On the Tautomerism of 2-Phenacyl-4-pyrimidinones and Related Compounds

José Elguero*, Pilar Goya, Ana Martínez, and Isabel Rozas

Instituto de Química Médica, C. S. I. C.,
Juan de la Cierva, 3, E-28006 Madrid, Spain

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3-Methyl-2-phenacyl-4-pyrimidinones 1, 2 have been synthesized using the sulfide contraction. According to the NMR data, the compounds 1, 2 exist exclusively as the benzoylmethylene tautomers a both in solution and in the solid state. AM1 calculations of the parent system are in agreement with the experimental observations. The study of the tautomeric equilibrium by this semiempirical method has been extended to other cases of enaminoketone/enolimine tautomerism.

Zur Tautomerie von 2-Phenacyl-4-pyrimidinonen und verwandten Verbindungen

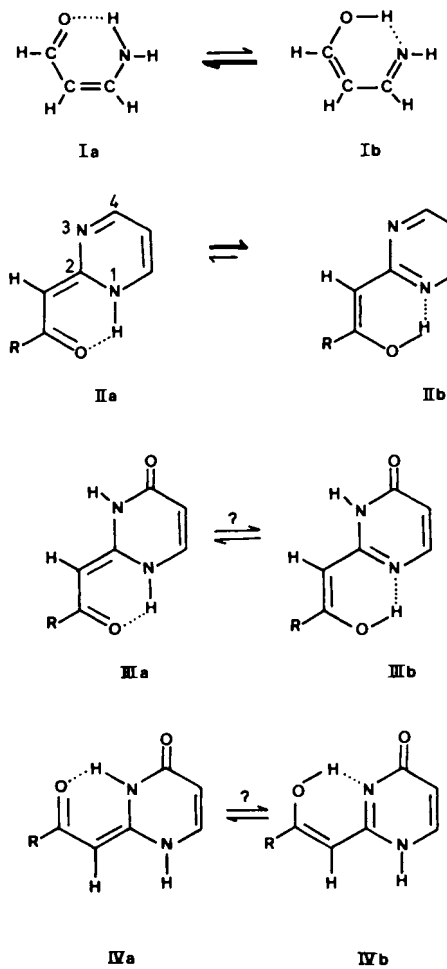
3-Methyl-2-phenacyl-4-pyrimidinone 1, 2 werden durch Sulfidkontraktion synthetisiert. Aufgrund der NMR-Daten existieren die Verbindungen ausschließlich in der Benzoylmethylen-Form, sowohl in Lösung als auch als Festkörper. Diese Ergebnisse werden durch AM1-Berechnungen für die Stammverbindung bestätigt. Die Untersuchung des Tautomeren-Gleichgewichts mittels dieser semiempirischen Methode wurde auf andere Fälle von Enaminoketon/Enolimin-Tautomerie erweitert.

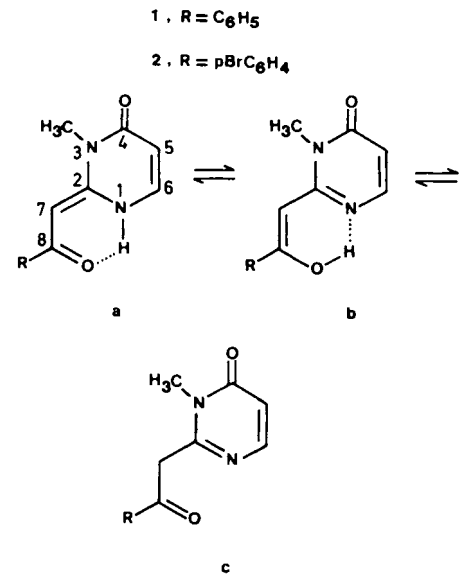
Although the information accumulated on tautomeric equilibria in solution is so large and consistent that most problems are either solved or predictable, a few cases still remain where the position of the equilibrium is uncertain. One such case concerns enaminoketones forming part of a heteroaromatic compound.

Enaminoketone/enolimine tautomerism in alicyclic systems is strongly shifted towards the enaminoketone form[1,2], as shown in the simplest case of the enaminoaldehyde **Ia**.

When the CN bond is part of an aromatic heterocycle (pyridine, pyrimidine, purine), all the evidence[3,4,5] points to stabilization of the enol form, which becomes predominant. For instance, the equilibrium **IIa** ⇌ **IIb** is displaced to **IIb** due to the aromaticity of pyrimidine[6]. Between these situations, the controversial case of pyrimidinone derivatives **III** and **IV** is found.

In such cases, it is not known whether the reduced aromaticity of the ring[6] can overcome the tendency of enaminoketones to exist as such or not.





