Registry No.—**1a**, 16733-97-4; **1b**, 4984-82-1; **1c**, 30994-24-2; **1d** (X = Cl), 34766-85-3; **1f**, 2726-34-3; *anti*-**2f**, 57496-94-3; **3** 1-phenyl isomer, 1961-98-4; **3** 2-phenyl isomer, 2327-56-2; **4**, 4453-90-1; **5**, 2542-07-6; benzyne, 462-80-6; sodium amide, 7782-92-5; 1,4-diphenylcyclopentadiene, 57496-95-4; 1,2,3,4,5-pentaphenylcyclopentadiene, 2519-10-0; potassium amide, 17242-52-3; ethylmagnesium chloride, 2386-64-3; diethylaminotrimethylstannane, 1068-74-2; cyclopentadiene, 542-92-7.

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Highly Stereoselective Preparations of *anti*-7-Benzonorbornadienyl Grignard Reagents

Gary R. Buske[1a] and Warren T. Ford*[1b]

Roger Adams Laboratory, Department of Chemistry, University of Illinois, Urbana, Illinois 61801

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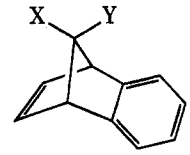
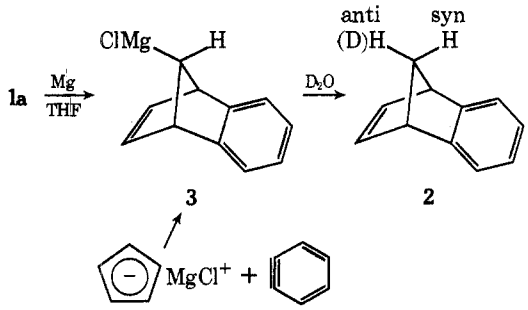
Grignard reagents have been prepared in tetrahydrofuran from *anti*- and *syn*-7-chlorobenzonorbornadiene (*anti*-Cl and *syn*-Cl) and *anti*- and *syn*-7-bromobenzonorbornadiene (*anti*-Br and *syn*-Br) by three methods: reaction with magnesium turnings, reaction with activated magnesium prepared by reduction of magnesium halide with potassium metal, and reaction with sodium naphthalenide (NaNaph) in the presence of magnesium halide. Deuterolyses of the Grignard solutions give deuterated benzonorbornadiene (**2**) with >85% overall retention of configuration from *anti*-Cl and *anti*-Br by the magnesium metal methods. Carbonation of the Grignard reagent from *anti*-Br and magnesium turnings also proceeds with high overall retention of configuration. The stereoselectivity does not depend on particle size or purity of the magnesium. In contrast, *syn*-Cl and *syn*-Br give deuterated **2** by the same methods with little or no stereoselectivity. The NaNaph method gives little stereoselectivity with any of the substrates but produces the Grignard reagents in higher yields. Sizable amounts of undeuterated benzonorbornadiene are formed in all of the preparations using magnesium turnings or activated magnesium. Grignard reagent formation and deuterolysis with *anti*-7-bromobenzonorbornene (**5**) also proceed with high retention of configuration. The Grignard reactions at saturated carbon with *anti*-Br, *anti*-Cl, and **5** are far more stereoselective than any previously reported. The results are discussed in terms of a mechanism of Grignard formation which proceeds by rate-limiting electron transfer to give a radical intermediate bound to the magnesium surface.

Both reaction of *anti*-7-chlorobenzonobornadiene (**1a**) with magnesium turnings in tetrahydrofuran (THF)[2] and cycloaddition of benzyne to the cyclopentadienyl Grignard reagent in THF[3] followed by deuterolysis give benzonorbornadiene-7-*d* (**2**) with the D incorporated >90% stereoselectively anti. Assuming that deuterolysis proceeds with retention of configuration,[4] both preparations must lead to the *anti*-7-benzonorbornadienyl Grignard reagent (**3**).

Three possible reasons for the stereoselectivity of these reactions are: (1) Both proceed stereoselectively to form **3**, and **3** is configurationally stable under the preparation and trapping conditions. (2) Both **3** and its syn isomer are formed but



1a, X = Cl; Y = H; *anti*-Cl
b, X = H; Y = Cl; *syn*-Cl
c, X = Br; Y = H; *anti*-Br
d, X = H; Y = Br; *syn*-Br

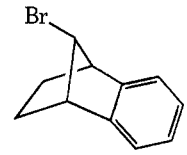


the mixture equilibrates rapidly to >90% **3**, which is then captured by deuterolysis. (3) Both **3** and its syn isomer are formed, but the syn Grignard reagent is rapidly destroyed under the reaction conditions. The third possibility would require that the isomeric Grignard reagents interconvert slowly or not at all during the time required to prepare them.

Previous studies of Grignard reagents show that the configurational stabilities are highly dependent on structure. Some acyclic primary Grignard reagents undergo configurational inversion on the NMR time scale at room temperature.[9] The tertiary Grignard reagent from optically active 1-bromo-1-methyl-2,2-diphenylcyclopropane (**4**) is configurationally stable for ≥30 min in refluxing di-*n*-butyl ether.[6] *endo*-2-Norbornylmagnesium bromide reverts to an equilibrium endo/exo mixture in ≤24 h in ether at room temperature.[5] A variety of secondary Grignard reagents fail to show inversion at ≥120 °C on the NMR time scale.[9a,10] On the other hand, Δ^3-cyclohexenylmagnesium bromide and Δ^3-cyclopentenylmagnesium bromide undergo rapid inversion on the NMR time scale at 25 °C in THF, presumably by a reversible homoallyl–cyclopropylcarbinyl rearrangement.[11]

The first possibility is most interesting because never before has any Grignard reagent been prepared with such high stereoselectivity at saturated carbon. The Grignard reagents from **4** and the corresponding chlorocyclopropane have been prepared and carbonated. The carboxylic acid obtained from bromide **4** had 59% retained and 41% inverted configuration, and that obtained from the corresponding chloride had 62.5% retained and 37.5% inverted configuration.[6] All other Grignard preparations from alkyl halides and magnesium have led to equilibrium mixtures of isomers. The loss of configuration has been established clearly in the cases of **4**[6] and the *exo*- and *endo*-2-bromonorbornanes[5] to occur during the Grignard formation step, not during subsequent deuterolysis or carbonation. Stereoselectivity of ≥90% has been reported for Grignard preparations from vinyl bromides such as the β-bromostyrenes, 1-bromopropenes, and 1-bromo-1-hexenes.[7,8]

In this paper we report details of Grignard preparations from *anti*-Cl, *syn*-7-chlorobenzonorbornadiene (**1b**), and the corresponding *anti*- and *syn*-7-bromobenzonorbornadienes (**1c,d**) by a variety of methods. The results clearly establish that stereoselective production of 2-*anti*-7-*d* is due to the first possibility, stereoselective formation of Grignard reagent **3**. To learn more about the mechanism of this unprecedented stereoselective Grignard reaction we have also tested effects of the state and purity of the magnesium metal on the reaction, thermal stabilities of the Grignard reagents, equilibration of the *anti*- and *syn*-7-carbomethoxybenzonorbornadienes, and preparation of the Grignard reagent from *anti*-7-bromobenzonorbornene (**5**).

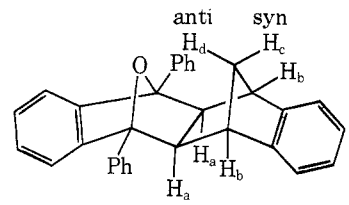


5

Previous attempts to prepare and carbonate Grignard reagents from **1c**[12] and **5**[13] led to poor yields of carboxylic acids and considerable 7,7′-dimer formation. Earlier experience with **3** formed by cycloaddition indicated that deuterolysis was a much more effective trapping method than carbonation,[3b] so we chose to trap the Grignard reagents prepared from **1a–d** and **5** by deuterolysis.

