This compound was synthesized from **1b** (90%): mp 88–90 °C (ether); $[\alpha]_D$ −183° (*c* 0.80, $CHCl_3$); IR (KBr) 2930, 1460, 1430, 1175, 1130, 1060 cm^{-1}; MS *m/z* 438 ($M^+ + 1$), 437 (M^+), 380 (100), 117 (51), 73 (95). Anal. Calcd for $C_{21}H_{31}O_3NS_2Si$: C, 57.63; H, 7.14; N, 3.19; S, 14.65. Found: C, 57.90; H, 7.23; N, 2.99; S, 14.35.

Methyl 2,3,4-Trideoxy-6-*O*-(*tert*-butyldimethylsilyl)-2-*S*-(2-benzothiazolyl)-2-thio-α-D-*threo*-hex-3-enopyranoside (4b). This compound (85%) was synthesized from **1d**: $[\alpha]_D$ −23° (*c* 0.9, $CHCl_3$); IR (film) 2940, 2860, 1465, 1430, 1255, 1115, 1060 cm^{-1}; MS *m/z* 424.4 ($M^+ + 1$), 423.4 (M^+), 366 (67), 73 (100). Anal. Calcd for $C_{20}H_{29}O_3NS_2Si$: C, 56.70; H, 6.90; H, 3.31; S, 15.14. Found: C, 56.90; H, 7.02; N, 3.27; S, 14.98.

General Procedures for the Reaction of (Allyloxy(thio))benzothiazole Derivatives with Organocopper Reagents. (A) The Grignard reagent was prepared in diethy ether (5 mL) from Mg (3.07 mmol) and MeI (3.07 mmol). This solution was cooled to −30 °C, and CuI (1.5 mmol) was added in one portion under argon. Stirring was continued during 30 min at −30 °C, and then a solution (15 mL) of the substrate (1.06 mmol) in ether was added; the mixture was allowed to warm slowly to room temperature and stirred for 6 h. The reaction was diluted with diethyl ether and treated with concentrated aqueous NH_4Cl and a few drops of NH_4OH, while vigorously stirring, to obtain a green suspension in a blue aqueous solution. The two layers were separated, and the ethereal phase was filtered and dried over anhydrous sodium sulfate and concentrated in vacuo. The residue was directly desilylated with tetrabutylammonium fluoride (4 mmol) in THF (20 mL). After 2 h at room temperature, the mixture was diluted with diethyl ether (20 mL) and washed with water (10 mL). The organic layer was dried ($MgSO_4$) and evaporated. Column chromatography of the residue (hexane–ethyl acetate, 7:3) yielded the product.

(B) CuI (1.5 mmol) was added to a solution of the substrate (1.06 mmol) in diethyl ether (15 mL) at 0 °C under argon. After 30 min the Grignard reagent (3.07 mmol), prepared in Et_2O, was then added dropwise with stirring. After 1 h the reaction was worked up as above.

Identical procedures were followed by changing diethyl ether to THF, stoichiometric amounts of CuI to catalytic amounts (5%), and $IMgCH_3$ to MeLi. We also tested the effect of substituting CuI by CuBr. In no case these changes have an appreciable effect on the final products.

Ethyl 2,3,4-Trideoxy-2-*C*-methyl-α-D-*erythro*-hex-3-enopyranoside (3a). This compound was synthesized from **2a** (68%): $[\alpha]_D$ +21.9° (*c* 0.42, $CHCl_3$); IR (film) 3435, 2975, 1660, 1455 cm^{-1}. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.93; H, 9.45.

Ethyl 2,3,4-Trideoxy-2-*C*-methyl-α-D-*threo*-hex-3-enopyranoside (3b). This compound was synthesized from **2b** (70%): $[\alpha]_D$ +194° (*c* 0.3, $CHCl_3$); IR (film) 3440, 2980, 2880, 1660, 1455, 1370, 1190, 1115 cm^{-1}. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.86; H, 9.48.

Methyl 2,3,4-Trideoxy-4-*C*-methyl-α-D-*erythro*-hex-2-enopyranoside (5a). This compound was synthesized from **4a** (68%): $[\alpha]_D$ +89.2° (*c* 0.42, $CHCl_3$); IR (film) 3430, 2970, 1660, 1400, 1185, 1100 cm^{-1}. Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.87; H, 8.97.

