NEW SYNTHETIC ROUTE TO 1,2,4-THIADIAZOLINES AND 1,3-THIAZOLINES *via* THIADIAZOLOPYRIDINIUM SALTS

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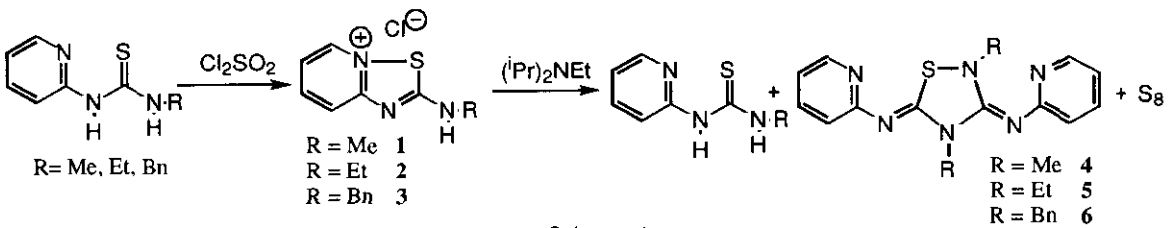
Abstract- A new efficient synthesis of 1,2,4-thiadiazolidines and 1,3-thiazolidines bearing 2-pyridylimino substituents using thiadiazolo-pyridinium chlorides as intermediates is described. The mechanism probably involves a base promoted nucleophilic addition of thiadiazolopyridinium salts to nitriles and ketones.

The high reactivity of 1,2,4-thiadiazolo[2,3-*a*]pyridinium salts against electrophiles has been shown to be an easy and efficient synthetic pathway to many five membered heterocycles bearing pyridylimino substituents.[1] In this paper, we described a new route for the preparation of 1,2,4-thiadiazolines and 1,3-thiazolines using thiadiazolopyridinium salts as intermediates in the key step.

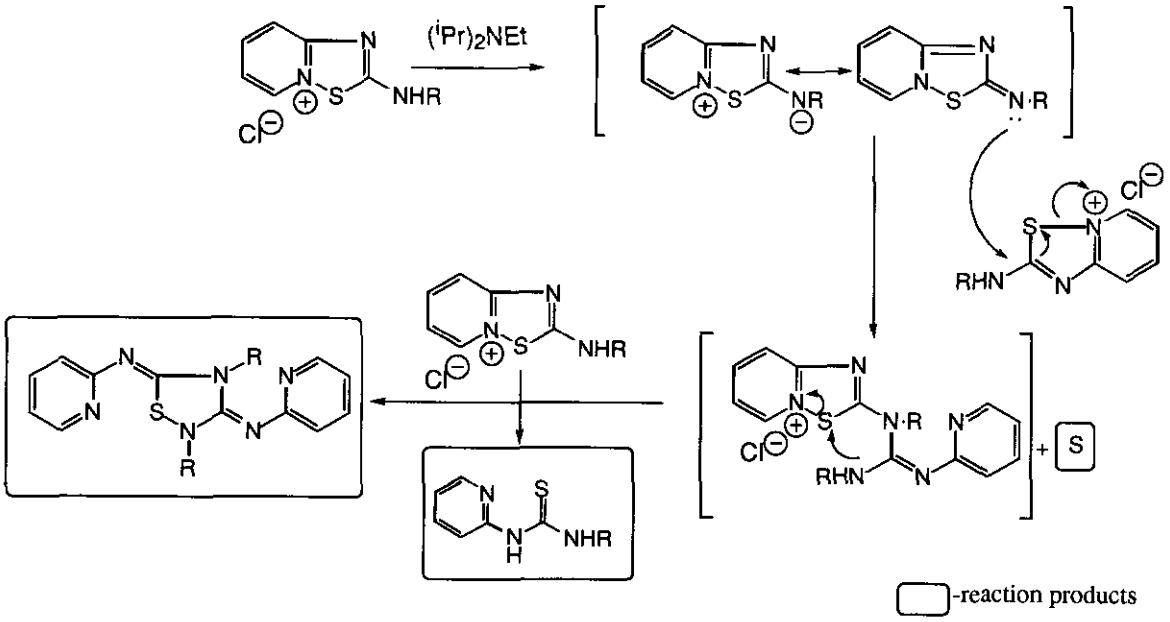
There are several reports dealing with the oxidation reaction of *N*-heteroarylthioureas.[2-4] However, the synthetic applications of the resulting thiadiazoloheteroarylium salts have not yet been reported.

Oxidation of *N*-alkyl- and *N*-benzyl-*N'*-(2-pyridyl)thioureas with sulphuryl chloride in toluene at room temperature gave regioselectively the corresponding 2-alkylamino- or 2-benzylamino[1,2,4]thiadiazolo[2,3-*a*]pyridinium chlorides in good yields after short reaction time (Scheme 1). The structure of these organic salts was established according to their analytical and spectroscopic data (^{1}H and ^{13}C nmr). In the ^{1}H nmr spectra the coupling between the the alkyl or benzylic protons and the exocyclic NH can be observed .



