Journal of Molecular Structure 923 (2009) 19–23

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

Synthesis and structural characterization of the C-6 fluoroalkylated pyrimidine derivatives

Svjetlana Krištafor [a], Tatjana Gazivoda [a], Mario Cetina [b], Damjan Makuc [c], Janez Plavec [c], Silvana Raić-Malić [a,*]

[a] Department of Organic Chemistry, Faculty of Chemical Engineering and Technology, University of Zagreb, Marulićev trg 20, P.O. Box 177, HR-10000 Zagreb, Croatia
[b] Department of Applied Chemistry, Faculty of Textile Technology, University of Zagreb, Prilaz baruna Filipovića 28a, HR-10000 Zagreb, Croatia
[c] Slovenian NMR Centre, National Institute of Chemistry, Hajdrihova 19, SI-1000 Ljubljana, Slovenia

ARTICLE INFO

Article history:
Received 20 October 2008
Received in revised form 8 December 2008
Accepted 12 December 2008
Available online 25 December 2008

Keywords:
C-6 fluoroalkylated pyrimidines
X-ray crystal structure analysis
π···π interactions

ABSTRACT

C-6 substituted fluoroalkenyl 2,4-dimethoxypyrimidine derivative (**4**) was synthesized by lithiation of 2,4-dimethoxy-6-methylpyrimidine (**3**) and subsequent reaction of thus obtained organolithium intermediate with ethyl pentafluoropropionate. The novel 2,4-pyrimidinedione containing 3,3,4,4,4-pentafluoro-1-butenyl side chain (**5**) was prepared by demethoxylation of **4** using sodium iodide and chlorotrimethylsilane. The structures of **4** and **5** were confirmed by ^{1}H, ^{13}C and ^{19}F NMR spectra, as well as IR spectra. The structure of **4** was also unambiguously confirmed by X-ray crystal structure analysis. The molecules of **4** are weakly linked by aromatic π···π stacking interactions into infinite chains parallel to the *a* axis.

© 2009 Elsevier B.V. All rights reserved.

1. Introduction

Fluorine containing compounds are widely used in the synthesis of pharmaceuticals due to their favourable chemical and biological properties such as solubility and bioavailability, they enhance the lipophilicity and thus increase the rate of cell penetration and transport of drug to an active site [1]. The excellent biological activities exhibited by 6-substituted uracil derivatives provide a new emphasis to explore the chemistry and biological activities of these pyrimidine derivatives [2–7]. A large number of acyclic nucleoside analogues showed antiviral activities against herpes viruses due to their selective and efficient activation through monophosphorylation by the viral enzyme in the intact cells [8,9]. Therefore, radiolabeling of these antiviral agents with the positron-emitting isotope ^{18}F allows in non-invasive imaging of the viral thymidine kinase (TK) enzyme activity by means of positron-emission tomography (PET) [10,11]. Besides, the PET technique has proven to be vital in early detection of cancer and monitoring the efficacy of chemo- or radiotherapy response [12,13]. Furthermore, we have reported that ^{18}F-radiolabeled C-6 acyclic pyrimidine nucleosides can be suitable candidates for the development of non-toxic PET-tracer molecules that are specifically and efficiently phosphorylated by the herpes simplex virus type 1 TK [10,11].

In this paper, we report the synthesis and structural study of C-6 3,3,4,4,4-pentafluoro-2-hydroxy-1-butenyl substituted 2,4-dimethoxypyrimidine (**4**) and 2,4-pyrimidinedione (**5**).

