  Bull. Chem. Soc. Jpn., 59, 3519—3522 (1986)

Bromochlorination of Alkenes with Dichlorobromate(1−) Ion. V. Regio- and Stereochemistry for the Bromochlorination of Styrene Derivatives with Dichlorobromate(1−) Ion in Protic Solvents

Takeshi NEGORO* and Yoshitsugu IKEDA
Department of Chemistry, Faculty of Education, Wakayama University,
Sakaedani, Wakayama 640
(Received April 24, 1986)

The bromochlorination of styrene derivatives with tetrabutylammonium dichlorobromate(1−) (**1**) in such protic solvents as acetic acid and methanol gives the corresponding bromo chloro adducts along with substantial amounts of solvent-incorporated products in a regiospecific manner (regioselective in the case of 3-nitro- or 2-chlorostyrenes). The reaction of 1-phenylpropenes with **1** gives nonstereospecific but regiospecific adducts. These results suggest that the addition of **1** to styrene derivatives in protic solvents involves an attack of chloride ion or solvent molecule to a bromonium ion intermediate.

In this series of studies, we have reported that the regiochemistry of the bromochlorination of alkenes with tetrabutylammonium dichlorobromate(1−) (**1**) is very sensitive to the structure of alkenes.[1-4] Meanwhile, the regio- and stereochemistries of the reaction of phenyl-substituted alkenes with **1** have been reported to be independent of the solvent polarity when the reaction is carried out in aprotic solvents.[1,2] However, only a few studies have been carried out on the addition of **1** to these alkenes in protic solvents.[1] As a continuation of our studies, the present work was initiated to examine the effect of protic solvents on the regio- and stereochemistries of the addition of **1** to styrene derivatives.

Results and Discussion

The reaction of $(n\text{-}C_4H_9)_4NBrCl_2$ (**1**) with styrene derivatives **2a—f** in acetic acid gave the corresponding bromo chloro compounds **3a—f** along with substantial amounts of solvent-incorporated products **4a—f** in good yields (Scheme 1 and Table 1).

$$XC_6H_4CH{=}CH_2 \;(\mathbf{2}) + \mathbf{1} \longrightarrow XC_6H_4CHClCH_2Br\;(\mathbf{3}) + XC_6H_4CH(OCOCH_3)CH_2Br\;(\mathbf{4})$$

a: X=H **b**: X=4-CH_3
c: X=4-F **d**: X=4-Cl
e: X=3-Cl **f**: X=4-Br

Scheme 1.

Table 1. Bromochlorination of **2** with **1** in Acetic Acid[a]

Alkene	Product composition/%[b]		
2	**3**	**3′**	**4**
2a	66.7(65.4)	0	33.3(34.6)
2b	72.2(70.0)	0	27.8(30.0)
2c	72.4(71.4)	0	27.6(28.6)
2d	69.8(70.0)	0	30.2(30.0)
2e	72.7(71.2)	0	27.3(28.8)
2f	72.9(71.6)	0	27.1(28.4)
2g	66.3	2.0	31.7
2h	71.8	6.8	21.4
2i	64.8[c]	0	35.2
2j	66.7[d]	0	33.3

a) Reactions were carried out with 10 mmol of **1**, 10 mmol of **2**, and 20 ml of acetic acid at 20 °C. b) Determined by ^1H NMR analysis. Figures in parentheses represent the product compositions determined by GLC analysis. Percentages are normalized to 100%. Total yields were found to be more than 80% in all runs. c) A mixture of **3i** (89.5%) and **3j** (10.5%). d) A mixture of **3i** (11.5%) and **3j** (88.5%).

On the other hand, the reaction of 2-chloro- and 3-nitrostyrenes (**2g** and **2h**) with **1** gave a mixture of two regioisomers, **3g** and **3h** and **3g′** and **3h′**, and **4g** and **4h**, respectively (Scheme 2 and Table 1).

$$XC_6H_4CH{=}CH_2 \;(\mathbf{2}) + \mathbf{1} \longrightarrow XC_6H_4CHClCH_2Br\;(\mathbf{3}) + XC_6H_4CHBrCH_2Cl\;(\mathbf{3'}) + XC_6H_4CH(OCOCH_3)CH_2Br\;(\mathbf{4})$$

g: X=2-Cl **h**: X=3-NO_2

Scheme 2.

