Purines

Part XVI[1])

Syntheses, Properties, and Reactions of 8-Aminoxanthines

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A series of *N*-substituted 8-aminoxanthines (= 8-amino-3,7(or 3,9)-dihydro-1*H*-purine-2,6-diones) **8**–**16** and **34**–**37** were synthesized from the corresponding 8-nitroxanthines **1**–**7**, **30**–**33**, and 8-(phenylazo)xanthines **17** and **18** by catalytic reduction. Another approach was derived from 6-amino-5-(cyanoamino)uracils (= *N*-(6-amino-1,2,3,4-tetrahydro-2,4-dioxopyrimidin-5-yl)cyanamides) **23**, **24**, and **27** by base-catalyzed cyclization yielding **25**–**28**. All 8-aminoxanthines **8**–**29** and **34**–**37** were acetylated to the corresponding 8-(acetylamino)xanthines **40**–**57**, and prolonged heating led to 8-(diacetylamino)xanthines **58** and **59**. Several 8-aminoxanthines **8**–**13** were diazotized forming 8-diazoxanthines **60**–**64**. Coupling reactions of isolated **62** and **64** and intermediary formed 8-diazoxanthines with 1,3-dimethylbarbituric acid (= 1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione; **66**) resulted in 5-[(xanthin-8-yl)diazenyl]-1,3-dimethylbarbituric acids = 3,7(or 3,9)-dihydro-8-[2-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-diones) **67**–**80**. The newly synthesized xanthine derivatives were characterized by the determination of their pK_a values, the UV- and NMR spectra, as well as elemental analyses.

Introduction. – Ever since the structural elucidation of the purine-ring system by *Emil Fischer* in 1898 [2], this heterocycle [3] has attracted much attention due to its wide distribution in nature in form of alkaloids, intermediates or end products of metabolism, and nucleosides and nucleic acid components. Numerous purine derivatives have been synthesized by the *Traube* synthesis [4] starting from pyrimidine-5,6-diamines and fusing the imidazole moiety or by attachment of the pyrimidine ring onto properly substituted imidazole derivatives [5]. In continuation of our efforts in the purine field, we concentrated our interest, after the 8-nitroxanthines [6], now on the little investigated 8-amino-*N*-methylxanthine derivatives. A few derivatives of this type have been described in the literature [7–16], but no systematic investigations of their properties and reactivities has been reported.

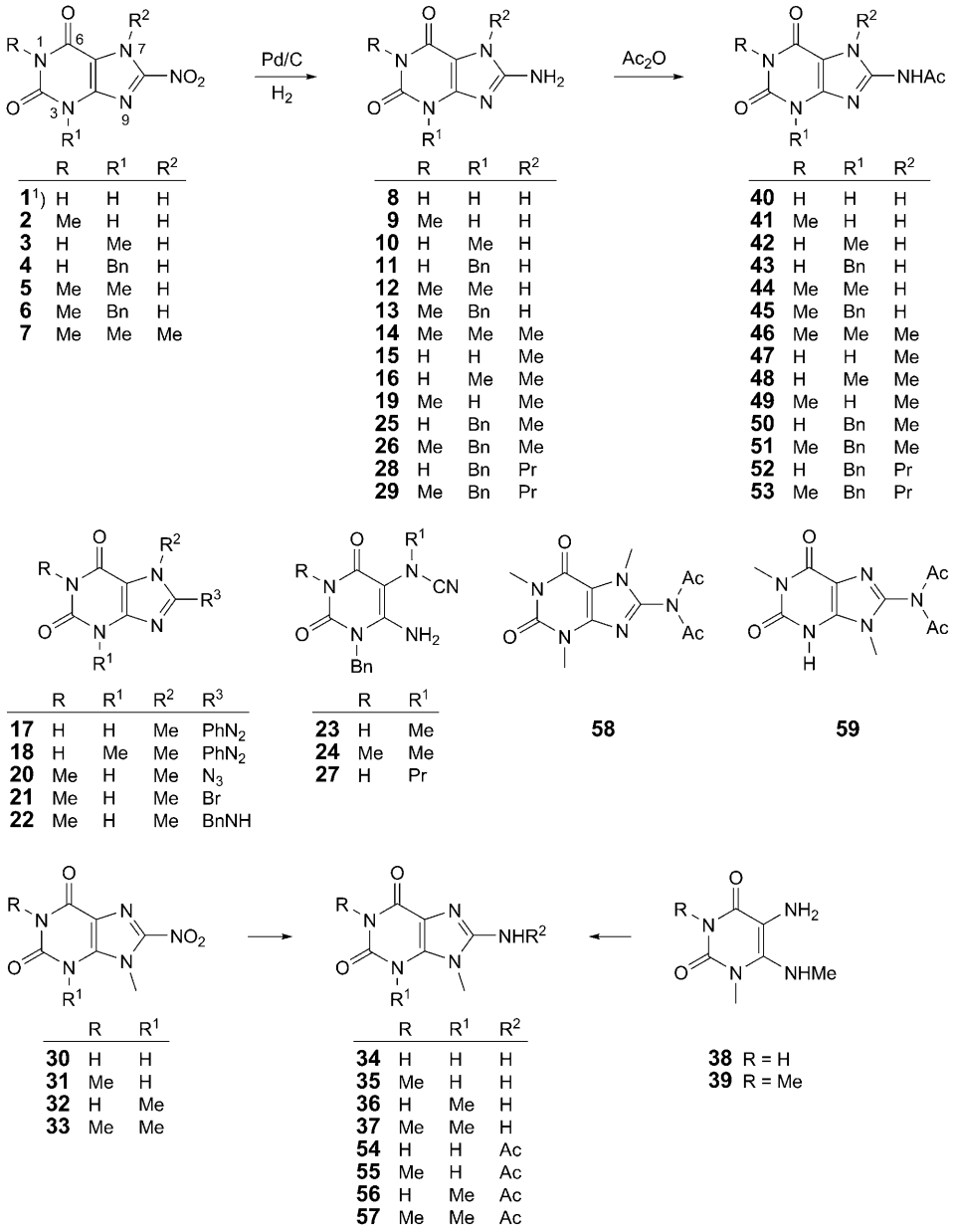
Synthesis. – The most straightforward syntheses of 8-aminoxanthines is the catalytic reduction of the corresponding 8-nitroxanthines of type **1**[2]) [6]. Thus, we obtained from **1** and its 1-methyl- (**2**), 3-methyl- (**3**), 3-benzyl- (**4**), 1,3-dimethyl- (**5**), 3-benzyl-1-methyl- (**6**), and 1,3,7-trimethyl derivative **7** with Pd/C catalyst and H_2 in a

[1]) Part XV: [1].

[2]) The xanthine structure has the same atom numbering as 1*H*-purine.

shaking apparatus in good yields the 8-aminoxanthines **8**–**14** (*Scheme 1*). Aminoxanthine **8** was prepared earlier by $Na_2S_2O_4$ reduction of 8-[(2,4-dichlorophenyl)azo]-[10][12] and 8-[(4-chlorophenyl)azo]xanthine [15], and 8-aminotheophylline (**12**) was synthesized from 8-chlorotheophylline with ethanolic ammonia [11] or by treatment of

Scheme 1



	R	R^1	R^2
1[1])	H	H	H
2	Me	H	H
3	H	Me	H
4	H	Bn	H
5	Me	Me	H
6	Me	Bn	H
7	Me	Me	Me

	R	R^1	R^2
8	H	H	H
9	Me	H	H
10	H	Me	H
11	H	Bn	H
12	Me	Me	H
13	Me	Bn	H
14	Me	Me	Me
15	H	H	Me
16	H	Me	Me
19	Me	H	Me
25	H	Bn	Me
26	Me	Bn	Me
28	H	Bn	Pr
29	Me	Bn	Pr

	R	R^1	R^2
40	H	H	H
41	Me	H	H
42	H	Me	H
43	H	Bn	H
44	Me	Me	H
45	Me	Bn	H
46	Me	Me	Me
47	H	H	Me
48	H	Me	Me
49	Me	H	Me
50	H	Bn	Me
51	Me	Bn	Me
52	H	Bn	Pr
53	Me	Bn	Pr

	R	R^1	R^2	R^3
17	H	H	Me	PhN_2
18	H	Me	Me	PhN_2
20	Me	H	Me	N_3
21	Me	H	Me	Br
22	Me	H	Me	BnNH

	R	R^1
23	H	Me
24	Me	Me
27	H	Pr

58 **59**

	R	R^1
30	H	H
31	Me	H
32	H	Me
33	Me	Me

	R	R^1	R^2
34	H	H	H
35	Me	H	H
36	H	Me	H
37	Me	Me	H
54	H	H	Ac
55	Me	H	Ac
56	H	Me	Ac
57	Me	Me	Ac

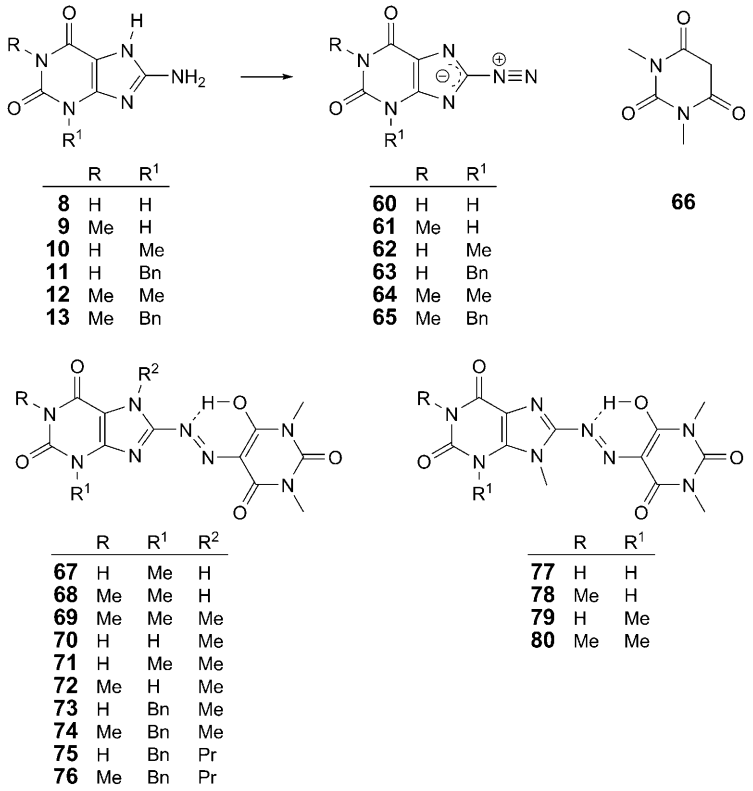
38 R = H
39 R = Me

8-(benzylamino)theophylline in concentrated H_2SO_4 solution at room temperature [16]. Aminoxanthine **14** was also obtained already in 1882 from 8-bromocaffeine in a sealed tube at 130° with saturated alcoholic ammonia [7]. The 8-amino-7-methylxanthine (**15**) [17] and 8-aminotheobromine (**16**) [18] resulted from catalytic reductions of the corresponding 8-(phenylazo) derivatives **17** and **18**, and 8-amino-1,7-dimethylxanthine (**19**) was obtained by three different routes: *i*) catalytic reduction of 8-azido-1,7-dimethylxanthine (**20**), *ii*) treatment of 8-bromo-1,7-dimethylxanthine (**21**) with methanolic ammonia in an autoclav at 160°, and *iii*) by reaction of 8-(benzylamino)-1,7-dimethylxanthine (**22**) with concentrated H_2SO_4 solution at 50° giving the best yield, *i.e.*, 82%. Another approach to 8-aminoxanthines was achieved by base-catalyzed cyclization of 6-amino-1-benzyl-5-[cyanomethylamino]uracil (=6-amino-1-benzyl-5-[cyano(methyl)amino]pyrimidine-2,4-(1*H*,3*H*)-dione = *N*-(6-amino-1-benzyl-1,2,3,4-tetrahydro-2,4-dioxopyrimidin-5-yl)-*N*-methylcyanamide; **23**) and its 3-methyl derivative **24** on treatment with 1N NaOH at 80° to give 8-amino-3-benzyl-7-methyl- (**25**) and 8-amino-3-benzyl-1,7-dimethylxanthine (**26**). Aminoxanthine **26** could also be obtained by methylation of **25** in DMF/K_2CO_3 with MeI. Analogously reacted 6-amino-1-benzyl-5-[cyano(propyl)amino]uracil (**27**) and its 3-methyl derivative to **28** and **29**. Since the 8-nitro-9-methylxanthines **30**–**33** are easily available by nitration [6], the corresponding 8-amino-9-methylxanthines **34**–**37** were prepared again by catalytic reductions. Furthermore, 5-amino-1-methyl- (**38**) and 5-amino-1,3-dimethyl-6-(methylamino)uracil (**39**) yielded on treatment with bromocyan at pH 4.5 and room temperature directly **36** and **37**. All synthesized 8-aminoxanthines were converted into the corresponding 8-(acetylamino) derivatives **40**–**57** by heating in Ac_2O for a time depending on the solubility of the starting material. Prolonged heating of 8-aminocaffeine (**14**) and 8-amino-1,9-dimethylxanthine (**35**) yielded the 8-(diacetylamino) derivatives **58** and **59**, of which **58** is described in [19][20] but has never been fully characterized.

Various 8-aminoxanthines have been applied to diazotization reactions which were tried for the first time by *Gomberg* in 1900 [21] starting with 8-aminocaffeine (**14**) but without success of isolation of the reaction product. More successful was *H. Fischer* [10] in 1909 with 8-aminoxanthine (**8**) and *Robins* [15] in 1960 with 8-aminotheophylline (**12**) isolating 8-diazoxanthine (**60**) and 8-diazotheophylline (**64**), respectively, as yellowish solids. Analogously reacted **8**–**13** at low temperature to the corresponding 8-diazoxanthines **60**–**65** in high yields (*Scheme 2*). According to the instability of the diazofunction on heating, recrystallization of the reaction products was not possible, but their characterization could be achieved by their UV and NMR spectra.

