Domino Reactions

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One-Step Synthesis and Exploratory Chemistry of [5]Dendralene**

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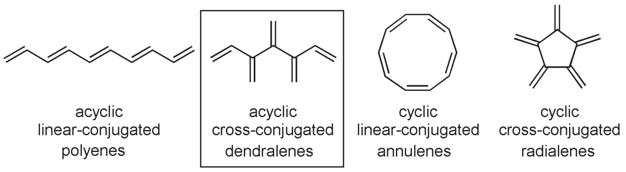
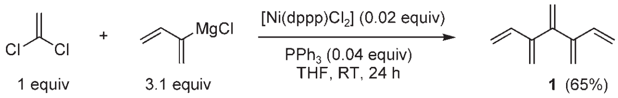


Scheme 1. Four fundamental classes of conjugated oligoalkene structures.

The fundamental hydrocarbons known as dendralenes are the neglected members of the family of conjugated oligoalkenes (Scheme 1).[1–5] Whereas the synthesis and physical and chemical properties of the linear polyenes, the annulenes, and the radialenes have been examined in detail, little is known about the dendralenes.[2,6] We recently reported a practical synthetic approach to [4]dendralene and some of its cycloaddition reactions.[7] Herein we present the first practical synthesis of the higher "ethenologue", [5]dendralene (3,4,5-trimethyleneheрta-1,6-diene), and for the first time we demonstrate its fascinating reactivity through domino sequences of pericyclic reactions.

To date, the chemistry of [5]dendralene has remained completely unexplored,[1–6] since the hydrocarbon has not been available in synthetically useful amounts. Indeed, the only published synthesis of the hydrocarbon from 3-sulfolene takes five steps and proceeds with an overall yield of less than 2%.[6] In contrast, the practical synthesis of [5]dendralene (**1**), which we now report (Scheme 2), avoids protection, proceeds in one step, and uses cheap and widely available starting materials. Thus, the chloroprene Grignard reagent[8] undergoes twofold Tamao–Kumada–Corriu coupling[9] with vinylidene chloride at room temperature.[10] An aqueous workup and vacuum distillation[11] affords [5]dendralene in 65% yield. We routinely prepare five-gram batches of **1** using this procedure. [5]Dendralene is a little more prone to decomposition than the lower homologue [4]dendralene. Nevertheless, the hydrocarbon can be stored as an approximately 0.75 M solution in light petrol, methylene chloride, or THF at −15 °C with minimal decomposition over several months.



Scheme 2. Practical synthesis of [5]dendralene (**1**); dppp = 1,3-bis(diphenylphosphanyl)propane.

In principle, [5]dendralene could undergo a domino sequence of diene-transmissive Diels–Alder reactions[12] with four dienophile molecules. In practice, the hydrocarbon reacts with an excess of *N*-methylmaleimide (NMM) at room temperature in methylene chloride to furnish a mixture of six products: two diastereomeric bis adducts **4** and **5** and four diastereomeric tris adducts **10**, **11**, **12**, and **13** (Scheme 3).[13] The pathway from **1** to the six multiple adducts was elucidated by a series of reactions involving the addition of one equivalent of dienophile to **1**, the mono adducts **2** and **3** and the bis adducts **4**–**9**.

