Transition-Metal-Based Synthesis of Dendralenes

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This paper is dedicated to Professor Paul Wender on the occasion of his 60th birthday.

Abstract: The consecutive ring-closing enyne metathesis of allylsilyl propargyl ethers with Grubbs’ ruthenium–alkylidene catalyst, followed by rhenium oxide mediated 1,4-elimination of the Si–O moiety from the siloxenes, provides [3]- and [4]dendralenes in good yields.

Key words: dendralenes, enynes, ring-closing metathesis, 1,4-eliminations, rhenium oxide

Dendralenes make up a novel class of cross-conjugated acyclic polyenes, and are represented by the two lowest homologues [3]dendralene (3-methylenepenta-1,4-diene) and [4]dendralene (3,4-bismethylenehexa-1,5-diene) (Figure 1).1 Compared to other unsaturated hydrocarbon compounds, such as linear conjugated polyenes, annulenes, cumulenes, fulvenes, and radialenes, the dendralene class of compounds is the least explored. Although the first dendralene derivatives were prepared more than half a century ago, general synthetic methods for the efficient preparation of dendralenes and their application have been limited.2 However, dendralenes have started attracting interest recently in the context of transmissive Diels–Alder reactions.3

Figure 1

Dendralenes have generally been prepared by thermal isomerization or elimination from rather elaborate precursors. Two recent representative examples by Sherburn and Fallis include the extrusion of sulfur dioxide from sulfolene derivatives at high temperatures (Scheme 1, reaction 1) and the removal of water from the adduct between the divinymethyl anion and an aldehyde (Scheme 1, reaction 2).4 Alternatively, bis-Negishi coupling of 1,1-dibromoalkenes with vinylmetal species has been employed by Sherburn (Scheme 1, reaction 3).5

From the perspective of expanding the utility of dendralenes in the area of diversity-oriented synthesis, the transmissive Diels–Alder reaction would be an ideal strategy to achieve molecular diversity and complexity.6 To serve this goal, the development of a mild and efficient synthesis protocol to generate dendralenes with various substituent patterns is crucial. In this regard, we envisioned that the ring-closing metathesis (RCM) of 1 catalyzed by the Grubbs ruthenium complex 4,7 followed by 1,4-elimination of siloxane 2 catalyzed by rhenium(VII) oxide would be an effective method to deliver various dendralenes 3 (Scheme 2). Although the acid-promoted9 1,4-elimination reaction of a siloxene related to 2 has been reported, the corresponding transition-metals-catalyzed 1,4-elimination reaction is unprecedented.10

We surmised that the easy formation of silyl ether 1 from various propargylic alcohols and allylsilyl chloride or triflate, followed by the well-established ring-closing enyne metathesis11 would render 2 an ideal substrate for testing the rhenium oxide catalyzed 1,4-elimination reaction.
Especially a one-pot sequence of RCM followed by the metal-catalyzed 1,4-elimination without isolation of RCM product 2 would provide a significant advantage over the corresponding two-step sequence, because of the operational simplicity. Herein, we report our preliminary results for the efficient synthesis of mono- and disubstituted [3]- and [4]-dendralenes by the RCM of 1 to 2, followed by 1,4-elimination of 2 with rhenium oxide (Scheme 2).\(^1\)\(^2\) First, various allyldimethylsilyl ethers 1 derived from simple monosubstituted propargyl alcohols 5a–e and allyl(chloro)dimethylsilane were subjected to typical RCM conditions in dichloromethane at 40 °C in the presence of second-generation Grubbs’ catalyst 4 to provide RCM products 2a–e (Table 1, entries 1–5). Upon completion of RCM, the reaction mixture was cooled to room temperature and was treated with a catalytic amount of rhenium(VII) oxide (5 mol%) for four hours; this, to our delight, delivered the desired [3]-dendralenes 3a–d (Table 1, entries 1–4) in good yields after simple flash column chromatography on silica gel. The elimination of 2e, derived from dihydrolinalool, gave cyclic dendralene

<table>
<thead>
<tr>
<th>Table 1</th>
<th>One-Pot Synthesis of Dendralenes</th>
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<tr>
<td>Entry</td>
<td>Alcohol 5</td>
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<tr>
<td>1</td>
<td>5a, (R = \text{CH}_2\text{CH}_2\text{Ph})</td>
</tr>
<tr>
<td>2</td>
<td>5b, (R = \text{CH}_2\text{CH}_2\text{OTHP})</td>
</tr>
<tr>
<td>3</td>
<td>5c, (R = \text{Ph})</td>
</tr>
<tr>
<td>4</td>
<td>5d, (R = \text{OMe})</td>
</tr>
<tr>
<td>5</td>
<td>5e, (R = \text{OH})</td>
</tr>
<tr>
<td>6</td>
<td>5f</td>
</tr>
<tr>
<td>7</td>
<td>5g</td>
</tr>
<tr>
<td>8</td>
<td>5h</td>
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\(^{a}\) Overall yield of 3 over three steps (silylation of 5, RCM of 1, elimination of 2 by method B), as determined by \(^1\)H NMR spectroscopy of the unpurified reaction mixture against an external standard.