2. Experimental

Melting points were determined on a Kofler micro hot-stage apparatus (Reichert, Wien) and are uncorrected. The electron impact mass spectra were recorded with an EXTREL FT MS 2002 instrument with ionizing energy of 70 eV. ^{1}H and ^{13}C NMR 1D and 2D spectra were recorded on a Bruker Avance 600 MHz NMR spectrometer, operating at 150.92 MHz for the ^{13}C resonance, and Varian Unity Inova 300 MHz NMR spectrometer. The samples of **4** and **5** were dissolved in CD_3OD and DMSO-d_6, respectively, and measured in 5 mm NMR tubes. The ^{1}H, ^{13}C and ^{19}F NMR chemical shift values (δ) are expressed in ppm and coupling constants (J) in Hz. Proton and carbon chemical shifts are referred to TMS, whereas fluorine chemical shifts are given with respect to CCl_3F. The sample temperature was set at 298 K and controlled to approximately ±0.5 K. ^{1}H NMR measurements were performed under the following spectral and processing conditions: 4.0 kHz sweep width, 90° pulse (11 μs), 2 s relaxation delay, 32 K time domain, zero filling to 64 K and line broadening of 0.5 Hz. *2D NMR spectra*: NOESY: 4096 ($\omega 2$) × 256 ($\omega 1$) data points, 16 scans per FID, 32 dummy scans, a pulse delay of 2 s, with mixing time of 150 ms, 4.0 kHz ($\omega 2$) × 4.0 kHz ($\omega 1$) spectral width, transformed after multiplication with a sine-bell squared filter shifted by π/2

* Corresponding author. Tel.: +385 1 45 97 213; fax: +385 1 45 97 224.
E-mail address: sraic@fkit.hr (S. Raić-Malić).

0022-2860/$ - see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.molstruc.2008.12.037

in both $\omega 2$ and $\omega 1$ to give 4 K × 1 K matrix. The infrared spectra were recorded by a Fourier transform infrared (FTIR) spectrometer Bruker Vertex 70 equipped with an attenuated total reflection (ATR) accessory with a diamond crystal. Sixteen scans were collected for each measurement over the spectral range of 400–4000 cm^{-1} with resolution of 4 cm^{-1}. Precoated Merck Silica Gel 60F-254 plates were used for thin layer chromatography (TLC) and the spots were detected under UV light (254 nm). Column chromatography (CLC) was performed using silica gel (0.063–0.2 mm) Fluka; glass column was slurry-packed under gravity. Compounds purity was analyzed by HPLC with DAD detector.

2.1. Synthesis

2,4-Dichloro-6-methylpyrimidine (**2**) and 2,4-dimethoxy-6-methylpyrimidine (**3**) were synthesized using an analogous procedures given in the literature [10].

The novel fluoroalkenyl substituted pyrimidine derivative containing free 2,4-diketo functionalities (**5**) was prepared by treatment of **4** with sodium iodide and chlorotrimethylsilane. In comparison with other synthetic methods used for hydrolysis of 2,4-dimethoxy groups, such as acetyl chloride and water or 35% aqueous hydrochloric acid, applied method gave compound **5** in higher yield [7] (Scheme 1).

2.1.1. 6-(3,3,4,4,4-Pentafluoro-2-hydroxy-1-butenyl)-2,4-dimethoxypyrimidine (**4**) [7]

The solution of 2,4-dimethoxy-6-methylpyrimidine (**3**) (300 mg, 1.95 mmol) in THF (5 mL) was cooled at −70 °C and lithium diisopropylamide (2.1 mL, 2 M in THF/heptane/ethyl benzene) was added. After the reaction mixture was stirred for 30 min at −55 °C ethyl pentafluoropropionate (0.35 mL, 2.34 mmol) was added. Mixture was additionally stirred for 3 h and neutralized with glacial acetic acid. The solvent was evaporated and the residual oily product was extracted with CH_2Cl_2 and water. The organic layer was dried over Na_2SO_4 and purified by silica gel column chromatography using petroleum ether:EtOAc = 5:1 as eluent to give compound **4** as yellow solid (424 mg, 72.5%, m.p. = 58–60 °C).

