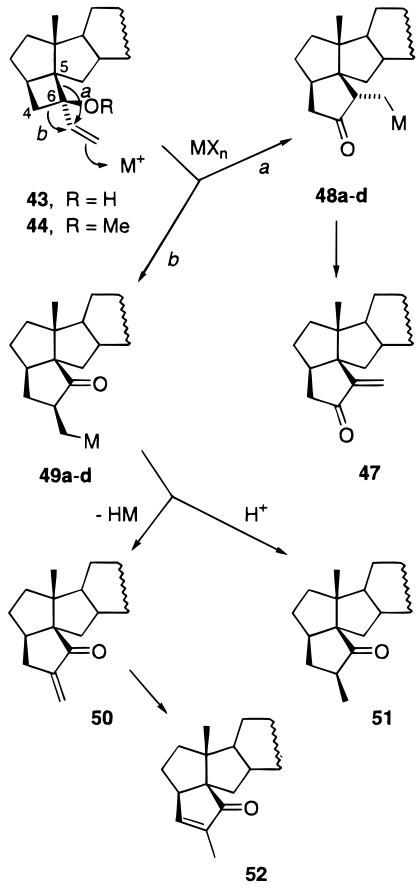


Figure 1. ORTEP diagram of the organomercurial **49c**.

Triquinane-Type Structures Synthesized by Ring-Expansion of Cyclobutane Derivatives via Electrophilic Rearrangements. As an alternative strategy, we envisioned that generation of an electron-deficient center at a substituent on the cyclobutane C(6) may trigger an expansion[11,67,68] of the four-membered ring via a Wagner–Meerwein-type migration. It occurred to us that the vinyl group in **43** would be particularly suitable for carrying out such transformation since its π-system should be prone to a Markovnikov-controlled electrophilic attack,[69] thereby creating electron deficiency at the desired position.

The reaction of **43** with thallium(III) nitrate in THF (rt, 15 min) afforded mainly the α-methylene ketone **47** (Table 1, entry 1) as a result of the expected[68] preferential migration of the quaternary carbon (Scheme 9; path a); isomeric α-methylene ketone **50** (path b) was isolated as a minor product[70] (entry 1). The isoelectronic mercury(II) nitrate in THF (rt, 15 min; NaCl quench) again furnished mainly **47** (entry 2) accompanied by a small amount of its isomer **50**. However, a third product has now been intercepted, namely, the organomercurial **49c** (arising from treatment of the prime product **49b** with aqueous NaCl), which suggests that **49b** is the precursor of **50**.[71] The structure of **49c** was determined by single-crystal X-ray crystallography (Figure 1).[72] Experiments with two other isoelectronic ions were less successful.

Scheme 9. **a**, M = $Tl(NO_3)_2$; **b**, M = $HgNO_3$; **c**, M = HgCl; **d**, M = PdL_nX



Thus, silver(I) triflate proved inert even at elevated temperatures, whereas the reaction with lead(IV) tetraacetate gave an intractable mixture of a number of products.

Palladium(II), which often exhibits reactivity somewhat similar to that of mercury(II), enjoys the advantage that it can be used catalytically, so that its toxicity is much less of a problem compared to that of Hg(II) or Tl(III). However, since Pd(II) would be reduced to Pd(0) in this reaction, developing a catalytic cycle required that an efficient oxidant be employed in a stoichiometric amount.[73–77]

In an initial, stoichiometric reaction, $Pd(NO_3)_2$[78] in THF (rt, 15 min) gave rise mainly to the enone **47** and its isomer **52** in ca. 2:3 ratio (entry 3). By contrast, in the

(67) (a) Clark, G. R.; Thiensatmit, T. *Tetrahedron Lett.* **1985**, *26*, 2503. (b) Demuth, M.; Pandey, B.; Wietfeld, B.; Said, H.; Viader, J. *Helv. Chim. Acta* **1988**, *71*, 1392. (c) de Almeida Barbosa, L.-C.; Mann, J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 177. (d) Nemoto, H.; Nagamochi, M.; Fukumoto, K. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2329.

(68) Kim, S.; Uh, K. H. *Tetrahedron Lett.* **1992**, *33*, 4325.

(69) Kočovský, P.; Tureček, F. *Tetrahedron Lett.* **1981**, *22*, 2699.

(70) The structural assignment for the isomers **47** and **50** is based on the signals of their *exo*-methylene protons in the ^1H NMR spectra: whereas **50** exhibits homoallylic coupling, there is none for **47**. The structure of **50** is further corroborated by chemical correlation.[71]

(71) Mass spectrum of **49c** lacks the molecular ion and closely resembles the spectrum of **50**, which further supports this mechanism. Moreover, on reaction with $Pd(NO_3)_2$, **49c** was converted into **52** (via **50**).

(72) For the structural details of **49c**, see the Supporting Information.

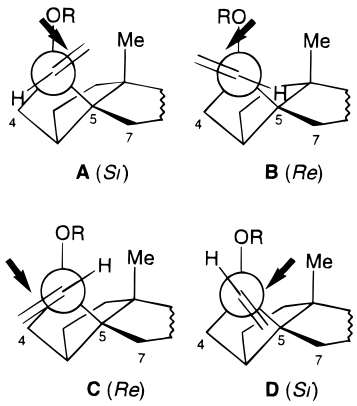
(73) Among the mild oxidants known to serve this purpose, copper(II),[74] *p*-benzoquinone,[67,75,76] and oxygen[77] play a dominant role, as documented by their successful use in methoxycarbonylation reactions,[74] Bäckvall oxidation,[75] and allylic oxidation.[33,76]

catalytic experiment, carried out in the presence of $Cu(NO_3)_2$[78] as the oxidant (THF, rt 15 h), formation of the enone **47** was largely suppressed in favor of pathway b (entry 4). With oxygen as the oxidant (in DMF), we observed the most selective reaction, affording almost exclusively **52**, though in a relatively low yield (entry 5). Palladium(II) chloride with $CuCl_2$ (in THF) gave rise mainly to **51** and **52** in ca. 1:1 ratio (entry 6), whereas $(CF_3CO_2)_2Pd$ and $(AcO)_2Pd$ did not exhibit any significant catalytic activity, due to either decomposition or low solubility of the catalyst.

A stoichiometric reaction of **43** with $(PhCN)_2PdCl_2$ afforded a mixture of **47** and **51**[79] in ca. 1:2 ratio (entry 7). By contrast, its catalytic version, using *p*-benzoquinone as oxidant (THF, rt, 15 h) and either the same complex or $(MeCN)_2PdCl_2$, proved more selective, producing **51** in high yield (entries 8 and 9).

These experiments have demonstrated a high preference for pathway a in the case of Tl(III)-mediated ring-expansions, whereas reactions catalyzed by Pd(II) preferred pathway b. Although potentially useful as a means of reactivity control by the reagent/catalyst, the need for a stoichiometric amount of thallium might be viewed as a deterent if large-scale operations are intended. Ideally, a less toxic and preferably catalytic system, whose selectivity could be tuned (in favor of either pathway a or b) either by ligands or by other structural modification, should be developed. Since coordination of the metal to the OH group of **43** can be anticipated, we reasoned that *O*-alkylation might dramatically influence the relative preference of the molecule for the two pathways a/b. Moreover, a comparison of the reactivity of alcohol **43** and its derivatives would also shed more light on the mechanisms of these intriguing reactions. To this end, methyl ether **44** was prepared from alcohol **43** (Scheme 7) by conventional methylation (MeI, NaH, THF, 45 °C, 1 h; 87%). With Hg(II), this methoxy derivative **44** reacted in the same way as the alcohol **43**, giving mainly **47** (64%), though the reaction was rather slow, presumably owing to the energetically more demanding cleavage

Scheme 10



of the C−O bond (Scheme 9).[80,81] With $(MeCN)_2PdCl_2$ (5 mol %), the reaction took a different turn compared to **43**: instead of pathway b, the methyl ether **44** now reacted almost exclusively via pathway a to afford **47** (rt; 75%), showing that the reaction outcome can be effectively controlled by alkylation of the hydroxy group. Hence, for both alternative pathways the same catalyst can be employed, thereby avoiding the necessity of using a stoichiometric amount of toxic reagent.

The reactivity patterns, exhibited by individual electrophiles in these ring-expansion reactions, are noteworthy. Thus, Tl(III) and Hg(II), being strong, soft electrophiles, favor the migration of the more substituted carbon (path a), suggesting an electronically controlled process. By contrast, Pd(II), a transition metal, clearly favors path b (with **43**). Catalytic reactions turned out to be more selective than their stoichiometric counterparts, which can be attributed to the modification of the reactivity of Pd in the transient species by coordination[75c−h] to the oxidant. The propensity of the organopalladium intermediate to β-elimination (i.e., **49d** → **50**, followed by isomerization to **52**) dramatically decreases in favor of protonolysis (**49d** → **51**)[82] by appending chloride and nitrile ligands (compare entries 4, 6, and 8).

The reactivity preferences for **43** and **44** are intriguing. In the classical, charge-controlled Wagner-Meerwein rearrangement, it is the migration of the more substituted carbon, i.e., C(5), that should be favored (pathway a), which is the case of **44**. By contrast, **43** follows this route only with Tl(III) and Hg(II), whereas Pd(II) clearly favors path b. Generally, for the rearrangement to occur, the π^* orbital of the double bond should be aligned with the σ orbital of the migrating C−C bond (with the maximum deviation believed to be ≤30°).[83] This requirement is met by conformations **A** − **D** (Scheme 10), of which the latter two are higher in energy due to eclipsing interactions of the vinyl group with the skeletal carbons. For conformation **A**, the electrophile should approach from the much less hindered Si face, thereby encouraging

(74) (a) Hosokawa, T.; Murahashi, S. *Acc. Chem. Res.* **1990**, *23*, 49. (b) Semmelhack, M. F.; Kim, C.; Zhang, N.; Bodurow, C.; Sanner, M.; Dobler, W.; Meier, M. *Pure Appl. Chem.* **1990**, *62*, 2035. (c) Kočovský, P.; Pour, M. *J. Org. Chem.* **1990**, *55*, 5580. (d) Semmelhack, M. F.; Cheung, A. W. H.; Gu, Y.; Kim, C.; Zhang, N.; Lew, W. *J. Am. Chem. Soc.* **1994**, *116*, 7455.

(75) (a) Bäckvall, J.-E. *Acc. Chem. Res.* **1983**, *16*, 335. (b) Bäckvall, J.-E. *Pure Appl. Chem.* **1983**, *55*, 1669. (c) Bäckvall, J.-E. *New J. Chem.* **1990**, *14*, 447. (d) Bäckvall, J.-E. *Pure Appl. Chem.* **1992**, *64*, 429. (c) Grennberg, H.; Gogoll, A.; Bäckvall, J.-E. *Organometallics* **1993**, *12*, 1790. (d) Tschoerner, M.; Trabesinger, G.; Albinati, A.; Pregosin, P. S. *Organometallics* **1997**, *16*, 3447. (e) Milani, B.; Anzilutti, A.; Vicentini, L.; Santi, A. S. O.; Zangrando, E.; Geremia, S.; Mestroni, G.; *Organometallics* **1997**, *16*, 5064. (f) Klein, R. A.; Elsevier: C. J.; Hartl, F. *Organometallics* **1997**, *16*, 1284. (g) Klein, R. A.; Witte, P.; van Belzen, R.; Fraanje, J.; Goubitz, K.; Numan, M.; Schenk, H.; Ernsting, J. M.; Elsevier, C. J. *Eur. J. Inorg. Chem.* **1998**, 319. (h) Szabó, K. J. *Organometallics* **1998**, *17*, 1677.

(76) (a) McMurry, J. E.; Kočovský, P. *Tetrahedron Lett.* **1984**, *25*, 4187. (b) Hansson, S.; Heumann, A.; Rein, T.; Åkermark, B. *J. Org. Chem.* **1990**, *55*, 975 and references therein. (c) Grennberg, H.; Bäckvall, J.-E. *Chem.-Eur. J.* **1998**, *4*, 1083.

(77) (a) Larock, R. C.; Hightower, T. R. *J. Org. Chem.* **1993**, *58*, 5298. (b) Rönn, M.; Bäckvall, J.-E.; Andersson, P. G. *Tetrahedron Lett.* **1995**, *36*, 7749. For a combination of Cu(II) and O_2, see: (c) Andersson, P. G.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1992**, *114*, 8696.

(78) Nitrate was employed in order to allow direct comparison with the Tl^{3+} and Hg^{2+} reagents.

(79) The structure of **51** was corroborated by a chemical correlation: reduction of **49c** with $LiAlH_4$ followed by Jones oxidation furnished an α-methyl ketone, identical with **51**. The β-orientation of the methyl group is evidenced by NOESY spectra, in which cross-peaks 4aβ-CH_3 ↔ 19-H and 4aα-H ↔ 7β-H have been identified.

(80) A similar retardation effect was observed for the Hg(II)-mediated cyclopropane cleavage in the methyl ether **4** as compared to alcohol **3** (*vide supra*).

(81) Thallium(III) nitrate gave an intractable mixture of a number of products.

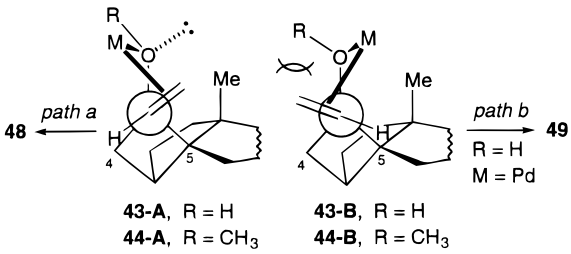
(82) Hydrogenolysis, as an alternative mechanism, seems unlikely in the oxidative medium.

(83) Saunders, M.; Chandrasekhar, J.; Schleyer, P. v. R. Rearrangements of Carbocations. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 1, p 24.

migration of the antiperiplanar C(5) (pathway a).[84] By contrast, conformation **B** should favor Re attack, followed by the migration of C(4).[85] Hence, pathway a should result from **A** (Si), whereas **B** (Re) is the prerequisite for pathway b. The observed reactivity of Tl(III) is consistent with the former and that of Pd(II) with the latter alternative for the free alcohol (R = H). Although coordination of any of the metals to the hydroxy group cannot, a priori, be excluded, it seems more likely that the initial electrophilic attack by Tl(III) and Hg(II) occurs on the double bond. As discussed above (Scheme 1), both Tl(III) and Hg(II) are very soft electrophiles[21,27] and, as such, prefer the attack on the cyclopropane ring (soft center) of **3**.[21] By contrast, all other electrophiles, including Pd(II), attack **3** on the hydroxyl (hard center), triggering a retro-iso-steroid rearrangement that leads to cholesterol-type structures.[21] Therefore, in the case of **43**, Pd(II) can be assumed to initially coordinate to the OH, followed by an attack on the double bond, stereodirected by the hydroxyl. There are numerous examples of this type of steering of transition metals by an OH group to bring about reaction at a neighboring double bond, such as in Sharpless epoxidation (with V or Ti),[86] catalytic hydrogenation,[87] hydroboration,[88] etc,[89] which support this rationalization; the recently observed effects of a neighboring OH, NH, or carbonyl groups on the course of Wacker oxidation[90,91] lend additional credence.

According to the latter scenario, Pd(II) should preferentially form chelate **43-B** (R = H; Scheme 11) on reaction with **43**, leading to pathway b. However, analogous coordination to the methoxyl, as in **44-B**, would impose a repulsive interaction between the methyl (R = Me) and the terminal atoms of the vinyl group.[92] Since the latter clash is avoided in **44-A**, the high preference for pathway a in the case of **44** can be understood.[93] On the other hand, in the case of the methyl ether **44**, the coordination may be impaired (in contrast to free alcohol **43**), as it is, e.g., in the case of Sharpless epoxidation (with V or Ti),[86] so that the "normal", i.e., electronically controlled, pathway a can prevail (**A** in Scheme 10). The latter alternative appears to be more likely. For further discussion of the Hg(II)-mediated ring expansion (a/b pathway competition), see the Note Added in Proof.

Scheme 11



Palladium(II)-Catalyzed Carbonylation. Pentalenolactones (Chart 1)[1d,48] and their congeners are characterized by their α-methylene lactone unit. The olefinic alcohol **34** seems a logical precursor to this type of molecules since its Pd(0)-catalyzed carbonylation should give rise to the corresponding α-methylene-δ-lactone.[94] However, all attempts at carbonylation (with carbon monoxide and with the corresponding chlorocarbonate derived from **34**) in the presence of a variety of Pd catalysts failed. Apparently, the steric congestion around the vinyl group is detrimental to coordination of palladium so that the reaction cannot take place.[95]

In view of the failure to produce δ-lactone from **34**, we explored the carbonylation of organomercurials. In a preliminary communication,[33] we have shown that halomercurials of the R−HgCl type can be carbonylated in the presence of a catalytic amount of $(MeCN)_2PdCl_2$ and excess of *p*-benzoquinone, provided that a hydroxyl group is located in a suitable position to allow the formation of a lactone ring; a number of *cis*- and *trans*-annulated γ-lactones have been synthesized from suitable organomercurio alcohols via this route.[33] These studies have also demonstrated that *p*-benzoquinone is required not only for the reoxidation of Pd(0) generated in the catalytic cycle but also to suppress the competing β-elimination. Application of this methodology to the bromomercurio alcohol **20** was carried out as a test of its scope and, in particular, to address the issue of whether δ-lactones could also be accessed via this route in addition to γ-lactones.

In a stoichiometric experiment, a mixture of **20**, $(MeCN)_2PdCl_2$, and *p*-benzoquinone was stirred in THF at room temperature for 17 h under an atmospheric pressure of carbon monoxide (Scheme 12). Under these

(84) The Hg(II)-mediated reaction via **C** (Re) can be excluded in view of the β-configuration of the CH_2HgCl group in **49c**: if the reaction proceeded via **C**, the latter configuratuion would have to be α. Conformation **D** appears to be most congested so that its attack by the electrophile is unlikely.

