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# Novel Ene Trimerization of 1-Phenylcyclopropene

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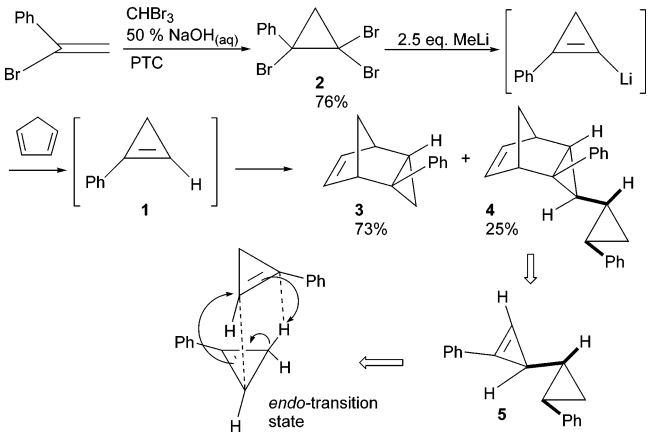
**Abstract:** 1-Phenylcyclopropene (**1**) was synthesized by treatment of 1,1,2-tribromo-2-phenylcyclopropane (**2**) with 2.5 equiv of methyllithium followed by protonation. Compound **1** underwent ene dimerization to form ene dimer **5** followed by ene reaction with monomer **1** (enophile) to give an ene trimer **6**. Both of these two ene reactions derived endo transition states. In the meantime, the [2+2] adduct, *trans*-1,2-diphenylbicyclo[3.1.0.0$^{2,4}$]hexane (**7**), was also formed. When the adduct **7** was heated at THF refluxing temperature, 1,2-diphenylcyclohexa-1,4-diene (**8**) was obtained. Compound **8** was treated with DDQ to yield *o*-diphenylbenzene.

Cyclopropene is known to dimerize and polymerize at room temperature via ene reactions to release the olefinic strain.[1] Substituted cyclopropenes are generally more stable and can dimerize via ene reactions to give 3-cyclopropylcyclopropenes,[2] [2+2] cyclizations to form tricycle-[3.1.0.0$^{2,4}$]hexanes,[3] and coupling reactions to yield 1,3,5-hexatriene[3c−f,4] at higher temperature. Due to their high strain energy, cyclopropenes containing 3-hydrogen usually undergo ene dimerizations. Asymmetric cyclopropenes usually undergo ene reactions to form several regio- and stereodimers.[3e,4b,5] In the literature, there are only a few cyclopropenes which undergo crossed ene reactions faster than ene dimerizations. Baird and coworker reported that 3,3-dimethylcyclopropenecarboxylic acid and 2-*tert*-butylcyclopropenecarboxylic acid only underwent crossed ene reactions via an exo approach of the dimethylcyclopropene and the ene dimer of 2-*tert*-butylcyclopropenecarboxylic acid was not obtained.[5c] This crossed ene reaction resulted from two different cyclopropenes but only one of them contained 3-hydrogen. Therefore the regio- and stereochemistry of this crossed ene reaction are less complicated than that of both cyclopropenes containing 3-hydrogen. Okamoto and coworker reported that 1,2-diarylcyclopropenes did react with strong enophiles such as tetracyanoethylene, dibenzoylacetylene, and dimethyl acetylenedicarboxylate but did not show any reactivity toward hydrocabonenes (e.g., 3-phenylpropene) or enophiles (e.g., diphenylacetylene).[5b] There was only one cyclopropene, bicyclo[5.1.0]hept-1(8)-ene, reported that underwent ene trimerization, another type of crossed ene reaction of monomer with ene dimer, to give an ene trimer.[3e] This ene trimer was only determined by $^1$H NMR and mass spectrometry in crude mixture and was not isolated or trapped to prove its existence and the stereochemistry and regiochemistry of these ene reactions were still unknown. Although 1-phenylcyclopropene (**1**) has been synthesized,[6] the chemistry of **1** has not been investigated yet. In this paper we describe an easier synthetic route and the characteristic facile ene trimerization of 1-phenylcyclopropene (**1**).

