Electrophilic Approach on Norbornene Systems. Preferential Endo Attack of Halogens on Hindered 2-Phenylnorbornenes

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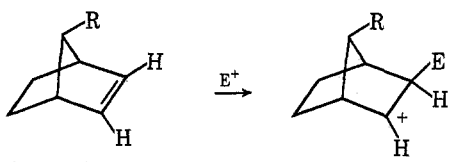
The results from the electrophilic addition of bromine to *anti*-7-bromo-5-phenylbenzonorbornadiene (**3**) and *syn*-7-bromo-2-phenylnorbornene (**2**) suggest that initial approach of the bulky electrophile to these hindered systems is endo. This is in contrast to typical stepwise electrophilic additions to hindered norbornene systems without the phenyl group where exo attack is usually observed. The observations are interpreted to indicate that some stereoelectronic factor must be operating, at least in part, in controlling the preference for exo approach of an electrophile to a norbornene system.

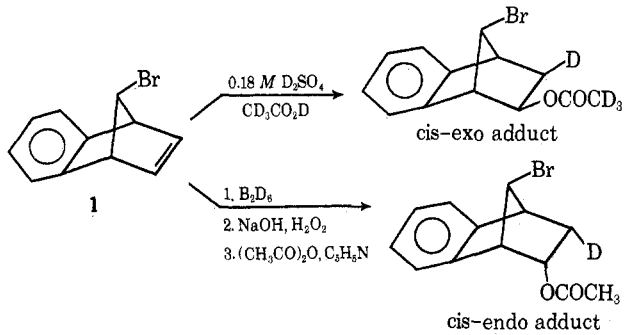
A recent generalization[2,3] suggests that those reagents of small or moderate steric requirements which add in a stepwise fashion to a norbornene system should not be prevented from attacking the exo face by the presence of a bulky group located at a syn-7 position. This generalization accounts for a large number of observations in this area.[4-9]



R = bulky group such as CH_3 or Br

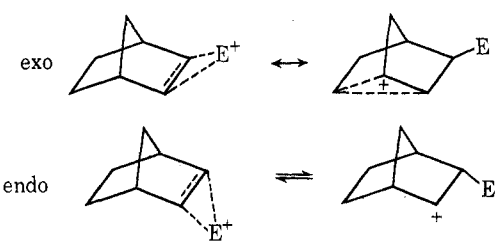
E^+ = electrophilic species such as Br^+, D^+, $HgOAc^+$

It is not entirely clear, however, why this exo selectivity should prevail, as even attack at the corners of the above hindered systems from the exo side must result in some interaction with the syn-7 substituent, an interaction which could be avoided by endo approach. As emphasized by Brown, interaction with a syn-7 substituent can result in an inversion of the steric approach control factor with those reagents which add in a single stage.[2,3] A comparison of the stereochemical course of reaction for these two types of reagents is illustrated for the acid-catalyzed addition of acetic acid-d_4 and deuterioboration of *anti*-7-bromobenzonorbornadiene (**1**).[5] The first reaction is a stepwise elec-

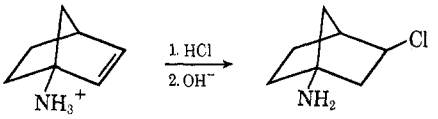


trophilic addition, whereas the second proceeds by a concerted process.

The magnitude of the energy term associated with a torsional strain factor,[10] although favoring exo approach, would appear to be too small to account for the preference observed for exo approach of an electrophile in a hindered system. Another factor that has received some consideration is an electronic factor.[7,11]



The orientation of the π orbital is such as to permit σ delocalization in the transition state for exo approach of the electrophile but not for endo attack. This consideration has been criticized, in part owing to the lack of a strong directive effect of a bridgehead substituent.[12-14] A comparison with the effect of a 1-methyl substituent in the solvolysis of an exo norbornyl derivative is usually made.[12,13] However, the directive effect should not be felt to the same extent in these two independent reactions. Furthermore, there is an example where a deactivating group does exert a strong directive influence. The 1-ammonium function in the following reaction leads to a regiospecific addition,[15] presumably by avoiding the accumulation of positive charges at some intermediate stage. By similar reasoning, one could explain the orientation of addition in the hydrochlorination of 1-chloronorbornene in terms of the inductive effect of chlorine.[14]



