A Quantitative Study of Substituent Effects on Oxidative Cyclization of Some 2-Aryl-substituted Aldehyde Thiosemicarbazones Induced by Ferric Chloride and Cupric Perchlorate

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As a development of our previous work, we performed a kinetic study of the oxidative cyclization reaction of some 2,4-diaryl-substituted aldehyde thiosemicarbazones **1a-n** induced by ferric chloride and by cupric perchlorate. The results of cyclization of **1a-n** were compared to those of the corresponding 2-methyl derivatives. The kinetic data were analyzed by means of the Hammett's equation.

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Introduction.

It is well known that heterocyclic compounds as 1,2,4-triazole, 1,3,4-oxadiazole and 1,3,4-thiadiazole derivatives can be obtained by oxidative cyclization of suitable open chain molecules as, for example, semicarbazones and thiosemicarbazones [1-5]. It may be useful to remind that both the starting semi- and thiosemicarbazones as well as the triazolic, oxa- and thiadiazolic cyclic products have received attention by pharmacologists. Semicarbazones have been considered as peptide isosteres and as possible urea peptide mimetics [6], while thiosemicarbazones and their copper complexes have been used as antimalarial agents [7,8]. Furthermore, 1,2,4-triazoline-5-ones and 1,2,4-triazoline-5-thiones have shown biological acivity and have been used as antiinflammatories, cardiotonics, or dopamine β-hydroxylase inhibitors [9], as well as fungicides and herbicides [10].

Several oxidizing agents can be used for the cyclization of semi- and thiosemicarbazones, and it has been investigated how the oxidant as well as the structure of the open chain molecules can affect regiochemistry and yield of the process. Previously, we examined the reactivity of several aldehyde thiosemicarbazones towards ferric chloride [1,4] and the behavior of aldehyde semicarbazones methyl substituted on the N(2) nitrogen atom towards different oxidizing agents [2,3]. We found that the presence of a substituent (methyl) on the N(2) nitrogen atom was a decisive factor for the regiochemistry of cyclization. In fact, aldehyde thiosemicarbazones unsubstituted on the N(2) nitrogen atom afforded only the 1,3,4-thiadiazolic derivatives, while the cyclization of 2-*N*-methyl substituted aldehyde thiosemicarbazones generally led to the formation of both the triazoline and thiadiazoline products (the second one being favored by electron withdrawing groups linked to the -CH=N-N< hydrazonic moiety).

Good linear correlations between kinetic data and Hammett's substituent constants σ were found for the oxidative cyclization of 2-methyl-4-arylthiosemicarbazones of substituted benzaldehydes induced by ferric chloride [4], while a more complex dependence from substituent effects was found using cupric perchlorate [5].

In order to achieve a deeper mechanistic insight into the process and to investigate the effect of the group linked to N(2) nitrogen atom, we performed a study of some variously substituted 2-*N*-aryl benzaldehyde thiosemicarbazones **1a-n** with ferric chloride and copper perchlorate.

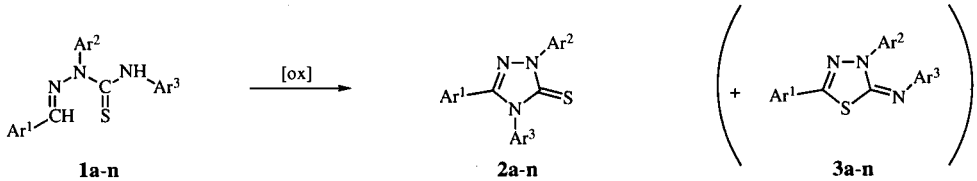
Results and Discussion.

In principle thiosemicarbazones **1a-n** treated with boiling ethanolic ferric chloride hexahydrate solutions could give the corresponding **2a-n** and **3a-n** cyclic derivatives (Scheme 1). Indeed, as it can be seen from data reported in Table 1 the formation of thiadiazoline derivatives was observed only when a strong electron withdrawing group (trifluoromethyl or nitro groups) is present on the phenyl group bonded to the carbon nitrogen double bond. Since under the reaction conditions adopted for the cyclization interconversion between **2** and **3** was not observed, it can be deduced that for substrates studied the nitrogen intramolecular attack always predominates over the sulfur attack.

It should be noticed that in the case of 2-*N*-methyl substituted aldehyde thiosemicarbazones analogues of **1a-n**, substituents on the phenyl group bonded to the carbon-nitrogen double bond were able to modify the regiochemistry of the cyclization [1,4]. Indeed, for the thiosemicarbazones bearing strong electron withdrawing substituents (trifluoromethyl and nitro groups) the sulfur intramolecular attack predominates over the nitrogen attack. The different behavior between 2-*N*-phenyl and 2-*N*-methylthiosemicarbazones seems to indicate that the electronic density on the nitrogen atom N(2) influences differently the rates of the two intramolecular attacks. However, as it can be seen from data relative to the thiosemicarbazones **1e-f**, little variations of electronic effects do not cause significant variations in the **2/3** ratio.

The kinetic data were collected (Table 2) in order to allow a deeper insight into the reaction. Although kinetic determinations were carried out in different conditions,

Scheme 1



1a-n **2a-n** **3a-n**

Substrate	Ar^1	Ar^2	Ar^3
a	C_6H_5	C_6H_5	C_6H_5
b	p-$CH_3OC_6H_4$	C_6H_5	C_6H_5
c	m-BrC_6H_4	C_6H_5	C_6H_5
d	p-$CF_3C_6H_4$	C_6H_5	C_6H_5
e	p-$NO_2C_6H_4$	C_6H_5	C_6H_5
f	p-$NO_2C_6H_4$	p-$CH_3OC_6H_4$	C_6H_5
g	C_6H_5	p-$CH_3OC_6H_4$	C_6H_5
h	C_6H_5	p-$CH_3C_6H_4$	C_6H_5
i	C_6H_5	m-$CH_3C_6H_4$	C_6H_5
j	C_6H_5	p-ClC_6H_4	C_6H_5
k	C_6H_5	C_6H_5	p-$CH_3OC_6H_4$
l	C_6H_5	C_6H_5	p-ClC_6H_4
m	C_6H_5	C_6H_5	m-ClC_6H_4
n	C_6H_5	C_6H_5	p-$NO_2C_6H_4$

Table 1

Reaction Times and Yields for the Reaction of Substrates **1a-n** with Ferric Chloride Hexahydrate in Boiling Ethanol. Data Accurate to within a ±5% in Determination

Substrate	% **2**	% **3**	Time (minutes)
a	>95	0	5
b	>95	0	4
c	66	0	15
d	90	4	20
e [a]	58	17	180
f [b]	51	16	60
g	>95	0	5
h	>95	0	5
i	>95	0	5
j	>95	0	5
k	81	0	15
l	80	0	15
m	90	0	15
n	>95	0	30

[a] Starting substrate 25% is recovered unchanged; [b] Starting substrate 21% is recovered unchanged.