Results

Three methods were employed to prepare Grignard reagents from **1a–d.** (1) The alkyl halide was added to a refluxing THF solution over ordinary magnesium turnings. (2) Activated magnesium was prepared from anhydrous magnesium halide and potassium metal in THF,[14] and the alkyl halide was added to the resulting mixture. (3) A 0.7–0.9 M THF solution of 2.3 equiv of sodium naphthalenide (NaNaph) was added to a solution of 1.0 equiv of the alkyl halide and 1.3 equiv of anhydrous magnesium halide at room temperature.[15] All three procedures were completed by deuterolysis of the Grignard reagent, determination of yield and purification of benzonorbornadiene (**2**) by GLC, and conversion of **2** to its diphenylisobenzofuran Diels–Alder adduct **6**.[16]



6

Deuterium analyses of **6** were performed by low eV mass spectrometry for total deuterium content and by ^{1}H NMR for both amount and location of deuterium. Because of low deuterium incorporation in many experiments, the ^{1}H NMR results were determinations of small differences in areas of large proton signals and are reliable only to ±0.05 atom D at each isomeric position (anti or syn). Usually the total deuterium found by ^{1}H NMR at the two positions agreed within ±0.08 atom D with the mass spectra. Complete results are in Table I. To check the accuracy of the ^{1}H NMR results, four representative samples were analyzed by Fourier transform deuterium NMR at 33.77 MHz with the help of Professor L. K. Montgomery at Indiana University. No internal standard was used in the deuterium NMR analyses, so only relative amounts of anti and syn D were obtained. Use of mass spectral results for total D and deuterium NMR for location of D gave the analyses in the last two columns of Table II, which agree well with the ^{1}H NMR analyses.

Numerous attempts to trap the Grignard reagents with electrophiles other than D_2O were disappointing. No simple derivatives were isolated after treatment with chlorotrimethylsilane, dimethyl sulfate, ethyl chloroformate, *N*-chlorosuccinimide, methyl iodide, benzaldehyde, acetic anhydride, or ethyl bromoacetate. Carbonation produced the expected carboxylic acids in much lower yield than deuterolysis produced **2**. Oxidation with O_2 of the Grignard reagent **3** from cycloaddition of benzyne and CpMgBr gave only a 4%

Table I. Stereochemistry of Formation and Deuterolysis of 7-Benzonorbornadienyl Grignard Reagents in THF

Expt no.	Reactant	Reagents	Temp, °C	Time, h	% yield of 2	Atom excess D in 6		
						By ^{1}H NMR[a]		
						Anti	Syn	By MS
1[b]	C_5H_5MgBr	Benzyne	65	1.0	29	0.91	0.00	0.91
2	*anti*-Cl	Mg turnings	65	20	86	0.56	0.05	0.68
3	*anti*-Cl	Mg turnings[c]	70	24	56	0.47	0.00	0.53
4	*anti*-Cl	$MgCl_2$/NaNaph	25	0.25	95	0.31	0.25	0.59
5	*anti*-Cl	$MgCl_2$/NaNaph	25	0.25	92	0.39	0.30	0.72
6	*anti*-Cl	NaNaph	25	0.25	66	0.00	0.00	−0.02
7	*anti*-Cl	Mg turnings[d]	65	23	81	0.39	0.07	0.49
8	*anti*-Cl	$MgCl_2$/NaNaph[e]	65	24	70	0.00	0.00	0.03
9	*anti*-Cl	$MgCl_2$/NaNaph[e]	65	24	71	0.00	0.02	0.13
10	*anti*-Cl	Activated Mg	25	780		No reaction		
11	*syn*-Cl	Mg turnings	65	4	41	0.00	0.00	0.08
12	*syn*-Cl	Mg turnings	65	15	47	0.24	0.16	0.39
13	*syn*-Cl	Activated Mg	65	20	41	0.11	0.05	0.08
14	*syn*-Cl	$MgCl_2$/NaNaph	25	0.25	36	0.64	0.33	0.86
15	*syn*-Cl	$MgCl_2$/NaNaph	25	0.25	32	0.63	0.18	0.91
16	*anti*-Br	Mg turnings	65	0.017	67	0.19	0.00	0.20
17	*anti*-Br	Mg turnings	65	0.5	73	0.24	0.07	0.28
18	*anti*-Br	Mg turnings	65	4	74	0.23	0.04	0.29
19[f]	*anti*-Br	Mg turnings	65	0.083	72	0.24	0.06	0.30
			65	0.5	75	0.25	0.00	0.28
			65	4	71	0.15	0.00	0.23
			65	10	66	0.11	0.01	0.09
			65	20	65	0.01	0.00	0.00
20[f]	*anti*-Br	Mg turnings	65	0.5	74	0.30	0.05	0.37
			25[g]	0.1	77	0.25	0.08	0.33
21	*anti*-Br	Activated Mg	25	6.33	82[h]	0.25	0.05	0.28
22[f]	*anti*-Br	Activated Mg	25	6.33	74	0.28	0.11	0.36
			65	4	70	0.25	0.09	0.30
23[f]	*anti*-Br	Activated Mg	25	7	72	0.21	0.00	0.21
			65	20	58	0.01	0.01	−0.01
24[f]	*anti*-Br	Activated Mg	25	3.83	60	0.25	0.03	0.28
			65	4	66	0.10	0.00	0.18
			65	20	49	0.00	0.00	0.00
25[f]	*anti*-Br	Sublimed Mg	65	0.083	76	0.28	0.04	0.38
			65	4	80	0.27	0.07	0.36
			65	20	67	0.05	0.01	0.07
26	*anti*-Br	$MgBr_2$/NaNaph	25	0.25	85	0.30	0.29	0.60
27[f]	1*syn*-Br	Mg turnings	65	0.25	60	0.08	0.02	0.10
			65	0.75	68	0.19	0.23	0.38
			65	4.25	71	0.10	0.06	0.13
28[f]	*syn*-Br	Activated Mg	25	2.25	72	0.25	0.15	0.37
			65	0.5	68	0.23	0.15	0.35
			65	4	68	0.21	0.13	0.30
29	*syn*-Br	Activated Mg	25	20.5	37	0.00	0.00	−0.01
30	*anti*-Br	Mg turnings[i]	65	0.5	90	0.01	0.02	0.01
31[f]	*anti*-Br	Mg turnings[j]	65	0.5	76	0.72	0.21	0.95
			65	240	31	0.14	0.08	0.21
32	*anti*-Br	Mg turnings[i]	65	0.5	59	0.01	0.00	0.02

[a] Estimated error ±0.05 atom excess D. [b] Reference 3. [c] The solvent was 7-oxabicyclo[2.2.1]heptane instead of THF. [d] The solution was treated with NaNaph at 25 °C for 0.25 h before deuterolysis. [e] The reaction with NaNaph was carried out at 25 °C for 0.25 h before heating to reflux. [f] Aliquots were withdrawn from a single reaction mixture at the times indicated. [g] Reaction mixture from preceding line was cooled to 25 °C and 3.65 equiv of HMPA was added. [h] Estimated yield ±10%, no internal standard. [i] THF-d_8, hydrolyzed with H_2O. [j] THF-d_8. Aliquot at 0.5 h was hydrolyzed with D_2O. Remainder at 240 h was hydrolyzed with H_2O.

yield of *anti*-7-benzonorbornadienol which required a tedious chromatography for purification.

