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# Effect of the Structure of 1- and 3-Methyl-5-fluoropyrimidin-4-ones on H–D Exchange in Position *6* under Conditions of Base Catalysis

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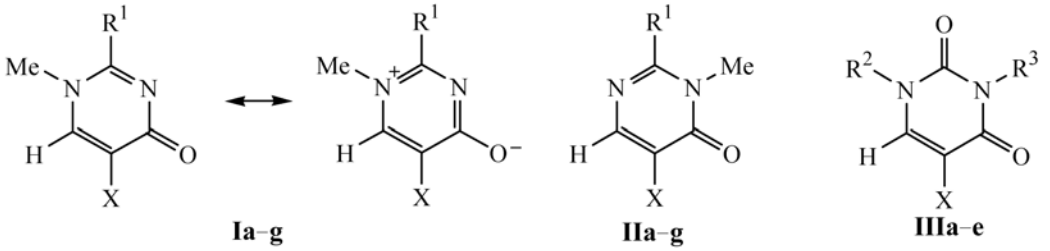
**Abstract**—Hydrogen atom in position *6* of 5-fluoro-1-methylpyrimidin-4(1*H*)-one and its 2-methylsulfan-yl, 2-methoxy and 2-butylamino derivatives is readily replaced by deuterium in 90% methanol-$d_4$ at ~20єC under conditions of base catalysis. The rate of H–D exchange decreases in the series H, SMe > OMe >> NHBu. Isomeric 5-fluoro-3-methylpyrimidin-4-ones, as well as their 5-unsubstituted analogs, do not undergo H–D exchange. Ready deuterium exchange in 5-fluoro-1-methylpyrimidin-4-ones is explained by synergistic effect of the zwitterionic structure and 5-fluorine atom on the $C^6$–H acidity. The gain in energy due to this effect, expressed through the enthalpy of dissociation of the $C^6$–H bond, is ~15 kcal/mol provided that effect of the medium is absent; the contribution of the 5-fluorine atom is 5.3–6.0 kcal/mol.

In the preceding study [1], while measuring the rate of alkaline methanolysis of compounds **Ia**, **Ib**, **IIa**, and **IIb**, we have found that the 6-H signal of pyrimidinone **Ib** disappeared from the $^1$H NMR spectrum immediately (in less than 1 min) after addition of a solution of NaOD in $D_2O$ to a solution of **Ib** in methanol-$d_4$ at room temperature.

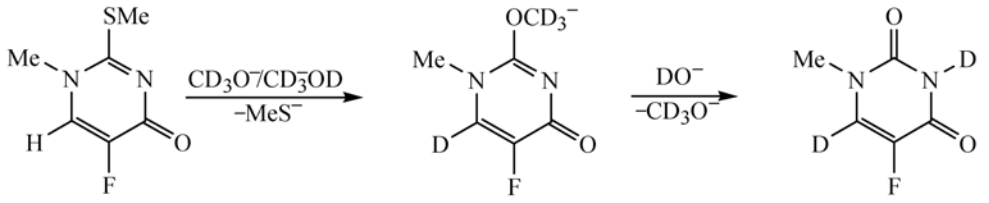



**Ia–g** **IIa–g** **IIIa–e**

**I**, **II**, X = H, $R^1$ = SMe (**a**); X = F, $R^1$ = SMe (**b**), OMe (**c**), H (**d**), $Et_2N(CH_2)_2S$ (**e**), NHBu (**f**); X = $R^1$ = H (**g**); **III**, X = F, $R^2$ = Me, $R^3$ = H (**a**); X = F, $R^2$ = H, $R^3$ = Me (**b**), X = F, $R^2$ = $R^3$ = Me (**c**); X = Br, $R^2$ = $R^3$ = Me (**d**); X = Br, $R^2$ = $R^3$ = OMe (**e**); X = Br, $R^2$ = $R^3$ = H (**f**).

