Remarkably Facile Hexatriene Electrocyclizations as a Route to Functionalized Cyclohexenones via Ring Expansion of Cyclobutenones

Nabi A. Magomedov, Piero L. Ruggiero, and Yuchen Tang

Department of Chemistry, University of Rochester, Rochester, NY 14627-0216
magomedov@chem.rochester.edu

Supporting Information

General Information. All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring. Solvents and reagents were purified prior to use following the guidelines of Perrin and Armarego,¹ except for THF, toluene, acetonitrile, dichloromethane and ether, which were dispensed using the Glass Contour solvent purification system. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated *in vacuo* below 45 °C at approximately 20 mm Hg. Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and potassium permanganate solution or ceric ammonium molybdate solution followed by heating. Melting points were measured with a Unimelt Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer. ¹H NMR spectra were recorded on a Bruker Avance-400 (400 MHz) or Bruker AMX-400 (400 MHz) spectrometer and are reported in ppm using the solvent as an internal standard (CDCl₃ at 7.26 ppm). Data are reported as (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant(s) in Hz; integration). Proton-decoupled ¹³C NMR spectra were recorded on a Bruker Avance-400 (100 MHz) or Bruker AMX-400 (100 MHz) spectrometer and are reported in ppm using the solvent as the internal standard (CDCl₃ at 77.23 ppm). High-resolution mass spectra were obtained on a VG-7070 spectrometer at the UC Riverside Mass Spectrometry Facility. 4-Methyl-3-phenylcyclobutenone,² 2,3-diethylcyclobutene-2-one,³ compound **11**,⁴ 2,3-dihydrothiophene-1,1-dioxide,⁵ (2,2-diphenyl)ethenesulfonylbenzene,⁶ and (hex-1*Z*-ene-1-sulfonyl)benzene⁷ were prepared according to the literature procedures. Except for the

¹ Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*; Butterworth-Heinemann: Bath, 2002.

² Schmit, C.; Sahraoui-Taleb, S.; Differding, E.; Dehasse-De Lombaert, C. G.; Ghosez, L. *Tetrahedron Lett.* **1984**, 25, 5043-5046.

³ Ammann, A. A.; Rey, M.; Dreiding, A. S. *Helv. Chim. Acta* **1987**, 70, 321-328.

⁴ Danheiser, R. L.; Savariar, S.; Cha, D. D. *Org. Synth.* **1990**, 68, 32-40.

⁵ Bailey, W. J.; Cummins, E. W. *J. Am. Chem. Soc.* **1954**, 76, 1932.

⁶ Ager, D. J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 183-194.

⁷ Iwata, N.; Morioka, T.; Kobayashi, T.; Asada, T.; Kinoshita, H.; Inomata, K. *Bull. Chem. Soc. Jpn.* **1992**, 65, 1379-1388.

cyclopropyl substituted sulfone, all trans sulfones are known compounds and were prepared according to the following general procedure:⁸

To a solution of 1.95 g (6.67 mmol) of (benzenesulfonylmethyl)phosphonic acid diethyl ester and 0.695 g (8.01 mmol) of LiBr in 12 mL of CH₃CN at room temperature, was added dropwise 1.02 mL (0.743 g, 7.34 mmol) of triethylamine. Once the reaction mixture became heterogenous, it was cooled to 0 °C and a solution of 0.50 mL (0.468 g, 6.67 mmol) of cyclopropanecarboxaldehyde in 10 mL of CH₃CN was added while vigorously stirring. After the addition was complete, the reaction mixture was warmed to room temperature and stirred for 4 h. A solution of 30 mL of 0.1N HCl and 30 mL of H₂O was added, and the reaction was diluted with 50 mL Et₂O. The organic phase was separated and the aqueous one was extracted with Et₂O (4x40 mL). The combined organic solutions were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Recrystallization from Et₂O/hexanes provided 1.10 g of the desired sulfone as a colorless solid (79% yield). Characterization data: mp 74-75 °C (Et₂O/hexanes); IR (CHCl₃) 3053, 3007, 2900, 1625, 1446, 1306, 1143, 954 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.71-0.75 (m, 2H), 1.00-1.05 (m, 2H), 1.53-1.61 (m, 1H), 6.36 (d, *J* = 14.8 Hz, 1H), 6.44 (dd, *J* = 14.8, 9.6 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.88 (dd, *J* = 7.6, 1.4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 151.9, 141.0, 132.9, 129.1, 127.2, 126.7, 45.9, 13.8, 9.0; LRMS (APCI): Mass calcd for C₁₁H₁₃O₂S (M+H⁺) 209.1. Found 209.0.

