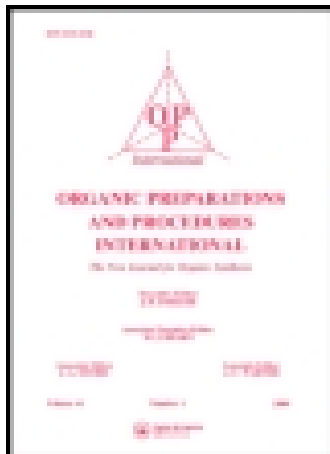


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A FACILE SYNTHESIS OF 3 β -ACETOXYLANOST-8-EN-24-ONE (24-KETOLANOSTERYL ACETATE)

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**A FACILE SYNTHESIS OF 3 β -ACETOXYLANOST-8-EN-24-ONE
(24-KETOLANOSTERYL ACETATE)**

Submitted by
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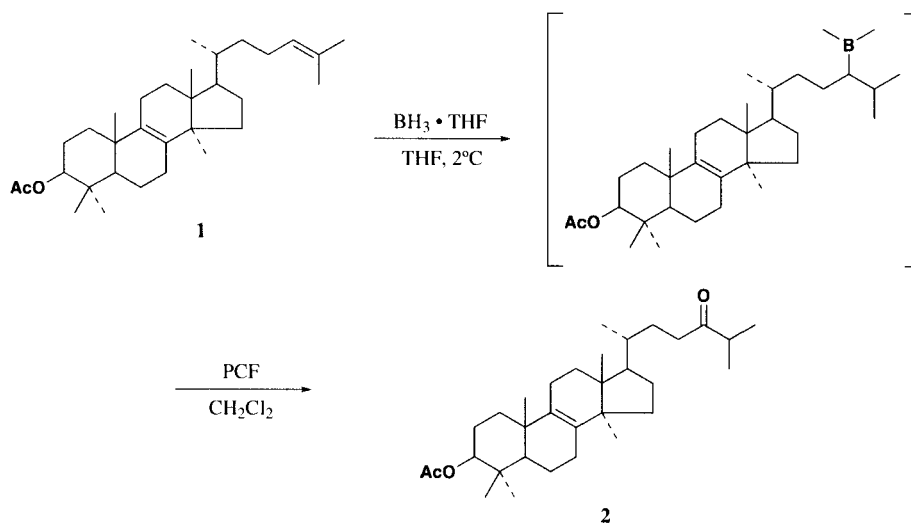
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The C-24 carbon of lanosterol is a major site of the sterol metabolism in plants, fungi, and animals.¹⁻³ As a result of our continuing studies on sterol biosynthesis, we have devised a simplified chemical synthesis of 3 β -acetoxy-lanost-8-en-24-one (**2**, 24-ketolanosteryl acetate), a key intermediate in the synthesis of C-24 alkylated metabolites and potential regulators of sterol biosynthesis. We now report a rapid and convenient chemical synthesis of **2** utilizing commercial lanosterol as a starting material.

Previous syntheses have required multiple-step procedures resulting in poor yields.⁴⁻⁷ In the present study, we have utilized the technique of hydroboration to form an organoborane intermediate, oxidation of which by pyridinium fluorochromate (PFC) in refluxing methylene chloride gave ketone **2**, in high yield. PFC is a mild and selective oxidant and has been used in the oxidation of a number of organic compounds.⁸⁻¹⁰



The high yield, anhydrous conditions and easy work-up make this a highly convenient method for the synthesis of **2** and expands the scope and utility of using PFC in organic oxidations.

EXPERIMENTAL SECTION

Procedures and conditions for the recording of melting points, infrared (IR) spectra, proton magnetic resonance (^1H -NMR) spectra, mass spectra (MS), thin-layer chromatography (TLC), gas liquid chromatography (GLC) and column chromatography have been detailed previously.¹¹ Commercial lanosterol (Sigma Chemical Co., St. Louis, MO) was purified by four recrystallizations from acetone/water and after recrystallization was found to be a mixture of lanosterol (61%) and 24,25-dihydrolanosterol (39%) upon GLC analysis. Acetylation of purified commercial lanosterol was accomplished by using acetic anhydride and pyridine which yielded lanosteryl acetate. PFC and borane-tetrahydrofuran complex ($\text{BH}_3\cdot\text{THF}$, 1.0 *M* solution in THF) were obtained from Aldrich Chemical Co. (Milwaukee, WI).

3 β -Acetoxylanost-8-en-24-one (24-ketolanosteryl acetate, 2).- Lanosteryl acetate (**1**, 12.0 g, approx. 15.6 mmol based on 61% purity), prepared as above, was dissolved in THF (75 mL) and cooled to 2° in an ice- H_2O bath. While maintaining a N_2 atmosphere, 10 mL (10 mmol) of a 1 *M* $\text{BH}_3\cdot\text{THF}$ solution was added over a 10 min period. The reaction was stirred for 1 h at 2° under N_2 . Ice was then cautiously added to decompose the excess hydride, H_2O (100 mL) was added, and the reaction mixture thoroughly extracted with ether (1000 mL). The extracts were dried over anhydrous MgSO_4 evaporated at reduced pressure, toluene was added and the solvent evaporated at reduced pressure (rotovap) to remove traces of H_2O (azeotrope).

The residue was dried in a vacuum dessicator over P_2O_5 for 2 h and dissolved in methylene chloride (100 mL), PFC (15 g) and molecular sieves (100 mg, type 4) were added, and the reaction mixture refluxed for 3 h. Saturated aqueous sodium chloride (500 mL) was added and the mixture was extracted with methylene chloride. The solvent was removed at reduced pressure and the residue subjected to column chromatography using an increasing gradient (50-95%) of toluene in hexane as the eluting solvent. The less polar component eluted first and after removal of the solvent, under reduced pressure, was recrystallized from acetone/water to yield 3.93 g (approx. 84% from the 24,25-dihydrolanoesteryl acetate portion of lanosteryl acetate) of 24,25-dihydrolanosteryl acetate, mp. 118-119°, lit.¹² 119°.

Continued elution resulted in the isolation of the more polar component. After evaporation of the solvent, the dried residue was recrystallized from acetone/water (cooling to -15°) to yield 6.65 g (approx. 88%) of 3 β -acetoxylanost-8-en-24-one (**2**) melting at 136-137°, *lit.* 137°;⁵ 135-137°;⁶ 140-142° (impure sample)⁷; IR: 1729 (acetate) 1702 (ketone), 1240, 1025 cm^{-1} ; ^1H NMR: δ 0.68 (s, 3H, C-18- CH_3), 1.00 and 2.05 (s, 3H, acetate), 4.48 (m, 1H, C-3-H). MS : *m/e* 484 (m, 9%), 469 (M- CH_3 , 16%), 424 (M-acetic acid, 2%), 409 (M- CH_3 -acetic acid, 35%), 71 (98%), 43 (acetoxyl, 100%). TLC analysis (toluene, 1% ether/toluene, 10% ether/hexane) indicated a single component and GLC analysis indicated one major component of 98% purity.

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