(85) Alternatively, if the attack occurred on the *Si*-face of the double bond in the conformation **B** (a less likely scenario), *syn* migration (rather than the usual *anti*) would have to follow in order to give the observed product. However, a clockwise rotation of the coordinated vinyl group prior to the Wagner-Meerwein migration would lead to the conformation **A** (*Si*), which would then trigger the migration of C(5).-

(86) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1985; Vol. 5, p 159.

(87) (a) Stork, G.; Kahne, D. E. *J. Am. Chem. Soc.* **1983**, *105*, 1072. (b) Crabtree, R. H.; Davis, M. W. *Organometallics* **1983**, *2*, 681. (c) Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655. (d) Burk, M. J.; McGrath, M. P.; Wheeler, R.; Crabtree, R. H. *J. Am. Chem. Soc.* **1988**, *110*, 5034. (e) Watanabe, Y.; Mizuhara, Y.; Shiota, M. *J. Org. Chem.* **1966**, *31*, 3785.

(88) Garrett, C. E.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 1370.

(89) For reviews on steering the reagent/catalyst by a neighboring group, see: (a) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307. (b) Brown, J. M. *Angew. Chem., Int Ed. Engl.* **1987**, *26*, 190.

(90) (a) Bose, A. K.; Krishnan, L.; Wagle, D. R.; Manhas, M. S. *Tetrahedron Lett.* **1986**, *27*, 5955. (b) Alonso, R. A.; Burgey, C. S.; Rao, B. V.; Vite, C. D.; Vollerthun, R.; Zottola, M. A.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1993**, *115*, 6666. (c) Hamed, O.; Henry, P. M. *Organometallics* **1997**, *16*, 4903. (d) Hamed, O.; Thompson, C.; Henry, P. M. *J. Org. Chem.* **1997**, *62*, 7082. (e) Pellisier, H.; Michellys, P.-Y.; Santelli, M. *Tetrahedron* **1997**, *53*, 10733. (f) Nemoto, H.; Miyata, J.; Yoshida, M.; Raku, N.; Fukumoto, K. *J. Org. Chem.* **1997**, *62*, 7850.

(91) For theoretical approach, see: (a) Siegbahn, P. E. M. *J. Am. Chem. Soc.* **1995**, *117*, 5409. (b) Strömberg, S.; Svensson, M.; Zetterberg, K. *Organometallics* **1997**, *16*, 3165.

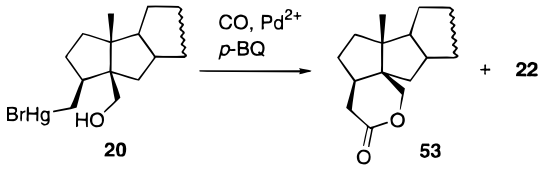
(92) Note that the MeO group is unlikely to assume a different conformation by rotating about the MeO−C(6) bond and, at the same time, offer one of the electron pairs to coordination, as this would impose a clash with the angular methyl.

(93) The "5,5,4" system reported by Snider,[11] which lacks the 10β-CH_3 but contains an additional angular methyl at position corresponding to 3α in **43**, exhibited high preference for pathway *a*, which further demonstrates the importance of conformational effects.

(94) For the Pd(0)-catalyzed method, see: (a) Henin, F.; Pete, J.-P. *Tetrahedron Lett.* **1983**, *24*, 4687. (b) Henin, F.; Muzart, J.; Pete, J.-P. *Tetrahedron Lett.* **1986**, *27*, 6332. For Ni-catalyzed carbonylation, see: (c) Semmelhack, M. F.; Brickener, J. S. *J. Org. Chem.* **1981**, *46*, 1723 and refs cited therein. Other methods make use of Pd-catalyzed carbonylation of acetylenic alcohols: (d) Chaudarian, C. G.; Woo, S. L.; Clark, R. D.; Heathcock, C. H. *Tetrahedron Lett.* **1976**, 1769. (e) Murray, T. F.; Norton, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 4107 and refs cited therein.

(95) Note that the less congested α-methylene-γ-lactones have been successfully synthesized.[94]

Scheme 12



conditions, a mixture of the desired lactone **53** (55%) and the tetrahydrofuran derivative **22** (11%) was formed. A catalytic experiment with 8 mol % of $(MeCN)_2PdCl_2$ and 2 equiv of *p*-benzoquinone required heating at 60 °C for 7 days[96] and gave the same products **53** (14%) and **22** (44%) but in an essentially reversed ratio.

These experiments have demonstrated that the Pd(II)-mediated/catalyzed carbonylation of hydroxy organomercurials can, indeed, be employed in the construction of the triquinane-type molecules with a *δ*-lactone ring. However, this methodology is less successful if a competing 5(*O*)^n-*exo*-tet cyclizatio[97] is available, which is the case in the synthesis of *δ*-lactones. By contrast, *γ*-lactones do not suffer from this competition as the conceivable 4(*O*)^n-*exo*-tet cyclization is less favorable.

Conclusions

The organomercurial **8**, obtained from the readily available alcohol **3** via a unique, mercury(II)-mediated cyclopropane opening (Scheme 1), has been utilized as a pivotal building block for the construction of a variety of triquinane-like structures annulated to the steroid skeleton, namely, lactones **13**, **30**, and **53**, conjugated ketones **39** and **52**, and α-methylene ketones **47** and **50**. Salient features of this strategy include: (1) Selective protection/deprotection of the C−HgX functionality via methylation with MeCu (**8** → **14**), followed by demethylation with $HgBr_2$ (**16** → **20**); the protected organomercurials are stable to common hydride reagents, such as $NaBH_4$, L-Selectride, superhydride, and $LiAlH(OBu^t)_3$, but not to $LiAlH_4$. This strategy allows selective reduction of a carbonyl group (**14** → **16**) and Tebbe olefination (**14** → **31**). (2) Activation of the C−HgX toward an intramolecular addition to a carbonyl group by treatment with Me_3CuLi_2 (**14** → **26**) which, in this case, can be regarded as a means of stereospecific annulation of a cyclobutane ring. (3) Oxidative demercuration with $O_2/NaBH_4$ (**8** → **28** + **11**; **20** → **28**; **31** → **34**); the resulting diol **28** was converted into the corresponding lactone via Dess−Martin and Jones oxidation (**28** → **29** → **30**). (4) Tebbe olefination of the sterically hindered carbonyl groups (**14** → **31**; **40** → **41**) where Wittig-type olefination failed. (5) Intramolecular aldol condensation (**38** → **39**). (6) Reagent/catalyst-controlled cyclobutane ring-expansion of the allylic alcohol **43** (Scheme 9) in favor of either path a (Tl^{3+} or Hg^{2+}) or b (Pd^{2+}); in the case of the methyl ether **44**, Pd(II)-catalyzed reaction switched to pathway a, so that both systems, i.e., **47** vs **50**, **51**, and **52** can be obtained by a catalytic method. Single-crystal X-ray crystallography confirmed the structure of the organomercurial intermediate **49c**, whose formation was used as evidence for the mechanism of the Hg(II)-mediated rearrangement. (7) Palladium(II)-catalyzed carbonylation (**20** → **53**).

Although the experiments were confined to the steroid realm, we are confident that the strategies and methods we have developed are of general nature and can be applied to the synthesis of triquinanes and other biologically significant products.

Experimental Section

General Methods. Melting points were determined on a Kofler block and are uncorrected. Optical rotations were recorded in $CHCl_3$ at 25 °C unless otherwise indicated with an error of $<\pm 0.1$. All reactions were carried out under a nitrogen atmosphere unless otherwise indicated. Dry THF and toluene were obtained by distillation form sodium metal in the presence of benzophenone. Dichloromethane and xylene were distilled from calcium hydride. Ether was distilled from $LiAlH_4$ or was sodium dried prior to use. Methanol and ethanol were dried by distillation from magnesium and iodine. Triethylamine and pyridine were dried over sodium hydroxide pellets. Petroleum ether refers to fraction with bp 40−60 °C. Routine drying of organic solutions was carried out with anhydrous magnesium sulfate. Standard workup of an ethereal solution means washing with 5% aqueous HCl solution, saturated aqueous $NaHCO_3$ solution, and water, drying with $MgSO_4$, and removal of the solvent under reduced pressure. All products were dried under high vacuum before recording their yields. The identity of samples prepared by different routes was checked by TLC, IR, MS, and NMR. Yields are given for isolated products showing one spot on TLC with no impurities detectable in the NMR spectrum. All flash chromatography was carried out with Kieselgel 60 (230−400 mesh) (Merck and Co), unless otherwise indicated. The amount of silica gel and the column size used for each separation was varied, with respect to the number of products, their relative polarities, and the quantity of crude mixture being purified. Separation of products using a chromatotron were performed on model 7924T with Kieselgel 60 (PF 254) plates (Merck and Co). The IR spectra were measured in chloroform. The ^1H NMR spectra were recorded with 250-, 300-, or 400-MHz instruments (FT mode) for $CDCl_3$ solutions at 25 °C. The ^{13}C NMR spectra were recorded with a 63-MHz instrument (FT mode) for $CDCl_3$ solutions at 25 °C unless stated otherwise. Chemical shifts were indirectly referenced to TMS via the solvent signals ($CDCl_3$, 7.26 ppm for ^1H and 77.00 ppm for ^{13}C, and CD_2Cl_2, 5.35 ppm for ^1H and 53.85 ppm for ^{13}C). The coupling constants were obtained by first-order analysis. The different types of carbon in the structures have been identified by DEPT techniques. Standard mass spectra and accurate mass measurements were recorded with direct inlet and the lowest temperature enabling evaporation. Chemical ionization was used in certain cases (with NH_3). The molecular ions and accurate mass values for compounds containing mercury and/or bromine are reported for the ^{202}Hg and ^{79}Br isotopes, respectively. Crystal data for **49c**: $C_{29}H_{47}ClOHg$, $M = 647.71$. Crystals were obtained from wet acetone solution via a slow evaporation at room temperature; they are monoclinic of space group $P2_1$, with $a = 10.319(2)$ Å, $b = 7.0740(11)$ Å, $c = 19.837(2)$ Å, $V = 1447.9(4)$ Å^3, $Z = 2$, $d_{calc} = 1.486$ g cm^{-3}, $\mu = 5.425$ mm^{-1}. Data were collected at 22 °C on a CCD detector-based SMART diffractometer (Siemens) using Mo Kα radiation ($\lambda = 0.710\ 73$ Å), a graphite monochromator, and the ω scan mode with frames of 0.3°. A total of 5573 reflections were measured, from which 3847 were unique ($R_{int} = 0.0810$), with 2872 having $I > 2\sigma_I$. All reflections were used in the structure refinement based on F^2 by full-matrix least-squares techniques with hydrogen atoms calculated into theoretical positions, riding during refinement on the respective pivot atom (297 parameters). Final $R_F = 0.0596$ for the observed data and $wR(F^2) = 0.1269$ for all data. The estimated error in C−C bond lengths is in the range of 0.02−0.04 Å as a result of the presence of a

(96) Note that heating for ≤4 days is required to close up *γ*-lactones.[33] See also: Kočovský, P.; Grech, J. M.; Mitchell, W. L. *Tetrahedron Lett.* **1996**, *37*, 1125.

(97) For the notation, see: Kočovský, P.; Stieborová, I. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1969.

(98) Johnson, C. K. Technical Report ORNL-5138; Oak Ridge National Laboratory: Oak Ridge, TN, 1976.

heavy atom. The absolute configuration was determined with the Flack factor (Flack, H. D. *Acta Cryst.* **1983**, *A39*, 876) = −0.03(2).

[6β-^{2}H]-3α,5-Cyclo-5α-cholestan-6α-ol (6). A solution of ketone **2** (2.8 g; 7.279 mmol) in dry ether (50 mL) was added dropwise to lithium aluminum deuteride (305 mg; 7.264 mmol) in dry ether (50 mL) at 0 °C. The mixture was stirred for 1.5 h at 0 °C; the excess reagent was then decomposed by successive addition of H_2O (0.3 mL), 15% aqueous NaOH solution (0.3 mL), and H_2O (1 mL). The solid residue was filtered off and the organic layer washed with 5% aqueous HCl solution (20 mL), saturated aqueous $NaHCO_3$ solution (20 mL), and H_2O (2 × 20 mL). The solution was dried and evaporated yielding amorphous **6** (2.65 g; 6.836 mmol; 94%): IR ν_{max}(OH) 3610 cm^{-1}; ^{1}H NMR (250 MHz) δ 0.24 (t, J = 4.1 Hz, 1 H, 4β-H), 0.60 (dd, J = 8.1 and 4.6 Hz, 1 H, 4α-H), 0.68 (s, 3 H, 18-H), 0.863 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.866 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.92 (s, 3 H, 19-H); ^{13}C NMR (62.90 MHz) δ 6.58 (C-4), 12.05 (C-18), 17.94 (C-19), 18.64 (C-21), 18.67 (C-3), 22.57 (C-26 or C-27), 22.82 (C-26 or C-27), 23.17 (CH_2), 23.83 (CH_2), 24.24 (CH_2), 25.07 (CH_2), 28.01 (CH), 28.24 (CH_2), 32.75 (CH_2), 34.94 (CH), 35.78 (CH), 36.13 (CH_2), 39.14 (CH_2), 39.50 (C-13), 39.72 (CH_2), 40.12 (CH_2), 42.72 (C-5 or C-10), 44.94 (C-5 or C-10), 47.65 (CH), 56.23 (CH), 56.26 (CH), 66.93 (t, C-6); MS (CI) m/z (%) 405 (100, $[M + NH_4]^+$); MS >98% ^{2}H (d_1).

3α,5-Cyclo-6β-methyl-5α-cholestan-6α-ol (7). Cerium chloride heptahydrate (1.802 g; 4.837 mmol) was placed in a flask equipped with a stirring bead. The flask was gradually heated to 140 °C while stirring under vacuum. After 3 h the solid was cooled under nitrogen. THF (15 mL) was added with vigorous stirring and the resultant suspension was stirred overnight at room temperature. The flask was then immersed in an ice bath and methyllithium (1.38 M in ether; 3.5 mL; 4.830 mmol) was added. After stirring for 1 h at 0 °C, a solution of ketone **2** (1.236 g; 3.213 mmol) in THF (10 mL) was added. The mixture was stirred at 0 °C for 1 h, then quenched with 5% aqueous HCl solution (5 mL) and diluted with ether (60 mL). The organic layer was washed with 5% aqueous NaCl solution (30 mL), saturated aqueous $NaHCO_3$ solution (30 mL), and 5% aqueous NaCl (30 mL), dried, and then evaporated. The crude product was purified by column chromatography using a petroleum ether−ether mixture (9:1) as the eluent, to afford unreacted **2** (148 mg; 385 μmol; 12%) as the least polar and amorphous **7** (940 mg; 2.346 mmol; 73%) as the most polar component: $[\alpha]_D$ +35.2 (*c* 1.9; literature[17] gives $[\alpha]_D$ +38.2); IR ν_{max}(OH) 3603 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.29 (dd, J = 4.7 Hz, 1 H, 4β-H), 0.54 (dd, J = 8.2 and 4.7 Hz, 1 H, 4α-H), 0.70 (s, 3 H, 18-H), 0.864 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.868 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.91 (d, J = 6.6 Hz, 3 H, 21-H), 0.92 (s, 3 H, 19-H), 0.98 (m, 1 H, 7α-H), 1.15 (m, 1 H, 12α-H), 1.27 (bd, 3 H, 6β-CH_3), 1.32 (m, 1 H, 3-H), 1.76 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.1 Hz, $J_{7\beta-H,8\beta-H}$ = 3.7 Hz, 1 H, 7β-H), 1.98 (ddd, J = 12.5, 6.9, 6.9 Hz, 1 H, 12β-H); NOE 0.29 (4β-H) ↔ 0.92 (19-H), 0.54 (4α-H) ↔ 1.27 (6β-Me), 0.54 (4α-H) ↔ 1.32 (3-H), 1.27 (6β-Me) ↔ 1.76 (7β-H); ^{13}C NMR (100.60 MHz) δ 6.81 (C-4), 12.17 (C-18), 18.69 (C-21), 20.10 (C-19), 22.37 (C-3), 22.57 (C-26 or C-27), 22.82 (C-26 or C-27), 23.06 (C-11), 23.19 (CH_2), 23.84 (CH_2), 24.31 (C-1), 27.30 (6β-CH_3), 28.02 (C-25), 28.27 (CH_2), 33.93 (C-2), 34.54 (C-14), 35.79 (C-20), 36.16 (CH_2), 39.51 (CH_2), 40.08 (C-12), 42.46 (C-5), 42.77 (C-13), 44.71 (C-10), 46.29 (C-7), 47.97 (C-9), 56.28 (C-17),56.29 (C-8), 69.90 (C-6); MS (EI) m/z (%) 400 (40, M^+).