The solvent-incorporated products **4** were found to be formed in a completely regiospecific Markownikoff manner from all the styrene derivatives.

The reaction of *trans*-1-phenylpropene (**2i**) with **1** in acetic acid gave a mixture of *erythro*- and *threo*-2-bromo-1-chloro-1-phenylpropanes (**3i** and **3j**) along with a substantial amount of *erythro*-1-acetoxy-2-bromo-1-phenylpropane (**4i**). When *cis*-1-phenylpropene (**2j**) was allowed to react with **1**, a mixture of **3i**, **3j**, and *threo*-1-acetoxy-2-bromo-1-phenylpropane (**4j**) was obtained (Scheme 3 and Table 1).

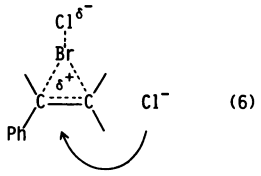
$$PhCH{=}CHCH_3 + \mathbf{1} \longrightarrow PhCHClCHBrCH_3 + PhCH(OCOCH_3)CHBrCH_3$$

2i	**3i**, 58.0%	**4i**, 35.2%
	3j, 6.8%	
2j	**3i**, 7.7%	**4j**, 33.3%
	3j, 59.0%	

Scheme 3.

The formation of the solvent-incorporated products **4** cannot be ascribed to the subsequent secondary reaction of the bromo chloro compounds **3** with acetic acid, since prolonged reaction did not cause any change in the isomer ratio of the products.

We have previously reported that the reaction of **2d—h** with **1** in chloroform occurred in a nonregiospecific manner, although the Markownikoff adducts were formed mainly.[4] The reactions of *trans*- and *cis*-1-phenylpropenes (**2i** and **2j**) with **1** have been found to proceed in an *anti*-stereospecific and nonregiospecific manner in aprotic solvents.[2] Therefore, we have suggested that the addition of **1** to alkenes in aprotic solvents involves a rate- and product-determining attack of chloride ion on a three-center bound π-complex **6**.



(6)

As shown in Table 1, the regio- and stereochemistries of the reaction of **2** with **1** in acetic acid are very different from those of the previous reaction in aprotic solvents.[2,4] Obviously, a different product-determining step is involved in the reaction in acetic acid.

Furthermore, in order to determine the effect of solvent on the regiochemistry of the addition, the reactions of **2e** or **2h** with **1** have been investigated in various solvents. Table 2 presents the data on the effect of solvents on the regiochemistry of bromo chloro adducts obtained from the reactions of **2e** or **2h** with **1**. No change in the regiochemistry has been observed with the reactions in the aprotic solvents. Similar regiochemical results have been observed previously for the reactions of **2i** and **2j**.[2]

On the other hand, the reaction of 3-chlorostyrene (**2e**) in methanol gave a solvent-incorporated product, 2-bromo-1-(3-chlorophenyl)-1-methoxyethane (**5e**, 78%) as the major product. In analogy with the reaction in acetic acid, the resulting bromo chloro adduct **3e** (22%) was found to be formed in a regiospecific Markownikoff manner. Similarly, the reaction of 3-nitrostyrene (**2h**) in methanol also gave 2-bromo-1-methoxy-1-(3-nitrophenyl)ethane (**5h**, 73%) along with a mixture of **3h** and **3h′** (**3h**:**3h′**=93:7) (Table 2).