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The Eschenmoser sulfide contraction[7] has been used for introducing C-substituents into α or γ position to the heterocyclic nitrogen of nucleosides[7-9] and heterocycles[10]. The general synthetic procedure involves *S*-alkylation and sulfur extrusion. We have used this procedure to prepare compounds **1** and **2**. These compounds can exist in three different tautomeric forms, **a**, **b**, and **c**.

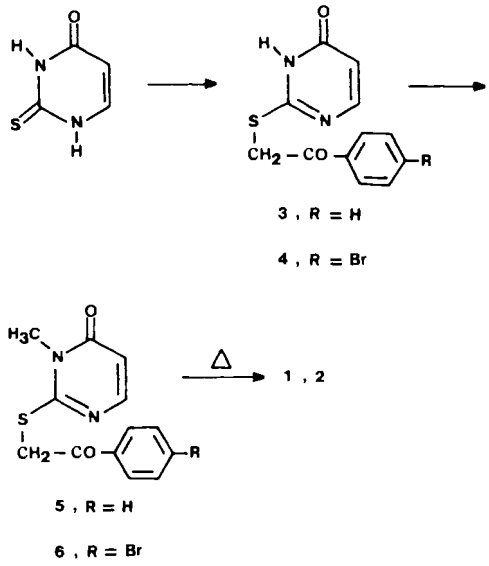
Of these, the nonconjugated keto tautomer **c** can be readily differentiated, whereas it is harder to distinguish the hydrogen-bonded enol **b** from the enaminoketone **a**.

With the aim of definitely establishing the correct tautomeric form, we have carried out a detailed study of these compounds both in solution (^1H, ^{13}C and ^{15}N NMR) and solid state (^{13}C CP/MAS). Theoretical calculations using the AM1 semiempirical approach have also been performed.

Synthesis

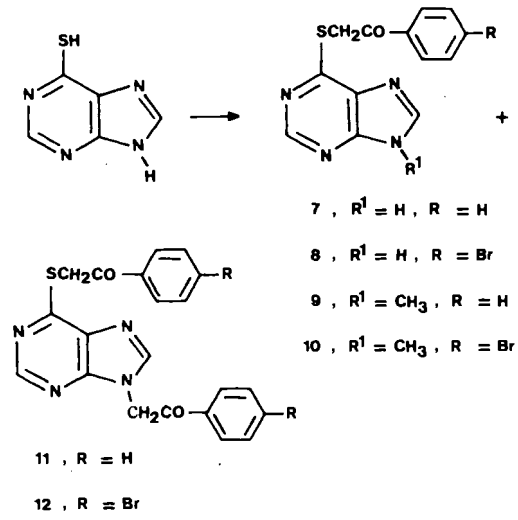
Compounds **1** and **2** were prepared according to Scheme 1. 2-Thiouracil was readily alkylated with phenacyl and *p*-bromophenacyl bromides to give the *S*-phenacyl compounds **3** and **4**[10]. Treatment of the latter with methyl iodide afforded complex mixtures from which it was possible to isolate the N-3 monomethyl derivatives **5** and **6**. Sulfur extrusion to the desired compounds **1** and **2** was achieved by heating in DMF.

Scheme 1



In order to investigate the tautomerism in purine derivatives as well, a similar reaction sequence was attempted with 6-mercaptopurine (Scheme 2). This compound reacted with the phenacyl bromides to give, in each case, two compounds: the *S*-monoalkyl 7, **8**, and the *N,S*-dialkyl derivatives **11** and **12**. Treatment of **7** and **8** with methyl iodide afforded the corresponding N-9 methyl derivatives **9** and **10**. However, all attempts to extrude sulfur from these, including prolonged heating in DMF and treatment with potassium *tert*-butylate and triphenylphosphine[9], were unsuccessful.

Scheme 2



Tautomeric Structure in Solution

The structures of all compounds were established by their analytical and spectroscopic data. The tautomeric structure of **1** and **2** was assigned by NMR.

The 300-MHz ^1H-NMR spectrum ([D_6]DMSO) of compound **1** (Table 2) shows two singlets at δ = 3.34 (*N*-methyl group) and δ = 5.90 (7-H). There are no traces of a singlet around 5 ppm, corresponding to the CH_2 group of tautomer **1c**.

Useful information concerning the tautomeric structure is gained from the signals of the protons of the uracil moiety: 5-H and 6-H cause quadruplets at 5.82 and 7.75 ppm. After addition of D_2O, these signals become doublets ($J_{5,6}$ = 7.2 Hz). The small coupling constant of 5-H (^4J = 1.2 Hz) is due to an allylic coupling with the NH proton at N-1, whereas at 6-H the 5.2 Hz coupling constant corresponds to a vicinal coupling with 1-H. This proton causes a broad singlet at δ = 14.59. The fact that it is shifted so far downfield indicates a strong hydrogen bond with the C=O group at the 8 position. Neither the NH signal nor its coupling constants can be detected in the $CDCl_3$ spectrum, probably due to traces of hydrochloric acid in this solvent. However, the chemical shifts in both solvents are very similar, indicating that the same tautomer is present. The reported coupling constants are only compatible with tautomer **1a**.

