SYNTHESIS OF 4-ALKYL- OR 4-PHENYL-7-METHYL-1,2-DIHYDRO-7*H*-IMIDAZO[1,2,3-*cd*]PURINE-6,8-DIONES

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Received September 1, 1997
Accepted February 5, 1998

Dedicated to Professor Wolfgang Pfleiderer on the occasion of his 70th birthday.

New 4-alkyl- or 4-phenyl-7-methyl-1,2-dihydro-7*H*-imidazo[1,2,3-*cd*]purine-6,8-diones **1** were obtained by intramolecular alkylation of 8-alkyl- or 8-phenyl-9-(2-mesyloxyethyl)-1-methyl-9*H*-purine-2,6(1*H*,3*H*)-diones **5**. The necessary compounds **5** were prepared from 6-[(2-hydroxyethyl)-amino]-3-methyl-5-nitrosopyrimidine-2,4(1*H*,3*H*)-dione (**2**), which was hydrogenated to 5-amino-6-[(2-hydroxyethyl)amino]-3-methyl derivative **3**; consecutive reactions of the latter with an orthocarboxylate and mesyl chloride afforded 8-alkyl- or 8-phenyl-9-(2-hydroxyethyl)-1-methyl-9*H*-purine-2,6(1*H*,3*H*)-diones **4** and compounds **5**, respectively.

Key words: Imidazo[1,2,3-*cd*]purines; 3,9-Annelated purines; Xanthine derivatives; Acyclic nucleoside analogues.

Our recent studies on fused purine derivatives[1,2] concerned compounds in which a heterocycle was peri-fused to a purine ring system[3]. The present paper dealing with the synthesis of alkyl and phenyl derivatives of the hitherto not described imidazo[*cd*]purinedione skeleton is to be regarded as a continuation of our research programme. Some of these derivatives, after functionalization of their alkyl groups, are aimed to serve as precursors for preparation of potentionally hypocholesterolemic effective 3-hydroxy-3-methylglutaryl CoA reductase inhibitors[4] and potentionally effective A_2 receptor antagonists[5,6].

The synthesis of tricyclic 4-alkyl- and 4-phenyl-7-methyl-1,2-dihydro-7*H*-imidazo[1,2,3-*cd*]purine-6,8-diones **1** was attempted in two ways. The first one started from the known 6-[(2-hydroxyethyl)amino]-3-methyl-5-nitrosopyrimidine-2,4(1*H*,3*H*)-dione (**2**) (refs[7,8]), and continued by its hydrogenation to the corresponding diamino derivative **3** and cyclization with orthocarboxylates to 8-alkyl- or 8-phenyl-9-(2-hydroxy-

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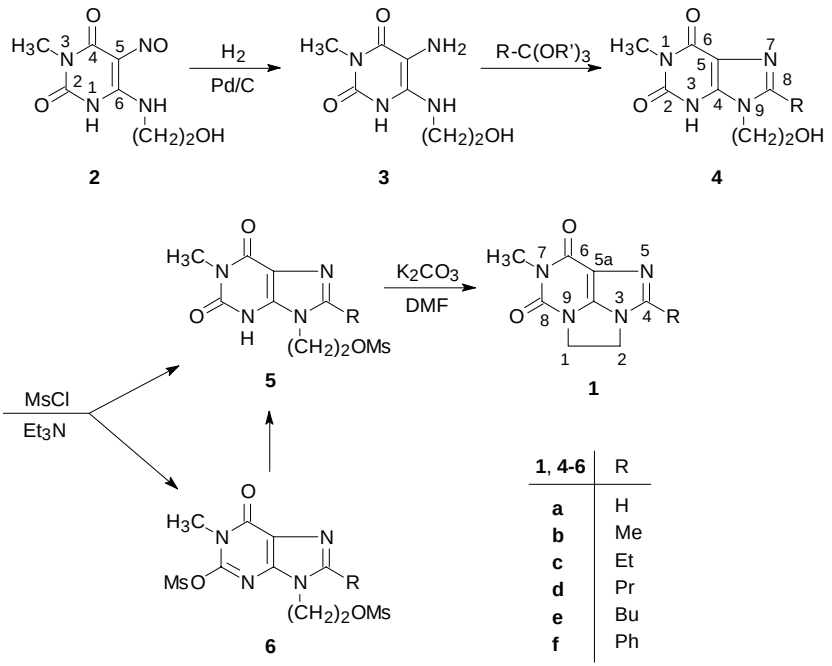
ethyl)-1-methyl-9*H*-purine-2,6(1*H*,3*H*)-diones **4**. Mesylation of 9-(2-hydroxyethyl) derivatives **4** produced 8-alkyl- or 8-phenyl-9-(2-mesyloxyethyl)-1-methyl-9*H*-purine-2,6(1*H*,3*H*)-diones **5** affording the final compounds **1** on intramolecular alkylation (Scheme 1).



