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# A SYNTHESIS OF TRANS-TRISUBSTITUTED OLEFINS USING THE CLAISEN REARRANGEMENT

D. John Faulkner and Michael R. Petersen
Scripps Institution of Oceanography, La Jolla, California 92037

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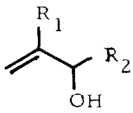
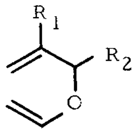
We wish to describe a simple and convenient route to *trans*-trisubstituted olefinic bonds, employing highly stereoselective examples of the Claisen rearrangement. Owing to the success of polyolefinic cyclisation reactions (1) and to recent interest in the synthesis of the insect juvenile hormone (2) and related polyolefinic compounds, several stereoselective approaches to the synthesis of trans-trisubstituted olefins have been described (3). Few of these methods, however, lend themselves to repetitive use for the synthesis of polyolefinic chains.

Since the Claisen rearrangement was known (4) to yield olefin mixtures in which the *trans* isomer was predominant, we set out to determine quantitatively the stereoselectivity of this reaction. The allylic alcohols (I a-c) were prepared by the addition of a Grignard reagent to a 2-substituted acrolein. By treatment with a large excess of ethyl vinyl ether containing mercuric acetate (5), the allylic alcohols were converted into the corresponding allyl vinyl ethers (II a-c) in variable yields. The allyl vinyl ethers were pyrolysed in sealed tubes to obtain stereoisomeric mixtures of the unsaturated aldehydes (III a-c) in quantitative yields (6). The *trans*:*cis* isomer ratios were determined by vapor phase chromatography (7) and are tabulated below:

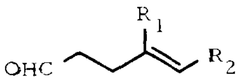


I

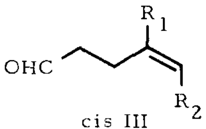


II

a) $R_1$ = Me $R_2$ = Et
b) $R_1$ = Me $R_2$ = iPr
c) $R_1$ = Et $R_2$ = Et



*trans* III

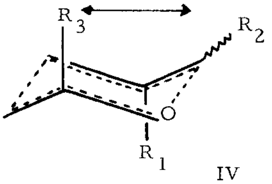


*cis* III

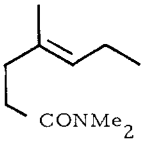
TABLE I

| Reaction | Temp. | trans:cis ratio |
|---|---|---|
| IIa → IIIa | 110°C | 90:10 |
| IIa → IIIa | 205°C | 86:14 |
| IIb → IIIb | 110°C | 93:7 |
| IIc → IIIc | 110°C | 90:10 |

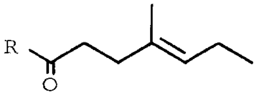
These results, together with some examples from the literature, led to the hypothesis (8) that the trans:cis isomer ratios in the Claisen and Cope rearrangements could be predicted using the recommended values of $\Delta G^{o}$, the free-energy change for the conversion of a substituent from the equatorial to the axial position of a cyclohexane. Furthermore, using the well-established (9) chair model (IV) for the transition state, we expected that the almost axial substituent $R_3$ would introduce a relatively large 1, 3-diaxial interaction with substituent $R_2$ and thus increase the stereoselectivity of the Claisen rearrangement (10).



IV



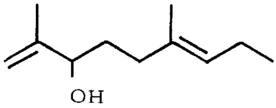
V



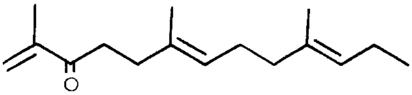
VI R = Me

VII R = isopropenyl

In order to test this prediction, we reacted the allylic alcohol (Ia) with dimethylacetamide dimethyl acetal in xylene at 140° (11). We obtained a high yield of the amide (V) which was contaminated with only 0.6% of the cis isomer. Similarly, a mixture of the allylic alcohol (Ia), two molar equivalents of isopropenyl methyl ether and catalytic quantities of oxalic acid and hydroquinone was heated in a sealed tube at 110° for 24 hours (12) to obtain a 76% yield of the ketone (VI), containing less than 1% of its cis isomer (13). Thus we had demonstrated that the introduction of a substitutent $R_3$ was sufficient to cause a profound increase in the stereoselectivity of the Claisen rearrangement.

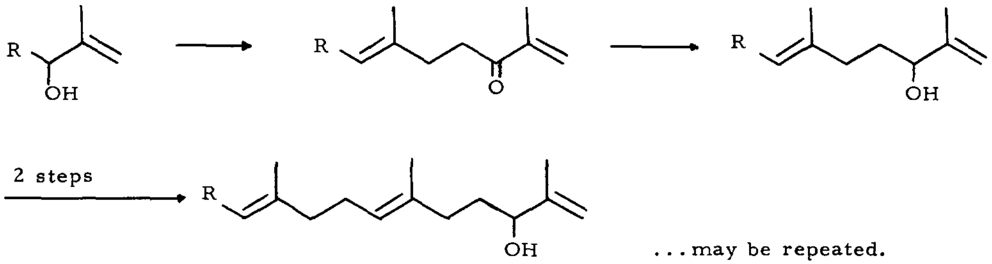


VIII



IX

A similar reaction between the allylic alcohol (Ia) and 2-methoxy-3-methylbutadiene [prepared in 40-45% overall yield from 2-methyl-1-buten-3-yne (14)] gave the $\alpha,\beta$-unsaturated ketone (VII), which was immediately reduced with sodium borohydride in methanol to the allylic alcohol (VIII). We were unable to detect any cis isomer by vapor phase chromatography although a 90:10 mixture of stereoisomers, prepared by the reactions of 2-propenyl magnesium bromide with the aldehyde (IIIa), was clearly separable under identical conditions. Repetition of the treatment with 2-methoxy-3-methyl butadiene converted the allylic alcohol (VIII) to the ketone (IX) in good yield, demonstrating the potential of this simple two-step process for the preparation of polyolefinic natural products (15). The envisioned reaction sequence is illustrated below.



...may be repeated.

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6. Satisfactory analytical data have been obtained for all new compounds described.

7. We wish to express our thanks to Prof. R.C. Fahey for allowing us to use his Varian 1200 gas chromatogram, equipped with a 300 ft. capillary column containing 150 ft. of XF 1150 and 150 ft. of Carbowax 400.

8. C.L. Perrin and D.J. Faulkner, Tetrahedron Letters, in press.

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10. Since the nature of the substituent $R_1$ will have very little effect on the stereoselectivity of the Claisen rearrangement, the reaction sequences below may also be employed for the synthesis of *trans*-disubstituted olefinic bonds.

11. A. E. Wick, D. Felix, K. Steen, and A. Eschenmoser, *Helv.*, **47**, 2425 (1964).

12. cf. G. Saucy and R. Marbet, *Helv.*, **50**, 2091 (1967).

13. To show that the very small peak on the vapor phase chromatogram was indeed due to the *cis* isomer, we reacted the stereoisomeric mixture of aldehydes (IIIa) with methyl magnesium iodide and oxidized the resulting alcohol with Jones reagent to obtain a mixture of stereoismeric ketones, in which the 90:10 *trans*:*cis* isomer ratio was clearly defined on vapor phase chromatography.

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15. Work in progress