Further evidence in favour of structure **a** was obtained from the ^{13}C-NMR spectra, both in [D_6]DMSO and $CDCl_3$ (Tables 3 and 4). The signals were assigned by comparing them to literature data on related pyrimidinones[11]. The long-range allylic coupling constant between C-4 and 6-H (^3J = 9.6 Hz) is useful for assigning the signal at δ = 160 to the C=O at C-4 and not at C-8. It is worth mentioning that the coupling between C-5 and the *N*-methyl group (^4J = 5.7 Hz) is unusually high, due to the W disposition[12].

The bromo derivative **2** shows similar features both in ^1H NMR (Table 2) and in ^{13}C NMR (Tables 3 and 4). Thus, tautomer **2a** is present in both [D_6]DMSO and $CDCl_3$.

The ^{15}N-NMR spectrum of compound **1** was recorded in [D_6]DMSO at room temperature. The proton-decoupled

spectrum (20 MHz, reference: external neat nitromethane) shows lines at −251.9 ppm and −234.6 ppm, which are due to N-3 (methyl) and N-1 (H) by analogy with uracil (−245.2 and −217.7 ppm, respectively)[13].

These chemical shifts are consistent only with tautomer **1a**, since N-1 of tautomer **1b** would appear at about −120 ppm (2-methoxypyridine nitrogen resonates at −112 ppm)[13].

In conclusion, the NMR study in solution shows that tautomer **1a** is much more stable than tautomer **1b**.

Tautomeric Structure in the Solid State

The most striking feature in the ^{13}C-CP/MAS spectra is the almost perfect coincidence of the chemical shifts with those found in solution (Table 3). Some signals are split, either because of interactions with the quadrupolar nitrogen atoms[14] or the existence of two independent molecules in the crystal (with, for example, two different conformations of the phenyl groups). However, these splittings cannot arise from a mixture of tautomers since they are too small and since they do not affect some carbons sensitive to tautomerism, such as C-2 and C-8 (in **2a**).

The obvious conclusion of this study is that only tautomer **a** exists in the solid state, since in crystals only *one* tautomer is present[3].

Theoretical Calculations of the Tautomerism of Heterocyclic Enaminoketones

Tautomerism in heterocycles may also be studied by quantum-mechanical calculations, since the relative stability of two tautomers depends on the difference between their lowest energies[15]. Therefore, for a better understanding of the predominance of the enaminoketone in compound **1**, semiempirical calculations of simplified structures of tautomers **1a** and **1b** (i.e. **IIIa** and **IIIb**) have been carried out. The AM1 method[16] (MOPAC package)[17] was chosen since it takes hydrogen bonds into account. The results predict tautomer **a** to be 2.6 kcal·mol^{-1} more stable than tautomer **b**.

The good agreement found between the theoretical calculations and results in solution enabled us to extend this study, and thus isomeric structures **IVa** and **IVb** have also been calculated.

The simplest case, that of the enaminoketone/enolimine equilibrium has also been studied, both in an alicyclic system (**Ia**, **Ib**) and in an aromatic heterocycle (**IIa**, **IIb**). All the calculations were done with full-geometry optimizations starting from standard parameters. Optimized geometries are available on request.

Regarding the final geometries, there is a slight difference in the relative disposition of the phenyl ring with respect to the rest of the structure. Thus, in all the **a** tautomers, this torsion angle is 35−37°, whereas in the **b** tautomers it is around 32°. Conjugation of the phenyl ring with two double bonds in the **a** cases can account for this more planar situation.

The energy values and the relative energy difference between the tautomers are presented in Table 1. As expected, the equilibrium in an alicyclic system, **I**, is strongly shifted to the keto form. When the CN bond is included in an aromatic structure such as pyrimidine (case **II**), the equilibrium is reversed and the enolimine form **b** becomes the more stable. In the case of pyrimidinone **III**, the predominant form is the keto species **a**, as in **I**, but with a smaller energy difference probably due to a certain degree of aromaticity in this system. The results obtained for pyrimidinones **IV** also indicate predominance of the keto form; however, the energy difference is of the same order as in the alicyclic system **I**, since the pyrimidinone moiety cannot, in this case, contribute to aromaticity.