SCHEME 1

The starting nitroso derivative **2** was hydrogenated[8] according to a modified procedure (palladium on charcoal in ethanol) which afforded very pure 5-amino-6-[(2-hydroxyethyl)amino]-3-methylpyrimidine-2,4(1*H*,3*H*)-dione (**3**).

Curiously enough, 1-substituted 8-alkyl- or 8-phenyl-9-(2-hydroxyethyl)purinediones **4** were not described as yet. To obtain them from diamine **3** possessing an *N*-hydroxyalkyl group, an acid-catalyzed reaction with orthocarboxylates was considered most suitable for the synthesis of the imidazole ring embodied in compound **4**. Hydrochloric acid-catalyzed condensation of diamine **3** with an excess of orthocarboxylates at room temperature required a long reaction time (*cf.*, *e.g.*, ref.[9]). The *p*-toluenesulfonic acid-catalyzed reaction in dimethylformamide at 100 °C made it possible to shorten the reaction time to 2–4 h. Substantially more problematic appeared to be the mesylation of compounds **4**. In contrast to that of 8-alkyl- or 8-phenyl-9-(3-hydroxypropyl) derivatives described in our preceding paper[3], compounds **4** formed double mesylated products, *i.e.* 8-alkyl- or 8-phenyl-2-mesyloxy-9-(2-mesyloxyethyl)-1-

methyl-9*H*-purine-6(1H)-ones **6**, in addition to the expected 8-alkyl- or 8-phenyl-9-(2-mesyloxyethyl) derivatives **5**. Structure of compound **6** was supported by both the IR spectra (absence of absorption bands associated with the second C=O and R–SO_2N groups, presence of an R–SO_2–O group) and easy elimination of the second mesyl group. It was therefore necessary to optimize the reaction conditions leading to compound **5**, namely to ensure a full consumption of the starting 9-(2-hydroxyethyl) derivative **4** and minimize the formation of double-mesylated derivatives **6**. The TLC-monitored 4–24 h reaction revealed that at a molar ratio intermediate 4 : mesyl chloride : triethylamine (1 : 1.1–1.5 : 1.1–1.5) in dichloromethane at 0–25 °C, both compound **6** and the triethylammonium salt of compound **5** (**5**·Et_3N) were formed in virtually the same relative amounts, but accompanied by a great amount of unreacted starting intermediate **4**. To ensure a complete reaction of intermediate **4**, the reactant ratio must be increased up to 1 : 3 : 8. Such a great excess of triethylamine had a positive impact on the ratio of compounds **6** and **5**. Triethylamine, namely, minimizes successively the content of compound **6** in the mixture during a relatively short reaction time. Thus, not only the starting material was consumed during 1 h, but also compound **6** appeared in trace amounts. A thorough acidification of the triethylammonium salts remaining in the filtrate led to the required compounds **5**.

To evidence the mesylation course as monitored by TLC, *i.e.*, that compounds **6** were converted into triethylammonium salt of mesyloxyethyl derivatives **5** with triethylammonium chloride and the already mentioned great excess of triethylamine in dichloromethane, we prepared pure 8-ethyl derivative **6c** and converted it into the corresponding **5c** under the already given conditions.

In conclusion, this method enables a facile preparation of 4-alkyl- or 4-phenyl-7-methyl-1,2-dihydro-7*H*-imidazo[1,2,3-*cd*]purine-6,8-diones (**1**) in 4 steps with overall yields 13–36%. Further application of this methodology is a facile preparation of 8-alkyl- or 8-phenyl-9-(2-hydroxyethyl)-1-methyl-9*H*-purine-2,6(1*H*,3*H*)-diones (**4**) in 2 steps with overall yields 39–55%.

