

# Molybdenum(V)-Mediated Skeletal Rearrangement of an Organomercury Steroid. Stereoelectronic Control and Mechanism

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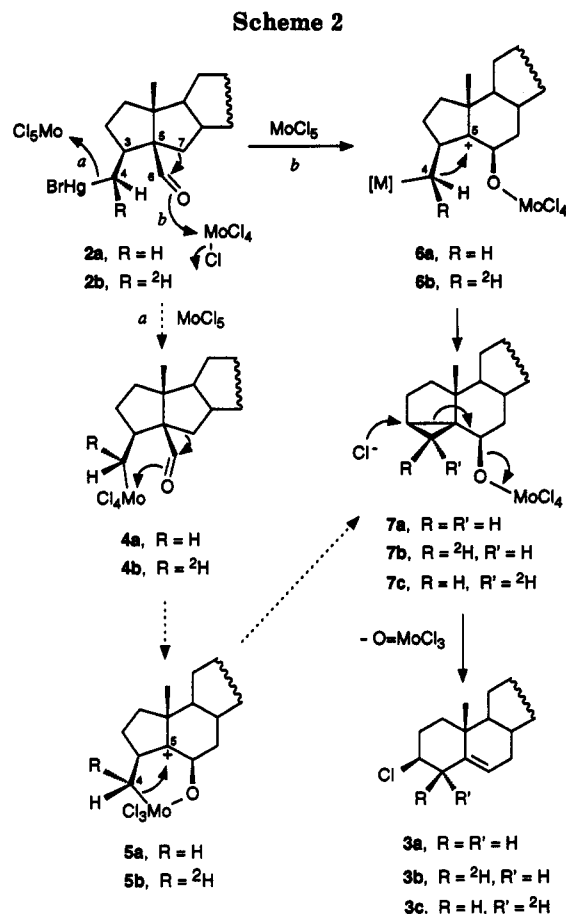
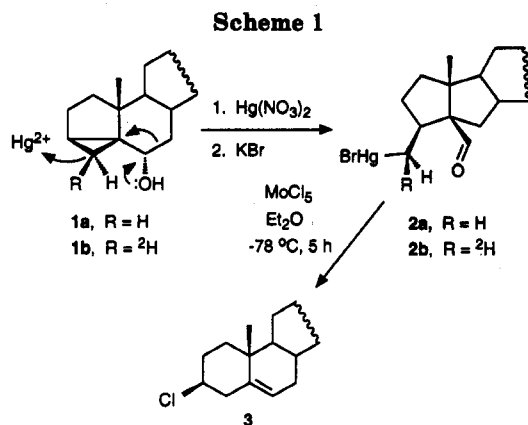
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The reactivity of organometallic species has been in the forefront of interest to synthetic organic chemists for a number of years.<sup>1</sup> While alkyllithiums, Grignard reagents, and organocuprates are highly reactive and sensitive, other organometallics, such as those with C-B, C-Sn or C-Hg bonds, are relatively stable and often require activation prior to the reaction.<sup>1</sup>

We have recently described a stereoelectronically controlled cleavage of 3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestan-6 $\alpha$ -ol (1a) by mercury(II)<sup>2,3</sup> that afforded the rearranged organomercurial 2a (97%) as a stable compound (Scheme 1).<sup>2-4</sup> We have also shown that transmetalation of 2a with Pd, Li, Cu, or Mo can be employed to synthesize various products and that the reactivity of the intermediate organometallics can be further controlled by added ligands.<sup>3,5</sup> Herein, we report on the stereospecific rearrangement of the organomercurial 2 initiated by molybdenum(V) chloride and other Lewis acids, discuss the mechanism, and show that, in contrast to other molybdenum reagents, transmetalation Hg  $\rightarrow$  Mo might not occur in this instance.