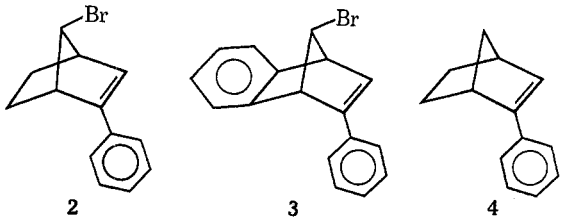
The electronic factor has also been criticized owing to the slight preference shown for cis-exo addition over rearrangement with certain protonic reagents.[16,17] The symmetrical norbornyl intermediate should provide

(1) National Science Foundation Undergraduate Research Participant, 1970.
(2) H. C. Brown and J. H. Kawakami, *J. Amer. Chem. Soc.*, **92**, 201 (1970).
(3) H. C. Brown and K.-T. Liu, *ibid.*, **92**, 3502 (1970).
(4) R. Caple, F. M. Hsu, and C. S. Ilenda, *J. Org. Chem.*, **33**, 4111 (1968).
(5) R. Caple and C. S. Ilenda, *J. Amer. Chem. Soc.*, **92**, 3817 (1970).
(6) H. C. Brown, J. H. Kawakami, and K.-T. Liu, *ibid.*, **92**, 3816 (1970); **89**, 1525 (1967).
(7) T. T. Tidwell and T. G. Traylor, *J. Org. Chem.*, **33**, 2614 (1968).
(8) W. C. Baird, Jr., and M. Buza, *ibid.*, **33**, 4105 (1968).
(9) H. C. Brown, M.-H. Rei, and K.-T. Liu, *J. Amer. Chem. Soc.*, **92**, 1760 (1970).
(10) P. v. R. Schleyer, *ibid.*, **89**, 701 (1967).
(11) C. W. Jefford and W. Wojnarowski, *Tetrahedron Lett.*, 193 (1968).
(12) H. C. Brown and K.-T. Liu, *J. Amer. Chem. Soc.*, **89**, 3898 (1967).
(13) P. v. R. Schleyer, *ibid.*, **89**, 3901 (1967).
(14) A. J. Fry and W. B. Farnham, *Tetrahedron Lett.*, 3345 (1968).
(15) J. W. Wilt, *et al.*, *J. Org. Chem.*, **33**, 694 (1965).
(16) J. K. Stille and R. D. Hughes, *ibid.*, **36**, 340 (1971).
(17) H. C. Brown and K.-T. Liu, *J. Amer. Chem. Soc.*, **89**, 3900 (1967).

exactly equal amounts of the two products, although one should consider the possibility that with certain reagents the initially formed ion pair, which includes the nucleophile, is not necessarily as symmetrically disposed as the delocalized cation itself.

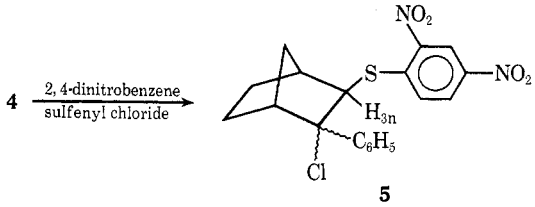
It was of interest to us to test further the stereoelectronic hypothesis by examining the stereochemistry of approach of an electrophile to hindered 2-phenylnorbornene systems where presumably the question of σ delocalization would not be involved. The *tert*-2-phenyl-2-norbornyl cation intermediate should be classical in nature.[18,19]

We chose to examine the approach of an electrophile to the hindered phenylnorbornene systems **2** and **3**. Our selection of an electrophilic reagent was somewhat limited. The oxymercuration of 2-phenylnorbornenes



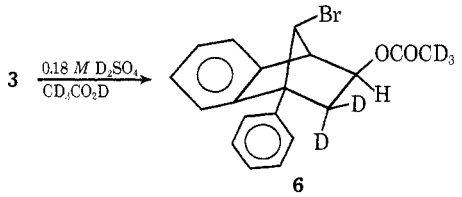
2 **3** **4**

is not straightforward, apparently leading to divinylmercury compounds.[20] The use of arylsulfenyl halides is not useful, as the reaction involves a cyclic transition state and endo attack is not unexpected[3] in syn-7 substituted norbornenes. In fact, we have observed no reaction of 2,4-dinitrobenzenesulfenyl chloride with **2**, whereas 2-phenylnorbornene (**4**) reacts readily to give the exo addition product **5** as confirmed by nmr.[21,22] The signal for H_{3n} in **5** occurs at δ 3.91 as a narrow doublet, J = 1.8 Hz.



