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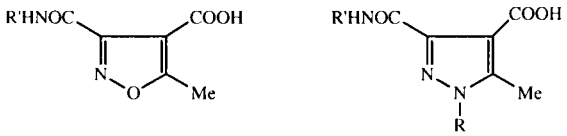
Received May 25, 1999

Ethyl 2-amino-3-methoxycarbonyl-4-oxo-2-pentenoate (3) reacts with hydroxylamine or hydrazines to give isoxazole and pyrazole ortho-dicarboxylic acid esters 4 and 5, respectively. Partial hydrolysis of diesters 4 and 5 afforded the corresponding dicarboxylic acid monoesters 6 and 7. Amidation of the intermediate acid chlorides 8,9 followed by hydrolysis of 4-methylesters 10,11 gave the title compounds 1 and 2, respectively.

J. Heterocyclic Chem., **37**, 175 (2000).

Pyrazoles and isoxazoles play an important role among a wide variety of nitrogen heterocycles that have been used for developing useful herbicides [1]. In particular, it was found by BASF that some 3-carboxamido-4-isoxazolecarboxylic acids **1** [2] display herbicidal activity as inhibitors of photosynthesis. They affected the photosynthetic electron transport in photosystem II and the rate of carbon dioxide assimilation. To this end we decided to extend the investigation to 3-carboxamido-4-pyrazolecarboxylic acid derivatives **2** as potential herbicides.

The only preparative route to isoxazole amide derivatives **1** reported in literature starts from β-ketoesters and 2-chloro-2-hydroxyiminoacetamide as nitrile equivalents, available by reaction of diketene with amines, subsequent nitrosation of the activated methylene group and removal of the acetyl group by chlorination [2].



1 2

Figure 1

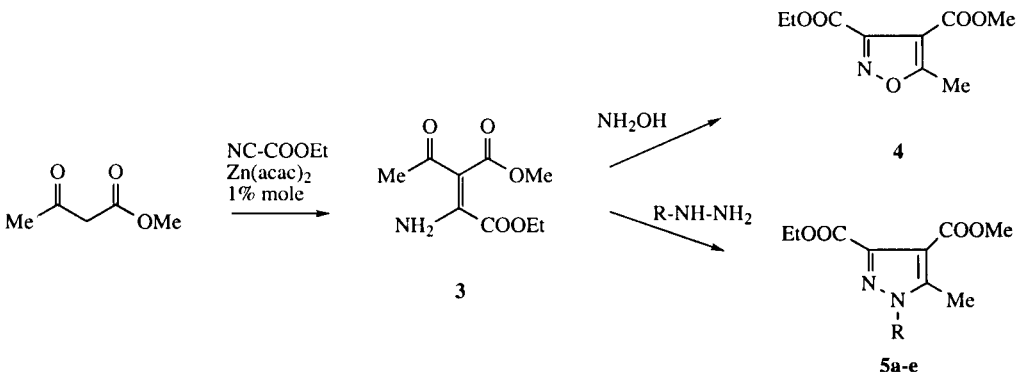
Earlier work in our laboratory has shown that ethyl 2-amino-3-methoxycarbonyl-4-oxo-2-pentenoate (**3**), easily prepared from methyl acetoacetate and ethyl cyanoformate in the presence of catalytic amount of zinc acetylacetonate [3], reacts with hydroxylamine and hydrazines to give respectively isoxazole and pyrazole *ortho*-dicarboxylic acid esters as the only or the major reaction products in high yields [4].

Therefore we decided to investigate a new synthetic entry to unknown 3-carboxamido-4-pyrazolecarboxylic acid derivatives **2** by a simple and straightforward method, also applicable to the known 3-carboxamido-4-isoxazolecarboxylic acid derivatives **1**.

The reaction of **3** with hydroxylamine afforded the isoxazole **4**, whereas **3** reacted with alkyl and aryl hydrazines to give pyrazolo derivatives **5** in high yield (Scheme 1).

The selective hydrolysis of ester group in the position 3 was achieved in mild conditions by treatment of diesters **4** and **5** with one equivalent of KOH in water at 0° for 24 hours to give the dicarboxylic acid monoesters **6** and **7**, respectively. The acid chlorides **8** and **9** were obtained by treatment of monocarboxylic acids **6** and **7** with phosphorus pentachloride in anhydrous diethyl ether at low temperature. Amidation with *tert*-butylamine or cyclopropylamine of the intermediate acid chlorides **8** and **9** afforded the corresponding carboxamido esters **10** and **11**. The hydrolysis of these compounds with an excess of KOH in ethanol under reflux gave finally the title compounds **1** and **2**. The 1-*tert*-butyl group of the pyrazole moiety is cleavable in acidic medium [5]: 1-*tert*-butyl-3-cyclopropylcarboxamido-5-methyl-4-pyrazolecarboxylic acid (**2g**) when heated under reflux in formic acid gave the dealkylated homologue **2k** (Scheme 2).