Organomercury steroid 2a was treated with MoCl<sub>5</sub> in ether at -78 °C and the reaction was monitored by TLC. When the starting material could no longer be detected (ca. 5 h), the mixture was worked up to afford cholesteryl chloride (3) as a single product (Scheme 1) in 78% isolated yield. This rather surprising outcome was tentatively rationalized in our preliminary communication<sup>5</sup> as follows (Scheme 2). Transmetalation of 2a with Mo was assumed as the initial step (pathway a) which would generate molybdenum species 4a (with extrusion of HgBrCl). Interaction of the highly oxophilic Mo(V) with the carbonyl oxygen would then trigger a stereoelectronically controlled Wagner-Meerwein migration to create the electron-deficiency at C<sub>(5)</sub> (4a  $\rightarrow$  5a). The cationic center in 5a is likely to interact with the nucleophilic carbon C<sub>(4)</sub> to



generate cyclopropyl intermediate 7a. The latter species should subsequently collapse to cholesteryl chloride (3a) via the well known<sup>6</sup> "iso-steroid" rearrangement.<sup>7</sup>

Taking advantage of the accessibility of the stereospecifically deuterated organomercurial 2b,<sup>8</sup> we have now been able to elucidate this mechanism in detail. According to our original mechanism (pathway a),<sup>5</sup> and assuming

(6) Kirk, D. N.; Hartshorn, M. P. *Steroid Reaction Mechanisms*; Elsevier: Amsterdam, 1968.

(7) Model experiments demonstrated that both 3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholestan-6 $\beta$ -ol and cholesterol are readily converted to 3 on treatment with MoCl<sub>5</sub> in Et<sub>2</sub>O at rt. 5 $\alpha$ -Cholestan-3 $\beta$ -ol was converted by the same reagent to a ca. 1:1 mixture of the corresponding 3 $\alpha$ - and 3 $\beta$ -chlorides, which indicates S<sub>N</sub>1 mechanism, in contrast to the former, stereoelectronically controlled substitutions.

(8) The (4*R*) configuration in 2b was established via chemical correlation. On treatment with Pd(II), the organomercurial 2b was converted into the lactol 14b in which the configuration at C<sub>(4)</sub> was determined using NOE experiments. For details, see refs 2 and 4.

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(1) (a) Davies, S. G. *Organotransition Metal Chemistry. Applications to Organic Synthesis*; Pergamon Press: Oxford, 1983. (b) Yamamoto, A. *Organotransition Metal Chemistry. Fundamental Concepts and Applications*; J. Wiley: New York, 1986. (c) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways for Organic Synthesis*; Plenum: New York, 1984. (d) Harrington, P. J. *Transition Metals in Total Synthesis*; J. Wiley: New York, 1990. (e) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. (f) Kočovský, P.; Tureček, F.; Hájíček, J. *Synthesis of Natural Products: Problems of Stereoselectivity*; CRC Press: Boca Raton, FL, 1986; Vols. I and II.

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

(3) (a) Kočovský, P.; Šrogl, J. *J. Org. Chem.* 1992, 57, 4565. (b) Kočovský, P.; Šrogl, J.; Hanuš, V.; Polášek, M. *J. Chem. Soc., Chem. Commun.* 1992, 1086.

(4) For a related reaction with Tl(III), see: Kočovský, P.; Pour, M.; Gogoll, A.; Hanuš, V.; Smrčina, M. *J. Am. Chem. Soc.* 1990, 112, 6735.

(5) Šrogl, J.; Kočovský, P. *Tetrahedron Lett.* 1992, 33, 5991.

retention of configuration in the transmetalation step<sup>10</sup> (2b → 4b), the coordination of Mo to the carbonyl oxygen requires rotation about the C<sub>(3)</sub>-C<sub>(4)</sub> bond. Subsequent Wagner–Meerwein migration will generate cationic species 5b in which the C<sub>(4)</sub>-C<sub>(5)</sub> bond formation should occur with retention of configuration at C<sub>(4)</sub> owing to the geometry imposed by the cyclic structure. The resulting cyclopropyl intermediate 7c should then produce 4α-<sup>2</sup>H-cholesteryl chloride (3c). Alternatively, MoCl<sub>5</sub> can be assumed to first coordinate to the aldehyde oxygen (path b) which may also trigger the Wagner–Meerwein migration generating carbocation 6b. The subsequent cyclopropane ring-closure is most likely to occur with inversion of configuration at C<sub>(4)</sub> (6b → 7b) due to the preferred conformation (6b) so that 4β-<sup>2</sup>H-cholesteryl chloride (3b) can be expected as the final product. Hence, utilizing the stereospecifically deuterated organomercurial 2b as the starting material should provide the answer as to which of the two proposed mechanisms does actually operate.

