# Reactivity of *p*-Phenyl Substituted β-Enamino Compounds Using K-10/Ultrasound. I. Synthesis of Pyrazoles and Pyrazolinones



Claudete J. Valduga, Hugo S. Braibante and Mara E. F. Braibante*

Departamento de Química, Universidade Federal de Santa Maria, 97105-900 Santa Maria, RS, Brazil

Received April 2, 1997

The reactivity of the β-enamino ketones, 3-amino-1-(*p*-phenyl-substituted)-2-buten-1-ones **1a-d** and β-enamino esters, ethyl 3-amino-3-(*p*-phenyl-substituted)-2-propenoates **5a-d** was systematically studied when allowed to react with hydrazine and methylhydrazine under solid support K-10/ultrasound conditions and in homogeneous media (reflux in ethanol or dichloromethane). The products were pyrazoles **2a-d**, *N*-methylpyrazoles **3a-d**, **4a-d** and *N*-methylpyrazolinones **6a-c** and **7a-c**. The regiochemistry of the cyclization reactions showed dependence upon the reaction conditions employed as well as upon the substituent in the aromatic ring.

*J. Heterocyclic Chem.*, **34**, 1453 (1997).

Heterocyclic compounds such as pyrazoles and its derivatives continue to be a rich source of innovative chemistry because a number of pharmaceuticals and dyestuffs contain these ring systems [1]. The most important derivatives of pyrazole are pyrazolones which have important pharmacological properties, although there are a few naturally-occurring examples. The standard syntheses for these compounds involve the reaction of β-dicarbonyl compounds with hydrazine [2]. The use of new bielectrophilic reagents for preparing pyrazoles and its derivatives have been studied [3-5].

β-Enamino ketones and esters have found application as 1,3-bielectrophilic synthons in the syntheses of heterocycles [6,7]; different types of heterocycles may be formed depending upon the reaction conditions employed.

We have been exploring the use of montmorillonite, K-10, as a solid support in the synthesis and reactivity of β-enamino compounds [8-10]. In order to study the reactivity of the electrophilic center in the *p*-phenyl-substituted-β-enamino ketones **1a-d** and esters **5a-d** we allowed these compounds to react with 1,2-dinucleophiles. We describe in this work the reactions of these compounds with hydrazine and methylhydrazine in heterogeneous media, K-10/ultrasound to obtain substituted pyrazoles and pyrazolinones.

The reaction of β-enamino ketones **1a-d** with hydrazine under K-10/ultrasound (method A) afforded pyrazoles **2a-d** (Scheme 1). We also tested this reaction under reflux conditions in ethanol for 16 hours (method B) to obtain information of the media dependence of the regiochemistry of the pyrazole formed. In both media used (heterogeneous and homogeneous), the pyrazoles formed possessed the same spectral data, $^1H$ and $^{13}C$ nmr but with different melting points, indicating that probably different tautomeric mixture were obtained. According to $^1H$ nmr spectral data of pyrazoles **2a,b,d** ($R^1$ = H, Me, $NO_2$), the chemical shift of the nitrogen proton appears at 11-13 ppm, while for **2c** at 8.6 ppm. This observed variation can be attributed to a different isomeric form or the possibility of an intermolecular hydrogen bond.

The tautomerism of 5(3)-methyl-3(5)-phenylpyrazole was studied by Parrilla [11] in the liquid state using multinuclear nmr spectroscopy at low temperatures and in the solid state by X-ray crystallography to determine the tautomeric equilibrium constants. They observed that the major tautomer in solution was the 5-methyl-3-phenyl tautomer whereas in the solid state both tautomeric were present.

In view of this situation, we decided to study the reaction of *p*-phenyl-substituted-β-enamino compounds **1a-d** and **5a-d** with an unsymmetrical hydrazine.

