A Convenient Synthesis of Pyrazolo[3,4-*d*]pyrimidine-4,6-dione and Pyrazolo[4,3-*d*]pyrimidine-5,7-dione Derivatives

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Pyrazolo-[3,4-*d*]pyrimidine-4,6-diones **5** and pyrazolo[4,3-*d*]pyrimidine-5,7-diones **7** were synthesized by Curtius rearrangement of pyrazolic mono-esters **2** and **3** followed by hetero-cyclization *via* the ureas derivatives **4** and **6** under alkaline conditions.

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In recent years, considerable attention has been focused on the development of new methodologies to synthesize many kinds of pyrazolopyrimidine ring system [1]. Indeed, these compounds are, by now widely recognized as important organic materials showing interesting biological activities. The most important biologically active compounds of this class are the formycin, allopurinol and their corresponding nucleosides. Formicyn A is used as a substitute of adenosine in a variety of biochemical reactions and, also extensively, in biological systems because of its intense fluorescence [2]. Allopurinol is the most widely used drug for treatment of hyperuracemia and gouty arthritis. Its efficiency was attribute to xanthine oxidase inhibition, which is responsible of purines conversion into uric acid [3]. In addition, some nucleosides of the pyrazolo[3,4-*d*]pyrimidine ring are potential immunotherapeutic agents [4] and have also demonstrated antitumor [5] and antiviral activity [6]. Recently it has been proved that, some of them are potent and selective inhibitors of PDE1 and PDE5 cGMP phosphodiesterase *in vitro* and potent oral antihypertensive *in vivo* [7]. It is noteworthy that, derivatives of the pyrazolo[3,4-*d*]pyrimidine ring system are potent inhibitors of tyrosine kinase and of the epidermal growth factor receptors (EGF-R) PTK [8].

These hetero-bicyclic structures are prepared by known reactions on analogous benzenic compounds. The general method described in the literature for their preparation involve the reaction of bifunctional pyrazole derivatives with the appropriate amines (or isocyanates), followed by the cyclization of the ureido derivatives with base [9]. However, other methods to synthesize the pyrazolo[3,4-*d*]-pyrimidine ring system were applied for example cyclization of 6-(benzylidenehydrazino)uracil derivatives [10]. We have shown that the phthalic mono-esters and pyrazolic mono-esters are versatile compounds for the synthesis of different fused heterocyclic systems with a potential therapeutic interest, quinazoline-2,4-diones [11], isomeric nitroquinazoline-2,4-diones [12], benzodiazepines [13] and pyrazolo[3,4-*d*]diazepinediones [14].

In our ongoing research program for new heterocycles containing quinazoline or pyrimidine ring systems, we report here a new rapid and convenient preparation of the two regioisomeric pyrazolo[3,4-*d*]pyrimidine-4,6-dione **5** and pyrazolo[4,3-*d*]pyrimidine-5,7-dione **7** derivatives.

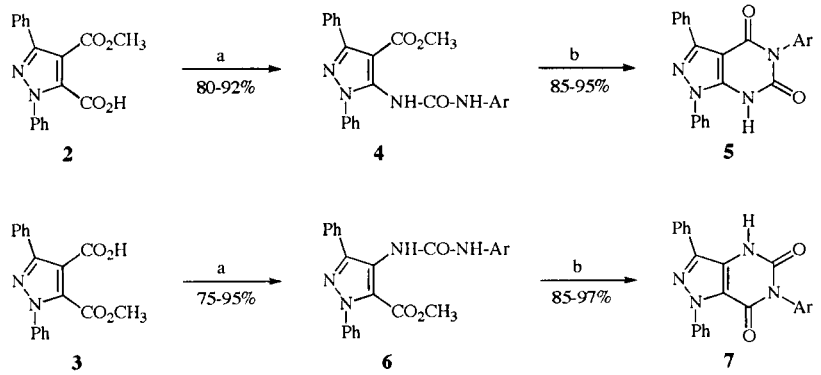
The pyrazolic mono-ester **2** was prepared in good yield from methyl-4,5-pyrazolodicarboxylate **1** by partial saponification and the ester **3** was successfully obtained by treatment of **1** with NaOH 2N (two equivalents), acetic anhydride and methanol, successively [15].

