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3 + 2 Cycloaddition Via a Diels-Alder/Retro-Diels-Alder Sequence: Tandem Cyclopentadienyl Annulation of a 1,5-Cyclooctadiyne Synthetic Equivalent.

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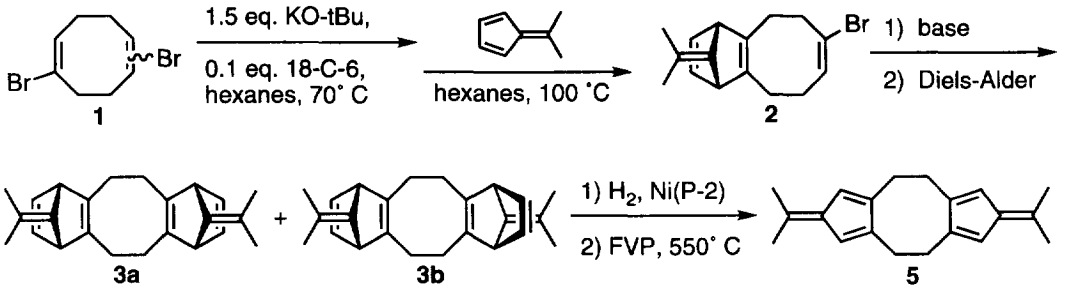
Abstract: A novel method of synthesizing a 1,2-bis(ethano) bridged bis(cyclopentadienyl) compound, 6,13-diisopropylidenetricyclo[9.3.0^{1,11}.0^{4,8}]tetradeca-1(14),4,7,11-tetraene, **5**, via a tandem Diels-Alder/retro-Diels-Alder sequence using a 1,5-cyclooctadiyne synthetic equivalent and 6,6-dimethylfulvene is reported.

The Diels-Alder reaction is a very efficient method of synthesizing six-membered carbocycles. The analogous reaction of enes and dipolarophiles is limited to the synthesis of functionalized five-membered carbocycles.[1] Unfortunately, dipolarophiles require synthesis themselves and are far less structurally diverse than Diels-Alder dienes. Trost's 3 + 2 cycloaddition methodology is one of the most general methods of synthesizing five-membered carbocycles, but it is limited to Michael acceptor enes.[2] This communication reports the synthetic equivalent of a 3 + 2 cycloaddition, using a Diels-Alder/retro-Diels-Alder approach. Diels-Alder/retro-Diels-Alder sequences have seen modest use as a method to protect or stabilize dienophiles,[3] with the diene component remaining unchanged. Jung reported a Diels-Alder based cyclopentanoid synthesis wherein oxidative cleavage was used to cleave the norbornene ring of a Diels-Alder adduct.[4] However, Katz's synthesis of dihydropentalene marked an early use of a Diels-Alder/retro-Diels-Alder sequence in the synthesis of a cyclopentadienyl ring compound, Eqn 1.[5]

Eqn. 1

Interest in catalytically active ansa bridged metallocene complexes has spurred the development of synthetic methods to prepare bridged bis(cyclopentadienyl) (bis(Cp)) compounds.[6] Recently, a few doubly bridged metallocene complexes have been synthesized.[7] Singly bridged bis(Cp) compounds have generally been prepared by alkylation of Cp anions with bis(electrophiles)[8] or by reductive coupling of 6,6-dimethylfulvene derivatives to prepare tetramethylethano bridged bis(Cp)s.[9] The bridged systems have been developed to inhibit Cp-metal rotation so that chiral pendant groups on the Cps cannot rotate away from approaching substrates or so that the chirality of the metallocene complex is set by the ansa bridge itself.[6] The synthesis of 1,2-diethano bridged bis(Cp) systems are inherently more challenging compared to the singly bridged systems because the dialkylation of Cp anions is difficult to direct to yield predominantly the 1,2 dialkylation of the Cp derivative. This problem has been cleverly solved when spirocyclopentadienyl compounds can be thermally rearranged to 1,2-cyclopentadienyl products.[10] The alternative is to annulate Cp rings onto a 1,2-bridged starting material. This is the approach described herein with an improved synthesis

of a known 1,2-diethano bridged cyclopentadienophane using a novel tandem Diels-Alder/retro-Diels-Alder sequence.



Scheme 1.

