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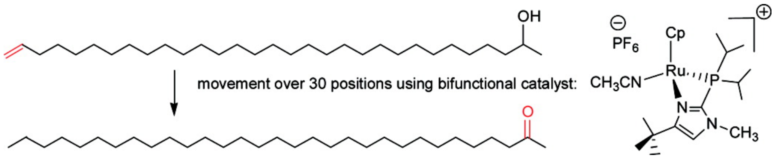

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# Extensive Isomerization of Alkenes Using a Bifunctional Catalyst: An Alkene Zipper

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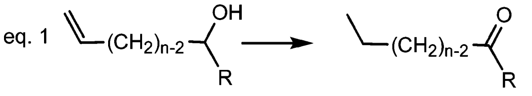
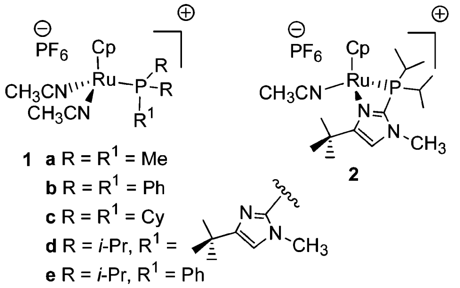
Redox isomerizations are examples of atom-economical processes[1] in which one site in an organic substrate is oxidized with concomitant reduction of another site. One especially well-studied example is the conversion of allylic alcohols to aldehydes or ketones,[2,3] which involves movement of the alkene double bond[4−7] over two positions (eq 1, $n = 2$). Far fewer catalysts exist for the movement of a more remote double bond ($n > 2$). For example, Kirchner et al. reported[8] that, although $[CpRu(PR_3)(CH_3CN)_2]^+$ (**1a**−**1c**) were improved catalysts for allylic alcohol isomerization relative to $CpRu(PR_3)_2Cl$, it failed in the case of 3-buten-1-ol ($n = 3$) or alkenes devoid of alcohol functionality. The apparent record for alkene isomerization of any kind is over 20 positions on the hydrocarbon $CH_3(CH_2)_{19}CH{=}CH(CH_2)_{19}CH_3$ by *stoichiometric* amounts of the reagent $Cp_2Zr(H)(Cl)$.[9] The apparent record for *catalyzed* double bond movement is on 9-decene-1-ol (nine positions, $n = 9$) using $Fe_3(CO)_{12}$.[10,11] However, 30 mol % was required, which means that nearly a mole of metal was used per mole of alkenol.

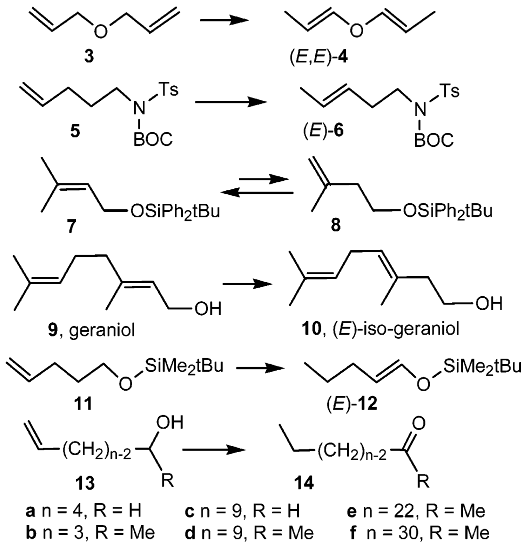
double bond movement over n positions





Here we highlight the discovery and development of a novel catalyst (**2**) whose notable and attractive features include the following: (1) ability to isomerize a variety of heterofunctionalized alkene derivatives, (2) formation of (*E*)-isomer products of high purity, (3) useful activity in many cases at low loadings (2−5 mol %), and (4) a heterocyclic ligand which appears to act not merely as a hemilabile group but rather as an internal base. Finally, we show that bifunctional catalyst **2** is truly an alkene zipper[12] by reporting *the catalyzed movement of an alkene double bond over 30 positions* along an alkyl chain (eq 1, $n = 30$).

***Scheme 1.*** Reactants and Products



Initial screening experiments were conducted on the alkenes 1-pentene and pent-4-en-1-ol, representing two different classes of substrate, one lacking any polar or protic group and the other featuring the alkene and OH separated by three carbons (eq 1, $n = 4$). Such substrates were inert to **1a**−**1c**.[13] From these preliminary studies, which included phosphines with both imidazol-2-yl and pyrid-2-yl substituents on P as well as *t*-Bu, *i*-Pr, Ph, and Me groups, the phosphine ligand[14,15] in **2** emerged as a superior choice for its ability to promote isomerization of both substrates.

To prepare **2**, $[CpRu(CH_3CN)_3]^+PF_6^-$ in acetone was allowed to react with the required ligand, forming a mixture of **1d** and chelate **2**.[16] This mixture could be used but for purposes of catalyst characterization and further testing as described in this paper was converted to >90% pure **2** by repeated coevaporation of added acetone with the acetonitrile liberated. Complex **2** showed diagnostic NMR data consistent with a chiral structure and four unique, diastereotopic methyl groups.

Because pent-4-en-1-ol (**13a**) represented a more challenging class of substrate, its isomerization to pentanal (**14a**) was optimized with respect to solvent, catalyst amount, and reaction temperature. At the 2 mol % level, heating at 70 °C was advised, whereas by using 5 mol %, reactions could be completed at 25 °C within 1 d. Acetone emerged as the solvent of choice, although dichloromethane could also be used. The effects of a substrate hydroxyl group were apparent by noting that under the optimized conditions, isomerization of 1-pentene to (*E*)-2-pentene required only minutes at room temperature using 2 mol % catalyst (Scheme 1).

