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One-Step Synthesis of Alloxazines, Alloxazine-5-oxides, 5-Aryl-5-deazaalloxazines, and Fervenulin-4-oxides

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Summary. 1-Methylalloxazines and 1-methylalloxazine-N-oxides were prepared by the treatment of 1-methyl-6-anilinouracils with diethyl azodiformate (*DAD*) and potassium nitrate, and sulfuric acid in acetic acid, respectively. In addition, 1-methyl-5-aryl-5-deazaalloxazines were prepared by refluxing of 1-methyl-6-anilinouracils with aryl aldehydes in acetic acid. Treatment of 6-benzylidenehydrazinouracils with potassium nitrate and sulfuric acid in acetic acid gave fervenulin-4-oxides.

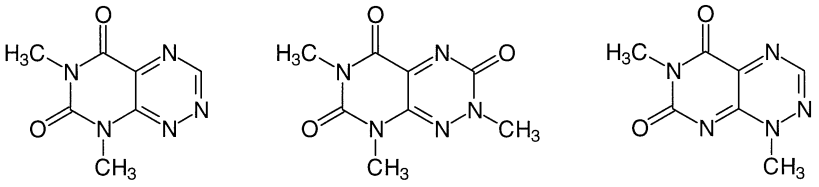
Keywords. 6-Anilino-1-methyluracils; Alloxazines; Alloxazine 5-oxides; 5-Aryl-5-deazaalloxazines; Fervenulin-4-oxides.

Einstufige Synthese von Alloxazinen, Alloxazin-5-oxiden, 5-Aryl-5-deazaalloxazinen und Fervenulin-4-oxiden

Zusammenfassung. 1-Methylalloxazine und 1-Methylalloxazin-N-oxide wurden durch Behandeln von 1-Methyl-6-anilinouracilen mit Diethylazadiformiat (*DAD*) und Kaliumnitrat sowie Schwefelsäure in Essigsäure hergestellt. Zusätzlich wurden durch Kochen von 1-Methyl-6-anilinouracilen mit aromatischen Aldehyden in Essigsäure unter Rückfluß 1-Methyl-5-aryl-5-deazaalloxazine erhalten. Aus 6-Benzylidenhydrazinouracilen entstehen durch Reaktion mit Kaliumnitrat und Schwefelsäure in Eisessig Fervenulin-4-oxide.

Introduction

5-Deazaalloxazines and 5-deazaflavins have been prepared by intramolecular cyclization of substituted 6-anilinouracils with one-carbon reagents, including the *Vilsmeier* type of reaction or triethyl orthoformate [1], by the condensation of 6-chloro-5-formylpyrimidines with N-substituted anilines, and by oxidative cyclization of aryl-*bis*(6-alkylamino-3-methyluracil-5-yl)methanes [2] with *DAD* (diethyl azodiformate) which led to the formation of 10-arly-5-deazaflavins. Coenzyme F_{420} from methanogenic bacteria contains the 8-hydroxy-5-deazaflavin moiety [3], and attractive biological activities are displayed by the antibiotics fervenulin (**1**), 2-methylfervenulone (MSD-92) (**2**), and toxoflavin (**3**) [4]. This promoted me to prepare a variety of 3-substituted N-oxide analogues.

