INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN CHEMISTRY AND PHARMACEUTICAL SCIENCES
(p-ISSN: 2348-5213: e-ISSN: 2348-5221)
www.ijcrcps.com
DOI: 10.22192/ijcrcps Coden: IJCROO(USA) Volume 5, Issue 3 - 2018

Research Article

DOI: http://dx.doi.org/10.22192/ijcrcps.2018.05.03.002

Synthesis, characterization and antifungal activity of some aromatic thiosemicarbazones and their 1,3,4- thiadiazolines derivatives

Houssou Raymond FATONDJI[1], Salomé KPOVIESSI[1*], Bardieu ATCHADE[1], Fernand GBAGUIDI[2] ,Kamirou CHABI SIKA[4], Joachim GBENOU[2], Georges Coffi ACCROMBESSI[1], Mansourou MOUDACHIROU[2] and Jacques POUPAERT[3]

[1] Laboratoire de Chimie Organique Physique et de Synthèse, Université d'Abomey-Calavi, Faculté des Sciences et Techniques Cotonou BP 4521, Bénin.
[2]Laboratoire National de Pharmacognosie/Centre Beninois de la Recherche Scientifique et Technique (CBRST). Bp 06 Oganla Porto-Novo
[3]Ecole de Pharmacie de l'Université Catholique de Louvain, 73.40 B-1200 Bruxelles-Belgique.
[4] Laboratoire de Biologie et de Typage Moléculaire en Microbiologie (LBTMM)

*Corresponding Author: salome.kpoviessi@fast.uac.bj

Abstract

The thiosemicarbazones of six aromatic ketones and aldehydes were synthesized as well as their 1,3,4-thiadiazolines derivatives obtained by cyclization under acetylating condition with yields going from 32 to 94%. The products purity was confirmed by mass spectrometry coupled with high-performance liquid chromatography (LC/MS) and they were characterized using spectrometry IR, NMR ^{1}H and ^{13}C (nuclear magnetic resonance). These compounds were then tested *in vitro* on *Candida abicans* MHMR according to the macro-dilution method in liquid environment for a comparison of their antifungal activity on *Candida albic*ans MHMR. Thiosemicarbazone has been shown to be more active than other products.

Keywords: Thiosemicarbazone, 1,3,4-thiadiazolines, characterization, antifungal activity.

Introduction

Candida albicans is a yeast found in human mucous membranes. This saprophyte, which is usually harmless to humans, is however responsible for important oral fungal and gynecological infections in certain immunocompromised patients (Laine L et al., 1994; Bretagne S et al., 1994; Baehr P et al 1996). In recent decades, candidiasis caused by this yeast is a real public health problem because of the spread of diseases such as AIDS and diabetes that weaken the immune system of affected people **(**Bonacini M et al., 1991**)**. Antifungal medications commonly used against *Candida albicans* are becoming less effective (Citak S et al., 2005**)**. It is then necessary to develop new antifungal molecules active on *Candida albicans*. Thiosemicarbazones have many biological activities such as: antiviral **(**Garcia CC et al., 2003), antibacterial **(**Sau DK et al., 2003; Rebolledo AP et al., 2003; Kasuga NC et al., 2003), antimalarial **(**Klayman

DL et al., 1984) antitumor **(**Quiroga AGet al., 1998; Perez JM et al., 1999; Easmon J et al., 2001; Hall IH et al., 2000; Kovala-Demertzi D et al., 2002; Afrasiabi Z et al., 2003; Afrasiabi Z et al., 2004).

Thiosemicarbazones are also known for their antifungal properties **(**Kovač T et al., 2017; De Araújo Neto LN et al., 2017**)**. In addition, thiosemicarbazones are important intermediates in drugs synthesis, formation of metal complexes and heterocycles such as thiadiazolines preparation **(**Sau DK et al., 2003**;** Chapleo CB et al., 1988). The 1,3,4-thiadiazoles and 1,3,4-thiadiazolines which are cyclic derivatives of the thiosemicarbazones exhibit various biological activities such as antituberculosis antimicrobial (Mamolo et al., 1996) anti-inflammatory (Labanauskas et al., 2001) antiviral, anticonvulsant (Chapleo et al., 1988) antihypertensive (Mazzone et al.,1993) anticancer (Chou et al., 2003) and hypoglycemic activities (Hanna et al., 1993). Therefore, 1,3,4-Thiadiazole and related compounds are of great interest in chemistry owing to their bioactivity of certain plant growth regulating effects as well as antimicrobial activity (Sancak et al., 2007). The thiosemicarbazones and 1,3,4-thiadiazolines thus presented have about the same biological properties however there is little information about the antifungal activity of 1,3,4-thiadiazolines. The aim of this work is to synthesize thiosemicarbazones and their corresponding 1,3,4-thiadiazolines in order to compare their antifungal activities.

