COMMUNICATIONS TO THE EDITOR

An Enantiospecific Synthesis of 4-Hexanolate (γ-Caprolactone), the Sex Pheromone of the Female Dermestid Beetle Trogoderma glabrum (Herbst)

Suk-Ku Kang* and Dong-Soo Shin

Department of Chemistry, Sung Kyun Kwan University, Natural Science Campus, Suwon 170
Received December 3, 1986

The (R)-enantiomeric form of (R)-(+)4-hexanolate (1), γ-caprolactone (Figure 1), is the sex pheromone of the dermestid beetle Trogoderma glabrum (Herbst), an economically important insect pest that infests nearly all forms of stored products, including grain, meat, dairy products, carpets and clothing. Although (R)-(+)4-hexanolate (1) have a simple structure, synthesis is difficult for the reason that (R)-1 contain an asymmetric carbon center in the molecule.

![Figure 1](image_url)

Several synthesis have been reported in the literature. Silvestrin have synthesized the (R)-form from (S)-glutamic acid. D-Ribonolactone was used as a chiral starting material in the J. Font's synthesis. Two synthesis have been reported by asymmetric reduction of acetylenic ketone or acetylenic keto ester. R. Bernardi also reported the synthesis of (R)-1 from (2S, 3R)-5-phenyl-4-pentene-2,3-diol, which was obtained by microbial transformation of cinnamaldehyde with baker's yeast.

Since the absolute stereochemistry of pheromones is important in pheromone activity, this fact demands a highly efficient chiral synthesis on a large scale and in high optical purity. Here, we wish to report an enantiospecific synthesis of (R)-1 using (R)-2,3-O-isopropylideneacetaldehyde (4) as a chiral starting material.

Bond formation between C-6 and C-7 can be accomplished with tosylate and dialkycuprate. A simple retrosynthetic analysis (Scheme 1) reveals that (S)-(+-5-hydroxymethyl-2-oxotetrahydrofuran (3) is the key intermediate. We have prepared (S)-(+-5-hydroxymethyl-2-oxotetrahydrofuran (3), the key intermediate. We have prepared (S)-(+-5-hydroxymethyl-2-oxotetrahydrofuran (3), the key intermediate from (R)-2,3-O-isopropylideneacetaldehyde (4) and synthesized (R)-1 by C-C coupling reaction of (S)-5-p-toluenesulfonylaminomethyl-2-oxotetrahydrofuran (2) with dimethylcuprate.

![Scheme 1](image_url)

Optically active (R)-2,3-O-isopropylidene-D-glyceraldehyde (4) was readily available from naturally occurring inexpensive carbohydrate, D-mannitol. The bis-acetone of D-mannitol was prepared in a moderate yield and the resulting diol acetone was cleaved with lead tetraacetate to yield (R)-glyceraldehyde acetone (4). Wittig-Emmons olefination of the aldehyde 4 with the anion of dimethyl methoxyacarbonylmethylphosphonate furnished the unsaturated ester 5 as a mixture of (E)-olefin 5:15 in 82% yield. Without separation of the mixture, the unsaturated ester 5 was subjected to hydrogenation at atmospheric pressure at room temperature to yield the saturated ester 6 in good yield. Esterhydrolysis with LiOH in THF-H₂O (3:1) for 3hr followed by deprotection of the acetone with aqueous AcOH at 75-80°C for 2hr provided (S)-(+-2-oxotetrahydrofuran 3. On treatment of (S)-(+-2-oxotetrahydrofuran 3 with tosyl chloride in dichloromethane in the presence of pyridine, the corresponding crystalline tosylate 2 was obtained in 96% yield. Addition of a benzene solution of the (S)-tosylate 2 to an ether solution of lithium dimethylcuprate gave (R)-(+-1 in 66% yield (Scheme 2). The compound synthesized was identical in all respects (TLC, IR, NMR, MS) with the compound reported in the
Facile Cleavage of Tetrahydrofurin Derivatives with S-2-Pyridyl Thioates / CuBr₂ / CH₃CN

Sunggak Kim* and Young Kwan Ko

Department of Chemistry, Korea Advanced Institute of Science and Technology, Seoul 131

