Bromochlorination of Alkenes with Dichlorobromate(1−) Ion. II.[1] Regio- and Stereochemistry for the Bromochlorination of 1-Phenylpropenes with Dichlorobromate(1−) Ion

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The bromochlorinations of 1-phenylpropenes with tetrabutylammonium dichlorobromate(1−) in aprotic solvents (dielectric constants 5—36) were found to be completely *anti* stereospecific and nonregiospecific, although Markownikoff adduct was mainly formed. In marked contrast, addition of molecular bromine chloride to the same alkenes was found to give nonstereospecific and regiospecific adducts. These results suggest that the addition of bromine chloride in the form of $(n\text{-}C_4H_9)_4NBrCl_2$ involves a rate- and product-determining attack of a chloride ion to a three-center bound π complex.

The stereochemistry of bromine addition to aryl-substituted alkenes has been shown to be markedly dependent both on the brominating agents and on the solvents employed.[2] The *anti* stereospecific additions were observed for the reaction with a tribromide ion[3,4] or with pyridine–bromine complex[4] as brominating agents. However, only a few systematic studies have been carried out on reaction with a dichlorobromate-(1−) ion as a bromochlorinating agent. It has been reported that 1-phenylpropenes give bromochlorinated adducts by reaction with $(CH_3)_4NBr_2Cl$ and pyridine–bromine chloride in a completely *trans* manner, while addition of molecular bromine chloride gives significant amounts of *cis*-adduct.[4] We have reported that tetrabutylammonium dichlorobromate(1−) reacted with stilbenes and 2-butenes to give the corresponding bromo chloro adducts in almost quantitative yields, and that the additions were in a completely *anti*-stereospecific manner.[1] In an attempt to gather more detailed information on bromochlorination with a dichlorobromate(1−) ion, we have investigated the regio- and stereochemistry of the addition to 1-phenylpropenes in solvents with widely different polarities. The reactions of 1-phenylpropenes with molecular bromine chloride were also carried out for comparison with the reactions of a dichlorobromate(1−) ion. This paper will describe reaction features of bromochlorination of 1-phenylpropenes with a dichlorobromate(1−) ion.

Results and Discussion

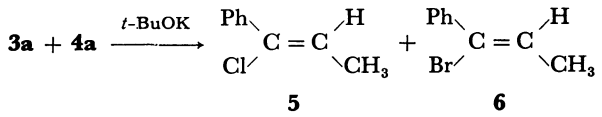
The reaction of tetrabutylammonium dichlorobromate(1−) [$(n\text{-}C_4H_9)_4NBrCl_2$, **1**] with *cis*-1-phenylpropene (**2a**) in chloroform gave a mixture of *threo*-2-bromo-1-chloro-1-phenylpropane (**3a**) and *threo*-1-bromo-2-chloro-1-phenylpropane (**4a**) in almost quantitative yield. *trans*-1-Phenylpropene (**2b**) was reacted with **1** to give a mixture of *erythro*-2-bromo-1-chloro and *erythro*-1-bromo-2-chloro adducts (**3b** and **4b**, respectively).

$$PhCH=CHCH_3 + \mathbf{1} \longrightarrow PhCHClCHBrCH_3 + PhCHBrCHClCH_3$$

2a	**3a**, 76%	**4a**, 24%
2b	**3b**, 95%	**4b**, 5%

Fig. 1.

Structural assignments of the bromo chloro compounds **3a** and **4a** were deduced by dehydrohalogenation to haloalkenes (Fig. 2). When a mixture of **3a** and **4a** was treated with 0.78 equivalent of potassium *t*-butoxide in *t*-butyl alcohol, the alkene (**5**) with recovery of the unreacted bromo chloro compound (**4a**) was obtained in good yield.



5 **6**

Fig. 2.

