



## The Inclusion Complex of Ferrocene with a Dithiolene Functionalized $\beta$ -Cyclodextrin

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### Abstract

A new  $\beta$ -cyclodextrin derivative with the anion side-arm, mono[6-deoxy-6-(2-sodium thio-1,2-dicyane ethylenylthio)]- $\beta$ -cyclodextrin (6-mnt- $\beta$ -CD), and its inclusion complex with ferrocene (6-mnt- $\beta$ -CD/Fc), have been prepared and characterized by elemental analysis, IR spectroscopy, UV spectroscopy, mass spectrometry, <sup>13</sup>C-NMR spectroscopy, thermogravimetry, and cyclic voltammetry (CV). Thermogravimetry analysis of the compound shows that the thermal stabilities of both the host and the guest in the inclusion complex have been greatly improved due to an additional interaction between the side-arm of the host and the guest. The interplay between the guest and the host with side-arm in the complex resulted in smaller positive potential shifts in CV compared to that in the inclusion complex  $\beta$ -CD/Fc.

### Introduction

Molecular complexes, in which two or more molecules are weakly bound by noncovalent bonds, have received much attention because of their characteristic chemical and physical properties and in relation to the function of biologically important substances [1].

Natural cyclic oligosaccharides, cyclodextrins (CDs) having the shape of a truncated cone are able to hold in the molecular cavity, a variety of single guest molecules of suitable size and shape [2]. Usually, the chemical stability and thermal stability of guests in the CD's cavity are remarkably increased. There have been many reports on molecular complexes of CDs with both organic and inorganic compounds, but few concern the inclusion complexes with organometallic compounds. Harada and Takahashi first reported in 1984 the solid inclusion complexes of CDs and organometallics of the ferrocene series [3–5]. To date, most of these works either in the solid phase or in the solution phase have concentrated on simple ferrocene derivatives [6–9]. To the best of our knowledge, little has been done to investigate the inclusion complexes of functionalized CDs with these organometallic guest compounds. In this paper, we synthesized a dithiolene functionalized  $\beta$ -CD and its inclusion complex with ferrocene. It was experimentally evident that the novel host has such a good ability to hold the guest that the new inclusion complex, 6-mnt- $\beta$ -CD/Fc, shows better thermal stability than does the complex  $\beta$ -CD/Fc.

### Experimental

#### General methods

A Bruker IFS66V FT-IR spectrophotometer was used, and the measurements were made by the KBr disk method. The UV spectra were recorded on a Shimadzu UV-3100 spectrometer. The mass spectra were performed on a Finnigan mat APISSQ-710 mass spectrometer. All <sup>13</sup>C-NMR and <sup>1</sup>H-NMR spectra were recorded on a Bruker AVANCE-300 spectrometer in dimethylsulfoxide-d<sub>6</sub> (DMSO-d<sub>6</sub>) solution at 15 °C. Elemental analysis was determined by a Perkin-Elmer 240C elemental analyzer. Thermogravimetric analysis curves were recorded on an American SDT-2960 thermal analyzer. Cyclic voltammetry was done with an EG&G model 273 instrument in *N,N*-dimethylformamide (DMF) solution. The three-electrode electrochemical cell used was equipped with a platinum disc working electrode, a platinum auxiliary electrode, and a Ag/AgCl reference electrode. Ethanol was of an analytically pure grade. DMF was distilled under reduced pressure in an N<sub>2</sub> atmosphere before use. 2-Butenedinitrile-2,3-dimercapto disodium salt (Na<sub>2</sub>mnt) and mono-(6-O-tolylsulfonyl)- $\beta$ -cyclodextrin (6-Ots- $\beta$ -CD) were synthesized according to the methods described in the literature [10, 11].

