

Pyrazolo[3,4-*d*]pyrimidines Related to Lonidamine

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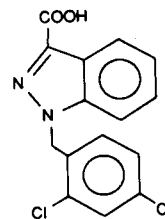
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This paper describes the synthesis of several pyrazolo[3,4-*d*]pyrimidines and tricyclic compounds with an imidazole, triazole or tetrazole ring fused to the pyrazolo[3,4-*d*]pyrimidine ring system, in an angular position (C-4 and N-5). All compounds reported herein contain the same substituent as "Lonidamine", namely the 2,4-dichlorobenzyl group, attached to the pyrazole nucleus.

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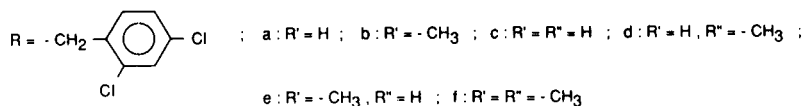
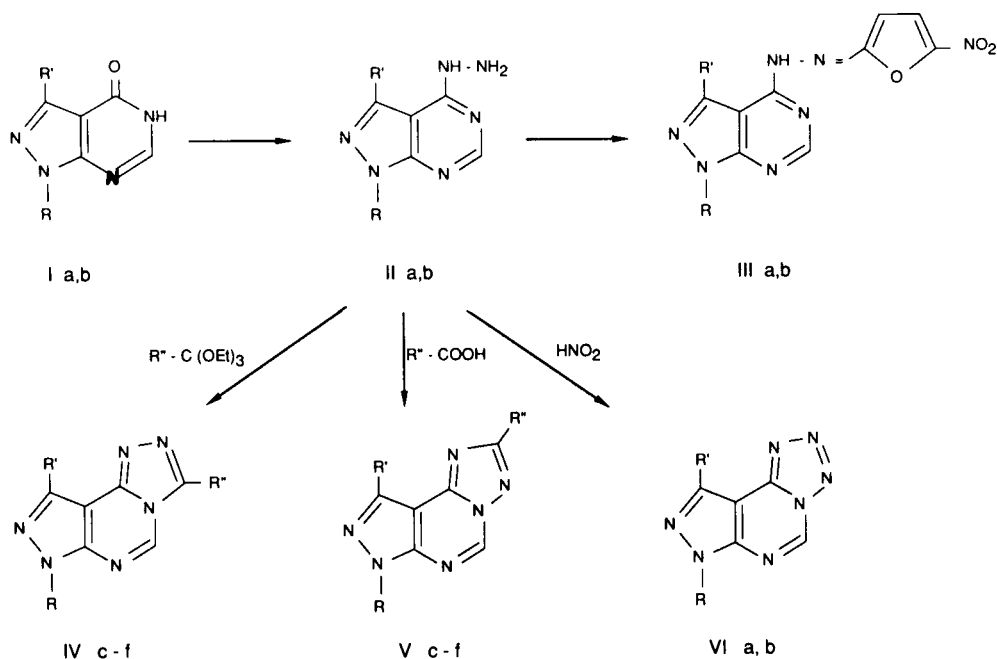
Lonidamine, an antispermatogenic and anticancer agent [1,2] has been recently investigated as a trypanocidal drug "in vitro". A survival decrease and morphological change in the culture of *Trypanosoma lewisi* treated with Lonidamine have been observed [3].

On the other hand, some derivatives of pyrazolo[3,4-*d*]pyrimidine, such as allopurinol and its related compounds, structural analogs of purine, have been intensively studied as they are biologically active in the treatment of experi-



Lonidamine

Scheme 1



mental acute Chagas' disease caused by *Trypanosoma cruzi* [4].

This paper describes the synthesis of some pyrazolo[3,4-*d*]pyrimidines containing the same substituent as Lonidamine, namely the 2,4-dichlorobenzyl group attached to the pyrazole nucleus, as potentially active chemotherapeutic agents.

