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Convenient syntheses of 1,3-dimethyluracil-6- (**7**) and -7-carboxaldehyde (**19**) are described. The reactivity of the carboxaldehyde group has been investigated by oxidations, reductions and various carbonyl reactions forming a series of new derivatives. The newly synthesized compounds were characterized by elemental analysis, uv and ¹H-nmr spectra.

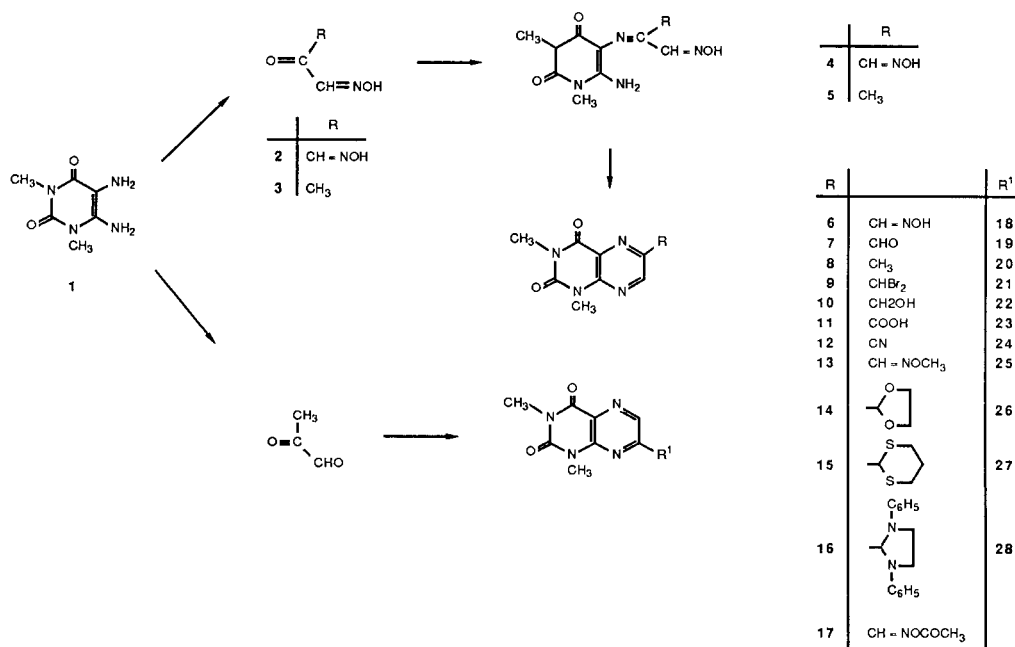
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Most pteridine syntheses are achieved by the Gabriel-Isay reaction [2] in condensing the easily available 5,6-diaminopyrimidines with vicinal dicarbonyl compounds. Problems regarding the regioselectivity arises on condensation with unsymmetrical 1,2-dicarbonyl derivatives in leading commonly to 6- and 7-substituted isomeric mixtures. In special cases pH-variation effects the orientation [2] but a defined regioselective synthesis affords usually an unambiguous approach as demonstrated by the Timmis [2] and the Taylor reaction [2] respectively. Since most naturally occurring pteridines bear a side-chain in 6-position special interest towards such synthetic approaches are obvious.

In this work we focussed our attention on the synthesis of the 1,3-dimethyluracil-6- (**7**) and -7-carboxaldehyde (**19**) as versatile intermediates for further structural modifications. The synthesis of **7** was based on an old observa-

tion by Karrer and Schwyzer [3] using propanetrione-1,3-dioxime (**2**) [4-6] in condensation reactions. 5,6-Diamino-1,3-dimethyluracil (**1**) reacts preferentially with its 5-amino group with **2** to form the corresponding Schiff base **4** in 95% yield. Short boiling of this orange coloured compound in dilute sodium bicarbonate solution caused clean cyclization to 1,3-dimethyluracil-6-carboxaldoxime (**6**) in 86% yield. This cyclization takes also place in methanol even at room temperature with a half life time of 40 minutes as monitored uv-spectrophotometrically.

