Notes

Solvation and Steric Effects on Electrophilic Reactivity of Ethylenic Compounds. 3. Stereo-, Regio-, and Chemoselectivity of Alkene Bromination in Methanol

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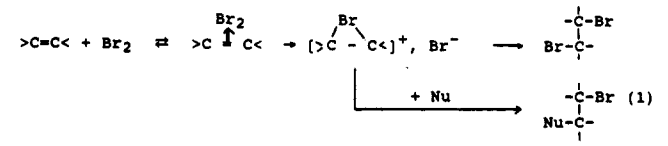
The bromination of ethylenic compounds is a basic organic reaction, the mechanism of which has been widely studied.[1] Nevertheless, this electrophilic addition is rarely used for synthetic purposes[2] although interesting β-bromo derivatives can be readily obtained by brominating a double bond in the presence of a nucleophile. In fact, mechanistic studies have been focused mainly on the first, rate-limiting steps leading to a more or less bridged bromocation[3] by ionization of the bromine-alkene charge transfer complex, CTC.[4] In contrast, there are few significant data on the last, product-forming step. Consequently, it is difficult to predict, and still more to control, the selectivity of product formation. The situation is all the more complicated in that electrophilic addition can show three kinds of selectivity: stereo-, regio-, and chemoselectivity. According to eq 1, the two first selectivities depend, at least in part, on the magnitude of bromine bridging in the ionic intermediates.[3,5] When bromonium ions are involved, it is expected that the bromo adducts will be formed stereospecifically but not 100% regioselectively.[1] In contrast, for β-bromo carbocations, as for instance in the case of enol derivatives, the reaction must be regiospecific but not stereoselective. It is now possible to determine from kinetic data how the substituents control the magnitude of bromine bridging in the intermediates.[3] The only work relevant to chemoselectivity concerns the bromination of methyl-substituted ethylenes in methanol.[6] The chemoselectivity is highly dependent on the number of methyl groups on the ethylenic bond; this has been interpreted in terms of the charge densities of the carbon atoms of the bromonium intermediates[7] and the relative hardness of the two competing nucleophiles.[8] However, many other factors (bromine bridging, substituent crowding, nucleophilic solvation, ion pairing, etc.) may be involved.



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In this paper we report the results of a systematic study on the influence of linear and branched alkyl groups on the three selectivities of alkene bromination in methanol.

Results

The products of brominating 30 mono-, di-, tri-, and tetrasubstituted alkenes in methanol containing 0.2 M sodium bromide were measured by GC analysis of the reaction mixture, without any workup after the end of bromine addition. The results collected in Table I were obtained at 25 °C by using experimental conditions very similar to those used for kinetic measurements.[9] The initial alkene concentration is 10^{-3} M; electrochemically generated bromine[10] is added slowly, its concentration being maintained at 10^{-5} M. Under these conditions, the bromine and tribromide ion concentrations are constant throughout the reaction.[11] The major brominating agent is the tribromide ion resulting from the well-known equilibrium,[12] $Br_2 + Br^- \rightleftarrows Br_3^-$, the $[Br_3^-]/[Br_2]$ ratio being 35.4. However, since free bromine reacts much faster than tribromide,[13] the two routes for bromonium ion formation, either from Br_2 or from Br_3^-, are of similar importance (vide infra). In the presence of 0.2 M NaBr, the two nucleophiles, Br^- and MeOH, which trap the bromonium ion intermediates competitively, are in a ratio, [MeOH]/[Br^-], of 120. This leads to dibromide and solvent-incorporated adducts in relative amounts readily accessible by GC.

Under these conditions, the only bromination products are dibromides (DB) and methoxy bromides (MB), except for the reaction of the two congested *gem*-disubstituted alkenes 11 and 12 for which significant amounts of bromoalkenes are obtained. For most of the dissymmetrically substituted alkenes, two solvent-incorporated products are observed; the Markovnikov and anti-Markovnikov adducts are denoted MB_α and MB_β, respectively, the most substituted carbon atom being C_α. The analytical data of the bromination products are given in Table SI of the supplementary material.