Coupling reactions of the 8-diazoxanthines **62** and **64** with 1,3-dimethylbarbituric acid (=1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione; **66**) led to the corresponding azo dyes **67** and **68** which exist most likely according to their NMR spectra in the (*E*)-form stabilized by an intramolecular H-bond but also other tautomeric forms cannot be excluded *a priori*. The 8-amino-7- and 8-amino-9-methylxanthines did not allow to isolate the corresponding diazonium salts indicating that the imidazole moiety is responsible for the stabilization of the zwitterion structures. To show that diazotizations of **14**–**16**, **19**, **25**, **26**, **28**, **29**, and **34**–**37** took place in solution, the corresponding diazonium salts were also coupled with 1,3-dimethylbarbituric acid (**66**) to give, in analogy to **67** and **68**, the azo dyes **69**–**80**. The 8-diazoxanthines are stable in acidic

Scheme 2



	R	R^1
8	H	H
9	Me	H
10	H	Me
11	H	Bn
12	Me	Me
13	Me	Bn

	R	R^1
60	H	H
61	Me	H
62	H	Me
63	H	Bn
64	Me	Me
65	Me	Bn

66

	R	R^1	R^2
67	H	Me	H
68	Me	Me	H
69	Me	Me	Me
70	H	H	Me
71	H	Me	Me
72	Me	H	Me
73	H	Bn	Me
74	Me	Bn	Me
75	H	Bn	Pr
76	Me	Bn	Pr

	R	R^1
77	H	H
78	Me	H
79	H	Me
80	Me	Me

solution but, in alkaline media, decomposition to unidentified products was observed. Interestingly, diazotheophylline (**64**) reacted in MeOH within 2 days to give 8-methoxy-1,3-dimethylxanthine [22] as shown in the *Figure*.

The UV spectra of 8-diazoxanthine (**60**) and 8-diazotheophylline (**64**) measured at pH 11 by *Jones* and *Robins* [15] have to be revised (*cf. Table 3*) since the authors have not realized the base lability of diazoxanthines leading to degradation.

Structures and Physical Properties. – The structures of the newly synthesized xanthine derivatives were characterized by UV spectra based on the pK_a values (*Tables 1–4*), by NMR spectra, and C,H,N analyses. Aminoxanthine **8** shows in the normal pH range one basic pK_a value at 2.00 and two acidic pK_a values at 8.48 and 12.01 describing the equilibria between cation (+) and neutral form (0), neutral form and monoanion (–) as well as monoanion and dianion (– –). The cations of all 8-aminoxanthines show very similar UV spectra indicating that protonation takes place in 7- or 9-position of the imidazole ring. The basic properties differ to some extent depending on the position of the various substituents. The 9-methyl derivatives are stronger bases than the 3-methyl- and 3-benzyl analogs which hinder partially the

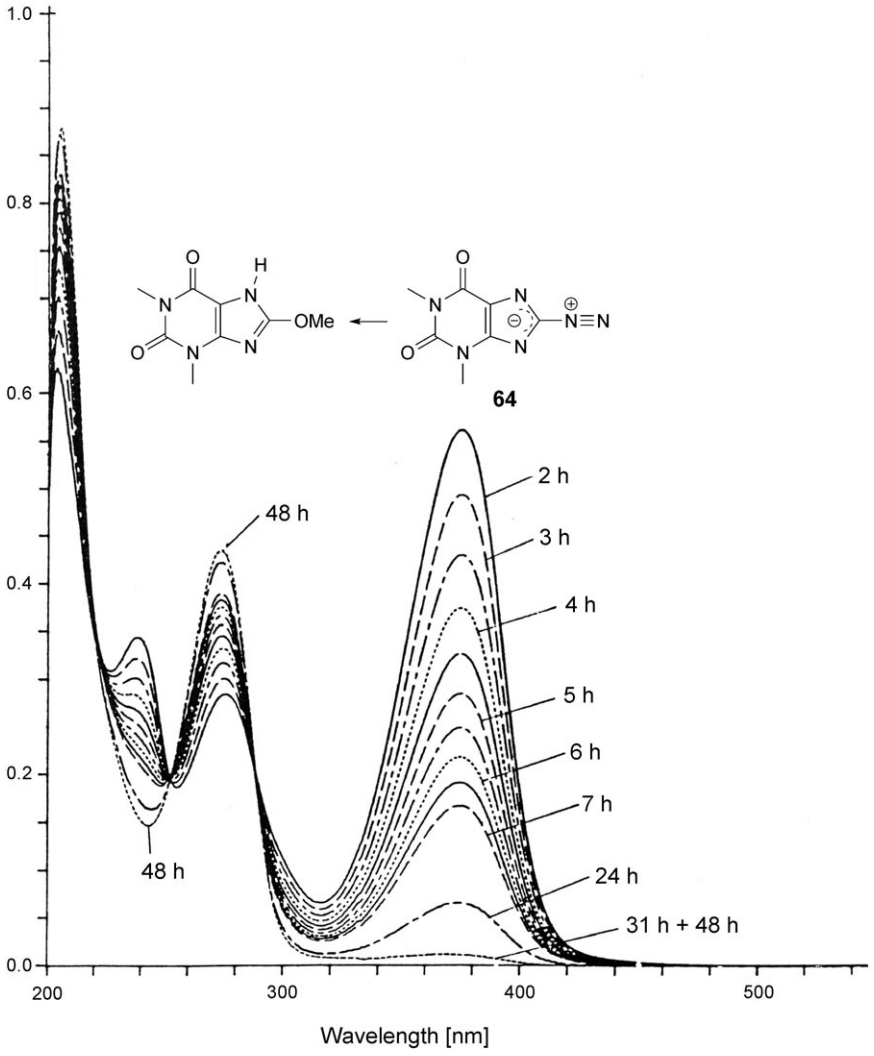


Figure. *Kinetics of 8-diazotheophylline* (**64**) *in MeOH in the dark*

adjacent protonation site (see, *e.g.*, **34** *vs.* **10** and **11**). The first deprotonation step takes place in the pyrimidine moiety at H–N(3) whereby a substituent at N(9) acidifies this H-atom again for steric reasons. The second ionization in 8-aminoxanthine (**8**) takes place at the NH of the imidazole ring as seen from the similarity of the second pK_a values of **9**–**11**. If the imidazole moiety is substituted, a second acidic pK_a value could not been determined in the normal pH range. The ionization sequence in the unsubstituted **8** can also be derived from the NMR spectra comparing the chemical shifts of the H–N sites with those of the various *N*-methyl derivatives.

Table 1. *Physical Properties of 8-Aminoxanthines*

	Substitution	pK_a	UV-Absorption spectra[a])		pH	Molecular form
			λ_{max}	log ε		
8	–	2.00	231, 278	4.05, 4.01	1.0	+
		8.48	[236], 287	[3.66], 4.21	6.0	0
		12.01	218, [247], 293	4.36, [3.75], 4.05	11.0	–
			[249], 294	[3.75], 4.02	2N NaOH	– –
9	1-methyl	2.12	233, 277	4.02, 4.07	1.0	+
		8.88	[238], 287	[3.60], 4.23	7.0	0
		12.44	216, [246], 291	4.40, [3.75], 4.09	11.0	–
			[250], 293	[3.72], 4.04	14.0	– –
10	3-methyl	1.29	235, 281	4.08, 4.09	– 1.0	+
		9.77	[240], 289	[3.66], 4.23	7.0	0
		12.72	214, [249], 292	4.21, [3.71], 4.14	11.0	–
			[247], 290	[3.70], 4.18	2N KOH	– –
11	3-benzyl	1.10	234, 281	4.02, 4.07	– 1.0	+
		9.42	[244], 290	[3.55], 4.22	5.0	0
		12.66	208, [250], 292	4.32, [3.64], 4.13	11.0	–
			228, 290	3.73, 4.13	14.3	– –
15	7-methyl	1.58	232, 277	4.06, 4.05	– 1.0	+
		8.97	[240], 289	[3.63], 4.21	6.0	0
			218, [246], 292	4.49, [3.64], 4.10	12.0	–
34	9-methyl	2.31	233, 278	3.99, 4.03	– 1.0	+
		6.59	241, 288	4.00, 3.99	6.0	0
			218, [246], 290	4.33, 4.03, 3.95	9.0	–
12	1,3-dimethyl	1.68	235, 282	3.96, 4.08	– 1.0	+
		10.20	[241], 289	[3.56], 4.22	6.0	0
			212, [255], 292	4.20, [3.67], 4.12	13.0	–
13	3-benzyl-1-methyl	1.34	234, 280	4.07, 4.15	– 1.0	+
		9.90	[244], 290	[3.52], 4.24	6.0	0
			212, [252], 294	4.31, [3.66], 4.15	13.0	–
19	1,7-dimethyl	1.85	233, 277	4.00, 4.02	– 1.0	+
		9.10	[240], 286	[3.60], 4.18	6.0	0
			218, [250], 291	4.47, [3.55], 4.07	12.0	–
16	3,7-dimethyl	1.33	235, 281	4.04, 4.03	– 1.0	+
		11.02	[240], 286	[3.70], 4.15	6.0	0
			214, [233], 285	4.17, [3.82], 4.18	13.0	–
25	3-benzyl-7-methyl	0.99	235, 281	4.05, 4.09	– 1.0	+
		10.80	[244], 290	[3.62], 4.23	6.0	0
			210, [234], 286	4.52, [3.92], 4.21	13.0	–
28	3-benzyl-7-propyl	0.88	235, 282	4.04, 4.09	– 1.0	+
		10.90	[246], 290	[3.59], 4.23	6.0	0
			210, [234], 287	4.51, [3.94], 4.21	13.0	–
35	1,9-dimethyl	3.26	234, 278	4.00, 4.09	– 1.0	+
		6.74	242, 287	4.02, 4.05	6.0	0
			207, 248, 290	4.41, 4.05, 3.99	9.0	–
36	3,9-dimethyl	3.66	236, 283	4.03, 4.02	– 1.0	+
		10.77	242, 290	4.01, 3.95	6.0	0
			213, 243, 284	4.30, 3.94, 3.96	9.0	–
26	3-benzyl-1,7-dimethyl	1.12	236, 280	4.01, 4.07	– 1.0	+
			[244], 289	[3.56], 4.21	6.0	0

Table 1 (cont.)

	Substitution	pK_a	UV-Absorption spectra[a])		pH	Molecular form
			λ_{max}	log ε		
29	3-benzyl-1-methyl-7-propyl	1.06	236, 281	4.00, 4.07	−1.0	+
			[244], 290	[3.50], 4.20	6.0	0
14	1,3,7-trimethyl	1.52	236, 280	3.97, 4.00	−1.0	+
			214, [245], 288	4.26, [3.54], 4.15	6.0	0
37	1,3,9-trimethyl	3.69	237, 283	3.95, 3.97	1.0	+
			244, 289	3.92, 3.89	6.0	0

[a]) Values within brackets are those of shoulders.

Similar conclusions can been drawn from the pK_a values and UV spectra of the 8-(acetylamino)xanthines **40**–**57** (*Table 2*). These xanthine derivatives are expectedly weaker bases than their precursors due to the acetylation of the amino groups.

The 8-diazoxanthines show a similar pattern identifying **60** and **61** as stronger acids as **62** indicating that the most acidic position is located at H–N(3). Anion formation at this site is associated with a strong bathochromic shift of the long-wavelength absorption band, whereas H–N(1) deprotonation in **62** causes a little red shift.

From a comparison of the pK_a values and UV spectra of the 5-[(xanthin-8-yl)diazenyl]-1,3-dimethylbarbituric acids **67**–**80** can be concluded that protonation in the cations takes place again at the imidazole moiety due to the very similar shape of the cation spectra (*Table 4*). The neutral molecular species are also very similar and exist most likely in the intramolecularly H-bonded (*E*)-form which show a characteristic signal in the NMR spectra at low field, at δ(H) 14.00–14.20. The first acidic pK_a in all derivatives is due to deprotonation at the barbituric acid moiety leading to a monoanion with an elongated chromophore associated with a red-shift of the long-wavelength absorption band.

Experimental Part

General. Products were dried under high vacuum. The pK_a values were determined by the spectrophotometric method [23]. M.p.: *Büchi-B-545* melting-point apparatus; uncorrected. TLC: precoated silica gel thin-layer sheets *60 F_{254}* (SiO_2; *Merck*) and cellulose sheets *F 1440 LS 254* (*Schleicher & Schüll*). Column chromatography (CC): SiO_2 *60* (*Merck*). Flash chromatography (FC): SiO_2 (30–60 μm; *Baker*). UV/VIS: *Perkin-Elmer Lambda 5*; λ_{max} (log ε) in nm, sh = shoulder. ^{1}H-NMR: *Bruker AC 250*; δ in ppm rel. to Me_4Si or $CDCl_3$ ((D$_6$)DMSO) as internal standard. Elemental analyses were performed by the Analytical Laboratory of the Department of Chemistry, Konstanz University.

1. *8-Aminoxanthine* (= *8-Amino-3,7-dihydro-1*H-*purine-2,6-dione*; **8**) [7][10][15]. A suspension of 8-nitroxanthine (**1**) [6] (0.6 g, 3.05 mmol) in H_2O (100 ml) was dissolved by addition of conc. NH_3 soln. (4 ml). Then 10% Pd/C (50 mg) was added and reduction performed in a shaking apparatus under H_2. When H_2 uptake stopped, the catalyst was filtered off and the filtrate acidified with AcOH (10 ml). The formed precipitate was washed with H_2O and dried to give 0.407 g (80%). Recrystallization from H_2O (900 ml) with charcoal gave 0.31 g (61%) of **8**. Colorless solid. M.p. >300°. ^{1}H-NMR ((D$_6$)DMSO): 10.30 (*s*, H–N(7)); 10.20 (br. *s*, H–N(1), H–N(3)); 6.30 (*s*, NH_2). Anal. calc. for $C_5H_5N_5O_2 \cdot 0.5\ H_2O$ (176.1): C 34.09, H 3.43, N 39.77; found: C 33.99, H 3.40, N 39.20.