Reactions of Cyclobutenones with Functionalized Vinyl Lithium Compounds

General procedure A. To a solution of 200 mg (0.77 mmol) of sulfone **9** in 5.7 mL of dry THF, cooled to -50 °C, was added 0.5 mL of a 1.87 M solution of *n*-BuLi (0.93 mmol) in cyclohexane dropwise over 3 minutes. After 15 minutes at -50 °C, 134 mg (0.93 mmol) of **11** in 2 mL of dry THF was added dropwise. The reaction mixture was stirred at this temperature for 15 minutes and then warmed to room temperature over 1 h, after which time TLC (silica gel, 3:1 hexanes/ethyl acetate) indicated complete consumption of starting sulfone. The reaction mixture was quenched with 5 mL of saturated aqueous NH₄Cl solution. The aqueous phase was extracted with CH₂Cl₂ (3x5 mL) and the combined organic solutions were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Flash chromatography (hexanes/ethyl acetate, 4:1) provided 252 mg of cyclohexenone **12** as a colorless solid (81% yield).

General procedure B. To a solution of 47 mg (65 μL, 0.47 mmol) of *i*-Pr₂NH in 2.2 mL of dry THF cooled to 0 °C, was added 0.25 mL of a 1.87 M solution of *n*-BuLi (0.47 mmol) in cyclohexane, dropwise over 1 minute. After stirring for 15 min at 0 °C, the solution was cooled to -78 °C and a solution of 50 mg (0.42 mmol) of 2,3-dihydrothiophene-1,1-dioxide in 0.5 mL of dry THF was added. The reaction was stirred for 15 min at -78 °C, and then a solution of 67 mg (0.47 mmol) of cyclobutenone **11** in 1

⁸ Adapted from Enders, D.; Berg, S.; Jandeleit, B. *Org. Synth.* **2000**, 78, 177-188.

mL of dry THF was added dropwise. The reaction mixture was stirred at -78 °C for 20 min and then was warmed to room temperature over 1 h, after which time TLC (silica gel, 2:1 hexanes/ethyl acetate) indicated complete consumption of the dihydrothiophene. The reaction mixture was quenched with 5 mL of saturated aqueous NH₄Cl. The aqueous phase was extracted with CH₂Cl₂ (3x5 mL) and the combined organic solutions were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Flash chromatography (hexanes/ethyl acetate, 1:1) provided 58 mg of 1,1-dioxo-5-phenyl-1,2,3,3a,4,7a-hexahydro-1λ⁶-benzo[*b*]thiophen-7-one (52% yield) as a white crystalline solid.

Characterization data for all new compounds (in the order they appear in the text)

3,5-Diphenyl-6-(toluene-4-sulfonyl)-cyclohex-2-enone (12).

Following **General procedure A**, was obtained in 81% yield. Characterization data: colorless solid, mp 133-134 °C (CH₂Cl₂/Hexane); IR (CHCl₃) 3085, 3060, 3030, 2918, 2848, 1658, 1607, 1495, 1448, 1317, 1145 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.47 (s, 3H), 3.16 (d, *J* = 19.0 Hz, 1H), 3.89 (ddd, *J* = 19.0, 6.4, 2.5 Hz, 1H), 4.10 (s, 1H), 4.64 (d, *J* = 6.4 Hz, 1H), 6.63 (d, *J* = 2.5 Hz, 1H), 7.13-7.19 (m, 2H), 7.20-7.30 (m, 3H), 7.38 (d, *J* = 8.6 Hz, 2H), 7.42-7.51 (m, 3H), 7.58-7.62 (m, 2H), 7.76 (d, *J* = 8.1 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 188.3, 158.9, 145.1, 141.6, 137.8, 135.2, 130.6, 129.7, 128.9, 128.8, 127.2, 127.1, 126.3, 125.0, 124.9, 73.9, 38.0, 31.3, 21.6; HRMS (DEI): Exact mass calcd for C₂₅H₂₃O₃S (M+H⁺) 403.1368. Found 403.1359.