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(1) (a) Freeman, F. *Chem. Rev.* **1975**, *75*, 441. (b) Schmid, G. H.; Garratt, D. G. *Double Bonded Functional Groups*; Patai, S., Ed.; Wiley: New York, 1977; Suppl. A, p 725. (c) de la Mare, P. B. D.; Bolton, R. *Electrophilic Additions to Unsaturated Systems*, 2nd ed.; Elsevier: Oxford, 1982. (d) Ruasse, M. F. *Adv. Phys. Org. Chem.* **1993**, *28*, 207.
(2) (a) Rodriguez, J.; Dulcère, J. P.; Bertrand, M. *Tetrahedron Lett.* **1984**, 527. (b) Giordano, C.; Castaldi, G. *J. Org. Chem.* **1989**, *54*, 1470.
(3) Ruasse, M. F. *Acc. Chem. Res.* **1990**, *23*, 87.
(4) Dubois, J. E.; Garnier, F. *Spectrochim. Acta* **1967**, *23A*, 2279. Bellucci, G.; Bianchini, R.; Ambrosetti, R.; Ingrosso, G. *J. Am. Chem. Soc.* **1985**, *107*, 2464. Brown, R. S.; Slebocka-Tilk, H.; Bunnett, A. J.; Bellucci, G.; Bianchini, R.; Ambrosetti, R. *Ibid.* **1990**, *112*, 6310.
(5) Galland, B.; Evleth, E. M.; Ruasse, M. F. *J. Chem. Soc., Chem. Commun.* **1990**, 898.
(6) Dubois, J. E.; Chrétien, J. R. *J. Am. Chem. Soc.* **1978**, *100*, 3506.
(7) Olah, G. A.; Westerman, P. W.; Melby, E. G.; Mo, Y. K. *J. Am. Chem. Soc.* **1974**, *96*, 3565.
(8) Pearson, R. G. *Hard and Soft Acids and Bases*; Dowden, Hutchinson, Ross: Stroudsburg, PA, 1977. Ho, T. L. *Chem. Rev.* **1975**, *75*, 1.
(9) Dubois, J. E.; Ruasse, M. F.; Poupard, D. *J. Electroanal. Chem. Interfacial Electrochem.* **1983**, *152*, 85.
(10) Poupard, D.; Ruasse, M. F.; Dubois, J. E. *J. Electroanal. Chem. Interfacial Electrochem.* **1983**, *152*, 77.
(11) Bartlett, P. D.; Tarbell, D. S. *J. Am. Chem. Soc.* **1936**, *58*, 466. Dubois, J. E.; Bienvenue-Goëtz, E. *Bull. Soc. Chim. Fr.* **1968**, 2089.
(12) Bienvenue-Goëtz, E.; Msika, R.; Dubois, J. E. *J. Chim. Phys. Phys-Chim. Biol.* **1980**, *77*, 803. Ruasse, M. F.; Aubard, J.; Galland, B.; Adenier, A. *J. Phys. Chem.* **1986**, *90*, 4382.
(13) Dubois, J. E.; Huynh, X. Q. *Bull. Soc. Chim. Fr.* **1968**, 1436.

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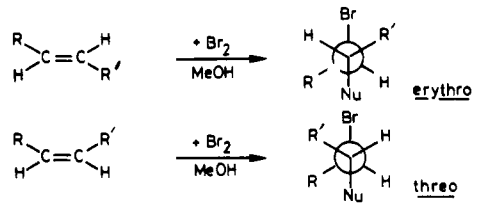
Discussion

Stereospecificity of *cis*- and *trans*-Alkene Bromination. The first striking result of Table I concerns the stereospecificity[14] of the reaction of 1,2-disubstituted alkenes (compounds 13–28), even when one substituent is as bulky as *tert*-butyl. *cis*-Alkenes lead to threo or *dl* adducts whereas their trans stereoisomers give the erythro or meso adducts only. The two nucleophiles, bromide and



methanol, trap the intermediate with the same stereospecificity,[14] exclusively anti with respect to the first bromine atom. This unambiguous and substituent-independent result confirms that the intermediates of the bromination of 1,2-disubstituted alkenes are totally bridged. This was established previously from kinetics,[15] product analyses,[16] and calculations.[5,17]

The important finding of the present study is that crowding and dissymmetric substitution, as in *t*-BuCH=CHMe, do not modify the bromonium ion nature of the bromination intermediates of 1,2-disubstituted alkenes.

