J. Braz. Chem. Soc., Vol. 16, No. 2, 275-279, 2005.
Printed in Brazil - ©2005 Sociedade Brasileira de Química
0103 - 5053 $6.00+0.00

Short Report

Regiospecific Synthesis of 1,2-Bis(azolyl)ethanes

Marcos A. P. Martins [a], *Wilson Cunico* [a], *Geonir M. Siqueira* [b], *Victor L. Leidens* [a], *Nilo Zanatta* [a], *Helio G. Bonacorso*[a] *and Alex F. C. Flores*[*,a]

[a] *Departamento de Quimica, Universidade Federal de Santa Maria, 97105-900 Santa Maria - RS, Brazil*

[b] *Departamento de Química Orgânica, Universidade Federal de Pelotas, 96040-160 Pelotas - RS, Brazil*

Este trabalho mostra a síntese de 1,2-bis-(5'-trialometilisoxazol-3'-il)etanos (**3**-**6**) e 1,2-bis(5'-trialometilpirazol-3'-il)etanos (**7**-**10**) a partir da ciclocondensação de 1,1,1,10,10,10-hexahalo-4,7-dimetoxideca-3,7-dien-2,9-dionas (**1** e **2**) com hidroxilamina e hidrazinas. Também é mostrada a síntese dos 1,2-bis(5'-alcoxicarbonilpirazol-3'-il)etanos (**11**-**14**) via reação da dienona **2**, triclorometil-substituída, e hidrazina.

The synthesis of 1,2-bis(5'-trihalomethylisoxazol-3'-yl)ethanes (**3**-**6**) and 1,2-bis(5'-trihalomethylpyrazol-3'-yl)ethanes (**7**-**10**) from the cyclocondensation of 1,1,1,10,10,10-hexahalo-4,7-dimethoxydeca-3,7-dien-2,9-diones (**1** and **2**) with hydroxylamine and hydrazines is reported. In addition, the one-pot synthesis of 1,2-bis(5'-alkoxycarbonylpyrazol-3'-yl)ethanes (**11**-**14**) by reaction of chloro-substituted dienone **2** and hydrazines is also described.

Keywords*:* bis(azolyl)ethanes, pyrazoles, isoxazoles, enones

Introduction

Most organic compounds belong to the heterocyclic class and a great number of heterocycles have been of significant help for the human beings. Isoxazoles and pyrazoles belong to this class of compounds and are known to be important intermediates for the preparation of agrochemicals and pharmaceutical compounds.[1,2] The 1,2-bis(azolyl)ethanes consist of two N-donor units linked by a flexible spacer. These compounds show desirable characteristics to be used as ligands of metals because they can either bridge two different metal ions, or act as bidentate chelants of single metal ions.[3]

We developed a general procedure for preparing 1,1,1-trihalo-4-alkoxy-3-alken-2-ones (β-haloacetylated enol ethers) using halogenated acylating groups CX_3CO.[4-7] These compounds are of general interest as precursors for a variety of halomethyl-substituted heterocyclic compounds, e.g. isoxazoles,[8,9] pyrazoles,[10-12] pyrimidines[13,14] and diazepines.[15]

Results and Discussion

In the course of our investigations on heterocyclic chemistry, we focused on the synthesis of trihalomethyl azoles by cyclocondensation reaction of 1,1,1,10,10,10-hexahalo-4,7-dimethoxydeca-3,7-dien-2,9-diones (**1** and **2**), a (2 × CCC) block, with (NO) hydroxylamine and (NN) hydrazine blocks. Compounds **1** and **2** were previously synthesised from the reaction of hexen-2,5-dione dimethyl acetal with trichloroacetyl chloride or trifluoroacetic anhydride in pyridine using chloroform as solvent.[5]

The cyclization of **1** and **2** with two equivalent of hydroxylamine hydrochloride was carried out in pyridine and ethanol. The mixture was refluxed for 16 hours and gave regiospecifically the 1,2-bis(5'-trihalomethyl-5'-hydroxy-4',5'-dihydroisoxazol-3'-yl) ethanes **3** and **4** (Scheme 1, Table 1). The mild reaction condition used for the synthesis of 1,2-bis(isoxazolyl)ethanes **3**-**6** was appropriate to preserve the trichloromethyl group on the heterocycle and to define the regiochemistry of the cyclocondensation.[16,17] The structure of 4,5-dihydro-isoxazole was evidenced by the presence of two doublets in the ^{1}H NMR spectrum in the range of δ 3.10 to 3.70 assigned to H4'a e H4'b. The observation of a peak around δ 47.0 in the ^{13}C NMR spectrum from methylene C4', further confirmed the structure of 4,5-dihydroisoxazoles **3** and **4** (Table 3). Compounds **3** and **4** were dehydrated with concentrated sulphuric acid at 45 °C for 3 hours to afford the corresponding 1,2-bis(5'-trihalomethyl-isoxazol-3'-yl) ethanes **5** and **6** in high yields (Scheme 1).