Methyl 2,3,4-Trideoxy-4-*C*-methyl-α-D-*threo*-hex-2-enopyranoside (5b). This compound was synthesized from **4b** (72%): $[\alpha]_D$ −10.9° (*c* 0.25; $CHCl_3$); IR (film) 3430, 2970, 1660, 1400, 1120 cm^{-1}. Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.93. Found: C, 60.95; H, 9.05.

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Registry No. **1a**, 23339-15-3; **1b**, 58888-62-3; **1c**, 51385-38-7; **1d**, 124944-63-4; **2a**, 124944-64-5; **2b**, 124944-65-6; **3a**, 124944-68-9; **3b**, 124944-69-0; **4a**, 124944-66-7; **4b**, 124944-67-8; **5a**, 124944-70-3; **5b**, 124944-71-4; tri-*O*-acetyl-D-glucal, 2873-29-2; methyl 2,6-di-*O*-benzoyl-α-D-glucopyranoside, 26927-44-6; 2-chlorobenzothiazole, 615-20-3; 2-mercaptobenzothiazole, 149-30-4.

Solvation and Steric Effects on Electrophilic Reactivity of Ethylenic Compounds. 1. Stereochemistry and Bromination of Congested Adamantylidenealkanes

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In order to evaluate the dependence of the steric effects of alkyl groups on the crowding of the double bond, bromination rate constants of adamantylidenealkanes **1**, Ad=CRR′ with R = H or Me and R′ = H, Me, *i*-Pr, *t*-Bu, or *neo*-Pe, and similarly substituted isopropylidenealkanes **2**, Me_2C=CRR′, are compared. Since the bromination rate of **1a** (R = R′ = H) is that expected by considering only the polar effect of two *gem*-isopropyls, the adamantyl group in **1**, like the *gem*-methyls in **2**, clearly does not exhibit any intrinsic steric effect. However, branched substituents R′ slow the reaction of **1** twice as much as that of **2**. This difference between the effects on **1** and **2** does not arise from differences in the stereoarrangement of R and R′ since, according to MM2 calculations, they adopt exactly the same conformation in both alkene series. Comparison of the bromination rates of **1** in methanol with those measured in acetic acid reveals that the solvent effect (k_{MeOH}/k_{AcOH} about 4) is markedly smaller than that (k_{MeOH}/k_{AcOH} = 25) on linear alkenes, which suggests that greater steric retardation in adamantylidenealkanes can be attributed to mechanistic changes: inhibition of nucleophilic solvent assistance in the ionization step and/or return resulting from a slow product-forming step.

That there is no general method of describing steric effects quantitatively severely limits the scope of structure–reactivity relationships for the quantitative analysis and prediction of reactivity data, as well as for the un-

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derstanding of mechanisms.[1,2] Neither the earlier approaches based on steric parameter scales[2,3] nor more recent methods such as force field calculations[2,4] or topological treatments[2,5] give satisfactory results over wide reactivity ranges. Most of the difficulties arise from the fact that, because of nonbonded interactions which vary along the reaction pathway, kinetic steric effects are not additive.

Among the numerous reactions whose sensitivity to steric effects has been investigated, electrophilic addition to olefins is of particular interest since up to four branched substituents can interact mutually and with the entering electrophile.[6] It is well known, for example, that steric effects considerably retard the bromination of alkenes with branched alkyl substituents.[7,8] The rate reduction is noticeable, even when the double bond bears only one moderately bulky group: 3-methyl-1-butene, iPrCH=CH_2, reacts in methanol 1.7 times more slowly than 1-butene.[7] The effect is significantly more important in tetrasubstituted alkenes:[8] from 2,3-dimethyl-2-butene, Me_2C=CMe_2, to 2,3,4-trimethyl-2-pentene, iPrMeC=CMe_2, the rate falls by a factor of 9. The limit, where steric effects totally inhibit any reaction of the double bond with bromine, is reached for alkenes which do not appear very highly congested, such as tetraisobutyl-[9] or tetraisopropylethylene.[10]

Not only steric but also polar effects of alkyl groups contribute to the bromination rates.[11] The additive polar contribution is easily determined by the previously established equation[12] (eq 1) where log k_0 is 6.89 in methanol,[12] 13.8 in water,[13] and 5.51 in acetic acid,[14] and d = 1 for *gem*-disubstituted and trisubstituted alkenes and d = 0 for the others. The steric contribution[6] can then be estimated from the difference between the experimental rate constant and that predicted by eq 1. Numerous attempts have been made to analyze the steric effects on bromination rates quantitatively by various methods, in particular, steric parameter scales which work more or less satisfactorily for alkenes involving only one bulky substituent.[7,8] Relationships valid for limited sets of data have thus been obtained. For example, Grosjean et al. found for the reactivity of 15 tetrasubstituted alkenes a fairly good correlation with Hancock's E_s^c (eq 2), erroneously suggesting that poiar effects are negligible in the bromination of these olefins.[8] The failure of the Taft type analysis is not unexpected since interactions between the entering bromine and the double bond substituents are probably the main rate-controlling factors.

