6 might really arise by the mechanism we looked for, involving precomplexation of the palladium reagent to the Ph_2P- group and formation of the complex **5**. But still, the competing anti mechanism in the first step remains the dominant reaction pathway giving finally the epimer **4** as the major product.

Although the stereoselectivity we achieved was not good,[12] this result was encouraging, and we turned our attention to sterically biased substrates **7**, **10**, and **11** (Scheme II). The acetate **7** is known[5] to form the intermediate Pd complex **8** via an ordinary anti mechanism and produce phenyl derivative **9** on the subsequent syn reaction with PhZnCl. In contrast, the epimeric acetate **10** is inert for the severe steric hindrance.[5] It turned out, to our delight, that the ester **11** of the same configuration as the inert acetate **10** readily reacted with PhZnCl/Pd(0), giving **9** as the sole product, identical with the compound obtained from the acetate **7** (Scheme II). Since the second step is known[4,5] to proceed stereospecifically in a syn fashion, the intermediate complex **8** formed from **11** should be the same as that arising from **7**. This is, again, consistent with the syn mechanism of the first step. Similarly, the phosphino ester **12** derived from (-)-*trans*-verbenol readily affords the corresponding phenyl derivative **14** as the result of the syn,syn two-step pathway (Scheme III). In contrast, the acetate **15** is inert under the same reaction conditions, while its epimer **16** reacts sluggishly, producing finally **14** via the ordinary anti,syn mechanism involving the complex **13**.

Since we have observed a clean syn mechanism of the complex formation with our sterically biased allylic esters, it was of interest to explore the reaction with a substrate free of any steric hindrance. (-)-Acetate **18** (58% ee) is known to produce (-)-**20** (58% ee) via the anti,anti sequence (Scheme IV) on a Pd(0)-catalyzed reaction with dimethyl sodiomalonate.[2c] We have prepared (diphenylphosphino)acetate (+)-**21** from the enantiomeric alcohol (+)-**17** of >99% ee[13] and carried out the Pd(0)-catalyzed reaction under the standard conditions. To our surprise, the reaction furnished a dextrorotatory product, which is consistent with the anti,anti pathway. Optical rotation of the product (+)-**20** indicated about 84% optical purity,[17] while ^1H NMR spectrum taken in the presence of $Eu(tfc)_3$ implied 74% ee.[18] It is obvious that in this case the precoordination of the Pd(0) reagent largely failed. However, the lower enantiomeric purity of the product suggests that **21** reacts via a mixture of two mechanisms, the classical anti,anti fashion (87%) accompanied by ca. 13% of the syn,anti pathway in contrast to the acetate **18** where the former clearly dominates. Hence, the anti,anti mechanism is apparently lower in energy even for the phosphinoacetate **21**.

In conclusion, these experiments bring, for the first time, an evidence that syn mechanism of the formation of palladium η^3-complex from allylic substrates may be enforced by precoordination of the Pd(0) reagent to a specially designed leaving group.[19] This finding broadens the applicability of the transition-metal-catalyzed allylic substitution, since it shows that in substrates where the classical anti route of the complex formation is impaired by steric congestion, our new leaving group enables the reaction to occur.

Acknowledgment. We thank Drs. M. Buděšinský and J. Zajíček for taking NMR spectra and Dr. A. Jegorov for a generous gift of (diphenylphosphino)acetic acid.

Supplementary Material Available: IR and NMR characterization of **2**, **11**, **12**, **14**, and **21** (2 pages). Ordering information is given on any current masthead page.

(12) In contrast to the cuprates, no substantial syn pathway could be detected in the Pd-catalyzed reaction of carbamates (**1**, R = $NHCH_2Ph$, NHPh, and $N(CH_3)_2$). We have always isolated **4** in good yields and with high diastereoisomeric excess (>10:1), while **1**, R = NH_2, remained unreacted.