EXPERIMENTAL

Melting points were determined on Kofler apparatus and are uncorrected. Samples for analysis were dried over P_4O_{10} at 60 °C and 30 Pa for 8–10 h. The ^{1}H (300 MHz) and ^{13}C (75.45 MHz) NMR spectra were obtained on a Bruker AM-300 spectrometer. Chemical shifts (δ) are reported in ppm, using TMS as internal reference. Mass spectra were obtained on a Finnigan MAT SSQ 710 instrument using the electron impact ionization technique (100–210 °C, 70 eV). The reaction progress and purity of all prepared compounds was followed by TLC (SILUFOL UV_{254}, Kavalier, Votice, Czech Republic) in the system chloroform–methanol 9 : 1 using UV detection.

5-Amino-6-[(2-hydroxyethyl)amino]-3-methylpyrimidine-2,4(1*H*,3*H*)-dione (**3**)

Compound **2** (21.4 g, 0.1 mol) was suspended in ethanol (300 ml) and hydrogenated over 10% palladium on carbon (1.0 g) at room temperature for 3 h. The orange colour of the starting material **2**

TABLE I
Yields and physicochemical properties of compounds **1**, **4** and **5**

Compound	Yield %	M.p., °C Solvent	Formula M.w.	Calculated/Found			
				% C	% H	% N	% S
1a	52	295–297	$C_8H_8N_4O_2$	50.00	4.20	29.15	–
		ethanol	192.2	50.29	4.41	29.04	
1b	73	251–253	$C_9H_{10}N_4O_2$	52.42	4.89	27.17	–
		acetone	206.2	52.49	5.15	27.04	
1c	62	161–163	$C_{10}H_{12}N_4O_2$	54.54	5.49	25.44	–
		propan-2-ol	220.2	54.75	5.71	25.20	
1d	68	186–188	$C_{11}H_{14}N_4O_2$	56.40	6.02	23.92	–
		hexane	234.3	56.66	6.00	23.66	
1e	72	128–130	$C_{12}H_{16}N_4O_2$	58.05	6.50	22.57	–
		hexane–propan-2-ol	248.3	57.89	6.58	22.41	
1f	60	320–323	$C_{14}H_{12}N_4O_2$	62.68	4.51	20.88	–
		ethanol	268.3	62.39	4.63	21.09	
4a	65	278–280	$C_8H_{10}N_4O_3$	45.71	4.80	26.66	–
		water	210.2	45.58	4.99	26.52	
4b	80	301–303	$C_9H_{12}N_4O_3$	48.21	5.39	24.99	–
		water	224.2	48.10	5.65	24.84	
4c	72	330–333	$C_{10}H_{14}N_4O_3$	50.41	5.92	23.52	–
		water	238.3	50.23	6.11	23.50	
4d	68	288–290	$C_{11}H_{16}N_4O_3$	52.37	6.39	22.21	–
		ethanol	252.3	52.49	6.51	22.00	
4e	65	257–259	$C_{12}H_{18}N_4O_3$	54.12	6.81	21.04	–
		ethanol	266.3	54.38	6.96	20.93	
4f	60	317–318	$C_{14}H_{14}N_4O_3$	58.74	4.93	19.57	–
		water	286.3	58.68	5.01	19.41	
5a	52	283–285	$C_9H_{12}N_4O_5S$	37.50	4.20	19.43	11.12
		methanol–water	288.3	37.43	4.51	19.30	11.34
5b	83	238–240	$C_{10}H_{14}N_4O_5S$	39.73	4.67	18.53	10.61
		water	302.3	39.34	4.96	18.49	10.58
5c	68	206–208	$C_{11}H_{16}N_4O_5S$	41.77	5.10	17.71	10.13
		ethanol–acetone	316.3	41.89	5.12	17.90	10.09

TABLE I
(*Continued*)