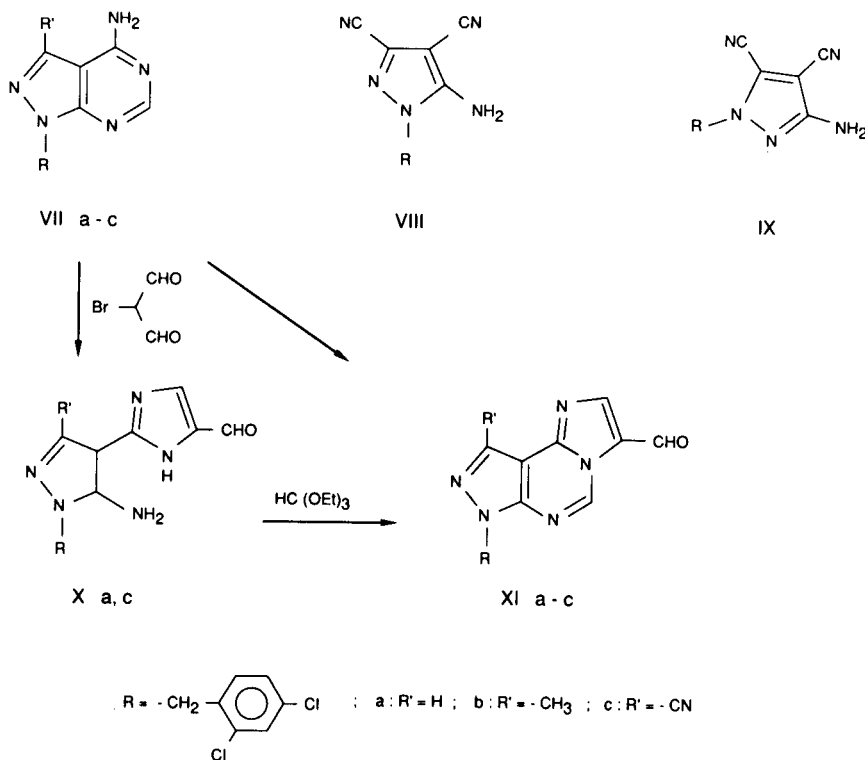
The readily available 1-(2,4-dichlorobenzyl)-5*H*-pyrazolo[3,4-*d*]pyrimidin-4-ones **I**, obtained according to the described procedures [5] from 2,4-dichlorobenzylhydrazine [6], served as starting materials for the syntheses outlined in Scheme 1. Compounds **I**, by refluxing with phosphorus oxychloride gave the 4-chloro derivatives, which on reaction with ethanolic hydrazine hydrate at room temperature yielded the 1-(2,4-dichlorobenzyl)-4-hydrazinopyrazolo[3,4-*d*]pyrimidines **II**. The latter were found to react with 5-nitrofurfural diacetate, with triethylorthoformate or orthoacetate, with refluxing formic or acetic acid, and with sodium nitrite in hydrochloric acid to give compounds **III**, **IV**, **V** and **VI** respectively. The proposed structures for isomers **IV** and **V** were differentiated through a comparison of their ¹H nmr spectra. For compound **IVc** two peaks were observed at δ 9.33 (H-3 and H-5) and one at 8.46 (H-9), while compound **Vc** showed one peak at δ 9.63 (H-5) and two peaks at 8.53 (H-3 and H-9) in agreement with similar triazole isomerization previously observed in the same type of tricyclic ring

system [7]. Also compound **IVe** was characterized by two peaks at δ 9.33 whereas the corresponding H-3 singlet of the isomeric **Ve** appeared at a higher field (8.56).

