was refluxed for 1 h, 0.2 mL (2.6 mmol) of ethyl bromide was added at room temperature, and the mixture was gently refluxed for 5 h. After the usual workup, the products were isolated by column chromatography (silica gel, hexane–ethyl acetate) to give 0.204 g (0.615 mmol, 40%) of **44b** as the first fraction and 0.268 g (0.883 mmol, 57%) of **44a** as the second fraction.

9-Ethyl-5,6,9,10,11,11a-hexahydro-2,3-dimethoxy-8,10-dioxo-8*H*-benzo[*a*]quinolizine (44a),[73] oil.

9,9-Diethyl-5,6,9,10,11,11a-hexahydro-2,3-dimethoxy-8,10-dioxo-8*H*-benzo[*a*]quinolizine (44b), mp 135–140 °C.

Transformation of 44a to 38. Under an atmosphere of nitrogen, 0.313 g of the ethylene ketal[74] of **44a** was reduced with 50 mg (1.3 mmol) of $LiAlH_4$ in 30 mL of dry THF to yield 0.215 g of crude **9-ethyl-5,6,9,10,11,11a-hexahydro-2,3-dimethoxy-8*H*-benzo[*a*]quinolizine-10-spiro-2′-1′,3′-dioxolane,** oil.

The crude product was dissolved in 5 mL of THF and 10 mL of 10% aqueous sulfuric acid and refluxed under a nitrogen atmosphere for 8 h. After the usual workup, 0.163 g (0.563 mmol, 70% based on **44a**) of **38** was isolated by column chromatography (silica gel, ethyl acetate).

Michael Addition and Robinson Annelation[32,33,45,72,75] of 43a and 47. Under an atmosphere of nitrogen, a solution of 0.210 g (0.609 mmol) of the keto amide **47** and 0.35 mL (4.19 mmol) of pyrrolidine in 60 mL of dry benzene was refluxed for 1 h with continuous removal of water by aluminum oxide placed in a small Soxhlet extractor and concentrated to dryness to yield 0.298 g of crude **12-benzyl-1,6,7,12b-tetrahydro-4-oxo-2-(1-pyrrolidinyl)-4*H*-indolo[2,3-*a*]quinolizine** as an oil.

The crude amido-enamine and 0.1 g (0.78 mmol) of freshly prepared methyl 3-oxo-4-pentenoate were dissolved in 20 mL of dry benzene and refluxed under a nitrogen atmosphere for 4 h. Into the reaction mixture was added a solution of 10 g of sodium acetate in 20 mL of acetic acid and 20 mL of water, and the mixture was refluxed for 3 h under an atmosphere of nitrogen. After the usual workup, the crude product was subjected to column chromatography (silica gel, hexane–ethyl acetate) to afford 0.246 mmol (89%) of **$\Delta^{15,16}$- or $\Delta^{15,20}$-1-benzyl-16-(methoxycarbonyl)-17,21-dioxoyohimbane (48)** as an oil.

In a similar manner, **45** and **46** were obtained from **43a**.

5,6,11,11a-Tetrahydro-2,3-dimethoxy-8-oxo-10-(1-pyrrolidinyl)-8*H*-benzo[*a*]quinolizine (45),[76] mp 211–213 °C (from benzene).

5,6,9,10,11,11a-Hexahydro-2,3-dimethoxy-8,10-dioxo-9-(3-oxobutyl)-8*H*-benzo[*a*]quinolizine (46), oil.

(73) This compound was exactly identical with the compound obtained by acid hydrolysis of **40b**.
(74) With the usual method, 0.244 g (0.804 mmol) of **44a** gave 0.313 g of the crude ethylene ketal of **44a**.
(75) Brossi, A.; Bruderer, H.; Rachlin, A. I.; Teitel, S. *Tetrahedron* **1968**, *24*, 4277.
(76) Cf.: Akhrem, A. A.; Chrnov, Y. G. *Syntesis* **1980**, 996.

Acknowledgment. We thank the Ministry of Education, Science, and Culture, Japan, for a Grant-in-Aid for Developmental Scientific Research(2) (No. 56850203), and they also thank the Asahi Glass Foundation for Industrial Technology.