The reaction of deuterated 2b with MoCl<sub>5</sub> was carried out in the same way as for its unlabeled counterpart 2a. Analysis of the <sup>1</sup>H NMR spectrum of the resulting deuterated cholesteryl chloride established the configuration of deuterium as being 4β (i.e. 3b rather than 3c)<sup>9</sup> and revealed that the whole reaction sequence was remarkably stereospecific, as no other diastereoisomer could be detected by NMR. The 4β-<sup>2</sup>H configuration is compatible with inversion of configuration at C<sub>(4)</sub> in the C<sub>(4)</sub>-C<sub>(5)</sub> bond-forming step (6b → 7b). The other pathway (5b → 7c) can thus be excluded as it would require retention at C<sub>(4)</sub>.<sup>11</sup> The exact structure of 6 is unknown and it would be premature to make conclusions at this stage as to whether M = Hg or Mo. We believe that both species can serve as intramolecular nucleophiles to trap the C<sub>(5)</sub>-electron-deficient center. If, however, transmetalation had occurred, retention of configuration at C<sub>(4)</sub> is assumed.<sup>12</sup>

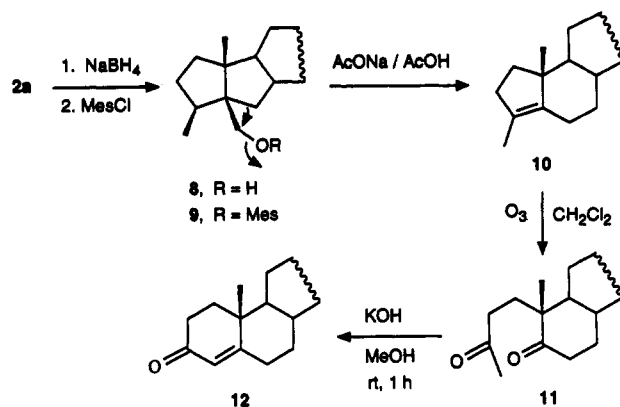
This analysis suggests that MoCl<sub>5</sub> serves as a Lewis acid and that transmetalation may not be required. To address this issue, the organomercurial 2a was treated with other Lewis acids, namely with AlCl<sub>3</sub>, SiCl<sub>4</sub>, and TiCl<sub>4</sub>. In all cases the reaction produced cholesteryl chloride (3a) in

(9) Diagnostic was the signal of 3α-H (at 3.77 ppm). While the width of this multiplet was 32.7 Hz for 3a, in the spectrum of the deuterated compound 3b (in which ≥95% of deuterium was revealed by HRMS) it was only 19.7 Hz, which indicated that one large (i.e. axial) coupling was missing. This is only compatible with the 4β-<sup>2</sup>H configuration. Compared with the spectrum of 3a, where the C(4) protons appear at 2.49 (4α-H) and 2.56 (4β-H) ppm, the latter signal is absent in the spectrum of 3b, and the former has lost its geminal coupling (13.5 Hz). For a detailed description of the <sup>1</sup>H NMR patterns in 4α-<sup>2</sup>H- and 4β-<sup>2</sup>H-cholesterol, see ref 10.

(10) Rabinowitz, M. H. *Tetrahedron Lett.* 1991, 32, 6081.

(11) An alternative explanation that would encompass transmetalation with inversion followed by the C<sub>(4)</sub>-C<sub>(5)</sub> bond formation with retention at C<sub>(4)</sub> (5 → 7) is unlikely in view of the generally accepted mechanism of transmetalations.<sup>10</sup>

(12) (a) A recent precedent<sup>13</sup> suggests that the carbon atom adjacent to HgX can serve as an effective nucleophile to quench an electron-deficient center. Hence, transmetalation of Hg for Mo may not be required in our case. (b) In order to address this issue, we have explored the reaction of PhCH<sub>2</sub>HgCl with MoCl<sub>5</sub>. The only product formed at rt over a period of 2 h was PhCH<sub>2</sub>Cl; no intermediate could be intercepted (by TLC and NMR). This transformation can be attributed either to the transmetalation followed by reductive elimination or to a disproportionation MoCl<sub>5</sub> → MoCl<sub>3</sub> + Cl<sub>2</sub> followed by chlorination of PhCH<sub>2</sub>HgCl. Thus, this experiment did not provide the conclusive evidence; however, transmetalation, if any, can be assumed to be considerably slower than our reaction. For a related transformation R<sub>2</sub>HgX → RCl by means of CuCl<sub>2</sub>, see: (c) Artamkina, G. A.; Beletskaya, I. P.; Reutov, O. A. *Zh. Org. Khim.* 1973, 9, 1769; *J. Org. Chem. USSR* 1973, 9, 1795. (d) Beletskaya, I. P.; Artamkina, G. A.; Reutov, O. A. *J. Organomet. Chem.* 1975, 99, 343. (e) Budnik, R. A.; Kochi, J. K. *J. Organomet. Chem.* 1976, 116, C3. (f) Heck, R. F. *J. Am. Chem. Soc.* 1968, 90, 5538.