In the $^{13}$C NMR spectrum of 5-fluoro-1-methyluracil (**IIIa**) isolated from the reaction mixture (Scheme 1), the $C^6$ signal appeared as a doublet of triplets. In the IR spectrum of this compound, the C–H stretching vibration band was displaced toward lower frequencies (2289 $cm^{-1}$; Figs. 1, 2). These data indicated that the 6-H atom in **IIIa** was replaced by deuterium. According to the NMR data, in the absence of alkali, compound **Ib** in $D_2O$ and $CD_3OD$ remained unchanged as long as 3 years. In the transformation of pyrimidinone **Ib** into uracil **IIIa** according to Scheme 1, H–D exchange occurs just in 2-methylsulfanyl derivative **Ib**, for the rate of replacement of 6-H by deuterium is much greater than the rate of methoxylation and incommensurably greater than the conversion of 5-fluoro-2-methoxy-1-methylpyrimidine-4(1*H*)-one (**Ic**) into uracil **IIIa** [1]. Insofar as no deuterium exchange was observed with both 3-methyl isomer **IIb** and its protium analog **Ia**, such a ready isotope exchange in compound **Ib** is likely to result from synergistic effect of the structure of **I** and fluorine atom in the 5-position.

**Scheme 1.**




**Ia** **Ic** **IIIc**

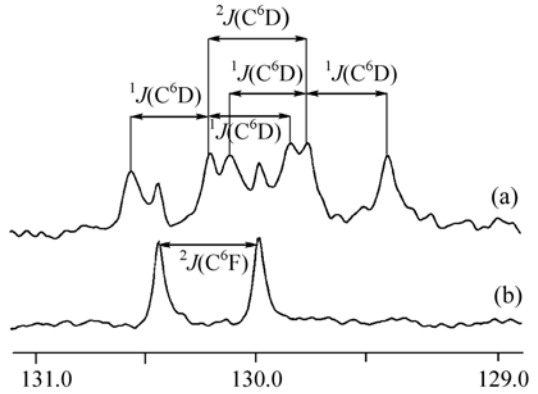



**Fig. 1.** Fragments of the $^{13}C$ NMR spectra corresponding to the $C^6$ signal of 5-fluoro-1-methyluracil obtained by methanolysis of 5-fluoro-1-methyl-2-methylpyrimidin-4(1*H*)-one (**Ib**) (a) in a mixture of methanol-$d_4$ and a 0.2 M solution of NaOD in $D_2O$ and (b) in a mixture of methanol and a 0.2 M solution of NaOH in $H_2O$. The other fragments of the spectra are identical.

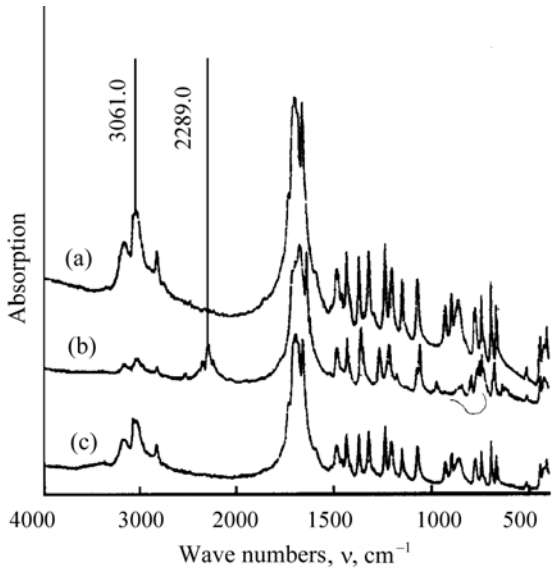



**Fig. 2.** IR spectra (KBr) of 5-fluoro-1-methyluracil obtained from 5-fluoro-1-methyl-2-methylpyrimidin-4(1*H*)-one (**Ib**) by (a) hydrolysis in 1 N hydrochloric acid, (b) methanolysis in a 0.2 M solution of NaOD in 90% $CD_3OD$, and (c) methanolysis in a 0.2 M solution of NaOH in 90% methanol.

