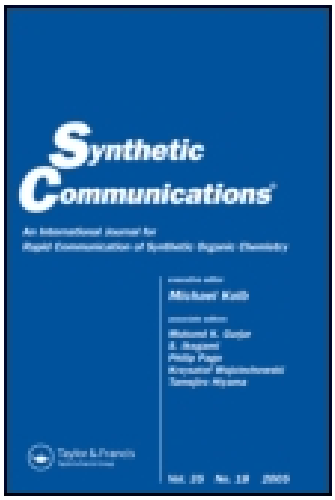


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

SYNTHESIS OF 3-METHYLISOXAZOLE- 5-CARBOXAMIDES AND 5-[(1H-PYRAZOL-1-YL)CARBONYL]- 3-METHYLISOXAZOLES

Marcos A. P. Martins [a], Marcelo Neto [a], Adilson P. Sinhorin [a], Giovani P. Bastos [a], Nilo E. K. Zimmermann [a], Adriano Rosa [a], Helio G. Bonacorso [a] & Nilo Zanatta [a]

[a] Departamento de Química, Núcleo de Química de Heterociclos (NUQUIMHE), Universidade Federal de Santa Maria, Santa Maria, RS, 97.105-900, Brazil

Published online: 16 Aug 2006.

To cite this article: Marcos A. P. Martins, Marcelo Neto, Adilson P. Sinhorin, Giovani P. Bastos, Nilo E. K. Zimmermann, Adriano Rosa, Helio G. Bonacorso & Nilo Zanatta (2002) SYNTHESIS OF 3-METHYLISOXAZOLE- 5-CARBOXAMIDES AND 5-[(1H-PYRAZOL-1-YL)CARBONYL]- 3-METHYLISOXAZOLES, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 32:3, 425-433

To link to this article: http://dx.doi.org/10.1081/SCC-120002127

SYNTHETIC COMMUNICATIONS, 32(3), 425–433 (2002)

SYNTHESIS OF 3-METHYLISOXAZOLE-5-CARBOXAMIDES AND 5-[(1*H*-PYRAZOL-1-YL)CARBONYL]-3-METHYLISOXAZOLES

Marcos A. P. Martins,* Marcelo Neto, Adilson P. Sinhorin, Giovani P. Bastos, Nilo E. K. Zimmermann, Adriano Rosa, Helio G. Bonacorso, and Nilo Zanatta

Departamento de Química, Núcleo de Química de Heterociclos (NUQUIMHE), Universidade Federal de Santa Maria, 97.105-900 Santa Maria, RS, Brazil

ABSTRACT

The one-pot synthesis of six 3-methylisoxazole-5-carboxamides **2** [where the *N*-substituents are $R^1 = H$, Me and $R^2 = Ph$, CH_2Ph, *n*-Bu, $C(CH_3)_2Et$, 3-methylisoxazol-5-yl] and twelve 5-[(1*H*-pyrazol-1-yl)carbonyl]-3-methyl isoxazoles **3** and **4** [where the pyrazole substituents are R^3 (C5/C3) = CO_2Et, CF_3 and R^5 (C3/C5) = H, Me, Et, Ph] from the 3-methyl isoxazole-5-carboxylic acid, thionyl chloride and the corresponding amine or pyrazole is reported. In the synthesis of 5-[(1*H*-pyrazol-1-yl)carbonyl]-3-methylisoxazoles we obtained a mixture of *1,3-* and *1,5-isomers* **3** and **4** in variable

*Corresponding author. E-mail: mmartins@base.ufsm.br; http://www.ufsm.br/nuquimhe

ratios, i.e., the substituent R^3 (CO_2Et and CF_3) are present in position 3 or 5 on the pyrazole ring.

Isoxazole derivatives possess very interesting pharmacological properties, especially isoxazolecarbonyl compounds that show marked action as diuretic,[1] antiinflammatory, analgesic, antipyretic, anticoagulant, and antireumatic. Isoxazolecarbonyl compounds are also important precursors for the synthesis of other compounds such as agrochemicals and microbicides.[2] As a part of our research program, we developed a general one-step procedure for preparing a series of analytically pure 4-alkoxy-1,1,1-trihalo-3-alken-2-ones, from the acylation of several enol ethers (or acetals), in molar quantities.[3] These compounds have been used as precursors of a variety of substituted five-, six- and seven-membered heterocyclic compounds, e.g., isoxazoles,[3,4] pyrazoles,[5] pyrimidines[6] and diazepines.[7] Recently,[8] we reported a one-pot synthesis of isoxazole-5-carboxylic acids from the cyclocondensation of 4-alkoxy-1,1,1-trichloro-3-alken-2-ones with hydroxylamine, in hydrochloric acid or sulfuric acid medium. The aim of this work is to show the one-pot synthesis of a series 3-methylisoxazole-5-carboxamides (**2**) and 5-[(1*H*-pyrazol-1-yl)carbonyl]-3-methylisoxazoles (**3, 4)** from the 3-methyl isoxazole-5-carboxylic acid (**1**), thionyl chloride and the corresponding amine or pyrazole (scheme).