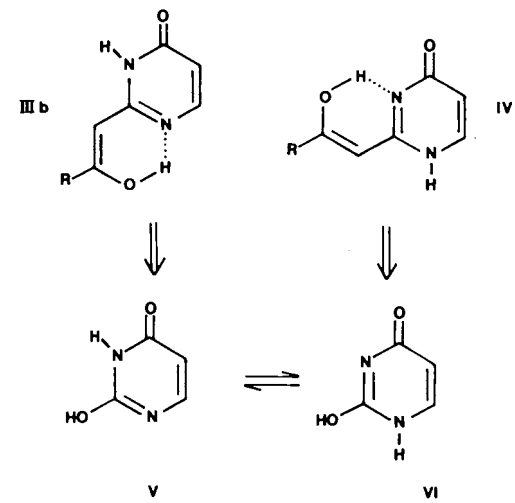
There is no controversy regarding the tautomeric structure of compounds related to **III**[7]; however, for 1-ribosyl derivatives of 4-pyrimidinone (type **IV**) tautomer **b** has been proposed[5], and according to our results, this form is very unlikely to occur.

Table 1. Heats of formation [kcal·mol^{-1}] for the enaminoketone (**a**) and enolimine (**b**) tautomers of structures **I**, **II**, **III**, and **IV**

Structure	ΔH_f (a)	ΔH_f (b)	ΔH_f (a − b)
I	−28.3	−17.4	−11.1
II	45.1	42.0	3.1
III	−8.8	−6.2	−2.6
IV	−6.6	4.5	−11.1

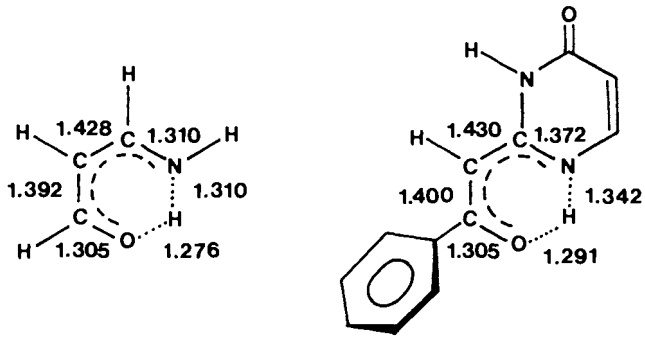
Finally, it is interesting to compare the ΔH_f values (Table 1) of tautomeric pairs **III** and **IV**. As can be seen, the heats of formation of tautomers **IIIa** and **IVa** are quite similar, a result that can be understood if we consider them to be vinylogous forms of uracil. On the other hand, there is a considerable difference in ΔH_f values for tautomers **IIIb** and **IVb**, the former being 10.7 kcal·mol^{-1} more stable. Again, if we make a comparison with lactim tautomers of uracil (Scheme 3), we can conclude that the observed differences should correspond to differences in stability in uracil tautomers.

Scheme 3



Theoretical calculations show that tautomer **V** should be more stable than tautomer **VI** by 8.9 kcal·mol^{-1} (3-21G basis set) or 9.2 kcal·mol^{-1} (MNDO)[18], values that agree remarkably well with our result (AM1). Since compounds **III** and **IV** are *E*/*Z* isomers, a practical consequence of our calculations is that, in the case of N^1,N^3-unsubstituted pyrimidinones, the most stable form may be **IIIa**.

The prototropic barriers for **I** and **III** have also been estimated. Thus, the transition states (TS) (Figure 2) were obtained using a reaction coordinate that is a linear combination of the O···H and N···H distances[17], and starting from the less stable tautomer.

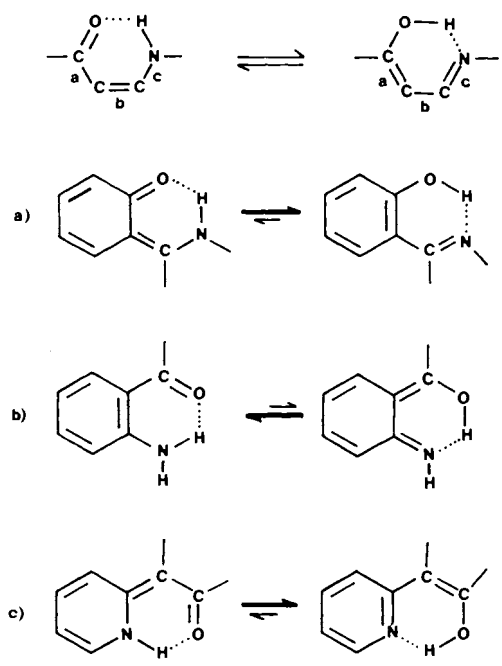


I-TS III-TS

Figure 1. Energies and optimized geometric parameters of transition states of **I** and **III**

In both cases the barriers are quite similar (**Ia** → **I**-TS = 31.1 kcal·mol^{-1}; **IIIa** → **III**-TS = 25.2 kcal·mol^{-1}). No experimental data are available on these activation energies. However, theoretical calculations for intra- or intermolecular proton transfers[19,20] provide values ranging from 12 to 44 kcal·mol^{-1} depending on the size of the hydrogen-bonded pseudoring (six in our case), and on the theoretical method used. It must be taken into account that in this kind of process tunnelling is important and, as a consequence, experimental barriers are much lower than calculated ones.

