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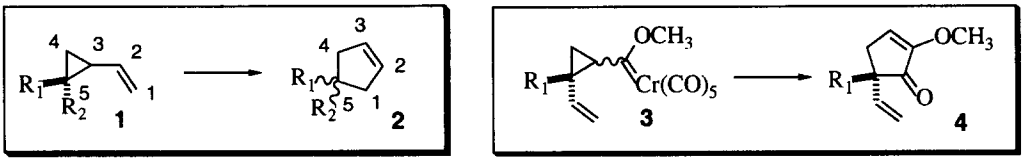
Conversion of 2-Alkenylcyclopropylcarbene-Chromium Complexes to 5-Alkenyl-2-cyclopentenones: A Stereospecific Three- to Five-Carbon Ring Expansion Reaction

James W. Herndon*, David K. Hill, and Leonard A. McMullen
Department of Chemistry and Biochemistry
University of Maryland
College Park, Maryland 20742-2021

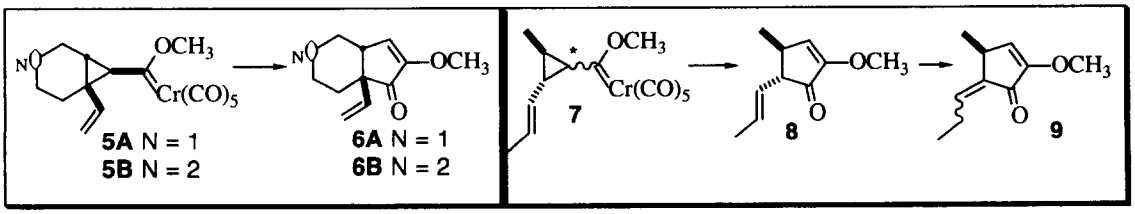
Summary: Upon thermolysis, 2-alkenylcyclopropylcarbene-chromium complexes are converted to 5-alkenyl-2-cyclopentenones. The reaction appears to proceed with retention of configuration in the absence of steric factors.

The conversion of vinylcyclopropane derivatives (**1**) to cyclopentene derivatives (**2**) (the vinylcyclopropane rearrangement, Scheme 1) has proven to be a very valuable reaction for the synthesis of five-membered rings.[1] One disadvantage of this reaction is that it typically proceeds with loss of stereochemistry at the migrating carbon atom (carbon 5). This is due either to isomerization of the vinylcyclopropane derivative followed by stereospecific rearrangement[2] or rearrangement via a radical mechanism.[3] There are a few notable examples of vinylcyclopropane derivatives which undergo a stereospecific ring expansion reaction.[4] We recently reported a novel three- to five-carbon ring expansion reaction involving the thermal conversion of 2-alkenylcyclopropylcarbene-chromium complexes (**3**) to 5-alkenyl-2-cyclopentenones (**4**), which appeared to proceed with retention of configuration in two of the examples studied (Scheme 2).[5] In this communication, evidence is provided which suggests that ring expansion with retention of configuration is an intrinsic mechanistic feature of this reaction.

SCHEME 1



SCHEME 2

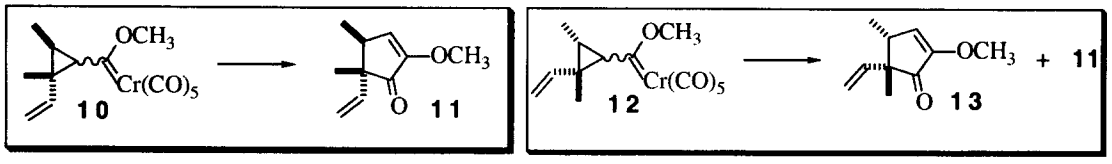


Ring-fused compounds **5A** and **B** appeared to undergo the ring expansion reaction with retention of configuration (Scheme 2),[5] however examination of the trans ring fusion stereoisomer was not attempted due to perceived synthetic difficulties. Compound **7** (mixture of isomers at the asterisked carbon) underwent ring expansion to cyclopentenone **8**, which had partially isomerized to the α,β–unsaturated cyclopentenone **9** under the reaction conditions. Unisomerized