Similar results are obtained in tetrachloromethane, methanol, and acetic acid.[18] Therefore, the stereospecificity of the reaction of 1,2-disubstituted alkenes is probably solvent-independent.

Regiochemistry of Methanol Attack. Another unambiguous result is the complete regioselectivity of the reaction of the *gem*-disubstituted bromination intermediates with methanol. Even when one of the substituents is branched (10–12), no anti-Markovnikov methoxy bromide, MB_β, is observed. A bulky group does not change the regioselectivity but favors the collapse of the intermediate by proton elimination instead of by nucleophilic trapping. Trimethylethylene, **29**, exhibits the same regioselectivity. These observations strongly suggest that, when one of the two ethylenic carbon atoms bears two substituents, the bromination intermediate is not a symmetrical bromonium ion but resembles a β-bromo carbocation. This conclusion agrees with MNDO calculations[5] and ^{13}C NMR results[7] on the 1,1-dimethyl bromocation which show that the C_α-carbon atom is markedly charged as compared with the C_β atom. In contrast, kinetic substituent effects[15] imply a symmetrical charge distribution in the 1,1-disubstituted transition states.[19] The reason for this discrepancy is not understood.[1d]

Table I. Products[a,b] of Alkene Bromination[c] in Methanol at 25 °C

compd	R	R′	DB	MB_α	MB_β
		RCH=CH_2			
1	Me	H	39	50	11
2	Et	H	47	38	15
3	*n*-Pr	H	51	37	12
4	*n*-Hex	H	51	37	12
5	*i*-Pr	H	60	19	21
6	*t*-Bu	H	70	0	29
7	*neo*-Pe	H	43	48	9
		gem-RR′CH=CH_2			
8	Me	Me	15	85	0
9	Et	Et	20	80	0
10	*i*-Pr	Me	26	74	0
11	*t*-Bu[d]	Me	21	66	0
12	*neo*-Pe[e]	Me	12	48	0
		cis-RCH=CHR′			
13	Me	Me	41*dl*	59*dl*	
14	Et	Me	48T[f]	19T	33T
15	Et	Et	51*dl*	49*dl*	
16	*n*-Pr	Me	50T	21T	29T
17	*n*-Pr	*n*-Pr	57*dl*	43*dl*	
18	*i*-Pr	Me	51T	11T	38T
19	*i*-Pr	*i*-Pr	69*dl*	31*dl*	
20	*t*-Bu	Me	65T	0	35T
		trans-RCH=CHR′			
21	Me	Me	37m[g]	63m	
22	Et	Me	41E	17E	42E
23	Et	Et	46m	54m	
24	*n*-Pr	Me	43E	22E	35E
25	*n*-Pr	*n*-Pr	52m	48m	
26	*i*-Pr	Me	45E	0	55E
27	*i*-Pr	*i*-Pr	81m	19m	
28	*t*-Bu	Me	43E	0	57E
29	Me_2C=CHMe		19	81	0
30	Me_2C=CMe_2		44	56	

[a] In %, determined by GC; reproducibility from 4–6 runs is generally better than ±3%. [b] Obtained in overall yield >98%. [c] In the presence of 0.2 M NaBr. DB = dibromide; MB_α and MB_β = Markovnikov and anti-Markovnikov methoxy bromides, respectively. [d] *t*-BuMeC=CHBr: 13%. [e] *neo*-PeMeC=CHBr: 40%. [f] E: erythro; T: threo. [g] m: meso.

For the other alkenes, the regioselectivity ($\mathcal{R} = 100 \times MB_\alpha/[MB_\alpha + MB_\beta]$; Table II) is more varied and less easy to interpret. $\mathcal{R}$ values between 0.5 and 1.00 indicate a preference for Markovnikov addition, whereas for $0 < \mathcal{R} < 0.5$ the addition is anti-Markovnikov. The completely anti-Markovnikov regioselectivity of alkenes bearing a *tert*-butyl (**20** and **28**) suggests that steric effects are important. However, the preponderance of anti-Markovnikov addition on 1-ethyl-2-methyl- and 1-*n*-propyl-2-methylethylenes, where bulky substituents are not involved, makes this interpretation doubtful. When $\mathcal{R}$ is plotted against σ^*_R or $\Delta\sigma^*_{R,R'}$[23] for the reactions of RCH=CH_2 and RCH=CHR′ (Figure 1), respectively, it appears that the regioselectivity is *inversely* proportional to the polar effects. The steric effects are not, therefore, the only factors responsible for the anti-Markovnikov behavior. The chemoselectivity data confirm this surprising role of polar effects (vide infra), which disagrees with the general belief regarding electrophilic addition.