Compound	Yield %	M.p., °C Solvent	Formula M.w.	Calculated/Found			
				% C	% H	% N	% S
5d	92	238–240	$C_{12}H_{18}N_4O_5S$	43.63	5.49	16.96	9.70
		water–acetone	330.4	43.40	5.68	17.21	10.10
5e	71	220–222	$C_{13}H_{20}N_4O_5S$	45.34	5.85	16.27	9.31
		ethanol–water	344.4	45.52	5.67	16.24	9.20
5f	88	211–213	$C_{15}H_{16}N_4O_5S$	49.44	4.43	15.38	8.80
		water	364.4	49.15	4.63	15.49	9.03

disappeared, a grey powdery product was filtered off together with the catalyst, and crystallized from water. Yield 15.0 g (75%) of light yellow crystals with no characteristic m.p. (decomposition around 220 °C; ref.[8] reports 220 °C slow decomposition). The diamine **3** is light- and air-instable and, therefore, it has to be consumed within 2 weeks. ^{1}H NMR spectrum (DMSO-d_6): 3.19 s, 3 H (N-3-CH_3); 3.40 q, 2 H (NH-C**H**$_2$); 3.48 bs, 1 H (OH); 3.60 t, 2 H (C**H**$_2$OH); 6.18 t, 1 H (6-NH). ^{13}C NMR spectrum (DMSO-d_6): 26.9 (N-3-CH_3); 44.2 (NH-CH_2); 60.7 (CH_2OH); 94.5 (C-5); 145.0 (C-6); 149.7 (C-2); 160.3 (C-4).

8-Alkyl- or 8-Phenyl-9-(2-hydroxyethyl)-1-methyl-9*H*-purine-2,6(1*H*,3*H*)-diones **4**

A stirred mixture of compound **3** (2.0 g, 10 mmol), dimethylformamide (25 ml), trimethyl or triethyl orthocarboxylate (15 mmol) and *p*-toluenesulfonic acid (10–12 mg) was heated to 100 °C (2 h for **4e** and **4f**; 3 h for **4a**, **4c** and **4d**; 4 h for **4b**). The catalytic amount of *p*-toluenesulfonic acid was neutralized with ethanolic ammonia and the volatile portion was distilled off under diminished pressure. The crude dry residue was crystallized from a suitable solvent with addition of charcoal.

8-Alkyl- or 8-Phenyl-9-(2-mesyloxyethyl)-1-methyl-9*H*-purine-2,6(1*H*,3*H*)-diones **5**

Mesyl chloride (0.69 g, 0.45 ml, 6.0 mmol) in dichloromethane (10 ml) was added gradually (15 min) to a stirred solution of intermediate **4** (2.0 mmol) in dichloromethane (30 ml) and triethylamine (1.62 g, 2.23 ml, 16 mmol) at 20–25 °C. The mixture was stirred for 1 h at the same temperature, the volatile components were removed under reduced pressure, the residue was dissolved in water, the light turbidity being filtered off, and pH of the clear filtrate was adjusted with acetic acid to 6–7 under cooling. Compounds **5a–5c**, **5f** and **5d**, **5e** were separated from filtrate within 10–5 min and 2–4 h, respectively. The resulting mixture was left standing in refrigerator overnight, product was filtered off and re-crystallized from a suitable solvent with addition of charcoal.

