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Regio- and Stereochemistry of Bromochlorinations of Alkynes with Molecular Bromine Chloride and Dichlorobromate(1−) Ion

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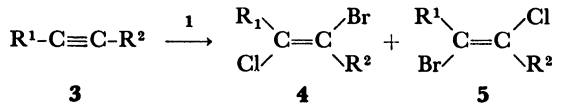
The bromochlorination of phenyl- and alkyl-substituted acetylenes with tetrabutylammonium dichlorobromate(1−) (**1**) in dichloromethane was found to be *anti*-stereospecific and nonregiospecific (regiospecific in the case of phenylacetylene). Whereas the addition of molecular bromine chloride (**2**) to phenyl-substituted acetylenes was found to give nonstereospecific and regiospecific adducts, the reaction of alkyl-substituted acetylenes gave *anti*-stereospecific and nonregiospecific adducts. These results suggest that the addition of **1** involves an attack of chloride ion to a three-centered π-complex in the product-forming stage, and that the addition of **2** to phenyl-substituted acetylenes involves a vinyl cation intermediate (but a bridged bromonium ion intermediate in the case of alkyl-substituted acetylenes).

The stereochemistry of bromine addition to alkynes has been known to markedly depend both on reaction conditions and on the structure of alkynes.[1,2] *Anti*-stereospecific addition was observed for the bromination of alkynes in the presence of bromide ion.[1,2] However, only a few scattered data have been made available on the bromochlorination of alkynes. The reaction of diphenylacetylene,[3] ethyl 3-butynoate,[4] or 1-hexyne[5] with molecular bromine chloride (**2**) has been reported to give the corresponding bromo chloro adducts in an *anti*-stereospecific manner. We have reported that tetrabutylammonium dichlorobromate(1−) (**1**) reacted with phenyl- or alkyl-substituted ethylenes to give bromo chloro adducts in nearly quantitative yields, and that the addition took place in an *anti*-stereospecific manner,[6,7] while that the regio- and stereochemistries of the bromochlorination of alkenes[6,7] or dienes[8] with **1** are strikingly different from those with **2**. As a continuation of our studies, we have studied on the regio- and stereochemistries of the reaction of **1** and **2** with various alkynes.

Results and Discussion

The reaction of 1-phenylpropyne (**3a**), 1-hexyne (**3c**), or 2-hexyne (**3d**) with tetrabutylammonium dichlorobromate(1−) (**1**) in CH_2Cl_2 gave a mixture of (*E*)-Markownikoff and (*E*)-*anti*-Markownikoff adducts (**4a**, **c**, and **d** and **5a**, **c**, and **d**, respectively) in nearly quantitative yields (Scheme 1 and Table 1).



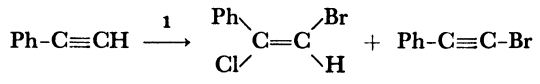
3 **4** **5**

a: R^1=Ph, R^2=Me **c**: R^1=*n*-Bu, R^2=H
d: R^1=*n*-Pr, R^2=Me

Scheme 1.

Similarly, treatments of symmetrical alkynes such as diphenylacetylene (**3e**: R^1=R^2=Ph) and 3-hexyne (**3f**: R^1=R^2=Et) with **1** also gave the corresponding bromo chloro adducts (**4e** and **4f**, respectively) in an *anti*-stereospecific manner (Table 1).

On the other hand, the reaction of phenylacetylene (**3b**: R^1=Ph, R^2=H) with **1** gave a mixture of (*E*)-2-bromo-1-chloro-1-phenylethene (**4b**) and 1-bromo-2-phenylethyne (**6b**) (Scheme 2 and Table 1).



3b **4b** **6b**

Scheme 2.