2. *8-Amino-1-methylxanthine* (= *8-Amino-3,7-dihydro-1-methyl-1*H-*purine-2,6-dione*; **9**). To a soln. of 1-methyl-8-nitroxanthine (**2**) [6] (1.0 g, 4.74 mmol) in DMF (150 ml) was added 10% Pd/C (60 mg),

Table 2. *Physical Properties of 8-(Acetylamino)xanthines*

	Substitution	pK_a	UV-Absorption spectra[a])		pH	Molecular form
			λ_{max}	log ε		
40	–	– 0.60	247, 278	4.00, 4.22	– 3.0	+
		7.50	214, [241], 286	4.36, [3.79], 4.22	4.0	0
		10.92	219, [257], 290	4.17, [3.90], 4.12	9.0	–
			222, [248], 296	4.28, [4.03], 4.07	13.0	– –
41	1-methyl	– 0.51	250, 278	3.94, 4.22	– 3.0	+
		7.96	214, [240], 287	4.39, [3.71], 4.22	4.0	0
		11.12	218, [232], 291	4.19, [4.11], 4.11	9.0	–
			224, [240], 298	4.23, [4.19], 4.06	13.0	– –
42	3-methyl	– 1.31	248, 281	4.03, 4.14	– 4.0	+
		8.03	219, [244], 289	4.37, [3.76], 4.18	4.0	0
		11.91	217, [252], 286	4.24, [3.79], 4.15	10.0	–
			218, [236], 287	4.27, [3.92], 4.14	13.0	– –
43	3-benzyl		217, [235], 286	4.41, [4.00], 4.17	13.0	– –
47	7-methyl	– 0.39	245, 277	3.90, 4.23	– 3.0	+
		8.32	210, 277	4.30, 4.10	4.0	0
		11.35	215, 290	4.35, 3.98	10.0	–
			218, 295	4.33, 4.07	13.0	– –
54	9-methyl		216, 252, 286	4.27, 4.16, 4.16	13.0	– –
44	1,3-dimethyl	– 1.07	218, 256, 282	4.06, 4.02, 4.18	– 4.0	+
		8.16	219, [246], 289	4.42, [3.69], 4.22	4.0	0
			217, [254], 286	4.27, [3.79], 4.16	11.0	–
45	3-benzyl-1-methyl		217, [252], 286	4.29, [3.80], 4.14	11.0	–
49	1,7-dimethyl	– 0.14	[244], 278	[3.86], 4.26	– 4.0	+
		8.44	210, 277	4.39, 4.14	4.0	0
			216, 294	4.41, 4.35	11.0	–
48	3,7-dimethyl	– 1.09	[250], 279	[3.93], 4.17	– 4.0	+
		9.39	212, 280	4.32, 4.10	4.0	0
			213, [235], 288	4.31, [4.01], 4.18	12.0	–
50	3-benzyl-7-methyl		217, [236], 288	4.46, [3.97], 4.25	12.0	–
52	3-benzyl-7-propyl		216, [237], 288	4.60, [4.00], 4.32	12.0	–
55	1,9-dimethyl	0.86	250, 278	3.98, 4.19	– 1.0	+
		5.59	243, 266	4.00, 4.09	3.0	0
			254, 279	4.05, 4.04	8.0	–
56	3,9-dimethyl	0.10	255, 280	4.03, 4.06	– 1.0	+
		10.57	244, 269	4.00, 4.00	3.0	0
			218, 251, 282	3.89, 4.07	13.0	–
51	3-benzyl-1,7-dimethyl		210, 279	4.40, 4.14	MeOH	0
			223, 290	4.28, 4.22	13.0	–
53	3-benzyl-1-methyl-7-propyl		209, 278	4.39, 4.14	MeOH	0
			223, 290	4.33, 4.29	13.0	–
46	1,3,7-trimethyl	– 1.03	[248], 280	[3.92], 4.22	– 4.0	+
			214, 279	4.40, 4.10	MeOH	0
57	1,3,9-trimethyl	0.30	256, 280	4.06, 4.14	– 2.0	+
			245, 267	4.05, 4.03	MeOH	0

[a]) Values within brackets are those of shoulders.

Table 3. *Physical Properties of 8-Diazoxanthines*

	Substitution	pK_a	UV-Absorption spectra		pH	Molecular form
			λ_{max}	log ε		
60	–	7.68	234, 276, 366	4.03, 3.52, 4.37	5.0	0
			222, 250, 290, 411	3.92, 4.07, 3.69, 4.08	10.0	–
61	1-methyl	7.72	236, 282, 367	3.87, 3.54, 4.25	5.0	0
			228, 253, 298, 415	3.81, 3.99, 3.64, 4.00	10.0	–
62	3-methyl	9.37	237, 279, 371	4.10, 3.59, 4.35	5.0	0
			212, 239, 274, 384	4.11, 3.81, 3.78, 4.19	12.0	–
63	3-benzyl		238, 280, 370	4.14, 3.63, 4.31	5.0	0
64	1,3-dimethyl		239, 284, 372	4.03, 3.66, 4.31	7.0	0
65	3-benzyl-1-methyl		239, 286, 372	4.08, 3.70, 4.29	7.0	0

for reduction under H_2 in a shaking apparatus. After uptake of the theoretical amount of H_2 (320 ml), the catalyst was filtered off and the filtrate evaporated. The residue was washed with H_2O and then recrystallized from H_2O: 0.592 g (69%) of **9**. Colorless solid. M.p. $>300°$. ^{1}H-NMR ((D_6)DMSO): 10.60 (*s*, H–N(7)); 10.20 (*s*, H–N(3)); 6.30 (*s*, NH_2); 3.20 (*s*, Me–N(1)). Anal. calc. for $C_6H_7N_5O_2 \cdot 0.25\ H_2O$ (185.2): C 38.81, H 3.94, N 37.72; found: C 39.05, H 3.83, N 37.77.

3. *8-Amino-3-methylxanthine* (=*8-Amino-3,7-dihydro-3-methyl-1*H-*purine-2,6-dione*; **10**). As described for **9**, with 3-methyl-8-nitroxanthine (**3**) [6] (1.0 g, 4.74 mmol), DMF (100 ml), and 10% Pd/C (60 mg): 0.496 g (58%) of **10**. Colorless solid. M.p. $>300°$. ^{1}H-NMR ((D_6)DMSO): 11.50 (*s*, H–N(7)); 10.80 (*s*, H–N(1)); 6.45 (*s*, NH_2); 3.40 (*s*, Me–N(1)). Anal. calc. for $C_6H_7N_5O_2$ (181.2): C 39.78, H 3.90, N 38.66; found: C 39.38, H 4.08, N 38.41.

4. *8-Amino-3-benzylxanthine* (=*8-Amino-3-benzyl-3,7-dihydro-1*H-*purine-2,6-dione*; **11**). To a soln. of 3-benzyl-8-nitroxanthine (**4**) [6] (1.5 g, 5.23 mmol) in H_2O (300 ml) and conc. NH_3 soln. (5 ml), 10% Pd/C was added and reduction achieved under H_2 in a shaking apparatus. When reduction stopped, the catalyst was filtered off, and the filtrate evaporated. The residue was treated with H_2O and filtered, and the solid recrystallized from dil. AcOH with charcoal: 0.806 g (60%) of **11**. Colorless crystals. M.p. 350–352°. ^{1}H-NMR ((D_6)DMSO): 11.29 (*s*, H–N(7)); 10.60 (*s*, H–N(1)); 7.35–7.25 (*m*, 5 arom. H); 6.45 (*s*, NH_2); 5.04 (*s*, CH_2). Anal. calc. for $C_{12}H_{11}N_5O_2$ (257.3): C 56.02, H 4.31, N 27.23; found: C 55.70, H 4.63, N 26.82.

5. *8-Amino-1,3-dimethylxanthine* (=*8-Amino-3,7-dihydro-1,3-dimethyl-1*H-*purine-2,6-dione*; **12**) [15][16]. *i*) As described for **11**, with 8-nitrotheophylline (**5**) [6] (1.2 g, 5.33 mmol), Pd/C (80 mg), H_2O (200 ml) and conc. NH_3 soln. (2 ml): 0.541 g (52%) of **12**. Colorless powder. M.p. $>310°$.

ii) A suspension of **5** (0.8 g, 3.56 mmol) in H_2O (15 ml) was treated at 90° under stirring with $Na_2S_2O_4$ (2.0 g) by gradual addition. After 1 h, the soln. was cooled overnight, and the solid recrystallized from dil. AcOH: 0.263 g (38%) of **12**. Colorless crystals. M.p. $>310°$. ^{1}H-NMR ((D_6)DMSO): 11.65 (*s*, H–N(7)); 6.45 (*s*, NH_2); 3.40 (*s*, Me–N(3)); 3.20 (*s*, Me–N(1)). Anal. calc. for $C_7H_9N_5O_2$ (195.2): C 43.02, H 4.64, N 35.88; found: C 43.06, H 4.46, N 35.49.

6. *8-Amino-3-benzyl-1-methylxanthine* (=*8-Amino-3-benzyl-3,7-dihydro-1-methyl-1*H-*purine-2,6-dione*; **13**). A soln. of 3-benzyl-1-methyl-8-nitroxanthine (**6**) [6] (0.5 g, 1.66 mmol) in H_2O (50 ml) and 10% KOH soln. (2 ml) was treated with Pd/C (50 mg) and H_2 in a shaking apparatus. After uptake of 110 ml of H_2, the mixture was filtered and the filtrate neutralized by AcOH and partially concentrated. The resulting precipitate was purified by dissolving in H_2O (50 ml) and dil. H_2SO_4 soln., heating, treatment with charcoal, and neutralization by NH_3: 0.297 g (66%) of **13**. Colorless crystals. M.p. 365–368°. ^{1}H-NMR ((D_6)DMSO): 9.80 (*s*, H–N(7)); 10.60 (*s*, H–N(1)); 7.35–7.25 (*m*, 5 arom. H); 6.49 (*s*, NH_2); 5.07 (*s*, CH_2); 3.18 (*s*, Me–N(1)). Anal. calc. for $C_{13}H_{13}N_5O_2$ (271.3): C 57.56, H 4.80, N 25.83; found: C 57.53, H 4.92, N 25.56.

7. *8-Amino-1,3,7-trimethylxanthine* (=*8-Amino-3,7-dihydro-1,3,7-trimethyl-1*H-*purine-2,6-dione*; **14**) [20]. A soln. of 8-nitrocaffeine (**7**) [6] (1.5 g, 6.28 mmol) in H_2O/MeOH 1:1 (200 ml) was treated with

Table 4. *Physical Properties of 5-[(Xanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acids*

	Substitution	pK_a	UV-Absorption spectra		pH	Molecular form
			λ_{max}	log ε		
67	3-methyl	−1.95	230, 267, 386	4.02, 4.22, 4.28	−4.0	+
		5.26	224, 272, 411	4.06, 4.21, 4.27	0.0	0
		9.06	215, 235, 276, 408, 445	4.17, 4.12, 4.02, 4.29, 4.37	7.0	−
			205, 240, 281, 394, 437	4.31, 4.04, 3.94, 4.37, 4.35	11.0	− −
68	1,3-dimethyl	−1.55	230, 266, 388	3.98, 4.19, 4.26	−4.0	+
		5.13	230, 272, 414	4.24, 4.02, 4.28	1.0	0
		9.48	216, 240, 274, 416, 446	4.16, 4.10, 3.97, 4.30, 4.36	7.0	−
			240, 282, 394, 436	4.02, 3.92, 4.38, 4.33	13.0	− −
70	7-methyl		211, 225, 290, 413	4.14, 4.33, 4.02, 4.38	13.0	− −
77	9-methyl	−0.22	228, 261, 384	4.06, 4.24, 4.23	−4.0	+
		4.29	238, 266, 409	4.12, 4.13, 4.25	0.0	0
			233, 283, 428, 450	4.23, 4.07, 4.24, 4.31	7.0	−
72	1,7-dimethyl	−1.13	227, 266, 387	3.98, 4.15, 4.29	−3.0	+
		4.72	238, 270, 408	3.99, 4.10, 4.31	2.0	0
		9.17	218, 235, 273, 405, 442	4.18, 4.12, 3.85, 4.44, 4.38	7.0	−
			223, 248, 281, 418, 452	4.34, 4.01, 3.88, 4.33, 4.36	12.0	− −
71	3,7-dimethyl	−1.74	230, 269, 388	4.01, 4.17, 4.27	−4.0	+
		4.13	208, 232, 275, 408	4.25, 4.00, 4.13, 4.29	1.0	0
			220, 242, 279, 406, 441	4.21, 4.08, 3.86, 4.43, 4.37	7.0	−
73	3-benzyl-7-methyl		218, 253, 274, 410, 453	4.30, 4.04, 3.99, 4.47, 4.38	13.0	− −
75	3-benzyl-7-propyl		220, 250, 278, 410, 450	4.37, 4.15, 4.01, 4.48, 4.44	13.0	− −
78	1,9-dimethyl	−0.08	230, 260, 386	4.05, 4.25, 4.25	−3.0	+
		4.51	240, 266, 411	4.14, 4.14, 4.30	2.0	0
			237, 282, 426, 461	4.20, 4.00, 4.25, 4.34	7.0	−
79	3,9-dimethyl	−0.54	234, 266, 386	4.03, 4.26, 4.19	−4.0	+
		4.66	238, 271, 408	4.10, 4.16, 4.22	2.0	0
			226, 237, 285, 403, 444	4.18, 4.15, 3.93, 4.34, 4.30	9.0	−
			233, 249, 414, 455	4.15, 4.09, 3.86, 4.29, 4.38	13.0	− −
74	3-benzyl-1,7-dimethyl	−2.35	230, 268, 390	4.04, 4.19, 4.28	−4.2	+
		4.10	242, 274, 410	4.00, 4.16, 4.30	2.0	0
			218, 242, 280, 407, 445	4.25, 4.10, 3.88, 4.43, 4.39	7.0	−
76	3-benzyl-1-methyl-7-propyl	−2.19	232, 269, 394	4.02, 4.19, 4.27	−4.0	+
		4.87	241, 274, 413	4.01, 4.15, 4.30	2.0	0
			248, 280, 407, 446	4.07, 3.88, 4.41, 4.37	7.0	−
69	1,3,7-trimethyl	−1.62	231, 268, 390	3.97, 4.13, 4.24	−4.0	+
		3.92	206, 239, 274, 410	4.28, 3.97, 4.09, 4.27	1.0	0
			220, 242, 278, 406, 444	4.15, 4.03, 3.77, 4.39, 4.33	7.0	−
80	1,3,9-trimethyl	−0.36	234, 265, 388	4.03, 4.26, 4.20	−3.0	+
		4.38	240, 272, 410	4.01, 4.14, 4.23	2.0	0
			228, 236, 284, 404, 444	4.19, 4.16, 3.92, 4.33, 4.30	7.0	−