[6-^{2}H]-3β-[(Bromomercurio)methyl]-A,B-bisnor-5β-cholestane-5-carbaldehyde (9). Mercury(II) nitrate monohydrate (2.2 g; 6.421 mmol) was added to a stirred solution of deuterated cyclopropyl alcohol **6** (2.48 g; 6.397 mmol) in DME (30 mL) and acetonitrile (75 mL), then the mixture was stirred for 1.5 h and worked up by adding 10% aqueous KBr solution (20 mL) and ether (70 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 50 mL) and H_2O (50 mL); then it was dried and the solvent evaporated. The crude product was recrystalized from a mixture of $CHCl_3$ and EtOH (3:2), which yielded pure **9** (3.92 g; 5.876 mmol; 92%): mp 148−150 °C (148−149.5 °C for the nondeuterated compound); IR (CH_2Cl_2) ν(C=O) 1700 cm^{-1}; ^{1}H NMR (300 MHz, CD_2Cl_2) δ 0.62 (s, 3 H, 18-H), 0.858 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.862 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.92 (d, J = 6.5 Hz, 3 H, 21-H), 0.94 (s, 3 H, 19-H), 2.44 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.1 Hz, $J_{7\beta-H,8\beta-H}$ = 6.8 Hz, 1 H, 7β-H); ^{13}C NMR (75.47 MHz, CD_2Cl_2) δ 12.33 (C-18), 18.92 (C-21), 19.79 (C-19), 21.47 (CH_2), 22.69 (C-26 or C-27), 22.93 (C-26 or C-27), 24.22 (CH_2), 24.73 (CH_2), 28.38 (C-25), 28.83 (C-11), 35.09 (C-4), 36.03 (C-20), 36.59 (C-22), 37.03 (C-7), 39.15 (C-2), 39.71 (C-1), 39.83 (C-12 or C-24), 39.90 (C-12 or C-24), 44. 05 (C-13), 44.67 (C-8), 53.34 (C-3), 56.08 (C-17), 57.12 (C-14), 58.41 (C-10), 59.52 (C-9), 70.84 (C-5), 206.07 (t, C-6); MS (CI) m/z (%) 685 (1, $[M + NH_4]^+$), 405 (100).

5-Acetyl-3β-[(bromomercurio)methyl]-A,B-bisnor-5β-cholestane (10). Method A. Mercury(II) nitrate monohydrate (130 mg; 379 μmol) was added to a stirred solution of **7** (150 mg; 374 μmol) in DME (6 mL) and acetonitrile (12 mL); then the mixture was stirred at room temperature. After 2 h 10% aqueous KBr solution (5 mL) was added, followed by ether (40 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 20 mL) and H_2O (20 mL) and then dried and the solvent removed. Purification by column chromatography using a petroleum ether−ether mixture (24:1) as the eluent furnished 120 mg of a single product by TLC. Mass spectrum showed the presence of the required molecular ion; however, ^{13}C NMR indicated the presence of additional species, which could not be separated, therefore an alternative route was used to obtain a pure sample of **10**.

Method B. To a stirred solution of methyl mercurial **27** (165 mg; 268 μmol) in DME (10 mL) was added mercuric bromide (98 mg; 286 μmol) and the resulting mixture was stirred at room temperature for 2 h. Then the reaction was diluted with water (5 mL) and ether (40 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (20 mL) and H_2O (2 × 20 mL) and then dried and the solvent evaporated. The aqueous phase was treated with an excess of solid $NaBH_4$ to reduce CH_3HgBr formed as byproduct; the excess of $NaBH_4$ was then decomposed with acetone. The crude product was chromatographed by elution with a petroleum ether−acetone mixture (97:3), which furnished amorphous **10** (149 mg; 220 μmol; 82%): $[\alpha]_D$ +45.6 (*c* 4.1); IR ν_{max}(C=O) 1684 cm^{-1}; ^{1}H NMR δ 0.65 (s, 3 H, 18-H), 0.862 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.866 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.89 (s, 3 H, 19-H), 0.92 (d, J = 6.6 Hz, 3 H, 21-H), 2.13 (s, 3 H, COCH_3); ^{13}C NMR δ 12.29 (C-18), 18.71 (C-21), 9.89 (C-19), 21.48 (CH_2), 22.51 (C-26 or C-27), 22.76 (C-26 or C-27), 23.83 (CH_2), 24.41 (CH_2), 27.94 (CH), 28.47 (CH_2), 31.99 (COCH_3), 35.04 (CH_2), 35.60 (CH), 36.17 (CH_2), 37.94 (CH_2), 38.16 (CH_2), 39.43 (CH_2), 39.55 (CH_2), 40.02 (CH_2), 43.91 (C-13), 43.37 (CH), 55.25 (CH), 55.64 (CH), 56.97 (CH), 57.68 (CH), 59.40 (C-10), 73.52 (C-5), 213.28 (C-6); MS (CI) m/z (%) 698 (5.6, $[M + NH_4]^+$), 399(100).

4a-Oxa-A-bishomo-B-nor-3α,5-cyclo-5α-cholestan-6α-ol (11). Method A.[16] Thallium(III) nitrate trihydrate (190 mg; 428 μmol) was added to a solution of cyclopropyl alcohol **3** (165 mg; 427 μmol) in dioxane (20 mL) containing 2 drops of 10% aqueous $HClO_4$ and the solution was stirred at room temperature for 5 h. A 10% aqueous $HClO_4$ solution (5 mL) was then added and the mixture was stirred for a further 5 h, then diluted with ether (20 mL), and worked up. The crude product was chromatographed by elution with a petroleum ether−ether mixture (9:1), to afford lactol **11** (103 mg; 256 μmol; 66%), identical to an authentic sample:[21,26] mp 156−158 °C (acetone); IR ν_{max}(OH) 3620 and 3395 cm^{-1}; ^{1}H NMR δ 0.64 (s, 3 H, 18-H), 0.865 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.867 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.91 (s, 3 H, 19-H), 2.27 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.8 Hz, $J_{7\beta-H,8\beta-H}$ = 6.0 Hz, 1 H, 7β-H), 2.40 (m, 1 H, 3α-H), 2.76 (s, 1 H, 6α-OH), 3.41 (dd, $J_{4\alpha-H,4\beta-H}$ = 8.7 Hz, $J_{3\alpha-H,4\beta-H}$ = 4.7 Hz, 1 H, 4β-H), 4.18 (dd, $J_{4\alpha-H,4\beta-H}$ = 8.7 Hz, $J_{3\alpha-H,4\alpha-H}$ = 9.1 Hz, 1 H, 4α-H), 5.18 (s, 1 H, 6β-H); ^{13}C NMR δ 12.22 (C-18), 18.53 (CH_3), 18.76 (CH_3), 22.19 (CH_2), 22.54 (C-26 or C-27), 22.80 (C-26 or C-27), 23.82 (CH_2), 24.48 (CH_2), 27.98 (CH), 28.45 (CH_2), 28.56 (CH_2), 35.65 (CH), 36.08 (CH_2), 36.21 (CH_2), 37.88 (CH_2), 39.47 (CH_2), 39.73 (CH_2), 40.92 (CH), 43.67 (C-13), 49.24 (CH), 53.03 (C-10), 55.08 (CH), 55.67 (CH), 56.56

(CH), 66.46 (C-5), 71.93 (C-4), 101.17 (C-6); MS (EI) *m/z* (%) 402 (18, M^+).

Method B.[22] Lithium chloride (23 mg; 542 μmol) was added to a solution of palladium(II) chloride (2.4 mg; 5 mol %) in DME (10 mL) and H_2O (2 drops) and the mixture was stirred at room temperature for 15 min. Copper(II) chloride (228 mg; 1.337 mmol) was then added and the mixture was stirred for an additional 15 min. Then a solution of bromomercurio aldehyde **8** (180 mg; 270 μmol) in DME (2 mL) was added and the mixture was stirred at room temperature for 12 h. The solution was diluted with ether (15 mL), washed with H_2O (5 × 10 mL) and saturated aqueous $NaHCO_3$ solution (10 mL), and dried with $MgSO_4$. The solvent was evaporated and the product chromatographed by elution with a petroleum ether−ether mixture (9:1) to produce lactol **11** (95 mg; 236 μmol; 87%), identical to the compound prepared by Method A.

5-(Hydroxymethyl)-3β-methyl-A,B-bisnor-5β-cholestane (12).[22] Oxidative demercuration (for the method, see below) of bromomercurial **8** furnished alcohol **12** (2%), identical with an authentic sample:[22] IR ν_{max}(OH) 3615, 3455 cm^{-1}; ^1H NMR δ 0.63 (s, 3 H, 18-H), 0.85 (s, 3 H, 19-H), 0.86 (d, J = 6.9 Hz, 6 H, 26-H and 27-H), 0.99 (d, J = 6.9 Hz, 3 H, 4-H), 3.42 and 3.66 (AB system, J = 10.7 Hz, 2 H, 6-H); ^{13}C NMR δ 12.66 (C-18), 16.39 (C-4), 19.17 (CH_3), 19.33 (CH_3), 22.49 (CH_2), 22.98 (C-26 or C-27), 23.23 (C-26 or C-27), 24.27 (CH_2), 24.97 (CH_2), 28.41 (CH), 29.01 (CH_2), 31.42 (CH_2), 36.10 (CH), 36.65 (CH_2), 38.97 (CH_2), 39.91 (CH_2), 40.32 (CH_2), 40.77 (CH), 41.57 (CH_2), 43.20 (CH), 44.16 (C-13), 52.05 (C-10), 56.16 (CH), 56.76 (CH), 58.11 (C-5), 58.14 (CH), 65.12 (C-6); MS (EI) *m/z* (%) 389 (30), 388 (100).

4a-Oxa-A-bishomo-B-nor-3α,5-cyclo-5α-cholestan-6-one (13).[26] Jones reagent (0.25 mL; 2.67 M) was added to a solution of lactol **11** (146 mg; 363 μmol) in acetone (15 mL) and the mixture was stirred for 15 min at room temperature. Methanol (5 mL) and ether (50 mL) were then added, the mixture was stirred for 5 min, and the ethereal layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 20 mL) and H_2O (2 × 20 mL). The solvent was dried and evaporated yielding lactone **13** (143 mg; 357 μmol; 98%): mp 137−139 °C (authentic sample[26] had mp 139−141 °C); IR ν_{max}(C=O) 1758 cm^{-1}; ^1H NMR δ 0.66 (18-H), 0.862 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.866 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.92 (d, J = 6.6 Hz, 3 H, 21-H), 0.98 (s, 3 H, 19-H), 2.26 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.3 Hz, $J_{7\beta-H,8\beta-H}$ = 6.0 Hz, 1 H, 7β-H), 2.73 (m, 1 H, 3α-H), 3.76 (t, J = 9.4 Hz, 1 H, 4-H) 4.31 (t, J = 9.4 Hz, 1 H, 4-H); ^{13}C NMR δ 12.28 (C-18), 18.77 (C-19), 20.83 (C-21), 22.12 (CH_2), 22.57 (C-26 or C-27), 22.82 (C-26 or C-27), 23.86 (CH_2), 24.32 (CH_2), 27.53 (CH_2), 28.00 (CH), 28.54 (CH_2), 35.62 (CH), 36.22 (CH_2), 36.38 (CH_2), 39.48 (CH_2), 39.52 (CH_2), 41.73 (CH_2), 41.90 (CH), 43.81 (C-13), 49.12 (CH), 54.96 (CH), 55.70 (CH), 56.53 (CH), 58.04 (C-10), 62.16 (C-5), 69.29 (C-4), 182.15 (C-6); MS (EI) *m/z* (%) 400 (2, M^+).

A,B-Bisnor-5β-cholestan-3β-[(methylmercurio)methyl]-5-carbaldehyde (14). Methyllithium (1.4 M in ether; 1.3 mL; 1.820 mmol) was added to a suspension of copper(I) iodide (355 mg; 1.864 mmol) in dry ether (30 mL) at −35 °C. The resulting mixture was stirred at −35 °C for 10 min and then cooled to −78 °C. A solution of organomercurial **8** (250 mg; 375 μmol) in THF (5 mL) was added and the mixture was stirred for a further 5 min. The excess reagent was decomposed by addition of 5% aqueous HCl solution (10 mL); then the mixture was diluted with ether (20 mL) and allowed to warm to room temperature. The organic layer was separated and washed with saturated aqueous $NaHCO_3$ solution (2 × 15 mL) and H_2O (2 × 15 mL) and then dried and the solvent evaporated yielding oily methylmercurial **14** (221 mg; 368 μmol; 98%), which was identical to an authentic sample:[21] IR ν_{max}(C=O) 1710 cm^{-1}; ^1H NMR δ 0.28 (s (83%) and d (17%), $J_{H,Hg}$ = 101.0 Hz, 3 H, $HgCH_3$), 0.59 (s, 3 H, 18-H), 0.86 (d, J = 6.9 Hz, 6 H, 26-H and 27-H), 0.91 (s, 3 H, 19-H), 2.36 (m, 1 H, 3α-H), 2.50 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.1 Hz, $J_{7\beta-H,8\beta-H}$ = 6.8 Hz, 1 H, 7β-H), 9.77 (s, 1 H, 6-H); ^{13}C NMR δ 12.19 (C-18), 18.76 (C-21), 19.57 (C-19), 20.97 ($HgCH_3$), 21.08 (CH_2), 22.55 (C-26 or C-27), 22.80 (C-26 or C-27), 23.85 (CH_2), 24.37 (CH_2), 27.97 (C-25), 28.49 (C-11), 35.63 (CH), 36.21 (CH_2), 36.48 (CH_2), 39.45 (CH_2),39.59 (CH_2), 39.71 (CH_2), 39.89 (CH_2), 42.24 (CH_2), 43.67 (C-13), 44.04 (C-8), 54.37 (CH), 55.74 (CH), 56.88 (CH), 57.36 (C-10), 59.45 (C-14), 71.56 (C-5), 207.26 (C-6); MS (EI) *m/z* (%) 587 (1, $M^+ - CH_3$), 385 (100); MS (CI) *m/z* (%) 621 (0.1, $[M + NH_4]^+$), 603 (1.3, MH^+).

[6-^{2}H]-3β-[(Methylmercurio)methyl]-A,B-bisnor-5β-cholestane-5-carbaldehyde (15). Methyllithium (1.4 M in ether; 1.7 mL; 2.365 mmol) was added to a suspension of copper(I) iodide (450 mg; 2.365 mmol) in dry ether (30 mL) at −35 °C. The resulting mixture was stirred at −35 °C for 10 min and then it was cooled to −78 °C. A solution of organomercurial **9** (312 mg; 468 μmol) in THF (5 mL) was added and the mixture was stirred for a further 5 min. The excess reagent was decomposed by addition of 5% aqueous HCl solution (5 mL); then the mixture was diluted with ether (20 mL) and allowed to warm to room temperature. The organic layer was separated and washed with saturated aqueous $NaHCO_3$ solution (2 × 15 mL) and H_2O (2 × 15 mL) and then dried and the solvent evaporated yielding oily methylmercurial **15** (270 mg; 449 μmol; 96%): IR ν_{max}(C=O) 1707 cm^{-1}; ^1H NMR (250 MHz) δ 0.28 (s (83%) and d (17%), $J_{H,Hg}$ = 101.0 Hz, 3 H, $HgCH_3$), 0.59 (s, 3 H, 18-H), 0.855 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.857 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.89 (s, 3 H, 19-H), 2.35 (m, 1 H, 3α-H), 2.45 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.1 Hz, $J_{7\beta-H,8\beta-H}$ = 6.8 Hz, 1 H, 7β-H); ^{13}C NMR (62.90 MHz) δ 12.18 (C-18), 18.74 (C-21), 19.55 (C-19), 20.97 ($HgCH_3$), 21.06 (CH_2), 22.54 (C-26 or C-27), 22.79 (C-26 or C-27), 23.83 (CH_2), 24.36 (CH_2), 27.96 (C-25), 28.47 (C-11), 35.61 (CH), 36.19 (CH_2), 36.39 (CH_2), 39.43 (CH_2), 39.56 (CH_2), 39.71 (CH_2), 39.89 (CH_2), 42.24 (CH_2), 43.65 (C-13), 44.00 (C-8), 54.33 (CH), 55.72 (CH), 56.85 (CH), 57.31 (C-10), 59.44 (C-14), 71.38 (C-5), 206.91 (t, C-6); MS (EI) *m/z* (%) 602 (0.2, M^+), 386 (100), 368 (11); MS (CI) *m/z* (%) 621 (4, $[M + NH_4]^+$).

5-(Hydroxymethyl)-3β-[(methylmercurio)methyl]-A,B-bisnor-5β-cholestane (16). Method A. Sodium borohydride (50 mg; 1.322 mmol) was added to a cooled (0 °C) stirred solution of aldehyde **14** (161 mg; 268 μmol) in ether (5 mL) and methanol (20 mL). The mixture was allowed to warm to room temperature and was stirred for 5 h. Then the excess reagent was decomposed with 10% aqueous HCl solution (5 mL) and the mixture was diluted with petroleum ether (40 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 20 mL) and H_2O (2 × 20 mL) and then dried and the solvent removed under vacuum, to afford amorphous **16** (144 mg; 239 μmol; 89%): $[\alpha]_D$ +14.5 (*c* 2.5), identical to an authentic sample with $[\alpha]_D$ +14 (*c* 2.5):[33] IR ν_{max}(OH) 3628 cm^{-1}; ^1H NMR (300 MHz) δ 0.25 (s (85%) and d (15%), $J_{H,Hg}$ = 96.8 Hz, 3 H, $HgCH_3$), 0.62 (s, 3 H, 18-H), 0.861 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.865 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.89 (s, 3 H, 19-H), 0.91 (d, J = 6.6 Hz, 3 H, 21-H), 3.52 and 3.73 (AB system, J = 10.9 Hz, 2 H, 6-H); ^{13}C NMR (75.47 MHz) δ 12.30 (C-18), 18.77 (C-21), 19.07 (C-19), 21.59 ($HgCH_3$), 21.83 (CH_2), 22.56 (C-26 or C-27), 22.81 (C-26 or C-27), 23.85 (CH_2), 24.53 (CH_2), 27.99 (CH), 28.58 (CH_2), 35.67 (CH), 35.81 (CH_2), 36.24 (CH_2), 38.71 (CH_2), 39.49 (CH_2), 39.90 (CH_2), 40.87 (CH_2), 41.28 (CH), 43.41 (CH_2), 43.79 (C-13), 49.58 (CH), 52.19 (C-10), 55.74 (CH), 56.66 (CH), 58.28 (CH), 59.96 (C-5), 64.96 (C-6); MS (EI) *m/z* (%) 604 (1.1, M^+), 369 (100).

