On the Synthesis of 3(5)-Carbomethoxy-4-hetarylpyrazoles

Carlos Cativiela*, Maria D. Diaz de Villegas, José A. Mayoral

Instituto de Ciencia de Materiales de Aragón,
Departamento de Química Orgánica, Universidad de Zaragoza-CSIC,
50009 Zaragoza, Spain

Alberto Avenoza, Miguel A. Roy

Departamento de Química Orgánica, Colegio Universitario de La Rioja,
Logroño, Spain

Received September 22, 1987

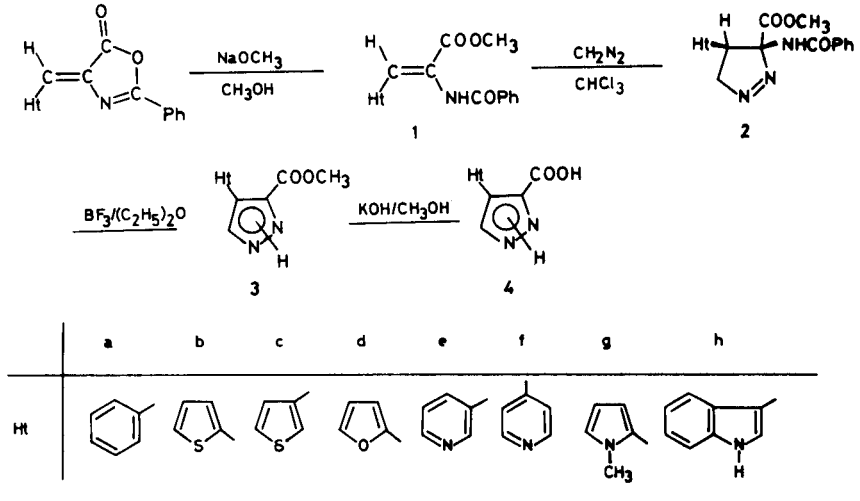
3(5)-Carbomethoxy-4-hetarylpyrazoles **3** can be obtained by the aromatization of the corresponding *cis*-3-benzamido-3-carbomethoxy-4-hetaryl-Δ^1-pyrazolines **2** obtained by 1,3-dipolar cycloaddition of diazomethane with methyl *Z*-2-benzamido-3-hetarylpropenoates **1**. An explanation, based on FMO theory, for the different reactivity of the dipolarophiles with diazomethane is given.

J. Heterocyclic Chem., **25**, 851 (1988).

Pyrazole chemistry has been and still is the subject of a good deal of research and has recently been reviewed [1]. One of the most useful synthetic routes to pyrazoles is the creation of two bonds of the pyrazole ring by means of 1,3-dipolar cycloaddition of diazo compounds and dipolarophiles [2]. When the dipolarophile is an olefinic compound, cycloaddition affords Δ^1-pyrazolines and provided there is a good leaving group these Δ^1-pyrazolines can be aromatized to the corresponding pyrazoles [3].

As a contribution to the research into pyrazole chemistry we have recently communicated [4] a new synthetic procedure to obtain 3(5)-carbomethoxy-4-arylpyrazoles from 3-aryl-2,3-dehydroamino acid derivatives. Our aim in this paper is to extend this new synthetic procedure to the synthesis of 3(5)-carbomethoxy-4-hetarylpyrazoles **3**. To this end various methyl *Z*-2-benzamido-3-hetarylpropenoates **1**, with different heterocyclic rings and different substitution positions, were used to obtain *cis*-3-benzamido-3-carbomethoxy-4-hetaryl-Δ^1-pyrazolines **2** (Scheme 1). Different behaviour was observed depending on the heterocyclic ring. Whereas compounds **1b-d** underwent total cycloaddition in about the same time as **1a** (3 days) [4], **1e** and **1f** underwent faster cycloaddition (total reaction in about 1 day), in the case of **1g** the reaction rate was too slow to be synthetically useful (no more than 40% in 7 days) and **1h** did not react at all.

