Competitive Reactions between Sigmatropic Reaction and Cycloaddition Affected by the Geometry of *o*-Quinodimethanes

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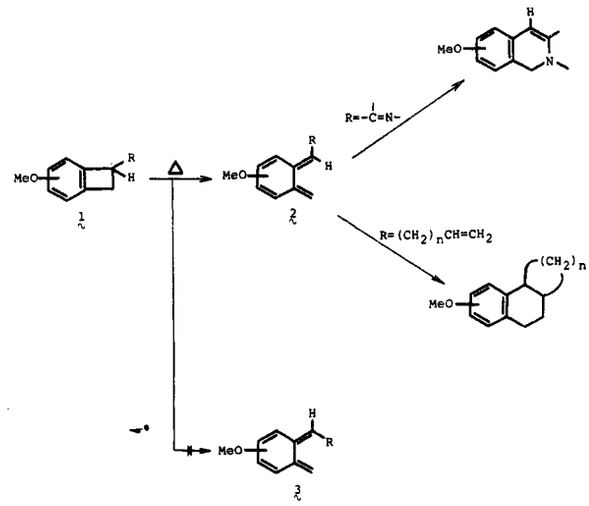
This paper describes a new type of reaction, [1,5]-sigmatropic hydrogen migration, of benzocyclobutenes, and also reports a direction of ring opening of benzocyclobutenes and a geometry of *o*-quinodimethanes.

Benzocyclobutenes (**1**)[1] are one kind of charming and effective intermediates for a construction of the natural products[2] having a complicated ring system, such as chelidonine,[3] hibaene,[4] atisine,[5] alnusenone,[6] and estrone.[7] The key reactions in these syntheses are electrocyclic reaction[8-11] and inter-[12-15] or intramolecular[3-7,16,17] cycloaddition reaction[18] between *o*-quinodimethanes (**2**), generated from benzocyclobutenes (**1**), and olefins or imines as shown in Scheme I. In some case, five-membered spiro compounds are formed[19-21] instead of an electrocyclic reaction. The intermolecular cycloaddition of *o*-quinodimethanes has been considered in terms of frontier orbital theory[22] and ease of electrocyclic ring opening of benzocyclobutenes has been related to their ^{13}C NMR chemical shifts.[23]

As benzocyclobutenes used in the above reactions have one substituent on the cyclobutene ring, *o*-quinodimethanes generated from **1** by conrotatory ring opening[18] could take an *E* form (**2**) which is thermodynamically more stable, but not a *Z* form (**3**).[9,13] Therefore, we are interested in the geometry of *o*-quinodimethanes formed from benzocyclobutenes having geminal substituents on a cyclobutene ring, and here we wish to report the structure of *o*-quinodimethanes and also the [1,5]-sigmatropic reaction of the *o*-quinodimethane system, the latter of which is a new reaction[1,24] of benzocyclobutenes.

Firstly, we reinvestigated[13] a reaction of the *o*-quinodimethane (**6**), derived from the 1-cyano-1-methylbenzocyclobutene (**5**), with maleic anhydride in order to reveal a geometry of **6**, because we must investigate which is more bulky in a stereochemical comparison of methyl and cyano groups. The starting compound **5** has been prepared by a usual methylation[19,20] of 1-cyano-5-methoxybenzocyclobutene (**4**)[11] with methyl iodide in the presence of sodium amide in liquid ammonia. Heating[5] the benzocyclobutene **5** with maleic anhydride in toluene at 240 °C for 5 h in a sealed tube gave α-(2-methyl-5-methoxyphenyl)acrylonitrile (**9**) [12% yield; *m/e* 173 (M^+); δ (CCl_4) 2.30 (3 H, s, ArMe), 5.83 (1 H, s, =CHH), and 6.07 (1 H, s, =CHH)], the tetralin-2,3-dicarboxylic acid anhydride (**7a**) [41%; *m/e* 271 (M^+); ν_{max} ($CHCl_3$) 1780 cm^{-1}; δ (CF_3CO_2H) 2.28 (3 H, s, >CMe)] and the dicarboxylic acid (**8b**) [24%; *m/e* 289 (M^+); ν_{max} ($CHCl_3$) 1715 and 1690 cm^{-1}; δ (CF_3CO_2H) 1.87 (3 H, s, >CMe)]. The stereochemistry of anhydride could be determined for the structure **7a** by NMR spectral analysis which showed that the methyl group resonated at an abnormally lower field due to a deshielding effect by the carbonyl group. On the other hand, the *C*-methyl group of the dicarboxylic acid **8b** showed a normal chemical shift, indicating the relationship of methyl group to a carboxylic function to be trans. This is supported by the fact that the dicarboxylic acid **8a**, derived from the anhydride **7a** by alkaline treatment, is a stereoisomer of **8b**. Thus, the formation of these products could be explained by a secondary orbital