Method B. L-Selectride (1 M in THF; 0.1 mL; 100 μmol) was added to a solution of aldehyde **14** (35 mg; 58 μmol) in ether (10 mL) at −78 °C. After stirring for 30 min the excess reagent was decomposed with H_2O. The mixture was treated with 30% aqueous H_2O_2 solution (0.25 mL) and 25% aqueous KOH solution (0.15 mL) and stirred for 2 h at 0 °C. Then ether (25 mL) and H_2O (5 mL) were added and the ethereal layer was separated. It was washed with 5% aqueous HCl solution (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and H_2O (2 × 10 mL), and the solvent was evaporated to yield **16** (31 mg; 51 μmol; 89%), identical to a sample prepared by method A.

(6*R*)-[6-^{2}H]-5-(Hydroxymethyl)-3β-[(methylmercurio)-methyl]-A,B-bisnor-5β-cholestane (17). Method A. A solution of *tert*-butyl alcohol (542 mg; 7.301 mmol) in ether (10 mL) was added dropwise to a stirred solution of lithium aluminum deuteride (99 mg; 2.357 mmol) in ether (15 mL), at

−78 °C. The mixture was allowed to warm to room temperature and was stirred for 1 h. Then it was cooled to −78 °C and a solution of methyl mercurio aldehyde **14** (140 mg; 232.8 μmol) in ether (5 mL) was added and the reaction mixture was stirred for 30 min at the same temperature. After this time, the excess reagent was quenched by addition of saturated aqueous NH_4Cl solution (5 mL). The white precipitate was filtered off and the organic layer worked up to furnish amorphous **17** as the major epimer (85% rel.), which was isolated along with minor epimer **18** (126 mg; 209 μmol; 90%; total yield). The major epimer **17** was characterized in the presence of **18**: IR ν_{max}(OH) 3620 and 3460 cm^{-1}; ^1H NMR (250 MHz) δ 0.25 (s (83%) and d (17%), $J_{H,Hg}$ = 97.5 Hz, 3 H, $HgCH_3$), 0.62 (s, 3 H, 18-H), 0.861 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.865 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.90 (s, 3 H, 19-H), 3.50 (s, 6-H); ^{13}C NMR (62.90 MHz) δ 12.26 (C-18), 18.75 (CH_3), 19.06 (CH_3), 21.58 ($HgCH_3$), 21.82 (CH_2), 22.56 (C-26 or C-27), 22.81 (C-26 or C-27), 23.84 (CH_2), 24.53 (CH_2), 27.98 (CH), 28.57 (CH_2), 35.67 (CH), 35.76 (CH_2), 36.23 (CH_2), 38.70 (CH_2), 39.48 (CH_2), 39.89 (CH_2), 40.83 (CH_2), 41.25 (CH), 43.42 (CH_2), 43.78 (C-13), 49.49 (CH), 52.15 (C-10), 55.73 (CH), 56.64 (CH), 58.26 (CH), 59.90 (C-5), 64.66 (t, C-6); MS (EI) m/z (%) 605 (0.5, M^+), 370 (100).

Method B. Super Deuteride (1 M in THF; 0.2 mL; 200 μmol) was added to a solution of methyl mercurio aldehyde **14** (80 mg; 133 μmol) in THF (20 mL) at −78 °C. The mixture was stirred for 10 min; then the excess reagent was decomposed by adding H_2O (0.5 mL). The reaction was completed by addition of 30% aqueous H_2O_2 solution (0.6 mL) and 25% aqueous KOH solution (0.4 mL), followed by stirring for 3 h. Then the mixture was diluted with ether (40 mL) and worked up to afford amorphous **17** as the major epimer (87% rel.), which was isolated with minor epimer **18** (73 mg; 121 μmol; 91%; total yield). The major epimer **17** characterized in the presence of **18**: ^1H NMR (250 MHz) δ 0.25 (s (82%), d (18%), $J_{H,Hg}$ = 97.8 Hz, 3 H, $HgCH_3$), 0.62 (s, 3 H, 18-H), 0.861 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.864 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.91 (s, 3 H, 19-H), 3.52 (s, 6-H).

(6*S*)-[6-^{2}H]-5-(Hydroxymethyl)-3*β*-[(methylmercurio)-methyl]-A,B-bisnor-5*β*-cholestane (18). A solution of *tert*-butyl alcohol (185 mg; 2.491 mmol) in ether (20 mL) was added dropwise to a stirred solution of lithium aluminum hydride (31.5 mg; 830 μmol) in ether (15 mL), at −78 °C. The mixture was allowed to warm to room temperature and was stirred for 1 h. Then it was cooled to −78 °C and a solution of methyl mercurio aldehyde **15** (57 mg; 95 μmol) in ether (5 mL) was added and the reaction mixture was stirred for 30 min at the same temperature. After this time, the excess reagent was quenched by addition of saturated aqueous NH_4Cl solution (5 mL). The white precipitate was filtered off and the organic layer worked up to furnish amorphous **18** as the major epimer (84% rel.), which was isolated with minor epimer **17** (52 mg; 86 μmol; 91%; total yield). The major epimer **18** was characterized in the presence of **17**: ^1H NMR (250 MHz) δ 0.25 (s (83%) and d (17%), $J_{H,Hg}$ = 97.5 Hz, 3 H, $HgCH_3$), 0.61 (s, 3 H, 18-H), 0.861 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.865 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.90 (s, 3 H, 19-H), 3.71 (s, 6-H).

(6*S*)-[6-^{2}H]-3*β*-[(Bromomercurio)methyl]-5-(hydroxymethyl)-A,B-bisnor-5*β*-cholestane (19). Mercuric bromide (51 mg; 142 μmol) was added to a stirred solution of **18** (82 mg; 136 μmol) in DME (10 mL). The reaction mixture was stirred at room temperature for 2 h and then diluted with ether (40 mL) and H_2O (15 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 20 mL) and H_2O (20 mL), then the solution was dried and evaporated, to furnish **19** as the major epimer (81%), isolated along with the minor epimer **21** (82.4 mg; 123 μmol; 91%; total yield): mp 153−155 °C ($CHCl_3$/MeOH) (154−156 °C for the nondeuterated compound); ^1H NMR (250 MHz, CD_2Cl_2) δ 0.63 (s, 3 H, 18-H), 0.856 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.860 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.90 (s, 3 H, 19-H), 3.69 (s, 6-H). The aqueous phase from the workup was treated with an excess of solid $NaBH_4$ to reduce CH_3HgBr formed as byproduct; the excess of $NaBH_4$ was then decomposed with acetone.

3*β*-[(Bromomercurio)methyl]-5-(hydroxymethyl)-A,B-bisnor-5*β*-cholestane (20). Mercuric bromide (48 mg; 133 μmol) was added to a stirred solution of **16** (80 mg; 133 μmol) in DME (10 mL). The mixture was stirred for 2 h, then diluted with ether (40 mL), and quenched with H_2O (15 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 20 mL) and H_2O (20 mL) and then dried and the solvent removed. The aqueous phase was treated with an excess of solid $NaBH_4$ to reduce CH_3HgBr formed as byproduct; the excess of $NaBH_4$ was then decomposed with acetone. The organic crude product was chromatographed with a petroleum ether−ether mixture (19:1) as the eluent, which afforded **20** (80 mg; 120 μmol; 90%): mp 154−156 °C ($CHCl_3$/MeOH); $[\alpha]_D$ +24.6 (*c* 1.1, CH_2Cl_2); IR (CH_2Cl_2) ν(OH) 3610 and 3480 cm^{-1}; ^1H NMR (300 MHz, CD_2Cl_2) δ 0.63 (s, 3 H, 18-H), 0.857 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.860 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.90 (s, 3 H, 19-H), 3.54 and 3.71 (AB system, J = 10.7 Hz, 2 H, 6-H); ^{13}C NMR (62.90 MHz, CD_2Cl_2) δ 12.39 (C-18), 18.87 (C-21), 19.04 (C-19), 22.83 (CH_2), 22.67 (C-26 or C-27), 22.91 (C-26 or C-27), 23.98 (CH_2), 24.63 (CH_2), 28.09 (CH), 28.64 (CH_2), 35.77 (CH), 35.98 (CH_2), 36.33 (CH_2), 36.67 (CH_2), 38.53 (CH_2), 39.59 (CH_2), 39.88 (CH_2), 40.98 (CH_2), 41.29 (CH), 43.89 (C-13), 49.67 (CH), 52.73 (C-10), 55.84 (CH), 56.60 (CH), 58.31 (CH), 58 69 (C-5), 64.27 (C-6); MS (CI) m/z (%) 686 (0.4, $[M + NH_4]^+$), 656 (0.2), 404 (77), 388 (77), 371 (46), 358 (85), 341 (21), 247 (40), 231 (50), 203 (48).

(6*R*)-[6-^{2}H]-3*β*-[(Bromomercurio)methyl]-5-(hydroxymethyl)-A,B-bisnor-5*β*-cholestane (21). Mercuric bromide (415 mg; 1.151 mmol) was added to a stirred solution of **17** (679 mg; 1.124 mmol) in DME (25 mL). The mixture was stirred at room temperature for 2 h and then diluted with ether (60 mL) and H_2O (20 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 30 mL) and H_2O (30 mL) then the solution was dried and evaporated. The crude product was chromatographed using a petroleum ether−ether mixture (19:1) as the eluent, which afforded **21** as the major epimer (82% rel.), isolated along with the minor epimer **19** (689 mg; 1.030 mmol; 89%; total yield). The major epimer **21** characterized in the presence of **19**: mp 152−154 °C ($CHCl_3$/MeOH) (154−156 °C for the nondeuterated compound); IR (CH_2Cl_2) ν(O−H) 3600 and 3470 cm^{-1}; ^1H NMR (250 MHz, CD_2Cl_2) δ 0.63 (s, 3 H, 18-H), 0.857 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.861 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.90 (s, 3 H, 19-H), 3.52 (s, 6-H); ^{13}C NMR (62.90 MHz, CD_2Cl_2) δ 12.39 (C-18), 18.94 (C-21), 19.08 (C-19), 22.13 (CH_2), 22.71 (C-26 or C-27) 22.96 (C-26 or C-27), 24.23 (CH_2), 24.87 (CH_2), 28.42 (CH), 28.93 (CH_2), 36.06 (CH_2), 36.10 (CH), 36.63 (2 CH_2), 38.80 (CH_2), 39.88 (CH_2), 40.24 (CH_2), 41.22 (CH_2), 41.49 (CH_2), 41.49 (CH), 44.16 (C-13), 49.84 (CH), 52.88 (C-10), 56.14 (CH), 56.91 (CH), 58.57 (CH), 58.89 (C-5), 64.06 (t, C-6); MS (CI) m/z (%) 687 (3, $[M + NH_4]^+$), 405 (100). The aqueous phase from the workup was treated with an excess of solid $NaBH_4$ to reduce CH_3HgBr formed as byproduct; the excess of $NaBH_4$ was then decomposed with acetone.

4a-Oxa-A-bishomo-B-nor-3α,5-cyclo-5α-cholestane (22). A solution of bromine (0.5 M in chloroform; 0.3 mL; 150 μmol) was added to a solution of bromomercurio alcohol **20** (70 mg; 105 μmol) in DME (10 mL) at 0 °C. The mixture was allowed to warm to room temperature and was stirred for 5 h. After that time, the TLC analysis showed the reaction to be complete hence the excess reagent was decomposed by addition of saturated aqueous sodium thiosulfate solution (5 mL). Extraction of the product with ether (25 mL) followed by the workup and removal of the solvent gave the crude product, which was recrystalized from a mixture of chloroform and methanol to yield pure **22** (35 mg; 91 μmol; 86%): mp 106−108 °C ($CHCl_3$/MeOH); $[\alpha]_D$ +37.1 (*c* 10); ^1H NMR (400 MHz) δ 0.65 (s, 3 H, 18-H), 0.876 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.880 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.91 (s, 3 H, 19-H), 0.94 (d, J = 6.5 Hz, 3 H, 21-H), 1.06 (m, 1 H, 12*β*-H), 1.25 (m, 1 H, 7α-H), 1.71 (m, 1 H, 7*β*-H), 2.04 (m, 1 H, 12α-H), 2.26 (m, 1 H, 3α-H), 3.38 (d, J = 9.1 Hz, 1 H, 6α-H), 3.43 (dd, $J_{4\alpha-H,4\beta-H}$ = 8.9 Hz, $J_{3\alpha-H,4\beta-H}$ = 4.8 Hz, 1 H, 4*β*-H), 3.92 (t, J = 8.9 Hz, 1 H, 4α-H), 3.97 (d, J = 9.1 Hz, 1 H, 6*β*-H); NOE: 2.26 (3-H) ↔ 1.25 (7α-H), 3.38 (6α-H), 3.92 (4α-H), 2-H and 3.43 (4*β*-H), 3.38 (6α-

H) ↔ 1.71 (7β-H), 1.25 (7α-H) and 0.91 (19-H), 3.43 (4β-H) ↔ 2-H, 2.26 (3-H), 3.92 (4α-H) ↔ 2.26 (3-H), 3.97 (6β-H) ↔ 2-H and 0.91 (19-H); ^{13}C NMR (100.60 MHz) δ 12.25 (C-18), 18.44 (C-19), 18.78 (C-21), 22.11 (C-11), 22.57 (C-26 or C-27), 22.82 (C-26 or C-27), 23.86 (CH_2), 24.53 (CH_2), 28.00 (C-25), 28.55 (2 × CH_2), 35.67 (C-20), 36.25 (CH_2), 37.01 (C-1), 39.50 (C-24), 39.78 (C-12), 41.04 (C-7), 41.19 (C-8), 43.75 (C-13), 52.56 (C-10), 53.26 (C-3), 54.94 (C-9), 55.71 (C-17), 56.67 (C-14), 62.75 (C-5), 74.59 (C-4), 76.43 (C-6); MS (EI) *m*/*z* (%) 387 (30), 386 (100, M^+), 246 (12), 237 (29), 231 (89); MS (CI) *m*/*z* 404 ($[M + NH_4]^+$).

[6β-^{2}H]-4a-Oxa-A-bishomo-B-nor-3α,5-cyclo-5α-cholestane (23). Bromine (0.5 M in chloroform; 0.4 mL; 200 μmol) was added to a solution of bromomercurio alcohol **21** (110 mg; 164 μmol) in DME (10 mL), at 0 °C and the mixture was warmed to room temperature and then stirred for 5 h. The excess reagent was decomposed by addition of saturated aqueous sodium thiosulfate solution (5 mL), the product was extracted with ether (30 mL), and the organic layer was worked up. The crude product was purified by column chromatography, eluting with a petroleum ether−ether mixture (19:1), which furnished deuterated tetrahydrofuran **23** as the major product (76%), isolated in the presence of minor epimer **24**, (57 mg; 147 μmol; 90%; total yield). The major epimer **23** characterized in the presence of **24**: mp 104−107 °C ($CHCl_3$/MeOH) (106−108 °C for the nondeuterated compound); ^{1}H NMR (250 MHz) δ 0.63 (s, 3 H, 18-H), 0.86 (d, J = 6.5 Hz, 6 H, 26-H and 27-H), 0.89 (s, 3 H, 19-H), 0.92 (d, J = 6.6 Hz, 3 H, 21-H), 2.02 (m, 1 H, 12α-H), 2.27 (m, 1 H, 3α-H), 3.43 (dd, $J_{4\alpha-H,4\beta-H}$ = 8.9 Hz, $J_{3\alpha-H,4\beta-H}$ = 4.8 Hz, 1 H, 4β-H), 3.91 (t, J = 8.9 Hz, 1 H, 4α-H), 3.36 (s, 6α-H); ^{13}C NMR (62.90 MHz) δ 12.20 (C-18), 18.39 (C-19), 18.73 (C-21), 22.07 (CH_2), 22.53 (C-26 or C-27), 22.78 (C-26 or C-27), 23.84 (CH_2), 24.49 (CH_2), 27.97 (CH), 28.50 (CH_2), 28.53 (CH_2), 35.66 (CH), 36.23 (CH_2), 36.97 (CH_2), 39.48 (CH_2), 39.76 (CH_2), 40.94 (CH_2), 41.16 (CH), 43.71 (C-13), 52.46 (C-10), 53.20 (CH), 54.91 (CH), 55.70 (CH), 56.65 (CH), 62.61 (C-5), 74.54 (C-4), 75.98 (t, C-6); MS (EI) *m*/*z* (%) 388 (30), 387 (100, M^+); MS > 97% ^{2}H (d_1).

[6α-^{2}H]-4a-Oxa-A-bishomo-B-nor-3α,5-cyclo-5α-cholestane (24). Bromine (0.5 M in chloroform; 0.45 mL; 225 μmol) was added to a solution of bromomercurio alcohol **19** (142 mg; 212 μmol) in DME (10 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 5 h and then the excess reagent was decomposed by addition of saturated aqueous sodium thiosulfate solution (5 mL). The product was extracted with ether (30 mL) and the organic layer worked up. Purification by column chromatography, using a petroleum ether−ether mixture (19:1) as the eluent, furnished **24** as the major product (79%), isolated in the presence of the minor epimer **23** (71 mg; 184 μmol; 87%; total yield). The major epimer **24** was characterized in the presence of **23**: mp 104−106 °C ($CHCl_3$/MeOH) (106−108 °C for the nondeuterated compound); ^{1}H NMR (250 MHz) δ 0.64 (s, 3 H, 18-H), 0.86 (d, J = 6.6 Hz, 6 H, 26-H and 27-H), 0.89 (s, 3 H, 19-H), 0.92 (d, J = 6.6 Hz, 3 H, 21-H), 2.03 (m, 1 H, 12α-H), 2.26 (m, 1 H, 3α-H), 3.43 (dd, $J_{4\alpha-H,4\beta-H}$ = 8.8 Hz, $J_{3\alpha-H,4\beta-H}$ = 4.7 Hz, 1 H, 4β-H), 3.91 (t, J = 8.8 Hz, 1 H, 4α-H), 3.94 (s, 6β-H); MS > 97% ^{2}H (d_1).