The results on bromination regioselectivity are in contrast with those for other electrophilic additions. For example, it is commonly agreed that hydroboration with

(14) For definitions of selectivity and specificity, see Glossary of terms used in physical organic chemistry IUPAC. *Pure Appl. Chem.* **1979**, *51*, 1725. Ward, R. S. *Chem. Br.* **1991**, 803.
(15) Bienvenue-Goëtz, E.; Dubois, J. E. *Tetrahedron* **1978**, *34*, 2021. Dubois, J. E.; Mouvier, G. *Bull. Soc. Chim. Fr.* **1968**, 1426.
(16) Fahey, R. C. *J. Am. Chem. Soc.* **1966**, *88*, 4681.
(17) Hamilton, T. P.; Schaefer, H. F. *J. Am. Chem. Soc.* **1990**, *112*, 8360.
(18) (a) Rolston, J. H.; Yates, K. *J. Am. Chem. Soc.* **1969**, *91*, 1477. (b) Yates, K.; McDonald, R. S. *J. Org. Chem.* **1973**, *38*, 2465.
(19) Ruasse, M. F.; Zhang, B. L. *J. Org. Chem.* **1984**, *49*, 3207.
(20) Bienvenue-Goëtz, E.; Dubois, J. E.; Pearson, D. W.; Williams, D. L. H. *J. Chem. Soc. B* **1970**, 1275.
(21) de Ficquelmont, M. Doctoral Thesis, CNRS AO8355, Paris, 1973.
(22) Dubois, J. E.; Bienvenue-Goëtz, E. *Bull. Soc. Chim. Fr.* **1968**, 2086.
(23) Shorter, J. *Advances in Linear Free Energy Relationships*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: London, 1972; p 2.

Table II. Regio- ($\mathcal{R}$) and Chemoselectivity (C) of Alkene Bromination, Compared with Kinetic Data on the Competition between Free Bromine and Bromide- and Methanol-Assisted Pathways

compd	$\mathcal{R}$[a]	C[b]	Q[c]	% k_{Br_2}[d]	R_{Nu}[e]
		RCH=CH$_2$			
1	0.82	0.39	20[f]	40	
2	0.72	0.47	15[f]	40	
3	0.76	0.51	17[f]	35	6.2
5	0.49	0.61	16[g]	30	
6	0	0.70	15[g]	30	
7	0.84	0.43	22[g]	35	
		gem-RR'C=CH$_2$			
8	1.0	0.15			
9	1.0	0.20	30[g]	45	
10	1.0	0.26			
11	1.0	0.21	25[g]	40	
12	1.0	0.12			
		cis-RCH=CHR'			
13		0.41			
14	0.37	0.48	15[h]	30	4.1
15		0.51	24[g]	40	
16	0.42	0.54	26[g]	40	
17		0.57	28[g]	45	
18	0.22	0.51	26[h]	40	
19		0.69	54[g]	60	
20	0	0.65	29[h]	45	1.5
		trans-RCH=CHR'			
21		0.37			
22	0.29	0.41	16[g]	30	1.7
23		0.45	20[g]	35	
24	0.39	0.47	31[g]	50	
25		0.51	31[g]	50	
26	0	0.45	19[h]	35	
27		0.81	25[g]	40	
28	0	0.43	70[g]	65	1.6
29	1.0	0.19	39[g]	50	
30		0.44	27[g]	45	3.3

[a] $100 \times MB_\alpha/(MB_\beta + MB_\beta)$. [b] $100 \times (DB)/(DB + MB_\alpha + MB_\beta)$. [c] $k_{Br_2}/k_{Br_3^-}$. [d] $(k_{Br_2}/(k_{Br_2} + Kk_{Br_3^-}[Br^-])) \times 100$. [e] $(k_{aqEtOH}/k_{AcOH})_Y$; ref 19. [f] Reference 20. [g] Reference 21. [h] References 13 and 22.

