

BORATE PROMOTED ELECTROPHILIC ADDITIONS OF ALKYL HYPOHALITES

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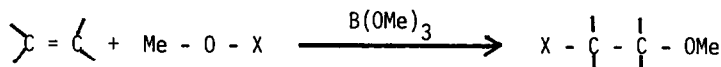
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Abstract: Catalysis by trimethyl borate promotes a rapid ionic reaction of methyl hypobromite with alkenes and dienes in methylene chloride.

Alkyl hypohalites belong to a group of "sluggish" electrophiles¹ which are resistant to ionic addition² to alkenes in aprotic, non-polar solvents. On the other hand, radical reactions³ of hypohalites with alkenes occur easily in aprotic solvents and ionic addition can be selected by using protic, nucleophilic solvents such as methanol and acetic acid.^{3a-3d, 4}

We were intrigued with the possibility that the lack of ionic reactivity of the hypohalites in aprotic solvents could be exploited as a basis for promoting ionic reactions with the aid of catalysts⁵. We hoped that the outcome of these catalyzed ionic reactions might differ markedly from either radical reactions or ionic reactions in protic solvents.

On the basis of our preliminary investigations, we wish to report that trimethyl borate (1) promotes the clean ionic addition of methyl hypobromite (2) in methylene chloride to alkenes and dienes. Reactions are rapid at 0°C and afford bromoethers in yields of 50-70%. Unlike catalysis by a number of other Lewis acids,⁶ products were not isomerized. Ionic addition of methyl hypochlorite (3) is also promoted by 1, but the reaction is slower and inhibitors must be used to prevent radical reactions of 3.



The results of the reactions of 2 and 3 with cyclopentadiene (4), presented in Table I, show that the borate catalyzed reaction gives a strikingly different product composition from that obtained by radical addition or by reaction in the protic solvent, methanol. Both 2 and 3 give mostly the cis-1,4 adduct (70% from 2 and 52% from 3) in the catalyzed reaction. By contrast, reaction in methanol gives mainly trans products (1,2 and 1,4). In radical addition of 2 and 3 the trans-1,4 adduct is major and the 1,2 products are anti-Markownikoff.

The products from reaction of methyl hypobromite with two acyclic, conjugated dienes, isoprene (5) and cis-3-methyl-1,3-pentadiene (6) are shown in Table II. Isoprene yields different major products at each of the three reaction conditions. In the borate catalyzed reaction attack occurs at the methyl substituted (1,2 bond) to yield 78% of the corresponding 1,4 isomer, whereas in methanol, attack occurs at the same bond but leads to 80% of the 1,2 isomer. In the radical reaction the methoxyl radical mainly attacks the 1,2 bond leading to 85% of the opposite 1,4 adduct (4-bromo-1-methoxy-2-methyl-2-butene).

The borate catalyzed addition of 2 to *cis*-3-methyl-1,3-pentadiene is especially interesting. In this reaction the 1,4 adduct resulting from attack at the trisubstituted double bond (3,4 bond) is the major product whereas it is a trace product in both the methyl hypobromite-methanol reaction and the radical reaction. Methyl hypobromite attacks both the 1,2 and 3,4 bonds of 6 to about an equal extent in the catalyzed reaction and in methanol. The difference is that the protic solvent gives mainly the 1,2 adducts but 1,4 adducts predominate in the catalyzed reaction.

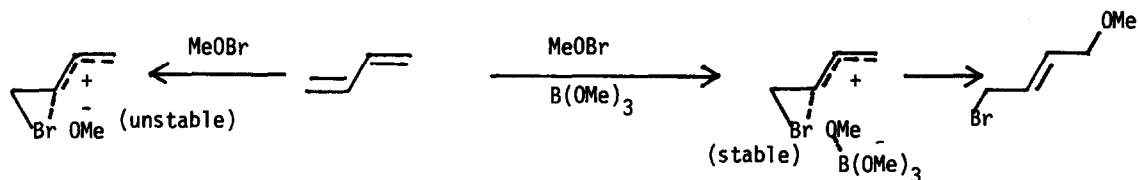
Table I. Reactions^a of CH₃OCl and CH₃OBr with Cyclopentadiene

Reactants	Products ^b (%)					
<u>4</u> , CH ₃ OBr, B(OCH ₃) ₃	70	7	15	8		
<u>4</u> , CH ₃ OBr, CH ₃ OH	16	25	57	1		
<u>4</u> , CH ₃ OBr (radical)	30	35			34	
<u>4</u> , CH ₃ OCl, B(OCH ₃) ₃	52	8	14	26		
<u>4</u> , CH ₃ OCl, CH ₃ OH ^c	26	31	36	7		
<u>4</u> , CH ₃ OCl, (radical) ^c	17	50			28	5

^aReactions were conducted at 0-5°C. In a typical borate catalyzed reaction, 1.5 mmol of CH₃OBr was added last to a solution consisting of: 1, 1.5 mmol; 4, 6.1 mmol; CH₂Cl₂, 261 mmol. Reactions in methanol were identical to the above with 1 omitted. In borate catalyzed reactions with 2, the radical inhibitor, 2,6-di-*t*-butyl-4-methylphenol was present at 0.5 M concentration. (constant oxygen saturation also prevented radical addition to 4 but yields were lower). Radical reactions were obtained by adding the solution of hypohalite directly to neat 4. Methyl hypobromite was prepared^{3c} from HgO and Br₂ as a solution (ca 0.4M) in CH₂Cl₂ and methyl hypochlorite^{3a} was prepared from commercial bleach as a solution (ca 1 M) in CH₂Cl₂. ^bProduct mixtures were analyzed by vpc. Chloromethoxy products were identified previously.^{3b} Bromomethoxy products were identified by nmr and by conversion to chloromethoxy compounds with LiCl/DMSO. ^cReference 3b.