Treatment of mono-esters **2** and **3** by ethyl chloroformate with triethylamine and sodium azide in the presence of a small amount of water give the acyl azide derivatives which were transformed by Curtius rearrangement in isocyanates. They react immediately with the corresponding amines to give, respectively, the *N,N*-disubstituted ureas **4** and **6**. The preparation of pyrazolopyrimidinediones **5** and **7** was achieved, respectively, by cyclization of the **4** and **6** urea derivatives in alkaline conditions (Scheme 1).

This new methodology is applicable to a wide range of aromatic amines substituted in ortho, meta or para position with several groups like alkyl, alkoxy or halogen, but also to heteroaromatic amines such as 2-aminopyridine. In addition, the starting material used in this approach is readily available, and suitable for preparation of derivatives having a wide variety of substituents. All the compounds were fully caracterized by ir, ^{1}H nmr, ^{13}C nmr, mass-spectrometry data and elemental analyses.

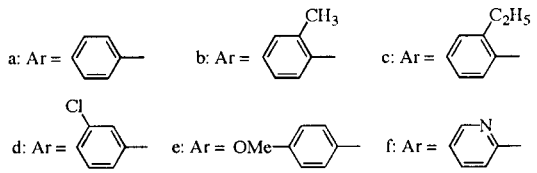
In conclusion, we have described a mild, general and efficient new methodology for the preparation of the two regioisomeric pyrazolo[3,4-*d*]pyrimidine-4,6-dione **5** and pyrazolo[4,3-*d*]pyrimidine-5,7-dione **7** derivatives in good yields.

Scheme 1



a) i) $ClCO_2Et$, Et_3N,THF, 0°C, ii) NaN_3, H_2O, 0°C, iii) $ArNH_2$,DME, Reflux

b) EtONa, EtOH, 80°C



EXPERIMENTAL

Melting points were determined in cappilary tubes with an electrothermal apparatus and are uncorrected. The ir spectra were performed on a ATI Mattson Genesis Series FTIR™ UNICAM instrument and the nmr spectra were recorded on a Bruker Avance DPX250 (^1H nmr; 250 MHz and ^{13}C nmr; 62.9 MHz) Chemical shifts (δ) are reported in parts per million downfield from internal tetramethylsilane. Mass spectra were obtained with a Perkin Elmer SCIEX spectrometer type API 300 (ionspray or heat nebuliser). Reagents and solvents were purified in the usual way [16]. Mono-esters **2** and **3** were prepared as described in reference [15].

General procedure for the preparation of the ureido derivatives **4** and **6**.

All of these reactions were carried out under a argon atmosphere. To a solution of half-esters **2** or **3** (1.0 g, 3.05 mmoles) in dry tetrahydrofuran (15 ml) cooled at -10°C was added dropwise triethylamine (0.62 ml, 4.48 mmoles) then ethyl chloroformate (0.59 ml, 7.13 mmoles). The mixture was stirred for 30 minutes at -10°C. Analysis by tlc showed complete conversion to a very non-polar product. A solution of sodium azide (0.525 g, 8.07 mmoles) in water (3 ml) was then added dropwise with continued stirring for 1 hour at -10°C. The resulting mixture was filtered, evaporated and the aqueous phase was extracted with ethyl acetate (3 x 15 ml). The combined organic layer were washed with brine, dried (magnesium sulfate), filtered and concentrated *in vacuo*. To the acyl azide intermediate in 1,2-dimethoxyethane (20 ml) was added 1.2 equivalents of arylamine. The solution was heated to reflux under stirring for 8 hours. After cooling to room temperature, the 1,2-dimethoxyethane was evaporated to dryness and the residue was precipitated from an appropriate solvent.

Methyl 5-[(anilinocarbonyl)amino]-1,3-diphenyl-1*H*-4-pyrazole carboxylate (**4a**).

This compound was obtained as a white solid (85%) from diethyl ether, mp 212°C, ir (potassium bromide): ν 3357 (NH), 1720 (CO), 1630 (CO), 1551 (C=N) cm^{-1}; ^1H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 3.68 (s, 3H, OCH_3), 6.96-7.76 (m, 15H, aryl protons), 8.66 (broad s, 1H, CO-NH), 9.29 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 51.21 (OCH_3), 105.69, 118.36 (2 C), 122.29, 123.95 (2 C), 127.9 (2 C), 128.11, 128.44, 128.78 (2 C), 128.8 (2 C), 129.13, 132.54, 138.5, 139.22, 140.46 (CO), 151.3 (C_5), 152.25 (C_3), 162.94 (CO); ms: m/z 413 (M+1).