5

The use of a mineral acid, such as hydrogen bromide (deuterium bromide), or acid solution such as acetic acid–sulfuric acid, leads to prior equilibration, and, in the latter case, rearrangement. This rearrangement is illustrated by the dideuteration and almost quantitative rearrangement accompanying the acetic acid-d_4–sulfuric acid-d_2 addition to **3** to produce **6**.



6

(18) H. C. Brown and K. Takeuchi, *J. Amer. Chem. Soc.*, **90**, 2691, 2693 (1968).

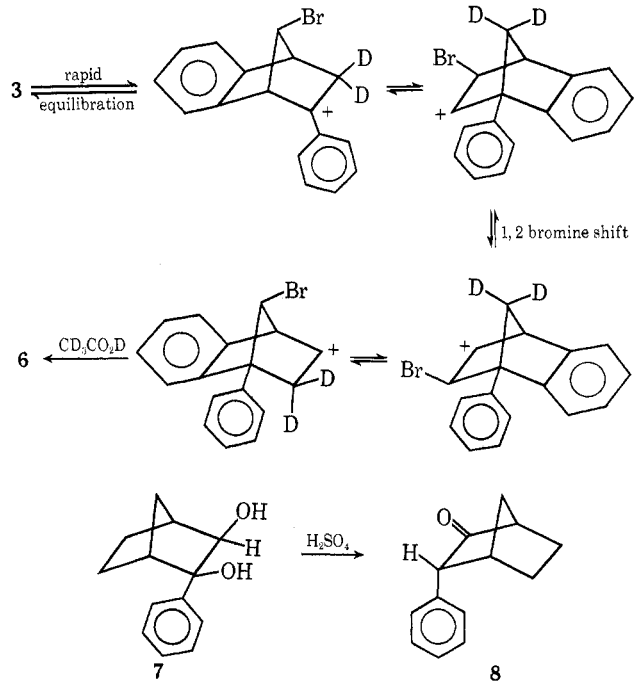
(19) D. G. Farnum and G. Mehta, *ibid.*, **91**, 3256 (1969).

(20) J. M. Coxon, M. P. Hartshorn, and A. J. Lewis, *Tetrahedron Lett.*, 3521 (1969).

(21) S. J. Cristol and G. W. Nachtigall, *J. Org. Chem.*, **32**, 3738 (1967).

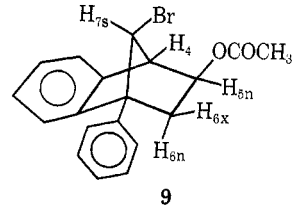
(22) Chemical shifts are relative to tetramethylsilane (60 MHz).

A multiple-step carbonium ion rearrangement, after an acid-catalyzed equilibration, is suggested to account for the origin of **6**. A rearrangement from a benzylic norbornyl cation to a secondary norbornyl cation, as required in the indicated scheme, has been postulated to occur in the rearrangement of the pinacol **7** to 3-*endo*-phenyl-2-norbornanone (**8**).[23,24]



7 **8**

The structure of **6** is readily confirmed by nmr[21,22] by comparison with the undeuterated acetate **9**. The signal for H_{5n} in the undeuterated acetate **9** occurs at δ 4.82 with $J_{5n,6n}$ = 7.5, $J_{5n,6x}$ = 3.7, and $J_{5n,7s}$ = *ca.* 1.2 Hz. The syn proton at C-7 occurs as a multiplet at δ 4.41 with a half-height width of 4.0 Hz, and the bridgehead hydrogen H_4 appears as a narrow signal at δ 3.85. The exo methylene hydrogen at C-6 exists as a quartet centered at δ 2.78 with $J_{6x,6n}$ = 13.0 and $J_{6x,5n}$ = 3.7 Hz. The endo hydrogen at C-6 appears as an octet at δ 2.40 with $J_{6n,6x}$ = 13.0, $J_{6n,5n}$ = 7.5, and $J_{6n,7s}$ = 1.5 Hz. In the deuterated adduct **6** the signals for H_{6x} and H_{6n} are missing. The signal for H_{5n} collapses to a narrow multiplet of 3.5 Hz at half-height. The signal for H_7 is a triplet with J values of *ca.* 1.2 Hz. The signal for H_4 is unchanged.