(13) We were unable to reproduce the asymmetric reduction of benzylidene acetone described in the literature.[14] On the other hand, we have achieved an excellent kinetic resolution of the racemic alcohol **17** via the stoichiometric Sharpless epoxidation using (+)-diisopropyl tartrate.[15] This procedure gave us (+)-**17** whose $[\alpha]_D$ +24.5° (*c* 2.8, $CHCl_3$) indicates >99% ee[16] in agreement with the ^1H NMR spectra taken in the presence of $Eu(tfc)_3$.

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(17) According to ref 2c, the maximum specific rotation of (+)-**20** is $[\alpha]_D$ +68.9° (*c* 1.0, $CHCl_3$). Our product had $[\alpha]_D$ +58° (*c* 3.9, $CHCl_3$).

(18) In addition to **20**, 5% of allylic isomer was formed as revealed by ^1H NMR spectrum of the crude product.

(19) For a recent report of syn substitution of aliphatic allylic acetate catalyzed by Mo(0), see: Faller, J. W.; Linebarrier, D. *Organometallics* **1988**, *7*, 1670.

A Model Reaction for Mo(VI) Reduction by Molybdopterin

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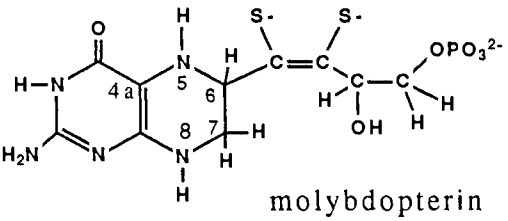
The molybdenum cofactor, Mo-co, is a dissociable cofactor common to xanthine oxidase, sulfite oxidase, nitrate reductase, and other enzymes involved in oxygen atom transfer.[1] Mo-co possesses one molybdenum atom and a pterin component known as molybdopterin.[2] The proposed structure for molybdopterin is supported by spectroscopic and chemical data.[2-4]



molybdopterin

The function of molybdopterin in Mo-co has not been determined. Molybdopterin may be present to coordinate the molybdenum atom through the dithiolene sulfur atoms.[4] On the basis of the known redox roles played by tetrahydropterin cofactors in other metalloenzymes,[5] we propose a different, perhaps additional, role for molybdopterin. We show that a tetrahydropterin is capable of reducing molybdenum(VI) in a sulfur coordination environment.

$MoO_2(detc)_2$ [detc = diethyldithiocarbamate] has been intensely studied because it mimics certain aspects of the Mo site in Mo-co-containing enzymes.[6-8] The reaction chemistry of $MoO_2(detc)_2$ includes the oxo-transferase activity characteristic of molybdoenzyme substrate reactions.[9-12] We have found that 6,7-dimethyl-5,6,7,8-tetrahydropterin (H_4dmp) is able to reduce

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(7) Cramer, S. P.; Gray, H. B.; Rajagopalan, K. V. *J. Am. Chem. Soc.* **1979**, *101*, 2772.

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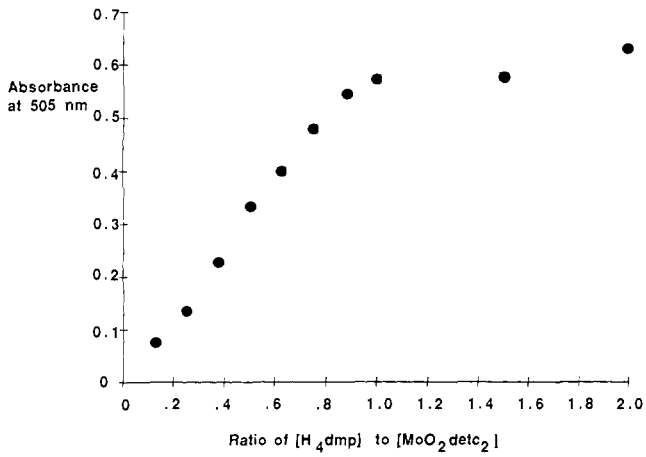