TABLE II
^{1}H NMR spectra of compounds **1**, **4** and **5**

Compound	^{1}H NMR ($CDCl_3$/TMS), δ (ppm)
1a	3.24 s, 3 H (N-7-CH_3); 4.67 m, 2 H (H-2); 4.83 m, 2 H (H-1); 7.78 s, 1 H (H-4)
1b	2.41 s, 3 H (4-CH_3); 3.31 s, 3 H (N-7-CH_3); 4.54 m, 2 H (H-2); 4.87 m, 2 H (H-1)
1c	1.30 t, 3 H ($CH_2C\mathbf{H}_3$); 2.76 q, 2 H ($C\mathbf{H}_2CH_3$); 3.21 s. 3 H (N-7-CH_3); 4.62 m, 2 H (H-2); 4.81 m, 2 H (H-1)
1d	1.03 t, 3 H ($CH_2C\mathbf{H}_3$); 1.75 sextet, 2 H ($C\mathbf{H}_2CH_3$); 2.71 t, 2 H (C-4-$C\mathbf{H}_2$); 3.22 s, 3 H (N-7-CH_3); 4.61 m, 2 H (H-2); 4.82 m, 2 H (H-1)
1e	0.94 t, 3 H ($CH_2C\mathbf{H}_3$); 1.40 sextet, 2 H ($C\mathbf{H}_2CH_3$); 1.70 quintet, 2 H (C-4-$CH_2C\mathbf{H}_2$); 2.69 t, 2 H (C-4-$C\mathbf{H}_2$); 3.30 s, 3 H (N-7-CH_3); 4.56 t, 2 H (H-2); 4.87 t, 2 H (H-1)
1f	3.27 s, 3 H (N-7-CH_3); 4.94 m, 4 H (H-2, H-1); 7.92–7.96 m, 5 H (C_6H_5)
4a	3.28 s, 3 H (N-1-CH_3); 3.73 t, 2 H (N-9-CH_2); 4.19 t, 2 H (OCH_2); 7.73 s, 1 H (H-8)
4b	2.41 s, 3 H (8-CH_3); 3.25 s, 3 H (N-1-CH_3); 3.69 t, 2 H (N-9-CH_2); 4.10 t, 2 H (OCH_2)
4c	1.30 t, 3 H ($CH_2C\mathbf{H}_3$); 2.78 q, 2 H ($C\mathbf{H}_2CH_3$); 3.27 s, 3 H (N-1-CH_3); 3.69 t, 2 H (N-9-CH_2); 4.11 t, 2 H (OCH_2)
4d	1.00 t, 3 H ($CH_2C\mathbf{H}_3$); 1.77 sextet, 2 H ($C\mathbf{H}_2CH_3$); 2.71 t, 2 H (C-8-CH_2); 3.25 s, 3 H (N-1-CH_3), 3.70 t, 2 H (N-9-CH_2); 4.11 t, 2 H (OCH_2)
4e	0.90 s, 3 H ($CH_2C\mathbf{H}_3$); 1.42 sextet, 2 H ($C\mathbf{H}_2CH_3$); 1.75 quintet, 2 H (C-8-$CH_2C\mathbf{H}_2$); 2.75 t, 2 H (C-8-$C\mathbf{H}_2$); 3.25 s, 3 H (N-1-CH_3); 3.68 t, 2 H (N-9-CH_2); 4.10 t, 2 H (OCH_2)
4f	3.30 s, 3 H (N-1-CH_3); 3.65 t, 2 H (N-9-CH_2); 4.27 t, 2 H (OCH_2); 7.50–7.80 m, 5 H (C_6H_5)
5a	3.29 s, 3 H (N-1-CH_3); 3.22 s, 3 H (CH_3SO_2); 4.53 m, 4 H (N-9-CH_2,OCH_2)[a]; 7.78 s, 1 H (H-8)
5b	2.44 s, 3 H (8-CH_3); 3.23 s, 3 H (CH_3SO_2); 3.27 s, 3 H (N-1-CH_3); 4.48 m, 4 H (N-9-CH_2, OCH_2)[a]
5c	1.32 t, 3 H ($CH_2C\mathbf{H}_3$); 2.80 q, 2 H ($C\mathbf{H}_2CH_3$); 3.23 s, 3 H (CH_3SO_2); 3.28 s, 3 H (N-1-CH_3); 4.48 m, 4 H (N-9-CH_2, OCH_2)[a]
5d	1.07 t, 3 H ($CH_2C\mathbf{H}_3$); 1.83 sextet, 2 H ($C\mathbf{H}_2CH_3$); 2.75 t, 2 H (C-8-$C\mathbf{H}_2$); 3.21 s, 3 H (CH_3SO_2); 3.28 s, 3 H (N-1-CH_3); 4.48 bs, 4 H (N-9-CH_2, OCH_2)[a]
5e	1.01 t, 3 H ($CH_2C\mathbf{H}_3$); 1.48 sextet, 2 H ($C\mathbf{H}_2CH_3$); 1.78 quintet, 2 H (C-8-$CH_2C\mathbf{H}_2$); 2.76 t, 2 H (C-8-$C\mathbf{H}_2$); 3.21 s, 3 H (CH_3SO_2); 3.28 s, 3 H (N-1-CH_3); 4.48 bs, 4 H (C-9-CH_2, OCH_2)[a]
5f	3.05 s, 3 H (CH_3SO_2); 3.32 s, 3 H (N-1-CH_3); 4.39 t, 2 H (OCH_2); 4.59 t, 2 H (N-9-CH_2); 7.58–7.69 m, 5 H (C_6H_5)

[a] Determined by single-frequency decoupling.

