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Selective Access to New Semicarbazones and Thiosemicarbazones Derived from Benzil. Study of their Conversion Reactions

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Abstract:

New Schiff bases from benzil with semicarbazide and thiosemicarbazide are reported. An open chain molecule, benzilbissemicarbazone **1** was prepared in presence of lithium hydroxide. A cycle 6-methoxy-1,6-diphenyl-4-thio-3,4,5,6-tetrahydro-2,3,5-triazine **7** was obtained from thiosemicarbazide. A cyclic molecule, 1,6-diphenyl-4-oxo-3,4,5,6-tetrahydro-2,3,5-triazine **4** was produced from the recrystallization of **3** in chloroform. A new macrocyclic complex **8** was isolated from the open chain **6** in the presence of iron (III) chloride hexahydrated. Compounds **1**, **2** convert into the cyclic **3** heated under reflux. In addition, we have got an iron complex **5** of **1** using the compound **2** as precursor. The crystal structure of **7** was obtained by single crystal X-Ray diffraction.

Keyword: Macromolecules; hydrazones; template; X-ray structure.

INTRODUCTION

Schiff base macroligands derived from thiosemicarbazide are of significative interest not only for their pharmacological properties as antibacterial and anticancer agents [1-8], but also for their capacity for chemical recognition of anions and metals of biochemical, medical and environmental importance [9-18]. Furthermore, they can act either as bidentate or polydentate ligands yielding mono or polynuclear complexes, some of which are biologically relevant [19-24].The range of their application depends on the structure of the precursor diamine and dicarbonyl. The number and relative position of the donor atom and the cavity size in the macrocyclic compound give to these new molecules special reactivity. For a particular dicarbonyl compound, the control of the reaction conditions and

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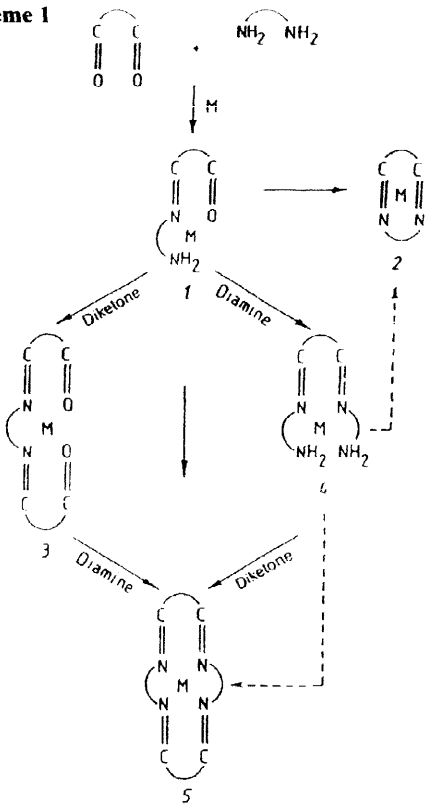
nature of reactants, permits to design the condensation product formed: cyclic or open chain compounds, [1+1], [1+2] or [2+2] condensation products [25]. The most important factors involved in these reactions are: nature and relative proportion of reactants; chain length and presence of heteroatoms in the precursor molecules; type of condensation to join the ends of both chains; experimental conditions such as solvent, pH and temperature.

Synthesis of organic molecules mediated by transition metal salts has attracted great attention in recent years. Known examples in this area employ metals complexes as catalyst [26-30]. Sometimes macrocyclic Schiff bases were prepared by metals salts as template [25,31,32]. A variety of metal ions were found effective as templating ions [33,34] for example, Ba(II), Ca(II), La(III), Pb(II), Sr(II). Surprising absent from this list are copper(II) and nickel(II), both of which have been utilized in the preparation of N4 aza crowns [33] and iron (III). If a metal salt is present as a template in the reaction, the size, charge and favourable geometries of the metal have to be considered.

Scheme 1



As it is shown in Scheme 1, in all cases the initial step lead to the open chain[1+1], product 1. If the chain length of the diamine is sufficient or the template metal ion is bonded to the residual carbonyl group, the intermolecular condensation leading to the cycle [1+1], product 2, is favourable. But, if the diamine has insufficient chain length or it is too rigid to fit by folding, [2+2] macrocycle 5, is obtained. The intermediate 1 can react with diamine or dicarbonyl compounds, giving open chain products 3 and 4, both can react again with the precursor molecules yielding the macrocycle 5. When the reaction is carried out in the presence of a template metal cation, if the template cation is large in relation to the cavity size of the [1+1] ring, then again the [2+2] compound is formed [25].

As part of a program on synthesis of Schiff base macroligands derived from benzil and carbohydrazides and thiocarbazides, cyclic molecules from hydrazides and open chain one from thiosemicarbazide were prepared [35], besides their coordination compounds with divalent metal salts were synthesized [36,37]. Since, we are currently interested in developing efficient and metal selective organic compounds, to incorporate them as modifiers in standard carbon paste electrode, for electrochemical measurements of toxic metal in aqueous or non aqueous media [38,39]. We decided to explore the optimum conditions to get specific (variable number of donor atoms and structures) macroligands from semicarbazide and thiosemicarbazide

In this paper, we report new semicarbazone and thiosemicarbazone macroligands: An [1+2] open chain and a triazine from semicarbazide and two cyclic

molecules [1+1] and [2+2], from thiosemicarbazide, which were obtained from benzil controlling the reaction conditions (pH, relative proportion of reactants, temperature and presence of iron(III)chloride hexahydrate). In addition we describe their intercorversion reactions

RESULTS AND DISCUSSION

The reactions of benzil with semicarbazide and thiosemicarbazide yield two new molecules **1** and **7** respectively. The analytical data agree with a condensation [1+2] for **1** and [1+1] or [2+2] with methanol for the thiosemicarbazone **7**.