Reactions of *anti*-Br and *anti*-Cl with magnesium turnings in refluxing THF followed by deuterolysis immediately after the starting halide was consumed gave benzonorbornadiene (**2**) in about 70 and 86% yields, respectively. However, the **2** was only partly deuterated, 27% D from *anti*-Br (average of expt 16–20) and 68% D from *anti*-Cl (expt 2). If the yield of Grignard reagent is equal to the yield of benzonorbornadiene-*d* [(% yield of **2**) × (atom excess D in **2** determined by mass spectrometry)], *anti*-Br and *anti*-Cl gave 20 and 58% yields of Grignard reagent, respectively. The higher yield of Grignard reagent from the alkyl chloride is consistent with previous reports of the 1-halo-1-methyl-2,2-diphenylcyclopropanes.[6] Complete consumption of *anti*-Cl required 20 h at reflux, while all of the *anti*-Br usually reacted in 0.5 h. Prolonged reflux of the Grignard solutions from *anti*-Br led to still smaller degrees of deuteration of **2** but only a slight

Table II. Comparison of ^{1}H NMR and ^{2}H NMR Analyses of 6

	Atom excess D in 6			
	By ^{1}H NMR		By ^{2}H NMR	
Expt	Anti	Syn	Anti	Syn
2	0.56	0.05	0.60	0.08
12	0.24	0.16	0.23	0.16
24	0.25	0.03	0.25	0.03
28	0.25	0.15	0.22	0.15

decrease in the yield of **2** (expt 19). This indicates that much of the Grignard reagent which disappeared from the solution was converted to undeuterated **2**, either by reaction with adventitious moisture or by reaction with THF. The deuterium in **2** from *anti*-Br averaged 86% anti, and from *anti*-Cl was >90% anti even after 20 h at reflux. Since prolonged reflux of the solutions from *anti*-Br destroyed both anti and syn Grignard reagents (expt 19), the experiments with the shortest reflux times (0.5 h or less) are the best indicators of the stereoselectivity of Grignard formation. In an attempt to prepare a Grignard reagent from *anti*-Cl with activated magnesium, no reaction occurred at 25 °C (expt 10). Activated magnesium did enable preparation of Grignard solutions from *anti*-Br at 25 °C with essentially the same stereoselectivity as magnesium turnings gave at 65 °C (expt 22–24). Use of turnings from Dow sublimed magnesium crystal gave the same results as the ordinary grade of magnesium (expt 25).

Often hexamethylphosphoramide (HMPA) greatly increases the reactivity and ionic character of organomagnesium compounds.[17] In expt 20 a Grignard solution prepared from *anti*-Br and magnesium turnings was treated with 3.65 equiv of HMPA at 25 °C for 0.1 h before deuterolysis. No change in yield and only a slight decrease in stereoselectivity of deuteration in **2** resulted.

Reactions of *anti*-Br and *anti*-Cl with NaNaph and anhydrous magnesium halides (expt 4, 5, 26) gave better yields of Grignard reagents than reactions with magnesium metal. Presumably the Grignard reagent is formed by an electron transfer–transmetalation sequence.[18]

$$RX + Na^+Naph\cdot^- \rightarrow R\cdot + Naph + NaX$$

$$R\cdot + Na^+Naph\cdot^- \rightarrow RNa + Naph$$

$$RNa + MgX_2 \rightarrow RMgX + NaX$$

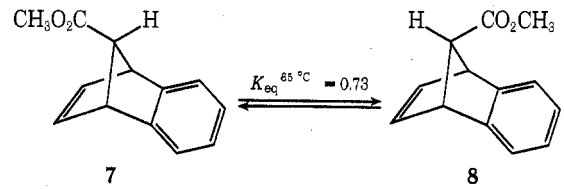
That an organomagnesium rather than an organosodium species reacts with D_2O is shown in expt **6**, where NaNaph treatment of *anti*-Cl in the absence of $MgCl_2$ led to a lower yield of **2** which contained no deuterium. The NaNaph/MgX_2 reactions usually gave **2** with only a small excess of *anti-d* over *syn-d*. The lack of selectivity occurs during Grignard formation and is not due to isomerization of a more stereoselectively formed Grignard reagent by excess NaNaph, because treatment of a preformed Grignard reagent from *anti*-Cl and magnesium turnings with NaNaph still allowed highly stereoselective formation of **2**-*anti*-7-*d* (expt 7). Unlike the Grignard reagent from *anti*-Cl and magnesium turnings, the one from NaNaph/$MgCl_2$ did not survive in refluxing THF (expt 8, 9).

Treatment of *syn*-Cl with magnesium turnings gave much lower yields of benzonorbornadiene than the corresponding reaction of *anti*-Cl, and much less deuterium was incorporated (expt 11, 12). Although the two experiments gave widely different degrees of deuteration, there was little stereoselectivity. *syn*-Cl also reacted with activated magnesium at 65 °C (expt 13) with about the same yield and extent of deuteration as with magnesium turnings. With NaNaph/$MgCl_2$ *syn*-Cl gave only 32–36% of **2** which was about 90% deuterated with more D anti than syn (expt 14, 15).

syn-Br behaved still differently from the other halides. With either Mg turnings at reflux or activated Mg at room temperature it gave about 70% of **2** which contained a total of 0.37 atom excess D distributed about equally between the syn and anti positions (expt 27, 28). An attempted Grignard preparation from *syn*-Br and activated Mg which required 20.5 h at 25 °C gave completely undeuterated **2** (expt 29). Experiment 27 gave a higher degree of deuteration after 0.75 h than after 0.25 h, probably because freshly formed Grignard reagent consumed a small amount of adventitious water in the first few minutes of the reaction to give undeuterated **2**. Since expt 27 is the only one where an increase in deuterium content was found in two successive samples, adventitious water does not appear to be a problem in the other experiments where the Grignard solution was sampled at different times.

The source of the undeuterated benzonorbornadiene is not known in the reactions of benzonorbornadienyl halides with magnesium turnings or activated magnesium followed by deuterolysis. The reproducibility of the atom excess D in **2** from nine experiments which varied in scale from 0.25 g to 2.25 g of *anti*-Br demonstrates that hydrolysis by H_2O was not a major source of undeuterated **2**. Since the most likely source of hydrogen was the THF, Grignard reagents were prepared in THF-d_8. In expt 30 and 31 two samples of the same lot of THF-d_8 were dried over sodium metal and used to prepare Grignard reagent from magnesium turnings and *anti*-Br under identical conditions. One Grignard solution was hydrolyzed with H_2O (expt 30) and part of the other was hydrolyzed with D_2O (expt 31). The remainder of the second solution was refluxed for 10 days and then hydrolyzed with H_2O. Surprisingly the benzonorbornadiene recovered after hydrolysis contained only 0.01 atom excess D while that recovered after deuterolysis contained 0.95 atom excess D. Continued reflux of the Grignard solution of expt 31, conditions known to destroy the Grignard reagent, led to a much lower yield of **2** which contained 0.21 atom excess D, indicating that most of the D in the portion deuterolyzed after 0.5 h came from the D_2O. Because of the apparent anomaly of expt 30, it was repeated (expt 32) with a new batch of THF-d_8 which was purified by distillation from the sodium ketyl of benzophenone. Although the yield of **2** was lower in expt 32 than in expt 30, the deuterium content was the same within experimental error by both mass spectrometry and ^{1}H NMR analyses.

In expt 20 samples of the Grignard solution were poured onto solid CO_2 before and after HMPA was added to the THF solution. The resulting mixtures of carboxylic acids were converted to mixtures of *anti*- and *syn*-7-carbomethoxybenzonorbornadiene (**7** and **8**). Without HMPA a 10.3% yield



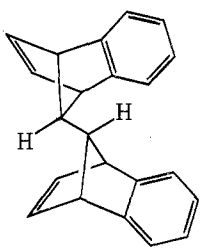
7 **8**

of carboxylic acids was isolated and the mixture of esters was 87% **7** by GLC, the same as the anti/syn distribution of deuterolysis products (Table I). With HMPA a 6.5% yield of carboxylic acids was isolated and the ester mixture was 75% **7** by GLC, also within experimental error of the deuterolysis results. Yields of benzonorbornadiene-*d* from deuterolysis were 27 and 25%, respectively, much better than the yields of carboxylic acids.

To establish the structures of **7** and **8**, anti ester **7** was syn-

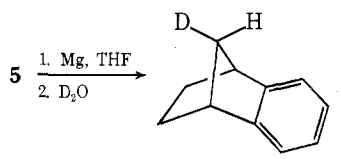
thesized stereospecifically by treatment of *anti*-Br with *sec*-butyllithium in hexane at −78 °C followed by carbonation and esterification in 17.6% overall yield after preparative GLC isolation. Its structure was proven by the characteristic four-bond coupling of 0.35 Hz between the syn-7 proton and the vinyl protons in its ^{1}H NMR spectrum.[19] Treatment of **7** in refluxing 0.4 M sodium methoxide in 80/20 (v/v) methanol/HMPA produced an equilibrium mixture of 58% **7** and 42% **8**. The ^{1}H NMR spectrum of **8** showed no coupling between the anti-7 proton and the vinyl protons.