$$(\log k)_{pol} = -3.03\sum\sigma^* + 0.43d + \log k_0 \quad (1)$$

$$\log k = 1.29\sum E_s^c + 6.32 \quad (2)$$

Table I. Rate Constants[a] for Free Bromine Addition to Adamantylidenealkanes 1 in Methanol and in Acetic Acid at 25 °C

			k,[b] M^{-1} s^{-1}	
1	R	R′	MeOH	AcOH
a	H	H	4.2×10^5	4.8×10^4
b	H	Me	1.6×10^6	
c	H	Et	1.2×10^6	
d	H	*i*-Pr	8.3×10^4	
e	H	*t*-Bu	1.6×10^3	7.0×10^2
f	H	*neo*-Pe	9.1×10^3	
g	Me	Me	2.5×10^7	8.2×10^6
h	Et	Et	2.9×10^6	
i	Me	*i*-Pr	5.7×10^5	1.9×10^5
j	*i*-Pr	*i*-Pr	*c*	*c*

[a] Obtained by extrapolation to zero bromide ion concentration from measurements in the presence of sodium bromide (methanol) or lithium bromide (acetic acid). [b] To ±4%. [c] No reaction.

A rational approach to understanding steric effects on electrophilic addition should, therefore, be based on a stereochemical analysis of branched alkenes in order to identify the most favorable conformations for electrophilic attack and, then, to estimate their stabilities and the rotational barriers for conformational exchange. Unfortunately, experimental data on this topic, which calls for dynamic NMR and crystallography, are scarce;[15a] empirical force field calculations are more accessible[15b] but have mainly been applied to highly congested alkenes, tetraisopropylethylene[16] or the elusive tetra-*tert*-butylethylene,[17] which do not react with bromine. Recently, the static and dynamic stereochemistry of five alkenes bearing four primary alkyl groups has been investigated experimentally and theoretically.[9] These first results are of interest; for example, a barrier of 8.6 kcal mol^{-1} to the rotation of one isobutyl group has been measured in solution, in agreement with the MM2 calculated value. It is, however, too early to apply this method extensively to the interpretation of the numerous olefin bromination data.

To tackle this problem more simply, we chose to investigate the electrophilic bromination of conformationally locked alkenes **1**, derived from methylideneadamantane, **1a**. The adamantyl cage, the tied-back equivalent of two eclipsed *gem*-isopropyl groups, is so inflexible that substituents R and R′ are expected to adopt conformations probably different from and more constrained than those they have in acyclic isopropylidenealkanes **2** and **3**. The comparison of the effect of the branched group R on the bromination rates of **1**, **2**, and **3** should give information as to the relationship between the conformation of R and the reactivity of the double bond toward bromine.

Results

Olefins **1a–h** were synthesized from the corresponding tertiary alcohols[18] obtained by the reaction of adamantanone and the appropriate organolithium reagents, according to classical procedures.[19] **1i** and **1j** were prepared

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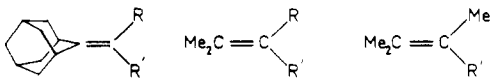


1 2 3

a, R = R′ = H; **b**, R = H, R′ = Me; **c**, R = H, R′ = Et; **d**, R = H, R′ = *i*-Pr; **e**, R = H, R′ = *t*-Bu; **f**, R = H, R′ = *neo*-Pe; **g**, R = R′ = Me; **h**, R = Et, R′ = Et; **i**, R = Me, R′ = *i*-Pr; **j**, R = R′ = *i*-Pr

by the McMurry method.[20]