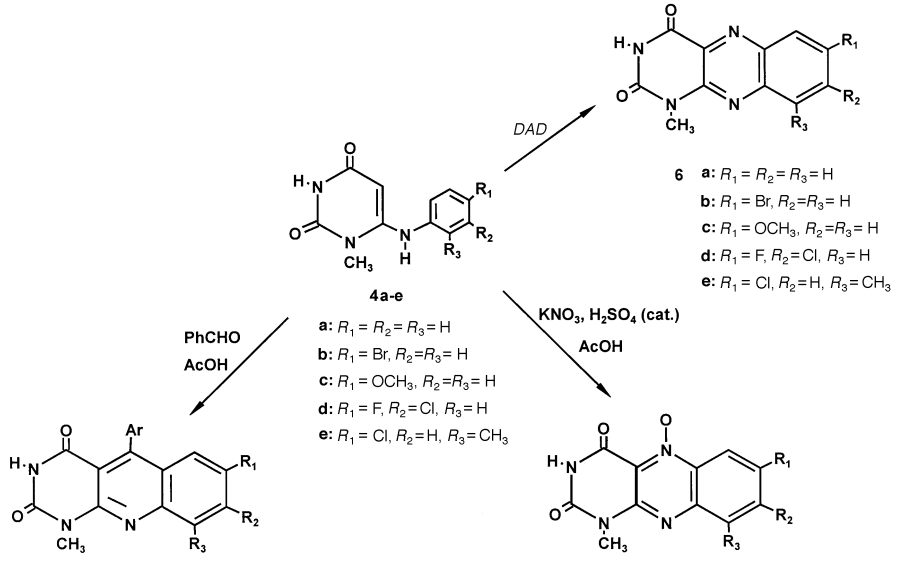


1 **2** **3**

In a previous paper [5], the synthesis of some derivatives of 5-deazaalloxazines and fervenulin by cyclocondensation of 6-arylamino- and 6-arylidinehydrazino-1-methyluracils using the *Vilsmeier* reagent and nitrous acid has been studied. The present work describes a convenient method for the synthesis of 1-methylalloxazine, 1-methylalloxazine-5-oxides, 5-aryl-5-deazaalloxazines, and 6-demethylfervenulin-4-oxides.

Results and Discussion

Heating a mixture of 6-anilino-1-methyluracils **4a–e** [5, 6] and a slight excess of *DAD* [7] which acts as a dehydrogenating agent as well as a nitrogen source for the direct cyclization at 200°C for 1 h under reflux gave 1-methylalloxazines **6a–e** in 35–83% yield, whereas treatment of **4a–e** with potassium nitrate and acetic acid in the presence of a few drops of sulfuric acid afforded compounds **7a–e** in 40–85%



4a-e

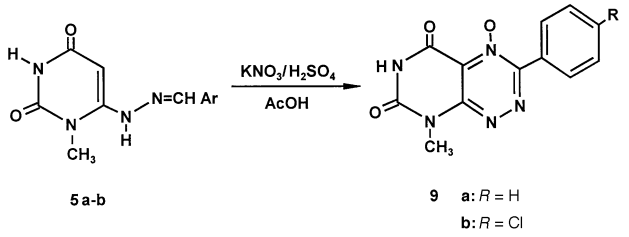
a: $R_1 = R_2 = R_3 = H$
b: $R_1 = Br$, $R_2 = R_3 = H$
c: $R_1 = OCH_3$, $R_2 = R_3 = H$
d: $R_1 = F$, $R_2 = Cl$, $R_3 = H$
e: $R_1 = Cl$, $R_2 = H$, $R_3 = CH_3$

6 **a:** $R_1 = R_2 = R_3 = H$
b: $R_1 = Br$, $R_2 = R_3 = H$
c: $R_1 = OCH_3$, $R_2 = R_3 = H$
d: $R_1 = F$, $R_2 = Cl$, $R_3 = H$
e: $R_1 = Cl$, $R_2 = H$, $R_3 = CH_3$

8 **a:** $R_1 = R_2 = R_3 = H$, Ar = Ph
b: $R_1 = Br$, $R_2 = R_3 = H$, Ar = Ph
c: $R_1 = OCH_3$, $R_2 = R_3 = H$, Ar = Ph
d: $R_1 = R_2 = R_3 = H$, Ar = P.$OCH_3C_6H_4$
e: $R_1 = Br$, $R_2 = R_3 = H$, Ar = P.$OCH_3C_6H_4$
f: $R_1 = OCH_3$, $R_2 = R_3 = H$, Ar = P.$OCH_3C_6H_4$

7 **a:** $R_1 = R_2 = R_3 = H$
b: $R_1 = Br$, $R_2 = R_3 = H$
c: $R_1 = OCH_3$, $R_2 = R_3 = H$
d: $R_1 = F$, $R_2 = Cl$, $R_3 = H$
e: $R_1 = Cl$, $R_2 = H$, $R_3 = CH_3$

