A HIGHLY STEREOSELECTIVE SYNTHESIS OF THE C\textsubscript{18} 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 \( \text{R} - \text{OLi} \) provide an efficient method for the preparation of \( Z \)-homoallylic alcohols (\( \text{ii} \)). We describe here an application of the rearrangement to the synthesis of the C\textsubscript{18} Cecropia juvenile hormone.

\[
\begin{align*}
\text{i} & \quad \text{R} - \text{OLi} \\
\text{ii} & \\
\end{align*}
\]

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 \( \text{i} \). Although \( \text{l} (R = \text{CH}_{3}) \) has been prepared previously from farnesol, the difficulties in obtaining all-trans farnesol and the poor overall yields of published sequences led us to develop a more efficient preparation of \( \text{l} \):

\[
\begin{align*}
\text{OH} & \quad \text{OH} \\
\end{align*}
\]

Addition of isopropenyllithium (THF, \(-78^\circ\text{C}, 10\text{ min}\)) to aldehyde \( \text{2} \) gave the expected adduct \( \text{3} \) (93% yield). When this product was treated with \( t\)-butyllithium (2.5 mmol \( t\)-BuLi/mmol \( \text{3} \), \( \text{Et}_2\text{O}, -78 \rightarrow 0^\circ\text{C}, 2\text{h}\)), a dianion was formed which added to aldehyde \( \text{4} \) at \( 0^\circ\text{C} \) to give directly the monoprotected tris-allylic alcohol \( \text{l} \) (R = CH(CH\(_3\))OCH\(_2\)CH\(_3\), 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 alkylation of 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%.

**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:**
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).
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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