Rate constants, k, for free bromine addition to **1a–i** in methanol and acetic acid are given in Table I; they have been obtained by extrapolating kinetic measurements carried out in the presence of added sodium bromide to zero bromide ion concentration.[21,22] In protic solvents, bromination leads not only to the usual dibromide but also to solvent-incorporated products whose formation releases bromide ions. These latter react with bromine rapidly, forming tribromide ions, according to eq 3. Since Br_3^- is

$$Br_2 + Br^- \rightleftharpoons Br_3^- \quad (3)$$

an electrophilic species, two brominating agents coexist in the medium so that kinetic experiments carried out by following the overall bromine uptake give only composite rate constants related to both free bromine and tribromide ion additions. To simplify the situation, bromination is followed in the presence of bromide ions in excess with respect to alkene and bromine, thus keeping the ratio Br_2/Br_3^- constant during the course of the reaction. The constants, k, for bromine addition and $k_{Br_3^-}$ for tribromide addition, are then obtained from bromide ion effects on the experimental rate constants, k_{exp}, by the following equation:

$$k_{exp}(1 + K[Br^-]) = k + Kk_{Br_3^-}[Br^-] \quad (4)$$

where K is the constant of eq 3. The constants k_{exp} at several bromide concentrations and k and $k_{Br_3^-}$ calculated from eq 4 are given in Table SI (see supplementary material). $k_{Br_3^-}$ is not necessarily related to a single process since it can include not only the tribromide addition but also the bromide medium effect or free bromine addition assisted by bromide ion, these being kinetically indistinguishable processes.[22,23] Consequently, only constant k, which is unambiguously related to free bromine addition unassisted by bromide, is considered in the following discussion.

In Table II, the log k values for the reaction of acyclic alkenes **2** in methanol are presented with those of **1**. The rate constants of **2**, k_{exp}, were previously obtained in methanol with 0.2 M added NaBr.[24] The data reported here result from extended kinetic measurements, as described above, and correspond to the constants k for unassisted free bromine addition. Steric contributions[6] of the branched substituents R and R′ to the bromination rates of alkenes **1** and **2** in methanol are also given in Table II. They have been estimated by subtracting the polar contributions (calculated by eq 1) from the experimental data.

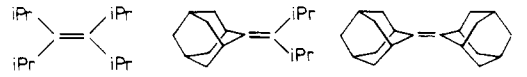
In Table III are collected the rate data[8] and the steric contributions of tetrasubstituted alkenes, **3**.

It has been observed that, in methanol, bromine does not add to alkene **1j**, the semi-tied-back analogue of tetraisopropylethylene. This result is not unexpected in view of the inertness of the highly crowded tetraneopentylethylene[25] and tetraisopropylethylene toward this electrophile.[9]

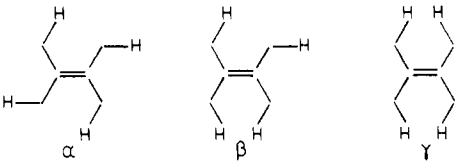
Molecular mechanics calculations (MM2 program) have been performed on alkenes **1** and **2**. For none of these is any distorsion of the ethylenic double bond plane observed. The most relevant geometrical feature of these alkenes is a noticeable pinching of the ethylenic bond angles. In **1**, and in **2** as well, the angle RCR′ between the substituents and that between the bonds involved in the adamantyl cage or between the two methyls of **2** is in the 112–115° range; it is as small as 111° in the case of the highly congested **1i** and **2i**. This angle pinching is not associated with a significant C=C nor =C—C bond elongation. Strain energies and some relevant dihedral angles are shown in Tables IV and V, respectively (data for the whole set of alkenes are given in Table SIV, supplementary material).

Discussion

Tetraisopropylethylene Analogues. The different behavior toward bromine of the three tetraisopropylethylenes, either non-tied-back, **4**, or semi-tied-back, **1j**, or totally tied-back adamantylideneadamantane, **5**, deserves comment. Molecular mechanics calculations on **4**, which does not react with bromine, reveal[16] a strong preference for the C_{2h} conformation, α (barrier to the rotation of one isopropyl group is about 15 kcal mol^{-1}). When two *gem*-isopropyls are locked as in **1j**, the stabler conformation becomes β but bromine attack is not easier. Finally, for **5** the sole conformation is γ and the electrophilic reactivity toward bromine is partially restored;[26] bromine adds to **5** in carbon tetrachloride, but the reaction stops at the formation of the bromonium–tribromide ion pair[27] insoluble in this solvent. Nucleophilic attack on this bromonium ion, usually the product-forming step, is totally inhibited; dissolution of the ion pair in methanol leads to the starting reagents.