6-Benzenesulfonyl-3-phenyl-5-thiophen-2-yl-cyclohex-2-enone (Entry 1).

Following **General procedure A**, a colorless oil was obtained in 86% yield. Characterization data: IR (CHCl₃) 1657, 1601, 1307 cm⁻¹; ¹H NMR (400 MHz, CHCl₃) δ 3.20 (d, *J* = 18.6 Hz, 1H), 3.89 (ddd, *J* = 18.6, 5.9, 2.5 Hz, 1H), 4.14 (s, 1H), 4.91 (d, *J* = 5.9 Hz, 1H), 6.59 (d, *J* = 2.5 Hz, 1H), 6.83-6.85 (m, 2H), 7.10 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.44-7.46 (m, 3H), 7.57-7.60 (m, 4H), 7.70 (t, *J* = 7.4 Hz, 1H), 7.87 (dd, *J* = 8.6, 1.4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 187.9, 158.9, 144.5, 138.5, 138.2, 134.5, 131.0, 129.4, 129.2, 129.1, 127.0, 126.7, 125.5, 125.2, 124.8, 73.8, 35.3, 33.2; HRMS (DEI): Exact mass calcd for C₂₂H₁₉O₃S₂ (M+H⁺) 395.0776. Found 395.0761.

6-Benzenesulfonyl-5-tert-butyl-3-phenyl-cyclohex-2-enone (Entry 2).

Following **General procedure A**, a colorless oil was obtained in 57% yield. Characterization data: IR (CHCl₃) 2916, 1656, 1317, 1309, 1146 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.94 (s, 9H), 2.97 (d, *J* = 19.5 Hz, 1H), 3.06 (d, *J* = 7.2 Hz, 1H), 3.45 (ddd, *J* = 19.5, 7.2, 2.6 Hz, 1H), 4.08 (s, 1H), 6.49 (d, *J* = 2.6 Hz, 1H), 7.45-7.47 (m, 3H), 7.57-7.60 (m, 4H), 7.70 (t, *J* = 7.3 Hz, 1H), 7.85 (dd, *J* = 8.0, 1.4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 189.2, 160.7, 138.2, 138.0, 133.9, 130.5, 129.0, 128.9, 128.8, 126.2, 124.4, 70.8, 42.3, 34.8, 28.1, 26.7; HRMS (DEI): Exact mass calcd for C₂₂H₂₅O₃S (M+H⁺) 369.1524. Found 369.1531.

2,3-Diethyl-5-phenyl-6-(toluene-4-sulfonyl)-cyclohex-2-enone (Entry 3).

Following **General procedure A**, was obtained in 73%

yield. Characterization data: thick colorless oil, IR (CHCl₃) 2968, 2934, 1655, 1119 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.99 (t, *J* = 7.2 Hz, 3H); 1.11 (t, *J* = 7.3 Hz, 3H), 2.28-2.47 (m, 4H), 2.47 (s, 3H), 2.62 (d, *J* = 19.0 Hz, 1H), 3.49 (dd, *J* = 19.0, 6.5 Hz, 1H), 4.02 (s, 1H), 4.39 (d, *J* = 6.5 Hz, 1H), 7.11 (d, *J* = 7.1 Hz, 2H), 7.20-7.28 (m, 3H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 188.0, 159.5, 145.0, 142.3, 136.9, 135.5, 129.6, 128.8, 128.7, 127.1, 74.0, 37.3, 33.5, 27.9, 21.6, 18.5, 13.5, 11.9; HRMS (EI): Exact mass calcd for C₂₃H₂₆O₃S (M⁺) 382.1597. Found 382.1600.