Scheme 1

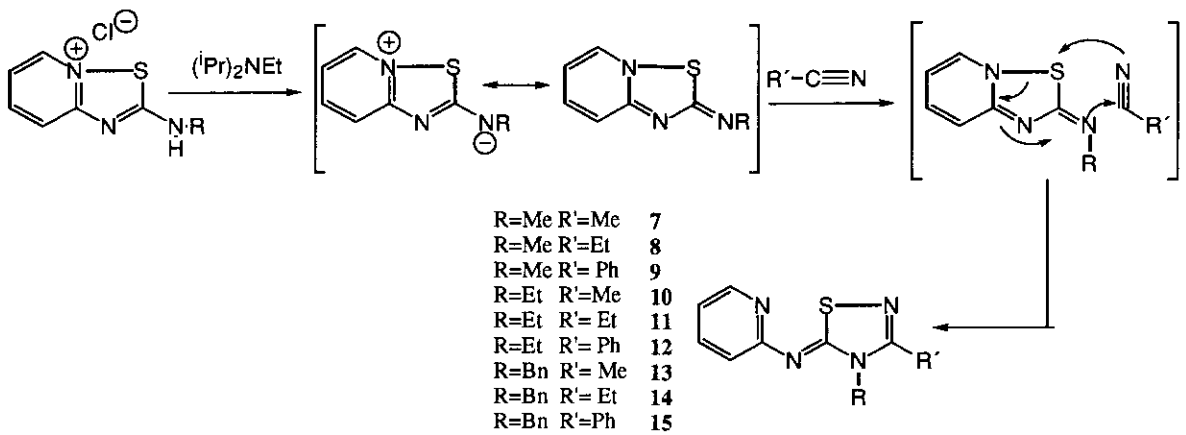
These salts are white solids and perfectly stable, the same as their solutions in dichloromethane or toluene at room or reflux temperature. However, when a weak base (tertiary amine or potassium carbonate) is present, a facile transformation proceeds to give a mixture of products from which we can isolate sulfur, the corresponding thiourea and 2,4-dialkyl-3,5-diimino-1,2,4-thiadiazolidines (Scheme 1). These last compounds, which have been the subject for a detailed structural study,[5] can be considered structurally related to Hector's bases.[6] Presumably, the transformation involves deprotonation of the exocyclic NH. In these conditions an intermediate free base is formed that can be observed as a transient yellow colour which rapidly faded. All attempts to isolate this intermediate were unsucessful. The nucleophilic base addition to the remaining thiadiazolopyridinium chloride and subsequent ring closure including redox reaction could explain all the process (Scheme 2).



Scheme 2

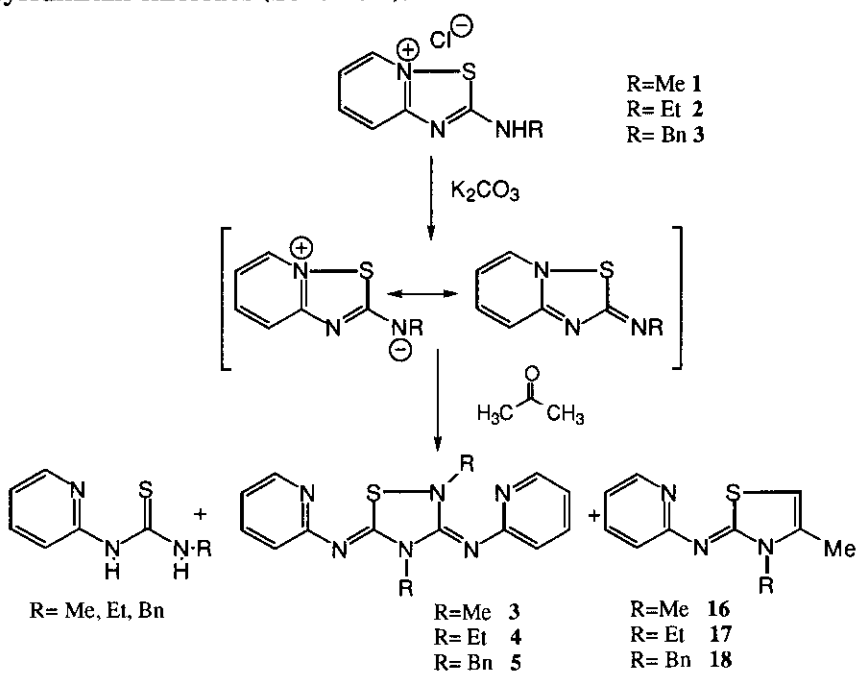
The oxidizing power of these thiadiazolopyridinium chlorides was established by standard methods (*e.g.* , liberation of iodine from iodide).