2.1.2. 6-(3,3,4,4,4-Pentafluoro-2-hydroxy-1-butenyl)-2,4-pyrimidinedione (**5**)

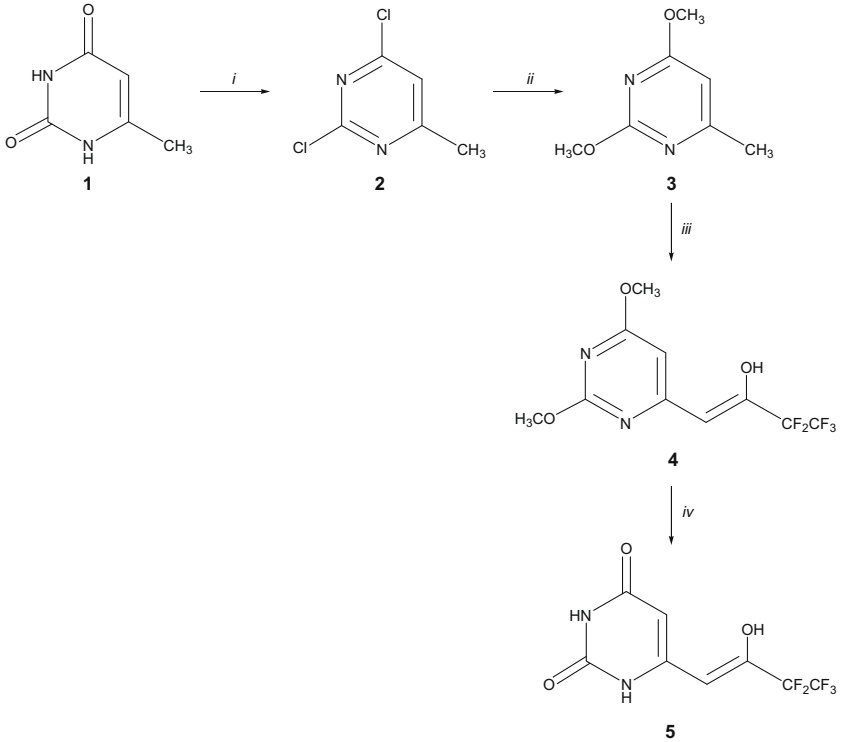
A mixture of **4** (0.1 g, 0.33 mmol), Me_3SiCl (0.15 mL, 1.16 mmol), and NaI (0.17 g, 1.16 mmol) in dry MeCN (7 mL) was stirred at room temperature for 18 h and then at 60 °C for 3 h, under argon atmosphere. The solvent was evaporated under reduced pressure, and the residue was chromatographed using CH_2Cl_2:MeOH = 15:1 as eluent to give crystalline compound **5** (60 mg, 66.6%, m.p. = 278–281 °C).

MS *m/z* 273.02 $[MH]^+$. Anal. Found: C, 35.23; H, 1.85; N, 10.26; Calcd for $[C_8H_5F_5N_2O_3]$: C, 35.31; H, 1.85; N, 10.29.

2.2. Crystal structure determination

Single crystal of **4** suitable for X-ray single crystal analysis was obtained at room temperature by partial evaporation from the CH_2Cl_2/*n*-hexane solution (1:1). The intensities were collected at 295 K on a Oxford Diffraction Xcalibur2 diffractometer with a Sapphire 3 CCD detector using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The data collection and reduction were carried out with the *CrysAlis* programs [14]. The *SHELXS97* and *SHELXL97* [15] programs were used for structure solution and refinement. The *PLATON* [16] program was used for structure analysis and molecular and crystal structure drawings preparation.

The crystal structure was solved by direct methods. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares calculations based on F^2. The hydroxyl hydrogen atom H3 was found in a difference Fourier map and its coordinates and isotropic thermal parameter have been refined freely. The O3−H3 bond amounts 1.17(6) Å, as a result of an involvement of



1 **2** **3** **4** **5**

Scheme 1. Reagents and conditions: (i) $POCl_3$; (ii) Na/MeOH; (iii) LDA, THF, ethyl pentafluoropropionate; (iv) NaI, Me_3SiCl, MeCN.

hydroxyl hydrogen atom in intramolecular hydrogen bond (see Section 3). All other hydrogen atoms were included in calculated positions as riding atoms, with *SHELXL97* [15] defaults. Details of crystal data, data collection and refinement parameters are given in Table 1. CCDC 685948 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

3. Results and discussion

3.1. Antitumoral activity

Fluoroalkylated pyrimidine derivatives **4** [7] and **5** were evaluated for their activity against human carcinoma cell lines. Comparison of cytostatic activities of **4** and **5** against acute lymphoblastic leukemia (Molt-4), colon carcinoma (HCT 116 and SW 620), breast carcinoma (MCF-7) and lung carcinoma (H 460) cell lines showed that demethoxylation caused the absence of inhibitory effect of novel 2,4-pyrimidinedione derivative **5**. While compound **4** showed moderate activity against cell lines (IC_{50} = 43–76 μM), its demethoxylated structural congener showed no activity (IC_{50} > 100 μM).

