Br^+ and I^+ Transfer from the Halonium Ions of Adamantylideneadamantane to Acceptor Olefins. Halocyclization of 1,ω-Alkenols and Alkenoic Acids Proceeds via Reversibly Formed Intermediates

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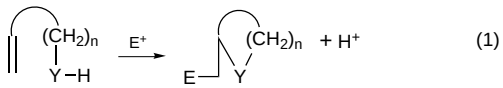
The kinetics of the transfer of X^+ from the bromonium and iodonium ions of adamantylideneadamantane (**1**-Br^+ and **1**-I^+) to some 1,ω-alkenols and alkenoic acids in $ClCH_2CH_2Cl$ at 25 °C was investigated. In all cases, the expected products of halocyclization were observed. For the iodonium ion transfer the reaction kinetics are second order overall, first order in both **1**-I^+ and acceptor olefin. Transfer of the bromonium ion from **1**-Br^+ to these acceptor olefins exhibits different kinetic characteristics. In most cases, the rate of the Br^+ transfer is subject to strong retardation in the presence of added parent olefin (Ad═Ad), suggestive of a common species rate depression. In some cases, such as 4-penten-1-ol (**2b**) and 4-pentenoic acid (**4b**), the reaction can be completely suppressed at high [Ad═Ad]. In other cases, such as 3-buten-1-ol (**2a**), 5-hexen-1-ol (**2c**), cyclohexene, 4-(hydroxymethyl)cyclohexene (**3**), and 5-*endo*-carboxynorbornene (**5**), added Ad═Ad does not suppress the reaction completely. In the cases of the 1,ω-alkenols, the reactions appear to exhibit kinetic terms that are greater than first order in alkenol. In these cases, alcohols such as 1-pentanol also accelerate the reaction, pointing to the involvement of the hydroxyl group of the second alkenol as a catalytic species. A unifying mechanism consistent with the data that involves two reversibly formed intermediates is presented.

Introduction

Electrophile-promoted cyclization of ω-substituted alkenes[1] (eq 1) is an increasingly important method for synthesis of heterocyclic ethers (X = OH),[2] lactones (X = CO_2H),[3] and lactams (X = C(O)NRH).[4] Much recent work



(1)

has centered on the well-known bromo- and iodocyclizations of substituted pentenols, hexenols, or their unsaturated acid counterparts which form cyclic 5- and 6-membered rings with defined stereochemical preferences for the ring closures.[2,3] Less comprehensively studied, in our opinion, are the mechanistic details of these reactions, although several early reports have delineated the overall reaction rates for bromo- and iodocyclizations of 1-ω-alkenols and 1-ω-alkenoic acids in various solvents.[5] The latter experimental work has been complemented by theoretical work on the facial selectivity in electrophilic addition to allylic alcohols and related amines,[6a] as well as on the details for cyclization of what is considered to be the Br^+-Π complex of 4-penten-1-ol.[6b]

Of interest in this work, particularly insofar as the product stereochemistry is concerned, is the question of reversibly-formed intermediates which could lead to thermodynamically controlled products in competition with kinetically controlled ones.[2b,d] Although the suggestions of reversibly formed intermediates in these cyclization reactions are reasonable and appealing, to our knowledge there is scant hard evidence for this. In one recent study, Rodebaugh and Fraser-Reid[7] have shown, on the basis of changing product ratios as a function of initial substrate concentrations, that there is communication between the bromonium ion of an *n*-pentenyl or *n*-hexenyl glycoside and the two parent olefins.[7] Kinetic evidence pertaining to this mechanistic question would be invaluable, and this forms the subject of the present report.

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(1) For reviews on this subject see: (a) Staninets, V. I.; Shilov, E. A. *Russ. Chem. Rev.* **1971**, *40*, 277. (b) Dowle, M. D.; Davies, D. I. *Chem. Soc. Rev.* **1979**, 171−197. (c) Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, **1984**; Chapter 6, Vol. 3.

(2) (a) Lipshutz, B. H.; Barton, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 1084. (b) Reitz, A. B.; Norley, S. O.; Maryanoff, B. E.; Liotta, D.; Monahan, R. *J. Org. Chem.* **1987**, *52*, 4191 and references therein. (c) Cook, C. H.; Cho, Y. S.; Jew, S. S.; Jung, Y. H. *Arch. Pharmacol. Res.* **1985**, *8*, 39 and references therein. (d) Rychnovsky, S. D.; Bartlett, P. A. *J. Am. Chem. Soc.* **1981**, *103*, 3963.

(3) (a) Corey, E. J.; Fleet, W. J.; Kato, M. *Tetrahedron Lett.* **1973**, 3963. (b) Rengevitch, E. N.; Staninets, V. L.; Shilov, E. A. *Proc. Natl. Acad. Sci. USSR* **1962**, *146*, 781. (c) Toshimitsu, A.; Teras, K.; Uemura, S. *Tetrahedron Lett.* **1984**, 5917. (d) Bartlett, P. A.; Richardson, D. P.; Meyerson, J. *Tetrahedron* **1984**, *40*, 2317 and references therein. (e) Collado, I. G.; Maders, J. G.; Massanet, G. M.; Luis, F. R. *Tetrahedron Lett.* **1990**, 563. (f) Cambie, R. C.; Rutledge, P. S.; Somerville, R. F.; Woodgate, P. D. *Synthesis* **1988**, 1009. (g) Davies, D. I.; Dowle, M. D. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2267. (h) Evans, D.; Magee, J. W.; Schauble, J. H. *Synthesis* **1988**, 862.

(4) (a) Balko, T. W.; Brinkmeyer, S.; Terando, N. H. *Tetrahedron Lett.* **1989**, *30*, 2045. (b) Bilosk, A. J.; Wood, R. D.; Ganem, B. *J. Am. Chem. Soc.* **1982**, *104*, 3233. (c) Knapp, S.; Levorse, A. T. *J. Org. Chem.* **1988**, *53*, 4006 and references therein.