Additionally, if different electrophiles as nitriles or ketones are present in the reaction medium, the nucleophilic addition of the free base provides a new synthetic route to substituted 1,2,4-thiadiazolines and 1,3-thiazolines respectively. Thus, reactions of thiadiazolopyridinium salts in basic medium (diisopropylethylamine) with alkyl and aryl nitriles afforded 5-pyridylimino-3 substituted-1,2,4-thiadiazolines in good yields for 2 h at nitrile reflux temperature. Only when trimethylacetonitrile was used the reaction did not proceed probably due to the steric hindrance of the *tert*-butyl group (Scheme 3).



Scheme 3

Synthesis of 1,3-thiazolines derivatives was achieved by reaction of thiadiazolopyridinium salts and acetone in the presence of weak base such as potassium carbonate or tertiary amines. In this case, the reaction time was longer and a mixture of compounds was obtained from which it was possible to isolate by silica gel column chromatography, the pyridylimino-1,3-thiazolines (**16-18**) together with *N*-alkyl-*N'*-(2-pyridyl)thiourea and 1,2,4-thiadiazolidines (**3-5**). These two last compounds appear in the reaction medium due to a kinetic competion between the nucleophilic addition of the free base to the acetone or to the thiadiazolopyridinium chlorides (Scheme 4).



Scheme 4

When acetophenone was used as the carbonyl compound, only the products corresponding to the internal reaction were isolated probably due to the lower reactivity of this electrophile.

The structures of the new synthesized compounds were established according to their analytical and ^{1}H and ^{13}C nmr spectroscopic data complemented with NOE, COSY and HETCOR experiments (Tables 1 and 2). Thus, the spatial proximity of the alkyl residues of the 1,2,4-thiadiazolines (**7-15**) and 1,3-thiazolines (**16-18**), one derived from electrophile (nitrile or ketone), and the other from thiadiazolopyridinium salt was confirmed by NOE experiments.

The X-ray diffraction study of molecule (**12**) confirms unequivocally the proposed structure (Figure 1). The dimensions of the central heterocycle are similar to those of several compounds containing 1,2,4-thiadiazole rings found in literature.[7] This ring is nearly planar owing to the charge delocalization which extends along N5 and C6 atoms to the pyridine ring. Pyridine and phenyl rings are also planar and form with the central ring dihedral angles of 9.2 and 36.0 degrees respectively. The molecules in the crystal are held together mainly by van der Waals interactions and are packed forming a ladder along the *a* axis (Figure 2).

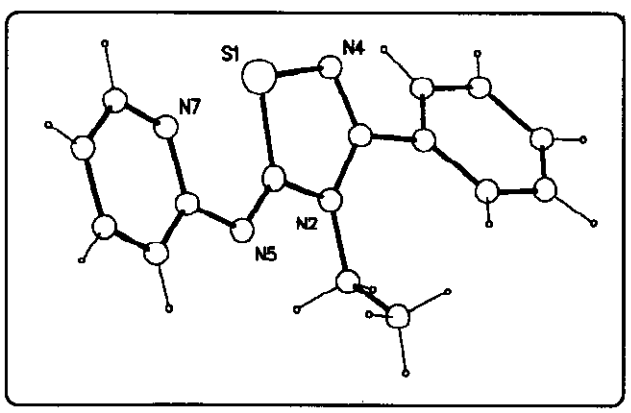


Figure 1.- X-ray crystal structure of 1,2,4-thiadiazoline (**12**)

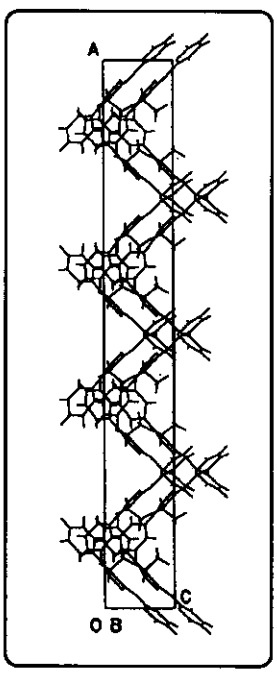
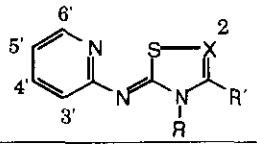


Figure 2.- Crystal packing of compound (**12**)

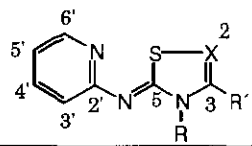
Table 1. ^{1}H Nmr chemical shifts (ppm) and coupling constants (Hz) of 1,2,4-thiadiazolines (**7-15**) and 1,3-thiazolines (**16-18**)