The formation of **6b** cannot be ascribed to the subsequent secondary reaction of **4b**, since prolonged reaction time did not cause any change in the ratio of the products. Further, the bromo chloro adduct **4b** was stable under the reaction conditions. Formation

Table 1. Regio- and Stereochemistries of the Bromochlorination of Alkynes with **1**[a]

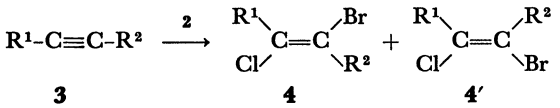
Alkynes	Product composition/%[b]			Yield/%[c]
	(*E*)-M[d]	(*E*)-*a*M[d]	(*Z*)	
3a	89.2	10.8	0	76(97)
3b	100	0	0	42[e]
3c	86.5	13.5	0	81(97)
3d	50.2	49.8	0	81(98)
	(*E*)		(*Z*)	
3e	100		0	93
3f	100		0	80(96)

a) Reactions were carried out with 20 mmol of **1**, 20 mmol of **3**, and 50 ml of CH_2Cl_2 at 20 °C. b) Percentages are normalized to 100%. Determined by ^{1}H NMR analysis. c) Isolated yield. Yields in parentheses were determined by ^{1}H NMR using 1,2-dibromo-1-phenylethane as the internal standard. d) M=Markownikoff adduct (**4**). *a*M=*anti*-Markownikoff adduct (**5**). e) The other product was 1-bromo-2-phenylethyne (**6b**, 58%). Determined by GLC analysis.

of 1-bromo-2-phenylethyne (**6b**) has already been reported for the reaction of **3b** with bromine.[2]

Although attempts to separate two regioisomers (**4** and **5**) were unsuccessful, the orientation of halogen atoms was elucidated mainly on the basis of the chemical shifts of the protons in the ^{1}H NMR spectra of the adducts. The structures of **4** and **5** have been determined by a comparison of their ^{1}H NMR or ^{13}C NMR spectra with those of the corresponding dibromo and dichloro adducts. It has been known that the proton β to a bromine atom is deshielded relative to the one β to a chlorine atom, and that the proton α to a chlorine atom is deshielded relative to the one α to a bromine atom.[5,9] Thus, the methyl protons of **4a** give δ=2.56 but those of **5a** δ=2.45, in agreement with the observation that the methyl protons (δ=2.60) of (*E*)-1,2-dibromo-1-phenylpropene are deshielded relative to those (δ=2.41) of (*E*)-1,2-dichloro-1-phenylpropene. Similarly, the methyl protons (=C–CH$_3$) of **4d** give δ=2.38 but those of **5d** δ=2.27 (Experimental). Control experiments revealed that all the bromo chloro adducts are stable under the reaction conditions.

Treatments of alkynes (**3a** and **3b**) with molecular bromine chloride (**2**) in CH_2Cl_2 gave the corresponding (*E*)- and (*Z*)-Markownikoff adducts (**4** and **4'**) in a regiospecific and nonstereospecific manner (Scheme 3 and Table 2).



3 **4** **4'**

a: R^1=Ph, R^2=Me **b**: R^1=Ph, R^2=H

Scheme 3.

Table 2. Regio- and Stereochemistries of the Bromochlorination of Alkynes with **2**[a]

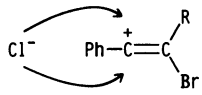
Alkynes	Product composition/%[b]			Yield/%[c]
	(*E*)-M[d]	(*Z*)-M[d]	(*E*)-*a*M[d]	
3a	78.1(77.9)	21.9(22.1)	0	69
3b	62.8	37.2	0	70
3c	90.9	0	9.1	71
3d	47.5[e]	0	52.5[e]	73
	(*E*)	(*Z*)		
3e	100	0		20[f]
3f	(100)	(0)		75

a) Reactions were carried out with 10 mmol of **2**, 20 mmol of **3**, and 50 ml of CH_2Cl_2 at 20 °C. b) Percentages are normalized to 100%. Determined by ^{1}H NMR analysis. Yields in parentheses were determined by GLC analysis. c) Determined by GLC analysis. d) M=Markownikoff adduct. *a*M=*anti*-Markownikoff adduct. e) Determined by ^{13}C NMR analysis. f) Ref. 3. Isolated yield.

As with the reaction with **1**, the reaction of alkyl-substituted acetylenes (**3c** and **3d**) with **2** gave a mixture of (*E*)-Markownikoff and (*E*)-*anti*-Markownikoff adducts (**4** and **5**) in a nonregiospecific and *anti*-stereospecific manner, and the reaction of 3-hexyne (**3f**) gave the *anti*-stereospecific adduct (**4f**) (Table 2). The yields of the bromo chloro adducts were lower than those in the reaction of **1** because dibromo- and dichloroalkenes were formed as by-products in every case.