In expt 21 we attempted to isolate and identify the side products from reaction of *anti*-Br with activated magnesium. The unsymmetrical dimer **9** was obtained in 5.7% yield by silica gel chromatography, but no other compounds could be isolated in a form suitable for identification.



9

To test whether the C_2–C_3 double bond of *anti*-Br and *anti*-Cl is a structural requirement for highly stereoselective Grignard formation, *anti*-7-bromobenzonorbornene (**5**) was treated with magnesium turnings in refluxing THF, and the mixture was hydrolyzed with D_2O. A 79% yield of benzonorbornene (**10**) was purified by GLC and analyzed by mass



10

spectrometry to contain 0.40 atom excess D. A 220-MHz ^{1}H NMR spectrum of **10**, in which the *anti*- and *syn*-7 proton resonances were clearly resolved from all other multiplets, showed 0.38 ± 0.05 atom excess D anti and 0.00 ± 0.05 atom excess D syn. This stereoselectivity is as high as or higher than in Grignard formation from *anti*-Br or *anti*-Cl.

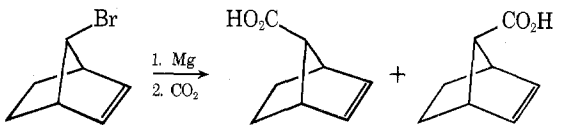
Discussion

anti-Br, *anti*-Cl, and *anti*-7-bromobenzonorbornene (**5**) react with magnesium with high retention of configuration. Under similar conditions *syn*-Br and *syn*-Cl give mixtures of *anti* and *syn*-7-benzonorbornadienyl Grignard reagents in which the syn Grignard reagent neither isomerizes rapidly to its anti isomer nor is selectively destroyed. Therefore, the formation of Grignard reagents from *anti*-Br, *anti*-Cl, and **5** and the cycloaddition of benzyne to cyclopentadienyl Grignard reagents are kinetically controlled. *anti*-Br, *anti*-Cl, and **5** react with magnesium and deuterolyze to produce benzonorbornadiene-7-*d* with at least a 6.1/1.0 preference for retention of configuration (based on expt 16–20). Only with vinyl bromides has such high stereoselectivity been observed before.[7,8] The only other Grignard preparations from halides and magnesium at saturated carbon known to proceed stereoselectively gave a maximum retention/inversion ratio of 1.67.[6]

In refluxing THF Grignard reagents from *anti*-Br start to decompose in less than 4 h and are completely consumed in 20 h. The thermal stability of the Grignard reagent from *anti*-Cl has not been tested directly, but it must be more stable than that from *anti*-Br because its formation required 20 h in refluxing THF. The data in Table I indicate that the configurational stabilities of the Grignard reagents from *anti*-Br must be at least as great as their thermal stabilities. Thus they are at least comparable in configurational stability to many secondary Grignard reagents studied previously.[5,9a,10] They do not invert configuration rapidly by homoallyl-cyclopropylcarbinyl rearrangement as Δ^3-cyclohexenyl- and Δ^3-cyclopentenylmagnesium halides do.[11]

Methyl esters **7** and **8** were designed to test the relative stabilities of anti- and syn-7-substituted benzonorbornadienes. Much greater stability of the anti isomer would help explain stereoselective formation of anti Grignard reagents. However, insofar as **7** and **8** are reasonable models for Grignard reagents, the anti isomer is only slightly favored at equilibrium.

We hypothesized at one time that the C_2–C_3 double bond of **3** could stabilize the anti Grignard reagent by coordinating to the magnesium atom more strongly than the benzene ring coordinates to magnesium in the syn Grignard reagent. However, such coordination is not a necessary feature for stereoselective Grignard formation because the saturated analogue **5** forms a Grignard reagent with as high retention of configuration as *anti*-Br and *anti*-Cl. Also treatment of *syn*-7-bromonorbornene (**11**) with magnesium in ether fol-



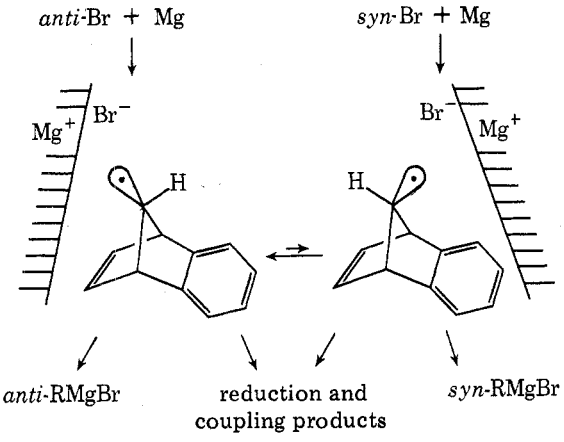
11 **2** : **1**

lowed by carbonation gives a 2/1 mixture of the corresponding anti and syn carboxylic acids.[20]

Since the origin of the stereoselectivity is kinetic, an explanation for our unusual results must lie in the mechanism of Grignard reagent formation. Diverse evidence supports a mechanism which proceeds by a free radical at the magnesium surface. For example, reaction of 1-chloro-2-methyl-2-phenylpropane with magnesium gives several products expected from free-radical rearrangement.[21] Grignard preparations from **1c**[12] and **5**[13] give substantial amounts of dimers from apparent free-radical coupling. Radical disproportionation and coupling account for the side products from treatment of 1-bromo-1-methyl-2,2-diphenylcyclopropane with magnesium in ether.[6] CIDNP in ^{1}H NMR spectra of alkyl Grignard reagents has been detected, but it must arise from coupling of free radicals in solution rather than at the magnesium surface.[22] The relative rates of reaction of alkyl halides with magnesium metal correlate better with their polarographic reduction potentials than with their rates of carbanion, SN2, lithium–halogen exchange, or tributyltin hydride reactions.[23] This suggests that the rate-limiting step is electron transfer from the metal to the alkyl halide.[23] Finally, the loss of configuration in formation of Grignard reagents at saturated carbon has long been cited as evidence for a radical intermediate. Radical surface mechanisms have been discussed recently by several authors.[6,22,23]

In spite of the high stereoselectivity, reactions of *anti*-Cl and *anti*-Br with magnesium may still proceed by a rate-limiting electron transfer to form a 7-benzonorbornadienyl radical at the magnesium surface as shown in Scheme I. This mechanism requires only that capture by magnesium of the anti surface-bound radical proceed faster than rearrangement to the syn surface-bound radical. Within the framework of Scheme I several experimental facts support stronger anti than syn binding to the magnesium surface: (a) *anti*-Br and *anti*-Cl react faster than *syn*-Br and *syn*-Cl, respectively. (b) *anti*-Cl gives much higher yields of deuterated benzonorbornadiene than *syn*-Cl. Yields from *anti*-Br and *syn*-Br are

Scheme I



about the same, however. (c) *syn*-Br and *syn*-Cl give approximately equal amounts of anti and syn Grignard reagents. The much faster reactions of the bromides than of the chlorides with magnesium also supports qualitatively a rate-limiting electron transfer step. A possible reason for stronger anti binding than syn binding of benzonorbornadienyl species to the metal is substantial steric hindrance between the benzene ring and the metal surface. On the other hand, highly stereoselective Grignard formation from *anti*-7-bromobenzonorbornene (**5**) and lack of stereoselectivity in reaction of *syn*-7-bromonorbornene (**11**)[20] suggest little difference in the abilities of ethano and etheno bridges of norbornene-like structures to bind to magnesium.