Table 2

Second Order Kinetic Constants for the Reaction of Substrates **1a-n** with Anhydrous Ferric Chloride in Methanol at 25°. Data Accurate to within a ±10% in Determination

Substrate	$k_R \cdot 10^3$ [a] ($M^{-1}s^{-1}$)	$k_N \cdot 10^3$ [b] ($M^{-1}s^{-1}$)	$k_S \cdot 10^3$ [c] ($M^{-1}s^{-1}$)
a	27.3	27.3	—
b	540	540	—
c	4.10	4.10	—
d	1.39	1.39	—
e	0.31	0.25	0.063
f	0.38	0.30	0.079
g	34.7	34.7	—
h	31.1	31.1	—
i	27.3	27.3	—
j	12.6	12.6	—
k	18.6	18.6	—
l	12.0	12.0	—
m	19.7	19.7	—
n	27.8	27.8	—

[a] Kinetic constant for the disappearing of the substrate **1**; [b] Kinetic constant for the formation of the triazole **2**; [c] Kinetic constant for formation of the thiadiazole **3**.

i.e. methanol at 25° and anhydrous salt instead of boiling ethanol with the hydrated salt, the kinetic data confirmed the results reported in Table 1. The reaction appears to be first order in both the substrate and the metallic salt, at least in the range of concentrations examined. As it can be seen, the reactivity of **1** is strongly influenced by substitution on the phenyl group bonded to the carbon-nitrogen double bond (k_{1b}/k_{1e} = 1700), the reactivity decreasing with the electron donating or electron repelling and increasing with the electron withdrawing character of the substituent. In contrast, the reactivity of **1** is only slightly influenced by substitution on the 2-*N*-phenyl ($k_{1g}/k_{1j} < 3$) or 4-*N*-phenyl ($k_{1k}/k_{1n} < 3$) groups. A careful comparative analysis of these data with those reported for the corresponding reaction of 2-methylthiosemicarbazones [4] shows several analogies but also some interesting differences. The replacement of a methyl with a phenyl group on the N(2) atom seems to have the overall effect to

increase the rate of formation of the triazoline **2** and to decrease strongly the rate of formation of the thiadiazoline **3**. In fact, **1d** took only 20 minutes to react and gave a 90% of **2d** (and a 4% of **3d**) while the corresponding 2-*N*-methyl substrate gave in 60 minutes respectively a 35% of the triazoline and a 50% of the thiadiazoline [4]. Furthermore, within the same reaction time (180 minutes) **1e** gave only a 17% yield in **3e**, while its 2-*N*-methyl analogue gave its thiadiazoline in a 54% yield [4]. In order to quantify the effect of the substituents we attempted to correlate data reported in Table 2 with substituent constants in terms of the Hammett's equation. From correlation results it follows that the oxidative cyclization is more sensitive to substitution on the phenyl ring bonded to the carbon-nitrogen double bond when a phenyl group rather than a methyl group is linked to N(2). In fact a ρ value (-3.02 ±0.23) may be calculated for substrates **1a-e** which is higher in module than that found for the corresponding 2-*N*-methyl derivatives (ρ = -2.07 ±0.11) [4]. A remarkable difference between the two series is nonetheless observed for the effect of substituents on the phenyl group linked to the N(4) atom: the effect reported for 2-*N*-methyl derivatives (ρ = -0.96 ±0.10) is not showed by the corresponding 2-*N*-phenyl substrates **1k-n** (no Hammett correlation was observed).

A different behavior was observed for the cyclization reaction carried out with cupric perchlorate. If the concentrations of both the reagents are enough high (>0.01 *M*) the formation of abundant amounts of brown precipitates, presumably a mixture of copper thiosemicarbazone complexes [13] which were quite stable in boiling methanol, was observed. In diluite systems thiosemicarbazones **1a-d,g-n** gave only formation of triazoline derivatives.

The kinetic constant values collected for the reaction of **1** performed in methanolic solution at various concentrations of cupric salt at 25° follow a hyperbolic relationship which can be explained within a Michaelis-Menten-like mechanistic scheme, with a fast substrate-metal complexation equilibrium before the rate determining step. Results of kinetic measurements are shown in Table 3, where both thermodynamic association constant and kinetic constant are reported for each substrate (see Experimental).

Association constants, even though affected by large experimental errors, show a regular trend, increasing with the electron donating properties of substituents placed on the phenyl groups linked to the carbon-nitrogen double bond or the N(4) atom, while the effect for the substitution on the 2-*N*-phenyl group is reversed. About kinetic constants, the effect of the substitution on the carbon-nitrogen double bond linked phenyl group is similar to that showed in the reaction with ferric chloride (a Hammett-type correlation gives ρ = -2.07 ±0.12); the effects for the substitution on 2-*N*- and 4-*N*-phenyl groups are reversed

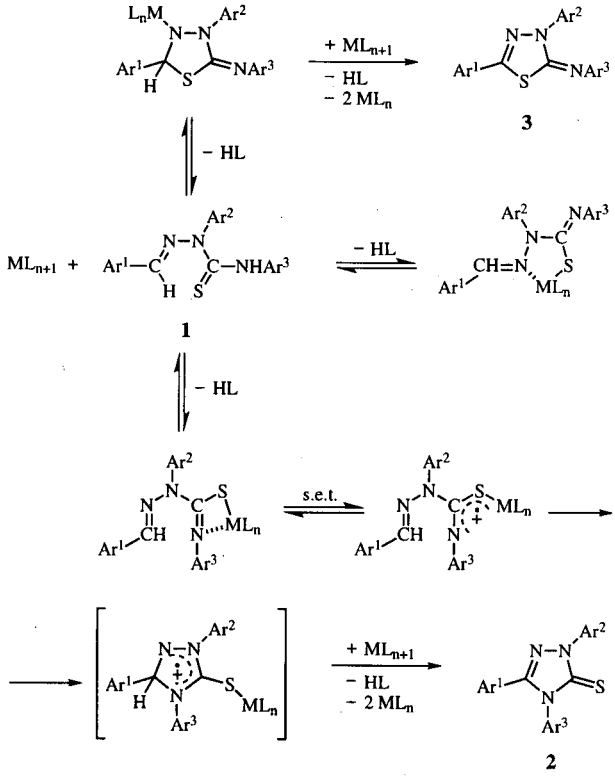
Table 3

Association (K) and Kinetic (k) Constants for the Reaction of Substrates **1a-n** with Cupric Perchlorate Hexahydrate in Methanol at 25°. Data Accurate to within a ±20% in Determination for K, and to within ±5% for k