Anal. Calcd. for $C_{24}H_{20}N_4O_3$: C, 69.89; H, 4.89; N, 13.58. Found: C, 69.72; H, 4.81; N, 13.62.

Methyl 5-{[(2-methylanilino)carbonyl]amino}-1,3-diphenyl-1*H*-4-pyrazolecarboxylate (**4b**).

This compound was obtained as a white solid (85%) from diethyl ether, mp 218°C, ir (potassium bromide): ν 3463 (NH), 1723 (CO), 1635 (CO), 1560 (C=N) cm^{-1}; ^1H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 2.18 (s, 3H, CH_3), 3,70 (s, 3H, OCH_3), 6.99-7.79 (m, 14H, aryl protons), 8,43 (broad s, 1H, CO-NH), 8.87 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 17.09 (CH_3), 51.23 (OCH_3), 103.75, 122.93, 123.65 (2 C), 123.95, 125.96, 127.65 (2 C), 128.05, 128.28, 128.44, 128.73 (2 C), 128.93 (2 C), 132.20, 135.36, 135.78, 138.44, 140.35 (CO), 151.05 (C_5), 152.52 (C_3), 162.65 (CO); ms: m/z 427 (M+1).

Anal. Calcd. for $C_{25}H_{22}N_4O_3$: C, 70.41; H, 5.20; N, 13.14. Found: C, 70.65; H, 5.23; N, 13.20.

Methyl 5-{[(2-ethylanilino)carbonyl]amino}-1,3-diphenyl-1*H*-4-pyrazolecarboxylate (**4c**).

This compound was obtained as a white solid (89%) from diethyl ether, mp 260°C, ir (potassium bromide): ν 3281 (NH), 1721 (CO), 1637 (CO), 1561 (C=N) cm^{-1}; ^1H-nmr (dimethyl-d_6

sulfoxide, ppm): δ 1.10 (t, 3H, CH_3, J = 7.5 Hz), 2.53 (q, 2H, CH_2, J = 7.5 Hz), 3.71(s, 3H, OCH_3), 6.98-7.21 (m, 3H, aryl protons), 7.36-7.75 (m, 11H, aryl protons), 8.42 (broad s, 1H, CO-NH), 8.85 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 14.23 (CH_2-CH_3), 23.84 (CH_2-CH_3), 51.23 (OCH_3), 105.68, 123.59, 123.87 (2 C), 124.27, 126.07, 127.88 (2 C), 128.09, 128.42, 128.54, 128.8 (2 C), 129.09 (2 C), 132.54, 135.51, 135.85, 138.54, 140.49 (CO), 151.31 (C_5), 152.74 (C_3), 162.93 (CO); ms: m/z 441 (M+1).

Anal. Calcd. for $C_{26}H_{24}N_4O_3$: C, 70.89; H, 5.49; N, 12.72. Found: C, 70.71; H, 5.48; N, 12.66.

Methyl 5-{[(3-chloroanilino)carbonyl]amino}-1,3-diphenyl-1*H*-4-pyrazolecarboxylate (**4d**).

This compound was obtained as a solid (83%) from diethylether/ petroleum ether, mp 230°C, ir (potassium bromide): ν 3326 (NH), 1718 (CO), 1658 (CO), 1558 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 3.67 (s, 3H, OCH_3), 6.90-7.80 (m, 14H, aryl protons), 8.71 (broad s, 1H, CO-NH), 9.45 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 51.43 (OCH_3), 95.39, 116.99, 117.93, 122.1, 124.19, 127.01 (2 C), 128.08 (2 C), 128.39, 128.95 (2 C), 129.35 (2 C), 130.56, 132.65, 133.3, 138.49, 140.29, 140.97 (CO), 151.51 (C_5), 152.5 (C_3), 162.99 (CO); ms: m/z 447.5 (M+1).

Anal. Calcd. for $C_{24}H_{19}ClN_4O_3$: C, 64.50; H, 4.29; N, 12.54. Found: C, 64.26; H, 4.32; N, 12.40.

Methyl 5-{[(4-methoxyanilino)carbonyl]amino}-1,3-diphenyl-1*H*-4-pyrazolecarboxylate (**4e**).