A radical mechanism for formation of 7-benzonorbornadienyl Grignard reagents must proceed at the metal surface rather than in solution. Tri-*n*-butyltin deuteride reductions of *anti*-Br and *syn*-Br, which proceed by a free-radical chain mechanism, give identical mixtures of 57% syn- and 43% anti-deuterated benzonorbornadiene.[16] Also, preparation of Grignard reagents by the NaNaph method proceeds via an alkyl free radical and perhaps an alkylsodium compound in solution.[18] Although the lifetimes of the 7-benzonorbornadienyl free radical and 7-benzonorbornadienylsodium under the NaNaph/MgX_2 conditions are not known, the lack of stereoselectivity in all such experiments in Table I must be due to rapid configurational inversion of one or both of them.

If *anti*-Br, *anti*-Cl, and **5** react with magnesium by the same mechanism as other alkyl halides, why do only they give high retention of configuration? We hypothesize that two major factors are involved.

First, the 7 position of benzonorbornadiene is strained. The average C_1–C_7–C_4 bond angle in norbornyl compounds studied by diffraction methods is 94°.[24] The ^{13}C–^1H coupling constants in the ^1H NMR spectrum of benzonorbornadiene are 134.6 and 136.2 Hz for the syn-7 and anti-7 protons, respectively,[25] which imply that the exocyclic carbon orbitals of the C–H bonds are $sp^{2.7}$ hybrids. Recent ESR studies suggest that 7-norbornenyl[26] and 7-benzonorbornadienyl[27] radicals are pyramidal rather than planar, presumably because of the high s character in the exocyclic carbon orbitals. The high s character should slow the rate of configurational inversion at C_7 in the 7-benzonorbornadienyl radical just as it causes high inversion barriers in analogous 7-azabenzonorbornadienes.[28] The inversion barrier cannot be high enough to prevent complete equilibration of the anti and syn radicals in solution, but it might still affect reaction of the radicals bound to a magnesium surface.

Second, there is a substantial difference in steric hindrance to approach of the anti- and syn-7 faces of benzonorbornadienyl halides to the magnesium surface. The argument that high s character slows configurational inversion of pyramidal radicals applies even better to Grignard formation from 1-bromo-1-methyl-2,2-diphenylcyclopropane (**4**) which proceeds with 18% retention of configuration.[6] However, the strengths of binding of the two enantiomeric pyramidal radicals from **4** to the metal are equal. Our hypothesis suggests that other alkyl halides which meet the requirements, (a) high s character in the carbon orbital of the carbon–halogen bond and (b) a substantial difference in hindrance to binding of the two isomers to the metal surface, may also form Grignard reagents with high retention of configuration.

The results of expt 30–32 in which Grignard reagents were prepared from *anti*-Br in THF-d_8 are most puzzling. Even though only about 0.02 atom excess D was incorporated into benzonorbornadiene using THF-d_8 and H_2O hydrolysis, THF still is the most intuitively likely source of hydrogen to account for the undeuterated **2** in THF/D_2O experiments. If this intuition is right, the results indicate a kinetic isotope effect of ≥60 for reaction of solvent with some intermediate benzonorbornadienyl species. Such a large isotope effect could occur only if hydrogen atom or proton transfer proceeded by a quantum mechanical tunneling mechanism, or by a multistep mechanism which would cause the experimental isotope effect to be a product of two or more primary kinetic isotope effects.

Experimental Section

General. Microanalyses were performed by J. Nemeth and associates. All temperatures, including melting points, are uncorrected. Infrared spectra were obtained either as a thin film between sodium chloride plates on Perkin-Elmer Model 137 or Model 237B instruments or as a potassium bromide pellet on Perkin-Elmer Model 521 or Beckman IR-12 instruments. Routine ^1H NMR spectra were obtained on Varian T-60, A-60A, A-56/60, or HA-100 spectrometers. The HA-100 equipped with a Hewlett-Packard Model 200ABR audio oscillator was used for decoupling experiments. Mass spectra were recorded on a Varian-MAT CH-5 mass spectrometer.

Analytical and Preparative GLC. Unless stated otherwise, analyses were performed with a 4 ft × 0.125 in. 20% Apiezon L on 60/80 Chromosorb W column at a He flow rate of 20 ml/min and 155 °C on a Hewlett-Packard Model 700 instrument equipped with a thermal conductivity detector. Naphthalene and *n*-tetradecane were used as internal standards. The thermal conductivity response factor per unit weight [(weight compd) (area standard)/(area compd) (weight standard)] of benzonorbornadiene (**2**) to naphthalene is 1.01, of **2** to n-$C_{14}H_{30}$ is 1.23, of *anti*-7-chlorobenzonorbornadiene (**1a**) to naphthalene is 1.19, and of *anti*-7-bromobenzonorbornadiene (**1c**) to naphthalene is 1.57. These response factors are averages of at least three determinations. The response factors of **1a** to n-$C_{14}H_{30}$ and **1c** to n-$C_{14}H_{30}$ calculated from these values are 1.45 and 1.91, respectively. The response factors of deuterated **2**, *syn*-Cl (**1b**), *syn*-Br (**1d**), and benzonorbornene are assumed to be the same as those for **2**, **1a**, **1c**, and **2**, respectively. Preparative GLC purifications of **2** were performed on a Varian Model A-90-P instrument at 200° on either a 0.25 in. × 10 ft 20% Apiezon L on 60/80 Chromosorb W column or a 0.375 in. × 10 ft 20% Apiezon L on 60/80 Chromosorb W column.

Materials. Unless noted otherwise Baker reagent grade magnesium turnings were washed with benzene and dried overnight under nitrogen at 120 °C, and tetrahydrofuran was distilled from the sodium ketyl of benzophenone just before use. Hexamethylphosphoramide, 1,2-dibromoethane, and 1,2-dichloroethane were distilled from calcium hydride under nitrogen. Tetrahydrofuran-d_8 was Merck Sharp & Dohme minimum 99% D, analyzed by mass spectrometry in our laboratory to contain 7% d_7 and 93% d_8 species. By ^1H NMR the residual protium was 21% at the α position and 79% at the β position. *anti*-7-Bromobenzonorbornadiene (**1c**),[12] *anti*-7-chlorobenzonorbornadiene (**1a**),[29] *anti*-7-bromobenzonorbornene (**5**),[13] and 7-oxabicyclo[2.2.1]heptane[30] were prepared by literature methods.

***syn*-7-Chlorobenzonorbornadiene (1b).** The literature method[31] for acetophenone-sensitized photolysis of *anti*-7-benzonorbornadienol after removal of solvent and evaporative distillation gave a 68% yield of a mixture of two compounds: the expected *exo*-tetracyclo[5.4.0.$0^{2,4}$.$0^{3,6}$]undeca-1(7),8,10-trien-5-ol and another tentatively identified as *syn*-7-benzonorbornadienol by similarity of ir and ^1H NMR spectral frequencies to those reported earlier.[31] Treatment of this mixture with thionyl chloride in ether by the literature method[31] gave a 47% yield of **1b** after sublimation at 40–50 °C (0.03 Torr) and

recrystallization from hexane: mp 57.5–58.5 °C (lit.[32] mp 59.0–59.5 °C). Its ^{1}H NMR spectrum agreed with a previous report.[19c] Ir (KBr) 6.87 (m), 7.73 (m), 7.90 (m), 11.50 (m), 11.68 (m), 12.40 (s), 13.00 (s), 13.85 (m), and 14.53 μ (s).

***syn*-7-Bromobenzonorbornadiene (1d).** By a method suggested earlier[31,33] a solution of 5.16 g (23.4 mmol) of *anti*-Br and 500 mg of acetophenone in 250 ml of freshly distilled, nitrogen-purged benzene was photolyzed in a Rayonet reactor at 3500 Å for 360 h. The reaction was followed by ^{1}H NMR in which the 7-H of *syn*-Br appeared at δ 4.38 and the 7-H of *anti*-Br at δ 4.15. The solvent was removed under vacuum, and the resultant yellow oil was crystallized from petroleum ether (bp 30–60 °C). Recrystallization gave 1.91 g (8.65 mmol, 37.0%) of **1d**, mp 59.5–61.5 °C. Molecular distillation of the recrystallization mother liquors at 75–125 °C (0.5–0.6 Torr) followed by recrystallization from petroleum ether yielded an additional 0.59 g (2.67 mmol, 11.8%) of **1d**, mp 57–59 °C (lit.[34] mp 61.1–61.7 °C) Ir[34,35] and ^{1}H NMR[34] spectra agreed with the literature. GLC analysis on an 0.125 in. × 4 ft 20% Apiezon L on 60/80 Chromosorb W column at 200 °C showed this material to contain <0.5% of *anti*-Br.

