

Molecular and Crystal Structure of (2RS,3RS)-2-Methyl-3-(p-Chloro Aniline)3-Phenyl-1-Propiofenone

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O composto $C_{22}H_{20}ONCl$ com $M_r = 349,9$ é monoclinico, grupo espacial $P2_1/n$, com dimensões de cela $a = 16,755(3)$, $b = 5,856(2)$, $c = 20,125(2)\text{Å}$, $\beta = 113(3)$, $V = 1811,4\text{Å}^3$; $Z=4$, $D_{\text{calc}} = 1,28 \text{ Mg m}^{-3}$, $\lambda(\text{Mo K}\alpha) = 0,71073\text{Å}$, $\mu = 1,78 \text{ cm}^{-1}$, $F(000) = 736$, $T = 298 \text{ K}$, $R=5,7\%$ para 1754 reflexões observadas com $I \geq 3.0 \sigma(I)$. A estrutura foi investigada para determinar a configuração relativa dos carbonos C(2) e C(3), que não pôde ser estabelecida por RMN. As moléculas estão ligadas por pontes de hidrogênio $N-H \cdots O$.

The compound $C_{22}H_{20}ONCl$ with $M_r = 349,9$ is monoclinic, space group $P2_1/n$ with cell dimension $a = 16,755(3)$, $b = 5,858(2)\text{Å}$, $c = 20,125(2)\text{Å}$, $\beta = 113,50(1)$, $V = 1811,4\text{Å}^3$; $Z=4$, $D_{\text{calc}} = 1,28 \text{ Mg m}^{-3}$, $\lambda(\text{Mo K}\alpha) = 0,71073\text{Å}$, $\mu = 1,78 \text{ cm}^{-1}$, $F(000) = 736$, $T = 298 \text{ K}$, $R=5,7\%$ for 1754 observed reflections with $I \geq 3.0 \sigma(I)$. The structure was investigated to determine the relative configuration at C(2) and C(3), which could not be established unambiguously by NMR. The molecules are linked by $N-H \cdots O$ hydrogen bonding.

Key words: $C_{22}H_{20}ONCl$; β -aminoketones.

Introduction

The widespread interest in the stereochemistry of the condensation between imines and lithium enolates of carboxylic acid derivatives has been greatly stimulated by synthesis of β -lactam derivatives¹. Evans *et alii*.² concluded that ester enolates which prefer the E-geometry react with the more stable E configuration of the imine through a chair-like transition state to give mainly *syn* products whereas amide enolates preferring the A geometry give mostly *anti* products (Fig. 1). Examples of addition of kinetically formed ketone enolates to imines are scarce in the literature compared to those of carboxylic acid derivatives^{3,4} although some functionalized β -aminoketones can conceivably be transformed into β -lactame.

Among the routes we have explored so far^{5,6}, moderate stereoselection was observed either with the lithium enolates of ketones or with the corresponding trimethylsilylenol ethers

under kinetic conditions. Since the assignment of the relative configuration by ¹H- and ¹³C-NMR spectroscopy is not straightforward the structure of the major compound obtained in the reaction of p-chlorobenzylamine with the trimethylsilylenol ether of propiophenone was solved by X-ray diffraction analysis.

Experimental

A clear yellow needle shaped crystal of approximate dimensions 0.45 x 0.45 x 0.20 mm was mounted on an Enraf-Nonius CAD-4 diffractometer. The unit cell dimensions and the orientation matrix for the data collection were obtained by a least squares fit of 25 reflections ($10.0 < \theta < 20.3^\circ$). The intensity data were collected with graphite-monochromated MoK α radiation, using ω -2 θ scan technique, and scan width calculated using the expression $(0.80 + 0.35 \tan \theta)^\circ$, with a max. time spent on any reflection measurement of 20 s. The range of hkl