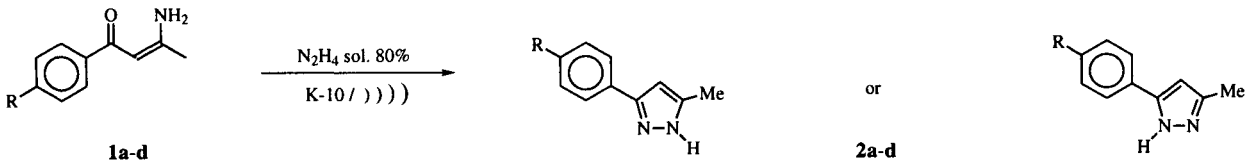
The reaction of **1a** with methylhydrazine using K-10 as the solid support with ultrasound affords *N*-methyl-3-methyl-5-phenylpyrazole **3a** only, however for **1b-d** a regioisomeric mixture of pyrazoles **3,4b-d** results (see Scheme 2).

When β-enamino ketones **1a** and **1d** were allowed to react with methylhydrazine in ethanol under reflux for 5 hours, isomers **4a** and **4d** were isolated. But when an unsymmetrical hydrazine was condensed with **1b-c** in homogeneous media a regioisomeric mixture of **3,4b,c** resulted.

The ratio of the isomeric products **3** and **4** formed showed dependence upon the reaction conditions used as well as the substituent on the aromatic ring.

This results indicated the influence of the K-10 support on the regiochemistry of these reactions. Presumably for steric reasons in the first step of this reaction, the interaction of K-10 with the nitrogen of the amino group makes the carboxylic carbon more electrophillic and the addition of the methylhydrazine occurs by initial addition of the unsubstituted nitrogen followed by cyclization to give the pyrazole **3**. However, when **1d** was treated with methylhydrazine under K-10/ultrasound conditions a mixture of **3** and **4** was isolated in a ratio of 1:4 respectively, indicating that the regiochemistry was inverted. It can be attributed to a more effective interaction of K-10 with the nitro group than with the nitrogen or oxygen atoms of the enamino ketones and the reaction has a similar path to that of the reactions in homogeneous media.

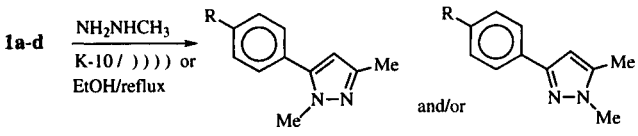
Scheme 1




**1a-d** **2a-d**

| | a | b | c | d |
|---|---|---|---|---|
| R | H | Me | OMe | $NO_2$ |

Scheme 2




**3a-d** **4a-d**

Ratio of isomers **3,4a-d** [a]

| | R | EtOH | | K-10 | |
|---|---|---|---|---|---|
| | | **3** | **4** | **3** | **4** |
| **a** | H | – | 100 | 100 | – |
| **b** | Me | 55 | 45 | 93 | 7 |
| **c** | OMe | 45 | 55 | 94 | 6 |
| **d** | $NO_2$ | – | 100 | 20 | 80 |

[a] The ratio was determined by gas chromatography.

In homogeneous media the reactivity of these systems is not affected by steric hindrance in the first step and the formation of **4** is favored. For the β-enamino ketones bearing a methyl substituent, (**1b**) or OMe, **1c** on the aromatic ring, the reactivity changes and the steric hindrance is important. A mixture of the regioisomers **3** and **4** in a ratio of 1:1 results.

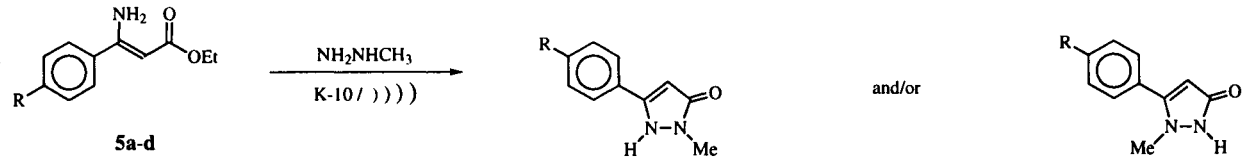
The synthesis of *N*-methyl-5(3)-methyl-3(5)-phenylpyrazole was described in the literature [12] by the reaction between benzoylacetone and methylhydrazine in the presence of alumina, mixtures of **3,4a** were isolated in a ratio of 2:3. In our case when K-10/ultrasound was employed the only product isolated was pyrazolone **3a**, indicating the selectivity of K-10 in these reaction.