10% Pd/C (0.1 g) under H_2 in a shaking apparatus. After uptake of H_2 stopped, the catalyst was filtered off, and the filtrate concentrated. The residue was purified by recrystallization from EtOH/AcOH: 0.563 g (43%) of **14**. Colorless crystals. M.p. >300°. ^{1}H-NMR ((D$_6$)DMSO): 6.80 (*s*, NH_2); 3.60 (*s*, Me−N(7)); 3.40 (*s*, Me−N(3)); 3.25 (*s*, Me−N(1)). Anal. calc. for $C_8H_{11}N_5O_2$ (209.2): C 45.93, H 5.30, N 33.48; found: C 46.01, H 5.42, N 32.90.

8. *8-Amino-7-methylxanthine* (= *8-Amino-3,7-dihydro-7-methyl-1*H-*purine-2,6-dione*; **15**). A soln. of 7-methyl-8-(phenylazo)xanthine (**17**; 0.5 g, 4.0 mmol) in H_2O (200 ml) and 1N KOH (10 ml) was reduced by 10% Pd/C (80 mg) under H_2 in a shaking apparatus. The catalyst was filtered off, and the filtrate acidified by AcOH. After evaporation to half of the volume, the formed precipitate was recrystallized from dil. AcOH with charcoal: 0.521 g (72%) of **15**. Colorless powder. M.p. >320°. ^{1}H-NMR ((D_6)DMSO): 10.70 (br. *s*, H–N(3), H–N(1)); 6.54 (*s*, NH_2); 3.60 (*s*, Me–N(7)). Anal. calc. for $C_6H_7N_5O_2$ (181.2): C 39.78, H 3.90, N 38.66; found: C 39.80, H 3.90, N 38.65.

9. *8-Amino-3,7-dimethylxanthine* (= *8-Amino-3,7-dihydro-3,7-dimethyl-1*H-*purine-2,6-dione*; **16**) [18]. As described for **15**, with 8-(phenylazo)theobromine (**18**; 1.4 g, 4.93 mmol) and 10% Pd/C (75 mg) in H_2O (400 ml) and 1N KOH (25 ml). The catalyst was filtered off after uptake of 220 ml of H_2. The filtrate was acidified by AcOH and then concentrated to half of the volume, and the formed precipitate recrystallized from dil. AcOH (500 ml) with charcoal: 0.442 g (46%) of **16**. Colorless crystals. M.p. >300°. ^{1}H-NMR ((D_6)DMSO): 10.40 (*s*, H–N(1)); 6.80 (*s*, NH_2); 3.55 (*s*, Me–N(7)); 3.25 (*s*, Me–N(3)). Anal. calc. for $C_7H_9N_5O_2$ (195.2): C 43.08, H 4.64, N 35.88; found: C 42.83, H 4.98, N 36.00.

10. *7-Methyl-8-(phenylazo)xanthine* (= *3,7-Dihydro-7-methyl-8-(2-phenyldiazenyl)-1*H-*purine-2,6-dione*; **17**). A mixture of 8-(phenylazo)xanthine [24] (2.6 g, 10.2 mmol), K_2CO_3 (1.41 g, 10.2 mmol), and MeI (0.8 ml, 12.85 mmol) in DMF (100 ml) and dry acetone (100 ml) was stirred at r.t. for 12 h. After evaporation to half of the volume and addition of H_2O (300 ml) under stirring, the resulting precipitate was recrystallized from AcOH (200 ml): 1.62 g (59%) of **17**. Orange crystals. M.p. 307–309°. UV (pH 6): 230 (3.97), 260 (3.77), 310 (3.80), 398 (4.27), 450 (sh, 3.86). ^{1}H-NMR ((D_6)DMSO): 12.28 (*s*, H–N(3)); 11.50 (*s*, H–N(1)); 8.30–7.69 (*m*, 5 arom. H); 4.41(*s*, Me–N(7)). Anal. calc. for $C_{12}H_{10}N_6O_2 \cdot 0.5\ H_2O$ (279.3): C 51.61, H 3.94, N 30.11; found: C 51.20, H 4.20, N 29.71.

11. *3,7-Dimethyl-8-phenylazoxanthine* (= *3,7-Dihydro-3,7-dimethyl-8-(2-phenyldiazenyl)-1*H-*purine-2,6-dione*; **18**). As described for **17**, with 3-methyl-8-(phenylazo)xanthine (2.70 g, 10 mmol), K_2CO_3 (1.38 g, 10 mmol), MeI (1 ml, 16 mmol), DMF (100 ml), and abs. acetone (200 ml). After stirring for 12 h at r.t., the acetone was evaporated and the remaining soln. diluted with H_2O (100 ml). The precipitate was collected and recrystallized from AcOH (200 ml): 2.13 g (75%) of **18**. Orange crystals. M.p. 312°. UV (pH 7): 232 (4.04), 266 (sh, 3.87), 326 (3.91), 404 (4.26). ^{1}H-NMR (CF_3COOD): 8.20–7.5 (*m*, 5 arom. H); 4.55 (*s*, Me–N(7)); 3.80 (*s*, Me–N(3)). Anal. calc. for $C_{13}H_{12}N_6O_2$ (284.3): C 54.92, H 4.26, N 29.56; found: C 54.65, H 4.41, N 29.37.

12. *8-Amino-1,7-dimethylxanthine* (= *8-Amino-3,7-dihydro-1,7-dimethyl-1*H-*purine-2,6-dione*; **19**). *i*) A soln. of 8-azido-1,7-dimethylxanthine (**20**; 0.15 g, 0.68 mmol) in EtOH (100 ml) was catalytically reduced by 10% Pd/C (75 mg) under H_2 in a shaking apparatus. After stop of the H_2-uptake, the mixture was heated and filtered and the filtrate concentrated. The residue was recrystallized from 50% AcOH: 60 mg (45%) of **19**. Colorless powder. M.p. >350°.

ii) A mixture of 8-bromo-1,7-dimethylxanthine (**21**; 0.26 g, 1.0 mmol) in sat. methanolic ammonia (20 ml) was heated in an autoclav to 160° for 30 h. After cooling, the mixture was concentrated and the residue recrystallized from 50% AcOH: 74 mg (38%) of **19**.

iii) A soln. of 8-(benzylamino)-1,7-dimethylxanthine (**22**; 0.56 g, 1.97 mmol) in conc. H_2SO_4 soln. (7 ml) was heated in an oilbath to 50° for 20 min. After cooling, the mixture was poured into ice water (70 ml), and then the pH was adjusted to 6–7 with 10% KOH soln. The mixture was stirred overnight, and the obtained precipitate recrystallized from AcOH/H_2O 1:1 (100 ml): 0.314 g (82%) of **19**. Colorless crystals. M.p. >350°. ^{1}H-NMR ((D_6)DMSO): 11.47 (*s*, H–N(3)); 6.68 (*s*, NH_2); 3.52 (*s*, Me–N(7)); 3.12 (*s*, Me–N(1)). Anal. calc. for $C_7H_9N_5O_2$ (195.2): C 43.08, H 4.64, N 35.88; found: C 43.02, H 4.62, N 35.65.

13. *8-Hydrazino-1,7-dimethylxanthine* [25]. A mixture of 8-bromo-1,7-dimethylxanthine (**21**; 1.0 g, 3.86 mmol) and 99% hydrazine hydrate (50 ml) was heated in an oilbath to 100° with stirring for 30 min. The precipitate formed was collected after cooling, washed with EtOH, and dried at 80°: 0.64 g (79%) of fine needles. M.p. 293–295° (dec.). UV (pH 13): 216 (4.23), 236 (sh, 3.75), 288 (3.91). ^{1}H-NMR ((D_6)DMSO): 11.60 (*s*, H–N(3)); 8.01 (br. *s*, NH–C(8)); 4.30 (br. *s*, NH_2); 3.49 (*s*, Me–N(7)); 3.10 (*s*, Me–N(1)). Anal. calc. for $C_7H_{10}N_6O_2$ (210.2): C 40.00, H 4.80, N 39.99; found: C 40.17, H 4.76, N 39.40.

14. *8-Azido-1,7-dimethylxanthine* (= *8-Azido-3,7-dihydro-1,7-dimethyl-1*H-*purine-2,6-dione*; **20**). A soln. of 8-hydrazino-1,7-dimethylxanthine (0.4 g, 1.91 mmol) in 3% HCl soln. (40 ml) was cooled in ice to 0–5°, and then under stirring, a soln. of $NaNO_2$ (0.15 g, 2.17 mmol) in H_2O (5 ml) was added dropwise.

After 30 min, the mixture was neutralized with 1N $NaHCO_3$. The formed precipitate was recrystallized from EtOH/H_2O 2:1 (60 ml): 0.219 g (52%) of **20**. Yellowish crystals. M.p. 185–190°. UV (MeOH): 218 (3.99), 289 (4.11). ^{1}H-NMR ((D$_6$)DMSO): 11.95 (*s*, H–N(3)); 3.59 (*s*, Me–N(7)); 3.14 (*s*, Me–N(1)). Anal. calc. for $C_7H_7N_7O_2$ (221.2): C 38.01, H 3.17, N 44.34; found: C 38.01, H 3.23, N 43.96.

15. *8-Bromo-1,7-dimethylxanthine* (= *8-Bromo-3,7-dihydro-1,7-dimethyl-1*H-*purine-2,6-dione*; **21**). To a warm soln. of 1,7-dimethylxanthine [26] (5.0 g, 27.78 mmol) in AcOH (50 ml) was dropwise added bromine (3 ml, 51.8 mmol). Then, the mixture was heated to 80° for 2 h. After cooling, the mixture was diluted with acetone (500 ml), and the formed precipitate purified by recrystallization from AcOH/EtOH 1:2 (250 ml): 3.02 g (42%) of **21**. Colorless crystals. M.p. 305–307°. UV (pH 13): 218 (4.49), 249 (sh, 3.84), 293 (3.98). ^{1}H-NMR (CF_3COOD): 4.10 (*s*, Me–N(7)); 3.50 (*s*, Me–N(1)). Anal. calc. for $C_7H_7BrN_4O_2$ (259.1): C 32.45, H 2.72, N 21.63; found: C 32.66, H 2.76, N 21.85.

16. *8-(Benzylamino)-1,7-dimethylxanthine* (= *8-(Benzylamino)-3,7-dihydro-1,7-dimethyl-1*H-*purine-2,6-dione*; **22**). A mixture of **21** (1.0 g, 3.86 mmol) in dist. benzylamine (10 ml) was heated in an oilbath with stirring to 130°. After 1 h, the mixture was cooled, diluted with H_2O (50 ml), and then extracted with $CHCl_3$. The $CHCl_3$ extract was dried (Na_2SO_4) and concentrated, and the residue stirred in Et_2O for 30 min. The resulting solid was then recrystallized from EtOH (20 ml): 0.68 g (62%) of **22**. Slightly yellowish crystals. M.p. 223–224°. UV (pH 13): 222 (4.68), 297 (4.28). ^{1}H-NMR ((D$_6$)DMSO): 11.53 (*s*, H–N(3)); 7.52 (*t*, NH–C(8)); 7.31–7.22 (*m*, 5 arom. H); 4.50 (*d*, CH_2); 3.58 (*s*, Me–N(7)); 3.09 (*s*, Me–N(1)). Anal. calc. for $C_{14}H_{15}N_5O_2$ (285.3): C 58.93, H 5.30, N 24.55; found: C 59.01, H 5.34, N 24.23.

17. *6-Amino-1-benzyl-5-[cyano(methyl)amino]uracil* (= N-*(6-Amino-1-benzyl-1,2,3,4-tetrahydro-2,4-dioxopyrimidin-5-yl)*-N-*methylcyanamide*; **23**). To a soln. of 6-amino-1-benzyl-5-(methylamino)uracil [26] (1.0 g, 4.07 mmol) in AcOH (10 ml) were added a soln. of $NaHCO_3$ (0.8 g) in H_2O (3 ml) and then bromocyan (0.5 g, 4.72 mmol). After 1 h, H_2O (10 ml) was added, and the mixture stirred overnight. The obtained precipitate was washed with H_2O and EtOH and dried under high vacuum: 1.0 g (91%) of crude **23**. Recrystallization from H_2O/EtOH 1:1 (100 ml) gave 0.84 g (76%) of **23**. Colorless crystals. M.p. 287–299°. UV (MeOH): 203 (4.23), 264 (4.28). ^{1}H-NMR ((D$_6$)DMSO): 10.95 (*s*, H–N(3)); 7.37–7.16 (*m*, 5 arom. H, NH_2); 5.06 (*s*, CH_2); 2.90 (*d*, MeN–C(5)). Anal. calc. for $C_{13}H_{13}N_5O_2$ (271.3): C 57.55, H 4.80, N 25.83; found: C 57.03, H 4.86, N 25.49.