^{1}H-NMR analysis of the reaction mixture revealed that one isomer (**3a**), which gives **5**, was consumed faster than the other (**4a**); this other isomer (**4a**), which gives **6**, disappeared slowly. Thus, the more facile elimination of **3a** (than that of **4a**) would be due to either differences in eclipsing effect of the bulky substituents or in the ability of the leaving groups. The relative reactivities of **3a** and **4a** are in accordance with the usual reactivities of hydrogen halide eliminations.[5]

The structures of the major and minor products from **2a** and **2b** were also determined by comparisons of their ^{13}C- and ^{1}H-NMR spectra with those of the corresponding dibromo and dichloro adducts. Selected ^{1}C- and ^{1}H-NMR spectra of *threo*- and *erythro*-1,2-dihalo-1-phenylpropanes are listed in Tables 1 and 2, respectively. NMR analysis of the mixture of two regioisomers could be used to determine the amounts of each isomer.

TABLE 1. ^{13}C CHEMICAL SHIFTS FOR *threo*- AND *erythro*-1,2-DIHALO-1-PHENYLPROPANES IN $CDCl_3$ (δ VALUE)

$C_6H_5\text{-}C^1H(X)\text{-}C^2H(Y)\text{-}CH_3$

X	Y	C^1	C^2	CH_3
threo				
Br	Br	58.9	52.7	22.3
Cl	Cl	67.4	61.2	21.6
Br	Cl	59.2	61.0	22.0
Cl	Br	67.4	53.0	22.4
erythro				
Br	Br	59.1	51.1	25.7
Cl	Cl	67.4	60.1	22.1
Br	Cl	58.8	59.6	24.0
Cl	Br	67.5	51.5	23.4

Table 2. ^1H chemical shifts for *threo*- and *erythro*-1,2-dihalo-1-phenylpropanes in $CDCl_3$ (δ value)

C_6H_5-CX(H_a)-CY(H_b)-CH_3

X	Y	CH_3	H_a	H_b
threo				
Br	Br	1.67	5.22	4.59
Cl	Cl	1.44	5.00	4.38
Br	Cl	1.46	5.06	4.45
Cl	Br	1.62	5.06	4.47
erythro				
Br	Br	2.03	5.05	4.57
Cl	Cl	1.67	4.91	4.38
Br	Cl	1.80		
Cl	Br	1.90	4.98	4.45

The present addition reaction appeared to be stereospecific but not regiospecific. The lack of regiospecificity cannot be ascribed to the subsequent isomerization of the bromochloroalkanes, since prolonged reaction time did not cause a change of the isomer ratio of the products. Interconversions between two regioisomers (pure **3a** or the mixed isomers; **3a**:**4a**=60:40) were examined. However, no isomerization was observed in chloroform at room temperature for 3 h by using either 2 equivalents of **1** or of tetrabutylammonium chloride. Another possibility for the formation of *anti*-Markownikoff adduct (**4a** or **4b**) from dichloro adduct of alkenes can also be excluded, since no dichloroalkane was found in the reaction product.

When the reaction was carried out in the presence of a free radical inhibitor, 2,6-di-*t*-butyl-4-methylphenol, the product composition did not change within experimental error. Moreover, the same product ratio was obtained under either an oxygen or nitrogen atmosphere. These results indicate that the reaction proceeds in an electrophilic process rather than in a free radical one.

The regio- and stereochemistry of the reactions of **2a** and **2b** were investigated in solvents with widely different polarities in order to determine the mechanism of the reaction. Table 3 presents data for the effect of solvents on the regiochemistry of the addition to **2a** and **2b**. The reactions were completely *anti* stereospecific and nonregiospecific in all the aprotic solvents employed. No solvent effects on the regiochemistry have been observed (Table 3). A similar stereochemical result has been previously observed for the reaction of *cis*-stilbene with **1**.[1]

In contrast to the present results, Heasley *et al.*[4] have reported that the reactions of **2a** and **2b** with molecular bromine chloride (BrCl) in dichloromethane and carbon tetrachloride occurred in a nonstereospecific manner, although *anti* additions were favored. We have reinvestigated the reaction of the same alkenes with BrCl in various solvents to compare the results with that of **1**. Although the bromo chloro adducts were the major products in all cases, as expected, substantial amounts of dichloro and dibromo adducts were also found in the product. None of the *anti*-Markownikoff adducts were detected by ^1H- and ^{13}C-NMR analyses of the product mixtures in any of the solvents employed. The results are shown in Table 4.