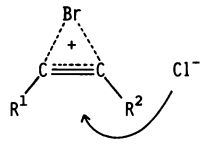
An inspection of the data in Tables 1 and 2 clearly reveals that the regio- and stereochemistries of the bromochlorinations of alkynes depend greatly both on the structure of alkynes and on the bromochlorinating agents employed. Therefore, the electronic structure of the intermediate in the product-forming step must depend both on the substituent on the acetylene linkage and on the bromochlorinating agents.

Regio- and Stereochemistries of the Reaction of 3 with 2. As shown in Table 2, the addition of molecular bromine chloride (**2**) to phenyl-substituted alkynes such as **3a** and **3b** is nonstereospecific and regiospecific. This result can be explained by assuming a mechanism involving the attack of chloride ion on an open vinyl cation intermediate **7**, in which the cationic character of the phenyl-substituted carbon atom is stabilized by overlap of *p*-orbitals of the phenyl group; a similar reaction intermediate has been suggested for the bromination of these alkynes with molecular bromine.[1,2]



(7)

On the other hand, the addition of **2** to alkyl-substituted acetylenes **3c**, **3d**, and **3f** gave only *trans*-bromo chloro adducts (Table 2). Such an *anti*-stereospecific addition of **2** to these alkynes are fully in accordance with the mechanism involving a bridged bromonium ion intermediate **8**.[2]

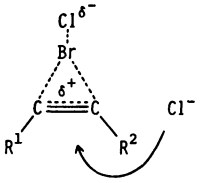


(8)

Meanwhile, the addition of **2** to monoalkyl-substituted acetylene **3c** gave the Markownikoff adduct **4c** as the major product. This implies that the attack of chloride ion on the intermediate **8** occurs at the alkyl-substituted carbon atom. Thus, the orientation of the addition of **2** would be due to the electronic effect of the alkyl substituent which stabilizes the developed cationic character on the alkyl-substituted carbon atom in the intermediate **8**.[5]

Regio- and Stereochemistries of the Reaction of 3 with 1. In contrast to the addition of **2** to alkynes, the

addition of **1** is in an *anti*-stereospecific manner irrespective of substituents on the acetylene linkage (Table 1). Thus, the addition of **1** to phenyl-substituted alkynes **3a** and **3b** gave only the *anti*-stereospecific adducts. This result cannot be explained on the basis of the mechanism involving an open vinyl cation intermediate **7** for the addition of **2** to **3a—b** as described above. We would like to suggest another possible mechanism which involves the attack of chloride ion on a three-centered π-complex intermediate **9** in a product-forming step with a very little charge development on the unsaturated carbon; a similar intermediate has been suggested for the addition of **1** to alkenes and dienes.[6-8]



(9)

Meanwhile, the addition of **1** to phenylacetylene (**3b**) gave only the regiospecific Markownikoff adduct **4b**. The addition to 1-phenylpropyne (**3a**) was in a regioselective Markownikoff manner. These results imply that the attack of chloride ion on the intermediate **9** occurs on the phenyl-substituted carbon atom. Thus, the orientation of the bromochlorination with **2** would depend on the electronic effect of phenyl substituent which stabilizes the developed cationic character on the phenyl-substituted carbon atom in the intermediate **9**. The addition of **1** to 1-hexyne (**3c**) gave the regioselective Markownikoff adduct **4c**. Thus, the orientation of addition with **1** can be influenced also by the electronic effect of the alkyl substituent.

Experimental

All the melting points and boiling points are uncorrected. NMR spectra were recorded on a JEOL JNM FX-60Q and a JEOL C-60HL spectrometer, with TMS as the internal standard. Mass spectra were recorded on a JMS-D-300 mass spectrometer. GLC analyses were performed on a Yanako G-180 gas chromatograph with a Silicone SE-30(10%)-Chromosorb WAW DMCS (2 m) column, with helium as the carrier gas. All the organic starting materials, including the solvents, were distilled just before use.

Tetrabutylammonium dichlorobromate(1−) (**1**) was prepared by the known procedure.[10] Bromine chloride (**2**) was prepared by adding an equimolar amount of bromine to a chlorine-carbon tetrachloride solution.

Reaction of Alkynes with 1. General Procedure: To a solution of **3** (20 mmol) in dichloromethane (50 ml) was added **1** (7.87 g, 20 mmol) at 20 °C over 20 min with stirring. After the yellow color disappeared, the reaction mixture was washed with water and dried over Na_2SO_4. After the solvent was removed by evaporation, the products were purified by distillation. The results are shown in Table 1. Although attempts to separate **4** and **5** were unsuccessful, these structures were determined by a comparison of their ^1H NMR spectra (^{13}C NMR spectra in some cases) with those of the corresponding dibromo and dichloro analogs.

