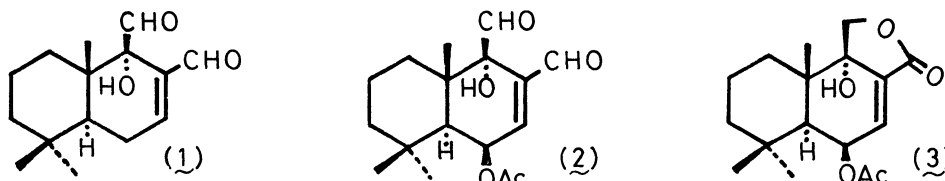


SYNTHESES OF (+)-CINNAMODIAL AND (+)-CINNAMOSMOLIDE

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Syntheses of (+)-cinnamodial and (+)-cinnamosmolide were achieved starting from the intermediate used in the synthesis of (+)-warburganal.

Warburganal (1), a unique member of drimanic sesquiterpenes, has attracted much attention of synthetic organic chemist because it has remarkably potent biological activities.¹⁾ Since its total synthesis has been achieved by us²⁾ and other several groups³⁾, our efforts were then focussed on the syntheses of the compounds possessing the related structure to examine the structure-activity relationship. We now report the total syntheses of (+)-cinnamodial (2)^{4a,b)} and (+)-cinnamosmolide (3)^{4a)} starting from the allyl alcohol (4)²⁾, an intermediate used in the synthesis of 1.

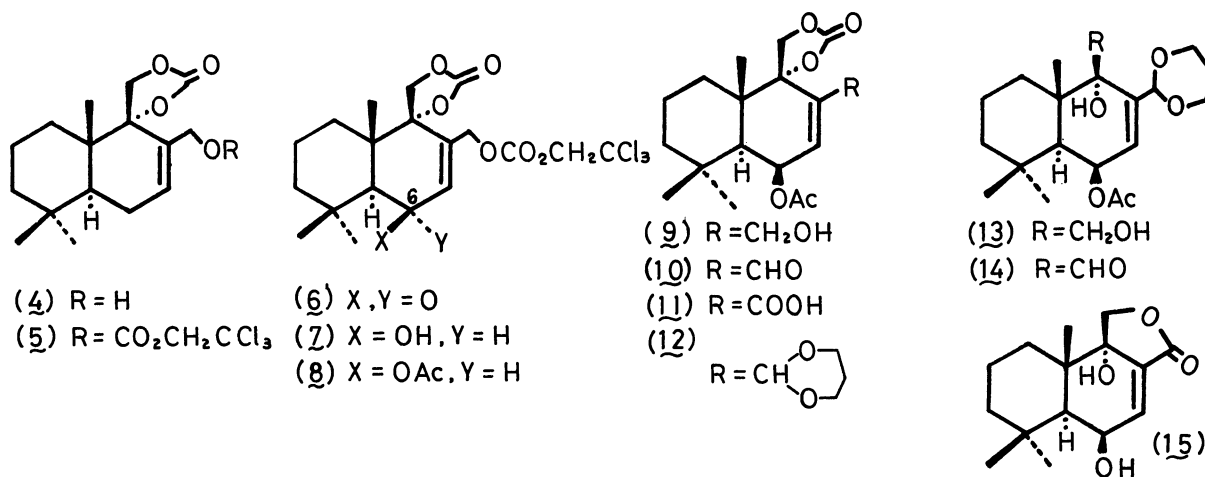


The allyl alcohol in 4 was protected by the conversion into the trichloroethoxycarbonate (5): trichloroethoxycarbonyl chloride⁵⁾-pyridine; 96% yield; mp 121-2°C; IR(CHCl₃) 1790, 1760 cm⁻¹. Oxidation of 5 with CrO₃ in AcOH produced the ketone (6)⁶⁾: 64% yield; mp 145-6°C; IR(CHCl₃) 1815, 1765, 1690 cm⁻¹; NMR(CDCl₃) δ 2.70(1H, br.s, C₅-H). The fact that the keto group was introduced into C₆-position was confirmed by the appearance of one proton broad singlet at δ 2.70 in NMR spectrum. Reduction of the keto group should be carried out under neutral condition because base sensitive two carbonate groups were involved in 6. In fact, the reduction with NaBH₄ gave only a mixture of unidentified products. However, when Zn(BH₄)₂⁷⁾, the ether solution of which was presumed to be almost neutral, was employed, reduction proceeded cleanly but rather slowly at room temperature to afford the desired alcohol (7): 73% yield; mp 131-2°C; IR(CHCl₃) 3600, 1800, 1760 cm⁻¹. Here, no conjugate reduction product was detected. The configuration of the C₆-OH was assigned as β-configuration because the reagent should attack from the less hindered α-side. This severely hindered hydroxy group was successfully acetylated with Ac₂O-pyridine in the presence of a catalytic amount of 4-dimethylaminopyridine⁸⁾ affording the acetate (8): 98% yield; mp 146-9°C; IR(CHCl₃) 1800, 1760, 1735 cm⁻¹; NMR(CDCl₃) δ 5.65(1H, t, J= 5.0 Hz, C₆-H). Then, trichloroethoxy-

carbonyl group was selectively removed by Zn-AcOH in the presence of other functional groups to produce the allyl alcohol (9): 84% yield; mp 157-9°C; IR(CHCl₃) 3400, 1795, 1730 cm⁻¹.

Conversion of this compound into 2 was performed in the same way as in the synthesis of warburganal. Jones oxidation of 9 at 0°C afforded a mixture of the corresponding aldehyde (10) [78% yield; mp 195-200°C(decomp.)] and the acid (11): 20% yield; mp 196-9°C. After the aldehyde (10) had been converted to the acetal (12) (80% yield; mp 235-7°C), the carbonate group in 12 was selectively cleaved by 10% NaOH-dioxane (1:1) treatment (room temp., 2 h) to afford the glycol (13): 77% yield; mp 117-8°C. Moffatt oxidation of the primary alcohol (13) (DMSO, pyridine, CF₃COOH, DCC, benzene, room temp.) produced the hydroxy aldehyde (14): 82% yield; mp 149-151°C. Acid hydrolysis (p-TsOH, acetone, 30 min, reflux) of 14 gave (+)-cinnamodial (2, mp 128-130°C) in 97% yield. The NMR and IR spectral data were identical with those reported in the literature.^{4a,b)}

(+)-Cinnamosmolide (3) was synthesized from the carboxylic acid (11) by two steps. The compound (11) was prepared this time from the alcohol (9) by use of an excess of Jones reagent in quantitative yield. Deprotection of the carbonate group using 4% NaOH-dioxane (1:1) yielded mostly the diol-lactone (15), the C₆-OAc group being hydrolysed in this case. Reacetylation of the crude product with Ac₂O-pyridine-4-dimethylaminopyridine afforded (+)-cinnamosmolide (3, mp 147-150°C) in 89% yield from 11. The NMR and IR spectral data were all identical with those reported in the literature.^{4a)}



References and Notes

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