Table 3. Solvent dependency on regiochemistry of the reactions of **2a** and **2b** with **1** at 0 °C

Solvent	Dielectric constant[a]	Product composition/%[b]			
		from **2a**		from **2b**	
		% **3a**	% **4a**	% **3b**	% **4b**
$CHCl_3$	4.81	76.0(76.8)	24.0(23.2)	94.5(95.8)	5.5(4.2)
$CH_3COOC_2H_5$	6.02	77.1	22.9	94.6	5.4
CH_2Cl_2	9.08	77.5(77.9)	22.5(22.1)	95.5(93.9)	4.5(6.1)
CH_2ClCH_2Cl	10.36	78.4	21.6	93.2	6.8
$(CH_3CO)_2O$	20.7	75.2(75.9)	24.8(24.1)	94.1(94.6)	5.9(5.4)
CH_3NO_2	35.87	78.0(76.2)	22.0(23.8)	92.2(92.9)	7.8(7.1)

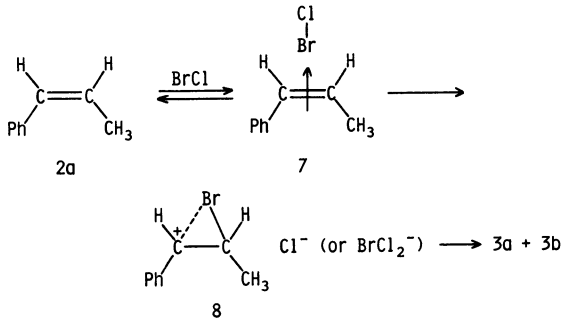
a) J.A.Riddick and E.E.Toops,"Technique of Organic Chemistry," ed by A. Weissberger, Interscience, New York (1955), Vol. VII. b) Percentages are normalized to 100%. Determined by ^1H-NHR analysis. Figures in parentheses represent the product distributions determined by ^{13}C-NMR analysis.

Table 4. Solvent dependency on stereochemistry of bromo chloro compounds obtained from the addition of molecular bromine chloride to **2a** and **2b** at 0 °C

Solvent	Dielectric constant[b]	Product composition/%[a]			
		from **2a**		from **2b**	
		% **3a**	% **3b**	% **3a**	% **3b**
Dioxane[c]	2.21	21.4	78.6	18.3	81.7
CCl_4	2.23	76.1(75.5)[d]	23.9(24.5)[d]	11.8	88.2
$CHCl_3$	4.81	75.2	24.8	9.8	90.2
CH_2Cl_2	9.08	75.7(79)[d]	24.3(21)[d]	6.3(8.5)[d]	93.7(91.5)[d]
$(CH_3CO)_2O$	20.7	51.4	48.6	14.5	85.5
CH_3NO_2	35.87	49.8	50.2	9.1	90.9

a) Based on the amount of bromo chloro compounds, as determined by GLC analysis. Values were not corrected for FID response factors. Percentages are normalized to 100%. Yields of bromo chloro compounds were determined by GLC and found to be more than 70% in all runs. Other products were 5—10% of the dichloride and 12—20% of the dibromide. b) See footnote a in Table 3. c) At 20 °C. d) Data from Ref. 4.

These results show that the stereochemistry of the addition to *cis*-alkene (**2a**) is dependent on the polarity of the solvent. The addition in acetic anhydride or in nitromethane was nonstereospecific. The results of *trans*-alkene (**2b**) showed a much smaller dependency on the nature of the solvent. All the additions to **2b** were found to be *anti* stereoselective. A similar stereochemistry has been observed for the addition of bromine to these alkenes.[2] Since it is quite reasonable to consider that the process is the same for both bromine and bromine chloride additions,[4,6] a mechanism such as that illustrated in Fig. 3, similar to bromine addition, would be involved in the addition with bromine chloride.



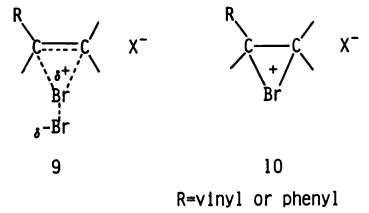
2a 7 8

Fig. 3.