**SCHEME 1**




Compound **1** was prepared and trapped in solution by the method shown in Scheme 1. 1,1,2-Tribromo-2-phenylcyclopropane (**2**),[4b,9] the immediate precursor via dehalogenation, halo-lithium exchanged reaction, and protonation to compound **1**, was generated by dibromocarbene addition to α-bromostyrene.[4b] When cyclopropane **2**[4b,9] was treated with 2.5 equiv of methyllithium followed by cyclopentadiene at −40 °C, two compounds were isolated (73 and 25%) (Scheme 1). The major product **3** was formed from cylopropene **1** with cyclopentadiene. The structure of the minor product **4** was shown by X-ray crystallography (Figure 1) and it was formed from an ene dimer **5** and cyclopentadiene. The ene dimer **5** was formed via an endo transition state. Cyclopropene **1** is very active and one-quarter of **1** undergoes ene reaction before reacting with cyclopentadiene.

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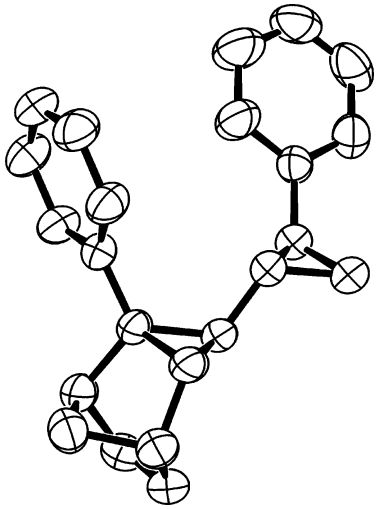


**FIGURE 1.** The structure of compound **4** (hydrogen atoms omitted).

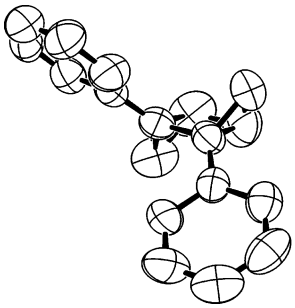


**FIGURE 2.** The structure of compound **7** (hydrogen atoms omitted).

To generate high-yield ene dimer **5**, compound **1** was synthesized and kept at −30 °C for 48 h followed at 0 °C for 24 h and two adducts **6** and **7** were isolated in the yields of 88% and 8%, respectively. The $^{13}C$ NMR spectrum of **6** showed 21 signals (triple of monomer's signals) including 14 alkene carbons as expected for an ene trimer **6**. The structure of **7**, *trans*-1,2-diphenylbicyclo-[3.1.0.0$^{2,4}$]hexane, was shown by X-ray crystallography (Figure 2) and it was formed via a head-to-head [2+2] dimerization reaction. When the adduct **7** was heated at THF refluxing temperature, 1,2-diphenylcyclohexa-1,4-diene (**8**) was obtained.[7] Compound **8** was treated with DDQ to yield *o*-diphenylbenzene.[8]

It is interesting to note that, despite the ready ene dimerization of **1**, there was no evidence of products other than **6** and **7**. Because the ene trimer **6** was unstable in the presence of water and oxygen, compound **6** was trapped with cyclopentadiene to form a stable adduct **9** to study the regio- and stereochemistry of **6** (Scheme 2). This is the first confirmed ene trimerization. The structure of adduct **9** was shown by single-crystal X-ray analysis (Figure 3). Compound **6** was generated by the endo transition state from **1** (enophile) and **5** (hydrogen donator). We also attempted to prepare the ene tetramer of **1** by treatment of **6** with **1** but only compound **6** was obtained.

The PM3 theoretical calculations of heats of formation of **1**, **5**, **6**, and the endo tetramer are 90.4, 135.1, 177.4, and 226.4 kcal/mol, respectively. The heat of ene dimerization is − 45.7 kcal/mol, and the heat of the reaction of **1** and **5** to give **6** is −48.1 kcal/mol, supportive of the favored ene trimerization over the ene dimerization. The heat of the reaction of **6** and **1** to yield the endo tetramer is −41.4 kcal/mol, indicating why there is no observation of ene tetramerization.

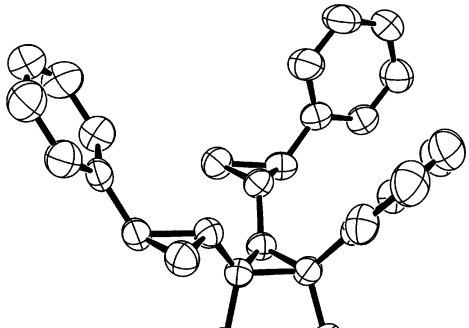
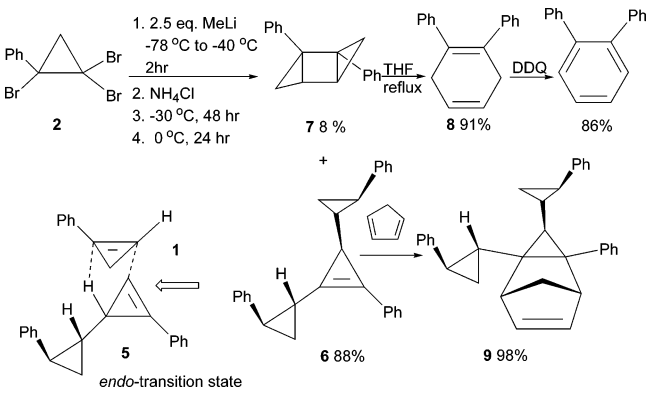