Registry No. 1, 30045-07-9; **2a**, 100-39-0; **2b**, 2746-25-0; **2c**, 21852-32-4; **2d**, 2417-73-4; **2e**, 76177-36-1; **2f**, 3433-80-5; **2g**, 53207-00-4; **2h**, 78946-25-5; **3a**, 47210-20-8; **3b**, 1934-93-6; **3c**, 1699-51-0; **3d**, 85222-32-8; **3e**, 85222-33-9; **3f**, 85222-34-0; **3g**, 54712-52-6; **3h**, 85222-35-1; **4a**, 75-30-9; **4b**, 107-08-4; **4c**, 106-95-6; **4d**, 105-36-2; **4e**, 535-11-5; **4f**, 1117-71-1; **4g**, 26536-93-6; **4h**, 13381-65-2; **4i**, 107-30-2; **4j**, 81701-41-9; **4k**, 81701-42-0; **5a**, 19253-43-1; **5b**, 18368-38-2; **5c**, 22191-92-0; **5d**, 70593-94-1; *erythro*-**5e**, 85222-36-2; *threo*-**5e**, 85222-38-4; **5f**, 85222-38-4; **5g**, 85222-39-5; *erythro*-**5h**, 85222-40-8; *threo*-**5h**, 85222-41-9; **5i**, 85222-42-0; **6**, 2786-31-4; **7a**, 56864-80-3; **7b**, 85222-43-1; **8**, 73554-70-8; **9a**, 29903-66-0; **9b**, 85222-44-2; **10**, 40004-92-0; **11a**, 85222-45-3; **11b**, 85222-46-4; **11b** picrate, 85222-47-5; **11c**, 85222-48-6; **11d**, 78946-26-6; **11d** picrate, 85222-49-7; **12**, 538-51-2; **13a**, 38924-78-6; **13b**, 85222-50-0; **13c**, 85222-51-1; **13d**, 76177-43-0; **13e**, 85222-52-2; **13f**, 85222-53-3; **14**, 622-29-7; **15**, 53663-25-5; **16**, 6319-84-2; **17**, 85222-54-4; **18**, 33797-51-2; **19a**, 1126-71-2; **19b**, 25314-75-4; **20**, 35287-11-7; **21**, 30936-27-7; **22a**, 6940-49-4; **22b**, 40125-46-0; **22c**, 73563-23-2; *threo*-**23a**, 73554-64-0; *erythro*-**23a** picrate, 85222-55-5; *threo*-**23b**, 55219-41-5; *erythro*-**23b**, 55563-22-9; *threo*-**23c**, 85280-87-1; *erythro*-**23c** picrate, 85280-89-3; *threo*-**23d** picrate, 85222-57-7; *erythro*-**23d** picrate, 85222-59-9; *threo*-**23e**, 85222-60-2; *erythro*--**23e**, 85222-61-3; *erythro*-**23e** picrate, 85222-62-4; *threo*-**23f** picrate, 85280-17-7; *erythro*-**23f**, 85280-18-8; *erythro*-**23f** picrate, 85280-19-9; *threo*-**23g**, 85222-63-5; *erythro*-**23g**, 85222-64-6; *threo*-**23h**, 85222-65-7; *erythro*-**23h**, 85222-66-8; *threo*-**23i**, 85222-67-9; *threo*-**23j**, 85280-20-2; **24a**, 5096-82-2; **24b**, 81701-39-5; **24c**, 81701-40-8; **24d**, 85222-69-1; *threo*-**25**, 85222-69-1; *erythro*-**25**, 85222-70-4; *erythro*-**25** picrate, 85222-71-5; *threo*-**26**, 85222-77-1; *erythro*-**26**, 85222-78-2; *erythro*-**26** picrate, 85222-79-3; **28**, 85222-80-6; **29**, 85222-81-7; **30**, 85222-72-6; **31**, 15889-93-7; **32**, 4787-30-8; *cis*-**33**, 85222-73-7; *trans*-**33**, 85222-74-8; **34**, 84690-25-5; **35** picrate, 85222-76-0; **36a**, 85222-82-8; **36b**, 81701-43-1; **36c**, 81701-44-2; **36d**, 81701-45-3; **37b**, 1876-67-1; **37c**, 81701-50-0; **37d**, 81701-51-1; **38**, 846-66-2; **39a**, 81701-46-4; **39b**, 81701-47-5; **39c**, 85222-83-9; **39d**, 81701-49-7; **39e**, 85222-84-0; **40a**, 81701-54-4; **40b**, 81701-55-5; **40c**, 81701-52-2; **40d**, 81701-53-3; **40e**, 85222-85-1; **41a**, 81701-57-7; **41b**, 81701-56-6; **42a**, 841-95-2; **43a**, 5911-65-9; **43b**, 85222-86-2; **44a**, 85222-87-3; **44b**, 85222-88-4; **45**, 85222-89-5; **46**, 81701-58-8; **47**, 85222-90-8; **48**, 85222-92-0; 12-benzyl-1,6,7,12b-tetrahydro-4-oxo-2-(1-pyrrolidinyl)-4*H*-indolo[2,3-*a*]quinolizine, 85222-93-1.