Scheme I

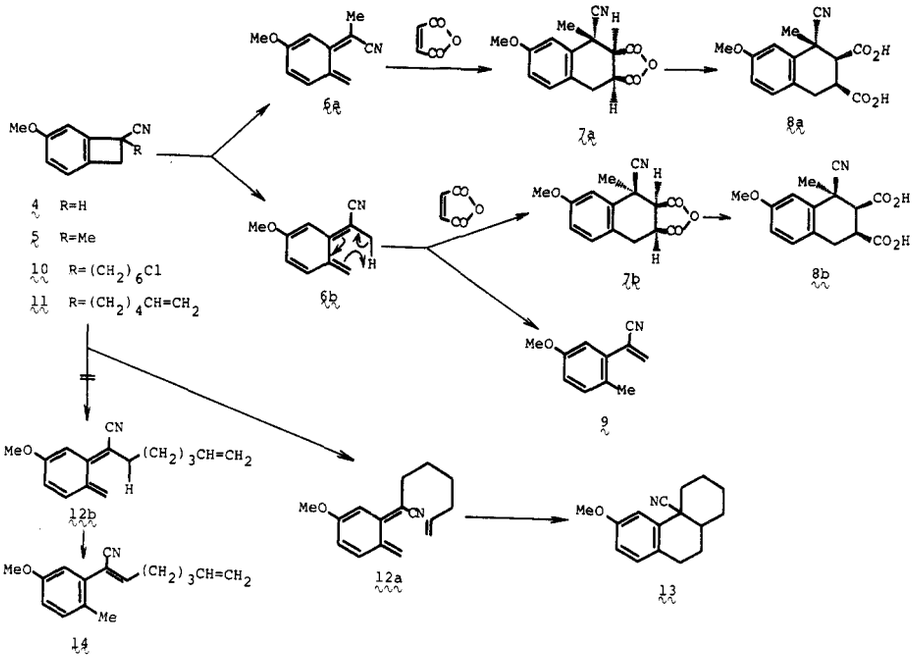


interaction in the Woodward–Hoffmann rule[18] as follows: a cycloaddition of *E* formed *o*-quinodimethane (**6b**), generated in situ from **5**, with maleic anhydride gives the dicarboxylic acid (**8b**) through the anhydride (**7b**), and the anhydride (**7a**) forms by a cycloaddition of *Z* formed *o*-quinodimethane (**6a**) with maleic anhydride. Moreover, the formation of the acrylonitrile derivative **9** is rationalized by [1,5]-sigmatropic hydrogen migration[18] of the *o*-quinodimethane **6b** but not **6a** in which the suprafacial [1,5]-hydrogen migration would not proceed from a geometrical point of view. Thus it is clear that on thermolysis of 1-cyano-1-methylbenzocyclobutene **5**, *Z* formed (**6a**) and *E* formed *o*-quinodimethanes (**6b**) are formed in almost the same ratio in a similar manner as in our previous work,[13] and then the former is transformed into the anhydride (**7a**) straightforwardly, but the latter intermediate (**6b**) results in the intermolecular cycloaddition and the [1,5]-sigmatropic rearrangement in competitive manner to form **8b** and **9**, respectively.

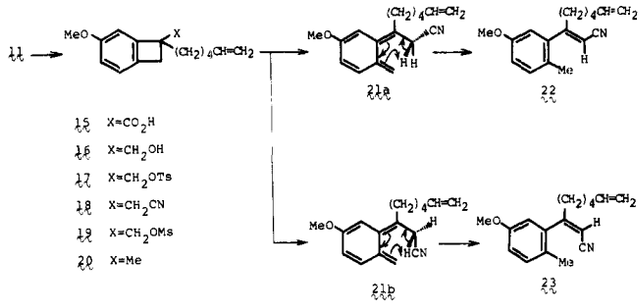
Secondly, we investigated a direction of ring opening of the benzocyclobutene (**11**), in which two substituents located at the geminal position have a different bulkiness. The starting benzocyclobutene (**11**) is synthesized as follows. Alkylation[5] of the 1-cyanobenzocyclobutene (**4**) with 6-chlorohexyl bromide in the presence of sodium amide, followed by a dehydrochlorination[5] of the resulting compound **10** with potassium *tert*-butoxide in dimethylformamide, afforded the 1,1-disubstituted benzocyclobutene **11** in 38.5% overall yield.

Thermolysis[8] of **11** was carried out in boiling *o*-dichlorobenzene for 6 h to give, in 80% yield, the cycloaddition product octahydrophenanthrene derivative (**13**), but the diolefin **14**, a [1,5]-sigmatropic hydrogen migration product, has not been

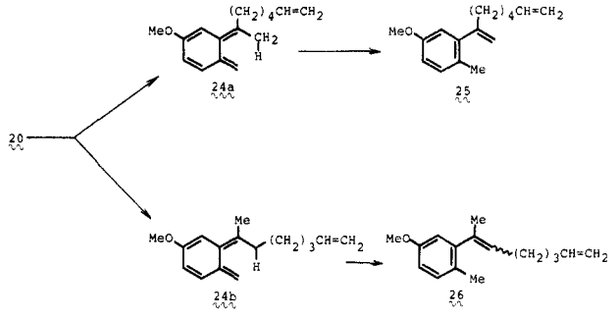
Scheme II



Scheme III



Scheme IV



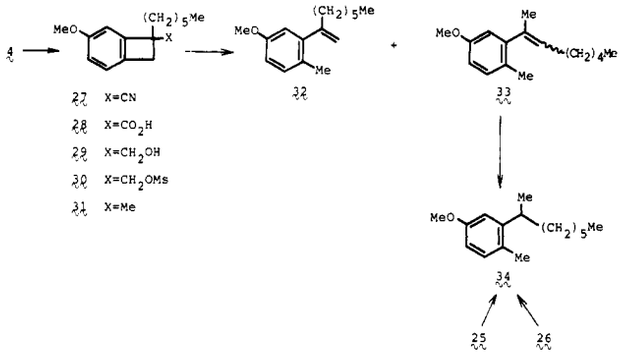
obtained. The structure of **13** was determined by its NMR spectrum showing no olefinic and methyl protons. This fact reveals that the benzocyclobutene **11** has been transformed regioselectively into the *Z*-type *o*-quinodimethane (**12a**), but not into *E*-type one (**12b**), by electrocyclic conrotatory ring opening. Thus steric effects of substituents on the cyclobutene ring fix a geometry of the *o*-quinodimethane, which determines a direction of the reaction of the intermediate. On the grounds of this finding, we are interested in investigation of a direction of ring opening of 1,1-dialkylated benzocyclobutenes (**18, 20, 31**) and of a reactivity of *o*-quinodimethanes.

