Regioselectivity of the Ene Reaction: Dimerization of 8-Chlorobicyclo[5.1.0]oct-1(8)-ene

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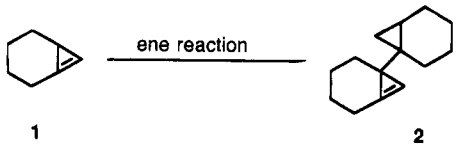
Cyclopropene has attracted the attention of both theoretical and experimental chemists because of its special place as the simplest small ring cycloalkene.[1-3] Cyclopropene contains 55.2 kcal/mol of strain energy and 27.7 kcal/mol of olefinic strain energy.[4] Consequently, cyclopropene undergoes many unusual reactions such as ring opening reactions and ene reactions to release olefinic strain.[5] Asymmetric cyclopropenes usually undergo ene reactions to form several regiodimers. Therefore, control of the regiochemistry of the ene reaction of cyclopropenes is an important issue in the synthesis of functionalized polycyclopropyl compounds. To the best of our knowledge, there is only one reported ene reaction of 1,3-fused bicyclic cyclopropene, in which bicyclo[4.1.0]-hept-1(7)-ene (**1**) has undergone the ene reaction at low temperature to give 6-(1-bicyclo[4.1.0]heptyl)bicyclo[4.1.0]-hept-1(7)-ene (**2**).[6] Unlike **1**, 7-chlorobicyclo[4.1.0]hept-1(7)-ene (**3**) produced, in neat condition, no dimeric product. Rather, 2-chlorocyclohepta-1,3-diene (**5**) was the only isolable compound, formed via cyclopropene–vinyl carbene rearrangement followed by intramolecular carbene insertion.[6,7]



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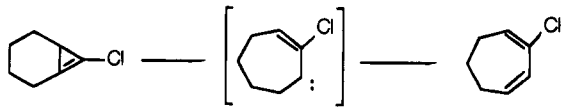

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Although the 2-chlorinated 1,3-fused bicyclic cyclopropene, 8-chlorobicyclo[5.1.0]oct-1(8)-ene (**6**), has been trapped as an intermediate with diphenylisobenzofuran (DPIBF) in the reaction of 1-(trimethylsilyl)-8,8-dichlorobicyclo[5.1.0]octane and tetrabutylammonium fluoride,[8] the purification and isolation of **6** was not feasible. We report here an easier route to the synthesis and isolation of **6** and describe the regioselectivity of its ene dimerization.

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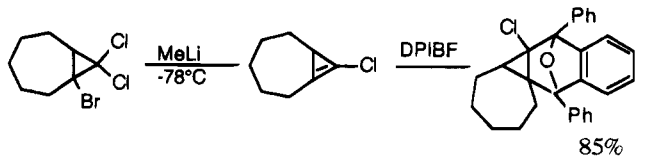
(1) Liebman, J. F.; Greenberg, A. *Chem. Rev.* **1976**, *76*, 311.
(2) Billups, W. E.; Haley, M. M.; Lee, G.-A. *Chem. Rev.* **1989**, *89*, 1147.
(3) Halton, B; Banwell M. B. Cyclopropenes. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed. Wiley: New York, 1987; Chapt. 21.
(4) Wiberg, K. B. Structures, Energies and Spectra of Cyclopropanes. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed. Wiley: New York, 1987; Chapt. 1.
(5) Dowd, D.; Gold, A. *Tetrahedron Lett.* **1969**, 85.
(6) Billups, W. E.; Lee, G.-A.; Arney, B. E., Jr.; Whitmire, K. H. *J. Am. Chem. Soc.* **1991**, *113*, 7980.
(7) Chan, T. H.; Massuda, D. *Tetrahedron Lett.* **1975**, 3383.
(8) Banwell, M. G.; Corbett, M.; Gulbis, J.; Mackay, M. F.; Reum, M. E. *J. Chem. Soc., Perkin Trans. 1* **1993**, 945.

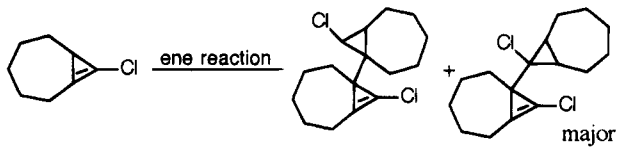
Results and Discussion

1-Bromo-8,8-dichlorobicyclo[5.1.0]octane (**7**), the immediate precursor via dehalogenation to compound **6**, was generated from cycloheptene. Cycloheptene proceeded via bromination, dehydrobromination, and dichlorocarbene addition to give trihalocyclopropane **7**. Trihalocyclopropane **7** reacted with methyllithium in ether at −78 °C to give a 47% isolated yield of **6**, which further formed a DPIBF adduct **8** with an 85% yield.