5-(Hydroxymethyl)-6ξ-methyl-3β-[(methylmercurio)-methyl]-A,B-bisnor-5β-cholestane (25).[38] A solution of methylmercurio aldehyde **14** (1. 053 g; 1.751 mmol) in ether (50 mL) was added dropwise, over 10 min, to a solution of methyllithium (1.4 M in ether; 1.4 mL; 1.960 mmol) in dry ether (100 mL) at −78 °C. After stirring for 1 min, the mixture was quenched with 5% aqueous HCl solution (10 mL) and allowed to warm to room temperature. The ethereal layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 40 mL) and H_2O (2 × 40 mL) and then dried and the solvent was removed under vacuum. The products were separated by column chromatography, using a petroleum ether−ether mixture (97:3), to furnish methyl mercurio derivative **25** (346 mg; 560 μmol; 32%), as a ∼2:1 mixture of diastereoisomers[38] (which was oxidized to achieve full characterization): IR ν_{max}(OH) 3616 cm^{-1}; ^{1}H NMR for the major diastereoisomer δ 0.28 (s, (83%) and d (17%), $J_{H,Hg}$ = 97.3 Hz, 3 H, $HgCH_3$), 0.64 (s, 3 H, 18-H), 0.88 (d, J = 6.6 Hz, 6 H, 26-H and 27-H), 0.89 (s, 3 H, 19-H), 0.93 (d, J = 6.6 Hz, 3 H, 21-H), 1.37 (d, J = 6.3 Hz, 3 H, CHOHCH_3), 4.04 (m, 1 H, 6-H); ^{13}C NMR for the major isomer δ 12.47 (C-18), 18.78 (C-21), 20.04 (CH_3), 21.76 (CH_3), 22.02 (CH_3), 22.06 (CH_2), 22.57 (C-26 or C-27), 22.81 (C-26 or C-27), 23.85 (CH_2), 24.54 (CH_2), 27.99 (CH), 28.65 (CH_2), 35.68 (CH), 36.27 (CH_2), 38.97 (CH_2), 39.52 (CH_2), 39.91 (CH_2), 40.14 (CH_2), 40.41 (CH_2), 42.04 (CH), 43.79 (CH_2), 43.96 (C-13), 51.29 (CH), 53.44 (C-10), 55.78 (CH), 57.35 (CH), 58.43 (CH), 63.10 (C-5), 71.63 (C-6); MS (EI) *m*/*z* (%) 600 (2.9, M^+ − OH). Cyclobutanol **26** (427 mg; 1.104 mmol; 63%) was isolated as the more polar product by eluting with a petroleum ether−ether mixture (17:3).

A-Homo-B-nor-3α,5-cyclo-5α-cholestan-6α-ol (26).[21] Methyllithium (1.46 M in ether; 0.54 mL; 788 μmol) was added to a suspension of copper(I) iodide (50 mg; 262 μmol) in dry ether (10 mL) under nitrogen at −35 °C. The resulting mixture was stirred at −35 °C for 10 min and then it was cooled to −78 °C. A solution of organomercurial **14** (75 mg; 113 μmol) in THF (2 mL) was added and the mixture was stirred for a further 5 min. The excess reagent was decomposed by addition of 5% aqueous HCl solution (2 mL), and then the mixture was diluted with ether (20 mL) and allowed to warm to room temperature. The organic layer was separated and washed with saturated aqueous $NaHCO_3$ solution (2 × 15 mL) and H_2O (2 × 15 mL) and then dried and the solvent evaporated yielding **26** (42 mg; 109 μmol; 97%): mp 98−99.5 °C (acetone), identical to an authentic sample, which had mp 97−99 °C;[21] IR ν_{max}(OH) 3600 and 3430 cm^{-1}; ^{1}H NMR δ 0.63 (s, 3 H, 18-H), 0.87 (d, J = 6.6 Hz, 6 H, 26-H and 27-H), 0.90 (s, 3 H, 19-H), 2.23 (dd, $J_{7\alpha-H,7\beta-H}$ = 13.4 Hz, $J_{7\beta-H,8\beta-H}$ = 7.8 Hz, 1 H, 7β-H), 2.40 (m, 1 H, 3α-H), 4.16 (dd, J = 5.4 and 4.6 Hz, 1 H, 6β-H); ^{13}C NMR δ 12.28 (C-18), 17.15 (C-19), 18.75 (C-21), 21.82 (CH_2), 22.54 (C-26 or C-27), 22.79 (C-26 or C-27), 23.80 (CH_2), 24.47 (CH_2), 27.98 (CH), 28.54 (CH_2), 28.93 (CH_2), 32.85 (CH_2), 34.93 (CH_2), 35.64 (CH), 36.22 (CH_2), 36.26 (CH_2), 39.48 (CH_2), 39.79 (CH_2), 40.93 (CH), 43.95 (C-13), 45.55 (CH), 53.46 (CH), 53.59 (C-10), 55.70 (CH), 57.05 (CH), 63.79 (C-5), 68.98 (C-6); MS (EI) *m*/*z* (%) 386 (14, M^+), 342 (100).

5-Acetyl-3β-[(methylmercurio)methyl]-A,B-bisnor-5β-cholestane (27). Pyridinium chlorochromate (54 mg; 251 μmol) was added to a solution of methylmercurio derivative **25** (75 mg; 121 μmol) in dichloromethane (10 mL). The mixture was stirred at room temperature for 3 h, then filtered through a Celite pad and the solvent was evaporated. The crude product was flushed through a short chromatography column using a petroleum ether−ether mixture (19:1), which yielded amorphous **27** (70 mg; 114 μmol; 93%): $[\alpha]_D$ +45.3 (*c* 2.5); IR ν_{max}(C=O) 1698 cm^{-1}; ^{1}H NMR δ 0.26 (s (87%) and d (13%), $J_{Hg,H}$ = 100.5 Hz, 3 H, $HgCH_3$), 0.64 (s, 3 H, 18-H), 0.87 (d, J = 6.6 Hz, 3 H, 26-H and 27-H), 0.88 (s, 3 H, 19-H), 2.12 (s, 3 H, COCH_3), 2.42 (m, 1 H, 4-H); ^{13}C NMR δ 12.30 (C-18), 14.14 ($HgCH_3$), 18.72 (C-21), 19.36 (C-19), 21.54 (CH_2), 22.52 (C-26 or C-27), 22.77 (C-26 or C-27), 23.84 (CH_2), 24.41 (CH_2), 27.96 (CH_2), 28.53 (CH_2), 32.00 (COCH_3), 34.25 (CH_2), 35.63 (CH_2), 36.22 (CH_2), 37.64 (CH_2), 38.89 (CH_2), 39.47 (CH_2), 39.76 (2 CH_2), 43.16 (CH), 43.98 (C-13), 50.03 (CH), 55.71 (CH), 57.16 (CH), 57.56 (CH), 57.81 (C-10), 72.82 (C-5), 212.74 (C=O); MS (EI) *m*/*z* (%) 616 (0.3, M^+), 345 (100).

3β,5-Bis(hydroxymethyl)-A,B-bisnor-5β-cholestane (28). Method A. Organomercurial **8** (1.494 g; 2.243 mmol) was placed in a Dreschler bottle and dissolved in DMF (45 mL). A septum was fixed to the bottle and one large bore needle was used as a vent. Three syringe needles were extended to the base of the container and were used to pass oxygen through the mixture for 10 min, maintaining a pressure of 8 lb/in^2. A mixture of sodium borohydride (270 mg; 7.137 mmol) and DMF (31 mL) was then added dropwise, over a period of 10 min. Oxygen was bubbled through the mixture during this time and for an additional 5 min after the addition of the sodium borohydride mixture. The oxygen supply was then turned off and the reaction quenched with H_2O (5 mL). Allowing the mixture to stand facilitated precipitation of elemental mercury, which was then separated from the solution by decantation. (If the mercury did not drop out of solution, the mixture was centrifuged.) Ether (60 mL) and 15% aqueous NaCl solution

(30 mL) were added to the supernatant and the organic layer was separated. The ethereal layer was washed with saturated aqueous $NaHCO_3$ (30 mL) and 15% aqueous NaCl solution (2 × 30 mL) and then the solution was dried and the crude product chromatographed. Elution with a petroleum ether−ether mixture (23:2) yielded alcohol **12** (17 mg; 44 μmol; 2%) as the least polar component. A petroleum ether−ether mixture (4:1) eluted lactol **11** (334 mg; 829 μmol; 37%), identical with an authentic sample. Finally, elution with a petroleum ether−ether−acetone mixture (8:1:1) furnished diol **28** (445 mg; 1.100 mmol; 49%): mp 145−146.5 °C (acetone); $[\alpha]_D$ +16.8 (*c* 1.5); IR ν_{max}(OH) 3610 and 3420, ν_{max}(C−O) 1040 cm^{-1}; ^1H NMR δ 0.63 (s, 3 H, 18-H), 0.83 (s, 3 H, 19-H), 0.86 (d, J = 6.6 Hz, 6 H, 26-H and 27-H), 0.89 (d, J = 6.6 Hz, 3 H, 21-H), 3.05 (br s, 2 H, OH), 3.38 and 3.83 (AB system, $J_{6\text{-H},6\text{-H}'}$ = 11.0 Hz, 2 H, 6-H, 6-H′), 3.62 and 3.79 (ABX system, $J_{4\text{-H},4\text{-H}'}$ = 11.2 Hz, $J_{3\alpha-\text{H},4-\text{H}}$ = 3.6 Hz, 2 H, 4-H, 4-H′); ^{13}C NMR δ 12.22 (C-18), 18.61 (C-19), 18.74 (C-21), 21.94 (CH_2), 22.53 (C-26 or C-27), 22.79 (C-26 or C-27), 23.83 (CH_2), 24.51 (CH_2), 27.54 (CH_2), 27.98 (CH), 28.56 (CH_2), 35.65 (CH), 36.20 (CH_2), 39.45 (CH_2), 39.46 (CH_2), 39.79 (CH_2), 40.39 (CH), 42.06 (CH_2), 43.69 (C-13), 51.73 (CH), 52.13 (C-10), 55.79 (CH), 56.32 (CH), 57.83 (CH), 57.86 (C-5), 64.14 (C-4 or C-6), 64.97 (C-4 or C-6); MS (EI) *m*/*z* (%) 404 (2, M^+), 386 (100).

Method B. Bromomercurio alcohol **20** (712 mg; 1.066 mmol) was dissolved in DMF (21 mL) and the solution was saturated with oxygen. A mixture of sodium borohydride (56 mg; 1.480 mmol) and DMF (7 mL) was added dropwise, over a period of 10 min, and the mixture was worked up. The crude product was purified by chromatography using a petroleum ether−ether mixture (4:1) to elute alcohol **12** (8 mg; 21 μmol; 2%), as the least polar component. Elution with a petroleum ether−ether−acetone mixture (8:1:1) furnished diol **28** (362 mg; 895 μmol; 84%).

Method C. A solution of lactone **13** (60 mg; 150 μmol) in ether (10 mL) was added to lithium aluminum hydride (11 mg; 295 μmol) in ether (15 mL) at 0 °C. The mixture was stirred at room temperature for 45 min and then worked up. The solvent was removed yielding diol **28** (54 mg; 134 μmol; 89%), which was identical to a sample prepared by oxidative demercuration.

4a-Oxa-A-bishomo-B-nor-3α,5-cyclo-5α-cholestan-4α-ol (29). *o*-Iodoxybenzoic acid[50] (435 mg; 1.553 mmol) was added to a solution of diol **28** (420 mg; 1.038 mmol) in DMSO (20 mL) and the mixture was stirred at room temperature for 45 min. The reaction mixture was then diluted with ether (60 mL) and quenched with H_2O (10 mL). The white precipitate was filtered off through a Celite pad and the organic layer was washed with 5% aqueous NaCl solution (3 × 30 mL) and H_2O (30 mL). The solvent was dried and removed; then the crude mixture was flushed through a short column using a petroleum ether−acetone mixture (3:1). The products were separated on a chromatotron by elution with a petroleum ether−acetone mixture (19:1), which furnished **13** and **30** (17 mg; 4%; not separated), **11** (92 mg; 228 μmol; 22%), identical with an authentic sample,[21] and finally, **29** (296 mg; 735 μmol; 71%): mp 122.5−124 °C (acetone); $[\alpha]_D$ +61.4 (*c* 2.4); IR ν_{max}(OH) 3602 cm^{-1}; ^1H NMR δ 0.63 (s, 3 H, 18-H), 0.87 (d, J = 6.6 Hz, 6 H, 26-H and 27-H), 0.90 (s, 3 H, 19-H), 2.73 (br s, 1 H, 4-OH), 3.90 and 4.00 (AB system, J = 9.1 Hz, 2 H, 6-H), 5.09 (d, J = 1.9 Hz, 1 H, 4-H); ^{13}C NMR δ 12.21 (C-18), 18.74 (C-21), 19.11 (C-19), 22.08 (CH_2), 22.54 (C-26 or C-27), 22.79 (C-26 or C-27), 23.83 (CH_2), 24.47 (CH_2), 26.67 (CH_2), 27.98 (CH), 28.52 (CH_2), 35.64 (CH), 36.21 (CH_2), 37.48 (CH_2), 39.47 (CH_2), 39.68 (CH_2), 39.90 (CH_2), 41.04 (CH), 43.70 (C-13), 52.40 (C-10), 54.83 (CH), 55.66 (CH), 56.52 (CH), 61.23 (CH), 62.63 (C-5), 74.00 (C-6), 105.08 (C-4); MS (EI) *m*/*z* (%) 402 (4, M^+), 245 (100).

4a-Oxa-A-bishomo-B-nor-3α,5-cylco-5α-cholestan-4-one (30). Jones reagent (0.15 mL; 2.67 M) was added to a solution of lactol **29** (71 mg; 176 μmol) in acetone (10 mL) and the mixture was stirred for 15 min at room temperature. Methanol (5 mL) and ether (50 mL) were added, then the mixture was stirred for 5 min and the ethereal layer was washed with saturated aqueous $NaHCO_3$ solution (2 × 20 mL) and H_2O (2 × 20 mL). The solvent was dried and evaporated, yielding lactone **30** (69 mg; 172 μmol; 98%): mp 111−112.5 °C (MeOH); $[\alpha]_D$ +72.4 (*c* 1.46); IR ν_{max}(C=O) 1762 cm^{-1}; ^1H NMR δ 0.64 (s, 3 H, 18-H), 0.87 (d, J = 6.6 Hz, 26-H and 27-H), 0.92 (d, 3 H, J = 6.6 Hz, 21-H), 0.95 (s, 3 H, 19-H), 2.61 (d, J = 6.6 Hz, 1 H, 3-H), 4.06 and 4.43 (AB system, J = 9.4 Hz, 2 H, 6-H); ^{13}C NMR δ 12.19 (C-18), 18.73 (C-21), 20.03 (C-19), 20.05 (CH_2), 22.53 (C-26 or C-27), 22.77 (C-26 or C-27), 23.83 (CH_2), 24.41 (CH_2), 26.23 (CH_2), 27.97 (CH), 28.47 (CH_2), 35.60 (CH), 36.19 (CH_2), 37.42 (CH_2), 39.47 (2 × CH_2), 40.55 (CH), 41.96 (CH_2), 43.72 (C-13), 52.66 (CH), 53.21 (C-10), 55.39 (CH), 55.63 (CH), 56.18 (CH), 58.04 (C-5), 74.44 (C-6), 180.33 (C-4); MS (EI) *m*/*z* (%) 401 (22), 245 (100).

3β-[(Methylmercurio)methyl]-5-vinyl-A,B-bisnor-5β-cholestane (31). Titanocene dichloride (243 mg; 976 μmol) was placed in a dry two neck flask with a condenser and a septum attached. Freshly dried toluene (2 mL) was added, and the flask was cooled to −78 °C. Trimethyl aluminum (2 M in toluene; 1 mL; 2 mmol) was added and the mixture was warmed slowly to 65 °C, then heated at this temperature for 18 h. After cooling to 0 °C, a solution of methyl mercurio aldehyde **14** (197 mg; 327 μmol) in THF (10 mL) was added to the flask. The solution was allowed to warm to room temperature and was stirred for 30 min. The mixture was then poured into cooled ether (40 mL) and worked up with 15% aqueous NaOH solution (5 mL). After leaving to stand for 10 min, to allow precipitation of the titanium salts, the ethereal solution was dried and the residue was purified by column chromatography, using hexane as the eluent, affording **31** (192 mg; 32 μmol; 98%) as a colorless oil: $[\alpha]_D$ +25.7 (*c* 2.0); IR ν_{max}(C=C) 1632 cm^{-1}, ν_{max}(CH=CH_2) 906 cm^{-1}; ^1H NMR δ 0.19 [s (81%) and d (19%), $J_{H,Hg}$ = 101.1 Hz, 3 H, $HgCH_3$], 0.61 (s, 3 H, 18-H), 0.74 (s, 3 H, 19-H), 0.862 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.866 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 2.10 (dd, $J_{7\alpha-\text{H},7\beta-\text{H}}$ = 12.3 Hz, $J_{7\beta-\text{H},8\beta-\text{H}}$ = 6.9 Hz, 1 H, 7β-H), 2.30 (m, 1 H, 4-H), 5.03 (m, 2 H, CHCH_2), 5.84 (dd, J_{trans} = 17.3 Hz, J_{cis} = 11.0 Hz, 1 H, 6-H); ^{13}C NMR δ 12.31 (C-18), 18.80 (C-21), 20.96 (CH_3), 21.49 (CH_3), 21.72 (CH_2), 22.59 (C-26 or C-27), 22.84 (C-26 or C-27), 23.91 (CH_2), 24.58 (CH_2), 28.02 (CH), 28.61 (CH_2), 35.73 (CH), 36.30 (CH_2), 38.40 (CH_2), 38.86 (CH_2), 38.90 (CH_2), 39.54 (CH_2), 39.95 (CH_2), 41.96 (CH_2), 43.39 (CH), 43.82 (C-13), 54.87 (C-10), 55.08 (CH), 55.83 (CH), 57.10 (CH), 59.02 (CH), 63.01 (C-5), 111.28 (CH=CH_2), 142.44 (C-6); MS (EI) *m*/*z* (%) 599 (4, M^+), 384 (35, M^+- $HgCH_3$), 383 (100).