18. *6-Amino-1-benzyl-5-[cyano(methyl)amino]-3-methyluracil* (= N-*(6-Amino-1-benzyl-1,2,3,4-tetrahydro-3-methyl-2,4-dioxopyrimidin-5-yl)*-N-*methylcyanamide*; **24**). As described for **23**, with 6-amino-1-benzyl-5-(methylamino)-3-methyluracil [26] (1.0 g, 3.85 mmol) and bromocyan (0.5 g, 4.72 mmol). Recrystallization from EtOH (90 ml) gave 0.9 g (82%) of **24**. Colorless crystals. M.p. 195°, solidifing and a second m.p. at 223°. UV (MeOH): 203 (4.30), 264 (4.28). ^{1}H-NMR ((D$_6$)DMSO): 7.37–6.90 (*m*, 5 arom. H, NH_2); 5.12 (*s*, CH_2); 3.14 (*s*, Me–N(3)); 2.90 (*d*, MeN–C(5)). Anal. calc. for $C_{14}H_{15}N_5O_2$ (285.3): C 58.93, H 5.30, N 24.55; found: C 58.87, H 5.28, N 24.28.

19. *8-Amino-3-benzyl-7-methylxanthine* (= *8-Amino-3-benzyl-3,7-dihydro-7-methyl-1*H-*purine-2,6-dione*; **25**). A soln. of **23** (0.8 g, 2.95 mmol) in 1N NaOH (15 ml) was stirred at r.t. for 10 h and then diluted with H_2O (30 ml) and neutralized with AcOH. The resulting precipitate was washed with H_2O and dried to give 0.712 g (89%) of chromatographically pure **25**. Recrystallization from H_2O/EtOH 1:1 (100 ml) gave 0.84 g (76%) of **25**. Colorless crystals. M.p. 305–306°. ^{1}H-NMR ((D$_6$)DMSO): 10.65 (*s*, H–N(1)); 7.35–7.27 (*m*, 5 arom. H); 6.83 (*s*, NH_2); 5.01 (*s*, CH_2); 3.54 (*s*, Me–N(3)). Anal. calc. for $C_{13}H_{13}N_5O_2$ (271.3): C 57.55, H 4.80, N 25.83; found: C 57.47, H 4.83, N 25.82.

20. *8-Amino-3-benzyl-1,7-dimethylxanthine* (= *8-Amino-3-benzyl-3,7-dihydro-1,7-dimethyl-1*H-*purine-2,6-dione*; **26**). *i*) As described for **25** with **24** (0.8 g, 1.4 mmol) by boiling in 1N NaOH (20 ml) and EtOH (20 ml) for 30 min. The mixture was neutralized with AcOH, and the precipitate recrystallized from EtOH (40 ml): 0.52 g (65%) of **26**. Colorless crystals. M.p. 224–225°.

ii) A mixture of **25** (0.2 g, 0.74 mmol), K_2CO_3 (0.1 g, 0.72 mmol), and MeI (0.2 ml) in DMF (20 ml) was stirred at r.t. for 24 h and then concentrated. The residue was treated with H_2O (50 ml), and the resulting solid recrystallized from EtOH (15 ml): 0.12 g (57%) of **26**. Colorless crystals. M.p. 224–225°. ^{1}H-NMR ((D$_6$)DMSO): 7.27 (*m*, 5 arom. H); 6.88 (*s*, NH_2); 5.00 (*s*, CH_2); 3.57 (*s*, Me–N(7)); 3.17 (*s*, Me–N(1)). Anal. calc. for $C_{14}H_{15}N_5O_2$ (285.3): C 58.93, H 5.30, N 24.55; found: C 58.75, H 5.64, N 24.00.

21. *6-Amino-1-benzyl-5-(propylamino)uracil* (= *6-Amino-1-benzyl-5-(propylamino)pyrimidine-2,4(1*H,*3*H*)-dione*). A suspension of 6-amino-1-benzyl-5-bromouracil [26] (15.4 g, 52.03 mmol) in 50% aq. propylamine (50 ml) was heated in an autoklav to 80° for 5 h. After cooling, the formed precipitate was washed with MeOH (20 ml) and Et_2O (20 ml) and dried in a vacuum desiccator: 9.27 g of crude product. Recrystallization from PrOH (500 ml) gave 7.84 g (55%) of a yellowish powder. M.p. 204–206°. ^{1}H-NMR ((D$_6$)DMSO): 10.58 (br. *s*, H–N(3)); 7.35–7.10 (*m*, 5 arom. H); 6.33 (*s*, NH_2); 5.00 (*s*, CH_2N); 2.75 (br. *s*, NH–C(5)); 2.60 (*t*, $MeCH_2CH_2N$); 1.45–1.20 (*m*, $MeCH_2CH_2N$); 0.80–0.60 (*t*, *Me*CH_2CH_2). Anal. calc. for $C_{14}H_{18}N_4O_2$ (274.3): C 61.30, H 6.61, N 20.43; found: C 61.12, H 6.50, N 20.28.

22. *6-Amino-1-benzyl-5-[cyano(propyl)amino]uracil* (= N-*(6-Amino-1-benzyl-1,2,3,4-tetrahydro-2,4-dioxopyrimidin-5-yl)*-N-*propylcyanamide*; **27**). A suspension of 6-amino-1-benzyl-5-(propylamino)uracil (4.0 g, 14.6 mmol) in 1N AcOH/0.5M AcONa (100 ml; pH 4.5) was treated with bromocyan (2.0 g, 18.80 mmol) at r.t. for 15 h. The obtained precipitate was recrystallized from EtOH (200 ml): 3.0 g (69%) of **27**. Colorless crystals. M.p. 259–260°. UV (MeOH): 203 (4.25), 265 (4.29). ^{1}H-NMR ((D$_6$)DMSO): 10.90 (br. *s*, H–N(3)); 7.29–7.00 (*m*, 5 arom. H, NH_2); 5.09 (*s*, $CH_2N(1)$); 3.21–2.89 (br. *t*, $MeCH_2CH_2N$); 1.63–1.38 (*m*, $MeCH_2CH_2N$); 0.97–0.80 (br. *t*, *Me*CH_2CH_2). Anal. calc. for $C_{15}H_{17}N_5O_2$ (299.3): C 60.20, H 5.69, N 23.41; found: C 60.14, H 5.66, N 23.60.

23. *8-Amino-3-benzyl-7-propylxanthine* (= *8-Amino-3-benzyl-3,7-dihydro-7-propyl-1*H-*purine-2,6-dione*; **28**). Addition of **27** (2.0 g, 6.69 mmol) to 1N NaOH (100 ml) under stirring gave a soln. from which, after 5 min, a solid precipitated. The suspension was stirred at r.t. for 2 h and then acidified with AcOH (30 ml). The formed precipitate was washed with H_2O and EtOH, dried, and then recrystallized from EtOH/H_2O 4:1 (100 ml): 1.6 g (80%) of **28**. Colorless crystals. M.p. 263–264°. ^{1}H-NMR ((D$_6$)DMSO): 10.80 (br. *s*, H–N(3)); 7.35–7.25 (*m*, 5 arom. H); 6.90 (*s*, NH_2); 5.02 (*s*, $CH_2N(3)$); 4.20–3.90 (*t*, $MeCH_2CH_2N$); 1.90–1.60 (*m*, $MeCH_2CH_2N$); 0.90 (br. *t*, *Me*CH_2CH_2). Anal. calc. for $C_{15}H_{17}N_5O_2$ (299.3): C 60.20, H 5.69, N 23.41; found: C 60.32, H 5.74, N 23.53.

24. *8-Amino-3-benzyl-1-methyl-7-propylxanthine* (= *8-Amino-3-benzyl-3,7-dihydro-1-methyl-7-propyl-1*H-*purine-2,6-dione*; **29**). A soln. of **28** (0.8 g, 2.68 mmol) in 1N NaOH (20 ml) was heated to 40°, and then Me_2SO_4 (0.4 ml, 4.22 mmol) was added dropwise. The mixture was stirred for 15 h at r.t., and the formed precipitate washed with H_2O and dried: 0.5 g (60%) of crude **29**. Recrystallization from EtOH (40 ml) gave 0.377 g (45%) of **29**. Colorless crystals. M.p. 209–210°. ^{1}H-NMR ((D$_6$)DMSO): 7.30–7.25 (*m*, 5 arom. H); 6.84 (*s*, NH_2); 5.03 (*s*, $CH_2N(3)$); 3.99–3.41 (*t*, $MeCH_2CH_2N$); 3.14 (*s*, Me–N(1); 1.66–1.50 (*m*, $MeCH_2CH_2N$); 0.88–0.72 (*t*, *Me*CH_2CH_2). Anal. calc. for $C_{16}H_{19}N_5O_2$ (313.4): C 61.32, H 6.11, N 22.35; found: C 61.35, H 6.16, N 22.30.

25. *8-Amino-9-methylxanthine* (= *8-Amino-3,9-dihydro-9-methyl-1*H-*purine-2,6-dione*; **34**) [15]. A soln. of 9-methyl-8-nitroxanthine (**30**) [15] (0.75 g, 3.55 mmol) in H_2O (100 ml) and conc. NH_3 soln. (5 ml) was reduced with 10% Pd/C (45 mg) under H_2 in a shaking apparatus. After uptake of 230 ml of H_2, the catalyst was filtered off, and the filtrate concentrated. The residue was recrystallized from H_2O (500 ml) with charcoal: 0.373 g (58%) of **34**. Colorless powder. M.p. >300°. ^{1}H-NMR ((D$_6$)DMSO): 11.80 (*s*, H–N(3)); 10.60 (*s*, H–N(1)); 6.10 (*s*, NH_2); 3.50 (*s*, Me–N(9)). Anal. calc. for $C_6H_7N_5O_2 \cdot 0.25\ H_2O$ (185.7): C 38.80, H 4.04, N 37.72; found: C 38.74, H 4.25, N 37.11.

26. *8-Amino-1,9-dimethylxanthine* (= *8-Amino-3,9-dihydro-1,9-dimethyl-1*H-*purine-2,6-dione*; **35**). As described for **34**, with 1,9-dimethyl-8-nitroxanthine (**31**) [15] (1.0 g, 4.44 mmol), 10% Pd/C (60 mg) and H_2. The crude product was recrystallized from H_2O/AcOH 4:1 (250 ml): 0.581 g (67%) of **35**. Colorless powder. M.p. >300°. ^{1}H-NMR ((D$_6$)DMSO): 12.40 (*s*, H–N(3)); 6.20 (*s*, NH_2); 3.50 (*s*, Me–N(9)); 3.20 (*s*, Me–N(1)). Anal. calc. for $C_7H_9N_5O_2$ (195.2): C 43.08, H 4.54, N 35.88; found: C 43.01, H 4.57, N 35.93.

27. *8-Amino-3,9-dimethylxanthine* (= *8-Amino-3,9-dihydro-3,9-dimethyl-1*H-*purine-2,6-dione*; **36**). *i*) As described for **34**, with 3,9-dimethyl-8-nitroxanthine (**32**) [15] (0.3 g, 0.134 mmol), 10% Pd/C (30 mg), and H_2. The crude product was recrystallized from H_2O/AcOH 1:1 (50 ml): 0.136 g (52%) of **36**. Colorless powder. M.p. 320–322°.

ii) A suspension of 1-methyl-6-(methylamino)-5-nitrosouracil [27] (3.0 g, 16.03 mmol) in $(NH_4)_2S$ soln. (20 ml) was heated to 70° for 20 min, and after cooling, the formed precipitate **38** was dissolved in 1N AcOH/0.5M AcONa (20 ml, pH 4.5). Then bromocyan (0.8 g, 7.55 mmol) was added, and the mixture stirred at r.t. overnight. The formed precipitate was purified by recrystallization from H_2O (400 ml) with

charcoal: 0.447 g (39%) of **36**. Colorless crystals. M.p. 320–322°. ^{1}H-NMR ((D$_6$)DMSO): 10.80 (*s*, H–N(1)); 5.99 (*s*, NH$_2$); 3.60 (*s*, Me–N(9)); 3.55 (*s*, Me–N(3)). Anal. calc. for $C_7H_9N_5O_2$ (195.2): C 43.08, H 4.54, N 35.88; found: C 42.83, H 4.81, N 35.66.

