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A HIGHLY STEREOSELECTIVE SYNTHESIS OF THE C_{18} CECROPIA JUVENILE HORMONE

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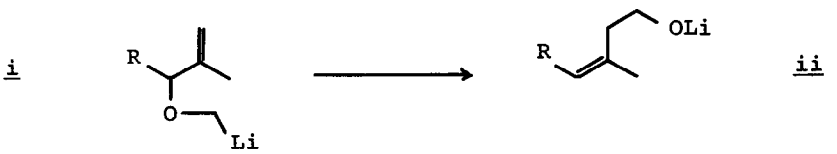
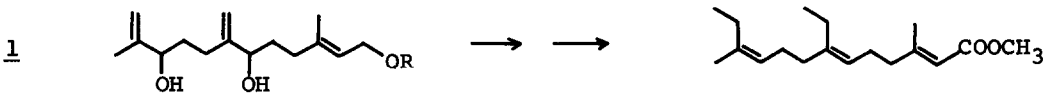
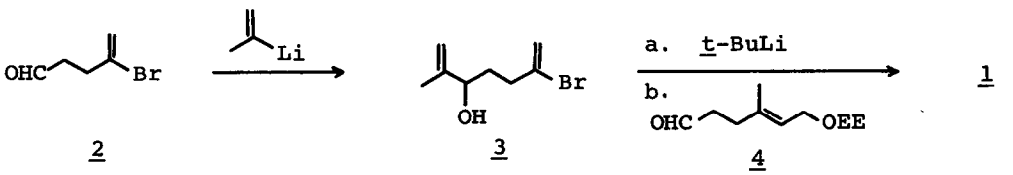
A short time ago we reported that [2,3]-sigmatropic rearrangements of alkoxy-organolithium reagents like i provide an efficient method for the preparation of Z-homoallylic alcohols (ii).[2] We describe here an application of the rearrangement to the synthesis of the C_{18} Cecropia juvenile hormone.[3]



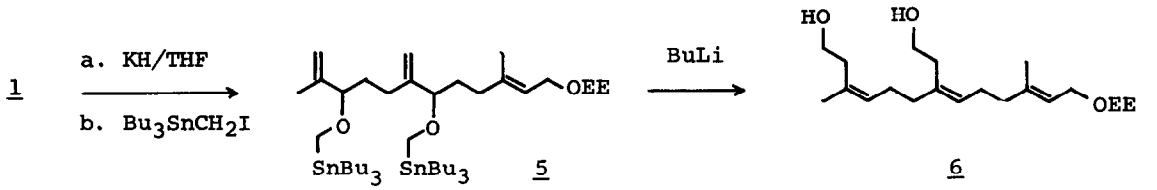
The general approach is related to several previous juvenile hormone syntheses in which two of the three intermediate trisubstituted olefins are created simultaneously from allylic alcohol 1.[4] Although 1 (R = $C\Phi_3$) has been prepared previously



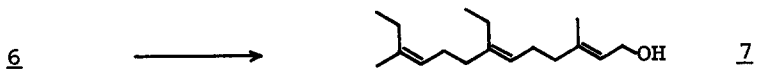
from farnesol,[4] the difficulties in obtaining all-trans farnesol and the poor overall yields of published sequences led us to develop a more efficient preparation of 1:



Addition of isopropenyllithium (THF, -78° C, 10 min) to aldehyde 2[5] gave the expected adduct 3 (93% yield). When this product was treated with t-butyllithium (2.5 mmol t-BuLi/mmol 3, Et_2O, -78 → 0° C, 2h),[6] a dianion was formed which added to aldehyde 4[7] at 0° C to give directly the monoprotected tris-allylic alcohol 1 (R = $CH(CH_3)OCH_2CH_3$, 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 iodomethyltributyltin[9] (88% yield) and rearranging the intermediate product 5 with n-butyllithium (THF, -78 → -20° C, 79% yield). Finally tosylation (excess TsCl/pyr, 0° C, 18 h, 93%), reduction ($LiAlH_4/Et_2O$, 0° C, 30 min, 98%), and deprotection (H_2O-HOAc, 45° C, 4 h, 92%) gave bis-homofarnesol 7 which has been converted previously to the C_{18} 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 ($CDCl_3$): 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).

2. W. C. Still and A. Mitra, J. Am. Chem. Soc., 100, 1927 (1978).

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) $LiAlH_4$ reduction (95%); and (3) CrO_3•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.

9. W. C. Still, J. Am. Chem. Soc., 100, 1481 (1978).

10. E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman and B. W. Erickson, J. Am. Chem. Soc., 90, 5618 (1968).

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