3β-[(Bromomercurio)methyl]-5-vinyl-A,B-bisnor-5β-cholestane (32). Mercuric bromide (18 mg; 50 μmol) was added to a solution of methyl mercurial **31** (30 mg; 49 μmol) in DME (10 mL) and the mixture stirred at room temperature for 2 h. Ether (40 mL) and H_2O (10 mL) were added and the ethereal layer was washed with saturated aqueous $NaHCO_3$ solution (20 mL) and H_2O (2 × 20 mL), and the solution was dried and evaporated. The aqueous phase was treated with an excess of solid $NaBH_4$ to reduce CH_3HgBr formed as byproduct; the excess of $NaBH_4$ was then decomposed with acetone. Purification of the organic crude product by column chromatography using petroleum ether as the eluent furnished **32** (31 mg; 47 μmol; 96%): mp 97−98 °C (petroleum ether/MeOH); $[\alpha]_D$ +28.0 (*c* 1.5); IR ν_{max}(C=C) 1632 cm^{-1}, ν_{max}(CH=CH_2) 907 cm^{-1}; ^1H NMR δ 0.62 (s, 3 H, 18-H), 0.78 (s, 3 H, 19-H), 0.872 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.875 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 2.15 (dd, $J_{7\alpha-\text{H},7\beta-\text{H}}$ = 12.3 Hz, $J_{7\beta-\text{H},8\beta-\text{H}}$ = 6.9 Hz, 1 H, 7β-H), 2.32 (m, 1 H, 4-H), 5.18 (m, 2 H, CH=CH_2), 5.82 (dd, J_{trans} = 17.6 Hz, J_{cis} = 11.0 Hz, 1 H, 6-H); ^{13}C NMR δ 12.23 (C-18), 18.72 (C-21), 20.61 (C-19), 21.51 (CH_2), 22.52 (C-26 or C-27), 22.78 (C-26 or C-27), 23.80 (CH_2), 24.47 (CH_2), 27.91 (CH), 28.47 (CH_2), 35.59 (CH), 35.67 (CH_2), 36.17 (CH_2), 36.92 (CH_2), 38.01 (CH_2), 38.29 (CH_2), 39.42 (CH_2), 39.71 (CH_2), 43.27 (CH), 43.72 (C-13), 53.39 (CH), 55.24 (C-10), 55.67 (CH), 56.84 (CH), 58.77 (CH), 62.36 (C-5), 113.78 (C=CH_2), 140.76 (C-6); MS (EI) *m*/*z* (%) 665 (2), 384 (100); MS (CI) *m*/*z* (%) 683 (0.1, $[M + NH_4]^+$).

Oxidative Demercuration of Bromomercurial 32. This reaction was carried out using the same apparatus and procedure as described for bromomercurial **8** (for details, see the preparation of **28**). A mixture of sodium borohydride (450 mg; 11.895 mmol) and DMF (50 mL) was added dropwise to

an oxygen saturated solution of bromomercurial **32** (5.303 g; 7.984 mmol) in DMF (135 mL). The reaction was worked up and the crude mixture was chromatographed by using petroleum ether−ether mixtures to obtain the products. Compound **33** (46 mg; 120 μmol; 1%) was eluted first using a (97:3) mixture of the solvents. A 95:5 mixture of the same solvents eluted alcohol **34** (2.431 g; 6.067 mmol; 51%), and a 90:10 mixture furnished peroxide **35** (2.082 g; 4.997 mmol; 42%).

3β-Methyl-5-vinyl-A,B-bisnor-5β-cholestane (33). Obtained as the least polar side-product (1%), along with **34** and **35**, on the oxidative demercuration of bromomercurial **32** (see above). **33:** $[\alpha]_D$ +39.1 (*c* 3.2); IR ν_{max}(C=C) 1632 cm^{-1}, ν_{max}(CH=CH$_2$) 906 cm^{-1}; ^{1}H NMR δ 0.62 (s, 3 H, 18-H), 0.76 (s, 3 H, 19-H), 0.80 (d, J = 6.9 Hz, 3 H, 4-H), 0.872 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.875 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.92 (d, J = 6.6 Hz, 3 H, 21-H), 2.12 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.6 Hz, $J_{7\beta-H,8\beta-H}$ = 6.6 Hz, 1 H, 7β-H) 5.00 (m, 2 H, CH=CH_2), 5.80 (dd, J_{trans} = 16.7 Hz, J_{cis} = 11.6 Hz, 1 H, 6-H); ^{13}C NMR δ 12.28 (C-18), 15.28 (C-4), 18.77 (C-21), 20.96 (C-19), 21.87 (CH$_2$), 22.56 (C-26 or C-27), 22.81 (C-26 or C-27), 23.88 (CH$_2$), 24.55 (CH$_2$), 28.00 (CH), 28.61 (CH$_2$), 33.48 (CH$_2$), 35.71 (CH), 36.28 (CH$_2$), 38.45 (CH$_2$), 38.81 (CH$_2$), 39.52 (CH$_2$), 39.95 (CH$_2$), 42.42 (CH), 43.80 (C-13), 47.86 (CH), 54.53 (C-10), 55.79 (CH), 56.96 (CH), 58.52 (CH), 61.09 (C-5), 110.71 (CH=*C*H$_2$), 141.30 (C-6); MS (EI) *m*/*z* (%) 384 (66, M$^+$), 369 (100).

3β-(Hydroxymethyl)-5-vinyl-A,B-bisnor-5β-cholestane (34). Obtained as the medium polar product (51%) from the oxidative demercuration of bromomercurial **32** (see above). **34:** $[\alpha]_D$ +45.4 (*c* 1.9); IR ν_{max}(OH) 3628 cm^{-1}, ν(C=C) 1632 cm^{-1}, ν(C−O) 1080 cm^{-1}, ν(CH=CH$_2$) 906 cm^{-1}; ^{1}H NMR δ 0.62 (s, 3 H, 18-H), 0.77 (s, 3 H, 19-H), 0.875 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.879 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.92 (d, J = 6.6 Hz, 3 H, 21-H), 2.23 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.6 Hz, $J_{7\beta-H,8\beta-H}$ = 6.6 Hz, 1 H, 7β-H), 3.53 (ABX system, $J_{4\alpha-H,4\beta-H}$ = 11.1 Hz, $J_{3\alpha-H,4-H}$ = 7.2 Hz, 2 H, 4-H), 5.07 (dd, J_{cis} = 10.9 Hz, J_{gem} = 1.6 Hz, 1 H, CH=CH_2), 5.11 (dd, J_{trans} = 17.5, J_{gem} = 1.6 Hz, 1 H, CH=CH_2), 5.88 (dd, J_{trans} = 17.5 Hz, J_{cis} = 10.9 Hz, 1 H, 6-H); ^{13}C NMR δ 12.25 (C-18), 18.76 (C-21), 20.42 (C-19), 21.85 (CH$_2$), 22.55 (C-26 or C-27), 22.80 (C-26 or C-27), 23.87 (CH$_2$), 24.50 (CH$_2$), 27.99 (CH), 28.57 (CH$_2$), 28.79 (CH$_2$), 35.68 (CH), 36.25 (CH$_2$), 38.46 (CH$_2$), 39.50 (CH$_2$), 39.60 (CH$_2$), 39.83 (CH$_2$), 42.48 (CH), 43.77 (C-13), 55.22 (C-10), 55.74 (CH), 56.24 (CH), 56.80 (CH), 58.36 (CH), 59.89 (C-5), 64.09 (C-4), 111.44 (CH=*C*H$_2$), 140.44 (C-6); MS (EI) *m*/*z* (%) 400 (21, M$^+$), 369 (100).

3β-(Peroxymethyl)-5-vinyl-A,B-bisnor-5β-cholestane (35). Obtained as the most polar product (42%) from the oxidative demercuration of bromomercurial **32** (see above). **35:** $[\alpha]_D$ +62.3 (*c* 3.0); IR ν_{max}(OH) 3533, 3425 cm^{-1}, ν_{max}(C=C) 1632 cm^{-1}, ν_{max}(CH=CH$_2$) 906 cm^{-1}, ν_{max}(O−O) 855 cm^{-1}; ^{1}H NMR δ 0.62 (s, 3 H, 18-H), 0.77 (s, 3 H, 19-H), 0.87 (d, J = 6.6 Hz, 3 H, 26-H and 27-H), 0.90 (d, J = 6.6 Hz, 3 H, 21-H), 2.19 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.7 Hz, $J_{7\beta-H,8\beta-H}$ = 6.8 Hz, 7β-H), 3.81 (t, J = 9.5 Hz, 1 H, 4-H), 3.98 (dd, J = 5.4 and 9.5 Hz, 1 H, 4-H), 5.05 (m, 2 H, CH=CH_2), 5.77 (dd, J_{trans} = 17.8 Hz, J_{cis} = 11.0 Hz, 1 H, 6-H); ^{13}C NMR δ 12.23 (C-18), 18.74 (C-21), 20.37 (C-19), 21.77 (CH$_2$), 22.53 (C-26 or C-27), 22.78 (C-26 or C-27), 23.86 (CH$_2$), 24.48 (CH$_2$), 27.97 (CH), 28.55 (CH$_2$), 29.52 (CH$_2$), 35.66 (CH), 36.24 (CH$_2$), 38.29 (CH$_2$), 38.86 (CH$_2$), 39.49 (CH$_2$), 39.82 (CH$_2$), 42.46 (CH), 43.76 (C-13), 51.26 (CH), 54.75 (C-10), 55.74 (CH), 56.82 (CH), 58.32 (CH), 60.25 (C-5), 78.52 (C-4), 111.66 (CH=*C*H$_2$), 139.60 (C-6); MS (EI) *m*/*z* (%) 416 (3, M$^+$), 385 (100).

5-Vinyl-A,B-bisnor-5β-cholestane-3β-carbaldehyde (36). PCC (1.262 g; 5.855 mmol) was added to a stirred solution of **34** (1.272 g; 3.175 mmol) in dichloromethane (30 mL) and the mixture was stirred at room temperature for 2.5 h. Then the solution was filtered through a Celite pad, the solvent was removed and the residue was adsorbed onto silica gel. The silica mixture was then placed on the top of a column and purified by chromatography using a petroleum ether−ether mixture (49:1) as the eluent, which afforded oily **36** (1.044 g; 2.619 mmol; 82%): $[\alpha]_D$ +76.4 (*c* 3.7); IR ν_{max}(CHO) 2733 cm^{-1}, ν_{max}(C=O) 1712 cm^{-1}, ν_{max}(C=C) 1634 cm^{-1}, ν_{max}(CH=CH$_2$) 909 cm^{-1}; ^{1}H NMR δ 0.63 (s, 3 H, 18-H), 0.82 (s, 3 H, 19-H), 0.87 (d, J = 6.6 Hz, 6 H, 26-H and 27-H), 0.92 (d, J = 6.6 Hz, 3 H, 21-H), 2.31 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.7 Hz, $J_{7\beta-H,8\beta-H}$ = 6.6 Hz, 1 H, 7β-H), 2.67 (dt, J = 7.2 and 2.2 Hz, 1 H, 3α-H), 5.09 (m, 2 H, CH=CH_2), 5.83 (m, J_{trans} = 17.6 Hz, J_{cis} = 10.7 Hz, 1 H, 6-H), 9.64 (d, J = 2.5 Hz, 1 H, 4-H); ^{13}C NMR δ 12.25 (C-18), 18.75 (C-21), 20.02 (C-19), 21.96 (CH$_2$), 22.54 (C-26 or C-27), 22.78 (C-26 or C-27), 23.86 (CH$_2$), 24.47 (CH$_2$), 25.49 (CH$_2$), 27.98 (CH), 28.53 (CH$_2$), 35.66 (CH), 36.23 (CH$_2$), 38.21 (CH$_2$), 39.49 (CH$_2$), 39.75 (CH$_2$), 40.89 (CH$_2$), 42.03 (CH), 43.81 (C-13), 55.34 (C-10), 55.73 (CH), 56.66 (CH), 57.89 (CH), 60.83 (C-5), 65.41 (CH), 112.95 (CH=*C*H$_2$), 139.83 (C-6), 204.60 (C-4); MS (EI) *m*/*z* (%) 398 (66, M$^+$).

3β-Acetyl-5-vinyl-A,B-bisnor-5β-cholestane (37). Methyllithium (1.9 mL; 1.35 M, 2.565 mmol) was added to a cooled (−78 °C), stirred solution of **36** (986 mg; 2.473 mmol) in ether (30 mL) and the mixture was stirred at −78 °C for 15 min. The excess reagent was quenched with H_2O (1 mL); then the mixture was diluted with ether (30 mL) and the ethereal layer was separated and worked up. The solvent was dried and evaporated, then the residue was redissolved in dichloromethane (30 mL). PCC (990 mg; 4.593 mmol) was added to the flask and the mixture was stirred at room temperature for 2 h. Then the solution was filtered through a Celite pad, the solvent was removed, and the residue was adsorbed onto silica gel. The silica mixture was then placed on the top of a column and purified by chromatography using a petroleum ether−ether mixture (49:1) as the eluent, which afforded **37** (898 mg; 2.176; 88%): mp 84−85 °C (MeOH); $[\alpha]_D$ +102.0 (*c* 4.5); IR ν_{max}(C=O) 1698 cm^{-1}, ν_{max}(C=C) 1636 cm^{-1}, ν_{max}(CH=CH$_2$) 914 cm^{-1}; ^{1}H NMR δ 0.63 (s, 3 H, 18-H), 0.77 (s, 3 H, 19-H), 0.871 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.874 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.93 (d, J = 6.6 Hz, 3 H, 21-H), 2.02 (s, 3 H, COCH$_3$), 2.37 (dd, J = 12.4 Hz, 5.8 Hz, 1 H, 7β-H), 2.82 (dd, J = 10.1 and 6.3 Hz, 1 H, 3α-H), 4.99 (m, J_{cis} = 10.9 Hz, 1 H, CH=C*H*H), 5.03 (m, J_{trans} = 17.5 Hz, 1 H, CH=C*H*H), 5.68 (dd, J_{trans} = 17.5 Hz, J_{cis} = 10.9 Hz, 1 H, 6-H); ^{13}C NMR δ 12.22 (C-18), 18.75 (C-21), 20.72 (C-19), 21.89 (CH$_2$), 22.54 (C-26 or C-27), 22.78 (C-26 or C-27), 23.85 (CH$_2$), 24.51 (CH$_2$), 27.77 (CH$_2$), 27.98 (CH), 28.54 (CH$_2$), 30.56 (CO*C*H$_3$), 35.66 (CH), 36.25 (CH$_2$), 38.91 (CH$_2$), 39.49 (CH$_2$), 39.74 (CH$_2$), 41.94 (CH$_2$), 43.16 (CH), 43.70 (C-13), 55.75 (CH), 56.16 (C), 56.69 (CH), 59.15 (CH), 60.57 (C), 67.26 (CH), 111.48 (CH=*C*H$_2$), 140.09 (*C*H=CH$_2$), 209.74 (C-4); MS (EI) *m*/*z* (%) 413 (25).

3β-Acetyl-A,B-bisnor-5β-cholestane-5-carbaldehyde (38). A solution of the olefin **37** (238 mg; 577 μmol) in dichloromethane (10 mL) was placed into a three-necked flask that was fitted with a septum, a bubbling device, and a gas outlet. The apparatus was flushed with nitrogen and the solution was cooled to −35 °C, then ozone was bubbled into the solution until TLC showed that all the starting material had reacted (approximately 1 h). The apparatus was flushed with nitrogen then a solution of thiourea (45 mg; 591 μmol) in MeOH (5 mL) was added. The reaction mixture was stirred at −35 °C for 1 h, 0 °C for 30 min, and room temperature for 1 h, then the solution was diluted with dichloromethane (25 mL) and filtered. The filtrate was adsorbed onto silica gel and the solvent was evaporated. The mixture was then placed on the top of a column and was purified by chromatography, eluting with various petroleum ether−ether mixtures. The polarity of the solvent mixture was gradually increased from (97:3) to (88:12), which facilitated removal of the impurities followed by elution of the most polar constituent that was the required product. Removal of the solvent afforded **38** (155 mg; 374 μmol; 65%): mp 127−129 °C ($CHCl_3$/MeOH); $[\alpha]_D$ +24.9 (*c* 3.8); IR ν_{max}(C=O) 1700 and 1713 cm^{-1}; ^{1}H NMR δ 0.64 (s, 3 H, 18-H), 0.863 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 0.866 (d, J = 6.6 Hz, 3 H, 26-H or 27-H), 1.01 (s, 3 H, 19-H), 2.14 (s, 3 H, COCH$_3$), 2.38 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.9 Hz, $J_{7\beta-H,8\beta-H}$ = 6.3 Hz, 1 H, 7β-H), 2.87 (t, J = 7.9 Hz, 1 H, 3α-H), 9.57 (s, 1 H, 6-H); ^{13}C NMR δ 12.19 (C-18), 18.73 (C-21), 19.67 (C-19), 21.64 (CH$_2$), 22.52 (C-26 or C-27), 22.76 (C-26 or C-27), 23.83 (CH$_2$), 24.32 (CH$_2$), 27.97 (CH), 28.45 (CH$_2$), 29.46 (CH$_2$), 29.53 (CO*C*H$_3$), 35.59 (CH), 36.19 (CH$_2$), 39.36 (CH$_2$), 39.45 (CH$_2$), 39.47 (CH$_2$), 40.69 (CH$_2$), 43.67 (C-13), 43.73 (CH), 55.67 (CH), 56.50 (CH), 56.78

(C-10), 58.67 (CH), 64.03 (CH), 68.35 (C-5), 204.68 (C-6), 209.29 (C-4); MS (EI) *m/z* (%) 414 (100, M^+).