4 1j 5



α β γ

Absence of Intrinsic Steric Effect of the Adamantyl Group in the Bromination of 1. Methylideneadamantane, **1a**, the least congested of series **1**, is highly reactive (log k = 5.62) as compared with its non-tied-back analogue,[6,14] *gem*-diisopropylethylene, **6**, (log k = 2.04). The polar contribution of two *gem*-isopropyls estimated by eq 1 is 5.53. There is, therefore, no steric contribution to the reactivity of **1a** whereas it is as great as −3.5 for the corresponding unlocked alkene.[6] Consequently, the adamantyl group does not exhibit any intrinsic steric effect in the bromination of **1a** whose reactivity arises only from

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Table II. Reactivity Data, log k, and Steric Contributions,[a] SterCo, to the Bromination Rates of Adamantylidenealkanes 1 and Isopropylidenealkanes 2 in Methanol at 25 °C

			1		2	
	R	R′	log k	SterCo	log k^b	SterCo
a	H	H	5.62	0	4.57	0
b	H	Me	6.20	−0.8	6.11	0
c	H	Et	6.08	−1.2	6.13	0
d	H	*i*-Pr	4.92	−2.6	5.66	−0.8
e	H	*t*-Bu	3.20	−4.7	5.22	−1.5
f	H	*neo*-Pe	3.96	−3.5	5.02	−1.3
g	Me	Me	7.40	−0.7	7.15	0
h	Et	Et	6.46	−2.2	6.46	−1.0
i	Me	*i*-Pr	5.75	−2.9	6.27	−1.2

[a] Obtained by subtracting the polar contribution, calculated by eq 1, from the experimental log k value. [b] The values given here correspond to the rate constants of free bromine addition; in refs 8 and 24, the rate constants are those experimentally obtained with 0.2 M added NaBr.

Table III. Reactivity Data, log k, and Steric Contributions,[a] SterCo, to the Bromination Rates of Trimethyl-R-ethylenes 3 in Methanol at 25 °C

R	log k^b	SterCo[a]
Me	7.15	0.0
Et	7.13	0.0
i-Pr	6.27	−1.2
t-Bu	6.23	−1.6
neo-Pe	4.61	−2.8

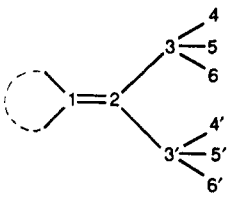
[a,b] See Table II.

Table IV. Strain Energies,[a] in kcal mol^{-1}, of Adamantylidenealkanes 1 and Isopropylidenealkanes 2

	1	2
a	12.34	−0.01
b	13.93	1.94
c	14.28	2.55
d	14.40	2.78
e	16.68	5.41
f	15.22	3.83
g	17.33	5.26
h	18.34	7.04
i	20.12	8.24

[a] Calculated by MM2.

Table V. Dihedral Angles $C_1C_2C_3X$ (X = H or C) in Some Adamantylidenealkanes 1 and Isopropylidenealkanes 2



	X	1	2
e	C_4	−62.6	−62.6
	C_5	180.0	180.0
	C_6	62.0	62.6
h	C_4	−87.8	−90.4
	H_5	150.3	147.7
	H_6	35.7	32.9
	C_4'	−87.8	−90.4
	H_5'	150.3	147.7
	H_6'	35.7	32.9
i	C_4	−89.3	−93.8
	C_5	145.3	140.9
	H_6	29.5	24.8
	H_4'	−76.0	−103.8
	H_5'	161.7	135.7
	H_6'	44.4	18.3

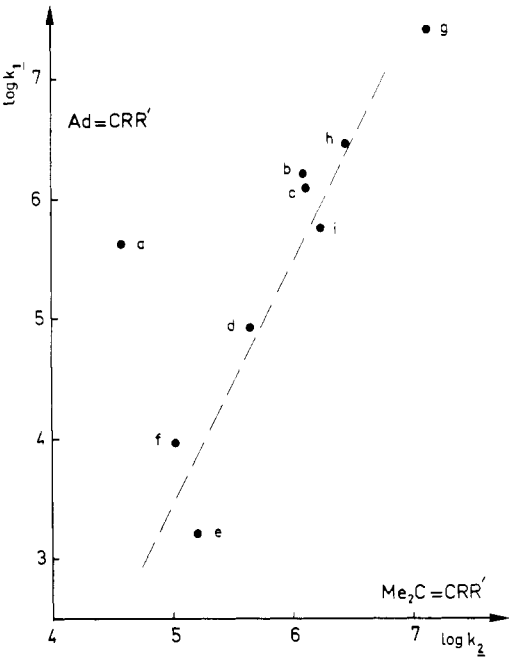


Figure 1. Comparison of R and R′ substituent effects on bromination rates of adamantylidenealkanes 1 and isopropylidenealkanes 2 in methanol at 25 °C.

expected polar effects of two isopropyl groups.