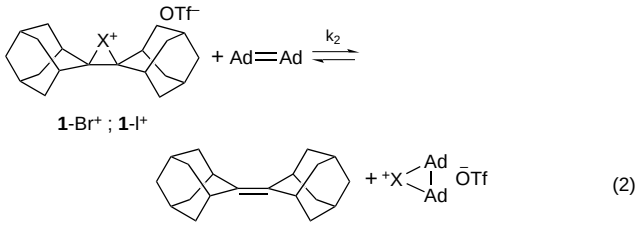
(5) (a) Williams, D. L. H. *Tetrahedron Let.* **1967**, 2001. (b) Rengevich, E. N.; Staninets, V. I.; Shilov, E. A. *Dokl. Akad. Nauk.* **1962**, *146*, 111. (c) Bienvenüe-Goetz, E.; Dubois, J. E.; Pearson, D. W.; Williams, D. L. H. *J. Chem. Soc. B* **1969**, 1275. (d) Williams, D. L. H.; Bienvenüe-Goetz, E.; Dubois, J. E. *Ibid.* **1969**, 517. (e) Hooley, S. R.; Williams, D. L. H. *J. Chem. Soc. B* **1975**, 503. (f) DoAmaral, L.; Melo, S. C. *J. Org. Chem.* **1973**, *38*, 800. (g) Lown, J. W.; Joshua, A. V. *Can. J. Chem.* **1977**, *55*, 131.

(6) (a) Chamberlin, A. R.; Mulholland, R. L.; Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 672. (b) Sperka, J.; Liotta, D. C. *Heterocycles* **1993**, *35*, 701. (c) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondan, N. G.; Jäger, V.; Schohe, R.; Franczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880.

(7) Rodebaugh, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1994**, *116*, 3155.

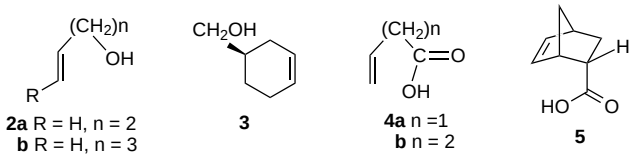
0022-3263/96/1961-0962$12.00/0

In earlier studies we have shown that the stable, structurally characterized, bromonium and iodonium ions (**1**-Br^+, **1**-I^+) of adamantylideneadamantane (Ad=Ad) undergo remarkably fast degenerate X^+ transfer between ion and parent olefin (eq 2).[8]



(2)

The second-order rate constants (k_2) at −80 °C in $ClCD_2CD_2Cl$ are 2×10^6 M^{-1} s^{-1} for $X^+ = Br^+$ and 8×10^6 M^{-1} s^{-1} for $X^+ = I^+$, and from the activation parameters, the process appears to be diffusionally controlled.[8b] The facility of this process suggested that 3-membered halonium ion/olefin exchanges might be general, but previously overlooked, phenomena. Should this be true, one might be able to probe the question of reversible X^+ transfer from **1**-X^+ to 1,ω-alkenols or alkenoic acids to form the putative halonium ion precursors believed to be on the pathway for halocyclizations.



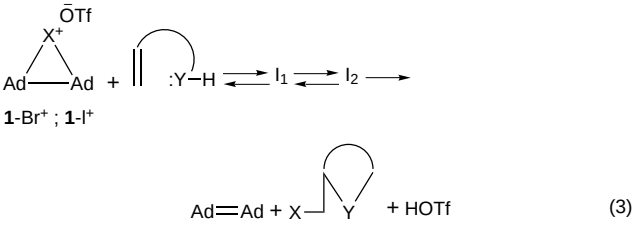
2a R = H, n = 2
b R = H, n = 3
c R = H, n = 4
d R = CH_3, n = 3

3

4a n =1
b n = 2

5

Herein we report the full details of a study[9] wherein bromo and iodocyclization of 1-ω-alkenols and alkenoic acids (**2**−**5**) is initiated using **1**-Br^+ and **1**-I^+ (eq 3). We believe that this study provides unambiguous kinetic evidence for the existence of at least two reversibly formed intermediates along the reaction pathway.



(3)

Experimental Section

(a) Materials. Adamantylideneadamantane (Ad=Ad) was prepared as previously described[10] as were the corresponding bromonium and iodonium triflate salts.[8b] All unsaturated alcohols and acids used in this study except 2-norbornene-5-carboxylic acid were commercially available (Aldrich) and purified by distillation. The latter olefin was provided by Professor Richard Gedye, Department of Chemistry, Laurentian University, Sudbury, Ontario.

4-Penten-1-ol-d_1 was synthesized from 4-penten-1-ol and CH_3OD. One mL of the olefin and 4 mL of the CH_3OD were mixed, and the methanol was removed by rotary evaporation. The procedure was repeated four times, and the final product was purified by distillation. ^1H NMR and IR analyses indicated less than 5% residual H in the hydroxyl group.

(b) Kinetics. The kinetics of the various transfer reactions were monitored by observing the disappearance of the halonium ion in purified[11] 1,2-dichloroethane (DCE) as a solvent at 25 °C under pseudo-first-order conditions of excess olefin. In the case of **1**-Br^+/OTf^-, 3.5×10^{-4} M solutions were used and the reaction was followed at 260 nm ($\epsilon_{260} = 3200$ M^{-1} cm^{-1}). For **1**-I^+/OTf^-, 8×10^{-5} M solutions were used, and the reaction was followed at 250 nm ($\epsilon_{250} = 13\,900$ M^{-1} cm^{-1}). The observed rate constants were determined from initial rate methods, monitoring the ΔAbs for the initial 5−10% of the reaction using an OLIS modified Cary 17 UV−vis spectrophotometer or, for faster reactions, an Applied Photophysics SX-17MV stopped-flow reaction analyzer. The pseudo-first-order rate constants, k_{obs}, were evaluated as $k_{obs} = (\Delta Abs)/(\Delta t[\mathbf{1}\text{-}X^+]\epsilon)$, where X = Br or I, Δt = the initial time span, and ϵ the extinction coefficients at 260 or 250 nm given above. The second-order rate constants, k_2, were determined from plots of k_{obs} vs [alkene] using three to six different concentrations of olefin from 0 to 2×10^{-2} M.