Scheme 4



The simultaneous use of experimental studies and theoretical calculations has clarified a controversial case of tautomerism. It is possible now to predict that, in the gas phase, enaminoketones should exist as such, unless they are included in an aromatic structure that stabilizes the enolimine tautomer. Thus, starting form one enaminoketone, three situations are possible (Scheme 4).

By convenient modulation of the aromaticity (fused rings, heteroatoms in the ring, *C*-substituents) it is possible to alter these basic situations. Conversely, knowledge (either experimental or theoretical) of the tautomeric equilibria sheds light on the always interesting problem of aromaticity[21].

We thank Prof. *S. Olivella* for helpful advice in the theoretical calculations, and the *CICYT* for financial support (PA86-0431). Cooperation of Dr. *D. Sanz* and Dr. *J. Sanz* in spectral acquisition is gratefully acknowledged.

Experimental

Melting points were determined with a Reichert-Jung Thermovar and are uncorrected. – UV spectra: Perkin-Elmer 402. – IR spectra: Perkin-Elmer 257. – Column chromatography was performed on Merck silica gel 60 (70–230 mesh). Compounds were detected with UV light (254 nm). – ^{1}H-NMR spectra were obtained at 298 K using TMS as internal standard on a Varian EM-90 and a Varian XL-300, operating at 90 MHz and 300 MHz, respectively. – ^{13}C-NMR spectra were recorded with a Varian XL-300, operating at 75 MHz and using TMS as internal reference, under the following conditions: sweep width 16 kHz; pulse width 9 μs; acquisition time 1 s; number of data points 64 K. – ^{15}N-NMR spectra were recorded with broad-band proton decoupling on a Bruker-AM-200 instrument operating at 20.28 MHz using CH_3NO_2 as external standard, under the following conditions: relaxation delay 5 s; pulse width 15 μs; acquisition time 0.4 s. – ^{13}C-CP/MAS-NMR spectra were recorded with a TOSS sequence on a Bruker-CXP-400 instrument operating at 100 MHz, under the following conditions: spinning rate 4.1 kHz; spectral width 50.0 kHz; acquisition time 5.0 s.

2-Phenacylthio-4(3H)-pyrimidinone (**3**): A solution of 13.8 g (0.07 mol) of phenacylbromide in 50 ml of ethanol was added to a solution of 9.0 g (0.07 mol) of 2-thiouracil and 2.0 g of potassium carbonate in 150 ml of water. The reaction mixture was stirred at room temperature for 1 h. The solution was then acidified with 25 ml of 12 N hydrochloric acid. The colorless solid formed was filtered and recrystallized from ethanol: 14.6 g (84%) of **3**, colorless needles; m.p. 184–185°C (ref.[10] 180°C). – IR (nujol): $\tilde{\nu}$ = 1680 and 1660 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 204 nm (4.35), 235 (4.30), 280 (3.88).

2-[(4-Bromophenacyl)thio]-4(3H)-pyrimidinone (**4**): In the same way, 5.0 g (0.04 mol) of 2-thiouracil and 10.8 g (0.04 mol) of 4-bromophenacyl bromide gave, after recrystallization from methanol, 12.0 g (94%) of **4**; m.p. 208–210°C (dec.) [ref.[10] 185–187°C (dec.)]. – IR (KBr): $\tilde{\nu}$ = 1680 and 1660 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 200 nm (4.32), 228 (4.17), 255 (4.15).

6-(Phenacylthio)purine and 9-Phenacyl-6-(phenacylthio)purine (**7** and **9**): To a solution of 3.9 g (0.02 mol) of phenacyl bromide in 75 ml of DMF, 3.0 g (0.02 mol) of 6-mercaptopurine and 1.0 g of

potassium carbonate were added. The reaction mixture was stirred at room temperature for 6 h. 50 ml of water was then added in order to dissolve the inorganic salt. The product was extracted with ethyl acetate (4 × 50 ml). The organic phase was dried with sodium sulfate, and the solvent evaporated in vacuo, to give a residue which was chromatographed on a silica gel column using chloroform/methanol (10:1) as eluent. The first fraction collected was evaporated under reduced pressure and the solid recrystallized from ethanol: 0.5 g (13%) of **9**, colorless needles; m.p. 154–156°C. – IR (nujol): $\tilde{\nu}$ = 1680 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 203 nm (4.57), 242 (4.39), 280 (4.36). – ^{1}H NMR ([D$_6$]DMSO): δ = 8.55 (s, 1 H, 2-H), 8.45 (s, 1 H, 8-H), 8.1–7.5 (m, 10 H, aromatic H), 6.0 (s, 2 H, NCH_2), 5.1 (s, 2 H, SCH_2).