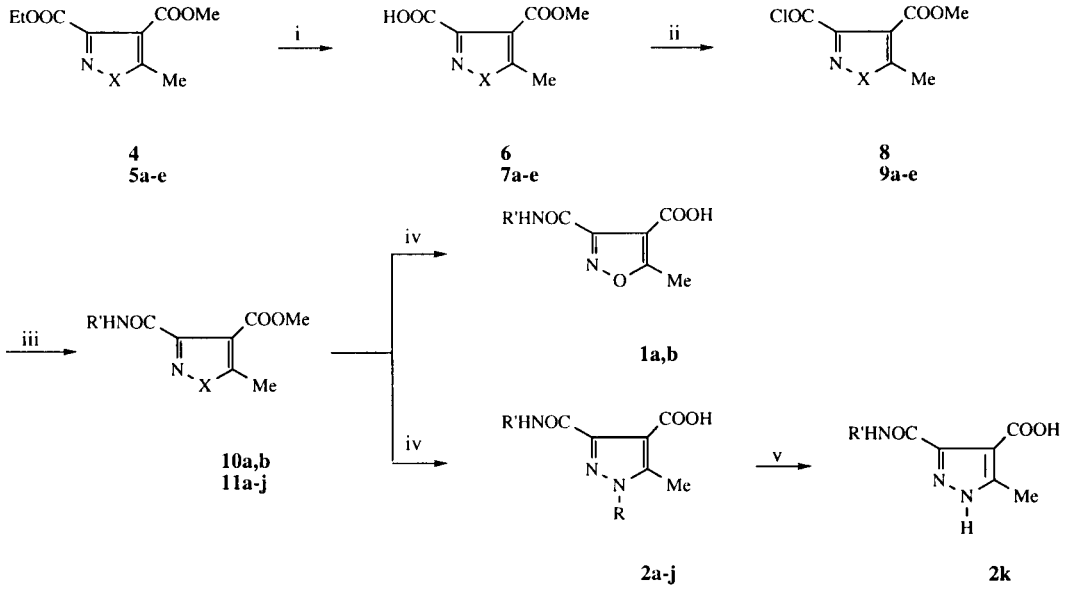
Scheme 1



3 4 5a-e

All these reactions gave the desired compounds in good yields. The spectral data agree with the reported structures. The structure of ethyl 4-(methoxycarbonyl)-5-methyl-3-pyrazolecarboxylate **5** was confirmed based upon two chemical shifts at *ca.* 144 ppm attributable to C-3 and C-5 carbon atoms of the pyrazole ring and on the ^{13}C nmr spectra reported by us for similar compounds [4].

Scheme 2



i: KOH; ii: PCl_5; iii: R'-NH_2 (R' = *t*-Bu, cyclopropyl); iv: KOH; v: HCOOH, reflux
For compounds **4,6,8,10**: X = O; for compounds **5,7,9,11**: X = NR
For compounds **5,7,9**: **a**: R = Me; **b**: R = *t*-Bu; **c**: R = Ph; **d**: R = 4-ClPh; **e**: R = 2,6-Cl-4-CF_3Ph
For compounds **1,10**: **a**: R' = *t*-Bu; **b**: R' = cyclopropyl
For compounds **2,11**: **a**: R = Me, R' = *t*-Bu; **b**: R,R' = *t*-Bu; **c**: R = Ph, R' = *t*-Bu; **d**: R = 4-ClPh, R' = *t*-Bu; **e**: R = 2,6-Cl-4-CF_3Ph, R' = *t*-Bu; **f**: R = Me, R' = cyclopropyl; **g**: R = *t*-Bu, R' = cyclopropyl; **h**: R = Ph, R' = cyclopropyl; **i**: R = 4-ClPh, R' = cyclopropyl; **j**: R = 2,6-Cl-4-CF_3Ph, R' = cyclopropyl; **k**: R' = cyclopropyl

EXPERIMENTAL

Melting points were determined with a Büchi capillary apparatus. The ir spectra were recorded on a Perkin-Elmer Paragon 500 FT-IR spectrophotometer. The ^1H nmr spectra were recorded on a Bruker AC 200 spectrometer. Chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane as internal standard. Column chromatography was performed using Merck silica gel (70-230 mesh).

Compounds **5a-c**, **4** and **7c** were prepared according to the reported procedure [4].

General Procedure for the Synthesis of Ethyl 4-(Methoxycarbonyl)-5-methyl-3-pyrazolecarboxylate 5.

To a stirred and cooled (0°) solution of ethyl 2-amino-3-methoxycarbonyl-4-oxo-2-pentenoate (3) (2 g, 9.2 mmoles) in methylene chloride (17 ml), a cooled (0°) solution (23 ml) of the appropriate hydrazine (13.8 mmoles) was added dropwise for ten minutes. The mixture was stirred at the same temperature for 24 hours. The solvent was evaporated in vacuo to give a residue which was dissolved in ethyl acetate, washed with 1 M hydrochloric acid and water, dried (sodium sulfate) and evaporated to yield a residue which was purified by column chromatography (eluent ethyl acetate:petroleum ether 3:7, v/v).

Ethyl 1-(4-Chlorophenyl)-4-(methoxycarbonyl)-5-methyl-3-pyrazolecarboxylate (**5d**).