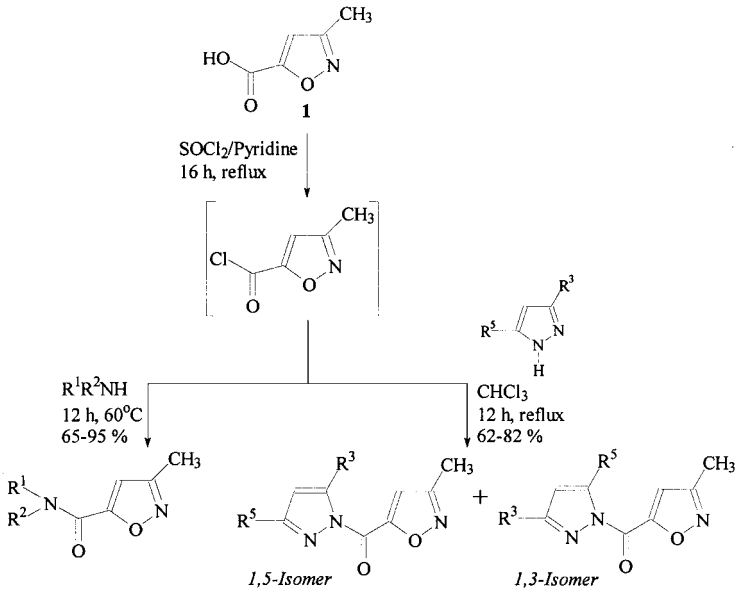
3-Methylisoxazole-5-carboxylic acid (**1**) was synthesized from the cyclocondensation reaction of 4-alkoxy-1,1,1-trichloro-3-alken-2-ones with hydroxylamine in sulfuric acid.[8] The 3(5)-trifluoromethylpyrazoles and pyrazole-3(5)-carboxylic acid ethyl ester were synthesized according as previous report.[5] The preparation of 3-methylisoxazole-5-carbonyl chloride from **1** was carried out with an excess of thionyl chloride and catalytic amounts of pyridine, following by reflux for 16 h.

Compounds **2a–f** were obtained by addition of amines to equimolar amounts of 3-methylisoxazole-5-carbonyl chloride, obtained *in situ*. The mixture was stirred for 12 h at 60°C, and isolated products were recrystallized. Compounds **3a–d** and **4a–d** were obtained by addition of pyrazoles to 3-methylisoxazole-5-carbonyl chloride as described for **2** with chloroform as solvent. The mixture was stirred for 12 h at reflux. The recrystallized products were identified by ^1H and ^{13}C NMR spectroscopy.

The assignments of *Z*- and *E*-isomers in the carboxamide group of **2a–f** were done based on the literature data.[9] Then, we assign compounds **2a–e** as *E*-isomer and **2f** shown a 1 : 1 mixture of *Z*- and *E*-isomers.

The assignments of *1,3*- and *1,5-isomers* of compounds **3** and **4** were done experimentally by the aromatic solvent induced shifts (ASIS)[5,10] and a two-dimensional correlation spectrum HMBC (*Heteronuclear Multiple Bond*

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016



Compd. 2	R^1	R^2
a	H	Ph
b	H	CH_2Ph
c	H	$C(CH_3)_2Et$
d	H	5-methylisoxazol-3-yl
e	Me	Ph
f	Me	*n*-Bu

Compd.	R^3
3	COOEt
4	CF_3

Compd. 3, 4	R^5
a	H
b	Me
c	Et
d	Ph

Scheme.

Correlation).[11,12] In the ASIS experiment, the ^{1}H NMR spectra are recorded in chloroform-d_1 and benzene-d_6 as solvents and all ^{1}H signals were shifted to upfield in benzene-d_6 when compared with the initial positions in chloroform-d_1. Due to the anisotropy *solvatation*[9,5] of the aromatic solvent, the hydrogens closer to N-1 (an amidic nitrogen, with partial positive charge) experience more shielding than the others hydrogens of the molecule. Then we observed that R^5 (hydrogen or alkyl groups) in compounds **3a–c** and **4a–c** was shifted upfield more in one isomer than in the other.