\(^{b}\) Overall yield of 3g over three steps in one pot (by method A).
3e, which was too unstable to be isolated without polymerization (Table 1, entry 5). Propargylic alcohols with internal alkynes 5f and 5g provided RCM products 2f and 2g, which subsequently underwent 1,4-elimination to give mono- and disubstituted [3]dendralenes 3f and 3g in respectable yields (Table 1, entries 6 and 7). The stereochemistry of 3g was unambiguously assigned on the basis of NOE experiments. Similarly, symmetrical propargylic diols 3h was silylated, ring-closed, and 1,4-eliminated to give bis-[3]dendralene 3h in good yield (Table 1, entry 8).

Next, we also briefly examined the synthesis of [4]dendralenes. The tandem RCM of silicon-tethered dienynes 6a and 6b, derived from the corresponding diols, provided bis-siloxyenes 7a and 7b at an elevated temperature (110 °C in toluene) (Scheme 3). Double 1,4-elimination of 7a and 7b afforded mono- and disubstituted [4]dendralenes 8a and 8b, respectively, in good yields (Scheme 3).13

Scheme 3

Although the exact mechanism of this rhenium oxide catalyzed 1,4-elimination is yet to be elucidated, our current working hypothesis is depicted in Scheme 4. On the basis of the known Lewis acidity of rhenium(VII) oxide,14 we surmise that Lewis acid mediated and sigmatropic-rearrangement-mediated pathways12b–e compete at multiple stages along the catalytic cycle. That Lewis acid mediated elimination takes place was further supported by the formation of 2a from 1a in the presence of other Lewis acids, such as SnCl4 (75%), HfOTf (92%), and Ph3PAuCl (<20%).

In conclusion, we have developed a one-pot method for the synthesis of [3]- and [4]dendralenes under mild conditions via two consecutive transition-metal-catalyzed reactions. This method should constitute a more general alternative for the synthesis of a variety of substituted dendralenes compared to the existing methods.1,2c

All reagents and solvents were purchased from Sigma-Aldrich and used as received. NMR spectra were recorded on a Bruker AC-300 spectrometer. Chemical shifts are relative to TMS as an internal standard. Siloxy-tethered enyne precursors 1a–h for RCM and RCM products were prepared according to a literature procedure.15

5-[3-(Benzyloxy)prop-1-en-2-yl]-2,2-dimethyl-3,6-dihydro-2H-1,2-oxasiline (2f); Typical Procedure

To a soln of 5f (0.176 g, 1.0 mmol) in anhyd CH2Cl2 (5 mL) were added AllylSiMe2Cl (0.114 g, 1.05 mmol) and imidazole (0.071 g, 1.05 mmol) at 0 °C. The mixture was stirred at 0 °C for 10 min and at r.t. for an additional 3 h. The solvent was removed under reduced pressure, and the residue was diluted with anhyd Et2O (10 mL) and filtered through a Celite plug. After removal of the Et2O, the siloxy-tethered enyne 1f was redissolved in anhyd CH2Cl2 (20 mL) and treated with the Grubbs catalyst 4 (0.042 g, 5 mol%) under heating at reflux for 5 h under N2. Conversion was monitored by TLC analysis.

[1,2,3-Dimethylenepent-4-enyloxy)methyl]benzene (3f); Typical Procedures

Method A. One-pot procedure: To the crude reaction mixture containing 2f in CH2Cl2 (see above) was added Re2O7 (0.024 g, 5 mol%), and the soln was stirred at r.t. for 4 h and then concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, Et2O–pentane, 1:10); this provided 3f as a colorless oil.

Yield: 0.106 g (53%).

Method B. Stepwise procedure: The solvent from the crude reaction mixture containing 2f in CH2Cl2 (see above) was removed under reduced pressure, and the residue was filtered through a Celite pad with Et2O. After addition of Re2O7 (0.024 g, 5 mol%) to the Et2O soln, the mixture was stirred at r.t. for 3 h and then concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, Et2O–pentane, 1:10); this provided 3f as a colorless oil.

Yield: 0.144 g (72%).

1H NMR (300 MHz, CDCl3): δ = 7.25–7.36 (m, 5 H), 6.44 (d, J = 17.4, 10.7 Hz, 1 H), 5.15–5.38 (m, 6 H), 4.34 (s, 2 H), 4.16 (s, 2 H).

13C NMR (75 MHz, CDCl3): δ = 146.04, 143.70, 138.52, 137.28, 128.58, 127.92, 127.78, 116.52, 115.71, 115.19, 72.32, 71.96.


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References


(13) The stereochemistry of 8a and 8b was assigned in analogy to that of 3g.