Materials and Methods

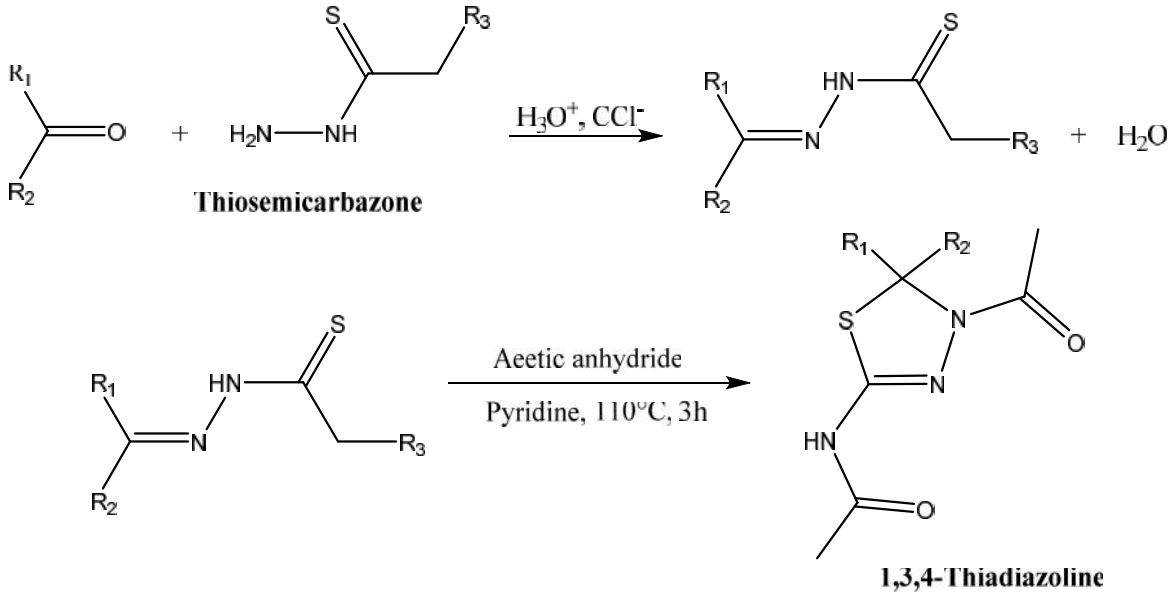
Chemistry

We used thin layer chromatography (TLC) to estimate the purity of the compounds, to follow the evolution of the reaction and then to achieve their purification on silica gel column. The solvent used is the mixture of dichloromethane/ethylacetate (2/1) or dichloromethane /methanol (9/1). The thiosemicarbazones were purified by recrystallization. Compounds purity was confirmed by LC/MS. The melting points were taken on the fusionometer *eletrothermal 1A 9000.* The spectrometric data were recorded with the following instruments: IR, Perkin Elmer FT-IR 286; ^{1}H NMR and ^{13}C NMR, Bruker 400; LC/MS in mode APCI on column C18. The thiosemicarbazones and 1,3,4-thiadiazolines are synthesized as follows:

1) Synthesis of the thiosemicarbazones. A mixture of ketone (20mmol dissolved in 100 mL of ethanol) and thiosemicarbazide (20 mmol dissolved in 20 ml of 1 N hydrochloric acid) is stirred until the thiosemicarbazone precipitates. The precipitate is filtered, dried and then recrystallized in ethanol (96°C) to give thiosemicarbazone crystals (Figure 1).