(c) Products. A typical preparative experiment was conducted as follows. Roughly 10 mg (0.02 mmol) of **1**-X^+/OTf^- was dissolved in 1 mL of CD_2Cl_2 (distilled from CaH_2) in a Teflon tube, and then equimolar olefin was added. The resulting solution was transferred to an NMR tube, and the ^1H NMR spectrum was recorded and compared with literature data. In a few cases where the product spectrum overlaps with that of Ad=Ad, the solution was extracted with D_2O to remove HOTf and dried ($CaCl_2$), and the CD_2Cl_2 was removed by evaporation with a stream of Ar. After the residue was dissolved in CD_3CN, the ^1H NMR spectrum was recorded. In several cases, the bromocyclization products were synthesized independently using NBS and the 1,ω-unsaturated system in $ClCD_2CD_2Cl$, monitoring the reaction progress by ^1H NMR. In these cases, the products had NMR spectra identical with those found using **1**-Br^+ as the halogen source.

Results and Discussion

Products. Given in Table 1 are the products identified from the reaction of equimolar **1**-X^+/OTf^- and various olefins in DCE-d_4 at room temperature. These products, based on ^1H NMR analysis and comparison with the spectra reported for the authentic materials, amount to greater than 90% of the material balance and are directly analogous to those observed from bromocyclization of the given olefin with other X^+ sources such as Br_2, NBS, I_2, or $I^+NO_3^-(pyridine)_2$.

Kinetics. (a) In the absence of added Ad=Ad. Given in Table 2 are the second-order rate constants for reaction of **1**-Br^+ or **1**-I^+ with various substituted alkenes in $ClCH_2CH_2Cl$ at 25 °C. These were evaluated under pseudo-first-order conditions of excess alkene by observing the rate of loss of the absorbance attributable to the halonium ion at 260 or 250 nm (for **1**-I^+ or **1**-Br^+) using conventional UV−vis spectrophotometry or stopped-flow techniques. No other components such as Ad=Ad or ROH were added. There are two observations of note for the kinetics determined in this way. First, the reactions appear to be second order overall, first order in each of the alkene and halonium ion. When the reaction mixtures are initially generated and their UV/vis spectra monitored, there is no evidence for the buildup of transient intermediates or complexes. Second, in all

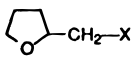
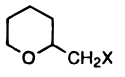
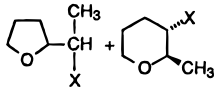
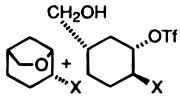
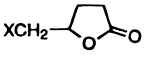
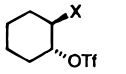
(8) (a) Bennet, A. J.; Brown, R. S.; McClung, R. E. D.; Klobukowski, M.; Aarts, G. H. M.; Santarsiero, B. D.; Bellucci, G.; Bianchini, R. *J. Am. Chem. Soc.* **1991**, *113*, 8532. (b) Brown, R. S.; Nagorski, R. W.; Bennet, A. J.; McClung, R. E. D.; Aarts, G. H. M.; Klobukowski, M.; McDonald, R.; Santarsiero, B. D. *J. Am. Chem. Soc.* **1994**, *116*, 2448.

(9) A preliminary account of this work has appeared: Neverov, A. A.; Brown, R. S. *Can. J. Chem.* **1994**, *72*, 2540.

(10) Flemming, M. P.; McMurry, J. E. *Org. Synth.* **1981**, *60*, 113.

(11) Perrin, D. D.; Armagero, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*, 2nd ed.; Pergamon Press: Oxford, 1980; p 204.

Table 1. Products Formed from Reaction of Equimolar 1-Br$^+$/OTf$^-$ or 1-I$^+$/OTf$^-$ and Various Olefins in $ClCD_2CD_2Cl$[a]

olefin	product	ref.	olefin	product	ref.
2a		X=Br[b] X=I[c]	**2b**		X=Br[d] X=I[c,e]
2c		X=Br[f] X=I[e]	**2d**[g]		X=Br[h,i] X=I[c]
3		j	**4b**		X=Br[k] X=I[c]
5		X=Br[l] X=I[e,m]			X=Br[n] X=I[o]

[a] Identified by ^{1}H NMR analysis and comparison with published data as identified below. [b] Product characterized on the basis of the following ^{1}H NMR spectrum: δ = 2.2−2.6 (m, 2 H); 4.0−4.3 (m, 4 H); 4.5−4.6 (m, 1 H). [c] Evans, R. D.; Magee, J. W.; Schanble, J. M. *Syntheses* **1988**, *11*, 862. [d] Lown, J. W.; Joshua, A. V. *Can. J. Chem.* **1977**, *55*, 508. [e] Lown, J. W.; Joshua, A. V. *Can. J. Chem.* **1977**, *55*, 122. [f] *Aldrich Library of ^{13}C and ^{1}H FT-NMR Spectra*; Aldrich: Milwaukee, 1993; Vol. 1, p 392(B). [g] Products in an 85:15 ratio for 5- and 6-membered ring with X = Br; only 6-membered ring formed with X = I. [h] Srebnik, M.; Mechowlam, R. *J. Chem. Soc., Chem. Commun.* **1984**, 1070. [i] Barti, G.; Catelani, G.; Monti, L.; Ventresca, G. *Tetrahedron* **1986**, *42*, 3973. [j] Identified on basis of the following ^{1}H NMR spectra data: δ = 1.5−2.5 (m, 7 H); 3.8 (m, 2 H); 4.2 (m, 1 H); 4.3 (m, 1 H) and 1.5−2.6 (m, 7 H); 4.0 (d, 2 H); 4.1 (m, 1 H); 4.8 (m, 1 H); ^{19}F δ = −79.2. [k] Cambie, R. C.; Rutledge, P. S.; Somerville, R. F.; Woodgate, P. D. *Synthesis* **1988**, *12*, 1009. [l] Ramey, K. C.; Lini, C.; Moriarty, R. M.; Gopal, H.; Welsh, H. G. *J. Am. Chem. Soc.* **1967**, *89*, 2401. [m] Davies, D. I.; Dowle, M. D. *J. Chem. Soc., Perkin Trans. 1* **1967**, 2267. [n] Bennet, A. J.; Brown, R. S.; McClung, R. E. D.; Klobukowski, M.; Aarts, G. H. M.; Santarsiero, B. D.; Bellucci, G.; Bianchini, R. *J. Am. Chem. Soc.* **1991**, *113*, 8532. [o] Product observable by ^{1}H NMR at −80 °C but decomposes on warming to room temperature.