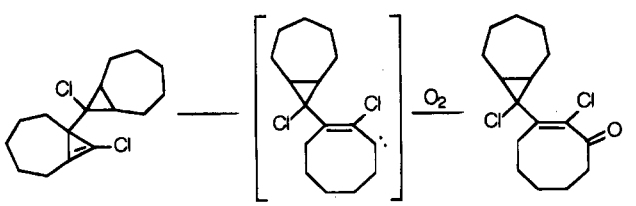
7 6 8

The ene reactions of compound **6**, in principle, can generate two 1,3-fused cyclopropenes, 8-chloro-7-(8-chlorobicyclo[5.1.0]oct-1-yl)bicyclo[5.1.0]oct-1(8)-ene (**9**) and 8-chloro-7-(8-chlorobicyclo[5.1.0]oct-8-yl)bicyclo[5.1.0]oct-1(8)-ene (**10**). After compound **6** was synthesized and purified at low temperature, it was kept neat under vacuum at room temperature for 5 days. Two compounds, both shown by mass spectrometry to be dimers of **6** (MS m/z = 284), could be isolated in 65 and 2.1% yields, respectively, by using HPLC. According to the ^{13}C-NMR (δ_C = 119.3 (=C), 109.4 (=C), and 67.1 ppm



6 9 10

(CCl)) and IR (1695 cm^{-1} cyclopropenyl stretching mode) spectral data, the major dimer is believed to be ene dimer **10** which contains a cyclopropenyl fragment. As expected, compound **10** cannot react with dienes (such as DPIBF, cyclopentadiene, and butadiene) to yield *trans* fused bicyclo[5.1.0]heptanes due to the high strained energy of these adducts. When the major dimer **10** was isolated and treated with oxygen, an α,β-unsaturated carbonyl compound, 2-chloro-3-(8-chlorobicyclo[5.1.0]oct-8-yl)cyclooct-2-enone (**11**) (δ_C = 202.4, 142.4, and 128.7 ppm; MS m/z = 300), was obtained. This compound was generated from the dimer **10** via cyclopropene–vinyl carbene rearrangement followed by oxidization with molecular oxygen.



10 11

The minor dimer **12** is a diene product (δ_C = 139.6 (=C), 136.7 (=C), 130.3 (=CH), 124.5 (=CH), and 67.1 (CHCl) ppm; δ_H = 6.00 (s, 1H), 5.54 (t, J = 7.9 Hz, 1H), 3.10 (d, J = 7.1 Hz, 1H, CHCl)) which was presumably formed from dimer **9**. Compound **9** is believed to undergo

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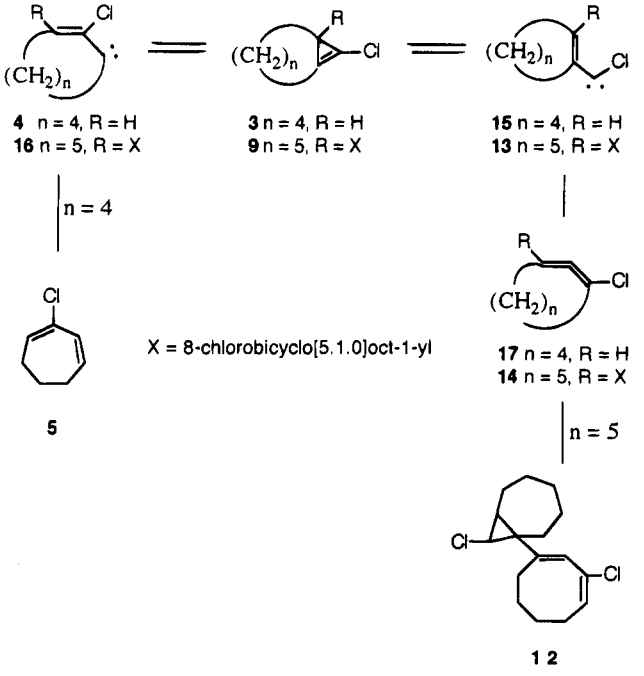
ring opening reaction to give vinyl carbene **13** followed by intramolecular carbene insertion to generate cyclic allene **14** which then isomerizes to afford 2-chloro-4-(8-chlorobicyclo[5.1.0]oct-1-yl)cycloocta-1,3-diene (**12**).

