STEROIDS AND RELATED NATURAL PRODUCTS

XXXI. SELECTIVE REDUCTION OF ESTERS. PART B. CARBONATES[1]

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ABSTRACT

Direct reduction of several pivalate esters to neopentyl ethers has been accomplished with boron trifluoride – sodium borohydride. The utility of the reduction reaction was illustrated with esters I*c*, II*b*, and IV*a*. Under the same conditions, a selection (I*d*, II*d*, and IV*a*) of carbonate esters was found to be relatively resistant to reduction. In this respect, the carbonate esters resembled benzoate esters, and selective reduction of a ketone (II*d*) or another ester (IV*a* → IV*b*) in their presence was possible. For comparison, one xanthate ester (I*e*) was allowed to react with boron trifluoride – sodium borohydride, and only the corresponding alcohol (I*a*) was isolated. Raney nickel desulfurization of xanthate 1*a* was shown to provide alcohol 1*a* and hydrocarbon I*f* as principal products.

Prior studies of ester → ether reduction reactions with diborane – boron trifluoride type reagents indicated that the alcohol segment of the ester influences the yield of ether while the carbonyl portion can influence the ease of reduction. For example, a series of otherwise equivalent *n*-, *s*-, and *t*-butyl esters, when allowed to react with boron trifluoride – sodium borohydride, were transformed to the corresponding ethers with marked increments in yield (7–76%) as alkyl branching adjacent to the ester alcohol group increased (2). Under the same conditions, benzoate esters were found to be essentially unaffected (1). To define further the scope of these observations and to increase biological knowledge of steroidal ethers (e.g. see ref. 3), we have examined the reaction between boron trifluoride – sodium borohydride and several pivalate- and carbonate-type esters.

Appropriate esters derived from primary alcohol I*a* were chosen for initial model experiments. The requirements for 24-hydroxy-5β-cholane (I*a*) were conveniently met by modifying a prior route (see ref. 2 for leading literature citations) to this substance. Cholic acid was oxidized to dehydrocholic acid by a modification of the Jones' chromic acid technique, and after Wolff–Kishner reduction, the 5β-cholanic acid was reduced with commercial diborane in tetrahydrofuran.[4] Treating alcohol I*a* in pyridine solution with pivaloyl chloride gave ester I*b*. Previous experience (2) suggested that reduction of pivalate I*b* would provide neopentyl ether I*c* in approximately 10% yield, and indeed 13% conversion was realized. Although the actual reagent used in this experiment was diborane – boron trifluoride,[5] all subsequent reduction reactions were carried out with a boron trifluoride – sodium borohydride reagent.[6] Next, pivalate ester II*b*, prepared from

[1]*For part XXX in this series, refer to ref. 1. The present contribution is based on part of the Ph.D. dissertation submitted by W. J. Evers to the Graduate School, University of Maine, Orono, Maine, December 1964.*

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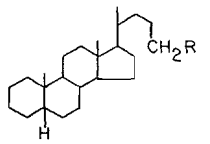
[4]*Carboxylic acids may even be reduced selectively by diborane in the presence of ketones (4a). For example, by employing a calculated amount of diborane, levulinic acid has been reduced to 4-oxopentanol (4b).*

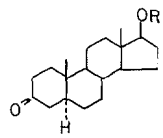
[5]*Reaction between diborane, boron trichloride, and diethyl ether or tetrahydrofuran has been shown to yield a dichloroborane etherate with the composition* $HCl_2B \cdot OR_2$ *or, when a limited amount of boron trichloride is used, a monochloroborane etherate* ($H_2ClB \cdot OR_2$) *(5). At room temperature, chloroborane etherate was found to reduce (rapidly) certain ketones, but did not affect esters such as ethyl acetate (compare with ref. 6). Interestingly, Brown and Tierney (5a) did not detect a similar reaction between diborane and boron trifluoride. Boron trifluoride etherate has recently been expressed (5b) as* $F_2B[O(CH_2CH_3)_2]_2BF_4$.