Substrate	$K \cdot 10^{-3}$ (M^{-1})	$k \cdot 10^{4}$ (s^{-1})
a	2.9	1.76
b	3.1	5.10
c	2.5	0.23
d	1.9	0.13
g	1.9	1.02
h	2.1	1.45
j	7.3	2.34
k	6.9	0.88
l	2.2	2.16
m	1.5	2.71
n	1.0	1.26

(the latter result being very similar to that reported for 2-methyl thiosemicarbazones). Comparatively, it is very interesting to notice that with cupric perchlorate as oxidizing agent the effect of the replacement of the 2-*N*-methyl group with a phenyl group is opposite to that shown by ferric chloride, as **1a** appears less reactive than 2-methyl-4-phenylthiosemicarbazone of benzaldehyde [5].

Scheme 2



Data examined here seem to confirm our hypothesis of the occurrence of two different mechanistic pathways [4] for the formation of the cyclic products **2** and **3** (Scheme 2), and in particular appear to rule out that the formation of the triazolines **2** may proceed *via* an attack of the metal oxidizing cation on the hydrazonic moiety -CH=N-N< of the substrate. The latter topic may be expressed also saying that it could be excluded, at least for the formation of the triazoline ring, the occurrence of a nitrilimine-type intermediate in the reaction mechanism. It has been reported that in the oxidation with lead tetraacetate of substituted phenylhydrazones of benzaldehyde [11], for which nitrilimine intermediates have been demonstrated, substituents on the 2-*N*-phenyl group have a strong effect on the reaction rate, giving a Hammett correlation with $\rho = -1.95$; differently, in the oxidation with lead tetraacetate of some (5-phenyl-1,2,4-triazol-3-yl)hydrazones of substituted benzaldehydes to the corresponding 3-aryl-6-phenyl-7*H*-*s*-triazolo[3,4-*b*]-*s*-triazoles [12] the effect of the substituent on the benzaldehyde residue is almost weaker ($\rho = -0.65$). By contrast, in the oxidation of substrates **1g-j** with ferric chloride the accelerating effect of electron donating substituents on the 2-*N*-phenyl group appears weaker than the one observed for the substitution on the benzaldehyde or the thioamide substrate moieties.

Furthermore, in the oxidation with cupric perchlorate electron donating substituents on the 2-*N*-phenyl group show a decelerating effect, as well as the effect shown by substitution on the 4-*N*-phenyl group. In the latter case, plotting data *vs.* Hammett's σ constants we obtained a bell-shaped curve similar to the one reported for 2-methylthiosemicarbazones [5]. Such a finding was caused by contrasting effects on the rate determining ring closure step for the formation of the triazoline product. In other words, data may be rationalized admitting that the formation of the triazole ring starts with a reversible attack of the oxidizing cation on the *N*(4)-nitrogen atom, followed by a relatively fast single electron transfer step and by a relatively slow ring closure step. This hypothesis easily explains the trends for the association constants: an attack of the metal cation on the *N*(4)-atom is favored by both electron donating substituents on the 4-*N*-phenyl group (which make the N(4) more nucleophilic) and electron withdrawing substituents on the 2-*N*-phenyl group (making the substrate more acidic and prone to lose the N(4) hydrogen atom). The trend due to the substitution on the phenyl group linked to the carbon-nitrogen double bond may be explained admitting also the reversible formation of an unreactive association species [5,7,13]. Furthermore substituent effects on the association constants for 2-*N*-phenyl group rule out an attack of the cation on N(2). Thus, the 2-*N*-group offers only a mild support for the stabilization of the reaction intermediates. In this light, the observation should probably be rationalized that the replacement of the N(2)-methyl group with a phenyl group increases the reaction rate with the ferric salt, but decreases the rate with the cupric salt. In the first case the apparent second order kinetic law seems to indicate that both the association equilibrium and the electron transfer step could play an important role in determining the reaction rate, so that the presence of one more phenyl group on the molecular framework makes **1a** more prone to electron abstraction and consequently more reactive than its 2-*N*-methyl analogue; by contrast in the second case the reaction rate depends only on the ring-closure step, and the radical cation intermediate from **1a**, being more stable, is less reactive than the other one. This observation implies that in the reaction with the ferric salt a different effect should be observed for the substitution on the 4-*N*-phenyl group passing from 2-*N*-methyl to 2-*N*-phenyl substrates. Actually, the apparent lack of an effect for substrates **1k-n** may be interpreted as a ρ value increasing nearly to zero, while the ρ value for the corresponding 2-*N*-methyl substrates is -0.96.

Our data also seem to suggest that the possibility to obtain the thiadiazoline product **3** by reaction with ferric chloride is linked to both the electrophilicity of the hydrazone carbon-nitrogen double bond and the nucleophilicity of the sulfur atom, which increases in electronic density by conjugation from both the N(2) and N(4) nitrogen atoms. In fact we observe that the presence of both factors at the same time on a phenyl group (which in this case behaves as π-electron withdrawing) hampers the formation of thiadiazole ring. In other terms, **3** is allowed to be formed when either at least one of the nitrogen atoms bears a group as electron repelling as a methyl group or the hydrazone double bond is sufficiently electrophile. In the latter case an electron donating substituent on the *N*(2)-phenyl group (substrate **1f**) shows an accelerating effect on the reaction rate, which is comparable to that observed for the N(4)-phenyl substitution. These considerations allow us to assume that in the formation of the thiadiazole product the metal cation acts first as a Lewis acid catalyzing the ring closure [14] and that it causes the oxidative formation of the unsaturation only in a second step, as proposed earlier by us [4].

EXPERIMENTAL

Materials: anhydrous methanol was prepared by refluxing the commercial product (Labscan, hplc grade) with magnesium turnings for 24 hours and distilling. Anhydrous ferric chloride was purified by sublimation of small amounts of the commercial product just before use. Commercial cupric perchlorate hexahydrate was kept for 1 hour at 60° and stored in a desiccator. All other reagents and solvents commercially avaliable (Aldrich, Fluka, Carlo Erba, Labscan) were used as such without further purification.