Numerous examples of facile isotope exchange in heteroaromatic compounds, including those containing a pyrimidine ring, have been reported [2–6]. The exchange process in pyrimidinones and pyrimidinediones is favored by the presence of onium nitrogen atom [4, 5] or halogen atom (as in 5-halouracils or 5-halouridines) [6] in the vicinity of the ring carbon atom involved. Base-catalyzed H–D exchange in the 5-halo derivatives is strongly accelerated due to desolvation upon replacement of water or methanol by DMSO [6]. In our case, i.e., with a substrate which has a betaine-like structure **I** [7] but is not a true onium salt, the exchange process readily occurs in a protic medium. There are two examples of very fast H–D exchange in such pyrimidine derivatives at pD ≥ 6, namely replacement of hydrogen by deuterium at $C^5$ in 4,6-dihydroxypyrimidine and its mono-*N*-methyl derivative. However, these compounds are fairly strong acids (p$K_a$ 5.4 and 5.75, respectively), and deuterium exchange therein occurs during their tautomeric transformations involving a common anion [8].

Another even more interesting aspect of the problem under study is the lack of H–D exchange at $C^6$ in 3-methyl isomer **IIb**. The 2-H atom neighboring to the *N*-methyl group is replaced by deuterium both in 1-methyl-pyrimidin-4(1*H*)-one (**Ig**) and in isomeric 3-methyl-pyrimidin-4(3*H*)-one (**IIg**) in $D_2O$ at 90–100°C in the absence of a catalyst [4, 5]. These compounds, as well as their 5-fluoro-substituted analogs **Id** and **IId**, also undergo deuterium exchange at $C^2$ on prolong storage in $D_2O$ at room temperature.

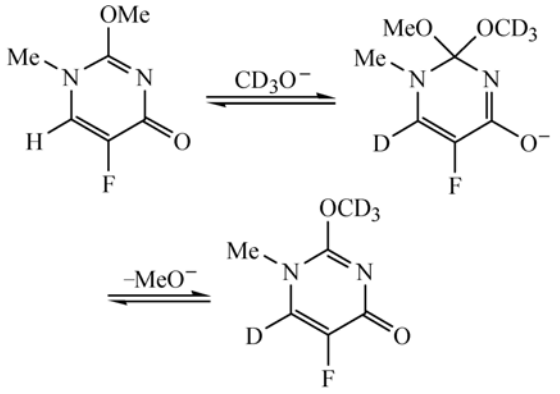
Presumably, the observed relations in H–D exchange at $C^6$ reflect most clearly differences in the reactivity of 1- and 3-methylpyrimidin-4-ones, depending on the position of the *N*-methyl group, which were discussed previously [1, 9, 10]. These relations attract interest from the viewpoint of similarity between the exchange reaction and many chemical [11] and biological [12] processes inherent to heterocycles. In additon, compounds of the 5-fluoro-1-methylpyrimidin-4-one series can be regarded as models of some *N*-glycosylated physiologically active substances [7].

In order to understand reasons for the different behaviors of isomers **Ib** and **IIb** it was necessary to elucidate whether deuterium exchange of 6-H occurs only with compound **Ib** or this is a general property of 5-fluoro-1-methylpyrimidin-4-one derivatives and how the substituent at $C^2$ affects the exchange process. Table 1 contains the rates of H–D exchange at $C^6$ in *N*-methyl derivatives of 5-fluoropyrimidin-4-one and some structurally related compounds, which were determined by $^1$H NMR spectroscopy at ~20°C. None of the compounds given in Table 1 exchanges hydrogen in the absence of a base. An exception is pyrimidinone **Ie.** In this case, a very slow H–D exchange at $C^6$ occurs due to autocatalysis by the side-chain diethylamino group. We also examined the ability of the corresponding 5-protium analogs to undergo base-catalyzed H–D exchange. In no cases, even at an alkali concentration of 0.2–0.3 M, introduction of deuterium to $C^6$ or $C^5$ was detected. We did not examine the behavior of these compounds at elevated temperature, though deuterium exchange for some derivatives becomes possible under more severe conditions. For example, replacement of 6-H (together with 2-H) by deuterium in compound **Ig** was observed in a buffer solution with pD = 11.8, $\tau_{0.5} \approx$ 113 h, 70°C [3], while its 3-methyl isomer **IIg** undergoes H–D exchange at $C^2$ (but not at $C^6$) in a 0.3 M solution of NaOD in $D_2O$ at 90°C [5]. 5-Fluoro-1-methyluracil (**IIIa**) and 5-fluorouridine exchange 6-H in 0.5 M NaOD/$D_2O$ ($\tau_{0.5} \approx$ 20 min, 60°C [13]; cf. Table 1).