The structure of the pyrazoles **3a-d** and **4a-d** were confirmed by spectral data. The $^1H$ nmr spectra showed significant differences in the chemical shifts. The appearance of the phenyl signal at position 3 (two multiplets, $H_o$ and $H_m + H_p$) for **3** is very different from that of the phenyl at position 5 (a singlet due to the steric hindrance of NMe) for **4**, for example: **3a** 7.36 ppm (phenyl at position 5); **4a** 7.20-7.79 ppm (phenyl at position 3). Similar variations were observed in the $^{13}C$ nmr data (see Table).

The reaction of β-enamino esters, ethyl 3-amino-3-(*p*-phenyl-substituted)-2-propenoates **5a-d** with methylhydrazine to afford pyrazolinones (Scheme 3) was performed using the same methodology used for β-enamino ketones in order to evaluate the effect of the K-10/ultrasound system and the substitution of the *p*-substituted phenyl group at position 3 in the regiochemistry of this reaction.

The reaction of **5a** with methylhydrazine under K-10/ultrasound for 6 hours gave only the pyrazolinone **6a**, however in homogeneous media, reflux in dichloromethane for 20 hours a mixture of **6a** and **7a** was isolated. This was observed in $^1H$ nmr spectra where the methyl protons of the *N*-Me group exhibit different chemical shifts and give two separate signals at 3.49 ppm and 2.60 ppm corresponding of the pyrazolinones **6a** and **7a** respectively. In the $^{13}C$ nmr spectra, the carbon of the *N*-methyl group appears at 31.3 ppm for the pyrazolinone **6a** and 36.9 ppm for pyrazolinone **7a**; this was confirmed by a DEPT 135 experiment. The cyclization of **5b** with methylhydrazine results in a mixture of **6b** and **7b** independent of the media employed. For ethyl 3-amino-3-(*p*-methoxy)-phenyl-2-propenoate **5c**, the cyclization with methylhy-

Scheme 3




**5a-d** **6a-c** **7a-c**

| | a | b | c | d |
|---|---|---|---|---|
| R | H | Me | OMe | $NO_2$ |

Table

Selected Physical and Spectral [a] Data of Pyrazoles **2,3,4a-d** and *N*-Methylpyrazolinones **6a,c**

