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DMF Acetals as Alkylating and Cyclizing Agents: A Facile Route to Substituted Pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones

S. Youssif

Department of Chemistry, Faculty of Science, Zagazig University, Zagazig, Egypt

Summary. Several 7-methyl-5-alkyl-2-vinylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones were prepared. The successful cyclization and alkylation of 6-(α-methylbenzylidenehydrazino)-1-methyluracils **2a–d** using dimethylformamide acetals at high temperature provided **6a–d**, **7a–d**, and **8a–d**. Treatment of **6a–d** and **7a–d** with acid afforded 7-methyl-5-alkylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones **9a**, **b**; under the same conditions, **3a–d** reacted to 7-methylpyrazolo[3,4-*d*]-pyrimidine-4,6(5*H*)-dione (**4**) in good yield.

Keywords. 6-(α-Methylbenzylidenehydrazino)-1-methyluracils; 2-Vinylarylpyrazolo[3,4-*d*]-pyrimidine, -4,6(5*H*,7*H*)-diones; Pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones.

***DMF*-Acetale als Alkylierungs- und Ringschlußreagentien: ein einfacher Weg zu substituierten Pyrazolo[3,4-*d*]pyrimidin-4,6(5*H*,7*H*)-dionen**

Zusammenfassung. Es wurden verschiedene 7-Methyl-5-alkyl-2-vinylpyrazolo[3,4-*d*]pyrimidin-4,6(5*H*,7*H*)-dione hergestellt. Cyclisierung und Alkylierung der 6-(α-Methylbenzylidenhydrazino)-1-methyl-uracile **2a–d** mit Hilfe von Dimethylformamidacetalen bei hohen Temperaturen ergab **6a–d**, **7a–d** und **8a–d**. Behandlung von **6a–d** und **7a–d** mit Säure lieferte die 7-Methyl-5-alkylpyrazolo[3,4-*d*]pyrimidin-4,6(5*H*,7*H*)-dione **9a,b**; unter den gleichen Bedingungen reagierten **3a–d** in guter Ausbeute zu 7-Methylpyrazolo[3,4-*d*]pyrimidin-4,6(5*H*)-dion (**4**).

Introduction

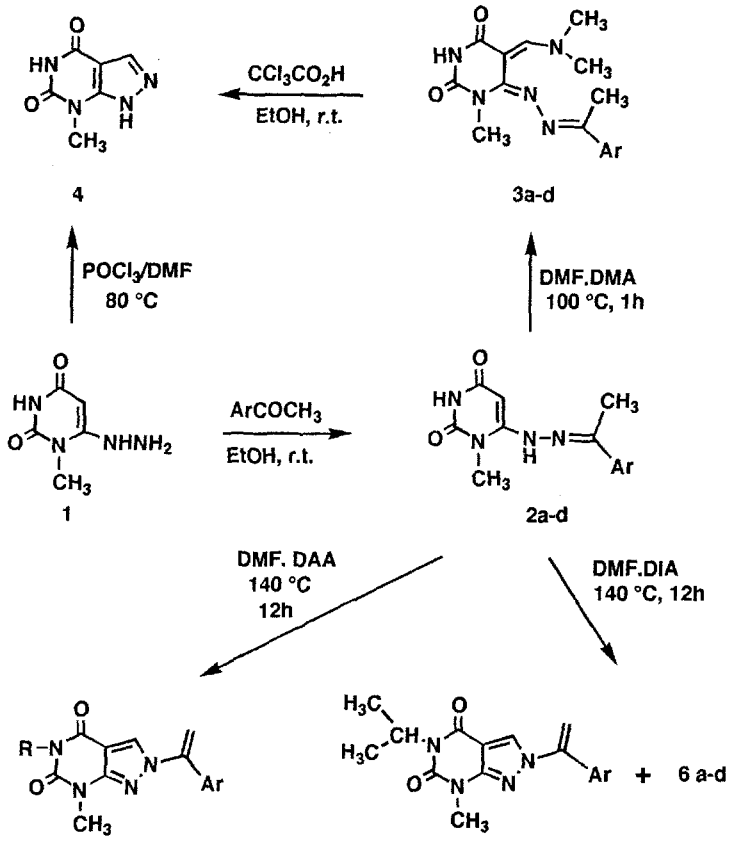
The antitumor activity [1, 2] and the potential therapeutic applications [3] of several pyrazolo[3,4-*d*]pyrimidine derivatives has prompted a more thorough investigation of these compounds. It has been reported that the preparation of pyrazolo[3,4-*d*]pyrimidines may involve suitably substituted pyrazole precursors, followed by annelation of the pyrimidine ring [4–6], cyclocondensation of 6-hydrazinopyrimidine derivatives [7, 8], and thermal and photochemical cyclization of 6-benzylidenehydrazinouracils and 6-(α-methylbenzylidenehydrazino)uracils, followed by dehydrogenation [9, 10].