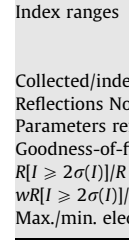
3.2. NMR and IR spectra of *4* and *5*

The structures of **4** [7] and **5** have been confirmed by ^{1}H, ^{13}C and ^{19}F NMR spectra (Table 2). The analysis of the spectra was performed on the basis of the chemical shift, signal multiplicity and magnitude of C–F coupling.^{19}F NMR resonances were well resolved (Table 2). ^{1}H decoupled ^{13}C NMR showed C–F coupling constants that enables straightforward identification of fluorinated carbon atoms and their neighbours. Namely, CF_2 group displayed triplet of quartets due to the coupling with three neighbouring fluorine atoms, while CF_3 group displayed quartet

Table 1
Crystal data and summary of data collection and refinement for **4.**

Formula	$C_{10}H_9F_5N_2O_3$
Formula weight	300.19
Crystal size [mm]	0.10 × 0.16 × 0.71
Crystal colour	Colourless
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	
a [Å]	6.9062 (4)
b [Å]	23.5039 (11)
c [Å]	9.6244 (5)
β [°]	126.763 (6)
V [Å^3]	1251.55 (11)
Z	4
$D_{calc.}$ [g cm^{-3}]	1.593
μ [mm^{-1}]	0.165
F(000)	608
Scan-mode	ω
θ range [°]	4.07–26.99
Index ranges	$-7 \leqslant h \leqslant 8$
	$-25 \leqslant k \leqslant 30$
	$-12 \leqslant l \leqslant 9$
Collected/independent reflections No.	8914/2707
Reflections No. [$I \geqslant 2\sigma(I)$]/$R_{int.}$	1321/0.0684
Parameters refined	187
Goodness-of-fit on F^2	0.922
$R[I \geqslant 2\sigma(I)]/R$ [all data]	0.0489/0.1083
$wR[I \geqslant 2\sigma(I)]/wR$ [all data]	0.1274/0.1601
Max./min. electron density [e^{-3}]	0.253/−0.242

Table 2
^{1}H NMR, ^{13}C NMR, ^{19}F NMR and IR spectra of **4** and **5.**

Compound	^{1}H NMR[a] δ (ppm)	^{19}F NMR δ (ppm)	^{13}C NMR δ (ppm), J (Hz)	IR ν (cm^{-1})
 **4**	6.47 (1H, s, H-1′) 6.32 (1H, s, H-5) 4.07 (3H, s, OCH_3) 4.01 (3H, s, OCH_3)	−81.19 (s, CF_3) −120.37 (s, CF_2)	173.71 (C-4) 163.59 (C-6) 162.71 (C-2) 96.15 (C-5) 103.20 (C-1′) 167.63 (td, $^{2}J_{CF}$ = 19.7; $^{3}J_{CF}$ = 1.2 Hz, C-2′) 110.49 (tq, $^{1}J_{CF}$ = 257.1; $^{2}J_{CF}$ = 37.9 Hz, CF_2CF_3) 120.27 (qt, $^{1}J_{CF}$ = 286.2; $^{2}J_{CF}$ = 37.1 Hz, CF_2CF_3) 164.99 (C-4) 155.68 (C-6) 151.68 (C-2) 87.17 (C-5)	O—H stretch: 2959, 2923, 2854 C=C and C—H ring stretch: 1600, 1567, 1380, 1326 C=C—H rock: 1486, 1469 C=C—H bend: 746–938 C—O—C stretch: asymm 1191, 1139–1013, symm 1096 C—F stretch: 571–680
5	10.12 (1H, s, NH) 12.29 (1H, s, NH) 4.91 (1H, s, H-1′) 4.77 (1H, s, H-5)	−81.29 (s, CF_3) −120.53 (s, CF_2)	82.96 (C-1′) 165.17 (td, $^{2}J_{CF}$ = 20.6; $^{3}J_{CF}$ = 0.8 Hz, C-2′) 109.38 (tq, $^{1}J_{CF}$ = 261.3; $^{2}J_{CF}$ = 33.2 Hz, CF_2CF_3) 119.5 (qt, $^{1}J_{CF}$ = 287.1; $^{2}J_{CF}$ = 37.7 Hz, CF_2CF_3)	N—H and O—H stretch: 3391–3014 C=O stretch: 1668 C=C and C—H ring stretch: 1601, 1539, 1395, 1324 C=C—H rock: 1443 C=C—H bend: 807–1005 1155–1033 and 680 C—F stretch: 754