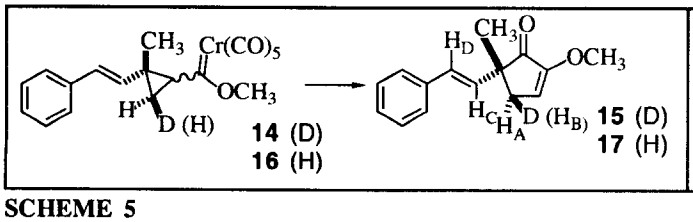
cyclopentenone **8** appeared to be exclusively the trans cyclopentenone based on the crude ^{1}H NMR spectrum.[6] Although all of the compounds in Scheme 2 underwent ring expansion with retention of configuration at the migrating carbon atom, the stereochemical fate of the ring expansion process is ambiguous since the opposite diastereomer has not been tested for each compound.

Appropriately-substituted carbene complexes from which the stereospecificity of the ring expansion could be delineated were prepared. Carbene complexes **10** and **12** were prepared from commercially available E- and Z 3-methyl-1,3-pentadiene (Scheme 3). Ring expansion of compound **10** proceeded readily at 100 °C, and provided cyclopentenone **11** as the only product of the reaction. Ring expansion of compound **12** was considerably slower, and ultimately provided a 60:40 mixture of cyclopentenones **13** and **11**. The equilibrium ratio for compounds **13** and **11** was also 60:40. Stereospecifically isotopically labelled compound **14** (Scheme 4) was prepared from bromostyrene according to the route in Scheme 5; deuterium incorporation in diene **18** was 90%, and completely stereospecific.[8] Thermolysis of compound **14** at 100 °C led to cyclopentenone derivative **15** in 35% yield. Purification of the reaction mixture was difficult in this case due to the formation of arene complexes, which did not undergo clean decomplexation reactions. The protio analog **16** underwent a similar conversion. In compound **17** H_A and H_B appear as doublets of doublets at δ 2.75 and δ 2.45 respectively. In compound **15** the ratio of the resonances at δ 2.75: δ 2.45 was 9:1. The resonance at δ 2.75 was a broad singlet, while the resonance at δ 2.45 was a sharp doublet of doublets. This implies that the reaction is completely stereospecific, and that the minor resonance at δ 2.45 is due to the undeuterated impurity (*i.e.* **17**) and not the opposite diastereomer. The assignment of stereochemistry for compound **15** is supported by enhancement in the intensity of the vinylic hydrogens upon irradiation of H_A.