Hydrolysis of the nitrile **11** with ethanolic potassium hydroxide, followed by lithium aluminum hydride reduction of the resulting carboxylic acid (**15**), afforded the alcohol (**16**), which was converted into the corresponding tosylate (**17**) with tosyl chloride in pyridine. A cyanation of **17** with sodium cyanide in dimethyl sulfoxide gave the starting 1,1-dialkylated benzocyclobutene (**18**). On the other hand, a mesylation of the alcohol (**16**) with mesyl chloride in pyridine afforded the mesylate (**19**), which on lithium aluminum hydride reduction furnished the second 1,1-dialkylated benzocyclobutene (**20**). Similarly, 1-cyano-1-*n*-hexyl-5-methoxybenzocyclobutene (**27**), which was obtained from **4** by an alkylation with *n*-hexyl bromide as usual, was converted into the 1-hexyl-1-methylbenzocyclobutene (**31**) through the carboxylic acid (**28**), the alcohol (**29**), and then the mesylate (**30**) by the same method as for a preparation of **20** as shown in Scheme V.

Heating the 1,1-dialkylated benzocyclobutene **18** in dry toluene at 250 °C for 72 h in a sealed tube gave a separable mixture of (*E*)- (**22**) [ν_{max} ($CHCl_3$) 2230 cm^{-1}; δ (CCl_4) 2.16 (3 H, s, ArMe)] and (*Z*)-styrenes (**23**) [ν_{max} ($CHCl_3$) 2230 cm^{-1}; δ (CCl_4) 2.19 (3 H, s, ArMe)] in a ratio of 3:2. The structure of both products was determined spectroscopically. The IR spectrum of both compounds showed the presence of the conjugated cyano group, and the NMR spectrum revealed the characteristic vinyl resonances in the above products. Moreover, an olefinic proton in the styrene system resonated at δ 5.36 in the major product and at δ 5.10 in the minor one. This phenomenon indicated that the major product was (*E*)-styrene **22** and the minor compound (*Z*)-styrene **23**. Therefore, a ring opening of the benzocyclobutene **18** occurred regioselectively to generate (*Z*)-*o*-quinodimethane **21**, and formation of **22** as a major product would be due to the fact that **21a** had a more stable conformation than **21b** from a stereochemical point of view.

Similarly, thermolysis of the benzocyclobutene **20** gave a mixture of the styrenes **25** and **26** via a [1,5]-sigmatropic hydrogen migration of (*E*)-*o*-quinodimethane (**24a**) and *Z* intermediate **24b**. Furthermore, the benzocyclobutene **31** was converted into a separable mixture of the styrenes **32** [δ 2.17 (3 H, s, ArMe), 4.79 (1 H, br, >CHH), and 5.07 (1 H, br, >CHH)] and **33** [δ 1.88 (3 H, s, =CMe), 2.15 (3 H, s, ArMe), and 5.23 (1 H, t, J = 7 Hz, =CH–)] in a ratio of 1:1 in 95% yield. The structure of **33** was correlated with the styrenes **25** and **26** by a conversion into the same *o*-octyltoluene **34** by the catalytic hydrogenation of these compounds **25, 26,** and **33.**

Scheme V



Thus, we could find out that the *o*-quinodimethanes derived from 1,1-dialkylated benzocyclobutenes or 1-substituted 1-methylbenzocyclobutene cause competitively sigmatropic and cycloaddition reactions depending on a geometry of *o*-quinodimethanes and also the direction of ring opening of cyclobutenes is controlled by a bulkiness of substituents.

Experimental Section

Melting points are uncorrected. NMR spectra were taken with a JNM-PMX-60 spectrometer (tetramethylsilane as an internal reference), IR spectra with a Hitachi 215 spectrophotometer, and mass spectra with a Hitachi RMU-7 spectrometer.

1-Cyano-5-methoxy-1-methylbenzocyclobutene (5). A solution of 4.77 g (30.0 mmol) of 1-cyano-5-methoxybenzocyclobutene (**4**) in 15 mL of dry tetrahydrofuran was added dropwise under stirring to a suspension of sodium amide in liquid ammonia, which was prepared as usual from 0.83 g (36.1 mmol) of sodium in 150 mL of liquid ammonia in the presence of a trace amount of ferric chloride. After 10 min, 6.40 g (44.8 mmol) of methyl iodide was added dropwise to the above mixture, which was stirred for 2 h. After addition of an excess of ammonium chloride, the liquid ammonia was evaporated. The residue was partitioned between ether and water. The ethereal solution was washed with saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate, and evaporated to give a solid, which was recrystallized from ethanol to afford 3.5 g (67.4%) of **5** as colorless needles: mp 72–74 °C; IR ($CHCl_3$) 2240 cm^{-1} (CN); NMR (CCl_4) δ 1.73 (3 H, s, CH_3), 3.13 and 3.71 (each 1 H, each d, J = 14 Hz, C_2 H_2), 3.76 (3 H, s, OCH_3), 6.77 (1 H, d, J = 2 Hz, C_6 H), 6.91 (1 H, dd, J = 2 and 5 Hz, C_4 H) and 7.04 (1 H, d, J = 5 Hz, C_3 H).

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.27; H. 6.40; N, 8.09. Found: C, 75.91; H, 6.29; N, 8.23.

