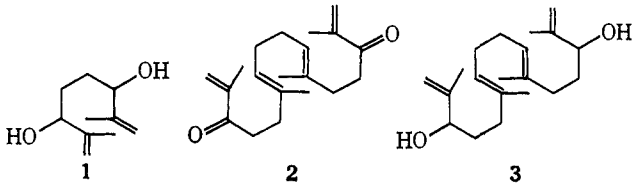
Acknowledgment. We wish to thank the U. S. Public Health Service, the National Science Foundation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

William S. Johnson, Tsung-tee Li
Charles A. Harbert, William R. Bartlett
Thomas R. Herrin, Benjamin Staskun, Daniel H. Rich
Department of Chemistry, Stanford University
Stanford, California 94305
Received April 14, 1970

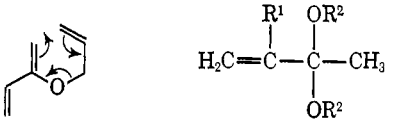
Olefinic Ketal Claisen Reaction. A Facile Route to Juvenile Hormone[1]

Sir:

The methoxyisoprene Claisen method[2] for the production of successive head-to-tail isoprene units with *trans* olefinic bonds has been used in connection with a stereoselective synthesis of squalene.[3] Thus the dienediol **1** on heating at 140° in xylene with excess 3-methoxyisoprene and catalytic amounts of hydroquinone and perchlorohomocubanecarboxylic acid for 25 hr gave the tetraenedione **2**, which was reduced with sodium borohydride to give the tetraenediol **3** in 53% yield.[4] The rearrangement almost certainly involves vinyl allylic ethers like **4**, which are produced *in situ*.



1 **2** **3**

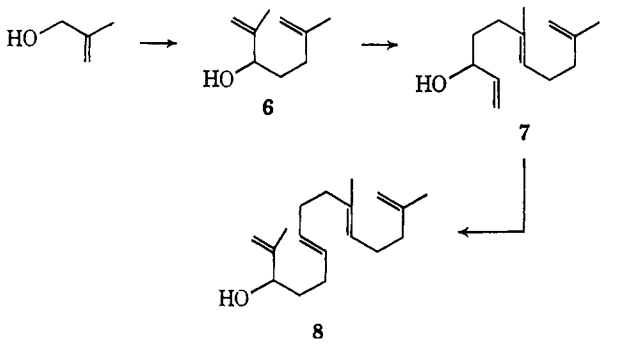


4

5a, $R^1 = H$; $R^2 = Et$
b, $R^1 = Me$; $R^2 = Me$
c, $R^1 = Me$; $R^2 = Et$
d, $R^1 = Et$; $R^2 = Me$

Some time ago we noted that the ketal from ethylene glycol and mesityl oxide, on heating with geraniol at 192° for 2 days, produced a product with nmr, ir, and mass spectral properties that were consistent with an α,β-unsaturated ketone structure resulting from a Claisen rearrangement involving an intermediary species like **4**. This discovery prompted us to undertake a detailed study of the use of olefinic ketals in the Claisen rearrangement and has led to the development of a procedure for effecting the transformation in good yield under relatively mild conditions.

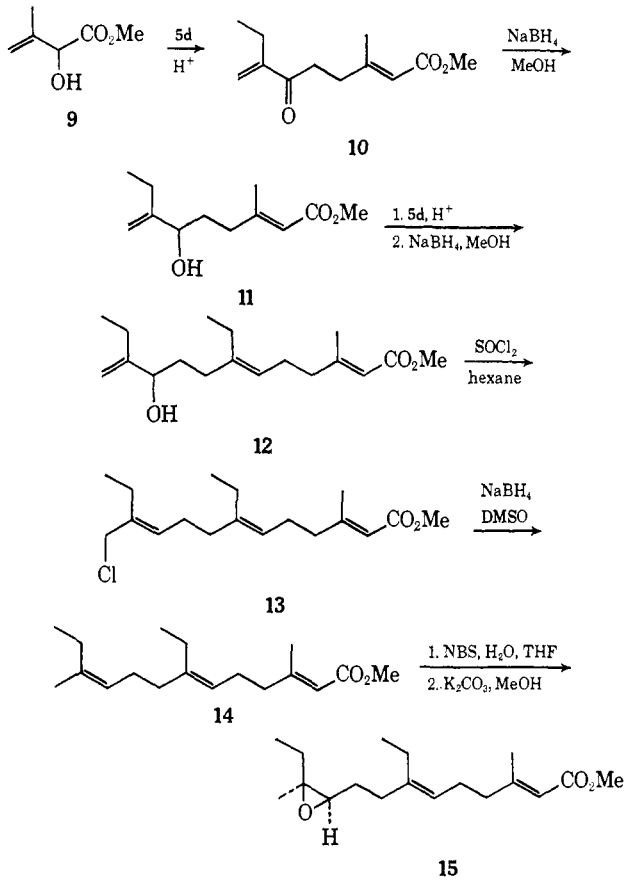
In order to allow a direct comparison of the olefinic ketal Claisen reaction with the aforementioned method, we have examined the conversion of **1** → **2** using the ketal **5b**. Our currently favored procedure involves heating at 100° for about 8 hr a solution of 1.18 mmol of **1** in 2.6 ml of toluene containing 1.19 mmol of 2,4-dinitrophenol[5] and a total of 13 mmol of **5b**.[6] Chromatography on Florisil afforded diketone **2** which was reduced with sodium borohydride in methanol at 0° to give the diol **3** in 62% yield after distillation[7] at 145° (0.01 mm) (97% pure by vpc, with no detectable *cis* isomers).[8] This procedure has advantages over the former method:[3] the ketals **5**, prepared by direct ketalization (orthoformate and excess alcohol) of the corresponding α,β-unsaturated ketones, are more readily accessible than the corresponding dienol ethers. Also the considerably lower temperature, shorter heating period, and weaker acidity of the reaction mixture give a relatively clean product which is readily purified and afford somewhat better yields. There are no appreciable competing Diels–Alder additions or polymerizations; hence the hydroquinone can be omitted. Moreover these milder conditions minimize tendency for geometric isomerization in sensitive systems (see below).