[6]*The present series of experiments was performed by adding a solution of sodium borohydride in diglyme to the ester – boron trifluoride mixture. Except for possible lower overall ester → ether conversion (cf. ref. 2), no other important differences were noted when this "reverse" technique was used.*

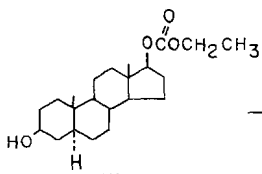
3-oxo-17β-hydroxy-5α-androstane and trimethylacetyl chloride, was reduced by boron trifluoride – sodium borohydride in diglyme–tetrahydrofuran. The product was subjected to oxidation with an 8 *N* chromic acid reagent, and neopentyl ether II*c* was isolated in 55% yield. The oxidation step eliminated separation of the 3β- and 3α-hydroxy epimers formed during reduction. Interestingly, when reduction was repeated with diethyl ether in place of tetrahydrofuran, only 17% conversion into ether II*c* was noted and 21% of ester II*b* was recovered. The lower yield suggests that the rate of reduction is temperature dependent, but this point was not pursued further. Reduction of the pivalate esters illustrates a new and convenient route to neopentyl ethers[7] and further confirms that alkyl branching adjacent to the carbonyl moiety has little influence on the yield of corresponding ether(s).



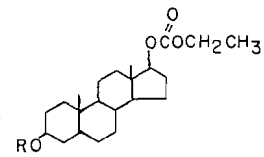
Ia, R=OH
Ib, R=OCOC(CH$_3$)$_3$
Ic, R=OCH$_2$C(CH$_3$)$_3$
Id, R=OCOCH$_2$CH$_3$
Ie, R=OCSCH$_3$
If, R=H



IIa, R = H
IIb, R = COC(CH$_3$)$_3$
IIc, R = CH$_2$C(CH$_3$)$_3$
IId, R = C-OCH$_2$CH$_3$



III



IVa, R = COC(CH$_3$)$_3$
IVb, R = CH$_2$C(CH$_3$)$_3$

Extending the reduction reaction to ethyl carbonate I*d*, prepared from alcohol I*a* and ethyl chloroformate,[8] was expected either to yield a methylenedioxy derivative or to provide an example of relative unreactivity.[9] In practice, ester I*d* was essentially unaffected (98% recovery), and when an attempt at reduction was repeated with boron trichloride (6*b*) in place of boron trifluoride, carbonate I*d* was recovered in 92% yield. Also, 3-oxo-17β-ethoxycarbonyloxy-5α-androstane (II*d*) was prepared and reduced, and the product reoxidized as with ester II*b*; a significant quantity (33%) of the starting ketoester was recovered. Decreased reactivity of carbonate ester II*d* was then demonstrated by a selective reduction sequence. Ketone II*d* was reduced by sodium borohydride in methanol

[7]*Recently, Eliel and Daignault (6a) have applied the lithium aluminium hydride – boron trifluoride reagent to reduction of thiol esters and have, for example, converted cyclohexyl thiopivalate into cyclohexyl neopentyl sulfide (33% yield).*

[8]*A recent review of reactions between chloroformates and alcohols has been prepared (7).*

[9]*If one assumes a molecular orbital picture for carbonate esters with the carbonyl group in an extended π bond overlap system, a reduced rate of reaction with diborane – boron trifluoride, as already experienced with benzoate esters (1), might be predicted.*

to a mixture of the corresponding C-3 epimeric alcohols. The more polar constituent, assumed to be equatorial alcohol III, was isolated by column chromatography and treated with trimethylacetyl chloride in pyridine. Applying the same reduction conditions (see II*b*) to diester IV*a* gave a mixture composed principally of neopental ether IV*b* and starting material (IV*a*) in essentially equal amounts (approximately 20% each). Results of the preceding reduction reactions suggest that carbonate esters, like benzoate esters, will, in general, display reduced reactivity.

