Novel 4-(3-Bromo-2-hydroxy-5-methylphenyl)-1,3-Dithiol-2-ylidene Derivatives

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Novel 4-(3-bromo-2-hydroxy-5-methylphenyl)-1,3-dithiol-2-ylidene derivatives have been synthesized from the reaction of the corresponding 1,3-dithiol-2-ylium salts with various methylene active compounds using DBU as base. The 1,3-dithiol-2-ylium compounds have been obtained from the reaction of the substituted w-bromoacetophenone with various salts of dithiocarbamic acids. The newly obtained derivatives were characterized by NMR spectrometry, UV-Vis and IR spectroscopy.

Keywords: dithiocarbamates, 1,3-dithiolium salts, mesoionic compounds, acetophenones

The development of new organic superconductors is a major topic in the field of molecular conductors [1]. Since the discovery of the metallic conductivity in a tetrathiafulvalene-tetracyanoquinodimethane complex [2] tetrachalcogenafulvalenes have played a leading role in the development of new molecular metals and superconductors [3, 4]. For many years, all the organic *ð*-electron donors with conductivity properties were limited to the tetrachalcogenafulvalenes compounds [5,6]. Recently, the non-tetrachalcogenafulvalenes containing a 1,3-dithiol-2-ylidene based *ð*-donor unity proved to give superconducting salts [7]. Moreover, novel dye-sensitized solar cells based on 1,3-dithiol-2-ylidene derivatives have been recently reported [8]. In general, charge-transfer [9-26] or push-pull [27-38] compounds have important applications in the field of conducting materials. For these reasons heterocyclic compounds - especially those containing sulfur and nitrogen - represent an important resource for the material chemistry [39-50] and not only (e.g. biologically active compounds) [51-59]. An important precursor for 1,3-dithiol-2-ylidene derivatives are the 1,3-dithiolium-2-yl compounds [60-62]. 1,3-Dithiolium salts contain a positive charge located at the C(2) position and consequently these systems are prone to nucleophilic interactions at this position [24, 63].

We are reporting here the synthesis of novel 4-(3-bromo-2-hydroxy-5-methylphenyl)-1,3-dithiol-2-ylidene derivatives from the corresponding 1,3-dithiolium salts, via mesoionic compounds by the nucleophilic attack at the C(2) position of the 1,3-dithiolium ring.

Experimental part

Analysis methods

Melting points were obtained on a Mel-Temp II apparatus and are uncorrected. IR spectra were recorded on a Bruker Tensor 27 instrument. NMR spectra were recorded on a Bruker 500 MHz spectrometer. Chemical shifts are reported in ppm downfield from TMS. Uv-Vis spectra were recorded on a Varian BioChem 100 spectrophotometer. Elemental analyses (C, H, N and S) were conducted using a CE440 Elemental Analyser; the results were found to be in good agreement (±0.24%) with the calculated values.

Synthesis

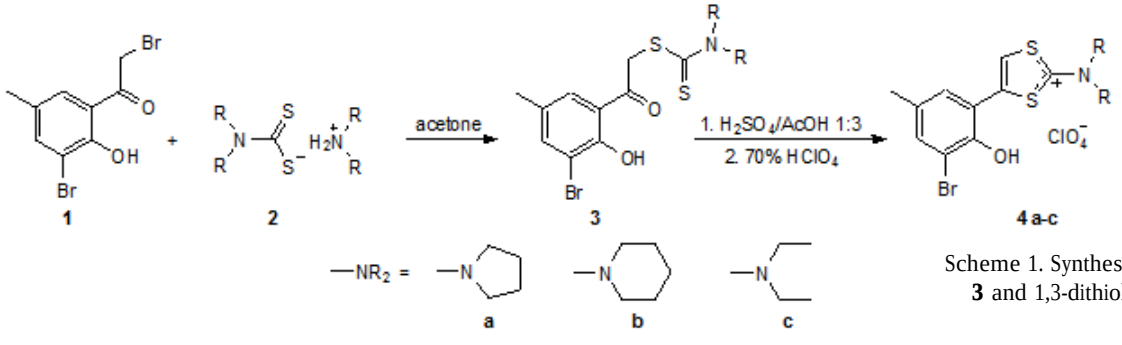
The reaction sequence for the synthesis of dithiocarbamate **3** and 1,3-dithiolium perchlorate **4** is described in scheme 1 and were performed in accordance with the previously reported procedures [64-66]. 1,3-Dithiol-2-ylidene derivatives **6a-c** were accomplished using the reaction pathway presented in scheme 2.