Scheme 1



Scheme 2

yield (Scheme 1). The structures of **6b–e** and **7b–e** were established by comparison of their spectroscopic data with those of authentic samples for **6a** and **7a** [6]. On the other hand, refluxing **4a–c** with a slight excess of aryl aldehydes such as benzaldehyde and/or anisaldehyde in glacial acetic acid for 6 h afforded 1-methyl-5-aryl-5-deazaalloxazines **8a–f** but no 1-methyl-10-aryl-5-deazaalloxazines as was expected (Scheme 1). The structures of **8a–f** were established from their analytical and spectroscopic data, in particular from the absence of the C-5 proton in the ^{1}H NMR spectrum which should appear 8.82–9.20 ppm [5]. Treatment of 6-benzylidinehydrazino-1-methyluracils **5a**, **b** [5] with potassium nitrate and acetic acid in the presence of a few drops of sulfuric acid [8] at 100°C for 50 min gave 6-demethylfervenulin-4-oxides **9a**, **b** in 55–70% yield (Scheme 2).

Experimental

Melting points are uncorrected. UV spectra were recorded on Perkin-Elmer Lambda 5 or 15 spectrophotometers. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AC 250 spectrometer (*TMS* as internal standard). Mass spectra were recorded on a Mat 1125 instrument (EI, 70 eV).

1-Methylalloxazines **6a–e** *(general procedure)*

A mixture of **4** (1.6 mmol) and *DAD* (2.0 mmol) was heated under reflux at 200°C for 1 h. After cooling, the mixture was triturated with ether. The resulting product was collected by filtration, washed with ether and recrystallized from the appropriate solvent (Table 1).

1-Methylalloxazine (**6a**)

6a was obtained from **4a** in 46% yield. M.p.: >330°C (*DMF*/EtOH; Ref. [6]: m.p.: >360°C); UV (MeOH): λ_{max} (lg ε) = 214 (4.83), 242 (4.91), 321 (4.31) 379 (4.44) nm; $C_{11}H_8N_4O_2$; calcd.: C 57.89, H 3.53, N 24.55; found: C 57.75, H 3.50, N 24.21.

1-Methyl-7-bromoalloxazine (**6b**)

Obtained from **4b**; UV (MeOH): λ_{max} (lg ε) = 215 (4.71), 252 (4.99), 313 (4.16), 388 (4.43) nm; ^{13}C NMR (*DMSO*-d_6): δ = 28.29 (N–C1), 120.98, 129.12, 131.59, 132.74, 136.15, 138.90, 140.87, 147.18, 150.05 (C=O), 159.03 (C=O) ppm; $C_{11}H_7BrN_4O_2$; calcd.: C 43.01, H 2.29, N 18.24; found: C 43.25, H 2.35, N 17.99.

1-Methyl-7-methoxyalloxazine (**6c**)

Obtained from **4c**; UV (MeOH): λ_{max} (lg ε) = 219 (4.65), 258 (4.79), 316 (4.10), 409 (4.35) nm; ^{13}C NMR (*DMSO*-d_6/CF_3COOH): δ = 28.58 (N–C1), 56.33 (O–C7), 101.07, 127.35, 129.17, 131.67,

139.42, 141.20, 146.20, 146.40, 150.91 160.42 (C=O), 160.50 (C=O) ppm; $C_{12}H_{10}N_4O_3$; calcd.: C 55.81, H 3.90, N 21.69; found: C 56.01, H 3.79, N 21.82.

1-Methyl-7-flouro-8-chloroalloxazine (**6d**)

Obtained from **4d**; UV (MeOH): λ_{max} (lg ε) = 219 (4.95), 246 (4.89), 316 (4.30), 383 (4.50) nm; ^{13}C NMR (*DMSO*-d_6): δ = 28.94 (C1), 105.50, 105.94, 127.89, 129.95, 134.83, 140.04, 149.23, 150.04, 154.40 (C=O), 158.13 (C=O) ppm; MS: *m/z* (%) = 282 (32), 281 (15), 280 (M^+, 100), 211 (18), 210 (9), 209 (52), 182 (90), 155 (39), 142 (18), 105 (13); $C_{11}H_6FClN_4O_2$; calcd.: C 47.07, H 2.15, N 19.96; found: C 46.88, H 2.14, N 19.65.