This compound was obtained as an oil, 2.8 g, yield 94%; ir (neat): 2984, 2952, 1720, 1550, 1501; ^1H nmr (deuteriochloroform): δ 1.39 (t, J = 7.1 Hz, Me), 2.50 (s, 3H, Me), 3.87 (s, 3H, OMe), 4.43 (q, J = 7.1 Hz, 2H, OCH_2), 7.39-7.51 (A_2B_2, J = 8.7 Hz, 4H, Ph); ^{13}C nmr (deuteriochloroform): δ 11.96 (q, J = 126 Hz, Me), 14.18 (q, J = 130 Hz, Me), 51.79 (q, J = 146 Hz, OMe), 61.77 (t, J = 147 Hz, OCH_2), 112.78 (s, C-4), 127.03 (d, J = 164 Hz, Ph), 129.56 (d, J = 167 Hz, Ph), 135.21 (s, Ph), 136.63 (s, Ph), 144.13 (s, C-5), 144.99 (s, C-3), 162.52 (s, COO), 163.26 (s, COO).

Anal. Calcd. for $C_{15}H_{15}ClN_2O_4$: C, 55.82; H, 4.68; Cl, 10.98; N, 8.68. Found: C, 55.72; H, 4.72; Cl, 10.90; N, 8.57.

Ethyl 1-(2,6-Dichloro-4-trifluoromethylphenyl)-4-(methoxycarbonyl)-5-methyl-3-pyrazolecarboxylate (**5e**).

This compound was obtained as an oil, 2.7 g, yield 70%; ir (neat): 2987, 1723, 1562; ^1H nmr (deuteriochloroform): δ 1.39

(t, J = 7.1 Hz, Me), 2.33 (s, 3H, Me), 3.89 (s, 3H, OMe), 4.41 (q, J = 7.1 Hz, 2H, OCH_2), 7.76 (s, 2H, Ph); ^{13}C nmr (deuteriochloroform): δ 10.74 (q, J = 130 Hz, Me), 14.20 (q, J = 126 Hz, Me), 51.93 (q, J = 146 Hz, OMe), 61.91 (t, J = 147 Hz, OCH_2), 112.72 (s, C-4), 122 (q, J_{C-F} = 272 Hz, CF_3), 125.89 (d, J = 160 Hz, Ph), 134.00 (q, J_{C-F} = 34 Hz, Ph), 136.23 (s, Ph), 136.67 (s, Ph), 144.09 and 146.21 (s, C-3 and C-5), 161.91 (s, COO), 163.02 (COO).

Anal. Calcd. for $C_{16}H_{13}C_{12}F_3N_2O_4$: C, 45.20; H, 3.08; Cl, 16.68; F, 13.40; N, 6.59. Found: C, 45.10; H, 3.14; Cl, 16.60; F, 13.35; N, 6.42.

General Procedure for the Synthesis of 3-Isoxazolecarboxylic Acid **6** or 3-Pyrazolecarboxylic Acids **7**.

To a cooled (0°) solution of isoxazole or pyrazole diester **4,5** (3 mmoles) in methanol (8 ml), a solution (3 ml, 3 mmoles) of 1 *M* potassium hydroxide was added. The mixture was stirred at the same temperature for 24 hours. The solvent was concentrated to a volume of 2 ml *in vacuo*, diluted with ethyl acetate and extracted with water. The aqueous layer was separated, acidified with 6 *M* hydrochloric acid and extracted with ethyl acetate. The organic layer was dried (sodium sulfate) and evaporated to dryness.

4-(Methoxycarbonyl)-5-methyl-3-isoxazolecarboxylic Acid (**6**).

This compound was obtained as colorless crystals, 0.41 g, yield 75%, mp 104-105° (triturated with diethyl ether); ir (potassium bromide): 2967, 2615, 1757, 1629, 1484; ^1H nmr (deuteriochloroform): δ 2.79 (s, 3H, Me), 4.07 (s, 3H, OMe), 9.5 (br s, 1H, OH).

Anal. Calcd. for $C_7H_7NO_5$: C, 45.41; H, 3.81; N, 7.57. Found: C, 45.22; H, 3.87; N, 7.41.

1,5-Dimethyl-4-(methoxycarbonyl)-3-pyrazolecarboxylic Acid (**7a**).

This compound was obtained as colorless crystals, 0.34 g, yield 57%, mp 155-156° (triturated with diethyl ether); ir (potassium bromide): 2627, 1748, 1627, 1491; ^1H nmr (deuteriochloroform): δ 2.57 (s, 3H, Me), 3.93 (s, 3H, NMe or OMe), 4.00 (s, 3H, NMe or OMe), 14.11 (br s, 1H, OH).

Anal. Calcd. for $C_8H_{10}N_2O_4$: C, 48.49; H, 5.09; N, 14.14. Found: C, 48.39; H, 5.14; N, 14.04.

1-*tert*-Butyl-4-(methoxycarbonyl)-5-methyl-3-pyrazolecarboxylic Acid (**7b**).