The solvent dependency of the stereochemistry and the regiospecific addition observed for the reaction with these alkenes are fully in accordance with the mechanism involving a very weakly bridged benzylic carbonium ion intermediate (**8**) prior to the product-determining step.[2] The fact that the stereochemistry of the addition to **2a** is more sensitive to solvent polarity than that of the addition to **2b** gives strong evidence for the presence of the intermediate (**8**). The intermediate (**8**) for the reaction of **2a** tends to take a more energetically favored conformation due to the eclipsing effect of the adjacent methyl and phenyl groups. Furthermore, the peculiarity of stereochemistry observed in dioxane is easily explained in terms of specific solvation for the carbonium ion intermediate.[2]

As has been described above, the additions to alkenes appeared to be strikingly different in reactions with **1** and with BrCl in all aprotic solvents employed. These marked differences in the reactions of **1** and BrCl suggest that these two reactions are quite different in their mechanisms. The formation of completely *anti* stereospecific and *anti*-Markownikoff adducts in reaction with **1** rules out a weakly bridged benzylic-like ion intermediate (**8**), such as is shown in Fig. 3. If an intermediate such as **8** was involved, the complete formation of Markownikoff adduct would be expected.

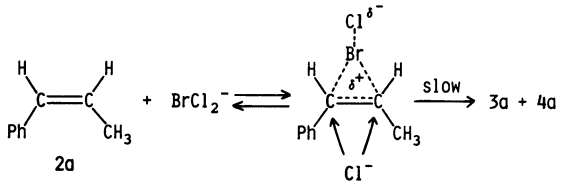
The large differences of product distribution obtained by the reaction with **1** are consistent with the previous proposal that this reagent is an independent electrophile rather than a precursor of BrCl.[1] The reactions of $BrCl_2^-$ presently studied and Br_2Cl^- (or Br_3^-) reported by Heasley *et al.*[4] seem to involve similar mechanisms. Two possible mechanisms have been proposed by them, involving attack of a halide ion on a three-center bound π complex (**9**)[7] or on the bromonium ion intermediate (**10**).



9 10

R=vinyl or phenyl

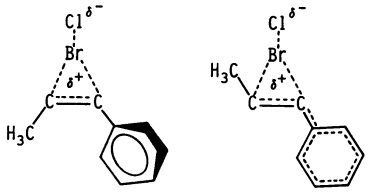
The bromonium ion intermediate (**10**), however, is hardly acceptable for the reaction of $BrCl_2^-$ since the present reaction gave nonregiospecific products. Thus, the $AdEC_2$ process involving an intermediate like **9** at the product-determining step would be applicable to the reaction of $BrCl_2^-$, as depicted in Fig. 4.



2a 11

Fig. 4.

The regiochemistry of the reaction of **1** would be dependent on the electronic effect of the phenyl ring which stabilizes the developing cationic character on the carbon in the complex (**11**). The *cis*- and *trans*-alkenes gave somewhat different regiochemical results. Markownikoff adducts were obtained mainly from both *cis*- and *trans*-alkenes (**2a** and **2b**) as given in Table 3. The *cis*-alkene gave less regioselectivity than the *trans*-alkene. The differences may be ascribed to the ability of stabilization of a cationic center by phenyl groups. The phenyl ring of the intermediate (**12**) formed from the *cis*-alkene would be skewed by the eclipsing effect.



12 13

The intermediate (**13**) formed from the *trans*-alkene would be free from such an eclipsing effect and the developing cationic character would be delocalized over the phenyl ring. This type of stabilization may develop the cationic character on the carbon adjacent to the phenyl ring. Thus, attack of a chloride ion to the benzylic carbon atom would be more favored in the intermediate from *trans*-alkene than in that from *cis*-alkene. In fact, the *trans*-alkene (**2b**) was found to react faster than the *cis*-alkene (**2a**).[8]

Experimental

NMR spectra were recorded on a JEOL JNM FX-60Q and a JEOL C-60HL spectrometer using TMS as an internal standard. Mass spectra were recorded on a JMS-D-300 Mass

spectrometer. The GLC analyses were performed on a Yanako G-180 Gas Chromatograph. Tetrabutylammonium dichlorobromate(1-) (**1**) was prepared by the literature procedure.[9] All the organic starting materials, including the solvents, were distilled before use. Bromine chloride was prepared by adding an equimolar amount of bromine to a chlorine-carbon tetrachloride solution.