1,9-Dimethyl-7-chloroalloxazine (**6e**)

Obtained from **4e**; UV (MeOH): λ_{max} (lg ε) = 216 (4.50), 253 (4.70), 325 (3.94), 393 (4.12) nm; ^{13}C NMR (*DMSO*-d_6): δ = 16.25 (C9–CH_3), 28.15 (N1–CH_3), 125.92, 132.28, 132.46, 132.96, 137.87, 138.72, 139.83, 146.23, 150.07 (C=O), 159.04 (C=O) ppm; MS: *m/z* (%) = 278 (32), 277 (18), 276 (M^+, 100), 265 (6), 203 (7), 205 (24), 188 (8), 190 (22), 176 (14), 178 (52), 163 (9), 142 (8), 114 (7), 102 (9); $C_{12}H_9ClN_4O_2$; calcd.: C 52.09, H 3.27, N 20.25; found: C 51.98, H 3.23, N 19.97.

1-Methylalloxazine 5-oxides **7a–e** *(general procedure)*

Sulfuric acid (1.0 mmol) was added dropwise to a hot mixture of **4b–e** (2.0 mmol) and KNO_3 (2.3 mmol) in acetic acid (5 ml) which was kept at 90°C in an oil bath for 1 h. The mixture was evaporated *in vacuo*, and the residue was diluted with water (10 ml). The resulting product was collected by filtration and, washed with ethanol or ether (Table 1).

1-Methyl-7-bromoalloxazine-5-oxide (**7b**)

Obtained from **4b**; UV (MeOH): λ_{max} (lg ε) = 202 (4.52), 270 (5.12), 335 (4.35), 410 (4.33) nm; ^{13}C NMR (*DMSO*-d_6): 28.91 (N–Cl), 120.80, 121.10, 122.66, 130.36, 135.87, 136.85, 141.63, 149.27, 149.70 (C=O), 154.65 (C=O) ppm; MS: *m/z* (%) = 325 (13), 324 (97), 323 (M^+, 14), 322 (M^+-1, 100), 307 (M^+-16, 38), 306 (40), 235 (13), 233 (12), 208 (78), 207 (62), 206 (74), 181 (27), 179 (25), 115 (24); $C_{11}H_7BrN_4O_3$; calcd.: C 40.88, H 2.18, N 17.34; found: C 40.87, H 2.26, N 17.61.

1-Methyl-7-methoxyalloxazine-5-oxide (**7c**)

Obtained from **4c**; UV (MeOH): λ_{max} (lg ε) = 204 (4.47), 271 (4.92), 334 (4.18), 429 (4.23) nm; ^{13}C NMR (*DMSO*-d_6): 28.73 (N–C1), 56.13 (O–C7) 97.77, 121.80, 125.99, 129.84, 136.19, 138.47, 147.81, 149.39, 154.90 (C=O), 159.46 (C=O) ppm; MS: *m/z* (%) = 274 (M^+, 100), 258 (M^+-16, 77), 244 (18), 227 (9), 187 (20), 160 (52), 144 (18), 117 (23); $C_{12}H_{10}N_4O_4$; calcd.: C 52.55, H 3.67, N 20.43; found: C 52.91, H 3.56, N 19.98.

1-Methyl-7-flouro-8-chloroalloxazine-5-oxide (**7d**)

Obtained from **4d**; UV (MeOH): λ_{max} (lg ε) = 210 (4.18), 267 (4.54), 338 (3.96), 405 (3.89) nm; MS: *m/z* (%) = 298 (29), 297 (12), 296 (M^+, 82), 280 (M^+-16, 43), 209 (19), 184 (34), 183 (35), 182 (100), 181 (70), 157 (14), 156 (15), 155 (40), 154 (20); $C_{11}H_6FClN_4O_3$; calcd.: C 44.53, H 2.03, N 18.88; found: C 44.67, H 2.14, N 19.28.

1,9-Dimethyl-7-chloroalloxazine-5-oxide (**7e**)

Obtained from **4e**; UV (MeOH): λ_{max} (lg ε) = 203 (4.50), 264 (5.03), 313 (3.35), 413 (4.34) nm; ^{13}C NMR ($CDCl_3/CF_3COOH$): δ = 17.60 (C–C9), 30.99 (N–C1), 109.01, 117.35, 121.85, 138.25, 140.05, 142.19, 144.45, 148.25, 152.57 (C=O), 158.96 (C=O) ppm; MS: *m/z* (%) = 294 (33), 293 (14), 292 (M^+, 100), 278 (22), 277 (10), 276 (M^+-16, 60), 205 (14), 190 (24), 180 (23), 179 (18), 178 (72); $C_{12}H_9ClN_4O_3$; calcd.: C 49.24, H 3.09, N 19.14; found: C 49.32, H 3.22, N 19.02.