The mass spectrum of **1** confirms the proposed formula, showing a peak at 325 amu corresponding to the molecular ion. The pattern of this spectrum is the same of benzilbisthiosemicarbazone, **6** previously obtained [35] and it shows a series of peaks corresponding to the sucessive fragments as it is reflected in the Table 1. These data suggest a open chain disposition for the new compound. Moreover, as all the open chain molecules,**1**, **2** and **6** spectra, this one shows a peak corresponding to the interaction between two molecules, it is probably due to hydrogen bonding through the terminal amine group. The FAB mas spectrum of **7** confirms the condensation, showing the molecular ion peak at 298 amu, and a peak corresponding to the loss of the methanol molecule (Table 1). It exhibits a pattern of breakdown similar to the cycle semicarbazone**3**, but the intensity of the peak corresponding to $M\text{-}OCH_3^+$ is smaller than that of the oxygen derivative, which suggests a minor stability for the new cyclothiosemicarbazone **7**.

Table 1

Mass spectra of organic molecules in THF solutions[a]

	M^++1	$M\text{-}OCH_3^+$	$M\text{-}N_3H_5CX^+$+1 X=O,S	$M\text{-}N_5H_6C_2X_2^+$ X=O,S	$2M^+$+1
1	325(80)		250(30)	192(20)	649(5)
2	268(95)				535(20)
3	282(45)	250(100)			499(15)
4	250(80)				499(15)
6	357(45)		266(20)	192(10)	713(20)
7	298(35)	266(10)			595(1)

[a] Published data have been included for comparison

^1H NMR spectrum of **1** in DMSO (Table 2) exhibits two signals at 6.59 and 9.09 ppm, corresponding to four and two protons, which support the presence of two terminal and two secondary amine group magnetically equivalent. The spectrum of **7** confirms the absence of terminal amine group and the presence of the methanol inserted, as well as two signal assigned to the NH groups. The ^{13}C NMR spectrum of **1** (Fig.1) shows signals corresponding to one imine carbon, one carbonyl group and four phenyl carbons . The signals

observed in the spectrum of 7 (Figure 2) supports the presence of a new imine group and the inserted methanol molecule. The NMR data (Tables 2 and 3) confirm a [1+2] condensation in a symmetric open chain disposition for compound **1** and a cyclic molecule [1+1] with a methanol inserted in an imine group for the compound **7**.

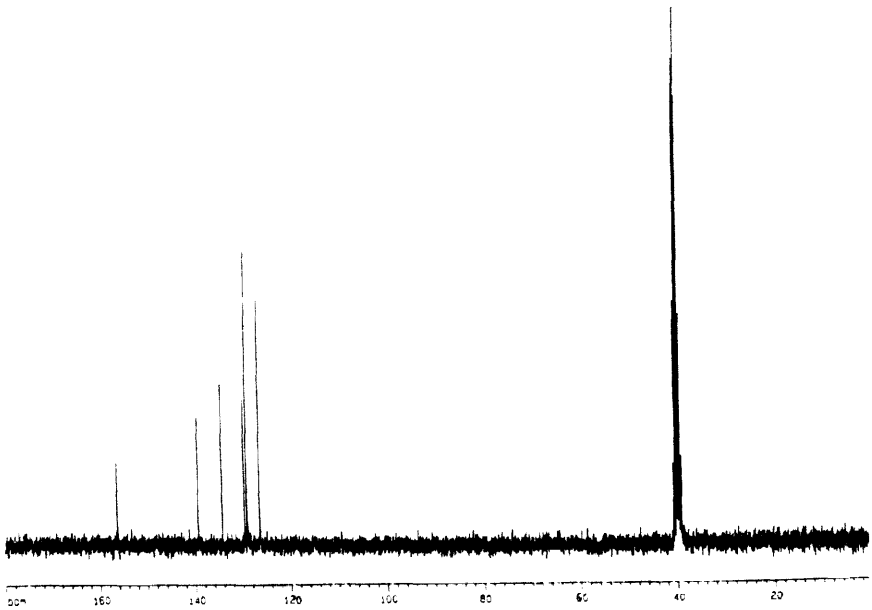


Figure 1 ^{13}C NMR spectrum of $C_{16}H_{16}N_6O_2$ (1)