Scheme 3<sup>a</sup>

<sup>a</sup> Mes = CH<sub>3</sub>SO<sub>2</sub>

good yields; MoCl<sub>5</sub>, however, turned out to be superior in terms of the reaction rate and purity of the product.<sup>14</sup> The stereochemistry of this transformation was tested for AlCl<sub>3</sub> and found to be identical with that of the MoCl<sub>5</sub> reaction (i.e. 2b → 3b).<sup>2</sup>

In order to gain further insight into the chemistry of this Lewis acid-mediated rearrangement and to assess the natural tendency of this [3.3.0] skeleton to rearrange, mesylate 9 was prepared from alcohol 8 which, in turn, was obtained by hydride reduction of 2a (Scheme 3). We reasoned that the presence of a good leaving group, such as CH<sub>3</sub>SO<sub>3</sub>, in place of the aldehyde oxygen might also induce the skeletal rearrangement<sup>15</sup> and provide further mechanistic support for the above conclusions. Standard solvolytic conditions (AcONa, AcOH, reflux) led to the formation of 10 as a single product, the structure of which was deduced from spectral data and confirmed by chemical correlation; ozonolysis resulted in the formation of diketone 11 which readily underwent a base-catalyzed aldol condensation to afford cholestenone (12). In the solvolysis of 9, the departure of the CH<sub>3</sub>SO<sub>3</sub> group is accompanied by Wagner–Meerwein rearrangement to generate the corresponding C<sub>(5)</sub>-cation which, in this instance, undergoes proton elimination to give 10. The behavior of mesylate 9 lends further credence to the above mechanistic considerations and suggests that MoCl<sub>5</sub> and other Lewis acids activate 2 as shown in pathway b (Scheme 2). Thus, while proton elimination is the best avenue for stabilizing the rearranged carbocation derived from mesylate 9, the cation 6 prefers to react with the neighboring nucleophilic center at C<sub>(4)</sub>.

Interestingly, the reactivity of MoCl<sub>5</sub> proved to be solvent dependent. In THF, chloro aldehyde 13a was formed as the major product from 2a (Scheme 4), rather than cholesteryl chloride.<sup>16</sup> Since 13a could not be fully

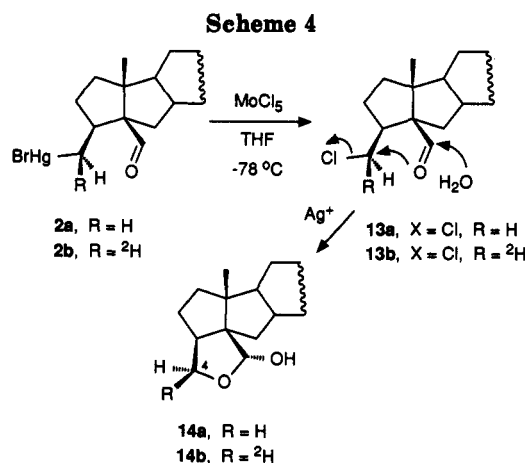
(13) (a) Takemoto, Y.; Ohra, T.; Yonetoku, Y.; Imanishi, T.; Iwata, C. *J. Chem. Soc., Chem. Commun.* 1992, 192. (b) Takemoto, Y.; Ohra, T.; Yonetoku, Y.; Nishimine, K.; Iwata, C. *J. Chem. Soc., Chem. Commun.* 1994, 81.

(14) While the reaction of 2a with MoCl<sub>5</sub> is complete in 5 h at -78 °C, only 50% conversion has been observed with AlCl<sub>3</sub> at rt over 5 days (!) and complete conversion has been achieved (with AlCl<sub>3</sub>) at 45 °C over 12 h.