TABLE III
^{13}C NMR spectra of compounds **1**, **4** and **5**

Compound	^{13}C NMR ($CDCl_3$/TMS), δ (ppm)
1a	28.0 (N-7-CH_3); 47.7 (C-2); 54.0 (C-1); 108.3 (C-5a); 133.6 (C-4); 149.8 (C-9a); 151.8 (C-8); 157.8 (C-6)
1b	13.9 (4-CH_3); 28.6 (N-7-CH_3); 46.5 (C-2); 53.9 (C-1); 107.7 (C-5a); 142.5 (C-4); 149.9 (C-9a); 151.5 (C-8); 157.6 (C-6)
1c	11.2 (CH_2**C**H_3); 20.8 (**C**H_2CH_3); 27.9 (N-7-CH_3); 47.0 (C-2); 54.0 (C-1); 106.4 (C-5a); 147.1 (C-4); 149.7 (C-9a); 152.2 (C-8); 157.5 (C-6)
1d	13.4 (CH_2**C**H_3); 20.1 (**C**H_2CH_3); 27.9 (N-7-CH_3); 29.2 (C-4-**C**H_2); 47.0 (C-2); 54.1 (C-1); 106.4 (C-5a); 146.0 (C-4); 149.8 (C-9a); 152.2 (C-8); 157.5 (C-6)
1e	13.5 (CH_2**C**H_3); 22.0 (**C**H_2CH_3); 27.8 (N-7-CH_3); 28.3 (C-4-CH_2**C**H_2); 29.2 (C-4-**C**H_2); 46.8 (C-2); 53.8 (C-1); 107.2 (C-5a); 146.4 (C-4); 149.6 (C-9a); 151.3 (C-8); 157.6 (C-6)
1f	28.1 (N-1-CH_3); 49.7 (C-2); 54.0 (C-1); 108.2 (C-5a); 125.5, 128.1, 129.0, 129.3 (C_6H_5); 153.1 (C-8); 157.6 (C-6)
4a	27.0 (N-1-CH_3); 46.5 (N-9-CH_2); 59.5 (OCH_2); 114.8 (C-5); 137.5 (C-8); 138.8 (C-4); 150.7 (C-2); 157.5 (C-6)
4b	13.6 (2-CH_3); 27.5 (N-1-CH_3); 46.2 (N-9-CH_2); 59.9 (OCH_2); 113.1 (C-5); 140.2 (C-8); 146.0 (C-4); 151.3 (C-2); 157.9 (C-6)
4c	11.5 (CH_2**C**H_3); 19.9 (**C**H_2CH_3); 27.4 (N-1-CH_3); 45.7 (N-9-CH_2); 59.8 (OCH_2); 113.2 (C-5); 140.1 (C-8); 149.9 (C-4); 151.3 (C-2); 157.8 (C-6)
4d	14.1 (CH_2**C**H_3); 20.4 (**C**H_2CH_3); 27.5 (N-1-CH_3); 28.4 (C-8-CH_2); 45.8 (N-9-CH_2); 59.9 (OCH_2); 113.4 (C-5); 140.0 (C-8); 149.0 (C-4); 151.2 (C-2); 157.9 (C-6)
4e	14.2 (CH_2**C**H_3); 22.2(**C**H_2CH_3); 26.2 (C-8-CH_2**C**H_2); 27.6 (N-1-CH_3); 29.1 (C-8-**C**H_2); 45.8 (N-9-CH_2); 59.9 (OCH_2); 113.4 (C-5); 140.0 (C-8); 149.1 (C-4); 151.3 (C-2); 157.9 (C-6)
4f	27.7 (N-1-CH_3); 47.0 (N-9-CH_2); 59.4 (OCH_2); 114.7 (C-5); 129.5, 2 × 129.8, 130.0 (C_6H_5); 141.0 (C-8); 147.3 (C-4); 151.3 (C-2); 158.2 (C-6)
5a	27.0 (N-1-CH_3); 36.7 (CH_3SO_2); 43.1 (N-9-CH_2); 67.9 (OCH_2); 114.4 (C-5); 137.2 (C-8); 138.8 (C-4); 150.7 (C-2); 157.4 (C-6)
5b	13.1 (8-CH_3); 27.0 (N-1-CH_3); 36.6 (CH_3SO_2); 42.3 (N-9-CH_2); 68.0 (OCH_2); 113.0 (C-5); 139.4 (C-8); 144.3 (C-4); 150.6 (C-2); 157.1 (C-6)
5c	10.9 (CH_2**C**H_3); 19.4 (**C**H_2CH_3); 26.9 (N-1-CH_3); 36.7 (CH_3SO_2); 41.9 (N-9-CH_2); 68.0 (OCH_2); 113.1 (C-5); 139.4 (C-8); 148.6 (C-4); 150.6 (C-2); 157.2 (C-6)
5d	13.7 (CH_2**C**H_3); 19.7 (**C**H_2CH_3); 26.9 (N-1-CH_3); 27.7 (C-8-**C**H_2); 38.6 (CH_3SO_2); 41.9 (N-9-CH_2); 68.0 (OCH_2); 113.5 (C-5); 139.3 (C-8); 147.5 (C-4); 150.7 (C-2); 157.2 (C-6)
5e	13.7 (CH_2**C**H_3); 21.8 (**C**H_2CH_3); 25.5 (C-8-CH_2**C**H_2); 27.0 (N-1-CH_3); 28.4 (C-8-**C**H_2); 36.7 (CH_3SO_2); 41.9 (N-9-CH_2); 68.0 (OCH_2); 113.2 (C-5); 139.3 (C-8); 147.7 (C-4); 150.7 (C-2); 157.2 (C-6)
5f	27.1 (N-1-CH_3); 36.6 (CH_3SO_2); 43.1 (N-9-CH_2); 67.1 (OCH_2); 113.0 (C-5); 128.7, 129.0, 129.3, 129.5 (C_6H_5); 140.2 (C-8); 146.2 (C-4); 150.6 (C-2); 157.4 (C-6)