* e-mail: alexflores@smail.ufsm.br

The cyclization of **1** and **2** with hydrazine hydrate or phenyl hydrazine, in a molar ratio of 1:2, in chloroform at 0 °C for 4 hours, furnished regiospecifically, the aromatic 5-trihalomethylpirazoles **7**-**10** (Scheme 1, Table 1). The products, as oils, were crystallized from a mixture of hexane/ethyl acetate (5:1). The expected 4,5-dihydropyrazole intermediates were not isolated.

On the other hand, the reaction of **2** with two equivalents of hydrazines in a mixture of pyridine and methanol (or ethanol) under reflux for 24 hours led to 5-alkoxycarbonyl pyrazoles **11**-**14** (Scheme 2, Table 2). This reaction condition promoted the cyclocondensation and the hydrolysis of the trichloromethyl group.[18,19] In addition, the treatment of 5-trichloromethylpyrazoles **8** and **10** in pyridine with an appropriate alcohol under reflux, also led to the carboxypyrazoles **11**-**14**, in good yields (Scheme 2, Table 2).

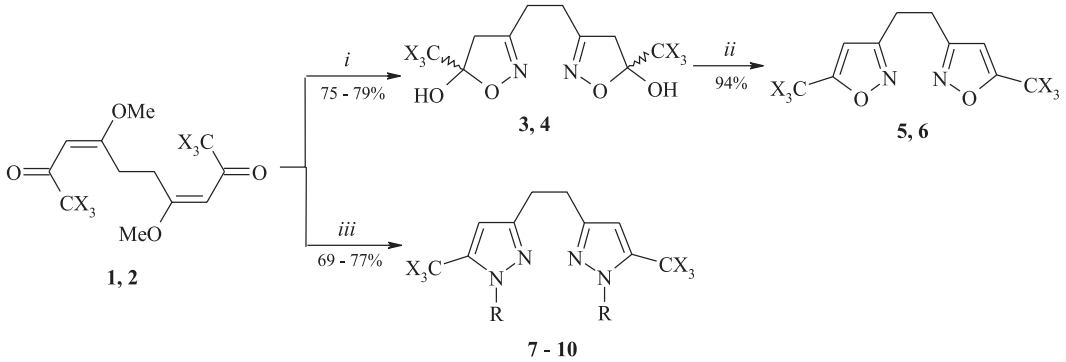
The structure of pyrazoles **7** - **15** was assigned by their NMR spectra. The ^{1}H NMR spectrum of aromatic pyrazoles displays the signal for methylene-3' at δ 3.19 - 3.85, for the aromatic H-4' at δ 6.33 – 6.85 and for **15** the N-Me appeared at δ 2.97. In the ^{13}C NMR spectra of **7**-**15** the signal from C-3' appeared at δ 138.7 - 155.3 and signal from C-5' at δ 140.3 – 145.0. For the pyrazole **15** they were assigned with two-dimensional correlation spectra HMBC (*Heteronuclear Multiple Bond Correlation)* by observing a cross peak between the C-5' (142.5 ppm) and the N-methyl hydrogen signal at 3.85 ppm that confirms the 5-ethoxycarbonylpyrazole isomers. The signals for C-4' of the pyrazole ring for compounds **7**-**15** appeared around δ 102.6 – 111 (Table 3).