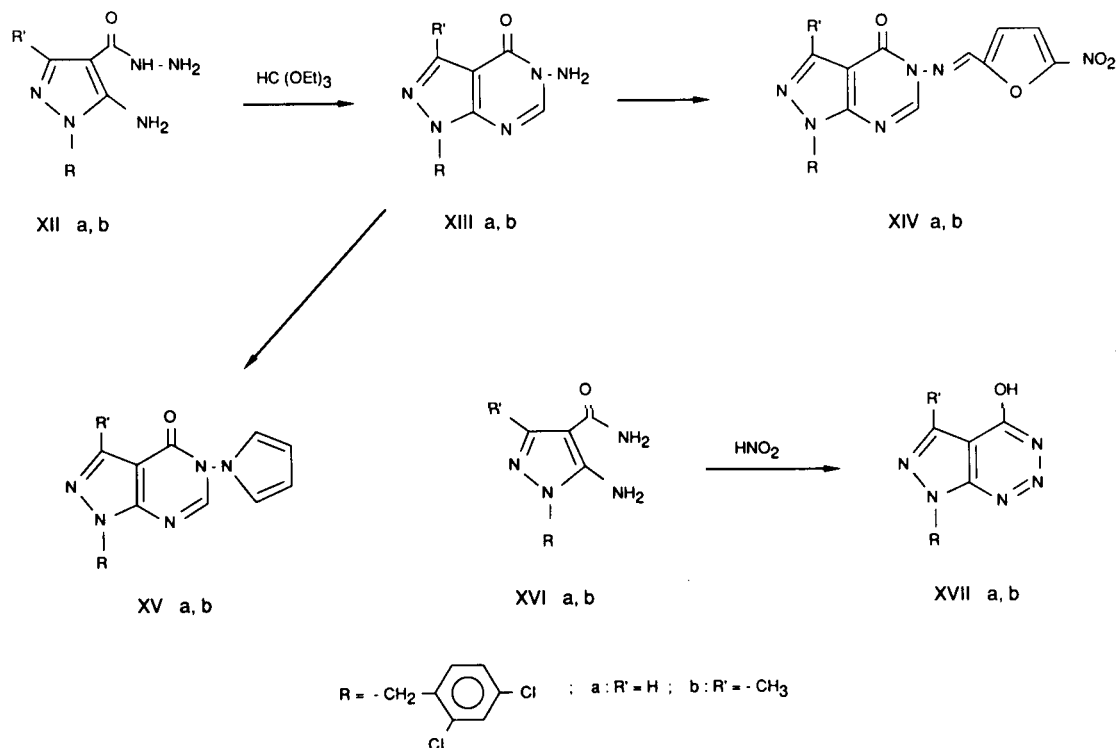
Compound **VIIa** (R' = H) and **VIIb** (R' = -CH₃) (Scheme 2) have been easily synthesized starting from 5-amino-4-cyano-1-(2,4-dichlorobenzyl)pyrazoles by ring-closure synthetic methods as previously described [8].

Compound **VIIc** (R' = CN) was prepared from 5-amino-1-(2,4-dichlorobenzyl)-3,4-dicyanopyrazole **VIII** by reaction with triethylorthoformate followed by ring closure with ethanolic ammonia. It was reported that the treatment of tetracyanoethylene with methylhydrazine afforded both possible *N*-methylpyrazole isomers, with the predominant product being the 3-amino-4,5-dicyano-1-methylpyrazole [9], and reaction of 5-amino-3,4-dicyanopyrazole with dimethylsulfate was found to yield principally the 5-amino-3,4-dicyano-1-methylpyrazole [10]. On the contrary, the desired compound **VIII** was directly obtained in good yield from 2,4-dichlorobenzylhydrazine and tetracyanoethylene, whereas the reaction of 5-amino-3,4-dicyanopyrazole with 2,4-dichlorobenzylchloride and sodium hydroxide in aqueous ethanol at 60° yielded, as the only characterizable product, a lower melting isomer to which was assigned the structure **IX**. This was supported by comparison of nmr and uv spectra of the isomers **VIII** and **IX** with those reported for the corresponding *N*-methyl derivatives.

Scheme 2



Scheme 3



By analogy with what reported for 9-ethyladenine [11], we examined the reaction of 4-aminopyrazolo[3,4-*d*]pyrimidines VII with bromomalondialdehyde in order to prepare the still unknown 3-formylpyrazolo[4,3-*e*]imidazo[1,2-*c*]pyrimidines XI. Compound VIIb ($R' = -\text{CH}_3$) in aqueous dioxane at 60-70° for 20 hours gave the expected XIb. Compounds VIIa ($R' = \text{H}$) and VIIc ($R' = -\text{CN}$) instead, yielded only the corresponding imidazolypyrazoles X. The formation of these products indicates that the initial cyclization to pyrazolo[4,3-*e*]imidazo[1,2-*c*]pyrimidines was followed by ring opening of the pyrimidine part of the tricyclic compounds. Nevertheless, compounds XIa,c could be subsequently cyclized with triethylorthoformate to give XIa,c.

