Stereoselective Synthesis of (Z)-11- and (E)-11-Eicosenyl Acetate

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Recently we found the acetates of octadecanol and (Z)-11-eicosenol in the defensive secretion of *Gastrophysa atrocyanea* Motschulsky.¹⁾ The latter alcohol has been known as a components of waxes or triglycerides in plants and animals,²⁾ especially in fish.^{2b~d)} The synthesis of (Z)-11-eicosenol was accomplished by starting from the naturally occurring stereoisomers,^{2b), 3)} however, stereoselective synthesis of (Z)-11- and (E)-11-eicosenol has not been appeared. To determine the stereochemistry of 11-eicosenyl acetate in the insect defensive secretion, the direct comparison with the synthetic (Z)- and (E)-isomers was required because that the two protons attached to the unsaturated carbons are equivalent on NMR even in the presence of the shift reagent and the coupling constant between vinyl protons could not be obtained.

This report describes stereoselective synthesis of (Z)-11- and (E)-11-eicosenyl acetates through the reductions of the common key intermediate, 11-eicosynol, to the corresponding alcohols with the easiest procedure and high yield.

As shown in the schema, 11-eicosynol (IIIb) was prepared by the alkylation of 1-decyne (I) with THP ether of 10-bromodecanol (II) under the condition developed by Beroza *et al.*⁴⁾ When partial hydrogenations of the triple bond to the corresponding (Z)-double bond were performed with Lindlar catalyst, P-2 nickel and quinoline poisoned Pd-BaSO₄, the contamination of 2~5% of (E)-isomer was unavoidable. The semihydrogenation of (IIIb) over Pd-BaSO₄ with pyridine as the solvent appeared to be the most satisfactory (less than 2% of E-isomer on GLC) to yield the pure (Z)-isomer after the recrystallization from pentane with high yield.

Reduction to the (E)-alcohol (Va) was accomplished by lithium aluminum hydride in diglyme-tetrahydrofuran following the method of Rossi *et al.*⁵⁾ The product was obtained as a single stereoisomer after the recrystallization same as the case of the (Z)-isomer.

The (Z)- and (E)-alcohols were acetylated quantitatively with acetic anhydride and pyridine respectively.

All steps of this synthetic procedure are simple and the yields are unexceptionally very high. The total

yields of (Z)- and (E)-11-eicosenyl acetates are above 50% based on 1-decyne (I), therefore, this method seems applicable to the stereoselective preparations of the (Z)- and (E)-unsaturated higher fatty alcohols.

EXPERIMENTAL

Infrared spectra were recorded on a JASCO IR-1 grating IR spectrometer. PMR spectra were determined as a solution in CCl₄ on a JEOL MH-60 (60 MHz) NMR spectrometer using TMS as an internal standard. Gas liquid chromatography was carried out under two different conditions. Condition A; 2 m × 2 mm stainless steel column packed with 20% DEGS on chromosorb W, N₂ flow rate = 20 ml/min, 200°C isothermal state. Condition B; 30 m × 0.25 mm glass capillary column coated with OV-101, N₂ flow rate = 2 ml/min. Temperature was programmed from 150°C to 220°C with the rate of 2°C/min and then the isothermal condition was maintained.

11-Eicosynol (IIIb): A solution of *n*-butyllithium in hexane (1.40 M, 16 ml) was added to 25 ml of dry THF solution of 1-decyne (I, 2.8 g, commercially available) with stirring at 0°C. After stirring for 2 hr 8.0 g of THP ether of 10-bromodecanol (II)⁶⁾ dissolved in 25 ml of HMPA was added dropwise at 0°~5°C. Stirring was continued for 6 hr at 0°C and then for 10 hr at room temperature. The reaction mixture was poured on ice-water and extracted with hexane. The hexane solution was washed with brine, dried on MgSO₄ and concentrated. The residue was chromatographed over silica gel (100 g packed with hexane) to give IIIa by elution with hexane-ethyl acetate (10: 1). Yield; 6.1 g (82%).