Scheme 1 shows the approach wherein a synthetic equivalent of 1,5-cyclooctadiyne is treated with excess 6,6-dimethylfulvene. 1,5-Cyclooctadiene is tetrabrominated and partially dehydrobrominated to form a mixture of 1,5- and 1,6-dibromo-1,5-cyclooctadiene (**1a** and **1b**).[11] The formation of these dibromides requires two syn eliminations and nonpolar solvents and strong bases enhance the formation of these dibromides. Treatment of the tetrabromides with excess DBU in dry, refluxing hexanes gave the best results with yields in excess of 32% on scales as high as 0.5 mol. Other products include 1,3,5,7-cyclooctatetraene which is why excess base must be used. These dibromides are selectively monodehydrobrominated using 1.5 eq. potassium *t*-butoxide and 0.1 eq. 18-crown-6 in refluxing hexanes for 4 hr. to give 5-bromo-5-cyclooctene-1-yne, which is not isolated, but a 10% solution in hexanes is treated with 1.7 eq. of 6,6-dimethylfulvene and a crystal of BHT at 100° C in a sealed tube to give the monoDiels-Alder adduct, **2** in 50% yield.[12] The ^{1}H NMR spectrum of this compound is consistent with the structure, but the lack of molecular symmetry and small chemical shift dispersion leads to a complex spin system. In the ^{13}C NMR spectra, 15 of the 16 expected peaks are observed. The missing ^{13}C peak is consistent with the overlap of the two nearly identical methyl groups. Dehydrobromination of **2** as above gives an ene-yne, that is treated as above with excess 6,6-dimethylfulvene giving a nearly equal mixture of anti and syn diastereomers **3a** and **3b** in a 32% yield. This mixture of diastereomers was difficult to separate, but the ^{1}H and ^{13}C NMR are consistent with the mixture of two diDiels-Alder adducts; each having a plane of symmetry that bisects the bicycloheptadiene units through the bridging isopropylidene unit. There should be 7 ^{13}C peaks for each compound, but the bridgehead carbons at approximately 56 ppm are apparently not resolved. Selective hydrogenation of the disubstituted double bonds of **3** using 1 atm. of H_2 over Ni (P-2) catalyst[13] gave the diastereomers **4a** and **4b** in 82% yield. The regioselective hydrogenation of the diadducts was confirmed by the absence of the vinylic protons of **3**. The mass spectrum of **4a** and **4b** shows the loss of two 28 Dalton fragments consistent with the expected tandem retro-Diels-Alder elimination of ethylene. The reaction mixture was purified by silica gel column chromatography using 1:4 chloroform:hexane which eluted the anti isomer, **4a**, and the syn isomer, **4b**, respectively. The ^{13}C spectra of **4a** and **4b** each gave 7 of the expected 7 peaks. Recrystallization of **4a** from 1:4 chloroform:hexane gave X-ray quality crystals that confirmed the tentative stereochemical assignments based upon the ^{1}H NMR, Fig. 1.[14] Flash vacuum pyrolysis[15] of **4** through a quartz tube at 550° C and 0.05 mmHg produces the difulvene, **5**, in 93% yield. Recrystallization of **5** from 1:1 chloroform:hexane gives X-

ray quality crystals of **5**, Fig. 1.[16] The spectra of **5** match those reported previously.[7b] The overall yield using this method is poor, but is still considerably better than the known route. The known route starting with 1,2-bis(cyclopentadienyl)ethane, which also has to be synthesized, gave **5** in 5 steps with an overall yield of less than 1%. The procedure described above gave an overall yield from the easily prepared **1** of 12%. The alternative of starting with 1,5-cyclooctadiyne can be done via the original procedure which gives a very poor yield[17] or by treating **1** with two or more equivalents of base.[12] The formation of 1,5-cyclooctadiyne from **1** and Diels-Alder reaction with excess 6,6-dimethylfulvene gave poorer overall yields than the stepwise method described above due to the competing addition of base to the highly reactive diyne. The low yields from the elimination/Diels-Alder reaction steps are due to side products generated during the elimination steps. GC verified by GC-MS chromatograms showed that the ene-ynes gave clean Diels-Alder adduct formation.

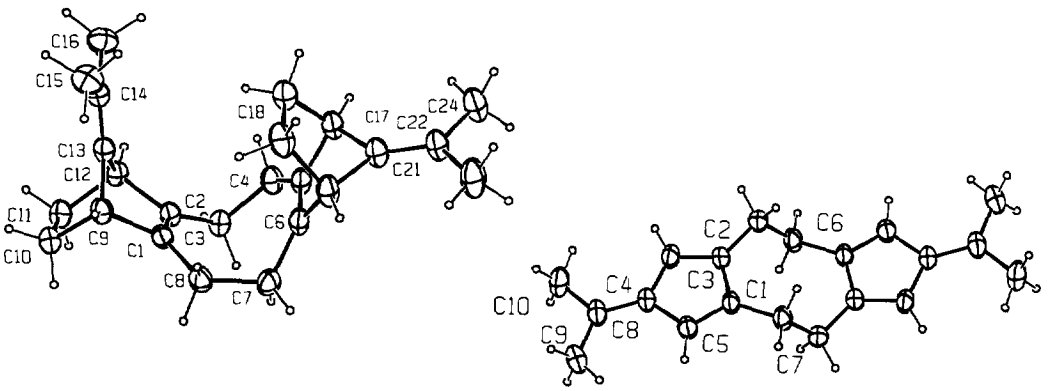


Figure 1. ORTEP Diagrams of **4a** and **5**.