Comp.	no.	H-2	H-3'	H-4'	H-5'	H-6'	R	R'
R=Me R´=Me X=N	**7**[a]	-	7.21 (dd)	7.62 (td)	6.86 (td)	8.40 (dd)	3.65 (s)	2.41 (s)
R=Me R´=Et X=N	**8**[b]	-	7.17 (ddd)	7.56 (td)	6.80 (td)	8.38 (ddd)	3.58 (s)	2.62 (q), 1.29 (t)
R=Me R´=Ph X=N	**9**[c]	-	7.20 (ddd)	7.35 (m)	6.82 (td)	8.40(dd)	3.40 (s)	7.20-7.50 (m)
R=Et R´=Me X=N	**10**[d]	-	7.27 (dd)	7.66(td)	6.90 (td)	8.48 (ddd)	5.22 (c), 1.42 (t)	2.48 (s)
R=Et R´=Et X=N	**11**[e]	-	7.20 (ddd)	7.66 (td)	6.90 (td)	8.50 (ddd)	4.20 (c), 1.32 (t)	2.80 (q), 1.42 (s)
R=Et R´=Ph X=N	**12**[f]	-	7.27 (dd)	7.65 (td)	6.80 (td)	8.48 (dd)	4.80 (c), 1.32 (t)	7.50-7.60 (m)
R=Bn R´=Me X=N	**13**[g]	-	7.2-7.5(m)	7.70 (td)	6.90 (t)	8.50 (dd)	5.47 (s), 7.2-7.5 (m)	2.37 (s)
R=Bn R´=Et X=N	**14**[h]	-	7.2-7.3(m)	7.70 (td)	7.00 (td)	8.60 (ddd)	5.50 (s), 7.2-7.3 (m)	2.60 (q), 1.38 (s)
R=Bn R´=Ph X=N	**15**[i]	-	7.11 (ddd)	7.68 (td)	6.95 (td)	8.55 (ddd)	5.42 (s), 7.35 (m)	7.80 (m)
R=Me R´=Me X=CH	**16**[j]	6.23 (d)	6.96 (ddd)	7.59 (td)	6.81 (td)	8.29 (ddd)	3.53 (s)	2.22 (s)
R=Et R´=Me X=CH	**17**[k]	5.88 (d)	7.06 (dd)	7.53 (td)	6.76 (td)	8.38 (dd)	4.11(q), 1.31(t)	2.20 (s)
R=Bn R´=Me X=CH	**18**[l]	5.83 (d)	6.92 (ddd)	7.43 (td)	6.69 (td)	8.32 (ddd)	5.32 (s), 7.1-7.2 (m)	2.00 (s)

a: $J_{H6'H5'}$= 5.1 Hz; $J_{H6'H4'}$= 2.1 Hz; $J_{H5'H4'}$= 8.0 Hz; $J_{H5'H3'}$= 2.0 Hz; $J_{H4'H3''}$= 9.1 Hz. b: $J_{H6'H5'}$= 5.2 Hz; $J_{H6'H4'}$= 1.0 Hz; $J_{H6'H3''}$= 2.0 Hz; $J_{H5'H4'}$= 7.1 Hz; $J_{H5'H3''}$= 2.1 Hz; $J_{H4'H3''}$= 9.1 Hz. c: $J_{H6'H5'}$= 6.0 Hz; $J_{H5'H4'}$= 6.2 Hz; $J_{H5'H3''}$= 1.1 Hz; $J_{H4'H3''}$= 8.1 Hz. d: $J_{H6'H5'}$= 5.1 Hz; $J_{H6'H4'}$= 2.1 Hz; $J_{H6'H3''}$= 1.0 Hz; $J_{H5'H4'}$= 8.1 Hz; $J_{H5'H3''}$= 2.1 Hz; $J_{H4'H3''}$= 8.0 Hz. e: $J_{H6'H5'}$= 5.1 Hz; $J_{H6'H4'}$= 2.0 Hz; $J_{H6'H3''}$= 1.0 Hz; $J_{H5'H4'}$= 7.2 Hz; $J_{H5'H3''}$= 2.0 Hz; $J_{H4'H3''}$= 8.2 Hz. f: $J_{H6'H5'}$= 5.1 Hz; $J_{H6'H4'}$= 2.10 Hz; $J_{H5'H4'}$= 8.0 Hz; $J_{H5'H3''}$= 2.0 Hz; $J_{H4'H3''}$= 8.0 Hz. g: $J_{H6'H5'}$= 5.2 Hz; $J_{H6'H4'}$= 2.1 Hz; $J_{H5'H4'}$= 7.2 Hz; $J_{H5'H3''}$= 1.2 Hz; $J_{H4'H3''}$= 7.4 Hz. h: $J_{H6'H5'}$= 5.1 Hz; $J_{H6'H4'}$= 2.0 Hz; $J_{H6'H3''}$= 1.10 Hz; $J_{H5'H4'}$= 7.2 Hz; $J_{H4'H3''}$= 8.0 Hz. i: $J_{H6'H5'}$= 5.1 Hz; $J_{H6'H4'}$= 2.1 Hz; $J_{H6'H3''}$= 1.1 Hz; $J_{H5'H4'}$= 6.4 Hz; $J_{H5'H3''}$= 1.0 Hz; $J_{H4'H3''}$= 8.1 Hz. j: J_{CHCH3}= 2.1 Hz; $J_{H6'H5'}$= 5.4 Hz; $J_{H6'H4'}$= 1.2 Hz; $J_{H5'H4'}$= 7.2 Hz; $J_{H5'H3''}$= 1.0 Hz; $J_{H4'H3''}$= 8.1 Hz. k: J_{CHCH3}= 1.3 Hz; $J_{H6'H5'}$= 4.1 Hz; $J_{H6'H4'}$= 2.1 Hz; $J_{H6'H3''}$= 1.0 Hz; $J_{H5'H4'}$= 7.2 Hz; $J_{H5'H3''}$= 1.0 Hz; $J_{H4'H3''}$= 8.2 Hz. l: J_{CHCH3}= 2.1 Hz; $J_{H6'H5'}$= 5.2 Hz; $J_{H6'H4'}$= 2.0 Hz; $J_{H6'H3''}$= 0.9 Hz; $J_{H5'H4'}$= 7.1 Hz; $J_{H5'H3''}$= 1.0 Hz; $J_{H4'H3''}$= 8.1 Hz.