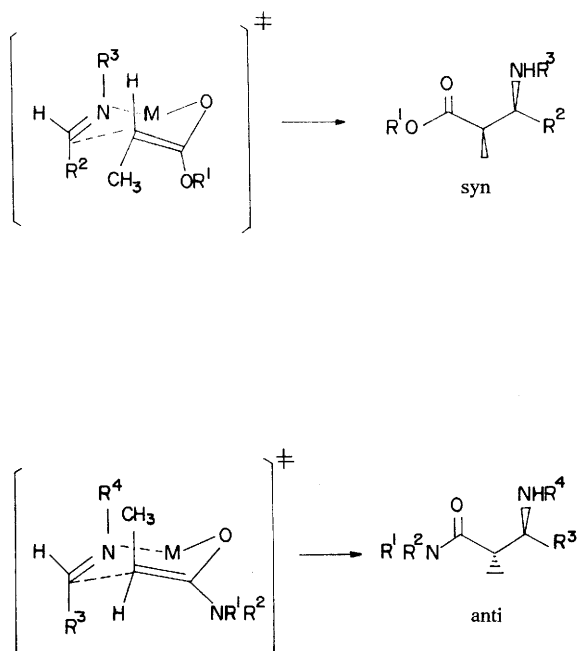


Figure 1. A diagram of the title molecule with atom numbering. Atoms are of arbitrary size.

was $-19 \leq h \leq 18$; $0 \leq k \leq 6$; $0 \leq l \leq 23$ with $\theta_{\max.} = 24.9^\circ$. Two standard reflections 7,0,11 and 0,0,14, measured every 30 min., varied $\pm 1.4\%$ of the mean intensities over data collection. A total number of 3608 reflections measured out of which 3121 were unique and 1754 were significant [$I \geq 3 \sigma(I)$]. Lp correction was applied, but no absorption correction, after which the equivalent reflections were merged with $R_{\text{int}} = 1.55\%$.

The structure was solved using MULTAN80⁷. The hydrogen atoms have been found from difference electron density map, placed with $B = B_{\text{eq}}$ of attached atoms. All non-hydrogen atoms were refined with anisotropic thermal parameters. Blocked-matrix refinement led to an R of 0.057 and $\omega R = 0.064$ with the function minimized $\sum w(|F_o| - |F_c|)^2$, where $w = 1.825 [\sigma(F_o) + (0.000853 F_o)]^{-1}$ and $\sigma(I)$ is based on counting statistics. Maximum shift to estimated standard deviation was 0.08, and the largest feature in the final difference electron map were 0.46 and -0.49 \AA^{-3} . The number of refined parameters was 227 and the standard deviations of unitary weight was 4.05. Programs from SHELX76⁸. Atomic scattering factors from *International Tables for X-ray Crystallography*⁹. Most of the calculations were performed on a IBM 3090 computer.

Discussion and Conclusion

The final atomic coordinates are given in Table 1 and bond distances and angles in Table 2. Selected torsion angles are shown in Table 3. Anisotropic temperature factors and the hy-

Table 1. Final positional parameters and equivalent isotropic temperature factors with *e.s.d.*'s in parentheses

	x	y	z	$B_{\text{eq}}(\text{\AA}^2)^*$
Cl	0.8586 (1)	-0.1565 (3)	0.9021 (1)	5.73 (4)
N	0.5006 (2)	0.0095 (6)	0.6892 (2)	3.5 (1)
O	0.3747 (2)	0.6307 (5)	0.6129 (2)	5.3 (1)
C(1)	0.3339 (3)	0.4576 (7)	0.5885 (2)	3.3 (1)
C(2)	0.3787 (3)	0.2260 (7)	0.6040 (2)	3.4 (1)
C(3)	0.4516 (2)	0.2196 (7)	0.6809 (2)	3.1 (1)
C(4)	0.2402 (3)	0.4742 (7)	0.5377 (2)	3.3 (1)
C(5)	0.2119 (3)	0.6691 (8)	0.4960 (2)	3.9 (1)
C(6)	0.1265 (3)	0.690 (1)	0.4476 (3)	4.9 (2)
C(7)	0.0690 (3)	0.515 (1)	0.4406 (3)	5.5 (2)
C(8)	0.0961 (3)	0.322 (1)	0.4822 (3)	5.5 (2)
C(9)	0.1821 (3)	0.2930 (8)	0.5303 (3)	4.5 (1)
C(10)	0.5835 (2)	-0.0218 (7)	0.7410 (2)	3.0 (1)
C(11)	0.6253 (3)	-0.2315 (7)	0.7413 (2)	3.7 (1)
C(12)	0.7093 (3)	-0.2743 (8)	0.7910 (2)	3.7 (1)
C(13)	0.7515 (3)	-0.1050 (8)	0.8398 (2)	3.6 (1)
C(14)	0.7126 (3)	0.1008 (8)	0.8407 (2)	3.6 (1)
C(15)	0.6292 (3)	0.1422 (7)	0.7919 (2)	3.3 (1)
C(16)	0.4147 (2)	0.2489 (7)	0.7382 (2)	3.0 (1)
C(17)	0.4315 (3)	0.4436 (7)	0.7814 (2)	3.7 (1)
C(18)	0.3988 (3)	0.4641 (8)	0.8347 (2)	4.3 (1)
C(19)	0.3477 (3)	0.2914 (9)	0.8443 (2)	4.6 (2)
C(20)	0.3298 (3)	0.1007 (8)	0.8010 (3)	4.4 (1)
C(21)	0.3636 (3)	0.0781 (7)	0.7490 (2)	3.7 (1)
C(22)	0.4113 (3)	0.1829 (9)	0.5446 (2)	5.0 (2)