A Mixture of (*E*)-2-Bromo-1-chloro- and (*E*)-1-Bromo-2-chloro-1-phenylpropenes (4a and 5a) from 1-Phenylpropyne (3a): Bp 78—79 °C/2 mmHg (1 mmHg=133.322 Pa); MS *m/z* (rel intensity) 230 (M^+; 100), 232 (135), and 234 (32). Found: *m/z* 229.9488. Calcd for C_9H_8BrCl: M, 229.9498. ^1H NMR ($CDCl_3$) (an asterisk indicates **5a**) δ=2.45,* 2.56 (3H, s, CH_3), and 7.30—7.40 (5H, m, C_6H_5). These assignments were supported for the dibromo and dichloro analogs as follows: (*E*)-1,2-dibromo-1-phenylpropene, ^1H NMR ($CDCl_3$) δ=2.60 (3H, s, CH_3) and 7.20—7.40 (5H, m, C_6H_5); (*E*)-1,2-dichloro-1-phenylpropene, ^1H NMR ($CDCl_3$) δ=2.41 (3H, s, CH_3) and 7.20—7.50 (5H, m, C_6H_5).

(*E*)-2-Bromo-1-chloro-1-phenylethene (4b) and 1-Bromo-2-phenylethyne (6b) from Phenylacetylene (3b): **4b**: bp 85—90 °C/6 mmHg; MS *m/z* (rel intensity) 216 (M^+; 100), 218 (128), and 220 (32). Found: *m/z* 215.9310. Calcd for C_8H_6BrCl: M, 215.9342. ^1H NMR ($CDCl_3$) δ=6.56 (1H, s, CH) and 7.30—7.67 (5H, m, C_6H_5). **6b**: bp 76—78 °C/6 mmHg (lit,[11] bp 40—41 °C/0.1 mmHg); MS *m/z* (rel intensity) 180 (M^+; 100) and 182 (100). Found: *m/z* 179.9550. Calcd for C_8H_5Br: M, 179.9575. ^1H NMR ($CDCl_3$) δ=7.28—7.53 (m, C_6H_5). The ^1H NMR spectrum of **4b** corresponds well with that reported in the literature.[12]

A Mixture of (*E*)-1-Bromo-2-chloro- and (*E*)-2-Bromo-1-chloro-1-hexenes (4c and 5c): Bp 55—56 °C/25 mmHg; MS *m/z* (rel intensity) 196 (M^+; 100), 198 (132), and 200 (32). Found: *m/z* 195.9648. Calcd for $C_6H_{10}BrCl$: M, 195.9655. ^1H NMR ($CDCl_3$) (an asterisk indicates **5c**) δ=0.75—1.10 (3H, br. t), 1.15—1.90 (4H, m), 2.40—2.80 (2H, m), 6.20, and 6.27* (1H, 2s); ^{13}C NMR ($CDCl_3$) (an asterisk indicates **5c**) δ=13.8, 21.6, 21.7,* 28.5,* 29.2, 34.5, 34.9,* 101.1,* 114.8, 127.0, and 136.9.* The ^1H and ^{13}C NMR of a mixture (**4c** and **5c**) correspond well with those reported in the literature.[5]

A Mixture of (*E*)-2-Bromo-3-chloro- and (*E*)-3-Bromo-2-chloro-2-hexenes (4d and 5d) from 2-Hexyne (3d): Bp 35—36 °C/5 mmHg; MS *m/z* (rel intensity) 196 (M^+; 100), 198 (133), and 200 (32). Found: *m/z* 195.9650. Calcd for $C_6H_{10}BrCl$: M, 195.9655. ^1H NMR ($CDCl_3$) (an asterisk indicates **5d**) δ=0.93 (3H, t, *J*=7.3 Hz), 1.18—1.79 (2H, m), 2.27,* 2.38 (3H, 2s), and 2.43—2.74 (2H, m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates **5d**) δ=13.0,* 13.1, 20.3, 20.9,* 25.8,* 25.9, 39.6,* 40.1, 115.9, 121.7,* 125.4,* and 130.5. These assignments were supported for the dibromo and dichloro analogs as follows: (*E*)-2,3-dibromo-2-hexene: ^1H NMR ($CDCl_3$) δ=0.94 (3H, t, *J*=6.7 Hz), 1.28—1.85 (2H, m), 2.41 (3H, s), and 2.65 (2H, t, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ=13.0, 20.8, 28.8, 42.4, 115.2, and 121.8. (*E*)-2,3-dichloro-2-hexene: ^1H NMR ($CDCl_3$) δ=0.93 (3H, t, *J*=6.7 Hz), 1.26—1.88 (2H, m), 2.00 (3H, s), and 2.52 (2H, t, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ=13.1, 20.2, 23.2, 37.5, 124.9, and 129.9.