1,3-Dithiol-2-ylidene derivative **6a**; *General Procedure*

To a suspension of 1,3-dithiolium perchlorate **4b** (0.47g, 1mmol) in acetonitrile (15mL) under nitrogen atmosphere, dimedone (**6a**, 0.14g, 1mmol) was added and the reaction mixture was brought to 60 °C. DBU (0.34mL, 2.2mmol) was then added and the reaction was left over night under stirring. The solution was then poured into water (100mL) and concentrated hydrochloric acid was added (3mL). After stirring for 10 min, the precipitate that formed was filtered under vacuum and recrystallized from ethanol; yield 0.36g (81%). The spectral data for the 1,3-dithiol-2-ylidene derivatives **6a-c** are presented in table 1.

Results and discussions

One of the most used synthetic procedure for 1,3-dithiolium salts consist of the acid catalyzed intramolecular cyclization of phenacyl carbodithioates [25-27] that, in turn,



Scheme 1. Synthesis of dithiocarbamate **3** and 1,3-dithiolium perhlorates **4**

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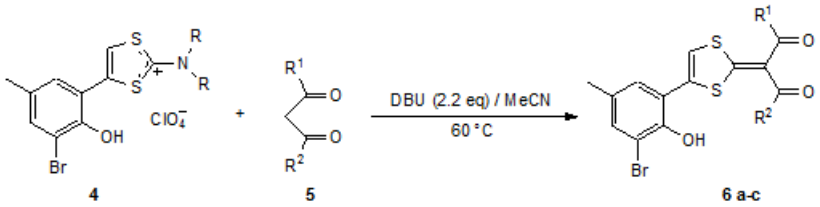
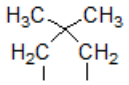


5, 6	R^1	R^2
a		
b		
c	CH_3	OEt

Scheme 2. Synthesis of 1,3-dithiol-2-ylidene derivatives **6a-c**

are obtained by the reaction of secondary amine with carbon disulfide [64] and then with *w*-bromo-acetophenones. Following this reaction pathway, 1-(3-bromo-2-hydroxy-5-methylphenyl)-1-oxaethan-2-yl carbodithioates **3a-c** have been synthesized by reacting 2-bromo-1-(3-bromo-2-hydroxy-5-methylphenyl)ethan-1-one (**1**) [67] with pyrrolidinium pyrrolidine-1-carbodithioate (**2a**), piperidinium piperidine-1-carbodithioate (**2b**) and sodium *N,N*-diethylamino carbodithioate (**2c**), in acetone under heating (scheme 1). Acid catalyzed cyclization of phenacyl carbodithioates **3a-c** provided the corresponding 1,3-dithiol-2-ylium cations, which where isolated as salts of perchloric acid **4a-c**. The analytical and spectral data of compound **3** and **4** are in agreement with those previously reported [65].

Due to the positive charge located at the C(2) position, 1,3-dithiol-2-ylium ring readily interact with nucleophiles [24]. In order to synthesize the target 1,3-dithiol-2-ylidene derivatives **6** we reacted 1,3-dithiolium perchlorates **4** with carbanions derived from various methylene active compounds **5** (scheme 2). In order to generate the *C*-nucleophiles we used 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as base (but week nucleophile) to extract a proton from the active methylene moiety. The reactions have been performed using 2.2 eq. of DBU, in acetonitrile, at 60 °C, under nitrogen, providing 1,3-dithiol-2-ylidene derivatives **6** in good isolated yields (table 1).