$$B_{\text{eq}}^* = 4/3 \sum_i \sum_j \beta_{ij} a_i \cdot a_j$$

Table 2. Bond lengths (Å) and angles (°) with e.s.d.'s in parentheses

Cl - C(13)	1.757(4)	C(4) - C(5)	1.384(6)
C(13) - C(14)	1.374(7)	C(5) - C(6)	1.378(6)
C(14) - C(15)	1.373(5)	C(6) - C(7)	1.376(8)
C(15) - C(10)	1.390(5)	C(7) - C(8)	1.375(8)
C(10) - C(11)	1.413(6)	C(8) - C(9)	1.388(6)
C(11) - C(12)	1.386(5)	C(9) - C(4)	1.408(7)
C(12) - C(13)	1.376(6)	C(3) - C(16)	1.519(7)
N - C(10)	1.376(4)	C(16) - C(21)	1.390(6)
N - C(3)	1.452(5)	C(21) - C(20)	1.379(8)
C(3) - C(2)	1.542(5)	C(20) - C(19)	1.375(7)
C(2) - C(1)	1.521(6)	C(19) - C(18)	1.387(7)
C(1) - O	1.212(5)	C(18) - C(17)	1.391(8)
C(1) - C(4)	1.497(5)	C(17) - C(16)	1.393(6)
C(2) - C(22)	1.522(8)		
C(10) - N - C(3)	123.7(3)	C(3) - C(16) - C(17)	121.6(4)
N - C(3) - C(2)	108.8(3)	C(16) - C(21) - C(20)	121.0(4)
N - C(3) - C(16)	113.0(3)	C(21) - C(20) - C(19)	120.5(5)
C(2) - C(3) - C(16)	111.1(3)	C(20) - C(19) - C(18)	119.6(5)
C(3) - C(2) - C(1)	110.9(3)	C(19) - C(18) - C(17)	120.0(4)
C(2) - C(3) - N	108.8(3)	C(18) - C(17) - C(16)	120.6(4)
C(2) - C(1) - C(4)	119.7(3)	N - C(10) - C(15)	124.0(4)
O - C(1) - C(4)	119.4(4)	C(10) - C(15) - C(14)	120.7(4)
C(1) - C(4) - C(5)	118.7(4)	C(15) - C(14) - C(13)	129.9(4)
C(1) - C(4) - C(9)	121.1(4)	C(14) - C(13) - Cl	119.7(3)
C(4) - C(5) - C(6)	120.8(4)	Cl - C(13) - C(12)	118.3(4)
C(5) - C(6) - C(7)	119.4(5)	C(14) - C(13) - C(12)	122.0(3)
C(6) - C(7) - C(8)	120.4(4)	C(13) - C(12) - C(11)	118.0(4)
C(7) - C(8) - C(9)	121.5(5)	C(12) - C(11) - C(10)	121.3(4)
C(9) - C(4) - C(5)	120.1(3)	C(8) - C(9) - C(4)	117.7(4)
C(3) - C(16) - C(21)	120.0(4)	C(11) - C(10) - N	118.1(3)
C(1) - C(2) - C(22)	106.7(4)	C(11) - C(10) - C(15)	118.1(3)
C(3) - C(2) - C(22)	113.3(4)		