A-Bishomo-B-nor-3α,5-cyclo-5α-cholest-4a-en-4-one (39). A 10% aqueous NaOH solution (3 mL) was added to a solution of **38** (40 mg; 96 μmol) in THF (3 mL) and the resultant mixture was stirred at room temperature for 45 min. Then the mixture was diluted with ether (35 mL) and the ethereal layer was extracted and worked up. The crude mixture was purified by column chromatography using a petroleum ether−ether mixture (97:3) as the eluent, which allowed separation of enone **39** (13 mg; 33 μmol; 34%): mp 104−105 °C (MeOH); IR ν_{max}(C=O) 1692 cm^{-1}, ν_{max}(C=C) 1635 cm^{-1}; ^{1}H NMR δ 0.69 (s, 3 H, 18-H), 0.84 (s, 3 H, 19-H), 0.871 (d, *J* = 6.6 Hz, 3 H, 26-H or 27-H), 0.874 (d, *J* = 6.6 Hz, 3 H, 26-H or 27-H), 0.94 (d, *J* = 6.6 Hz, 21-H), 6.03 (d, *J* = 5.7 Hz, 1 H, 6-H), 7.44 (d, *J* = 5.3 Hz, 1 H, 4a−H); MS (EI) *m/z* (%) 396 (83, M^+), 241 (100).

6-Methylene-A-homo-B-nor-3α,5-cyclo-5α-cholestane (41). Titanocene dichloride (184 mg; 739 μmol) was placed in a dry two-necked flask fitted with a condenser and a septum. Freshly dried toluene (3 mL) was added and the mixture cooled to −78 °C. Trimethylaluminum (2 M in toluene; 0.8 mL; 1.6 mmol) was added to the flask; then the mixture was allowed to warm slowly and was heated at 65 °C for 18 h. The mixture was then cooled to 0 °C and a solution of cyclobutanone **40**[21] (80 mg; 208 μmol) in THF (10 mL) was added. The mixture was heated at 65 °C for 2 h, allowed to cool, poured into ice-cold ether (40 mL), and worked up with a 15% aqueous NaOH solution (5 mL). After it was left to stand for 10 min to allow precipitation of the titanium salts, the ethereal solution was dried and the solvent was removed. The residue was adsorbed onto silica gel, and the mixture was placed on the top of a chromatography column. The product was flushed through the column with petroleum ether as the eluent, and the solvent was evaporated, to furnish **41** (69 mg; 180 μmol; 87%) as a colorless oil: $[\alpha]_D$ +15.1 (*c* 3.6); IR ν_{max}(C=C) 1666 cm^{-1}, ν_{max}(C=CH_2) 872 cm^{-1}; ^{1}H NMR δ 0.65 (s, 3 H, 18-H), 0.86 (s, 3 H, 19-H), 0.872 (d, *J* = 6.6 Hz, 3 H, 26-H or 27-H), 0.875 (d, *J* = 6.6 Hz, 3 H, 26-H or 27-H), 0.93 (d, *J* = 6.6 Hz, 3 H, 21-H), 2.30 (m, 1 H, 4-H), 2.57 (dddd, *J* = 15.5, 8.4 2.0 and 1.9 Hz, 1 H, 4-H), 4.70 (dd, *J* = 2.7 and 2.7 Hz, 1 H, C=CH*H*), 4.74 (dd, *J* = 2.0 and 2.0 Hz, 1 H C=C*H*H); ^{13}C NMR δ 12.34 (C-18), 18.78 (C-21), 19.18 (C-19), 22.23 (CH_2), 22.56 (C-26 or C-27), 22.81 (C-26 or C-27), 23.87 (CH_2), 24.50 (CH_2), 28.01 (CH), 28.58 (CH_2), 29.38 (CH_2), 31.99 (CH_2), 35.61 (CH_2), 35.69 (CH), 36.27 (CH_2), 39.52 (CH_2), 39.87 (CH_2), 41.53 (CH), 41.91 (CH_2), 44.00 (C-13), 46.39 (CH), 53.41 (CH), 54.72 (C-10), 55.76 (CH), 57.03 (CH), 68.04 (C-5), 103.96 (C=*C*H_2), 154.29 (C-6); MS (EI) *m/z* (%) 382 (100, M^+).

6α-Ethynyl-A-homo-B-nor-3α,5-cyclo-5α-cholestan-6β-ol (42). A solution of cyclobutanone **40**[21] (147 mg; 382 μmol) in THF (4 mL) was added dropwise to a stirred suspension of lithium acetylide−ethylenediamine complex (336 mg; 1.887 mmol) in THF (4 mL) at room temperature. After stirring for 5 min, the reaction mixture was cooled to 0 °C and quenched with saturated aqueous NH_4Cl solution (5 mL). The resulting mixture was diluted with ether (30 mL) and the organic layer was washed with H_2O (10 mL) and 15% aqueous NaCl solution (2 × 10 mL). The ethereal solution was dried and evaporated and the crude product was resubjected to the reaction with the lithium acetylide suspension. Column chromatography using a petroleum ether−ether mixture (24:1) afforded unreacted ketone **40** (21 mg; 55 μmol; 14%) as the least polar and alcohol **42** (97 mg; 236μmol; 62%) as the most polar component: mp 99.5−101 °C (MeOH); IR ν_{max}(OH) 3595 cm^{-1}, ν_{max}(C≡CH) 3303 cm^{-1}; ^{1}H NMR δ 0.65 (s, 3 H, 18-H), 0.87 (d, *J* = 6.6 Hz, 6 H, 26-H and 27-H), 0.92 (d, *J* = 6.6 Hz, 3 H, 21-H), 1.23 (s, 3H, 19-H), 2.41 (m, 1H, 4-H), 2.49 (m, 1 H, 4-H), 2.64 (s, 1 H, C≡CH); ^{13}C NMR δ 12.27 (C-18), 18.75 (C-19 or C-21), 18.77 (C-19 or C-21), 21.40 (CH_2), 22.56 (C-26 or C-27), 22.80 (C-26 or C-27), 23.82 (CH_2), 24.47 (CH_2), 27.98 (CH), 28.59 (2 × CH_2), 35.65 (CH), 36.23 (CH_2), 36.94 (CH_2), 37.89 (CH_2), 39.49 (CH_2), 39.71 (CH_2), 40.39 (CH), 41.46 (CH_2), 42.16 (CH), 43.86 (C-13), 54.85 (CH), 55.65 (CH), 56.49 (C-10), 57.11 (CH), 65.60 (C-5), 72.25 (C-6 or *C*≡CH), 72.87 (C-6 or *C*≡CH), 88.91 (C≡*C*H); MS (EI) *m/z* (%) 410 (20, M^+), 342 (100).

6α-Vinyl-A-homo-B-nor-3α,5-cyclo-5α-cholestan-6β-ol (43). Magnesium (340 mg; 14 mmol) was placed into a three-necked flask, fitted with a pressure-equalized dropping funnel, an acetone−dry ice condenser (equipped with a nitrogen bubbler), and a septum, and then covered with dry THF (10 mL). A crystal of iodine was added to activate the magnesium and initiate the formation of the Grignard reagent. Vinyl bromide (0.6 mL; 910 mg; 8.508 mmol) was condensed from a cylinder into a sealed measuring tube at −35 °C. The cylinder was removed, then a cannula was fitted to the tube and placed under the surface of the THF, in the reaction flask. The tube was gently heated so that vinyl bromide could slowly bubble into the THF over a period of approximately 5 min. After the fizzing had ceased, the mixture was stirred at room temperature for an additional 15 min. A solution of cyclobutanone **40** (1.095 g; 2.847 mmol) in THF (20 mL) was then added dropwise and the mixture stirred at 40 °C for 1 h. The reaction was then cooled by an ice bath and quenched with saturated aqueous NH_4Cl solution (5 mL). The product was taken up into ether and the organic layer worked up. Column chromatography using petroleum ether and ether (49:1), as the eluent, furnished amorphous **43** (1.139 g; 97%): $[\alpha]_D$ +44.2 (*c* 1.6); IR ν_{max}(OH) 3595 cm^{-1}, ν_{max}(C=C) 1640 cm^{-1}, ν_{max}(CH=CH_2) 912 cm^{-1}; ^{1}H NMR δ 0.63 (s, 3 H, 18-H), 0.93 (s, 3 H, 19-H), 5.04 (dd, J_{cis} = 10.7 Hz, J_{gem} = 1.2 Hz, 1 H, CH=C*H*H), 5.12 (dd, J_{trans} = 17.3 Hz, J_{gem} = 1.2 Hz, 1 H, CH=C*H*H), 6.11 (dd, J_{trans} = 17.3 Hz, J_{cis} = 10.7 Hz, 1 H, C*H*=CH_2); ^{13}C NMR δ 12.26 (C-18), 18.76 (C-21), 18.87 (C-19), 21.36 (CH_2), 22.55 (C-26 or C-27), 22.80 (C-26 or C-27), 23.81 (CH_2), 24.43 (CH_2), 27.97 (CH), 28.59 (CH_2), 28.77 (CH_2), 35.64 (CH), 36.22 (CH_2), 36.48 (CH_2), 36.94 (CH_2), 39.48 (CH_2), 39.75 (CH_2), 39.89 (CH_2), 40.41 (CH), 42.13 (CH), 43.86 (C-13), 54.06 (CH), 55.65 (CH), 56.62 (C-10), 57.19 (CH), 65.63 (C-5), 77.42 (C-6), 108.59 (CH_2), 145.79 (CH); MS (EI) *m/z* (%) 412 (54, M^+), 342 (100).

6β-Methoxy-6α-vinyl-A-homo-B-nor-3α,5-cyclo-5α-cholestane (44). Sodium hydride, (20 mg; 833 μmol; obtained from a 60% oil suspension by washing with petroleum ether) was placed in a flask and covered with THF (5 mL) and then cooled to 0 °C. A solution of vinyl cyclobutanol **43** (69 mg; 167 μmol) dissolved in THF (5 mL) was added and the mixture was stirred for 30 min. Then methyl iodide (0.1 mL; 288 mmol) was added and the reaction mixture stirred at 45 °C for a further 1 h. The mixture was diluted with ether (15 mL), quenched with water (1 mL), and then worked up. The product was chromatographed with a petroleum ether−ether mixture (99:1), which afforded methoxy derivative **44** (60 mg; 145 μmol; 87%) as a colorless oil: $[\alpha]_D$ +32.8 (*c* 3.5); IR ν_{max}(C=C) 1638 cm^{-1}; ^{1}H NMR δ 0.63 (s, 3 H, 18-H), 0.869 (d, *J* = 6.6 Hz, 3 H, 26-H or 27-H), 0.871 (d, *J* = 6.6 Hz, 3 H, 26-H or 27-H), 1.21 (s, 3 H, 19-H), 3.05 (s, 3 H, OC*H*$_3$), 5.17 (m, 2 H, CH=C*H*$_2$), 5.87 (m, J_{trans} = 14.1 Hz, J_{cis} = 6.7 Hz, 1 H, C*H*=CH_2); ^{13}C NMR δ 12.26 (C-18), 18.78 (C-21), 19.09 (C-19), 21.48 (CH_2), 22.55 (C-26 or C-27), 22.79 (C-26 or C-27), 23.84 (CH_2), 24.46 (CH_2), 27.99 (CH), 28.54 (CH_2), 28.61 (CH_2), 30.05 (CH_2), 35.66 (CH), 36.27 (CH_2), 37.21 (CH_2), 39.42 (CH_2), 39.52 (CH_2), 39.86 (CH_2), 40.37 (CH), 42.49 (CH), 43.89 (OCH_3), 50.18 (C-13), 54.33 (CH), 55.73 (CH), 56.70 (C-10), 57.19 (CH), 64.76 (C-5), 81.99 (C-6), 112.30 (CH=*C*H_2), 142.49 (*C*H=CH_2); MS (EI) *m/z* (%) 426 (100, M^+).

6-Methylene-A-bishomo-B-nor-3α,5-cyclo-5α-cholestan-4a-one (47). Method A. Manganese(III) picolinate (172 mg; 461 μmol) and **42** (76 mg; 186 μmol) were dissolved in degassed DMF (5 mL) and the mixture was heated at 100 °C for 3 h. Then the reaction was quenched with H_2O (5 mL) and diluted with ether (40 mL). The ethereal layer was washed with 15% aqueous NaCl solution (2 × 15 mL) and H_2O (15 mL) and then dried and the solvent removed under vacuum. Purification by column chromatography using a petroleum ether−ether mixture (19:1) furnished **47** (24 mg; 58 μmol; 32%): mp 85.5−87 °C (MeOH/$CHCl_3$); $[\alpha]_D$ −21.5 (*c* 1); IR ν_{max}(C=CH_2) 3000 cm^{-1}, ν(C=O) 1712 cm^{-1}, ν(C=C) 1630 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.67 (s, 3 H, 19-H), 0.68 (s, 3 H, 18-H), 1.10 (m, 1 H, 12α-H), 1.27 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.2 Hz, $J_{7\alpha-H,8\beta-H}$ = 12.2 Hz, 1 H, 7α-

H), 1.60 (dd, $J_{2\alpha-H,2\beta-H}$ = 12.9 Hz, $J_{1\beta-H,2\beta-H}$ = 5.9 Hz, 1 H, 2β-H), 1.95 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.2 Hz, $J_{7\beta-H,8\beta-H}$ = 5.4 Hz, 1 H, 7β-H), 1.96 (dddd, $J_{2\alpha-H,2\beta-H}$ = 12.9 Hz, $J_{2\alpha-H,1\beta-H}$ = 12.9 Hz, $J_{2\alpha-H,1\alpha-H}$ = 6.5 Hz, $J_{2\alpha-H,3\alpha-H}$ = 5.9 Hz, 1 H, 2α-H), 2.03 (dd, $J_{4\alpha-H,4\beta-H}$ = 19.2 Hz, $J_{3\alpha-H,4\beta-H}$ = 9.4 Hz, 1 H, 4β-H), 2.06 (ddd, $J_{12\alpha-H,12\beta-H}$ = 12.8 Hz, $J_{11\alpha-H.12\beta-H}$ = 3.4 Hz, $J_{11\beta-H,12\beta-H}$ = 3.4 Hz, 1 H, 12β-H), 2.33 (ddd, $J_{3\alpha-H,3\beta-H}$ = 19.2 Hz, $J_{3\alpha-H,4\alpha-H}$ = 9.4 Hz, $J_{3\alpha-H,4\beta-H}$ = 9.4 Hz, $J_{2\alpha-H,3\alpha-H}$ = 5.9 Hz, 1 H, 3α-H), 2.50 (dd, $J_{4\alpha-H,4\beta-H}$ = 19.2 Hz, $J_{3\alpha-H,4\alpha-H}$ = 9.4 Hz, 1 H, 4α-H), 5.22 (d, J = 1 Hz, 1 H, (*E*)-C=C*H*H), 6.04 (d, J = 1 Hz, 1 H, (*Z*)-C=C*H*H); ^{13}C NMR δ 12.21 (C-18), 18.70 (C-21), 22.29 (CH_2), 22.51 (C-26 or C-27), 22.59 (C-26 or C-27), 22.76 (C-19), 23.80 (CH_2), 24.56 (CH_2), 27.71 (CH_2), 27.74 (CH), 28.52 (CH_2), 35.61 (CH), 36.17 (CH_2), 36.54 (CH_2), 39.44 (CH_2), 39.63 (CH_2), 42.07 (CH_2), 42.45 (CH), 43.64 (C-13), 46.14 (CH), 48.04 (CH_2), 54.86 (C-10), 55.62 (CH), 55.97 (CH), 56.39 (CH), 64.19 (C-5), 116.54 (C-6a), 154.17 (C-6), 208.44 (C-4a); MS (EI) *m*/*z* (%) 410 (100, M^+); MS (CI) *m*/*z* 428 ([M + NH_4]$^+$), 411 (MH^+).

Method B. Obtained from **43** on the $Tl(NO_3)_3$-mediated reaction (76%); see below.

Reaction of 43 with Thallium(III) Nitrate. Thallium(III) nitrate trihydrate (229 mg; 514 μmol) was added to a solution of **43** (204 mg; 495 μmol) in THF (15 mL). The mixture was stirred at room temperature for 15 min then diluted with 15% aqueous NaCl solution (2 mL) and ether (35 mL), and the organic layer was worked up. The crude mixture was chromatographed with a petroleum ether−ether mixture (49:1), to afford **50** (24 mg; 12%) as the less polar compound and **47** (154 mg; 76%) as the more polar component.

Reaction of 43 with Mercury(II) Nitrate. Mercury(II) nitrate monohydrate (160 mg; 466 μmol) was added to a solution of **43** (192 mg; 495 μmol) in THF (15 mL). The mixture was stirred at room temperature for 15 min then treated with 15% aqueous NaCl solution (15 mL) and stirred for a further 5 min. The crude product was taken up into ether and the ethereal solution was worked up. Separation of the products was achieved by chromatography: elution with a petroleum ether−ether mixture (49:1) afforded **50** (25 mg; 13%) as the less polar and **47** (100 mg; 52%) as the more polar component. Further elution with a petroleum ether−ether mixture (9:1) furnished **49c** (69 mg; 23%).