The formation of 1,3-dithiol-2-ylidene derivatives **6a-c** is supported by analytical and spectral data (table 1). IR spectroscopy indicates the presence of new carbonyl or ester bands, which come from the active methylene compounds. ^{1}H NMR spectra reveals the presence of new methyl/methylene aliphatic signals for derivatives **6a-c**. It should be noted that the regeneration of the phenolic group is always indicated by the presence of a broad singlet at various chemical shifts depending on the nature of deuterated solvent. ^{13}C NMR spectra indicates the disappearance of the signal of the positively charged C(2) atom and the appearance of the new signals corresponding to the new double bonded carbon atoms. Also, the new signals corresponding to the carbonyl groups and ester groups confirm the structures of the new 1,3-dithiol-2-ylidene derivatives. The compound **6c** has been obtained as a mixture of two isomers due to the asymmetry of ethyl acetoacetate. The spectral data are presented for one isomer. UV/Vis spectra also confirm the formation of 1,3-dithiolium-2-ylidene derivatives. A strong absorption band was recorded for the new double bond in compound **6b**

Table 1
ANALYTICAL AND SPECTRAL DATA OF 1,3-DITHIOL-2-YLIDENE DERIVATIVES **6a-c**

	M.p., °C	η, %	IR-ATR, cm^{-1}	NMR, ppm
6a	214-215	81	2947, 1558, 1369, 843, 600	*^{1}H NMR* (DMSO-*d6*) δ : 1.07 (6H, s, 2 CH_3); 2.28 (3H, s, CH_3); 2.53 (2H, s, CH_2); 2.55 (2H, s, CH_2); 6.76 (1H, bs, OH); 6.83 (1H, s); 7.35 (1H, d, H-6); 7.75 (1H, d, H-4). *^{13}C NMR* ($CDCl_3$) δ : 14.3, 28.4, 30.9, 50.4, 50.6, 112.3, 116.9, 120.1, 128.9, 130.5, 133.5, 135.7, 137.1, 150.1, 174.45, 193.0 .
6b	271-272	75	1641, 1568, 1475, 1211, 814, 641	*^{1}H NMR* (DMSO-*d6*) δ : 2.25 (3H, s, CH_3); 6.88 (1H, s); 7.57 (1H, d, H-6); 7.76 (4H, m); 7.88 (1H, s, H-4); 10.11 (1H, bs, OH). *^{13}C NMR* (DMSO-*d6*) δ : 14.4, 111.8, 113.1, 120.9, 122.1, 122.3, 128.3, 128.9, 133.1, 134.8, 135.7, 136.4, 139.8, 140.7, 152.1, 166.4, 186.8, 186.8 .
6c	149-150	77	2958, 1644, 1631, 1579, 1439, 1244, 1027, 937, 674	*^{1}H NMR* ($CDCl_3$) selected data for one isomer, δ : 1.41 (3H, t, CH_3); 2.21 (3H, s, CH_3); 2.85 (3H, s, CH_3); 4.39 (2H, q, CH_2); 6.79 (1H, s); 7.13 (1H, d, H-6); 7.51 (1H, s, H-6); 11.01 (1H, bs, OH). *^{13}C NMR* ($CDCl_3$) selected data for one isomer, δ : 14.7, 14.9, 30.1, 61.1, 111.0, 121.1, 121.7, 128.7, 132.9, 134.2, 135.5, 159.5, 167.2, 167.8, 177.9, 191.8 .