In view of this different behaviour, we tried to determine the electronic configuration of the 1,3-dipole and of the acetamido models of the dipolarophiles by the MNDO method [5] in order to explain the observed reactivity scale by the FMO theory [6]. The dipolarophiles show a considerable mobility around their σ bonds. However, as Ajò *et al.* [7] have studied the structure of *N*-acetyl-α,β-dehydroalanine and its ethyl ester and have shown that these compounds exhibit non planar conformation as far as the ω torsion angle is concerned (Figure 1), we considered our



SCHEME 1

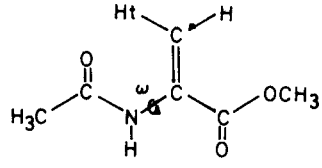
Table 1

Frontier orbital energies of the acetamido dipolarophiles and HOMO-LUMO energy gaps as calculated by MNDO, given in eV

Compound	E(HOMO)	E(LUMO DIPOLE)-E(HOMO DIPOLAROPHILE) [a]	E(LUMO)	E(LUMO DIPOLAROPHILE)-E(HOMO DIPOLE) [a]
5a	-9.174	10.175	-0.805	7.863
5b	-9.196	10.197	-1.021	7.647
5c	-9.375	10.376	-0.826	7.842
5d	-8.972	9.973	-0.793	7.875
5e	-9.406	10.407	-1.026	7.642
5f	-9.813	10.814	-1.062	7.606
5g	-8.559	9.560	-0.576	8.092
5h	-8.438	9.439	-0.523	8.145

[a] Energies of the HOMO and the effective LUMO of diazomethane calculated by MNDO are -8.668 and 1.001 eV respectively.

dipolarophiles to be planar, with the exception of the double bond-amide group torsion angle which was optimized [8].



5

Figure 1

The reactivity in 1,3-dipolar cycloadditions depends on the energy separations of the frontier orbitals which show up in the denominators of the second order terms of the perturbation equation [9]. The frontier orbital energies of **5**, as calculated by MNDO, as well as the HOMO-LUMO energy gaps are gathered in Table 1.

In spite of the presence of the amido group, the reactions are mainly controlled by the HOMO(dipole)-LUMO(dipolarophile) interaction and, with the exception of the 2-thiophene derivative **1b**, there is a relationship between the corresponding energy separations and the experimental reactivity. Dewar and Mckee [10] have shown that, for molecules containing sulphur, MNDO calculated MO energies are greater than vertical ionization energies derived from photoelectron spectroscopy, and that the correction for a given MO should be proportional to the contribution to it by AOs of sulphur. Although there is no similar study for unoccupied orbitals, the lack of a good correlation with thiophene compounds was not unexpected.

Cis-3-benzamido-3-carbomethoxy-4-hetaryl-Δ^1-pyrazolines **2b-2g** were obtained by 1,3-dipolar cycloaddition of diazomethane with methyl *Z*-2-benzamido-3-hetarylpropenoates **1b-g**.

Cis-3-benzamido-3-carbomethoxy-4-hetaryl-Δ^1-pyrazolines **2b-2f** were aromatized to 3(5)-carbomethoxy-4-hetarylpyrazoles **3b-3f** in good yields using boron trifluoride etherate as an aromatizing agent, as previously described [4], but 3 moles of boron trifluoride etherate per mole of pyrazoline were necessary in order to accelerate the reaction when a new coordinating centre, proceeding from the pyridine, was present in the molecule.

Saponification of 3(5)-carbomethoxy-4-hetarylpyrazoles **3b-f** using methanolic potassium hydroxide afforded 4-hetaryl-3(5)-pyrazolecarboxylic acids in good yields.

In summary, the method above-described is a quite general one to obtain 3(5)-carbomethoxy-4-hetarylpyrazoles using easily obtainable reactants (3-hetaryl-2,3-dehydroamino acid derivatives) the scope of which is only limited by the rate of 1,3-dipolar cycloaddition of diazomethane.