[a] ^{1}H NMR chemical shifts for compound **4** are given in the literature [7].

of triplets due to the long-range coupling constants with two fluorine atoms. One-bond and two-bond C–F coupling values are in agreement with those found for related fluorinated compounds [17].

Although fluoroalkenyl substituted pyrimidine derivatives **4** and **5** are structurally alike, the demethoxylation of **4** caused significant shielding of pyrimidine ring carbon atoms ($\Delta\delta$ values were between 9 and 11 ppm). The most pronounced shielding was observed for C1′, where $\Delta\delta$ exceeds 20 ppm (Table 2). Related upfield chemical shift changes were observed for H5 and H1′ protons.

The configuration along C1′=C2′ double bond in **5** was evaluated through $^3J_{C3'H1'}$ coupling constant. Its small value of 1.4 Hz is in agreement with *Z*-configuration along C1′=C2′ double bond. The conformational properties of **5** were assessed also by 1D difference NOE experiments. Unfortunately proton signals were overlapped and therefore enhancements could not be quantified unequivocally.

Besides characteristic bands that can be ascribed to pyrimidine moiety [18], the IR spectrum of **4** showed bands at 1191 and 1096 cm^{-1} arising from asymmetric C–O–C stretching and symmetric C–O–C stretching vibrations, respectively. On the contrary to this, strong band at 1668 cm^{-1} in the spectrum of **5** is caused by C=O stretching vibration. Besides, the frequencies at 1155–1050 and 680–750 cm^{-1} can be associated with C–F stretching vibrations, which are typical for the fluorinated pyrimidines [17].

3.3. X-ray crystal structure of *4*

The compound **4** (Fig. 1) crystallized in monoclinic space group $P2_1/c$. In **4**, two methoxy groups are bonded to pyrimidine ring atoms C-2 and C-4, and a 2-hydroxy-3,3,4,4,4-pentafluoro-1-butenyl moiety is bonded to the pyrimidine ring atom C-6. The bond lengths and angles of 2,4-dimethoxypyrimidine (Table 3) agree well with the equivalent ones in similar structures [19]. The molecule is essentially planar, with the exception of the F1 and F2 atoms, and terminal trifluoromethyl group. The dihedral angle between the mean plane defined by the C9/C10/O3/C11 atoms and the mean plane of the pyrimidine ring is 0.8(2)°. Both methoxy groups in three closely related structures [19] adopt a *synperiplanar* conformation with respect to the N1 and N3 atoms of the pyrimidine ring, whereas in **4**, the C7 atom with respect to the N1 atom adopts an *antiperiplanar* conformation (Table 3). Furthermore, the F1 atom is *antiperiplanar* with respect to the hydroxyl oxygen atom O3, and F3 and F4 atoms are *synclinal* with respect to the fluorine atom F1. The bond lengths in 3,3,4,4,4-pentafluoro-1-butenyl moiety are within the expected values [20–22]. The hydroxyl hydrogen atom is directed towards the N1 atom of pyrimidine ring (Fig. 1), thus forming intramolecular hydrogen bond [O3···N1 = 2.567(2) Å; O3-H···N1 = 152(5)°] and six-membered ring which can be described by graph-set notation as *S*(6) [23]. Besides, the hydrogen H9 atom participates in intramolecular C–H···F interaction, so forming *S*(5) ring [C9···F1 = 2.713(3) Å; C9–H···F1 = 102°].