Table 2. ^{13}C Nmr chemical shifts (ppm) of 1,2,4-thiadiazolines (**7-15**) and 1,3-thiazolines (**16-18**)



Comp.	**no.**	C-2	C-3	C-5	C-2'	C-3'	C-4'	C-5'	C-6'	R	R'
R=Me R´=Me X=N	**7**	-	155.96	167.56	153.06	116.98	137.57	118.45	144.80	32.83	16.50
R=Me R´=Et X=N	**8**	-	157.79	167.50	156.72	116.27	137.27	119.14	144.98	31.67	23.33, 9.91
R=Me R´=Ph X=N	**9**	-	157.79	167.64	n.o	116.56	137.45	119.43	145.01	34.40	[a]
R=Et R´=Me X=N	**10**	-	157.90	166.27	152.42	116.22	137.21	119.32	144.91	40.46, 13.55	16.43
R=Et R´=Et X=N	**11**	-	157.99	166.70	156.43	116.11	137.15	119.28	144.93	40.05, 13.59	23.00, 10.19
R=Et R´=Ph X=N	**12**	-	157.81	166.58	155.34	116.38	137.33	119.51	144.91	41.77, 13.77	[b]
R=Bn R´=Me X=N	**13**	-	157.83	167.00	153.08	116.53	137.36	119.56	145.07	48.32, [c]	16.85
R=Bn R´=Et X=N	**14**	-	157.89	167.45	157.05	116.43	137.32	119.50	145.10	47.90, [d]	23.30, 9.87
R=Bn R´=Ph X=N	**15**	-	157.73	167.08	155.64	116.63	137.38	119.70	144.98	49.62, [e]	[e]
R=Me R´=Me X=CH	**16**	99.51	133.33	160.48	159.94	115.59	136.77	119.14	145.81	31.39	14.54
R=Et R´=Me X=CH	**17**	99.52	132.85	159.54	159.10	115.42	136.67	119.29	145.78	39.97, 11.26	13.17
R=Bn R´=Me X=CH	**18**	99.82	133.45	160.51	158.93	115.73	136.76	119.50	145.86	47.85, [f]	14.51

a: C-Ar 120.75; 130.42. b: C-Ar: 128.51; 128.73; 130.27. 130.80; c: C-Ar: 126.83; 127.80; 128.34; 135.80. d: C-Ar: 126.73; 127.72; 128.81; 135.96; e: C-Ar: 127.01; 127.49; 128.51; 128.55; 128.75; 130.34; 130.58; 136.44. f: C-Ar: 126.70, 127.22, 128.61, 137.31.

In conclusion, we have shown that base promoted nucleophilic addition of thiadiazolopyridinium salts to nitriles and ketones represents an efficient synthesis of 1,2,4-thiadiazolines and 1,3-thiazolines providing a new entry to several heterocycles.

ACKNOWLEDGEMENTS

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EXPERIMENTAL

General. Column Chromatography was performed on Merck silicagel 60 (70-230 mesh). ^1H Nmr spectra were obtained on Varian XL-300 and Gemini-200 spectrometers operating at 300 and 200 MHz respectively. Typical spectral parameters were: spectral width 10 ppm, pulse width 9 μs (57°), data size 32 K. NOE difference spectra were measured under the same conditions, using a presaturation time of 3 s. ^{13}C Nmr experiments were carried out on the Varian Gemini-200 spectrometer operating at 50 MHz. The acquisition parameters were: spectral width 16kHz, acquisition time 0.99 s, pulse width 9 μs (57°) and data size 32 K.