EXPERIMENTAL

Melting points were determined on a Büchi 510 capillary melting point apparatus and are uncorrected; melting points of *cis*-3-benzamido-3-carbomethoxy-4-hetaryl-Δ^1-pyrazolines **2** were not determined as these compounds decompose thermically. The ir spectra were recorded on a Perkin-Elmer 283 infrared spectrophotometer. The nmr spectra were measured at 80 MHz on a Bruker CW-80-SY spectrometer with tetramethylsilane as the internal standard. Microanalyses were carried out on a Perkin-Elmer 240-C microanalyzer and were in good agreement with the calculated values.

General Procedures.

Methyl *Z*-2-Benzamido-3-hetarylpropenoates **1b-h**.

A total of 3 mmoles of the corresponding *Z*-2-phenyl-4-hetarylmethylene-5(4*H*)-oxazolone, obtained by standard procedures [11], were stirred at room temperature with sodium methylate (0.01 g) in absolute methanol (20 ml) until the solid went into solution. The solution was concentrated *in vacuo* and water was added. Filtration and washing with water of the solid afforded pure samples of the corresponding methyl *Z*-2-benzamido-3-hetarylpropenoates **1b-h**.

Methyl *Z*-2-Benzamido-3-(2-thienyl)propenoate (**1b**).

This compound was obtained as a white solid (methanol/water), in 87% yield, mp 187-188°; ir (nujol): 3250 (NH), 1705 (C=O), 1645 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.71 (s, 3H, CO_2CH_3), 7.10-7.20 (m, 1H, thienyl protons), 7.5-7.8 (m, 5H, phenyl and thienyl protons), 7.93 (s, 1H, HC=), 7.90-8.20 (m, 2H, phenyl protons), 9.84 (broad s, 1H, NH).

Anal. Calcd. for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87. Found: C, 62.92; H, 4.31; N, 5.01.

Methyl *Z*-2-Benzamido-3-(3-thienyl)propenoate (**1c**).

This compound was obtained as a white solid (methanol/water), in 65% yield, mp 157-159°; ir (nujol): 3260 (NH), 1715 (C=O), 1640 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.77 (s, 3H, CO_2CH_3), 7.50-7.80 (m, 6H, phenyl and thienyl protons), 8.04 (s, 1H, HC=), 8.05-8.20 (m, 2H, phenyl protons), 10.05 (broad s, 1H, NH).

Anal. Calcd. for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87. Found: C, 62.83; H, 4.60; N, 4.83.

Methyl *Z*-2-Benzamido-3-(2-furyl)propenoate (**1d**).

This compound was obtained as a white solid (methanol/water), in 75% yield, mp 140-142°; ir (nujol): 3290 (NH), 1685 (C=O), 1645 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.77 (s, 3H, CO_2CH_3), 6.35-6.65 (m, 2H, furyl protons), 7.05 (s, 1H, HC=), 7.30-7.60 (m, 4H, phenyl and furyl protons), 7.85-8.05 (m, 2H, phenyl protons), 8.42 (broad, s, 1H, NH).

Anal. Calcd. for $C_{15}H_{13}NO_4$: C, 66.42; H, 4.83; N, 5.16. Found: C, 66.25; H, 4.91; N, 5.03.

Methyl *Z*-2-Benzamido-3-(3-pyridyl)propenoate (**1e**).

This compound was obtained as a white solid (ethyl acetate/hexane), in 48% yield, mp 119-120°; ir (nujol): 3300 (NH), 1705 (C=O), 1650 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.80 (s, 3H, CO_2CH_3), 7.05-7.30 (m, 1H, pyridyl protons), 7.35-7.55 (m, 4H, phenyl protons and HC=), 7.60-7.95 (m, 3H, phenyl and pyridyl protons), 8.22 (broad s, 1H, NH), 8.35-8.50 (m, 1H, pyridyl protons), 8.55-8.70 (m, 1H, pyridyl protons).