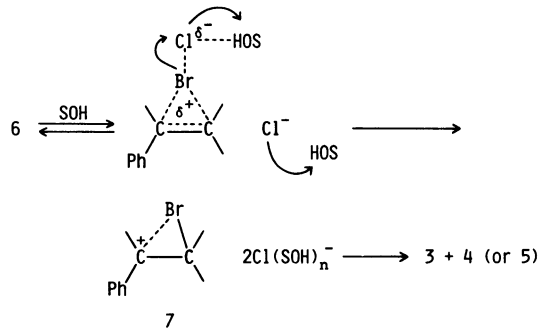
As shown in Table 2, the reaction in protic solvents proceeded in a more regioselective (or regiospecific) manner than the reaction in aprotic solvents. The effect of protic solvents on the regiochemistry cannot be related to the dielectric constant of the medium, since in both acetic acid and ethyl acetate having similar dielectric constants, the regiochemistry was different, whereas chloroform and acetic anhydride have different dielectric constants but gave similar regiochemical results.

Table 2. Regiochemistry of Bromo Chloro Adducts Obtained from the Reactions of **2e** or **2h** with **1** in Various Solvents[a]

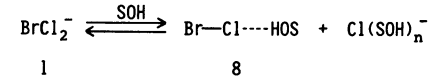
Solvent	Dielectric constant[c]	Product composition/%[b] from **2e**		from **2h**	
		3e	**3e′**	**3h**	**3h′**
$CHCl_3$	4.81	87.6	12.4	71.3	28.7
$CH_3COOC_2H_5$	6.02	87.2	12.8	69.1	30.9
CH_2Cl_2	9.08	87.0	13.0	71.7	28.3
$(CH_3CO)_2O$	20.7	87.7	12.3	70.0	30.0
CH_3COOH[d]	6.19	100	0	91.3	8.7
CH_3OH[e]	32.6	100	0	93.1	6.9

a) At 0 °C. b) Determined by ^1H NMR analysis. Percentages are normalized to 100%. c) J. A. Riddick and E. E. Toops, "Technique of Organic Chemistry," ed by A. Weissberger, Interscience, New York (1955), Vol. VII. d) At 20 °C. From the data of Table 1. e) The yield of **3e** was 22%. The yield of a mixture of **3h** and **3h′** was 27%.

Two different mechanisms can account for the role of such protic solvents as acetic acid and methanol. They are indicated in Schemes 4 and 5.



Scheme 4.



Scheme 5.

According to Scheme 4, the major role of protic solvent is assumed to be the solvation of the external chloride ion (Cl^-) in a three-center bound π-complex **6**, and promoting the ionization of **6** by stabilizing the negatively polarized chlorine atom ($Br^{\delta+}\cdots Cl^{\delta-}$) via hydrogen bonding. The solvent molecule may then assist catalytically the bromine–chlorine bond cleavage, followed by the formation of the cationic intermediate **7**. Evidence for such a specific role of the solvent has been observed by Dubois et al.[5] for the bromination of 1-pentene in methanol.

In Scheme 5, we assume the initial formation of solvated BrCl **8** and chloride ion by the solvation of $BrCl_2^-$ (**1**) in protic solvent. The solvated BrCl **8** thus formed is assumed to react with alkene (**2**) to give the cationic intermediate **7**, which is in turn attacked by chloride ion or solvent molecule to form a mixture of **3** and **4** (or **5**). Although we cannot decide by which mechanism the reactions proceed, the present results clearly show that the addition of **1** to alkenes in protic solvent proceeds via a cationic intermediate **7** prior to the product-determining step.

The regiochemical results in protic solvents (Tables 1 and 2) show that all the styrene derivatives (except **2g** and **2h**) were attacked by chloride ion exclusively on the phenyl-substituted carbon atom of the double bond. Furthermore, the addition of 1-phenylpropenes (**2i** and **2j**) was nonstereospecific, although the trans-addition product was formed mainly (Scheme 3). These results would be taken as evidence supporting that such a cationic intermediate resembles a weakly bridged benzylic carbonium ion intermediate **7**.[6] In the case of the reaction of **2h**, the formation of *anti*-Markownikoff adduct **3h′** would suggest that the intermediate resembles a fully bridged bromonium ion. A similar intermediate has been suggested for the bromination of 3-nitro- and 4-nitrostyrenes in acetic acid.[7] In the case of 2-chlorostyrene (**2g**), a small amount of *anti*-Markownikoff adduct **3g′** was also isolated in the reaction in acetic acid (Table 1). Probably, the formation of this product is due to the combination of polar and steric effects.