This compound was obtained as colorless crystals, 0.32 g, yield 44%, mp 207-209° (triturated with diethyl ether); ir (potassium bromide): 2993, 2607, 1748, 1634, 1493; ^1H nmr (deuteriochloroform): δ 1.73 (s, 9H, *t*-Bu), 2.76 (s, 3H, Me), 4.00 (s, 3H, OMe), 14.00 (br s, 1H, OH).

Anal. Calcd. for C11H16N2O4: C, 54.99; H, 6.71; N, 11.66. Found: C, 54.85; H, 6.79; N, 11.54.

1-(4-Chlorophenyl)-4-(methoxycarbonyl)-5-methyl-3-pyrazolecarboxylic Acid (**7d**).

This compound was obtained as colorless crystals, 0.72 g, yield 81%, mp 163-165° (triturated with diethyl ether); ir (potassium bromide): 2684, 1742, 1632, 1495; ^1H nmr (deuteriochloroform): δ 2.55 (s, 3H, Me), 4.05 (s, 3H, OMe), 7.36-7.52 (A_2B_2, J = 8.7 Hz, 4H, Ph), 12.5 (br s, 1H, OH).

Anal. Calcd. for $C_{13}H_{11}ClN_2O_4$: C, 52.98; H, 3.76; Cl, 12.03; N, 9.51. Found: C, 52.82; H, 3.74; Cl, 12.07; N, 9.44.

1-(2,6-Dichloro-4-trifluoromethylphenyl)-4-(methoxycarbonyl)-5-methyl-3-pyrazolecarboxylic Acid (**7e**).

This compound was obtained as colorless crystals, 0.90 g, yield 75%, mp 180-183° (triturated with diethyl ether); ir (potassium bromide): 2962, 2697, 1751, 1637, 1486; ^1H nmr (deuteriochloroform): δ 2.42 (s, 3H, Me), 4.07 (s, 3H, OMe), 7.78 (s, 2H, Ph).

Anal. Calcd. for $C_{14}H_9Cl_2F_3N_2O_4$: C, 42.34; H, 2.28; Cl, 17.85; F, 14.35; N, 7.05. Found: C, 42.18; H, 2.35; Cl, 17.75; F, 14.26; N, 6.98.

General Procedure for the Synthesis of Methyl 3-Carboxamido-4-isoxazolecarboxylates **10** or Methyl 3-Carboxamido-4-pyrazolecarboxylates **11**.

To a cooled (-10°) suspension of 3-isoxazole- or pyrazolecarboxylic acid **6,7** (1.5 mmoles) in anhydrous diethyl ether (15 ml) 0.342 g (1.65 mmoles) of phosphorus pentachloride was added. After being warmed to 0° gradually, the mixture was stirred at that temperature for 1 hour. The solvent was evaporated to dryness *in vacuo*, the solid was washed twice with anhydrous diethyl ether and dried under reduced pressure. The resulting acyl chlorides **8** or **9** were directly reacted as follows. A solution of **8** or **9** in chloroform (15 ml) was added dropwise for ten minutes to a stirred mixture of pertinent amine (3 mmoles) in chloroform (30 ml) and of sodium hydrogen carbonate (0.13 g, 1.6 mmoles) in water (30 ml). The mixture was stirred with the aid of a magnetic stirrer for four hours at room temperature. The organic layer was washed with 1 *M* hydrochloric acid, aqueous 5% sodium carbonate and water, dried (sodium sulfate) and evaporated. The solid was triturated with diethyl ether and collected.

Methyl 3-*tert*-Butylcarboxamido-5-methyl-4-isoxazolecarboxylate (**10a**).

This compound was obtained as colorless crystals, 0.23 g, yield 64%, mp 77-80° (triturated with diethyl ether); ir (potassium bromide): 3259, 2992, 1738, 1650, 1570; ^1H nmr (deuteriochloroform): δ 1.46 (s, 9H, *t*-Bu), 2.67 (s, 3H, Me), 3.88 (s, 3H, Me), 7.38 (br s, 1H, NH).

Anal. Calcd. for $C_{11}H_{16}N_2O_4$: C, 54.99; H, 6.71; N, 11.66. Found: C, 54.81; H, 6.78; N, 11.52.

Methyl 3-Cyclopropylcarboxamido-5-methyl-4-isoxazolecarboxylate (**10b**).

This compound was obtained as colorless crystals, 0.26 g, yield 77%, mp 77-79° (triturated with diethyl ether); ir (potassium bromide): 3267, 1731, 1657, 1567; ^1H nmr (deuteriochloroform): δ 0.61-0.69 (m, 2H, CH_2), 0.83-0.93 (m, 2H, CH_2), 2.69 (s, 3H, Me), 2.91-3.00 (m, 1H, CH), 3.90 (s, 3H, OMe), 8.07 (br s, 1H, NH).

Anal. Calcd. for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.49. Found: C, 53.43; H, 5.43; N, 12.32.

Methyl 3-*tert*-Butylcarboxamido-1,5-dimethyl-4-pyrazolecarboxylate (**11a**).