Dimethylformamide acetals have been widely used in nucleoside [11] and nucleotide [12] chemistry as alkylating agents of the acidic amide group of

heterocyclic bases. In the present work, this approach is extended to introduce an efficient one-pot synthesis of 7-methyl-5-alkyl-2-vinylpyrazolo[3,4-*d*]pyrimidines using *DMF* acetals as cyclizing and alkylating agent with respect to the acidic amide group of the starting material **1**.

Results and Discussion

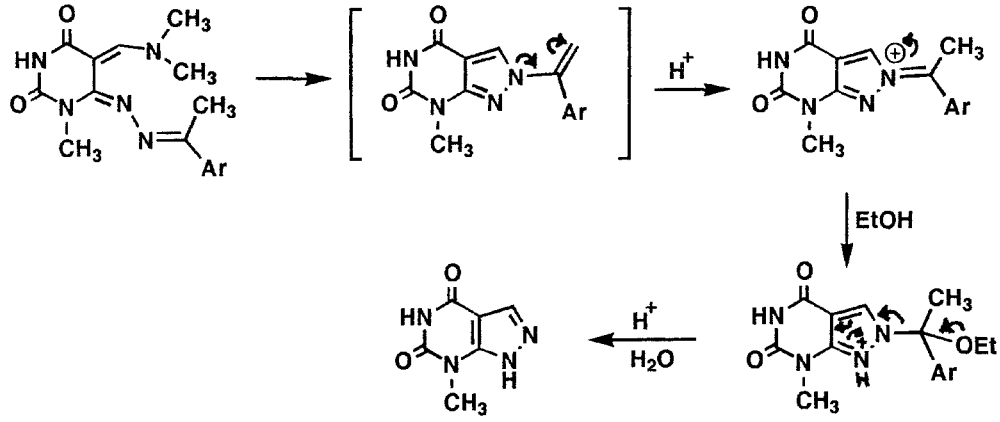
6-Hydrazino-1-methyluracil (**1**, [13]) was reacted with an equimolar amount of acetophenones (acetophenone, *p*-methyl-, *p*-chloro-, and *p*-methoxyacetophenone) in ethanol at room temperature with stirring to give 6-(α-methylbenzylidene-hydrazino)-1-methyluracils **2a–d**. Heating the latter with an excess of *DMF* dimethylacetal at 100°C for 1 h led to the formation of 6-(α-methylbenzylidene-hydrazino)-5-dimethylaminomethylene-1-methyluracils **3a–d** in good yields.



	Ar	
a	C_6H_5	8a : 6a = 35 : 46
b	p-C_6H_4. CH_3	8b : 6b = 37 : 14
c	p-C_6H_4. Cl	8c : 6c = 21 : 35
d	p-C_6H_4. OCH_3	8d : 6d = 29 : 32

Scheme 1

Treatment of the products with trichloroacetic, trifluoroacetic, or hydrochloric acid (ethanol, room temperature, 15 min) gave rise to a ring closure with the loss of one mole of acetophenone and dimethylamine, affording 7-methylpyrazolo[3,4-*d*]-pyrimidine-4,6(5*H*)-dione (**4**, Scheme 1). The structure of **4** was proven by an independent synthesis (action of *DMF*/$POCl_3$ (*Vilsmeier*'s reagent) on compound **1**). As depicted in Scheme 2, this reaction involves the formation of 7-methyl-2-



Scheme 2

arylvinylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*)-dione as intermediate which cannot be separated.

On the other hand, heating **2a–d** with an excess of *DMF* acetals for 12 h at 140°C resulted in a ring closure and a subsequent alkylation of HN-5, *i.e.* in a one-pot formation of 7-methyl-5-alkyl-2-vinylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones **6a–d** (Table 1) and **7a–d** (Scheme 1). Heating of **2a–d** under the same conditions with *DMF* diisopropylacetal afforded a mixture of **6a–d** and **8a–d** in poor yield. Separation was accomplished by silica gel column chromatography using AcOEt:toluene = 1:2 (Scheme 1). The definite mechanism for the formation of **6a–d** in the latter reaction is currently under investigation.

The structures of **7a–d** and **8a–d** were assigned on the basis of their spectroscopic data and elemental analyses. In particular, the ^{1}H NMR spectra ($CDCl_3$) of **7a, c** and **8a, c** revealed two vinylic protons (Table 2).

