A Stereoselective Synthesis of *dl*-C₁₇-*Cecropia* Juvenile Hormone

Sir:

The first stereoselective total synthesis of *dl*-C₁₈-*Cecropia* juvenile hormone (I) was announced by Corey *et al.* in 1968.¹⁾ Since then seven other stereoselective syntheses have been reported as preliminary communications.^{2~4)} These works greatly improved our modern methodology for the stereo-controlled construction of a trisubstituted double bond.⁴⁾

We here record another stereoselective synthesis of *dl*-C₁₇-*Cecropia* juvenile hormone (II). The starting materials were C₆-(III) and C₁₀-(IV) units. The former was prepared stereoselectively as described by us⁵⁾ and the latter as reported by Corey *et al.*⁶⁾ with slight modifications. We also developed an alternative and more convenient route to the latter. Geranyl acetate (V) was oxidized with selenium dioxide in ethanol to give an aldehyde (VIa)^{cf. 7)} stereoselectively. This was treated with aqueous ethanolic potassium hydroxide at -10°C.

The resulting alcohol (VIb) was converted to a tetrahydropyranyl ether (VIc) in the usual manner with dihydropyran and *p*-toluenesulfonic acid. Its reduction with sodium borohydride in isopropanol-ethanol yielded the C₁₀-unit (IV) bp 120~121°C (0.1 mmHg); δ (CCl₄, 100 MHz) 1.60 (3H, s), 1.64 (3H, s), 3.83 (2H, s), 4.51 (1H, br. s), 5.25 (2H, br. t) ppm (overall yield of IV from V: 16%).

For the coupling of III and IV to form a C-C bond, a method developed by Biellmann and Ducep⁸⁾ for squalene synthesis was employed which consisted in the alkylation of an allylic carbanion stabilized by the sulfur atom of a phenyl sulfide (VII+VIII→IXa) and subsequent removal of the sulfur (IXb→X). The phenyl sulfide (VII), bp 107~110°C (3 mmHg); δ 0.94 (3H, t, *J*=7Hz), 1.70 (3H, s), 1.99 (2H, q, *J*=7Hz), 3.95 (2H, d, *J*=7Hz), 5.21 (1H, t, *J*=7Hz), 6.90~7.30 (5H, m) ppm, was obtained from III by treatment with

thiophenol and sodium ethoxide in ethanol at 0~5°C. The conversion of IV into a bromide (VIII) was accomplished by Stork's method.⁹⁾ Thus IV in HMPA (hexamethylphosphoramide) was treated successively with *n*-butyllithium, tosyl chloride and lithium bromide to give VIII in 59% yield, δ 1.67 (3H, s), 1.73 (3H, s), 3.93 (2H, s), 4.51 (1H, br. s), 5.28 (2H, br. t) ppm, without isomerization of the terminal *trans* double bond. The sulfide (VII) in THF was treated with *n*-butyllithium in the presence of DABCO (diazabicyclo [2.2.2] octane) and then alkylated with VIII in THF to give IXa in 58% yield after chromatography over alumina. The tetrahydropyranyl protective group was removed with *p*-toluenesulfonic acid in methanol. The product was purified by chromatography over silicic acid to give IXb in 88% yield, δ 0.77 (3H, t, $J=7\text{Hz}$), 1.23 (1H, s, -OH), 1.58, 1.62, 1.90~2.35 (m), 3.70~4.10 (3H), 4.80~5.20 (2H), 5.33 (1H, t, $J=7\text{Hz}$), 7.00~7.40 (5H, m) ppm. Desulfurization of this phenyl sulfide (IXb) with lithium-ethylamine gave 12-homofarnesol (X) in 33% yield, ν_{max} ~3320, 1670, 1440, 1380, 1000 cm^{-1} ; δ 0.94 (3H, t, $J=7\text{Hz}$), 1.57, 1.63 [1.50~1.70 (9H)], 1.80~2.30 (10H), 3.99 (2H, d, $J=6\text{Hz}$), 5.00 (2H, br.), 5.31 (1H, t, $J=7\text{Hz}$) ppm. This was oxidized by Corey's method¹⁾ to give methyl 12-homofarnesoate (XI) in 35% yield, ν_{max} 1725, 1650, 1380, 1360, 1220, 1140, 1020, 860 cm^{-1} ; δ 0.93 (3H, t, $J=7\text{Hz}$), 1.56 (3H, s), 1.61 (3H, s), 2.11 (3H, s), 3.58 (3H, s), 5.00 (2H, br), 5.54 (1H, br. s); MS: m/e 264. 2080 (M^+). These spectral data were identical with those of an authentic sample.¹⁰⁾ The identity was also proved by co-GLC with an authentic sample, t_R 12.0 min (LAC-2R-446 at 180°C with N_2 , 1.2 kg/cm^2). This completed the stereoselective synthesis of *dl*- C_{17} -*Cecropia* juvenile hormone (II), since the conversion of XI into II was well-documented.^{4,10,11)}

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- 11) A somewhat similar but different synthesis was orally reported by Prof. E. E. van Tamelen employing tri-*n*-butylphosphine as a leaving group. He used III obtained by a non-stereoselective synthesis (First Swiss Symposium on Juvenile Hormones, Basel, Switzerland, October 16th, 1970).

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