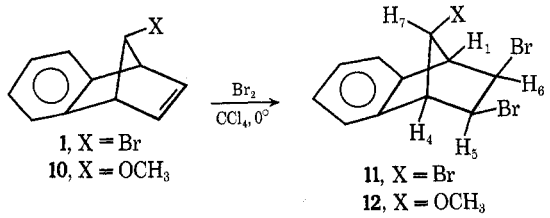
9

The halogens bromine and chlorine were found to add to the hindered systems **2** and **3** under controlled conditions. Bromine, furthermore, has been shown to attack exo in hindered norbornene systems. The addition of bromine to *anti*-7-bromobenzonorbornadiene

(23) D. C. Kleinfelter and T. E. Dye, *J. Amer. Chem. Soc.*, **88**, 3174 (1966).

(24) C. J. Collins, Z. K. Cheema, R. G. Werth, and B. M. Benjamin, *ibid.*, **86**, 4913 (1964).

(**1**) and *anti*-7-methoxybenzonorbornadiene (**10**) forms the cis-exo adducts **11**[4] and **12**, respectively.



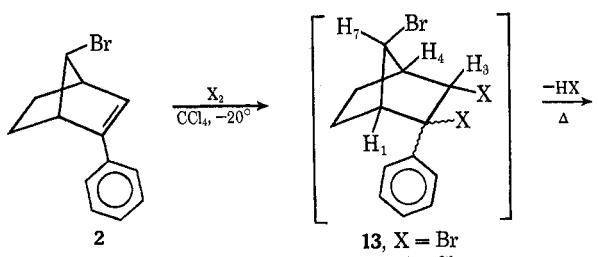
1, X = Br
10, X = OCH_3

11, X = Br
12, X = OCH_3

With the tribromide **11** a three-proton multiplet centered at δ 4.43 is observed with a width at half-height of 1.5 Hz for the isochronous protons (chloroform-*d*) on the carbons bearing bromine. The isochronous protons can be separated into a narrow two-proton peak and a narrow one-proton peak using acetone as the solvent. The chemically equivalent bridgehead protons, H_1 and H_4, produce a doublet, J = 1.2 Hz, centered at δ 4.04. Typically larger bridgehead-exo vicinal coupling[21] is not observed and the corresponding cis-endo structure is not likely. In the dibromide **12**, in addition to the aromatic and methyl absorptions, a two-proton signal, H_5 and H_6, centered at δ 4.16 with a width at half-height of 1.5 Hz is observed. A three-proton multiplet centered at δ 3.79 with a width at half-height of 2.0 Hz is also observed and again the absence of trans or bridgehead-exo coupling is noted.[21]

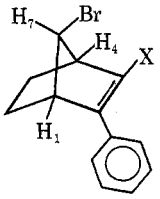
The polar addition of bromine or chlorine in carbon tetrachloride at −20° to *syn*-7-bromo-2-phenylnorbornene (**2**) produces the adducts **13** and **14**, which appear to have resulted from initial endo attack of the electrophilic halogen. Consistent with this assignment is the observation that the adducts gradually lose 1 mol of hydrogen halide upon warming to room temperature to form the substitution products **15** and **16**, respectively. A facile elimination of hydrogen halide leading to the conjugated system is not unexpected.[25]

The nmr signal for H_7 in **13** occurs as a triplet at δ 4.14 with $J_{1,7} = J_{4,7}$ = 1.4 Hz. The signal for H_3 in **13** occurs as a quartet at δ 5.45 with $J_{3,5}$ = 1.6 and $J_{3,4}$ = 3.7 Hz. The latter coupling in H_3 is consistent with a bridgehead-exo coupling,[21] and the former coupling is consistent with a long-range interaction with



