A HIGHLY STEREOSSELECTIVE SYNTHESIS OF THE C₁₈ CECROPIA JUVENILE HORMONE

W. Clark Still, John H. McDonald, III, David B. Collum, and Abhijit Mitra

Department of Chemistry, Columbia University, New York, N Y 10027

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

\[ \text{i} \quad \begin{array}{c} \text{R} \text{O} \text{Li} \\ \text{O} \text{Li} \end{array} \quad \text{→} \quad \begin{array}{c} \text{R} \text{OLi} \end{array} \quad \text{ii} \]

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 = C₃) 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:

\[ \begin{array}{c} \text{OH} \text{OH} \text{OR} \\ \text{OH} \text{OH} \text{OR} \quad \text{→} \quad \begin{array}{c} \text{COOCH₃} \end{array} \end{array} \]

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 tri-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 alkyllating the dipotassium salt of 1 with iodomethyltributyltin (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 (LiAlH₄/Et₂O, 0° C, 30 min, 98%), and deprotection (H₂O-HOAc, 45° C, 4 h, 92%) gave bis-homofarnesol 7 which has been converted previously to the C₁₈ Cecropia juvenile hormone. Analysis by VPC and CMR showed the product 7 to consist of a single isomer to the extent of at least 95%.

Notes and References:
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).
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