The addition of precursor **2** to one equivalent of hydrazine hydrate in acetonitrile at room temperature for 4 hours, furnished the trichloromethylated tetrahydro-

Table 1. Reaction conditions,[a] yields and melting points of alkoxycarbonyl pyrazoles **3**-**10**

Precursor	X	R	Products	Found/calculated			m.p. (°C)[b]	Yields (%)[c]
				C	H	N		
1	F	-	dihydroisoxazole **3**	35.7/35.73	3.00/3.00	8.3/8.33	165-167	75
2	Cl	-	dihydroisoxazole **4**	27.5/27.62	2.40/2.32	6.5/6.44	201-203	79
3	F	-	isoxazole **5**	40.0/40.02	2.10/2.01	9.33/9.30	Oil	94
4	Cl	-	isoxazole **6**	30.0/30.11	1.50/1.52	7.10/7.02	156-158	94
1	F	H	pyrazole **7**	40.2/40.28	2.70/2.70	18.8/18.79	222-225	69
2	Cl	H	pyrazole **8**	30.3/30.26	2.00/2.03	14.1/14.12	160-162	73
1	F	Ph	pyrazole **9**	48.3/48.12	3.00/2.94	10.20/10.20	188-190	74
2	Cl	Ph	pyrazole **10**	58.7/58.67	3.60/6.58	12.40/12.44	184-186	77

[a] See experimental part; [b] The melting points are uncorrected; [c] Yields of isolated compounds.

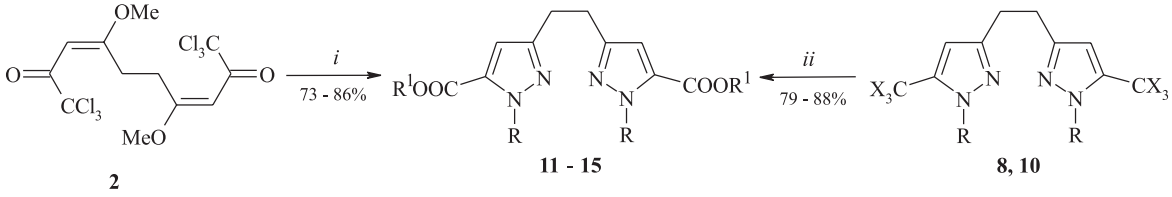


i. $NH_2OH.HCl$, Pyridine, EtOH, reflux (85° C), 16 hours
ii.H_2SO_4 98%, 40° C, 4 hours
iii.NH_2NHR, $CHCl_3$, 0° C, 4 hours

	X
1, 3, 5, 7, 9	F
2, 4, 6, 8, 10	Cl

	R
7, 8	H
9, 10	Ph

Scheme 1. Synthesis of 1,2-bis(5'-trihalomethylisoxazol-3'-yl)ethanes and 1,2-bis(5'-trihalomethylpyrazol-3'-yl)ethanes.



2 **11 - 15** **8, 10**

i. NH_2NHR, Pyridine, R^1OH, alcohol reflux, 24 hours
ii.Pyridine, R^1OH, alcohol reflux, 4 hours

	R	R^1
11	H	Me
12	H	Et
13	Ph	Me
14	Ph	Et
15	Me	Et

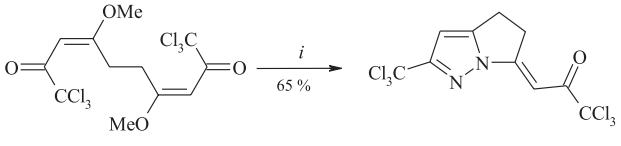
Scheme 2. Synthesis of the 1,2-bis(5'-alkoxycarbonylpyrazol-3'-yl)ethanes.

Table 2. Reaction conditions,[a] yields and melting point of pyrazole compounds **11-15**

Precursor	X	R	R^1	Products	Found/calculated			m.p. (°C)[b]	Yields (%)[c]
					C	H	N		
2 / 8	Cl	H	Me	**11**	58.50/58.53	5.80/5.73	22.90/22.75	185-187	74 / 77
2 / 8	Cl	H	Et	**12**	61.30/61.30	6.60/6.61	20.40/20.42	186-188	79 / 82
2 / 10	Cl	Ph	Me	**13**	72.50/72.34	5.65/5.57	14.10/14.06	128-130	82 / 86
2 / 10	Cl	Ph	Et	**14**	73.20/73.22	6.15/6.14	13.20/13.14	140-142	86 / 73
2	Cl	Me	Et	**15**	61.70/61.30	6.80/6.61	20.40/20.42	-	75

[a] See experimental part; [b] The melting points are uncorrected; [c] Yields of isolated compounds.

pyrrolo [1,5-b]pyrazole **16** (Scheme 3). The product was characterized by ^1H, ^{13}C NMR and 2D HMQC and HMBC spectroscopy data (Table 3). The presence of two CCl_3 groups with different chemical shift and the absence of methoxy group agree with the structure. To our knowledge there are no reports in the literature of this condensed heterocyclic compound. The formation of this condensed product was not observed when precursor **1** was used under the same conditions.