This compound was obtained as a white solid (92%) from diethyl ether, mp 224°C, ir (potassium bromide): ν 3301 (NH), 1733 (CO), 1631 (CO), 1560 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 3.68 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 6.81 (d, 2H, aryl protons, J = 9.0 Hz), 7.23 (d, 2H, aryl protons, J = 9.0 Hz), 7.43-7.70 (m, 10H, aryl protons), 8.54 (broad s, 1H, CO-NH), 9.07 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 51.12 (OCH_3), 55.06 (OCH_3), 113.87, 120.16 (2 C), 123.81 (2 C), 125.38 (2 C), 127.8 (2 C), 127.98, 128.34, 128.69 (2 C), 129.01 (2 C), 132.07, 132.45, 138.46, 140.56 (CO), 151.17 (C_{23}, C_5, C_3), 152.23 (C_{23}, C_5, C_3), 154.68 (C_{23}, C_5, C_3), 162.87 (CO); ms: m/z 443 (M+1).

Anal. Calcd. for $C_{25}H_{22}N_4O_4$: C, 67.86; H, 5.01; N, 12.66. Found: C, 67.95; H, 4.98; N, 12.68.

Methyl 5-{[(2-aminopyridyl)carbonyl]amino}-1,3-diphenyl-1*H*-4-pyrazolecarboxylate (**4f**).

This compound was obtained as a yellow solid (80%) from diethylether/petroleum ether, mp 178°C, ir (potassium bromide): ν 3385 (NH), 1725 (CO), 1631 (CO), 1560 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 3.70 δ s, 3H, OCH_3), 6.69 (d, 1H, aryl proton, J = 7.7 Hz), 6.97 (dd, 1H, aryl proton, J = 0.9, 7.7 Hz), 7.26-7.45 (m, 6H, aryl protons), 7.60-7.75 (m, 5H, aryl protons), 8.20 (d, 1H, aryl proton, J = 4.0 Hz), 8.83 (broad s, 1H, CO-NH), 12.00 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 52.51 (OCH_3), 106.8, 112.95, 115.08, 129.76 (2 C), 129.86 (2 C), 130.14 (2 C), 130.31, 130.44 (2 C), 130.74 (2 C), 133.64, 140.71, 142.23, 142.36, 148.78, 152.46 (CO), 152.64, 153.01, 163.95 (CO); ms: m/z 414 (M+1).

Anal. Calcd. for $C_{23}H_{19}N_5O_3$: C, 66.82; H, 4.63; N, 16.94. Found: C, 66.75; H, 4.62; N, 16.97.

Methyl 4-[(anilinocarbonyl)amino]-1,3-diphenyl-1*H*-5-pyrazole carboxylate (**6a**).

This compound was obtained as a white solid (87%) from diethyl ether, mp 218°C, ir (potassium bromide): ν 3356 (NH), 1724 (CO), 1632 (CO), 1556 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 3.69 (s, 3H, OCH_3), 6.94-7.85 (m, 15H, aryl protons), 8.63 (broad s, 1H, CO-NH), 9.04 (broad s, 1H, NH-CO);^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 55.54 (OCH_3), 105.07 (C_5), 117.6 (C_3), 121.26 (2 C), 121.46, 123.35, 124.37 (2 C), 126.29 (2 C), 128.19, 128.21 (2 C), 128.29 (2 C), 131.09, 139.14, 139.21(C_4), 146.03 (CO), 151.97, 152.8, 158.78 (CO); ms: m/z 413 (M+1).

Anal. Calcd. for $C_{24}H_{20}N_4O_3$: C, 69.89; H, 4.89; N, 13.58. Found: C, 69.65; H, 4.88; N, 13.55.

Methyl 4-{[(2-methylanilino)carbonyl]amino}-1,3-diphenyl-1*H*-5-pyrazolecarboxylate (**6b**).

This compound was obtained as a white solid (85%) from diethyl ether, mp 230°C, ir (potassium bromide): ν 3463 (NH), 1723 (CO), 1637 (CO), 1556 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 2.17 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 6.93-7.20 (m, 2H, aryl protons), 7.34-7.79 (m, 12H, aryl protons), 8.54 (broad s, 1H, CO-NH), 9.00 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 17.8 (CH_3); 51.21 (OCH_3); 105.71 (C_5); 115.98 (C_3); 122.51; 122.98; 123.72; 123.92 (2 C); 126.12; 127.88 (2 C); 128.10; 128.42; 128.79 (2 C); 129.11 (2 C); 130.22; 136.74; 138.52; 140.50 (CO); 151.30; 152.63; 162.93 (CO); ms: m/z 427 (M+1).

Anal. Calcd. for $C_{25}H_{22}N_4O_3$: C, 70.41; H, 5.20; N, 13.14. Found: C, 70.47; H, 5.19; N, 13.37.