The two-step condensation reaction of an α -ketocarboxaldoxime with a 5,6-diaminopyrimidine was then extended to **1** and oximinoacetone (**3**). The Schiff base **5** has to be cyclized in this case, however, by 80% sulfuric acid to form 1,3,6-trimethyluracil (**8**) in 72% yield, whereas weaker acidic conditions always led to a mixture of the 6- and 7-methyl isomers. The conversion of **6** into 1,3-



Scheme 1

Table 1

¹H-NMR Spectra of 1,3-Dimethylumazine-6- and -7-carboxaldehyde Derivatives (δ -values in ppm)

Compound	1-CH ₃	3-CH ₃	6-H	7-H	Side chain	Solvent
4	3.35	3.10			11.3 bs (OH), 7.80 bs (CH), 6.95 bs (NH ₂)	D ₆ -DMSO
5	3.33	3.13			11.5 bs (OH), 7.73 bs (CH), 6.65 bs (NH ₂) 1.88 s (CH ₃)	D ₆ -DMSO
6	3.50	3.30		9.05	11.9 bs (OH), 8.15 s (CH)	D ₆ -DMSO
18	3.52	3.32	8.88		12.54 bs (OH), 8.23 s (CH)	D ₆ -DMSO
7	3.74	3.53		9.16	10.18 s (CHO)	CDCl ₃
19	3.77	3.55	9.07		10.17 s (CHO)	CDCl ₃
8	3.65	3.49		8.46	2.65 s (CH ₃)	CDCl ₃
20	3.66	3.53	8.40		2.65 s (CH ₃)	CDCl ₃
9	3.73	3.53		9.26	6.81 s (CHBr ₂)	CDCl ₃
21	3.72	3.54	8.92		6.67 s (CHBr ₂)	CDCl ₃
10	3.53	3.30		8.78	5.68 t (OH), 4.68 d (CH ₂)	D ₆ -DMSO
22	3.51	3.31	8.63		5.80 t (OH), 4.72 d (CH ₂)	D ₆ -DMSO
11	3.56	3.33		9.21	COOH not detected	D ₆ -DMSO
23	3.56	3.34	9.05		COOH not detected	D ₆ -DMSO
12	3.72	3.53		8.90		CDCl ₃
24	3.69	3.53	8.81			CDCl ₃
13	3.75	3.55		9.20	8.3 s (CH), 4.10 s (OCH ₃)	CDCl ₃
25	3.70	3.53	9.03		8.15 s (CH), 4.13 s (OCH ₃)	CDCl ₃
14	3.70	3.50		8.85	6.00 s (CH), 3.95-4.35 m (CH ₂ CH ₂)	CDCl ₃
26	3.71	3.52	8.72		5.94 s (CH), 4.12-4.24 m (CH ₂ CH ₂)	CDCl ₃
15	3.70	3.50		8.85	5.50 s (CH), 2.85-3.20 m (CH ₂ -C-CH ₂), 1.90-2.25 m (C-CH ₂ -C)	CDCl ₃
27	3.74	3.54	8.67		5.35 s (CH), 3.01-3.14 m (CH ₂ -C-CH ₂), 2.03-2.28 m (C-CH ₂ -C)	CDCl ₃
16	3.55	3.50		8.61	6.65-7.25 m (C ₆ H ₅), 6.30 s (CH), 3.60-4.20 m (CH ₂ CH ₂)	CDCl ₃
28	3.72	3.44	8.53		6.68-7.25 m (C ₆ H ₅), 6.22 s (CH), 3.85-4.05 m (CH ₂ -CH ₂)	CDCl ₃
17	3.72	3.52		9.35	8.60 s (CH), 2.25 s (COCH ₃)	CDCl ₃

s = singlet; bs = broad singlet; d = doublet; t = triplet; m = multiplet.

dimethylumazine-6-carboxaldehyde (**7**) [7] can best be achieved by boiling in dilute hydrochloric acid in presence of a large excess of formaldehyde to give a 94% yield of **7**. On the other hand **8** can easily be brominated with bromine in boiling acetic acid to 6-dibromomethyl-1,3-dimethylumazine (**9**), which hydrolyzes fast in boiling water to form **7** in 94% yield.