Thus, it was possible to assign the isomer that resonates more upfield as the *1,3-isomer* (R^5 is closer to N-1). The assignment proposed were confirmed with the HMBC method. In the HMBC experiment, the long range coupling constant ($^{2,3}J_{C\text{-}H}$) was optimized for 7 Hz. The experiment showed that the carbonyl carbon (attached on N-1) presented a cross-peak with the hydrogen attached on C-5 ($R^5 = H$) for compounds **3a** and **4a** which were used as standard compounds. This fact identified the *1,3-isomers*, where $R^5 = H$ is three bonds from the N-1 carbonyl carbon.

EXPERIMENTAL

Unless otherwise indicated all common reagents and solvents were used as obtained from commercial suppliers without further purification. Yields listed in Table 1 are of isolated compounds and all melting points were taken on a melting point microscope Reichert-Thermovar. Elemental analysis was carried out on an Elemental Analysensysteme Vario EL equipment. ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 400, at 298 K, digital resolution of ± 0.01 ppm, 0.5 M in chloroform-d_1/TMS.

Synthesis of 3-Methylisoxazole-5-carboxamides 2a–f

General Procedure

A mixture of **1** (10 mmol), with catalytic amounts of pyridine, and thionyl chloride (1.43 g, 12 mmol) was refluxed for 12–16 h. The mixture was cooled to room temperature, the amine (R^1R^2NH, 12 mmol) added slowly, and the mixture stirred for 8–12 h at 60°C. The crude product was washed with water and then diluted in chloroform. The solvent was evaporated and the products **2a–f** were recrystallized from a mixture of hexane/ethyl acetate. Yields and selected physical and spectroscopic data are presented in Tables 1 and 2.

Synthesis of 5-[(1*H*-Pyrazol-1-yl)carbonyl]-3-methylisoxazoles 3a–d and 4a–d

General Procedure

A mixture of **1** (10 mmol), with catalytic amounts of pyridine, and thionyl chloride (1.43 g, 12 mmol) was refluxed for 12–16 h. The mixture

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Table 1. Selected Physical and Elemental Analysis Data of Compounds **2a–f, 3a–d** and **4a–d**

Compound	Molecular Formula (M. wt.)	Isomer Ratio *1,3* : *1,5*[a]	Yield (%)[b]	M.P. (°C)	Elemental Analysis (%) Calcd./Found C	H
2a	$C_{11}H_{10}N_2O_2$ (202.21)	–	95	155–156	65.34 65.16	4.98 4.97
2b	$C_{12}H_{12}N_2O_2$ (216.23)	–	88	148–150	66.66 66.60	5.59 5.58
2c	$C_{10}H_{16}N_2O_2$ (196.24)	–	72	140–141	61.21 61.04	8.22 8.20
2d	$C_9H_9N_3O_3$ (207.18)	–	78	149–153	52.18 51.90	4.38 4.35
2e	$C_{12}H_{12}N_2O_2$ (216.23)	–	88	158–160	66.66 66.43	5.59 5.57
2f	$C_{10}H_{16}N_2O_2$ (196.24)	–	55	164–166	61.21 61.00	8.22 8.19
3a	$C_{11}H_{11}N_3O_4$ (249.21)	4 : 1	73	122–124	53.02 52.82	4.45 4.40
3b	$C_{12}H_{13}N_3O_4$ (263.24)	2 : 3	72	84–85	54.75 54.55	4.98 4.95
3c	$C_{13}H_{15}N_3O_4$ (277.26)	4 : 5	70	98–99	56.32 56.10	5.45 5.43
3d	$C_{17}H_{15}N_3O_4$ (325.31)	3 : 5	62	111–113	62.77 62.53	4.65 4.63
4a	$C_9H_6F_3N_3O_2$ (245.15)	2 : 1	82	102–103	44.09 43.95	2.47 2.46
4b	$C_{10}H_8F_3N_3O_2$ (259.18)	4 : 1	80	108–109	46.34 46.19	3.11 3.09
4c	$C_{11}H_{10}F_3N_3O_2$ (273.21)	3 : 1	78	148–150	48.36 48.20	3.69 3.67
4d	$C_{15}H_{10}F_3N_3O_2$ (321.25)	5 : 1	78	99–100	56.08 55.90	3.14 3.13