#### Synthesis of 6-mnt- $\beta$ -CD

To a solution of Na<sub>2</sub>mnt (0.2 g, 1.08 mmol) in water (30 mL) was added 6-Ots- $\beta$ -CD (0.5 g, 0.39 mmol), and the mixture was stirred at 65 °C for 3–4 h under a N<sub>2</sub> at-

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mosphere. After cooling down to room temperature, the yellow solution was concentrated. The dark-red residue (about 3–4 mL) was then added in drops to stirred ethanol (120 mL) to precipitate 0.4 g crude 6-mnt- $\beta$ -CD. The crude product was dissolved in 1 mL of water, and was then added in drops to stirred ethanol (10 mL) again. After standing overnight, the final product precipitated from the ethanol solution as a yellow powder.  $^{13}\text{C}$ -NMR (300Hz DMSO):  $\delta$  59.94, 72.12, 72.49, 73.15, 80.94, 81.15, 81.62, 102.05, 118.38, 118.79. IR (KBr):  $\nu/\text{cm}^{-1}$  2189.7 (CN). UV (H<sub>2</sub>O):  $\lambda_{\text{max}}/\text{nm}$  371 ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$  8800), UV (DMF):  $\lambda_{\text{max}}/\text{nm}$  385.5 ( $\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$  9200). MS  $m/z$ : 1258.0 [Calcd for C<sub>46</sub>H<sub>69</sub>O<sub>34</sub>N<sub>2</sub>S<sub>2</sub> ([M-Na]<sup>-</sup>): 1258.2]. Anal. Calcd for C<sub>46</sub>H<sub>69</sub>O<sub>34</sub>N<sub>2</sub>NaS<sub>2</sub>·8H<sub>2</sub>O: C, 38.76, H, 6.01, N, 1.97; found: C, 38.85, H, 6.21, N, 2.08.

#### Preparation of the inclusion complexes of ferrocene

The inclusion complex of 6-mnt- $\beta$ -CD with ferrocene (6-mnt- $\beta$ -CD/Fc) was prepared by the coprecipitation method [12].  $0.53 \times 10^{-3}$  Mol of 6-mnt- $\beta$ -CD was dissolved in 50 mL of water, and then  $1.06 \times 10^{-3}$  mol of ferrocene was added to the aqueous solution. After stirring at 60 °C for 2 h, the solution was cooled down to room temperature and yielded a dark yellow solid precipitate. It was then collected by filtration and washed twice with water and ethanol. Finally, drying of the solid in air for 4 h yielded the inclusion complex as a yellow solid. The inclusion complex of  $\beta$ -CD with ferrocene ( $\beta$ -CD/Fc) was prepared in the same way.

## Results and discussion

### The new host 6-MNT- $\beta$ -CD

Both the electronic spectrum and the IR spectrum analyses of 6-mnt- $\beta$ -CD have shown the presence of the mnt group in the compound (see the Experimental). Moreover, electro-spray MS provided structural evidence of the existence of mnt-modified  $\beta$ -CD ( $m/z$  1258.0, see the Experimental). In addition, the  $^{13}\text{C}$ -NMR spectrum of the host molecule (6-mnt- $\beta$ -CD) displayed the resonances due to one C=C bond at  $\delta$  118.38 and 118.79 ppm, and two nitrile groups at  $\delta$  80.94 and 81.15 ppm (Table 1). The prominent upfield shift of the signal of C-6 ( $-0.08$  ppm, Table 1) in the  $^{13}\text{C}$ -NMR spectrum of 6-mnt- $\beta$ -CD, compared to that of pure  $\beta$ -CD, was observed. This upfield shift was considered to result mainly from the introduction of electron-rich mnt onto the  $\beta$ -CD rim [13]. Figure 1 shows thermogravimetric (TG) and differential thermogravimetric (DTG) curves of 6-Ots- $\beta$ -CD, Na<sub>2</sub>mnt, and 6-mnt- $\beta$ -CD. Two peaks were observed in the DTG curve of the hydrate 6-Ots- $\beta$ -CD (curve *a'*). The first peak (around 59 °C) corresponded to the dehydration process, and the other (around 185 °C) was related to the degradation of the 6-Ots- $\beta$ -CD structure. In the case of Na<sub>2</sub>mnt (curve *b'*), peaks of the desolvation and decomposition were clearly seen (at around 48 °C and 98 °C, respectively). However, in that of 6-mnt- $\beta$ -CD (curve *c'*), no obvious peaks were recorded at around 98 °C or 185 °C. In addition to the