A similar route is leading to 1,3-dimethylumazine-7-carboxaldehyde (**19**) since condensation of **1** with methylglyoxal forms first under neutral to weak acidic conditions regioselectively the 1,3,7-trimethylumazine (**20**) [7,8] as the main reaction product. Bromination in acetic acid gave in 88% yield 7-dibromomethyl-1,3-dimethylumazine (**21**), which turned out to be unexpectedly resistant towards aqueous hydrolyses. Reaction with hydroxylamine caused on prolonged heating conversion to 1,3-dimethylumazine-7-carboxaldoxime (**18**), from which the corresponding 7-carboxaldehyde **19** could again be generated by acid hydrolysis in presence of formaldehyde in high yield.

Both carboxaldehydes **7** and **19** are valuable intermediates for synthetic purposes due to their high carbonyl reactivity. Sodium borohydride reduction in dilute acetic acid solution leads to the corresponding 6- (**10**) and 7-hydroxymethyl-1,3-dimethylumazines (**22**) and permanganate oxidation gave rise to the formation of the 6- (**11**) and 7-carboxylic acid (**23**), respectively, which could also be obtained on acid hydrolysis of the corresponding 6- (**12**) and 7-cyano-1,3-dimethylumazine (**24**). The latter two compounds are derived from the carboxaldoximes **6** and **18** by dehydration on boiling in acetic anhydride. In the case of **6** an intermediate could be isolated and identified as 1,3-dimethylumazine-6-(*O*-acetyl)-carboxaldoxime (**17**), whereas **18** reacted much faster with subsequent elimination to form directly **24**.

The carbonyl reactivity of **7** and **19** was proven by reaction of *O*-methylhydroxylamine forming the corresponding 6- (**13**) and 7-(*O*-methyl)carboxaldoximes (**25**) in excellent yields. Acetal formation was easily achieved with ethylglycol in an acid catalysed reaction to give **14** and **26**

respectively and in a similar manner reacted propane-1,3-dithiole to the dithianes **15** and **27** and *N,N'*-diphenyl-ethylenediamine to the amins **16** and **28**.

The newly synthesized compounds have been characterized by various physical data. The ¹H-nmr spectra (Table 1) indicate as a characteristic feature a lower field signal of the corresponding 7-H over the 6-H isomer due to the stronger electron-attracting power of the 4-carbonyl function on the C-7 center. The *N*-methyl absorptions are not altered significantly by the 6- and 7-substituents but always N¹-CH₃ appears at lower field than N³-CH₃.

The uv spectra also differ very little between the corresponding isomeric pairs what the maxima of the absorption bands is concerned, but the extinctions are mostly higher with the 7-substituted derivatives. An anomaly is recognized with the 1,3-dimethylumazine-6- (**7**) and 7-carboxaldehyde (**19**) comparing their uv-spectra with those of the corresponding 6- and 7-acetyl-1,3-dimethylumazines [8]. There should be a more distinct spectral difference between **7** and **19** due to the interaction of the carboxaldehyde function with the lumazine chromophor giving rise to a three band spectrum in the former and a two band absorption in the latter case. The striking similarity of the

spectral behaviour of **7** and **19** in methanol has therefore to be explained by hemiacetal formation in both cases leading to a simple 1,3-dimethylumazine spectrum as indicated by the trimethylumazines **8** and **20**.

The acidic p*K*_a of the carboxaldoximes **6** and **18** reflect the π-electron-deficient character of the lumazine nucleus showing similar acidity like 2,4-dinitrobenzaldoxime [9].

EXPERIMENTAL

The uv spectra were determined with a Cary Model 118 (Applied Physics Corporation) and an Uvikon 820 (Kontron) recording spectrometer. The ¹H-nmr spectra were obtained with a Jeol FX-90-Q and Bruker WM-250 spectrometer, with chemical shifts (δ) reported in ppm downfield from tetramethylsilane. DC was performed on silica gel plates F 1500 LS 254 and cellulose sheets F 1440 LS 254 of Schleicher & Schüll. For column chromatography silica gel 60 (0.05-0.2 mm) of Merck was used. Melting points were taken in capillary tubes in a Dr. Tottoli apparatus of Büchi Comp. and are uncorrected.