2-Methylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride (1): *N*-Methyl-*N'*-(2-pyridyl)thiourea (1.00 g, 5.9 mmol) was dissolved in dry toluene (30 ml) and stirred at room temperature during the dropwise addition of sulphuryl chloride (0.89 g, 6.6 mmol). After 30 min the product was collected by filtration and recrystallized from ethyl acetate/hexane to give **1** (1.2 g, 78%): mp 167°C;^1H nmr (200 MHz, DMSO-d_6) δ: 10.00 (m, 1H, NH); 9.02 (d, 1H, J_{H6H5}=6.1 Hz, H6-Pyr); 8.12 (dd, 1H, J_{H5H4}=7.2 Hz, J_{H3H4}=8.2 Hz, H4-Pyr); 7.70 (d, 1H, J_{H3H4}=8.2 Hz, H3-Pyr); 7.36 (dd, 1H, J_{H5H4}=7.2 Hz, J_{H6H5}=6.1 Hz, H5-Pyr); 3.1 (d, 3H, J_{NHCH3}=4.7 Hz, CH_3). ^{13}C Nmr (50 MHz, DMSO-d_6) δ: 171.03 (C-2 thiadiazole moiety); 156.52, 140.61, 134.97, 116.76, 116.67 (C-2, C-6, C-4, C-5 and C-3 pyridine moiety); 30.61 (NCH_3). Anal. Calcd for $C_7H_8N_3ClS$: C, 41.16; H, 3.97; N, 20.84; S, 15.88; Cl, 17.61. Found: C, 41.02; H, 3.82; N, 20.71; S, 15.63; Cl, 17.24.

2-Ethylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride (2): To a solution of *N*-ethyl-*N'*-(2-pyridyl)thiourea (0.5 g, 2.7 mmol) in dry toluene (50 ml) was added dropwise sulphuryl chloride (0.41 g, 3.0 mmol). The reaction mixture was refluxed for 2 h. After cooling, the solid was removed by filtration and recrystallized from ethyl acetate/hexane to give **2** (0.31 g, 51%): mp 136°C;^1H nmr (200 MHz, DMSO-d_6) δ: 10.10 (m, 1H, NH); 8.52 (d, 1H, J_{H6H5}=6.0 Hz, H6-Pyr); 7.81 (td, 1H, J_{H5H4}=7.1 Hz, J_{H3H4}=8.0 Hz, H4-Pyr); 7.50 (dd, 1H, J_{H3H4}=8.0 Hz, J_{H3H5}=1.3 H, H3-Pyr); 7.10 (td, 1H, J_{H5H4}=7.1 Hz, J_{H3H5}=1.3 Hz, H5-Pyr); 3.60 (dd, 2H, J_{NHCH2}=5.0 Hz, J_{CH2CH3}=7.1 Hz, CH_2); 1.30 (t, 3H, J_{CH2CH3}=7.1 Hz, CH_3). ^{13}C Nmr (50 MHz, DMSO-d_6) δ: 170.78 (C-2 thiadiazole moiety); 157.19, 139.75,

134.97, 117.28, 116.43 (C-2, C-6, C-4, C-5 and C-3 pyridine moiety); 40.03 (NCH_2); 13.85 (CH_3). Anal. Calcd for $C_8H_{10}N_3ClS$: C, 44.54; H, 4.64; N, 19.48; S, 14.85; Cl, 16.47. Found: C, 44.22; H, 4.66; N, 19.26; S, 14.59; Cl, 16.40.

2-Benzylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride (3): Following the above mentioned procedure, *N*-benzyl-*N'*-(2-pyridyl)thiourea (1.0 g, 4.1 mmol) and sulphuryl chloride (0.55 g, 4.1 mmol) were refluxed for 3 h. After cooling, the solid was collected by filtration and recrystallized from ethyl acetate/hexane to give **3** (0.59 g, 52%): mp 160°C; ^1H nmr (200 MHz, DMSO-d6) δ: 10.40 (m, 1H, NH); 8.51 (dd, 1H, J_{H6H5}=6.2 Hz, J_{H6H4}=1.2 Hz, H6-Pyr); 7.72 (td, 1H, J_{H5H4}=7.0 Hz, J_{H3H4}=8.1 Hz, H4-Pyr); 7.39 (d, 1H, J_{H3H4}=8.1 Hz, H3-Pyr); 7.20 (m, 5H, H-Ar); 7.00 (t, 1H, J_{H5H4}=7.0 Hz, H5-Pyr); 4.70 (m, 2H, J_{NHCH2}=5.0 Hz, N-CH_2). ^{13}C nmr (50 MHz, DMSO-d6) δ: 171.46 (C-2 thiadiazole moiety); 157.10, 139.72, 138.49, 117.69, 116.61 (C-2, C-6, C-4, C-5 and C-3 pyridine moiety); 136.16, 128.68, 127.71, 127.51 (C_i, C_o, C_m and C_p); 48.61 (NCH_2). Anal. Calcd for $C_{13}H_{12}N_3ClS$: C, 56.21; H, 4.32; N, 15.13; S, 11.53; Cl, 12.70. Found: C, 56.02; H, 4.27; N, 15.23; S, 11.02; Cl, 12.32.