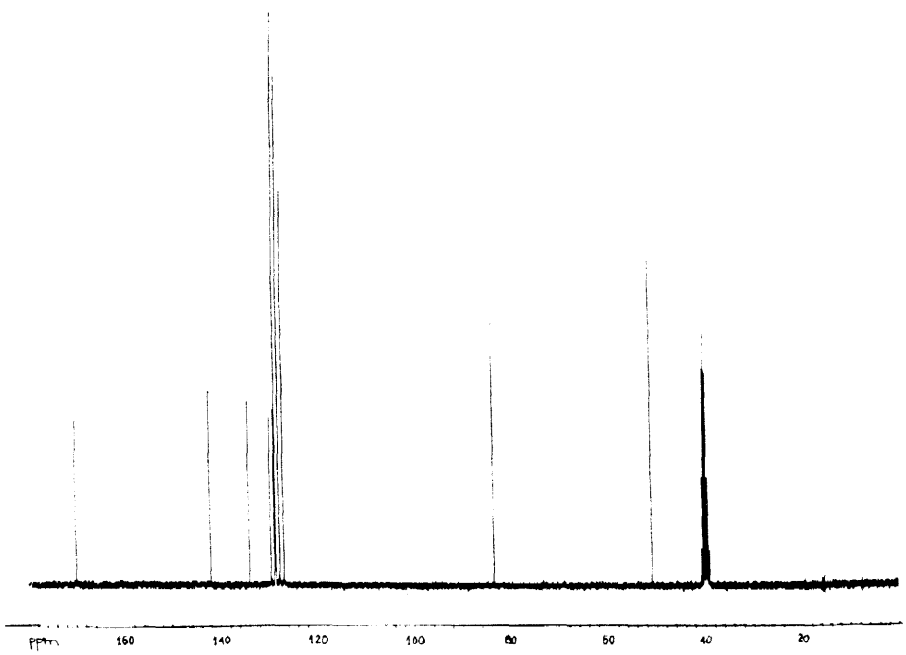


Figure 2 ^{13}C NMR spectrum of $C_{16}H_{15}N_3OS$ (7)

Table 2

^{1}H NMR spectral data (δ, ppm) of compounds in DMSO solutions[a].

	NH/NH_2	NH	H_{Ph}	$H_{Ph\ orto}$	CH_3
1	6.59(4H,s)	9.09(2H,s)	7.25-7.51(6H,m)	7.65,4H,m)	
2	6.63(2H,s)	9.91(1H,s)	7.33-7.63(7H,m)	7.71-7.80(3H,m)	
3	8.34(1H,s)	10.88(1H,s)	7.12-7.29(6H,m)	7.33-7.51(4H,m)	3.21(3H,s)
4		11.1(1H,s)	7.10-7.30(6H,m)	7.30-7.50(4H,m)	
6	8.35(2H,s)	9.89(2H,s)	7.35(6H,m)	7.70(4H,m)	
	8.64(2H,s)				
7	10.01(H,d)	12.14(1H,d)	7.20-7.37(8H,m)	7.53(2H,m)	3.15(3H,s)

[a] Published data have been included for comparison

Table 3

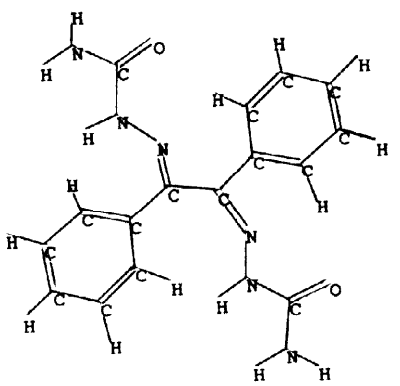
^{13}C NMR spectral data for compounds in DMSO solutions

	C=X	C=N	C_{Ph}	$C_{Ph\ orto}$	$C{=}O_{benzil}$	C-N	CH_3
	X=O,S						
1	156.3	138.9	126.2-129.4	133.9			
2	156.3	143.4	128.1-131.2	134.1	195.2		
3	149.1	142.4	126.3-129.3	134.3-139.6		86.7	49.7
4	167	142	129.1-131.3	134			
6	179.1	140.5	126.7-130.1	133.1			
7	169.7	142.4	126.5-129-3	133.7-141.7		83.2	50.7

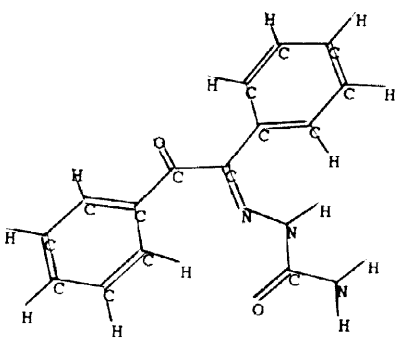
[a] Published data have been included for comparison

The bands observed in the IR spectrum are consistent with the functional groups present in the molecules[35,40]. From the molecular modelling for **1, 2 and 6**, we have obtained the lowest energy minimised structures (Figure 3), which suggest that the semicarbazone moieties are located on opposite sides of the carbon backbone which minimizes their intermolecular interactions.

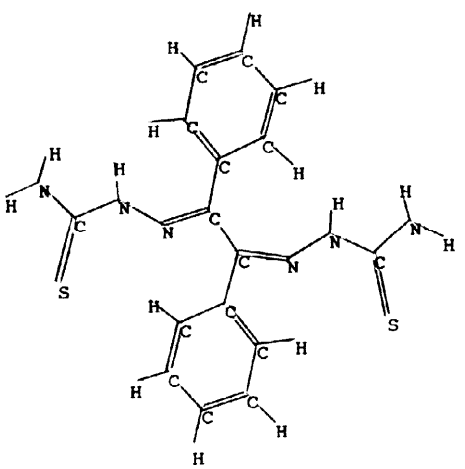
Figure 3 Minimum energy structure from Hyperchem for



$C_{16}H_{16}N_6O_2$ (**1**)



$C_{15}H_{13}N_3O_2$ (**2**)



$C_{16}H_{16}N_6S_2$ (**6**)

Pale yellow crystals of 7 were grown by slow evaporation of a methanolic solution. The Figure 6 shows a ORTEP [41] view of the molecule, Which confirms the structure proposed from the analytical and spectroscopic data. The new 6-membered ring formed differs of the cyclosemicarbazone **3** because it deviates significantly from the planarity. The angles with the phenyl planes are 36.94° and 95.07°. The two phenyl rings are plane and the angle between them is 79.55°. Table 4 contains the atomic coordinates, Table 5 summarizes the most important bond lengths and angles and Table 6 includes the crystal data. These data are less regular than in the oxygen derivative [35] probably due to the larger volume of the sulphur atom.