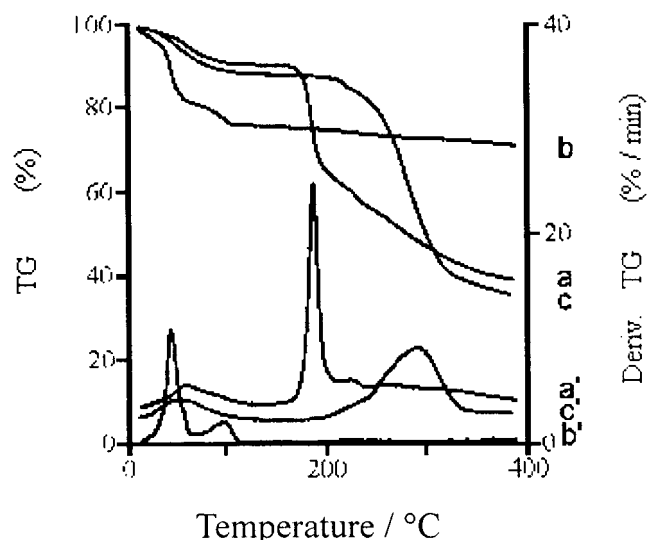
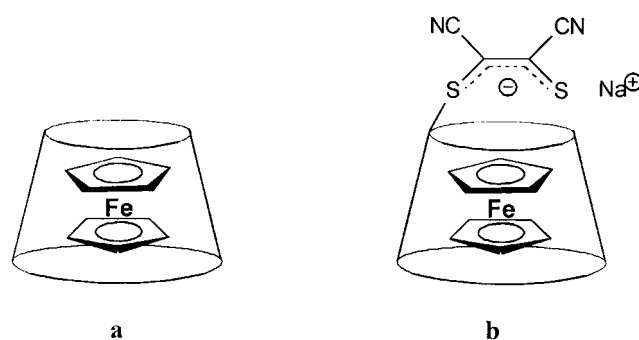


Figure 1. TG and DTG curves of 6-Ots- $\beta$ -CD (*a*, *a'*), Na<sub>2</sub>mnt (*b*, *b'*), and 6-mnt- $\beta$ -CD (*c*, *c'*).



Scheme 1. Proposed inclusion modes of the inclusion complexes  $\beta$ -CD/Fc (*a*), and 6-mnt- $\beta$ -CD/Fc (*b*).

dehydration occurring at around 53 °C, a new peak (around 291 °C) appeared clearly, which should be assigned to the decomposition of the 6-mnt- $\beta$ -CD structure.

### Inclusion complexes of ferrocene

Electro-spray MS spectra of the inclusion complex, 6-mnt- $\beta$ -CD/Fc, have shown the presence of the 6-mnt- $\beta$ -CD anion ( $m/z$  1258.1). We could presume that the ferrocene guest penetrates into  $\beta$ -CD cavities (as proposed in Scheme 1) just as the ferrocene molecule has done in the inclusion complex  $\beta$ -CD/Fc [3, 6]. The stoichiometries (1:1 molar ratio) of both the inclusion complexes that were isolated as solid complexes in our experiments have also been confirmed by  $^1\text{H}$ -NMR spectroscopy (Table 2).

The effect of the inclusion phenomenon on the molecular structures of both the host and guest has been observed by  $^{13}\text{C}$ -NMR (Table 1). The signal of C-1 shifted from 102.05 to 102.40 ppm in the inclusion complex  $\beta$ -CD/Fc, and from 73.15 to 73.05 ppm for C-3 in the inclusion complex 6-mnt- $\beta$ -CD/Fc. The signals of ferrocene in the two inclusion complexes  $\beta$ -CD/Fc and 6-mnt- $\beta$ -CD/Fc were observed at  $\delta$  67.69 and 67.68 ppm, respectively (Table 1).