This conclusion is supported by the very high rate constant of **1g**, 2.5×10^7 M^{-1} s^{-1}. It was accepted until now that the alkene the most reactive toward bromine[7,8] was 2,3-dimethyl-2-butene, $Me_2C{=}CMe_2$, whose bromination rate constant in methanol is 1.40×10^7 M^{-1} s^{-1}; even the replacement of one methyl by the hardly bigger ethyl group slightly decreases the rate. This upper limit of alkene reactivity is now revised since **1g** beats tetramethylethylene by a short head (×1.7).

Enhancement of the Steric Effects of Branched Alkyl Groups in the Bromination of 1 as Compared with That of 2. In Table II, the kinetic effects of alkyl groups R and R′ on the bromination of **1** and **2** are compared. It might seem more appropriate to compare **1** with the *i*-$Pr_2C{=}CRR'$ series involving two *gem*-isopropyls, but these latter are not available. However, **2** is a suitable surrogate since neither the adamantyl cage alone in **1a** nor the two *gem*-methyls in **2** exhibit any intrinsic steric effect. Figure 1, where the rate data of **1** are plotted against those of **2**, shows that there is no linear relationship but only some similarity between the effects of the branched groups on the two alkene series. According to the best regression line shown in Figure 1, the rates of **1** are about twice as

Table VI. Relative Contributions of R and R′ to the Strain Energies, SE, and to the Bromination Rates of Alkenes 1 and 2

R	R′	$(\Delta SE)_{2\rightarrow 1}$[a]	$(\Delta \log k)_{2\rightarrow 1}$[b]
H	H	−0.01	−1.05
H	Me	0.33	−0.09
H	Et	0.61	0.05
H	*i*-Pr	0.72	0.74
H	*t*-Bu	1.07	2.02
H	*neo*-Pe	0.95	1.06
Me	Me	0.27	−0.25
Et	Et	1.04	0.00
Me	*i*-Pr	0.46	0.52

[a] $(\Delta SE)_{2\rightarrow 1} = (SE)_2 - (SE)_1 + (SE)_{Ad=CH_2}$, in kcal mol^{-1}. [b] $(\Delta \log k)_{2\rightarrow 1} = \log k_2 - \log k_1$.

sensitive to R and R′ as those of **2**. This result is also evident when the steric contributions of these groups to the reactivities of the two sets of alkenes are compared (Table II); *i*-Pr, *t*-Bu or *neo*-Pe substituents reduce the rates of **1** at least twice as much as those of **2**.

It has been claimed[8] that branched alkyl groups exhibit the most important steric effects in bromination when they are included in tetrasubstituted alkenes, $Me_2C{=}CMeR$, **3**. However, it can be seen by comparing the steric contributions in series **2** (**2a–f**) and in series **3** (**3a–f**) (Table III) that their values are about in the same range whatever the number of methyls on the double bond. The differences between **3** and **1** are, therefore, similar to those between **2** and **1**.

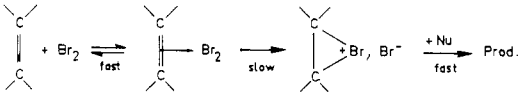
Consequently, the bromination rates of adamantylidenealkanes, Ad=CRR′, are much more sensitive to steric effects than those of isopropylidenealkanes, $Me_2C{=}CRR'$. The rate retardation caused by bulky alkyl groups in the adamantyl series, where their preferred conformation is probably very constrained, is significantly greater than that of the same groups in acyclic series where their conformation is less rigid.

Similar Conformations of Branched Alkyl Substituents in 1 and 2. As suggested above, the enhancement of the steric effects in the adamantylidene compounds could result from some special characteristic of their stereochemistry. However, the calculations in Table V do not reveal any significant differences in the stabler conformations of R and R′, whether the associated substituents are locked adamantyl or *gem*-dimethyls. For example, *i*-Pr or *t*-Bu groups adopt exactly the same stereoarrangement with respect to the double bond in Ad=CHR as in $Me_2C{=}CHR$. The different sensitivities of the reactivities to the steric effect cannot be attributed to differences in alkene stereochemistries.