Reaction of cis-*1-Phenylpropene (**2a**) with **1**.* Details of the reaction have been reported previously.[1] The mixture of **2a** (5.90 g, 50 mmol) and **1** (19.7 g, 50 mmol) in 100 ml of chloroform was stirred at 0 °C for 10 min. After the usual work-up procedure, distillation afforded 9.3 g (80%) of a mixture of two isomeric bromochloroalkanes (**3a** and **4a**): bp 90—91 °C/1 mmHg (1 mmHg≈133.322 Pa); MS M^+ at m/z= 232, 234, 236 (100:128:32); Found: m/z 231.9649. Calcd for $C_9H_{10}BrCl$: M, 231.9655. Although attempts to separate **3a** and **4a** by GLC were unsuccessful, ^{1}H-NMR analysis by integration of methyl protons revealed the product composition to be 76% of **3a** and 24% of **4a**. The major product was characterized as **3a** on the basis of the ^{1}H- and ^{13}C-NMR spectra of an authentic sample.[4]

Reaction of trans-*1-Phenylpropene (**2b**) with **1**.* The reaction was carried out similarly to that of **2a**. Distillation afforded 9.6 g (82%) of mixed bromochloroalkanes (**3b** and **4b**): bp 91—92 °C/1 mmHg; MS M^+ at m/z=232, 234, 236 (100:128:32); Found: m/z 231.9648. Calcd for $C_9H_{10}BrCl$: M, 231.9655. ^{1}H-NMR analysis established the product composition as 96% of **3b** and 4% of **4b**. The major product was also characterized as **3b** on the basis of the ^{1}H- and ^{13}C-NMR spectra of an authentic sample.[4]

*Dehydrohalogenation of Regioisomers (**3a** and **4a**).* To 2.34 g (10 mmol) of the mixture composed of **3a** (76%) and **4a** (24%) in *t*-butyl alcohol (50 ml) was added 6 ml (2.23 mmol) of potassium *t*-butoxide in *t*-butyl alcohol (0.372 mol dm^{-3}); the mixture was stirred at 20 °C. After 30 min, 1 ml of the solution was taken up, shaken with water, and extracted with pentane. The pentane layer was washed with dilute acid and dried over $MgSO_4$. Evaporation of the pentane and analysis of the residue by ^{1}H NMR showed the composition to be: **3a**, 53.3%; **4a**, 25%; **5**, 21.7%; and **6**, 0%. The reaction was carried out further by the addition of 15 ml (5.58 mmol) of potassium *t*-butoxide solution (0.372 mol dm^{-3}); this mixture was stirred for 1 h. The reaction mixture was then worked up in a fashion similar to that described above. Evaporation of the pentane gave 1.58 g of the crude product. ^{1}H NMR showed the composition to be: **3a**, 0.5%; **4a**, 23%; **5**, 76.5%; and **6**, 0%. Column chromatography of this residue on silica gel with hexane as the eluent gave almost pure **4a** (150 mg) and **5** (711 mg). The data for **4a** are as follows: ^{1}H NMR ($CDCl_3$) δ=1.46 (3H, d, J=6.6 Hz, CH_3), 4.45 (1H, approx. quintet, CHCl), 5.06 (1H, d, J=6.6 Hz, CHBr), and 7.32 (5H, m, C_6H_5); MS M^+ at m/z=232, 234, 236 (100:127:32); Found: m/z 231.9649. Calcd for $C_9H_{10}BrCl$: M, 231.9655. The data for **5** are as follows: ^{1}H NMR (CCl_4) δ=1.90 (3H, d, J=6.7 Hz, CH_3), 6.31 (1H, d, J=6.7 Hz, CHCl), and 7.28—7.62 (5H, m, C_6H_5); MS M^+ at m/z=152, 154 (100:32); Found: m/z 152.0388. Calcd for C_9H_9Cl: M, 152.0393. The ^{1}H-NMR spectrum for **5** corresponds well with that reported in the literature.[10]