Jae In Lee

Department of Chemistry, Duksvang Women’s College, Seoul 132. Received February 2, 1987

Previously we have reported a rapid and convenient preparation of sterically hindered carboxylic esters by the reaction of S-2-pyridyl thioates with alcohols in the presence of cupric bromide in acetonitrile.¹ We wish to report that S-2-pyridyl thioates/cupric bromide rapidly and cleanly

cleaves tetrahydrofuran derivatives in acetonitrile at room temperature,² although S-2-pyridyl thioates/cupric bromide was inert to tetrahydrofuran derivatives at room temperature for a long period of time.³ Thus, the success of the reaction depends crucially on the use of acetonitrile as a solvent, although the reason for this observation is rather unclear.

The reaction was carried out with equimolar amounts of S-2-pyridyl methanethioate and cupric bromide using a slight

†This paper is dedicated to Professor Sae-Hee Chang on the occasion of his 60th birthday.

References

8. Satisfactory physical properties and spectroscopic data (¹H-NMR, IR, MS) were obtained for the compounds: (R)-2,3-O-isopropylideneglyceraldehyde (4); bp 39°C/15 mmHg; IR(NaCl, neat) 2850, 2750, 1725, 1180 cm⁻¹; ¹H-NMR (60MHz, CDCl₃) δ 1.35 (3H, s, CH₃), 1.46 (3H, s, CH₃), 4.01-4.18 (2H, d, OCH₂), 4.24-4.39 (1H, m, CH₂CHO), 9.85 (1H, s, CHCHO). Methyl (4S, 2E)-4,5-isopropylidenedioxepin-2-enoate (5): hexane: ethyl acetate (9:1); [α]D + 37.5° (c = 0.29, CHCl₃); IR (neat) 1700, 1650 cm⁻¹; ¹H-NMR δ 1.42 (3H, s, CH₃), 1.45 (3H, d, OCH₂), 3.63 (1H, m, CHCH₂O), 3.75 (3H, s, OCH₃), 4.1 (1H, m, OCH₂CHO), 4.05 (1H, m, CH₂CHO), 6.04 (1H, dd, J₁5 and 1.5Hz, CH = CH-O), and 6.87 (1H, dd, J₁5 and 1.5Hz, CH = CH-O). Methyl(4S)-4,5-isopropylidenedioxepinato (6): bp 67-75°C/8 mmHg; IR (neat) 1700, 1650 cm⁻¹; ¹H-NMR δ 1.42 (3H, s, CH₃), 1.45 (3H, s, CH₃), 1.92 (2H, m, CH₂), 2.5 (2H, m, CH₂CO₂H₄), 3.63 (1H, m, CH-O), 3.75 (3H, s, OCH₃), 4.1 (2H, m, CH₂O). (S)(+)-5-hydroxymethyl-2-oxotetrahydrofuran (3); chloroform: methanol (98:2); [α]D + 33.1° (c = 3.17, EtOH); IR (neat) 3400, 1765 cm⁻¹; ¹H-NMR δ 2.0-2.8 (4H, m, CH₂CHO), 3.1 (1H, br.s, OH), 3.5-4.1 (2H, m, CH₂O), 4.6 (1H, m, -CH-O). (S)(+)-p-toluenesulfonyl methyl-2-oxotetrahydrofuran (2); mp 85-7°C (ether; dichloromethane); [α]D + 46.3° (c = 1.33, CHCl₃); IR (KBr, pellet) 1765 cm⁻¹; ¹H-NMR δ 1.8-2.7 (4H, m, CH₂CH₂), 2.45 (3H, s, CH₃), 4.18 (2H, d, CH₂O); 4.70 (1H, m, CH-O); 7.42 (2H, d, J = 10Hz), 7.85 (2H, d, J = 10Hz); MS 270 (M⁺), 85 (base); (R)+hexan-4-olide (1); ether: hexane (3:2); [α]D + 30.4° (c = 1.0, MeOH); lit. [2] [α]D + 42.7° (c = 1, MeOH); IR (neat) 1770, 1170 cm⁻¹; ¹H-NMR δ 1.01 (3H, t, CH₃), 1.6-2.7 (6H, m, -CH₂CH₂), 4.61 (1H, m, CH-O).