This compound was obtained as colorless crystals, 0.23 g, yield 60%, mp 154-155°; ir (potassium bromide): 3263, 2965, 1716, 1670, 1554; ^{1}H nmr (deuteriochloroform): δ 1.46 (s, 9H, *t*-Bu), 2.48 (s, 3H, Me), 3.84 (s, 3H, NMe or OMe), 3.87 (s, 3H, NMe or OMe), 8.81 (br s, 1H, NH).

Anal. Calcd. for $C_{12}H_{19}N_3O_3$: C, 56.90; H, 7.56; N, 16.59. Found: C, 56.78; H, 7.62; N, 16.48.

Methyl 1-*tert*-Butyl-3-*tert*-butylcarboxamido-5-methyl-4-pyrazolecarboxylate (**11b**).

This compound was obtained as an oil, 0.36 g, yield 82%; ir (neat): 3296, 2971, 1714, 1681, 1538; ^{1}H nmr (deuteriochloroform): δ 1.46 (s, 9H, *t*-Bu), 1.67 (s, 9H, *t*-Bu), 2.63 (s, 3H, Me), 3.87 (s, 3H, OMe), 7.95 (br s, 1H, NH).

Anal. Calcd. for $C_{15}H_{25}N_3O_3$: C, 60.99; H, 8.53; N, 14.23. Found: C, 60.82; H, 8.59; N, 14.13.

Methyl 3-*tert*-Butylcarboxamido-5-methyl-1-phenyl-4-pyrazolecarboxylate (**11c**).

This compound was obtained as colorless crystals, 0.34 g, yield 72%, mp 147-149°; ir (potassium bromide): 3315, 2966, 1728, 1670, 1540, 1497; ^{1}H nmr (deuteriochloroform): δ 1.48 (s, 9H, *t*-Bu), 2.47 (s, 3H, Me), 3.91 (s, 3H, OMe), 7.38-7.51 (m, 5H, Ph), 8.12 (br s, 1H, NH).

Anal. Calcd. for $C_{17}H_{21}N_3O_3$: C, 64.74; H, 6.71; N, 13.32. Found: C, 64.78; H, 6.64; N, 13.42.

Methyl 3-*tert*-Butylcarboxamido-1-(4-chlorophenyl)-5-methyl-4-pyrazolecarboxylate (**11d**).

This compound was obtained as colorless crystals, 0.36 g, yield 69%, mp 112-114°; ir (potassium bromide): 3298, 2974, 1712, 1657, 1557, 1501; ^{1}H nmr (deuteriochloroform): δ 1.48 (s, 9H, *t*-Bu), 2.48 (s, 3H, Me), 3.91 (s, 3H, OMe), 7.34-7.50 (A_2B_2, J = 8.7 Hz, 4H, Ph), 8.27 (br s, 1H, NH).

Anal. Calcd. for $C_{17}H_{20}ClN_3O_3$: C, 58.37; H, 5.76; Cl, 10.13, N, 12.01. Found: C, 58.19; H, 5.82; Cl, 10.04, N, 12.13.

Methyl 3-*tert*-Butylcarboxamido-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methyl-4-pyrazolecarboxylate (**11e**).

This compound was obtained as colorless crystals, 0.53 g, yield 78%, mp 150-151°; ir (potassium bromide): 3286, 2969, 1697, 1671, 1573, 1507; ^{1}H nmr (deuteriochloroform): δ 1.48 (s, 9H, *t*-Bu), 2.33 (s, 3H, Me), 3.93 (s, 3H, OMe), 7.75 (s, 2H, Ph), 8.23 (br s, 1H, NH).

Anal. Calcd. for $C_{18}H_{18}Cl_2F_3N_3O_3$: C, 47.80; H, 4.01; Cl, 15.68; F, 12.60; N, 9.29. Found: C, 47.88; H, 4.09; Cl, 15.77; F, 12.48; N, 9.19.

Methyl 3-Cyclopropylcarboxamido-1,5-dimethyl-4-pyrazolecarboxylate (**11f**).

This compound was obtained as colorless crystals, 0.25 g, yield 71%, mp 115-117°; ir (potassium bromide): 3085, 1675, 1654, 1587, 1493; ^{1}H nmr (deuteriochloroform): δ 0.61-0.66 (m, 2H, CH_2), 0.79-0.89 (m, 2H, CH_2), 2.50 (s, 3H, Me), 2.94-3.01 (m, 1H, CH), 3.87 (s, 3H, NMe or OMe), 3.89 (s, 3H, NMe or OMe), 9.36 (br s, 1H, NH).

Anal. Calcd. for $C_{11}H_{15}N_3O_3$: C, 55.69; H, 6.37; N, 17.71. Found: C, 55.53; H, 6.45; N, 17.59.

Methyl 1-*tert*-Butyl-3-cyclopropylcarboxamido-5-methyl-4-pyrazolecarboxylate (**11g**).

This compound was obtained as colorless crystals, 0.30 g, yield 71%, mp 119-121°; ir (potassium bromide): 3213, 3006, 1688, 1663, 1560, 1504; ^{1}H nmr (deuteriochloroform): δ 0.60-0.62 (m, 2H, CH_2), 0.79-0.84 (m, 2H, CH_2), 1.65 (s, 9H, *t*-Bu), 2.61 (s, 3H, Me), 2.87-2.89 (m, 1H, CH), 3.86 (s, 3H, OMe), 7.95 (br s, 1H, NH).