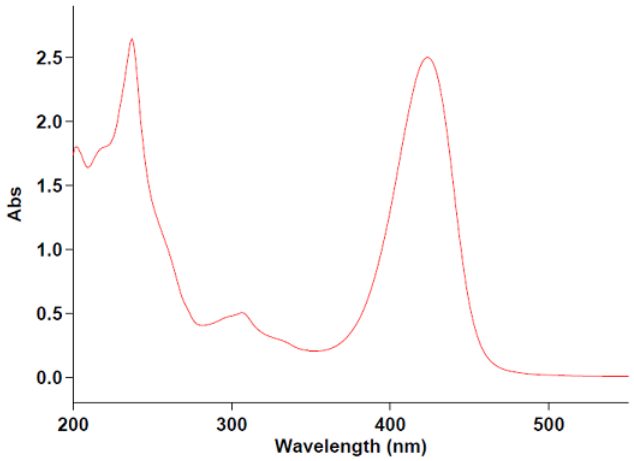


Fig. 1. UV/Vis absorption spectra of compound **6b** in ethanol

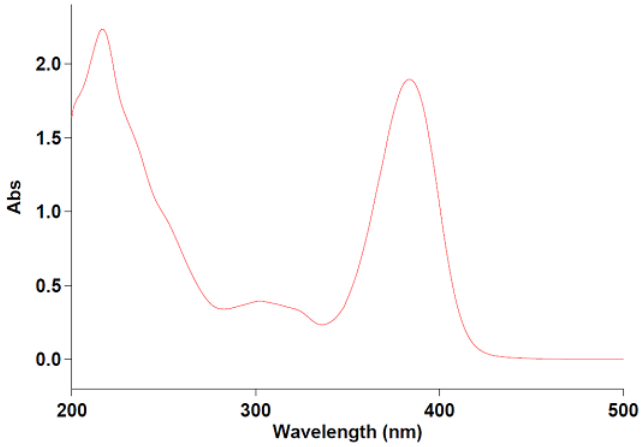


Fig. 2. UV/Vis absorption spectra of compound **6c** in ethanol

(424 nm, fig. 1). Due to the lack of extended conjugation a hypsochromic effect was recorded for compound **6a** (384 nm, fig. 2). The spectrum of compounds **6a** (not shown here) shows a weak absorption for the 2-ylidene double bond along the characteristic signals displayed by the previous two compounds (ca. 300 and 215 nm).

Conclusions

The synthesis of new 4-(3-bromo-2-hydroxy-5-methylphenyl)-1,3-dithiol-2-ylidene derivatives has been performed by reacting the corresponding 1,3-dithiolium perchlorates with various active methylene compounds. The latter have been *in situ* converted into nucleophiles, using DBU, a non-nucleophilic base.