6-Amino-5-diformaldoximomethyleneamino-1,3-dimethyluracil (4).

To 10.0 g (59 mmoles) of 5,6-diamino-1,3-dimethyluracil (**1**) in 150 ml of ethanol were added gradually at 0-5° 7.3 g (63 mmoles) of propane-1,3-dioxime (**2**) with stirring. An orange coloured precipitate is formed, which is filtered off after stirring for 1 hour at room temperature. The precipitate is washed with water, ethanol and ether and dried in a vacuum desiccator to give 15.0 g (89%) of an orange powder of mp 137° dec.

Anal. Calcd. for C₉H₁₂N₆O₄·H₂O: C, 37.77; H, 4.93; N, 29.36. Found: C, 38.00; H, 4.91; N, 29.00.

6-Amino-5-(2-methyloximinoethylideneamino)-1,3-dimethyluracil (5).

To 1.0 g (5.9 mmoles) of **1** in 30 ml of ethanol is added 0.6 g (6.9 mmoles) of methylglyoxalmonoaldoxime (**3**) [10] and 5 drops of 1*N* hydrochloric acid. After stirring for 3 hours at room temperature, the yellow precipitate is collected, washed with ethanol and ether and dried in a vacuum desiccator over night to give 1.13 g (80%) of a yellow powder of mp 193° dec.

Anal. Calcd. for C₉H₁₃N₅O₃: C, 45.18; H, 5.48; N, 29.28. Found: C, 44.84; H, 5.43; N, 29.15.

1,3-Dimethylumazine-6-carbaldoxime (6).

To 100 ml of a 5% sodium bicarbonate solution is added 5.3 g (20 mmoles) of **4** and then the mixture heated under reflux for 5 minutes whereby the colour changes from orange to yellow. After cooling the precipitate is filtered off, washed with water, methanol and ether and dried in vacuum at 80° to 4.0 g (86%) of a yellow powder of mp 280° dec, lit [12] mp 280-283°.

6-Formyl-1,3-dimethylumazine (7).

A mixture of 5.0 g (21 mmoles) of **6**, 80 ml of a 37% aqueous formaldehyde solution, 40 ml of water, and 10 ml of 5*N* hydrochloric acid is heated under reflux for 30 minutes. After cooling the solution is neutralized with 5*N* sodium hydroxide, filtered and the filtrate extracted several times with chloroform. The organic layer is dried over sodium sulfate and evaporated to dryness. The oily residue is treated several times with toluene to give a solid on evaporation. The product is dissolved in chloroform and purified by silica gel column chromatography in the same solvent to give after evaporation 4.4 g (94%) of a colourless material of mp 170-171°, lit [7] mp 171°.

1,3,6-Trimethylumazine (8).

To 25 ml of 80% of sulphuric acid is added 0.5 g (2.1 mmoles) of **5** and the mixture then heated to 100° for 30 minutes. After cooling the mixture is poured on 40 g of ice, extracted three times with 120 ml of chloroform, the organic layer dried over potassium carbonate and then evaporated