6-Benzenesulfonyl-2,3-diethyl-5,5-diphenyl-cyclohex-2-enone

(Entry 4). Following **General procedure A**, was obtained in 63% yield. Characterization data: white crystalline solid, mp 174-176 °C (CH₂Cl₂/hexane); IR (CHCl₃) 3058, 2970, 2933, 1660, 1625, 1447, 1318, 1148 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.82 (t, *J* = 7.5 Hz, 3H), 0.97 (t, *J* = 7.6 Hz, 3H), 2.15-2.39 (m, 4H), 3.21 (d, *J* = 17.9 Hz, 1H), 4.50 (d, *J* = 17.9 Hz, 1H), 5.03 (d, *J* = 1.8 Hz, 1H), 7.05-7.20 (m, 10H), 7.35-7.39 (m, 2H), 7.46-7.54 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 189.5, 159.2, 146.2, 143.5, 140.9, 136.6, 133.2, 128.7, 128.3, 128.2, 128.1, 127.0, 126.6, 126.3, 126.0, 78.4, 49.8, 37.7, 28.0, 18.5, 13.3, 11.5; HRMS (DEI): Exact mass calcd for C₂₈H₂₉O₃S (M+H⁺) 445.1832. Found 445.1836.

5-Benzenesulfonyl-7-methyl-2-phenyl-octa-2,6-dien-4-one (16).

Following **General procedure A**, a thick colorless oil was obtained in 85% yield. Characterization data: IR (CHCl₃) 1679, 1593, 1446, 1307 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.51 (d, *J* = 1.0 Hz, 3H), 1.80 (d, *J* = 1.0 Hz, 3H), 2.55 (d, *J* = 1.0 Hz, 3H), 4.92 (d, *J* = 10.3 Hz, 1H), 5.49 (dm, *J* = 10.3 Hz, 1H), 6.84 (d, *J* = 1.0 Hz, 1H), 7.42-7.44 (m, 3H), 7.53-7.58 (m, 4H), 7.65 (t, *J* = 6.4 Hz, 1H), 7.87 (d, *J* = 7.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 189.2, 158.3, 143.7, 141.9, 137.9, 133.8, 129.7, 129.2, 128.8, 128.6, 126.7, 123.2, 112.3, 76.9, 26.1, 19.0, 18.4; HRMS (DEI): Exact mass calcd for C₂₁H₂₃O₃S (M+H⁺) 355.1368. Found 355.1385.

6-Benzenesulfonyl-5-cyclopropyl-3-phenylcyclohex-2-enone

(Entry 5). Following **General procedure A**, was obtained in 80%

yield. Characterization data: colorless solid, mp 110-111 °C (Ethyl Acetate/Hexane); IR (CHCl₃) 3063, 3001, 2924, 2851, 1659, 1652, 1606, 1447, 1309, 1251, 1149 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.21-0.27 (m, 1H), 0.34-0.41 (m, 1H), 0.49-0.61 (m, 2H), 0.93-1.03 (m, 1H), 2.32 (dd, *J* = 10.7, 5.7 Hz, 1H), 2.94 (d, *J* = 18.5 Hz, 1H), 3.61 (ddd, *J* = 18.5, 5.7, 2.5 Hz, 1H), 3.96 (s, 1H), 6.54 (d, *J* = 2.5 Hz, 1H), 7.45-7.46 (m, 3H), 7.59 (m, 4H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.84 (d, *J* = 7.5 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 189.0, 159.5, 138.6, 138.5, 134.3, 130.8, 129.3, 129.1, 126.6, 124.1, 73.8, 40.0, 31.5, 16.0, 6.3, 5.0; HRMS (DEI) Exact mass calcd for C₂₁H₂₁O₃S (M+H⁺) 353.1211. Found 353.1205.

1,1-Dioxo-5-phenyl-1,2,3,3a,4,7a-hexahydro-1λ⁶-benzo[b]thiophen-7-one (Entry 6).

Following **General procedure B**, was obtained in 52% yield. Characterization data: colorless solid, mp 163-164 °C

(Ether/CH₂Cl₂/Hexane); IR (CHCl₃) 3059, 3005, 2950, 2850, 1656, 1604, 1446, 1308, 1140, 1117 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.27-2.35 (m, 1H), 2.40-2.49 (m, 1H), 2.90-3.03 (m, 2H), 3.27-3.36 (m, 3H), 3.96 (d, *J* = 7.6 Hz, 1H), 6.60 (s, 1H), 7.41-7.47 (m, 3H), 7.52-7.55 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 186.6, 159.0, 138.0, 131.1, 129.2, 126.6, 125.2, 67.8, 51.0, 35.8, 29.3, 26.4; HRMS (DEI): Exact mass calcd for C₁₄H₁₅O₃S (M+H⁺) 263.0742. Found 263.0738.