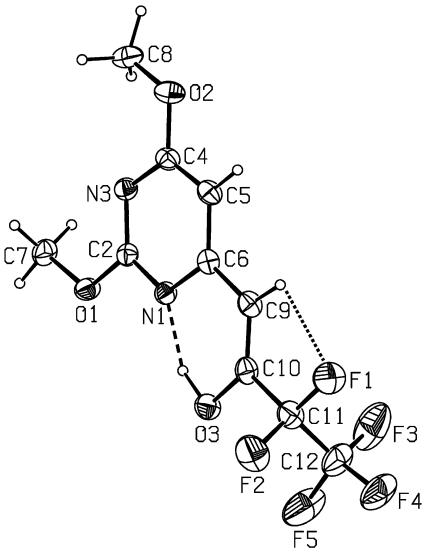


Fig. 1. A molecular structure of **4**, with the atom-numbering scheme. Displacement ellipsoids for non-hydrogen atoms are drawn at the 20% probability level.

Table 3
Selected bond lengths (Å), bond and torsion angles (°) for **4.**

Bond lengths		Bond and torsion angles	
N1–C2	1.330(3)	N1–C2–N3	126.4(2)
C2–N3	1.319(3)	N1–C2–O1	113.30(19)
C2–O1	1.326(3)	C2–O1–C7	117.65(19)
O1–C7	1.441(3)	O1–C2–N3	120.3(2)
N3–C4	1.323(3)	C2–N3–C4	115.6(2)
C4–O2	1.341(3)	N3–C4–O2	118.7(2)
O2–C8	1.437(3)	C4–O2–C8	118.1(2)
C4–C5	1.381(3)	O2–C4–C5	117.4(2)
C5–C6	1.381(3)	N3–C4–C5	123.9(2)
C6–N1	1.363(3)	C4–C5–C6	116.7(2)
C6–C9	1.439(3)	C5–C6–C9	123.7(2)
C9–C10	1.343(4)	C9–C6–N1	116.3(2)
O3–C10	1.319(3)	C5–C6–N1	120.0(2)
F1–C11	1.353(3)	C6–N1–C2	117.4(2)
F2–C11	1.342(3)	C7–O1–C2–N1	178.40(19)
F3–C12	1.300(5)	C8–O2–C4–N3	1.4(3)
F4–C12	1.313(4)	O3–C10–C11–F1	178.1(2)
F5–C12	1.315(4)	O3–C10–C11–F2	61.2(3)
		F1–C11–C12–F3	71.5(3)
		F1–C11–C12–F4	−50.2(4)
		F1–C11–C12–F5	−168.1(3)

The molecules of **4** are aligned along the *b* axis and are mutually parallel (Fig. 2). The 3,3,4,4,4-pentafluoro-1-butenyl moieties of neighbouring molecules are oriented in such manner that they generate hydrophobic layers. Such orientation of the molecules prevents hydrogen bonds formation and C–H···π interactions, but enables a weak aromatic π···π stacking interactions [24] between the pyrimidine rings of the neighbouring molecules. An interplanar angle between the pyrimidine rings is 0.00°, interplanar spacings are *ca* 3.43^{i} and 3.46^{ii} Å, a centroid separations 3.6452(17)^{i} and 3.6136(17)^{ii} Å, and a corresponding centroid–centroid offsets 1.225^{i} and 1.039^{ii} Å, respectively [symmetry codes: (*i*) $1-x, -y, 1-z$; (*ii*) $2-x, -y, 1-z$]. The π···π interactions link the molecules of **4** into infinite chains parallel to the *a* axis. One short intermolecular F···F contact is also present in this structure [F1···F2^{iii} = 2.886(3) Å; (*iii*): $x, -1/2-y, -1/2+z$]. This F···F interaction can be classified as type-I interaction [25], as C11–F1···F2^{iii} and F1···F2^{iii}–C11^{iii} angles are 141.3(2)° and 159.0(2)°, respectively. The recent charge density study of intermolecular interactions involving organic fluorine has classified F···F contacts as a well-defined weak intermolecular interactions [26]. In the absence of any other significant intermolecular interactions, these interactions can also provide stability of molecular assembly.