Methyl 4-{[(2-ethylanilino)carbonyl]amino}-1,3-diphenyl-1*H*-5-pyrazolecarboxylate (**6c**).

This compound was obtained as a white solid (93%) from diethyl ether, mp 217°C, ir (potassium bromide): ν 3448 (NH), 1721 (CO), 1638 (CO), 1561 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 1.10 (t, 3H, CH_3, J = 7.5 Hz), 2.51 (q, 2H, CH_2, J = 7.5 Hz), 3.68 (s, 3H, OCH_3), 6.9-7.20 (m, 3H, aryl protons), 7.3-7.75 (m, 11H, aryl protons), 8.41 (broad s, 1H, CO-NH), 8.85 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 13.95 (CH_2-CH_3), 23.34 (CH_2-CH_3), 51.24 (OCH_3), 104.65 (C_5), 117.35 (C_3), 122.20, 122.88, 123.65, 123.82 (2 C), 126.05, 127.78 (2 C), 128.02, 128.14, 128.72 (2 C), 129.10 (2 C), 130.18, 136.65, 138.45, 140.45 (CO), 151.18, 152.29,160.12 (CO); ms: m/z 441 (M+1).

Anal. Calcd. for $C_{26}H_{24}N_4O_3$: C, 70.89; H, 5.49; N, 12.72. Found: C, 70.82; H, 5.50; N, 12.68.

Methyl 4-{[(3-chloroanilino)carbonyl]amino}-1,3-diphenyl-1*H*-5-pyrazolecarboxylate (**6d**).

This compound was obtained as a solid (80%) from diethyl ether/ petroleum ether, mp 226°C, ir (potassium bromide): ν 3317 (NH), 1728 (CO), 1650 (CO), 1597 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 3.68 (s,3H, OCH_3), 6.90-7.78 (m, 12H, aryl protons), 7.80-7.84 (m, 2H, aryl protons), 8.29 (broad s, 1H, CO-NH), 9.26 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 52.35 (OCH_3), 112.52 (C_5), 113.12 (C_3), 115.08, 116.8, 117.7, 121.64, 121.9, 125.18 (2 C), 126.61 (2 C), 127.02, 128.53 (2 C), 128.78 (2 C), 130.56, 131.72, 133.32 (C_4), 140.12, 141.6, 153.56 (CO), 159.44 (CO); ms: m/z 447.5 (M+1).

Anal. Calcd. for $C_{24}H_{19}ClN_4O_3$: C, 64.50; H, 4.29; N, 12.54. Found: C, 64.36; H, 4.38; N, 12.57.

Methyl 4-{[(4-methoxyanilino)carbonyl]amino}-1,3-diphenyl-1*H*-5-pyrazolecarboxylate (**6e**).

This compound was obtained as a white solid (95%) from diethyl ether, mp 260°C, ir (potassium bromide): ν 3405 (NH), 1734 (CO), 1630 (CO), 1559 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 3.68 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 6.82 (d, 2H, aryl protons, J = 9.1 Hz), 7.29 (d, 2H, aryl protons, J = 9.1 Hz), 7.37-7.83 (m, 10H, aryl protons), 8.29 (broad s, 1H, CO-NH), 8.8 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 52.31 (OCH_3), 55.34 (OCH_3), 113.9 (C_5), 114.12 (C_4), 120.17 (2 C), 122.43 (2 C), 125.12 (2 C), 127.04 (2 C), 128.30, 128.44, 128.61, 128.72 (2 C), 129.08 (2 C), 131.88, 133.02, 140.16, 153.72 (CO), 154.63 (C-OCH_3), 159.57 (CO); ms: m/z 443 (M+1).

Anal. Calcd. for $C_{25}H_{22}N_4O_4$: C, 67.86; H, 5.01; N, 12.66. Found: C, 67.76; H, 5.02; N, 12.77.

Methyl 4-{[(2-aminopyridyl)carbonyl]amino}-1,3-diphenyl-1*H*-5-pyrazolecarboxylate (**6f**).