Unless otherwise stated, all measurements were performed in methanol-$d_4$ after addition of NaOH in $D_2O$. This medium contained 90% of methanol-$d_4$, and the catalytic species was strongly nucleophilic trideuteromethoxide ion ($CD_3O^-$). This follows from the fact that H–D exchange at $C^6$ in compound **Ic** is accompanied by replacement of the methoxy group on $C^2$ by $CD_3O$ (Scheme 2).

The rates of the based-catalyzed reactions were estimated by the pseudofirst-order rate constants $k_{ap}$ ($s^{-1}$) and catalytic constants $k_{cat} = k_{ap}/c(OH^-)$ ($l\ mol^{-1}\ s^{-1}$) which were calculated from the initial concentrations of the base. The progress of the reaction was monitored following the disappearance of

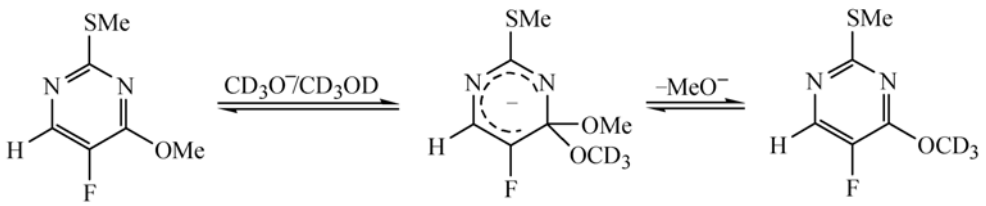
**Scheme 2.**




the doublet signal from 6-H in the $^1$H NMR spectrum and the transformation of the $C^6$ signal from doublet to doublet of triplets, the other signals retaining their position and multiplicity. The rate of H–D exchange was determined from the decrease in the intentsity of the 6-H signal relative to signals of the other groups and DSS signal (internal reference). Under conditions of base catalysis, compounds containing a methylsulfanyl or methoxy group in position *2* can undergo methoxylation followed by transformation into the corresponding uracils [1]. These processes were monitored by NMR spectroscopy, but their rate was negligible as compared to the rate of deuterium exchange.

As follows from the data in Table 1, appreciable exchange of 6-H is possible only under base catalysis. The rate of exchange in $D_2O$ increases in the presence of 20% of DMSO. All the examined 5-fluoro-1-methylpyrimidin-4-ones **I** were found to undergo H–D exchange, whereas isomeric 5-fluoro-3-methylpyrimidin-4-ones **II** were not. With respect to the substituent on $C^2$, the rate of H–D exchange decreases in the series H, SMe > OMe >> NHBu. Strong deceleration of the process in going to the 2-butylamino derivative may be due to ionization of the exocyclic amino group in basic medium. No H–D exchange at $C^6$ was observed for compounds with an aromatic character of the heteroring. In the $^1$H NMR spectra of 5-fluoro-4-methoxy-2-methylsulfanylpyrimidine (**IVa**) we observed slow decrease in intensity (by 95% in