$C_{21}H_{16}N_4O_2S$ (388.3) Calcd. C 64.95 H 4.12 N 14.43 S 8.24
Found C 64.78 H 4.29 N 14.45 S 8.65

The second fraction was evaporated in vacuo and the residue recrystallized from ethanol to yield 2.1 g (39%) of **7**, yellow crystalline solid; m.p. 158–160°C. – IR (nujol): $\tilde{\nu}$ = 1680 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 204 nm (4.34), 243 (4.16), 279 (4.29). – ^{1}H NMR ([D$_6$]DMSO): δ = 8.6 (s, 1 H, 2-H), 8.5 (s, 1 H, 8-H), 8.1–7.5 (m, 5 H, aromatic H), 5.1 (s, 2 H, SCH_2).

$C_{13}H_{10}N_4OS$ (270.2) Calcd. C 57.77 H 3.70 N 20.74 S 11.85
Found C 57.89 H 3.90 N 20.74 S 11.86

6-[(4-Bromophenacyl)thio]purine and 6-[(4-Bromophenacyl)-thio]-9-(4-bromophenacyl)purine (**8** and **10**): Following the procedure described above, 3.0 g (0.02 mol) of 6-thiopurine was allowed to react with 5.5 g (0.02 mol) of 4-bromophenacyl bromide. The first fraction of the column (chloroform/methanol, 25:1) was evaporated in vacuo, and the solid was washed with chloroform and ethanol: 0.2 g (4%) of **10**; m.p. 215–217°C. – IR (KBr): $\tilde{\nu}$ = 1700 and 1680 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 204 nm (3.79), 255 (3.82), 273 (3.75). – ^{1}H NMR ([D$_6$]DMSO): δ = 8.5 (s, 1 H, 2-H), 8.4 (s, 1 H, 8-H), 8.0–7.6 (m, 8 H, aromatic H), 5.9 (s, 2 H, NCH_2), 4.9 (s, 2 H, SCH_2).

$C_{21}H_{14}Br_2N_4O_2S$ (546.1) Calcd. C 46.15 H 2.56 N 10.25 S 5.86
Found C 46.43 H 2.13 N 10.17 S 5.41

The second fraction was evaporated to dryness, and the solid was washed with chloroform and ethanol: 1.1 g (16%) of **8**; m.p. 223–225°C. – IR (KBr): $\tilde{\nu}$ = 1680 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 205 nm (4.36), 255 (4.31), 275 (4.34). – ^{1}H NMR ([D$_6$]DMSO): δ = 8.6 (s, 1 H, 2-H), 8.5 (s, 1 H, 8-H), 8.1–7.8 (m, 4 H, aromatic H), 5.1 (s, 2 H, SCH_2).

$C_{13}H_9BrN_4OS$ (349.1) Calcd. C 44.69 H 2.57 N 16.04 S 9.16
Found C 45.38 H 2.86 N 16.24 S 9.10

3-Methyl-2-phenacylthio-4(3H)-pyrimidinone (**5**): A stirred solution of 14.0 g (0.05 mol) of **3** in 100 ml of anhydrous acetone was treated with 3.0 g of potassium carbonate and 7.5 g (0.05 mol) of methyl iodide. The mixture was heated for 1 h at reflux, and the precipitate was filtered off. The solvent was removed in vacuo, and the residue was purified by silica gel column chromatography using ethyl acetate as eluent. The less polar fractions were collected, the solvent was evaporated under reduced pressure, and the residue recrystallized from ethanol: 8.0 g (54%) of **7**, yellow crystalline solid; m.p. 132–134°C. – IR (nujol): $\tilde{\nu}$ = 1680 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 208 nm (4.17), 238 (4.24), 285 (4.05).

$C_{13}H_{12}N_2O_2S$ (260.2) Calcd. C 60.00 H 4.61 N 10.76 S 12.30
Found C 59.60 H 4.58 N 10.56 S 12.58

2-[(4-Bromophenacyl)thio]-3-methyl-4(3H)-pyrimidinone (**6**): Following the procedure described above, 11.0 g (0.03 mol) of **4** was allowed to react with 4.3 g (0.03 mol) of methyl iodide. Once the solvent was evaporated to dryness, the residue was recrystallized from ethanol: 7.9 g (71%) of **6**; m.p. 130–131°C. – IR (KBr): $\tilde{\nu}$ = 1700 and 1670 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 206 nm (4.57), 259 (4.51), 285 (4.30).

