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AN ISOMERIZATION→CLAISEN REARRANGEMENT ROUTE TO OLEFINIC DICARBONYL STARTING MATERIALS FOR CONJUGATE CYCLIZATION

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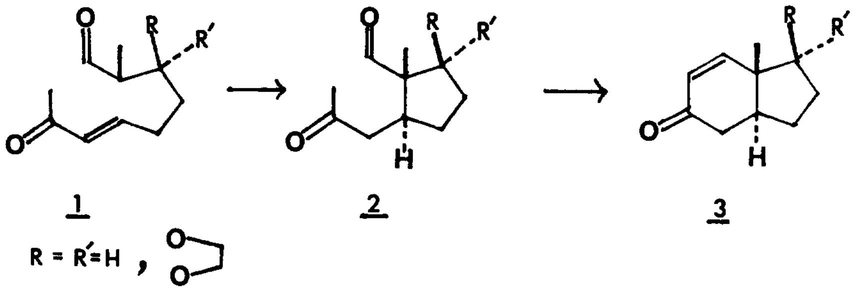
Summary: Unsaturated dicarbonyl compounds which are useful in conjugate cyclization processes are synthesized by a route which makes use of a sequential isomerization and Claisen rearrangement of the allyl ether of a substituted allyl alcohol.

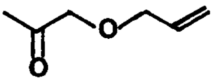
We have recently shown that intramolecular conjugate addition of systems such as 1 can be controlled to give the vicinal stereochemistry which corresponds to trans hydrindane systems: 1→2→3[1].



The potential importance of this route made it desirable to devise versatile syntheses of molecules of type 1 which would also be flexible with respect to the nature of substituent R. We report here the results obtained in our investigation of the possibility of using the regiocontrolled rearrangement of a diallylic ether coupled with Claisen rearrangement of the resulting allyl vinyl ether as a route to the desired systems (9→10)[2].

The starting material for the synthesis of substrate 6 was the easily available allyloxy acetone (4)[3]. Wittig condensation of 4 with the Wittig reagent 5[4] at 0°C using butyl lithium as a base provided the olefin 6 in 70% yield[5]. Acid treatment of the allyl ether 6 to the alcohol 7 was followed by oxidation[6] to give the aldehyde 8 in 91% yield. The aldehyde 8 was condensed with 1-triphenylphosphoranylidene-2-propanone[8] in refluxing benzene to provide the enone 9 in 90% yield[9]: IR (Neat) 1690, 1620 cm^{-1}; NMR ($CDCl_3$)δ 7.0-6.6 (m, 1 H), 6.1 (d, J = 16 Hz, 1 H).

It was necessary to find conditions which would effect the rearrangement of the terminal allyl ether moiety selectively, under conditions which would neither decarbonylate the resulting aldehyde nor lead to premature formation of the five membered ring by thermal cyclization[11]. After considerable experimentation, we were able to achieve the desired result by heating the allyloxy enone 9 (500 mg) and 10% palladium on charcoal[12] (150 mg) in dry xylene (30 ml) for



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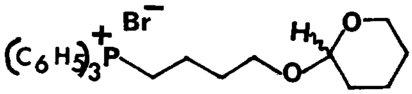

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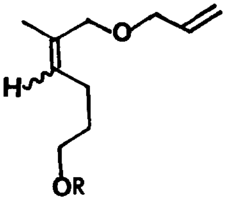
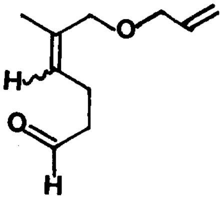


6 R=THP
7 R=H



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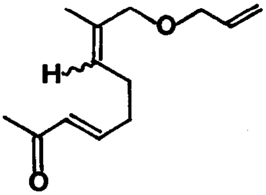

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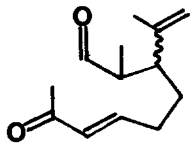

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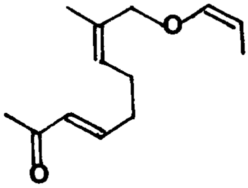

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24 hours and the aldehyde 10[14] (NMR ($CDCl_3$) δ 9.6 (d, J = 2.2 Hz, 1 H), 7.0 - 6.6 (m, 1 H), 6.07 (d, J = 16 Hz, 1 H)) was obtained in 58% yield along with the starting material (8%) and the propenyl ether 11 (12.6%)[13]. Both the starting material and the propenyl ether 11 could be recycled.

Acknowledgement:

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References and Notes

1. G. Stork, C. Shiner and J. Winkler, J. Am. Chem. Soc., J. Am. Chem. Soc., 1o4, 310 (1982).
2. J. Reuter and R. Solomon J. Org. Chem., 42, 3360 (1977).
3. We found the oxidation method of Swern[6] to be particularly effective for the preparation of allyloxyacetone (80%) from the corresponding alcohol: D. Swern, G. Billen and H. Knight, J. Am. Chem. Soc., 71, 1152 (1949).
4. A. Kreft, Ph. D. thesis, Columbia University, 1976; L. Long and G. Freeguard, Nature, 207, 403 (1965).
5. The Z : E ratio[7] of the isomers was 3 : 1 as determined by VPC analysis (3% FFAP, 159°C; Z elutes faster than E).
6. A. Mancuso, S. Hung and D. Swern, J. Org. Chem., 43, 2480 (1978).
7. C. Sreekumar, K. Darst and W. C. Still, J. Org. Chem., 45, 4260 (1980).
8. F. Ramirez and S. Dershowitz, J. Org. Chem.,22. 41 (1957); Triphenylphosphoranylidene-2-propanone is available from Aldrich Chem. Co..
9. A small amount (5%) of the Z-isomer was easily separable by flash chromatography[10].
10. W. C. Still, M. Kahn and A. Mitra, J. Org. Chem., 43, 2923 (1978).
11. This has to be avoided because we found that thermal cyclization shows

essentially no stereoselectivity in these systems.

12. H. A. J. Carless and D. J. Hayward, J. Chem. Soc. Chem. Comm., 980 (1980)

13. The Z-stereochemistry of the propenyl ether 11 was proved by irradiating the methyl group at δ 1.55 whereby the vinylic proton signal at δ 5.9 collapsed to a doublet (J = 6.4 Hz). A small amount (7%) of what seems to be the therma cyclization product was also obtained. The three products were easily separated by flash chromatography[10] with 15% ether in hexane,when the desired compound eluted last.

14. It is, at this stage, of uncertain mechanistic significance that the metal alcoxide-catalyzed cyclization of 10 was much less stereoselective than that of 1 With zirconium propoxide in benzene[1],we were able to show that the eventual enones 3(R or R' = isopropenyl) were formed with a trans : cis ratio of only 3 : 1. It was possible to show that in the minor component (~18%) in which the isopropenyl ends up trans to the angular methyl (cf 3, R'= isopropenyl) the cis indane derivative actually predominates. The stereochemistry of the four isopropenyl indenones was determined by conversion to the mixture of two cis and two trans 7a-methyl-1-acetylindanes. Ratios followed from the NMR integration of the angular methyl groups which are known to be characteristic for each of these subtances : B. Zech, G. Jones and C. Djerassi, Chem. Ber., 101, 1018 (1965) . The details of this transformation and an improved synthesis of trans-hydrindane will be the subject of a forthcoming publication.

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