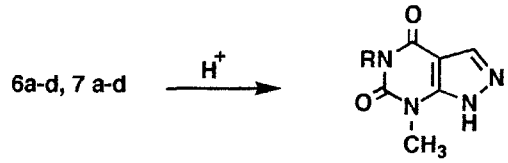
Table 1. Compounds **6a–d**

	m.p. (°C)	Method of preparation	Yield (%)
6a	145 (Ref. [10]: 148–149)	A	67
		B	56
6b	198–199 (Ref. [10]: 200–201)	A	78
		B	64
6c	205 (Ref. [10]: 210)	A	83
		B	72
6d	190 (Ref. [10]: 186–188)	A	73
		B	65

Table 2. ^{1}H NMR data of 7-methyl-5-alkyl-2-vinylpyrazolo[3,4-d]pyrimidine-4, 6(5H, 7H)-diones **7a**, **7c**, **8a**, and **8c**

Compd No.	$=CH_2$	NCH_2CH_3-5	CH-3	NCH_3-7	$NCH(CH_3)_2$-5
7a	5.28 (d, 1H, $J = 0.48$ Hz) 5.82 (d, 1H, $J = 0.48$ Hz)	1.24 (t, 3H), 4.05 (q, 2H)	7.90 (s, 1H)	3.57 (s, 3H)	–
7c	5.30 (d, 1H, $J = 0.80$ Hz) 5.79 (d, 1H, $J = 0.80$ Hz)	1.24 (t, 3H), 4.05 (q, 2H)	7.92 (s, 1H)	3.55 (s, 3H)	–
8a	5.27 (d, 1H, $J = 0.50$ Hz) 5.80 (d, 1H, $J = 0.50$ Hz)	– –	7.88 (s, 1H)	3.54 (s, 3H)	1.49 (d, 6H) 5.27 (m, 1H)
8c	5.26 (d, 1H, $J = 0.80$ Hz)	–	7.87 (s, 1H)	3.49 (s, 3H)	1.46 (d, 6H) 5.27 (m, 1H)

Heating of **6a–d** and **7a–d** with trichloroacetic acid in ethanol for 30 min at 60°C furnished **9a, b** in a good yield (Scheme 3).



9-a, b
a; R = CH_3
b; R = C_2H_5

Scheme 3

Experimental

Melting points were taken on a Büchi 530 melting point apparatus and are uncorrected; UV spectra were recorded on a Perkin-Elmer Lambda 5 or 15 spectrophotometer (λ_{max} in nm ($\log \varepsilon$)); ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AC 250 spectrometer δ (ppm), *TMS* as internal standard).

General procedure for the preparation of 6-(α-methylbenzylidene-hydrazino)-1-methyluracils (**2a–d**)

To a suspension of 6-hydrazino-1-methyluracil (**1**, 12.8 mole) in absolute ethanol (15 ml), the appropriate acetophenones (12.8 mole) were added dropwise. The mixture was stirred at room temperature for 30 min. The precipitate was filtered, washed with ethanol, dried in the oven, and recrystallized from *DMF*: $CH_3OH = 2:3$.

2a: Yield: 3.2 g (97%); m.p.: 270–272°C; UV (MeOH): $\lambda_{max} = 204$ (4.80), 252 (4.33), 306 (4.38); ^{1}H NMR (*DMSO*-d_6): $\delta = 10.73$ (s, 1H, NH-3), 8.90 (s, 1H, NH-6), 7.41–7.85 (m, 5H, aromatic), 5.43 (s, 1H, CH-5), 3.48 (s, 3H, NCH_3-1), 2.38 (s, 3H, α-CH_3); $C_{13}H_{14}N_4O_2$; calcd.: C 60.45, H 5.46, N 21.69; found: C 60.33, H 5.41, N 21.15.

2b: Yield: 3.48 g (92%); m.p.: 268°C; UV (MeOH): $\lambda_{max} = 204$ (4.36), 255 (4.42), 308 (4.49); ^{1}H NMR (*DMSO*-d_6): $\delta = 10.71$ (s, 1H, NH-3), 8.84 (s, 1H, NH-6), 7.22–7.79 (dd, 4H, aromatic), 5.42 (s, 1H, CH-5), 3.39 (s, 3H, NCH_3-1), 3.33 (s, 3H, CH_3-*p*), 2.35 (s, 3H, α-CH_3); $C_{14}H_{16}N_4O_2$; calcd.: C 61.75, H 5.92, N 20.27; found: C 61.68, H 5.88, N 20.23.

2c: Yield: 3.50 (94%); m.p.: 265–67°C; UV (MeOH): $\lambda_{max} = 210$ (3.90), 256 (3.87), 308 (3.87); ^{1}H NMR (*DMSO*-d_6): $\delta = 10.76$ (s, 1H, NH-3), 8.95 (s, 1H, NH-6), 7.47–7.93 (dd, 4H, aromatic),

5.44 (s, 1H, CH-5), 3.40 (s, 3H, NCH_3-1), 2.37 (s, 3H, α-CH_3); $C_{13}H_{13}ClN_4O_2$; calcd.: C 53.43, H 4.48, N 19.17; found: C 53.18, H 4.33, N 18.91.