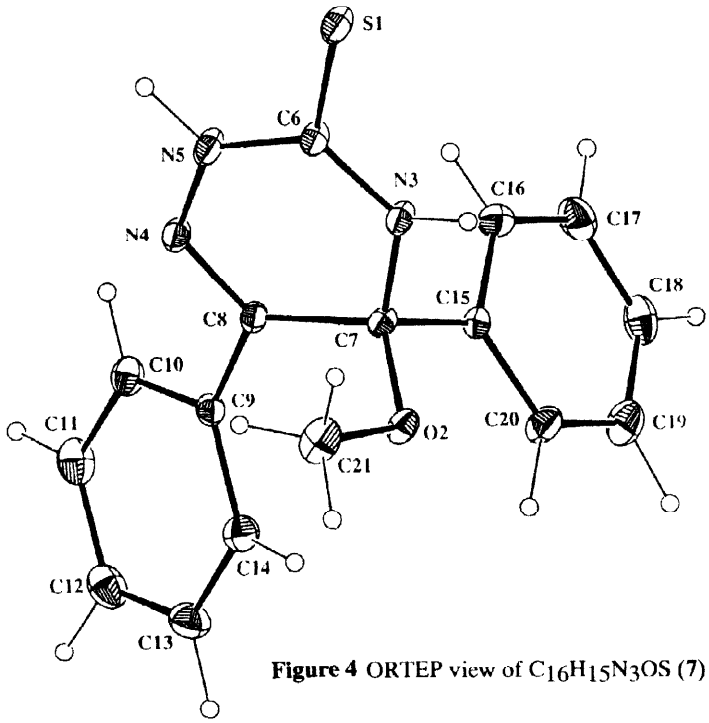


Figure 4 ORTEP view of $C_{16}H_{15}N_3OS$ (7)

Table 4 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
S(1)	-157(1)	3795(1)	7827(1)	45(1)
O(2)	954(2)	1404(2)	5652(1)	37(1)
N(3)	1226(2)	2514(2)	6846(1)	36(1)
N(4)	1489(2)	5293(2)	6144(1)	38(1)
N(5)	898(2)	5142(2)	6765(1)	42(1)
C(6)	687(2)	3796(2)	7103(1)	33(1)
C(7)	1809(2)	2395(2)	6167(1)	30(1)
C(8)	1908(2)	4049(2)	5852(1)	31(1)
C(9)	2495(2)	4330(3)	5170(1)	33(1)
C(10)	3210(2)	5729(3)	5113(1)	41(1)
C(11)	3678(3)	6105(3)	4468(2)	51(1)
C(12)	3446(3)	5078(3)	3866(1)	54(1)
C(13)	2760(3)	3699(3)	3918(1)	51(1)
C(14)	2283(3)	3309(3)	4563(1)	43(1)
C(15)	3241(2)	1633(2)	6349(1)	31(1)
C(16)	4202(3)	2176(3)	6952(1)	44(1)
C(17)	5537(3)	1561(4)	7115(1)	55(1)
C(18)	5922(3)	398(3)	6678(2)	55(1)
C(19)	4979(3)	-165(3)	6083(2)	56(1)
C(20)	3643(2)	442(3)	5917(1)	46(1)
C(21)	-450(2)	1949(3)	5415(2)	54(1)

Table 5 Bond lengths [A] and angles [deg] for (7)

S(1)-C(6)	1.682(2)
O(2)-C(7)	1.410(2)
O(2)-C(21)	1.434(3)
N(3)-C(6)	1.332(3)
N(3)-C(7)	1.459(2)
N(4)-C(8)	1.284(3)
N(4)-N(5)	1.370(2)
N(5)-C(6)	1.333(3)
C(7)-C(15)	1.520(3)
C(7)-C(8)	1.528(3)
C(8)-C(9)	1.482(3)
C(9)-C(14)	1.389(3)
C(9)-C(10)	1.392(3)
C(10)-C(11)	1.377(3)
C(11)-C(12)	1.386(4)
C(12)-C(13)	1.362(4)
C(13)-C(14)	1.383(3)
C(15)-C(16)	1.381(3)
C(15)-C(20)	1.384(3)
C(16)-C(17)	1.383(3)
C(17)-C(18)	1.365(4)
C(18)-C(19)	1.369(4)
C(19)-C(20)	1.382(3)
C(7)-O(2)-C(21)	114.7(2)
C(6)-N(3)-C(7)	126.7(2)
C(8)-N(4)-N(5)	118.8(2)
C(6)-N(5)-N(4)	126.0(2)
N(3)-C(6)-N(5)	115.7(2)
N(3)-C(6)-S(1)	124.0(2)
N(5)-C(6)-S(1)	120.3(2)
O(2)-C(7)-N(3)	109.1(2)
O(2)-C(7)-C(15)	107.1(2)
N(3)-C(7)-C(15)	109.6(2)
O(2)-C(7)-C(8)	111.8(2)
N(3)-C(7)-C(8)	108.5(2)
C(15)-C(7)-C(8)	110.7(2)
N(4)-C(8)-C(9)	114.7(2)
N(4)-C(8)-C(7)	123.6(2)
C(9)-C(8)-C(7)	121.7(2)
C(14)-C(9)-C(10)	118.4(2)
C(14)-C(9)-C(8)	122.8(2)
C(10)-C(9)-C(8)	118.6(2)
C(11)-C(10)-C(9)	120.9(2)
C(10)-C(11)-C(12)	119.9(2)
C(13)-C(12)-C(11)	119.7(2)
C(12)-C(13)-C(14)	121.0(2)
C(13)-C(14)-C(9)	120.1(2)
C(16)-C(15)-C(20)	118.2(2)
C(16)-C(15)-C(7)	119.3(2)
C(20)-C(15)-C(7)	122.4(2)
C(15)-C(16)-C(17)	121.0(2)
C(18)-C(17)-C(16)	120.0(2)
C(17)-C(18)-C(19)	119.8(2)
C(18)-C(19)-C(20)	120.5(2)
C(19)-C(20)-C(15)	120.4(2)