Table 2. Second-Order Rate Constants for Reaction of 1-Br$^+$ and 1-I$^+$ with Various Alkenes, T = 25 °C, $ClCH_2CH_2Cl$[a]

	k_2 (M^{-1} s^{-1})		
olefin	**1**-Br$^+$	**1**-I$^+$	k_I/k_{Br}
2a	1.0×10^{-2}	0.75	75
2b	3.4	2.4×10^2	70
2c	0.35	1.0×10^1	28
2d	3.4×10^1	1.75×10^3	50
3	2.0		
cyclohexene	1.1	*c*	
5-decene	2.0		
1-octene	7.5×10^{-2}		
4a	N.O.[b]	N.O.[d]	
4b	7.6×10^{-2}	2.7	35
5	3.3	3.76×10^2	114

[a] Determined from initial rate methods using 10-fold or more excess of alkene/[**1**]. k_2 determined from the slope of the plot of initial pseudo-first-order rate constant (k_{obs}) vs [alkene]. Error limits ±10% of quoted number. [b] Not observable by ^{1}H NMR after 24 h. [c] By ^{1}H NMR, the reaction proceeds at −80 °C to give *trans*-2-iodotrifluoromethane sulfonate, but at higher temperatures this product is unstable, which precludes kinetic analysis. [d] By ^{1}H NMR, the reaction occurs slowly (~50% conversion in 24 h) to give presumably the β-iodo-γ-lactone (it is too slow for kinetic analysis).

cases investigated, the reactions slow down as a function of time, suggesting that one or more of the reaction products (Ad=Ad, HOTf, or cyclized material) is inhibitory. Therefore, the initial rates for 5−10% of the reaction were used to determine the rate constants given in Table 2.

Two major conclusions can be drawn. First, from the ratios of the k_2 constants for reactions using **1**-I$^+$ and **1**-Br$^+$ given in column 4 of Table 2, it can be seen that the I$^+$-reactions are 30−110-fold faster than the corresponding Br$^+$-ones. This observation stands in contrast to halocyclizations of 1,ω-alkenols and alkenoic acids using Br_2 or I_2 as the source of electrophilic halogen. In those cases, the Br_2 reactions are much faster than the I_2 reactions and the product mixtures of the former often contain 1,2-dibromides and bromosolvates as well as cyclized material.[1a,5d,e] By contrast, the iodocyclizations, while slower, appear to be far more selective and give very little of the noncyclized 1,2-addition products.

Of course, in the present case the only possible products are those of cyclization or X$^+$/OTf$^-$ 1,2-addition. In the case of cyclohexene, decene, and 1-octene, these latter products are exclusively formed, but the iodotriflate products are unstable at ambient temperatures in the media which precludes detailed kinetic analysis of the I$^+$ transfer. We suggest that the higher kinetic reactivity of **1**-I$^+$ relative to **1**-Br$^+$ stems from a higher ground state energy of the former ion which is destabilizing and leads to a lower transition state energy for the transfer of I$^+$ to the acceptor olefin.

Second, for the series of alcohols **2a**−**c**, reactivity with either **1**-Br$^+$ or **1**-I$^+$ follows the order **2a** < **2b** > **2c** which is analogous to the situation using Br_2 or I_2 as the halogenating agent.[5] Williams, Bievenüe-Goetz, and Dubois[5d] have explained this in terms of a complex mixture of OH inductively withdrawing effects, which decrease the reactivity of the Π-bond, superimposed upon an anchimeric assistance of the X$^+$ addition to the Π-bond which is optimized when the assisting OH group can cyclize to form a 5-membered ring. It is notable that this reactivity behavior contrasts what is reported for the additions and cyclizations promoted by I$^+$ (pyridine)$_2$·NO_3^+ in 70% $CHCl_3$/30% pyridine.[5g] In that study, the order of reactivity is **2a** > **2b** > **2c**, the total rate difference being only 2.5-fold. The constancy of these values, and indeed the similar kinetic values for several other olefins reported which are noncyclizable,[5g] suggests that the rate-limiting step for that reaction is largely independent of the olefin, e.g., reversible separation of the complex into a reactive form[12] (pyridine)$_2$ I$^+$ ⇌ (pyridine)$_1$ I$^+$ + pyridine).

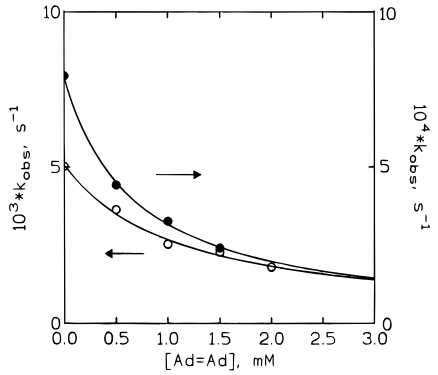


Figure 1. Plots of the observed pseudo-first-order rate constants for reaction of **1**-Br^+/OTf^- with (1.6×10^{-3} M) **2b** (○), and (10^{-2} M) **4b** (●) as a function of added [Ad=Ad] in $ClCH_2CH_2Cl$ at 25 °C. Lines through the data computed by NLLSQ fits to eq 4 where k_3 and $k'_3 = 0$.