Stoichiometric Reaction of 43 with Palladium(II) Nitrate. Palladium(II) nitrate (35 mg; 152 μmol) was added to a solution of **43** (56 mg; 135 μmol) in THF (5 mL) and the resulting solution was stirred at room temperature for 15 min. The mixture was then treated with 15% aqueous NaCl solution (5 mL) and diluted with ether. The organic layer was washed with H_2O (2 × 10 mL) and then dried, and the solvent was evaporated. Separation of the products was carried out by column chromatography: elution with a petroleum ether−ether mixture (49:1) gave products in the following order: **51** (1.3 mg; 2%), **50** (1.3 mg; 2%), **52** (30 mg; 54%), and **47** (20 mg; 36%).

Catalytic Reaction of 43 with Palladium(II) Nitrate. Palladium(II) nitrate (13 mg; 5 mol %) and copper(II) nitrate (725 mg; 3 mmol) were added to a solution of **43** (438 mg; 1.061 mmol) in THF (10 mL) and the resulting solution was stirred at room temperature for 15 h. The mixture was then treated with 15% aqueous NaCl solution (5 mL) and diluted with ether. The organic layer was washed with H_2O (2 × 20 mL) and then dried and the solvent was evaporated. Separation of the products was carried out by column chromatography: elution with a petroleum ether−ether mixture (49:1) gave products in the following order: **50** and **51** (14 mg; 3%; not separated), **52** (263 mg; 60%), and **47** (58 mg; 13%).

Catalytic Reaction of 43 with Bis(benzonitrile)palladium(II) Chloride. $(PhCN)_2PdCl_2$ (3.6 mg; 8 mol %) and *p*-benzoquinone (26 mg; 242 μmol) were added to a solution of **43** (50 mg; 121 μmol) in THF (5 mL) and the resulting solution was stirred at room temperature for 15 h. The mixture was then diluted with ether (25 mL) and the ethereal solution was washed with 10% aqueous sodium dithionite solution (2 × 10 mL) and water (2 × 10 mL). The solution was dried and the solvent evaporated; then chromatography was used to separate the mixture of products. Elution with petroleum ether and ether (49:1) gave products in the following order: **51** (36 mg; 72%), **50** (0.9 mg; 2%), **52** (5.5 mg; 11%), **47** (5.8 mg; 12%).

4a-[(Chloromercurio)methyl]-A-bishomo-B-nor-3α,5-cyclo-5α-cholestan-6-one (49c). Obtained from **43** on a mercury(II) nitrate-mediated reaction as described above (23%). **49c**: mp 158−159.5 °C (MeOH/$CHCl_3$); $[\alpha]_D$ −48.6 (*c* 3.0); IR ν_{max}(C=O) 1712 cm^{-1}; ^{1}H NMR δ 0.66 (s, 3 H, 18-H), 0.74 (s, 3 H, 19-H), 0.86 (d, J = 6.6 Hz, 26-H and 27-H), 0.91 (d, J = 6.6 Hz, 3 H, 21-H); ^{13}C NMR δ 12.29 (C-18), 18.73 (C-21), 22.06 (CH_2), 22.53 (C-26 or C-27), 22.79 (C-26 or C-27), 23.02 (C-19), 23.82 (CH_2), 24.32 (CH_2), 26.59 (CH_2), 27.96 (CH), 28.02 (CH_2), 28.54 (CH_2), 35.58 (CH), 36.18 (CH_2), 36.85 (CH_2), 39.44 (CH_2), 39.57 (CH_2), 42.24 (CH), 43.44 (CH_2), 43.76 (C-13), 47.83 (CH), 50.55 (CH), 55.65 (CH), 55.78 (CH), 56.48 (CH), 58.04 (C-10), 68.81 (C-5), 226.84 (C-6); MS (EI) *m*/*z* (%) 411 (32, M^+ − HgCl), 410 (100, M^+ − HHgCl); MS (CI) *m*/*z* 412 (MH^+ − HgCl).

4a-Methylene-A-bishomo-B-nor-3α,5-cyclo-5α-cholestan-6-one (50). Obtained from **43** on a mercury(II) nitrate-mediated reaction as described above (12%). **50**: mp 92−94 °C ($CHCl_3$/MeOH); $[\alpha]_D$ +22.6 (*c* 1.5); IR ν_{max}(C=O) 1710 cm^{-1}, ν_{max}(C=C) 1635 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.67 (s, 3 H, 18-H), 0.77 (s, 3 H, 19-H), 0.84 (dd, $J_{7\alpha-H,7\beta-H}$ = 11.8 Hz, $J_{7\alpha-H,8\beta-H}$ = 11.8 Hz, 1 H, 7α-H), 1.44 (m, 1 H, 1β-H), 1.65 (m, 2 H, 1α-H and 2β-H), 1.71 (m, 1 H, 8β-H), 1.92 (m, 1 H, 2α-H), 2.05 (dd, $J_{7\alpha-H,7\beta-H}$ = 11.8 Hz. $J_{7\beta-H,8\beta-H}$ = 5.8 Hz, 1 H, 7β-H), 2.28 (m, 1 H, 3α-H), 2.72 (m, 1 H, 4α-H), 5.19 (narrow m, 1 H, (*E*)-C=C*H*H), 5.92 (narrow m, 1 H, (*Z*)-C=C*H*H); NOESY cross-peaks have been identified for (*E*)-4b−H ↔ 4α-H and 4β-H, 7α-H ↔ 3α-H, 2α-H ↔ 3α-H, 4β-H ↔ 2β-H, 4β-H ↔ 1β-H; ^{13}C NMR δ 12.30 (C-18), 18.76 (C-21), 20.82 (C-19), 22.15 (CH_2), 22.54 (C-26 or C-27), 22.80 (C-26 or C-27), 23.85 (CH_2), 24.36 (CH_2), 27.98 (CH), 28.58 (CH_2), 29.71 (C-4), 32.02 (CH_2), 35.63 (CH), 36.22 (CH_2), 36.78 (CH_2), 39.47 (CH_2), 39.69 (CH_2), 42.18 (CH), 42.46 (CH_2), 43.79 (C-13), 46.91 (C-3), 55.72 (CH), 55.89 (CH), 56.70 (CH), 58.30 (C-10), 69.43 (C-5), 116.06 (C-4b), 146.86 (C-4a), 212.01 (C-6); MS (EI) *m*/*z* (%) 410 (100, M^+).

4a-Methyl-A-bishomo-B-nor-3α,5-cyclo-5α-cholestan-6-one (51). Obtained from **43** on a $(PhCN)_2PdCl_2$-catalyzed reaction as described above (72%). **51**: mp 87.5−89 °C (MeOH−$CHCl_3$); $[\alpha]_D$ +34.4 (*c* 0.7); IR ν_{max}(C=O) 1718 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.66 (s, 3 H, 18-H), 0.77 (s, 3 H, 19-H), 0.81 (dd, $J_{7\alpha-H,7\beta-H}$ = 11.9 Hz, $J_{7\alpha-H,8\beta-H}$ = 11.5 Hz, 1 H, 7α-H), 1.04 (d, J = 6.8 Hz, 3 H, 4aβ-CH_3), 1.05 (m, 1 H, 12α-H), 1.14 (m, 1 H, 4β-H), 1.45 (ddd, $J_{1\alpha-H,1\beta-H}$ = 12.8 Hz, $J_{1\beta-H,2\alpha-H}$ = 12.8 Hz, $J_{1\beta-H,2\beta-H}$ = 6.5 Hz, 1 H, 1β-H), 1.62 (m, 1 H, 2-H), 1.62 (dd, $J_{1\alpha-H,1\beta-H}$ = 12.8 Hz, $J_{1\alpha-H,2\alpha-H}$ = 7.1 Hz, $J_{1\alpha-H,2\beta-H}$ ≅ 0 Hz, 1 H, 1α-H), 1.71 (dddd, J = 11.5, 11.5, 11.2 and 5.7 Hz, 1 H, 8β-H), 1.88 (m, 1 H, 2α-H), 1.89 (dd, $J_{7\alpha-H,7\beta-H}$ = 11.9 Hz, $J_{7\beta-H,8\beta-H}$ = 5.7 Hz, 1 H, 7β-H), 2.02 (ddd, J = 12.7, 3.3 and 3.3 Hz, 1 H, 12β-H), 2.09 (m, $J_{4\alpha-H,4\beta-H}$ = 12.3 Hz, $J_{3\alpha-H,4\alpha-H}$ = 7.9 Hz, $J_{4\alpha-H,4a\alpha-H}$ = 7.9 Hz, 1 H, 4α-H), 2.17 (m, 1 H, 4aα-H), 2.20 (m, 1 H, 3α-H); NOESY cross-peaks have been identified for 4aβ-CH_3 ↔ 19-H, 4aα-H ↔ 7β-H, 3α-H ↔ 4α-H, 7β-H ↔ 8β-H, and 3α-H ↔ 7α-H; ^{13}C NMR δ 12.24 (C-18), 13.57 (C-4b), 18.72 (C-21), 22.09 (C-11), 22.42 (C-26 or C-27), 22.49 (C-19), 22.77 (C-26 or C-27), 23.82 (CH_2), 24.32 (CH_2), 27.95 (C-25), 28.06 (C-2), 28.55 (CH_2), 33.72 (C-4), 35.60 (C-20), 36.20 (CH_2), 36.88 (C-1), 39.45 (CH_2), 39.67 (C-12), 42.53 (C-8), 43.43 (C-7), 43.73 (C-13), 44.87 (C-4a), 48.69 (C-3), 55.68 (C-17), 55.77 (C-8), 56.57 (C-14), 57.23 (C-10), 68.41 (C-5), 225.87 (C-6); MS (EI) *m*/*z* (%) 413 (32), 412 (100, M^+), 272 (31), 262 (11), 258 (22), 257 (62), 151 (36); MS (CI) *m*/*z* 413 (MH^+), 430 ([M + NH_4]$^+$), 397 (M^+ − CH_3).

4a-Methyl-A-bishomo-B-nor-3α,5-cyclo-5α-cholest-4-en-6-one (52). Obtained from **43** on a $Pd(NO_3)_2$-catalyzed reaction as described above (60%). **52**: mp 113.5−115.5 °C (MeOH); $[\alpha]_D$ −54.6 (*c* 1.2); IR ν_{max}(C=CH_2) 3005 cm^{-1}, ν_{max}(C=O) 1690 cm^{-1}, ν_{max}(C=C) 1640 cm^{-1}; ^{1}H NMR δ 0.66 (s, 3 H, 18-H), 0.73 (s, 3 H, 19-H), 0.86 (d, J = 6.6 Hz, 6 H, 26-H and 27-H), 0.89 (d, J = 6.6 Hz, 3 H, 21-H), 1.73 (t, ^4J = 1.7 Hz, 3 H, 4b−H), 2.12 (dd, $J_{7\alpha-H,7\beta-H}$ = 12.3 Hz, $J_{7\beta-H,8\beta-H}$ = 6.6 Hz, 1 H, 7β-H), 2.71 (d, $J_{2\alpha-H,3\alpha-H}$ = 6.9 Hz, 1 H, 3α-H), 6.96 (br s, 1 H, 4-H); ^{13}C NMR (75.5 MHz) δ 10.17 (C-4b), 12.36 (C-18), 18.79 (C-21), 20.93 (C-19), 22.07 (CH_2), 22.56 (C-26 or

C-27), 22.82 (C-26 or C-27), 23.88 (CH_2), 24.40 (CH_2), 27.43 (CH_2), 28.01 (CH), 28.59 (CH_2), 35.21 (CH_2), 35.66 (CH), 36.26 (CH_2), 38.48 (CH_2), 39.50 (CH_2), 39.69 (CH_2), 41.81 (CH), 43.95 (C-13), 53.35 (CH), 55.41 (CH), 55.77 (CH), 56.19 (C-10), 57.02 (CH), 67.20 (C-5), 141.50 (C-4a), 158.30 (C-4), 213.19 (C-6); MS (EI) *m*/*z* (%) 410 (100, M^+); MS (CI) *m*/*z* 411 (MH^+).

Stoichiometric Palladium(II)-Mediated Carbonylation of 20. *p*-Benzoquinone (32 mg; 296 μmol) and **20** (89 mg; 133 μmol) were added to a mixture of $(MeCN)_2PdCl_2$ (38 mg; 145 μmol) and THF (10 mL), then the flask was fitted with a CO balloon, the air was evacuated from the flask, and the CO was let in. The mixture was stirred at room temperature for 17 h, then quenched with H_2O (5 mL), and diluted with ether (50 mL). The ethereal layer was washed with 10% aqueous sodium dithionite solution (2 × 25 mL) and H_2O (20 mL). The solution was dried and the solvent evaporated, then the residue was adsorbed onto silica gel. Column chromatography was used to purify the mixture with petroleum ether and ether (4:1) as the eluent, which furnished the tetrahydrofuran derivative **22** (5.4 mg; 14 μmol; 11%) as the least polar and lactone **53** (30 mg; 73 μmol; 55%) as the more polar component.

Palladium(II)-Catalyzed Carbonylation of 20. *p*-Benzoquinone (51 mg; 472 mmol) and bromomercurio alcohol **20** (134 mg; 200 μmol) were added to a mixture of $(MeCN)_2PdCl_2$ (4 mg; 15 μmol; 8 mol %) and THF (10 mL), then the flask was fitted with a CO balloon, the air was evacuated from the flask, and the CO was let in. The mixture was stirred at 60 °C for 7 days, then quenched with H_2O, and diluted with ether. The ethereal layer was washed with 10% aqueous sodium dithionite solution (2 × 25 mL) and H_2O (20 mL); then the solution was dried and the solvent evaporated. The crude product was chromatographed with a petroleum ether−ether mixture (49:1) to furnish tetrahydrofuran **22** (35 mg; 89 μmol; 44%), identical with an authentic sample (see above). Continued elution with a 4:1 mixture afforded lactone **53** (12 mg; 29 μmol; 14%).

4b-Oxa-A-trishomo-B-nor-3α,5-cyclo-5α-cholestan-4a-one (53). A stoichiometric, palladium(II)-mediated carbonylation of **8**, as described above, furnished lactone **53** (55%): mp 142−144 °C (MeOH); $[\alpha]_D$ +25.6 (*c* 1.7); IR ν_{max}(C=O) 1740 cm^{-1}; ^1H NMR δ 0.65 (s, 3 H, 18-H), 0.87 (d, J = 6.6 Hz, 6 H, 26-H and 27-H) 0.92 (d, J = 6.3 Hz, 21-H), 0.98 (s, 3 H, 19-H), 2.56 (m, 1 H, 4-H), 4.02 and 4.16 (AB system, J = 11.6 Hz, 2 H, 6-H); ^{13}C NMR δ 12.21 (C-18), 17.97 (C-19), 18.72 (C-21), 21.68 (CH_2), 22.53 (C-26 or C-27), 22.77 (C-26 or C-27), 23.80 (CH_2), 24.41 (CH_2), 27.97 (CH), 28.46 (CH_2), 30.63 (CH_2), 35.32 (CH_2), 35.61 (CH), 36.18 (CH_2), 36.77 (CH_2), 39.45 (CH_2), 39.50 (CH_2), 40.76 (CH), 43.73 (C-13), 44.99 (CH_2), 46.86 (CH), 53.78 (C-10), 54.54 (CH), 54.67 (C-5), 55.61 (CH), 56.50 (CH), 72.55 (C-6), 174.27 (C-4a); MS (EI) *m*/*z* (%) 414 (83, M^+), 259 (100).

Acknowledgment. We thank the EPSRC for Grant GRH/65535 and an earmarked studentship to V.D.

Supporting Information Available: Experimental procedures and spectral data for the known compounds, HRMS and elemental analyses for new compounds, and details of the crystallographic analysis with a fully labeled ORTEP diagram,[98] atomic coordinates, selected bond lengths and angles, anisotropic displacement parameters, and hydrogen coordinates (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Note Added in Proof: While this paper was in press, Paquette reported on oxymercuration stereocontrolled by an homoallylic hydroxy group (Paquette, L. A.; Bolin, D. A.; Stepanian, M.; Branan, B. M.; Mallavadhani, U. V.; Tae, J.; Eisenberg, S. W. E.; Rogers, R. D. *J. Am. Chem. Soc.* **1998**, *120*, 11603; for an earlier observation, see: Thaisrivongs, S.; Seebach, D. *J. Am. Chem. Soc.* **1983**, *105*, 7407). These convincing examples of steering Hg^{2+} to the olefinic double bond by precoordination to a neighboring hydroxyl seem to be in direct conflict with our explanation of the preferential reactivity of **43**, i.e., coordination of Pd^{2+} and no coordination of Hg^{2+} and Tl^{3+} (Schemes 9−11). However, one has to bear in mind that whereas our system **43** is an *allylic* alcohol with a *tertiary* OH and a sterically well accessible *monosubstituted* C=C bond, the steering above was observed for *homoallylic*, *secondary* alcohols having a *1,2-disubstituted* C=C bond, so that differences in behavior would not be unexpected. Moreover, little difference was observed by us in the reactivity of **43** (an alcohol) and **44** (a methyl ether) toward Hg^{2+}, which does not seem to be compatible with the coordination model (compare this with the striking differences observed for Pd^{2+}). Finally, another homoallylic alcohol, namely 3β-acetoxy-cholest-5-en-19-ol (having a primary, *neopentyl* OH and a *trisubstituted* C=C bond), is known to react with Hg^{2+} in a "normal" way, i.e., by attack on the double bond from the sterically more accessible α-face, ignoring the coordination potential of the 19-hydroxyl (Kočovský, P. *Organometallics* **1993**, *12*, 1969), which is in sharp contrast to the vanadium-catalyzed epoxidation that has been shown to be directed by the 19-OH group (Kočovský, P. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1975). Hence, not even an homoallylic hydroxyl is always capable of stereodirection via precoordination, and that may also be the case of the tertiary allylic hydroxyl in **43**.

JO9812882