Figure 2 shows DTG curves of pure ferrocene, pure  $\beta$ -CD hydrate, and the inclusion complex  $\beta$ -CD/Fc. Only one

Table 1.  $^{13}\text{C}$ -NMR spectra of the inclusion complex 6-mnt- $\beta$ -CD/Fc<sup>a</sup>

Complex	C1	C2	C3	C4	C5	C6	C'
$\beta$ -CD	102.05	72.15	73.16	81.63	72.50	60.02	
6-mnt- $\beta$ -CD	102.05	72.12	73.15	81.62	72.49	59.94	118.38 <sup>b</sup> , 118.79 <sup>b</sup> 80.94 <sup>c</sup> , 81.15 <sup>c</sup>
$\beta$ -CD/Fc	102.40	72.20	73.09	81.88	72.57	59.96	67.69 <sup>d</sup>
6-mnt- $\beta$ -CD/Fc	102.15	72.11	73.05	81.69	72.47	59.91	67.68 <sup>d</sup>

<sup>a</sup>Relative to internal DMSO- $d_6$  ( $\delta = 39.51$  ppm), C1 to C6 refer to carbon atoms of the cyclodextrin structure.

<sup>b</sup>Carbon atoms of the double bond in mnt.

<sup>c</sup>Carbon atoms of the nitrile group in mnt.

<sup>d</sup>Carbon atoms in the cyclopentene ring of ferrocene.

Table 2.  $^1\text{H}$ -NMR spectra of the two inclusion complexes<sup>a</sup>

Complex	H-1	H-2	H-3	H-4	H-5	H-6	H <sup>b</sup>	C <sub>p.a.</sub> <sup>c</sup>
$\beta$ -CD/Fc	4.86	3.31	3.67	3.40	3.66	3.71	4.16	1.47
6-mnt- $\beta$ -CD/Fc	4.86	3.32	3.68	3.40	3.65	3.70	4.16	1.40

<sup>a</sup>H-1 to H-6 refer to protons of the cyclodextrin structure.

<sup>b</sup>Protons in the cyclopentene ring of ferrocene.

<sup>c</sup>Value of the comparison of peak areas of the guest molecule and H-1.

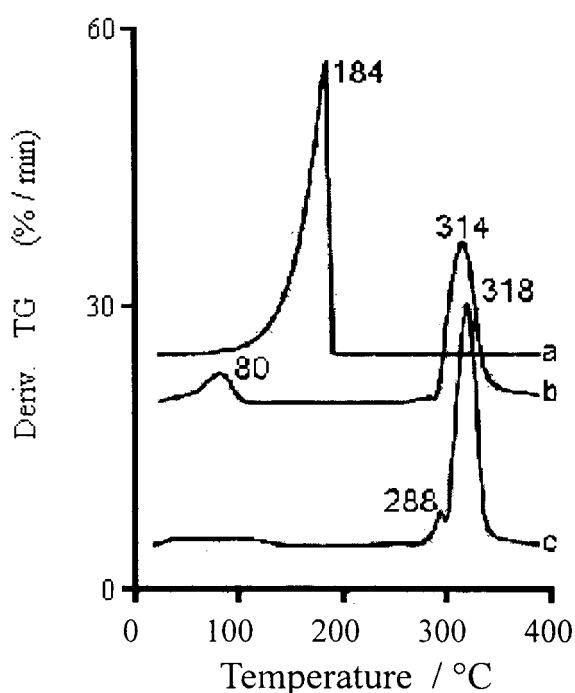


Figure 2. DTG curves of pure ferrocene (a), pure  $\beta$ -CD hydrate (b), and the inclusion complex  $\beta$ -CD/Fc (c).

peak was observed in curve *a* at 184 °C, which was attributed to the decomposition of pure ferrocene. The two peaks (around 80 and 314 °C, respectively) in curve *b* corresponded to the dehydration and decomposition of pure  $\beta$ -CD hydrate. In curve *c*, the peak at around 288 °C should be assigned to the liberation of the guest from the inclusion complex  $\beta$ -CD/Fc, and the decomposition of the host was clearly seen at around 318 °C, which were consistent with the literature [9]. The decomposition temperature difference between the free host and the host in the inclusion complex