Table 2

UV-Absorption Spectra of 1,3-Dimethylumazine-6- and 7-carboxaldehyde Derivatives

Compound	p <i>K</i> _a in H ₂ O	UV-Absorption Spectra							
		λ max (nm)		log ε					
4		242	283	416	4.09	4.16	3.65	MeOH	
5		243	284	360	4.11	4.12	3.70	MeOH	
6	9.57	[257]	283	351	[4.13]	4.25	3.95	7.0	
			300	372		4.39	3.88	12.0	
18	9.15	[255]	284	351	[4.08]	4.28	3.88	MeOH	
			225	250	352	4.30	4.14	4.12	7.0
			237	304	375	4.25	3.87	4.39	12.0
		227	257	351	4.26	4.07	4.07	MeOH	
7		239		331	4.22		3.87	MeOH	
19		237		332	4.14		3.89	MeOH	
8		238		336	4.21		3.86	MeOH	
20		235		329	4.09		3.89	MeOH	
9		248	[258]	337	4.19	[4.08]	3.92	MeOH	
21		242		342	4.12		3.91	MeOH	
10		238		335	4.22		3.86	MeOH	
22		236		331	4.18		3.94	MeOH	
11		247	[264]	331	4.14	[4.01]	3.88	MeOH	
23		236		331	4.18		3.94	MeOH	
12		252	[270]	338	4.24	[4.10]	3.96	MeOH	
24		246	[286]	352	4.17	[3.10]	3.87	MeOH	
13		[256]	289	351	[4.04]	4.33	3.95	MeOH	
25		229	257	352	4.33	4.17	4.20	MeOH	
14		240		331	4.25		3.88	MeOH	
26		237		332	4.32		4.04	MeOH	
15		242		339	4.30		3.91	MeOH	
27		237		340	4.26		4.14	MeOH	
16		248	287	331	4.74	3.95	3.85	MeOH	
28		247	[292]	334	4.63	[3.80]	3.92	MeOH	
17		255	289	341	4.08	4.26	4.00	MeOH	

ated to dryness to give 0.31 g (72%) of a colourless powder of mp 202-203°.

6-Dibromomethyl-1,3-dimethylumazine (9).

In 60 ml of glacial acetic acid is dissolved 2.4 g (11 mmoles) of **8** and then with stirring 1 ml (20 mmoles) of bromine added dropwise. The mixture is then heated under reflux in an oil bath for 1 hour and then evaporated to dryness. The residue is treated with 100 ml of chloroform, washed three times with water, the organic layer dried over sodium sulfate and then evaporated to dryness. The residue consists of a mixture of 6-bromomethyl- and 6-dibromomethyl-1,3-dimethylumazine, which are separated by silica gel column chromatography first with toluene/ethyl acetate (9/1) to elute **9**, of which was obtained after evaporation and drying 1.62 g (40%) of mp 215-216°.

Anal. Calcd. for $C_8H_{10}Br_2N_4O_2$: C, 29.70; H, 2.21; N, 15.39. Found: C, 29.93; H, 2.38; N, 15.39.

Continuation of the chromatographic separation on the silica gel column with the mixture toluene/ethyl acetate (4/1) elutes 1.3 g (42%) of 6-bromomethyl-1,3-dimethylumazine of mp 228° dec.

6-Hydroxymethyl-1,3-dimethylumazine (10).

In a mixture of 75 ml of acetonitrile and 4 ml of 5 *N* acetic acid is dissolved 0.5 g (2.3 mmoles) of **7** and then small amounts of sodium borohydride added with stirring in small amounts until the starting material could not any more be detected chromatographically. Stirring is continued for another 20 minutes and then the mixture evaporated to dryness. The residue is dissolved in 40 ml of water, then extracted 5 times with each 50 ml of chloroform, the organic layer dried over sodium sulfate and evaporated to dryness. Crystallization of the residue from 20 ml of ethanol yielded 0.395 g (78%) of colourless needles of mp 211-212° lit [11] mp 208-209°.

1,3-Dimethylumazine-6-carboxylic Acid (11).

a) In 30 ml of 50% sulphuric acid is heated under reflux 0.25 g (1.2 mmoles) of **12** for 1.5 hours. After cooling the mixture is diluted with 30 ml of water and then stored in the ice box for several days. The precipitate is filtered off, washed with water and dried in vacuum to give 0.2 g (74%) of colourless needles of mp 249° dec, lit [13] mp 249-250°.

b) Thirty ml of water is adjusted by 0.1 *N* sodium hydroxide to a pH of 10, then 0.22 g (1 mmole) of **7** added and the mixture then treated by slow addition of 10 ml of a 1% potassium permanganate solution at room temperature for 1.5 hours. Then 6 ml of methanol is added and the mixture heated to 90° for a few minutes. The precipitate of MnO_2 is filtered off, the filtrate acidified by concentrated hydrochloric acid to pH 0 and then the solution stored in the ice box over night to give 0.18 g (76%) of colourless needles of mp 250° dec.