2d: Yield: 3.2 g (87%); m.p.: 250–252°C; UV (MeOH): $\lambda_{max} = 207$ (4.40), 263 (4.53), 312 (4.66); ^{1}H NMR (*DMSO*-d_6): $\delta = 10.70$ (s, 1H, NH-3), 8.82 (s, 1H, NH-6), 6.95–7.85 (dd, 4H, aromatic), 5.37 (s, 1H, CH-5), 3.78 (s, 3H, OCH_3-*p*), 3.37 (s, 3H, NCH_3-1), 2.33 (s, 3H, α-CH_3); $C_{14}H_{16}N_4O_3$; calcd.: C 58.32, H 5.59, N 19.43; found: C 58.22, H 5.61, N 19.41.

General procedure for the preparation of 6-(α-methylbenzylidene)-5-dimethylaminomethylene-1-methyluracils (**3a–d**)

A mixture of the appropriate uracil **2** (0.001 mole) and *DMF* dimethylacetal (3 ml) was heated at 100°C for 1 h. After cooling, the resulting precipitate was filtered, washed with ethanol, and recrystallized from a mixture of C_2H_5OH: *DMF* = 2:1.

3a: Yield: (63%); m.p.: 230°C; UV (MeOH): $\lambda_{max} = 203$ (4.59), 244 (4.58), 277 (4.72), 323 (4.71); ^{1}H NMR (*DMSO*-d_6): $\delta = 10.13$ (s, 1H, NH-3), 8.08 (s, 1H, CH-5), 7.36–7.74 (m, 5H, aromatic), 3.32 (s, 3H, NCH_3-1), 3.20 (s, 3H, NCH_3-5), 3.09 (s, 3H, NCH_3-5), 2.40 (s, 3H, α-CH_3); ^{13}C NMR (*DMSO*-d_6): $\delta = 13.97$ (α-C), 28.93 (NC-1), 42.79, 46.16 (2NC-5), 82.92 (=CH-), 125.34, 128.54, 138.52, 151.12, 154.22, 155.13, 159.08, 163.79; MS: *m/z* (relative intensity) = 313 (M^+, 100), 269 (60), 255 (42), 193 (57), 167 (56), 123 (38), 104 (37), 95 (46), 77 (65), 44 (47); $C_{16}H_{19}N_5O_2$; Calcd.: C 61.32, H 6.11, N 22.34; found: C 61.00, H 6.09, N 22.04

3b: Yield: (65%); m.p.: 242–244°C; UV (MeOH): $\lambda_{max} = 203$ (4.65), 245 (4.61), 284 (4.80), 318 (4.77); ^{1}H NMR (*DMSO*-d_6): $\delta = 10.17$ (s, 1H, NH-3), 8.08 (s, 1H, CH-5), 7.22–7.64 (dd, 4H, aromatic), 3.31 (s, 3H, NCH_3-1), 3.21 (s, 3H, NCH_3-5), 3.07 (s, 3H, NCH_3-5), 2.37 (s, 3H, CH_3-*p*), 2.33 (s, H, α-CH_3); ^{13}C NMR (*DMSO*-d_6): $\delta = 13.96$ (α-C), 20.72 (C-*p*), 28.96 (NC-1), 42.6, 46.3 (2NC-5), 83.35 (=CH-), 125.41, 128.85, 135.93, 138.11, 151.15, 153.9, 155.54, 159.41, 163.34; MS: *m/z* (relative intensity) = 327 (M^+, 46), 283 (32), 282 (25), 269 (24), 193 (34), 167 (25), 123 (21), 118 (23), 117 (100), 105 (25), 95 (25), 91 (34); $C_{17}H_{21}N_5O_2$; calcd.: C 62.36, H 6.46, N 21.39; found: C 62.20, H 6.45, N, 21.23.

3c: Yield: (58%); m.p.: 245–247°C; UV (MeOH): $\lambda_{max} = 204$ (4.61), 250 (4.66), 276 (4.76), 325 (4.78); ^{1}H NMR (*DMSO*-d_6): $\delta = 10.21$ (s, 1H, NH-3), 8.05 (s, 1H, CH-5), 7.48–7.73 (dd, 4H, aromatic), 3.31 (s, 3H, NCH_3-1), 3.22 (s, 3H, NCH_3-5), 3.11 (s, 3H, NCH_3-5), 2.38 (s, 3H, α-CH_3); ^{13}C NMR (*DMSO*-d_6): $\delta = 13.87$ (α-C), 28.93 (NC-1), 42.85, 46.23 (2NC-5), 83.04 (=C-5), 127.01, 128.29, 133.11, 137.51, 151.11, 154.15, 154.56, 159.06, 163.84; MS: *m/z* (relative intensity) = 347 (M^+, 80), 303 (55), 289 (50), 193 (98), 183 (42), 167 (83), 166 (64), 152 (34), 139 (45), 137 (100), 125 (34), 111 (39), 103 (52), 95 (72), 83 (41); $C_{16}H_{18}ClN_5O_2$; calcd.: C 55.25, H 5.21, N 20.13; found: C 55.14, H 5.22, N, 19.96.