The first dienophile addition to [5]dendralene occurs with a preference for the terminal mono adduct **2** over its internal congener **3**. The latter gives rise to two diastereomeric bis adducts **4** and **5** in roughly equal amounts at ambient temperature and pressure. In contrast, terminal mono adduct **2** furnishes a mixture of all six possible bis adducts **4**–**9** along with tris adducts **11** and **12**. Linear conjugated trienes **4** and **5** do not undergo further reaction with NMM under these conditions. In contrast, the other four bis adducts **6**–**9**, which contain cross-conjugated trienes, undergo cycloadditions to form the triple cycloadducts **10**–**13**. Complete site selectivity for the acyclic diene but very low π-diastereofacial selectivity is witnessed during NMM cycloadditions to **7** and **9**, whereas the more symmetrical structures **6** and **8** exhibit marked π-diastereofacial selectivities in reactions with NMM. Thus, each of the six isolated products from the exhaustive reaction depicted in Scheme 3 is formed from two different precursors. The two major products from the reaction, tris adducts **11** and **12**, are the result of high levels of π-diastereofacial selectivity in reactions of the *meso* and C_2-symmetric intermediates **6** and **8**, respectively. It seems safe to assume that the major pathway for the reaction is **1**→**2**→**6**→**11**, which represents a diene-transmissive terminal-terminal-internal triple cycloaddition to [5]dendralene. Inspection of the X-ray crystal structures of the four tris adducts **10**–**13** reveals a preference for a skewed *s-cis*-1,3-butadiene conformation, albeit one in which the diene is very sterically hindered. None of the tris adducts underwent a fourth cycloaddition with either NMM, diethyl acetylene dicarboxylate, or *N*-phenyl triazolinedione under thermal, Lewis acid promoted, or ultra-high-pressure conditions.

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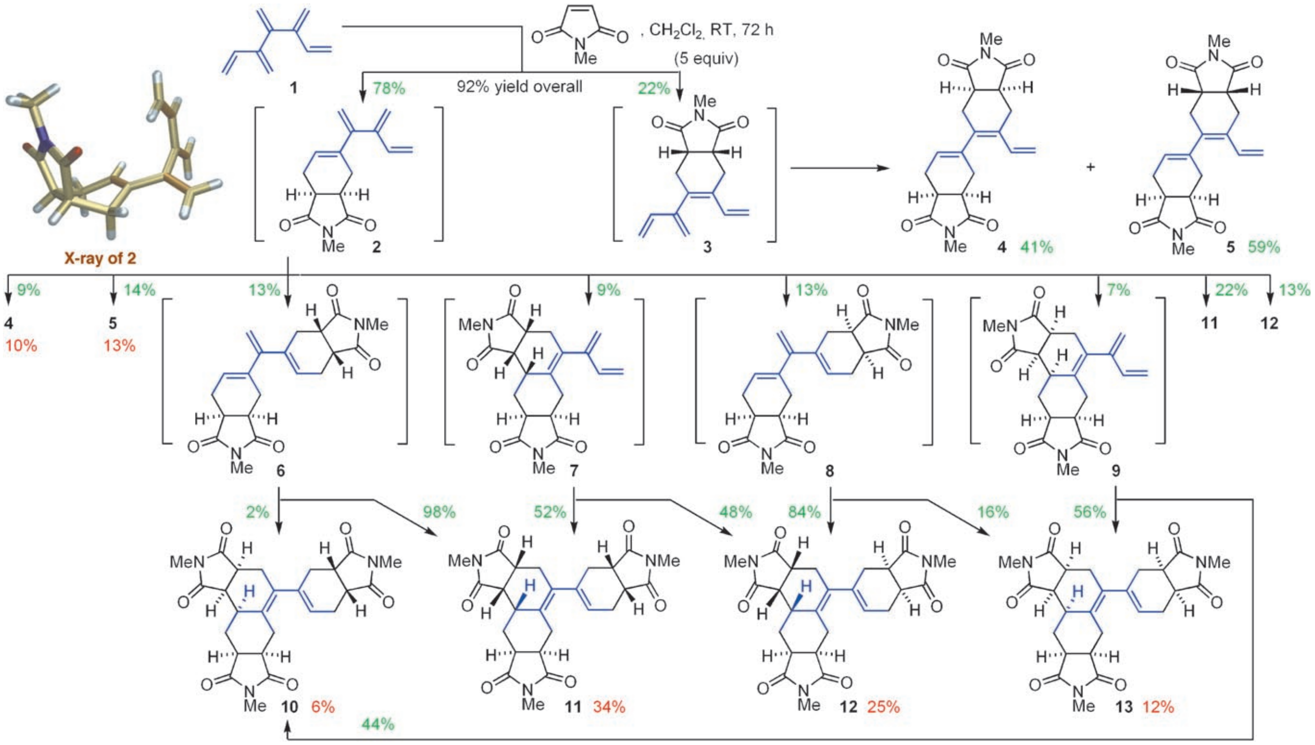
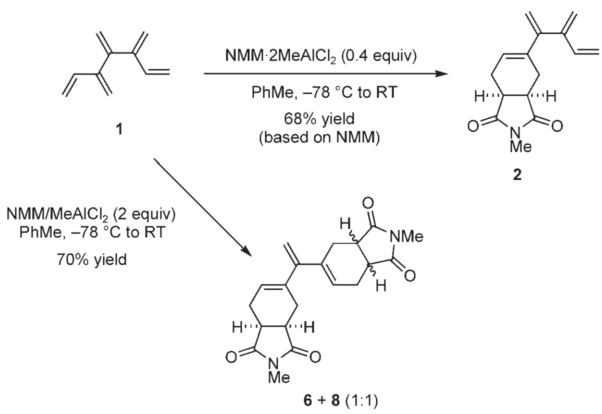