Experimental

NMR spectra were recorded on a JEOL JNM FX-60Q and a JEOL C-60HL spectrometer, using TMS as the internal standard. GLC analyses were performed on a Yanako G-180 gas chromatograph with a Silicone SE-30(2.5%)-Chromosorb WAW DMCS (2 m) column, with helium as the carrier gas. All the organic starting materials, including the solvents, were distilled before use. Tetrabutylammonium dichlorobromate(1−) (**1**) was prepared by the known procedure.[8]

Reaction of 2a—j with 1 in Acetic Acid. General Procedure: To a solution of **2** (10 mmol) in acetic acid (20 ml) was added **1** (3.93 g, 10 mmol) at 20 °C over 5 min with stirring. After the yellow color disappeared, the product was isolated by pouring the reaction mixture into a cold saturated aq NaCl solution, followed by extraction with ether (200 ml) and washing with aq $NaHCO_3$ and then with water. The ethereal extract was dried over $MgSO_4$ and concentrated. The crude products were subjected to GLC and NMR. All the results are given in Table 1. Furthermore, the crude products were separated by column chromatography (silica gel) with hexane–ether as the eluent. The structures of the bromo chloro adducts **3** and **3′** were determined by a comparison of their GLC and NMR spectra with those of the authentic samples prepared by the reaction of **1** with styrene derivatives **2** in chloroform.[4] The spectral data of each bromo chloro adduct have been reported in the previous papers.[2,4] The structures of the acetoxy bromide (**4**) were determined by a comparison of their GLC and NMR spectra with those of the authentic samples prepared by the reaction of **2** with bromine in acetic acid.[9] The spectral data are as follows.

1-Acetoxy-2-bromo-1-phenylethane (4a): ^1H NMR ($CDCl_3$) δ=2.12 (3H, s, $OCOCH_3$), 3.61, 3.62 (2H, 2d, J=5.9 and 7.0 Hz, CH_2Br), 5.97 (1H, approx. t, CH), and 7.34 (5H, s, C_6H_5); ^{13}C NMR ($CDCl_3$) δ=20.9, 34.2, 74.7, 126.4, 128.5, 128.6, 137.5, and 169.6.

1-Acetoxy-2-bromo-1-(4-methylphenyl)ethane (4b): ^1H NMR ($CDCl_3$) δ=2.11 (3H, s, $OCOCH_3$), 2.33 (3H, s, CH_3), 3.59, 3.60 (2H, 2d, J=5.9 and 7.3 Hz, CH_2Br), 5.95 (1H, approx. t, CH), and 7.26 (4H, s, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=21.0, 21.2, 34.2, 74.8, 126.5, 129.3, 134.7, 138.6, and 169.7.

1-Acetoxy-2-bromo-1-(4-fluorophenyl)ethane (4c): ^1H NMR ($CDCl_3$) δ=2.12 (3H, s, $OCOCH_3$), 3.58, 3.59 (2H, 2d, J=6.1 and 7.2 Hz, CH_2Br), 5.94 (1H, approx. t, CH), and 6.9—7.6 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=20.9, 34.1, 74.1, 114.9, 116.4, 128.1, 128.7, 133.4, 133.6, 154.5, 169.6, and 170.9.

1-Acetoxy-2-bromo-1-(4-chlorophenyl)ethane (4d): ^1H NMR ($CDCl_3$) δ=2.12 (3H, s, $OCOCH_3$), 3.57, 3.58 (2H, 2d, J=5.9 and 6.7 Hz, CH_2Br), 5.93 (1H, approx. t, CH), and 7.31 (4H, s, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=20.8, 33.8, 74.0, 127.9, 128.8, 134.6, 136.1, and 169.6.