$C_{13}H_{11}BrN_2O_2S$ (339.2) Calcd. C 46.01 H 3.24 N 8.25 S 9.43
Found C 46.10 H 3.44 N 8.42 S 9.13

9-Methyl-6-(phenacylthio)purine (**11**): According to the procedure described for **5**, 1.0 g (0.004 mol) of **7** was allowed to react with 0.6 g (0.004 mol) of methyl iodide. The solvent was evaporated under reduced pressure and the residue recrystallized from ethanol: 0.5 g (48%) of **11**, yellow needles; m.p. 170–172°C. – IR (nujol): $\tilde{\nu}$ = 1670 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 205 nm (4.13), 222 (4.05), 242 (4.01), 280 (4.17). – ^{1}H NMR ([D$_6$]DMSO): δ = 8.5 (s, 1 H, 2-H), 8.4 (s, 1 H, 8-H), 8.1–7.5 (m, 5 H, aromatic H), 5.0 (s, 2 H, CH_2), 3.8 (s, 3 H, CH_3).

$C_{14}H_{12}N_4OS$ (284.2) Calcd. C 59.15 H 4.22 N 19.72 S 11.26
Found C 58.87 H 3.99 N 19.71 S 11.07

6-[(4-Bromophenacyl)thio]-9-methylpurine (**12**): Following the procedure described for **5**, 1.1 g (0.003 mol) of **8** and 0.5 g (0.003 mol) of methyl iodide yielded after recrystallization from methanol, 0.5 g (44%) of **12**; m.p. 175–177°C. – IR (KBr): $\tilde{\nu}$ = 1670 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 201 nm (4.36), 255 (4.30), 278 (4.35). – ^{1}H NMR ([D$_6$]DMSO): δ = 8.6 (s, 1 H, 2-H), 8.5 (s, 1 H, 8-H), 8.1–7.7 (m, 4 H, aromatic, H), 5.0 (s, 2 H, CH_2), 3.7 (s, 3 H, CH_3).

$C_{14}H_{11}BrN_4OS$ (363.2) Calcd. C 46.28 H 3.03 N 15.42 S 8.81
Found C 46.02 H 3.23 N 15.24 S 9.14

Table 2. ^{1}H-NMR parameters: chemical shifts (ppm) and coupling constants [Hz]

	5-H	6-H	$J_{5,6}$	NH	$J_{NH,6}$	$J_{NH,5}$	7-H	CH_3	Ar-H	J_{AB}
1[b]	5.82 (dd)	7.75 (q)	7.2	14.59 (bs)	5.2	1.2	5.90 (s)	3.34 (s)	7.99–7.44 (m)	–
1[c]	5.84 (d)	7.28 (d)	7.3	–	–	–	5.72 (bs)	3.39 (s)	7.87–7.39 (m)	–
2[b]	5.83 (dd)	7.74 (q)	7.4	14.55 (bs)	5.2	1.3	5.86 (s)	3.16 (s)	7.92 (d) 7.65 (d)	8.7
2[c]	5.89 (d)	7.35 (d)	7.3	–	–	–	5.69 (bs)	3.42 (s)	7.75 (d) 7.57 (d)	8.6
3[a]	6.1 (d)	7.7 (d)	6.0	–	–	–	4.9 (s)	–	8.1–7.4 (m)	–
4[a]	6.1 (d)	7.7 (d)	6.0	–	–	–	4.7 (s)	–	7.9 (d) 7.7 (d)	6.0
5[a]	6.1 (d)	8.0 (d)	6.0	–	–	–	4.9 (s)	3.5 (s)	8.1–7.5 (m)	–
6[a]	6.2 (d)	7.7 (d)	6.0	–	–	–	4.9 (s)	3.5 (s)	8.1 (d) 7.9 (d)	6.0

[a] 90 MHz, in [D$_6$]DMSO. – [b] 300 MHz, in [D$_6$]DMSO. – [c] 300 MHz, in $CDCl_3$.

Table 3. ^{13}C-NMR parameters: chemical shifts (ppm)

	C-2	C-4	C-5	C-6	C-7	C-8	N-CH_3	C-*i*	C-*o*	C-*m*	C-*p*
1[a]	156.2	160.5	103.6	139.6	79.4	186.8	28.7	139.3	126.8	131.3	128.4
1[b]	155.4	159.8	102.3	140.8	78.6	185.3	28.4	139.3	126.7	131.0	128.3
1[c]	157.9	162.3	103.9	143.9	82.4	189.3	30.9	143.9	130.3	133.3	130.3
2[a]	155.6	159.9	102.6	140.9	78.7	183.9	28.6	138.5	128.9	131.3	124.8
2[b]	156.4	160.4	104.0	139.4	79.0	185.8	28.8	138.1	128.4	131.6	126.0
2[c]	157.5	161.8	101.9	144.7	79.9	186.9	30.8	139.1	129.9	134.1	120.8

[a] 75 MHz, in [D_6]DMSO. – [b] 75 MHz, in $CDCl_3$. – [c] 100 MHz, CP/MAS.

