Regioselective Ring Opening in Substituted Benzocyclopropenes. An Alternative or Complementary Mechanism for Electrophilic Substitution Involving Attack at a σ Bond

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Abstract: 2-Methylbenzocyclopropene (**5**) reacts with bromine, iodine, and HCl to give the *m*-xylenes **12a,c,d** as the major products, whereas it reacts with silver nitrate in the presence of ethanol and aniline to give the *o*-xylenes **11e,f** as the major products. Similarly, 3-methylbenzocyclopropene (**10**) gives mainly *m*-xylenes **14a,c,d** with halogens and HCl and gives *p*-xylenes **13e,f** with silver nitrate and ethanol or aniline. Cyclopropa[3,4]benzocyclobutene (**15**) also gives different products with halogens and silver nitrate, but in this case HCl gives the same type of product as the silver ion. The difference in electrophilic behavior of **5**, **10**, and **15** toward the two types of reagents is suggested to arise from attack of the silver ion (and the proton in the case of **15**) on the σ electrons of the cyclopropyl ring.

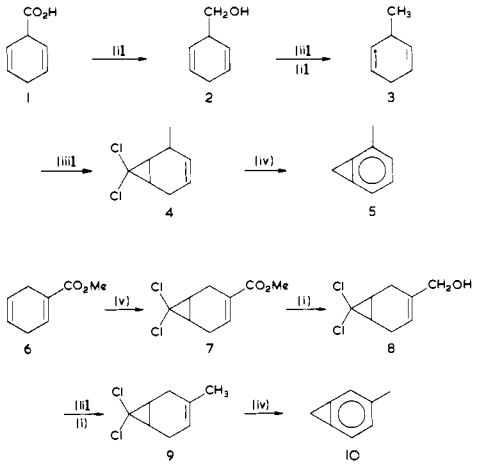
Substituted benzocyclopropenes have considerable potential both as synthetic intermediates and as model compounds for the study of the mechanism of electrophilic aromatic substitution. The three-membered ring is readily cleaved by electrophiles,[1] and if the ring opening of asymmetrically substituted benzocyclopropenes can be regiospecifically controlled, then the value of benzocyclopropenes in synthesis would be considerably enhanced. We have prepared a number of simple asymmetrically substituted benzocyclopropanes and have explored their behavior with electrophiles under a variety of conditions. We now report that the direction of ring cleavage can be controlled by the selection of the appropriate electrophile and suggest that the variation in product composition may arise because of attack on either the π- or σ-electron system.

Results

2-Methylbenzocyclopropene (**5**) and 3-methylbenzocyclopropene (**10**) were prepared by the sequence of reactions illustrated in Scheme I. 1,4-Dihydrobenzoic acid (**1**)[2] was reduced with $LiAlH_4$ to **2**,[3] which on treatment with tosyl chloride followed by $LiAlH_4$ gave **3**.[4] Reaction of **3** with $CHCl_3$ and KO-*t*-Bu gave **4** which was converted into **5** with KO-*t*-Bu in Me_2SO. Compound **5** showed all the spectroscopic properties associated with benzocyclopropenes. Methyl 2,5-dihydrobenzoate (**6**)[5] was treated with $CHCl_3$ and NaOH in the presence of benzyltriethylammonium chloride to give **7**. Compound **7** was reduced with $LiAlH_4$ to give **8**, which was then tosylated and reduced to give **9**. Reaction of **9** with KO-*t*-Bu in Me_2SO gave **10**, which again exhibited the expected spectroscopic properties of a benzocyclopropene.

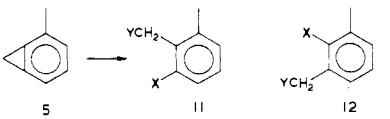
Reaction of **5** with Br_2 in CCl_4 at 15 °C gave a mixture of 2-(bromomethyl)-3-methylbromobenzene (**11a**) and 6-(bromomethyl)-2-methylbromobenzene (**12a**). These compounds could not be separated by GLC, so the mixture was treated with *n*-Bu_3SnH when a mixture of 2,3-dimethylbromobenzene (**11b**) and 2,6-dimethylbromobenzene (**12b**) was obtained which could be separated into its components. Treatment of **5** with I_2 gave a mixture of the iodides **11c** and **12c**,[6] and treatment with HCl gave

Scheme I



(i) $LiAlH_4$; (ii) TosCl; (iii) $CHCl_3$, KO-*t*-Bu; (iv) KO-*t*-Bu, Me_2SO; (v) $CHCl_3$, NaOH, Et_3BzNCl

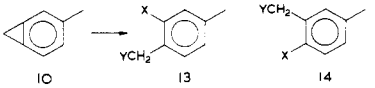
a mixture of **11d** and **12d**. A solution of **5** in CCl_4 when treated with EtOH and $AgNO_3$ gave the ethers **11e** and **12e** and with aniline and $AgNO_3$ gave a mixture of the amines **11f** and **12f** (see eq 1).