The comparison of strain energies of congested cyclic and acyclic alkenes, after deduction of the intrinsic contribution of the adamantylidene moiety estimated from that of **1a**, shows (Table VI) that the additional strain provided by a branched group is in fact smaller in Ad=CRR′ than in $Me_2C{=}CRR'$. Moreover there is no relationship between the reactivity differences of the two alkene sets and their strain energy differences. Clearly, the kinetic effect of alkyl groups in alkene bromination is not determined by the geometrical features of the alkenes.

This conclusion is not totally unexpected since it is well-known that the bromination transition states closely resemble the bromonium ion intermediates rather than the ethylenic substrates.[28] There is a priori no reason that steric strain and intramolecular interactions in the alkene and in the intermediate should be similar. Consequently, calculations on the corresponding bromonium ions would be more appropriate. Unfortunately, there is no available force field for these ions; attemps to model them by other onium ions, calculations of which are possible at present, have not led to a satisfactory interpretation of the bromination rates of even moderately congested alkenes. In any case, the following comparison of the rate data of **1** in methanol and in acetic acid suggests that mechanistic change could occur when the alkene structure is modified. Before going further with the calculations, it is, therefore, important to examine the possible consequences on the magnitude of steric effects.

Mechanistic Changes Induced by Steric Effects: Return and Inhibition of Nucleophilic Solvent Assistance. In the preceding discussion it has been implicitly accepted, in agreement with what is currently postulated, that rate constants measured by following bromine uptake correspond to the same rate-limiting step, namely unassisted formation of bromonium ions by CTC ionization according to the Ad_ECl mechanism.[28] Now, there are two



recent series of experiments which suggest that this assumption can fail: the ionization step could be reversible[29] and/or solvent assisted.[14] Return could be favored by bromonium ion congestion which would hinder the nucleophilic trapping; the product forming step could, therefore, become slow enough to compete with collapse of the intermediate into alkene and bromine. If so, the measured rate constant is smaller than the ionization rate.[30] Since adamantylidenealkanes **1** are more congested than isopropylidenealkanes **2**, return is more probable for **1** than for **2**. The enhancement of steric effects in series **1** could, therefore, arise at least in part from the ionization step reversibility, the extent of which increases as the substituents R and R′ become more and more bulky.

Solvent nucleophilic assistance is also related to double-bond crowding: the more bulky the substituents, the less important is solvent participation[14] in the second step of the Ad_ECl mechanism. The bromination rates of highly congested **1** could, therefore, correspond to an unassisted ionization[31] and be smaller as compared to those for the eventually assisted reaction of the less bulky **2**. Consequently, the fact that branched substituents slow the reaction of **1** more than that of **2** could also result from steric inhibition of solvent assistance in the ionization step. This phenomenon has been invoked to explain the differences between the bromination rates of acyclic alkenes in methanol and in the less nucleophilic acetic acid: a fairly linear relationship between the data in the two solvents is obtained only if the double bond substituents are linear alkyl groups.[14] Alkenes with branched substituents react

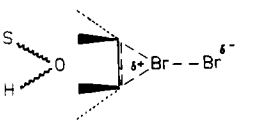


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Table VII. Comparison of Bromination Data of 1 in Methanol and in the Less Nucleophilic Acetic Acid[a]

R	R′	log k_{obs} MeOH	log k_{obs} AcOH	(log k_{calc})$_{MeOH}$[b]	Δ[c]	SterCo[d]
H	H	5.62	4.68	6.15	0.5	0
H	*t*-Bu	3.20	2.84	4.30	1.1	−3.2
Me	Me	7.40	6.91	8.43	0.9	−0.6
Me	*i*-Pr	5.76	5.28	6.75	1.0	−1.7
t-Bu	*i*-Pr[e]	2.29	1.08	2.52	0.3	−3.5

[a] The large deviation Δ suggests that part of the high steric contribution comes from a significant change in the bromination mechanism on going from acyclic alkenes to adamantylidenealkanes. [b] (log k_{calc})$_{MeOH}$ = 1.02 log k_{AcOH} + 1.42; this value includes methanol assistance as high as that observed for linear alkenes (see ref 14). [c] (log k_{obs} − log k_{calc})$_{MeOH}$. [d] SterCo in MeOH: see Table II. [e] *gem-tert*-Butylisopropylethylene, ref 6.

systematically slower in methanol than what is expected, indicating steric inhibition of solvent assistance (0.5 log unit at most). The decrease in adamantylidenealkane bromination rates arising from inhibition of nucleophilic methanol assistance can be as high as 1 log unit, as estimated by comparing the data in methanol and acetic acid (Δ in Table VII).