The chemistry of formation of **12** is different from that for **5**. There are two effects that influence the outcome. One is that the chloro vinyl carbene is more stable than an alkyl vinyl carbene; another is that the stability of the seven-membered cyclic allene is less than that of the eight-membered cyclic allene, cycloocta-1,2-diene.[9,10] Considering the former effect, carbenes **13** and **15** are more stable than **16** and **4**. Hence, compound **9** rearranges to carbene **13** followed by insertion reaction to form cycloocta-1,2-diene **14**. However, cyclopropene **3** isomerizes to carbene **4** followed by intramolecular carbene insertion to give diene **5** because of the dominant effect of the latter one.



Finally, the reason for different regiochemistry in the dimerization of **1** and **6** is a chlorine effect. The carbocation on the fused carbon (C-1) in bicyclo[4.1.0]hept-1(7)-ene is more stable than that on C-7, but in 8-chlorobicyclo-[5.1.0]oct-1(8)-ene the carbocation on C-1 is less stable than that on C-8 due to the resonance effect of the Cl atom.

Experimental Section

Melting points are uncorrected. Chemical shifts (δ) are expressed in ppm downfield from tetramethylsilane. Coupling constants are expressed in hertz. HPLC was carried out with a Lichrosorb (Merck) column. The silica gel (60–200 mesh) for column chromatography and silica gel (230 mesh) for flash chromatography were made by E. Merck. Solvents are of reagent grade.

1-Bromo-8,8-dichlorobicyclo[5.1.0]octane (7). 1-Bromocycloheptene (6.0 g, 34.2 mmol), 25 mL chloroform, 10 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 24 h at room temperature, 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 magnesium sulfate. Filtration and distillation gave **7** (80–81°C, 0.8 torr, 7.4 g, 84%). Compound **7**: IR (neat, cm^{-1}) 2920, 2850, 1440, 825, 750; ^1H NMR ($CDCl_3$) δ 2.48–2.41 (m, 1H), 2.25–2.16 (m, 1H), 2.03–1.76 (m, 6H), 1.57–1.43 (m, 1H), 1.35–1.18 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 70.53 (C), 50.31 (C), 43.52 (CH), 37.39 (CH_2), 31.33 (CH_2), 27.42 (CH_2), 27.28 (CH_2), 27.11 (CH_2); MS *m/z* 256 (M^+, 39%), 258 ($M^+ + 2$, 61%), 260 ($M^+ + 4$, 24%), 262 ($M^+ + 6$, 0.9%), 177 (100%); HRMS calcd for $C_8H_{11}BrCl_2$ *m/z* 255.9422, found 255.9424.

8-Chlorobicyclo[5.1.0]oct-1(8)-ene (6). Compound **7** (1.0 g, 3.9 mmol) in 5 mL of dry ether was cooled to −78 °C, and 5 mL of 1.5 M methyllithium in ether was added. The mixture was stirred for 10 min at −78 °C. The reaction was quenched with water (1 mL) and allowed to warm to room temperature. The ethereal solution was dried, concentrated, and chromatographed to give **6**. Compound **6**: ^1H NMR ($CDCl_3$) δ 2.48–2.41 (m, 1H), 2.25–2.16 (m, 1H), 2.03–1.76 (m, 6H), 1.57–1.43 (m, 1H), 1.35-1.18 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 116.75 (C), 111.04 (C), 33.40 (CH_2), 29.58 (CH_2), 29.40 (CH_2), 28.55 (CH), 26.93 (CH_2), 24.50 (CH_2).

Trapping 8-Chlorobicyclo[5.1.0]oct-1(8)-ene (6) with Diphenylisobenzofuran. To a solution of compound **7** (1.0 g, 3.9 mmol) and diphenylisobenzofuran (1.89 g, 7.0 mmol) in 5 mL dry ether at −78 °C was added methyllithium (10 mL, 1.5 M) in ether over 10 min. The mixture was stirred for 20 min and then allowed to warm to room temperature and stirred 2.5 h. Water was added, and the mixture was extracted with ether (3 × 25 mL). The ethereal solution was dried, concentrated, and chromatographed to give **8** (1.32 g, 82.3%, mp 141.0–142.0 °C). Compound **8**: IR (neat, cm^{-1}) 3030, 2910, 2850, 1470, 1430, 1270, 750, 730, 690, 670; ^1H NMR ($CDCl_3$) δ 7.90–7.79 (m, 4H), 7.73–7.67 (m, 1H), 7.57–7.41 (m, 6H), 7.38–7.22 (m, 3H), 2.95–2.86 (m, 1H), 2.39–2.20 (m, 1H), 1.94–1.78 (m, 3H), 1.77–1.15 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 148.59 (C), 147.12 (C), 136.14 (C), 134.00 (C), 129.15 (CH), 128.88 (CH), 128.41 (CH), 128.27 (CH), 128.12 (CH), 126.87 (CH), 126.26 (CH), 126.15 (CH), 122.61 (CH), 121.33 (CH), 89.80 (C), 89.67 (C), 65.35 (C), 42.17 (C), 34.01 (CH), 32.77 (CH_2), 28.23 (CH_2), 27.39 (CH_2), 27.27 (CH_2), 25.51 (CH_2); MS *m/z* 412 (M^+, 3%), 377 (100%); HRMS calcd for $C_{28}H_{25}ClO$ *m/z* 412.1596, found 412.1597.