The structure assignments of compounds X and XI were substantiated by nmr and ir spectroscopy and by elemental analysis. The nmr spectra of XI showed two peaks at δ 9.90-10.00 which could be assigned to $-\text{CHO}$ and H-5, whereas the imidazolypyrazoles X were characterized by the absence of the H-5 signal and by a broad singlet at 6.50-6.60, integrating for two protons, undoubtedly due to a NH_2 group; this was also supported by their ir spectra (nujol) which revealed a ν NH band at 3240 cm^{-1} .

In Scheme 3, 5-amino-1-(2,4-dichlorobenzyl)pyrazole-4-carboxylic acid hydrazides XII, obtained by refluxing the corresponding ethyl esters in ethanolic hydrazine hydrate,

were treated at 150-160° for 24 hours with triethylorthoformate in diethylene glycol to give the 5-amino-1-(2,4-dichlorobenzyl)-4,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-ones XIII. The latter ones with 5-nitro-2-furfural diacetate gave the Schiff bases XIV, and by reaction with 2,5-diethoxytetrahydrofuran the pyrrolo derivatives XV.

Finally treatment of 5-amino-1-(2,4-dichlorobenzyl)pyrazole-4-carboxamides XVI with nitrous acid yielded the pyrazolo[3,4-*d*]-1,2,3-triazines XVII.

The compounds described herein were shown to be less effective than Lonidamine when tested, according to the procedure previously reported [3], on the culture forms of *Trypanosoma lewisi*.

EXPERIMENTAL

Melting points are uncorrected. The ^1H nmr spectra were determined on a T-60 Varian instrument with TMS as internal standard; uv and ir spectra were recorded on a Perkin Elmer 554 and on a Perkin Elmer 580 spectrophotometer respectively. Column chromatography was performed on silica gel Merck (70-230 mesh). Purity of each compound was checked by tlc Merck silica gel plates. Sodium sulfate was used to dry organic solutions.

1-(2,4-Dichlorobenzyl)-5H-pyrazolo[3,4-*d*]pyrimidin-4-ones Ia,b.

These compounds were prepared from 5-amino-4-carboxamido-1-(2,4-dichlorobenzyl)pyrazoles XVI according to the synthetic pathway described for the corresponding 1-alkyl derivatives [8].

Compound **Ia** had mp 288-290°, dimethylformamide, 81%.

Anal. Calcd. for $C_{12}H_9Cl_2N_4O$: C, 48.83; H, 2.73; N, 18.98. Found: C, 48.81; H, 2.75; N, 19.08.

Compound **Ib** had mp 213-215°, ethanol, 79%.

Anal. Calcd. for $C_{13}H_{10}Cl_2N_4O$: C, 50.50; H, 3.26; N, 18.12. Found: C, 50.66; H, 3.17; N, 18.41.

1-(2,4-dichlorobenzyl)-4-hydrazinopyrazolo[3,4-*d*]pyrimidines **IIa,b**.

Compounds **I** (5 g) were suspended in phosphorus oxychloride (30 ml) and the mixture was refluxed for two hours. The excess phosphorus oxychloride was distilled under reduced pressure and the residual syrup was poured, while stirring, into finely crushed ice (100 g). The white suspension was extracted with ether, the solvent was removed and the residue crystallized to give 1-(2,4-dichlorobenzyl)-4-chloropyrazolo[3,4-*d*]pyrimidine, mp 90-92°, *n*-hexane, 88%; and 1-(2,4-dichlorobenzyl)-4-chloro-3-methylpyrazolo[3,4-*d*]pyrimidine, mp 120-122°, ethanol 84%.

A solution of the above 4-chloro derivatives (5 g) and 99% hydrazine hydrate (5 g) in ethanol (100 ml) was stirred at room temperature for 3 hours. The white solid which separated was filtered and crystallized.

Compound **IIa** had mp 222-224°, dimethylformamide, 74%.

Anal. Calcd. for $C_{12}H_{10}Cl_2N_6$: C, 46.62; H, 3.26; N, 27.18. Found: C, 46.88; H, 3.20; N, 27.22.

Compound **IIb** had mp 194-196°, dimethylformamide, 70%.