Table 6 Crystal data and structure refinement for $C_{16}H_{15}N_3OS$ (7)

Identification code	m22
Empirical formula	C16 H15 N3 O S
Formula weight	297.37
Temperature	293(2) K
Wavelength	1.54180 A
Crystal system	Monoclinic
Space group	P21/c
Unit cell dimensions	a = 9.7660(10) A alpha = 90 deg. b = 8.4990(8) A beta = 100.940(10) deg. c = 18.202(2) A gamma = 90 deg.
Volume	1483.3(3) A^3
Z	4
Density (calculated)	1.332 Mg/m^3
Absorption coefficient	1.953 mm^-1
F(000)	624
Crystal size	0.10 x 0.10 x 0.22 mm
Theta range for data collection	4.61 to 65.98 deg.
Index ranges	0<=h<=11, -10<=k<=10, -21<=l<=21
Reflections collected	4815
Independent reflections	2521 [R(int) = 0.0478]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2521 / 0 / 199
Goodness-of-fit on F^2	1.096
Final R indices [I>2sigma(I)]	R1 = 0.0397, wR2 = 0.1053
R indices (all data)	R1 = 0.0510, wR2 = 0.1256
Extinction coefficient	0.029(2)
Largest diff. peak and hole	0.259 and -0.246 e.A^-3

We tried to find alternative ways to get **1** from the [1+1] open chain molecule **2**. We carried out the reaction with a additional semicarbazide molecule in different experimental conditions (room temperature, under reflux, basic or acid) but, in all cases the analysis, NMR, mass and IR spectra confirm that the cycle **3** was obtained.

The semicarbazide and thiosemicarbazide reactions with benzil are a good example of the great importance of the experimental conditions in these condensation reactions [35] The pH of the solution is the most of important factor to get the [1+2] product instead the [1+1], but the temperature is the principal parameter to obtain an open chain or a cyclic [1+1] product in the oxygen derivatives. However, in the thiosemicarbazide reactions the most important factor is the molar ratio of the precursor molecules.

On the other hand, all of our attemps to prepare the macrocycle[2+2] from benzil with semicarbazide and thiosemicarbazide in absence of metal template have been unsuccessful. As it is indicated in the experimental section, semicarbazone open chain, **1** and **2** convert to the cycle one, **3**, when they are boiled in methanol. The same compound is obtained from the reactions of the open chain molecules **1** and **2** with benzil, as an attemp to get the semicarbazone macrocycle, in the working conditions described in the experimental section.

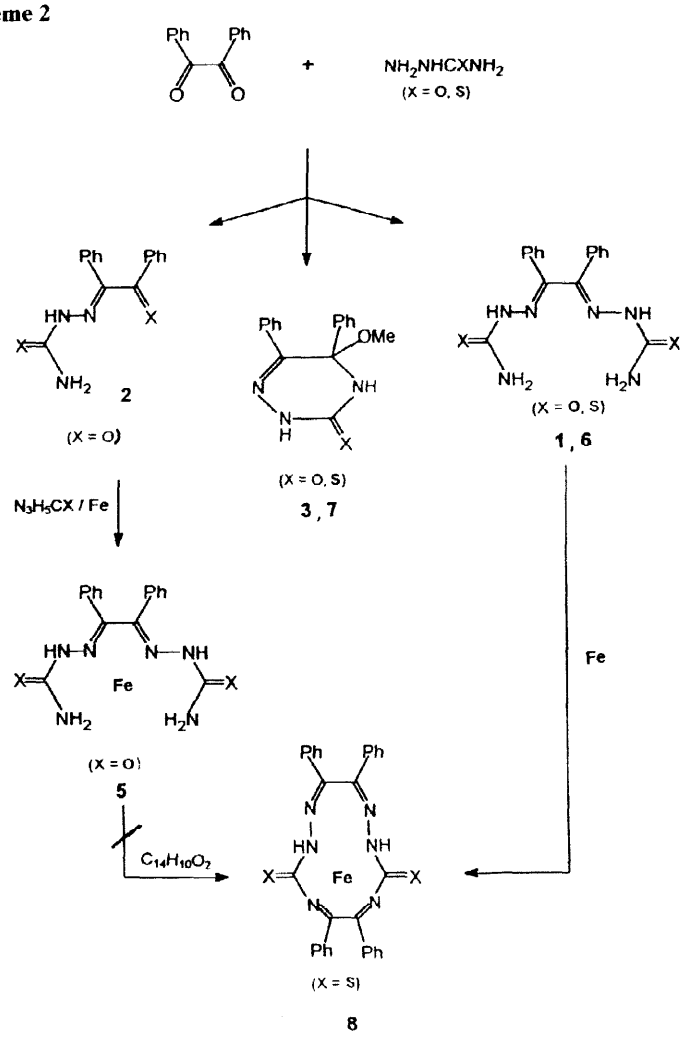
The methanol inserted in **3** can be removed if the compound is recrystallized in chloroform giving a new molecule **4**, whose analytical and spectroscopic data support a cyclic triazine (Table 1, 2 and 3). However, the thiosemicarbazone compounds[1+2] and [1+1] **6** and **7** respectively have to be synthetized independently.

