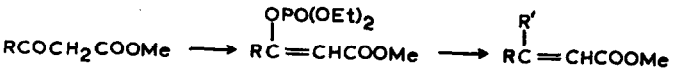
Tetrahedron Letters No. 8, pp 707 - 708. 0040-4039/79/0215-0707$02.00/0

STEREOSELECTIVE SYNTHESIS OF LATIA LUCIFERIN

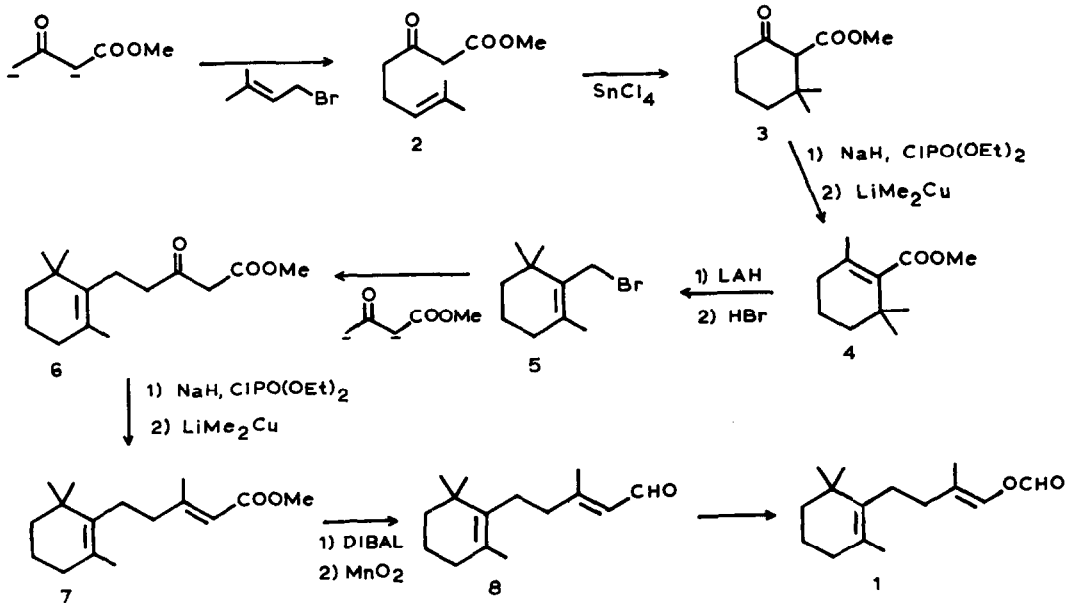
F.W. Sum and Larry Weiler*
Department of Chemistry, University of British Columbia
Vancouver, British Columbia, Canada, V6T 1W5

In the past few years β-keto esters have been very useful in the construction of complex molecules. The increased interest in these building blocks no doubt follows from the fact that all four carbons in the simplest unit, esters of acetoacetic acid, may be activated under different reaction conditions. Recently, we have found another reaction of β-keto esters which should even further enhance the utility of these systems. This sequence involves converting the β-keto ester to an enol phosphate and coupling the enol phosphate with dialkylcuprates to yield alkenes as shown in equation 1.[1,2] For acyclic β-keto esters this reaction is stereospecific depending on the geometry of the enol phosphate. We would



(1)

like to report two applications of this reaction in the synthesis of Latia neritoides luciferin (1),[3,4] shown below.



The dianion of methyl acetoacetate[5] was alkylated with dimethylallyl bromide to give 2 in 85% yield. This alkylation product 2 was cyclized with $SnC\ell_4$ and $CH_2C\ell_2$ to produce 3. Then in one of the applications of our new alkene synthesis, the β-keto ester was converted into the enol phosphate on treatment with NaH in THF followed by diethyl chlorophosphate. Subsequent reaction of the enol phosphate with 2 eq. of Me_2CuLi in ether gave the alkene 4 in 89% yield from 2. The ester 4 was reduced with LAH and treated with conc HBr[6] to give the bromide 5 in over 80% yield. The bromide 5 was alkylated in ca. 80% yield with the dianion of methyl acetoacetate[5] to give 6 which again was converted into a α,β-unsaturated ester by conversion into the enol phosphate and subsequent coupling with lithium dimethylcuprate as above. The desired E isomer of 7 was obtained in 93% yield and the isomeric Z product could not be detected by chromatographic or spectral analysis. We have found that acyclic β-keto esters are stereoselectively converted into Z enol phosphates under these conditions and the dialkylcuprate coupling occurs with retention of geometry about the double bond.[1]

The α,β-unsaturated ester 7 was reduced to the corresponding alcohol with DIBAL and then oxidized to the α,β-unsaturated aldehyde 8 with MnO_2.[7] This aldehyde had spectral data identical to that reported for the E isomer 8[4b] and this isomer has been stereoselectively converted into the luciferin 1 by treating 8 with anhydrous H_2O_2 and SeO_2.[4b]

The above synthesis illustrates the utility of β-keto esters (acetogenins) in the synthesis of isoprenoids. The cyclized ester 4 is an obvious terminal unit in the synthesis of retinals and carotenoids. Finally, we have shown that this new alkene synthesis is stereoselective, it is successful for cyclic and acyclic β-keto esters, and it is directly compatible with products of dianion reactions[5] of β-keto esters.[8]

1. F.W. Sum and L. Weiler, submitted for publication.
2. For a coupling of enol phosphates with dialkylcuprates see L. Blaszczak, J. Winkler, and S. O'Kuhn, Tet. Letters, 4405 (1976).
3. Structure: O. Shimomura and F.H. Johnson, Biochemistry, 7, 1734 (1968).
4. Previous non-stereoselective synthesis: (a) M.G. Fracheboud, O. Shimomura, R.K. Hill, and F.H. Johnson, Tet. Letters, 3951 (1969) (b) F. Nakatsubo, Y. Kishi, and T. Goto, Tet. Letters, 381 (1970).
5. S.N. Huckin and L. Weiler, J. Amer. Chem. Soc., 96, 1082 (1974).
6. E.E. van Tamelen, R.A. Holton, R.E. Hopla, and W.E. Konz, J. Amer. Chem. Soc., 94, 8228 (1972).
7. J.A. Attenburrow, A.F.B. Cameron, J.H. Chapman, R.M. Evans, B.A. Hems, A.B.A. Jansen, and T. Walker, J. Chem. Soc., 1094 (1952).
8. We are grateful to the National Sciences and Engineering Research Council Canada and the University of British Columbia for financial support of this work.

(Received in USA 10 November 1978)