2

13, X = Br
14, X = Cl

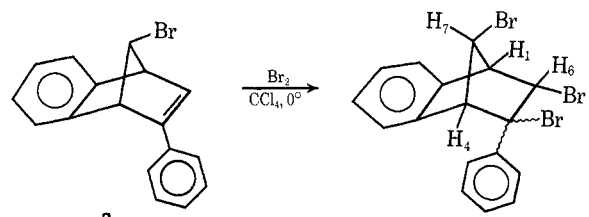


15, X = Br
16, X = Cl

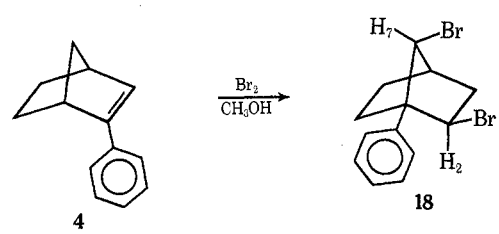
an exo hydrogen at C-5.[26,27] The corresponding signals for **14** are as follows: H_7, δ 4.14, $J_{1,7} = J_{4,7}$ = 1.5 Hz; H_3, δ 5.37, $J_{3,5}$ = 1.2 and $J_{3,4}$ = 3.8 Hz. In the substitution product **15**, H_7 occurs as a triplet at δ 3.80 with $J_{4,7} = J_{1,7}$ = 1.5 Hz and H_1 and H_4 are centered at δ 3.09 and 3.30, respectively. In **16**, H_7 is at δ 3.87 with $J_{4,7} = J_{1,7}$ = 1.5 Hz and H_1 and H_4 are at δ 3.08 and 3.42, respectively.

The addition of bromine to *anti*-7-bromo-5-phenylbenzonorbornadiene (**3**) was also examined, as elimination of hydrogen bromide and net substitution is less likely. In this instance the crystalline adduct **17**, again resulting from initial endo electrophilic attack, could be isolated in an 85% yield. In the nmr spectrum for **17**, H_6 occurs as a doublet at δ 5.67 with $J_{1,6}$ = 3.5 Hz, H_7 occurs as a triplet at δ 4.60 with $J_{1,7} = J_{4,7}$ = 1.5 Hz, H_4 occurs as a triplet at δ 4.32 with $J_{4,7}$ = 1.5 and $J_{1,4}$ = 1.5 Hz, and H_1 occurs as a doublet of triplets at δ 3.73 arising from $J_{1,6}$ = 3.5, $J_{1,7}$ = 1.5, and $J_{1,4}$ = 1.5 Hz. Quite significantly, the small long-range coupling, $H_{3\,exo}$ with $H_{5\,exo}$, observed for H_3 in **13** and **14**, is not observed in the benzonorbornene system **17** where H_6 occurs as a clean doublet.

The addition of bromine to 2-phenylnorbornene (**4**) in methanol produces the rearranged adduct **18** as the only major addition product. This observation is consistent with reactions of other unhindered norbornene systems.[28] The multiplet for the endo proton at C-2 in **18** occurs at δ 4.47 arising from J_{cis} = 8.0, J_{trans} = 3.0, and $J_{2,7}$ = *ca.* 1.5 Hz. The signal for the anti-7 proton occurs as a narrow multiplet at δ 4.33.



3 **17**



4 **18**

In conclusion, it appears that in the hindered phenylnorbornene systems **2** and **3** electrophilic attack of a halogen is governed by steric-approach control even though exo electrophilic attack at the corner should be just as feasible here as without the phenyl group. These surprising results are in contrast to the hindered norbornene systems **1** and **10** where initial exo approach of the electrophile was observed. The results suggest that the phenyl substituent is removing or altering the factor that favors exo approach of an electrophile in nonphenyl-substituted norbornenes. It is difficult to see how the original factor could be only steric or torsional in nature, and it would appear that

(25) J. K. Stille, F. M. Sonnenberg, and T. H. Kinstle, *J. Amer. Chem. Soc.*, **88**, 4922 (1966).

(26) R. M. Moriarty, H. Gopel, H. G. Walsh, K. C. Ramey, and D. C. Lini, *Tetrahedron Lett.*, 4555 (1966).

(27) D. N. Ford, W. Kitching, and P. R. Wells, *Aust. J. Chem.*, **22**, 1157 (1969).