*Dehydrochlorination of Pure Regioisomer (**4a**).* To 120 mg (0.51 mmol) of **4a** in *t*-butyl alcohol (5 ml) was added 2 ml (0.74 mmol) of potassium *t*-butoxide solution (0.372 mol dm^{-3}); this mixture was stirred at 20 °C. After 30 min, the reaction mixture was worked up as described above. Evaporation of pentane gave 75 mg of crude product **6** as a colorless oil: ^{1}H NMR (CCl_4) δ=2.00 (3H, d, J=7.5 Hz, CH_3), 6.40 (1H, d, J=7.5 Hz, CHBr), and 7.35—7.80 (5H, m, C_6H_5); MS M^+ at m/z=196, 198 (100:97); Found: m/z 195.9898. Calcd for C_9H_9Br: M, 195.9888. The spectral patterns of this product were identical with those of a sample prepared by dehydromination of *threo*-1,2-dibromo-1-phenylpropane.

*Reaction of **1** with **2a** or **2b** in Various Solvents.* To 2 mmol of the alkene in 20 ml of the solvent was added 2 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 and washing with aq $NaHCO_3$ then water. After the solvent was removed under reduced pressure, the residues were analyzed by ^{1}H NMR and ^{13}C NMR in some cases. The relative amounts of products were determined from the ratio of the peak areas of the methyl protons of the bromo chloro compounds (**3a** and **4a** or **3b** and **4b**), and also from the ratio of peak heights of aliphatic carbons (^{13}C NMR). The results are given in Table 3.

*Reaction of Bromine Chloride with **2a** or **2b** in Various Solvents.* To 2.1 mmol of the solvent, was added 1.7 ml of BrCl solution in CCl_4(1.2 mol dm^{-3}) at 0 °C with stirring. Products of the reactions in acetic anhydride and dioxane were isolated by extraction with ether as described above. Products of the reactions in carbon tetrachloride, chloroform, dichloromethane, and nitromethane were obtained by direct evaporation of the solvent. GLC analysis of the residue gave six peaks with retention times of 12.3, 13.7, 18.9, 21.1, 27.6, and 32.8 min. These were assigned to be *erythro*-1,2-dichloro-, *threo*-1,2-dichloro-, *erythro*-2-bromo-1-chloro-, *threo*-2-bromo-1-chloro-, *erythro*-1,2-dibromo-, and *threo*-1,2-dibromo-1-phenylpropanes, except for unreacted alkene, respectively. GLC analyses were performed on a High vacuum silicon grease (25%)-Celite 545 (2 m) column at 120 °C with helium as a carrier gas (35 ml/min). The results are given in Table 4.

*The Reaction of **1** with **2a** in the Presence of a Radical Inhibitor.* When **2a** was treated with **1** in chloroform as described above, O_2 was bubbled during the reaction. The product ratio of 76.5:23.5 was obtained by ^{1}H-NMR analysis for **3a** and **4a**, respectively. The reaction was carried out with 1.18 g (10 mmol) of **2a**, 3.93 g (10 mmol) of **1**, and 0.70 g (0.3 mmol) of 2.6-di-*t*-butyl-4-methylphenol in chloroform (30 ml). After the usual work-up, the product ratio of 77.8: 22.2 was obtained by ^{1}H-NMR analysis for **3a** and **4a**, respectively. ^{13}C-NMR analysis also showed a 76.5:23.5 mixture of **3a** and **4a**, respectively.

Stability of the Bromo Chloro Compounds under the Reaction Conditions. To 1 mmol of the two regioisomers (**3a** and **4a**) in chloroform (10 ml) was added 2 mmol of **1** and allowed to stand for 3 h at room temperature with stirring. The mixture was shaken with aq sodium sulfite. The chloroform layer was separated, washed with water, and dried over $MgSO_4$. After the solvent was removed, the residue was analyzed by ^{1}H-NMR spectrum. No interconversion was observed. Namely, the same isomer compositions were observed within experimental error: Starting from a 60:40 mixture of **3a** and **4a** recovered a 59:41 mixture of **3a** and **4a**, and only **3a** was recovered from **3a** without contamination with **4a**.

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8) The rates of the reactions of **2a** and **2b** with **1** were determined in chloroform relative to the rate of the reaction of styrene. Relative rates were measured at 0 °C by the competition method using ^{1}H-NMR analysis. The relative rates were found to be: styrene, 1.00; **2a**, 1.27±0.05; **2b**, 1.54±0.05.

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