Anal. Calcd. for $C_{16}H_{14}N_2O_3$: C, 68.08; H, 5.00; N, 9.92. Found: C, 67.93; H, 5.22; N, 10.03.

Methyl *Z*-2-Benzamido-3-(4-pyridyl)propenoate (**1f**).

This compound was obtained as a white solid (ethyl acetate/hexane) in 52% yield, mp 103-104°; ir (nujol): 3160 (NH), 1735 (C=O), 1650 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.83 (s, 3H, CO_2CH_3), 7.28 (s, 1H, HC=), 7.40-7.65 (m, 5H, phenyl and pyridyl protons), 7.80-8.05 (m, 2H, phenyl protons), 8.45-8.65 (m, 2H, pyridyl protons), 9.97 (broad s, 1H, NH).

Anal. Calcd. for $C_{16}H_{14}N_2O_3$: C, 68.08; H, 5.00; N, 9.92. Found: C, 68.21; H, 5.24; N, 9.67.

Methyl *Z*-2-Benzamido-3-(*N*-methyl-2-pyrrolyl)propenoate (**1g**).

This compound was obtained as a white solid (methanol/water), in 70% yield, mp 186-188°; ir (nujol): 3230 (NH), 1710 (C=O), 1650 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.70 (s, 3H, N-CH_3), 3.85 (s, 3H, CO_2CH_3), 6.10-6.25 (m, 1H, pyrrolyl protons), 6.50-6.65 (m, 1H, pyrrolyl protons), 6.70-6.85 (m, 1H, pyrrolyl protons), 7.40-7.60 (m, 4H, phenyl protons and HC=), 7.85-8.05 (m, 3H, phenyl protons and NH).

Anal. Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.66; H, 5.48; N, 10.02.

Methyl-*Z*-2-Benzamido-3-(3-indolyl)propenoate (**1h**).

This compound was obtained as a white solid (methanol/water), in 75% yield, mp 246-248°; ir (nujol): 3340 (NH), 1705 (C=O), 1670 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.72 (s, 3H, CO_2CH_3), 7.00-7.25 (m, 2H, indolyl protons), 7.35-7.65 (m, 4H, phenyl protons and HC=), 7.65-7.90 (m, 3H, indolyl protons), 7.95-8.15 (m, 2H, phenyl protons), 9.75 (broad s, 1H, NH).

Anal. Calcd. for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 70.97; H, 5.31; N, 8.96.

Cis-3-benzamido-3-carbomethoxy-4-hetaryl-Δ¹-pyrazolines (**2b-g**).

In a typical procedure, the methyl *Z*-2-benzamido-3-hetarylpropenoate **1b-g** (4 mmoles) dissolved in chloroform (20 ml) was treated with a solution of diazomethane in chloroform (from 2 g of *N*-methyl-*N*-nitrosourea in 20 ml of chloroform) in a stoppered flask protected from the light at room temperature until completion (tlc using chloroform/dioxane 4:1 as eluting agent). The solution was then treated with anhydrous calcium chloride to destroy the excess of diazomethane, filtered and concentrated *in vacuo*. The residue was dissolved in acetone and precipitated with water, filtered, and dried to afford analytically pure samples of the corresponding pyrazoline **2b-f** in good yields. With analytical pourpouses a sample of *cis*-3-benzamido-3-carbomethoxy-4-(*N*-methyl-2-pyrrolyl)-Δ¹-pyrazoline **2g** was isolated by column chromatography by using ether as eluting agent.

Cis-3-benzamido-3-carbomethoxy-4-(2-thienyl)-Δ¹-pyrazoline (**2b**).