**FIGURE 3.** The structure of compound **9** (hydrogen atoms omitted).

**SCHEME 2**




$$\Delta H(H_f \text{ of dimer} - H_f \text{ of monomer} \times 2) = -45.7 \text{ (kcal/mol)} \quad (1)$$

$$\Delta H(H_f \text{ of trimer} - H_f \text{ of monomer} - H_f \text{ of dimer}) = -48.1 \text{ (kcal/mol)} \quad (2)$$

$$\Delta H(H_f \text{ of tetramer} - H_f \text{ of monomer} - H_f \text{ of trimer}) = -41.4 \text{ (kcal/mol)} \quad (3)$$

In summary, we discovered an easier route to synthesize 1-phenylcyclopropene (**1**). Compound **1** underwent ene dimerization to from ene dimer **5** followed by ene reaction with monomer **1** (enophile) to give an ene trimer **6**. Both of these ene reactions derived endo transition states. In the meantime, the [2+2] adduct **7** was also formed and this reaction provides a feasible route to *o*-diarylbenzene.

## Experimental Section

**General.** Melting points are determined and uncorrected. Proton and carcon-13 NMR spectra were measured in $CDCl_3$ with $CHCl_3$ as the internal standard. Chemical shifts ($\delta$) are expressed in ppm downfield from tetramethylsilane and coupling

constants are expressed in hertz. X-ray data were recorded on a Siemens P4 diffractometer for compounds **4**, **7**, and **9**. Calculations were performed with the HyperChem Molecular Modeling System for Windows, Version 6.03, geometry optimization, semiempirical, PM3. Silica gel (70−230 mesh) for column chromatography and silica gel (230 mesh) for flash chromatography were from E. Merck. Solvents are reagent grade.

**1,1,2-Tribromo-2-phenylcyclopropane (2).** α-Bromostyrene (14.2 g, 78 mmol), 21 mL of bromoform, 21 mL of 50% of sodium hydroxide, and 0.1 g of *n*-tetrabutylammonium bromide were placed into a 100-mL flask. The mixture was stirred for 20 h at 80 °C, and then 25 mL of methylene chloride and 20 mL of water were added. The water layer was extracted with methylene chloride (3 × 25 mL). The combined organic solution was washed with water and brine and dried over anhydrous sodium sulfate, filtered, concentrated, and chromatographed (hexanes) to give white solid **2** (21.04 g, 76%, mp 83.5−84.5 °C).