1-Methyl-5-aryl-5-deazaalloxazines (**8a–f**)

A mixture of **4** (2.0 mmol) and benzaldehyde or anisaldehyde (2.5 mmol) in glacial acetic acid (6 ml) was refluxed for 6 h. The precipitate was filtered off, washed with ethanol, and dried in the oven (Table 1).

1-Methyl-5-phenyl-5-deazaalloxazines (**8a**)

Obtained from **4a** and benzaldehyde; UV (0.1 *N*, NaOH): λ_{max} (lg ε) = 359 (3.74), 295 (3.39), 248 (4.71), 211 (4.27), 200 (3.78) nm; ^{13}C NMR (*DMSO*-d_6): δ = 28.52 (N–C1), 111.84, 117.50, 124.21, 125.49, 127.93, 127.99, 128.48, 129.76, 137.33, 144.98, 149.21, 151.66, 152.61, 157.26, 160.18 ppm; $C_{18}H_{13}N_3O_2$; calcd.: C 71.27, H 4.32, N 42.01; found: C 71.31, H 4.30, N 42.12.

1-Methyl-7-bromo-5-phenyl-5-deazaalloxazine (**8b**)

Obtained from **4b** and benzaldehyde; UV (0.1 *N*, NaOH): λ_{max} (lg ε) = 372 (3.63), 317 (3.56), 258 (3.74), 211 (4.35), 206 (3.56) nm; ^{13}C NMR (*DMSO*-d_6): δ = 28.76 (N–C1), 101.31, 109.65, 113.44, 118.19, 126.26, 127.84, 127.90, 128.19, 129.91, 135.99, 146.92, 150.70, 152.71, 159.76 ppm; $C_{18}H_{12}BrN_3O_2$; calcd.: C 56.56, H 3.16, N 10.99; found: C 56.81, H 3.20, N 12.00.

1-Methyl-7-methoxy-5-phenyl-5-deazaalloxazine (**8c**)

Obtained from **4c** and benzaldehyde; UV (0.1 *N*, NaOH): λ_{max} (lg ε) = 383 (4.06), 308 (4.05), 257 (4.77), 215 (4.57), 204 (4.38) nm; ^{13}C NMR (*DMSO*-d_6): δ = 28.61 (N–C1), 55.59 (OCH_3), 106.77, 108.96, 124.56, 125.93, 127.62, 127.78, 128.29, 129.33, 137.00, 144.48, 148.94, 150.56, 152.30, 156.90, 160.12 ppm; MS: *m/z* (%) = 333 (M^+, 100), 318 (5), 304 (6), 261 (5), 235 (7), 218 (7), 166 (8), 44 (5); $C_{19}H_{15}N_3O_3$; calcd.: C 68.45, H 4.53, N 12.60; found: C 68.37, H 4.66, N 12.70.

1-Methyl-5-(4-methoxyphenyl)-5-deazaalloxazine (**8d**)

Obtained from **4a** and anisaldehyde; UV (0.1 *N*, NaOH): λ_{max} (lg ε) = 363 (3.68), 313 (3.77), 251 (4.39), 211 (4.24), 202 (4.20) nm; ^{13}C NMR (*DMSO*-d_6): δ = 28.77 (N–Cl), 55.25 (OC), 113.73, 116.56, 123.33, 125.13, 126.75, 127.90, 129.03, 129.62, 132.47, 136.04, 140.27, 146.70, 150.47, 157.74, 161.29 ppm; MS: *m/z* (%) = 333 (M^+, 100), 332 (27), 304 (18), 261 (22), 228 (20), 190 (19), 188 (12), 128 (10); $C_{19}H_{15}N_3O_3$; calcd.: C 68.45, H 4.53, N 12.60; found: C 68.23, H 4.61, N 12.47.