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References

1.ISHIGURO, T., YAMAJI, K., SAITO, G., Organic Superconductors (Springer Series in Solid-State Sciences), 2nd edition, Ed. FULDE, P., Springer, Berlin, vol. 88, 1998.
2.FERRARIS, J., COWAN, D.O., WALATKA Jr., V., PERLSTEIN, J.H., J. Am. Chem. Soc., **95**, 1973, p. 948.
3.BECHGAARD, K., CARNEIRO, K., RASMUSSEN, F.B., OLSEN, M., RINDORF, G., JACOBSEN, C.S., PEDERSEN, H.J., SCOTT, J.C., J. Am. Chem. Soc., **103,** 1981, p. 2440.
4.YAMADA, J., SUGIMOTO, T., TTF Chemistry - Fundamentals and Applications of Tetrathiafulvalene, Kodansha-Springer, 2004.
5.ADACHI, T., OJIMA, E., KATO, K., KOBAYASHI, H., MIYAZAKI, T., TOKUMOTO, M., KOBAYASHI, A., J. Am. Chem. Soc., **122**, 2000, p. 3238.
6.OTSUBO, T., TAKIMIYA, K., Bull. Chem. Soc. Jpn., **77**, 2004, p. 43.
7.YAMADA, J.-i., J. Mater. Chem., **14**, 2004, p. 2951.
8.WADA, A., NISHIDA, J.-i., MAITANI, M.M., WADA, Y., YAMASHITA, Y., Chem. Lett., **43**, 2014, p. 296.
9.LUNGU, N.C., SANDU, I., CHIRITA, P., BIRSA, M.L., Rev. Chim. (Bucharest), **64**, no. 7, 2013, p. 697.
10. BELEI, D., FORNA, N.C., SANDU, I., BIRSA, M.L., Rev. Chim. (Bucharest), **65**, no. 1, 2014, p. 80.
11.BAHRIN, L.G., LUNGU, N.C., FORNA, N.C., SANDU, I., BIRSA, M.L., Rev. Chim. (Bucharest), **64**, no. 11, 2013, p. 1343.
12.SARBU, L.G., LUNGU, N.C., ASAFTEI, I.V., SANDU, I., BIRSA, M.L., Rev. Chim. (Bucharest), **65**, no. 3, 2014, p. 325.
13.BUHACEANU, R., LUNGU, N.C., FORNA, N.C., ASAFTEI, I.V., CHIRITA, P., BIRSA, M.L., Rev. Chim. (Bucharest), **64**, no. 8, 2013, p. 802.
14. BUHACEANU, R., LUNGU, N.C., FORNA, N.C., ASAFTEI, I.V., CHIRITA, P., BIRSA, M.L., Rev. Chim. (Bucharest), **64**, no. 9, 2013, p. 960.
16.SELIGER, H., HAPP, E., CASCAVAL, A., BIRSA, M.L., An. Stiint. Univ. Al.I. Cuza Iasi, **5**, 1997, p. 111.
17.BIRSA, M.L., An. St. Univ. Al. I. Cuza Iasi, s. Chimie, **8**, 2000, p. 325.
18.BIRSA, M.L., An. St. Univ. Al. I. Cuza Iasi, s. Chimie, **6**, 1998, p. 57.
19. BIRSA, M.L., An. St. Univ. Al. I. Cuza Iasi, s. Chimie, **7**, 1999, p. 341.
20.BIRSA, M.L., An. St. Univ. Al. I. Cuza Iasi, s. Chimie, **7**, 1999, p. 349.
21. BIRSA, M.L., An. St. Univ. Al. I. Cuza Iasi, s. Chimie, **8**, 2000, p. 71.
22.BIRSA, M.L., An. St. Univ. Al. I. Cuza Iasi, s. Chimie, **8**, 2000, p. 329.
23. BIRSA, M.L., GANJU, D., J. Phys. Org. Chem., **16**, 2003, p. 207.
24. BIRSA, M.L., Synth. Commun., **33**, 2003, p. 3071.
25. SARBU, L.G., BIRSA, M.L., Acta Chem. Iasi, **19**, 2011, p. 125.
26. BIRSA, M.L., ASAFTEI, I.V., Monat. Chem., **139**, 2008, p. 1433.
27. SARBU, L.G., BIRSA, A., HOPF, H., BIRSA, M.L., Phosphorus, Sulfur, and Silicon, and the Related Elements, **186**, 2011, p. 1246.
28. BIRSA, M.L., HOPF, H., Phosphorus, Sulfur, and Silicon, and the Related Elements, **180**, 2005, p. 1453.
29. BIRSA, M.L., JONES, P.G., BRAVERMAN, S., HOPF, H., Synlett, **2005**, p. 640.
30. BIRSA, M.L., JONES, P.G., HOPF, H., Eur. J. Org. Chem., **2005**, p. 3263.
31. BIRSA, M.L., HOPF, H., Synlett, **2007**, p. 2753.
32. BIRSA, M.L., HOPF, H., Synlett, **2009**, p. 3000.
33. BIRSA, M.L., HOPF, H., Heteroatom Chem., **21**, 2010, p. 126.
34. BIRSA, M.L., JONES, P.G., HOPF, H., Synlett, **2011**, p. 259.
35. SARBU, L.G., HOPF, H., GRUENENBERG, J., BIRSA, M.L., Synlett, **26**, 2015, p. 87.
36. SARBU, L.G., BICU. E., HOPF, H., BIRSA, M.L., Rev. Chim. (Bucharest), **65**, no. 4, 2014, p. 398.
37. SARBU, L.G., HOPF, H., JONES, P.G., BIRSA, M.L., Beilstein J. Org. Chem., **10**, 2014, p. 2550.
38. BAHRIN, L.G., SARBU, L.G., JONES, P.G., BIRSA, M.L., HOPF, H., Chem. Eur. J., **23**, 2017, p. 0000. DOI: 10.1002/chem.201701593
39. SELIGER, H., CASCAVAL, A., BIRSA, M.L., An. Stiint. Univ. Al.I. Cuza Iasi, **5**, 1997, p. 129.
40. SELIGER, H., HAPP, E., CASCAVAL, A., BIRSA, M.L., NICOLAESCU, T., POINESCU, I., COJOCARIU, C., Eur. Polym. J., **35**, 1999, p. 827.
41.BRAVERMAN, S., CHERKINSKY, M., BIRSA, M.L., TICHMAN, S., GOLDBERG, I., Tetrahedron Lett., **42**, 2001, p. 7485.
42. BIRSA, M. L., Synth. Commun., **32**, 2002, p. 115.
43.BRAVERMAN, S., CHERKINSKY, M., BIRSA, M.L., ZAFRANI, Y., Eur. J. Org. Chem., **2002**, p. 3198.
43. BIRSA, M.L., CHERKINSKY, M., BRAVERMAN, S., Tetrahedron Lett., **43**, 2002, p. 9615.
44.LEVI, M.D., GOFER, Y., CHERKINSKY, M., BIRSA, M.L., AURBACH, D., BERLIN, A., Phys. Chem. Chem. Phys., **5**, 2003, p. 2886.
45. BRAVERMAN, S., CHERKINSKY, M., BIRSA, M.L., GOTTLIEB, H.E., Synthesis, **2003**, p. 849.
46.BELEI, D., BICU, E., BIRSA, M.L., Acta Chem. Iasi, **17**, 2009, p. 197.