2) Synthesis of 1,3,4-thiadiazolines. Thiosemicarbazone (0.25 mmol) was dissolved in 0.5 mL of pyridine and 0.5 ml of acetic anhydride and the mixture was heated at 110°C during 3 h with magnetic stirring to give the 1,3,4- thiadiazoline derivative which is filtered and purified by flash chromatography (Figure 1).

Figure 1: Synthesis of 1,3,4-thiadiazolines (1-15)



Microbiologie

Determination of Minimal Inhibitory Concentration (MIC)

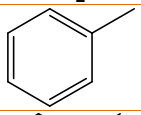
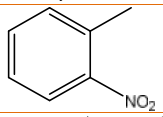
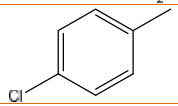
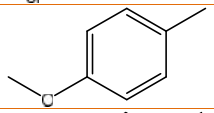
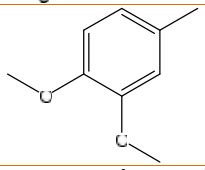
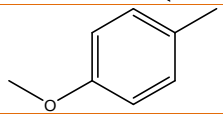
It is *Candida albicans* MHMR strain that was used for this study. MIC was determined by the liquid macro-dilution method described by Delarras (1998) with visual assessment of growth in microorganisms. One milliliter of sterile distilled water was introduced into a series of 11 test tubes numbered from T1 to T11. One milliliter of the stock solution of thiosemicarbazone concentration 20 mg / ml was added to tube T1 from which successive (half) dilutions were made up to tube T10 to have concentrations of thiosemicarbazone of 10 mg / ml; 5 mg / mL; 2.5 mg / mL; 1.25 mg mL; 0.625 mg / mL; 0.312 mg / mL; 0.156 mg / mL; 0.078 mg / mL and 0.039 mg / mL. All tubes (T1-T11) inoculated with 1 mL of inoculum (106 CFU / mL) were incubated at 37 ° C for 24 h and examined for bacterial growth resulting in turbidity. The tube T11 is considered as a control. The MIC of an extract against a given strain is the smallest of the concentrations showing no visible growth of the seed with the naked eye.

Results and Discussion

Chemistry

Six thiosemicarbazones and their corresponding 1,3,4-thiadiazolines were synthesized with yields going from 65to 90% for the thiosemicarbazone and 32 to 94% for 1'3'4-thiadiazolines. The physical and spectrometric data of the 12 compounds are reported in Table 1. Thin layer chromatography (TLC) shows that thiosemicarbazones with Rf ranging from 0.75 to 0.82 in hydrophobic mobile phases are generally more lipophilic than their corresponding 1,3,4-thiadiazolines, which have Rf up 0.33 to 0.60. The spectrometric data of this table are in conformity with the structures suggested for the products.

Table 1 Chemical structure, yield, and melting point of synthesized thiosemicarbazones **(1-6)**

Compounds		R_1	R_2	Yield (%)		*R*f		M. P (°C)	
1	**1C**	H		65	87	0.80	0.40	162-163	221-222
2	**2C**	H		90	94	0.78	0.37	254-255	245-246
3	**3C**	H		78	77	0.82	0.77	212-213	228-230
4	**4C**	$-CH_3$		89	32	0.82	0.60	180-181	188-189
5	**5C**	$-CH_3$		82	49	0.75	0.33	224-225	156-157
6	**6C**	$-CH_2-CH_3$		78	66	0.80	0.60	126-127	209-210

Thus the IR spectra of the thiosemicarbazones and 1,3,4-thiadiazolines show bands in the range of 3437-3145 cm^{-1}due to the stretching vibration of NH in both types of compounds. The thiosemicarbazones C=N stretching band which corresponds between the thiosemicarbazide part and carbonyl part of the molecule, appears at 1596 or 1525 cm^{-1}. In the ^1H NMR spectra the most deshielded proton, which is linked to the central nitrogen atom appears as a broadened singlet between 7.85 and 11.86 ppm for both types of molecules. In the ^{13}C NMR spectra, the thiosemicarbazones C=N bond is indicated by chemical shifts between 140 and 152 ppm while the chemical shift of the, the C=S bond corresponding to the chemical shift between 177 and 179 ppm. Ring closure in 1,3,4-thiadiazolines may be observed by (1) the disappearance of the signal between 177 and 179corresponding to the thiocarbonyl group, (2)

the appearance of a signal between 63 and 85 ppm assigned to C-2 and (3) the signals of the carbonyl and methyl moieties of the acetyl groups incorporated to the molecule. In mass spectrometry, the $[MH]^+$ peaks obtained in APCI mode correspond to molecular weights expected for all products. In LC mode, all 1,3,4-thiadiazoles have a single peak confirming their purity. The synthesized compounds were tested for their antifungal activity on *Candida albicans* MHMR. The test results are reported in table 2.