**Scheme 3.**




**IVa** **IVb**

**Table 1.** Hydrogen–deuterium exchange at $C^6$ in 1-methyl- and 3-methylpyrimidin-4-one derivatives and related compounds in a solution of NaOD in $CD_3OD$–$D_2O$ (9 : 1) at (20 ± 1)°C and enthalpies of dissociation $\Delta_d H^0(0)$ (kcal/mol) of the $C^6$–H bond, calculated by the PM3 semiempirical method

| Compd. no. | Pyrimidine concentration, M | *c*(NaOD), M | $k_{ap}\times10^4$, $s^{-1}$ | $k_{cat}\times10^2$,[a] $l\ mol^{-1}\ s^{-1}$ | $\Delta_d H^0(0)$, kcal/mol |
|---|---|---|---|---|---|
| **Ia** | 0.11 | 0.22 | No exchange[b] | | 344.01 |
| **Ib** | 0.08 | 0.013 | 26.0 | 20.0 | 338.67 |
| | 0.08 | 0.025 | 44.0 | 18.0 | |
| | 0.08 | 0.037 | 75.8 | 20.5 | |
| | 0.03 | 0.250 | [c] | [c] | |
| | 0.15 | 0.330 | [c] | [c] | |
| | 0.07 | 0.014[d] | 68.0 | 48.6 | |
| | 0.30 | 0.33[e] | 0.33 | – | |
| **Ic** | 0.07 | 0.013 | 3.40 | 2.6 | 341.02 |
| | 0.07 0.07 | 0.024 0.043 | 7.00 14.00 | 2.9 3.2 | |
| | 0.07 | 0.200 | [f] | – | |
| **Id** | 0.073 | 0.013 | 54.5 | 42.0 | 341.84 |
| **Ie**[g] | 0.20 | 0 | – | – | – |
| **If** | 0.010 | 0.093 | 2.4 | 0.25 | – |
| **Ig** | – | – | No exchange[b, h] | | 347.77 |
| **IIb** | 0.1 | 0.36 | No exchange[b,i] | | 353.06 |
| **IIc** | 0.1 | 0.36 | No exchange[b] | | – |
| **IId** | 0.090 | 0.013 | No exchange[b] | | 356.67 |
| **IIf** | 0.014 | 0.093 | No exchange[b,j] | | – |
| **IIg** | – | – | No exchange[b] | | 363.05 |
| **IIIa** | 0.15 | 0.33 | No exchange[b] | | – |
| **IIIb** | 0.10 | 0.36 | No exchange[b] | | – |
| **IIIc** | 0.11 | 0.013 | 5.0 | 3.9 | 339.52 |
| | 0.11 | 0.024 | 8.9 | 3.8 | |
| **IIId** | – | 0.08[k] | 10[m] | | 336.90 |
| **IIIe** | – | 0.08[k] | 30[m] | | 342.07 |
| **IIIf** | – | 0.08[k] | 60[m] | | 344.97 |
| **IVa** | 0.125 | 0.23 | No exchange[b,m] | | – |

[a] $k_{cat} = k_{ap}/c$(NaOD).
[b] No exchange was observed over a period of several hours or tens hours.
[c] The rate of exchange was too high to be measured.
[d] In a solution of NaOD in DMSO-$d_6$–$D_2O$ (1 : 5).
[e] In a solution of $Et_3N$ in $D_2O$.
[f] $\tau_{0.5} \le 16$ s.
[g] In a $CD_3OD$–$D_2O$ mixture (9:1) in the absence of a base, 80% of 6-H was replaced by deuterium in 90 days, and 50% of 2-methoxy derivative **Ic** was formed [1].
[h] In a buffer solution with pD = 11.2 at 70°C, $k_{ap} \approx 1.6 \times 10^{-6}\ s^{-1}$ [3].
[i] The resulting 2-methoxy derivative **IIb** (R = $OCH_3$) [1] contained no deuterium.
[j] No exchange of 6-H was observed in a 0.3 M solution of NaOD in $D_2O$ at 90°C [5].
[k] In a solution of NaOD in DMSO-$d_6$.
[l] $\tau_{0.5}$ (s) at 38°C (data of [6]).
[m] Only replacement of the 4-methoxy group by $CD_3O$ was observed (94% in 7 h).