Anal. Calcd. for $C_{13}H_{12}Cl_2N_6$: C, 48.31; H, 3.74; N, 26.01. Found: C, 48.26; H, 3.74; N, 25.90.

1-(2,4-Dichlorobenzyl)-4-(5-nitro-2-furfurylidene)hydrazinopyrazolo[3,4-*d*]pyrimidines **IIIa,b**.

A solution of each compound **II** (3 g) and 5-nitro-2-furfuryl diacetate (4.5 g) in glacial acetic acid (50 ml) was heated at 80° for 4 hours. After cooling the separated solid was filtered and crystallized.

Compound **IIIa** had mp 219-222°, ethanol, 62%.

Anal. Calcd. for $C_{17}H_{11}Cl_2N_7O_3$: C, 47.24; H, 2.56; N, 22.68. Found: C, 47.51; H, 2.50; N, 22.67.

Compound **IIIb** had mp 215-217°, ethanol, 71%.

Anal. Calcd. for $C_{18}H_{13}Cl_2N_7O_3$: C, 48.44; H, 2.94; N, 21.97. Found: C, 48.70; H, 2.88; N, 22.00.

7-(2,4-Dichlorobenzyl)pyrazolo[4,3-*e*]-1,2,4-triazolo[4,3-*c*]pyrimidines **IVc-f**.

Compounds **II** (1 g) were heated and stirred at 70° in triethylorthoformate or orthoacetate (50 ml) for 1 hour. The white crystals which had formed were collected by filtration and crystallized.

Compound **IVc** had mp 253-255°, ethanol, 58%.

Anal. Calcd. for $C_{13}H_9Cl_2N_6$: C, 48.91; H, 2.52; N, 26.33. Found: C, 48.72; H, 2.33; N, 26.29.

Compound **IVd** had mp 252-254°, ethanol, 52%.

Anal. Calcd. for $C_{14}H_{10}Cl_2N_6$: C, 50.46; H, 3.02; N, 25.22. Found: C, 50.61; H, 2.77; N, 25.49.

Compound **IVe** had mp 244-246°, ethanol, 64%.

Anal. Calcd. for $C_{14}H_{10}Cl_2N_6$: C, 50.46; H, 3.02; N, 25.22. Found: C, 50.32; H, 2.81; N, 25.24.

Compound **IVf** had mp 236-239°, ethanol, 61%.

Anal. Calcd. for $C_{15}H_{12}Cl_2N_6$: C, 51.88; H, 3.48; N, 24.21. Found: C, 51.89; H, 3.34; N, 24.07.

7-(2,4-Dichlorobenzyl)pyrazolo[4,3-*e*]-1,2,4-triazolo[1,5-*c*]pyrimidines **Vc-f**.

The hydrazines **II** (1 g) were refluxed for 5 hours in the respective acid (99% formic or glacial acetic acid, 15 ml). The mixture was evaporated to dryness and the residue obtained suspended in 10% sodium carbonate solution (20 ml) and chloroform (50 ml). After shaking, the insoluble material was filtered and the organic layer separated. The crude product resulting from the solvent evaporation was purified by column chromatography (ethyl acetate as eluent), then crystallized.

Compound **Vc** had mp 201-203°, ethanol, 48%.

Anal. Calcd. for $C_{13}H_9Cl_2N_6$: C, 48.91; H, 2.52; N, 26.33. Found: C, 48.72; H, 2.58; N, 26.47.

Compound **Vd** had mp 184-186°, ethanol, 46%.

Anal. Calcd. for $C_{14}H_{10}Cl_2N_6$: C, 50.46; H, 3.02; N, 25.22. Found: C, 50.72; H, 3.05; N, 25.44.

Compound **Ve** had mp 202-204°, ethanol, 48%.

Anal. Calcd. for $C_{14}H_{10}Cl_2N_6$: C, 50.46; H, 3.02; N, 25.22. Found: C, 50.38; H, 2.82; N, 25.20.

Compound **Vf** had mp 185-188°, ethanol, 54%.

Anal. Calcd. for $C_{15}H_{12}Cl_2N_6$: C, 51.88; H, 3.48; N, 24.21. Found: C, 51.89; H, 3.35; N, 24.07.