(15) For skeletal rearrangements of a normal steroid skeleton with electron deficiency created at the angular methyl (C-19), see e.g.: (a) Kočovský, P.; Tureček, F. *Tetrahedron Lett.* 1981, 22, 2691. (b) Kočovský, P.; Tureček, F.; Langer, V.; Podlahová, J.; Podlaha, J. *J. Org. Chem.* 1986, 51, 4888 and references therein.

(16) Since MoCl<sub>5</sub> is known to react with THF to give (THF)<sub>2</sub>MoOCl<sub>3</sub>,<sup>17</sup> the latter is likely to be the actual reagent in this case.

(17) McAuliffe, C. A.; Werfali, A. *Inorg. Chim. Acta* 1980, 60, 87.



purified and characterized, its structure was determined by the silver(I)-mediated conversion<sup>18</sup> to lactol **14a**. The same reaction carried out with **2b** showed that **13** was formed nonstereospecifically as a ~2:1 mixture of **13b** and its C(4)-epimer.

In summary, we have observed interesting, stereoelectronically controlled, skeletal rearrangements. The key reaction **2** → **3** is apparently controlled by the combination of high oxophilicity of Mo(V) and stereoelectronic effects. The proposed mechanism is supported by stereospecific labeling and by analogous results in the solvolysis of **9**. Although the experiments were confined to the steroid skeleton, we believe that our findings are general and may be used for synthetic purposes, particularly in view of a number of methods for preparation of organomercurials.<sup>19</sup>

### Experimental Section

**General Methods.** Melting points were determined on a Kofler block and are uncorrected. The optical rotations were measured in CHCl<sub>3</sub> with a Perkin-Elmer 141 polarimeter at 22 °C with an error of  $\pm 1^\circ$ . The NMR spectra were recorded for CDCl<sub>3</sub> solutions at 25 °C on a Varian Unity 400 (operating at 400 MHz for <sup>1</sup>H, 100.6 MHz for <sup>13</sup>C, and 61.4 MHz for <sup>2</sup>H), Varian XL-300, or Bruker AM 300 spectrometer. Chemical shifts were indirectly referenced to TMS *via* the solvent signals (7.26 ppm for <sup>1</sup>H and <sup>2</sup>H, and 77.0 ppm for <sup>13</sup>C). The IR spectra were recorded in CHCl<sub>3</sub> on a Perkin-Elmer 621 instrument. The mass spectra were measured on a JEOL JMSD-100 spectrometer using direct inlet and the lowest temperature enabling evaporation. All reactions were carried out under nitrogen. Standard workup of an ethereal solution means washing with 5% HCl (aqueous), water, and 5% KHCO<sub>3</sub> (aqueous) and drying with MgSO<sub>4</sub>. Petroleum ether refers to the fraction boiling in the range 40–60 °C. The identity of samples prepared by different routes was checked by TLC and IR and NMR spectra. Yields are given for isolated product showing one spot on a chromatographic plate and no impurities detectable in the NMR spectrum.

**3 $\beta$ -Chloro-5-cholestene (3a).** Molybdenum(V) chloride (50 mg; 1.2 equiv) was added in small portions to a solution of organomercurial **2a** (100 mg; 0.15 mmol) in ether (10 mL) at -78 °C over a period of 1 h. The mixture was then stirred at the same temperature for 4 h. The mixture was then gradually warmed to rt, diluted with ether (20 mL), washed with water (5  $\times$  5 mL), 5% aqueous KHCO<sub>3</sub> (5  $\times$  5 mL), and water (5 mL), and dried with MgSO<sub>4</sub>. The solvent was evaporated and the residue was chromatographed on a column of silica gel with petroleum ether to yield **3a** (47 mg; 79%), identical with an authentic sample