Microbiology

Considering thiosemicarbzone**1** as a reference compound, the determination of the minimum inhibitory concentration (MIC) of the twelve compounds on *Candida albicans* MHMR shows that benzaldehydethiosemicarbazone (**1**) and its thiadiazoline derivative (**1C**) have the same inhibitory activity on *Candida albicans* is 5 mg/mL. The addition of a nitro group *ortho* to the benzene ring at the level of thiosemicarbazone **2**, is enough to double the inhibitory activity to 2.5 mg/mL. At the corresponding thiadiazoline derivative (**2C**), the observed activity is four times greater, ie 1.25 mg/mL. However, the presence of a chlorine atom in *para* position on the nucleus of compound **3**; results in a loss of the antifungal activity of thiosemicarbazone 3 and its thiadiazoline derivative **3C**. Thiosemicarbazone **4** has antifungal power (0.625 mg/mL) eight times higher due to the presence of a methoxy group in the para position on the ring and a methyl group in **R1**. These same modifications in the corresponding thiadiazoline derivative (**4C**) lead to a loss of inhibitory power. This inhibitory activity however reappears at 5 mg/mL as regards the place of the methyl group, there is an ethyl substituent (**6C**). The presence of an additional methoxy group on the thiosemicarbazone **5** nucleus results in a significant loss of the activity which passes 5 mg/mL. The corresponding thiadiazoline (**5C**) remains inactive.

Table 2: Minimal inhibitory concentration (MIC) of synthesized compounds

Compounds	MIC (mg/mL)	Compounds	MIC (mg/mL)
1	**5.00**	**1C**	**5.00**
2	**2.50**	**2C**	**1.25**
3	**--**	**3C**	**--**
4	**0.625**	**4C**	**--**
5	**5.00**	**5C**	**--**
6	**--**	**6C**	**5.00**

From the foregoing, it appears that the presence of highly electroattractive groups such as the nitro substituent on the benzene ring is good for the antifungal power of the two categories of compounds. However, the presence of the methyl group in the **R1** position is favorable to the antifungal activity of certain thiosemicarbazones. This is not the case for the corresponding 1,3,4-thiadiazolines.

References

Afrasiabi Z, Sinn E, Chen JN, Ma YF, Rheingold AL, Zakharov LN, Rath N, Padhye S. Appended 1,2-naphthoquinones as anticancer agents 1: synthesis, structural, spectral and antitumor activities of ortho-naphthoquinone thiosemicarbazone and its transition metal complexes. InorgChimActa 2004; 357(1):271–278.

Afrasiabi Z, Sinn E, Padhye S, Dutta S, Newton C, Anson CE, Powell AK. Transition metal complexes of phenanthrenequinonethiosemicarbazone as potential anticancer agents: synthesis, structure, spectroscopy, electrochemistry and *in vitro* anticancer activity against human breast cancer cell-line T47D. J Inorg Biochem 2003; 95(4):306–314.

Baehr P. H., MC Donald G.B. Esophageal infections: risk factors, presentation, diagnosis and treatment. Gastroenterology 1994; 106, 509-532.

Bonacini M., Young T., Laine L. The causes of esophageal symptoms in human immunodeficiency virus infection. A prospective study of 110 patients. Arch. Intern. Med 1991; Vol. 151, 1567-1571.

Bretagne S. Les candidoses muqueuses au cours du SIDA. Le concours médical 1996 ; 118-33.

Chapleo CB, Myers PL, Smith ACB, Stillings MR, Tulloch IF, Walter SD. Substituted 1,3,4-thiadiazolines with anticonvulsant activity. 4. Amidines. J Med Chem 1988;31:7.

Chou JY, Lai SY, Pan SL, Chern JW, Guh JH (2003). Investigation ofanticancer mechanism of thiadiazole-based compound in human non-small cell lung cancer A549 cells. Biochem. Pharmacol., 66: 115.