6-Cyano-1,3-dimethylumazine (12).

In 30 ml of acetic anhydride is boiled under reflux 1.0 g (4.3 mmoles) of **6** for 24 hours. It is then evaporated to dryness, the residue dissolved in little ethyl acetate and then purified by silica gel column chromatography with the system toluene/ethyl acetate (95/5) and collection of the main fraction. After evaporation the residue is recrystallized from 40 ml of a mixture of water/ethanol (7/3) to give 0.695 g (75%) of colourless needles of mp 165° dec.

Anal. Calcd. for $C_9H_{11}N_5O_2$: C, 49.77; H, 3.25; N, 32.25. Found: C, 49.54; H, 3.21; N, 32.15.

1,3-Dimethyl-6-(*O*-methyl)carboxaldoxime (13).

To a mixture of 40 ml of ethanol and 10 ml of water is added 0.3 g *O*-methylhydroxylammonium chloride, 0.26 g sodium bicarbonate and 0.25 g (1.1 mmoles) of **7** with stirring. After treatment for 4 hours at room temperature the precipitate is filtered off and washed with water. The filtrate is evaporated to dryness, the residue dissolved in little water and then acidified to give another crop. After filtration the unified precipitates are dried at 100° to give 0.275 g (97%) of a colourless powder of mp 215°.

Anal. Calcd. for $C_{10}H_{11}N_5O_3$: C, 48.19; H, 4.45; N, 28.10. Found: C, 48.20; H, 4.42; N, 27.90.

6-(1,3-Dioxolan-2-yl)-1,3-dimethylumazine (14).

A mixture of 0.5 g (2.3 mmoles) of **7**, 80 mg of *p*-toluenesulfonic acid monohydrate and 0.3 ml of ethylene glycol were refluxed in 50 ml of absolute chloroform for 8 hours in such a manner that in between the reaction vessel and the condenser a Soxhlet apparatus, filled with molecular sieve (3-4 A), is fitted to remove the water formed during the reaction. The reaction solution is then treated twice with 30 ml of 0.5 *N* sodium hydroxide and subsequently washed three times with water. The organic layer is dried over potassium carbonate, the solution concentrated to a small volume and then chromatographed over a silica gel column with chloroform to give from the main fraction after evaporation 0.462 g (77%) of a colourless powder of mp 191° dec.

Anal. Calcd. for $C_{11}H_{12}N_4O_4$: C, 50.00; H, 4.58; N, 21.20. Found: C, 49.70; H, 4.73; N, 21.00.

6-(1,3-Dithian-2-yl)-1,3-dimethylumazine (15).

A mixture of 0.25 g (1.1 mmoles) of **7**, 0.15 ml of 1,3-propanedithiole and 60 mg of *p*-toluenesulfonic acid monohydrate is stirred in 30 ml of absolute chloroform at room temperature for 15 hours. The reaction solution is treated three times with 90 ml of 5% potassium hydroxide, three times with water and then dried over sodium sulfate. The reaction solution is then evaporated to give an oil, which solidifies after treatment and coevaporation several times with toluene. The residue is dissolved in little chloroform and purified by column chromatography on silica gel with chloroform as the eluant. The main fraction is collected and yielded on evaporation and drying 0.253 g (72%) of a slightly yellowish powder of mp 196°.

Anal. Calcd. for $C_{12}H_{14}N_4O_2S_2$: C, 46.43; H, 4.55; N, 18.05. Found: C, 46.63; H, 4.49; N, 17.61.

6-(*N,N'*-Diphenylimidazolidin-2-yl)-1,3-dimethylumazine (16).