4-Alkyl- or 4-Phenyl-7-methyl-1,2-dihydro-7*H*-imidazo[1,2,3-*cd*]purine-6,8-diones **1**

Compound **5** (2.0 mmol), potassium carbonate (0.33 g, 2.4 mmol) and dimethylformamide (30 ml) were heated at 120 °C (30 min for **1b–1d** and **1f**; 45 min for **1e**; 60 min for **1a**). Dimethylformamide was distilled off under reduced pressure, the dry residue was extracted with chloroform (3 × 50 ml) and the solvent was removed. The dry residue was crystallized from a suitable solvent with addition of charcoal. For all prepared compounds **1**, **4** and **5** melting points, yields and elemental analyses are summarized in Table I, ^{1}H NMR spectra in Table II, ^{13}C NMR spectra in Table III, and mass spectra in Table IV.

8-Ethyl-2-mesyloxy-9-(2-mesyloxyethyl)-1-methyl-9*H*-purin-6(1*H*)-one (**6c**)

Mesyl chloride (0.48 g, 0.33 ml, 4.2 mmol) in dichloromethane (5 ml) was added gradually (10 min) to a stirred suspension of **4c** (0.63 g, 2.0 mmol) in dichloromethane (10 ml) and triethylamine (0.51 g, 0.70 ml, 5.0 mmol) at 20 °C. After 1 h the content dissolved at the same temperature; the volatile components were distilled off under diminished pressure and water (5 ml) was added to the residue. The white precipitate was filtered off, dried and dissolved in acetone (20 ml) at room temperature.