Equipment: melting points were determined with a Kofler hot-stage apparatus and are uncorrected; ir spectra were recorded in nujol mulls on a Perkin-Elmer 1310 infrared spectrophotometer; ^{1}H nmr spectra were recorded on a Bruker AC-E series 250 or 200 MHz spectrometer, chemical shifts are reported in δ values (ppm) relative to tetramethylsilane as internal standard; uv kinetic measurements were performed on a Beckman DU7 UV spectrophotometer. Analyses by hplc were performed with a Shimadzu Class-VP apparatus equipped with an ET 250/4 NUCLEOSIL® 100-10 C_{18} column (250 mm length, 4 mm diameter) and a uv-vis detector (measurements were performed at λ = 280 nm), a mixture 80:20 v/v acetonitrile-water was used as eluent with a flow of 2 ml/minute.

Synthesis of the Substrates.

All thiosemicarbazones were synthesized by reaction of the proper thiosemicarbazide and aldehyde. The thiosemicarbazides were in turn prepared as follows: 10 mmoles of the proper hydrazine hydrochloride were dissolved at 0° in 5 ml of water, 5 ml of ethanol and 1 ml of pyridine, and to the solution 10 mmoles of the proper phenyl isothiocyanate dissolved or suspended in 10 ml of ethanol was slowly added with stirring; the mixture was stirred at room temperature for an additional 30 minutes and the product filtered. Because of thermal instability (2,4-diphenylthiosemicarbazide is transformed on heating to 1,4-diphenylthiosemicarbazide [15]) they cannot be recrystallized.

2-(*p*-Methoxyphenyl)-4-phenylthiosemicarbazide.

This compound had mp 148°; ir: 3250, 3155 (NH) cm^{-1}; ^{1}H nmr (250 MHz, dimethyl-d_6 sulfoxide): δ 3.83 (s, 3H, CH_3O), 5.71 (s, 2H, NH_2), 7.00 (d, 2H, J = 8.9 Hz, *p*-$CH_3OC_6H_4$), 7.18 (t, 1H, J = 7.3 Hz, C_6H_5), 7.34-7.42 (m, 4H, 2H of C_6H_5 overlapped with 2H of *p*-$CH_3OC_6H_4$), 7.69 (d, 2H, J = 7.4 Hz, C_6H_5), 10.47 (s, 1H, NH).

Anal. Calcd. for $C_{14}H_{15}N_3OS$: C, 61.52; H, 5.53; N, 15.37. Found: C, 61.48; H, 5.45; N, 15.12.

2-(*p*-Methylphenyl)-4-phenylthiosemicarbazide.

This compound had mp 121-124°; ir: 3240, 3125 (NH) cm^{-1}; ^{1}H nmr (250 MHz, dimethyl-d_6 sulfoxide): δ 2.38 (s, 3H, CH_3), 5.73 (s, 2H, NH_2), 7.15-7.25 (m, 3H, ArH), 7.35-7.41 (m, 4H, ArH), 7.70 (d, 2H, J = 8.1 Hz, ArH), 10.48 (s, 1H, NH).

Anal. Calcd. for $C_{14}H_{15}N_3S$: C, 65.34; H, 5.87; N, 16.33. Found: C, 65.45; H, 5.85; N, 16.12.

2-(*m*-Methylphenyl)-4-phenylthiosemicarbazide.

This compound had mp 113-120°; ir: 3330, 3230, 3150 (NH) cm^{-1}; ^{1}H nmr (250 MHz, dimethyl-d_6 sulfoxide): δ 2.39 (s, 3H, CH_3), 5.75 (s, 2H, NH_2), 7.12-7.23 (m, 2H, ArH), 7.29-7.42 (m, 5H, ArH), 7.71 (d, 2H, J = 7.9 Hz, ArH), 10.50 (s, 1H, NH).

Anal. Calcd. for $C_{14}H_{15}N_3S$: C, 65.34; H, 5.87; N, 16.33. Found: C, 65.10; H, 5.80; N, 16.22.

2-(*p*-Chlorophenyl)-4-phenylthiosemicarbazide.

This compound had mp 139-143°; ir: 3340, 3300, 3290, 3170 (NH) cm^{-1}; ^{1}H nmr (200 MHz, dimethyl-d_6 sulfoxide): δ 5.78 (s, 2H, NH_2), 7.17 (t, 1H, J = 6.1 Hz, C_6H_5), 7.28-7.40 (m, 2H, C_6H_5), 7.47, 7.51 (2d, 4H of AA'BB', J = 9.75 Hz, *p*-ClC_6H_4), 7.65 (d, 2H, J = 8.55 Hz, C_6H_5), 10.59 (s, 1H, NH).

Anal. Calcd. for $C_{13}H_{12}N_3S$: C, 56.21; H, 4.35; N, 15.13. Found: C, 56.08; H, 4.44; N, 15.31.

2-Phenyl-4-(*p*-methoxyphenyl)thiosemicarbazide.

This compound had mp 136-138°; ir: 3340, 3300, 3290, 3170 (NH) cm^{-1}; ^{1}H nmr (250 MHz, dimethyl-d_6 sulfoxide): δ 3.81 (s, 3H, CH_3O), 5.74 (s, 2H, NH_2), 6.88 (d, 2H, J = 8.5 Hz, *p*-$CH_3OC_6H_4$), 7.25-7.32 (m, 2H, C_6H_5), 7.37-7.54 (m, 5H, 3H of C_6H_5 overlapped with 2H of *p*-$CH_3OC_6H_4$), 10.36 (s, 1H, NH).

Anal. Calcd. for $C_{14}H_{15}N_3OS$: C, 61.52; H, 5.53; N, 15.37. Found: C, 61.31; H, 5.47; N, 15.48.

2-Phenyl-4-(*p*-chlorophenyl)thiosemicarbazide.

This compound had mp 139-143°; ir: 3220, 3120 (NH) cm^{-1}; ^{1}H nmr (200 MHz, dimethyl-d_6 sulfoxide): δ 5.82 (s, 2H, NH_2), 7.35 (t, 1H, J = 6.9 Hz, C_6H_5), 7.53-7.71 (m, 6H, 4H of C_6H_5 overlapped with 2H of *p*-ClC_6H_4), 7.74 (d, 2H, J = 8.75 Hz, *p*-ClC_6H_4), 10.59 (s, 1H, NH).

Anal. Calcd. for $C_{13}H_{12}N_3S$: C, 56.21; H, 4.35; N, 15.13. Found: C, 56.30; H, 4.29; N, 15.13.