Substrate scope was explored. Table 1 shows results which are in most cases unoptimized for a particular substrate but are designed to give an idea of the capabilities and limitations of the catalyst. In general, full isomerization of substrates with polar groups (OH, amide) required heating at 70 °C, whereas partial isomerization of these compounds or full isomerization of nonpolar substrates could be done at 25 °C. Most dramatically, alkenol isomerization over 9, 22, and even 30 positions could be achieved (entries 9−12). The silyl ether **11** (entry 8) gave enol ether (*E*)-**12** in which only traces

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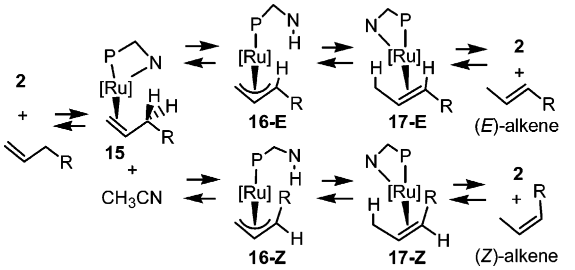
***Table 1.*** Scope and Limitations Using **2**[a]

| entry | reactant | product | **2** (%) | temp (°C) | time | yield (%) |
|---|---|---|---|---|---|---|
| 1 | 1-pentene | (*E*)-2-pentene | 2 | 25 | 15 min | 95 |
| 2 | **3** | (*E*, *E*)-**4** | 2 | 25 | 40 min | 96 |
| 3 | **5** | (*E*)-**6** | 2 | 25 | 4 h | 75[b] |
| 4 | **7** | **8** | 2 | 25 | 26 h | 70:30[c] |
| 5 | **9** | **10** | 2 | 25 | 4 d | 61[d] |
| 6 | **13a** | **14a** | 2 | 70 | 1 h | 95[e] |
| 7 | **13b** | **14b** | 2 | 70 | 1 h | 97 |
| 8 | **11** | (*E*)-**12** | 5 | 70 | 4 h | 90 |
| 9 | **13c** | **14c** | 5 | 70 | 4 h | 84 |
| 10 | **13d** | **14d** | 5 | 70 | 4 h | 97 |
| 11 | **13e** | **14e** | 20 | 70 | 3.6 d | 91[b] |
| 12 | **13f** | **14f** | 30 | 70 | 3 d | 81[b] |

[a] Acetone-$d_6$ solvent, yields determined by $^{1}$H NMR and internal standard unless otherwise indicated. [b] Isolated. [c] Equilibrium ratio of **7** and **8**, also reached from either side within 2−4 h using 2 mol % of **2** at 70 °C. [d] Unreacted **9** (29%) and an unidentified isomer (10%) also present. [e] Isomerization could also be completed using 5 mol % of **2** for 1 d at 25 °C.

***Scheme 2.*** Mechanistic Hypothesis



(<2%) of (*Z*)-isomer are detected in 500 MHz $^{1}$H NMR spectra. Remarkably, diallyl ether (entry 2) gave (*E*,*E*)-**4** in high yield without Claisen rearrangement of the intermediate allyl propenyl ether[17−19] and without any detectable (*Z*,*E*)-isomer, providing rapid entry under neutral conditions to a little-explored class of compounds which have typically been made as mixtures using strong base.[20]

Preliminary experiments are thus far consistent with the mechanistic hypothesis advanced in Scheme 2. Rather surprisingly, bubbling ethylene (∼25 equiv) into an acetone solution of **2** leads to formation of *free acetonitrile* and an ethylene complex similar to **15**, rather than a chelate-opened species. Therefore, we propose that the first step of the catalytic cycle is exchange of acetonitrile for alkene, forming **15**. The role of the basic nitrogen of the imidazole could then be deprotonation at an allylic position, forming **16** with an anionic allyl and a protonated heterocyclic ligand, which could then return the proton to either end of the allyl moiety and promote isomerization. Preliminary experiments using propene instead of ethylene show formation of **15** but no other detectable complexes; thus, the concentration of **16** during the catalysis must be low.

Additional compelling evidence for the role of the heterocycle in the catalyst[21] is that complex **1e** is 330 times slower at isomerizing 1-pentene than is **2** and, moreover, is 10000 times slower at isomerizing pent-4-en-1-ol. Our mechanistic hypothesis for high (*E*)-selectivity is that either the transition states (e.g., from **15** to allyl complex **16**) or intermediates (e.g., **16**) leading to (*Z*)-alkene are sufficiently high in energy to leave the system shuttling between terminal and (*E*)-alkene(s), creating “semi-thermodynamic” mixtures consisting of almost exclusively these latter isomers. The mechanistic hypothesis in Scheme 2 helps rationalize the unusual ability of **2** to convert geraniol to (*E*)-isogeraniol rather than to the aldehyde, because formation of the enol isomer would require the catalyst to form an allyl intermediate like **16-Z**. Finally, we note that, since isomerization of the longer substrates presumably occurs by a random walk of the double bond up and down the chain en route to the most stable isomer, the observed movement of the double bond is actually just a lower estimate of the number of times the catalyst acts on a substrate.

In summary, catalyst **2** is unusual in its activity (in many cases 2−5 mol % is sufficient), selectivity, and unprecedented ability to move unhindered double bonds over many positions. Ongoing studies are designed to elucidate further the mechanism of action and the capabilities of this bifunctional catalyst design, and these will be reported in due course.

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**Supporting Information Available:** Details of compound preparation, characterization, and use of the catalysts. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) In eq 1, isomerization to the enol requires a movement over $n-1$ positions, all of which can be reasonably attributed to catalysis by metal. The final enol−keto tautomerization may or may not involve metal catalyst but for simplicity is included in the total count of $n$.
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