6-Benzenesulfonyl-5-butyl-3-phenylcyclohex-2-enone (Entry 7).

72% yield. Characterization data: thick colorless oil; IR (CH₂Cl₂) 3057, 2932, 1657, 1607, 1448, 1319, 1150 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 0.86 (t, *J* = 7.0 Hz, 3H), 1.25-1.34 (m, 3H), 1.42-1.52 (m, 3H), 2.74 (d, *J* = 18.7 Hz, 1H), 3.24 (m, 1H), 3.60 (ddd, *J* = 18.7, 5.6, 2.5 Hz, 1H), 3.77 (s, 1H), 6.49 (d, *J* = 2.5 Hz, 1H), 7.42-7.45 (m, 3H), 7.54-7.59 (m, 4H), 7.67 (t, *J* = 7.3 Hz, 1H), 7.84 (d, *J* = 7.5 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 14.1, 22.6, 29.6, 30.7, 33.5, 33.6, 73.6, 124.0, 126.6, 129.1, 129.1, 129.3, 130.9, 134.3, 138.6, 138.8, 159.3, 189.1; HRMS (DEI): Exact mass calcd for C₂₂H₂₅O₃S (M+H⁺) 369.1524. Found 369.1534.

2-Benzenesulfonyl-5,7-diphenylcycloocta-1,3,7-trienol (21).

Following General procedure A, was obtained in 45% yield. Characterization data: white crystalline solid, mp 155-156 °C (CH₂Cl₂/hexane), IR (CHCl₃) 3185, 3060, 1587, 1446, 1297, 1221 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.73 (d, *J* = 12.4 Hz, 1H), 3.11 (dd, *J* = 13.2, 13.2 Hz, 1H), 3.41 (m, 1H), 5.73 (dd, *J* = 12.4, 5.6 Hz, 1H), 6.14 (d, *J* = 12.0 Hz, 1H), 6.40 (s, 1H), 6.49 (d, *J* = 7.6 Hz, 2H), 7.05-7.15 (m, 3H), 7.39-7.40 (m, 3H), 7.47-7.48 (m, 2H), 7.63 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.75 (t, *J* = 7.2 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 2H), 11.01 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 160.6, 150.3, 143.0, 141.4, 139.9 (bs), 137.0 (bs), 133.8, 129.6, 129.2, 129.0, 128.7, 127.8, 127.3, 126.8, 126.7, 121.9, 118.8, 107.8, 43.5, 37.8; HRMS (DEI): Exact mass calcd for C₂₆H₂₃O₃S (M+H⁺) 415.1368. Found 415.1355.

3-Bromo-1-methyl-4-phenyl-5,6-dihydro-1H-pyridin-2-one (22).

To a solution of 1.06 g (5.67 mmol) of 1-methyl-4-phenyl-5,6-dihydro-1H-pyridin-2-one⁹ in 10 mL of CH₂Cl₂, cooled to 0 °C (water/ice bath), was added 337 μL (6.52 mmol) of Br₂. The reaction mixture was stirred at room temperature for 10 min and then concentrated in vacuo to give orange foam. The foam was dissolved in 5 mL of dioxane and 1.72 g of DBU (11.34 mmol) was added in one portion. After 1 h at room temperature, TLC (silica gel, EtOAc) indicated complete consumption of starting material. The reaction mixture was partitioned between 30 mL of 1N aqueous HCl and 150 mL of CH₂Cl₂. The organic solution was dried (MgSO₄), concentrated in vacuo to give a solid residue. The residue was flash chromatographed over 20 g of silica gel (EtOAc:Hex, 3:1) to produce 1.11 g (74%) of amide **22** as a white crystalline solid: mp 116-117 °C; IR (CH₂Cl₂) 3054, 1652, 1490, 1340, 1270, 1264, 1258 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.79 (t, *J* = 7.0 Hz,

⁹ Soldatenkov, A. T.; Temesgen, A. V.; Bekro, I. A.; Soldatova, S. A.; Golovtsov, N. I.; Sergeeva, N. D. *Chem. Heterocycl. Compd.* **2000**, 36, 1426-1430.