4. Conclusion

Pyrimidine derivatives (**4** and **5**) with C-6 3,3,4,4,4-pentafluoro-1-butenyl side chain were synthesized, and their structures were elucidated by ^{1}H, ^{13}C and ^{19}F NMR spectra, and IR spectra. The *Z*-

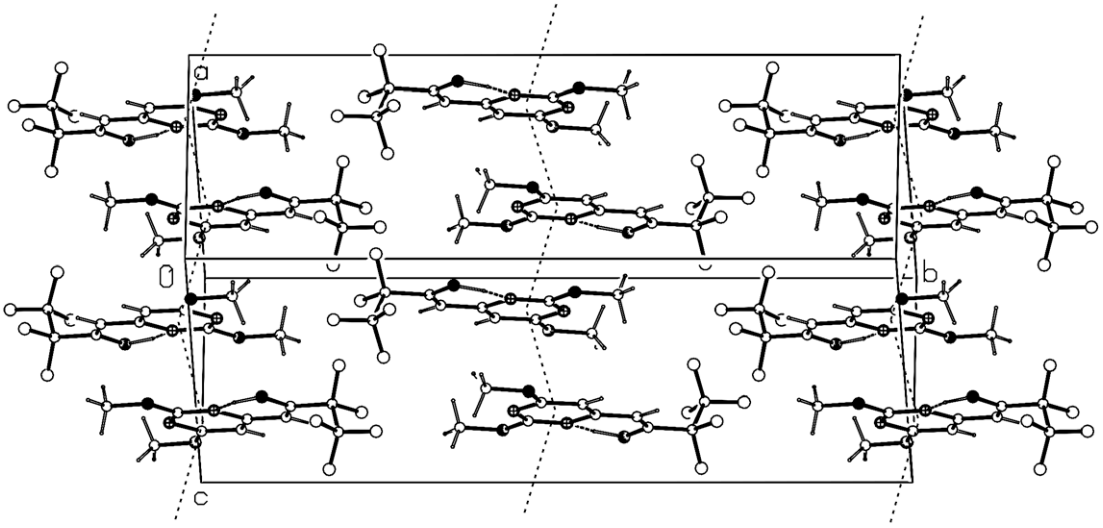


Fig. 2. Crystal packing diagram of **4**, showing the π···π interactions that link the molecules of **4** into infinite chains. π···π interactions are indicated by dotted lines.

configuration of C1′=C2′ double bond in **5** was determined through $^3J_{CH}$ coupling constant. X-ray crystal structure analysis of **4** showed that the molecule is essentially planar, and that the mutually parallel molecules are aligned along the *b* axis. Aromatic π···π stacking interactions link the molecules of **4** into infinite chains parallel to the *a* axis.

Acknowledgements

Support for this study was provided by the Ministry of Science of the Republic of Croatia (Projects #125-0982464-2925 and #119-1193079-3069). The authors wish to thank Dr. Marijeta Kralj for cytostatic evaluation of 6-(3,3,4,4,4-pentafluoro-2-hydroxy-1-butenyl)-2,4-pyrimidinedione (**5**).