7-(2,4-Dichlorobenzyl)pyrazolo[4,3-*e*]tetrazolo[4,5-*c*]pyrimidines **VIa,b**.

Hydrochloric acid (2 *N*, 15 ml) was added dropwise to a stirred homogeneous mixture of **II** (1 g) and powdered sodium nitrite (1.2 g). The mixture was stirred for 6 hours at room temperature, then made alkaline with diluted sodium hydroxide and extracted with chloroform. The solvent was removed and the residue crystallized.

Compound **VIa** had mp 176-178°, ethanol, 68%.

Anal. Calcd. for $C_{12}H_7Cl_2N_7$: C, 45.02; H, 2.19; N, 30.63. Found: C, 45.18; H, 2.22; N, 30.79.

Compound **VIb** had mp 160-162°, ethanol, 60%.

Anal. Calcd. for $C_{13}H_9Cl_2N_7$: C, 46.72; H, 2.71; N, 29.34. Found: C, 46.88; H, 2.68; N, 29.14.

4-Amino-1-(2,4-dichlorobenzyl)pyrazolo[3,4-*d*]pyrimidines **VIIa,b**.

These compounds were prepared by reaction of 5-amino-4-cyano-1-(2,4-dichlorobenzyl)pyrazole and 5-amino-4-cyano-1-(2,4-dichlorobenzyl)-3-methylpyrazole [12] with formamide, according to the already described methods [8].

Compound **VIIa** had mp 247-250°, ethyl acetate, 77%.

Anal. Calcd. for $C_{12}H_9Cl_2N_5$: C, 49.00; H, 3.08; N, 23.81. Found: C, 48.96; H, 2.99; N, 23.93.

Compound **VIIb** had 178-180°, ethyl acetate, 62%.

Anal. Calcd. for $C_{13}H_{11}Cl_2N_5$: C, 50.66; H, 3.60; N, 22.73. Found: C, 50.38; H, 3.50; N, 22.84.

5-Amino-1-(2,4-dichlorobenzyl)-3,4-dicyanopyrazole **VIII**.

To a cooled stirred solution of 2,4-dichlorobenzylhydrazine (3.8 g) in ethanol (70 ml) tetracyanoethylene (3 g) was added in one portion. An immediate reaction occurred, the mixture turning dark red with a raise in temperature. The suspension was stirred at 0° for 1 hour and then heated on a steam bath for 1 hour. The solid precipitated from the cooled solution was separated by filtration and crystallized from ethanol. 4.3 g (74%), mp 204-206°, uv (ethanol): λ max 272 nm (2600); λ min 248 (1200); 1H

nmr (dimethyl sulfoxide-*d*₆): δ 7.42 (broad, 2H, NH₂, partially overlapped by aromatic protons), 5.32 (s, 2H, ϵ CH₂-Ph).

Anal. Calcd. for C₁₂H₈Cl₂N₅: C, 49.33; H, 2.41; N, 23.97. Found: C, 49.61; H, 2.28; N, 24.24.

3-Amino-1-(2,4-dichlorobenzyl)-4,5-dicyanopyrazole IX.

5-Amino-3,4-dicyanopyrazole [13] (1.3 g) was added with stirring to a solution of sodium hydroxide (0.5 g) in water (30 ml) until a clear solution was obtained. 2,4-Dichlorobenzylchloride (2.4 g) in ethanol (30 ml) was then added and the mixture was stirred and heated at 60° for 8 hours. After cooling the reaction mixture was diluted with water and extracted with chloroform. The solvent was evaporated and the crude product, purified by column chromatography by eluting with ethyl acetate/*n*-hexane (1:2) mixture, crystallized from ethanol. 1.2 g (42%), mp 162-164°; uv (ethanol): λ max 310 nm (2200); λ min 262 (800). ¹H nmr (dimethyl sulfoxide-*d*₆): δ 6.34 (broad, 2H, NH₂), 5.40 (s, 2H, ϵ CH₂-Ph).

Anal. Calcd. for C₁₂H₇Cl₂N₅: C, 49.33; H, 2.41; N, 23.97. Found: C, 49.52; H, 2.20; N, 24.42.

4-Amino-3-cyano-1-(2,4-dichlorobenzyl)pyrazolo[3,4-*d*]pyrimidine VIIc.