(Fluka): mp 95–97 °C (ethyl acetate) (Fluka catalogue gives 94–96 °C); <sup>1</sup>H NMR  $\delta$  0.68 (s, 3H, 18-H), 1.04 (s, 3 H, 19-H), 2.49 (ddd,  $J_{\text{gem}} = 13.5$ ,  $J_{4\alpha\text{-H},3\alpha\text{-H}} = 5.1$ ,  $J_{4\alpha\text{-H},6\text{-H}} = 2.1$  Hz, 1 H, 4 $\alpha$ -H), 2.56 (m, 1 H, 4 $\beta$ -H), 3.77 (m,  $W = 32.7$  Hz, 1 H, 3 $\alpha$ -H), 5.38 (br d,  $J = 5.2$  Hz, 6-H); <sup>13</sup>C NMR  $\delta$  11.87 (q), 18.73 (q), 19.27 (q), 20.97 (t), 22.58 (q), 22.84 (q), 23.85 (t), 24.28 (t), 28.03 (d), 28.23 (t), 31.79 (d), 31.84 (t), 33.39 (t), 35.79 (t), 36.19 (t), 36.38 (s), 39.12 (t), 39.52 (t), 39.71 (t), 42.31 (s), 43.41 (t), 50.07 (d), 56.14 (d), 56.69 (d), 60.33 (d), 122.46 (d), 140.77 (s); MS  $m/z$  M<sup>+</sup> 406 (34%)/404 (91%).

**[4 $\beta$ <sup>2</sup>H]-3 $\beta$ -Chloro-5-cholestene (3b):** mp 94–96 °C; <sup>1</sup>H NMR  $\delta$  0.71 (s, 3 H, 18-H), 1.06 (s, 3 H, 19-H), 2.50 (m,  $W = 6$  Hz, 1 H, 4 $\alpha$ -H), 3.80 (m,  $W = 19.7$  Hz, 1 H, 3 $\alpha$ -H), 5.48 (dd,  $J = 5.5$  and 2.0 Hz, 1 H, 6-H); MS  $\geq 95\%$  <sup>2</sup>H (*d*<sub>1</sub>).

**3 $\beta$ -Methyl-5-(hydroxymethyl)-A,B-bisnor-5 $\beta$ -cholestane (8).** To a solution of **2a** (120 mg; 0.18 mmol) in ether (20 mL) and methanol (2 mL) was added sodium borohydride (321 mg; 8.48 mmol) and the mixture was stirred at 0 °C for 10 min. The excess of reagent was then decomposed with 5% aqueous HCl at -78 °C, and the mixture was diluted with ether and worked up to give alcohol **8** (44 mg; 0.113 mmol; 83%):  $[\alpha]_D^{+15}$  (c 1.2); IR  $\nu(\text{OH})$  3420, 3595 cm<sup>-1</sup>; <sup>1</sup>H NMR  $\delta$  0.66 (s, 3 H, 18-H), 0.88 (s, 3 H, 19-H), 1.02 (d, 3 H,  $J = 7.1$  Hz, 3 $\beta$ -CH<sub>3</sub>), 3.46 (d,  $J = 10.7$  Hz, 1 H, CH<sub>2</sub>OH), 3.70 (dd,  $J = 10.7$  and 1.0 Hz, CH<sub>2</sub>OH); <sup>13</sup>C NMR  $\delta$  12.27 (q), 15.98 (q), 18.79 (q), 18.93 (q), 22.10 (t), 22.57 (q), 22.83 (q), 23.88 (t), 24.57 (t), 28.02 (d), 28.61 (d), 31.05 (t), 35.70 (d), 36.26 (t), 38.57 (t), 39.51 (t), 39.92 (t), 40.40 (d), 41.17 (t), 42.85 (d), 43.77 (s), 51.67 (s), 55.76 (d), 56.37 (d), 57.75 (d), 64.72 (t). Anal. Calcd for C<sub>27</sub>H<sub>48</sub>O: C, 83.44; H, 12.45. Found: C, 83.17; H, 12.66.