This compound was obtained as a white solid (acetone/water), in 80% yield; ir (nujol): 3320 (NH), 1725 (C=O), 1655 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.80 (s, 3H, CO_2CH_3), 4.39 (dd, 1H, H_X, J_{AX} = 8.80 Hz, J_{BX} = 5.50 Hz), 5.12 (dd, 1H, H_B, J_{BX} = 5.50 Hz, J_{AB} = -17.60 Hz), 5.36 (dd, 1H, H_A, J_{AX} = 8.80 Hz, J_{AB} = -17.60 Hz), 6.70-6.90 (m, 2H, thienyl protons), 6.95-7.15 (m, 1H, thienyl protons), 7.20-7.50 (m, 5H, phenyl protons).

Anal. Calcd. for $C_{16}H_{15}N_3O_3S$: C, 58.35; H, 4.59; N, 12.76. Found: C, 57.93; H, 4.84; N, 11.87.

Cis-3-benzamido-3-carbomethoxy-4-(3-thienyl)-Δ¹-pyrazoline (**2c**).

This compound was obtained as a white solid (acetone/water), in 82% yield; ir (nujol): 3320 (NH), 1765 (C=O), 1670 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.83 (s, 3H, CO_2CH_3), 4.22 (dd, 1H, H_X, J_{AX} = 8.60 Hz, J_{BX} = 4.60 Hz), 5.06 (dd, 1H, H_B, J_{BX} = 4.60 Hz, J_{AB} = -17.80 Hz), 5.30 (dd, 1H, H_A, J_{AX} = 8.60 Hz, J_{AB} = -17.80 Hz), 6.50-6.80 (m, 1H, thienyl protons), 6.90-7.00 (m, 1H, thienyl protons), 7.05-7.25 (m, 1H, thienyl protons), 7.25-7.65 (m, 5H, phenyl protons).

Anal. Calcd. for $C_{16}H_{15}N_3O_3S$: C, 58.35; H, 4.59; N, 12.76. Found: C, 57.86; H, 4.54; N, 12.67.

Cis-3-benzamido-3-carbomethoxy-4-(2-furyl)-Δ¹-pyrazoline (**2d**).

This compound was obtained as a white solid (acetone/water), in 85% yield; ir (nujol): 3315 (NH), 1740 (C=O), 1665 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 3.82 (s, 3H, CO_2CH_3), 4.38 (dd, 1H, H_X, J_{AX} = 8.50 Hz, J_{BX} = 4.30 Hz), 5.12 (dd, 1H, H_B, J_{BX} = 4.30 Hz, J_{AB} = -18.00 Hz), 5.37 (dd, 1H, H_A, J_{AX} = 8.50 Hz, J_{AB} = -18.00 Hz), 6.65-6.85 (m, 2H, furyl protons), 7.00-7.15 (m, 1H, furyl protons), 7.20-7.65 (m, 5H, phenyl protons).

Anal. Calcd. for $C_{16}H_{15}N_3O_4$: C, 61.34; H, 4.83; N, 13.41. Found: C, 61.53; H, 4.83; N, 13.24.

Cis-3-benzamido-3-carbomethoxy-4-(3-pyridyl)-Δ¹-pyrazoline (**2e**).

This compound was obtained as a white solid (acetone/water), in 90% yield; ir (nujol): 3150 (NH), 1750 (C=O), 1660 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.67 (s, 3H, CO_2CH_3), 4.22 (dd, 1H, H_X, (J_{AX} + J_{BX})/2 = 6 Hz), 5.07 (d, 2H, (H_A + H_B)/2) 7.00-7.50 (m, 7H, phenyl and pyridyl protons), 8.00-8.35 (m, 2H, pyridyl protons).

Anal. Calcd. for $C_{17}H_{16}N_4O_3$: C, 62.96; H, 4.97; N, 17.27. Found: C, 63.01; H, 4.95; N, 17.33.

Cis-3-benzamido-3-carbomethoxy-4-(4-pyridyl)-Δ¹-pyrazoline (**2f**).