**Trapping 1-Phenylcyclopropene (1) with Cyclopentadiene.** Methyllithium (1.5 M in ether, 23.5 mL, 35.0 mmol) was added dropwise from a syringe to a stirred solution of 1,1,2-tribromo-2-phenylcyclopropane (**2**) (5.0 g, 14.0 mmol) in 30.0 mL of dry ether at −78 °C. The mixture was stirred at −40 °C for 2 h, then cyclopentadiene (11.5 mL, 0.14 mol) was added and the mixture was allowed to warm to room temperature and stirred for 12 h. About 20 mL of ether was added, then the mixture was pour into a 250-mL beaker with 100 g of crushed ice. The organic layer was separated and washed with water and brine, dried over anhydrous magnesium sulfate, filtered, and then concentrated and chromatographed (hexanes) to give colorless oil **3** (1.86 g, 73%) and white solid **4** (0.52 g, 25%). Compound **3**: IR (neat, $cm^{-1}$) 3058, 2971, 2863, 1600, 1497, 1446, 1329, 1245, 1026, 852, 792, 754, 727, 696; $^1H$ NMR ($CDCl_3$) $\delta$ 7.35−7.15 (m, 5H), 6.09−6.06 (m, 1H), 5.90 (dd, 1H, $J$ = 3.2, 5.2 Hz), 3.08−3.06 (m, 1H), 3.04−3.02 (m, 1H), 2.12 (dt, 1H, $J$ = 6.9, 1.7 Hz), 1.79−1.75 (m, 2H), 1.12−1.10 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 144.6 (C), 133.2 (CH), 132.6 (CH), 128.3 (CH), 127.4 (CH), 125.4 (CH), 62.1 ($CH_2$), 48.4 (CH), 43.9 (CH), 28.8 (C), 26.2 ($CH_2$), 22.6 (CH); MS (EI) *m/z* (%) 182 ($M^+$, 53), 167 (100), 115 (39), 91 (36); HRMS calcd for $C_{14}H_{14}$ *m/z* 182.1096, found 182.1097. Anal. Calcd for $C_{14}H_{14}$: C 92.26, H 7.74. Found: C 92.54, H 7.68. Compound **4**: mp 38.0−39.0 °C; IR (neat, $cm^{-1}$) 3052, 2979, 2949, 2923, 2856, 1600, 1495, 1444, 1324, 1257, 1146, 875, 830, 754, 736, 698; $^1H$ NMR ($CDCl_3$) $\delta$ 7.41−7.04 (m, 8H), 6.73−6.71 (m, 2H), 6.09−6.06 (m, 1H), 5.98−5.95 (m, 1H), 3.09 (s, 1H), 2.98 (s, 1H), 2.07 (d, 1H, $J$ = 6.9 Hz), 1.82−1.79 (m, 1H), 1.72−1.65 (m, 2H), 1.01 (dd, 1H, $J$ = 2.7, 7.1 Hz), 0.84−0.77 (m, 1H), 0.72−0.65 (m, 1H), 0.54−0.47 (m, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 143.2 (C), 141.8 (C), 132.9 (CH), 132.4 (CH), 130.4 (CH), 128.0 (CH), 127.9 (CH), 126.2 (CH), 125.9 (CH), 125.1 (CH), 60.6 ($CH_2$), 51.8 (CH), 43.8 (CH), 39.4 (CH), 34.9 (C), 23.4 (CH), 23.3 (CH), 22.1 (CH), 15.8 ($CH_2$); MS (EI) *m/z* (%) 298 ($M^+$, 3.5), 232 (38), 207 (47), 165 (49), 91 (100); HRMS calcd for $C_{23}H_{22}$ *m/z* 298.1722, found 298.1723. Anal. Calcd for $C_{23}H_{22}$: C 92.57, H 7.43. Found: C 92.57, H 7.45.

**Ene Trimerization and [2+2] Cyclization of 1-Phenylcyclopropene (1).** To a stirred solution of compound **2** (15.0 g, 42.0 mmol) in 80 mL of dry ether at − 78 °C was added methyllithium (1.5 M in ether, 70.5 mL, 0.105 mol) dropwise from a syringe. The mixture was stirred at −40 °C for 2 h, then ammonium chloride (5.6 g, 0.105 mol) was added. Ether was removed under reduced pressure and the residue was kept at −30 °C for 48 h followed at 0 °C for 24 h, then allowed to warm to room temperature. Hexanes (100 mL) was added, and the mixture was filtrated, concentrated, and chromatographed (hexanes) to give white solid **6** (4.29 g, 88%) and **7** (0.39 g, 8%). Compound **6**: $^1H$ NMR ($CDCl_3$) $\delta$ 7.54−7.07 (m, 15H), 2.43−2.30 (m, 2H), 2.03 (d, 1H, $J$ = 3.9 Hz), 1.80−1.74 (m, 1H), 1.67−1.53 (m, 2H), 1.31−1.21 (m, 1H), 1.02−0.92 (m, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 143.8 (C), 143.3 (C), 130.1 (C), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 127.5 (CH), 126.1 (CH), 126.0 (CH), 125.9 (CH), 125.2 (CH), 120.7 (C), 111.4 (C), 27.6 (CH), 26.3 (CH), 22.5 (CH), 21.8 (CH), 20.5 (CH), 16.3 ($CH_2$), 15.7 ($CH_2$). Compound **7**: mp 43.0−43.5 °C; IR (neat, $cm^{-1}$) 3054, 3026, 2972, 1600, 1497, 1446, 1290, 1230, 1118, 1024, 819, 784, 747, 697; $^1H$ NMR ($CDCl_3$) $\delta$ 7.14−7.32 (m, 10H), 2.02 (dd, 2H, $J$ = 2.5, 3.7 Hz), 1.82−1.85 (m, 4H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 140.4 (C), 128.3 (CH), 125.5 (CH), 125.1 (CH), 32.4 (C), 31.3 ($CH_2$), 29.3 (CH); MS (EI) *m/z* (%) 232 ($M^+$, 100), 215 (74), 141 (66), 91 (89); HRMS calcd for $C_{18}H_{16}$ *m/z* 232.1252, found 232.1253. Anal. Calcd for $C_{18}H_{16}$: C 93.06, H 6.94. Found: C 92.99, H 7.04.