| No. | Yield (%) [b] Method [c] | | Mp [d] °C | Molecular Folmula | Analysis (%) Calcd./Found | | | $^1$H-NMR δ, J (Hz) | $^{13}$C-NMR δ |
|---|---|---|---|---|---|---|---|---|---|
| | A | B | | | C | H | N | | |
| **2a** | 58 | | 126-128 | $C_{10}H_{10}N_2$ 158.20 | 75.92 75.78 | 6.37 6.35 | 17.71 17.69 | 2.09 (s, 3H, $CH_3$), 6.16 (s, 1H, CH), 7.12-7.63 (m, 5H, arom), 11.69 (s, 1H, NH) | 11.5, 102.0, 125.8, 127.7, 128.6, 143.2, 149.9, 132.6 |
| **2b** | 40 | | 118-119 | $C_{11}H_{12}N_2$ 172.23 | 76.71 76.59 | 7.02 7.04 | 16.27 16.15 | 2.16 (s, 3H, $CH_3$), 2.28 (s, 3H, $CH_3$), 6.21 (s, 1H, CH), 6.66-7.70 (m, 4H, arom), 11.74 (s, 1H, NH) | 11.6, 21.1, 101.7, 125.6, 129.2, 129.2, 137.4, 143.5, 149.2 |
| **2c** | 70 | | 70-73 | $C_{11}H_{12}N_2O$ 188.23 | 70.19 69.96 | 6.43 6.35 | 14.88 14.80 | 2.18 (s, 3H, $CH_3$), 3.71 (s, 3H, $CH_3$), 6.17 (s, 1H, CH), 6.73-7.62 (m, 4H, arom), 8.60 (s, 1H, NH) | 11.6, 55.1, 101.4, 114.0, 125.2, 127.0, 143.5, 149.2, 159.3 |
| **2d** | 42 | | 179 | $C_{10}H_9N_3O$ 203.20 | 59.11 59.16 | 4.46 4.44 | 20.68 20.42 | 2.31 (s, 3H, $CH_3$), 6.60 (s, 1H, CH), 7.95-8.29 (m, 4H, arom), 12.99 (s, 1H, NH) | 10.2, 102.2, 123.8, 125.5, 140.2, 146.0 148.4, 150.3 |
| **3a** | 65 | - | 265 | $C_{11}H_{12}N_2$ 172.23 | 76.71 76.59 | 7.02 7.08 | 16.27 16.11 | 2.27 (s, 3H, $CH_3$), 3.76 (s, 3H, $CH_3$), 6.05 (s, 1H, CH), 7.36 (s, 5H, arom) | 13.1, 36.7, 105.3, 128.0, 128.4, 128.4. 130.7, 144.1, 147.3 |
| **3b** | 53 | 37 | 275 | $C_{12}H_{14}N_2$ 186.26 | 77.37 77.21 | 7.58 7.37 | 15.05 14.94 | 2.27 (s, 3H, $CH_3$), 2.36 (s, 3H, $CH_3$), 3.76 (s, 3H, $CH_3$), 6.02 (s, 1H, CH), 7.22 (s, 4H, arom) | 13.1, 20.9, 36.7, 105.1, 127.8, 128.3, 129.0, 130.7, 144.2, 147.2 |
| **3c** | 60 | 43 | 73 | $C_{12}H_{14}N_2O$ 202.26 | 71.26 71.30 | 6.98 7.10 | 13.85 13.62 | 2.27 (s, 3H, $CH_3$), 3.75 (s, 3H, $CH_3$), 3.80 (s, 3H, $CH_3$), 6.01 (s, 1H, CH), 6.82-7.31 (m, 4H, arom) | 13.2, 36.7, 55.1, 105.0, 113.8, 123.2, 129.7, 144.0, 147.2, 159.5 |
| **3d** | 8 | - | 191 | $C_{11}H_{11}N_3O_2$ 217.23 | 60.82 60.69 | 5.10 5.11 | 19.34 19.01 | 2.33 (s, 3H, $CH_3$), 3.86 (s, 3H, $CH_3$), 6.45 (s, 1H, CH), 7.82-8.3 (m, 4H, arom) | 11.1, 36.3, 103.5, 123.9, 125.6, 140.1, 140.4, 146.8, 147.5 |
| **4a** | - | 94 | 292 | $C_{11}H_{12}N_2$ 172.23 | 76.71 76.50 | 7.02 7.10 | 16.27 16.18 | 2.17 (s, 3H, $CH_3$), 3.70 (s, 3H, $CH_3$), 6.24 (s, 1H, CH), 7.20-7.79 (2d, 5H, arom) | 10.9. 35.8, 102.3, 125.2, 127.1, 128.3, 133.6, 139.5, 149.7 |
| **4b** | 4 | 30 | 95-97 | $C_{12}H_{14}N_2$ 186.26 | 77.37 77.28 | 7.58 7.35 | 15.05 14.98 | 2.21 (s, 3H, $CH_3$), 2.32 (s, 3H, $CH_3$), 3.73 (s, 3H, $CH_3$), 6.23 (s, 1H, CH), 7.09-7.68 (2d, 4H, arom) | 11.0, 21.0, 37.8, 102.2, 125.2, 129.1, 131.0, 136.8, 139.5, 150.0 |
| **4c** | 4 | 52 | 91 | $C_{12}H_{14}N_2O$ 202.26 | 71.26 71.14 | 6.98 6.93 | 13.85 13.61 | 2.21 (s, 3H, $CH_3$), 3.73 (s, 6H, $CH_3$), 6.19, (s, 1H, CH), 6.82-7.72 (2d, 4H, arom) | 10.8, 35.6, 54.9, 101.7, 113.7, 126.3, 139.4, 139.4, 149.5, 158.9 |
| **4d** | 36 | 89 | 166 | $C_{11}H_{11}N_3O_2$ 217.23 | 60.82 60.51 | 5.10 5.15 | 19.34 19.05 | 2.26 (s, 3H, $CH_3$), 3.86 (s, 3H, $CH_3$), 6.22 (s, 1H, CH), 6.82-7.72 (2d, 4H, arom) | 12.3, 36.5, 105.8, 123.0, 128.2, 136.1, 141.0, 146.3, 146.7 |
| **6a** | 65 | - | 219-221 | $C_{10}H_{10}N_2O$ 174.20 | 68.95 68.72 | 5.79 5.70 | 16.08 16.04 | 3.49 (s, 4H, $CH_3$), 7.22 (br, 7H, CH, NH and arom) | 31.3, 100.3, 127.4, 127.9, 128.2, 131.1, 144.7, 157.8 |
| **6c** | - | 52 | 214-217 | $C_{11}H_{12}N_2O_2$ 204.23 | 64.69 64.72 | 5.92 6.01 | 13.72 13.51 | 3.47 (s, 3H, $CH_3$), 3.75 (s, 3H, $CH_3$), 6.3 (br, 2H, NH and CH), 6.69-7.22 (m, 4H, arom) | 31.6, 55.0 100.3, 113.8, 124.3, 129.1, 144.9, 158.2, 159.1 |