2 **16**

i. $NH_2NH_2.H_2O$ (1 eq.), MeCN, r.t., 4 hours

Scheme 3. Synthesis of the Tetrahydropyrrolo[1,5-b]pyrazole.

Conclusion

In conclusion, compounds **1** and **2** demonstrated high versatility as building blocks for the synthesis of many types of heterocycles that could provide potential biological activity. In addition, the use of 1,2-bis(5'-trihalomethylpyrazol-3'-yl)ethane (**7** and **9**) as ligands in coordination chemistry, is under investigation.[20] Also, a new type of condensed heterocycle (**16**) has been synthesized.

Experimental

Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial suppliers without further purification. Yields listed in Table 1 and 2 are for isolated compounds. ^1H, ^{13}C NMR spectra were recorded on a Bruker DPX 400 spectrometer (^1H at 400.13 MHz and ^{13}C at 100.63 MHz) at 298 K, digital resolution of ±0.01 ppm, 0.5 mol L^{-1} in $CDCl_3$, Acetone-d_6 or DMSO-d_6 containing TMS as in internal standard. All spectra were acquired in a 5 mm tube, at natural abundance. Mass spectra were registered in a HP 5973 MSD spectrometer connected to a HP 6890 GC and interfaced by a Pentium PC. The GC was equipped with a split-splitless, injector, auto sampler, cross-linked HP-5 capillary column (30 m, 0.32 mm of internal diameter), and helium was used as the carrier gas.