Dimerizations of 8-Chlorobicyclo[5.1.0]oct-1(8)-ene (6). Compound **6** (1.06 g, 7.44 mmol) was generated as described above and sealed in vaccum tube. After 5 days, the mixture was purified by HPLC (n-hexane, 1.0 mL/min) to give two compounds. The first compound (t_R = 9.5 min) is **10** (0.69 g, yield 65%). The second compound (t_R = 17.9 min) is **12**. Spectral data of **10** are as follows: IR (neat, cm^{-1}) 2915, 2855, 1695, 1440; ^1H NMR (300 MHz, $CDCl_3$) δ 2.85–2.59 (m, 1H), 2.45–2.28 (m, 1H), 2.27–1.90 (m, 20H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 119.27 (C), 109.45 (C), 67.14 (C), 44.70 (C), 32.96 (CH_2), 32.70 (CH_2), 29.19 (CH_2), 29.08 (CH_2), 29.04 (CH_2), 28.90 (CH_2), 28.22 (CH), 28.16 (CH), 26.6 (CH_2), 26.4 (CH_2), 26.0 (CH_2), 23.4 (CH_2); MS *m/z* 284 (M^+, 4%), 247 (42%), 193 (100%); HRMS calcd for $C_{16}H_{22}Cl_2$ *m/z* 284.1098, found 284.1094. Spectral data for **12**: IR (neat, cm^{-1}) 2890, 2830, 1595, 1425, 1245, 990, 840; ^1H NMR ($CDCl_3$) δ 6.00 (s, 1H), 5.54 (t, J = 7.9 Hz, 1H), 3.10 (d, J = 7.1 Hz, 1H), 2.42–1.22 (m, 19H); ^{13}C NMR ($CDCl_3$) δ 139.60 (C), 136.65 (C), 130.31 (CH), 124.48 (CH), 46.70 (CH), 36.87 (CH_2), 34.90 (CH), 32.18 (CH_2), 28.67 (CH_2), 28.35 (CH_2), 28.07 (CH), 27.66 (CH_2), 25.58 (CH_2), 25.17 (CH_2), 24.18 (CH_2), 21.67 (CH_2); MS *m/z* 286 ($M^+ + 2$, 14%), 284 (M^+, 21%), 249 (100%), 213 (65%); HRMS calcd for $C_{16}H_{22}Cl_2$ *m/z* 284.1098, found 284.1092.

Reaction of Dimer 10 with Oxygen. Compound **10** (0.51 g, 1.79 mmol) was generated as described above and exposed to oxygen. After 7 days the mixture was purified by column chromatography (methylene chloride:hexanes = 1:1) to give 0.35 g of compound **11** (65%): IR (neat, cm^{-1}) 2940, 2865, 1690, 1440, 1260, 1080, 1020, 860, 800; ^1H NMR ($CDCl_3$) δ 2.70–2.65 (m, 1H), 2.56–2.52 (m, 1H), 2.17–1.30 (m, 20H); ^{13}C NMR ($CDCl_3$) δ 202.34 (C), 142.41 (C), 128.66 (C), 58.24 (C), 42.50 (CH_2), 32.60 (CH_2), 32.26 (CH_2), 29.95 (CH), 28.82 (CH_2), 26.94 (CH_2), 26.31 (CH_2), 24.27 (CH_2), 22.80 (CH_2); MS *m/z* 302 ($M^+ + 2$, 7%), 300 (M^+, 10%), 265 (100%), 229 (57%); HRMS calcd for $C_{16}H_{22}Cl_2O$ *m/z* 300.1048, found 300.1049.

(9) Johnson, R. P. *Chem. Rev.* **1989**, *89*, 1111.
(10) Price, J. D.; Johnson, R. P. *Tetrahedron Lett.* **1986**, *27*, 4679.

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for compounds **6**, **7**, **8**, **10**, **11**, and **12** (15 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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