2H), 3.12 (s, 3H), 3.55 (t, $J = 7.0$ Hz, 2H), 7.35-7.43 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 32.3, 36.0, 47.1, 116.7, 127.5, 128.5, 128.8, 140.0, 149.3, 161.2; LRMS (APCI): Mass calcd for $\text{C}_{12}\text{H}_{13}\text{BrNO}$ ($\text{M}+\text{H}^+$) 266.0 and 268.0. Found 266.0 and 268.0 (1:1 in intensity).

8-Hydroxy-2-methyl-4a,6-diphenyl-3,4,4a,5-tetrahydro-2H-isoquinolin-1-one (24). To a solution of 58 mg (0.218 mmol) of bromide **22** in 1 mL of THF, cooled to -92 $^{\circ}\text{C}$ ($\text{CH}_2\text{Cl}_2/\text{liquid N}_2$) was added 120 μL of 2M solution of *n*-BuLi in cyclohexane (0.240 mmol) dropwise over a period of 1 minute. After 5 minutes at bath temperature, a solution of 31 mg (0.218 mmol) cyclobutenone in 0.5 mL of THF was added dropwise via syringe over a period of 3 minutes. The reaction mixture was left to warm to room temperature and then heated in an oil bath at 65 $^{\circ}\text{C}$ for 1 h. The reaction mixture was cooled down to room temperature and then quenched with 1 mL of saturated aqueous NH_4Cl solution. The mixture was partitioned between 100 mL of dichloromethane and 10 mL of water. The organic phase was separated and the aqueous one was extracted with dichloromethane (20 mL). The combined organic solutions were dried (MgSO_4), and then concentrated in vacuo to provide thick yellow oil. The oil was flash chromatographed over 15 g of silica gel ($\text{EtOAc}:\text{Hex}$, 1:1, then 2:1) to provide 37 mg (52%) of the bicyclic amide **24**. Characterization data for **24**: yellow crystalline solid, mp $167\text{--}168$ $^{\circ}\text{C}$ ($\text{CH}_2\text{Cl}_2/\text{Hexane}$); IR (CH_2Cl_2) 3070, 2925, 1643, 1586, 1503, 1446, 1368, 1323 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 2.26 (ddd, $J = 12.9, 12.9, 4.7$ Hz, 1H), 2.38 (ddd, $J = 12.9, 3.4, 2.0$ Hz, 1H), 2.89 (ddd, $J = 12.9, 12.5, 3.4$ Hz, 1H), 2.95 (dd, $J = 16.4, 2.9$ Hz, 1H), 2.97 (s, 3H), 3.09 (ddd, $J = 12.5, 4.7, 2.0$ Hz, 1H), 3.27 (d, $J = 16.4$ Hz, 1H), 6.29 (d, $J = 2.9$ Hz, 1H), 7.21 (t, $J = 7.1$ Hz, 1H), 7.26-7.32 (m, 7H), 7.37-7.38 (m, 2H), 14.56 (bs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 34.3, 37.2, 41.9, 42.4, 46.4, 97.4, 120.7, 125.9, 126.9, 127.0, 128.6, 128.7, 128.8, 139.2, 143.9, 145.3, 165.6, 169.7; HRMS (ESI): Exact mass calcd for $\text{C}_{22}\text{H}_{22}\text{NO}_2$ ($\text{M}+\text{H}^+$) 332.1645. Found 332.1650.

Control Experiments

a) Reaction of **11** with β -(*E*)-lithiostyrene.