3d: Yield: (63%); m.p.: 230–232°C; UV (MeOH): $\lambda_{max} = 202$ (4.66), 246 (4.61), 284 (4.77), 322 (4.74); ^{1}H NMR (*DMSO*-d_6): $\delta = 10.13$ (s, 1H, NH-3), 8.07 (s, 1H, CH-5), 6.97–7.68 (dd, 4H, aromatic), 3.78 (s, 3H, OCH_3-*p*), 3.29 (s, 3H, NCH_3-1), 3.20 (s, 3H, NCH_3-5), 3.05 (s, 3H, NCH_3-5), 2.35 (s, 3H, α-CH_3); ^{13}C NMR (*DMSO*-d_6): $\delta = 13.92$ (α-C), 28.94 (NC-1), 42.58, 46.09 (2NC-5), 55.14 (C-*p*), 83.14 (=C-5), 113.72, 126.86, 131.13, 151.16, 153.63, 155.20, 159.39, 159.88, 163.31; MS: *m/z* (relative intensity) = 343 (M^+, 30), 328 (10), 299 (25), 285 (14), 193 (15), 183 (6), 150 (10), 134 (23), 133 (100), 123 (11), 95 (15), 92 (7), 83 (10); $C_{17}H_{21}N_5O_3$; calcd.: C 59.46, H 6.16, N 20.39; found: C 59.61, H 6.24, N 20.42.

7-Methylpyrazolo[3,4-d]pyrimidine-4,6(5H)-dione (**4**)

Method A: To a suspension of **3a**, **b**, **c**, or **d** (0.001 mol) in ethanol (10 ml), trichloroacetic acid (0.003 mol) in ethanol (5 ml) was added with stirring over 15 min at room temperature. The resulting

precipitate was filtered, washed with water, dried in the oven, and recrystallized from ethanol to give 0.13 g **4**.

Yield: 88%; m.p.: > 330°C; UV (MeOH): λ_{max} = 204 (4.44), 257 (3.97); ^{1}H NMR (*DMSO*-d_6): δ = 13.43 (s, 1H, NH-1), 10.43 (s, 1H, NH-5), 8.29 (s, 1H, CH-3), 3.31 (s, 3H, NCH_3-7); ^{13}C NMR (*DMSO*-d_6): δ = 28.60 (NC-7), 100.57 (C-3), 129.96 (C-4), 151.30 (C-5), 151.89, 158.84 (2C=O).
Method B: To a mixture of **1** (0.6 g, 3.8 mmol) and $POCl_3$ (0.6 ml), *DMF* (10 ml), was added. The mixture was heated at 80°C for 1 h. The excess of $POCl_3$ and *DMF* was removed by evaporation under reduced pressure. Water was added to the residue, the resulting precipitate was filtered, washed with ethanol, and dried in the oven to give 0.11 g (75%) colourless crystals.

5,7-Dimethyl-2-vinylpyrazolo[3,4-d]pyrimidine-4,6(5H, 7H)-dione (**6a–d** [10])

Method A: A mixture of **2a–d** (0.001 mol) and *DMF* dimethylacetal (2.5 ml) was heated at 140°C for 12 h with stirring. After cooling, the resulting precipitate was filtered, washed with ethanol and recrystallized from ethanol to give colourless crystals (Table 1).
Method B: A mixture of **2a–d** (0.001 mol) and *DMF* dimethylacetal (2.5 ml) in *DMF* (3 ml) was heated for 30 min. After cooling, the resulting precipitate was filtered, washed with ethanol, and recrystallized from ethanol (Table 1).

6a: UV (MeOH): λ_{max} = 207 (4.4), 239 (4.06); 273 (4.10); ^{1}H NMR (*DMSO*-d_6): δ = 8.54 (s, 1H, CH-3), 7.36–7.48 (m, 5H, aromatic), 5.57, 5.71 (dd, 2H, J = 0.9 Hz, $=CH_2$), 3.35 (s, 3H, NCH_3-5), 3.22 (s, 3H, NCH_3-7); ^{13}C NMR (*DMSO*-d_6): δ = 27.58 (NC-7), 29.75 (NC-5), 101.67, 109.00 (C=C-2), 127.37, 128.56, 129.47, 131.74, 134.21, 144.63, 150.73, 151.21, 157.77; MS: *m/z* (relative intensity)= 283 (MH^+, 17), 282 (M^+, 100), 281 (M^+-1, 32), 225 (8), 197 (18), 180 (20), 123 (18), 103 (37), 95 (11), 77 (19); $C_{15}H_{14}N_4O_2$; calcd.: C 63.81, H 4.99, N 19.84; found: C 63.68, H 5.01, N, 19.70.