(28) S. J. Cristol and G. W. Nachtigall, *J. Org. Chem.*, **32**, 3727 (1967).

the factor favoring exo approach of an electrophile is comprised in part by a stereoelectronic effect. A conceivable origin of a stereoelectronic factor is the one related to σ delocalization in the transition state for exo but not endo approach of an electrophile as discussed earlier. The phenyl group would be expected to reduce this delocalization and hence remove it as a factor favoring exo approach of an electrophile.[29]

Experimental Section

Analytical.—Nuclear magnetic resonance spectra were obtained on a Varian Associates Model A-60 spectrometer where the internal standard was tetramethylsilane. Galbraith Laboratories, Inc., Knoxville, Tenn., performed all the microanalyses. The melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected.

3-Chloro-3-phenyl-2-*exo*-norbornyl-2′4′-dinitrophenyl Sulfide (5).—The necessary starting olefin, 2-phenylnorbornene (4), was synthesized according to the procedure of Kleinfelter and Schleyer.[30] The sulfide **5** was made using a modification of a basic procedure of Kwart and Miller.[31] The olefin **4**, 0.323 g. (1.92 mmol), was dissolved in 5 ml of reagent ethylene chloride. The solution was stirred and a slurry of 2,4-dinitrobenzenesulfenyl chloride (Aldrich Chemical Co.), 0.439 g (1.87 mmol), in 5 ml of ethylene chloride was slowly added. Stirring was continued for 1 hr and then the solvent was removed under vacuum. Only the exo addition product **5** could be detected by nmr in the crude material. The light orange product was recrystallized from benzene–carbon tetrachloride, mp 158–160°.

Anal. Calcd for $C_{19}H_{17}SClN_2O_4$: C, 56.55; H, 4.23; Cl, 8.76. Found: C, 56.65; H, 4.39; Cl, 9.09.

***anti*-7-Methoxy-*cis*-*exo*-5,6-dibromobenzonorbornene (12).**—*anti*-7-Methoxybenzonorbornadiene (**10**),[32] 0.44 g (2.6 mmol), was dissolved in 20 ml of carbon tetrachloride and placed in an aluminum foil wrapped flask. Bromine, 0.45 g (2.8 mmol), in 10 ml of carbon tetrachloride was added and the solution was stirred in an ice bath for 2.5 hr. The excess solvent was then removed under vacuum and a brown, gummy solid was obtained. This crude material, almost exclusively **12** by nmr, was recrystallized from ether three times to yield colorless crystals, 0.36 g (42%), mp 139–140°°.

Anal. Calcd for $C_{12}H_{12}Br_2O$: C, 43.40; H, 3.65; Br, 48.12. Found: C, 43.48; H, 3.60; Br, 47.97.

***anti*-7-Bromo-5-phenylbenzonorbornadiene (3).**—*anti*-7-Bromo-5-benzonorbornenone (**19**),[4] 2.01 g (8.4 mmol), in 10 ml of anhydrous tetrahydrofuran (freshly distilled from lithium aluminum hydride) was added to preformed phenylmagnesium bromide (*ca.* 13 mmol) in 10 ml of dry tetrahydrofuran under a nitrogen atmosphere. The mixture was stirred and refluxed for 0.5 hr. Crushed ice and 25 ml of a saturated ammonium chloride solution were then added to the cooled mixture and stirring was continued for 1 hr. The mixture was extracted with ether and washed with a saturated sodium carbonate solution. The ether layer was dried over anhydrous magnesium sulfate and the solvent was removed under aspirator vacuum. The oily product recovered (no carbonyl by ir) was dehydrated without further purification. The crude reaction product was dissolved in 20 ml of anhydrous ether and 3 ml of boron trifluoride etherate was added. The solution was stirred at room temperature overnight. The solution was then washed with a 10% sodium bicarbonate solution. The ether layer was dried over anhydrous magnesium sulfate and the solvent was removed under vacuum. The crude product crystallized upon standing and was recrystallized from ethanol to yield 1.58 g (75%), mp 130°.

Anal. Calcd for $C_{17}H_{13}Br$: C, 68.70; H, 4.41; Br, 26.88. Found: C, 68.49; H, 4.45; Br, 26.62.

***syn*-7-Bromo-2-phenylnorbornene (2).**—The phenyl olefin **2** was synthesized by the reaction of phenylmagnesium bromide with *syn*-7-bromo-2-norbornanone (**20**)[33] and a subsequent dehydration. The procedure used was the same as that used in the preparation of **3** from the bromo ketone **19**. The product was recrystallized from ethanol, mp 62–63°, and was obtained in a 54% yield from **20**.