The reaction of **2** with iron (III) chloride hexahydrated yielded in a first step the cyclosemicarbazone **3**, but finally a complex **5** was obtained. The same products were isolated if the reaction were carried out in presence of semicarbazide. The analytical data of **5** correspond to a C:N:H relation of 16:16:6 which indicate a [1+2] condensation with iron, two chlorine and water molecules. The mass spectrum confirms the presence the metal ion, a additional semicarbazone moiety and coordinated water molecules, therefore a organic reaction has been realized with iron (III) as template. The IR spectrum shows the absence of residual carbonyl group presented in the compound **2** supporting the additional imine group [

35]. The band assigned to C=O from the semicarbazone moieties in **1** and **2** has been shifted to lower frequencies, which indicates their coordination to the iron atom. The electronic spectrum, in solid state, agrees with a distorted octahedral geometry for the metal[42]. The conductivity measurements indicate that **5** is a molecular complex. Taking into account all these data, the hexacoordinated iron must be bonded to two carbonyl groups, two chlorine atoms and two water molecules.

The reaction of **6** with iron choride in presence of lithium hydroxide and under reflux yields a solid which analytical data correspond to an iron complex **8** with a CHN ratio different to the free ligand and close to the cyclothiosemicarbazone **7**. The mass spectrum shows a peak at 529 amu (Table 1) corresponding to the $C_{30}H_{20}N_6S_2+1^+$, which supports that a new macrocyclic [2+2] complex was formed in this reaction. The IR spectrum does not show stretching and deformation modes of teminal amine group and it exhibits bands assigned to imine group slighly shiftted to higher frequencies, confirming the iron imine nitrogen bond. ^{1}HNMR confirms the presence of a paramagnetic species, besides the reflectance spectrum shows a band at 520 nm corresponding to a d-d transition.

Scheme 2



This reaction involves a self-condensation of two molecules of the diamine-diimine species **6** (4 to 5 in the Scheme 1) leading through to an overall amine exchange (transamination) [43]. The open chain ring closure [44,45] is only observed from benzilbisthiosemicarbazone **6** in presence of iron (III) chloride. A mechanism involving a sequence of inter and intra-molecular nucleophilic additions followed by deamination of NH_2 to cooordinated C=N group is proposed. All new molecules prepared in this work and the conversion of previously sinthesized ligand into the new ones are indicated in the Scheme 2.

EXPERIMENTAL

Melting points were measured in sealed tubes and were uncorrected. Microanalyses were carried out using a Perkin-Elmer 2400 CHN Elemental Analyser. IR spectra in the 4000-400 cm^{-1} range were recorded as KBr pellets on a Bomen spectrophotometer MB-100. ^{1}H and ^{13}C NMR were registred on a Bruker AMX-300 spectrometer. Chemical shifts are given in ppm relative to tetramethylsilane. Fast atom bombardment mass spectra were recorded on a VG Auto Spec instrument using Cs as the fast atom and *m*-mitrobenzylalcohol (*m*NBA) as the matrix. Solid reflectance spectra were run on a Pye Unicam SP8-100 spectrophotometer. Conductivity data were measured using freshly prepared dimethylformamide solutions (*ca* 10^{-3}M) at 25°C with a Metrohm Herisau model E-518 instrument. Semicarbazide hydrochloride, thiosemicarbazide, benzil, iron (III) chloride hexahydrate and litium hydroxide monohydrate were commercial products of highest chemical grade. Solvent were purified according to standard procedures.

Preparation of Semicarbazide Derivatives

Benzilbissemicarbazone 1. Semicarbazide hydrochloride (4.50 g, 40.30 mmol), benzil (4.24 g, 20.20 mmol) and lithium hydroxide monohydrate (0.98 g, 23 mmol) in ethanol (50 cm^3) were heated under reflux for 3 h giving a yellow solution. The white solid formed at room temperature was filtered off, washed with ethanol and methanol and dried *in vacuo* (85%), mp 236 °C (Found: C, 59.06; H, 4.90; N, 25.89. Calc. for $C_{16}H_{16}N_6O_2$: C, 59.26; H, 4.90; N, 25.92 %). IR/cm^{-1} 3411, 3325, 3255 and 3158 (NH+NH_2), 1682 (amide I), 1584 (C=N), 1569 (NH_2).