Supplementary Material Available: Full spectral and analytical data for all compounds (24 pages). Ordering information is given on any current masthead page.

Syntheses of Azolopyrimido[5,4-*e*]-*as*-triazines and Azolopyrimido[4,5-*c*]pyridazines Related to Fervenulin

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Received August 30, 1982

Syntheses of some azolopyrimido[5,4-*e*]-*as*-triazines and azolopyrimido[4,5-*c*]pyridazines, new heterocyclic systems related to the antibiotic fervenulin, are described. Synthesis of the 4-deaza analogue of the antibiotic 2-methylfervenulone (MSD-92) is also reported.

Because of the natural occurrence of the triad of antibiotics fervenulin, 2-methylfervenulone (MSD-92), and toxoflavin, the pyrimido[5,4-*e*]-*as*-triazine nucleus has aroused considerable recent attention.[1] As a part of our

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Scheme I

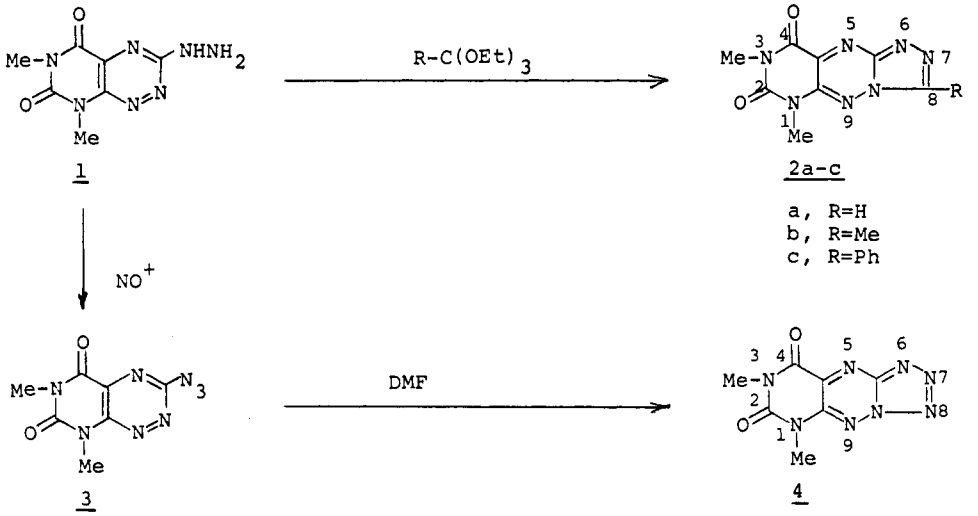


Table I. Azolopyrimido[5,4-*e*]-*as*-triazines and Azolopyrimido[4,5-*c*]pyridazines[a]

compd	yield, %	mp, °C	UV (EtOH) λ_{max}, nm (log ϵ)
2a	84	272 dec[b]	232 (4.25), 340 (3.63)
2b	75	>300[b]	232 (4.37), 347 (3.83)
2c	60	>300[b]	227 (4.67), 268 (4.54), 360 (3.99)
4	42	225 dec[b]	238 (4.37), 310 (3.56)
11a	52	238-240[b]	233 (4.25), 315 (3.66)
11b	57	210-211[c]	233 (4.57), 325 (3.85)
11c	74	>300[d]	228 (4.13), 268 (4.16), 335 (3.30)
12	95	265-268[b]	235 (4.45), 295 (3.79)

[a] Satisfactory analytical data (±0.3% for C, H, and N) were reported for all compounds in the table except 11a, which required 0.10 mol of H_2O to fit the calculated value. [b] Recrystallization from EtOH. [c] Recrystallization from EtOAc. [d] Recrystallization from DMF.