Thermolysis of 1-Cyano-5-methoxy-1-methylbenzocyclobutene (5) in the Presence of Maleic Anhydride. A mixture of 500 mg (2.9 mmol) of the benzocyclobutene and 350 mg (3.6 mmol) of maleic anhydride in 35 mL of toluene was heated for 5 h at 240 °C in a sealed tube. After cooling, the solvent was evaporated to give a gummy residue, which was chromatographed on silica gel. Elution with benzene gave 60 mg (12%) of α-(5-methoxy-2-methylphenyl)-acrylonitrile (**9**) as an oil: IR ($CHCl_3$) 2250 cm^{-1} (CN); NMR (CCl_4) δ 2.30 (3 H, s, $ArCH_3$), 3.73 (3 H, s, OCH_3), 5.83 (1 H, s, >C=CHH), 6.07 (1 H, s, >C=CHH), and 6.53–7.00 (3 H, m, ArH); MS *m/e* 173 (M^+).

Further elution with benzene gave a powder, which was recrystallized from benzene–*n*-hexane to afford 300 mg (41%) of the tetralin-2,3-dicarboxylic acid anhydride (**7a**) as colorless crystals: mp 102–103 °C; IR ($CHCl_3$) 2240 (CN) and 1780 cm^{-1} (C=O); NMR ($CDCl_3$) δ 2.13 (3 H, s, CH_3), 3.80 (3 H, s, OCH_3), and 6.90–7.03 (3 H, m, 3, ArH); NMR (CF_3CO_2H) δ 2.28 (3 H, s, CH_3), 4.03 (3 H, s, OCH_3), and 7.00–7.33 (3 H, m, ArH); MS *m/e* 271 (M^+) and 173.

Anal. Calcd for $C_{15}H_{13}NO_4 \cdot 0.5H_2O$: C, 64.28; H, 5.04; N, 5.00. Found: C, 64.53; H, 4.81; N, 4.91.

Further elution with benzene–methanol (9:1 v/v) gave a powder, which was recrystallized from methanol to afford 200 mg (24%) of the dicarboxylic acid (**8b**) as colorless crystals: mp >250 °C; IR (KBr) 1715 and 1690 cm^{-1} (C=O); NMR (CF_3CO_2H) δ 1.87 (3 H, s, CH_3), 3.93 (3 H, s, OCH_3), and 6.85–7.30 (3 H, m, ArH); MS *m/e* 289 (M^+) and 173.

Anal. Calcd for $C_{15}H_{15}NO_5$: C, 62.28; H, 5.23; N, 4.84. Found: C, 61.87; H, 5.27; N, 4.62.

Hydrolysis of the Anhydride (7a). A mixture of 10 mg (0.037 mmol) of the anhydride (**7a**) in 1 mL of saturated aqueous sodium bicarbonate solution was stirred for 48 h at room temperature and then washed with ether. After acidification by addition of 10% hydrochloric acid, the resulting mixture was extracted several times with ethyl acetate. The combined extracts were washed with saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate, and evaporated. Recrystallization of the resulting powder from ethyl acetate–*n*-hexane gave 9.5 mg (88.3%) of the dicarboxylic acid (**8a**) as colorless needles: mp 175–176 °C; IR (KBr) 1720 and 1700 cm^{-1} (C=O); NMR (CF_3CO_2H) 2.13 (3 H, s, CH_3), 4.03 (3 H, s, OCH_3), and 6.96–7.10 (3 H, m, ArH); MS *m/e* 289 (M^+) and 271.

Anal. Calcd for $C_{15}H_{15}NO_5 \cdot 0.25H_2O$: C, 61.32; H, 5.31. Found: C, 61.28; H, 5.06.

1-Cyano-1-(6′-chloro-*n*-hexyl)-5-methoxybenzocyclobutene (10). A solution of 22 g (138.3 mmol) of 1-cyano-5-methoxybenzocyclobutene (**4**) and sodium amide (prepared from 3.7 g of sodium in liquid ammonia) in 1 L of liquid ammonia was stirred for 10 min at −33 °C, and then a solution of 34 g (170 mmol) of 1-bromo-6-chlorohexane in 100 mL of dry tetrahydrofuran was added dropwise.

The resulting mixture was further stirred for 6 h at −33 °C and treated with an excess of crystalline ammonium chloride and the solvent was removed to give a reddish residue, which was diluted with 100 mL of saturated aqueous ammonium chloride solution and extracted with 3 × 200 mL of ether. The organic layer was washed with 2 × 50 mL of saturated aqueous sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent gave a reddish gum, which was purified by column chromatography on 300 g of silica gel (using *n*-hexane–benzene for elution) to give 27.2 g (70%) of compound **10** as a colorless oil: IR ($CHCl_3$) 2245 cm^{-1} (CN); NMR (CCl_4) δ 1.36–2.30 (8 H, m, 4 CH_2), 3.00–3.70 (4 H, m, CH_2Cl, C_1 H_2), 3.75 (3 H, s, OCH_3), 6.83 (1 H, d, J = 2 Hz, $C_{6'}$ H), 6.96 (1 H, dd, J = 2 and 6 Hz, $C_{4'}$ H), 7.13 (1 H, d, J = 6 Hz, $C_{3'}$ H); MS *m/e* 277 (M^+); R_f 0.42 (benzene).

Anal. Calcd for $C_{16}H_{20}NOCl$: C, 69.18; H, 7.25; N, 5.04; Cl, 12.76. Found: C, 69.27; H, 7.09; N, 4.82; Cl, 12.46.