The possibility that xanthate-type esters might be of greater utility than carbonates was discounted when thiocarbonate I*e* was found to yield (82%) alcohol I*a*. Since the fate of the alkoxy group during Raney nickel desulfurization of xanthate esters has, to our knowledge, not been determined (8), the present series of experiments was concluded by subjecting xanthate I*e* to desulfurization with an acid-washed (8*c*) W-4 Raney nickel. The major product was alcohol I*a* accompanied by 5β-cholane (I*f*).[10]

EXPERIMENTAL

All solvents were redistilled. A description of reagents and pretreatment of several solvents used in the present study appears in the Experimental sections of two prior contributions (1, 6*b*). Diborane (1 *M*) in tetrahydrofuran was employed as received from Metal Hydrides Division, Ventron Corp. Except for column chromatographic grade (0.02–0.5 mm) silica gel (E. Merck, A.G.) and Mallinckrodt chemical silicic acid (100 mesh), all other chromatographic and thin-layer techniques have been noted in refs. 1 and 6*b*.

After a crude reaction product had been partitioned between solvent and aqueous phase, the solvent layer was dried over anhydrous sodium sulfate or potassium carbonate. Each analytical sample was colorless, and its melting point was determined on a Kofler melting point apparatus. Unless otherwise indicated, the remaining melting points were determined in open Kimble glass capillary tubes immersed in a silicone oil bath. Optical rotation measurements (in the laboratory of Dr. C. Janssen, Beerse, Belgium) were conducted in chloroform solution. Infrared (in potassium bromide) and proton magnetic resonance (on a Varian Associates model A-60 nuclear magnetic resonance spectrometer) spectra were recorded by Dr. R. A. Hill, University of Maine. Elemental analyses were provided by Dr. A. Bernhardt, Mülheim, Germany.

3,7,12-Trioxo-5β-cholanic Acid

A solution of cholic acid (62 g) in acetic acid (370 ml) – acetone (1.5 l) was treated (room temperature, stirring) with an 8 *N* chromic acid reagent (9) until the orange color persisted for 15 min. Excess chromic acid was reduced with methanol, and solvent was removed (steam bath, *in vacuo*) until a precipitate began to separate. The solid was redissolved by adding acetic acid and the resulting solution was diluted with approximately 2 l of water. The solid product was collected, washed with water, and recrystallized from methanol (300 ml) to yield 40 g of dehydrocholic acid melting at 234–237° (ref. 10 reports m.p. 237–238°). The product was used without further purification for reduction.

24-Hydroxy-5β-cholane (Ia)

Commercial 1 *M* diborane in tetrahydrofuran (15 ml) was added to 5β-cholanic acid (2.7 g) in the same solvent (28 ml) at room temperature. Sixteen hours later the solution was diluted with water (15 ml) and diethyl ether (100 ml). The ethereal phase was separated, washed with water, and evaporated. The solid residue was recrystallized from ethyl acetate to give alcohol I*a* (2.2 g), m.p. 129.5–131° (ref. 10 reports m.p. 130.5–132.5°).

24-(2,2-Dimethyl)propionyloxy-5β-cholane (Ib)

A reaction mixture prepared from pyridine (16 ml), 24-hydroxy-5β-cholane (2.2 g), and 5 ml of 2,2-dimethylpropionyl chloride (11) was allowed to remain at room temperature for 1 h. After dilution with water (20 ml) – diethyl ether (60 ml), the ethereal solution was washed successively with water, 10% hydrochloric acid, and water. Removal of solvent (*in vacuo*) gave a viscous residue (2.3 g) which was crystallized from acetone–methanol to yield 1.8 g, m.p. 59.5–61.5°. Two recrystallizations from the same solvent system gave an analytical specimen as plates melting at 63–64°, $[\alpha]_D^{20}$ +9° (*c*, 5.63); ν_{max} 1 730, 1 282, and 1 158 cm^{-1}.