2-Phenyl-4-(*m*-chlorophenyl)thiosemicarbazide.

This compound had mp 125-127°; ir: 3325, 3260, 3200 (NH) cm^{-1}; ^{1}H nmr (250 MHz, dimethyl-d_6 sulfoxide): δ 5.63 (s, 2H, NH_2), 7.22-7.26 (m, 1H, *m*-Cl-C_6H_4), 7.29-7.35 (m, 1H, C_6H_5), 7.37-7.53 (m, 5H, 4H of C_6H_5 overlapped with 1H of *m*-ClC_6H_4), 7.61-7.65 (m, 1H, *m*-ClC_6H_4), 7.98 (d, 1H, J = 1.19 Hz, *m*-ClC_6H_4), 10.59 (s, 1H, NH).

Anal. Calcd. for $C_{13}H_{12}N_3S$: C, 56.21; H, 4.35; N, 15.13. Found: C, 56.00; H, 4.36; N, 15.17.

2-Phenyl-4-(*p*-nitrophenyl)thiosemicarbazide.

This compound had mp 156-157°; ir: 3300, 3180, 3150 (NH) cm^{-1}; ^{1}H nmr (200 MHz, dimethyl-d_6 sulfoxide): δ 7.26-7.35 (m, 1H, C_6H_5), 7.40-7.48 (m, 4H, C_6H_5), 8.14, 8.22 (2d, 4H of AA'BB', J = 9.15 Hz, *p*-$NO_2C_6H_4$); signals relative to NH and NH_2 were too broadened to be detected.

Anal. Calcd. for $C_{14}H_{15}N_4O_2S$: C, 54.16; H, 4.19; N, 19.43. Found: C, 54.37; H, 4.11; N, 19.09.

The synthesis of 2,4-diphenylbenzaldehyde thiosemicarbazone was reported for the first time by the following method [15]: equimolar amounts of thiosemicarbazide and benzaldehyde are placed in a vial and allowed to react for one hour on a steam bath; the product is then isolated by crystallization. For similar reactions yields are not particularly high (50-80%) and the reaction cannot be performed when both the reagents are solid. We preferred to prepare our substrates as follows: 10 mmoles of both reagents were dissolved in 5 ml of dimethyl sulfoxide, two drops of acetic acid was added and the mixture was kept overnight at room temperature; finally 25 ml of ethanol was added and the precipitated product was filtered (yield 65-95%); another amount of less pure product can be precipitated by addition of water. Further purification, if necessary, can be accomplished by crystallization from ethanol.

2,4-Diphenylthiosemicarbazone of *p*-Methoxybenzaldehyde (**1b**).

This compound had mp 125-127°; ir: 3315 (NH), 1610, 1590 (CN) cm^{-1}; ^{1}H nmr (200 MHz, deuteriochloroform): δ 3.83 (s, 3H, CH_3O), 6.91, 7.72 (2d, 4H of AA'BB', J = 8.5 Hz, *p*-$CH_3OC_6H_4$), 7.16 (s, 1H, CH), 7.23-7.45 (m, 5H, C_6H_5), 7.50-7.62 (m, 5H, C_6H_5), 10.13 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{19}N_3OS$: C, 69.78; H, 5.30; N, 11.63. Found: C, 69.90; H, 5.31; N, 11.47.

2,4-Diphenylthiosemicarbazone of *m*-Bromobenzaldehyde (**1c**).

This compound had mp 133-137°; ir: 3280 (NH), 1598 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 7.13 (s, 1H, CH), 7.23-7.31 (m, 4H, 3H of C_6H_5 overlapped with 1H of *m*-BrC_6H_4), 7.45 (t, 2H, J = 7.75 Hz, C_6H_5), 7.51-7.64 (m, 5H, 3H of C_6H_5 overlapped with 2H of *m*-BrC_6H_4), 7.71-7.75 (m, 3H, 2H of C_6H_5 overlapped with 1H of *m*-BrC_6H_4), 10.05 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{16}BrN_3S$: C, 58.54; H, 3.93; N, 10.24. Found: C, 58.36; H, 3.88; N, 10.19.

2,4-Diphenylthiosemicarbazone of *p*-Trifluoromethylbenzaldehyde (**1d**).

This compound had mp 112-115°; ir: 3300 (NH), 1590 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 7.21 (s, 1H CH), 7.23-7.31 (m, 3H, C_6H_5), 7.39-7.46 (m, 2H, C_6H_5), 7.50-7.73 (m, 9H, 5H of C_6H_5 overlapped with 4H of *p*-$CF_3C_6H_4$), 10.15 (s, 1H NH).

Anal. Calcd. for $C_{21}H_{16}F_3N_3S$: C, 63.15; H, 4.04; N, 10.52. Found: C, 62.98; H, 4.05; N, 10.73.

2,4-Diphenylthiosemicarbazone of *p*-Nitrobenzaldehyde (**1e**).

This compound had mp 153-155°; ir: 3300 (NH), 1590 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 7.21 (s, 1H, CH), 7.23-7.30 (m, 3H, C_6H_5), 7.42 (t, 2H, J = 7.65 Hz, C_6H_5), 7.53-7.64 (m, 3H, C_6H_5) 7.66-7.71 (m, 2H, C_6H_5), 7.74, 8.23 (2d, 4H of AA'BB', J = 8.85 Hz, *p*-$NO_2C_6H_4$), 10.03 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{16}N_4O_2S$: C, 63.81; H, 4.28; N, 14.88. Found: C, 63.59; H, 4.25; N, 14.97.

2-(*p*-Methoxyphenyl)-4-phenylthiosemicarbazone of *p*-Nitrobenzaldehyde (**1f**).

This compound had mp 136°; ir: 3180 (NH), 1590 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 3.89 (s, 3H, CH_3O), 7.10, 7.19 (2d, 4H of AA'BB', J = 9.0 Hz, *p*-$CH_3OC_6H_4$), 7.25-7.30 (m, 2H, 1H of C_6H_5 overlapped with 1H of CH), 7.43 (d, 2H, J = 7.95 Hz, C_6H_5), 7.69 (t, 2H, J = 7.95 Hz, C_6H_5), 7.75, 8.24 (2d, 4H of AA'BB', J = 8.8 Hz, *p*-$NO_2C_6H_4$), 10.03 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{18}N_4O_3S$: C, 62.06; H, 4.46; N, 13.78. Found: C, 61.89; H, 4.65; N, 14.00.

2-(*p*-Methoxyphenyl)-4-phenylbenzaldehyde Thiosemicarbazone (**1g**).