*1,2-Bis(5'-trihalomethyl-4',5'-dihydroisoxazol-3'-yl) ethanes (**3**,**4**)*

To a solution of 1,1,1,10,10,10-hexahalo-4,7-

Table 3. Spectral data[a] of compounds **3-16**

Product	GC-MS *m/z* (%)	^{1}H NMR δ (ppm), *J* (Hz) ^{13}C NMR, δ (ppm), *J* (Hz)
3[b]	336 (M^+, 13), 319 (27), 301 (25), 2 49 (37), 203 (30), 164 (62), 69 (100)	3.52 (d, 2H, H4'a, 18.6), 3.19 (d, 2H, H4'b, 18.6), 2.75 (s, 4H, H1,H2); 160.1 (C3'), 124.7 (q, CF_3, ^1J 281.4), 103.9 (q, C5', ^2J 33.4), 46.5 (C4'), 25.5 (C1,C2)
4[b]	399 (M^+- 36, 9), 381 (9), 353 (49), 297 (58), 214 (54), 54 (100)	3.76 (d, 2H, H4'a, 18.8), 3.29 (d, 2H, H4'b, 18.8), 2.76 (s, 4H, H1,H2); 159.6 (C3'), 111.9 (C5'), 102.5 (CCl_3), 47.0 (C4'), 24.8 (C1,C2)
5	300 (M^+, 5), 231 (10), 203 (100), 176 (28), 149 (29), 94 (49), 69 (84)	6.64 (s, 2H, H4'), 3.22 (s, 4H, H1,H2); 162.1 (C3'), 158.9 (q, C5', ^2J 42.2), 117.7 (q, CF_3, ^1J 268.6), 105.1 (C4'), 24.0 (C1,C2)
6[b]	398 (M^+, <1), 363 (12), 279 (26), 251 (34), 216 (100)	6.52 (s, 2H, H4'), 3.16 (s, 4H, H1,H2)169.0 (C5'), 162.3 (C3'), 103.5 (C4'), 84.5 (CCl_3), 24.4 (C1,C2)
7	298 (M^+, 42), 279 (14), 149 (100), 101 (62)	6.46 (s, 2H, H4'), 3.19 (s, 4H, H1,H2); 145.7 (C3'), 144.2 (q, C5', ^2J 37.0), 123.5 (q, CF_3, ^1J 265.7), 103.6 (C4'), 26.5 (C1,C2)
8	382 (M^+- 48, <1), 347 (23), 319 (12), 263 (100), 228 (58)	6.48 (s, 2H, H4'), 3.17 (s, 4H, H1,H2)155.3 (C3'), 145.0 (C5'), 102.6 (C4'), 92.3 (CCl_3), 25.5 (C1,C2)
9	450 (M^+, 17), 301 (16), 225 (100), 205 (42), 77 (65)	7.51-7.19 (m, 10H, Ph), 6.33 (s, 2H, H4'), 2.99 (s, 4H, H1,H2)143.4 (C3'), 142.8 (q, C5', ^2J 40.6), 138.5, 129.3, 129.2 ,125.8 (Ph), 121.1 (q, CF_3, ^1J 267.1), 103.7 (C4'), 25.3 (C1,C2)
10	458 (M^+ - 91, 100), 429 (9), 385 (10), 229 (24), 201 (26), 77 (49)	7.54-7.44 (m, 10H, Ph), 6.68 (s, 2H, H4'), 3.08 (s, 4H, H1,H2)150.4 (C3'), 144.9 (C5'), 139.9, 129.4, 128.6, 128.4 (Ph), 108.0 (C4'), 86.8 (CCl_3), 27.7 (C1,C2)
11[c]	278 (M^+, 60), 246 (100), 214 (22), 139 (24), 108 (42), 79 (52)	6.53 (s, 2H, H4'), 3.78 (s, 6H, OMe), 3.03 (s, 4H, H1,H2)162.0 (C=O), 145.4 (C3'), 140.7 (C5'), 106.3 (C4'), 51.5 (OMe), 25.1 (C1,C2)
12[c]	306 (M^+, 64), 260 (100), 232 (10), 214 (36), 186 (18), 108 (36)	6.46 (s, 2H, H4'), 4.19 (q, 4H, OCH_2), 2.96 (s, 4H, H1,H2), 1.21 (t, 6H, Me); 162.1 (C=O), 143.2 (C3'), 143.2 (C5'), 106.1 (C4'), 60.1 (OCH_2), 24.3 (C1,C2), 14.1 (Me)
13	306 (M^+, 64), 260 (100), 232 (10), 214 (36), 186 (18), 108 (36)	7.43 (m, 10H, Ph), 6.84 (s, 2H, H4'), 3.77 (s, 6H, OMe), 3.13 (s, 4H, H1,H2); 161.2 (C=O), 152.3 (C3'), 140.3 (C5'), 133.4, 129.0, 128.5, 125.9 (Ph), 111.4 (C4'), 51.9 (OMe), 27.8 (C1,C2)
14	458 (M^+, 100), 385 (11), 229 (28), 201 (27), 77 (43)	7.47-7.25 (m, 10H, Ph), 6.65 (s, 2H, H4'), 4.39 (q, 4H, OCH_2), 2.92 (s, 4H, H1, H2), 1.39 (t, 6H, Me); 162.3 (C=O), 144.0 (C5'), 138.7 (C3'), 138.7, 129.3, 129.1, 125.9 (Ph), 108.0 (C4'), 61.0 (OCH_2), 25.3 (C1,C2), 14.3 (Me)
15	-	6.63 (s, 2H, H4'), 4.39 (q, 4H, OCH_2), 3.85 (s, 4H, H1,H2), 2.97 (s, 6H, N-Me), 1.38 (t, 6H, Me); 162.2 (C=O), 142.5 (C5'), 142.3 (C3'), 107.3 (C4'), 60.9 (OCH_2), 36.9 (N-Me), 24.4 C1,C2), 14.3 (Me)
16[b]	382 (M^+, <5), 347 (14), 319 (8), 263 (100), 228 (43)	7.10 (t, 1H, CHC=O, 4.4), 6.75 (s, 1H, H3), 3.85 (m, 2H, H5), 3.25 (m, 2H, H4); 181.9 (C=O), 164.7 (C6), 161.5 (C2), 155.9 (C3a), 102.4 (CHC=O), 98.4 (C(O)CCl_3), 97.0 (C3), 91.8 (CCl_3), 35.3 (C5), 22.9 (C4)

[a] NMR spectra were recorded on a Bruker DPX 400 in $CDCl_3$/TMS; [b] aceton-d_6; [c] DMSO-d.

dimethoxydeca-3,7-dien-2,9-dione (**1** or **2**) (2 mmol) in pyridine (4.2 mmol) was added hydroxylamine hydrochloride (4.2 mmol) in ethanol (15 mL). The mixture was stirred for 16 hours at 78 °C. The solvent was removed under reduced pressure and the residue was extracted with ethyl acetate and recrystallized from a mixture of hexane/ethyl acetate (5:1).