Anal. Calcd. for $C_{29}H_{50}O_2$: C, 80.86; H, 11.56; O, 7.43. Found: C, 81.34; H, 11.85; O, 6.90.

24-(2,2-Dimethyl)propoxy-5β-cholane (Ic)

Diborane (1 *M*) in tetrahydrofuran (4 ml) was added to pivalate ester I*b* (0.90 g) in tetrahydrofuran (10 ml) – boron trifluoride etherate (10 ml) and the solution was heated at reflux for 1 h. After it was cooled

[10]*Hydrocarbon If may have arisen by a Chugaev-type elimination leading to 5β-chol-23-ene, which would undergo ready hydrogenation in the presence of Raney nickel catalyst.*

water was added and the mixture extracted with hexane. The combined hexane extracts were chromatographed on activated alumina. Elution with the same solvent gave 0.12 g of neopentyl ether I*c*, which was recrystallized from acetone as plates melting at 69.5–70°, $[\alpha]_D^{20}$ +17° (*c*, 1.21), ν_{max} 1 120 cm^{-1}.

Anal. Calcd. for $C_{29}H_{52}O$: C, 83.58; H, 12.58. Found: C, 83.57; H, 12.46.

*3-Oxo-17β-(2,2-dimethyl)propionyloxy-5α-androstane (II*b*)*

Except for a 2 day reaction period at room temperature, 3-oxo-17β-hydroxy-5α-androstane (II*a*, 2.0 g) in pyridine (15 ml) – diethyl ether (20 ml) was converted into pivalate II*b* with pivaloyl chloride (5 ml) as noted for ester I*b*. Recrystallizing the product from ethyl acetate – ethanol yielded 1.4 g of ester II*b* melting at 199–200° (Fisher–Johns melting point apparatus). A pure sample was recrystallized from acetone–methanol as waxy needles, m.p. 194.5–196°, $[\alpha]_D^{20}$ +28° (*c*, 7.15); ν_{max} 1 720, 1 282, 1 171, and 1 032 cm^{-1}.

Anal. Calcd. for $C_{24}H_{38}O_3$: C, 76.96; H, 10.22; O, 12.82. Found: C, 76.94; H, 10.10; O, 12.86.

*3-Oxo-17β-(2,2-dimethyl)propoxy-5α-androstane (II*c*)*

Sodium borohydride (0.16 g) in diethylene glycol dimethyl ether (diglyme, 6 ml) was added to an ice-cold solution of pivalate II*b* (0.51 g) in tetrahydrofuran (20 ml) – boron trifluoride etherate (8 ml). Before the mixture was heated at reflux for 1 h, cooling was continued for 50 min. Next, water was added and the mixture extracted with chloroform. The combined extracts were washed with water and solvent removed *in vacuo*. Residual solid (0.47 g) was dissolved in acetone (50 ml) and treated with an 8 *N* chromic acid reagent (9) until the orange color remained for 5 min. After dilution with water (50 ml) and extraction with chloroform, removal (*in vacuo*) of solvent yielded 0.38 g of crystalline residue. A solution of the residue in benzene–chloroform (7:3) was chromatographed on activated alumina (13 g). Elution with the same solvent mixture gave 0.28 g of neopentyl ether II*c*. A thin-layer chromatogram (13:3 hexane – diethyl ether as the mobile phase) of the product displayed only one spot, and recrystallization from ethanol–water yielded 0.20 g melting at 189–191.5°. A second recrystallization from acetone gave crystals with the same melting point. The analytical sample exhibited $[\alpha]_D^{20}$ +13° (*c*, 0.73) and ν_{max} 1 715, 1 145, 1 119, and 1 102 cm^{-1}.

Anal. Calcd. for $C_{24}H_{40}O_2$: C, 79.94; H, 11.18; O, 8.88. Found: C, 79.80; H, 11.20; O, 8.82.