(1)

a, X = Y = Br; b, X = Br, Y = H; c, X = Y = I; d, X = H, Y = Cl; e, X = H, Y = OEt; f, X = H, Y = NHC_6H_5

The hydrocarbon **10** was reacted with the same reagents under similar conditions to give mixtures of products of type **13** and **14** (see eq 2).



(2)

a, X = Y = Br; b, X = Br, Y = H; c, X = Y = I; d, X = H, Y = Cl; e, X = H, Y = OEt; f, X = H, Y = NHC_6H_5

The mixtures were analyzed by a variety of methods. In many cases the ^1H NMR spectra of the two components were distinct so that ratios of the methyl and methylene groups could be compared by integration. The ^1H NMR spectra of these mixtures were also matched to ^1H NMR spectra of mixtures of authentic

(1) See: Halton, B. *Chem. Rev.* **1973**, *73*, 113; Billups, W. E. *Acc. Chem. Res.* **1978**, *11*, 245.
(2) Kuehne, M. E.; Lambert, B. F. *Org. Synth.* **1963**, *43*, 22.
(3) Nelson, N. A.; Fassnacht, J. H.; Piper, J. U. *J. Am. Chem. Soc.* **1961**, *83*, 210.
(4) Paquette, L. A.; Kuhla, D. E.; Barrett, J. H.; Haluska, R. J. *J. Org. Chem.* **1969**, *34*, 2866.
(5) Petrov, A. A.; Rall, K. B. *J. Gen. Chem. USSR (Engl. Transl.)* **1956**, *26*, 1779.
(6) No diiodoheptatriene was observed in this reaction unlike that of the parent benzocyclopropene with I_2 (Vogel, E.; Grimme, W.; Korte, S. *Tetrahedron Lett.* **1965**, 3625), but this may have been due to our method of isolation.

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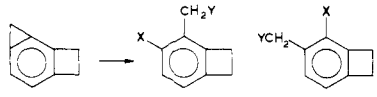
Table I

substrate	reagent	anal. method	products, % proportion (% error)[a]	isolated yield, %
5	Br_2	^{1}H NMR	11a, 40 (±5); 12a, 60 (±5)	70
		GLC	11b, 42 (±3); 12b, 58 (±3)	
	I_2	^{1}H NMR	11c, 45 (±2); 12c, 55 (±2)	77
	HCl	^{1}H NMR	11d, 15 (±2); 12d, 85 (±2)	55
	$AgNO_3$, EtOH	^{1}H NMR	11e, 72 (±2); 12e, 28 (±2)	65
	$AgNO_3$, $C_6H_5NH_2$	LC	11f, 93 (±2); 12f, 7 (±2)	54
10	Br_2		13a; 14a	65
		GLC	13b, 13 (±2); 14b 87 (±2)	
	I_2	^{1}H NMR	13c, 42 (±3); 14c, 58 (±3)	78
	HCl	GLC	13e, 24 (±2); 14e, 76 (±2)	77
	$AgNO_3$, EtOH	GLC	13e, 76 (±3); 14e, 24 (±3)	69
	$AgNO_3$, $C_6H_5NH_2$	LC	13f, 53 (±4); 14f, 47 (±4)	58

[a] At least two experiments were carried out in each case, and the proportion of isomers, within the limits of analysis, was within ±3%.

compounds, the authentic compounds having been obtained commercially or prepared by conventional methods. In selected cases the components of the mixture were also separated by GLC or LC and the peak areas compared by integration. In the case of **11a** and **12a** the mixture was converted to **11b** and **12b** and the product composition of this mixture determined by both GLC and ^{1}H NMR, the results being both internally consistent and consistent with the composition obtained for **11a** and **12a**. The composition of the product mixtures, the methods of analysis, the estimated reliability, and the isolated yields are given in Table I and further details are in the Experimental Section.

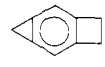
We also investigated the reaction of cyclopropa[3,4]benzocyclobutene (**15**)[7] with electrophiles. Again, two possible products can be formed depending on which of the cyclopropyl bonds is cleaved. In this case we found that I_2 gave predominately, and Br_2 exclusively, products of type **16** whereas HCl and $AgNO_3$ in EtOH gave exclusively products of type **17** (see eq 3).



