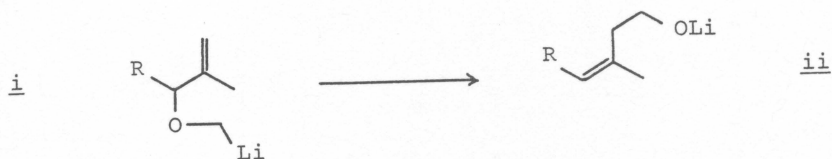


A HIGHLY STEREOSELECTIVE SYNTHESIS OF THE C₁₈
 CECROPIA JUVENILE HORMONE

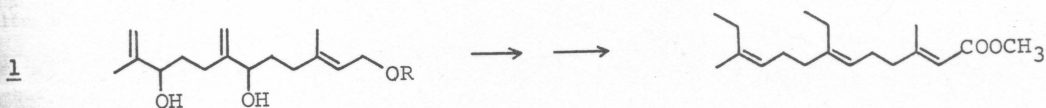
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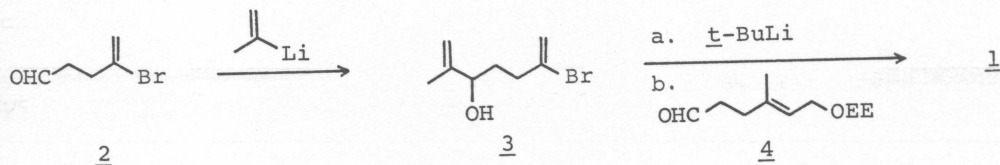
A short time ago we reported that [2,3]-sigmatropic rearrangements of alkoxy-organolithium reagents like i provide an efficient method for the preparation of Z-homoallylic alcohols (ii).² We describe here an application of the rearrangement to the synthesis of the C₁₈ Cecropia juvenile hormone.³



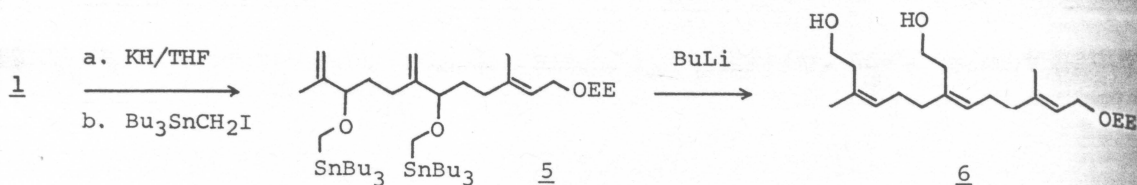
The general approach is related to several previous juvenile hormone syntheses in which two of the three intermediate trisubstituted olefins are created simultaneously from allylic alcohol 1.⁴ Although 1 (R = C₆H₅) has been prepared previously



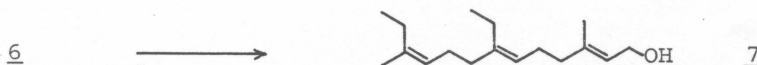
from farnesol,⁴ the difficulties in obtaining all-trans farnesol and the poor overall yields of published sequences led us to develop a more efficient preparation of 1:



Addition of isopropenyllithium (THF, -78° C, 10 min) to aldehyde 2⁵ gave the expected adduct 3 (93% yield). When this product was treated with t-butyllithium (2.5 mmol t-BuLi/mmol 3, Et₂O, -78 → 0° C, 2h),⁶ a dianion was formed which added to aldehyde 4⁷ at 0° C to give directly the monoprotected tris-allylic alcohol 1 (R = CH(CH₃)OCH₂CH₃, 77% yield). This product was in all ways identical with that prepared from all-trans farnesol.^{4b, 8}



Highly stereoselective rearrangement to the bis-homoallylic alcohol 6 was then effected by alkylating the dipotassium salt of 1 with iodomethyltributyltin⁹ (88% yield) and rearranging the intermediate product 5 with *n*-butyllithium (THF, -78 \rightarrow -20 $^\circ$ C, 79% yield). Finally tosylation (excess TsCl/pyr, 0 $^\circ$ C, 18 h, 93%), reduction (LiAlH₄/Et₂O, 0 $^\circ$ C, 30 min, 98%), and deprotection (H₂O-HOAc, 45 $^\circ$ C, 4 h, 92%) gave bis-homofarnesol 7 which has been converted previously to the C₁₈ Cecropia juvenile hormone.¹⁰ Analysis by VPC and CMR showed the product 7 to consist of a single isomer to the extent of at least 95%.



CMR 7 (CDCl₃): 141.6, 139.9, 137.3, 124.3, 123.7 (2C), 59.1, 39.6, 36.5, 26.2, 25.6, 24.4, 22.8, 22.4, 15.8, 12.7, 12.3.

Notes and References:

1. A. P. Sloan Foundation Fellow (1978-1980).
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3. Reviewed by C. H. Heathcock, "The Total Synthesis of Natural Products," Vol. 2, J. ApSimon, Ed., Wiley, New York, 1973, pp 207-222.
4. (a) R. J. Anderson, C. A. Henrick and J. B. Siddall, *J. Am. Chem. Soc.*, 92, 735 (1970); (b) E. E. Van Tamelen and J. P. McCormick, *ibid.*, 92, 737 (1970); (c) S. Tanaka, H. Yamamoto, H. Nozaki, K. B. Sharpless, R. C. Michaelson and J. D. Cutting, *ibid.*, 96, 5254 (1974).
5. Aldehyde 2 was prepared by: (1) alkylation of lithio *tert*-butylacetate with 2,3-dibromopropene (93%); (2) LiAlH₄ reduction (95%); and (3) CrO₃·2 Pyr oxidation (42%, low yield due largely to product volatility).
6. Cf. E. J. Corey and G. N. Widiger, *J. Org. Chem.*, 40, 2975 (1975).
7. Aldehyde 4 was prepared by low temperature ozonolysis of ethoxyethyl-protected geraniol (cf. P. A. Grieco, Y. Masaki and D. Boxler, *J. Am. Chem. Soc.*, 97, 1597 (1975)) (54% yield and 77% conversion).
8. We wish to thank Dr. John S. Baran at G. D. Searle for a generous sample of all-trans farnesol.
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10. E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman and B. W. Erickson, *J. Am. Chem. Soc.*, 90, 5618 (1968).