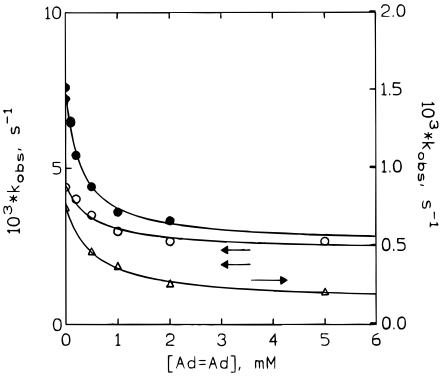


Figure 2. Plots of the observed pseudo-first-order rate constants for reaction of **1**-Br^+/OTf^- with (2×10^{-3} M) **2c** (△), (2×10^{-4} M) **2d** (●), and (2×10^{-3} M) **3** (○) as a function of added [Ad=Ad] in $ClCH_2CH_2Cl$ at 25 °C. Lines through data computed from NLLSQ fits to eq 4.

(b) In the Presence of Added Ad=Ad. While the kinetic information presented above is consistent with a bimolecular process involving direct transfer of X^+ to the acceptor olefins, it provides no information concerning the existence of intermediates. However, as indicated above, the reactions slow down as they proceed, which suggests that some of the products formed are inhibitory. We have confirmed this by investigating the initial reaction rates as a function of added HOTf and Ad=Ad. However, triflic acid, at the small concentrations which would be formed by reaction of the halonium ion at UV concentrations (8×10^{-5}–3.5×10^{-4} M), is not inhibitory.

The situation with added Ad=Ad is different, and there are several observations of note leading to the conclusion that there must be reversibly formed intermediates. First, in the bulk of the cases, added Ad=Ad markedly suppresses the reaction of **1**-Br^+ + alkene. In some cases, e.g., **2b** and **4b** as shown in Figure 1, plots of k_{obs} vs [Ad=Ad] asymptotically approach the X-axis, signifying complete reaction suppression at high [Ad=Ad]. In other cases, e.g., **2a**,**c**,**d**, **3**, **5**, and cyclohexene, the added [Ad=Ad] does not suppress the reaction completely. Rather, the plots of k_{obsd} vs [Ad=Ad] plateau at some limiting value as is shown in Figure 2 for **2c**,**d** and 4-(hydroxymethyl)cyclohexene (**3**). Only in the case of

(12) For the analogous process involving bis(quinuclidine)−Br^+/Br^- oxidation of secondary alcohols → ketones see: Blair, L. K.; Hobbs, S.; Bagnoli, N.; Husband, L.; Badika, N. *J. Org. Chem.* **1992**, *57*, 1600.

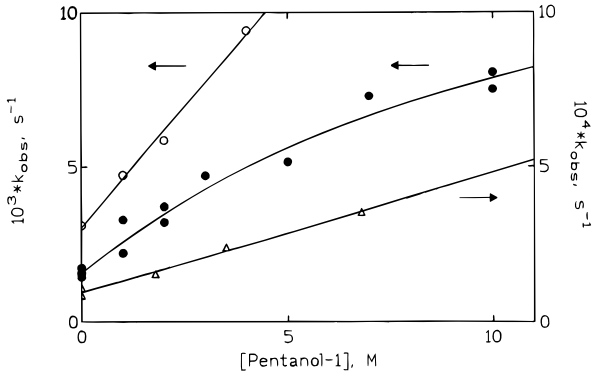


Figure 3. Plots of the observed pseudo-first-order rate constant for reaction of **1**-Br^+/OTf^- with **2b** (●), **2c** (△), and **5** (○) as a function of [ROH] in $ClCH_2CH_2Cl$ at 25 °C. For **2b**, **2c**, and **5**, ROH = pentanol. Key: [**2b**] = 1.6×10^{-3} M, [Ad=Ad] = 2×10^{-3} M; [**2c**] = 2×10^{-3} M, [Ad=Ad] = 5×10^{-3} M; [**5**] = 1×10^{-3} M, [Ad=Ad] = 0 M.

reaction of 5-decene or 1-octene with **1**-Br^+ is the rate observed to be independent of [Ad=Ad]. Notably, the above rate depression behavior is not seen for any substrate with **1**-I^+, all reaction rates being independent of [Ad=Ad] up to the highest concentrations we have used ($\sim 1 \times 10^{-2}$ M).

Second, in some cases that we have investigated the reaction exhibits kinetic terms that are second order in added [alkenol]. These cases include **2b**,**c**,**d**, although the latter two examples contain both first and second order in [alkenol] terms. Notably, none of the reactions using **1**-I^+ and any alkene shows such behavior, nor does the reaction of **1**-Br^+ with any alkenoic acid or alkene that does not contain a hydroxyl functionality.

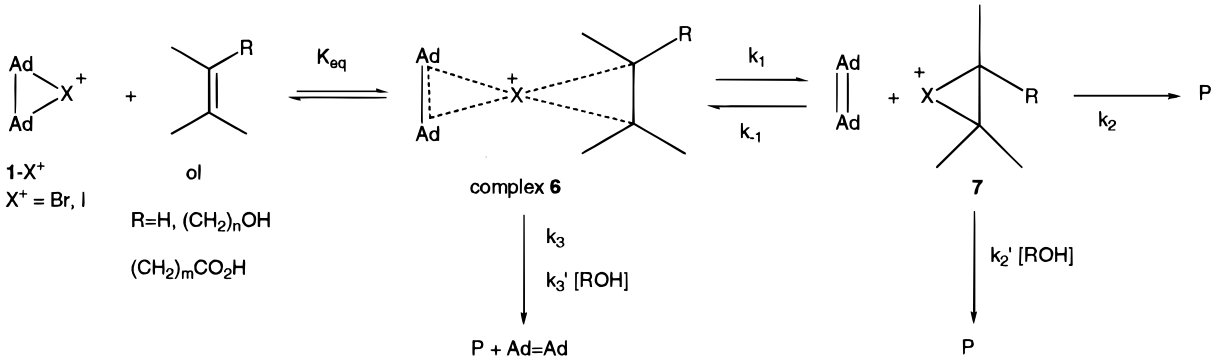
Third, in the cases we have investigated in most detail, namely reaction of **1**-Br^+ with **2b**,**c** and 2-norbornene-5-carboxylic acid (**5**), added alcohols such as pentanol accelerate the reaction. The behavior is shown in Figure 3, which depicts the k_{obsd} vs [ROH] plots for these reactions. Once again, this behavior is not seen for any reaction using **1**-I^+.