The product compositions from the reactions of the dienes and methyl hypobromite with borate catalysis closely resembles the products from bromination of dienes in aprotic solvents. Bromination gives largely 1,4 dibromides⁷ with a stereochemical preference for *syn* 1,4 addition.⁸ An ion pair mechanism can explain both reactions. Trimethyl borate may promote the reaction by helping to form a more stable anion than would be possible from the hypobromite itself. In the aprotic

non-polar solvent, the carbocation intermediate would be stabilized by charge dispersal across the



allylic system. The high charge density at the # 4 carbon, steric effects encountered by the bulky anion, and the increased stability with the catalyst would favor 1,4 collapse of the ion pair.

Table II. Reaction^a of CH_3OBr with Isoprene and *cis*-3-Methyl-1,3-pentadiene

Diene, 	Reagents	Products (%)			
<u>5</u> ($R_1 \text{ \& } R_2 = \text{H}$)	CH_3OBr , $\text{B}(\text{OCH}_3)_3$	78	2	20	b
	CH_3OBr , CH_3OH	6		94	b
	CH_3OBr (radical)	17	83		
<u>6</u> ($R_1 = \text{H}$, $R_2 = \text{CH}_3$)	CH_3OBr , $\text{B}(\text{OCH}_3)_3$	41	38	15	6
	CH_3OBr , CH_3OH	3	26	47	23
	CH_3OBr (radical)	7	93		

^aReaction conditions are the same as for 4 in Table I. ^bThis isomer could have been formed in small amounts but it was not identified. ^cProducts were analyzed by vpc. Products from 5 were identified by nmr analysis of mixtures which were rich in a single isomer. Products from 6 were identified by preparatory vpc isolation of individual isomers followed by nmr analysis.

Additional evidence for an analogy to the bromination mechanism was obtained by comparing bromination and the catalyzed addition of methyl hypobromite to the 1-phenylpropenes. The borate catalyzed reaction took place with 95% stereoselectivity (*erythro* : *threo*, 95:5) for the *trans* alkene and with 82% stereoselectivity (*erythro* : *threo*, 18:82) for the *cis* alkene. A comparable degree of stereoselectivity was observed in bromination of these alkenes in methylene chloride where a weakly bridged bromonium ion intermediate was proposed to account for the result.⁹ Further investigations are planned in which we will explore a number of borate esters and a variety of hypohalites and other positive halogen electrophiles. These experiments should serve to further elucidate the mechanism of the catalysis.

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REFERENCES

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2. In a previous investigation (V.L. Heasley, C.L. Frye, G.E. Heasley, K.A. Martin, D.A. Redfield, and P.A. Wilday, Tetrahedron Lett., 1573 (1970) of the reaction of 2 with 1-hexene and styrene in methylene chloride, we found that if the radical reaction was prevented with inhibitors that a polar addition of 2 could be observed. But reactions did not go to completion and yields were low. We found in this current investigation that dienes such as isoprene and cyclopentadiene continue to react by a radical mechanism even under oxygen saturation.
3. (a) G.E. Heasley, V.M. McCully, R.T. Wiegman, V.L. Heasley, and R.A. Skidgel, J. Org. Chem., 41, 644 (1976); (b) G.E. Heasley, W.E. Emery III, R. Hinton, D.F. Shellhamer, V.L. Heasley, and S.L. Rodgers, J. Org. Chem., 43, 361 (1978); (c) P. Brun and B. Waegell, Tetrahedron, 32, 517 (1976); (d) A. Bresson, G. Dauphin, J. -M. Geneste, A. Kergomard, and A. LaCourt, Bull. Soc. Chim. France, 2432 (1970).
4. Ionic reactions of the sluggish electrophiles in protic solvents is not a simple addition (i.e., $C=C + E-Y \longrightarrow E-C-C-Y$) but is instead a solvent incorporation process ($C=C + E-Y + SOH \longrightarrow E-C-C-OS + H-Y$). The solvent probably provides catalysis, as well, by hydrogen-bonded stabilization of the anion of the electrophile.
5. Recently we found that boron fluoride effectively catalyzed the reaction of methyl hypochlorite with alkenes in methylene chloride. Chloro fluorides were major products from many alkenes (V.L. Heasley, D.F. Shellhamer, R.K. Gipe, H.C. Wiese, M.L. Oakes, and G.E. Heasley, Tetrahedron Lett., 21, 4133 (1980)).
6. We briefly explored catalysis of the addition of methyl hypochlorite to several alkenes and dienes in methylene chloride by the following Lewis acids: BCl_3 , $Ti(OMe)_4$, $TiCl_4$, $FeCl_3$, $SbCl_5$, and $SnCl_4$. These proved to be less promising than 1 because of problems such as equilibration of products, formation of dichlorides, and low yields.
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