This compound was obtained as a white solid (acetone/water), in 87% yield; ir (nujol): 3200 (NH), 1730 (C=O), 1660 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.72 (s, 3H, CO_2CH_3), 4.25 (dd, 1H, H_X, (J_{AX} + J_{BX})/2 = 7 Hz), 5.13 (d, 2H, (H_A + H_B)/2), 6.75-7.00 (d, 2H, J = 7 Hz, pyridyl protons), 7.15-7.65 (m, 5H, phenyl protons), 8.15-8.35 (d, 2H, J = 7 Hz pyridyl protons).

Anal. Calcd. for $C_{17}H_{16}N_4O_3$: C, 62.96; H, 4.97; N, 17.27. Found: C, 63.05; H, 4.83; N, 17.17.

Cis-3-benzamido-3-carbomethoxy-4-(*N*-methyl-2-pyrrolyl)-Δ¹-pyrazoline (**2g**).

This compound was obtained as a white solid, isolated on a silica gel column eluted with ether, in 20% yield; nmr (deuteriochloroform): δ 3.44 (s, 3H, N-CH_3), 3.72 (s, 3H, CO_2CH_3), 4.00 (dd, 1H, H_X, J_{AX} = 7.30 Hz, J_{BX} = 3.75 Hz), 4.89 (dd, 1H, H_B, J_{BX} = 3.75 Hz, J_{AB} = -18.90 Hz), 5.08 (dd, 1H, H_A, J_{AX} = 7.30 Hz, J_{AB} = -18.90 Hz), 5.50-5.70 (m, 1H, pyrrolyl pro-

tons), 5.80-5.95 (m, 1H, pyrrolyl protons), 6.25-6.45 (m, 1H, pyrrolyl protons), 7.00-7.40 (m, 5H, phenyl protons).

Anal. Calcd. for $C_{17}H_{18}N_4O_3$: C, 62.57; H, 5.56; N, 17.17. Found: C, 62.67; H, 5.34; N, 17.19.

3(5)-Carbomethoxy-4-hetarylpyrazoles **3b-d**.

In a typical procedure, the *cis*-3-benzamido-3-carbomethoxy-4-hetaryl-Δ^1-pyrazoline **2b-d** (4 mmoles) dissolved in chloroform (40 ml) was treated with boron trifluoride etherate (8 mmoles) under reflux conditions for 30 minutes. The solution was cooled, filtered, and evaporated to dryness. The residue was heated with a saturated solution of sodium bicarbonate (40 ml) for 1 hour and the resultant solid filtered, washed with warm water (2 x 10 ml), and dried over phosphorous pentoxide to afford the corresponding 3(5)-carbomethoxy-4-hetarylpyrazole **3b-d** in good yields.

3(5)-Carbomethoxy-4-(2-thienyl)pyrazole (**3b**).

This compound was obtained as a white solid in 85% yield, mp 162-164°; ir (nujol): 3230 (NH), 1700 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.77 (s, 3H, CO_2CH_3), 7.00-7.15 (m, 1H, thienyl protons), 7.40-7.65 (m, 2H, thienyl protons), 8.10 (s, 1H, pyrazole protons).

Anal. Calcd. for $C_9H_8N_2O_2S$: C, 51.91; H, 3.87; N, 13.45. Found: C, 51.76; H, 4.01; N, 13.65.

3(5)-Carbomethoxy-4-(3-thienyl)pyrazole (**3c**).

This compound was obtained as a white solid in 86% yield, mp 180-182°; ir (nujol): 3225 (NH), 1705 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.85 (s, 3H, CO_2CH_3), 7.35-7.60 (m, 2H, thienyl protons), 7.75-7.95 (m, 1H, thienyl protons), 8.10 (s, 1H, pyrazole protons).

Anal. Calcd. for $C_9H_8N_2O_2S$: C, 51.91; H, 3.87; N, 13.45. Found: C, 51.98; H, 3.97; N, 13.65.

3(5)-Carbomethoxy-4-(2-furyl)pyrazole (**3d**).