Table II. ^{13}C Chemical Shifts[a] of the Pyrimido[4,5-*c*]pyridazines in Me_2SO-d_6

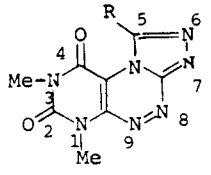
carbon	compd 7	compd 8	$\Delta\delta$(7-8)
C_3	148.6	133.6	15.0
C_4	124.7	130.5	-5.8
C_{4a}	113.7	104.3	9.4
C_5	151.6	152.7	-1.1
Me (N_6)	28.2	28.1	0.1
C_7	150.6	150.8	-0.2
Me (N_8)	29.3	29.2	0.1
C_{8a}	160.6	158.8	1.8

[a] ^{13}C NMR spectra were performed on a JEOL JMS-PS-100 spectrometer, and the chemical shifts are reported in parts per million downfield from internal Me_4Si.

study on the chemistry of this attractive heterocycle[2,3] and its 4-deaza analogue pyrimido[4,5-*c*]pyridazine,[4] we now report the syntheses of some azolopyrimido[5,4-*e*]-*as*-triazines and azolopyrimido[4,5-*c*]pyridazines, new heterocyclic systems related to fervenulin.[5] Additionally, we also describe the synthesis of 4-deaza analogue of MSD-92.

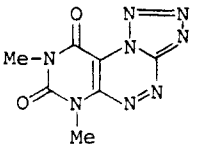
The triazolo- and tetrazolopyrimidotriazines were readily synthesized by starting with 3-hydrazinofervenulin (1)[6] as shown in the Scheme I. Thus, the condensation of 1 with the appropriate ortho esters under reflux directly afforded the corresponding triazolopyrimidotriazines (**2a-c**) in 60–84% yields,[7] while the diazotization of 1 with nitrous acid to 6-azidofervenulin (**3**, 44%) followed by thermal (150 °C) cyclization in DMF furnished the tetrazolopyrimidotriazine **4**[8] in 42% yield.[9]

Although the structure of **2** is isomeric with that of **5**, the possibility of the latter was excluded since models of **2b** and **2c** indicated the steric hindrance between the methyl (or phenyl) substituent and peri carbonyl group at C-4. Moreover, the close proximity of the chemical shift of **2a** (particularly at H-8, δ 9.74) with that of the triazolopyrimidopyridazine **11a** (δ 9.77, vide infra) also eliminated structure **5a**. If the cyclization occurred at the N-4