15 16 17 (3)

16a, X = Y = I; 16b, X = Y = Br; 16c, X = Y = H

17a, X = Y = I; 17b, X = H, Y = Cl; 17c, X = H, Y = OEt; 17d, X = Y = H



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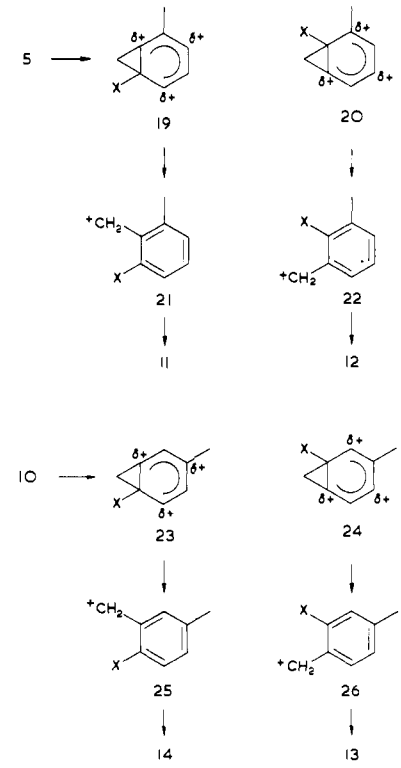
The structure of the diodide **16a** was determined by treatment with *n*-Bu_3SnH in boiling benzene to give 3-methylbenzocyclobutene (**16c**).[7] The ^{1}H NMR spectrum was consistent with this structure and different from that reported for 4-methylbenzocyclobutene (**17d**).[8] About 5% of the isomeric diiodide **17a** was detected in the ^{1}H NMR spectrum of the diiodide **16a**. Bromide **16b** was assigned this structure on the basis of a comparison of its spectral data with that for **16a**. The product from the reaction of **15** with HCl was in all observed respects identical with the sample obtained from the reaction of cyclopropa[4,5]benzocyclobutene (**18**)[7,9] with HCl. The chloride **17b** and ether **17c** were correlated by conversion of the former into the latter. All of the reactions of **15** were carried out on a small scale, but conversions were high. The detection of the diodide **17a** indicates that ca. 5–10% of a minor isomer would have been detected.

Scheme II



Discussion

As shown in Table I the reactions of **5** and **10** with Br_2, I_2, and HCl favor one type of isomer whereas $AgNO_3$ in the presence of ethanol or aniline favors the other. The major isomer obtained in the reaction of **5** and **10** with the halogens and HCl is that expected from a comparison of the relative stabilities of the two possible Wheland intermediates (Scheme II). Thus electrophilic addition to **5** can give either **19** or **20**, and in the latter ion there is a canonical form in which the positive charge is situated on the carbon bearing the methyl group whereas in the former there is not. If this is the product-determining step then compounds **12a,c,d** should predominate over **11a,c,d**. A similar analysis applied to electrophilic addition to **10** predicts that **14a,c,d** should predominate over **13a,c,d**. The regioselectivity observed with these reagents is small by comparison with that found for the electrophilic substitution of toluene.[10] This may indicate that the process is partially concerted, concommitant ring cleavage providing the benzyl cation as a good leaving group.[12] The relatively poor discrimination also implies that rapid equilibrium between the ipso positions does not occur in this system.[12,13] It should also be noted that the benzyl cations show the inverse stability to the Wheland intermediates, the benzylic cation **21**, derived from **19**, being more stable than **22**, derived from **20**. Exactly similar arguments apply to the Wheland intermediates **23** and **24** and their associated benzylic ions **25** and **26**, resulting from the reaction of **10** with halogens or HCl.

Electrophilic addition mediated by the silver ion gives opposite results and clearly the Wheland intermediate cannot be product

(7) Davalian, D.; Garratt, P. J.; Mansuri, M. M. *J. Am. Chem. Soc.* **1978**, *100*, 980. Davalian, D.; Garratt, P. J.; Koller, W.; Mansuri, M. M. *J. Org. Chem.*, in press.

(8) Garrett, J. M.; Fonken, G. J. *Tetrahedron Lett.* **1969**, *191*.

(9) Davalian, D.; Garratt, P. J. *J. Am. Chem. Soc.* **1975**, *97*, 6883. Saward, C. J.; Vollhardt, K. P. C. *Tetrahedron Lett.* **1975**, 4539.

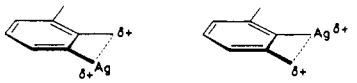
(10) See: Taylor, R. *Compr. Chem. Kinet.* **1972**, *13*, 33.

(11) Eaborn, C.; Waters, J. A. *J. Chem. Soc.* **1961**, 542. Bott, R. W.; Eaborn, C.; Waters, J. A. *Ibid.* **1963**, 681. Leaving group participation is equivalent to the involvement of the σ electrons in the transition state (vide infra).

(12) See: Hahn, R. C.; Shosenji, H.; Strack, D. L. *ACS Symp. Ser.* **1975**, No. *22*, 99.