[a] NMR-Spectra in deuteriochloroform/tetramethylsilane (dimethyl sulfoxide-$d_6$/tetramethylsilane for **2d**); [b] Yields given for pure isolated products; [c] Methods: A: K-10/ultasound; B: reflux in ethanol (dichloromethane for **7a** and **7c**); [d] Melting points were determined with a Microquimica APF-301 apparatus and are uncorrected.

drazine under K-10/ultrasound conditions results in a mixture of **6c** and **7c**, but the same reaction under reflux in dichloromethane gives only **6c**. The pyrazolinones **6,7b** were not separated from the mixture. The structures of compounds **6a-c** were established based on the $^1H$ and $^{13}C$ nmr spectra which show different chemical shifts, see the Experimental.

When ethyl 3-amino-3-(*p*-nitro)phenyl-2-propenoate **5d** was treated with methylhydrazine, reaction did not take place, only starting material was isolated from the reaction, independent of the conditions employed (K-10/ultrasound or reflux in dichloromethane). This is probably due the influence of the aromatic ring bonded directly on the α,β-unsaturated system.

From the results described here we conclude that β-enamino ketones **1a-d** are more reactive than β-enamino esters **5a-d** in the cyclization proposed. The regiochemistry of the cyclization showed dependence upon the reaction conditions employed as well as the substituent on the aromatic ring. The influence of the K-10 system was demonstrated in the regiochemistry of the products obtained as well in compounds that have polar groups due the interactions of the substrate/support system.