6b: UV (MeOH): λ_{max} = 205 (4.46), 252 (4.26), 292 (4.22); ^{1}H NMR (*DMSO*-d_6): δ = 8.48 (s, 1H, CH-3), 7.22–7.29 (dd, 4H, aromatic), 5.50, 5.64 (dd, 2H, J = 1.06 Hz=CH_2), 3.35 (s, 3H, NCH_3-5), 3.23 (s, 3H, NCH_3-7), 2.34 (s, 3H, CH_3-*p*);^{13}C NMR (*DMSO*-d_6): δ = 20.73 (C-*p*), 27.57 (NC-7), 29.74 (NC-5), 101.67, 108.13 (C=C-2), 127.29, 129.12, 131.44, 131.58, 139.16, 144.65, 150.74, 151.26, 157.80; $C_{16}H_{16}N_4O_2$; calcd.: C 64.85, H 5.44, N 18.90; found: C 65.21, H 5.51, N 19.23.

6c: UV (MeOH); λ_{max} = 206 (4.36), 251 (4.25), 290 (4.17); ^{1}H NMR (*DMSO*-d_6): δ = 8.63 (s, 1H, CH-3), 7.39–7.52 (dd, 4H, aromatic), 5.62, 5.73 (dd, 2H, J = 1.29 Hz, $=CH_2$), 3.34 (s, 3H, NCH_3-5), 3.23 (s, 3H, NCH_3-7); ^{13}C NMR (*DMSO*-d_6): δ = 27.59 (NC-7), 29.75 (NC-5), 101.78, 109.71 (C=C-2), 128.56, 129.17, 132.04, 133.10, 134.10, 143.53, 150.77, 151.21, 157.77; $C_{15}H_{13}ClN_4O_2$; calcd.: C 56.87, H 4.13, N 17.68; found: C 56.82, H 4.23, N, 17.88.

6d: UV (MeOH): λ_{max} = 204 (4.90), 270 (4.80); ^{1}H NMR (*DMSO*-d_6): δ = 8.49 (s, 1H, CH-3), 6.96–7.33 (dd, 4H, aromatic), 5.45, 5.59 (dd, 2H, $=CH_2$), 3.36 (s, 3H, NCH_3-5), 3.80 (s, 3H, OCH_3-*p*), 3.22 (s, 3H, NCH_3-7); ^{13}C NMR (*DMSO*-d_6): δ = 27.56 (NC-7), 29.72 (NC-5), 55.14 (OC-*p*), 101.57, 107.23 (C=C-2), 113.95, 126.49, 128.82, 131.60, 144.32, 150.66, 151.21, 157.77, 160.14; MS: *m/z* (relative intensity) = 313 (MH^+, 8), 312 (M^+, 45), 311 (M^+-1, 3), 156 (2), 134 (10), 133 (100), 118 (4), 102 (2), 89 (5), 77 (5), 66 (4), 63 (3); $C_{16}H_{16}N_4O_3$; calcd.: C 61.51, H 5.16, N 17.93; found: C 61.38, H 5.29, N, 17.76.

7-Methyl-5-ethyl-2-vinylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-diones (**7a–d**)

A mixture of **2** (0.001 mol) and *DMF* diethylacetal (2.5 ml) was heated at 140°C for 12 h. The mixture was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography using AcOEt: toluene = 1 : 2. The residue was recrystallized from ethanol: water = 4 : 1.

7a: Yield: (60%); m.p.: 110–112°C; UV (MeOH): λ_{max} = 205 (4.8), 247 (4.5), 288 (4.55); ^{1}H NMR ($CDCl_3$): δ = 7.9 (s, 1H, CH-3), 7.37–7.46 (m, 5H, aromatic), 5.28, 5.82 (dd, 2H, J = 0.48 Hz, =CH_2-2), 4.06 (q, 2H, NCH_2), 3.57 (s, 3H, NCH_3), 1.24 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 13.36 (NC-5), 30.05 (NC-5), 36.6 (C-7), 102.7, 107.02 (C=C), 128.31, 128.90, 129.94, 130.41, 134.27, 144.92, 151.38, 151.55, 158.30; MS: *m/z* (relative intensity) = 296 (100), 281 (17), 268 (22), 253 (8), 225 (11), 197 (18), 166 (7), 123 (8), 104 (6), 95 (11); $C_{16}H_{16}N_4O_2$; calcd.: C 64.85, H 5.44, N 18.90; found: C 64.50, H 5.53, N 18.65.