1-Methyl-7-bromo-5-(4-methoxyphenyl)-5-deazaalloxazine (**8e**)

Obtained from **4b** and anisaldehyde; UV (0.1 *N*, NaOH): λ_{max} (lg ε) = 372 (3.94), 312 (3.88), 312 (3.88), 258 (4.68), 214 (4.55), 202 (3.92) nm; ^{13}C NMR (*DMSO*-d_6): δ = 28.67 (N–C1), 55.05 (OC), 109.59, 113.35, 118.04, 126.18, 127.56, 128.86, 129.49, 135.21, 146.37, 150.32, 152.43, 158.95, 159.82 ppm; MS: *m/z* (%) = 414 (24), 413 (M^++1, 100), 412 (M^+, 43), 411 (95), 410 (19), 382 (12), 332 (15), 190 (15), 177 (13), 151 (15), 135 (14); $C_{19}H_{14}BrN_3O_3$; calcd.: C 55.35, H 3.42, N 10.19; found: C 55.64, H 3.50, N 10.00.

Table 1. Physical data of compounds **6b–d**, **7a–d**, **8a–d**, and **9a**, **b**

	Yield (%)	M.p. (°C)	Solvent of crystallization	^{1}H NMR data (*DMSO*-d_6, *TMS*) δ (ppm)
6b	83	305–307	Benzene	3.51 (3H, s, NCH_3), 8.02 (1H, d, H9, $J_o = 9$ Hz), 8.03 (1H, dd, H8, $J_o = 9$ Hz, $J_m = 2$ Hz), 8.40 (1H, d, H6, $J_m = 2$ Hz), 11.98 (1H, s, NH)
6c	69	328	*DMF*	3.60 (3H, s, NCH_3), 3.98 (3H, s, OCH_3), 7.51 (1H, d, H9, $J_o = 9$ Hz), 7.58 (1H, d, H8, $J_o = 9$ Hz, $J_m = 2$ Hz), 7.88 (1H, d, H6, $J_m = 2$ Hz), 11.62 (1H, bs, NH)
6d	60	258–260	Ethanol	3.50 (3H, s, NCH_3), 8.22 (1H, d, H6, $J_o = 7$ Hz), 8.23 (d, 1H, H9, $J_m = 3$ Hz), 11.73 (1H, s, NH)
6e	35	283–285	*DMF*	3.57 (3H, s, CH_3), 7.79 (d, 1H, H8, $J_m = 2$ Hz), 8.01 (1H, d, H6, $J_m = 2$ Hz), 11.86 (1H, s, NH)
7b	62	258	*DMF*	3.51 (3H, s, NCH_3), 7.89 (1H, d, H9, $J_o = 8$ Hz), 8.05 (1H, dd, H8, $J_o = 8$ Hz), 8.46 (1H, d, H6, $J_m = 2$ Hz), 11.86 (1H, s, NH)
7c	80	268–314	*DMF*	3.51 (3H, s, NCH_3), 3.95 (3H, s, OCH_3), 7.58 (1H, d, H9, $J_o = 6$ Hz), 7.68 (1H, dd, H8, $J_m = 2$ Hz),$J_o = 8$ Hz), 7.87 (1H, d, H6, $J_m = 2$ Hz), 11.84 (1H, s, NH)
7d	52	275–277	*DMF*	3.47 (3H, s, NCH_3), 8.20 (1H, d, H9, $J_m = 3$ Hz), 8.23 (1H, d, H6, $J_o = 7$ Hz), 11.86 (1H, s, NH)
7e	49	>330	*DMF*	2.84 (3H, s, CH_3), 3.92 (3H, s, NCH_3), 7.80 (1H, d, H8, $J_m = 2$ Hz), 8.07 (1H, d, H6, $J_m = 2$ Hz), 11.70 (1H, s, NH)
8a	62	>340	*DMF*/H_2O (2:1)	3.02 (3H, s, NCH_3), 7.02–6.87 (4H, m, ArH), 7.95–7.29 (SH, m, ArH), 11.07 (1H, s, NH)
8b	56	338	*DMF*/H_2O (2:1)	3.65 (3H, s, NCH_3), 6.81 (1H, d, ArH), 7.44 (5H, m, ArH), 7.89 (2H, d, ArH), 11.09 (1H, s, NH)
8c	71	>340	*DMF*/H_2O (2:1)	3.62 (3H, s, NCH_3), 3.63 (3H, s, OCH_3), 6.56 (2H, m, ArH), 7.24–7.20 (2H, m, ArH), 7.52–7.45 (4H, m, ArH), 7.88 (1H, dd, ArH), 10.93 (1H, s, NH)
8d	49	>340	*DMF*/H_2O (2:1)	3.65 (3H, s, NCH_3), 3.86 (3H, s, OCH_3), 6.71 (2H, d, ArH), 7.16 (2H, m, ArH), 7.28 (2H, d, ArH), 7.38 (1H, d, ArH), 7.92 (1H, d, ArH), 11.07 (1H, s, NH)
8e	76	305	*DMF*/H_2O (2:1)	3.59 (3H, s, NCH_3), 3.87 (3H, s, OCH_3), 7.06 (2H, m, ArH), 7.18 (2H, d, ArH), 7.39 (1H, d, ArH), 7.85 (2H, m, ArH), 11.42 (1H, s, NH)
8f	69	339	*DMF*/H_2O (2:1)	3.60 (3H, s, NCH_3), 3.63 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 6.64 (1H, d, ArH), 7.05 (2H, dd, ArH), 7.13 (2H, dd, ArH), 7.48 (1H, d, ArH), 7.85 (1H, d, ArH), 11.20 (1H, s, NH)
9a	70	318–321	AcOH	3.61 (1H, s, NCH_3), 7.60 (3H, m, ArH), 8.40 (2H, m, ArH), 12.27 (1H, s, NH)
9b	56	236–238	AcOH	3.36 (3H, s, NCH_3), 7.60 (2H, d, ArH), 8.19 (2H, d, ArH), 11.03 (1H, s, NH)