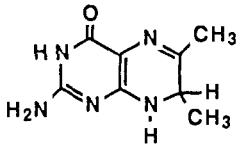
Figure 1. Titration plot for the reduction of MoO_2detc_2 by H_4dmp. The reaction progress was monitored with the strong absorption band of $MoO(detc)_2$ at 505 nm. Titration of $MoO_2(detc)_2$ by H_4dmp was performed in a 50% CH_2Cl_2/50% CH_3OH solvent mixture. A constant total molybdenum concentration of 0.107 mM was maintained for all samples, and, at this concentration, the dimer $Mo_2O_3(detc)_4$ represents less than 1.5% of the total molybdenum in solution.[13] The reaction solutions were stirred for 5 h to attain equilibrium.[13]

$MoO_2(detc)_2$ to $MoO(detc)_2$ quantitatively.[13]

Titration of $MoO_2(detc)_2$ with H_4dmp shows that the redox reaction is complete after addition of one tetrahydropterin per $MoO_2(detc)_2$ (Figure 1). These data show that H_4dmp is a two-electron reductant and is oxidized to a 6,7-dimethyldihydropterin (H_2dmp) as in reaction 1. $Mo^{IV}O(detc)_2$ and H_2dmp have been identified spectroscopically,[13] and the removed oxo ligand is presumably protonated to form water.

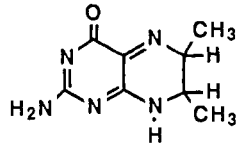
$$Mo^{VI}O_2(detc)_2 + H_4dmp \rightarrow Mo^{IV}O(detc)_2 + H_2dmp + H_2O \quad (1)$$

Dihydropterins exist in several tautomeric structures. Two of these tautomers are shown in A and B. Quinonoid dihydropterin, B, is the product of tetrahydropterin oxidation in thermodynam-



7,8-H_2dmp

A



quinonoid-H_2dmp

B

ically reversible redox reactions.[15,16] The quinonoid structure is unstable and rearranges to 7,8-dihydropterin, A. Only the quinonoid dihydropterin is recycled enzymatically during substrate reactions of phenylalanine hydroxylase, a metalloenzyme requiring a tetrahydropterin cofactor.[5] *We find that the quinonoid H_2dmp is the product of reaction 1 and that this normally reactive dihydropterin is significantly stabilized when generated by $MoO_2(detc)_2$ oxidation.*

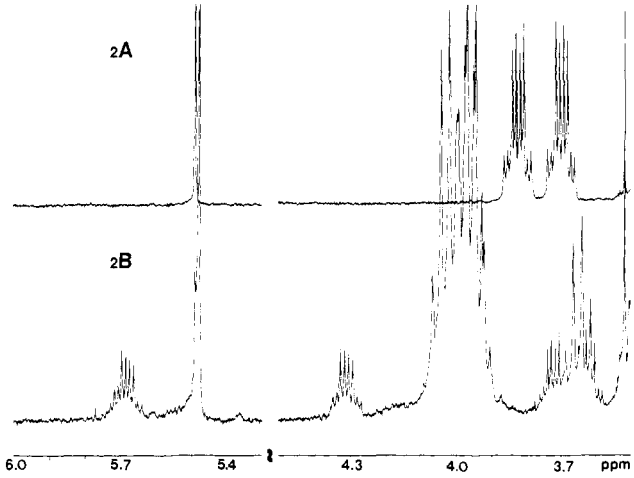


Figure 2. Spectrum 2A is 0.001 M H_4dmp in CD_3OD. Spectrum 2B is of 0.001 M H_4dmp and 0.001 M MoO_2detc_2 in 30% $CDCl_3/CD_3OD$ 30 min after mixing. Signals marked with an * are due to CH_2Cl_2. The broad signal in 2B centered at 4.0 ppm is due to $-CH_2-$ resonances of detc. The multiplet centered near 3.7 ppm is due to H6 and H7 of unreacted H_4dmp; these signals are slightly shifted from spectrum 2A due to the different solvent composition.