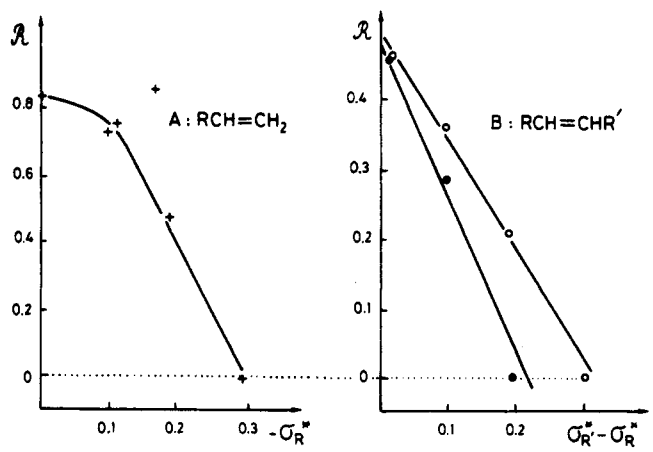


Figure 1. The inverse relationship between regioselectivity, $\mathcal{R}$, of alkene bromination in methanol and the difference between polar effects of the substituents R and R' on C_α and C_β [(○) *cis*; (●) *trans*]. Electron donation favors the anti-Markovnikov adduct. Deviation occurs in A for R = *neo*-Pe.

moderately crowded boranes is mainly anti-Markovnikov[24] whereas oxymercuration is considered as a Markovnikov reaction.[25] These differences can be interpreted in terms of the transition state structures of the various product-forming steps. Since the bromonium–nucleophile reaction is fast, its transition state is loose, so the selectivity is controlled by the charge distribution in the bromination intermediate. Calculations on bromonium ions from ethylene[17] and its methylated derivatives[5] indicate that the positive charge is neither on bromine nor on C_α and C_β but on the substituents. Earlier calculations on carbocation solvation[26] support this unexpected result. Because of charge delocalization by the alkyl groups, interaction energies between water and small carbocations decrease markedly on going from Me^+, *i*-Pr^+, to *t*-Bu^+. It is, therefore, likely that the preferentially attacked carbon atom of a bromonium ion is the less substituted, in agreement with the favored anti-Markovnikov behavior.

Chemoselectivity, the Competition between Bromide and Methanol Trapping of Bromonium Ions. Chemoselectivity data (C = {DB/(DB + MB)}%) are also highly variable and not readily interpretable. When C is close to unity, bromide attack is favored over that of methanol, although the methanol concentration is 120 times that of bromide.

Again, *gem*-disubstituted alkenes and trimethylethylene, which lead mainly to methoxy bromo adducts ($0.1 < C < 0.2$), behave very differently from the other alkenes. The marked carbocationic character of these bromonium ions is probably at the origin of this high chemoselectivity. It is interesting to note that other brominations going through β-bromo carbocations, such as those of α-methylstilbenes[27] and α-methoxystyrenes,[28] lead to methoxy bromo adducts only, even in the presence of 0.5 M bromide.

Chemoselectivity for the bromination of monosubstituted and 1,2-disubstituted alkenes varies more with the substituents, $0.4 < C < 0.8$. It can be influenced by a variety of factors such as the polar and steric effects of the substituents, the nature of the counterion of the intermediate, preassociation with nucleophiles, the life-times of the ion pairs, etc.

Under the conditions used in this work, bromonium ions are formed by two routes, either from free bromine addition or from the so-called tribromide addition.[11] Early unsuccessful attempts were made to relate the solvent-incorporated adducts to the free bromine route and dibromide to that of tribromide.[11,29] This suggestion received some support later when it was found that free bromine addition is nucleophilically assisted by the solvent[30] and that the "tribromide" reaction is mainly bromide-assisted free bromine addition,[31] at least as long as the double bond substituents are not bulky. Consequently, the competition between bromide and methanol attack on the bromonium ion could be determined in the rate-limiting step and estimated from the relative im-

(24) Cragg, G. M. L. *Organoboranes in Organic Synthesis*; Marcel Dekker: New York, 1973; pp 63–84, 137–197. Regioselectivity determining transition state of hydroboration is that of the electrophilic step.