## EXPERIMENTAL

Melting points were determined with a Microquímica APF-301 apparatus and are uncorrected. The $^1H$ and $^{13}C$ nmr spectra were recorded on a Bruker AC-80 and Varian XL-200 spectrometers in deuteriochloroform/tetramethylsilane or DMSO-$d_6$/tetramethylsilane. Elemental analyses were determined with a Vario CHN-standard analyser. Capillary gc analyses were performed on a Carlo Erba, Mega Series 5400 chromatograph equipped with a split/splitless injector and a FID detector. An ultrasound bath (water), Thornton, 50-60 Hz, 110/220 volts, 1.0 Amps was used, the water bath was maintained at rt. β-Enamino compounds **1** and **5** were prepared by a known procedure [10].

5(3)-Methyl-3(5)-(*p*-phenyl-substituted)-1*H*-pyrazoles **2a-d**.

General Procedure.

Hydrazine hydrate (80%) (4 mmoles) in dichloromethane (1 ml) was added dropwise to the 3-amine-1-(*p*-phenyl-substituted)-2-buten-1-ones **1a-d** (2 mmoles) dispersed on montmorillonite K-10 (0.6 g, Fluka). The mixture was placed in the ultrasound bath for 5 hours. The products were extracted by washing the montmorillonite with dichloromethane, the organic layer was washed with water, dried over magnesium sulfate, filtered and the solvent was removed *in vacuo* to yield the crude products. Compounds **2a**, **2b** and **2c** which were purified by recrystallization from petroleum ether/diisopropyl ether 10%. Compound **2d** was recrystallized from ethanol. The yields of products were **2a** (58%), **2b** (40%), **2c** (70%) and **2d** (42%).

3-Methyl-5-(*p*-phenyl-substituted)-*N*-methylpyrazole **3a-d**, 5-Methyl-3-(*p*-phenyl-substituted)-*N*-methylpyrazoles **4a-d** and 3(5)-(*p*-Phenyl-substituted)-*N*-methyl-5(3)-pyrazolinones **6,7a-c**.

General Procedure.

Method A.

Methylhydrazine (3 mmoles) in dichloromethane (1 ml) was added dropwise to the 3-amino-1-(*p*-phenyl-substituted)-2-buten-1-ones **1a-d** or ethyl 3-amino-3-(*p*-phenyl-substituted)-2-propenoates (1 mmole) **5a-c** dispersed on montmorillonite K-10 (0.3 g, Fluka). The mixture was placed in the ultrasound bath for 6 hours and the solvent was evaporated in a rotary evaporator under vacuum. The crystals were dissolved with dichloromethane and the organic layer was washed with water, dried over magnesium sulfate, filtered and the solvent was removed *in vacuo* to yield **3a** (65%) and a mixture of **3,4b-d**. The mixtures were separated by column chromatography on silica gel (Aldrich, 230-400 mesh), using dichloromethane as eluent resulting **3b** (53%), **4b** (4%), **3c** (60%), **4c** (4%), **3d** (8%) and **4d** (36%). The isomeric mixture of **6,7b** (78%), **6,7c** (78%) were obtained; **6a** was obtained in 65% yield.

Method B.

Methylhydrazine (3 mmoles) was added dropwise to a stirred solution of the 3-amino-1-(*p*-phenyl-substituted)-2-buten-1-ones **1a-d** or ethyl 3-amino-3-(*p*-phenyl-substituted)-2-propenoate (1 mmole) **5a-c** in ethanol (15 ml). The mixture was stirred and refluxed for 5 hours. The solvent was evaporated in a rotary evaporator under vacuum. The crystals were dissolved in dichloromethane and the organic layer was washed with water, dried over magnesium sulfate, filtered and the solvent was removed *in vacuo*, resulting in **4a** (94%) and **4d** (89%). The mixture of the **3,4b** and **3,4c** was applied to a silica gel (Aldrich, 230-400 mesh) column and eluated with dichloromethane to give **3b** (37%), **4b** (30%), **3c** (43%) and **4c** (52%). The isomeric mixture of **6,7a** (62%), **6,7b** (72%) were obtained; **6c** was obtained in 52% yield.

Compound **6b**.