Citak S, Ozcelik B, Cesur S, Abbasoglu U. *In vitro* susceptibility of *Candida* species isolated from blood culture to some antifungal agents. *Japanese Journal of Infectious Diseases* 2005; 58: 44-46.

De AraújoNeto LN,do CarmoAlves de Lima M,de Oliveira JF, de Souza ER, Buonafina MDS, Victor Anjos MN, Brayner FA, Alves LC, Neves RP, Mendonça-JniorFJB.Synthesis, cytotoxicity and antifungal activity of 5-nitro-thiophene-thiosemicarbazones derivatives. ChemBiol Interact.Jun 2017; 25;272:172-181.

Delarrascamille. , Microbiologie. 90 heures de travaux pratiques. Gaétan Morien Editeur. P 169-178.

Easmon J, Purstinger G, Heinisch G, Roth T, Fiebig HH, Holzer W, Ja¨ger W, Jenny M, Hofmann J. Synthesis, cytotoxicity, and antitumor activity of copper (II) and iron (II) complexes of (4) N-azabicyclo [3. 2. 2] nonanethiosemicarbazones derived from acyldiazines. Med Chem 2001; 44:2164.

Garcia CC, Brousse BN, Carlucci MJ, Moglioni AG, Martins AM, Moltrasio GY, D'Accorso NB, Damonte EB. Inhibitory effect of thiosemicarbazone derivatives on Junin virus replication in vitro. AntivirChemChemother 2003; 14:99–105.

Hall IH, Lachey CB, Kistler TD, Durham RW, Jouad EM, Khan M, Thanh XD, Djebbar-Sid S, Benali-Baitich O, Bouet GM. Cytotoxicity of copper and cobalt complexes of furfural semicarbazone and thiosemicarbazone derivatives in murine and human tumor cell lines. Pharmazie 2000; 55(12):937–941.

Hanna MA, Girges MM, Rasala D, Gawinecki R (1993). Synthesis and pharmacological evaluation of some novel 5-(pyrazol-3-yl)thiadiazole et oxadiazole derivatives as potential hypoglycemic agents. Arzneim-Forsch./ Drug Res., 45: 1074.

Kasuga NC, Sekino K, Ishibawa. Synthesis, crystal structures and antibacterial activity of monomeric 7-cordinate bismuth (III) complexes with tridentate and pentadentatethiosemicarbazones ligand. InorgBiochem 2003; 96:298.

Klayman DL, Scovill JP, Bruce J, Bartosevich JF. 2-Acethylpyridine thiosemicarbazones derivatives of acethylisoquinoline as potential antimalarial agents. J Med Chem1984 ; 27:84.

Kovač T, Kovač M, Strelec I, Nevistić A, Molnar M. Antifungal and antiaflatoxigenic activities of coumarinylthiosemicarbazides against Aspergillusflavus NRRL 3251. DOI: 10.1515/aiht-2017-68-2883.

Kovala-Demertzi D, Demertzis MA, Miller JR, Papadopoulou C, Dodorou C, Filousis G Structure of bis(2-acetylpyridine 3-hexamethyleneiminyl thiosemicarbazonato) palladium (II), a potential antitumor complex. J InorgBiochem 2002; 92:137.

Labanauskas L, Kalcas V, Udrenaite E, Gaidelis P, Brukstus A, Dauksas V (2001). Synthesis of 3-(3,4-dimethoxyphenyl)-1 H-1,2,4- triazole-5-thiol et 2-amino-5-(3,4-dimethoxyphenyl)-1,3,4-thiadiazole derivatives exhibiting anti-inflammatory activity. Pharmazie., 56: 617.

Laine L. The natural history of esophageal candidiasis after successful treatment in patients with AIDS.Gastroenterology1994 ; 107, 744-746.

Mamolo MG, Vio L, Banfi E (1996). Synthesis etantimycobacterial activity of some indole derivatives of pyridine-2-carboxamidrazone et quinoline-2-carboxamidrazone. Farmaco, 51:71

Mazzone G, Pignatello R, Mazzone S, Panico A, Pennisi G, Castana R, Mazzone P (1993). Synthesis et local anesthetic activity of alkylaminoacyl derivatives of 2-amino-1,3,4-thiadiazole. Farmaco, 48: 1207.