(13) A low discrimination was also observed in the reaction of 3-chlorobenzocyclopropene with HCl: Garratt, P. J.; Koller W. *Tetrahedron Lett.* **1976**, 4177.

controlling. Silver ions are known to interact with strained cyclopropane rings,[14] and if the silver ion attacks the σ electrons of the cyclopropyl ring rather than the π system then two possible intermediates can be formed, **27** and **28**. These intermediates



27 28

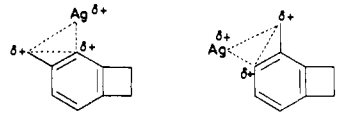
are shown with the silver ion bonded to the ring and only partially bonded to the potential benzylic carbon atom. The stabilities of **27** and **28** will probably parallel the benzylic cation stability, **27** being more stable than **28**. This assumes that the benzylic carbon atom is at least partially conjugated with the π system, which requires some rotation of the benzylic carbon atom for the orbitals to become nonorthogonal. Although the silver ion is attached by an orbital orthogonal to the π system, if any charge is relayed from it through the π system, this effect would also favor **27** over **28**. The low discrimination exhibited by **10** to attack by the silver ion in the presence of aniline is difficult to understand. There would appear to be no difference between the two silver–cyclopropene intermediates (whereas **27** would appear sterically preferred to **28**), and it may be that the more reactive nucleophile attacks the intermediate before the benzylic charge has greatly developed, thus reducing discrimination.

The reaction of **15** with halogens presumably proceeds by attack on the π electrons to give the intermediate in which the positive charge is located at the α position to the four-membered ring. Electrophilic substitution of benzocyclobutene and biphenylene occurs at the β position because of charge stabilization at the α position in the intermediate cation. This has found a statisfying explanation in the rehybridization of the σ framework which occurs in these molecules because of the bond angle requirements of the small ring.[15] The ^{13}C NMR spectrum of **15** shows the C-3 carbon at significantly higher field than that at C-4, indicating that the former carbon should more readily stabilize the positive charge. Following this argument, **29** should be preferred to **30**.

29 30

The benzylic cations resulting from the cleavage of **29** and **30** are equivalently substituted and consequently should not influence the product composition. This may in part explain the greater regioselectivity of the reactions of **15** compared to those of **5** and **10**.

If the reaction of **15** with silver ions proceeds through the cyclopropyl σ electrons, then **31** should be preferred to **32**. In



31 32

31 the positive charge is located at the α-carbon atom, albeit in this case in an orbital orthogonal to the π system, and the greater s character of the orbital should accommodate the charge better than the orbital on **32**. The benzylic cations are again both equivalently substituted.

The reaction of HCl with **15** gives the same type of product as for the silver mediated reaction and is not in accord with our findings for **5** and **10**. Presumably this reaction now proceeds by attack on the σ framework, but why this change in the mode of reaction should have occurred is not clear. Certainly **15** is much more strained than either **5** or **10**, and this strain appears to be concentrated more in the σ framework than in the π electrons if the normality of the electronic spectrum of **15** is a valid guide.[7] Presumably the reactivity of the cyclopropane ring toward protons is now greater than that of the π system. It is possible that the minor isomer from iodination of **15** also arises from the σ route rather than via **30**, and the σ route may also contribute to the minor isomers found when **5** and **10** react with halogens and HCl.

The studies suggest that, by a choice of suitably substituted benzocyclopropenes, considerable insight into the mechanism of electrophilic substitution may be obtained, in particular with regard to ipso attack and leaving group participation. The ring cleavage of complex benzocyclopropenes would appear to be capable of regioselective control. We are continuing our investigation in both of these areas.

Experimental Section

^1H NMR spectra were obtained on either a Varian T-60 or HA-100 spectrometer and are reported in δ units, using Me_4Si as internal standard. The areas of relevant signals were measured by electronic integration and by planimetry. Mass spectra were taken on an AEI MS-12 or MS-9 spectrometer. Gas liquid chromatography was carried out on a Varian Model 920 chromatogram, peak areas were measured by planimetry, and authentic samples were used as standards. High pressure liquid chromatography was carried out with a Waters ALC 100 chromatogram. Silica for preparative TLC was Merck Kieselgel PF_{254}. Solvents were purified by standard methods.

7,7-Dichloro-2-methylbicyclo[4.1.0]hept-3-ene (4). Dry, alcohol-free $CHCl_3$ (16.1 g, 0.14 mol) was added to a stirred solution of 1,4-dihydrotoluene (**3**)[4] (2.12 g, 0.02 mol) in dry pentane (300 cm^3) under N_2 at −20 °C. KO-*t*-Bu (10.1 g, 0.09 mol) was then added and the mixture stirred at −20 °C for 2 h. The mixture was allowed to warm to room temperature and was stirred for a further 14 h. The mixture was poured into water (200 cm^3) and the organic layer separated, washed with water (2 × 200 cm^3), and dried ($MgSO_4$). Removal of the solvent gave a yellow liquid which on PTLC (silica, pentane:ether 4:1) gave **4** as a pale yellow liquid (1.41 g, 40%): mass spectrum, *m/e* 176.0159 ($C_8H_{10}{}^{35}Cl_2$ requires 176.0160) 180, 178, 176 (M^+, 1:6:9, 100%), 143, 141 ($M^+ - Cl$, 1:3, 90%), 106 ($M^+ - Cl_2$, 50%); ^1H NMR δ 5.40 (b s, 2 H), 2.50–2.10 (m, 3 H), 1.36–1.07 (m, 5 H).