7b: Yield: (68%); m.p.: 114–115°C UV (MeOH): λ_{max} = 205 (4.90), 248 (4.63), 286 (4.60); ^{1}H NMR ($CDCl_3$): δ = 7.91 (s, 1H, CH-3), 7.21–7.29 (dd, 4H, aromatic), 5.24, 5.77 (dd, 2H, =CH_2), 4.06 (q, 2H, NCH_2), 3.57 (s, 3H, NCH_3), 2.41 (s, 3H, CH_3-*p*), 1.24 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 13.38 (NC-5), 21.31 (C-2-*p*), 30.03 (NC-5), 36.58 (NC-7), 102.63, 106.37 (C=C),128.21, 129.55, 130.37, 131.39, 140.13, 144.9, 151.34, 151.57, 158.29; MS: *m/z* (relative intensity) = 310 (M^+, 100), 295 (13), 282 (13), 267 (5), 239 (7), 211 (8), 194 (5), 166 (7), 123 (9), 118 (5), 115 (20); $C_{17}H_{18}N_4O_2$; calcd.: C 65.78, H 5.84, N 18.05; found: C 66.01, H 5.89, N 18.10.

7c: Yield: (40%); m.p.: 130°C; UV (MeOH): λ_{max} = 205 (4.88), 251 (4.67), 281 (4.57); ^{1}H NMR ($CDCl_3$): δ = 7.92 (s, 1H, CH-3), 7.29–7.35 (dd, 4H, aromatic), 5.30, 5.79 (dd, 2H, J = 0.8 Hz, =CH_2), 4.07 (q, 2H, CH_2), 3.55 (s, 3H, NCH_3), 1.24 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 13.37 (C-5), 30.06 (NC-5), 36.64 (NC-7), 102.91, 107.66 (C=C), 129.18, 129.50, 130.31, 132.7, 136.1, 144.0, 151.4, 151.5, 158.18; MS: *m/z* (relative intensity) = 332 (34), 331 (21), 330 (M^+, 100), 315 (17), 302 (24), 231 (17), 139 (12), 123 (11), 102 (19); $C_{16}H_{15}ClN_4O_2$; calcd.: C 58.09, H 4.57, N 16.93; found: C 58.13, H 4.51, N 16.78.

7d: Yield: (46%); m.p.: 108°C; UV (MeOH): λ_{max} = 204 (4.81), 257 (4.56), 272 (4.62); ^{1}H NMR ($CDCl_3$): δ = 7.93 (s, 1H, CH-3), 6.92–7.33 (dd, 4H, aromatic), 5.29, 5.72 (dd, 2H, =CH_2), 4.07 (q, 2H, NCH_2), 3.86 (s, 3H, OCH_3), 3.57 (s, 3H, NCH_3), 1.24 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 13.39 (C-5), 30.05 (NC-5), 36.59 (NC-7), 55.45 (OC-*p*), 102.61, 105.9 (C=C), 114.27, 126.57, 129.67, 130.36, 144.6, 151.33, 151.58, 158.31, 160.87); MS: *m/z* (relative intensity) = 326 (M^+, 55), 325 (3), 311 (3), 298 (2), 156 (2), 134 (10), 133 (100), 123 (2), 118 (5), 103 (3); $C_{17}H_{18}N_4O_3$; calcd.: C 62.56, H 5.56, N 17.16; found: C 62.33, H 5.54, N 17.21.

7-Methyl-5-isopropyl-2-vinylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-diones (**8a–d**)

Method A: A mixture of **2** (0.001 mol) and *DMF* diisopropylacetal (2.5 ml) in *DMF* (1 ml) was heated at 140°C for 0.5 h with stirring. The mixture was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography (AcOEt: toluene = 1:2) to give two fractions. The second fraction consists of **6a–d**; and the first one was purified again using preparative silica gel chromatography (AcOEt: toluene = 1:2) to give colourless crystals of **8a–d**.
Method B: A mixture of **2** (0.001 mol) and *DMF* diisopropylacetal (2.5 ml) was heated at 120°C for 12h with stirring. The mixture was separated as expained in method A.

8a: M.p.: 80°C; ^{1}H NMR ($CDCl_3$): δ = 7.88 (s, 1H, CH-3), 7.35–7.47 (m, 5H, aromatic), 5.27, 5.80 (dd, 2H, J = 0.5Hz, =CH_2), 5.26 (m, 1H, NCH-5), 3.54 (s, 3H, NCH_3-7), 1.48–1.50 (d, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): δ = 19.62 (2C-5), 29.91 (NC-7), 45.74 (NC-5), 102.95, 106.90 (C=C), 128.29, 128.87, 129.91, 130,55, 144.90, 151.42, 151.60, 158.84; MS: *m/z* (relative intensity)= 310 (M^+, 86), 295 (25), 269 (21), 268 (100), 197 (19), 122 (20), 103 (74), 95 (19), 77 (53), 66 (26); $C_{17}H_{18}N_4O_2$; calcd.: C 65.79, H 5.85, N 18.05; found: C 65.51, H 5.83, N 17.91.