^1H NMR spectra of H_4dmp and of a 1:1 reaction mixture of $MoO_2(detc)_2$ and H_4dmp are shown respectively in Figure 2 (parts A and B).[13] The spectrum of H_4dmp has a unique pattern of double quartets at 3.70 and 3.83 ppm due to H6 and H7. This same pattern is seen in spectrum 2B at 4.32 and 5.68 ppm indicating that the reaction product is quinonoid-H_2dmp. The downfield shifts observed are similar to those found in spectra of quinonoid-H_2dmp in aqueous solution.[17] Quinonoid-H_2dmp generated by bromine oxidation of H_4dmp in the same solvent mixture used above rearranged to 7,8-dihydropterin and fully oxidized pterin within 3 min.[18] In contrast, the quinonoid-H_2dmp resonances in spectrum 2B are stable for over 6 h at ambient temperature and retain 50% of the original intensity after 6 days. The improved solution stability of quinonoid-H_2dmp formed in reaction 1 may be due to H_2dmp coordination to a molybdenum complex. $MoOdetc_2$ is known to add nucleophiles such as phosphine and pyridine.[10]

The oxidation of H_4pterin by MoO_2detc_2 may proceed by a mechanism similar to the scheme proposed for tetrahydrobiopterin oxidation by an iron-peroxo species in phenylalanine hydroxylase.[5,19,20] Within this analogy, transfer of an oxygen atom from the MoO_2 group to carbon 4a in H_4pterin would precede formation of the 4a-carbinolamine. Subsequent dehydration would yield the quinonoid dihydropterin.

Our results provide the first data on redox reactions of reduced pterins and molybdenum complexes. The data support the hypothesis that molybdopterin is involved in electron transfer between molybdenum, substrate, and other prosthetic groups[1] (cytochromes, Fe_4S_4 centers, FAD) present in molybdoenzymes. These results

(13) All solutions used in this study were prepared and handled under anaerobic conditions with use of a drybox or standard Schlenk techniques. Reaction of $MoO_2(detc)_2$ ([Mo] < 0.001 M) with 6,7-dimethyl-5,6,7,8-tetrahydropterin hydrochloride (H_4dmp) is immediate in CH_3OH/CH_2Cl_2 solution as indicated by a change in solution color from yellow to red due to formation of $MoO(detc)_2$ (λ_{max} = 508 nm). At higher Mo concentrations ([Mo] > 0.01 M) the resultant solution is purple due to formation of $Mo_2O_3(detc)_4$ (λ_{max} = 513 nm) in the facile dimerization of $MoO_2(detc)_2$ and $MoO(detc)_2$.[14] ^1H NMR samples were prepared by mixing solutions of $MoO_2(detc)_2$ in $CDCl_3$ and H_4dmp in CD_3OD to give final concentrations of 0.001 M in both reagents with a solvent composition of 30% $CDCl_3$ and 70% CD_3OD. Data for spectrum 2B were collected 30 min after mixing the reagents. Chemical shifts for pterin resonances in spectra 2A and 2B: 2A, δ 1.27 (d, $CH_3(6)$), δ 1.33 (d, $CH_3(7)$), δ 3.70 (d of q, H6), 3.83 (d of q, H7); $J_{H6,Me6}$ = 6.8 Hz, $J_{H7,Me7}$ = 6.8 Hz, $J_{H6,H7}$ = 3.3 Hz; 2B, δ 1.63 (d, $CH_3(6)$), δ 5.68 (d of q, H6), δ 4.32 (d of q, H7); $J_{H6,Me6}$ = 6.8 Hz, $J_{H7,Me7}$ = 6.8 Hz, $J_{H6,H7}$ = 3.5 Hz. The resonance for $CH_3(7)$ is obscured by dithiocarbamate methyl signals at 1.32 ppm. H6 and H7 assignments are made according to ref 17. The H_4dmp obtained from Aldrich is the cis-6,7 stereoisomer (as a racemic mixture) as judged from comparison of spectral data from 2A with data from ref 17. NMR is not useful for identifying the dithiocarbamate products since typical sample concentrations (>0.01 M) cause the dimer concentration to be dominant. The complex detc signals of the dimer obliterate both the $-CH_2-$ and $-CH_3$ regions.

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(15) Pfleiderer, W. *J. Inher. Metab. Dis.* **1978**, *1*, 54.