1-Methyl-5-(4-methoxyphenyl)-7-methoxy-5-deazaalloxazine (**8f**)

Obtained from **4c** and anisaldehyde; UV (0.1 *N* NaOH): λ_{max} (lg ε) = 364 (4.18), 310 (4.33), 257 (4.86), 213 (4.78), 202 (4.35) nm; ^{13}C NMR (*DMSO*-d_6): δ = 28.55 (N–C1), 55.29 (O=C), 55.42 (O=C), 106.32, 109.02, 113.57. 124.37, 126.03, 128.78, 129.20, 129.59, 144.13, 148.73, 150.47, 152.16, 156.58, 159.14, 160.14 ppm; MS: *m/z* (%) = 363 (M^+, 100), 362 (9), 348 (8), 335 (4), 332 (7), 320 (4), 305 (6), 291 (5), 277 (6), 261 (7), 248 (12); $C_{20}H_{17}N_3O_4$; calcd.: C 66.11, H 4.71, N 11.56; found: C 65.98, H 4.77, N 11.74.

6-Demethyl-3-substituted fervenulin-4-oxides (**9**) *(general procedure)*

Concentrated sulfuric acid was added to a hot mixture of compound **5** (2.0 mmol) and KNO_3 (4.0 mmol) in acetic acid (10 ml). The mixture was heated at 100°C for 1 h in an oil bath. The inorganic residue was separated by filtration, and water (20 ml) was added. The resulting product was collected by filtration, washed with ethanol and ether and recrystallized from acetic acid to give yellow crystals.

6-Demethyl-3-phenylfervenulin-4-oxide (**9a**)

Obtained from **5a**; UV (MeOH): λ_{max} (lg ε) = 203 (4.47), 279 (4.75), 373 (3.96) nm; MS: *m/z* (%) = 271 (M^+, 38), 255 (M^+-16, 32), 228 (8), 200 (12), 199 (100), 115 (18), 105 (64), 81 (63); $C_{12}H_9N_5O_3$; calcd.: C 53.13, H 3.34, N 25.82; found: C 52.90, H 3.22, N 25.49.

6-Demethyl-3-(4-chloro)-phenylfervenulin-4-oxide (**9b**)

Obtained from **5b**; UV (MeOH): λ_{max} (lg ε) = 202 (4.22), 286 (4.43), 374 (3.50) nm; MS: *m/z* (%) = 306 (M^++1, 7), 305 (M^+, 6), 304 (M^+-1, 33), 289 (M^+-16, 81), 278 (33), 276 (100), 261 (11), 23 (57), 205 (75), 161 (25), 139 (26), 138; $C_{12}H_8ClN_5O_3$; C 47.15, H 2.63, N 22.91; found: C 46.89, H 2.61, N 22.47.

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