28. *8-Amino-1,3,9-trimethylxanthine* (= *8-Amino-3,9-dihydro-1,3,9-trimethyl-1*H-*purine-2,6-dione*; **37**). *i*) A soln. of 1,3,9-trimethyl-8-nitroxanthine (**33**) [15] (0.3 g, 0.134 mmol) in DMF (50 ml) was reduced with 10% Pd/C (30 mg) under H_2 in a shaking apparatus. After filtration of the catalyst, the filtrate was concentrated, and the residue treated with H_2O (20 ml), filtered, and recrystallized from EtOH/H_2O 1:1 (40 ml): 0.56 g (60%) of **37**. Colorless crystals. M.p. 319–320°.

ii) A suspension of 1,3-dimethyl-6-(methylamino)-5-nitrosouracil [27] (3.0 g, 16.03 mmol) and *Raney*-Ni (1.5 g) in MeOH (50 ml) was reduced under H_2 in a shaking apparatus. After filtration, the mixture was evaporated, and the residue **39** dried in a vacuum desiccator. A soln. of **39** (0.9 g, 4.89 mmol) in 1N AcOH/0.5M AcONa (30 ml, pH 4.5) was then treated with bromocyan (0.6 g, 5.66 mmol) under stirring at r.t. for 3 h. The resulting precipitate was purified by recrystallization from EtOH/H_2O 1:1 (150 ml) with charcoal: 0.45 g (44%) of **37**. Colorless crystals. M.p. 320°. ^{1}H-NMR ((D$_6$)DMSO): 6.00 (*s*, NH$_2$); 3.60 (*s*, Me–N(9)); 3.58 (*s*, Me–N(3)); 3.20 (*s*, Me–N(1)). Anal. calc. for $C_8H_{11}N_5O_2$ (209.2): C 45.93, H 5.30, N 33.48; found: C 45.90, H 5.10, N 33.07.

29. *8-(Acetylamino)xanthine* (= N-*(3,7-Dihydro-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **40**). A suspension of **8** (0.1 g, 0.6 mmol) in Ac_2O (10 ml) was heated under reflux for 5 h. The precipitate was collected after cooling and washed with H_2O and EtOH. The solid was dissolved in hot DMSO (20 ml), and then H_2O was added slowly until a precipitate started to separate. After cooling, the mixture was filtered, and the solid washed and dried at 100°: 70 mg (56%) of **40**. Colorless powder. M.p. >320°. ^{1}H-NMR ((D$_6$)DMSO): 11.83 (*s*, H–N(7)); 11.49 (br. *s*, H–N(1), H–N(3)); 10.05 (*s*, NH–C(8)); 2.10 (*s*, MeCO). Anal. calc. for $C_7H_7N_5O_3$ (209.2): C 40.16, H 3.35, N 33.46; found: C 40.03, H 3.49, N 32.82.

30. *8-(Acetylamino)-1-methylxanthine* (= N-*(3,7-Dihydro-1-methyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **41**). As described for **40**, with **9** (0.15 g, 0.83 mmol) and Ac_2O (5 ml) for 4 h. The precipitate was collected after cooling, washed with H_2O and EtOH, and purified by recrystallization from dil. AcOH: 0.113 g (61%) of **41**. Colorless crystals. M.p. >300°. ^{1}H-NMR ((D$_6$)DMSO): 11.81 (*s*, H–N(7), H–N(3)); 11.76 (*s*, NH–C(8)); 3.15 (*s*, Me–N(1)); 2.10 (*s*, MeCO). Anal. calc. for $C_8H_9N_5O_3$ (223.2): C 43.05, H 4.06, N 31.38; found: C 43.10, H 4.07, N 31.50.

31. *8-(Acetylamino)-3-methylxanthine* (= N-*(3,7-Dihydro-3-methyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **42**). As described for **40**, with **10** (0.1 g, 0.55 mmol) and Ac_2O (5 ml) for 4 h. The precipitate was collected after cooling and washed with H_2O and EtOH. Partial evaporation of the filtrate gave a second crop. Both solids were purified by recrystallization from dil. AcOH: 0.086 g (70%) of **42**. Colorless crystals. M.p. >350°. ^{1}H-NMR ((D$_6$)DMSO): 12.40 (*s*, H–N(7)); 12.00 (*s*, H–N(1)); 11.30 (*s*, NH–C(8)); 3.35 (*s*, Me–N(3)); 2.10 (*s*, MeCO). Anal. calc. for $C_8H_9N_5O_3$ (223.2): C 43.05, H 4.06, N 31.38; found: C 43.05, H 4.17, N 31.20.

32. *8-(Acetylamino)-3-benzylxanthine* (= N-*(3-Benzyl-3,7-dihydro-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **43**). As described for **40**, with **11** (0.1 g, 0.39 mmol) in AcOH (2 ml) and Ac_2O (3 ml) for 3 h. After cooling, the precipitate was collected, washed with H_2O and EtOH, and purified by recrystallization from H_2O/AcOH 3:1 (20 ml): 0.07 g (60%) of **43**. Colorless crystals. M.p. 317–318°. ^{1}H-NMR ((D$_6$)DMSO): 12.11 (*s*, H–N(7)); 11.64 (*s*, H–N(1)); 11.05 (*s*, NH–C(8)); 7.28 (*m*, 5 arom. H); 5.07 (*s*, CH$_2$N); 2.08 (*s*, MeCO). Anal. calc. for $C_{14}H_{13}N_5O_3 \cdot 0.5\ H_2O$ (223.2): C 54.55, H 4.54, N 22.73; found: C 54.70, H 4.92, N 22.53.

33. *8-(Acetylamino)-1,3-dimethylxanthine* (= N-*(3,7-Dihydro-1,3-dimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **44**). As described for **40**, with **12** (0.5 g, 2.56 mmol) and Ac_2O (10 ml) for 2 h. After evaporation, the solid was washed with H_2O and EtOH and then purified by recrystallization from H_2O (200 ml) with charcoal: 0.405 g (67%) of **44**. Colorless crystals. M.p. >330°. ^{1}H-NMR ((D$_6$)DMSO): 12.00 (br. *s*, H–N(7), NH–C(8)); 3.40 (*s*, Me–N(3)); 3.25 (*s*, Me–N(1)); 2.10 (*s*, MeCO). Anal. calc. for $C_9H_{11}N_5O_3$ (237.2): C 45.57, H 4.67, N 29.53; found: C 45.58, H 4.73, N 29.63.

34. *8-(Acetylamino)-3-benzyl-1-methylxanthine* (= N-*(3-Benzyl-3,7-dihydro-1-methyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **45**). As described for **40**, with **13** (0.2 g, 0.74 mmol) and Ac_2O (3 ml) for 1 h. After cooling, H_2O (5 ml) was added and the mixture heated for 30 min and then cooled. The formed precipitate was recrystallized from EtOH/H_2O 5:1 (60 ml): 0.141 g (61%) of **45**. Colorless crystals. M.p.

286–288°. ^{1}H-NMR ((D$_6$)DMSO): 12.09 (*s*, H–N(7)); 11.66 (*s*, NH–C(8)); 7.28 (*m*, 5 arom. H); 5.12 (*s*, CH_2N); 3.23 (*s*, Me–N(1)); 2.09 (*s*, MeCO). Anal. calc. for $C_{15}H_{15}N_5O_3$ (313.3): C 57.51, H 4.79, N 22.36; found: C 57.40, H 4.98, N 22.20.

35. *8-(Acetylamino)-1,3,7-trimethylxanthine* (= N-*(3,7-Dihydro-1,3,7-trimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **46**). As described for **40**, with **14** (0.21 g, 1.0 mmol) and Ac_2O (3 ml) for 2 h. Recrystallization from H_2O (120 ml) gave 0.141 g (56%) of **46**. Colorless crystals. M.p. 265–266°. ^{1}H-NMR ((D$_6$)DMSO): 9.80 (*s*, NH–C(8)); 3.70 (*s*, Me–N(7)); 3.30 (*s*, Me–N(3)); 3.00 (*s*, Me–N(1)); 2.10 (*s*, MeCO). Anal. calc. for $C_{10}H_{13}N_5O_3$ (251.2): C 47.80, H 5.21, N 27.88; found: C 47.83, H 5.24, N 27.16.

36. *8-(Acetylamino)-7-methylxanthine* (= N-*(3,7-Dihydro-7-methyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **47**). As described for **40**, with **15** (0.1 g, 0.55 mmol) and Ac_2O (3 ml) for 1.5 h. After evaporation, H_2O (20 ml) was added, and the mixture stirred at r.t. for 1 h. The precipitate was purified by recrystallization from H_2O (10 ml): 73 mg (59%) of **47**. Colorless crystals. M.p. 358–360°. ^{1}H-NMR ((D$_6$)DMSO): 11.46 (*s*, H–N(3)); 10.76 (*s*, H–N(1)); 10.55 (*s*, NH–C(8)); 3.60 (*s*, Me–N(7)); 2.09 (*s*, MeCO). Anal. calc. for $C_8H_9N_5O_3 \cdot 0.5\ H_2O$ (232.2): C 41.35, H 4.31, N 30.15; found: C 41.56, H 4.63, N 29.92.

37. *8-(Acetylamino)-3,7-dimethylxanthine* (= N-*(3,7-Dihydro-3,7-dimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **48**). As described for **40**, with **16** (0.1 g, 0.52 mmol) and Ac_2O (5 ml) for 2 h. Recrystallization from H_2O (10 ml) gave 91 mg (75%) of **48**. Colorless crystals. M.p. 315°. ^{1}H-NMR ((D$_6$)DMSO): 10.20 (*s*, H–N(1)); 9.85 (*s*, NH–C(8)); 3.60 (*s*, Me–N(7)); 3.35 (*s*, Me–N(3)); 2.00 (*s*, MeCO). Anal. calc. for $C_9H_{11}N_5O_3$ (237.2): C 45.57, H 4.67, N 29.53; found: C 45.20, H 4.85, N 29.22.

38. *8-(Acetylamino)-1,7-dimethylxanthine* (= N-*(3,7-Dihydro-1,7-dimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **49**). As described for **40**, with **19** (0.2 g, 1.0 mmol) and Ac_2O (6 ml) for 2 h. Recrystallization from H_2O/AcOH 1:1 (40 ml) gave 0.136 g (59%) of **49**. Colorless crystals. M.p. 350–354°. ^{1}H-NMR ((D$_6$)DMSO): 11.80 (*s*, H–N(3)); 10.56 (*s*, NH–C(8)); 3.63 (*s*, Me–N(7)); 3.16 (*s*, Me–N(1)); 2.10 (*s*, MeCO). Anal. calc. for $C_9H_{11}N_5O_3$ (237.2): C 45.57, H 4.67, N 29.53; found: C 45.52, H 4.59, N 29.45.

39. *8-(Acetylamino)-3-benzyl-7-methylxanthine* (= N-*(3-Benzyl-3,7-dihydro-7-methyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **50**). As described for **40**, with **25** (0.25 g, 0.92 mmol) and Ac_2O (5 ml) for 3 h. Recrystallization from H_2O/EtOH 1:1 (20 ml) gave 0.159 g (55%) of **50**. Colorless crystals. M.p. 259–260°. ^{1}H-NMR ((D$_6$)DMSO): 11.17 (*s*, H–N(1)); 10.76 (*s*, NH–C(8)); 7.28 (*m*, 5 arom. H); 5.05 (*s*, CH_2N); 3.62 (*s*, Me–N(7)); 2.08 (*s*, MeCO). Anal. calc. for $C_{15}H_{15}N_5O_3$ (313.3): C 57.51, H 4.79, N 22.36; found: C 57.50, H 4.85, N 22.28.

40. *8-(Acetylamino)-3-benzyl-1,7-dimethylxanthine* (= N-*(3-Benzyl-3,7-dihydro-1,7-dimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **51**). As described for **40**, with **26** (0.3 g, 1.03 mmol) in AcOH (10 ml) and Ac_2O (2 ml) for 2 h. Recrystallization from MeOH (15 ml) gave 0.138 g (40%) of **51**. Colorless crystals. M.p. 216–217°. ^{1}H-NMR ((D$_6$)DMSO): 10.72 (*s*, NH–C(8)); 7.20 (*m*, 5 arom. H); 5.11 (*s*, CH_2N); 3.65 (*s*, Me–N(7)); 3.23 (*s*, Me–N(1)); 2.08 (*s*, MeCO). Anal. calc. for $C_{16}H_{17}N_5O_3$ (327.3): C 58.70, H 5.24, N 21.40; found: C 58.68, H 5.36, N 21.38.

41. *8-(Acetylamino)-3-benzyl-7-propylxanthine* (= N-*(3-Benzyl-3,7-dihydro-2,6-dioxo-7-propyl-1*H-*purin-8-yl)acetamide*; **52**). As described for **40**, with **28** (0.3 g, 1.03 mmol) in AcOH (10 ml) and Ac_2O (2 ml) for 2 h. Recrystallization from EtOH (30 ml) gave 0.216 g (63%) of **52**. Colorless crystals. M.p. 261°. ^{1}H-NMR ((D$_6$)DMSO): 11.17 (*s*, H–N(1)); 10.51 (*s*, NH–C(8)); 7.28 (*m*, 5 arom. H); 5.05 (*s*, CH_2N); 4.00 (*t*, CH_2–N(7)); 2.07 (*s*, MeCO); 1.74–1.58 (*m*, CH_2CH_2N); 0.85–0.69 (*t*, *Me*CH_2CH_2). Anal. calc. for $C_{17}H_{19}N_5O_3$ (341.4): C 59.82, H 5.57, N 20.53; found: C 59.76, H 5.64, N 20.41.

42. *8-(Acetylamino)-3-benzyl-1-methyl-7-propylxanthine* (= N-*(3-Benzyl-3,7-dihydro-1-methyl-2,6-dioxo-7-propyl-1*H-*purin-8-yl)acetamide*; **53**). As described for **40**, with **29** (0.1 g, 0.32 mmol) in AcOH (10 ml) and Ac_2O (2 ml) for 2 h. Recrystallization from EtOH (20 ml) gave 65 mg (58%) of **53**. Colorless crystals. M.p. 234°. ^{1}H-NMR ((D$_6$)DMSO): 11.17 (*s*, H–N(1)); 10.60 (*s*, NH–C(8)); 7.31–7.23 (*m*, 5 arom. H); 5.11 (*s*, CH_2N); 4.02 (*t*, CH_2–N(7)); 3.23 (*s*, Me–N(1)); 2.08 (*s*, MeCO); 1.75–1.66 (*m*, CH_2CH_2N); 0.81–0.75 (*t*, *Me*CH_2CH_2). Anal. calc. for $C_{18}H_{21}N_5O_3$ (355.4): C 60.84, H 5.92, N 19.72; found: C 61.06, H 5.88, N 19.72.