This compound was obtained as a white solid in 80% yield, mp 150-152°; ir (nujol): 3130 (NH), 1720 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 3.85 (s, 3H, CO_2CH_3), 6.50-6.70 (m, 1H, furyl protons), 7.00-7.20 (m, 1H, furyl protons), 7.60-7.75 (m, 1H, furyl protons), 8.15 (s, 1H, pyrazole protons).

Anal. Calcd. for $C_9H_8N_2O_3$: C, 56.25; H, 4.20; N, 14.58. Found: C, 56.43; H, 4.18; N, 14.67.

3(5)-Carbomethoxy-4-hetarylpyrazoles **3e-f**.

In a typical procedure the *cis*-3-benzamido-3-carbomethoxy-4-hetaryl-Δ^1-pyrazoline **2e-f** (4 mmoles), dissolved in chloroform (40 ml) was treated with boron trifluoride etherate (12 mmoles) under reflux conditions for 30 minutes. The solution was cooled, filtered, and evaporated to dryness. The resultant residue was heated with a saturated solution of sodium bicarbonate (50 ml) for 1 hour and the resultant solid filtered and dried to afford the corresponding 3(5)-carbomethoxy-4-hetarylpyrazole **3e-f**. Concentration *in vacuo* of the filtrate afforded a new portion of pyrazole.

3(5)-Carbomethoxy-4-(3-pyridyl)pyrazole (**3e**).

This compound was obtained as a white solid in 73% yield, mp 136-138°; ir (nujol): 1720 (C=O); nmr (dimethylsulfoxide-d_6): δ 3.77 (s, 3H, CO_2CH_3), 7.25-7.60 (m, 1H, pyridyl protons), 7.80-8.00 (m, 1H, pyridyl protons), 8.05 (s, 1H, pyrazole protons), 8.40-8.60 (m, 1H, pyridyl protons), 8.65-8.85 (m, 1H, pyridyl protons).

Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.46; N, 20.68. Found: C, 58.96; H, 4.54; N, 20.67.

3(5)-Carbomethoxy-4-(4-pyridyl)pyrazole (**3f**).

This compound was obtained as a white solid in 75% yield, mp 192-193°; ir (nujol): 1720 (C=O); nmr (dimethylsulfoxide-d_6): δ 3.81 (s, 3H, CO_2CH_3), 7.53 (d, 2H, J = 7 Hz, pyridyl protons), 8.18 (s, 1H, pyrazole protons), 8.55 (d, 2H, J = 7 Hz, pyridyl protons).

Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.46; N, 20.68. Found: C, 59.23; H, 4.61; N, 20.77.

4-Hetaryl-3(5)-pyrazolecarboxylic Acids **4b-f**.

In a typical procedure, the 3(5)-carbomethoxy-4-hetarylpyrazole **3b-f** (1 mmole) in 10% methanolic potassium hydroxide (10 ml) was stirred at 65° for 30 minutes. Methanol was removed *in vacuo* and water (10 ml) added. The solution was neutralized with 5% hydrochloric acid. The product was then isolated by filtration, washed with cold water (1 x 5 ml), and dried to afford the corresponding 4-hetaryl-3(5)-pyrazolecarboxylic acid **4e-f** in good yields.

4-(2-Thienyl)-3(5)-pyrazolecarboxylic Acid (**4b**).

This compound was obtained as a white solid in 80% yield, mp 244-245°; ir (nujol): 3240 (NH), 1720 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 6.90-7.20 (m, 1H, thienyl protons), 7.25-7.65 (m, 2H, thienyl protons), 7.95 (s, 1H, pyrazole protons).

Anal. Calcd. for $C_8H_6N_2O_2S$: C, 49.47; H, 3.11; N, 14.42. Found: C, 49.23; H, 3.17; N, 14.54.

4-(3-Thienyl)-3(5)-pyrazolecarboxylic Acid (**4c**).

This compound was obtained as a white solid in 62% yield, mp 278-279°; ir (nujol): 3250 (NH), 1725 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 7.40-7.65 (m, 2H, thienyl protons), 7.85-7.95 (m, 1H, thienyl protons), 8.05 (s, 1H, pyrazole protons).