1-Cyano-1-(5′-*n*-hexenyl)-5-methoxybenzocyclobutene (11). A solution of 25 g (90 mmol) of the above chloride **10** in 50 mL of dry dimethylformamide was added dropwise to a solution of 20 g (180 mmol) of potassium *tert*-butoxide in 200 mL of dry dimethylformamide and the resulting mixture was stirred for 10 h at room temperature and poured into 500 mL of ice-cold water. The mixture was extracted with 3 × 200 mL of ether and the combined ethereal layers were washed with 2 × 100 mL of saturated aqueous sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent afforded a pale yellow oil, which was purified by column chromatography on 350 g of silica gel (using *n*-hexane–benzene for elution) to give 11.9 g (55%) of the compound **11** as a colorless oil: IR ($CHCl_3$) 2240 (CN) and 1642 cm^{-1} (C=O); NMR (CCl_4) δ 1.20–2.33 (8 H, m, 4 CH_2), 2.90 (1 H, d, J = 13 Hz, ArCHH), 3.60 (1 H, d, J = 13 Hz, ArCHH), 3.72 (3 H, s, OCH_3), 4.73–6.17 (3 H, m, $-CH{=}CH_2$), 6.68 (1 H, d, J = 2 Hz, $C_{6'}$ H), 6.86 (1 H, dd, J = 2 and 6 Hz, $C_{4'}$ H), 7.02 (1 H, d, J = 6 Hz, $C_{3'}$ H); MS *m/e* 241 (M^+).

Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.80; H, 7.80; N, 5.89.

4a-Cyano-1,2,3,4,4a,9,10,10a-octahydro-6-methoxyphenanthrene (13). A solution of 1.6 g (6.6 mmol) of the hexenylbenzocyclobutene **11** in 400 mL of *o*-dichlorobenzene was refluxed for 6 h under an atmosphere of nitrogen. After evaporation of the solvent, the residue was recrystallized from *n*-hexane to give 1.6 g (80%) of the compound **13** as colorless needles: mp 138–140 °C; IR ($CHCl_3$) 2240 cm^{-1} (CN); NMR (CCl_4) δ 3.75 (3 H, s, OCH_3), 6.70 (1 H, d, J = 2 Hz, C_5 H), 6.82 (1 H, dd, J = 2 and 4 Hz, C_7 H), 7.00 (1 H, d, J = 4 Hz, C_8 H); MS *m/e* 241 (M^+).

Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.43; H. 7.85; N, 5.48.

1-(5′-*n*-Hexenyl)-5-methoxybenzocyclobutene-1-carboxylic Acid (15). A solution containing 6 g (29.8 mmol) of the nitrile **11** and 5 g (89.2 mmol) of potassium hydroxide in 20 mL of ethanol was refluxed for 4 h. After evaporation of the ethanol, 100 mL of water was added and extracted with ether. The aqueous phase was acidified with 10% hydrochloric acid and extracted with ether. The ethereal extract was washed with saturated aqueous sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent gave a white solid, which was recrystallized from *n*-hexane to give 5.0 g (77%) of the carboxylic acid **15** as colorless prisms: mp 60–60.5 °C; IR ($CHCl_3$) 1700 cm^{-1} (C=O); NMR (CCl_4) δ 1.10–2.28 (8 H, m, 4 CH_2), 2.90 (1 H, d, J = 13 Hz, ArCHH), 3.53 (1 H, d, J = 13 Hz, ArCHH), 3.65 (3 H, s, OCH_3), 4.60–6.02 (3 H, m, $-CH{=}CH_2$), 6.48–6.94 (3 H, m, ArH), 11.45 (1 H, br s, COOH); MS *m/e* 260 (M^+).

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.94; H, 7.81.

1-(5′-*n*-Hexenyl)-1-hydroxymethyl-5-methoxybenzocyclobutene (16). To a slurry of 1.52 g (40 mmol) of lithium aluminum hydride in 30 mL of anhydrous tetrahydrofuran was added dropwise a solution of 5 g (19.2 mmol) of the carboxylic acid (**15**) in 30 mL of anhydrous tetrahydrofuran and the solution was stirred for 5 h at room temperature. After quenching with 30% aqueous sodium hydroxide solution, filtration of inorganic compound, and evaporation of tetrahydrofuran, the residue was extracted with 3 × 100 mL of ether. The ethereal extract was washed with 2 × 50 mL of saturated aqueous sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of ether afforded a colorless gum, which was purified by column chromatography on 100 g of silica gel (using benzene as eluent) to give 4.0 g (85%) of the alcohol **16** as a colorless oil: R_f 0.31 (benzene); IR ($CHCl_3$) 3600 cm^{-1} (OH); NMR (CCl_4) δ 1.10–2.33 (9 H, m, 4 CH_2 and OH), 2.78 (2 H, s, $ArCH_2$), 3.61 (2 H, s, CH_2OH), 3.67 (3 H, s, OCH_3), 4.68–6.10 (3 H, m, $-CH{=}CH_2$), 6.55 (1 H, d, J = 2 Hz, $C_{6'}$ H), 6.73 (1 H, dd, J = 2 and 8 Hz, $C_{4'}$ H), 6.92 (1 H, d, J = 8 Hz, $C_{3'}$ H); MS m/e 246 (M^+).

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.04; H, 9.02.

1-(5′-*n*-Hexenyl)-5-methoxy-1-*p*-toluenesulfonylmethylbenzocyclobutene (17). To a solution of 4 g (16.2 mmol) of the alcohol **16** in 30 mL of pyridine was added 6.1 g (32.1 mmol) of *p*-toluenesulfonyl chloride and the solution was stirred for 3 h at room temperature. The resulting mixture was poured into water and extracted with 3 × 100 mL of ether. The ethereal phase was washed with 5% hydrochloric acid, water, and saturated aqueous sodium bicarbonate solution. After drying over anhydrous sodium sulfate, the organic solvent was removed to give 6.0 g (93%) of the tosylate **17** as a yellow oil. This crude tosylate **17** was used for the next reaction without further purification because of its instability.