The above seemingly complex variety of behaviors can be accommodated by a general mechanism given in Scheme 1, the individual product-forming pathways of which have prominence depending upon the nature of the olefin and **1**-X^+.[13] The proposed process stems from the observation that increasing [Ad=Ad] suppresses the reaction rate which requires that there be, at least in some cases, a reversibly formed intermediate having a sufficient lifetime that it can be driven backward by a common species reaction with Ad=Ad. From Scheme 1 can be derived the general kinetic expression given in eq 4 assuming steady state concentration of the nascent halonium ion **7**.

$$k_{obs} = (k_3 + k_3'[ROH])K_{eq}[ol] + \frac{k_1K_{eq}[ol](k_2'[ROH] + k_2)}{k_{-1}[Ad{=}Ad] + (k_2'[ROH] + k_2)} \quad (4)$$

(13) A kinetically equivalent scheme can be drawn where there are two independent pathways leading away from the starting material. One of the pathways involves a complex similar to that shown in Scheme 1, but that complex does not spontaneously evolve to products (i.e., k_3, $k_3' = 0$). The other independent pathway involves a true bimolecular concerted process leading to products with no interceptable intermediates. For the sake of simplicity we prefer the overall mechanism presented in Scheme 1.

Scheme 1[a]



[a] ol signifies acceptor olefins given in Table 2 and ROH indicates either added pentanol or propanol, or starting alkenol.

In eq 4, ROH and ol can refer to the same material if the starting olefin contains an alcohol portion; otherwise, ROH refers to added alkanols. In Scheme 1 there are several channels for product formation involving (a) direct collapse of a putative[14] ol:**1**-X^+ complex **6**, (b) breakdown of this complex assisted by added alcohol (ROH) or a second substrate alkene provided that olefin possesses an OH group, (c) reversible dissociation of the complex **6** into free Ad═Ad and a nascent halonium ion **7**, the latter undergoing spontaneous cyclization, or (d) a similar reversible dissociation of the complex followed by cyclization of **6** promoted by some hydroxyl-bearing molecule (i.e., ROH or alkenol).

Scheme 1 is sufficiently complex that evaluation of the individual rate and equilibrium constants in every case is not possible. Fortunately, some of the molecules exhibit limiting behavior that allows considerable simplification of eq 4 and a good definition of the kinetic terms for product formation.

We deal first with two such examples (**2b** and **4b**) where at high added [Ad═Ad] the reaction with **1**-Br^+ is completely suppressed, thereby signifying that the (k_3 + k_3'[ROH]) terms are negligible. After removal of the k_3, k_3' terms and linearization, eq 4 adopts the form of eq 5.

$$\frac{[\text{ol}]}{k_{\text{obs}}} = \frac{k_{-1}[\text{Ad=Ad}]}{k_1 K_{\text{eq}}(k_2 + k_2'[\text{ROH}])} + \frac{1}{k_1 K_{\text{eq}}} \qquad (5)$$

Thus, plots of [ol]/k_{obs} vs [Ad═Ad] should yield straight lines having slopes relating to the partitioning of nascent halonium ion **7** between reversal and product formation and slopes relating to k_1K_{eq} For clarity, when no other alcohol is present, ROH in eqs 4 and 5 = ol. Shown in Figures 4 and 5 are such plots for the cyclization of **2b** and **4b** using **1**-Br^+ in the presence of varying amounts of the former olefins. The plots reveal that the reactions exhibit greater than first order dependence on starting material for 4-penten-1-ol (**2b**) and a first order dependence for alkenoic acid **4b**. Thus, for **2b**, a second molecule of alkenol is required to promote product formation from **7**, while for **4b** product formation appears not to require this.

Numerical evaluation of the partitioning of the nascent bromonium ions (**7**) involved above is accomplished by

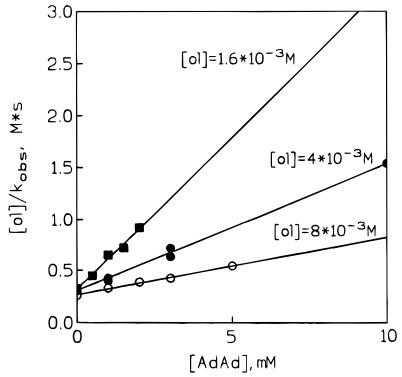


Figure 4. Plots of [ol]/k_{obs} vs [Ad═Ad] for reaction of **2b** with **1**-Br^+/OTf^- at three different [ol] in $ClCH_2CH_2Cl$ at 25 °C.

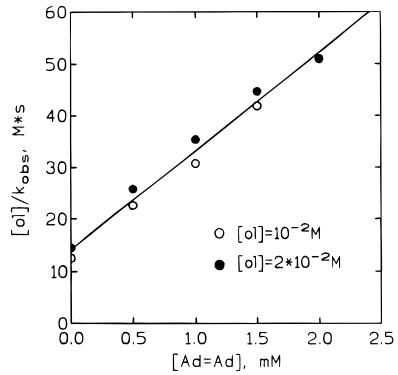


Figure 5. Plots of [ol]/k_{obs} vs [Ad═Ad] for reaction of **4b** with **1**-Br^+/OTf^- at two different [ol] in $ClCH_2CH_2Cl$ at 25 °C.

plotting the intercept/slope ratio (from eq 5) as a function of [ol] as in eq 6. For **2b**, the slope of such a plot is ~0.67

$$\text{intercept/slope} = \frac{k_2'[\text{ol}]}{k_{-1}} + \frac{k_2}{k_{-1}} \qquad (6)$$

and the intercept is indistinguishable from zero: thus, for **2b** spontaneous breakdown to product is kinetically insignificant and can only occur if a second molecule of alkenol is involved. By contrast, a similar plot for alkenoic acid **4b** shows that the slope of the plot in eq 6 is zero, while the intercept is 7.2×10^{-4} M. In this case, product formation occurs primarily by spontaneous breakdown and another molecule of alkenoic acid is not active in promoting this process: the relatively small value for k_2/k_{-1} represents the inefficiency of spontaneous breakdown of **7** in this case.