[a]Isomer ratio obtained from ^{1}H NMR data. [b]Yields of isolated products.

was cooled to room temperature, the pyrazole (10 mmol) in chloroform (5 mL) added slowly, and the mixture stirred for 8–12 h reflux. The crude product was washed with water and then diluted in chloroform. The solvent was evaporated and the products **2a–f** were recrystallized from a mixture of

Table 2. Selected ^{1}H and ^{13}C NMR Data[a] of Compounds **2a–f, 3, 4a–d**

Compound	δ ^{1}H	δ ^{13}C, J (Hz)
2a	8.29 (NH, s), 6.85 (H4, s), 2.38 (H6, s), 7.67–7.22 (H phenyl)	161.2 (C3), 108.4 (C4), 153.7 (C5), 11.4 (C6), 163.0 (C7), 136.6–121.2 (C phenyl).
2b	9.48 (NH, s), 6.90 (H4, s), 2.35 (H6, s), 4.38 (CH_2, s), 7.41–7.22 (H phenyl)	160.5 (C3), 107.0 (C4), 155.8 (C5), 11.0 (C6), 163.0 (C7), 138.7–126.9 (C phenyl), 42.2 (CH_2).
2c	6.30 (NH, s), 6.70 (H4, s), 2.35 (H6, s), 1.82 (CH2, q), 1.43 (2CH3, s), 0.90 (CH3, t)	160.9 (C3), 107.3 (C4), 155.3 (C5), 11.4 (C6), 163.8 (C7), 55.1 (CH28), 32.9 (CH29), 26.3 (CH210), 8.3 (CH311).
2d	3.50 (NH, s), 7.25 (H4, s), 2.35 (H6, s), 6.69 (H4, s), 2.52 (Me5, s)	160.6 (C3), 108.4 (C4), 154.1 (C5), 11.1 (C6), 161.5 (C7), 169.9 (C8), 97.0 (C9), 157.5 (C10), 12.1 (Me11).
2e	7.20 (H4, s), 2.20 (H6, s), 3.45 (Me, s), 7.40–7.22 (H phenyl)	159.0 (C3), 108.2 (C4), 157.5 (C5), 11.0 (C6), 162.7 (C7), 142.6–126.7 (C phenyl).
2f	9.48; 6.79 (H4, s), 6.74 (H4′, s), 2.31 (H6, s), 2.30 (H6′, s), 3.07 (Me, s), 2.98 (Me′, s), 3.44 (CH2, t), 3.37 (CH2′, t), 1.31 (CH2, qui), 1.20 (CH2′, qui), 1.55 (CH2, sex), 0.90 (CH3, t)	160.5 (C3), 160.7 (C3′), 107.3 (C4), 106.9 (C4′), 157.8 (C5), 157.7 (C5′), 10.8 (C6), 163.3 (C7), 35.8 (Me), 33.0 (Me′), 49.5 (C8), 47.0 (C8′), 29.9 (CH2), 28.3 (CH2′), 19.4 (2CH3), 19.0 (2CH2′), 13.6 (CH3), 13.4 (CH3′).
3a	7.67 (H4, s), 2.47 (H6, s), 2.40 (H6′, s), 8.47 (H10, s), 7.60 (H10′, s), 7.01 (H11, s), 6.90 (H11′, s), 4.47 (H15, s), 4.45 (H15′, s), 1.45 (H16, s)	160.8 (C3), 115.6 (C4), 158.0 (C5), 159.4 (C5′), 11.5 (C6), 160.4 (C7), 159.4 (C7′), 149.0 (C10), 153.5 (C10′), 111.6 (C11), 108.0 (C11′), 131.2 (C12), 132.5 (C12′), 161.0 (C13), 161.5 (C13′), 61.8 (C15), 61.0 (C15′), 14.2 (C16).
3b	7.51 (H4, s), 2.43 (H6, s), 2.39 (H6′, s), 2.70 (Me, s), 6.71 (H11, s), 6.60 (H11′, s), 4.43 (H15, s), 4.35 (H15′, s), 1.41 (H16, s), 1.30 (H16′, s)	160.7 (C3), 115.1 (C4), 155.4 (C5), 11.2 (C6), 159.4 (C7), 158.8 (C7′), 14.0 (Me), 147.0 (C10), 146.4 (C10′), 111.6 (C11), 107.4 (C11′), 140.9 (C12), 143.0 (C12′), 161.0 (C13), 161.2 (C13′), 61.5 (C15), 61.0 (C15′), 14.1 (C16).