This compound had $^1H$ nmr (deuteriochloroform/tetramethylsilane): δ 2.32 (s, 3H, $CH_3$), 3.47 (s, 3H, $CH_3$), 4.00 (br, 1H, NH), 7.01-7.12 (s, 5H, CH and arom); $^{13}C$ nmr (deuteriochloroform/tetramethylsilane): δ 31.7, 20.9, 100.7, 124.1, 127.8, 113.9, 129.1, 144.6, 158.2.

Compound **7a**.

This compound had $^1H$ nmr (deuteriochloroform/tetramethylsilanle): δ 2.60 (s, 3H, $CH_3$), 7.19 (br, 7H, NH, CH and arom); $^{13}C$ nmr (deuteriochloroform/tetramethylsilane): δ 36.9, 99.2, 127.6, 128.1, 128.1, 133.7, 145.1, 157.9.

Compound **7b**.

This compound had $^1H$ nmr (deuteriochloroform/tetramethylsilane): δ 2.32 (s, 3H, $CH_3$), 2.58 (s, 3H, $CH_3$), 4.00 (br, H, NH), 7.01-7.12 (s, 5H, CH and arom); $^{13}C$ nmr (deuteriochloroform/-tetramethylsilane): δ 36.9, 20.9, 100.7, 124.1, 127.8, 113.9, 129.1, 144.6, 158.2.

Compound **7c**.

This compound had $^1H$ nmr (deuteriochloroform/tetramethylsilane): δ 2.63 (s, 3H, $CH_3$), 3.76 (s, 3H, $CH_3$), 6.70-7.23 (6H, m, CH, NH and arom); $^{13}C$ nmr (deuteriochloroform/tetramethylsilane): δ 37.0, 55.0, 100.4, 113.9, 124.1, 129.2, 144.9, 158.2, 159.2.

Acknowledgements.

We are grateful to the Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS) for financial support and to the fellowship from Coordenação de Aperfeiçoamento de Pessoal de Nivel Superior (CAPES) (C. J. V.). Our thanks to Dr. Robert Burrow for helpful comments on the manuscript.

REFERENCES AND NOTES

* Author to whom correspondence should be addressed.

[1] S. Sugiura, S. Ohno, O. Ohtani, K. Izumi, T. Kitamikado, H. Asai, K. Kato, M. Hori and H. Fujimura, *J. Med. Chem.*, **20**, 80 (1977).

[2] A. R. Katritzky, Handbook of Heterocyclic Chemistry, Pergamon Press, New York, 1985, p 416.

[3] M. Pätzel and J. Liebscher, *J. Heterocyclic Chem.*, **28**, 1257 (1991).

[4] L. Birkofer and K. Richzenhain, *Chem. Ber.*, **112**, 2829 (1979).

[5] L. F. Tietze and A. Steinmetz, *Synlett.*, **667** (1996).

[6] M. E. F. Braibante, H. S. Braibante and L. Missio, *J. Heterocyclic Chem.*, **33**, 1243 (1996).

[7] E. Bejan, H. A. Haddou, J. C. Daran and G. G. A. Balavoine, *Synthesis*, 1012 (1996).

[8] M. E. F. Braibante, H. S. Braibante and S. Salvatore, *Quim. Nova*, **13**, 67 (1990).

[9] M. E. F. Braibante, H. S. Braibante, L. Missio and A. Andricopulo, *Synthesis*, 898 (1994).

[10] C. J. Valduga, Dissertation, Universidade Federal de Santa Maria (1996).

[11] F. Aguilar-Parrilla, C. Cativiela, M. D. D. de Villegas, J. Elguero, C. Foces-Foces, J. I. G. Laureiro, F. H. Cano, H. H. Limbach, J. A. S. Smith and C. Toiron. *J. Chem. Soc., Perkin Trans. 2*, 1737 (1992).

[12] F.-T.-Boullet, B. Klein and J. Hamelin, *Synthesis*, 409 (1986).