(25) Matteson, D. S. *Organometallic Reaction Mechanisms of the Nontransition Elements*; Academic Press: New York, 1974; p 202. If the nucleophile–mercurinium reaction is rate-limiting, this product-forming step is slow and its transition state is tight. This implies a significant steric control of the regioselectivity in agreement with Markovnikov behavior.

(26) Jorgensen, W. L. *J. Am. Chem. Soc.* **1978**, *100*, 1049.

(27) Ruasse, M. F.; Argile, A. *J. Org. Chem.* **1983**, *48*, 202.

(28) Ruasse, M. F.; Dubois, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 3230.

(29) Kanyaev, N. P. *J. Gen. Chem. URSS* **1959**, *29*, 825. Atkinson, J. R.; Bell, R. P. *J. Chem. Soc.* **1963**, 3260.

(30) Ruasse, M. F.; Motallebi, S.; Galland, B. *J. Am. Chem. Soc.* **1991**, *113*, 3440.

(31) Dubois, J. E.; Huynh, X. Q. *Tetrahedron Lett.* **1971**, 3369. Bellucci, G.; Bianchini, R.; Ambrosetti, R.; Ingrosso, G. *J. Org. Chem.* **1985**, *50*, 3313.

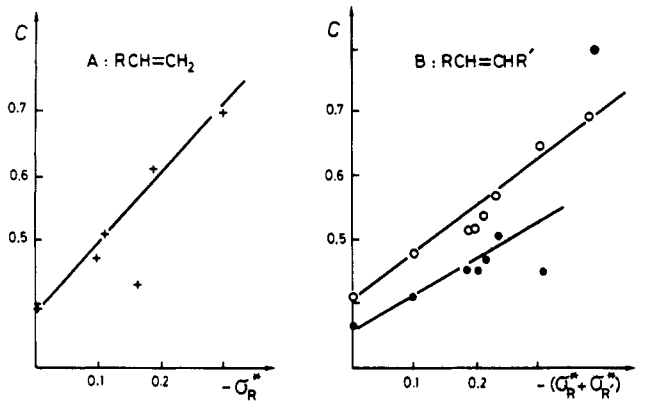
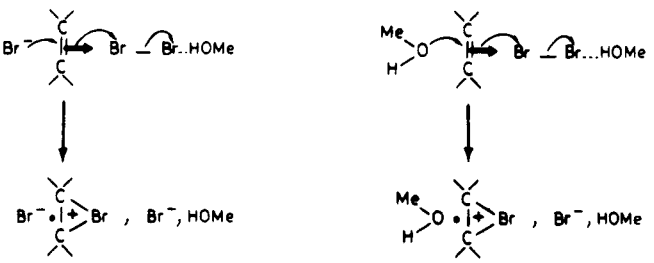


Figure 2. Dependence of the chemoselectivity, *C*, on the polar effects of alkyl groups on alkene bromination in methanol. A, RCH=CH_2; B, RCH=CHR' [(O) cis; (●) trans]. Electron donation favors the dibromide over the solvent-incorporated adduct. Deviations are observed in A for R = *neo*-Pe and in B for *trans*-*t*-BuCH=CHMe and *trans*-*i*-PrCH=CH*i*-Pr.

portance of the two reaction pathways involving either free bromine or "tribromide ion". With this objective in



mind, the *Q* ratios[13] ($k_{Br_2}/k_{Br_3^-}$), the proportion of the free bromine pathway, and the available R_{Nu} ratios,[30] which estimate the magnitude of methanol assistance, are shown in Table II. Clearly, there is no simple relationship between these kinetic data and the chemoselectivity. Other factors play a more important role in determining the fate of the bromonium ions. Among them, the life-times of the intermediates[32] must influence the chemoselectivity. On this life-time depends the extent of ion-pair dissociation and, therefore, the microenvironment of the bromonium ion when it reacts with the nucleophile. The scarce data on the life-times of these species[33] show that they are short, but it is not possible to know much they dissociate. Previous results in acetic acid[34] where dibromide is the major adduct suggest that there are no free ions in this solvent. In the more dissociating methanol, it is possible that ion-pairs and free ions coexist.