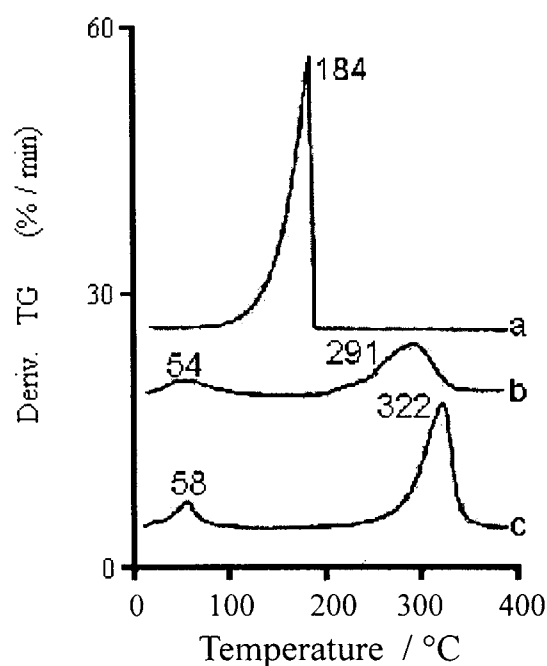


Figure 3. DTG curves of pure ferrocene (a), pure 6-mnt- $\beta$ -CD hydrate (b), and the inclusion complex 6-mnt- $\beta$ -CD/Fc (c).

$\beta$ -CD/Fc ( $\Delta T_{\text{host}}$ ) is +4 °C, and the decomposition temperature difference between the free guest and the guest in the inclusion complex  $\beta$ -CD/Fc ( $\Delta T_{\text{guest}}$ ) is +104 °C [9]. Obviously, the thermal stabilities of both the host and the guest in the inclusion complex  $\beta$ -CD/Fc were higher than in their free forms.

DTG curves of pure ferrocene, pure 6-mnt- $\beta$ -CD hydrate, and the inclusion complex 6-mnt- $\beta$ -CD/Fc are shown in Figure 3. The inclusion complex, 6-mnt- $\beta$ -CD/Fc, decomposed at around 322 °C [9]. The decomposition temperature difference between free (around 291 °C) and bonded

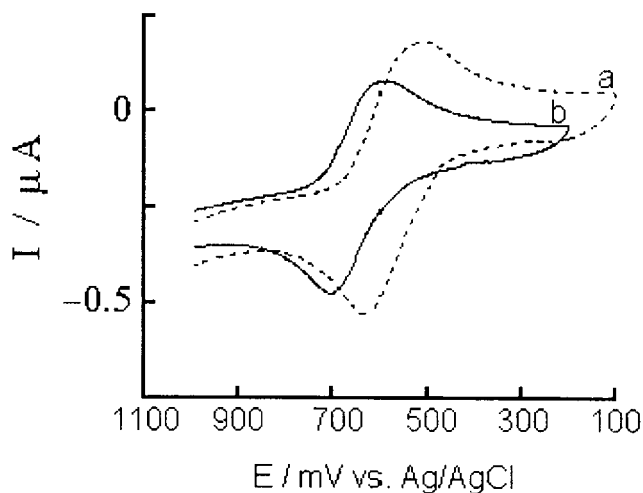


Figure 4. Cyclic voltammogram of  $0.1 \times 10^{-3}$  M ferrocene + 0.1 M  $(n\text{-Bu})_4\text{NClO}_4$  in DMF in the absence (---) and presence (—) of 1.0 M  $\beta\text{-CD}$ . Scan rate: 100 mV/s.

6-mnt- $\beta\text{-CD}$  ( $\Delta T_{\text{host}}$ ) was +31 °C, and the decomposition temperature difference between free and included ferrocene ( $\Delta T_{\text{guest}}$ ) was +138 °C.

By closer inspection of Figures 2 and 3, we came to the following conclusions: (a) Compared with pure ferrocene, the inclusion complexation of both  $\beta\text{-CD}$  and 6-mnt- $\beta\text{-CD}$  with the guest improved the thermal stability of the guest ( $\Delta T_{\text{guest}}$  was +104 °C and +138 °C, respectively). (b) Compared with the free host, the inclusion improved the thermal stability of the host ( $\Delta T_{\text{host}}$  was +4 °C and +31 °C, respectively). It was interesting that a much higher  $\Delta T_{\text{host}}$  was achieved in 6-mnt- $\beta\text{-CD}/\text{Fc}$ , which is probably due to the additional interaction between the side-arm anion of the host and the guest ferrocene. Thus, it was experimentally evident that the new host, 6-mnt- $\beta\text{-CD}$ , exhibited a better binding ability with the organometallic guest than did the natural  $\beta\text{-CD}$ .