5a-c

a, R=H
b, R=Me
c, R=Ph

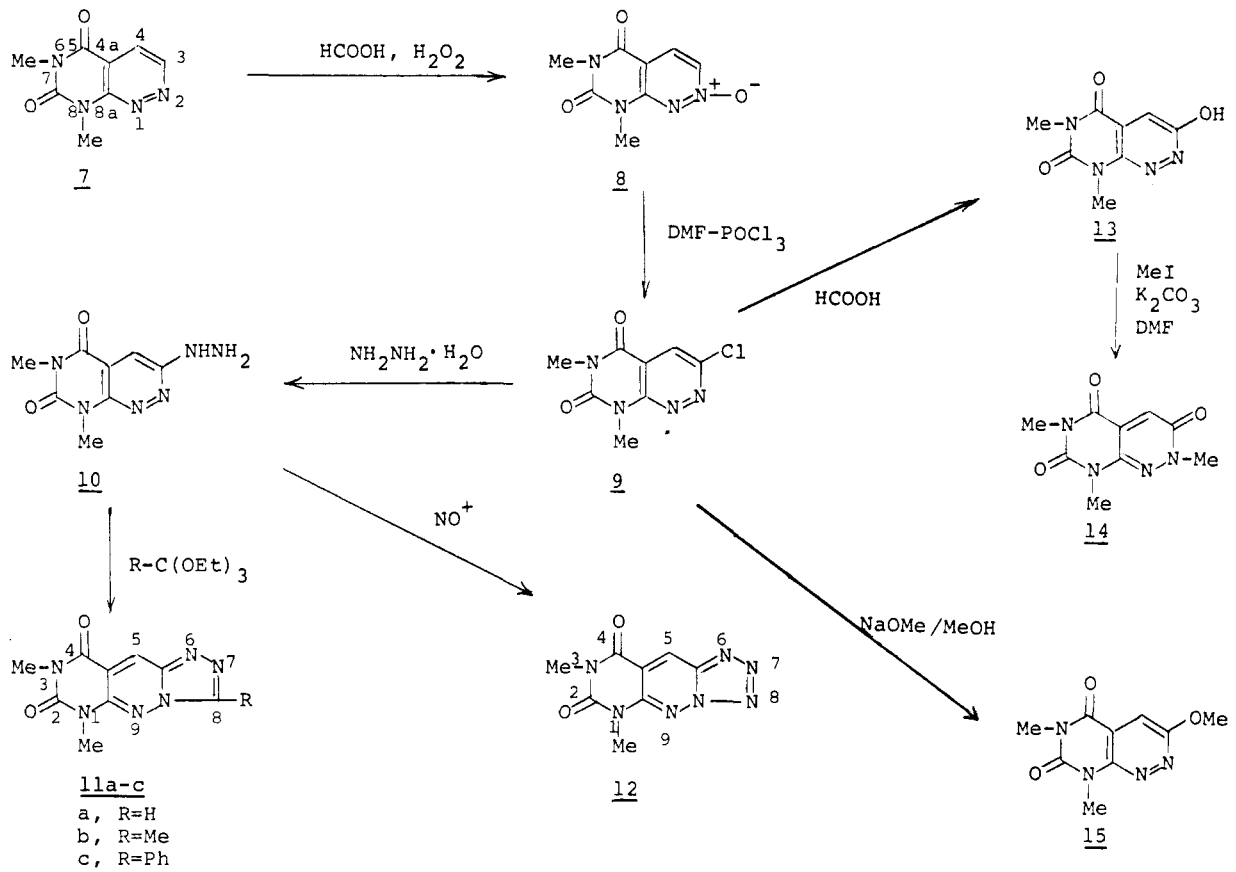


6

of 1, the H-5 of **5a** would undergo some degree of anisotropic effect by the carbonyl group at C-4. The preferential ring closure mode of 1 can be explained by the enhanced nucleophilicity of N-2 as compared to N-4.[10] Analogously, the structure of 4 is isomeric with that of **6**; however, the latter structure was eliminated by the previous finding that thermal cyclization of 3-azido-*as*-triazines affords exclu-

(1) For a review on the pyrimido[5,4-*e*]-*as*-triazines, see: Brown, D. J.; Lynn, R. K. "Chemistry and Biology of Pteridines"; Pfleiderer, W., Ed.; Walter de Gruyter: New York, 1975; pp 575–601.
(2) Ichiba, M.; Nishigaki, S.; Senga, K. *J. Org. Chem.* **1978**, *43*, 469.
(3) Senga, K.; Ichiba, M.; Nishigaki, S. *J. Org. Chem.* **1979**, *44*, 3830.
(4) Senga, K.; Sato, J.; Kanamori, Y.; Ichiba, M.; Nishigaki, S.; Noguchi, M.; Yoneda, F. *J. Heterocycl. Chem.* **1978**, *15*, 781.
(5) For the sake of convenience, the same numbering system was used for the azolopyrimidotriazines and the azolopyrimidopyridazines.
(6) Taylor, E.C.; Sowinski, F. *J. Org. Chem.* **1975**, *40*, 2321.
(7) 3-(Ethoxymethylenehydrazino)fervenulin [mp 165–167 °C (MeOH). Anal. Calcd for $C_{10}H_{13}N_7O_3$: C, 43.00; H, 4.70; N, 35.11. Found: C, 42.95; H, 4.68; N, 35.15] could also be isolated in the reaction of 1 with triethyl orthoformate to give **2a**.
(8) No absorption band due to the azido tautomer (ca. 2000–2200 cm^{-1}) was detected in the IR spectrum.
(9) Castillon et al. have recently reported on the synthesis, structural elucidation, and equilibria of azido-*as*-triazines: Castillon, S.; Vilarrasa, J. *J. Org. Chem.* **1982**, *47*, 3168. Castillon, S.; Melendez, E.; Pascual, C.; Vilarrasa, J. *Ibid.* **1982**, *47*, 3886.
(10) Daunis, J.; Lopez, H.; Maury, G. *J. Org. Chem.* **1977** *42*, 1018.