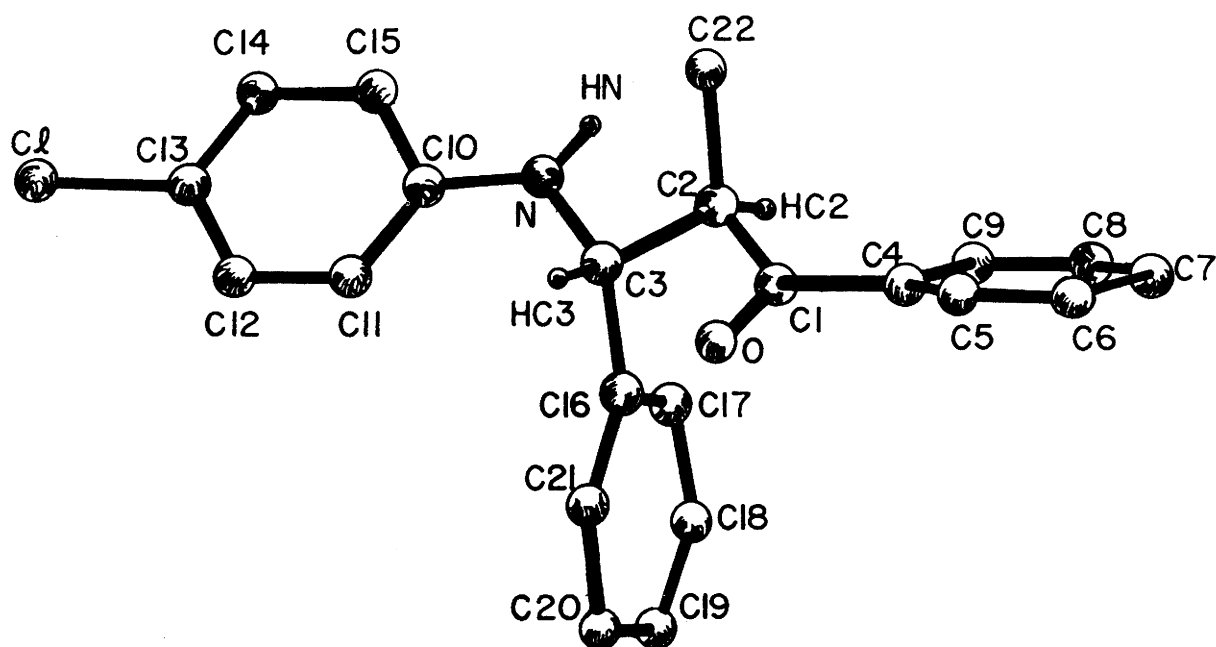
**Figure 2.** Stereodrawing of the molecular packing with the hydrogen bonds shown by broken lines.

Table 3. Selected torsion angles ($^{\circ}$). The estimated standard deviation is 0.9°

HN	- N	- C(3)	- C(2)	-33.4
HN	- N	- C(3)	- HC3	-150.1
HN	- N	- C(10)	- C(11)	16.5
HN	- N	- C(10)	- C(15)	-165.1
C(10)	- N	- C(3)	- C(2)	160.0
C(10)	- N	- C(3)	- HC3	43.3
C(3)	- N	- C(10)	- C(11)	-117.4
C(3)	- N	- C(10)	- C(15)	1.1
C(4)	- C(1)	- C(2)	- C(3)	-150.4
C(2)	- C(1)	- C(4)	- C(5)	-147.7
C(2)	- C(1)	- C(4)	- C(9)	30.2
O	- C(1)	- C(4)	- C(5)	27.3
O	- C(1)	- C(4)	- C(9)	-154.8
C(1)	- C(2)	- C(3)	- HC3	-52.5
C(1)	- C(2)	- C(3)	- C(16)	63.4
C(1)	- C(2)	- C(3)	- N	171.6
C(2)	- C(3)	- C(16)	- C(21)	68.5
C(2)	- C(3)	- C(16)	- C(17)	-112.2
HC3	- C(3)	- C(16)	- C(17)	3.8
HC3	- C(3)	- C(16)	- C(21)	-175.6
C(3)	- C(16)	- C(17)	- C(18)	-178.4
C(3)	- C(16)	- C(21)	- C(20)	179.7
C(22)	- C(2)	- C(3)	- N	51.5
HC2	- C(2)	- C(3)	- C(16)	-52.4
HC2	- C(2)	- C(3)	- N	72.6
C(22)	- C(2)	- C(3)	- HC3	67.6
HC2	- C(2)	- C(3)	- HC3	-168.4
C(22)	- C(2)	- C(3)	- C(16)	-176.5

drogen atoms coordinates are given in Tables 4 and 5, respectively. The crystallographic atomic numbering and a view of the molecule are shown in Fig. 2.