(14) An asymmetric complex having X^+ closer to one olefin unit than the other has been computed as being energetically favored relative to a free halonium ion plus olefin for the ethylene/bromonium ion system.[8b]

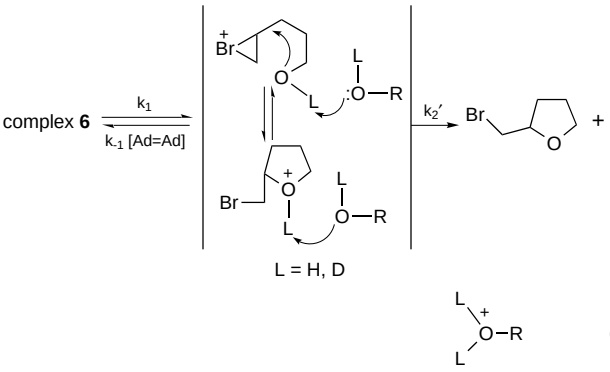
Table 3. Kinetic Parameters for Br^+ transfer from 1-Br^+ to various acceptor olefins in $ClCH_2CH_2Cl$ at 25 °C

olefin	k_1K_{eq} (M^{-1} s^{-1})[a]	$(k_3 + k_3'[ROH])K_{eq}$ [a] (M^{-1} s^{-1})[a]	$(k_2 + k_2'[ROH])/k_{-1}$
2a	1.0×10^{-2} [b]		
2b-OH	3.5 ± 0.3	N.O.[c]	0.63 ± 0.04[a,d]
	3.0 ± 0.2[e]	N.O.[c]	0.71 ± 0.04[d,e]
2b-OD	4.8 ± 1.0[e]	N.O.[c]	0.30 ± 0.3[d,e]
	4.9 ± 1.0	N.O.[c]	0.29 ± 0.04[a,d]
2c	$(2.5 \pm 0.5) \times 10^{-1}$	$(8.4 \pm 1.2) \times 10^{-2}$	0.39 ± 0.25[d]
2d	23 ± 3	11 ± 3	0.37 ± 0.13[d]
			$(1.9 \pm 0.6) \times 10^{-4}$ [f]
4b	$(7.2 \pm 0.6) \times 10^{-2}$	N.O.[c]	$(7.4 \pm 1.3) \times 10^{-4}$ [f]
5	1.6 ± 0.4	1.7 ± 0.4	$(2 \pm 1) \times 10^{-3}$ [f]
3	0.67 ± 0.2	1.3 ± 0.05	$(4.5 \pm 1.2) \times 10^{-4}$ [f]
cyclohexene	0.6 ± 0.1	0.5 ± 0.1	$(5 \pm 2) \times 10^{3}$
5-decene	2[b]		
1-octene	1.0×10^{-2} [b]		

[a] From NLLSQ fits to eq 4. [b] From Table 2; strictly speaking, it refers to $(k_1 + k_3 + k_3'[ROH])K_{eq}$ since we have no evidence that product formation comes exclusively from $(k_2 + k_2')$. [c] Not observable; cannot be defined from plot of k_{obsd} vs [Ad=Ad] since limiting k_{obsd} at high [Ad=Ad] → 0. [d] Unitless; refers to k_2'/k_{-1}. [e] Calculated from linear plot of eq 5. [f] Units M^{-1}, refers to k_2/k_{-1}.

The effectiveness of a second alkenol but ineffectiveness of the second molecule of alkenoic acid in promoting product formation from reaction of **1**-Br^+ with **2b** and **4b** suggests that the hydroxyl group is the important component. Consistent with this is the fact that an alkanol such as 1-pentanol promotes the cyclization of **2b**, **2c** and **5**. The concentration dependences of the rates for these reactions are shown in Figure 3, that for **2b** vs [pentanol] being particularly significant because it shows evidence of saturation behavior. The latter is consistent with the process given in eq 7 which is an expansion of the product-forming steps in Scheme 1, wherein the added alcohol, and by inference the second molecule of alkenol, acts as a base to remove a proton from **7** to assist its cyclization. The saturation behavior for **2b** stems from the competition of ROH-dependent deprotonation of **7**, or its reversibly cyclized intermediate,[2b] with Ad=Ad-promoted reversal such that at high [ROH], there is a change in rate-limiting step from breakdown, to formation, of **7**.

As a final piece of evidence in support of the role of the ROH or second molecule of alkenol as a base, we note that the assisted breakdown depicted in eq 7 should be subject to a normal deuterium kinetic isotope effect. Accordingly, when the slope and intercept data obtained from the plots of [**2b**-OL]/k_{obs} vs [Ad=Ad] (eq 5) are manipulated as in eq 6, it is found that $(k_2'/k_{-1})_{\mathbf{2b}\text{-OH}/\mathbf{2b}\text{-OD}} = 2.0$.



(7)

For the other olefins that we have investigated where **1**-Br^+-promoted cyclization cannot be completely suppressed by the addition of [Ad=Ad], $(k_3 + k_3'[ROH])K_{eq}$[ol] in eq 4 cannot be negligible, and we suggest that product formation occurs by direct cyclization within complex **6**. In the cases of noncyclizable cyclohexene, 5-decene, and 1-octene where the reaction shows little suppression with added [Ad=Ad], we further suggest that product formation results from OTf^-/bromonium ion pair collapse within the complex to afford 1,2-addition products. For these more complex cases, NLLSQ fitting of the k_{obs} vs [Ad=Ad] data to eq 4 yields the parameters k_1, K_{eq}, $(k_3 + k'_3[ROH])K_{eq}$, and $(k_2 + k'_2[ROH])/k_{-1}$. These are given in Table 3 along with the comparable parameters for **2b** and **4b** derived as above.