2-Methylbenzocyclopropene (5). Compoumd **4** (360 mg, 2.0 mmol) in dry Me_2SO (5 cm^3) was added over 5 min to a stirred solution of KO-*t*-Bu (850 mg, 7.6 mmol) in dry Me_2SO (6 cm^3) under N_2. The dark reaction mixture was stirred for 30 min and the volatile material then removed by bulb-to-bulb distillation under low pressure (0.05mmHg) at room temperature. The distillate was extracted with CCl_4 (15 cm^3) and the organic layer washed with water (8 × 10 cm^3) and dried (Na_2SO_4). The solvent was removed by distillation under reduced pressure (room temperature, 40mmHg) to give **5** (56 mg, 27%) as a pale yellow oil (the yield varied from 20–48%): mass spectrum, *m/e* 104.0574 (C_8H_8 requires 104.0626), 105 ($M^+ + 1$, 100%), 104 (M^+, 30%), 103 ($M^+ - 1$, 20%); ^1H NMR δ 7.08–6.80 (m, 3 H), 3.06 (s, 2 H), 2.34 (s, 3 H); γ_{max} (liquid film) 2960, 2860, 1680, 1620, 1470, 1360, 1260, 1090, 1015, 785, and 760 cm^{-1}; λ_{max} (cyclohexane) 255 nm (ϵ 1655), 263 (1665), 276 (1355).

Methyl 7,7-Dichlorobicyclo[4.1.0]hept-3-ene-3-carboxylate (7). A chilled solution of NaOH (50%, 160 cm^3) was added to a stirred solution of methyl 2,5-dihydrobenzoate (**6**)[5] (15.9 g, 0.12 mol) and $C_6H_5CH_2Et_3NCl$ (1.27 g, 5.6 mmol) in alcohol-free $CHCl_3$ (68.0 g, 0.57 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 14 h. Water (500 cm^3) was added, the mixture was extracted with ether (4 × 250 cm^3), and the combined organic layers were washed (HCl, 5%, 2 × 30 cm^3) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue distilled to give **7** and 1-carbomethoxy-4,4,8,8-tetrachlorotricyclo[5.1.0.$0^{3,5}$]octane. Compound **7**: pale yellow oil (14.57 g, 55%), bp 86–88 °C (0.05mmHg); mass spectrum, *m/e* 220.0056 ($C_9H_{10}O_2{}^{35}Cl_2$ requires 220.0058), 224, 222, 220 (M^+, 1:6:9, 100%), 193, 191, 189 ($M^+ - OCH_3$, 1:6:9, 56%), 165, 163, 161 ($M^+ - CH_3CO_2$, 1:6:9, 89%); ^1H NMR δ 7.00–6.66 (bs, 1 H), 3.73 (s, 3 H), 2.76–2.33 (m, 4 H), 2.00–1.69 (m, 2 H). **1-Carbomethoxy-4,4,8,8-tetrachlorotricyclo[5.1.0.$0^{3,5}$]octane**: colorless oil (8.92 g, 24%), bp 97 °C (0.1mmHg); isomeric mixture (5.5:1); *m/e* 301.9435 ($C_{10}H_{10}O_2{}^{35}Cl_4$ requires 301.9435) 310, 308, 306, 302 (M^+, 1:12:55:114:87, 100%), 273, 271, 269, 267 ($M^+ - Cl$, 1:9:28:28, 76%), 236, 234, 232 ($M^+ - Cl_2$, 1:6:9, 69%); ^1H NMR δ 3.90 (s, 0.5 H), 3.76 (s, 2.5 H), 2.59–2.03 (m, 5 H), 1.86–1.53 (m, 2 H).

7,7-Dichloro-3-hydroxymethyl[4.1.0]hept-3-ene (8). The ester **7** (14.57 g, 0.07 mol) in dry ether (200 cm^3) was added dropwise to a stirred slurry of $LiAlH_4$ (26.6 g, 0.70 mol) in dry ether (1000 cm^3) at 0 °C under N_2.

(14) See: Beverivizk, C. D. M.; Van der Kerk, G. J. M.; Lensink, A. J.; Noltes, J. G. *Organomet. Chem. Rev., Sect. A* **1970**, 5, 218; Paquette, L. A. *Acc. Chem. Res.* **1971**, *4*, 280.

(15) Finnegan, R. A. *J. Org. Chem.* **1965**, *30*, 1333. Streitwieser, A.; Ziegler, G. R.; Mowery, P. C.; Lewis, A.; Lawler, R. G., *J. Am. Chem. Soc.* **1968**, *90*, 1357.