7 h) only of the methoxy group signal (δ 4.06 ppm), while the other signals (including that from 6-H) did not change their position and intensity and the signal from methanol increased in intensity. These data suggest replacement of the 4-methoxy group by $CD_3O$ (with formation of compound **IVb**) under conditions of base catalysis, as shown in Scheme 3.

Unlike 1- and 3-methyl-5-fluorouracils which give rise to an appreciable amount of the corresponding anions under the H–D exchange conditions, 5-fluoro-1,3-dimethyluracil (**IIIc**) exchanges 6-H by deuterium fairly readily, though the exchange rate is considerably lower than in 5-fluoro-1-methylpyrimidin-4-ones **Ib** and **Ie**. These data indicate that the absence of deuterium exchange of 6-H in 5-fluoro-3-methyl isomers **II** cannot be explained in terms of spatial arrangement of the *N*-methyl group with respect to the $C^6$ atom.

Assuming that H–D exchange in the series of 5-fluoro derivatives **I** involves formation of partially saturated intermediate **A** which then eliminates $CD_3OH$ molecule, there are no factors preventing formation of an analogous intermediate from isomers **II**. Moreover, anchimeric effect of the methyl group, which hinders the exchange process, could be expected just for 1-methyl isomers **I**. Cushley *et al*. [13] previously proposed a mechanism for H–D exchange at $C^6$ in 5-fluorouracil derivatives, which involved addition at the $C^5$–$C^6$ bond. This mechanism was later ruled out [6]. An alternative path of the exchange includes direct deprotonation at $C^6$ by the action of a base to give intermediate anion; however, in this case isomers **I** and **II** should be characterized by different kinetic or thermodynamic acidities. Although quasi-*p*-quinoid isomers **I** are contributed mainly by the zwitterionic structure while the contribution of ionic structure to quasi-*o*-quinoid isomers **II** is equal to zero (due to small volume of the $\Psi_1$ molecular orbital) [7], different CH acidities of isomers **I** and **II** do not directly follow from their structure. According to the NMR data, the shielding parameters of $C^6$ and 6-H in isomers **I** and **II** are very similar (Table 2). The gas-phase enthalpies of dissociation of the $C^6$–H bond ($\Delta_d H^0$) at 0 K, calculated by the PM3 method with no regard to effect of the medium (Table 1), indicate that proton abstraction from $C^6$ in compounds **I** requires a smaller energy (by about ~15 kcal/mol) as compared to structures **II**. Within the series of compounds with the same structure (**I** or **II**), the presence of a fluorine atom in position *5* gives an energy gain (in the $C^6$–H bond dissociation energy) of 5.4–6.4 kcal/mol (see Table 1). The

**Table 2.** Chemical shifts of $C^6$ in the $^{13}C$ NMR spectra of 1- and 3-methyl-5-fluoropyrimidin-4-ones **I** and **II** and 1-methylpyrimidin-4-one[a]

| Substituent at $C^2$ | Solvent | $\delta_C{}^6$, ppm | | |
|---|---|---|---|---|
| | | **I** | **II** | 1-methylpyrimidin-4-(1*H*)-ones |
| H | $D_20$ | 131.3 | 136.9 | 146.5 |
| | $CD_3OD$ | 131.3 | 137.3 | 146.4 |
| | DMCO-$d_6$ | 129.1 | 136.5 | 143.8 |
| MeS | $CD_3OD$ | 133.3 | 136.7 | 147.1 |
| | DMCO-$d_6$ | 131.2 | 135.0 | 145.7 |
| BuNH | DMCO-$d_6$ | 128.6 | 136.8 | 144.1 |
| MeO | DMCO-$d_6$ | 129.3 | 134.1 | – |
| | $CDC1_3$ | 127.2 | 133.65 | – |
| | $CD_3OD$ | – | – | 147.3 |