(16) The tautomer B is indicated from studies reported by Benkovic et al. (Benkovic, S. J.; Sammons, D.; Armarego, W. L. F.; Waring, P.; Iners, R. *J. Am. Chem. Soc.* **1985**, *107*, 3706).

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(18) The 7,8-H_2dmp formed by bromine oxidation in 50% CD_3Cl/CD_3OD has the following chemical shifts: δ 1.47 (d, $CH_3(7)$), δ 2.44 (s, $CH_3(6)$), δ 4.71 (q, H7).

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suggest that changes in the Mo oxidation states during substrate turnover may be coupled to pterin oxidation/reduction reactions. The nature of the quinonoid dihydropterin stabilization is currently under study by experiments in progress. We are also investigating H_4Pterin reductions of other dioxomolybdenum model complexes.

Acknowledgment. We thank Bryn Mawr College and the Exxon Education Foundation for financial support of this research.

1-Silylvinyl Radical Cyclization: Silicon-Mediated Regio- and Stereoselective Hydroacylation and Hydrovinylation of Allyl Alcohols[1]

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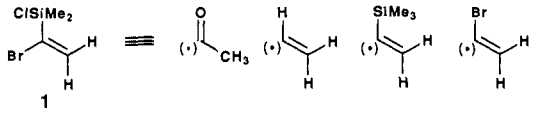
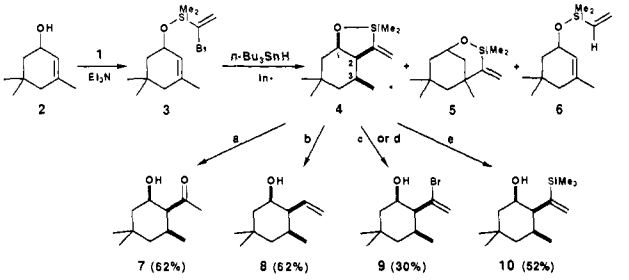
Radical cyclization has recently become a new useful methodology for carbon–carbon bond formation, especially for efficient synthesis of carbocyclic compounds and for regio- and stereoselective introduction of functionalized carbon chains.[2] Utility of vinyl radical cyclization has also been demonstrated by Stork's work.[3] Described herein is the first demonstration of 1-silylvinyl radical[4] cyclization as new tools for regio- and stereoselective hydroacylation[5] or hydrovinylation[6] of allyl alcohols.

The reagent for the purpose is 1-bromovinyldimethylsilyl chloride (**1**),[7] a new member of multifunctional silicon reagents[8] (Scheme I). Typical transformations starting with isophorol (**2**) are summarized in Scheme II. The hydroxy group is silylated with **1** to give **3**. When refluxed (80 °C, 8 h) with tri-*n*-butylstannane (1.2 equiv) in the presence of azobisisobutyronitrile (AIBN) (5 mol%) in benzene, **3** gave a mixture of a five-membered ring product **4**[9] (5-exo)[10] as the major cyclization product,

Scheme I

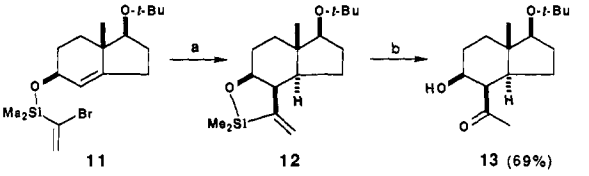


Scheme II[a]



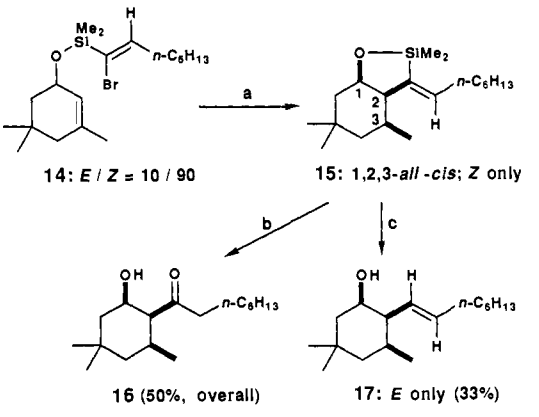
[a] (a) 30% H_2O_2/KF/$KHCO_3$/MeOH/THF/room temperature/1 day; (b) *t*-BuOK/DMSO–H_2O (17:1)/room temperature/2 days; (c) NBS/DMF/0 °C to room temperature/1 day; (d) (1) Br_2/CCl_4/0 °C; (2) KHF_2/MeOH/room temperature/1 day; (e) MeLi/Et_2O.