Benzilsemicarbazone 2 [35]. Semicarbazide hydrochloride (4.50 g, 40.30 mmol) was dissolved in 40 cm^3 of methanol, 40 cm^3 of 2N HCl and 1 cm^3 of conc. HCl and then added to a suspensión of benzil (4.24 g, 20.20 mmol) in 50 cm^3 of methanol and some drops of conc. HCl. The mixture was stirred for 6 h at room temperature, the yellow solid was filtered off, washed with methanol and dried *in vacuo*. (75 %) mp 160 °C (Found: C, 67.35; H, 4.82; N, 15.54. Calc. for $C_{15}H_{13}N_3O_2$: C, 67.41; H, 4.94; N, 15.73 %). IR/cm^{-1} 3480 and 3198 (NH+NH_2), 1710 (C=O)benzil, 1705 (amide I),1580 (C=N),

6-Methoxy-1,6-diphenyl-4-oxo-3,4,5,6-tetrahydro-2,3,5-triazine 3[35]. The semicarbazide hydrochloride (4.50 g, 40.30 mmol) was dissolved in 40 $cm^3$of methanol, 40 cm^3 of 2N HCl and 1 cm^3 of conc. HCl and then added to a suspensión of benzil (4.24 g, 20.20 mmol) in 50 cm^3 of methanol. The mixture was boiled under reflux for 6 h. A white crystalline solid, which formed on standing overnight, was isolated by filtration, washed with methanol and

dried *in vacuo*.(70 %).mp 224 °C (Found: C, 68.32; H, 5.34; N, 15.10. Calc for $C_{16}H_{15}N_3O_2$: C, 68.36; H, 5.31; N, 15.10 %). IR/cm^{-1} 3220 and 3062 (NH), 1688 (amide I), 1610 (C=N).

Conversion of the open chain molecules **1** and **2** to the cycle one **3.**

A suspension of **1** (0.50 g, 1.54 mmol) in methanol (20 cm^3) was boiled under reflux for 6 h. The crystalline solid formed was filtered off, washed with methanol and dried *in vacuo*.

A methanolic suspension of **2** (0.2 g, 1.2 mmol) in 30 cm^3 was heated under reflux for 6 h. A crystalline solid, which was formed on standing overnight, was filtered off, washed with methanol and dried *in vacuo*.

A methanolic solution of **2** (0.3 g, 12 mmol) in 20 cm^3 was added to a suspension of semicarbazide (0.12 g, 12 mmol) in 10 cm^3 of methanol. At this moment the mixtures was: a) stirred at room temperature for 6 h in presence of HCl or LiOH, b) heated under reflux for 6 h in presence of HCl or LiOH, c) at room temperature. The solid formed was filtered off, washed and dried *in vacuo*.

A solution of $FeCl_3$ $6H_2O$ (0.30g, 1.12 mmol) in 10 cm^3 of methanol was added to a solution of **2** (0.30g, 1.12 mmol) in the same solvent. The solution was stirred for 6 h and then a solution of semicarbazide (0.12g, 1.12 mmol) was added. The reaction mixture was: a) heated under reflux with HCl; b) boiled with LiOH. After evaporated a part of the solvent, a white solid was separated in both cases.

A solution of benzil (0.16 g, 0.7 mmol) in 20 cm^3 of methanol was added to a warm suspension of **1** (0.16 g, 0.8 mmol) in 10 cm^3 of methanol. The mixture was refluxed for 6 h. The solution formed was evaporated to 10 cm^3 and then a crystalline white solid was formed. This precipitate was filterd off, washed and dried *in vacuo*.

1,6-diphenyl-4-oxo-3,4,5,6-tetrahydro-2,3,5-triazine 4. A solution of **3** (0.70 g, 2.5 mmol) in 30 cm^3 of chloroform was stirred for 3 h. The resulting solution was evaporated to half volume, the solid formed was collected by filtration, washed with chloroform and dried *in vacuo*. (29 %). mp 220 °C. (Found: C, 71.95; H, 4.61; N, 16.57: Calc. for $C_{15}H_{11}N_3O$: C, 72.30; H, 4.41; N, 16.87 %). IR/cm^{-1} 3060 (NH), 1560, 1420 and 808 (CNNCNC).

Dichlorobenzilbissemicarbazonediaquoiron(III)monohydrate 5. A solution of iron(III)chloride (0.20 g, 0.7 mmol) in 10 cm^3 of methanol was added to a suspension of **2** (0.19 g, 0.7 mmol,). The reaction mixture was stirred for 12 h and then heated under reflux for 12 h again. The orange solution was concentrated until a white solid was formed, which was separated by filtration. The brown solid precipitated from the filtrate, was filtered off, washed with methanol and dried *in vacuo*. (57 %). mp 260 °C. (Found: C, 38.18; H, 4.17; N, 16.56. Calc. for $C_{16}H_{18}N_6O_5FeCl_2$: C, 38.10, H, 4.16; N, 16.66 %). m/z (FAB) 415 ($C_{16}H_{14}N_6O_2FeCl_2(H_2O)_2+1^+$, 40%), 379 $C_{16}H_{14}N_6O_2Fe^+1^+$,100), 325 ($C_{16}H_{16}N_6O_2+1^+$, 20), 250 ($C_{15}H_{11}N_3O+1^+$,15), 192 ($C_{14}H_{10}N+1^+$, 25). IR/$cm^{-1}$ 3450

(OH), 3410, 3325, 3220 and 3160 (NH_2+NH),1668 (CO), 1586 (C=N).λ_{max}(solid)/nm 590Ω_M /cm^2/mol, 27.