General method for the obtention of 5-(2-pyridylimino)-1,2,4-thiadiazolines

To a suspension of the corresponding 2-alkylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride (2.3 mmol) in 15 ml of alkyl or arylnitrile, *N,N'*-diisopropylethylamine (0.29 g, 2.3 mmol) was added. The reaction mixture was refluxed for 2 h. The solvent was evaporated *in vacuo* and the residue was recrystallized from the appropiate solvents.

3,4-Dimethyl-5-(2-pyridylimino)-1,2,4-thiadiazoline (7). Following the general procedure reacts 2-methylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride and acetonitrile. Recrystallization solvent: water; yield 67%; mp 144-146°C. Anal. Calcd for $C_9H_{10}N_4S$: C, 52.42; H, 4.85; N, 27.18; S, 15.53. Found: C, 52.49; H, 4.98; N, 27.31; S, 15.14.

3-Ethyl-4-methyl-5-(2-pyridylimino)-1,2,4-thiadiazoline (8). According to the general procedure reacts 2-methylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride and propionitrile. Recrystallization solvent: methanol/water; yield 62%; mp 124-126°C. Anal. Calcd for $C_{10}H_{12}N_4S$: C, 54.54; H, 5.45; N, 25.45; S, 14.54. Found: C, 54.72; H, 5.69; N, 25.36; S, 14.81.

4-Methyl-3-phenyl-5-(2-pyridylimino)-1,2,4-thiadiazoline (9). Following the general procedure reacts 2-methylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride and benzonitrile. Recrystallization solvent: methanol/water; yield 60%; mp 168-170°C. Anal. Calcd for $C_{14}H_{12}N_4S$: C, 62.68; H, 4.47; N, 20.89; S, 11.94. Found: C, 62.39; H, 4.29; N, 20.48; S, 11.62.

4-Ethyl-3-methyl-5-(2-pyridylimino)-1,2,4-thiadiazoline (10). According to the general procedure reacts 2-ethylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride and acetonitrile.

Recrystallization solvent: methanol/water; yield 75%; mp 78-80°C. Anal. Calcd for $C_{10}H_{12}N_4S$: C, 54.54; H, 5.45; N, 25.45; S, 14.54. Found: C, 54.88; H, 5.52; N, 25.16; S, 14.90.

3,4-Diethyl-5-(2-pyridylimino)-1,2,4-thiadiazoline (11). Following the general procedure reacts 2-ethylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride and propionitrile. Recrystallization solvent: water; yield 52%; mp 90-92°C. Anal. Calcd for $C_{11}H_{14}N_4S$: C, 56.41; H, 5.98; N, 23.93; S, 13.67. Found: C, 56.23; H, 5.66; N, 23.70; S, 14.03.

4-Ethyl-3-phenyl-5-(2-pyridylimino)-1,2,4-thiadiazoline (12). According to the general procedure reacts 2-ethylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride and benzonitrile. Recrystallization solvent: methanol/water; yield 53%; mp 92-94°C. Anal. Calcd for $C_{15}H_{14}N_4S$: C, 63.83; H, 4.96; N, 19.86; S, 11.34. Found: C, 64.07; H, 5.18; N, 19.81; S, 11.62.

X-Ray analysis of ***12****:* A prismatic single crystal of dimensions 0.38 x 0.32 x 0.21 mm was used to collect 1376 independent reflections (1211 considered as observed with I > 2 s (I) criterion) up to q=134° with graphite monochromated Cu Kα radiation on a Seifert XRD 3000 s four circle diffractometer by using an w/2q scan mode. No crystal decomposition was observed. Unit cell parameters were refined using L.s. on Fobs. The structure was solved using direct methods. The following programs were used to solve and refine the structure: MULTAN80,[8] DIRDIF,[9] DIFABS,[10] XRAY80,[11] PESOS,[12] and PARST.[13]An empirical weighting scheme was used to avoid depences in $< wD^2F >$ vs $< F_o >$ and vs <sin q/l>. Final disagreement indices are R=0.040 and Rw=0.045. Crystal data: symmetry:orthorombic, Fdd^2; Formula: $C_{14}H_{14}N_4S$; Unit cell dimensions: 44.269 (4), 22.335 (2), 5.654 (1) Å. a=b=g=90°; Packing: v=5590 (1) $Å^3$; Z=16; D_c=1.3419 g. cm^{-3}; M=270.358; F(000)=2368; m=19.641 cm^{-1}. Fractional coordinates and thermal parameters have been deposited as supplementary materia