**1,2-Diphenylcyclohexa-1,4-diene (8).**[7] A solution of **7** (0.46 g, 2.0 mmol) in THF (20 mL) was stirred and heated at THF refluxing temperature for 8 h. The reaction mixture was concentrated and the residue was purified by chromatography (hexanes) to give white solid **8** (0.42 g, 91%). Compound **8**: $^1H$ NMR ($CDCl_3$) $\delta$ 7.15−7.05 (m, 10H), 5.86 (t, 2H, $J$ = 2.7 Hz), 3.13 (d, 4H, $J$ = 1.4 Hz).

**Oxidation of Compound 8.** A solution of **8** (0.11 g, 0.48 mmol) in glacial acetic acid (60 mL) containing 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (0.13 g, 0.57 mmol) was stirred for 0.5 h at room temperature. About 30 mL of hexanes was added, and the mixture was poured into a 250-mL beaker with 100 mL of iced water. The organic layer was separated and washed with water and brine, then dried over anhydrous magnesium sulfate, filtered, concentrated, and chromatographed (hexanes) to give *o*-diphenylbenzene (0.095 g, 86%).[8] *o*-Diphenylbenzene: $^1H$ NMR ($CDCl_3$) $\delta$ 7.47−7.42 (m, 4H), 7.27−7.15 (m, 10H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 141.6 (C), 140.7 (C), 130.7 (CH), 130.0 (CH), 127.9 (CH), 127.5 (CH), 126.5 (CH).

**Diels−Alder Reaction of Ene Trimer 6 and Cyclopentadiene.** Compound **6** (4.0 g, 11.0 mmol) was generated as described above and dissolved in 40 mL of hexanes at room temperature. After cyclopentadiene (9.0 mL, 0.11 mol) was added the mixture was stirred for 12 h, concentrated, and chromatographed (hexanes) to give white solid **9** (4.46 g, 98%). Compound **9**: mp 107.0−108.0 °C; IR (neat, $cm^{-1}$) 3054, 3021, 2981, 2965, 2936, 2866, 1600, 1496, 1461, 1449, 1442, 1326, 1245, 1227, 1102, 1085, 1028, 910, 876, 857, 773, 747, 695; $^1H$ NMR ($CDCl_3$) $\delta$ 7.42−7.02 (m, 13H), 6.84−6.81 (m, 2H), 6.05 (dd, 1H, $J$ = 3.3, 5.0 Hz), 5.98−5.95 (m, 1H), 2.75 (d, 1H, $J$ = 1.1 Hz), 2.50 (s, 1H), 2.21 (d, 1H, $J$ = 7.0 Hz), 2.02−1.95 (m, 1H), 1.84−1.78 (m, 1H), 1.61 (d, 1H, $J$ = 7.0 Hz), 1.30−1.24 (m, 1H), 1.18−1.07 (m, 2H), 0.82−0.74 (m, 2H), 0.59−0.53 (m, 1H), 0.46−0.38 (m, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 143.4 (C), 143.1 (C), 140.7 (C), 133.9 (CH), 133.2 (CH), 131.3 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 126.2 (CH), 126.1 (CH), 125.9 (CH), 125.3 (CH), 125.2 (CH), 59.2 ($CH_2$), 53.5 (CH), 44.2 (CH), 41.9 (CH), 35.8 (C), 31.2 (C), 24.9 (CH), 22.4 (CH), 22.3 (CH), 21.3 (CH), 16.3 ($CH_2$), 11.9 ($CH_2$); MS (FAB) *m/z* (%) 414 ($M^+$, 9), 310 (39), 165 (19), 115 (17); HRMS calcd for $C_{32}H_{30}$ *m/z* 414.2348, found 414.2358. Anal. Calcd for $C_{32}H_{30}$: C 92.71, H 7.29. Found: C 92.94, H 7.05.

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**Supporting Information Available:** Crystal structures for **4**, **7**, and **9**, and $^1H$ and $^{13}C$ NMR spectra for compounds **2**, **3**, **4**, **6**, **7**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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