This compound was obtained as a yellow solid (75%) from ethyl acetate, mp 165°C, ir (potassium bromide).ν 3460 (NH), 1736 (CO), 1630 (CO), 1550 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 3.65 (s, 3H, OCH_3), 7.04 (dd, 1H, aryl proton, J = 4.8, 7.0 Hz), 7.26 (d, 1H, aryl proton, J = 7.0Hz), 7.38-7.80 (m, 11H, aryl protons), 8.26 (dd, 1H, aryl proton, J = 1.0, 4.8 Hz), 9.90 (broad s, 1H, CO-NH), 11.03 (broad s, 1H, NH-CO); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 52.04 (OCH_3), 106.21 (C_5), 112.84 (C_4), 118.78, 124.86 (2 C), 128.76 (2 C), 129.05, 129.32, 129.62 (2 C), 130.0 (2 C), 132.29, 139.32, 139.71, 140.46, 147.47, 152.17 (CO), 152.78, 153.17, 163.58 (CO); ms: m/z 414 (M+1).

Anal. Calcd. for $C_{23}H_{19}N_5O_3$: C, 66.82; H, 4.63; N, 16.94. Found: C, 66.77; H, 4.74; N, 16.97.

General procedure for the preparation of the pyrazolopyrimidinediones derivatives **5** and **7**.

The appropriate urea derivatives **4** or **6** (0.5 g) in ethanol (10 ml) were added to a solution of sodium (1.1 equivalents) in ethanol (10 ml). The mixture was stirred at 80°C for 6 hours. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was dissolved in water and acidified with acetic acid (10 %) to *p*H = 2. The precipitate was collected by filtration and washed with diethylether to give the corresponding pyrazolopyrimidine.

1,3,5-Triphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*d*]pyrimidine-4,6-dione (**5a**).

This compound was obtained as a yellow solid (89%) from ethyl acetate, mp 336°C, ir (potassium bromide): ν 3443 (NH); 1720 (CO), 1662 (CO), 1557 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 7.29-7.36 (m, 2H, aryl protons), 7.40-7.56 (m, 8H, aryl protons), 7.64-7.70 (m, 2H, aryl protons), 7.84-7.90 (m, 2H, aryl protons), 11.67 (broad s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 97.1, 125.0 (2 C), 127.9, 128.2 (2 C), 128.3, 128.8 (2 C), 128.9, 129.1, 129.3 (2 C), 129.5 (2 C), 131.0, 136.3, 136.5, 144.8, 149.2 (CO), 156.6 (CO), 158.2; ms: m/z 381 (M+1).

Anal. Calcd. for $C_{23}H_{16}N_4O_2$: C, 72.62; H, 4.24; N, 14.73. Found: C, 72.56; H, 4.12; N, 14.69.

5-(2-Methylphenyl)-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*d*]pyrimidine-4,6-dione (**5b**).

This compound was obtained as a yellow solid (92%) from ethyl acetate, mp 318°C, ir (potassium bromide): ν 3431 (NH); 1724 (CO), 1665 (CO), 1557 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 2.08 (s, 3H, CH_3), 7.18-7.65 (m, 10H, aryl protons), 7.68-7.76 (m, 2H, aryl protons), 8.14-8.24 (m, 2H, aryl protons), 12.30 (broad s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 17.0 (CH_3), 96.9, 125.1 (2 C), 126.6, 128.1, 128.3 (2 C), 128.9, 129.1, 129.3, 129.5 (2 C), 130.3, 131.0 (2 C), 135.3, 136.0, 136.5, 145.0, 149.3 (C_3), 150.1 (CO), 150.1, 157.7 (CO); ms: m/z 395 (M+1).

Anal. Calcd. for $C_{24}H_{18}N_4O_2$: C, 73.08; H, 4.60; N, 14.20. Found: C, 72.89; H, 4.58; N, 14.23.

5-(2-Ethylphenyl)-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*d*]pyrimidine-4,6-dione (**5c**).

This compound was obtained as a yellow solid (92%) from ethyl acetate, mp 314°C, ir (potassium bromide): ν 3466 (NH), 1720 (CO), 1667 (CO), 1560 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 1.10 (t, 3H, CH_3, J = 7.5 Hz), 2.44 (q, 2H, CH_2, J = 7.5 Hz), 7.17-7.65 (m, 10H, aryl protons), 7.68-7.76 (m, 2H, aryl protons), 8.14-8.22 (m, 2H, aryl protons), 12.63 (broad s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 14.1 (CH_3), 23.4 (CH_2), 95.7, 125.1 (2 C), 126.5, 128.1 (2 C), 128.3 (2 C), 128.5, 128.6, 128.9, 129.1, 129.5 (2 C), 131.0, 134.7, 136.5, 141.5, 145.0, 149.2 (CO), 150.4, 158.0 (CO); ms: m/z 409 (M+1).