The benzene rings are planar with only slight deviations from planarity. The average bond length of each ring, A, B and C is $1.385(8)\text{\AA}$. The dihedral angles between rings A and B, rings A and C, and rings B and C, are $47.0(3)^{\circ}$, $92.5(3)^{\circ}$ and $79.2(3)^{\circ}$, respectively. The corresponding dihedral angles found in the similar compound (1SR, 3RS)-3-p-Chloro Anilino-1,3-Diphenyl-1-Propanol¹¹ are $3.6(3)^{\circ}$, $92.0(2)^{\circ}$ and $95.3(2)^{\circ}$, respectively. This difference in molecular conformation may be due to the electronic repulsion that occurs when the C(2) carbon atom is bonded to a methyl group instead of a hydrogen atom (H¹C2) as in the previous compound.

The C(sp³)-Cl bond length do not differ significantly from the values determined in crystal structures of similar compounds. So, the C(13)-Cl bond is almost symmetrical in the plane of the phenyl ring and does not undergo any bending as indicated by the angles Cl-C(13)-C(14) [$118.3(4)^{\circ}$] and Cl-C(13)-C(12) [$119.7(3)^{\circ}$] and the distances Cl-C(14) [$2.715(4)\text{\AA}$] and Cl-C(12) [$2.697(4)\text{\AA}$].

The molecular packing is assured by the hydrogen bond where the N atom acts as donor of H atom and the Oⁱ atom as an acceptor of H atom, with the distances and angles N - HN...O_i [N...O_i $3.029(9)\text{\AA}$, N - HN 1.02\AA , N - HN...O_i $167.0(9)^{\circ}$, with $i = x, y-1, z$]. A stereodrawing of the molecular packing with the hydrogen bonds is shown in Figure 3.

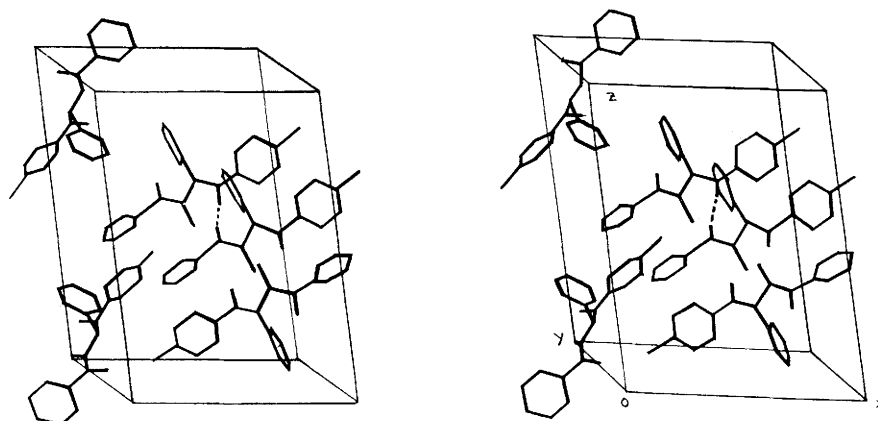
The *syn* relative configuration for the major isomer isolated in the condensation between p-chlorobenzylideneaniline and the trimethylsilylenolether of propiofenone. This