Anal. Calcd for $C_{13}H_{13}Br$: C, 62.67; H, 5.26; Br, 32.07. Found: C, 62.87; H, 5.48; Br, 31.88.

Addition of Bromine to *syn*-7-Bromo-2-phenylnorbornene (2).—Bromine could be added to the olefin **2** at −20° in the dark using either carbon tetrachloride or pentane as the solvent. The reaction could be followed by running it in an nmr tube. Under the above conditions the addition product **13** and the substitution product **15** were observed in *ca.* a 30:70 ratio. These two products accounted for better than 90% of the products. Upon warming to room temperature the adduct **13** was gradually converted to **15** with the evolution of hydrogen bromide. Essentially pure **15** could be obtained by running the reaction in methanol at room temperature. A short-path distillation, 80° (0.2 mm), of **15** obtained in this way produced an analytical sample.

Anal. Calcd for $C_{13}H_{12}Br_2$: C, 47.60; H, 3.69; Br, 48.72. Found: C, 47.86; H, 3.75; Br, 48.50.

Addition of Chlorine to *syn*-7-Bromo-2-phenylnorbornene (2).—The highest ratio of addition (**14**) to substitution (**16**) in the reaction of chlorine with **2** was obtained in carbon tetrachloride at −20°, where *ca.* a 50:50 ratio of **14**:**16** was observed. These two products accounted for *ca.* 90% of the products, the other minor product possibly being a tricyclic product. The chlorination was carried out by saturating a carbon tetrachloride solution of **2** at −20° with chlorine and allowing the reaction flask to remain in the dark at the reaction temperature for 3 hr. The chlorine adduct only slowly lost hydrogen chloride at room temperature and the substitution product **16** was obtained by first distilling twice at 85° (0.3 mm) and then recrystallizing from ethanol–water to yield pure **16**, mp 74–75°.

Anal. Calcd for $C_{13}H_{12}BrCl$: C, 55.05; H, 4.27; Br, 28.18. Found: C, 54.81; H, 4.37; Br, 28.34.

***anti*-7,*endo*-6,5-Tribromo-5-phenylbenzonorbornene (17).**—*anti*-7-Bromo-5-phenylbenzonorbornadiene (**3**), 0.446 g (1.5 mmol), was dissolved in 20 ml of carbon tetrachloride and then placed in an aluminum foil wrapped flask. Bromine, 0.25 g (1.6 mmol), was dissolved in 10 ml of carbon tetrachloride and added dropwise to the above solution. The solution was stirred in an ice bath for 0.5 hr and stirring was continued at room temperature for another 20 hr. Excess solvent was removed under reduced pressure. The crude adduct was recrystallized from cyclohexane to yield white, needlelike crystals of **17**, 0.585 g (85.4%), mp 100–100.5°.

Anal. Calcd for $C_{17}H_{13}Br_3$: C, 44.68; H, 2.86; Br, 52.46. Found: C, 44.49; H, 2.95; Br, 52.51.

***exo*-2,*syn*-7-Dibromo-1-phenylnorbornane (18).**—2-Phenylnorbornene (**4**), 1.19 g (7.0 mmol), was dissolved in 20 ml of dry methanol and placed in an aluminum foil wrapped flask. Bromine, 1.2 g (7.5 mmol), was dissolved in 10 ml of dry methanol and added dropwise to the above solution. The reaction solution was stirred for 1.5 hr in an ice bath. The excess solvent was then removed under reduced pressure and a near quantitative yield of a brown, viscous product was obtained. This crude product was almost exclusively **18** (nmr), and methyl ethers were not noted Recrystallization from absolute ethanol produced pure *exo*-2,*syn*-7-dibromo-1-phenylnorbornane (**18**), mp 102–102.5°.

Anal. Calcd for $C_{13}H_{14}Br_2$: C, 47.30; H, 4.27; Br, 48.43. Found: C, 47.10; H, 4.29; Br, 48.19.

Registry No.—**2**, 30783-70-1; **3**, 30783-71-2; **5**, 30783-72-3; **12**, 30783-73-4; **15**, 30783-74-5; **16**, 30783-75-6; **17**, 30783-76-7; **18**, 30783-77-8; Br, 7726-95-6; Cl, 7782-50-5.

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