When the reduction was repeated with 0.27 g of pivalate ester II*b* and diethyl ether (20 ml) in place of tetrahydrofuran, only 0.047 g, m.p. 188–191°, of neopentyl ether II*c* was obtained. Continued elution of the column chromatogram with chloroform gave 0.06 g of starting ester II*b* melting at 193–195°.

*24-Ethoxycarbonyloxy-5β-cholane (I*d*)*

Ethylchloroformate (6 ml) was added during a 10 min period to 24-hydroxy-5β-cholane (I*a*, 2.0 g) in pyridine (15 ml) – benzene (40 ml). After the solution had stood for 5 min at room temperature, water (20 ml) was added, the aqueous phase discarded, and the benzene solution washed with 2 *N* hydrochloric acid and water. The benzene solution was concentrated to an oily residue, which was dissolved in 1:1 hexane–benzene and chromatographed on activated alumina (60 g). Elution with the same solvent mixture gave an oil which crystallized on standing. Recrystallization from methanol–acetone yielded 1.9 g melting at 69.5–72°. Three recrystallizations from the same solvent system gave a pure specimen as plates, m.p. 69.5–72°, $[\alpha]_D^{22}$ +28° (*c*, 1.23); ν_{max} 1 742, 1 250, 1 030, 1 010, 995, 953, 875, 859, and 792 cm^{-1}.

Anal. Calcd. for $C_{27}H_{46}O_3$: C, 77.45; H, 11.07; O, 11.46. Found: C, 77.74; H, 11.05; O, 11.47.

*Attempted Diborane – Boron Trihalide Reduction of 24-Ethoxycarbonyloxy-5β-cholane (I*d*)*

Procedure A

Reaction between carbonate ester I*d* (0.5 g) and sodium borohydride (0.11 g) – boron trifluoride etherate (13 g) was attempted essentially as described for ester II*b*, except that the hour at reflux (increased reductive cleavage) was not employed. After recrystallization from acetone–methanol, the product weighed 0.43 g, m.p. 69.5–71°, and was identical with ester I*d*.

Procedure B

The experimental approach summarized in procedure A was repeated with boron trichloride (7 ml) in place of boron trifluoride etherate. Here, reaction was carried out with diglyme (20 ml) as solvent and 0.59 g of carbonate ester I*d*. The product,[11] 0.50 g, m.p. 69.5–71°, was carbonate I*d*.

*3-Oxo-17β-ethoxycarbonyloxy-5α-androstane (II*d*)*

Preparation of ethyl carbonate II*d* (10 g crude yield, m.p. 129–136°) was accomplished by the method summarized above for obtaining ester I*d*, with appropriately adjusted quantities of reagents. The analytical specimen was recrystallized from 95% ethanol as fine plates, m.p. 138–139°, $[\alpha]_D^{22}$ +27° (*c*, 4.76); ν_{max} 1 738, 1 710, 1 270, 1 020, 992, 972, 890, 879, and 790 cm^{-1}.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.89; H, 9.45; O, 17.65. Found: C, 72.80; H, 9.20; O, 17.86.

*Reaction of 3-Oxo-17β-ethoxycarbonyloxy-5α-androstane (II*d*) with Sodium Borohydride – Boron Trifluoride*

Ketone II*d* (1.1 g) was allowed to react with the boron trifluoride – sodium borohydride reagent as noted with pivalate ester II*b*. The crude product (1.1 g) was reoxidized with 8 *N* chromic acid reagent (cf. II*b*),

[11]*Identification was supported by the results of mixture melting point determination and infrared spectral comparison.*

and a solution of the oxidation product (0.85 g) in 17:3 benzene–chloroform was chromatographed on activated alumina (15 g). Elution with the same solvent mixture gave 0.33 g of starting carbonate ester (II*d*). Two recrystallizations from hexane gave 0.26 g of carbonate ester II*d* melting at 136–137°.[11] Continued elution with more polar solvents gave fractions with a combined weight of 0.39 g, but each was shown (by thin-layer chromatography) to contain substances considerably more polar than ester II*d*. The mixtures were not further separated.