47.BELEI, D., BICU, E., JONES, P. G., BIRSA, M. L., Synlett, **2010**, p. 931.
48. BELEI, D., BICU, E., JONES, P. G., BIRSA, M.L., J. Heterocycl. Chem., **48**, 2011, p. 129.
49.BELEI, D., ABUHAIE, C., BICU, E., JONES, P. G., HOPF, H., BIRSA, M.L., Synlett, **23**, 2012, p. 545.
50.HOPF, H., JONES, P.G., NICOLESCU, A., BICU, E., BIRSA, M.L., BELEI, D., Chem. Eur. J., **20**, 2014, p. 5565.
51.GOSAV, S., PRAISLER, M., BIRSA, M.L., Int. J. Mol. Sci., **12**, 2011, p. 6668.
52.BIRSA, M.L., SANDU, I., BAHRIN, L.G., Rev. Chim. (Bucharest), **65**, no. 2, 2014, p. 174.
53. BAHRIN, L.G., LUCA, A., BIRSA, M.L., Rev. Chim. (Bucharest), **65**, no. 2, 2014, p. 199.
54.BAHRIN, L.G., APOSTU, M.O., BIRSA, M.L., STEFAN, M., Bioorg. Med. Chem. Lett., **24**, 2014, p. 2315.
55.GOSAV, S., BIRSA, M.L., Rom. Rep. Phys., **66**, 2014, p. 411.
56.GOSAV, S., BIRSA, M.L., Acta Chem. Iasi, **18**, 2010, p. 150.
57.BABII, C., BAHRIN, L.G., NEAGU, A., GOSTIN, I., MIHASAN, M., BIRSA, M.L., STEFAN, M., J. Appl. Microbiology, **120**, 2016, p. 630.
58.BAHRIN, L.G., HOPF, H., JONES, P.G., SARBU, L.G., BABII, C., MIHAI, A.C., STEFAN, M., BIRSA, M.L., Beilstein J. Org. Chem., **12**, 2016, p. 1065.
59.BAHRIN, L.G., SARBU, L.G., HOPF, H., JONES, P.G., BABII, C., STEFAN, M., BIRSA, M.L., Bioorg. Med. Chem., **24**, 2016, p. 3166.
60. DIRTU, D., LUNGU, N.C., CHIRITA, P., SANDU, I.G., BIRSA, M.L., EARAR, K., SARBU, L.G., Rev. Chim. (Bucharest), **67**, no. 3, 2016, p. 534.
61.MATEI, M., SANDU, I., BIRSA, M.L., SARBU, L.G., SIMION, L., Rev. Chim. (Bucharest), **68**, no. 1, 2017, p. 81.
62.BAHRIN, L.G., CRACIUN, B.F., SANDU, I., BIRSA, M.L., Rev. Chim. (Bucharest), **65**, no. 5, 2014, p. 525.
63.SARBU, L.G., BAHRIN, L.G., JONES, P.G., BIRSA, M.L., HOPF, H., Beilstein J. Org. Chem., **11**, 2015, p. 1917.
64.BRAVERMAN, S., CHERKINSKY, M., BIRSA, M.L., Science of Synthesis, **18.2**, Georg Thieme Verlag, Stuttgart, 2005, p 55.
65.GOANTA, M., CIOBANU, A.S., BIRSA, A., ASAFTEI, I.V., BIRSA, M.L., Acta Chem. Iasi, **17**, 2009, p. 35.
66.BIRSA, M.L., Synth. Commun., **31**, 2001, p. 1271.
67.BUU-HOI, Ng. Ph., LAVIT, D., J. Chem. Soc., **1955**, p. 18.

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