1-Acetoxy-2-bromo-1-(3-chlorophenyl)ethane (4e): ^1H NMR ($CDCl_3$) δ=2.14 (3H, s, $OCOCH_3$), 3.58 (2H, d, J=6.3 Hz, CH_2Br), 5.93 (1H, t, J=6.3 Hz, CH), and 7.28 (4H, br. s, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=20.9, 33.8, 74.0, 124.8, 126.6, 128.9, 129.9, 134.5, 139.6, and 169.5.

1-Acetoxy-2-bromo-1-(4-bromophenyl)ethane (4f): ^1H NMR ($CDCl_3$) δ=2.12 (3H, s, $OCOCH_3$), 3.58 (2H, d, J=6.3 Hz, CH_2Br), 5.91 (1H, t, J=6.3 Hz, CH), and 7.13—7.68 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=20.8, 33.7, 74.0, 122.7, 128.2, 131.8, 136.6, and 169.4.

1-Acetoxy-2-bromo-1-(2-chlorophenyl)ethane (4g): ^1H NMR ($CDCl_3$) δ=2.17 (3H, s, $OCOCH_3$), 3.63, 3.68 (2H, 2d, J=6.9 and 4.4 Hz, CH_2Br), 6.36 (1H, q, 6.9 and 4.4 Hz, CH), and 7.20—7.70 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=20.8, 33.1, 71.4, 127.0, 127.4, 129.7, 132.2, 135.3, and 169.3.

1-Acetoxy-2-bromo-1-(3-nitrophenyl)ethane (4h): ^1H NMR ($CDCl_3$) δ=2.18 (3H, s, $OCOCH_3$), 3.65 (2H, d, J=6.2 Hz, CH_2Br), 6.04 (1H, t, J=6.2 Hz, CH), and 7.70—8.30 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=20.9, 33.5, 73.4, 121.5, 123.6, 129.6, 132.8, 139.6, 148.3, and 169.4.

***erythro*-1-Acetoxy-2-bromo-1-phenylpropane (4i):** ^1H NMR ($CDCl_3$) δ=1.64 (3H, d, J=6.7 Hz, CH_3), 2.15 (3H, s, $OCOCH_3$), 4.15—4.57 (1H, m, CHBr), 5.95 (1H, d, J=5.3 Hz, CH), and 7.34 (5H, s, C_6H_5); ^{13}C NMR ($CDCl_3$) δ=20.8, 20.9, 50.0, 78.2, 127.0, 128.3, 128.4, 137.1, and 169.5.

***threo*-1-Acetoxy-2-bromo-1-phenylpropane (4j):** ^{1}H NMR ($CDCl_3$) δ=1.53 (3H, d, J=6.7 Hz, CH_3), 2.11 (3H, s, $OCOCH_3$), 4.08—4.56 (1H, m, CHBr), 5.82 (1H, d, J=7.8 Hz, CH), and 7.34 (5H, s, C_6H_5); ^{13}C NMR ($CDCl_3$) δ=21.0, 22.4, 50.5, 79.2, 127.1, 128.5, 128.6, 137.1, and 169.5.

Reaction of 2e and 2h with 1 in Aprotic Solvents. To a solution of the alkene (10 mmol) in the solvent (20 ml) was added 10 mmol of **1** at 0 °C over 5 min with stirring. After the yellow color disappeared, the mixture was washed with water and dried over Na_2SO_4. The product of the reaction in acetic anhydride was isolated by pouring the reaction mixture into water, followed by extraction with ether (200 ml) and washing with aq $NaHCO_3$ and then with water. After the solvent was evaporated, the residues were analyzed by ^{1}H NMR. The relative amounts of products were determined from the ratio of the peak areas of the methylene protons of the bromo chloro adducts **3** and **3′**.[4] The results are given in Table 2.

Reaction of 2e and 2h with 1 in Methanol. To a solution of the alkene (10 mmol) in methanol (20 ml) was added **1** (10 mmol) at 0 °C over 5 min with stirring. The solvent was removed by evaporation and ether (200 ml) was added to the residue. The ether solution was washed with aq $NaHCO_3$ and then with water. The ethereal extract was dried over Na_2SO_4 and concentrated. In the case of **2e**, the ^{1}H NMR spectrum of the residue showed a 78:22 mixture of **5e** and **3e** (by integration of the methine protons). In the case of **2h**, the ^{1}H NMR spectrum of the residue showed a 73:27 mixture of **5h** and **3h** with a trace amount of **3h′**.