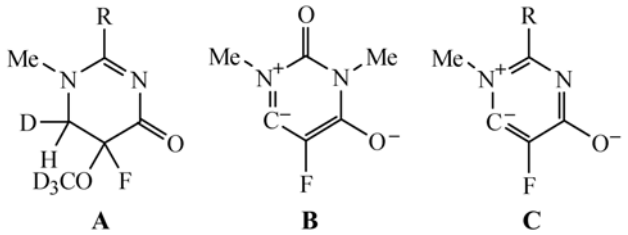
[a] The difference in the chemical shifts δ of 6-H in 5-fluoro derivatives of 1-methyl and 3-methyl isomers is +(0.02–0.11) ppm, and for the 5-protium analogs, –(0.13–0.45) ppm [7].

enthalpies of dissociation of the $C^6$–H bond in 1,3-dimethyluracils having acceptor substituents in position *5* show a satisfactory correlation with the rates of base-catalyzed H–D exchange at $C^6$ in DMSO-$d_6$:

$$\ln k = 71.8 - 0.22\,\Delta_d H^0(0)\ (\text{kcal/mol});\ r = 0.999.$$

Obviously, the ease of isotope exchange in 5-fluoro-1-methylpyrimidin-4-ones **I,** in contrast to their 3-methyl isomers **II**, is explained primarily by their different structure in the initial state, which becomes crucial at the exchange moment.

In keeping with the mechanism proposed for H–D exchange at $C^6$ in 5-halouridines [6], the reaction with 5-fluoro-1,3-dimethyluracil (**IIIc**) involves proton abstraction from $C^6$ with formation of intermediate anion **B** which is stabilized due to electron-withdrawing effect of the neighboring positively charged nitrogen atom.




The H–D exchange at $C^6$ in 5-fluoro-1-methylpyrimidin-4-ones **I** may occur through intermediate carbanion **C** whose formation requires no additional energy for charge separation. Anion **C** is stabilized by the positive charge on the nitrogen atom, as well as by resonance

delocalization of electron density on the reaction center. The presence of a fluorine atom in position *5* provides an additional stabilizing effect. According to the $^{13}C$ NMR data, deshielding effect ($\Delta\delta_C$) of fluorine atom in position *5* of 1- and 3-methylpyrimidin-4-ones on $C^5$ is equal to 36 ppm, while the $C^6$ atom is shielded by 15–18 ppm [7]; these values are very consistent with the chemical shifts of carbon nuclei in vinyl fluoride which may be regarded as a model of the $FC^5C^6$ fragment in pyrimidin-4-ones **I**. The corresponding $\Delta\delta_C$ values for vinyl fluoride are 25 and –59.2 ppm (relative to ethylene) [14]. There are no factors favoring "internal" stabilization of intermediate anion derived from 5-fluoro-3-methylpyrimidin-4-ones **II**; here, the thermodynamic barrier is the main reason for the absence of H–D exchange at $C^6$. This barrier (~15 kcal/mol) is so high that solvation of the neutral molecule and/or carbanion cannot reduce it to a sufficient extent. A different pattern is observed with 5-bromo- (**IIId**) and 5-methoxy-1,3-dimethyluracils (**IIIe**) for which the $\Delta\Delta_dH^0(0)$ values relative to 5-unsubstituted 1,3-dimethyluracil (**IIIf**) are –8 and –3 kcal/mol, respectively. All these compounds readily exchange 6-H by deuterium in DMSO-$d_6$ in the presence of NaOD [6]. 1-Methyl derivatives **Id** and **Ig** are characterized by a $\Delta\Delta_dH^0(0)$ value of –5.93 kcal/mol, and the half-conversion period $\tau_{0.5}$ (corresponding to replacement of 50% of 6-H by D) in 90% methanol-$d_4$ in a buffer solution with pD ≈11.8 is 2 min at 21°C (**Id**) and 113 h at 70°C (**Ig**) [3]. Kurinovich and Lee [15] showed a leveling effect of solvation on the calculated enthalpies of protolytic dissociation of the $N^1$–H and $N^3$–H bonds in uracil, which attained 8 kcal/mol in going from an inert solvent to aqueous medium. For 5-fluoro-1-methylpyrimidin-4-ones **I**, the calculated values of $\Delta\Delta_dH^0(0) = \Delta_dH^0(0)$(**Ib** or **Ic**) – $\Delta_dH^0(0)$(**Id**) are –3.2 and –0.8 kcal/mol, respectively, though the rates of H–D exchange in 90% methanol-$d_4$ differ by factors of 2 and 15 (Table 1). The observed inversion may be interpreted in terms of different effects of solvation of the neutral molecules and/or carbanions derived therefrom.