Scheme 3. Reaction of [5]dendralene with NMM. (Red = product breakdown (%) for reaction of **1** with excess NMM. Green = product breakdown (%) for reactions with 1:1 precursor/NMM stoichiometry.) X-ray structure of **2**: red O, blue N, yellow C, white H. X-ray crystal structures of **4**, **7**, and **10**–**13** can be found in the Supporting Information.

If the Diels–Alder sequences between [5]dendralene and dienophiles are to be useful in chemical synthesis, these processes must be rendered more selective. Towards this end, preliminary investigations show that the Diels–Alder reaction site selectivities of [5]dendralene are dramatically improved under Lewis acid promoted conditions (Scheme 4). Thus, whereas an uncatalyzed single addition reaction with NMM gives the products of terminal and internal addition in a 72:28 ratio (**2**/**3**; Scheme 2), promotion with methylaluminium dichloride leads to significantly enhanced selectivity for **2** (terminal/internal = 96:4). Furthermore, whereas mono adduct **2** undergoes a very unselective uncatalyzed reaction with NMM to give no less than eight products (Scheme 2), under Lewis acid promotion, a smooth conversion into the terminal-terminal double addition products **6** and **8** is witnessed.

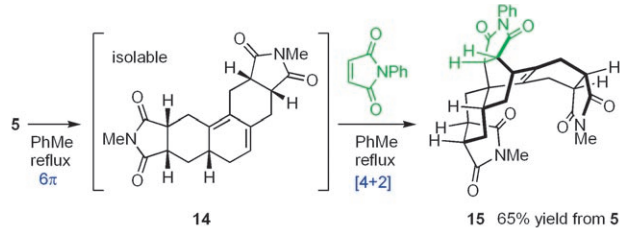


Scheme 4. Enhanced Diels–Alder site selectivities with Lewis acid promoters.

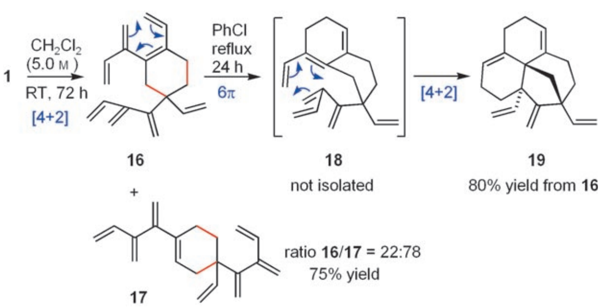
The X-ray crystal structure of terminal mono adduct **2** (Scheme 3) is, to our knowledge, the first reported crystal structure of a [4]dendralene. The tetraene system comprises two *s-trans*-1,3-butadiene residues in an orthogonal relationship. The solution UV spectrum of **2** is consistent with this conformation, with a single absorption maximum at 225 nm (CH_2Cl_2)—the same wavelength observed for the parent [4]dendralene, [5]dendralene, and isoprene.[14] Electron diffraction studies and calculations on the parent [4]dendralene point to a 72° angle between the two π systems.[15] Perhaps crystal packing forces are the origin of the conformational difference between the parent hydrocarbon and mono adduct **2**.[16] We are unable to identify any steric or electronic effects within the structure which might explain this difference in conformation.