*1,2-Bis(5'-trihalomethylisoxazol-3'-yl) ethanes (**5**,**6**)*

A mixture of 1,2-bis(5'-trihalomethyl-4',5'-dihydro isoxazol-3'-yl)ethane (**3** or **4**) (1 mmol) in 97% sulphuric acid (8 mL) was stirred at 40 °C for 4 hours. The mixture was poured slowly on 25 mL of ice-water and the solution was extracted with ethyl acetate (3 × 10 mL). The solvent was removed under reduced pressure and the product was obtained in high purity.

*1,2-Bis(5'-trihalomethylpyrazol-3'-yl) ethanes (**7**-**10**)*

The appropriate hydrazine (4,2 mmol, 0.20 mL of hydrazine monohydrate or 4.2 mmol, 0.42 mL of 97% phenylhydrazine) was added dropwise at 0 °C to a stirred solution of 1,1,1,10,10,10-hexahalo-4,7-dimethoxydeca-3,7-dien-2,9-dione (**1** or **2**) (2 mmol) in chloroform (15 mL) or acetonitrile (15 mL). The mixture was stirred for 4

hours at room temperature. The solution was washed with 0.1 mol L^{-1} HCl (3 × 15 mL) and extracted with ethyl acetate (3×10 mL). The solvent was removed under reduced pressure and the product was recrystallized from a mixture of hexane/ethyl acetate (5:1).

*1,2-Bis(5'-alkoxycarbonylpyrazol-3'-yl) ethanes (**11-15**)*

To a stirred solution 1,1,1,10,10,10-hexachoro-4,7-dimethoxydeca-3,7-dien-2,9-dione (**2**) (2 mmol) in pyridine (4.2 mmol) was added the appropriate hydrazine hydrochloride (4.2 mmol) in methanol (or ethanol) (15 mL) at room temperature. The mixture was stirred under reflux for 16 hours. The solution was washed with 0.1 mol L^{-1} HCl (3 × 15 mL) and extract with ethyl acetate (3 × 10 mL). After removal of the solvent under reduced pressure, the product was recrystallized from a mixture of hexane/ethyl acetate (5:1).

*Tetrahydropyrrolo[1,5-b] pyrazole (**16**)*

Hydrazine hydrate (2.1 mmol) was added drop wise at room temperature to a stirred solution of 1,1,1,10,10,10-hexachloro-4,7-dimethoxydeca-3,7-dien-2,9-dione (**2**) (2 mmol) in acetonitrile (20 mL). The mixture was stirred for 4 hours at room temperature. The solution was washed with 0.1 mol L^{-1} HCl (3 × 15 mL) and extracted with ethyl acetate (3 × 10 mL). The solvent was removed under reduced pressure and the product was recrystallized from hexane furnishing a gray solid. Yield 65%, m.p. 136-138 °C.

Acknowledgments

The authors thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), PADCT-III/CNPq 62.0228/97-0-QEQ, and Fundação de Apoio a Pesquisa do Estado do Rio Grande do Sul (FAPERGS) for financial support. Fellowship from CAPES (W.C.) is also acknowledged.