Exclusion of Water and Oxygen from Grignard Reactions. All preparations were run under dry nitrogen at slightly above atmospheric pressure. All deuterolyses were performed under nitrogen at room temperature (23–25 °C). All solvents, solutions, and liquid reagents were transferred by syringes which were dried at 160 °C and stored in a desiccator. Grignard reactions were performed in 14/20 standard taper glassware that consisted of a three-neck round-bottom flask, magnetic stirring bar, condenser, addition funnel, and rubber septum. All but the septum were dried at 160 °C overnight and then flame dried under a dry nitrogen flow. The alkyl halides were vacuum dried and weighed into oven-dried vials. They were dissolved in THF under nitrogen and transferred to the addition funnel by syringe.

Typical Procedure for Grignard Preparations with Magnesium Turnings (Expt 16–18). To 0.55 g (22.6 mg-atoms) of magnesium turnings under 5 ml of THF, 0.212 g (1.13 mmol) of 1,2-dibromoethane was added dropwise at a rate which maintained reflux. Another 7 ml of THF was added, the mixture was refluxed for 1–2 h, and 0.250 g (1.13 mmol) of *anti*-Br in 3 ml of THF was added dropwise in 2–5 min at reflux. After the additional heating time indicated in Table I the mixture was cooled to room temperature, 5 ml of D_2O was added, and the mixture was stirred for at least 15 min.

This procedure was used on scales of 0.25–2.25 g of **1c**, 0.10 g of **1a** and **1b**, and 0.60 g of **1d**. Progress of the reaction was followed by quenching a 5–10-μl aliquot of the reaction mixture in saturated NH_4Cl (aqueous) and analyzing an ether extract by GLC. Naphthalene (ca. 100 mg) was added to the deuterolyzed mixture as an internal standard for the GLC analysis, and the excess Mg was destroyed with 3 ml of saturated NH_4Cl (aqueous). The phases were separated, and the aqueous phase was extracted with several portions of ether. The combined ethereal extracts were washed with saturated NaCl (aqueous), dried ($MgSO_4$), and concentrated to about 2 ml. Yield was determined by GLC analysis of the concentrate, and **2** was isolated by preparative GLC. By the method of Cristol and Noreen,[16] a 10% molar excess of 1,3-diphenylisobenzofuran was added to **2** and heated in a sealed tube at 120 °C for 20 h. The adduct (**6**) was recrystallized one or two times from ethanol/chloroform, vacuum dried, and analyzed for deuterium content.

Typical Procedure for Grignard Preparations from Activated Magnesium (Expt 21–24). This procedure is based on the method of Rieke and co-workers.[14] A solution of 0.565 g (3.00 mmol) of 1,2-dibromoethane in 5 ml of THF was added dropwise with stirring to 153.6 mg (6.3 mg-atoms) of magnesium turnings in 10 ml of THF at a rate which maintained reflux, and the mixture was refluxed for another 1–2 h. Freshly cut potassium metal (217 mg, 5.54 mg-atoms) was added, and the mixture was refluxed for 2 h to produce a gray suspension of activated magnesium. After cooling to room temperature, 0.50 g (2.26 mmol) of *anti*-Br in 5 ml of THF was added and the progress of the reaction was checked by GLC. The reaction was usually complete in 3–7 h. In expt 22, naphthalene was added as an internal GLC standard, and half of the reaction mixture was removed by syringe and quenched in D_2O. The remaining half was refluxed for 4 h, cooled to room temperature, and quenched with D_2O. Products from each half of the reaction were isolated independently in the manner described for mgnesium turning experiments. Experiments 23 and 24 were done similarly, except that the naphthalene was added to each aliquot after removal and quench.

Typical Procedure for Grignard Preparation from Magnesium Halide and Sodium Naphthalenide (Expt 4, 5, 14, 15, 26). A. Standard Magnesium Halide Solutions. A solution of 1.5 g (15 mmol) of 1,2-dichloroethane in 10 ml of THF was added dropwise with stirring to 730 mg (30.0 mg-atoms) of magnesium turnings in 10 ml of THF at a rate which maintained reflux. Another 30 ml of THF was added, and the mixture was filtered under nitrogen through a course porosity sintered glass frit into a dry flask. Typical quantities used in preparing the analogous $MgBr_2$/THF solutions were 4.51 g (24.0 mmol) of 1,2-dibromoethane, 1.22 g (50.0 mg-atoms) of Mg, and a total of 80 ml of THF. This resulted in a saturated $MgBr_2$/THF solution as indicated by a white, crystalline precipitate. Molarities of these solutions (typically 0.30 M $MgCl_2$ and 0.23 M $MgBr_2$) were determined by both EDTA titration of Mg^{2+} and Ag^+ titration for X^-, which indicated that the reactions were quantitative.

B. Sodium Naphthalenide (NaNaph) Solutions. A large excess of sodium metal was added to 3.84 g (30.0 mmol) of naphthalene in 30 ml of THF. The solution turned green within seconds after the addition of the sodium and was stirred for 2–10 h. The green solution was separated from the excess sodium and transferred to a dry flask under nitrogen by syringe. The solution was analyzed by quenching an aliquot in ethanol and titrating with standard HCl (aqueous) solution to the bromcresol green end point.[36] NaNaph was usually 0.7–0.9 M. Only fresh solutions of NaNaph worked satisfactorily. Solutions aged for 1 week or more still showed the same total base concentration, but failed to consume all the starting halide in the Grignard preparations.

C. Grignard Preparations. By the method of Bank and Bank,[15] 1.3 mmol of NaNaph from a standardized solution was added dropwise with stirring at room temperature to a solution prepared from 100.0 mg (0.57 mmol) of *anti*-Cl in 0.4 ml of THF and 0.75 mmol of standardized $MgCl_2$ solution. In the case of *anti*-Br 250 mg (1.13 mmol) of *anti*-Br, 1.7 mmol of $MgBr_2$, and 2.67 mmol of NaNaph were used. The solution was stirred for about 15 min after the addition was complete, quenched with D_2O, and stirred for at least 15 min. The product **2** was isolated in the usual manner using ca. 150 or 250 mg of n-$C_{14}H_{30}$ as the internal GLC standard rather than naphthalene.

Procedural Variations in Specific Experiments. In Table I, 65 °C refers to refluxing THF and 25 °C means room temperature. Times refer to time after addition of the alkyl halide was complete. In experiments with more than one data point a single reaction mixture was prepared and aliquots were withdrawn by syringe at the times indicated. The reaction mixture was chilled briefly in an ice bath before sample withdrawal, and heating was resumed immediately afterward. In reactions of chlorides **1a** and **1b**, 1,2-dichloroethane, rather than 1,2-dibromoethane, was used to precondition the magnesium turnings or to generate the $MgCl_2$ from which activated magnesium was prepared.

Expt 3. 7-Oxabicyclo[2.2.1]heptane was used as solvent in place of THF.

Expt 6. The $MgCl_2$ was omitted from the NaNaph procedure.

Expt 7. A Grignard solution was prepared from *anti*-Cl and Mg turnings by the standard procedure and cooled to room temperature. Standard NaNaph solution (2.5 equiv) was added, the mixture was stirred for 15 min, and deuterolysis was carried out by the standard procedure. .

Expt 8, 9. After the standard $MgCl_2$/NaNaph treatment the reaction mixture was refluxed for 24 h before deuterolysis.

Expt 25. Turnings from Dow singly sublimed magnesium crystal rather than reagent grade magnesium turnings were used.