Table 4. ^{13}C-NMR parameters: coupling constants [Hz]

	C-2	C-4	C-5	C-6	C-7	N-CH_3	C-*i*	C-*o*	C-*m*	C-*p*
1[a]	$^3J_{2,6}$ = 8.2	$^2J_{4,5}$ = 1.1 $^3J_{4,6}$ = 9.4	^1J = 175.9 $^2J_{5,6}$ = 5.7 $^4J_{5,9}$ = 5.7	^1J = 184.3 $^2J_{6,5}$ = 2.9	^1J = 163.1	^1J = 141.7	^3J = 6.6	^1J = 158.9 ^2J = 6.3	^1J = 160.8 ^2J = 6.4	^1J = 159.7 ^2J = 6.8
1[b]	$^3J_{2,6}$ = 5.6	$^3J_{4,6}$ = 6.7	^1J = 174.6 $^2J_{5,6}$ = 4.4 $^4J_{5,9}$ = 4.4	^1J = 180.7	^1J = 163.1	^1J = 142.2	^3J = 7.2	^1J = 154.9 ^2J = 7.1	^1J = 159.8 ^2J = 8.7	^1J = 162.0 ^2J = 9.0
2[a]	$^3J_{2,6}$ = 7.6	$^3J_{4,6}$ = 9.7	^1J = 175.8 $^2J_{5,6}$ = 3.3	^1J = 184.8 $^2J_{6,5}$ = 3.5	^1J = 163.8	^1J = 141.7	^3J = 7.0	^1J = 165.5 ^2J = 7.2	^1J = 169.5 ^2J = 5.0	^2J = 3.0
2[b]	$^3J_{2,6}$ = 7.1	$^3J_{4,6}$ = 9.3	^1J = 175.8 $^2J_{5,6}$ = 4.1 $^4J_{5,9}$ = 5.8	^1J = 181.3 $^2J_{6,5}$ = 3.1	^1J = 145.6	^1J = 141.7	–	^1J = 163.0 ^2J = 6.9	^1J = 167.9 ^2J = 5.4	–

[a] 300 MHz, in [D_6]DMSO. – [b] 300 MHz, in $CDCl_3$.

2-(Benzoylmethylene-1,2-dihydro-3-methyl-4(3H)-pyrimidinone (**1**): A solution of 8 g (0.03 mol) of **5** in 100 ml of DMF was heated for 2 h at reflux. After cooling, the solvent was evaporated in vacuo and the solid recrystallized from ethanol: 3.8 g (55%) of **1**, colorless needles; m.p. 166–168°C. – IR (nujol): $\tilde{\nu}$ = 1680 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 201 nm (3.11), 222 (3.13), 243 (3.00), 346 (3.40).

$C_{13}H_{12}N_2O_2$ (228.0) Calcd. C 67.53 H 5.19 N 12.12
Found C 67.80 H 5.27 N 12.40

2-[(4-Bromobenzoyl)methylene]-1,2-dihydro-3-methyl-4(3H)-pyrimidinone (**2**): A solution of 6 g (0.02 mol) of **6** in 150 ml of DMF was heated for 3 h at reflux. After cooling, the solid which appeared was filtered and recrystallized from methanol: 0.9 g (16%) of **12**, thin colorless needles; m.p. 210–212°C. – IR (KBr): $\tilde{\nu}$ = 1710 and 1700 cm^{-1} (C=O). – UV (methanol): λ_{max} (lgε) = 200 nm (4.13), 215 (4.12), 250 (4.07), 350 (4.45).

$C_{13}H_{11}BrN_2O_2$ (307.1) Calcd. C 50.81 H 3.58 N 9.12
Found C 51.02 H 3.50 N 9.26

CAS Registry Numbers

1: 119011-48-2 / **2**: 119011-49-3 / **3**: 17649-29-5 / **4**: 74195-45-2 / **5**: 119038-85-6 / **6**: 119038-86-7 / **7**: 5454-50-2 / **8**: 80985-23-5 / **9**: 119415-01-9 / **10**: 111780-42-8 / **11**: 119011-46-0 / **12**: 119011-47-1 / $PhCOCH_2Br$: 70-11-1 / 4-$BrC_6H_4COCH_2Br$: 99-73-0 / 6-thiouracil: 141-90-2 / 6-mercaptopurine: 50-44-2

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