

SYNTHESIS OF  $\gamma$ -ACORADIENE ( $\alpha$ -ALASKENE) AND  $\delta$ -ACORADIENE

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(Received in USA 6 July 1973; received in UK for publication 25 September 1973)

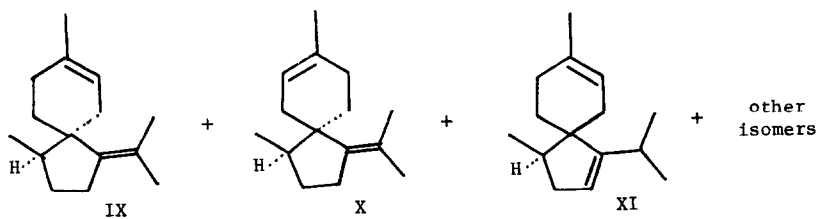
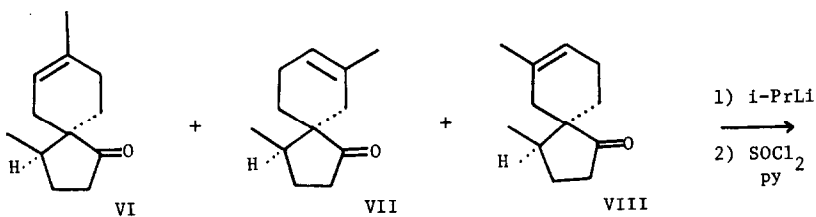
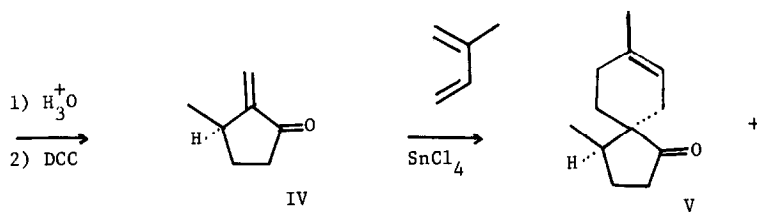
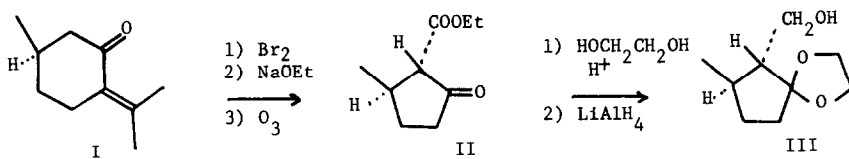
We wish to report syntheses of  $\gamma$ -acoradiene (IX) and  $\delta$ -acoradiene (X), two spirocyclic sesquiterpenes isolated from Juniperus rigida.<sup>1</sup>  $\gamma$ -Acoradiene has been shown to be identical to  $\alpha$ -alaskene, isolated from Alaska cedar, Chamaecyparis nootkatensis,<sup>2</sup> though  $\delta$ -acoradiene is enantiomeric to  $\beta$ -alaskene from the same source.<sup>2,3</sup>

Previous syntheses of members of the acorane class have been reported for racemic forms of an unnamed acoradiene<sup>5</sup> and for a compound which was an intermediate in a biogenetic-like synthesis of  $\alpha$ -cedrene<sup>6</sup> and which has the structure assigned later to  $\alpha$ -acorenol.<sup>1</sup> Some other synthetic approaches toward acoranes have also been reported.<sup>7-9</sup>

The synthesis of  $\gamma$ - and  $\delta$ -acoradiene is summarized in Chart I. R(+)-Pulegone (I) was converted into 3-methyl-2-carbethoxycyclopentanone (II), bp<sub>0.1</sub> 72-74°, [ $\alpha$ ]<sub>D</sub> + 53° in 57% yield by improvement of published procedures.<sup>10</sup> Conversion of II into its ethylene ketal and reduction with LiAlH<sub>4</sub> gave the ketal alcohol III (64%). Careful hydrolysis (25% HCl, 2.0 min) gave the corresponding keto alcohol (98%), which was dehydrated with dicyclohexylcarbodiimide<sup>11</sup> to 3-methyl-2-methylenecyclopentanone (IV), 69%, [ $\alpha$ ]<sub>D</sub> + 53.5°, bp<sub>0.1</sub> 32-33°, semicarbazide adduct, mp 177-179.5°.

Stirring the easily-polymerized IV with isoprene and a 0.2 eq. of SnCl<sub>4</sub><sup>12</sup> gave a 69:27:3:1 mixture (39% yield) of the Diels-Alder adducts V, VI, VII, and VIII.<sup>13</sup> The two major products are the "para" isomers V and VI, as predicted from increased electronic control of orientation in the Lewis acid-catalyzed Diels-Alder reaction<sup>12,14</sup> and verified by model experiments.<sup>15</sup> The well-known sensitivity of the Diels-Alder reaction to steric effects<sup>16</sup> allows one to assign structure V to the major isomer, in which the isoprene has attacked from the side opposite

## CHART I



the methyl group in IV. The structures of the two minor isomers follow from their predicted relative abundances and their relative retention times on vpc, as judged from the model work.<sup>15</sup>

Treatment of the ketone mixture V + VIII with *i*-propyl lithium gave a 1:1 mixture of unchanged ketones (enolization) and stereoisomeric alcohols. This was resubmitted to the reaction conditions, then the total material treated with  $\text{SOCl}_2$  in pyridine (5 min at 0°) and chromatographed on silica gel to give a mixture of dienes (60% based on ketones consumed).

The diene mixture was well resolved by vpc into an exocyclic fraction (40%) and an endocyclic fraction (XI) (60%). The exocyclic fraction contained four compounds in approximately the same ratios as their ketonic precursors. The major isomers were purified by preparative vpc on SE-30. The major component (longest retention time) was identical by chromatographic and spectral comparisons with  $\gamma$ -acoradiene ( $\alpha$ -alaskene) IX,  $[\alpha]_D - 82^\circ$  (lit.<sup>1</sup>  $-88 \pm 10^\circ$ ), and was cyclized to  $\alpha$ -cedrene with formic acid as reported.<sup>2</sup> The other major exocyclic diene was identified as  $\delta$ -acoradiene (X)  $[\alpha]_D + 14^\circ$  (lit.<sup>1</sup>  $+16^\circ$ ) by vpc and spectral comparisons.

Since a formal total synthesis of pulegone is on record<sup>17</sup> and the absolute configuration of the methyl group has been shown<sup>18</sup> to be R, the present formal total synthesis confirms the relative and absolute stereochemistry proposed for  $\gamma$ - and  $\delta$ -acoradiene.

Acknowledgment. Financial support by the Robert A. Welch Foundation is gratefully acknowledged. L. R. N. wishes to thank the National Science Foundation for a Traineeship grant, administered by Texas Tech University. We also thank Professor Niels H. Anderson for comparison samples and spectra.

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13. The compounds were partially separated by vpc ( $\frac{1}{8}$  in x 40 ft 3% SE-30 on Chromasorb G at 165°). The ratios were estimated from the ratios of acoradienes formed (which were separated under these conditions) and by analogy with a model reaction.<sup>15</sup>
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15. In model experiments, heating 2-methylenecyclopentanone with isoprene gave a 2:1 ratio of "para" to "meta" adducts (the desmethyl analogs of V or VI and VII or VIII respectively). This ratio was changed to 24:1 by the use of SnCl<sub>4</sub>.<sup>12</sup>
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