Anal. Calcd. for $C_8H_6N_2O_2S$: C, 49.47; H, 3.11; N, 14.42. Found: C, 49.23; H, 3.27; N, 14.61.

4-(2-Furyl)-3(5)-pyrazolecarboxylic Acid (**4d**).

This compound was obtained as a white solid in 75% yield, mp 230-231°; ir (nujol): 3260 (NH), 1710 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 6.40-6.70 (m, 1H, furyl protons), 6.95-7.20 (m, 1H, furyl protons), 7.55-7.75 (m, 1H, furyl protons), 8.00 (s, 1H, pyrazole protons).

Anal. Calcd. for $C_8H_6N_2O_3$: C, 53.93; H, 3.39; N, 15.72. Found: C, 54.06; H, 3.44; N, 15.65.

4-(3-Pyridyl)-3(5)-pyrazolecarboxylic Acid (**4e**).

This compound was obtained as a white solid in 68% yield, mp 250-251°; ir (nujol): 3390 (NH), 1710 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 7.85-8.10 (m, 1H, pyridyl protons), 8.20 (s, 1H, pyrazole protons), 8.55-8.85 (m, 2H, pyridyl protons), 9.22 (s, 1H, pyridyl protons).

Anal. Calcd. for $C_9H_7N_3O_2$: C, 57.14; H, 3.73; N, 22.21. Found: C, 57.32; H, 3.65; N, 22.33.

4-(4-Pyridyl)-3(5)-pyrazolecarboxylic Acid (**4f**).

This compound was obtained as a white solid in 74% yield, mp 255-256°; ir (nujol): 3390 (NH), 1720 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 7.95 (d, 2H, J = 7 Hz, pyridyl protons) 8.27 (s, 1H, pyrazole protons), 8.67 (d, 2H, J = 7 Hz, pyridyl protons).

Anal. Calcd. for $C_9H_7N_3O_2$: C, 54.17; H, 3.73; N, 22.21. Found: C, 57.28; H, 3.67; N, 22.23.

REFERENCES AND NOTES

[1] J. Elguero, in "Comprehensive Heterocyclic Chemistry", Vol **6**, A. R. Katritzky, ed, Pergamon Press, Oxford, 1981, p 167.

[2] A. Pawda, in "1,3-Dipolar Cycloaddition Chemistry", John Wiley and Sons, Inc, New York, 1984.

[3] D. S. Wulfman, G. Linstrumelle and C. F. Cooper, in "The Chemistry of the Diazonium and Diazo Groups", Part 2, S. Patai, ed, Interscience, 1978, p 854.

[4] C. Cativiela, M. D. Diaz de Villegas and M. P. Gainza, *Synth. Commun.*, **17**, 165 (1987).

[5] M. J. S. Dewar and W. H. Thiel, *J. Am. Chem. Soc.*, **99**, 4917 (1977).

[6] R. Huisgen in ref [2], p 130 and references therein.

[7] D. Ajò, V. Busetti, H. C. J. Ottenheijm and R. Plate, *Acta Cryst.*, **C40**, 4917 (1984); D. Ajò, M. Casarin, G. Granozzi and V. Busetti, *Tetrahedron*, **37**, 3507 (1981); D. Ajò, M. Casarin, G. Granozzi, H. C. J. Ottenheijm and R. Plate, *Rec. Trav. Chim.*, **103**, 385 (1984).

[8] Geometries were fully optimized except the mentioned dihedral angles.

[9] J. Sauer, *Angew. Chem., Int. Ed. Engl.*, **6**, 16 (1967).

[10] M. J. S. Dewar and M. L. Mckee, *J. Comp. Chem.*, **4**, 84 (1983).

[11] C. Cativiela, M. D. Diaz de Villegas, J. I. García, J. A. Mayoral, E. Meléndez, *An. Quim. Ser. C*, **81**, 56 (1985).