The potential generality of this synthetic approach is more significant than the improved synthesis of **5**. The approach requires an acetylenic dienophile or an ene that allows specific unsaturation of the Diels-Alder adduct at the ene derived carbons and a Diels-Alder adduct that can be selectively reduced to allow clean retro-Diels-Alder reaction of the 2,3-carbons of the diene component of the original 4 + 2 adduct. The Diels-Alder/retro-Diels-Alder reaction sequence using a cyclopentadienyl compound described herein gives the synthetic equivalent of a 3 + 2 cycloaddition of a 1,3-dicarbene to the ene. We are investigating the scope of this Diels-Alder/retro-Diels-Alder reaction methodology as a means of synthesizing new cyclopentadienophanes and the metal complexation of these cyclopentadienophanes. These studies will be reported in due course.[18]

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12. General experimental data. 6,6-Dimethylfulvene was prepared according to: W. Freiesleben, *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 396. A horizontal Thermolyne type 21100 tube furnace was used for the pyrolysis with a 2 cm x 30.5 cm contact zone. **4** was sublimed into the pyrolysis tube. Bright yellow product collected at the exit of the contact zone. Data for **2**: mp: 78-80° C, ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.46 (s, 6H, Me), 2.03-3.08 (m, 8H, 3,4,7,8-CH_2), 3.56-3.72 (m, 2H, 1,10-CH), 5.96 (t, J = 7.5Hz, 1H, 6-CH), 6.83-6.93 (m, 2H, 11,12-CH); ^{13}C NMR (75 MHz, $CDCl_3$) 18.41, 27.50, 31.16, 31.86, 36.49, 57.14, 57.19, 94.36, 125.29, 130.53, 141.99, 142.03, 144.61, 145.08, 161.26 ppm; IR (thin film, cm^{-1}) 3060, 2980, 2910, 2873, 2821; HRMS, calcd 290.0670, obsd 290.0681. Data for **3** mp: 122-123° C, ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.39 (s, 12H, Me), 1.43 (s, 12H, Me), 2.05-2.17 (m, 4H, CH_2), 2.31-2.56 (m, 8H, CH_2), 3.56-3.60 (m, 8H, CH), 6.67 (t, J = 2Hz, 4H, CH), 6.75 (t, J = 2Hz, 4H, CH); ^{13}C NMR (50 MHz, $CDCl_3$) 18.28, 18.42, 28.59, 29.00, 56.47, 93.07, 93.84, 141.55, 141.67, 145.84, 146.09, 161.64, 162.41 ppm; IR (thin film, cm^{-1}) 3060, 2979, 2919 2869, 2820; HRMS, calcd 316.2191, obsd 316.2210. Data for **4a** (anti) mp: 157-158° C, ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.97-1.04 (m, 4H, CH_2), 1.50 (s, 12H, Me), 1.57 (m, 4H, CH_2), 2.39 (m, 8H, CH_2), 2.89 (m, 4H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) 19.45, 26.63, 28.52, 48.89, 105.75, 140.05, 147.40 ppm; IR (thin film, cm^{-1}) 2953, 2927, 2867, 1439. **4b** (syn) mp: 148-149° C, ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.02-1.09 (m, 4H, CH_2), 1.54 (s, 12H, Me), 1.61 (m, 4H, CH_2), 2.14-2.26 (m, 4H, CH_2), 2.66-2.82 (m, 4H, CH_2), 2.66-2.82 (m, 4H, CH_2), 2.96 (m, 4H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) 19.34, 25.98, 27.86, 48.53, 104.71, 140.27, 147.79 ppm; IR (thin film, cm^{-1}) 2968, 2927, 2866, 1440; HRMS, calcd 320.2504, obsd 320.2472; Anal. calcd for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.59; H, 10.37. The spectra for compound **5** match those reported in 7(b).
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16. Crystallographic Data for **5:** yellow lath, T = 297 K; triclinic, space group P $\bar{1}$, with a = 5.139 (1) Å, b = 6.352 (1) Å, c = 12.384 (1) Å, α = 88.85 (1)°; β = 87.55 (1)°; γ = 73.99 (1)°; V = 388.2 (1) Å^3, and Z = 1 (D_c = 1.131 gcm^{-3}); μ (Cu Kα) 4.4 cm^{-1} absorption corrected by ψ scans; 1599 unique data; 1263 data with, 2 < θ < 75°, I > 3σ (I) were used in the refinement; R = 0.061, Rw = 0.071. H atoms were refined. The authors have deposited atomic coordinates for these structures with the Cambridge Crystallographic Centre. The coordinates can be obtained on request from The Director, Cambridge Crystallographuc Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.
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