A solution of VIII (3 g) in triethylorthoformate (30 ml) was refluxed for 20 hours. Excess orthoformate was removed *in vacuo* and the crude crystalline ethoxymethyleneimino derivative which formed was added to a stirred solution of ethanol saturated with ammonia. The reaction mixture was stirred at room temperature and the separated solid was collected by filtration and crystallized from ethanol. 1.4 g (44%, mp 219-221°).

Anal. Calcd. for C₁₃H₈Cl₂N₆: C, 48.92; H, 2.53; N, 26.33. Found: C, 49.10; H, 2.26; N, 26.49.

5-Amino-1-(2,4-dichlorobenzyl)-4-(4-formyl-2-imidazolyl)pyrazoles Xa,c and 7-(2,4-Dichlorobenzyl)-3-formylpyrazolo[4,3-*e*]imidazo[1,2-*c*]pyrimidines XIa,c.

Compounds VII (1 g) and bromomalondialdehyde (0.8 g) [14] were added to a dioxane/water (2:1) mixture (50 ml). The reaction mixture was heated at 60° for 20 hours. After water addition, the crude product Xc was filtered and crystallized, while compounds Xa and XIb were extracted with chloroform and chromatographed on a silica gel column by eluting with ethyl acetate/*n*-hexane (2:1) mixture, then crystallized. Compounds XIa,c were prepared by refluxing a solution of Xa,c (1 g) in triethylorthoformate (15 ml) for 2 hours. The reaction mixture was evaporated *in vacuo*, and the residue crystallized.

Compound Xa had mp 210-212°, ethanol, 55%.

Anal. Calcd. for C₁₄H₁₁Cl₂N₅O: C, 50.01; H, 3.30; N, 20.83. Found: C, 50.04; H, 3.26; N, 21.10.

Compound Xc had mp 265-268°, dimethylformamide/ethanol, 74%.

Anal. Calcd. for C₁₅H₁₀Cl₂N₆O: C, 49.87; H, 2.79; N, 23.27. Found: C, 49.63; H, 2.66; N, 23.30.

Compound XIa had mp 194-196°, ethanol, 88%.

Anal. Calcd. for C₁₅H₉Cl₂N₅O: C, 52.04; H, 2.62; N, 20.23. Found: C, 51.85; H, 2.67; N, 20.24.

Compound XIb had mp 181-183°, ethanol, 58%.

Anal. Calcd. for C₁₆H₁₁Cl₂N₆O: C, 53.35; H, 3.08; N, 19.44. Found: C, 53.38; H, 2.83; N, 19.60.

Compound XIc had mp 227-230°, ethanol, 90%.

Anal. Calcd. for C₁₆H₈Cl₂N₆O: C, 51.77; H, 2.17; N, 22.64. Found: C, 51.84; H, 2.06; N, 22.87.

5-Amino-1-(2,4-dichlorobenzyl)pyrazole-4-carboxylic Acid Hydrazides XIIa,b.

A solution of each 5-amino-1-(2,4-dichlorobenzyl)-4-ethoxy-carbonylpyrazole (5 g) (R' = H, mp 85-86°, cyclohexane, 96%; R' = -CH₃, mp 138-140°, ethyl acetate/*n*-hexane, 92%) [15] and 99% hydrazine hydrate (5 g) in ethyleneglycol monomethylether (25 ml) was refluxed for 48 hours. The solvent was evaporated under reduced pressure and the residue crystallized.

Compound XIIa had mp 269-272°, ethanol, 92%.

Anal. Calcd. for C₁₁H₁₁Cl₂N₅O: C, 44.01; H, 3.69; N, 23.33. Found: C, 43.88; H, 3.70; N, 23.51.

Compound XIIb had mp 232-234°, ethanol, 84%.

Anal. Calcd. for C₁₂H₁₃Cl₂N₅O: C, 45.88; H, 4.17; N, 22.30. Found: C, 46.02; H, 4.25; N, 22.22.

5-Amino-1-(2,4-dichlorobenzyl)-4,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-ones XIIIa,b.

