[3 + 2] Cycloadditions are among the most powerful strategies for the synthesis of five-membered carbocyclic and heterocyclic ring systems.1 Among the reactions useful in the synthesis of cyclopentanes, trimethylene methane precursors,2 activated cyclopropanes,3 and allyl and propargylsilanes4 are arguably the most useful three-carbon units in [3 + 2] cycloadditions. Methylene cyclopropanes are known to be versatile precursors in metal-catalyzed [3 + 2] cycloadditions involving either trimethylene methane intermediates or four-membered metallacycles, depending on whether the o-bond proximal or distal to the exocyclic methylene undergoes oxidative addition with the low-valent transition metal.3 Vinylvyclopropanes are also excellent substrates in metal-catalyzed cycloadditions and rearrangements in several contexts.5 However, cyclopropanes that lack exomethylene or vinyl substituents have received relatively little attention as useful precursors in metal-catalyzed cycloaddition processes. Donor—acceptor cyclopropanes are highly versatile substrates in five-membered ring synthesis via Lewis acid catalysis.6 However, Lewis acid-promoted [3 + 2] cycloadditions of simple cyclopropyl ketones are typically not efficient. Given the lack of utility of simple cyclopropyl ketones in both Lewis acid-catalyzed and transition metal-catalyzed cycloadditions, we have initiated an exploratory investigation of this potentially useful substrate class in nickel-catalyzed reactions.

In gauging the reactivity of cyclopropyl ketone 1a with a catalyst derived from Ni(COD)2, imidazolium chloride 2, and potassium tert-butoxide,7 we made the surprising observation that 1a undergoes an efficient and highly diastereoselective dimerization to trisubstituted cyclopentane 3a in 85% yield. A variety of aromatic ketones undergo the process efficiently (Table 1, entries 1–5), and aliphatic ketones were significantly less reactive in the process. Variation of the cyclopropyl unit was difficult since even a simple methyl substituent led to low yields of expected adduct 3f along with 66% yield of 3-methyl-1-phenylbut-2-en-1-one (Table 1, entry 6). We reasoned that this remarkable transformation likely involves the oxidative addition of Ni(0) to 1 to afford metallacycle 4a or 4b,8 which undergoes a sequence involving β-hydride elimination to afford enone 5a or 5b along with regeneration of Ni(0) (Scheme 1).9 Enone 5a then undergoes addition to another equivalent of 4b to afford [3 + 2] cycloaddition product 3 (when R2 = H, note that 4a = 4b and 5a = 5b, with alkene stereochemistry arbitrarily shown). The formation of an enone as the major product in reactions of substrate 1f provided direct evidence for the 1 to 5b conversion. Analysis of the overall mass balance of entry 6 (Table 1) illustrates that metallacycle 4b is favored via oxidative addition to the least hindered carbon—carbon bond of 1, although both 4b and 5a are required for the formation of 3f.

The crossed reaction of differentially substituted cyclopropyl ketones and enones was attempted in order to advance the synthetic utility of the process and to provide further evidence for the proposed reaction pathway. However, initial attempts failed since stoichiometric addition of the enone effectively inhibits the [3 + 2] process, presumably due to its π-acidity. However, keeping the enone concentration low by syringe drive addition over 2 h duplicates the slow release of enone suggested in the proposed mechanism, and crossed reactions now become possible (Table 2). Yields were typically modest to good, and the cyclopropyl ketone dimer 3 is nearly always observed as a component of the reaction mixture. While not strictly required, Ti(O-iPr)4 or Ti(O-i-Bu)4 as an additive improves yields and increases reaction rates. The crossed reactions of differentially substituted cyclopropyl ketones and

Table 1. Cyclopropyl Ketone Dimers

<table>
<thead>
<tr>
<th>entry (substrate)</th>
<th>R1</th>
<th>R2</th>
<th>product (% yield, dr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (1a)</td>
<td>Ph</td>
<td>H</td>
<td>3a (85, 98:2)</td>
</tr>
<tr>
<td>2 (1b)</td>
<td>4-MeO(C6H4)H</td>
<td>H</td>
<td>3b (90, 99:1)</td>
</tr>
<tr>
<td>3 (1c)</td>
<td>4-F(C6H4)H</td>
<td>H</td>
<td>3c (85, 98:2)</td>
</tr>
<tr>
<td>4 (1d)</td>
<td>thiophen-2-yl</td>
<td>H</td>
<td>3d (88, 99:1)</td>
</tr>
<tr>
<td>5 (1e)</td>
<td>furan-2-yl</td>
<td>H</td>
<td>3e (83, 90:10)</td>
</tr>
<tr>
<td>6 (1f)</td>
<td>Ph</td>
<td>Me</td>
<td>3f (24)*</td>
</tr>
</tbody>
</table>

* 3-Methyl-1-phenylbut-2-en-1-one was obtained in 66% yield.

Scheme 1. Proposed Mechanism

1. Ketone dimerization
2. Oxidative addition
3. Metallacycle formation
4. Diastereoselective dimerization
5. Metal elimination
6. Enone formation
7. Crossed reaction
8. Metallacycle degradation
9. Enone formation
enones that both possess aromatic substitution at the carbonyl proceed efficiently by this procedure (entries 1–4). Notably, a comparison of entries 3 and 4 illustrates that diastereoselectivities are kinetically controlled, and that either cis–trans diastereomer may be obtained by simply swapping the ketone substituents on the two reaction partners. Additionally, use of an enone reactant now allows additional flexibility in the R4 functionality, as illustrated by incorporation of n-hexyl (entry 5), phenyl (entry 6), or trimethylsilyl (entry 7) substituents. Whereas dimerization of cyclopropyl methyl ketone was inefficient, a crossed reaction under conditions optimized for the dimerization or crossed reaction. 10 Future studies will focus on further development of cyclopropyl imine cycloadditions and elucidation of the mechanistic basis for reaction acceleration with imine derivatives.

**Acknowledgment.** The authors wish to acknowledge receipt of NSF Grant CHE-0553895. We thank Dr. Beth Knapp-Reed for helpful discussions, and the Roush group for assistance with and use of their preparative HPLC.

**Supporting Information Available:** Full experimental details and copies of NMR spectral data (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

## References


