Grubbs' Catalyst in Paraffin: An Air-Stable Preparation for Alkene Metathesis

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Abstract: A homogeneous mixture of Grubbs' catalyst in paraffin wax was shown to catalyze three important types of metathesis reactions: ring-closing metathesis, alkene dimerization, and alkene cross-metathesis (e.g., $\ce{11 \to 13}$). This catalyst preparation demonstrated no loss in catalytic activity after 22 months of storage open to the air.

The ruthenium 4,5-dihydroimidazo-2-ylidene complex 1 developed by Grubbs is widely known for its applications in organic and polymer synthesis.1,2 Despite the obvious utility of Grubbs' catalyst, its routine use is hindered by special storage requirements. Prolonged exposure to air and moisture deactivates the complex, and it is typically stored under inert atmosphere. Recently, it has been shown that attaching the active ruthenium complex to a polymer support improves the stability of the catalyst while retaining full activity.3 Here, we report that Grubbs' catalyst dispersed in paraffin4 is easily handled and retains its activity indefinitely with no special storage precautions.

The Grubbs catalyst, complex 1, was weighed in a nitrogen atmosphere drybox and dispersed (11 wt %) in molten paraffin wax to give a homogeneous purple liquid. This mixture was allowed to cool before removal from the drybox. The ruthenium complex—paraffin mixture was cut into useful pieces and stored without protection from laboratory air. This makes it convenient to weigh out small quantities of the otherwise easily dispersed ruthenium complex. The mixture can be stored under normal laboratory conditions for many months without concern over the loss of catalytic activity. A sample stored for 22 months with no special storage precautions showed no loss of activity.

Entries 1 and 2 in Table 1 illustrate ring-closing metathesis (RCM) reactions using this catalyst preparation. The diene was dissolved in distilled CH$_2$Cl$_2$, the paraffin—catalyst mixture was added, and the reaction mixture was stirred for 10 h. Flash chromatography then separated the paraffin from the cyclized product. The reaction mixture was stirred for 10 h. Flash chromatography then separated the paraffin from the cyclized product. Reactions with the paraffin—catalyst mixture appear to run at the same rate as the same reactions with pure catalyst. Entry 3 illustrates the homo-dimerization metathesis of a terminal alkene by an analogous procedure. Entry 4 demonstrates the cross-metathesis reaction between diethyl malonate and methyl acrylate.5

Table 1. Examples of Metathesis Reaction Using Grubbs' Catalyst in Paraffin

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Percent Yield</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>5</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>7</td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>9</td>
<td>91b</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>12</td>
<td>86</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Isolated yield based on recovered starting material. b Trans/cis ratio 20:1 by integration of the $^1$H NMR spectrum.

Notes:
4. The coating of air-sensitive catalysts with paraffin is a common industrial practice, with many references in the patent literature. For a recent example, see: Fang, Y.; Liu, Y.; Ke, Y.; Guo, C.; Zhu, N.; Mi, X.; Ma, Z.; Hu, Y. Applied Catalysis, A: General 2002, 235, 33.
Entry 5 is an example of olefin cross-metathesis using the inexpensive cis-1,4-butenediol to yield the allylic alcohol 13.6 Such trans allylic alcohols are important as, inter alia, substrates for Sharpless asymmetric epoxidation. This is also the first synthesis of 13, a natural product isolated from the rhizomes of Zingiber cassumunar, a medicinal plant from Southeast Asia possessing antioxidant and antiinflammatory properties.7

We believe that these examples demonstrate that Grubbs' catalyst in paraffin is a useful reagent for routine organic synthesis. This easily handled preparation will facilitate the use of the Grubbs' catalyst in trial metathesis reactions and small-scale synthesis. There are many catalysts in common usage in the organic synthesis laboratory that are much more air and moisture sensitive than the Grubbs catalyst. It is remarkable that dispersion in paraffin to protect them has not been more widely employed.