A solution of XII (2 g) and triethylorthoformate (1 g) in diethylene glycol (15 ml) was stirred at 150-160° until tlc (ethyl acetate) indicates the absence of the starting material (24 hours). After cooling, the mixture was diluted with water and extracted with ethyl acetate. The solvent was removed and the residue crystallized.

Compound XIIIa had mp 189-191°, 2-propanol, 72%.

Anal. Calcd. for C₁₂H₉Cl₂N₅O: C, 46.47; H, 2.92; N, 22.58. Found: C, 46.69; H, 3.07; N, 22.62.

Compound XIIIb had mp 161-163°, 2-propanol, 66%.

Anal. Calcd. for C₁₃H₁₁Cl₂N₅O: C, 48.16; H, 3.42; N, 21.60. Found: C, 48.21; H, 3.41; N, 21.68.

1-(2,4-Dichlorobenzyl)-5-(5-nitro-2-furfurilidene)amino-4,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-ones XIVa,b.

These compounds were prepared following the procedure described for III.

Compound XIVa had mp 192-194°, ethyl acetate, 72%.

Anal. Calcd. for C₁₇H₁₀Cl₂N₆O₄: C, 47.13; H, 2.32; N, 19.40. Found: C, 47.30; H, 2.41; N, 19.43.

Compound XIVb had mp 208-210°, ethanol, 66%.

Anal. Calcd. for C₁₈H₁₂Cl₂N₆O₄: C, 48.34; H, 2.70; N, 18.79. Found: C, 48.23; H, 2.74; N, 19.00.

1-(2,4-Dichlorobenzyl)-5-(1-pyrryl)-4,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-ones XVa,b.

2,5-Dimethoxytetrahydrofuran (1 g) was added to a stirred solution of each compound XII (1 g) in glacial acetic acid (15 ml). The solution was refluxed and stirred for 2 hours, evaporated under reduced pressure and the residue crystallized.

Compound XVa had mp 178-180°, 2-propanol, 84%.

Anal. Calcd. for C₁₆H₁₁Cl₂N₅O: C, 53.35; H, 3.08; N, 19.44. Found: C, 53.39; H, 3.14; N, 19.36.

Compound XVb had mp 170-172°, 2-propanol, 86%.

Anal. Calcd. for C₁₇H₁₃Cl₂N₅O: C, 54.56; H, 3.50; N, 18.72. Found: C, 54.44; H, 3.38; N, 18.66.

5-Amino-4-carboxamido-1-(2,4-dichlorobenzyl)pyrazoles XVIa,b.

These compounds were obtained by reaction of the related 5-amino-4-cyanopyrazoles, described in the preparation of VIIa,b, with ethanolic sodium hydroxide, as reported for the corresponding benzyl derivatives [5].

Compound XVIa had mp 205-207°, ethanol, 80%.

Anal. Calcd. for C₁₁H₁₀Cl₂N₄O: C, 46.33; H, 3.53; N, 19.65.

Found: C, 46.65; H, 3.42; N, 19.68.

Compound **XVIb** had 164-166°, benzene, 84%.

Anal. Calcd. for $C_{12}H_{12}Cl_2N_4O$: C, 48.17; H, 4.04; N, 18.73.
Found: C, 48.30; H, 3.88; N, 18.95.

1-(2,4-Dichlorobenzyl)-4-hydroxypyrazolo[3,4-*d*]-1,2,3-triazines **XVIIa,b**.

To a stirred finely powdered suspension of each compound **XVI** (3 g) in hydrochloric acid (40 ml, 10%) cooled at 0° sodium nitrite (1.5 g) in water (15 ml) was added dropwise over 15 minutes. The mixture was stirred for 3 hours at room temperature, then left at the same temperature overnight. Water was added and the precipitate was filtered and crystallized.

Compound **XVIIa** had mp 161-163°, ethanol, 88%.

Anal. Calcd. for $C_{11}H_7Cl_2N_5O$: C, 44.61; H, 2.38; N, 23.65.
Found: C, 44.53; H, 2.32; N, 23.68.

Compound **XVIIb** had mp 144-146°, ethanol 82%.

Anal. Calcd. for $C_{12}H_9Cl_2N_5O$: C, 46.47; H, 2.92; N, 22.58.
Found: C, 46.28; H, 2.90; N, 22.64.

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