Expt 30, 32. THF-d_8 (see Materials section) rather than THF was used and H_2O rather than D_2O was used for hydrolysis.

Expt 31. The solvent was THF-d_8. An aliquot was removed after 30 min at reflux and hydrolyzed with D_2O. The remaining solution was refluxed for 240 h and hydrolyzed with H_2O.

Benzonorbornadiene Dimer 9 (Expt 21). The usual activated magnesium with 1.00 g (4.52 mmol) of *anti*-Br was used. No naphthalene was added. After the usual extractions the solvent was removed under vacuum and replaced with hexane. The hexane solution was chromatographed on 100 g of silica gel taking 25-ml fractions. Fractions 1–80 were eluted with hexane, 81–150 with 1% ether in hexane, 151–200 with 2% ether in hexane, 201–250 with 5% ether in hexane, and 251–300 with 10% ether in hexane. Fractions 1–30 contained **2** and were combined and concentrated to a solution weighing 0.6728 g. By GLC analysis, the area of **2** compared to the total area of **2** and the solvent peak was 78%, which corresponds to a yield of 525 mg (82%). This solution was treated with 1.0 g (3.7 mmol) of 1,3-diphenylisobenzofuran and adduct **6** was purified in the usual manner.

Fractions 40–80 were combined and evaporated to dryness to yield 36.5 mg (0.130 mmol, 5.7%) of dimer **9**: ^{1}H NMR (CCl_4) δ 2.00 (broad d, 1 H, J = 10 Hz), 2.78 (broad d, 1 H, J = 10 Hz), 3.32–3.64 (broad m, 4 H), 6.42–6.60 (m, 4 H), 6.60–7.16 (m, 8 H); ir (KBr) 1448 (m), 1300 (m), 1285 (m), 757 (s), 727 (s), 682 (s), and 632 cm^{-1} (m); mass spectrum (70 eV) *m/e* (rel intensity) 284 (0.81), 283 (4.05), 282 (16.38), 281 (5.24), 167 (15.83), 155 (5.85), 154 (36.46), 153 (28.72), 142 (13.62), 141

(100.00), 128 (26.15), 115 (20.82). Other column fractions yielded no identifiable products.

Hexamethylphosphoramide Treatment and Carbonation of Grignard Reagent from *anti*-Br (Expt 20). The Grignard reagent was prepared from 2.25 g (10.2 mmol) of *anti*-Br and magnesium turnings in 70 ml of THF. A 7-ml aliquot was removed and quenched in D_2O, and a 20-ml aliquot was removed and injected into a flask of freshly powdered dry ice. As quickly as possible, 8 ml (45.7 mmol) of HMPA was added to the remaining Grignard solution. An 8.3-ml aliquot was removed and quenched in D_2O, a 23.7-ml aliquot was removed and quenched in dry ice, and 1.0 g (9.3 mmol) of chlorotrimethylsilane was added to the remaining 19 ml of solution. The deuterolyzed mixtures were purified in the usual manner. The chlorotrimethylsilane mixture was stirred overnight, saturated NH_4Cl solution was added to destroy excess magnesium, the phases were separated, the aqueous phase was extracted with ether, and the ether extracts were dried ($MgSO_4$). Analysis by GLC showed four peaks in the volatility range expected for 7-trimethylsilylbenzonorbornadienes, so no further isolation was attempted.

After warming to room temperature, water was added to the mixture carbonated without HMPA and it was acidified with concentrated HCl. The aqueous phase was extracted with several portions of ether, and the combined ether phases were extracted with three 50-ml portions of 1 N NaOH. The combined NaOH extracts were washed with ether, acidified, and extracted with ether. The ether was evaporated and the resultant solid was vacuum dried to yield 56.0 mg (0.301 mmol, 10.3%) of 7-benzonorbornadienecarboxylic acids. The acids were esterified by refluxing overnight in 5 ml of methanol with 0.1 ml of concentrated H_2SO_4. Addition of water followed by ether extraction and evaporation gave 46.6 mg (0.233 mmol, 78%) of 7-carbomethoxybenzonorbornadienes (**7** and **8**). The aliquot that was carbonated after addition of HMPA was treated in an analogous manner to give 35.0 mg (0.188 mmol, 6.5%) of 7-benzonorbornadienecarboxylic acids and 24.1 mg (0.121 mmol; 64.5%) of **7** and **8**. GLC analyses of these samples on a 0.125 in. × 4 ft 10% FFAP on 60/80 Chromosorb G column at 200 °C showed anti/syn ratios of esters of 6.8 and 3.0, respectively, for the carbonations with and without HMPA. The structures of **7** and **8** were confirmed by comparison of their GLC properties and NMR spectra with those of known samples (vide infra).

Deuterium Analyses. Mass spectra of adduct **6** were run at ca. 8.5 eV to minimize fragmentation. The data were processed as follows. Let P_0 = peak height of parent peak of **6** at *m/e* 412 and P_1 = peak height of peak at *m/e* 413. The experimentally measured natural abundance P_1/P_0 ratio was 0.3485 (theory, 0.3348). Thus atom excess $D = [P_1 - (0.3485)(P_0)]/[P_1 - (0.3485)(P_0) + P_0]$. Duplicate analyses of three different samples gave values which never differed by more than 0.008 atom excess D.

^1H NMR spectra of **6** in $CDCl_3$ were obtained on a Varian HA-100 spectrometer using either Me_4Si or CH_2Cl_2 for the lock signal. The spectra were integrated five times and the deuterium incorporation was determined from the sum of the five integrals for each adsorption as follows. Let H_a = the area for protons H_a (δ 2.45) in **6**, H_b = the area for protons H_b (δ 3.04), H_c = the area for proton H_c (δ 1.27), and H_d = the area for proton H_d (δ 2.88). Three spectra of two independently prepared all-protio samples of **6** were run. Using a Me_4Si lock H_c and H_d integrated on the average to 1.05 ± 0.05 protons when the total areas for H_a and H_b divided by 4 was considered equal to the area per proton. Using this correction factor

$$\text{atom excess D syn} = 1 - \left[\frac{H_c}{(H_a + H_b)/4}\right]\left[\frac{1}{1.05}\right]$$

$$\text{atom excess D anti} = 1 - \left[\frac{H_d}{(H_a + H_b)/4}\right]\left[\frac{1}{1.05}\right]$$

With a CH_2Cl_2 lock, the corresponding correction factors were 1.01 for the syn position and 1.04 for the anti position. Occasionally ^1H NMR analyses gave total deuterium content which differed from the mass spectral analysis by >0.10 atom excess D. In such cases the ^1H NMR analyses were repeated and closer agreement with mass spectrometry was found. However, we do not claim that the ^1H NMR analyses are any better than ±0.05 atom excess D at each position.