This compound had mp 182-185°; ir: 3270 (NH), 1598 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 3.89 (s, 3H, CH_3O), 7.10, 7.22 (2d, 4H of AA'BB', J = 9.0 Hz, *p*-$CH_3OC_6H_4$), 7.23-7.29 (m, 2H, 1H of C_6H_5 overlapped with 1H of CH), 7.39-7.46 (m, 5H, C_6H_5), 7.60-7.64 (m, 2H, C_6H_5), 7.73-7.77 (m, 2H, C_6H_5), 10.17 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{19}N_3OS$: C, 69.78; H, 5.30; N, 11.63. Found: C, 69.91; H, 5.39; N, 11.78.

2-(*p*-Methylphenyl)-4-phenylbenzaldehyde Thiosemicarbazone (**1h**).

This compound had mp 179-181°; ir: 3345 (NH), 1595 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 2.47 (s, 3H, CH_3), 7.18 (d, 2H, J = 8.2 Hz, *p*-$CH_3C_6H_4$), 7.22-7.28 (m, 2H, 1H of C_6H_5 overlapped with 1H of CH), 7.38-7.46 (m, 7H, 5H of C_6H_5 overlapped with 2H of *p*-$CH_3C_6H_4$), 7.57-7.63 (m, 2H, C_6H_5), 7.70-7.77 (m, 2H, C_6H_5), 10.15 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{19}N_3S$: C, 73.01; H, 5.54; N, 12.16. Found: C, 72.88; H, 5.41; N, 12.32.

2-(*m*-Methylphenyl)-4-phenylbenzaldehyde Thiosemicarbazone (**1i**).

This compound had mp 127-132°; ir: 3290 (NH), 1588 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 2.45 (s, 3H, CH_3), 7.09-7.11 (m, 2H, ArH), 7.21-7.52 (m, 9H, 8H of ArH overlapped with 1H of CH), 7.58-7.64 (m, 2H, ArH), 7.71-7.77 (m, 2H, ArH), 10.14 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{19}N_3S$: C, 73.01; H, 5.54; N, 12.16. Found: C, 10.10; H, 5.05; N, 52.12.

2-(*p*-Clorophenyl)-4-phenylbenzaldehyde Thiosemicarbazone (**1j**).

This compound had mp 153-154°; ir: 3275 (NH), 1590 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 7.20-7.29 (m, 4H, 3H of C_6H_5 overlapped with 1H of CH), 7.37-7.46 (m, 5H, C_6H_5), 7.53-7.64 (m, 4H, 2H of C_6H_5 overlapped with 2H of *p*-ClC_6H_4), 7.71 (d, 2H, J = 8.5 Hz, *p*-ClC_6H_4), 10.11 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{16}ClN_3S$: C, 65.66; H, 4.41; N, 11.48. Found: C, 65.89; H, 4.35; N, 11.67.

2-Phenyl-4-(*p*-methoxyphenyl)benzaldehyde Thiosemicarbazone (**1k**).

This compound had mp 125-127°; ir: 3320 (NH), 1605, 1587 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 3.82 (s, 3H, *p*-CH_3O), 6.95 (d, 2H, J = 9.75 Hz, *p*-$CH_3OC_6H_4$), 7.20 (s, 1H, CH), 7.25-7.31 (m, 2H, C_6H_5), 7.36-7.40 (m, 3H, C_6H_5) 7.50-7.63 (m, 7H, 5H of C_6H_5 overlapped with 2H of *p*-$CH_3OC_6H_4$), 9.94 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{19}N_3OS$: C, 69.78; H, 5.30; N, 11.63. Found: C, 69.43; H, 5.35; N, 11.75.

2-Phenyl-4-(*p*-chlorophenyl)benzaldehyde Thiosemicarbazone (**1l**).

This compound had mp 157-160°; ir: 3320 (NH), 1592 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 7.21 (s, 1H, CH), 7.27, 7.69 (2d, 4H of AA'BB', J = 8.55 Hz, *p*-ClC_6H_4), 7.33-7.44 (m, 5H, C_6H_5), 7.52-7.63 (m, 5H, C_6H_5), 10.10 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{16}ClN_3S$: C, 65.66; H, 4.41; N, 11.48. Found: C, 65.84; H, 4.30; N, 11.55.

2-Phenyl-4-(*m*-chlorophenyl)benzaldehyde Thiosemicarbazone (**1m**).

This compound had mp 145-148°; ir: 3265 (NH), 1588 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 7.22 (s, 1H, CH), 7.25-7.34 (m, 4H, 3H of C_6H_5 overlapped with 1H of *m*-ClC_6H_4), 7.37-7.43 (m, 3H, 2H of C_6H_5 overlapped with 1H of *m*-ClC_6H_4), 7.52-7.63 (m, 5H, C_6H_5), 7.65-7.70 (m, 1H, *m*-ClC_6H_4), 7.81 (t, 1H, *m*-ClC_6H_4), 10.15 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{16}ClN_3S$: C, 65.66; H, 4.41; N, 11.48. Found: C, 65.91; H, 4.49; N, 11.41.

2-Phenyl-4-(*p*-nitrophenyl)benzaldehyde Thiosemicarbazone (**1n**).

This compound had mp 158-161°; ir: 3260 (NH), 1593 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 7.25-7.31 (m, 3H, 2H of C_6H_5 overlapped with 1H of CH), 7.41-7.47 (m, 2H, C_6H_5), 7.53-7.68 (m, 6H, C_6H_5), 8.11, 8.28 (2d, 4H of AA'BB', J = 9.15 Hz, *p*-$NO_2C_6H_4$), 10.57 (s, 1H, NH).

Anal. Calcd. for $C_{21}H_{16}N_4O_2S$: C, 63.81; H, 4.28; N, 14.88. Found: C, 64.01; H, 4.38; N, 14.99.

Oxidation of Substrates with Ferric Chloride Hexahydrate.

Thiosemicarbazones (10 mmoles) were dissolved or suspended in 25 ml of boiling ethanol and the ferric salt (5.7 g, 21 mmoles) dissolved in 15 ml of ethanol was added. The mixture was refluxed until the reaction was complete - the color of the solution changes from brown-orange to yellow. After cooling overnight most of the triazoline precipitated and was filtered, the mother liquors were distilled under vacuum and the residue was extracted with water/chloroform to remove most of the inorganic salts. The organic layer was dried over sodium sulfate and distilled. The residue was chromatographated on silica (using cyclohexane-ethyl acetate mixtures as eluents) to obtain the pure thiadiazoline (when present) and another small amount of triazoline.