Scheme II



sively the tetrazolo[1,5-*b*]-*as*-triazines.[11] Further support on the structures of azolopyrimidotriazines **2a–c** and **4** was derived from the comparison of their UV spectra with those of the azolopyrimidopyridazines **11a–c** and **12**. The longest wavelength bands of the azolopyrimidotriazines exhibit a bathochromic shift of 17–25 nm compared with those of the azolopyrimidopyridazines (Table I).

The triazolo- and tetrazolopyrimido[4,5-*c*]pyridazines were unequivocally synthesized in four steps by starting with 4-deazafervenulin (**7**)[12] as shown in the Scheme II. Treatment of **7** with performic acid at 70 °C gave the 4-deazafervenulin 2-oxide (**8**) in 65% yield. Compound **7** has two possible sites for the N-oxidation, i.e., N-1 and N-2; however, the former was tentatively eliminated by taking into account the steric hindrance of the peri methyl group at N-8.[13] The structure of **8** was confirmed by comparison of the chemical shift changes of the corresponding ^{13}C resonances in the pyrimidopyridazine **7** with their counterparts in the *N*-oxides 8[14] (Table II). Namely, the resonances at 148.6 (C_3) and 113.7 (C_{4a}) ppm exhibit upfield shifts of 15 and 9.4 ppm, respectively, while the resonance at 124.7 (C_4) ppm exhibits a downfield shift of 5.8 ppm when the *N*-oxide is introduced. In contrast to the large shifts for the C_3, C_{4a}, and C_4 carbons, the resonance at 160.6 ppm (C_{8a}) did not undergo any appreciable effect by the N-oxidation. Therefore, the N-oxidation site in compound **7** must be N-2 and not N-1.

Treatment of **8** with a mixture of phosphorus oxychloride and DMF (Vilsmeier–Haack reagent) gave 3-chloro-4-deazafervenulin (**9**) in 45% yield. The structural assignment of **9** was derived from its hydrolytic conversion with formic acid to 3-hydroxy-4-deazafervenulin (**13**), which exhibits a melting point and spectroscopic properties different from those of the known 4-hydroxy-4-deazafervenulin.[12] Refluxing of **9** with hydrazine hydrate in *n*-BuOH gave 3-hydrazino-4-deazafervenulin (**10**) in 80% yield. Heating of **10** with the appropriate ortho esters afforded the desired triazolopyrimidopyridazines **11a–c** in 52–74% yields.[15] Diazotization of **10** with nitrous acid directly gave the tetrazolopyrimidopyridazine **12** in 95% yield.

Compound **13** served as a useful starting material for the synthesis of 4-deaza-MSD-92 (**14**). Thus treatment of **13** with methyl iodide in DMF containing anhydrous potassium carbonate readily gave **14** in 73% yield. The structure of **14** was supported by comparison of the UV spectrum with that of 3-methoxy-4-deazafervenulin (**15**) prepared from the reaction of **9** with sodium methoxide in MeOH.

Experimental Section

Melting points were taken on a YANACO micro-hot-stage melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO A-100 spectrophotometer from samples

(11) For example: Goodman, M. M.; Atwood, J. L.; Carlin, R.; Hunter, W.; Paudler, W. W. *J. Org. Chem.* **1976**, *41*, 2860.

(12) Pfleiderer, W.; Ferch, H. *Justus Liebigs Ann. Chem.* **1958**, *615*, 48.

(13) Broom and Bartholomew reported that the reaction of 1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione with peracid did not give the desired *N*-oxide: Broom, A. D.; Bartholomew, D. G. *J. Org. Chem.* **1976**, *41*, 3027.

(14) The structure of **8** was also supported by the following precedents: Klinge, D. F.; van der Plas, H. C.; van Veldhuizen, A. *Recl. Trav. Chim. Pays-Bas* **1976**, 21. Radel, R. J.; Keen, B. T.; Wong, C.; Paudler, W. W. *J. Org. Chem.* **1977**, *42*, 546. Paudler, W. W.; Jovanovic, M. V. *Heterocycles* **1982**, *19*, 93.