8b: M.p.: 74°C; ^{1}H NMR ($CDCl_3$): δ = 7.89 (s, 1H, CH-3), 7.24–7.29 (dd, 4H, aromatic), 5.23, 5.75 (dd, 2H, =CH2), 5.25 (m, 1H, NCH-5), 3.53 (s, 3H, NCH_3), 2.40 (s, 3H, CH_3-*p*), 1.47–1.50 (d, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): δ = 19.62 (2C-5), 21.33 (C-*p*), 29.90 (NC-7), 45.72 (NC-5), 102.87, 106.30 (C=C), 128.18, 129.53, 130.55, 131.42, 140.09, 144.90, 151.38, 151.63, 158.88; MS: *m/z* (relative intensity) = 324 (M^+, 100), 309 (22), 283 (20), 282 (93), 124 (15), 118 (13), 117 (86),

95 (18), 66 (30), 57 (11), 43 (33); $C_{18}H_{20}N_4O_2$; calcd.: C 66.65, H 6.21, N 17.27; found: C 66.35, H 6.27, N, 17.19.

8c: M.P.: 45°C; ^{1}H NMR ($CDCl_3$): $\delta = 7.87$ (s, 1H, CH-3), 7.27–7.40 (dd, 4H, aromatic), 5.26, 5.74 (dd, 2H, $J = 0.8$ H_2, $=CH_2$), 5.26 (m, 1H, CH-5), 3.49 (s, 3H, NCH_3), 1.44–1.47 (d, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 19.61$ (2C-5), 29.92 (NC-7), 45.81 (NC-5), 103.14, 107.58 (C=C), 129.14, 129.47, 130.48, 132.74, 136.06, 144.02, 151.50, 151.63, 158.77; $C_{17}H_{17}ClN_4O_2$; calcd.: C 59.22, H 4.97, N 16.25; found: C 58.97, H 4.99, N 16.02.

8d: Oil; ^{1}H NMR ($CDCl_3$): $\delta = 7.87$ (s, 1H, CH-3), 6.87–7.29 (dd, 4H, aromatic), 5.17, 5.66 (dd, 2H, $=CH_2$), 5.24 (m, 1H, NCH-5), 3.82 (s, 3H, OCH_3-*p*), 3.50 (s, 3H, NCH_3-7), 1.44–1.47 (d, 6H, $2CH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 19.59$ (2C-5), 29.85 (NC-7), 45.71 (NC-5), 55.38 (C-*p*), 102.82, 105.76 (=CH2), 114.20, 126.61, 129.59, 130.48, 144.61, 151.35, 151.59, 158.84, 160.83; $C_{18}H_{20}N_4O_3$; C 63.51, H 5.92, N 16.46; found: C 63.29, H 6.14, N, 16.32.

5,7-Dimethylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-dione (**9a**)

A mixture of **6a–d** (0.001 mol) and 36% hydrochloric acid (0.5 ml) in ethanol (10 ml) was refluxed for 2 h. After cooling, the resulting precipitate was filtered to give 0.15 g (88%).

9a: M.P.: 274°C (Ref. [5]: 277–279°C); ^{1}H NMR (*DMSO*-d_6): $\delta = 13.48$ (s, 1H, NH-1), 8.45 (s, 1H, CH-3), 3.37 (s, 3H, NCH_3-7), 3.18 (s, 3H, NCH_3-5); ^{13}C NMR (*DMSO*-d_6): $\delta = 27.46$ (NC-7), 29-66 (NC-5), 9.88 (C-4), 130.19 (C-3), 150.11, 151.36, 158.32; $C_7H_8N_4O_2$; calcd.: 46.66, H 4.47, N 31.09; found: C 46.79, H 4.43, N 31.12.

7-Methyl-5-ethylpyrazolo[3,4-d]pyrimidine-4,6(5H,7H)-dione (**9b**)

A mixture of **7a–d** (0.001 mol) and 36% hydrochloric acid (0.003 mol) in ethanol (10 ml) was refluxed for 1 h. The mixture was evaporated under reduced pressure, and the residue was recrystallized from methanol to give 0.14 g (74%)

9b: M.P.: 243°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 13.48$ (s, 1H, NH-1), 8.46 (s, 1H, CH-3), 3.85 (q, 2H, NCH_2-5), 3.37 (s, 3H, NCH_3-7), 1.08 (t, 3H, CH_3); ^{13}C NMR (*DMSO*-d_6): $\delta = 13.16$ (C-5), 29.58 (NC-7), 35.45 (NC-5), 100.01 (C-4), 130.18 (C-3), 150.26, 150.97, 157.98; $C_8H_{10}N_4O_2$; C 49.47, H 5.19, N 28.85; found: C 49.21, H 5.06, N 28.63.

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