To a solution of 45 μL of β -(*E*)-bromostyrene (63 mg, 0.35 mmol) in 2 mL of dry THF cooled to -78 $^{\circ}\text{C}$, was added dropwise 0.54 mL of a 1.30 M solution of *t*-BuLi in

pentane (0.70 mmol). After stirring 15 minutes at -78°C , 50 mg (0.35 mmol) of **11** in 1.5 mL of dry THF was added over a period of 1 minute. The reaction mixture was stirred at bath temperature for 20 minutes then at room temperature for 2 hours. Then the reaction mixture was quenched with 1 mL of saturated aqueous NH_4Cl . The aqueous phase was extracted with CH_2Cl_2 (3x5 mL) and the combined organic solutions were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. Flash chromatography (hexanes/ethyl acetate, 4:1) provided 38 mg (44%) of 1,5-diphenylhexa-1,5-dien-3-one as a yellow oil. Characterization data: IR (CHCl_3) 3081, 3057, 3027, 2918, 1684, 1610, 1576, 1496, 979 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 3.83 (s, 2H), 5.27 (s, 1H), 5.65 (s, 1H), 6.87 (d, $J = 16.0$ Hz, 1H), 7.34 (m, 6H), 7.44 (m, 2H), 7.51 (m, 2H), 7.62 (d, $J = 16.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 197.4, 143.2, 141.7, 140.0, 134.4, 130.5, 128.9, 128.5, 128.4, 127.9, 125.9, 124.7, 116.6, 48.5; LRMS (APCI): Mass calcd for $\text{C}_{18}\text{H}_{17}\text{O}$ ($\text{M}+\text{H}^+$) 249.1. Found 249.1.

In an attempt to thermally induce the 6π -ERC, the same experiment was repeated and the reaction mixture was heated under reflux. Analysis of an aliquot collected after 1 h at 65°C indicated that the reaction mixture still contained only the ring opened enone. After 14 h at reflux, this reaction produced a complex mixture of products. Careful analysis of the crude ^1H NMR of the reaction mixture revealed no peaks characteristic of 3,5-diphenylcyclohex-2-enone.¹⁰

b) Reaction of **10** and **11** at -78°C .

To a solution of 85 mg (0.33 mmol) of sulfone **9** in 1 mL of THF, cooled to -78°C , was added 180 μL (0.36 mmol) of 2M solution of *n*-BuLi in cyclohexane. After 10 min at bath temperature, a solution of 43 mg (0.30 mmol) of **11** in 0.5 mL of THF was added dropwise via syringe. The reaction mixture was stirred at bath temperature for 1 h and then quenched with 36 mg (0.60 mmol) of glacial acetic acid. The reaction mixture was partitioned between 5 mL of water and 30 mL of CH_2Cl_2 , the organic layer was separated, dried (MgSO_4), and concentrated *in vacuo* to provide a thick oil. The oil was flash chromatographed over 15 g of silica gel (EtOAc:Hex, 1:3) to afford 74 mg (61%) of **13** and 28 mg (23%) of **14** as thick colorless oils: Characterization data for **13**: IR (neat) 3492 (br), 1658, 1596, 1447, 1311, 1301, 1144 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 2.37 (s, 3H), 2.68 (d, $J = 13.0$ Hz, 1H), 2.88 (d, $J = 13.0$ Hz, 1H), 3.24 (bs, 1H), 6.27 (s, 1H), 7.01-7.04 (m, 2H), 7.01-7.04 (m, 2H), 7.20-7.22 (m, 3H), 7.29 (d, $J = 8.2$ Hz, 2H), 7.42-7.46 (m, 3H), 7.69-7.74 (m, 2H), 7.81 (d, $J = 8.2$ Hz, 2H), 7.88 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.7, 44.7, 72.6, 125.5, 127.6, 128.4, 128.6, 129.1, 129.5,

¹⁰ Zhang, F. Y.; Corey, E. J. *Org. Lett.* **2000**, 2, 1097-1100.

129.9, 130.2, 130.9, 133.3, 133.5, 138.7, 142.2, 143.5, 144.3, 147.7; LRMS (APCI): Mass calcd for C₂₅H₂₃O₃S (M+H⁺) 403.1. Found 403.1. Characterization data for **14**: IR (neat) 1707, 1610, 1596, 1319, 1304, 1147, 1084 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.41 (s, 3H), 3.81 (s, 2H), 5.04 (s, 1H), 5.52 (s, 1H), 7.27-7.34 (m, 11H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.85 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 21.9, 29.9, 117.7, 126.2, 127.9, 128.5, 128.8, 129.4, 130.0, 130.1, 131.4, 131.8, 136.6, 139.9, 140.0, 140.1, 142.3, 145.1, 199.2; LRMS (APCI): Mass calcd for C₂₅H₂₃O₃S (M+H⁺) 403.1. Found 403.1.

c) Base-mediated transformation of **13** to **12**.