**3 $\beta$ -Methyl-5-[(methanesulfonyl)oxy]methyl]-A,B-bisnor-5 $\beta$ -cholestane (9).** To a solution of the alcohol **8** (100 mg; 0.26 mmol) and triethylamine (0.4 mL) in THF (20 mL) was added mesyl chloride (0.2 mL) at -10 °C and the mixture was kept at this temperature for 1 h. The mixture was then poured onto ice and water, the product was extracted with ether, and the ethereal solution was worked up to furnish sufficiently pure mesylate **9** (117 mg; 97%): <sup>1</sup>H NMR  $\delta$  0.74 (s, 3 H, 18-H), 0.99 (s, 3 H, 19-H), 1.08 (d,  $J = 7.1$  Hz, 3 H, 3 $\beta$ -CH<sub>3</sub>), 3.12 (s, 3 H, CH<sub>3</sub>SO<sub>3</sub>), 4.14 and 4.30 (AB system,  $J_{\text{gem}} = 9.3$  Hz, 2 H, CH<sub>2</sub>OMes); <sup>13</sup>C NMR  $\delta$  12.16 (q), 15.42 (q), 18.62 (q), 18.83 (q), 21.85 (t), 22.43 (q), 22.68 (q), 23.71 (t), 24.35 (t), 27.86 (d), 28.41 (t), 31.07 (t), 35.50 (d), 36.09 (t), 37.03 (q), 38.19 (t), 39.35 (t), 39.60 (t), 40.32 (d), 41.36 (t), 43.01 (d), 43.62 (s), 52.56 (s), 55.56 (d), 55.77 (s), 56.05 (d), 57.52 (d), 72.04 (t).

**3-Methyl-A-norcholest-3(5)-ene (10).** A mixture of the mesylate **9** (100 mg; 0.21 mmol) and sodium acetate (200 mg; 2.44 mmol) in acetic acid (30 mL) was refluxed for 30 min. The mixture was then cooled to rt, diluted with ether and the ethereal solution was washed successively with water (10  $\times$  10 mL), KHCO<sub>3</sub> (aqueous; 5  $\times$  10 mL), and water and dried with MgSO<sub>4</sub>. The solvent was evaporated and the residue was chromatographed on silica gel (5 g) with petroleum ether as eluent to yield **10** (65 mg; 82%): mp 62–64 °C (acetone; lit.<sup>20</sup> gives 64–65 °C);  $[\alpha]_D^{+54}$  (c 5.3; lit.<sup>20</sup> gives +59°); <sup>1</sup>H NMR  $\delta$  0.68 (s, 3 H, 18-H), 0.76 (m, 1 H, 9 $\alpha$ -H), 0.87 (two d,  $J = 6.6$  Hz, 6 H, 26-H and 27-H), 0.90 (s, 3 H, 19-H), 0.91 (d,  $J = 6.6$  Hz, 3 H, 21-H), 1.11 (m, 1 H, 12  $\alpha$ -H), 1.47 (m, 1 H, 1 $\beta$ -H), 1.57 (br s, 3 H, =C-CH<sub>3</sub>), 1.64 (ddd,  $J = 12.4, 8.2$ , and 1.1 Hz, 1 H, 1 $\alpha$ -H), 1.71 (m, 1 H, 7 $\alpha$ -H), 1.81 (m, 1 H, 6 $\beta$ -H), 1.97 (ddd,  $J = 12.5, 3.6$ , and 3.0 Hz, 1H, 12 $\beta$ -H), 2.08 (ddm,  $J = 15.7$  and 9.6 Hz, 1 H, 2 $\beta$ -H), 2.27 (m, 1 H, 2 $\alpha$ -H), 2.33 (ddd,  $J = 14.1, 4.5$ , and 2.4 Hz, 1 H, 6 $\alpha$ -H); <sup>13</sup>C NMR  $\delta$  11.90 (q, C-18), 13.46 (q, C-4), 17.93 (q, C-19), 18.59 (q, C-21), 22.43 (q, C-26/27), 22.61 (two t, C-6 and C-11), 22.69 (q, C-26/27), 23.71 (t, C-23), 24.30 (t, C-15), 27.88 (d, C-25), 28.08 (t, C-12), 31.96 (t, C-7), 35.37 (t, C-2), 35.65 (d, C-20), 35.96 (d, C-8), 36.05 (t, C-16), 38.00 (t, C-1), 39.38 (t, C-24), 39.83 (t, C-22), 42.73 (s, C-13), 49.62 (s, C-10), 55.00 (d, C-9), 55.93 (d, C-17), 56.07 (d, C-14), 125.60 (s, C-3), 141.62 (s, C-5); MS  $m/z$  (%) 370 (34, M<sup>+</sup>), 355 (69), 147 (47), 135 (26), 122 (39), 109 (42), 93 (90), 57 (100).