Perez JM, Matesanz AI, Martin A, Navaro P, Alonso C, Sousa P. Synthesis and characterization of complexes of p-isopropylbenzaldehyde and methyl 2-pyridyl ketone thiosemicarbazones with Zn(II) and Cd(II) metallic centers. Cytotoxic activity and induction of apoptosis in Pam-ras cells. J InorgBiochem 1999;75:255–261.

Quiroga AG, Pe´rez JM, Lo´pez-Solera I, Montero EI, Masaguer JR, Luque A, Roma´n P, Edwards A, Alonso C, Navarro-Ranninger C. Novel tetranuclearorthometalated complexes of Pd (II) and Pt(II) derived from p-isopropylbenzaldehyde thiosemicarbazone with cytotoxic activity in cis-DDP resistant tumor celllines. Interaction of these complexes with DNA. J Med Chem1998 ;41(9):1399–1408.

Rebolledo AP, de Lima GM, Gambi LN, Speziali NL, Maia DF,Pinheiro CB, Ardisson JD, Cortes ME, Beraldo HI (2003) Tin (IV) complexes of 2-benzoylpyridine N (4)-phenylthiosemicarbazone: spectral characterization, structural studies and antifungal activity. Appl Organomet Chem 2003;17:945.

Sancak K, ¨Unver Y, Er M (2007). Synthesis of 2-a, 2-aroylamino et ethoxycarbonyl imino-1,3,4-thiadiazolines as antitumor agents. Turk. J. Chem., 31: 125

Sau DK, Butcher RJ, Chandhuri S, Saha N (2003) Spectroscopic, structural and antibacterial properties of copper (II) complexes with bio-relevant 5-methyl-3-formylpyrazole N(4)-benzyl-N(4) methylthiosemicarbazone. Mol Cell Biochem 2003; 253(1–2):21–22.

Appendix: Spectral data of thioseicarbazones

Benzaldehyde-thiosemicarbazone(1)

IR m (KBr cm^{-1}): 3401, 3145 (NH), 1600, 1584 (C=N).
^{1}H NMR d (DMSO-$d_6$ppm): 7.39–7.79 (5H, several signals, ArH), 8.00 (1H, s, NH_2), 8.06 (1H, s, CH=N); 8.21 (1H, s, NH_2), 11.44 (1H, s, NH).
^{13}C NMR d (DMSO-$d_6$ppm): 127.26–134.15 (Aromatic C), 142.24 (C=N), 177.97 (C=S).

2'-Nitrobenzaldehyde-thiosemicarbazone (2)

IR m (KBr cm^{-1}): 3424, 3245, 3159 m (NH), 1539 (C=N, C=C).
^{1}H NMR d (DMSO-d_6 ppm): 7.63–8.02 and 8.41 (4H, several signals, ArH), 8.11 (1H, s, NH_2), 8.39 (1H, s, NH_2), 8.47 (1H, s, CH=N), 11.74 (1H, s, NH). ^{13}C NMR d (DMSO-d_6 ppm): 124.44–137.19 (Aromatic C), 148.22 (C=N), 178.45 (C=S).

4'-Chlorobenzaldehyde-thiosemicarbazone (3)

IR m (KBr cm^{-1}): 3437, 3281, 3165 m (NH), 1600, 1525 (C=N).
^{1}H NMR d (DMSO-$d_6$ppm): 7.43–7.84 (4H, several signals, ArH), 8.03 (1H, s, CH=N), 8.07 (1H, s, NH_2); 8.24 (1H, s, NH), 11.49 (1H, s, NH).
^{13}C NMR d (DMSO-$d_6$ppm): 128.65–134.22 (Aromatic C), 140.85 (C=N), 178.06 (C=S).

4-Methoxyacetophenone-thiosemicarbazone (4)

IR m (KBr cm^{-1}): 3400, 3247, 3162 (NH), 1588 (C=N).
^{1}H NMR d (DMSO-d_6 ppm): 2.26 (3H, s, CH_3), 3.78 (3H, s, O–CH_3), 7.39–7.52 (several signals, 4H of ArH and 1H of NH_2) 8.19 (1H, s, NH_2) 10.10 (1H, s, NH).
^{13}C NMR d (DMSO-d_6 ppm): 13.24 (CH_3) 54.59 (O–CH_3) from 112.94 to 129.45 and 159.61 (Aromatic C), 147.21 (C=N), 178.02 (C=S).