Table 4. Anisotropic temperature factors

Atom	U(1,1)	U(2,2)	U(3,3)	U(2,3)	U(1,3)	U(1,2)
Cl	0.0465(7)	0.091(1)	0.0631(8)	0.0112(8)	0.0043(6)	0.0209(7)
N	0.038(2)	0.034(2)	0.051(2)	-0.008(2)	0.006(2)	0.000(2)
O	0.063(2)	0.042(2)	0.066(2)	-0.003(2)	-0.005(2)	-0.014(2)
C(1)	0.048(2)	0.035(3)	0.036(2)	-0.002(2)	0.008(2)	-0.011(2)
C(2)	0.037(2)	0.040(3)	0.044(2)	-0.004(2)	0.007(2)	-0.005(2)
C(3)	0.035(2)	0.032(2)	0.040(2)	-0.001(2)	0.004(2)	-0.004(2)
C(4)	0.042(2)	0.039(3)	0.043(2)	-0.010(2)	0.016(2)	0.007(2)
C(5)	0.056(3)	0.042(3)	0.045(3)	-0.005(2)	0.016(2)	0.006(2)
C(6)	0.058(3)	0.068(4)	0.049(3)	0.003(3)	0.011(2)	0.018(3)
C(7)	0.042(3)	0.085(4)	0.066(3)	-0.020(3)	0.004(3)	0.013(3)
C(8)	0.040(3)	0.072(4)	0.085(4)	-0.014(3)	0.014(3)	-0.007(3)
C(9)	0.040(2)	0.061(3)	0.065(3)	-0.013(3)	0.016(2)	-0.010(2)
C(10)	0.036(2)	0.044(3)	0.034(2)	0.000(2)	0.013(2)	-0.003(2)
C(11)	0.044(2)	0.039(3)	0.058(3)	-0.003(2)	0.022(2)	-0.003(2)
C(12)	0.045(2)	0.048(3)	0.049(3)	0.006(2)	0.021(2)	0.002(2)
C(13)	0.037(2)	0.058(3)	0.041(2)	0.011(2)	0.015(2)	0.010(2)
C(14)	0.042(2)	0.048(3)	0.038(2)	-0.002(2)	0.007(2)	0.002(2)
C(15)	0.045(2)	0.034(2)	0.042(2)	-0.003(2)	0.014(2)	0.001(2)
C(16)	0.032(2)	0.037(2)	0.037(2)	0.003(2)	0.007(2)	0.001(2)
C(17)	0.049(2)	0.036(2)	0.053(3)	-0.006(2)	0.018(2)	-0.001(2)
C(18)	0.060(3)	0.050(3)	0.052(3)	-0.005(2)	0.020(2)	0.006(2)
C(19)	0.062(3)	0.062(3)	0.056(3)	0.005(3)	0.029(2)	0.011(3)
C(20)	0.054(3)	0.053(3)	0.061(3)	0.011(2)	0.025(2)	-0.002(2)
C(21)	0.047(2)	0.042(3)	0.049(2)	-0.001(2)	0.015(2)	-0.007(2)
C(22)	0.066(3)	0.074(4)	0.046(3)	-0.002(3)	0.019(2)	0.015(3)

Table 5. Hydrogen atoms coordinates and equivalent isotropic temperature factors.

Atom	x	y	z	Beq(Å ²)*
HN	0.4657	-0.1288	0.6621	3.5
HC2	0.3324	0.0956	0.6080	3.4
HC3	0.4900	0.3559	0.6850	3.1
HC5	0.2568	0.8083	0.5031	3.9
HC6	0.1040	0.8400	0.4146	4.9
HC7	0.0031	0.5308	0.4019	5.5
HC8	0.0478	0.1909	0.4778	5.5
HC9	0.2319	-0.1283	-0.0296	4.5
H11	0.5975	0.3027	0.7923	3.3
H12	0.7490	0.2305	0.8800	3.6
H14	0.4289	-0.0746	-0.0667	3.7
H15	0.5911	-0.3598	0.7022	3.7
HC17	0.3503	-0.0730	0.7156	3.7
HC18	0.2896	-0.0335	0.8079	4.4
HC19	0.329	0.3055	0.8860	4.6
HC20	0.4117	0.6136	0.8679	4.4
HC21	0.4702	0.5778	0.7731	3.7
H22	0.4556	0.3186	0.5443	4.9
H ^o 22	0.3575	0.1784	0.4917	4.9
H ⁿ 22	0.4459	0.0216	0.5534	4.9

**Figure 3.** Stereodrawing of the molecular packing with the hydrogen bond shown by a broken line.

result will enable us to correlate the ¹³C-NMR data and the relative configuration for the whole series of β-aminoketones prepared.

Supplementary Material

The list of the observed and calculated structure factors is available from one of the authors (I.V.) upon request.

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