A mixture of 0.5 g (2.3 mmoles) of **7**, 80 mg of *p*-toluenesulfonic acid monohydrate and 0.725 g of *N,N'*-diphenylethylenediamine is boiled under reflux in 50 ml of absolute chloroform for 10 hours in such a manner that a Soxhlet apparatus, filled with molecular sieve (3-4 A), is fitted in between the reaction vessel and the condenser in order to remove the water formed during the reaction. The reaction solution is then treated three times with 90 ml of 0.5 *N* sodium hydroxide followed by washing three times with water. The organic layer is dried over potassium carbonate, filtered and then the filtrate evaporated to dryness. The residue is dissolved in little ethyl acetate, put on a silica gel column (80 g) and then developed with toluene/ethyl acetate (95/5). The main fraction is collected and evaporated to dryness to give a 1/1-adduct of **16** and toluene. Drying of this material in high vacuum at 100° yielded 0.807 g (86%) of **16** as a yellowish powder of mp 226°.

Anal. Calcd. for $C_{23}H_{22}N_6O_2$: C, 66.65; H, 5.35; N, 20.28. Found: C, 67.00; H, 5.46; N, 20.16.

1,3-Dimethylumazine-6-(*O*-acetyl)carboxaldoxime (17).

In 30 ml of acetic anhydride is boiled under reflux for 2 hours 1.0 g (4.3 mmoles) of **6**. On cooling a precipitate separates out, which is filtered off after standing over night. Crystallization from 40 ml of water/ethanol (1/1) yielded 0.465 g (40%) of yellowish needles of mp 178-180° dec.

Anal. Calcd. for $C_{11}H_{11}N_5O_4$: C, 47.66; H, 4.00; N, 25.26. Found: C, 47.55; H, 3.98; N, 25.35.

1,3-Dimethylumazine-7-carboxaldoxime (18).

A mixture of 1.0 g (2.74 mmoles) of **6** and 1.04 g sodium bicarbonate in 20 ml of ethanol is combined with a solution of 0.96 g (13.7 mmoles) of hydroxylamine hydrochloride in 150 ml of water and then the mixture refluxed for 16 hours. After cooling the precipitate is filtered off, washed with water and ethanol to yield after drying in vacuum at 60° 0.53 g (82%) of a yellowish powder of mp 253-254° dec.

Anal. Calcd. for $C_9H_9N_3O_3$: C, 45.96; H, 3.86; N, 29.77. Found: C, 45.85; H, 3.78; N, 29.60.

1,3-Dimethylumazine-7-carboxaldehyde (19).

The same procedure as described for **7** yielded from 5 g (21 mmoles) of **18** after purification by silica gel column chromatography in the system toluene/ ethyl acetate (15/1) 4.12 g (88%) of a colourless powder of mp 168-170°.

Anal. Calcd. for $C_9H_9N_3O_3$: C, 49.09; H, 3.66; N, 25.44. Found: C, 49.38; H, 3.72; N, 25.08.

7-Dibromomethyl-1,3-dimethylumazine (21).

In 20 ml of glacial acetic acid is dissolved 0.5 g (2.4 mmoles) of **20** [8] and than 1 g of bromine added dropwise. The mixture is then refluxed for 3-4 hours until the intense colour has disappeared. It is evaporated to dryness, the residue dissolved in chloroform and then washed several times with water. The organic layer is dried over magnesium sulfate, filtered, evaporated, and finally the residue crystallized from methanol to give 0.785 g (88%) of slightly yellowish needles of mp 203-204°.

Anal. Calcd. for $C_9H_9Br_2N_3O_2$: C, 29.70; H, 2.21; N, 15.39; Br, 43.91. Found: C, 29.64; H, 2.09; N, 15.11; Br, 44.08.

7-Hydroxymethyl-1,3-dimethylumazine (22).

Compound **19** (0.5 g) is treated analogously to the procedure of **10**. Purification is done by crystallization from ethanol by the adding of ether to give 0.466 g (92%) of colourless crystals of mp 158-159° dec.

Anal. Calcd. for $C_9H_{10}N_3O_3$: C, 48.65; H, 4.54; N, 25.22. Found: C, 48.46; H, 4.78; N, 24.98.

1,3-Dimethylumazine-7-carboxylic Acid (23).

Compound **24** (0.25 g) is treated analogously to the procedure of **11 a**) to yield 0.203 g (75%) and from **19** by procedure **11 b**) to form 0.251 g (93%) of colourless crystals of mp 226-227° lit [8] mp 215-216°.