## EXPERIMENTAL

The $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker DPX-300 spectrometer at 300 and 75.47 MHz, respectively. Samples were examined as 0.01–0.030 M solutions which were placed in 5-mm NMR ampules (while recording the $^{13}C$ NMR spectra from dilute solutions, the number of scans attained 6000–7000). The chemical shifts (ppm) and signal intensities were measured relative to DSS. The IR spectra were measured on a Bruker IFS-88 spectrometer in KBr.

The kinetic experiments were performed in NMR ampules. A sample was dissolved in a required volume of methanol-$d_4$, and the initial spectrum was recorded relative to DSS. A solution of NaOD in $D_2O$ was then added (it was prepared in such a way that the resulting solution contained 90% of methanol-$d_4$). A concentrated (2.5 M) solution of NaOD was prepared by dissolution of metallic sodium in $D_2O$, and its concentration was determined by titration. After addition of NaOD solution, the ampule was shaken, and this moment was taken as initial (the time elapsed from the moment of addition of the base to recording of the first spectrum did not exceed 1 min). The rate of H–D exchange was determined from the decrease in the 6-H signal intensity, taking into account the intensities of signals from unexchangeable protons. The rate constants were determined by the graphical method from the semilog plots of the intensity ratio between the 6-H and DSS signals versus time. The site of H–D exchange was checked each time by the $^{13}C$ NMR spectra: replacement of 6-H by D was accompanied by conversion of the doublet $C^6$ signal into a doublet of triplets, while the other carbon signals did not change their position and multiplicity.

The enthalpies of dissociation of the $C^6$–H bond in pyrimidine derivatives $\Delta_dH^0(0)$ were calculated (according to the Hess law) as the heat effect of the reaction $AH \rightarrow A^- + H^+$ using the equation $\Delta_dH^0(0) = \Delta_dH^0(0)(A^-) + \Delta_dH^0(0)(H^+) - \Delta_dH^0(0)$ (AH), where $\Delta_dH^0(0)$(AH), $\Delta_dH^0(0)(A^-)$, and $\Delta_dH^0(0)(H^+)$ are the standard gas-phase enthalpies of formation (at 0 K) of the corresponding pyrimidin-4-one derivatives, their anions, and a proton, which were calculated by the PM3 semiempirical method with the aid of GAMESS software package [16]; $\Delta_dH^0(0)$ $(H^+) = 353.58$ kcal/mol.

The procedures for the preparation of compounds used in this work and their properties were reported in [1, 7]. A sample of 5-fluoro-1,3-dimethyluracil, mp 131–134°C [17], was kindly provided by E.P. Studentsov.

**5-Fluoro-1-methyluracil.** 5-Fluoro-1-methyl-2-methylsulfanylpyrimidin-4(1*H*)-one (**Ib**), 0.11 mmol, was dissolved in 5.8 ml of 90% methanol containing 0.22 mmol of sodium hydroxide, and the mixture was left to stand for 5 days at room temperature. The mixture was then neutralized with hydrochloric acid (without separation of crystal), the precipitate was filtered off, and the filtrate was evaporated to obtain an additional amount of the product. Overall yield 90%. The product was purified by recrystallization from water. mp 261°C; published data [18]:

mp 263–264°C. UV spectrum, $\lambda_{max}$ (log ε): 0.1 N HCl: 274 (3.92); 0.1 N NaOH: 271 (3.80).

**[6-$^2$H]-5-Fluoro-1-methyluracil** was synthesized by a similar procedure using methanol-$d_4$ and NaOD in $D_2O$.

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