1,4-Diphenyl-3-(*p*-methoxyphenyl)-1,2,4-triazoline-5-thione (**2b**).

This compound had mp 177-178°; ir: 1605, 1595 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 3.78 (s, 3H, CH_3O), 6.89 (d, 2H, J = 9.75 Hz, *p*-$CH_3OC_6H_4$), 7.25-7.56 (m, 10H, 8H of C_6H_5 overlapped with 2H of *p*-$CH_3OC_6H_4$), 8.14 (d, 2H, J = 7.3 Hz, C_6H_5).

Anal. Calcd. for $C_{21}H_{17}N_3OS$: C, 70.17; H, 4.77; N, 11.69. Found: C, 70.45; H, 4.91; N, 11.70.

1,4-Diphenyl-3-(*m*-bromophenyl)-1,2,4-triazoline-5-thione (**2c**).

This compound had mp 177-179°; ir: 1595 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 7.07-7.16 (m, 1H, *m*-BrC_6H_4), 7.19-7.29 (m, 1H, *m*-BrC_6H_4), 7.36-7.47 (m, 3H, C_6H_5), 7.47-7.58 (m, 6H, 4H of C_6H_5 overlapped with 2H of *m*-BrC_6H_4), 7.64-7.73 (m, 1H, C_6H_5), 8.13 (d, 2H, J = 7.85 Hz, C_6H_5).

Anal. Calcd. for $C_{21}H_{14}BrN_3S$: C, 58.83; H, 3.46; N, 10.29. Found: C, 58.61; H, 3.45; N, 10.12.

1,4-Diphenyl-3-(*p*-trifluoromethylphenyl)-1,2,4-triazoline-5-thione (**2d**).

This compound had mp 164-169°; ir: 1590 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 7.37-7.43 (m, 2H, C_6H_5), 7.43-7.49 (m, 1H, C_6H_5), 7.51-7.54 (m, 1H, C_6H_5), 7.54-7.61 (m, 8H, 4H of C_6H_5 overlapped with 4H of *p*-$CF_3C_6H_4$) 8.12-8.17 (m, 2H, C_6H_5).

Anal. Calcd. for $C_{21}H_{14}F_3N_3S$: C, 63.47; H, 3.55; N, 10.57. Found: C, 63.51; H, 3.65; N, 10.48.

1,4-Diphenyl-3-(*p*-nitrophenyl)-1,2,4-triazoline-5-thione (**2e**).

This compound had mp 189-190°; ir: 1590 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 7.37-7.43 (m, 2H, C_6H_5), 7.43-7.49 (m, 1H, C_6H_5), 7.52-7.62 (m, 7H, 5H of C_6H_5 overlapped with 2H of *p*-$NO_2C_6H_4$) 8.11-8.19 (m, 4H, 2H of C_6H_5 overlapped with 2H of *p*-$NO_2C_6H_4$).

Anal. Calcd. for $C_{21}H_{14}N_4O_2S$: C, 64.16; H, 3.77; N, 14.96. Found: C, 64.10; H, 3.84; N, 15.05.

1-(*p*-Methoxyphenyl)-3-(*p*-nitrophenyl)-4-phenyl-1,2,4-triazoline-5-thione (**2f**).

This compound had mp 191-194°; ir: 1595 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 3.88 (s, 3H CH_3O), 7.05, 7.98 (2d, 4H of AA'BB', J = 9.1 Hz, *p*-$CH_3OC_6H_4$), 7.37-7.42 (m, 2H, C_6H_5), 7.54-7.61 (m, 5H, 3H of C_6H_5 overlapped with 2H of *p*-$NO_2C_6H_4$), 8.16 (d, 2H, J = 8.8 Hz, *p*-$NO_2C_6H_4$).

Anal. Calcd. for $C_{21}H_{16}N_4O_3S$: C, 62.37; H, 3.95; N, 13.85. Found: C, 67.54; H, 4.00; N, 13.71.

1-(*p*-Methoxyphenyl)-3,4-diphenyl-1,2,4-triazoline-5-thione (**2g**).

This compound had mp 204-207°; ir: 1595 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 3.91 (s, 3H, CH_3O), 7.19, 8.03 (2d, 4H of AA'BB', J = 9.0 Hz, *p*-$CH_3OC_6H_4$), 7.43-7.60 (m, 10H, C_6H_5).

Anal. Calcd. for $C_{21}H_{17}N_3OS$: C, 70.17; H, 4.77; N, 11.69. Found: C, 69.98; H,4.98; N, 11.83.

1-(*p*-Methylphenyl)-3,4-diphenyl-1,2,4-triazoline-5-thione (**2h**).

This compound had mp 203-205°; ir: 1590 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 2.47 (s, 3H CH_3), 7.43-7.61 (m, 10H, 8H of C_6H_5 overlapped with 2H of *p*-$CH_3C_6H_4$), 8.04 (d, 2H, J = 8.5 Hz, *p*-$CH_3C_6H_4$).

Anal. Calcd. for $C_{21}H_{17}N_3S$: C, 73.44; H, 4.99; N, 12.23. Found: C, 73.26; H, 5.09; N, 12.36.

1-(*m*-Methylphenyl)-3,4-diphenyl-1,2,4-triazoline-5-thione (**2i**).

This compound had mp 184-187°; ir: 1601 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 2.49 (s, 3H, CH_3), 7.43-7.61 (m, 12H, ArH), 7.96-8.00 (m, 2H, ArH).

Anal. Calcd. for $C_{21}H_{17}N_3S$: C, 73.44; H, 4.99; N, 12.23. Found: C, 73.19; H, 5.04; N, 12.41.

1-(*p*-Chlorophenyl)-3,4-diphenyl-1,2,4-triazoline-5-thione (**2j**).

This compound had mp 189-190°; ir: 1590 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 7.25-7.41 (m, 7H, C_6H_5), 7.45-7.54 (m, 5H, 3H of C_6H_5 overlapped with 2H of *p*-ClC_6H_4), 8.20 (d, 2H, J = 8.55 Hz, *p*-ClC_6H_4).

Anal. Calcd. for $C_{21}H_{14}ClN_3S$: C, 66.02; H, 3.88; N, 11.55. Found: C, 66.15; H, 3.75; N, 11.73.

1,3-Diphenyl-4-(*p*-methoxyphenyl)-1,2,4-triazoline-5-thione (**2k**).

