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THE STEREOSELECTIVE SYNTHESIS OF C_{18}-JUVENILE HORMONE ANALOGUE

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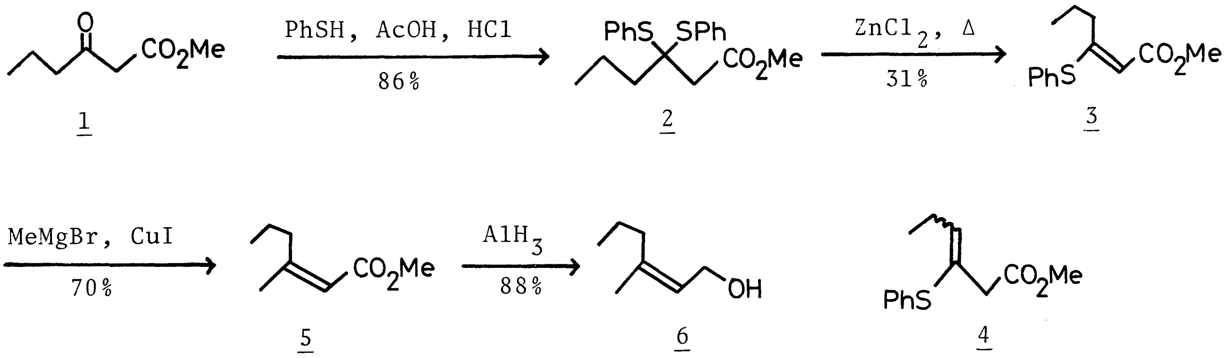
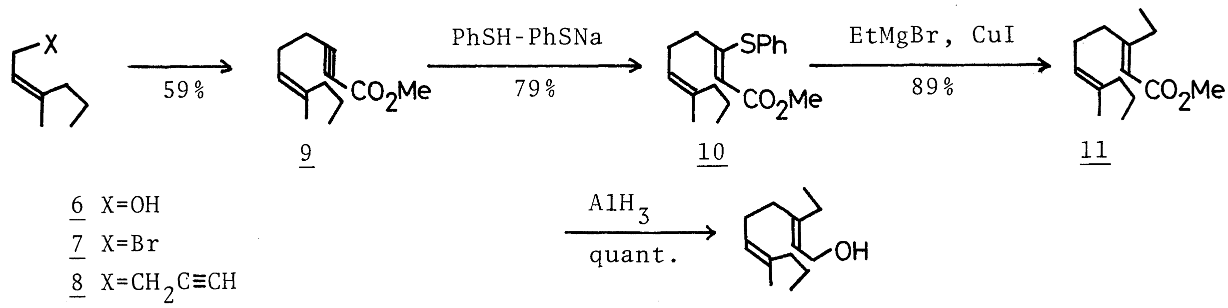
The new method for the stereoselective preparation of 1,5-diene units was successfully applied to the synthesis of C_{18}-juvenile hormone analogue 16 of high biological activity.

In the preceding paper we have reported a new route to the stereoselective preparation of 1,5-diene unit and its application to the synthesis of C_{18}- and C_{17}-juvenile hormones.[1)] The key steps involved in the route are (1) the stereoselective trans addition of benzenethiol to an α,β-acetylenic ester and (2) the stereospecific preparation of trisubstituted olefin.[2)]

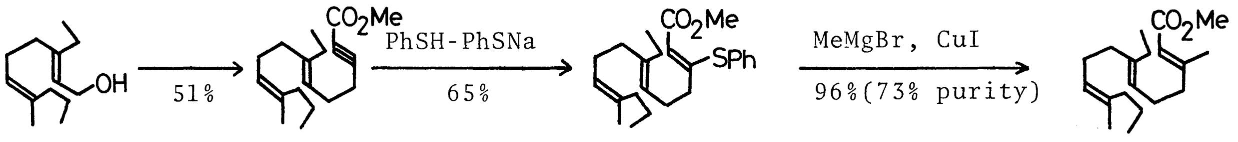
We now describe a stereoselective synthesis of C_{18}- juvenile hormone analogue which was reported to have a high biological activity by Mori et al.[3)] When diphenylthioacetal 2, prepared from β-ketoester 1 and benzenethiol in 86% yield, was heated to 110°C in the presence of a catalytic amount of $ZnCl_2$, elimination of benzenethiol occurred and E-β-phenylthio-α,β-ethylenic ester 3 and β-phenylthio-β,γ-ethylenic ester 4 were obtained in 31% and 20% yields, respectively. 4 was found to isomerize to the desired E-β-phenylthio-α,β-ethylenic ester 3 on treating with potassium-tert-butoxide in tert-butyl alcohol. 3 was methylated by the coupled use of methylmagnesium bromide and cuprous iodide in tetrahydrofuran at -78°C to afford α,β-ethylenic ester 5 in 70% yield, which was reduced to C_7-alcohol 6 in 88% yield.



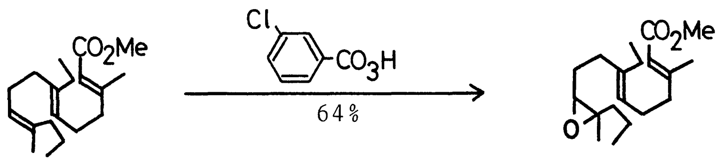
The homologation of C_7- alcohol 6 to the C_{13}- alcohol 12 was achieved by the same reaction sequence described previously[1)2)]; (1) propynylation followed by methoxycarbonylation(59% yield), (2) base catalyzed addition of benzenethiol(79% yield), (3) ethylation with ethylmagnesium bromide and cuprous iodide(89% yield) and (4) aluminum hydride reduction (quant.).



The preparation of the trienic ester 15[4)], the precursor of juvenile hormone analogue, was accomplished starting from C_{13}- alcohol 12 by a repetitive application of the above mentioned procedure.



The epoxidation of the trienic ester with m-chloroperbenzoic acid in methylene chloride at 0°C followed by TLC purification afforded the desired C_{18}-juvenile hormone analogue 16[5)] in 64% yield, and the product exhibited fully consistent of n.m.r. and i.r. spectra with the assigned structure 16.



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1) S. Kobayashi and T. Mukaiyama, Chem. Lett., 1425 (1974).
2) S. Kobayashi and T. Mukaiyama, Chem. Lett., 705 (1974).
3) K. Mori, T. Mitui, J. Fukami, and T. Ohtaki, Agr. Biol. Chem., 35, 1116 (1971).
4) n.m.r.(δ_{TMS} ppm, CCl_4): 0.97(m, 6H), 1.64(s, 3H), 1.18 ∿ 1.51(m, 2H), 1.75 ∿ 2.30(m, 12H), 2.13(s, 3H), 3.61(s, 3H), 5.02(m, 2H), 5.59(bs, 1H).
i.r.: $\nu_{C=O}$ 1720, $\nu_{C=C}$ 1650 cm^{-1}.
Anal. calcd. for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 78.33; H, 11.23%.
5) n.m.r.(δ_{TMS} ppm, CCl_4): 0.96(m, 3H), 0.99(m, 3H), 1.20(s, 3H), 1.25 ∿ 1.75(m, 6H), 1.75 ∿ 2.30(m, 8H), 2.14(s, 3H), 2.49(t, J=6 Hz, 1H), 3.61(s, 3H), 5.05(m, 1H), 5.59(bs, 1H).
i.r.: $\nu_{C=O}$ 1720, $\nu_{C=C}$ 1650 cm^{-1}.

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