Anal. Calcd. for $C_{14}H_{21}N_3O_3$: C, 60.20; H, 7.58; N, 15.04. Found: C, 60.03; H, 7.66; N, 14.95.

Methyl 3-Cyclopropylcarboxamido-5-methyl-1-phenyl-4-pyrazolecarboxylate (11h).

This compound was obtained as colorless crystals, 0.31 g, yield 69%, mp 134-136°; ir (potassium bromide): 3247, 1711, 1661, 1498; ^{1}H nmr (deuteriochloroform): δ 0.62-0.68 (m, 2H, CH_2), 0.80-0.89 (m, 2H, CH_2), 2.47 (s, 3H, Me), 2.93-3.00 (m, 1H, CH), 3.91 (s, 3H, OMe), 7.37-7.51 (m, 5H, Ph), 8.73 (br s, 1H, NH).

Anal. Calcd. for $C_{16}H_{17}N_3O_3$: C, 64.20; H, 5.72; N, 14.04. Found: C, 64.08; H, 5.79; N, 13.92.

Methyl 3-Cyclopropylcarboxamido-1-(4-chlorophenyl)-5-methyl-4-pyrazolecarboxylate (11i).

This compound was obtained as colorless crystals, 0.25 g, yield 51%, mp 153-155°; ir (potassium bromide): 3257, 1717, 1653, 1558, 1499; ^{1}H nmr (deuteriochloroform): δ 0.64-0.67 (m, 2H, CH_2), 0.80-0.90 (m, 2H, CH_2), 2.47 (s, 3H, Me), 2.93-3.02 (m, 1H, CH), 3.91 (s, 3H, OMe), 7.33-7.50 (A_2B_2, J = 8.7 Hz, 4H, Ph), 8.79 (br s, 1H, NH).

Anal. Calcd. for $C_{16}H_{16}ClN_3O_3$: C, 57.58; H, 4.83; Cl, 10.62, N, 12.59. Found: C, 57.36; H, 4.88; Cl, 10.50, N, 12.41.

Methyl 3-Cyclopropylcarboxamido-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methyl-4-pyrazolecarboxylate (11j).

This compound was obtained as colorless crystals, 0.39 g, yield 60%, mp 124-126°; ir (potassium bromide): 3273, 1718, 1653, 1557; ^{1}H nmr (deuteriochloroform): δ 0.64 (m, 2H, CH_2), 0.80-0.87 (m, 2H, CH_2), 2.33 (s, 3H, Me), 2.98-3.03 (m, 1H, CH), 3.93 (s, 3H, OMe), 7.75 (s, 2H, Ph), 8.91 (br s, 1H, NH).

Anal. Calcd. for $C_{17}H_{14}Cl_2F_3N_3O_3$: C, 46.81; H, 3.23; Cl, 16.25, F, 13.07; N, 9.63. Found: C, 46.73; H, 3.28; Cl, 16.15, F, 12.96; N, 9.69.

General Procedure for the Synthesis of 3-Carboxamido-5-methyl-4-isoxazole- or 4-Pyrazolecarboxylic Acids 1 and 2.

To a solution of 4-isoxazole- or 4-pyrazolecarboxylic acid methyl ester **10,11** (1 mmole) in ethanol (6 ml) ethanolic 1*N* potassium hydroxide (6 ml) was added. After the addition, the mixture was heated under reflux for 1 hour. The solvent was evaporated to dryness *in vacuo* to give a residue which was dissolved in ethyl acetate. The organic solution was extracted with water. The aqueous layer was separated, acidified with 6*M* hydrochloric acid and extracted with ethyl acetate. The organic layer was dried (sodium sulfate) and evaporated to dryness.

3-tert-Butylcarboxamido-5-methyl-4-isoxazolecarboxylic Acid (**1a**).

This compound was obtained as colorless crystals, 0.20 g, yield 91%, mp 95-97°; ir (potassium bromide): 2967, 1704, 1645, 1441;

^{1}H nmr (deuteriochloroform): δ 1.50 (s, 9H, *t*-Bu), 2.82 (s, 3H, Me), 7.16 (br s, 1H, NH), 14.69 (br s, 1H, OH).

Anal. Calcd. for $C_{10}H_{14}N_2O_4$: C, 53.09; H, 6.24; N, 12.38. Found: C, 53.25; H, 6.31; N, 12.19.

3-Cyclopropylcarboxamido-5-methyl-4-isoxazolecarboxylic Acid (**1b**).

This compound was obtained as colorless crystals, 0.16 g, yield 76%, mp 123-125°; ir (potassium bromide): 3325, 1726, 1608, 1465; ^{1}H nmr (deuteriochloroform): δ 0.73-0.79 (m, 2H, CH_2), 0.88-0.96 (m, 2H, CH_2), 2.77 (s, 3H, Me), 2.94 (m, 1H, CH), 7.65 (br s, 1H, NH), 13.62 (br s, 1H, OH); ^{13}C nmr (deuteriochloroform): δ 6.56 (t, J = 163 Hz, $2CH_2$), 13.51 (q, J = 131 Hz, Me), 23.25 (d, J = 182 Hz, CH), 109.64 (s, C-4), 152.41 (s, C-3), 160.68 and 162.62 (two s, COO and CONH), 180.29 (s, C-5).