This compound had mp 164-167°; ir: 1603-1595 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 3.85 (s, 3H, CH_3), 7.00 (d, 2H, J = 8.55 Hz, *p*-$CH_3OC_6H_4$), 7.25-7.44 (m, 8H, 6H of C_6H_5 overlapped with 2H of *p*-$CH_3OC_6H_4$), 7.48-7.56 (m, 2H, C_6H_5), 8.13 (d, 2H, J = 7.3 Hz, C_6H_5).

Anal. Calcd. for $C_{21}H_{17}N_3OS$: C, 70.17; H, 4.77; N, 11.69. Found: C, 70.01; H, 4.61; N, 11.56.

1,3-Diphenyl-4-(*p*-chlorophenyl)-1,2,4-triazoline-5-thione (**2l**).

This compound had mp 157-160°; ir: 1595 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 7.29-7.56 (m, 12H, 8H of C_6H_5 overlapped with 4H of *p*-Cl-C_6H_4), 8.12 (d, 2H, J = 7.3 Hz, C_6H_5).

Anal. Calcd. for $C_{21}H_{14}ClN_3S$: C, 66.02; H, 3.88; N, 11.55. Found: C, 65.89; H, 3.96; N, 11.73.

1,3-Diphenyl-4-(*m*-chlorophenyl)-1,2,4-triazoline-5-thione (**2m**).

This compound had mp 173°; ir: 1590 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 7.25-7.29 (m, 2H, ArH), 7.32-7.57 (m, 10H, ArH), 8.12 (d, 2H, J = 7.3 Hz, C_6H_5).

Anal. Calcd. for $C_{21}H_{14}ClN_3S$: C, 66.02; H, 3.88; N, 11.55. Found: C, 61.91; H, 3.88; N, 11.32.

1,3-Diphenyl-4-(*p*-nitrophenyl)-1,2,4-triazoline-5-thione (**2n**).

This compound had mp 203-204°; ir: 1590 (CN) cm^{-1}; ^1H nmr (200 MHz, deuteriochloroform): δ 7.32-7.40 (m, 4H, C_6H_5), 7.42-7.62 (m, 6H, 4H of C_6H_5 overlapped with 2H of

p-$NO_2C_6H_5$), 8.10 (d, 2H, J = 8.5 Hz, C_6H_5), 8.36 (d, 2H, J = 8.5 Hz, *p*-$NO_2C_6H_5$).

Anal. Calcd. for $C_{21}H_{14}N_4O_2S$: C, 64.16; H, 3.77; N, 14.96. Found: C, 64.10; H, 3.86; N, 15.09.

2-(*p*-Trifluoromethylphenyl)-3-phenyl-5-phenylimino-Δ^2-1,3,4-thiadiazoline (**3e**).

This compound had mp 72-78°; ir: 1610, 1583 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 7.05-7.18 (m, 3H, C_6H_5), 7.30 (t, 1H, J = 7.3 Hz, C_6H_5), 7.39 (t, 2H, J = 7.8 Hz, C_6H_5) 7.43-7.56 (m, 2H, C_6H_5), 7.67, 7.80 (2d, 4H of AA'BB', J = 8.3 Hz, *p*-$CF_3C_6H_4$), 8.08 (d, 2H, J = 7.8 Hz, C_6H_5).

Anal. Calcd. for $C_{21}H_{14}F_3N_3S$: C, 63.47; H, 3.55; N, 10.57. Found: C, 63.41; H, 3.27; N,10.84.

2-(*p*-Nitrophenyl)-3-phenyl-5-phenylimino-Δ^2-1,3,4-thiadiazoline (**3f**).

This compound had mp 154-155°; ir: 1608,1578 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 7.04-7.09 (m, 2H, C_6H_5), 7.14 (t, 1H, J = 7.3 Hz, C_6H_5), 7.31 (t, 1H, J = 7.3 Hz, C_6H_5), 7.36-7.44 (m, 4H, C_6H_5) 7.84, 8.26 (2d, 4H of AA'BB', J = 8.3 Hz, *p*-$NO_2C_6H_4$), 8.03-8.09 (m, 2H, C_6H_5).

Anal. Calcd. for $C_{21}H_{14}N_4O_2S$: C, 64.16; H, 3.77; N, 14.96. Found: C, 64.19; H, 3.68; N, 15.01.

2-(*p*-Nitrophenyl)-3-(*p*-methoxyphenyl)-5-phenylimino-Δ^2-1,3,4-thiadiazoline (**3g**).

This compound had mp 82-84°; ir: 1610, 1580 (CN) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 3.85 (s, 3H, CH_3O), 7.00, 7.89 (2d, 4H of AA'BB', J = 9.05 Hz, *p*-$CH_3OC_6H_4$), 7.05 (d, 2H, J = 7.6 Hz, C_6H_5), 7.13 (t, 1H, J = 7.6 Hz, C_6H_5), 7.38 (t, 2H, J = 7.6 Hz, C_6H_5), 7.84, 8.27 (2d, 4H of AA'BB', J = 8.9 Hz, *p*-$NO_2C_6H_4$).

Anal. Calcd. for $C_{21}H_{16}N_4O_3S$: C, 62.37; H, 3.95; N, 13.85. Found: C, 62.15; H, 4.07; N, 13.99.

Kinetic Measurements for the Reaction with Anhydrous Ferric Chloride in Methanol at 25°.

Reaction systems were prepared by mixing reagent solutions, thermostated at 25°, in such a way as to have twenty times or more excess of the oxidizing agent (pseudo-first order conditions), at a concentration ranging from 10 to 50 m*M*. During each kinetic experiment small volumes (0.2-0.4 ml) of the reaction system were taken away time by time and rapidly chromatographed on a silica micro column (4 mm diameter, 6 cm height) eluting with 5 ml of a cyclohexane/ethyl acetate 1:1 mixture in order to remove the excess of inorganic salts; the eluate was concentrated and the residue analyzed by hplc to evaluate the concentrations of the species in the system. From the relative concentrations of the reactant substrate and of the products the second order kinetic constants were evaluated using standard mathematical methods.

Kinetic Measurements for the Reaction with Cupric Perchlorate Hexahydrate in Methanol at 25°.

For each substrate several kinetic experiments were performed at an initial substrate concentration of 7.5 μ*M*, while the copper salt concentration ranged from 0.1 to 10 m*M*. We monitored the disappearance of the substrates following their absorbance at 320 nm. Observed rate constats followed the Michaelis-Menten-type law $k_{obs} = k{\bullet}K{\bullet}[Cu]/(1+K{\bullet}[Cu])$. Control experiments for the oxidation of **1a** were performed by hplc in order to confirm uv data.

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