3β-Hydroxy-17β-ethoxycarbonyloxy-5α-androstane (III)

A solution composed of 3-oxo-17β-ethoxycarbonyloxy-5α-androstane (II*d*, 8.0 g), sodium borohydride (3.0 g), and methanol (350 ml) was allowed to remain at room temperature for 3 h. After dilution with *N* hydrochloric acid (250 ml) and water (750 ml), the aqueous mixture was extracted repeatedly with diethyl ether. The combined extracts were washed with water and concentrated to a crystalline residue (6.0 g). A thin-layer chromatogram (1:1 hexane – diethyl ether as the mobile phase) of the residue indicated the presence of two substances with very similar R_f values: presumably the 3α- and 3β-isomers. A solution of the mixture in hexane – diethyl ether (3:2) was chromatographed on silica gel (430 g). A fraction eluted with the same solvent mixture gave 1.1 g of the more polar (on a thin-layer chromatogram) component. Two recrystallizations from hexane–chloroform and one from acetone led to a pure specimen of the 3β-isomer III, m.p. 132–133°, $[\alpha]_D^{20}$ +6° (*c*, 1.33); ν_{max} 3 500, 1 750, 1 740, 1 265 (broad), 1 050, 1 030, 1 014, 975, 881, and 790 cm^{-1}.

Anal. Calcd. for $C_{22}H_{36}O_4$: C, 72.49; H, 9.95; O, 17.56. Found: C, 72.52; H, 9.84; O, 17.56.

3β-(2,2-Dimethyl)propionyloxy-17β-ethoxycarbonyloxy-5α-androstane (IVa)

Alcohol III (0.16 g) was converted into pivalate ester IV*a* as described for ester II*b*. After recrystallization from 95% ethanol, ester IV*a* weighed 0.12 g and melted at 114–117°. A second recrystallization from the same solvent gave an analytical specimen as leaflets, m.p. 116–117°, $[\alpha]_D^{20}$ −10.9° (*c*, 1.83); ν_{max} 1 740, 1 720, 1 280 (broad with shoulders at 1 290 and 1 260), 1 172, 1 010, 969, 881, and 792 cm^{-1}.

Anal. Calcd. for $C_{27}H_{44}O_5$: C, 72.28; H, 9.88; O, 17.83. Found: C, 72.51; H, 10.01; O, 17.44.

3β-(2,2-Dimethyl)propoxy-17β-ethoxycarbonyloxy-5α-androstane (IVb)

Reduction of 3β-(2,2-dimethyl)propionyloxy-17β-ethoxycarbonyloxy-5α-androstane (IV*a*, 0.54 g) with boron trifluoride etherate (15 ml) – sodium borohydride (0.14 g) in tetrahydrofuran (25 ml) – diglyme (7 ml) was performed essentially as described for ester II*b*. However, 15 min at ice-bath temperature and 45 min at reflux were employed here. A solution of crude product (0.52 g) in hexane–benzene (1:1) was chromatographed on activated alumina (15 g). The same solvent eluted 0.1 g of neopentyl ether IV*b*, which was crystallized from ethanol–water as fine needles, m.p. 98–99°, $[\alpha]_D^{20}$ 0.0°; ν_{max} 1 740, 1 270, 1 109 (shoulder at 1 100), 1 018 (shoulder at 1 005), 980, 880, and 795 cm^{-1}.

Anal. Calcd. for $C_{27}H_{46}O_4$: C, 74.60; H, 10.59; O, 14.70. Found: C, 74.74; H, 10.59; O, 14.64.