Anal. Calcd. for $C_9H_{10}N_2O_4$: C, 51.43; H, 4.80; N, 13.33. Found: C, 51.25; H, 4.84; N, 13.19.

3-*tert*-Butylcarboxamido-1,5-dimethyl-4-pyrazolecarboxylic Acid (**2a**).

This compound was obtained as colorless crystals, 0.20 g, yield 83%, mp 171-172°; ir (potassium bromide): 3384, 2981, 1713, 1610, 1560; ^{1}H nmr (deuteriochloroform): δ 1.46 (s, 9H, *t*-Bu), 2.62 (s, 3H, Me), 3.82 (s, 3H, NMe), 7.30 (br s, 1H, NH), 15.48 (br s, 1H, OH).

Anal. Calcd. for $C_{11}H_{17}N_3O_3$: C, 55.22; H, 7.16; N, 17.56. Found: C, 55.08; H, 7.22; N, 17.39.

1-*tert*-Butyl-3-*tert*-butylcarboxamido-5-methyl-4-pyrazolecarboxylic Acid (**2b**).

This compound was obtained as colorless crystals, 0.22 g, yield 78%, mp 168-169°; ir (potassium bromide): 3285, 2983, 1708, 1562, 1519; ^{1}H nmr (deuteriochloroform): δ 1.47 (s, 9H, *t*-Bu), 1.68 (s, 9H, *t*-Bu), 2.85 (s, 3H, Me), 7.26 (br s, 1H, NH), 15.62 (br s, 1H, OH).

Anal. Calcd. for $C_{14}H_{23}N_3O_3$: C, 59.77; H, 8.24; N, 14.93. Found: C, 59.58; H, 8.35; N, 14.76.

3-*tert*-Butylcarboxamido-5-methyl-1-phenyl-4-pyrazolecarboxylic Acid (**2c**).

This compound was obtained as colorless crystals, 0.27 g, yield 90%, mp 184°; ir (potassium bromide): 3382, 2975, 1703, 1596, 1561, 1488; ^{1}H nmr (deuteriochloroform): δ 1.48 (s, 9H, *t*-Bu), 2.62 (s, 3H, Me), 7.39-7.58 (m, 6H, Ph + NH), 15.57 (br s, 1H, OH).

Anal. Calcd. for $C_{16}H_{19}N_3O_3$: C, 63.77; H, 6.36; N, 13.94. Found: C, 63.59; H, 6.42; N, 13.77.

3-*tert*-Butylcarboxamido-1-(4-chlorophenyl)-5-methyl-4-pyrazolecarboxylic Acid (**2d**).

This compound was obtained as colorless crystals, 0.25 g, yield 74%, mp 200-203°; ir (potassium bromide): 3381, 2971, 2414, 1713, 1619, 1560; ^{1}H nmr (deuteriochloroform): δ 1.47 (s, 9H, *t*-Bu), 2.61 (s, 3H, Me), 7.30 (br s, 1H, NH), 7.34-7.55 (m, 4H, Ph), 15.55 (br s, 1H, OH).

Anal. Calcd. for $C_{16}H_{18}ClN_3O_3$: C, 57.23; H, 5.40; Cl, 10.56; N, 12.51. Found: C, 57.11; H, 5.46; Cl, 10.42; N, 12.39.

3-*tert*-Butylcarboxamido-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methyl-4-pyrazolecarboxylic Acid (**2e**).

This compound was obtained as colorless crystals, 0.42 g, yield 95%, mp 63-66°; ir (potassium bromide): 3396, 2973, 1720, 1622, 1560; ^{1}H nmr (deuteriochloroform): δ 1.49 (s, 9H, *t*-Bu), 2.47 (s, 3H, Me), 7.26 (br s, 1H, NH), 7.81 (s, 2H, Ph), 15.58 (br s, 1H, OH).

Anal. Calcd. for $C_{17}H_{16}Cl_2F_3N_3O_3$: C, 46.59; H, 3.68; Cl, 16.18; F, 13.01; N, 9.59. Found: C, 46.40; H, 3.73; Cl, 16.05; F, 13.14; N, 9.42.

3-Cyclopropylcarboxamido-1,5-dimethyl-4-pyrazolecarboxylic Acid (**2f**).

This compound was obtained as colorless crystals, 0.18 g, yield 81%, mp 140-142°; ir (potassium bromide): 3282, 1712, 1600, 1567; ^{1}H nmr (deuteriochloroform): δ 0.66-0.73 (m, 2H, CH_2), 0.86-0.93 (m, 2H, CH_2), 2.62 (s, 3H, Me), 2.85-2.94 (m, 1H, CH), 3.81 (s, 3H, NMe), 7.41 (br s, 1H, NH), 15.15 (br s, 1H, OH); ^{13}C nmr (deuteriochloroform): δ 6.47 (t, J = 162 Hz, $2CH_2$), 11.04 (q, J = 129 Hz, Me), 22.62 (d, J = 181 Hz, CH), 36.94 (q, J = 140 Hz, N-Me), 112.63 (s, C-4), 140.30 (s, C-3), 147.81 (s, C-5), 163.03 and 165.38 (two s, COO and CONH).