(*continued*)

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Table 2. Continued

Compound	δ ^{1}H	δ ^{13}C, J (Hz)
3c	7.53 (H4, s), 2.44 (H6, s), 2.38 (H6′, s), 3.71 (CH2, q), 1.40 (CH3, t), 6.75 (H11, s), 6.60 (H11′, s), 4.43 (H15, s), 4.35 (H15′, s), 1.41 (H16, s), 1.30 (H16′, s)	161.7 (C3), 115.0 (C4), 156.8 (C5), 11.3 (C6), 159.5 (C7), 19.2 (CH2), 13.1 (CH3), 149.0 (C10), 105.8 (C11), 141.3 (C12), 160.3 (C13), 60.9 (C15), 14.1 (C16).
3d	7.67 (H4, s), 2.40 (H6, s), 2.30 (H6′, s), 7.76–7.40 (H phenyl), 7.20 (H11, s), 7.03 (H11′, s), 4.39 (H15, s), 4.31 (H15′, s), 1.36 (H16, s), 1.32 (H16′, s)	160.0 (C3), 110.3 (C4), 159.4 (C5), 11.4 (C6), 160.0 (C7), 129.1–126.0 (C phenyl), 148.0 (C10), 105 (C11), 140.0 (C12), 160.0 (C13), 61.4 (C15), 13.9 (C16).
4a	7.60 (H4, s), 2.49 (H6, s), 2.37 (H6′, s), 8.53 (H10, s), 7.76 (H10′, s), 6.83 (H11, s), 6.70 (H11′, s)	160.1 (C3), 115.6 (C4), 153.1 (C5), 11.4 (C6), 157.7 (C7), 131.8 (C10), 130.5 (C10′), 104.4 (C11), 108.0 (C11′), 147.0 (C12 $J = 39.3$), 120.0 (C13 $J = 270.1$).
4b	7.43 (H4, s), 2.45 (H6, s), 2.34 (H6′, s), 2.73 (Me, s)	160.6 (C3), 115.1 (C4), 155.2 (C5), 11.4 (C6), 159.3 (C7), 14.3 (Me), 147.2 (C10), 143.0 (C10′), 108.1 (C11), 102.9 (C11′), 146.0 (C12 $J = 39.1$), 118.0 (C13).
4c	7.43 (H4, s), 2.45 (H6, s), 2.47 (H6′, s), 3.16 (CH2, q), 2.75 (CH2′, q), 1.35 (CH3, t), 1.32 (CH3′, t)	160.8 (C3), 115.0 (C4), 155.1 (C5), 11.3 (C6), 158.8 (C7), 21.6 (CH2), 18.6 (CH2′), 11.9 (CH3), 12.7 (CH3′), 153.6 (C10), 148.1 (C10′), 106.3 (C11), 104.3 (C11′), 145.0 (C12 $J = 39.0$), 118.0 (C13 $J = 270.0$).
4d	7.54 (H4, s), 2.46 (H6, s), 2.34 (H6′, s), 7.06 (H11, s), 6.97 (H11′, s), 7.85–7.54 (H phenyl)	162.0 (C3), 116.0 (C4), 155.5 (C5), 11.5 (C6), 159.7 (C7), 131.2–127.6 (C phenyl), 154.0 (C10), 113.8 (C11), 136.3 (C12), 120.0 (C13).

[a] ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 400, at 298 K, 0.5 M in chloroform-d_1/TMS. For compound **2f** the data labeled as (′) refers to *E*-isomer (R^2 is *syn* to carbonyl oxygen in the carboxamide group) and for **3**, **4** the data refers to *1,5-isomer* (see scheme).

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

hexane/ethyl acetate. Yields and selected physical and spectroscopic data are presented in Tables 1 and 2.

ACKNOWLEDGMENTS

The authors thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq/PADCT), Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS) for financial support. The fellowhips from CNPq, CAPES and FAPERGS are also acknowledged.