THP protective group was removed by refluxing ethanol solution of IIIa (4.5 g in 50 ml) containing 1 ml of conc. HCl for 2 hr. The contents was diluted with water and ether-extracted. After washing with NaHCO₃ sol and brine, drying on MgSO₄ and distilling off the solvent, residual mass was recrystallized from pentane at -60°C. IIIb was obtained as white leaflet crystal. mp 40~41°C. Yield; 3.1 g (85%). *Anal.* Found C, 81.46; H, 12.94. Calcd. for C₂₀H₃₈O; C, 81.56; H, 13.01%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3280, 1455, 1050, 720.

(Z)-11-Eicosenol (IVa): 11-Eicosynol (600 mg) was dissolved in 30 ml of dry pyridine and was shaken with 100 mg of 5% Pd-BaSO₄ under hydrogen gas. The calculated amount of hydrogen was absorbed during 2 hr and shaking was continued for additional 0.5 hr (No absorption of H₂ was observed during last period). The catalyst was filtered off and the content was diluted with water followed by hexane extraction. The crude product was recrystallized from pentane at -10°C. White plate crystal. mp 25~26°C, 470 mg (78%).

SCHEME. i) BuLi/THF, HMPA, ii) Pd-BaSO₄/Pyridine, iii) LAH/Diglyme, THF.

Anal. Found; C, 80.73; H, 13.54. Calcd. for C₂₀H₄₀O: C, 81.00; H, 13.60%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3320, 3020, 1460, 1050, 720. GLC: Condition B; t_R =38.2 min.

(*E*)-11-Eicosenol (Va): Under N₂-flow LiAlH₄ (1.0 g), 2 ml of dry THF and 20 ml of dry diglyme were heated up to 180°C with stirring to correct 3 ml of the distillate. The content was cooled to 10°C and 11-eicosynol (400 mg) in 2 ml of diglyme was added. Stirring and heating at 140°C were continued for 45 hr. After cooling the mixture was decomposed with ice-conc. HCl and the product was extracted with hexane. The crude crystalline product was recrystallized from hexane at 0°C, mp 43~44°C. Yield: 360 mg (90%). *Anal.* Found: C, 80.80; H, 13.56. Calcd. for C₂₀H₄₀O: C, 81.00; H, 13.60%. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3350, 3010, 1470, 1460, 1070, 965, 730, 720. GLC: Condition B; t_R =39.0 min.

(*Z*)-11-Eicosenyl acetate (IVb): The mixture of (*E*)-11-eicosenol (IVa, 400 mg), pyridine (1 ml) and acetic anhydride (0.8 ml) was placed overnight at room temperature and was decomposed on ice-water. The hexane extract was washed with dil. HCl and brine and dried on MgSO₄. Theoretical amount of the acetate was obtained, which showed single peak on GLC (Condition A: t_R =23.6 min. Condition B: t_R =51.8 min). bp_{0.04 mm Hg} 156°C. *Anal.* Found: C, 78.33; H, 12.57. Calcd. for C₂₂H₄₂O₂: C, 78.04; H, 12.50%. IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 3020, 1740, 1230, 1030. PMR δ : 0.90 (3H, t, J =4.0 Hz), 1.1~1.5 (28H, m), 1.9~2.2 (4H, m), 1.98 (3H, s), 4.03 (2H, t, J =6.0 Hz), 5.33 (2H, t, J =5.5 Hz). TLC (20 cm×5 cm silica gel H impregnated

with 10% AgNO₃ sol, developed with hexane-ether (5:1)); R_f =0.18.

(*E*)-11-Eicosenyl acetate (Vb): The same procedure described above was applied to (*E*)-11-eicosenol (Va, 400 mg). After evaporating of the solvent the residue was recrystallized from pentane at -10°C. mp 19.5°C. Yield: 230 mg (80%). *Anal.* Found: C, 78.66; H, 12.41. Calcd. for C₂₂H₄₂O₂: C, 78.04; H, 12.50%. IR $\nu_{\text{max}}^{\text{film}}$ cm⁻¹: 3020, 1740, 1230, 1030, 960. PMR δ : 0.90 (3H, t, J =4.0 Hz), 1.1~1.7 (28H, m), 1.8~2.2 (4H, m), 1.97 (3H, s), 4.00 (2H, t, J =6.0 Hz), 5.33 (2H, t, J =4.2 Hz). TLC (The conditions were the same as described above.); R_f =0.26. GLC: Condition A; t_R =23.6 min. Condition B; t_R =52.3 min.

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