References

[1] D. Chopra, T.N.G. Row, CrystEngComm. 10 (2008) 54.
[2] P. Das, C.P. Spears, A.H. Shahinian, S.K. Dasgupta, N.G. Kundu, Bioorg. Med. Chem. Lett. 6 (1996) 2477.
[3] M. Baba, E. De Clercq, H. Tanaka, M. Ubasawa, H. Takashima, K. Sekiya, I. Nitta, K. Umezu, R.T. Walter, S. Mori, Mol. Pharmacol. 39 (1991) 805.
[4] J. Balzarini, A. Karlsson, E. De Clercq, Mol. Pharmacol. 44 (1993) 694.
[5] A. Mai, M. Artico, G. Sbardella, S. Quartarone, S. Massa, A.G. Loi, A. De Montis, F. Scintu, M. Putzolu, P. LaColla, J. Med. Chem. 40 (1997) 1447.
[6] S. Prekupec, D. Makuc, J. Plavec, S. Kraljević, M. Kralj, K. Pavelić, G. Andrei, R. Snoeck, J. Balzarini, E. De Clercq, S. Raić-Malić, M. Mintas, Antiviral Chem. Chemother. 16 (2005) 327.
[7] S. Prekupec, D. Makuc, J. Plavec, L. Šuman, M. Kralj, K. Pavelić, J. Balzarini, E. De Clercq, M. Mintas, S. Raić-Malić, J. Med. Chem. 50 (2007) 3037.
[8] P. Pospisil, D.B. Pilger, S. Marveggio, P. Schelling, C. Wurth, L. Scapozza, G. Folkers, M. Pongračić, M. Mintas, S. Raić-Malić, Helv. Chim. Acta 85 (2002) 3237.
[9] T. Kulikowski, Pharm. World Sci. 16 (1994) 127.
[10] S. Raić-Malić, A. Johayem, S. Ametamey, S. Batinac, E. De Clercq, G. Folkers, L. Scapozza, Nucleosides Nucleotides Nucleic Acids 23 (2004) 1707.
[11] A. Johayem, S. Raić-Malić, K. Lazzati, P.A. Schubiger, L. Scapozza, S.M. Ametamey, Chem. Biodiversity 3 (2006) 274.
[12] J. Eary, D.A. Mankoff, A.M. Spence, M.S. Berger, A. Olshen, J. Link, F. O'Sullivan, K.A. Krohn, Cancer Res. 59 (1999) 615.
[13] D.A. Mankoff, A.F. Shields, J.M. Link, M.M. Graham, M. Muzi, L.M. Peterson, J.F. Eary, K.A. Krohn, J. Nucl. Med. 40 (1999) 614.
[14] Oxford Diffraction, Xcalibur CCD System. CrysAlis CCD and CrysAlis RED, Versions 171.32.4, Oxford Diffraction, Oxford, United Kingdom, 2007.
[15] G.M. Sheldrick, Acta Crystallogr. A64 (2008) 112.
[16] A.L. Spek, J. Appl. Crystallogr. 36 (2003) 7.
[17] L.M. Popova, A.U. Trishina, S.V. Vershilov, A.I. Ginak, B.N. Maksimov, J. Fluorine Chem. 96 (1999) 51.
[18] M. Futamata, D. Diesing, Vibr. Spectrosc. 19 (1999) 187.
[19] T. Gazivoda, S. Krištafor, M. Cetina, A. Nagl, S. Raić-Malić, Struct. Chem. 19 (2008) 441.
[20] V.F. Snegirev, M.Y. Antipin, V.N. Khrustalev, Y.T. Struchkov, Russ. Chem. Bull. 43 (1994) 1009.
[21] G.F. Jiang, J. Sun, Y. Shen, J. Fluorine Chem. 108 (2001) 207.
[22] V.I. Filyakova, D.S. Yufit, Y.T. Struchkov, K.I. Pashkevich, Russ. Chem. Bull. 39 (1990) 936.
[23] J. Bernstein, R.E. Davis, L. Shimoni, N.L. Chang, Angew. Chem. Int. Ed. Engl. 34 (1995) 1555.
[24] C.A. Hunter, J.K.M. Sanders, J. Am. Chem. Soc. 112 (1990) 5525.
[25] G.R. Desiraju, R. Parthasarathy, J. Am. Chem. Soc. 111 (1989) 8725.
[26] D. Chopra, T.S. Cameron, J.D. Ferrara, T.N. Guru Row, J. Phys. Chem. A 110 (2006) 10465.