1-Cyanomethyl-1-(5′-*n*-hexenyl)-5-methoxybenzocyclobutene (18). A solution containing 5.7 g (14.2 mmol) of the crude tosylate **17** and 1.5 g (32.0 mmol) of sodium cyanide in 50 mL of anhydrous dimethyl sulfoxide was stirred for 60 h at room temperature. The resulting mixture was poured into water and extracted with 3 × 150 mL of ether. The ethereal phase was washed with 2 × 50 mL of water and dried over anhydrous sodium sulfate. Removal of the solvent afforded a yellow oil, which was purified by column chromatography on 150 g of silica gel (using *n*-hexane–benzene as eluent) to give 2.9 g (80%) of the nitrile **18** as a colorless oil: R_f 0.41 (benzene); IR ($CHCl_3$) 2255 cm^{-1} (CN); NMR (CCl_4) δ 1.00–2.33 (8 H, m, 4 CH_2), 2.58 (2 H, s, CH_2CN), 2.92 (2 H, s, $ArCH_2$), 3.70 (3 H, s, OCH_3), 4.70–6.13 (3 H, m, $-CH{=}CH_2$), 6.65 (1 H, d, J = 2 Hz, $C_{6'}$ H), 6.79 (1 H, dd, J = 2 and 7 Hz, $C_{4'}$ H), 6.95 (1 H, d, J = 7 Hz, $C_{3'}$ H); MS *m/e* 255 (M^+).

Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 80.34; H, 8.49; N, 5.79.

(*E*)- (22) and (*Z*)-1-Cyano-2-(5′-methoxy-2′-methyl)phenyl-1,7-octadiene (23). Thermolysis of the Nitrile. A solution of 120 mg (0.47 mmol) of the nitrile **18** in 50 mL of dry toluene was heated in a sealed tube for 72 h at 250 °C. After evaporation of the solvent, the resulting residue was purified by preparative thin layer chromatography (*n*-hexane–benzene, 30:70). The first fraction (R_f 0.53) afforded 16 mg (13%) of (*Z*)-1-cyano-2-(5′-methoxy-2′-methyl)phenyl-1,7-octadiene (**23**) as a colorless oil: IR ($CHCl_3$) 2230 cm^{-1} (CN); NMR (CCl_4) δ 1.15–2.30 (8 H, m, 4 CH_2), 2.19 (3 H, s, CH_3), 3.70 (3 H, s, OCH_3), 4.6–6.07 (3 H, m, $CH{=}CH_2$), 5.10 (1 H, s, >C=CH–), 6.50 (1 H, d, J = 2 Hz, $C_{6'}$ H) 6.67 (1 H, dd, J = 2 and 8 Hz, $C_{4'}$ H), 7.03 (1 H, d, J = 8 Hz, $C_{3'}$ H); MS *m/e* 255 (M^+).

Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 80.30; H, 8.60; N, 5.37.

The second fraction (R_f 0.34) gave 20 mg (17%) of (*E*)-1-cyano-2-(5′-methoxy-2′-methyl)phenyl-1,7-octadiene (**22**) as a colorless oil: IR ($CHCl_3$) 2230 cm^{-1} (CN); NMR (CCl_4) δ 1.20–2.60 (8 H, m, 4 CH_2), 2.16 (3 H, s, CH_3), 3.70 (3 H, s, OCH_3), 4.50–6.00 (3 H, m, $-CH{=}CH_2$), 5.36 (1 H, s, >C=CH–), 6.55 (1 H, d, J = 2 Hz, $C_{6'}$ H), 6.70 (1 H, dd, J = 2 and 8 Hz, $C_{4'}$ H), 7.12 (1 H, d, J = 8 Hz, $C_{3'}$ H); MS *m/e* 255 (M^+).

Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 80.06; H, 8.46; N, 5.22.

1-(5′-*n*-Hexenyl)-1-mesyloxymethyl-5-methoxybenzocyclobutene (19). A solution of 150 mg (0.61 mmol) of 1-(5′-*n*-hexenyl)-1-hydroxymethyl-5-methoxybenzocyclobutene (**16**) in 10 mL of pyridine was added dropwise to a solution of 200 mg (1.74 mmol) of methanesulfonyl chloride in 10 mL of pyridine and allowed to stand at room temperature for 24 h. This was poured into 50 mL of water and extracted with ether. The organic layer was washed with water, 10% hydrochloric acid, water, saturated sodium bicarbonate solution, and then water, dried over anhydrous sodium sulfate, and evaporated to give 163 mg (89.1%) of **19** as a yellow oil, which was used without purification because of its instability.

1-(5′-*n*-Hexenyl)-5-methoxy-1-methylbenzocyclobutene (20). A solution of 146 mg (0.49 mmol) of **19** in 10 mL of dry ether was added to a stirred suspension of 100 mg (2.62 mmol) of lithium aluminum hydride in 5 mL of dry ether in a nitrogen atmosphere under cooling and this was heated under reflux for 2 h. The workup as above gave 98 mg (87.58%) of **20** as a yellow oil: NMR (CCl_4) δ 1.17–1.73 (6 H, m, 3 CH_2), 1.34 (3 H, s, CH_3), 1.93–2.20 (2 H, m, $CH_2CH{=}CH_2$), 2.82 (2 H, s, $ArCH_2$), 3.67 (3 H, s, OCH_3), 4.70–5.14 (2 H, m, $-CH{=}CH_2$), 5.39–6.00 (1 H, m, $-CH{=}CH_2$), 6.49 (1 H, d, J = 1 Hz, $C_{6'}$ H), 6.55 (1 H, dd, J = 8 and 1 Hz, $C_{4'}$ H), 6.85 (1 H, d, J = 8 Hz, $C_{3'}$ H).

Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.29; H, 9.71.

Thermolysis of 1-(5′-*n*-Hexenyl)-5-methoxy-1-methylbenzocyclobutene (20). A solution of 77 mg (0.335 mmol) of **20** in 60 mL of dry toluene was heated in a sealed tube at 230 °C for 24 h. Evaporation of the solvent gave an oil, which was chromatographed on 10 g of silicic acid using *n*-hexane as eluent to afford 54 mg of a mixture of **25** and **26** [NMR (CCl_4) δ 1.87 (s, $=CCH_3$), 2.08 and 2.17 (s, $ArCH_3$)].

1-Cyano-1-*n*-hexyl-5-methoxybenzocyclobutene (27). To a stirred solution of sodium amide in liquid ammonia which was prepared from 0.52 g (22.61 mmol) of sodium, 200 mL of redistilled liquid ammonia, and a small amount of ferric chloride was added a solution of 3.0 g (18.87 mmol) of 1-cyano-5-methoxybenzocyclobutene (**4**) in 10 mL of dry tetrahydrofuran and the stirring was continued for 30 min. A solution of 3.7 g (22.42 mmol) of *n*-hexyl bromide in 5 mL of dry tetrahydrofuran was added to the above reaction mixture. After evaporation of the liquid ammonia, the residue was treated with an excess of crystalline ammonium chloride and water. The resulting mixture was extracted with 20 mL of ether and the organic layer was washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Evaporation of the solvent gave 3.8 g (82.97%) of a pale yellow oil: IR ($CHCl_3$) 2220 cm^{-1} (CN); NMR (CCl_4) δ 0.92 (3 H, br t, CH_3), 1.10–2.05 (10 H, m, 5 CH_2), 3.10 (1 H, d, J = 14 Hz, C_2 H), 3.60 (1 H, d, J = 14 Hz, C_2 H), 3.72 (3 H, s, OCH_3), 6.68 (1 H, d, J = 2 Hz, C_6 H), 6.73 (1 H, dd, J = 8 and 2 Hz, C_4 H), 6.97 (1 H, d, J = 8 Hz, C_3 H).

Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.62; H, 8.51; N, 6.11.

1-Carboxy-1-*n*-hexyl-5-methoxybenzocyclobutene (28). A solution of 4.1 g (16.87 mmol) of 1-cyano-1-*n*-hexyl-5-methoxybenzocyclobutene (**27**) and 4.0 g (71.43 mmol) of potassium hydroxide in 30 mL of water and 30 mL of ethanol was heated under reflux for 12 h. This was treated under the same manner as **15** to give 4.0 g (90.5%) of a colorless powder, which was recrystallized from *n*-hexane to give colorless prisms: mp 73–74 °C; IR ($CHCl_3$) 1695 cm^{-1} (C=O); NMR (CCl_4) δ 0.88 (3 H, br t, CH_3), 1.13–2.20 (10 H, m, 5 CH_2), 2.93 (1 H, d, J = 14 Hz, C_2 H), 3.57 (1 H, d, J = 14 Hz, C_2 H), 3.72 (3 H, s, OCH_3), 6.57–6.95 (3 H, m, ArH), 11.43 (1 H, s, CO_2H).

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.24; H, 8.31.

1-Hydroxymethyl-1-*n*-hexyl-5-methoxybenzocyclobutene (29). To a stirred suspension of 2.0 g (52.62 mmol) of lithium aluminum hydride in 100 mL of dry tetrahydrofuran was added a solution of 3.8 g (14.5 mmol) of 1-carboxy-1-*n*-hexyl-5-methoxybenzocyclobutene (**28**) in 50 mL of dry tetrahydrofuran under nitrogen and the stirring was continued for 3 h. This was treated in the same manner as **16** to give 3.2 g (88.96%) of a pale yellow oil: NMR (CCl_4) δ 0.85 (3 H, br t, CH_3), 1.10–1.90 (10 H, m, 5 CH_2), 2.50 (1 H, s, OH), 2.77 (2 H, s, $ArCH_2$), 3.60 (2 H, s, CH_2OH), 3.63 (3 H, s, OCH_3), 6.53 (1 H, d, J = 2 Hz, C_6 H), 6.58 (1 H, dd, J = 8 and 2 Hz, C_4 H), 6.84 (1 H, d, J = 8 Hz, C_3 H).

Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.37; H, 9.47. Found: C, 77.15; H, 9.69.

1-*n*-Hexyl-1-mesyloxymethyl-5-methoxybenzocyclobutene (30). A solution of 3.0 g (12.10 mmol) of 1-hydroxymethyl-1-*n*-hexyl-5-methoxybenzocyclobutene (**29**) in 20 mL of pyridine was added in small portions to a solution of 4.0 g (33.90 mmol) of methanesulfonyl chloride in 50 mL of pyridine and this was allowed to stand at room temperature under a nitrogen atmosphere for 24 h. The workup as above gave 3.2 g (88.96%) of a pale yellow oil: NMR (CCl_4) δ 0.90 (3 H, br t, CH_3), 1.13–2.07 (10 H, m, 5 CH_2), 2.83 (3 H, s, OSO_2CH_3), 2.93 (2 H, s, $ArCH_2$), 3.72 (3 H, s, OCH_3), 4.27 (2 H, s, CH_2OSO_2), 6.61 (1 H, d, J = 2 Hz, C_5 H), 6.67 (1 H, dd, J = 8 and 2 Hz, C_4 H), 6.92 (1 H, d, J = 8 Hz, C_3 H).