The effects of inclusion of ferrocene with  $\beta\text{-CD}$  upon the electrochemical properties are clearly evident in Figure 4. The association constant of ferrocene with  $\beta\text{-CD}$  was determined to be approximately  $(1.65 \pm 0.04) \times 10^4$  ( $\text{dm}^3 \text{mol}^{-1}$ ) by the solubility measurements method [14]. In our experiments, a  $10^4$ -fold molar excess of host was added to the DMF solution of ferrocene to ensure that the guest would work as the corresponding inclusion complex. The electrochemical behavior of the DMF solution of the inclusion complex  $\beta\text{-CD}/\text{Fc}$  retained the same reversible shape as ferrocene itself, but the peak potentials were displaced toward more positive potentials by approximately +76 mV. Compared with pure ferrocene, a substantial decrease of the peak currents in the inclusion complex  $\beta\text{-CD}/\text{Fc}$  was observed. This decrease was caused by the fact that the charged species,  $\beta\text{-CD}/\text{Fc}$ , is more bulky and more slowly diffusing than ferrocene [15]. The +76 mV shifts of potentials in CV is probably because the neutral ferrocene was strongly bound with the hydrophobic cavity of the  $\beta\text{-CD}$  moiety in the inclusion complex  $\beta\text{-CD}/\text{Fc}$ . In other words, ferrocene is more difficult to oxidize in the presence of  $\beta\text{-CD}$  be-

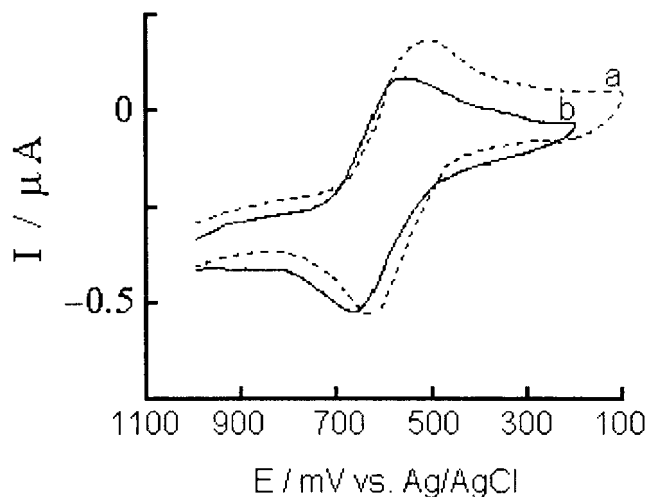


Figure 5. Cyclic voltammogram of  $0.1 \times 10^{-3}$  M ferrocene + 0.1 M  $(n\text{-Bu})_4\text{NClO}_4$  of DMF in the absence (---) and presence (—) of 1.0 M 6-mnt- $\beta\text{-CD}$ . Scan rate: 100 mV/s.

cause it is more strongly bound than is the oxidized form, ferrocenium ( $\text{Fc}^+$ ) [15].

For the inclusion complex, 6-mnt- $\beta\text{-CD}/\text{Fc}$ , its CV resembled that of pure ferrocene (Figure 5). But compared with pure ferrocene, positive shifts (+43 mV) of potentials were observed. The host, 6-mnt- $\beta\text{-CD}$ , has an anion side-arm which could interact with the oxidized form of the guest ( $\text{Fc}^+$ ) in the cavity and finally stabilize the ferrocenium species. So compared with that in  $\beta\text{-CD}/\text{Fc}$ , the guest ferrocene was easier to oxidize to ferrocenium in the inclusion complex 6-mnt- $\beta\text{-CD}/\text{Fc}$ . Consequently, in the CV of 6-mnt- $\beta\text{-CD}/\text{Fc}$ , positive shifts of potentials were only +43 mV. And in the CV of  $\beta\text{-CD}/\text{Fc}$ , bigger shifts (+76 mV) of potentials were obtained.

Generally speaking, inclusion complexation made improvements in the physical and chemical properties of the ferrocene guest. After inclusion, the ferrocene guest was thermally more stable than, not only in its pure form, but also its simple complex with pure  $\beta\text{-CD}$ , which was due to the introduction of the substituent group to the host. The interaction between the substituent group and the ferrocene guest was then confirmed experimentally by the CV spectra.

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