(15) 3-[(α-Methylethoxy)methylenehydrazino]-6,8-dimethylpyrimido-[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione [mp 168–170 °C (EtOH). Anal. Calcd for $C_{12}H_{16}N_6O_3$: C, 49.30; H, 5.53; N, 28.75. Found: C, 49.19; H, 5.40; N, 28.78.] could also be isolated in the reaction of **10** with triethyl orthoacetate to give **11b**.

mulled in Nujol. NMR spectra were determined at 90 MHz with a Varian EM-390 spectrometer with tetramethylsilane as the internal standard. UV spectra were performed on a Hitachi 124 spectrophotometer in EtOH.

The molecular weights for all compounds were correctly analyzed by mass spectroscopy with a JEOL JMS D-300 spectrometer with a direct-inlet system at 70 eV.

1,3-Dimethyl-s-triazolo[3,4-b]pyrimido[5,4-e]-as-triazine-2,4(1H,3H)-diones (2a–c) and 1,3-Dimethyl-s-triazolo[3,4-f]pyrimido[4,5-c]pyridazine-2,4(1H,3H)-diones (11a–c). A mixture of 3-hydrazinofervenulin (1;[3] 0.223 g, 0.001 mol) or 3-hydrazino-4-deazafervenulin (**10**; 0.222 g, 0.001 mol) and the appropriate ortho esters (0.5 mL) was heated at 95 °C (at 140 °C for **2c** and **11c**) for 1 h. The reaction mixture was evaporated in vacuo, and the residue was recrystallized to give the corresponding **2a–c** and **11a–c**, respectively.

2a: NMR (Me_2SO-d_6) δ 3.38 (s, 3 H, NMe), 3.52 (s, 3 H, NMe), 9.74 (s, 1 H, H-8).

11a: NMR (Me_2SO-d_6) δ 3.30 (s, 3 H, NMe), 3.50 (s, 3 H, NMe), 8.97 (s, 1 H, H-5), 9.77 (s, 1 H, H-8).

11b: NMR (Me_2SO-d_6) δ 2.75 (s, 3 H, C^8 Me), 3.27 (s, 3 H, NMe), 3.55 (s, 3 H, NMe), 8.87 (s, 1 H, H-5).

3-Azidofervenulin (3). To a stirring mixture of **1** (0.56 g, 0.0026 mol) and sodium nitrite (0.45 g, 0.0065 mol) in H_2O (15 mL) was added concentrated HCl (3 drops) at 0–3 °C. After the mixture was stirred for 30 min at the same temperature, the precipitates were filtered and recrystallized from EtOH to give **3**: 0.27 g (44%); mp 130–132 °C: IR, 2200 cm^{-1} (N_3). Anal. Calcd for $C_7H_6N_8O_2$: C, 35.90; H, 2.59; N, 47.85. Found: C, 35.83; H, 2.65; N, 47.53.

1,3-Dimethyltetrazolo[4,5-b]pyrimido[5,4-e]-as-triazine-2,4(1H,3H)-dione (4). A mixture of **3** (0.237 g, 0.001 mol) and DMF (5 mL) was heated at 150 °C for 10 min. The reaction mixture was evaporated to dryness in vacuo, and the residue was recrystallized to give **4**: 0.1 g; NMR (Me_2SO-d_6) δ 3.41 (s, 3 H, NMe), 3.60 (s, 3 H, NMe).

6,8-Dimethylpyrimido[4,5-c]pyridazine-5,7(6H,8H)-dione 2-Oxide (8). To a solution of 6,8-dimethylpyrimido[4,5-c]-pyridazine-5,7(6*H*,8*H*)-dione (**7**;[10] 0.68 g, 0.0035 mol) in 99% formic acid (30 mL) was added 30% hydrogen peroxide (8 mL) dropwise. The mixture was heated for 12 h at 70 °C with stirring. The reaction mixture was evaporated in vacuo, and the residue was triturated with H_2O. The insoluble material was filtered and recrystallized from EtOH to give **8**: 0.47 g (65%): mp 167–168 °C. Anal. Calcd for $C_8H_8N_4O_3$: C, 46.15; H, 3.87; N, 26.92. Found: C, 46.25; H, 3.84; N, 27.02.