6 **7** **8**

An interesting application of a succession of olefinic ketal Claisen reactions (combined with the reduction step) is exemplified by the conversion of methallyl alcohol into **6** using the ketal **5b**, of **6** into **7**[8] (*m/e* 194, M^+) using the ketal **5a**, and of **7** into **8** using the ketal **5b** or **5c**. The first two stages have been studied in only a preliminary way, but sufficiently to ascertain that products of very high stereochemical purity were produced. The last step, **7** → **8**, has been examined more thoroughly. Under conditions similar to those described above (4 equiv of ketal), yields as high as 81% of distilled[7] (150° (0.35 mm)) tetraenol **8** (98% pure by vpc; *m/e* 262, M^+) have been realized. Hence the olefinic ketal Claisen reaction is useful for preparing *trans*-disubstituted as well as *trans*-trisubstituted olefinic bonds.

(1) This work was reported, in essence, at the Metrochem Organic Synthesis Symposium at Stevens Institute of Technology, Hoboken, N. J., March 25, 1970.
(2) D. J. Faulkner and M. R. Petersen, *Tetrahedron Lett.*, 3243 (1969).
(3) W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. Li, D. J. Faulkner, and M. R. Petersen, *J. Amer. Chem. Soc.*, **92**, 741 (1970).
(4) This represents the yield of material after distillation (footnote 7) at 145° (0.01 mm).
(5) Ammonium nitrate is also effective as a catalyst, as are propionic, diphenylacetic, trimethylacetic, or mesitoic acids. The carboxylic acids, however, are gradually esterified under the reaction conditions.
(6) In the preparation of **2** the olefinic ketal was added in three portions and the methanol removed by distillation as the reaction progressed; however, in other instances comparable results were obtained when the ketal was added all at once or when the methanol was not removed. Also the ethyl ketal **5c** seemed to be as effective as **5b**.
(7) Evaporative bulb-to-bulb distillation using a Büchi kugelrohrofen.
(8) This substance was compared (vpc, tlc, nmr, and ir) and shown to be identical with that from the orthoester Claisen sequence.[3]



