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A METHOD FOR THE STEREOSPECIFIC SYNTHESIS OF TRISUBSTITUTED OLEFINS BY 1,5-PROTOTROPIC SHIFT

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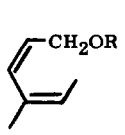
In connection with a new synthesis of Cecropia juvenile hormone, we recently reported (1) a novel stereospecific synthesis of cis-5-methylhept-4-en-1-al (III) from 2,3-cis-4,5-trans-4-methylhexa-2,4-dien-1-ol (I, R = H). The key step in this conversion was a 1,5-sigmatropic rearrangement of cyclopropane II to aldehyde III.

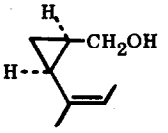
We have now extended the use of 1,5-sigmatropic rearrangements to a stereospecific conversion of the same dienol (I, R = H) to cis-4-methylhex-3-en-1-al (V), the lower homolog of III. The crucial step in this case is the rearrangement of I (R = $SiMe_3$) to the trimethylsilyl enol ether IV.

Pure dienol I was produced in 58% yield by reduction of trans-1-acetoxy-4-methylhex-4-en-2-yne (1) with disiamylborane (2) (18 hr. at -5 to 2°), followed by protonolysis (2), oxidation with alkaline hydrogen peroxide (2), and saponification (1). Conversion of I (R = H) to its trimethylsilyl ether (3a) was effected by heating (70°, 4 hr.) with excess hexamethyldisilazane and a catalytic amount of ammonium chloride. The reaction mixture was dissolved in pentane and extracted three times with cold 0.5 M HCl to remove ammonia and excess hexamethyldisilazane. Washing with 0.6 M $NaHCO_3$ and with brine, followed by evaporation of solvent and distillation, gave I (R = $SiMe_3$, b.p. 28-30°/0.2 mm. Hg, 86% yield). Dropwise addition of neat I (R = $SiMe_3$) to the top of a vertical quartz column heated to 300° under a stream of nitrogen gave a condensate (100% yield) consisting of IV (3a, b, c) (98% pure by v.p.c. analysis). The v.p.c. analysis and the n.m.r. spectrum of IV indicate that it consists of only one isomer. Assignment of trans geometry to the 1,2 double bond follows from the n.m.r. coupling constant of 11.5 Hz. observed (4) between the protons on C_1 and C_2 (5). The cis geometry of the 3,4 double bond follows from the known (6) stereochemistry of the 1,5-sigmatropic shift in 1,3 dienes, and from the ultimate stereospecific conversion of IV into the known (7) alcohol VI.

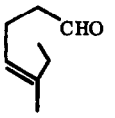
The enol ether IV (1.10 ml., 910 mg.) was converted to the aldehyde V by stirring with methanol (8.0 ml., stored over Linde 4A molecular sieves) and pH 7.0 phosphate buffer (0.80 ml., 0.05 M) under argon at 64-65° (oil bath) for 1.9 hr. The reaction mixture (which by v.p.c. analysis was found to contain V in 70% yield) was added to pentane and extracted with water. Back-extraction with pentane followed by



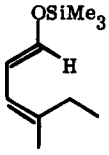
I



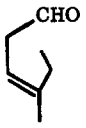
II



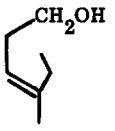
III



IV



V



VI

washing the combined pentane solutions twice with water and then with brine, evaporation of solvent at 0° (>100 mm. Hg), and distillation at 22° (0.1 mm. Hg) gave the aldehyde V (3a, b) as a colorless oil (95% pure by v.p.c. and n.m.r. analyses, 45% yield). The impurities present are hexamethyldisiloxane (2.5%) and the dimethyl acetal of V (2.5%).

The structure of V was confirmed by its reduction with lithium aluminum hydride in ether (0°, 15 min.) to the alcohol VI (77% yield), previously prepared in this laboratory (7) by a completely independent stereospecific route (8).

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3. Satisfactory (a) spectroscopic, (b) mass spectrometric, and/or (c) analytical data have been obtained for this compound.
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8. This work was assisted financially by the National Institutes of Health and the National Science Foundation.