A column chromatography of the residue (2.12 g) from the reaction of **2e** on silica gel with hexane–ether as the eluent gave 1.50 g of **5e** and 0.4 g of **3e**. The spectral data for 2-bromo-1-(3-chlorophenyl)-1-methoxyethane (**5e**) are as follows: ^{1}H NMR ($CDCl_3$) δ=3.32 (3H, s, OCH_3), 3.46, 3.47 (2H, 2d, J=5.9 and 6.7 Hz, CH_2Br), 4.36 (1H, approx. t, CH), and 7.26—7.35 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=35.7, 57.4, 82.7. 125.0, 126.8, 128.6, 129.9, 134.6, and 141.1. The ^{1}H and ^{13}C NMR spectra of **5e** correspond well with those of the authentic sample prepared by the reaction of **2e** with N-bromosuccinimide (NBS) in methanol.[10] The data for 2-bromo-1-chloro-1-(3-chlorophenyl)ethane (**3e**) have been reported in the previous paper.[4]

Similarly, a column chromatography of the residue (2.13 g) from the reaction of **2h** gave 1.30 g of **5h** and 0.45 g of a mixture of **3h** and **3h′**. The spectral data for 2-bromo-1-methoxy-1-(3-nitrophenyl)ethane (**5h**) are as follows: ^{1}H NMR ($CDCl_3$) δ=3.36 (3H, s, OCH_3), 3.53 (2H, d, J=5.9 Hz, CH_2Br), 4.51 (1H, t. J=5.9 Hz, CH), and 7.67—8.22 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=35.3, 57.6, 82.1, 121.8, 123.4, 129.6, 132.8, 141.4, and 148.4. The ^{1}H and ^{13}C NMR spectra of **5h** correspond well with those of the authentic sample prepared by the reaction of **2h** with NBS in methanol.[10] The ^{1}H NMR spectrum of the isolated bromo chloro adducts showed a 93:7 mixture of **3h** and **3h′**. The data for 2-bromo-1-chloro- and 1-bromo-2-chloro-1-(3-nitrophenyl)ethanes (**3h** and **3h′**) have been reported in the previous paper.[4]

The authors sincerely wish to thank Professor Shigeru Oae of Okayama University of Science for his kind guidance.

References

1) T. Negoro and Y. Ikeda, *Bull. Chem. Soc. Jpn.*, **57**, 2111 (1984).
2) T. Negoro and Y. Ikeda, *Bull. Chem. Soc. Jpn.*, **57**, 2116 (1984).
3) T. Negoro and Y. Ikeda, *Bull. Chem. Soc. Jpn.*, **58**, 3665 (1985).
4) T. Negoro and Y. Ikeda, *Bull. Fac. Edu. Wakayama Univ. Nat. Sci.*, **35**, 15 (1986).
5) F. Garnier, R. H. Donnay, and J. E. Dubois, *J. Chem. Soc., Chem. Commun.*, **1971**, 829.
6) J. H. Rolston and K. Yates, *J. Am. Chem. Soc.*, **91**, 1477 (1969); G. E. Heasley, J. M. Bundy, V. L. Heasley, S. Arnold, A. Gipe, D. McKee, R. Orr, S. L. Rodgers, and D. F. Shellhamer, *J. Org. Chem.*, **43**, 2793 (1978).
7) J. H. Rolston and K. Yates, *J. Am. Chem. Soc.*, **91**, 1483 (1969).
8) A. I. Popov and R. E. Buckles, *Inorg. Synth.*, Vol. **V**, 172 (1957).
9) J. H. Rolston and K. Yates, *J. Am. Chem. Soc.*, **91**, *1469 (1969)*.
10) V. L. Heasley, R. A. Skidgel, G. E. Heasley, and D. Strickland, *J. Org. Chem.*, **39**, 3953 (1974).