Scheme III[a]



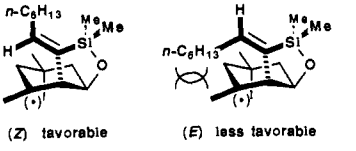
[a] (a) 0.02 M solution; *n*-Bu_3SnH (×1.2)/AIBN/benzene/reflux/4 h; (b) 30% H_2O_2 (×8)/KF (×4.4)/$KHCO_3$ (×4.4)/MeOH/THF/room temperature/15 h.

Scheme IV[a]



[a] (a) *n*-Bu_3SnH/*n*-Bu_3B/benzene/room temperature/24 h; (b) 30% H_2O_2/KF/$KHCO_3$/MeOH/THF/room temperature; (c) *t*-BuOK/DMSO–H_2O (17:1)/room temperature.

Scheme V



a six-membered isomer **5**[9] (6-endo),[10] and a direct reduction product **6**. While with 0.4 M *n*-Bu_3SnH the direct reduction was the major course of the reaction (**4**:**5**:**6** = 25:2:73), the cyclization proceeded efficiently (**4**:**5**:**6** = 80:8:12) under high dilution con-

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(3) (a) Stork, G.; Baine, N. H. *J. Am. Chem. Soc.* **1982**, *104*, 2321. (b) Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 3720. (c) Beckwith, A. L. J.; O'Shea, D. M. *Tetrahedron Lett.* **1986**, *27*, 4525. (d) Stork, G.; Mook, R., Jr. *Tetrahedron Lett.* **1986**, *27*, 4529. (e) Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547. (f) Stork, G.; Mook, R., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 2829.

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(5) Transition-metal-catalyzed hydroacylation of olefins has been known. Recent papers: (a) Marder, T. B.; Roe, D. C.; Milstein, D. *Organometallics* **1988**, *7*, 1451. (b) Fairlie, D. P.; Bosnich, B. *Organometallics* **1988**, *7*, 936. (c) Kondo, T.; Tsuji, Y.; Watanabe, Y. *Tetrahedron Lett.* **1987**, *28*, 6229.

(6) Transition-metal-catalyzed hydrovinylation: Buono, G.; Siv, C.; Peiffer, G.; Triantaphylides, C.; Denis, P.; Mortreux, A. Petit, F. *J. Org. Chem.* **1985**, *50*, 1781.

(7) Compound **1** was readily prepared from commercially available $[(CH_2{=}CH)Me_2Si]_2O$ by the following reactions: Bromination (neat, −78 °C), followed by dehydrobromination (Et_2NH, reflux, 3 h) gave $[(CH_2{=}CBr)Me_2Si]_2O$ (bp 70 °C/3 mmHg; 71%) which was heated with $MeSiCl_3$ (2/3 equiv) at 50 °C for 3 days in the presence of 5 mol% of HMPA. Direct distillation from the reaction mixture gave **1** in 52% overall yield (bp 80 °C/120 mmHg).

(8) Review: Tamao, K. *J. Synth. Org. Chem., Jpn.* **1988**, *46*, 861.

(9) In ^1H NMR (400 MHz, $CDCl_3$), **4** showed the NOE (6%) between the 3-Me (1.244, d, J = 7.3 Hz) and the lower field proton of the two olefin protons (5.499, t, J = 2.6 Hz and 5.916, t, J = 2.6 Hz). **5**: The bridgehead Me appeared as a singlet at 1.079.

(10) (a) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073. (b) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

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