This was used in the following reaction without purification because of its instability.

1-*n*-Hexyl-5-methoxy-1-methylbenzocyclobutene (31). To a

stirred suspension of 2.0 g (52.63 mmol) of lithium aluminum hydride in 50 mL of dry ether was added a solution of 3.2 g (9.79 mmol) of 1-*n*-hexyl-1-mesyloxymethyl-5-methoxybenzocyclobutene (**30**) under nitrogen and this was heated under reflux for 2 h. The workup as above gave 1.5 g (66.08%) of a pale yellow oil: NMR (CCl_4) δ 0.88 [3 H, br t, $(CH_2)_5CH_3$], 1.10–1.87 (10 H, m, 5 CH_2), 1.50 (3 H, s, C_1 CH_3), 2.79 (2 H, br, $ArCH_2$), 3.69 (3 H, s, OCH_3), 6.50 (1 H, d, J = 2 Hz, C_6 H), 6.58 (1 H, dd, J = 7 and 2 Hz, C_4 H), 6.85 (1 H, d, J = 7 Hz, C_3 H).

Thermolysis of 1-*n*-Hexyl-5-methoxy-1-methylbenzocyclobutene (31). A solution of 1.0 g (4.31 mmol) of 1-*n*-hexyl-5-methoxy-1-methylbenzocyclobutene (**31**) in 50 mL of dry toluene was heated in a sealed tube for 12 h at 220 °C. The evaporation of the solvent gave 0.95 g (95.0%) of a pale yellow oil, which was chromatographed on 50 g of silicic acid using *n*-hexane as eluent. The first eluate gave 420 mg (42.0%) of 2-(5′-methoxy-2′-methylphenyl)octene-1 (**32**) as a colorless oil: NMR (CCl_4) δ 0.87 [3 H, br t, $(CH_2)_5CH_3$], 1.07–1.60 (10 H, m, 5 CH_2), 2.17 (3 H, s, $ArCH_3$), 3.69 (3 H, s, OCH_3), 4.79 (1 H, m, C=CH), 5.07 (1 H, m, C=CH), 6.46 (1 H, d, J = 2 Hz, $C_{6'}$ H), 6.58 (1 H, dd, J = 8 and 2 Hz, $C_{4'}$ H), 6.94 (1 H, d, J = 8 Hz, $C_{3'}$ H).

Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.53; H, 10.16.

The second eluate gave 410 mg (41%) of 2-(5′-methoxy-2′-methylphenyl)octene-2 (**33**) as a colorless oil: NMR (CCl_4) δ 0.93 [3 H, br t, $(CH_2)_4CH_3$], 1.17–1.63 (8 H, m, 4 CH_2), 1.88 (3 H, s, olefinic CH_3), 2.15 (3 H, s, aromatic CH_3), 3.69 (3 H, s, OCH_3), 5.23 (1 H, br t, J = 7 Hz, C=CH), 6.49 (1 H, d, J = 2 Hz, $C_{6'}$ H), 6.58 (1 H, dd, J = 9 and 2 Hz, $C_{4'}$ H), 6.93 (1 H, d, J = 9 Hz, $C_{3'}$ H).

2-(5′-Methoxy-2′-methylphenyl)octane (34). A. From the Styrene 24 and 25. A suspension of 53 mg (0.23 mmol) of a mixture of **24** and **25** and 3 mg of platinum oxide in 5 mL of ethanol was shaken in hydrogen atmosphere for 24 h. After removal of the catalyst, the ethanol was evaporated off to give an oil, which was chromatographed on 5 g of silica gel using benzene as eluent to afford 51 mg (94.6%) of **34** as a colorless oil: NMR δ (CCl_4) 2.21 (3 H, s, $ArCH_3$) 2.88 (1 H, sextet, ArCH–), 3.67 (3 H, s, OCH_3), 6.43 (1 H, dd, J = 3 and 8 Hz, $C_{4'}$ H), 6.58 (1 H, d, J = 3 Hz, $C_{6'}$ H), 6.87 (1 H, d, J = 8 Hz, $C_{3'}$ H).

B. From the Styrene 33. A suspension of 268 mg (1.155 mmol) of **33** and 10 mg of platinum oxide in 30 mL of ethanol was treated in the same way as above to give 254 mg (94.1%) of **34** as a colorless oil, whose physical data were identical with those of the sample obtained by method A.

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Nucleophilic Displacements on Halogen Atoms. 9.[1] Reactions of Triarylphosphines with Halomethylpyridyl Phenyl Sulfones

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The rates of reactions of halomethylpyridyl phenyl sulfones with triphenylphosphine have been used to determine σ^- values for the heterocyclic ring in 2-, 3- and 4-substituted pyridine derivatives, e.g., pyridines, pyridine *N*-oxides, and *N*-methylpyridinium salts.

The reactions of α-halo sulfones with tertiary phosphorus compounds (e.g., alkyl and aryl phosphines and phosphites) have been studied extensively.[1-3] These reactions occur by S_N2 displacement by the nucleophile on the halogen atom to give α-sulfonyl carbanions which are subsequently protonated by solvent to give the reduced sulfone (eq 1). The rates of these reactions were shown to be very sensitive to changes in structure in both the α-halo sulfones and in the nucleophiles.[1-4] In particular, the Hammett ρ values associated with the reactions of α-bromobenzyl and α-iodobenzyl phenyl sulfones with both triphenylphosphine[1] and sodium benzenesulfinate[4] in aqueous dimethylformamide (DMF) are