7-Cyano-1,3-dimethylumazine (24).

Treatment of 1.0 g (4.3 mmoles) of **18** analogously to procedure **12** yielded 0.77 g (83%) of yellowish crystals of mp 158-159°.

Anal. Calcd. for $C_9H_9N_5O_2$: C, 49.77; H, 3.25; N, 32.25. Found: C, 49.83; H, 3.24; N, 31.85.

1,3-Dimethylumazine-7-(O-methyl)carboxaldoxime (25).

Compound **19** (0.25 g) is treated analogously to the procedure **13** to yield 0.275 g (97%) of a colourless powder of mp 206-207°.

Anal. Calcd. for $C_{10}H_{11}N_3O_3$: C, 48.19; H, 4.45; N, 28.10. Found: C, 48.22; H, 4.34; N, 28.20.

7-(1,3-Dioxolan-2-yl)-1,3-dimethylumazine (26).

Compound **19** (0.5 g) is treated analogously to procedure **14** to give on crystallization from ethanol 0.475 g (79%) colourless crystals of mp 177-178°.

Anal. Calcd. for $C_{11}H_{12}N_4O_4$: C, 50.00; H, 4.58; N, 21.20. Found: C, 50.00; H, 4.68; N, 21.27.

7-(1,3-Dithian-2-yl)-1,3-dimethylumazine (27).

Compound **19** (0.25 g) is treated analogously to procedure **15** to give after work-up 0.274 g (78%) of a yellowish powder of mp 194-195°.

Anal. Calcd. for $C_{12}H_{14}N_4O_2S_2$: C, 46.43; H, 4.55; N, 18.05. Found: C, 46.40; H, 4.34; N, 17.81.

7-(N,N'-Diphenylimidazolidin-2-yl)-1,3-dimethylumazine (28).

Compound **19** (0.5 g) is treated analogously to procedure **16** to yield after the chromatographical purification and evaporation a yellowish oil, which is dissolved in hot ethanol to yield on cooling 0.685 g (73%) of yellowish crystals of mp 173-174°.

Anal. Calcd. for $C_{23}H_{22}N_6O_7$: C, 66.65; H, 5.35; N, 20.28. Found: C, 66.27; H, 5.40; N, 20.11.

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REFERENCES AND NOTES

- [1] M. Böhme, W. Hutzenlaub, W. J. Richter, E. F. Elstner, G. Huttner, J. v. Seyerl and W. Pfeleiderer, *Ann. Chem.*, 1705 (1986).
- [2] W. Pfeleiderer in "Comprehensive Heterocyclic Chemistry", A. R. Katritzky and C. W. Rees, eds, Vol 3, Part 2B, Pergamon Press, Oxford, 1984, p 263.
- [3] P. Karrer and R. Schwyzer, *Helv. Chim. Acta*, **31**, 777 (1948).
- [4] H. von Pechmann and K. Wehsarg, *Ber.*, **19**, 2466 (1886).
- [5] K.K. Koessler and M. H. Hauke, *J. Am. Chem. Soc.*, **40**, 1717 (1918).
- [6] T. A. Geissman, M. J. Schlatter and I. D. Webb, *J. Org. Chem.*, **11**, 736 (1946).
- [7] G. Henseke and H. G. Patzwaldt, *Chem. Ber.*, **89**, 2904 (1956).
- [8] R. Baur, E. Kleiner and W. Pfeleiderer, *Ann. Chem.*, 1798 (1984).
- [9] O. L. Brady and G. F. Goldstein, *J. Chem. Soc.*, 1918 (1926).
- [10] G. Charrier, *Gazz. Chim. Ital.*, **37**, 145 (1907).
- [11] H. Zondler, H. S. Forrest and J. M. Lagowski, *J. Heterocyclic Chem.*, **4**, 124 (1967).
- [12] H. Fuchs and W. Pfeleiderer, *Heterocycles*, **11**, 247 (1978).
- [13] R. B. Angier and W. V. Curran, *J. Org. Chem.*, **27**, 892 (1962).