TABLE IV
Mass spectra of compounds **1**, **4** and **5**

Compound	EI MS[a], *m/z* (rel. int.%)
1a	192 (M^+, 34), 135 (100), 108 (33), 81 (14)
1b	206 (M^+, 36), 149 (100), 121 (26), 107 (4), 81 (11)
1c	220 (M^+, 51), 163 (100), 134 (21), 120 (2), 107 (8), 83 (64), 81 (10)
1d	234 (M^+, 30), 177 (100), 149 (14), 121 (25), 107 (4), 97 (30)
1e	248 (M^+, 47), 206 (68), 191 (98), 149 (100), 134 (9), 121 (38)
1f	268 (M^+, 65), 211 (100), 182 (18), 131 (56), 103 (74)
4a	210 (M^+, 75), 180 (9), 153 (23), 123 (19), 109 (100)
4b	224 (M^+, 89), 193 (27), 167 (18), 137 (18), 123 (100), 109 (9)
4c	238 (M^+, 100), 207 (58), 153 (19), 150 (25), 137 (85), 109 (62)
4d	252 (M^+, 47), 224 (32), 221 (21), 208 (17), 180 (100), 151 (10), 136 (10), 123 (76)
4e	266 (M^+, 56), 237 (14), 224 (48), 209 (10), 194 (17), 180 (100), 123 (26)
4f	286 (M^+, 100), 255 (40), 185 (46), 157 (16), 104 (89)
5a	192 (M^+ – MsOH, 32), 166 (3), 134 (4), 108 (22), 96 (75), 81 (52), 79 (100)
5b	206 (M^+ – MsOH, 16), 180 (5), 149 (3), 108 (8), 96 (89), 81 (58), 79 (100)
5c	220 (M^+ – MsOH, 32), 180 (7), 163 (100), 134 (13), 83 (42), 79 (8)
5d	234 (M^+ – MsOH, 23), 206 (7), 177 (84), 149 (15), 121 (22), 96 (87), 79 (100)
5e	248 (M^+ – MsOH, 11), 224 (14), 206 (38), 191 (48), 149 (59), 96 (100), 79 (83)
5f	268 (M^+ – MsOH, 100), 242 (49), 236 (17), 185 (11), 108 (18), 104 (59), 79 (50)

[a] MsOH = CH_3SO_3H.

The filtered solution was concentrated to one half of its original volume and the product was precipitated with diethyl ether. Yield 0.51 g (65%). Analytical sample was purified by crystallization from water, m.p. 138–140 °C. For $C_{12}H_{18}N_4O_7S_2$ (394.4) calculated: 36.54% C, 4.60% H, 14.20% N, 16.26% S; found: 36.40% C, 4.82% H, 14.32% N, 16.41% S. ^{1}H NMR spectrum (DMSO-d_6): 1.39 t, 3 H ($CH_2C\mathbf{H}_3$); 2.49 s, 3 H (C-2-OSO_2-CH_3); 2.95 q, 2 H ($C\mathbf{H}_2CH_3$); 3.26 s, 3 H (CH_2-OSO_2-$C\mathbf{H}_3$); 3.30 s, 3 H (N-1-CH_3); 4.52–4.58 overlapped m, 4 H (N-9-CH_2CH_2). ^{13}C NMR spectrum (DMSO-d_6): 10.8 ($CH_2\mathbf{C}H_3$); 19.0 ($\mathbf{C}H_2CH_3$); 27.1 (N-1-CH_3); 36.7 (CH_2-OSO_2-$\mathbf{C}H_3$); 39.7 (C-2-OSO_2-$\mathbf{C}H_3$); 42.7 (N-9-CH_2); 67.5 (CH_2O); 109.8 (C-5); 139.1 (C-8); 149.8 (C-4); 150.7 (C-2); 155.7 (C-6).

8-Ethyl-9-(2-mesyloxyethyl)-1-methyl-9*H*-purine-2,6(1*H*,3*H*)-dione (**5c**)

Suspension of **6c** (0.79 g, 2 mmol) and triethylamine hydrochloride (0.28 g, 2 mmol) in triethylamine (1.42 g, 1.95 ml, 14 mmol) and dichloromethane (20 ml) was stirred at room temperature for 1 h during which compound **6c** dissolved. Stirring was continued for another 1 h, the volatile components were removed under diminished pressure, the residue was dissolved in water (5 ml) and the solution was neutralized to pH 7 with aqueous acetic acid (1 : 1). The product separated on standing in refrigerator was filtered off and crystallized from water. Yield 0.39 g (62%). Product **5c** obtained in this way proved to be identical (mixed m.p., EI MS, ^{1}H NMR) with that prepared according to the above-mentioned general procedure for compounds **5**.

Financial support from the Slovak Grant Agency (project No. 2/568/96) is gratefully acknowledged.

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