Anal. Calcd. for $C_{25}H_{20}N_4O_2$: C,73.51; H, 4.94; N, 13.72. Found: C, 73.31; H, 4.98; N, 13.70.

5-(3-Chlorophenyl)-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*d*]pyrimidine-4,6-dione (**5d**).

This compound was obtained as a white solid (95%) from ethyl acetate, mp 330°C, ir (potassium bromide): ν 3419 (NH), 1719 (CO), 1665 (CO), 1557 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 7.23-7.70 (m, 12H, aryl protons), 8.05-8.10 (m, 2H, aryl protons), 12.50 (broad s, 1H, NH); ^{13}C-nmr dimethyl-d_6 sulfoxide, ppm): δ 98.3, 116.6, 122.6, 126.3 (2 C), 129.6 (2 C), 130.2 (2 C), 130.4, 130.8, 130.8 (2 C), 131.6, 132.2, 134.1, 137.7, 139.0, 146.1, 151.8 (CO); 152.7, 159.3 (CO); 160.7; ms: m/z 415.5 (M+1).

Anal. Calcd. for $C_{23}H_{15}ClN_4O_2$: C, 66.59; H, 3.64; N, 13.51. Found: C, 66.63; H, 3.60; N, 13.55.

5-(2-Pyridyl)-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo-[3,4-*d*]pyrimidine-4,6-dione (**5f**).

This compound was obtained as a yellow solid (85%) from ethyl acetate, mp 310°C, ir (potassium bromide): ν 3434 (NH), 1722 (CO), 1668 (CO), 1560 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 7.30-7.90 (m, 11H, aryl protons), 7.98-8.11 (m, 1H, aryl protons), 8.18-8.30 (m, 2H, aryl protons), 12.60 (s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 95.7, 122.7, 123.4, 123.8 (2 C), 126.9 (2 C), 127.0 (2 C); 127.7, 127.9, 128.3 (2 C), 129.7, 135.3, 137.4, 144.0, 148.0 (CO), 148.1, 148.6, 149.3 (CO), 156.8; ms: m/z 382 (M+1).

Anal. Calcd. for $C_{22}H_{15}N_5O_2$: C,69.28; H, 3.96; N, 18.36. Found: C, 69.45; H, 3.91; N, 18.34.

1,3,6-Triphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*d*]pyrimidine-5,7-dione (**7a**).

This compound was obtained as a yellow solid (85%) from ethyl acetate, mp 305°C, ir (potassium bromide): ν 3447 (NH),

1722 (CO), 1670 (CO), 1559 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 7.25-7.95 (m, 15H, aryl protons), 8.15 (broad s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 118.59, 123.0, 125.0, 127.4, 127.7, 128.6, 128.7 (2 C), 128.8 (2 C), 129.2, 123.0 (2 C), 137.6 (2 C); 138.7, 141.2, 151.1, 151.8, 162.6 (CO), 163.6 (CO); ms: m/z 381 (M+1).

Anal. Calcd. for $C_{23}H_{16}N_4O_2$: C, 72.62; H, 4.24; N, 14.73. Found: C, 72.45; H, 4.29; N, 14.69.

6-(2-Methylphenyl)-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo-[4,3-*d*]pyrimidine-5,7-dione (**7b**).

This compound was obtained as a yellow solid (87%) from ethyl acetate, mp 323°C, ir (potassium bromide): ν 3542 (NH), 1720 (CO), 1662 (CO), 1557 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 2.16 (s, 3H, CH_3), 7.25-7.71 (m, 12H, aryl protons), 7.75-7.82 (m, 2H, aryl protons), 12.47 (broad s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 18.3 (CH_3), 99.8, 125.1 (2 C), 126.6, 128.1, 128.3 (2 C); 128.9, 129.1, 129.3, 129.5 (2 C), 130.3, 131.0 (2 C), 135.3, 136.0, 136.49, 144.8, 149.3, 150.0, 150.1 (CO), 157.7 (CO); ms: m/z 395 (M+1).

Anal. Calcd. for $C_{24}H_{18}N_4O_2$: C, 73.08; H, 4.60; N, 14.20. Found: C, 73.12; H, 4.65; N, 14.16.

6-(2-Ethylphenyl)-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo-[4,3-*d*]pyrimidine-5,7-dione (**7c**).