Variations in the symmetry of the bromine bridging could also result in steric retardation of these highly crowded alkenes as compared with **1a**; on going from the unsubstituted methylideneadamantane to **1j**, the bromonium ion like transition states could change from unsymmetrical, where the adamantyl group effect could be minimized, to symmetrical, where the cage and the alkyl groups could interact significantly. The transition-state structure has been observed to be independent of the substituent pattern of the double bond, at least for *n*-alkyl groups: symmetrically bridged transition states are found for *cis*-, *trans*-, and *gem*-disubstituted alkenes.[12] However, the influence of the crowding of the ethylenic bond on the bridging in the transition states has still not been evaluated. Calculations and mechanistic studies designed to investigate the relative contributions of these various factors to the large steric retardation of highly congested alkenes are in progress.

Experimental Section

2-R′-2-adamantanols were synthesized, according to the previously described procedure[19,32] by condensing adamantanone in diethyl ether with the organolithium compounds, R′Li, obtained from the corresponding chlorides, R′Cl, at −40 °C for the secondary and at room temperature for the primary chlorides, with vigorous stirring. After the reaction mixture was worked up, adamantanols purified by column chromatography on alumina in pentane were obtained in 80–95% yield.

Adamantylidenealkanes 1b–h. They were prepared from the corresponding 2-R′-2-adamantanols by dehydration[18] with thionyl chloride in the presence of pyridine at −5 °C. After purification by alumina chromatography, the alkene yields were about 60%. Apart from **1g** which is solid (mp 42 °C), alkenes **1b–h** are oily liquids. The analytical and NMR spectral characteristics are given in Tables SII and SIII of the supplementary material.

Methylideneadamantane 1a. Dehydration of 2-Me-2-adamantanol[33] was carried out with 85% phosphoric acid in 85% yield. This procedure applied to the other 2-R′-2-adamantanols gives the corresponding alkenes with a yield markedly poorer than that obtained with thionyl chloride.

Adamantylidenealkanes 1i and 1j were prepared by reductive coupling of adamantanone and the corresponding ketone (MeCO-*i*-Pr and *i*-PrCO-*i*-Pr, respectively) in equimolar ratio, catalyzed by the $TiCl_3$/Li couple.[20] Symmetrical alkenes are the major products; mixed alkenes, obtained in about 7% yield, were separated from the product mixture by preparative GC (SE30, 10%, 1.4 m, *T* 150 °C). The yield is still poorer when the $TiCl_3$/Zn couple[34] is used. **1i** is an oily liquid and **1j** is solid (mp 42 °C).

Kinetic Measurements. Methanol and acetic acid were analytical grade Merck reagents; they were purified by previously described procedures.[14] Sodium and lithium bromides were Merck Suprapur grade, dried at 120 °C overnight before use.

Two different methods both using TFCR-EXSEL conditions[35] (very low concentration in reagents–salt excess) have been used: couloamperometry[35] for rate constants above 5×10^3 M^{-1} s^{-1} and UV spectroscopy[36] for rate constants below this limit. In the couloamperometric method, bromine is produced in situ by quantitative electrolysis[37] of NaBr (in methanol) or LiBr (in acetic acid); its uptake is followed by the decrease in the bromine diffusion current between Pt electrodes. Second-order conditions (first order in bromine and in alkene) are used: the bromine concentration is in the range 10^{-5}–10^{-8} M and the initial alkene concentration is approximately half this. In the UV spectroscopic method,[36] alkene (10^{-3}–10^{-4} M) is syringed into the reaction cell containing the bromine solution, and bromine consumption is followed by the absorbance change at a fixed wavelength (280–320 nm). In both methods, the reproducibility is within 3%.

Registry No. **1a**, 875-72-9; **1b**, 13376-16-4; **1c**, 13376-17-5; **1d**, 13376-19-7; **1e**, 38424-21-4; **1f**, 125413-48-1; **1g**, 20441-18-3; **1h**, 99810-86-3; **1i**, 125413-49-2; **1j**, 125413-50-5.

Supplementary Material Available: Tables SI (experimental bromination rate constant of **1**) SII (elemental analysis of **1**), SIII (NMR data on **1**), and SIV (full MM2 calculations) (4 pages). Ordering information is given on any current masthead page.

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