(*E*)-1-Bromo-2-chloro-1,2-diphenylethene (4e) from Diphenylacetylene (3e): Mp 170—172 °C (lit,[3] 173—175 °C); ^1H NMR ($CDCl_3$) δ=7.30—7.66 (m, $2C_6H_5$); ^{13}C NMR ($CDCl_3$) δ=117.7, 128.2, 128.8, 129.0, and 129.1.

(*E*)-3-Bromo-4-chloro-3-hexene (4f) from 3-Hexyne (3f): Bp 55—57 °C/25 mmHg; MS *m/z* (rel intensity) 196 (M^+;

100), 198 (130), and 200 (33). Found: *m/z* 195.9649. Calcd for $C_6H_{10}BrCl$: M, 195.9655. ^1H NMR ($CDCl_3$) δ=1.10 (6H, t, J=7.3 Hz) and 2.41—2.83 (4H, m); ^{13}C NMR ($CDCl_3$) δ=11.4, 12.2, 31.7, 32.2, 122.1, and 130.8.

Reaction of Alkynes (3) with Bromine Chloride (2). To a solution of **3** (20 mmol) in CH_2Cl_2 (50 ml) was added 5.5 ml of BrCl (**2**) solution in CCl_4 (1.8 mol dm^{-3}) at 20 °C over 5 min with stirring. After the reaction completed, the solvent and unreacted alkyne were removed under reduced pressure and the residues were analyzed by GLC and ^1H NMR or ^{13}C NMR. The results are given in Table 2. In all cases, GLC analyses showed the presence of 11—15% of the dichloro adduct and 12—17% of the dibromo adduct as by-products.

The reaction of 1-phenylpropyne (**3a**) with **2** gave a mixture of (*E*)-2-bromo-1-chloro- and (*Z*)-2-bromo-1-chloro-1-phenylpropenes (**4a** and **4a'**, 69%) (**4a**:**4a'**=78:22) with dichloro and dibromo adducts (31%) by GLC analysis. After the bromo chloro adducts were separated by distillation, a column chromatography (silica gel, with hexane as the eluent) of the mixture of **4a** and **4a'** gave almost pure **4a** and **4a'**. **4a**: MS *m/z* (rel intensity) 230 (M^+; 100), 232 (132), and 234 (32). Found: *m/z* 229.9487. Calcd for C_9H_8BrCl: M, 229.9498. ^1H NMR ($CDCl_3$) δ=2.56 (3H, s, CH_3) and 7.30—7.40 (5H, m, C_6H_5). **4a'**: MS *m/z* (rel intensity) 230 (M^+; 100), 232 (133), and 234 (30). Found: *m/z* 229.9485. Calcd for C_9H_8BrCl: M, 229.9498. ^1H NMR ($CDCl_3$) δ=2.32 (3H, s, CH_3) and 7.30—7.40 (5H, m, C_6H_5).

The reaction of phenylacetylene (**3b**) with **2** gave a mixture of (*E*)-2-bromo-1-chloro- and (*Z*)-2-bromo-1-chloro-1-phenylethenes (**4b** and **4b'**, 70%) (**4b**:**4b'**=63:37 by ^1H NMR analysis) with dichloro and dibromo adducts (26%) and a small amount of 1-bromo-2-phenylethyne (**6b**, 4%) by GLC analysis. Although the isolation of **4b** and **4b'** was not carried out, the retention time of GLC and the ^1H NMR (δ=6.56, vinyl proton of **4b** and δ=6.82, vinyl proton of **4b'**) agreed with those of a sample prepared by the reaction of **3b** with copper(II) chloride and bromine.[12]

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