A solution of $FeCl_3$ $6H_20$ (0.30g, 1.12 mmol) in 10 cm^3 of methanol was added to a solution of **2** (0.30g, 1.12 mmol) in the same solvent. The solution was stirred for 6 h and then a solution of semicarbazide (0.12g, 1.12 mmol) was added. The reaction mixture was stirred at room temperature for 48 h, then the solvent was partially removed and a white solid was formed. From the filtrate a new solid was isolated after several days. The analytical and spectroscopic data were those indicated above.

Preparation of Thiosemicarbazide Derivatives

Benzilbisthiosemicarbazone 6 [35]. The thiosemicarbazide (3.64 g, 40.30 mmol) was dissolved in 40 cm^3 of methanol, 40 cm^3 of 2N HCl and 1 cm^3 of conc. HCl and then added to a suspensión of benzil (4.24 g, 20.20 mmol) in 50 cm^3 of methanol and some drops of conc, HCl. The mixture was stirred for 6 h at room temperature, the yellow solid was filtered off, washed with methanol and dried *in vacuo*. (75%) mp 241 °C. (Found: C, 54.15; H, 4.49; N, 23.29. Calc. For $C_{16}H_{16}N_6S_2$: C, 53.93; H, 4.59; N, 23.08 %). IR/cm^{-1} 3420, 3330, 3250 and 3150 (NH+NH_2), 1610 (C=N), 1585 (NH_2), 1465 (thioamide I), 840 (thioamide IV).

A suspension of **6** (0.30 g, 0.84 mmol) in 20 cm^3 of methanol was boiled under reflux for 6 h. The yellow solid was filtered off, washed with methanol and dried *in vacuo*. This reaction in presence of litium hydroxide or HCl yielded the same results.

A solution of benzil (0.06 g, 0.3 mmol) in 10 cm^3 of methanol was added to a warm suspension of **6** (0.10 g, 0.3 mmol) in 20 cm^3 the same solvent The mixture was boiled under reflux for 6 h. El yellow solid was separated by filtration. Analytical data and melting point of the solid and the previous one corresponding with compound **6**.

6-Methoxy-1,6-diphenyl-4-thio-3,4,5,6-tetrahydro-2,3,5-triazine 7. A solution of thiosemicarbazide (1.82 g, 20 mmol) in 40 cm^3 of methanol, 40 cm^3 of 2N HCl and 1 cm^3 of conc. HCl was added to a suspensión of benzil (4.24 g, 20.20 mmol) in 50 cm^3 of methanol. The mixture was stirred for 6 h at room temperature, the pale yellow solid formed was filtered off, washed with methanol and dried *in vacuo*. (43 %) mp 222 °C. (Found: C, 64.45; H, 5.09; N, 14.05. Calc. For $C_{16}H_{15}N_3SO$: C, 64.64; H, 5.05; N, 14.14 %). IR/cm^{-1} 3184 and 3131 (NH), 1608(C=N), 1550 (thioamide I), 780 (thioamide IV).

Bis3,4,9,10-tetraphenyl-1,2,5,6,8,11-hexaaza-cyclododeca-7,11-dithione-2,4,8,10-tetraeneiron(III) 8. A solution of iron (III) chloride (0.08 g, 0.30 mmol) in 10 cm^3 of methanol was added to a warm solution of **6** (0.10 g, 0.3 mmol) and lithium hydroxide (0.01 g, 0.3mmol) in 20 cm^3 of methanol. The reaction mixture was boiled under reflux for 2 h. The yellow solid formed was filtered off, washed with methanol and dried *in vacuo*.(21 %). mp

260 °C. (Found: C, 64.67; H, 3.62; N, 15.09. Calc. for $C_{60}H_{40}N_{12}S_4Fe$: C, 64.75, H, 3.61, N, 15.11%). m/z(FAB) 529.1 ($C_{30}H_{20}N_6S_2+1^+$,100%), 266 ($C_{15}H_{10}N_3S+1^+$,20). IR/cm^{-1}. 3450 (OH), 1620 (CN), 1550 (thioamide I). λ_{max}/nm 520.

A solution of $FeCl_36H_2O$ (0.09 g, 0.33 mmol) in 10 cm^3 of methanol was adedd to a solution of **7** (0.10 g, 0.33 mmol) in 20 cm^3 of the same solvent. The reaction mixture was boiled under reflux for 6 h. Then, the yellow solid formed was filtered off, washed with methanol and dried *in vacuo* (15%).

X-ray Structure Determination

A pale-yellow crystal was mounted on a four-circle Seifert XRD-3000S diffractometer. Exact cell dimension were refined by full matrix least-squares (SHELXL-93). The intensities were corrected for Lorentz and polarization effects. Scattering factors for neutral atoms were taken from the International Tables for X-Ray Crystallography[46]. The structure was solved by direct methods [47] and Fourier syntheses.

The final refinement was made with anisotropic thermal parameters for the non-hydrogen atoms and fixed isotropic thermal parameters and coordinates for hydrogen atoms.

Molecular Modelling

Molecular mechanics and molecular dynamics calculations were undertaken with Hyperchem Version 3. Molecular mechanics was carried out using $MM^+$the Polak-Riviere algorithm of Hyperchem. Molecular dynamics was also used. Computing was performed with a PC containing a 486DX2 processor. The quality of the results were evaluated for comparison with crystallographic data of similar molecules [35].

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