3-Chloro-4-deazafervenulin [3-Chloro-6,8-dimethylpyrimido[4,5-c]pyridazine-5,7(6H,8H)-dione (9)]. To a solution of **8** (0.21 g, 0.001 mol) in DMF (3 mL) was added phosphorus oxychloride (0.6 mL). The solution was heated at 95 °C for 3 h with stirring. The reaction mixture was evaporated in vacuo, and the residue was covered with ice-cold water. The insoluble material was filtered and recrystallized from EtOH to give **9**: 0.1 g (45%); mp 178-180 °C. Anal. Calcd for $C_8H_7ClN_4O_2$: C, 42.39; H, 3.12; N, 24.73. Found: C, 42.52; H, 3.10; N, 24.66.

3-Hydrazino-4-deazafervenulin [3-Hydrazino-6,8-dimethylpyrimido[4,5-c]pyridazine-5,7(6H,8H)-dione (10)]. A mixture of **9** (0.36 g, 0.0016 mol) and 100% hydrazine hydrate (0.28 g, 0.0048 mol) in *n*-BuOH (4 mL) was heated at 120–130 °C for 2 h. After the mixture was cooled, the precipitates were filtered, washed with H_2O and then with EtOH, and recrystallized from DMF to give **10**: 0.28 g (80%); mp 221–223 °C. Anal. Calcd for $C_8H_{10}N_6O_2$: C, 43.23; H, 4.54; N, 37.82. Found: C, 43.46; H, 4.59; N, 37.47.

1,3-Dimethyltetrazolo[4,5-f]pyrimido[4,5-c]pyridazine-2,4(1H,3H)-dione (12). To a suspension of **10** (0.22 g, 0.001 mol) in 1 N HCl (10 mL) was added sodium nitrite (0.22 g, 0.003 mol) at 0–5 °C. After the mixture was stirred for 1 h at the same temperature, the precipitates were filtered, washed with water, and recrystallized to give **12** (0.22 g).

4-Deazafervenulone [3-Hydroxy-6,8-dimethylpyrimido-[4,5-c]pyridazine-5,7(6H,8H)-dione (13)]. A suspension of **9** (0.23 g, 0.001 mol) in 99% formic acid (2 mL) was heated at 120 °C for 1 h with stirring. The reaction mixture was evaporated in vacuo, and the residue was recrystallized from EtOH to give **13**: 0.19 g (91%); mp 248–249 °C. Anal. Calcd for $C_8H_8N_4O_3 \cdot 0.25H_2O$: C, 45.17; H, 4.03; N, 26.35. Found: C, 44.85; H, 3.66; N, 26.16.

4-Deaza-MSD-92 [2,6,8-Trimethylpyrimido[4,5-c]-pyridazine-3,5,7(2H,5H,7H)-trione (14)]. A mixture of **13** (0.104 g, 0.0005 mol) and anhydrous potassium carbonate (0.04 g, 0.000 29 mol) in DMF (3.5 mL) was heated at 80–90 °C for 1.5 h with stirring, and then methyl iodide (0.11 g, 0.000 75 mol) was added. The mixture was heated at 80 °C for 3 h with stirring. The reaction mixture was evaporated in vacuo, and the residue was washed with H_2O. The insoluble material was filtered and recrystallized from EtOH to give **14**: 0.08 g (73%); mp 190–193 °C; UV λ_{max} 233 nm (log ε 4.25), 380 (3.08). Anal. Calcd for $C_9H_{10}N_4O_3 \cdot 0.2\ H_2O$: C, 47.86; H, 4.65; N, 24.81. Found: C, 47.68; H, 4.32; N, 24.88.

3-Methoxy-4-deazafervenulin [3-Methoxy-6,8-dimethylpyrimido[4,5-c]pyridazine-5,7(6H,8H)-dione (15)]. A suspension of **13** (0.09 g, 0.0004 mol) in absolute MeOH (3 mL) with dissolving metallic Na (0.1 mol) was refluxed for 45 min. The precipitates were filtered and recrystallized from MeOH to give **15**: 0.07 g (79%); mp 190–192 °C; UV λ_{max} 228 nm (log ε 4.55), 347 (3.17). Anal. Calcd for $C_9H_{10}N_4O_3$: C, 48.65; H, 4.54; N, 25.22. Found: C, 48.43; H, 4.44; N, 25.04.

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