To a solution of 12 μL (0.086 mmol) of *i*-Pr₂NH in 1 mL of dry THF, cooled to –78 °C, was added 43 μL (0.086 mmol) of a 2M solution of *n*-BuLi in cyclohexane. After 10 min at bath temperature, a solution of 29 mg (0.072 mmol) of alcohol **13** in 0.5 mL of THF was added dropwise over a period of 1 minute. Then the cooling bath was removed and the reaction mixture was stirred for 1 h, after which time TLC (silica gel, EtOAc:Hex, 1:3) indicated complete consumption of starting material. The reaction mixture was quenched with 1 mL of saturated aqueous NH₄Cl and then partitioned between 5 mL of water and 30 mL of CH₂Cl₂. The organic phase was dried (MgSO₄) and concentrated *in vacuo* to provide a light yellow residue, which was flash chromatographed over 15 g of silica gel (EtOAc:Hex, 1:3) to afford 27 mg (94%) of **12**.

d) Preparation of **15**.

To a solution of 90 mg (0.35 mmol) of sulfone **9** in 1 mL of THF, cooled to –50 °C, was added 0.18 mL (0.36 mmol) of a 2M solution of *n*-BuLi in cyclohexane dropwise. After 15 minutes at –50 °C, the reaction mixture was cooled to –78 °C. The red reaction mixture was then cannulated into a cooled (–78 °C) solution of 50 mg (0.32 mmol) of 4-methyl-3-phenylcyclobutenone in 1 mL of THF. The reaction mixture was warmed to –35 °C and stirred for 1 hour at the bath temperature. After quenching with 50 μL of AcOH at –35 °C, the reaction mixture was warmed to room temperature and then concentrated *in vacuo*. The crude oil was flash chromatographed (hexanes:EtOAc, 5:1) to obtain 74 mg of 1,5-diphenyl-2-(toluene-4-sulfonyl)hepta-1,5-dien-3-one (57% yield) as a yellow oil. Characterization data: IR (CDCl₃) 3058, 3027, 2924, 2858, 1708, 1597,

1146, 1318, 1146, 1085 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.70 (d, $J = 7.0$ Hz, 3H), 2.41 (s, 3H), 3.86 (s, 2H), 6.03 (q, $J = 7.0$ Hz, 1H), 7.14-7.18 (m, 2H), 7.18-7.27 (m, 5H), 7.27-7.30 (m, 3H), 7.35-7.41 (m, 2H), 7.71 (d, $J = 8.1$ Hz, 2H), 7.84 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 21.7, 46.0, 126.3, 126.7, 128.1, 128.4, 128.6, 129.1, 129.7, 129.8, 131.0, 131.6, 131.8, 136.4, 139.7, 142.1, 142.4, 144.8, 198.3; LRMS (APCI): Mass calcd for $\text{C}_{26}\text{H}_{25}\text{O}_3\text{S}$ ($\text{M}+\text{H}^+$) 417.1. Found 417.1.

ppm

189.21

160.68

138.23

138.03

133.91

130.45

128.94

128.80

128.77

126.20

124.38

77.19

76.87

76.55

70.77

42.30

34.78

28.13

26.74

CDCl₃, 100 MHz

CDCl₃, 100 MHz

CDCl₃, 100 MHz

ppm

CDCl₃, 400 MHz

129.20
126.56

77.55
77.23
76.91

21

CDCl₃, 100 MHz

22

CDCl₃, 100 MHz

CDCl₃, 400 MHz

CDCl₃, 100 MHz

169.652
165.558

145.302
143.925
139.198

128.749
128.687
128.590
126.958
126.856
125.885
120.706

97.351

77.549
77.437
77.231
76.914

46.435
42.427
41.920
37.229
34.281