**4,5-Secocholestane-3,5-dione (11).** Ozone was bubbled to a solution of olefin **10** (70 mg; 0.189 mmol) in dichloromethane (20 mL) at -48 °C and the progress of ozonization was monitored by

(18) (a) Kočovský, P. *J. Org. Chem.* 1988, 53, 5816. (b) Kočovský, P.; Pour, M. *J. Org. Chem.* 1990, 55, 5580 and references cited therein.

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TLC. When the reaction was complete, acetic acid (1 mL) and powdered zinc (500 mg) were added and the mixture was stirred at rt for 8 h. The inorganic solid was then filtered off and the filtrate was washed with water, 5% aqueous potassium hydrogen carbonate, and water, and dried with anhydrous  $\text{MgSO}_4$ . The solvent was evaporated in vacuo and the residue was chromatographed on silica gel (5 g) with a petroleum ether-ether mixture (9:1) to yield diketone 11 (70 mg; 92%):  $[\alpha]_D^{29} +29^\circ$  (c 5.8);  $^1\text{H NMR } \delta$  0.74 (s, 3 H, 18-H), 1.13 (s, 3 H, 19-H), 2.17 (s, 3 H, 4-H);  $^{13}\text{C NMR } \delta$  11.97 (q), 18.58 (q), 20.50 (q), 21.40 (t), 22.54 (q), 22.79 (q), 23.78 (t), 24.22 (t), 27.99 (d), 28.06 (t), 28.37 (t), 29.88 (q), 31.44 (t), 34.87 (d), 35.69 (d), 36.09 (t), 38.19 (t), 38.80 (t), 39.36 (t), 39.47 (t), 42.51 (s), 48.05 (d), 50.31 (s), 55.79 (d), 56.01 (d), 209.18 (s), 215.20 (s). Anal. Calcd for  $\text{C}_{27}\text{H}_{46}\text{O}_2$ : C, 80.54; H, 11.51. Found: C, 80.26; H, 11.75.

**Cholest-4-en-3-one (12).** To a solution of 11 (70 mg; 0.174 mmol) in methanol (10 mL) was added a 10% solution of NaOH in water (0.2 mL) and the mixture was stirred at rt for 1 h. The mixture was then diluted with ether and the ethereal solution was worked up to afford 12 (60 mg; 90%), identical with an authentic sample (Aldrich): mp 75–78 °C (acetone; Aldrich catalogue gives 79–81 °C).

**3 $\beta$ -Chloromethyl-A,B-bisnor-5 $\beta$ -cholestane-5-carbaldehyde (13a).** Molybdenum(V) chloride (200 mg) was introduced in small portions to a solution of organomercurial 2a (245 mg; 0.68 mmol) in THF (10 mL) at -78 °C over a period of 2 h. After this time, TLC indicated a completion of the reaction and, along with the main product 13a (ca. 90%), lactol 14a (ca. 5–10%) was

identified. The TLC analysis also revealed a slow conversion of 13a to 14a on silica gel, e.g. during the attempted flash chromatography. Therefore the chloride 13a could not be isolated in pure state and fully characterized:  $^1\text{H NMR } \delta$  0.66 (s, 3 H, 18-H), 0.97 (s, 3 H, 19-H), 2.50 (dd,  $J_{\text{gem}} = 12.9$  Hz,  $J_{7\beta\text{-H},8\beta\text{-H}} = 6.5$  Hz, 1 H, 7 $\beta$ -H), 3.68 (t,  $J = 7.5$  Hz, 2 H, 4-H), 9.68 (s, 1 H, CH=O). Treatment of the crude product with silver nitrate (120 mg; 0.7 mmol) in wet DME (10 mL) at rt for 5 h resulted in the deposition of AgCl and formation of 14a (119 mg; 80%), identical with an authentic sample,<sup>2,4</sup> which was purified by flash chromatography.

**Lactol (14a).** To a solution of chloro aldehyde 13a (80 mg; 0.19 mmol) in DME (5 mL) were added water (0.2 mL) and silver nitrate (50 mg; 0.29 mmol). The mixture was stirred at rt overnight and then filtered, and the filtrate was diluted with ether, washed with water, and dried with  $\text{MgSO}_4$ . The crude product was chromatographed on silica gel (5 g) with a petroleum ether-ether mixture (8:2) to furnish lactol 14a (71 mg; 91%), identical with an authentic sample.<sup>2,4</sup>

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