SCHEME 3

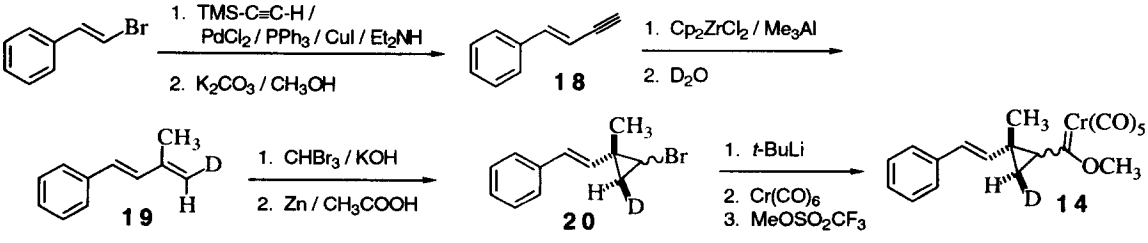


SCHEME 4



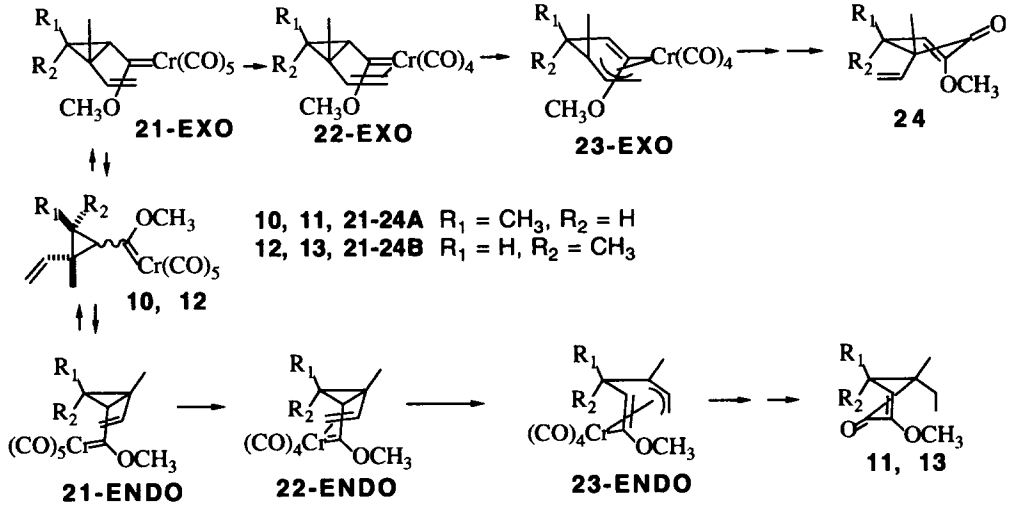
NOE Enhancements In Cyclopentenone 15				
H Irradiated	H_A	H_C	H_D	CH_3
H_A		3%	9%	0%
CH_3	0%	5%	9%	

SCHEME 5



The result in Scheme 4 definitively establishes that the ring expansion reaction proceeds with retention of configuration at the migrating carbon atom. The stereochemical ambiguity presented in Scheme 3 is puzzling, and can possibly be attributed to steric interactions between the carbene complex and the methyl group in complex **12** (isomer where carbene complex and alkene are cis). Previous mechanistic studies have established that ring expansion occurs primarily from the isomer where carbene complex and alkene are cis, that the carbene complex undergoes epimerization at elevated temperatures and in basic solvents, and that dissociation of carbon monoxide is required in the reaction.[5] The mechanistic argument depicted in Scheme 6 might account for the differing degrees of stereospecificity observed for ring expansion of stereoisomers **10** and **12**. First, loss of carbon monoxide, alkene complexation, and conversion to internally-coordinated π-allyl complex **23** occurs.[9] Carbon monoxide insertion and reductive elimination affords cyclopentenone derivatives **11** and **13**. If the double bond and carbene complex are in the exo orientation, a trans double bond in a five-membered ring must ultimately result (*e.g.* **24**). Only the endo reacting conformation can eventually lead to the observed cis cyclopentenone derivatives **11** and **13**. In the endo conformation of compound **12** there is significant steric interaction between the methyl group (R_2) and the carbene complex which would suppress formation of this conformation, and thus cyclopropane stereoisomerization can compete with ring expansion. A similar argument has been used to explain steric effects in the related divinylcyclopropane rearrangement.[10]

SCHEME 6



In summary, the conversion of 2-alkenylcyclopropylcarbene-chromium complexes to 5-alkenyl-2-cyclopentenones proceeds with retention of configuration in the absence of steric interactions which suppress the preferred reacting conformation. Further examination of the conformational factors affecting the ring expansion process is presently underway in these laboratories.

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2. For a recent example supporting this viewpoint, see Gajewski, J.J.; Olson, L.P. *J. Am. Chem. Soc.* **1991**, *113*, 7432-7433.

3. For a recent example supporting this viewpoint, see Baldwin, J.E.; Villarica, K.A.; Freedberg, D.I.; Anet, F.A.L. *J. Am. Chem. Soc.* **1994**, *116*, 10845-10846.

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6. ^{1}H NMR ($CDCl_3$): δ 6.27 (d, 1 H, J = 3.2 Hz), 5.72 (dq, 1 H, J = 16.0, 7.1 Hz), 5.41 (dd, 1 H, J = 16.0, 8.0 Hz), 3.78 (s, 3 H), 2.64 (ddq, 1 H, J = 3.4, 3.2, 8.0 Hz), 2.56 (br d, 1 H, J = 8.0 Hz), 1.78 (br d, 3 H, J = 7.1 Hz), 1.24 (d, 3 H, J = 8.0 Hz). The coupling constant between the hydrogens at C-4 and C-5 (IUPAC numbering) is 3.4 Hz, which is more consistent with the trans orientation of cyclopentenone substituents.[7]

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