REFERENCES

1. Fossa, P.; Menozzi, G.; Schenone, P.; Filippelli, W.; Russo, S.; Lucarelli, C.; Marmo, E. Farmaco **1991**, *46*, 789; Bartlett, R.R.; Schleyerbach, R. Int. J. Immunopharmac. **1985**, *7*, 7.
2. Kuene, S.; Kaestner, G.; Mueller, J.; Borgman, E. Heterocycles **1988**, *28*, 110.
3. Martins, M.A.P.; Colla, A.; Clar, G.; Fischer, P.; Krimmer, S. Synthesis **1991**, *6*, 483; Martins, M.A.P.; Siqueira, G.M.; Flores, A.F.C.; Clar, G.; Zanatta, N. Química Nova **1994**, *17*, 24. Chem. Abstr. **1995**, *122*, 187063a; Martins, M.A.P.; Flores, A.F.C.; Siqueira, G.M.; Freitag, R.; Zanatta, N. Química Nova **1994**, *17*, 298. Chem. Abstr. **1994**, *121*, 230377z.
4. Martins, M.A.P.; Zoch, A.N.; Bonacorso, H.G.; Zanatta, N.; Clar, G. J. Heterocycl. Chem. **1995**, *32*, 739; Martins, M.A.P.; Flores, A.F.C.; Freitag, R.A.; Zanatta, N. J. Heterocycl. Chem. **1995**, *32*, 731; Martins, M.A.P.; Flores, A.F.C.; Freitag, R.A.; Zanatta, N. J. Heterocycl. Chem. **1996**, *33*, 1223; Martins, M.A.P.; Siqueira, G.M.; Bastos, G.P.; Zanatta, N. J. Heterocycl. Chem. **1996**, *33*, 1.
5. Martins, M.A.P.; Freitag, R.A.; Rosa, A.; Flores, A.F.C.; Zanatta, N.; Bonacorso, H.G. J. Heterocycl. Chem. **1999**, *36*, 217; Martins, M.A.P.; Freitag, R.A.; Flores, A.F.C.; Zanatta, N. Synthesis **1995**, 1491; Martins, M.A.P.; Braibante, M.E.F.; Clar, G. J. Heterocycl. Chem. **1993**, *30*, 1159; Bonacorso, H.G.; Wastowski, A.D.; Zanatta, N.; Martins, M.A.P.; Naue, J.A. J. Fluorine Chem. **1998**, *92*, 23; Bonacorso, H.G.; Wastowski, A.D.; Zanatta, N.; Martins, M.A.P.; Naue, J.A. Tetrahedron **1999**, *55*, 345.

6. Zanatta, N.; Pacholski, I.L.; Blanco, I.; Martins, M.A.P. J. Braz. Chem. Soc. **1991**, *2*, 118; Chem. Abstr. **1994**, *120*, 323443n; Zanatta, N.; Madruga, C.C.; Clerici, E.; Martins, M.A.P. J. Heterocycl. Chem. **1995**, *32*, 735; Zanatta, N.; Cortelini, M.F.M.; Carpes, M.J.S.; Bonacorso, H.G.; Martins, M.A.P. J. Heterocycl. Chem. **1997**, *34*, 509; Zanatta, N.; Fagundes, M.B.; Ellensohn, R.; Bonacorso, H.G.; Martins, M.A.P. J. Heterocycl. Chem. **1998**, *35*, 451.
7. Bonacorso, H.G.; Bittencourt, S.T.; Wastowski, A.D.; Wentz, A.P.; Zanatta, N.; Martins, M.A.P. Tetrahedron Lett. **1996**, *37*, 9155; Bonacorso, H.G.; Bittencourt, S.T.; Wastowski, A.D.; Wentz, A.P.; Zanatta, N.; Martins, M.A.P. J. Heterocycl. Chem. **1999**, *36*, 45.
8. Martins, M.A.P.; Flores, A.F.C.; Bastos, G.P.; Sinhorin, A.; Bonacorso, H.G.; Zanatta, N. Tetrahedron Lett. **2000**, *41*, 293.
9. Stewart, W.E.; Siddall III, T.H. Chem. Rev. **1970**, *70*(5), 517; Bonacorso, H.G.; Caro, M.S.B.; Zanatta, N.; Martins, M.A.P. Spectrosc. Lett. **1993**, *26*(8), 1381.
10. Elguero, J.; Jacquier, R.; Tien Duc, H.C.N. Bull. Soc. Chim. Fr. **1996**, 3727.
11. Kolehmainen, E.; Gawinecki, R.; Osmialowski, B.; Trzebiatowska, K. Magn. Reson. Chem. **1997**, *35*, 778.
12. Kolehmainen, E.; Lappalainen, K.; Saman, D.; Holy, A.; Günter, J. Magn. Reson. Chem. **1998**, *36*, 442.

Received in the USA March 19, 2001

Request Permission or Order Reprints Instantly!