4-Benzyl-3-methyl-5-(2-pyridylimino)-1,2,4-thiadiazoline (13). Following the general procedure reacts 2-benzylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride and acetonitrile. Recrystallization solvent: methanol/water; yield 58%; mp 146-148°C. Anal. Calcd for $C_{15}H_{14}N_4S$: C, 63.83; H, 4.90; N, 19.86; S, 11.34. Found: C, 63.60; H, 4.97; N, 19.57; S, 11.55.

4-Benzyl-3-ethyl-5-(2-pyridylimino)-1,2,4-thiadiazoline (14). According to the general procedure reacts 2-benzylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride and propionitrile. Recrystallization solvent: methanol/water; yield 70%; mp 112-114°C. Anal. Calcd for $C_{16}H_{16}N_4S$: C, 64.86; H, 5.40; N, 18.91; S, 10.81. Found: C, 64.54; H, 5.57; N, 18.70; S, 10.58.

4-Benzyl-3-phenyl-5-(2-pyridylimino)-1,2,4-thiadiazoline (15).- Following the general procedure reacts 2-benzylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride and benzonitrile. Recrystallization solvent: methanol/water; yield 43%; mp 134°C. Anal. Calcd

for $C_{20}H_{16}N_4S$: C, 69.76; H, 4.65; N, 16.27; S, 9.30. Found: C, 70.07; H, 4.38; N, 16.21; S, 9.60.

General method for the synthesis of 2-(2-pyridylimino)-1,3-thiazolines and 3,5-[Bis(2-pyridyl)imino]-1,2,4-thiadiazolidines

To a suspension of the corresponding 2-alkylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride (2 mmol) in 20 ml of acetone, potassium carbonate (2.76 g, 20 mmol) was added. The reaction mixture was refluxed for 2 h. After cooling, the solid was removed by filtration. The filtrate was evaporated to dryness in vacuo and the residue was purified by column chromatography using the adequated mixtures of solvents. From the first fraction were isolated the corresponding 1,3-thiazolines while from the last ones, 1,2,4-thiadiazolidines were obtained.

3,4-Dimethyl-2-(2-pyridylimino)-1,3-thiazoline (16) *and* **3,5-[Bis(2-pyridyl)imino]-2,4-dimethyl-1,2,4-thiadiazolidine (3)**. Following the general procedure, 2-methylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride reacts with acetone. Silica gel column chromatography eluent: methanol/ dicloromethane 1:100. Compound (**16**): yield, 63%; mp 90-92°C. Anal. Calcd for $C_{10}H_{11}N_3S$: C, 58.50; H, 5.40; N, 20.47; S, 15.61. Found: C, 58.89; H, 4.67; N, 20.25; S, 15.65. Compound (**3**): yield, 12%; mp 130-132°C.[5]

3-Ethyl-4-methyl-2-(2-pyridylimino)-1,3-thiazoline (17) *and* **3,5-[Bis(2-pyridyl)-imino]-2,4-diethyl-1,2,4-thiadiazolidine (4)**. According to the general procedure, 2-ethylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride reacts with acetone. Silica gel column chromatography eluent: hexane/ethyl acetate 1:1. Compound (**17**) (oil): yield, 12%. Anal. Calcd for $C_{11}H_{13}N_3S$: C, 60.64; H, 5.97; N, 19.16; S, 14.62. Found: C, 60.52; H, 6.10; N, 19.27; S, 14.50. Compound (**4**): yield, 8%; mp 136-138°C.[5]

3-Benzyl-4-methyl-2-(2-pyridylimino)-1,3-thiazoline (18) *and* **3,5-[Bis(2-pyridyl)-imino]-2,4-dibenzyl-1,2,4-thiadiazolidine (5)**. Following the general procedure, 2-benzylamino-1,2,4-thiadiazolo[2,3-*a*]pyridinium chloride reacts with acetone. Silica gel column chromatography eluent: hexane/ethyl acetate 3:1. Compound (**18**): yield, 8%; mp 98-100°C. Anal. Calcd for $C_{16}H_{15}N_3S$: C, 68.29; H, 5.37; N, 14.93; S, 11.39. Found: C, 68.02; H, 5.56; N, 14.69; S, 11.58. Compound (**5**): yield, 9%; mp 133-135°C.[5]

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