This compound was obtained as a yellow solid (93%) from ethyl acetate, mp 319°C, ir (potassium bromide): ν 3466 (NH), 1720 (CO), 1667 (CO), 1560 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 1.05 (t, 3H, CH_3, J = 7.5 Hz), 2.46 (q, 2H, CH_2, J = 7.5 Hz), 7.17-7.65 (m, 10H, aryl protons), 7.68-7.76 (m, 2H, aryl protons), 8.14-8.22 (m, 2H, aryl protons), 12.53 (broad s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 16.0 (CH_2-CH_3), 25.3 (CH_2-CH_3), 98.8, 127.0 (2 C), 127.3, 128.4 (2 C), 130.0, 130.2, 130.4, 130.5 (2 C), 130.8, 131.0, 131.4 (2 C), 132.9, 136.6, 138.4, 143.4, 147.0, 151.1, 152.4 (CO); 156.0 (CO); ms: m/z 409 (M+1).

Anal. Calcd. for $C_{25}H_{20}N_4O_2$: C, 73.51; H, 4.94; N, 13.72. Found: C, 73.36; H, 4.90; N, 13.76.

6-(3-Chlorophenyl)-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo-[4,3-*d*]pyrimidine-5,7-dione (**7d**).

This compound was obtained as a white solid (97%) from ethyl acetate, mp 345°C, ir (potassium bromide): ν 3445 (NH), 1725 (CO), 1668 (CO), 1583 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 7.29-7.71 (m, 12H, aryl protons), 8.13-8.20 (m, 2H, aryl protons), 12.55 (broad s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 119.2, 123.9 (2 C), 127.1 (2 C), 127.2 (2 C), 127.3, 127.9, 128.1, 128.4, 128.5 (2 C), 129.3, 129.9, 131.8, 135.4, 136.6, 143.8, 148.2, 149.4, 156.9 (CO), 160.2 (CO); ms: m/z 415.5 (M+1).

Anal. Calcd. for $C_{23}H_{15}ClN_4O_2$: C, 66.59; H, 3.64; N, 13.51. Found: C, 66.39; H, 3.61; N, 13.57.

6-(4-Methoxyphenyl)-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[4,3-*d*]pyrimidine-5,7-dione (**7e**).

This compound was obtained as a white solid (95%) from ethyl acetate, mp 342°C, ir (potassium bromide): ν 3446 (NH), 1720 (CO), 1665 (CO), 1557 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 3.85 (s, 3H, OCH_3), 7.02 (d, 2H, aryl protons, J = 8.2 Hz), 7.23 (d, 2H, aryl protons, J = 8.2 Hz), 7.40-7.85 (m, 8H, aryl protons), 8.15-8.30 (m, 2H, aryl protons), 12.48 (broad s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 55.3 (OCH_3), 97.1, 114.0 (2 C), 125.0 (2 C), 128.1 (2 C), 128.3 (2 C), 128.6, 128.9, 129.1, 129.5 (2 C), 130.2 (2 C), 131.0, 136.5, 144.7, 149.2, 150.8 (CO), 158.3, 158.8 (CO); ms: m/z 411 (M+1).

Anal. Calcd. for $C_{24}H_{18}N_4O_3$: C, 70.23; H, 4.42; N, 13.65. Found: C, 70.39; H, 4.39; N, 13.70.

6-(2-Pyridyl)-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo-[4,3-*d*]pyrimidine-5,7-dione (**7f**).

This compound was obtained as a yellow solid (85%) from ethyl acetate, mp 327°C, ir (potassium bromide): ν 3434 (NH), 1722 (CO), 1668 (CO), 1560 (C=N) cm^{-1}; ^{1}H-nmr (dimethyl-d_6 sulfoxide, ppm): δ 7.43-7.75 (m, 10H, aryl protons), 8.01 (m, 1H, aryl proton), 8.18 (m, 2H, aryl protons), 8.61 (m, 1H, aryl proton), 12.67 (broad s, 1H, NH); ^{13}C-nmr (dimethyl-d_6 sulfoxide, ppm): δ 98.1, 125.2, 125.9, 126.3 (2 C), 129.4 (2 C), 129.4 (2 C), 130.1, 130.3, 130.7 (2 C), 132.1, 137.7, 139.8, 146.4, 150.5, 150.5 (CO), 151.0, 151.8, 159.3 (CO); ms: m/z 382 (M+1).

Anal. Calcd. for $C_{22}H_{15}N_5O_2$: C,69.28; H, 3.96; N, 18.36. Found: C, 69.16; H, 3.96; N, 18.40.

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