(c) Generalities That Can Be Drawn from Data in Table 3. In the cases where either Ad=Ad does not inhibit the rate or it has not been added to the reaction (e.g., for the k_2 data in Table 2), eq 4 can be recast as eq 8, which shows that the observed rate constant is really

$$\frac{k_{obs}}{[ol]} = K_{eq}(k_1 + k_3 + k_3'[ROH]) \qquad (8)$$

the product of K_{eq} and the sum of all steps leading toward product from complex **6**. Without additional information for those cases (e.g., **2a**, 5-decene, 1-octene), we cannot further partition k_{obs}/[ol] into its individual rate constants.

Inspection of the process shown in Scheme 1 indicates that the numerical value of k_1K_{eq}/k_{-1} should represent the equilibrium constant for eq 9.

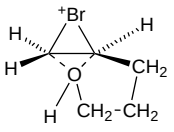
$$\mathbf{1}\text{-}Br^+ + ol \rightleftharpoons Ad{=}Ad + \mathbf{7} \qquad (9)$$

Fortunately, for those reactions where Ad=Ad can be shown to depress the rate, exact kinetic evaluation of k_1K_{eq} is possible, those values being given in column 2 of Table 3.

For those cases where it is possible to dissect the k_1K_{eq} term from k_{obs}/[ol], we can provide conditional values for the equilibrium constant for the process depicted in eq 8, assuming that k_{-1} is a constant value approaching the diffusion limit. This assumption is reasonable since we have previously shown[8] that the thermoneutral X^+ exchange between two Ad=Ad molecules occurs with a rate constant of 4×10^7 M^{-1} s^{-1} at 25 °C, the associated $\Delta H^‡$ and $\Delta S^‡$ values being 1.8 kcal/mol and −21 cal/K·mol. Such exchange should be at least as fast for transfer of Br^+ from less stable bromonium ions to Ad=Ad in the thermodynamically favored direction (k_{-1} in Scheme 1).

The so-calculated ordering of stability for the bromonium ions formed from the 1,ω-alkenols is **2d** > **2b** > **3** > **2c** > **2a**, the range of stabilities being ~100-fold. The **2d** > **2b** ordering can easily be explained on the basis

that the former double bond is disubstituted, while the latter is monosubstituted; compare **5** > **4b**, cyclohexene ~ 5-decene > 1-octene. The ordering of **2b** > **2c** > **2a** must be a reflection of a complex mixture of inductive effects which should attenuate in passing from **2a** → **2b** → **2c**, coupled to some internal stabilization of the bromonium ion as in **8** which is similar to what was

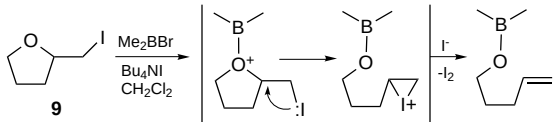


8

described by Williams, Bienvenüe-Goetz, and Dubois[5a] as being an anchimeric assistance to cyclization. In our case, however, there is an important distinction since an anchimerically assisted cyclization would describe a transition state and not an intermediate which is capable of common species reversal. Rather, the process involved here must be akin to the solvent-assisted ionization[15] described first by Grunwald and Winstein[16] and later applied to electrophilic bromination by Ruasse and coworkers.[17]

Conclusions

The behavior of **1**-Br^+ in transferrring its halogen to acceptor olefins in inducing bromocyclizations provides for the first time kinetic evidence supporting the involvement of at least two intermediates, namely complex **6** and nascent bromonium ion **7**. The kinetic details of this investigation are made possible by the rapidity with which Ad=Ad captures the intermediate halonium ions, thereby causing a common species rate depression. Notably, the corresponding iodonium ion, **1**-I^+, exhibits none of this kinetic behavior in its reactions with the same olefins. Because of the similarity in the reactions and halogenating agents, it seems unwarranted to suggest that the gross mechanism for iodocyclization differs from that of bromocyclization. Rather, we suggest that the common mechanism of Scheme 1 works in both cases, with the k_1K_{eq} and/or $(k_3 + k_3'[ROH])K_{eq}$ values for the iodonium ion being larger than the corresponding ones in the bromonium case. The most likely source of the extra activity which would not be subject to common species rate depression by added Ad=Ad is in the k_3, k_3' terms which pertain to an internally assisted cyclization of the iodonium ion within the complex. Pertinent to this is the finding by Gauthier and Guindon[18] that iodomethyl cyclic ethers of the type **9** can easily be opened to the corresponding 1,ω-alkenols via the proposed intermediacy of an iodonium ion, while the corresponding bromomethyl ethers are inert. Additionally, it is well-known that neighboring group participation in internal displacements leading to 3-membered halonium ions by iodine is at least 1000−3000-fold better than the corresponding bromine participation.[19] By microscopic reversibility, if iodine closure is faster, opening of the iodonium ion should also be faster, which may explain why Ad=Ad is ineffectual in suppressing the rate.



9 (10)

Acknowledgment. The authors gratefully acknowledge the financial assistance of the University of Alberta and the Natural Sciences and Engineering Research Council of Canada.

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(15) For discussions about solvent-assisted ionizations in S_N1 processes see: Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper and Row: New York, 1987; pp 335−340.
(16) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc.* **1948**, *70*, 846.
(17) Ruasse, M. F.; Motallebi, S.; Galland, B. *J. Am. Chem. Soc.* **1991**, *113*, 3440.
(18) Gauthier, J. Y.; Guindon, Y. *Tetrahedron Lett.* **1987**, 5985.
(19) (a) Winstein, S.; Grunwald, E.; Ingraham, L. L. *J. Am. Chem. Soc.* **1948**, *70*, 821. (b) Winstein, S.; Grunwald, E. *Ibid.* **1948**, *80*, 828.