The olefinic ketal Claisen reaction has been employed in a facile stereoselective synthesis of the juvenile hormone **15**. The hydroxy ester **9**,[9] on treatment with ketal **5d** as described above, gave after chromatography on Florisil the keto ester **10** which was then reduced with sodium borohydride in methanol at 0°. The product, after chromatography on silica gel, was obtained in 51% yield and consisted of the *trans* hydroxy ester **11** contaminated with 13% of the *cis* isomer as estimated by vpc. The loss of high stereoselectivity here represents a unique case. Fortunately, the *cis* isomer is relatively volatile and could be easily removed by distilling it away from the *trans* isomer using a moderately efficient fractionating column. The residue (mass spectrum of purified material *m/e* 212, M^+), on retreatment by the Claisen-reduction sequence, was transformed into the hydroxy ester **12**. After chromatography on silica gel the yield was 70% of material (*m/e* 294, M^+) containing (as shown by vpc analysis) none of the *cis,trans* isomer. (Authentic *cis,trans* isomer was produced for comparison by applying the Claisen-reduction sequence to the pure *cis* form of **11**.) It is noteworthy, however, that extensive isomerization about the double bond conjugated with the ester was observed when carboxylic acid catalysis[5] was employed. The hydroxy ester **12** was submitted to conditions (thionyl chloride in hexane at 0° for 17 hr) for the SNi′ reaction,[10] to give in 85% yield the chloride **13** contaminated, as shown by vpc, with 12% of an impurity containing what appeared to be the secondary chloride **12** (Cl in place of OH). This mixture (*m/e* 312, M^+) was reduced at 50° with 1 equiv of sodium borohydride in DMSO containing 1,5-hexadiyne as a borane trapping agent. Under these conditions the reduction was selective giving predominantly the known[11] *trans,trans,cis*-trienic ester **14** contaminated (as shown by vpc) with a mixture rich in the aforementioned impurity. The known conversion of **14** into juvenile hormone **15**[11] was performed with our material. Reaction with N-bromosuccinimide in aqueous THF gave a bromohydrin which was readily separated from the chloride impurities (see above) by chromatography on silica gel. The bromohydrin, on treatment with potassium carbonate in methanol, afforded after distillation[7] at 85° (0.02 mm) *dl*-juvenile hormone (**15**) in 35% overall yield from **13**, identified with authentic material[12] by vpc, ir, nmr, and mass spectroscopy. By vpc and nmr analysis of the trienic ester,[13] as well as the juvenile hormone, it was possible to demonstrate that none of the small amounts of detectable impurities in our final product were stereoisomers of the juvenile hormone. Although the yields and purifications have not been optimized, this synthesis in its present state represents a short, highly stereoselective route to the hormone.[14]

Acknowledgment. We wish to thank the U. S. Public Health Service and the National Science Foundation for support of this research.

(9) The acetoxy methyl ester (**9**, OAc in place of OH) was prepared by a method analogous to that for formation of the acetoxy ethyl ester (see footnote 9 of R. J. Anderson, C. A. Henrick, and J. B. Siddall, *J. Amer. Chem. Soc.*, **92**, 735 (1970)). Methanolysis of the acetate in the presence of anhydrous potassium carbonate at 0° for 1 min afforded the hydroxy ester **9** (mass spectrum *m/e* 130, M^+) in 81% yield. We wish to thank Dr. John Siddall and Mr. Richard Anderson of Zoecon Corp. for providing us with samples and information regarding the preparation of the acetoxy ethyl ester.

(10) W. S. Johnson, T. Li, C. A. Harbert, W. R. Bartlett, T. R. Herrin, B. Staskun, and D. H. Rich, *J. Amer. Chem. Soc.*, **92**, 4461 (1970).

(11) K. H. Dahm, B. M. Trost, and H. Röller, *ibid.*, **89**, 5292 (1967).

(12) W. S. Johnson, T.-t. Li, D. J. Faulkner, and S. F. Campbell, *ibid.*, **90**, 6225 (1968).

(13) We wish to thank Dr. J. B. Siddall of Zoecon Corp. for providing us with an authentic mixture of the *trans,trans,cis*-, *trans,trans,trans*-, *cis,trans,trans*-, and *cis,trans,cis*-trienic ester isomers which are all resolvable by vpc.

(14) All new compounds reported in this paper have been fully characterized by ir, nmr, and mass spectrometry. Satisfactory combustion analyses were obtained for all of these substances except for some of the α,β-unsaturated ketone intermediates which have not yet been obtained completely pure.

William S. Johnson, Timothy J. Brocksom
Peter Loew, Daniel H. Rich, Lucius Werthemann
Robert A. Arnold, Tsung-tee Li, D. John Faulkner
Department of Chemistry, Stanford University
Stanford, California 94305
Received April 14, 1970

Stoichiometric Reduction of Molecular Nitrogen by Iron Complexes

Sir:

A fair number of stoichiometric[1-3] or even catalytic[4,5] reductions of molecular nitrogen with group IV to VI transition metal systems have been described in the

(1) M. E. Volpin and V. B. Shur, *Nature*, **209**, 1236 (1966), and earlier references quoted there.

(2) E. E. Van Tamelen, R. B. Fechter, S. W. Schneller, G. Boche, R. H. Greeley, and B. Akermark, *J. Amer. Chem. Soc.*, **91**, 1551 (1969), and earlier references quoted there.

(3) G. Henrici-Olive and S. Olive, *Angew. Chem., Int. Ed. Engl.*, **8**, 650 (1969), and earlier references quoted there.

(4) M. E. Volpin, M. A. Ilatovskaya, L. V. Kosyakova, and V. B. Shur, *Chem. Commun.*, 1074 (1968).

(5) E. E. Van Tamelen and D. A. Seeley, *J. Amer. Chem. Soc.*, **91**, 5194 (1969).