The mixture was allowed to come to room temperature and was stirred for 14 h. Excess $LiAlH_4$ was destroyed by the addition of water (51 cm^3) and then concentrated HCl (63 cm^3). The mixture was filtered, the filtrate was extracted with ether (2 × 250 cm^3), and the ethereal extracts were dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue distilled to give **8** (7.53 g, 56%), colorless oil: bp 99–103 °C (0.05 mmHg); mass spectrum, *m/e* 192.0108 ($C_8H_{10}O^{35}Cl_2$ requires 192.0109) 196, 194, 192 (M^+, 1:6:9, 39%), 178, 176, 174 ($M - H_2O$, 1:6:9, 13%), 141, 139 ($M^+ - H_2ClO$, 1:3, 100%); ^1H NMR δ 5.43 (bs, 1 H), 3.86 (bs, 2 H), 2.56–2.17 (m, 5 H), 2.00–1.66 (m, 2 H); γ_{max} (film) 3370 cm^{-1}.

7,7-Dichloro-3-methylbicyclo[4.1.0]hept-3-ene (9). *p*-Toluenesulfonyl chloride (10.9 g, 0.06 mol) was added to a stirred solution of **8** (7.53 g, 0.04 mol) and dry Et_3N (10.9 g, 0.06 mol) in CH_2Cl_2 (200 cm^3) at 0 °C under N_2. The mixture was stirred at 0 °C for 4 h and then allowed to stand at 5 °C for 14 h. Water (200 cm^3) was then added and the organic layer separated, washed with cold HCl (10%, 500 cm^3), saturated Na_2CO_3 solution (100 cm^3), and water (2 × 200 cm^3), and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave the tosylate as a yellow oil (10.0 g, 72%) which was used without further purification. The tosylate (10.0 g, 0.03 mol) in dry ether (100 cm^3) was added dropwise to a rapidly stirred slurry of $LiAlH_4$ (4.6 g, 0.12 mol) in dry ether (1000 cm^3) under N_2. The mixture was heated to reflux for 14 h and was then cooled in an icebath. Water (25 cm^3), NaOH solution (30%, 25 cm^3), and water (75 cm^3) were added. The inorganic salts were removed by filtration, the precipitate was washed with ether (2 × 100 cm^3), and the combined filtrate and washings were dried ($MgSO_4$). The solvent was removed and the residue distilled to give **9** as a colorless liquid (1.91 g, 36% from tosylate): bp 45–55 °C (0.5mmHg); mass spectrum, *m/e* 176.0159 ($C_8H_{10}{}^{35}Cl_2$ requires 176.0160) 180, 178, 176 (M^+, 1:6:9, 22%), 143, 141 ($M^+ - Cl$, 1:3, 100%), 106 ($M^+ - Cl_2$, 50%); ^1H NMR δ 5.17 (bs, 1 H), 2.56–1.92 (m, 4 H), 1.86–1.59 (m, 5 H).

3-Methylbenzocyclopropene. The dichloride **9** (200 mg, 1.10 mmol) in dry Me_2SO (5 cm^3) was added over 5 min to a stirred solution of freshly sublimed KO-*t*-Bu (510 mg, 4.50 mmol) in dry Me_2SO (6 cm^3) under N_2. The reaction mixture was stirred at room temperature for 2 h and the volatile material removed by bulb-to-bulb distillation at 0.1 mm. CCl_4 (5 cm^3) was added to the distillate and the organic layer separated, washed with water (6 × 10 cm^3), and dried ($NaSO_4$). The solvent was removed under reduced pressure (40–50 m) to leave **10** as a pale yellow oil (60 mg, 52%): mass spectrum, *m/e* 104.0621 (C_8H_8 requires 104.0626), 105 (M + 1, 100%), 104 (M^+, 22%), 103 ($M^+ - 1$, 20%); ^1H NMR δ 7.14–6.88 (m, 3 H), 3.18 (s, 2 H), 2.38 (s, 3 H); γ_{max} (film) 2940, 2860, 1660, 1465, 1260, 1085, 1055, 1010, 870, 800, and 785 cm^{-1}; λ_{max} (cyclohexane) 270 nm (ϵ 780), 277 (960), 284 (850).

Reaction of 5 with Bromine. A solution of Br_2 (286 mg, 1.79 mmol) in dry CCl_4 (10 cm^3) was added to a stirred solution of **5** (56 mg, 0.54 mmol) in CCl_4 (15 cm^3) at −10 °C under N_2. The reaction was stirred at −10 °C for 30 min and allowed to warm to room temperature, and the solvent was removed under reduced pressure to give a mixture of **11a** and **12a** as a yellow oil (100 mg, 70%): mass spectrum, *m/e* 261.9106 ($C_8H_8{}^{79}Br_2$ requires 261.8994); ^1H NMR δ 7.44–6.88 (m, 3 H), 4.61 (s, 0.68 H), 4.56 (s, 1.32 H), 2.45 (s, 1.17 H), 2.42 (s, 1.83 H).