A fraction eluted by 19:1 benzene–chloroform weighed 0.12 g and was identical[11] with starting diester IV*a*. Continued elution with 9:1 chloroform–methanol gave 0.23 g of a mixture of two alcohols (indicated by thin-layer chromatography), apparently arising from ester cleavage; these alcohols were not further characterized.

24-Methylthiolthiocarbonyloxy-5β-cholane (Ie)

A mixture of toluene (200 ml), 24-hydroxy-5β-cholane (I*a*, 15 g), and potassium (1.7 g) was heated at reflux for 16 h. After the solution was cooled to room temperature, carbon disulfide (5 g) was added, followed in 1 h by methyl iodide (5 ml). When a total of 4 h had elapsed, the solution was filtered and the solvent concentrated *in vacuo* to a red oil. The residue in hexane–benzene (1:1) was passed through a column of silicic acid to yield a yellow oil, which crystallized, m.p. 84–87°, upon trituration with methanol. When a thin-layer chromatogram (hexane as the mobile phase) indicated the presence of impurities, a 1.5 g portion of the product in hexane was chromatographed on acid-washed alumina (45 g). Of five fractions eluted by hexane–benzene (9:1), the fourth was pure as evidenced by a thin-layer chromatogram (hexane as the mobile phase); this fraction was recrystallized from 2-propanol–hexane to yield 0.35 g of needles melting at 87.5–89°, $[\alpha]_D^{20}$ +17.4° (*c*, 1.55); ν_{max} 1 379, 1 249, 1 225, 1 118, and 1 060 cm^{-1}.

Anal. Calcd. for $C_{26}H_{44}OS_2$: C, 71.50; H, 10.15; O, 3.66; S, 14.68. Found: C, 71.97; H, 10.10; O, 3.81; S, 14.08.

Reaction of 24-Methylthiolthiocarbonyloxy-5β-cholane (Ie) with Boron Trifluoride – Sodium Borohydride

Xanthate I*e* (2.0 g) was allowed to react with boron trifluoride (22 ml) – sodium borohydride (0.50 g) as described for ketone II*b*. A solution of crude product (1.6 g) in benzene–chloroform (4:1) was chromatographed on activated alumina. Elution with the same solvent gave 1.3 g of 24-hydroxy-5β-cholane (I*a*) melting at 130–131° after one recrystallization from ethyl acetate.[11]

Reaction of 24-Methylthiolthiocarbonyloxy-5β-cholane (Ie) with W-4 Raney Nickel

A sample (from 40 g of Raney nickel alloy) of W-4 Raney nickel (12) was washed successively with 0.4% acetic acid (2 × 500 ml), water (4 × 500 ml), 95% ethanol (2 × 100 ml), ethanol (3 × 150 ml), and tetrahydrofuran (3 × 150 ml). After the final washing, a mixture of xanthate I*e* (1.0 g) in tetrahydrofuran

(250 ml) and the nickel was heated at reflux for 14 h. The nickel residue was collected and washed with tetrahydrofuran (50 ml), and the combined filtrates were evaporated *in vacuo*. Chromatographing the crude product (0.96 g) in hexane on activated alumina and eluting with the same solvent gave 0.29 g of 5β-cholane melting at 91–92° (homogeneous on a thin-layer chromatogram with hexane as the mobile phase). Recrystallization from acetone gave 0.21 g, m.p. 91–92° (ref. 13 reports m.p. 90–91°); ν_{max} 2 950, 2 840, 1 450 (shoulder at 1 465), and 1 379 cm^{-1}; proton magnetic resonance (deuteriochloroform solution): broad response from 0.5 to 2.1 δ with methyl group signals at 0.65, 0.91, and 1.25 δ.

A series of fractions eluted by 13:7 hexane–benzene were found by thin-layer chromatography to consist of two or more components in small amounts, and were not further separated. However, the fraction eluted by chloroform provided 0.34 g of 24-hydroxy-5β-cholane[11] which melted at 130–131° after one recrystallization from ethyl acetate.

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