Anal. Calcd. for $C_{10}H_{13}N_3O_3$: C, 53.81; H, 5.87; N, 18.82. Found: C, 53.66; H, 5.95; N, 18.67.

1-*tert*-Butyl-3-cyclopropylcarboxamido-5-methyl-4-pyrazolecarboxylic Acid (**2g**).

This compound was obtained as colorless crystals, 0.22 g, yield 84%, mp 185-187°; ir (potassium bromide): 3246, 2921, 1703, 1560; ^{1}H nmr (deuteriochloroform): δ 0.69-0.75 (m, 2H, CH_2), 0.88-0.95 (m, 2H, CH_2), 1.67 (s, 9H, *t*-Bu), 2.84-2.91 (m, 1H, CH), 2.86 (s, 3H, Me), 7.40 (br s, 1H, NH), 15.31 (br s, 1H, OH).

Anal. Calcd. for $C_{13}H_{19}N_3O_3$: C, 58.85; H, 7.22; N, 15.84. Found: C, 58.92; H, 7.18; N, 15.93.

3-Cyclopropylcarboxamido-5-methyl-1-phenyl-4-pyrazolecarboxylic Acid (**2h**).

This compound was obtained as colorless crystals, 0.25 g, yield 78%, mp 160-166°; ir (potassium bromide): 3262, 1708, 1576, 1494; ^{1}H nmr (deuteriochloroform): δ 0.69-0.73 (m, 2H, CH_2), 0.86-0.92 (m, 2H, CH_2), 2.61 (s, 3H, Me), 2.92-2.95 (m, 1H, CH), 7.36-7.56 (m, 6H, Ph + NH), 15.28 (br s, 1H, OH).

Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.98; H, 5.36; N, 14.56.

3-Cyclopropylcarboxamido-1-(4-chlorophenyl)-5-methyl-4-pyrazolecarboxylic Acid (**2i**).

This compound was obtained as colorless crystals, 0.27 g, yield 84%, mp 178-181°; ir (potassium bromide): 3290, 1707, 1560, 1497; ^{1}H nmr (deuteriochloroform): δ 0.70-0.72 (m, 2H, CH_2), 0.90-0.94 (m, 2H, CH_2), 2.61 (s, 3H, Me), 2.92-2.96 (m, 1H, CH), 7.26-7.55 (m, 5H, Ph + NH), 15.22 (br s, 1H, OH).

Anal. Calcd. for $C_{15}H_{14}ClN_3O_3$: C, 56.35; H, 4.41; Cl, 11.09; N, 13.14. Found: C, 56.42; H, 4.37; Cl, 11.01; N, 13.02.

3-Cyclopropylcarboxamido-1-(2,6-dichloro-4-trifluoromethylphenyl)-5-methyl-4-pyrazolecarboxylic Acid (**2j**).

This compound was obtained as colorless crystals, 0.33 g, yield 78%, mp 78-81°; ir (potassium bromide): 3402, 1717,

1610; ^{1}H nmr (deuteriochloroform): δ 0.70-0.76 (m, 2H, CH_2), 0.88-0.98 (m, 2H, CH_2), 2.47 (s, 3H, Me), 2.90-2.97 (m, 1H, CH), 7.44 (br, 1H, NH), 7.81 (s, 2H, Ph), 15.24 (br s, 1H, OH).

Anal. Calcd. for $C_{16}H_{12}Cl_2F_3N_3O_3$: C, 45.52; H, 2.86; Cl, 16.79; F, 13.50; N, 9.95. Found: C, 45.35; H, 2.93; Cl, 16.59; F, 13.38; N, 9.77.

Cleavage of the *tert*-Butyl Group from **2g**.

3-Cyclopropylcarboxamido-5-methyl-4-pyrazolecarboxylic Acid (**2k**).

A suspension of **2g** (0.265 g, 1 mmole) in formic acid (5 ml) was heated under reflux for 2 hours. The solution was evaporated to give a solid which was taken up with water (10 ml): colorless crystals, 0.14 g, 70% yield, mp 248-250°; ir (potassium bromide): 3369, 3087, 2972, 2867, 1676, 1562, 1490; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 0.72 (s, 2H, CH_2), 0.75 (s, 2H, CH_2), 2.50 (s, 3H, Me), 2.93-2.95 (m, 1H, CH), 9.34 (br s, 1H, NH), 13.83 (br s, 1H, NH), 15.45 (br s, 1H, OH).

Anal. Calcd. for $C_9H_{11}N_3O_3$: C, 51.67; H, 5.30; N, 20.09. Found: C, 51.46; H, 5.36; N, 20.21.

Acknowledgments.

The authors are grateful to Dr. A. Casolari for carrying out nmr spectra. Research work supported by grants of MURST, ITALY.

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