**Experimental Section**

**Grubbs' Catalyst 1 in Paraffin.** In a nitrogen atmosphere (grade 4.8) drybox, Grubbs' catalyst (1.27 g, 1.50 mmol) was combined in a 25 mL beaker with paraffin (paraffin wax (petroleum wax) for canning, mp = 48–50 °C, 8.73 g). The mixture was warmed to melting in a heating mantle and stirred with a glass rod to apparent homogeneity (one min). After cooling, the solid was removed from the drybox, broken into useful-sized pieces, and stored in a brown glass bottle without further protection.

3,3-Dimethyl-2,4-dioxaspiro[5.5]undec-8-ene 3. Starting diene 2 (177 mg, 0.892 mmol) was dissolved in 4 mL of CH2Cl2, and Grubbs' catalyst in paraffin was added (0.15 mmol/g catalyst by wt, 273 mg, 0.016 mmol, 1.2 mol %). The reaction mixture was adsorbed directly onto silica gel and chromatographed to yield 3 as a colorless solid (210 mg, 1.08 mmol, 80% yield): TLC Rf = 0.45 (50% 1:1 CH2Cl2/MTBE; 20% 1:1 PE); 1H NMR δ = 1.57 (t, J = 7.5 Hz, 4 H), 3.85 (s, 6 H), 5.44 (m, 2 H), 7.09 (d, J = 8.5 Hz, 2 H), 7.30 (d, J = 7.4 Hz, 1 H); 13C NMR δ = 112.4, 119.5, 120.8, 129.6, 130.7, 131.0; m/z 241, 321, 38.0, 138.7, 159.8, 200.4; IR 2096, 1640 cm⁻¹; HRMS calcd for C24H28O4: C, 75.76; H, 7.42. Found: C, 75.42; H, 7.55.

5-Ethoxycarbonylhex-2-en-1-ylidene Acid 6-Ethyl Ester 1-Methyl Ester 10. Diethyl allyl malonate (206 mg, 1.03 mmol) was dissolved in 3 mL of CH2Cl2. Benzoic acid (9 mg, 0.075 mmol) was added as a cocatalyst along with Grubbs' catalyst in paraffin (488 mg, 0.073 mmol, 7.1 mol %). The reaction vial was vented to a bubbler via a nitrogen line and stirred for 22.5 h. The reaction mixture was adsorbed directly onto silica gel and chromatographed to yield 10 as a color oil (0.206 g, 0.798 mmol, 77% yield): TLC Rf = 0.39 (25% 1:1 CH2Cl2/MTBE–PE); 1H NMR δ = 1.27 (t, J = 7.8 Hz, 6 H), 2.80 (dt, J = 7.3, 1.5 Hz, 2 H), 3.50 (d, J = 7.5 Hz, 4 H), 3.77 (s, 6 H), 4.22 (m, 2 H); 13C NMR δ = 14.1, 50.6, 51.6, 123.4, 126.4; m/z 259.1182, obsd 259.1171. This was recrystallized from CHCl3 to give small colorless needles: mp = 95–96 °C; 1H NMR (CDCl3) δ = 3.33 (d, J = 6.3 Hz, 2 H), 3.88 (s, 3 H), 4.14 (m, 2 H), 5.73 (m, 1 H), 6.88 (m, 2 H), 6.85 (d, J = 8.5 Hz, 1 H); 1H NMR (CDCl3) δ = 3.15 (m, 5 H), 3.83 (d, J = 4.3 Hz, 2 H), 5.48 (m, 1 H), 5.66 (m, 1 H), 6.45 (d, J = 1.8, 1.9 Hz, 6.60 (dd, J = 6.3, 2.0 Hz, 1 H), 7.02 (d, J = 8.0 Hz, 1 H); 13C NMR(CDCl3) δ = 56.0, 111.1, 114.4, 121.2, 130.1, 132.1, 134.8, 63.7, 131.9, 144.1, 146.6; IR 2744, 1591. These data are congruent with those previously reported.7

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**Supporting Information Available:** 1H and 13C spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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