A more empirical approach is given in Figure 2 which shows fairly linear relationships between the polar constants of the substituents and *C*. An interpretation, similar to that suggested by the anti-Markovnikov regioselectivity, can be proposed. The more polar the substituents, the less charged the bromonium intermediates, because of charge delocalization, and the more favored the attack by the bromide. In this interpretation, the steric effects do not play a significant role. Nevertheless, it is noticeable that the slopes of Figure 2 decrease on going from monosubstituted to cis- and trans-substituted alkenes; in other words, the sensitivity of chemoselectivity to polar effects decreases from monosubstitution to cis and trans substitution, i.e. as nucleophile approach to the double bond is more and more inhibited. Moreover, deviations of bulky substituents from the regression line occur only for *trans*-alkenes the reaction of which are usually considered as more sensitive to steric effects than those of their cis isomers. The tendency of steric effects to favor methanol attack agrees with the idea that solvated bromide ions are more bulky than methanol.

In conclusion, despite recent progress on bromonium ion structure,[5,7,17,34] it is still difficult to fully understand what controls the product selectivities in bromination. From the present study, empirical rules useful for synthesis can be inferred:

(i) The bromination of *cis*- and *trans*-alkenes is stereospecific, which agrees with complete bridging in the intermediates. This stereochemistry does not depend on the crowding of the double bond, on the solvent, or on the nucleophilic species. In contrast, the regioselectivity is not complete and is generally in disagreement with the Markovnikov predictions, even when non bulky substituents are involved. Crowding by branched substituents reinforces this tendency.

(ii) The reaction of *gem*-disubstituted and probably trisubstituted alkenes is fully regioselective in agreement with a carbocation-like intermediate. This regioselectivity is associated with a high chemoselectivity in favor of methoxy bromides and, in more general terms, with trapping of the intermediate by the harder nucleophile.

(iii) The regioselectivity of monosubstituted alkenes is not completely Markovnikov; the anti-Markovnikov adduct is preponderant only for the *tert*-butyl substituent.

(iv) Chemoselectivity of the reaction of monosubstituted and cis- and trans-disubstituted alkenes is controlled by a variety of factors whose overall effect is fairly well described by the polar constants of the substituents. Unexpectedly, electron donation favors the trapping of the bromonium ions by bromide ion. Work is in hand to obtain information on the extent of bromonium–bromide association in methanol and on the role of ion pairing in determining chemoselectivity.

However, the surprising chemoselectivity of alkenes reacting via bromonium ions is consistent with their anti-Markovnikov behavior insofar as both phenomena can be attributed to an overall decrease in the positive charge on the more substituted carbon atom, due to charge delocalization by polar substituents. Theoretical calculations on bromonium ions are in progress.

Experimental Section

Materials. The alkenes were commercially available (Fluka, Chemical Samples); they were purified by preparative GC and their purity was checked by analytical GC and NMR. Methanol (Baker, analytical grade) was distilled over bromine and dried by distillation from magnesium. Sodium bromide (Merck, Suprapur) was dried at 120 °C overnight before use. Bromine was generated in the reaction medium by quantitative electrolysis of sodium bromide.[10]

Alkene Bromination and Analysis of Bromination Products. Alkene brominations were carried out as previously

(32) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161.
(33) Nagorski, R. W.; Brown, R. S. *J. Am. Chem. Soc.* **1992**, *114*, 7773.
(34) Rolston, J. H.; Yates, K. *J. Am. Chem. Soc.* **1969**, *91*, 1469, 1483.
(35) k_{cis}/k_{trs} for bromination are generally greater than unity because bromine approach is less hindered. The fact that *cis*-alkenes are less stable than their trans isomers has no influence on the reactivity since the steric constraints in the ground state are maintained at the transition state. Yates, K.; McDonald, R. S. *J. Org. Chem.* **1973**, *38*, 2465.
(36) Slebocka-Tilk, H.; Ball, R. G.; Brown, R. S. *J. Am. Chem. Soc.* **1985**, *107*, 4505. Bennett, A. J.; Brown, R. S.; McClung, R. E. D.; Aarts, G. M.; Klobukowski, M.; Santarsioro, B. D.; Bellucci, G.; Bianchini, R. *Ibid.* **1991**, *113*, 8532.

described[6,37] under the kinetic conditions used in the coulometric concentrostat technique.[38] Alkene solutions (ca. 10^{-3} M) were prepared in methanol containing 0.2 M NaBr at 25 °C. Stoichiometric amounts of bromine were slowly produced in situ by sodium bromide electrolysis at constant current, the bromine concentration being maintained below 10^{-5} M throughout the reaction.