3',4'-Dimethoxyacetophenone-thiosemicarbazone (5)

IR m (KBr cm^{-1}): 3376, 3267, 3155 (NH), 1588 (C=N).
^{1}H NMR d (DMSO-d_6 ppm): 2.27 (3H, s, CH_3), 3.78 (3H, s, O–CH_3), 3.82 (3H, s, O–CH_3), 6.92–7.51 (3H, several signals, ArH), 7.88 (1H, s, NH_2), 8.22 (1H, s, NH_2), 10.06 (1H, s, NH).
13C NMR d (DMSO-d_6 ppm): 12.95 (CH_3) 54.45 (O–CH_3) 54.65 (O–CH_3) from 108.60 to 129.19 and 149.12, 147.49 (Aromatic C), 147.19 (C=N), 177.52 (C=S).

4'-Methoxypropiophenone-thiosemicarbazone (6)

IR m (KBr cm^{-1}): 3433, 3278 (NH), 1596 (C=N).
^{1}H NMR d (DMSO-d_6 ppm): 1.01 (3H, t, CH_3), 2.83 (2H, q, CH_2), 3.78 (3H, s, O–CH_3), 6.92–7.87 (4H, several signals, ArH), 7.85 (1H, s, NH_2), 8.18 (1H, s, NH_2), 10.19 (1H, s, NH).
^{13}C NMR d (DMSO-d_6 ppm): 11.01 (CH_3) 19.11 (CH_2) 55.17 (O–CH_3) from 112.96 to 128.06 and 160.17 (Aromatic C) 151, 78 (C=N), 178.70 (C=S).

N-(4-acetyl-5-phenyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamide (1C) :

LC/MS : $[MH]^+$calculated : 264,0801 ; $[MH]^+$found : 264,0796.
IR m (KBr cm^{-1}): 3216, 3165 (NH) ; 1713, 1702, 1634 (C=O amides).
^{1}H NMR d (DMSO-d_6 ppm): 2,04 (3H, s, CH_3 amide) ; 2,21 (3H, s, CH_3amide); 6,84 (1H, s, CH); 7,24-7,37 (5H, several signals, ArH); 11,76 (1H,s, NH).
^{13}C NMR d (DMSO-d_6): 21,85 and 22,52 (2. CH_3 amides); 65,79 (C2 of thering) ; 125,04-141,37 (Aromatic C); 145,97 (C=N); 167,27 and 167,39(C=O amides).

N-(4-acetyl-5-(2-nitrophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamide (2C) :

LC/MS :$[MH]^+$calculated : 309,0652 ; $[MH]^+$found : 309,064
IR m (KBr cm^{-1}): 3232, 3192 (NH) ; 1682, 1664 and 1622 (C=O amides).
^{1}H NMR d (DMSO-d_6 ppm): 2,04 (3H, s, CH_3 amide) ; 2,26 (3H, s, CH_3amide); 7,06 (1H, s, CH_2); 7,33-8,18 (4H, several signals, ArH); 11,86 (1H,s, NH).
^{13}C NMR d (DMSO-d_6): 21,70 and 22,41 (2. CH_3 amides); 63,15 (C2 of the ring) ; 125,52-145,01 (Aromatic C); 146,31 (C=N); 167,77 et 169,66(C=O amides).

N-(4-acetyl-5-(4-chlorophenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamide (3C) :

LC/MS : $[MH]^+$calculated : 298,0412 ; $[MH]^+$found : 294,0407.
IR m (KBr cm^{-1}): 3216, 3163 (NH) ; 1698, 1637, 1612 (C=O amides).
^{1}H NMR d (DMSO-d_6 ppm): 2,04 (3H, s, CH_3 amide) ; 2,20 (3H, s, CH_3amide); 6,83 (1H, s, CH_2); 7,28-7,42 (4H, several signals, ArH); 11,78 (1H,s, NH).
^{13}C NMR d (DMSO-d_6) : 21,83 and 22,51 (2. CH_3 amides); 65,15 (C2 of the ring) ; 127,13-140,28 (Aromatic C); 145,88 (C=N); 167,44 and 169,44(C=O amides).