Reduction of the Mixture of 11a and 12a. Freshly prepared *n*-Bu_3SnH (442 mg, 1.52 mmol) was added to the mixture of **11a** and **12a** (70 mg, 0.27 mmol), and the reaction mixture was stirred for 24 h under N_2. PTLC (silica, pentane) gave a mixture of **11a** and **12b** (20 mg, 40%). The compounds were separated by GLC (140 °C, 6 ft × $^1/_8$ in., 5% benton 34 + 5% diisodecyl phthalate) as **11b** (42 ± 3%) and **12b** (58 ± 3%). An authentic mixture of **11b** and **12b** of the composition (39:61) had a ^1H NMR spectrum identical with that of the mixture obtained.

Reaction of 5 with Iodine. A solution of iodine (89 mg, 0.35 mmol) in dry CCl_4 (20 cm^3) was added dropwise to a stirred solution of **5** (30 mg, 0.29 mmol) in CCl_4 at 0 °C. The solution was then stirred at room temperature for 1 h, the solvent removed under reduced pressure, and the residue separated by PTLC (silica, CH_2Cl_2) to give a mixture of **11c** and **12c** as a yellow oil (80.0 mg, 77%): mass spectrum, *m/e* 357.8440 ($C_8H_8I_2$ requires 357.8719); ^1H NMR δ 7.06–7.24 (m, 3 H), 4.59 (s, 0.90 H), 4.57 (s, 1.10 H), 2.44 (s, 0.89 H), 2.40 (s, 1.11 H).

Reaction of 5 with HCl. A solution of **5** (32 mg, 0.31 mmol) in CCl_4 (15 cm^3) was added to a saturated solution of HCl in CCl_4 (10 cm^3). The solution was stirred for 1 h and then washed with water (4 × 20 cm^3) and dried ($MgSO_4$). The solvent was removed under reduced pressure to give a mixture of **11a** and **12d** (24.0 mg, 55%): ^1H NMR δ 7.26–6.90 (m, 4 H), 4.50 (s, 0.32 H), 4.46 (s, 1.68 H), 2.41 (s, 0.28 H), 2.15 (s, 1.72 H).

Reaction of 5 with $AgNO_3$ in the Presence of Ethanol. A solution of **5** (30 mg, 0.29 mol) in CCl_4 (5 cm^3) was added to a stirred solution of $AgNO_3$ (9 mg, 0.05 mmol) in dry EtOH (18 cm^3) under N_2. The mixture was stirred for 30 min and the solvent removed under reduced pressure. Ether (20 cm^3) was added to the residue, and the ethereal layer was washed with water (2 × 20 cm^3) and dried ($NaSO_4$). Removal of the solvent and PTLC (silica, pentane) of the residue gave a mixture of **11e** and **12e** (28.3 mg 65%): mass spectrum, *m/e* 150.1040 ($C_{10}H_{14}O$ requires 150.1045); ^1H NMR δ 7.28–7.00 (m, 4 H), 4.40 (s, 1.40 H), 4.37 (s, 0.60 H), 3.56–3.33 (m, 2 H), 2.34 (s, 0.87 H), 2.29 (s, 2.13 H), 1.28–1.14 (m, 3 H).

Preparation of α-Ethoxy-*o*-xylene (11e) from α-Chloro-*o*-xylene. Sodium ethoxide (2.7 g, 0.04 mol) was added to α-chloro-*o*-xylene (2.8 g, 0.02 mol) in dry EtOH (10 cm^3) at 0 °C, and the reaction mixture was then stirred at room temperature for 14 h. The solvent was removed by reduced pressure, ether (50 cm^3) and water (20 cm^3) were added, the ethereal layer was separated, washed with water (20 c^3), and dried ($CaCl_2$), and the solvent was removed under reduced pressure. The residue gave on PTLC (silica, pentane:ether, 95:5) α-ethoxy-*o*-xylene (**11e**) as a pale yellow oil (2.7 g, 90%): mass spectrum, *m/e* 105.1018 ($C_{10}H_{14}O$ requires 105.1045); ^1H NMR δ 7.33–6.96 (m, 4 H), 4.40 (s, 2 H), 3.63–3.30 (q, 2 H), 2.60 (s, 3 H), 1.30–1.10 (t, 3 H).

Preparation of α-Ethoxy-*m*-xylene (12e) from α-Chloro-*m*-xylene. The reaction was carried out as for **11e** to give **12e** (85%): mass spectrum, *m/e* 105.1037 ($C_{10}H_{14}O$ requires 150.1045); ^1H NMR δ 7.13–6.79 (m, 4 H), 4.33 (s, 2 H), 3.59–3.26 (q, 2 H), 2.33 (s, 3 H), 1.60–1.07 (t, 3 H).