The reaction mixture was GC analyzed directly with no prior workup (Carbowax 600, 5–20 ft, 80–100 °C). Bromination products were identified by comparing their retention times with those of authentic samples obtained from preparative experiments. Product ratios were obtained from the relative areas of the corresponding adducts, after calibration of the detector response. Reproducibility of 4–6 runs is generally 3%. The overall yield in bromination products calculated from alkene is better than 98%.

Product Identification. Authentic samples of dibromides and methoxy bromides were prepared by adding slowly the stoichiometric amount of bromine to a 10^{-2} M alkene solution at 4 °C in methylene chloride and methanol, respectively. The reaction mixtures were worked up as described in ref 35. Products were purified by distillation. Physical and analytical data of the bromoderivatives are given in Table SI (supplementary material). Bromination products were identified by their ^{1}H NMR spectra which were in agreement with those previously reported and discussed in a systematic investigation of similar alkene bromoadducts.[18b] Relevant chemical shifts and coupling constants were as follows.

Dibromides obtained from terminal alkenes, RCH=CH_2 (1–7), show a complex multiplet (δ 3.5–4.1, 3 H) for the bromomethine and bromomethylene hydrogens[39] whereas those from *gem*-disubstituted alkenes, RR'C=CH_2 (8–12), exhibit a singlet at 4.1–4.2 ppm (2 H). Diastereoisomeric dibromides from *cis*- and *trans*-alkenes, RCH=CHR' (13–28), are identified on the basis of the coupling constants (Table III in the supplementary material) of the two bromomethine hydrogens (δ 3.9–4.3 ppm). J_{HH} for the erythro is smaller than that for the threo isomer.[40]

^{1}H NMR spectra of regioisomeric methoxy bromides, MB_α and MB_β, from RCH=CH_2 (1–7), differ markedly in the 3–4 ppm region. For MB_β, $RCHBrCH_2OCH_3$, the three types of hydrogens are readily identified [δ 3.35 (s, 3 H), 3.3–3.6 (m, 2 H), and 3.8–4.1 (m, 1 H)], whereas for MB_α they are not distinguishable [δ 3.2–3.4 (m, 6 H) with a dominant signal at δ 3.3]. In the spectra of methoxy bromides derived from RMeC=CH_2 (8–12), three characteristic signals [δ 1.2–1.3 (s, 3 H), 3.1–3.2 (s, 3 H), and 3.8–3.9 (s, 2 H)] are clearly distinguishable from those of the alkyl substituents. Regioisomeric methoxy bromides from *cis*- and *trans*-RCH=CHMe are identified from the chemical shifts of the methyl group involved either in CHBrMe (MB_α) or in CH(OMe)Me (MB_β), δ_{Me} 1.6–1.8 and 1.2–1.3, respectively. Diastereoisomeric methoxybromides from *cis*- and *trans*-alkenes, RCH=CHR' (13–28), were identified by the vicinal coupling constants (Table III, supplementary material) of the bromomethine hydrogens. As for the analogous dibromides, J_{HH} for the erythro is systematically smaller than that for the threo isomer.

Supplementary Material Available: Table SI (physical and analytical data), which characterizes the bromo adducts, and Table III (coupling constants) (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(37) Chrétien, J. R.; Durand, M.; Mouvier, G. *Bull. Soc. Chim. Fr.* **1969**, 1966.
(38) Dubois, J. E.; Mouvier, G. *C. R. Acad. Sci.* **1962**, *255*, 1104.
(39) Snyder, E. I. *J. Am. Chem. Soc.* **1966**, *88*, 1155.
(40) Kingsbury, C. A.; Best, C. A. *J. Org. Chem.* **1967**, *32*, 6.