43. *8-(Acetylamino)-9-methylxanthine* (= N-*(3,9-Dihydro-9-methyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **54**). As described for **40**, with **34** (0.1 g, 0.55 mmol) and Ac_2O (5 ml) for 4 h. After cooling, the formed precipitate was washed with H_2O and EtOH, dried, and recrystallized from H_2O (20 ml) with charcoal: 62 mg (50%) of **54**. Colorless crystals. M.p. >350°. ^{1}H-NMR ((D$_6$)DMSO): 11.93 (*s*, H–N(3)); 10.77 (*s*, H–N(1)); 10.33 (*s*, NH–C(8)); 3.36 (*s*, Me–N(9)); 2.04 (*s*, MeCO). Anal. calc. for $C_8H_9N_5O_3 \cdot 0.125\ H_2O$ (225.6): C 42.58, H 4.10, N 31.05; found: C 43.03, H 4.17, N 30.82.

44. *8-(Acetylamino)-1,9-dimethylxanthine* (= N-*(3,9-Dihydro-1,9-dimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **55**). *i*) As described for **40**, with **35** (0.195 g, 1 mmol) in AcOH (10 ml) and Ac_2O (4 ml) for 1 h. After cooling, the formed precipitate was washed with H_2O and EtOH and recrystallized from EtOH/H_2O 1:1 (30 ml): 0.161 g (68%) of **55**. Colorless crystals. M.p. >310°.

ii) A soln. of 8-(diacetylamino)-1,9-dimethylxanthine (**59**; 0.1 g, 0.36 mmol) in H_2O (10 ml) was heated under reflux for 1.5 h. After cooling, the colorless crystals were washed with H_2O and dried at 100°: 50 mg (59%) of **55**. M.p. >310°. ^{1}H-NMR ((D$_6$)DMSO): 12.20 (*s*, H–N(3)); 10.31 (*s*, NH–C(8)); 3.40 (*s*, Me–N(9)); 3.18 (*s*, Me–N(1)); 2.12 (*s*, MeCO). Anal. calc. for $C_9H_{11}N_5O_3$ (237.2): C 45.57, H 4.67, N 29.53; found: C 45.43, H 4.77, N 29.75.

45. *8-(Acetylamino)-3,9-dimethylxanthine* (= N-*(3,9-Dihydro-3,9-dimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **56**). As described for **55** (*i*), with **36** (0.195 g, 1 mmol): 0.118 g (49%) of **56**. Colorless crystals. M.p. 310–311°. ^{1}H-NMR ((D$_6$)DMSO): 11.07 (*s*, H–N(1)); 10.27 (*s*, NH–C(8)); 3.62 (*s*, Me–N(9)); 3.58 (*s*, Me–N(3)); 2.05 (*s*, MeCO). Anal. calc. for $C_9H_{11}N_5O_3 \cdot 0.25\ H_2O$ (241.7): C 44.68, H 4.65, N 28.96; found: C 44.60, H 4.85, N 28.71.

46. *8-(Acetylamino)-1,3,9-trimethylxanthine* (= N-*(3,9-Dihydro-1,3,9-trimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **57**). As described for **40**, with **37** (0.1 g, 0.48 mmol) in AcOH (5 ml) and Ac_2O (1 ml) for 40 min. After cooling, the mixture was evaporated and the residue heated in H_2O (5 ml) for 30 min. Evaporation and recrystallization of the solid from EtOH (10 ml) gave 76 mg (63%) of **57**. Colorless crystals. M.p. 262–263°. ^{1}H-NMR ((D$_6$)DMSO): 10.30 (*s*, NH–C(8)); 3.66 (*s*, Me–N(9)); 3.65 (*s*, Me–N(3)); 3.21 (*s*, Me–N(1)); 2.05 (*s*, MeCO). Anal. calc. for $C_{10}H_{13}N_5O_3$ (251.2): C 47.80, H 5.21, N 27.88; found: C 47.94, H 5.13, N 27.66.

47. *8-(Diacetylamino)-1,3,7-trimethylxanthine* (= N-*Acetyl*-N-*(3,7-dihydro-1,3,7-trimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **58**) [20]. As described for **40**, with **14** (0.2 g, 0.96 mmol) and Ac_2O (10 ml) for 5 h. The mixture was concentrated, and the residue treated with Et_2O for 1 h at r.t. The precipitate was dissolved again in hot Ac_2O (5 ml), and after cooling, the soln. was diluted with Et_2O (3 ml): 0.1 g (36%) of **58**. Colorless crystals. M.p. 144–145°. ^{1}H-NMR ($CDCl_3$): 4.10 (*s*, Me–N(7)); 3.80 (*s*, Me–N(3)); 3.70 (*s*, Me–N(1)); 2.80 (*s*, 2 Ac). Anal. calc. for $C_{12}H_{15}N_5O_4$ (293.3): C 49.14, H 5.16, N 23.88; found: C 49.20, H 5.10, N 23.71.

48. *8-(Diacetylamino)-1,9-dimethylxanthine* (= N-*Acetyl*-N-*(3,9-dihydro-1,9-dimethyl-2,6-dioxo-1*H-*purin-8-yl)acetamide*; **59**). As described for **40**, with **35** (0.2 g, 1.03 mmol) and Ac_2O (8 ml) for 3 h. After evaporation, the residue was stirred in H_2O (20 ml) for 30 min, and then the solid collected. Recrystallization from Ac_2O (40 ml) and drying in a desiccator over KOH gave 0.178 g (62%) of **59**. Colorless crystals. ^{1}H-NMR ((D$_6$)DMSO): 12.40 (*s*, NH); 3.43 (*s*, Me–N(9)); 3.20 (*s*, Me–N(1)); 2.24 (*s*, 2 Ac). Anal. calc. for $C_{11}H_{13}N_5O_4$ (279.3): C 47.31, H 4.69, N 25.08; found: C 47.07, H 4.79, N 25.25.

49. *8-Diazoxanthine* (= *8-Diazo-3,8-dihydro-1*H-*purine-2,6-dione*; **60**) [15]. To a soln. of **8** (0.1 g, 0.6 mmol) in 5% KOH soln. (10 ml), $NaNO_2$ (43 mg, 0.62 mmol) was added, and then the mixture cooled in an ice bath (0–5°). Under stirring in the dark, conc. HCl soln. (5 ml) was added dropwise, and after 1 h, the resulting precipitate was washed with H_2O and MeOH and dried in a vacuum desiccator over P_4O_{10}: 97 mg (91%) of **60**. Yellowish solid. M.p. 145° (dec.). ^{1}H-NMR ((D$_6$)DMSO): 11.75 (*s*, H–N(3)); 11.16 (*s*, H–N(1)). Anal. calc. for $C_5H_2N_6O_2$ (178.1): C 33.72, H 1.13, N 47.19; found: C 33.62, H 1.20, N 47.01.

50. *8-Diazo-1-methylxanthine* (= *8-Diazo-3,8-dihydro-1-methyl-1*H-*purine-2,6-dione*; **61**). As described for **60**, with **9** (0.15 g, 0.83 mmol), 5% KOH soln. (8 ml), $NaNO_2$ (60 mg, 0.87 mmol), and conc. HCl soln. (3 ml): 0.14 g (88%) of **61**. Yellowish solid. M.p. 154° (dec.). ^{1}H-NMR ((D$_6$)DMSO): 12.01 (*s*, H–N(3)); 3.19 (*s*, Me–N(1)). Anal. calc. for $C_6H_4N_6O_2 \cdot 0.25\ H_2O$ (192.7): C 36.61, H 2.16, N 42.71; found: C 36.70, H 2.28, N 42.62.

51. *8-Diazo-3-methylxanthine* (= *8-Diazo-3,8-dihydro-3-methyl-1*H-*purine-2,6-dione*; **62**). As described for **60**, with **10** (0.181 g, 1 mmol), 5% KOH soln. (10 ml), $NaNO_2$ (0.1 g, 1.45 mmol), and conc. HCl soln. (3 ml): 0.15 g (78%) of **62**. Yellowish solid. M.p. 156° (dec.). ^{1}H-NMR ((D_6)DMSO): 11.43 (*s*, H–N(1)); 3.32 (*s*, Me–N(3)). Anal. calc. for $C_6H_4N_6O_2 \cdot 0.25\ H_2O$ (192.7): C 36.61, H 2.16, N 42.71; found: C 36.60, H 2.08, N 42.23.

52. *3-Benzyl-8-diazoxanthine* (= *3-Benzyl-8-diazo-3,8-dihydro-1*H-*purine-2,6-dione*; **63**). As described for **60**, with **11** (0.26 g, 1 mmol), 5% KOH soln. (10 ml), $NaNO_2$ (0.1 g, 1.45 mmol), and conc. HCl soln. (5 ml): 0.23 g (85%) of **63**. Yellowish solid. M.p. 130° (dec.). ^{1}H-NMR ((D_6)DMSO): 11.51 (*s*, H–N(1)); 7.30 (*m*, 5 arom. H); 5.06 (*s*, CH_2N). Anal. calc. for $C_{12}H_8N_6O_2$ (268.3): C 53.73, H 2.99, N 31.34; found: C 54.00, H 3.09, N 31.13.

53. *8-Diazo-1,3-dimethylxanthine* (= *8-Diazo-3,8-dihydro-1,3-dimethyl-1*H-*purine-2,6-dione*; **64**) [15]. A soln. of **12** (0.4 g, 2.05 mmol) in 5% HCl soln. (20 ml) was cooled to 0–5°, and then $NaNO_2$ (0.16 g, 2.32 mmol) was added in four portions. The mixture was stirred for 1.5 h, and the resulting precipitate washed with H_2O and MeOH and dried in a vacuum desiccator: 0.38 g (90%) of **64**. Yellowish powder. M.p. 155° (dec.). ^{1}H-NMR ((D_6)DMSO): 3.41 (*s*, Me–N(3)); 3.24 (*s*, Me–N(1)). Anal. calc. for $C_6H_6N_6O_2$ (194.2): C 37.11, H 3.11, N 43.28; found: C 37.20, H 3.00, N 43.11.

54. *3-Benzyl-8-diazo-1-methylxanthine* (= *3-Benyzl-8-diazo-3,8-dihydro-1-methyl-1*H-*purine-2,6-dione*; **65**). As described for **64**, with **13** (0.12 g, 0.44 mmol), 5% HCl soln. (20 ml), and $NaNO_2$ (40 mg, 0.58 mmol): 0.11 g (89%) of **65**. Yellowish powder. M.p. 120° (dec.). ^{1}H-NMR ((D_6)DMSO): 7.32–7.25 (*m*, 5 arom. H); 5.13 (*s*, CH_2N); 3.27 (*s*, Me–N(1)). Anal. calc. for $C_{13}H_{10}N_6O_2 \cdot 0.25\ H_2O$ (286.7): C 54.45, H 3.57, N 29.29; found: C 55.09, H 3.63, N 29.00.

55. *5-[(3-Methylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (= *3,7-Dihydro-3-methyl-8-[2-(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H-*purine-2,6-dione*; **67**). To a soln. of 1,3-dimethylbarbituric acid (**66**; 81 mg, 0.52 mmol) in buffer pH 8 (10 ml) was added under stirring **62** (0.1 g, 0.52 mmol) to form a reddish precipitate. After 5 min, the mixture was acidified by 1N HCl to pH 2–3, and stirring was continued for 30 min. The precipitate was washed with H_2O (10 ml) and EtOH (10 ml) and dried at 100°: 0.17 g (94%) of **67**. Light red solid. M.p. >350°. ^{1}H-NMR ((D_6)DMSO): 14.00 (br. *s*, HO–C(6), H–N(7′)); 11.05 (*s*, H–N(1′)); 3.23 (*s*, Me–N(3′)); 3.20 (*s*, 2 MeN). Anal. calc. for $C_{12}H_{12}N_8O_5$ (348.3): C 41.38, H 3.45, N 32.18; found: C 41.57, H 3.68, N 31.91.

56. *5-[(1,3-Dimethylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (= *3,7-Dihydro-1,3-dimethyl-8-[2-(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H-*purine-2,6-dione*; **68**). As described for **67**, with **66** (45 mg, 0.29 mmol) and **64** (60 mg, 0.29 mmol): 94 mg (90%) of **68**. Red powder. M.p. 328–330°. Recrystallization from DMF (8 ml) gave 83 mg (79%). ^{1}H-NMR ((D_6)DMSO): 14.10 (br. *s*, HO–C(6)); 14.00 (*s*, H–N(7′)); 3.42 (*s*, Me–N(3′)); 3.21 (*s*, Me–N(1′)); 3.20 (*s*, 2 MeN). Anal. calc. for $C_{13}H_{14}N_8O_5 \cdot 0.5\ H_2O$ (371.3): C 42.00, H 3.90, N 30.02; found: C 41.90, H 4.12, N 30.00.

57. *5-[(1,3,7-Trimethylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (= *3,7-Dihydro-1,3,7-trimethyl-8-[2-(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H-*purine-2,6-dione*; **69**). A soln. of **14** (0.1 g, 0.48 mmol) in 5% HCl soln. (15 ml) was cooled in an ice bath to 0–5°. Then, $NaNO_2$ (35 mg, 0.51 mmol) was added under stirring, and after 1 h, the yellow soln. was dropwise added to a cold soln. of **66** (75 mg, 0.48 mmol) in 1N NaOH (15 ml). The pH was adjusted to 8, and after stirring for 10 min, the mixture was acidified with 1N HCl to pH 1–2. The precipitate was washed with H_2O (10 ml) and MeOH (10 ml), and the red solid recrystallized from AcOH (8 ml): 70 mg (39%) of **69**. Light red crystals. M.p. 320°. ^{1}H-NMR ((D_6)DMSO): 14.19 (br. *s*, HO–C(6)); 3.95 (*s*, Me–N(7′)); 3.40 (*s*, Me–N(3′)); 3.20 (*s*, Me–N(1′)); 3.18 (*s*, 2 MeN). Anal. calc. for $C_{14}H_{16}N_8O_5$ (376.3): C 44.68, H 4.25, N 29.78; found: C 44.25, H 4.27, N 29.24.