Bis adducts **4** and **5** carry *Z*-triene moieties, which undergo a 6π electrocyclization/[4+2] cycloaddition cascade[7,17] with dienophiles in toluene heated at reflux. In the case of **5**, reaction with *N*-phenylmaleimide gives a single diastereomeric heptacycle **15** in 65 % yield (Scheme 5). It is noteworthy that **15** is produced in only two synthetic steps from [5]dendralene (**1**), through a sequence involving the generation of seven new C−C bonds and nine stereocenters.

As mentioned above, [5]dendralene undergoes decomposition: upon storage in neat form at ambient temperature, a colorless solid is formed. Nevertheless, under controlled conditions, Diels–Alder dimerization to **16** and **17** (Scheme 6)



Scheme 5. A highly stereoselective domino pericyclic reaction of **5**. The X-ray crystal structure of **15** is shown in the Supporting Information.



Scheme 6. Two-step synthesis of a fenestrane from [5]dendralene. The X-ray crystal structure of **19** is shown in the Supporting Information.

occurs in high yield. Intriguingly, both products result from the same olefinic residue reacting as the dienophile, with the major product **17** ensuing from union with a terminal 4π component.[18] Upon heating, the minor dimer **16** undergoes a remarkable domino electrocyclization/intramolecular cycloaddition sequence to form tetracyclic [5.6.6.6]fenestrane[19] hydrocarbon **19**.

In summary, an undemanding preparation of [5]dendralene employing standard laboratory equipment and methods has been developed. The hydrocarbon undergoes a rich variety of atom-efficient domino cycloaddition and electrocyclization reactions to furnish a diverse range of complex fused and bridged polycyclic structures.

Experimental Section

1: Vinylidene chloride (5.00 mL, 6.07 g, 62.6 mmol), triphenylphosphine (801 mg, 3.05 mmol), and [Ni(dppp)Cl$_2$] (789 mg, 1.46 mmol) were added successively to a cooled (0 °C) solution of the chloroprene Grignard reagent[20] (made from chloroprene (17.3 g, 195 mmol) and magnesium (8.00 g, 329 mmol) in THF (200 mL)). The reaction was then allowed to warm to room temperature, and stirring was continued for 20 h. The reaction mixture was poured into a stirred mixture of petroleum spirits (30–40 °C, 500 mL) and ice-cold water (1 L), then 1 M aqueous HCl (250 mL) was added to disperse the resulting suspension. The organic layer was collected and washed with saturated sodium carbonate solution (200 mL) and brine (200 mL), dried over anhydrous magnesium sulfate, and concentrated under reduced pressure (0 °C, 30 mbar). The resulting oil was subjected to bulb-to-bulb vacuum distillation to give [5]dendralene **1** (b.p. 25 °C, 0.4 Torr) as a colorless oil (5.37 g, 4.07 mmol, 65 %). ^{1}H NMR (300 MHz, CDCl$_3$): $\delta = 6.44$ (2H, dd, $J = 17.4$, 10.6 Hz), 5.34 (2H, dd, $J = 17.4$, 1.5 Hz), 5.26 (2H, s), 5.23 (2H, d, $J = 1.5$ Hz), 5.14 (2H, d, $J = 10.6$, 0.9 Hz), 5.12 ppm (2H, m); ^{13}C NMR (75 MHz, CDCl$_3$): $\delta = 146.9$ (C), 146.5 (C), 136.9 (CH), 116.8 (CH$_2$), 116.4 (CH$_2$), 116.2 ppm (CH$_2$); IR (thin film): $\tilde{\nu} = 3154$, 3091, 1579 cm^{-1}; UV/Vis (CH$_2$Cl$_2$): $\lambda_{max} = 224$ nm ($\varepsilon = 44\,000$ L M^{-1} cm^{-1}); MS (EI, 70 eV): *m*/*z* (%): 132 ([*M*]$^+$, 14), 131 (48), 117 (100); HRMS: calcd for C$_{10}$H$_{12}$ [*M*]$^+$: 132.0939; found: 132.0914.