N-(4-acetyl-5-(4-methoxyphenyl)-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamide(4C):

LC /MS :$[MH]^+$calculated : 308,1063 $[MH]^+$ found : 308,1059.
IR m (KBr cm^{-1}): 3171 (NH) ; 1691, 1643 and 1614 (C=O amides).

^{1}H NMR d ($CDCl_3$ ppm): 1,88 (3H, s, CH_3) ; 2,19 (3H, s, CH_3 amide) ; 2,27(3H, s, CH_3 amide); 3,34 (3H, s, O-CH_3); 6,75-7,27 (4H, several signals,ArH); 9,13 (1H, s, NH).
^{13}C NMR d ($CDCl_3$ ppm): 22,87 (CH_3) ; 23,89 and 26,86 (2. CH_3 amides);55,29 (O-CH_3) 80,03 (C2 of the ring) ; 124,99-142,82 (Aromatic C); 143,48(C=N); 168,84 and 169,27 (C=O amides).

N-(4-acetyl-5-(3,4-dimethoxyphenyl)-5-methyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamide (5C) :

LC /MS :$[MH]^+$calculated : 338,1169 $[MH]^+$found : 338,1165.
IR m (KBr cm^{-1}): 3214, 3169 (NH) ; 1698, 1646 and 1601 (C=O amides).
^{1}H NMR d ($CDCl_3$ ppm): 1,80 (3H, s, CH_3) ; 2,23 (3H, s, CH_3 amide) ; 2,25(3H, s, CH_3 amide); 3,78 (3H, s, O-CH_3); 3,79 (3H, s, O-CH_3); 6,68-6,91 (3H,several signals, ArH); 9,94 (1H, s, NH).
^{13}C NMR d ($CDCl_3$ ppm): 22,64 (CH_3) ; 23,86 et 26,68 (2. CH_3 amides);55,91 (O-CH_3) ; 56,91 (O-CH_3) 79,72 (C2 of the ring) ; 109,14-135,17 and148,83 ; 148,90 (Aromatic C); 144,22 (C=N); 169,33 and 169,34 (C=Oamides).

N-(4-acetyl-5-ethyl-5-(4-methoxyphenyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl)acetamide(6C) :

LC /MS : $[MH]^+$calculated : 322,1225 ; $[MH]^+$found : 322,1217.
IR m (KBr cm^{-1}): 3227, 3177 (NH) ; 1697, 1643 and 1610 (C=O amides).
^{1}H NMR d ($CDCl_3$ ppm): 1,06 (3H, t, CH_3); 2,18 (2H, q, CH_2) ; 2,23 (3H, s,CH_3 amide); 2,26 (3H, s, CH_3 amide); 3,67 (3H, s, O-CH_3); 7,73-7,25 (4H,several signals, ArH); 9,84 (1H, s, NH).
^{13}C NMR d ($CDCl_3$): 9,91 (CH_3-CH_2-) ; 22,61 and 23,80 (2. CH_3 amides);29,95 (CH_3-CH_2-) ; 55,29 (O-CH_3) ; 84,85 ($C_2$of the ring) ; 113,82-135,89and 159,07 (Aromatic C); 144,17 (C=N); 169,28 and 169,43 (C=O amides).

Access this Article in Online	
Quick Response Code	Website: www.ijcrcps.com
	Subject: Chemistry
DOI: 10.22192/ijcrcps.2018.05.03.002	

How to cite this article:
Houssou Raymond FATONDJI, Salomé KPOVIESSI, Bardieu ATCHADE, Fernand GBAGUIDI ,Kamirou CHABI SIKA, Joachim GBENOU, Georges Coffi ACCROMBESSI, Mansourou MOUDACHIROU and Jacques POUPAERT. (2018). Synthesis, characterization and antifungal activity of some aromatic thiosemicarbazones and their 1,3,4- thiadiazolines derivatives. Int. J. Curr. Res. Chem. Pharm. Sci. 5(3): 5-11.
DOI: http://dx.doi.org/10.22192/ijcrcps.2018.05.03.002