58. *5-[(7-Methylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (= *3,7-Dihydro-7-methyl-8-[2-(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H-*purine-2,6-dione*; **70**). A soln. of **15** (0.15 g, 0.83 mmol) in 5% KOH soln. (30 ml) was cooled in an ice bath to 0–5°, then, $NaNO_2$ (60 mg, 0.87 mmol) was added and the soln. acidified by dropwise addition of conc. HCl soln. (5 ml). After 15 min stirring, the yellow soln. was dropwise added to **66** (0.13 g, 0.83 mmol) in cold 5% KOH soln. (30 ml), the pH adjusted to 8, and stirring continued for another 15 min. The mixture was then acidified by 1N HCl (10 ml) and stirred at r.t. for 30 min. The formed precipitate was recrystallized

from AcOH (15 ml): 104 mg (36%) of **70**. Light red crystals. M.p. >350°. ^{1}H-NMR ((D$_6$)DMSO): 14.00 (br. *s*, HO–C(6)); 12.10 (*s*, H–N(3′)); 10.80 (*s*, H–N(1′)); 3.91 (*s*, Me–N(7′)); 3.21 (*s*, 2 MeN). Anal. calc. for $C_{12}H_{12}N_8O_5 \cdot 0.5\ H_2O$ (357.3): C 40.29, H 3.49, N 31.33; found: C 40.30, H 3.20, N 30.85.

59. *5-[(3,7-Dimethylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (*=3,7-Dihydro-3,7-dimethyl-8-[2-(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-dione*; **71**). As described for **70**, with **16** (0.1 g, 0.51 mmol), 5% KOH soln. (5 ml), $NaNO_2$ (40 mg, 0.58 mmol), and conc. HCl soln. (3 ml). The diazonium salt soln. was dropwise added to **66** (80 mg, 0.51 mmol) in buffer soln. of pH 8 (15 ml). Acidification and stirring for 5 h gave a red solid. Recrystallization from AcOH (5 ml) gave 71 mg (38%) of **71**. Light red solid. M.p. 337°. ^{1}H-NMR ((D$_6$)DMSO): 14.12 (br. *s*, HO–C(6)); 11.21 (*s*, H–N(1′)); 3.92 (*s*, Me–N(7′)); 3.32 (*s*, Me–N(3′)); 3.21 (*s*, 2 MeN). Anal. calc. for $C_{13}H_{14}N_8O_5$ (362.3): C 43.09, H 3.87, N 30.94; found: C 42.95, H 3.89, N 30.74.

60. *5-[(1,7-Dimethylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (*=3,7-Dihydro-1,7-dimethyl-8-[2-(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-dione*; **72**). As described for **70**, with **19** (0.1 g, 0.51 mmol), $NaNO_2$ (40 mg, 0.58 mmol), and **66** (80 mg, 0.51 mmol). Recrystallization from AcOH (5 ml) gave 50 mg (27%) of **72**. Reddish crystals. M.p. 330°. ^{1}H-NMR ((D$_6$)DMSO): 14.20 (br. *s*, HO–C(6)); 12.01 (*s*, H–N(3′)); 3.92 (*s*, Me–N(7′)); 3.21 (*s*, 2 MeN); 3.17 (*s*, Me–N(1′)). Anal. calc. for $C_{13}H_{14}N_8O_5 \cdot 0.25$ AcOH (377.3): C 42.97, H 4.00, N 29.70; found: C 42.97, H 4.06, N 29.53.

61. *5-[(3-Benzyl-7-methylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (*=3-Benzyl-3,7-dihydro-7-methyl-8-[2-(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-dione*; **73**). As described for **70**, with **25** (0.14 g, 0.51 mmol) in 5% KOH soln. (10 ml), $NaNO_2$ (40 mg, 0.58 mmol), and **66** (80 mg, 0.51 mmol). After final stirring for 3 h, the formed solid was recrystallized from AcOH (10 ml): 91 mg (41%) of **73**. Light red crystals. M.p. 330°. ^{1}H-NMR ((D$_6$)DMSO): 14.18 (br. *s*, HO–C(6)); 7.30 (*m*, 5 arom. H); 5.09 (*s*, CH_2N); 3.96 (*s*, Me–N(7′)); 3.21 (*s*, 2 MeN). Anal. calc. for $C_{19}H_{18}N_8O_5$ (438.4): C 52.06, H 4.13, N 25.56; found: C 51.92, H 4.07, N 25.31.

62. *5-[(3-Benzyl-1,7-dimethylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (*=3-Benzyl-3,7-dihydro-1,7-dimethyl-8-[(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-dione*; **74**). A soln. of **26** (0.1 g, 0.35 mmol) in 15% HCl soln. (10 ml) was cooled to 0–5°. Then, $NaNO_2$ (30 mg, 0.43 mmol) was added in small portions, and the mixture stirred for 15 min. The yellow soln. was added dropwise to **66** (55 mg, 0.35 mmol) in 5% KOH soln. (10 ml) and, after acidification with 1N HCl, stirred for 3 h. The formed precipitate was recrystallized from AcOH/MeOH 1:1 (10 ml): 71 mg (45%) of **74**. Light red crystals. M.p. 276–277°. ^{1}H-NMR ((D$_6$)DMSO): 14.20 (br. *s*, HO–C(6)); 7.37–7.30 (*m*, 5 arom. H); 5.16 (*s*, CH_2N); 4.00 (*s*, Me–N(7′)); 3.23 (*s*, Me–N(1′)); 3.21 (*s*, 2 MeN). Anal. calc. for $C_{20}H_{20}N_8O_5$ (452.4): C 53.10, H 4.42, N 24.78; found: C 53.03, H 4.37, N 24.76.

63. *5-[(3-Benzyl-7-propylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (*=3-Benzyl-3,7-dihydro-7-propyl-8-[2-(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-dione*; **75**). To a soln. of **28** (0.2 g, 0.57 mmol) and $NaNO_2$ (50 mg, 0.72 mmol) in 5% KOH soln. (10 ml) was added dropwise under cooling and stirring conc. HCl soln. (4 ml). After 30 min, the yellow diazonium salt soln. was added to a soln. of **66** (104 mg, 0.67 mmol) in buffer pH 8 (30 ml). Then, the mixture was acidified with HCl to pH 2 and stirred at r.t. overnight. The orange precipitate was recrystallized from AcOH/MeOH 1:1 (10 ml): 0.1 g (32%) of **75**. Orange crystals. M.p. 295°. ^{1}H-NMR ((D$_6$)DMSO): 14.20 (br. *s*, HO–C(6)); 11.29 (*s*, H–N(1′)); 7.30–7.27 (*m*, 5 arom. H); 5.08 (*s*, CH_2N); 4.33 (*t*, MeCH$_2$C*H*$_2$N); 4.00 (*s*, Me–N(7′)); 3.20 (*s*, 2 MeN); 1.89–1.75 (*m*, MeC*H*$_2$CH$_2$N); 0.93 (*t*, *Me*CH$_2$). Anal. calc. for $C_{21}H_{22}N_8O_5$ (466.4): C 54.08, H 4.72, N 24.03; found: C 54.08, H 4.75, N 23.82.

64. *5-[(3-Benzyl-1-methyl-7-propylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (*=3-Benzyl-3,7-dihydro-1-methyl-7-propyl-8-[2-(1,2,3,4-tetrahydro-6-hydroxy-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)-diazenyl]-1*H*-purine-2,6-dione*; **76**). To a cold soln. of **29** (0.2 g 0.64 mmol) in dioxane (20 ml) and conc. HCl soln. (2 ml) was added $NaNO_2$ (50 mg, 0.72 mmol) in H_2O (2 ml) dropwise with stirring, and after 10 min, this soln. was added to a soln. of **66** (0.1 g, 0.64 mol) in dioxane (20 ml) and AcONa (0.6 g, 0.74 mmol). After addition and stirring for 15 min, the mixture was acidified with HCl to pH 3 and the precipitate collected after another 2 h of stirring at r.t. Recrystallization from AcOH/MeOH 1:2 (15 ml) gave 61 mg (20%) of **76**. Orange crystals. M.p. 205°. ^{1}H-NMR ((D$_6$)DMSO): 14.16 (br. *s*, HO–C(6)); 7.32–7.28 (*m*, 5 arom. H); 5.15 (*s*, CH_2N); 4.41 (*t*, MeCH$_2$C*H*$_2$N); 3.23 (*s*, Me–N(1′)); 3.20 (*s*, 2 MeN);

1.82–1.79 (*m*, MeC*H*$_2$CH$_2$N); 0.89 (*t*, *Me*CH$_2$). Anal. calc. for $C_{22}H_{24}N_8O_5 \cdot 0.5$ AcOH (510.4): C 54.12, H 5.10, N 21.96; found: C 53.98, H 5.04, N 21.96.

65. *5-[(9-Methylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (= *3,9-Dihydro-9-methyl-8-[2-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-dione*; **77**). A soln. of **34** (0.1 g, 0.55 mmol) and $NaNO_2$ (40 mg, 0.68 mmol) in 5% KOH soln. (10 ml) was cooled with ice to 0–5°, and then conc. HCl soln. (3 ml) was dropwise added. After stirring for 10 min, this soln. was added slowly to **66** (86 mg, 0.55 mmol) in 5% KOH soln. (20 ml), and then the pH was adjusted to 7–8. After another 10 min, the soln. was acidified to pH 1–2 and stirred at r.t. for 3 h. The precipitate was washed with H_2O (10 ml) and MeOH (10 ml) and recrystallized from AcOH (5 ml): 77 mg (40%) of **77**. Orange powder. M.p. >350°. ^{1}H-NMR ((D$_6$)DMSO): 14.00 (br. *s*, HO–C(6)); 12.11 (*s*, H–N(3′)); 10.90 (*s*, H–N(1′)); 3.70 (*s*, Me–N(9′)); 3.21 (*s*, 2 MeN). Anal. calc. for $C_{12}H_{12}N_8O_5$ (348.3): C 41.38, H 3.45, N 32.18; found: C 41.40, H 3.53, N 31.70.

66. *5-[(1,9-Dimethylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (= *3,9-Dihydro-1,9-dimethyl-8-[2-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-dione*; **78**). As described for **77**, with **35** (0.1 mg, 0.51 mmol) and $NaNO_2$ (40 mg, 0.58 mmol). The diazonium salt soln. was added to **66** (80 mg, 0.51 mmol) and finally stirred for 3 h. The precipitate was recrystallized from AcOH/MeOH 1:1 (10 ml): 57 mg (32%) of **78**. Orange powder. M.p. 327–328°. ^{1}H-NMR ((D$_6$)DMSO): 14.10 (br. *s*, HO–C(6)); 12.70 (*s*, H–N(3′)); 3.69 (*s*, Me–N(9′)); 3.18 (*s*, Me–N(1′)); 3.20 (*s*, 2 MeN). Anal. calc. for $C_{13}H_{14}N_8O_5 \cdot H_2O$ (380.3): C 41.05, H 4.15, N 29.47; found: C 41.25, H 3.94, N 29.25.

67. *5-[(3,9-Dimethylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (= *3,9-Dihydro-3,9-dimethyl-8-[2-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-dione*; **79**). As described for **77**, with **36** (0.1 mg, 0.51 mmol) and $NaNO_2$ (40 mg, 0.58 mmol). The diazonium salt soln. was added to **66** (80 mg, 0.51 mmol) and finally stirred for 3 h. The precipitate was recrystallized from AcOH/MeOH 1:1 (10 ml): 62 mg (33%) of **79**. Orange powder. M.p. 290–291°. ^{1}H-NMR ((D$_6$)DMSO): 14.00 (br. *s*, HO–C(6)); 11.25 (*s*, H–N(1′)); 3.80 (*s*, Me–N(9′)); 3.61 (*s*, Me–N(3′)); 3.21 (*s*, 2 MeN). Anal. calc. for $C_{13}H_{14}N_8O_5 \cdot 0.25$ AcOH (377.3): C 42.97, H 4.00, N 29.70; found: C 43.17, H 4.16, N 29.29.

68. *5-[(1,3,9-Trimethylxanthin-8-yl)diazenyl]-1,3-dimethylbarbituric Acid* (= *3,9-Dihydro-1,3,9-trimethyl-8-[2-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)diazenyl]-1*H*-purine-2,6-dione*; **80**). To a cooled soln. of **37** (0.1 mg, 0.48 mmol) in 5% HCl soln. (15 ml) was added in small portions $NaNO_2$ (35 mg, 0.48 mmol). After stirring for 1 h, this soln. was added dropwise to **66** (75 mg, 0.48 mmol) in 1N NaOH (15 ml). The pH was adjusted to 8, and after 15 min, the mixture was acidified by 1N HCl (10 ml) and stirred for another 30 min. The precipitate was recrystallized from AcOH (5 ml): 80 mg (44%) of **80**. Light red crystals. M.p. 289–290°. ^{1}H-NMR ((D$_6$)DMSO): 14.00 (br. *s*, HO–C(6)); 3.87 (*s*, Me–N(9′)); 3.69 (*s*, Me–N(3′)); 3.21 (*s*, Me–N(1′)); 3.20 (*s*, 2 MeN). Anal. calc. for $C_{14}H_{16}N_8O_5$ (376.3): C 44.68, H 4.25, N 29.79; found: C 44.27, H 4.42, N 29.58.

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