Reaction of 5 with $AgNO_3$ in the Presence of Aniline. Compound **5** (30 mg, 0.29 mmol) in dry CCl_4 (5 cm^3) was added dropwise to a stirred solution of redistilled aniline (400 mg, 4.0 mmol) and $AgNO_3$ (30 mg, 0.18 mmol) in dry CCl_4 (5 cm^3). The reaction mixture was stirred for 30 min, then washed with water (2 × 10 cm^3), and dried ($NaSO_4$). The solvent was removed under reduced pressure to give an oil which on PTLC (silica, pentane:Et_2O, 9:1) gave a mixture of **11f** and **12f** (31 mg, 54%): mass spectrum, *m/e* 197.1204 ($C_{14}H_{15}N$ requires 197.1204); ^1H NMR δ 7.20–6.33 (m, 9 H), 4.13 (s, 2 H), 3.73–3.43 (bs. 1 H), 2.30 (s, 3 H). The products were separated by LC (250 mm × $^1/_4$ in., partisil-10) as **11f** (93 ± 2%) and **12f** (7 ± 2%).

Reaction of 10 with bromine was carried out as for **5** above to give a mixture of **13a** and **14a** (65%): mass spectrum, *m/e* 261.9002 ($C_8H_8{}^{79}Br_2$ requires 261.8994); ^1H NMR δ 7.56–6.82 (m, 3 H), 4.50, 4.47 (s, s, 2 H), 2.28 (s, 3 H).

Reduction of 13a, 14a with *n*-Bu_3SnH was carried out as for **5** above to give a mixture of **13b** and **14b** (43%); GLC separation gave **13b** (13 ± 2%) and **14b** (87 ± 2%). An authentic mixture of **13b** and **14b** of the composition (13:87) had a ^1H NMR spectrum identical with that of the mixture.

Reaction of 10 with iodine was carried out as for **5** to give a mixture of **13c** and **14d** (78%): mass spectrum, *m/e* 357.8645 ($C_8H_8I_2$ requires 357.8719); ^1H NMR δ 7.66–6.58 (m, 3 H), 4.45 (s, 0.8 H), 4.43 (s, 1.16 H), 2.28 (s, 3 H).

Reaction of 10 with HCl was carried out as for **5** to give a mixture of **13d** and **14c** (77%): ^1H NMR δ 7.25–6.92 (m, 4 H), 4.40 (s, 2 H), 2.28 (s, 3 H). The products were separated by GLC (80 °C, 6 ft × $^1/_8$ in., 5% bentone 34 + 5% diisodecyl phthalate) to give **13d** (24 ± 2%) and **14d** (76 ± 2%).

Reaction of 10 with $AgNO_3$ in the presence of ethanol was carried out as for **5** to give a mixture of **13e** and **14e** (69%): mass spectrum, *m/e* 105.1044 ($C_{10}H_{14}O$ requires 150.1045); ^1H NMR δ 7.30–6.80 (m, 4 H), 4.36 (s, 2 H), 3.56–3.30 (m, 2 H), 2.32 (s, 3 H), 1.30–1.10 (m, 3 H). The products were separated by GLC (100 °C, 6 ft × $^1/_8$ in., 5% bentone 34 + 5% diisodecyl phthalate) to give **13e** (76 ± 3%) and **14e** (24 ± 3%).

Preparation of α-Ethoxy-*p*-xylene (13e) from α-Chloro-*p*-xylene. The reaction was carried out as for **11e** to give **13e** (90%): mass spectrum, *m/e* 150.1040 ($C_{10}H_{14}O$ requires 150.1045); ^1H NMR δ 7.23–6.86 (s, 4 H), 4.33 (s, 2 H), 3.56–3.23 (q, 2 H), 2.30 (s, 3 H), 1.26–1.03 (t, 3 H).

Reaction of 10 with $AgNO_3$ in the presence of aniline was carried out as for **5** to give a mixture of **13f** and **14f** (58%): mass spectrum, *m/e* 197.1205 ($C_{14}H_{15}N$ requires 197.1204); ^1H NMR δ 7.96–6.33 (m, 9 H), 4.20 (s, 2 H), 3.83–3.59 (bs, 1 H), 2.33 (s, 3 H). The products were separated by LC (250 mm × $^1/_4$ in., partisil-10) to give **13f** (53 ± 4%) and **14f** (47 ± 4%).

Preparation of 17c from 17b was carried out as for **11e** to give **17c** (80%); mass spectrum and ^1H NMR spectra identical with those of the sample prepared by reaction of **15** with $AgNO_3$ and EtOH.

Acknowledgment. We thank the Science Research Council (U.K.) for support and Professor J. H. Ridd for valuable discussions.