References

1. Kromann, H.; Slok, F. A.; Johansen, T. N.; Krogsgaard-Larsen, P.; *Tetrahedron* **2001**, *57*, 2195; Hjeds, H.; Christensen, I. T.; Cornett, C.; Frolund, B.; Falch, E.; Pedersen, J. B.; Krogsgaard-Larsen, P.; *Acta Chem. Scand.* **1992**, *46*, 772; Bang-Andersen, B.; Lenz, S. M.; Skjaerbaek, N.; Soby, K. K.; Hansen, H. O.; Ebert, B.; Bogeso, K. P.; Krogsgaard-Larsen, P.; *J. Med. Chem.* **1997**, *40*, 2831; Bräuner-Osborne, H.; Nielsen, B.; Krogsgaard-Larsen, P.; *Eur. J. Pharmacol.* **1998**, *350*, 311; Zimmermann, D.; Janin, Y. L.; Brehm, L.; Bräuner-Osborne, H.; Ebert, B.; Johansen, T. N.; Madsen, U.; Krogsgaard-Larsen, P.; *Eur. J. Med.Chem.* **2000**, *35*, 69; Bräuner-Osborne, H.; Egebjerg, J.; Nielsen, E. O.; Madsen, U.; Krogsgaard-Larsen, P.; *J. Med. Chem.* **2000**, *43*, 2609.
2. Mello, C. F.; Souza, F. R.; Souza, V. T.; Reatzlaff, V.; Borges, L. P.; Oliveira, M. R.; Bonacorso, H. G.; Zanatta, N.; Martins, M. A. P.; *Eur. J. Pharmacol.* **2002**, *451*, 141
3. Driessen, W. L.; Schuitema, A. M.; Engelen, M.; Koval, I. A.; Gorter, S.; Reedijk, J.; *Inorg. Chim. Acta* **2001**, *324*, 57.
4. Martins, M. A. P.; Colla, A.; Clar, G. ; Krimmer, S.; Fischer, P.; *Synthesis* **1991**, 483.
5. Martins, M. A. P.; Bastos, G. P.; Bonacorso, H. G.; Zanatta, N.; Flores, A. F. C.; Siqueira, G.M.; *Tetrahedron Lett.* **1999**, *40*, 4309.
6. Bonacorso, H. G.; Martins, M. A. P.; Bittencourt, S. R.T.; Lourega, R. V.; Zanatta, N. ; Flores, A. F. C.; *J. Fluorine Chem.* **1999**, *99*, 177.
7. Flores, A. F. C.; Brondani, S.; Zanatta, N.; Rosa, A.; Martins, M. A. P.; *Tetrahedron Lett.* **2002**, *43*, 8701.
8. Martins, M. A. P.; Beck, P.; Cunico, W.; Pereira, C. M. P.; Sinhorin, A. P.; Blanco, R. F.; Peres, R.; Bonacorso, H. G.; Zanatta, N.; *Tetrahedron Lett.* **2002**, *43*, 7005.
9. Martins, M. A. P.; Sinhorin, A. P.; Zimmermann, N. E. K.; Zanatta, N.; Bonacorso, H. G.; Bastos, G. P.; *Synthesis* **2002**, 1959.
10. Flores, A. F. C.; Martins, M. A. P.; Rosa, A.; Flores, D. C.; Zanatta, N.; Bonacorso, H. G.; *Synth. Commun.* **2002**, *32*, 1585.
11. Flores, A. F. C.; Zanatta, N.; Rosa, A.; Brondani, S.; Martins, M. A. P.; *Tetrahedron Lett.* **2002**, *43*, 5005.
12. Martins, M. A. P.; Pereira, C. M. P.; Sinhorin, A. P.; Bastos, G. P.; Zimmermann, N. E. K.; Rosa, A.; Bonacorso, H. G.; Zanatta, N.; *Synth. Comm.* **2002**, *32*, 419.
13. Zanatta, N.; Lopes, E. C. S.; Fantinel, L.; Bonacorso, H. G.; Martins, M. A. P.; *J. Heterocyclic Chem.* **2002**, *39*, 943.
14. Bonacorso, H. G.; Lopes, I. S.; Wastowski, A. D.; Zanatta, N.; Martins, M. A. P.; *J. Fluorine Chem.* **2003**, *120*, 29.
15. Bonacorso, H. G.; Bittencourt, S. R. T.; Wastowski, A. D.; Wentz, A. P.; Zanatta, N. Martins, M. A. P.; *J. Heterocyclic Chem.* **1999**, *36*, 45.
16. Spiegler, W.; Götz, N.; *Synthesis* **1986**, 69.
17. Martins, M. A. P.; Flores, A. F. C.; Bastos, G. P.; Sinhorin, A. P.; Bonacorso, H. G.; Zanatta N.; *Tetrahedron Lett.* **2000**, *41*, 293.
18. Martins, M. A. P.; Freitag, R.; Flores, A. F. C.; Zanatta, N.; *Synthesis* **1995**, 1491.
19. Martins, M. A. P.; Freitag, R.; Rosa, A.; Flores, A. F. C.; Zanatta, N.; Bonacorso, H. G.; *J. Heterocyclic Chem.* **1999**, *36*, 217.
20. Martins, M. A. P.; Höerner, M., unpublished results.

Received: April 19, 2004
Published on the web: February 17, 2005