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[1] M. Gholami, R. R. Tykwinski, *Chem. Rev.* **2006**, *106*, 4997 – 5027.
[2] H. Hopf in *Organic Synthesis Highlights V* (Eds.: H.-G. Schmalz, T. Wirth), Wiley-VCH, Weinheim, **2003**, pp. 419 – 427.
[3] H. Hopf, *Classics in Hydrocarbon Chemistry: Syntheses, Concepts, Perspectives*, Wiley-VCH, Weinheim, **2000**.
[4] H. Hopf, *Angew. Chem.* **2001**, *113*, 727 – 729; *Angew. Chem. Int. Ed.* **2001**, *40*, 705 – 707.
[5] H. Hopf, *Angew. Chem.* **1984**, *96*, 947 – 958; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 948 – 960.
[6] S. Fielder, D. D. Rowan, M. S. Sherburn, *Angew. Chem.* **2000**, *112*, 4501 – 4503; *Angew. Chem. Int. Ed.* **2000**, *39*, 4331 – 4333.
[7] A. D. Payne, A. C. Willis, M. S. Sherburn, *J. Am. Chem. Soc.* **2005**, *127*, 12188 – 12189.
[8] S. Nunomoto, Y. Yamashita, *J. Org. Chem.* **1979**, *44*, 4788 – 4791.
[9] a) R. J. P. Corriu, J. P. Masse, *J. Chem. Soc. Chem. Commun.* **1972**, 144 – 144; b) K. Tamao, K. Sumitani, M. Kumada, *J. Am. Chem. Soc.* **1972**, *94*, 4374 – 4376.
[10] Similar results were obtained when [Ni(dppe)Cl$_2$] (dppe = 1,2-bis(diphenylphosphanyl)ethane) was used in place of [Ni(dppp)Cl$_2$].
[11] The crude product is contaminated with up to 10 % [4]dendralene, which is the result of an oxidative dimerization process. This more volatile contaminant is easily removed by vacuum distillation.
[12] For a review of diene-transmissive Diels–Alder reactions, see: J. D. Winkler, *Chem. Rev.* **1996**, *96*, 167 – 176.
[13] All cycloadditions involving maleimide dienophiles were found to proceed exclusively through the *endo* mode.
[14] The molar extinction coefficient measured for isoprene $\varepsilon \approx 20\,000$ L M^{-1} cm^{-1} is one-half that measured for the other three compounds.
[15] a) P. T. Brain, B. A. Smart, H. E. Robertson, M. J. Davis, D. W. H. Rankin, W. J. Henry, I. Gosney, *J. Org. Chem.* **1997**, *62*, 2767 – 2773; b) M. H. Palmer, J. A. Blair-Fish, P. Sherwood, *J. Mol. Struct.* **1997**, *412*, 1 – 18.
[16] See the Supporting Information for crystallographic details.
[17] R. von Essen, D. Frank, H. W. Sünnemann, D. Vidović, J. Magull, A. de Meijere, *Chem. Eur. J.* **2005**, *11*, 6583 – 6592.
[18] The *diene* site selectivity witnessed during this cycloaddition is identical to that seen in the reaction of **1** with NMM (Scheme 3).
[19] a) R. Keese, *Chem. Rev.* **2006**, *106*, 4787 – 4808; b) M. Thommen, R. Keese, *Synlett* **1997**, 231 – 240.
[20] S. Nunomoto, Y. Yamashita, *J. Org. Chem.* **1979**, *44*, 4788 – 4791.