***anti*-7-Carbomethoxybenzonorbornadiene (7).** At −78 °C 1.82 ml of 1.9 M *sec*-butyllithium (Alfa) was added to a solution of 601.5 mg (2.73 mmol) of *anti*-Br in 24 ml of dry ether. The solution was allowed to warm to 0 °C, was cooled back to −78 °C, and was added by syringe to freshly crushed dry ice. After the carbonated mixture had warmed to room temperature, the phases were separated, and the aqueous phase was extracted with several portions of ether. The combined ethereal extracts were extracted with two 60-ml portions of 1 N NaOH. The NaOH extracts were washed with ether and acidified with HCl. The precipitated carboxylic acid (200 mg) was filtered, vacuum dried, and esterified by refluxing in 10 ml of methanol with 0.25 ml of concentrated H_2SO_4 for 23 h. After the addition of 40 ml of ice water, the solution was extracted with several portions of CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with saturated NaCl, dried ($MgSO_4$), and evaporated to 216.7 mg of dry solid. Preparative GLC on a 0.25 in. × 10 ft 20% SE-30 on 60/80 Chromosorb W column at 210 °C gave 95.9 mg (0.48 mmol, 17.6%) of **7**. Only one minor component (1.2%) of comparable retention time could be seen by preparative GLC, but it was not isolated. No impurities or other isomers could be detected in the purified product by GLC analysis on a 0.125 in. × 4 ft 10% FFAP on 60/80 Chromosorb G column at 200 °C: ir (KBr) 3020 (m), 1733 (s), 1455 (m), 1440 (m), 1350 (m), 1295 (m), 1247 (s), 1220 (s), 1180 (m), 1170 (m), 1020 (m), 1012 (m), 918 (m), 772 (s), 743 (s), and 709 cm^{-1} (s); mass spectrum (70 eV) *m/e* (rel intensity) 202 (0.21), 201 (3.18), 200 (23.51), 185 (5.12), 169 (13.34), 168 (71.40), 157 (6.04), 142 (13.38), 141 (100.00), 129 (19.71), 116 (6.46), 115 (51.69); ^1H NMR (CCl_4) δ 3.17 (t of t, 1 H, J = 1.75, 0.35 Hz), 3.53 (s, 3 H), 4.08 (q, 2 H, J = 1.83 Hz), 6.61 (t of d, 2 H, J = 1.95, 0.35 Hz), 6.96 (AA'BB', 4 H); irradiation at δ 6.61 converts the δ 3.17 absorption to a simple triplet, J = 1.75 Hz, confirming the anti configuration.

Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 78.01; H, 5.94.

Equilibration of *anti*- and *syn*-7-Carbomethoxybenzonorbornadienes (7 and 8). A mixture of 70.6 mg (0.40 mmol) of **7**, 0.20 ml of HMPA, and 0.8 ml of 0.53 M sodium methoxide in methanol was heated at 65 °C. Aliquots of 3–5 μl were removed and analyzed by GLC on a 0.125 in. × 4 ft 10% FFAP on 60/80 Chromosorb G column at 200 °C. After 165 h equilibrium was attained since there was no further change in the ratio of anti to syn esters up to 333 h, K_{eq} = [8]/[7] = 0.73. Least-squares analysis of the composition vs. time data plotted as a first-order rate process gave a straight line with slope = 3.415 × 10^{-4} min^{-1} = $k_f + k_r$, the sum of the forward and reverse rate constants. Thus k_f = 1.44 × 10^{-4} min^{-1} and k_r = 1.97 × 10^{-4} min^{-1}. ^1H NMR (CCl_4) of the equilibrium mixture showed both **7** (vide supra) and **8**: δ 3.26 (t, 1 H, J = 1.75 Hz), 3.33 (s, 3 H), 4.01 (q, 2 H, J = 1.92 Hz), 6.70 (t, 2 H, J = 2 Hz), 6.8–7.2 (AA'BB').

Grignard Reagent from *anti*-7-Bromobenzonorbornene (5). The general procedure with magnesium turnings was used with 1.00 g (4.48 mmol) of **5** and a reaction time of 5 min at reflux. The reaction mixture was hydrolyzed with 40 ml of D_2O, and the resultant benzonorbornene (79% by GLC) was isolated by preparative GLC under identical conditions with isolation of **2**. Deuterium analyses were carried out by mass spectrometry and by 220-MHz ^1H NMR using methods analogous to those described for **2**.

Registry No.—**1a**, 10239-89-1; **1b**, 14518-75-3; **1c**, 7605-10-9; **1d**, 22436-26-6; **2**, 4453-90-1; **2** (*7-d*), 31893-09-1; **5**, 7605-11-0; **6**, 58473-66-8; **7**, 58473-67-9; **8**, 58525-37-4; **9**, 14518-80-0; *anti*-7-benzonorbornadienol, 6991-42-0; magnesium, 7439-95-4; 1,2-dibromoethane, 106-93-4; sodium naphthalenide, 3481-12-7; 1,2-dichloroethane, 107-06-2; $MgCl_2$, 7786-30-3; $MgBr_2$, 7789-48-2; hexamethylphosphoramide, 680-31-9.

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Effects of a Remote Double Bond or Cyclopropane Ring on Electrophilic Aromatic Substitution[1]

Mark W. Galley and Roger C. Hahn*

Department of Chemistry, Syracuse University, Syracuse, New York 13210

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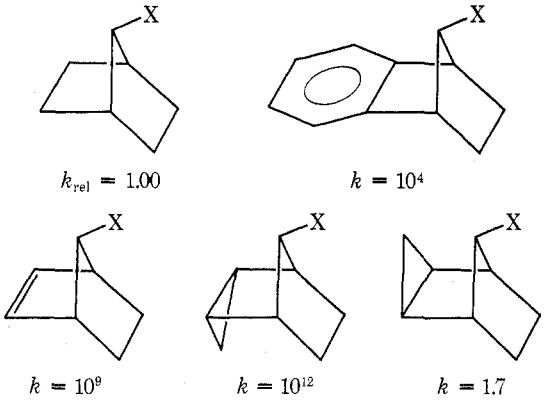
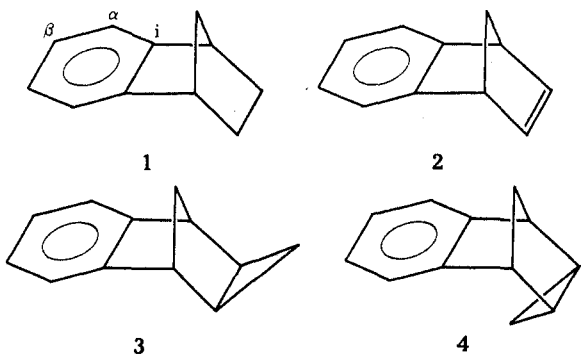
Relative positional reactivities have been determined for nitration of benzonorbornene (**1**), benzonorbornadiene (**2**), and the corresponding *exo*- and *endo*-benzotricyclo[3.2.1.$0^{2,4}$]octenes (**3** and **4**). For β positions, homoconjugation in **2** and **3** dominates over hyperconjugative effects; for α and ipso positions, inductive effects dominate. A "buttressed fused ortho effect" is proposed to account for the lower α reactivity of **3** than of **4**.

There is continued widespread interest in interactions between electron-deficient centers and remote (i.e., nonconjugated) double bonds, arenes, and cyclopropane rings.[2] However, little attention has been turned to the effects of a remote double bond or cyclopropane ring on electrophilic substitution reactions of an aromatic ring; experimental approaches to determination of optimum geometries for such interactions have not been reported. Consideration of the literature on remote participation effects facilitated a choice of substrates for this type of study. As summarized recently,[2a] conformationally mobile molecules thus far have afforded no kinetic evidence of significant contributions from cyclopropane participation. In contrast, fusion of a cyclopropane ring into a rigid framework has produced some of the most dramatic solvolysis rate variations known, as exemplified by the group of compounds formulated below (X = brosylate or *p*-nitrobenzoate).[3]



It was anticipated, therefore, that kinetically detectable interaction between arene and remote cyclopropane (or double bond) moieties would be found in a study of the series of rigid structures **1–4**. Further impetus was given to this work by the discovery[4] that **1** undergoes detectable (~3%) ipso[5] (i) nitration; thus the influence of remote substituents might be accessible via measured reactivities at each of three distinct arene positions.



Results and Discussion

Benzonorbornadiene (**2**), prepared by established methods,[6] was converted to **1** by catalytic hydrogenation and to a 95:5 mixture of **3** and **4** by Simmons–Smith cyclopropanation.[7,8] Pure **3** was obtained by crystallization from the mixture; pure **4** was obtained by chromatography of the enriched mother liquor.

Certain features of the nitration study by Tanida and Muneyuki[9] were adapted to the present work; indan and tetralin were nitrated for comparison purposes, with the latter used as a standard (rel rate = 1.00) for computation of substrate reactivities. Because of the sensitivity of **2**, **3**, and **4** toward other nitrating agents, nitrations were performed with copper nitrate in acetic anhydride (0 °C). Product mixtures were subjected to VPC analysis; product distributions were checked against artificial mixtures of similar composition. Percentages of nitro compounds (α and β) for **1**, indan, and tetralin were nearly identical with those previously re-